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Total Synthesis of Silyl-Protected Early Intermediates of Polyketide Biosynthesis

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Dedicated to Prof. Volker Schurig on the occasion of his 70th birthday

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The ketal- or dithioketal-protected isocoumarins **15**–**18** gave the corresponding 1-naphthols **21**–**26** in their reactions with the acetoacetate (**10**) or pentane-2,4-dione (**19**) dianions and the acetone monoanion. Subjection of the dithioketal-protected ester **28** to Baker–Venkataraman reaction conditions led to the 8-deoxy tautomeric, protected forms **29**/**30** of the early decaketide antibiotic intermediate **2b**. However, the dithioketal protecting groups could not be removed without destruction of the molecule. Consequently the silyl-protected unstable early tri- and tetracyclic decaketide biosynthesis intermediates **37a**, **37b**, and **38a** (precursors of angucycline and anthracycline antitumor antibiotics) were prepared through silylation of **33a** and **33b**, to afford **34a** and **34b**, and subsequent treatment with acetylacetone dianion. The ultimate synthetic goal, the silyl-protected 2,3-dialkylated naphthol derivative **41**, was achieved by selective elongation of the bottom chain of the bis-silyl-protected methyl ester **36** with acetylacetone dianion.

Introduction

The important polyketide antibiotics can essentially be divided into two classes:[1] firstly, those in which polyketide synthethase I (PKS I) is involved, which are mostly macrolides and other branched chain derivatives, and secondly, the aromatic or quinoid polyketides, synthesized by polyketide synthethase II (PKS II). Acetate/mevalonate is incorporated in the synthesis of the hypothetical linear oligo- or polyketide **1** (Scheme 1), which then cyclizes through different folding patterns[2] into a large variety of secondary metabolites. Prominent examples of decaketide-derived classes of antibiotics are the anthracyclines,[3] angucyclines,[2,4] and anthrapyrans.[5,6]

UWM6 (**3**, Scheme 1) is one of the earliest known intermediates in decaketide-derived angucycline biosynthesis.[7] In addition, the new product S2502 (**4**), derived from the cultivation of a hybrid strain in which genes of *Streptomyces nogalater* originally producing nogalamycin were expressed in *Streptomyces lividans*, was described in 1999.[8,9] In biological investigations, compound **4**, recently synthesized by our group,[10] exerted outstanding activities against adeno-, cytomegalo-, herpes simplex, and influenza B viruses at a concentration of 1 μm.[11] Metabolites **3** and **4** both point to the dihydroxynaphthalene **2a**, with two lateral short ketide side chains, as a putative early precursor in decaketide biosynthesis, provided that a stepwise cyclization of the open chain **2a** is assumed. It is not certain at this stage whether the methyl ketone **2b** is a genuine precursor.

Available information on the early steps in the biosynthesis is currently rather scarce, whereas the later stages in the biosynthesis of these antibiotics, in which most of the condensation steps into cyclic intermediates have already occurred, are far better documented.[4,5,12–26] In UWM6 (**3**), as in most anthracyclines and angucyclines, the initial ester group on the right hand ring is eliminated, but in S2502 (**4**) this group is still present. In spite of this, it is reasonable to assume that the initial ester group is indeed present in the early intermediates of polyketide biosynthesis, and so the initial synthetic targets of our investigation were the open-chain ketide **2a** and the related derivative **2b** (without the ester group). The reasons for this are, firstly, that the putative linear oligoketides **2a** and **2b** are extremely reactive molecules that tend to cyclize spontaneously by aldol-type reaction mechanisms, and secondly, apart from related quin-

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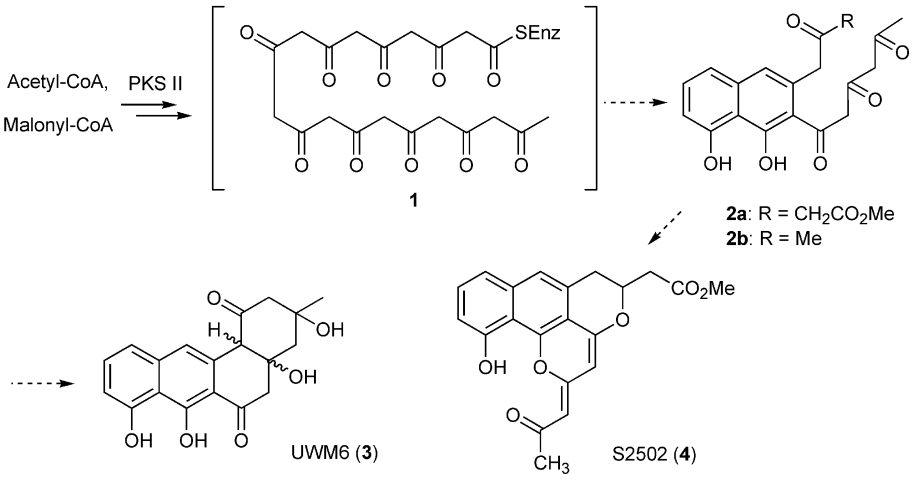


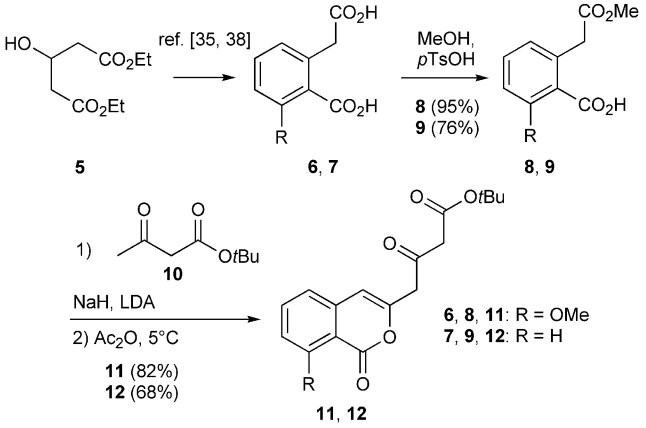
Scheme 1. Biosynthesis of decaketides **3** and **4** via the hypothetical early intermediates **1** and **2a**.

oid analogues,[27–31] compounds such as **2a** or **2b** have not yet been made available by synthesis and so no feeding experiments could be performed to confirm that naphthalene derivatives such as **2a** are in fact biosynthetic precursors. The aim of this study was therefore to explore the possibility of a chemical synthesis of the reactive intermediates **2a** or **2b** for subsequent feeding experiments.

Results and Discussion

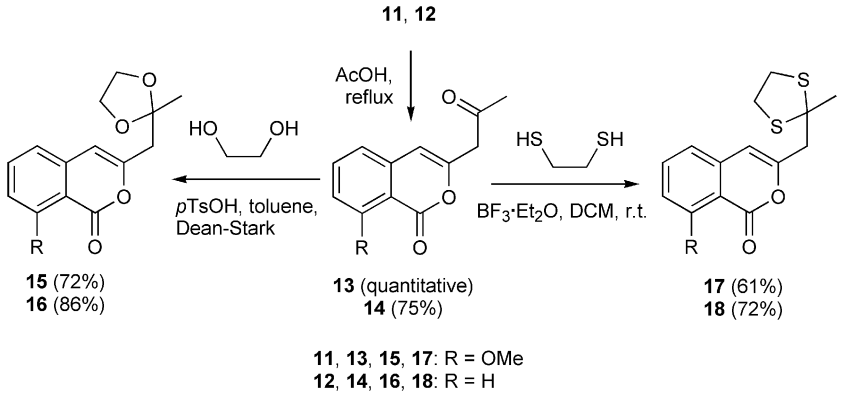
On the basis of the pioneering work of Harris,[32–34] Yamaguchi,[35–37] and our own extension of this chemistry,[37,38] we first selected isocoumarins such as **11** and **12** (Scheme 2) as the starting materials for the synthesis of naphthalene-derived oligoketides such as **2b**. The synthesis of the methoxy isocoumarin **11** started from diethyl 3-hydroxyglutarate (**5**), which was transformed into the monoester **8**. The demethoxy isocoumarin **12** was included as an additional analogue because the diacid **7** is commercially available and the possible "non-natural" demethoxy precursors can easily be detected as "artificial" in a fermentation broth for biosynthetic studies. Interestingly, on treatment of diacids **6** and **7** with acidified methanol, the aliphatic carboxylic acid group was in each case chemoselectively converted, to provide the monoesters **8** and **9**.

In our initial synthetic investigations directed towards the putative precursors **2a** and **2b**, we planned to decarboxylate the esters **11** and **12** and to protect the remaining subsequently formed keto group. For that purpose, the two *tert*-butyl esters were heated at reflux in acetic acid to yield the corresponding ketones **13** and **14** in quantitative and 75% yields, respectively (Scheme 3). The keto function was then protected by standard methods either as the ketals **15** and **16** with the aid of a Dean–Stark trap to remove water or by treatment with 1,2-dithiane in the presence of boron trifluorate etherate to yield the dithioketals **17** and **18** in 61 and 72% yields, respectively.

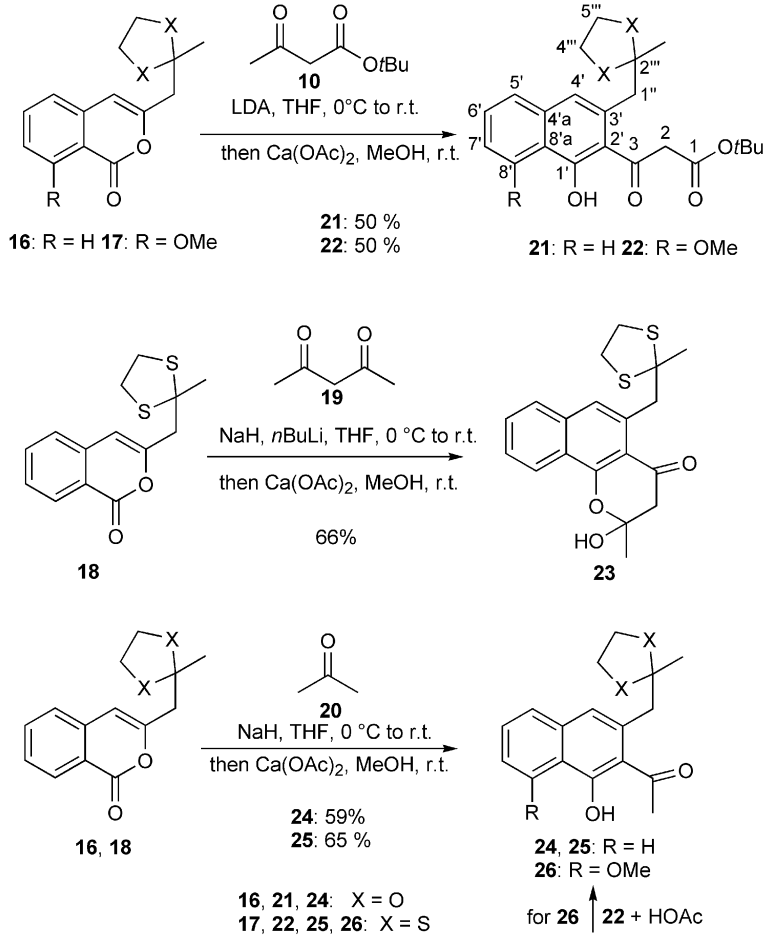


Scheme 2. Synthesis of the starting isocoumarins **11** and **12** from the monoacids **8** and **9**.

