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Synthesis of chromanes by sequential '[3 + 3]-cyclization/Williamson' reactions of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes

Van Thi Hong Nguyen,[a] Bettina Appel[a] and Peter Langer[b,c,*]

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

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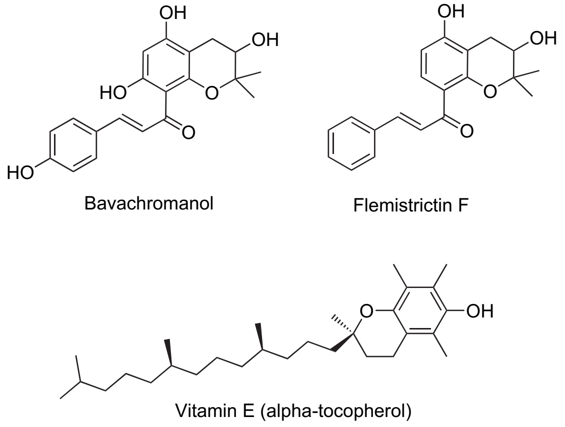
Abstract—Functionalized chromanes were prepared by sequential '[3+3]-cyclization/Williamson' reactions of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes with 1,1,3,3-tetramethoxypropane, 3-silyloxyalk-2-en-1-ones, and 1,1-diacetylcyclopropane. The first step of the sequence involves [3+3] cyclizations of the starting materials to give 2-(3-chloropropyl)phenols. The subsequent cyclization proceeds by intramolecular nucleophilic substitution. 6-(2-Hydroxybenzoyl)chromanes were prepared based on sequential '[3+3]-cyclization/Williamson' reactions of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes with 3-formylchromones.

1. Introduction

3,4-Dihydro-2*H*-chromenes (chromanes) represent pharmacologically relevant heterocycles, which occur in a variety of natural products (Scheme 1).[1,2] For example, bavachromanol has been isolated from leaves of *Maclura tinctoria* L. (Venezuela).[2a] The chromanol moiety of vitamin E (α-tocopherol) exhibits anti-androgen properties. Many synthetic approaches to 3,4-dihydro-2*H*-chromenes are based on intramolecular Friedel–Crafts alkylations.[2] Finn et al. have prepared chromanes from salicylic aldehydes and vinylboronic acids in the presence of catalytic amounts of dibenzylamine.[3] Jones et al. reported the synthesis of chromanes by Diels–Alder reactions of *o*-quinone methides, which were generated from salicylic aldehydes and alcohols.[4]



Scheme 1. Chromane natural products.

Chan and co-workers reported an efficient one-pot synthesis of salicylates based on [3+3] cyclizations of 1,3-bis-silyl enol ethers[5] with 3-silyloxyalk-2-en-1-ones or 1,1,3,3-tetramethoxypropane.[6] Recently, we have reported[7] an extension of this method by the first use of 1,3-bis-(trimethylsilyloxy)-7-chlorohepta-1,3-dienes (chloro-substituted 1,3-bis-silyl enol ethers)[8] in [3+3] cyclizations. The combination of these [3+3] cyclizations with subsequent intramolecular Williamson reactions allows for the synthesis of functionalized chromanes. Herein, we report full details of these studies. With regard to our preliminary communication in this field,[7] we herein report, for the first time, the synthesis of 6-(2-hydroxybenzoyl)-3,4-dihydro-2*H*-chromenes based on sequential '[3+3]-cyclization/Williamson' reactions of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes with 3-formylchromones. The general strategy reported herein allows for a convenient synthesis of a variety functionalized chromanes. Notably, the substitution patterns of these products are not readily available by other methods.

Keywords: Benzopyrans; Cyclizations; Ethers; Lewis acids; Silyl enol ethers.

* Corresponding author. Tel.: +49 381 4986410; fax: +49 381 4986412; e-mail: peter.langer@uni-rostock.de

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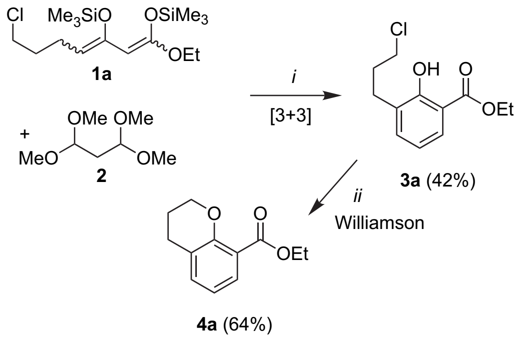
2. Results and discussion

2.1. [3 + 3] Cyclization of 1,1,3,3-tetramethoxypropane

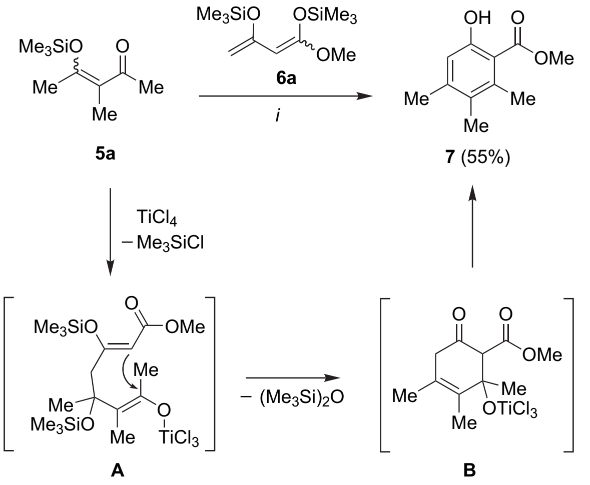
The key substrates of this study—1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes **1a**,**b**—were prepared in three steps from ethyl acetoacetate as previously reported.[7,9] The $TiCl_4$-mediated [3+3] cyclization of **1a** with 1,1,3,3-tetramethoxypropane (**2**) afforded the 2-(3-chloropropyl)phenol **3a**. The formation of **3a** proceeds by attack of carbon atom C-4 of **1a** onto **2**, cyclization via carbon C-2, and finally aromatization. Notably, the chloride functionality remained unattacked during the reaction. Treatment of a THF solution of **3a** with sodium hydride (NaH), in the presence of tetrabutylammonium iodide (TBAI), afforded chromane **4a** (Scheme 2).



Scheme 2. Synthesis of chromane **4a**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C; (ii) NaH, TBAI, THF, 20 °C.

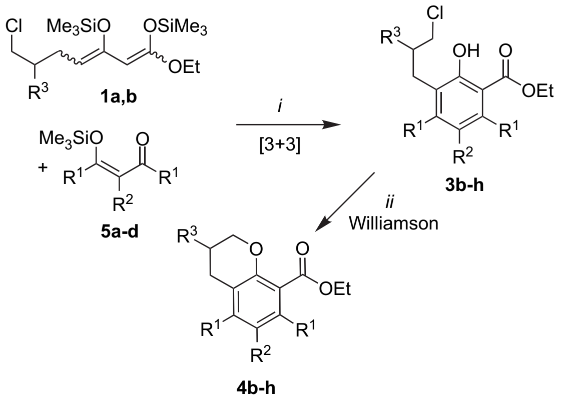
2.2. [3 + 3] Cyclizations of 3-silyloxyalk-2-en-1-ones

The [3+3] cyclization of 1,3-bis-silyl enol ether **6a** with 3-silyloxyalk-2-en-1-one **5a** has been reported to give salicylate **7**.[6] The cyclization proceeds by $TiCl_4$-mediated conjugate addition of the terminal carbon atom of the bis-silyl enol ether onto **5a**, cyclization, extrusion of siloxane, and aromatization (Scheme 3).



Scheme 3. Synthesis of salicylate **7** by Chan et al. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C.

The [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes **1a**,**b** with 3-silyloxyalk-2-en-1-ones **5a–d** afforded the 2-(3-chloropropyl)phenols **3b–h**. The latter were transformed (by NaH and TBAI) into chromanes **4b–h** (Scheme 4, Table 1). The formation of **3b–h** can be explained, following the mechanism proposed by Chan,[6] by initial attack of carbon atom C-4 of **1a**,**b** onto the carbon atom attached to the silyloxy group of **5a–d**, cyclization by attack of carbon C-2 onto the carbonyl group and subsequent aromatization.



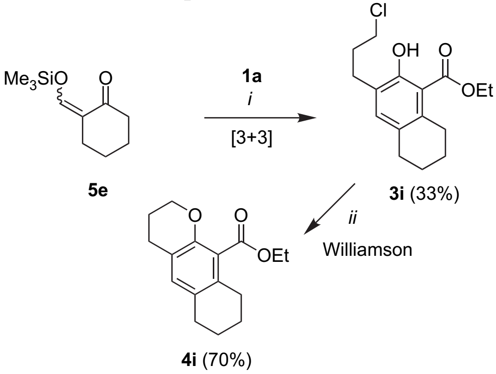
Scheme 4. Synthesis of chromanes **4b–h**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C; (ii) NaH, TBAI, THF, 20 °C.

Table 1. Synthesis of chromanes **4b–h**

5	3,4	R^1	R^2	R^3	% (**3**)[a]	% (**4**)[a]
a	**b**	Me	Me	H	52	90
b	**c**	Me	H	H	46	70
c	**d**	Me	Et	H	43	82
d	**e**	Et	H	H	42	65
a	**f**	Me	Me	Me	44	94
b	**g**	Me	H	Me	46	80
c	**h**	Et	H	Me	53	97

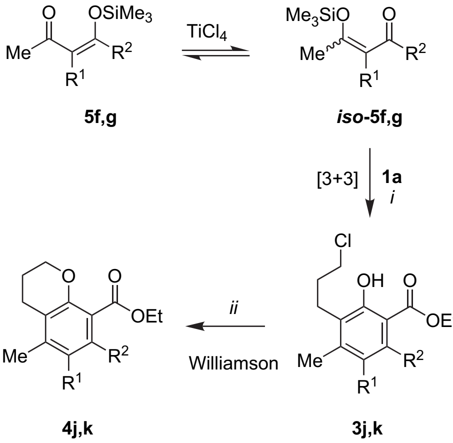
[a] Yields of isolated products.

The [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-diene **1a** with 3-silyloxyalk-2-en-1-one **5e**, prepared from 2-(hydroxymethylidene)cyclohexan-1-one, furnished tetrahydronaphthalene **3i** (Scheme 5). In contrast to **3b–h**, the formation of regioisomers is theoretically possible in case of **3i**. The regioselective formation of **3i** can be explained by the same mechanism as described for **3b–h**, i.e. by initial attack of carbon atom C-4 of **1a** onto the carbon attached to the silyloxy group of **5e**. Treatment of **3i** with NaH/TBAI afforded the tricyclic benzopyran **4i**. The structure of **4i** was established by H,H-COSY, C,H-COSY, HMBC, and NOESY experiments.



Scheme 5. Synthesis of chromane **4i**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C; (ii) NaH, TBAI, THF, 20 °C.

The [3+3] cyclization of **1a** with 3-silyloxyalk-2-en-1-one **5f**, available by silylation of 2-acetylcyclohexanone, regioselectively afforded **3j**, which was transformed into the tricyclic chromane **4j** (Scheme 6, Table 2). The formation of **3j** can be explained by $TiCl_4$-mediated isomerization of **5f** into *iso*-**5f** and subsequent attack of carbon C-4 of **1a** onto the carbon attached to the silyloxy group of *iso*-**5e**. The structure of **4j** was established by H,H-COSY, C,H-COSY, HMBC, and NOESY experiments. The cyclization of **1a** with 3-silyloxyalk-2-en-1-one **5g**, prepared from 2-acetyltetralone, regioselectively afforded **3k**, which was transformed into the tetracyclic chromane **4k**. The formation of **3k** presumably follows the mechanism as discussed for **3j**. The structure of **4k** was established by H,H-COSY, C,H-COSY, HMBC, and NOESY experiments. Notably, the structures of **3j**,**k** and **4j**,**k** have to be revised with respect to our preliminary communication.



Scheme 6. Synthesis of chromanes **4j**,**k**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, $-78\rightarrow 20$ °C; (ii) NaH, TBAI, THF, 20 °C.

Table 2. Products and yields

3,4	R^1	R^2	% (**3**)[a]	% (**4**)[a]
j	$-(CH_2)_4-$		34	87
k	$-(CH_2)_2C_6H_4-$		27	88

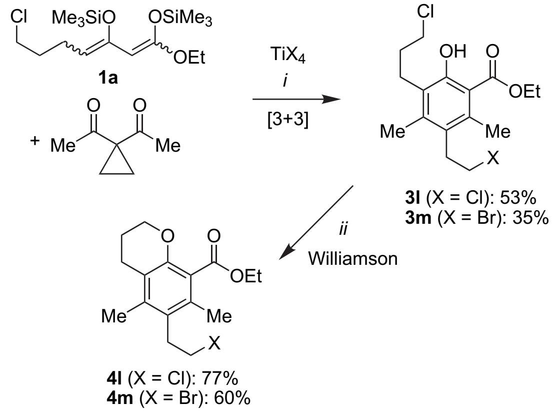
[a] Isolated yields.

