An Oxidative Dimerization of Anthrones by Oxygen-Metal Acetate System

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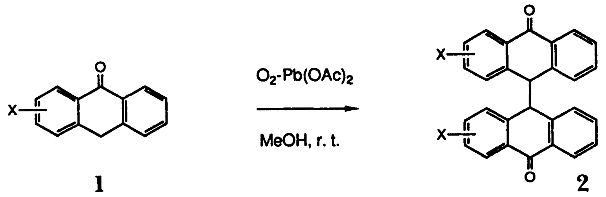
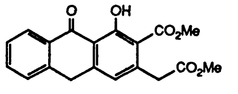
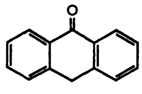
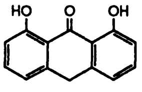
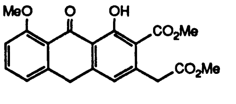
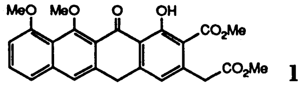
Synopsis. Anthrones were oxidatively dimerized with oxygen in the presence of $Pb(OAc)_2$ giving 9,9′-bianthracene-10,10′(9*H*,9′*H*)-diones. The dimerization proceeds under mild reaction conditions, and gives products in good yields. Binaphthacenedione and bipentacenedione were also synthesized.

9′9-Bianthracene-10,10′(9*H*,9*H*)-diones and their derivatives possess interesting chemical, physical, or biological properties. For example, sennosides are natural purgatives,[1] and photochromism, thermochromism, or piezochromism of $\Delta^{10,10'}$-bianthrone, dehydro derivative of 9,9′-bianthracene-10,10′(9*H*, 9′*H*)-dione, has been known.[2] As for the synthesis of 9,9′-bianthracene-10,10′(9*H*,9′*H*)-diones, oxidative dimerization of anthrones has been conducted using several oxidants,[1–6] of which $FeCl_3$ was most frequently employed.[1a,2a,3] Although the dimerization can be carried out with oxygen more conveniently,[7] the reaction was sluggish, and relatively strong basic conditions were required for promotion. During our investigations on the synthesis of polycyclic aromatic compounds,[8] a novel oxygen-induced dimerization of anthrones, which proceeds under mild reaction conditions, was found.

Table 1. Oxidative Dimerization of Anthrones



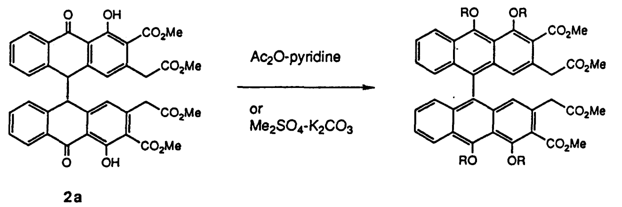
1 2

Entries	Anthrones		Yields/%
1		1a	92[a], 41[a,b]
2		1b	84
3		1c	41, 23[b]
4		1d	73[a]
5		1e	59[a]

a) The products were a 1 : 1 mixture of two diastereomers.
b) Instead of $Pb(OAc)_2$, $Cd(OAc)_2$ was used.

When 2-methoxycarbonyl-3-methoxycarbonylmethyl-1,9-anthracenediol (**1a**)[8f] was treated with $Pb(OAc)_2$ in methanol at room temperature, oxidative dimerization reaction proceeded smoothly and 4,4′-dihydroxy-3,3′-bis(methoxycarbonyl)-2,2′-bis(methoxycarbonylmethyl)-9,9′-bianthracene-10,10′(9*H*,9′*H*)-dione (**2a**) was obtained in quantitative yield. The use of $Cd(OAc)_2$ gave **2a** in lower yield. Other metal acetates were less effective. Under oxygen atmosphere the reaction was accelerated. Although mass spectra of **2a** showed the parent peak corresponding to the monomer, the dimeric structure was determined by conversion to acetate **3a** or methyl ether **4a**, which gave parent peaks of dimers (Scheme 1). ^1H NMR spectra of **1a** showed the presence of two stereoisomers. Since **1a** exists in keto-form, they are *meso*- and *dl*-isomers concerning 9- and 9′-chiral centers.[9]

