[Chem. Pharm. Bull. 30(7)2440—2446(1982)]

Studies on Ketene and Its Derivatives. CIX.[1] Synthesis of naturally Occurring Anthracene-9,10-diones

NOBUYA KATAGIRI,[a] TETSUZO KATO,*,[a] and JUN NAKANO[b]

Pharmaceutical Institute, Tohoku University,[a] Aobayama, Sendai, 980, Japan and Kakenyaku-Kako, Kyoto Research Laboratories,[b] 14 Shionomiya Minami Kawara-cho, Yamashina-ku, Kyoto 607, Japan

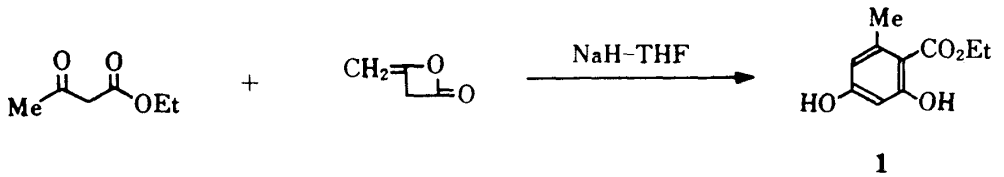
(Received January 23, 1982)

The synthesis of naturally occurring anthracene-9,10-diones (**12a**—**c**) from ethyl 2-benzyl-4,6-dihydroxybenzoates (**7a**—**d**), prepared by the reaction of diketene with ethyl 4-aryl-3-oxobutanoates (**6a**—**d**), is described. Reaction of diketene with **6a**—**d** in the presence of sodium hydride in tetrahydrofuran gave **7a**—**d**. Treatment of **7a**—**d** with methyl iodide in the presence of potassium carbonate, followed by ethanolic sodium hydroxide, gave 2-benzyl-4,6-dimethoxybenzoic acids (**9a**—**d**). Cyclization of **9a**—**d** with trifluoroacetic acid-trifluoroacetic anhydride gave anthrone derivatives (**10a**—**d**) which, without purification, were oxidized with chromium trioxide to give the anthracene-9,10-diones (**11a**—**d**). Selective demethylation of **11a**—**c** with boron tribromide gave **12a**—**c**.

Keywords——ethyl 4-aryl-3-oxobutanoates; diketene; orsellinic acid derivatives; cyclization; anthracene-9,10-diones; selective demethylation

A large number of naturally occurring anthracene-9,10-diones have been found,[2] and used practically as dyes. The anthracene-9,10-dione nucleus can be obtained from the following three reactions; (a) oxidation of anthracene derivatives, (b) cyclization of 2-benzoylbenzoic acid derivatives (obtainable by Friedel–Crafts reaction), and (c) Diels–Alder reaction of benzoquinones with butadienes, followed by oxidation. Among them method (b) has been most extensively used. However, this reaction is not effective for the preparation of anthracene-9,10-diones having a number of substituents, because of the low yield and low regioselectivity.

