The Synthesis of Benzofuroquinolines. IX. A Benzofuroisoquinolinone and a Benzofuroisocoumarin

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Some procedures for a benzofuroisoquinolinone **1** were studied. Its *O*-analogous benzofuroisocoumarin **2** was synthesized from methyl salicylate with diethyl α-bromohomophthalate (**9**). And, the benzofuroisoquinolinone **1** was obtained by treating **2** with ammonia gas in a sealed tube.

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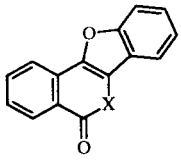
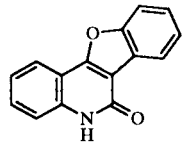
In our course of polycyclic heteroaromatic compounds, we already reported some benzofuroquinolines [1a-d]. Some derivatives of 6(5*H*)-benzofuro[3,2-*c*]quinolinone (**3**) showed interesting activities for osteoporosis [2a,b]. Now we will describe some studies for an isomeric benzofuroisoquinolinone, 5(6*H*)-benzofuro[3,2-*c*]isoquinolinone (**1**), and an *O*-analogous benzofuroisocoumarin, 5-benzofuro[3,2-*c*][2]benzopyranone (**2**), in this paper.



1) X = NH
2) X = O



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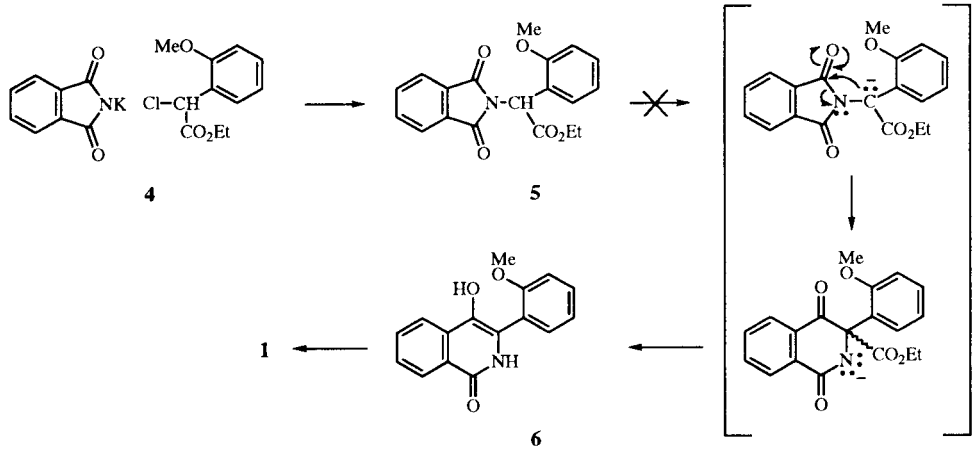
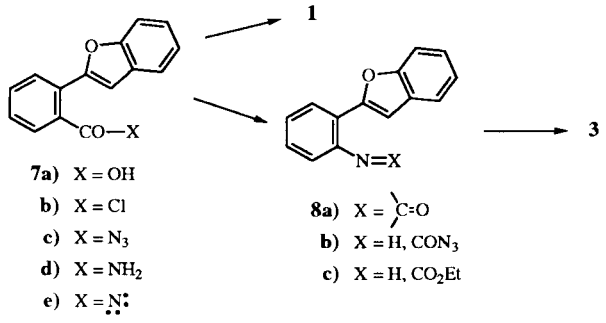
Our first approach for benzofuroisoquinolinone **1** was a Gabriel-Colmann method [3]. Gabriel-Colmann reaction of ethyl α-(*o*-methoxyphenyl)-α-(phthalimino)acetate (**5**) might give 4-hydroxy-3-(*o*-methoxyphenyl)-1(2*H*)-isoquinolinone (**6**), a precursor of **1**. But any Gabriel-Colmann procedure of **5**, prepared from ethyl α-chloro-α-(*o*-methoxyphenyl)acetate (**4**) and potassium phthalimido, could not afford our desired **6** [4].

