STUDIES ON CLAISEN REARRANGEMENT OF BIS-PROPARGYL ETHERS SYNTHESIS OF NAPHTHODIPYRANS, NAPHTHODIFURANS AND NAPHTHOFUROPYRANS+

Bindumadhavan Venugopalan and Kalpattu Kuppuswamy Balasubramanian*

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

Abstract- The Claisen Rearrangement of bis-propargyl ethers of naphthalenes yields naphthodipyrans when refluxed in N,N-diethyl-aniline and naphthodifurans in HMPT in the presence of sodium bicarbonate.

Growing interest in the area of Claisen rearrangement has motivated several studies from mechanistic as well as synthetic view points[1,2,3]. The thermal rearrangement of aryl propargyl ethers has been recognised as one of the general method for the synthesis of (2H)-benzopyrans[4].

In a preliminary communication[5] we have reported the facile double Claisen rearrangement of bis-propargyl ethers 1 and 7 to yield novel benzodipyrans. This double Claisen rearrangement of bis-propargyl ethers has been subsequently exploited by Murray et al. in the synthesis of natural products like dipetalolactone[15].

A detailed study of the various naphthalene bis-propargyl ethers and hydroquinone bis-propargyl ethers was undertaken to gain information regarding

1. The ease and the course of the migration
2. The nature of the migration - whether it is synchronous or step-wise.
3. To study the generality of the reaction, so as to make it a useful synthetic route to benzodipyrans, benzodimethylfurans and furopyrans.

We herein report a detailed study regarding the generality and synthetic utility of the reaction.

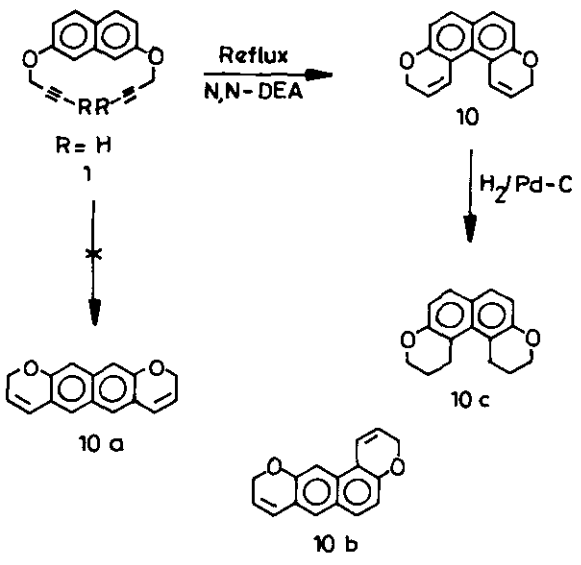
The rearrangement of 2,7-bis(2'-propynyloxy)naphthalene 1 was carried out

---

+ Dedicated to Prof.S.Swaminathan, on the occasion of his 60th birthday

by refluxing the ether in N,N-diethylaniline. The reaction was complete in five minutes. The NMR of the product obtained showed it to be the dipyran 10. The rearrangement was seen to be regiospecific as regioisomers 10a and 10b could not be detected (Scheme 1). The regiospecific migration of the propargyl groups to 1,8 positions contrasts with that reported for the double Fries rearrangement of 2,7-diacetoxynaphthalene to 1,6-diacetyl-2,7-dihydroxy-naphthalene[6].

SCHEME - 1



Catalytic hydrogenation of the dipyran 10 using Pd-C (10%) furnished the tetrahydro derivative 10c.

Other naphthalene bis-propargyl ethers 2,3 and 4 and 6 rearranged on refluxing in N,N-diethylaniline to yield the respective dipyrans (see Table I). In contrast to these bis-ethers 1,6-bis(2'-propynyloxy)-naphthalene 5 failed to rearrange when refluxed in N,N-diethylaniline. When 5 was refluxed in N,N-diethylaniline for 10 min in nitrogen atmosphere a viscous liquid (40% yield) was obtained which showed presence of starting material along with either the monofuro ether or monopyrano ether. The rearrangement was continued for 20 min with a view to drive the reaction to completion. This resulted in extensive polymerisation and systematic work up afforded a viscous liquid which showed three new spots in addition to that of the starting material. In view of its complex nature the rearrangement of this ether was not further

investigated. The contrasting behaviour of the ether 5 was rather unexpected (see Table I).