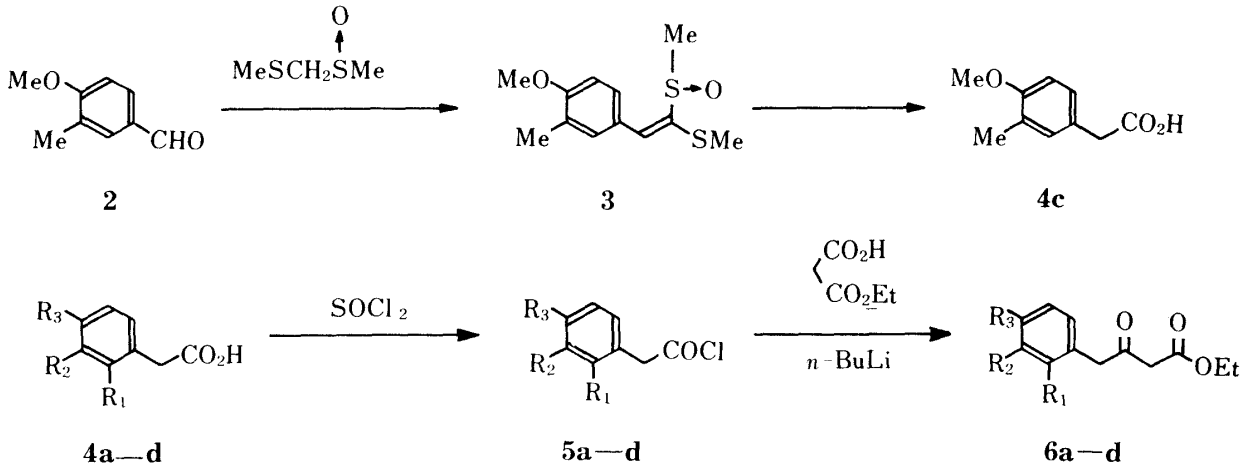
We have previously reported the reaction of diketene with ethyl acetoacetate to give ethyl orsellinate (**1**).[3] Applying this reaction, we have prepared some orsellinic acid derivatives starting from various β-keto esters.[4] The synthesis of natural products such as lichexanthone[5] and bikaverin[6] by using compound **1** has been also reported by us. In the present paper we wish to report the synthesis of naturally occurring anthracene-9,10-diones such as xanthopurpurin 3-methyl ether (**12a**), 6-methylxanthopurpurin 3-methyl ether (**12b**), and macrosporin 3-methyl ether (**12c**), from 2-benzylbenzoic acids prepared by the reaction of diketene with ethyl 4-aryl-3-oxobutanoates (**6a**—**d**).



1

Chart 1

Ethyl 4-aryl-3-oxobutanoates (**6a**—**d**) were synthesized from arylacetic acids (**4a**—**d**), which were obtained commercially (**4a**, **b**, and **d**) except for 4-methoxy-3-methylphenylacetic acid (**4c**). The last compound was prepared as follows; 4-methoxy-3-methylbenzaldehyde (**2**), prepared by the regioselective formylation of *o*-methoxytoluene with hexamine in trifluoro-



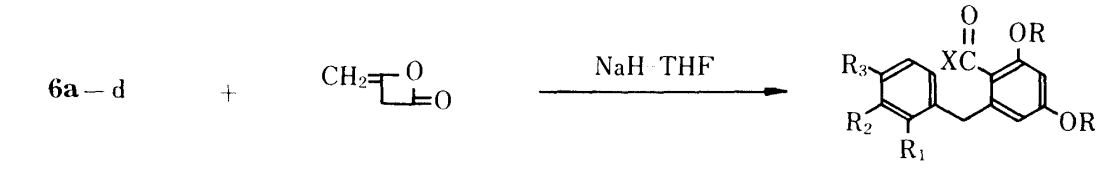
a: $R_1=R_2=R_3=H$ **c**: $R_1=H$, $R_2=Me$, $R_3=OMe$
b: $R_1=R_3=H$, $R_2=Me$ **d**: $R_1=OMe$, $R_2=R_3=H$

Chart 2

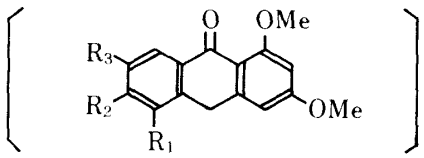
TABLE I. Ethyl 4-Aryl-3-oxobutanoates (**6a—d**)

Compd. No.	Yield (%)	bp (mmHg) (°C)	Formula	Analysis (%) Calcd (Found) C	H	IR ν_{max}^{neat} cm^{-1}	MS *m/e* (M$^+$)
6a	85	118—120(1.6)[a]				1740, 1717	206
6b	73	134(2.3)	$C_{13}H_{16}O_3$	70.89 (70.72)	7.32 (7.36)	1740, 1718	220
6c	77	155(0.7)	$C_{14}H_{18}O_4$	69.39 (69.21)	7.49 (7.50)	1740, 1717	250
6d	79	147(0.9)	$C_{13}H_{16}O_4$	68.39 (68.16)	7.06 (7.18)	1740, 1718	236

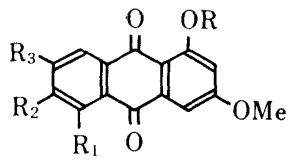
a) Lit.[14] 153—155 °C (9 mmHg).



