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CLAISEN REARRANGEMENT OF META-SUBSTITUTED ARYL PROPARGYL ETHERS IN POLY(ETHYLENE GLYCOL)

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Abstract - The thermal rearrangement of meta-substituted aryl propargyl ethers was studied in poly(ethylene glycol)-200. The rearrangement was not regiospecific.

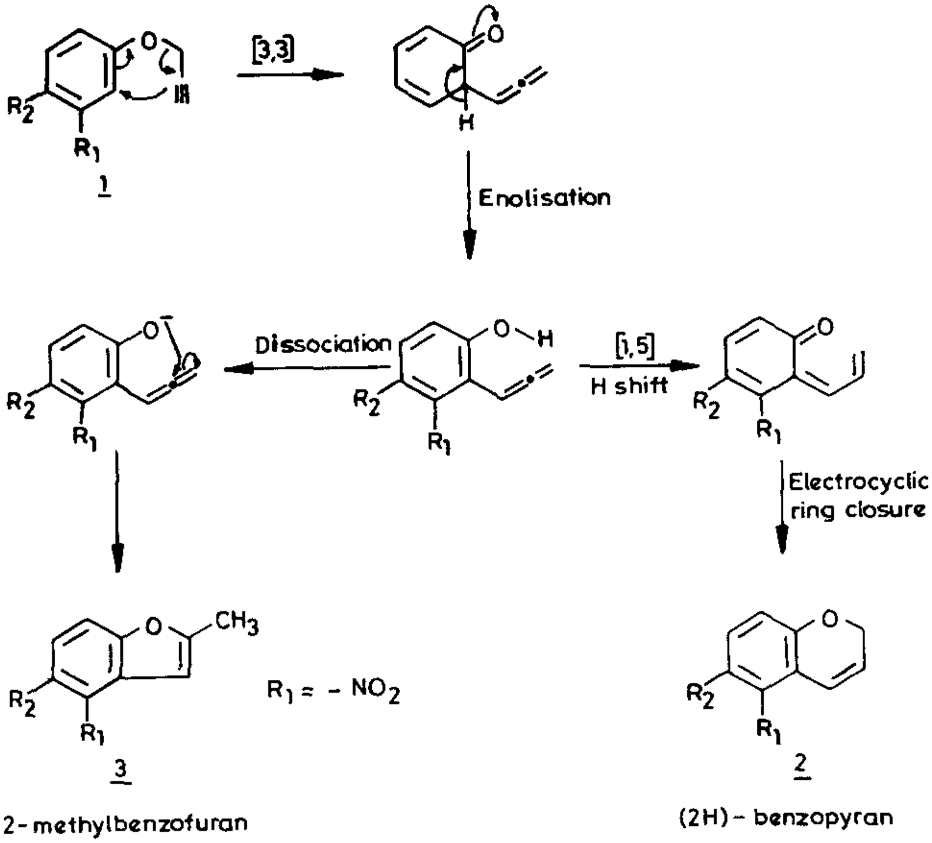
The thermal rearrangement of aryl propargyl ethers is one of the most versatile routes to the synthesis of (2H)-benzopyrans[1]. Several reports have appeared in literature on this rearrangement but no detailed report on the rearrangement of meta-substituted aryl propargyl ethers has appeared so far.

Earlier reports on the Claisen rearrangement of meta-substituted allyl phenyl ethers[2] has shown that when the meta-substituent is electron accepting, the rearrangement occurs ortho to the substituent predominantly, whereas when the substituent is electron donating the major product obtained is that in which the migration of the allyl group has occurred para to the substituent. We thus undertook a study of the thermal rearrangement of meta-substituted aryl propargyl ethers with electron donating and electron accepting substituents to study the regiochemical outcome of the rearrangement.

Recent work in our laboratory[3] has proved poly(ethylene glycol)-200 (PEG-200) to be a versatile solvent for the rearrangement of aryl propargyl ethers. We therefore employed PEG-200 as a solvent for the present study also.

