Synthesis of Dibenzofurans by Palladium-Catalysed Intramolecular Dehydrobromination of 2-Bromophenyl Phenyl Ethers

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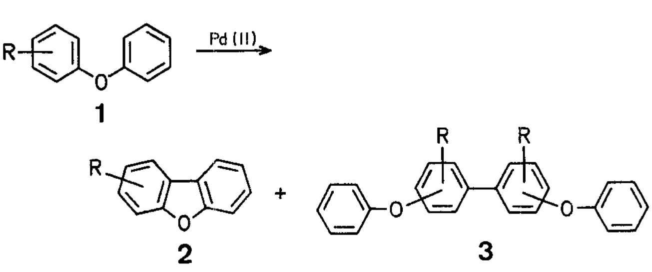
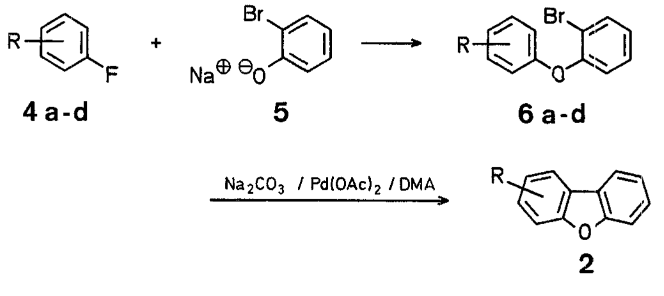
Previous preparations of substituted dibenzofurans **2** by the palladium-promoted intramolecular cyclisation of substituted diphenyl ethers **1** have required heating these with stoichiometric amounts of palladium(II) acetate (more than 1 equivalent if an electron-withdrawing group is present) in acidic solvents[1,2]. This dehydrogenative process can be made catalytic with respect to palladium, by performing the reaction at high pressure in a 1 to 1 mixture of oxygen and nitrogen under neutral conditions. Unfortunately the reaction suffers from lack of selectivity due to the formation of the coupled products **3** by competing intermolecular dehydrogenative coupling[3].



We report here a convenient, general process using a catalytic amount of palladium(II) acetate for the cyclisation of substituted 2-bromophenyl phenyl ethers **6a–h** to substituted dibenzofurans **2a–h**, under basic conditions. This reaction is based on a previously reported dehydrohalogenative process[4], which is not directly applicable in this series[5].

The bromophenyl phenyl ethers **6a–d** were prepared by coupling the appropriately substituted fluorobenzene **4a–d** with sodium 2-bromophenoxide (**5**). The reaction requires the substituted fluorobenzene to be activated by an electron-withdrawing group and, in the case of strong activation as in **4c**, the coupling occurs at room temperature. The other bromophenyl ethers **6e–h** were prepared by standard methods (Table 1).



The dibenzofurans **2a–h** were prepared in good yield by heating 2-bromophenyl phenyl ethers **6a–h** under nitrogen with 0.1 equivalent of palladium(II) acetate in *N,N*-dimethylacetamide (DMA) in the presence of sodium carbonate. In example **6b**, it might be possible to obtain two products, 1-nitro- and 3-nitrodibenzofuran, but only 3-nitrodibenzofuran was isolated. However when **6g** was used, a mixture of two products was obtained and these were not separated; the ^{1}H-N.M.R. spectrum (in CDCl$_3$) of the mixture showed an aliphatic to aromatic proton ratio of 7 : 3 which indicated that cyclisation had occurred. Two methyl singlets were observed, one at $\delta = 2.4$ ppm, attributed to the methyl group of 3-methyldibenzofuran, and the other at $\delta = 2.65$ ppm, due to the methyl group of 1-methyldibenzofuran. G.L.C. and ^{1}H-N.M.R. data showed the ratio of 3-methyl to 1-methyldibenzofuran to be 9 : 1.

As can be seen from Table 2, the reaction tolerates strongly electron-withdrawing groups as well as electron-releasing groups, unlike the dehydrogenative coupling performed in acidic solvents[1]. Also the reaction proceeds catalytically, though no attempt was made to reduce the amount of catalyst to less than 10 mol% with respect to the bromodiphenyl ether.

2-Fluoronitrobenzene (**4a**), 3-fluoronitrobenzene (**4b**), 4-fluoronitrobenzene (**4c**), and 4-cyanofluorobenzene (**4d**) were obtained from Aldrich Chemical Co., Ltd.