7a—d : R=H, X=OEt
8a—d : R=Me, X=OEt
9a—d : R=Me, X=OH



10a—d



11a—d : R=Me
12a—c : R=H

a: $R_1=R_2=R_3=H$ **c**: $R_1=H$, $R_2=Me$, $R_3=OMe$
b: $R_1=R_3=H$, $R_2=Me$ **d**: $R_1=OMe$, $R_2=R_3=H$

Chart 3

acetic acid, was treated with methyl methylthiomethyl sulfoxide (FAMSO)[7] to give compound **3**, which was hydrolyzed to compound **4c**.

The acids (**4a—d**) were treated with thionyl chloride to give the corresponding arylacetyl chlorides (**5a—d**), which, according to the method reported by Wierenga *et al.*,[8] were treated with ethyl malonate in the presence of *n*-butyllithium to give ethyl 4-aryl-3-oxobutanoates (**6a—d**). The results are summarized in Table I.

When compounds **6a—d** were allowed to react with diketene in the presence of sodium hydride in tetrahydrofuran, crystalline products were obtained. Purification by silica gel column chromatography gave ethyl 2-benzyl-4,6-dihydroxybenzoates (**7a—d**) in *ca.* 30% yield. In order to prevent decarboxylation in the subsequent cyclization process, compounds **7a—d**

TABLE II. Ethyl 2-Benzyl-4,6-dihydroxybenzoates (**7a—d**)

Compd. No.	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	IR ν_{max}^{KBr} cm^{-1}	MS *m/e* (M$^+$)	^{1}H-NMR ($CDCl_3$) δ (ppm) $-CH_2-$	3,5-Ring H	4,6-OH	Others
7a	30.5	120—123	$C_{16}H_{16}O_4$	70.57 (70.29	5.92 6.01)	3340, 1640	272	4.31 (s)	6.23 (d, J= 2.5 Hz)	6.04 (br s)	1.16 (3H, t, J= 7.5 Hz)
									6.40 (d, J= 2.5 Hz)	11.64 (s)	4.26 (2H, q, J= 7.5 Hz)
											7.04—7.40 (5H, m)
7b	28.9	106—107	$C_{17}H_{18}O_4$	71.31 (71.16	6.34 6.39)	3350, 1641	286	4.23 (s)	6.15 (d, J= 2.5 Hz)	5.60 (br s)	1.19 (3H, t, J= 7.5 Hz)
									6.34 (d, J= 2.5 Hz)	11.55 (s)	2.28 (3H, s)
											4.25 (2H, q, J= 7.5 Hz)
											6.78—6.92 (2H, m)
											7.02 (1H, br s)
											7.11 (1H, d, J= 7.5 Hz)
7c	28.7	117—118	$C_{18}H_{20}O_5$	68.34 (68.54	6.37 6.61)	3340, 1640	316	4.20 (s)	6.15 (d, J= 2.5 Hz)	5.45 (br s)	1.15 (3H, t, J= 7.5 Hz)
									6.36 (d, J= 2.5 Hz)	11.50 (s)	2.18 (3H, s)
											3.80(3H, s)
											4.31 (2H, q, J= 7.5 Hz)
											6.80—6.95 (3H, m)
7d	26.4	138—139	$C_{17}H_{18}O_5$	67.54 (67.98	6.00 5.89)	3325, 1640	302	4.24 (s)	6.14 (d, J= 2.5 Hz)	11.51[a] (s)	1.11 (3H, t, J= 7.5 Hz)
									6.38 (d, J= 2.5 Hz)		3.84 (3H, s)
											4.21 (2H, q, J= 7.5 Hz)
											6.84—6.96 (4H, m)

a) 4-OH undetected.

