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The Reduction of 2-Benzylidene-3(2*H*)-benzofuranones with Lithium Aluminium Hydride–Aluminium Chloride

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Synopsis. The reduction of various 2-benzylidene-3(2*H*)-benzofuranones with lithium aluminium hydride–aluminium chloride in ether gave the corresponding 2-benzylbenzofurans in moderate yields. The reduction of 6-methoxy-2-(4-methoxybenzoyl)benzofuran also yielded 6-methoxy-2-(4-methoxybenzyl)benzofuran.

Although the syntheses of 2-benzylidene-3(2*H*)-benzofuranones (**1**) (aurones) were investigated in detail,[1] the synthesis of 2-benzylbenzofurans (**2**) which have the same carbon skeleton has not been reported. Our interest in the preparation of new C_6–C_3–C_6 type compounds[2,3] led us to examine the reduction of **1** with lithium aluminium hydride–aluminium chloride. It has often been observed that the reduction of α,β-unsaturated carbonyl compounds with lithium aluminium hydride–aluminium chloride proceeds with a double bond migration.[4–10] Therefore, it could be expected that the reduction of **1** with these reagents gives stable 2-benzylbenzofuran (**2**) rather than 2-benzylidene-2,3-dihydrobenzofuran (**3**) (Fig. 1).

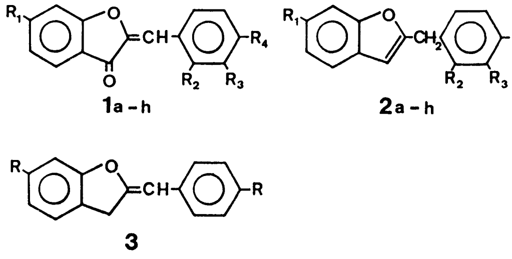
2-Benzylidene-3(2*H*)-benzofuranones (**1a**—**h**) were prepared from 2′-hydroxychalcones by the procedures reported by Donnelly *et al.*[11] and by one of the authors.[12] When 6-methoxy-2-(4-methoxybenzylidene)-3(2*H*)-benzofuranone (**1d**) was treated with lithium aluminium hydride in ether, followed by the addition of aluminium chloride, a single product was obtained. Its NMR showed the presence of two methoxyl groups [δ=3.72 (3H, s) and δ=3.75 (3H, s)], a methylene group [δ=3.93 (2H, s)], a vinylic proton [δ=6.11 (1H, broad s)], and aromatic protons [δ=6.5—6.9 (4H, m) and δ=6.95—7.3 (3H, m)]. The IR spectrum showed absorptions at 1625, 1615, and 1590 cm^{-1}. The reduction of 6-methoxy-2-(4-methoxybenzoyl)benzofuran[13] (**4**) with lithium aluminium hydride–aluminium chloride yielded identical **2d**. These results indicate that the product is not 6-methoxy-2-(4-methoxybenzylidene)-2,3-dihydrobenzofuran (**3**, R=OCH_3), but 6-methoxy-2-(4-methoxybenzyl)benzofuran (**2d**). The oxidation of **2d** with manganese(IV) oxide gave **4**.

Seven other 2-benzylidene-3(2*H*)-benzofuranones (**1a**—**c** and **1e**—**h**) were also subjected to the reduction, which gave the corresponding 2-benzylbenzofurans (**2a**—**c** and **2e**—**h**) in moderate yields. The results are shown in Table 1. The reduction of **1b** with lithium aluminium hydride without the addition of aluminium chloride gave an intractable mixture of products. This may be due to the instability of the allylic alcohol formed by the reduction of **1b**. In the reduction of **1a**, 3-(2-hydroxyphenyl)-1-phenyl-1-propene (**5**) was obtained together with 2-benzylbenzofuran (**2a**), which was the major product. There were a number of minor products which could not be purified.

Table 1. The reduction of 2-benzylidene-3(2*H*)-benzofuranones (**1**$_a$—**h**) with lithium aluminium hydride–aluminium chloride in ether at room temperature

Entry	Substrate	Reaction conditions: Molar ratio of substrate: $LiAlH_4$: $AlCl_3$	Reaction conditions: Time/min A[a]	Reaction conditions: Time/min B[b]	2-Benzylbenzofuran(**2**) (yield/%)[c]
1	**1a**[14]	1 : 2 : 2	60	60	36[d]
2	**1b**[12]	1 : 2 : 2	60	105	78
3	**1c**[15]	1 : 2 : 2	60	90	57
4	**1d**[12]	1 : 2 : 2	60	120	59
5	**1e**[12]	1 : 2 : 2	60	90	41
6	**1f**[12]	1 : 2 : 2	60	60	64
7	**1g**[12]	1 : 4 : 4	240	90	48[e]
8	**1h**[12]	1 : 2 : 2	60	60	40

a) Time before addition of $AlCl_3$. b) Time after addition of $AlCl_3$. c) The yields are based on the amount of the substrate used. d) **5** was obtained as a minor product in a 16% yield. e) **1g** (4%) was recovered.



