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Intramolecular aldol-type condensation between side chains of naphthoquinones: biomimetic synthesis of 1,6- and 1,8-dihydroxyanthraquinones †

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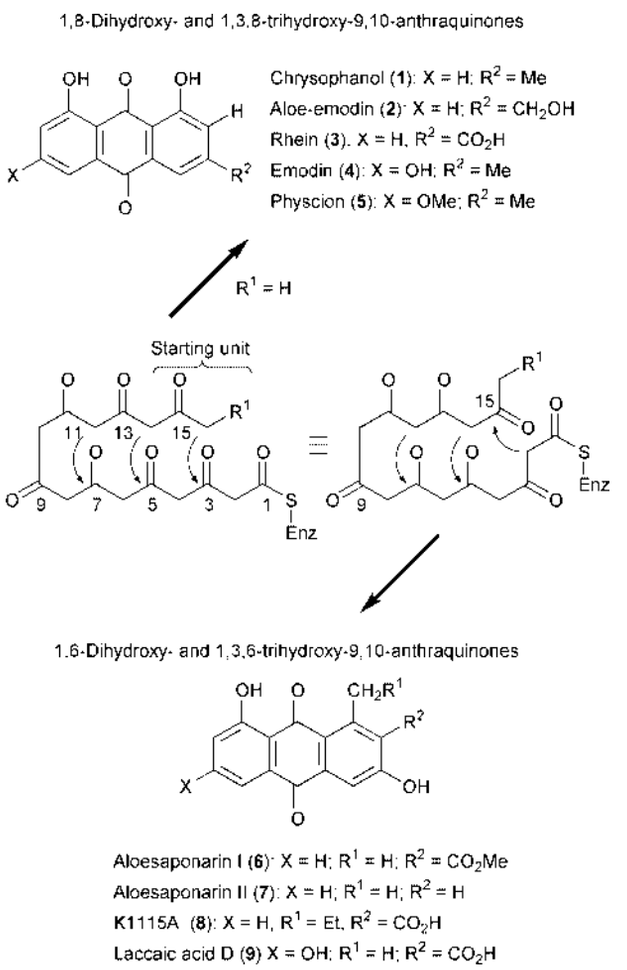
Intramolecular condensation of 2-(acetonyl)-3-acyljuglone derivatives under basic conditions gave 1,6- and/or 1,8-dihydroxyanthraquinones depending on the conditions employed. Treatment of 6-[(3-acetyl-5-methoxy-1,4-dioxo-1,4-dihydro-2-naphthyl)methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one with K_2CO_3 in alcohol brought about the intramolecular Knoevenagel-type reaction to give 3-hydroxy-8-methoxy-1-methyl-9,10-dioxo-9,10-dihydro-anthracene-2-carboxylates in good yields, while the same naphthoquinone gave 4-hydroxy-5-methoxy-9,10-dioxo-9,10-dihydroanthracene-2-acetic acid in good yield by treatment with potassium bis(trimethylsilyl)amide (KHMDS). Chrysophanol, aloe-emodin, aloesaponarin I, and K1115A were prepared in good yields.

Introduction

Among various kinds of naturally occurring quinones, dihydroxy- and trihydroxyanthraquinones are abundantly isolated from different sources.[1] These quinone skeletons are biologically synthesized from polyketides.[2] For example, chrysophanol (**1**), aloe-emodin (**2**), rhein (**3**), emodin (**4**), physcion (**5**), aloesaponarins (**6** and **7**), and laccaic acid D (**9**) are believed to be biosynthesized from the common octaketide having an acetyl group as a starting unit *via* different biosynthetic pathways, and the key step forming the skeletons is an aldol-type reaction such as a Knoevenagel or a Michael reaction (Scheme 1).[2] During the biosynthesis, the ending unit is variously modified and the oxygen functionality is occasionally removed from the 9-position of the octaketide. Contrary to the biosynthesis, most successful syntheses of these quinones involve the Diels–Alder or Friedel–Crafts reaction as a key construction step of the target quinone skeletons,[3] although some biomimetic syntheses of naturally occurring quinones have been reported by Krohn's, Yamaguchi's, Harris', and one of author's, groups.[4] One of the reasons for the different choice of routes between biological and artificial syntheses may be due to the labile nature of quinones under basic conditions.[5] Neutral or acidic conditions commonly employed in the Diels–Alder and Friedel–Crafts reactions are thought to be suitable for reactions using protected quinones or the quinones themselves. Basic conditions required for the aldol-type reactions would cause decomposition of quinones or simple reduction to hydroquinones mainly by the electron-transfer mechanism. We thought that this disadvantage under the aldol-type conditions would be overcome when the quinone side chains bearing carbonyl groups at appropriate positions are intramolecularly condensed. In such cases, a proper choice of the conditions would



Scheme 1 Biosynthesis of widely distributed 9,10-anthraquinones with hydroxy groups from an octaketide.

† Electronic supplementary information (ESI) available: preparation and experimental details of acetonylquinones. See http://www.rsc.org/suppdata/p1/b1/b104789m/

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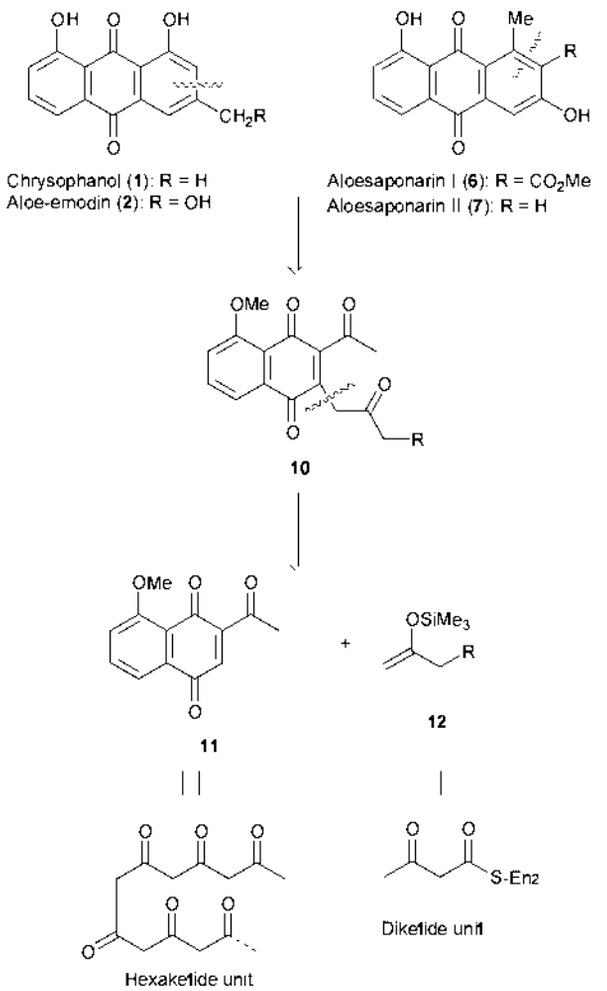
alter the reaction mode to provide various quinone homologues starting from the common precursor quinones. In this paper, we would like to report 1,6- and 1,8-dihydroxyanthraquinone syntheses from common naphthoquinone precursors by the suitable choice of conditions[6] and the total synthesis of chrysophanol (**1**), aloe-emodin (**2**), aloesaponarins I (**6**) and II (**7**), and K1115A (**8**).

Results and discussion

Our strategy

Our retro-synthesis of the dihydroxyanthraquinones **1**, **2**, **6**, and **7** is illustrated in Scheme 2. When the right-hand aromatic

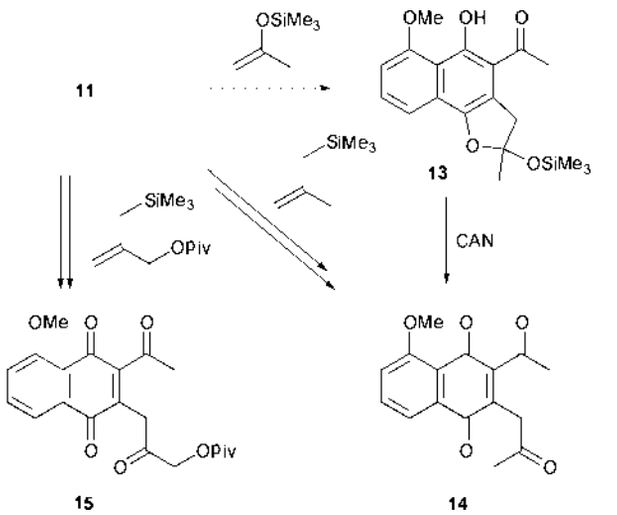


Scheme 2 Retro-synthesis of 1,8- and 1,6-dihydroxyanthraquinones with an acetyl group as the starting octaketide unit.

part of the dihydroxyanthraquinones is cleaved between the β,γ-carbons from the hydroxy group, the common skeleton of 2-acetonyl-3-acetyl-1,4-naphthoquinones **10** is obtained. These quinones should be obtained from the reaction of acetyljuglone derivative **11**[7] with enol silyl ethers **12**. This quinone **11** is considered as an equivalent of a hexaketide unit with an acetyl starter.

