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

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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-benzyloxybenzoic 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-benzyloxybenzoic acids prepared by the reaction of diketene with ethyl 4-aryl-3-oxobutanoates (6a—d).

![Chart 1](image)

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-
\[
\begin{align*}
\text{MeO} \quad \text{CHO} & \quad \xrightarrow{O} \quad \xrightarrow{\text{MeSCH}_2\text{SMe}} \quad \xrightarrow{\text{MeO}} \quad \xrightarrow{\text{Me}} \quad \xrightarrow{\text{S-O}} \quad \xrightarrow{\text{CO}_2\text{H}} \\
2 & \quad \xrightarrow{3} & \quad \xrightarrow{4c} \\
\text{R}_3 \quad \text{R}_1 \quad \text{CO}_2\text{H} & \quad \xrightarrow{\text{SOCl}_2} \quad \xrightarrow{\text{R}_5 \quad \text{R}_1} \quad \xrightarrow{\text{R}_5 \quad \text{R}_1} \quad \xrightarrow{n-\text{BuLi}} \quad \xrightarrow{\text{CO}_2\text{Et}} \quad \xrightarrow{6a \quad \text{a-d}} \\
4a-d & \quad \xrightarrow{5a-d} & \quad \xrightarrow{6a-d} \\
\text{a: R}_1 = \text{R}_2 = \text{R}_3 = \text{H} & \quad \text{c: R}_1 = \text{H}, \text{R}_2 = \text{Me}, \text{R}_3 = \text{OMe} \\
\text{b: R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{Me} & \quad \text{d: R}_1 = \text{OMe}, \text{R}_2 = \text{R}_3 = \text{H} \\
\text{Chart 2} \\
\text{TABLE I. Ethyl 4-Aryl-3-oxobutanoates (6a-d)} \\
\begin{tabular}{|c|c|c|c|c|c|c|c|c|}
\hline
\text{Compd.} & \text{Yield} & \text{bp (mmHg)} & \text{Analysis (\%)} & \text{Formula} & \text{IR (cm}^{-1}\text{)} & \text{MS (m/E \text{M}^+)}
\hline
\text{6a} & 85 & 118—120 (1.6) & 70.89 & \text{C}_{14}\text{H}_{14}\text{O}_3 & 1740, 1717 & 206 \\
\text{6b} & 73 & 134 (2.3) & 70.72 & \text{C}_{14}\text{H}_{14}\text{O}_3 & 1740, 1717 & 220 \\
\text{6c} & 77 & 155 (0.7) & 69.39 & \text{C}_{14}\text{H}_{14}\text{O}_3 & 1740, 1717 & 250 \\
\text{6d} & 79 & 147 (0.9) & 68.39 & \text{C}_{14}\text{H}_{14}\text{O}_3 & 1740, 1717 & 236 \\
\hline
\end{tabular}
\text{a) Lit.}^{10} \text{ 153—155 °C (9 mmHg).}
\]