It was observed that most of the dipyrans deteriorated upon standing, whereas the corresponding tetrahydro derivatives were quite stable. The dipyran derived from ether 6 was especially unstable and hence converted to the more stable tetrahydro derivative.

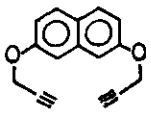
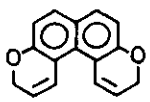
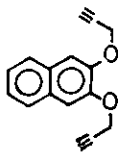
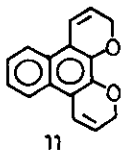
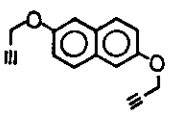
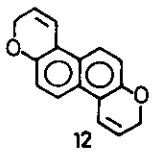
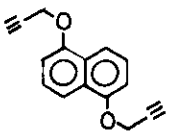
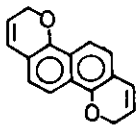
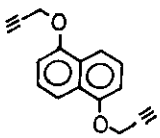
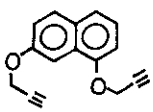
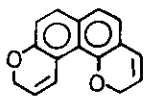
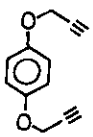
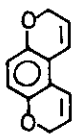
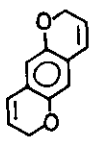
The rearrangement of 1 in refluxing decalin for 1.5 h did not yield any rearrangement product. Whereas on heating in HMPT for 10 min 1 yielded 10. Use of acid catalysts like p-toluenesulphonic acid did not bring about any change. Thus refluxing 1 in N,N-diethylaniline in the presence of catalytic amount of p-toluenesulphonic acid for 5 min afforded only the dipyran 10 in 50% yield.

1,2-bis(2'-propynyloxy)benzene 8 failed to rearrange even under longer hours of refluxing unlike the smooth rearrangement of 2. On prolonged heating of ether 8 only polymeric material was obtained. The ether 8 failed to rearrange even when refluxed in other solvents like decalin, o-dichlorobenzene and nitrobenzene. Similarly an attempted rearrangement of 1,3-bis (2'-propynyloxy)benzene 9 was also unsuccessful. A neat rearrangement in the absence of any solvent also failed to furnish any clean product. This again is in contrast to the behaviour of several of the derivatives of resorcinol monopropargyl ethers[7]. While no regioselectivity was observed in the case of the rearrangement of 3-methoxy- and 3-benzyloxypropargyl ethers, it was claimed by Box et al.[8] that 3-benzoyloxy propargyl ether underwent a rather unexpected regioselective migration to the 2-position. The cause of this regioselectivity (to the more hindered position) was not explained. Careful reinvestigation in our laboratory showed that the rearrangement of 3-benzoyloxy was not regioselective.

Hydroquinone bis-propargyl ether 7 could be rearranged to a 1:1 mixture of the benzo(1,2-b;4,3-b)dipyran 15 and benzo(1,2-b;4,5-b)dipyran 16 when refluxed in N,N-diethylaniline for 3 h. Dipyrans 15 and 16 were light sensitive and were hydrogenated to the more stable tetrahydro derivative 21 and 22.

The rearrangement of 1,4-bis(allyloxy)benzene has also been reported to

TABLE - 1

Compd No	Formula	Reaction time in min	Yield	Dipyran obtained
1		5	79	 10
2		10	63	 11
3		10	84	 12
4		10	67	 13
5		-	-	No reaction product
6		6	63	 14
7		3	76	 15  16

yield a mixture of the two isomeric phenols in a 1:1 ratio[9].

With a view to obtain additional confirmatory evidence for the proposed structure of the dipyran 10, an independent synthesis was attempted on the lines described by Bachman et al.[10] (Scheme II)