Direct attachment of the anion derived from (*Z*)-4-hydroxy-5-(2-methyl-1,3-dioxolan-2-yl)pent-3-en-2-one, described by Bringmann et al.,[39] to the ketals **15**–**18** was then attempted. However, no products of any defined structure could be isolated, and so treatment with dianions of shorter chain length – *tert*-butyl acetoacetate (**10**), pentane-2,4-dione (**19**), and even the monoanion of acetone (**20**) – with the ketal **16** and the dithioketals **17** and **18** was studied (Scheme 4). To our delight, clean reaction products **21**–**25** were formed in acceptable overall yields in each of these multistep transformations. Attack of the anionic species at the lactone carbonyl led to open-chain intermediates, which cyclized into the corresponding naphthols under the basic reaction conditions. In this way, the keto esters **21** and **22** were formed through the reactions between **16** or **17**, respectively, and the dianion of *tert*-butyl acetoacetate (**10**). However, the intermediate 1,3-diketone formed in the reaction between the dithioketal **18** and the dianion derived from pentane-2,4-dione (**19**) underwent spontaneous cyclization to form the more stable cyclic hemiketal **23**. Treatment of **16** and **18** with acetone monoanion directly af-



Scheme 3. Decarboxylation of the *tert*-butyl esters **11** and **12** and transformation into the corresponding ketals **15** and **16** and the dithioketals **17** and **18**.

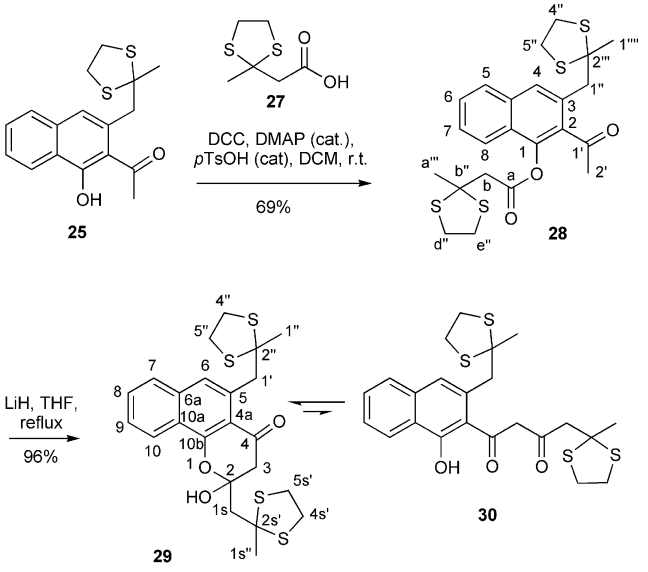


Scheme 4. Conversion of the lactones **16**–**18** into the 2,3-bisalkylated 1-naphthols **21**–**26**.

forded the acetyl naphthols **24** and **25**. An alternative route to the acetyl derivatives was demonstrated in the acidic cleavage of the *tert*-butyl keto ester **22** to afford the acetyl phenol **26**.

The *ortho*-hydroxy acetyl derivatives **24**–**26** are of paramount interest because chain extension of the acetyl group to form a triketide, as present in the target molecule **2b**, should be particularly easy by means of the Baker–Venkataraman rearrangement,[40,41] so we decided to focus our attention in this direction. Consequently, the naphthol dithioketal **25** was esterified with the dithioprotected acid **27**[42] (Scheme 5) to afford the naphthol ester **28**. With lithium hydride as the base as described earlier,[38] the intramolecular Baker–Venkataraman acyl transfer of **28** afforded the hemiketal **29** in 96% yield.

It is evident, as already observed with the diketonaphthol **23**, that the cyclic hemiacetal **29** form of these compounds is more stable in solution than the corresponding open-

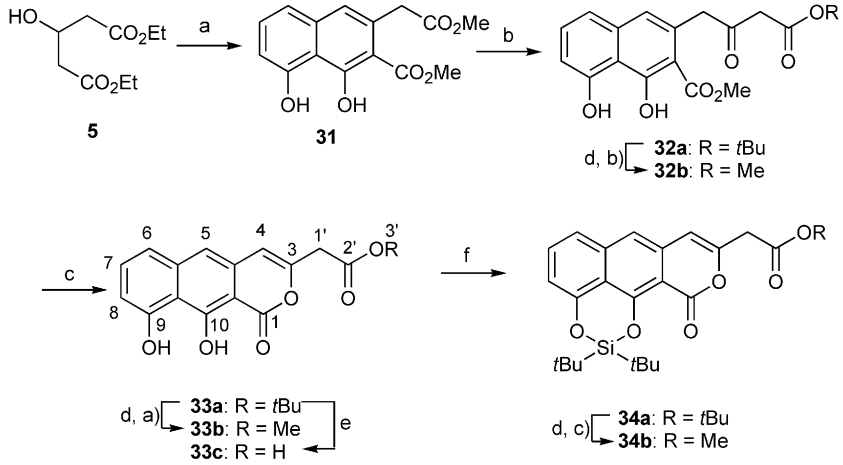


Scheme 5. Chain elongation of the naphthol **25** (via the ester **28**) to the protected tetraketide **29** through the Baker–Venkataraman reaction.

chain diketone **30**. From their NMR spectra, however, the hemiacetals appear to exist in two isomeric forms as observed by their splitting patterns, as expected for all possible keto–enol tautomeric forms. The synthesis of the model mononaphthol-ketide **29/30** thus represents an 8-deoxybisdithioketal-protected form of our synthetic goal and so the essential framework of the first target analogue molecule **2b** had been achieved. Unfortunately, though, and to our frustration, the protecting groups could not be removed without destruction of the molecule, notwithstanding the use of a large variety of different cleaving reagents,[42–44] and so this approach, although successful for the construction of the carbon skeleton of **2b**, had to be abandoned at this stage to allow us to pursue alternative routes.

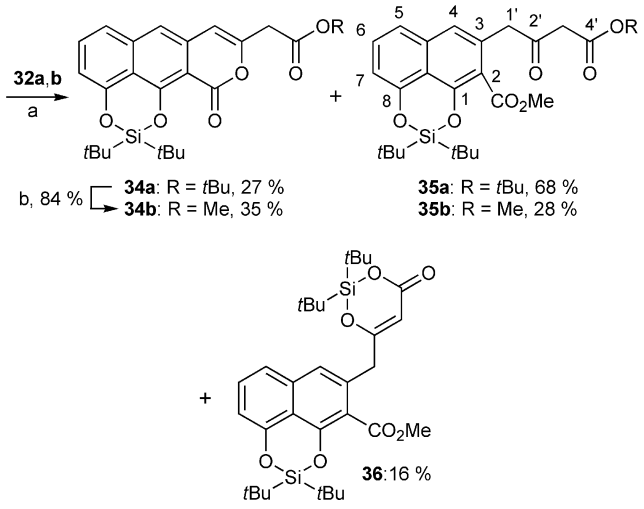
This result had, however, demonstrated that compounds such as **2** are fundamentally extremely unstable and tend to undergo spontaneous aldol-type cyclizations to yield polycyclic systems. To address, and potentially to solve, this problem of inherent instability, the synthetic protocol would have to be achieved either without the involvement of any protection groups or at least with protecting groups that are much easier to remove, such as silyl groups. Our next efforts were therefore focused in this direction, culminating in the preparation of the silyl-protected tricyclic decaketide precursors **36** (Scheme 7, below), **38** (Scheme 8, below), and **41** (Scheme 10, below) through the employment of substituted 1,8-dihydroxynaphthalenes instead of the isocoumarins as the starting materials in these cases.

Diethyl 3-hydroxyglutarate (**5**), as described by Yamaguchi,[35] was used as the starting material in the preparation of the dimethyl ester **31**, which involved a double Claisen condensation (Scheme 6). This compound was then treated with an excess of the *tert*-butyl acetate anion without protection of the two free hydroxy groups. Evidently, the formation of the phenoxide, in the presence of the *tert*-butyl acetate anion as the base and reagent, protects the vicinal methyl ester through resonance, leading to exclusive attack of the *tert*-butyl acetate anion at the aliphatic ester group to yield the keto ester **32a** in an excellent 96% yield.[37] Subsequent lactonization of the ketodiester **32a** to **33a** proceeded without any difficulty and in nearly quantitative yield by treatment with the mild base triethylamine in dichloromethane solution. To prepare the corresponding methyl ester **33b**, BBr_3 in methanol was the reagent of choice for a facile transesterification of **33a**. Hydrolysis of ester **33a** to produce the acid **33c** was achieved by treatment of the *tert*-butyl ester **33a** with trifluoroacetic acid. The two *peri* phenolic groups of both the *tert*-butyl and methyl esters **33a** and **33b** were subsequently protected as their di-*tert*-butyldisilyl ethers **34a** and **34b**, both in 91% yields, with use of di-*tert*-butyldichlorosilane in acetonitrile containing triethylamine.



Scheme 6. Synthesis of the silyl-protected tricyclic starting materials **34a** and **34b**. a) 1. LDA, MAA, THF, –78 °C, 2. $Ca(OAc)_2$, MeOH, 57%; b) LDA, TBA, THF, –78 °C, 96%; c) NEt_3, CH_2Cl_2, 99%; d) 1. BBr_3, CH_2Cl_2, 2. MeOH, 0 °C, (a) 92%, (b) 84%, (c) 91%; e) TFA, CH_2Cl_2 (98%); f) NEt_3, $SiCl_2(tBu)_2$, acetonitrile, 91%.

Interestingly, under the standard conditions for silylation of **33a** and **33b** to afford **34a** and **34b**, the phenolic groups were more readily silylated than the enolic form of the ester side chain that might have formed. Our initial plans actually involved a possible twofold silylation of both 1,3-diol groups possible for compounds **32a** and **32b** and in addition, it was also considered very important for us to study the behavior of the open-chain keto esters **35** (Scheme 7) in the dianion reactions. Therefore, the non-lactonized keto diesters **32a** and **32b** were subjected to the silylation procedure. After some experimentation, the open-chain cyclic silyl-protected keto diesters **35a** and **35b** were in fact isolated in reasonable yields together with the previously prepared lactonization products **34a** and **34b**. To our delight, careful separation of the reaction mixture obtained after the silylation of the methyl ester **32b** produced a 16% isolated yield of the much desired bis-silylation product **36**.



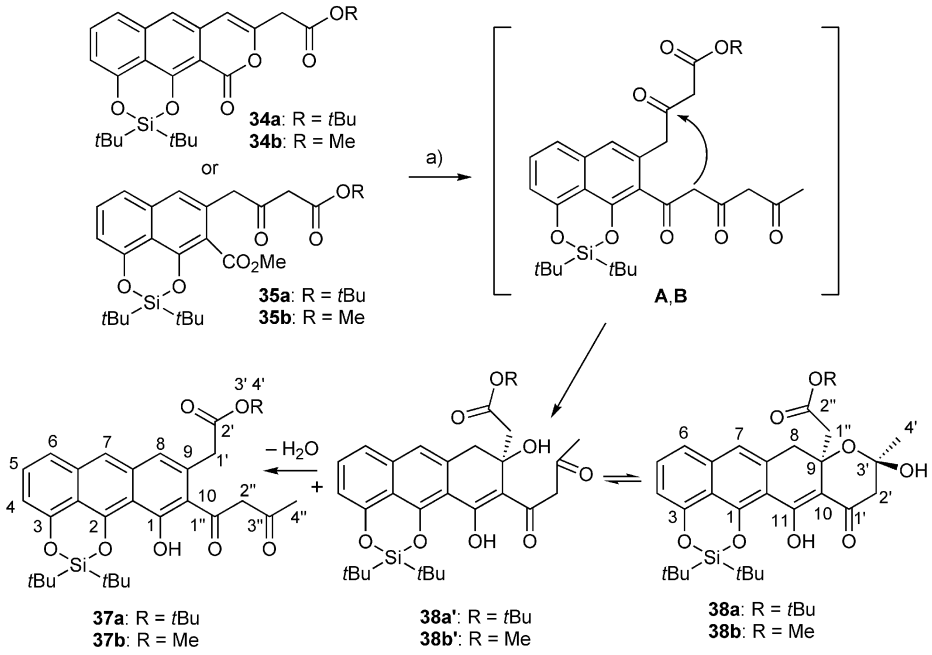
Scheme 7. Synthesis of the silyl-protected *tert*-butyl esters **34a** and **35a**, the methyl esters **34b** and **35b**, and the bis-silylation product **36**. a) NEt_3, $SiCl_2(tBu)_2$, acetonitrile; b) 1. BBr_3, CH_2Cl_2, 2. MeOH, 0 °C.