\[
\begin{align*}
6a-d + \text{CH}_2=\text{O} \xrightarrow{\text{NaH THF}} \text{7a-d : R = H, X = OEt} \\
8a-d : R = \text{Me}, X = \text{OEt} \\
9a-d : R = \text{Me}, X = \text{OH} \\
\text{10a-d} \\
\text{11a-d : R = Me} \\
\text{12a-c : R = H} \\
a: \text{R}_1 = \text{R}_3 = \text{R}_4 = \text{H} & \quad \text{c: R}_1 = \text{H}, \text{R}_2 = \text{Me}, \text{R}_3 = \text{OMe} \\
b: \text{R}_1 = \text{R}_3 = \text{H}, \text{R}_4 = \text{Me} & \quad \text{d: R}_1 = \text{OMe}, \text{R}_3 = \text{R}_4 = \text{H} \\
\text{Chart 3}
\end{align*}
\]
acetic acid, was treated with methyl methylthiomethyl sulfoxide (FAMSO)\textsuperscript{71} 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.,\textsuperscript{81} were treated with ethyl maleonitrile in the presence of \textit{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>
<thead>
<tr>
<th>Compd. No.</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Formula</th>
<th>Analysis (%)</th>
<th>IR ν\textsubscript{max} cm\textsuperscript{-1}</th>
<th>MS m/e (M\textsuperscript{+})</th>
<th>\textsuperscript{1}H-NMR (CDCl\textsubscript{3}) δ (ppm)</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>30.5</td>
<td>120–123</td>
<td>C\textsubscript{14}H\textsubscript{16}O\textsubscript{4}</td>
<td>70.57, 5.92</td>
<td>3340, 1640</td>
<td>272 4.31</td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td>7b</td>
<td>28.9</td>
<td>106–107</td>
<td>C\textsubscript{14}H\textsubscript{16}O\textsubscript{4}</td>
<td>71.31, 6.34</td>
<td>3350, 1641</td>
<td>286 4.23</td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td>7c</td>
<td>28.7</td>
<td>117–118</td>
<td>C\textsubscript{16}H\textsubscript{20}O\textsubscript{4}</td>
<td>68.34, 6.37</td>
<td>3340, 1640</td>
<td>316 4.20</td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td>7d</td>
<td>26.4</td>
<td>138–139</td>
<td>C\textsubscript{12}H\textsubscript{16}O\textsubscript{4}</td>
<td>67.54, 6.00</td>
<td>3325, 1640</td>
<td>302 4.24</td>
<td>6.14 (d, J = 2.5 Hz) 5.51 (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)</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a)} 4-OH undetected.
### TABLE III. Ethyl 2-Benzyl-4,6-dimethoxybenzoates (8a—d)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%)</th>
<th>IR ν max cm⁻¹</th>
<th>MS m/e (M⁺)</th>
<th>¹H NMR (CDCl₃) δ (ppm)</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd (Found)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8a</td>
<td>92.0</td>
<td>C₁₈H₂₅O₄</td>
<td>71.98 6.71</td>
<td>1720 300</td>
<td>3.73(s)</td>
<td>3.98(s) 6.30 1.23 (3H, t, J = 7.5 Hz) (d, J = 2 Hz) 4.26 (2H, q, J = 7.5 Hz) 6.37 7.18—7.30 (5H, m)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(71.73 6.79)</td>
<td></td>
<td>3.79(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8b</td>
<td>94.2</td>
<td>C₁₈H₂₅O₄</td>
<td>72.59 7.05</td>
<td>1722 314</td>
<td>3.81(s)</td>
<td>4.01(s) 6.38 1.33 (3H, t, J = 7.5 Hz) (d, J = 2 Hz) 2.38 (2H, s) 6.46 4.35 (2H, q, J = 7.5 Hz) (d, J = 2 Hz) 7.02—7.30 (4H, m)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(72.28 7.17)</td>
<td></td>
<td>3.88(s)</td>
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<tr>
<td>8c</td>
<td>90.1</td>
<td>C₂₀H₂₄O₆</td>
<td>69.75 7.02</td>
<td>1720 344</td>
<td>3.71(s)</td>
<td>3.75(s) 6.26 1.26 (3H, t, J = 7.5 Hz) (d, J = 2 Hz) 2.16 (3H, s) 6.33 4.25 (2H, q, J = 7.5 Hz) (d, J = 2 Hz) 6.71 (1H, d, J = 9 Hz) 6.95 (2H, br s)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(69.56 7.08)</td>
<td></td>
<td>3.77(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8d</td>
<td>95.1</td>
<td>C₁₉H₂₄O₄</td>
<td>69.50 6.14</td>
<td>1720 330</td>
<td>3.74(s)</td>
<td>3.82 3.98(s) 6.30 1.25 (3H, t, J = 7.5 Hz) (d, J = 2 Hz) 4.30 (2H, q, J = 7.5 Hz) 6.38 6.78—7.28 (4H, m)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(69.24 6.23)</td>
<td></td>
<td>(6H, s)</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Formula</th>
<th>Analysis (%)</th>
<th>IR ν max cm⁻¹</th>
<th>MS m/e (M⁺)</th>
<th>¹H NMR (CDCl₃) δ (ppm)</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Calcd (Found)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9a</td>
<td>91.5</td>
<td>173—175³</td>
<td>C₁₈H₂₄O₄</td>
<td>70.57 5.92</td>
<td>3420 272</td>
<td>3.79(s) 4.30 (s) 6.40 Undetected 7.24—7.38 (5H, br s)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(70.33 5.98)</td>
<td></td>
<td>1686</td>
<td>(s)</td>
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<tr>
<td>9b</td>
<td>93.8</td>
<td>131—132³</td>
<td>C₁₇H₁₉O₄</td>
<td>71.31 6.34</td>
<td>3430 286</td>
<td>3.76(s) 4.16 (s) 6.39 10.21 (br s) (3H, s) 2.30</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(71.28 6.23)</td>
<td></td>
<td>1693</td>
<td>(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9c</td>
<td>91.9</td>
<td>127³</td>
<td>C₁₈H₂₄O₅</td>
<td>68.34 6.37</td>
<td>3450 316</td>
<td>3.73(s) 4.06 (s) 6.29 9.98—10.60 2.14 (br s) (3H, s) 3.84 (s) 6.35 (d, J = 2 Hz) 6.69 (1H, d, J = 9 Hz) 6.89—7.05 (2H, br s)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(68.54 6.61)</td>
<td></td>
<td>1680</td>
<td>(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9d</td>
<td>91.0</td>
<td>156³</td>
<td>C₁₇H₁₉O₅</td>
<td>67.54 6.00</td>
<td>3420 302</td>
<td>3.73(s) 4.22 (s) 6.34 Undetected 6.83—6.97 (2H, m) 3.78 (s) 6.41 (d, J = 2 Hz) 7.96—7.15 (2H, m) 3.90 (s)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