Preparation of quinones

The highly electrophilic nature of 2-acylnaphthoquinones at the 3-position was well exemplified by their reactions with allylsilanes,[4d,7] allylstannanes,[7,8] enamines,[9] ketene acetals,[7,10] and 2-siloxyfuran,[11] and various kinds of naturally occurring quinones were successfully synthesized. Simple acetonylation of the acylquinones, however, has not been employed for the construction of higher quinone skeletons, though acetonylations of alkylated naphthoquinones were accomplished by the reaction with an acetonylpyridinium reagent.[12] The 2-acetonyl-3-acetylnaphthoquinone **14** was prepared either in 40% yield *via* acetonylation of **11** with 2-(trimethylsiloxy)propene to give **13**, followed by oxidation with cerium(IV) ammonium nitrate (CAN) or in 45% yield *via* 2-methylallylation of **11** with trimethyl(2-methylprop-2-enyl)silane followed by sequential oxidation with CAN and ozone (Scheme 3). The pivaloyloxy derivative **15** was prepared in 58% yield. The detailed discussion for the preparation of **14** and **15** is in the Experimental section.

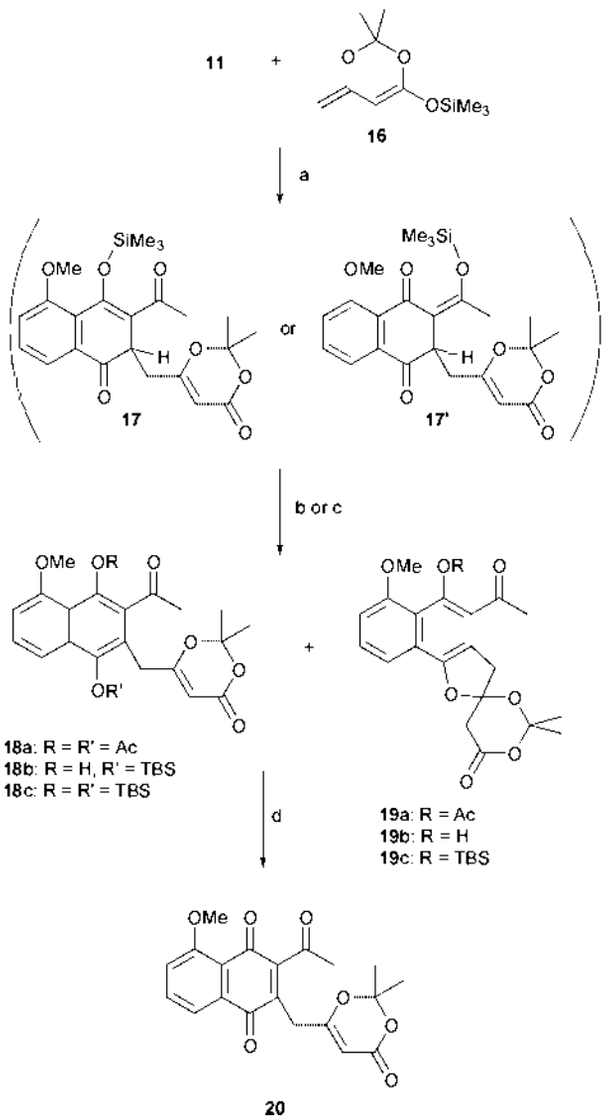


Scheme 3 Preparation of acetonylnaphthoquinones **14** and **15**. Details are in the Experimental section.

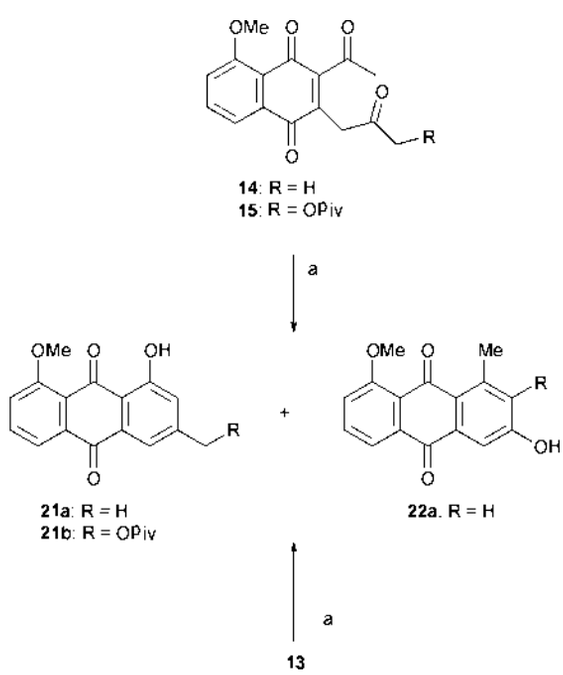
For the synthesis of aloesaponarin I **6**, an acetoacetate unit was to be introduced to the quinone **11**. 1-Methoxy-1,3-bis(trimethylsiloxy)buta-1,3-diene[13] seemed to be a promising candidate. However, the reaction of **11** with the reagent resulted in formation of a very complex mixture. 2,2-Dimethyl-4-methylene-6-trimethylsiloxy-4*H*-1,3-dioxine[14] **16** was next chosen as the introducing reagent. The reaction of **11** and the dioxine reagent **16** (1.7 molar ratio) was examined in an NMR tube (Scheme 4). The signals due to the quinone **11** disappeared within 1 h at −20 °C without any additive and new signals assigned to adduct **17** by COSY were observed (the position of a trimethylsilyl group could not be determined; **17** *vs.* **17′**). Conversion of the cyclohexadienone form **17** to the corresponding phenolic form would be very slow due to the steric encumbrance around the ring sp^3 carbon.[15] As the adduct **17** could not be isolated, the reaction mixture was treated with Ac_2O and pyridine to give a spiro compound **19a** in 6% yield in addition to hydroquinone diacetate **18a** (70%). When the reaction mixture was treated with *tert*-butyldimethylsilyl chloride (TBDMSCl) and imidazole, *mono*-silyl ether **18b** (35%), bis-silyl ether **18c** (16%), and spiro compounds (**19b**, 17%; **19c**, trace) were obtained. As both the spiro compounds **19b** and **19c** could be converted to the quinone **20** by oxidation, the mixture from the reaction of **11** with the dioxine reagent **16** was oxidized by CAN after treatment with trimethylsilyl chloride (TMSCl) and Et_3N. The quinone compound **20** was obtained in 84% yield from the starting quinone **11**.

Condensation between the side chain carbonyl groups

Intramolecular aldol-type condensation reactions were examined using both quinone and hydroquinone derivatives (**13**–**15**) (Scheme 5). Treatment of the dihydrofuran derivative **13** with potassium *tert*-butoxide in THF gave a mixture of chrysophanol 8-*O*-methyl ether (**21a**; 35%) and aloesaponarin II 8-*O*-methyl ether (**22a**; 4%). Similar treatment of the quinone **14** gave **21a** (16%) and **22a** (37%). When the reaction of **14** was carried out using KHMDS, an intractable mixture was



Scheme 4 Reaction of **11** with **16**. *Reagents and conditions*: a) CH_2Cl_2, below 0 °C; b) Ac_2O, pyridine, rt; c) TBSCI, imidazole, DMF, rt; d) **18b**, **18c**, **19b**, or **19c**, CAN aq. MeCN, rt.

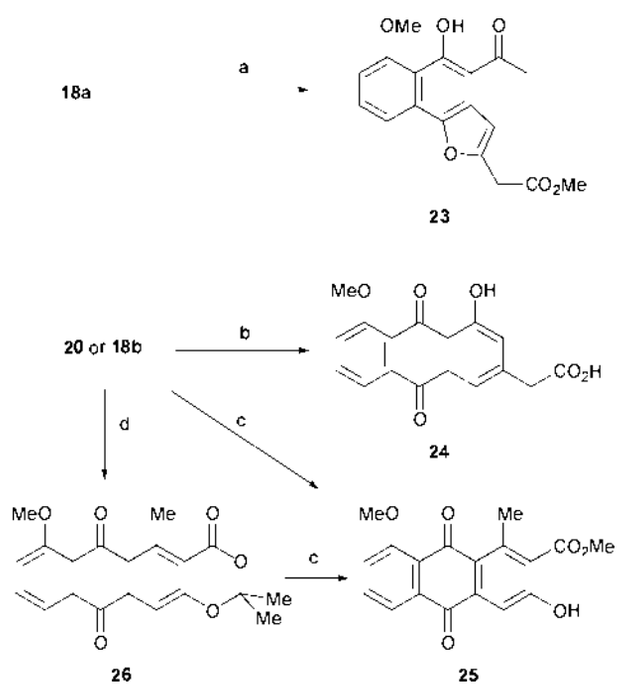


Scheme 5 Intramolecular condensation. *Reagents and conditions*: a) *t*-BuOK, THF, rt.

obtained. Treatment of the quinone bearing a pivaloyloxy group, compound **15**, with potassium *tert*-butoxide in THF gave the quinone **21b** as the sole product in 65% yield.

The preference observed in the reaction of **13**, **14** and **15** is rationalized as follows. In the case of **13**, proton abstraction from the phenolic hydroxy group would first occur to give a 6-membered cyclic potassium chelate and then base-induced rearrangement to the corresponding acetonylhydroquinone derivative would occur. In this intermediate, the methyl moiety of the acetyl group would be directed to the neighbouring acetonyl group. Therefore, attack from the methyl moiety to the acetonyl carbonyl carbon would be favoured. On the other hand, the carbonyl oxygen of the acetyl group would be directed to the neighbouring acetonyl group in the quinone **14** due to the dipole–dipole interaction between the quinone and acetyl carbonyl groups. Therefore, attack from the methyl moiety to the acetonyl carbonyl carbon would be disfavoured. In the case of **15**, the steric hindrance of the pivaloyloxy group would thwart the proton abstraction from the acetonyl methylene, and the intramolecular condensation reaction caused by the proton abstraction from the acetyl group would be predominant to give **21b**.

