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THIOCYANATES AND ISOTHIOCYANATES. EQUILIBRIUM, KINETICS AND MECHANISMS OF ISOMERIZATION

A. Iliceto, A. Fava and U. Mazzucato

Istituti di Chimica della Facolta' di Scienze,
Universita' di Padova, Italy

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THIOCYANIC acid esters have long been known to undergo thermal isomerization to give the corresponding isothiocyanic acid esters. Although the isomerization reaction is believed to be quite general and is frequently used as a synthetic route to isothiocyanates, little is known about its nature and mechanism. We wish to report here a number of observations which may have considerable mechanistic significance.

Saturated systems, kinetics

In all cases recorded in the literature,[1] drastic temperature conditions are required to obtain isomerization; this

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[1] See for istance: [a] A.W.Hofmann, Ber. **13**, 1349 (1880); [b] J.Gillis, Rec. Trav. Chim. **39**, 330 (1920); [c] E.Schimdt W. Striewsty, M.Seefelder and F.Hitzler, Ann. **568**, 192 (1950); [d] H.Hennicke, Ann. **344**, 24 (1906); [e] H.L.Wheeler, Amer. Chem. Jour. **26**, 345 (1901).

appears to be often accompanied by extensive decomposition. Milder conditions can be adopted, however, in the presence of electrophilic catalysts, such as $ZnCl_2$ or CdI_2.[1b,1c] The catalytic action of electrophilic agents suggests that the isomerization may occur by way of an ionization mechanism. To test this hypothesis, we have investigated a number of systems which, because of the nature of the organic substrate, would be expected to ionize readily. The benzhydryl substrate has been proved ideal in this respect, since the isomerization was found to take place at relatively low temperatures, smoothly and to the exclusion of side reactions. Some representative kinetic results are reported under Table I. The rate of isomerization appears to be considerably accelerated by polar media, by the presence of 'inert' salts and by the introduction of electron releasing substituents in the organic moiety: the latter effect is comparable in magnitude [in methyl ethyl ketone, $\rho \simeq 3{,}5$ (calculated from Brown's σ^+)[2]] to that observed for the solvolysis of benzhydryl chlorides in ethanol ($\rho = 4{,}05$).[2] These

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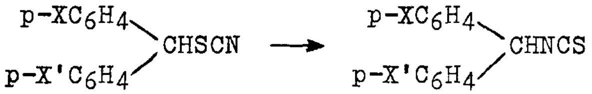
[2] Y. Okamoto and H.C. Brown, J. Org. Chem. 22, 485 (1957).

TABLE I

First-order rate coefficients [a] for the isomerization of benzhydryl thiocyanates:



$$(p\text{-}XC_6H_4)(p\text{-}X'C_6H_4)CHSCN \longrightarrow (p\text{-}XC_6H_4)(p\text{-}X'C_6H_4)CHNCS$$

Compound		Solvent	t° C	10^5 k (sec^{-1})
X	X'			
H	H	MeEtCO	90	2.2
		MeCN	90	32
		MeEtCO + $NaClO_4$ 0.1M	90	6.0
		MeEtCO	50[b]	0.026
CH_3	CH_3		50	7.8
H	H		130[b]	77
NO_2	H		130	0.25

[a] Determined by I.R. spectrophotometry.

[b] Extrapolated from data taken between 70° and 90°.

effects point consistently towards a rate determining ionization. Whether ionization involves dissociation, or stops to some kind of ion-pair,[3] the results cannot tell. Experiments of exchange and **simultaneous** isomerization which are now under way, will clarify this point. Whatever the detailed mechanism may be, it appears likely that an ionization mechanism is applicable for most saturated systems.

Allylic systems, kinetics

Allylic thiocyanates appear to isomerize at much faster rates than other systems (e.g. benzyl) of comparable electron releasing ability. This behaviour is attributed to the allylic structure providing a path to isomerization through an intramolecular rearrangement. The correctness of this view was proved in 1940 by Mumm and Richter[4] who showed that, upon heating, crotyl thiocyanate is converted to α-methylallyl isothiocyanate:

$$CH_3CH{=}CHCH_2SCN \longrightarrow CH_3CH(NCS)CH{=}CH_2$$

and more recently by us[5] for γ,γ-dimethylallyl thiocyanate. Although these are the only mechanistic studies so far performed, an intramolecular mechanism is believed to hold for most allylic

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[3] S. Winstein, E. Clippinger, A.H. Fainberg, R. Heck and G.C. Robinson, J. Amer. Chem. Soc. **78**, 328 (1956).

[4] O. Mumm and H. Richter, Ber. **73**, 483 (1940).