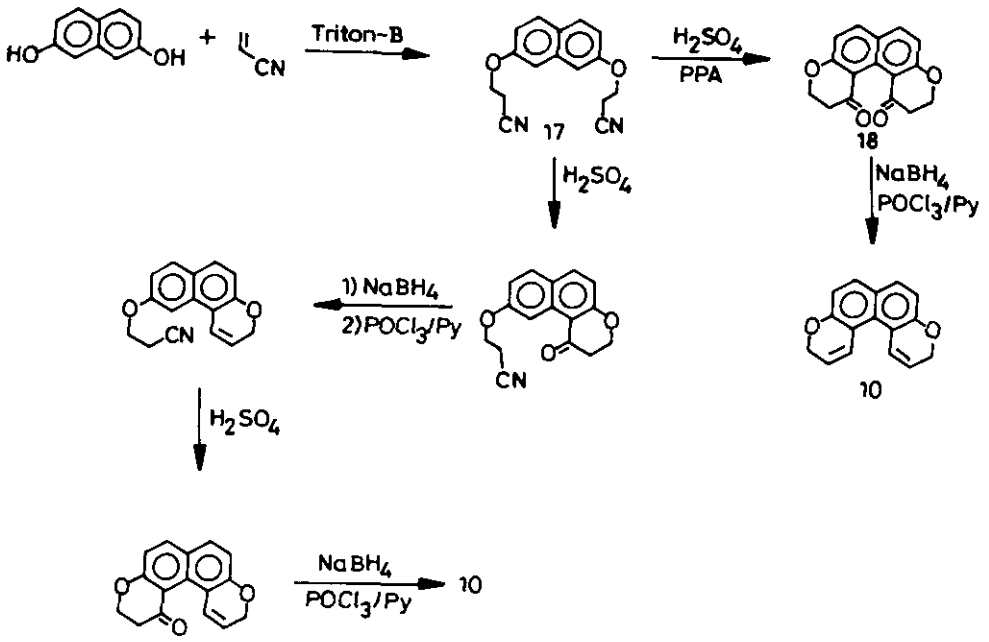
The dinitrile 17 was obtained as a crystalline solid when 2,7-dihydroxy-naphthalene was refluxed in acrylonitrile and in the presence of triton-B. The dinitrile however, failed to yield the desired product 18 when treated with conc. H_2SO_4 at R.T. or PPA at 60°c in contrast to the facile cyclisation of the β-naphthyloxypropionitrile to naphthochromonone.

The rearrangement of bis-propargyl ethers of naphthalenes shows considerable rate acceleration, the reaction times ranging from 5 to 10 min only, compared to the rearrangement of β-naphthyl propargyl ether which has been found to require 45 min for completion. Similar rate accelerations have been observed in the rearrangement of bis-allyl ethers also[11,12]. This remarkable acceleration obviously stems from the electronic effect of the additional ether linkage present in the starting material as well as in the several intermediates leading to the bis-pyrans, whereas, it is known that the rates of the Claisen rearrangements of aryl allyl ethers[13] and or aryl propargyl ethers[14] are not very much affected by the electronic nature of the substituents. It is unlikely that the migration of the two propargyl groups proceeds synchronously since the transition state of such a pathway will be highly unstable due to the simultaneous destruction of aromaticity of both the rings.

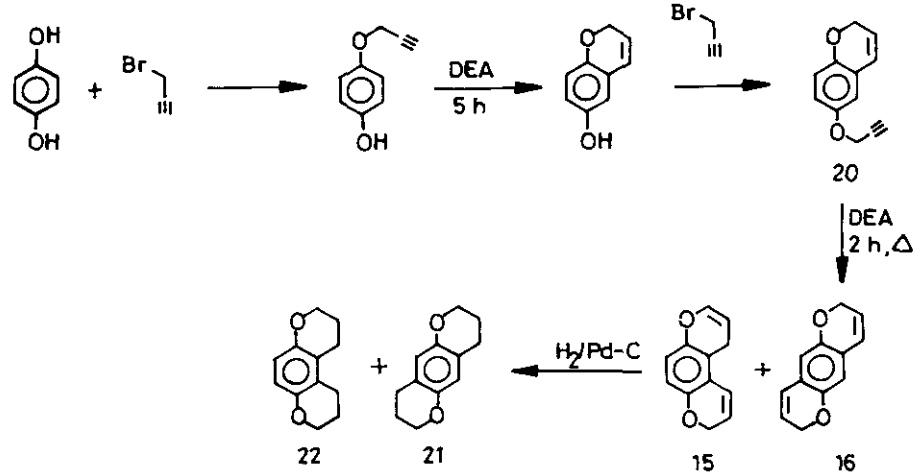
The simultaneous migration of the two propargyl groups in the case of hydroquinone bis-propargyl ethers also seems less feasible on entropy and delocalisation considerations. Moreover, such synchronous migration of the two propargyl groups would have to be regioselective unlike in ether 7 which gives rise to two dipyrans 15 and 16 in a 1:1 ratio.

