

Reaction of Dimethyloxosulphonium Methylide with o-Hydroxybenzylideneanilines.

A Facile Synthesis of 3-Amino-2,3-dihydrobenzofurans

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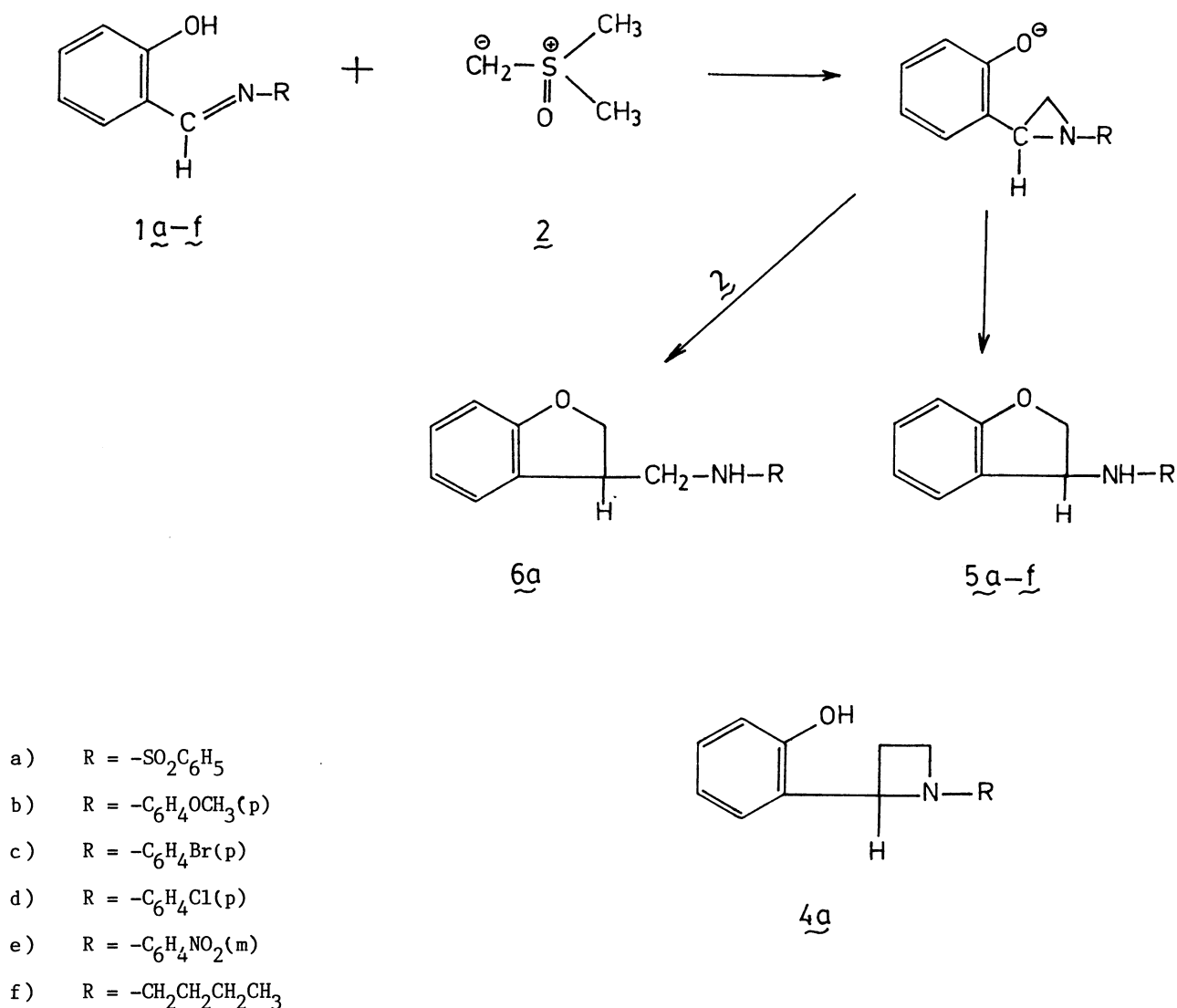
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o-Hydroxybenzylideneanilines react with dimethyloxosulphonium methylide to give 3-amino-2,3-dihydrobenzofurans in good yields.