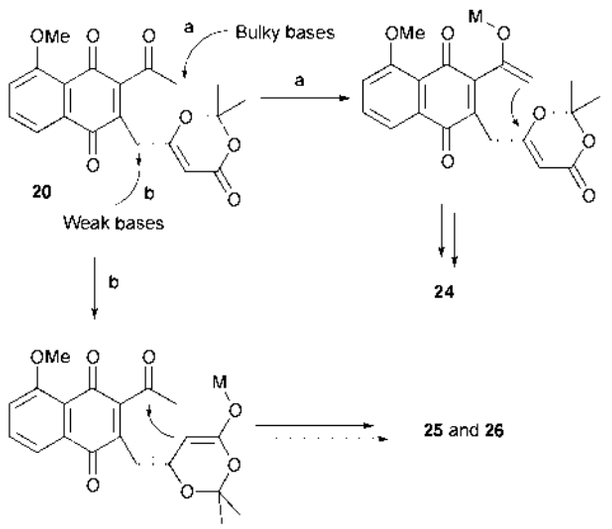
Next, we turned our attention to the preparation of aloesaponarin from the adducts **18** and **20**. Deprotection of the diacetate **18a** under acidic conditions gave only **23** in low yield (12%; Scheme 6), whereas the treatment of **18a** with K_2CO_3 in



Scheme 6 Intramolecular condensation of masked octaketides. *Reagents and conditions*: a) $BF_3{\cdot}OEt_2$, MeOH, rt; b) KHMDS, THF, −78 ° ⟶ rt; c) K_2CO_3, MeOH, rt; d) Et_3N, THF, rt.

THF–MeOH gave an intractable mixture. Hydroquinone *mono*-silyl ether **18b** and quinone **20** were employed as the substrate. When the quinone **20** was treated with KHMDS, a clean intramolecular Michael-type reaction between the acetyl and β-alkoxy α,β-unsaturated ester moieties occurred to give only 4-hydroxy-5-methoxy-9,10-dioxo-9,10-dihydroanthracene-2-acetic acid **24** in 62% yield (Scheme 6). On the other hand, a completely different condensation route was observed in the reaction of the same quinone compound **20** with a weak base. When the quinone **20** was treated with K_2CO_3 in methanol, an intramolecular condensation between the acetyl and masked β-keto ester moieties was observed to give only 3-hydroxy-8-methoxy-1-methyl-9,10-dioxo-9,10-anthracene-2-carboxylate **25** in 70% yield. When the quinone **20** was treated with Et_3N in THF, a similar cyclization leading to **26** occurred in 94% yield.

The anthraquinone **26** was converted to aloesaponarin I 8-*O*-methyl ether **25** under the same conditions as the transformation of **20** to **25**. The alteration of condensation route depends on the steric bulkiness and basicity of the base employed. A strong and bulky base such as KHMDS can only deprotonate from the less-hindered acetyl moiety, while weak bases such as an alkoxide and Et_3N cannot deprotonate from the acetyl moiety but from the most acidic methylene moiety (Scheme 7).



Scheme 7 Reaction pathways of **20**.

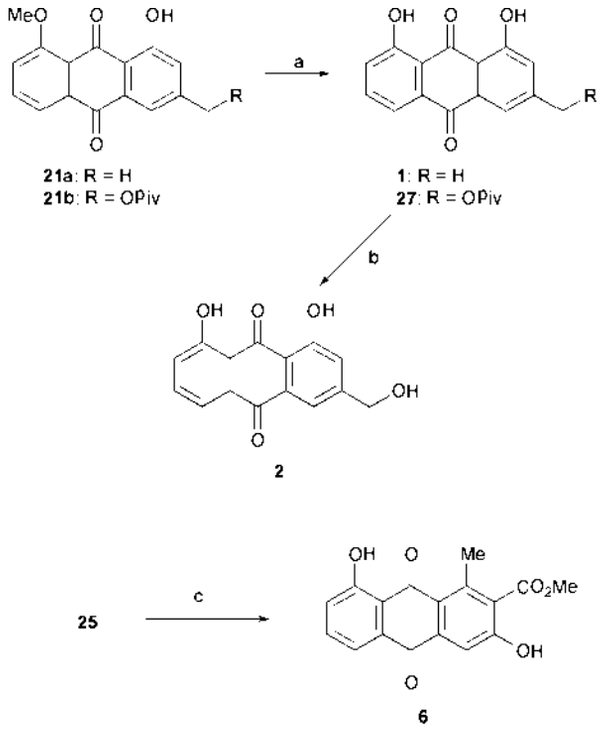
A similar transformation to 1,6- and 1,8-dihydroxyanthraquinones was also achieved by employing the TBS ether **18b** as the substrate. Treatment of **18b** with KHMDS in THF and with K_2CO_3 in MeOH brought about the similar ring closures followed by air oxidation to give the quinones **24** and **25**. The yields were slightly lower (50% and 56% yield, respectively) than those from the quinone **20**.

Conversion to naturally occurring 1,8- and 1,6-dihydroxyanthraquinones

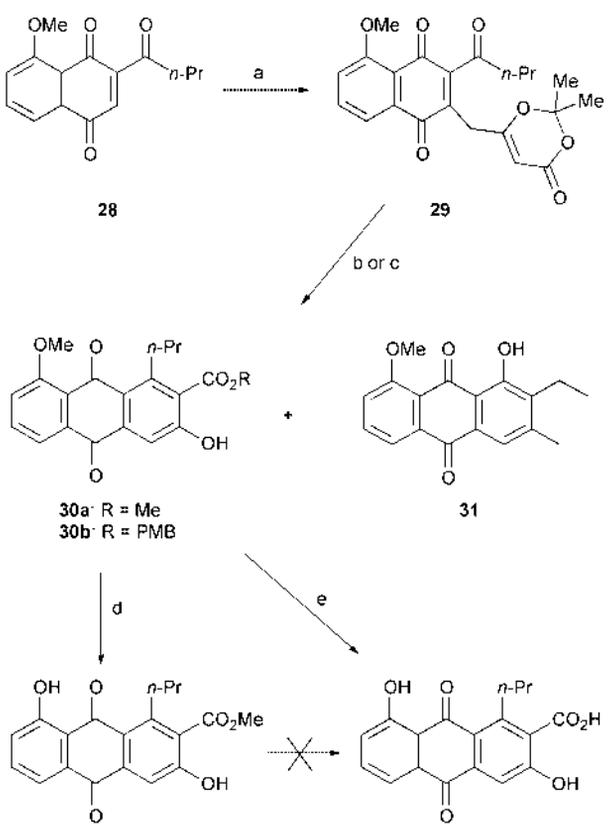
Deprotection of the *O*-methyl group of **21a**, **21b**, and **25** with $AlCl_3$ or BBr_3 gave chrysophanol **1**, aloe-emodin ω-pivalate **27**, and aloesaponarin I **6** in 91, 84, and 69% yield (Scheme 8). The physical and spectroscopic data of chrysophanol[16] **1** and aloesaponarin I[17] **6** were identical with those reported. The pivaloyl group of **27** was hydrolyzed with NaOH to give aloe-emodin **2** in 39% yield.

Synthesis of K1115A

K1115A[18] **8** was thought to be biologically derived from an octaketide bearing a butyryl group as the starting unit (Scheme 9). Therefore, we employed butyryljuglone derivative **28** as the starting quinone. The reaction of **28** with the dioxine reagent **16** gave an adduct, which was treated successively with TMSCl–Et_3N and CAN to give quinone **29** in 90% yield. Treatment of **29** with K_2CO_3 in MeOH gave a mixture of **30a** (62%) and **31** (6%). The latter compound **31** was derived from the intramolecular Michael-type reaction followed by decarboxylation. The methyl ether of **30a** was removed by treatment with BBr_3 to afford **32** in 87% yield. Since attempted saponification of the methyl ester **32** to K1115A failed, the nucleophile in the reaction of **29** was changed to *p*-methoxybenzyl alcohol (PMB alcohol) and the PMB ester **30b** was obtained in 72% yield. Simultaneous deprotection of the methyl ether and PMB ester of **30b** was achieved by treatment with BBr_3 at −78 °C to provide K1115A **8** in 59% yield. Identity of the synthetic and authentic K1115A was confirmed by NMR investigation of the mixed sample.



Scheme 8 Synthesis of crysophanol **1** aloe-emodin **2** and aloesaponarin I **6**. *Reagents and conditions*: a) $AlCl_3$, CH_2Cl_2, rt; b) NaOH, aq. THF–MeOH, rt; c) BBr_3, CH_2Cl_2, −78 °C ⟶ rt.



Scheme 9 Synthesis of K1115A **8**. *Reagents and conditions*: a) **16**, CH_2Cl_2, −78 °C; TMSCl, Et_3N, rt; CAN, MeCN; b) K_2CO_3, MeOH, rt; c) K_2CO_3, 4-$MeOC_6H_4CH_2OH$, rt; d) **30a**, BBr_3, CH_2Cl_2, −78 °C ⟶ rt; e) **30b**, BBr_3, CH_2Cl_2, −78 °C ⟶ rt.

