Tetrahedron Letters No. 21, pp. 1753-1756, 1971. Pergamon Press. Printed in Great Britian.

NUCLEOPHILIC SUBSTITUTION AT AN ACETYLENIC CARBON: 1-ALKOXY-2-PHENYLACETYLENES FROM 1-CHLORO-2-PHENYLACETYLENE

Ryuichi Tanaka and Sidney I. Miller

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616, USA

(Received in USA 20 January 1971; received in UK for publication 14 April 1971)

The usual routes to acetylenic ethers, e.g. from acetylenes, aldehydes, or vinyl ethers, involve many steps (1). Here we describe a short route to phenylalkoxyacetylenes (**2**) from phenylacetylene _via_ phenylchloroacetylene (**1**): nucleophilic attack on **1** by some alkoxides in certain aprotic solvents _may_ lead to the desired ethers.

$$\underset{\mathbf{1}}{C_6H_5C{\equiv}CCl} + RO^- \longrightarrow \underset{\mathbf{2}}{C_6H_5C{\equiv}COR} + Cl^- \qquad (1)$$

$$(R = CH_3,\ C_2H_5,\ \underline{i}\text{-}C_3H_7,\ \underline{t}\text{-}C_4H_9)$$

Of the title ethers, only phenylmethoxyacetylene has been described in any detail (2), although a large number of 1-alkoxy-2-alkylacetylenes have been synthesized (1). Jacobs and Scott had many difficulties in their preparation of low yields of somewhat impure 1-methoxy-2-phenylacetylene from the bromomethoxystyrenes (2). 1-Ethoxy-2-phenylacetylene is mentioned in a patent (3), but not in a comprehensive review by the same authors (1). The formation of phenyl-_t_-butoxyacetylene from the reaction between potassium-_t_-butoxide and a 2-chloro-2-fluorostyrene was reported but no experimental details were disclosed (4). It does, in fact, appear that the normal susceptibility of ethynyl ethers to attack by a variety of reagents (1) is enhanced by the phenyl substituent, so that problems of preparation and separation are magnified.

To illustrate both the simplicity and the problems of carrying out process 1, four illustrative examples will be given. The sodium alkoxides were prepared by treating sodium with an excess of the appropriate alcohol under nitrogen, at reflux if necessary, and evaporating the alcohol at ca. 200, then 0.1 torr. Phenylchloroacetylene (0.1 mole) in solvent (20 ml) and a suspension of sodium alkoxide (0.2 mole) in solvent (25 ml) were mixed in a flask which was immersed in ice water. The flask was quickly stoppered and swirled to dissipate any evolved heat. After the flask was shaken mechanically, its contents were poured into ice water and the mixture was extracted with ether. The extract was dried over sodium sulfate, stripped, and fractionally distilled.

For phenylethoxyacetylene, the solvent was DMSO and the shaking time at ca. 25° was 60 min. Using tetraethylene glycol dimethyl ether (20 ml) as a chaser, we obtained a middle fraction (6.2 g, 42% yield): bp 40-42° (0.06 torr); ir (neat) 2258, 1320, and 1062 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.39 (t, 3H, J = 7.25 Hz), 4.11 (q, 2H, J = 7.25 Hz) and 7.05-7.45 (m, 5H); mass spec. 146 (P^+). Calcd. for $C_{10}H_{10}O$: C, 82.13; H, 6.89; Found, C, 82.0; H, 6.77

For phenylisopropoxyacetylene, the solvent was DMSO and the shaking time at ca. 25° was 20 hr. The crude liquid gave a middle fraction (4.8 g, 31.5% yield): bp 54-55° (0.15 torr); ir (neat) 2253, 1379, 1316 and 889 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.38 (d, 6H, J = 6.2 Hz), 4.32 (septet, 1H, J = 6.2 Hz) and 7.0-7.3 (m, 5H); mass spec. 160 (P^+). Calcd. for $C_{11}H_{12}O$: C, 82.45; H, 7.55; Found: C, 82.41; H, 7.47.

For phenyl-t-butoxyacetylene at double scale, commercial potassium t-butoxide powder was used. The solvent was HMPA and the shaking time at ca. 0° was 60 min. The unreacted phenylchloroacetylene (20-50% depending on the runs) was removed at 1 torr in 2 hr. The residue (ca. 8 g in one of the runs, 46% yield) was chromatographed on alumina with pentane. A portion of the middle fraction (ca. 1 g) was distilled at ca. 25°C (0.008 torr) through two cold traps. The condensate (ca. 0.5 g) in the first ice trap had: ir (neat) 2238, 1398, 1375, and 1332 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.44 (s), and 7.0-7.5 (m); mass spec. 174 (P^+). The later fractions of the chromatographic run gave 1,4-diphenylbutadiyne (0.3 g), confirmed by its ir spectrum and mp 87.5-88.0° (lit. (5) 88°), from ethanol-water.