Five different silyl-protected methyl esters **34a**–**36** representing a wide range of functionalities were now available for study of the crucial chain-extension reaction with the dianion of acetylacetone. We envisioned that rapid transformation of the top keto ester group into the enolate anion should protect this chain ester from attack by the dianion. Indeed, as was also observed in the transformation of **32a** into **33a**, the dianion exclusively attacked the bottom lactone carbonyl or methyl ester. Systematic studies also revealed that the relatively sterically less hindered lactones **34a** and **34b** reacted much more rapidly and gave better yields than the more hindered open-chain analogues **35a** and **35b**. In all cases mild reaction conditions were employed, with quenching of the basic solutions with acetic acid at low temperatures at the end of the reactions.

In this way both the cyclic lactonized forms **34a** and **34b** and the open-chain *tert*-butyl and methyl esters **35a** and **35b** were transformed in clean reactions (Scheme 8) into two series of products: the major tetracyclic hemiketal **38a** (ca. 80%), together with trace amounts of **38b** (analyzed in analogy to **38a**), and the open-chain keto esters **37a** and **37b** (ca. 20%). Initial attack both on the lactones **34a** and **34b** as well as on the methyl esters **35a** and **35b** would lead to the intermediates **A** and **B**: silyl-protected molecules (*tert*-butyl and methyl ester respectively) very similar to our target molecule **2** (Scheme 1). However, under the operating basic reaction conditions, spontaneous cyclization becomes unavoidable. Attack of the carbon nucleophile of the bottom side chain (shown in square brackets in Scheme 8) at the first keto group of the top side chain initially leads to the tertiary alcohols **38a′** and **38b′**. This equilibrium can be seen in the signals of the NMR spectra and also in the typical tailing on TLC, whereas the minor products **37a** and **37b** each appeared as a single spot on TLC. Structure elucidation of the major products **38** was hampered by the complex NMR spectra due to the tautomeric equilibrium in solution. Fortunately, the *tert*-butyl ester **38a** crystallized, and single-crystal X-ray analysis (Figure 1) unambiguously revealed the stereochemistry of the hemiacetal structure **38a** (Scheme 8), in which both alkyl sides chains are on the same side of the molecule.

In solution, the major products **38a′** and **38b′** slowly undergo elimination of water to form the thermodynamically more stable protected anthracenetriols **37a** and **37b** quantitatively. These anthracene derivatives have a close resemblance to the anthraquinone aklanonic acid (**39**, Scheme 9), a shunt product in the biosynthesis of anthracycline antibiotics.[49] Aklanonic acid (**39**) is converted into the anthracycline aklavinone (**40**) by *Streptomyces galilaeus* and *Streptomyces peucetius*[46] and even a synthetic 4-deoxy derivative was microbially cyclized to a the corresponding 4-deoxyaklavinone by the same microorganisms.[47] However, it is more probable that it is in fact not the anthraquinones but rather the phenolic tricyclic anthracenes related to **37** that are the true early intermediates in the anthracycline biosynthesis, and so in considering our compounds **37a** and **37b**, we are confident that we have in fact prepared these putative silyl-protected early tricyclic anthracyclin precursors. The methyl ester **37b** was selected for feeding experiments, and it will be interesting to discover if our assumption that this is indeed the true early intermediate is establishable experimentally.

The successful syntheses of the silyl-protected anthracenetriols **37** represents just how close we are to our goal. The experiments clearly showed that the cyclization of the open-chain precursors to the corresponding anthracene derivatives was unavoidable, even at low temperatures. In order to prevent this undesired cyclization, there is no alternative other than the protection of the keto ester of the side chain and, for obvious reasons, preferably also as the di-*tert*-butylsilyl ether. This was in fact a vital component of our initial synthetic strategy. We found that the *tert*-butyl ester of the top side chain keto ester moiety was too stable to undergo the required transesterification process under basic conditions. However, as shown in Scheme 7, the bis-silyl ether **36** was indeed formed with the starting methyl



Scheme 8. Reactions between the acetylacetone dianion and the esters **34a**–**35b** to form the major tetracyclic hemiketals **38a** and **38b** and the minor tricyclic esters **37a** and **37b**. a) 1. NaH, 2. LDA, AA, THF, –40 °C.

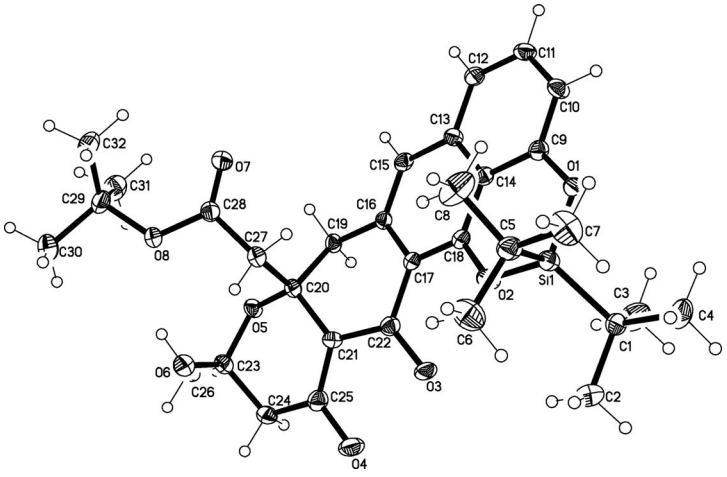
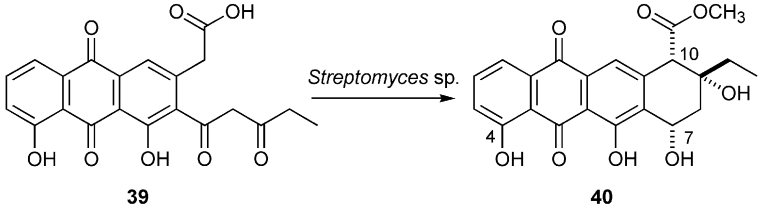
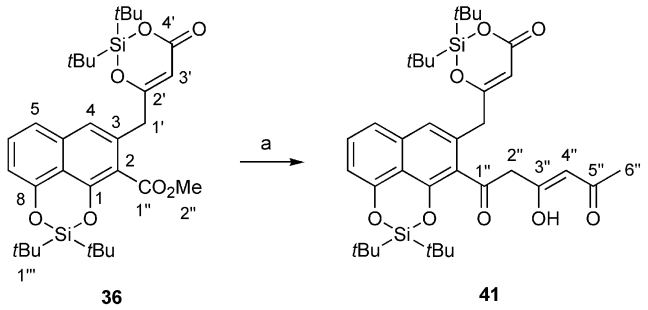


Figure 1. Single crystal X-ray analysis of the hemiketal **38a**.



Scheme 9. Conversion of aklanonic acid (**39**) into the anthracycline aklavinone (**40**) by *Streptomyces galilaeus* and *Streptomyces peucetius*.[46]

ester **32b**, albeit in a 16% yield, which in our hands proved to be sufficient to probe the reaction between **36** and the dianion of acetylacetone. Consequently, under reaction conditions similar to those described above, it was most gratifying to isolate a single product identified as **41** in 43% yield (Scheme 10). The NMR spectra showed signals for the intact top silyl-protected side chain very clearly. The bottom side chain is again able to undergo tautomerization to produce two enolic forms, as observed from the overlapping signals in the NMR spectra.



Scheme 10. Reaction between the bis-silyl-protected methyl ester **36** and the dianion of acetylacetone to form the bis-silyl-protected form **41** of the putative precursor **2**. a) 1. NaH, 2. LDA, acetylacetone, –78 °C, 43%.

Conclusions

In summary, appropriately substituted 2,3-bisalkylnaphthols were obtained in a single step starting from readily available isocoumarins. Baker–Venkataraman reactions of the corresponding esters such as **28** led to protected forms of the tetraketide target molecule **2b**. However, it was not possible to remove the dithioacetal protecting groups in **29** without destroying the molecule. Consequently, different approaches involving either no or more easily removable protecting groups were adopted. With silyl ethers as the protecting groups and substituted naphthalene-1,8-diols as starting materials, the synthesis of compound **41**, a bis-silyl-protected form of the early intermediate, could be achieved. Experience in our group has clearly found that the unprotected form **2a** of **41** easily cyclizes into the tricyclic phenolic anthracenes, and so we envisage an in situ fluoride-mediated deprotection of **41** and immediate submission of the formed product to feeding experiments.

Experimental Section

General Procedures: For instrumentation and general methods see references.[45]

Abbreviations: MAA: methyl acetoacetate, TBA: *tert*-butyl acetoacetate, AA: acetylacetone, PE: petroleum ether, EA: ethyl acetate.

8-Methoxy-3-(2′-oxopropyl)-1*H*-isochromen-1-one (13): A solution of isocoumarin (**11**,[38,48] 1.9 g, 5.7 mmol) in acetic acid (22 mL) was heated under reflux for 3 h. After dilution with toluene, the solvent was removed under reduced pressure. Purification by flash chromatography (dichloromethane/methanol, 100:0 to 98:2) afforded the ketone **13** (1.33 g, quantitative yield) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, 3′-H), 3.5 (s, 2 H, 1′-H), 3.94 (s, 3 H, OCH_3), 6.26 (s, 1 H, 4-H), 6.86 (dd, $J_{5,6}$ = 7.8, $J_{5,7}$ = 0.7 Hz, 1 H, 5-H), 6.90 (dd, $J_{7,6}$ = 8.4, $J_{7,5}$ = 0.7 Hz, 1 H, 7-H), 7.55 (dd, $J_{6,7}$ = 8.4, $J_{6,5}$ = 7.8 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 29.9 (q, C-3′), 47.7 (t, C-1′), 56.3 (q, OCH_3), 106.3 (d, C-4), 109.0 (s, C-4a or C-8a), 110.1 (d, C-7), 117.5 (d, C-5), 135.9 (d, C-6), 139.8 (s, C-4a or C-8a), 151.0 (s, C-3), 159.1 (s, C-1), 161.6 (s, C-8), 202.4 (s, C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3021, 1707, 1701, 1589, 1486, 1470, 1425, 1319, 1294, 1262, 1064, 752 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 232 (42) $[M]^+$, 190 (58), 149 (50), 122 (44), 85 (70), 57 (65), 43 (100). HRMS (EI, 70 eV): calcd. for $C_{13}H_{12}O_4$ 232.0736; found 232.0736.

3-(2′-Oxopropyl)isochromen-1-one (14): A solution of the keto ester **12**[38] (1.92 g, 6.4 mmol) in acetic acid (30 mL) was heated under reflux for 2 h and the solvent was co-evaporated with toluene. The product was crystallized from ethanol to afford the isochromenone **14** (480 mg, 37%) as fine white needles. The mother liquor was further purified by flash chromatography (dichloromethane) to afford further **14** (another 482 mg, 38%, total yield 75%); m.p. 73.5–75 °C (ethanol). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, 3′-H), 3.61 (s, 2 H, 1′-H), 6.40 (s, 1 H, 4-H), 7.38 (br. d, 1 H, 5-H), 7.49 (ddd, J = 7.9, J = 1.1 Hz, 1 H, 7-H), 7.69 (ddd, J = 7.9, J = 1.1 Hz, 1 H, 6-H), 8.25 (br. d, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.0 (q, C-3′), 47.9 (t, C-1′), 106.3 (d, C-4), 120.4 (s, C-4a), 125.4 (d), 128.4 (d), 129.6 (d), 134.9 (d), 136.9 (s, C-8a), 150.6 (s, C-3), 162.3 (s, C-1), 202.2 (s, C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 1747, 1708, 1664, 1325, 1290, 1174, 1023, 759, 693 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 202 (39) $[M]^+$, 160 (100), 131 (41), 77 (15), 43 (53). HRMS: calcd. for $C_{12}H_{10}O_3$ 202.0630; found 202.0628. $C_{12}H_{10}O_3$ (200.21): calcd. C 71.28, H 4.98; found C 70.63, H 4.69.

