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ADDITION REACTIONS OF ETHOXYCARBONYLNITRENE AND ETHOXYCARBONYLNITRENIUM ION TO ALLYLIC ETHERS[1]

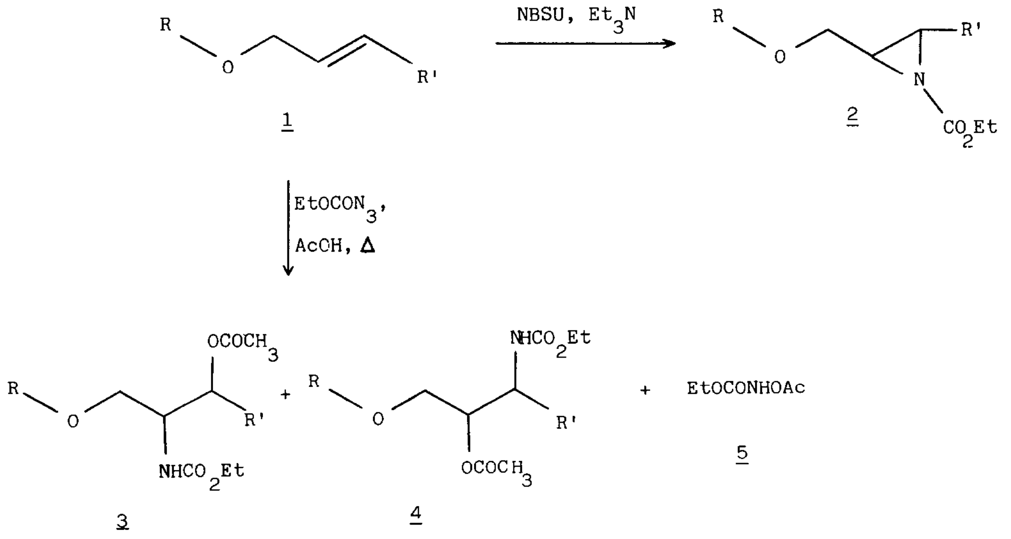
M. Antonietta Loreto,* Lucio Pellacani,* Paolo A. Tardella,* and Elena Toniato

Dipartimento di Chimica, Università "La Sapienza", I-00185 Roma, Italy

SUMMARY. Ethoxycarbonylnitrene (EtOCON) generated by α-elimination adds cleanly to allylic ethers giving substituted aziridines. Similar addition via nitrenium ion (EtOCONH$^+$) gives derivatives of β-amino alcohols.

While reactions of carbenes and carbenoids on allylic compounds have been thoroughly investigated,[2] little attention has been paid to the reaction between nitrenes and allylic derivatives.[2,3] Our interest in the reaction of ethoxycarbonylnitrene (EtOCON) on unsaturated systems[4] and consideration of recent results of addition reactions of ethoxycarbonylnitrenium ion (EtOCONH$^+$) to alkenes[5] prompts us to report the addition of EtOCON and EtOCONH$^+$ to the allylic ethers:[6] diallyl ether 1a, allyl phenyl ether 1b, and 2,5-dihydrofuran 1c.

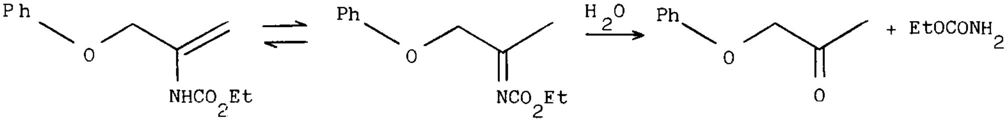
Using EtOCON generated by α-elimination from 4-nitrobenzenesulfonyloxyurethan (NBSU) we confirmed that there is a large preference for addition of EtOCON over insertion into a C–H bond: the only products detectable were the aziridines 2a-c.



a: R = CH_2=CH–CH_2, R' = H b: R = C_6H_5, R' = H c: R·····R' = CH_2

GLC analysis and proton NMR spectra of crude reaction mixtures pointed to high yields of aziridines (up to 77 %, 73 %, and 95 % respectively by GLC), but only low yields (16 %, 7 %, and 10 %) were isolated after silica gel column chromatography. This parallels the results of Ando[3a] using MeOCON generated by photolysis of methyl azidoformate in other allylic ethers, but he found up to 30 % of products of formal insertion.

