Thiocyanates and Isothiocyanates. III.[1] Kinetics and Mechanism of Benzhydryl Thiocyanates Isomerization

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The isomerization of benzhydryl thiocyanates to isothiocyanates follows first-order kinetics. The rate is strongly affected by solvent polarity and by addition of salts to the reaction medium, the effects being of the same magnitude as for reactions in which ions are formed from neutral substrates. Substitution in the 4- and 4'-positions of the phenyl rings causes large variations in the isomerization rate. Treatment of the structural effects by means of the Hammett equation (using Brown's σ^+)[16] yields a ρ-value of -3.4. Isomerization of benzhydryl thiocyanate in the presence of S^{35}-labeled thiocyanate ions indicates that ion pairs are the major intermediate, even in a polar solvent like acetonitrile.

Although the isomerization of alkyl thiocyanates to give isothiocyanates has been known for nearly a century, its nature and mechanism has received little attention up to very recently. In a preliminary communication[1a] we have presented a number of observations of mechanistic significance dealing with the isomerization of thiocyanates of allylic and of benzhydrylic structure. While for the former an intramolecular route seems to be preferred, for the latter systems the evidence indicated that the isomerization takes place by way of a rate-determining ionization. Supported by a few scattered observations existing in the literature (catalysis by electrophilic agents, ease of isomerization paralleling the stability of the carbonium ion) the suggestion was also made that an ionization mechanism is likely to apply to most saturated systems. The same suggestion was recently made by Rensom, who reviewed this matter.[2]

Shortly after our first report, two other independent investigations have appeared on this subject: In the first of these, Rao and Balasubrahmanyam[3] give some rate data on the isomerization of methyl thiocyanate; in the second, Smith and Emerson[4] report a number of observations on a variety of structurally different thiocyanates and also arrive at the conclusion that ionization is likely to be the critical step in the isomerization of most saturated thiocyanates.

In this paper we report the detailed kinetic results obtained from thiocyanates with benzhydrylic structure. These results supplement those previously given[1a] and, together with some tracer experiments which are also reported, allow a better understanding of the ionization mechanism.

Results and Discussion

The kinetic results are collected in Table I.

Reaction Order.—The reaction order appears to be unity. This arises from the linearity of the semilog plots of the isomerization fraction *versus* time up to 80% reaction (see Experimental) and more significantly from runs 14 and 15 in which a 300-fold variation of the initial concentration was

TABLE I
RATE OF ISOMERIZATION OF BENZHYDRYL THIOCYANATES[a]

Run	Substituent in position 4	4'	Solvent	Salt, molarity × 10²		Temp., °C.	10^5k, sec.⁻¹
1	H	H	Benzene			90.0	0.187
2						130.0	5.28
3			MEK[b]			75.0	0.390
4						90.0	1.88
5				NaClO₄	1.98		2.40
6					4.07		2.85
7					6.14		3.34
8					10.1		4.17
9				NaSCN	2.03		2.57
10					4.09		3.34
11					7.70		4.20
12					10.7		5.40
13			MeCN[c]			75.0	6.65
14						80.0	11.1 ± 0.1
15[d]							11.4 ± 0.3
16						85.0	18.6
17						90.0	28.6 ± 0.3
18						70.0	3.91
19				NaClO₄	2.08		4.20
20					4.12		4.40
21					6.14		4.69
22					10.2		5.09
23				NaSCN	2.00		4.47
24					4.27		4.90
25					6.47		5.31
26					10.6		5.76
27			DMF[e]			70.0	7.1
28	Cl	H	MEK[b]			85.0	1.03
29						90.0	1.58
30			MeCN[c]			70.0	2.57
31						75.0	3.62
32						80.0	6.80
33						85.0	11.3
34						90.0	17.5
35	Cl	Cl	MEK[b]			90.0	0.894
36			MeCN[c]			90.0	10.0
37	NO₂	H	MEK[b]			131.0	0.4
38			MeCN[c]			110.0	0.77
39	CH₃	H	MEK[b]			70.0	4.68
40			MeCN[c]			50.0	8.47
41	CH₃	CH₃	MeC₆H₁₁[f]			100.0	2.1
42			Benzene			70.5	3.40
43						75.0	5.05
44						80.0	7.34
45						90.1	17.7
46			MEK[b]			50.0	7.80
47			MeCN[c]			0.0	0.36
48						20.0	4.97
49						25.0	8.79
50						30.0	14.7
51						35.0	25.5

[a] Except for Run 15, initial concentration 0.15 M and analysis by infrared spectrophotometry. [b] Methyl ethyl ketone. [c] Acetonitrile. [d] Initial concentration 5 × 10⁻⁴ M and analysis by ultraviolet spectrophotometry. [e] Dimethylformamide. [f] Methylcyclohexane.

