

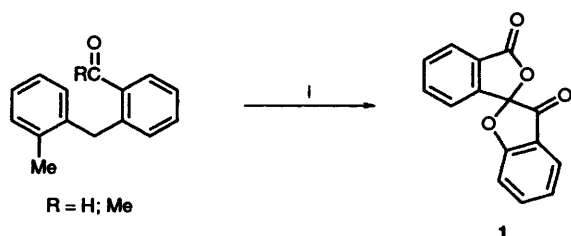
## First Synthesis of Spiro[benzofuran-2,1'-isobenzofuran]-3,3'-dione and its X-Ray Crystal Structure

Roy M. Letcher,\* Nai-Chiu Kwok and Kung-Kai Cheung

Department of Chemistry, University of Hong Kong, Bonham Road, Hong Kong

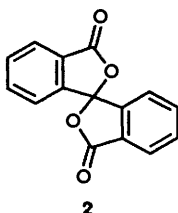
The title compound has been synthesised by selenium dioxide oxidation of 2'-carboxy-2-hydroxydeoxybenzoin **3** and its structure has been confirmed spectroscopically and by X-ray crystallography. An earlier report of this compound's synthesis is shown to be erroneous. The synthesis of 3-(2-hydroxyphenyl)isoquinolin-1(2*H*)-ones from 2'-carboxy-2-hydroxydeoxybenzoin **3** is also described.

Although the title compound **1** has been reported as being synthesised according to Scheme 1,<sup>1a</sup> the structural assignment



Scheme 1 Reagent: i, CrO<sub>3</sub>

was clearly in error, the known compound 3,3'-spirobipthalide **2**,<sup>2</sup> having been prepared.† We now report the first synthesis of, and data for, the novel compound, spiro[benzofuran-2,1'-isobenzofuran]-3,3'-dione **1**.



Oxidation of 2'-carboxy-2-hydroxydeoxybenzoin **3** with selenium dioxide in refluxing acetic acid gave compound **1** (36% yield, not optimised). The structure **1** was indicated from its IR spectrum which exhibited carbonyl absorptions for a lactone and ketone at 1790 and 1735 cm<sup>-1</sup> respectively, and from its <sup>13</sup>C NMR spectrum which exhibited a signal for a quaternary carbon at δ 103.8, indicative of an sp<sup>3</sup> carbon attached to two oxygen atoms. <sup>1</sup>H NMR, mass spectra, and remaining <sup>13</sup>C NMR data are all consistent with the spiro structure **1**. Confirmation of the structure was obtained from a single crystal X-ray analysis (see Fig. 1) in which all bond distances and angles were found to be normal, and with the two planes of the spiro system being almost perfect, and at an angle of 90.2° to each other.

The formation of compound **1** from the deoxybenzoin **3** almost certainly follows the route shown in Scheme 2 in which oxidation by SeO<sub>2</sub> furnishes the diketo intermediate **4** which is presumed to be dehydrated spontaneously to give the product **1** since compound **4** was not detected. This is supported by the

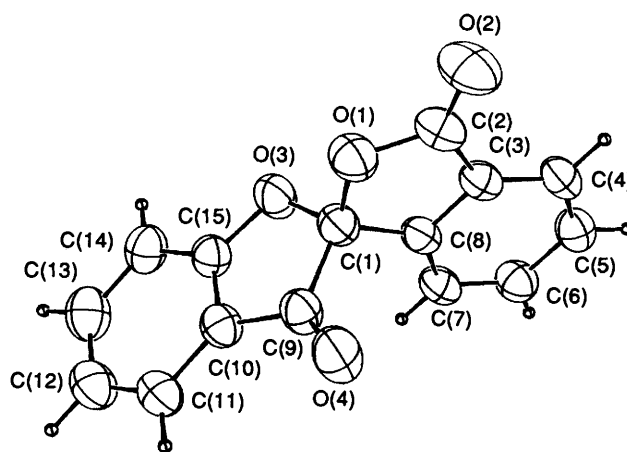
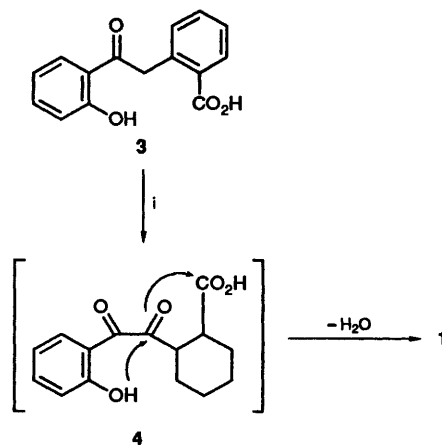