Meta-substituted aryl propargyl ethers rearranged cleanly on heating in PEG-200 at 220°C and gave rise to (2H)-benzopyrans <u>2</u> when electron donating substituents were present in the aromatic ring. On the other hand meta-nitrophenylpropargyl ether <u>1i</u> gave rise to the corresponding 2-methylbenzofurans <u>3i A</u> and <u>3i B</u> on heating in PEG-200 at 220°C for 1.5 h. The Claisen rearrangement of other aryl propargyl ethers containing electron-withdrawing groups like -CHO, $-COOC_2H_5$ and COOH did not give rise to the expected 2-methylbenzofuran as the sole product. Meta-formylphenyl propargyl ether gave rise to a mixture of 2-methylbenzofurans <u>3j A</u> and <u>3j B</u> and (2H)-benzopyran <u>2j A</u> and <u>2j B</u> whereas meta-ethoxycarbonyloxyphenylpropargyl ether <u>1h</u> gave rise to only (2H)-benzopyran <u>2h A</u> and <u>2h B</u> quite contrary to our expectations. Surprisingly meta-carboxyphenylpropargyl ether did not rearrange at all even on heating in PEG-200 for 3 h, only starting material was recovered.

Scheme I



When meta-nitrophenylpropargyl ether 1i was refluxed in N,N-diethylaniline for 10 h a mixture of the 2-methylbenzofuran <u>3i A</u> and <u>3i B</u> and (2H)-benzopyran <u>2i A</u> and <u>2i B</u> was obtained. A similar observation was made by Schmid et al.[4]. They have reported the formation of the two isomeric methylfurans <u>5</u> and <u>6</u> when 3-pyridylpropargyl ether <u>4</u> was heated in a polar solvent like N,N-dimethylformamide at 208°C, whereas when it was heated in a non-polar solvent like decane at 208°C the two isomeric methylfurans 5 and 6 as well as the pyranopyridine 7 was obtained (see Scheme II).

Scheme II

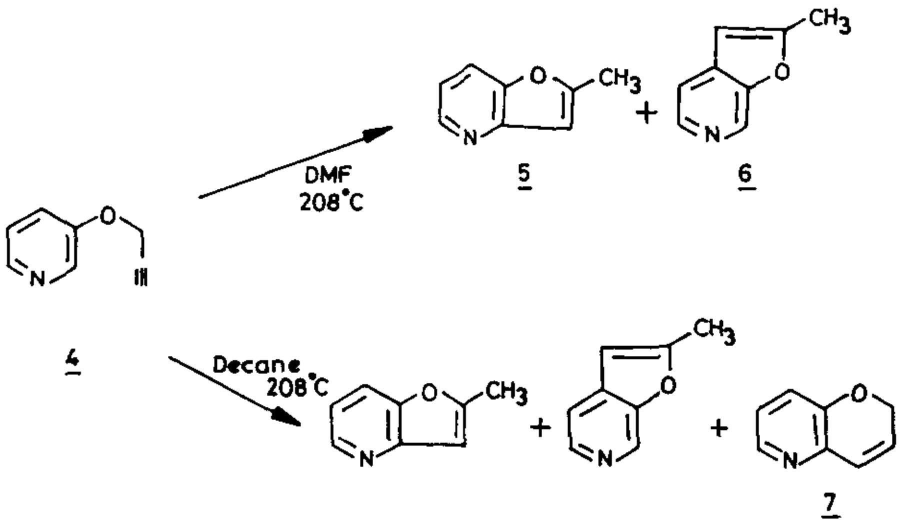


TABLE I

Yields§ of (2H)-benzopyrans and 2-methylbenzofurans obtained from the rearrangement of aryl propargyl ethers in PEG-200 at 220°C.

Compd No.	R_1	R_2	Rxn. time in min	Yield		
				2	3	2+3
1a	CH_3	H	45	77		
1b	CH_3	Cl	45	64		
1c	OCH_3	H	45	70		
1d	OCH_2Ph	H	45	75		
1e	OCOPh	H	60	60		
1f	$OCOCH_3$	H	180	55		
1g	COOH	H	180	-	-	-
1h	COOEt	H	360	48		
1i	NO_2	H	90		23	
1j	CHO	H	45			40

§ For ratios of the two isomeric 2H-benzopyrans and 2-methylbenzofurans see Table II.

Iwai et al.[5] have reported that with meta-substituted aryl propargyl ethers the migration occurs regioselectively para to the meta substituent and electron donating meta-substituents increase the yields of the (2H)-benzopyrans. These authors have also reported that during the rearrangement of meta-methoxyphenylpropargyl ether 1c, the product obtained was exclusively the (2H)-benzopyran 2c A (see Scheme III). Later investigations by Anderson et al.[6] have shown that the rearrangement of meta-methoxyphenylpropargyl ether 1c is not regiospecific. They have obtained the two isomeric (2H)-benzopyrans 2c A and 2c B in the ratio of 46:54 when 1c was refluxed in N,N-diethylaniline for 15 h.

