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REACTION PATHS OF 1,3-OXAZOLINIUM SALTS WITH STABILIZED CARBANIONS

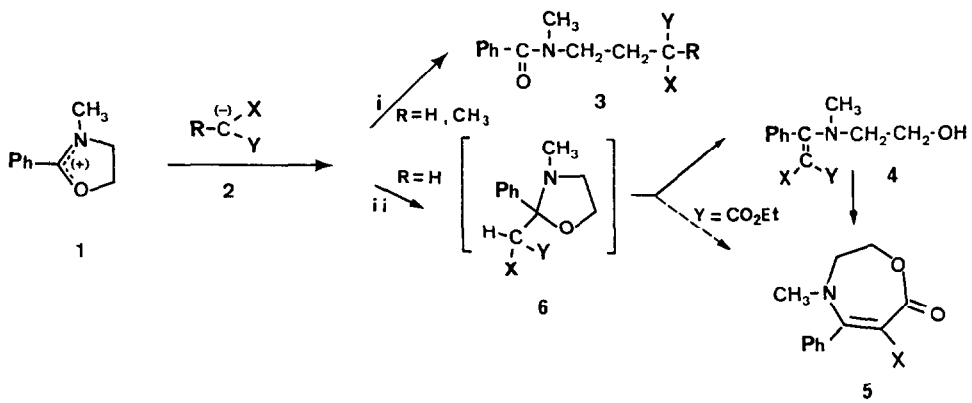
Martine DREME[1], Pierre LE PERCHEC[1], Jacques GARAPON[2] and Bernard SILLION[2]

[1]Laboratoire des Matériaux Organiques - CNRS - BP 24 - 69390 VERNAISON (France)
[2]Institut Français du Pétrole - BP 3 - 69390 VERNAISON (France)

ABSTRACT Reaction of stabilized carbanions with 3-methyl-2-phenyl-1,3-oxazolinium triflate occurs at both C_5 and C_2 sites with a regioselectivity depending partially on steric effects. The reaction at C_2 site can result in the formation of 1,4-oxazepin derivatives.

1,3-Oxazolinium salts are known to react readily with nitrogen[1], oxygen[2], sulfur[3] and halogen[2,4]nucleophiles. However, literature reports on reaction with carbon nucleophiles are limited to the formylation of organolithium and organomagnesium derivatives[5].

The condensation of 3-methyl-2-phenyl-1,3-oxazolinium triflate (1)[6] with stabilized carbanions (2) can follow two different paths : nucleophilic substitution (i) giving rise to a stable amido alkyl derivative (3) and addition (ii) forming opened product (4) and (or) heterocycle (5)[7], probably through an oxazolidine intermediate (6) :



1 + 2a (R = H,X = CN,Y = CO_2Et)	5a (85%)[8]
1 + 2b (R = H,X = Y = CN)	4b (85%)[9]
1 + 2c (R = CH_3,X = CN,Y = CO_2Et)	3c (50%)
1 + 2d (R = CH_3,X = Y = CN)	3d (75%)
1 + 2e (R = H,X = Y = SO_2Ph)	3e (85%)
1 + 2f (R = H,X = Y = CO_2Et)	3f (63%) + 5f (7%)[8]

The sodium salts of various carbanions (2) have been generated in THF using NaH as base. Thereafter, they were reacted at room temperature with one equivalent of (1) in THF solution. During the addition, the temperature of the mixture reached about 35°C. After standing for one night, the mixture was evaporated and its ethereal solution washed with water, dried and purified by liquid column chromatography. In most cases a single product was obtained. However, we have isolated 30% of N-(2-hydroxyethyl)N-methylbenzamide with 3c and 25% of ethyl bis(2-(N-benzoyl,N-methyl)aminoethyl)propanedioic acid ethylester issuing from 3f alkylation.

Our results point out that the regioselectivity of attack by carbanions (2) on the ambident salt (1) is at least partially governed by steric effects. Actually, the use of C.P.K. models shows that carbanions (2c-f) are indeed sterically crowded.

Related examples of ambident electrophilic reactivity have been analysed by Hünig[2] in terms of a competition between a kinetically controlled but reversible reaction at the sp^2 site and a thermodynamically controlled reaction at the sp^3 site. Further work is in progress to bring insight on this question and precise the factors (electronic versus steric) that govern this condensation.

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6) Salt (1) is prepared from 2-phenyl-oxazoline with methyl-trifluoromethane sulfonate at room temperature in ether. After crystallization in ethylacetate, white needles (mp = 81°C) are obtained, having a satisfactory elemental analysis : ($C_{11}H_{12}F_3NO_4S$) C, H, F, N, S.

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8) All compounds reported gave satisfactory IR and NMR spectra, exact mass and combustion analyses. Yields are based on purified products.
More particularly 5a and 5f have been fully identified :

5a : mp = 250°C ; IR (KBr) : 2200, 1665, 1660, 1590 cm^{-1}
^1H NMR (350 MHz, 40°C, DMSO d_6, TMS) δ: 2,77 (s,3H), 3,87-3,89 (m,2H), 4,51-4,53 (m,2H), 7,38-7,41 (m,2H meta), 7,52-7,54 (m,2H ortho + 1H para). ^{13}C NMR (20,1 MHz, DMSO d_6) δ: 43,9 (CH_3), 56,2 (N-CH_2), 64,6 (O-CH_2), 76,6 (C=C), 120,2 (CN), 127,7, 129,2, 130,1 (CH aromatic), 136,4 (C aromatic), 164,5 (C=C), 166,8 (O-C=O).

5f : mp = 175°C ; IR (KBr) : 1710, 1630, 1553 cm^{-1}
^1H NMR (350 MHz, DMSO d_6, TMS) : 0,73 (t, J = 7 Hz,3H), 2,68 (s,3H), 3,52 (q,J =7Hz 2H), 3,74-3,76 (m,2H), 4,41-4,43 (m,2H), 7,27-7,30 (m,2H meta), 7,41-7,43 (m, 2H ortho + 1H para). ^{13}C NMR (20,1 MHz, DMSO d_6) : 13,4 (CH_3), 42,8 (N-CH_3), 56,1 (N-CH_2), 60,2 (O-CH_2-CH_3), 65,5 (O-CH_2), 99,1 (C=C), 128,5 128,7 129,6 (CH aromatic), 136,1 (C aromatic), 158,2 (C=C), 167,5, 168,1 (O-C=O).

These two products 5a and 5f have also been studied by X-ray crystallography. Preliminary results gave structures consistent with our expectations. All the data will be reported in detail in a next paper with the collaboration of R. Faure and H. Loiseleur, Laboratoire de Chimie Analytique II, Université Claude Bernard, 43 boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex.

9) Alcohol 4b, a low melting solid, turned out to be difficult to purify. It was therefore converted into a stable urethane derivative with para-chlorophenyl isocyanate and the resulting solid characterized by IR, ^1H and ^{13}C NMR spectra and elemental analysis : ($C_{20}H_{17}N_4O_2Cl$) C, H, N, Cl; mp = 150°C.

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