Synthesis of Carba- and Heterocycles based on novel One-Pot Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetals and 1,3-Bis(Silyl Enol Ethers)

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Ehsan Ullah

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“Dedicated to Mama and Papa,

my beloved brothers and sisters to whom I owe everything”

Contents

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Acknowledging people who in one way or the other have contributed to my life and achievements, if there are any, is always most difficult task encountered. Writing this page is much more difficult for me than writing the whole thesis because I don't find any words, infact there are no such words that can justify their contributions and encouragements.

So then let me take pride in acknowledging Prof. Dr. Peter Langer, my supervisor, for his guidance, support, patience and encouragement. Without all these favours from him, accomplishment of this work would have been extremely difficult.

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Abbreviations

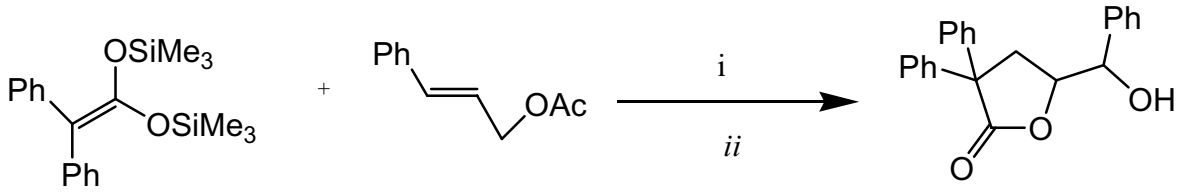
Ar	Aromatic
APT	Attached Proton Test
*n*BuLi	*n*-Butyllithium
DEPT	Distortionless Enhancement by Polarisation Trasfer
EI	Electronic Ionization
ESI	Electronspray Ionization
EtOAc	Ethylacetate
HRMS	High Resolution Mass Spectroscopy
IR	Infrared Spectroscopy
LDA	Lithium diisopropylamine
HMDS	Hexamethyldisilazine
MS	Mass Spectrometry
Ph	Phenyl
Et_3N	Triethylamine
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhause and Exchange SpectroscopY
Me_3SiOTf	Trimethylsilyl trifluoro methanesulfonate
Me_3SiCl	Trimethylsilylchloride
mp.	Melting point
TBAI	Tetrabutyl ammonium iodide
TFA	Trifluoroacetic acid
THF	Tetrahedrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy
EXSY	EXchange SpectroscopY
HMBC	Heteronuclear Multiple Quantum Coherence
HSQC	Heteronuclear Single Quantum Coherence
Oct	Octyl
Pent	Pentyl
Bu	Butyl
MTO	Methyltrioxorhenium

INTRODUCTION

One-Pot Cyclization Reactions of 1,1-Bis(trimethylsilyloxy)ketene acetals

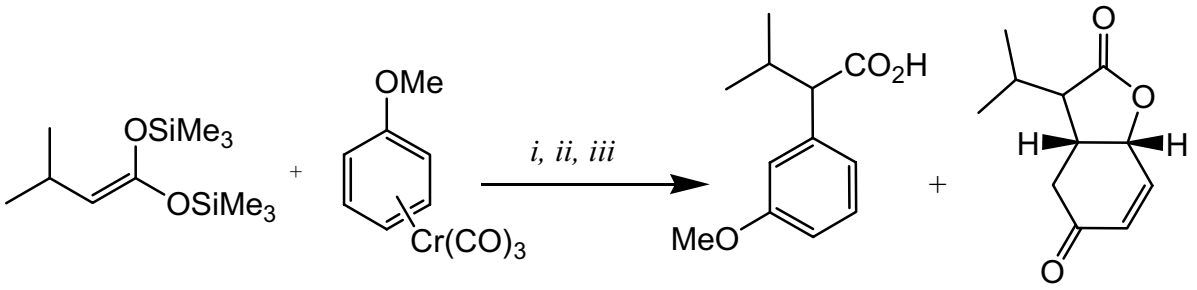
1,1-Bis(trimethylsilyloxy)ketene acetals represent useful synthetic building blocks which can be regarded as masked carboxylic acid dianions. In recent years, a number of cyclization reactions of 1,1-bis(trimethylsilyloxy)ketene acetals have been reported.

The palladium(0) catalysed reaction of 1,1-bis(trimethylsilyloxy)ketene acetals, such as **1**, with allyl acetates, such as **2**, has been reported to give γ-unsaturated carboxylic acids which were transformed into 5-(hydroxymethyl)-γ-lactones (e. g. **3**) by addition of H_2O_2 in the presence of catalytic amounts of methyltrioxorhenium (MTO) (Scheme 1).[1]



1 **2** **3** (65%)

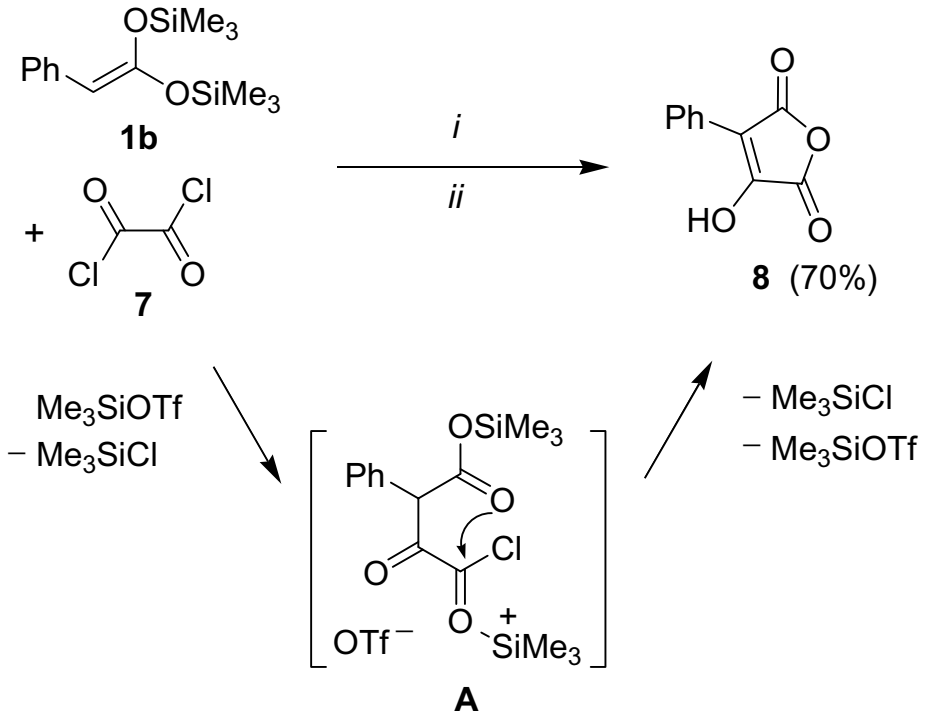
Scheme 1. Synthesis of **3**: *i*, **1** (1.1 equiv.), **2** (1.0 equiv.), THF, $Pd(PPh_3)_4$ (0.02 equiv., 2%), 24 , reflux; *ii*, MTO (5%), 30% H_2O_2 (1.1 equiv.), 72 h



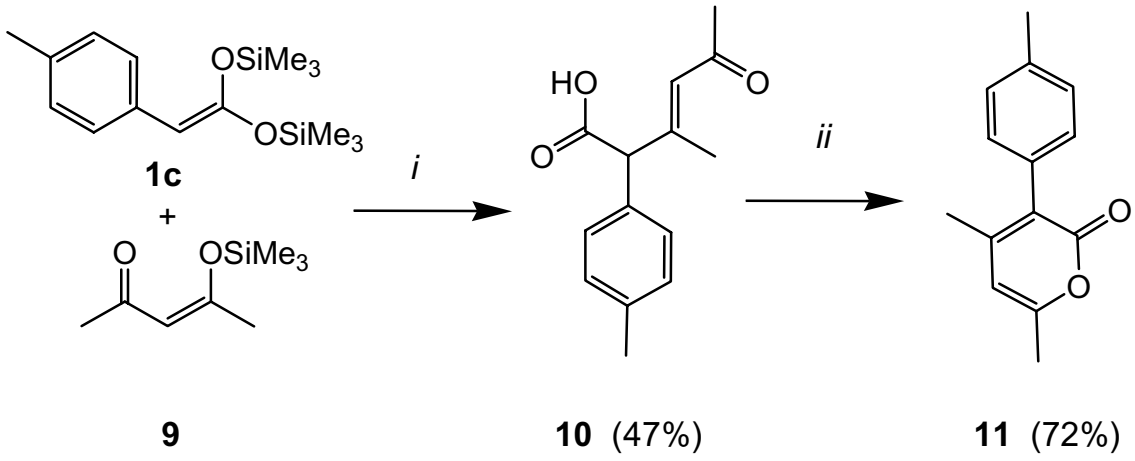
1a **4** **5** (41%) **6** (23%)

Scheme 2. Synthesis of **5, 6**: *i*, **1a** (1.5 equiv.), **4** (1.0 equiv.), THF, → -78 °C, *t*-BuOK (1M) in THF, HMPA (6 mL), 1.5 h stirring; *ii*, I_2 (5.0 equiv.) in THF, → 20 °C; *iii*, H_2O

3-Hydroxymaleic anhydrides, such as **8**, have been prepared by cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride (**7**) (Scheme 3).[5]



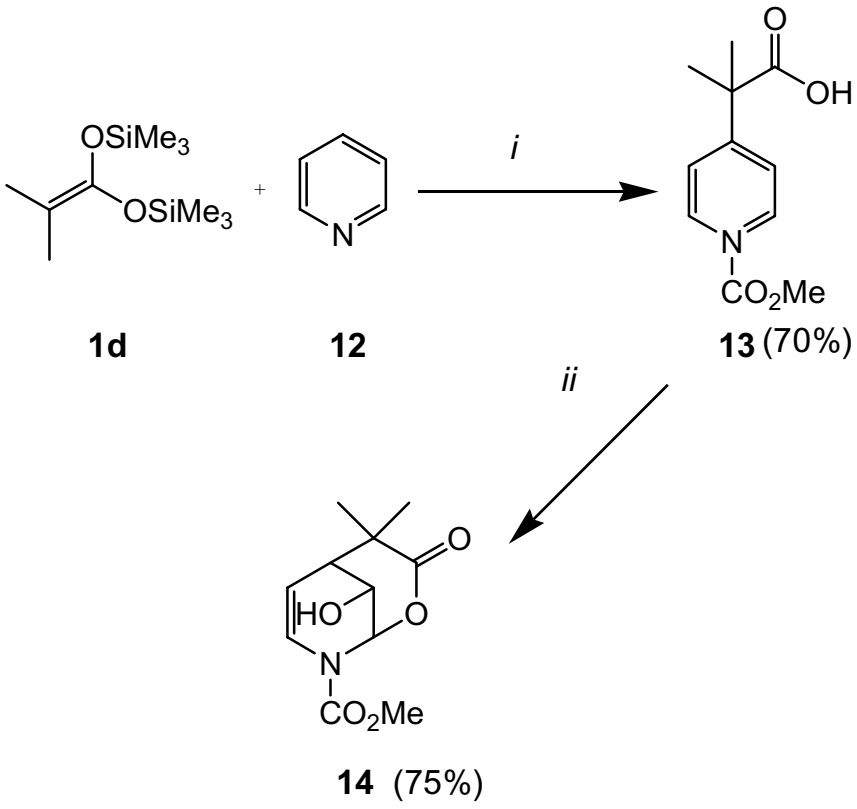
Scheme 3. Synthesis of **8**: *i*, **1b** (1.0 equiv.), CH_2Cl_2, −78 °C, **7** (1.3 equiv.), Me_3SiOTf (0.5equiv.); *ii*, −78 → 20 °C, 12 h, then 20 °C, 3 h



Scheme 4. Synthesis of **11**: *i*, **1c** (1.0 equiv.), **9** (1.0 equiv.), Me_3SiOTf (0.5 equiv.), CH_2Cl_2, –78 → 20 °C, 12 h, 20 °, 3 h, 2) H_2O; *ii*, TFA, CH_2Cl_2, 20 °C, 72 h

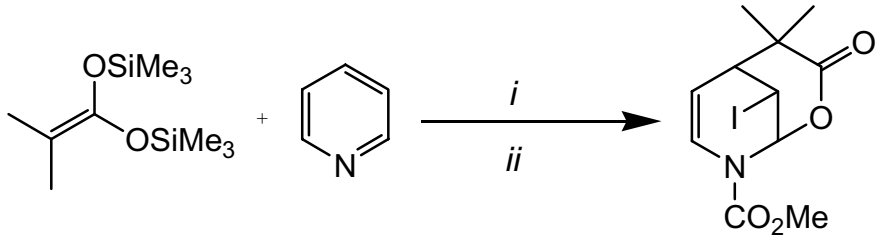
The Me_3SiOTf mediated reaction of 1,1-bis(trimethylsilyloxy)ketene acetals with 3-silyloxyalk-2-en-1-ones, such as **9**, afforded 5-ketoacids, such as **10**.[6] Treatment of the latter with TFA in CH_2Cl_2 afforded pyran-2-ones, such as **11** (Scheme 4).[6]

Very recently, Rudler *et al.* have reported the two-step cyclocondensation of silyl ketene acetals, such as **1d**, with pyridinium salt **12** to give open-chained products (**13**).[7] The latter were transformed into bicyclic products, such as **14**, by treatment with *m*CPBA (Scheme 5).



Scheme 5. Synthesis of hydroxylactone **14.** *i*, **1d** (1.4 equiv.), **12** (1.0 equiv.), CH_2Cl_2, $ClCO_2Me$ (2.0 equiv.), 2 h; *ii*, **13** (1.0 equiv.), MCPBA (1.4 equiv.), 2 h, NaOH, H_2O.

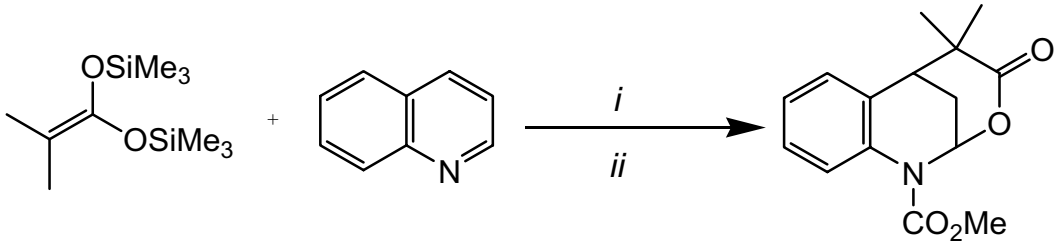
The iodolactonization of the open-chained products again resulted in the formation of bicyclic products, such as **15** (Scheme 6).[7]



1d **12** **15** (90%)

Scheme 6. Synthesis of iodolactone **15**: *i*, **1d** (1.4 equiv.), **12** (1.0 equiv.), CH_2Cl_2, $ClCO_2Me$ (2.0 equiv.), 2 h; *ii*, I_2 (1.1 equiv.), $NaHCO_3$ (10 mL), 12 h, $NaHSO_4$ soln.

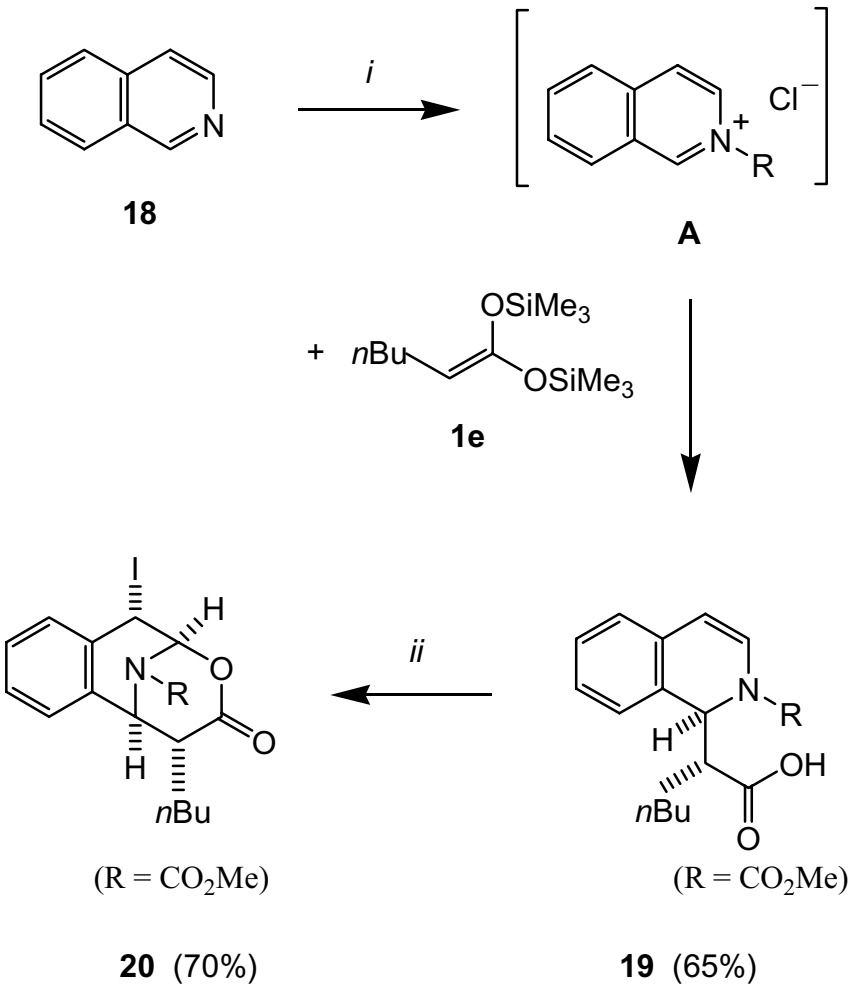
Related bicyclic products were prepared based on the reaction of bis(trimethylsilyl) ketene acetals with quinoline (Scheme 7).[7]



1d **16** **17** (32%)

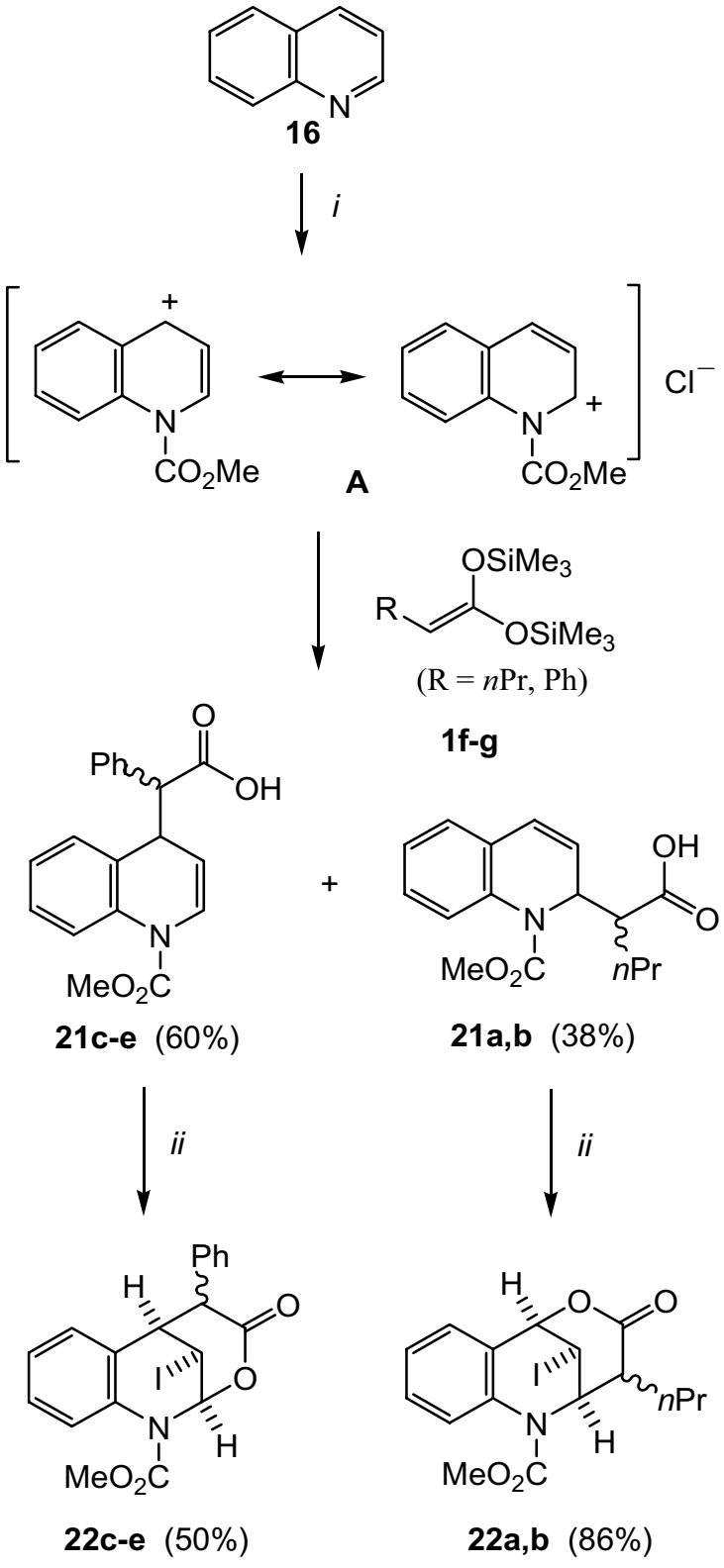
Scheme 7. Synthesis of **17**: *i*, **1d** (1.4 equiv.), **16** (1.0 equiv.), $ClCO_2Me$ (2.0 equiv.), 2 h; *ii*, SiO_2 (10.0 equiv.), CH_2Cl_2, reflux, 2 h.

7,8-Benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones were prepared by cyclocondensation of 1,1-bis(trimethylsilyloxy)ketene acetals with isoquinolinium salts. For example, the reaction of **1e** with isoquinoline (**18**) in the presence of methyl chloroformate afforded the condensation product **19** (Scheme 8). Treatment of **19** with iodine in the presence of sodium bicarbonate afforded 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-one **20** (Scheme 8)[8].



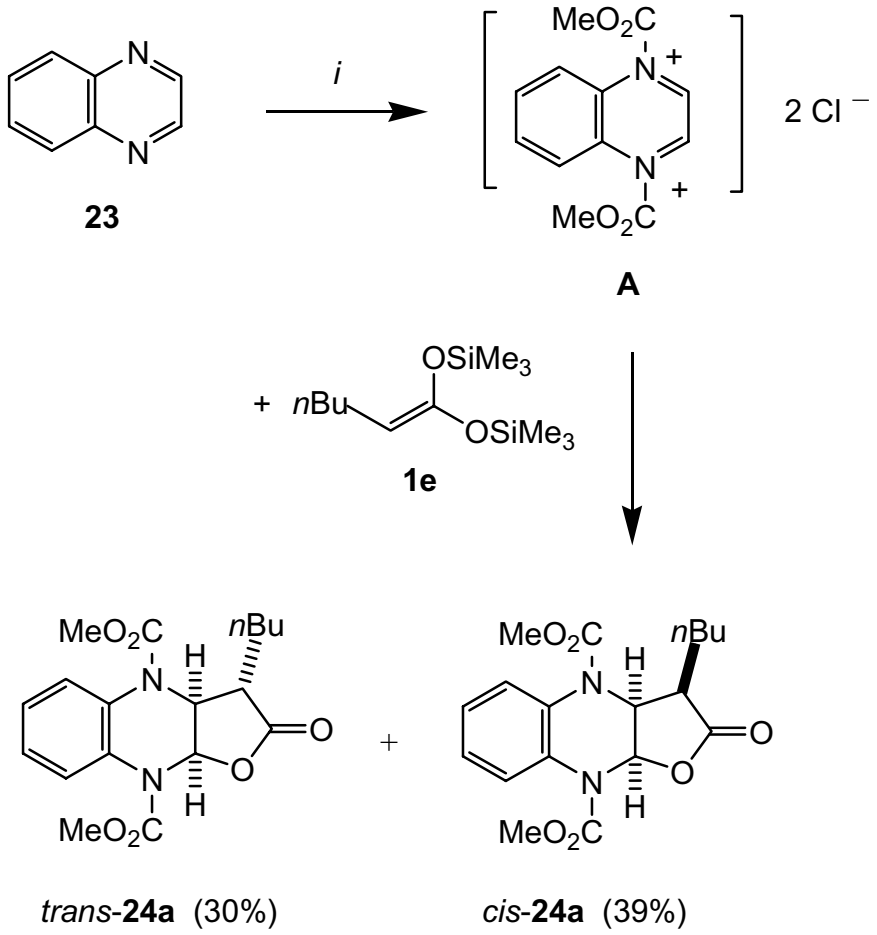
Scheme 8. Cyclization of bis ketene acetal with isoquinoline: *i*, **18** (1.0 equiv.), **1e** (2.0 equiv.), $ClCO_2Me$ (1.2 equiv.), CH_2Cl_2, 0 °C, 2 h, 20 °C, 12 h; *ii*, I_2 (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h

The methyl chloroformate mediated reaction of quinoline (**16**) with **1f** and **1g** afforded the regioisomeric condensation products **21a** and **21b** (Scheme 9). Treatment of **21a** and **21b** with iodine in the presence of sodium bicarbonate afforded **22a** and **22b**, respectively.

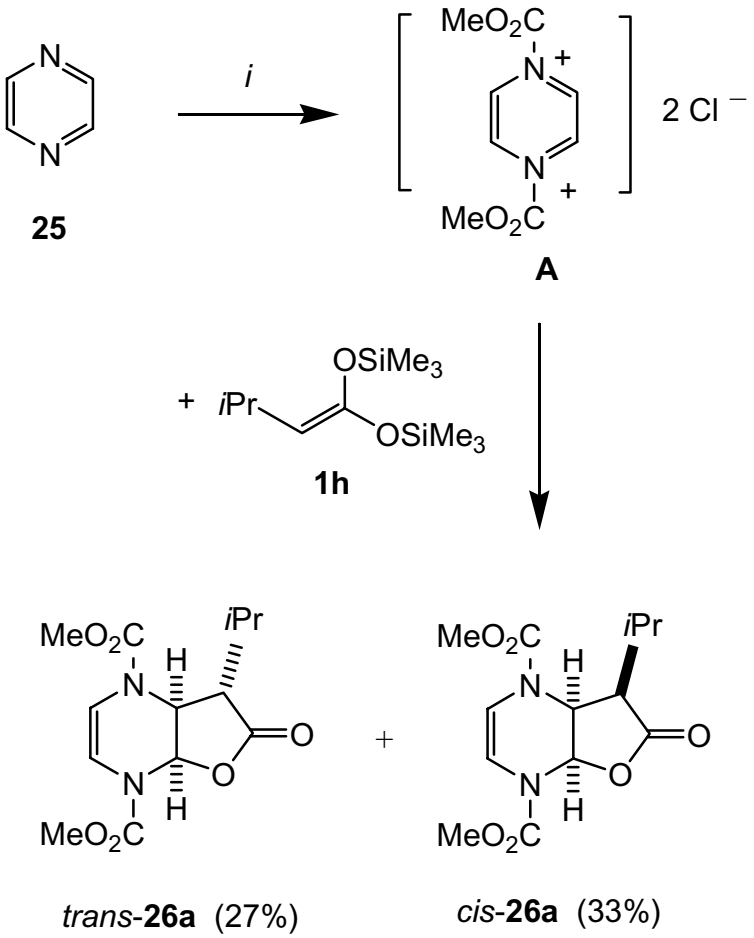


Scheme 9. Cyclization of **1f, g** with **16**: *i*, **16** (1.0 equiv.), **1f, g** (2.0 equiv.), $ClCO_2Me$ (1.2 equiv.), CH_2Cl_2, 0 °C, 2 h, 20 °C, 12 h; *ii*, I_2 (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h

Rudler and our group recently reported the reaction of silyl ketene acetals with pyrazine and quinoxaline.[9] These reactions provide a facile access to a variety of 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones and 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones (Schemes 10 and 11).



Scheme 10. Cyclization of bis ketene acetal **1e** with **23**: *i*, **1e** (1.0 equiv.), **23** (1.4 equiv.), $ClCO_2Me$ (4.0 equiv.), CH_2Cl_2, 20 °C, 12 h



Scheme 11. Cyclization of bis ketene acetal **1h** with **25**: *i*, **1h** (1.0 equiv.), **25** (1.4 equiv.), $ClCO_2Me$ (4.0 equiv.), CH_2Cl_2, 20 °C, 12 h

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Publication 1

Ehsan Ullah, Peter Langer*, "One-Pot Synthesis of 3-Hydroxymaleic Anhydrides by Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Oxalyl Chloride", *Synlett* **2004**, 2782.

One-Pot Synthesis of 3-Hydroxymaleic Anhydrides by Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Oxalyl Chloride

Ehsan Ullah, Peter Langer*

Institut für Chemie und Biochemie der Ernst-Moritz-Arndt-Universität Greifswald, Soldmannstr. 16, 17487 Greifswald, Germany
Fax +49(3834)864373; E-mail: peter.langer@uni-greifswald.de

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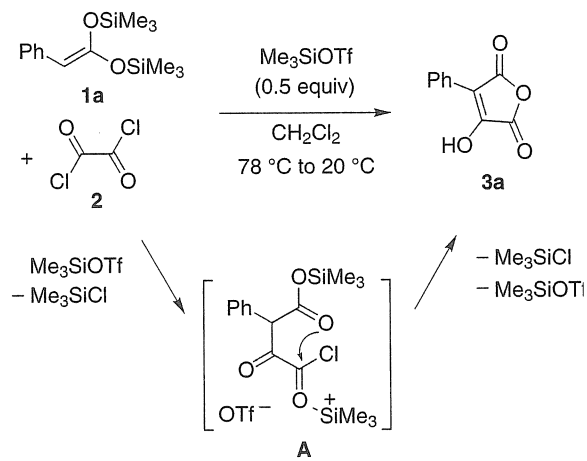
Abstract: Functionalized 3-hydroxymaleic anhydrides were prepared by cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride.

Key words: anhydrides, cyclizations, ketene acetals, oxalyl chloride, silyl enol ethers

Functionalized maleic anhydrides represent versatile building blocks for organic synthesis.[1] For example, pharmacologically relevant γ-alkylidenebutenolides have been prepared by Wittig reactions of maleic anhydrides.[2] Maleic anhydrides have been transformed into maleimides[3] which represent key-intermediates for the synthesis of 5-alkylidene-5*H*-pyrrol-2-ones.[3] The employment of maleic anhydrides as dienophiles in [4+2], [3+2] and [2+2] cycloaddition reactions allows the synthesis of a variety of carba- and heterocyclic frameworks.[4] Functionalized 3-alkanoylacrylic acids and naphthoquinones were prepared by Friedel–Crafts acylations using maleic anhydrides as reagents. The reaction of maleic anhydrides with enolates provides a convenient approach to 4-alkylidenebutane-1,3-diones.[5] A variety of functionalized α,β-unsaturated carbonyl compounds were prepared by reaction of maleic anhydrides with nucleophiles.[6]

Functionalized maleic anhydrides have been prepared by conjugate addition of nucleophiles onto parent maleic anhydride and subsequent halogenation and elimination.[7] 2-Methoxy-3-methylmaleic anhydride has been prepared by base-mediated condensation of ethyl propionate with diethyl oxalate[8] and subsequent methylation.[2a] 2-Methoxy-3-arylmaleic anhydrides are available by condensation of arylacetonitriles with diethyl oxalate to give open-chained pyruvates, subsequent methylation and treatment with acid.[9] 3-Hydroxymaleic anhydrides are of potential synthetic usefulness as precursors of enol triflates to be employed in palladium-catalyzed cross-coupling reactions. For example, the synthesis of (symmetrical) 2,3-dihydroxymaleic anhydride,[10a] 2,3-diacetoxymaleic anhydride[10b,c] and 2,3-dimethoxymaleic anhydride[10d] has been reported. In contrast, unsymmetrical 2,3-dihydroxymaleic anhydrides, containing one free and one protected hydroxy group, have not been prepared so far. Herein, we wish to report a new method for the synthesis of 3-hydroxymaleic anhydrides based on what are, to the best of our knowledge, the first cyclization reactions of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride.[11–14] This methodology allows a convenient one-pot synthesis of a variety of maleic anhydrides which are in many cases not directly available by other methods.



Scheme 1 Cyclization of 1,1-bis(trimethylsilyloxy)ketene acetal **1a** with oxalyl chloride.

The known 1,1-bis(trimethylsilyloxy)ketene acetal **1a** was prepared by deprotonation of phenylacetic acid with lithio-1,1,1,3,3,3-hexamethyldisilazane and subsequent addition of trimethylchlorosilane to the dianion thus formed.[15] The reaction of **1a** with oxalyl chloride (**2**) in the presence of trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf) afforded the 3-hydroxymaleic anhydride **3a** in up to 70% yield (Scheme 1).[16] The direct reaction of the dianion of phenylacetic acid[17] with oxalyl chloride or diethyl oxalate resulted in the formation of complex mixtures. In fact, the employment of 1,1-bis(trimethylsilyloxy)ketene acetal **1a**, which can be regarded as a masked dianion, proved mandatory to induce a clean cyclization. During the optimization, the following parameters proved to be important: a) the employment of 0.5 equivalents of Me_3SiOTf (the use of stoichiometric amounts of $TiCl_4$ resulted in the formation of complex mixtures), b) the solvent (CH_2Cl_2), c) the reaction time and d) the temperature. The formation of **3a** can be explained by Me_3SiOTf-mediated attack of the carbon atom of **1a** onto **2** to give intermediate **A** and subsequent cyclization via the oxygen atom.

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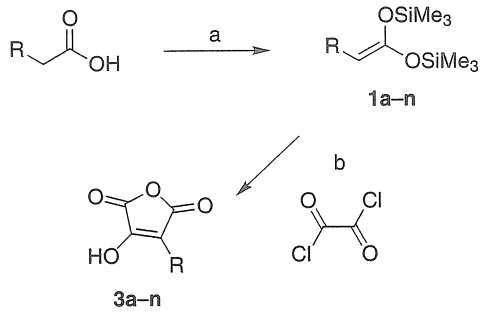

Scheme 2 Synthesis of **3a–n**: *a*, (1) $Li[N(SiMe_3)_2]$ (2.0 equiv), THF, –78 °C, (2) Me_3SiCl (2.2 equiv), –78 °C → 20 °C; *b*, Me_3SiOTf (0.5 equiv), CH_2Cl_2, –78 °C → 20 °C, 12 h, then 20 °C, 3 h.

Table 1 Products and Yields

3	R	Yield (%)[a]
a	Ph	70
b	4-MeC_6H_4	73
c	4-ClC_6H_4	65
d	4-$(MeO)C_6H_4$	53
e	3,4-$(MeO)_2C_6H_3$	70
f	Me	20
g	Et	36
h	*n*-Pr	42
i	*n*-Pent	50
j	*n*-Oct	56
k	Allyl	20
l	MeO	53
m	PhO	50
n	BnO	40

[a] Yields of isolated products.

To study the preparative scope, the substituents of the 1,1-bis(trimethylsilyloxy)ketene acetal were systematically varied (Scheme 2, Table 1). The cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals **1a–e** with oxalyl chloride afforded the aryl-substituted 3-hydroxymaleic anhydrides **3a–e**. The ketene acetals **1f–j** were prepared from propionic-, butanoic-, pentanoic-, heptanoic- and decanoic acid, respectively. The cyclization of **1f–j** with oxalyl chloride afforded the alkyl-substituted 3-hydroxymaleic anhydrides **3f–j**. The cyclization of oxalyl chloride with **1k**, prepared from pent-4-enoic acid, gave the allyl-substituted maleic anhydride **3k**. The methoxy-, phenyloxy- and benzyloxy-substituted 3-hydroxymaleic anhydrides **3l–n** were prepared from the corresponding 1,1-bis(trimethylsilyloxy)ketene acetals **1l–n**. All cyclizations proceeded in good to moderate yields and with very good regioselectivity.

We currently study the functionalization of the 3-hydroxymaleic anhydrides by palladium-catalyzed cross-coupling reactions of the corresponding enol triflates.

Acknowledgment

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(16) To a CH_2Cl_2 solution (17.8 mL) of oxalyl chloride (0.20 mL, 2.3 mmol) and **1a** (0.50 g, 1.8 mmol) was added a CH_2Cl_2 solution (5 mL) of TMSOTf (0.16 mL, 0.9 mmol) at 78 °C. The temperature of the solution was allowed to rise to 20 °C during 12 h. After stirring for 3 h at 20 °C, an aq solution of HCl (10%) was added. The organic and the aqueous layer were separated and the latter was extracted three times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane–EtOAc) to give **3a** as a yellow solid (240 mg, 70%), mp 164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.50 (m, 3 H, Ar), 8.05–8.08 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.0 (C), 126.9 (C), 128.8 (CH), 129.1 (CH), 130.3 (CH), 149.4 (C), 163.4 (C), 163.5 (C). IR (neat): 3244 (s), 3123 (w), 1840 (s), 1760 (s), 1673 (s), 1393 (s), 1262 (s), 939 (s), 762 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 190 (43) [M$^+$], 162 (100), 145 (22), 118 (27), 105 (15), 89 (81), 77 (8). Anal. Calcd for $C_{10}H_6O_4$: C, 63.16; H, 3.18. Found: C, 62.87; H, 3.63.

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Publication 2

Ehsan Ullah, Sven Rotzoll, Helmar Görls, and Peter Langer*

"One-Pot Synthesis of 3-Hydroxymaleic Anhydrides by Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Oxalyl Chloride", Manuscript in preparation.

One-Pot Synthesis of 3-Hydroxymaleic Anhydrides by Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Oxalyl Chloride

Sven Rotzoll,[a, b] Ehsan Ullah,[a, b] Helmar Görls,[c] Christine Fischer,[b] and Peter Langer* [a, b]

[a] Institut für Chemie, Universität Rostock,

Albert-Einstein-Str. 3a, 18059 Rostock, Germany

Fax: +381 4986412, E-mail: peter.langer@uni-rostock.de

[b] Leibniz-Institut für Katalyse e. V. an der Universität Rostock,

Albert-Einstein-Str. 29a, 18059 Rostock, Germany

[c] Institut für Anorganische und Analytische Chemie, Universität Jena,

August-Bebel-Str. 2, 07740 Jena, Germany

Abstract: Functionalized 3-hydroxymaleic anhydrides were prepared by cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride.

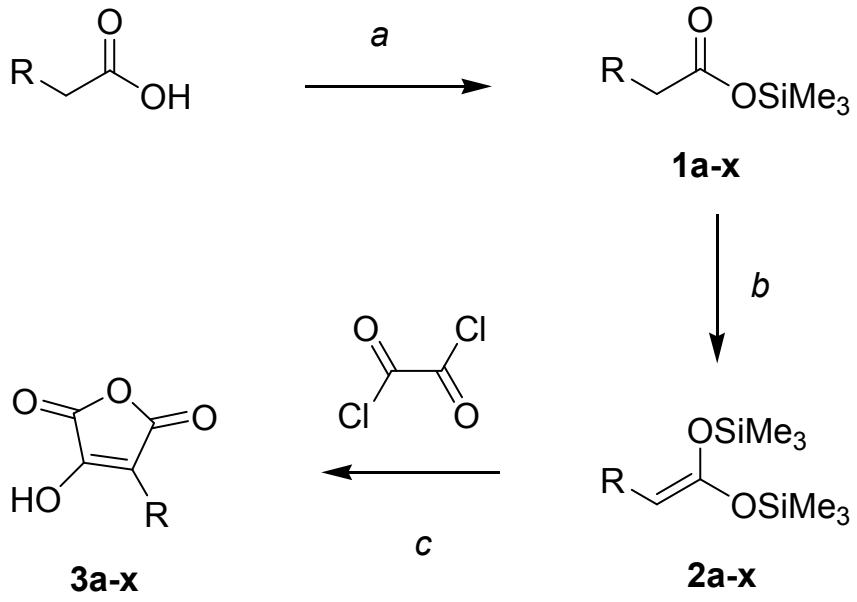
Keywords: anhydrides, cyclizations, ketene acetals, oxalyl chloride, silyl enol ethers

Functionalized maleic anhydrides represent important synthetic building blocks[1] which have been employed, for example, in the synthesis of γ-alkylidenebutenolides,[2a-c] maleimides,[2d] 5-alkylidene-5*H*-pyrrol-2-ones,[2d] numerous carba- and heterocycles (by [4+2], [3+2] and [2+2] cycloaddition reactions),[3] functionalized 3-alkanoylacrylic acids and naphthoquinones (by Friedel-Crafts acylations of maleic anhydrides), 4-alkylidenebutane-1,3-diones (by reaction with enolates),[4a] and various α,β-unsaturated carbonyl compounds (by reaction with nucleophiles).[4b] Substituted maleic anhydrides are available by Michael reaction of nucleophiles with parent maleic anhydride and subsequent halogenation and elimination,[4c] or by $TiCl_4$ / $N(nBu)_3$ mediated reaction of α-ketoesters with alkanoic acid anhydrides.[5] The condensation of ethyl propionate with diethyl oxalate and subsequent methylation afforded 2-methoxy-3-methylmaleic anhydride.[6a] 3-Methoxy-4-arylmaleic anhydrides are available by condensation of arylacetonitriles with diethyl oxalate, methylation and subsequent treatment with acid.[6b] Notably, whereas 3,4-dihydroxymaleic anhydride,[6c] 3,4-diacetoxymaleic anhydride[6d,e] and 3,4-dimethoxymaleic anhydride[6f] are known for a long time, methods for the synthesis of unsymmetrical 3-hydroxyanhydrides have only scarcely been reported.

Oxalyl chloride represents an important building block for the synthesis of *O*-heterocycles. For example, 2,3-dihydrofuran-2,3-diones have been prepared by cyclization of silyl enol ethers[7] with oxalyl chloride.[8] The cyclization of 1,3-bis(silyl enol ethers)[9] with oxalyl chloride provides a convenient access to γ-alkylidenebutenolides.[10] Recently, we reported a new method for the synthesis of 3-hydroxymaleic anhydrides by one-pot cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride.[11] Herein, we report full details of these studies. With regard to our preliminary communication,[11] we considerably extended the preparative scope.

Results and Discussion

The 1,1-bis(trimethylsilyloxy)ketene acetals **2a-x** were prepared, according to known procedures,[12] in two steps. The reaction of the carboxylic acid with pyridine, 1,1,1,3,3,3-hexamethyldisilazane (HMDS) and trimethylchlorosilane afforded the trimethylsilyl carboxylates **1a-x** (52-92% yield). The latter were deprotonated by lithium-1,1,1,3,3,3-hexamethyldisilazide and subsequently silylated to give the 1,1-bis(trimethylsilyloxy)ketene acetals **2a-x** (47-94% yield). The reaction of **2a-x** with oxalyl chloride, in the presence of trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf), afforded the 3-hydroxymaleic anhydride **3a-x** in 20-73% yield (Scheme 1, Table 1). The formation of **3** can be explained by Me_3SiOTf mediated attack of the carbon atom of **2** onto oxalyl chloride and subsequent cyclization via the oxygen atom. The best yields were obtained when the Lewis acid Me_3SiOTf (0.5 equiv.) was employed. The yields dropped when the amount of Lewis acid was reduced.



Scheme 1. Synthesis of **3a-x**: *a*, 1) pyridine (0.5 mL per 10 mmol of **1**, THF (1 mL per 10 mmol of **1**), 0 °C, 30 min, 2) $H[N(SiMe_3)_2]$ (1.0 equiv.), Me_3SiCl (0.5 equiv.), 0 → 20 °C, 12 h; *b*, 1)

Li[N($SiMe_3$)$_2$] (1.25 equiv.), THF, 15 min, −78 °C, 2) Me_3SiCl (1.5 equiv.), −78 → 20 °C, 12 h; *c*, Me_3SiOTf (0.5 equiv.), CH_2Cl_2, −78 → 20 °C, 12 h, then 20 °C, 3 h

Table 1. Products and yields

3	R	% (**1**)[a]	% (**2**)[a]	% (**3**)[a]
a	Me	54	62	20
b	Et	66	70	36
c	*n*Pr	80	74	42
d	*n*Pent	74	75	50
e	*n*Oct	78	64	56
f	*n*Dodec	89	94	71
g	*t*Bu	61	92	17
h	*c*Hex	80	87	60
i	(*c*Pent)CH_2	84	85	62
j	(*c*Hex)$(CH_2)_2$	89	78	63
k	Ph_2CH	91	92	30
l	Ph	92	92	70
m	4-MeC_6H_4	83	87	73
n	4-ClC_6H_4	77	86	65
o	4-FC_6H_4	83	91	53
p	4-MeO(C_6H_4)	78	83	70
q	3,4-$(MeO)_2(C_6H_3)$	85	70	45
r	4-PhC_6H_4	84	88	57

s	Thien-2-yl	96	83	62
t	MeO	53	53	53
u	PhO	72	92	50
v	BnO	69	47	40
w	PhS	84	86	50
x	Allyl	52	82	20

[a] Yields of isolated products

The preparative scope was studied. The cyclization of oxalyl chloride with 1,1-bis(trimethylsilyloxy)ketene acetals **2a-k**, prepared from various alkanoic acids, afforded the alkyl-substituted 3-hydroxymaleic anhydrides **3a-k**. The products were generally isolated in moderate to good yields (except for **3a**, **3g**, and **3k**). The low yield of **3g** and **3k** can be explained by steric hindrance of the *tert*-butyl and the diphenylmethyl groups, respectively. The ketene acetals **2l-r** were prepared from various arylacetic acids. The cyclization of **2l-r** with oxalyl chloride afforded the aryl-substituted 3-hydroxymaleic anhydrides **3l-r** in moderate to good yields. The cyclization of oxalyl chloride with **2s**, prepared from (2-thienyl)acetic acid, gave the thienyl-substituted anhydride **3s**. The methoxy-, phenyloxy- and benzyloxy-substituted 3-hydroxymaleic anhydrides **3t-v** were prepared from 1,1-bis(trimethylsilyloxy)ketene acetals **1t-v**. The cyclization of oxalyl chloride with silyl ketene acetal **2w**, prepared from (thiophenoxy)acetic acid, afforded the thiophenoxy-substituted maleic anhydride **3w**. Allyl-substituted anhydride **3x** was prepared, albeit in low yield, from silyl ketene acetal **1x** (which is available from pent-4-enoic acid).

Due to the unstable character of silyl esters **1** and silyl ketene acetals **2**, ^{13}C NMR and MS spectra could not be obtained for all compounds; in addition, elemental analyses could not be

obtained. However, the purity and identity was clearly shown for all derivatives by ^{1}H NMR. The structure of anhydrides **3** was established by spectroscopic methods. The structure of **3o** was independently confirmed by X-ray crystal structure analysis (Figure 1).[13]

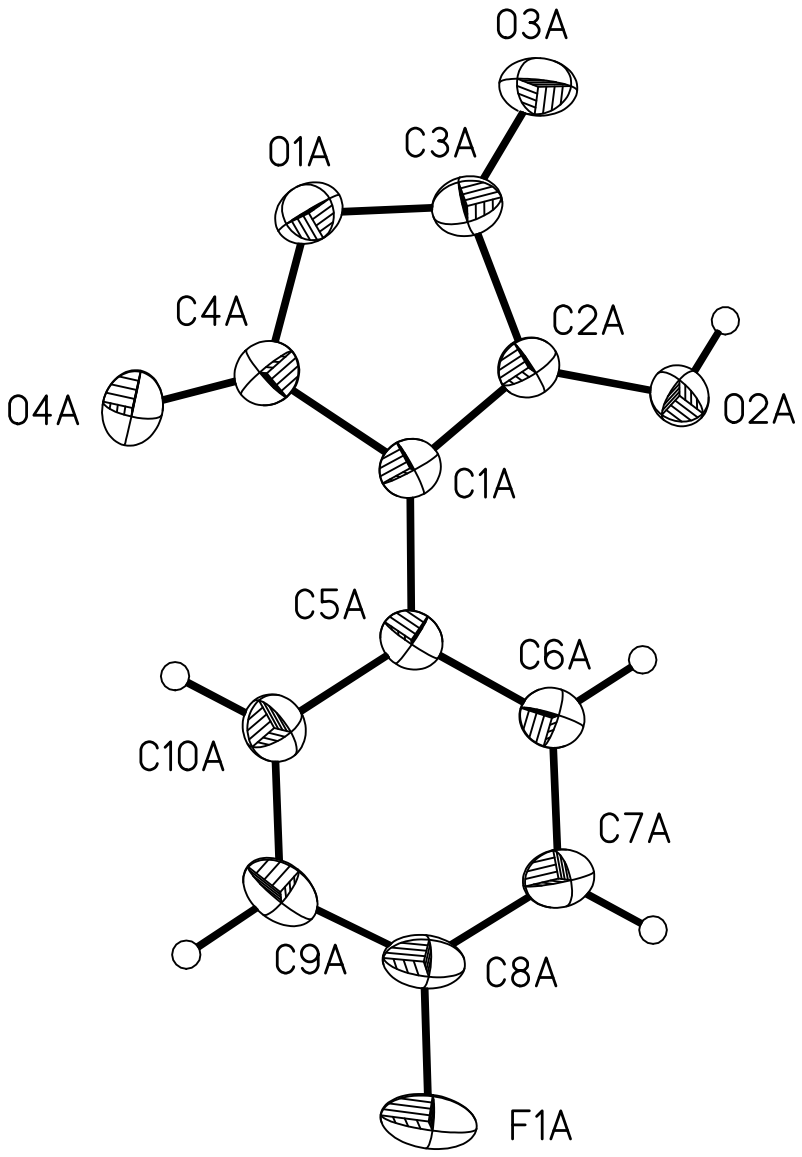


Figure 1. ORTEP plot of **3o**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms

In conclusion, a variety of functionalized 3-hydroxymaleic anhydrides were prepared by cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride.

Experimental section

General. All solvents were dried by standard methods and all reactions were carried out under inert atmosphere. For ^{1}H and ^{13}C NMR spectra (^{1}H NMR: 300, 600 MHz; ^{13}C NMR: 75, 150 MHz), the deuterated solvents indicated were used. Mass spectrometry (MS) data were obtained by using the electron ionization (70 eV), chemical ionization (CI, H_2O), or electrospray (ESI) techniques. For preparative scale chromatography, silica gel (60-200 mesh) was used.

Typical procedure for the preparation of 2-substituted Trimethylsilylacetates (1a-x): Trimethylsilyl propionate (1a): To a stirred solution of propionic acid (5.00 g, 67.56 mmol) in THF (6.7 mL) and pyridine (3.4 mL) at 0 °C was added HMDS (14.0 mL, 67.56 mmol), followed by dropwise addition of Me_3SiCl (4.24 mL, 33.78 mmol). After stirring of the solution for 12 h, to the mixture was added hexane (10 mL) and the solution was filtered under Argon. The solvent was removed under reduced pressure to give **1a** (5.30 g, 54%) as colorless oil. The spectroscopic data are in accordance with the data provided in the literature.[12a] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (q, 2H, ^{3}J = 7.5 Hz, CH_2), 1.04 (t, 3H, ^{3}J = 7.5 Hz, CH_3), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl butyrate (1b): Starting with butyric acid (5.00 g, 56.80 mmol), HMDS (11.8 mL, 56.80 mmol), Me_3SiCl (3.8 mL, 28.40 mmol), THF (5.7 mL), and pyridine (2.9 mL), **1b**

(6.00 g, 66%), was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12e] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (t, 2H, ^3J = 7.5 Hz, CH_2), 1.58-1.53 (m, 2H, CH_2), 0.88 (t, 3H, ^3J = 7.5 Hz, CH_3), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl pentanoate (1c): Starting with pentanoic acid (5.00 g, 49.00 mmol), HMDS (10.2 mL, 49.00 mmol), Me_3SiCl (3.1 mL, 24.50 mmol), THF (4.9 mL), and pyridine (2.5 mL), **1c** (6.80 g, 80%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (t, 2H, ^3J = 7.2 Hz, CH_2), 1.61-1.51 (m, 2H, CH_2), 1.36-1.25 (m, 2H, CH_2), 0.89 (t, 3H, ^3J = 7.5 Hz, CH_3), 0.27 (s, 9H, $SiMe_3$).

Trimethylsilyl heptanoate (1d): Starting with heptanoic acid (5.00 g, 43.04 mmol), HMDS (9.0 mL, 43.04 mmol), Me_3SiCl (2.7 mL, 21.52 mmol), THF (4.3 mL), and pyridine (2.2 mL), **1d** (6.00 g, 74%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (t, 2H, ^3J = 7.5 Hz, CH_2), 1.60-1.55 (m, 4H, CH_2), 1.32-1.26 (m, 4H, CH_2), 0.86 (t, 3H, ^3J = 7.5 Hz, CH_3), 0.27 (s, 9H, $SiMe_3$).

Trimethylsilyl decanoate (1e): Starting with decanoic acid (5.00 g, 29.02 mmol), HMDS (6.0 mL, 29.02 mmol), Me_3SiCl (1.8 mL, 14.51 mmol), THF (3.0 mL), and pyridine (1.5 mL), **1e** (5.20 g, 78%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (t, 2H, ^3J = 7.5 Hz, CH_2), 1.58 (t, 2H, ^3J = 7.5 Hz, CH_2), 1.26 (br s, 12H, CH_2), 0.87 (t, 3H, ^3J = 7.5 Hz, CH_3), 0.27 (s, 9H, $SiMe_3$).

Trimethylsilyl tetradecanoate (1f): Starting with tetradecanoic acid (7.00 g, 30.65 mmol), HMDS (6.3 mL, 30.65 mmol), Me_3SiCl (2.0 mL, 15.33 mmol), THF (3.1 mL) and pyridine (1.5 mL), **1f** (8.19 g, 89%) was isolated as yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$):

δ = 2.23 (t, 2H, ^3J = 7.6 Hz, CH_2), 1.49-1.56 (m. 2H, CH_2), 1.20 (m, 20H, CH_2), 0.83 (t, 3H, ^3J = 7.0 Hz, CH_3), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl 3,3-dimethylbutanoate (1g): Starting with 3,3-dimethylbutyric acid (7.30 g, 62.84 mmol), HMDS (13.0 mL, 62.84 mmol), Me_3SiCl (4.0 mL, 31.42 mmol), in THF (6.2 mL) and pyridine (3.1 mL), (**1g**) (7.21 g, 61%), was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided by literature[12d]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.03 (s, 2H, CH_2), 0.82 (s, 9H, CH_3), 0.13 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(cyclohexyl)acetate (1h): Starting with cyclohexylacetic acid (10.00 g, 70.32 mmol), HMDS (14.6 mL, 70.32 mmol), Me_3SiCl (4.5 mL, 35.16 mmol), THF (7.0 mL) and pyridine (3.5 mL), **1h** (12.06 g, 80%) was isolated as yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.11 (d, 2H, ^3J = 6.7 Hz, CH_2), 1.63-1.77 (m, 6H, CH/CH_2), 0.83-1.32 (m, 5H, CH_2), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl 3-(cyclopropyl)propionate (1i): Starting with 3-cyclopropylpropionic acid (8.00 g, 56.25 mmol), HMDS (11.6 mL, 56.25 mmol), Me_3SiCl (3.6 mL, 28.13 mmol), THF (5.6 mL) and pyridine (2.8 mL), **1i** (10.15 g, 84%) was isolated as yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.25 (m, 2H, CH_2), 1.67-1.74 (m, 3H, CH, CH_2), 1.44-1.60 (m, 6H, CH_2), 1.00-1.08 (m, 2H, CH_2), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl 4-(cyclohexyl)butyrate (1j): Starting with 4-cyclohexylbutyric acid (5.00 g, 29.39 mmol), HMDS (6.1 mL, 29.39 mmol), Me_3SiCl (1.9 mL, 14.69 mmol), THF (2.9 mL) and pyridine (1.5 mL), **1j** (6.33 g, 89%) was isolated as yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.21 (t, 2H, ^3J = 7.3 Hz, CH), 1.51-1.67 (m, 5H, CH, CH_2), 1.09-1.22 (m, 6H, CH_2), 0.80-0.85 (m, 4H, CH_2), 0.22 (s, 9H, $SiMe_3$).

Trimethylsilyl 3,3-diphenylpropionate (1k): Starting with 3,3-diphenylpropionic acid (7.00 g, 30.93 mmol), HMDS (6.4 mL, 30.93 mmol), Me_3SiCl (2.0 mL, 15.47 mmol), THF (3.1 mL) and pyridine (1.5 mL), **1k** (8.40 g, 91%) was isolated as colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.14-7.31 (m, 10H, Ph), 4.49 (t, 1H, ^3J = 8.0 Hz, CH), 3.05 (d, 2H, ^3J = 8.0 Hz, CH_2), 0.12 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-phenylacetate (1l): Starting with phenylacetic acid (5.00 g, 36.72 mmol), HMDS (7.63 mL, 36.72 mmol), Me_3SiCl (2.3 mL, 18.36 mmol), THF (3.6 mL), and pyridine (1.8 mL), **1l** (7.05 g, 92%) was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12a] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17-7.09 (m, 5H, Ph), 3.46 (s, 2H, CH_2), 0.12 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(4-tolyl)acetate (1m): Starting with *p*-tolylacetic acid (5.00 g, 33.30 mmol), HMDS (6.9 mL, 33.30 mmol), Me_3SiCl (2.1 mL, 16.65 mmol), THF (3.3 mL), and pyridine (1.7 mL), **1m** (6.15 g, 83%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, 2H, ^3J = 6.7 Hz, Ar), 7.08 (d, 2H, ^3J = 8.1 Hz, Ar), 3.78 (s, 1H, CH_2), 2.27 (s, 3H, CH_3), 0.29 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(4-chlorophenyl)acetate (1n): Starting with (4-chlorophenyl)acetic acid (5.00 g, 29.30 mmol), HMDS (6.1 mL, 29.30 mmol), Me_3SiCl (1.8 mL, 14.65 mmol), THF (3.0 mL), and pyridine (1.5 mL), **1n** (5.50 g, 77%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25-7.08 (m, 4H, Ar), 3.51 (s, 2H, CH_2), 0.25 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(4-fluorophenyl)acetate (1o): Starting with (4-fluorophenyl)acetic acid (6.00 g, 38.93 mmol), HMDS (8.1 mL, 38.93 mmol), Me_3SiCl (2.5 mL, 19.46 mmol), THF

(3.9 mL) and pyridine (2.0 mL), **1o** (7.29 g, 83%) was isolated as colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.03-7.11 (m, 2H, Ar), 6.80-6.90 (m, 2H, Ar), 3.44 (s, 2H, CH_2), 0.12 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(4-methoxyphenyl)acetate (1p): Starting with (4-methoxyphenyl)acetic acid (5.00 g, 30.09 mmol), HMDS (6.3 mL, 30.09 mmol), Me_3SiCl (1.9 mL, 15.04 mmol), THF (3.0 mL), and pyridine (1.5 mL), **1p** (5.60 g, 78%) was isolated as yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.09 (d, 2H, ^3J = 8.5 Hz, Ar), 6.76 (d, 2H, ^3J = 8.5 Hz, Ar), 3.70 (s, 3H, OCH_3), 3.46 (s, 2H, CH_2), 0.18 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(3,4-dimethoxyphenyl)acetate (1q): Starting with (3,4-dimethoxyphenyl)acetic acid (5.00 g, 25.48 mmol), HMDS (5.3 mL, 25.48 mmol), Me_3SiCl (1.6 mL, 12.74 mmol), THF (2.6 mL), and pyridine (1.3 mL), **1q** (5.80 g, 85%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80 (br s, 3H, Ar), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.53 (s, 2H, CH_2), 0.25 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(4-biphenyl)acetate (1r): Starting with (4-biphenyl)acetic acid (8.00 g, 37.69 mmol), HMDS (7.8 mL, 37.69 mmol), Me_3SiCl (2.4 mL, 18.85 mmol), THF (3.8 mL) and pyridine (1.9 mL), **1r** (8.97 g, 84%) was isolated as yellowish solid (mp 38 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.38-7.45 (m, 4H, Ph/Ar), 7.13-7.30 (m, 5H, Ph/Ar), 3.51 (s, 2H, CH_2), 0.15 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(thien-2-yl)acetate (1s): Starting with (thien-2-yl)acetic acid (7.00 g, 49.24 mmol), HMDS (10.1 mL, 49.24 mmol), Me_3SiCl (3.1 mL, 24.62 mmol), THF (4.9 mL) and pyridine (2.5 mL), **1s** (10.13 g, 96%) was isolated as yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$):

δ = 7.13 (dd, 1H, ^3J = 4.9 Hz, ^3J = 5.2 Hz, Hetar), 6.83-6.90 (m, 2H, Hetar), 3.77 (s, 2H, CH_2), 0.24 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-methoxyacetate (1t): Starting with methoxyacetic acid (5.00 g, 50.97 mmol), HMDS (10.6 mL, 50.97 mmol), Me_3SiCl (3.2 mL, 25.48 mmol), THF (6.0 mL), and pyridine (3.0 mL), **1t** (4.40 g, 53%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12b] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.94 (s, 2H, CH_2), 3.40 (s, 3H, OCH_3), 0.27 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(phenoxy)acetate (1u): Starting with phenoxyacetic acid (5.00 g, 32.90 mmol), HMDS (6.8 mL, 32.90 mmol), Me_3SiCl (2.1 mL, 16.44 mmol), THF (3.3 mL), and pyridine (1.6 mL), **1u** (5.30 g, 72%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17-7.09 (m, 5H, Ph), 3.46 (s, 2H, CH_2), 0.12 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(benzyloxy)acetate (1v): Starting with (benzyloxy)acetic acid (2.00 g, 11.44 mmol), HMDS (2.4 mL, 11.44 mmol), Me_3SiCl (0.7 mL, 5.72 mmol), THF (1.1 mL), and pyridine (0.6 mL), **1v** (1.88 g, 69%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12c] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37-7.25 (m, 5H, Ph), 4.63 (s, 2H, OCH_2), 4.06 (s, 2H, CH_2), 0.31 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-(thiophenoxy)acetate (1w): Starting with (thiophenoxy)acetic acid (8.00 g, 47.56 mmol), HMDS (9.8 mL, 47.56 mmol), Me_3SiCl (3.0 mL, 23.78 mmol), THF (4.7 mL), and pyridine (2.4 mL), **1w** (9.56 g, 84%) was isolated as yellow oil. The spectroscopic data are in accordance with the data provided in the literature.[12f] ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.10-7.34 (m, 5H, PhH), 3.55 (s, 2H, CH_2), 0.17 (s, 9H, $SiMe_3$).

Trimethylsilyl 2-allylacetate (1x): Starting with pent-4-enoic acid (2.00 g, 19.40 mmol), HMDS (4.0 mL, 19.40 mmol), Me_3SiCl (1.2 mL, 9.70 mmol), THF (1.9 mL), and pyridine (1.0 mL), **1x** (1.73 g, 52%) was isolated as colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.87-5.78 (m, 1H, CH), 5.08-4.97 (m, 2H, CH_2), 2.44-2.31 (m, 4H, CH_2), 0.28 (s, 9H, $SiMe_3$).

Typical procedure for the preparation of 1,1-bis(trimethylsilyloxy)ketene acetals (2a-x):

2-Methyl-1,1-bis(trimethylsilyloxy)ethene (2a): To a solution of HMDS (7.1 mL, 34.25 mmol) in THF (28.0 mL) was dropwise added *n*-BuLi (13.7 mL, 2.5 M solution in hexane, 34.25 mmol) at 0 °C. After stirring for 30 min at 45 °C, the mixture was cooled to −78 °C, stirred for 20 minutes at −78 °C and, subsequently, **1a** (4.00 g, 27.40 mmol) was slowly added. The reaction mixture was stirred for 15 min at −78 °C. Subsequently, Me_3SiCl (5.2 mL, 41.10 mmol) was dropwise added to the solution. After holding the -78 °C for additional 15 min, the solution was allowed to warmup over night. The solvent was removed under reduced pressure and the filtration of the residue through a sintered glass funnel under Argon atmosphere gave (**2a**) (3.70 g, 62%). The obtained spectroscopic data are in accordance with the data provided in the literature.[12a] ^1H NMR (300 MHz, $CDCl_3$): δ = 3.51-3.42 (m, 1H, CH), 1.47 (d, 3H, ^3J = 6.6 Hz, CH_3), 0.20 (s, 18H, $SiMe_3$).

2-Ethyl-1,1-bis(trimethylsilyloxy)ethene (2b): Starting with **1b** (5.90 g, 36.87 mmol), HMDS (9.6 mL, 46.08 mmol), *n*-BuLi (18.4 mL, 46.08 mmol), Me_3SiCl (8.7 mL, 55.30 mmol), and THF (37.0 mL), **2b** (6.00 g, 70%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12g] ^1H NMR (300

MHz, $CDCl_3$): δ = 3.57 (t, 1H, ^3J = 7.2 Hz, CH), 1.97-1.90 (m, 2H, CH_3), 0.91 (t, 3H, ^3J = 7.5 Hz, CH_3), 0.20 (s, 18H, $SiMe_3$).

2-Propyl-1,1-bis(trimethylsilyloxy)ethene (2c): Starting with **1c** (6.73 g, 38.67 mmol), HMDS (10.1 mL, 48.33 mmol), *n*-BuLi (19.3 mL, 48.33 mmol), Me_3SiCl (6.9 mL, 55.00 mmol), and THF (39.0 mL), **2c** (7.05 g, 74%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.55 (t, 1H, ^3J = 7.2 Hz, CH), 1.31 (q, 2H, ^3J = 7.2 Hz, ^3J = 14.4 Hz, CH_2), 1.34-1.27 (m, 2H, CH_2), 0.88 (t, 3H, ^3J = 7.3 Hz, CH_3). 0.28 (s, 18H, $SiMe_3$).

2-Pentyl-1,1-bis(trimethylsilyloxy)ethene (2d): Starting with **1d** (5.00 g, 24.70 mmol), HMDS (6.4 mL, 30.88 mmol), *n*-BuLi (12.4 mL, 30.88 mmol), Me_3SiCl (4.6 mL, 37.05 mmol), and THF (25.0 mL), **2d** (5.10 g, 75%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.55 (t, 1H, ^3J = 7.2 Hz, CH), 1.92-1.89 (m, 2H, CH_2), 1.33-1.26 (m, 6H, CH_2), 0.88 (t, 3H, ^3J = 7.3 Hz, CH_3). 0.28 (s, 18H, $SiMe_3$).

2-Octyl-1,1-bis(trimethylsilyloxy)ethene (2e): Starting with **1e** (5.05 g, 22.17 mmol), HMDS (5.8 mL, 27.71 mmol), *n*-BuLi (11.1 mL, 27.71 mmol), Me_3SiCl (4.2 mL, 33.25 mmol) and THF (23.0 mL), **2e** (4.50 g, 64%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.54 (t, 1H, ^3J = 7.2 Hz, CH), 1.41-1.27 (m, 2H, CH_2), 1.26 (br s, 12H, CH_2), 0.88 (t, 3H, ^3J = 7.3 Hz, CH_3), 0.20 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$).

2-Dodecyl-1,1-bis(trimethylsilyloxy)ethene (2f): Starting with **1f** (8.19 g, 27.25 mmol), HMDS (7.0 mL, 34.06 mmol), *n*-BuLi (13.6 mL, 34.06 mmol), and Me_3SiCl (5.2 mL, 40.88 mmol), and THF (27.0 mL), **2f** (9.51 g, 94%) was isolated as yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.54 (t, 1H, ^3J = 7.3 Hz, CH), 1.65-1.95 (m, 2H,CH_2), 1.26 (m, 20H, CH_2), 0.87 (t, 3H, ^3J = 6.4 Hz, CH_3), 0.18 (s, 9H, $SiMe_3$), 0.05 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 150.3 (COSi), 83.7 (CH), 32.0, 30.7, 29.8, 29.8, 29.8, 29.6, 29.5, 29.3, 25.0, 22.8 (CH_2), 14.1 (CH_3), 2.7, 0.6 ($SiMe_3$).

2-(*t*-Butyl)-1,1-bis(trimethylsilyloxy)ethene (2g): Starting with **1g** (7.21 g, 38.28 mmol), HMDS (9.9 mL, 47.85 mmol), *n*-BuLi (19.1 mL, 47.85 mmol), Me_3SiCl (7.3 mL, 57.42 mmol), and THF (38.0 mL), **2g** (9.16 g, 92%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12a] ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.32 (s, 1H, CH), 0.82 (s, 9H, CH_3), 0.17 (s, 9H, $SiMe_3$), 0.14 (s, 9H, $SiMe_3$).

2-Cyclohexyl-1,1-bis(trimethylsilyloxy)ethene (2h): Starting with **1h** (12.07 g, 56.30 mmol), HMDS (14.6 mL, 70.35 mmol), *n*-BuLi (28.1 mL, 70.35 mmol), Me_3SiCl (10.8 mL, 84.40 mmol), and THF (56.0 mL), **2h** (14.07 g, 87%) was isolated as yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.42 (d, 2H, ^3J = 8.8 Hz), 1.97-2.12 (m, 1H, CH), 1.51-1.62 (m, 5H, CH_2), 0.86-1.29 (m, 5H, CH_2), 0.15 (s, 9H, $SiMe_3$), 0.14 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.2 (COSi), 90.8, 34.8 (CH), 34.5, 26.6, 26.5(CH_2), 0.8, 0.4 ($SiMe_3$).

2-(Cyclopentyl)-1,1-bis(trimethylsilyloxy)ethene (2i): Starting with **1i** (10.15 g, 47.35 mmol), HMDS (12.2 mL, 59.18 mmol), *n*-BuLi (23.7 mL, 59.18 mmol), Me_3SiCl (9.1 mL, 71.03 mmol), and THF (47.0 mL), **2i** (11.52 g, 85%) was isolated as yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.51 (t, 1H, ^3J = 7.0 Hz, CH), 1.83-1.89 (m, 2H, CH_2), 1.41-1.74 (m, 7H, CH, CH_2), 1.04-1.11 (m, 2H, CH_2), 0.16 (s, 9H, $SiMe_3$), 0.13 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9 (COSi), 82.4, 40.7 (CH), 32.0, 30.7, 24.9 (CH_2), 0.8, 0.4 ($SiMe_3$).

2-(Cyclohexylethyl)-1,1-bis(trimethylsilyloxy)ethene (2j): Starting with **1j** (6.33 g, 26.11 mmol), HMDS (6.8 mL, 32.64 mmol), *n*-BuLi (13.1 mL, 32.64 mmol), Me_3SiCl (5.0 mL, 39.16 mmol), and THF (26.0 mL), **2j** (6.42 g, 78%) was isolated as yellowish oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.47 (t, 1H, ^3J = 7.3 Hz, CH), 1.55-1.90 (m, 7H, CH, CH_2), 1.09-1.19 (m, 6H, CH_2), 0.77-0.86 (m, 2H, CH_2), 0.16 (s, 9H, $SiMe_3$), 0.12 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.3 (COSi), 84.0 (CH), 38.6 (CH_2), 37.1(CH), 33.4, 27.0, 26.9, 22.5 (CH_2), 0.9, 0.4 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 314 ($[M]^+$, 5), 299 (11), 271 (19), 217 (100), 204 (12), 147 (61), 73 (72). HRMS (EI): calcd for $C_{16}H_{34}O_2Si_2$ ($[M]^+$) 314.20918, found 314.209123.

2-Benzhydryl-1,1-bis(trimethylsilyloxy)ethene (2k): Starting with **1k** (8.40 g, 35.53 mmol), HMDS (9.2 mL, 44.41 mmol), *n*-BuLi (17.8 mL, 44.41 mmol), Me_3SiCl (6.8 mL, 53.29 mmol), and THF (36.0 mL), **2k** (12.13 g, 92%) was isolated as colorless oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.02-7.11 (m, 10H, Ph), 4.84 (d, 1H, ^3J = 9.2 Hz, CH), 4.06 (d, 1H, ^3J = 9.2 Hz, CH), 0.17 (s, 9H, $SiMe_3$), 0.06 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.2 (COSi), 146.7 (C_{Ph}), 128.7, 126.1 (CH_{Ph}), 87.7 (CH), 47.7 ($CHPh_2$), 0.9, 0.5 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 370 ($[M]^+$, 82), 293 (31), 207 (24), 180 (100), 167 (99), 147 (55), 131 (44), 73 (69). HRMS (EI): calcd for $C_{28}H_{30}O_2Si_2$ ($[M]^+$) 370.17788, found 370.177791.

2-Phenyl-1,1-bis(trimethylsilyloxy)ethene (2l): Starting with **1l** (6.87 g, 32.02 mmol), HMDS (8.6 mL, 41.28 mmol), *n*-BuLi (16.5 mL, 41.28 mmol), Me_3SiCl (6.2 mL, 49.53 mmol), and THF (34.0 mL), **2l** (8.50 g, 92%) was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12a] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.35-7.31 (m, 1H, Ph), 7.18-7.12 (m, 2H, Ph), 6.96-6.90 (m, 2H, Ph), 4.55 (s, 1H, CH), 0.24 (s, 18H, $SiMe_3$).

2-(*p*-Tolyl)-1,1-bis(trimethylsilyloxy)ethene (2m): Starting with **1m** (6.10 g, 27.43 mmol), HMDS (7.1 mL, 34.28 mmol), *n*-BuLi (13.7 mL, 34.28 mmol), Me_3SiCl (5.2 mL, 41.14 mmol), and THF (27.0 mL), **2m** (7.00 g, 87%) was isolated as yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.28 (d, 2H, ^3J = 8.4 Hz, Ar), 7.02 (d, 2H, ^3J = 7.8 Hz, Ar), 4.58 (s, 1H, CH_2), 2.27 (s, 3H, CH_3), 0.29 (s, 9H, $SiMe_3$), 0.25 (s, 9H, $SiMe_3$).

2-(4-Chlorophenyl)-1,1-bis(trimethylsilyloxy)ethene (2n): Starting with **1n** (5.00 g, 20.60 mmol), HMDS (5.4 mL, 25.75 mmol), *n*-BuLi (10.3 mL, 25.75 mmol), Me_3SiCl (3.9 mL, 30.90 mmol), and THF (21.0 mL), **2n** (5.60 g, 86%) was isolated as yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25-7.08 (m, 4H, Ar), 4.48 (s, 1H, CH), 0.25 (s, 9H, $SiMe_3$), 0.24 (s, 9H, $SiMe_3$).

2-(4-Fluorophenyl)-1,1-bis(trimethylsilyloxy)ethene (2o): Starting with **1o** (7.29 g, 32.20 mmol), HMDS (8.3 mL, 40.25 mmol), *n*-BuLi (16.1 mL, 40.25 mmol), Me_3SiCl (6.2 mL, 48.30 mmol), and THF (32.0 mL), **2o** (8.79 g, 91%) was isolated as yellowish oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.25-7.30 (m, 2H, Ar), 6.81-6.88 (m, 2H, Ar), 4.52 (s, 1H, CH), 0.26 (s, 9H,$SiMe_3$), 0.12 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2 (d, $^1J_{F,C}$ = 242.3 Hz, FC_{Ar}), 151.1 (COSi), 132.8 (C_{Ar}), 126.9 (d, $^3J_{F,C}$ = 6.8 Hz, CH_{Ar}), 114.2 (d, $^2J_{F,C}$ = 21.1 Hz, CH_{Ar}), 83.8 (CH), 0.8, 0.4 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 298 ($[M]^+$, 27), 197 (23), 147 (35), 136 (100). HRMS (EI): calcd for $C_{14}H_{23}FO_2Si_2$ ($[M]^+$) 298.12151, found 298.121185.

