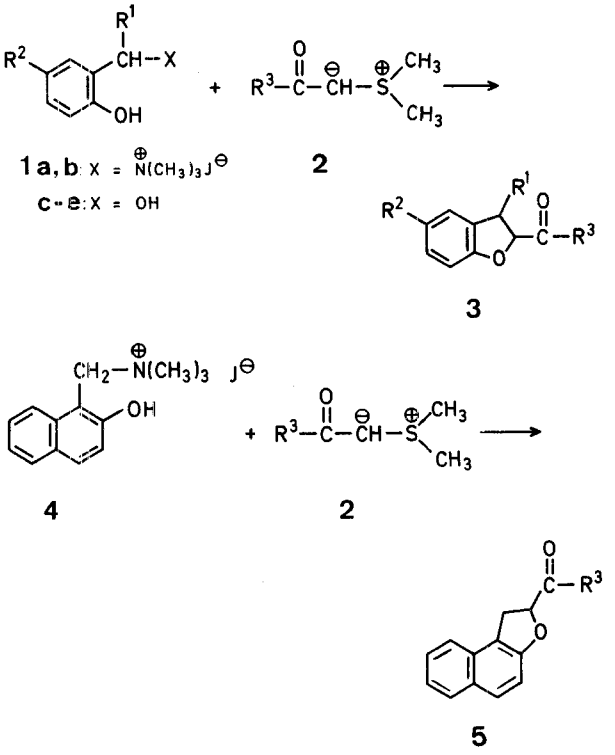
A Convenient Synthesis of 2-Acyl- or 2-Aroyl-substituted 2,3-Dihydrobenzofurans and 1,2-Dihydronaphtho[2,1-*b*]furans[1,2]

Luciano CADONA, Piero DALLA CROCE*

Istituto di Chimica Industriale dell'Università e Centro C.N.R., Via Golgi 19, I-20133 Milano, Italy

In the course of certain pharmacological studies we needed a variety of 2-acyl- or 2-aroyl-2,3-dihydrobenzofurans. None of the reported syntheses[3] was satisfactory for our purposes owing to poor yields and lack of generality. We therefore developed a simple, general route to the 2,3-dihydrobenzofurans (**3a–h**) and the 1,2-dihydronaphtho[2,1-*b*]furans (**5a–f**), substituted in position 2 by an acyl or aroyl group, starting from phenolic Mannich base methiodides (**1** or **4**) and the carbonyl-stabilised sulphonium ylide (**2**).



The reaction proceeds readily at room temperature and usually affords the desired products in good yields. The formation of the products can be rationalised by assuming the known behaviour of stabilised sulphonium ylides towards systems bearing an electrophilic centre and a nucleophilic heteroatom[4].

Analytical and spectroscopic data (I.R. and N.M.R.[5]) of the compounds prepared are consistent with the assigned structures. These were also confirmed by the dehydrogenation of **5b** with *N*-bromosuccinimide and triethylamine to give the corresponding 2-ethoxycarbonylnaphtho[2,1-*b*]furan.

Some of the products listed in the Table may be useful intermediates for the preparation of highly functionalised 2,3-dihydrobenzo- and 1,2-dihydronaphtho[2,1-*b*]furans.

The carbonyl-stabilised sulphonium ylides (**2**)[6,7], the phenolic Mannich base methiodides (**1a, b,** and **4**)[8], and the *o*-hydroxybenzyl alcohol derivatives (**1c–e**)[9,10,11] were prepared according to the reported methods.

Preparation of Dimethylsulphonium 4-Acetoxyphenacylide (2; R^3 = 4-H_3C—COO—C_6H_4):

To a stirred solution of sodium hydroxide (20 g) in water (200 ml) at 5° is added dimethyl 4-acetoxyphenacylsulphonium bromide (26 g, 0.80 mol; prepared from dimethyl sulphide and 4-acetoxyphenacyl bromide[12] in acetonitrile; yield: 95%; m.p. 130–132°) and the mixture is stirred for 15 min. The mixture is then extracted with dichloromethane (3 × 50 ml). The extract is evaporated under reduced pressure to leave a pale yellow oil which slowly crystallises. The crystals are washed with cyclohexane and recrystallised from ether; yield: 16 g (85%); m.p. 115–116°.

$C_{12}H_{14}O_3S$	calc.	C 60.47	H 5.92
(238.31)	found	60.32	5.87

Table. Preparation of 2-Substituted 2,3-Dihydrobenzofurans (**3a–h**) and 1,2-Dihydronaphtho[2,1-*b*]furans (**5a–f**)