Synthesis of benzofuran and its 2,3-dihydro derivatives has received some attention in recent years.¹⁾ However, no good method is available for obtaining the 3-amino derivatives^{2,3)} and only a few are known. It is in this context that we report a facile procedure for these compounds involving reaction of easily available o-hydroxybenzylideneanilines with dimethyloxosulphonium methylide.

During the course of our investigations related to the synthesis of azetidines from the corresponding azomethines⁴⁾ and aziridines,⁵⁾ we treated the azomethine 1a with an excess (2.5 equiv.) of dimethyloxosulphonium methylide (2). We were surprised to get, instead of the expected azetidine 4a, the 2,3-dihydrobenzofuran derivatives 5a and 6a. Structural assignment to these was made on the basis of ¹H and ¹³C NMR data. Thus 5a showed in the ¹H NMR (100 MHz, CDCl₃) signals at δ 4.3 (m, 2H), δ 5.0 (m, 2H), δ 6.73-7.94 (m, 9H, ArH), D₂O exchange: δ 4.3 (m, 2H), δ 5.0 (dd, 1H, J₇ 7 Hz and 4 Hz) and 6a exhibited signals at δ 3.15 (m, 2H), δ 3.57 (m, 1H), δ 4.43 (m, 2H), δ 4.88 (m, 1H), and δ 6.73-8.06 (m, 9H, ArH). The corresponding ¹³C NMR showed signals at δ 55.31(d), δ 76.99(t), δ 110.42-159.7(ArC) and δ 42.0(d), δ 46.34(t), δ 74.21(t), δ 109.74-160.03 (ArC). Since we had observed that aziridines in which the arylsulphonyl group had been replaced by a phenyl ring did not add a methylene under these reaction conditions,⁶⁾ it was expected that such a replacement would improve the yield of the 3-aminobenzofuran derivative by suppressing the aziridine ring opening by the ylide. This was borne out by experiment. Treatment of 1b-f (1 equiv.) with excess dimethyloxosulphonium methylide (2.5 equiv.) in DMSO at ambient temperatures under dry nitrogen atmosphere led to the formation of 5b-f in 60-80% yield (unoptimised) of pure isolated products. No other product could be detected in the reaction mixture. The 2,3-dihydrobenzofuran derivatives analysed correctly for C, H, and N and showed the expected spectral properties. Thus

they were characterised by $\nu_{\text{N-H}}$ at 3300–3400 cm^{-1} in the IR spectra, a typical ABX pattern between δ 4.2 to 5.2 and a broad singlet at δ 3.6 (N–H) in ^1H NMR and a triplet at δ 77.5 and a doublet at δ 55.5 in off resonance ^{13}C NMR.⁷⁾



Scheme 1.

This synthesis is simple and uses easily available Schiff bases as starting materials. R may be an alkyl or aryl group. The effect of substitution of an alkyl or an aryl group on the azomethine carbon and the scope and limitations of this procedure for synthesising benzofuran derivatives generally is being investigated. Its extension to other heterocycles having a nitrogen or sulfur atom in place of oxygen is also being studied.

A typical procedure for the preparation of 5b is as follows: A solution of the imine 1b⁸⁾ (1.135 g, 5 mmol) was added with stirring and in an atmosphere of nitrogen gas to dimethyloxosulphonium methyllide (2)⁹⁾ (1.15 g, 12.5 mmol) obtained by the reaction of trimethyloxosulphonium iodide (2.75 g, 12.5 mmol) with NaH(67%) (0.448 g, 12.5 mmol) contained in a three necked flask fitted with a dropping funnel, nitrogen gas inlet tube, and a condenser at ambient temperature. Stirring was continued till disappearance of the imine (TLC, 3 h). After the reaction was completed, the reaction mixture was poured into ice cold water (150 ml). It was extracted with ether (3 x 30 ml), the organic layer was washed with water and dried (Na₂SO₄). Ether was distilled off and the residue was chromatographed on silica gel (60 - 120 mesh). The benzofuran 5b was eluted with benzene : hexane mixture (1 : 1), yield 72%, mp 49-50 °C.

