998. *Thiocyanogen, Thiocyanates, and Isothiocyanates. Part IV.*[1] *Addition, Substitution, and Substitutive Reduction between Triphenylmethyl Isothiocyanate and Alcohols or Amines*

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Competitive reactions of the types $Ph_3C{\cdot}NCS \longrightarrow Ph_3CH$, Ph_3CX, or $Ph_3C{\cdot}NH{\cdot}CS{\cdot}X$ are reported. Uncatalysed reaction with some secondary alcohols results in reduction of the isothiocyanate to triphenylmethane and dehydrogenation of the alcohol to a ketone; triphenylmethyl bromide reacts similarly. Analogous oxidation–reduction occurs between the isothiocyanate and some tertiary amines. Alkoxide-catalysed reaction of a primary or secondary alcohol with the isothiocyanate gives an ether by substitution or a thiocarbamate by addition. Non-aromatic primary or secondary amines react additively, and in some cases reversibly, giving thiourea derivatives; substitution is more difficult than with alcohols. Aniline, ammonia, and acetamide react only by substitution.

Triphenylmethyl isothiocyanate is known to behave exceptionally towards nucleophiles in the sense that substitution, with release of thiocyanate ion, competes strongly with addition to the N:C:S group, which is a more characteristic reaction of isothiocyanates. Using alcohols or amines, we have observed not only these types of reaction, but also reduction to triphenylmethane. These three alternatives are represented in the following generalised scheme (R = Ph_3C), in which the possibility of reversibility is indicated for the addition (1) and the substitution (2):

$$R{\cdot}NCS \rightleftharpoons R{\cdot}\overset{-}{N}{\cdot}CS{\cdot}\overset{+}{X}{\cdot}H \rightleftharpoons R{\cdot}NH{\cdot}CS{\cdot}X \quad (1)$$

$$\downarrow\uparrow\ (\pm XH)$$

$$R^+NCS^- \rightleftharpoons RX + NCS^- + H^+ \quad (2)$$

$$\downarrow\ (+XH)$$

$$RH + NCS^- + X^+;\ X^+ \longrightarrow (X - H) + H^+ \quad (3)$$

Previously reported reactions of triphenylmethyl isothiocyanate with salts and acids [1] were substitutions, except that formic acid caused reduction (3; X − H = CO_2), and the reaction with trifluoroacetic acid probably proceeded through an intermediate addition product.

The experiments of Iliceto *et al.*,[2] in which n-butylamine and aniline were compared, indicate that a reagent of high nucleophilicity is needed if addition to the N:CS bond of triphenylmethyl isothiocyanate is to be achieved; otherwise substitution occurs, this process being aided by solvents which favour formation of the Ph_3C^+ ion. Alcohols are weaker nucleophiles than amines and show little tendency to add to isothiocyanates except in the presence of basic catalysts.[3,4] We have shown [1] that methanol and ethanol react reversibly and substitutively with triphenylmethyl isothiocyanate to give the triphenylmethyl alkyl ethers. Reaction has now been examined with the secondary alcohols, propan-2-ol, octan-2-ol, cyclopentanol, and cyclohexanol, at their boiling points. In no case was addition observed; cyclohexanol caused ether formation and reduction to triphenylmethane in an approximately 1 : 4 ratio; in octan-2-ol and cyclopentanol the reduction was nearly quantitative and no ether was isolated.