Fig. 1 Perspective view of the molecule **1** showing non-hydrogen-atom labelling



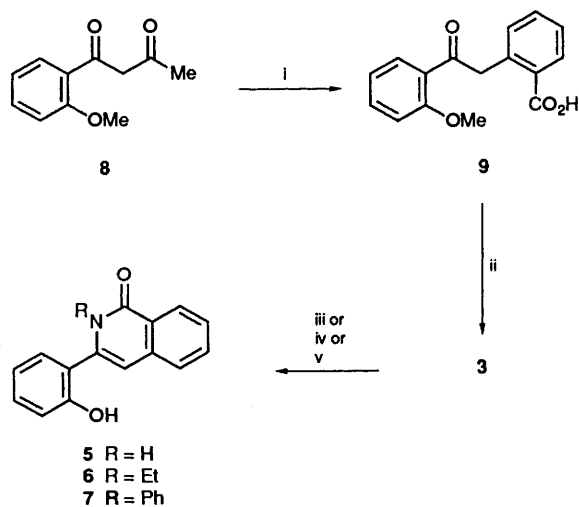
Scheme 2 Reagent: i, SeO<sub>2</sub>

fact that in SeO<sub>2</sub> oxidation of ketones, the most readily enolizable CH<sub>2</sub> is oxidised to a ketone.<sup>3</sup>

We also report a new synthetically useful reaction of the deoxybenzoin **3**. Treatment of compound **3** with a variety of amines gives 3-(2-hydroxyphenyl)isoquinolin-1(2*H*)-ones in good yield: ammonium acetate, ethylamine and aniline gave compounds **5**, **6** and **7** respectively (see Scheme 3). All structures were confirmed from spectral data. 3-Arylisoquinolin-1(2*H*)-ones have previously been synthesised either by treating 3-arylisocoumarins with amines,<sup>4</sup> or by oxidising 3-arylisquinolines.<sup>5</sup>

Our synthetic route (Scheme 3) to the deoxybenzoin **3** is different from that reported<sup>6</sup> in which it was obtained by

† Although compound **1** was not synthesised earlier its name appears in *Chemical Abstracts*<sup>1b</sup> with a Registry number.



**Scheme 3** Reagents: i, *o*-BrC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H/Cu; ii, NaCN; iii, NH<sub>4</sub>OAc; iv, EtNH<sub>2</sub>; v, PhNH<sub>2</sub>

alkaline hydrolysis of [2]benzopyrano[4,3-*c*]benzopyran-5,12-dione. We have found a convenient route starting with a Hurltley reaction<sup>7,8</sup> between the butane-1,3-dione **8**<sup>9</sup> and 2-bromobenzoic acid, which gave 2'-carboxy-2-methoxydeoxybenzoin **9**. Careful demethylation of the acid **9** with sodium cyanide in dimethyl sulfoxide<sup>10</sup> (DMSO) gave compound **3**, with a similar m.p. to that reported,<sup>6</sup> and with NMR, IR, and mass spectra consistent with the structure.