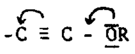
For phenylmethoxyacetylene, the solvent was DMSO and the shaking time at *ca.* 25° was 60 min. If the sodium methoxide was freshly prepared, the initial reaction evolved much heat and led to substantial polymerization. If commercially available sodium methoxide was used, the reaction was milder and did not go to completion. Because this ether and phenylchloroacetylene distill together at *ca.* 45° (0.7 torr), we were unable to separate them. Typically, we obtained: phenylmethoxyacetylene (*ca.* 53%); ir (neat) 2277 and 1328 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 3.93 (s) and 7.1-7.5 (m); phenylchloroacetylene (*ca.* 40%), ir 2225 cm^{-1}; minor components (<10%) of phenylacetylene, methyl phenylacetate, methyl orthophenylacetate, and the bromomethoxystyrenes.

It is interesting that for the three ethers for which mass spectra were obtained, m/e = 118 was a major peak. This species must involve rearrangement and may correspond to positively charged phenylethynyl alcohol or phenylketene.

$$\underset{\sim}{\mathbf{2}}(R = C_2H_5,\ \underline{i}\text{-}C_3H_7,\ \underline{t}\text{-}C_4H_9) \xrightarrow{e^-} C_8H_6O^+ \qquad (2)$$

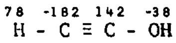
Compared to the usual conditions for alkoxide promoted additions of alcohols to alkynes (6), the present conditions for process 1 are extremely mild. Besides enhancing the nucleophilicity of the alkoxide, the use of an aprotic solvent permits the survival of the phenylalkoxyalkynes; phenylmethoxyacetylene in methanolic base for example, is a transient, having a rate constant for decomposition by methoxide of $\underline{k} \simeq 10^{-3}\ M^{-1}\ sec^{-1}$ at 78° (7). An important factor in the success of process 1 derives from the fact that the alkoxide probably attacks the terminal carbon rather than abstracting positive halogen, as is largely the case with phenylbromoacetylene (7). Several mechanistic alternatives are discussed in detail elsewhere (7-9).

A comment on the vulnerability of ethynyl ethers to various reagents is in order. With respect to orientation, one can make the proper predictions by using the valence bond representations (I) of Arens, *et al.* (1). As for their reactivity, relative to fluoro- or amino-



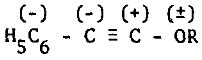
$-C \equiv C - \overline{\underline{O}}R$

I



$\overset{78}{H} - \overset{-182}{C} \equiv \overset{142}{C} - \overset{-38}{OH}$

II



$\overset{(-)}{H_5C_6} - \overset{(-)}{C} \equiv \overset{(+)}{C} - \overset{(\pm)}{OR}$

III

alkynes, with variations in substituents, or compared to other unsaturated ethers, one can begin to draw on MO theory. The CNDO/2 charge densities in II, $(q_\pi + q_\sigma) \times 10^4$, show a strong polarization within the triple bond (10,11), an effect which should be accentuated by an aryl substituent as in III (11). Although enhanced reactivity of arylethynyl ethers may pose problems in their preparation, it could be advantageous in synthetic applications (1).

This investigation was supported by Public Health Service Grant GM 7021.

References

(1) L. Brandsma, H.J.T. Bos, and J.F. Arens, in "Chemistry of Acetylenes," H.G. Viehe, Ed., Marcel Dekker, New York, N.Y. 1969, Chap. 10.

(2) T.L. Jacobs and W.R. Scott, Jr., J. Amer. Chem. Soc. **75**, 5497 (1953).

(3) J.F. Arens, U.S. Patent 2813862; Nov. 19 (1957).

(4) H.G. Viehe, Angew. Chem. **75**, 638 (1963).

(5) J.S. Salkind and F.B. Fundyler, Chem. Ber., **69**, 128 (1936).

(6) S.I. Miller and R. Tanaka, in "Selective Organic Transformations," B.S. Thyagarajan, Ed., Wiley-Interscience, New York, N.Y., 1970, p. 143.

(7) R. Tanaka, M. Rodgers, R. Simonaitis, and S.I. Miller, unpublished results.

(8) A. Fujii, J.I. Dickstein, and S.I. Miller, Tetrahedron Letters 3435 (1970).

(9) G.R. Ziegler, C.A. Welch, C.E. Orzech, S. Kikkawa, and S.I. Miller, J. Amer. Chem. Soc., **85**, 1648 (1963).

(10) W.J. Hehre and J.A. Pople, ibid., **92**, 2191 (1970).

(11) R.T.C. Brownlee and R.W. Taft, ibid., **92**, 7007 (1970).