Isothiocyanate–alcohol interactions are obviously complex, and the result is probably governed by several polar, steric, and environmental factors. The dominant effect for

[1] Part III, R. G. R. Bacon, J. Köchling, and T. A. Robinson, *J.*, 1964, 5600.
[2] A. Iliceto, A. Fava, and U. Mazzuccato, *J. Org. Chem.*, 1960, **25**, 1445.
[3] S. J. Assony in "Organic Sulfur Compounds," vol. I, ed. N. Kharasch, Pergamon Press, 1961.
[4] C. N. R. Rao and R. Venkataraghavan, *Tetrahedron*, 1962, **18**, 531; 1963, **19**, 1509.

these readily oxidised secondary alcohols (at ~140—180°) was displacement of NCS by H, which can plausibly be represented as a hydride-ion transfer to the CPh_3^+ ion:

$$Ph_3C^+NCS^- + RR'CH{\cdot}OH \longrightarrow Ph_3CH + NCS^- + (RR'C^+{\cdot}OH \longleftrightarrow RR'C{\cdot}\overset{+}{O}H) \longrightarrow RR'CO + H^+$$

As was expected, triphenylmethyl bromide responded even more readily than the isothiocyanate, and was reduced by all the alcohols, including propan-2-ol at its boiling point (~80°). Ketones produced by the dehydrogenation of the alcohols were identified. These reactions are closely related to those discussed by Bartlett and McCollum,[5] whose experiments with aryl-substituted alcohols in strongly acidic media were considered to involve formation of the carbonium ion, to which hydride ion was transferred from a molecule of the same alcohol (disproportionation) or from a different alcohol, such as propan-2-ol, *e.g.*,

$$Ar_3C{\cdot}OH + H^+ \rightleftharpoons Ar_3C^+ + H_2O$$
$$Ar_3C^+ + Me_2CH{\cdot}OH \longrightarrow Ar_3CH + Me_2CO + H^+$$

Addition of alcohols to isothiocyanates, giving thiocarbamates, is known to be catalysed by alkoxides,[3] or by a tertiary amine.[4] Observations were made with the former type of catalyst, the action of which may be represented:

$$Ph_3C{\cdot}N{:}C{:}S: + RO^- \longrightarrow Ph_3C{\cdot}\overset{-}{N}{\cdot}CS{\cdot}OR \xrightarrow{(ROH)} Ph_3C{\cdot}NH{\cdot}CS{\cdot}OR + RO^-$$

Use of the appropriate alkoxide in the refluxing alcohol proved to be an inadequate method for additions to triphenylmethyl isothiocyanate; the reagents ethanol–ethoxide or isopropyl alcohol–isopropoxide gave the corresponding thiocarbamate in only ~20% yield, in competition with formation of the ethyl or isopropyl ether by substitution, while, as reported earlier,[1] methanol–methoxide gave the methyl ether exclusively. An effective method of preparing the thiocarbamate was to use the alkoxide, at ordinary temperature, as a suspension in xylene containing some of the corresponding alcohol.[6] Substitution was then absent in all the cases examined, probably because of the suppression of carbonium-ion formation from triphenylmethyl isothiocyanate in this largely hydrocarbon medium; the behaviour of n-butylamine towards solutions of the isothiocyanate has been similarly explained.[2] The observed ease of conversion of the isothiocyanate into thiocarbamates was in the order R = ethyl > isopropyl or cyclohexyl > methyl. Kinetic studies of these reactions are desirable. The limited data so far available indicate that the more basic species $RCH_2{\cdot}O^-$ and $RRCH{\cdot}O^-$ are more effective in addition than $CH_3{\cdot}O^-$. On the other hand, reported results of studies [4] of addition reactions in systems of the type aryl isothiocyanate–alcohol–triethylamine were the reverse of those expected from considerations of relative basicity of the alcohols and were attributed to the operation of a steric factor.

Triphenylmethyl isothiocyanate reacted exclusively by addition, at ordinary temperatures, with an excess of a non-aromatic primary or secondary amine, giving thiourea derivatives, *e.g.*,

$$Ph_3C{\cdot}N{:}C{:}S + NHR_2 \rightleftharpoons Ph_3C{\cdot}NH{\cdot}CS{\cdot}NR_2$$