Conclusions

We have demonstrated that naturally occurring 1,6- and 1,8-dihydroxy-9,10-anthraquinones are prepared *via* the intramolecular aldol-type condensation of common naphthoquinones

bearing acyl and acetonyl groups. We have achieved the syntheses of chrysophanol, aloe-emodin, aloesaponarin, and K1115A, the last of which is reported to show an inhibitory activity towards activation protein I (AP-I).

Experimental

General details

Melting points are uncorrected. Unless otherwise specified, NMR spectra were obtained with a JEOL GSX-270 or JNM-400 spectrometer at ambient temperature using $CDCl_3$ as solvent and tetramethylsilane as internal standard for ^1H and ^{13}C. *J*-values are given in Hz. Mass spectra and high-resolution mass spectra were measured with a Hitachi M80B spectrometer under EI (20 eV) ionizing conditions. Column chromatography and TLC analysis were carried out using Wakogel C-200 and Kieselgel 60 F_{254} (Merck), respectively. Ether (Et_2O) and THF were freshly distilled from sodium diphenyl ketyl. Dichloromethane, benzene, toluene, diisopropylamine, and triethylamine were distilled from CaH_2 under an inert atmosphere and stored over molecular sieves 4Å. Other commercially available materials were used without further purification.

Reaction of 11 with 2-(trimethylsiloxy)propene

To a solution of compound **11**[7] (460 mg, 2.0 mmol) in dry CH_2Cl_2 (40 mL) were added $SnCl_4$ (1.0 mol L^{-1} in CH_2Cl_2, 2.2 mL) and 2-(trimethylsiloxy)propene (0.40 mL, 2.4 mmol) at −78 °C. After the addition, the mixture was stirred for 1 h at the same temperature. Ethyldiisopropylamine (0.418 mL, 2.4 mmol) was added and then the mixture was allowed to warm to room temperature. After 1 h, the reaction was quenched with water. The organic phase was separated and the aqueous phase was extracted with dichloromethane. The combined organic phase was washed successively with 5% HCl, water and brine, dried over Na_2SO_4, and concentrated by a rotary evaporator to give a crude product, which was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 290 mg (40%) of 4-acetyl-5-hydroxy-6-methoxy-2-methyl-2-trimethylsiloxy-1,2-dihydronaphtho[1,2-*b*]furan **13** as pale yellow crystals (Found: C, 63.6; H, 6.65. $C_{19}H_{24}O_5Si$ requires C, 63.3; H, 6.7%); mp 109–110 °C (yellow needles from CH_2Cl_2–hexane); R_f (40% EtOAc–hexane) 0.65; δ_H 0.05 (9 H, s, $SiMe_3$), 1.75 (3 H, s, 2-Me), 2.67 (3 H, s, COMe), 3.54 (2 H, br s, H^3), 4.05 (3 H, s, OMe), 6.82 (1 H, d, *J* = 7.3, H^7), 7.45 (1 H, m, H^8), 7.47 (1 H, m, H^9) and 11.81 (1 H, br s, OH); δ_C 1.4 ($SiMe_3$), 29.1 (2-Me), 32.3 (CO*Me*), 48.2 (C3), 56.2 (OMe), 105.4 (C7), 110.4 (C2), 114.9 (C5a), 115.0 (C9), 115.6 (C4), 118.3 (C3a), 125.2 (C9a), 128.9 (C9), 145.4 (C9b), 154.8 (C5), 158.1 (C6) and 201.4 (*C*OMe); ν_{max} (KBr) 3332, 1651, 1633, 1591, 1403, 1282, 1250 and 997 cm^{-1}; *m*/*z* (rel. intensity) 360 (M^+, 100%), 318 (59), 270 (13) and 240 (11).

2-Acetonyl-3-acetyl-5-methyl-1,4-naphthoquinone 14

To a solution of **13** (184 mg, 0.51 mmol) in acetonitrile (13 mL) was added a solution of CAN (0.84 g, 1.53 mmol) in water (6 mL). After 10 min brine and $CHCl_3$ were added. The organic phase was separated and the aqueous phase was extracted with $CHCl_3$. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated by a rotary evaporator to give 144 mg (100%) of **14**. An analytically pure sample was obtained by recrystallization from CH_2Cl_2–ether–hexane. **14**: yellow needles (Found: C, 66.75; H, 5.05. $C_{16}H_{14}O_5$ requires C, 67.1; H, 4.9%); mp 117–119 °C (from CH_2Cl_2–hexane); R_f (40% EtOAc–hexane) 0.3; δ_H 2.30 (3 H, s), 2.51 (3 H, s), 3.75 (2 H, s), 4.03 (3 H, s), 7.34 (1 H, dd, *J* = 7.8 and 2.0) and 7.73 (2 H, m); δ_C 30.5, 31.6, 40.3, 56.5, 116.3, 118.3, 119.1, 119.6, 133.5, 135.4, 137.6, 148.3, 159.8, 182.6, 184.6, 202.3 and 202.9; ν_{max} (KBr) 1716, 1700, 1660, 1587, 1475 and 1271 cm^{-1}; *m*/*z* (rel. intensity) 286 (M^+, 1%), 245 (17), 244 (100), 243 (16), 229 (67) and 201 (18).

3-Acetyl-5-methoxy-2-[2-oxo-3-(pivaloyloxy)propyl]-1,4-naphthoquinone 15

For the experimental procedure, see the electronic supplementary information. †

Yellow crystals (Found: C, 65.0; H, 5.75. $C_{21}H_{22}O_7$ requires C, 65.3; H, 5.7%); R_f (40% EtOAc–hexane) 0.45; mp 120–122 °C; δ_H 1.25 (9 H, s), 2.50 (3 H, s), 3.69 (2 H, s), 4.01 (3 H, s), 4.79 (2 H, s), 7.32 (1 H, d, *J* = 7.8), 7.69 (1 H, t, *J* = 7.8) and 7.72 (1 H, d, *J* = 7.8); δ_C 27.1, 31.7, 36.1, 38.7, 56.6, 68.0, 118.4, 119.1, 119.6, 133.4, 135.5, 136.8, 148.8, 159.9, 177.6, 182.4, 184.4, 199.3 and 202.1; ν_{max} (KBr) 2976, 1750, 1728, 1708, 1664, 1640, 1584, 1272 and 1160 cm^{-1}; *m*/*z* (rel. intensity) 388 (M^+ + 2, 4%), 386 (M^+, 3), 368 (17), 356 (25), 284 (25), 271 (94), 244 (57) and 143 (100).

Reaction of 11 with 16

To a $CDCl_3$ solution (0.5 mL) of **11** (20 mg, 0.087 mmol) in an NMR sample tube was added **16** (32 mg) at −70 °C. This mixture was immediately subjected to NMR measurements at −20 °C. The structure of the adduct was elucidated by COSY. 6-[(3-Acetyl-5-methoxy-1-oxo-4-trimethylsiloxy-1,2-dihydro-2-naphthyl)methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one **17** showed δ_H 0.22 (9 H, s), 1.39 (3 H, s), 1.59 (3 H, s), 1.91 (1 H, dd, *J* = 13.9 and 12.0), 2.25 (1 H, dd, *J* = 13.9 and 5.6), 2.34 (3 H, s), 3.93 (4 H, m), 4.12 (1 H, s), 7.20 (1 H, br d, *J* = 8.3), 7.42 (1 H, br d, *J* = 7.3) and 7.51 (1 H, dd, *J* = 8.3 and 7.3).

Work-up with acetylation. To a solution of **11**[7] (230 mg, 1.0 mmol) in dry CH_2Cl_2 (30 mL) was added **16** (210 mg, 1.2 mmol) at −78 °C. The mixture was stirred for 1 h at that temperature and then warmed up to room temperature. After disappearance of **11** (TLC), the solvent was removed. Pyridine (1 mL) and acetic anhydride (1 mL) were added to the residue and the resulting mixture was stirred overnight. The volatile material was removed under reduced pressure (*ca.* 13 Pa). The residue was chromatographed on silica gel (30–50% EtOAc–hexane) to give 26 mg (6%) of 6-[(1,4-diacetoxy-3-acetyl-5-methoxy-2-naphthyl)methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one **18a** and 294 mg (71%) of 5′-acetoxy-4′-acetyl-6′-methoxy-2,2-dimethylspiro{1,3-dioxane-4,2′(3′*H*)-naphtho[1,2-*b*]furan}-6-one **19a**. **18a**: pale yellow crystals (Found: C, 63.1; H, 5.4. $C_{24}H_{24}O_9$ requires C, 63.15; H, 5.3%); mp 132–133.5 °C; R_f (40% EtOAc–hexane) 0.15; δ_H 1.60 (6 H, s), 2.36 (3 H, s), 2.47 (3 H, s), 2.56 (3 H, s), 3.63 (2 H, s), 3.93 (3 H, s), 5.15 (1 H, s), 6.92 (1 H, d, *J* = 8.5), 7.27 (1 H, d, *J* = 8.5) and 7.50 (1 H, t, *J* = 8.5); δ_C 20.6, 20.8, 24.8, 31.2, 32.3, 56.2, 94.5, 107.0, 107.7, 114.4, 119.0, 120.4, 128.9, 130.0, 132.2, 141.8, 143.9, 155.8, 160.8, 168.0, 168.5, 169.0 and 202.1; ν_{max} (KBr) 1763, 1748, 1735, 1700, 1377, 1275 and 1205 cm^{-1}; *m*/*z* (rel. intensity) 372 ($M^+ - 2\ CH_2{=}C{=}O$, 5%), 330 (22) and 270 (100). **19a**: pale yellow crystals (Found: C, 63.7; H, 5.45%. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.35%); mp 121–123 °C; R_f (40% EtOAc–hexane) 0.4; δ_H 1.60 (3 H, s), 1.79 (3 H, s), 2.41 (3 H, s), 2.60 (3 H, s), 3.09 (1 H, d, *J* = 17.8), 3.20 (1 H, d, *J* = 17.8), 3.60 (1 H, d, *J* = 17.8), 3.63 (1 H, d, *J* = 17.8), 3.94 (3 H, s), 6.88 (1 H, dd, *J* = 7.1 and 1.5) and 7.40–7.45 (2 H, m); δ_C 21.2, 28.8, 29.9, 31.8, 38.8, 45.1, 56.2, 106.8, 107.3, 109.0, 114.2, 117.2, 118.8, 124.0, 126.4, 128.8, 140.9, 150.7, 156.3, 165.2, 169.9 and 198.9; ν_{max} (KBr) 1768, 1751, 1681, 1394, 1363 and 1205 cm^{-1}; *m*/*z* (rel. intensity) 414 (M^+, 2%), 356 (7), 312 (22), 270 (100) and 255 (38).