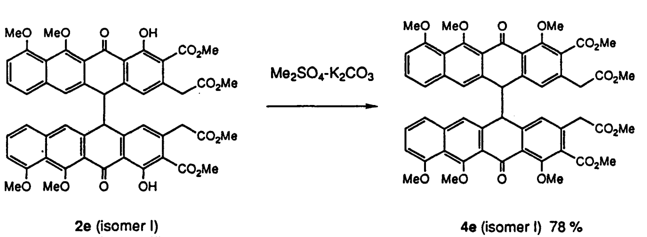
Several other anthrones were oxidatively dimerized in the presence of $Pb(OAc)_2$ in good yields (Table 1). Under the reaction conditions, 1,8-dihydroxyanthrone (**1c**) gave dimer **2c** of thermodynamically less stable *pseudoaxial-pseudoaxial*-type conformation rather than *pseudoequatorial-pseudoequatorial*-type.[7b] Two stereoisomers synthesized by the dimerization of anthrone **1d** or 12-naphthacenone **1e** were separable by silica gel chromatography. Equilibration between *meso*- and *dl*-isomer was not observed. The intercon-



2a

3a (R = Ac) 82 %
4a (R = Me) 53 %

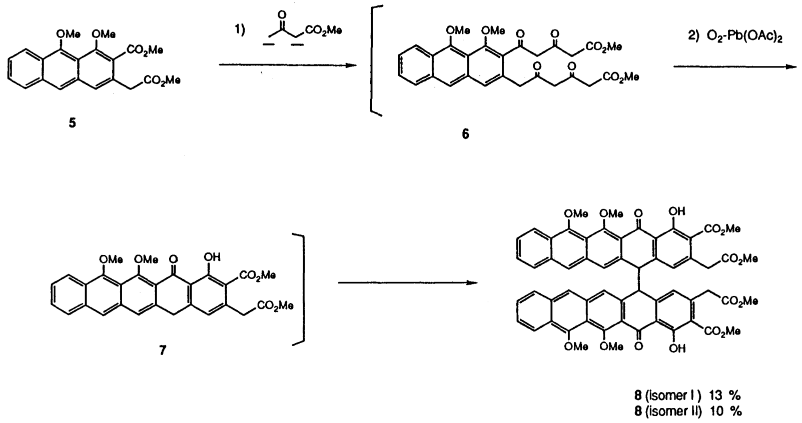
Scheme 1.



2e (isomer I)
2e (isomer II)

4e (isomer I) 78 %
4e (isomer II) 62 %

Scheme 2.



Scheme 3.

version did not proceed even under basic conditions. Each of the two isomers of **2e** gave distinct methylated product at 1-hydroxy group by treating with dimethyl sulfate and K_2CO_3 (Scheme 2). It is presumed that enolization is inhibited by severe steric repulsion between 12-hydroxyl group and substituents at 1- and 11-position in the planar structure of enol form. The behavior of **2e** is contrasted to that of **2a** lacking 8-substituent, which readily aromatized to **4a** (Cf. Scheme 1).

The dimerization reaction was applied to pentacenone **7** formed from dimethoxyanthracene **5** (Scheme 3). According to the reactions developed in our laboratory,[8)] **5** was treated with methyl acetoacetate dianion followed by $Pb(OAc)_2$, and 5,5′-dipentacene-14,14′(5*H*,5′*H*)-dione (**8**) was obtained as a separable mixture of two stereoisomers. Here, $Pb(OAc)_2$ serves as the promoter of intramolecular condensation of polyketide intermediate **6** and oxidative dimerzation of **7**.

Experimental

Melting points were not corrected. NMR spectra were obtained on a JEOL JNM-FX-60. Chemical shift values are given in ppm relative to internal Me_4Si. IR spectra were recorded on a Shimadzu IR-408. High-resolution mass spectra were taken with JEOL JMS-DX-300. UV spectra were obtained on a Hitachi Model 150-20 double beam spectrophotometer.