2.3. [3+3] Cyclizations of 1,1-diacetylcyclopropane

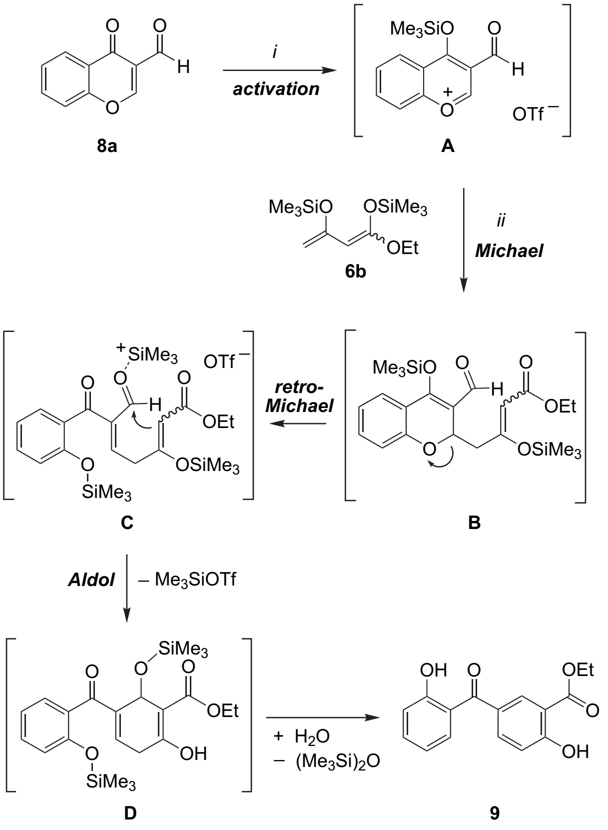
We have recently reported[9] the synthesis of 2-(3-chloropropyl)-4-(2-chloroethyl)phenol **3l** by $TiCl_4$-mediated cyclization of **1a** with 1,1-diacetylcyclopropane (**6**) (Scheme 7). The formation of **3l** can be explained by initial [3+3] cyclization to give a spirocyclopropane, which is cleaved by attack of $TiCl_4$ (homo-Michael reaction).[10] Likewise, the $TiBr_4$-mediated cyclization of **1a** with **6** furnished 2-(3-chloropropyl)-4-(2-bromoethyl)phenol **3m**. Treatment of **3l**,**m** with NaH/TBAI afforded the novel functionalized chromanes **4l**,**m**.

2.4. [3+3] Cyclizations of 3-formylchromones

We have recently reported the reaction of 1,3-bis-silyl enol ethers with 3-formylchromones to give functionalized benzophenones.[11] The formation of the products can be explained by a domino 'Michael/Retro-Michael/Aldol' reaction following the mechanism as given in Scheme 8. The reaction can be formally regarded as a [3+3] cyclization of an activated enal and resemble the [3+3] cyclizations of 1,3-bis-silyl enol ethers with 3-silyloxyalk-2-en-1-ones discussed above. Herein, we report the reaction of formylchromones with 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes, which allow for an efficient synthesis of 6-(2-hydroxybenzoyl)-3,4-chromanes.

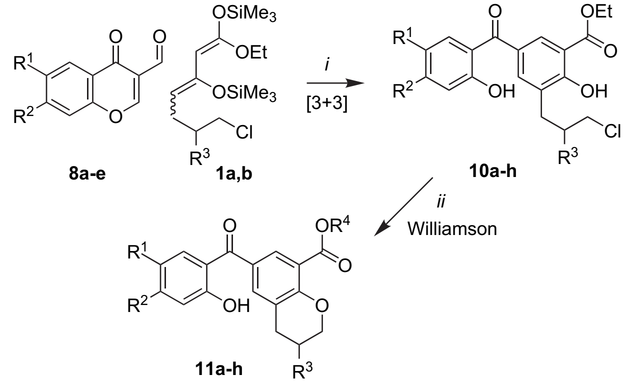


Scheme 7. Synthesis of chromanes **4l**,**m**. Reagents and conditions: (i) TiX_4 (X=Cl, Br, 2 equiv), CH_2Cl_2, $-78\rightarrow 20$ °C; (ii) NaH, TBAI, THF, 20 °C.



Scheme 8. Mechanism of the cyclization of 1,3-bis-silyl enol ethers with 3-formylchromones (Ref. 11). Reagents and conditions: (i) Me_3SiOTf (0.3 equiv), 20 °C, 10 min; (ii) (1) **2a** (1.3 equiv), CH_2Cl_2, $0\rightarrow 20$ °C, 12 h; (2) HCl (10%).

The TMSOTf catalyzed reaction of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes **1a**,**b** with 3-formylchromones **8a**–**e** afforded the 4-(2-hydroxybenzoyl)salicylates **10a**–**h** containing a remote chloride group (Scheme 9, Table 3). The mechanism of these reactions can be explained analogously to the formation of **9** (Scheme 8). Treatment of **10a**–**h** with NaH/TBAI afforded the 6-(2-hydroxybenzoyl)-3,4-dihydro-2*H*-chromenes **11a**,**b**,**e**–**h** by intramolecular Williamson reaction. These products were isolated in the form of their carboxylic acids (except for **11a**); the hydrolysis of the ester group presumably occurred during the aqueous work-up using hydrochloric acid (10%). Notably, the employment of the latter proved to be mandatory for a successful isolation of any type of product of this reaction.



Scheme 9. Synthesis of **11a–h**. Reagents and conditions: (i) (1) Me_3SiOTf (0.3 equiv), 0 °C, 10 min; (2) **1a**,**b** (1.3 equiv), CH_2Cl_2, 20 °C, 12 h; (3) HCl (10%); (ii) NaH (1.5 equiv), TBAI (2.0 equiv), THF, 20 °C, 20 h; for **11b**,**e–h**: HCl (10%).

Table 3. Products and yields

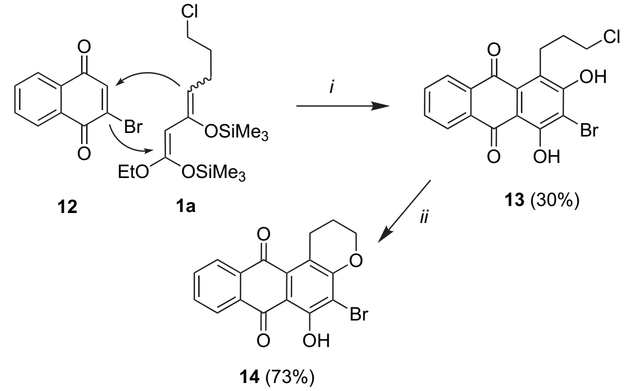
8	**1**	**10/11**	R^1	R^2	R^3	R^4	% (**10**)	% (**11**)[a]
a	**a**	**a**	H	H	H	Et	41	68
b	**a**	**b**	Me	H	H	H	54	94
c	**a**	**c**	Et	H	H	H	48	—[b]
d	**a**	**d**	Cl	H	H	H	51	—[b]
e	**a**	**e**	Cl	Me	H	H	47	70
a	**b**	**f**	H	H	Me	H	43	71
b	**b**	**g**	Me	H	Me	H	41	86
d	**b**	**h**	Cl	H	Me	H	38	73

[a] Isolated yields.

[b] Experiment not carried out.

2.5. [4 + 2] Cyclization of 2-bromonaphthalene-1,4-dione

Some years ago, Brassard et al. reported the [4+2] cycloaddition of 1,3-bis-silyl enol ethers with bromoquinones to give anthraquinones.[12] The reaction of **1a** with 2-bromonaphthalene-1,4-dione (**12**) afforded the functionalized anthraquinone **13**. Surprisingly, the product contained a bromide group located at the benzene moiety formed during the reaction. Treatment of **13** with NaH/TBAI afforded chromane **14** (Scheme 10). The formation of **13** can be explained by a radical mechanism.



Scheme 10. Synthesis of **14**. Reagents and conditions: (i) (1) THF, 1 h, −78 °C, (2) 14 h, −78 → 20 °C, (3) HCl (10%); (ii) NaH, TBAI, THF, 20 °C.

3. Conclusions

We have reported the synthesis of functionalized chromanes by double-annulation reactions of 1,3-bis(trimethylsilyloxy)-7-chlorohepta-1,3-dienes with 1,1,3,3-tetramethoxypropane, 3-silyloxyalk-2-en-1-ones, and 1,1-diacetylcyclopropane. The products were formed by [3+3] cyclization of the starting materials to give 2-(3-chloropropyl)phenols and subsequent cyclization by intramolecular nucleophilic substitution. 6-(2-Hydroxybenzoyl)chromanes were prepared based on double-annulation reactions of 3-formylchromones; an anthraquinone derived chromane was prepared from 2-bromonaphthoquinone. The general strategy reported herein allows for a convenient synthesis of a variety of functionalized chromanes. Notably, the substitution patterns of these products are not readily available by other methods.

4. Experimental

4.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H and ^{13}C NMR spectra, the deuterated solvents indicated were used. Mass spectrometric 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.

4.2. General procedure for the synthesis of salicylates 3a–k

To a CH_2Cl_2 solution of **1a**,**b** and **2** or **5a–g** was dropwise added $TiCl_4$ at −78 °C under argon atmosphere. The solution was stirred at −78 °C for 30 min and was subsequently warmed to 20 °C within 18 h. To the solution was added a saturated aqueous solution of $NaHCO_3$. The organic and the aqueous layer were separated and the latter was extracted with ether. 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*-hexane/EtOAc).

4.2.1. Ethyl 3-(3-chloropropyl)-2-hydroxybenzoate (3a). Starting with **1a** (1.75 g, 5.0 mmol), **2** (0.8 g, 5.0 mmol), and $TiCl_4$ (0.94 g, 5.0 mmol) in CH_2Cl_2 (15 mL), **3a** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.5 g, 42%). ^1H NMR ($CDCl_3$, 300 MHz): δ=1.41 (t, J=7.1 Hz, 3H, CH_3), 2.11 (quint, J=6.5 Hz, 2H, CH_2), 2.82 (t, J=7.1 Hz, 2H, CH_2), 3.54 (t, J=6.6 Hz, 2H, CH_2–Cl), 4.41 (q, J=7.1 Hz, 2H, OCH_2), 6.18 (m, 1H, CH of Ar), 7.32–7.35 (m, 1H, CH of Ar), 7.75 (d, 1H, CH of Ar), 11.13 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.2 (CH_3), 21.2, 31.9, 44.6, 61.4 (CH_2), 112.3, 118.6, 128.0, 128.9 (C), 135.9 (CH), 159.9, 170.6 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3140 (m), 2986 (m), 1671 (s), 1615 (s), 1449 (s), 1401 (s), 1374 (s), 1297 (s), 1249 (s), 1178 (s), 1152 (s), 1087 (m), 1026 (m), 761 (s), 725 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=212 (4.42), 242 (3.92), 310 (3.55) nm. MS (EI, 70 eV): m/z (%)=244 ($M^+[^{37}Cl]$, 11), 242 ($M^+[^{35}Cl]$, 34), 196 (19), 161 (100), 134 (44), 105 (21), 77 (24), 51 (9), 27 (10). HRMS (ESI): calcd for $C_{12}H_{16}ClO_3$ ([M+1]$^+$): 245.07584 [^{37}Cl], 243.07879 [^{35}Cl]; found: 245.07565 [^{37}Cl], 243.0787 [^{35}Cl]. Anal. Calcd for $C_{12}H_{15}ClO_3$ (242.699): C, 59.39; H, 6.23. Found: C, 60.88; H, 6.36.

4.2.2. Ethyl 3-(3-chloropropyl)-2-hydroxy-4,5,6-trimethylbenzoate (3b). The synthesis of **3b** has been previously reported.[9] Starting with **1a** (1.23 g, 3.5 mmol), **5a** (0.61 g, 3.5 mmol), and $TiCl_4$ (0.66 g, 3.5 mmol) in CH_2Cl_2 (10 mL), **3b** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.516 g, 52%).

4.2.3. Ethyl 3-(3-chloropropyl)-2-hydroxy-4,6-dimethylbenzoate (3c). Starting with **1a** (2.90 g, 8.2 mmol), **5b** (1.42 g, 8.2 mmol), and $TiCl_4$ (1.55 g, 8.2 mmol) in CH_2Cl_2 (15 mL), **3c** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (1.02 g, 46%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.42 (t, *J*=7.1 Hz, 3H, CH_3), 2.00 (quint, *J*=6.6 Hz, 2H, CH_2), 2.25 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.78 (t, *J*=7.7 Hz, 2H, CH_2), 3.61 (t, *J*=6.7 Hz, 2H, CH_2–Cl), 4.42 (q, *J*=7.1 Hz, 2H, OCH_2), 6.54 (s, 1H, CH), 11.76 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.2, 19.8 (CH_3), 23.6, 23.9, 31.8, 45.3, 61.4 (CH_2), 109.7 (C), 124.8 (CH), 125.2, 138.4, 143.1, 161.1, 172.2 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2977 (s), 2937 (s), 1938 (w), 1653 (s), 1563 (m), 1447 (s), 1396 (s), 1376 (s), 1349 (s), 1311 (s), 1273 (s), 1232 (s), 1175 (s), 1037 (s), 848 (s), 811 (s). UV–vis (CH_3CN, nm): λ_{max} (log ε)= 216 (4.45), 253 (4.00), 316 (3.60) nm. MS (EI, 70 eV): *m*/*z* (%)=272 (M$^+$[^{37}Cl], 6), 270 (M$^+$[^{35}Cl], 21), 224 (20), 189 (100), 162 (25), 133 (7), 105 (5), 91 (10), 27 (5.3). HRMS (ESI): calcd for $C_{14}H_{20}ClO_3$ ([M+1]$^+$): 273.10714 [^{37}Cl], 271.11009 [^{35}Cl]; found: 273.10647 [^{37}Cl], 271.10950 [^{35}Cl]. Anal. Calcd for $C_{14}H_{19}ClO_3$ (270.752): C, 62.11; H, 7.10. Found: C, 61.20; H, 7.80.

4.2.4. Ethyl 3-(3-chloropropyl)-5-ethyl-2-hydroxy-4,6-dimethylbenzoate (3d). Starting with **1a** (1.75 g, 5.0 mmol), **5c** (1.42 g, 5.0 mmol), and $TiCl_4$ (0.94 g, 5.0 mmol) in CH_2Cl_2 (15 mL), **3d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.630 g, 43%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ_C=1.10 (t, *J*=7.2 Hz, 3H, CH_3), 1.39 (t, *J*=7.1 Hz, 3H, CH_3), 1.99 (quint, *J*=6.7 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 2.65 (q, *J*=7.5 Hz, 2H, CH_2), 2.85 (m, *J*=6.0 Hz, 2H, CH_2), 3.61 (t, *J*=6.7 Hz, 2H, CH_2–Cl), 4.43 (q, *J*=7.1 Hz, 2H, OCH_2), 10.83 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=13.7, 14.2, 15.9, 18.3 (CH_3), 22.8, 24.1, 30.1, 45.3, 61.4 (CH_2), 111.5, 125.3, 133.1, 135.1, 141.3, 157.3, 172.1 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2967 (s), 2874 (m), 1726 (m), 1651 (s), 1599 (s), 1448 (s), 1701 (s), 1375 (s), 1322 (s), 1269 (s), 1195 (s), 1090 (s), 1037 (s), 806 (s), 768 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=218 (4.42), 256 (3.95), 320 (3.58) nm. MS (EI, 70 eV): *m*/*z* (%)=300 (M$^+$[^{37}Cl], 3), 298 (M$^+$[^{35}Cl], 14), 252 (20), 217 (100), 189 (16), 176 (40), 161 (30), 91 (8), 28 (44). Anal. Calcd for $C_{16}H_{23}ClO_3$ (298.805): C, 64.31; H, 7.76. Found: C, 64.35; H, 8.10.