This was a rapid reaction for n-butyl-, isopropyl-, cyclohexyl-, diethyl-, and di-n-butylamine, and for pyrrolidine, and was slower for piperidine and morpholine. The reversibility indicated for the reaction in the above equation was clearly shown in the behaviour of the thiourea derivatives of all the secondary amines; thermal decomposition occurred on melting, regenerating the isothiocyanate. The thermal decomposition of some other thiourea derivatives is known as a method for preparing isothiocyanates, but has had limited success.[7] The reversibility of thiourea formation was probably responsible for the inferior results obtained at the boiling point with secondary amines; diethylamine thus

[5] P. D. Bartlett and J. D. McCollum, *J. Amer. Chem. Soc.*, 1956, **78**, 1441.
[6] M. Roshdestwenski, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 107, 1438.
[7] N. Bortnick, L. S. Luskin, M. D. Hurtwitz, and A. W. Rytina, *J. Amer. Chem. Soc.*, 1956, **78**, 4358.

gave a much reduced yield of adduct, while piperidine and morpholine gave no adducts but reacted substitutively to give high yields of the corresponding triphenylmethylamines:

$$Ph_3C{\cdot}NCS + NHR_2 \longrightarrow Ph_3C{\cdot}NR_2 + HNCS$$

Also, the thiourea derivatives obtained from diethylamine or morpholine decomposed in hot ethanol, giving triphenylmethyl ethyl ether, either by solvolysis of isothiocyanate regenerated from the adduct, or by direct displacement of the CPh_3 group from the adduct; the thiourea derivative from morpholine also decomposed in boiling morpholine, affording *N*-triphenylmethylmorpholine in high yield.

With nucleophiles less basic than non-aromatic primary or secondary amines, only substitution, $Ph_3C{\cdot}NCS \longrightarrow Ph_3CX$, was observed. This occurred with excess of aniline at room temperature.[2] In refluxing methyl cyanide, a solvent favouring carbonium-ion formation, ammonia gave a quantitative yield of triphenylmethylamine. In the higher-boiling polar solvent, phenyl cyanide, even acetamide slowly gave the corresponding substitution product:

$$Ph_3C{\cdot}NCS + AcNH_2 \longrightarrow Ph_3C{\cdot}NHAc + HNCS$$

To test the capacity of amines to reduce triphenylmethyl isothiocyanate, some compounds of tertiary type, which should be incapable of the competitive addition or substitution reactions, were selected. As in the case of alcohols, reduction readily occurred if the temperature was high enough. Nearly quantitative yields of triphenylmethane were isolated from solutions of the isothiocyanate in refluxing tri-n-propylamine, tri-n-butylamine, or *NN*-diethylaniline, which boil in the range 155—215°, while only a trace of reduction occurred in the lower-boiling triethylamine. Gums which also appeared were probably polymers from dehydrogenation products of the amines. The reaction may again be represented as a hydride-ion transfer, and, as in the dehydrogenation of amines by other methods,[8] the carbon centre adjacent to the nitrogen atom is likely to be the initial source of hydrogen:

$$Ph_3C^+NCS^- + R_2N{\cdot}CH_2{\cdot}CH_2R' \longrightarrow Ph_3CH + NCS^- + (R_2N{\cdot}\overset{+}{C}H{\cdot}CH_2R \longleftrightarrow R_2\overset{+}{N}{:}CH{\cdot}CH_2R) \longrightarrow H^+ + (\text{polymers of } R_2N{\cdot}CH{:}CHR)$$

Experimental

Reduction by Secondary Alcohols.—(*a*) Triphenylmethyl isothiocyanate was recovered unchanged after 48 hr. in refluxing anhydrous propan-2-ol. A solution of triphenylmethyl bromide (2 mmoles) in propan-2-ol (25 ml.) was refluxed for 24 hr., evaporated, and the residue chromatographed on alumina. Triphenylmethane (93%), m. p. and mixed m. p. 92—93°, was eluted with light petroleum, and triphenylmethanol (7%; from unreduced bromide), m. p. and mixed m. p. 158—162°, was eluted with benzene.