## Experimental

**General Experimental Details.**—<sup>1</sup>H and <sup>13</sup>C NMR spectra were determined at 89.56 and 22.50 MHz respectively on a JEOL FX90Q Fourier Transform spectrometer for [<sup>2</sup>H<sub>6</sub>]-DMSO solutions with tetramethylsilane as internal standard; *J*-values are given in Hz, and the multiplicities in <sup>13</sup>C spectra were obtained by off-resonance decoupling. IR spectra were determined as Nujol mulls. Mass spectra were recorded on an Hitachi RMS-4 spectrometer.

**2'-Carboxy-2-hydroxydeoxybenzoin 3.**—To a solution of absolute ethanol (400 cm<sup>3</sup>) and sodium (6.0 g, 0.26 mol) was added 1-(2-methoxyphenyl)butane-1,3-dione **8**<sup>9</sup> (27.4 g, 0.14 mol), copper powder (1 g), and 2-bromobenzoic acid (26.1 g, 0.13 mol). After being heated under reflux for 12 h, the solution was cooled and filtered and the filtrate diluted with cold water (500 cm<sup>3</sup>) before extraction with CH<sub>2</sub>Cl<sub>2</sub>. The aqueous layer was acidified with conc. HCl, cooled overnight and filtered. Recrystallisation of the product (benzene) yielded 2'-carboxy-2-methoxydeoxybenzoin **9** (26.0 g, 74%), m.p. 147.5–148 °C (Found: C, 70.9; H, 5.0. Calc. for C<sub>16</sub>H<sub>14</sub>O<sub>4</sub>: C, 71.1; H, 5.2%);  $\nu_{\max}/\text{cm}^{-1}$  1685s and 1672s;  $\delta_{\text{H}}$  3.92 (3 H, s, OMe), 4.64 (2 H, s, CH<sub>2</sub>) and 6.98–8.00 (9 H, m, ArH, CO<sub>2</sub>H);  $\delta_{\text{C}}$  49.64 (t, CH<sub>2</sub>), 55.52 (q, OCH<sub>3</sub>), 111.78, 120.26, 126.57, 129.88, 130.50, 131.53, 132.37, 133.07 (all d, aryl CH), 128.33, 130.69, 137.30, 158.18 (all s, quaternary aryl C), 168.42 (s, CO<sub>2</sub>H) and 198.51 (s, C=O); *m/z* 270 (M<sup>+</sup>, 100%), 253 (41), 252 (53) and 224 (24).

A mixture of **9** (21.4 g, 0.079 mol) and sodium cyanide (11.6 g, 0.23 mol) in dimethyl sulfoxide (20 cm<sup>3</sup>) was heated to 160 °C under nitrogen for 2 days, after which dilute HCl was added to give a solid which on recrystallisation (benzene) gave pale yellow needles of the title compound **3** (9.3 g, 45%), m.p. 164–166 °C (lit.,<sup>6</sup> m.p. 160–161 °C);  $\nu_{\max}/\text{cm}^{-1}$  3500–2300br, 1684s and 1638s;  $\delta_{\text{H}}$  4.77 (2 H, s, CH<sub>2</sub>), 6.90–8.11 (8 H, m, ArH) and 12.09 (1 H, s, CO<sub>2</sub>H);  $\delta_{\text{C}}$  44.47 (t, CH<sub>2</sub>), 110.01, 118.93, 127.22, 130.09, 131.15, 132.01, 132.50, 136.00 (all d, aryl CH), 119.50,

128.20, 130.36, 161.97 (all s, quaternary aryl), 168.61 (s, CO<sub>2</sub>H) and 203.85 (s, C=O); *m/z* 256 (M<sup>+</sup>, 100%), 238 (23), 210 (15) and 181 (16).