2-Bromodiphenyl ether (**6e**) was prepared from 2-aminodiphenyl ether according to Ref.[6]; 2-bromo-4′-hydroxymethyldiphenyl ether (**6f**) was prepared by sodium borohydride reduction of 2-bromo-4′-formyldiphenyl ether (m.p. 53–55 °C), obtained by coupling of 4-fluorobenzaldehyde with **5** at 100 °C for 15 h; 2-bromo-3-methyldiphenyl ether (**6g**) was prepared from 1,2-dibromobenzene and *m*-cresol according to Ref.[7]; 2-bromo-4′-carboxydiphenyl ether (**4h**) was prepared by basic hydrolysis of the corresponding ethyl ester obtained by coupling of ethyl 4-fluorobenzoate with **5** at 150 °C for 24 h.

2-Bromo-4′-nitrodiphenyl Ether (6c); Typical Procedure:

Sodium hydride (4.8 g, 50% dispersion in oil) is washed with toluene, then suspended in dry dimethyl sulphoxide (90 ml). 2-Bromophenol (17.3 g) is added dropwise to the stirred suspension and, after hydrogen evolution has ceased, the solution is heated to 80 °C. To the stirred solution of **5** is added 4-fluoronitrobenzene (**4c**; 14.1 g) and stirring is continued at room temperature for 18 h. Water (500 ml) is added and the precipitated solid is collected, dried, and recrystallised from ethanol to give 2-bromo-4′-nitrodiphenyl ether (**6c**); yield: 23.1 g (78%); m.p. 80–82 °C (Ref.[9], m.p. 82 °C).

2-Nitrodibenzofuran (2c):

2-Bromo-4′-nitrodiphenyl ether (**6c**; 2.94 g, 10 mmol), anhydrous sodium carbonate (1.3 g), and palladium(II) acetate (0.22 g, 1 mol) in di-

Table 1. 2-Bromodiphenyl Ethers **6a-h** prepared

Product No.	R	Reaction Conditions temp./time	Yield [%]	m.p. [°C][a] or b.p. [°C]/torr	Molecular Formula[b] or Lit. m.p. [°C]	
6a	2-O_2N—	100 °C/18 h	42	49-51°	54°[8]	
6b	3-O_2N—	140 °C/24 h	53	164°/1.5	$C_{12}H_8BrNO_3$	(294.1)
6c	4-O_2N—	25°/18 h	78	80-82°	82°[9]	
6d	4-NC—	100°/18 h	24	63-65°	$C_{13}H_8BrNO$	(274.1)
6e	H	see text	28	43-44°	43.5-44.5°[6]	
6f	4-HO—CH_2—	see text	99	oil	$C_{13}H_{11}BrO_2$	(279.1)
6g	3-H_3C—	see text	9	102-104°/0.15	$C_{13}H_{11}BrO$	(263.1)
6h	4-HOOC—	see text	90	151-153°	$C_{13}H_9BrO_3$	(293.1)

[a] Not corrected.

[b] Satisfactory microanalyses obtained: C ±0.41, H ±0.31, N ±0.30; exception: **6f**, C −0.50.

Table 2. Dibenzofurans **2a-h** prepared

Product No.	R	Reaction time	Yield [%]	m.p. [°C][a]	
				found (solvent)	reported
2a	4-O_2N—	2 h	78	137-138° (C_2H_5OH)	141°[10]
2b	3-O_2N—	3 h	68	181-182° (C_2H_5OH)	181-182°[10]
2c	2-O_2N—	4 h	76	153-155° (C_2H_5OH)	150°[11]
2d	2-NC—	1.5 h	80	141-143° (C_2H_5OH)	137.5-138°[11]
2e	H	0.75 h	74[b]	86-87° (i-C_3H_7OH)	87°[12]
2f	2-HO—CH_2—	24 h	56[b]	120-122° (C_2H_5OH)	124°[13]
2g	1-H_3C— + 3-H_3C—	0.75 h	73[b]	—[c]	—
2h	2-HOOC	7 h	66	253-255° (C_2H_5OH)	252-255°[14]

[a] Not corrected.

[b] Purified by chromatography on silica gel.

[c] 1:9 mixture of 1-methyl- and 3-methyldibenzofuran.

methylacetamide (20 ml) are heated and stirred under nitrogen at 170 °C for 2 h. Water (100 ml) is added to the cooled solution and the precipitated solid is collected by filtration. Crystallisation from ethanol gives 2-nitrobenzofuran (**2c**); yield: 1.62 g (78%); m.p. 153-155 °C (Ref.[11], m.p. 150 °C).

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