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ETHOXYCARBONYLNITRENE ADDITION TO VINYL CHLORIDES. SYNTHESIS AND THERMAL REARRANGEMENT OF α-CHLOROAZIRIDINES

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SUMMARY: The addition of ethoxycarbonylnitrene to vinyl chlorides gives N-ethoxycarbonyl-α-chloroaziridines which undergo an easy rearrangement mainly or exclusively to N-ethoxycarbonyl-2-chloro-2-alkenylamines.

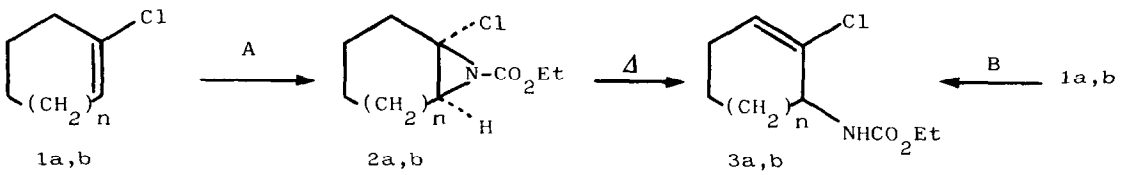
The low selectivity of ethoxycarbonylnitrene in addition and insertion reactions is exemplified in its reaction with cyclohexene, where all possible products have been found.[1] Later it was found that EtOCON in the singlet state seems to be coordinated by chlorine atoms of the solvent as well as of the substrate, in some cases.[2]

In this letter we report that vinyl chlorides add ethoxycarbonylnitrene, produced by triethylamine-induced α-elimination of ethyl p-nitrobenzensulphonyloxycarbamate,[3] to afford N-ethoxycarbonyl-α-chloroaziridines without appreciable contamination by insertion products. As shown in the Scheme, 1-chlorocyclohexene (1a), 1-chlorocycloheptene (1b), (Z) and (E)-5-chloro-4-nonene (4 and 8), all gave the corresponding addition product in yields ranging from 17 to 48%, the reaction being highly stereospecific as can be seen in the reaction of the last two substrates. The absence of any insertion product has been noted. The chlorine atom seems to have the power to sequestrate singlet EtOCON and to allow its stereospecific addition to a double bond. In fact, both singlet and triplet nitrenes are known to give addition reactions, but only the former species in a stereospecific fashion.[4]

When $EtOCON_3$ was thermolysed in the cyclic vinyl chlorides 1a and 1b, in a sealed tube at 100°C overnight, a 49% yield of 3a and a 22% yield of 3b were obtained. From 4 and 8 allylic and vinylic urethans 6 (probably the Z-isomer, vide infra) and 7 in a 2:1 ratio were isolated, together with variable amounts of 5 from 4.

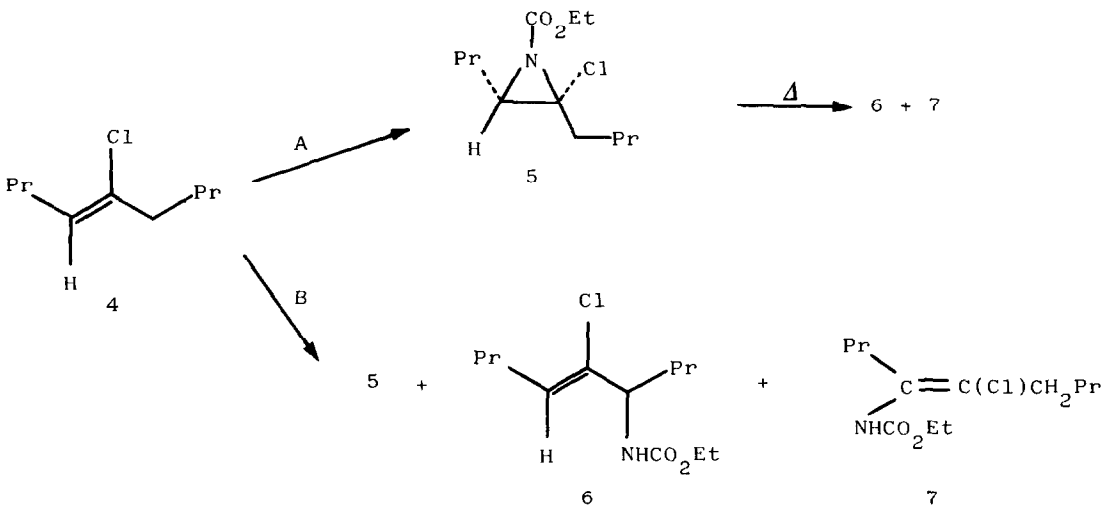
If the aziridines 2a, 2b, 5, and 9 were chromatographed on silica gel or allowed to stand for several days at room temperature or submitted to the thermolysis conditions, the same products from thermolysis were also obtained in

