Reactions of Benzofuran Oxidation, Nitration and Bromination of 7-Hydroxy- and 7-Methoxy-benzofuran Derivatives

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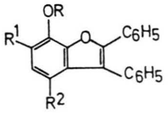
Benzofuran, Benzoin, Pyrocatechol

Condensation of benzoin and pyrocatchol gave 7-hydroxy-2,3-diphenylbenzofuran (**1a**), which on oxidation yielded the quinone **3a** whereas, its methyl ether **1b** gave the benzophenone **2a** on oxidation. Nitration of **1a** and **1b** led to the formation 4,6-dinitro- (**1c**) and 4-nitro (**1h**) derivatives, respectively, also bromination of **1a** and **1b** gave 4,6-dibromo- (**1f**) and 6-bromo- (**1j**), respectively.

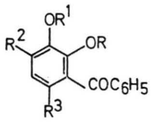
In the previous publications[1, 2], both nitration and bromination of 5-hydroxy- and 5-methoxy- or 6-hydroxy- and 6-methoxy-2,3-diphenylbenzofuran have been studied. The present investigation deals with oxidation, nitration and bromination of 7-hydroxy- and 7-methoxy-2,3-diphenylbenzofuran.

Condensation of benzoin and pyrocatechol in presence of dilute sulphuric acid, two products were obtained. The first product was 2,3,6,7-tetraphenylfuro[3,2-g]benzofuran[3], and the second product was namely 7-hydroxy-2,3-diphenylbenzofuran (**1a**).



	R	R¹	R²
1a	H	H	H
1b	CH_3	H	H
1c	H	NO_2	NO_2
1d	CH_3	NO_2	NO_2
1e	$COCH_3$	NO_2	NO_2
1f	H	Br	Br
1g	$COCH_3$	Br	Br
1h	CH_3	H	NO_2
1i	CH_3	H	NH_2
1j	CH_3	Br	H

The structure of **1a** was confirmed by the following reactions. Methylation of **1b** with dimethylsulphate and sodium hydroxide gave the 7-methoxy derivative (**1b**). Oxidation of **1b** with chromic-acetic acid mixture yielded 2-benzoyloxy-3-methoxybenzophenone (**2a**), which on alkaline hydrolysis led to the formation of the known 2-hydroxy-3-methoxybenzophenone[4] (**2b**).



	R	R¹	R²	R³
2a	COC_6H_5	CH_3	H	H
2b	H	CH_3	H	H
2c	COC_6H_5	$COCH_3$	NO_2	NO_2
2d	H	H	NO_2	NO_2
2e	COC_6H_5	$COCH_3$	Br	Br
2f	H	H	Br	Br
2g	COC_6H_5	CH_3	H	NO_2
2h	H	CH_3	H	NO_2
2i	COC_6H_5	CH_3	Br	H
2j	H	CH_3	Br	H

Oxidation of 7-hydroxy-2,3-diphenylbenzofuran (**1a**) with chromic-acetic acid mixture afforded 2,3-diphenyl-4,7-benzofuranquinone (**3a**). The infrared spectrum of **3a** showed a band at 1668 cm^{-1} due to *p*-benzoquinone system[5].

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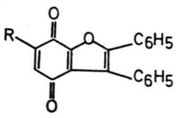
This is in agreement with the finding of Inouye *et al.*[6] who found that oxidation of 3-methyl-4-hydroxybenzofuran[7] afforded the 3-methyl-4,7-benzofuranquinone. However, oxidation of 2-(3′,4′-dimethoxyphenyl) - 5 - (3″ - hydroxypropyl) - 7 - methoxybenzofuran by using hydrogen peroxide followed by basic hydrolysis gave styroxenolic acid and veratric acid[7].



	R
3a	H
3b	NO_2
3c	Br

It has been reported that nitration of benzofuran with nitric acid in acetic acid gave 2-nitro derivative[8] along with an isomeric nitro compound thought to be the 5-nitro derivatives[9–11], as 5-nitro salicyclic acid was found among the product of the reaction.

However, when the group present in position 2 is easily replaced, displacement sometimes occurred on nitration. Thus, 2-bromobenzofuran yielded 2-nitrobenzofuran[12].