4.2.5. Ethyl 3-(3-chloropropyl)-4,6-diethyl-2-hydroxybenzoate (3e). Starting with **1a** (1.75 g, 5.0 mmol), **5d** (1.00 g, 5.0 mmol), and $TiCl_4$ (0.94 g, 5.0 mmol) in CH_2Cl_2 (15 mL), **3e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.62 g, 41%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.21 (t, *J*=7.5 Hz, 6H, 2×CH_3), 1.42 (t, *J*=7.2 Hz, 3H, CH_3), 2.02 (quint, *J*=7.2 Hz, 2H, CH_2), 2.62 (q, *J*=7.6 Hz, 2H, CH_2), 2.79 (m, *J*=6.0 Hz, 2H, CH_2), 2.91 (q, *J*=7.5 Hz, 2H, CH_2), 3.61 (t, *J*=6.6 Hz, 2H, CH_2–Cl), 4.44 (q, *J*=7.2 Hz, 2H, OCH_2), 6.58 (s, 1H, CH), 11.68 (s, 1H, OH). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2969 (m), 1654 (s), 1614 (m), 1453 (m), 1401 (s), 1317 (m), 1264 (s), 1171 (s), 1073 (m), 1024 (m), 816 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=217 (4.44), 254 (4.04), 316 (3.64) nm. MS (EI, 70 eV): *m*/*z* (%)=300 (M$^+$[^{37}Cl], 3), 298 (M$^+$[^{35}Cl], 11), 252 (15), 217 (100), 189 (14), 133 (9), 70 (10), 28 (29). Anal. Calcd for $C_{16}H_{23}ClO_3$ (298.805): C, 64.31; H, 7.76. Found: C, 64.24; H, 9.30.

4.2.6. Ethyl 3-(3′-chloroisobutyl)-2-hydroxy-4,5,6-trimethylbenzoate (3f). The synthesis of **3f** has been previously reported.[9] Starting with **1b** (1.09 g, 3.0 mmol), **5a** (0.56 g, 3.0 mmol), and $TiCl_4$ (0.56 g, 3.0 mmol) in CH_2Cl_2 (10 mL), **3f** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.398 g, 44%).

4.2.7. Ethyl 3-(3-chloro-2-methylpropyl)-2-hydroxy-4,6-dimethylbenzoate (3g). Starting with **1b** (1.46 g, 4.0 mmol), $TiCl_4$ (0.75 g, 4.0 mmol), and **5b** (0.69 g, 4.0 mmol) in CH_2Cl_2 (10 mL), **3g** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (520 mg, 46%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.05 (d, *J*=6.7 Hz, 3H, CH_3), 1.42 (t, *J*=7.1 Hz, 3H, CH_3), 2.23 (m, 1H, CH), 2.27 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.59–2.79 (m, *J*=24, 6.9 Hz, 2H, CH_2), 3.42–3.56 (dq, *J*=7.0 Hz, 2H, CH_2–Cl), 4.43 (q, *J*=7.2 Hz, 2H, OCH_2), 6.55 (s, 1H, CH), 11.78 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=15.3, 18.9, 21.2, 24.9 (CH_3), 31.8, 36.8 (CH), 52.5, 62.5 (CH_2), 109.8, 124.6 (C), 125.9 (CH), 138.4, 143.6, 161.4, 172.3 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2959 (m), 2933 (m), 1654 (s), 1618 (m), 1449 (m), 1397 (m), 1268 (s), 1174 (m), 1097 (m), 1042 (m), 846 (m), 808 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=216 (4.45), 254 (4.02), 315 (3.62) nm. MS (EI, 70 eV): *m*/*z* (%)=286 (M$^+$[^{37}Cl], 1.4), 284 (M$^+$[^{35}Cl], 8), 203 (57), 194 (22), 161 (40), 148 (32), 147 (76), 120 (20), 91 (20), 32 (23), 28 (100). Anal. Calcd for $C_{15}H_{21}ClO_3$ (284.778): C, 63.25; H, 7.14. Found: C, 62.62; H, 7.49.

4.2.8. Ethyl 3-(3-chloro-2-methylpropyl)-4,6-diethyl-2-hydroxybenzoate (3h). Starting with **1b** (1.82 g, 5.0 mmol), $TiCl_4$ (0.95 g, 5.0 mmol), and **5d** (1.0 g, 5.0 mmol) in CH_2Cl_2 (10 mL), **3h** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.820 g, 53%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.07 (d, *J*=6.8 Hz, 3H, CH_3), 1.19 (m, *J*=7.1 Hz, 6H, 2×CH_3), 1.45 (t, *J*=7.1 Hz, 3H, CH_3), 2.28 (m, *J*=4.5 Hz, 1H, CH), 2.62 (m, *J*=7.0 Hz, 2H, CH_2), 2.75 (q, *J*=7.0 Hz, 2H, CH_2), 2.91 (q, *J*=7.3 Hz, 2H, CH_2), 3.51 (dq, *J*=6.8, 5.0 Hz, 2H, CH_2–Cl), 4.44 (q, *J*=7.1 Hz, 2H, OCH_2), 10.77 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.4, 15.5, 16.7, 18.3 (CH_3), 26.6, 30.1, 31.8 (CH_2), 36.5 (CH), 51.9, 61.8 (CH_2), 109.1 (C), 121.9 (CH), 123.9, 144.9, 149.7, 161.3, 172.1 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2972 (s), 2877 (s), 1654 (s), 1613 (m), 1564 (m), 1460 (s), 1399 (s), 1376 (s), 1315 (s), 1267 (s), 1171 (s), 1071 (m), 946 (m), 867 (m), 813 (m), 725 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=217 (4.48), 255 (4.05), 317 (3.64) nm. MS (EI, 70 eV): *m/z* (%)=314 ($M^+[^{37}Cl]$, 2), 312 ($M^+[^{35}Cl]$, 9), 232 (43), 231 (100), 190 (12), 189 (51), 176 (29), 133 (13), 28 (25). HRMS (ESI): calcd for $C_{17}H_{25}ClO_3$ ($[M+1]^+$): 315.15410 [^{37}Cl], 313.15705 [^{35}Cl]; found: 315.15432 [^{37}Cl], 313.15664 [^{35}Cl].

4.2.9. Ethyl 3-(3-chloropropyl)-5,6,7,8-tetrahydro-2-hydroxynaphthalene-1-carboxylate (3i). Starting with **1a** (2.8 g, 8.0 mmol), $TiCl_4$ (1.5 g, 8.0 mmol), and **5e** (1.59 g, 8.0 mmol) in CH_2Cl_2 (20 mL), **3i** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.72 g, 33%). ^1H NMR ($CDCl_3$, 300 MHz): δ=1.42 (t, *J*=7.1 Hz, 3H, CH_3), 1.74 (m, *J*=3.3 Hz, 4H, 2×CH_2), 2.11 (quint, *J*=6.9 Hz, 2H, CH_2), 2.69 (m, 2H, CH_2), 2.75 (m, *J*=7.0 Hz, 2H, CH_2), 2.97 (m, 2H, CH_2), 3.55 (t, *J*=6.7 Hz, 2H, CH_2–Cl), 4.43 (q, *J*=7.1 Hz, 2H, OCH_2), 7.01 (s, 1H, CH), 11.18 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.4 (CH_3), 22.5, 23.6, 27.5, 29.6, 29.9, 32.2, 44.9, 61.6 (CH_2), 115.3, 126.2, 128.0 (C), 136.4 (CH), 137.2, 155.3, 172.2 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2934 (s), 2860 (m), 1653 (s), 1431 (s), 1373 (s), 1316 (s), 1283 (s), 1159 (m), 1023 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=213 (4.41), 252 (3.99), 324 (3.80) nm. MS (EI, 70 eV): *m/z* (%)=298 ($M^+[^{37}Cl]$, 7), 296 ($M^+[^{35}Cl]$, 25), 250 (56), 215 (100), 188 (42), 160 (10), 114 (9), 91 (10), 28 (7). HRMS (ESI): calcd for $C_{16}H_{22}ClO_3$ ($[M+1]^+$): 299.12279 [^{37}Cl], 297.12574 [^{35}Cl]; found: 299.12179 [^{37}Cl], 297.12495 [^{35}Cl]. Anal. Calcd for $C_{16}H_{22}ClO_3$ (297.797): C, 64.85; H, 7.14. Found: C, 64.58; H, 7.35.

4.2.10. Ethyl 3-(3-chloropropyl)-5,6,7,8-tetrahydro-2-hydroxy-4-methylnaphthalene-1-carboxylate (3j). Starting with **1a** (1.40 g, 4.0 mmol), $TiCl_4$ (0.72 g, 4.0 mmol), and **5f** (0.85 g, 4.0 mmol) in CH_2Cl_2 (15 mL), **3j** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.42 g, 34%). ^1H NMR ($CDCl_3$, 300 MHz): δ=1.41 (t, *J*=7.1 Hz, 3H, CH_3), 1.68 (m, *J*=2.5 Hz, 2H, CH_2), 1.76 (m, *J*=2.0 Hz, 2H, CH_2), 1.98 (quint, *J*=6.8 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.58 (t, *J*=6.5 Hz, 2H, CH_2), 2.86 (m, *J*=7.0 Hz, 2H, CH_2), 2.98 (t, *J*=6.2 Hz, 2H, CH_2), 3.61 (t, *J*=6.7 Hz, 2H, CH_2–Cl), 4.42 (q, *J*=7.1 Hz, 2H, OCH_2), 11.23 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.2, 15.7 (CH_3), 22.8, 23.0, 23.9, 27.9, 30.3, 32.2, 45.3, 61.4 (CH_2), 110.2, 125.2, 127.4, 136.9, 142.4, 158.1, 172.2 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3416 (w), 2931 (s), 2863 (m), 1650 (s), 1598 (m), 1434 (s), 1401 (s), 1375 (s), 1316 (s), 1275 (s), 1241 (s), 1202 (s), 1149 (m), 1035 (m), 804 (m), 651 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=216.5 (4.36), 257.9 (3.98), 320.7 (3.59) nm. MS (EI, 70 eV): *m/z* (%)=312 ($M^+[^{37}Cl]$, 5), 310 ($M^+[^{35}Cl]$, 17), 264 (27), 230 (16), 229 (100), 202 (15), 28 (13). Anal. Calcd for $C_{17}H_{23}ClO_3$ (310.816): C, 65.69; H, 7.46. Found: C, 65.39; H, 7.78.

4.2.11. Ethyl-2-(3-chloropropyl)-9,10-dihydro-3-hydroxy-1-methylphenanthrene-4-carboxylate (3k). Starting with **1a** (2.8 g, 8.0 mmol), **5g** (2.08 g, 8.0 mmol), and $TiCl_4$ (1.52 g, 8.0 mmol) in CH_2Cl_2 (20 mL), **3k** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1) as a colorless oil (0.78 g, 27%). ^1H NMR ($CDCl_3$, 300 MHz): δ=1.00 (t, *J*=7.1 Hz, 3H, CH_3), 2.03 (quint, 7.5 Hz, 2H, CH_2), 2.32 (s, 3H, CH_3), 2.65 (t, *J*=5.6 Hz, 2H, CH_2), 2.81 (t, *J*=6.7 Hz, 2H, CH_2), 2.92 (t, *J*=6.2 Hz, 2H, CH_2), 3.64 (t, *J*=7.7 Hz, 2H, CH_2–Cl), 4.16 (q, *J*=7.1 Hz, 2H, OCH_2), 7.06–7.09 (dd, 1H, CH of Ar), 7.12–7.18 (m, 2H, 2×CH of Ar), 7.21–7.24 (dd, 1H, CH of Ar), 9.95 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=13.4, 15.7 (CH_3), 24.2, 25.7, 29.2, 31.1, 45.2, 61.3 (CH_2), 109.0 (C), 125.4 (CH), 126.7 (C), 126.8, 126.9, 129.2 (CH), 130.6, 134.6 (C), 137.6 (2C), 139.7, 156.5, 172.2 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3293 (w), 2956 (m), 1662 (s), 1592 (m), 1443 (m), 1397 (m), 1373 (m), 1313 (s), 1246 (s), 1188 (s), 1162 (m), 1071 (m), 1029 (m), 765 (s). UV–vis (CH_3CN, nm): λ_{max} (log ε)=204 (4.48), 232 (4.40), 280 (3.94), 341 (3.89) nm. MS (EI, 70 eV): *m/z* (%)=358 ($M^+[^{35}Cl]$, 6), 344 (6), 312 (5), 277 (16), 263 (32), 242 (24), 196 (13), 161 (100), 134 (41), 105 (19), 77 (22), 28 (39). Anal. Calcd for $C_{21}H_{23}ClO_3$ (358.859): C, 70.28; H, 6.46. Found: C, 70.44; H, 6.11.

4.3. General procedure for the preparation of salicylates (3l,m)

The synthesis of **3l**,**m** has been previously reported.[9] To a stirred CH_2Cl_2 solution (100 mL) of 1,1-diacetylcyclopropane (**6**) (1.1 mmol) and 1,3-bis-silyl enol ether **1a** (1.6 mmol) was added $TiCl_4$ (2.0 mmol in 2 mL 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 during 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), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc) to give **3l**,**m**.