Table III. Ethyl 2-Benzyl-4,6-dimethoxybenzoates (**8a—d**)

Compd. No.	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	IR ν_{max}^{neat} cm^{-1}	MS m/e (M^+)	^{1}H-NMR ($CDCl_3$) δ (ppm) OMe	$-CH_2-$	3,5-Ring H	Others
8a	92.0	$C_{18}H_{20}O_4$	71.98 (71.73	6.71 6.79)	1720	300	3.73(s) 3.79(s)	3.98(s)	6.30 (d, J=2 Hz) 6.37 (d, J=2 Hz)	1.23 (3H, t, J=7.5 Hz) 4.26 (2H, q, J=7.5 Hz) 7.18—7.30 (5H, m)
8b	94.2	$C_{19}H_{22}O_4$	72.59 (72.28	7.05 7.17)	1722	314	3.81(s) 3.88(s)	4.01(s)	6.38 (d, J=2 Hz) 6.46 (d, J=2 Hz)	1.33 (3H, t, J=7.5 Hz) 2.38 (3H, s) 4.35 (2H, q, J=7.5 Hz) 7.02—7.30 (4H, m)
8c	90.1	$C_{20}H_{24}O_5$	69.75 (69.56	7.02 7.08)	1720	344	3.71(s) 3.75(s) 3.77(s)	3.85(s)	6.26 (d, J=2 Hz) 6.33 (d, J=2 Hz)	1.26 (3H, t, J=7.5 Hz) 2.16 (3H, s) 4.25 (2H, q, J=7.5 Hz) 6.71 (1H, d, J=9 Hz) 6.95 (2H, br s)
8d	95.1	$C_{19}H_{20}O_5$	69.50 (69.24	6.14 6.23)	1720	330	3.74(s) 3.82 (6H, s)	3.98(s)	6.30 (d, J=2 Hz) 6.38 (d, J=2 Hz)	1.25 (3H, t, J=7.5 Hz) 4.30 (2H, q, J=7.5 Hz) 6.78—7.25 (4H, m)

Table IV. 2-Benzyl-4,6-dimethoxybenzoic Acids (**9a—d**)

Compd. No.	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	IR ν_{max}^{KBr} cm^{-1}	MS m/e (M^+)	^{1}H-NMR ($CDCl_3$) δ (ppm) OMe	$-CH_2-$	3,5-Ring H	COOH	Others
9a	91.5	173—175[a]	$C_{16}H_{16}O_4$	70.57 (70.33	5.92 5.98)	3420 1686	272	3.79 (s) 3.84 (s)	4.30 (s)	6.40 (d, J= 2 Hz) 6.46 (d, J= 2 Hz)	Unde-tected	7.24—7.38 (5H, br s)
9b	93.8	131—132[b]	$C_{17}H_{18}O_4$	71.31 (71.28	6.34 6.25)	3430 1693	286	3.76 (s) 3.89 (s)	4.16 (s)	6.39 (d, J= 2 Hz) 6.45 (d, J= 2 Hz)	10.21 (br s)	2.30 (3H, s) 6.95—7.23 (4H, m)
9c	91.9	127[a]	$C_{18}H_{20}O_5$	68.34 (68.54	6.37 6.61)	3450 1680	316	3.73 (6H, s) 3.84 (s)	4.06 (s)	6.29 (d, J= 2 Hz) 6.35 (d, J= 2 Hz)	9.98—10.60 (br s)	2.14 (3H, s) 6.69 (1H, d, J=9 Hz) 6.89—7.05 (2H, br s)
9d	91.0	156[b]	$C_{17}H_{18}O_5$	67.54 (67.89	6.00 6.06)	3420 1676	302	3.73 (s) 3.78 (s) 3.90 (s)	4.22 (s)	6.34 (d, J= 2 Hz) 6.41 (d, J= 2 Hz)	Unde-tected	6.83—6.97 (2H, m) 7.06—7.15 (2H, m)

a) Recrystallization from benzene–hexane (5:1).
b) Recrystallization from benzene.

were methylated with methyl iodide in the presence of potassium carbonate in acetone to give dimethoxy derivatives **8a**—**d**. Compounds **8a**—**d** were hydrolyzed with alcoholic sodium hydroxide to give the corresponding 2-benzyl-4,6-dimethoxybenzoic acids (**9a**—**d**).

Next, cyclization of **9a**—**d** was carried out. Compounds **9a**—**d** were treated with a mixture of trifluoroacetic acid and trifluoroacetic anhydride to give anthrone derivatives **10a**—**d**.[9] However, compounds **10a**—**d** were difficult to isolate owing to their instability. Therefore, compounds **10a**—**d**, without purification, were oxidized with chromium trioxide (CrO_3) in acetic acid to give the anthracene-9,10-diones **11a**—**d**.[9,10] Selective demethylation of **11a**—**c** with boron tribromide in methylene chloride gave anthracene-9,10-diones **12a**—**c**,[11] which were identical with naturally occurring samples. The results are summarized in Tables II—V.