2-(4-Methoxyphenyl)-1,1-bis(trimethylsilyloxy)ethene (2p): Starting with **1p** (5.50 g, 23.07 mmol), HMDS (6.0 mL, 28.84 mmol), *n*-BuLi (11.5 mL, 28.84 mmol), Me_3SiCl (5.4 mL, 43.26 mmol), and THF (23.0 mL), **2p** (6.00 g, 83%) was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12h] ^1H

NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, 2H, ^3J = 8.8 Hz, Ar), 6.73 (d, 2H, ^3J = 8.6 Hz, Ar), 4.52 (s, 1H, CH_2), 3.68 (s, 3H, OCH_3), 0.24 (s, 9H, $SiMe_3$), 0.21 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8 (C_{Ar}), 151.0 (COSi), 130.1 (C_{Ar}), 127.0, 113.8 (CH_{Ar}), 84.8 (CH), 55.3 (OCH_3), 0.7, 0.4 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 310 ($[M]^+$, 39), 267 (6), 238 (6), 209 (20), 179 (14), 148 (100), 120 (20). HRMS (EI): calcd for $C_{15}H_{26}O_3Si_2$ ($[M]^+$) 310.14150, found 310.14146.

2-(3,4-Dimethoxyphenyl)-1,1-bis(trimethylsilyloxy)ethene (2q): Starting with **1q** (5.67 g, 21.15 mmol), HMDS (5.5 mL, 26.44 mmol), *n*-BuLi (10.6 mL, 26.44 mmol), Me_3SiCl (4.0 mL, 31.72 mmol), and THF (21.0 mL), **2q** (5.00 g, 70%) was isolated as yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.21-7.15 (m, 1H, Ar), 6.80-6.78 (m, 2H, Ar), 4.57 (s, 1H, CH). 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 0.29 (s, 18H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.1 (COSi), 148.9, 145.5, 130.6 (C_{Ar}), 118.6, 111.3, 109.4 (CH_{Ar}), 84.8 (CH), 56.0, 55.6 (OCH_3), 1.0, 0.4 ($SiMe_3$).

2-(4-Biphenyl)-1,1-bis(trimethylsilyloxy)ethene (2r): Starting with **1r** (8.97 g, 31.54 mmol), HMDS (8.2 mL, 39.42 mmol), *n*-BuLi (15.8 mL, 39.42 mmol), Me_3SiCl (6.0 mL, 47.31 mmol), and THF (32.0 mL), **2r** (9.88 g, 88%) was isolated as yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.13-7.53 (m, 9H, Ph/Ar), 4.60 (s, 1H, CH), 0.22 (s, 9H, $SiMe_3$), 0.12 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.7 (COSi), 140.7, 136.1, 135.4 (C_{Ar}), 128.7, 127.3, 127.1, 126.6, 126.5 (CH_{Ar}), 84.3 (CH), 0.7, 0.3 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 356 ($[M]^+$, 16), 284 (66), 269 (35), 240 (44), 194 (32), 165 (36), 73 (100). HRMS (EI): calcd for $C_{20}H_{28}O_2Si_2$ ($[M]^+$) 356.16223, found 356.162565.

2-(Thien-2-yl)-1,1-bis(trimethylsilyloxy)ethene (2s): Starting with **1s** (10.55 g, 49.20 mmol), HMDS (12.7 mL, 61.50 mmol), *n*-BuLi (24.6 mL, 61.50 mmol), Me_3SiCl (9.4 mL, 73.80 mmol), and THF (49.0 mL), **2s** (11.37 g, 83%) was isolated as yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 6.97-7.00 (m, 1H, Hetar), 6.89 (dd, 1H, ^3J = 5.2 Hz, ^3J = 4.9 Hz, Hetar), 6.70-6.73 (m, 1H, Hetar), 4.99 (s, 1H, CH), 0.32 (s, 9H, $SiMe_3$), 0.18 (s, 9H,$SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.2 (COSi), 140.8 (C_{Hetar}), 126.0, 120.7, 120.4 (CH_{Hetar}), 81.2 (CH), 2.5, 0.6 ($SiMe_3$). MS (EI, 70 eV): *m/z* (%) = 286 ($[M]^+$, 22), 185 (98), 147 (32), 124 (61), 73 (100). HRMS (EI): calcd for $C_{18}H_{22}O_2SSi_2$ ($[M]^+$) 286.08736, found 286.086880.

2-Methoxy-1,1-bis(trimethylsilyloxy)ethene (2t): Starting with **1t** (4.36 g, 26.91 mmol), HMDS (7.0 mL, 33.64 mmol), *n*-BuLi (13.5 mL, 33.64 mmol), Me_3SiCl (5.1 mL, 40.36 mmol), and THF (27.0 mL), **2t** (4.00 g, 53%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12g] ^1H NMR (300 MHz, $CDCl_3$): δ = 5.26 (s, 1H, CH). 3.43 (s, 3H, OCH_3), 0.22 (s, 18H, $SiMe_3$).

2-Phenoxy-1,1-bis(trimethylsilyloxy)ethene (2u): Starting with **1u** (5.20 g, 23.18 mmol), HMDS (6.0 mL, 28.97 mmol), *n*-BuLi (11.6 mL, 28.97 mmol), Me_3SiCl (5.5 mL, 43.45 mmol), and THF (29.0 mL), **2u** (8.50 g, 92%) was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided by literature.[12g] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.35-7.31 (m, 1H, Ph), 7.18-7.12 (m, 2H, Ph), 6.96-6.90 (m, 2H, Ph), 4.55 (s, 1H, CH), 0.24 (s, 18H, $SiMe_3$).

2-Benzyloxy-1,1-bis(trimethylsilyloxy)ethene (2v): Starting with **1v** (1.86 g, 7.81 mmol), HMDS (2.0 mL, 9.77 mmol), *n*-BuLi (3.9 mL, 9.77 mmol), Me_3SiCl (1.5 mL, 11.72 mmol), and THF (8.0 mL), **2v** (1.14 g, 47%) was isolated as colorless oil. The obtained spectroscopic

data are in accordance with the data provided in the literature[12c]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.33 (m, 5H, Ph), 5.35 (s, 1H, CH), 4.63 (s, 2H, CH_2), 0.24 (s, 18H, $SiMe_3$).

2-Thiophenyl-1,1-bis(trimethylsilyloxy)ethene (2w): Starting with **1w** (9.56 g, 39.76 mmol), HMDS (10.3 mL, 49.70 mmol), *n*-BuLi (19.9 mL, 49.70 mmol), Me_3SiCl (10.8 mL, 59.64 mmol), and THF (39.0 mL), **2w** (10.66 g, 86%) was isolated as yellow oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12f] ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.94-7.21 (m, 5H, Ph), 4.31 (s, 1H, CH), 0.22 (s, 9H, $SiMe_3$), 0.19 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8 (COSi), 140.4 (C_{Ph}), 128.5, 125.5, 124.3 (CH_{Ph}), 70.1 (CH), 0.9, 0.4 ($SiMe_3$).

1,1-Bis(trimethylsilyloxy)penta-1,4-diene (2x): Starting with **1x** (1.71 g, 9.94 mmol), HMDS (2.6 mL, 12.42 mmol), *n*-BuLi (4.0 mL, 9.94 mmol), Me_3SiCl (1.9 mL, 14.91 mmol), and THF (10.0 mL), **2x** (2.00 g, 82%) was isolated as colorless oil. The obtained spectroscopic data are in accordance with the data provided in the literature.[12i] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.83-5.74 (m, 1H, CH), 5.01-4.84 (m, 2H, $=CH_2$), 3.57 (t, 1H, ^3J = 7.3 Hz, CH), 2.05 (t, 2H, ^3J = 2.4 Hz, CH_2), 0.20 (s, 18H, $SiMe_3$).

Typical procedure for the preparation of substituted hydroxymaleic anhydrides (3a-x):

3-Hydroxy-4-methylmaleic anhydride (3a): To a CH_2Cl_2 solution (22.0 mL) of oxalyl chloride (0.252 g, 2.80 mmol) and of **2a** (0.500 g, 2.15 mmol) was added a CH_2Cl_2 solution (5 mL) of TMSOTf (0.19 mL, 1.07 mmol) at −78 °C. The temperature of the solution was allowed to rise to 20 °C during 12 h. After stirring for 3 h at 20 °C, an aqueous solution of HCl (10%) was added. The organic and the aqueous layer were separated and the latter was extracted three times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered

and the solvent of the filtrate was removed *in vacuo*. The residue was purified by chromatography (silica gel, hexane/EtOAc) to give **3a** (68 mg, 20%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7, 163.6 (CO), 152.6 (COH), 111.9 (C), 6.9 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3430 (br), 2959 (m); 1729 (s), 1666 (s), 1614 (m), 1378 (m), 1239 (m), 1090 (m). MS (EI, 70 eV): *m/z* (%) = 128 ($[M]^+$, 34), 100 (28), 83 (100), 55 (96), 27 (56). Anal. Calcd for $C_5H_4O_4$ (128.08): C 46.89, H 3.15; found: C 47.02, H 3.33.

3-Ethyl-4-hydroxymaleic anhydride (3b): Starting with **2b** (0.500 g, 2.15 mmol), oxalyl chloride (0.251 g, 2.80 mmol) and TMSOTf (0.19 mL, 1.07 mmol), **3b** (0.100 g, 36%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.78 (s, 1H, OH), 2.40 (q, 2H, ^{3}J = 7.5 Hz, CH_2), 1.20 (t, 3H, ^{3}J = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 163.6 (CO), 151.8 (COH), 116.9 (C), 15.6 (CH_2), 11.4 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3440 (br), 2979 (w), 1766 (s), 1699 (s), 1398 (m), 1255 (m), 1167 (w), 899 (w). MS (EI, 70 eV): *m/z* (%) = 142 (M^+, 25), 113 (14), 97 (100), 70 (58), 55 (24), 41 (37), 28 (36). Anal. Calcd for $C_6H_6O_4$ (142.11): C 50.71, H 4.26; found: C 50.90, H 4.39.

3-Hydroxy-4-propylmaleic anhydride (3c): Starting with **2c** (0.500 g, 2.03 mmol), oxalyl chloride (0.231 g, 2.64 mmol) and TMSOTf (0.18 mL, 1.01 mmol), **3c** (0.132 g, 42%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 3.59 (t, 2H, ^{3}J = 7.2 Hz, CH_2), 2.85 (sex, 2H, ^{3}J = 7.8 Hz, CH_2), 2.20 (t, 3H, ^{3}J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 167.4, 164.0 (CO), 155.1 (COH), 115.7 (C), 24.9, 22.0 (CH_2), 14.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3355 (br), 2935 (w), 2875 (m), 1771 (s), 1701 (s), 1393 (s), 1233 (s), 1167 (s), 909 (s), 750 (w). MS (EI, 70 eV): *m/z* (%) = 156 ($[M]^+$, 14), 110 (78), 97 (27), 83 (19), 70

(23), 55 (51), 41 (40), 28 (100). Anal. Calcd for $C_7H_8O_4$ (156.14): C 53.85, H 5.16; found: C 53.35, H 6.00.

3-Hydroxy-4-pentylmaleic anhydride (3d): Starting with **2d** (0.500 g, 1.82 mmol), oxalyl chloride (1.180 g, 2.37 mmol) and TMSOTf (0.16 mL, 0.91 mmol), **3d** (0.168 g, 50%) was isolated as colorless oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 11.35 (s, 1H, OH), 2.32 (t, 2H, ^3J = 7.2 Hz, CH_2), 1.59-1.51 (m, 2H, CH_2), 1.36-1.26 (m, 4H, CH_2), 0.96 (t, 3H, ^3J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 167.4, 164.0 (CO), 155.0 (COH), 115.8 (C), 32.7, 28.3, 23.6, 22.9 (CH_2), 14.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3356 (br), 2923 (s), 1775 (s), 1703 (s), 1394 (s), 1207 (s), 749 (m). MS (EI, 70 eV): *m/z* (%) = 184 ($[M]^+$, 2), 156 (10), 139 (27), 128 (50), 112 (66), 100 (34), 85 (26), 55 (50), 43 (100), 29 (50). Anal. Calcd for $C_9H_{12}O_4$ (184.19): C 58.69, H 6.57; found: C 58.90, H 7.02.

3-Hydroxy-4-octylmaleic anhydride (3e): Starting with **2e** (0.500 g, 1.58 mmol), oxalyl chloride (0.258 g, 2.97 mmol) and TMSOTf (0.21 mL, 1.14 mmol), **3e** (0.200 g, 56%) was isolated as colorless solid; mp. 87 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 11.18 (s, 1H, OH), 2.36 (t, 2H, ^3J= 7.2 Hz, CH_2), 1.61-1.17 (m, 12H, CH_2), 0.89 (t, 3H, ^3J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.7, 163.4 (CO), 154.3 (COH),115.4 (C), 32.5, 29.9, 28.0, 23.3, 22.3 (CH_2), 14.3 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3358 (s), 2924 (s), 2854 (m), 1780 (s), 1705 (s), 1397 (s), 903 (m), 750 (m). MS (EI, 70 eV): *m/z* (%) = 226 ($[M]^+$, 7), 198 (16), 180 (17), 155 (34), 128 (57), 112 (60), 57 (79), 43 (89), 41 (100), 28 (98). Anal. Calcd for $C_{12}H_{18}O_4$ (226.27): C 63.70, H 8.02; found: C 63.33, H 7.85.

3-Dodecyl-4-hydroxymaleic anhydride (3f): Starting with **2f** (0.932 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3f** (0.544 g, 71%) was

isolated as a colorless solid; mp. 98 °C. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 2.40 (t, 2H, ^{3}J = 7.3 Hz, CH_2), 1.61 (m, 2H, CH_2), 1.19-1.45 (m, 18H, CH_2), 0.91 (t, 3H, ^{3}J = 6.4 Hz, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.3, 163.0 (CO), 154.0 (COH), 114.8 (C), 32.2, 30.2, 30.0, 29.9, 29.7, 29.6, 28.9, 28.7, 27.6, 22.9, 21.9 (CH_2), 14.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3353 (m), 1849 (m), 1790 (s), 1705 (s), 1275 (m), 1254 (m), 1231 (m). MS (EI, 70 eV): *m/z* (%) = 282 ($[M]^+$, 9), 254 (40), 209 (17), 155 (25), 113 (100). Anal. Calcd for $C_{16}H_{26}O_4$ (284.38): C 68.06, H 9.28; found: C 67.73, H 9.40.

3-*t*-Butyl-4-hydroxymaleic anhydride (3g): Starting with **2g** (0.651 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3g** (0.070 g, 17%) was isolated as colorless oil. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 1.21 (s, 9H, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 164.2, 162.5 (CO), 151.7 (COH), 118.8 (C), 46.3 (CMe_3), 31.4 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3353 (br, m), 3057 (br, m), 1845 (m), 1773 (s), 1757 (br, s), 1684 (br, s), 1472 (br, s), 1116 (s). MS (EI, 70eV): *m/z* (%) = 170 ($[M]^+$, 1), 127 (100), 109 (59), 97 (73), 39 (58). HRMS (ESI): calcd for $C_8H_9O_4$ ($[M-H]^-$) 169.0506, found: 169.0498.

3-Cyclohexyl-4-hydroxymaleic anhydride (3h): Starting with **2h** (0.716 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3h** (0.292 g, 60%) was isolated as a colorless solid; mp. 88 °C. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 2.52-2.64 (m, 1H, CH), 1.68-2.09 (m, 6H, CH_2), 1.25-1.45 (m, 4H, CH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.6, 164.2 (CO), 154.1 (COH), 119.1 (C), 34.9 (CH), 31.0, 27.3, 26.9 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3558 (m), 3451 (m), 2667 (br, s), 1834 (m), 1756 (s), 1687 (s), 934 (m). MS (EI, 70 eV): *m/z* (%) = 196 ($[M]^+$, 33), 178 (18), 124 (23), 81 (62), 150 (100). HRMS (EI): calcd for $C_{10}H_{12}O_4$ ($[M]^+$) 196.0730, found 196.0729.

3-(Cyclopentylmethyl)-4-hydroxymaleic anhydride (3i): Starting with **2i** (0.716 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3i** (0.303 g, 62%) was isolated as colorless oil. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 2,37 (d, 2H, ^{3}J = 3,8 Hz, CH_2), 2.14-2.24 (m, 1H, CH), 1.45-1.83 (m, 6H, CH_2), 1.19-1.26 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.6, 163.2 (CO), 154.4 (COH), 114.6 (C), 39.2 (CH), 32.7, 27.7, 25.2 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3441 (m), 3351(s), 2953 (s), 2868 (m), 1844 (s), 1774 (s), 1703 (s), 1443 (m), 1394 (s). MS (EI, 70 eV): *m/z* (%) = 196 ($[M]^+$, 1), 178 (3), 161 (13), 147 (12), 128 (100), 100 (55). HRMS (ESI): calcd for $C_{10}H_{11}O_4$ ($[M-H]^-$) 195.06573, found 195.06702.

3-(Cyclohexylethyl)-4-hydroxymaleic anhydride (3j): Starting with **2j** (0.787 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3j** (0.354 g, 63%) was isolated as a colorless solid; mp. 87 °C. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 2.37 (t, 2H, ^{3}J = 7.5 Hz, CH_2), 1.61-1.80 (m, 5H, CH, CH_2), 1.41-1.50 (m, 2H, CH_2), 1.13-1.32 (m, 4H, CH_2), 0.85-0.98 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.5, 163.3 (CO), 154.4 (COH), 114.6 (C), 37.7 (CH), 35.1, 33.4, 26.9, 26.6, 19.5 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3349 (s), 3261 (m), 2926 (s), 2852 (m), 1839 (m), 1779 (br, s), 1708 (s), 1456 (m), 1391 (s). MS (CI pos.): *m/z* (%) = 225 ($[M+H]^+$, 100). Anal. Calcd for $C_{12}H_{16}O_4$ (284.38): C 64.27, H 7.19; found: C 64.44, H 9.31.

3-Benzhydryl-4-hydroxymaleic anhydride (3k): Starting with **2k** (0.927 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3k** (0.212 g, 30%) was isolated as colorless oil. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 7.27-7.37 (m, 10H, Ph), 5.43 (s, 1H, CH). ^{13}C NMR (62.5 MHz, $(CD_3)_2CO$): δ = 165.9, 163.0 (CO), 155.0 (COH), 140.8 (C_{Ph}), 129.2, 128.8, 127.3 (CH_{Ph}), 114.8 (C), 45.5 (CH). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3596 (w),

3062 (m), 3029 (m), 2633 (br, m), 1849 (s), 1763 (s), 909 (s). MS (EI, 70 eV): *m/z* (%) = 280 ($[M]^+$, 59), 262 (9), 252 (34), 235 (50), 167 (100). HRMS (EI): calcd for $C_{17}H_{12}O_4$ ($[M]^+$) 280.0730, found: 280.0729.

3-Hydroxyphenylmaleic anhydride (3l): Starting with **2l** (0.500 g, 1.8 mmol), oxalyl chloride (0.20 ml, 2.3 mmol) and TMSOTf (0.16 ml, 0.9 mmol), **3l** (240 mg, 70%) was isolated as a yellow solid; mp. 164 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42-7.50 (m, 3H, Ph), 8.05-8.08 (m, 2H, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.5, 163.4 (CO), 149.4 (COH), 130.3, 129.1, 128.8 (CH_{Ph}), 126.9 (C_{Ph}), 112.0 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3244 (s), 3123 (w), 1840 (s), 1760 (s), 1673 (s), 1393 (s), 1262 (s), 939 (s), 762 (s). MS (EI, 70 eV): *m/z* (%) = 190 ($[M]^+$, 43), 162 (100), 145 (22), 118 (27), 105 (15), 89 (81), 77 (8). Anal. Calcd. for $C_{10}H_6O_4$(190.15): C 63.16, H 3.18; found: C 62.87, H 3.63.

3-hydroxy-4-(4-tolyl)maleic anhydride (3m): Starting with **2m** (0.501 g, 1.70 mmol), oxalyl chloride (0.192 g, 2.21 mmol) and TMSOTf (0.15 mL, 0.85 mmol), **3b** (0.253 g, 73%) was isolated as brown solid; mp. 102 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 7.95 (d, 2H, ^3J = 8.4 Hz, Ar), 7.30 (d, 2H, ^3J = 8.4 Hz, Ar), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.0, 163.9 (CO), 153.0 (COH), 140.7 (C_{Ar}), 130.7, 129.6 (CH_{Ar}), 126.8 (C_{Ar}), 111.9 (C), 22.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3455 (br), 2925 (w), 1767 (s), 1680 (m), 1387 (s), 1173 (w), 825 (w). MS (EI, 70 eV): *m/z* (%) = 204 ($[M]^+$, 36), 176 (76), 149 (31), 131 (30), 105 (100), 77 (40), 51 (18), 28 (10). Anal. Calcd for $C_{11}H_8O_4$ (204.18): C 64.71, H 3.95; found: C 65.00, H 4.01.

4-(4-Chlorophenyl)-3-hydroxymaleic anhydride (3n): Starting with **2n** (0.500 g, 1.60 mmol), oxalyl chloride (1.042 g, 2.0 mmol) and TMSOTf (0.14 mL, 0.80 mmol), **3n** (0.230 g, 65%) was isolated as yellow solid; mp. 150 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 8.09 (d,

2H, ^{3}J = 2.4 Hz, Ar), 7.55 (d, 2H, ^{3}J = 7.2 Hz, Ar). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 165.9, 163.6 (CO), 154.2 (COH), 135.9, 135.5 (C_{Ar}), 132.5, 131.2, 130.3, 129.8 (CH_{Ar}), 110.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3319 (s), 3100 (w), 1755 (s), 1697 (s), 1388 (s), 1092 (m), 864 (m). MS (EI, 70 eV): *m/z* (%) = 224 ($[M]^+$, 36), 196 (100), 151 (32), 125 (57), 89 (52), 63 (24), 28 (10). Anal. Calcd for $C_{10}H_5ClO_4$ (224.60): C 53.48, H 2.24; found: C 53.29, H 2.56.

4-(4-Fluorophenyl)-3-hydroxymaleic anhydride (3o): Starting with **2o** (0.746 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3o** (0.232 g, 45%) was isolated as colorless solid; mp. 115 °C. ^{1}H NMR (500.13 MHz, $(CD_3)_2CO$): δ = 10.9 (br, 1H, OH); 8.12 (m, 2H, $^{4}J_{F,H}$ = 5.5 Hz, *o*-Ph); 7.27 (m, 2H, $^{3}J_{F,H}$ = 9.0 Hz, *m*-Ph). ^{13}C NMR (125.8 MHz, $(CD_3)_2CO$): δ = 165.3, 160.0 (C-1, C-4); 163.6 (d, $^{1}J_{F,C}$ = 249.3 Hz, *p*-Ph); 152.6 (d, $^{6}J_{F,C}$ = 1.5 Hz, C-2); 131.3 (d, $^{3}J_{F,C}$ = 8.4 Hz, *o*-Ph); 125.4 (d, $^{4}J_{F,C}$ = 3.4 Hz, *i*-Ph); 116.4 (d, $^{2}J_{F,C}$ = 22.0 Hz, *m*-Ph); 110.3 (C-3). ^{19}F NMR (235 MHz): δ = -111.8 (*p*-CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3308 (br, s), 1843 (m), 1773 (br, s), 1676 (m), 1606 (m), 1514 (m), 1419 (w), 1392 (br, s). MS (EI, 70 eV): *m/z* (%) = 208 ($[M]^+$, 34), 180 (100), 163 (12), 135 (45), 107 (89). HRMS (EI): calcd for $C_{10}H_5FO_4$ ($[M]^+$) 208.0166, found: 208.0168.

3-Hydroxy-4-(4-methoxyphenyl)maleic anhydride (3p): Starting with **2p** (0.500 g, 1.61 mmol), oxalyl chloride (0.180 g, 2.10 mmol) and TMSOTf (0.15 mL, 0.80 mmol), **3p** (0.190 g, 53%) was isolated as yellow solid; mp. 115 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 8.07-8.02 (m, 2 H, Ar), 7.07-7.02 (m, 2 H, Ar), 3.85 (s, 3 H, OCH_3); ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 165.8, 163.6, 161.2 (CO), 151.8 (COH), 131.3, 130.6, (CH_{Ar}), 121.7 (C), 115.0, 114.6 (CH_{Ar}), 111.1 (C), 55.8 (OCH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3484 (br), 2927 (m), 1761 (s), 1604 (s), 1515 (s), 1251 (s), 1028 (m), 836 (m). MS (EI, 70 eV): *m/z* (%) = 220 ($[M]^+$,

43), 192 (100), 135 (64), 121 (85), 77 (36), 51 (45), 28 (50). Anal. Calcd for $C_{11}H_8O_5$ (220.18): C 60.00, H 3.66; found: C 59.95, H 4.17.

4-(3,4-Dimethoxyphenyl)-3-hydroxymaleic anhydride (3q): Starting with **2q** (0.500 g, 1.47 mmol), oxalyl chloride (0.161 g, 1.91 mmol) and TMSOTf (0.14 mL, 0.17 mmol), **3e** (0.261 g, 70%) was isolated as yellow solid; mp. 214 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 7.72-7.68 (m, 2H, Ar), 7.07 (t, 1H, ^3J = 8.4 Hz, Ar), 3.87 (s, 6H, OCH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.2, 163.9 (CO), 151.9 (COH), 151.7, 150.7 (C_{Ar}), 123.4 (CH_{Ar}), 122.8 (C_{Ar}), 113.1, 113.1 (CH_{Ar}), 112.2 (C) 56.7, 56.7 (OCH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3401 (s), 2927 (m), 1765 (s), 1714 (s), 1242 (s), 1022 (s), 915 (m), 822 (m). MS (EI, 70 eV): *m/z* (%) = 250 ($[M]^+$, 46), 220 (100), 207 (18), 148 (20), 77 (10), 28 (33). Anal. Calcd for $C_{12}H_{10}O_6$ (250.20): C 57.60, H 4.03; found: C 58.01, H 3.72.

4-(4-Biphenyl)-3-hydroxymaleic anhydride (3r): Starting with **2r** (0.892 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3r** (0.379 g, 57%) was isolated as yellowish solid; mp. 180 °C. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 8.31 (d, 2H, ^3J = 8.5 Hz, Ph/Ar), 7.58-7.64 (m, 4H, Ph/Ar), 7.37-7.44 (m, 2H, Ph/Ar), 7.27-7.34 (m, 1H, Ph/Ar). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 177.5, 168.0 (CO), 150.3 (COH), 141.7, 139.4, 131.8 (C), 129.9, 128.2, 127.7, 127.7, 127.4 (CH_{Ar}). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1810 (br, s), 1733 (br, m), 1620 (br, s), 1300 (br, m), 1240 (m), 1181 (m), 1077 (w). HRMS (ESI): calcd for $C_{16}H_9O_4$ ($[M-H]^-$) 265.0506, found: 265.0622.

3-Hydroxy-4-(thien-2-yl)maleic anhydride (3s): Starting with **2s** (0.716 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3s** (0.305 g, 62%) was isolated as yellowish solid; mp. 151 °C. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 7.88 (dd,

1H, ^{3}J = 3.7 Hz, ^{4}J = 1.2 Hz, Hetar), 7.77 (dd, 1H, ^{3}J = 5.2 Hz, ^{4}J = 1.2 Hz, Hetar), 7.27 (dd, 1H, ^{3}J = 5.2 Hz, ^{3}J = 3.7 Hz, Hetar). ^{13}C NMR (62.5 MHz, $(CD_3)_2CO$): δ = 165.2, 163.4 (CO), 150.3 (COH), 130.4, 130.1 (CH_{Hetar}), 130.0 (C_{Hetar}), 129.0 (CH_{Hetar}), 109.3 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3182 (br, m), 3109 (m), 1829 (m), 1758 (s), 1676 (m), 1277 (s), 1230 (m). MS (CI pos.): *m/z* (%) = 197 ($[M+H]^+$, 100). HRMS (CI, neg.): calcd for $C_8H_3O_4S$ ($[M-H]^-$) 194.9747, found: 194.9750.

3-Hydroxy-4-methoxymaleic anhydride (3t): Starting with **2t** (0.500 g, 2.13 mmol), oxalyl chloride (0.252 g, 2.77 mmol) and TMSOTf (0.19 mL, 1.06 mmol), **3t** (0.159 g, 53%) was isolated as yellow oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 4.10 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 163.5, 162.4 (CO), 153.3 (COH), 133.6 (C), 60.0 (OCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3436 (br), 2966 (m), 1773 (s), 1714 (s), 1353 (s), 1155 (s), 917 (w). MS (EI, 70 eV): *m/z* (%) = 144 ($[M]^+$, 3), 118 (6), 89 (7), 73 (14), 59 (23), 45 (100), 29 (77), 28 (21). Anal. Calcd for $C_5H_4O_5$ (144.08): C 41.68, H 2.80; found: C 41.80, H 3.20.

3-Hydroxy-4-phenoxymaleic anhydride (3u): Starting with **2u** (0.500 g, 1.69 mmol), oxalyl chloride (0.192 g, 2.19 mmol) and TMSOTf (0.15 mL, 0.84 mmol), **3u** (0.178 g, 50%) was isolated as colorless solid; mp.164 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 8.67-8.60 (m, 2H, Ph), 8.49-8.38 (m, 3H, Ph). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 162.6, 162.3 (CO), 157.1 (COH), 143.8, 133.1 (C), 131.3, 125.4, 117.8 (CH_{Ph}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3220 (br), 2960 (w), 1766 (s), 1721 (s), 1489 (s), 1381 (s), 1198 (s), 930 (s). MS (EI, 70 eV): *m/z* (%) = 206 ($[M]^+$, 6), 180 (35), 151 (36), 107 (47), 105 (54), 77 (100), 51 (33), 28 (10). Anal. Calcd for $C_{10}H_6O_5$ (206.15): C 58.26, H 2.93; found: C 58.00, H 3.02.

3-Hydroxy-4-benzyloxymaleic anhydride (3v): Starting with **2v** (0.500 g, 1.61 mmol), oxalyl chloride (1.051 g, 2.10 mmol) and TMSOTf (0.14 mL, 0.80 mmol), **3n** (0.145 g, 40%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 7.49-7.34 (m, 5H, Ph), 5.46 (s, 2H, CH_2); ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 163.4, 162.6 (CO), 137.6, 136.8 (C), 130.1, 130.0, 129.9, 129.8, 129.7 (CH), 128.0 (C), 74.6 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3428 (br), 3035 (w), 1747 (s), 1208 (m), 743 (m), 699 (m). MS (EI, 70 eV): *m/z* (%) = 220 ($[M]^+$, 1), 107 (4), 91 (100), 66 (14), 39 (6), 29 (6). Anal. Calcd for $C_{11}H_8O_5$ (220.18): C 60.00, H 3.66; found: C 59.69, H 3.20.

3-Hydroxy-4-thiophenoxymaleic anhydride (3w): Starting with **2w** (0.782 g, 2.50 mmol), oxalyl chloride (0.413 g, 3.25 mmol) and TMSOTf (0.14 mL, 0.75 mmol), **3w** (0.277 g, 50%) was isolated as yellow oil. ^{1}H NMR (250 MHz, $(CD_3)_2CO$): δ = 7.06-7.57 (br m, 5H, Ph). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 172.1, 167.8, 167.0, 138.8 (C), 128.9, 126.3, 125.0 (CH_{Ph}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3419 (br, m), 3058 (m), 1829 (m), 1696 (m), 1618 (s), 1480 (m), 1439 (m), 1402 (m). HRMS (ESI): calcd for $C_{10}H_5O_4$ ($[M-H]^-$) 220.9914, found: 220.9925.

3-Allyl-4-hydroxymaleic anhydride (3x): Starting with **2x** (1.900 g, 7.78 mmol), oxalyl chloride (5.061 g, 10.12 mmol) and TMSOTf (0.70 mL, 3.90 mmol), **3x** (0.134 g, 20%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 5.82 (q, 1H, ^{3}J = 10.2 Hz, CH), 5.17 (d, 2H, $^{3}J_{trans}$ = 17 Hz, $^{3}J_{gem}$ = 2 Hz, 1H, CH), 5.01 (d, 2H, $^{3}J_{cis}$ = 12 Hz, $^{3}J_{gem}$ = 2 Hz, 1H, CH). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.4, 163.4 (CO), 155.1 (COH), 133.3 (CH), 117.1 (CH), 112.2 (C), 26.3 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3344 (Br), 2982 (m), 1769 (s), 1673 (m), 1227 (m), 923 (m), 759 (m). MS (EI, 70 eV): *m/z* (%) = 154 ($[M]^+$, 17), 108 (60), 107 (89), 83 (50), 55 (100), 27 (50). Anal. Calcd for $C_7H_6O_4$ (154.12): C 54.55, H 3.92; found: C 54.92, H 4.01.

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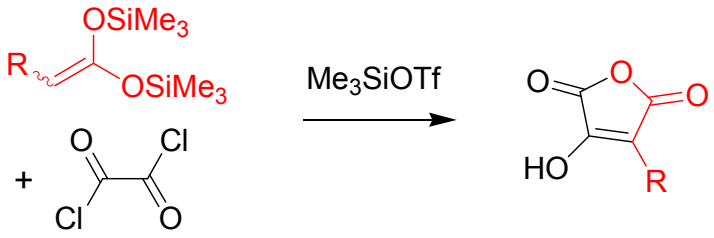

Publication 3

Ehsan Ullah, and Peter Langer* , “Synthesis of Pyran-2-ones by Reaction of 1,1-Bis(silyloxy)ketene Acetals with 3-(Silyloxy)alk-2-en-1-ones ”, *Synthesis* **2005**, 3189.

Synthesis of Pyran-2-ones by Reaction of 1,1-Bis(trimethylsilyloxy)ketene Acetals with 3-Silyloxyalk-2-en-1-ones

Ehsan Ullah,[a] Peter Langer*[a,b]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany

[b] Leibnitz-Institut für Organische Katalyse an der Universität Rostock e. V. (IfOK), Albert-Einstein-Str. 29a, 18059 Rostock, Germany
E-mail: peter.langer@uni-rostock.de

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Dedicated to Professor S. V. Ley, FRS, on the occasion of his 60th birthday

Abstract: Functionalized pyran-2-ones were prepared in two steps by the reaction of 1,1-bis(trimethylsilyloxy)ketene acetals with 3-silyloxyalk-2-en-1-ones.

Key words: cyclizations, ketene acetals, pyran-2-ones, silyl enol ethers

Functionalized pyran-2-ones (α-pyrones) occur in a variety of pharmacologically relevant natural products, such as 5,6-dehydrokawaine, hispidine, geogenine, hymenoquinone, or the antibiotically active myxopyronins (Figure 1).[1] In addition, a wide range of annulated pyran-2-ones are present in nature, e.g. furocumarins or aflatoxins.[1] Many syntheses of pyran-2-ones involve the ring-closure of 5-keto-acids or their derivatives which are available by reaction of an appropriate enolate with an α,β-unsaturated carbonyl compound or a related 1,3-di-electrophile.[2] For example, Effenberger and co-worker reported a versatile approach to 4-hydroxypyran-2-ones by [3+3] cyclization of silyl enol ethers[3] – masked enolates – with malonyl dichloride.[4] Some years ago, Chan and co-workers developed an efficient approach to salicylic esters by [3+3] cyclization of 1,3-bis-silyl enol ethers[5] – masked 1,3-dicarbonyl dianions – with 3-silyloxyalk-2-en-1-ones.[6] Herein, we wish to report what are, to the best of our knowledge, the first [3+3] cyclizations of 1,1-bis(trimethylsilyloxy)ketene acetals – masked carboxylic acid dianions – with 3-silyloxyalk-2-en-1-ones.[7] This methodology allows a convenient two-step synthesis of pyran-2-ones and offers a mild variant of the general strategy outlined above.

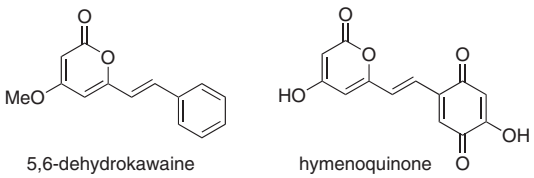
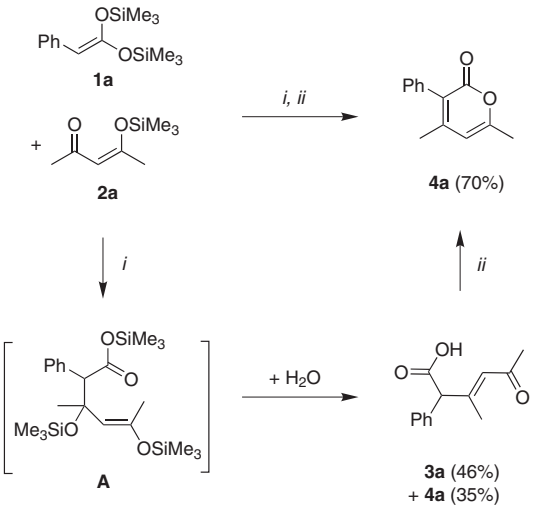


Figure 1

The known 1,1-bis(trimethylsilyloxy)ketene acetal **1a** was prepared by deprotonation of phenylacetic acid with Li-HMDS and subsequent addition of trimethylchlorosilane to the dianion thus formed.[8] The Me_3SiOTf mediated reaction of **1a** with acetylacetone-derived 3-silyloxyalk-2-en-1-one **2a** afforded a separable mixture of the desired pyran-2-one **4a** (35%) and 5-keto-acid **3a** (46%).[9] Treatment of the latter with TFA in CH_2Cl_2 afforded **4a** in 70% yield (Scheme 1).[9] The direct reaction of dilithiated phenylacetic acid with **2a** resulted in the formation of a complex mixture. During the optimization, the use of Me_3SiOTf proved to be important; the employment of stoichiometric amounts of $TiCl_4$ resulted in the formation of a complex mixture.



Scheme 1 Cyclization of 1,1-bis(trimethylsilyloxy)ketene acetal **1a** with 3-silyloxyalk-2-en-1-one **2a**: (*i*) 1) Me_3SiOTf (0.5 equiv), CH_2Cl_2, –78 → 20 °C, 12 h, 20 °C, 3 h, 2) H_2O; (*ii*) TFA, CH_2Cl_2, 20 °C, 72 h.

To study the preparative scope, the substituents were systematically varied (Scheme 2, Table 1). The Me_3SiOTf-mediated reaction of 1,1-bis(trimethylsilyloxy)ketene acetals **1b–d** with **2a** afforded the 5-keto-acids **3b–d** which were transformed into the aryl-substituted pyran-2-ones **4b–d** by treatment with TFA.[9] The reaction of **1e–h** with **2a** gave the 5-keto-acids **3e–h** which were transformed

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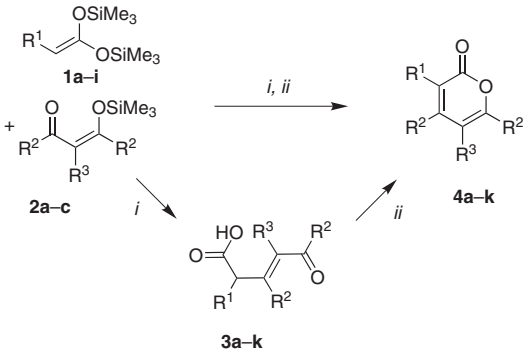
into the alkyl-substituted pyran-2-ones **4e–h**.[9] The phenyloxy-substituted pyran-2-one **4i** was prepared from 1,1-bis(trimethylsilyloxy)ketene acetal **1i**. The 3-silyloxyalk-2-en-1-ones **2b** and **2c** were prepared from heptane-3,5-dione and from 3-methylpentane-2,4-dione, respectively. The reaction of **1a** with **2b** and **2c** afforded the 5-keto-acids **3j** and **3k**, which were transformed into the pyran-2-ones **4j** and **4k**, respectively.



Scheme 2 Synthesis of **4a–k**: (*i*) 1) Me_3SiOTf (0.5 equiv), CH_2Cl_2, –78 → 20 °C, 12 h, 20 °C, 3 h, 2) H_2O; (*ii*) TFA, CH_2Cl_2, 20 °C, 72 h.

Table 1 Products and Yields of Pryran-2-ones

3,4	R^1	R^2	R^3	**3** (%)[a]	**4** (%)[a]
a	Ph	Me	H	46 + 35[b]	70
b	4-MeC_6H_4	Me	H	47 + 42[b]	72
c	4-ClC_6H_4	Me	H	48	68
d	3,4-$(MeO)_2C_6H_3$	Me	H	40	62
e	Et	Me	H	34	45
f	*n*-Pr	Me	H	45	55
g	*n*-Bu	Me	H	42	60
h	*n*-Oct	Me	H	40	58
i	PhO	Me	H	40	50
j	Ph	Et	H	40	62
k	Ph	Me	Me	42	64

[a] Yields of isolated products.
[b] Isolated yields of **4a**,**b**.

4,6-Dimethyl-3-phenylpyran-2-one (4a); Typical Procedure

To a CH_2Cl_2 soln (29 mL) of **1a** (0.81 g, 2.90 mmol) and **2** (0.50 g, 2.90 mmol) was added a CH_2Cl_2 soln (5 mL) of TMSOTf (0.26 mL, 1.45 mmol) at –78 °C. The temperature of the soln was allowed to rise to 20 °C over 12 h. After stirring for 3 h at 20 °C, a sat. aq soln of $NaHCO_3$ (20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel; hexane–EtOAc, 3:2) to give **3a** (0.30 g, 46%) as a colorless oil and **4a** (0.16 g, 35%) as a light yellow solid. To a CH_2Cl_2 soln (0.5 mL) of **3a** (0.10 g, 0.45 mmol) was added TFA (0.70 mL, 9.16 mmol) and the soln was stirred at 20 °C for 72 h. The solvent was removed in vacuo and the residue was purified by chromatography (silica gel; hexane–EtOAc, 3:1) to give **4a** (0.06 g, 70%) as a light yellow solid.

Mp 94 °C.

IR (neat): 2924 (s), 1698 (s), 1645 (s), 1437 (m), 1247 (m), 969 (m), 704 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.77–7.58 (m, 5 H, Ar), 6.30 (s, 1 H, CH), 2.68 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.0, 159.3, 151.4 (C), 129.9, 128.3, 127.8 (CH), 123.0 (C), 107.5 (CH), 29.3 (CH_3), 19.6 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 200 (M^+, 84), 172 (100), 129 (74), 104 (18), 77 (17), 43 (36), 28 (48).

HRMS (ESI): *m*/*z* (%) Calcd. for $C_{13}H_{13}O_2$ ($[M + 1]^+$): 201.09155; found: 201.09094.

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(7) For the cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals with oxalyl chloride, see: Ullah, E.; Langer, P. *Synlett* **2004**, 2782.
(8) For the synthesis of 1,1-bis(trimethylsilyloxy)ketene acetals, see: (a) Ainsworth, C.; Kuo, Y.-N. *J. Organomet. Chem.* **1972**, *46*, 73. (b) Wissner, A. *J. Org. Chem.* **1979**, *44*, 4617. (c) Takai, K.; Heathcock, C. H. *J. Org. Chem.* **1985**, *50*, 3247.
(9) All new compounds gave satisfactory spectroscopic and analytical and/or HRMS data.

Publication 4

Ehsan Ullah, Gopal Bose, Helmar Görls, Peter Langer*

"Synthesis of Pyran-2-ones by Reaction of 1,1-Bis(silyloxy)ketene Acetals with 3-(Silyloxy)alk-2-en-1-ones and 1,1-Diacetylcyclopropane", manuscript in preparation.

Synthesis of Pyran-2-ones by Reaction of 1,1-Bis(silyloxy)ketene Acetals with 3-(Silyloxy)alk-2-en-1-ones and 1,1-Diacetylcyclopropane

Ehsan Ullah,[a, b, c] Gopal Bose, [c] Helmar Görls,[d] Peter Langer* [a, b]

[a] Institut für Chemie, Universität Rostock,
Albert-Einstein-Str. 3a, D-18059 Rostock, Germany

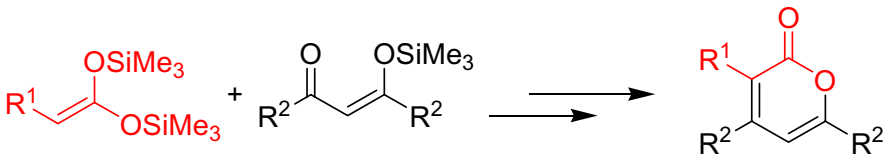
[b] Leibniz-Institut für Katalyse e.V. an der Universität Rostock,
Albert-Einstein-Str. 29a, D-18059 Rostock, Germany

[c] Institut für Biochemie, Universität Greifswald,
Friedrich-Ludwig-Jahn-Str. 18c, D-17487 Greifswald, Germany

[d] Institut für Anorganische und Analytische Chemie, Universität Jena,
August-Bebel-Str. 2, 07740 Jena, Germany

Abstract: Functionalized pyran-2-ones were prepared in two steps by reaction of 1,1-bis(trimethylsilyloxy)ketene acetals with 3-silyloxyalk-2-en-1-ones.

Keywords: cyclizations, ketene acetals, pyran-2-ones, silyl enol ethers

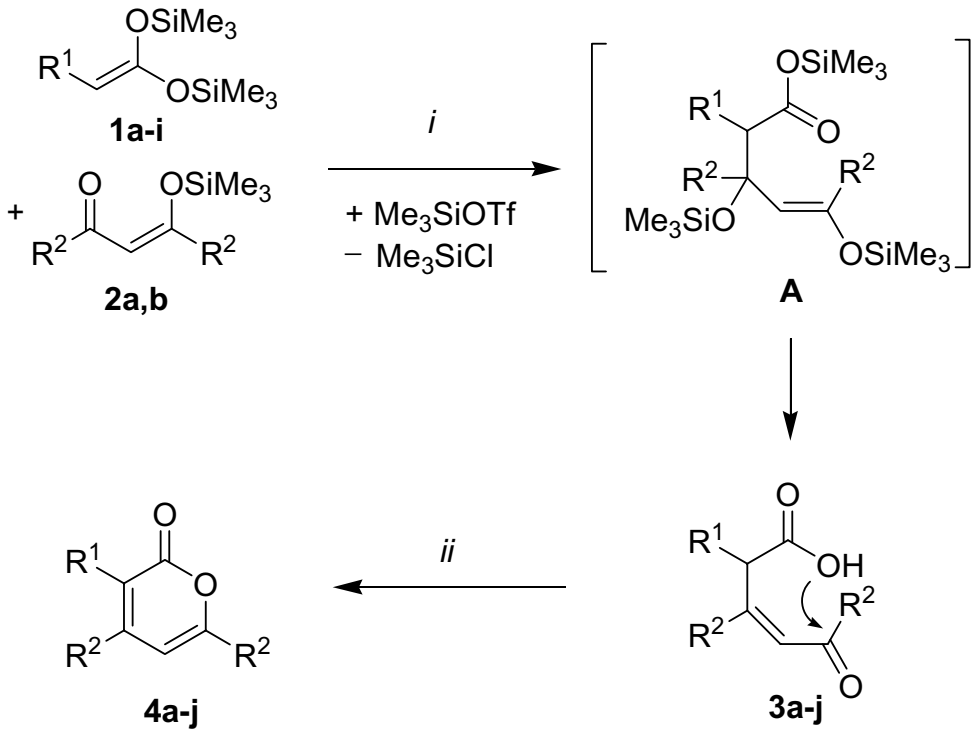


Functionalized pyran-2-ones (α-pyrones) occur in a variety of pharmacologically relevant natural products, such 5,6-dehydrokawaine, hispidine, geogenin, hymenoquinone or the antibiotically active myxopyronins.[1] In addition, a wide range of annulated pyran-2-ones

are present in nature, e. g. the furocumarins or aflatoxins.[1] Many syntheses of α-pyrones involve the ring-closure of 5-keto-acids or derivatives which are available by reaction of an appropiate enolate with an α,β-unsaturated carbonyl compound or a related 1,3-dielectrophile.[2] For example, Effenberger and coworker reported a versatile approach to 4-hydroxypyran-2-ones by [3+3] cyclization of silyl enol ethers[3] – masked enolates – with malonyl dichloride.[4] Some years ago, Chan and coworkers developed an efficient approach to salicylic esters by [3+3] cyclization of 1,3-bis-silyl enol ethers[5] – masked 1,3-dicarbonyl dianions – with 3-silyloxyalk-2-en-1-ones.[6] Herein, we wish to report what are, to the best of our knowledge, the first [3+3] cyclizations of 1,1-bis(trimethylsilyloxy)ketene acetals – masked carboxylic acid dianions – with 3-silyloxyalk-2-en-1-ones.[7] This methodology allows a convenient two-step synthesis of α-pyrones and offers a mild variant of the general strategy outlined above.

The known 1,1-bis(trimethylsilyloxy)ketene acetal **1a** was prepared by deprotonation of phenylacetic acid with lithio-1,1,1,3,3,3-hexamethyldisilazane (Li-HMDS) and subsequent addition of trimethylchlorosilane to the dianion thus formed.[8] The Me_3SiOTf mediated reaction of **1a** with acetylacetone-derived 3-silyloxyalk-2-en-1-one **2a** afforded a separable mixture of the desired pyran-2-one **4a** (35%) and of the 5-keto-acid **3a** (46%).[9] Treatment of the latter with TFA in CH_2Cl_2 afforded **4a** in 70% yield (Scheme 1).[9] The direct reaction of dilithiated phenylacetic acid with **2a** resulted in the formation of a complex mixture. During the optimization, the use of Me_3SiOTf proved to be important; the employment of stoichiometric amounts of $TiCl_4$ resulted in the formation of a complex mixture.

To study the preparative scope, the substituents were systematically varied (Scheme 2, Table 1). The Me_3SiOTf mediated reaction of 1,1-bis(trimethylsilyloxy)ketene acetals **1b-d** with **2a** afforded the 5-keto-acids **3b-d** which were transformed into the aryl-substituted pyran-2-ones **4b-d** by treatment with TFA. The reaction of **1e-h** with **2a** gave the 5-keto-acids **3e-h**, which was transformed into the alkyl-substituted pyran-2-ones **4e-h**. The phenyloxy-substituted pyran-2-one **4i** was prepared from 1,1-bis(trimethylsilyloxy)ketene acetal **1i**. The 3-silyloxyalk-2-en-1-ones **2b** and **2c** were prepared from heptane-3,5-dione and from 3-methylpentane-2,4-dione, respectively. The reaction of **1a** with **2b** afforded the 5-keto-acids **3j** which were transformed into the pyran-2-ones **4j**.



Scheme 1. Synthesis of **4a-j**: *i*, 1) Me_3SiOTf (0.5 equiv.), CH_2Cl_2, –78 → 20 °C, 12 h, 20 °C, 3 h, 2) H_2O; *ii*, TFA, CH_2Cl_2, 20 °C, 72 h

Table 1. Products and yields

3,4	R^1	R^2	R^3	% (**3**) [a]	% (**4**) [a]
A	Ph	Me	H	46 + 35[b]	70
b	4-MeC_6H_4	Me	H	47 + 42[b]	72
c	4-ClC_6H_4	Me	H	48	68
D	3,4-$(MeO)_2C_6H_3$	Me	H	40	62
E	Et	Me	H	34	45
F	*n*Pr	Me	H	45	55
G	*n*Bu	Me	H	42	60

h	*n*Oct	Me	H	40	58
i	PhO	Me	H	40	50
J	Ph	Et	H	40	62

[a] Yields of isolated products. [b] Isolated yields of **4a,b**

The structure of **4d** was independently confirmed by crystal structure analysis (Figure 1).

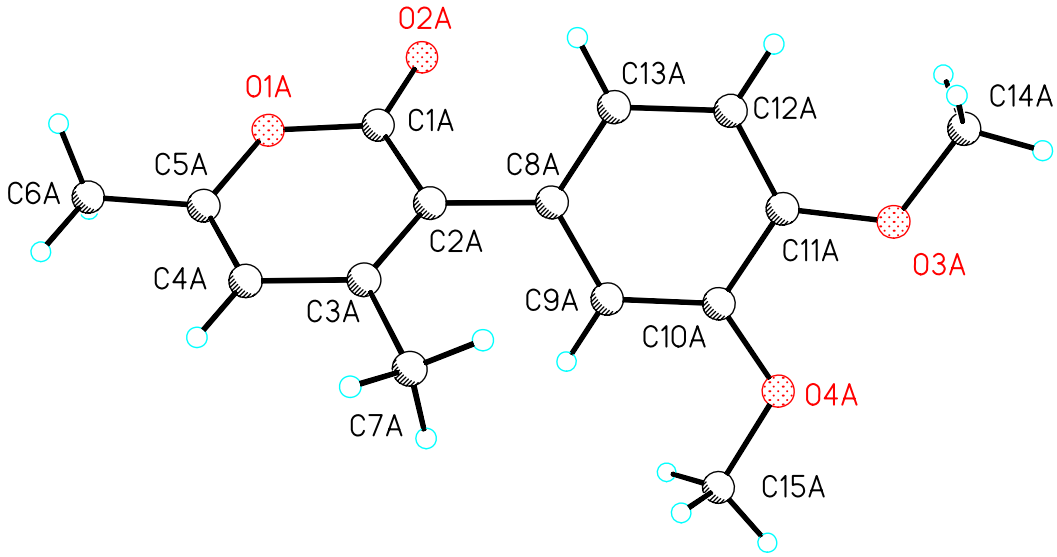
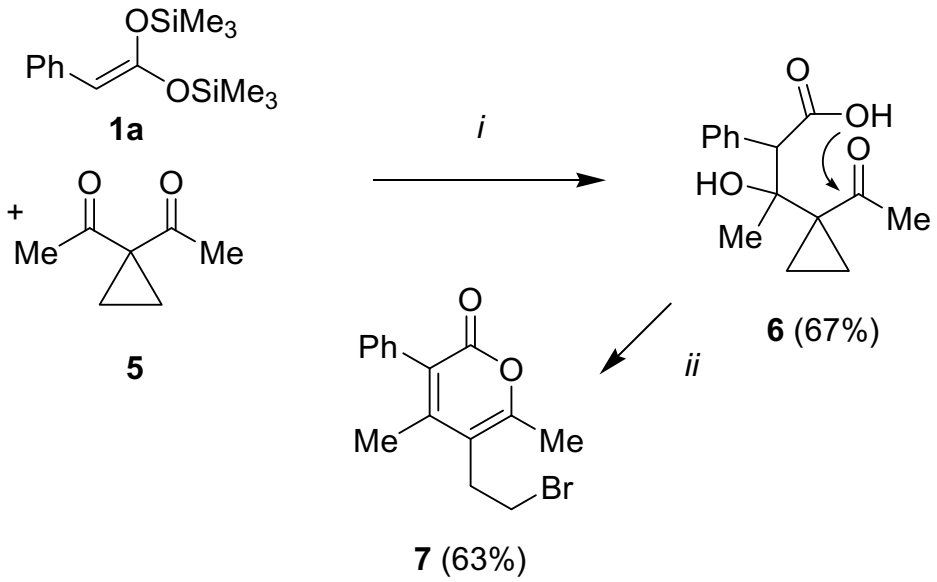


Figure 1. Crystal structure of **4d**

The reaction of silyl ketene acetal **1a** with 1,1-diacetylcyclopropane afforded the condensation product 6 which was transformed into the pyrone **7** by treatment with $TiBr_4$ (Scheme 2). The formation of **7** can be explained by $TiBr_4$-mediated attack of the carboxylic acid onto the carbonyl group and $TiBr_4$-mediated ring-opening of the cyclopropane moiety.



Scheme 2. Synthesis of **7**: *i*, 1) $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 12 h, 20 °, 2 h, 2) H_2O; *ii*, $TiBr_4$, CH_2Cl_2, 20 °C, 3 h

Experimental Section:

Typical procedure: synthesis of 4,6-dimethyl-3-phenylpyran-2-one (**4a**): To a CH_2Cl_2 solution (29 ml) of **1a** (0.81 g, 2.90 mmol) and of **2** (0.50 g, 2.90 mmol) was added a CH_2Cl_2 solution (5 ml) of TMSOTf (0.26 ml, 1.45 mmol) at −78 °C. The temperature of the solution was allowed to rise to 20 °C during 12 h. After stirring for 3 h at 20 °C, a saturated aqueous solution of $NaHCO_3$ was added. The organic and the aqueous layer were separated and the latter was extracted three times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane/EtOAc) to give **3a** (0.30 g, 46%) as colourless oil and **4a** (0.16 g, 35%) as a light yellow solid. To a CH_2Cl_2 solution (0.5 mL) of **3a** (0.10 g, 0.45 mmol) was added TFA (0.70 mL, 9.16 mmol) and the solution was stirred at 20 °C for 72 h. The solvent was removed in vacuo and the residue was purified by chromatography (silica gel, hexane/EtOAc) to give **4a** (0.06 g, 70%) as a light yellow solid.

3-Methyl-5-oxo-2-phenyl-hex-3-enoic acid (3a): Starting with (2,2-bis-trimethylsilanyloxy-vinyl)-benzene (**1a**) (0.810 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol) and TMSOTf (0.26 mL, 1.45 mmol), (**3a**) (0.292 g, 46%), was isolated as colorless oil and (4a) (0.203 g, 35%), was also isolated as yellow

solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.35 (s, 1H, OH), 7.38-7.25 (m, 5H, ArH), 6.19 (s, 1 H, CH), 4.42 (s, 1H, CH), 2.19 (s, 3H, CH_3), 2.04 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.0 (CO), 176.3 (COOH), 152.6 (C-CH_2), 136.3 (C-Ph), 130.3, 129.9, 129.8, 129.6, 129.4 (CH-Ph), 126.3, 60.5 (CH), 21.6, 19.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3062 (br), 1698 (s), 1680 (m), 1646 (s), 1562 (m), 1243 (w), 705 (m). MS (EI, 70 eV): m/z (%) = 218.0 (M^+, 40), 199 (17), 188 (40), 144 (68), 91 (23), 43 (56), 28 (100). Anal. Calcd for $C_{13}H_{14}O_3$ (218.09): C 71.54, H 6.47; found: C 71.30, H 6.10.

3-Methyl-5-oxo-2-*p*-tolylhex-3-enoic acid (3b): Starting with 2-(4-*p*-tolyl)-1,1-bis(trimethylsilyloxy) ethene (**1b**) (0.854 g, 2.901 mmol)**,** 4-trimethylsilanyl-pent-3-en-2-one **(2)** (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3b**) (0.315 g, 47%), was isolated as colorless oil and (4b) (0.261 g, 42%) was also isolated as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.30 (s, 1H, OH), 7.28-7.15 (m, 5H, ArH), 6.19 (s, 1H, CH), 4.39 (s, 1H, CH), 2.34 (s, 1H, CH_3), 2.19 (s, 3H, CH_3), 2.04 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.9 (CO), 176.3 (COOH), 152.5 (C-CH_3), 137.8, 132.0 (C-Ph), 129.5, 129.2, 128.9, 128.8 (CH-Ph), 126.0, 60.5 (CH), 32.0, 21.10, 18.8 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3455 (br), 2926 (w), 1690 (s), 1614 (m), 1437 (m), 1176 (w), 788 (w). MS (EI, 70 eV): m/z (%) = 232.0 (M^+, 2), 214 (30), 188 (38), 144 (78), 104 (26), 91 (16), 77 (16), 43 (63), 28 (100). HRMS (Maldi+): calcd for $C_{14}H_{18}NO_3$ ($[M+2]^+$): 234.18630; found: 234.1856.

2-(4-chlorophenyl)-3-methyl-5-oxohex-3-enoic acid (3c): Starting with 2-(4-chlorophenyl)-1,1-bis(trimethylsilyloxy)ethane (**1c**) (0.912 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3c**) (0.350 g, 48%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.02 (s, 1H, OH), 7.35 (d, 2H, *J* = 8.4 Hz, ArH), 7.35 (d, 2H, *J* = 8.4 Hz, ArH), 6.17 (s, 1H, CH), 4.04 (s, 1H, CH), 2.21 (s, 3H, CH_3), 2.12 (CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.9 (CO), 175.7 (COOH), 151.7 (C-CH_3), 134.3, 133.4 (C-Ph), 130.3 (2C), 129.0 (2C)(CH-Ph), 126.2, 59.9 (CH), 31.9, 18.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2976 (w), 2928 (w), 1712 (s), 1616 (s), 1490 (s), 1091 (s), 792 (m). MS (CI): *m/z* (%) = 255.0 (M^++1, [^{37}Cl], 10), 253.0 (M^++1, [^{37}Cl], 33), 237 (30), 235 (100), 227 (5), 225 (10), 207 (7), 101 (7). Anal. Calcd for $C_{13}H_{13}ClO_3$ (252.05): C 61.79, H 5.19; found: C 62.01, H 5.40.

2-(3,4-Dimethoxy-phenyl)-3-methyl-5-oxohex-3-enoic acid (3d): Starting with 2-(3,4-dimethoxy-phenyl)-1,1-bis(trimethylsilyloxy)ethene (**1d**) (0.328 g, 1.47 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.252 g, 1.47 mmol), and TMSOTf (0.13 mL, 0.73 mmol), (**3d**) (0.290 g, 38%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.21 (s, 1 H, OH), 6.95 (d, 1 H, *J* = 8.1 Hz, ArH), 6.82 (dd, 2 H, *J* = 8.1 Hz, 9.6 Hz, ArH), 5.92 (s, 1 H, CH), 4.50 (s, 1 H, CH), 3.92 (s, 1 H, OCH_3), 3.85 (s, 3 H, OCH_3), 2.24 (s, 3 H, CH_3), 2.02 (s, 1 H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.4 (CO), 178.4 (COOH), 151.3 (C-CH_3), 148.4, 148.7 (C-Ph), 129.6, 128.8 , 126.5 (CH-Ph), 122.8, 54.7 (CH), 55.5, 54.6 (OCH_3), 20.3, 19.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3236 (s), 2954 (s), 2832 (m), 1710 (s), 1375 (s), 920 (m). MS (EI, 70 eV): m/z (%) = 278.0 (M^+, 16), 260 (21), 232 (42), 189 (34), 113 (6), 28 (100). Anal. Calcd for $C_{15}H_{18}O_5$ (278.11): C 64.74, H 6.52; found: C 64.50, H 6.30.

2-Ethyl-3-methyl-5-oxo-hex-3-enoic acid (3e): Starting with 2-(3,4-dimethoxy-phenyl)-1,1-bis(trimethylsilyloxy)ethene (**1e**) (0.667 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3e**) (0.170 g, 34%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (s, 1H, OH), 6.21 (s, 1H, CH), 2.96 (t, 1H, *J* = 7.5 Hz, CH), 2.21 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.94-1.87 (m, 1H, CH_2), 1.72-1.65 (m, 1H, CH_2), 0.90 (t, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.5 (CO), 177.8 (COOH), 153.0 (C-CH_3), 126.4, 57.0 (CH), 31.7 (CH_3), 23.1 (CH_2), 16.9, 12.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2975 (s), 2888 (m), 1733 (s), 1617 (s), 1382 (s), 1118 (m). MS (EI, 70 eV): *m/z* (%) = 170.0 (M^+, 4), 151 (14), 124 (24), 108 (62), 43 (100), 28 (69). Anal. Calcd for $C_9H_{14}O_3$ (170.09): C 63.51, H 8.29; found: C 63.25, H 8.01.

3-Methyl-5-oxo-2-propyl-hex-3-enoic acid (3f) Starting with 1,1-bis(trimethylsilyloxy)propene (**1f**) (0.713 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3f**) (0.212 g, 40%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (s, 1H, CH), 3.06 (t, 1H, *J* = 7.5 Hz, CH), 2.21 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.89-1.82 (m, 1H, CH_2), 1.65-1.58 (m, 1H, CH_2), 1.34-1.24 (m, 2H, CH_2), 0.90 (t, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7 (CO), 177.5 (COOH), 153.0 (C-CH_3), 126.3, 54.9 (CH), 32.0 (CH_3), 31.9, 20.61 (CH_2), 17.0, 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2963 (s), 2873 (m), 1717 (s), 1618 (m), 1382 (m), 1115 (m), 1071 (w). MS (EI, 70 eV): *m/z* (%) = 184.0 (M^+, 5),

167 (22), 124 (44), 108 (30), 96 (52), 43 (100), 28 (46). Anal. Calcd for $C_{10}H_{16}O_3$ (184.10): C 65.19, H 8.75; found: C 64.78, H 8.54.

.**2-(1-Methyl-3-oxo-but-1-enyl)-heptanoic acid (3g):** Starting with 1,1-bis(trimethylsilyloxy)-but-1-ene (**1g**) (0.754 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3g**) (0.240 g, 42%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (s, 1H, CH), 3.04 (t, 1H, *J* = 7.5 Hz, CH), 2.21 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.94-1.83 (m, 1H, CH_2), 1.69-1.60 (m, 1H, CH_2), 1.38-1.20 (m, 4H, CH_2), 0.90 (t, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.5 (CO), 177.0 (COOH), 152.8 (C-CH_3), 126.1, 55.0 (CH), 31.7 (CH_3), 29.4, 29.3, 22.2 (CH_2), 16.7, 13.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 2959 (s), 2867 (m), 1734 (s), 1695 (s), 1360 (s), 1211 (m), 969 (w). MS (EI, 70 eV): *m/z* (%) = 198.0 (M^+, 1), 180 (6), 138 (25), 124 (62), 108 (65), 96 (100), 43 (78).

2-(1-Methyl-3-oxo-but-1-enyl)-3-decanoic acid (3h): Starting with 2-octyl-1,1-bis(trimethylsilyloxy)ethene (**1h**) (0.920 g, 2.90 mmol), 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3h**) (0.297 g, 40%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.27 (s, 1H, OH), 6.21 (s, 1H, CH), 3.04 (t, 1H, *J* = 7.5 Hz, CH), 2.22 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.90-1.60 (m, 2H, CH_2), 1.26 (br s, 12H, CH_2), 0.89 (t, 3H, *J* = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.9 (CO), 177.9 (COOH), 153.3 (C-CH_3), 126.3, 55.5 (CH), 31.8 (CH_3), 31.7, 29.9 (2C), 29.3, 29.1, 27.3, 22.6 (CH), 16.9, 14.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2977 (s), 2930 (s), 2862 (m), 1734 (m), 1691 (m), 1447 (s), 1128 (s), 794 (m). MS (EI, 70 eV): *m/z* (%) = 254.0 (M^+, 1), 236 (2), 142 (4), 124 (15), 96 (12), 43 (30), 28 (100). HRMS (CI; pos.): calcd for $C_{15}H_{27}NO_3$ ($[M+1]^+$): 255.19547; found: 255.19617.

3-Methyl-5-oxo-2-phenoxy-hex-3-enoic acid (3i): Starting with 2-phenoxy-1,1-bis(trimethylsilyloxy)ethene (**1i**) (0.858 g, 2.90 mmol) **,** 4-trimethylsilanyl-pent-3-en-2-one (**2**) (0.500 g, 2.90 mmol), and TMSOTf (0.26 mL, 1.45 mmol), (**3i**) (0.270 g, 40%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (t, 2 H, *J* = 7.5 Hz, ArH), 7.0 (q, 3 H, *J* = 7.2 Hz, ArH), 6.39 (s, 1H, CH), 3.28 (s, 1H, CH), 2.21 (s, 3H, CH_3), 1.70 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.7 (CO), 157.5 (COOH), 157.0 (C-CH_3), 137.9, 131.0, 129.5 (C-Ph), 122.4 (CH), 122.4, 116.0 (CH-Ph), 113.8 (C), 29.2, 17.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2931 (s), 2857 (m), 1721 (s), 1685 (s), 1341 (s),

1120 (m), 956 (w). MS (EI, 70 eV): m/z (%) = 234 (M^+, 5), 215 (20), 190 (40), 146 (64), 91 (100), 43 (34). Anal. Calcd for $C_{13}H_{14}O_4$ (234.00): C 66.66, H 6.02; found: C 66.40, H 5.93.

3-Ethyl-5-oxo-2-phenyl-hept-3-enoic acid (3j): Starting with (2,2-bis-trimethylsilanyloxy-vinyl)-benzene (**2a**) (0.700 g, 2.50 mmol), and 5-trimethylsilanyl-hept-4-en-3-one (**2**) (0.500 g, 2.50 mmol), and TMSOTf (0.23 ml, 1.25 mmol)**,** (**3j**) (0.230 g, 37%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.28 (m, 5H, ArH), 6.16 (s, 1H, CH), 4.50 (s, 1H, CH), 2.67 (q, 2H, *J* = 7.5 Hz, CH_2), 2.50-2.36 (m, 2H, CH_2), 1.11-104 (m, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.3 (CO), 176.0 (COOH), 157.4 (C-CH_3), 135.2 (C-Ph), 129.3, 129.2, 129.0 (2C), 128.3 (CH-Ph), 125.0, 58.2 (CH), 38.0, 26.2 (CH_2), 13.4, 8.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2940 (s), 2834 (m), 1729 (s), 1693 (s), 1618 (s), 1455 (m), 1169 (m), 700 (w). MS (EI, 70 eV): *m/z* (%) = 246.0 (M^+, 6), 228 (84), 100 (49), 173 (30), 144 (73), 129 (75), 57 (100), 29 (69). Anal. Calcd for $C_{15}H_{18}O_3$ (246.29): C 73.15, H 7.36; found: C 73.42, H 7.78

General procedure for the synthesis of 4,6-Dimethyl-pyran-2-one (4): To a CH_2Cl_2 solution (0.5 mL) of enoic acid (1.00 mmol) was added TFA (20.00 mmol) and the solution was stirred at 20 °C for 72 h. The solvent was removed in vacuo and the residue was purified by chromatography.

4,6-Dimethyl-3-phenyl-pyran-2-one (4a): The intermediate (**3a**) (0.100 g, 0.45 mmol), was then treated with TFA (0.70 mL, 9.16 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4a**) (0.063 g, 70%), was isolated as yellow solid; mp. 94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77-7.58 (m, 5H, ArH), 6.30 (s, 1H, CH), 2.68 (s, 3H, CH_3), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.0 (CO), 159.3, 151.4 (C-CH_3), 134.0 (C-Ph), 129.9 (2C), 128.3 (2C), 127.8 (CH-Ph), 123.0 (C), 107.5 (CH), 29.3, 19.6 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2924 (s), 1698 (s), 1645 (s), 1437 (m), 1247 (m), 969 (m), 704 (s). MS (EI, 70 eV): *m/z* (%) = 200.0 (M^+, 84), 172 (100), 129 (74), 104 (18), 77 (17), 43 (36), 28 (48). HRMS (Maldi+): calcd for $C_{13}H_{13}O_2$ ($[M+1]^+$): 201.09155; found: 201.09094.

4,6-Dimethyl-3-*p*-tolyl-pyran-2-one (4b): The intermediate (**3b**) (0.100 g, 0.43 mmol), was then treated with TFA (0.671 mL, 8.76 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4b**) (0.066 g, 72%), was isolated as yellow solid; mp. 86 °C. ^{1}H NMR (300 MHz,

$CDCl_3$): δ = 7.25 (d, 2H, *J* = 8.1 Hz, Ar), 7.14 (d, 2H, *J* = 8.4 Hz, Ar), 5.95 (s, 1H, CH), 2.37 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2 (CO), 159.1, 151.2 (C-CH_3), 137.9, 131.0 (C-Ph), 129.7 (2C), 129.0 (2C) (CH), 123.0 (C), 107.5 (CH), 21.3, 20.3, 19.6 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 1705 (s), 1650 (s), 1567 (s), 1366 (m), 919 (m), 818 (m). MS (EI, 70 eV): m/z (%) = 214.0 ($[M]^+$, 15), 186 (23), 143 (34), 91 (2), 32 (23), 28 (100). HRMS (Maldi+): calcd for $C_{14}H_{15}O_2$ ($[M+1]^+$): 215.10666; found: 215.10689.

3-(4-Chloro-phenyl)-4,6-Dimethyl-pyran-2-one (4c): The intermediate (3c) (0.180 g, 0.71 mmol), was then treated with TFA (1.02 mL, 14.22 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (4c) (0.114 g, 68%), was isolated as yellow solid; mp. 80 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39 (dd, 2H, ^3J = 8.9 Hz, ^4J = 2.4 Hz, Ar), 7.21 (dd, 2H, ^3J = 8.9 Hz, ^4J = 2.4 Hz, Ar), 5.98 (s, 1H, CH), 2.26 (s, 3H, CH_3), 2.02 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.8 (CO), 151.7, 133.7 (C-CH_3), 132.4 (C-Ph), 131.3 (2C), 128.5 (2C) (CH), 128.5, 121.8 (C), 107.4 (CH), 20.3, 19.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3426 (w), 2872 (m), 1705 (s), 1647 (s), 1565 (m), 1337 (m), 1091(m), 825 (w), 504 (w). MS (EI, 70 eV): *m/z* (%) = 236.0 (M^+ [^{37}Cl], 2), 234 (M^+ [^{35}Cl], 5), 208 (2), 206 (6), 165 (1), 163 (5), 130 (42), 83 (17), 32 (28), 28 (100). Anal. Calcd for $C_{13}H_{12}ClO_3$ (235.50): C 66.24, H 4.69; found: C 65.91, H 4.40.

3-(3,4-Dimethoxy-phenyl)-4,6-Dimethyl-pyran-2-one (4d): The intermediate (**3c**) (0.100 g, 0.36 mmol), was then treated with TFA (0.55 mL, 7.20 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4d**) (0.058 g, 62%), was isolated as yellow solid; mp. 93 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.91 (d, 1H, *J* = 8.1 Hz, ArH), 6.80 (dd, 2H, *J* = 8.1 Hz, 9.6 Hz, ArH), 5.95 (s, 1H, CH), 3.90 (s, 1H, OCH_3), 3.87 (s, 3H, OCH_3), 2.24 (s, 3H, CH_3), 2.02 (s, 1H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.3 (CO), 159.1 (C), 151.4, 148.4 (C-CH_3), 148.7, 126.5, 122.8 (C-ph), 122.8 (C), 122.4, 113.0, 111.0 (CH-Ph), 107.4 (CH), 55.9 (2C, OCH_3), 20.3, 19.6 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3282 (w), 2960 (w), 1719 (s), 1517 (s), 1266 (m), 1025 (m), 798 (m). MS (EI, 70 eV): m/z (%) = 260.0 (M^+, 100), 232 (42), 188 (22), 114 (6), 28 (73). HRMS (Maldi+): calcd for $C_{15}H_{17}O_4$ ($[M+1]^+$): 261.1127; found: 261.1128.

3-Ethyl-4, 6-Dimethyl-pyran-2-one (4e): The intermediate **3e** (0.100 g, 0.58 mmol), was then treated with TFA (0.88 mL, 11.60 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4e**) (0.040 g, 45%), was isolated as colorleass needle; mp. 57 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.80 (s, 1H, CH), 2.17 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 1.52 (q, 2H, *J* = 6.0 Hz, CH_2), 0.95 (t, 3H, *J* = 7.5 Hz CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.13 (CO), 157.53, 149.94 (C-CH_3), 122.40 (C), 107.52 (CH), 28.60 (CH_2), 19.40, 19.02, 14.04 (CH_3). IR (KBr, cm^{-1}): $\widetilde{\nu}$ = 3089 (br), 2872 (s), 1708 (s), 1612 (s), 1206 (m), 745 (w). MS (EI, 70 eV): m/z (%) = 152.0 (M^+, 21), 124 (19), 109 (34), 81 (8). Anal. Calcd for $C_9H_{12}O_2$ (152.08): C 71.01, H 7.89; found: C 71.03, H 7.68.