8-Methoxy-3-[(2′′-methyl-1′′,3′′-dioxolan-2′′-yl)methyl]-1*H*-isochromen-1-one (15): A solution of the ketone **13** (506 mg, 2.2 mmol), *p*-toluenesulfonic acid (10 mg), and ethylene glycol (0.24 mL, 4.31 mmol) in dry toluene (22 mL) was heated at reflux for 3 h under a Dean–Stark trap. After addition of anhydrous sodium carbonate and filtration, the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane to dichloromethane/methanol 98:2) afforded the unstable ketal **15** (430 mg, 72% yield) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (s, 3 H, 3′′′-H), 2.79 (s, 2 H, 1′-H), 3.95 (m, 4 H, 4′′-H, 5′′-H), 3.97 (s, 3 H, OCH_3), 6.30 (s, 1 H, 4-H), 6.88 (d, J = 8.0 Hz, 1 H, 5-H, 7-H), 7.56 (dd, $J_{6,5}$ = $J_{6,7}$ = 8.0 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.3 (q, C-1′′′), 42.9 (t, C-1′), 56.2 (q, OCH_3), 64.8 (t, C-4′′, C-5′′), 105.9 (d, C-4), 108.5 (s, C-2′′), 109.1 (q, C-4a or C-8a), 109.6 (d, C-7), 117.4 (d, C-5), 135.6 (d, C-6), 140.3 (q, C-4a or C-8a), 153.9 (s, C-3), 159.5 (s, C-1), 161.6 (s, C-8) ppm. UV (CH_2Cl_2): λ_{max} (lg ε) = 245 (3.84), 300 (3.31) nm. MS (EI, 70 eV): *m*/*z* (%) = 276 (45) $[M]^+$, 232 (90), 190 (100), 161 (85).

3-[(2-Methyl-1,3-dioxolan-2-yl)methyl]isochromen-1-one (16): A solution of the ketone **14**, a catalytic amount of *p*-toluenesulfonic acid (10 mg), and ethylene glycol in dry toluene were heated at reflux for 2 h under a Dean–Stark trap to separate the water formed. After addition of potassium sulfate, the mixture was filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (dichloromethane/diethyl ether, 100:0 to 95:5) afforded the product (966 mg, 86%) as a slightly yellow oil, which crystallized slowly in the fridge; m.p. 58–59 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.46 (s, 3 H, 1′′′-H), 2.85 (s, 2 H, 1′-H), 3.95–3.97, 3.98–4.01 (2 × m, 2 × 2 H, 4′′-H, 5′′-H), 6.41 (m, 1 H, 4-H), 7.38 (m, 1 H, 5-H), 7.46 (ddd, J = 8.0, J = 7.3, J = 1.1 Hz, 1 H, 7-H), 7.68 (ddd, J = 8.0, J = 7.3, J = 1.1 Hz, 1H-6), 8.26 (m, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.3 (q, C-1′′′), 43.1 (t, C-1′), 64.9 (t, C-4′′, C-5′′), 106.0 (d, C-4), 108.5 (s, C-2′′), 120.4 (s, C-4a or C-8a), 125.3 (d, C-5), 127.9 (d, C-7), 129.5 (d, C-8), 134.7 (d, C-6), 137.4 (s, C-4a or C-8a), 153.5 (s, C-3), 162.8 (s, C-1) ppm. IR (KBr): $\tilde{\nu}$ = 2987, 2886, 1723, 1655, 1482, 1320, 1193, 1159, 1057, 1029, 759 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 246 (21) $[M]^+$, 231 (50), 160 (50), 131 (62), 103 (49), 87 (95), 43 (100). HRMS: calcd. for $C_{14}H_{14}O_4$ 246.0892; found 246.0894.

8-Methoxy-3-[(2′′-methyl-1′′,3′′-dithiolan-2′′-yl)methyl]-1*H*-isochromen-1-one (17): Boron trifluoride etherate (0.25 mL, 2 mmol) was added at 0 °C to a solution of the ketone **13** (235 mg, 1.0 mmol) and ethane-1,2-dithiol (0.17 mL, 2.0 mmol) in dry

dichloromethane (6 mL). The mixture was stirred for 24 h at room temp. After addition of saturated aqueous sodium hydrogencarbonate (2 mL) at 0 °C, the mixture was stirred for 30 min and extracted with dichloromethane. The combined organic phases were washed with brine and dried with anhydrous sodium sulfate, and the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane/methanol 98:2) afforded the dithioketal **17** (189 mg, 61%) as a slightly yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.86 (s, 3 H, 1′′′-H), 3.11 (s, 2 H, 1′-H), 3.34 (m, 4 H, 4′′-H, 5′′-H), 3.97 (s, 3 H, OCH_3), 6.39 (s, 1 H, 4-H), 6.91 (dd, $J_{7,6}$ = 8.3, $J_{7,5}$ = 0.8 Hz, 1 H, 7-H), 6.92 (dd, $J_{5,6}$ = 7.9, $J_{5,7}$ = 0.8 Hz, 1 H, 5-H), 7.57 (dd, $J_{6,7}$ = 8.3, $J_{6,5}$ = 7.9 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.0 (q, C-1′′′), 40.1 (t, C-4′′, C-5′′), 49.2 (t, C-1′), 56.3 (q, OCH_3), 65.38 (s, C-2′′), 106.4 (d, C-4), 109.3 (s, C-4a or C-8a), 109.7 (d, C-7), 117.6 (d, C-5), 135.7 (d, C-6), 140.0 (s, C-4a or C-8a),154.8 (s, C-3), 159.2 (s, C-1), 161.6 (s, C-8) ppm. IR (KBr): $\tilde{\nu}$ = 2920, 1730, 1666, 1629, 1570, 1477, 1450, 1435, 1320, 1281, 1256, 1152, 1012, 980, 832, 691 cm^{-1}. UV (CH_2Cl_2): λ_{max} (lg ε) = 238 (3.95), 342 (3.47) nm. EI-MS (EI, 70 eV): *m*/*z* (%) = 308 (18) $[M]^+$, 279 (13), 232 (24), 190 (62), 161 (52), 119 (92), 85 (48), 43 (100). HRMS (EI, 70 eV).: calcd. for $C_{15}H_{16}O_3S_2$ 308.0541; found 308.0541.

3-[(2-Methyl-1,3-dithiolan-2-yl)methyl]isochromen-1-one (18): $BF_3{\cdot}OEt_2$ (0.25 mL, 2 mmol) was added to a mixture of 3-(2-oxopropyl)-isochromen-1-one (**14**, 2.0 g, 9.93 mmol) and ethanedithiol (1.7 mL, 19.8 mmol) in dry dichloromethane (66 mL). Workup was performed as described for **17** to afford the dithioketal **18** as a pale yellow solid (2.0 g, 72% yield); m.p. 87 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, 1′′′-H), 3.16 (s, 2 H, 1′-H), 3.32–3.41 (m, 4 H, 4′′-H, 5′′-H), 6.49 (s, 1 H, 4-H), 7.40 (br. d, 1 H, 5-H), 7.47 (ddd, *J* = 8.1, *J* = 7.6, *J* = 1.1 Hz, 1 H, 7-H), 7.68 (ddd, *J* = 8.1, *J* = 7.6, *J* = 1.1 Hz, 1 H, 6-H), 8.25 (br. d, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.0 (q, C-1′′′), 40.1 (t, C-4′′, C-5′′), 49.4 (t, C-1′), 65.2 (s, C-2′′), 106.5 (d, C-4), 120.5 (s, C-4a or C-8a), 125.5 (d, C-5), 128.1 (d, C-7), 129.5 (d, C-8), 134.7 (d, C-6), 137.1 (s, C-4a or C-8a), 154.4 (s, C-3), 162.5 (s, C-1) ppm. IR (KBr): $\tilde{\nu}$ = 2917, 1726, 1652, 1238, 1025, 763 cm^{-1}. UV (CH_2Cl_2): λ_{max} (lg ε) = 240 (4.23), 275 (4.08), 325 (3.84) nm. MS (EI, 70 eV): *m*/*z* (%) = 278 (18) $[M]^+$, 217 (3), 160 (40), 119 (100), 89 (76), 59 (90). HRMS: calcd. for $C_{14}H_{14}O_2S_2$ 278.0435; found 278.0436. $C_{14}H_{14}O_2S_2$ (278.39): calcd. C 60.40, H 5.07; found C 59.88, H 4.94.

***tert*-Butyl 3-[1-Hydroxy-8-methoxy-3-(2-methyl-[1,3]dioxolan-2-ylmethyl)naphthalen-2-yl]-3-oxopropionate (21):** A solution of the acetal **16** (246 mg, 1.0 mmol) in dry THF (2 mL) was added dropwise to a solution of the dianion of *tert*-butyl acetoacetate, prepared from *tert*-butyl acetoacetate (0.5 mL, 3.0 mmol) and LDA (5.3 mL, 6.6 mmol) [from a solution of *n*-butyllithium in hexane (1.23 mol L^{-1}) and dry diisopropylamine (1.0 mL, 7.0 equiv., 7.0 mmol) in dry THF at 0 °C]. After the system had been stirred for 3 h at room temp., a saturated ammonium chloride solution (12 mL) and diethyl ether were added, the mixture was extracted with diethyl ether, the combined organic phases were dried with anhydrous sodium sulfate, and the solvents were removed under reduced pressure. The residue was then diluted with dry methanol (3 mL) and stirred overnight at room temp. with calcium acetate (940 mg). The mixture was acidified with saturated ammonium chloride and extracted with diethyl ether, the combined organic phases were dried with anhydrous magnesium sulfate, and the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane) afforded the keto ester **21** (354 mg, 50%) as a yellow solid; m.p. 72 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (s, 3 H, Me), 1.38 [s, 9 H, $C(CH_3)_3$], 3.36–3.38 (m, 4 H, 4′′′-H, 5′′′-H, 1′′-H), 3.71–3.74 (m, 2 H, 4′′′-H, 5′′′-H), 4.02 (s, 2 H, 2-H), 7.20 (s, 1 H, 4′-H), 7.48 (ddd, *J* = 8.2, *J* = 6.8, *J* = 1.2 Hz, 1 H, 7′-H), 7.57 (ddd, *J* = 8.2, *J* = 6.8, *J* = 1.2 Hz, 1 H, 6′-H), 7.69 (m, 1 H, 5′-H), 8.38 (m, 1 H, 8′-H), 12.19 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.7 (q, Me), 27.8 [q, $C(CH_3)_3$], 45.2 (t, C-1′′), 51.6 (t, C-2), 64.9 (t, C-4′′′, C-5′′′), 82.2 [s, $C(CH_3)_3$], 109.4 (s, C-2′′′), 117.7 (s, C-2′), 123.6 (d, C-4′), 124.1 (d, C-8′), 124.5 (s, C-8′a), 125.6 (d, C-7′), 127.0 (d, C-5′), 129.5 (d, C-6′), 130.8 (s, C-3′), 135.5 (s, C-4′a), 159.1 (s, C-1′), 167.1 (s, C-1), 200.7 (s, C-3) ppm. IR (KBr): $\tilde{\nu}$ = 3252, 2983, 2880, 1723, 1705, 1683, 1346, 1327, 1145, 1046, 750 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 386 (5) $[M]^+$, 271 (10), 224 (15), 197 (7), 149 (10), 87 (100), 59 (75). HRMS ($M^+ - CH_2O$) calcd. for $C_{22}H_{26}O_6$ 386.1729; found 386.1730.