a: R_1=R_2=R_3=R_4=H b: R_1=R_2=R_3=H, R_4=OCH_3
c: R_2=R_3=R_4=H, R_1=OCH_3 d: R_2=R_3=H, R_1=R_4=OCH_3
e: R_1=R_3=H, R_2=R_4=OCH_3 f: R_3=H, R_1=R_2=R_4=OCH_3
g: R_2=H, R_1=R_3=R_4=OCH_3 h: R_1=R_2=R_3=R_4=OCH_3

Fig. 1.

Thus it can be concluded that the reduction of 2-benzylidene-3(2*H*)-benzofuranones (**1**) with lithium aluminium hydride–aluminium chloride can be used for a preparation of 2-benzylbenzofuran derivatives (**2**).

Experimental

All the ^{1}H NMR spectra were recorded for the carbon tetrachloride solution with a Hitachi-Perkin-Elmer R-24 spectrometer, with tetramethylsilane as the internal standard. The IR spectra were taken for the chloroform solution on a JASCO grating spectrometer, while the UV spectra were recorded for the methanol solution, unless otherwise stated, with a Hitachi EPS-3T spectrophotometer. The high-resolution mass spectra were recorded on JMS-OlSG-2 instrument with direct inlet at 75 eV. The melting points were determined with a Yanagimoto micro-melting point apparatus and were not corrected.

2-Benzylidene-3(2H)*-benzofuranones* (*1a—h*). **1a**—**e** and **1g** were prepared by the procedure described by Donnelly *et al.*,[11] and **1f** and **1h** were obtained by the oxidation[12] of the corresponding 2′-hydroxychalcones with manganese(III) acetate.

*Reduction of 2-Benzylidene-3(2H)-benzofuranones (**1a—h**) with Lithium Aluminium Hydride–Aluminium Chloride.* The general procedure for the reduction of **1** was as follows. To a stirred solution of lithium aluminium hydride (2 mmol) in anhydrous ether (30 ml), a 2-benzylidene-3(2*H*)-benzofuranone (**1**) (1 mmol) was added and the reaction mixture was stirred at room temperature for the time shown in Table 1. Then aluminium chloride (2 mmol) was added and the mixture was again stirred for the time shown in Table 1. The reaction mixture was passed through a silica gel column, eluting with ether, and the ether was evaporated. The crude product was chromatographed on TLC and crystalline products were recrystallized from ethanol. In the case of **1a**, the reaction mixture was treated with 1 M sulfuric acid (30 ml) and extracted with ether. The ethereal solution was washed with a saturated sodium chloride solution and then evaporated. The resulting liquid was chromatographed on TLC with benzene as the developing solvent.

*2-Benzylbenzofuran (**2a**)*: Colorless liquid (lit,[16] bp$_{15}$ 180—185 °C); IR 1600 and 1618 cm^{-1}; UV λ_{max} (ε) 251 (17000), 280 (4770), and 287 nm (4690); NMR δ=3.97 (2H, s, $-CH_2-$), 6.17 (1H, s, =CH–), and 6.9—7.5 (9H, m, aromatic).

*3-(2-Hydroxyphenyl)-1-phenyl-1-propene (**5**)*: Colorless liquid (lit,[4] mp 67—68 °C); IR 975, 3340, and 3600 cm^{-1}; UV (EtOH)[4] λ_{max} (ε) 254 (18100), 277$_{sh}$ (6260), 284$_{sh}$ (4950), 293$_{sh}$ (2180), and 304 nm (1240); NMR δ=3.58 (2H, m, $-CH_2-$), 5.0 (1H, broad s, OH), 6.32 (2H, m, –CH=CH–), and 6.5—7.4 (9H, m, aromatic). When the methylene group at δ=3.58 was irradiated, the vinyl protons became singlet.

*2-(4-Methoxybenzyl)benzofuran (**2b**)*: MP 60—62 °C; IR 1590 and 1615 cm^{-1}; UV λ_{max} (ε) 253 (17000), 280 (6310), and 287 nm (6170); NMR δ=3.73 (3H, s, OCH_3), 4.00 (2H, s, $-CH_2-$), 6.28 (1H, broad s, =CH–), 6.6—7.4 (8H, m, aromatic) (Found: C, 80.78; H, 5.61%. Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92%).

