Tetrahedron Letters,Vol.29,No.27,pp 3335-3338,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

RADICAL CYCLISATION : SYNTHESIS OF 4H-FURO(3,2-c)-1-BENZOPYRANS

G. ARIAMALA and K.K. BALASUBRAMANIAN*

Indian Institute of Technology,
Department of Chemistry,
Madras - 600 036, INDIA.

Abstract - 3,4-dihydro-3-bromo-4-(prop-2-ynyloxy)-2H-1-benzopyrans (3) undergo radical cyclisation when treated with nBu_3SnH and AIBN to give good yield of 2,3,3a,9b-tetrahydro-3-methylene-4H-furo (3,2-c)benzopyrans (4).

Carbon-Carbon bond formation by free radical methods[1] are becoming increasingly important in organic synthesis and five and six membered ring construction by intramolecular radical cyclisation for carbocycles[2] and heterocycles[3] has become an established part of the synthetic strategies. The most obvious manifestation of radical cyclisation is the stereo and regioselectivity[4]. Though the strategy has shown considerable promise for the construction of dihydrobenzofuran systems[5], little attention has been given to the furan annulation on an existing heterocycle.

In continuation of our project aimed at the synthesis of pterocarpans[6] we have developed a new synthesis based on radical cyclisation, for 2,3,3a,9b-tetrahydro-3-methylene-4H-furo (3,2-c)-1-benzopyrans (4), potential intermediates, which would not only lead to pterocarpans (6) (see Scheme I), but also to unnatural pterocarpans.

Thermal rearrangement of aryl propargyl ethers (1) in polyethylene glycol-200 afforded 2H-1-benzopyrans (2) in 60% yield[7]. The 2H-1-benzopyrans on treatment with N-Bromo-succinimide in the presence of propargyl alcohol[8] using dichloromethane as solvent at 0°C gave rise to 3,4-dihydro-3-bromo-4-(prop-2-ynyloxy)-2H-1-benzopyrans (3) in good yields (see Table I). Cyclisation was carried out by refluxing a 0.02M solution of (3) in benzene with 1.02 equivalents of nBu_3SnH with a catalytic amount of AIBN for 4h. Removal of the solvent followed by chromatography over silica gel (benzene-hexane 1:1) furnished the cyclised

Scheme - I

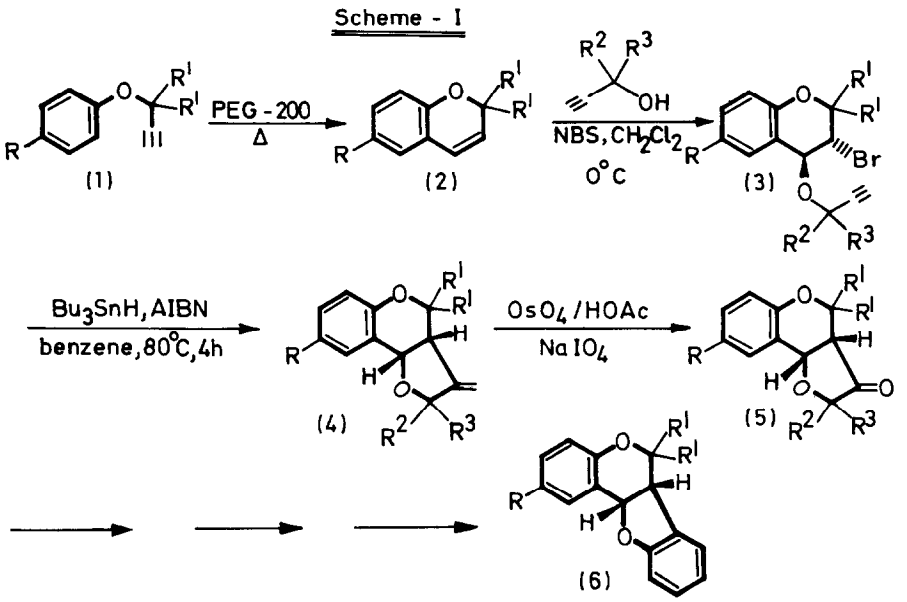

Table - I

Synthesis of 2,3,3a,9b-tetrahydro-3-methylene-4H-furo(3,2-c)-1-benzopyrans (4).