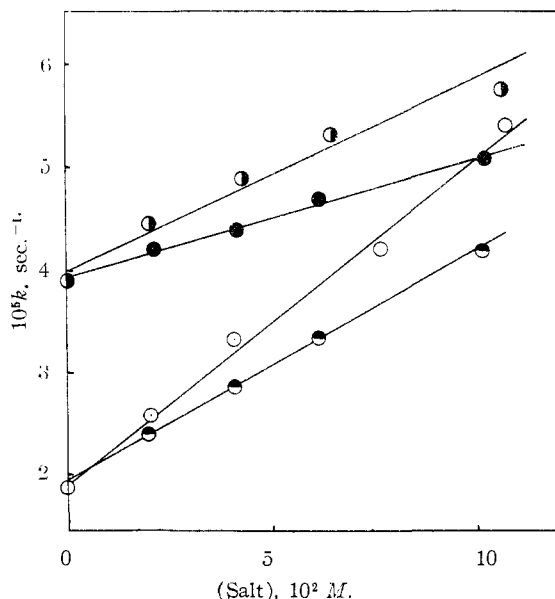made; the resulting variation of the first-order specific rate is less than 3%.

(1) Previous papers in this series: (a) I, A. Iliceto, A. Fava and U. Mazzucato, *Tetrahedron Letters*, **11**, 27 (1960); (b) II, A. Iliceto, A. Fava, U. Mazzucato and P. Radici, *Gazz. chim. ital.*, **90**, 919 (1960).

(2) M. Rensom, *Bull. Soc. roy. Sci. (Liège)*, **29**, 78 (1960); this and ref. 1a,b and 4 should be consulted for the existing literature.

(3) C. N. R. Rao and S. N. Balasubrahmanyam, *Chemistry & Industry*, 625 (1960).

(4) P. A. S. Smith and D. W. Emerson, *J. Am. Chem. Soc.*, **82**, 3076 (1960).

Fig. 1.—Plots of k vs. salt concentration for the isomerization of benzhydryl thiocyanate. The symbols   and O apply to NaClO₄ and NaSCN, respectively, in methyl ethyl ketone at 90°; ● and ◑ apply to NaClO₄ and NaSCN in acetonitrile to 70°.

Solvent Effect.—For the study of the solvent effect the selection of media has been made among solvents which would neither react with isothiocyanates, nor divert the reaction course by intercepting electron-deficient intermediates eventually formed during isomerization. The latter possibility, although offering an interesting way to get information concerning the reaction mechanism, was felt as an unnecessary complication at this stage. The media employed (methylcyclohexane, benzene, methyl ethyl ketone, acetonitrile and dimethylformamide) span a sufficiently large polarity range to allow an easy appreciation of the effect. For the benzhydryl substrate, at 90°, the rates in methyl ethyl ketone (run 4), acetonitrile (run 17) and dimethylformamide (run 27) relative to benzene (run 1) are 10, 150 and 280,[5] respectively. Runs 42 through 51 allow a similar comparison to be made for the 4,4'-dimethylbenzhydryl substrate. At 50°, the rates in methylcyclohexane, methyl ethyl ketone and acetonitrile, relative to benzene, are 0.06,[6] 16 and 220, respectively. Thus the isomerization rate is quite sensitive to solvent change, *the magnitude of the effect being of the same order as for reactions in which ions are produced from neutral substrates.* For example, the ratio of the rate in methyl ethyl ketone to that in benzene (10 and 16) is comparable to the ratio in acetone to that in benzene (13) for the reaction of pyridine with methyl iodide.[7] Similarly, the ratio of the isomerization rate in benzene to that in methylcyclohexane (17) is similar to the ratio in benzene to that in hexane (17) observed for formation of p-nitrobenzyltrimethylammo-

(5) Estimated from the rate ratio dimethylformamide to acetonitrile at 70°.

(6) At 100°.

(7) J. F. Norris and S. W. Prentiss, *J. Am. Chem. Soc.*, **50**, 3042 (1928).

nium chloride from p-nitrobenzyl chloride and trimethylamine.[8] More to the point is the comparison with reactions which proceed by way of a rate-determining unimolecular ionization. Thus, the ratio of rates in acetonitrile and benzene (150 and 220) compare with the ratios, *ca.* 120, observed for the rearrangement of camphene hydrochloride,[9] and 28, observed for the rearrangement of 9-decalyl perbenzoate.[10] Both of these reactions are believed to occur by way of ionization processes which in the solvents above probably stop at the intimate ion-pair stage.[11]
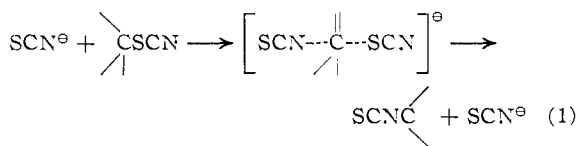
Salt Effect.—The addition of salts to the reaction medium increases the rate of isomerization, the effect being greater in the less polar solvents. The pertinent runs are 4–12 for methyl ethyl ketone, and 18–26 for acetonitrile solvent.