Work-up with silylation. To a solution of **11**[7] (230 mg, 1.0 mmol) in dry CH_2Cl_2 (30 mL) was added **16** (360 mg, 1.7 mmol) at −78 °C. The mixture was stirred for 1 h at that temperature and then warmed up to room temperature. After

disappearance of **11** (TLC, within 1 h), the solvent was removed on a rotary evaporator to give a crude material. To the crude material in DMF (3 mL) were added TBDMSCl (226 mg, 1.5 mmol) and imidazole (225 mg, 3.3 mmol). The mixture was stirred overnight at room temperature, the reaction was quenched with water, and the mixture was extracted with ether. The ethereal phase was washed successively with water and brine, dried over Na_2SO_4, and concentrated on a rotary evaporator to give a residue, which was dissolved in MeCN (16 mL) and 50% HF (1.8 mL, 60 mmol) was added. After being stirred for 20 h, the mixture was quenched with saturated aq. $NaHCO_3$ (10 mL) and ether. The organic phase was separated and the aqueous phase was extracted with ether. The combined ethereal phase was washed successively with saturated aq. $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated by rotary evaporator. The residue was chromatographed on silica gel (30–50% EtOAc–hexane) to give 171 mg (35%) of 6-[(3-acetyl-1-*tert*-butyldimethylsiloxy-4-hydroxy-5-methoxy-2-naphthyl)methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one **18b**, 95 mg (16%) of 6-{[3-acetyl-1,4-bis(*tert*-butyldimethylsiloxy)-5-methoxy-2-naphthyl]methyl}-2,2-dimethyl-4*H*-1,3-dioxin-4-one **18c**, 62 mg (17%) of 4′-acetyl-5′-hydroxy-6′-methoxy-2,2-dimethylspiro{1,3-dioxane-4,2′(3′*H*)-naphtho[1,2-*b*]furan}-6-one **19b**, and trace amounts of 4′-acetyl-5′-*tert*-butyldimethylsiloxy-6′-methoxy-2,2-dimethylspiro{1,3-dioxane-4,2′-(3′*H*)-naphtho[1,2-*b*]furan}-6-one **19c**. **18b**: pale yellow needles (Found: C, 64.0; H, 6.8. $C_{26}H_{34}O_7Si$ requires C, 64.2; H, 7.0%); mp 121–123 °C (from CH_2Cl_2–hexane); R_f (40% EtOAc–hexane) 0.59; δ_H 0.11 (6 H, s), 1.05 (9 H, s), 1.63 (6 H, s), 2.59 (3 H, s), 3.77 (2 H, s), 4.05 (3 H, s), 4.81 (1 H, s), 6.85 (1 H, d, J = 7.9), 7.36 (1 H, dd, J = 8.5 and 7.9), 7.62 (1 H, d, J = 8.5) and 9.60 (1 H, s, OH); δ_C −3.3, 18.6, 25.0, 26.0, 30.9, 32.4, 56.4, 93.5, 105.6, 106.5, 114.9, 117.4, 117.7, 123.3, 126.6, 130.8, 142.4, 148.1, 156.5, 161.3, 171.0 and 204.4; ν_{max} (KBr) 3342, 1720, 1687, 1637 and 1384 cm^{-1}; *m*/*z* (rel. intensity) 486 (M^+, 4%), 428 (29) and 386 (100). **18c**: pale yellow needles (Found: C, 63.7; H, 7.8. $C_{32}H_{48}O_7Si_2$ requires C, 64.0; H, 8.05%); mp 116.5–117.5 °C (from CH_2Cl_2–hexane); R_f (40% EtOAc–hexane) 0.73; δ_H −0.09 (6 H, s), 0.15 (6 H, s), 0.99 (9 H, s), 1.05 (9 H, s), 1.62 (6 H, s), 2.57 (3 H, s), 3.76 (2 H, s), 3.91 (3 H, s), 4.75 (1 H, s), 6.83 (1 H, d, J = 7.7), 7.38 (1 H, dd, J = 8.4 and 7.7) and 7.60 (1 H, d, J = 8.6); δ_C −4.2, −3.2, 18.5, 18.7, 20.0, 26.1, 26.3, 30.9, 33.0, 55.2, 93.5, 106.2, 106.6, 115.9, 116.4, 120.1, 126.8, 130.5, 131.2, 144.7, 145.4, 156.9, 161.3, 171.0 and 205.1; ν_{max} (KBr) 1720, 1691, 1631, 1570, 1376 and 1294 cm^{-1}; *m*/*z* (rel. intensity) 600 (M^+, 3%), 542 (18), 485 (100) and 426 (73). **19b**: yellow needles (Found: C, 64.2; H, 5.4. $C_{20}H_{20}O_7$ requires C, 64.5; H, 5.4%); mp 169.5–172.5 (from CH_2Cl_2–hexane); R_f (40% EtOAc–hexane) 0.4; δ_H 1.58 (3 H, s), 1.77 (3 H, s), 2.70 (3 H, s), 3.08 (1 H, d, J = 18.5), 3.17 (1 H, d, J = 18.5), 3.61 (1 H, d, J = 18.1), 3.72 (1 H, d, J = 18.1), 4.09 (3 H, s), 6.86 (1 H, m), 7.44 (2 H, m) and 11.08 (1 H, s); δ_C 28.8, 30.0, 32.7, 38.8, 46.5, 56.4, 105.7, 106.7, 108.2, 114.8, 115.0, 116.3, 118.3, 124.9, 129.2, 145.0, 154.4, 157.8, 165.6 and 200.4; ν_{max} (KBr) 3294, 1741, 1653, 1637, 1400, 1286 and 1014 cm^{-1}. **19c**: pale yellow, waxy crystals (Found: C, 63.9; H, 7.1. $C_{26}H_{34}O_7Si$ requires C, 64.2; H, 7.0%); R_f (40% EtOAc–hexane) 0.75; δ_H −0.11 (3 H, s), −0.09 (3 H, s), 1.09 (9 H, s), 1.60 (3 H, s), 1.80 (3 H, s), 2.65 (3 H, s), 3.07 (1 H, d, J = 17.4), 3.20 (1 H, d, J = 17.4), 3.51 (1 H, d, J = 18.1), 3.55 (1 H, d, J = 18.1), 3.92 (3 H, s), 6.82 (1 H, m) and 7.41 (2 H, m); δ_C −4.7, −4.5, 18.4, 26.4, 28.8, 29.9, 31.7, 39.0, 45.0, 55.2, 106.0, 106.7, 108.6, 113.6, 117.1, 120.1, 124.2, 126.2, 128.3, 147.2, 147.6, 157.7, 165.5 and 202.7; ν_{max} (KBr) 1763, 1680, 1631, 1570, 1514, 1394 and 1267 cm^{-1}; *m*/*z* (rel. intensity) 486 (M^+, 2%), 384 (10), 327 (100), 312 (22) and 297 (17).