One of the possible intermediates in the double Claisen rearrangement of ether 7 viz. 6-propargyloxy benzopyran 20 which would be involved in a step-wise migration process has been independently synthesised as shown in Scheme III.

SCHEME - 2



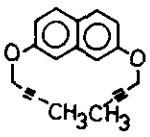
SCHEME - 3



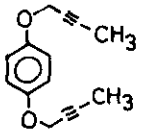
Rearrangement of the monopyran ether 20 was complete within 2 h on refluxing in N,N-diethylaniline. The NMR of the product indicated it to be a mixture of the two isomeric dipyrans 15 and 16 in a 1:1 ratio. These experimental findings are consistent with the step-wise nature of the above transformation.

In contrast to the facile rearrangement undergone by the naphthalene bis-propargyl ethers, the rearrangement of 2,7-bis(but-2-ynyloxy)naphthalene 23 was found to be slow and complex too. The starting material disappeared

completely after refluxing a N,N-diethylaniline for 15 min. The NMR spectrum revealed the presence of the dimethylnaphthodipyran along with other uncharacterisable material. Attempts to obtain it in pure state failed. Similarly the rearrangement of 1,4-bis(but-2-ynyloxy)benzene 24 furnished a complex mixture upon refluxing in N,N-diethylaniline for 3.5 h. The NMR spectrum of the crude product indicated the presence of monopyran and the dipyran. On prolonged heating extensive polymerisation was obtained.



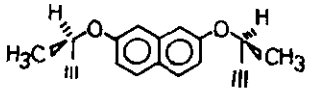
23



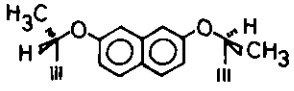
24

A few cases of rearrangement of optically active alkyl propargyl ethers leading to the formation of optically active allenes has been described in literature[16]. But there has been no study on the behaviour of optically active aryl propargyl ethers.

It was thus interest to see whether optically active bis-propargyl ether would yield naphthodipyrans which would exhibit optical activity. It was also of interest to see whether the rearrangement of diastereomeric bis-propargyl ethers 30 and 31 would exhibit stereospecificity or stereoselectivity.



30



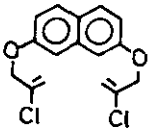
31

Thus with this objective in view the synthesis of 2,7-bis(2'-but-3'-ynyloxy)-naphthalene 30 was attempted. While β-naphthol as a model compound could be easily converted into the unknown 2-but-3-ynylether, under similar conditions or under better o-alkylation conditions viz. sodium and DMF, 2,7-dihydroxynaphthalene failed to furnish the desired ether. The reaction of but-3-yn-2-yl tosylate was tried in different solvents like DMF, DMSO, HMPT and bases like K_2CO_3, KOH, NaOH as well as preformed sodium salt of 2,7-dihydroxynaphthaline were tried without any success.

Schmid et al. have reported for formation of 2-methylbenzofuran by the Claisen

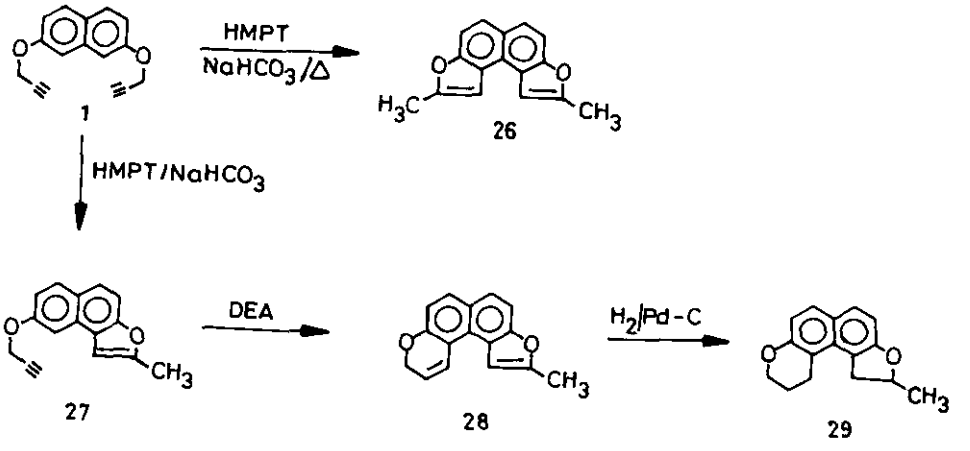
rearrangement of aryl propargyl ethers in sulfolane in the presence of potassium carbonate[17]. Extension of such a reaction to the bis propargyloxy benzene and naphthalenes might thus provide a simple and convenient route for the synthesis of various types of known and unknown condensed benzofurans. Further, if the rearrangement could be intercepted at the monofuran stage, one could exploit such an intermediate for a simple synthesis of a condensed furopyran ring system also.