4, 6-Dimethyl-3-propyl-pyran-2-one (4f): The intermediate (**3f**) (0.100 g, 0.54 mmol), was then treated with TFA (0.83 mL, 10.80 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4f**) (0.049 g, 55%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.79 (s, 1H, CH), 2.44 (t, 2H, *J* = 7.8 Hz, CH_2), 2.17 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.55-1.47 (m, 2H, CH_2), 0.95 (t, 3H, *J* = 7.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0 (CO), 157.5, 149.9 (C-CH_3), 122.4 (C), 107.5 (CH), 28.6, 21.4 (CH_2), 19.4, 19.0, 14.0 (CH_3). IR (KBr, cm^{-1}): $\widetilde{\nu}$ = 3416 (w), 2968 (s), 2874 (m), 1764 (s), 1724 (s), 1382 (m), 1115(m), 930 (w). MS (EI, 70 eV): *m/z* (%) = 166.0 (M^+, 24), 137 (44), 108 (100), 96 (12), 43 (85), 28 (85). Anal. Calcd for $C_9H_{12}O_2$ (166.08): C 72.28, H 8.43; found: C 72.37, H 8.65.

3-Butyl-4, 6-Dimethyl-pyran-2-one (4g): The intermediate (**3g**) (0.120 g, 0.60 mmol), was then treated with TFA (0.92 mL, 12.00 mmol), in CH_2Cl_2 (0.920 mL), at 20 °C for 72 hr, (**4g**) (0.065 g, 60%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.80 (s, 1H, CH), 2.45 (t, 1H, *J* = 7.2 Hz, CH_2), 2.17 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.48-1.32 (m, 4H, CH_2), 0.92 (t, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0 (CO), 157.4, 149.6 (C-CH_3), 122.6 (C), 107.1 (CH), 30.3, 26.4, 22.7 (CH_2), 19.2, 18.9, 13.9 (CH_3). IR (KBr, cm^{-1}): $\widetilde{\nu}$ = 3087 (w), 2959 (s), 2867 (m), 1734 (s), 1695 (s), 1360 (s), 1211 (m), 969 (w). MS (EI, 70 eV): *m/z* (%) = 180.2 (M^+, 2), 142 (10), 124 (62), 108 (65), 43 (78), 28 (100). HRMS (Maldi+): calcd for $C_{11}H_{17}O_2$ ($[M+1]^+$): 181.1223; found: 181.12245.

4, 6-Dimethyl-3-octyl-pyran-2-one (4h): The intermediate (**3h**) (0.700 g, 0.275 mmol), was then treated with TFA (0.42 mL, 5.50 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4h**) (0.038 g, 58%), was isolated as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.80 (s, 1H, CH), 2.44 (t, 2H, *J* = 7.2 Hz, CH_2), 2.17 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 1.48-1.21(m, 14H, CH_2), 0.87 (t, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0 (CO), 157.4, 149.6 (C-CH_3), 122.6 (C), 107.4 (CH), 31.8, 29.6, 29.4, 29.2, 28.1, 26.7, 22.6 (CH_2), 19.3, 18.9, 14.6 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3208 (w), 2923 (w), 1713 (s), 1614 (s), 1210 (m), 1111 (m). MS (EI, 70 eV): m/z (%) = 236.0 (M^+, 24), 221 (32), 108 (38), 43 (62), 28 (100). HRMS (Maldi+): calcd for $C_{15}H_{17}O_2$ ($[M+1]^+$): 237.18491; found: 237.18536.

4, 6-Dimethyl-3-phenoxy-pyran-2-one (4i): The intermediate (**3i**) (0.100 g, 0.42 mmol), was then treated with TFA (0.65 mL, 8.60 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4i**) (0.045 g, 50%), was isolated as yellow oil. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 7.43-7.25 (m, 5H, Ph), 6.14 (s, 1H, CH), 2.23 (s, 3H, CH_3), 2.00 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.7 (CO), 160.4, 152.1 (C-CH_3), 135.7 (C-Ph), 131.0, 128.8, 128.3 (CH-Ph), 123.4 (C), 107.8 (CH), 20.3, 19.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2924 (s), 1751 (s), 1362 (m), 1107 (m), 553 (w). MS (EI, 70 eV): m/z (%) = 215.0 (M^+, 8), 186 (100), 143 (68), 119 (34), 28 (56). Anal. Calcd for $C_{13}H_{12}O_3$ (216.23): C 72.21, H 5.59; found: C 72.46 H 5.70.

3-Benzyl-4, 6-Dimethyl-pyran-2-one (4j): The intermediate (**3j**) (0.100 g, 0.40 mmol), was then treated with TFA (0.62 mL, 8.00 mmol), in CH_2Cl_2 (0.50 mL), at 20 °C for 72 hr, (**4j**) (0.057 g, 62%), was isolated as colorless solid; mp = 60 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44-7.35 (m, 3H, Ar), 7.26-7.22 (m, 2H, Ar), 5.98 (s, 1H, CH), 2.67 (q, 2H, *J* = 7.2 Hz, CH_2), 2.30 (q, 2H, *J* = 7.5 Hz, CH_2), 1.26 (t, 3H, *J* = 7.8 Hz, CH_3), 1.08 (t, 3H, *J* = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.8 (CO), 163.4, 156.8 (C-CH_3), 134.1 (C), 129.8, 128.4 (2C), 127.8 (CH-Ph), 103.9 (CH), 26.8, 26.4 (CH_2), 13.5, 11.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2977 (s), 2934 (m), 2864 (s), 1726 (m), 1382 (m), 1123 (s), 700 (w). MS (EI, 70 eV): *m/z* (%) = 228.0 (M^+, 2), 185 (24), 143 (4), 32 (25), 28 (100). Anal. Calcd for $C_{15}H_{16}O_2$ (228.29): C 78.91, H 7.06; found: C 78.71, H 7.07.

3-(1-Acetylcyclopropyl)-3-hydroxy-2-phenylbutyric acid (**6**): To a CH_2Cl_2 solution (50 mL) of 1-(1-acetylcycopropyl)ethanone (0.261 g, 2.07 mmol) and 1,1-bis-trimethylsilanyloxy-2-phenylethene (0.870 g, 3.10 mmol) was added $TiCl_4$ (0.23 mL, 2.09 mmol) at –78 °C. The temperature of the reaction mixture was allowed to rise to 20 °C during 12 h. After stirring for 2 h at 20 °C, an aqueous solution of HCl (10%; 50 mL) was added. The aqueous layer was separated and extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. The solvent of the filtrate was removed *in vacuo* and the residue was purified by column chromatography (silica gel, *n*-hexane / EtOAc) to give **6** as a colourless solid (0.361 g, 67%); mp = 171-172 °C; R_f = 0.15 (*n*-hexane / EtOAc = 1:1); IR (KBr): $\tilde{\nu}$ = 3452 (w), 1701 (s), 1634 (s), 1395 (m), 1361 (m), 1322 (m), 1211 (s), 1090 (w), 700 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45-7.41 (m, 2 H, ArH), 7.33-7.30 (m, 3 H, ArH), 4.74 (s, 1 H, CH), 4.45 (brs, 1 H, OH), 1.89 (s, 3 H, CH_3), 1.40-1.33 (m, 1 H, CH_2), 1.18-0.96 (m, 3 H, CH_2), 1.12 (s, 3 H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.3, 177.6, 134.8 (C), 130.1 (2C), 128.3 (2C), 127.9 (CH), 73.9 (C), 55.6 (CH), 39.1 (C), 25.0, 23.2 (CH_3), 12.8, 11.8 (CH_2). MS (EI, 70 eV): *m/z* (%) = 262 (M^+, 1), 216 (1), 201 (1), 173 (1), 136 (1), 127 (3), 91 (4), 43 (5), 28 (100). HRMS (EI, 70 eV): calcd for $C_{15}H_{18}O_4$: *m/z* = 261.98478; found: 261.98478 ± 2 ppm. Anal. Calcd. for $C_{15}H_{18}O_4$: C 68.68, H 6.91; found: C 68.86, H 7.27

5-(2-Bromoethyl)-4,6-dimethyl-3-phenylpyran-2-one (**7**). To a CH_2Cl_2 solution (2.0 mL) of 3-(1-Acetylcyclopropyl)-3-hydroxy-2-phenylbutyric acid (0.131 g, 0.50 mmol) was added $TiBr_4$ (0.184 g, 0.50 mmol) at 20 °C and the stirring was continued for 3.0 h when all reactant was converted into products (monitored by TLC). CH_2Cl_2 (25 mL) was added to the reaction mixture and extracted from an aqueous solution of HCl (10%; 50 mL). The aqueous layer was separated and washed with CH_2Cl_2 (2 x 25 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. The solvent of the filtrate was removed *in vacuo* and the residue was purified by column chromatography (silica gel, *n*-hexane / EtOAc) to give **7** as a colourless oil (0.096 g, 63%); R_f = 0.49 (*n*-hexane / EtOAc = 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45-7.21 (m, 3 H, ArH), 7.23-7.20 (m, 2 H, ArH), 3.41 (t, 2 H, *J* = 8.4 Hz, CH_2Br), 2.98 (t, 2 H, *J* = 8.4 Hz, CH_2), 2.35 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0, 157.8, 151.2, 134.6 (C), 129.9 (2C), 128.5 (2C), 128.0 (CH), 124.9, 113.8 (C), 31.0, 29.7 (CH_2), 17.9, 17.8 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 1765 (m), 1701 (s), 1633 (m),

1548 (s), 1439 (s), 1218 (w), 702 (m). MS (EI, 70 eV): *m/z* (%) = 308 (M^+, [^{81}Br], 6), 306 (M^+, [^{79}Br], 6), 280 (19), 278 (16), 234 (10), 200 (6), 185 (36), 136 (26), 114 (20), 91 (88), 43 (77), 28 (100). Anal. Calcd. for $C_{15}H_{15}BrO_2$: C 58.63, H 4.80; found: C 58.78, H 4.93.

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Publication 5

Ehsan Ullah, Sven Rotzoll, Andreas Schmidt, Dirk Michalik, and Peter Langer*

"Synthesis of 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones by sequential 'condensation-iodolactonization' reactions of 1,1-bis(trimethylsilyloxy)ketene acetals with isoquinolines", *Tetrahedron Lett.* **2005**, *46*, 8997.

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Synthesis of 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones by sequential 'condensation–iodolactonization' reactions of 1,1-bis(trimethylsilyloxy)ketene acetals with isoquinolines

Ehsan Ullah,[a] Sven Rotzoll,[b] Andreas Schmidt,[b] Dirk Michalik[c] and Peter Langer[b,c,*]

[a]*Institut für Chemie und Biochemie, Universität Greifswald, Soldmannstr. 16, D-17487 Greifswald, Germany*
[b]*Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, D-18059 Rostock, Germany*
[c]*Leibniz-Institut für Organische Katalyse an der Universität Rostock e. V. (IfOK), Albert-Einstein-Str. 29a, D-18059 Rostock, Germany*

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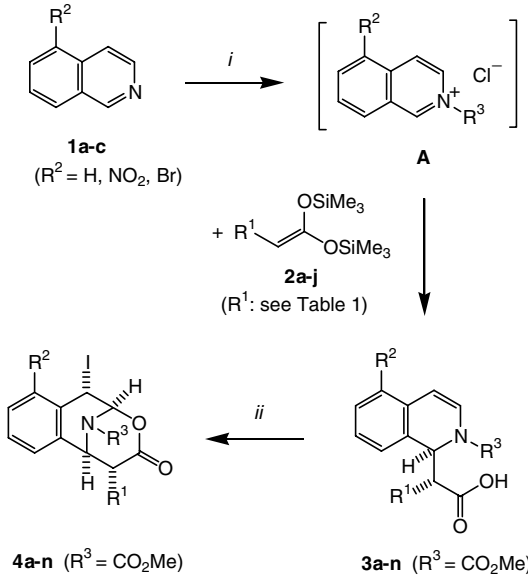
Abstract—Functionalized 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones were prepared by regio- and diastereoselective condensation of 1,1-bis(silyloxy)ketene acetals with isoquinolinium salts and subsequent regioselective and stereospecific iodolactonization.

Quinolinium- and isoquinolinium salts represent important synthetic building blocks.[1] They are readily generated by alkylation or acylation of quinolines and isoquinolines and have been used in a number of reactions, for example, with Grignard reagents, cyanide (Reissert reaction),[2] trimethylsilylacetonitrile, allylsilanes, silyl enol ethers[3,4] or diazoesters.[5] We have studied the synthesis of 7,8-benzo-3-hydroxy-9-azabicyclo-[3.3.1]non-3-enes based on cyclocondensations of 1,3-bis-silyl enol ethers with isoquinolinium salts.[6] Very recently, Rudler et al. have reported the two-step cyclocondensation of silyl ketene acetals with pyridinium salts.[7] The publication of this work prompted us to disclose our own findings in this field: herein, we report what are, to the best of our knowledge, the first cyclocondensations of 1,1-bis(trimethylsilyloxy)ketene acetals with isoquinolinium salts. These reactions allow a convenient synthesis of densely functionalized 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones. Notably, bicyclic N/O-acetals are present in a number of natural products, such as quinocarcin, tetrazomine and the bioxalomycins, showing good antitumour or antimicrobial activity.[8]

1,1-Bis(trimethylsilyloxy)ketene acetal **2a** ($R^1 = Me$) was prepared by deprotonation of trimethylsilyl propionic acid using lithio-1,1,1,3,3,3-hexamethyldisilazane (LiHMDS) and subsequent addition of trimethylchlorosilane.[9] The reaction of **2a** with isoquinoline (**1a**,



Scheme 1. Cyclization of silyl enol ethers **2a–j** with **1a–c**: (i), **1** (1.0 equiv), **2** (2.0 equiv), $ClCO_2Me$ (1.2 equiv), CH_2Cl_2, 0 °C, 2 h, 20 °C, 12 h; (ii), I_2 (2.0 equiv), CH_2Cl_2, 20 °C, 12 h.

Keywords: Cyclizations; Heterocycles; Iminium salts; Isoquinoline; Silyl ketene acetals.
* Corresponding author. Tel.: +49 381 4986410; fax: +49 381 4986412; e-mail: peter.langer@uni-rostock.de

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$R^2 = H$) in the presence of methyl chloroformate afforded the condensation product **3a** (Scheme 1).[†] Treatment of **3a** with iodine in the presence of sodium bicarbonate afforded 7,8-benzo-9-aza-4-oxabicyclo-[3.3.1]nonan-3-one **4a**.[‡] In contrast, the reaction of **3a** with TFA resulted in decomposition. During the optimization of the cyclocondensation, the activating agent, temperature and concentration played an important role.

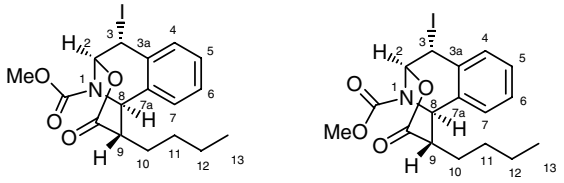
The preparative scope of our methodology was studied (Scheme 1 and Table 1). The reaction of **1a** ($R^2 = H$) with 1,1-bis(silylyloxy)ketene acetals **2a–e** (R^1 = Me, Et, *n*Pr, *n*Bu, *n*Oct), prepared from the corresponding alkanoic acids, afforded the condensation products **3a–e**, which were transformed into the alkyl-substituted 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones **4a–e**. The reaction of **1a** with **2f–h** (R^1 = Ph, 4-MeC_6H_4, 4-ClC_6H_4), prepared from the corresponding arylacetic acids, afforded the condensation products **3f–h**, which were transformed into **4f–h**. The transformation of **3i** into **4i** (R^1 = 4-(MeO)C_6H_4) was not successful. Starting with 5-nitroisoquinoline (**1b**, $R^2 = NO_2$) and 5-bromoisoquinoline (**1c**, R^2 = Br) the 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones **4j–n** were prepared.

Table 1. Products and yields

3, 4	R^1	R^2	% (3)[a]	% (4)[a]
a	Me	H	56	46
b	Et	H	62	61
c	*n*Pr	H	60	48
d	*n*Bu	H	65	70
e	*n*Oct	H	60	67
f	Ph	H	47	65
g	4-MeC_6H_4	H	54	64
h	4-ClC_6H_4	H	83	72
i	4-(MeO)C_6H_4	H	75	0
j	*n*Oct	NO_2	30	71
k	OPh	Br	70	50
l	*n*Bu	Br	36	73
m	*n*Oct	Br	54	67
n	Ph	Br	36	53

[a] Yields of isolated products.

The condensation of 1,1-bis(trimethylsilyloxy)ketene acetals **2** with isoquinolines **1** afforded the carboxylic acids **3** with very good regio- and diastereoselectivity (step 1). The formation of 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones **4a–n** can be explained by regioselective formation of an iminium salt from **3** and subsequent trans-stereospecific iodolactonization (step 2). The formation of regioisomeric products, by generation of benzylic rather than iminium cations, was not observed. The configuration of all products was established by spectroscopic methods. For example, the NMR signals of **4d** were assigned by DEPT and two-dimensional $^1H,^1H$ COSY, $^1H,^1H$ NOESY and $^1H,^{13}C$ correlation spectra (HSQC, HMBC). In the NOESY spectrum of **4d** cross peaks were found for protons H-2 with H-3, H-3 with H-4, and H-7 with H-8,9. Besides the relevant NOESY signals, EXSY signals have been found between the signals of protons H-$2_{(I)}$ and H-$2_{(II)}$ as well as H-$8_{(I)}$ and H-$8_{(II)}$, which confirm the presence of two exchanging isomers (rotamers I and II). In the HMBC spectrum cross peaks were found for C-3 with H-4, C-8 with H-7, and for COO with H-2,8,9,10, which confirm the given structures (Scheme 2). The two rotamers were observed owing to the rigidity of the urethane



Scheme 2. Relative configuration and rotamers of **4d**.

[†] *Typical procedure:* To a CH_2Cl_2 solution (20 ml) of isoquinoline (0.250 g, 1.9 mmol) were added the 1,1-bis(trimethylsilyloxy)hex-1-ene (1.0 g 3.8 mmol) and methyl chloroformate (0.218 g, 2.3 mmol) at 0 °C. The solution was stirred for 2 h at 0 °C and for 12 h at 20 °C. A saturated aqueous solution of ammonium chloride (20 ml) was added and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 × 100 ml). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane → *n*-heptane/EtOAc = 2:1) to give **3d** as a slightly brownish solid (0.384 g, 65%), mp 82 °C.

[‡] *Typical procedure*: To a CH_2Cl_2 solution (6 ml) of **3d** (0.1 g, 0.35 mmol) and I_2 (0.17 g 0.70 mmol) was added a saturated solution of $NaHCO_3$ (3.5 ml) and the solution was stirred for 12 h at 20 °C. The excess of iodine was removed by addition of a saturated aqueous solution of sodium sulfite (20 ml). The organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 × 30 ml). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane → *n*-heptane/EtOAc = 2:1) to give **4d** as a yellow oil (0.10 g, 70%). Due to the amide resonance and formation of *E*/*Z*-isomers, doubling of some signals was observed. ^1H NMR (500.13 MHz, $CDCl_3$) δ = 7.40–7.35 (m, $1H_{(I)}$, $1H_{(II)}$, H-$4_{(I)}$, H-$4_{(II)}$); 7.30–7.24 (m, $2H_{(I)}$, $2H_{(II)}$, H-$5,6_{(I)}$, H-$5,6_{(II)}$); 7.02–6.97 (m, $1H_{(I)}$, $1H_{(II)}$, H-$7_{(I)}$, H-$7_{(II)}$); 6.82 ('t', 1H, $^3J_{2,3}$ = 1.8 Hz, $^4J_{2,8}$ = 1.5 Hz, H-$2_{(II)}$); 6.68 ('t', 1H, $^3J_{2,3}$ = 1.8 Hz, $^4J_{2,8}$ = 1.5 Hz, H-$2_{(I)}$); 5.69 (d, 1H, $^3J_{2,3}$ = 1.8 Hz, H-$3_{(II)}$); 5.68 (d, 1H, $^3J_{2,3}$ = 1.8 Hz, H-$3_{(I)}$); 5.50 (br s, 1H, $^4J_{2,8}$ = 1.5 Hz, $^3J_{8,9}$ = 1.0 Hz, H-$8_{(I)}$); 5.36 (br s, 1H, $^4J_{2,8}$ = 1.5 Hz, $^3J_{8,9}$ = 1.0 Hz, H-$8_{(II)}$); 3.89 (s, 3H, $MeO_{(I)}$); 3.88 (s, 3H, $MeO_{(II)}$); 2.56–2.50 (m, $1H_{(I)}$, $1H_{(II)}$, H-$9_{(I)}$, H-$9_{(II)}$); 1.75–1.35 (m, $6H_{(I)}$, $6H_{(II)}$, H-$10,11,12_{(a,b),(I)}$, H-$10,11,12_{(a,b),(II)}$); 0.944 (t, 3H, J = 7.2 Hz, H-$13_{(II)}$); 0.936 (t, 3H, J = 7.2 Hz, H-$13_{(I)}$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 169.3 ($COO_{(I)}$); 169.0 ($COO_{(II)}$); 153.8 ($NCO_{(I)}$); 154.3 ($NCO_{(II)}$); 132.2, 132.2 (C-$3a_{(II)}$, C-$7a_{(II)}$); 131.9, 132.2 (C-$3a_{(I)}$, C-$7a_{(I)}$); 131.6 (C-$4_{(II)}$); 131.5 (C-$4_{(I)}$); 129.5, 128.9 (C-$5,6_{(I)}$); 129.4, 129.1 (C-$5,6_{(II)}$); 126.6 (C-$7_{(I)}$); 126.4 (C-$7_{(II)}$); 85.4 (C-$2_{(I)}$); 84.8 (C-$2_{(II)}$); 53.8 ($OMe_{(I)}$); 53.6 ($OMe_{(II)}$); 52.2 (C-$9_{(I)}$); 51.9 (C-$9_{(II)}$); 51.8 (C-$8_{(II)}$); 50.6 (C-$8_{(I)}$); 30.7 (C-$10_{(I)}$); 30.5 (C-$10_{(II)}$); 29.4 (C-$11_{(I)}$); 29.3 (C-$11_{(II)}$); 23.5 (C-$3_{(I)}$); 23.0 (C-$3_{(II)}$); 22.2 (C-$12_{(I)}$); 22.3 (C-$12_{(II)}$); 13.8 (C-$13_{(I)}$); 13.8 (C-$13_{(II)}$). IR (KBr): $\tilde{\nu}$ = 772(m), 1109 (w), 1231 (s), 1450 (s), 1780 (s), 3430 (br) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 429 (M^+, 2), 302 (7), 204 (19), 188 (100), 144 (25), 129 (36). All products were prepared as racemic material. All new compounds gave satisfactory spectroscopic and analytical and/or high resolution mass data.

moiety, which possesses a considerable double bond character and, thus, a high rotation barrier.

Our current studies are directed towards extension of the preparative scope, development of an enantioselective version and towards synthetic applications of our methodology.

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Publication 6

Ehsan Ullah, Andreas Schmidt, Sven Rotzoll, Christine Fischer, Dirk Michalik, Helmut Reinke, Peter Langer*, “Synthesis of Benzo-azoxabicyclo[3.3.1]nonanones by Cyclocondensation of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Isoquinoline and Quinoline”, manuscript in preparation.

Synthesis of Benzo-azoxabicyclo[3.3.1]nonanones by Cyclocondensation of 1,1-Bis(trimethylsilyloxy)ketene Acetals with Isoquinoline and Quinoline

Ehsan Ullah,[a, b, c] Andreas Schmidt,[a] Sven Rotzoll,[a, c] Christine Fischer,[c] Dirk Michalik,[c] Helmut Reinke,[a] Peter Langer* [a, c]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, D-18059 Rostock, Germany

[b] Institut für Biochemie, Universität Greifswald, Soldmannstr. 16, D-17487 Greifswald, Germany

[c] Leibniz-Institut für Katalyse e. V. an der Universität Rostock, Albert-Einstein-Str. 29a, D-18059 Rostock, Germany

Abstract: Functionalized benzo-azoxabicyclo[3.3.1]nonanones were prepared by regio- and diastereoselective condensation of 1,1-bis(silyloxy)ketene acetals with isoquinolinium and quinolinium salts and subsequent regioselective and stereospecific iodolactonization.

Keywords: cyclizations, heterocycles, iminium salts, isoquinoline, silyl ketene acetals

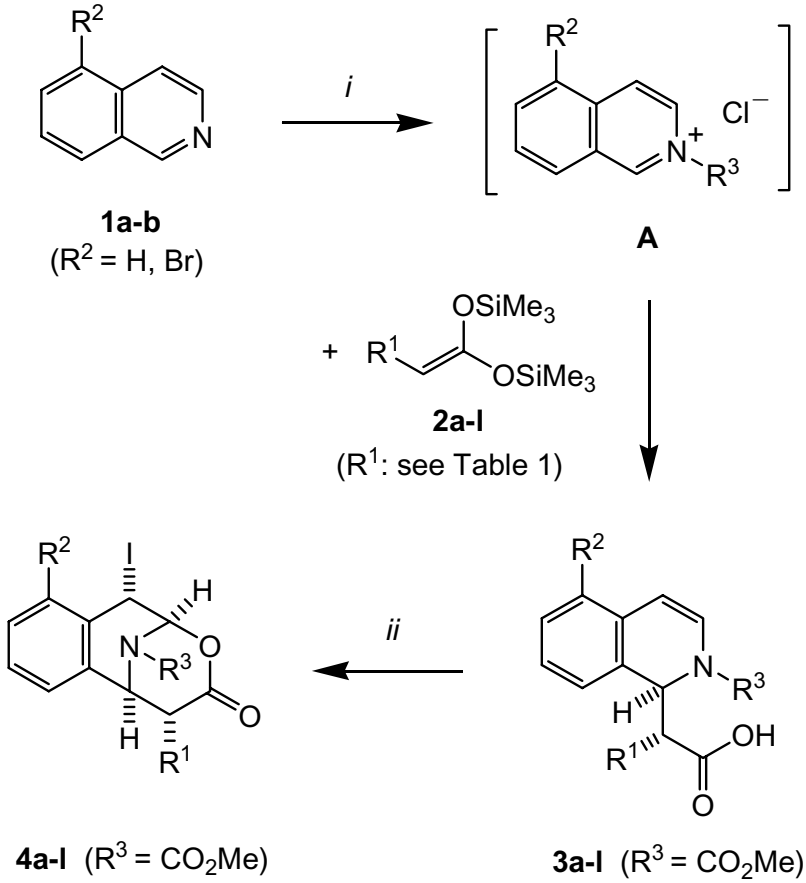
Introduction

Heterocyclic iminium salts represent important synthetic building blocks[1] which have been used in a number of reactions (e. g. with Grignard reagents, cyanide,[2] trimethylsilylacetonitrile, allylsilanes, silyl enol ethers[3,4] or diazoesters[5]). We have studied the synthesis of 7,8-benzo-3-hydroxy-9-azabicyclo[3.3.1]non-3-enes based on cyclocondensations of 1,3-bis-silyl enol ethers with isoquinolinium salts.[6] Very recently, Rudler *et al.* have reported the two-step cyclocondensation of silyl ketene acetals with pyridinium salts.[7] We have reported the synthesis of 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones by cyclocondensation of 1,1-bis(trimethylsilyloxy)ketene acetals with isoquinolinium salts. Herein, we report full details of these studies. With regard to our preliminary communication, we report for the first time cyclocondensation reactions of 1,1-bis(trimethylsilyloxy)ketene acetals with quinolinium salts.

Results and Discussion

Isoquinoline. 1,1-Bis(trimethylsilyloxy)ketene acetals 2 are available by generation of the dianion of the appropriate carboxylic acid (by means of lithio-1,1,1,3,3,3-hexamethyldisilazane, LiHMDS) and subsequent addition of trimethylchlorosilane.9 The reaction of 2a with isoquinoline (1a, R2 = H) in the presence of methyl chloroformate afforded the condensation product 3a (Scheme 1). Treatment of 3a with iodine in the presence of sodium bicarbonate afforded 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-one 4a. The preparative scope was studied (Scheme 1, Table 1). The reaction of 1a (R2 = H) with 1,3-bis-silyl enol ethers 2a-d (R1 = Me, Et, nBu, nOct), prepared from the corresponding alkanoic acids, afforded the condensation products **3a-d** which were transformed into the alkyl-substituted 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones **4a-d**. The reaction of **1a**

with **2e-g** (R^1 = Ph, 4-MeC_6H_4, 4-ClC_6H_4), prepared from the corresponding arylacetic acids, afforded the condensation products 3e-g which were transformed into 4e-g. The transformation of **3h** into **4h** (R^1 = 4-$(MeO)C_6H_4$) was not successful. Starting with 5-bromoisoquinoline (1b, R^2 = Br) the 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones 4i-l were prepared.



Scheme 1. Cyclization of bis ketene acetal **2a-l** with **1a-b**: *i*, **1** (1.0 equiv.), **2** (2.0 equiv.), $ClCO_2Me$ (1.2 equiv.), CH_2Cl_2, 0 °C, 2 h, 20 °C, 12 h; *ii*, I_2 (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h

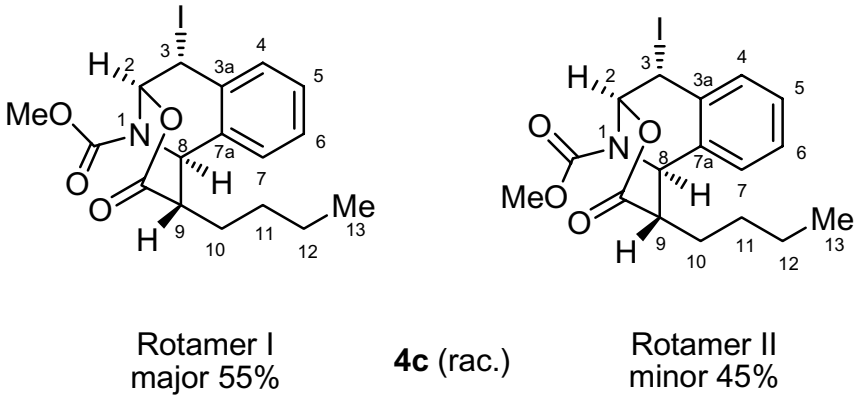
Table 1. Products and yields

3,4	R^1	R^2	% (**3**) [a]	% (**4**) [a]
a	Me	H	56	46
b	Et	H	62	61
c	*n*Bu	H	65	70
d	*n*Oct	H	60	67
e	Ph	H	47	65

f	4-MeC_6H_4	H	54	64
g	4-ClC_6H_4	H	83	72
h	4-$(MeO)C_6H_4$	H	75	0
i	OPh	Br	70	50
j	*n*Bu	Br	36	73
k	*n*Oct	Br	54	67
l	Ph	Br	36	53

[a] Yields of isolated products

The condensation of 1,1-bis(trimethylsilyloxy)ketene acetals 2 with isoquinolines 1 afforded the carboxylic acids 3 with very good regio- and diastereoselectivity (step 1). The formation of 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones 4a-i can be explained by regioselective formation of an iminium salt from 3 and subsequent trans-stereospecific iodolactonization (step 2). The formation of regioisomeric products, by generation of benzylic rather than iminium cations, was not observed. The configuration of all products was established by spectroscopic methods. For example, the NMR signals of 4c were assigned by DEPT and two-dimensional ^1H, ^1H COSY, ^1H, ^1H NOESY and ^1H, ^{13}C correlation spectra (HSQC, HMBC) recorded on a Bruker AVANCE 500. In the NOESY spectrum of 4c cross peaks were found for protons H-2 with H-3, H-3 with H-4, and H-7 with H-8,9. Besides the relevant NOESY signals, EXSY signals have been found between the signals of protons H-$2_{(I)}$ and H-$2_{(II)}$ as well as H-$8_{(I)}$ and H-$8_{(II)}$ which confirm the presence of two exchanging isomers (rotamers I and II). In the HMBC spectrum cross peaks were found for C-3 with H-4, C-8 with H-7, and for COO with H-2,8,9,10, which confirm the given structures (Scheme 2). The two isomers were observed owing to the double bond character of the CN-bond in the urethane moiety leading to a high rotation barrier.



Scheme 2. Relative configuration and rotamers of **4c**

Quinoline. The methyl chloroformate mediated reaction of quinoline (5) with 2a, prepared from butanoic acid, afforded the condensation product 7a (Scheme 2). The product was formed by regioselective attack of 2a onto carbon atom C-2 of the quinolinium salt. The product was isolated as an unseparable mixture of diastereomers (dr = 1:1). Treatment of 7a with iodine in the presence of sodium bicarbonate afforded 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-one 8a. The preparative scope was studied (Scheme 1, Table 1). The reaction of 1a (R^2 = H) with 1,3-bis(trimethylsilyloxy)ketene acetals 2a-b (R^1 = *n*Pr, *n*Oct), prepared from the corresponding alkanoic acids, afforded the condensation products 7a-b which were transformed into the alkyl-substituted 7,8-benzo-9-aza-4-oxabicyclo[3.3.1]nonan-3-ones 8a-b. The reaction of 1a with 2c (R^1 = Ph), prepared from the corresponding arylacetic acid, afforded the condensation product 7c, which were transformed into 8c. The transformation of 3i into 4i (R^1 = 4-(MeO)C_6H_4) was not successful.

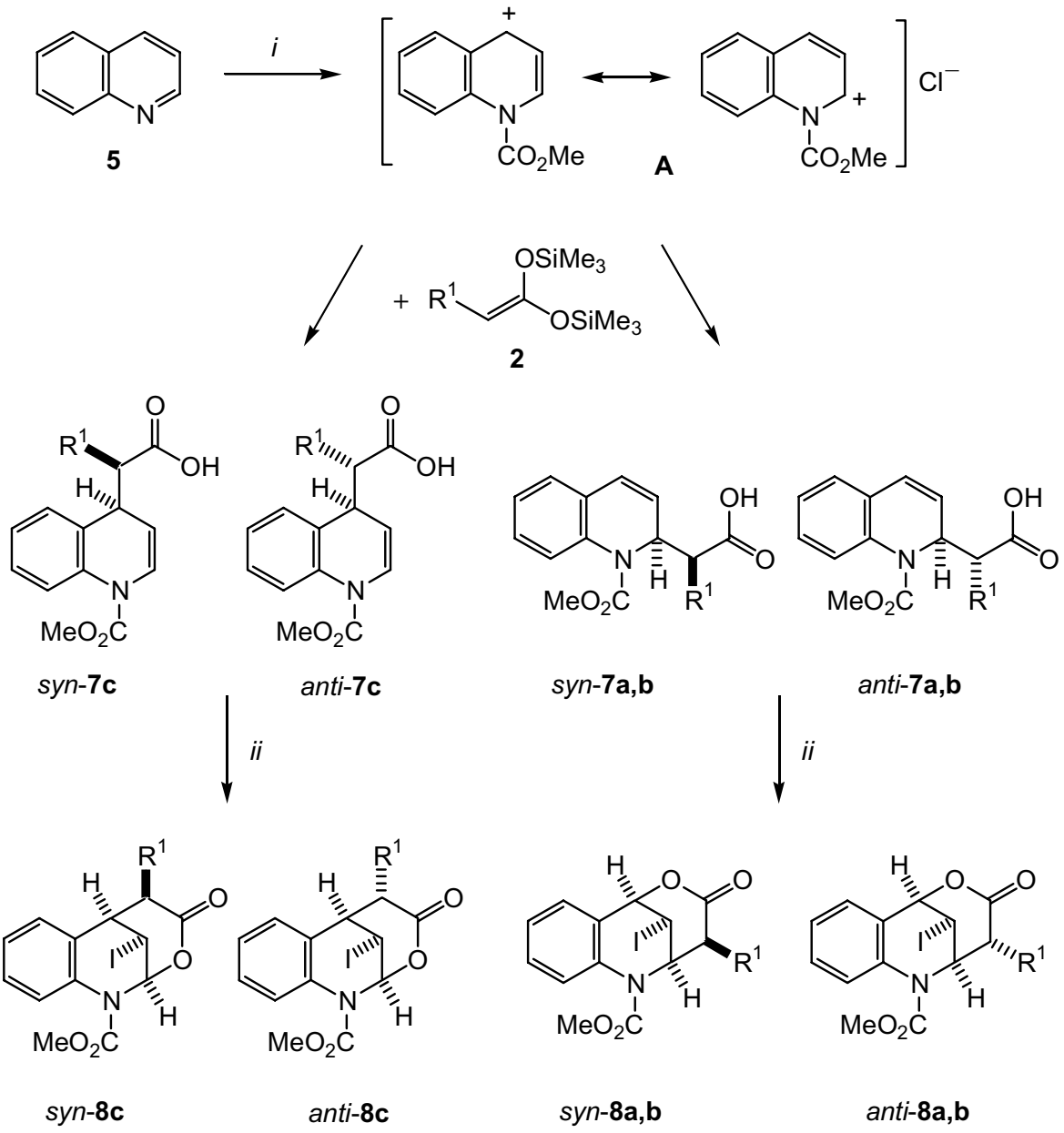


Table 2. Products and yields

entry	R^1	% (**7**) [a]	*Syn/anti*	% (**8**) [a]	*syn/anti*
a	*n*Pr	38	1:1	86	1:1
b	*n*Oct	46	3:2	52	> 98:2
		30	< 2:98	0	-
c	Ph	56	1.2:1	50	> 98:2

[a] Yields of isolated products

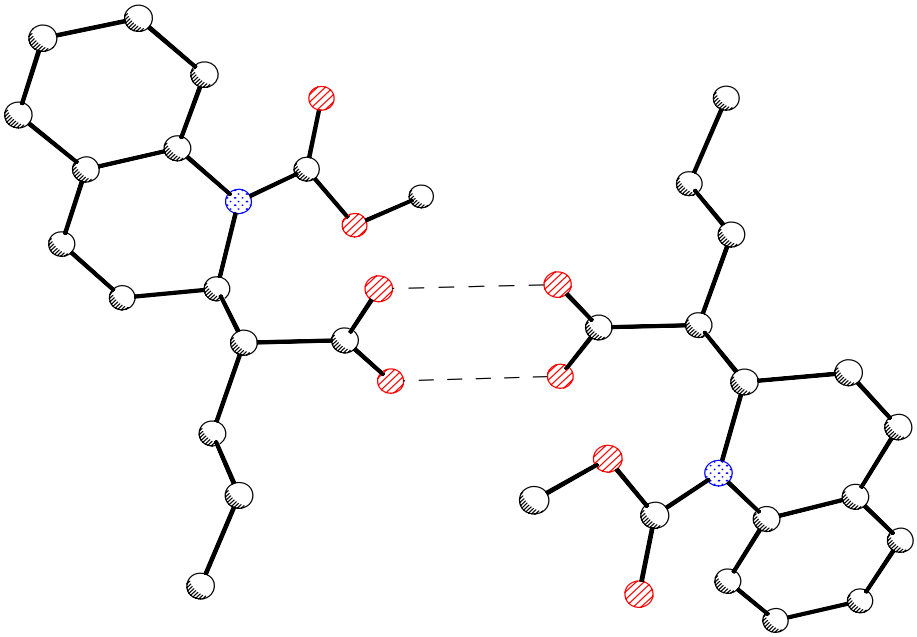


Figure 1. ORTEP plot of 7a

Experimental section

General. All solvents were dried by standard methods and all reactions were carried out under an inert atmoshphere. For ^{1}H and $^{13}CNMR$ spectra ($^{1}HNMR$: 300, 600 MHz; $^{13}CNMR$: 75, 150 MHz), the deutrated solvents indicated were used. Mass spectrometry (MS) data were obtained by using the electron ionization (70eV), chemical ionization (CI, H_2O), or electrospray (ESI) techaniques. For preparative scale chromatography, silica gel (60-200 mesh) was used.

Typical procedure for the preparation of 1H-isoquinoline-2-carboxylic acid methyl ester (3): To a CH_2Cl_2 solution (20 mL) of isoquinoline (0.250 g, 1.90 mmol) was added the 1,1-bis(trimethylsilyloxy)hex-1-ene (1.00 g 3.80 mmol) and methyl chloroformate (0.218 g, 2.30 mmol) at 0 °C. The solution was stirred for 2 h at 0 °C and for 12 h at 20 °C. A saturated aqueous solution of ammonium chloride (20 mL) was added and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1) to give 3c as a slightly brownish solid (0.384 g, 65%), m.p. 82 °C.

Due to the restricted rotation in the urethane moiety, 3c appeared as a racemic mixture of two rotamers in a ratio of 55% (I) to 45% (II).

1-(1-Carboxy-ethyl)-1*H*-isoquinoline-2-carboxylic acid (3a): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2a**) (0.632 g, 2.90 mmol) and methyl chloroformate (0.363 g, 3.87 mmol), (**3a**) (0.283 g, 56%), was isolated as colorless solid; mp. 126 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.23-7.20 (m, 1H, ArH), 7.16-7.13 (br m, 4H, ArH), 7.09-7.06 (m, 3H, ArH), 6.96 (br d, 1H, *J* = 7.6 Hz, H-2), 6.80 (br d, 1H, *J* = 7.6 Hz, H-2), 5.98 (d, 1H, *J* = 7.6 Hz, H-3), 5.89 (d, 1H, *J* = 7.6 Hz, H-3), 5.71 (br d, 1H, *J* = 8.2 Hz, H-8), 5.58 (d, 1H, *J* = 7.6 Hz, H-8), 3.80 (s, 6H, OMe), 2.89-2.78 (m, 2H, H-9), 1.19-1.14 (m, 6H, Hz, H-10). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 179.8, 179.6 (COOH), 154.5, 154.4 (NCO), 130.8, 130.6, 128.6 (C-Ar), 128.5, 127.5, 127.4, 127.1, 126.8, 125.6, 125.3, 125.2, 124.9 (CH-Ar/C-2), 110.7, 110.5 (C-3), 57.4, 57.0 (C-8), 53.9, 53.5 (OMe), 45.6, 45.2 (C-9), 14.0, 13.9 (C-10). IR (KBr, cm^{-1}): ν = 3414 (s), 2959 (s), 1712 (s), 1686 (m), 1603 (w), 1453 (s), 1340 (m), 775 (m). MS (EI; 70 eV) m/z (%) = 262.4 ($[M+1]^+$, 12), 203 (40), 188 (58), 129 (100), 102 (61), 75 (13). HRMS (EI): calcd for $C_{14}H_{16}NO_4$ ($[M+1]^+$): 262.1074; found: 262.1094.

1-(1-Carboxy-propyl)-1*H*-isoquinoline-2-carboxylic acid (3b): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2b**) (0.903 g, 3.87 mmol) and methyl chloroformate (0.363 g, 3.87 mmol), (**3b**) (0.330 g, 62%), was isolated as light brown solid; mp. 102-103 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18-7.06 (m, 8H, ArH), 6.94 (br d, 1H, *J* =7.6 Hz, H-2), 6.78 (d, 1H, *J* = 7.6 Hz, H-2), 6.01 (d, 1H, *J* = 7.6 Hz, H-3), 5.91 (d, 1H, *J* = 7.9 Hz, H-3), 5.67 (d, 1H, *J* = 8.5 Hz, H-8), 5.54 (d, 1H, *J* = 8.8 Hz, H-8), 3.80 (s, 6H, OMe), 2.75-2.65 (m, 2H, H-9), 1.86-1.65 (m, 2Ha, H-10), 1.59-1.49 (m, 2Hb, H-10), 0.88 (t, 6H, *J* = 7.3 Hz, H-11). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.8, 178.7 (COOH), 154.2, 153.9 (NCO), 130.6, 130.4, 130.4, 130.2 (C-Ar), 128.2, 128.1, 127.1, 126.9, 126.7, 126.5, 126.4, 125.0, 124.8 (2C) (CH-Ar/C-2), 110.8, 110.4 (C-3), 56.9, 56.4 (C-8), 53.5, 53.2 (OMe), 52.8, 52.6 (C-9), 22.7, 21.6 (C-10), 11.8 (2C, C-11). IR (KBr, cm^{-1}): ν = 3443 (m), 3282 (m), 2964 (m), 1728 (s), 1684 (s), 1636 (m), 1458 (s), 1363 (s), 779 (s). MS (EI; 70 eV) m/z (%) = 275.0 (M^+, 2), 188 (100), 129 (98), 115 (60), 102 (85), 59 (60). HRMS (EI): calcd for $C_{15}H_{17}NO_4$ ($[M]^+$): 275.1152; found: 275.1153.

1-(1-Carboxy-pentyl)-1*H*-isoquinoline-2-carboxylic acid (3c): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2c**) (1.00 g, 3.87 mmol) and methyl chloroformate (0. 218 g, 2.32 mmol), (**3c**) (0.380 g, 65%) was isolated as light brown solid; mp. 82-83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.40 (br s, 1H, OH $_{(II)}$), 8.50 (br s, 1H, OH $_{(I)}$), 7.24-7.04 (m, $4H_{(I)}$, $4H_{(II)}$, H-4,5,6,$7_{(I)}$, H-4,5,6,$7_{(II)}$), 6.94 (br d, 1H, $^{3}J_{2,3}$ = 7.5 Hz, $^{4}J_{2,8}$ = 1.0 Hz, H-$2_{(II)}$), 6.78 (br d, 1H, $^{3}J_{2,3}$ = 7.5 Hz, $^{4}J_{2,8}$ = 1.0 Hz, H-$2_{(I)}$), 6.01 (d, 1H, $^{3}J_{2,3}$ = 7.5 Hz, H-$3_{(II)}$), 5.90 (d, 1H, $^{3}J_{2,3}$ = 9.0 Hz, H-$3_{(I)}$), 5.67 (br d, 1H, $^{3}J_{8,9}$ = 8.5 Hz, $^{4}J_{2,8}$ = 1.0 Hz, H-$8_{(I)}$), 5.52 (br d, 1H, $^{3}J_{8,9}$ = 9.0 Hz, $^{4}J_{2,8}$ = 1.0 Hz, H-$8_{(II)}$), 3.81 (s, 3H, $OMe_{(II)}$), 3.80 (s, 3H, $OMe_{(I)}$), 2.79-2.73 (m, $1H_{(I)}$, $1H_{(II)}$, H-$9_{(I)}$, H-$9_{(II)}$), 1.78-1.65 (m, 1H, H-$10_{(II)}$), 1.49-1.39 (m, 1H, H-$10_{(I)}$), 1.32-1.13 (m, $2H_{(I)}$, $2H_{(II)}$, H-$11,12_{(I)}$, H-$11,12_{(II)}$), 0.84 (t, $3H_{(I)}$, $3H_{(II)}$, *J* = 7.2 Hz, H-$13_{(I)}$, H-$13_{(II)}$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ: 178.8 ($COOH_{(II)}$), 178.7 ($COOH_{(I)}$), 154.2 ($NCO_{(II)}$), 153.9 ($NCO_{(I)}$), 130.6 (C-$7a_{(II)}$), 130.4 (C-$3a_{(II)}$), 130.4 (C-$7a_{(I)}$), 130.2 (C-$3a_{(I)}$), 128.2, 126.9, 126.3, 125.0 (C-4,5,6,$7_{(II)}$), 128.1, 127.1, 126.7, 124.8 (C-4,5,6,$7_{(I)}$), 125.0 (C-$2_{(II)}$), 124.4 (C-$2_{(I)}$), 110.8 (C-$3_{(II)}$), 110.4 (C-$3_{(I)}$), 56.4 (C-$8_{(I)}$), 57.0 (C-$8_{(II)}$), 53.5 ($OMe_{(I)}$), 53.2 ($OMe_{(II)}$), 50.4 (C-$9_{(I)}$), 50.5 (C-$9_{(II)}$), 29.5 (C-$11_{(I)}$), 29.4 (C-$11_{(II)}$), 28.1 (C-$10_{(I)}$), 28.0 (C-$10_{(II)}$), 22.4 (C-$12_{(I)}$), 22.4 (C-$12_{(II)}$), 13.8 (C-$13_{(I)}$), 13.8 (C-$13_{(II)}$). IR (KBr, cm^{-1}): ν = 3437 (m), 2956 (m), 1710 (s), 1693 (s), 1632 (m), 1456 (s), 1356 (s), 765 (m). MS (CI; 70 eV) m/z (%) = 304.0 ($[M+1]^+$, 47), 204 (5), 188 (100), 130 (20), 79 (5). HRMS (EI): calcd for $C_{17}H_{21}NO_4$ ($[M]^+$): 303.1465 found: 303.1472.

1-(1-Carboxy-nonyl)-1*H*-isoquinoline-2-carboxylic acid (3d): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2d**) (0.914 g, 2.90 mmol) and methyl chloroformate (0.363 g, 3.87 mmol), (**3d**) (0.420 g, 60%), was isolated as colorless solid; mp. 120 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.23 -7.17 (m, 2H, ArH), 7.13-7.06 (br m, 6H, ArH), 6.93 (d, 1H, *J* = 7.6 Hz, H-2), 6.79 (br d, 1H, *J* = 7.6 Hz, H-2), 6.03 (br d, 1H, *J* = 7.9 Hz, H-3), 5.91 (d, 1H, *J* = 7.6 Hz, H-3), 5.66 (d, 1H, *J* = 8.8 Hz, H-8), 5.52 (d, 1H, *J* = 8.5 Hz, H-8), 3.81 (s, 6H, OMe), 2.81-2.72 (m, 2H, H-9), 1.81-1.67 (m, 2Ha, H-10), 1.50-1.41 (br m, 2Hb, H-10), 1.22 (br s, 24H, H-12, H-13, H-14, H-15, H-16), 0.87 (t, 6H, *J* = 7.0 Hz, H-17). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.2, 178.0 (COOH), 154.0 (br, NCO), 130.5, 130.1, 130.4 (C-Ar), 128.6 (2C), 128.5 (2C), 127.5, 127.0 (CH-Ar), 126.7 (C-Ar), 126.3, 125.4 (2C), 125.0, 124.8, 124.4 (CH-Ar/C-2), 110.8, 110.4 (C-3), 57.0, 56.8 (C-8), 53.5, 53.2 (OMe), 50.3 (2C, C-9), 32.2, 31.8 (C-11), 29.8 (2C, C-10), 29.6 (2C, C-12), 29.5 (2C, C-13), 28.8 (2C, C-14), 27.9 (2C, C-15), 23.0 (2C, C-16), 14.9 (2C,

C-17). IR (KBr, cm^{-1}): ν = 3444 (br), 3288 (m), 2919 (m), 1727 (s), 1683 (s), 1635 (m), 1460 (s), 1360 (s), 778 (s). MS (EI, 70 eV) m/z (%) = 358.8 (M^+, 2), 301 (4), 188 (100), 144 (90), 129 (84), 103 (44), 43 (49). HRMS (EI): calcd for $C_{21}H_{29}NO_4$ ($[M]^+$): 359.2091; found: 359.2074.

1-(1-Carboxy-phenyl-methyl)-1*H*-isoquinoline-2-carboxylic acid (3e): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2e**) (1.08 g, 3.87 mmol) and methyl chloroformate (0. 218 g, 2.32 mmol), (**3e)** (0.290 g, 47%), was isolated as colorless solid; mp. 178 °C. (Major rotamer 57%, minor 43%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22-7.00 (m, 7H, H-4, 5,o, m, p-Ph), 6.97 (d, 1H, $^3J_{2,3}$ = 7.5 H-$2_{(II)}$), 6.81-6.77 (m, $2H_{(I)}$, $1H_{(II)}$, H-$2,6_{(I)}$, H-$2,6_{(II)}$), 6.39 (d, 1H, $^3J_{6,7}$ = 8.0 Hz, H-$7_{(I)}$), 6.34 (d, 1H, $^3J_{6,7}$ = 8.0 Hz, H-$7_{(II)}$), 6.03 (d, 1H, $^3J_{2,3}$ = 7.5 Hz, H-$3_{(II)}$), 6.01 (d, 1H, $^3J_{8,9}$ = 9.5, H-$8_{(I)}$), 5.93 (d, 1H, $^3J_{2,3}$ = 7.5, H-$3_{(I)}$), 5.83 (d, 1H, $^3J_{8,9}$ = 9.5, H-$8_{(II)}$), 3.99 (d, 1H, $^3J_{8,9}$ = 9.5 Hz, H-$9_{(II)}$), 3.97 (d, 1H, $^3J_{8,9}$ = 9.5 Hz, H-$9_{(I)}$), 3.82 (s, 3H, $OMe_{(II)}$), 3.75 (s, 3H, $OMe_{(I)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.6 ($COOH_{(II)}$), 176.0 ($COOH_{(I)}$), 154.0 ($NCO_{(II)}$). 153.6 ($NCO_{(I)}$), 134.1 (i-$Ph_{(I)}$), 134.1 (i-$Ph_{(II)}$), 130.4 (C-$3a_{(II)}$), 130.1 (C-$3a_{(I)}$), 129.7 (o-$Ph_{(I)}$), 129.5 (o-$Ph_{(II)}$), 128.9 (C-$7a_{(I)}$), 128.7 (C-$7a_{(II)}$), 128.1 (m-$Ph_{(I)}$), 128.1 (m-$Ph_{(II)}$), 128.0 (C-$5_{(II)}$), 127.9 (C-$5_{(I)}$), 127.7 (p-$Ph_{(I)}$), 127.7 (p-$Ph_{(II)}$), 127.4 (C-$7_{(I)}$), 127.2 (C-$7_{(II)}$), 126.3 (C-$6_{(I)}$), 126.0 (C-$6_{(II)}$), 125.1(C-$2_{(II)}$), 124.6 (C-$4_{(II)}$), 124.5 (C-$4_{(I)}$), 124.4 (C-$2_{(I)}$), 110.5 (C-$3_{(II)}$), 110.3 (C-$3_{(I)}$), 58.6 (C-$8_{(II)}$), 57.9 (C-$8_{(I)}$), 54.0 (C-$9_{(I)}$), 54.0 (C-$9_{(II)}$), 53.5 ($OMe_{(I)}$), 53.3 ($OMe_{(II)}$). IR (KBr, cm^{-1}): ν = 3429 (br), 2956 (m), 1716 (s), 1698 (s), 1630 (m), 1444 (s), 1353 (s), 766 (s). MS (CI; neg.) m/z (%) = 322.0 ($[M-H]^-$, 2), 188 (8), 174 (10), 130 (100), 91 (32), 85 (63), 79 (69). Anal. Calcd for $C_{19}H_{17}N_1O_4$ (323.00): C 70.58, H 5.26, N 4.33; found: C 70.85, H 5.01, N 3.41.

1-(1-Carboxy-*p*-tolyl-methyl)-1*H*-isoquinoline-2-carboxylic acid (3f): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2f**) (0.850 g, 2.90 mmol) and methyl chloroformate (0.365 g, 3.87 mmol), (**3f**) (0.350 g, 54%), was isolated as colourless solid; mp. 208 °C. ^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.60 (s, 2H, OH), 7.30-7.20 (m, 11H, Ar/Ph), 7.15-7.08 (m, 5H, Ar/Ph), 6.77 (d, 1H, *J* = 7.6 Hz, H-2), 6.66 (d, 1H, *J* = 7.6 Hz, H-2), 6.23 (d, *J* = 7.6 Hz, 1H, H-3), 6.18 (d, *J* = 7.6 Hz, 1H, H-3), 5.88 (d, 1H, *J* = 11.3 Hz, H-8), 5.72 (d, 1H, *J* = 10.7 Hz, H-8), 3.73-3.65 (m, 2H, H-9), 3.36 (s, 3H, OMe), 3.33 (s, 3H, OMe), 2.28 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 172.2, 172.1 (COOH), 152.7, 152.4 (NCO), 136.8, 132.0 (C-Ar/Ph), 130.5, 130.1 (C-Ar/Ph), 129.6,

129.5, 128.9, 128.7 (CH-Ar/Ph), 128.9, 128.7 (C-Ar/Ph), 128.5, 127.2 (C-5), 127.1 (C-Ar/Ph), 127.0, 125.5, 125.2, 124.8 CH-Ar/Ph), 110.3, 110.0 (C-3), 57.0, 55.7 (C-8), 54.2, 54.0 (C-9), 52.9, 52.2 (OMe), 20.5 (2C, Me). IR (KBr, cm^{-1}): ν = 3410 (br), 2940 (s), 1709 (m), 1692 (m), 1349 (m), 1245 (w), 778 (w). MS (CI; pos.) m/z (%) = 338.2 ($[M+1]^+$, 14), 226 (2), 188 (100), 130 (4), 91 (32), 69 (2). HRMS (CI, neg.): calcd for $C_{20}H_{18}NO_4$ ($[M]^-$): 336.1230; found: 336.1224.

1-[Carboxy-(4-chloro-phenyl)-methyl]-1*H*-isoquinoline-2-carboxylic acid (3g): Starting with isoquinoline (**1a**) (0.250 g, 1.93 mmol), (**2g**) (0.916 g, 2.90 mmol) and methyl chloroformate (3.86 g, 3.87 mmol), (**3g**) (0.583 g, 83%) was isolated as colourless solid; mp. 181 °C. 1H NMR (500.13 MHz, DMSO-d_6): δ = 12.60 (s, 2H, OH), 7.43-7.34 (m, 8H, ArH/Ph), 7.29-7.23 (m, 8H, ArH/Ph), 6.78 (d, 1H, *J* = 8.5 Hz, H-2), 6.68 (d, 1H, *J* = 7.0 Hz, H-2), 6.25 (d, 1H, *J* = 8.2 Hz, H-3), 6.18 (d, 1H, *J* = 7.9 Hz, H-3), 5.89 (d, 1H, *J* = 10.0 Hz, H-8), 5.74 (d, 1H, *J* = 10.3, H-8), 3.81-3.72 (m, 2H, H-9), 3.40 (s, 3H, OMe), 3.30 (s, 3H, OMe). ^{13}C NMR (62 MHz, DMSO-d_6): δ = 172.5, 172.0 (COOH), 152.8, 152.7 (NCO), 134.3, 134.2, 134.0, 132.7 (C-Ar/Ph), 132.5, 131.5, 130.7 (CH-Ar/Ph), 130.6, 130.4, 130.1 (C-Ar/Ph), 128.5, 128.4, 128.3, 128.2 (2C), 127.2, 127.0, 126.9, 125.1, 125.1, 124.6 (2C) (CH-Ar/Ph, C-2), 110.6, 110.5 (C-3), 57.3, 56.1 (C-8), 54.1, 54.0 (C-9), 53.3, 52.6 (OMe). IR (KBr, cm^{-1}): ν = 3430 (br), 3028 (m), 1732 (s), 1706 (s), 1491 (s), 1334 (s), 1253 (s), 705 (s). MS (CI; pos.) m/z (%) = 358.0 ($[M+1]^+$, 2), 314 (45), 188 (75), 130 (55), 81 (39), 69 (100). ESI could not confirm mass.

1-[Carboxy-(4-methoxy-phenyl)-methyl]-1*H*-isoquinoline-2-carboxylic acid (3h): Starting with isoquinoline (**1a**) (0.258 g, 2.00 mmol), (**2h**) (0.846 g, 3.00 mmol) and methyl chloroformate (0. 376 g, 4.00 mmol), (**3h**) (0.263 g, 75%) was isolated as colorless solid; mp. 213 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 12.47 (s, 2H, OH), 7.29-7.24 (m, 11H, ArH/Ph), 7.23-6.90 (m, 5H, ArH/Ph), 690-6.79 (m, 5H, ArH/Ph), 6.77 (d, 1H, *J* = 7.3 H-2), 6.67 (d, 1H, *J* = 8.5 H-2), 6.24 (d, 1H, *J* = 7.0 Hz, H-3), 6.19 (d, 1H, *J* = 7.6 Hz, H-3), 5.88 (d, 1H, *J* = 9.7 Hz, H-8), 5.73 (d, 1H, *J* = 10.9 Hz, H-8), 3.73 (br s, 2H, H-9), 3.72 (s, 6H, OMe), 3.30 (s, 6H, *p*-OMe). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 173.0, 172.5 (COOH), 158.8, 158.7 (C-Ph), 152.3, 152.0 (NCO), 130.9, 130.6 (C-Ar/Ph), 130.9, 130.6, 130.3 (C-Ar/Ph.), 130.2 (CH-Ar/Ph), 130.0 (C-Ar/Ph), 129.8 (CH-Ar/Ph), 128.2 (C-Ar/Ph), 128.1, 126.9, 126.8, 126.7, 126.6 (CH-Ar/Ph), 125.0 (C-Ar/Ph), 124.9, 124.6 (C-2), 113.3, 110.3 (C-3), 57.1, 55.8 (C-8), 55.1, 55.0 (C-9), 53.9, 53.7, 53.0, 52.5

(OMe). IR (KBr, cm^{-1}): ν = 3443 (br), 3214 (s), 1725 (s), 1679 (s), 1458 (s), 1364 (s), 1248 (s), 779 (s). MS (CI; 70 eV) m/z (%) = 354.0 (M^+, 2), 188 (100), 148 (26), 129 (23), 91 (5), 85 (30), 69 (72). Anal. Calcd for $C_{20}H_{19}N_1O_5$ (353.36): C 67.98, H 5.42, N 3.96; found: C 67.87, H 5.43, N 3.73.

5-Bromo-1-(carboxy-phenoxy)-1*H*-isoquinoline-2-carboxylic acid methyl ester (3i): Starting from 5-bromo-isoquinoline (0.416 g, 2 mmol), 2-phenoxy-1,1-bis-trimethyl silanyloxy-ethene (1.072 g, 4 mmol) and methyl chloroformate (0.230 g, 2.4 mmol) (**3i**) (0.580 g, 69%), was isolated as a colourless solid; mp. 62-63 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (br s, 1H, OH), 7.47 (d, 1H, ^3J = 8.0 Hz, Ph/ArH), 6.90– 7.33 (m, 7H, Ph/ArH), 6.81, 6.67 (2 x d, 1H, ^3J = 8.0 Hz, H-2), 6.20–6.41 (m, 1H, 1H, ^3J = 8.0 Hz, H-3), 5.72–6.01 (m, 1H, H-8), 4.65–4.73 (m, 1H, H-9), 3.88, 3.80, 3.72 (3 x s, 3H, OMe). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 173.8, 173.3 (COOH), 157.1, 154.0, 153.8, 153.7 (C-Ar, NCO), 131.8, 131.0, 130.7, 129.7, 129.6, 129.5, 129.1, 128.7, 128.3, 126.7, 120.6, 120.3, 120.2 (C-Ar), 133.1, 132.9, 129.6, 128.0, 127.8, 127.1, 126.6, 126.4, 122.5, 122.3, 122.0, 115.3, 115.1, 114.6 (C-2) (CH-Ar), 108.0, 107.7 (C-3), 77.9, 77.2 (C-9), 57.3, 56.6 (C-8), 53.9, 53.6 (OMe). IR (KBr): $\widetilde{\nu}$ = 3430 (br, m), 1994 (m), 1729 (s), 1448 (s), 1359 (s), 1280 (m), 1237 (s), 1225 (s), 1199 (m), 766 (m), 756 (m) cm^{-1}. MS (CI): *m/z* (%) = 420 ([M+1]$^+$, ^{81}Br, 26), 418 ([M+1]$^+$, ^{79}Br, 26), 285 (16), 268 (100), 266 (99), 188 (27). HRMS (CI neg.): calcd for $C_{19}H_{16}BrNO_5$ ([M]$^-$, ^{79}Br) 417.0217, found 417.0210.

5-Bromo-1-(carboxy-butyl)-1*H*-isoquinoline-2-carboxylic acid methyl ester (3j): Starting from 5-bromo-isoquinoline (0.416 g, 2 mmol), 1,1-bis-trimethyl silanyloxy-pent-1-ene (1.042 g, 4 mmol) and methyl chloroformate (0.230 g, 2.4 mmol), (**3j**) (0.271 g, 36%), was isolated as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.45 (d, 1H, ^3J = 8.0 Hz, ArH), 6.94 – 7.08 (m, 3H, H-2, ArH), 6.88 (d, 1H, ^3J = 8.0 Hz, H-2), 6.37 (d, 1H, ^3J = 8.0 Hz, H-3), 6.27 (d, 1H, ^3J = 8.0 Hz, H-3), 5.63 (d, 1H, ^3J = 8.5 Hz, H-8), 5.49 (d, 1H, ^3J = 8.5 Hz, H-8), 3.82 (s, 3H, OMe), 2.76 (m, 1H, H-9), 1.14–1.74 (m, 6H, H-10, H-11, H-12), 0.85 (t, 3H, ^3J = 7.0 Hz, H-13). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 178.7, 178.7 (COOH), 153.9, 153.7 (NCO), 132.4, 132.3, 127.9, 127.7, 126.7, 126.1, 125.9, 125.6 (CH-Ar, C-2), 131.9, 130.2, 130.0, 120.5 (C-Ar), 109.4, 109.0 (C-3), 57.0, 56.4, 53.7, 53.4 (C-8, C-9), 50.0 (OMe), 29.4, 28.1, 22.4 (C-10, C-11, C-12), 13.8 (C-13). MS (CI): *m/z* (%) = 384 ([M+1]$^+$, ^{81}Br, 40), 382 ([M+1]$^+$, ^{79}Br, 40), 269 (13), 268 (100), 267 (13),

266 (100), 188 (9). HRMS (CI-neg.): calcd for $C_{17}H_{20}BrNO_4$ ([M]$^-$, ^{79}Br) 381.0576. found 381.0559, calcd for $C_{17}H_{20}BrNO_4$ ([M]$^-$, ^{81}Br) 383.0556, found 383.0536.

5-Bromo-1-(carboxy-octyl)-1*H*-isoquinoline-2-carboxylic acid methyl ester (3k): Starting from 5-bromo-isoquinoline (0.416 g, 2 mmol), 1,1-bis-trimethyl silanyloxy-dec-1-ene (1.264 g, 4 mmol) and methyl chloroformate (0.230 g, 2.4 mmol), (**3k**) (0.472 g, 54%), was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.54 (br s, 1H, COOH), 7.44 (d, 1H, ^3J = 8.0 Hz, ArH), 6.94-7.07 (m, 3H, ArH, H-2), 6.87 (d, 1H, ^3J = 7.8 Hz, H-2), 6.37 (d, 1H, ^3J = 7.8 Hz, H-3), 6.26 (d, 1H, ^3J = 7.8 Hz, H-3), 5.63 (d, 1H, ^3J = 8.7 Hz, H-8), 5.48 (d, 1H, ^3J = 8.7 Hz, H-8), 3.81, 3.73 (2 x s, 3H, OMe), 2.71-2.79 (m, 1H, H-9), 1.07-1.76 (m, 14H, CH_2), 0.84-0.88 (m, 3H, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.1, 179.1 (COO), 153.9, 153.6 (NCO), 132.4, 132.2, 127.9, 127.7, 126.7, 126.1, 125.9, 125.6 (CH-Ar, C-2), 132.1, 131.9, 130.2, 130.0, 120.6, 120.4 (C-Ar), 109.4, 109.0 (C-3), 57.0, 56.4, 53.7, 53.4 (C-8, C-9), 50.1 (OMe), 42.8, 31.8, 31.8, 29.4, 29.3, 29.2, 29.2, 28.4, 27.3, 27.2, 22.6, 22.6, 22.6 (CH_2), 14.1 (Me). IR (kap.): $\widetilde{\nu}$ = 3072 (br, w), 2954 (s), 2925 (s), 2855 (s), 2671 (br, w), 1728 (s), 1707 (s), 1628 (m), 1555 (w), 1447 (s), 1410 (m), 1352 (s), 1276 (s), 1231 (m), 1195 (m), 1111 (m), 941 (m), 767 (m) cm^{-1}. MS (CI pos.): *m/z* (%) = 440 ([M+1]$^+$, ^{81}Br, 34), 438 ([M+1]$^+$, ^{79}Br, 36), 360 (9), 283 (9), 268 (100), 266 (99), 188 (8). HRMS (CI neg.): calcd for $C_{21}H_{27}BrNO_4$ ([M-H]$^-$, ^{81}Br) 436.1129, found 436.1120; calcd for $C_{21}H_{27}BrNO_4$ ([M-H]$^-$, ^{79}Br) 438.1109, found 438.1100.

5-Bromo-1-(carboxy-phenyl)-1*H*-isoquinoline-2-carboxylic acid methyl ester (3l): Starting from 5-bromo-isoquinoline (0.416 g, 2 mmol), 2-phenyl-1,1-bis-trimethyl silanyloxy- ethene (1.122 g, 4 mmol) and methyl chloroformate (0.230 g, 2.4 mmol) (**3l)** (0.292 g, 36%), was isolated as a colourless solid; mp. 202-203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.49 (m, 7H, Ph/ArH), 6.98 (d, 1H, ^3J = 8.0 Hz, H-2), 6.88–6.95 (m, 1H, Ph/ArH), 6.74 (d, 1H, ^3J = 8.0 Hz, H-2), 6.47 (d, 1H, ^3J = 8.0 Hz, H-3), 6.38 (d, 1H, ^3J = 8.0 Hz, H-3), 6.04 (d, 1H, ^3J = 10.5 Hz, H-8), 5.79 (d, 1H, ^3J = 10.5 Hz, H-8), 4.01 (d, 1H, ^3J = 10.5 Hz, H-9), 3.96 (d, 1H, ^3J = 10.5 Hz, H-9), 3.44 (s, 3H, OMe), 3.29 (s, 3H, OMe). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.5, 176.4 (COOH), 153.2, 152.9 (NCO), 132.5, 132.4, 132.5, 132.4, 129.8, 129.1, 128.9, 128.4, 128.3, 128.3, 128.2, 128.0, 127.8, 126.9, 126.3, 126.2 (CH-Ph/Ar, C-2), 133.7, 133.5, 132.2, 131.7, 130.2, 128.7, 120.6, 120.5 (C-Ph/Ar), 109.1, 109.0 (C-3), 57.8, 56.4 (C-8), 54.1, 53.7 (C-9), 53.3, 52.7 (OMe).

IR (KBr): $\tilde{\nu}$ = 3440 (w), 3089 (br, m), 1730 (s), 1671 (s), 1465 (s), 1449 (s), 1413 (m), 1366 (s), 1323 (m), 1257 (s), 1202 (w), 1166 (m), 1120 (w) cm^{-1}. MS (CI): *m/z* (%) = 404 ($[M+1]^+$, ^{81}Br, 18), 402 ($[M+1]^+$, ^{79}Br, 19), 268 (99), 266 (100), 137 (50), 71 (83), 69 (87), 67 (56). Anal. Calcd for $C_{19}H_{16}BrNO_4$ (402.24): C 56.73, H 4.01, N 3.48. Found: C 56.54, H 4.14, N 3.19.

Typical procedure for the preparation 0f (4): To a CH_2Cl_2 solution (6 mL) of **3c** (0.1 g, 0.35 mmol) and I_2 (0.17 g 0.70 mmol) was added a saturated solution of $NaHCO_3$ (3.5 mL) and the solution was stirred for 12 h at 20 °C. The excess of iodine was removed by addition of a saturated aqueous solution of sodium sulfite (20 mL). The organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1) to give **4c** as yellow oil (0.10 g, 70%). Due to the restricted rotation in the urethane moiety, **4c** appeared as a racemic mixture of two rotamers in the same ratio of 55% (I) to 45% (II), as observed in **3c**.

8-Iodo-12-methyl-11-oxo-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4a): The intermediate (**3a**) (0.080 g, 0.30 mmol) was treated with I_2 (0.084 g, 0.34 mmol) and saturated $NaHCO_3$ soln (3.5mL) in CH_2Cl_2 (6.0 mL), (**4a**) (0.054 g, 46%) was isolated as brown solid; mp. 53 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, 2H, *J* = 6.2 Hz, ArH), 7.35-7.24 (m, 4H, ArH), 7.01 (d, 2H, *J* = 6.0 Hz, ArH), 6.81 (br s, 2H, H-2), 5.76 (br s, 2H, *J* = 1.6 Hz, H-3), 5.32 (br s, 1H, H-8), 3.92 (s, 6H, OMe), 3.00 (m, 2H, H-9), 1.15 (d, 6H, *J* = 5.2 Hz, H-10). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 170.2 (COOH), 155.1, 154.5 (NCO), 134.6, 133.0, 132.8, 132.3 (C-Ar), 131.1, 130.0, 129.8, 129.4 (2C), 129.4, 128.8, 128.5 (CH-Ar), 87.0, 86.8 (C-2), 68.54 (C-9), 54.4, 53.0 (OMe), 43.1 (C-8), 24.5 (br C, C-3), 13.5, 13.3 (C-10). IR (KBr, cm^{-1}): ν = 3428 (br), 2956 (w), 1708 (s), 1635 (s), 1454 (m), 1333 (m), 1254 (m), 1250 (m), 766 (m). MS (EI, 70 eV): m/z (%) = 389.0 ($[M+2]^+$, 10), 331 (39), 271 (19), 204 (39), 188 (100), 142 (9).

12-Ethyl-8-iodo-11-oxo-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4b): The intermediate (**3b**) (0.120 g, 0.43 mmol) was treated with I_2 (0.120 g, 0.48 mmol) and saturated $NaHCO_3$ soln (4.36 mL) in CH_2Cl_2

(7.0 mL), (**4b**) (0.107 g, 61%), was isolated as light yellow solid; mp. 63 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43 (d, 1H, ArH), 7.33-7.23 (m, 3H, ArH), 7.02 (d, 2H, *J* = 5.9 Hz, ArH), 6.66 (br s, 1H, H-2), 5.74 (s, 1H, H-3), 5.45 (br s, 1H, H-8), 3.91 (s, 3H, OMe), 2.70 (br s, 1H, H-9), 1.94-1.87 (m, 1Ha, H-10), 1.35-1.26 (m, Hb, H-10), 1.17 (t, 3H, *J* = 7.4 Hz, H-11). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.4 (COOH), 154.2 (NCO), 134.4 (C-Ar), 132.4 (CH-Ar), 132.0 (C-Ar), 129.7, 129.3, 128.6. 128.4, (CH-Ar), 86.1 (C-2), 54.4 (OMe), 50.7 (C-9), 50.0 (C-8), 24.6 (C-3), 20.6 (C-10), 12.6 (C-11). IR (KBr, cm^{-1}): ν = 3439 (br), 2961 (s), 1743 (s), 1730 (s), 1442 (m), 1318 (m), 1250 (m), 1097 (m), 765 (m). MS (EI, 70 eV): m/z (%) = 401.0 (M^+, 2), 314 (8), 204 (100), 188 (90), 144 (30), 129 (60). HRMS (EI): calcd for $C_{15}H_{16}INO_4$ ($[M]^+$): 401.0119; found: 401.0112.