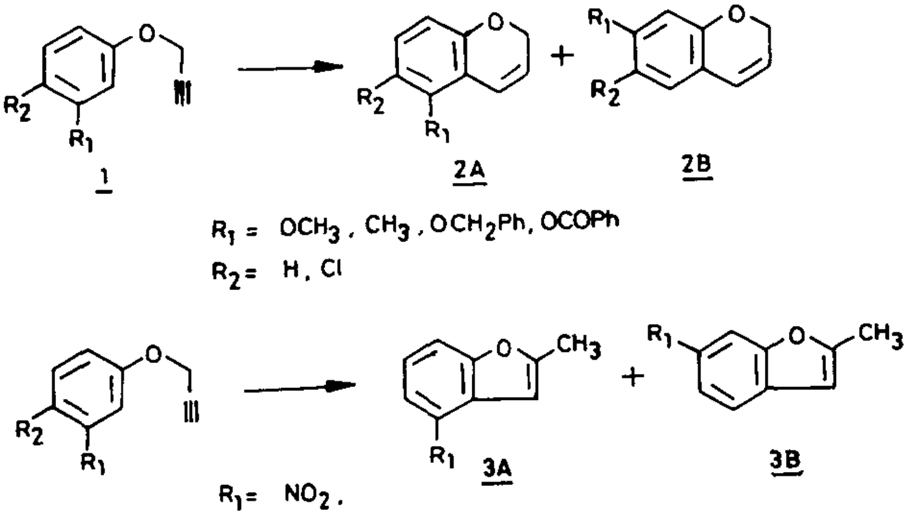
Our studies on the rearrangement of meta-methoxyphenylpropargyl ether 1c has shown that it rearranges on heating in PEG-200 at 220°C for 1 h under argon atmosphere to yield the two isomeric (2H)-benzopyrans (Table II) as evidenced by tlc, glc and NMR. On prolonged heating (3 h) of 1c in PEG-200 at 220°C only one isomer could be obtained viz. 5-methoxy-1-(2H)-benzopyran 2c A. In order to see whether the 7-methoxy-1-(2H)-benzopyran 2c B was getting destroyed during the process of heating, or if by some means it was getting converted to the 5-methoxy-1-(2H)-benzopyran 2c A, the two isomeric methoxy-(2H)-benzopyrans were separated by preparative thin layer chromatography using hexane-benzene (7:3) system as eluent. The 7-methoxy-1-(2H)-benzopyran thus obtained was heated in PEG-200 at 220°C for 3 h. It was seen from tlc that it did not get converted to 5-methoxy-1-(2H)-benzopyran. No tractable product could be obtained. 7-methoxy-1-(2H)-benzopyran 2c B was synthesised[7] independently and heated in PEG-200 at 220°C for 3 h. No tractable product could be obtained after work up of the reaction mixture. It was thus evident that 7-methoxy-1-(2H)-benzopyran was getting destroyed on prolonged heating in PEG-200.

On the other hand, when 1c was refluxed for 10 h in N,N-diethylaniline the two isomeric (2H)-benzopyrans could still be obtained in the ratio of 6.45 : 6.48. We have observed that the solvent employed has no effect on the regioselectivity of the rearrangement as the ratios of the two isomeric (2H)-benzopyrans obtained from the rearrangement of 1c in various solvents like PEG-200, N,N-diethylaniline and o-dichlorobenzene were more or less the same (Table II).

Aryl propargyl ethers 1a, 1b, 1d and 1f gave a mixture of two isomeric (2H)-benzopyrans when the solvent employed for the rearrangement was either

PEG-200 or N,N-diethylaniline. Our preliminary attempts to separate the two isomeric (2H)-benzopyrans or 2-methylbenzofurans were unsuccessful except in the case of 2c and 2d.

Scheme III



In 1979 Box et al.[8] reported that meta-benzoyloxyphenyl propargyl ether 1e rearranged in a regiospecific manner when refluxed in N,N-diethylaniline to yield the 5-benzoyloxy-1-(2H)-benzopyran. Since the exact experimental conditions were not mentioned in the paper, we reinvestigated the rearrangement of ether 1e at shorter reaction times (4 h) and longer reaction times (12 h) in N,N-diethylaniline in view of our experience with the rearrangement of the ether 1c.