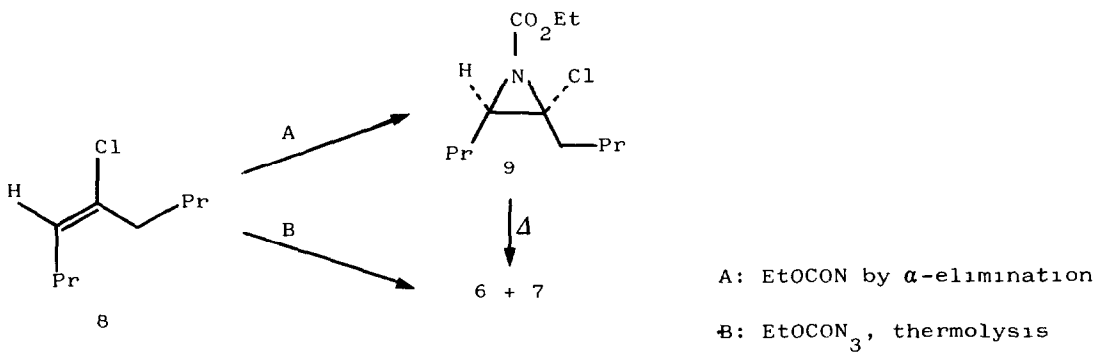
Scheme



1a,b 2a,b 3a,b

a,n=1;b,n=2





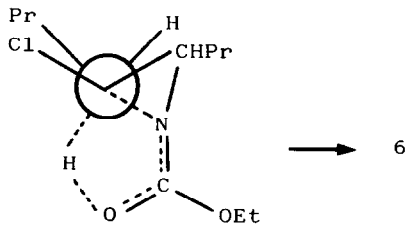
A: EtOCON by α-elimination

B: $EtOCON_3$, thermolysis

every case, suggesting that also in thermolysis the first products could have been aziridines,[5] which then rearranged in the reaction medium.

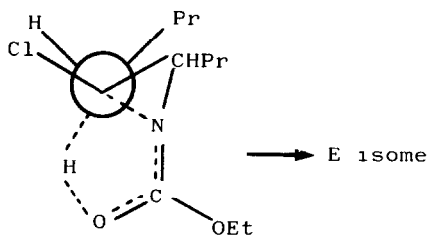
Interestingly, the rearrangement was regiospecific and, in the case of 5 and 9, highly stereoselective.[6]

The thermal isomerization of N-ethoxycarbonylaziridines has been reported to be only partial in similar or more severe conditions,[1] whereas some examples of facile isomerizations of N-acylaziridines are known.[7-9] For the latter cases a cyclic transition state was postulated and, if such a mechanism operates in our case, the stereoselective rearrangement of 5 and 9 to 6, can be accounted for by transition state 10a rather than 10b, since the latter requires eclipsing of the relatively bulky propyl groups, irrespective of the stereochemistry of the starting aziridines.



10a (preferred)

→ 6



10b

→ E isomer of 6

A zwitterionic intermediate, as proposed for N-sulphonylaziridines,[10] can be excluded, considering the observed stereoselectivity.

Experimental Procedure

N-Ethoxycarbonyl-1-chloro-7-azabicyclo[4.1.0]heptane (2a)

To a solution of 1.75 g (6.8 mmol) of ethyl p-nitrobenzensulphonyloxycarbamate in 21.5 ml of a mixture of 4.8 g (41.2 mmol) of 1-chlorocyclohexene and 23 ml of dichloromethane a solution of 8.4 ml (17 mmol) of triethylamine dissolved in 7.1 ml of the same 1-chlorocyclohexene : dichloromethane solution was added dropwise.

After stirring 3 hours at 35-40°C the solution was concentrated and diethyl ether was added. After salt filtration, the solvent and the unreacted 1-chlorocyclohexene were removed under vacuum at room temperature. A residue of 690 mg (50%) was obtained; IR (CCl_4) 1730, 1250 cm^{-1}; NMR (CCl_4) δ 4.15 (q, 2H); 2.8

(m, 1H); 2.2-0.9 (m+t, 11H); mass spectrum m/e 205, 203 (M^+), 168, 130, 69 (100%).

N-Ethoxycarbonyl-2-chloro-2-cyclohexenylamine (3a)

5 ml of 1-chlorocyclohexene (1a) and 0.5 ml of $EtOCON_3$ were heated at 100°C for 12 hours in a sealed tube. The unreacted 1-chlorocyclohexene was removed by vacuum distillation. The residue after chromatography on SiO_2, C_6H_6/EtOAc (99 : 1) afforded 480 mg (49% yield) of pure 3a, m.p. 65-67°C; IR (CCl_4) 3440, 3040, 1720, 1650 cm^{-1}; NMR (CCl_4) δ 5.92 (m, 1H); 4.80 (m, 1H); 4.05 (q+m, 3H); 2.05 (m, 2H); 2-1.4 (m, 4H); 1.23 (t, 3H); mass spectrum m/e 205, 203 (M^+), 90 (100%). Li/NH_3 reduction of 3a gave N-ethoxycarbonyl-2-cyclohexenylamine.[1]

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5. The intermediacy of a triazoline seems unlikely since 4 and 8 were recovered unchanged after exposure to $EtOCON_3$ at room temperature for two weeks.
6. The isomeric purity of 6 and 7, as well as the identity of products obtained starting from both 4 and 8 was verified by "double g.l.c." with glass capillary columns of Apiezon L and methylsilicone (OV 1).
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