12-Butyl-8-iodo-11-oxo-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4c): The intermediate (**3c**) (0.100 g, 0.35 mmol) was treated with I_2 (0.177 g, 0.70 mmol) and saturated $NaHCO_3$ soln (2.0 mL) in CH_2Cl_2 (6.0 mL), (**4c**) (0.105 g, 70%) was isolated as yellow oil (major rotamer 55%, 45%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40-7.35 (m, $1H_{(I)}$, $1H_{(II)}$, H-$4_{(I)}$, H-$4_{(II)}$), 7.30-7.24 (m, $2H_{(I)}$, $2H_{(II)}$, H-$5,6_{(I)}$, H-$5,6_{(II)}$), 7.02-6.97 (m, $H_{(I)}$, $H_{(II)}$, H-$7_{(I)}$, H-$7_{(II)}$), 6.82 („t“, H, $^{3}J_{2,3}$ = 1.8 Hz, $^{4}J_{2,8}$ = 1.5 Hz, H-$2_{(II)}$), 6.68 („t“, 1H, $^{3}J_{2,3}$ = 1.8 Hz, $^{4}J_{2,8}$ = 1.5 Hz, H-$2_{(I)}$), 5.69 (d, 1H, $^{3}J_{2,3}$ = 1.8 Hz, H-$3_{(II)}$), 5.68 (d, 1H, $^{3}J_{2,3}$ = 1.8 Hz, H-$3_{(I)}$), 5.50 (br s, 1H, $^{4}J_{2,8}$ = 1.5 Hz, $^{3}J_{8,9}$ = 1.0 Hz, H-$8_{(I)}$), 5.36 (br s, 1H, $^{4}J_{2,8}$ =1.5 Hz, $^{3}J_{8,9}$ = 1.0 Hz, H-$8_{(II)}$), 3.89 (s, 3H, $OMe_{(I)}$), 3.88 (s, 3H, $OMe_{(II)}$), 2.56-2.50 (m, $1H_{(I)}$, $1H_{(II)}$, H-$9_{(I)}$, H-$9_{(II)}$), 1.75-1.35 (m, $6H_{(I)}$, $6H_{(II)}$, H-$10,11,12_{(a,b),(I)}$, H-$10,11,12_{(a,b),(II)}$), 0.944 (t, 3H, *J* = 7.2 Hz, H-$13_{(II)}$), 0.936 (t, 3H, *J* = 7.2 Hz, H-$13_{(I)}$). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.3 ($COO_{(I)}$), 169.0 ($COO_{(II)}$), 154.3 ($NCO_{(II)}$), 153.8 ($NCO_{(I)}$), 132.2, 132.2 (C-$3a_{(II)}$, C-$7a_{(II)}$), 131.9, 132.2 (C-$3a_{(I)}$, C-$7a_{(I)}$), 131.6 (C-$4_{(II)}$), 131.5 (C-$4_{(I)}$), 129.5 (C-$5_{(I)}$), 129.4 (C-$5_{(II)}$), 129.1 (C-$6_{(II)}$), 128.9 (C-$6_{(I)}$), 126.6 (C-$7_{(I)}$), 126.4 (C-$7_{(II)}$), 85.4 (C-$2_{(I)}$), 84.8 (C-$2_{(II)}$), 53.8 ($OMe_{(I)}$), 53.6 ($OMe_{(II)}$), 52.2 (C-$9_{(I)}$), 51.9 (C-$9_{(II)}$), 51.8 (C-$8_{(II)}$), 50.6 (C-$8_{(I)}$), 30.7 (C-$10_{(I)}$), 30.5 (C-$10_{(II)}$), 29.4 (C-$11_{(I)}$), 29.3 (C-$11_{(II)}$), 23.5 (C-$3_{(I)}$), 23.0 (C-$3_{(II)}$), 22.2 (C-$12_{(I)}$), 22.3 (C-$12_{(II)}$), 13.8 (C-$13_{(I)}$), 13.8 (C-$13_{(II)}$). IR (KBr, cm^{-1}): ν = 3467 (br), 2956 (s), 1760 (s), 1716 (s), 1456 (m), 1333 (m), 1254 (m), 1002 (m), 763 (m). MS (EI, 70 eV): m/z (%) = 429 (M^+, 2), 302 (7), 204 (19), 188 (100), 144 (25), 129 (36). HRMS (EI): calcd for $C_{17}H_{20}INO_4$ ($[M]^+$): 429.0432; found: 429.0426.

8-Iodo-12-octyl-11-oxo-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4d): The intermediate (**3d**) (0.100 g, 0.27 mmol) was treated with I_2 (0.077 g, 0.30 mmol) and saturated soln of $NaHCO_3$ (2.0 mL) in CH_2Cl_2 (5.0 mL), (**4d**) (0.088 g, 67%), was isolated as yellow oil. Single rotamer. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52-7.45 (m, 1H, ArH), 7.44-7.23 (m, 2H, ArH), 7.03-7.00 (m, 1H, ArH), 7.78-6.67 (br d, 1H, H-2), 5.75 (d, 1H, *J* = 1.8 Hz, H-3), 5.42 (br s, 1H, H-8), 3.92 (s, 3H, OMe), 2.75 (br s, 1H, H-9), 1.92-1.78 (m, 1Ha, H-10), 1.60 (br s, 1Hb, 2H, H-10, H-11), 1.59-1.24 (m, 10H, H-12, H-13, H-14, H-15, H-16), 0.89 (t, 3H, *J* = 7.2 Hz, H-17). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.4 (COOH), 154.0 (NCO), 132.7 (C-Ar), 132.0, 129.4 (CH-Ar), 128.6 (C-Ar), 128.3, 127.7 (CH-Ar), 86.2 (C-2), 54.0 (OMe), 50.8 (C-9), 48.4 (C-8), 31.8 (C-10), 29.6, 29.4, 29.3, 29.2, 27.2, 26.6 (C-11, C-12,C-13,C-14,C-15,C-16), 22.6 (C-3), 14.1 (C-17). MS (CI; pos.): m/z (%) = 486.1 ([M+2]$^+$, 1), 430 (2), 360 (40), 222 (12), 188 (100), 130 (7). HRMS (CI; neg.): calcd for $C_{21}H_{27}INO_4$ ([M]$^+$): 484.0979; found: 484.0984.

8-Iodo-11-oxo-12-phenyl-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4e): The intermediate (**3e**) (0.100 g, 0.30 mmol) was treated with I_2 (0.152 g, 0.60 mmol) and saturated $NaHCO_3$ (2.5 mL) in CH_2Cl_2 (5.0 mL), (**4e**) (0.088 g, 65%) was isolated as yellow oil (major rotamer 70%, minor 30%). ^{1}H NMR (500 Hz, $CDCl_3$): δ = 7.45-7.21 (m, 9 H, H-4,5,6,7, Ph), 7.01 (t 1H, $^3J_{2,3}$ = 1.8 Hz, $^4J_{2,8}$ = 1.8 Hz, H-2$_{(I)}$), 6.85 („t“, 1H, $^3J_{2,3}$ = 1.8 Hz, $^4J_{2,8}$ = 1.5 Hz, H-2$_{(II)}$), 5.78 (d, 1H, $^3J_{2,3}$ = 1.8 Hz, H-3$_{(I)}$), 5.76 (d, 1H, $^3J_{2,3}$ = 1.8 Hz, H-3$_{(II)}$), 5.61 (br s, 1H, $^4J_{2,8}$ = 1.5 Hz, $^3J_{8,9}$ = 1.0 Hz, H-8$_{(II)}$), 5.45 (br s, 1H, $^4J_{2,8}$ = 1.5 Hz, $^3J_{8,9}$ = 1.0 Hz, H-8$_{(I)}$), 3.96 (br s, 1H$_{(II)}$,H-9$_{(II)}$), 3.95 (br s, 1H$_{(I)}$, H-9$_{(I)}$), 3.68 (s, 3H, OMe$_{(II)}$), 3.18 (s, 3H, OMe$_{(I)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.8 (COO$_{(I)}$), 167.0 (COO$_{(II)}$), 154.5 (NCO$_{(I)}$), 153.2 (NCO$_{(II)}$), 136.2 (I-Ph$_{(I)}$), 135.9 (I-Ph$_{(II)}$), 132.4 (C-3a$_{(I)}$), 132.1 (C-3a$_{(II)}$). 131.8 (C-7a$_{(II)}$), 131.7 (C-4$_{(I)}$), 131.6 (C-4$_{(II)}$), 131.5 (C-7a$_{(I)}$), 129.7, 129.3 (C-5,6$_{(II)}$), 129.6, 129.5 (C-5,6$_{(I)}$), 129.1 (m-Ph$_{(I)}$), 129.0 (m-Ph$_{(II)}$), 128.3 (p-PH$_{(I)}$), 128.0 (p-Ph$_{(I)}$), 127.7 (o-Ph$_{(I)}$), 127.5 (o-Ph$_{(II)}$), 126.9 (C-7$_{(II)}$), 126.7 (C-7$_{(I)}$), 86.1 (C-2$_{(II)}$), 85.7 (C-2$_{(II)}$), 57.5 (C-8$_{(II)}$),, 57.4 (C-9$_{(I)}$), 56.4 (C-8$_{(I)}$), 54.9 (C-9$_{(II)}$), 53.7 (OMe$_{(II)}$), 53.0 (OMe$_{(I)}$), 23.4 (C-3$_{(II)}$), 22.8 (C-3$_{(I)}$). IR (KBr, cm^{-1}): ν = 3429 (br), 2953 (w), 1745 (s), 1721 (s), 1444 (m), 1322 (m), 1238 (m), 1002 (m), 726 (w). MS (EI; 70 eV) m/z (%) = 449.0 (M$^+$, 2), 355(3), 279 (30), 225 (15), 118 (100), 167 (63), 77 (50). HRMS (EI): calcd for $C_{19}H_{16}INO_4$ (449.0): 449.0119; found: 449.0138.

8-Iodo-11-oxo-12-*p*-tolyl-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4f): The intermediate (**3f**) (0.090 g, 0.26 mmol) was treated with I_2 (0.073 g, 0.30 mmol) and saturated $NaHCO_3$ (2.5 mL) in CH_2Cl_2 (5 mL), (**4f**) (0.077 g, 64%) was isolated as brown solid; mp. 82 °C. single rotamer. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (d, 1H, *J* = 8.5 Hz, ArH), 7.26 (t, 1H, *J* = 6.8 Hz, ArH), 7.03 (d, 2H, *J* = 7.8 Hz, ArH), 6.93-6.88 (m, 2H, ArH), 6.66 (d, 2H, *J* = 7.3 Hz, ArH), 5.86 (br s, 1H, *J* = 8.3 Hz, H-2), 5.41 (br s, 1H, H-3), 4.28 (br s, 1H, H-9), 3.98 (s, 3H, OMe), 2.32 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.3 (COOH), 154.2 (NCO), 136.7, 132.2 (C-Ar/Ph), 131.3, 130.2, 130.2 (C-Ar/Ph), 130.1 (CH-Ar/Ph), 129.8 (C-Ar/Ph), 129.5, 129.3, 128.9, 127.4 (CH-Ar/Ph), 86.8 (C-2), 54.5 (C-8, C-9), (OMe), 22.70 (C-3), 21.0 (Me). IR (KBr, cm^{-1}): ν = 3433 (br), 2955 (w), 1758 (s), 1718 (s), 1443 (s), 1316 (s), 1251 (m), 1044 (m), 767 (w). MS (EI; 70 eV) m/z (%) = 463.0 (M^+, 10), 313 (18), 253 (53), 204 (25), 188 (100), 132 (87), 44 (48). HRMS (EI): calcd for $C_{20}H_{18}INO_4$ ($[M]^+$): 463.0275; found: 463.0270.

12-(4-Chloro-phenyl)-8-Iodo-11-oxo-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6.triene-13-carboxylic acid methyl ester (4g): The intermediate (**3g**) (0.200 g, 0.56 mmol) was treated with I_2 (0.156 g, 0.61 mmol) and saturated $NaHCO_3$ (5.6 mL) in CH_2Cl_2 (9.0 mL), (**4g**) (0.195g, 72%), was isolated as colourless solid; mp. 93 °C. Single rotamer. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.51 (d, 1H, *J* = 7.8 Hz, ArH), 7.36-7.26 (m, 4H, ArH), 7.00 (t, 1H, *J* = 8.5 Hz, ArH), 6.85 (br s, 3H, ArH), 5.95-5.89 (m, 2H, H-2, H-3), 5.48 (br s, 1H, H-8), 4.33 (br s, 1H, H-9), 4.04 (s, 3H, OMe). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0 (COO), 154.1 (NCO), 134.1 (C-Ar/Ph), 132.3 (2C), 132.0 (CH-Ar/Ph), 131.6, 131.5 (C-Ar/Ph), 129.6 (CH-Ar/Ph), 129.2 (C-Ar/Ph), 128.5, 127.4 (2C), 127.2 (CH-Ar/Ph), 86.8 (C-2), 58.3 (C-8), 54.7 (C-9), 54.6 (OMe), 22.6 (C-3). IR (KBr, cm^{-1}): ν = 3433 (br), 2925 (w), 1727 (s), 1717 (s), 1445 (s), 1360 (m), 1249 (m), 1092 (m), 764 (w). MS (CI; 70eV) m/z (%) = 484.2 ($[M+2]^+$, 3), 372 (100), 326 (31), 204 (66), 188 (26). HRMS (CI; neg.): calcd for $C_{19}H_{15}INO_4Cl$ ($[M]^+$): 482.9729; found: 482.9716.

6-Bromo-8-iodo-11-oxo-12-phenoxy-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5- triene-13-carboxylic acid methyl ester (4i): Starting from (**3i**) (0.400 g, 0.96 mmol) and I_2 (0.366 g, 1.44 mmol), (**4i**) (0.285 g, 49%), was isolated as a light-yellow solid; mp. 75-77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.3

Hz, Ph/ArH), 7.30-7.37 (m, 3H, Ph/ArH), 7.00-7.12 (m, 4H, Ph/ArH), 6.88-6.89, 6.71-6.80 (2 x m, 1H, H-2), 5.74-5.83 (m, 1H, H-8), 5.60 (d, 1H, ^3J = 2.3 Hz, H-3), 4.88-5.01 (m, 1H, H-9), 3.98, 3.97 (2 x s, 3H, OMe). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 162.9, 162.5 (COO), 156.9, 156.7, 156.4, 154.8, 153.9, 153.7 (C-Ph/Ar, NCO), 134.8, 134.6, 130.7, 129.9, 129.8, 129.8, 129.0, 126.8, 126.5, 123.0, 122.8, 117.0, 115.8, 115.4 (CH-Ph/Ar), 132.8, 130.8, 129.5, 129.1, 127.0, 126.7, 126.1, 123.3 (C-Ph/Ar), 86.1 (br), 85.4 (C-2), 54.4, 54.1, 53.7, 53.5, 52.7, 50.7 (OMe, C-8, C-9), 24.8 (br), 24.3, 23.7 (C-3). IR (KBr): $\tilde{\nu}$ = 3435 (br, w), 2955 (w), 2924 (w), 2853 (w), 1766 (s), 1727 (s), 1590 (m), 1494 (m), 1445 (s), 1416 (m), 1352 (m), 1304 (m), 1226 (s), 1097 (m) cm^{-1}. MS (ESI): *m/z* = 545.92 ([M+1]$^+$, ^{81}Br), 543.93 ([M+1]$^+$, ^{79}Br). Anal. Calcd for $C_{19}H_{15}BrINO_5$ (544.13): C, 41.94; H, 2.78; N, 2.57. Found: C, 41.96; H, 2.92; N, 2.23.

6-Bromo-8-iodo-11-oxo-12-butyl-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-13-carboxylic acid methyl ester (4j): Starting from (**3j**) (0.237 g, 0.62 mmol) and I_2 (0.236 g, 0.93 mmol), (**4j**) (0.229 g, 73%), was isolated as a colourless solid; mp. 123-124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, 1H, ^3J = 8.0 Hz, ArH), 7.21 („t“, 1H, ^3J = 8.0 Hz, H-6), 7.02-7.05 (m, 1H, ArH), 6.68-6.91 (m, 1H, H-2), 5.57 (d, 1H, ^3J = 2.1 Hz, H-3), 5.34-5.50 (m, 1H, H-8), 3.94 (s, 3H, OMe), 2.69-2.87 (m, 1H, H-9), 1.79-1.90 (m, 1H, CH_2), 1.48-1.62 (m, 2H, CH_2), 1.30-1.46 (m, 2H, CH_2), 1.15-1.27 (m, 1H, CH_2), 0.95 (t, 3H, ^3J = 7.3 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1 (br, COO), 153.8 (NCO), 134.1, 129.4, 127.1 (br) (CH-Ar), 131.8 (br), 130.9 (br) (C-Ar), 85.8, 85.2 (C-2), 54.0 (OMe), 51.6, 50.9, 49.4, 48.7 (C-8, C-9), 29.4, 26.2, 22.4 (C-10, C-11, C-12), 26.1 (C-3), 13.8 (C-13). IR (KBr): $\tilde{\nu}$ = 3433 (br, m), 2956 (m), 2928 (m), 2863 (w), 1756 (s), 1718 (s), 1561 (w), 1445 (s), 1416 (m), 1345 (s), 1300 (m), 1105 (m), 959 (s) cm^{-1}. MS (ESI): *m/z* = 509.96 ([M+1]$^+$, ^{81}Br), 507.96 ([M+1]$^+$, ^{79}Br). Anal. Calcd for $C_{17}H_{19}BrINO_4$ (508.15): C, 40.18; H, 3.77; N, 2.76. Found: C, 40.54; H, 3.73; N, 2.67.

6-Bromo-8-iodo-11-oxo-12-octyl-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-13-carboxylic acid methyl ester (4k): Starting from (**3k**) (0.365 g, 0.83 mmol) and I_2 (0.316 g, 1.245 mmol) (**4k**) (0.324 g, 67%), was isolated as a colourless solid; mp. 113-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, 1H, ^3J = 8 Hz, ArH), 7.18-7.27 (m, 1H, ArH), 7.03 (d, 1H, ^3J = 7.4 Hz, ArH), 6.66-6.89 (m, 1H, H-2), 5.57 (d, 1H, ^3J = 2.1 Hz, H-3), 5.31-5.54 (m, 1H, H-8), 3.94 (s, 3H, OMe), 2.68-2.90 (m, 1H, H-9), 1.16-1.95 (m, 14H, CH_2), 0.89 (t, 3H, ^3J = 6.7 Hz, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2 (br),

168.9 (COO), 153.8 (NCO), 134.1, 129.5, 127.1 (br) (CH-Ar), 131.9 (br), 131.0 (br) (C-Ar), 85.8, 85.2 (C-2), 54.0 (OMe), 51.6, 50.9, 49.3, 48.8 (C-8, C-9), 31.8, 29.3, 29.2, 27.3 (br), 26.5 (br), 22.6 (CH_2), 26.2 (C-3), 14.1 (Me). IR (KBr): $\tilde{\nu}$ = 3432 (br, w), 2952 (m), 2922 (m), 2853 (m), 1754 (s), 1709 (s), 1449 (s), 1420 (w), 1355 (s), 1299 (m), 1115 (m), 959 (m), 765 (m) cm^{-1}. MS (CI pos., Isobutan): *m/z* (%) = 566 ($[M+1]^+$, ^{81}Br, 5), 564 ($[M+1]^+$, ^{79}Br, 5), 456 (52), 454 (71), 440 (63), 438 (74), 284 (38), 282 (39), 268 (100), 266 (100) HRMS (EI): calcd for $C_{21}H_{27}BrINO_4$ (M^+, ^{79}Br) 563.0163, found 563.0149.

6-Bromo-8-iodo-11-oxo-12-phenyl-10-oxa-13-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-13-carboxylic acid methyl ester (4l): Starting from (**3l**) (0.229 g, 0.57 mmol) and I_2 (0.217 g, 0.86 mmol) (**4l**) (0.160 g, 53%), was isolated as a light-yellow solid; mp. 71-73 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.52 (m, 1H, ^3J = 7.9 Hz, Ph/ArH), 7.21–7.49 (m, 3H, Ph/ArH), 6.77–6.85 (m, 4H, Ph/ArH), 5.80 (m, 1H, H-2), 5.68 (d, 1H, ^3J = 1.9 Hz, H-3), 5.37– 5.56 (m, 1H, H-8), 4.26–4.44 (m, 1H, H-9), 4.00 (br s, 3H, OMe). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.2 (br, COO), 153.9 (NCO), 134.1 (br), 130.2, 128.7, 128.5, 128.3, 128.2 (CH-Ar/Ph), 133.2, 131.6 (br), 129.8 (br), 126.2 (br) (C-Ar/Ph), 86.3 (br, C-2), 55.0 (br), 54.6, 54.5 (C-8, C-9), 54.3 (br, OMe), 25.8 (br, C-3). IR (KBr): $\tilde{\nu}$ = 3449 (br, s), 1755 (m), 1725 (s), 1445 (m), 1354 (m), 1303 (m), 1264 (w), 753 (w) cm^{-1}. MS (CI pos.): *m/z* (%) = 530 ($[M+1]^+$, ^{81}Br, 3), 528 ($[M+1]^+$, ^{79}Br, 3), 404 (15), 402 (22), 360 (26), 358 (32), 268 (57), 266 (53), 204 (29). HRMS (CI neg., Isobutane): calcd for $C_{19}H_{15}BrINO_4$ ($[M-H]^-$) 527.9307, found 527.9291.

Typical procedure for the preparation of 2*H*-quinoline-1-carboxylic acid methyl ester (7): To a CH_2Cl_2 solution (20 mL) of quinoline (0.250 g, 1.90 mmol) was added the 1,1-bis(trimethylsilyloxy)pent-1-ene (0.713 g, 2.90 mmol) and methyl chloroformate (0.362 g, 3.86 mmol) at 0 °C. The solution was stirred for 2 h at 0 °C and for 12 h at 20 °C. A saturated aqueous solution of ammonium chloride (20 mL) was added and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1) to give **7a** as a colorless crystal (0.214 g, 38%), m.p. 105-106 °C.

2-(1-Carboxy-butyl)-2*H*-quinoline-1-carboxylic acid methyl ester (7a): Starting with quinoline (**5**) (0.250 g, 1.93 mmol), (**2a**) (0.713 g, 2.90 mmol) and methyl chloroformate (0.362 g, 3.86 mmol), (**7a**) (0.214 g, 38%), was isolated as colorless crystal; mp. 105-106°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54 (d, 1H, *J* = 8.2 Hz, ArH), 7.28-7.21 (m, 1H, ArH), 7.11-7.09 (d, 2H, ArH), 6.57 (d, 1H, *J* = 9.4 Hz, H-4), 6.10 (dd, 1H, *J* = 6.1 Hz, *J* = 9.4 Hz, H-3), 5.26 (dd, 1H, *J* = 6.1 Hz, *J* = 9.4 Hz, H-2), 3.76 (s, 3H, OMe), 2.52-2.42 (m, 1H, H-9), 1.76-1.63 (m, 1Ha, H-10), 1.47- 1.13 (m, 1Hb, 2H, H-10, H-11), 0.85 (t, 3H, *J* = 7.0 Hz, H-12). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.0 (COOH), 154.8 (NCO), 134.3 (C-Ar), 127.8, 127.1, 126.5, 126.1 (CH-Ar), 125.6 (C-Ar), 124.7 (CH-Ar) 54.1 (OMe), 53.8 (C-2), 49.0 (C-9), 30.0 (C-10), 20.7 (C-11), 14.0 (C-12). IR (KBr, cm^{-1}): ν = 3430 (br), 2953 (m), 1697 (s), 1443 (m), 1305 (s), 753 (w). MS (CI pos.; 70eV) m/z (%) = 290.1 ($[M+1]^+$, 10), 330 (5), 290 (80), 188 (100). HRMS (CI; neg.): calcd for $C_{16}H_{18}NO_4$ ($[M]^-$): 288.1230; found: 288.1230.

2-(1-Carboxy-nonyl)-2*H*-quinoline-1-carboxylic acid methyl ester (7b): Starting with quinoline (**5**) (0.250 g, 1.93 mmol), (**2b**) (0.919 g, 2.89 mmol) and methyl chloroformate (0.364 g, 3.88 mmol), (**7b**) (0.320 g, 46%), was isolated as colorless solid; mp. 77-78 °C. Second diastereomer **7b** (0.120 g, 17%), was also isolated as colorless oil.

7b (*syn*): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (br s, 1H, H-8), 7.23 (m, 1H, H-7), 7.11-7.08 (br m, 2H, H-5, 6), 6.55 (d, 1H, $^{3}J_{3,4}$ = 9.5 Hz, H-4), 6.09 (dd, 1H, $^{3}J_{3,4}$ = 9.5 Hz, $^{3}J_{2,3}$ = 6.0 Hz,H-3), 5.23 (br m, 1H, H-2), 3.79 (s, 3H, OMe), 2.38 (dt, 1H, $^{3}J_{9,10}$ = $^{3}J_{9,10}$ = 9.8 Hz, $^{3}J_{2,9}$ = 4.0 Hz, H-9), 1.58 (m, 2H, H-10), 1.31-1.11 (m, 12H, H-11,12,13,14,15,16), 0.88 (t, 3H, $^{3}J_{CH2,CH3}$ = 7.0 Hz, H-$17_{(Me)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.6 (COOH), 155.1 (NCO), 134.1 (C-8a), 127.7 (C-7), 127.4 (C-3), 127.3 (C-4a), 126.4, 126.4 (C-4, C-5), 125.0 (C-8), 124.8 (C-6), 53.2 (OMe), 53.0 (C-2), 48.4 (C-9), 31.8, 29.3, 29.2, 29.1, 26.7 (C-11, C-12, C-13, C-14, C-15), 28.5 (C-10), 22.6 (C-16), 14.0 (C-$17_{(Me)}$). IR (Nujol, cm^{-1}): ν = 3433 (br), 2925 (w), 1727 (m), 1445 (m), 1359 (m), 1249 (w), 764 (w). MS (EI; 70eV) m/z (%) = 359.2 (M^+, 1), 347(2), 204 (2), 188 (100), 144 (48), 129 (12). HRMS (EI): calcd for $C_{21}H_{29}NO_4$ ($[M]^+$): 359.2091; found: 359.2084.

7b (*anti*): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52 (br s, 1H, H-8), 7.24 (m, 1H, H-7), 7.10 (br d, 2H, H-5, 6), 6.57 (d, 1H, $^{3}J_{3,4}$ = 9.5 Hz, H-4), 6.09 (dd, 1H, $^{3}J_{3,4}$ = 9.5 Hz, $^{3}J_{2,3}$ = 6.0 Hz,H-2), 5.26 (dd, 1H, $^{3}J_{2,9}$ = 9.5 Hz, $^{3}J_{2,3}$ = 6.0 Hz,H-2), 3.76 (s, 3H, OMe), 2.45 (ddd, 1H, $^{3}J_{2,9}$ = 9.5 Hz, $^{3}J_{9,10}$ = 11.0 Hz, $^{3}J_{9,10}$ = 3.6 Hz, H-9), 1.69 (m, 1Ha H-10), 1.46 (m,

1Hb, H-10), 1.30-1.13 (m, 12H, H-11,12,13,14,15,16), 0.88 (t, 3H, $^3J_{CH2,CH3}$ = 7.0 Hz, H-$17_{(Me)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.3 (COO), 154.8 (NCO), 134.4 (C-8a), 127.8 (C-7), 127.2 (C-4a), 126.5 (C-3), 126.5 (C-4), 126.1 (C-5), 125.6 (br, C-8), 124.7 (C-6), 53.5 (C-2), 53.1 (OMe), 49.2 (C-9), 31.8, 29.5, 29.2, 29.1 (C-11, C-12, C-13, C-14), 27.8 (C-10), 27.5 (C-5), 22.6 (C-16), 14.1 (C-$17_{(Me)}$). IR (Nujol, cm^{-1}): ν = 3224 (br), 2945 (m), 1742 (s), 1671 (m), 1342 (m), 1277 (m), 1180 (m), 763 (w). MS (EI; 70eV) m/z (%) = 359.2 (M^+, 1), 347 (2), 188 (100), 144 (48), 129 (12). Anal. Calcd for $C_{21}H_{29}NO_4$ (359.45): C 70.17, H 8.13, N 3.90; found: C 70.36, H 8.36, N 4.20.

4-(Carboxy-phenyl-methyl)-4H-quinoline-1-carboxylic acid methyl ester (7c): Starting with quinoline (**5**) (0.250 g, 1.93 mmol), (**2c**) (0.810 g, 2.90 mmol) and methyl chloroformate (0.362 g, 3.86 mmol), (**7c**) (0.350 g, 56%), was isolated as colorless solid; mp. 42-43 °C. Product was a diastereomeric mixture of enantiomeres (55%, 45%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.55 (br, 1H, $OH_{(I)}$), 8.94 (br, 1H, $OH_{(II)}$), 7.90 (dd, 1H, $^3J_{7,8}$ = 8.5 Hz, $^4J_{6,8}$ = 1.2 Hz, H-$8_{(I)}$), 7.84 (dd, 1H, $^3J_{7,8}$ = 8.5 Hz, $^4J_{6,8}$ = 1.2 Hz, H-$8_{(II)}$), 7.30-7.04 (m, $6H_{(I)}$, 8-$H_{(II)}$, H-$7_{(I)}$, $Ph_{(I)}$, H-$5_{(II)}$, $6_{(II)}$, $7_{(II)}$, $Ph_{(II)}$), 7.06 (d, 1H, $^3J_{2,3}$ = 7.6 Hz, H-$2_{(I)}$), 6.88 (d, 1H, $^3J_{2,3}$ = 7.6 Hz, H-$2_{(II)}$), 6.77 (d,,t", 1H, $^3J_{5,6}$ =7.6 Hz, $^4J_{6,8}$ =1.2 Hz, H-$6_{(I)}$), 6.33 (dd, 1H, $^3J_{5,6}$ =7.6 Hz, $^4J_{5,7}$ = 1.6 Hz, H-$5_{(I)}$), 5.60 (dd, 1H, $^3J_{2,3}$ = 7.6 Hz, $^3J_{3,4}$ =6.0 Hz, H-$3_{(I)}$), 5.19 (dd, 1H, $^3J_{2,3}$ = 7.6 Hz, $^3J_{3,4}$ = 6.0 Hz, H-$3_{(II)}$), 4.17 (dd, 1H, $^3J_{4,9}$ =7.8 Hz, $^3J_{3,4}$ = 6.0 Hz, H-$4_{(II)}$), 3.95 (dd, 1H, $^3J_{4,9}$ = 9.5 Hz, $^3J_{3,4}$ = 6.0 Hz, H-$4_{(I)}$), 3.87 (s, 3H, $OMe_{(I)}$), 3.76 (s, 3H, $OMe_{(II)}$), 3.72 (d, 1H, $^3J_{4,9}$ = 7.8 Hz, H-$9_{(II)}$), 3.52 (d, 1H, $^3J_{4,9}$ = 7.8 Hz, H-$9_{(I)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.9 ($COOH_{(I)}$), 177.8 ($COOH_{(II)}$), 152.8 ($NCO_{(I)}$). 152.5 ($NCO_{(II)}$), 137.0 (C-$8a_{(I)}$), 136.7 (C-$8a_{(II)}$), 135.5 (i-$Ph_{(I)}$), 134.7 (i-$Ph_{(II)}$), 129.2 (C-$5_{(I)}$), 129.1, 128.9 (o-$Ph_{(I)}$, o-$Ph_{(II)}$), 128.7 (C-$4a_{(II)}$), 128.4 (C-$5_{(II)}$), 128.3, 128.0 (m-$Ph_{(I)}$, m-$Ph_{(II)}$), 128.1 (C-$2_{(I)}$), 128.1 (C-$2_{(II)}$), 127.7 (C-$4a_{(I)}$), 127.6 (p-$Ph_{(I)}$), 127.4 (p-$Ph_{(II)}$), 126.9 (C-$7a_{(II)}$), 126.4 (C-$7a_{(I)}$), 125.0 (C-$6_{(II)}$), 124.2 (C-$6_{(I)}$), 121.5 (C-$8_{(I)}$), 121.1 (C-$8_{(II)}$), 111.6 (C-$3_{(I)}$), 110.0 (C-$3_{(II)}$), 58.2 (C-$9_{(II)}$), 57.9 (C-$9_{(I)}$), 53.3 ($OMe_{(II)}$), 53.1 ($OMe_{(I)}$), 42.2 (C-$4_{(I)}$), 41.1 (C-$4_{(II)}$). IR (Nujol, cm^{-1}): ν = 3155 (br), 2945 (m), 1729 (m), 1708 (m), 1339 (m), 1239 (w), 1353 (s), 764 (w). MS (CI pos.; 70 eV) m/z (%) = 323.0 ($[M+1]^+$, 80), 244 (12), 220 (66), 188 (100), 130 (15), 85 (33). HRMS (CI neg.): calcd for $C_{19}H_{16}NO_4$ ($[M]^-$): 322.1074; found: 322.1075.

Typical procedure for the preparation of (8): To a CH_2Cl_2 solution (6 mL) of **7b** (0.1 g, 0.35 mmol) and I_2 (0.17 g 0.70 mmol) was added a saturated solution of $NaHCO_3$ (3.5

mL) and the solution were stirred for 12 h at 20 °C. The excess of iodine was removed by addition of a saturated aqueous solution of sodium sulfite (20 mL). The organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1) to give **8a** (0.110 g, 86%), as yellow oil.

13-Iodo-11-oxo-10-propyl-12-oxa-8-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene-8-carboxylic acid methyl ester (8a): A mixture of intermediate (7a) (0.090 g, 0.31 mmol) was treated with I_2 (0.086 g, 0.34 mmol) and saturated $NaHCO_3$ soln (3.6 mL) in CH_2Cl_2 (7.0 mL), (**8a**) (0.110 g, 86%), was isolated as yellow oil. There was a bit unreacted intermediate as well. ^{1}H NMR (500 MHz, $CDCl_3$, dr = 1:1): δ = 7.78 (br s, 1H, H-8), 7.38 (m, 1H, H-7), 7.35-7.31 (m, 2H, H-7, H-5), 7.17 (m, 2H, H-6,6), 5.62 (br s, 1H, H-2), 5.35-5.27 (m, 4H, H-2, H-3, H-4,4), 4.92 („t“, 1H, $^3J_{2,3} = {}^3J_{3,4} = 3.0$ Hz, H-3), 3.88 (s, 3H, OMe), 3.78 (s, 3H, OMe), 2.90-2.86 (m, 1H, H-9), 2.74 (br m, 1H, H-9), 1.91-1.84 (m, 1H, H-10), 1.66-1.36 (m, 7H, H-10, H-11), 0.95 (t, 3H, J = 7.3 Hz, Me), 0.90 (t, 3H, J = 7.3 Hz, Me). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3 (COO), 155.3 (NCO), 136.3, 133.3 (C-8a), 131.2, 130.4 (C-7), 129.6 (C-5), 127.8, 127.7 (br, C-5, C-8), 126.9 (br), 125.4 (C-6), 124.4 (C-8), 123.0 (C-4a), 81.4, 77.5 (C-4), 55.4, 55.2 (C-2), 53.8 (OMe), 45.3, 43.3 (br) (C-9), 31.0, 27.3 (C-10), 20.8, 20.3 (C-11), 14.0, 13.8 (Me). IR (KBr, cm^{-1}): ν = 3432 (br), 2923 (w), 1698 (s), 1494 (m), 1213 (m), 921 (w), 703 (s). MS (EI, 70 eV): m/z (%) = 415.0 (M^+, 17), 314 (28), 288 (62), 204 (100), 188 (27), 144 (27), 128 (21). HRMS (EI): calcd for $C_{16}H_{18}INO_4$ ($[M]^+$): 415.0275; found: 415.0268.

13-Iodo-10-0ctyl-11-oxo-12-oxa-8-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene-8-carboxylic acid methyl ester (8b, *syn*): The intermediate 7b (*syn*) (0.147 g, 0.41 mmol) was treated with I_2 (0.133 g, 0.45 mmol) and saturated $NaHCO_3$ soln (4.0 mL) in CH_2Cl_2 (7.0 mL), **(8b)** (0.103 g, 52%), was isolated as brown solid; mp. 101-102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97 (br d, 1H, $^3J_{7,8} = 8.5$ Hz, H-8), 7.39 (ddd, 1H, $^3J_{7,8} = 8.5$ Hz, $^3J_{6,7} = 7.5$ Hz, $^4J_{5,7} = 1.5$ Hz, H-7), 7.35 (dd, 1H, $^3J_{5,6} = 7.7$ Hz, $^4J_{5,7} = 1.5$ Hz, H-5), 7.15 (d„t“, 1H, $^3J_{5,6} = 7.7$ Hz, $^3J_{6,7} = 7.5$ Hz, $^4J_{6,8} = 1.0$ Hz, H-6), 5.34 („t“, 1H, $^3J_{3,4} = 3.0$ Hz, $^4J_{2,4} = 2.5$ Hz, H-4), 4.98 (br, 1H, H-2), 4.77 („t“, 1H, $^3J_{3,4} = {}^3J_{2,3} = 3.0$ Hz, H-3), 3.89 (s, 3H, OMe), 2.73 (ddd, 1H, $^3J_{9,10} = 8.5$ Hz, $^3J_{9,10} = 4.5$ Hz, $^3J_{9,10'} = 4.5$ Hz, $^3J_{2,9} = 1.0$ Hz, H-9), 1.91 (m, 1Ha, H-10), 1.77 (m, 1Hb, H-10), 1.53 (m, 1Ha, H-11), 1.42 (m, 1Hb, H-11),

1.36-1.23 (m, 10H, H-12,13,14,15,16), 0.88 (t, 3H, $^3J_{CH2,CH3}$ = 7.0 Hz, H-17$_{(Me)}$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5 (COO), 154.2 (NCO), 134.0 (C-8a), 131.5 (C-5), 130.7 (C-7), 124.6 (C-6), 123.0 (C-8), 121.7 (C-4a), 77.6 (C-4), 56.8 (C-2), 53.6 (OMe), 47.4 (C-9), 33.2 (C-10), 31.8, 29.3, 29.3, 29.2, (C-12,13,14,15), 26.7 (C-11), 22.6 (C-16), 17.8 (C-3), 14.0 (C-17$_{(Me)}$). IR (KBr, cm^{-1}): ν = 3416 (br), 2916 (s), 1771 (s), 1716 (s), 1442 (m), 1331 (s), 1166 (m), 950 (m), 759 (m). MS (EI, 70 eV): m/z (%) = 485.0 (M^+, 74), 314 (82), 204 (20), 188 (100), 144 (30), 129 (15). HRMS (EI): calcd for $C_{21}H_{28}NIO_4$ ($[M]^+$): 485.10575; found: 4485.10581.

13-Iodo-11-oxo-12-phenyl-10-oxa-8-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene-8-carboxylic acid methyl ester (8c, *anti*): The intermediate (**7c)** (0.300 g, 0.93 mmol), was treated with I_2 (0.260 g, 1.02 mmol) and saturated $NaHCO_3$ soln (10.0 mL) in CH_2Cl_2 (15.0 mL), **(8c)** (0.210 g, 50%), was isolated as light yellow solid; mp. 73 °C. 1H NMR (500 MHz, $CDCl_3$): δ = 8.27 (dd, 1H, $^3J_{7,8}$ = 8.5 Hz, $^4J_{6,8}$ = 1.0 Hz, H-8), 7.44 (m, 2H, *m*, *m*-Ph), 7.39-7.35 (m, 2H, H-7,*p*-Ph), 7.28 (m, 3H, H-5, *o*, *o*'-Ph), 7.21 (d,,t", 1H, $^3J_{5,6}$ = $^3J_{6,7}$ = 7.3 Hz, $^4J_{6,8}$ = 1.0 Hz, H-6), 6.84 (dd, 1H, $^3J_{2,3}$ = 3.8 Hz, $^4J_{2,4}$ = 2.0 Hz, H-2), 4.94 (dd, 1H, $^3J_{2,3}$ = 3.8 Hz, $^3J_{3,4}$ = 2.2, H-3), 4.18 (d, 1H, $^3J_{4,9}$ = 2.2 Hz, H-9), 3.93 (s, 3H, OMe), 3.55 („q", 1H, $^3J_{4,9}$ = $^3J_{3,4}$ = 2.2 Hz, $^4J_{2,4}$ = 2.0 Hz, H-4). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.2 (COO), 153.5 (NCO), 136.6 (*i*-Ph), 132.2 (C-8a), 129.5 (C-5); 129.4 (*m*-Ph), 129.3 (C-7), 128.2 (*p*-Ph), 127.6 (*o*-Ph), 125.1 (C-6), 124.6 (C-4a), 122.0 (C-8), 84.4 (C-2), 57.8 (C-9), 53.9 (OMe); 48.0 (C-4), 12.8 (C-3). MS (CI; 70 eV) m/z (%) = 449.0 (M^+, 9), 321(53), 219 (34), 203 (100), 159 (32), 129 (54), 90 (25). HRMS (CI): calcd for $C_{19}H_{16}NIO_4$ ($[M]^+$): 449.0119; found: 449.0113.

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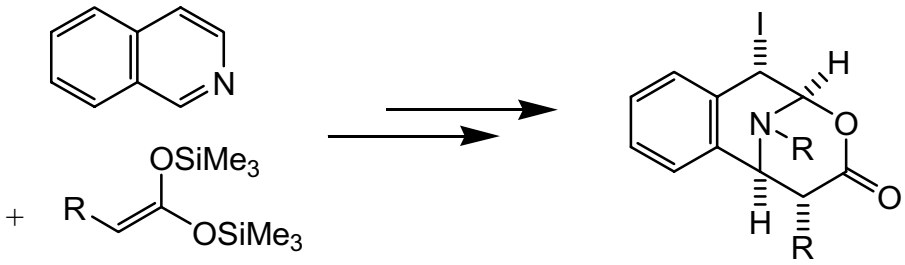
Graphic abstract



Publication 7

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Synthesis of 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline

Sven Rotzoll,[a,b] Ehsan Ullah,[a,b,c] Christine Fischer,[b] Dirk Michalik,[b] Anke Spannenberg[b] and Peter Langer[a,b,*]

[a]*Institut für Chemie, Universität Rostock, Albert-Einstein-Strasse 3a, D-18059 Rostock, Germany*
[b]*Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Strasse 29a, D-18059 Rostock, Germany*
[c]*Institut für Biochemie, Universität Greifswald, Friedrich-Ludwig-Jahn-Strasse 18c, D-17487 Greifswald, Germany*

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Abstract—1,4-Diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones were prepared by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline.

1. Introduction

1,1-Bis(trimethylsiloxy)ketene acetals represent interesting synthetic building blocks, which can be regarded as masked carboxylic acid dianions.[1–3] Rudler et al. were the first to report the use of 1,1-bis(trimethylsiloxy)ketene acetals as 1,3-dinucleophiles in cyclization reactions: In 1999, they reported the synthesis of lactones by reaction of 1,1-bis(trimethylsiloxy)ketene acetals with chromium(0) complexes.[4] In 2000, Rudler et al. developed the palladium(0) catalysed reaction of 1,1-bis(trimethylsiloxy)ketene acetals with allyl acetates to give γ-unsaturated carboxylic acids, which were transformed into 5-(hydroxymethyl)-γ-lactones by addition of H_2O_2 in the presence of catalytic amounts of methyltrioxorhenium (MTO).[5] Rudler et al. also reported interesting reactions of 1,1-bis(trimethylsiloxy)ketene acetals with tropylium derivatives.[6] We reported the cyclocondensation of 1,1-bis(trimethylsiloxy)ketene acetals with oxalyl chloride[7] and 3-(siloxy)alk-2-en-1-ones to give maleic anhydrides and pyran-2-ones, respectively.[8]

Pyridinium salts represent important synthetic building blocks, which can be generated in situ by acylation of pyridines.[9] They have been used in various reactions with Grignard reagents, cyanide (Reissert reaction), trimethylsilylacetonitrile, allylsilanes, silyl enol ethers or diazoesters.[10] We reported the cyclization of 1,3-bis(silyl enol ethers)[11]—masked 1,3-dicarbonyl dianions—with isoquinoline.[12] In 2002, Rudler et al. reported the first cyclocondensations of 1,1-bis(trimethylsiloxy)ketene acetals with pyridine[13a] and later extended this interesting concept to other *N*-heterocycles.[13b] We reported the cyclocondensation of 1,1-bis(trimethylsiloxy)ketene acetals with isoquinoline.[14] Recently, Rudler et al. reported the first cyclizations of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine[13b,15] and quinoxaline.[15] These reactions provide a facile access to 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones and 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones, respectively. Herein, we report our own findings in this field. With regard to the previous report of Rudler et al.,[15] we extensively studied the preparative scope of the reactions. In addition, 2-monosubstituted 1,1-bis(trimethylsiloxy)ketene acetals have been employed by us, which give rise to questions of stereochemistry. The isomeric products could be successfully separated for the first time and their structure unambiguously assigned.

2,3-Benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones and 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones are of biological relevance as they represent analogues of clofazimine, riboflavin (vitamin B_2) and lumiflavin. The substituted dihydrophenazine clofazimine represents an important drug against leprosy and is also effective against a number of diseases related to the autoimmune system.[16] However, there are serious problems, such as bacterial resistance.[16] Therefore, the development of suitable clofazimine analogues is of pharmacological relevance.

Keywords: Cyclizations; Heterocycles; Iminium salts; Pyrazine; Quinoxaline; Silyl enol ethers.
* Corresponding author. Tel.: +49 381 4986410; fax: +49 381 4986412; e-mail: peter.langer@uni-rostock.de

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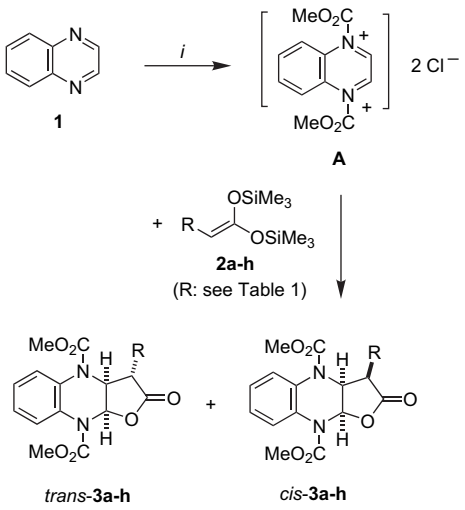
2. Results and discussion

The reaction of 1,1-bis(trimethylsiloxy)ketene acetal **2a** (1.4 equiv)[17] with quinoxaline (**1**) (1.0 equiv) in the presence of methyl chloroformate (4.0 equiv) afforded the 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-one **3a** as a separable mixture of diastereomers *trans*-**3a** and *cis*-**3a** (Scheme 1 and Table 1). During the optimization of the cyclocondensation, the activating agent, stoichiometry, temperature and concentration played an important role. The formation of **3a** can be explained by formation of bis(iminium salt) **A**, attack of the carbon atom of **2a** onto **A** and subsequent cyclization. Alternatively, the reaction may proceed by formation of a simple iminium salt, reaction of the latter with **2a**, acylation of the second nitrogen atom and subsequent cyclization.



Scheme 1. Cyclization of 1,1-bis(siloxy)ketene acetals **2a**–**h** with **1**. *i*, **1** (1.0 equiv), **2** (1.4 equiv), $ClCO_2Me$ (4.0 equiv), CH_2Cl_2, 20 °C, 12 h.

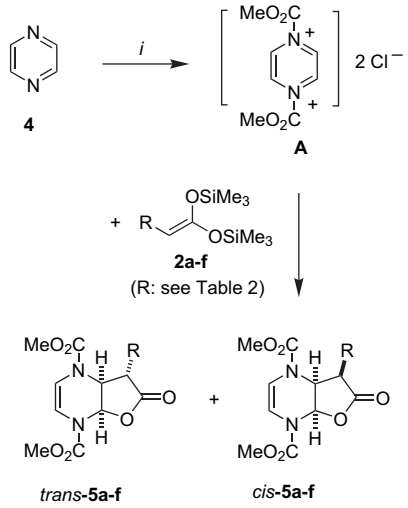
The preparative scope of the methodology was studied (Scheme 1 and Table 1). The reaction of **1** with 1,1-bis(trimethylsiloxy)ketene acetals **2b**–**h**, prepared from the corresponding alkanoic acids, afforded the 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones **3b**–**h** as separable mixtures of diastereomers. As expected, a cis-annulation was observed for all 5,6-bicyclic products, due to steric reasons. In contrast to the reaction of isoquinoline with 1,1-bis(trimethylsiloxy)ketene acetals, the reaction of the latter with quinoxaline proceeded with low 1,2-diastereoselectivity. However, the isomers could be separated by chromatography, due to their different polarity.

Table 1. Products and yields

3	R	% (*trans*-**3**)[a]	% (*cis*-**3**)[a]
a	Et	19	28
b	^{n}Pr	29	21
c	^{n}Bu	11	25
d	^{n}Dodec	30	15
e	^{i}Pr	27	33
f	^{c}Hex	28	27
g	$CH_2(^c$Pent)	32	24
h	$(CH_2)_2(^c$Hex)	25	12

[a] Yields of isolated products.

The reaction of 1,1-bis(trimethylsiloxy)ketene acetal **2a** (1.4 equiv) with pyrazine (**4**) (1.0 equiv) in the presence of methyl chloroformate (4.0 equiv) afforded the 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-one **5a** as a separable mixture of diastereomers *trans*-**5a** and *cis*-**5a** (Scheme 2 and Table 2). The reaction of **4** with 1,1-bis(trimethylsiloxy)-ketene acetals **2b–f** afforded the 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones **5b–f** as separable mixtures of diastereomers.



Scheme 2. Cyclization of 1,1-bis(siloxy)ketene acetals **2a–f** with **4**: *i*, **4** (1.0 equiv), **2** (1.4 equiv), $ClCO_2Me$ (4.0 equiv), CH_2Cl_2, 20 °C, 12 h.

The relative configurations for chinoxalines **3** and pyrazines **5** were proved by NOESY experiments. In the NOESY spectra recorded for **3b**, **3f**, **3g** and **5e** cross peaks could be observed for the hydrogen atoms H-2 with H-9 (**3b**, **3f**, **3g**) and H-2 with H-7 (**5e**), respectively, only in the case of cis-compounds. The atom numbering for NMR assignment of **3** and **5** is given in Scheme 3. The cis- or trans-configuration of the other compounds **3** and **5** could be confirmed based on chemical shifts. Thus, the H-3 signals for the cis-compounds are generally shifted downfield compared to the trans-compounds. It should be noted that some signals in the ^{1}H and ^{13}C spectra appeared as broadened or doubled signals due to dynamic processes (hindered rotation about the NCO bonds).

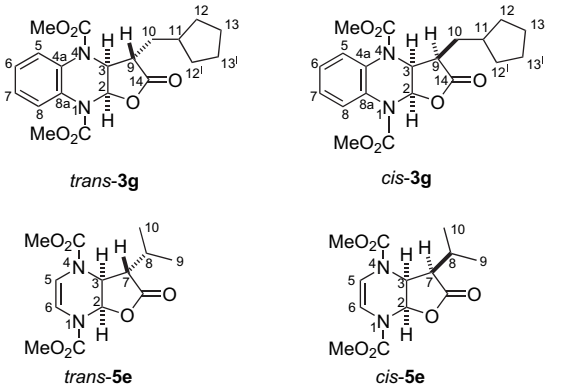
The configuration of *cis*-**5e** was independently confirmed by X-ray crystal structure analysis (Fig. 1).[18] The trans-isomers generally proved to be less polar (R_f value) than the cis-isomers.

In conclusion, we have reported—based on previous work of Rudler et al.[15]—the synthesis of a number of

Table 2. Products and yields

5	R	% (*trans*-**5**)[a]	% (*cis*-**5**)[a]
a	Et	24	0
b	^{n}Pr	40	26
c	^{n}Bu	30	39
d	^{n}Dodec	26	20
e	^{i}Pr	20	35
f	^{c}Hex	38	11

[a] Yields of isolated products.



Scheme 3. Atom numbering of quinoxaline **3g** and pyrazine **5e** for NMR assignment.

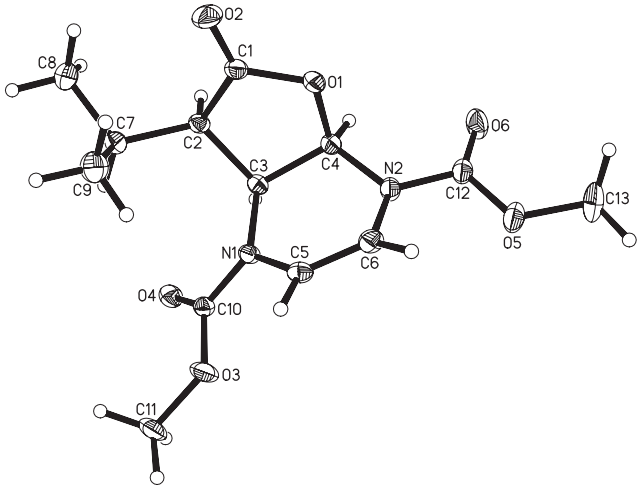


Figure 1. Ortep plot of *cis*-**5e**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms.

1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline.

3. Experimental

3.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR, the deuterated solvents indicated were used. The ^{1}H NMR (250.13 and 300.13 MHz) and ^{13}C NMR (62.9 and 75.5 MHz) were recorded on Bruker spectrometers AC 250 and ARX 300, respectively, at 300 K. In addition to the routine measurements, the spectra of **3b**, **3f**, **3g** and **5e** were recorded on a Bruker spectrometer AVANCE 500 (^{1}H: 500.13 MHz and ^{13}C: 125.8 MHz). Calibration of spectra was carried out on solvent signals ($CDCl_3$: δ ^{1}H=7.25, δ ^{13}C=77.0; DMSO-d_6: δ ^{1}H=2.50, δ ^{13}C=39.7). The NMR signals were assigned by DEPT and two-dimensional $^{1}H,^{1}H$ COSY, $^{1}H,^{1}H$ NOESY and $^{1}H,^{13}C$ correlation spectra (HSQC, HMBC). Mass spectrometric data (MS) were obtained by electron ionization (70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

3.1.1. Typical procedure for the synthesis of 2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxalines 3a–h and 6-oxo-7,7a-dihydrofuro[3,2-*b*]pyrazines 5a–f. To a CH_2Cl_2 solution (50 mL) of quinoxaline (0.325 g, 2.5 mmol) and 2-methylcyclopentyl-1,1-bis(trimethylsilyloxy)ethene (1.003 g 3.5 mmol) was slowly added methyl chloroformate (0.945 g, 10.0 mmol) at 20 °C. The solution was stirred for 12 h at 20 °C. The solvent was removed in vacuo and the residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 20:1 to 5:1) to give *trans*-**3g** (0.315 g, 32%) and *cis*-**3g** (0.225 g, 24%) as colourless solids. Due to the restricted rotation in the urethane moiety, compounds **3** and **5** appeared as mixtures of two rotamers. All compounds were formed as racemates.

3.1.1.1. Dimethyl 3-ethyl-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3a). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-ethyl-1,1-bis-(trimethylsilyloxy)ethene (**2a**) (0.650 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3a** (0.125 g, 19%) was isolated as a colourless solid, mp 147 °C; *cis*-**3a** (0.185 g, 27%) was isolated as a colourless solid, mp 147 °C.

Data of *trans*-**3a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.23–7.17 (m, 2H, Ar), 6.70 (d, 1H, $^{3}J_{2,3}$=8.8 Hz, H-2), 5.50 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.45–2.36 (m, 1H, H-9), 1.92–1.84 (m, 1H, CH_2), 1.82–1.65 (m, 1H, CH_2), 1.03 (t, 3H, ^{3}J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.6 (COO), 153.9 (br) (2NCO), 130.5, 130.3 (C_{Ar}), 126.5, 126.2, 126.1, 125.9 (CH_{Ar}), 86.0 (C-2), 59.1 (C-3), 53.9, 53.7 (OCH_3), 43.2 (C-9), 22.7 (CH_2), 10.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br), 2965 (m), 1715 (s), 1506 (m), 1325 (s), 1165 (s), 950 (s), 755 (w). MS (EI; 70 eV): *m*/*z* (%)=334 ([M]$^+$, 100), 306 (39), 247 (43), 235 (54), 145 (25), 59 (21). HRMS (EI) calcd for $C_{16}H_{18}N_2O_6$ ([M]$^+$): 334.1159; found: 334.1154.

Data of *cis*-**3a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.30–7.19 (m, 2H, Ar), 6.92 (d, 1H, $^{3}J_{2,3}$=8.0 Hz, H-2), 5.73 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.66 (m, 1H, H-9), 1.71–1.50 (m, 2H, CH_2), 1.12 (t, 3H, ^{3}J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.3 (COO), 155.0, 153.6 (2NCO), 130.9, 130.3 (C_{Ar}), 126.8, 126.4, 126.3, 125.6 (CH_{Ar}), 86.4 (C-2), 58.9 (C-3), 53.9, 53.8 (OCH_3), 44.7 (C-9), 19.1 (CH_2), 12.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br), 2965 (m), 1715 (s), 1506 (m), 1325 (s), 1165 (s), 950 (s), 755 (w). MS (EI; 70 eV): *m*/*z* (%)=334 ([M]$^+$, 100), 306 (39), 247 (43), 235 (54), 145 (25), 59 (21). HRMS (EI) calcd for $C_{16}H_{18}N_2O_6$ ([M]$^+$): 334.1159; found: 334.1153.

3.1.1.2. Dimethyl 3-propyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3b). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 2-propyl-1,1-bis-(trimethylsilyloxy)ethene (**2b**) (0.863 g, 3.5 mmol) and methyl

chloroformate (0.78 mL, 10.25 mmol), *trans*-**3b** (0.252 g, 29%) was isolated as a colourless solid, mp 99–100 °C; *cis*-**3b** (0.183 g, 21%) was isolated as a colourless solid, mp 142–143 °C.

Data of *trans*-**3b**: ^{1}H NMR (500 MHz, DMSO-d_6): δ=7.51–7.48 (m, 1H, H-8), 7.41 (br, 1H, H-5), 7.28–7.23 (m, 2H, H-6,7), 6.73 (d, 1H, $^3J_{2,3}$=8.8 Hz, H-2), 5.53 (br t, 1H, H-3), 3.78 (s, 3H, OCH_3), 3.73 (br s, 3H, OCH_3), 2.34 (m, 1H, H-9), 1.70–1.59 (m, 2H, CH_2), 1.45–1.36 (m, 2H, CH_2), 0.84 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=175.1 (COO), 153.8, 153.5 (br) (2NCO), 130.8 (C-4a), 130.6 (C-8a), 126.5 (br), 126.3 (br), 126.2, 125.6 (C-5,6,7,8), 86.6 (C-2), 59.6 (C-3), 53.9, 53.5 (OCH_3), 41.6 (C-9), 31.4, 19.2 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3427 (br, w), 2961 (m), 2974 (w), 1792 (s), 1730 (br, s), 1596 (w), 1505 (s), 1441 (s). MS (EI, 70 eV): *m*/*z* (%)=348 ([M]$^+$, 100), 320 (68), 291 (97), 261 (34), 235 (77), 145 (30). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (348.35): C, 58.61; H, 5.79; N, 8.04. Found: C, 58.37; H, 5.81; N, 7.85.

Data of *cis*-**3b**: ^{1}H NMR (500 MHz, DMSO-d_6): δ=7.47–7.43 (m, 1H, H-8), 7.39 (br, 1H, H-5), 7.27–7.22 (m, 2H, H-6,7), 6.92 (d, 1H, $^3J_{2,3}$=8.0 Hz, H-2), 5.61 (br t, 1H, H-3), 3.80 (s, 3H, OCH_3), 3.70 (br s, 3H, OCH_3), 3.00 (ddd, 1H, $^3J_{3,9}$=9.5 Hz, $^3J_{9,10a}$=7.5 Hz, $^3J_{9,10b}$=6.3 Hz, H-9), 1.53–1.30 (m, 4H, CH_2), 0.87 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=175.1 (COO), 154.3 (br, NCO), 153.4 (NCO), 131.2 (C-4a), 130.7 (C-8a), 126.6 (br), 126.5 (br), 126.2 (C-5,6,7), 125.3 (C-8), 86.8 (C-2), 59.1 (C-3), 53.9 (OCH_3), 53.7 (br, OCH_3), 41.9 (C-9), 27.2, 20.3 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br, w), 2963 (m), 2867 (w), 1774 (s), 1713 (br, s), 1597 (m), 1508 (s), 1441 (s), 1330 (br, s). MS (EI, 70 eV): *m*/*z* (%)=348 ([M]$^+$, 94), 320 (55), 291 (100), 261 (25), 235 (55), 145 (37). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (348.35): C, 58.61; H, 5.79; N, 8.04. Found: C, 58.23; H, 5.91; N, 7.97.

3.1.1.3. Dimethyl 3-butyl-2-oxo-3,3a-dihydrofuro[2,3-*b*]-quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3c). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-butyl-1,1-bis(trimethylsilyloxy)ethene (**2c**) (0.728 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3c** (0.083 g, 11%) was isolated as a colourless solid, mp 125–126 °C; *cis*-**3c** (0.180 g, 25%) was isolated as a colourless oil.

Data of *trans*-**3c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.50 (br, 1H, Ar), 7.32 (br, 1H, Ar), 7.25–7.17 (m, 2H, Ar), 6.69 (d, 1H, $^3J_{2,3}$=8.8 Hz, H-2), 5.48 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.48–2.34 (m, 1H, H-9), 1.90–1.78 (m, 1H, CH_2), 1.71–1.56 (m, 1H, CH_2), 1.46–1.22 (m, 4H, CH_2), 1.03 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.0 (2NCO), 130.6, 130.3 (C_{Ar}), 126.5, 126.2 (2), 126.0 (CH_{Ar}), 86.0 (C-2), 59.6 (C-3), 54.0, 53.7 (OCH_3), 41.8 (C-9), 29.4, 28.2, 22.2 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3425 (br), 2960 (m), 1789 (s), 1507 (s), 1332 (s), 1162 (s), 971 (s), 745 (w). MS (EI; 70 eV): *m*/*z* (%)=362 ([M]$^+$, 100), 291 (65), 275 (33), 235 (55), 189 (14), 145 (26), 59 (20). HRMS (EI) calcd for $C_{18}H_{22}N_2O_6$ ([M]$^+$): 362.1472; found: 362.1461.

Data of *cis*-**3c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, ArH), 7.23–7.19 (m, 3H, ArH), 6.92 (d, 1H, $^3J_{2,3}$=8.2 Hz, H-2), 5.74 (br, 1H, H-3), 3.87 (s, 3H, OCH_3), 3.78 (br s, 3H, OCH_3), 2.75–2.66 (m, 1H, H-9), 1.59–1.29 (m, 6H, CH_2), 0.91 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.4 (COO), 154.9 (br) (2NCO), 131.0, 130.3 (C_{Ar}), 126.8, 126.4, 126.3, 125.6 (CH_{Ar}), 86.5 (C-2), 58.8 (C-3), 53.9, 53.7 (OCH_3), 43.0 (C-9), 29.7, 25.2, 22.5 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3420 (br), 2954 (m), 1715 (s), 1508 (s), 1331 (s), 1160 (s), 965 (s), 754 (w). MS (EI; 70 eV): *m*/*z* (%)=362 ([M]$^+$, 100), 291 (63), 275 (32), 235 (51), 189 (17), 145 (28), 59 (21). HRMS (EI) calcd for $C_{18}H_{22}N_2O_6$ ([M]$^+$): 362.1472; found: 362.1462.

3.1.1.4. Dimethyl 3-dodecyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3d). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 2-dodecyl-1,1-bis-(trimethylsilyloxy)ethene (**2d**) (1.304 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**3d** (0.355 g, 30%) was isolated as a colourless solid, mp 100–101 °C; *cis*-**3d** (0.178 g, 15%) was isolated as a colourless solid, mp 119–120 °C.

Data of *trans*-**3d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.31 (br, 1H, Ar), 7.26–7.21 (m, 2H, Ar), 6.70 (d, 1H, $^3J_{2,3}$=8.7 Hz, 1H, H-2), 5.49 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.82 (br s, 3H, OCH_3), 2.47–2.42 (m, 1H, H-9), 1.85–1.60 (br m, 2H, CH_2), 1.46–1.39 (m, 2H, CH_2), 1.38–1.24 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=6.7 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.1, 154.0 (NCO), 130.6, 130.4 (C_{Ar}), 126.6, 126.2 (2), 125.9 (CH_{Ar}), 86.0 (C-2), 59.7 (C-3), 53.9, 53.7 (OCH_3), 41.8 (C-9), 31.9, 29.7, 29.6 (3), 29.5, 29.4, 29.3, 29.2, 26.1, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3413 (br, w), 2919 (s), 2849 (m), 1771 (s), 1716 (br, s), 1595 (w), 1508 (s), 1441 (m). MS (EI, 70 eV): *m*/*z* (%)=474 ([M]$^+$, 100), 387 (19), 291 (62), 235 (55), 145 (20). HRMS (EI) calcd for $C_{26}H_{38}N_2O_6$ ([M]$^+$): 474.27244; found: 474.27190.

Data of *cis*-**3d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, Ar), 7.26–7.19 (m, 3H, Ar), 6.92 (d, 1H, $^3J_{2,3}$=8.3 Hz, H-2), 5.73 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.71 (m, 1H, H-9), 1.62–1.52 (m, 4H, CH_2), 1.47–1.13 (m, 18H, CH_2), 0.87 (t, 3H, ^3J=6.7 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.4 (COO), 153.6 (2NCO), 131.0, 130.4 (C_{Ar}), 126.8, 126.4 (2), 125.6 (CH_{Ar}), 86.4 (C-2), 58.8 (C-3), 53.8, 53.7 (br) (OCH_3), 43.1 (C-9), 31.9, 29.6 (3), 29.5 (2), 29.3 (2), 27.5, 25.6, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3419 (br, w), 2918 (s), 2849 (m), 1773 (s), 1715 (br, s), 1596 (w), 1509 (s), 1472 (m). MS (EI, 70 eV): *m*/*z* (%)=474 ([M]$^+$, 100), 387 (13), 291 (40), 235 (34), 145 (15). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (474.58): C, 65.80; H, 8.07; N, 5.90. Found: C, 66.00; H, 8.20; N, 5.59.

3.1.1.5. Dimethyl 3-isopropyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3e). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-isopropyl-1,1-bis(trimethylsilyloxy)ethene (**2e**) (0.728 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3e** (0.185 g, 27%) was isolated as a brownish solid, mp

159–160 °C; *cis*-**3e** (0.232 g, 33%) was isolated as a brownish solid, mp 168–169 °C.

Data of *trans*-**3e**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.50 (br, 1H, Ar), 7.26–7.19 (m, 3H, Ar), 6.67 (d, 1H, $^3J_{2,3}$=8.9 Hz, H-2), 5.60 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (br s, 3H, OCH_3), 2.40 (dd, 1H, $^3J_{3,9}$=7.6 Hz, $^3J_{9,CH}$=4.2 Hz, H-9), 2.32–2.22 (m, 1H, CH), 1.03 (d, 3H, ^3J=7.0 Hz, CH_3), 1.00 (d, 3H, ^3J=6.8 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.1 (COO), 153.8 (2NCO), 130.7, 130.4 (C_{Ar}), 126.5, 126.2 (2), 125.7 (CH_{Ar}), 86.2 (C-2), 56.2 (C-3), 53.9, 53.6 (OCH_3), 48.0 (C-9), 28.2 (CH), 19.5, 18.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3413 (br), 2959 (m), 1715 (s), 1507 (m), 1330 (s), 1165 (s), 959 (s), 766 (w). MS (EI; 70 eV): *m/z* (%)=348.1 ([M]$^+$, 100), 320 (48), 305 (49), 261 (73), 235 (64), 145 (27). HRMS (EI) calcd for $C_{17}H_{20}N_2O_6$ ([M]$^+$): 348.13159; found: 348.13137.

Data of *cis*-**3e**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.26–7.14 (m, 3H, Ar), 6.84 (d, 1H, $^3J_{2,3}$=7.8 Hz, H-2), 5.77 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.75 (br s, 3H, OCH_3), 2.56 (dd, 1H, $^3J_{3,9}$=9.2 Hz, $^3J_{9,CH}$=6.1 Hz, H-9), 2.08–2.00 (m, 1H, CH), 1.11 (d, 3H, ^3J=6.8 Hz, CH_3), 1.04 (d, 3H, ^3J=6.8 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.3 (COO), 153.8 (2NCO), 130.8, 130.5 (C_{Ar}), 127.1, 127.0, 126.0, 125.4 (CH_{Ar}), 85.4 (C-2), 59.7 (C-3), 53.8 (2 OCH_3), 49.0 (C-9), 25.5 (CH), 22.7, 19.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3428 (br), 2954 (m), 1711 (s), 1507 (m), 1328 (s), 1161 (s), 1008 (s), 765 (w). MS (EI; 70 eV): *m/z* (%)=348.1 ([M]$^+$, 100), 320 (81), 305 (58), 261 (78), 235 (68), 145 (29). Anal. Calcd for $C_{19}H_{22}N_2O_6$ (348.35): C, 58.61; H, 5.79, N, 8.04. Found: C, 58.98; H, 5.86; N, 7.83.

3.1.1.6. Dimethyl 3-cyclohexyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3f). Starting with quinoxaline (**1**) (0.190 g, 1.45 mmol), 2-cyclohexyl-1,1-bis(trimethylsilyloxy)ethene (**2f**) (0.580 g, 2.03 mmol) and methyl chloroformate (0.54 mL, 5.80 mmol), *trans*-**3f** (0.160 g, 28%) was isolated as a colourless solid, mp 169–170 °C; *cis*-**3f** (0.150 g, 27%) was isolated as a colourless solid, mp 205–206 °C.

Data of *trans*-**3f**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.60 (br, 1H, Ar), 7.27 (br, 1H, Ar), 7.23–7.18 (m, 2H, Ar), 6.66 (d, 1H, $^3J_{2,3}$=8.5 Hz, H-2), 5.62 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.40 (dd, 1H, $^3J_{3,9}$=7.0 Hz, $^3J_{9,10}$=4.5 Hz, H-9), 1.89–1.55 (m, 6H, ring CH, ring CH_2), 1.31–1.15 (m, 5H, ring CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=174.2 (COO), 153.9 (br, 2NCO), 130.7, 130.4 (C-4a,8a), 126.7, 126.5, 126.2, 125.9 (CH_{Ar}), 86.3 (C-2), 56.9 (C-3), 53.9, 53.7 (OCH_3), 48.2 (C-9), 38.4 (CH), 30.0, 28.5, 26.3, 26.0, 25.8 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (br), 2927 (m), 1715 (s), 1506 (m), 1329 (s), 1157 (s), 960 (s), 751 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 360 (21), 301 (21), 252 (25), 192 (19), 145 (18). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.81; H, 6.16; N, 6.77.

Data of *cis*-**3f**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.45 (br, 1H, Ar), 7.30 (br, 1H, Ar), 7.24–7.15 (m, 2H, Ar), 6.83 (d, 1H, $^3J_{2,3}$=7.9 Hz, H-2), 5.76 (br s, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.57 (dd, 1H, $^3J_{3,9}$=9.5 Hz, $^3J_{9,10}$=5.4 Hz, H-9), 1.75–1.61 (m, 6H, ring CH, ring CH_2), 1.28–1.12 (m, 5H, ring CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=172.5 (COO), 155.2, 153.5 (NCO), 131.1, 130.5 (C-4a,8a), 127.0 (br), 126.8 (br), 126.0, 125.5 (CH_{Ar}), 85.6 (C-2), 59.5 (C-3), 53.8 (2C, OCH_3), 48.2 (C-9), 35.5 (CH), 32.7, 29.1, 26.6, 26.2, 25.9 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3428 (br), 2928 (m), 1714 (s), 1506 (s), 1327 (s), 1159 (m), 966 (s), 753 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 360 (25), 301 (19), 252 (24), 235 (40), 192 (20), 145 (22). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.80; H, 6.08; N, 6.62.

3.1.1.7. Dimethyl 3-(cyclopentylmethyl)-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3g). Starting with quinoxaline (**1**) (0.325 g, 2.5 mmol), 2-methylcyclopentyl-1,1-bis(trimethylsilyloxy)ethene (1.003 g, 3.5 mmol) and methyl chloroformate (0.945 g, 10.0 mmol), *trans*-**3g** (0.315 g, 32%) was isolated as a colourless solid, mp 129 °C; *cis*-**3g** (0.225 g, 24%) was isolated as a colourless solid, mp 174 °C.

Data of *trans*-**3g**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.51 (br, 1H, Ar), 7.30 (br, 1H, Ar), 7.24–7.19 (m, 2H, Ar), 6.69 (d, 1H, $^3J_{2,3}$=8.5 Hz, H-2), 5.50 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (br s, 3H, OCH_3), 2.43 (m, 1H, H-9), 2.06 (br m, 1H, H-11), 1.82–1.48 (m, 8H, H-10,12a,12′a,13,13′), 1.09–0.97 (m, 2H, H-12b,12′b). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=175.2 (C-14), 154.1 (br, NCO), 154.0 (NCO), 126.6 (CH_{Ar}), 126.3 (br, CH_{Ar}), 126.2, 125.9 (CH_{Ar}), 86.0 (C-2), 60.1 (C-3), 53.9 (OCH_3), 53.7 (br, OCH_3), 40.9 (C-9), 36.7 (C-11), 36.3 (C-10), 32.9, 31.8 (C-12,12′), 25.1, 25.0 (C-13,13′). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (br, w), 2958 (m), 2870 (w), 1787 (s), 1725 (s), 1593 (m), 1507 (s). MS (EI, 70 eV): *m/z* (%)=388 ([M]$^+$, 99), 291 (100), 235 (45), 189 (25), 145 (28). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 62.16; H, 6.43; N, 6.84.

Data of *cis*-**3g**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.27 (br, 1H, Ar), 7.23–7.17 (m, 2H, Ar), 6.92 (d, 1H, $^3J_{2,3}$=8.2 Hz, H-2), 5.73 (br, 1H, H-3), 3.76 (br s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.76 (m, 1H, H-9), 2.16 (m, 1H, H-11), 1.78 (m, 2H, H-12a,12′a), 1.65–1.43 (m, 6H, H-10,13,13′), 1.08 (m, 2H, H-12b,12′b). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=174.5 (C-14), 155.0, 153.5 (NCO), 126.8 (br, CH_{Ar}), 126.5 (br, CH_{Ar}), 126.3, 125.6 (CH_{Ar}), 86.4 (C-2), 59.0 (C-3), 53.8 (OCH_3), 53.7 (br, OCH_3), 42.1 (C-9), 37.1 (C-11), 32.5, 32.4 (C-12,12′), 31.6 (C-10), 25.1, 25.0 (C-13,13′). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3427 (br, w), 2955 (m), 2867 (w), 1785 (s), 1719 (s), 1594 (m), 1506 (s). MS (EI, 70 eV): *m/z* (%)=388 ([M]$^+$, 100), 291 (97), 235 (43), 189 (20), 145 (23). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.90; H, 6.38; N, 6.90.

3.1.1.8. Dimethyl 3-(2-cyclohexylethyl)-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3h). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 4-cyclohexyl-1,1-bis(trimethylsilyloxy)but-1-ene (**2h**) (1.100 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**3h** (0.258 g, 25%) was isolated as a

colourless solid, mp 128–130 °C; *cis*-**3h** (0.123 g, 12%) was isolated as a colourless solid, mp 115–116 °C.

Data of *trans*-**3h**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.24–7.20 (m, 2H, Ar), 6.70 (d, 1H, $^3J_{2,3}$=8.8 Hz, 1H, H-2), 5.49 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.81 (br s, 3H, OCH_3), 2.47–2.33 (m, 1H, H-9), 1.99–1.80 (br m, 1H, CH), 1.78–1.51 (m, 6H, CH_2), 1.39–1.05 (m, 6H, CH_2), 1.00–0.75 (m, 2H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.0 (br, 2NCO), 130.6, 130.4 (C_{Ar}), 126.5, 126.2 (2), 125.9 (CH_{Ar}), 86.0 (C-2), 59.5 (C-3), 53.9, 53.6 (br) (OCH_3), 41.9 (C-9), 37.2 (CH), 33.4, 33.1, 32.8, 26.9, 26.4, 26.2, 26.1 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3448 (br, m), 2923 (s), 2852 (m), 1771 (s), 1716 (br, s), 1593 (w), 1507 (s), 1441 (s). MS (EI, 70 eV): *m*/*z* (%)=416 ([M]$^+$, 100), 357 (3), 291 (11), 235 (27), 188 (30), 145 (16). HRMS (EI) calcd for $C_{22}H_{28}N_2O_6$ ([M]$^+$): 416.19419; found: 416.19472.