Product[a]	R^1	R^2	R^3	Yield [%]	Method	m.p.[b] or b.p./torr	Molecular formula[c]	I.R. spectra ($CHCl_3$)[d] ν [cm^{-1}]
3a	H	H	C_6H_5	85	A	94–95°[e]	$C_{15}H_{12}O_2$ (224.3)	1680 (C=O)
3b	H	H	C_2H_5O	84	A	140°/10	$C_{11}H_{12}O_3$ (192.2)	1695 (C=O)
3c	H	H	4-H_3CCOO—C_6H_4	75	A	152–153°[f]	$C_{17}H_{14}O_4$ (266.3)	1680 (C=O), 1725 (C=O)
3d	H	H	4-HO—C_6H_4	60	B	184–185°[f]	$C_{15}H_{12}O_3$ (240.3)	1680 (C=O), 3320 (OH)
3e	H	Cl	4-HO—C_6H_4	65	B	158–160°[f]	$C_{15}H_{13}ClO_3$ (274.7)	1675 (C=O), 3315 (OH)
3f[g]	H	NO_2	C_6H_5	82	C	95–96°[f]	$C_{15}H_{11}NO_4$ (269.3)	1680 (C=O)
3g[g]	CH_3	H	C_6H_5	50	C	83–84°[e]	$C_{16}H_{14}O_2$ (238.3)	1675 (C=O)
3h[g]	C_6H_5	CH_3	C_6H_5	65	C	124–126°[f]	$C_{22}H_{18}O_2$ (314.4)	1670 (C=O)
5a	—	—	C_6H_5	65	A	131–132°[f]	$C_{19}H_{14}O_2$ (274.3)	1670 (C=O)
5b	—	—	C_2H_5O	75	A	140°/0.1	$C_{15}H_{14}O_3$ (242.3)	1695 (C=O)
5c	—	—	CH_3	70	A	130°/0.1	$C_{14}H_{12}O_2$ (212.2)	1690 (C=O)
5d	—	—	4-H_3C—C_6H_4	72	A	135–136°[f]	$C_{20}H_{16}O_2$ (288.3)	1670 (C=O)
5e	—	—	4-O_2N—C_6H_4	75	A	190–191°[f]	$C_{19}H_{13}NO_4$ (319.3)	1675 (C=O)
5f	—	—	4-HO—C_6H_4	70	B	214–215°[f]	$C_{19}H_{14}O_3$ (290.3)	1675 (C=O), 3320 (OH)

[a] The structures of the products were consistent with their ^{1}H-N.M.R. data[5].

[b] Melting points were determined on a Büchi apparatus (capillary method) and were uncorrected.

[c] All products gave satisfactory microanalyses (C ± 0.29%), (H ± 0.18%), (N ± 0.25%).

[d] The I.R. spectra were recorded with a Perkin-Elmer 137 spectrophotometer as ~2% solutions.

[e] Recrystallised from diisopropyl ether.

[f] Recrystallised from ethanol.

[g] Compounds **3f–h** were prepared starting from the appropriate *o*-hydroxybenzyl alcohol derivative.

Preparation of 2-Substituted 2,3-Dihydrobenzofurans (3a–h) and 1,2-Dihydronaphtho[2,1-*b*]furans (5a–f):

Method A: To a stirred suspension of **1a, b** or **4** (0.01 mol) in acetonitrile (50 ml) is added the ylide **2** (0.02 mol) and the mixture is stirred for 12 h at room temperature. The solvent is removed and the residue taken up in ether and 1 *N* hydrochloric acid. The solvent is distilled off and the residue purified by recrystallisation or distillation.

Method B: The procedure is identical to Method A except that at the end of the 12 h, the reaction mixture is treated with 3 *N* hydrochloric acid (25 ml) and refluxed for 3 h to effect hydrolysis of the acetyl derivative of the phenol.

Method C: A solution of **1c–e** (0.01 mol) in benzene (100 ml) at 0° is treated with thionyl chloride (0.01 mol) and stirred for 2 h. The solution is thoroughly purged with nitrogen, treated with **2** (0.02 mol) and stirred for 12 h at room temperature. The reaction mixture is washed with 1 *N* hydrochloric acid, the solvent is distilled off, and the residue purified as above.

Preparation of 2-Ethoxycarbonylnaphtho[2,1-*b*]furan:

A solution of **5b** (2.4 g, 0.01 mol) in tetrachloromethane (50 ml) is treated with *N*-bromosuccinimide (2.0 g, 0.011 mol) and refluxed for 2 h. Triethylamine (1 g, 0.01 mol) is added and the reaction mixture is refluxed for a further 2 h. The mixture is then cooled, succinimide is removed by filtration, and the solvent evaporated to give the product as colourless needles; yield: 1.96 g (82%); m.p. 96–97° (from diisopropyl ether); Lit.[13] m.p. 97–98°.

Received: July 8, 1976

[1] Part VI[2] of the series Heterocycles from Ylides.

[2] Part V, P. Dalla Croce, *J. Heterocycl. Chem.* in press.

[3] A. Mustafa, *Benzofurans*, Interscience, New York, 1974, p. 143–191.

[4] B. M. Trost, L. S. Melvin, Jr., *Sulfur Ylides*, Academic Press, New York, 1975, p. 77–95.

[5] P. Dalla Croce, R. Stradi, *Org. Magn. Reson.* submitted.

[6] K. W. Ratts, A. N. Yao, *J. Org. Chem.* **31**, 1185 (1966).

[7] H. Koenig, H. Metzger, R. Werner, *U.S. Patent* 3821277 (1974), BASF A.G.; *C.A.* **81**, 135487 (1974).

[8] P. D. Gardener, H. S. Rafsenjani, L. Rand, *J. Am. Chem. Soc.* **81**, 3364 (1959).

[9] J. Arct, Z. Eckstein, H. Krzywicka, *Przem. Chem.* **43**, 87 (1964); *C.A.* **61**, 3000 (1964).

[10] S. Mitsui, Y. Takeuchi, *Nippon Kagaku Zasshi* **82**, 499 (1961).

[11] H. D. Becker, T. Bremholt, *Tetrahedron Lett.* **1973**, 197.

[12] K. W. Rosenmund, K. Pfroepffer, *Chem. Ber.* **90**, 1922 (1957).

[13] F. Duro, G. Scapini, P. Condorelli, *Boll. Sedute Accad. Gioenia Sci. Nat. Catania* **1970**, 337; *C.A.* **75**, 20065 (1971).