Radical Cyclisation of 4-(*o*-Bromophenoxy)-2*H*-1-benzopyrans; an Efficient Synthesis of Pterocarpans

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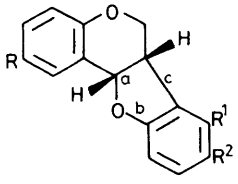
The preparation of 4-(*o*-bromophenoxy)-2*H*-1-benzopyrans and their conversion into the pterocarpan skeleton *via* radical cylisation are reported.

The 6a,11a-dihydro-6*H*-benzofuro[3,2-*c*]benzopyran (**1**) is representative of a wide range of pterocarpan[1] phytoalexins[2] produced by Leguminosae plants when challenged by fungal infections. The chemistry of pterocarpans has attracted some attention[3] recently and several synthetic routes[4] have been developed which involve the formation of one of the C–O bonds a or b [see (**1**)] in the last stage. However, we have developed a general and more flexible approach by constructing the furan C–C bond c in the final step.

A synthesis of (**1**) based on radical cyclisation[5] for the construction of the five membered ring was developed to make use of the stereo- and regio-specific nature of these reactions. The route is depicted in Scheme 1. Thermal rearrangement of aryl propynyl ether (**2**) in Polyethyleneglycol-200 gave rise to 2*H*-1-benzopyran (**3**) in 60% yield,[6] which on treatment with *N*-bromosuccinimide in aqueous dimethyl sulphoxide (DMSO) gave bromohydrin (**4**) in 85% yield. Bromohydrin (**4**) was converted to the epoxide (**5**) (in KOH ether) in 80% yield. Opening of the epoxide (**5**)

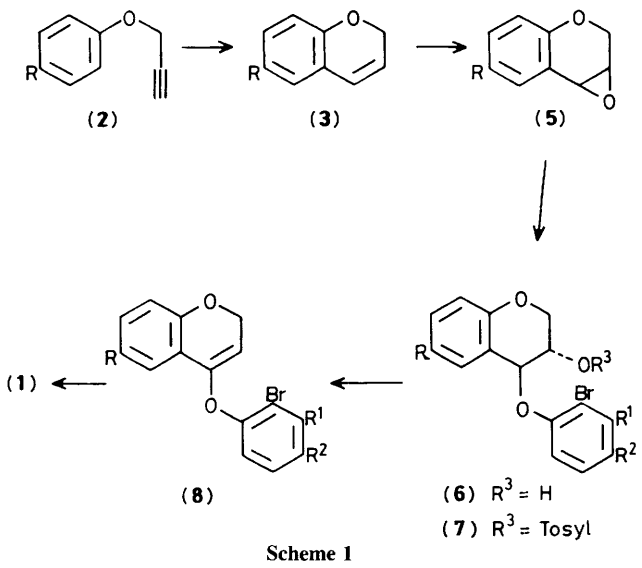


(**1**)

Table 1. Synthesis of 6a,11a-dihydro-6*H*-benzofuro[3,2-*c*]benzopyrans *via* radical cyclisation.

R	Alkene (**8**) R¹	R²	Cyclised product (**1**), m.p./°C	Cyclisation yield (%)
H	H	H	125—126[a]	82
OMe	–CH=CH–CH=CH–		201	90
Cl	–CH=CH–CH=CH–		205	88

[a] Lit. 125—126 °C.[8]



Scheme 1

with *o*-bromophenol or 2-bromonaphthol afforded the 4-phenoxychroman-3-ol (**6**)[7] (90%), which was converted to the tosylate (**7**). Treatment of the tosylate (**7**) with potassium t-butoxide in DMSO gave the enol ether (**8**) in 70% yield.

Cyclisation of (**8**) was carried out by refluxing a 0.02 M solution in benzene with 1.1 equiv. of Bu^n_3SnH in the presence of a catalytic amount of azoisobutyronitrile (AIBN). Usual work-up and purification by column chromatography gave rise to the cyclised products (**1**) in 90% yield.† The cyclisation proceeded smoothly in all cases (Table 1) and no reduction product was detected.‡ Successful isolation of product (**1c**) from (**8c**) shows the compatibility of the chloro substituent under the cyclisation conditions.

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† New compounds were characterised by i.r., n.m.r., and mass spectroscopy, and in some cases elemental analysis.

‡ Careful analysis of the crude cyclised product (**1a**) did not reveal the presence of the *trans*-fused isomer. The n.m.r. spectrum of (**1a**) was identical with the reported spectrum.

References

1 A. C. Jain and D. K. Tuli, *J. Sci. Ind. Res.*, 1978, **37**, 287.
2 F. M. Dean, 'The Total Synthesis of Natural Products', vol 1, ed. J. Apsimon, Wiley, New York, 1973; D. Gross, *Fortschr. Chem. Org. Naturst.*, 1977, **34**, 187; J. L. Ingham, *ibid.*, 1982, **43**, 1.
3 U. Rao, S. Ramakanth, K. Narayanan, and K. K. Balasubramanian, *J. Chem. Soc., Chem. Commun.*, 1983, 842; S. Ramakanth, K. Narayanan, K. Rajagopalan, and K. K. Balasubramanian, *Tetrahedron*, 1986, **42**, 863; P. J. Van der Merwe, G. J. H. Rall, and D. G. Roux, *J. Chem. Soc., Chem. Commun.*, 1978, 224; E. V. Brandt, B. C. B. Bezuidenhoudt, and D. G. Roux, *ibid.*, 1982, 1409.
4 H. Suginone and T. Iwadare, *Bull. Chem. Soc. Jpn*, 1960, **33**, 567; K. Fukui and M. Nakayama, *Tetrahedron Lett.*, 1965, 2559; M. Corina and L. Merlini, *J. Chem. Soc., Chem. Commun.*, 1975, 428; H. Horino and N. Inoue, *ibid.*, 1976, 500; A. V. K. Prasad, R. S. Kapil, and S. P. Papil, *J. Chem. Soc. Perkin Trans. 1*, 1986, 1561; S. E. N. Mohamed, P. Thomas, and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 431, 1987.
5 W. P. Neumann, *Synthesis*, 1987, 665.
6 U. Rao and K. K. Balasubramanian, *Tetrahedron Lett.*, 1983, **24**, 5023.
7 Opening the 3,4-epoxyflavan with phenol gives the *cis*-alcohol and opening with phenoxide the *trans*-alcohol. G. Bateman, B. R. Brown, J. B. Campbell, C. A. Cotton, P. Johnson, P. Mulqueen, D. O'Neill, M. R. Shaw, R. A. Smith, and J. A. Troke, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2903. However, in our case 3,4-epoxychroman gave rise to the same alcohol with phenol or phenoxide, with the stereochemistry tentatively assigned as *trans*.
8 H. Suginome and T. Iwadare, *Bull. Chem. Soc. Jpn.*, 1966, **39**, 1535.