In the present work nitration of **1a** with nitric acid in acetic acid gave the dinitro compound namely 4,6-dinitro-7-hydroxy-2,3-diphenylfuran (**1c**) which on oxidation led to the formation of 6-nitro-2,3-diphenyl-4,7-benzofuranquinone (**3b**).

The IR spectrum of **3b** showed the presence of benzoquinone system (1670 cm^{-1})[5].

Methylation of **1c** with dimethylsulphate and sodium hydroxide gave 4,6-dinitro-7-methoxy-2,3-diphenylbenzofuran (**1d**). Compound **1c** was converted to the acetoxy derivative **1e** by the reaction with acetic anhydride and acetic acid, which gave on hydrolysis 2,3-dihydroxy-4,6-dinitrobenzophenone (**2d**) *via* oxidation.

The infrared spectrum of **1e** showed a band at 1646 cm^{-1} characteristic for ester group[5], and the infrared spectrum of **2d** showed a band at 1655 cm^{-1} attributable to the carbonyl group-.

Bromination of benzofuran and its derivatives has been previously investigated by several authors. It has been reported that benzofuran on bromination gave unstable 2,3-dibromo-2,3-dihydrobenzofuran[13,14]. 2-Methylbenzofuran formed 3-bromo-2-methylbenzofuran[14]. Also, 3-phenylbenzofuran furnished 2-bromo derivative[15].

In this investigation it was found that bromination of 7-hydroxy-2,3-diphenylbenzofuran (**1a**) with bromine in carbon tetrachloride formed the 4,6-dibromo derivative (**1f**). Oxidation of **1f** gave 2,3-diphenyl-6-bromo-4,7-benzofuranquinone (**3c**). The infrared spectrum of **3c** showed a band at 1675 cm^{-1} characteristic for *p*-benzoquinine moiety[5].

In a similar manner as in nitration, 4,7-dibromo-7-hydroxy-2,3-diphenylbenzofuran (**1f**) was converted to the acetoxy derivative (**1g**), which on oxidation followed by hydrolysis led to the formation of 2,3-dihydroxy-4,6-dibromobenzophenone (**2f**).

Nitration of 7-methoxy-2,3-diphenylbenzofuran (**1b**) gave 4-nitro-7-methoxy-2,3-diphenylbenzofuran (**1h**) which on reduction was converted to the 4-amino derivative (**1i**) Oxidation of **1i** led to the formation of 2,3-diphenyl-4,7-benzofuranquinone (**3a**), m. p. and mixed m. p., element test for nitrogen was negative).

IR spectrum of **1h** showed bands at 1360 and 1543 cm^{-1} attributable to the nitro group[5].

Oxidation of **1h** followed by hydrolysis gave 2-hydroxy-3-methoxy-6-nitrobenzophenone (**2h**).

Bromination of 7-methoxy-2,3-diphenylbenzofuran (**1b**) gave a monobromo derivative namely 6-bromo-7-methoxy-2,3-diphenylbenzofuran (**1j**). This was in agreement with the finding of Angeloni *et al.*[16] who found that bromination of 7-methyl-2,3-diphenylbenzofuran gave the 6-bromo derivative.

Oxidation of **1j** gave 3-methoxy-2-benzoyloxy-4-bromobenzophenone (**2i**) as on oil, hydrolysis of the crude oil afforded 2-hydroxy-3-methoxy-4-bromobenzophenone (**2j**).

The infrared spectrum of **21** showed bands at 1672 cm^{-1} ($>$C=O) and a broad band at 3550–3350 cm^{-1} (OH)[5].

Experimental

Melting points were not corrected. The IR spectra were carried out on S. P. 1000 spectrophotometer.

7-Hydroxy-2,3-diphenylbenzofuran (**1a**)

A mixture of benzoin (100 g) and pyrocatechol (150 g) was fused on oil bath at 140 °C for 15 minutes. Water (200 ml) was added to the reaction mixture after cooling followed by 200 ml of conc. sulphuric acid. The reaction mixture was heated again at 120 °C for 10 min then left to cool, the solid so obtained was dissolved in 10% sodium hydroxide and filtered while hot. The undisolved substance was crystallised from acetone to give 20% of 2,3,6,7-tetraphenylfuro[3,2-g]benzofuran, m. p. 237 °C.