Our second approach for **1** was an intramolecular cyclization of nitrene **7e**. *o*-(2-Benzofuranyl)benzoic acid (**7a**), a key compound in this approach, was prepared from salicylaldehyde and diethyl α-bromohomophthalate (**9**). Condensation of salicylaldehyde with **9** gave ethyl 5-oxo-5*H*,6a*H*-benzofuro[3,2-*c*][2]benzopyran-11a-carboxylate (**12**) in 46% yield, *via* diethyl α-(*o*-formylphenyloxy)homophthalate (**10**) and ethyl 2-(*o*-ethoxycarbonylphenyl)-3-hydroxy-2,3-dihydrobenzofuran-2-carboxylate (**11**) [5]. Acidic hydrolysis of **12** readily gave the desired acid **7a** in 82% yield. But treating acid chloride **7b** with sodium azide in aqueous acetone gave *o*-(2-benzofuranyl)phenylaminocarbonyl azide (**8**) (**8b**) [6]. This azide **8b** might be derived by addition of ammonia to isocyanate **8a**. A Hofmann reaction of amide **7d**, another approach *via* nitrene **7e**, also gave a carbamate **8c** after treating **7d** with bromine-sodium ethoxide in ethanol [7]. Treating **8b** with ethanol gave carbamate **8c** with evolution of nitrogen gas, and heating of **8b** or **8c** around 130-150° gave 5(6*H*)-benzofuro[3,2-*c*]quinolinone **3**. These experiments showed that, in nitrene **7e**, the rearrangement to isocyanate **8a** might be more favorable than the electrophilic attack of the electron deficient nitrogen for **1**. Because some steric hindrances set the electron deficient nitrogen far from the C=C double bond. Therefore, a Schmidt reaction of 10-indeno[1,2-*b*]benzofuranone (**13**), keeping the electron defficient nitrogen near the C=C double bond in an intermediate nitrene **15**, was attempted next. Treating acid **7a** with trifluoroacetic anhydride gave



13, but a Schmidt reaction of **13** with hydrogen azide gave only a tarry mixture. All attempts from *o*-(2-benzofuranyl)benzoic acid **7a** to 5(6*H*)-benzofuroisoquinolinone **1** were thus unsuccessful, but the formation of the intermediate **12** suggested another route for **1** *via* benzofuroisocoumarin **2**.

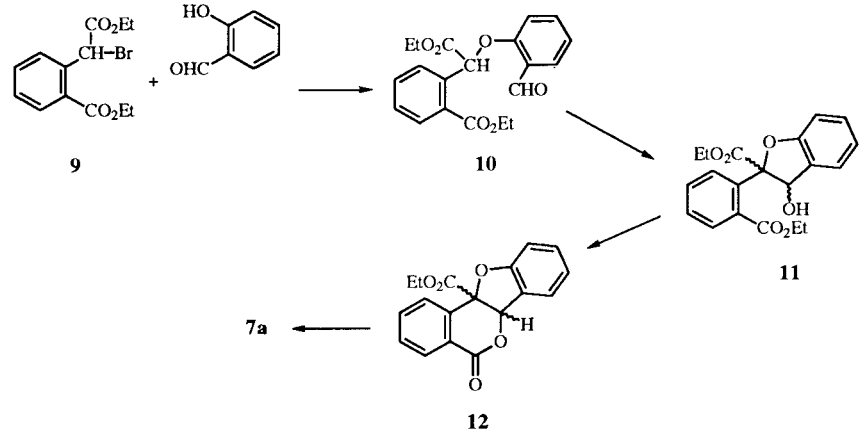


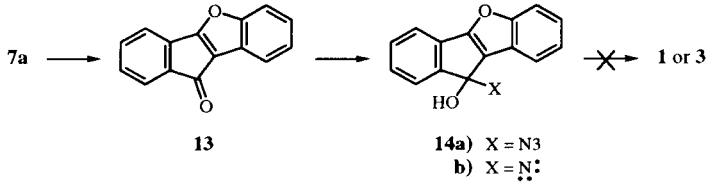
acidic decarboxylation-dehydration (80%) *via* 2-(*o*-carboxyphenyl)-3-oxo-2,3-dihydro-2-benzofurancarboxylic acid (**16**). The desired benzofuroisoquinolinone **1** was obtained by treating benzofuroisocoumarin **2** with ammonia gas at 100° for 24 hours in a sealed tube.