However, we obtained a large amount (32 %, GLC) of a byproduct in the thermolysis of ethyl azidoformate ($EtOCON_3$) in allyl phenyl ether 1b, which we identified as phenoxyacetone, probably formed as shown below:



Similarly, thermolysis of $EtOCON_3$ in diallyl ether 1a gave the aziridine 2a (77 %, GLC) but accompained by an isomeric (GC-MS) product (22 %, GLC).

Nitrene insertion into a vinylic C-H bond is a common reaction with alkenes. We did not observe the usual insertion product into the α C-H bonds of saturated ethers,[7] nor the product of a [2,3]-sigmatropic rearrangement as reported by Ando.[3a]

On the basis of our results and Ando's, and considering the results of the photolysis and thermolysis of $ROCON_3$ in the presence of Pd catalysts,[8] the α-elimination route is the method of choice for a clean addition of EtOCON to the double bond of allylic ethers.

The aziridines 2a-c are potentially useful precursors of β-amino alcohols[9] of potential interest as β-blockers.[10] Thus the acetolysis[11] of the aziridine 2c gave the acethoxyurethan 3c in 52 % yield. However, the same reaction products might be obtained in a one-pot reaction via a nitrenium ion.[5] Thermolysis of $EtOCON_3$ in 2,5-dihydrofuran (equimolar amounts, 5:5 mmol) dissolved in acetic acid (160 mmol) gave the same acethoxyurethan 3c in 16 % yield (55 %, GLC). The main byproduct (32 %, GLC) was identified as ethyl O-acetyl-N-hydroxycarbamate 5 from its spectroscopic data as reported by Takeuchi.[5] When the thermolysis of $EtOCON_3$ in AcOH was run with the ether 1a (1:160:5) the expected products 3a and 4a were produced in 15 and 38 % yields in addition to 5 (47 % yield). The amount of 5 was substantially reduced when the thermolysis was carried out with less acetic acid ($EtOCON_3$:AcOH:1a = 1:6:2).

Finally, thermolysis of $EtOCON_3$ in AcOH with the ether 1b gave the two products 3b and 4b in 68 % and 25 % yield. Thus the major product 3b was derived from the attack of acetic acid on the less substituted carbon of the aziridinium ion, in contrast to the formation of

2a: ^{1}H-NMR (CCl_4) δ 5.75 (1H, m), 5.15 (2H, m), 4.05 (2H, q), 3.95 (2H, d), 3.50 (2H, m), 2.50 (1H, m), 2.15 (1H, d), 2.10 (1H, d), 1.2 (3H, t); MS: m/z 185 (M^+, 1 %), 41 (100 %); high resolution MS, calcd for $C_9H_{15}NO_3$: 185.1052, found: 185.1047.

2b: ^{1}H-NMR (CCl_4) δ 7.4-6.5 (5H, m), 4.4-3.7 (4H, q + 2d + 2d), 2.7 (1H, m), 2.35 (1H, d), 2.2 (1H, d), 1.2 (3H, t); MS: m/z 221 (M^+, 35 %), 56 (100 %); high resolution MS, calcd for $C_{12}H_{15}NO_3$: 221.1052, found: 221.1057.

2c: ^{1}H-NMR (CCl_4) δ 4.0 (4H, d, J=10 Hz + q), 2.95 (2H, dd, J=10 Hz, J<1 Hz), 2.45 (2H, d, J<1 Hz), 1.0 (3H, t); MS: m/z 157 (M^+, 1%), 56 (100 %); high resolution MS, calcd for $C_7H_{11}NO_3$ 157.0739, found: 157.0730.

3a: ^{1}H-NMR ($CDCl_3$) δ 5.75 (1H, m), 5.1 (3H, m), 4.1 (7H, m), 3.55 (2H, d), 2.05 (3H, s), 1.25 (3H, t); CI/CH_4 MS: m/z 246 (MH^+, 52 %), 188 (100 %).