The salt effect may be conveniently analyzed by treating the data by means of the Winstein[12] equation for "normal" salt effects and evaluating the

$$k = k_0 (1 + b \, [\text{salt}])$$

values of the coefficient b. The plots of k *versus* molarities of added salt (Fig. 1) yield good straight lines up to the highest concentration employed (0.1 M). For sodium thiocyanate and sodium perchlorate the b-values are (in parentheses the average fit % of k): 16.7 (2.3) and 11.7 (1.2) in methyl ethyl ketone and 4.27 (2.3) and 2.93 (0.6) in acetonitrile. These values *fit nicely the general pattern of normal salt effect for ionization reactions in poorly ionizing media.*[13]

Sodium thiocyanate appears to be more effective than sodium perchlorate in promoting isomerization in both solvents. The greater effect of sodium thiocyanate could perhaps be due to a concurrent isomerization arising from a direct displacement by the nitrogen end of thiocyanate ion

$$\text{SCN}^\ominus + \begin{matrix}\backslash \\ /\end{matrix}\text{CSCN} \longrightarrow \left[\text{SCN}\cdots\overset{\parallel}{\underset{/}{\text{C}}}\cdots\text{SCN} \right]^\ominus \longrightarrow$$

$$\text{SCN}\overset{/}{\underset{\backslash}{\text{C}}} + \text{SCN}^\ominus \quad (1)$$

However, although this latter possibility cannot be entirely eliminated, a specific salt effect seems more likely. This view is strongly supported by the consideration of the ratio $b_{\text{MeEtCO}}/b_{\text{MeCN}}$ which appears to be independent of the nature of the salt (3.99 and 3.92 for sodium perchlorate and sodium thiocyanate, respectively). The effect lies well within the limits of the specificity of different salts in promoting ionization.[13,14]

Structural Effects.—The isomerization rate appears to be very sensitive to substituent effects, the reaction being favored by increasing the elec-

(8) H. V. Halban, *Z. physik. Chem.*, **84**, 129 (1913).

(9) H. Meerwein and K. V. Einster, *Ber.*, **55**, 2500 (1922). The relative rate reported here is a rough estimate made by utilizing data at different temperatures.

(10) R. Criegee and R. Kaspar, *Ann.*, **560**, 127 (1948).

(11) For a discussion of these rearrangements see for instance: (a) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956); (b) S. Winstein and G. C. Robinson, *J. Am. Chem. Soc.*, **80**, 169 (1958).
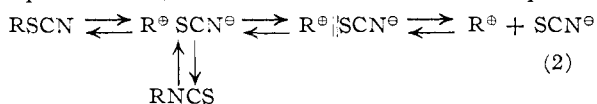
(12) S. Winstein, E. Clippinger, A. Fainberg and G. C. Robinson, *ibid.*, **76**, 2597 (1954), and subsequent papers in the series.

(13) S. Winstein, S. Smith and D. Darwish, *ibid.*, **81**, 5511 (1959).

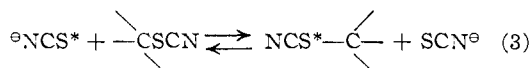(14) S. Winstein and J. S. Gall, *Tetrahedron Letters*, **2**, 31 (1960).

tron releasing power of the organic moiety. The results in Table I can be correlated by the Hammett plot of Fig. 2.[15] With Brown's σ^+,[16] the rate data fit very closely a linear free energy relationship with slopes of -3.33 in acetonitrile at 70°, and -3.40 in methyl ethyl ketone at 90° (correlation coefficients 0.998 and 0.996, respectively). While there seems not to be any appreciable solvent effect on the reaction constant, the value of the latter appears to be of the same order as for solvolytic reactions which occur by a rate-determining ionization. For instance, the solvolysis of benzhydryl chlorides in ethanol yields $\rho = -4.05$.[16,17]

Tracer Experiments and Mechanism.—The evidence outlined above with regard to kinetic order, solvent, salt and substituent effects leaves little doubt that *the isomerization of benzhydryl thiocyanates occurs by way of a rate-determining ionization.* The evidence, however, does not indicate whether the ionization process involves dissociation into separate ions, or into some kind of ion-pair.[18]

$$RSCN \rightleftarrows R^\oplus SCN^\ominus \rightleftarrows R^\oplus{}_{||}SCN^\ominus \rightleftarrows R^\oplus + SCN^\ominus$$

$$\uparrow\downarrow \qquad\qquad (2)$$

$$RNCS$$

Exchange experiments (see below) give some information about this point. When isomerization was allowed to occur in the presence of labeled ionic thiocyanate, isotopic exchange took place simultaneous to isomerization. Under the conditions: 0.01 M NaS^{35}CN, 0.1 M benzhydryl thiocyanate, 0.09 M sodium perchlorate in acetonitrile at 70°, an initial rate of exchange of 1.6 × 10^{-6} mole. l.$^{-1}$sec.$^{-1}$ was measured. In a particular experiment, in which isomerization proceeded for 10% and exchange for 25%, the specific activities of all reactants and product were separately measured and found to be (relative values): thiocyanate 1.00, isothiocyanate 2.19, inorganic thiocyanate 36.5.

Since the activity of the isothiocyanate is greater than that of thiocyanate, at least part of the activity must have entered the organic substrates by way of a reaction which is not a direct displacement

$$^\ominus NCS^* + {}^{\textstyle\diagdown}\!\!-\overset{\textstyle\diagup}{\underset{\textstyle\diagdown}{C}}SCN \rightleftarrows NCS^*-\overset{\textstyle\diagup}{\underset{\textstyle\diagdown}{C}}- + SCN^\ominus \quad (3)$$

From the above considerations of the salt effects on the rate of isomerization it does not seem likely that reaction 1 is responsible for the excess activity in the isothiocyanate. More likely this excess activity arises from a reaction of thiocyanate ion with an electron-deficient intermediate common to isomerization. However, the *total* activity of the organic reactants is far less than would be calculated had the isomerization occurred by an ionization mechanism in which the "organic" SCN group becomes equilibrated with SCN$^-$ in solution.