4.3.1. Ethyl 5-(2-chloroethyl)-3-(3-chloropropyl)-2-hydroxy-4,6-dimethylbenzoate (3l). The synthesis of **3l** has been previously reported.[9] Starting with CH_2Cl_2 (250 mL), **6** (0.48 g, 3.8 mmol), **1a** (2.0 g, 5.7 mmol), and $TiCl_4$ (2.16 g, 11.4 mmol), **3l** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 25:1) as a colorless solid (0.672 g, 53%).

4.3.2. Ethyl 5-(2-bromoethyl)-3-(3-chloropropyl)-2-hydroxy-4,6-dimethylbenzoate (3m). The synthesis of **3m** has been previously reported.[9] Starting with **1a** (1.58 g, 4.5 mmol), **6** (0.38 g, 3.0 mmol), $TiBr_4$ (2.21 g, 6.0 mmol), and CH_2Cl_2 (200 mL), **3m** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.397 g, 35%).

4.4. General procedure for the synthesis of 5-(2-hydroxybenzoyl)salicylates (10a–h)

To the 3-formylchromone **8a**–**e** (1.0 equiv) was added Me_3SiOTf (0.3 equiv) at 20 °C. After stirring for 10 min, CH_2Cl_2 (8 mL) was added, the solution was cooled to 0 °C and the 1,3-bis-silyl enol ether **1a**,**b** (1.3 equiv) was added. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic and the aqueous layer were separated and the latter was extracted with $\mathrm{Et_2O}$ (3×80 mL). The combined organic layers were washed with water, dried ($\mathrm{Na_2SO_4}$), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc = 10:1→3:1).

4.4.1. Ethyl 3-(3-chloropropyl)-5-(2-hydroxybenzoyl)-salicylate (10a). Starting with **8a** (268 mg, 1.54 mmol), $\mathrm{Me_3SiOTf}$ (103 mg, 0.46 mmol), and 1,3-bis-silyl enol ether **1a** (703 mg, 2.00 mmol), **10a** was isolated as a yellow solid (229 mg, 41%), mp=107 °C. ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ=1.41 (t, *J*=7.1 Hz, 3H, $\mathrm{OCH_2C}H_3$), 2.15 (m, 2H, $\mathrm{CH_2C}H_2\mathrm{CH_2}$), 2.90 (t, *J*=7.1 Hz, 2H, $\mathrm{ArCH_2}$), 3.58 (t, *J*=6.5 Hz, 2H, $\mathrm{CH_2}$–Cl), 4.44 (q, *J*=7.2 Hz, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.92 (m, 1H, Ar), 7.09 (dd, *J*=8.4, 1.0 Hz, 1H, Ar), 7.53 (m, 1H, Ar), 7.59 (dd, *J*=8.0, 1.5 Hz, 1H, Ar), 7.40 (d, *J*=2.3 Hz, 1H, Ar), 8.18 (d, *J*=2.3 Hz, 1H, Ar), 11.65 (s, 1H, OH), 11.88 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $\mathrm{CDCl_3}$): δ=14.1 ($\mathrm{CH_3}$), 27.2, 31.6 ($\mathrm{CH_2}$), 44.4 ($\mathrm{CH_2Cl}$), 62.1 ($\mathrm{O}C\mathrm{H_2CH_3}$), 111.9 (C), 118.5, 118.7 (CH), 119.0, 128.4, 129.5 (C), 130.5, 132.9, 136.1, 136.6 (CH), 162.9, 163.0 (C-OH), 169.9, 199.2 (C═O). IR (KBr): $\tilde{\nu}$ = 3329 (m), 3095 (m), 3070 (m), 2991 (m), 2963 (m), 2938 (m), 1675 (s), 1624 (s), 1590 (s), 1483 (s), 1450 (s), 1407 (s), 1381 (s), 1348 (s), 1328 (s), 1289 (s), 1264 (s), 1237 (s), 1192 (s), 1158 (s), 1134 (w), 1023 (m), 807 (w), 770 (s), 738 (m), 706 (m), 659 (w) cm^{-1}. UV–vis ($\mathrm{CH_3CN}$): $\lambda_{\max}$ (log ε): 316 (3.93), 289 (3.99), 240 (4.28), 214 (4.47) nm. MS (EI, 70 eV): *m/z* (%)=362 (M$^+$, 64), 317 (4), 281 (67), 252 (19), 242 (24), 197 (6), 161 (10), 121 (100), 93 (9). HRMS (FT-ICR): calcd for $\mathrm{C_{19}H_{19}O_5Cl}$ ([M+1]$^+$): 363.09938; found: 363.09970. Anal. Calcd for $\mathrm{C_{19}H_{19}ClO_5}$: C, 62.90; H, 5.28. Found: C, 62.72; H, 5.51.

4.4.2. Ethyl 3-(3-chloropropyl)-2-hydroxy-5-(2-hydroxy-5-methylbenzoyl)benzoate (10b). Starting with **8b** (376 mg, 2.00 mmol), $\mathrm{Me_3SiOTf}$ (133 mg, 0.60 mmol), and 1,3-bis-silyl enol ether **1a** (917 mg, 2.60 mmol), **10b** was isolated as a yellow solid by column chromatography with *n*-hexane/EtOAc = 25:1 (410 mg, 54%). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ=1.43 (t, *J*=7.1 Hz, 3H, $\mathrm{OCH_2C}H_3$), 2.16 (m, *J*=6.6 Hz, 2H, $\mathrm{CH_2C}H_2\mathrm{CH_2Cl}$), 2.28 (s, 3H, $\mathrm{CH_3}$), 2.90 (t, *J*=7.1 Hz, 2H, $\mathrm{ClCH_2CH_2C}H_2$), 3.58 (t, *J*=6.5 Hz, 2H, $\mathrm{CH_2CH_2C}H_2\mathrm{Cl}$), 4.46 (q, *J*=7.2 Hz, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 7.00 (d, *J*=2.3 Hz, 1H, Ar), 7.26 (d, *J*=2.0 Hz, 1H, Ar), 7.36 (dd, *J*=1, 2 Hz, 1H, Ar), 7.74 (d, *J*=2.0 Hz, 1H, Ar), 8.19 (d, *J*=2.3 Hz, 1H, Ar), 11.63 (s, 1H, OH), 11.68 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $\mathrm{CDCl_3}$): δ=14.2, 20.5 ($\mathrm{CH_3}$), 27.2, 31.5, 44.3, 62.0 ($\mathrm{CH_2}$), 112.1 (C), 118.3 (CH), 118.8, 127.9, 128.6, 129.4 (C), 130.6, 132.7, 136.7, 137.2 (CH), 160.0, 163.0, 170.1, 199.2 (C). MS (EI, 70 eV): *m/z* (%)=378 (M$^+$[^{37}Cl ^{35}Cl], 18), 376 (M$^+$[^{35}Cl ^{35}Cl], 55), 340 (34), 295 (55), 206 (31), 135 (100), 44 (72). IR (KBr): $\tilde{\nu}$ = 2990 (w), 1674 (s), 1631 (s), 1583 (s), 1484 (m), 1406 (s), 1378 (s), 1348 (s), 1290 (s), 1236 (s), 1177 (s), 1023 (m), 786 (m), 705 (m) cm^{-1}. UV–vis ($\mathrm{CH_3CN}$): $\lambda_{\max}$ (log ε)=214.9 (4.45), 240.3 (4.29), 285.3 (3.99), 343.5 (3.74) nm. Anal. Calcd for $\mathrm{C_{20}H_{21}O_5Cl}$: C, 63.74; H, 5.62. Found: C, 63.60; H, 5.72.

4.4.3. Ethyl 3-(3-chloropropyl)-2-hydroxy-5-(2-hydroxy-5-ethylbenzoyl)benzoate (10c). Starting with **8c** (505 mg, 2.50 mmol), $\mathrm{Me_3SiOTf}$ (167 mg, 0.75 mmol), and 1,3-bis-silyl enol ether **1a** (1.147 mg, 3.25 mmol), **10c** was isolated as a yellow solid by column chromatography with *n*-hexane/EtOAc = 25:1 (472 mg, 48%). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ=1.20 (t, *J*=7.6 Hz, 3H, $\mathrm{C}H_3\mathrm{CH_2}$), 1.42 (t, *J*=7.2 Hz, 3H, $\mathrm{OCH_2C}H_3$), 2.15 (m, *J*=6.4 Hz, 2H, $\mathrm{CH_2C}H_2\mathrm{CH_2Cl}$), 2.57 (q, *J*=7.5 Hz, 2H, $\mathrm{CH_3C}H_2$), 2.89 (t, *J*=7.2 Hz, 2H, $\mathrm{ClCH_2CH_2C}H_2$), 3.59 (t, *J*=6.5 Hz, 2H, $\mathrm{CH_2CH_2C}H_2\mathrm{Cl}$), 4.45 (q, *J*=7.2 Hz, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 7.02 (d, *J*=8.4 Hz, 1H, Ar), 7.35–7.41 (m, *J*=2.1 Hz, 2H, Ar), 7.77 (t, *J*=1.5 Hz, 1H, Ar), 8.19 (d, *J*=2.3 Hz, 1H, Ar), 11.64 (s, 1H, OH), 11.68 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $\mathrm{CDCl_3}$): δ=14.1, 15.9 ($\mathrm{CH_3}$), 27.2, 27.9, 31.7, 44.4, 62.0 ($\mathrm{CH_2}$), 111.9 (C), 118.3, 118.8 (CH), 128.5, 129.6 (C), 130.8, 131.6 (CH), 134.4 (C), 136.1, 136.7 (CH), 161.1, 163.1, 170.1, 199.1 (C). IR (KBr): $\tilde{\nu}$ = 3167 (br), 2961 (m), 1675 (s), 1629 (m), 1588 (s), 1476 (m), 1342 (m), 1290 (m), 1254 (s), 1200 (s), 1166 (m), 1023 (m), 841 (m) cm^{-1}. UV–vis ($\mathrm{CH_3CN}$): $\lambda_{\max}$ (log ε)=251.0 (4.42), 239.6 (4.26), 287.9 (3.96), 344.5 (3.71) nm. MS (EI, 70 eV): *m/z* (%)=392 (M$^+$[^{37}Cl], 8), 390 (M$^+$[^{35}Cl], 29), 310 (45), 226 (38), 225 (100), 148 (61), 147 (51), 133 (19), 74 (17), 28 (71). HRMS (ESI): calcd for $\mathrm{C_{21}H_{23}O_5Cl}$: 390.12340; found: 390.12216.

4.4.4. Ethyl 3-(3-chloropropyl)-2-hydroxy-5-(2-hydroxy-5-chlorobenzoyl)benzoate (10d). Starting with **8d** (522 mg, 2.50 mmol), $\mathrm{Me_3SiOTf}$ (167 mg, 0.75 mmol), and 1,3-bis-silyl enol ether **1a** (1.147 g, 3.25 mmol), **10d** was isolated as yellow solid by column chromatography with *n*-hexane/EtOAc = 25:1 (507 mg, 51%). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ=1.42 (t, *J*=7.1 Hz, 3H, $\mathrm{OCH_2C}H_3$), 2.16 (m, *J*=6.5 Hz, 2H, $\mathrm{CH_2C}H_2\mathrm{CH_2Cl}$), 2.92 (t, *J*=7.0 Hz, 2H, $\mathrm{ClCH_2CH_2C}H_2$), 3.59 (t, *J*=6.5 Hz, 2H, $\mathrm{CH_2CH_2C}H_2\mathrm{Cl}$), 4.48 (q, *J*=7.2 Hz, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 7.05 (d, *J*=8.5 Hz, 1H, Ar), 7.35–7.41 (dd, *J*=2.6 Hz, 6.2 Hz, 1H, Ar), 7.58 (d, *J*=2.6 Hz, 1H, Ar), 7.75 (t, *J*=1 Hz, 1H, Ar), 8.18 (d, *J*=2.3 Hz, 1H, Ar), 11.70 (s, 1H, OH), 11.74 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $\mathrm{CDCl_3}$): δ=14.1 ($\mathrm{CH_3}$), 27.3, 31.6, 44.3, 62.2 ($\mathrm{CH_2}$), 112.1, 119.7 (C), 120.1 (CH), 123.5, 127.8, 130.0 (C), 130.7, 131.9, 135.9, 136.4 (CH), 161.4, 163.5, 169.9, 198.2 (C). IR (KBr): $\tilde{\nu}$ = 3089 (br), 2956 (w), 1675 (m), 1630 (m), 1464 (m), 1335 (m), 1256 (m), 1206 (m), 1017 (w), 843 (m) cm^{-1}. UV–vis ($\mathrm{CH_3CN}$): $\lambda_{\max}$ (log ε)=218.9 (4.39), 293.1 (3.84) nm. MS (EI, 70 eV): *m/z* (%)=398 (M$^+$[^{37}Cl ^{35}Cl], 4), 390 (M$^+$[^{35}Cl ^{35}Cl], 10), 363 (4), 320 (8), 291 (40), 275 (19), 219 (33), 217 (31), 203 (18), 146 (20), 129 (29), 74 (100), 28 (59). Anal. Calcd for $\mathrm{C_{19}H_{18}O_5Cl_2}$: C, 57.63; H, 4.58. Found: C, 56.75; H, 5.43.