Entry	R	R^1	R^2	R^3	Yield of* (3) %	Yield of* (4) %
a	OCH_3	H	H	H	82	85
b	CH_3	H	H	H	85	82
c	Cl	H	H	H	68	82
d	OCH_3	CH_3	H	H	78	80
e	OCH_3	H	CH_3	H	+	78
f	OCH_3	H	H	CH_3	+	75
g#	OCH_3	H	CH_3	CH_3	-	-

* All the yields recorded here are based upon isolated material
\+ A 1:1 mixture of (3e) & (3f) was isolated in 75% yield.
\# No reaction.

product[9] viz, 2,3,3a,9b-tetrahydro-3-methylene-4H-furo(3,2-c)-1-benzopyrans (4) (see Table I). The cyclisation was found to be facile and no reduced product was observed. It was also found to be highly regio and stereospecific, for only the five membered ring formation was observed (5-Exo-dig) and only the cis isomer was formed. The successful isolation of the

furan (4c) shows the compatability of the chloro substituent under the cyclisation conditions (see entry c).

This synthetic sequence was found to be successful when but-3-yn-2-ol was reacted with 6-methoxy-2H-1-benzopyran and NBS to afford a 1:1 mixture[10] of both the diastereomers epimeric at C2- position (which were separated by fractional crystalisation) (3e) and (3f). Cyclisation of each of the isomers afforded the furans (4e) and (4f). In the case of the tertiary ethynyl carbinol viz, 2-methyl-but-3-yn-2-ol, reaction with 6-methoxy-2H-1-benzopyran and NBS in dichloromethane failed to furnish (3g). Instead, 3-bromo-4-succinimido-6-methoxy-2H-1-benzopyran was isolated in quantitative yield. Another significant observation was that the presence of gem dimethyl group adjacent to the cyclisation centre did not impede the reaction (see entry 4d). Oxidation[11] of (4b) with 1.2 equivalent of osmium tetroxide in acetic acid followed by sodium periodate (2 equivalents) furnished, 3a,9b-dihydro-4H-furo(3,2-c)-1-benzopyran-3(2H)-one (5b) in 84% yield, the potential intermediate for the synthesis of pterocarpans.

The chemistry of 4H-furo(3,2-c)-1-benzopyrans remains less explored when compared to 4H-furo(3,2-c)-1-benzopyran-4-ones. Although a few syntheses of furo(3,2-c)-1-benzopyran-4-ones are known in the literature, there are not many for 4H-furo(3,2-c)-1-benzopyran and its derivatives, some of which are biologically important[12]. Thus, the reactions described here represent a new and easy access to variously substituted 4H-furo(3,2-c) 1-benzopyrans.

We acknowledge the support of this investigation by Department of Science and Technology. We thank RSIC, IIT, Madras, Prof. Schröder and Dr. H. Röttele, Karlsruhe, West Germany and Prof. T.C. Gallagher, University of Bath for Spectral Data and Messers BASF, West Germany for the generous gift of propargyl alcohol, but-3-yn-2-ol and 2-methyl-but-yn-2-ol samples.

Selected spectral data :

3,4-dihydro-6methyl-3-bromo-4-(prop-2-ynyloxy)-2H-1-benzopyran (3b) : ^{1}H NMR ($CDCl_3$/TMS, 250MHz) : δ 2.3(s, 3H), 2.58(t, J:1.5Hz, 1H), 4.25-4.52(m, 5H), 4.7(dd, J_1:3Hz, J_2:0.8Hz, 1H) and 6.8-7.1 (m, 3H).