*2-Benzyl-6-methoxybenzofuran (**2c**)*: Colorless liquid; IR 1580 and 1625 cm^{-1}; UV λ_{max} (ε) 252 (17000) and 292 nm (6780); NMR δ=3.69 (3H, s, OCH_3), 3.97 (2H, s, $-CH_2-$), 6.11 (1H, broad s, =CH–), 6.5—6.85 (2H, m, $H_{(5)}$ and $H_{(7)}$), 7.11 (1H, d, J=8.5 Hz, $H_{(4)}$), and 7.13 (5H, s, Ph); MS *m/e* 238.0989 (100%, M$^+$) (Calcd for $C_{16}H_{14}O_2$, MW 238.0994), 223 (49%, M$^+$–15), and 161 (26%, $C_{10}H_9O_2$).

*6-Methoxy-2-(4-methoxybenzyl)benzofuran (**2d**)*: Mp 90—91 °C; UV λ_{max} (ε) 255 (18600) and 291 nm (8320) (Found: C, 76.44; H, 5.81%. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01%).

*2-(2,4-Dimethoxybenzyl)benzofuran (**2e**)*: Colorless liquid; IR 1585 and 1610 cm^{-1}; UV λ_{max} (ε) 251 (16200), 280 (7550), and 287 nm (7650); NMR δ=3.62 (3H, s, OCH_3), 3.64 (3H, s, OCH_3), 3.90 (2H, s, $-CH_2-$), 6.10 (1H, broad s, =CH–), 6.0—6.4 (2H, m, aromatic), and 6.9—7.4 (5H, m, aromatic); MS *m/e* 268.1144 (100%, M$^+$) (Calcd for $C_{17}H_{16}O_3$, MW 268.1099) 253 (78%, M$^+$ –15), 237 (62%, M$^+$ –31), and 131 (90%, C_9H_7O).

*2-(2,4-Dimethoxybenzyl)-6-methxybenzofuran (**2f**)*: Colorless liquid; IR 1585 and 1615 cm^{-1}; UV λ_{max} (ε) 253 (19400) and 289 nm (8780); NMR δ=3.69 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 3.90 (2H, s, $-CH_2-$), 6.03 (1H, broad s, =CH–), 6.2—7.3 (6H, m, aromatic); MS *m/e* 298.1161 (43.8%, M$^+$) (Calcd for $C_{18}H_{18}O_4$, MW 298.1205), 283 (16%, M$^+$–15), 267 (14%, M$^+$–31), and 161 (13%, $C_{10}H_9O_2$).

*2-(3,4-Dimethoxybenzyl)-6-methoxybenzofuran (**2g**)*: Mp 63—64 °C; IR 1595 and 1625 cm^{-1}; UV λ_{max} (ε) 253 (20000) and 290 nm (10100); NMR δ=3.68 (9H, s, 3×OCH_3), 3.87 (2H, s, $-CH_2-$), 6.09 (1H, broad, s, =CH–), 6.55—7.3 (6H, m, aromatic) (Found: C, 72.41; H, 6.22%. Calcd for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08%).

*6-Methoxy-2-(2,3,4-trimethoxybenzyl)benzofuran (**2h**)*: Colorless liquid; IR 1580, 1590, and 1620 cm^{-1}; UV λ_{max} (ε) 253 (17300) and 292 nm (6900); NMR δ=3.71 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.78 (6H, s, 2×OCH_3), 3.93 (2H, s, $-CH_2-$), 6.11 (1H, broad s, =CH–), 6.45 (1H, d, J=9.0 Hz, $H_{(5')}$), 6.5—6.9 (3H, m, $H_{(5)}$, $H_{(6')}$, and $H_{(7)}$), and 7.19 (1H, m, $H_{(4)}$); MS *m/e* 328.1316 (100%, M$^+$) (Calcd for $C_{19}H_{20}O_5$, MW 328.1311), 313 (55%, M$^+$–15), 297 (25%, M$^+$–31), and 161 (49%, $C_{10}H_9O_2$).

*Reduction of 6-Methoxy-2-(4-methoxybenzoyl)benzofuran (**4**).* To a stirred solution of lithium aluminium hydride (43.4 mg) in anhydrous ether (20 ml), **4** (140.8 mg) was added at room temperature and the reaction mixture was stirred for 50 min. Aluminium chloride (141.7 mg) was added and the reaction mixture was further stirred for 96 min. After working-up in a manner similar to the above experiments, **2d**, mp 90—91 °C (111 mg, 83%), was obtained.

*Oxidation of 6-Methoxy-2-(4-methoxybenzyl)benzofuran (**2d**).* A mixture of **2d** (134 mg), freshly prepared manganese(IV) oxide (1 g), and anhydrous ether (30 ml) was heated under reflux for 8 h. After manganese (IV) oxide was removed by filtration, the ether was distilled off and the resulting solid was recrystallized from ethanol to give **4** (93.4 mg, 66%), mp 149 °C (lit,[13] mp 149 °C).

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