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UNCATALYZED INSERTION REACTION OF ISOCYANIDES INTO A CARBON-SULFUR BOND

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Summary *Tert-butylisocyanide and tert-octylisocyanide insert into the carbone-sulfur bond of activated sulfides 2 yielding thioimidates 5 which rearrange to enamines 6.*

Isocyanides are stable nucleophilic carbenes. They gave insertion reactions into carbon-halogen bonds [1,2] or heteroatom-hydrogen bonds [1,3]. These last reactions can be catalyzed by groups IB and IIB metals and their salts, by acids or radical initiators [1,3]. Some uncatalyzed α-addition reactions to N-S bond [4], S-H bond [5] and S-Cl bond [6] are also known. In the present communication, we wish to report a new uncatalyzed formal insertion of isocyanide C atom into a carbon-sulfur bond activated by two electronegative groups.

Sulfides 2 were prepared by sulfenylation reaction of α-cyanoester anions 3 with N-alkylthio or N-phenylthiosuccinimides [7]. The reaction of isocyanides 1 (R^1 = tert-Bu, R^1 = tert-$BuCH_2CMe_2$) with sulfides was carried out without solvent at room temperature (method A) or in refluxing acetonitrile (method B), according to the reactivity of the sulfides 2. The method A allows to isolate most of the thioimidates 5A with R^2 given in table I [8]. Thioimidates 5A, except when R^3 = Ph, are unstable in solution. They rearrange at room temperature to give enamines 6A (two isomers). In other cases (R^2 = aryl, $PhCH_2$), the insertion reaction, slow at room temperature, requires a heating (method B) and yields the enamines 6B only (table II)[8] Thioimidates 5, precursors of compounds 6B, probably very unstable, were not obtained even through method A.

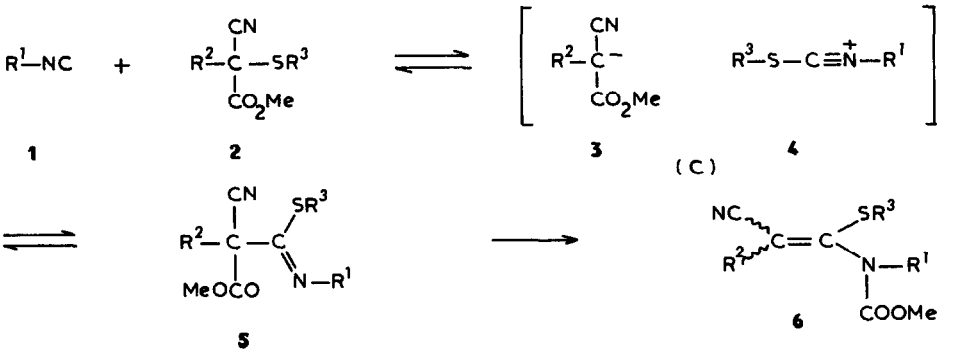
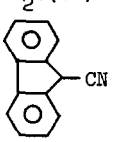


Table I - Thioimidates 5A and enamines 6A (method A)

R^1	R^2	R^3	Reaction time (hr)[a]	Thioimidates 5A m.p.(°C)	yield(%)[b]	Enamines 6A m.p.(°C)[c]	yield(%)(E+Z)[b]
tert-Bu	$Ph_2C(CN)$	Me	17	136	40	177	40
tert-Bu	$Ph_2C(CN)$	Ph	112	130	84	-	d
tert-Bu	$Ph_2C(CN)$	$PhCH_2$	18	145	75	192	6
tert-Oct	$Ph_2C(CN)$	Me	48	108	37	158, 128[e]	50
tert-Bu		Me	113	f	-	228	82
tert-Bu	$(PhCH_2)_2C(CN)$	Me	66	f	-	156, 125[e]	60
tert-Bu	Ph(Me)C(CN)	Me	114	94[g]	45	165	10
tert-Oct	Ph(Et)C(CN)	Me	72	125[g]	36	118	10

a - Reaction time corresponding to the complete conversion of the starting product 2 in the presence of 3 equiv. of isocyanide. Yields of 5A were optimized. b - Isolated product yield. c - One purified isomer (E or Z). d - The rearrangement 5 → 6 was not observed. e - Two purified isomers. f - Observed by NMR. A pure compound was not obtained. g - Only one diastereoisomer was observed.

Table II - Enamines 6B (method B)

R^1	R^2	R^3	Reaction time (hr)[a]	Yield (%) (E+Z)	m.p. (°C)
tert-Bu	$pCl\text{-}C_6H_4$	Me	7	94	114 [b]
tert-Bu	$pMeC_6H_4$	Me	48	75 [d]	154, 81 [c]
tert-Bu	$pMeOC_6H_4$	Me	68	82	100 [e]
tert-Bu	$pNO_2C_6H_4$	Me	87	68	110 [e]
tert-Bu	$PhCH_2$	Me	144 [f]	19	74 [b]
tert-Bu	Ph	Ph	20	50	66-68 [b]
tert-Bu	$pMeC_6H_4$	$PhCH_2$	22	90	130, 100 [c]
tert-Oct	$pClC_6H_4$	Me	6	40	88 [b]

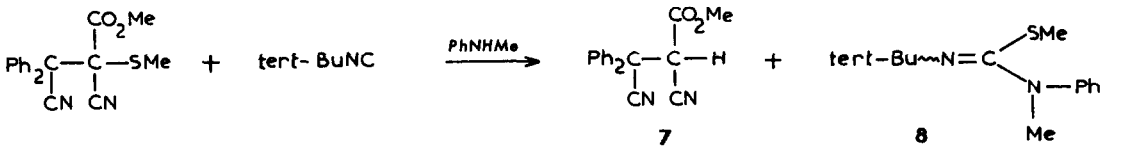
a - Reaction time corresponding to the complete conversion of the starting products. Isolated enamines yield. b - one purified isomer E or Z. c - two purified isomers. d - The enamine 6 was formed along with the coupling product [7] $(pMeC_6H_4C(CN)CO_2Me)_2$ (8 % yield). e - mixture of two isomers. f - solvent nitromethane.