1,1′-Dihydroxy-2,2′-bis(methoxycarbonyl)-3,3′-bis(methoxycarbonylmethyl)-10,10′,11,11′-tetramethoxy-5,5′-binaphthacene-12,12′(5*H*,5′*H*)-dione (2e). A mixture of (**1e**,[8f)] 60 mg, 0.13 mmol) and $Pb(OAc)_2 \cdot 3H_2O$ (184 mg, 0.68 mmol) in methanol (4 mL) was stirred overnight vigorously. The mixture was filtered, and washed with dichloromethane. Solvents were removed in vacuo, and the residue was chromatographed on silica gel to give 16 mg (26%) of Isomer I (with higher R_f) and 19 mg (32%) of Isomer II (with lower R_f). Isomer I: Mp 222—225 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.57 (6H, s), 3.77 (6H, s), 3.90 (4H, s), 3.94 (6H, s), 3.98 (6H, s), 4.59 (2H, s), 6.36 (2H, s), 6.83 (2H, d, J=7 Hz), 7.04 (2H, s), 7.06 (2H, d, J=7 Hz), 7.50 (2H, t, J=7 Hz), 12.99 (2H, s). IR (KBr) 3400, 1740, 1720, 1630, 1605 cm^{-1}. HRMS Calcd for $C_{25}H_{22}O_8$: 450.1314. Found: 450.1282 (M/2+H). Isomer II: Mp 228—230 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.70 (16H, s), 3.92 (6H, s), 3.98 (6H, s), 4.66 (2H, s), 6.36 (2H, s), 6.85 (2H, d, J=8 Hz), 6.98 (2H, s), 7.09 (2H, d, J=8 Hz), 7.47 (2H, t, J=8 Hz), 12.94 (2H, s). IR (KBr) 3300, 1735, 1710, 1630, 1610 cm^{-1}. HRMS Calcd for $C_{25}H_{22}O_8$: 450.1314. Found: 450.1321 (M/2+H).

4,4′-Dihydroxy-3,3′-bis(methoxycarbonyl)-2,2′-bis(methoxycarbonylmethyl)-9,9′-bianthracene-10,10′(9*H*,9′*H*)-dione (2a). ^{1}H NMR ($CDCl_3$) δ=3.71 (5H, s), 3.74 (5 H, s), 3.93 (3H, s), 3.96 (3H, s), 4.61 (1H, s), 4.63 (1H, s), 6.33 (1H, s), 6.3—6.9 (2H, m), 6.68 (1H, s), 7.2—7.5 (4H, m), 7.7—8.0 (2H, m), 12.83 (1H, s), 12.88 (1H, s). IR (KBr) 3400, 1735, 1630, 1595 cm^{-1}. HRMS Calcd for $C_{19}H_{16}O_6$: 340.0947. Found: 340.0950 (M/2+H).

9,9′-Bianthracene-10,10′(9*H*,9′*H*)-dione (2b). Mp 270—272 °C decomp ($CHCl_3$). Lit, 264—266 °C decomp.[10)] ^{1}H NMR spectra was identical to the reported data.[10)]

4,4′,8,8′-Tetrahydroxy-9,9′-bianthracene-10,10′ (9*H*,9′*H*)-dione (2c). Mp 237 °C decomp (benzene). Lit, 230 °C decomp.[7b)] ^{1}H NMR was identical to the reported data of *pseudoaxial-pseudoaxial*-type conformation.[7b)]