***tert*-Butyl 3-{1-Hydroxy-8-methoxy-3-[(2-methyl-1,3dithiolan-2-yl)-methyl]naphthalen-2-yl}-3-oxopropionate (22):** The dithiane **17** (500 mg, 1.62 mmol), dissolved in dry THF (1 mL), was added dropwise to a solution of the dianion of *tert*-butyl acetoacetate, prepared from *tert*-butyl acetoacetate (0.9 mL, 4.87 mmol) and LDA (9.2 mL, 10.7 mmol). Workup was performed as described for **21** to afford the keto ester **22** (366 mg, 50%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (s, 9 H, *t*Bu-H), 1.76 (s, 3 H, Me), 3.17–3.22, 3.26–3.31 (2 × m, 2 × 2 H, 4′′′-H, 5′′′-H), 3.52 (s, 2 H, 2-H), 4.06 (s, 5 H, OCH_3, 1′′-H), 6.78 (dd, 1 H, 6′-H), 7.36 (m, 3 H, 4′-H, 5′-H, 7′-H), 9.86 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.1 [q, $C(CH_3)_3$], 31.1 (q, Me), 39.8 (t, C-4′′′, C-5′′′), 46.2 (t, C-1′′), 52.5 (t, C-2), 56.3 (q, OCH_3), 67.0 (s, C-2′′′), 80.9 [s, $C(CH_3)_3$], 104.7 (d, C-6′), 113.6 (s), 121.7 (d), 122.7 (d, C-4′), 123.8 (s), 127.5 (d), 135.2 (s), 136.2 (s), 153.6 (s), 156.5 (s), 167.2 (s, C-1), 198.5 (s, C-3) ppm. IR (NaCl, film): $\tilde{\nu}$ = 3342, 2977, 2925, 1737, 1731, 1628, 1603, 1452, 1367, 1307, 1265, 1173, 1138, 1092 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 448 (25) $[M]^+$, 330 (30), 299 (14), 274 (25), 258 (41), 216 (38), 178 (15), 119 (68), 87 (19), 59 (100). HRMS: calcd. for $C_{23}H_{28}O_5S_2$ 448.1378; found 448.1371.

2-Hydroxy-2-methyl-5-[(2-methyl-1,3-dithiolan-2-yl)methyl]-2,3-dihydrobenzo[*H*]chromen-4-one (23): A solution of the isocoumarin **18** (280 mg, 1.01 mmol) in dry THF (2 mL) was added dropwise to a solution of the dianion of acetylacetone [prepared under argon at 0 °C from sodium hydride (350 mg, 8.48 mmol), *n*BuLi (3.7 mL of a 1.13 mol L^{-1} solution, 4.2 mmol) and acetylacetone (0.41 mL, 4.04 mmol)] in dry THF (8 mL). The mixture was stirred for 3 h at room temp. and after addition of dilute HCl the mixture was extracted with ethyl acetate. The combined organic phases were washed with brine and dried with anhydrous sodium sulfate, and the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane/diethyl ether, 100:0 to 95:5) afforded the hemiacetal **23** (240 mg, 66%) as a yellow gum. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.76 (s, 3 H, 1′′′′-H), 1.80 (s, 3 H, 1′-H), 2.96 (2 × d, 2 × *J* = 15.6 Hz, 2 × 1 H, 3-H), 3.06, 3.20 (2 × m, 2 × 2 H, 4′′′-H, 5′′′-H), 3.93, 4.04 (2 × d, 2 × *J* = 13.3 Hz, 2 1 H, 1′′-H), 7.37 (s, 1 H, 6-H), 7.44 (ddd, *J* = 8.2, *J* = 6.8, *J* = 1.2 Hz, 1 H, 9-H), 7.56 (ddd, *J* = 8.1, *J* = 6.8, *J* = 1.2 Hz, 1 H, 8-H), 7.72 (m, 1 H, 7-H), 8.27 (m, 1 H, 10-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.8 (q, C-1′), 32.1 (q, C-1′′′′), 39.7 (t, C-4′′′, C-5′′′), 46.0 (t, C-1′′), 49.5 (t, C-3), 68.1 (s, C-2′′′), 101.5 (s, C-2), 115.5 (s, C-5), 123.6 (d, C-10), 124.5 (s, C-10a), 125.2 (d, C-6), 125.8 (d, C-9), 127.4 (d, C-7), 129.5 (d, C-8), 134.2 (s, C-4a), 135.8 (s, C-6a), 156.9 (s, C-10b), 193.5 (s, C-4) ppm. IR (NaCl, film): $\tilde{\nu}$ = 3342, 2923, 1681, 1438 cm^{-1}. UV (CH_2Cl_2): λ_{max} (lg ε) = 255 (3.91), 335 (2.87) nm. MS (EI, 70 eV): *m*/*z* (%) = 360 (6) $[M]^+$, 286 (6), 242 (8), 198 (8), 165 (15), 140 (84), 85 (100), 43 (89). HRMS: calcd. for $C_{19}H_{20}O_3S_2$ 360.0854; found 360.0854.

1-{1-Hydroxy-3-[(2-methyl-1,3-dioxolan-2-yl)methyl]naphthalen-2-yl}ethanone (24): A solution of the isocoumarin **16** (280 mg, 1.01 mmol) in dry THF (2 mL) was added dropwise to a solution of the anion of acetone [prepared under argon at 0 °C from acetone (0.30 mL, 4.04 mmol) and sodium hydride (350 mg, 8.48 mmol) in dry THF (8 mL)]. The mixture was stirred for 3 h at room temp. After addition of dilute hydrochloric acid, the mixture was extracted with ethyl acetate, the combined organic phases were washed with brine and dried with anhydrous sodium sulfate, and the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane/diethyl ether, 100:0 to 95:5) afforded the acetyl-naphthol **24** (166 mg, 59%) as a yellow solid; m.p. 83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, 1′′′′-H), 2.73 (s, 3 H, 2-H), 3.30, 3.70 (2×m, 2×2 H, 4′′′-H, 5′′′-H), 3.45 (s, 2 H, 1′′-H), 7.19 (s, 1 H, 4′-H), 7.46 (ddd, J = 8.2, J = 7.0, J = 0.8 Hz, 1 H, 7′-H), 7.56 (ddd, J = 8.2, J = 7.0, J = 0.8 Hz, 1 H, 6′-H), 7.68 (d, J = 8.1 Hz, 1 H, 5′-H), 8.39 (m, 1 H, 8′-H), 13.22 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.9 (q, C-1′′′′), 32.5 (q, C-2), 45.8 (t, C-1′′), 60.4 (t, C-4′′′, C-5′′′), 109.4 (s, C-2′′′), 117.3 (s, C-2′), 123.4 (d, C-4′), 124.2 (d, C-8′), 124.6 (s, C-8′a), 125.6 (d, C-7′), 127.0 (d, C-5′), 129.5 (d, C-6′), 131.5 (s, C-3′), 135.5 (s, C-4′a), 160.1 (s, C-1′), 206.2 (s, C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3447, 2985, 2953, 2923, 2883, 1618, 1570, 1396, 1375, 1344, 1254, 1215, 1153, 1098, 1034, 825, 765 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 286 (8) [M]$^+$, 224 (4), 163 (59), 145 (55), 87 (64), 43 (100). HRMS: calcd. for $C_{17}H_{18}O_4$ 286.1205; found 286.1205.

1-{1-Hydroxy-3-[(2-methyl-1,3-dithiolan-2-yl)methyl]naphthalen-2-yl}ethanone (25): A solution of isocoumarin **18** (280 mg, 1.01 mmol) in dry THF (2 mL) was added dropwise to a solution of the anion of acetone [prepared under argon at 0 °C from freshly distilled acetone (0.30 mL, 4.04 mmol) and sodium hydride (240 mg, 6.06 mmol) in dry THF (8 mL)]. The mixture was stirred for 3 h at room temp. Workup was performed as described for **24** to afford the naphthol **25** (207 mg, 64%) as a yellow solid; m.p. 81–82 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.71 (s, 3 H, 1′′′′-H), 2.75 (s, 3 H, 2-H), 2.92, 3.20 (2×m, 2×2 H, 4′′′-H, 5′′′-H), 3.70 (s, 2 H, 1′′-H), 7.26 (s, 1 H, 4′-H), 7.49 (ddd, J = 8.2, J = 7.0, J = 1.1 Hz, 1 H, 7′-H), 7.59 (ddd, J = 8.2, J = 7.0, J = 1.1 Hz, 1 H, 6′-H), 7.71 (m, 1 H, 5′-H), 8.41 (m, 1 H, 8′-H), 13.28 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.1 (2×q, C-2, C-1′′′′), 40.3 (t, C-4′′′, C-5′′′), 50.6 (t, C-1′′), 67.2 (C-2′′′), 117.1 (s, C-2′), 124.0 (d, C-4′), 124.4 (d, C-8′), 124.8 (s, C-8′a), 125.9 (d, C-7′), 127.1 (d, C-6′), 129.7 (d, C-5′), 132.5 (s, C-3′), 160.1 (s, C-1′), 205.5 (s, C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2959, 2921, 1612, 1569, 1402, 1348, 1252, 1094, 752 cm^{-1}. UV (CH_2Cl_2): λ_{max} (lg ε) = 243 (4.21), 264 (4.18), 371 (3.65) nm. MS (EI, 70 eV): *m*/*z* (%) = 318 (34) [M]$^+$, 279 (8), 225 (26), 182 (76), 119 (100), 57 (85), 43 (72). HRMS: calcd. for $C_{17}H_{18}O_2S_2$ 318.0748; found 318.0748. $C_{17}H_{18}O_2S_2$ (318.45): calcd. C 64.12, H 5.70; found C 64.62, H 5.84.

3-{1-Hydroxy-8-methoxy-3-[(2-methyl-1,3-dithiolan-2-yl)methyl]-naphthalen-2-yl}ethanone (26): The keto ester **22** (320 mg, 0.71 mmol) was heated under reflux for 1 h in acetic acid (4 mL). After dilution with toluene, the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane) afforded the ketone **26** (90 mg, 36%) as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.76 (s, 3 H, 1′′′′-H), 2.70 (s, 3 H, 2-H), 3.16, 3.28 (2×m, 2×2 H, 4′′′-H, 5′′′-H), 3.51 (s, 2 H, 1′′-H), 4.06 (s, 3 H, OCH_3), 6.78 (dd, J = 7.0, J = 1.3 Hz, 1 H, 7′-H), 7.32–7.37 (m, 3 H, 4′-H, 5′-H, 6′-H), 9.77 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.2 (q, C-1′′′), 33.4 (q, C-2), 39.6, 39.8 (2×t, C-4′′′, C-5′′′), 46.3 (t, C-1′′), 56.3 (q, OCH_3), 67.0 (s, C-2′′′), 104.6 (d, C-7′), 113.7 (s, C-4′a or C-8′a), 121.7 (d, C-5′ or C-6′), 122.7 (d, C-4′), 125.4 (s, C-2′), 127.2 (C-6′ or C-5′), 134.8 (s, C-3′), 135.9 (s, C-8′a or C-4′a), 153.0 (s, C-1′), 156.4 (s, C-8′), 205.1 (s, C-1) ppm. IR (NaCl, film): $\tilde{\nu}$ = 3352, 2923, 1687, 1681, 1626, 1613, 1581, 1494, 1450, 1370, 1255, 1239, 1164, 1091 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 348 (42) [M]$^+$, 279 (14), 255 (38), 230 (75), 215 (65), 167 (18), 149 (32), 119 (100), 59 (41), 43 (33). HRMS: calcd. for $C_{18}H_{20}O_3S_2$ 348.0854; found 348.0853.