We suggest that the first step of the reaction occurs via the heterolytic and reversible cleavage of the C-S bond of the sulfide giving an ion pair (C), according to the three following observations

Pure thioimidate 5A, R^1 = t-$BuCH_2CMe_2$, R^2 = $Ph_2C(CN)$, R^3 = Me was dissolved in $CDCl_3$ at room temperature. After 23 hr, NMR spectra of the solution showed the formation of a mixture of two isomers 6A and a small quantity of the starting sulfide 2.

When the reaction of tert-butylisocyanide with a pure diastereoisomer 2, R^2 = Ph(Me)C(CN), R^3 = Me, was stopped before the total conversion of the sulfide, we observed the formation of one diastereoisomer 5A and a mixture (60 40) of two diastereoisomers 2. This epimerization of the sulfide is in agreement with the reversible formation of the ion pair C.

Treatment of 2, R^2 = $Ph_2C(CN)$, R^3 = Me, with tert-butylisocyanide at room temperature in the presence of N-methylaniline (excess) yielded cyanoester 7 (70 %) and isothiourea 8 [10] (one isomer, 83 %). This result is in agreement with the trapping of anion 3 and nitrilium cation 4 (ion pair C) by the N-methylaniline.



We have shown that the isocyanide C atom can insert into some S-C bonds giving thioimidates which have been assuming much importance as intermediates in organic synthesis [9]. However, the reaction is restricted to electrophilic sulfides with good living group. For example, sulfides 9 and 10 do not react with isocyanides. Reactions of the sulfides 2 with isocyanides that carry an α-hydrogen atom and the mechanism of the transposition 5 → 6 are under investigation.

Me—CO—CH(Ph)SPh

9

Ph—C(Me)(CN)—SMe

10

References and notes

1 - I. UGI, Isonitrile Chemistry, Academic Press, New York, 65 (1971).

2 - M. TORDEUX and C. WAKSELMAN, Tetrahedron, 37, 315 (1981).

3 - T. SAEGUSA and Y. ITO, Synthesis, 291 (1975).
D. MARMET, P. BOULLANGER and G.DESCOTES, Tetrahedron Lett., 21, 1459 (1980).
A.F. HEGARTY and A. CHANDLER, Tetrahedron Lett., 21, 885 (1980).

4 - J.P. CHUPP, J.J. D'AMICO and K.L. LESCHINSKY, J. Org. Chem., 43, 3553 (1978).

5 - J.P. CHUPP and K.L. LESCHINSKY, J. Org. Chem., 40, 66 (1975).

6 - A.J. HAVLICK and M.M. WALD, J. Amer. Chem. Soc., 77, 5171 (1955).

7 - G.MOREL, E. MARCHAND and A. FOUCAUD, Tetrahedron Lett. 3719 (1978).
G.MOREL, M.A. LE MOING-ORLIAC, S. KHAMSITTHIDETH and A. FOUCAUD, Tetrahedron, in press.

8 - All isolated compounds had spectral properties (IR, NMR) and elemental analysis in accord with their assigned structures. For instance, spectral data for 6B, R^1 = tert-Bu, R^2 = pMeC$_6$H$_4$, R^3 = Me, isomer m.p. 81° IR 2195, 1717, 1552 cm^{-1}, ^{1}H NMR ($CDCl_3$, δ) 1.65 (s, 9H) 2.14 (s, 3H) 2.38 (s, 3H) 3.74 (s, 3H) 7.4 (m, 4H). ^{13}C NMR ($CDCl_3$, δ) 15.5 (q, S-$\underline{C}H_3$) 21.4 (q, C_6H_4-$\underline{C}H_3$) 28.7 (m, C($\underline{C}H_3$)$_3$) 52.9 (q, O$\underline{C}H_3$) 60.8 (m, $\underline{C}(CH_3)_3$) 114.8 (t, ^3J = 3.9 Hz, C_6H_4-$\underline{C}$=) 118.1 (s, $\underline{C}$≡N) 129.0, 129.4, 129.5, 139.7 ($\underline{C}_6H_4$) 153.9 (q, ^3J = 3.9 Hz, =$\underline{C}$-SMe) 154.0 (q, ^3J = 3.9 Hz, $\underline{C}$=O).

9 - D.G. NEILSON, in "The Chemistry of amidines and imidates", S. Patai Ed., J. Wiley and Sons, London, 385 (1975).

10 - Isothiourea 8, $E_{0.02}$ = 80°C, ^{1}H NMR ($CDCl_3$) δ = 1.37 (s, 9H) , 2.03 (s, 3H) , 3.12 (s, 3H) , 7.15 (m, 5H). MS exact mass at m/e 236.1335 (calc. for $C_{13}H_{20}N_2S$ 236.1347).

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