## UNCATALYZED INSERTION REACTION OF ISOCYANIDES INTO A CARBON-SULFUR BOND

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<u>Summary</u> Tert-butylisocyanide and tert-octylisocyanide insert into the carbone-sulfur bond of activated sulfides 2 yielding this  $\frac{5}{2}$  which rearrange to enamines  $\frac{6}{2}$ .

Isocyanides are stable nucleophilic carbenes. They gave insertion reactions into carbon-halogen bonds <sup>1,2</sup> or heteroatom-hydrogen bonds <sup>1,3</sup>. These last reactions can be catalyzed by groups IB and IIB metals and their salts, by acids or radical initiators <sup>1,3</sup>. Some uncatalyzed  $\alpha$ -addition reactions to N-S bond <sup>4</sup>, S-H bond <sup>5</sup> and S-Cl bond <sup>6</sup> 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  $\underline{2}$  were prepared by sulfenylation reaction of  $\alpha$ -cyanoester anions  $\underline{3}$  with N-alkylthio or N-phenylthiosuccinimides <sup>7</sup>. The reaction of isocyanides  $\underline{1}$  (R<sup>1</sup> = tert-Bu, R<sup>1</sup> = tert-BuCH<sub>2</sub>CMe<sub>2</sub>) 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  $\underline{2}$ . The method A allows to isolate most of the thioimidates  $\underline{5A}$  with R<sup>2</sup> given in table I <sup>8</sup>. Thioimidates  $\underline{5A}$ , except when R<sup>3</sup> = Ph, are unstable in solution. They rearrange at room temperature to give enamines  $\underline{6A}$  (two isomers). In other cases (R<sup>2</sup> = aryl, PhCH<sub>2</sub>), the insertion reaction, slow at room temperature, requires a heating (method B) and yields the enamines  $\underline{6B}$  only (table II)<sup>8</sup> Thioimidates  $\underline{5}$ , precursors of compounds  $\underline{6B}$ , probably very unstable, were not obtained even through method A.



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

R <sup>1</sup>	R <sup>2</sup>	r <sup>3</sup>	Reaction time (hr) <sup>a</sup>	Thioimic m.p.(°C)	lates <u>5A</u> yıeld(%) <sup>b</sup>	Enar m.p.(°C) <sup>C</sup>	nines <u>6A</u> yield(%)(E+Z) <sup>b</sup>
tert-Bu	Ph <sub>2</sub> C(C <sup>™</sup> )	Me	17	136	40	177	40
tert-Bu	Ph <sub>2</sub> C(CN)	Ph	112	130	84	-	d
tert-Bu	Ph <sub>2</sub> C(CN)	PhCH <sub>2</sub>	18	145	75	192	6
tert-Oct	Ph <sub>2</sub> C(CN)	Me	48	108	37	158, 128 <sup>e</sup>	50
tert-Bu		Me	113	f	-	228	82
tert-Bu	(PhCH <sub>2</sub> ) <sub>2</sub> C(CN)	Me	66	f	-	156, 125 <sup>e</sup>	60
tert-Bu	Ph(Me)C(CN)	Me	114	94 <sup>66</sup>	45	165	10
tert-Oct	Ph(Et)C(CN)	Me	72	125 <sup>8</sup>	36	118	10
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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  $5 \rightarrow 6$  was not observed. e - Two purified isomers. f - Observed by NMR. A pure compound was not obtained. g - Only one diastereoisomer was observed.