Mixed m.p. with an authentic sample[3] gave no depression. The filtrate was left to cool and acidified with hydrochloric acid, extracted with ether, washed with water several times, dried and evaporated the ether. The solid so obtained was crystallized from petrol. ether (b.p. 60–80 °C); m.p. 59 °C, yield is *ca.* 65%. It gave green colour with alcoholic ferric chloride.

Analysis

$C_{20}H_{14}O_2$ (286.332)
Calcd C 83.89 H 4.93,
Found C 83.81 H 4.82.

7-Methoxy-2,3-diphenylbenzofuran (**1b**)

A mixture of 4 g of **1a** in 50 ml of 50% of sodium hydroxide was treated with 10 ml of dimethylsulphate and stirred will till vigorous reaction occurred. The reaction mixture was left to cool, filtered and the solid so obtained was crystallized from petrol ether (60–80 °C) yielded 72% of **1b** as white crystals, m.p. 78–80 °C.

Analysis

$C_{21}H_{16}O_2$ (300.359)
Calcd C 83.98 H 5.37,
Found C 83.91 H 5.31.

2-Benzoyloxy-3-methoxybenzophenone (**2a**)

0.4 g of **1b** was added to a hot solution of 0.4 g of chromic anhydride in 20 ml glacial acetic acid. After adding another 0.15 of chromic anhydride and refluxing for 30 min, the mixture was diluted with water (20 ml) and left to cool, then filtered. White crystals was obtained, m.p. 90–92 °C petrol ether (b.p. 60–80 °C); yield 78%.

Analysis

$C_{21}H_{16}O_4$ (332.359)
Calcd C 75.89 H 4.85,
Found C 75.92 H 5.14.

2-Hydroxy-3-methoxybenzophenone (**2b**)

A mixture of 1 g of **2a** and 0.25 g of potassium hydroxide in 150 ml of ethanol was refluxed for 1 h. The solvent was then concentrated to about 10 ml, poured over water (75 ml), left to cool and acidified with conc. hydrochloric acid to give 2-hydroxy-3-methoxybenzophenone (**2b**) in 73% yield. M.p. and mixed m.p. between **2b** and the authentic sample-, gave no depression.

2,3-Diphenyl-4,7-benzofuranquinone (**3a**)

Oxidation of **1a** with chromic-acetic acid mixture as in case of **2a** gave pale yellow crystals, m.p. 180–182 °C (ethanol); yield 73%.

Analysis

$C_{20}H_{12}O_3$ (300.316)
Calcd C 79.99 H 4.02,
Found C 79.61 H 4.32.

4,6-Dinitro-7-hydroxy-2,3-diphenylbenzofuran (**1c**)

A mixture of 0.46 ml of conc. nitric acid and 0.5 ml of glacial acetic acid was added to a suspension of 1 g of **1a** in 2.5 ml of glacial acetic acetic acid. The reaction mixture was warmed at 80 °C for 5 min and left for 2 h at room temperature. Orange-red needles separated after pouring on water, which was filtered and crystallized from methanol, m.p. 255–257 °C, yield is *ca.* 55%. Ferric chloride test gave red colour.

Analysis

$C_{20}H_{12}N_2O_6$ (376.332)
Calcd C 63.83 H 3.21 N 7.44,
Found C 63.82 H 3.11 N 7.52.

2,3-Diphenyl-6-nitro-4,7-benzofuranquinone (**3b**)

Oxidation of 1 g of **1c** with chromic-acetic acid mixture gave 6-nitro-4,7-benzofuranquinone (**3b**) as yellow crystals from methanol, m.p. 260 °C; yield is *ca.* 65%.

Analysis

$C_{20}H_{11}N_2O_5$ (345.316)
Calcd C 69.57 H 3.21 N 4.06,
Found C 70.10 H 3.22 N 4.02.