Oxidative work-up. To a solution of compound **11** (464 mg, 2.0 mmol) in dry CH_2Cl_2 (20 mL) was added **16** (730 mg, 3.4 mmol) at −78 °C and then the cooling bath was removed. After the mixture had been stirred for 1 h at room temperature, TMSCl (1.27 mL, 10 mmol) and Et_3N (2.78 mL, 20 mmol) were added and the mixture was stirred for 2 h. The reaction was quenched with saturated aq. $NaHCO_3$. The organic phase was separated and the aqueous phase was extracted with $CHCl_3$. The combined organic phase was washed successively with water and brine, dried over Na_2SO_4, and concentrated by rotary evaporator. The residue was dissolved in MeCN (20 mL) and a solution of CAN (1.64 g, 3 mmol) in water (10 mL) was added at room temperature. After 10 min, the mixture was extracted with $CHCl_3$. The organic extract was washed with brine, dried over Na_2SO_4, and concentrated by rotary evaporator to give crude 6-[(3-acetyl-5-methoxy-1,4-dioxo-1,4-dihydro-2-naphthyl)methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one **20**. Chromatography on silica gel (30–50% EtOAc–hexane) gave 314 mg (84%) of pure **20** as yellow crystals (Found: C, 64.2; H, 4.7. $C_{20}H_{18}O_7$ requires C, 64.9; H, 4.9%); mp 130 °C (decomp.); R_f (40% EtOAc–hexane) 0.25; δ_H 1.65 (6 H, s), 2.51 (3 H, s), 3.49 (2 H, s), 4.04 (3 H, s), 5.31 (1 H, s), 7.37 (1 H, m) and 7.76 (2 H, m); δ_C 24.9, 30.4, 31.8, 56.6, 94.9, 107.0, 113.3, 118.5, 118.9, 119.7, 135.8, 136.2, 149.0, 159.9, 160.5, 166.7, 182.2, 183.9 and 200.9; ν_{max} (KBr) 1728, 1699, 1658, 1639, 1630, 1585, 1390, 1261 and 1203 cm^{-1}.

Intramolecular condensation of 13

To a solution of **13** (89 mg, 0.25 mmol) in dry THF (5 mL) was added *t*-BuOK (1.0 M; 0.62 mL, 0.62 mmol) in THF at 0 °C. After the cooling bath had been removed the mixture was stirred for 14 h at room temperature. The reaction mixture was quenched with saturated aq. NH_4Cl. The aqueous phase was extracted with EtOAc. The combined extract was washed successively with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporator. The residue was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 23 mg (35%) of 1-hydroxy-8-methoxy-3-methyl-9,10-anthraquinone (chrysophanol 8-*O*-methyl ether; **21a**) and 2 mg (4%) of 3-hydroxy-8-methoxy-1-methyl-9,10-anthraquinone (aloesaponarin II 8-*O*-methyl ether; **22a**). **21a**: yellow crystals, mp 195–197 °C (lit., 197 °C,[16a] 198 °C,[19] 196–197 °C[20]); R_f (40% EtOAc–hexane) 0.45; δ_H 2.43 (3 H, s), 4.06 (3 H, s), 7.07 (1 H, d, J = 1.0), 7.33 (1 H, d, J = 8.1), 7.58 (1 H, d, J = 1.0), 7.73 (1 H, t, J = 8.1), 7.94 (1 H, d, J = 8.1) and 12.89 (1 H, s, OH); δ_C 22.0, 56.6, 114.9, 118.1, 120.0, 120.1, 120.8, 124.6, 132.4, 135.6, 135.8, 147.6, 160.8, 162.7, 182.9 and 188.5; ν_{max} (KBr) 3409, 1637, 1583, 1446, 1301, 1274 and 1246 cm^{-1}; *m*/*z* (rel. intensity) 268 (M^+, 100%), 250 (43), 239 (20), 222 (49) and 181 (22). **22a**: yellow crystals; mp 218–220 °C; R_f (30% EtOAc–hexane) 0.2; δ_H (DMSO-d_6; 50 °C) 2.94 (3 H, s), 3.93 (3 H, s), 7.01 (1 H, d, J = 2.6), 7.37 (1 H, d, J = 2.6), 7.52 (1 H, dd, J = 8.3 and 2.5), 7.72 (2 H, m) and 10.7 (1 H, br, OH); ν_{max} (KBr) 3465, 1662, 1646, 1604, 1585, 1568, 1458, 1342 and 1247.

Intramolecular condensation of 14

The reaction was carried out according to the procedure described above by using 111 mg of **14**. Chromatographic purification (silica gel) gave 17 mg (16%) of **21a** and 39 mg (37%) of **22a**.

Intramolecular condensation of 15

The reaction was performed according to the procedure described above by using 50 mg (0.13 mmol) of **15**. Chromatographic purification (silica gel) gave 31 mg (65%) of **21b** as yellow crystals (Found: C, 68.4; H, 5.5. $C_{21}H_{20}O_6$ requires C, 68.5; H, 5.5%), mp 163–165 °C; R_f (40% EtOAc–hexane) 0.35; δ_H 1.28 (9 H, s), 4.09 (3 H, s), 5.17 (2 H, s), 7.25 (1 H, d, J = 2.0), 7.38 (1 H, dd, J = 8.3 and 1.5), 7.71 (1 H, d, J = 2.0), 7.77 (1 H, dd, J = 8.3 and 7.8), 7.98 (1 H, dd, J = 7.8 and 1.5) and 12.98 (1 H, s, OH); δ_C 27.1, 38.8, 56.6, 64.6, 116.3, 116.9, 118.1, 120.1, 120.5, 122.1, 132.8, 135.5, 135.8, 145.3, 160.8, 162.7, 177.9,

182.3 and 188.3; ν_{max} (KBr) 3432, 2920, 1724, 1676, 1632, 1584, 1284 and 1166 cm^{-1}; *m/z* (rel. intensity) 368 (M^+, 100%), 284 (98), 267 (20) and 239 (30).

Treatment of 18a with acid in MeOH

To a solution of diacetate **18a** in MeOH (10 mL)–CH_2Cl_2 (10 mL) was added $BF_3{\cdot}OEt_2$ (0.24 mL, 0.24 mmol) at room temperature. The mixture was stirred overnight. As some starting material remained (TLC), conc. H_2SO_4 (10 drops) was added and the mixture was warmed to 50 °C. After disappearance of the starting material (TLC), the reaction was quenched with saturated aq. $NaHCO_3$. The mixture was extracted with EtOAc, and the extract was washed with brine, dried over Na_2SO_4, and concentrated on a rotary evaporator. The residue was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 8 mg (12%) of methyl 4-acetyl-5-hydroxy-6-methoxynaphtho[1,2-*b*]furan-2-acetate **23** as colourless crystals (HRMS Found: M^+, 328.0943. $C_{18}H_{16}O_6$ requires *M*, 328.0946); mp 159–161 °C (needles from CH_2Cl_2–hexane); R_f (50% EtOAc–hexane) 0.4; δ_H 2.79 (3 H, s), 3.77 (3 H, s), 3.92 (2 H, s), 4.09 (3 H, s), 6.88 (1 H, d, J = 7.5), 7.01 (1 H, s), 7.56 (1 H, dd, J = 8.5 and 7.5), 7.78 (1 H, d, J = 8.5) and 13.52 (1 H, br s); δ_C 31.9, 34.4, 52.4, 56.3, 105.6, 105.7, 107.4, 109.9, 113.0, 122.2, 126.6, 130.6, 144.0, 150.6, 159.0, 160.5, 169.2 and 201.4; ν_{max} (KBr) 3311, 1730, 1647, 1633, 1589, 1389, 1244, 1214 and 1029 cm^{-1}; *m/z* (rel. intensity) 328 (M^+, 100%), 313 (49), 269 (43) and 239 (14).

Treatment of 20 with KHMDS in THF

To a solution of **20** (230 mg, 0.6 mmol) in dry THF (10 mL) was added KHMDS (4.46 mL, 2.23 mmol; 0.5 M in toluene) at −78 °C. After the addition, the mixture was allowed to warm to room temperature and was stirred for 1 h. The reaction was quenched by acidification with 5% HCl. The mixture was extracted with EtOAc, and the extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was triturated with CH_2Cl_2–ether–hexane. Filtration gave 118 mg (63%) of 4-hydroxy-5-methoxy-9,10-dioxo-9,10-dihydroanthracene-2-acetic acid **24** as a yellow powder (Found: C, 61.7; H, 4.5. $C_{17}H_{12}O_6{\cdot}H_2O$ requires C, 61.8; H, 4.3%); mp 234–237 °C; R_f (40% EtOAc–hexane) 0.5; δ_H (DMSO-d_6) 3.75 (2 H, s), 3.99 (3 H, s), 7.25 (1 H, s), 7.59 (1 H, s), 7.60 (1 H, d, J = 6.8), 7.83 (2 H, m), 12.35 (1 H, br, OH) and 12.77 (1 H, br, OH); δ_C (DMSO-d_6) 40.3, 56.3, 115.2, 119.0, 119.2, 119.3, 119.8, 124.4, 131.9, 134.7, 135.8, 143.7, 160.4, 161.1, 170.9, 181.8 and 187.3; ν_{max} (KBr) 3438, 1716, 1670, 1635, 1585, 1282 and 1226 cm^{-1}; *m/z* (rel. intensity) 312 (M^+, 73%), 294 (21), 268 (100), 250 (49), 222 (61) and 181 (28).