4,4′-Dihydroxy-5,5′-dimethoxy-3,3′-bis(methoxycarbonyl)-2,2′-bis(methoxycarbonylmethyl)-9,9′-bianthracene-10,10′(9*H*,9′*H*)-dione (2d). Isomer I (with higher R_f): Mp 185—186 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.74 (6H, s), 3.81 (4H, s), 3.85 (6H, s), 3.95 (6H, s), 4.51 (2H, s), 5.88 (2H, d, J=7 Hz), 6.87 (2 H, s), 6.88 (2H, d, J=7 Hz), 7.26 (2H, t, J=7 Hz), 12.93 (2H, s). IR (KBr) 3500, 1735, 1620 cm^{-1}. UV ($CHCl_3$) λ_{max} 353 nm. HRMS Calcd for $C_{20}H_{18}O_7$: 370.1052. Found: 370.1079 (M/2+H). Isomer II (with lower R_f): Mp 192—194 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.65 (4H, s), 3.70 (6H, s), 3.92 (12H, s), 4.48 (2H, s), 6.25 (2H, s), 6.44 (2H, d, J=8 Hz), 6.93 (2H, s), 7.40 (2H, t, J=8 Hz), 12.87 (2H, s). IR (KBr) 3400, 1735, 1625 cm^{-1}. UV ($CHCl_3$) λ_{max} 353 nm. HRMS Calcd for $C_{20}H_{18}O_7$: 370.1052. Found: 370.1043 (M/2+H).

3,3′-Bis(methoxycarbonyl)-2,2′-bis(methoxycarbonylmethyl)-4,4′,10,10′-tetramethoxy-9,9′-bianthracene (4a). Under a nitrogen atmosphere, a mixture of **2a** (68 mg, 0.21 mmol), K_2CO_3 (119 mg, 0.86 mmol), dimethyl sulfate (0.5 mL), and acetone (5 mL) was stirred at reflux for 3 h. Then 2 M hydrochloric acid (1 M=1 mol dm^{-3}) was added, and organic materials were extracted twice with chloroform. Combined extracts were washed with water and brine, dried (Na_2SO_4), concentrated, and chromatographed on silica gel to give **4a** (41 mg, 53%). Mp 167—172 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.46 (10H, s), 3.96 (6H, s), 4.16 (6H, s), 4.22 (6H, s), 6.76 (2H, s), 6.7—7.6 (6H, m), 8.53 (2H, d, J=8 Hz). IR (KBr) 1740 cm^{-1}. UV ($CHCl_3$) λ_{max} 417, 395, 375, 269 nm. HRMS Calcd for $C_{42}H_{38}O_{12}$: 734.2364. Found: 734.2403.

1,1′,10,10′,11,11′-Hexamethoxy-2,2′-bis(methoxycarbon-

yl)-3,3′-bis(methoxycarbonylmethyl)-5,5′-binaphthacene-12,12′(5*H*,5′*H*)-dione (4e). Two isomers I and II of **2e** were methylated in 78 and 62% yields, respectively. **4e** (isomer I) synthesized from **2e** (isomer I): Mp 239—242 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.68 (6H, s), 3.70 (6H, s), 3.90 (6H, s), 3.91 (12H, s), 3.96 (4H, s), 4.53 (2H, s), 6.61 (2H, s), 6.7—7.1 (4H, m), 6.96 (2H, s), 7.36 (2H, t, *J*=8 Hz). IR (KBr) 1735, 1675, 1615, 1595, 1560 cm^{-1}. UV ($CHCl_3$) λ_{max} 383 nm. HRMS Calcd for $C_{26}H_{23}O_8$: 463.1392. Found: 463.1374 (M/2). **4e** (isomer II) synthesized from **2e** (isomer II): Mp 259—262 °C ($CHCl_3$-hexane). ^{1}H NMR ($CDCl_3$) δ=3.64 (10H, s), 3.73 (6H, s), 3.87 (6H, s), 3.89 (6H, s), 3.99 (6H, s), 4.57 (2H, s), 6.58 (2H, s), 6.7—7.2 (4H, m), 6.98 (2H, s), 7.42 (2H, t, *J*=7Hz). IR (KBr) 1740, 1685, 1620, 1600, 1565 cm^{-1}. UV ($CHCl_3$) λ_{max} 382 nm. HRMS Calcd for $C_{26}H_{24}O_8$: 464.1471. Found: 464.1494 (M/2+H).