2-Acetyl-[(2-methyl-1,3-dithiolan-2-yl)methyl]naphthalen-1-yl (2-Methyl-1,3-dithiolan-2-yl)acetate (28): A solution of the phenol **25** (100 mg, 0.36 mmol) was treated with the acid **27**,[42] DCC (111 mg, 0.54 mmol), *p*-toluenesulfonic acid (5 mg), and DMAP (10 mg) in dry dichloromethane (2 mL). The mixture was stirred for 3.5 h at room temp. and filtered, and the solvent was removed under reduced pressure. Purification by flash chromatography (*n*-hexane/ethyl acetate, 9:1 to 8:2) afforded the product **28** as a colorless oil (118 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.77 (s, 3 H, 1′′′′-H), 2.03 (s, 3 H, a′′′-H), 2.63 (s, 3 H, 2′-H), 3.06, 3.26 (2×m, 2×2 H, 4′′′-H, 5′′′-H), 3.42 (m, 4 H, d′′-H, e′′-H), 3.46 (s, 2 H, b-H), 3.49 (s, 2 H, 1′′-H), 7.52–7.55, 7.83–7.85 (2×m, 2×2 H, 5-H, 6-H, 7-H, 8-H), 7.88 (s, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.5, 31.5 (2×q, C-a′′′, C-1′′′′), 33.0 (q, C-2′), 40.0 (t, C-4′′′, C-5′′′), 40.2 (t, C-d′′, C-e′′), 46.7 (t, C-1′′), 50.4 (t, C-b), 62.0 (q, C-b′′), 66.9 (s, C-2′′′), 122.0, 127.1, 127.6, 128.0 (4×d, C-5, C-6, C-7, C-8), 125.6, 133.8 (2×s, C-4a, C-8a), 132.3 (s, C-3), 133.2 (s, C-2), 143.6 (s, C-1), 168.2 (s, C-a), 202.4 (s, C-1) ppm (letters refer to the acid part, numbers to the "alcohol" part). IR (NaCl, film): $\tilde{\nu}$ = 3053, 2967, 2922, 2857, 1766, 1692, 1444, 1333, 1275, 1254, 1120, 1166 cm^{-1}. UV (CH_2Cl_2): λ_{max} (lg ε) = 230 (3.88) nm. MS (EI, 70 eV): *m*/*z* (%) = 478 (8) [M]$^+$, 414 (1), 282 (3), 360 (15), 318 (2), 279 (5), 240 (23), 224 (6), 119 (100), 98 (29), 49 (48). HRMS: calcd. for $C_{23}H_{26}O_3S_4$ 478.0765; found 478.0765.

2-Hydroxy-2,5-bis[(2-methyl-1,3-dithiolan-2-yl)methyl]-2,3-dihydrobenzo[*H*]chromen-4-one (29): Lithium hydride (28 mg) was added at 0 °C under argon to a solution of the ester **28** (100 mg, 0.21 mmol) in dry THF (21 mL). The mixture was heated under reflux for 24 h and then cooled to 0 °C, dilute hydrochloric acid was added, the mixture was extracted with dichloromethane, the combined organic phases were washed with hydrochloric acid and brine and dried over anhydrous sodium sulfate, and the solvents were removed under reduced pressure. Purification by flash chromatography (dichloromethane) afforded the hemiacetal **29** (96 mg, 96%) as a yellow solid; m.p. 60–61 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.79 (s, 3 H, 1′′′-H), 2.14 (s, 3 H, 1s′′′-H), 2.66, 2.88 (2×d, J = 15.2 Hz, 2×1 H, 1s-H), 3.01–3.05 (m, 2 H, 3-H), 3.10, 3.23 (2×m, 2×2 H, 4′′-H, 5′′-H), 3.40, 3.45 (2×m, 2×2 H, 4s′-H, 5s′-H), 3.91, 4.12 (2×d, J = 13.6 Hz, 2×1 H, 1′-H), 5.75 (d, J = 1.8 Hz, 1 H, OH), 7.42 (s, 1 H, 6-H), 7.50 (ddd, J = 8.4, J = 7.0, J = 1.5 Hz, 1 H, 9-H), 7.59 (ddd, J = 8.2, J = 7.0, J = 1.3 Hz, 1 H, 8-H), 7.75 (m, 1 H, 7-H), 8.32 (m, 1 H, 10-H) ppm (s refers to the hemiketal side chain). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.2 (q, C-1′′′), 33.3 (q, C-1s′′), 39.2 (t, C-4s′, C-5s′), 39.8 (t, C-4′′, C-5′′), 46.0 (t, C-1′), 50.8 (t, C-3), 52.2 (t, C-1s), 63.2 (s, C-2s′), 68.1 (s, C-2′′), 102.7 (s, C-2), 116.0 (s, C-5), 123.8 (d, C-10), 124.5 (s, C-10a), 125.5 (d, C-6), 126.0 (d, C-9), 127.6 (d, C-7), 129.4 (d, C-8), 134.2 (s, C-4a), 135.8 (s, C-6a), 156.6 (s, C-10b), 192.8 (s, C-4) ppm (s refers to the hemiketal side chain). IR (KBr): $\tilde{\nu}$ = 3431, 2921, 1683, 1675, 1653, 1624, 1569, 1437, 668 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 478 (10) [M]$^+$, 342 (62), 276 (10), 249 (8), 224 (7), 152 (8), 119 (100), 43 (80). HRMS: calcd. for $C_{23}H_{26}O_3S_4$ 478.0765; found 478.0768.

Methyl 1,8-Dihydroxy-3-(4-methoxy-2,4-dioxobutyl)-2-naphthoate (32b): The *tert*-butyl ester **32a** (300 mg, 0.80 mmol) in CH_2Cl_2

(10 mL) was treated with BBr_3 (1 M, 1.6 mL in CH_2Cl_2) as described for **33b** to afford the dimethyl ester **32b** as yellow crystals (224 mg, 0.67 mmol, 84%); m.p. 184–188 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.49 (s, 2 H, CH_2), 3.74 (s, 3 H, CO_2CH_3), 3.95 (s, 3 H, CO_2CH_3), 4.13 (s, 2 H, CH_2) 6.91 (dd, $J_{7,6}$ = 8.0, $J_{7,5}$ = 1.0 Hz, 1 H, 7-H), 7.01 (s, 1 H, 4-H), 7.15 (dd, $J_{5,6}$ = 8.0, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 7.48 (t, $J_{6,5}$ = $J_{6,7}$ = 8.0 Hz, 1 H, 6-H), 9.74 (s, 1 H, OH), 14.21 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.23 (CH_2), 51.37 (CH_2), 52.35 (C-2′′), 52.64 (C-5′), 104.21 (C-2), 111.94 (C-5), 113.37 (C-8a), 118.17 (C-7), 124.13 (C-4), 129.59 (C-4a), 132.04 (C-6), 137.77 (C-3), 156.94 (C-8), 164 (C-1), 167.51 (C-4′), 172.34 (C-1′′), 199.83 (C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3423, 2972, 1748, 1585, 1460, 1351, 1215, 1074, 981, 764 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 251 (4.69), 359 (3.98) nm. MS (EI, 70 eV): *m*/*z* (%) = 300 (100), 268 (10), 226 (50), 199 (20), 171 (15), 149 (10), 115 (20), 61 (60). HRMS (EI): calcd. for $C_{17}H_{16}O_7$ 332.0900; found 332.0896.

***tert*-Butyl 2-(9,10-Dihydroxy-1-oxo-1*H*-benzo[*g*]isochromen-3-yl)-acetate (33a):** A solution of the methyl ester **32a**[10,48] (5.00 g, 13.4 mmol) in CH_2Cl_2 (10 mL) was treated with NEt_3 (16 mmol, 2.2 mL) and heated under reflux under argon for ca. 3 h. The solvent was evaporated under reduced pressure, aqueous HCl (2 N, 50 mL) was added, and the mixture was extracted with dichloromethane (100 mL). The organic phase was washed with water (50 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was triturated with dichloromethane (5 mL) and the solid was filtered to afford bright yellow crystals of the lactone **33a** (4.50 g, 99%); m.p. 152 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50 [s, 9 H, $C(CH_3)_3$], 3.46 (s, 2 H, CH_2), 6.44 (s, 1 H, 4-H), 6.91 (dd, $J_{8,7}$ = 8.0, $J_{8,6}$ = 1.0 Hz, 1 H, 8-H), 7.16 (s, 1 H, 5-H), 7.24 (d, $J_{6,7}$ = 8.0 Hz, 1 H, 6-H), 7.52 (t, $J_{7,8}$ = $J_{7,6}$ = 8.0 Hz, 1 H, 7-H), 9.36 (s, 1 H, OH), 13.47 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.04 (3 × CH_3), 40.11 (C-1′), 82.33 (C-3′), 99.27 (C-10a), 107.11 (C-4), 111.00 (C-8), 112.57 (C-9a), 114.58 (C-5), 118.78 (C-6), 130.23 (C-4a), 132.48 (C-7), 139.81 (C-5a), 148.72 (C-3), 156.94 (C-9), 162.20 (C-10), 167.25 (C-2′), 167.83 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3368, 2924, 1682, 1460, 1387, 1273, 1093, 1051, 881, 700 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 262 (4.78), 350 (4.03), 404 (4.17) nm. MS (EI, 70 eV): *m*/*z* (%) = 342 (80), 286 (100), 242 (35), 213 (30), 150 (45), 122 (15), 57 (95), 43 (30). HRMS (EI): calcd. for $C_{19}H_{18}O_6$ 342.1103; found 342.1103.

Methyl 2-(9,10-Dihydroxy-1-oxo-1*H*-benzo[*g*]isochromen-3-yl)acetate (33b): A solution of the lactone **33a** (1 g, 2.9 mmol) in CH_2Cl_2 (100 mL) was treated at 0 °C with BBr_3 (5.85 mL, 1 M in CH_2Cl_2). After 1 h dry methanol (10 mL) was added and the temperature was allowed to rise to room temp. over 4 h. The solvent was removed under reduced pressure and the residue was dissolved in MeOH (20 mL). Aqueous HCl (2 N, 20 mL) was added, the mixture was extracted with ethyl acetate (50 mL), the organic phase was washed with water, dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 7:3) to afford the lactone **33b** (0.80 g, 92%); m.p. 178 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.49 (s, 2 H, CH_2), 3.71 (s, 3 H, CH_3), 6.39 (s, 1 H, 4-H), 6.83 (d, $J_{8,7}$ = 8.0 Hz, 1 H, 8-H), 7.10 (s, 1 H, 5-H), 7.18 (d, $J_{6,7}$ = 8.0 Hz, 1 H, 6-H), 7.45 (t, $J_{7,8}$ = $J_{7,6}$ = 8.0 Hz, 1 H, 7-H), 9.28 (s, 1 H, OH), 13.36 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.76 (CO_2CH_3), 52.60 (C-1′), 99.25 (C-10a), 107.43 (C-4), 111.15 (C-8), 112.63 (C-9a), 114.75 (C-5), 118.83 (C-6), 130.02 (C-4a), 132.57 (C-7), 139.79 (C-5a), 147.91 (C-3), 156.95 (C-9), 162.26 (C-10), 167.70 (C-2′), 168.49 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3467, 2961, 1748, 1683, 1444, 1384, 1275, 1123 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 251 (4.15), 362 (3.30) nm. MS (EI, 70 eV): *m*/*z* (%) = 300 (100), 226 (50), 213 (40), 149 (25), 97 (10), 57 (30), 43 (25). HRMS (EI): calcd. for $C_{16}H_{12}O_6$ 300.0634; found 300.0631.

