Selective Preparations; 27. A Convenient Preparation of 1-Hydroxydibenzofuran from 2-Bromo-4,6-di-*t*-butylphenol[1]

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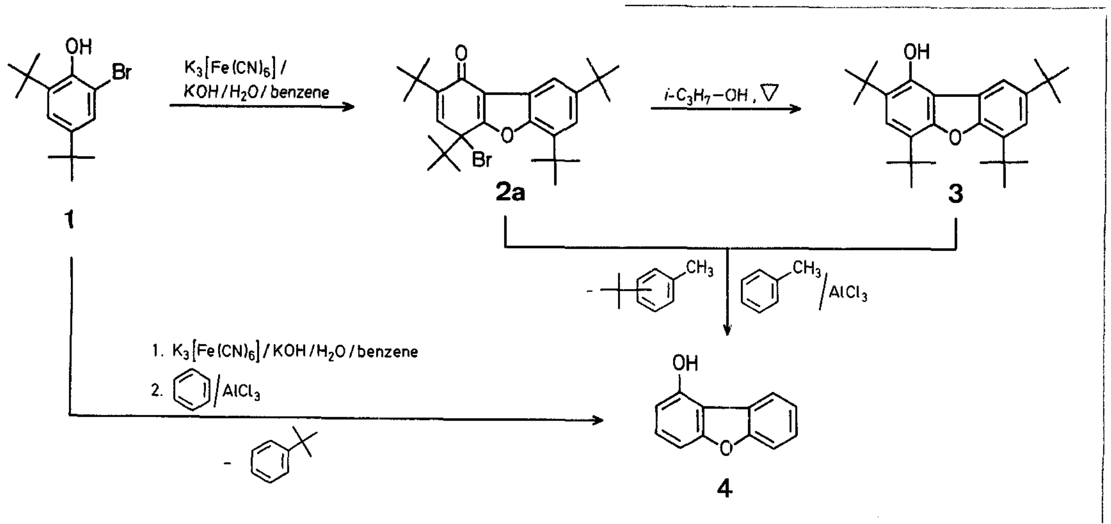
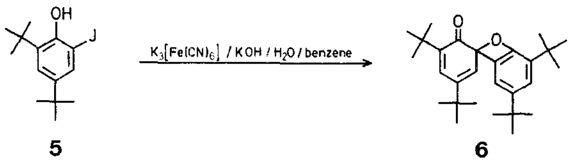
1-Hydroxydibenzofuran (**4**), a benzofuran derivative of some importance, has hitherto been prepared from readily available starting materials only by laborious methods[2]. We wish to report here a convenient synthesis of **4** from 2-bromo-4,6-di-*t*-butylphenol (**1**) in only a few steps. The starting material **1** is obtained by bromination of commercially available 2,4-di-*t*-butylphenol.

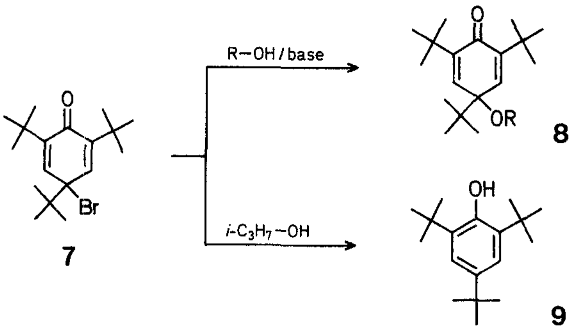


Müller et al.[4] reported that oxidation of 2-iodo-4,6-di-*t*-butylphenol (**5**) with potassium hexacyanoferrate(III) affords the spiro compound **6**.



Contrary to this, oxidation of the bromo derivative **1** with potassium hexacyanoferrate(III) in benzene gives the bromo-1-oxo-2,4,6,8-tetra-*t*-butyldihydrodibenzofuran **2a**[3] in 81% yield. When compound **2a** is heated in isopropanol, hydrodebromination occurs to afford the 1-hydroxydibenzofuran derivative **3** in 85% yield.

It has been reported[5] that the reaction of 4-bromo-2,4,6-tri-*t*-butyl-2,5-cyclohexadienone (**7**) with methanol or ethanol in the presence of bases such as pyridine or DBU affords the corresponding 4-alkoxy derivatives **8**. On the other hand, heating of **7** with isopropanol in the absence of a base results in hydrodebromination of **7** to give 2,4,6-tri-*t*-butylphenol (**9**) in 95% yield.



Conversion of compounds **2a** or **3** into the desired 1-hydroxydibenzofuran (**4**) is achieved in ∼75% yield by aluminum chloride-catalyzed transalkylation with toluene; in the case of **2a**, bromotoluenes are formed as side products. Compound **4** may also be directly obtained in 53% yield by oxidation of **1** with potassium hexacyanoferrate(III) in benzene, drying the reaction solution, and treating it with aluminum chloride.

4-Bromo-1-oxo-2,4,6,8-tetra-*t*-butyl-1,4-dihydrodibenzofuran (2a): The reaction flask is a 1000 ml three-neck separatory funnel-type flask equipped with a stirrer. The flask is charged with a solution of

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2-bromo-4,6-di-*t*-butylphenol[6] (**1**; 1.72 g, 6 mmol) in benzene (100 ml) and a solution of potassium hexacyanoferrate(III) (10 g, 30 mmol) and potassium hydroxide (10 g, 180 mmol) in distilled water (150 ml). The mixture is stirred at room temperature under oxygen-free nitrogen for 20 min. The aqueous layer is then removed and the organic layer is washed with distilled water (5 × 100 ml) whereby the color is changed to red-brown. The organic solution is dried with sodium sulfate and evaporated in vacuo to give crude **2a** in 81% yield; m.p. 175–182 °C. The product is recrystallized from ether to give **2a** as pale yellow prisms; yield: 0.94 g (64%); m.p. 181–183 °C.