3,3′-Bis(methoxycarbonyl)-2,2′-bis(methoxycarbonylmethyl)-4,4′,10,10′-tetraacetoxy-9,9′-bianthracene (3a). Under a nitrogen atmosphere, a mixture of **2a** (34 mg, 0.10 mmol), a catalytic amount of 4-dimethylaminopyridine, pyridine (2 mL), and acetic anhydride (0.5 mL) was stirred overnight at room temperature. Saturated aqueous $KHSO_4$ was added and organic materials were extracted twice with chloroform. Organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), concentrated, and chromatographed on silica gel to give **3a** (34 mg, 82%). Mp 140—144 °C (benzene-hexane). ^{1}H NMR ($CDCl_3$) δ=2.50 (6H, s), 2.65 (6H, s), 3.45 (6H, s), 3.60 (4H, s), 3.87 (6H, s), 6.8—7.7 (6H, m), 6.94 (2H, s), 8.08 (2H, d, *J*=8Hz). IR (KBr) 1770, 1730, 1615 cm^{-1}. MS 847 (M+H)

1,1′-Dihydroxy-2,2′-bis(methoxycarbonyl)-3,3′-bis(methoxycarbonylmethyl)-12,12′,13,13′-tetramethoxy-5,5′-bipentacene-14,14′(5*H*,5′*H*)-dione (8). Under a nitrogen atmosphere, a THF (4 mL) solution of methyl acetoacetate dianion[11] was prepared from methyl acetoacetate (132 mg, 1.7 mmol), sodium hydride (42 mg, 1.9 mmol), and hexane solution (1.1 mL) of butyllithium (1.7 mmol). Methyl 4,10-dimethoxy-3-methoxycarbonyl-2-anthraceneacetate (**5**,[8f] 78 mg, 0.21 mmol) in THF (2 mL) was added at 0 °C, and stirring was continued for 2 h at room temperature. The reaction mixture was poured on cooled 2 M hydrochloric acid, and organic materials were extracted twice with ethyl acetate. The combined organic layer was washed with water and brine, dried (Na_2SO_4), and concentrated. Methanol (2 mL) and $Pb(OAc)_2 \cdot 3H_2O$ (380 mg, 1.0 mmol) were added to the residue, and the mixture was stirred vigorously for 3 h at room temperature. Then, 2 M hydrochloric acid was added, and organic materials were extracted twice with ethyl acetate. Organic layer was washed with water and brine, dried (Na_2SO_4), concentrated, and chromatographed on silica gel giving isomer I (10 mg, 10%) and isomer II (13 mg, 13%) of **8**. Isomer I (with higher R_f): Mp 170—172 °C (AcOEt-hexane). ^{1}H NMR ($CDCl_3$) δ=3.67 (6H, s), 3.81 (6H, s), 3.93 (4H, s), 3.99 (12H, s), 4.62 (2H, s), 6.59 (2H, s), 7.09 (2H, s), 7.3—7.6 (4H, m), 7.87 (2H, s), 7.7—8.0 (2H, m), 8.1—8.4 (2H, m), 12.79 (2H, s). IR (KBr) 3400, 1735, 1630, 1600 cm^{-1}. UV ($CHCl_3$) λ_{max} 455, 339, 281, 258 nm. HRMS Calcd for $C_{29}H_{24}O_8$: 500.1470. Found: 500.1461 (M/2+H). Isomer II (with lower R_f): Mp 156—157 °C (AcOEt-hexane). ^{1}H NMR ($CDCl_3$) δ=3.72 (16H, s), 3.94 (6H, s), 4.01 (6H, s), 4.76 (2H, s), 6.40 (2H, s), 7.25 (2H, s), 7.4—7.7 (4H, m), 7.7—8.0 (2H, m), 7.88 (2H, s), 8.2—8.5 (2H, m), 12.90 (2H, s). IR(KBr) 3400, 1735, 1625, 1600 cm^{-1}. UV ($CHCl_3$) λ_{max} 454, 339, 264 nm. HRMS Calcd for $C_{29}H_{24}O_8$: 500.1470. Found: 500.1468 (M/2+H).

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