EXPERIMENTAL

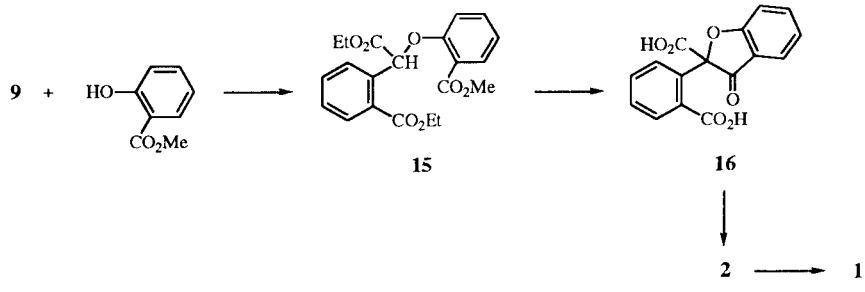
All melting points and boiling points were uncorrected. The ir spectra were recorded on a Hitachi 260-50 spectrometer in liquid films or potassium bromide disks. The uv spectra were recorded on a Hitachi 220A spectrophotometer in ethanol solution. The ^{1}H nmr spectra were recorded on a JEOL PMX-60Si or FX-90Q nmr spectrometer in deuteriochloroform solutions, and the mass spectra were recorded on a JEOL JMS-OISG-2 mass spectrometer.

Ethyl α-Chloro-α-(*o*-methoxyphenyl)acetate (**4**).





To a mitxure of *o*-methoxybenzaldehyde (26.0 g, 0.191 mole) and sodium cyanide (13.1 g, 267 mmoles) in ethanol (100 ml) and water (100 ml) was slowly added concentrated hydrochloric acid (50 ml) over a period of 2 hours with ice-cooling, and the mixture was stirred at room temperature for 2 hours. After dilution by adding water (50 ml) the mixture was extracted with ether. The ether layer was washed with saturated



A similar condensation of methyl salicylate with **9** gave diethyl α-(*o*-methoxycarbonylphenyl)homophthalate (**15**) in 43% yield, which was converted to benzofuroisocoumarin **2** by an alkaline cyclization (57%) followed by

sodium carbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue, which was crystallized from benzene-cyclohexane to give α-hydroxy-α-(*o*-methoxyphenyl)acetonitrile (25.6 g, 89%), mp 77.5-78°; ir: ν OH 3400, ν CN 2250 cm^{-1}.

α-Hydroxy-α-(*o*-methoxyphenyl)acetonitrile (25.6 g, 169 mmoles) was added to concentrated hydrochloric acid (200 ml) with ice-cooling, and the mixture was stirred for 2 hours with ice-cooling and then allowed to warm to room temperature for 4 hours. The mixture was concentrated under reduced pressure, and the residue was then diluted with acetone. The precipitates were collected by filtration to yield crude α-hydroxy-α-(*o*-methoxyphenyl)acetic acid; ir: ν OH 3500-2500, ν CO 1700 cm^{-1}. Crude α-hydroxy-α-(*o*-methoxyphenyl)acetic acid was dissolved in ethanol (200 ml) containing concentrated sulfuric acid (20 ml) and the mixture was refluxed for 5 hours. The mixture was poured onto cold water and extracted with ether. The ether layer was washed with saturated sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residual oil, which was distilled to give ethyl α-hydroxy-α-(*o*-methoxyphenyl)acetate (18.4 g, 52%), bp 146-148° (6 mm Hg); ir: ν OH 3600-3300, ν CO 1730 cm^{-1}; ^1H nmr: δ 1.2 (t, 3H, OCH_2CH_3, J = 7 Hz), 3.4 (br d, 1H, OH, J = 6 Hz), 3.8 (s, 3H, OCH_3), 4.1 (q, 2H, OCH_2CH_3, J = 7 Hz), 5.2 (d, 1H, α-CH, J = 6 Hz), 6.7-7.3 ppm (m, 4H, aromatic protons).

Ethyl α-hydroxy-α-(*o*-methoxyphenyl)acetate (16.0 g, 76.0 mmoles) was dissolved in thionyl chloride (36.0 g, 303 mmoles), and the mixture was stirred for 16 hours and refluxed for 30 minutes. Evaporation of excess thionyl chloride under reduced pressure gave a residual oil, which was poured onto ice-water and then extracted with ether. The ether layer was washed with saturated sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residual oil, which was distilled to give **4** (15.3 g, 88%), bp 134-136° (6 mm Hg); ir: ν CO 1750, 1600 cm^{-1}; ^1H nmr: δ 1.2 (t, 3H, OCH_2CH_3, J = 7 Hz), 3.8 (s, 3H, OCH_3), 4.2 (q, 2H, OCH_2CH_3, J = 7 Hz), 5.7 (s, 1H, α-CH-), 6.7-7.5 ppm (m, 4H, aromatic protons); ms: m/z 157 and 155 (M^+).