$C_{28}H_{39}BrO_2$	calc.	C 68.98	H 8.06
(487.5)	found	69.15	8.07

I.R. (KBr): $\nu_{C=O} = 1660\ cm^{-1}$.

^{1}H-N.M.R. (CCl_4): $\delta = 1.27$ (s, 9H); 1.35 (s, 9H); 1.40 (s, 9H); 1.51 (s, 9H); 6.81 (s, 1H); 7.22 (d, $J = 2$ Hz, 1H); 7.99 ppm (d, $J = 2$ Hz, 1H).

1-Hydroxy-2,4,6,8-tetra-*t*-butyldibenzofuran (3):

A suspension of 4-bromo-1-oxo-2,4,6,8-tetra-*t*-butyl-1,4-dihydrodibenzofuran (**2a**; 2.44 g, 5 mmol) in isopropanol (50 ml) is heated to reflux until **2a** has completely dissolved. Refluxing is continued for 30 min, and the solvent then removed in vacuo. The residue is recrystallized from methanol to give colorless prisms; yield: 1.73 g (85%); m.p. 213–214 °C.

$C_{28}H_{40}O_2$	calc.	C 82.30	H 9.87
(408.6)	found	82.11	9.91

M.S.: $m/e = 408$ (M^+).

I.R. (KBr): $\nu_{OH} = 3660\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.44$ (s, 9H); 1.53 (s, 9H); 1.55 (s, 9H); 1.60 (s, 9H); 5.36 (s, 1H; disappears with D_2O); 7.31 (s, 1H); 7.46 (d, $J = 2$ Hz, 1H); 7.99 ppm (d, $J = 2$ Hz, 1H).

1-Hydroxydibenzofuran (4):

From **1**: The reaction flask is a 1000 ml three-neck separatory funnel-type flask equipped with a stirrer. The flask is charged with a solution of 2-bromo-4,6-di-*t*-butylphenol[6] (**1**; 5.7 g, 20 mmol) in benzene (330 ml) and a solution of potassium hexacyanoferrate (33 g, 100 mmol) and potassium hydroxide (33 g, 590 mmol) in distilled water (500 ml). The mixture is stirred at room temperature under oxygen-free nitrogen for 20 min. The aqueous layer is then removed and the organic layer is washed with distilled water (5 × 150 ml) whereby the color is changed to red brown. The organic solution is dried with sodium sulfate, finely powdered aluminum chloride (9.3 g, 70 mmol) is added, and the mixture is stirred for 3 h at room temperature. The mixture is then poured into ice/water (500 ml). The organic phase is separated and the aqueous phase extracted with benzene (2 × 100 ml). The combined organic solutions are extracted with 10% aqueous sodium hydroxide (3 × 100 ml). The aqueous-alkaline extract is acidified with 10% hydrochloric acid and extracted with benzene (3 × 200 ml). The organic extract is dried with sodium sulfate and evaporated in vacuo. The residue is recrystallized from hexane to give **4** as colorless needles; yield: 0.98 g (53%); m.p. 142–143 °C (Ref.[2], m.p. 140–140.5 °C).

$C_{12}H_8O_2$	calc.	C 78.25	H 4.38
(184.2)	found	77.90	4.38

M.S.: $m/e = 184$ (M^+).

I.R. (KBr): $\nu_{OH} = 3280\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 5.5$ (broad s, 1H; disappears with D_2O); 6.67 (d-d, $J = 8$ Hz, 2 Hz, 1H); 7.1–7.6 (m, 5H); 8.02–8.12 ppm (m, 1H).

From **2a**: Finely powdered aluminum chloride (1.2 g, 9 mmol) is added to a solution of 4-bromo-1-oxo-2,4,6,8-tetra-*t*-butyl-1,4-dihydrodibenzofuran (**2a**; 1.46 g, 3 mmol) in dry toluene (60 ml) and the mixture is stirred for 3 h at room temperature. The solution is then poured into ice/water (100 mml) and worked up as described above; yield: 0.42 g (75%).

In the toluene layer treated with the alkaline solution, the formation of bromotoluene was confirmed by G.L.C. analysis (conditions: Yanagimoto gas chromatograph, YANACO G 180; 30% high-vacuum silicon grease, 75 cm; programmed temperature raise: 12 °C/min; carrier gas: helium, 25 ml/min).

From **3**: A solution of 1-hydroxy-2,4,6,8-tetra-*t*-butyldibenzofuran (**3**; 1.22 g, 3 mmol) in dry toluene (60 ml) is treated with aluminum chloride (1.2 g, 9 mmol) and worked up as described above; yield: 0.42 g (76%).

Reaction of 4-Bromo-2,4,6-tri-*t*-butyl-2,5-cyclohexadienone (7) with Isopropanol:

A suspension of 4-bromo-2,4,6-tri-*t*-butyl-2,5-cyclohexadienone[5] (**7**; 3.4 g, 10 mmol) in isopropanol (100 ml) is refluxed for 1 h and then evaporated in vacuo. The residual crude **9** (2.5 g, 95%) is recrystallized from ethanol to give *2,4,6-tri-t-butylphenol* (**9**) as colorless prisms; yield: 2.1 g (80%); m.p. 135–136 °C (Ref.[7], m.p. 135–136 °C).

Received: October 10, 1979
(Revised form: November 23, 1979)

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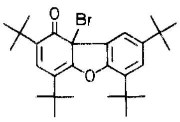
[3] Structure **2b** might also be considered for the bromodienone **2a**. A clear distinction between structures **2a** and **2b** is not possible on the basis of the presently available data.



2b

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