Treatment of 20 with K_2CO_3 in MeOH

To a solution of **20** (314 mg, 0.85 mmol) in dry MeOH (10 mL) was added K_2CO_3 (1.17 mg) at room temperature. The suspension was stirred overnight and then 5% HCl was added to neutralize. The mixture was extracted with EtOAc, and the extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel (50% EtOAc–hexane) to give 193 mg (70%) of methyl 3-hydroxy-8-methoxy-1-methyl-9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (aloesaponarin I 8-*O*-methyl ether; **25**) as yellow crystals (Found: M^+, 326.0786. $C_{18}H_{14}O_6$ requires *M*, 326.0790); mp 200–201 °C; R_f (50% EtOAc–hexane) 0.55; δ_H 2.88 (3 H, s, 1-Me), 4.03 (3 H, s, 8-OMe), 4.05 (3 H, s, CO_2Me), 7.33 (1 H, d, J = 8.3, H^7), 7.65 (1 H, dd, J = 8.3 and 7.3, H^6), 7.67 (1 H, s, H^4), 7.83 (1 H, d, J = 7.3, H^5) and 10.53 (1 H, br s, OH); δ_C 20.6 (1-Me), 52.8 (CO_2Me), 56.6 (8-OMe), 113.4 (C4), 118.5 (C7), 119.1 (C5), 121.8 (C2 or C9a), 124.8 (C8a), 128.1 (C9a or C2), 133.8 (C6), 134.8 (C10a), 137.5 (C4a), 144.9 (C1), 159.5 (C8), 161.8 (C3), 170.4 (CO_2), 183.3 (C10) and 184.3 (C9); ν_{max} (KBr) 3572, 3459, 1712, 1670, 1587, 1336 and 1240 cm^{-1}; *m/z* (rel. intensity) 326 (M^+, 100%), 311 (54), 294 (17), 276 (47) and 220 (23).

Treatment of 20 with Et_3N in THF

To a solution of **20** (180 mg, 0.49 mmol) in dry THF (10 mL) was added Et_3N (0.68 mL, 4.9 mmol) at room temperature. The solution was stirred overnight and then water was added. The mixture was extracted with $CHCl_3$, and the extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel (30–50% EtOAc–hexane) to give 163 mg (94%) of 7-methoxy-2,2,5-trimethyl-4*H*-anthra-[2,3-*d*][1,3]dioxin-4,6,11-trione **26** as yellow needles (Found: C, 67.8; H, 4.6. $C_{20}H_{16}O_6$ requires C, 68.2; H, 4.6%); mp 222–225 °C; R_f (40% EtOAc–hexane) 0.4; δ_H 1.74 (6 H, s, 2-Me), 3.10 (3 H, s, 5-Me), 4.01 (3 H, s, 7-OMe), 7.32 (1 H, d, J = 8.1, H^{10}), 7.63 (1 H, s, H^{12}), 7.64 (1 H, t, J = 8.1, H^9) and 7.78 (1 H, d, J = 8.1, H^8); δ_C 19.2 (5-Me), 25.7 (2-Me), 56.6 (7-OMe), 105.8 (C2), 113.5 (C12), 118.0, 118.5, 119.0, 124.6, 130.8, 134.1, 134.4, 138.8, 148.6, 159.0, 159.0, 159.4, 182.9 (CO) and 184.1 (CO); ν_{max} (KBr) 1738, 1672, 1595, 1585, 1323 and 1221 cm^{-1}; *m/z* (rel. intensity) 352 (M^+, 73%), 294 (100), 276 (82), 248 (20) and 220 (40).

Conversion of 26 to 25

To a solution of **26** (163 mg, 0.46 mmol) in THF (5 mL) were added MeOH (20 mL) and K_2CO_3 (640 mg, 4.6 mmol) at room temperature. The suspension was stirred for 30 min and then aq. NH_4Cl was added. The mixture was extracted with EtOAc, and the extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel to give 128 mg (85%) of **25**.

Treatment of 18b with KHMDS in THF

The reaction of **18b** (97 mg, 0.2 mmol) was performed according to the procedure described above to give 31 mg (50%) of **24**.

Treatment of 18b with K_2CO_3 in MeOH

The reaction of **18b** (97 mg, 0.2 mmol) was carried out according to the procedure described above to give 36 mg (56%) of **25**.

1,8-Dihydroxy-3-methyl-9,10-anthraquinone (chrysophanol; 1)

To a solution of compound **21a** (44 mg, 0.16 mmol) in dry CH_2Cl_2 (5 mL) was added $AlCl_3$ (0.8 mmol) at 0 °C. After the addition, the mixture was allowed to warm to room temperature. After disappearance of the starting compound **21a**, the reaction was quenched with 1 M HCl. The mixture was extracted with $CHCl_3$, and the organic phase was washed with brine, dried over Na_2SO_4, and concentrated by rotary evaporator. The residue was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 37 mg (91%) of chrysophanol **1** as yellow crystals, mp 192.5–193.3 °C (lit., 195–196 °C,[16a] 194–195 °C[19]), R_f (30% EtOAc–hexane) 0.45; δ_H 2.46 (3 H, s), 7.10 (1 H, s), 7.28 (1 H, d, J = 8.8), 7.66 (1 H, s), 7.66 (1 H, dd, J = 8.8 and 7.4), 7.82 (1 H, d, J = 7.4), 12.00 (1 H, s) and 12.11 (1 H, s); ν_{max} (KBr) 3255, 3050, 1676, 1628, 1606, 1475, 1452, 1373 and 1268 cm^{-1}; *m/z* (rel. intensity) 254 (M^+, 100%), 226 (9), 197 (9) and 152 (8).

1,8-Dihydroxy-3-(pivaloyloxymethyl)-9,10-anthraquinone 27

To a solution of compound **21b** (736 mg, 2.0 mmol) in dry CH_2Cl_2 (10 mL) was added $AlCl_3$ (6 mmol). After the addition, the mixture was stirred overnight at room temperature. The reaction was quenched with water (10 mL) and conc. HCl (1.2 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated.

The residue was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 592 mg (84%) of **27** as yellow crystals (Found: C, 67.8; H, 5.15. $C_{20}H_{18}O_6$ requires C, 67.8; H, 5.1%); mp 164–166 °C (needles from CH_2Cl_2–hexane); R_f (CH_2Cl_2) 0.65; δ_H 1.29 (9 H, s), 5.19 (2 H, s), 7.25 (1 H, d, J = 1.7), 7.31 (1 H, dd, J = 8.3 and 1.0), 7.69 (1 H, dd, J = 8.3 and 7.8), 7.77 (1 H, d, J = 1.7), 7.84 (1 H, dd, J = 7.8 and 1.0), 12.05 (1 H, s) and 12.07 (1 H, s); δ_C 27.2, 38.9, 64.5, 115.2, 115.8, 118.2, 120.1, 122.0, 124.8, 133.5, 133.9, 137.3, 147.0, 162.6, 162.8, 177.9, 181.5 and 192.7; ν_{max} (KBr) 3452, 3220, 3080, 2972, 1730, 1676, 1622, 1456, 1440, 1278, 1168, 1154 and 772 cm^{-1}; *m*/*z* (rel. intensity) 354 (M^+, 84%), 270 (100), 254 (40), 253 (50) and 225 (56).

1,8-Dihydroxy-3-(hydroxymethyl)-9,10-anthraquinone (aloe-emodin; 2)

To a solution of *t*-BuOK (954 mg, 8.5 mmol) in dry ether (17 mL) was added water (0.04 mL) at 0 °C. After 5 min, a solution of **27** (354 mg, 1.0 mmol) dry THF (4 mL)–dry CH_2Cl_2 (10 mL) was added and then the cooling bath was removed. After 12 h, trifluoroacetic acid (10 mL) was added. After 1 h, the reaction was quenched with water (20 mL). The organic phase was separated and the aqueous phase was extracted with $CHCl_3$. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporator. The residue was purified by silica gel chromatography (30% EtOAc–hexane) to give 106 mg (39%) of **2** as yellow crystals, mp 215–217 °C (lit., 222–223 °C,[21] 220 °C[22]); R_f (30% EtOAc–hexane) 0.3; δ_H (DMSO-d_6) 4.63 (2 H, d, J = 5.4), 5.59 (1 H, t, J = 5.4, OH), 7.28 (1 H, br s), 7.37 (1 H, d, J = 7.3), 7.68 (1 H, br s), 7.70 (1 H, d, J = 7.3), 7.80 (1 H, t, J = 7.3), 11.89 (1 H, s, OH) and 11.96 (1 H, s, OH); δ_C 62.0, 114.4, 115.9, 117.1, 119.3, 120.6, 124.4, 133.1, 133.3, 137.3, 153.7, 161.3, 161.6, 181.4 and 191.6; ν_{max} (KBr) 3404, 1676, 1628, 1572, 1456 and 1288 cm^{-1}.

Methyl 3,8-dihydroxy-1-methyl-9,10-dioxo-9,10-dihydro-anthracene-2-carboxylate (aloesaponarin I; 6)

To a solution of **25** (14 mg, 0.04 mmol) in dry CH_2Cl_2 (5 mL) was added a 1 mol L^{-1} solution of BBr_3 in CH_2Cl_2 (0.45 mL, 0.45 mmol) at −78 °C. After disappearance of **25** (*ca.* 1 h), saturated aq. NH_4Cl was added (pH *ca.* 2). The mixture was extracted with EtOAc, and the extract was washed with brine, dried over Na_2SO_4, and concentrated. The residual solid was triturated with ether–hexane to afford 10 mg (69%) of **6** as yellow powdery crystals, mp 204–206 °C [lit., 199–203 °C (decomp.),[17a] 206.5–207 °C,[17b] 202.5–207 °C[17c]]; R_f (40% EtOAc–hexane) 0.45; δ_H 2.99 (3 H, s), 4.06 (3 H, s), 7.30 (1 H, dd, J = 8.3 and 1.0), 7.62 (1 H, dd, J = 8.3 and 7.8), 7.76 (1 H, dd, J = 7.8 and 1.0), 7.78 (1 H, s), 10.45 (1 H, br) and 12.92 (1 H, s); ν_{max} (KBr) 3318, 1728, 1668, 1631, 1579, 1367 and 1215 cm^{-1}; *m*/*z* (rel. intensity) 312 (M^+, 70%), 297 (13), 280 (100), 252 (17), 224 (26), 196 (10) and 168 (19).