The implication of these results is that *the isomerization of benzhydryl thiocyanate in acetonitrile*

(15) Since the various compounds span a reactivity range of over four powers of ten, extrapolation of relative rates to lower or higher temperatures has been extensively used in making the plot.

(16) Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957).

(17) J. F. Norris and C. Banta, *J. Am. Chem. Soc.*, **50**, 1804 (1928).

(18) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **78**, 328 (1956).
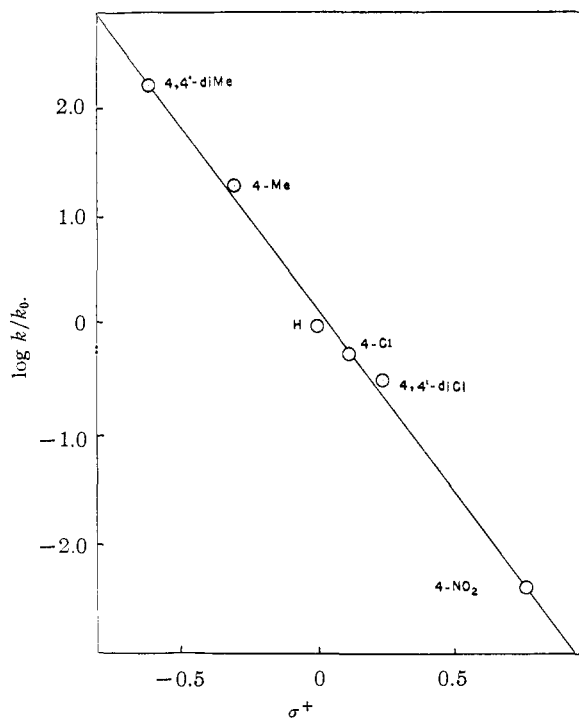

Fig. 2.—Plot of log k/k_0 *vs.* σ^+ for the isomerization of benzhydryl thiocyanates in acetonitrile at 70°

proceeds by way of an ionization mechanism which does not involve dissociation, except possibly to a small extent.

Establishment of the fraction of intermediate ion-pairs which undergo exchange rather than internal return is a difficult task since it requires the knowledge of (i) the fraction of radioactivity which has entered the organic substrates *via* the direct displacement 3 and (ii) the fraction of intimate ion-pairs which return to thiocyanate. To obtain these quantities a great deal of systematic work is necessary. At the present time we can only set an upper limit for the *fraction of ionic intermediates which undergo exchange rather than internal return to isothiocyanate.* This limit is calculated by simply assuming that all activity in the organic substrates has entered *via* the ionization path. Thus, from the first-order rate coefficients for exchange ($k_e = 1.6 \times 10^{-5}$) and isomerization ($k_t = 5.11 \times 10^{-5}$), an upper limit of 31% is calculated. (It may be observed that this is also the maximum fraction of intermediates which undergo exchange rather then internal return, either to thio- or to isothiocyanate.)

Nothing can be said about which particular ionic intermediate is involved in the exchange. Since the exchange cannot fail to occur on formation of separated ions, the minimum fraction of all ionic intermediates which do not dissociate is 69%. This percentage, however, is liable to be much greater since a sizable fraction of ionic intermediates also must return to thiocyanate.[19]

(19) L. G. Cannell and R. W. Taft, Jr. (129th National Meeting of the Am. Chem. Soc., Dallas, Tex., April 8–13, 1956: Abstracts of Papers, Organic Division, p. 40-N) have studied the reaction of thiocyanate ion with carbonium ion-forming substrates and evaluated competition factors, S to N, which range between 2 and 9.

The picture derived from these results and discussion is reminiscent of that which, since 1951,[20] has been give for a rather large number of systems which undergo molecular rearrangement simultaneous to solvolysis or exchange. The case most closely related to the present one is that of racemization and isotopic exchange of p-chlorobenzhydryl chloride which have been recently communicated by Winstein and collaborators.[14,21] Unfortunately our results are too preliminary to allow an interesting quantitative comparison between the two systems. Systematic work is now in progress in this Laboratory.

Activation Parameters.—The rate data collected in Table I allow the evaluation of the activation parameters for a number of systems (Table II). Two features are worth pointing out: (i) in a given solvent the structural effect acts essentially on the energy term; and (ii) for a given substrate, the solvent effect acts essentially on the entropy term.

TABLE II

ACTIVATION PARAMETERS FOR ISOMERIZATION OF BENZHYDRYL THIOCYANATES

Thiocyanate	Solvent	$E_{a,b}$	log A^a	ΔS^{*c}
4-Chlorobenzhydryl	Acetonitrile	25.22	11.42	− 8.5
Benzhydryl		24.84	11.41	− 8.5
4,4'-Dimethyl-		20.67	11.08	−10.0
benzhydryl	Benzene	20.76	8.72	−20.8

a Arrhenius parameters. *b* Kcal./mole. *c* At 70°; kcal./mole degree.