4.4.5. Ethyl 3-(3-chloropropyl)-2-hydroxy-5-(2-hydroxy-5-chloro-3-methylbenzoyl)benzoate (10e). Starting with **8e** (556 mg, 2.50 mmol), $\mathrm{Me_3SiOTf}$ (167 mg, 0.75 mmol), and 1,3-bis-silyl enol ether **1a** (1.147 mg, 3.25 mmol), **10e** was isolated as yellow solid by column chromatography with *n*-hexane/EtOAc = 25:1 (482 mg, 47%). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ=1.43 (t, *J*=7.2 Hz, 3H, $\mathrm{OCH_2C}H_3$), 2.16 (m, *J*=6.5 Hz, 2H, $\mathrm{CH_2C}H_2\mathrm{CH_2Cl}$), 2.42 (s, 3H, $\mathrm{CH_3}$), 2.92 (t, *J*=7.3 Hz, 2H, $\mathrm{ClCH_2CH_2C}H_2$), 3.59 (t, *J*=6.5 Hz, 2H, $\mathrm{CH_2CH_2C}H_2\mathrm{Cl}$), 4.48 (q, *J*=7.1 Hz, 2H,

$OC\mathit{H}_2CH_3$), 6.99 (d, J=1.0 Hz, 1H, Ar), 7.56 (s, 1H, Ar), 7.73 (dd, J=1, 2 Hz, 1H, Ar), 8.17 (d, J=2.3 Hz, 1H, Ar), 11.67 (s, 1H, OH), 11.77 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=14.1, 20.8 (CH_3), 27.3, 31.6, 44.3, 62.1 (CH_2), 112.1, 117.9 (C), 120.5 (CH), 124.1, 127.9, 129.9 (C), 130.5, 132.3, 136.4 (CH), 145.4, 161.4, 163.3, 169.9, 197.9 (C). IR (KBr): $\tilde{\nu}$ = 3110 (br), 2957 (m), 1678 (s), 1626 (m), 1587 (s), 1471 (m), 1381 (m), 1340 (s), 1264 (s), 1242 (s), 1181 (s), 1022 (m), 843 (s) cm^{-1}. UV–vis (CH_3CN): λ_{max} (log ε)=218.9 (4.39), 293.1 (3.84) nm. MS (EI, 70 eV): m/z (%)=413 ($M^+[^{37}Cl\ ^{35}Cl]$, 20), 411 ($M^+[^{35}Cl\ ^{35}Cl]$, 36), 371 (11), 329 (26), 219 (35), 217 (39), 169 (49), 129 (24), 74 (100), 29 (19). HRMS (ESI): calcd for $C_{20}H_{20}O_5Cl_2$: 410.06878; found: 410.06721.

4.4.6. Ethyl 3-(3-chloro-2-methylpropyl)-2-hydroxy-5-(2-hydroxybenzoyl)benzoate (10f). Starting with formylchromone **8a** (348 mg, 2.0 mmol), Me_3SiOTf (133 mg, 0.60 mmol), and 1,3-bis-silyl enol ether **1b** (949 mg, 2.6 mmol), **10f** was isolated by column chromatography (silica gel, n-hexane/EtOAc = 25:1) as a yellow solid (324 mg, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.08 (d, J=6.7 Hz, 3H, $C\mathit{H}_3(CH)CH_2$), 1.42 (t, J=7.2 Hz, 3H, $OCH_2C\mathit{H}_3$), 2.38 (m, J=5.7 Hz, 1H, $CH_3(C\mathit{H})CH_2$), 2.69 (q, J=7.2 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 2.87 (q, J=7.1 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 3.43–3.57 (qq, J=5.4, 9.2 Hz, 2H, $CH_3(CH)C\mathit{H}_2Cl$), 4.46 (q, J=7.1 Hz, 2H, $OC\mathit{H}_2CH_3$), 6.89–6.94 (td, J=6.3, 1.0 Hz, 1H, Ar), 7.08–7.10 (dd, J=7.6, 1.0 Hz, 1H, Ar), 7.49–7.56 (td, J=7.0, 2.0 Hz, 1H, Ar), 7.59–7.62 (dd, J=6.3, 2.0 Hz, 1H, Ar), 7.72 (d, J=2.2 Hz, 1H, Ar), 8.20 (d, 2.2 Hz, 1H, Ar), 11.66 (s, 1H, OH), 11.89 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=14.2, 17.7 (CH_3), 34.4 (CH_2), 34.9 (CH), 50.6, 62.1 (CH_2), 112.1 (C), 118.5, 118.7 (CH), 119.1, 128.4, 128.8 (C), 130.6, 132.9, 136.2, 137.4 (CH), 163.0, 163.2, 170.1, 199.3 (C). UV–vis (CH_3CN): λ_{max} (log ε)=214.9 (4.46), 240.2 (4.28), 289.6 (3.99), 317.2 (3.94) nm. IR (KBr): $\tilde{\nu}$ = 3418 (br), 2960 (w), 1675 (s), 1624 (s), 1587 (s), 1482 (m), 1458 (m), 1348 (s), 1296 (s), 1263 (s), 1240 (s), 1180 (s), 766 (m) cm^{-1}. MS (EI, 70 eV): m/z (%)=378 ($M^+[^{37}Cl]$, 1), 376 ($M^+[^{35}Cl]$, 5), 295 (8), 253 (8), 121 (14), 32 (24), 28 (100). Anal. Calcd for $C_{20}H_{21}O_5Cl$: C, 63.75; H, 5.62. Found: C, 63.52; H, 5.65.

4.4.7. Ethyl 3-(3-chloro-2-methylpropyl)-2-hydroxy-5-(2-hydroxy-5-methylbenzoyl)benzoate (10g). Starting with **8b** (376 mg, 2.0 mmol), Me_3SiOTf (133 mg, 0.60 mmol), and 1,3-bis-silyl enol ether **1b** (948 mg, 2.60 mmol), **10g** was isolated as yellow solid by column chromatography with n-hexane/EtOAc = 25:1 (320 mg, 41%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.09 (d, J=6.7 Hz, 3H, $C\mathit{H}_3(CH)CH_2$), 1.44 (t, J=7.2 Hz, 3H, $C\mathit{H}_3CH_2O$), 2.28 (s, 3H, CH_3), 2.38 (m, J=5.5 Hz, 1H, $CH_3(C\mathit{H})CH_2$), 2.69 (q, J=6.2 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 2.87 (q, J=6.5 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 3.45–3.58 (qq, J=5.2, 9.0 Hz, 2H, $CH_3(CH)C\mathit{H}_2Cl$), 4.46 (q, J=7.1 Hz, 2H, $CH_3C\mathit{H}_2O$), 7.00 (d, J=8.3 Hz, 1H, Ar), 7.31–7.38 (m, J=1.0, 2.0 Hz, 2H, Ar), 7.71 (d, J=2.2 Hz, 1H, Ar), 7.74 (d, J=2.0 Hz, 1H, Ar), 8.21 (d, J=2.3 Hz, 1H, Ar), 11.63 (s, 1H, OH), 11.68 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=14.2, 17.8, 20.5 (CH_3), 30.3 (CH), 34.4 (CH_2), 34.9 (CH_3), 50.6, 62.1 (CH_2), 112.1 (C), 118.3 (CH), 118.8, 127.9, 128.5 (C), 130.6, 132.7, 137.2, 137.5 (CH), 160.9, 163.1, 170.1, 199.3 (C). IR (KBr): $\tilde{\nu}$ = 2962 (w), 1676 (s), 1630 (s), 1586 (s), 1482 (m), 1349 (s), 1291 (s), 1265 (s), 1204 (s), 1173 (m), 791 (m) cm^{-1}. UV–vis (CH_3CN): λ_{max} (log ε)=213.3 (4.47), 240.6 (4.29), 287.8 (3.98), 345.1 (3.73) nm. MS (EI, 70 eV): m/z (%)=326 (M^+, 90), 175 (100), 134 (91), 77 (15), 28 (29). HRMS (ESI): calcd for $C_{21}H_{23}O_5Cl$: 390.12340; found: 390.12286.

4.4.8. Ethyl 3-(3-chloro-2-methylpropyl)-2-hydroxy-5-(2-hydroxy-5-chlorobenzoyl)benzoate (10h). Starting with **8d** (417 mg, 2.00 mmol), Me_3SiOTf (133 mg, 0.60 mmol), and 1,3-bis-silyl enol ether **1b** (948 mg, 2.6 mmol), **10h** was isolated as yellow solid by column chromatography with n-hexane/EtOAc=25:1 (410 mg, 38%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.08 (d, J=6.7 Hz, 3H, $C\mathit{H}_3(CH)CH_2$), 1.43 (t, J=7.1 Hz, 3H, $OCH_2C\mathit{H}_3$), 2.37 (m, J=5.4 Hz, 1H, $CH_3(C\mathit{H})CH_2$), 2.69 (q, J=7.0 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 2.88 (q, J=7.0 Hz, 1H, $CH_3(CH)C\mathit{H}_2$), 3.44–3.57 (qq, J=5.4, 8.0 Hz, 2H, $CH_3(CH)C\mathit{H}_2Cl$), 4.47 (q, J=7.2 Hz, 2H, $OC\mathit{H}_2CH_3$), 7.06 (d, J=8.9 Hz, 1H, Ar), 7.44–7.48 (m, J=2.5, 6.3 Hz, 1H, Ar), 7.57 (d, J=2.0 Hz, 1H, Ar), 7.71 (d, J=2.2 Hz, 1H, Ar), 8.19 (d, J=2.2 Hz, 1H, Ar), 11.69 (s, 1H, OH), 11.73 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=14.1, 17.7 (CH_3), 34.4 (CH_2), 34.9 (CH), 50.6, 62.2 (CH_2), 112.2, 119.7 (C), 120.1 (CH), 123.4, 127.5, 129.1 (C), 130.7, 131.9, 135.9, 137.2 (CH), 161.4, 163.5, 169.9, 198.1 (C). IR (KBr): $\tilde{\nu}$ = 3109 (br), 2970 (w), 1674 (s), 1629 (s), 1593 (s), 1464 (s), 1378 (m), 1347 (s), 1320 (s), 1287 (s), 1254 (s), 1231 (s), 1177 (s), 737 (m) cm^{-1}. UV–vis (CH_3CN): λ_{max} (log ε)=218.6 (4.52), 294.2 (3.95), 343.1 (3.78) nm. MS (EI, 70 eV): m/z (%)=413 ($M^+[^{37}Cl\ ^{35}Cl]$, 7), 412 (31), 411 ($M^+[^{35}Cl\ ^{35}Cl]$, 11), 410 (47), 374 (34), 287 (12), 220 (100), 155 (49). HRMS (ESI): calcd for $C_{20}H_{20}O_5Cl_2$: 410.06878; found: 410.06794. Anal. Calcd for $C_{20}H_{20}O_5Cl_2$: C, 58.41; H, 4.90. Found: C, 58.45; H, 4.89.

4.4.9. 2-Bromo-4-(3-chloropropyl)-1,3-dihydroxyanthracene-9,10-dione (13). A THF solution (50 mL) of **1a** (2.81 g, 8.0 mmol) and 2-bromonaphthalene-1,4-dione (**12**) (0.95 g, 4.0 mmol) was stirred at −78 °C for 1 h. The solution was allowed to warm to 20 °C during 14 h. To the solution was added hydrochloric acid (10 mL, 6 M). The THF was removed in vacuo and the residue was washed with water and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by column chromatography (silica gel, n-hexane/EtOAc = 20:1) to give **13** as a yellowish solid (0.375 g, 30%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.14 (m, J=6.9, 1.5 Hz, 2H, CH_2), 3.36 (m, J=5.7 Hz, 2H, CH_2), 3.74 (t, J=6.8 Hz, 2H, CH_2–Cl), 6.59 (s, 1H, OH), 7.71–7.83 (m, 2H, 2×CH of Ar), 8.22–8.29 (m, 2H, 2×CH of Ar), 14.44 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=25.1, 31.9, 45.3 (CH_2), 105.4, 110.6 (C), 126.3, 127.3 (CH), 127.5, 130.4, 132.1 (C), 134.5 (CH), 134.6 (C), 135.2 (CH), 160.5, 161.1, 184.2, 187.1 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (s), 1667 (s), 1626 (s), 1586 (s), 1439 (s), 1393 (s), 1358 (s), 1279 (s), 1183 (s), 1150 (s), 1013 (m), 838 (m), 732 (s), 628 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=206.7 (4.32), 248.9 (4.37), 272.5 (4.37), 338.6 (3.51), 408.4 (3.77) nm. MS (EI, 70 eV): m/z (%)=398 ($M^+[^{81}Br\ ^{37}Cl]$, 20), 397 (12), 396 ($M^+[^{81}Br\ ^{35}Cl]$, M$^+$[^{79}Br ^{37}Cl], 100), 395 (8), 394 (M$^+$[^{79}Br ^{35}Cl], 73), 331 (85), 264 (8), 210 (14), 139 (34), 105 (6), 77 (13), 28 (40). HRMS (ESI): calcd for $C_{17}H_{12}BrClO_4$ ([M+1]$^+$): 396.96562 [^{81}Br ^{35}Cl], 394.96857 [^{79}Br ^{35}Cl]; found: 396.94806 [^{81}Br ^{35}Cl], 394.95052 [^{79}Br ^{35}Cl]. Anal. Calcd for $C_{17}H_{12}BrClO_4$ (395.632): C, 51.59; H, 3.06. Found: C, 51.86; H, 3.60.

4.5. General procedure for the synthesis of chromanes (4a–m), (11a–h), and (14)

To a THF solution of **3a**–**m**, **10a**–**h**, or **13** and of NaH was added TBAI. After stirring at 20 °C for 20 h, the mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc) to give the product.

4.5.1. Ethyl 3,4-dihydro-2*H*-chromene-8-carboxylate (4a). Starting with **3a** (0.329 g, 1.36 mmol), NaH (0.040 g, 1.66 mmol), and TBAI (0.721 g, 2.21 mmol) in THF (22 mL), **4a** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.230 g, 64%). ^{1}H NMR (CDCl$_3$, 300 MHz): δ=1.37 (t, J=7.1 Hz, 3H, CH$_3$), 2.04 (m, J=5.3 Hz, 2H, CH$_2$), 2.82 (t, J=6.5 Hz, 2H, CH$_2$), 4.29 (t, J=5.3 Hz, 2H, CH$_2$), 4.35 (q, J=7.1 Hz, 2H, OCH$_2$), 6.83 (t, J=7.6 Hz, 1H, CH of Ar), 7.17 (m, J=6.5, 1 Hz, 1H, CH of Ar), 7.61 (dt, J=7.8, 1 Hz, 1H, CH of Ar). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=14.3 (CH$_3$), 21.7, 25.1, 60.6, 66.9 (CH$_2$), 111.1 (CH), 119.6, 123.4 (C), 129.3, 133.7 (CH), 154.9, 166.2 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (m), 2937 (m), 1726 (s), 1595 (s), 1473 (s), 1454 (s), 1367 (m), 1298 (s), 1265 (s), 1238 (s), 1176 (s), 1138 (s), 1094 (s), 1055 (s), 958 (m), 878 (m), 761 (s). UV–vis (CH$_3$CN, nm): λ_{max} (log ε)=209 (4.43), 298 (3.51) nm. MS (EI, 70 eV): m/z (%)=207 ([M+1]$^+$, 6), 206 (M$^+$, 46), 161 (100), 133 (34), 105 (31), 77 (27), 51 (18), 29 (8). HRMS (FT-ICR): calcd for $C_{12}H_{14}O_3$ ([M+1]$^+$): 207.10212; found: 207.10165. Anal. Calcd for $C_{12}H_{14}O_3$ (206.238): C, 69.89; H, 6.84. Found: C, 69.18; H, 6.75.