Data of *cis*-**3h**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.31 (br, 1H, Ar), 7.23–7.20 (m, 2H, Ar), 6.93 (d, 1H, $^3J_{2,3}$=8.0 Hz, 1H, H-2), 5.75 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.78 (br s, 3H, OCH_3), 2.75–2.61 (br m, 1H, H-9), 1.77–1.53 (m, 7H, CH, CH_2), 1.38–1.05 (m, 6H, CH_2), 1.01–0.75 (m, 2H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.3 (COO), 155.0, 153.5 (NCO), 131.0, 130.4 (C_{Ar}), 126.8 (br), 126.5 (br), 126.3, 125.6 (CH_{Ar}), 86.5 (C-2), 58.8 (C-3), 53.8, 53.7 (br) (OCH_3), 43.4 (C-9), 37.6 (CH), 33.2, 33.1, 32.9, 26.5, 26.3, 26.2 (2) (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3420 (br, m), 2920 (s), 2851 (s), 1773 (s), 1717 (br, s), 1597 (w), 1508 (s), 1440 (s), 1338 (br, s). MS (EI, 70 eV): *m*/*z* (%)=416 ([M]$^+$, 100), 388 (3), 291 (11), 235 (26), 145 (17). HRMS (EI) calcd for $C_{22}H_{28}N_2O_6$ ([M]$^+$): 416.19419; found: 416.19437. Anal. Calcd for $C_{22}H_{28}N_2O_6$ (416.47): C, 63.45; H, 6.78; N, 6.73. Found: C, 64.11; H, 7.07; N, 6.44.

3.1.1.9. Dimethyl 7-ethyl-6-oxo-7,7a-dihydrofuro[3,2-*b*]-pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5a). Starting with pyrazine (**4**) (0.200 g, 2.5 mmol), 2-ethyl-1,1-bis(trimethylsilyloxy)ethene (**2a**) (0.650 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**5a** (0.170 g, 24%) was isolated as a colourless oil.

Data of *trans*-**5a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.20 (br, 3H, H-2,5,6), 4.72 (br, 1H, H-3), 3.84 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.84 (br, 1H, H-7), 1.85–1.79 (m, 1H, CH_2), 1.62–1.53 (m, 1H, CH_2), 1.10 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.5 (COO), 153.1 (NCO), 152.7 (NCO), 108.7 (br, 2CH), 80.4 (C-2), 56.0 (br, C-3), 53.8, 53.7 (OCH_3), 46.0 (br, C-7), 21.4 (CH_2), 10.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2960 (s), 1716 (s), 1443 (s), 1339 (s), 1127 (s), 974 (s), 766 (w). MS (EI; 70 eV): *m*/*z* (%)=284.1 ([M]$^+$, 100), 240 (10), 185 (76), 139 (44), 95 (44), 59 (30). Anal. Calcd for $C_{12}H_{16}N_2O_6$ (284.00): C, 50.70; H, 6.63; N, 9.85. Found: C, 50.86; H, 6.09; N, 9.21.

3.1.1.10. Dimethyl 7-propyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5b). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-propyl-1,1-bis(trimethylsilyloxy)ethene (**2b**) (0.863 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5b** (0.299 g, 40%) was isolated as a colourless oil; *cis*-**5b** (0.196 g, 26%) was isolated as a colourless solid, mp 71–72 °C.

Data of *trans*-**5b**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.24 (br, 3H, H-2,5,6), 4.66 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.91 (br, 1H, H-7), 1.81–1.71 (m, 2H, CH_2), 1.64–1.45 (m, 2H, CH_2), 0.97 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.8 (br), 108.0 (br) (CH), 80.5 (C-2), 57.1 (br, C-3), 54.0, 53.7 (OCH_3), 46.2 (br), 45.0 (br) (C-7), 30.6, 19.7 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3546 (br, w), 3160 (s), 2960 (br, s), 2875 (s), 1785 (br, s), 1717 (br, s), 1540 (w), 1443 (br, s). MS (EI, 70 eV): *m*/*z* (%)=298 ([M]$^+$, 73), 198 (12), 185 (100), 139 (68), 95 (48). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.06; H, 6.19; N, 9.19.

Data of *cis*-**5b**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.28 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.83 (br m, 1H, H-7), 1.71–1.39 (m, 4H, CH_2), 0.92 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.7 (COO), 153.1 (2NCO), 110.6 (2CH), 81.7 (br, C-2), 54.0 (C-3), 54.0, 53.9 (OCH_3), 42.3 (C-7), 28.4, 20.5 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3545 (br, w), 3138 (m), 2960 (br, s), 2874 (s), 1783 (br, s), 1717 (br, s), 1540 (w), 1438 (br, s). MS (EI, 70 eV): *m*/*z* (%)=298 ([M]$^+$, 27), 198 (15), 185 (61), 139 (49), 95 (43), 59 (100). HRMS (EI) calcd for $C_{13}H_{18}N_2O_6$ ([M]$^+$): 298.11594; found: 298.11537. Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 51.83; H, 6.09; N, 8.84.

3.1.1.11. Dimethyl 7-butyl-6-oxo-7,7a-dihydrofuro[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5c). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-butyl-1,1-bis(trimethylsilyloxy)ethene (**2c**) (0.912 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5c** (0.234 g, 30%) was isolated as a colourless oil; *cis*-**5c** (0.297 g, 39%) was isolated as a colourless oil.

Data of *trans*-**5c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.24 (br, 3H, H-2,5,6), 4.68 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.90 (br m, 1H, H-7), 1.82–1.73 (m, 2H, CH_2), 1.63–1.25 (m, 4H, CH_2), 0.93 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.9 (br), 108.8 (br) (CH), 80.5 (C-2), 56.9 (C-3), 54.0, 53.7 (OCH_3), 46.5 (br), 44.9 (br) (C-7), 28.4, 28.2, 22.5 (CH_2), 13.8 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (br, s), 3140 (m), 2959 (s), 2863 (s), 1792 (br, s), 1734 (br, s), 1539 (w), 1437 (br, s), 1368 (br, s). MS (EI, 70 eV): *m*/*z* (%)=312 ([M]$^+$, 100), 268 (10), 185 (79), 139 (61), 95 (21), 59 (17). HRMS (EI) calcd for $C_{14}H_{20}N_2O_6$ ([M]$^+$): 312.13159; found: 312.13168. Anal. Calcd for $C_{14}H_{20}N_2O_6$ (312.32): C, 53.84; H, 6.45; N, 8.97. Found: C, 53.20; H, 6.42; N, 8.63.

Data of *cis*-**5c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.29 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.82 (br m, 1H, H-7), 1.64-1.24 (m, 6H, CH_2), 0.89 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.8 (COO), 153.4 (br, NCO), 153.1 (NCO), 110.6 (2 CH), 81.6 (br, C-2), 54.0 (C-3), 54.0, 53.8 (OCH_3), 42.5 (C-7), 29.4, 26.0, 22.5 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}):

$\tilde{\nu}$ = 3545 (br, w), 3435 (br, w), 3137 (m), 2958 (br, s), 2871 (s), 1782 (br, s), 1716 (br, s), 1540 (w), 1444 (br, s). MS (EI, 70 eV): *m/z* (%)=312 ([M]$^+$, 100), 198 (19), 185 (83), 139 (46), 95 (23), 59 (21). HRMS (EI) calcd for $C_{14}H_{20}N_2O_6$ ([M]$^+$): 312.13159; found: 312.13136.

3.1.1.12. Dimethyl 7-dodecyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5d). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-dodecyl-1,1-bis(trimethylsilyloxy)ethene (**2d**) (1.304 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5d** (0.275 g, 26%) was isolated as a colourless oil; *cis*-**5d** (0.214 g, 20%) was isolated as a colourless oil.

Data of *trans*-**5d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.23 (br, 3H, H-2,5,6), 4.67 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.89 (m, 1H, H-7), 1.82–1.71 (m, 2H, CH_2), 1.67–1.45 (br m, 2H, CH_2), 1.38–1.21 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.9 (br, 2CH), 80.5 (C-2), 56.9 (C-3), 54.0, 53.7 (OCH_3), 46.6, 45.1 (br) (C-7), 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.3, 29.3, 26.3, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3140 (w), 2924 (s), 2854 (s), 1790 (s), 1724 (br, s), 1540 (w), 1444 (s), 1344 (br, s). MS (EI, 70 eV): *m/z* (%)=424 ([M]$^+$, 100), 380 (5), 281 (4), 185 (20), 139 (15). HRMS (EI) calcd for $C_{22}H_{36}N_2O_6$ ([M]$^+$): 424.25679; found: 424.25793.

Data of *cis*-**5d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.28 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.81 (br m, 1H, H-7), 1.75–1.55 (m, 2H, CH_2), 1.55–1.37 (m, 2H, CH_2), 1.37–1.18 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.3 (br, NCO), 153.0 (NCO), 110.6, 110.3 (br) (CH), 81.6 (C-2), 54.1 (C-3), 54.0, 53.8 (OCH_3), 42.5 (br, C-7), 31.9, 29.6 (3), 29.5, 29.4, 29.3 (2), 27.3, 26.3, 22.6 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3447 (br, w), 3144 (w), 2957 (m), 2920 (s), 2850 (s), 1763 (s), 1748 (s), 1678 (m), 1449 (s), 1349 (br, s). MS (EI, 70 eV): *m/z* (%)=424 ([M]$^+$, 100), 380 (1), 280 (3), 185 (40), 139 (28). HRMS (EI) calcd for $C_{22}H_{36}N_2O_6$ ([M]$^+$): 424.25679; found: 424.25795.

3.1.1.13. Dimethyl 7-isopropyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5e). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-isopropyl-1,1-bis-(trimethylsilyloxy)ethene (**2e**) (0.616 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5e** (0.146 g, 20%) was isolated as a colourless solid, mp 102–103 °C; *cis*-**5e** (0.265 g, 35%) was isolated as a colourless solid, mp 92–93 °C.

Data of *trans*-**5e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.30–6.05 (br, 3H, H-2,5,6), 4.79 (br, 1H, H-3), 3.80 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.75 (br s, 1H, H-7), 2.17 (br s, 1H, H-8), 1.12 (d, 3H, ^3J=7.0 Hz, CH_3), 1.04 (d, 3H, ^3J= 7.0 Hz, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=173.7 (COO), 152.9 (br, NCO), 152.6 (NCO), 108.7 (br, C-5,6), 80.5 (C-2), 55.4 (br), 54.6 (br) (C-3), 53.9, 53.5 (OCH_3), 52.1 (br), 50.1 (br) (C-7), 27.7 (C-8), 19.7, 18.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br, w), 3139 (w), 2964 (m), 1783 (s), 1727 (br, s), 1683 (m), 1441 (s), 1347 (br, s). MS (EI, 70 eV): *m/z* (%)=298 ([M]$^+$, 100), 211 (40), 198 (15), 185 (74), 139 (60). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.14; H, 6.08; N, 9.05.

Data of *cis*-**5e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.25–6.18 (br, 3H, H-2,5,6), 5.25 (br s, 1H, H-3), 3.82 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 2.79 (br s, 1H, H-7), 1.96 (br s, 1H, H-8), 1.13 (d, 3H, ^3J=7.0 Hz, CH_3), 0.94 (d, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=173.1 (COO), 153.4 (br, NCO), 153.0 (NCO), 110.8 (br), 110.2 (C-5,6), 81.2 (C-2), 54.4 (C-3), 53.9, 53.8 (OCH_3), 48.5 (C-7), 25.0 (C-8), 23.0, 18.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br, m), 3137 (w), 2965 (m), 1780 (s), 1728 (br, s), 1442 (s), 1337 (br, s). MS (EI, 70 eV): *m/z* (%)=298 ([M]$^+$, 92), 211 (24), 198 (45), 185 (100), 139 (67). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.24; H, 6.10; N, 9.20.

3.1.1.14. Dimethyl 7-cyclohexyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5f). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-cyclohexyl-1,1-bis(trimethylsilyloxy)ethene (**2f**) (0.989 g, 3.46 mmol) and methyl chloroformate (0.94 mL, 10.0 mmol), *trans*-**5f** (0.320 g, 38%) was isolated as a colourless solid, mp 129–130 °C; *cis*-**5f** (0.060 g, 11%) was isolated as a colourless oil.

Data of *trans*-**5f**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.22 (br, 3H, H-2,5,6), 4.73 (br, 1H, H-3), 3.83 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.76 (br, 1H, H-7), 1.78–1.64 (m, 6H, CH_2, ring CH), 1.46–1.11 (m, 5H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.0 (COO), 153.0, 152.7 (NCO), 109.4 (br) (C-5,6), 80.9 (C-2), 56.4 (br, C-3), 54.0, 53.6 (br) (OCH_3), 48.2 (br, C-7), 37.7 (ring CH), 30.2, 29.6, 26.3, 26.2, 25.8 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2931 (s), 1721 (s), 1449 (s), 1341 (s), 1120 (s), 956 (s), 765 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 211 (26), 185 (59), 139 (37), 95 (15), 59 (12). HRMS (EI) calcd for $C_{16}H_{22}N_2O_6$ ([M]$^+$): 338.1472; found: 338.1466.

Data of *cis*-**5f**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.29–6.12 (br m, 3H, H-2,5,6), 5.22 (br, 1H, H-3), 3.84 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.75 (br, 1H, H-7), 1.76–1.53 (m, 6H, CH_2, ring CH), 1.24–1.12 (m, 5H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=173.3 (COO), 153.1 (2NCO), 110.1 (C-5,6), 81.0 (C-2), 53.9 (C-3), 53.9 (2 OCH_3), 48.4 (C-7), 35.5 (CH), 33.2, 28.8, 27.0, 26.4, 25.7 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2931 (s), 1733 (s), 1428 (s), 1341 (s), 1121 (s), 957 (s), 766 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 211 (26), 185 (59), 139 (37), 95 (15), 59 (12). HRMS (EI) calcd for $C_{16}H_{22}N_2O_6$ ([M]$^+$): 338.14724; found: 338.14659.

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Publication 8

Ehsan Ullah, Bettina Appel, Christine Fischer, and Peter Langer*, "Synthesis of 7-Hydroxy-6*H*-Benzo[*c*]chromen-6-ones based on a ′[3+3] Cyclization / Domino Retro-Michael-Aldol-Lactonization′ Strategy", Tetrahedron **2006**. Accepted for publication.

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Synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones based on a '[3+3] cyclization/domino retro-Michael–aldol–lactonization' strategy

Ehsan Ullah,[a,b,c] Bettina Appel,[c] Christine Fischer[b] and Peter Langer[a,b,*]

[a]*Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, D-18059 Rostock, Germany*
[b]*Leibniz-Institut für Katalyse e. V. an der Universität Rostock, Albert-Einstein-Str. 29a, D-18059 Rostock, Germany*
[c]*Institut für Biochemie, Universität Greifswald, Soldmannstr. 16, 17487 Greifswald, Germany*

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Abstract—The $TiCl_4$-mediated [3+3] cyclization of 2,4-bis(trimethylsilyloxy)penta-1,3-diene with 3-silyloxyalk-2-en-1-ones afforded 2-acetylphenols, which were transformed into functionalized chromones. The Me_3SiOTf-mediated condensation of the latter with 1,3-bis(silyl enol ethers) and subsequent domino 'retro-Michael–aldol–lactonization' reaction afforded 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones.

1. Introduction

Functionalized 6*H*-benzo[*c*]chromen-6-ones (dibenzo[*b*,*d*]-pyran-6-ones) are present in a number of pharmacologically relevant natural products. For example, autumnariol has been isolated from *Eucomis autumnalis* Greab. (Liliaceae).[1] The isolation of related 6*H*-benzo[*c*]chromen-6-ones, such as autumnariniol,[2] alternariol,[3] or altenuisol,[4] has been reported (Chart 1).[5] It has been demonstrated that 6*H*-benzo[*c*]-chromen-6-ones are specific inhibitors of the growth of endothelic cells[6] and represent oestrogene receptors.[7] Ellagic and coruleoellagic acid, which have been isolated mainly from plant sources,[8] occur both as glycosides and aglycons. Dibenzo[*c*,*d*]chromen-6-ones occur in a number of natural antibiotics and antitumor agents, such as the gilvocarcins, chrysomycins, and ravidomycins.[9]

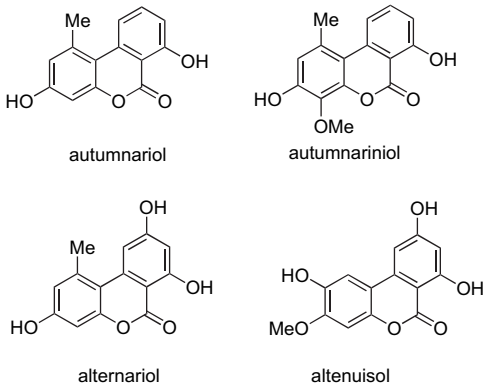

Chart 1. 7-Hydroxy-6*H*-benzo[*c*]chromen-6-ones in nature.

6*H*-Benzo[*c*]chromen-6-ones have been prepared by cyclizations of *o*-bromobenzoic acids with phenols,[10] intramolecular palladium(II) catalyzed coupling reactions of aryl benzoates,[11] and Suzuki reactions.[12,13] Harris et al. reported the synthesis of 9-*O*-methylalternariol by condensation of the dianion of acetylacetone with a protected salicylate.[15,16] We have recently reported[17] the synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones by condensation of 1,3-bis-silyl enol ethers[18] with 4-silyloxybenzopyrylium triflates, in situ generated from chromones,[19] and subsequent base-mediated domino 'retro-Michael–aldol–lactonization' reaction. The preparative scope of this method severely depends on the availability of the chromones as starting materials. Chan and co-workers developed an elegant approach to arenes by [3+3] cyclization of 1,3-bis(silyl enol ethers) with 3-siloxyalk-2-en-1-ones.[20] Based on this work we herein report a new approach to functionalized chromones by [3+3] cyclization of 2,4-bis(trimethylsilyloxy)penta-1,3-diene with 3-silyloxyalk-2-en-1-ones. The combination of these reactions with the domino reaction of chromones with 1,3-bis-silyl enol ethers provides a versatile strategy for the synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones. Notably, this strategy relies on the sequential use of 1,3-bis(silyl enol ethers)[18] at two stages of the synthesis.

Keywords: Chromones; Cyclizations; Domino reactions; Oxygen heterocycles; Silyl enol ethers.
* Corresponding author. Tel.: +49 381 4986410; fax: +49 381 4986412; e-mail: peter.langer@uni-rostock.de

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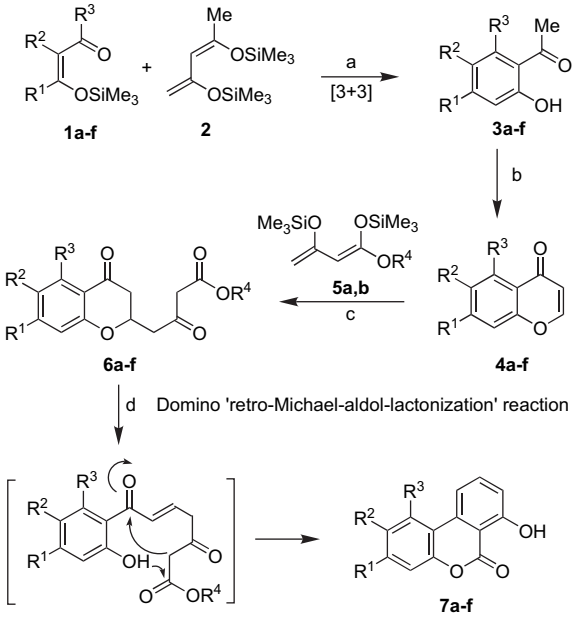
2. Results and discussion

The $TiCl_4$-mediated [3+3] cyclization of 2,4-bis(trimethylsilyloxy)penta-1,3-diene (**2**) with 3-silyloxyalk-2-en-1-ones, following the conditions reported by Chan[20] and us,[21] afforded the 2-acetylphenols **3a–f** (Scheme 1, Table 1). The synthesis of chloro-[21e] and acetoxy-substituted[21f] salicylates by [3+3] cyclizations of 1,3-bis(silyl enol ethers) with appropriate 3-silyloxyalk-2-en-1-ones has been previously reported. The cyclization of 1,3-bis(silyl enol ether) **2** with **1d** and **1e** proceeded with very good regioselectivity, which can be explained as previously reported.[20,21i] Treatment of the acetylphenols with $HC(OEt)_3$ and $HClO_4$ afforded the chromones **4a–f**. During the formation of **4f**, the acetoxy group was cleaved to give a hydroxyl group. The Me_3SiOTf-mediated condensation of **4a–f** with 1-ethoxy or 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5a**,**b**) gave the 2,3-dihydrobenzopyrans **6a–f**. Treatment of the latter with NEt_3 in EtOH afforded the novel 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones **7a–f**. The formation of the latter can be explained by a domino 'retro-Michael–aldol–lactonization' reaction.[17] The synthesis of compounds **3b**,[22] **3c**,[23] and **4c**[24] has been previously reported.



Scheme 1. Synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones **7a–f**: (a) $TiCl_4$, CH_2Cl_2, −78 °C; (b) $HC(OEt)_3$, $HClO_4$ (70%), reflux, 12 h; (c) (1) Me_3SiOTf (1.3 equiv), 20 °C, 1 h; (2) **5a**,**b** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (3) HCl (10%); (d) NEt_3 (2.0 equiv), EtOH, 20 °C, 12 h.

The combination of two different cyclization reactions of 1,3-bis(silyl enol ethers) allows a facile approach to a number of novel 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones. The core structure of the products contains 13 carbon atoms out of which 9 carbons are derived from the two 1,3-bis(silyl enol ethers), 3 carbons from the 3-silyloxyalk-2-en-1-one and 1 carbon from the orthoformate.

In conclusion, we have reported the synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones based on sequential reactions of 1,3-bis(silyl enol ethers) with 3-silyloxyalk-2-en-1-ones and chromones.

3. Experimental

3.1. General comments

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For the ^1H and ^{13}C NMR spectra the deuterated solvents indicated were used. Chemical shifts δ are reported in parts per million relative to $CHCl_3$ (^1H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm) as internal standards. ^{13}C NMR spectral assignments are supported by DEPT analyses. Mass spectral data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI). For preparative scale chromatography silica gel (60–200 mesh) was used. Melting points are uncorrected.

3.2. General procedure for the synthesis of 2-acetylphenols 3a–f

To a stirred CH_2Cl_2 solution (2 mL/mmol) of 1,3-bis(silyl enol ether) **2** (1.0 mmol) and 3-siloxyalk-2-en-1-one **1** (1.0 mmol) was added $TiCl_4$ (1.0 mmol) at −78 °C under argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C during 20 h and a saturated aqueous solution of $NaHCO_3$ (10 mL) was added. The organic layer was separated and extracted with diethyl ether (3×30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/heptane=1:4).

3.2.1. 1-(3-Chloro-2,4-diethyl-6-hydroxyphenyl)ethanone (3a). Starting with 4-chloro-5-(trimethylsilyloxy)hept-4-en-3-one (**1a**) (1.021 g, 4.3 mmol), 2,4-bis(trimethylsilyloxy)penta-1,3-diene (**2**) (1.041 g, 4.3 mmol), and $TiCl_4$ (0.812 g, 4.3 mmol), **3a** was obtained (0.490 g, 50%) as

Table 1. Products and yields

	R^1	R^2	R^3	R^4	**3** (%)[a]	**4** (%)[a]	**6** (%)[a]	**7** (%)[a]
a	Et	Cl	Et	Me	50	80	77	28 (48)
b	Me	Me	Me	Et	51	70	65	22 (42)
c	Me	H	Me	Et	40	84	68	24 (46)
d	Me		$-(CH_2)_4-$	Et	36	78	61	50
e	Me		$-(CH_2)_3-$	Me	20	69	73	35 (60)
f	Me	OAc	Me	Me	42	—	—	—
f	Me	OH	Me	Me	—	70	68	33 (40)

[a] Yields of isolated products; the synthesis of compounds **3b**,[22] **3c**,[23] and **4c**[24] has been previously reported; values in brackets: yields based on recovered starting material.

a yellow solid; mp 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 10.40 (s, 1H, OH), 6.74 (s, 1H, Ar-H), 3.00 (q, 2H, J=7.6 Hz, CH_2), 2.75 (q, 2H, J=7.3 Hz, CH_2), 2.67 (s, 3H, CH_3), 1.32–1.19 (m, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.8 (CO), 157.9 (C–OH), 148.7, 141.6 (C), 125.8 (C–Cl), 122.8 (C), 116.8 (CH), 32.8 (CH_3), 28.3, 26.0 (CH_2), 14.7, 13.7 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3229 (w), 1678 (m), 1225 (s), 1081 (s), 856 (w). MS (EI, 70 eV): *m/z* (%) 226 (M^+, 34), 211 (100), 193 (17), 173 (10). Anal. Calcd for $C_{12}H_{15}O_2Cl$ (226.0): C 63.57, H 6.62; found: C 63.97, H 6.57.

3.2.2. 1-(6-Hydroxy-2,3,4-trimethylphenyl)ethanone (3b). The synthesis of **3b** has been previously reported.[22] Starting with 3-methyl-4-(trimethylsilyloxy)pent-3-en-2-one (**1b**) (0.500 g, 2.68 mmol), **2** (0.653 g, 2.68 mmol), and $TiCl_4$ (0.506 g, 2.68 mmol), **3b** (0.241 g, 51%) was obtained as a slight yellow solid; mp 62 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 10.87 (s, 1H, OH), 6.66 (s, 1H, Ar-H), 2.58 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.12 (s, 3H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 206.3 (CO), 157.7, 144.2, 136.4, 128.1, 122.3 (C), 116.6 (CH), 32.7, 21.5, 20.2, 15.0 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3191 (m), 2975 (s), 1661 (m), 1450 (s), 1304 (m), 845 (s). MS (EI, 70 eV): *m/z* (%) 178 (M^+, 30), 163 (100), 135 (8), 91 (12), 44 (14). Anal. Calcd for $C_{11}H_{14}O_2$ (178.1): C 74.15, H 7.86; found: C 74.00, H 7.96.

3.2.3. 1-(6-Hydroxy-2,4-dimethylphenyl)ethanone (3c). The synthesis of **3c** has been previously reported.[23] Starting with 4-trimethylsilyloxy-pent-3-en-2-one (**1b**) (1.000 g, 5.81 mmol), **2** (1.417 g, 5.81 mmol), and $TiCl_4$ (1.098 g, 5.81 mmol), **3b** (0.380 g, 40%) was obtained as a slight yellow solid; mp 42 °C.

3.2.4. 1-(2-Hydroxy-4-methyl-5,6,7,8-tetrahydronaphthalen-1-yl)ethanone (3d). Starting with 1-(2-trimethylsilyloxycyclohex-1-enyl)ethanone (**1d**) (0.500 g, 2.35 mmol), **2** (0.573 g, 2.35 mmol), and $TiCl_4$ (0.444 g, 2.35 mmol), **3d** (0.172 g, 36%) was obtained as a brownish solid; mp 55 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.49 (s, 1H, OH), 6.67 (s, 1H, Ar-H), 2.93 (t, 2H, J=6.4 Hz, CH_2), 2.64 (s, 3H, CH_3), 2.57 (t, 2H, J=6.7 Hz, CH_2), 2.19 (s, 3H, CH_3), 1.87–1.68 (m, 4H, CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): δ 206.1 (CO), 158.9, 145.1, 137.6, 127.3, 121.0 (C), 117.2 (CH), 33.4 (CH_3), 31.3, 26.6, 22.9, 22.6 (CH_2), 20.4 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3410 (w), 2950 (s), 1629 (m), 1460 (s), 1340 (s), 1298 (m). MS (EI, 70 eV): *m/z* (%) 204 (M^+, 64), 189 (100), 161 (43), 146 (15), 44 (39). HRMS (EI) calcd for $C_{13}H_{16}O_2$ $[M]^+$: 204.1145; found: 204.1141.

3.2.5. 1-(5-Hydroxy-7-methylindan-4-yl)ethanone (3e). Starting with 2-(1-trimethylsilyloxy-ethylidene)cyclopentanone (**1a**) (1.000 g, 5.04 mmol), **2** (1.230 g, 5.04 mmol), and $TiCl_4$ (0.952 g, 5.04 mmol), **3e** (0.200 g, 20%) was obtained as a yellow solid; mp 58 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 12.18 (s, 1H, OH), 6.74 (s, 1H, Ar-H), 2.92 (t, 2H, J=7.3 Hz, CH_2), 2.83 (t, 2H, J=7.6 Hz, CH_2), 2.66 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.07 (quint, 2H, J=7.6 Hz, CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): δ 205.8 (CO), 161.8. 152.0, 135.4, 134.1, 120.3 (C), 111.6 (CH), 33.8 (CH_2), 33.0 (CH_3), 31.5, 24.3 (CH_2), 20.5 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 2952 (s), 1622 (w), 1470 (s), 1353 (s), 1234 (w), 841 (w). MS (EI, 70 eV): *m/z* (%) 190 (M^+, 40), 175 (100), 115 (12), 91 (16), 43.0 (24). HRMS (EI) calcd for $C_{12}H_{14}O_2$ $[M]^+$: 190.0988; found: 190.0985.

3.2.6. 1-[3-(Acetoxy)-6-hydroxy-2,4-dimethylphenyl]-ethanone (3f). Starting with **1f** (1.005 g, 4.37 mmol), **2** (1.066 g, 4.37 mmol), and $TiCl_4$ (0.825 g, 4.37 mmol), **3f** (0.410 g, 42%) was obtained as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.80 (s, 1H, OH), 6.71 (s, 1H, Ar-H), 2.61 (s, 3H, CH_3COO), 2.34 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.21 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.5, 169.1(CO), 159.5, 141.0, 138.6, 130.4, 121.2 (C), 118.3 (CH), 33.3, 20.7, 17.5, 16.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3407 (br), 2929 (w), 1760 (s), 1198 (s), 908 (w). MS (EI, 70 eV): *m/z* (%) 222 (M^+, 9), 180 (84), 165 (100), 43 (23). HRMS (EI) calcd for $C_{12}H_{14}O_4$ $[M]^+$: 222.0887; found: 222.0881.

3.3. General procedure for the synthesis of chromones 4a–f

To ethanone **3** (1.0 equiv) were slowly added triethyl orthoformate (20 equiv) and perchloric acid (70%, 1.3 equiv) and the reaction mixture was refluxed for 20 h at 80 °C. After cooling to 20 °C, the reaction mixture was filtered and washed with cold water. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel).

3.3.1. 6-Chloro-5,7-diethylchromen-4-one (4a). Starting with **3a** (0.302 g, 1.33 mmol), triethyl orthoformate (3.936 g, 26.60 mmol, 20 equiv), and perchloric acid (70%) (0.172 g, 1.72 mmol), **4a** (0.251 g, 80%) was obtained as a colorless solid; mp 80 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.68 (d, 1H, J=6.1 Hz, CH), 7.18 (s, 1H, Ar-H), 6.23 (d, 1H, J=5.8 Hz, CH), 3.55 (q, 2H, J=7.3 Hz, CH_2), 2.85 (q, 2H, J=7.6 Hz, CH_2), 1.32–1.19 (m, 6H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 178.4 (CO), 156.5 (C), 153.1 (CH), 148.0, 144.2, 131.7, 121.0 (C), 116.3, 114.4 (CH), 28.0, 24.3 (CH_2), 13.7, 13.3 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3436 (br), 2970 (w), 1648 (s), 1436 (s), 1254 (s), 843 (s). MS (EI, 70 eV): *m/z* (%) 236 (M^+, 89), 219 (100), 193 (20), 115 (11). Anal. Calcd for $C_{13}H_{13}O_2Cl$ (236.0): C 66.10, H 5.55; found: C 65.97, H 5.63.

3.3.2. 5,6,7-Trimethylchromen-4-one (4b). Starting with **3b** (0.202 g, 1.15 mmol), triethyl orthoformate (3.400 g, 23.00 mmol), and perchloric acid (70%) (0.152 g, 1.50 mmol), **4b** (0.151 g, 70%) was obtained as a white solid; mp 124 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.64 (d, 1H, J=5.8 Hz, CH), 7.07 (s, 1H, Ar-H), 6.20 (d, 1H, J=5.7 Hz, CH), 2.83 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.23 (s, 3H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 180.0 (CO), 156.0 (C), 153.0 (CH), 143.0, 138.5, 133.2, 121.3 (C), 116.2, 114.1 (CH), 21.6, 17.3, 15.2 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3438 (br), 2925 (w), 1647 (s), 1428 (s), 1236 (s), 1001 (s), 848 (s). MS (EI, 70 eV): *m/z* (%) 188 (M^+, 100), 173 (57), 145 (9), 91 (7). Anal. Calcd for $C_{12}H_{12}O_2$ (188.0): C 76.60, H 6.38; found: C 76.20, H 6.31.

3.3.3. 5,7-Dimethylchromen-4-one (4c). The synthesis of **4c** has been previously reported.[24] Starting with **3c**

(0.175 g, 1.07 mmol), triethyl orthoformate (3.502 g, 21.34 mmol), and perchloric acid (70%) (0.140 g, 1.40 mmol), **4c** (0.156 g, 84%) was obtained as a brownish solid; mp 58 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.66 (d, 2H, J=5.8 Hz, CH), 7.04 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 6.20 (d, 2H, J=6.1 Hz, CH), 2.80 (s, 3H, CH_3), 2.38 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.6 (CO), 158.1 (C), 153.5 (CH), 143.7, 140.7 (C), 129.2 (CH), 121.0 (C), 116.3, 114.5 (CH), 22.7, 21.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3432 (br), 2925 (m), 1648 (s), 1350 (s), 1239 (s), 827 (s). MS (EI, 70 eV): *m*/*z* (%) 174 (M^+, 100), 159 (12), 145 (30), 91 (36), 39 (21). Anal. Calcd for $C_{11}H_{10}O_2$ (174.1): C 75.58, H 5.74; found: C 75.23, H 5.80.

3.3.4. 6-Methyl-7,8,9,10-benzo[*f*]chromen-1-one (4d). Starting with **3d** (0.150 g, 0.73 mmol), triethyl orthoformate (2.161 g, 14.60 mmol), and perchloric acid (0.095 g, 0.95 mmol), **4d** (0.122 g, 78%) was obtained as a white solid; mp 70 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.66 (d, 1H, J=5.7 Hz, CH), 7.07 (s, 1H, Ar-H), 6.23 (d, 1H, J=6.1 Hz, CH), 3.45 (t, 2H, J=6.4 Hz, CH_2), 2.64 (t, 2H, J=5.4 Hz, CH_2), 2.31 (s, 3H, CH_3), 1.80–1.77 (m, 4H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.9 (CO), 156.2 (C), 153.3 (CH), 143.6, 139.7, 133.3, 120.9 (C), 116.5, 114.7 (CH), 30.1, 27.8, 23.1, 22.5 (CH_2), 20.8 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3437 (br), 2925 (s), 1620 (s), 1605 (s), 1455 (s), 1232 (s), 850 (m). MS (EI, 70 eV): *m*/*z* (%) 214 (M^+, 100), 199 (80), 181 (29), 131 (33), 69 (51). Anal. Calcd for $C_{14}H_{14}O_2$ (214.1): C 78.85, H 6.94; found: C 78.70, H 6.30.

3.3.5. 4-Methyl-2,3-dihydro-1*H*-6-oxacyclopenta[*a*]-naphthalen-9-one (4e). Starting with **3e** (0.240 g, 1.30 mmol), triethyl orthoformate (3.863 g, 26.10 mmol), and perchloric acid (0.170 g, 1.70 mmol), **4e** (0.180 g, 69%) was obtained as a colorless solid; mp 130 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.70 (d, 1H, J=6.1 Hz, CH), 7.03 (s, 1H, Ar-H), 6.21 (d, 1H, J=5.8 Hz, CH), 3.50 (t, 2H, J=7.6 Hz, CH_2), 2.81 (t, 2H, J=7.6 Hz, CH_2), 2.33 (s, 3H, CH_3), 2.15 (p, 2H, J=7.6 Hz, CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): δ 179.4 (CO), 157.0 (C), 154.6 (CH), 144.6, 141.3, 140.7, 133.9 (C), 116.4, 113.9 (CH), 34.0, 29.3, 24.0 (CH_2), 20.3 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3438 (br), 2914 (w), 1662 (s), 1603 (s), 1230 (m), 849 (m). MS (EI, 70 eV) *m*/*z* (%) 199 (M^+, 100), 184 (5), 128 (12), 115 (7). HRMS (EI, 70 eV) calcd for $C_{13}H_{11}O_2$ $[M]^+$: 199.0754; found: 199.0747.

3.3.6. 6-Hydroxy-5,6-dimethylchromen-4-one (4f). Starting with **3f** (0.205 g, 0.90 mmol), triethyl orthoformate (2.666 g, 18.01 mmol), and perchloric acid (70%) (0.117 g, 1.17 mmol), **4f** (0.120 g, 70%) was obtained as a colorless solid; mp 140 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.67 (d, 1H, J=5.8 Hz, CH), 7.10 (s, 1H, Ar-H), 6.20 (d, 1H, J=7.1 Hz, CH), 2.81 (s, 3H, CH_3), 2.36 (s, 3H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 177.0 (CO), 154.8 (CH), 149.5, 148.5, 131.6, 121.7, 119.4 (C), 117.0, 113.0 (CH), 17.7, 13.9 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3410 (br), 2950 (s), 1642 (w), 1634 (w), 1294 (w), 1280 (w). MS (EI, 70 eV): *m*/*z* (%) 190 (M^+, 94), 161 (56), 147 (54), 43 (100). HRMS (EI, 70 eV) calcd for $C_{11}H_{10}O_3$ $[M]^+$: 190.0624; found: 190.0621.

3.4. General procedure for the synthesis of 4-(chroman-2-yl)-3-oxobutyrates 6a–f

To chromone **4** (1.0 equiv) was added Me_3SiOTf (1.3 equiv) at 20 °C. After stirring for 1 h, CH_2Cl_2 (8 mL) and the 1,3-bis(silyl enol ether) **5** (1.3 equiv) were added at 0 °C. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×80 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified from polar side-products by column flash chromatography (silica gel, *n*-hexane/EtOAc=1:1) to give **6a–f**. Products **6a–f** were isolated and characterized and subsequently transformed into **7a–f**.

3.4.1. 4-(6-Chloro-5,7-diethyl-4-oxochroman-2-yl)-3-oxobutyric acid methyl ester (6a). Starting with **4a** (0.212 g, 0.89 mmol), TMSOTf (0.256 g, 1.15 mmol), and 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5a**) (0.300 g, 1.15 mmol), **6a** (0.240 g, 77%) was obtained as a brownish solid; mp 72 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.73 (s, 1H, Ar-H), 4.95–4.84 (m, 1H, CH chain), 3.76 (s, 3H, OCH_3), 3.56 (s, 2H, CH_2), 3.32–3.27 (m, 2H, CH_2), 3.14 (dd, 1H, ^2J=17.0 Hz, ^3J=7.3 Hz, CH_2), 2.90 (dd, 1H, ^2J=17.0 Hz, ^3J=7.1 Hz, CH_2), 2.79–2.70 (m, 4H, CH_2), 1.22 (t, 3H, J=7.6 Hz, CH_3), 1.16 (t, 3H, J=7.3 Hz, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 199.0, 191.4, 160.9 (CO), 150.3, 148.1, 148.5, 145.5, 145.4 (C), 115.9, 73.0 (CH), 53.0 (OCH_3), 50.0, 47.7, 44.4, 28.5, 24.7 (CH_2), 14.0 (2C, CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3437 (br), 2977 (m), 1746 (s), 1677 (s), 1417 (s), 1194 (s), 867 (m). MS (EI, 70 eV): *m*/*z* (%) 352 (M^+, 78), 320 (14), 237 (100), 167 (40), 115 (9). Anal. Calcd for $C_{18}H_{21}O_5Cl$ (352.0): C 61.27, H 5.95; found: C 61.19, H 6.10.

3.4.2. 3-Oxo-4-(5,6,7-trimethyl-4-oxochroman-2-yl)-butyric acid ethyl ester (6b). Starting with **4b** (0.13 g, 0.70 mmol), TMSOTf (0.20 g, 0.91 mmol), and 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5b**) (0.25 g, 0.91 mmol), **6b** (0.145 g, 65%) was obtained as a yellow solid; mp 56 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.63 (s, 1H, Ar-H), 4.90–4.79 (m, 1H, CH), 4.20 (q, 2H, J=7.0 Hz, CH_2), 3.53 (s, 2H, CH_2), 3.15 (dd, 1H, ^2J=16.7 Hz, ^3J=7.3 Hz, CH_2), 2.85 (dd, 1H, ^2J=16.7 Hz, ^3J=7.3 Hz, CH_2), 2.72–2.70 (m, 2H, CH_2), 2.67 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.28 (t, 3H, J=7.3 Hz, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 199.4, 193.2, 166.8 (CO), 159.9, 145.0, 139.7, 129.6, 118.0 (C), 116.2, 72.4 (CH), 61.6, 50.0, 47.5, 44.4 (CH_2), 21.7, 17.5, 14.9, 14.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3435 (br), 2982 (w), 1741 (s), 1677 (s), 1271 (s), 1100 (m), 857 (w). MS (EI, 70 eV): *m*/*z* (%) 318 (M^+, 60), 272 (20), 203 (9), 189 (42), 162 (100), 91 (16). HRMS (EI, 70 eV) calcd for $C_{18}H_{22}O_5$ $[M]^+$: 318.1462; found: 318.1458. Anal. Calcd for $C_{18}H_{22}O_5$ (318.0): C 67.92, H 6.91; found: C 68.44, H 6.75.

3.4.3. 4-(5,7-Dimethyl-4-oxochroman-2-yl)-3-oxobutyric acid ethyl ester (6c). Starting with **4c** (0.228 g, 1.30 mmol), TMSOTf (0.375 g, 1.70 mmol), and 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5b**) (0.465 g, 1.70 mmol), **6c** (0.265 g, 68%) was obtained as a yellow

oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.61 (s, 2H, Ar-H), 4.93–4.82 (m, 1H, CH), 4.21 (q, 2H, J=7.3 Hz, CH_2), 3.53 (s, 2H, CH_2), 3.14 (dd, 1H, ^2J=16.7 Hz, ^3J=7.3 Hz, CH_2), 2.85 (dd, 1H, ^2J=16.7 Hz, ^3J=7.3 Hz, CH_2), 2.71–2.67 (m, 2H, CH_2), 2.58 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.28 (t, 3H, J=7.3 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.3, 192.2, 166.5 (CO), 162.07, 146.0, 141.9 (C), 126.2 (CH), 117.2 (C), 116.3, 73.1 (CH), 61.9, 50.3, 47.8, 44.2 (CH_2), 23.0, 22.0, 14.5 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3436 (br), 2979 (m), 1744 (s), 1614 (s), 1326 (s), 1029 (s), 846 (w). MS (EI, 70 eV): *m*/*z* (%) 304 (M^+, 71), 189 (34), 175 (100), 148 (96), 91 (40). Anal. Calcd for $C_{17}H_{20}O_5$ (304.1): C 67.67, H 6.57; found: C 67.84, H 6.61.

3.4.4. 4-(6-Methyl-1-oxo-2,3,7,8,9,10-hexahydro-1*H*-benzo[*f*]chromen-3-yl)-3-oxobutyric acid ethyl ester (6d). Starting with **4d** (0.092 g, 0.43 mmol), TMSOTf (0.124 g, 0.56 mmol), and 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5b**) (0.153 g, 0.56 mmol), **6d** (0.091 g, 61%) was obtained as a yellow oil. ^{1}H NMR (keto/enol=10:1, 250 MHz, $CDCl_3$, only keto tautomer was listed): δ 6.63 (s, 1H, Ar-H), 4.91–4.80 (m, 1H, CH), 4.21 (q, 2H, J=7.3 Hz, CH_2), 3.53 (s, 2H, CH_2), 3.17–3.0 (m, 1H, CH_2), 2.85 (dd, 1H, ^2J=16.3 Hz, ^3J=7.1 Hz, CH_2), 2.70–2.67 (m, 2H, CH_2), 2.31 (s, 3H, CH_3), 1.19–1.17 (m, 2H, CH_2), 1.73–1.66 (m, 6H, CH_2), 1.28 (t, 3H, J=7.0 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.3, 192.7, 166.7 (CO), 159.9, 145.6, 140.7, 130.0, 117.1 (C), 116.3, 72.4 (CH), 61.3, 49.9, 47.3, 44.3, 30.9, 26.8, 23.3, 22.6 (CH_2), 20.41, 14.03 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3437 (br), 2925 (s), 1620 (s), 1605 (s), 1455 (s), 1232 (s), 850 (m). MS (EI, 70 eV): *m*/*z* (%) 344 (M^+, 73), 298 (15), 272 (17), 214 (100), 188 (85), 91 (11). Anal. Calcd for $C_{20}H_{24}O_5$ (344.2): C 69.73, H 6.97; found: C 69.72, H 7.16.

3.4.5. 4-(9-Methyl-8-oxo-1,2,3,6,7,8-hexahydro-5-oxacyclopenta[*b*]naphthalen-6-yl)-3-oxabutyric acid methyl ester (6e). Starting with **4e** (0.100 g, 0.54 mmol), TMSOTf (0.155 g, 0.70 mmol), and 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5a**) (0.182 g, 0.70 mmol), **6e** (0.125 g, 73%) was obtained as a yellow solid; mp 68 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.59 (s, 1H, Ar-H), 4.93–4.82 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 3.57 (s, 2H, CH_2), 3.28 (t, 2H, J=7.9 Hz, CH_2), 3.18 (dd, 1H, ^2J=16.7 Hz, ^3J=7.3 Hz, CH_2), 2.88 (dd, 1H, ^2J=16.5 Hz, ^3J=7.3 Hz, CH_2), 2.72–2.66 (m, 4H, CH_2), 2.24 (s, 3H, CH_3), 2.15–2.06 (m, 2H, CH_2). ^{13}C NMR (62 MHz, $CDCl_3$): δ 199.4, 192.4, 167.2 (CO), 160.8, 148.6, 146.4, 142.8, 138.0 (C), 116.6, 73.5 (CH), 53.0 (OCH_3), 50.0, 47.8, 43.8, 34.7, 30.5, 25.2 (CH_2), 21.0 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 3435 (br), 2982 (w), 1741 (s), 1677 (s), 1271 (s), 1100 (m), 857 (w). MS (EI, 70 eV): *m*/*z* (%) 316 (M^+, 59), 284 (15), 200 (100), 174 (50), 115 (12). HRMS (EI, 70 eV) calcd for $C_{18}H_{20}O_5$ $[M]^+$: 316.1305; found: 316.1303.

3.4.6. Methyl 4-(3,4-dihydroxy-5,7-dimethyl-4-oxo-2*H*-chromen-2-yl)-3-oxobutanoate (6f). Starting with **4f** (0.082 g, 0.45 mmol), TMSOTf (0.129 g, 0.58 mmol), and 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**5a**) (0.150 g, 0.58 mmol), **6f** (0.093 g, 68%) was obtained as a yellow oil. ^{1}H NMR (keto/enol=10:3, 250 MHz, $CDCl_3$, only keto tautomer was listed): δ 6.69 (s, 1H, Ar-H), 4.95–4.77 (m, 1H, ring CH), 3.75 (s, 3H, OCH_3), 3.56 (s, 2H, chain CH_2), 3.19–3.07 (m, 1H, ring CH_2), 2.91–2.80 (m, 1H, ring CH_2), 2.72–2.66 (m, 2H, chain CH_2), 2.55 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 199.2, 192.7, 169.0 (CO), 159.5 (C–OH), 147.1, 138.9, 133.4, 133.1 (C), 117.7, 73.1 (CH), 53.0 (OCH_3), 50.0, 47.8, 44.6 (CH_2), 17.6, 14.6 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3476 (br), 2955 (w), 1748 (s), 1614 (s), 1196 (s), 1073 (m), 862 (w). MS (EI, 70 eV): *m*/*z* (%) 306 (M^+, 97), 274 (18), 191 (51), 164 (100), 135 (10). HRMS (EI, 70 eV) calcd for $C_{16}H_{18}O_6$ $[M]^+$: 306.1098; found: 306.1097.

3.5. General procedure for the synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones 7a–f

To an EtOH solution (10 mL) of **6** was added NEt_3 (2.0 equiv) and the mixture was refluxed for 12 h at 80 °C. After cooling down to 20 °C, an aqueous solution of hydrochloric acid (1 M) and Et_2O (50 mL) was added. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×100 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc=20:1→3:1) to give product **7**.

3.5.1. 3-Chloro-2,4-diethyl-8-hydroxy-10*H*-phenanthren-9-one (7a). Starting with **6a** (0.170 g, 0.48 mmol) and NEt_3 (0.097 g, 0.96 mmol), **7a** (0.041 g, 28%; 48% based on recovered starting material) was obtained as a colorless solid; mp 140 °C. Starting material **6a** (0.070 g) was recovered. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.70 (s, 1H, OH), 8.14–8.06 (m, 2H, Ar-H), 7.55 (s, 1H, Ar-H), 7.47 (dd, 1H, J=6.4 Hz, J=2.7 Hz, Ar-H), 3.30 (q, 2H, J=7.3 Hz, CH_2), 2.82 (q, 2H, J=7.6 Hz, CH_2), 1.50 (t, 3H, J=7.3 Hz, CH_3), 1.28 (t, 3H, J=7.3 Hz, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$): δ 165.7, 163.2, 150.0, 145.0, 140.2 (C), 137.0 (CH), 135.8, 133.0, 117.3 (C), 116.7, 116.5, 116.0 (CH), 107.0 (C), 27.6, 26.2 (CH_2), 13.3, 12.7 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3430 (br), 2910 (s), 1678 (s), 1224 (m), 1081 (w), 856 (w). MS (EI, 70 eV): *m*/*z* (%) 302 (M^+, 100), 287 (44), 267 (20), 152 (15), 57 (20). HRMS (EI, 70 eV) calcd for $C_{17}H_{15}O_3Cl$ $[M]^+$: 302.0704; found: 302.0704.

3.5.2. 7-Hydroxy-1,2,3-trimethylbenzo[*c*]chromen-6-one (7b). Starting with **6b** (0.120 g, 0.37 mmol) and NEt_3 (0.076 g, 0.75 mmol), **7b** (0.021 g, 22%; 42% based on recovered starting material) was obtained as a white solid; mp 182 °C. Starting material (**6b**) (0.040 g) was recovered. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.68 (s, 1H, OH), 7.68 (d, 1H, J=7.9 Hz, Ar-H), 7.66 (s, 1H, Ar-H), 7.06–7.03 (m, 2H, Ar-H), 2.71 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.2, 162.8, 152.2, 149.9, 139.9 (C), 136.9 (CH), 135.0, 134.0, 117.9 (C), 116.6, 116.4, 115.9 (CH), 107.3 (C), 21.6, 21.5, 16.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ 2952 (s), 1671 (w), 1477 (s), 1371 (s), 1238 (w), 817 (w). MS (EI, 70 eV): *m*/*z* (%) 254 (M^+, 100), 239 (32), 211 (47), 149 (19), 91 (5). HRMS (EI, 70 eV) calcd for $C_{16}H_{14}O_3$ $[M]^+$: 254.0937; found: 254.0940.

3.5.3. 7-Hydroxy-1,3-dimethylbenzo[*c*]-6-one (7c). Starting with **6c** (0.091 g, 0.30 mmol) and NEt_3 (0.060 g, 0.60 mmol), **7c** (0.017 g, 24%; 46% based on recovered starting material) was obtained as a white solid; mp 180 °C.

Starting material (**6c**) (0.042 g) was recovered. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.79 (s, 1H, OH), 7.80 (d, 1H, J=7.6 Hz, Ar-H), 7.70 (t, 1H, J=8.2 Hz, Ar-H), 7.08 (s, 1H, Ar-H), 7.31 (d, 1H, J=7.0 Hz, Ar-H), 7.30 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 2.82 (s, 3H, CH_3), 2.40 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.2, 162.8, 152.2, 149.4, 140.1, 136.8, 136.7 (C), 136.6, 130.6, 116.6, 116.2, 115.7 (CH), 115.2, 106.3 (C), 25.4, 20.9, 16.7 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3410 (br), 2930 (s), 1675 (m), 1460 (s), 1225 (w), 814 (w). MS (EI, 70 eV): *m/z* (%) 240 (M^+, 100), 197 (15), 165 (10), 111 (21), 97 (30). HRMS (EI, 70 eV) calcd for $C_{15}H_{12}O_3$ $[M]^+$: 240.0781; found: 240.0781.

3.5.4. 4-Hydroxy-8-methyl-9,10,11,12-tetrahydro-6-oxabenzo[*c*]phenanthren-5-one (7d). Starting with **6d** (0.072 g, 0.20 mmol) and NEt_3 (0.041 g, 0.40 mmol), **7d** (0.028 g, 50%) was obtained as a slight yellow solid; mp 115 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.82 (s, 1H, OH), 7.78–7.66 (m, 2H, Ar-H), 7.08–7.03 (m, 2H, Ar-H), 3.45 (t, 2H, J=6.1 Hz, CH_2), 2.84 (t, 2H, J=5.4 Hz, CH_2), 2.31 (s, 3H, CH_3), 1.89–1.77 (m, 4H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6, 163.0, 149.4, 139.0, 137.4 (C), 136.6 (CH), 123.9, 118.5, 118.2 (C), 116.8, 115.9 (CH), 107.2 (C), 33.3, 30.9, 23.8, 22.7 (CH_2), 20.5 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3130 (br), 1719 (w), 1663 (w), 1098 (w), 700 (w). MS (EI, 70 eV): *m/z* (%) 280 (M^+, 100), 265 (25), 214 (15), 149 (13), 57 (18). HRMS (EI, 70 eV) calcd for $C_{18}H_{16}O_3$ $[M]^+$: 280.1094; found: 280.1090.

3.5.5. 8-Hydroxy-4-methyl-2,3-dihydro-1*H*-6-oxacyclopenta[*c*]phenanthren-7-one (7e). Starting with **6e** (0.100 g, 0.31 mmol) and NEt_3 (0.063 g, 0.63 mmol), **7e** was obtained (0.030 g, 35%; 60% based on recovered starting material) as a colorless solid; mp 202 °C. Starting material (**6e**) (0.041 g) was recovered. ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.74 (s, 1H, OH), 7.68 (t, 1H, J=7.0 Hz, Ar-H), 7.63 (s, 1H, Ar-H), 7.06–7.03 (m, 2H, Ar-H), 3.42 (t, 2H, J=7.3 Hz, CH_2), 2.90 (t, 2H, J=7.9 Hz, CH_2), 2.34 (s, 3H, CH_3), 2.30–2.18 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 181.6, 165.9, 162.6, 150.0, 141.4, 140.6, 136.8 (C), 135.8, 115.3, 114.6, 114.6 (CH), 106.2 (C), 35.1, 29.5, 23.8 (CH_2), 18.5 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3420 (br), 2910 (s), 1653 (w), 1320 (w), 1229 (w), 846 (w). MS (EI, 70 eV): *m/z* (%) 266 (M^+, 100), 251 (24), 207 (10), 165 (8), 57 (10). HRMS (EI, 70 eV) calcd for $C_{17}H_{14}O_3$ $[M]^+$: 266.0937; found: 266.0930.

3.5.6. 2,7-Dihydroxy-1,3-dimethyl-6*H*-benzo[*c*]chromen-6-one (7f). Starting with **6f** (0.120 g, 0.41 mmol) and NEt_3 (0.083 g, 0.82 mmol), **7f** (0.035 g, 33%; 40% based on recovered starting material) was obtained as a slight brownish solid mp 190 °C. Starting material (**6f**) (0.020 g) was recovered. ^{1}H NMR (250 MHz, DMSO-d_6): δ 11.69 (s, 1H, OH), 8.65 (s, 1H, OH), 7.87–7.77 (m, 2H, Ar-H), 7.12 (s, 1H, Ar-H), 7.09 (dd, 1H, J=8.2, 7.3 Hz, Ar-H), 2.64 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). ^{13}C NMR (62 MHz, DMSO-d_6): δ 165.3, 161.8, 151.0, 144.5 (C), 137.2 (CH), 136.6, 129.2, 122.8 (C), 117.6, 117.5, 116.3, 115.6 (CH), 106.3 (C), 17.3, 17.0 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ 3415 (br), 2940 (s), 1635 (m), 1240 (s), 1120 (m), 810 (w). MS (EI, 70 eV): *m/z* (%) 256 (M^+, 100), 213 (5), 207 (10), 165 (8), 57 (10). HRMS (ESI) calcd for $C_{15}H_{13}O_4$ $[M+H]^+$: 257.08084; found: 257.08069.

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Publication 9

Gopal Bose, Ehsan Ullah and Peter Langer*, "Synthesis of Spiro[5.4]decenones and their Transformation into Bicyclo[4.4.0]deca-1,4-dien-3-ones by Domino ′Elimination–Double-Wagner-Meerwein-Rearrangement′ Reactions", *Chem. Eur. J.* **2004**, *10*, 6015-6028.

Synthesis of Spiro[5.4]decenones and Their Transformation into Bicyclo[4.4]deca-1,4-dien-3-ones by Domino "Elimination–Double-Wagner–Meerwein-Rearrangement" Reactions

Gopal Bose, Ehsan Ullah, and Peter Langer*[a]

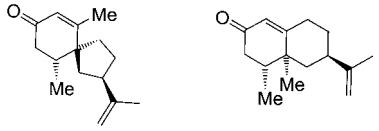
Abstract: The [3+3] cyclization of 1,3-bis-silyl enol ethers with 1,1-diacylcyclopentanes allows a convenient synthesis of spiro[5.4]decenones. Treatment of these compounds with trifluoroacetic acid (TFA) afforded a great variety of bicyclo[4.4.0]deca-1,4-dien-3-ones containing an angular alkyl group. This core structure occurs in a number of pharmacologically relevant natural products.

Keywords: cyclization · domino reactions · rearrangement · silyl enol ethers · spiro compounds

Introduction

1,3-Bis-silyl enol ethers can be regarded as electroneutral 1,3-dicarbonyl dianion equivalents (masked dianions).[1,2] They represent useful synthetic building blocks in Lewis acid mediated transformations. In cyclization reactions, 1,3-bis-silyl enol ethers can react as 1,3-dinucleophiles or, similarly to the well-known Danishefsky diene,[3] as functionalized 1,3-butadienes. Chan and co-workers have reported $TiCl_4$-mediated [3+3] cyclizations of 1,3-bis-silyl enol ethers with 3-silyloxyalk-2-en-1-ones and with ketals of β-ketoaldehydes, β-ketoesters, and β-ketocarboxylic chlorides to give benzene derivatives.[4] In addition, the synthesis of aromatic products by cyclization of free 1,3-dicarbonyl compounds with 1,3-dielectrophiles has been reported.[5,6]

We have recently reported the $TiCl_4$-mediated cyclization of 1,3-bis-silyl enol ethers with 1,1-diacetylcyclopentane to give spiro[5.4]decenones.[7] Treatment of these compounds with trifluoroacetic acid (TFA) resulted in a domino rearrangement[8] and formation of bicyclo[4.4.0]deca-1,4-dien-3-ones containing an angular methyl group. This type of rearrangement has been previously reported by Hagenbruch and Hünig[9a] and by others.[9b–g] The bicyclo[4.4.0]decane core structure is present in a variety of natural products, such as steroids and the eudesmane and eremophilane sesquiterpenes (for example, nootkaton; Scheme 1).[10,11] The spiro[5.4]decane skeleton also occurs in nature. This includes the spirovetivane sesquiterpenes (for example, solavetivone; Scheme 1), which are biosynthetically derived from the eudesmanes.[10] The biosynthetic pathways for the interconversion of eudesmane, eremophilane, and the spirovetivane sesquiterpenes involve Wagner–Meerwein rearrangements.[12–14]



Solavetivon Nootkaton

Scheme 1. Spiro[5.4]decanes and bicyclo[4.4.0]decanes in nature.

We have significantly extended the preparative scope of the methodology, with regard to our preliminary communication.[7] We have successfully developed regioselective cyclizations of unsymmetrical 1,1-diacylcyclopentanes, such as 1-acetyl-1-formylcyclopentane, and also studied cyclizations of 2,2-diacetylindane, 1,1-diacetylcyclopent-3-ene, and 3,3-dimethylpentane-2,4-dione. In addition, the mechanism of the domino process was studied.

Results and Discussion

Our starting point was the development of conditions for the cyclization of 3,3-dimethylpentane-2,4-dione (**2**) with 1,3-bis-silyl enol ether **1a**. Treatment of a CH_2Cl_2 solution of the starting materials with $TiCl_4$ (2 equiv) resulted in the formation of 3-hydroxycyclohex-5-en-1-one **3a** (Scheme 2). The product was formed by cyclization and subsequent extrusion of water. The use of other Lewis acids, such as $BF_3{\cdot}OEt_2$, Me_3SiOTf, or $ZnCl_2$, was unsuccessful. Optimal yields were obtained when the reaction was carried out at −78→20 °C.

[a] Dr. G. Bose, E. Ullah, Prof. Dr. P. Langer
Institut für Chemie und Biochemie
der Ernst-Moritz-Arndt Universität Greifswald
Soldmannstrasse 16, 17487 Greifswald (Germany)
Fax: (+49) 3834-864-373
E-mail: peter.langer@uni-greifswald.de

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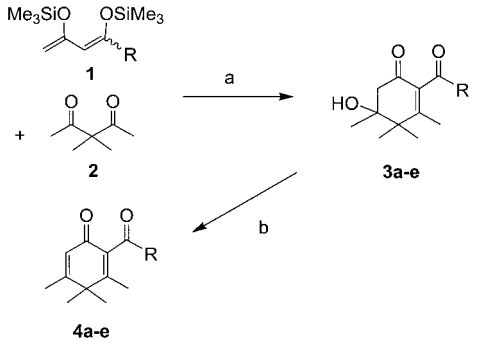


Scheme 2. Cyclization of 1,3-bis-silyl enol ethers with 3,3-dimethylpentane-2,4-dione: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å molecular sieves (MS), −78→20 °C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

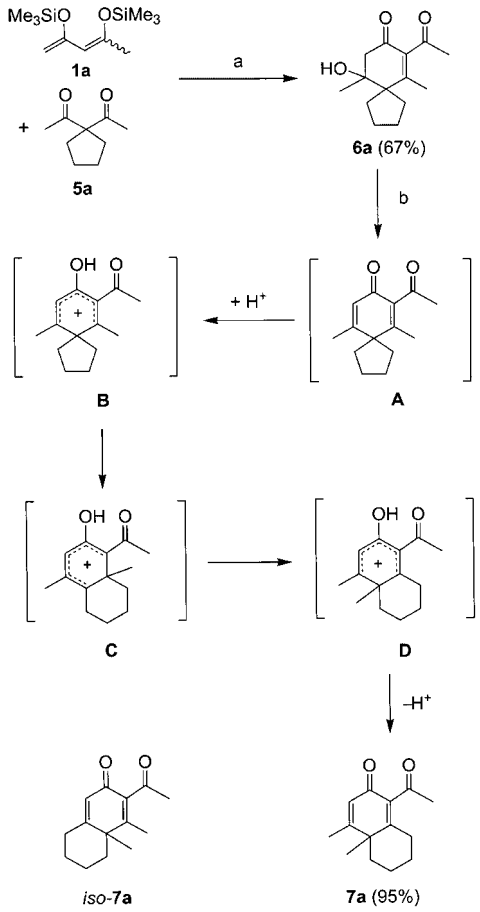
The use of molecular sieves (4 Å) proved to be mandatory. Treatment of a CH_2Cl_2 solution of **3a** with TFA afforded, after optimization of the reaction conditions, the cyclohexa-2,5-dien-1-one **4a** in 88% yield. A number of related products (**3b–e** and **4b–e**) were prepared by variation of the 1,3-bis-silyl enol ether (Table 1).

Table 1. Products and yields.

3,**4**	R	% **3**[a]	% **4**[a]
a	Me	47	88
b	OMe	61	95
c	OEt	63	96
d	O*i*Pr	56	90
e	$O(CH_2)_2Me$	61	92

[a] Yield of isolated products.

The $TiCl_4$-mediated cyclization of **1a** with 1,1-diacetylcyclopentane (**5a**), prepared by K_2CO_3-mediated cyclization of acetylacetone with 1,4-dibromobutane,[9,15] afforded the hydroxyspiro[5.4]decenone **6a** in good yield (Scheme 3). The following parameters proved to be important during the optimization of this reaction: a) the choice of the Lewis acid, b) the temperature (−78→20 °C), and c) the presence of molecular sieves (4 Å). Stirring of a TFA/CH_2Cl_2 solution of **6a** for 72 h afforded the bicyclo[4.4.0]deca-1,4-dien-3-one **7a** in high yield. The formation of **7a** can be explained as follows (Scheme 3): acid-mediated elimination of water gave the spiroannulated cyclohexa-2,5-dien-1-one **A**, which was protonated to give intermediate **B**. Ring enlargement by [1,2] rearrangement gave intermediate **C**. Rearrangement of the methyl group gave intermediate **D** and subsequent ex-

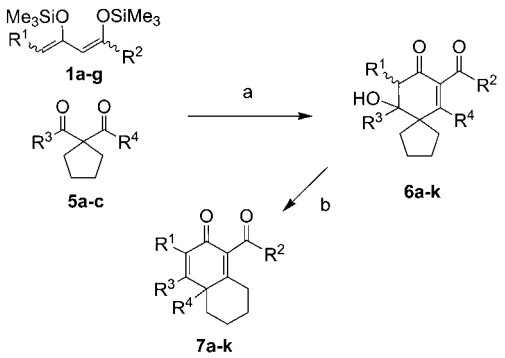


Scheme 3. Cyclization of 1,3-bis-silyl enol ether **1a** with 1,1-diacetylcyclopentane: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20 °C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

trusion of a proton afforded **7a**. The rearrangement proceeded with very good regioselectivity. The formation of the regioisomer *iso*-**7a** was not observed. The regioselectivity of the ring enlargement (**B**→**C**) can be explained by the fact that carbon atom C-5 of the delocalized carbocation **B** is more electron-poor than carbon atom C-3, due to the proximity of two electron-withdrawing carbonyl groups.

The preparative scope of our methodology was studied. The reaction of **5a** with ester-derived 1,3-bis-silyl enol ethers **1b–e** gave the spiro compounds **6b–e**, which were successfully transformed into the bicyclo[4.4.0]deca-1,4-dien-3-ones **7b–e** (Scheme 4, Table 2). The cyclization of **5a** with 1,3-bis-silyl enol ethers **1f** and **1g**, which contain either a methyl or an ethyl group at the terminal carbon atom, afforded the spiro compounds **6f** and **6g**, respectively. Treatment of these compounds with TFA resulted in formation of the bicyclo[4.4.0]decadienones **7f** and **7g** containing a methyl and an ethyl substituent, respectively. Variation of the 1,1-diacylcyclopentane was studied next. The reaction of **1b–d** with novel 1,1-dipropionylcyclopentane (**5b**), prepared by cyclization of heptane-3,5-dione with 1,4-dibromobutane, resulted in formation of spiro compounds **6h–j**, which were successfully transformed into **7h–j**. The cyclization of 1,3-bis-silyl enol ether **1c** with (unsymmetrical) 1-acetyl-1-benzoylcyclopentane (**5c**)[15d] gave the spiro[5.4]decenone **6k**.

Abstract in German: *Die [3+3] Cyclisierung von 1,3-Bis-Silylenolethern mit 1,1-Diacylcyclopentanen ermöglicht eine effiziente Synthese von Spiro[5.4]decenonen. Durch Behandlung dieser Verbindungen mit Trifluoressigsäure (TFA) konnte eine große Bandbreite von Bicyclo[4.4.0]deca-1,4-dien-3-onen mit angularer Alkylgruppe hergestellt werden. Dieses Gerüstsystem tritt in einer Reihe pharmakologisch relevanter Naturstoffe auf.*



Scheme 4. Synthesis of **6a–k** and **7a–k**: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20 °C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

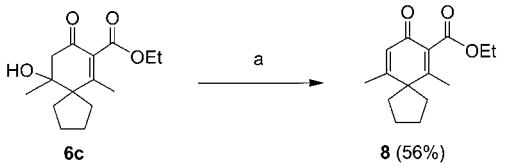
Table 2. Products and yields.

6,**7**	R^1	R^2	R^3	R^4	% **6**[a]	% **7**[a]
a	H	Me	Me	Me	67	95
b	H	OMe	Me	Me	72	98
c	H	OEt	Me	Me	78	96
d	H	O*i*Pr	Me	Me	66	97
e	H	$O(CH_2)_2OMe$	Me	Me	53	97
f	Me	OMe	Me	Me	23[b]	92
g	Et	OEt	Me	Me	41[b]	88
h	H	OMe	Et	Et	58	83
i	H	OEt	Et	Et	53	85
j	H	O*i*Pr	Et	Et	38	89
k	H	OEt	Me	Ph	20	91

[a] Yields of isolated products. [b] Diastereomeric mixture.

The TFA-mediated rearrangement of **6k** selectively afforded the bicyclo[4.4.0]decadienone **7k**.

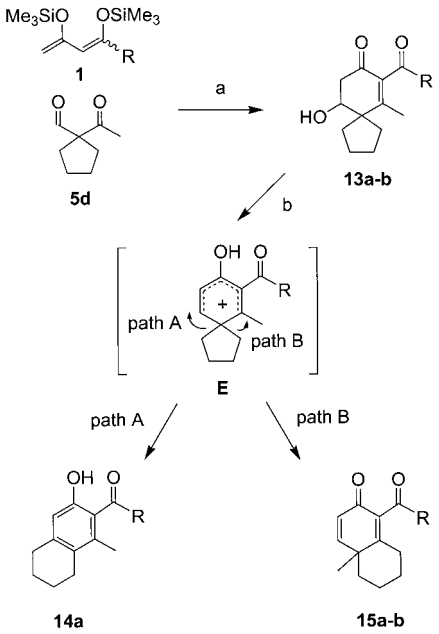
Treatment of hydroxyspiro[5.4]decenone **6c** with TFA for only 3 h (rather than for 72 h) afforded the spiro[5.4]decadienone **8** in 56% yield (Scheme 5). This experiment supports the intermediacy of spiro[5.4]decadienone **A** in the mechanism suggested (Scheme 3). The formation of a carbocation by extrusion of water and subsequent ring enlargement (without protonation of the carbonyl group) appears to be less likely.



Scheme 5. Synthesis of **8**: a) TFA, CH_2Cl_2, 3 h.

Cyclization reactions of 1-acetyl-1-formylcyclopentane (**5d**) were studied next. The synthesis of novel compound **5d** was accomplished as follows (see the Experimental Section). The cyclization of ethyl acetoacetate with 1,4-dibromobutane afforded ethyl 1-acetylcyclopentane-1-carboxylate (**9**). The keto group of **9** was protected by transformation into a ketal (**10**). The ester group was reduced to an alcohol (**11**), the acetal was hydrolyzed, and the alcohol (**12**) was transformed into an aldehyde by application of the Swern oxidation. This straightforward synthesis of **5d** is related to the procedure reported for the preparation of 1-acetyl-1-formylcyclopropane.[16]

The cyclization of 1,3-bis-silyl enol ether **1c** with 1-acetyl-1-formylcyclopentane (**5d**) gave the spiro compound **13a**, which was formed by regioselective attack of the terminal carbon atom of **1c** onto the aldehyde group (Scheme 6, Table 3). Treatment of **13a** with TFA afforded a separable mixture of the expected bicyclo[4.4.0]decadienone **14a** (43%, mechanism path B) and of the tetraline **15a** (22%, mechanism path A). The formation of **15a** can be explained by elimination of water and protonation to give intermediate **E** and subsequent ring enlargement and aromatization. The regioselectivity of the ring enlargement can be explained by the higher reactivity of the secondary carbocation located at C-3 (with respect to the tertiary carbocation located at C-5). The product **15a** is formed by a rapid ring enlargement (mechanism path A) and irreversible formation of a stable aromatic product. The cyclization of **5d** with 1,3-bis-silyl enol ether **1a** afforded **13b**. Treatment of the latter with TFA resulted in exclusive formation of the tetraline **15b** in 52% yield (mechanism path A).



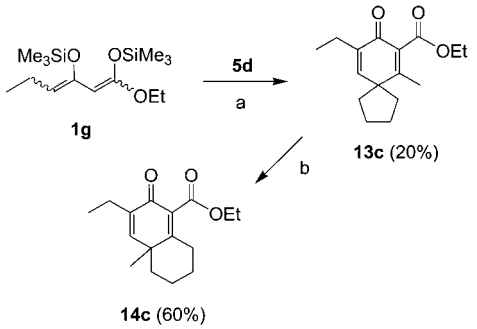
Scheme 6. Synthesis of **13a**, **13b**, **14a**, **15a**, and **15b**: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20 °C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

Table 3. Products and yields.

13,**14**,**15**	R	% **13**[a]	% **14**[a]	% **15**[a]
a	OEt	20	43	22
b	Me	27	0	52

[a] Yields of isolated products.

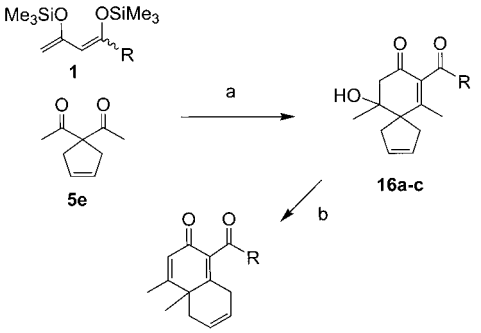
The reaction of **5d** with **1g** afforded the spiro compound **13c** (Scheme 7). Treatment of the latter with TFA exclusively afforded the bicyclo[4.4.0]decadienone **14c** in 60% yield (mechanism path B). The formation of an aromatic product



Scheme 7. Synthesis of **13c** and **14c**: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20°C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

15 by mechanism path A is disfavored, due to the presence of the ethyl group at carbon atom C-2 and steric repulsion during the ring enlargement.

Cyclization reactions of 1,1-diacetylcyclopent-3-ene (**5e**) were studied next. Direct base-mediated cyclization of acetylacetone with 1,4-dichlorobut-2-ene has been reported to give mixtures of regioisomeric products.[17] Therefore, we have developed a new synthesis of **5e**. The reaction of acetylacetone with allyl bromide afforded the known 3,3-diallylacetylacetone, which was subsequently transformed into **5e** by ring-closing metathesis (RCM) with the Grubbs catalyst and Ti(O*i*Pr)$_4$ (Fürstner conditions).[18] The reaction of 1,3-bis-silyl enol ethers **1b–d** with **5e** afforded the spiro compounds **16a–c** (Scheme 8, Table 4). Treatment of **16a–c** with TFA afforded the bicyclo[4.4.0]deca-1,4,6-trien-3-ones **17a–c**. The formation of the latter can be explained by a double Wagner–Meerwein rearrangement, as described for



Scheme 8. Synthesis of **16a–c** and **17a–c**: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20°C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

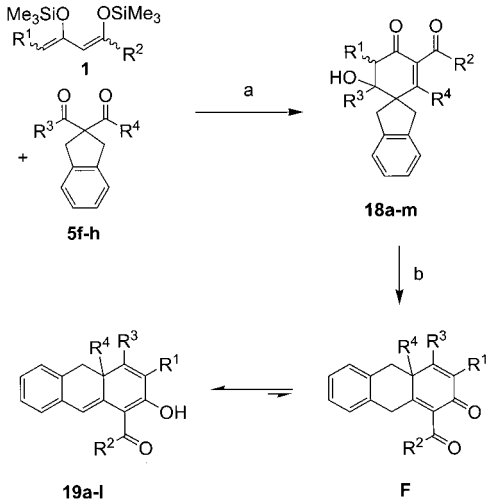
Table 4. Products and yields.

16, **17**	R	% **16**[a]	% **17**[a]
a	OMe	83	76
b	OEt	64	76
c	O*i*Pr	59	73

[a] Yields of isolated products.