**Spiro[benzofuran-2,1'-isobenzofuran]-3,3'-dione 1.**—A mixture of the deoxybenzoin **3** (0.6 g, 2.34 mmol) and selenium dioxide (0.35 g, 3.15 mmol) in glacial acetic acid was refluxed for 2 days and then filtered and neutralised with aqueous sodium hydrogen carbonate. The resulting product was filtered off, washed with water, and recrystallised (95% ethanol) to give the title spiro compound **1** (0.21 g, 36%), m.p. 182–185 °C (Found: C, 71.8; H, 3.0. Calc. for C<sub>15</sub>H<sub>8</sub>O<sub>4</sub>: C, 71.45; H, 3.2%);  $\nu_{\max}/\text{cm}^{-1}$  1789s (lactone) and 1734s (ketone);  $\delta_{\text{H}}$  7.3–7.4 (2 H, m, ArH) and 7.61–7.98 (6 H, m, ArH);  $\delta_{\text{C}}$  103.87 (s, quaternary sp<sup>3</sup> C), 117.98, 126.06, 141.63, 166.36 (all s, quaternary aryl C), 113.62, 123.19, 124.16, 125.60, 125.73, 132.34, 135.81, 140.39 (all d, aryl CH), 170.72 (s, lactone C=O) and 192.17 (s, ketone C=O); *m/z* 252 (M<sup>+</sup>, 70%), 224 (25), 223 (28), 180 (70) and 104 (100).

**3-(2-Hydroxyphenyl)isoquinolin-1(2H)-ones.**—**General method.** A stirred mixture of the deoxybenzoin **3** (1 g, 4 mmol) and the amine (20 mmol) was heated at 100 °C for 3 h and then cooled, acidified with dilute hydrochloric acid and extracted with ether. The extract on evaporation yielded the isoquinolinone.

Ammonium acetate gave 3-(2-hydroxyphenyl)isoquinolin-1(2H)-one **5**, 94%, m.p. > 255 °C (95% ethanol) (Found: C, 75.4; H, 4.85; N, 5.75. Calc. for C<sub>15</sub>H<sub>11</sub>NO<sub>2</sub>: C, 75.9; H, 4.65; N, 5.9%);  $\nu_{\max}/\text{cm}^{-1}$  3500–2700br, 3193w and 1644m;  $\delta_{\text{H}}$  6.75–8.26 (9 H, m, ArH and 4-H), 10.18 and 11.12 (both 1 H, br s, OH and NH);  $\delta_{\text{C}}$  104.22, 116.33, 119.31, 125.92, 126.38, 126.49, 129.52, 130.31, 132.23 (all d, aryl CH and C-4), 120.96, 124.62, 138.08, 138.73, 154.90 (all s, quaternary sp<sup>2</sup> C) and 161.86 (s, C=O); *m/z* 237 (M<sup>+</sup>, 100%).

Ethylamine (70% solution in ethanol) gave 2-ethyl-3-(2-hydroxyphenyl)isoquinolin-1(2H)-one **6**, 78%, m.p. 215.5–217 °C (95% ethanol) (Found: C, 76.95; H, 5.7; N, 5.0. Calc. for C<sub>17</sub>H<sub>15</sub>NO<sub>2</sub>: C, 76.95; H, 5.7; N, 5.3%);  $\nu_{\max}/\text{cm}^{-1}$  3500–2700br and 1649s;  $\delta_{\text{H}}$  1.02 (3 H, t, *J* 7.0, CMe), 3.61 (1 H, pentet, *J* 7.0, CH<sub>2</sub>), 4.28 (1 H, pentet, *J* 7.0, CH<sub>2</sub>), 6.47 (1 H, s, H-4), 6.94–8.32 (8 H, m, ArH) and 9.96 (1 H, s, OH);  $\delta_{\text{C}}$  13.70 (q, Me), 40.47 (t, CH<sub>2</sub>), 106.86, 115.51, 118.99, 125.84, 126.17, 126.95, 130.53, 130.66, 132.05 (all d, sp<sup>2</sup> CH), 122.92, 124.57, 136.38, 141.26, 154.80 and 161.30 (all s, quaternary sp<sup>2</sup> C); *m/z* 265 (M<sup>+</sup>, 100%).