TABLE V. Anthracene-9,10-diones (**11a**—**d** and **12a**—**c**)

Compd. No.	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	IR ν_{max}^{KBr} cm^{-1}	MS *m/e* (M+)	^{1}H-NMR ($CDCl_3$) δ (ppm) OMe	2-Ring H	4-Ring H	OH	Others
11a	36.7	160—161[a,g]	$C_{16}H_{12}O_4$	71.63 (71.84	4.51 4.71)	1668 1659	268	3.93 (s) 3.97 (s)	6.75(d, *J*=2 Hz)	7.41(d, *J*=2 Hz)	—	7.64—7.77 (2H, m) 8.16—8.24 (2H, m)
11b	54.8	191—192[h]	$C_{17}H_{14}O_4$	72.33 (72.21	5.00 4.83)	1670 1660	282	3.93 (s) 3.96 (s)	6.72(d, *J*=2 Hz)	7.38(d, *J*=2 Hz)	—	2.48 (3H, s) 7.50 (1H, dd, *J*=8, 1.5 Hz) 7.93 (1H, br s) 8.09 (1H, d, *J*=8 Hz)
11c	87.8	267[b,i]	$C_{18}H_{16}O_5$	69.22 (69.08	5.16 5.03)	1658	312	3.94 (s) 3.96 (6H, s)	6.71(d, *J*=2 Hz)	7.41(d, *J*=2 Hz)	—	2.30 (3H, s) 7.60 (1H, s) 7.93 (1H, s)
11d	58.0	204[c,g]	$C_{17}H_{14}O_5$	68.45 (68.50	4.73 4.66)	1658	298	3.98 (s) 4.03 (s) 4.06 (s)	6.80(d, *J*=2 Hz)	7.48(d, *J*=2 Hz)	—	7.31 (1H, dd, *J*=8, 1.3 Hz) 7.75 (1H, t, *J*=8 Hz) 7.99 (1H, dd, *J*=8, 1.3 Hz)
12a	85.0	193—194[d,j]	$C_{15}H_{10}O_4$	70.86 (70.59	3.96 4.20)	3430 1674 1630	254	3.90 (s)	6.68(d, *J*=2 Hz)	7.34(d, *J*=2 Hz)	12.47 (s)	7.67—7.83 (2H, m) 8.18—8.36 (2H, m)
12b	81.6	183—184[e,j]	$C_{16}H_{12}O_4$	71.63 (71.78	4.51 4.45)	3430 1670 1626	268	3.90 (s)	6.66(d, *J*=2.5 Hz)	7.31(d, *J*=2.5 Hz)	12.51 (s)	2.50 (3H, s) 7.55 (1H, d, *J*=8 Hz) 8.02 (1H, br s) 8.13 (1H, d, *J*=8 Hz)
12c	87.9	209—210[f,g]	$C_{17}H_{14}O_5$	68.45 (68.43	4.73 4.58)	3450 1670 1625	298	3.93 (s) 4.01 (s)	6.19(d, *J*=2 Hz)	7.35(d, *J*=2 Hz)	12.46 (s)	2.33 (3H, s) 7.63 (1H, s) 8.03 (1H, s)

a) Lit.[15] 155°C,[16a] 162—163°C,[16b] 163°C.
b) Lit.[17] 260—261°C,[18a] 260°C,[18a] 270—271°C.
c) Lit.[20] 203°C,[21] 201.5—202°C.
d) Lit.[16a] 193°C,[15] 193°C,[22] 193°C.
e) Lit.[19a] 184—185°C,[19b] 182°C.
f) Lit.[18a] 209—210°C,[18b] 208°C,[19a] 214°C.
g) Recrystallization from benzene.
h) Recrystallization from benzene–ethyl acetate (1:1).
i) Recrystallization from benzene–chloroform (1:1).
j) Recrystallization from benzene–*n*-hexane (4:1).