³ Recrystallization from benzene.
³ 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)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Formula</th>
<th>Analysis (% Calc'd) [Found]</th>
<th>IR (v_{max}) cm(^{-1})</th>
<th>MS (m/e)</th>
<th>(^1H)-NMR (CDCl(_3)) (\delta) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11a</td>
<td>36.7</td>
<td>160—161(^a, b)</td>
<td>C(<em>{16})H(</em>{14})O(_4)</td>
<td>71.63 (71.84) (C) 4.51 (H) 1668 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)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11b</td>
<td>54.8</td>
<td>191—192(^b)</td>
<td>C(<em>{17})H(</em>{13})O(_4)</td>
<td>72.33 (72.21) (C) 5.00 (H) 1670 282 3.93 (s) 3.96 (s) 6.72 (d, (J = 2) Hz) 7.38 (d, (J = 2) Hz) — 7.50 (1H, dd, (J = 8), 1.5 Hz) 7.93 (1H, br s) 8.09 (1H, d, (J = 8) Hz) 2.48 (3H, s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11c</td>
<td>87.8</td>
<td>267(^b, c)</td>
<td>C(<em>{18})H(</em>{14})O(_5)</td>
<td>69.22 (69.08) (C) 5.16 (H) 1658 312 3.94 (s) 3.96 (s) 6.71 (d, (J = 2) Hz) 7.41 (d, (J = 2) Hz) — 7.60 (1H, s) 7.93 (1H, s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11d</td>
<td>58.0</td>
<td>204(^a, b)</td>
<td>C(<em>{17})H(</em>{14})O(_5)</td>
<td>68.45 (68.50) (C) 4.73 (H) 1658 298 3.98 (s) 4.03 (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) 2.30 (3H, s) 2.60 (1H, s)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>12a</td>
<td>85.0</td>
<td>193—194(^a, f)</td>
<td>C(<em>{15})H(</em>{14})O(_4)</td>
<td>70.86 (70.59) (C) 3.96 (H) 3430 254 3.90 (s) 6.68 (d, (J = 2) Hz) 7.34 (d, (J = 2) Hz) — 7.67—7.83 (2H, m) 8.18—8.36 (2H, m)</td>
<td></td>
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<tr>
<td>12b</td>
<td>81.6</td>
<td>183—184(^a, f)</td>
<td>C(<em>{16})H(</em>{14})O(_4)</td>
<td>71.63 (71.78) (C) 4.51 (H) 3430 268 3.90 (s) 6.66 (d, (J = 2) Hz) 7.31 (d, (J = 2) Hz) — 7.30 (1H, d, (J = 8) Hz) 0.82 (1H, br s) 8.13 (1H, d, (J = 8) Hz) 2.50 (3H, s) 2.75 (1H, s)</td>
<td></td>
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<td></td>
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<tr>
<td>12c</td>
<td>87.9</td>
<td>209—210(^a, f)</td>
<td>C(<em>{17})H(</em>{14})O(_4)</td>
<td>68.45 (68.43) (C) 4.73 (H) 3450 298 3.93 (s) 6.19 (d, (J = 2) Hz) 7.35 (d, (J = 2) Hz) — 7.63 (1H, s) 8.03 (1H, s)</td>
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\(^a\) Lit.\(^11\) 165°C,\(^14\) 162—163°C,\(^18\) 163°C.
\(^b\) Lit.\(^19\) 260—261°C,\(^18\) 260°C,\(^14\) 270—271°C.
\(^c\) Lit.\(^20\) 205°C,\(^11\) 201.5—202°C.
\(^d\) Lit.\(^21\) 193°C,\(^11\) 193°C.
\(^e\) Lit.\(^22\) 184—185°C,\(^18\) 182°C.
\(^f\) Lit.\(^20\) 209—210°C,\(^19\) 208°C,\(^14\) 214°C.
Experimental