This behavior is in keeping with the notion that, independently of substrate and solvent, the essential nature of the transition state is that of an ion-pair. Thus, in a given solvent, while solvation phenomena stay nearly constant, less energy is needed to create the ion-pair as the carbonium ion becomes intrinsically more stable. On the other hand, for a given substrate the process of creating the ion-pair differs from one solvent to another, mainly in the nature and extent of solvation.
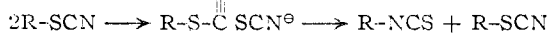
The lower activation entropy in benzene compared to that in acetonitrile simply reflects the fact that the latter is a highly associated liquid. Thus the formation of the ion-pair produces, relative to the transition state, a more orderly state of affairs in benzene than in acetonitrile.

The Possibility of Mechanisms other than Ionization.—It has been said in the introduction that apart from thiocyanates of allylic structure, for which an intramolecular concerted mechanism seems to be the preferred route,[1a,4] all other thiocyanates for which reliable information is available appear to fit the pattern of an ionization mechanism. Most of the pertinent information is summarized in refs. 1a and 4 and needs no elaboration. Since, however, other mechanisms have been proposed,[3,4] a brief discussion of their relative merits seems to be warranted.

(20) W. G. Young, S. Winstein and H. L. Goering, *J. Am. Chem. Soc.*, **73**, 1851 (1951).

(21) (a) S. Winstein, J. S. Gall, M. Hojo and S. Smith, *ibid.*, **82**, 1010 (1960); (b) S. Winstein, M. Hojo and S. Smith, *Tetrahedron Letters*, **22**, 12 (1960).

One such mechanism is bimolecular[4] in which the isomerization takes place by way of a direct dis-

$$\begin{array}{c} \text{R} \\ | \\ \text{N}^\oplus \qquad\qquad (4) \\ | \\ 2\text{R-SCN} \longrightarrow \text{R-S-C SCN}^\ominus \longrightarrow \text{R-NCS} + \text{R-SCN} \end{array}$$

placement by the nitrogen end of one thiocyanate molecule on the α-carbon of another, then a second displacement by the thiocyanate ion first formed. This mechanism seems, however, unlikely to apply to any substrate because of the very low nucleophilicity of the nitrogen atom of organic thiocyanates. Indeed, such a reaction could be effective only when the C–S bond is almost completely heterolyzed. The nitrogen end of the thiocyanate ion, formed within the same solvent cage, is a much more powerful nucleophile than the starting material, but is in a much more favorable position to collapse directly to rearranged product than to react with a second molecule of starting material. Thus an intramolecular process would be favored over an intermolecular one.

A second possibility involves an intramolecular cyclic mechanism in which the breaking of the C–S bond is simultaneous to, or follows, the formation of the C–N bond. Of course, the ionization mechanism which has been found to apply in the benzhydryl case is largely intramolecular in the sense that the two fragments, carbonium and thiocyanate ions, tend to remain within the same solvent cage. However, all the evidence is against a concerted process or a process in which the formation of the C–N bond is rate determining.[22] The geometry of the C—S—C≡N grouping provides a distance, alkyl-C to N, of about 4.5 Å.[23] Clearly the nitrogen atom is too far removed for the bond making and breaking to be included in the same transition state, without a prohibitive bending of the S–CN bond angle.

Experimental

Solvents.—Methylcyclohexane was shaken several times with a mixture of concentrated nitric and sulfuric acids in the cold. After repeated washings with water, the solvent was dried over Drierite and fractionally distilled from potassium; b.p. 100.8–100.9°. Reagent grade benzene was refluxed over sodium–potassium alloy and distilled. Reagent grade methyl ethyl ketone was refluxed over potassium permanganate, distilled, dried over Drierite and redistilled; b.p. 79.3–79.4°. Acetonitrile was first dried over Drierite, refluxed over phosphorus pentoxide and distilled. From the redistillation over anhydrous potassium carbonate the fraction b.p. 81.5–81.6° was collected. Reagent grade dimethylformamide was dried over Drierite and distilled under reduced pressure.

4-Nitrobenzhydryl Bromide.—4-Nitrodiphenylmethane, obtained by a Friedel–Crafts reaction of commercial 4-nitrobenzyl chloride with benzene, was oxidized with chromic acid in acetic acid to give 4-nitrobenzophenone.[24] The ketone was reduced by Meerwein–Ponndorf procedure to the corresponding alcohol which was converted to the

(22) This latter view has actually been taken by Rao and Balasubrahmanyam[2] for the isomerization of methyl thiocyanate, *against their own evidence*. In fact, beside finding a high and positive entropy of activation, they observe that the reaction becomes immeasurably slow when carried out in a non-polar solvent (toluene) rather than in the pure state. Both observations are obviously incompatible with the mechanism they assume, but in keeping with the ionization hypothesis.

(23) C. I. Beard and B. P. Dailey, *J. Am. Chem. Soc.*, **71**, 929 (1949).

(24) A. Baeyer and V. Villiger, *Ber.*, **37**, 605 (1904).

bromide on treatment with PBr_3, as reported for the preparation of benzhydryl bromide.[25] The substance was crystallized from petroleum ether; m.p. 32–34°.