2-(9,10-Dihydroxy-1-oxo-1*H*-benzo[*g*]isochromen-3-yl)acetic Acid (33c): A solution of the *tert*-butyl ester **33a**[10,48] (500 mg, 1.46 mmol) in CH_2Cl_2 (20 mL) was treated at room temp. for 12 h with trifluoroacetic acid (1 mL). The solvent was removed under reduced pressure, CH_2Cl_2 (10 mL) was added, and the solvent was removed again under reduced pressure. The procedure was repeated twice and the acid was triturated with MeOH (0.5 mL) and then precipitated by addition of CH_2Cl_2 (3 mL) to afford greenish yellow crystals of the lactone acid **33c** (410 mg, 1.43 mmol, 98%); m.p. 195–205 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.61 (s, 2 H, CH_2), 6.44 (s, 1 H, 4-H), 6.67 (s, 1 H, 5-H), 6.87 (d, $J_{8,7}$ = 8.0 Hz, 1 H, 8-H), 7.16 (d, $J_{6,7}$ = 8.0 Hz, 1 H, 5-H), 7.53 (t, $J_{7,8}$ = $J_{7,6}$ = 8.0 Hz, 1 H, 7-H), 9.36 (s, 1 H, OH), 13.47 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.97 (C-1′), 99.64 (C-10a), 107.04 (C-4), 110.79 (C-8), 113.05 (C-9a), 114.14 (C-5), 119.03 (C-6), 131.32 (C-4a), 132.45 (C-7), 140.17 (C-5a) 149.73 (C-3), 157.00 (C-9), 162.85 (C-10), 166.45 (C-2′), 170.39 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3447, 2981, 1731, 1647, 1447, 1384, 1241, 1132 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 258 (4.6), 347 (3.93), 405 (4.07) nm. MS (EI, 70 eV): *m*/*z* (%) = 286 (50), 242 (100), 227 (20), 213 (25), 200 (15), 199 (8), 171 (68), 157 (4), 139 (20), 125 (12), 115 (24), 99 (4), 85 (8), 63 (8), 44 (16). HRMS (EI): calcd. for $C_{15}H_{10}O_6$ 286.0477; found 286.0477.

***tert*-Butyl 2-[9,10-Di(*tert*-butylsilyloxy)-1-oxo-1*H*-benzo[*g*]isochromen-3-yl]acetate (34a):** A solution of the bisphenol **33a** (500 mg, 1.46 mmol) in acetonitrile was treated at room temp. with di-*tert*-butyldichlorosilane (0.4 mL, 1.90 mmol) and triethylamine (1.22 mL, 8.8 mmol). The reaction mixture was heated to 65 °C for ca. 3 h until the starting material was consumed (TLC monitoring). The solvent was removed under reduced pressure and HCl (2 N, 20 mL) was added to the residue. The mixture was extracted with dichloromethane and the solvent was again removed under reduced pressure. The organic phase was washed with water, dried (Na_2SO_4), filtered, and purified by column chromatography on silica gel (PE/EA 9:1) to afford the di-*tert*-butylsilyl ether **34a** as a viscous oil (641 mg, 1.33 mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 [s, 18 H, 2 × $C(CH_3)_3$], 1.48 (s, 9 H, 3 × CH_3), 3.40 (s, 2 H, CH_2), 6.29 (s, 1 H, 4-H), 6.87 (dd, $J_{8,7}$ = 8, $J_{8,6}$ = 0.7 Hz, 1 H, 8-H), 7.17 (s, 1 H, 5-H), 7.29 (d, $J_{6,7}$ = 7.5 Hz, 1 H, 6-H), 7.42 (t, $J_{7,6}$ = $J_{7,8}$ = 7.5 Hz, 1 H, 7-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.13 (C-1′), 26.15 (C-2′), 28.05 (3 × CH_3), 40.40 (C-1′), 81.86 (C-3′), 104.11 (C-10a), 105.43 (C-4), 112.06 (C-8), 114.82 (C-5), 115.46 (C-9a), 120.02 (C-6), 130.93 (C-7), 133.72 (C-4a), 138.44 (C-5a), 149.52 (C-3), 152.78 (C-9), 156.54 (C-10), 158.50 (C-1), 167.81 (C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3450, 3059, 2863, 1743, 1672, 1580, 1471, 1378, 1291, 1145 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 389 (4.34), 267 (5.27) nm. MS (EI, 70 eV): *m*/*z* (%) = 482 (80), 426 (100), 382 (40), 370 (30), 353 (20), 326 (10), 239 (15), 167 (20), 149 (40), 105 (20), 91 (80), 57 (50). HRMS (EI): calcd. for $C_{27}H_{34}O_6Si$ 482.2100; found 482.2126.

Treatment of *tert*-Butyl 2-[9,10-Di(*tert*-butylsilyloxy)-1-oxo-1*H*-benzo[*g*]isochromen-3-yl]acetate (34a) with the Acetylacetone Dianion: Acetylacetone (0.35 mL, 3.40 mmol) was added at –50 °C to a solution of LDA prepared from diisopropylamine (1 mL, 7.14 mmol) and *n*BuLi (2.9 mL, 6.97 mmol) in dry THF (40 mL) and the mixture was stirred for 30 min at this temperature and then cooled to –78 °C for storage. A solution of the methyl ester **34a** (175 mg) in THF (5 mL) was treated at 0 °C with NaH (40 mg) and this solution was added to the dianion solution. The mixture was allowed to warm to 0 °C over 1 h and then neutralized carefully

by addition of acetic acid (1 mL, 17.50 mmol). The mixture was extracted twice with ethyl acetate (30 mL), the organic phase was washed with water and brine and dried ($MgSO_4$), and the solvent was removed under reduced pressure. TLC analysis showed the presence of two products, which were separated by column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the major product **38a** (164 mg, 78%) and the minor product **37a** (40 mg, 19%, m.p. 165 °C).

***tert*-Butyl 2-[2,2-Di-*tert*-butyl-9,11-dihydroxy-10-(3-oxobutanoyl)-8,9-dihydroanthra[1,9-*de*][1,3,2]dioxasilin-9-yl]acetate (38a):** ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 [s, 18 H, 2 × $C(CH_3)_3$], 1.48 (s, 9 H, 3 × CH_3), 1.51 (s, 3 H, CH_3), 2.44 (s, 2 H, CH_2CO_2tBu), 2.96 (d, $J_{8a,8b}$ = 16 Hz, 1 H, 8a-H), 3.08 (d, $J_{8b,8a}$ = 16 Hz, 1 H, 8b-H), 6.82 (d, $J_{4,5}$ = 1 Hz, 1 H, 4-H), 7.42 (t, $J_{5,4}$ = $J_{5,6}$ = 8 Hz, 1 H, 5-H), 7.51 (d, $J_{6,5}$ = 8 Hz, 1 H, 6-H), 7.69 (s, 1 H, 7-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.75 (CH_3), 21.3 (C-1′′′′), 26.4 (C-2′′′′), 28.3 (C-2′′′), 42.8 (C-1′′), 48.8 (C-8), 59.5 (C-2′), 80.6 (C-1′′′), 81.0 (C-3′), 110.6 (C-4), 114.4 (C-3a), 117.4 (C-1a), 120.5 (C-7), 124.2 (C-6), 126.4 (C-7a), 128.5 (C-6a), 135.2 (C-5), 151.6 (C-1), 151.9 (C-3), 162.1 (C-11), 171.7 (C-2′′), 191.3 (C-1′) ppm. IR (KBr): $\tilde{\nu}$ = 3441, 2929, 1734, 1615, 1563, 1393, 1155, 1049, 829 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 274 (3.98), 381 (4.54), 432 (4.25) nm. MS (EI, 70 eV): *m*/*z* (%) = 582 (20), 564 (80), 508 (95), 467 (100), 450 (45), 424 (65), 409 (75), 383 (25), 279 (10), 149 (35), 91 (20), 57 (35). HRMS (EI): calcd. for $C_{32}H_{42}O_8Si$ 582.2610; found 582.2619.

Data for *tert*-Butyl 4-[2,2-Di-*tert*-butyl-4-(3,5-dioxohexanoyl)-naphtho[1,8-*de*][1,3,2]dioxasilin-5-yl]-3-oxobutanoate (37a): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 [s, 18 H, 2 × $C(CH_3)_3$], 1.46 (s, 9 H, 3 × CH_3), 2.46 (s, 3 H, $COCH_3$), 4.18 (s, 2 H, CH_2), 6.29 (s, 1 H, CH), 6.91 (dd, $J_{4,5}$ = 7, $J_{4,6}$ = 1 Hz, 1 H, 4-H), 7.39 (s, 1 H, 8-H), 7.41 (t, $J_{5,4}$ = $J_{5,6}$ = 8 Hz, 1 H, 5-H), 7.50 (d, $J_{6,5}$ = 8 Hz, 1 H, 6-H), 7.82 (s, 1 H, 7-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.63 (CH_3), 21.19 [$C(CH_3)_3$], 26.43 (C-1′′′), 28.2 (C-4′′), 42.88 (C-1′′), 80.45 (C-3′′), 110.43 (C-3a), 110.61 (C-4), 113.59 (C-2′), 114.44 (C-2a), 117.88 (C-7), 118.47 (C-10), 120.46 (C-6), 128.51 (C-8), 128.84 (C-5), 130.5 (C-9), 133.77 (C-7a), 135.58 (C-6a), 150.16 (C-2), 151.6 (C-1), 158.23 (C-3), 163.14 (C-3′), 171.57 (C-2′′), 178.8 (C-1′) ppm. IR (KBr): $\tilde{\nu}$ = 3447, 2981, 1731, 1647, 1376, 1295, 1132 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 224 (3.25), 418 (3.62) nm. MS (EI, 70 eV): *m*/*z* (%) = 564 (16), 535 (4), 508 (20), 467 (72), 450 (12), 424 (24), 409 (54), 383 (16), 364 (12), 307 (10), 255 (10), 198 (16), 167 (24), 149 (60), 113 (40), 85 (40), 71 (56), 57 (100). HRMS (EI, 70 eV): calcd. for $C_{32}H_{40}O_7Si$ 564.2500; found 564.2504.

Methyl 2-[9,10-Di(*tert*-butylsilyloxy)-1-oxo-1*H*-benzo[*g*]isochromen-3-yl]acetate (34b): A solution of the isochromene methyl acetate **33b** (136 mg, 0.45 mmol) in acetonitrile (5 mL) was treated at room temp. with di-*tert*-butyldichlorosilane (0.13 mL, 0.59 mmol) and triethylamine (0.38 mL, 2.7 mmol). The reaction conditions and workup were performed as described for **34a** to afford the silyl ether **34b** (182 mg, 91%); m.p. 151.2–156.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 [s, 18 H, 2 × $C(CH_3)_3$], 3.49 (s, 2 H, CH_2), 3.74 (s, 3 H, CH_3), 6.30 (s, 1 H, CH), 6.87 (dd, $J_{8,7}$ = 8.0, $J_{8,6}$ = 1.0 Hz, 1 H, 8-H), 7.17 (s, 1 H, 5-H), 7.29 (d, $J_{6,7}$ = 8.0 Hz, 1 H, 6-H), 7.43 (t, $J_{7,8}$ = $J_{7,6}$ = 8.0 Hz, 1 H, 7-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.13 (C-1′′), 26.13 (C-2′′), 39.10 (CH_2), 52.40 (C-3′), 104.04 (C-10a), 105.71 (C-4), 112.19 (C-8), 114.93 (C-5), 115.53 (C-9a), 120.03 (C-6), 131.01 (C-4a), 133.51 (C-7), 138.44 (C-5a), 148.73 (C-3), 152.81 (C-9), 156.66 (C-10), 158.41 (C-2′), 169.00 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3450, 2863, 1737, 1688, 1580, 1471, 1373, 1248, 1155, 1096, 1009, 845 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 265 (4.12), 346 (2.82), 380 (2.75) nm. MS (EI, 70 eV): *m*/*z* (%) = 440 (44), 382 (20), 326 (10), 279 (18), 206 (50), 191 (100), 149 (60), 119 (100), 92 (80), 65 (40), 65 (40), 57 (30), 43 (20). HRMS (EI, 70 eV): calcd. for $C_{24}H_{28}O_6Si$ 440.1700; found 440.1656.