Experimental

Melting points are uncorrected. Infrared (IR) spectra were taken with a Shimadzu IR 430 machine; proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded using tetramethylsilane as an internal standard on a JEOL PS-100 spectrometer at 100 MHz; mass spectra were recorded with a Hitachi M-52 spectrometer. Merck Kieselgel 60 and Merck Kieselgel 60F 254 were employed for column chromatography and thin-layer chromatography (TLC), respectively.

4-Methoxy-3-methylbenzaldehyde (**2**)——Hexamine (51.2 g) was added dropwise to a solution of 2-methoxytoluene (36.6 g) in trifluoroacetic acid (400 ml) with stirring. The mixture was stirred for 3 h. After removal of the solvent *in vacuo*, the residue was purified by distillation under reduced pressure to give **2**, bp 95°C (3.5 mmHg) [lit.[12] bp 80—85°C (1 mmHg)]. Yield, 25.7 g (57.2%). IR ν_{max}^{neat} cm^{-1}: 1685, 1600. ^{1}H-NMR ($CDCl_3$) δ: 2.19 (3H, s, ring Me), 3.80 (3H, s, OMe), 6.80 (1H, d, J=8 Hz, 5-H), 7.55 (1H, d, J=2 Hz, 2-H), 7.60 (1H, dd, J=8 Hz, 2 Hz, 6-H), 9.76 (1H, s, CHO). MS *m/e*: 150 (M^+), 135, 121, 91.

1-Methylsulfinyl-1-methylthio-2-(4-methoxy-3-methylphenyl)ethylene (**3**)——Methanolic Triton-B (40%, 8 ml) was added to a solution of **2** (18 g) and methyl methylthiomethyl sulfoxide (FAMSO) (10.3 g) in dioxane (20 ml). The mixture was stirred for 4 h at 80°C. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography (SiO_2 400 g, CH_2Cl_2 – ether=8: 1) to furnish **3** (18.0 g, 84.6%) as a yellow oil. *Anal.* Calcd for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29. Found: C, 56.05; H, 6.33. IR ν_{max}^{neat} cm^{-1}: 1600, 1500. ^{1}H-NMR ($CDCl_3$) δ: 2.14 (3H, s, ring Me), 2.22 (3H, s, SMe), 2.60 (3H, s, S(O)Me), 3.74 (3H, s, OMe), 6.74 (1H, d, J=9 Hz, 5-H), 7.42 (1H, s, olefinic H), 7.66 (1H, d, J=1.5 Hz, 2-H), 7.70 (1H, dd, J=9 Hz, 1.5 Hz, 6-H). MS *m/e*: 256 (M^+), 240.

4-Methoxy-3-methylphenylacetic Acid (**4c**)——A solution of **3** (17 g) in EtOH (40 ml) was added dropwise to a solution of EtOH (200 ml) saturated with dry hydrogen chloride under ice-salt cooling. Hydrogen chloride was bubbled through the mixture for 30 min with stirring. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was dissolved in 10% ethanolic NaOH (100 ml). The solution was refluxed for 1 h with stirring. The reaction mixture was then acidified with conc. HCl under cooling, and concentrated under reduced pressure to give a residue, which was extracted with ether. The extract was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a crystalline residue, which was recrystallized from *n*-hexane to furnish the product **4c**, mp 84°C (lit.[13] mp 84—85°C). Yield, 7.8 g (61.9%). IR ν_{max}^{KBr} cm^{-1}: 3420, 1717 (shoulder), 1690. MS *m/e*: 208 (M^+), 135, 120.

Arylacetyl Chlorides (**5a—d**)——A mixture of an arylacetic acid (**4**) (0.1 mol) and $SOCl_2$ (10 ml) in dry benzene (400 ml) was stirred for 2 h at 60°C. The mixture was concentrated *in vacuo* to give an oily residue, which was distilled under reduced pressure to furnish the product **5**. **5a**: bp 52—54°C (1.3 mmHg), **5b**: bp 70°C (1.7 mmHg), **5c**: bp 104°C (1.6 mmHg), **5d**: 88°C (1.3 mmHg).