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References

- 1) R.Rodrigo, G. Weeratinga, A. Jaworskiesobiesiak, and S. Horne, Can. J. Chem., 65, 2019(1987) and references cited therein.
- 2) P.Cagniant and D.Cagniant, Adv. Heterocycl. Chem., 18, 337, (1975).
- 3) M.V.Sargent, "Comprehensive Organic Chemistry," ed by D.H.R.Barton and W.D.Ollis, Wiley-Interscience (1979), Vol. 4, p.693.
- 4) U.K. Nadir and V.K. Koul, Synthesis, 1983, 554
- 5) U.K. Nadir and V.K. Koul, J. Chem. Soc., Chem. Commun., 1981, 417.
- 6) V.K.Koul, Ph.D. Thesis, IIT Delhi, (1982).
- 7) 5a, yield 45%, mp 126-127 °C, ¹H NMR: δ 4.3 (m, 2H), δ 5.0 (m, 2H), δ 6.73-7.94 (m, 9H, ArH) D₂O exchange: δ 4.3 (m, 2H), δ 5.0 (dd, 1H, J ≈ 7 Hz & 4 Hz), ¹³C NMR: δ 55.31(d), δ 76.99(t), δ 110.42-159.7 (ArC); 5b, yield 72%, mp 49-50 °C, ¹H NMR: δ 3.6(m, 1H), δ 3.67 (s, 3H), δ 4.35(m, 2H), δ 5.03(dd, 1H, J ≈ 7 Hz & 4 Hz), δ 6.45-7.29 (m, 8H, ArH), ¹³C NMR: δ 55.41(d), δ 56.04(q), δ 77.29(t), δ 110.1-159.78(ArC); 5c, yield 80%, mp 108-109 °C, ¹H NMR: δ 3.95(bs, 1H), δ 4.5 (m, 2H), δ 5.12(d, 1H), δ 6.43-7.34(m, 8H, ArH), ¹³C NMR: δ 55.21(d), δ 77.14(t), δ 109.64-159.98 (ArC); 5d, yield 76%, mp 106 °C, ¹H NMR: δ 3.95 (bs, 1H), δ 4.45(m, 2H), δ 5.10(dd, 1H), δ 6.40-7.33(m, 8H, ArH), ¹³C NMR: δ 55.21(d), δ 77.09(t), δ 110.23-159.93(ArC); 5e, yield 71%, mp 152-154 °C, ¹H NMR: δ 3.67(bs, 1H), δ 4.50 (m, 2H), δ 5.39(dd, 1H), δ 6.85-7.44(m, 8H, ArH), ¹³C NMR: δ 53.83(d), δ 76.89(t), δ 105.59-159.98(ArC); 5f, yield 45%, Viscous oil, ¹H

NMR: δ 0.89(t, 3H), δ 1.36 (m, 4H), δ 1.93(bs, 1H), δ 2.61(m, 2H), δ 4.45(m, 3H), δ 6.77–7.35(m, 4H, ArH), ^{13}C NMR: δ 9.47(q), δ 15.87(t), δ 28.27(t), δ 42.67(t), δ 56.67(d), δ 73.47(t), δ 106.27–125.47(ArC).

- 8) A. I. Vogel, "A Text Book of Practical Organic Chemistry Including Qualitative Organic Analysis", 3rd ed, London 1956, p. 653.
- 9) E.J.Corey and M.Chaykovsky, J. Am. Chem. Soc., 87, 1353 (1965).

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