(*b*) A solution of the isothiocyanate (1 mmole) in anhydrous octan-2-ol (10 ml.) was refluxed for 48 hr. and solvent removed. Infrared spectra indicated a carbonyl-containing constituent of distillate and residue. Chromatography yielded triphenylmethane (98%). A similar reaction, carried out for 12 hr. with triphenylmethyl bromide, gave triphenylmethane (42%) and triphenylmethanol (58%).

(*c*) A solution of the isothiocyanate (2 mmoles) in anhydrous cyclopentanol (10 ml.) was refluxed for 48 hr. and solvent removed. Chromatography of the tarry residue gave only triphenylmethane (91%). A similar reaction was carried out with triphenylmethyl bromide for 24 hr. The first portion of the solvent distillate contained hydrogen bromide and cyclopentanone, identified as its 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 142—146°, and the brown residue yielded triphenylmethane (98%) when chromatographed.

(*d*) A solution of the isothiocyanate (2 mmoles) in anhydrous cyclohexanol (25 ml.) was refluxed for 24 hr., the solvent removed, and the residual brown oil chromatographed on alumina. Triphenylmethane (~55%) was closely followed by triphenylmethyl cyclohexyl ether (~15%), both being eluted by light petroleum and identified by comparison of their infrared spectra

[8] *E.g.*, L. Horner and W. Kirmse, *Annalen*, 1955, **597** 48; G. M. Coppinger and J. D. Swalen, *J. Amer. Chem. Soc.*, 1961, **83**, 4900.

with those of authentic samples. Triphenylmethanol (30%) was eluted by benzene, and an oily fraction, with a carbonyl-containing constituent, by ether. Refluxing of a similar solution for 48 hr. gave triphenylmethane in 95% yield. Triphenylmethyl bromide in refluxing cyclohexanol (24 hr.) yielded triphenylmethane (95%); the first portion of solvent distillate contained hydrogen bromide and yielded cyclohexanone 2,4-dinitrophenylhydrazone, as shown by infrared spectroscopy.

Reactions with Alkoxides in Alcohols.—A solution of triphenylmethyl isothiocyanate (6 mmoles) and an excess (3·3 mol.) of sodium ethoxide in anhydrous ethanol was refluxed for 2 hr., added to water, and the product isolated with methylene chloride. The resulting oil, chromatographed on alumina, yielded triphenylmethyl ethyl ether (80%), m. p. and mixed m. p. 83—84° (from methanol), eluted by light petroleum, and *ethyl* N-*triphenylmethylthiocarbamate* (16%), m. p. 165—167° (from light petroleum), eluted by benzene (Found: C, 75·9; H, 5·8; N, 4·3; S, 9·1. $C_{22}H_{21}NOS$ requires C, 76·0; H, 6·1; N, 4·0; S, 9·2%). A similar reaction (3hr.) with sodium isopropoxide (6 mol.) in propan-2-ol gave, after isolation, an aqueous phase containing thiocyanate ion and an oily mixture of the ether and adduct. Treatment of the oil with hot ethanol yielded *isopropyl* N-*triphenylmethylthiocarbamate* (20%), m. p. 181—183° (Found: C, 76·7; H, 6·5; N, 3·9; S, 8·8. $C_{23}H_{23}NOS$ requires C, 76·4; H, 6·4; N, 3·9; S, 8·9%). Reaction of triphenylmethyl bromide with sodium isopropoxide in propan-2-ol yielded the isopropyl ether (45%), m. p. 114—116° (lit.,[9] 113°). A similar reaction (3 hr.) between the isothiocyanate and sodium cyclohexoxide (6 mol.) in cyclohexanol yielded only gums. Triphenylmethyl chloride was converted into the cyclohexyl ether in very poor yield by a reported process.[9]