When 1e was refluxed in N,N-diethylaniline for 4 h it gave rise to the two isomeric (2H)-benzopyrans along with some starting material. The formation of the two isomeric (2H)-benzopyrans was further confirmed by saponification of the crude product and methylation of the resultant phenolic product with dimethyl sulphate and potassium carbonate in refluxing acetone for 4 h. The tlc and NMR of the methylated product clearly showed it to be a mixture of 5-methoxy-1-(2H)-benzopyran and 7-methoxy-1-(2H)-benzopyran and also by comparison with an authentic mixture of 2c A and 2c B obtained from the rearrangement of 1c. When 1e was refluxed in N,N-diethylaniline for 12 h, the NMR spectrum of the crude product showed complete disappearance of starting material and the presence of only one isomeric (2H)-benzopyran. Saponification and methylation of the crude product thus obtained showed it to be 5-methoxy-1-(2H)-benzopyran from NMR and tlc and also by comparison with an authentic sample. It was thus evident that prolonged heating in N,N-diethylaniline destroyed one of the two isomeric chromenes viz. the 7-benzoyloxy-1-(2H)-benzopyran.

In contrast, when 1e was heated in PEG-200 at 220°C for 1 h it gave rise to the two isomeric benzopyrans. Prolonged heating of 1e in PEG-200 at 220°C for 3 h also yielded a mixture of the two isomeric (2H)-benzopyrans.

TABLE II

Ratios of the two isomeric (2H)-benzopyrans 2 and 2-methylbenzofurans 3 obtained from meta-substituted aryl propargyl ethers.

Compd No.	Rxn. time in h	Isomeric ratios of 2A:2B PEG	 DEA	 ODClB	Isomeric ratios of 3A:3B
1a	1.0	6.5:6.24	-	-	-
1b	1.0	1:2	-	-	-
1c	1.0	16:11	-	-	-
1c*	3.0	5.5:3.4	9:7.2	7:5.5	-
1d	0.75	1:1	-	-	-
1i	1.5	-	-	-	1:2

The ratios of the two isomeric (2H)-benzopyrans were determined by glc using flame ionisation detector and SE-30 column for compounds 1a-1c. The isomeric ratios for compounds 1d and 1i were determined by NMR analysis.

*1c was heated in poly(ethylene glycol) (PEG), N,N-diethylaniline (DEA) and o-dichlorobenzene (ODClB) for 3 h at 200°C. All other rearrangement studies were carried out in PEG at 220°C.

The isomeric ratios for compounds 1e, 1f, 1h and 1j could not be determined by glc or from NMR analysis.

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REFERENCES AND NOTES

1. 'Heterocyclic Compounds - Chromenes, chromones and chromonones', ed. by G.P. Willis, John Wiley and Sons, 1977.
2. J.M. Bruce and Y. Roshan Ali, J. Chem. Soc., Perkin Trans. I, 1981, 2677.
3. U. Rao and K.K. Balasubramanian, Tetrahedron Letters, 1983, **24**, 5023.
4. J. Bruhn, J. Zsindely, H. Schmid and G. Frater, Helv. Chim. Acta, 1978, **61**, 2542.
5. a) I. Iwai and J. Ide, Chem. Pharm. Bull., 1963, **11**, 1042.
   b) J. Hlubucek, E. Ritchie and W.C. Taylor, Aust. J. Chem., 1971, **24**, 2347.
6. W.K. Anderson and E.J. LaVoie, J. Org. Chem., 1973, **38**, 3832.
7. G.B. Bachman and H.A. Levine, J. Am. Chem. Soc., 1948, **70**, 599.
8. V.G.S. Box, A.B. Burke and C. McCaw, Heterocycles, 1979, **12**, 451.
9. Aryl propargyl ethers 1a-1j were prepared according to the general procedure outlined in Ref. 5a. Ether 1j was prepared in a similar manner except that the solvent used was dimethylformamide.
10. The compounds obtained from the rearrangement of aryl propargyl ethers were unequivocally characterised from their IR and NMR spectra. No elemental analysis was thought necessary (as also quoted by Box et al. in Ref. 8).
11. Part of this work has been accepted for presentation in the 'The Ninth International Congress of Heterocyclic Chemistry' to be held in Tokyo, Japan, August 1983.

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