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

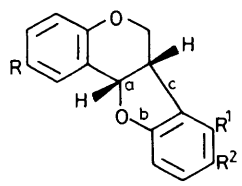
Ariamala Gopalsamy and K. K. Balasubramanian*

Department of Chemistry, Indian Institute of Technology, Madras-600 036, India

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**)

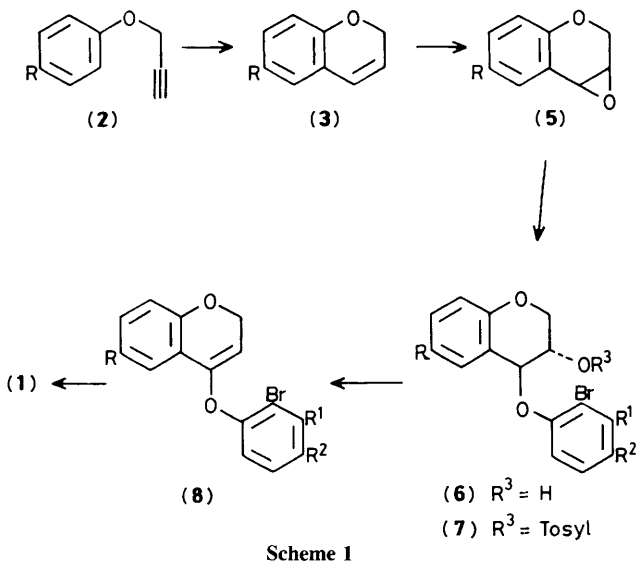


(**1**)

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.

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