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SOLVOLYSIS AND REARRANGEMENT OF ARYL VINYL COMPOUNDS IN PYRIDINE HYDROCHLORIDE

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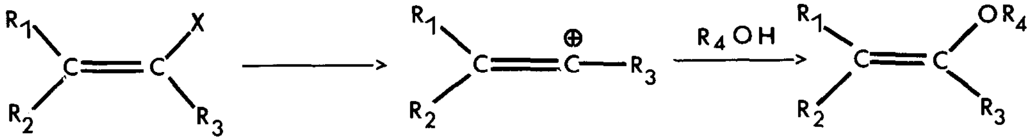
Summary Anisyl substituted stilbenes undergo concommitant thermal rearrangement and loss of a halogen atom with dealkylation in pyridine hydrochloride.

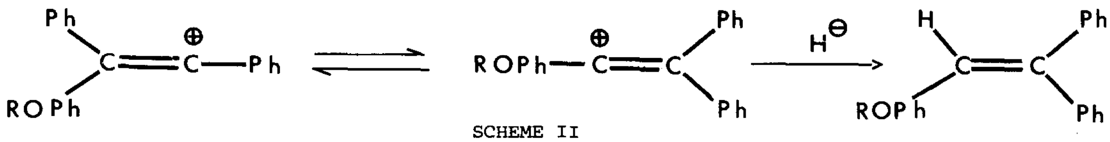
The reaction of aryl substituted vinyl halides in strongly ionizing solvents is thought to proceed via a vinyl cation intermediate (see review[1]), which subsequently reacts with solvent (or eliminates if β hydrogens are present) (Scheme I).



SCHEME I

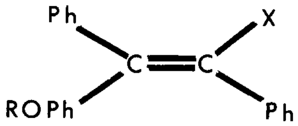
While attempting the dealkylation of chlomiphene[2] (1) and (2) to phenols (3) and (4) in search of a sensitive assay for chlomiphene, based on the fluorescence of the dansyl derivatives of phenols (3) and (4), a mixture of three isomeric phenols (5), (6) and (7) (approx. 1:1:1) was isolated[3]. The proposed structures of these three isomeric phenols were confirmed by their individual syntheses[4,5] and co-injection of their TMS ethers on GC with the silylated mixture obtained from the reaction of clomiphene[6].

The phenols (5), (6) and (7) may be rationalized to form by a reversible 1,2 aryl shift[7] within the initially formed vinyl cation followed by hydride abstraction, possibly from the dealkylated side chain (Scheme II).

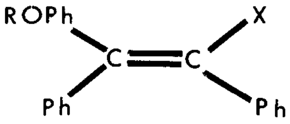


SCHEME II

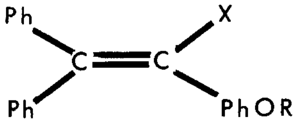
Extremely vigorous conditions are necessary to produce the vinyl cation since demethylation of ethers (8), (9) and (10) with pyridine hydrochloride (200°, 2h), employed to prepare phenols (3), (4) and (14) caused no detectable loss of chlorine, whereas a mixture of ethers (8) and (9) afforded phenols (5), (6) and (7) (1:1:1) under the conditions used for clomiphene[8].



(1) R = $(CH_2)_2$ NEt_2
X = Cl
(3) R = H, X = Cl
(5) R = H, X = H
(8) R = Me, X = Cl
(11) R = Me, X = H



(2) R = $(CH_2)_2$ NEt_2
X = Cl
(4) R = H, X = Cl
(6) R = H, X = H
(9) R = Me,X = Cl
(12) R = Me,X = H



(7) R = H, X = H
(10) R = Me,X = Cl
(13) R = Me,X = H
(14) R = H, X = Cl

The reaction was not limited to vinyl chlorides for, separately, ether (13) and a mixture of ethers (11) and (12) afforded phenols (5), (6) and (7) (1:1:1) when heated with pyridine hydrochloride at 230°.

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References and Footnotes

1. P.J. Stang, Prog. Phys. Org. Chem., 10, 257 (1973).
2. Clomiphene, a 1:1 mixture of *cis* and *trans* 2- (p - (2-Chloro-1,2-diphenyl-vinyl) phenoxy) triethylamine, is marketed as the citrate salt.
3. Clomiphene citrate (100 mg) and pyridine hydrochloride (2 g) were heated at 230° for 24 h
4. E.C. Dodds, L. Goldberg, E.I. Grunfeld, W. Larson, C.M. Saffer, Jnr, and R. Robinson, Proc. Roy. Soc., 132B, 83 (1944).
5. The p-toluenesulphonate of phenol (7), m.p. 116-117°, gave a satisfactory combustion analysis.
6. SE-30 SCOT column, 20 m x 0.5 mm ID, T = 240°, Neff = 15,000; Retention indices for the TMS derivatives of (5), (7) and (6) were 2467, 2495 and 2510 respectively; Resolution of (7) and (6) was 0.48.
7. D.Y. Curtin, J.H. Kampmeier and M.L. Farmer, J. Amer. Chem. Soc., 87, 863 (1965).

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