7. Despite the acidic conditions, no migration of the double bond was observed during the reaction.

The reaction of 1,3-bis-silyl enol ethers with 2,2-diacetylindane (**5f**), prepared by base-mediated cyclization of acetylacetone with 1,2-bis(bromomethyl)benzene,[19] was studied next (Scheme 9, Table 5). The cyclization of 1,3-bis-silyl enol



Scheme 9. Synthesis of **18a–m** and **19a–l**: a) 1. $TiCl_4$ (2.0 equiv), CH_2Cl_2, 4 Å MS, −78→20°C; 2. H^+, H_2O; b) TFA, CH_2Cl_2, 72 h.

Table 5. Products and yields.

18, **19**	R^1	R^2	R^3	R^4	% **18**[a]	% **19**[a]
a	H	Me	Me	Me	82	82
b	H	OMe	Me	Me	86	79
c	H	OEt	Me	Me	86	86
d	H	O*i*Pr	Me	Me	82	76
e	H	$O(CH_2)_2OMe$	Me	Me	61	85
f	Et	OEt	Me	Me	31[b]	–[c]
g	H	OMe	Me	Ph	23	73
h	H	OMe	Ph	Me	21	84
i	H	OEt	Me	Ph	22	84
j	H	OEt	Ph	Me	17	83
k	H	O*i*Bu	Me	Ph	21	83
l	H	O*i*Bu	Ph	Me	15	73
m	H	O*i*Pr	Et	Et	43	–[c]

[a] Yields of isolated products. [b] Diastereomeric mixture. [c] The product could not be isolated in pure form.

ether **1a** with **5f** afforded the benzo-annulated spiro[5.4]decenone **18a** in good yield. Treatment of **18a** with TFA afforded the tricyclic product **19a**, which can be regarded as a 9,9a-dihydroanthracene. Due to conjugation of the enol moiety with the aryl group, this compound resides in the enol tautomeric form. The reaction of 1,3-bis-silyl enol ethers **1b–e** with **5f** afforded the spiro[5.4]decenones **18b–e**, which were transformed into the 9,9a-dihydroanthracenes **19b–e**. The reaction of **1g** with **5f** afforded **18f**. Treatment of the latter resulted in the formation of the ethyl-substituted 9,9a-dihydroanthracene **19f**; however, this could not be isolated in pure form. The reaction of 1,3-bis-silyl enol ether **1b** with novel 2-acetyl-2-benzoylindane (**5g**) afforded a separable mixture of the regioisomeric spiro[5.4]decenones **18g** (23%) and **18h** (21%). These products were transformed

into the corresponding 9,9a-dihydroanthracenes **19g** and **19h**, respectively. The reaction of ethoxy- and isobutoxy-substituted 1,3-bis-silyl enol ethers with **5g** afforded separable mixtures of the regioisomers **18i** and **18j** and of the regioisomers **18k** and **18l**, respectively. These products were transformed into the 9,9a-dihydroanthracenes **19i–l**. The cyclization of **1d** with novel 2,2-dipropionylindane (**5h**) afforded **18m**. Treatment of the latter with TFA afforded **19m**; however, this could not be isolated in pure form.

Conclusion

The [3+3] cyclization of 1,3-bis-silyl enol ethers with 1,1-diacylcyclopentanes allows a convenient synthesis of spiro[5.4]decenones. Treatment of these compounds with TFA afforded a great variety of bicyclo[4.4.0]deca-1,4-dien-3-ones containing an angular alkyl group.

Experimental Section

General: All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For the ^{1}H and ^{13}C NMR spectra (^{1}H NMR: 300, 600 MHz; ^{13}C NMR: 75, 150 MHz), the deuterated solvents indicated were used. Mass spectrometry (MS) data were obtained by using the electron ionization (70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI) techniques. For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

Typical procedure for the preparation of 3-hydroxycyclohex-5-en-1-ones of 3: $TiCl_4$ (0.22 mL, 2.00 mmol) was added dropwise to a stirred CH_2Cl_2 solution (100 mL) of 3,3-dimethylpentane-2,4-dione (**2**; 0.133 g, 1.04 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **1a** (0.330 g, 1.35 mmol) at −78 °C under an argon atmosphere in the presence of molecular sieves (4 Å; 1.0 g). The temperature of the reaction mixture was allowed to rise to 20 °C over 6 h. The solution was stirred for an additional 6 h at 20 °C. The reaction mixture was filtered and the filtrate was poured into an aqueous solution of HCl (10%, 100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were dried (Na_2SO_4) and filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel; hexane/ethyl acetate 3:2) to give **3a** as a colorless oil (0.102 g, 47%).

2-Acetyl-5-hydroxy-3,4,4,5-tetramethylcyclohex-2-enone (3a): From 1-methyl-1,3-bis(trimethysilyloxy)buta-1,3-diene (**1a**; 0.330 g, 1.35 mmol), 3,3-dimethylpentane-2,4-dione (**2**; 0.133 g, 1.04 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3a** was obtained as a colorless oil (0.102 g, 47%). R_f=0.08 (hexane/ethyl acetate 7:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.65 (s, 2H; CH_2), 2.33 (s, 3H; CH_3), 2.05 (br, 1H; OH), 1.89 (s, 3H; CH_3), 1.30 (s, 3H; CH_3), 1.26 (s, 3H; CH_3), 1.20 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=205.19, 195.06, 163.03, 138.77 (C), 75.09 (C−OH), 49.06 (CH_2), 44.51 (C), 31.81, 24.51, 22.24, 20.61, 16.95 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3424 (br), 2986 (m), 1719 (s), 1663 (s), 1621 (m), 1384 (m), 1243 (s), 129 (s), 1092 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=240.5 (7) [M^+], 211.3 (10), 195.3 (34), 179.3 (14), 151.5 (30), 136.2 (100), 108.5 (22), 43.1 (14).

4-Hydroxy-2,3,3,4-tetramethyl-6-oxocyclohex-1-ene carboxylic acid methyl ester (3b): From 1-methoxy-1,3-bis(trimethysilyloxy)buta-1,3-diene (**1b**; 0.386 g, 1.48 mmol), 3,3-dimethylpentane-2,4-dione (**2**; 0.152 g, 1.18 mmol), and $TiCl_4$ (0.24 mL, 2.18 mmol), **3b** was obtained as a colorless solid (0.164 g, 61%). M.p. 114–115 °C; R_f=0.12 (hexane/ethyl acetate 7:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.78 (s, 3H; OCH_3), 2.62 (s, 2H; CH_2), 2.15 (s, 1H; OH), 1.90 (s, 3H; CH_3), 1.26 (s, 3H; CH_3), 1.22 (s, 3H; CH_3), 1.16 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ= 193.18, 167.47, 164.33, 132.34 (C), 74.96 (C−OH), 52.05 (OCH_3), 48.83 (CH_2), 44.49 (C), 24.40, 22.09, 20.66, 17.68 ppm (CH_3); IR (KBr): $\tilde{\nu}$= 3411 (br), 2987 (m), 1728 (s), 1661 (s), 1618 (m), 1436 (m), 1340 (m), 1225 (s), 1091 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=226.3 (5) [M^+], 211.1 (11), 194.2 (35), 179.2 (16), 151.5 (29), 136.1 (100), 107.2 (20), 43.0 (16); elemental analysis calcd (%) for $C_{12}H_{18}O_4$: C 63.70, H 8.31; found: C 63.64, H 8.39.

4-Hydroxy-2,3,3,4-tetramethyl-6-oxocyclohex-1-ene carboxylic acid ethyl ester (3c): From 1-ethoxy-1,3-bis(trimethysilyloxy)buta-1,3-diene (**1c**; 0.375 g, 1.37 mmol), 3,3-dimethylpentane-2,4-dione (**2**; 0.135 g, 1.05 mmol), and $TiCl_4$ (0.23 mL, 2.09 mmol), **3c** was obtained as a colorless solid (0.159 g, 63%). M.p. 116–117 °C; R_f=0.12 (hexane/ethyl acetate 7:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.31 (d, 2H, J=7.2 Hz; OCH_2), 2.64 (s, 2H; CH_2), 2.27 (s, 1H; OH), 1.95 (s, 3H; CH_3), 1.33 (t, 3H, J= 7.2 Hz; CH_3), 1.31 (s, 3H; CH_3), 1.26 (s, 3H; CH_3), 1.21 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=193.44, 167.19, 164.08, 132.39 (C), 74.99 (C−OH), 61.29 (OCH_2), 48.71 (CH_2), 44.35 (C), 24.34, 22.10, 20.59, 17.66, 14.11 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3424 (br), 2986 (m), 1719 (s), 1663 (s), 1621 (m), 1384 (m), 1243 (s), 129 (s), 1092 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=240.5 (7) [M^+], 211.3 (10), 195.3 (34), 179.3 (14), 151.5 (30), 136.2 (100), 108.5 (22), 43.1 (14); elemental analysis calcd (%) for $C_{13}H_{20}O_4$: C 64.98, H 8.39; found: C 64.80, H 8.24.

4-Hydroxy-2,3,3,4-tetramethyl-6-oxocyclohex-1-ene carboxylic acid isopropyl ester (3d): From 1-isopropyloxy-1,3-bis(trimethysilyloxy)buta-1,3-diene (**1d**; 0.380 g, 1.32 mmol), 3,3-dimethylpentane-2,4-dione (**2**; 0.130 g, 1.01 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3d** was obtained as a colorless solid (0.144 g, 56%). M.p. 68–69 °C; R_f=0.11 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.15 (sep, 1H, J=6.2 Hz; OCH), 2.62 (s, 2H; CH_2), 2.30 (s, 1H; OH), 1.93 (s, 3H; CH_3), 1.31 (s, 3H; CH_3), 1.25 (d, 6H, J=6.2 Hz; CH_3), 1.22 (s, 3H; CH_3), 1.16 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.41, 166.75, 163.45, 132.58 (C), 75.01 (C−OH), 68.93 (OCH), 48.75 (CH_2), 44.30 (C), 24.33, 22.13, 21.70 (2C), 20.60, 17.45 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3415 (br), 2982 (m), 1723 (s), 1658 (s), 1619 (m), 1461 (m), 1356 (s), 1226 (s), 1096 cm^{-1} (s); MS (EI, 70 eV): m/z (%)=254.6 (17) [M^+], 211.4 (77), 195.3 (69), 169.2 (65), 151.8 (44), 136.3 (100), 108.5 (24), 43.1 (52); elemental analysis calcd (%) for $C_{14}H_{22}O_4$ (254.33): C 66.11, H 6.81; found: C 65.93, H 9.38.

4-Hydroxy-2,3,3,4-tetramethyl-6-oxocyclohex-1-ene carboxylic acid 2-methoxyethyl ester (3e): From 1-(2-methoxy)ethoxy-1,3-bis(trimethysilyloxy)buta-1,3-diene (**1e**; 0.401 g, 1.32 mmol), 3,3-dimethylpentane-2,4-dione (**2**; 0.135 g, 1.05 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3e** was obtained as a colorless solid (0.164 g, 61%). M.p. 78–88 °C; R_f=0.11 (hexane/ethyl acetate 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.39 (t, 2H, J=4.8 Hz; OCH_2), 3.64 (t, 2H, J=4.8 Hz; OCH_2), 3.38 (s, 3H; OCH_3), 2.61 (s, 2H; CH_2), 2.29 (s, 1H; OH), 1.96 (s, 3H; CH_3), 1.29 (s, 3H; CH_3), 1.26 (s, 3H; CH_3), 1.19 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=193.31, 167.07, 164.57, 132.08 (C), 74.92 (C−OH), 70.22, 63.92 (OCH_2), 58.75 (OCH_3), 48.72 (CH_2), 44.42 (C), 24.33, 22.02, 20.62, 17.66 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3402 (br), 2987 (m), 1727 (s), 1660 (s), 1619 (m), 1456 (m), 1382 (s), 1245 (s), 1091 cm^{-1} (s); MS (EI, 70 eV): m/z (%)=270.5 (18) [M^+], 211.3 (40), 194.5 (79), 179.2 (41), 151.8 (68), 136.6 (100), 108.5 (32), 43.1 (37); elemental analysis calcd (%) for $C_{14}H_{22}O_5$ (270.33): C 62.20, H 8.20; found: C 62.35, H 8.59.

Typical procedure for the preparation of cyclohexa-2,5-dien-1-ones of 4: TFA (0.4 mL, 5.2 mmol) was added dropwise to a stirred CH_2Cl_2 solution (0.4 mL) of **3a** (0.065 g, 0.31 mmol) at 20 °C. The solution was stirred for 72 h until all starting material disappeared (TLC control). The solvent and TFA were removed in vacuo and the residue was purified by column chromatography (silica gel; hexane/ethyl acetate 7:3) to give **4a** as a colorless oil (0.052 g, 88%).

2-Acetyl-3,4,4,5-tetramethylcyclohexa-2,5-dienone (4a): From **3a** (0.065 g, 0.31 mmol), **4a** was obtained as a colorless oil (0.052 g, 88%). R_f=0.23 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.12 (d, 1H, J=1.2 Hz; =CH), 2.37 (s, 3H; CH_3), 2.05 (d, 3H, J=1.2 Hz; CH_3), 1.96 (s, 3H; CH_3), 1.29 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=205.32, 183.14, 165.71, 160.60, 139.12 (C), 126.40 (CH), 42.96 (C), 31.72, 24.51 (2C), 19.93, 16.17 ppm (CH_3); IR (KBr): $\tilde{\nu}$=1734 (s), 1664 (s), 1623 (s), 1386 (m), 1250 (s), 1048 (m), 888 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=192.2 (2) [M^+], 177.1 (100), 162.1 (5), 149.1 (11), 135.1 (9), 121.1 (8), 91.1 (7), 43.1 (13). The exact molecular mass for $C_{12}H_{16}O_2$: m/z=192.1150±2 mD was confirmed by HRMS (EI, 70 eV).

2,3,3,4-Tetramethyl-6-oxocyclohexa-1,4-dienecarboxylic acid methyl ester (4b): From **3b** (0.075 g, 0.33 mmol), **4b** was obtained as a colorless oil (0.065 g, 95%). R_f=0.18 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.07 (d, 1H, J=1.2 Hz; =CH), 3.79 (s, 3H; OCH_3), 1.99 (d, 3H, J=1.2 Hz; CH_3), 1.97 (s, 3H; CH_3), 1.23 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=181.43, 167.55, 165.32, 161.73, 132.72 (C), 125.92 (CH), 52.05 (CH_3), 42.69 (C), 24.33 (2C), 19.80, 16.82 ppm (CH_3); IR (KBr): $\tilde{\nu}$=1739 (s), 1662 (s), 1627 (s), 1390 (m), 1250 (s), 1048 (m), 870 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=208.2 (100) [M^+], 193.1, 177.1, 149.1, 121.1, 91.1. The exact molecular mass for $C_{12}H_{16}O_3$: m/z=208.1099±2 mD was confirmed by HRMS (EI, 70 eV).

2,3,3,4-Tetramethyl-6-oxocyclohexa-1,4-dienecarboxylic acid ethyl ester (4c): From **3c** (0.070 g, 0.29 mmol), **4c** was obtained as a colorless oil (0.062 g, 96%). R_f=0.22 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.11 (d, 1H, J=1.3 Hz; =CH), 4.32 (d, 2H, J=7.1 Hz; OCH_2), 2.03 (d, 3H, J=1.3 Hz; CH_3), 2.01 (s, 3H; CH_3), 1.32 (t, 3H, J=7.1 Hz; CH_3), 1.28 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=181.59, 167.18, 165.27, 161.30, 132.99 (C), 126.07 (CH), 61.18 (OCH_2), 42.69 (C), 24.40 (2C), 19.86, 16.71, 14.11 ppm (CH_3); IR (neat): $\tilde{\nu}$=2982 (w), 1733 (s), 1665 (s), 1632 (s), 1389 (m), 1244 (s), 1048 (s), 878 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=222.2 (98) [M^+], 207.2 (34), 177.1 (100), 149.1 (87), 135.1 (45), 121.1 (65), 105.5 (41), 91.1 (35). The exact molecular mass for $C_{13}H_{18}O_3$: m/z=222.1256±2 mD was confirmed by HRMS (EI, 70 eV).

2,3,3,4-Tetramethyl-6-oxocyclohex-1,4-dienecarboxylic acid isopropyl ester (4d): From **3d** (0.066 g, 0.26 mmol), **4d** was obtained as a colorless oil (0.055 g, 90%). R_f=0.23 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.12 (d, 1H, J=1.2 Hz; =CH), 5.23 (sep, 1H, J=6.3 Hz; OCH), 2.05 (d, 3H, J=1.2 Hz; CH_3), 2.04 (s, 3H; CH_3), 1.32 (d, 6H, J=6.3 Hz; CH_3), 1.27 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=181.43, 166.56, 165.14, 160.69, 132.99 (C), 125.91 (CH), 68.57 (OCH), 42.49 (C), 24.23 (2C), 21.55 (2C), 19.65, 16.32 ppm (CH_3); IR (neat): $\tilde{\nu}$=2982 (w), 1731 (s), 1667 (s), 1627 (s), 1386 (m), 1249 (s), 1039 cm^{-1} (s); MS (EI, 70 eV): m/z (%)=236.0 (42) [M^+], 220.9 (10), 177.1 (100), 149.1 (56), 135.1 (44), 121.1 (29), 91.0 (31), 43.1 (87). The exact molecular mass for $C_{14}H_{20}O_3$: m/z=236.1412±2 mD was confirmed by HRMS (EI, 70 eV).

2,3,3,4-Tetramethyl-6-oxocyclohex-1,4-dienecarboxylic acid 2-methoxyethyl ester (4e): From **3e** (0.080 g, 0.29 mmol), **4e** was obtained as a colorless oil (0.068 g, 92%). R_f=0.18 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.13 (d, 1H, J=1.2 Hz; =CH), 4.44 (m, 2H; OCH_2), 3.67 (m, 2H; OCH_2), 3.39 (s, 3H; OCH_3), 1.31 (s, 6H; CH_3), 1.05 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=181.31, 167.10, 165.08, 161.53, 132.77 (C), 126.05 (CH), 70.26, 63.84 (OCH_2), 58.76 (OCH_3), 42.68 (C), 24.36 (2C), 19.80, 16.69 ppm (CH_3); IR (KBr): $\tilde{\nu}$=1734 (s), 1664 (s), 1623 (s), 1386 (m), 1250 (s), 1048 (m), 888 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=252.0 (26) [M^+], 237.0 (12), 195.0 (27), 177.0 (100), 148.3 (29), 58.5 (44), 28.1 (29). The exact molecular mass for $C_{14}H_{20}O_4$: m/z=252.1362±2 mD was confirmed by HRMS (EI, 70 eV).

Typical procedure for the preparation of spiro[5.4]decenones 6, 13, 16, and 18: $TiCl_4$ (0.22 mL, 2.00 mmol) was added dropwise to a stirred CH_2Cl_2 solution (100 mL) of 1,1-diacetylcyclopentane (**5a**; 0.160 g, 1.04 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene (**1a**; 0.380 g, 1.54 mmol) at −78°C under an argon atmosphere in the presence of molecular sieves (4 Å; 1.0 g). The temperature of the reaction mixture was allowed to rise to 20°C over 6 h. The solution was stirred for additional 6 h at 20°C. The reaction mixture was filtered and the filtrate was poured into an aqueous solution of HCl (10%, 100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were dried (Na_2SO_4) and filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel; hexane/ethyl acetate 7:3) to give **6a** as colorless crystals (0.164 g, 67%).

7-Acetyl-10-hydroxy-6,10-dimethylspiro[5,4]dec-6-en-8-one (6a): From 1-methyl-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1a**; 0.380 g, 1.54 mmol), 1,1-diacetylcyclopentane (**5a**; 0.160 g, 1.04 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6a** was obtained as colorless crystals (0.164 g, 67%). M.p. 80–81°C; R_f=0.11 (hexane/ethyl acetate 7:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.60 (br, 2H; CH_2), 2.30 (br, 1H; OH), 2.25 (s, 3H; CH_3), 1.86 (s, 3H; CH_3), 1.73 (br, 8H; CH_2), 1.21 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=205.44, 195.65, 163.68, 137.63 (C), 75.40 (C–OH), 56.26 (C), 49.95, 32.93 (2C, CH_2), 31.75 (CH_3), 28.22 (2C, CH_2), 24.89, 17.04 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3414 (s), 2959 (m), 1704 (s), 1652 (s), 1603 (m), 1383 (m), 1344 (m), 1191 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=236.2 (26) [M^+], 218.0 (64), 193.1 (60), 149.1 (100), 43.0 (89); elemental analysis calcd (%) for $C_{14}H_{20}O_3$: C 71.15, H 8.53; found: C 71.31, H 8.53.

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid methyl ester (6b): From 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.390 g, 1.5 mmol), 1,1-diacetylcyclopentane (**5a**; 0.156 g, 1.0 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6b** was obtained as colorless crystals (0.184 g, 72%). M.p. 106–107°C; R_f=0.23 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.82 (s, 3H; OCH_3), 2.65 (br, 2H; CH_2), 2.22 (br, 1H; OH), 1.99 (br, 2H; CH_2), 1.98 (s, 3H; CH_3), 1.76 (br, 6H; CH_2), 1.27 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.83, 167.66, 164.91, 131.25 (C), 75.34 (C–OH), 56.13 (C), 52.20 (OCH_3), 49.64, 32.98 (2C), 28.23 (2C, CH_2), 24.86, 17.88 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3431 (s), 2961 (s), 1730 (s), 1663 (s), 1620 (s), 1344 (m), 1385 (s), 1231 (s), 1203 (s), 863 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=252.3 (4) [M^+], 220.2 (16), 162.1 (100), 134.1 (52), 91.1 (54), 43.0 (72); elemental analysis calcd (%) for $C_{14}H_{20}O_4$: C 66.64, H 7.99; found: C 66.58, H 8.23.

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid ethyl ester (6c): From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.415 g, 1.5 mmol), 1,1-diacetylcyclopentane (**5a**; 0.154 g, 1.0 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6c** was obtained as colorless crystals (0.208 g, 78%). M.p. 107–108°C; R_f=0.35 (hexane/ethyl acetate 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.29 (q, 2H, J=7.2 Hz; OCH_2), 2.64 (br, 2H; CH_2), 2.16 (br, 2H; CH_2), 1.98 (s, 3H; CH_3), 1.88 (br, 1H; OH), 1.76 (br, 6H; CH_2), 1.32 (t, 3H, J=7.2 Hz; CH_3), 1.26 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.15, 167.54, 164.61, 131.72 (C), 75.68 (C–OH), 61.53 (OCH_2), 56.35 (C), 49.95, 33.54 (2C), 28.50 (2C, CH_2), 25.11, 17.98, 14.40 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3410 (s), 2966 (s), 1724 (s), 1663 (s), 1619 (s), 1470 (m), 1385 (s), 1342 (s), 1237 (s), 1205 (s), 1089 (s), 1026 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=266.3 (9) [M^+], 220.2 (52), 162.2 (100), 134.1 (33); elemental analysis calcd (%) for $C_{15}H_{22}O_4$: C 67.64, H 8.32; found: C 67.38, H 8.45.

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid isopropyl ester (6d): From 1-isopropoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1d**; 0.430 g, 1.5 mmol) and 1,1-diacetylcyclopentane (**5a**; 0.154 g, 1.0 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6d** was obtained as a colorless oil (0.185 g, 66%). R_f=0.17 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.18 (sep, 1H, J=6.3 Hz; OCH), 2.63 (br, 2H; CH_2), 2.37 (br, 2H; CH_2), 1.97 (s, 3H; CH_3), 1.95 (br, 1H; OH), 1.75 (br, 6H; CH_2), 1.32 (s, 3H; CH_3), 1.28 ppm (d, 6H, J=6.3 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.97, 166.88, 163.89, 131.55 (C), 75.29 (C–OH), 68.84 (OCH), 56.01 (C), 49.66, 32.77 (2C), 28.19 (2C, CH_2), 24.75, 21.67 (2C), 17.47 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3460 (br), 2977 (s), 1728 (s), 1671 (s), 1619 (m), 1379 (m), 1248 (s), 1108 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=280.3 (5) [M^+], 237.2 (22), 220.2 (20), 195.2 (12), 178.2 (11), 162.1 (100), 134.1 (17), 43.0 (16); elemental analysis calcd (%) for $C_{16}H_{24}O_4$: C 68.54, H 8.62; found: C 67.38 H 8.97. The exact molecular mass for $C_{16}H_{24}O_4$: m/z=280.1675±2 mD was confirmed by HRMS (EI, 70 eV).

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid 2-methoxyethyl ester (6e): From 1-(2-methoxy)ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1e**; 0.455 g, 1.5 mmol), 1,1-diacetylcyclopentane (**5a**; 0.154 g, 1.0 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6e** was obtained as a colorless oil (0.156 g, 53%). R_f=0.21 (hexane/ethyl acetate 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.37 (t, 2H, J=6.0 Hz; OCH_2), 3.62 (t, 2H, J=6.0 Hz; OCH_2), 3.36 (s, 3H; OCH_3), 2.62 (br, 2H; CH_2), 2.09 (br, 2H; CH_2), 2.00 (s, 3H; CH_3), 1.95 (br, 1H; OH), 1.73 (br, 6H; CH_2), 1.22 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.76, 167.16, 164.91, 134.13 (C), 75.38 (C–OH), 70.23, 63.90 (OCH_2), 58.76 (OCH_3), 56.12 (C), 49.26, 32.82 (2C), 28.25 (2C, CH_2), 24.81, 17.71 ppm (CH_3); IR (neat): $\tilde{\nu}$=3462 (br), 2973 (s), 1733 (s), 1666 (s), 1621 (m), 1382 (s), 1253 (s), 1108 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=295.6 (8) [M^+], 219.7 (77), 177.9 (46), 162.0 (100), 133.9 (76), 90.9 (28), 43.1 (28). The exact molecular mass for $C_{16}H_{24}O_5$: m/z=296.1624±2 mD was confirmed by HRMS (EI, 70 eV).

10-Hydroxy-6,9,10-trimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid methyl ester (6f) (major isomer): From 1-methoxy-1,3-bis(trimethylsi-

lyloxy)penta-1,3-diene (**1f**; 0.410 g, 1.5 mmol), 1,1-diacetylcyclopentane (**5a**; 0.157 g, 1.0 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6f** was obtained as a colorless oil (0.061 g, 23%). R_f=0.23 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.36 (s, 3H; OCH_3), 2.88 (q, 1H, J=6.9 Hz; CH), 2.08 (s, 3H; CH_3), 1.96–1.92 (m, 3H; OH, CH_2), 1.41–1.21 (m, 6H; CH_2), 1.20 (d, 3H, J=7.2 Hz; CH_3), 1.08 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=196.32, 168.60, 163.67, 131.13 (C), 75.38 (C–OH), 57.23 (C), 52.42 (OCH_3), 49.48 (CH), 33.37 (2C), 28.60 (2C, CH_2), 17.71, 16.88, 14.09 ppm (CH_3); IR (neat): $\tilde{\nu}$=3462 (br), 2973 (s), 1733 (s), 1666 (s), 1621 (m), 1382 (s), 1253 (s), 1108 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=266.5 (2) [M^+], 234.4 (15), 192.3 (23), 162.2 (100), 134.2 (60), 91.2 (28), 43.0 (58). The exact molecular mass for $C_{15}H_{22}O_4$: m/z=266.1519±2 mD was confirmed by HRMS (EI, 70 eV).

9-Ethyl-10-hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid ethyl ester (6g): From 1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene (**1g**; 0.380 g, 1.56 mmol), 1,1-diacetylcyclopentane (**5a**; 0.160 g, 1.04 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6g** was obtained as a colorless oil (0.100 g, 41%). R_f=0.23 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.27 (q, 2H, J=7.2 Hz; OCH_2), 2.60–2.40 (m, 1H; CH), 2.10 (br, 1H; OH), 1.94 (s, 3H; CH_3), 1.92–1.40 (m, 10H; CH_2), 1.31 (t, 3H, J=7.2 Hz; CH_3), 1.08 (t, 3H, J=7.5 Hz; CH_3), 1.06 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=196.43, 167.44, 162.37, 131.58 (C), 61.13 (CH), 57.44 (C), 57.10 (CH_2), 33.36, 31.89, 28.72, 27.20, 19.55, 17.42, 16.44, 14.63, 14.10, 11.01 ppm; IR (neat): $\tilde{\nu}$=3515 (s), 2976 (s), 2875 (m), 1732 (s), 1670 (s), 1622 (m), 1457 (m), 1382 (m), 1257 (m), 1210 (m), 1112 (s), 1023 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=294.5 (6) [M^+], 265.5 (76), 219.3 (45), 162.2 (100), 134.2 (75), 43.0 (52). The exact molecular mass for $C_{17}H_{26}O_4$: m/z=294.1831±2 mD was confirmed by HRMS (EI, 70 eV).

6,10-Diethyl-10-hydroxy-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid methyl ester (6h): From 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.180 g, 0.69 mmol), 1,1-dipropionylcyclopentane (**5b**; 0.097 g, 0.53 mmol), and $TiCl_4$ (0.12 mL, 1.09 mmol), **6h** was obtained as a colorless oil (0.086 g, 58%). R_f=0.22 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.77 (s, 3H; OCH_3), 2.63 (br, 2H; CH_2), 2.30–2.22 (br, 2H; CH_2), 2.12 (br, 1H; OH), 1.93–1.53 (br, 10H; CH_2), 1.13 (t, 3H, J=7.5 Hz; CH_3), 0.87 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.20, 170.99, 167.75, 131.39 (C), 75.33 (C–OH), 57.53 (C), 52.08 (OCH_3), 44.08, 40.62 (CH_2), 29.63 (2C), 27.20 (2C), 24.62 (CH_2), 14.48, 7.38 ppm (CH_3); IR (neat): $\tilde{\nu}$=3496 (br), 2971 (s), 2875 (m), 1735 (s), 1666 (s), 1606 (w), 1436 (m), 1342 (m), 1228 (m), 1082 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=280.4 (10) [M^+], 248.4 (50), 192.2 (62), 176.3 (100), 147.6 (41), 120.5 (48), 91.1 (41), 29.0 (44). The exact molecular mass for $C_{16}H_{24}O_4$: m/z=280.1675±2 mD was confirmed by HRMS (EI, 70 eV).

6,10-Diethyl-10-hydroxy-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid ethyl ester (6i): From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.415 g, 1.60 mmol), 1,1-dipropionylcyclopentane (**5b**; 0.193 g, 1.06 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6i** was obtained as a colorless oil (0.167 g, 56%). R_f=0.28 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.30 (dq, 2H, J=7.2, 1.5 Hz; OCH_2), 2.67 (br, 2H; CH_2), 2.40–2.30 (br, 4H; CH_2), 2.04 (br, 1H; OH), 1.94–1.59 (br, 8H; CH_2), 1.31 (t, 3H, J=7.2 Hz; CH_3), 1.17 (t, 3H, J=7.5 Hz; CH_3), 0.91 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.20, 170.99, 167.75, 131.39 (C), 75.33 (C–OH), 57.53 (C), 52.08 (OCH_3), 44.08, 40.62 (CH_2), 29.63 (2C), 27.20 (2C), 24.62 (CH_2), 14.48, 7.38 ppm (CH_3); IR (neat): $\tilde{\nu}$=3496 (br), 2971 (s), 2875 (m), 1735 (s), 1666 (s), 1606 (w), 1436 (m), 1342 (m), 1228 (m), 1082 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=294.2 (10) [M^+], 248.2 (25), 219.0 (16), 192.1 (26), 176.1 (100), 91.0 (14), 29.0 (35). The exact molecular mass for $C_{17}H_{26}O_4$: m/z=294.1813±2 mD was confirmed by HRMS (EI, 70 eV).

6,10-Diethyl-10-hydroxy-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid isopropyl ester (6j): From 1-isopropoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1d**; 0.475 g, 1.65 mmol), 1,1-dipropionylcyclopentane (**5b**; 0.200 g, 1.10 mmol), and $TiCl_4$ (0.24 mL, 2.20 mmol), **6j** was obtained as a colorless solid (0.179 g, 53%). M.p. 96–97 °C; R_f=0.34 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.18 (sep, 1H, J=6.3 Hz; OCH), 2.65 (br, 2H; CH_2), 2.36–1.56 (m, 13H; OH, CH_2), 1.30 (d, 6H, J=6.3 Hz; CH_3), 1.19 (t, 3H, J=7.5 Hz; CH_3), 0.88 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.39, 169.99, 167.06, 132.11 (C), 75.33 (C–OH), 68.95 (OCH), 57.72 (C), 45.19, 28.07, 36.48 (2C), 28.48, 27.36, 24.64 (CH_2), 21.85 (2C), 14.72, 7.63 ppm (CH_3); IR (neat): $\tilde{\nu}$=3462 (br), 2975 (s), 1725 (s), 1698 (s), 1667 (s), 1612 (m), 1450 (m), 1102 (s), 827 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=308.1 (10) [M^+], 265.2 (19), 248.1 (22), 192.1 (22), 176.1 (100), 43.1 (14); elemental analysis calcd (%) for $C_{18}H_{28}O_4$: C 70.10, H 9.19; found: C 69.92, H 9.68.

10-Hydroxy-10-methyl-8-oxo-6-phenylspiro[4,5]dec-6-ene-7-carboxylic acid ethyl ester (6k): From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.415 g, 1.50 mmol), 1-acetyl-1-benzoylcyclopentane (**5c**; 0.216 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **6k** was obtained as a colorless oil (0.125 g, 38%). R_f=0.28 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.38–7.18 (m, 5H; ArH), 3.85 (q, 2H, J=7.2 Hz; OCH_2), 2.90–2.70 (m, 4H; CH_2), 2.07 (br, 1H; OH), 1.98–1.86 (m, 4H; CH_2), 1.55–1.42 (m, 2H; CH_2), 1.39 (s, 3H; CH_3), 0.81 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.63, 166.16 (2C), 136.50, 132.25 (C), 128.03 (2C), 127.83, 127.55 (2C, CH), 75.72 (C–OH), 60.88 (OCH_2), 57.17 (C), 50.07, 33.15 (2C), 27.25, 27.03 (CH_2), 24.83, 13.58 ppm (CH_3); IR (neat): $\tilde{\nu}$=3542 (m), 2953 (m), 1727 (s), 1677 (s), 1612 (m), 1341 (m), 1234 (s), 704 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=328.4 (6) [M^+], 282.8 (33), 224.6 (100), 104.8 (40), 43.1 (76), 28.1 (53). The exact molecular mass for $C_{20}H_{24}O_4$: m/z=328.1675±2 mD was confirmed by HRMS (EI, 70 eV).

10-Hydroxy-6-methyl-8-oxospiro[4.5]dec-6-en-7-carboxylic acid ethyl ester (13a): From 1-acetyl-1-formylcyclopentane (**5d**; 0.200 g, 1.42 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.585 g, 2.13 mmol), and $TiCl_4$ (0.31 mL, 2.84 mmol), **13a** was obtained as a yellow oil (0.068 g, 20%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.30 (q, 2H, J=7.2 Hz; OCH_2), 3.49 (br, 1H, J=6.9 Hz; CHOH), 2.79 (dd, 1H, J=16.8, 3.7 Hz; CH_2), 2.63 (dd, 1H, J=16.8, 7.2 Hz; CH_2), 2.04 (s, 1H; OH), 1.96 (s, 3H; CH_3), 1.81–1.77 (m, 8H; CH_2), 1.32 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.0, 167.12, 162.55, 132.54 (C), 72.85 (CH), 61.30 (CH_2), 52.57 (C), 43.04, 35.36, 32.48, 27.36, 27.01 (CH_2), 17.69, 14.16 ppm (CH_3); IR (neat): $\tilde{\nu}$=3430 (br), 2959 (m), 1729.2 (s), 1666 (s), 1614 (m), 1378 (m), 1239 (m), 1090 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=252.0 (7) [M^++1], 206.0 (19), 161.9 (83), 134.1 (30), 82.1 (33), 68.0 (67), 43.1 (53), 28.1 (100); elemental analysis calcd (%) for $C_{14}H_{19}O_4$: C 66.93, H 7.5; found: C 66.05, H 8.53.

7-Acetyl-10-hydroxy-10-methylspiro[5,4]dec-6-en-8-one (13b): From 1-acetyl-1-formylcyclopentane (**5d**; 0.150 g, 1.07 mmol), 2,4-bis-trimethylsilyloxypenta-1,3-diene (0.391 g, 1.60 mmol), and $TiCl_4$ (0.23 mL, 2.14 mmol), **13b** was obtained as a yellow oil (0.064 g, 27%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.96 (br, 1H; C*H*OH), 2.78 (dd, 1H, J=16.5, 3.6 Hz; CH_2), 2.61 (dd, 1H, J=16.8, 6.9 Hz; CH_2), 2.32 (s, 3H; CH_3), 2.09–2.01 (m, 3H; CH_2, OH), 1.90 (s, 3H; CH_3), 1.85–1.75 ppm (m, 6H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$); δ=205.48, 195.08, 161.81, 138.68 (C), 72.74 (CH), 52.72 (C), 43.25, 33.41, 32.65 (CH_2), 31.77 (CH_3), 27.30, 26.81 (CH_2), 17.05 ppm (CH_3); IR (neat): $\tilde{\nu}$=3461 (br), 2960 (m), 1703 (s), 1664 (s), 1355 (s), 1215 (m), 1074 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 223.0 (9) [M^++1], 222.0 (51) [M^+], 181.0 (100), 163 (38), 149.1 (81), 122 (40), 43.1 (97), 29.0 (7); elemental analysis calcd (%) for $C_{13}H_{18}O_3$: C 70.27, H 8.62; found: C 69.00, H 8.10.

9-Ethyl-10-methyl-8-oxospiro[5,4,0]deca-6,9-diene-7-carboxylic acid (13c): From 1-acetyl-1-formylcyclopentane (**5d**; 0.150 g, 1.07 mmol), 1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.485 g, 1.60 mmol), and $TiCl_4$ (0.23 mL, 2.14 mmol), **13c** was obtained as a colorless oil (56 mg, 20%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.47 (s, 1H; =CH), 4.33 (q, 2H, J=7.2 Hz; OCH_2), 2.54–2.42 (m, 1H; CH_2), 2.38–2.37 (m, 3H; CH_2), 2.05–1.95 (m, 1H; CH_2), 1.87–1.81 (m, 1H; CH_2), 1.73–1.67 (m, 2H; CH_2), 1.43–1.35 (m, 2H; CH_2), 1.34 (t, 3H, J=7.2 Hz; CH_3), 1.28 (s, 3H; CH_3), 1.07 ppm (t, 3H, J=7.5 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=182.98, 167.35, 162.83 (C), 151.30 (CH), 137.64, 130.67 (C) 61.14 (CH_2), 40.02 (C), 38.72, 29.40, 27.59 (CH_2) 23.16 (CH_3), 21.75, 20.70 (CH_2), 14.18, 12.36 ppm (CH_3); IR (neat): $\tilde{\nu}$=3440 (br), 2960 (m); 1730 (s), 1670 (s), 1365 (s), 1237 (m), 1092 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=262.1 (25) [M^+], 217.1 (29), 201.1 (55), 189.1 (100), 161.1 (21), 29.0 (10). The exact molecular mass for $C_{16}H_{22}O_3$: m/z=262.1570±2 mD was confirmed by HRMS (EI, 70 eV).

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]deca-2,6-diene-7-carboxylic acid methyl ester (16a): From 1-(1-acetylcyclopent-3-enyl)ethanone (**5e**; 0.155 g, 1.02 mmol), 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.400 g, 1.53 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **16a** was ob-

tained as a colorless solid (0.211 g, 83%). M.p. 123–124°C; R_f=0.22 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.76 (br, 1H; =CH), 5.70 (br, 1H; =CH), 3.81 (s, 3H; OCH_3), 2.74–2.64 (m, 6H; CH_2), 2.38 (br, 1H; OH), 1.88 (s, 3H; CH_3), 1.23 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.61, 167.13, 163.45, 130.57 (C), 129.80, 128.39 (CH), 75.22 (C–OH), 52.34 (OCH_3), 49.13 (CH_2), 42.70 (C), 38.73, 31.03 (CH_2), 24.75, 17.74 ppm (CH_3); IR (neat): $\tilde{\nu}$=3442 (br), 2977 (m), 1784 (m), 1734 (s), 1653 (s), 1609 (m), 1435 (m), 1246 (s), 1159 (s), 875 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=250.1 (3) [M^+], 232.1 (18), 218.1 (53), 200.0 (24), 185.1 (23), 160.0 (100), 132.0 (91), 91.0 (23), 43.1 (31); elemental analysis calcd (%) for $C_{14}H_{18}O_4$: C 67.18, H 7.24; found: C 67.00, H 7.22. The exact molecular mass for $C_{14}H_{18}O_4$: m/z=250.1205±2 mD was confirmed by HRMS (EI, 70 eV).

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-2,6-diene-7-carboxylic acid ethyl ester (16b): From 1-(1-acetylcyclopent-3-enyl)ethanone (**5e**; 0.149 g, 0.98 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.400 g, 1.47 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **16b** was obtained as a colorless solid (0.165 g, 64%). M.p. 89–90°C; R_f=0.26 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.75 (br, 1H; =CH), 5.70 (br, 1H; =CH), 4.29 (q, 2H, J=7.2 Hz; OCH_2), 2.74–2.32 (m, 7H; CH_2, OH), 1.95 (s, 3H; CH_3), 1.31 (t, 3H, J=7.2 Hz; CH_3), 1.24 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.73, 167.13, 163.16, 130.57 (C), 129.87, 128.39 (CH), 75.27 (C–OH), 61.24 (OCH_2), 54.59 (C), 48.71, 39.49, 38.21 (CH_2), 24.38, 17.38, 14.08 ppm (CH_3); IR (neat): $\tilde{\nu}$=3442 (br), 2977 (m), 1784 (m), 1734 (s), 1653 (s), 1609 (m), 1435 (m), 1246 (s), 1159 (s), 875 cm^{-1} (w); MS (EI, 70 eV): m/z (%)= 264.2 (3) [M^+], 246.1 (14), 218.1 (51), 200.1 (21), 185.1 (19), 160.1 (100), 132.0 (89), 91.0 (21), 43.1 (33); elemental analysis calcd (%) for $C_{15}H_{20}O_4$: C 68.16, H 7.63; found: C 68.62, H 7.38.

10-Hydroxy-6,10-dimethyl-8-oxo-spiro[4,5]dec-2,6-diene-7-carboxylic acid isospropyl ester (16c): From 1-(1-acetylcyclopent-3-enyl)ethanone (**5e**; 0.200 g, 1.31 mmol), 1-isopropoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.512 g, 1.97 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **16c** was obtained as a colorless solid (0.216 g, 59%). M.p. 90–91°C; R_f=0.27 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.75 (br, 1H; =CH), 5.70 (br, 1H; =CH), 5.18 (sep, 1H, J=6.3 Hz; OCH), 2.74–2.30 (m, 7H; CH_2, OH), 1.94 (s, 3H; CH_3), 1.31 (d, 6H, J=6.3 Hz; CH_3), 1.24 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.72, 166.70, 165.98, 130.82 (C), 128.75 (2C, CH), 69.54 (C–OH), 68.91 (OCH), 54.51 (C), 48.81, 42.35, 38.18 (CH_2), 24.38, 21.58 (2C), 14.11 ppm (CH_3); IR (neat): $\tilde{\nu}$=3392 (br), 2982 (w), 1719 (s), 1664 (s), 1618 (m), 1379 (m), 1249 (s), 1105 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 278.3 (3) [M^+], 260.3 (7), 218.2 (51), 200.2 (19), 186.2 (15), 160.1 (100), 132.2 (61), 91.1 (20), 43.1 (38); elemental analysis calcd (%) for $C_{16}H_{22}O_4$: C 69.04, H 7.97; found: C 69.09, H 8.70. The exact molecular mass for $C_{16}H_{22}O_4$: m/z= 278.1518±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18a: From 1-methyl-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1a**; 0.368 g, 1.51 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.202 g, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18a** was obtained as colorless crystals (0.230 g, 82%). M.p. 168–169°C; R_f=0.31 (hexane/ethyl acetate 3:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.20 (s, 4H; ArH), 3.90–3.65 (br, 1H; CH_2), 3.39 (d, 1H, J=17.1 Hz; CH_2), 3.02 (d, 2H, J=17.1 Hz; CH_2), 2.32 (br, 2H; CH_2), 2.28 (s, 3H; CH_3), 2.21 (br, 1H; OH), 1.67 (s, 3H; CH_3), 1.22 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ= 204.96, 195.26, 163.60, 141.80, 141.14, 137.37 (C), 127.03, 126.94, 124.25, 123.98 (CH), 74.54 (C–OH), 56.39 (C), 49.88, 39.24 (2C, CH_2), 31.77, 25.02, 17.49 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3396 (s), 2970 (w), 1700 (s), 1662 (s), 1612 (m), 1485 (w), 1380 (m), 1336 (m), 1192 (m), 742 cm^{-1} (m); MS (EI; 70 eV): m/z (%)=284.2 (32) [M^+], 266.1 (71), 251.2 (33), 223.1 (60), 183.1 (64), 155.1 (46), 115.1 (90), 43.1 (100); elemental analysis calcd (%) for $C_{18}H_{20}O_3$: C 76.03, H 6.97; found: C 75.94, H 6.97.

Compound 18b: From 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.390 g, 1.50 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.202 g, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18b** was obtained as a colorless solid (0.258 g, 86%). M.p. 164–165°C; R_f=0.24 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.19 (s, 4H; ArH), 3.81 (s, 3H; OCH_3), 3.90–3.65 (br, 1H; CH_2), 3.40 (d, 1H, J=16.8 Hz; CH_2), 3.05 (d, 2H, J=16.8 Hz; CH_2), 2.71 (br, 2H; CH_2), 2.20 (br, 1H; OH), 1.81 (s, 3H; CH_3), 1.28 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 193.55, 167.43, 164.00, 141.21, 141.09, 131.01 (C), 127.03, 126.92, 124.27, 123.98 (CH), 74.40 (C–OH), 56.52 (C), 52.29 (OCH_3), 49.56, 39.39 (2C, CH_2), 24.96, 18.31 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3398 (s), 2960 (w), 1732 (s), 1668 (s), 1629 (w), 1381 (m), 1241 (m), 1114 cm^{-1} (m); MS (EI, 70 eV): m/z (%)=300.2 (2) [M^+], 282.1 (61), 267.1 (21), 210.1 (27), 182.1 (100), 153.1 (47), 142.1 (40), 115.1 (26), 43.1 (58); elemental analysis calcd (%) for $C_{18}H_{20}O_4$: C 71.98, H 6.71; found: C 71.78, H 6.50.

Compound 18c: From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.415 g, 1.51 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.202 g, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18c** was obtained as colorless crystals (0.270 g, 86%). M.p. 132–133°C; R_f=0.31 (hexane/ethyl acetate 3:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.19 (s, 4H; ArH), 4.28 (q, 2H, J=7.2 Hz; OCH_2), 3.90–3.65 (br, 1H; CH_2), 3.39 (d, 1H, J=17.1 Hz; CH_2), 3.04 (d, 2H, J=17.1 Hz; CH_2), 2.70 (br, 2H; CH_2), 2.45 (br, 1H; OH), 1.81 (s, 3H; CH_3), 1.30 (s, 3H; CH_3), 1.28 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=193.68, 167.07, 163.74, 141.81, 141.21, 131.14 (C), 126.95, 126.84, 124.24, 12.94 (CH), 74.44 (C–OH), 61.36 (OCH_2), 56.28 (C), 49.59, 39.33 (2C, CH_2), 24.87, 18.11, 14.10 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3421 (s), 2975 (w), 2947 (w), 2904 (w), 1727 (s), 1665 (s), 1619 (m), 1445 (w), 1381 (m), 1239 (m), 1129 (m), 1030 (m), 866 (w), 745 cm^{-1} (w); MS (EI; 70 eV): m/z (%)=314.2 (5) [M^+], 296.2 (88), 210.1 (37), 182.1 (100), 142.1 (38), 115.1 (23), 43.1 (20); elemental analysis calcd (%) for $C_{19}H_{22}O_4$: C 72.59, H 7.05; found: C 72.75, H 6.94.

Compound 18d: From 1-isopropoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1d**; 0.430 g, 1.50 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.202 g, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18d** was obtained as a colorless solid (0.269 g, 82%). M.p. 185–186°C; R_f=0.33 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.20 (s, 4H; ArH), 5.18 (sep, 1H, J=6.3 Hz; OCH), 3.90–3.60 (br, 1H; CH_2), 3.38 (d, 1H, J= 17.1 Hz; CH_2), 3.02 (d, 2H, J=17.1 Hz; CH_2), 2.65 (br, 2H; CH_2), 2.38 (br, 1H; OH), 1.76 (s, 3H; CH_3), 1.31 (s, 3H; CH_3), 1.27 ppm (d, 6H, J= 6.3 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.58, 166.62, 163.70, 141.84, 141.24, 131.39 (C), 126.96, 126.86, 124.26, 123.96 (CH), 74.61 (C–OH), 69.04 (OCH), 56.25 (C), 49.52, 39.72 (2C, CH_2), 24.93, 21.71 (2C), 17.93 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3383 (s), 2978 (w), 1723 (s), 1655 (s), 1622 (w), 1381 (m), 1251 (m), 1104 cm^{-1} (m); MS (EI, 70 eV): m/z (%)= 328.8 (2) [M^+], 310.8 (64), 269.7 (32), 250.7 (36), 210.6 (66), 182.5 (96), 153.0 (65), 142.3 (53), 115.8 (38), 43.1 (100), 28.1 (38); elemental analysis calcd (%) for $C_{20}H_{24}O_4$: C 73.15, H 7.15; found: C 73.17, H 6.97.

Compound 18e: From 1-(2-methoxy)ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1e**; 0.455 g, 1.50 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.205 g, 1.01 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18e** was obtained as a colorless solid (0.213 g, 61%). M.p. 115–116°C; R_f=0.17 (hexane/ethyl acetate 3:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.18 (s, 4H; ArH), 4.81 (t, 2H, J=4.5 Hz; OCH_2), 3.90–3.65 (br, 1H; CH_2), 3.62 (t, 2H, J=4.5 Hz; OCH_2), 3.46 (d, 1H, J=17.1 Hz; CH_2), 3.35 (s, 3H; OCH_3), 3.03 (d, 2H, J=17.1 Hz; CH_2), 2.68 (brs, 2H; CH_2), 2.26 (brs, 1H; OH), 1.82 (s, 3H; CH_3), 1.28 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=195.28, 166.90, 163.63, 141.76, 141.13, 137.36 (C), 127.02, 126.92, 124.28, 123.98 (CH), 74.51 (C–OH), 70.28, 64.04 (OCH_2), 58.82 (OCH_3), 56.35 (C), 49.85, 39.29 (2C, CH_2), 25.01, 18.19 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3421 (s), 2946 (w), 1727 (s), 1665 (s), 1619 (m), 1381 (m), 1239 (s), 1129 (s), 866 (w), 745 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=344.9 (4) [M^+], 326.9 (45), 268.7 (42), 250.7 (44), 210.5 (43), 182.5 (100), 153.0 (43), 114.6 (31), 59.6 (36), 43.1 (45); elemental analysis calcd (%) for $C_{20}H_{24}O_5$ (344.41): C 69.74, H 7.02; found: C 69.48, H 6.86.

Compound 18f: From 1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene (**1g**; 0.453 g, 1.50 mmol), 1-(2-acetylindan-2-yl)ethanone (**5f**; 0.202 g, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18f** was obtained as a colorless solid (0.106 g, 31%). R_f=0.27 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.16 (br, 4H; ArH), 4.26 (q, 2H, J=7.2 Hz; OCH_2), 4.02 (d, 1H, J=16.8 Hz; CH_2), 3.47 (d, 1H, J=16.5 Hz; CH_2), 3.03 (d, 1H, J=16.8 Hz; CH_2), 2.92 (d, 1H, J=16.5 Hz; CH_2), 2.51 (br, 1H; CH), 1.95 (br, 1H; OH), 1.90–1.75 (m, 1H; CH_2), 1.69 (s, 3H; CH_3), 1.65–1.58 (m, 1H; CH_2), 1.29 (t, 3H, J=7.2 Hz; CH_3), 1.20 (s, 3H; CH_3), 1.11 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 196.16, 167.25, 162.43, 142.05, 141.23, 131.03 (C), 126.98, 126.79, 124.30, 123.72 (CH), 74.55 (C–OH), 61.24 (OCH_2), 57.69 (CH), 56.09 (C), 40.13, 37.47, 19.99 (CH_2), 17.54, 16.13, 14.52, 14.02 ppm (CH_3); IR (KBr): $\tilde{\nu}$= 3504 (s), 2983 (w), 1706 (s), 1676 (m), 1630 (w), 1380 (m), 1216 (m), 1129 (s), 760 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=342.3 (4) [M^+], 324.3 (53), 296.3 (42), 278.2 (24), 256.2 (30), 210.1 (57), 182.1 (100), 142.1 (70), 71.1

(38), 43.1 (54); elemental analysis calcd (%) for $C_{21}H_{26}O_4$: C 73.65, H 7.65; found: C 73.42, H 7.86.

Compound 18g: From 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.390 g, 1.50 mmol), 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.264 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18g** was obtained as a colorless solid (0.084 g, 23%). R_f=0.36 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.54–6.97 (m, 9H; ArH), 3.87 (s, 3H; OCH_3), 3.81–3.63 (br, 1H; CH_2), 3.45 (d, 1H, J=19.2 Hz; CH_2), 3.40–3.25 (br, 1H; CH_2), 3.15 (d, 1H, J=17.1 Hz; CH_2), 3.06 (d, 1H, J=17.1 Hz; CH_2), 2.95–2.70 (br, 1H; CH_2), 2.46 (brs, 1H; OH), 1.85 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.33, 167.38, 164.24, 142.74, 141.86, 140.61, 132.63 (C), 131.36, 128.63, 128.03, 127.77, 127.10, 127.05, 126.75, 126.50, 123.79 (CH), 78.76, 56.74 (C), 52.25 (OCH_3), 49.11, 45.45, 40.74 (CH_2), 18.60 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3556 (s), 1739 (s), 1665 (s), 1656 (s), 1623 (m), 1349 (m), 1241 (m), 1072 (w), 768 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=362.4 (7) [M^+], 330.4 (49), 312.3 (32), 210.2 (62), 182.2 (95), 142.2 (100), 104.7 (99), 77.4 (70), 43.2 (17), 28.1 (13); elemental analysis calcd (%) for $C_{23}H_{22}O_4$: C 76.22, H 5.96; found: C 75.40, H 5.96.

Compound 18h: From 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**; 0.390 g, 1.50 mmol), 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.264 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18h** was obtained as a colorless solid (0.076 g, 21%). M.p. 139–140°C; R_f=0.28 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.16–6.80 (m, 9H; ArH), 3.38 (s, 3H; OCH_3), 3.90–3.65 (br, 1H; CH_2), 3.33 (br, 1H; CH_2), 3.17 (d, 2H, J=18.0 Hz; CH_2), 2.85 (br, 2H; CH_2), 2.45 (brs, 1H; OH), 1.85 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.01, 166.56 (2C), 141.91, 140.88, 136.24 (C), 132.87 (CH), 132.70 (C), 127.13, 128.70, 128.08, 127.39, 126.72 (2C), 126.57, 123.69 (CH), 75.20, 56.85 (C), 52.91 (OCH_3), 49.51, 40.22 (2C, CH_2), 25.10 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3537 (s), 1736 (s), 1661 (s), 1615 (w), 1344 (m), 1233 (m), 1074 (w), 734 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=362.0 (17) [M^+], 344.0 (89), 311.9 (39), 244.0 (86), 214.9 (71), 104.6 (100), 77.4 (52), 43.2 (77), 28.1 (34). The exact molecular mass for $C_{23}H_{22}O_4$: m/z=362.1518±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18i: From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.410 g, 1.50 mmol), 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.263 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18i** was obtained as a colorless solid (0.083 g, 22%). M.p. 177–178°C; R_f=0.39 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.29–6.97 (m, 9H; ArH), 4.29 (q, 2H, J=7.2 Hz; OCH_2), 3.95–3.80 (br, 1H; CH_2), 3.48–3.25 (m, 2H; CH_2), 3.16 (d, 1H, J=17.1 Hz; CH_2), 3.06 (d, 1H, J=17.1 Hz; CH_2), 2.95–2.75 (m, 1H; CH_2), 2.56 (brs, 1H; OH), 1.85 (s, 3H; CH_3), 1.29 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.24, 166.95 (2C), 142.77, 141.91, 140.66, 131.66 (C), 128.66, 128.14, 127.83, 127.16 (2C), 126.79, 126.54, 123.89, 123.83 (CH), 78.86 (C), 61.36 (OCH_2), 56.76 (C), 49.21, 40.90, 39.50 (CH_2), 18.42, 14.15 ppm (CH_3); IR (KBr): $\tilde{\nu}$= 3400 (m), 1728 (s), 1656 (s), 1621 (m), 1447 (m), 1377 (m), 1240 (m), 1071 (w), 7660 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=376.0 (3) [M^+], 358.0 (3), 329.9 (12), 209.9 (23), 181.9 (66), 142.0 (68), 104.6 (58), 87.0 (100), 43.1 (63), 28.1 (77). The exact molecular mass for $C_{24}H_{24}O_4$: m/z= 376.1675±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18j: From 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.410 g, 1.50 mmol) and 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.263 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18j** was obtained as a colorless solid (0.064 g, 17%). M.p. 133–134°C; R_f=0.33 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.15–6.87 (m, 9H; ArH), 3.87 (q, 2H, J=7.2 Hz; OCH_2), 3.36 (d, 1H, J=16.8 Hz; CH_2), 3.18 (d, 1H, J=16.8 Hz; CH_2), 2.80 (br, 2H; CH_2), 2.43 (br, 1H; OH), 1.87 (br, 1H; CH_2), 1.37 (br, 3H; CH_3), 1.24 (br, 1H; CH_2), 0.80 ppm (t, 3H, J=7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.96, 166.95 (2C), 141.95, 141.91, 136.25, 133.00 (C), 128.71, 128.03, 127.34, 127.12, 126.94, 126.72, 126.57, 123.70 (2C, CH), 75.21 (C–OH), 61.04 (OCH_2), 56.92 (C), 49.56, 40.00 (2C, CH_2), 25.17, 13.61 ppm (CH_3); IR (KBr): $\tilde{\nu}$= 3447 (s), 1735 (s), 1664 (s), 1613 (w), 1373 (m), 1234 (s), 1026 (w), 763 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=376.9 (8) [M^+], 358.0 (6), 243.9 (42), 214.9 (28), 142.0 (43), 104.7 (100), 77.4 (41), 43.1 (89), 28.1 (63). The exact molecular mass for $C_{24}H_{24}O_4$: m/z=376.1675±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18k: From 1-isobutoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.455 g, 1.50 mmol), 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.264 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18k** was obtained as a colorless solid (0.085 g, 21%). M.p. 121–122°C; R_f=0.49 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.54–7.00 (m, 9H; ArH), 4.03 (d, 2H, J=6.7 Hz; OCH_2), 3.97–3.92 (br, 1H; CH_2), 3.49–3.42 (br, 1H; CH_2), 3.30–3.22 (br, 1H; CH_2), 3.16 (d, 1H, J=17.1 Hz; CH_2), 3.08 (d, 1H, J=17.1 Hz; CH_2), 2.92–2.86 (br, 1H; CH_2), 2.24 (brs, 1H; OH), 2.03 (sep, 1H, J=6.6 Hz; CH_2), 1.87 (s, 3H; CH_3), 0.94 ppm (d, 6H, J=6.6 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.23, 167.09, 163.61, 142.88, 141.90, 140.76, 131.82 (C), 128.69 (2C), 127.85, 127.16 (2C), 126.83, 126.59, 123.96, 123.85 (CH), 78.86 (C), 71.47 (CH_2), 56.80 (C), 52.25 (OCH_2), 49.32, 40.77, 39.36 (CH_2), 27.72 (CH), 19.11 (2C), 18.56 ppm (CH_3); IR (KBr): $\tilde{\nu}$=3368 (m), 2963 (w), 1719 (s), 1657 (s), 1616 (w), 1379 (m), 1240 (m), 1073 (w), 770 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 404.0 (9) [M^+], 386.1 (12), 330.0 (34), 311.9 (35), 210.1 (45), 182.0 (90), 142.1 (93), 104.7 (100), 77.4 (25), 41.2 (25); elemental analysis calcd (%) for $C_{26}H_{28}O_4$: C 77.20, H 6.98; found: C 77.58, H 7.49. The exact molecular mass for $C_{26}H_{28}O_4$: m/z=404.1988±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18l: From 1-isobutoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**; 0.455 g, 1.50 mmol), 1-(2-benzoylindan-2-yl)ethanone (**5f**; 0.264 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18l** was obtained as a colorless solid (0.060 g, 15%). M.p. 89–90°C; R_f=0.33 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.14–6.89 (m, 9H; ArH), 3.58 (d, 2H, J=6.7 Hz; OCH_2), 3.36 (d, 1H, J=17.1 Hz; CH_2), 3.17 (d, 1H, J=16.8 Hz; CH_2), 2.85 (brs, 2H; CH_2), 2.69 (brs, 1H; OH), 2.07–2.03 (m, 1H; CH_2), 1.57 (sep, 1H, J=6.9 Hz; CH_2), 1.36 (brs, 3H; CH_3), 0.95–0.85 (m, 1H; CH_2), 0.68 ppm (d, 6H, J=6.7 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.03, 166.24 (2C), 141.91, 140.92, 136.22, 133.01 (C), 128.63, 127.99, 127.35, 127.03, 126.80, 126.63, 126.47, 123.62 (2C, CH), 75.19, 71.30 (CH_2), 56.72 (C), 49.45, 40.70, 39.06 (CH_2), 27.27 (CH), 25.00, 18.88 ppm (2C, CH_3); IR (KBr): $\tilde{\nu}$=3472 (s), 1740 (s), 1656 (s), 1612 (w), 1351 (m), 1232 (m), 1068 (w), 773 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=403.9 (12) [M^+], 386.0 (75), 311.9 (53), 244.0 (100), 214.9 (77), 43.1 (25), 28.1 (54). The exact molecular mass for $C_{26}H_{28}O_4$: m/z= 404.1988±2 mD was confirmed by HRMS (EI, 70 eV).

Compound 18m: From 1-isopropoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.453 g, 2.11 mmol), 1-(2-propylindan-2-yl)propan-1-one (**5f**; 0.230 mg, 1.00 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **18m** was obtained as a colorless oil (0.160 g, 43%). R_f=0.50 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.18 (s, 4H; ArH), 4.00 (d, 2H, J= 6.6 Hz; OCH_2), 3.37 (d, 1H, J=16.5 Hz; CH_2), 3.07 (d, 1H, J=16.8 Hz; CH_2), 2.69 (br, 2H; CH_2), 2.69 (br, 2H; CH_2), 2.17–2.03 (m, 2H; CH_2), 2.01–1.97 (m, 1H; CH), 1.95 (br, 1H; OH), 1.67–1.54 (m, 2H; CH_2), 0.99–0.81 ppm (m, 12H; CH_3); IR (KBr): $\tilde{\nu}$=3466 (br), 2970 (m), 1279 (s), 1670 (s), 1609 (m), 1465 (m), 1230 (m), 785 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=370.0 (4) [M^+], 352.1 (24), 322.9 (65), 297.0 (58), 223.9 (60), 196.0 (63), 181.9 (78), 101.9 (100), 57.4 (78), 28.4 (70). The exact molecular mass for $C_{23}H_{30}O_4$: m/z=370.2144±2 mD was confirmed by HRMS (EI, 70 eV).

Typical procedure for the preparation of bicyclo[4.4.0]deca-1,4-dien-3-ones 7, 14, 15, 17, and 19: TFA (0.4 mL, 5.2 mmol) was added dropwise to a stirred CH_2Cl_2 solution (0.4 mL) of **6a** (0.100 g, 0.42 mmol) at 20°C. The solution was stirred for 72 h until all starting material disappeared (TLC control). The solvent and TFA were removed in vacuo and the residue was purified by column chromatography (silica gel; hexane/ethyl acetate 7:3) to give **7a** as a colorless solid (0.088 g, 95%).

1-Acetyl-4,10-dimethyl-5,6,7,8-tetrahydro-10*H*-naphthalen-2-one (7a): From **6a** (0.100 g, 0.42 mmol), **7a** was obtained as a colorless solid (0.088 g, 95%). M.p. 56–57°C; R_f=0.16 (hexane/ethyl acetate 7:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=6.10 (d, 1H, J=1.2 Hz; =CH), 2.45–2.30 (m, 2H; CH_2), 2.34 (s, 3H; CH_3), 2.10–1.95 (m, 2H; CH_2), 1.98 (d, 3H, J=1.2 Hz; CH_3), 1.75–1.62 (m, 2H; CH_2), 1.35–1.20 (m, 2H; CH_2), 1.32 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=205.22, 183.45, 166.72, 163.20, 137.41 (C), 126.22 (CH), 43.32, 37.62 (CH_2), 32.14 (CH_3), 28.62, 28.31 (CH_2), 22.63 (CH_3) 21.03 (CH_2), 18.98 ppm (CH_3); IR (KBr): $\tilde{\nu}$=2944 (m), 1704 (s), 1654 (s), 1610 (s), 1446 (m), 1391 (m), 1142 (w), 958 (w), 880 cm^{-1} (w); MS (EI, 70 eV): m/z (%)=218.5 (65), 203.5 (68), 189.5 (100), 175.5 (33), 161.4 (36), 43.1 (85) [M^+]; elemental analysis calcd (%) for $C_{14}H_{18}O_2$: C 77.03, H 8.31; found: C 76.89, H 9.26. The exact molecular mass for $C_{14}H_{18}O_2$ m/z=218.1307±2 mD was confirmed by HRMS (EI, 70 eV).

4,10-Dimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid methyl ester (7b): From **6b** (0.071 g, 0.28 mmol), **7b** was obtained as a colorless solid (0.064 g, 98%). M.p. 82–83 °C; R_f = 0.28 (hexane/ethyl acetate 3:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.15 (d, 1H, J = 1.2 Hz; =CH), 3.86 (s, 3H; OCH_3), 2.47–2.41 (m, 2H; CH_2), 2.14–2.04 (m, 2H; CH_2), 2.01 (d, 3H, J = 1.2 Hz; CH_3), 1.80–1.68 (m, 2H; CH_2), 1.46–1.28 (m, 2H; CH_2), 1.36 ppm (s, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 181.91, 167.60, 166.06, 164.21, 130.79 (C), 126.04 (CH), 52.19 (OCH_3), 43.22, 37.49, 29.91, 28.10 (CH_2), 22.58 (CH_3), 21.09 (CH_2), 18.98 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2951 (m), 1732 (s), 1660 (s), 1630 (m), 1608 (m), 1389 (m), 1268 (s), 1048 (m), 958 (w), 868 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 234.2 (31) [M^+], 203.1 (20), 187.1 (45), 175.1 (100), 147.1 (21), 91.1 (23); elemental analysis calcd (%) for $C_{14}H_{18}O_3$: C 71.77, H 7.14; found: C 71.90, H 7.12.

4,10-Dimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid ethyl ester (7c): From **6c** (0.134 g, 0.5 mmol), **7c** was obtained as colorless crystals (0.120 g, 96%). M.p. 79–80 °C; R_f = 0.30 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.14 (q, 1H, J = 1.2 Hz; =CH), 4.33 (q, 2H, J = 7.2 Hz; OCH_2), 2.47–2.41 (m, 2H; CH_2), 2.12–1.98 (m, 2H; CH_2), 2.01 (d, 3H, J = 1.2 Hz; CH_3), 1.78–1.71 (m, 2H; CH_2), 1.44–1.37 (m, 2H; CH_2), 1.36 (s, 3H; CH_3), 1.34 ppm (t, 3H, J = 7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.02, 167.23, 165.95, 163.77, 131.08 (C), 126.26 (CH), 61.27 (OCH_2), 43.23 (C), 37.60, 29.83, 28.13 (CH_2), 22.60 (CH_3), 21.19 (CH_2), 19.00, 14.24 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2941 (s), 1730 (s), 1658 (s), 1630 (m), 1447 (m), 1390 (m), 1324 (w), 1265 (s), 1245 (s), 1050 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 248.1 (71) [M^+], 233.1 (46), 203.1 (72), 178.1 (100); elemental analysis calcd (%) for $C_{15}H_{20}O_3$: C 72.55, H 8.11; found: C 72.59, H 8.39.

4,10-Dimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid isopropyl ester (7d): From **6d** (0.054 g, 0.19 mmol), **7d** was obtained as colorless crystals (0.049 g, 97%). M.p. 62–63 °C; R_f = 0.34 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.19 (q, 1H, J = 1.2 Hz; = CH), 5.23 (sep, 1H, J = 6.3 Hz; OCH), 2.53–2.37 (m, 2H; CH_2), 2.14–2.04 (m, 2H; CH_2), 2.02 (d, 3H, J = 1.2 Hz; CH_3), 1.80–1.70 (m, 2H; CH_2), 1.54–1.38 (m, 2H; CH_2), 1.36 (s, 3H; CH_3), 1.32 ppm (dd, 6H, J = 1.2, 6.3 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.55, 167.13, 166.72, 164.49, 131.08 (C), 125.95 (CH), 69.06 (OCH), 43.44 (C), 37.68, 29.75, 28.14 (CH_2), 22.54, 21.83 (2C, CH_3), 21.15 (CH_2), 19.09 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2939 (s), 1727 (s), 1660 (s), 1633 (m), 1450 (m), 1239 (m), 876 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 262.3 (51) [M^+], 203.2 (80), 187.2 (100), 175.2 (63), 161.2 (57), 91.1 (32), 43.1 (85); elemental analysis calcd (%) for $C_{16}H_{22}O_3$: C 73.25, H 8.45; found: C 73.38, H 8.71.

4,10-Dimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid 2-methoxyethyl ester (7e): From **6e** (0.078 g, 0.26 mmol), **7e** was obtained as colorless crystals (0.071 g, 97%). M.p. 64–65 °C; R_f = 0.23 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.14 (q, 1H, J = 1.2 Hz; =CH), 4.50–4.36 (m, 2H; OCH_2), 3.66 (t, 2H, J = 4.8 Hz; OCH_2), 3.38 (s, 3H; OCH_3), 2.55–2.37 (m, 2H; CH_2), 2.13–1.98 (m, 2H; CH_2), 2.01 (d, 3H, J = 1.2 Hz; CH_3), 1.79–1.70 (m, 2H; CH_2), 1.52–1.38 (m, 2H; CH_2), 1.35 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 181.95, 167.13, 166.16, 164.37, 130.77 (C), 126.13 (CH), 70.39, 63.99 (OCH_2), 58.90 (OCH_3), 43.31 (C), 37.65, 29.87, 28.14 (CH_2), 22.55 (CH_3), 21.17 (CH_2), 19.04 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2944 (s), 1733 (s), 1659 (s), 1630 (m), 1449 (m), 1268 (m), 1053 (m), 876 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 277.7 (54) [M^+], 220.9 (53), 203.2 (100), 187.9 (82), 175.7 (67), 161.0 (43), 90.9 (22); elemental analysis calcd (%) for $C_{16}H_{22}O_4$: C 69.04, H 7.97; found: C 68.83, H 7.95.

3,4,10-Trimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid methyl ester (7f): From **6f** (0.135 g, 0.5 mmol), **7f** was obtained as colorless crystals (0.114 g, 92%). M.p. 110–111 °C; R_f = 0.28 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3H; OCH_3), 2.43–2.38 (m, 2H; CH_2), 2.18–2.11 (m, 1H; CH_2), 2.03–1.98 (m, 1H; CH_2), 1.96 (s, 3H; CH_3), 1.89 (s, 3H; CH_3), 1.77–1.67 (m, 2H; CH_2), 1.44–1.34 (m, 1H; CH_2), 1.31 (s, 3H; CH_3), 1.29–1.22 ppm (m, 1H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.82, 168.09, 163.05, 159.57, 130.45, 130.19 (C), 52.19 (OCH_3), 43.21 (C), 37.37, 29.90, 28.06 (CH_2), 22.13 (CH_3), 21.21 (CH_2), 15.78, 11.01 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2951 (m), 1729 (s), 1656 (m), 1623 (s), 1438 (m), 1275 (m), 1219 (m), 1007 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 248.1 (45) [M^+], 201.0 (51), 189.1 (100), 173.0 (41), 144.8 (34), 91.0 (57), 41.2 (46); elemental analysis calcd (%) for $C_{15}H_{20}O_3$: C 72.55, H 8.11; found: C 72.59, H 8.39. The exact molecular mass for $C_{15}H_{20}O_3$ m/z = 248.1412 ± 2 mD was confirmed by HRMS (EI, 70 eV).

3-Ethyl-4,10-dimethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid ethyl ester (7g): From **6g** (0.060 g, 0.22 mmol), **7g** was obtained as a colorless oil (0.049 g, 88%). R_f = 0.31 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.35 (q, 2H, J = 7.2 Hz; OCH_2), 2.45–2.38 (m, 4H; CH_2), 2.16–2.11 (m, 1H; CH_2), 2.05–1.95 (m, 1H; CH_2), 1.98 (s, 3H; CH_3), 1.74–1.68 (m, 2H; CH_2), 1.45–1.22 (m, 2H; CH_2), 1.34 (t, 3H, J = 7.2 Hz; CH_3), 1.31 (s, 3H; CH_3), 0.98 ppm (t, 3H, J = 7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 181.42, 167.68, 162.67, 159.24, 136.23, 130.55 (C), 61.18 (OCH_2), 42.92 (C), 37.41, 29.73, 27.95 (CH_2), 22.17 (CH_3), 21.21, 18.63 (CH_2), 14.79, 14.19, 12.69 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2936 (s), 2870 (w), 1733 (s), 1656 (m), 1629 (s), 1447 (m), 1393 (m), 1268 (m), 1149 (m), 1028 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 276.1 (63) [M^+], 230.1 (77), 215.0 (100), 203.1 (37), 28.0 (60). The exact molecular mass for $C_{17}H_{24}O_3$ m/z = 276.1725 ± 2 mD was confirmed by HRMS (EI, 70 eV).

4,10-Diethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalene-1-carboxylic acid methyl ester (7h): From 6,10-diethyl-10-hydroxy-8-oxo-spiro[4,5]dec-6-ene-7-carboxylic acid methyl ester (**6h**; 0.080 g, 0.28 mmol), **7h** was obtained as a colorless oil (0.062 g, 83%). R_f = 0.32 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.34 (s, 1H; =CH), 3.85 (s, 3H; OCH_3), 2.42–2.13 (m, 6H; CH_2), 2.04–1.98 (m, 1H; CH_2), 1.83–1.67 (m, 3H; CH_2), 1.48–1.35 (m, 2H; CH_2), 1.15 (t, 3H, J = 7.2 Hz; CH_3), 0.53 ppm (t, 3H, J = 7.1 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.76, 169.75, 167.62, 163.44, 132.86 (C), 125.85 (CH), 52.21 (OCH_3), 48.52 (C), 37.74, 29.92, 28.12, 27.50, 23.02, 20.95 (CH_2), 12.15, 7.96 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2951 (m), 1729 (s), 1656 (m), 1623 (s), 1438 (m), 1275 (m), 1007 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 248.1 (45) [M^+], 201.1 (51), 189.1 (100), 173.0 (41), 144.8 (34), 91.0 (57), 77.4 (36), 41.2 (46); elemental analysis calcd (%) for $C_{16}H_{22}O_3$: C 73.25, H 8.45; found: C 73.20, H 8.68.