4,6-Dinitro-7-methoxy-2,3-diphenylbenzofuran (**1d**)

Compound **1c** was methylated with dimethyl sulphate as in case of **1b** to give yellow crystals from methanol, m.p. 208–210 °C, yield is *ca.* 78%.

Analysis

$C_{21}H_{14}N_2O_6$ (390.359)
Calcd C 64.62 H 3.62 N 7.18,
Found C 65.11 H 3.41 N 7.10.

7-Acetoxy-4,6-dinitro-2,3-diphenylbenzofuran (**1e**)

A mixture of 1 g of **1c** and 5 ml of glacial acetic acid and 5 ml of acetic anhydride was heated under reflux for 3 h. Water (20 ml) was added to the reaction mixture and left to cool, then filtered. The solid so obtained was crystallized from methanol as yellow crystals, m.p. 170 °C; yield is *ca.* 62%.

Analysis

$C_{22}H_{14}N_2O_7$ (418.37)
Calcd C 63.16 H 3.38 N 6.70,
Found C 63.22 H 3.65 N 6.91.

2-Benzoyloxy-3-acetoxy-4,6-dinitrobenzophenone (**2c**)

As in case of **2a**, 1 g of **1c** gave 72% of **2c** as yellow crystals from methanol, m.p. 260–262 °C, yield is *ca.* 81%.

Analysis

$C_{22}H_{14}N_2O_9$ (450.37)
Calcd C 58.67 H 3.13 N 6.22,
Found C 58.41 H 3.25 N 6.35.

2,3-Dihydroxy-4,6-dinitrobenzophenone (**2d**)

As in case of **2a**, hydrolysis of 1 g of 2-benzoyloxy-3-acetoxy-4,6-dinitrobenzophenone (**2c**) gave 68% of **2d** from ethanol, m.p. 264–265 °C; mixed m.p. with **2c** 155–159 °C.

Analysis

$C_{13}H_8N_2O_7$ (304.225)
Calcd C 51.33 H 2.65 N 9.21,
Found C 51.41 H 2.71 N 9.22.

4,6-Dibromo-7-hydroxy-2,3-diphenylbenzofuran (**1f**)

To a solution of 7-hydroxy-2,3-diphenylbenzofuran (**1a**) (1 g) in carbon tetrachloride (60 ml), the solution of bromine (0.46 g) in carbon tetrachloride (10 ml) was added, set aside over night at room temperature. The solvent was evaporated under reduced pressure, and the oily residue solidified by trituration with ethanol. Crystallization from ethanol gave white crystals, m.p. 216–218 °C; yield is *ca.* 78%. Ferric chloride test gave green colour.

Analysis

$C_{20}H_{12}Br_2O_2$ (444.148)
Calcd C 54.09 H 2.72 Br 35.99,
Found C 53.83 H 2.85 Br 36.21.

2,3-Diphenyl-6-bromo-4,7-benzofuranquinone (**3c**)

Oxidation of 1 g of **1f** with chromic-acetic acid mixture gave **3c** as white crystals from methanol, m.p. 228–230 °C; yield is *ca.* 72%, ferric chloride test was negative.

Analysis

$C_{20}H_{11}BrO_3$ (379.224)
Calcd C 63.35 H 2.92 Br 21.07,
Found C 63.52 H 2.91 Br 21.52.

7-Acetoxy-4,6-dibromo-2,3-diphenylbenzofuran (**1g**)

As in the case of **1e**, 1 g of **1f** gave white crystals from benzene, m.p. 230 °C; yield is *ca.* 75%.

Analysis

$C_{22}H_{14}Br_2O_3$ (486.186)
Calcd C 54.35 H 2.90 Br 32.87,
Found C 54.63 H 3.11 Br 32.72.

2-Benzoyloxy-3-acetoxy-4,6-dibromobenzophenone (**2e**)

Oxidation of 1 g of **1g** with chromic-acetic acid mixture gave **2e** as white crystals from ethanol, m.p. 212 °C; yield 70%.

Analysis

$C_{22}H_{14}Br_2O_5$ (518.186)
Calcd C 50.99 H 2.72 Br 30.84,
Found C 51.22 H 3.01 Br 31.33.