Anal. Calcd. for $C_{11}H_{13}ClO_3$: C, 57.78; H, 5.73. Found: C, 57.89; H, 5.72.

A Gabriel-Colmann Reaction of **5**.

To a solution of **4** (7.43 g, 32.5 mmoles) in DMF (60 ml) containing potassium iodide (130 mg) was added potassium phthalimide (7.25 g, 39.2 mmoles), and the mixture was refluxed for 3 hours. The mixture was poured onto ice-water and then extracted with ethyl acetate. The organic layer was washed with 5% sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave a residual oil, which was crystallized from ethanol to give **5** (7.50 g, 68%), mp 135-136°; ir: ν CO 1780, 1750, 1715 cm^{-1}; ^1H nmr: δ 1.3 (t, 3H, OCH_2CH_3, J = 7 Hz), 3.9 (s, 3H, OCH_3), 4.3 (q, 2H, OCH_2CH_3, J = 7 Hz), 6.5 (s, 1H, α-CH-), 6.8-7.9 ppm (m, 8H, aromatic protons); ms: m/z 339 (M^+), 293 (M^+-OEt).

Anal. Calcd. for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.18; H, 4.96; N, 4.04.

To an ethanolic solution of sodium ethoxide, prepared from sodium metal (120 mg, 8.7 mmoles) and absolute ethanol (10 ml), was added a solution of **5** (2.0 g, 5.9 mmoles) over a period of 30 minutes with stirring, and the mixture was refluxed for 14 hours. The mixture was treated with hot water (150 ml) and then the aqueous layer was acidified with ammonium chloride. The precipitates were collected and recrystallized from chloroform to give an unknown compound (340 mg), mp 231-232°; ir: ν CO 1710, 1680 cm^{-1}; uv: λ max 242 (log ε 4.03), 273 (log ε 3.61), 289 (log ε 3.49); ms: m/z 283 (M^+).

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 67.79; H, 4.65; N, 4.85.

Diethyl α-Bromohomophthalate (**9**).

To a stirred refluxing solution of diethyl homophthalate (14.5 g, 61.4 mmoles) in carbon tetrachloride (260 ml) was added bromine (3.6 ml, *ca.* 70 mmoles) with irradiation using a 100W electric bulb. After complete addition refluxing was continued for 3 hours. Evaporation of the solvent gave a residual oil, which was separated by column chromatography (silica gel-benzene) to give 9 (15.3 g, 79%); ir: ν CO 1735, 1710 cm^{-1}; ^1H nmr: δ 1.3 and 1.4 (two t, each 3H, $O\text{-}CH_2CH_3$, J = 7 Hz), 4.2 and 4.4 (two q, each 2H, $O\text{-}CH_2CH_3$, J = 7 Hz), 6.6 (s, 1H, α-CH-), 7.2-8.1 ppm (m, 4H, aromatic protons).

Condensation of Salicylaldehyde with **9**.

To a solution of salicylaldehyde (2.07 g, 17.0 mmoles) and **9** (4.45 g, 14.1 mmoles) in acetone (50 ml) was added anhydrous potassium carbonate (5.83 g, 42.2 mmoles), and the mixture was refluxed for 3 hours. After dilution with water the mixture was acidified with 10% hydrochloric acid and then extracted with ether. The ether layer was washed with 5% sodium hydroxide solution and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude crystalline residue, which was recrystallized from benzene-hexane to give **12** (2.02 g, 46%), mp 92-93°; ir: ν CO 1740, 1720 cm^{-1}; ^1H nmr: δ 1.2 (t, 3H, $O\text{-}CH_2CH_3$, J = 7 Hz), 4.3 (q, 2H, $O\text{-}CH_2CH_3$, J = 7 Hz), 6.4 (s, 1H, 6a-H), 6.8-8.4 ppm (m, 8H, aromatic protons); ms: m/z 310 (M^+).

Anal. Calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found: C, 69.97; H, 4.69.

o-(2-Benzofuranyl)benzoic Acid (**7a**).