4.5.2. Ethyl 3,4-dihydro-5,6,7-trimethyl-2*H*-chromene-8-carboxylate (4b). Starting with **3b** (0.307 g, 1.09 mmol), NaH (0.039 g, 1.63 mmol), and TBAI (0.771 g, 2.18 mmol) in THF (20 mL), **4b** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.235 g, 90%), mp=76 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ=1.36 (t, J=7.1 Hz, 3H, CH$_3$), 2.00 (m, 2H, CH$_2$), 2.13 (s, 6H, 2×CH$_3$), 2.17 (s, 3H, CH$_3$), 2.65 (t, J=6.5 Hz, 2H, CH$_2$), 4.11 (t, J=5.2 Hz, 2H, CH$_2$), 4.39 (q, J=7.1 Hz, 2H, OCH$_2$). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=14.3, 15.3, 15.5 (CH$_3$), 17.2, 22.5, 23.2, 60.9, 65.8 (CH$_2$), 118.6, 121.6, 126.8, 130.9, 136.8, 149.3, 169.4 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2983 (m), 2936 (m), 1724 (s), 1581 (m), 1455 (m), 1312 (m), 1277 (s), 1184 (s), 1114 (s), 1084 (m), 1046 (s), 964 (m). UV–vis (CH$_3$CN, nm): λ_{max} (log ε)=205 (4.49), 289 (3.43) nm. MS (EI, 70 eV): m/z (%)=249 ([M+1]$^+$, 14), 248 (M$^+$, 100), 203 (66), 202 (22), 174 (25), 161 (40), 133 (13), 105 (11), 77 (16), 51 (5), 29 (8). HRMS (ESI): calcd for $C_{15}H_{20}O_3$ ([M+1]$^+$): 249.14910; found: 249.14908.

4.5.3. Ethyl 5,7-dimethyl-3,4-dihydro-2*H*-chromene-8-carboxylate (4c). Starting with **3c** (0.059 g, 0.22 mmol), NaH (0.008 g, 0.33 mmol), and TBAI (0.144 g, 0.44 mmol) in THF (5 mL), **4c** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.036 g, 70%). ^{1}H NMR (CDCl$_3$, 300 MHz): δ=1.36 (t, J=7.1 Hz, 3H, CH$_3$), 2.02 (m, J=4.2, 1.2 Hz, 2H, CH$_2$), 2.16 (s, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 2.59 (t, J=6.6 Hz, 2H, CH$_2$), 4.14 (t, J=5.2 Hz, 2H, CH$_2$), 4.38 (q, J=7.1 Hz, 2H, OCH$_2$), 6.75 (s, 1H, CH of Ar). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=14.3, 18.9, 19.0 (CH$_3$), 22.0, 22.2, 60.9, 66.1 (CH$_2$), 118.6, 120.9 (C), 123.1 (CH), 133.1, 138.6, 151.9, 168.7 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3414 (m), 2977 (s), 2938 (s), 1716 (s), 1612 (m), 1574 (m), 1457 (s), 1369 (m), 1303 (s), 1273 (s), 1151 (s), 1106 (s), 1056 (s), 959 (m). UV–vis (CH$_3$CN, nm): λ_{max} (log ε)=207 (4.48), 285 (3.34) nm. MS (EI, 70 eV): m/z (%)=236 ([M+2]$^+$, 1), 235.1 ([M+1]$^+$, 12), 234 (M$^+$, 87), 189 (100), 161 (31), 132 (20), 103 (7), 77 (12), 28 (17). HRMS (ESI): calcd for $C_{14}H_{19}O_3$ ([M+1]$^+$): 235.13342; found: 235.13286. Anal. Calcd for $C_{14}H_{18}O_3$ (234.291): C, 71.77; H, 7.74. Found: C, 70.94; H, 7.37.

4.5.4. Ethyl-3,4-dihydro-5,7-dimethyl-6-ethyl-2*H*-chromene-8-carboxylate (4d). Starting with **3d** (0.274 g, 0.92 mmol), NaH (0.033 g, 1.37 mmol), and TBAI (0.600 g, 1.84 mmol) in THF (20 mL), **4d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.198 g, 82%). ^{1}H NMR (CDCl$_3$, 300 MHz): δ=1.06 (t, J=7.5 Hz, 3H, CH$_3$), 1.36 (t, J=7.2 Hz, 3H, CH$_3$), 2.01 (m, J=6.5 Hz, 2H, CH$_2$), 2.15 (s, 3H, CH$_3$), 2.20 (s, 3H, CH$_3$), 2.56–2.64 (m, J=7.4 Hz, 4H, 2×CH$_2$), 4.09 (t, J=5.2 Hz, 2H, CH$_2$), 4.37 (q, J=7.1 Hz, 2H, OCH$_2$). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=13.7, 14.1, 14.6, 16.0 (CH$_3$), 22.2, 22.3, 23.0, 60.8, 65.7 (CH$_2$), 118.8, 121.8, 130.2, 132.6, 136.1, 149.2, 169.3 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2968 (s), 2934 (s), 2872 (s), 1728 (s), 1583 (s), 1451 (s), 1372 (m), 1275 (s), 1187 (s), 1115 (s), 1087 (s), 1043 (s), 956 (m), 735 (m). UV–vis (CH$_3$CN, nm): λ_{max} (log ε)=207 (4.48), 289 (3.36) nm. MS (EI, 70 eV): m/z (%)=263 ([M+1]$^+$, 7), 262 (M$^+$, 50), 247 (66), 217 (32), 201 (28), 188 (20), 84 (56), 32 (25), 28 (100).

4.5.5. Ethyl 5,7-diethyl-3,4-dihydro-2*H*-chromene-8-carboxylate (4e). Starting with **3** (0.330 g, 1.10 mmol), NaH (0.040 g, 1.66 mmol), TBAI (0.721 g, 2.21 mmol) in THF (20 mL), **4e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.230 g, 80%). ^{1}H NMR (CDCl$_3$, 300 MHz): δ=1.19 (t, J=7.5 Hz, 6H, 2×CH$_3$), 1.36 (t, J=7.1 Hz, 3H, CH$_3$), 2.03 (m, J=4.4 Hz, 2H, CH$_2$), 2.53 (m, J=7.5 Hz, 4H, 2×CH$_2$), 2.67 (t, J=6.5 Hz, 2H, CH$_2$), 4.15 (t, J=5.2 Hz, 2H, CH$_2$), 4.38 (q, J=7.1 Hz, 2H, OCH$_2$), 6.61 (s, 1H, CH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=14.1, 14.2, 15.6 (CH$_3$), 21.6, 22.0, 25.4, 26.3, 60.8, 66.0 (CH$_2$), 117.8 (C), 119.8 (CH), 120.5, 139.5, 144.4, 151.6, 168.7 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2969 (s), 2937 (s), 2874 (s), 1728 (s), 1609 (s), 1571 (s), 1463 (s), 1442 (s), 1417 (s), 1370 (m), 1276 (s), 1248 (s), 1150 (s), 1113 (s), 1066 (s), 868 (m). UV–vis (CH$_3$CN, nm): λ_{max} (log ε)=207 (4.53), 284 (3.38) nm. MS (EI, 70 eV): m/z (%)=263 ([M+1]$^+$, 6), 262 (M$^+$, 50), 217 (73), 216 (100), 215 (34), 189 (15), 188 (15), 187 (17), 159 (9), 91 (13), 28 (36). Anal. Calcd for $C_{16}H_{22}O_3$ (262.344): C, 73.53; H, 8.10. Found: C, 73.49; H, 8.94.

4.5.6. Ethyl 3,4-dihydro-3,5,6,7-tetramethyl-2*H*-chromene-8-carboxylate (4f). Starting with **3f** (0.230 g, 0.77 mmol), NaH (0.028 g, 1.15 mmol), and TBAI (0.503 g, 1.54 mmol) in THF (12 mL), **4f** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.190 g, 94%), mp=111 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.05 (d, J=6.5 Hz, 3H, CH_3), 1.34 (t, J=7.1 Hz, 3H, CH_3), 2.09 (m, 1H, CH), 2.13 (s, 6H, $2\times CH_3$), 2.17 (s, 3H, CH_3), 2.22 (m, 1H, CH_2), 2.74 (dq, J=10.1, 1.8 Hz, 1H, CH_2), 3.57 (m, J=10 Hz, 1H, CH_2), 4.12 (m, J=5.3, 1.8 Hz, 1H, CH_2), 4.39 (q, J=7.1 Hz, 2H, OCH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.3, 15.3, 15.5, 17.1, 17.3 (CH_3), 27.3 (CH), 31.9, 60.9, 71.2 (CH_2), 118.4, 121.4, 126.9, 130.9, 136.6, 148.8, 169.4 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2983 (m), 1726 (s), 1464 (m), 1268 (s), 1185 (s), 1123 (m), 1042 (s). UV–vis (CH_3CN, nm): λ_{max} (log ε)=203 (4.57), 288 (3.43) nm. MS (EI, 70 eV): *m/z* (%)=263 ([M+1]$^+$, 16), 262 (M$^+$, 100), 217 (89), 216 (40), 188 (39), 175 (21), 146 (11), 91 (12), 32 (17), 28 (80). Anal. Calcd for $C_{16}H_{22}O_3$ (262.344): C, 73.25; H, 8.45. Found: C, 72.85; H, 7.98.

4.5.7. Ethyl 3,4-dihydro-3,5,7-trimethyl-2*H*-chromene-8-carboxylate (4g). Starting with **3g** (0.176 g, 0.62 mmol), NaH (0.039 g, 1.63 mmol), and TBAI (0.771 g, 2.18 mmol) in THF (12 mL), **4g** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.123 g, 80%), mp=71 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.05 (d, J=6.3 Hz, 3H, CH_3), 1.36 (t, J=7.1 Hz, 3H, CH_3), 2.10 (m, 1H, CH), 2.16 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.18 (m, 1H, CH_2), 2.68 (m, 1H, CH_2), 3.61 (m, J=12 Hz, 1H, CH_2), 4.15 (m, J=5.5 Hz, 1H, CH_2), 4.38 (q, J=7.1 Hz, 2H, OCH_2), 6.57 (s, 1H, CH of Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.3, 17.2, 18.9, 19.0 (CH_3), 26.9 (CH), 30.9, 60.9, 71.5 (CH_2), 110.9, 118.4, 120.7 (C), 123.2 (CH), 133.2, 138.5, 151.4, 168.7 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3442 (m), 2978 (s), 1728 (s), 1612 (m), 1574 (m), 1452 (m), 1282 (s), 1265 (s), 1151 (s), 1056 (s), 1042 (s), 862 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=206 (4.52), 284 (3.39) nm. MS (EI, 70 eV): *m/z* (%)=249 ([M+1]$^+$, 8), 248 (M$^+$, 100), 202 (66), 161 (21), 32 (22), 28 (100). Anal. Calcd for $C_{15}H_{20}O_3$ (248.318): C, 72.55; H, 8.12. Found: C, 72.10; H, 8.43.

4.5.8. Ethyl 5,7-diethyl-3,4-dihydro-3-methyl-2*H*-chromene-8-carboxylate (4h). Starting with **3h** (0.450 g, 1.44 mmol), NaH (0.052 g, 2.16 mmol), and TBAI (0.941 g, 2.88 mmol) in THF (24 mL), **4h** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.385 g, 97%), mp=42 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.05 (d, J=6.5 Hz, 3H, CH_3), 1.20 (q, J=7.0 Hz, 6H, $2\times CH_3$), 1.36 (t, J=7.1 Hz, 3H, CH_3), 2.14 (m, 1H, CH_2), 2.24 (m, 1H, CH_2), 2.53 (m, 4H, $2\times CH_2$), 2.75–2.79 (m, 1H, CH), 3.62 (dd, J=10 Hz, 1H, OCH_2), 4.15–4.19 (dd, J=2.4 Hz, 1H, OCH_2), 4.38 (q, J=7.1 Hz, 2H, OCH_2), 6.61 (s, 1H, CH of Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.6, 14.7, 16.1, 17.7 (CH_3), 25.9, 26.7 (CH_2), 27.3 (CH), 30.7, 61.3, 71.9 (CH_2), 117.7, 119.9 (C), 120.4 (CH), 139.6, 144.4, 151.2, 168.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2967 (s), 2933 (s), 2875 (s), 1728 (s), 1610 (m), 1571 (s), 1462 (s), 1417 (s), 1274 (s), 1242 (s), 1150 (s), 1261 (s), 1044 (s), 866 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=208 (4.53), 284 (3.39) nm. MS (EI, 70 eV): *m/z* (%)=277.6 ([M+1]$^+$, 21), 276.7 (M$^+$, 100), 231 (39), 230 (64), 229 (16), 189 (8), 188 (7), 29 (6). HRMS (ESI): calcd for $C_{17}H_{24}O_3$ ([M+1]$^+$): 277.18037, found: 277.18035.