Anal. Calcd. for $C_{13}H_{10}NO_2Br$: Br, 27.39. Found: Br, 26.77.

4-Chlorobenzhydryl Bromide.—Commercial 4-chlorobenzophenone was reduced (Meerwein–Ponndorf) to the alcohol. This was converted to the bromide by reaction with hydrogen bromide in ether. The product was crystallized from petroleum ether; m.p. 39–40°.

Anal. Calcd. for $C_{13}H_{10}ClBr$: Br, 28.41. Found: Br, 28.65.

4-Methylbenzhydryl Bromide was similarly obtained, starting from commercial 4-methylbenzophenone. The compound was crystallized from petroleum ether; m.p. 19–20.5°.

Anal. Calcd. for $C_{14}H_{13}Br$: Br, 30.64. Found: Br, 30.31.

4-Nitrobenzhydryl Thiocyanate.—A solution of 9 g. of 4-nitrobenzhydryl bromide and 3.6 g. of potassium thiocyanate in 50 ml. of acetone was allowed to stand at room temperature for 12 hours. After filtration of potassium bromide, the solvent was removed under vacuum and the residue shaken with water–benzene. The organic layer was washed with water, dried over sodium sulfate and the solvent removed under reduced pressure. The residue was crystallized from 1:1 benzene–ether; m.p. 105–106° (89%).

Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: N, 10.35; S, 11.85. Found: N, 10.34; S, 11.98.

4-Chlorobenzhydryl thiocyanate was similarly obtained and crystallized from 1:1 ether–petroleum ether at −20°; m.p. 38.5–39.5°.

Anal. Calcd. for $C_{14}H_{10}NClS$: N, 5.40; Cl, 13.58; Found: N, 5.45; Cl, 13.54.

4-Methylbenzhydryl Thiocyanate.—The crude product obtained from the reaction of 4-methylbenzhydryl bromide with alkali thiocyanate in acetone was found to contain about 10% of isothiocyanate. It was dissolved in cyclohexane and the solution treated with cyclohexylamine (100% excess on the isothiocyanate). After the mixture had stood at 0° for 1 hour the thiourea was removed by filtration and the solution was washed first with dilute hydrochloric acid, then with water and finally dried over Drierite. The solvent was removed under reduced pressure to give a viscous oil. Infrared analysis showed it to contain less than 2% of isothiocyanate. This product was used without further purification.

Anal. Calcd. for $C_{15}H_{13}NS$: N, 5.85; S, 13.41. Found: N, 5.79; S, 13.15.

4-Nitrobenzhydryl Isothiocyanate.—A solution of 0.5 g. of the corresponding thiocyanate and 0.01 g. of zinc chloride in 5 ml. of acetonitrile was heated at 70° for 40 hours and then poured into water–carbon tetrachloride. The organic layer was repeatedly washed with water, dried over Drierite and evaporated under vacuum to a thick oil. This was sublimed at 130° and 0.05 mm. pressure. The product was crystallized from 1:1 ether–petroleum ether; m.p. 52.4–53.8° (50%).

N-(4-Nitrobenzhydryl)-N′-phenylthiourea was obtained from 4-nitrobenzhydryl isothiocyanate and aniline in benzene. Crystallization from acetone–petroleum ether gave a product which melted at 143–144.5°.

Anal. Calcd. for $C_{20}H_{17}N_3O_2S$: C, 66.10; H, 4.68; N, 11.56. Found: C, 66.15; H, 4.81; N, 11.60.

4-Chlorobenzhydryl Isothiocyanate.—The corresponding thiocyanate was heated at 100° in acetonitrile for 6 hours. Distillation under reduced pressure gave a pale yellow oil, b.p. 150–152° (0.1 mm.), $n^{25}D$ 1.6298.

N-(4-Chlorobenzhydryl)-N′-phenylthiourea, prepared as for the 4-nitro derivative, melted at 168–168.5°.

Anal. Calcd. for $C_{20}H_{17}N_2ClS$: C, 68.10; H, 4.82; N, 7.94; S, 9.09; Cl, 10.05. Found: C, 67.68, H, 4.91; N, 7.93; S, 9.32; Cl, 10.21.

4-Methylbenzhydryl Isothiocyanate.—A concentrated solution in acetonitrile of the crude thiocyanate (see above) was refluxed for 2 hours. Distillation gave an oil, b.p. 139–141° (0.1 mm.), $n^{25}D$ 1.6165.

(25) L. Claisen, *Ann.,* **442**, 245 (1925).

N-(4-Methylbenzhydryl)-N′-cyclohexylthiourea was obtained from the isothiocyanate and cyclohexylamine in cyclohexane and had, after crystallization from acetone, m.p. 170–171°.

Anal. Calcd. for $C_{21}H_{26}N_2S$: N, 8.28; S, 9.49. Found: N, 8.48; S, 9.50.

All other thiocyanates and isothiocyanates used in this study and not described under this section are those previously reported.[1b]

Labeled sodium thiocyanate (S^{35}) was prepared as previously described.[26] Sodium perchlorate and sodium thiocyanate were commercial reagent grade dried and stored over P_2O_5.