General Procedure for the Synthesis of Ethyl 4-Aryl-3-oxobutanoates (**6a—d**)——*n*-BuLi (0.1 g/1 ml hexane solution) (124 ml, 0.2 mol) was added dropwise to a solution of ethyl malonate (13.5 g, 0.1 mol) and a trace of 2,2′-bipyridyl in abs. tetrahydrofuran (THF) (250 ml) under an argon atmosphere with vigorous stirring. The reaction temperature was initially kept at −78°C and then raised gradually to 0°C with addition of *n*-BuLi. The deep red color of the mixture no longer disappeared at this temperature. The reaction mixture was cooled again at −65°C, and then arylacetyl chloride (**5**) (0.057 mol) was added dropwise. After being stirred for 5 min, the whole was poured into a mixture of ether (400 ml) and 1 N aq. HCl (200 ml) with vigorous stirring. The organic layer was separated and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was distilled under reduced presure to furnish the product **6**. The results are summarized in Table I.

General Procedure for the Synthesis of Ethyl 2-Benzyl-4,6-dihydroxybenzoates (**7a—d**)——Sodium hydride (NaH) (50% dispersion, 2.2 g, 0.044 mol) was added in portions to a solution of **6** (0.04 mol) in abs. THF (50 ml) with stirring and cooling, and the mixture was kept standing for 10 min. A solution of diketene (3.7 g, 0.044 mol) in abs. THF (10 ml) was added dropwise to this mixture. The whole was stirred for 1 h at room temperature. The reaction mixture was poured into a mixture of conc. HCl (5 ml) and ice (50 g). The resulting mixture was extracted with ether (100 ml×2). The combined extract was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue, which was subjected to silica gel (250 g) column chromatography (*n*-hexane – ether=5: 1) to furnish the product **7** (from benzene–*n*-hexane=2: 1). The results are summarized in Table II.

General Procedure for the Synthesis of Ethyl 2-Benzyl-4,6-dimethoxybenzoates (**8a—d**)——A mixture of **7** (0.015 mol) and K_2CO_3 (0.035 mol) in acetone (30 ml) was refluxed for 30 min with vigorous stirring, then CH_3I (10 g) was added. The whole was stirred vigorously under reflux for 48 h. Water (20 ml) was added to the reaction mixture. The resulting mixture was extracted with ether (50 ml×2). The ethereal layer was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave an oily residue, which was purified by silica gel (50 g) column chromatography (*n*-hexane – ether=7: 1) to furnish the product **8** as a colorless oil. The results are summarized in Table III.

General Procedure for the Synthesis of 2-Benzyl-4,6-dimethoxybenzoic Acids (**9a—d**)——A mixture of **8** (0.02 mol) in 10% ethanolic NaOH (50 ml) was refluxed with stirring for 1 h. The mixture was adjusted

to pH 3—4 with conc. HCl under cooling. The resulting mixture was extracted with ether (50 ml × 3). The ethereal layer was washed with 1 N NaOH (20 ml × 2). The washing was adjusted to pH 3—4 with conc. HCl under cooling. The mixture was extracted with ether (50 ml × 2). The ethereal layer was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a crystalline residue, which was recrystallized from benzene–*n*-hexane (5: 1) to furnish the product **9**. The results are summarized in Table IV.

General Procedure for the Synthesis of 1,3-Dimethoxyanthracene-9,10-diones (11a—d)——Compound **9** (2 mmol) was dissolved in a mixture of trifluoroacetic acid (2.5 ml) and trifluoroacetic anhydride (2.5 ml). The mixture was stirred for 15 min at room temperature. The reaction mixture was poured onto ice (15 g), and K_2CO_3 was added until evolution of CO_2 gas ceased. The resulting mixture was extracted with methylene chloride (50 ml × 2). The extract was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue, which was dissolved in acetic acid (5 ml). A solution of CrO_3 (0.4 g, 4 mmol) in water (0.5 ml) was added to the above solution. The mixture was stirred for 2 h at room temperature. 2-Propanol (0.5 ml) was added to the reaction mixture. The whole was stirred for 10 min, then the solvent was removed *in vacuo* to give a residue, which was extracted with methylene chloride (30 ml × 2). The extract was washed with water and dried over $MgSO_4$. Removal of the solvent gave a residue which was purified by silica gel (20 g) column chromatography (CH_2Cl_2) to furnish the product **11**. The results are summarized in Table V.