4.5.9. Ethyl 3,4,6,7,8,9-hexahydro-2*H*-benzo[*g*]chromene-10-carboxylate (4i). Starting with **3i** (311 mg, 1.05 mmol), NaH (38 mg, 1.58 mmol), and TBAI (685 mg, 2.10 mmol) in THF (20 mL), **4i** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.189 g, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.36 (t, J=7.2 Hz, 3H, CH_3), 1.71–1.76 (m, J=3.3 Hz, 4H, $2\times CH_2$), 1.97 (m, J=4.3 Hz, 2H, CH_2), 2.65 (m, 6H, $3\times CH_2$), 2.71 (t, J=6.5 Hz, 2H, CH_2), 4.16 (t, J=5.2 Hz, 2H, CH_2), 4.36 (q, J=7.1 Hz, 2H, OCH_2), 6.77 (s, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.3 (CH_3), 22.2, 22.8, 22.9, 24.5, 26.2, 28.8, 60.9, 66.6 (CH_2), 111.9, 122.4, 128.7, 131.1, 132.3, 149.4, 168.7 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2977 (s), 2931 (s), 2858 (s), 1729 (s), 1582 (s), 1476 (s), 1446 (s), 1367 (s), 1285 (s), 1249 (s), 1179 (s), 1164 (s), 1108 (s), 1061 (s), 961 (s), 866 (s), 724 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=204 (4.41), 294 (3.55) nm. MS (EI, 70 eV): *m/z* (%)=261 ([M+1]$^+$, 6), 260 (M$^+$, 50), 214 (64), 186 (23), 168 (12), 153 (16), 128 (6), 114 (6), 91 (9), 28 (100). HRMS (ESI): calcd for $C_{16}H_{20}O_3$ ([M+1]$^+$): 261.14907; found: 261.14928. Anal. Calcd for $C_{16}H_{20}O_3$ (260.328): C, 73.81; H, 7.74. Found: C, 73.51; H, 8.02.

4.5.10. Ethyl 3,4,6,7,8,9-hexahydro-5-methyl-2*H*-benzo[*g*]chromene-10-carboxylate (4j). Starting with **3j** (0.305 g, 0.98 mmol), NaH (0.035 g, 1.47 mmol), and TBAI (0.640 g, 1.96 mmol) in THF (18 mL), **4j** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.234 g, 87%), mp=74 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.38 (t, J=7.2 Hz, 3H, CH_3), 1.69–1.79 (m, 4H, $2\times CH_2$), 2.00–2.06 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 2.58 (t, J=6.5 Hz, 2H, CH_2), 2.64 (m, 4H, 2 CH_2), 4.13 (t, J=5.2 Hz, 2H, CH_2), 4.36 (q, J=7.1 Hz, 2H, OCH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.2, 14.3 (CH_3), 22.4 (2 CH_2), 22.9, 23.1, 23.2, 26.9, 60.8, 65.8 (CH_2), 118.7, 120.6, 127.1, 131.9, 136.9, 149.3, 168.9 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3430 (w), 2931 (s), 1725 (s), 1579 (m), 1445 (m), 1272 (s), 1188 (s), 1076 (m), 1034 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=206 (4.51), 290 (4.47) nm. MS (EI, 70 eV): *m/z* (%)=275 ([M+1]$^+$, 3), 274 (M$^+$, 20), 229 (17), 228 (21), 174 (29), 114 (4), 91 (4), 32 (25), 28 (100). Anal. Calcd for $C_{17}H_{22}O_3$ (274.355): C, 74.42; H, 8.09. Found: C, 74.31; H, 8.18.

4.5.11. Ethyl 6,8,9,10-tetrahydro-7-methyl-5*H*-naphtho[2,1-*g*]chromene-12-carboxylate (4k). Starting with **3k** (0.353 g, 0.984 mmol), NaH (0.035 g, 1.48 mmol), and TBAI (0.643 g, 1.97 mmol) in THF (18 mL), **4k** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.280 g, 88%), mp=180 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.18 (t, J=7.1 Hz, 3H, CH_3), 2.09 (m, J=4.0 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.69–2.77 (m, 6H, $3\times CH_2$), 4.18 (t, J=5.2 Hz, 2H, CH_2), 4.29 (q, J=7.1 Hz, 2H, OCH_2), 7.17–7.23 (m, 3H, $3\times$CH of Ar), 7.54–7.57 (m, 1H, CH of Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=13.7, 15.1 (CH_3), 22.3, 23.4, 25.4, 29.4, 61.2, 65.9 (CH_2), 118.4, 120.7 (C), 126.2, 126.3, 127.2, 127.3 (CH), 129.5, 131.2, 133.9, 135.7, 138.6, 151.0, 169.7 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 3414$ (w), 2986 (m), 1717 (s), 1558 (m), 1415 (m), 1282 (s), 1188 (m), 1164 (m), 1070 (m), 1033 (m), 757 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=208 (4.49), 225 (4.38), 269 (4.12), 316 (3.87) nm. MS (EI, 70 eV): *m/z* (%)=323 ([M+1]$^+$, 22), 322 (M$^+$, 100), 277 (54), 32 (24), 28 (92). HRMS (ESI): calcd for $C_{21}H_{22}O_3$ ([M+1]$^+$): 323.16472; found: 323.16431. Anal. Calcd for $C_{21}H_{22}O_3$ (322.398): C, 78.23; H, 6.88. Found: C, 77.99; H, 7.29.

4.5.12. Ethyl 6-(2-chloroethyl)-5,7-dimethyl-3,4-dihydro-2*H*-chromene-8-carboxylate (4l). Starting with **3l** (0.308 g, 0.923 mmol), NaH (0.033 g, 1.36 mmol), and TBAI (0.603 g, 1.85 mmol) in THF (16 mL), **4l** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.211 g, 77%), mp=103 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.37 (t, *J*=7.2 Hz, 3H, CH_3), 2.02 (m, *J*=7.5 Hz, 2H, CH_2), 2.18 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.63 (t, *J*=6.6 Hz, 2H, CH_2), 3.10 (m, 2H, CH_2), 3.47 (m, 2H, CH_2–Cl), 4.12 (t, *J*=5.2 Hz, 2H, CH_2), 4.37 (q, *J*=7.1 Hz, 2H, OCH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.2, 15.2, 16.5 (CH_3), 22.3, 23.2, 33.2, 42.3, 61.1, 65.9 (CH_2), 119.4, 122.4, 126.5, 131.4, 137.3, 150.4, 168.9 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 2987$ (m), 2939 (m), 1727 (s), 1579 (m), 1453 (s), 1308 (s), 1278 (s), 1244 (s), 1186 (s), 1115 (s), 1042 (s), 722 (w). UV–vis (CH_3CN, nm): λ_{max} (log ε)=208 (4.58), 288 (4.35) nm. MS (EI, 70 eV): *m/z* (%)=298 (M$^+$[^{37}Cl], 10), 296 (M$^+$[^{35}Cl], 34), 247 (100), 201 (17), 173 (3), 114 (4), 28 (7). HRMS (ESI): calcd for $C_{16}H_{21}ClO_3$ ([M+1]$^+$): 299.12280 [^{37}Cl], 297.12575 [^{35}Cl]; found: 299.12162 [^{37}Cl], 297.12476 [^{35}Cl]. Anal. Calcd for $C_{16}H_{21}ClO_3$ (296.789): C, 64.73; H, 7.13. Found: C, 64.73; H, 7.72.

4.5.13. Ethyl 6-(2-bromoethyl)-3,4-dihydro-5,7-dimethyl-2*H*-chromene-8-carboxylate (4m). Starting with **3m** (0.129 g, 0.34 mmol), NaH (0.012 g, 0.51 mmol), and TBAI (0.222 g, 0.68 mmol) in THF (6 mL), **4m** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless solid (0.070 g, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.36 (t, *J*=7.1 Hz, 3H, CH_3), 2.02 (quint, *J*=5.3 Hz, 2H, CH_2), 2.17 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.63 (t, *J*=6.6 Hz, 2H, CH_2), 3.06–3.19 (m, 2H, CH_2), 3.44–3.49 (m, 2H, CH_2), 4.12 (t, *J*=5.3 Hz, 2H, CH_2), 4.36 (q, *J*=7.2 Hz, 2H, OCH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=14.3, 15.2, 16.4 (CH_3), 22.3, 23.2, 33.2, 33.6, 61.1, 65.9 (CH_2), 119.5, 126.5, 131.3, 137.3, 150.4, 219.7 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 3431$ (m), 2981 (m), 2961 (m), 2937 (m), 1726 (s), 1581 (m), 1451 (s), 1305 (s), 1277 (s), 1186 (s), 1115 (s), 1041 (s), 962 (m), 793 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=210 (4.52), 289 (3.38) nm. MS (EI, 70 eV): *m/z* (%)=342 (M$^+$[^{81}Br], 6), 340 (M$^+$[^{79}Br], 5), 296 (23), 260 (33), 247 (100), 215 (30), 153 (9), 114 (10), 84 (88), 41 (29), 28 (78). HRMS (ESI): calcd for $C_{16}H_{21}BrO_3$ ([M+1]$^+$): 343.07317 [^{81}Br], 341.07522 [^{79}Br]; found: 343.07428 [^{81}Br], 341.07612 [^{79}Br].

4.5.14. Ethyl 3,4-dihydro-6-(2-hydroxybenzoyl)-2*H*-chromene-8-carboxylate (11a). A THF solution (5 mL) of **10a** (149 mg, 0.41 mmol) was added to a mixture of NaH (14.8 mg, 0.61 mmol) and TBAI (304 mg, 0.82 mmol). After stirring for 20 h at 20 °C, an aqueous solution of NH_3Cl (1 M, 4 mL) was added. The organic layer was separated and the aqueous layer was extracted with Et_2O (5×10 mL). The layers were separated and the organic layer was 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 = 3:1 → 1:1) to give **11a** as a yellow solid (92 mg, 68%), mp=119 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.36 (t, *J*=7.1 Hz, 3H, OCH_2CH_3), 2.10 (m, 2H, $CH_2CH_2CH_2$), 2.90 (t, *J*=6.3 Hz, 2H, $ArCH_2$), 4.32–4.42 (m, 4H, CH_2Cl, OCH_2CH_3), 6.91 (m, 1H, Ar), 7.07 (dd, *J*=8.1 Hz, *J*=1.0 Hz, 1H, Ar), 7.51 (m, 1H, Ar), 7.61 (m, 2H, Ar), 7.99 (d, *J*=2.3 Hz, 1H, Ar), 11.89 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=14.25 (OCH_2CH_3), 21.33 ($CH_2CH_2CH_2$), 25.23 ($ArCH_2$), 61.10 (OCH_2CH_3), 67.64 (OCH_2), 118.41, 118.67 (CH), 119.16, 119.58, 123.76, 128.80 (C), 131.45, 133.08, 134.73, 136.04 (CH), 158.15, 162.96 (C), 165.30, 199.40 (C=O). IR (KBr): $\tilde{\nu} = 3070$ (w), 3035 (w), 2941 (w), 1692 (s), 1626 (s), 1622 (s), 1480 (s), 1456 (m), 1335 (m), 1276 (s), 1250 (s), 1216 (s), 1184 (s), 1159 (s), 1135 (m), 1021 (m), 762 (w) cm^{-1}. UV–vis (CH_3CN): λ_{max} (log ε): 302 (3.99), 248 (4.07), 214 (4.29) nm. Fluorescence (CH_3CN): λ_{Ex} ($F\lambda_{max}$): 340 (379) nm. MS (EI, 70 eV): *m/z* (%)=326 (M$^+$, 36), 270 (68), 234 (14), 210 (100), 182 (18), 161 (12), 128 (32), 77 (16). HRMS (FT-ICR): calcd for $C_{19}H_{19}O_5$ ([M+1]$^+$): 327.12270; found: 327.12296.

4.6. General procedure for the synthesis of (11b,e–h)

A THF solution of **10b**,**e–h** (1.0 equiv) was added to a mixture of NaH (1.5 equiv) and TBAI (2 equiv). After stirring for 20 h at 20 °C, an aqueous solution of hydrochloric acid (10%) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (5×10 mL). The layers were separated and the organic layer was 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 → 10:1) to give **11b**,**e–h**.

4.6.1. 3,4-Dihydro-6-(2-hydroxy-5-methylbenzoyl)-2*H*-chromene-8-carboxylic acid (11b). Starting with **10b** (102 mg, 0.27 mmol) in 4 mL THF, NaH (10 mg, 0.405 mmol), and TBAI (176 mg, 0.54 mmol), **11b** was isolated as a yellow solid (80 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.18 (quint, *J*=5.2 Hz, 2H, CH_2), 2.26 (s, 3H, CH_3), 2.97 (t, *J*=6.1 Hz, 2H, CH_2), 4.55 (t, *J*=5.4 Hz, 2H, CH_2), 6.96 (d, *J*=7.8 Hz, 1H, Ar), 7.32–7.35 (m, 2H, Ar), 7.69 (d, *J*=2.2 Hz, 1H, Ar), 8.30 (d, *J*=2.2 Hz, 1H, Ar), 11.62 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=20.5 (CH_3), 21.2, 24.6, 68.9 (CH_2), 116.7 (C), 118.2 (CH), 118.6, 124.1, 128.1, 130.9 (C), 132.7, 133.2, 135.8, 137.5 (CH), 156.5, 160.9, 164.8, 199.2 (C). IR (KBr): $\tilde{\nu} = 3225$ (m), 1731 (s), 1630 (m), 1594 (s), 1478 (s), 1427 (s), 1336 (s), 1249 (s), 1205 (s), 788 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=312 (M$^+$, 42), 264 (25), 57 (12), 44 (42), 28 (100). Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.64; H, 5.38.

4.6.2. 3,4-Dihydro-6-(5-chloro-2-hydroxy-4-methylbenzoyl)-2*H*-chromene-8-carboxylic acid (11e). Starting with **10e** (102 mg, 0.25 mmol) in 4 mL THF, NaH (9 mg, 375 mmol), and TBAI (163 mg, 0.5 mmol), **11e** was isolated as yellow viscous oil (60 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.19 (quint, *J*=5.0 Hz, 2H, C*H*$_2$), 2.40 (s, 3H, CH_3), 2.98 (t, *J*=6.2 Hz, 2H, C*H*$_2$), 4.56 (t, *J*=5.2 Hz, 2H, C*H*$_2$), 6.97 (s, 1H, Ar), 7.49 (s, 1H, Ar), 7.65 (t, *J*=1 Hz, 1H, Ar), 8.31 (d, *J*=2.3 Hz, 1H, Ar), 11.68 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=20.8 (CH_3), 21.2, 24.6, 68.9 (CH_2), 117.1, 117.9 (C), 120.5 (CH), 124.2, 130.5 (C), 132.3, 133.0, 135.6 (CH), 145.9, 156.7, 161.4, 164.5, 190.5, 197.9 (C). MS (EI, 70 eV): *m*/*z* (%)=348 ($M^+[^{37}Cl]$, 21), 346 ($M^+[^{35}Cl]$, 59), 205 (17), 178 (79), 168 (43), 161 (100), 77 (53).