4,10-Diethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalen-1-carboxylic acid ethyl ester (7i): From **6i** (0.060 g, 0.22 mmol), **7i** was obtained as a colorless oil (0.048 g, 85%). R_f = 0.36 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.29 (s, 1H; =CH), 4.29 (q, 2H, J = 7.2 Hz; OCH_2), 2.41–2.09 (m, 6H; CH_2), 2.00–1.95 (m, 1H; CH_2), 1.79–1.60 (m, 3H; CH_2), 1.58–1.33 (m, 2H; CH_2), 1.30 (t, 3H, J = 7.1 Hz; CH_3), 1.12 (t, 3H, J = 7.5 Hz; CH_3), 0.50 ppm (t, 3H, J = 7.1 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.67, 169.31, 167.20, 162.26, 133.11 (C), 125.97 (CH), 61.17 (OCH_2), 48.38 (C), 37.72, 29.71, 28.06, 27.42, 22.96, 20.96 (CH_2), 14.25, 12.15, 7.99 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 1733 (s), 1658 (s), 1632 (m), 1448 (m), 1236 (m), 1044 (w), 887 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 276.1 (32) [M^+], 247.1 (55), 203.0 (100), 175.1 (46), 231.0 (30), 91.0 (24), 28.0 (35).

4,10-Diethyl-2-oxo-2,5,6,7,8,10-hexahydronaphthalen-1-carboxylic acid isopropyl ester (7j): From **6j** (0.066 g, 0.21 mmol), **7j** was obtained as a colorless oil (0.055 g, 89%). R_f = 0.44 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.32 (d, 1H, J = 1.2 Hz; =CH), 5.22 (sep, 1H, J = 6.3 Hz; OCH), 2.45–2.13 (m, 7H; CH_2), 1.79–1.62 (m, 3H; CH_2), 1.46–1.35 (m, 2H; CH_2), 1.32 (d, 6H, J = 6.3 Hz; CH_3), 1.15 (t, 3H, J = 7.2 Hz; CH_3), 0.53 ppm (t, 3H, J = 7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.61, 169.40, 166.52, 162.30, 133.01 (C), 48.20 (C), 37.54, 29.38, 27.82, 27.22, 22.79 (CH_2), 21.66, 21.64 (CH_3), 20.77 (CH_2), 11.96, 7.81 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2933 (m), 1732 (s), 1659 (s), 1629 (m), 1439 (m), 1241 (m), 1044 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 290.0 (19) [M^+], 261.0 (19), 231.0 (46), 218.9 (85), 202.9 (96), 175.0 (62), 43.1 (78), 28.0 (100). The exact molecular mass for $C_{18}H_{26}O_3$: m/z = 290.1882 ± 2 mD was confirmed by HRMS (EI, 70 eV).

4-Methyl-2-oxo-10-phenyl-2,5,6,7,8,10-hexahydronaphthalen-1-carboxylic acid ethyl ester (7k): From **6k** (0.068 g, 0.22 mmol), **7k** was obtained as a colorless oil (0.088 g, 91%). R_f = 0.28 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.16 (m, 5H; ArH), 6.09 (q, 1H, J = 1.2 Hz; =CH), 4.45–4.29 (m, 2H; OCH_2), 3.00–2.94 (m, 1H; CH_2), 2.44–2.39 (m, 1H; CH_2), 1.95–1.79 (m, 3H; CH_3), 1.71 (d, 3H, J = 1.5 Hz; CH_3), 1.54–1.54 (m, 2H; CH_2), 1.36 (t, 3H, J = 7.2 Hz; CH_3), 1.28–1.23 ppm (m, 1H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.65, 166.90, 165.25, 164.05, 138.08, 131.87 (C), 129.21 (2C), 127.59 (2C), 127.45, 124.80 (CH), 61.37 (OCH_2), 52.25 (C), 35.37, 31.22, 29.17, 21.61 (CH_2), 19.39, 14.27 ppm (CH_3); MS (EI, 70 eV): m/z (%) = 310.9 (36) [M^+],

282.8 (100), 265.8 (39), 237.7 (60), 209.6 (63), 165.1 (43), 91.2 (30), 29.1 (57).

Compound 14a: From **13a** (0.050 g, 0.2 mmol) and TFA (0.15 mL, 2.00 mmol), **14a** was obtained as a colorless oil (0.025 g, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75 (d, 1H, J = 9.9 Hz; CH), 6.24 (d, 1H, J = 9.9 Hz; CH), 4.33 (q, 2H, J = 7.2 Hz; OCH_2), 2.51–2.46 (m, 1H; CH_2), 2.37 (dd, 1H, J = 13.5, 5.1 Hz; CH_2), 2.08–1.98 (m, 1H; CH_2), 1.90–1.83 (m, 1H; CH_2), 1.75–1.69 (m, 2H; CH_2), 1.48–1.38 (m, 2H; CH_2), 1.34 (t, 3H, J = 7.2 Hz; CH_3), 1.31 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.77, 167.01, 163.57 (C), 157.14 (CH), 131.02 (C), 126.25 (CH), 61.33 (CH_2), 40.62 (C), 38.46, 29.71, 27.65 (CH_2), 23.01 (CH_3), 20.68 (CH_2), 14.29 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2936 (s); 1659 (s), 1233 (s), 1038 (s), 838 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 234.1 (21) [M^+], 188.1 (100), 162.4 (19), 116.0 (6), 30.1 (7), 28.0 (5); elemental analysis calcd (%) for $C_{14}H_{18}O_3$: C 71.79, H 7.63; found: C 71.20, H 7.40.

Compound 15a: From **13a** (0.050 g, 0.2 mmol) and TFA (0.15 mL, 2.00 mmol), **15a** was obtained as a colorless solid (0.012 g, 22%). M.p. 216–217 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.46 (s, 1H; OH), 6.58 (s, 1H; ArH), 4.41 (q, 2H, J = 6.9 Hz; OCH_2), 2.73 (t, 4H, J = 6.3 Hz; CH_2), 2.58 (t, 4H, J = 6.3 Hz; CH_2), 2.39 (s, 3H; CH_3), 2.19–1.67 (m, 8H; CH_2), 1.43 ppm (t, 3H, J = 7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.78, 158.82, 144.73, 139.24, 128.01 (C), 115.21 (CH), 112.09 (C), 61.53, 30.99, 27.13, 23.80, 22.44 (CH_2), 18.07, 14.35 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3410 (br), 2932 (s), 1727 (m), 1658 (s), 1237 (s), 1155 (m), 1080 (m), 802 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 233.9 (17) [M^+], 187.9 (92), 160.9 (15), 86.9 (19), 43.0 (27), 28.0 (100); elemental analysis calcd (%) for $C_{14}H_{18}O_3$: C 71.79, H 7.63; found: C 71.38, H 7.23.

Compound 15b: From **13b** (0.047 g, 0.21 mmol) and TFA (0.16 mL, 2.11 mmol), **15b** was obtained as a colorless solid (0.022 g, 52%). M.p. 136–137 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.72 (s, 1H; OH), 6.57 (s, 1H; ArH), 2.74 (t, 2H, J = 6.3 Hz; CH_2), 2.59 (s, 3H; CH_3), 2.56 (t, 2H, J = 6.3 Hz; CH_2), 2.35 (s, 3H; CH_3), 1.85–1.82 (m, 2H; CH_2), 1.76–1.71 ppm (m, 2H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.40, 157.19, 144.80, 136.97, 127.86, 122.50 (C), 115.29 (CH), 32.71 (CH_3), 30.79, 26.68, 23.50, 22.27 (CH_2), 19.03 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3306 (br), 2933 (s), 1666 (s), 1599 (s), 1429 (s), 1302 (m), 1241 (m), 1149 (m), 855 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 204.2 (41) [M^+], 189.2 (100), 161.2 (9), 145.2 (5), 114.0 (7), 43.0 (8), 28.0 (12); elemental analysis calcd (%) for $C_{13}H_{16}O_2$: C 76.47, H 7.84; found: C 75.76, H 7.97.

Compound 14c: From **13c** (0.040 g, 0.152 mmol) and TFA (0.12 mL, 1.52 mmol), **14c** was obtained as a colorless oil (0.024 g, 60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.47 (s, 1H; =CH), 4.33 (q, 2H, J = 7.2 Hz; OCH_2), 2.36 (q, 2H, J = 7.1 Hz; CH_2), 1.99 (t, 2H, J = 3.0 Hz; CH_2), 1.43–1.38 (m, 4H; CH_2), 1.34 (t, 3H, J = 7.2 Hz; CH_3), 1.32–1.28 (m, 2H; CH_2), 1.27 (s, 3H; CH_3), 1.07 ppm (t, 3H, J = 7.5 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 183.03, 167.40, 162.84 (C), 151.30 (CH), 137.71, 130.73 (C), 61.19, 38.76, 29.44, 27.63 (CH_2), 23.21 (CH_3), 21.79, 20.74 (CH_2), 14.23, 12.40 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2936 (s), 1733 (s), 1663 (s), 1636 (s), 1440 (m), 1266 (s), 1184 (s), 1025 (m), 716 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 262.3 (22) [M^+], 247.3 (13), 217.2 (28), 189.2 (100), 161.2 (28), 91.0 (20), 28.0 (78); elemental analysis calcd (%) for $C_{16}H_{22}O_3$: C 73.00, H 8.36; found: C 72.32, H 8.34.

4,10-Dimethyl-2-oxo-2,5,6,10-tetrahydronaphthalene-1-carboxylic acid methyl ester (17a): From **16a** (0.118 g, 0.48 mmol), **17a** was obtained as a colorless oil (0.085 g, 76%). R_f = 0.32 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.38–6.33 (ddd, 1H, J = 1.5, 2.4, 9.9 Hz; =CH), 6.29–6.23 (m, 1H; =CH), 6.18 (q, 1H, J = 1.2 Hz; =CH), 3.88 (s, 3H; OCH_3), 2.47–2.39 (m, 2H; CH_2), 2.10–2.05 (m, 1H; CH_2), 2.04 (d, 3H, J = 1.2 Hz; CH_3), 1.71–1.61 (m, 1H; CH_2), 1.26 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.57, 167.12, 164.83, 157.79 (C), 137.99 (CH), 128.96 (C), 126.84, 124.60 (CH), 52.52 (OCH_3), 40.56 (C), 30.32 (CH_2), 25.12 (CH_3), 23.38 (CH_2), 19.23 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3442 (br), 2977 (m), 1784 (m), 1734 (s), 1653 (s), 1609 (m), 1435 (m), 1246 (s), 1159 (s), 875 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 232.1 (100) [M^+], 217.1 (36), 201.0 (46), 173.0 (74), 144.8 (99), 129.0 (63), 91.0 (18). The exact molecular mass for $C_{14}H_{16}O_3$: m/z = 232.1099 ± 2 mD was confirmed by HRMS (EI, 70 eV).

4,10-Dimethyl-2-oxo-2,5,6,10-tetrahydronaphthalen-1-carboxylic acid ethyl ester (17b): From **16b** (0.118 g, 0.48 mmol), **17b** was obtained as a colorless oil (0.044 g, 76%). R_f = 0.37 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.39–6.34 (ddd, 1H, J = 1.5, 2.7, 9.9 Hz; =CH), 6.27–6.22 (m, 1H; =CH), 6.17 (q, 1H, J = 1.2 Hz; =CH), 4.35 (q, 2H, J = 7.2 Hz; OCH_2), 2.47–2.39 (m, 2H; CH_2), 2.10–2.05 (m, 1H; CH_2), 2.03 (d, 3H, J = 1.2 Hz; CH_3), 1.72–1.62 (m, 1H; CH_2), 1.36 (t, 3H, J = 7.2 Hz; CH_3), 1.35 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.29, 166.54, 164.34, 156.89 (C), 137.47 (CH), 128.99 (C), 126.66, 124.27 (CH), 61.42 (OCH_2), 40.18 (C), 30.04 (CH_2), 24.85 (CH_3), 23.12 (CH_2), 19.01, 14.18 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3440 (br), 2922 (m), 1784 (m), 1726 (s), 1657 (s), 1610 (m), 1449 (m), 1241 (s), 1160 (s), 732 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 246.1 (70) [M^+], 231.0 (25), 201.0 (79), 187.0 (100), 173.0 (62), 144.8 (79), 129.0 (50), 91.0 (21). The exact molecular mass for $C_{15}H_{18}O_3$: m/z = 246.1256 ± 2 mD was confirmed by HRMS (EI, 70 eV).

4,10-Dimethyl-2-oxo-2,5,6,10-tetrahydronaphthalen-1-carboxylic acid isopropyl ester (17c): From **16c** (0.058 g, 0.21 mmol), **17c** was obtained as a colorless oil (0.039 g, 73%). R_f = 0.38 (hexane/ethyl acetate 7:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.38 (ddd, 1H, J = 1.5, 2.7, 9.9 Hz; = CH), 6.26–6.21 (m, 1H; =CH), 6.15 (q, 1H, J = 1.2 Hz; =CH), 5.25 (sep, 1H, J = 6.3 Hz; OCH), 2.44–2.39 (m, 2H; CH_2), 2.08–2.03 (m, 1H; CH_2), 2.02 (d, 3H, J = 1.2 Hz; CH_3), 1.71–1.61 (m, 1H; CH_2), 1.36 (d, 6H, J = 6.3 Hz; CH_3), 1.35 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 182.52, 166.34, 164.33, 156.52 (C), 137.33 (CH), 129.56 (C), 127.01, 124.51 (CH), 69.32 (OCH), 40.36 (C), 30.31 (CH_2), 25.05 (CH_3), 23.38 (CH_2), 22.07 (2C), 19.01 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3436 (br), 2982 (m), 1784 (m), 1722 (s), 1656 (s), 1610 (m), 1372 (s), 1246 (s), 732 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 260.0 (26) [M^+], 217.9 (37), 200.9 (57), 173.9 (100), 144.7 (28), 114.3 (23), 43.1 (48). The exact molecular mass for $C_{16}H_{20}O_3$: m/z = 260.1412 ± 2 mD was confirmed by HRMS (EI, 70 eV).

Compound 19a: From **18a** (0.110 g, 0.39 mmol), **19a** was obtained as a yellow oil (0.084 g, 82%). R_f = 0.45 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 16.55 (s, 1H; OH), 7.19–7.03 (m, 4H; ArH), 6.12 (s, 1H; =CH), 5.93 (q, 1H, J = 1.2 Hz; =CH), 2.93 (d, 1H, J = 15.0 Hz; CH_2), 2.85 (d, 1H, J = 15.0 Hz; CH_2), 2.38 (s, 3H; CH_3), 2.04 (d, 3H, J = 1.2 Hz; CH_3), 1.05 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.23, 182.27, 162.95, 138.40, 133.36, 131.57 (C), 128.17, 126.98, 126.65, 125.11 123.32, 122.53 (CH), 107.93, 43.53 (C), 38.19 (CH_2), 23.67, 20.50, 19.08 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2974 (m), 1735 (m), 1657 (s), 1630 (m); 1601 (w), 1571 (m), 1441 (m), 1268 (m), 1235 (m), 1156 (w), 869 (m), 759 cm^{-1} (m); MS (EI, 70 eV): m/z (%) = 266.7 (96) [M^+], 251.6 (100), 209.5 (47), 178.3 (19), 43.1 (79), 28.0 (73). The exact molecular mass for $C_{18}H_{18}O_2$: m/z = 266.1307 ± 2 mD was confirmed by HRMS (EI, 70 eV).

Compound 19b: From **18b** (0.097 g, 0.32 mmol), **19b** was obtained as a yellow oil (0.072 g, 79%). R_f = 0.48 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.28 (s, 1H; OH), 7.17–6.96 (m, 5H; ArH, = CH), 5.86 (q, 1H, J = 1.2 Hz; =CH), 3.88 (s, 3H; CH_3), 3.01 (d, 1H, J = 15.3 Hz; CH_2), 2.81 (d, 1H, J = 15.3 Hz; CH_2), 2.38 (s, 3H; CH_3), 2.00 (d, 3H, J = 1.2 Hz; CH_3), 1.25 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.80, 168.60, 157.38, 136.69, 134.26, 130.60 (C), 127.89, 126.84, 126.24, 125.97, 121.39, 119.35 (CH), 96.05 (C), 51.82 (OCH_3), 41.27 (C), 37.97 (CH_2), 29.67, 21.88 (CH_3); IR (neat): $\tilde{\nu}$ = 3436 (br), 1736 (m), 1658 (s), 1626 (m), 1567 (m), 1441 (m), 1269 (s), 751 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 281.9 (49) [M^+], 267.0 (34), 249.9 (35), 234.9 (100), 179.0 (41), 57.4 (18), 28.1 (22). The exact molecular mass for $C_{18}H_{18}O_3$: m/z = 282.1256 ± 2 mD was confirmed by HRMS (EI, 70 eV).

Compound 19c: From **18c** (0.115 g, 0.36 mmol), **19c** was obtained as orange crystals (0.093 g, 86%). M.p. 126–127 °C; R_f = 0.45 (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.37 (s, 1H; OH), 7.10–7.03 (m, 5H; ArH, =CH), 5.86 (q, 1H, J = 1.4 Hz; =CH), 4.44–4.33 (m, 2H; OCH_2), 3.02 (d, 1H, J = 15.2 Hz; CH_2), 2.80 (d, 1H, J = 15.2 Hz; CH_2), 2.01 (d, 3H, J = 1.4 Hz; CH_3), 1.45 (t, 3H, J = 7.2 Hz; CH_3), 1.03 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.05, 168.59, 157.18, 136.89, 134.43, 130.66 (C), 127.92, 126.86, 126.21, 125.94, 121.45, 119.45 (CH), 96.06 (C), 61.11 (CH_2), 41.31 (C), 38.04 (CH_2), 21.98, 19.14, 14.21 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 2960 (m), 1725 (w), 1659 (s), 1613 (s), 1574 (s), 1408 (m), 1306 (s), 1272 (s), 1239 (s), 1073 (m), 1017 (w), 869 (m), 752 cm^{-1} (m); MS (EI, 70 eV) m/z (%) = 296.2 (43) [M^+], 281.4 (28), 250.2 (41), 235.2 (100), 179.2 (43); elemental analysis calcd (%) for $C_{19}H_{20}O_3$: C 77.00, H 6.80; found: C 77.33, H 6.95.

Compound 19d: From **18d** (0.113 g, 0.34 mmol), **19d** was obtained as a yellow oil (0.081 g, 76%). R_f = 0.54 (hexane/ethyl acetate 3:2); ^{1}H NMR

(300 MHz, $CDCl_3$): $\delta = 13.44$ (s, 1H; OH), 7.19–6.98 (m, 5H; ArH, =CH), 5.85 (q, 1H, $J = 1.5$ Hz; =CH), 5.25 (sep, 1H, $J = 6.0$ Hz; CH), 3.00 (d, 1H, $J = 15.0$ Hz; CH_2), 2.80 (d, 1H, $J = 15.0$ Hz; CH_2), 2.00 (d, 3H, $J = 1.5$ Hz; CH_3), 1.45 (d, 3H, $J = 6.0$ Hz; CH_3), 1.39 (d, 3H, $J = 6.0$ Hz; CH_3), 1.03 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.57$, 168.40, 156.96, 136.95, 134.37, 130.62 (C), 127.89, 126.80, 126.12, 125.86, 121.42, 119.44 (CH), 96.23 (C), 69.04 (OCH), 41.27 (C), 38.02 (CH_2), 22.05, 21.19 (2C), 19.07 ppm (CH_3); IR (neat): $\tilde{\nu} = 2979$ (w), 1733 (s), 1657 (s), 1630 (s), 1603 (w), 1569 (m), 1454 (w), 1269 (s), 1105 (s), 862 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 310.0 (36) [M^+], 250.0 (53), 234.9 (100), 209.4 (24), 179.0 (45), 43.2 (44), 28.0 (23). The exact molecular mass for $C_{20}H_{22}O_3$: $m/z = 310.1569 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19e: From **18e** (0.113 g, 0.34 mmol), **19e** was obtained as a yellow oil (0.089 g, 85%). $R_f = 0.50$ (hexane/ethyl acetate 3:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 13.12$ (s, 1H; OH), 7.17–7.00 (m, 5H; ArH, =CH), 5.86 (q, 1H, $J = 1.2$ Hz; =CH), 4.57–4.51 (m, 1H; OCH_2), 4.39–4.32 (m, 1H; OCH_2), 3.77–3.73 (m, 2H; OCH_2), 3.48 (s, 3H; OCH_3), 3.00 (d, 1H, $J = 15.0$ Hz; CH_2), 2.80 (d, 1H, $J = 15.0$ Hz; CH_2), 2.00 (d, 3H, $J = 1.2$ Hz; CH_3), 1.03 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.05$, 168.59, 157.18, 136.89, 134.43, 130.66 (C), 127.92, 126.86, 126.21, 125.94, 121.45, 119.45 (CH), 96.06 (C), 61.11 (CH_2), 41.31 (C), 38.04 (CH_2), 21.98, 19.14, 14.21 ppm (CH_3); IR (neat): $\tilde{\nu} = 2969$ (w), 1714 (w), 1646 (s), 1621 (s), 1566 (s), 1454 (m), 1425 (s), 1283 (s), 962 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 326.0 (39) [M^+], 310.9 (20), 250.0 (51), 234.9 (100), 179.0 (32), 43.1 (55), 28.1 (48); elemental analysis calcd (%) for $C_{20}H_{22}O_4$: C 73.59, H 6.79; found: C 73.87, H 7.04. The exact molecular mass for $C_{20}H_{22}O_4$: $m/z = 326.1518 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19g: From **18g** (0.046 g, 0.13 mmol), **19g** was obtained as a yellow oil (0.032 g, 73%). $R_f = 0.82$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 13.21$ (s, 1H; OH), 7.30–6.92 (m, 10H; ArH, =CH), 5.99 (s, 1H; =CH), 3.96 (s, 3H; OCH_3), 2.97 (d, 1H, $J = 15.6$ Hz; CH_2), 2.48 (d, 1H, $J = 15.6$ Hz; CH_2), 1.26 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.47$, 167.80, 159.46, 139.55, 136.83, 134.10, 131.27 (C), 128.59 (2C), 128.25, 128.23 (2C), 127.93, 126.95, 126.61, 126.36, 122.16 (CH), 92.28 (C), 52.22 (CH_3), 41.62 (C), 39.31 (CH_2), 23.44 ppm (CH_3); IR (neat): $\tilde{\nu} = 3435$ (s), 2977 (w), 1739 (s), 1655 (s), 1601 (m), 1562 (m), 1441 (m), 1275 (m), 763 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 344.0 (47) [M^+], 329.0 (35), 311.9 (29), 297.0 (100), 241.0 (34), 70.0 (34), 28.1 (32). The exact molecular mass for $C_{23}H_{20}O_3$: $m/z = 344.1412 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19h: From **18h** (0.040 g, 0.11 mmol), **19h** was obtained as a yellow oil (0.032 g, 84%). $R_f = 0.39$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.29$–7.05 (m, 9H; ArH), 6.27 (d, 1H, $J = 1.2$ Hz; =CH), 3.90 (s, 3H; OCH_3), 3.88 (d, 1H, $J = 16.5$ Hz; CH_2), 3.63 (d, 1H, $J = 19.2$ Hz; CH_2), 3.33 (d, 1H, $J = 19.2$ Hz; CH_2), 3.08 (d, 1H, $J = 16.5$ Hz; CH_2), 1.79 ppm (d, 3H, $J = 1.1$ Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 182.18$, 166.85, 163.71, 159.88, 137.69, 132.22, 132.19, 131.37 (C), 129.00 (2C), 128.41, 128.00, 127.63, 127.11 (2C), 126.93, 126.86, 125.00 (CH), 52.41 (OCH_3), 50.47 (C), 38.36, 33.78 (CH_2), 19.50 ppm (CH_3); IR (neat): $\tilde{\nu} = 3435$ (s), 2977 (w), 1739 (s), 1655 (s), 1601 (m), 1562 (m), 1441 (m), 1275 (m), 763 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 344.4 (45) [M^+], 312.6 (100), 285.1 (8), 253.0 (19), 179.0 (12), 104.8 (12), 28.0 (9). The exact molecular mass for $C_{23}H_{20}O_3$: $m/z = 344.1412 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19i: From **18i** (0.050 g, 0.13 mmol), **19i** was obtained as a yellow oil (0.040 g, 84%). $R_f = 0.88$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 13.31$ (s, 1H; OH), 7.37–6.93 (m, 10H; ArH, =CH), 5.98 (s, 1H; =CH), 4.51–4.34 (m, 2H; OCH_2), 2.97 (d, 1H, $J = 15.6$ Hz; CH_2), 2.48 (d, 1H, $J = 15.6$ Hz; CH_2), 1.47 (t, 3H, $J = 7.2$ Hz; CH_3), 1.26 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.87$, 167.54, 159.10, 139.39, 136.77, 134.01, 131.08 (C), 128.40 (2C), 127.72 (3C), 126.72, 126.35, 126.09, 121.99 (2C, CH), 97.07 (C), 61.29 (CH_3), 41.42 (C), 39.13 (CH_2), 23.30, 14.18 ppm (CH_3); IR (neat): $\tilde{\nu} = 3435$ (s), 2977 (w), 1739 (s), 1655 (s), 1601 (m), 1562 (m), 1441 (m), 1275 (m), 763 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 358.4 (41) [M^+], 343.3 (28), 312.3 (33), 297.3 (100), 241.3 (39), 77.4 (3). The exact molecular mass for $C_{24}H_{22}O_3$: $m/z = 358.1569 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19j: From **18j** (0.043 g, 0.11 mmol), **19j** was obtained as a yellow oil (0.040 g, 83%). $R_f = 0.40$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.27 (m, 9H; ArH), 6.27 (d, 1H, $J = 1.2$ Hz; =CH), 4.38 (d, 2H, $J = 7.2$ Hz; OCH_2), 3.88 (d, 1H, $J = 16.5$ Hz; CH_2), 3.64 (d, 1H, $J = 19.2$ Hz; CH_2), 3.32 (d, 1H, $J = 19.2$ Hz; CH_2), 3.08 (d, 1H, $J = 16.5$ Hz; CH_2), 1.78 (d, 3H, $J = 1.2$ Hz; CH_3), 1.35 ppm (t, 3H, $J = 7.2$ Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 182.26$, 164.40, 163.65, 159.40, 137.73, 133.29, 132.25 (C), 128.97 (2C), 128.37, 128.00, 127.58, 127.12 (2C), 126.91, 126.81, 125.93 (CH), 61.52 (OCH_2), 50.39 (C), 38.32, 33.61 (CH_2), 19.48, 14.19 ppm (CH_3); IR (neat): $\tilde{\nu} = 3435$ (s), 2977 (w), 1739 (s), 1655 (s), 1601 (m), 1562 (m), 1441 (m), 1275 (m), 763 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 358.3 (45) [M^+], 312.1 (100), 297.1 (19), 284.1 (18), 235.1 (47), 179.1 (20), 144.8 (9), 28.0 (8). The exact molecular mass for $C_{24}H_{24}O_3$: $m/z = 358.1569 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19k: From **18k** (0.052 g, 0.13 mmol), **19k** was obtained as a yellow oil (0.041 g, 83%); a small amount of impurity could not be separated. $R_f = 0.93$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 13.32$ (s, 1H; OH), 7.45–6.93 (m, 10H; ArH, =CH), 5.99 (s, 1H; =CH), 4.24–4.09 (m, 2H; OCH_2), 2.96 (d, 1H, $J = 15.6$ Hz; CH_2), 2.47 (d, 1H, $J = 15.6$ Hz; CH_2), 2.20–2.11 (m, 1H; CH), 1.27 (s, 3H; CH_3), 1.10 ppm (d, 6H, $J = 6.7$ Hz; CH_3); IR (KBr): $\tilde{\nu} = 2938$ (s), 1736 (s), 1602 (m), 1453 (m), 1276 (s), 1115 (s), 706 cm^{-1} (w); MS (EI, 70 eV): m/z (%) = 386.0 (51) [M^+], 311.0 (100), 284.9 (15), 234.9 (38), 179.0 (18), 144.8 (9), 43.1 (10), 28.1 (41). The exact molecular mass for $C_{26}H_{26}O_3$: $m/z = 386.1882 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

Compound 19l: From **18l** (0.050 g, 0.12 mmol), **19l** was obtained as a yellow oil (0.035 g, 73%); a small amount of impurity could not be separated. $R_f = 0.46$ (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.30$–6.90 (m, 9H; ArH), 6.27 (d, 1H, $J = 1.2$ Hz; =CH), 4.16–4.05 (m, 2H; OCH_2), 3.95–3.80 (br, 1H; CH_2), 3.88 (d, 1H, $J = 16.7$ Hz; CH_2), 3.66 (d, 1H, $J = 19.1$ Hz; CH_2), 3.32 (d, 1H, $J = 17.2$ Hz; CH_2), 3.10 (d, 1H, $J = 16.7$ Hz; CH_2), 2.08–2.08 (m, 1H; CH), 1.78 (d, 3H, $J = 1.1$ Hz; CH_3), 0.98 ppm (dd, 6H, $J = 12.6$, 1.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 182.80$, 166.94, 164.31, 160.07, 138.18, 133.69 (C), 132.66, 132.00, 129.44, 129.20, 128.85, 128.80, 128.39, 120.36, 127.77, 127.60, 127.48, 126.34 (CH), 72.07 (CH_2), 50.90 (C–OH), 38.70, 34.18 (CH_2), 28.15 (CH), 20.00, 19.92, 19.57 ppm (CH_3); IR (KBr): $\tilde{\nu} = 2973$ (m), 1736 (s), 1677 (m), 1657 (s), 1600 (m), 1450 (m), 1257 (m), 1115 (m), 759 cm^{-1} (w); MS (EI, 70 eV): m/z (%): 386.0 (51) [M^+], 311.0 (100), 284.9 (15), 234.9 (38), 179.0 (18), 144.8 (9), 43.1 (10), 28.1 (41). The exact molecular mass for $C_{26}H_{26}O_3$: $m/z = 386.1882 \pm 2$ mD was confirmed by HRMS (EI, 70 eV).

6,10-Dimethyl-8-oxo-spiro[4,5]deca-6,9-dien-7-carboxylic acid ethyl ester (8): TFA (0.40 mL, 5.30 mmol) was added to a well-stirred CH_2Cl_2 solution (0.5 mL) of **7c** (0.130 g, 0.49 mmol) at 20 °C and the mixture was stirred for 1 h. The solvent and TFA were removed in vacuo and the residue was purified by column chromatography (silica gel, ethyl acetate/hexane 2:3) to give **8** as a colorless solid (0.068 g, 56%). M.p. 50–51 °C; $R_f = 0.30$ (ethyl acetate/hexane 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.06$ (s, 1H; =CH), 4.35 (q, 2H, $J = 7.2$ Hz; OCH_2), 2.02 (s, 3H; CH_3), 2.01 (s, 3H; CH_3), 1.93–1.85 (m, 8H; cyclopentane CH_2), 1.42 ppm (t, 3H, $J = 7.2$ Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 182.11$, 167.45, 164.76, 161.00, 132.09 (C), 125.08 (CH), 61.23 (CH_2), 53.40 (C), 37.33 (2C), 29.19 (2C, CH_2), 20.79, 17.46, 14.19 ppm (CH_3); IR (neat): $\tilde{\nu} = 2959$ (m), 1731 (s), 1657 (s), 1629 (m), 1607 (w), 1394 (m), 1243 (m), 1049 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 248.3 (20) [M^+], 233.2 (6), 203.3 (37), 187.2 (20), 175.2 (100), 161.2 (30), 146.8 (30), 91.1 (11), 29.2 (17); elemental analysis calcd (%) for $C_{15}H_{20}O_3$: C 72.55, H 8.11; found: C 72.61, H 8.29.

Synthesis of ethyl 1-acetylcyclopropanecarboxylate (9): 1,4-Dibromobutane (46.6 mL, 395.3 mmol) was added dropwise through a dropping funnel to a stirred solution of ethyl acetoacetate (51.4 g, 395.3 mmol) and potassium carbonate (136.0 g, 987.5 mmol) in dimethyl sulfoxide (120 mL) at 20 °C. After three days of stirring, the reaction mixture was filtered and the residue was washed with Et_2O (2 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude reaction mixture was purified by column chromatography (hexane/ethyl acetate 9:1) to give **9** as a colorless oil (60.0 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.19$ (q, 2H, $J = 7.2$ Hz; OCH_2), 2.15 (s, 3H; CH_3), 2.13–2.08 (m, 2H; CH_2), 1.68–1.61 (m, 2H; CH_2),

1.26 ppm (t, 3H, $J=7.2$ Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 203.09, 172.87, 66.38 (C) 60.79, 32.50 (2C, CH_2), 25.82 (CH_3), 25.21 (2C, CH_2), 13.54 ppm (CH_3); IR (neat): $\tilde{\nu}=2960$ (s), 2874 (m), 1739 (s); 1710 (s), 1623 (m), 1448 (s), 1246 (s), 1171 (s), 858 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 184.0 (5) [M^+], 139.0 (2), 84.9 (4), 55.3 (5), 43.1 (10), 28.0 (100).

Synthesis of 10: 4-Methyl benzenesulfonic acid (PTSA; 0.028 g, 0.16 mmol) was added to a stirred benzene solution (200 mL) of **9** (30.4 g, 165.3 mmol) and ethane-1,2-diol (110.6 mL, 198.4 mmol) at 20 °C. The reaction mixture was heated to reflux by using a Dean–Stark apparatus until water was completely removed from the reaction mixture (8 h). The benzene was distilled off and the product was collected by fractional distillation to give **10** as a colorless oil (32.0 g, 85 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=4.15$ (q, 2H, $J=7.2$ Hz; OCH_2), 3.96 (s, 4H; $COCH_2$), 2.20–2.07 (m, 2H; CH_2), 1.83–1.62 (m, 6H; CH_2), 1.33 (s, 3H; CH_3), 1.26 ppm (t, 3H, $J=6.9$ Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 174.26, 110.44 (C), 64.41 (2C, CH_2), 62.91 (C), 59.91, 31.25 (2C), 24.48 (2C, CH_2), 21.24, 13.44 ppm (CH_3); IR (neat): $\tilde{\nu}=2982$ (m), 2877 (m), 1719 (s), 1248 (s), 1043 (s), 890 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 229.0 (5) [M^++1], 213.0 (46), 142.0 (24), 88.0 (22), 87.2 (100); elemental analysis calcd (%) for $C_{12}H_{20}O_4$: C 63.15, H 8.71; found: C 62.86, H 8.41.

Synthesis of 11: Lithium aluminium hydride (2.0 g, 52.6 mmol) was added to a three-necked round-bottom flask containing Et_2O (200 mL) under argon at 20 °C. The suspension was cooled to 0 °C and an Et_2O solution (100 mL) of **10** (10.0 g, 43.8 mmol) was added dropwise over 0.5 h by using a dropping funnel. After completion of addition, the reaction was warmed to 20 °C and was stirred for additional 3 h. The reaction was quenched by the slow addition of water (1.5 mL), followed by addition of an aqueous solution of NaOH (4.0 mL, 1.0 M) and water (4.0 mL). The reaction mixture was filtered and the residue was washed with Et_2O (2× 50 mL). The combined organic filtrates were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give **11** as a colorless oil (7.35 g, 90 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=4.01$–3.96 (br, 4H; CH_2), 3.49 (d, 2H, $J=5.4$ Hz; C*H*$_2$OH), 3.12 (t, 1H, $J=5.4$ Hz; CH_2O*H*), 1.68–1.52 (m, 6H; CH_2), 1.48–1.44 (m, 2H; CH_2), 1.36 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=114.66$ (C), 67.31, 64.46 (2C, CH_2), 54.29 (C), 30.65 (2C), 25.65 (2C, CH_2), 20.03 ppm (CH_3); IR (neat): $\tilde{\nu}=3453$ (s), 2954 (s), 2873 (s), 1376 (s), 1126 (m), 1038 (s), 881.27 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 187.4 (2) [M^++1], 171.4 (36), 87.2 (100), 82.2 (54), 68.1 (71), 43.1 (48), 31.1 (39); elemental analysis calcd (%) for $C_{10}H_{18}O_3$: C 64.48, H 9.74; found: C 63.95, H 9.45.

Synthesis of 12: An acetone solution (50 mL) of **11** (4.67 g, 25.10 mmol) and PTSA (2.15 g, 12.55 mmol) was stirred for 24 h at 20 °C. The acetone was removed in vacuo and the reaction mixture was extracted with Et_2O (50 mL). The organic layer was washed with water (50 mL), dried over anhydrous Na_2SO_4, filtered, and and concentrated in vacuo to give **12** as a colorless oil (3.09 g, 87 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=3.57$ (s, 2H; CH_2), 2.45 (s, 1H; OH), 2.18 (s, 3H; CH_3), 1.91–1.62 ppm (m, 8H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=214.14$ (C), 66.92 (CH_2), 60.89 (C), 32.08 (2C), 25.28 (2C, CH_2), 20.40 ppm (CH_3); IR (neat): $\tilde{\nu}=3431$ (br), 2953 (s), 1700 (s), 1357 (m), 1041 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%)= 143.0 (12) [M^++1], 125.0 (17), 108.4 (88), 81.1 (39), 68.0 (68), 43.1 (100), 28.1 (40).

Synthesis of 5d: A CH_2Cl_2 solution (2 mL) of dimethyl sulfoxide (1.00 mL, 14.1 mmol) was added dropwise to a stirred CH_2Cl_2 solution (7 mL) of oxalyl chloride (0.88 mL, 7.04 mmol) at −78 °C under an argon atmosphere. After stirring for 10 min, a CH_2Cl_2 solution (3 mL) of **12** (1.00 g, 7.04 mmol) was added dropwise and the solution was stirred for 15 min. Triethylamine (3.9 mL, 28.2 mmol) was added slowly and the temperature of the mixture was allowed to rise to 20 °C over 30 min. Water (40 mL) was added to the reaction mixture and the latter was stirred for 10 min. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (2×25 mL). The combined organic layers were washed with an aqueous solution of Na_2CO_3 (30 mL, 10 %) and water (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give **5d** as a yellow oil (0.858 mg, 87 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=9.57$ (s, 1H; CHO), 2.20 (s, 3H; CH_3), 2.15–2.06 (m, 4H; CH_2), 1.71–1.61 ppm (m, 4H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 205.36 (C), 199.28 (CH), 72.23 (C), 30.05 (2C, CH_2), 27.10 (CH_3), 25.51 ppm (2C, CH_2); IR (neat): $\tilde{\nu}=2952$ (s), 2870 (m), 1702 (s), 1357 (m), 1158 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%)=141 (3) [M^++1], 125.0 (11), 111.1 (44), 98 (18), 81 (33), 67.9 (57), 43.1 (100), 28.1 (42).

1-(1-Propionylcyclopentyl)propan-1-one (5b): The reaction was carried out by following the procedure as given for the synthesis of **9**. From heptane-3,5-dione (3.20 g, 25.0 mmol), 1,4-dibromobutane (5.40 g, 25.0 mmol), and potassium carbonate (7.60 g, 55.0 mmol), **5b** was obtained as a colorless oil (3.00 g, 66 %). $R_f=0.66$ (hexane/ethyl acetate 9:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.37$ (q, 4H, $J=7.2$ Hz; CH_2), 2.12–2.18 (m, 4H; CH_2), 1.60–1.56 (m, 4H; CH_2), 1.04 ppm (t, 6H, $J=$ 7.2 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=208.26$ (2C), 74.52 (C), 32.00 (2C), 31.26 (2C), 25.29 (2C, CH_2), 8.11 ppm (2C, CH_3); IR (neat): $\tilde{\nu}=2973$ (s), 1697 (s), 1456 (m), 1346 (m), 1139 (m), 1024 cm^{-1} (w).

1-(2-Benzoylcyclopentyl)ethanone (5c): The reaction was carried out by following the procedure as given for the synthesis of **9**. From benzoylacetone (4.05 g, 25.0 mmol), 1,4-dibromobutane (5.40 g, 25.0 mmol), and potassium carbonate (7.60 g, 55.0 mmol), **5c** was obtained as a colorless oil (3.95 g, 75 %). $R_f=0.68$ (hexane/ethyl acetate 9:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.86$–7.82 (m, 2H; ArH), 7.53–7.50 (m, 1H; ArH), 7.44–7.38 (m, 2H; ArH), 3.43 (m, 1H; CH_2), 2.32–2.20 (m, 4H; CH_2), 2.01 (s, 3H; CH_3), 1.66–1.61 ppm (m, 3H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 205.75, 197.41, 135.21 (C), 132.95, 129.02 (2C), 128.50 (2C, CH), 72.32 (C), 33.09 (2C, CH_2), 27.05 (CH_3), 26.07 ppm (2C, CH_2); IR (neat): $\tilde{\nu}=$ 2957 (m), 1713 (m), 1674 (s), 1598 (w), 1447 (m), 1243 (s), 710 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 215.8 (1) [M^+], 173.9 (5), 144.6 (2), 104.5 (100), 77.3 (36), 43.0 (7).

Preparation of 1-(1-acetylcyclopent-3-enyl)ethanone (5e): Ti(O*i*Pr)$_4$ (0.3 mL, 1.01 mmol) was added to a CH_2Cl_2 solution (degassed, 70 mL) of 3,3-diallylpentane-2,4-dione (1.30 g, 7.22 mmol). After stirring for 1 h at 35 °C, Grubbs catalyst (0.594 g, 0.7 mmol in 5 mL of CH_2Cl_2) was added. The solution was stirred for 48 h at the same temperature. The solvent was removed in vacuo and the residue was purified by column chromatography (silica gel, ethyl acetate/hexane 1:9) to give **5e** as an oil (0.626 g, 57 %). $R_f=0.66$ (ethyl acetate/hexane 1:9); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.59$ (s, 2H; =CH), 2.90 (s, 4H; CH_2), 2.15 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=204.99$ (2C, C), 127.89 (2C, CH), 73.16 (C), 37.66 (2C, CH_2), 26.37 ppm (2C, CH_3); IR (neat): $\tilde{\nu}=1700$ (s), 1433 (m), 1358 (m), 1216 (m), 1151 (m), 633 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 151.3 (1) [M^+], 138.1 (2), 124.1 (5), 108.4 (15), 97.0 (5), 81.0 (4), 43.1 (100), 28.0 (7).

1-(2-Acetylindan-2-yl)ethanone (5f): The reaction was carried out by following the procedure as given for the synthesis of **9**. From acetylacetone (2.10 g, 25.0 mmol), 1,2-bis(bromomethyl)benzene (6.60 g, 25.0 mmol), and potassium carbonate (7.60 g, 55.0 mmol), **5f** was obtained as a colorless oil (4.10 g, 81 %). $R_f=0.66$ (hexane/ethyl acetate 9:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.17$–7.11 (m, 4H; ArH), 3.47 (s, 4H; CH_2), 2.14 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=214.56$ (2C), 139.53 (2C, C), 126.84 (2C), 124.22 (2C, CH), 74.39 (C), 37.38 (2C, CH_2), 26.29 ppm (2C, CH_3); IR (neat): $\tilde{\nu}=1695$ (s), 1585 (s), 1430 (s), 1357 (s), 1032 (m), 771 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 201.9 (1) [M^+], 186.8 (1), 158.8 (80), 144.6 (6), 114.3 (21), 88.9 (4), 43.0 (100), 28.0 (16).

1-(2-Propionylindan-2-yl)propan-1-one (5g): The reaction was carried out by following the procedure as given for the synthesis of **9**. From heptane-3,5-dione (3.20 g, 25.0 mmol), 1,2-bis(bromomethyl)benzene (6.60 g, 25.0 mmol), and potassium carbonate (7.60 g, 55.0 mmol), **5g** was obtained as a colorless oil (3.91 g, 68 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 7.20–7.13 (m, 4H; ArH), 3.51 (s, 4H; CH_2), 2.44 (q, 4H, $J=7.2$ Hz; CH_2), 1.04 ppm (t, 6H, $J=7.2$ Hz; CH_3); IR (neat): $\tilde{\nu}=2980$ (m), 1697 (s), 1456 (m), 1348 (m), 1163 (m), 995 (w), 745 cm^{-1} (m).

1-(2-Benzoylindan-2-yl)ethanone (5h): The reaction was carried out by following the procedure as given for the synthesis of **9**. From benzoylacetone (4.05 g, 25.0 mmol), 1,2-bis(bromomethyl)benzene (6.60 g, 25.0 mmol), and potassium carbonate (7.60 g, 55 mmol), **1** was obtained as a colorless oil (4.50 g, 68 %). $R_f=0.59$ (hexane/ethyl acetate 9:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.89$–7.84 (m, 2H; ArH), 7.56–7.51 (m, 1H; ArH), 7.45–7.39 (m, 2H; ArH), 7.18–7.11 (m, 4H; ArH), 3.78 (d, 2H, $J=16.5$ Hz; CH_2), 3.68 (d, 2H, $J=16.5$ Hz; CH_2), 2.11 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=204.51$, 196.41, 139.43 (2C), 134.86 (C), 133.29, 129.14 (2C), 128.72 (2C), 126.84 (2C), 124.18 (2C, CH), 72.02 (C), 39.05 (2C, CH_2), 26.75 ppm (CH_3); IR (neat): $\tilde{\nu}=2944$ (m),

1715 (m), 1679 (s), 1601 (m), 1589 (m), 1447 (m), 1355 (m), 1243 (s), 721 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 263.9 (1) [M^+], 248.8 (1), 220.7 (80), 158.9 (53), 104.5 (100), 77.3 (44), 43.0 (16).

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JOC Article

Domino "[3+3]-Cyclization-Homo-Michael" Reactions of 1,3-Bissilyl Enol Ethers with 1,1-Diacylcyclopropanes

Gopal Bose,[†] Van Thi Hong Nguyen,[†] Ehsan Ullah,[†] Sunanda Lahiri,[†] Helmar Görls,[‡] and Peter Langer*,[†]

Institut für Chemie und Biochemie, Ernst-Moritz-Arndt Universität Greifswald, Soldmannstrasse 16, D-17487 Greifswald, Germany, and Institut für Anorganische und Analytische Chemie, Universität Jena, August-Bebel-Strasse 2, 07740 Jena, Germany

peter.langer@uni-greifswald.de

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The Lewis acid mediated domino "[3+3]-cyclization-homo-Michael" reaction of 1,3-bissilyl enol ethers with 1,1-diacylcyclopropanes allows an efficient one-pot synthesis of functionalized salicylates containing a halogenated side chain. A great variety of substitution patterns could be realized by variation of the starting materials and of the Lewis acid. The mechanism of the domino process was studied.

1,3-Bissilyl enol ethers can be regarded as electroneutral 1,3-dicarbonyl dianion equivalents (masked dianions).[1,2] They represent useful synthetic building blocks in Lewis acid mediated transformations. In cyclization reactions, 1,3-bissilyl enol ethers can react as 1,3-dinucleophiles or, similar to the well-known Danishefsky diene,[3] as functionalized 1,4-butadienes. Chan and coworkers have reported $TiCl_4$-mediated [3+3] cyclizations of 1,3-bissilyl enol ethers with 3-silyloxyalk-2-en-1-ones and with ketals of β-keto aldehydes, β-ketoesters, and β-ketocarboxylic chlorides to give benzene derivatives.[2d,e] We have recently reported the $TiCl_4$-mediated domino "[3+3]-cyclization-homo-Michael" reaction of 1,3-bissilyl enol ethers with 1,1-diacetylcyclopropane.[4,5] This cyclization allows an efficient one-pot synthesis of functionalized salicylates containing a halogenated side chain. The strategic placement of the halide group in these products makes them versatile synthetic intermediates. With regard to our preliminary communication, we significantly extended the preparative scope and developed, for example, regioselective cyclizations of unsymmetrical 1,1-diacylcyclopropanes. In addition, we studied the mechanism of the domino process.

Results and Discussion

Mechanism. The $TiCl_4$-mediated reaction of 1,3-bissilyl enol ether **1a** with 1,1-diacetylcyclopropane (**2a**)[6] afforded the chlorinated salicylate **3a** in 82% yield. The best yields were obtained when 2 equiv of the Lewis acid were used. Two mechanisms can be discussed for the formation of **3a**. Path A: Titanium enolate **A** is formed by $TiCl_4$-mediated ring-opening of **2a**. The reaction of **A** with **1a** proceeds, in analogy to the known cyclization of 1,3-bissilyl enol ethers with 3-silyloxypent-3-en-2-one,[2e] by attack of **1a** onto the Michael position (intermediate **B**) and subsequent cyclization. Alternatively, the cyclization could proceed by formation of the spirocyclic intermediate **C** and subsequent $TiCl_4$-mediated ring cleavage (homo-Michael reaction) via intermediate **D**.

The mechanism of the cyclization was studied. Mechanism path A is supported by the following experiment: Treatment of **2a** with $TiCl_4$ and subsequent aqueous workup afforded 3-(2′-chloroethyl)pentane-2,4-dione (**4**) in 47% yield (Scheme 2). The formation of **4** can be explained by $TiCl_4$-mediated formation of titanium enolate **A** and subsequent hydrolysis. Although **4** fails to directly react with 1,3-bissilyl enol ethers, a cyclization of 1,3-bissilyl enol ethers with intermediate **A** cannot be ruled out. In fact, the related cyclization of 3-silyloxyalk-2-en-1-ones with 1,3-bissilyl enol ethers is known (vide supra).[2d,e]

However, we believe that the cyclization of the 1,3-bissilyl enol ether with 1,1-diacylcyclopropanes proceeds by mechanism type B, based on the following observa-

* Address correspondence to this author. Fax: (+49) 3834-864373.
† Ernst-Moritz-Arndt Universität Greifswald.
‡ Universität Jena.

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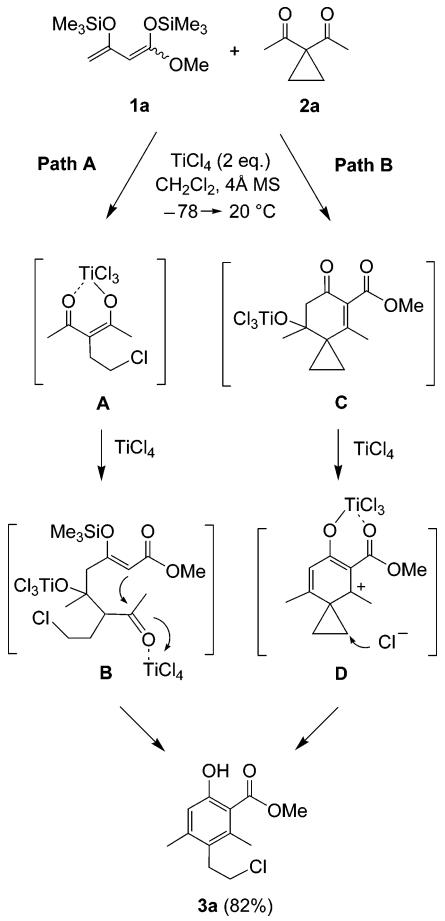
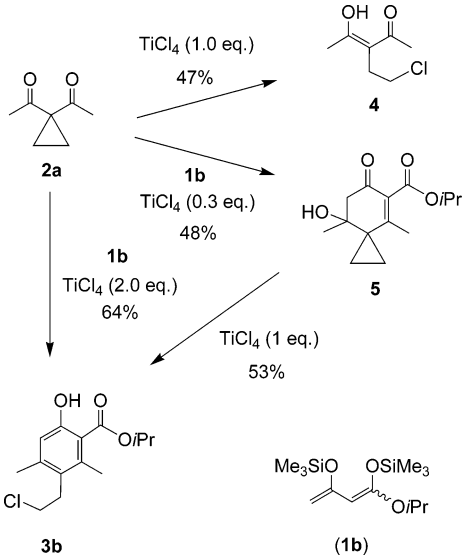
SCHEME 1. Possible Mechanisms of the Cyclization of 1,3-Bissilyl Enol Ether 1a with 1,1-Diacetylcyclopropane

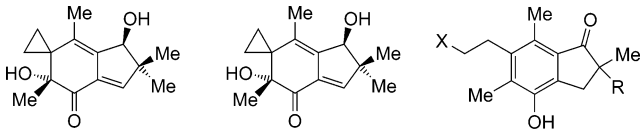


SCHEME 2. Mechanistic Studies



tions: The reaction of 1,3-bissilyl enol ether **1b** with **2a** in the presence of 0.3 rather than 2.0 equiv of $TiCl_4$ allowed the isolation of spirocyclopropane **5** in 48% yield.[7] The formation of **5** can be explained by $TiCl_4$-mediated cyclization, to give a spirocyclic titanium alkoxide (intermediate **C**, Scheme 1), and subsequent hydrolysis upon aqueous workup. Treatment of **5** with $TiCl_4$ afforded the salicylate **3b** in 53% yield. The yield was significantly improved when NBu_4Cl was employed. The use of more than 0.5 equiv of $TiCl_4$ in the reaction of **1b** with **2a** resulted in formation of significant amounts of **3b** at the expense of **5**. In fact, salicylate **3b** was isolated in 64% yield when the cyclization was carried out in the presence of 2.0 equiv of $TiCl_4$. The use of $BF_3{\cdot}OEt_2$, Me_3SiOTf, or TFA resulted in formation of complex mixtures.

CHART 1



Acceptor-substituted cyclopropanes represent important building blocks in homo-Michael reactions with various nucleophiles.[8] Reactions of acceptor-substituted cyclopropanes have been classified by Danishefsky in terms of "strictly nucleophilic ring openings", "electrophilically assisted ring openings", and "spiro-activations".[9] In the domino "[3+3]-cyclization-homo-Michael" reaction reported herein two effects are operating: (a) a "dynamic spiro-activation"[10] and (b) activation by an electrophile.

The second step of mechanism path B, the transformation of the spirocyclopropane into the salicylate, is related to the biosynthesis of the carcinogenic pterosins isolated from the bracken fern *Pteridium aquilinium*.[11] It was shown earlier that the pterosins are formed from their direct biogenetic precursor, the spirocyclopropane ptaquilosin, by treatment with acid. It was proposed that the pterosins, ptaquilosin, and illudin M (Chart 1) are all formed from farnesyl phosphate via a common biosynthetic intermediate.[12] The synthesis of analogues of these compounds is of considerable pharmacological relevance, due to their potential cytotoxic and cancerostatic activity.[13]

Preparative Scope. The $TiCl_4$-mediated reaction of 1,1-diacetylcyclopropane (**2a**) with a variety of 1,3-bissilyl enol ethers was studied. The reaction of **2a** with β-ketoester derived 1,3-bissilyl enol ethers **1a**−**d** afforded the

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SCHEME 3. Synthesis of Salicylates

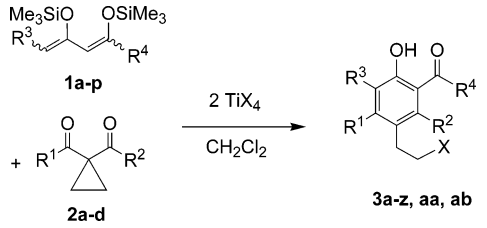


TABLE 1. Products and Yields

3	R^1	R^2	R^3	R^4	X	yield (%)[a]
a	Me	Me	H	OMe	Cl	82
b	Me	Me	H	O*i*Pr	Cl	64
c	Me	Me	H	OEt	Cl	72
d	Me	Me	H	$O(CH_2)_2OMe$	Cl	56
e	Me	Me	H	Me	Cl	82
f	Me	Me	Me	OMe	Cl	32
g	Me	Me	Et	OEt	Cl	38
h	Me	Me	*n*Pr	OEt	Cl	67
i	Me	Me	*n*Bu	OEt	Cl	44
j	Me	Me	*n*Hex	OEt	Cl	41
k	Me	Me	*n*Hept	OEt	Cl	51
l	Me	Me	*n*Oct	OEt	Cl	45
m	Me	Me	*n*Non	OEt	Cl	47
n	Me	Me	*n*Dec	OEt	Cl	55
o	Me	Me	OBn	OEt	Cl	45
p	Et	Et	H	OMe	Cl	47
q	Et	Et	H	OEt	Cl	42
r	Et	Et	H	O*i*Pr	Cl	37
s	Et	Et	H	$O(CH_2)_2OMe$	Cl	42
t	Me	Ph	H	OMe	Cl	73
u	Me	Ph	H	OEt	Cl	57
v	Me	Ph	H	O*i*Pr	Cl	34
w	Me	Ph	H	O*i*Bu	Cl	73
x	H	Me	H	OEt	Cl	42
y	H	Me	Et	OEt	Cl	33
z	Me	Me	H	OMe	Br	82
aa	Me	Me	*n*Bu	OEt	Br	43
ab	Me	Me	*n*Hex	OEt	Br	45

[a] Isolated yields.

functionalized salicyclates **3a**−**d** in good yields (Scheme 3, Table 1). Starting with **2a** and 2,4-bis(trimethylsilyloxy)-1,3-pentadiene (**1e**), the acetophenone **3e** was obtained. The reaction of **2a** with bissilyl enol ethers **1f**−**n** afforded the alkyl-substituted salicylates **3f**−**n**. The benzyloxy-substituted salicylate **3o** was prepared from **1o**. The 1,1-diacylcyclopropane was varied next. Cyclization of **1a**−**d** with 1,1-dipropionylcyclopropane (**2b**) afforded the ethyl-substituted salicylates **3p**−**s**. The reaction of β-ketoester derived 1,3-bissilyl enol ethers with (unsymmetrical) 1-acetyl-1-benzoylcyclopropane (**2c**) gave the methyl- and phenyl-substituted salicyclates **3t**−**w**. The products were formed with very good regioselectivity and the cyclizations proceeded by attack of the terminal carbon of the bissilyl enol ether onto the (more reactive) acetyl group rather than onto the benzoyl group. The cyclization of **1b** and **1g** with (unsymmetrical) 1-acetyl-1-formylcyclopropane (**2d**) afforded the salicylates **3x** and **3y**, respectively. The products were again formed with very good regioselctivity and the cyclizations proceeded by initial attack of the terminal carbon of the 1,3-bissilyl enol ethers onto the aldehyde and subsequent cyclization. The $TiBr_4$-mediated cyclization of **1a** with **2a** resulted in formation of salicylate **3z** containing a bromo-substituted side chain. Similarly, reaction of **1i** and **1j** with **2a** in the presence of $TiBr_4$ resulted in the formation of **3aa** and **3ab**.

The structure of all products was elucidated by spectroscopic methods. The structure of **3w** was independently confirmed by crystal structure analysis (see Supporting Information). As expected from the structure in solution, an intramolecular hydrogen bond O−H···O is observed. The two aryl moieties are orthogonally twisted.

In conclusion, we have reported the $TiCl_4$- or $TiBr_4$-mediated domino "[3+3]-cyclization-homo-Michael" reaction of 1,3-bissilyl enol ethers with 1,1-diacylcyclopropanes. These reactions allow a convenient one-pot synthesis of a great variety of functionalized salicylates containing a chlorinated or brominated side chain.

Experimental Section

General. All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For the ^1H and ^{13}C NMR spectra (^1H NMR, 300, 600 MHz; ^{13}C NMR, 75, 150 MHz) the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained with the electron ionization (70 eV), the chemical ionization (CI, H_2O), or the electrospray ionization technique (ESI). For preparative scale chromatography silica gel (60−200 mesh) was used. Melting points are uncorrected

Typical Procedure for the Preparation of Salicylates 3. To a stirred CH_2Cl_2 solution (100 mL) of 1,1-diacetylcyclopropane (**2a**) (0.136 g, 1.1 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene (**1a**) (0.421 g, 1.6 mmol) was added $TiCl_4$ (0.22 mL, 2.0 mmol in 2 mL of CH_2Cl_2) at −78 °C under argon atmosphere in the presence of molecular sieves (4 Å) (1.0 g). The temperature of the reaction mixture was allowed to rise to 20 °C over 6 h. The solution was stirred for an additional 6 h at 20 °C. The reaction mixture was filtered and the filtrate was poured into an aqueous solution of HCl (10%, 100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel; hexane/ethyl acetate = 4:1) to give **3a** (0.251 g, 82%) as colorless crystals.

Methyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3a). Starting with **2a** (0.136 g, 1.08 mmol), 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.420 g, 1.61 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3a** was isolated (0.215 g, 82%) as a colorless solid; mp 73−74 °C; R_f 0.53 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ = 2956 (m), 1722 (w), 1657 (s), 1601 (m), 1574 (m), 1437 (s), 1239 (s), 1072 (m), 804 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.68 (s, 1 H, OH), 6.70 (s, 1 H, ArH), 3.94 (s, 3 H, OCH_3), 3.51−3.46 (m, 2 H, CH_2), 3.12−3.06 (m, 2 H, CH_2), 2.48 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 160.3, 144.2, 139.0, 127.1, 117.2, 111.9, 52.1, 42.2, 32.9, 21.0, 18.5; MS (EI, 70 eV) *m/z* (%) 244.6 ($[M]^+$, 14), 242.5 ($[M]^+$, 42), 212.5 (37), 210.4 (85), 193.5 (21), 161.4 (100), 104.8 (14), 77.5 (13). Elemental analysis calcd for $C_{12}H_{15}O_3Cl$: C 59.39, H 6.22. Found: C 59.56, H 6.50.

Isopropyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3b). Starting with **2a** (0.126 g, 1.00 mmol), 1-isopropyloxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.375 g, 1.30 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3b** was isolated (0.173 g, 64%) as a colorless solid; mp 51−52 °C; R_f 0.66 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2982 (m), 1731 (w), 1656 (s), 1601 (w), 1574 (m), 1467 (m), 1372 (s), 1238 (s), 1105 (m), 804 (w), 703 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.77 (s, 1 H, OH), 6.70 (s, 1 H, ArH), 5.32 (sep, 1 H, J = 6.2 Hz, OCH), 3.53−3.46 (m, 2 H, CH_2), 3.12−3.06 (m, 2 H, CH_2), 2.50 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 1.46 (d, 6 H, J = 6.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 160.2, 143.9, 138.9,

127.0, 117.2, 112.3, 69.7, 42.2, 33.0, 21.9, 21.0, 18.6; MS (EI, 70 eV): *m/z* (%) 272.1 ([M]$^+$, 5), 270.1 ([M]$^+$, 15), 212.0 (26), 210.1 (74), 161.1 (100), 91.1 (8), 77.5 (7), 28.0 (35). Elemental analysis calcd for $C_{14}H_{19}O_3Cl$: C 62.10, H 7.07. Found: C 62.07, H 7.49.

Ethyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3c). Starting with **2a** (0.127 g, 1.00 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.355 g, 1.30 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3c** was isolated (0.186 g, 72%) as a colorless solid; mp 53−54 °C; R_f 0.57 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2978 (m), 1666 (s), 1606 (w), 1561 (m), 1467 (m), 1311 (s), 1072 (m), 699 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.74 (s, 1 H, OH), 6.70 (s, 1 H, ArH), 4.43 (q, 2 H, J = 7.2 Hz, OCH_2), 3.52−3.47 (m, 2 H, CH_2), 3.13−3.07 (m, 2 H, CH_2), 2.51 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 1.42 (t, 3 H, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 160.2, 144.0, 139.0, 127.0, 117.2, 112.0, 61.6, 42.2, 32.9, 21.0, 18.5, 14.1; MS (EI, 70 eV) *m/z* (%) 258.4 ([M]$^+$, 12), 256.4 ([M]$^+$, 38), 212.2 (34), 210.2 (88), 161.2 (100), 91.1 (5), 77.5 (4). Elemental analysis calcd for $C_{13}H_{17}O_3Cl$: C 60.82, H 6.67. Found: C 60.81, H 7.09.

2-Methoxyethyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3d). Starting with **2a** (0.127 g, 1.00 mmol), 1-(2-methoxy)ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.395 g, 1.30 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3d** was isolated (0.162 g, 56%) as a colorless solid; mp. 41−42 °C; R_f 0.51 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2960 (m), 1727 (m), 1659 (s), 1610 (m), 1573 (m), 1467 (m), 1237 (s), 1072 (m), 802 (w), 703 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.29 (s, 1 H, OH), 6.70 (s, 1 H, ArH), 4.50 (t, 2 H, J = 4.7 Hz, OCH_2), 3.72 (t, 2 H, J = 4.7 Hz, OCH_2), 3.52−3.46 (m, 2 H, CH_2), 3.42 (s, 3 H, OCH_3), 3.12−3.08 (m, 2 H, CH_2), 2.51 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 159.7, 144.1, 139.2, 127.0, 117.3, 112.4, 70.0, 64.1, 58.9, 42.2, 33.0, 21.0, 18.4; MS (EI, 70 eV) *m/z* (%) 288.1 ([M]$^+$, 6), 286.2 ([M]$^+$, 20), 212.0 (27), 210.0 (81), 161.0 (100), 91.1 (7), 77.5 (5), 28.1 (19). Elemental analysis calcd for $C_{14}H_{19}O_4Cl$: C 58.64, H 6.68. Found: C 58.54, H 6.97.

2-Acetyl-[4-(2-chloroethyl)]-1-hydroxy-3,5-dimethylbenzene (3e). Starting with **2a** (0.138 g, 1.09 mmol), 1-methyl-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.400 g, 1.64 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3e** (0.215 g, 82%) was obtained as a colorless oil; R_f 0.56 (hexane/ethyl acetate = 4:1); IR (neat) $\tilde{\nu}$ 3332 (br), 2956 (w), 1673 (s), 1600 (m), 1574 (m), 1446 (s), 1301 (s), 1239 (m), 723 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.72 (s, 1 H, OH), 6.67 (s, 1 H, ArH), 3.54−3.46 (m, 2 H, CH_2), 3.09−3.06 (m, 2 H, CH_2), 2.59 (s, 3 H, CH_3), 2.47 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 158.2, 143.9, 136.7, 127.2, 122.9, 117.4, 42.1, 32.8, 32.6, 20.7, 19.2; MS (EI, 70 eV) *m/z* (%) 228.3 ([M]$^+$, 20), 226.3 ([M]$^+$, 60), 213.2 (28), 211.2 (79), 177.3 (100), 159.3 (56), 91.1 (23), 77.5 (11). The exact molecular mass for $C_{12}H_{15}O_2Cl$ (*m/z* 226.0761 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Methyl 4-(2-Chloroethyl)-1-hydroxy-3,5,6-trimethyl-2-benzoate (3f). Starting with **2a** (0.128 g, 1.02 mmol), 1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene (**2f**) (0.363 g, 1.32 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3f** was isolated (0.083 g, 32%) as a colorless solid; mp 95−96 °C; R_f 0.63 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2955 (m), 1649 (s), 1599 (m), 1564 (m), 1442 (s), 1211 (s), 1099 (m), 811 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.94 (s, 1 H, OH), 3.95 (s, 3 H, OCH_3), 3.51−3.45 (m, 2 H, CH_2), 3.17−3.12 (m, 2 H, CH_2), 2.46 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 158.2, 142.4, 135.4, 126.5, 122.9 111.3, 52.1, 42.3, 33.5, 18.6, 16.9, 12.2; MS (EI, 70 eV) *m/z* (%) 258.4 ([M]$^+$, 13), 256.4 ([M]$^+$, 37), 226.3 (39), 224.3 (90), 189.3 (569, 175.3 (100), 146.8 (16), 91.2 (9). Elemental analysis calcd for $C_{13}H_{17}O_3Cl$: C 60.82, H 6.68. Found: C 61.01, H 7.13.

Ethyl 4-(2-Chloroethyl)-6-ethyl-1-hydroxy-3,5-dimethyl-2-benzoate (**3g**): Starting with **2a** (0.139 g, 1.10 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene (**2g**) (0.500 g, 1.65 mmol), and $TiCl_4$ (0.24 mL, 2.20 mmol), **3g** was isolated (0.119 g, 38%) as a colorless solid; mp 38−39 °C; R_f 0.61 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2971 (m), 1652 (s), 1597 (w), 1565 (w), 1452 (m), 1275 (s), 1198 (s), 809 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.91 (s, 1 H, OH), 4.42 (q, 2 H, J = 7.2 Hz, OCH_2), 3.52−3.47 (m, 2 H, CH_2), 3.16−3.11 (m, 2 H, CH_2), 2.70 (q, 2 H, J = 7.5 Hz, CH_2), 2.48 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 1.09 (t, 3 H, J = 7.5 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 158.0, 141.4, 135.6, 129.0, 126.7, 111.7, 61.6, 42.3, 33.6, 19.8, 18.6, 16.1, 14.2, 13.3; MS (EI, 70 eV) *m/z* (%) 286.2 ([M]$^+$, 9), 284.2 ([M]$^+$, 28), 240.2 (36), 238.2 (100), 212.1 (9), 210.1 (28), 203.1 (91), 189.2 (34), 91.1 (8), 29.1 (12). Elemental analysis calcd for $C_{15}H_{21}O_3Cl$: C 63.26, H 7.43. Found: C 63.12, H 7.43.

Ethyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-6-propyl-2-benzoate (3h). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)hepta-1,3-diene (0.711 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3h** was isolated (0.273 mg, 67%) as a colorless solid; mp 38−39 °C; R_f 0.66 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 2960 (m), 1653 (s), 1593 (w), 1449 (m), 1190 (s), 1041 (w), 769 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.90 (s, 1 H, OH), 4.44 (q, 2 H, J = 7.2 Hz, OCH_2), 3.50−3.46 (m, 2 H, CH_2), 3.15−3.08 (m, 2 H, CH_2), 2.48 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.38−1.46 (m, 4 H, CH_2), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 0.89 (t, 3 H, J = 6.9 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 158.3, 141.7, 135.6, 127.7, 126.7, 111.7, 61.6, 42.2, 33.6, 28.7, 22.3, 18.6, 16.4, 14.4, 14.2; MS (EI, 70 eV) *m/z* (%) 300.0 ([M]$^+$, 11), 298.0 ([M]$^+$, 35), 254.0 (34), 252.0 (100), 239.0 (8), 237.0 (29), 217.0 (58), 91.0 (9), 28.0 (36). The exact molecular mass for $C_{16}H_{23}O_3Cl$ (*m/z* 298.1336 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 6-Butyl-4-(2-chloroethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3i). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)octa-1,3-diene (0.743 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3i** was isolated (0.206 g, 44%) as a colorless oil; R_f 0.69 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ =2929 (m), 1654 (s), 1597 (w), 1567 (w), 1450 (m), 1195 (s), 1039 (w), 806 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.89 (s, 1 H, OH), 4.47 (q, 2 H, J = 7.2 Hz, OCH_2), 3.52−3.46 (m, 2 H, CH_2), 3.16−3.10 (m, 2 H, CH_2), 2.69−2.65 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.38−1.46 (m, 4 H, CH_2), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 0.89 (t, 3 H, J = 6.9 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 158.4, 141.8, 135.8, 128.1, 126.9, 111.9, 61.8, 42.5, 33.9, 31.5, 26.6, 23.2, 18.8, 16.5, 14.3, 14.2; MS (EI, 70 eV) *m/z* (%) 314.0 ([M]$^+$, 17), 312.0 ([M]$^+$, 55), 268.0 (28), 266.0 (81), 253.0 (26), 251.0 (81), 223.9 (100), 188.9 (41), 91.0 (21), 28.0 (67). The exact molecular mass for $C_{17}H_{25}O_3Cl$ (*m/z* 312.1492 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-6-hexyl-1-hydroxy-3,5-dimethyl-2-benzoate (3j). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)deca-1,3-diene (0.806 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3j** was isolated (0.208 g, 41%) as a colorless oil; R_f 0.67 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ 2927 (s), 1725 (w), 1654 (s), 1597 (w), 1566 (w), 1452 (m), 1195 (s), 1041 (w), 808 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.89 (s, 1 H, OH), 4.47 (q, 2 H, J = 7.2 Hz, OCH_2), 3.56−3.46 (m, 2 H, CH_2), 3.16−3.10 (m, 2 H, CH_2), 2.69−2.64 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 1.30−1.23 (br, 8 H, CH_2), 0.89 (t, 3 H, J = 6.9 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 158.4, 141.8, 135.8, 128.2, 126.9, 111.9, 61. 8, 42.5, 33.8, 31.9, 29.9, 29.3, 26.9, 22.9, 18.8, 16.6, 14.4, 14.3; MS (EI, 70 eV) *m/z* (%) 342.0 ([M]$^+$, 17), 340.0 ([M]$^+$, 51), 296.0 (22), 294.0 (58), 281.0 (11), 279.0 (43), 225.0 (35), 223.0 (100), 189.0 (34), 91.0 (15), 28.0 (32). The exact molecular mass for $C_{19}H_{29}O_3Cl$ (*m/z* 340.1805 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-6-heptyl-1-hydroxy-3,5-dimethyl-2-benzoate (3k). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)undeca-1,3-diene (0.865 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3k** was isolated (0.269 g, 51%) as a colorless oil; R_f 0.67 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 2927 (s), 1727 (w), 1655 (s), 1597 (w), 1567

(w), 1452 (m), 1195 (s), 1039 (w), 853 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.90 (s, 1 H, OH), 4.42 (q, 2 H, J = 7.2 Hz, OCH_2), 3.46−3.52 (m, 2 H, CH_2), 3.16−3.10 (m, 2 H, CH_2), 2.69−2.64 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 1.37−1.25 (br, 10 H, CH_2), 0.91−0.89 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 158.4, 141.8, 135.8, 128.2, 126.9, 111.9, 61. 8, 42.5, 33.9, 32.1, 30.2, 29.4, 29.4, 26.9, 22.9, 18.8, 16.6, 14.4, 14.3; MS (EI, 70 eV) *m/z* (%) 356.1 ($[M]^+$, 2), 354.1 ($[M]^+$, 7), 310.0 (2), 308.0 (6), 226.0 (4), 223.9 (15), 122.0 (24), 73.0 (36), 28.0 (100). The exact molecular mass for $C_{20}H_{31}O_3Cl$ (*m/z* 354.1962 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-6-octyl-2-benzoate (3*l*). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)dodeca-1,3-diene (0.869 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3*l*** was isolated (0.249 g, 45%) as a colorless oil; R_f 0.68 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ 2926 (s), 1697 (w), 1655 (s), 1597 (w), 1460 (m), 1195 (s), 1040 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.89 (s, 1 H, OH), 4.42 (q, 2 H, J = 7.2 Hz, OCH_2), 3.52−3.46 (m, 2 H, CH_2), 3.16−3.10 (m, 2 H, CH_2), 2.69−2.64 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 1.37−1.23 (br, 12 H, CH_2), 0.90−0.80 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 158.4, 141.8, 135.8, 128.2, 126.9, 111.9, 61.8, 42.5, 33.9, 32.1, 30.3, 29.7, 29.5, 29.4, 26.9, 22.9, 18.9, 16.6, 14.4, 14.3; MS (EI, 70 eV) *m/z* (%) 368.1 (M^+, 3), 296.1 (6), 281.0 (10), 240.0 (12), 196.9 (36), 122.1 (75), 73.1 (100), 28.0 (43). Elemental analysis calcd for $C_{21}H_{33}O_3Cl$: C 68.36, H 9.01. Found: C 68.37, H 8.40. The exact molecular mass for $C_{21}H_{33}O_3Cl$ (*m/z* 368.2118 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-1-hydroxy-3,5-dimethyl-6-nonyl-2-benzoate (3m). Starting with **2a** (0.190 g, 1.51 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)trideca-1,3-diene (0.901 g, 2.25 mmol), and $TiCl_4$ (0.33 mL, 3.00 mmol), **3m** was isolated (0.270 g, 47%) as a colorless oil; R_f 0.71 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ 2926 (s), 1698 (w), 1655 (s), 1597 (w), 1567 (w), 1461 (m), 1195 (s), 1040 (w), 847 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.93 (s, 1 H, OH), 4.47 (q, 2 H, J = 7.2 Hz, OCH_2), 3.56−3.51 (m, 2 H, CH_2), 3.21−3.15 (m, 2 H, CH_2), 2.69−2.63 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 1.42 (t, 3 H, J = 7.2 Hz, CH_3), 1.37−1.23 (br, 14 H, CH_2), 0.70 (t, 3 H, J = 6.6 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 158.5, 141.8, 135.8, 128.2, 126.9, 111.9, 61.8, 42.5, 33.9, 32.1, 30.3, 29.8, 29.6, 29.4, 26.9, 22.9, 18.9, 16.6, 14.4, 14.3; MS (EI, 70 eV) *m/z* (%) 384.3 ($[M]^+$, 7), 382.3 ($[M]^+$, 24), 338.1 (4), 336.1 (14), 265.1 (21), 240.0 (34), 197.1 (37), 122.1 (75), 73.7 (100), 43.1 (42). The exact molecular mass for $C_{22}H_{35}O_3Cl$ (*m/z* 382.2275 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-6-decyl-1-hydroxy-3,5-dimethyl-2-benzoate (3n). Starting with **2a** (0.380 g, 3.02 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)tetradeca-1,3-diene (1.864 g, 4.5 mmol), and $TiCl_4$ (0.66 mL, 6.00 mmol), **3n** was isolated (0.512 g, 55%) as a colorless oil; R_f 0.68 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 2926 (s), 1697 (w), 1655 (s), 1620 (w), 1460 (m), 1195 (s), 1040 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.89 (s, 1 H, OH), 4.42 (q, 2 H, J = 7.2 Hz, OCH_2), 3.51−3.46 (m, 2 H, CH_2), 3.16−3.10 (m, 2 H, CH_2), 2.69−2.64 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 1.41 (t, 3 H, J = 7.2 Hz, CH_3), 1.36−1.22 (br, 16 H, CH_2), 0.87 (t, 3 H, J = 6.6 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 158.5, 141.8, 135.8, 128.2, 126.9, 111.8, 61.8, 42.5, 32.9, 32.1, 30.3, 30.2, 29.8, 29.8, 29.6, 29.4, 27.0, 22.9, 18.8, 16.6, 14.4, 14.2; MS (EI, 70 eV) *m/z* (%) 398.0 ($[M]^+$, 15), 396.0 ($[M]^+$, 47), 352.0 (11), 350.0 (30), 265.1 (53), 223.9 (70), 167.1 (86), 70.1 (100), 41.1 (95), 28.0 (73). The exact molecular mass for $C_{23}H_{37}O_3Cl$ (*m/z* 396.2431 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 1-Benzyloxy-5-(2-chloroethyl)-2-hydroxy-4,6-dimethyl-3-benzoate (3o). Starting with **2a** (0.380 g, 3.00 mmol), 1-ethoxy-4-benzyloxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (1.71 g, 4.5 mmol), and $TiCl_4$ (0.65 mL, 6.00 mmol), **3o** was isolated (0.492 g, 45%) as a colorless solid; mp 52−53 °C; R_f 0.58 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 3429 (br), 2929 (w), 1654 (s), 1594 (w), 1449 (m), 1276 (s), 1067 (m), 807 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.53 (s, 1 H, OH), 7.48−7.43 (m, 5 H, ArH), 4.97 (s, 2 H, OCH_2Ph), 4.45 (q, 2 H, J = 7.2 Hz, OCH_2), 3.49−3.43 (m, 2 H, CH_2), 3.11−3.06 (m, 2 H, CH_2), 2.46 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 1.43 (t, 3 H, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 153.5, 143.6, 137.7, 136.8, 133.4, 128.6, 128.3, 127.2, 113.7, 74.5, 61.9, 42. 33.5, 18.4, 14.4, 13.5; MS (EI, 70 eV) *m/z* (%) 363.4 ($[M]^+$, 5), 361.4 ($[M]^+$, 16), 291.1 (16), 276.5 (24), 197.5 (10), 90.7 (100), 28.0 (79). Elemental analysis calcd for $C_{20}H_{32}O_4Cl$: C 66.20, H 6.38. Found: C 65.84, H 6.97. The exact molecular mass for $C_{20}H_{32}O_4Cl$ (*m/z* 362.1285 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Methyl 4-(2-Chloroethyl)-3,5-diethyl-1-hydroxy-2-benzoate (3p). Starting with **2b** (0.152 g, 0.99 mmol), 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.340 g, 1.30 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3p** was isolated (0.126 g, 47%) as a colorless oil; R_f 0.69 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 2966 (m), 1732 (w), 1663 (s), 1604 (m), 1570 (m), 1438 (s), 1335 (s), 1080 (m), 850 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.65 (s, 1 H, OH), 6.75 (s, 1 H, ArH), 3.96 (s, 3 H, OCH_3), 3.52−3.46 (m, 2 H, CH_2), 3.12−3.06 (m, 2 H, CH_2), 2.94 (q, 2 H, J = 7.5 Hz, CH_2), 2.65 (q, 2 H, J = 7.5 Hz, CH_2), 1.25 (t, 3 H, J = 7.5 Hz, CH_3), 1.19 (t, 3 H, J = 7.5 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 160.6, 150.5, 145.2, 125.7, 115.7, 111.1, 52.1, 43.1, 31.9, 26.5, 24.3, 15.9, 14.7; MS (EI, 70 eV) *m/z* (%) 272.2 ($[M]^+$, 6), 270.2 ($[M]^+$, 19), 240.2 (23), 238.1 (70), 221.2 (11), 189.2 (100), 91.1 (12); the exact molecular mass for $C_{14}H_{19}O_3Cl$ (*m/z* 270.1023 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-3,5-diethyl-1-hydroxy-2-benzoate (3q). Starting with **2b** (0.155 g, 1.00 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.355 g, 1.30 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3q** was isolated (0.119 g, 42%) as a colorless solid; mp 62−63 °C; R_f 0.74 (hexane/ethyl acetate = 7:3); IR (KBr) $\tilde{\nu}$ 3432 (w), 2970 (m), 1725 (w), 1657 (s), 1602 (m), 1570 (m), 1235 (s), 1078 (m), 711 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.77 (s, 1 H, OH), 6.74 (s, 1 H, ArH), 4.43 (q, 2 H, J = 7.1 Hz, OCH_2), 3.52−3.46 (m, 2 H, CH_2), 3.11−3.05 (m, 2 H, CH_2), 2.97 (q, 2 H, J = 7.4 Hz, CH_2), 2.64 (q, 2 H, J = 7.5 Hz, CH_2), 1.43 (t, 3 H, J = 7.2 Hz, CH_3), 1.24 (t, 3 H, J = 7.4 Hz, CH_3), 1.19 (t, 3 H, J = 7.4 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 160.8, 150.2, 145.3, 125.8, 115.8, 111.3, 61.7, 43.2, 32.0, 26.5, 24.3, 16.1, 14.8, 14.0; MS (EI, 70 eV) *m/z* (%) 286.2 ($[M]^+$, 6), 284.2 ($[M]^+$, 20), 240.2 (26), 238.2 (81), 189.2 (100), 91.1 (6). Elemental analysis calcd for $C_{15}H_{21}O_3Cl$: C 63.26, H 7.43. Found: C 63.32, H 7.69.