R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Reaction time (hr) <sup>a</sup>	Yield (%) (E+Z)	m.p. (°C)
tert-Bu	pc1-c6H4	Me	7	94	114 <sup>b</sup>
tert-Bu	$p^{MeC}6^{H}$	Me	48	75 <sup>d</sup>	154, 81 <sup>c</sup>
tert-Bu	$\mathtt{pMeOC}_{6}\mathtt{H}_{l_{j_{1}}}$	Me	68	82	100 <sup>e</sup>
tert-Bu	pn0 <sub>2</sub> c6 <sup>H</sup> 4	Me	87	68	110 <sup>e</sup>
tert-Bu	PhCH <sub>2</sub>	Me	144 <sup>f</sup>	19	74 <sup>b</sup>
tert-Bu	Ph	Ph	20	50	66-68 <sup>b</sup>
tert-Bu	р <sup>MeC</sup> 6 <sup>H</sup> ц	PhCH <sub>2</sub>	22	90	130, 100 <sup>c</sup>
tert-Oct	pClC <sub>6</sub> H <sub>4</sub>	Me	6	40	88 <sup>b</sup>

## Table II - Enamines <u>6B</u> (method 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  $\underline{6}$  was formed along with the coupling product  $7(pMeC_{6}H_{4}C(CN)CO_{2}Me)_{2}$  (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 <u>5A</u>,  $R^1 = t-BuCH_2CMe_2$ ,  $R^2 = Ph_2C(CN)$ ,  $R^3 = Me$  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 <u>6A</u> and a small quantity of the starting sulfide <u>2</u>.

When the reaction of tert-butylisocyanide with a pure diastereoisomer  $\underline{2}$ ,  $R^2 = Ph(Me)C(CN)$ ,  $R^3 = Me$ , was stopped before the total conversion of the sulfide, we observed the formation of one diastereoisomer  $\underline{5A}$  and a mixture (60 40) of two diastereoisomers  $\underline{2}$ . 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 <u>7</u> (70 %) and isothiourea <u>8</u> <sup>10</sup> (one isomer, 83 %). This result is in agreement with the trapping of anion <u>3</u> and nitrilium cation <u>4</u> (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 <sup>9</sup>. However, the reaction is restricted to electrophilic sulfides with good living group. For example, sulfides <u>9</u> and <u>10</u> do not react with isocyanides. Reactions of the sulfides <u>2</u> with isocyanides that carry an  $\alpha$ -hydrogen atom and the mechanism of the transposition  $\underline{5} + \underline{6}$  are under investigation.

## References and notes

- 1 I. UGI, Isonitrile Chemistry, Academic Press, New York, 65 (1971).
- 2 M. TORDEUX and C. WAKSEIMAN, 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., <u>43</u>, 3553 (1978).
- 5 J.P. CHUPP and K.L. LESCHINSKY, J. Org. Chem., <u>40</u>, 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 <u>6B</u>,
  R<sup>1</sup> = tert-Bu, R<sup>2</sup> = pMeC6H4, R<sup>3</sup> = Me, isomer m.p. 81° IR 2195, 1717, 1552 cm<sup>-1</sup>,
  <sup>1</sup>H NMR (CDC1<sub>3</sub>, δ) 1.65 (s, 9H) 2.14 (s, 3H) 2.38 (s, 3H) 3.74 (s, 3H) 7.4 (m, 4H).
  <sup>1</sup>3C NMR (CDC1<sub>3</sub>, δ) 15.5 (q, S-CH<sub>3</sub>) 21.4 (q, C6H4-CH<sub>3</sub>) 28.7 (m, C(CH<sub>3</sub>)<sub>3</sub>) 52.9 (q, 0CH<sub>3</sub>)
  60.8 (m,C(CH<sub>3</sub>)<sub>3</sub>) 114.8 (t, 3J = 3.9 Hz, C6H4-C=) 118.1 (s, C=N) 129.0, 129.4, 129.5, 139.7 (C6H4) 153.9 (q, 3J = 3.9 Hz, =C-SMe) 154.0 (q, 3J = 3.9 Hz, 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 = 80°C, <sup>1</sup>H NMR (CDCl<sub>2</sub>)  $\delta$  = 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<sub>13</sub>H<sub>20</sub>N<sub>2</sub>S 236.1347).

(Received in France 19 January 1982)