A mixture of **12** (6.72 g, 21.7 mmoles) and 30% sulfuric acid (100 ml) was refluxed with stirring for 20 hours. The mixture was diluted with ice-water and extracted with ether. The ether layer was extracted with saturated sodium hydrogen-carbonate solution. After acidification with 10% hydrchloric acid the extract was re-extracted with ether. The ether layer was washed with saturated sodium chloride and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude crystals, which were recrystallized from benzene-cyclohexane to give **7a** (4.22 g, 82%), mp 131-132°; ir: ν CO 1700 cm^{-1}; ^1H nmr: δ 7.0 (s, 1H, 3-H), 7.1-8.0 (m, 8H, aromatic protons), 10.3 ppm (s, 1H, $-CO_2H$); ms: m/z 238 (M^+).

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23. Found: C, 75.80; H, 4.24.

Curtius Reaction of **7a**.

To a solution of crude acid chloride **7b**, prepared from **7a** (200 mg, 840 mmoles) and thionyl chloride (5.00 g, 42 mmoles), in acetone (10 ml) was added a solution of sodium azide (93 mg, 1.4 mmoles) with ice-water cooling over a period of 15 minutes. The mixture was stirred at room temperature for 15 hours. The precipitates were filtered and the flitrate was concentrated under reduced pressure and the precipitates were collected by filtration and recrystallized from benzene-cyclohexane to give **8b** (108 mg, 46%), mp 116-117°; ir: ν NH 3250, ν N_3 2150, ν CO 1680 cm^{-1}; ^1H nmr: δ 7.0 (s, 1H, 3'-H), 7.1-7.8 ppm (m, 8H, aromatic protons); ms: m/z 235 (M^+-N_2).

Anal. Calcd. for $C_{15}H_{10}N_4O_2$: C, 64.74; H, 3.62; N, 20.14. Found: C, 65.00; H, 3.56; N, 20.23.

Heating azide **8b** at 130-150° gave 6(5*H*)-benzofuro[3,2-*c*]-quinolinone (**3**), mp 294-296°; ir: ν CO 1670 cm^{-1}, identical with an authentic sample [1b].

Hofmann Method of *o*-(2-Benzofuranyl)benzamide (**7d**).

A mixture of **7a** (340 mg, 1.43 mmoles), thionyl chloride (3.4 g, 28 mmoles), and dry benzene (20 ml) was refluxed for 2 hours. After evaporation of the solvent under reduced pressure the residual oil was dissolved again in dry benzene (30 ml). Through the benzene solution was bubbled ammonia gas with stirring for 2 hours. The precipitates were collected by filtration and recrystallized from benzene to give amide **7d** (277 mg, 83%), mp 190-190.5°; ir: ν NH 3350, 3170, ν CO 1640 cm^{-1}; ^1H nmr (deuteriochloroform-DMSO-d_6): δ 6.8 (br s, 2H, $CONH_2$), 7.1 (s, 1H, 3'-H), 7.0-8.0 ppm (m, 8-H, aromatic protons); ms: m/z 237 (M^+).

Anal. Calcd. for $C_{15}H_{11}NO_2$: C, 75.93; H, 4.67; N, 5.90. Found: C, 76.02; H, 4.60; N, 5.61.

To a solution of amide **7d** (264 mg, 1.11 mmoles) in absolute ethanol (5 ml) was added an ethanolic solution of sodium ethoxide, prepared from sodium metal (52 mg, 2.26 mmoles) and absolute ethanol (5 ml). To this mixture was added bromine (184 mg, 1.15 mmoles), and the mixture was refluxed for 10 minutes. After cooling the mixture was acidifed with 10% hydrochloric acid, diluted with water, and extracted with ether. The ether layer was washed with sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue, which was crystallized from benzene to recover **7d** (74 mg, 28%). After evaporation of benzene the filtrate gave an oily residue, which was purified by chromatography (silica gel-chloroform) to give **8c** (124 mg, 40%), mp 83-83.5°; ir: ν NH 3250, ν CO 1700 cm^{-1}; ^1H nmr: δ 1.3 (t, 3H, O-CH_2CH_3, J = 7 Hz), 4.3 (q, 2H, O-CH_2CH_3, J = 7 Hz), 7.0 (s, 1H, 3'-H), 7.1-8.4 (m, 8H, aromatic protons), 7.9 ppm (br s, 1H, NH); ms: m/z 281 (M^+).