Methyl 5-(4-*tert*-Butoxy-2,4-dioxobutyl)-2,2-di-*tert*-butylnaphtho-[1,8-*de*][1,3,2]dioxasiline-4-carboxylate (35a): A solution of the 1,8-dihydroxy-2-naphthoate (**32a**) (500 mg, 1.34 mmol) in acetonitrile (10 mL) di-*tert*-butyldichlorosilane (0.57 mL, 2.68 mmol), and triethylamine (0.56 mL, 4 mmol) was allowed to react as described for **34a** to afford the oily open-chain silyl ether **35a** (468 mg, 68%, along with 28% of **34a**). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09 [s, 18 H, 2 × $C(CH_3)_3$], 1.46 (s, 9 H, 3 × CH_3), 3.45 (s, 2 H, CH_2), 3.88 (s, 3 H, CO_2CH_3), 3.98 (s, 2 H, CH_2), 6.88 (dd, $J_{7,6}$ = 7.5, $J_{7,5}$ = 1.0 Hz, 1 H, 8-H), 7.19 (s, 1 H, 4-H), 7.26 (dd, $J_{5,6}$ = 7.5, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 7.33 (t, $J_{6,5}$ = $J_{6,7}$ = 7.5 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.14 (C-1′′′), 26.17 (C-2′′′), 27.99 (C-6′), 48.19 (CH_2), 49.88 (CH_2), 51.80 (CO_2CH_3), 81.79 (C-5′), 112.45 (C-7), 115.31 (C-8a), 116.53 (C-2), 120.06 (C-5), 122.38 (C-4), 129.14 (C-6), 130.48 (C-3), 136.14 (C-4a), 150.41 (C-1), 151.54 (C-8), 166.48 (C-4′), 168.17 (C-1′′), 200.43 (C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3418, 2863, 1721, 1629, 1476, 1384, 1280, 1172, 1096, 883 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 221 (4.96), 319 (4.02), 338 (4.29) nm. MS (EI, 70 eV): *m*/*z* (%) = 514 (80), 458 (60), 426 (100),382 (40), 370 (30), 326 (20), 257 (15), 57 (40). HRMS (EI, 70 eV): calcd. for $C_{28}H_{38}O_7Si$ 514.6800; found 514.2387.

Silylation of Methyl 1,8-Dihydroxy-3-(4-methoxy-2,4-dioxobutyl)-2-naphthoate (32b): A solution of the 1,8-dihydroxy-2-naphthoate **32b** (800 mg, 2.41 mmol), di-*tert*-butyldichlorosilane (1.5 mL, 7.23 mmol), and triethylamine (2 mL, 14.46 mmol) in acetonitrile (20 mL) was allowed to react as described for **34a** to afford the three silyl ethers **34b** (353 mg, 35%), **35b** (299 mg, 28%), and **36** (231 mg, 16%). The mixture was separated by column chromatography on silica gel (ca. 40 g of silica gel, (PE/EA 20:1, 15:1, 9:1).

Data for Methyl 2-(9,10-Di-*tert*-butylsilyloxy-1-oxo-1*H*-benzo[*g*]-isochromen-3-yl)acetate (35b): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 [s, 9 H, $C(CH_3)_3$], 1.14 [s, 9 H, $C(CH_3)_3$], 2.91 (d, $J_{3a',3b'}$ = 15 Hz, 1 H, 3a′-H), 3.12 (d, $J_{3b',3a'}$ = 15 Hz, 1 H, 3b′-H), 3.42 (d, $J_{1a',1b'}$ = 3 Hz, 1 H, 1a′-H), 3.43 (s, 3 H, CO_2CH_3), 3.49 (d, $J_{1b',1a'}$ = 3 Hz, 1 H, 1b′-H), 3.74 (s, 3 H, CO_2CH_3), 6.88 (dd, $J_{7,6}$ = 8.0, $J_{7,5}$ = 1.0 Hz, 1 H, 7-H), 7.14 (s, 1 H, 4-H), 7.26 (d, $J_{5,6}$ = 8 Hz, 1 H, 5-H), 7.41 (t, $J_{6,5}$ = $J_{6,7}$ = 8.0 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.02 (C-1′′′), 26.15 (C-2′′′), 37.78 (C-1′), 40.86 (C-3′), 50.31 (C-2′′), 52.04 (C-5′), 102.26 (C-2), 112.59 (C-5), 115.86 (C-8a), 118 (C-4), 119.76 (C-7), 130.65 (C-6), 133.41 (C-4a), 137.77 (C-3), 156.94 (C-8), 164 (C-1), 167.51 (C-4′), 172.34 (C-1′′), 199.83 (C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3439, 2945, 1743, 1629, 1476, 1373, 1270, 1101, 1052, 878 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 232 (4.73), 323 (3.96) nm. MS (EI, 70 eV): *m*/*z* (%) = 472 (30), 440 (40), 414 (80), 382 (100), 371 (20), 326 (50), 283 (20), 269 (20), 213 (10), 167 (10), 149 (30), 77 (15), 57 (20). HRMS (EI, 70 eV): calcd. for $C_{25}H_{32}O_7Si$ 472.1900; found 472.1919.

Data for Methyl 2,2-Di-*tert*-butyl-5-[(2,2-di-*tert*-butyl-4-oxo-4*H*-1,3,2-dioxasilin-6-yl)methyl]naphtho[1,8-*de*][1,3,2]dioxasiline-4-carboxylate (36): Yield 16% (231 mg, 0.39 mmol, m.p. 184–188 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01 [s, 18 H, 2 × $C(CH_3)_3$], 1.12 [s, 18 H, 2 × $C(CH_3)_3$], 3.79 (s, 3 H, CO_2CH_3), 4.40 (s, 2 H, CH_2), 5.42 (s, 1 H, CH), 6.87 (dd, $J_{7,6}$ = 7.5, $J_{7,5}$ = 1.0 Hz, 1 H, 7-H), 7.29 (dd, $J_{5,6}$ = 7.5, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 7.34 (t, $J_{6,5}$ = $J_{6,7}$ = 7.5 Hz, 1 H, 6-H), 7.41 (s, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.00 (C-1′′′′), 21.20 (C-1′′′), 26.17 (C-2′′′′), 26.72 (C-2′′′), 35.37 (C-1′), 51.10 (C-2′′), 100.67 (C-3′), 112.21 (C-7), 115.09 (C-8a), 119.56 (C-2), 120.08 (C-5), 121.37 (C-4), 129.19 (C-

6), 131.48 (C-3), 136.37 (C-4a), 150.14 (C-1), 151.69 (C-8), 161.34 (C-1′′), 168.22 (C-4′), 168.66 (C-2′) ppm. IR (KBr): $\tilde{\nu}$ = 3451, 2945, 1754, 1645, 1476, 1373, 1275, 1199, 1085, 970, 856 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 221 (5.47), 347 (3.74) nm. MS (EI, 70 eV): *m*/*z* (%) = 598 (100), 541 (8), 498 (4), 455 (10), 441 (20), 353 (4), 337 (10), 300 (12), 226 (4), 134 (8), 123 (10), 91 (10), 61 (12). HRMS (EI, 70 eV): calcd. for $C_{32}H_{46}O_7Si_2$ 598.2800; found 598.2782.

1-{2,2-Di-*tert*-butyl-5-[(2,2-di-*tert*-butyl-4-oxo-4*H*-1,3,2-dioxasilin-6-yl)methyl]naphtho[1,8-*de*][1,3,2]dioxasilin-4-yl}-3-hydroxyhex-2-ene-1,5-dione (41): A solution of acetylacetone (3.34 mmol, 0.34 mL) in dry THF (1 mL) was added to a solution of LDA [prepared from diisopropylamine (8.68 mmol, 1.22 mL) and *n*BuLi (7.68 mmol, 6.3 mL)] in dry THF (50 mL). A solution of **36** (200 mg) was then added as described in the case of **34a** to afford **41** (96 mg, 43%) as a viscous oil after column chromatographic purification on silica gel (PE/EA 9:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01 [s, 18 H, 2 × $C(CH_3)_3$], 1.12 [s, 18 H, 2 × $C(CH_3)_3$], 4.40 (s, 2 H, CH_2), 5.42 (s, 1 H, CH), 5.66 (s, 1 H, CH), 6.87 (dd, $J_{7,6}$ = 7.5, $J_{7,5}$ = 1.0 Hz, 1 H, 7-H), 7.29 (dd, $J_{5,6}$ = 7.5, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 7.34 (t, $J_{6,5}$ = $J_{6,7}$ = 7.5 Hz, 1 H, 6-H), 7.39 (s, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.00 (C-1′′′′), 21.20 (C-1′′′), 26.16 (C-2′′′′), 26.72 (C-2′′′), 30.30 (C-6′′), 36.44 (C-1′), 53.76 (C-4′′), 102.19 (C-2′′), 108.17 (C-3′), 112.16 (C-7), 115.09 (C-8a), 119.39 (C-2), 120.12 (C-5), 121.42 (C-4), 129.16 (C-6), 131.50 (C-3), 136.36 (C-4a), 150.26 (C-1), 151.69 (C-8), 161.24 (C-1′′), 167.58 (C-4′), 184.98 (C-3′′), 185.23 (C-2′), 202.21 (C-5′′) ppm. IR (KBr): $\tilde{\nu}$ = 3472, 2944, 1739, 1579, 1481, 1372, 1253, 1113, 824, 684 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 228 (5.01), 317 (4.55), 349 (4.57) nm. MS (EI, 70 eV): *m*/*z* (%) = 666.3 (100), 609 (20), 523 (10), 498 (75), 397 (30), 340 (10), 284 (10), 227 (10), 199 (10), 142 (25), 57 (100), 43 (50). HRMS (EI, 70 eV): calcd. for $C_{36}H_{50}O_8Si_2$ 666.3000; found 666.3043.

Treatment of Lactone 34b or Methyl Ester 35b with the Acetylacetone Dianion: A solution of acetylacetone (1.95 mmol, 0.20 mL) in dry THF (2 mL) was added to a solution of LDA [prepared from diisopropylamine (4.37 mmol, 0.61 mL) and *n*BuLi (4.13 mmol, 1.60 mL)] in dry THF (40 mL). A solution of **34b** (214 mg, 0.49 mmol) was then added as described in the case of **34a** to afford **37b** (237 mg, 92%) after column chromatographic purification on silica gel (petroleum ether/ethyl acetate, 3:1). The corresponding reaction of the methyl ester **35b** (300 mg, 0.64 mmol) afforded **37b** (274 mg, 82%) in addition to trace amounts of **38b**.

Data for Methyl 2-[2,2-Di-*tert*-butyl-11-hydroxy-10-(3-oxobutanoyl)-anthra[9,1-*de*][1,3,2]dioxasilin-9-yl]acetate (37b): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 [s, 18 H, 2 × $C(CH_3)_3$], 2.18 (s, 3 H, $COCH_3$), 3.71 (s, 3 H, CO_2CH_3), 3.85 (s, 2 H, CH_2), 5.96 (s, 1 H, CH), 6.84 (d, $J_{4,5}$ = 7.5 Hz, 1 H, 4-H), 7.12 (s, 1 H, 8-H), 7.38 (t, $J_{5,4}$ = $J_{5,6}$ = 7.5 Hz, 1 H, 5-H), 7.43 (d, $J_{6,5}$ = 7.5 Hz, 1 H, 6-H), 7.68 (s, 1 H, 7-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.76 [$C(CH_3)_3$], 24.95 (C-4′), 27.16 (C-2′′′), 39.35 (C-1′), 52.28 (C-3′), 77.20 (C-), 103.84 (C-2′′), 110.10 (C-3a), 115.00 (C-2a), 120.96 (C-10), 121.20 (C-8), 121.60 (C-7), 128.46 (C-6), 131.10 (C-9), 133.12 (C-7a), 135.15 (C-6a), 135.67 (C-5), 145.00 (C-2), 157.64 (C-3), 160.00 (C-1), 170.40 (C-2′), 185.00 (C-1′′), 191.18 (C-3′) ppm. IR (KBr): $\tilde{\nu}$ = 3436, 2929, 1739, 1646, 1465, 1387, 1268, 1051, 570 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 245 (4.31) nm. MS (EI, 70 eV): *m*/*z* (%) = 522 (32), 492 (10), 462 (30), 438 (20), 406 (10), 337 (20), 183 (50), 149 (54), 119 (75), 97 (60), 72 (68), 57 (100). HRMS (EI, 70 eV): calcd. for $C_{29}H_{36}O_8Si$ 522.2074; found 522.2075.

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