Melting points are uncorrected. Infrared (IR) spectra were taken with a Shimadzu IR 430 machine; proton nuclear magnetic resonance (1H-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 until reduced pressure to give 2, bp 95°C (3.5 mmHg) [lit.11] bp 80—85°C (1 mmHg)]. Yield, 25.7 g (57.2%). IR νcm⁻¹: 1685, 1600. 1H-NMR (CDCl₃) 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)ethylen (3)—Methanolic Triton-B (40%, 8 ml) was added to a solution of 2 (18 g) and methyl methyldimethyl 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 (SiO₂, 400 g, CH₂Cl₂ – ether = 8: 1) to furnish 3 (18.0 g, 84.6%) as a yellow oil. Anal. Calcd for C₁₇H₁₉O₃S₂: C, 56.22; H, 6.29. Found: C, 56.05; H, 6.33. IR νcm⁻¹: 1600, 1500. 1H-NMR (CDCl₃) δ: 2.14 (3H, s, ring Me), 2.22 (3H, s, SMe), 2.60 (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: 258 (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 MgSO₄. 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.12) mp 84—85°C. Yield, 7.8 g (61.9%). IR νcm⁻¹: 3420, 1717 (shoulder), 1600. MS m/e: 208 (M⁺), 135, 120.

Arylacetyl Chlorides (5a—d)—A mixture of an arylacetic acid (4) (0.1 mol) and SOCl₂ (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: bp 88°C (1.3 mmHg).

General Procedure for the Synthesis of Ethyl 4-Aryl-3-oxobutanoates (6a—d)—n-BuLi (0.1 g/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 mixture 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 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 MgSO₄. Removal of the solvent in vacuo gave an oily residue, which was distilled under reduced pressure 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 x 2). The combined extract was washed with water and dried over MgSO₄. 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 K₂CO₃ (0.035 mol) in acetone (30 ml) was refluxed for 30 min with vigorous stirring, then CH₂Cl₂ (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 x 3). The ether layer was washed with water and dried over MgSO₄. 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 x 3). The ethereal layer was washed with 1 N NaOH (20 ml x 2). The washing was adjusted to pH 3–4 with conc. HCl under cooling. The mixture was extracted with ether (50 ml x 2). The ethereal layer was washed with water and dried over MgSO<sub>4</sub>. 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<sub>2</sub>CO<sub>3</sub> was added until evolution of CO<sub>2</sub> gas ceased. The resulting mixture was extracted with methylene chloride (50 ml x 2). The extract was washed with water and dried over MgSO<sub>4</sub>. Removal of the solvent in vacuo gave a residue, which was dissolved in acetic acid (5 ml). A solution of CrO<sub>3</sub> (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 x 2). The extract was washed with water and dried over MgSO<sub>4</sub>. Removal of the solvent gave a residue which was purified by silica gel (20 g) column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) 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<sub>2</sub>Cl<sub>2</sub> (20 ml) and a solution of boron tribromide (0.5 g) in dry CH<sub>2</sub>Cl<sub>2</sub> (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 x 2). The extract was washed with water and dried over MgSO<sub>4</sub>. 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**


14) A. Sönn and W. Litten, Ber., 66B, 1512 (1933).