In a preliminary communication we have reported the formation of naphthodifurans from the rearrangement of 2,7-bis(2'-propynyloxy)naphthalene 26 and 2,7-di(β-chloroallyl)naphthyl diether 25 by refluxing the respective ethers in HMPT with two equivalents of sodium bicarbonate in nitrogen atmosphere[18].



25

SCHEME - 4



1 26 27 28 29

Intermediate 27 could be isolated by careful analysis of the reaction mixture as a low melting solid (10%). On refluxing 27 in N,N-diethylaniline for 20 min under nitrogen atmosphere the furopyran 28 was obtained while the furonaphthopyran 28 was highly unstable the dihydro derivative 29 obtained on hydrogenation was found to be stable.

The base induced thermal rearrangement when extended to 1,4-bis(2'-propynyloxy)

benzene 7, led to the formation of both the angular and linear difurans. Thus on refluxing 1,4-bis(2'-propynyloxy)benzene 7 and sodium bicarbonate (2 equiv.) in HMPT for 5 h furnished a viscous liquid which showed two closely moving spots in TLC. By column chromatography it was possible to isolate one of the isomers as a crystalline solid, mp 109-110°c.

2,6-Dimethyl benzo(1,2-b;4,5-b)difuran (mp 113-114°c) was found to be known in literature. This had been reportedly formed by the acid catalysed condensation of ethylacetoacetate and quinone. Though, an authentic sample of the literature compound could not be obtained for direct comparison, in view of the close similarity in their melting points, the isolated product from the rearrangement of 1,4-bis(2'-propynyloxy)benzene with mp 109-110°c has been tentatively assigned the structure as 2,6-dimethylbenzo(1,2-b;4,5-b)difuran.

EXPERIMENTAL

Melting points reported are uncorrected. NMR spectra were taken using a Varian A-60 instrument. Mass spectra were taken using a Varian Mat CA 7 Mass Spectrometer.

Preparation of bis-propargyloxynaphthalenes and bis-propargyloxybenzenes

A mixture of dihydroxynaphthalene or dihydroxybenzenes (0.1 mole) 3-bromo-1-propyne (0.02 mole) and anhydrous potassium carbonate (0.02 mole) in dry acetone (40 ml) was refluxed for about 10 to 20 h. The reaction mixture was cooled and diluted with 500 ml of water and extracted thoroughly with ether. The ether layer was washed with 10% sodium hydroxide, water and dried. Evaporation of the ether extract afforded the corresponding bispropargyloxynaphthalenes or bispropargyloxybenzenes. The crude bis-propargyloxynaphthalenes were purified by column chromatography over silica-gel.

General procedure for the rearrangement of bis-propargyl ethers - A mixture of bis-propargyl ethers (472 mg, 0.002 mole) and N,N-diethylaniline (5 ml) was refluxed in nitrogen atmosphere for 5-10 min. The aniline solution was cooled and poured into 1:1 hydrochloric acid and extracted with ether. The ether extract was washed with dil. hydrochloric acid and then with water and dried. Evaporation of the ether extract furnished in most cases, a viscous dark liquid which was homogeneous on tlc (benzene:pet.ether 1:4). The crude product was purified by column chromatography over silica gel.

General Procedure for the hydrogenation of dipyran - To a solution of the dipyrans (0.0005 mole) in acetone (10 ml) was added 10% Pd-C (35 mg) and the mixture was hydrogenated at atmospheric pressure. When no more hydrogen uptake was observed the hydrogenated solution was filtered and the filterate was evaporated to remove the solvent. The crude product was then purified by passing through a column of silica gel and eluting with pet-ether.