3b: ^{1}H-NMR ($CDCl_3$) δ 7.3 (2H, m), 6.9 (3H, m), 5.1 (1H, broad), 4.1 (7H, m), 2.05 (3H, s), 1.25 (3H, t); MS: m/z 281 (M^+, 7 %), 188 (100 %); high resolution MS, calcd for $C_{14}H_{19}NO_5$ 281.1263, found: 281.1263.

3c: ^{1}H-NMR ($CDCl_3$) δ 6.6 (1H, broad), 4.5-3.6 (8H, m), 2.1 (3H, s), 1.3 (3H, t); MS: m/z 217 (M^+, 2 %), 157 (100 %); high resolution MS, calcd for $C_9H_{15}NO_5$ 217.0950, found: 217.0929.

4a: ^{1}H-NMR ($CDCl_3$) δ 5.75(1H, m), 5.2 (3H, m), 4.1 (7H, m), 3.5 (2H, m), 2.0 (3H, s), 1.25 (3H, t); CI/CH_4 MS: m/z 246 (MH^+, 62 %), 162 (100 %).

4b: ^{1}H-NMR ($CDCl_3$) δ 7.3 (2H, m), 6.9 (3H, m),4.9 (1H, broad), 4.1 (5H, m), 3.55 (2H, m), 2.1 (3H, s), 1.25 (3H, t); MS: m/z 281 (M^+, 7 %), 188 (100 %); high resolution MS, calcd for $C_{14}H_{19}NO_5$ 281.1263, found: 281.1260.

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References

1. Part of this paper has been presented at the 3rd European Symposium on Organic Chemistry, Canterbury, U.K., September 5-9, 1983, Abstract PB 49.
2. a) Ando, W. Acc. Chem. Res. 1977, 10, 179.
   b) Jendralla, H.; Pflaumbaum, W. Chem. Ber. 1982, 115, 210.
3. a) Ando, W.; Fujii, H.; Nakamura, I.; Ogino, N.; Migita, T. Int. J. Sulfur Chem. 1973, 8, 13.
   b) Aktinson, R. S.; Awad, S. B. J. Chem. Soc. Perkin Trans. 1 1977, 346.
   c) Kozlowska - Gramsz, E.; Descotes, G. J. Heterocycl. Chem. 1983, 20, 671.
4. Lociuro, S.; Pellacani, L.; Tardella, P. A. Tetrahedron Lett. 1983, 24, 593 and refs therein.

5. Takeuchi, H.; Takahashi, T.; Mashuda, T.; Mitani, M.; Koyama, K. *J. Chem. Soc. Perkin Trans*. **2** 1979, 1321.

6. Oxyamination of allyl aryl ethers has been recently reported: Bäckvall, J. E.; Björkman, E. E.; Byström, S. E.; Solladié-Cavallo, A. *Tetrahedron Lett*. 1982, **23**, 943.

7. Shingaki, T.; Inagaki, M.; Torimoto, N.; Takebayashi, M. *Chem. Lett*. 1972, 859; Torimoto, N.; Shingaki, T.; Nagai, T. *Bull. Chem. Soc. Jpn*. 1976, **49**, 2572.

8. Migita, T.; Chiba, M.; Takahashi, K.; Saitoh, N.; Nakaido, S.; Kosugi, M. *Bull. Chem. Soc. Jpn*. 1982, **55**, 3943 and refs therein.

9. For several methods of preparing β-amino alcohols see Barton, D.; Ollis, W. D. "Comprehensive Organic Chemistry" Sutherland, I. O.,Ed.; Pergamon Press, 1979,Vol. 2. Some recent reports on alkene oxyaminations are remarkable: Dubey, S. K.; Knaus, E. E. *Can. J. Chem*. 1983, **61**, 565; Sharpless, K. B.; Hori, T. *J. Org. Chem*. 1976, **41**, 176.

10. Leclerc, G.; Rouot, B.; Velly, J.; Schwartz, J. *Trends Pharmacol. Sci*. 1981, **2**, 18.

11. Takeuchi,H.;Koyama,K.*J. Chem. Soc. Perkin Trans*. **2** 1981, 121.

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