General Procedure for Demethylation of Compounds (11a—c)——Compound **11** (1 mmol) was dissolved in dry CH_2Cl_2 (20 ml) and a solution of boron tribromide (0.5 g) in dry CH_2Cl_2 (1 ml) was added dropwise with stirring and cooling. After being stirred for 5 min, the reaction mixture was poured into a mixture of 10% aq. HCl (20 ml) and ice (20 g). The resulting mixture was extracted with methylene chloride (30 ml × 2). The extract was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a crystalline residue, which was recrystallized to furnish the product **12**. The results are summarized in Table V.

References and Notes

1) Part CVIII: T. Chiba, H. Takahashi, and T. Kato, *Heterocycles*, **19**, 703 (1982).
2) T.K. Devon and A.I. Scott, "Handbook of Naturally Occurring Compounds," Vol. 1, Academic Press Inc. N.Y., San Francisco and London, 1975, pp. 333—359.
3) T. Kato and T. Hozumi, *Chem. Pharm. Bull.*, **20**, 1574 (1972).
4) T. Kato, M. Sato, and H. Kimura, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 529.
5) T. Kato, N. Katagiri, and J. Nakano, *Heterocycles*, **5**, 167 (1976).
6) *a*) T. Kato, N. Katagiri, J. Nakano, and H. Kawamura, *J. Chem. Soc., Chem. Commun.*, **1977**, 645; *b*) N. Katagiri, J. Nakano, and T. Kato, *J. Chem. Soc., Parkin Trans. 1*, **1981**, 2710.
7) K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, **1972**, 1383.
8) W. Wierenga and H.I. Skulnick, *J. Org. Chem.*, **44**, 310 (1979).
9) K.S. Kim, M.W. Spatz, and F. Johnson, *Tetrahedron Lett.*, **1979**, 331.
10) M.G. Sarngadharan and T.R. Seshadri, *Indian J. Chem.*, **4**, 503 (1966).
11) J.F.W. McOmie, M.L. Watts, and D.E. West, *Tetrahedron*, **24**, 2289 (1968).
12) L. Gattermann, *Justus Liebigs Ann. Chem.*, **357**, 313 (1907).
13) A.A. Aroyan and T.R. Ovsepyan, *Izv. Akad. Nauk Arm. SSSR, Khim. Nauk*, **15**, 263 (1962).
14) A. Sonn and W. Litten, *Ber.*, **66B**, 1512 (1933).
15) A.R. Burnett and R.H. Thomson, *J. Chem. Soc. (C)*, **1968**, 2437.
16) *a*) S. Sibata, T. Murakami, O. Tanaka, G. Chihara, and M.Sumimoto, *Chem. Pharm. Bull.*, **3**, 247 (1955); *b*) T.F. Low, R.J. Park, M.D. Sutherland, and I. Vessey, *Aust. J. Chem.*, **18**, 182 (1965).
17) P.W. Briazz, P.J. Curtis, H.G. Hemming, E.G. Jefferys, C.H. Unwin, and J.M. Wright, *J. Gen. Microbiol.*, **5**, 619 (1951).
18) *a*) R. Suemitsu, M. Nakajima, and M. Hiura, *Bull. Agr. Chem. Soc. Japan*, **23**, 547 (1959); *b*) R. Suemitsu, M. Nakajima, and M. Hiura, *Agric. Biol. Chem.* (Tokyo), **25**, 100 (1961).
19) *a*) A. Stoessl, *Can. J. Chem.*, **47**, 767 (1969); *b*) S. Nakajima, *Chem. Pharm. Bull.*, **21**, 2083 (1973).
20) B.S. Joshi, N. Parkash, and K. Venkataraman, *J. Sci. Ind. Research*, **1313**, 246 (1954).
21) J. Banville, J.L. Grandmaison, G. Lang, and P. Brassard, *Can. J. Chem.*, **52**, 80 (1974).
22) B.S. Joshi, N. Parkash, and K. Venkataraman, *J. Sci. Ind. Research*, **1413**, 87 (1955).