Preparation of 4-hydroxyl-1-(2'-propynyloxy)benzene - The procedure described by Perkin et al.[19] for the preparation of 2-hydroxy-1-(2'-allyloxy)benzene was extended. In a three necked flask fitted with an efficient stirrer and condenser, was taken a mixture of hydroquinone (22 g; 0.2 mole), anhydrous potassium carbonate (27 g; 0.2 mole) and acetone (100 ml) heated and stirred for sometime. Then 3-bromo-1-propyne (24 g; 0.2 mole) was added dropwise while the reaction mixture was stirred and kept at 50-60°c. The addition was carried out over a period of 45 min. The reaction mixture was refluxed for 8 h. It was then poured into ice and extracted with ether. The ethereal layer was thoroughly washed with 10% sodium hydroxide solution. The alkaline washings were collected separately and then acidified with dilute hydrochloric acid, and re-extracted with chloroform. The chloroform extract was washed thoroughly with water to remove unreacted hydroquinone. The chloroform extract was dried and then evaporated. A clear liquid was obtained. Yield: 8 g. bp 110°c (18-20 Hg mm). Mass spectrum showed the molecular ion at m/z 148(39%). NMR $CDCl_3$/TMS: 2.45 (t, J = 2Hz, 1 H), 4.55 (d, J = 2Hz, 2H), 2.35 (s, 1H) exchangeable with D_2O), 6.75 (s, 4H). Ethereal solution on evaporation gave a low melting solid (6 g), mp 40°c, which was found to be 1,4-bis(2'-propynyloxy)benzene 7.

Rearrangement of 4-hydroxy 1-2(2'-propynyloxy)benzene to 6-hydroxy benzo-1,2-b)pyran - A solution of 4-hydroxy-1-2(2'-propynyloxy)benzene (1.5 g; 0.01 mole) in N,N-diethylaniline (10 cc) was refluxed under nitrogen atmosphere for 5 h. The aniline solution was then cooled and poured into dilute hydrochloric acid and extracted with ether. The ether extract was washed with more of dilute hydrochloric acid, then with water and dried. On evaporation of the ether was obtained a viscous gum, which distilled at 100°c/18-20 Hg mm to give the monopyran as a clear viscous liquid (yield: 990 mg, 66%). Mass spectrum showed the molecular ion at m/z 148 (68%). NMR $CDCl_3$/TMS: 2.43 (s, 1H), 4.75 (d d), J = 4.5 Hz, J allylic=1.5 Hz 2H), 5.79(m,1H),6.59(m,4H).

Preparation of 6-(2'-propynyloxy)benzopyran - A mixture of 6-hydroxybenzopyran (740 mg; 0.005 mole), 3-bromo-1-propyne (600 mg ; 0.005 mole) and anhydrous potassium carbonate (680 mg; 0.005 mole) in dry acetone (30 ml) was refluxed for about 6 h. The reaction mixture was cooled, diluted with 50 ml of water and extracted with ether. The ether layer was washed with 10% sodium hydroxide, then with water and dried. Evaporation of the ether extract furnished the 6-(2'-propynyloxybenzopyran: which distilled at 93°c(18-20 Hg mm) yield: 650 mg, 69%. Mass spectrum showed the molecular ion at 186 (50%). NMR ($CDCl_3$/TMS) 2.45(t, J = 2.5 Hz, 1H), 4.62(d, J = 2.5 Hz, 2H), 5.79(m,1H), 6.53 (m, 4H). Anal. calcd for $C_{12}H_{10}O_2$: C, 77.4; H, 5.41. Found: C, 77.26; H, 6.0%.

General Procedure for the base-catalysed rearrangement of bis-propargyl ethers A mixture of bis-propargyl ether (472 mg; 0.002 mole) and sodium bicarbonate (2 equiv.) was refluxed in HMPT (5 ml) in nitrogen atmosphere for 30 to 40 min. The reaction product was then extracted with benzene. The benzene layer was washed with water and then dried. Evaporation of the benzene solution yielded a thick viscous gum which showed single spot in tlc (benzene: hexane 1:4). The viscous gum was purified by passing through a column of silica gel and eluting with hexane (60-80). The difuran was obtained as a crystalline solid which on recrystallisation from benzene and hot hexane furnished analytically pure sample.