Anal. Calcd. for $C_{17}H_{15}NO_3$: C, 72.58; H, 4.97; N, 4.98. Found: C, 72.29; H, 5.20; N, 4.70.

Schimidt Method of 10-Indeno[1,2-*b*]benzofuranone (**13**).

With ice cooling **7a** (1.00 g, 4.20 mmoles) was added to trifluoroacetic anhydride (3.76 g, 17.9 mmoles), and the mixture was stirred at room temperature for 4 hours. The mixture was then poured onto saturated sodium hydrogencarbonate solution, and extracted with ether. The ether layer was washed with saturated sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude crystals, which were recrystallized from ethyl acetate-hexane to give **13** (251 mg, 27%), mp 142-145°; ir: ν CO 1720, 1695 cm^{-1}; ^1H nmr: δ 7.3-7.9 ppm (m, aromatic protons); ms: m/z 220 (M^+); uv: λ max 261 (log ε 4.57), (log ε 4.47), 276 sh (log ε 4.27), 302 sh (log ε 3.68), 315 sh nm (log ε 3.47).

Anal. Calcd. for $C_{15}H_8O_2$: C, 81.81; H, 3.66. Found: C, 81.62; H, 3.87.

To a solution of **13** (311 mg, 1.41 mmoles) in chloroform (20 ml) and concentrated sulfuric acid (1 ml) was added sodium azide (110 mg, 1.69 mmoles), and the mixture was stirred at 35-40° for 30 minutes. The mixture was then treated with water and the chloroform layer was washed with 5% sodium hydroxide solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oily residue (151 mg), which was heated in benzene to give a tarry mixture.

Condensation of Methyl Salicylate with **9**.

To a solution of methyl salicylate (3.86 g, 25.4 mmoles) and **9** (8.00 g, 25.4 mmoles) in acetone (190 ml) was added anhydrous potassium carbonate (10.6 g, 76.7 mmoles), and the mixture was refluxed for 4 hours. The precipitates were filtered off, and the filtrate was concentrated under reduced pressure. The residual oil was diluted with ether and the ether layer was washed with 5% sodium hydroxide solution and dried over anhydrous sodium sulfate. Evaporation of the ether gave an oily residue, which was purified by chromatography (silica gel-benzene) to give diethyl α-(*o*-methoxycarbonylphenyloxy)homophthalate (**15**) (5.17 g, 53%), bp 180° (2 mm Hg); ir: ν CO 1750, 1730, 1710 cm^{-1}; ^1H nmr: δ 1.2 and 1.4 (two t, each 3H, $COOCH_2CH_3$, J = 7 Hz), 3.9 (s, 3H, $COOCH_3$), 4.2 and 4.4 (two q, each 2H, $COOCH_2CH_3$, J = 7 Hz), 7.0 (s, α-C*H*), 6.8-8.1 ppm (m, 8H, aromatic protons); ms: m/z 386 (M^+).

Anal. Calcd. for $C_{21}H_{22}O_7$: C, 65.27; H, 5.74. Found: C, 65.37; H, 5.62.

Cyclization of **15** to **2**.

To 10% potassium hydroxide solution (124 ml) was added **15** (3.24 g, 8.38 mmoles), and the mixture was stirred at room temperature for 24 hours. After washing with ether, the mixture was acidified, and extracted with ethyl acetate. The ethyl acetate layer was extracted with saturated sodium hydrogencarbonate solution. The sodium carbonate solution was acidified and re-extracted with ethyl acetate. The ethyl acetate layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crystalline residue, which was recrystallized from ethyl acetate-hexane to give **16** as a dihydrate, mp 175°; ir: ν OH 3600-2400, ν CO 1735, 1710, 1685 cm^{-1}; ^1H nmr (DMSO-d_6): δ 7.0-8.3 (m, 8H, aromatic protons), 9.5 ppm (br s, 2H, COO*H*); ms: m/z 236 (M^+-CO_2).

Anal. Calcd. for $C_{16}H_{10}O_6 \cdot 2H_2O$: C, 57.48; H, 4.23. Found: C, 57.84; H, 3.99.