Aniline gave 3-(2-hydroxyphenyl)-2-phenyl-isoquinolin-1(2H)-one **7**, 72%, m.p. 234.5–237 °C (benzene-ethyl acetate) (Found: C, 80.3; H, 4.75; N, 4.4. Calc. for C<sub>21</sub>H<sub>15</sub>NO<sub>2</sub>: C, 80.5; H, 4.85; N, 4.45%);  $\nu_{\max}/\text{cm}^{-1}$  3500–2700br, 1646s and 1618s;  $\delta_{\text{H}}$  6.54–8.38 (14 H, m, ArH and 4-H) and 9.15 (1 H, s, OH);  $\delta_{\text{C}}$  107.42, 115.38, 118.34, 126.33, 127.33, 127.60, 127.71, 128.14, 128.95, 129.77, 130.82, 132.39 (all d, ArCH and C-4), 123.21, 125.27, 136.95, 139.03, 141.20, 154.42 (all s, quaternary sp<sup>2</sup> C) and 162.68 (C=O); *m/z* 313 (M<sup>+</sup>, 100%).

**X-Ray Crystal Structure Analysis of Compound 1.**—Intensity data were measured on an Enraf-Nonius CAD-4 diffractometer using graphite-monochromated Mo-K $\alpha$  radiation ( $\lambda$  0.710 73 Å) and scintillation counter; cell parameters by least squares from the setting angles of 25 reflections 10° < 2 $\theta$  < 15°. The  $\omega$ -2 $\theta$  scanning technique in the bisect mode was employed, extended 25% on each side for background measurement. No decay was observed in the three standard reflections measured every two hours. Lorentz and polarization corrections and no absorption correction, was applied. 2235 Independent reflections with *I* >  $\sigma(I)$ , where  $\sigma(I) = S + 4(B1 + B2)$ , *S* = scan, *B1* and *B2* = background counts, were

**Table 1** Atomic coordinates (esd) for compound 1

Atom	x	y	z
O(1)	0.2458(2)	0.6193(1)	0.2310(1)
O(2)	0.2490(2)	0.8392(1)	0.4099(1)
O(3)	0.4075(1)	0.3898(1)	0.1446(1)
O(4)	-0.0891(2)	0.3778(2)	0.1131(1)
C(1)	0.2444(2)	0.4402(2)	0.2055(1)
C(2)	0.2478(2)	0.6889(2)	0.3685(2)
C(3)	0.2485(2)	0.5510(2)	0.4388(1)
C(4)	0.2506(2)	0.5529(2)	0.5756(1)
C(5)	0.2516(2)	0.4007(2)	0.6124(1)
C(6)	0.2510(2)	0.2493(2)	0.5159(1)
C(7)	0.2498(2)	0.2465(2)	0.3793(1)
C(8)	0.2479(2)	0.4004(2)	0.3428(1)
C(9)	0.0717(2)	0.3525(2)	0.0993(1)
C(10)	0.1533(2)	0.2442(2)	-0.0079(1)
C(11)	0.0711(2)	0.1284(2)	-0.1274(1)
C(12)	0.1907(3)	0.0456(2)	-0.2107(2)
C(13)	0.3847(3)	0.0788(2)	-0.1779(2)
C(14)	0.4689(2)	0.1932(2)	-0.0596(2)
C(15)	0.3467(2)	0.2738(2)	0.0232(1)

considered observed and used. Wilson statistics indicated a centrosymmetrical space group:  $P\bar{1}$  was confirmed in the structure solution.

The structure was determined by direct methods using MULTAN 11/82<sup>11</sup> and refined by full matrix least squares using atomic scattering factors from International Tables for X-Ray Crystallography (1974) and the Enraf-Nonius SDP-1985 Programs on a MicroVAX II computer. The oxygen and carbon atoms were refined anisotropically and the hydrogen atoms placed in calculated positions were not refined.