Isopropyl 4-(2-Chloroethyl)-3,5-diethyl-1-hydroxy-2-benzoate (3r). Starting with **2b** (0.156 g, 1.01 mmol), 1-isopropyloxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.475 g, 1.65 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3r** was isolated (0.112 g, 37%) as a colorless oil; R_f 0.78 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ 2978 (m), 1725 (w), 1656 (s), 1601 (m), 1570 (m), 1457 (s), 1369 (s), 1104 (m), 838 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.81 (s, 1 H, OH), 6.73 (s, 1 H, ArH), 5.34 (sep, 1 H, J = 6.3 Hz, OCH), 3.51−3.46 (m, 2 H, CH_2), 3.11−3.05 (m, 2 H, CH_2), 2.94 (q, 2 H, J = 7.5 Hz, CH_2), 2.65 (q, 2 H, J = 7.5 Hz, CH_2), 1.41 (d, 6 H, J = 6.3 Hz, CH_3), 1.23 (t, 3 H, J = 7.2 Hz, CH_3), 1.21 (t, 3 H, J = 7.5 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 161.3, 150.5, 145.7, 126.2, 116.2, 112.1, 70.3, 43.8, 32.5, 27.0, 24.8, 22.3, 16.8, 15.3; MS (EI, 70 eV) *m/z* (%) 300.0 ($[M]^+$, 6), 298.1 ($[M]^+$, 20), 240.0 (33), 238.1 (100), 189.0 (97), 91.0 (8), 28.0 (28). The exact molecular mass for $C_{16}H_{23}O_3Cl$ (*m/z* 298.1336 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

2-Methoxyethyl 4-(2-Chloroethyl)-3,5-diethyl-1-hydroxy-2-benzoate (3s). Starting with **2b** (0.152 g, 0.99 mmol), 1-(2-methoxyethoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.450 g, 1.48 mmol), and $TiCl_4$ (0.22 mL, 2.00 mmol), **3s** was isolated (0.130 g, 42%) as a colorless oil; R_f 0.58 (hexane/ethyl acetate = 7:3); IR (neat) $\tilde{\nu}$ 2966 (m), 1736 (w), 1665 (s), 1602 (m), 1588

(m), 1444 (s), 1335 (s), 1074 (m), 834 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.26 (s, 1 H, OH), 6.73 (s, 1 H, ArH), 4.50 (t, 2 H, $J = 4.8$ Hz, OCH_2), 3.72 (t, 2 H, $J = 4.8$ Hz, OCH_2), 3.51−3.46 (m, 2 H, CH_2), 3.41 (s, 3 H, OCH_3), 3.11−3.05 (m, 2 H, CH_2), 2.94 (q, 2 H, $J = 7.5$ Hz, CH_2), 2.65 (q, 2 H, $J = 7.5$ Hz, CH_2), 1.23 (t, 3 H, $J = 7.5$ Hz, CH_3), 1.21 (t, 3 H, $J = 7.5$ Hz, CH_3); MS (EI, 70 eV) *m/z* (%) 316.0 ($[M]^+$, 7), 314.0 ($[M]^+$, 24), 240.0 (32), 238.1 (100), 189.0 (99), 91.0 (8), 28.0 (18); the exact molecular mass for $C_{16}H_{23}O_4Cl$ (*m/z* 298.1336 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Methyl 4-(2-Chloroethyl)-1-hydroxy-5-methyl-3-phenyl-2-carboxylate (3t). Starting with **2c** (0.376 g, 2.00 mmol), 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.780 g, 3.00 mmol), and $TiCl_4$ (0.44 mL, 4.00 mmol), **3t** was isolated (0.437 g, 73%) as a colorless solid; mp 95−96 °C; IR (KBr) $\tilde{\nu}$ 1663 (s), 1600 (m), 1572 (m), 1441 (s), 1347 (s), 1204 (s), 854 (m), 778 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.83 (s, 1 H, OH), 7.32−7.04 (m, 3 H, ArH), 7.09−7.06 (m, 2 H, ArH), 3.34 (s, 3 H, OCH_3), 3.30−3.24 (m, 2 H, CH_2), 2.79−2.56 (m, 2 H, CH_2), 2.04 (s, 3 H,CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 160.3, 144.8, 144.4, 141.3, 128.5, 127.8, 127.1, 119.1, 111.3 (C), 51.9, 42.8, 33.4, 20.9; MS (EI, 70 eV) *m/z* (%) 306.4 ($[M]^+$, 17), 304.3 ($[M]^+$, 50), 274.3 (36), 272.3 (88), 223.3 (100), 195.3 (17), 165.2 (36), 151.5 (28). Elemental analysis calcd for $C_{17}H_{17}O_3Cl$: C 66.99, H 5.62. Found: C 64.72, H 5.95. The exact molecular mass for $C_{17}H_{17}O_3Cl$ (*m/z* 304.0866 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Ethyl 4-(2-Chloroethyl)-1-hydroxy-5-methyl-3-phenyl-2-carboxylate (3u). Starting with **2c** (0.376 g, 2.00 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.822 g, 3.00 mmol), and $TiCl_4$ (0.44 mL, 4.00 mmol), **3u** was isolated (0.367 g, 57%) as a colorless solid; mp 104−105 °C; R_f 0.59 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2984 (m),1657 (s), 1597 (m), 1575 (m), 1462 (m), 1240 (s), 1015 (w), 776 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.04 (s, 1 H, OH), 7.38−7.33 (m, 3 H, ArH), 7.11−7.07 (m, 2 H, ArH), 6.88 (s, 1 H, ArH), 3.86 (q, 2 H, $J = 7.2$ Hz, OCH_2), 3.29−3.24 (m, 2 H, CH_2), 2.78−2.72 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 0.66 (t, 3 H, $J = 7.2$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 160.6, 144.7, 144.4, 141.5, 128.6, 127.1, 119.2, 111.3, 61.0, 42.8, 33.4, 20.9, 13.1; MS (EI, 70 eV) *m/z* (%) 319.4 ($[M]^+$, 13), 317.4 ($[M]^+$, 39), 273.5 (16), 271.5 (77), 222.6 (100), 164.7 (19), 150.8 (15), 128.2 (24). Elemental analysis calcd for $C_{18}H_{19}O_3Cl$: C 67.81, H 6.00. Found: C 67.89, H 5.94.

Isopropyl 4-(2-Chloroethyl)-1-hydroxy-5-methyl-3-phenyl-2-carboxylate (3v). Starting with **2c** (0.376 g, 2.00 mmol), 1-isopropyloxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.864 g, 3.00 mmol), and $TiCl_4$ (0.44 mL, 4.00 mmol), **3v** was isolated (0.229 g, 34%) as a colorless solid; R_f 0.62 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2981 (m), 1656 (s), 1599 (m), 1575 (m), 1458 (m), 1370 (s), 1240 (s), 1102 (m), 702 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.72 (s, 1 H, OH), 7.40−7.33 (m, 3 H, ArH), 7.10−7.06 (m, 2 H, ArH), 6.88 (s, 1 H, ArH), 4.87 (d, 1 H, $J =$ 6.3 Hz, OCH), 3.29−3.23 (m, 2 H, CH_2), 2.76−2.71 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 0.84 (d, 6 H, $J = 6.3$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 160.6, 144.5, 144.3, 141.6, 128.8, 127.9, 127.0, 119.0, 111.6, 68.8, 42.8, 33.4, 21.0, 20.9; MS (EI, 70 eV) *m/z* (%) 333.9 ($[M]^+$, 11), 331.9 ($[M]^+$, 34), 274.0 (33), 272.0 (100), 222.9 (99), 165.1 (17), 151.2 (13), 28.0 (25). Elemental analysis calcd for $C_{19}H_{21}O_3Cl$: C 68.56, H 6.36. Found: C 68.90, H 5.80.

Isobutyl 4-(2-Chloroethyl)-1-hydroxy-5-methyl-3-phenyl-2-carboxylate (3w). Starting with **2c** (0.376 g, 2.00 mmol), 1-isobutyloxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (0.980 g, 3.00 mmol), and $TiCl_4$ (0.44 mL, 4.00 mmol), **3w** was isolated (0.509 g, 73%) as a colorless solid; mp 74−75 °C; R_f 0.63 (hexane/ethyl acetate = 4:1); IR (KBr) $\tilde{\nu}$ 2980 (m), 1651 (s), 1598 (m), 1465 (m), 1244 (s), 755 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.04 (s, 1 H, OH), 7.38−7.32 (m, 3 H, ArH), 7.19−7.08 (m, 2 H, ArH), 6.89 (s, 1 H, ArH), 3.62 (d, 2 H, $J = 6.9$ Hz, OCH_2), 3.28−3.22 (m, 2 H, CH_2), 2.75−2.69 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 1.24−1.17 (m, 1 H, CH), 0.60 (d, 6 H, $J =$ 6.6 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 160.6, 144.7, 144.2, 141.4, 128.5, 128.3, 128.0, 127.1, 119.1, 71.8, 42.8, 33.4, 20.9, 19.3, 19.0; MS (EI, 70 eV) *m/z* (%) 348.0 ($[M]^+$, 10), 346.1 ($[M]^+$, 34), 274.0 (34), 272.0 (100), 222.9 (93), 210.0 (78), 104.6 (34), 28.0 (78). Elemental analysis calcd for $C_{19}H_{21}O_3Cl$: C 69.25, H 6.68. Found: C 69.72, H 6.45.

Ethyl 4-(2-Chloroethyl)-1-hydroxy-3-methyl-2-benzoate (3x). Starting with **2d** (0.100 g, 0.89 mmol), 1-ethoxy-1,3-bis-(trimethylsilyloxy)buta-1,3-diene (0.366 g, 1.33 mmol), and $TiCl_4$ (0.20 mL, 1.80 mmol), **3x** was obtained (0.090 g, 42%) as a colorless solid; mp 43−44 °C; IR (KBr) $\tilde{\nu}$ 2963 (m), 1727 (w), 1661 (s), 1598 (m), 1471 (m), 1221 (s), 839 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.26 (s, 1H, OH), 7.22 (d, 1 H, $J =$ 8.7 Hz, ArH), 6.81 (d, 1 H, $J = 9$ Hz, ArH), 4.46 (q, 2 H, $J =$ 7.2 Hz, OCH_2), 3.60 (t, 2 H $J = 6.9$ Hz, CH_2 Cl), 3.06 (t, 2 H, $J = 7.8$ Hz, CH_2), 2.49 (s, 3 H, CH_3), 1.43 (t, 3 H, $J = 6.3$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 160.9, 138.6, 136.1, 128.2, 115.4, 114.0, 61.2, 43.8, 37.1, 18.4, 14.2; MS (EI, 70 eV) *m/z* (%) 244.1 ($[M]^+$, 6), 242.0 ($[M]^+$, 20), 198 (26), 196.0 (76), 146.5 (100), 91.0 (11), 43.1 (3.5), 28.0 (35.8). Elemental analysis calcd for $C_{12}H_{15}O_3Cl$: C 59.50, H 6.96. Found: C 58.90, H 7.39.

Ethyl 4-(2-Chloroethyl)-6-ethyl-1-hydroxy-3-methyl-2-benzoate (3y). Starting with **2d** (0.150 g, 1.33 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene (0.607 mg, 2.00 mmol), and $TiCl_4$ (0.290 mL, 2.66 mmol), **3y** was obtained (0.903 g, 33%) as a colorless oil; IR (neat) $\tilde{\nu}$ 2968 (m), 1728 (w), 1656 (s), 1614 (w), 1448 (m), 1283 (m), 1187 (s), 807 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.98 (s, 1 H, OH), 7.10 (s, 1 H, ArH), 4.43 (q, 2 H, $J = 7.2$ Hz, OCH_2), 3.59 (t, 2 H, $J =$ 7.2 Hz, CH_2Cl), 3.04 (t, 2 H, $J = 7.5$ Hz, CH_2), 2.64 (q, 2 H, J = 7.5 Hz, CH_2), 2.45 (s, 3 H, CH_3), 1.42 (t, 3 H, $J = 7.2$ Hz, CH_3), 1.20 (t, 3 H, $J = 7.5$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 158.9, 135.6, 135.5, 130.0, 127.4, 113.4, 61.7, 43.9, 37.2, 22.9, 18.2, 14.2, 13.8; MS (EI, 70 eV) *m/z* (%) 272.0 ($[M]^+$, 9), 270.0 ($[M]^+$, 26), 225.9 (33), 223.9 (100), 195.9 (82), 175.0 (40), 91(18), 77(8), 28.0 (35). Elemental analysis calcd for $C_{14}H_{19}O_3Cl$: C 62.22, H 7.00. Found: C 62.33, H 6.96.

Methyl 4-(2-Bromoethyl)-1-hydroxy-3,5-dimethyl-2-benzoate (3z). Starting with **2a** (0.136 g, 1.08 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**2b**) (0.420 g, 1.61 mmol), **3z** was obtained (0.215 g, 82%) as a colorless solid; mp 73−74 °C; IR (KBr) $\tilde{\nu}$ 2950 (m), 1721 (w), 1656 (s), 1599 (m), 1574 (m), 1436 (s), 1355 (s), 1237 (s), 1071 (m), 805 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.69 (s, 1 H, OH), 6.69 (s, 1 H, ArH), 3.95 (s, 3 H, OCH_3), 3.35−3.29 (m, 2 H, CH_2), 3.19−3.15 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 160.3, 144.0, 138.8, 128.2, 117.3, 111.8, 52.2, 33.3, 29.7, 20.9, 18.5; MS (EI, 70 eV) *m/z* (%) 288.0 ($[M]^+$, 24), 286.0 ($[M]^+$, 26), 256.0 (63), 254.0 (62), 207.0 (62), 193.0 (23), 175.0 (31), 161.0 (100), 77.0 (12). Elemental analysis calcd for $C_{12}H_{15}O_3Br$ (287.15): C 50.13, H 5.26. Found: C 50.29, H 5.43.

Ethyl 4-(2-Bromoethyl)-6-butyl-1-hydroxy-3,5-dimethyl-2-benzoate (3aa). Starting with **2a** (0.252 g, 2.00 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)octa-1,3-diene (0.990 g, 3.00 mmol), and $TiBr_4$ (1.500 g, 4.00 mmol), **3aa** was isolated (0.308 g, 43%) as a colorless oil; IR (neat) $\tilde{\nu}$ 2959 (s), 1715 (m), 1653 (s), 1598 (s), 1567 (m), 1451 (m), 1193 (s), 1031 (m), 850 (m); ^1H NMR (300 MHz, $CDCl_3$) δ 10.91 (s, 1 H, OH), 4.42 (q, 2 H, $J = 7.2$ Hz, OCH_2), 3.34−3.30 (m, 2 H, CH_2), 3.23−3.20 (m, 2 H, CH_2), 2.70−2.63 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 1.46−1.25 (m, 7 H, 1 × CH_3, 2 × CH_2), 0.96−0.87 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 258.3, 141.5, 135.5, 128.0, 111.7, 61.6, 34.1, 31.3, 29.9, 26.4, 23.1, 18.6, 16.4, 14.2, 14.0; MS (EI, 70 eV) *m/z* (%) 358.5 ($M^+ + 2$, 21), 354.5 (M^+, 21), 312.3 (33), 310.3 (33), 270.3 (42), 268.3 (44), 231.3 (47), 189.2 (44), 91.1 (47), 73.7 (55), 41.2 (44), 29.1 (100); UV−vis λ_{max} (log ϵ) 222 (4.3), 255 (3.82), 320 (3.44); $C_{17}H_{25}O_3Br$.

Ethyl 4-(2-Bromoethyl)-6-hexyl-1-hydroxy-3,5-dimethyl-2-benzoate (3ab). Starting with **2a** (0.380 g, 3.00 mmol), 1-ethoxy-1,3-bis(trimethylsilyloxy)deca-1,3-diene (1.730 g, 4.5 mmol), and $TiBr_4$ (2.210 g, 6.00 mmol), **3ab** was isolated (0.520

g, 45%) as a colorless oil; IR (neat) $\tilde{\nu}$ 2927 (s), 1715 (s), 1654 (s), 1597 (m), 1460 (m), 1193 (s), 1031 (m), 848 (m); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.91 (s, 1 H, OH), 4.46 (q, 2 H, J = 7.2 Hz, OCH_2), 3.36−3.30 (m, 2 H, CH_2), 3.23−3.19 (m, 2 H, CH_2), 2.69−2.64 (m, 2 H, CH_2), 2.47 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 1.39 (t, 3 H, J = 7.2 Hz, CH_3), 1.34−1.21 (m, 8 H, CH_2), 0.91−0.88 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 258.2, 141.4, 135.5, 128.0, 127.9, 111.7, 61.6, 34.1, 31.7, 29.9, 29.7, 29.1, 26.7, 22.6, 18.6, 16.3, 14.2, 14.1; MS (EI, 70 eV) *m/z* (%) 386.0 (M^+ + 2, 3), 384.0 (M^+, 3), 340.0 (4), 337.9 (4), 269.9 (10), 268 (10), 189.0 (10), 161.0 (10), 73.7 (10), 43.1 (14), 28.0 (100); UV−vis λ_{max} (log ϵ) 222 (4.3), 255 (3.73), 320 (3.29); $C_{19}H_{29}O_3Br$.

Crystal Structure Determination of 3w. The intensity data for the compound were collected on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo Kα radiation. Data were corrected for Lorentz and polarization effects, but not for absorption effects.[14,15] The structures were solved by direct methods (SHELXS)[16] and refined by full-matrix least-squares techniques against F_o^2 (SHELXL-97).[17] For the hydroxy group O1 the hydrogen atom was located by difference Fourier synthesis and refined isotropically. All other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.[17] XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations.

Crystal Data for 3w: $C_{20}H_{23}ClO_3$, M_r = 346.83 g mol^{-1}, colorless prism, size 0.03 × 0.03 × 0.02 mm^3, monoclinic, space group $P2_1/n$, a = 8.8561(2) Å, b = 12.9712(3) Å, c = 15.8805(4) Å, β = 104.172(1)°, V = 1768.74(7) Å^3, T = −90 °C, Z = 4, $\rho_{calc.}$ = 1.302 g cm^{-3}, μ(Mo Kα) = 2.31 cm^{-1}, F(000) = 736, 6834 reflections in h (−11/11), k (−16/15), l (−20/20), measured in the range 2.42° ≤ Θ ≤ 27.48°, completeness Θ_{max} = 99.6%, 4050 independent reflections, R_{int} = 0.019, 3299 reflections with $F_o > 4\sigma(F_o)$, 221 parameters, 0 restraints, $R1_{obs}$ = 0.037, $wR2_{obs}$ = 0.090, $R1_{all}$ = 0.050, $wR2_{all}$ = 0.097, GOOF = 1.025, largest difference peak and hole 0.236/−0.268 e Å^{-3}.

Synthesis of 3-(2-Chloroethyl)pentane-2,4-dione (4). To a CH_2Cl_2 solution (100 mL) of **2a** (0.151 g, 1.2 mmol) was added dropwise $TiCl_4$ (0.13 mL, 1.2 mmol) at −78 °C under argon atmosphere. The reaction mixture was allowed to warm to 20 °C over 12 h and was stirred for an additional 6 h at 20 °C. The mixture was poured into an aqueous solution of HCl (1.0 M, 100 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1:4 → 1:1) to give **4** (0.086 g, 47%) as a colorless oil; IR (KBr) ν 3429 (br), 1725 (w), 1702 (m), 1605 (s), 1421 (s), 1284 (m), 985 (m), 688 (w) cm^{-1}; major isomer (enol from) ^{1}H NMR (300 MHz, $CDCl_3$) δ 16.88 (s, 1 H, OH), 3.49 (t, 2 H, J = 8.1 Hz, CH_2Cl), 2.73 (t, 2 H, J = 7.8 Hz, CH_2), 2.18 (s, 6 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 106.8, 43.3, 31.1, 23.1; minor isomer (keto form) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.01 (t, 1 H, J = 7.2 Hz, CH), 3.53 (t, 2 H, J = 7.5 Hz, CH_2Cl), 2.28 (q, 2 H, J = 7.2 Hz, CH_2), 2.24 (s, 6 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1, 64.8, 42.6, 31.3, 29.6; MS (EI, 70 eV) *m/z* (%) 164.0 (M^+, 7), 162.0 (M^+, 21), 148.3 (5), 146.5 (15), 227.2 (16), 112.1 (99), 70.0 (20), 43.1 (100). The exact molecular mass for $C_7H_{11}O_2Cl$ (*m/z* 162.0448 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Synthesis of Isopropyl 8-Hydroxy-4,8-dimethyl-6-oxospiro[5.2]oct-4-ene-5-carboxylate (5). A CH_2Cl_2 solution (1 mL) of $TiCl_4$ (0.03 mL, 0.3 mmol) was added dropwise at −78 °C under argon atmosphere to a stirred CH_2Cl_2 solution (100 mL) of **2a** (0.131 g, 1.0 mmol) and **1b** (0.450 g, 1.6 mmol) in the presence of molecular sieves (4 Å, 1.0 g). The reaction mixture was allowed to warm to 20 °C over 6 h, stirred for an additional 6 h at 20 °C, and subsequently filtered. The filtrate was poured into an aqueous solution of HCl (1.0 M, 100 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 4:1→1:1) to give **5** (0.125 g, 48%) as a colorless oil; R_f 0.18 (hexane/EtOAc = 1:1); IR (neat) ν 3399 (br), 2983 (w), 1729 (s), 1659 (s), 1617 (m), 1380 (m), 1243 (s), 1024 (m), 745 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.17 (sept, 1 H, J = 6.3 Hz, CH), 2.71 (d, 1 H, J = 15.6 Hz, CH_2), 2.59 (d, 1 H, J = 15.6 Hz, CH_2), 2.40 (br, 1 H, OH), 1.68 (s, 3 H, CH_3), 1.49−1.37 (m, 1 H, CH_2), 1.30 (d, 6 H, J = 6.3 Hz, CH_3), 1.26 (s, 3 H, CH_3), 1.15−1.04 (m, 2 H, CH_2), 0.88−0.81 (m, 1 H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 166.8, 160.5, 133.2, 70.5, 69.0, 51.5, 32.1, 25.4, 21.7, 16.7, 10.8, 9.5; MS (EI, 70 eV) *m/z* (%) 252.2 (M^+, 40), 237.1 (13), 193.1 (65), 177.1 (41), 164.1 (47), 148.1 (100), 91.1 (17), 43.1 (78); the exact molecular mass for $C_{14}H_{20}O_4$ (*m/z* 252.1362 ± 2 mD) was confirmed by HRMS (EI, 70 eV).

Procedure for the Preparation of 3b from 5. A CH_2Cl_2 solution (1 mL) of $TiCl_4$ (0.06 mL, 0.5 mmol) was added dropwise at 0 °C to a CH_2Cl_2 solution (20 mL) of **5** (0.126 g, 0.5 mmol) and the solution was stirred for 1 h (TLC monitoring). The reaction mixture was extracted with an aqueous solution of HCl (1.0 M, 20 mL) and the aqueous layer was washed with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica, hexane/EtOAc = 9:1→ 4:1) to give **3b** (0.072 g, 53%) as a colorless solid.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft. We are grateful to the government of Vietnam for a graduate scholarship for V.T.H.N.

Supporting Information Available: Details of the crystal structure analysis of **3w**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0485278

(14) *COLLECT*; Data Collection Software: Nonius B.V., The Netherlands, 1998.

(15) Otwinowski, Z.; Minor, W. Processing of X-ray Diffraction Data Collected in Oscillation Mode. In *Methods in Enzymology*; Vol. 276, Macromolecular Crystallography, Part A; Carter, C. W., Sweet, R. M., Eds.; Academic Press: New York, 1997; pp 307−326.

(16) Sheldrick, G. M. *Acta Crystallogr. Sect. A* **1990**, *46*, 467−473.

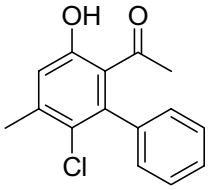
(17) Sheldrick, G. M. *SHELXL-97*, Release 97-2; University of Göttingen: Göttingen, Germany, 1997.

MANUSCRIPT IN PREPARATION

Manuscript in preparation

The following experimental data represent unpublished results from different projects.

1-(6-Chloro-3-hydroxy-5-methyl-biphenyl-2-yl)-ethanone (1):



Starting with 3-chloro-4-phenyl-4-(trimethylsilyloxy)but-3-en-2-one (0.748 g, 2.91 mmol), 2,4-bis(trimethylsilanyloxy)penta-1,3-diene (0.710 g, 2.91 mmol) and $TiCl_4$ (0.550 g, 2.91 mmol), (**1**) (0.324 g, 43%) was obtained as a yellow crystal; mp. 68 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 11.95 (s, 1H, OH), 7.50-7.43 (m, 3H, ArH), 7.30-7.25 (m, 2H, ArH), 6.95 (s, 1H, Ar-H), 2.42 (s, 3H, CH_3), 1.68 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.2 (CO), 159.8, 144.4, 141.7, 139.5 (C), 130.4 (2C), 128.9 (3C) (CH-Ph), 125.2, 121.0 (C), 120.2 (CH), 32.0, 22.1 (CH_3). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3206 (m), 1673 (m), 1330 (s), 1209 (m), 742 (s). MS (EI, 70 eV): *m/z* (%) = 262.0 (M^+, [^{37}Cl], 33), 260 (M^+, [^{35}Cl], 99), 247 (34), 245 (100), 212 (1), 210 (34), 183 (4), 181 (32), 152 (28). Anal. calcd for $C_{15}H_{13}O_2Cl$ (260.50): C 69.09, H 5.00; found: C 69.28, H 5.20.

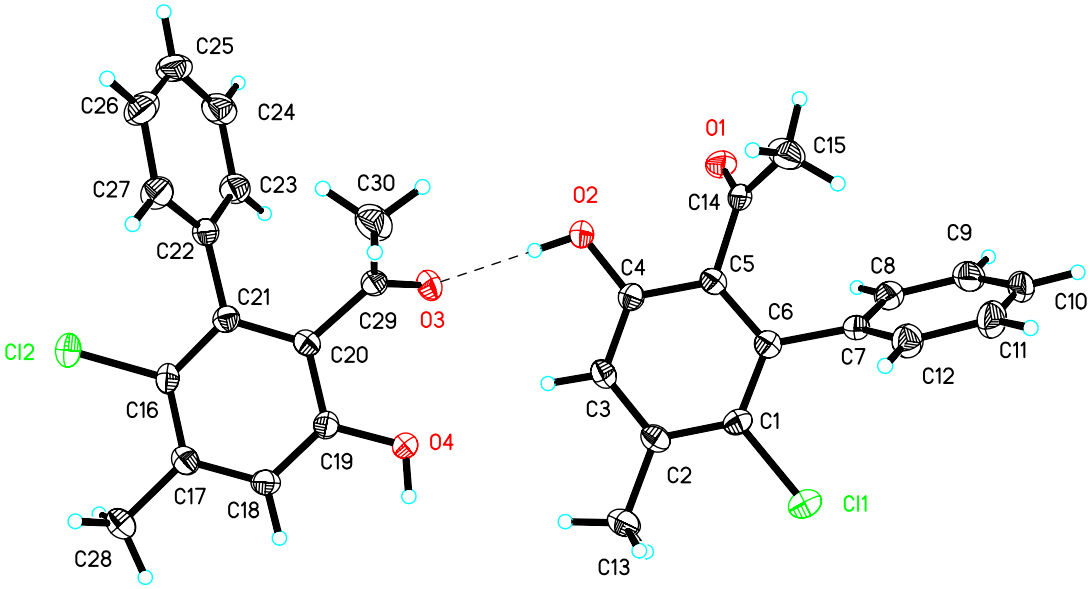
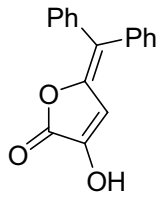


Figure 1. ORTEP plot of **1**

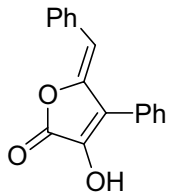
General procedure for the synthesis of compound (2) and (3): To a CH_2Cl_2 solution (42.20 mL) of (1-benzhydral-vinyloxy)-trimethyl-silane (1.190 g, 4.21 mmol) and of oxalyl chloride (0.44 mL, 5.05 mmol) was added a CH_2Cl_2 solution (5 ml) of TMSOTf (0.38 mL, 2.10 mmol) at −78 °C. The temperature of the solution was allowed to rise to 20 °C during 12 h. After stirring for 3 h at 20 °C, a saturated aqueous solution of $NaHCO_3$ was added. The organic and the aqueous layer were separated and the latter was extracted three times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane/EtOAc) to give compound (**2**) (0.290 g, 26%), as a yellow solid.

5-Benzhydrylidene-3-hydroxy-5*H*-furan-2-one (2):



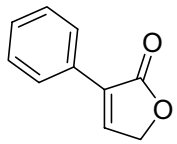
mp. 199 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.27-7.41 (m, 10 H, Ar-H), 6.48 (s, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6 (C=O), 146.7 (C-OH), 145.5, 139.3, 138.6 (C), 131.9 (2C), 131.6 (2C), 129.3 (2C), 129.1, 128.9 (2C), 128.7 (CH_2), 124.3 (C), 111.9 (CH). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3341 (m), 1743 (s), 1617 (m), 1208 (w), 1092 (m), 700 (m); UV-VIS (CH_3CN, nm): λ_{max} (Ig ε): 352 (4.12), 247 (4.02), 203 (4.44). MS (EI, 70 eV): *m/z* (%) = 264 (M^+, 100), 191 (58), 165 (62), 104 (23), 28 (65). Anal. Calcd for $C_{17}H_{12}O_3$ (264.07): C 77.26, H 4.58; found: C 77.12, H 4.32.

5-Benzylidene-3-hydroxy-4-phenyl-5*H*-furan-2-one (3):



Starting with (1-benzyl-2-phenyl-ethoxy)-trimethyl-silane (0.200 g, 0.70 mmol), oxalyl chloride (0.07 mL, 0.85 mmol), and TMSOTf (0.06 mL, 0.35 mmol), (**3**) (0.051 g, 27%), was isolated as a yellow solid; mp. 205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26-7.73 (m, 10H, Ar-H), 6.01 (s, 1H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.66 (C=O), 145.6 (C-OH), 138.2, 133.3 (2C), 130.2 (2C), 129.4 (2C), 129.1 (2C), 128.9 (2C), 128.7 ($2CH_2$), 126.10 (C), 111.4 (CH). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3294 (m), 1778 (s), 1407 (w), 1130 (m), 773 (w), 694 (w). UV-VIS (CH_3CN, nm): λ_{max} (Ig ε): 352 (4.12), 278 (3.96), 244 (3.85). MS (EI, 70 eV): *m/z* (%) = 265 ($[M+1]^+$, 20), 264 (M^+, 100), 191 (81), 118 (64), 90 (29), 28 (22). Anal. Calcd for $C_{17}H_{12}O_3$ (264.07): C 77.26, H 4.58; found: C 77.00, H 4.40.

General procedure for the synthesis of 3-phenyl-5H-furan-2-one (4):



To a CH_2Cl_2 solution (40.00 mL) of chloroacetaldehydedimethylacetal (0.500 g, 4.03 mmol) and of 2,2-(bis-trimethylsilyloxy-vinyl)-benzene (1.290 g, 4.63 mmol) was added a CH_2Cl_2 solution (5 ml) of TMSOTf (0.37 mL, 2.01 mmol) at −78 °C. The temperature of the solution was allowed to rise to 20 °C during 12 h. After stirring for 3 h at 20 °C, a solution of HCl (10%) was added. The organic and the aqueous layer were separated and the latter was extracted three times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane/EtOAc) to give intermediate acid (0.350 g, 38%), as colorless oil.

Data of intermediate acid: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.33-7.31 (m, 5H, Ar-H), 4.08-4.03 (m, 1H, CH), 3.94 (d, 1H, *J* = 8.5 Hz, CH_2), 3.70-3.65 (m, 1H, CH_2), 3.55 (s, 3H, CH_3), 3.12 (dd, *J* = 2.5 Hz, *J* = 10.3 Hz, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.5 (COOH), 134.3 (C-Ph), 130.1, 129.5, 129.0, 128.8, 18.4 (CH-Ph), 81.5, 58.6 (CH), 54.7 (OMe), 43.5 (CH_2). MS (EI, 70 eV): *m/z* (%) = 228.0 (M^+, 2), 192 (22), 136 (87), 118 (54), 93 (100), 44 (34).

The intermediate acid (0.175 g, 0.76 mmol), was then treated with NaH (0.027 g, 1.14 mmol), TBAI (0.56 g, 1.52 mmol) in THF (21 mL). The reaction was being stirred at 20 °C for 20 h. Solvent was removed at vacuo and product was purified by chromatography (silica gel, hexane/EtOAc) to give (**4**) (0.055 g, 45%), colorless oil.

Data of **4**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.84-7.83 (m, 2H, Ar-H), 7.65-7.64 (m, 1H, ArH), 7.42-7.24 (m, 3H, ArH, CH), 4.92 (d, 2H, *J* = 1.8 Hz, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.2 (C=O), 144.2 (CH), 131.7, 129.5 (C), 129.3, 128.6 (2C), 127.0 (2C) (C-Ph), 69.5 (CH_2). MS (EI, 70 eV): *m/z* (%) = 160.0 (M^+, 24), 132 (13), 103 (100), 77 (26), 51 (22). Anal. Calcd for $C_{10}H_8O_2$ (160.05): C 74.99, H 5.03; found: C 74.70, H 4.80.

X-RAY CRYSTAL DATA

X-Ray crystals data

Data of compound 4d (publication 4):

Table 1. Bond lengths [Å] and angles [°] for 4d

O(1B)-C(5B)	1.359(6)
O(1B)-C(1B)	1.389(6)
O(2B)-C(1B)	1.217(6)
O(3B)-C(11B)	1.371(6)
O(3B)-C(14B)	1.416(6)
O(4B)-C(10B)	1.365(5)
O(4B)-C(15B)	1.421(6)
C(1B)-C(2B)	1.450(7)
C(2B)-C(3B)	1.364(7)
C(2B)-C(8B)	1.484(7)
C(3B)-C(4B)	1.435(7)
C(3B)-C(7B)	1.500(7)
C(4B)-C(5B)	1.338(7)
C(5B)-C(6B)	1.492(7)
C(8B)-C(13B)	1.382(6)
C(8B)-C(9B)	1.406(6)
C(9B)-C(10B)	1.372(7)
C(10B)-C(11B)	1.424(6)
C(11B)-C(12B)	1.364(7)
C(12B)-C(13B)	1.398(7)
O(1A)-C(5A)	1.358(6)
O(1A)-C(1A)	1.384(6)
O(2A)-C(1A)	1.215(5)
O(3A)-C(11A)	1.368(6)
O(3A)-C(14A)	1.411(6)
O(4A)-C(10A)	1.362(5)
O(4A)-C(15A)	1.439(6)
C(1A)-C(2A)	1.456(6)
C(2A)-C(3A)	1.375(6)
C(2A)-C(8A)	1.481(6)
C(3A)-C(4A)	1.428(7)
C(3A)-C(7A)	1.503(6)
C(4A)-C(5A)	1.345(7)
C(5A)-C(6A)	1.489(7)

C(8A)-C(13A)	1.391(6)
C(8A)-C(9A)	1.401(7)
C(9A)-C(10A)	1.374(7)
C(10A)-C(11A)	1.414(7)
C(11A)-C(12A)	1.375(7)
C(12A)-C(13A)	1.402(7)

C(5B)-O(1B)-C(1B)	122.5(4)
C(11B)-O(3B)-C(14B)	116.5(4)
C(10B)-O(4B)-C(15B)	116.7(4)
O(2B)-C(1B)-O(1B)	115.2(4)
O(2B)-C(1B)-C(2B)	127.5(4)
O(1B)-C(1B)-C(2B)	117.3(4)
C(3B)-C(2B)-C(1B)	119.5(4)
C(3B)-C(2B)-C(8B)	123.6(4)
C(1B)-C(2B)-C(8B)	116.9(4)
C(2B)-C(3B)-C(4B)	119.5(4)
C(2B)-C(3B)-C(7B)	123.3(5)
C(4B)-C(3B)-C(7B)	117.2(4)
C(5B)-C(4B)-C(3B)	120.6(4)
C(4B)-C(5B)-O(1B)	120.5(4)
C(4B)-C(5B)-C(6B)	127.3(4)
O(1B)-C(5B)-C(6B)	112.2(4)
C(13B)-C(8B)-C(9B)	118.4(4)
C(13B)-C(8B)-C(2B)	122.2(4)
C(9B)-C(8B)-C(2B)	119.4(4)
C(10B)-C(9B)-C(8B)	121.5(4)
O(4B)-C(10B)-C(9B)	126.0(4)
O(4B)-C(10B)-C(11B)	114.9(4)
C(9B)-C(10B)-C(11B)	119.2(4)
C(12B)-C(11B)-O(3B)	126.5(4)
C(12B)-C(11B)-C(10B)	119.6(4)
O(3B)-C(11B)-C(10B)	113.9(4)
C(11B)-C(12B)-C(13B)	120.7(4)
C(8B)-C(13B)-C(12B)	120.7(4)
C(5A)-O(1A)-C(1A)	122.4(4)
C(11A)-O(3A)-C(14A)	117.5(4)
C(10A)-O(4A)-C(15A)	115.9(4)
O(2A)-C(1A)-O(1A)	115.7(4)

O(2A)-C(1A)-C(2A)	126.6(4)
O(1A)-C(1A)-C(2A)	117.7(4)
C(3A)-C(2A)-C(1A)	118.8(4)
C(3A)-C(2A)-C(8A)	123.4(4)
C(1A)-C(2A)-C(8A)	117.7(4)
C(2A)-C(3A)-C(4A)	120.0(4)
C(2A)-C(3A)-C(7A)	123.3(4)
C(4A)-C(3A)-C(7A)	116.7(4)
C(5A)-C(4A)-C(3A)	120.2(4)
C(4A)-C(5A)-O(1A)	120.9(4)
C(4A)-C(5A)-C(6A)	126.6(4)
O(1A)-C(5A)-C(6A)	112.5(4)
C(13A)-C(8A)-C(9A)	118.4(4)
C(13A)-C(8A)-C(2A)	122.7(4)
C(9A)-C(8A)-C(2A)	118.9(4)
C(10A)-C(9A)-C(8A)	121.5(5)
O(4A)-C(10A)-C(9A)	126.2(4)
O(4A)-C(10A)-C(11A)	114.1(4)
C(9A)-C(10A)-C(11A)	119.6(4)
O(3A)-C(11A)-C(12A)	125.6(5)
O(3A)-C(11A)-C(10A)	114.9(4)
C(12A)-C(11A)-C(10A)	119.5(4)
C(11A)-C(12A)-C(13A)	120.4(4)
C(8A)-C(13A)-C(12A)	120.5(4)

Symmetry transformations used to generate equivalent atoms:

Data of compound 7a (publication 6):

Table 1. Crystal data and structure refinement for 7a

Identification code	FO2669	
Empirical formula	C16 H19 N O4	
Formula weight	289.32	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 5.1502(3) Å	a= 90°.
	b = 11.2491(9) Å	b= 90.408(5)°.
	c = 26.050(2) Å	g = 90°.
Volume	1509.15(19) $Å^3$	
Z	4	
Density (calculated)	1.273 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	616	
Crystal size	0.03 x 0.03 x 0.03 mm^3	
Theta range for data collection	2.39 to 27.47°.	
Index ranges	-6<=h<=6, -14<=k<=12, -33<=l<=33	
Reflections collected	8536	
Independent reflections	3396 [R(int) = 0.0574]	
Completeness to theta = 27.47°	98.1 %	
Absorption correction	NONE	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3396 / 0 / 196	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2sigma(I)]	R1 = 0.0598, wR2 = 0.1252	
R indices (all data)	R1 = 0.1210, wR2 = 0.1518	
Largest diff. peak and hole	0.181 and -0.243 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for fo2669. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1975(3)	-2565(2)	1461(1)	47(1)
O(2)	3959(4)	-1348(1)	908(1)	53(1)
O(3)	-1561(3)	261(2)	613(1)	48(1)
O(4)	2160(3)	847(2)	270(1)	44(1)
N(1)	1955(3)	-543(2)	1583(1)	30(1)
C(1)	3179(4)	605(2)	1445(1)	31(1)
C(2)	4129(4)	1227(2)	1920(1)	34(1)
C(3)	3025(4)	1046(2)	2372(1)	34(1)
C(4)	901(4)	203(2)	2426(1)	33(1)
C(5)	-595(4)	157(2)	2871(1)	40(1)
C(6)	-2607(5)	-646(2)	2915(1)	46(1)
C(7)	-3173(4)	-1409(2)	2511(1)	41(1)
C(8)	-1716(4)	-1381(2)	2069(1)	36(1)
C(9)	340(4)	-587(2)	2026(1)	31(1)
C(10)	2581(4)	-1568(2)	1329(1)	37(1)
C(11)	4742(8)	-2388(3)	626(1)	89(1)
C(12)	1260(4)	1409(2)	1137(1)	31(1)
C(13)	657(4)	814(2)	631(1)	31(1)
C(14)	2350(5)	2653(2)	1041(1)	39(1)
C(15)	535(6)	3461(2)	736(1)	51(1)
C(16)	1616(7)	4708(3)	677(1)	75(1)

Table 3. Bond lengths [Å] and angles [°] for fo2669.

O(1)-C(10)	1.215(3)
O(2)-C(10)	1.335(3)
O(2)-C(11)	1.441(3)
O(3)-C(13)	1.301(3)
O(4)-C(13)	1.224(3)
N(1)-C(10)	1.368(3)
N(1)-C(9)	1.428(3)
N(1)-C(1)	1.482(3)
C(1)-C(2)	1.501(3)
C(1)-C(12)	1.558(3)
C(2)-C(3)	1.325(3)
C(3)-C(4)	1.455(3)
C(4)-C(5)	1.396(3)
C(4)-C(9)	1.400(3)
C(5)-C(6)	1.380(3)
C(6)-C(7)	1.386(4)
C(7)-C(8)	1.380(3)
C(8)-C(9)	1.390(3)
C(12)-C(13)	1.508(3)
C(12)-C(14)	1.529(3)
C(14)-C(15)	1.523(3)
C(15)-C(16)	1.518(4)
C(10)-O(2)-C(11)	114.91(19)
C(10)-N(1)-C(9)	120.04(18)
C(10)-N(1)-C(1)	121.05(17)
C(9)-N(1)-C(1)	118.49(17)
N(1)-C(1)-C(2)	110.05(17)
N(1)-C(1)-C(12)	111.16(16)
C(2)-C(1)-C(12)	110.91(17)
C(3)-C(2)-C(1)	121.4(2)
C(2)-C(3)-C(4)	120.9(2)
C(5)-C(4)-C(9)	118.8(2)
C(5)-C(4)-C(3)	121.7(2)
C(9)-C(4)-C(3)	119.50(19)
C(6)-C(5)-C(4)	120.8(2)
C(5)-C(6)-C(7)	119.7(2)

C(8)-C(7)-C(6)	120.4(2)
C(7)-C(8)-C(9)	120.1(2)
C(8)-C(9)-C(4)	120.1(2)
C(8)-C(9)-N(1)	122.44(19)
C(4)-C(9)-N(1)	117.50(19)
O(1)-C(10)-O(2)	122.9(2)
O(1)-C(10)-N(1)	125.5(2)
O(2)-C(10)-N(1)	111.64(19)
C(13)-C(12)-C(14)	109.74(17)
C(13)-C(12)-C(1)	108.57(17)
C(14)-C(12)-C(1)	112.52(17)
O(4)-C(13)-O(3)	123.11(19)
O(4)-C(13)-C(12)	122.08(19)
O(3)-C(13)-C(12)	114.81(18)
C(15)-C(14)-C(12)	113.99(19)
C(16)-C(15)-C(14)	112.4(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for fo2669. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	71(1)	29(1)	42(1)	1(1)	16(1)	-5(1)
O(2)	85(1)	30(1)	42(1)	-9(1)	28(1)	-15(1)
O(3)	39(1)	68(1)	36(1)	-16(1)	7(1)	-21(1)
O(4)	46(1)	57(1)	30(1)	-9(1)	8(1)	-20(1)
N(1)	37(1)	26(1)	28(1)	-1(1)	2(1)	-5(1)
C(1)	33(1)	29(1)	30(1)	-2(1)	3(1)	-6(1)
C(2)	34(1)	31(1)	36(1)	-5(1)	-3(1)	-1(1)
C(3)	36(1)	34(1)	33(1)	-7(1)	-6(1)	3(1)
C(4)	34(1)	35(1)	30(1)	2(1)	-2(1)	8(1)
C(5)	44(1)	44(2)	30(1)	4(1)	1(1)	8(1)
C(6)	47(1)	51(2)	40(1)	15(1)	11(1)	11(1)
C(7)	36(1)	38(2)	51(2)	14(1)	5(1)	3(1)
C(8)	36(1)	31(1)	42(1)	5(1)	-1(1)	0(1)
C(9)	33(1)	30(1)	31(1)	3(1)	0(1)	4(1)
C(10)	47(1)	34(1)	29(1)	0(1)	4(1)	-6(1)
C(11)	153(3)	41(2)	73(2)	-21(2)	69(2)	-22(2)
C(12)	35(1)	33(1)	26(1)	-1(1)	2(1)	-6(1)
C(13)	34(1)	29(1)	30(1)	1(1)	2(1)	-5(1)
C(14)	54(1)	32(1)	32(1)	0(1)	-2(1)	-8(1)
C(15)	76(2)	37(2)	38(1)	1(1)	-12(1)	-6(1)
C(16)	124(3)	37(2)	65(2)	13(1)	-19(2)	-17(2)

Data of compound 1 (manuscript in preparation):

Table 1. Crystal data and structure refinement for 1.

Identification code	euo35806	
Empirical formula	$C_{15}H_{13}ClO_2$	
Formula weight	260.70	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.2672(4) Å	α= 74.236(2)°.
	b = 10.0848(4) Å	β= 76.844(2)°.
	c = 15.2035(7) Å	γ = 70.0580(10)°.
Volume	1271.07(9) $Å^3$	
Z	4	
Density (calculated)	1.362 Mg/m^3	
Absorption coefficient	0.291 mm^{-1}	
F(000)	544	
Crystal size	0.71 x 0.42 x 0.08 mm^3	
Θ range for data collection	2.35 to 25.66°.	
Index ranges	$-11\leq h\leq 11$, $-11\leq k\leq 12$, $-18\leq l\leq 18$	
Reflections collected	21261	
Independent reflections	4729 [R(int) = 0.0310]	
Completeness to Θ = 25.66°	97.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9771 and 0.8202	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4729 / 0 / 327	
Goodness-of-fit on F^2	1.046	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0391, wR2 = 0.1031	
R indices (all data)	R1 = 0.0514, wR2 = 0.1098	
Largest diff. peak and hole	0.442 and -0.283 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for euo35806. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	7409(1)	8938(1)	3141(1)	31(1)
O(1)	2930(2)	5880(2)	5802(1)	30(1)
O(2)	5448(2)	5517(2)	6725(1)	28(1)
C(1)	6813(2)	7939(2)	4212(1)	22(1)
C(2)	7937(2)	7125(2)	4782(1)	22(1)
C(3)	7460(2)	6305(2)	5626(1)	23(1)
C(4)	5940(2)	6277(2)	5889(1)	21(1)
C(5)	4830(2)	7099(2)	5305(1)	21(1)
C(6)	5262(2)	7961(2)	4458(1)	20(1)
C(7)	4078(2)	8838(2)	3840(1)	22(1)
C(8)	3330(2)	8168(2)	3479(1)	27(1)
C(9)	2172(2)	8986(3)	2943(1)	32(1)
C(10)	1737(2)	10465(3)	2776(1)	34(1)
C(11)	2474(3)	11149(2)	3133(2)	35(1)
C(12)	3647(2)	10340(2)	3656(1)	29(1)
C(13)	9595(2)	7134(2)	4508(2)	30(1)
C(14)	3193(2)	7039(2)	5626(1)	23(1)
C(15)	1935(2)	8388(2)	5782(2)	35(1)
Cl(2)	12468(1)	1511(1)	10473(1)	32(1)
O(3)	7889(2)	4062(2)	7681(1)	30(1)
O(4)	10511(2)	5108(2)	6956(1)	31(1)
C(16)	11877(2)	2612(2)	9434(1)	22(1)
C(17)	13009(2)	3005(2)	8726(1)	23(1)
C(18)	12537(2)	3835(2)	7890(1)	23(1)
C(19)	10998(2)	4259(2)	7760(1)	22(1)
C(20)	9877(2)	3867(2)	8481(1)	21(1)
C(21)	10317(2)	3038(2)	9334(1)	20(1)
C(22)	9124(2)	2618(2)	10106(1)	23(1)
C(23)	8378(2)	1673(2)	10039(1)	28(1)
C(24)	7212(3)	1347(2)	10741(2)	35(1)
C(25)	6784(2)	1968(2)	11500(2)	36(1)

C(26)	7526(3)	2903(2)	11573(1)	35(1)
C(27)	8703(2)	3219(2)	10884(1)	29(1)
C(28)	14684(2)	2555(3)	8850(2)	34(1)
C(29)	8219(2)	4372(2)	8314(1)	23(1)
C(30)	7015(3)	5334(3)	8890(2)	39(1)

Table 3. Bond lengths [Å] and angles [°] for euo35806.

Cl(1)-C(1)	1.7463(18)
O(1)-C(14)	1.221(2)
O(2)-C(4)	1.362(2)
O(2)-H(2A)	0.8400
C(1)-C(6)	1.395(3)
C(1)-C(2)	1.396(3)
C(2)-C(3)	1.393(3)
C(2)-C(13)	1.501(3)
C(3)-C(4)	1.381(3)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.403(3)
C(5)-C(6)	1.403(3)
C(5)-C(14)	1.501(3)
C(6)-C(7)	1.492(3)
C(7)-C(8)	1.390(3)
C(7)-C(12)	1.393(3)
C(8)-C(9)	1.388(3)
C(8)-H(8A)	0.9500
C(9)-C(10)	1.372(3)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.389(3)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.383(3)
C(11)-H(11A)	0.9500
C(12)-H(12A)	0.9500
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-C(15)	1.494(3)
C(15)-H(15A)	0.9800
C(15)-H(15D)	0.9800
C(15)-H(15B)	0.9800
Cl(2)-C(16)	1.7483(18)
O(3)-C(29)	1.217(2)
O(4)-C(19)	1.361(2)
O(4)-H(4A)	0.8400
C(16)-C(21)	1.392(3)

C(16)-C(17)	1.397(3)
C(17)-C(18)	1.390(3)
C(17)-C(28)	1.503(3)
C(18)-C(19)	1.386(3)
C(18)-H(18A)	0.9500
C(19)-C(20)	1.402(3)
C(20)-C(21)	1.402(3)
C(20)-C(29)	1.502(3)
C(21)-C(22)	1.495(3)
C(22)-C(23)	1.390(3)
C(22)-C(27)	1.392(3)
C(23)-C(24)	1.393(3)
C(23)-H(23A)	0.9500
C(24)-C(25)	1.378(3)
C(24)-H(24A)	0.9500
C(25)-C(26)	1.381(3)
C(25)-H(25A)	0.9500
C(26)-C(27)	1.387(3)
C(26)-H(26A)	0.9500
C(27)-H(27A)	0.9500
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-C(30)	1.493(3)
C(30)-H(30A)	0.9800
C(30)-H(30B)	0.9800
C(30)-H(30C)	0.9800

C(4)-O(2)-H(2A)	109.5
C(6)-C(1)-C(2)	122.75(17)
C(6)-C(1)-Cl(1)	119.42(14)
C(2)-C(1)-Cl(1)	117.82(14)
C(3)-C(2)-C(1)	117.46(17)
C(3)-C(2)-C(13)	120.76(17)
C(1)-C(2)-C(13)	121.78(17)
C(4)-C(3)-C(2)	121.67(17)
C(4)-C(3)-H(3A)	119.2
C(2)-C(3)-H(3A)	119.2
O(2)-C(4)-C(3)	122.22(16)

O(2)-C(4)-C(5)	117.72(16)
C(3)-C(4)-C(5)	120.00(17)
C(4)-C(5)-C(6)	119.91(17)
C(4)-C(5)-C(14)	117.97(16)
C(6)-C(5)-C(14)	122.11(16)
C(1)-C(6)-C(5)	118.19(17)
C(1)-C(6)-C(7)	121.98(16)
C(5)-C(6)-C(7)	119.82(16)
C(8)-C(7)-C(12)	119.03(18)
C(8)-C(7)-C(6)	120.34(17)
C(12)-C(7)-C(6)	120.54(17)
C(9)-C(8)-C(7)	120.4(2)
C(9)-C(8)-H(8A)	119.8
C(7)-C(8)-H(8A)	119.8
C(10)-C(9)-C(8)	120.3(2)
C(10)-C(9)-H(9A)	119.9
C(8)-C(9)-H(9A)	119.9
C(9)-C(10)-C(11)	119.94(19)
C(9)-C(10)-H(10A)	120.0
C(11)-C(10)-H(10A)	120.0
C(12)-C(11)-C(10)	120.1(2)
C(12)-C(11)-H(11A)	120.0
C(10)-C(11)-H(11A)	120.0
C(11)-C(12)-C(7)	120.3(2)
C(11)-C(12)-H(12A)	119.8
C(7)-C(12)-H(12A)	119.8
C(2)-C(13)-H(13A)	109.5
C(2)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(2)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
O(1)-C(14)-C(15)	121.42(18)
O(1)-C(14)-C(5)	119.44(17)
C(15)-C(14)-C(5)	119.00(17)
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15D)	109.5
H(15A)-C(15)-H(15D)	109.5
C(14)-C(15)-H(15B)	109.5

H(15A)-C(15)-H(15B)	109.5
H(15D)-C(15)-H(15B)	109.5
C(19)-O(4)-H(4A)	109.5
C(21)-C(16)-C(17)	122.61(17)
C(21)-C(16)-Cl(2)	119.21(14)
C(17)-C(16)-Cl(2)	118.16(14)
C(18)-C(17)-C(16)	117.73(17)
C(18)-C(17)-C(28)	120.36(18)
C(16)-C(17)-C(28)	121.90(17)
C(19)-C(18)-C(17)	121.27(18)
C(19)-C(18)-H(18A)	119.4
C(17)-C(18)-H(18A)	119.4
O(4)-C(19)-C(18)	121.95(17)
O(4)-C(19)-C(20)	117.80(16)
C(18)-C(19)-C(20)	120.20(17)
C(19)-C(20)-C(21)	119.80(17)
C(19)-C(20)-C(29)	118.32(16)
C(21)-C(20)-C(29)	121.88(16)
C(16)-C(21)-C(20)	118.37(17)
C(16)-C(21)-C(22)	121.66(16)
C(20)-C(21)-C(22)	119.97(16)
C(23)-C(22)-C(27)	119.23(18)
C(23)-C(22)-C(21)	120.59(17)
C(27)-C(22)-C(21)	120.13(17)
C(22)-C(23)-C(24)	120.0(2)
C(22)-C(23)-H(23A)	120.0
C(24)-C(23)-H(23A)	120.0
C(25)-C(24)-C(23)	120.3(2)
C(25)-C(24)-H(24A)	119.8
C(23)-C(24)-H(24A)	119.8
C(24)-C(25)-C(26)	119.92(19)
C(24)-C(25)-H(25A)	120.0
C(26)-C(25)-H(25A)	120.0
C(25)-C(26)-C(27)	120.3(2)
C(25)-C(26)-H(26A)	119.9
C(27)-C(26)-H(26A)	119.9
C(26)-C(27)-C(22)	120.2(2)
C(26)-C(27)-H(27A)	119.9
C(22)-C(27)-H(27A)	119.9

C(17)-C(28)-H(28A)	109.5
C(17)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(17)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(3)-C(29)-C(30)	120.81(18)
O(3)-C(29)-C(20)	119.80(18)
C(30)-C(29)-C(20)	119.25(17)
C(29)-C(30)-H(30A)	109.5
C(29)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	109.5
C(29)-C(30)-H(30C)	109.5
H(30A)-C(30)-H(30C)	109.5
H(30B)-C(30)-H(30C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x 10^3)for euo35806. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	31(1)	33(1)	27(1)	1(1)	-1(1)	-15(1)
O(1)	28(1)	37(1)	29(1)	1(1)	-4(1)	-19(1)
O(2)	22(1)	35(1)	24(1)	6(1)	-7(1)	-11(1)
C(1)	24(1)	20(1)	21(1)	-3(1)	-1(1)	-9(1)
C(2)	19(1)	22(1)	28(1)	-8(1)	-3(1)	-5(1)
C(3)	19(1)	22(1)	27(1)	-4(1)	-7(1)	-3(1)
C(4)	22(1)	20(1)	21(1)	-3(1)	-4(1)	-6(1)
C(5)	18(1)	20(1)	23(1)	-5(1)	-4(1)	-6(1)
C(6)	21(1)	18(1)	22(1)	-6(1)	-3(1)	-5(1)
C(7)	18(1)	24(1)	20(1)	-3(1)	-1(1)	-5(1)
C(8)	27(1)	30(1)	24(1)	-5(1)	-3(1)	-10(1)
C(9)	27(1)	50(1)	24(1)	-9(1)	-5(1)	-14(1)
C(10)	23(1)	49(1)	20(1)	0(1)	-5(1)	-2(1)
C(11)	34(1)	27(1)	33(1)	1(1)	-7(1)	0(1)
C(12)	30(1)	26(1)	30(1)	-4(1)	-6(1)	-7(1)
C(13)	21(1)	35(1)	35(1)	-6(1)	-3(1)	-10(1)
C(14)	21(1)	33(1)	15(1)	-2(1)	-5(1)	-10(1)
C(15)	24(1)	42(1)	38(1)	-13(1)	0(1)	-6(1)
Cl(2)	31(1)	37(1)	25(1)	2(1)	-12(1)	-8(1)
O(3)	26(1)	40(1)	28(1)	-1(1)	-12(1)	-14(1)
O(4)	23(1)	43(1)	22(1)	8(1)	-7(1)	-16(1)
C(16)	24(1)	24(1)	19(1)	-2(1)	-8(1)	-5(1)
C(17)	20(1)	25(1)	25(1)	-7(1)	-4(1)	-5(1)
C(18)	21(1)	27(1)	23(1)	-5(1)	0(1)	-10(1)
C(19)	23(1)	23(1)	20(1)	-2(1)	-6(1)	-9(1)
C(20)	19(1)	22(1)	23(1)	-5(1)	-4(1)	-7(1)
C(21)	22(1)	22(1)	19(1)	-6(1)	-2(1)	-8(1)
C(22)	20(1)	22(1)	22(1)	0(1)	-4(1)	-4(1)
C(23)	28(1)	27(1)	30(1)	-3(1)	-5(1)	-10(1)
C(24)	30(1)	31(1)	43(1)	1(1)	-6(1)	-14(1)
C(25)	26(1)	35(1)	32(1)	7(1)	2(1)	-7(1)
C(26)	37(1)	39(1)	23(1)	-5(1)	1(1)	-7(1)

C(27)	33(1)	31(1)	25(1)	-6(1)	-3(1)	-12(1)
C(28)	21(1)	46(1)	32(1)	-2(1)	-7(1)	-8(1)
C(29)	21(1)	23(1)	24(1)	4(1)	-5(1)	-10(1)
C(30)	26(1)	42(1)	44(1)	-12(1)	-6(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for euo35806.

	x	y	z	U(eq)
H(2A)	6201	5086	7020	42
H(3A)	8198	5751	6030	27
H(8A)	3613	7144	3601	32
H(9A)	1678	8519	2690	39
H(10A)	932	11021	2417	41
H(11A)	2172	12173	3019	42
H(12A)	4160	10811	3890	35
H(13A)	10198	6498	4997	45
H(13B)	9642	8119	4419	45
H(13C)	10028	6792	3931	45
H(15A)	939	8178	5988	53
H(15D)	1882	9118	5204	53
H(15B)	2158	8751	6256	53
H(4A)	11259	5345	6597	46
H(18A)	13284	4117	7397	28
H(23A)	8662	1248	9514	34
H(24A)	6711	694	10696	42
H(25A)	5979	1754	11974	43
H(26A)	7230	3331	12097	43
H(27A)	9225	3847	10944	35
H(28A)	15288	2934	8278	51
H(28B)	15083	1499	8997	51
H(28C)	14773	2939	9356	51
H(30A)	6001	5567	8698	59
H(30B)	7281	6226	8806	59
H(30C)	6974	4840	9542	59

Table 6. Torsion angles [°] for euo35806.

C(6)-C(1)-C(2)-C(3)	0.2(3)
Cl(1)-C(1)-C(2)-C(3)	-178.51(14)
C(6)-C(1)-C(2)-C(13)	-179.18(18)
Cl(1)-C(1)-C(2)-C(13)	2.1(3)
C(1)-C(2)-C(3)-C(4)	0.8(3)
C(13)-C(2)-C(3)-C(4)	-179.78(18)
C(2)-C(3)-C(4)-O(2)	-177.80(17)
C(2)-C(3)-C(4)-C(5)	-0.6(3)
O(2)-C(4)-C(5)-C(6)	176.65(17)
C(3)-C(4)-C(5)-C(6)	-0.7(3)
O(2)-C(4)-C(5)-C(14)	-2.3(3)
C(3)-C(4)-C(5)-C(14)	-179.64(17)
C(2)-C(1)-C(6)-C(5)	-1.4(3)
Cl(1)-C(1)-C(6)-C(5)	177.26(14)
C(2)-C(1)-C(6)-C(7)	-179.99(18)
Cl(1)-C(1)-C(6)-C(7)	-1.3(2)
C(4)-C(5)-C(6)-C(1)	1.7(3)
C(14)-C(5)-C(6)-C(1)	-179.44(17)
C(4)-C(5)-C(6)-C(7)	-179.75(17)
C(14)-C(5)-C(6)-C(7)	-0.9(3)
C(1)-C(6)-C(7)-C(8)	116.6(2)
C(5)-C(6)-C(7)-C(8)	-62.0(2)
C(1)-C(6)-C(7)-C(12)	-66.9(2)
C(5)-C(6)-C(7)-C(12)	114.5(2)
C(12)-C(7)-C(8)-C(9)	0.1(3)
C(6)-C(7)-C(8)-C(9)	176.66(17)
C(7)-C(8)-C(9)-C(10)	-1.1(3)
C(8)-C(9)-C(10)-C(11)	1.0(3)
C(9)-C(10)-C(11)-C(12)	0.1(3)
C(10)-C(11)-C(12)-C(7)	-1.1(3)
C(8)-C(7)-C(12)-C(11)	1.0(3)
C(6)-C(7)-C(12)-C(11)	-175.59(18)
C(4)-C(5)-C(14)-O(1)	-58.8(2)
C(6)-C(5)-C(14)-O(1)	122.3(2)
C(4)-C(5)-C(14)-C(15)	117.1(2)
C(6)-C(5)-C(14)-C(15)	-61.8(3)
C(21)-C(16)-C(17)-C(18)	-1.0(3)

Cl(2)-C(16)-C(17)-C(18)	177.60(15)
C(21)-C(16)-C(17)-C(28)	178.99(19)
Cl(2)-C(16)-C(17)-C(28)	-2.4(3)
C(16)-C(17)-C(18)-C(19)	-0.1(3)
C(28)-C(17)-C(18)-C(19)	179.93(19)
C(17)-C(18)-C(19)-O(4)	177.99(18)
C(17)-C(18)-C(19)-C(20)	0.7(3)
O(4)-C(19)-C(20)-C(21)	-177.63(17)
C(18)-C(19)-C(20)-C(21)	-0.2(3)
O(4)-C(19)-C(20)-C(29)	1.6(3)
C(18)-C(19)-C(20)-C(29)	179.02(17)
C(17)-C(16)-C(21)-C(20)	1.4(3)
Cl(2)-C(16)-C(21)-C(20)	-177.14(14)
C(17)-C(16)-C(21)-C(22)	-179.34(18)
Cl(2)-C(16)-C(21)-C(22)	2.1(3)
C(19)-C(20)-C(21)-C(16)	-0.8(3)
C(29)-C(20)-C(21)-C(16)	179.99(17)
C(19)-C(20)-C(21)-C(22)	179.95(17)
C(29)-C(20)-C(21)-C(22)	0.8(3)
C(16)-C(21)-C(22)-C(23)	-112.5(2)
C(20)-C(21)-C(22)-C(23)	66.7(2)
C(16)-C(21)-C(22)-C(27)	70.2(2)
C(20)-C(21)-C(22)-C(27)	-110.6(2)
C(27)-C(22)-C(23)-C(24)	0.7(3)
C(21)-C(22)-C(23)-C(24)	-176.71(18)
C(22)-C(23)-C(24)-C(25)	0.6(3)
C(23)-C(24)-C(25)-C(26)	-0.9(3)
C(24)-C(25)-C(26)-C(27)	0.0(3)
C(25)-C(26)-C(27)-C(22)	1.3(3)
C(23)-C(22)-C(27)-C(26)	-1.6(3)
C(21)-C(22)-C(27)-C(26)	175.81(18)
C(19)-C(20)-C(29)-O(3)	57.4(2)
C(21)-C(20)-C(29)-O(3)	-123.4(2)
C(19)-C(20)-C(29)-C(30)	-118.4(2)
C(21)-C(20)-C(29)-C(30)	60.8(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for euo35806 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2A)...O(3)	0.84	1.89	2.7306(18)	178.3
O(4)-H(4A)...O(1)#1	0.84	1.87	2.7146(18)	179.6

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z

CURRICULUM VITAE

Ehsan Ullah

Date/Place of Birth: January 01, 1977 / Rawalpindi (Pakistan)

Work
Address: Fachbereich Chemie,
Albert-Einstein St 3a
18059 Rostock
Germany
Email: ehsan.ullah@uni-rostock.de
Phone: +49-381-4986416

Home
Address: Albert-Einstein St.28,
App. 1-02-04-1,
18059 Rostock
Germany
Email: eusatti@yahoo.com
Phone: +49-173-6329462

Academics:

2003 to date	**Ph.D**. Organic Chemistry, EMAU Greifswald, Germany **Title:** Synthesis of Carba-and Heterocycles based on novel One Pot Cyclization of 1,1-Bis(trimethylsilyloxy)ketene Acetal and 1,3-Bis(Silyl Enol Ether)
2002-2003	Junior research Fellow, HEJ (University of Karachi, Pakistan
2002	**M.Sc**.(Distinction), Organic Chemistry, University of Karachi, Pakistan
1997	**B.Sc**. University of Punjab, Pakistan **Majors**: *Chemistry, Zoology, Botany*
Till 1995	Higher secondary school (H.S.SC.)

Scholarships & Awards:

1. HEC Scholarship for higher education and research (April 2002 to March 2003)
2. Landesforschungsschwerpunkt 'Neue Wirkstoffe und Screeningverfahren' and DFG (June 2003 to July 2005)
3. Deutsche Forschungsgemeinschaft (August 2005 to December 2005)
4. Leibniz Fellowship (January 2006-present)

Research Interests:

- Synthetic Organic Chemistry
- Homogeneous Catalysis

Research Experience:

- Research Fellow (April 2005 till date)
  Fachbereich Chemie, Albert-Einstein St 3a 18059 Rostock Germany
- Research Fellow (June 2003 to March 2005)
  Institute of Organic Chemistry, EMAU Greifswald, Soldmann St. 16
  17489 Greifswald, Germany
- Junior Research Fellow (April 2002 to April2003)
  HEJ Research Institute of Chemistry, International Center for Chemical Sciences, University of Karachi, Pakistan.

Publications:

1. Ehsan Ullah and Peter Langer, *Synlett* **2004**, 2782-2784. "One-Pot Synthesis of 3-Hydroxymaleic Anhydrides by Cyclization of 1,1-Bis (trimethylsilyloxy) ketene Acetals with Oxalyl Chloride".

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4. Ehsan Ullah and Peter Langer, *Synthesis* **2005**, 3189-3190. "Synthesis of Pyran-2-ones by Reaction of 1,1- Bis-(trimethylsilyloxy)ketene Acetals with 3-Silyloxyalk-2-en-1-ones".

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7. Sven Rotzoll, Ehsan Ullah, Christine Fischer, Dirk Michalik, Helmut Reinke, Peter Langer " Synthesis of 1,4-Diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones by Cyclization of 1,1-Bis(trimethylsiloxy)ketene Acetals with Pyrazine and Quinoxaline", Tetrahedron **2006,** submitted.

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Declaration/Erklärung

Here by i declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the Ernst-Moritz-Arndt-University of Greifswald nor to any other scientific institution for the purpose of doctorate.
Furthermore, I declare that I have written this work by myself and that I have not used any other sources, other than mentioned earlier in this work.

Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Ernst-Moritz-Arndt-Universität Greifswald noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion eingereicht wurde.
Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe.

_____

Ehsan Ullah