[5] Unpublished results.

thiocyanates.[6] However, with no kinetic data at hand, the details of the mechanism remained obscure. The kinetic results summarized in Table II allow a better particularization of the

TABLE II

First-order rate coefficients[a] at 60° for the isomeric rearrangement of allylic thiocyanates:

$$RR'C{=}CHCH_2SCN \longrightarrow RR'C(NCS)C{=}CH_2$$

Compound		$10^5\ k_{60^o}(sec^{-1})$		$(k_A/k_C)_{60^o}$
R	R'	A[b]	C[b]	
H	H	1,8	3,3	0,5
CH_3[c]	H	27	31	0,9
CH_3	CH_3	270 [d]	96 [d]	3

[a] **Determined by U.V. spectrophotometry.**

[b] **A and C stand for acetonitrile and cyclohexane solver respectively.**

[c] **trans**

[d] **Extrapolated from lower temperature data.**

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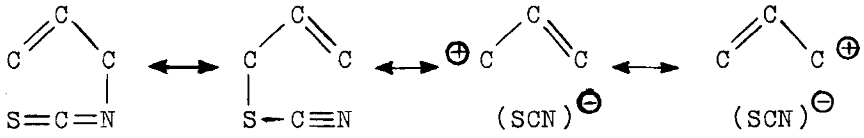
[6] R. H. DeWolfe and W. G. Young, Chem. Rev. **56**, 856 (1956).

intramolecular mechanism. Most helpful to this end, is the combined consideration of solvent and structure effects. As shown, the rate of isomerization increases in the sequence: allyl < γ-methylallyl < γ,γ-dimethylallyl, the variation being more pronounced in the more polar solvent. Thus, the reaction appears to be favored by electron releasing substituents, the more so in the more polar solvent. Moreover, it is interesting to remark that, while for allyl and γ-methylallyl thiocyanates the reaction is faster in cyclohexane than in acetonitrile, the reverse is true for γ,γ-dimethylallyl thiocyanate. In any case, it has to be noted that, considering the wide polarity difference of the solvents concerned, these medium effects are quite small.

In agreement with the above evidence, it appears that a satisfactory representation of the transition state can be given in terms of the following structures:



I II III IV

This description is essentially that given by Young, Winstein and Goering[7] for the rearrangement of α,α-dimethylallyl chloride. The main distinction between that rearrangement and the present ones, lies in the different weight carried by the ionic structures, III and IV, with respect to the purely covalent ones, I and II. In the present example, the smallness of the structure and solvent effects[8] and especially the direction of the latter for the first two members, strongly indicate that the bonding in the transition state is largely, though not wholly, covalent.

Equilibrium

The reverse change, isothiocyanate to thiocyanate has never been clearly established. We have now found evidence that in the isomerization of thiocyanates an equilibrium is reached in which substantial amounts of thiocyanate may be present.

Some representative results are collected in Table III.

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[7] W.G. Young, S. Winstein and H.L. Goering, J. Amer. Chem.Soc. 73, 1958 (1951).

[8] At first sight these effects may not seem to be small. However, in the reactions of allylic systems which occur by way of an ionization mechanism, much larger solvent and structure effects are observed. For a summary of data, see A. Streitweiser, Jr., Chem. Rev. 56, 650 (1956).

TABLE III

Equilibrium thiocyanate/isothiocyanate at 100° in different media.

Compound	% of thiocyanate at equilibrium[a]			Conc. m/l
	Pure	cyclohexane	acetonitrile	
Benzhydryl	-	<1	2-3	0.1-0.75
allyl	<1	<1	9-11 (3)[b]	10^{-3} - 10^{-1}
γ-methyl-allyl	11	5	27	10^{-3}
γ,γ-dimethyl-allyl	40	18	50	10^{-3}

[a] Analysis by U.V. and I.R. spectrophotometry.

[b] In methyl ethyl ketone.

As shown, either in the pure state or in non polar solvents, the fraction of thiocyanate at equilibrium is generally too small to be detected, while it becomes appreciable in polar media such as acetonitrile or methyl ethyl ketone. This behaviour is consistent with the greater dipole moment of thiocyanates, which consequently become stabilized in such media.

The equilibrium may be pushed further to the thiocyanate side whenever the isomerization proceeds by way of a molecular rearrangement which produces a less stable carbon skeleton. This appear to be the case of γ-methyl substituted allylic thiocyanates for which, in the isomeric rearrangement, there is loss of hyperconjugation energy due to the isolation of the double bond from the methyl group(s). In this connection, the observed[9] failure of γ-phenylallyl thiocyanate to undergo isomeric rearrangement can be conveniently explained on equilibrium grounds. In fact, due to the conjugation of the allylic double bond with the phenyl ring, γ-phenylallyl thiocyanate may be stabilized, with respect to α-phenylallyl isothiocyanate, to the point that, at equilibrium, the latter is not even detectable. This viewpoint is further substantiated by the fact that, in the attempted preparation of α-phenylallyl isothiocyanate from α-phenylallyl amine and carbon disulphide, the only product which could be isolated was γ-phenylallyl thiocyanate.[10]

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[9] E. Bergmann, J. Chem. Soc. **1935**, 1361.

[10] A. Iliceto and G. Gaggia, Gazz. Chim. Ital. **90**, 262 (1960).