4.6.3. 3,4-Dihydro-3-methyl-6-(2-hydroxybenzoyl)-2*H*-chromene-8-carboxylic acid (11f). Starting with **10f** (94 mg, 0.25 mmol) in 10 mL THF, NaH (9 mg, 0.37 mmol), and TBAI (163 mg, 0.50 mmol), **11f** was isolated as a yellow viscous oil (55 mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.22 (d, *J*=6.5 Hz, 3H, C*H*$_3$(CH)), 2.34 (m, 1H, CH_3(C*H*)), 2.62 (q, *J*=9.8, 6.5 Hz, 1H, C*H*$_2$), 3.00 (dd, *J*=5.0, 9.5 Hz, 1H, C*H*$_2$), 4.04 (t, *J*=10.5 Hz, 1H, C*H*$_2$), 4.54–4.59 (qq, *J*=2.0, 9.0 Hz, 1H, C*H*$_2$), 6.99 (d, *J*=8.1 Hz, 1H, Ar), 7.32 (s, 1H, Ar), 7.35 (d, *J*=2.2 Hz, 1H, Ar), 7.68 (t, *J*=1.1 Hz, 1H, Ar), 8.32 (d, *J*=2.2 Hz, 1H, Ar), 11.63 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=16.5 (CH_3), 26.3 (CH), 32.7, 73.8 (CH_2), 116.6 (C), 118.5 (CH), 118.8 (C), 119.0 (CH), 123.8, 130.9 (C), 133.0, 133.3, 135.9, 136.4 (CH), 156.1, 163.0, 164.6, 199.1 (C). MS (EI, 70 eV): *m*/*z* (%)=312 (M^+, 64), 267 (20), 219 (26), 192 (100), 175 (39), 121 (60). IR (KBr): $\tilde{\nu}$ = 3296 (br, m), 2926 (m), 1733 (m), 1625 (s), 1598 (s), 1479 (s), 1329 (s), 1249 (s), 1158 (s), 762 (m) cm^{-1}. HRMS (ESI): calcd for $C_{18}H_{16}O_5$: 312.09977; found: 312.09901.

4.6.4. 3,4-Dihydro-3-methyl-6-(2-hydroxy-5-methylbenzoyl)-2*H*-chromene-8-carboxylic acid (11g). Starting with **10g** (194 mg, 0.50 mmol) in 10 mL THF, NaH (18 mg, 0.75 mmol), and TBAI (326 mg, 1.0 mmol), **11g** was isolated as a yellow solid (140 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.15 (d, *J*=6.8 Hz, 3H, C*H*$_3$(CH)), 2.26 (s, 3H, CH_3), 2.34 (m, 1H, CH_3(C*H*)), 2.62 (q, *J*=9.8, 6.5 Hz, 1H, C*H*$_2$), 3.00 (dd, *J*=5.0, 9.5 Hz, 1H, C*H*$_2$), 4.04 (t, *J*=10.5 Hz, 1H, C*H*$_2$), 4.54–4.59 (qq, *J*=2.0, 9.0 Hz, 1H, C*H*$_2$), 6.99 (d, *J*=8.1 Hz, 1H, Ar), 7.32 (s, 1H, Ar), 7.35 (d, *J*=2.2 Hz, 1H, Ar), 7.68 (t, *J*=1.1 Hz, 1H, Ar), 8.32 (d, *J*=2.2 Hz, 1H, Ar), 11.63 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=16.5, 20.5 (CH_3), 26.3 (CH), 32.8, 73.8 (CH_2), 116.5 (C), 118.2 (CH), 118.6, 123.8, 128.1, 131.2 (C), 132.7, 133.2, 135.8, 137.5 (CH), 156.0, 160.9, 164.7, 199.2 (C). IR (KBr): $\tilde{\nu}$ = 2956 (m), 2926 (m), 1670 (s), 1596 (s), 1479 (s), 1336 (s), 1246 (s), 1219 (s), 1173 (s), 792 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=326 (M^+, 90), 175 (100), 134 (91), 77 (15), 28 (29). HRMS (ESI): calcd for $C_{19}H_{18}O_5$: 326.11542; found: 326.11530. Anal. Calcd for $C_{19}H_{18}O_5$: C, 69.93; H, 5.56. Found: C, 69.51; H, 5.56.

4.6.5. 3,4-Dihydro-3-methyl-6-(5-chloro-2-hydroxybenzoyl)-2*H*-chromene-8-carboxylic acid (11h). Starting with **10h** (261 mg, 0.64 mmol) in 10 mL THF, NaH (23 mg, 0.96 mmol), and TBAI (662 mg, 1.27 mmol), **11h** was isolated as a yellow solid (160 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.16 (d, *J*=6.8 Hz, 3H, C*H*$_3$(CH)), 2.34 (m, 1H, CH_3(C*H*)), 2.62 (q, *J*=9.8, 6.6 Hz, 1H, C*H*$_2$), 2.99–3.06 (dd, *J*=3.2, 13.3 Hz, 1H, C*H*$_2$), 4.04 (t, *J*=10.1 Hz, 1H, C*H*$_2$), 4.55–4.60 (qq, *J*=2.0, 8.6 Hz, 1H, C*H*$_2$), 7.04 (td, *J*=1.2, 6.9 Hz, 1H, Ar), 7.06–7.09 (dd, *J*=2.0, 7.6 Hz, 1H, Ar), 7.49–7.58 (m, 2H, Ar), 7.70 (quint, *J*=1.0 Hz, 1H, Ar), 8.34 (d, *J*=2.3 Hz, 1H, Ar), 11.82 (s, 1H, OH). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ=16.5 (CH_3), 26.2 (CH), 32.8, 73.8 (CH_2), 116.9, 119.6 (C), 120.1 (CH), 123.6, 123.9, 130.3 (C), 131.8, 133.1, 135.7, 136.3 (CH), 156.5, 161.5, 164.6, 198.2 (C). IR (KBr): $\tilde{\nu}$ = 3069 (w), 2959 (m), 1735 (m), 1706 (m), 1674 (s), 1627 (s), 1596 (s), 1474 (s), 1466 (s), 1330 (s), 1249 (s), 1226 (s), 1185 (s), 1140 (m), 1001 (m), 790 (m) cm^{-1}. UV–vis (CH_3CN): λ_{max} (log ε)=209.1 (4.49), 291.6 (3.93), 344.8 (3.77) nm. MS (EI, 70 eV): *m*/*z* (%)=348 ($M^+[^{37}Cl]$, 22), 346 ($M^+[^{35}Cl]$, 62), 192 (100), 175 (66), 155 (24). Anal. Calcd for $C_{18}H_{15}O_5Cl$: C, 62.35; H, 4.36. Found: C, 62.11; H, 4.34.

4.6.6. 5-Bromo-2,3-dihydro-6-hydroxy-1*H*-naphtho[2,3-*f*]chromene-7,12-dione (14). Starting with **13** (0.140 g, 0.44 mmol), NaH (0.016 g, 0.66 mmol), and TBAI (0.287 g, 0.88 mmol) in THF (7 mL), **14** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a yellowish solid (0.115 g, 73%), mp=235 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.10 (tt, *J*=5.5, 6.5 Hz, 2H, CH_2), 3.36 (t, *J*=6.7 Hz, 2H, CH_2), 4.44 (t, *J*=6.2 Hz, 2H, CH_2), 7.77–7.79 (m, 2H, 2×CH of Ar), 8.20–8.28 (m, 2H, 2×CH of Ar), 14.23 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=21.9, 25.0, 67.9 (CH_2), 106.5, 111.4, 121.2 (C), 126.4, 127.2 (CH), 129.9, 132.2 (C), 133.8, 134.3, 134.4 (CH), 159.4, 160.2, 184.3, 187.4 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 1661 (m), 1631 (s), 1586 (s), 1556 (m), 1439 (m), 1396 (s), 1355 (s), 1282 (s), 1152 (s), 959 (m), 797 (m), 729 (m). UV–vis (CH_3CN, nm): λ_{max} (log ε)=206 (4.46), 250 (4.42), 277 (4.43), 332 (3.43), 414 (3.89) nm. MS (EI, 70 eV): *m*/*z* (%)=360 ($M^+[^{81}Br]$, 16), 359 (96), 358 ($M^+[^{79}Br]$, 21), 357 (100), 342.7 (28), 164.9 (11), 139.0 (12), 77.4 (8), 32.0 (20), 28 (89). Anal. Calcd for $C_{17}H_{11}BrO_4$ (359.171): C, 56.83; H, 3.09. Found: C, 56.43; H, 3.64.

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References and notes

1. (a) *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Elsevier Science: Oxford, 1996; (b) *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Elsevier Science: Oxford, 1984.
2. (a) Bavachromanol: ElSohly, H. N.; Joshi, A. S.; Nimrod, A. C.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 87; (b) Calyxin L: Tezuka, Y.; Gewali, M. B.; Ali, M. S.; Banskota, A. H.; Kadota, S. *J. Nat. Prod.* **2001**, *64*, 208; (c) Vismiaguianone E: Seo, E.-K.; Wani, M. C.; Wall, M. E.;

Navarro, H.; Mukherjee, R.; Farnsworth, N. R.; Kinghorn, A. D. *Phytochemistry* **2000**, *55*, 35; (d) Ali, S.; Goundar, R.; Sotheeswaran, S.; Beaulieu, C.; Spino, C. *Phytochemistry* **2000**, *53*, 281; (e) Grandinal: Singh, I. P.; Hayakawa, R.; Etoh, H.; Takasaki, M.; Konoshima, T. *Biosci. Biotechnol. Biochem.* **1997**, *61*, 921; (f) Hericenone F: Kawagishi, H.; Ando, M.; Shinba, K.; Sakamoto, H.; Yoshida, S. *Phytochemistry* **1993**, *32*, 175; (g) Calomelanol A: Asai, F.; Iinuma, M.; Tanaka, T.; Mizuno, M. *Phytochemistry* **1991**, *30*, 3091; (h) Flemistrictin F: Subrahmanyam, K.; Rao, J. M.; Vemuri, V. S. S.; Babu, S. S.; Roy, C. P.; Rao, K. V. J. *Indian J. Chem., Sect. B* **1982**, *21*, 895; (i) Iryantherin E: Conserva, L. M.; Yoshida, M.; Gottlieb, O. R.; Martinez, V. J. C.; Gottlieb, H. E. *Phytochemistry* **1990**, *29*, 3911; (j) Bohlmann, F.; Vorwerk, E. *Chem. Ber.* **1981**, *114*, 147.

3. Wang, Q.; Finn, M. G. *Org. Lett.* **2000**, *2*, 4063.
4. Jones, R. M.; Selenski, C.; Pettus, T. R. R. *J. Org. Chem.* **2002**, *67*, 6915.
5. For a review of 1,3-bis-silyl enol ethers, see: Langer, P. *Synthesis* **2002**, 441.
6. (a) Chan, T.-H.; Brownbridge, P. *J. Chem. Soc., Chem. Commun.* **1979**, 578; (b) Molander, G. A.; Cameron, K. O. *J. Am. Chem. Soc.* **1993**, *115*, 830.
7. Nguyen, V. T. H.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 815.
8. For chloro-substituted mono-silyl enol ethers, see: (a) Fleming, F. F.; Shook, B. C.; Jiang, T.; Steward, O. W. *Tetrahedron* **2003**, *59*, 737; (b) Hydrio, J.; van de Weghe, P.; Collin, J. *Synthesis* **1997**, 68; (c) Limat, D.; Schlosser, M. *Tetrahedron* **1995**, *51*, 5799; (d) Masters, A. P.; Parvez, M.; Sorensen, T. S.; Sun, F. *J. Am. Chem. Soc.* **1994**, *116*, 2804; (e) Stack, D. E.; Dawson, B. T.; Rieke, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 4672; (f) Hambly, G. F.; Chan, T. H. *Tetrahedron Lett.* **1986**, *27*, 2563; (g) Chatani, N.; Fujii, S.; Yamasaki, Y.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1986**, *108*, 7361; (h) Poirier, J.-M.; Hennequin, L. *Synth. Commun.* **1985**, *15*, 217; (i) Schultz, A. G.; Dittami, J. P. *J. Org. Chem.* **1983**, *48*, 2318; (j) Chatani, N.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 1370; For bromo-substituted mono-silyl enol ethers, see: (k) Marko, I. E.; Dumeunier, R.; Leclercq, C.; Leroy, B.; Plancher, J.-M.; Mekhalfia, A.; Bayston, D. J. *Synthesis* **2002**, 958; (l) Oku, A.; Miki, T.; Abe, M.; Ohira, M.; Kamada, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 511; (m) Rigby, J. H.; Rege, S. D.; Sandanayaka, V. P.; Kirova, M. *J. Org. Chem.* **1996**, *61*, 842.
9. Nguyen, V. T. H.; Bellur, E.; Appel, B.; Langer, P. *Synthesis* **2006**, 1103.
10. (a) Langer, P.; Bose, G. *Angew. Chem.* **2003**, *115*, 4165; *Angew. Chem., Int. Ed.* **2003**, *42*, 4033; (b) Bose, G.; Nguyen, V. T. H.; Ullah, E.; Lahiri, S.; Görls, H.; Langer, P. J. *Org. Chem.* **2004**, *69*, 9128.
11. Langer, P.; Appel, B. *Tetrahedron Lett.* **2003**, *44*, 7921.
12. (a) Roberge, G.; Brassard, P. *Synthesis* **1981**, 381; (b) Roberge, G.; Brassard, P. *J. Org. Chem.* **1981**, *46*, 4161; (c) Couturier, M.; Brassard, P. *Synthesis* **1994**, 703.