*Crystal data.*  $C_{15}H_8O_4$ ,  $M = 252.23$ , triclinic, space group  $P\bar{1}$ ,  $a = 7.162(3)$ ,  $b = 8.122(3)$ ,  $c = 10.173(3)$  Å,  $\alpha = 102.95(3)^\circ$ ,  $\beta = 96.99(3)^\circ$ ,  $\gamma = 93.45(3)^\circ$ ,  $V = 570.1(8)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.469$  g cm<sup>-3</sup>,  $\mu(\text{Mo-K}\alpha) = 1.01$  cm<sup>-1</sup>,  $F(000) = 260$ ,  $T = 297$  K,  $R = 0.043$  for 1929 independent reflections with  $|F_o| > 2\sigma(|F_o|)$ . A crystal of dimensions  $0.1 \times 0.25 \times 0.3$  mm was used for the diffraction measurements. Intensity data with  $2\theta_{\text{max}} = 48^\circ$  in the range  $-8 \leq h \leq 8$ ,  $-9 \leq k \leq 9$ ,  $-11 \leq l \leq 11$  were measured with  $\omega$ -scan angle  $(0.80 + 0.344 \tan \theta)^\circ$  at a scan speed of 1.03 to 5.49 deg min<sup>-1</sup> for 4468 reflections, 2 unique and 4466 twice measured

( $R_{\text{int}} = 0.027$ ). Convergence for 172 variables by least squares method with  $w = 4 F_o^2/\sigma^2(F_o^2)$ , where  $\sigma^2(F_o^2) = [\sigma^2(I) + (0.04 F_o^2)^2]$  for reflections with  $F_o^2 \geq \sigma(F_o^2)$  and  $w = -2.0$  for all other reflections, was reached at  $R = 0.043$  and  $wR = 0.062$  and  $S = 1.931$  for 1929 reflections with  $|F_o| > 2\sigma(|F_o|)$ .  $(\Delta/\sigma)_{\text{max}} = 0.01$ . A final difference Fourier map was featureless, with maximum positive and negative peaks of 0.22 and 0.21 eÅ<sup>-3</sup> respectively. The non-hydrogen atomic coordinates are given in Table 1. Bond distances and bond angles (together with selected torsion angles) together with other crystallographic data has been deposited at the Cambridge Crystallographic Data Centre.\*

\* For full details of the CCDC deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1992, issue 1.

## References

- (a) B. Miller and A. K. Bhattacharya, *Tetrahedron Lett.*, 1981, 3753; (b) *Chem. Abstr.*, **96**, 68536s (CAS No. [80716-35-4]).
- W. R. Vaughan, M. V. Andersen and R. Q. Little, *J. Am. Chem. Soc.*, 1954, **76**, 1748.
- E. N. Trachtenberg, in *Oxidation*, vol. 1, ed. R. L. Augustine, Marcel Dekker, New York, 1969, ch. 3.
- A. Rose and N. P. Buu-Hoi, *J. Chem. Soc. C*, 1968, 2205.
- E. Dominguez, E. M. de Marigorta, L. Carrillo and R. Fananas, *Tetrahedron*, 1991, 9253.
- J. R. Merchant, N. M. Koshti and K. M. Bakre, *J. Heterocycl. Chem.*, 1981, **18**, 1655.
- K. A. Cirigottis, E. Ritchie and W. C. Taylor, *Aust. J. Chem.*, 1974, **27**, 2209.
- A. Bruggink and A. McKillop, *Tetrahedron*, 1975, **31**, 2607.
- A. O. Fitton, R. N. Patel and R. W. Millar, *J. Chem. Res. (M)*, 1986, 1101.
- J. R. McCarthy, J. L. Moore and R. J. Cregge, *Tetrahedron Lett.*, 1978, 5183.
- P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq and M. M. Woolson, MULTAN 11/82, a System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data, Universities of York and Louvain, 1982.

Paper 2/01623K

Received 27th March 1992

Accepted 9th April 1992