2,3-Dihydroxy-4,6-dibromobenzophenone (**2f**)

Alkaline hydrolysis of 1 g of **2e** gave 2,3-dihydroxy-4,6-dibromobenzophenone as white crystals from ethanol, m.p. 205 °C; mixed m.p. with **2e** 165–170 °C; yield is *ca.* 72%, ferric chloride test gave green colour.

Analysis

$C_{13}H_8Br_2O_3$ (372.039)
Calcd C 41.97 H 2.17 Br 42.96,
Found C 41.72 H 2.53 Br 43.22.

4-Nitro-7-methoxy-2,3-diphenylbenzofuran (**1h**)

Nitration of 1 g of 7-methoxy-2,3-diphenylbenzofuran (**1b**) with nitric acid in acetic acid as in case of **1d** gave **1h** as yellow crystals from ethanol, m.p. 161–163 °C; yield is *ca.* 83%.

Analysis

$C_{21}H_{15}NO_4$ (345.359)
Calcd C 73.03 H 4.38 N 4.06,
Found C 72.68 H 4.23 N 4.26.

4-Amino-7-methoxy-2,3-diphenylbenzofuran (**1i**)

A mixture of 1 g of **1h** in 20 ml of ethanol and 5 g of stannous chloride in 20 ml of hydrochloric acids was refluxed for 3 h. Water (20 ml) was added then left to cool, filtered and crystallized from ethanol as white crystals, m.p. 188–189 °C; yield 72%.

Analysis

$C_{21}H_{17}NO_2$ (315.375)
Calcd C 79.98 H 5.43 N 4.44,
Found C 80.20 H 5.53 N 4.31.

Oxidation of **1** g with chromic-acetic acid mixture gave 84% of **3a**, m.p. and mixed m.p. gave no depression.

2-Benzoyloxy-3-methoxy-6-nitrobenzophenone (**2g**)

Oxidation of 1 g of **1h** gave 2-benzoyloxy-3-methoxy-6-nitrobenzophenone (**2g**) as yellow crystals from petrol ether (b.p. 80–100 °C), m.p. 160–161 °C; mixed m.p. with **1f** 130–135 °C; yield 80%.

Analysis

$C_{21}H_{15}NO_6$ (377.359)
Calcd C 66.84 H 4.01 N 3.71,
Found C 66.76 H 3.99 N 3.73.

2-Hydroxy-3-methoxy-6-nitrobenzophenone (**2h**)

Alkaline hydrolysis of 1 g of **2g** gave yellow crystals from petrol ether (b.p. 60–80 °C), m.p. 72–73 °C; yield 70%.

Analysis

$C_{14}H_{11}NO_5$ (273.25)
Calcd C 61.54 H 4.06 N 5.13,
Found C 62.01 H 4.30 N 5.20.

6-Bromo-7-methoxy-2,3-dihydrobenzofuran (**1j**)

It was prepared in a similar manner as **1f** from 1 g of 7-methoxy-2,3-diphenylbenzofuran (**1b**). The oily residue gave white crystals from petrol ether (b.p. 40–60 °C), m.p. 85–86 °C; yield 70%.

Analysis

$C_{21}H_{15}BrO_2$ (379.267)

Calcd	C 66.50	H 3.99	Br 21.07,
Found	C 66.31	H 4.48	Br 21.40.

Attempts for the preparation of 2-benzoyloxy-3-methoxy-4-bromobenzophenone (**2i**)

Oxidation of 1 g of **2h** with chromic-acetic acid mixture gave 2-benzoloxy-3-methoxy-4-bromobenzophenone (**2i**) as oil, yield 65%. It was difficult to solidify and purify this compound and thus it was hydrolysed directly to the compound **2j**.

2-Hydroxy-3-methoxy-4-bromobenzophenone (**2j**)

Alkalive hydrolysis of the crude **2i** gave 2-hydroxy-3-methoxy-4-bromobenzophenone (**2j**) as white crystals from petrol ether (b.p. 80–100 °C), m.p. 240–243 °C; yield 70%.

Analysis

$C_{14}H_{11}BrO_3$ (307.158)

Calcd	C 54.75	H 3.61	Br 26.02,
Found	C 55.19	H 3.22	Br 26.30.

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