2,3,3a,9b-tetrahydro-8-methyl-3-methylene-4H-furo(3,2-c)-1-benzopyran (4b) : ^{1}H NMR $CDCl_3$/TMS, 250MHz) : δ 2.3(s, 3H), 3.0(m, 1H), 3.85(t, J:11Hz, 1H), 4.1(m, 1H), 4.4(m, 2H), 4.75(d, J:4.5Hz, 1H), 5.15(m, 2H) and 6.8-7.3(m, 3H).

^{13}C NMR (62.89MHz) : ppm:20(q), 42(d), 65(t), 70(d), 75(d), 98(s), 108(t), 118(d), 121(s), 130(d), 132(d), 148(s) and 154(s).

3a,9b-dihydro-8-methyl-4H-furo(3,2-c)-1-benzopyran-3(2H)-one (5b) : ^{1}H NMR ($CDCl_3$/TMS, 270MHz) : δ 2.3(s, 3H), 2.9(m, 1H), 3.93(d, J:16Hz, 1H), 4.04(d, J:16Hz, 1H), 5.32(d, J:6.5Hz, 1H) and 6.78-7.3(m, 3H).

IR : cm^{-1} : 2850-3000, 1780, 1500, 1210, 1050.

References and Notes :

1. a. B. Giese, Radicals in organic synthesis : Formation of Carbon-Carbon bonds, Pergamon, Oxford, 1986.
   b. M. Ramaiah, Tetrahedron, 1987, 43, 3541.

2. For a few recent reports :
   a. V.K. Yadav and A.G. Fallis, Tetrahedron Lett., 1988, 897.
   b. D.L.J. Clive, T.L.B. Boivin and A.G. Angoh, J. Org. Chem., 1987, 52,4943.
   c. T. Endo, M. Okawara, C. Tanaka, Y. Ueno and Y. Watanabe, Tetrahedron Lett., 1987, 3953.
   d. K.S. Groninger, K.F. Jager and B. Giese, Liebigs Ann. Chem., 1987, 8, 731.

3. a. G. Haaima and R.T. Weavers, Tetrahedron Lett., 1988, 1085.
   b. J.P. Dittami and H. Ramanathan, Tetrahedron Lett., 1988, 45.
   c. Srikrishna and Sunderbabu, Tetrahedron Lett., 1987, 6393.
   d. Y. Vero, K. Chino and M. Okawara, Tetrahedron Lett., 1982, 2575.

4. a. A.J.L. Beckwith, Tetrahedron, 1981, 37, 3073.
   b. D.L.J. Clive and D.R. Cheshire, J. Chem. Soc., Chem. Commun., 1987, 1520.

5. a, M. Osamu, K. Masato, U. Yoshikiyo, S. Toshio, K. Toshifumi, U. Yoshio and T. Endo, J. Chem. Soc., Chem. Commun., 1985, 1401.
   b. K. Shankaran, C.D. Sloan and V. Snieckus, Tetrahedron Lett., 1985, 6001, and see also ref. 3d.

6. G. Ariamala and K.K. Balasubramanian, J. Chem. Soc., Chem. Commun., 1988, 28.

7. Usha Rao and K.K. Balasubramanian, Tetrahedron Lett., 1983, 24, 5023.

8. M. Okabe, M. Abe and M. Tada, J. Org. Chem., 1982, 42, 1775.

9. The structure assigned to each compound was in accord with its IR, NMR(^{1}H and ^{13}C NMR) as well as HRMS (parent ion identification).

10. The stereochemistry of both the isomers is yet to be assigned.

11. H. Vorbrueggen and C. Djerassi, J. Am. Chem. Soc., 1962, 80, 2990.

12. The crop reduction by parasitism is known to be prevented by seed germination stimulant (of Orabanche Crenata)-2,3,3a,9b-tetrahydro-4H-furo(3,2-c)-1-benzopyrans. see-
M. Davis, M. Pettet, D.B. Scanlon and V. Ferrito, Aust. J. Chem., 1977, 30, 2289.

(Received in UK 16 May 1988)