Rearrangement of 2-methyl-5-(2'-propynyloxy)naphtho(2,1-b)furan in N,N-diethylaniline - A solutionof 2-methyl-5-(2'-propynyloxy)naphtho(2,1-b)furan (230 mg; 0.001 mole) in N,N-diethylaniline (5 ml) was refluxed for 20 min in nitrogen atmosphere. The aniline solution was cooled and poured into dilute hydrochloric acid and extracted with ether. Ether layer was washed with water and then dried. Evaporation of the ether furnished a viscous liquid which showed a thick heavy yellow spot in tlc (benzene : pet ether 1:4),yield 90%. Preparative tlc purification of this viscous liquid yielded a white solid, mp 92-96°c(yield: 190 mg, 82%). NMR($CDCl_3$/TMS) : 2.5 (d, J = 1 Hz, 3H), 3.75 (d, J = 4 Hz, $J_{allylic}$ = 1.5 Hz, 2 H), 5.75 (m, 1H), 6.8 (unresolved singlet, 1H), 7.6 (d, J = 10 Hz, 1H), 7.4 (s, 2H). Mass spectrum showed the molecular ion at m/z 236 (100%).

Hydrogenation of furo(2',3'; 7,8)naphtho(2,1-b)pyran - To a solution of furopyran (60 mg, 0.00025 mole) in acetone (10 ml) was added 10% Pd-C (50 mg)

and the mixture was hydrogenated at atmospheric pressure. When no more hydrogen uptake was observed the hydrogeneated solution was filtered. The filtrate was evaporated to furnish a solid, mp 112°c(yield: 90%). Recrystallisation of this solid from hexane-ether mixture raised the melting point to 125-126°c. Yield: 50 mg(83%). NMR($CDCl_3$|TMS) : 2.2 (m, 2H), 2.5(d, J = 1Hz, 3H), 3.2(t, J = 7 Hz, 2H), 4.2 (t, J = 5 Hz, 2H), 6.8 (singlet merging with one limb of the doublet at 6.95, 1H), 6.95,(d, J = 9 Hz, 1H), 7.55 (d, J = 9 Hz, 1H), 7.35 (s, 1H), 7.4 (s, 1H) (AB quartet two extreme limbs are not seen). Mass spectrum showed the molecular ion at m/z 238 (100%). Anal. calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.47; H, 6.25%.

ACKNOWLEDGEMENT

Support of this work by the Indian National Science Academy and Council of Scientific and Industrial Research, India, is gratefully acknowledged.

REFERENCES

1. S.J. Rhoads and N.R. Raulins in Organic Reactions, Vol.22, Chapter I, Wiley, 1975.
2. G.B. Bennett, Synthesis, 1979, 589.
3. A. Viola, J.J. Collins, N. Filipp, Tetrahedron, 1981, 37, 3765.
4. Heterocyclic compounds - 'Chromenes,Chromones and Chromonones', G.P. Ellis, Ed., John Wiley and Sons, 1977.
5. K.K. Balasubramanian and B.Venugopalan, Tetrahedron Lett., 1973, 2707.
6. A.W. Burgstahler, L.K. Gibbon and I.C. Nordin,J.Chem.Soc., 1963, 4986.
7. U. Rao and K.K. Balasubramanian, Heterocycles, 1984, 22,1351.
8. V.G.S. Box, G.B. Burke and C. MeCaw, Heterocycles, 1979 ,17,451.
9. D.S. Tarbell, 'Organic Reactions', Vol.II, Chapter I, Wiley, New York, 1944.
10. G.B. Bachman and H.A. Levine, J.Am.Chem.Soc., 1948, 70, 599.
11. L.F. Fieser, W.P. Campbell and Edward M.Fry, J.Am.Chem.Soc., 1939, 61, 2206.
12. De Mayo, 'Molecular Rearrangements', Part I, Chapter II, by S.J. Rhoads, Interscience Publishers, New York, 1963.
13. M. Harfenest and E. Thom, J.Org.Chem., 1972, 37, 841.
14. I. Iwai and J. Ide, Chem.Pharm.Bull. (Japan), 1963, 11, 1042.
15. R.D.H. Murray and I.T. Forbes, Tetrahedron, 1978, 38, 1411.
16. E.R.H. Jones, J.D. Loder and M.C. Whiting, Proc.Chem.Soc., 1960, 180.
17. N. Sarcevic, J. Zsindely and H. Schmid, Helv.Chim.Acta, 1973, 56, 1457.
18. K.K. Balasubramanian and B.Venugopalan, Chem. and Ind. 1975, 611.
19. W.H. Perkin and V.M. Trikojus, J.Chem.Soc., 1927, 1663.

Received, 1st June, 1984