Kinetic Measurements.—Weighed amounts of the organic thiocyanate (and salt, if any) were dissolved and brought to volume in the appropriate solvent to make up a nearly 0.15 M solution. This was divided into portions, sealed in vials and placed in a constant temperature bath (±0.1°). For each run, 7 to 10 samples were withdrawn at times such as to give a regular coverage up to 60 to 80% reaction, and subsequently analyzed for isothiocyanate by infrared spectrophotometry. The wave length was selected in the region 2040–2080 cm.$^{-1}$ (—N≡C≡S pseudo-asymmetrical stretching)[27] in conjunction with the absorption maximum for the respective isothiocyanate. A Perkin–Elmer model 21 double beam instrument was used. Standard solutions of sodium thiocyanate were used to compensate for the absorption of thiocyanate ion in those runs where the effect of sodium thiocyanate upon the rate was studied.

The rate of formation of isothiocyanate follows a first-order law,[28] at least up to 80% reaction, with deviations which stay within 5%. The greater deviations were observed for the less reactive compounds and solvents, *i.e.*, where rather high temperatures and long heating times were involved. A typical run (run 17 in Table I) is reported in detail below:

Time, sec. × 10^{-2}	6	9	12	15
Reacn., %	16.2	22.7	29.4	34.7
$10^4 k$, sec.$^{-1}$	2.92	2.85	2.90	2.83
Time, sec. × 10^{-2}	19.2	24	30	39
Reacn., %	42.3	49.6	59.6	67.0
$10^4 k$, sec.$^{-1}$	2.87	2.85	2.81	2.84

In an experiment (run 15 in Table I) the initial concentration was $5 \times 10^{-4} M$. In this case the analysis was carried out by ultraviolet spectrophotometry, the rate being obtained from the increase of the optical density at 255 mμ. At this wave length the molar extinction coefficients for benzhydryl thiocyanate and isothiocyanate, in acetonitrile, are, respectively, 1290 and 1680. A Beckman model DU instrument was used.

Tracer Experiments.—For measuring the rate of isotopic exchange between benzhydryl thiocyanate and sodium thiocyanate, a solution in acetonitrile of the organic reactant (0.2 M) was mixed with an equal volume of a solution in the same solvent of (labeled) sodium thiocyanate 0.02 M and sodium perchloride 0.18 M, divided in portions and sealed in vials. At intervals, samples were withdrawn and the separation effected by pouring in water–hexane. The organic layer was washed three times with water (containing some non-radioactive sodium thiocyanate), diluted with ethanolic silver nitrate and refluxed for 1 hour. The precipitate, which consisted of silver thiocyanate and silver sulfide, was oxidized to sulfuric acid with bromine. The inorganic thiocyanate in the aqueous layer was converted to sulfuric acid also by treating the solution with bromine. Counting was effected on "thick layer" barium sulfate disks. This separation procedure yielded practically nil zero-time exchange fractions.

As expected, the exchange data do not fit the usual McKay equation for stable exchanging systems.[29] In fact,

(26) A. Fava and A. Iliceto, *Ricerca Sci.,* **25**, 54 (1955).

(27) For a discussion of the infrared spectra of thio- and isothiocyanates see: U. Mazzucato, A. Foffani, A. Iliceto and G. Svegliado, IVth Meeting of European Molecular Spectroscopists, Bologna, Italy, September 7–12, 1959, and references therein.

(28) Since the equilibrium constant is of the order of ≥40,[1b] no appreciable contribution can be expected from the reverse reaction.

(29) A. C. Wahl and N. A. Bonner (Editors), "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 11.

the plots of log $(1 - F)$ versus time are non-linear and flatten considerably at the higher fractions of exchange. However, initial rates can be easily obtained graphically.

In the experiment where the activities of thio- and isothiocyanate were separately measured, the separation of the two organic species was performed by treating the hexane layer with cyclohexylamine (100% excess, calculated on the isothiocyanate formed) and cooling at 0° for 30 minutes. The crystals (N-cyclohexyl-N'-benzhydrylthiourea) were filtered, washed with hexane and dissolved in ethanol.

Silver nitrate was added and the mixture refluxed. Silver sulfide was filtered off and oxidized to sulfuric acid with bromine. The hexane solution containing the unreacted benzhydryl thiocyanate was diluted with ethanolic silver nitrate and refluxed. The precipitate consisted largely of silver thiocyanate, but contained also traces of silver sulfide, presumably in part from incompletely separated thiourea. It was therefore heated with aqueous ammonia, filtered and the solution treated with nitric acid to precipitate silver thiocyanate, which was oxidized.

# The Reinterpretation of Several Kharasch Reactions. A Question of Free Radical Displacements at Saturated Carbon Atoms

BY LYNN H. SLAUGH

Many reactions of Grignard reagents with organic halides in the presence of cobaltous salts apparently involve the formation of free radicals by the removal of a halogen atom from the organic halide. It has been found that interchange reactions between the Grignard reagent and the organic halide are important competing reactions and may determine the product. For example, an interchange reaction producing, transiently, 3-phenoxypropylmagnesium bromide and not the formation of the 3-phenoxypropyl radical, as previously postulated, is believed to be responsible for cyclopropane formation during the cobaltous bromide-catalyzed reaction of 3-phenoxypropyl bromide with Grignard reagents. Other reactions of this type have been reinterpreted in light of this finding. The decomposition of di-t-butyl peroxide in a chlorobenzene solution containing 1-iodobutane was studied in a further search for a reaction involving a free radical displacement at a saturated carbon atom. t-Butyl n-butyl ether, the anticipated product of displacement on 1-iodobutane by the t-butoxy radical, was not detected in the product.