The acid dihydrate **16** (867 mg, 2.59 mmoles) was once heated around 200° under reduced pressure (18 mm Hg), and the residue was dissolved in ethyl acetate. The ethyl acetate layer was washed with sodium hydrogencarbonate and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crystalline residue, which was recrystallized from benzene to give **2** (490 mg, 80%), mp 168-169°; ir: ν CO 1735 cm^{-1}; ^1H nmr: δ 7.2-8.5 (m, aromatic protons); ^{13}C nmr: δ 112.2, 118.6, 119.3, 119.4, 123.8, 126.7, 128.0, 129.3, 131.5, 135.3, 137.3, 153.9, 161.3 ppm; ms: m/z 236 (M^+); uv: λ max 225 (log ε 4.29), 245 sh (log ε 4.15), 256 sh (log ε 3.92), 290 sh (log ε 4.14), 301 (log ε 4.36), 314 (log ε 4.41), 353 nm (log ε 3.96).

Anal. Calcd. for $C_{15}H_8O_3$: C, 76.27; H, 3.41. Found: C, 76.18; H, 3.41.

Conversion of **2** to **1**.

In a sealed tube benzofuroisocoumarin **2** (671 mg, 2.84 mmoles) was treated with ammonia gas (7 kg/cm^2) at 100° for 24 hours. The residue was recrystallized from ethanol to give 5(6*H*)-benzofuro[3,2-*c*]isoquinolinone (**1**) (393 mg, 59%), mp 310°; ir: ν CO 1670 cm^{-1}; ^1H nmr: δ 7.4-8.4 (m, 8H, aromatic protons), 12.5 ppm (br s, 1H, CON*H*); ^{13}C nmr: δ 112.1, 119.4, 119.5, 119.9, 121.9, 123.4, 124.7, 126.7, 126.9, 127.8, 128.6,

133.2, 135.3, 154.2, 161.1 ppm; ms: m/z 235 (M^+); uv: λ max 231 (log ε 4.42), 260 (log ε 3.24), 300 sh (log ε 4.03), 312 sh (log ε 4.19), 323 (log ε 4.22), 353 (log ε 4.11), 372 sh nm (log ε 3.93).

Anal. Calcd. for $C_{15}H_9NO_2$: C, 76.58; H, 3.86; N, 5.96. Found: C, 76.81; H, 4.01; N, 6.03.

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[3] A. Ulrich, *Chem. Ber.*, **37**, 1689 (1904).

[4] An unknown compound ($C_{16}H_{13}NO_4$) obtained is supposed to be *N*-[α-hydroxy-α-(*o*-methoxyphenyl)methyl]phthalimide.

[5] A similar mild treatment at room temperature for 3 hours gave ethyl α-(*o*-ethoxycarbonylphenyl)-α-(*o*-formylphenoxy)acetate (**10**), ethyl 2-(*o*-ethoxycarbonylphenyl)-3-hydroxy-2,3-dihydrobenzofuran-2-carboxylate (**11**), and **12** in 58, 11, and 3% respectively. Spectral data of **10** and **11** are the following; **10**, ir: ν CO 1740, 1710, 1690 cm^{-1}; ^1H nmr: δ 1.2 and 1.4 (two t, each 3H, $CO_2CH_2CH_3$, J = 7 Hz), 4.1 and 4.4 (two q, each 2H, $CO_2CH_2CH_3$, J = 7 Hz), 7.0 (s, 1H, α-C*H*), 6.8-8.2 (m, 8H, aromatic protons), 10.6 ppm (s, 1H, C*H*O); ms: m/z 356 (M^+); **11**, ir: ν OH 3450, ν CO 1715 cm^{-1}; ^1H nmr: δ 1.2 and 1.4 (two t, each 3H, $CO_2CH_2CH_3$, J = 7 Hz), 4.1 and 4.4 (two q, each 2H, $CO_2CH_2CH_3$, J = 7 Hz), 5.5 (d, 1H, OH, J = 7 Hz), 7.0 (d, 1H, α-C*H*, J = 7 Hz), 6.7-7.8 ppm (m, 8H, aromatic protons); ms: m/z 338 (M^+-H_2O).

[6] Sodium azide was insoluble in other solvents.

[7] Another Hofmann reaction using 1,1-bis(trifluoro-acetoxy)-iodobenzene in aqueous acetonitrile was also attempted, but resulted in recovery of the starting materials.