6-[(3-Butanoyl-5-methoxy-1,4-dioxo-1,4-dihydro-2-naphthyl)-methyl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one 29

The reaction of **28**[7] (258 mg, 1.0 mmol) with **16** (322 mg, 1.5 mmol) was carried out according to the procedure described for the preparation of **20** to give 318 mg (90%) of **29** as yellow crystals (Found: C, 66.1; H, 5.8. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.6%); mp 90–92 °C; R_f (40% EtOAc–hexane) 0.25; δ_H 0.99 (3 H, t, J = 7.3), 1.65 (6 H, s), 1.74 (2 H, sextet, J = 7.3), 2.75 (2 H, t, J = 7.3), 3.42 (2H, s), 4.03 (3 H, s), 5.30 (1 H, s), 7.74 (1 H, m) and 7.76 (2 H, m); δ_C 13.6, 16.4, 24.9, 30.7, 46.1, 56.6, 94.8, 107.0, 118.5, 118.9, 119.6, 133.3, 135.8, 136.1, 149.3, 159.9, 160.6, 166.8, 182.4, 184.0 and 203.3; ν_{max} (KBr) 1729, 1698, 1664, 1657, 1632, 1585, 1280 and 1261 cm^{-1}; *m*/*z* (rel. intensity) 298 (M^+ − 100, 52%), 281 (14), 255 (100) and 240 (20).

Intramolecular cyclization of 29 with K_2CO_3 in MeOH

The reaction of **29** (360 mg, 0.9 mmol) with K_2CO_3 (1.2 g) in MeOH (30 mL) was carried according to the usual procedure as described for the reaction of **20** with K_2CO_3 and methanal to give compound **25**. Silica gel chromatography (30–50% EtOAc–hexane) gave 197 mg (62%) of methyl 3-hydroxy-8-methoxy-9,10-dioxo-1-propyl-9,10-dihydroanthracene-2-carboxylate **30a** and 16 mg (6%) of 2-ethyl-1-hydroxy-8-methoxy-3-methyl-9,10-anthraquinone **31**. **30a**: yellow crystals (Found: C, 67.5; H, 5.1. $C_{20}H_{18}O_6$ requires C, 67.8; H, 5.1%), mp 190–194 °C; R_f ($CHCl_3$–MeOH–AcOH = 92 : 5 : 3) 0.3; δ_H 1.06 (3 H, t, J = 7.3), 1.72 (2 H, m), 3.29 (2 H, m), 4.01 (3 H, s), 4.03 (3 H, s), 7.31 (1 H, dd, J = 8.3 and 1.0), 7.63 (1 H, dd, J = 8.3 and 7.8), 7.67 (1 H, s), 7.77 (1 H, dd, J = 7.8 and 1.0) and 10.12 (1 H, br); δ_C 14.6, 25.1, 33.6, 53.0, 56.6, 113.7, 118.2, 118.9, 121.4, 125.0, 127.4, 133.8, 134.6, 137.7, 149.1, 159.2, 161.7, 170.4, 183.6 and 184.4; ν_{max} (KBr) 3400, 1741, 1662, 1579, 1240 and 1215 cm^{-1}; *m*/*z* (rel. intensity) 354 (M^+, 89%), 339 (78), 337 (21), 321 (20), 307 (100), 305 (39) and 279 (24). **31**: yellow crystals (HRMS Found: M^+, 296.1068. $C_{18}H_{16}O_4$ requires *M*, 296.1049), mp 185–188 °C; R_f ($CHCl_3$–MeOH–AcOH = 92 : 5 : 3) 0.65; δ_H 1.17 (3 H, t, J = 7.5), 2.43 (3 H, s), 2.79 (2 H, q, J = 7.5), 4.07 (3 H, s), 7.34 (1 H, dd, J = 8.3 and 1.0), 7.58 (1 H, s), 7.72 (1 H, dd, J = 8.3 and 7.8), 7.96 (1 H, dd, J = 7.8 and 1.0) and 13.33 (1 H, s, OH); ν_{max} (KBr) 3444, 1672, 1631, 1585 and 1274 cm^{-1}; *m*/*z* (rel. intensity) 296 (M^+, 100%), 281 (79), 278 (28), 263 (15) and 251 (12).

Intramolecular cyclization of 29 with K_2CO_3 in *p*-methoxybenzyl alcohol

To a solution of compound **29** (50 mg, 0.13 mmol) in dry THF (0.5 mL) were added *p*-methoxybenzyl (PMB) alcohol (0.1 mL) and K_2CO_3 (174 mg, 1.3 mmol) at room temperature. After being stirred for 24 h, the reaction mixture was quenched with saturated aq. NH_4Cl. The mixture was extracted with EtOAc, and the organic phase was washed successively with water and brine, dried over Na_2SO_4, and concentrated by rotary evaporator. The residue was purified by silica gel chromatography (30–50% EtOAc–hexane) to give 42 mg (72%) of *p*-methoxybenzyl 3-hydroxy-8-methoxy-9,10-dioxo-1-propyl-9,10-dihydroanthracene-2-carboxylate **30b** as yellow crystals (Found: C, 70.2; H, 5.4. $C_{27}H_{24}O_7$ requires C, 70.4; H, 5.25%); mp 171–172 °C; R_f (40% EtOAc–hexane) 0.3; δ_H 0.84 (3 H, t, J = 7.0), 1.59 (2 H, m), 3.24 (2 H, m), 3.82 (3 H, s), 3.98 (3 H, s), 5.39 (2 H, s), 6.92 (2 H, m), 7.28 (1 H, d, J = 8.3), 7.40 (2 H, m), 7.60 (1 H, dd, J = 8.3 and 7.8), 7.65 (1 H, s), 7.77 (1 H, d, J = 7.8) and 10.14 (1 H, br, OH); δ_C 14.3, 25.2, 33.3, 55.3, 56.6, 68.3, 113.8, 114.2, 118.2, 118.9, 121.1, 125.2, 126.4, 127.5, 131.0, 133.7, 134.7, 137.8, 149.3, 159.2, 160.2, 161.9, 169.8, 183.6 and 184.4; ν_{max} (KBr) 3529, 3434, 1718, 1691, 1670, 1649, 1577, 1513, 1425, 1330, 1240 and 1213 cm^{-1}; *m*/*z* (rel. intensity) 460 (M^+, 5%), 339 (21), 228 (19), 197 (11) and 121 (100).

Methyl 3,8-dihydroxy-9,10-dioxo-1-propyl-9,10-dihydro-anthracene-2-carboxylate 32

The reaction of **30a** (177 mg, 0.5 mmol) was carried out according to the procedure described for the preparation of chrysophanol **1** except that BBr_3 was used instead of $AlCl_3$ to give 115 mg (87%) of **32** as orange crystals (Found: C, 65.3; H, 4.8. $C_{19}H_{16}O_6 \cdot 0.5H_2O$ requires C, 65.3; H, 4.9%); mp 190–193.5 °C; R_f (40% EtOAc–hexane) 0.45; δ_H (DMSO-d_6) 1.00 (3 H, t, J = 7.3), 1.60 (2 H, m), 3.03 (2 H, m), 3.89 (3 H, s), 7.32 (1 H, dd, J = 8.3 and 1.5), 7.63 (1 H, dd, J = 7.3 and 1.5), 7.66 (1 H, s), 7.71 (1 H, dd, J = 8.3 and 7.3), 11.42 (1 H, br) and 12.74 (1 H, br); δ_C (DMSO-d_6; 80 °C) 13.9, 23.1, 33.8, 51.8, 112.1, 116.6, 117.9, 121.8, 124.0, 129.4, 132.1, 135.6, 136.9, 145.4, 158.7, 161.2, 166.6, 181.5 and 188.7; ν_{max} (KBr) 3388, 1720, 1660, 1630, 1577, 1467, 1243, 1214 and 1080 cm^{-1}; *m*/*z* (rel. intensity) 340 (M^+, 57%), 325 (13), 307 (22), 290 (100) and 265 (20).

3,8-Dihydroxy-9,10-dioxo-1-propyl-9,10-dihydroanthracene-2-carboxylic acid (K1115A; 8)

An identical reaction of **30b** (40 mg, 0.09 mmol) was carried out as above to give 17 mg (59%) of **8** as orange crystals; mp 243–245 °C (lit.,[18] 255–258 °C); R_f ($CHCl_3$–MeOH–CH_3CO_2H = 94 : 5 : 1) 0.4; δ_H (DMSO-d_6) 1.02 (3 H, t, J = 7.3), 1.61 (2 H, m), 3.08 (2 H, m), 7.36 (1 H, dd, J = 8.3 and 1.0), 7.63 (1 H, s), 7.65 (1 H, dd, J = 7.6 and 1.5), 7.74 (1 H, dd, J = 8.3 and 7.6), 11.8 (1 H, br, OH), 12.91 (1 H, s, OH) and 13.4 (1 H, br, OH); ν_{max} (KBr) 3388, 1736, 1707, 1670, 1631, 1582, 1468, 1363, 1321, 1270, 1234 and 1215 cm^{-1}; MS *m*/*z* (rel. intensity) 326 (M^+, 48%), 293 (22), 290 (100) and 265 (19).

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