Introduction

Kharasch discovered that several transition metal salts, e.g., cobaltous chloride, catalyze a reaction between Grignard reagents and organic halides[1] (referred to hereafter as "Kharasch reactions"). He proposed the following mechanism to explain the formation of the observed products.

$$RMgX + CoX_2 \longrightarrow RCoX + MgX_2$$

$$RCoX \longrightarrow R\cdot + CoX$$

$$R'X + CoX \longrightarrow R'\cdot + CoX_2$$
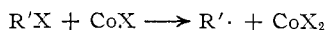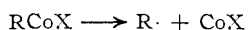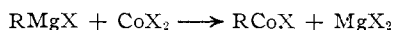
He postulated the formation of intermediate subhalides (CoX in the present case) which abstract halogen atoms from the organic halides to produce free radicals. The free radicals thus formed disproportionate, couple etc. The following are further evidences for the formation of free radicals. (a) 2,3-Dimethyl-2,3-diphenylbutane is formed when these reactions occur in a solvent containing cumene.[2] (b) Rearrangement products are obtained from the Kharasch reaction of neophyl chloride (1-chloro-2-methyl-2-phenylpropane).[3] (c) 9,-10-Dibenzyl-9,10-dihydroanthracene, 10,10'-dibenzyl-9,9'10,10'-tetrahydro-9,9'-dianthryl and a trace of 9,10-dibenzylanthracene result from the Kharasch reaction of benzyl chloride with benzylmagnesium chloride[4] in the presence of anthracene.[6]

Several particularly interesting Kharasch reactions have resulted in the formation of cyclopropane from 3-phenoxypropyl bromide (I),[7] bicyclo-[3.1.0]hexane from 1,3-dibromocyclohexane[8] and cyclobutane from 1,4-dibromobutane[9] or 4-phenoxybutyl bromide.[7,9] These reactions have been interpreted as involving free radical intermediates (eq. 1-3).[8,9]

$$C_6H_5OCH_2CH_2CH_2\cdot \longrightarrow \underset{CH_2-CH_2}{\overset{CH_2}{\diagup\diagdown}} \quad (1)$$

$$+ \text{ "acceptor molecule"} \longrightarrow \quad (2)$$

Br   Br-acceptor molecule

$$BrCH_2CH_2CH_2CH_2\cdot \longrightarrow \underset{CH_2-CH_2}{\overset{CH_2-CH_2}{\mid \quad \mid}} + Br\cdot \quad (3)$$

Although it is unlikely, there is the possibility that the formation of the above products involved free radical displacements at saturated carbon atoms. Since this type of displacement is rare, it seemed of interest to reinvestigate the Kharasch reaction of I to form cyclopropane. It was further hoped that this study would shed light on the mechanisms of these and other Kharasch reactions.

Results and Discussion

Decarbonylation of 4-Phenoxybutyraldehyde.—To check the possibility that the cyclopropane from the Kharasch reaction of I was formed via the 3-phenoxypropyl radical, the latter was generated,

(1) M. S. Kharasch and O. Reinmuth. "Grignard Reactions of Nonmetallic Substances." Prentice Hall, Inc., New York, N. Y., 1954.

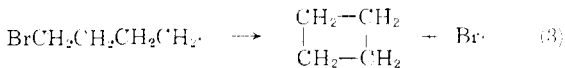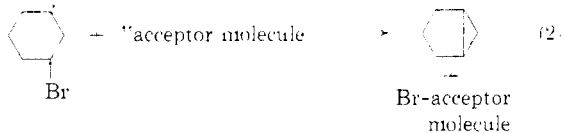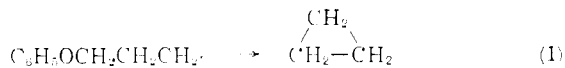(2) M. S. Kharasch and W. H. Urry, J. Org. Chem., **13**, 101 (1948).

(3) W. H. Urry and M. S. Kharasch. J. Am. Chem. Soc., **66**, 1438 (1944).

(4) Although evidences indicate that some Grignard reagents are best represented as $R_2Mg\cdot MgX_2$[5] they will be referred to as alkylmagnesium halides for simplicity in this publication.

(5) R. E. Dessy. G. S. Handler, J. H. Wotiz and C. A. Hollingsworth, J. Am. Chem. Soc., **79**, 3476 (1957); R. E. Dessy and G. S. Handler, ibid., **80**, 5824 (1958).

(6) R. O. C. Norman and W. A. Waters, J. Chem. Soc., 950 (1957).

(7) M. S. Kharasch. G. Stampa and W. Nudenberg, J. Org. Chem., **18**, 575 (1953).

(8) M. S. Kharasch. J. S. Sallo and W. Nudenberg. ibid., **21**, 129 (1956).

(9) W. B. Smith. ibid., **23**, 509 (1958).