Reactions with Alkoxides in Alcohol and Xylene.—The procedure was based on a reported process.[6] The alcohol (10 ml.) was treated with sufficient sodium to provide 20 mmoles of the alkoxide, which appeared as a suspension on addition of xylene (25 ml.). Triphenylmethyl isothiocyanate (3 mmoles) in xylene (15 ml.) was added, and the mixture was shaken for 12 hr. at room temperature, treated with ice-cold 0·25N-hydrochloric acid, and extracted with ether. In no case was thiocyanate ion found in the aqueous layer. The ethereal extracts yielded crystalline products, which were dissolved in the minimum amount of hot light petroleum and cooled, when most of the unchanged isothiocyanate crystallised. Concentration of the filtrate yielded, on cooling, the following thiocarbamates: *methyl* N-*triphenylmethylthiocarbamate* (24%; 58% isothiocyanate recovered), m. p. 190—192° (Found: C, 75·6; H, 6·0; N, 4·3; S, 9·5. $C_{21}H_{19}NOS$ requires C, 75·7; H, 5·7; N, 4·2; S, 9·2%); ethyl *N*-triphenylmethylthiocarbamate (65%; 25% isothiocyanate recovered), m. p. 165—167°; isopropyl *N*-triphenylmethylthiocarbamate (52%; 14% isothiocyanate recovered), m. p. 181—183°; *cyclohexyl* N-*triphenylmethylthiocarbamate* (54%; 42% isothiocyanate recovered), m. p. 179—181° (Found: C, 77·4; H, 6·5; N, 3·4; S, 8·0. $C_{26}H_{27}NOS$ requires C, 77·8; H, 6·8; N, 3·5; S, 8·0%).

Reactions with Cold Primary or Secondary Amines.—The isothiocyanate (3 mmoles) and an excess of the appropriate amine (5 ml.) were shaken at room temperature for 1 hr. Clear solutions resulted, from which the adducts rapidly crystallised, except in the case of mono- and di-n-butylamine. Addition of water and extraction with methylene chloride usually gave a nearly quantitative yield of fairly pure product. In no case was thiocyanate ion found in the aqueous layer. The following thiourea derivatives were thus prepared (yields refer to recrystallised products): N-*isopropyl*-N′-*triphenylmethylthiourea* (88%), m. p. 188—190° (from light petroleum) (Found: C, 76·8; H, 6·8; N, 8·0; S, 9·1. $C_{23}H_{24}N_2S$ requires C, 76·6; H, 6·7; N, 7·8; S, 8·9%); *N*-n-butyl-*N*′-triphenylmethylthiourea (78%), m. p. 134° (from ethanol) (lit.,[2] 134—134·5°); N-*cyclohexyl*-N′-*triphenylmethylthiourea* (78%), m. p. 191—192° (from ethanol) (Found: C, 77·9; H, 7·3; N, 7·4; S, 8·4. $C_{26}H_{28}N_2S$ requires C, 78·0; H, 7·0; N, 7·0; S, 8·0%); NN-*diethyl*-N′-*triphenylmethylthiourea* (61%), m. p. 118—124° (from acetone) (Found: C, 77·1; H, 7·4; N, 7·8; S, 8·5. $C_{24}H_{26}N_2S$ requires C, 77·0; H, 7·0; N, 7·5; S, 8·6%); NN-*di-n-butyl*-N′-*triphenylmethylthiourea* (81%), m. p. 94—96° (separated from the reaction mixture after standing for several days) (Found: C, 78·0; H, 7·7; N, 6·9; S, 7·4. $C_{28}H_{34}N_2S$ requires C, 78·1; H, 8·0; N, 6·5; S, 7·5%); N-(N′-*triphenylmethylthiocarbamoyl*)-*pyrrolidine* (83%), m. p. 155° (from 1 : 4 methylene chloride–ether) (Found: C, 77·5; H, 6·4; N, 7·7; S, 8·6. $C_{24}H_{24}N_2S$ requires C, 77·4; H, 6·5; N, 7·5; S, 8·5%); N-(N′-*triphenylmethylthiocarbamoyl*)*piperidine* (54%), m. p. 117—119° (from 1 : 4 benzene–light petroleum) (Found: C, 77·9; H, 6·7; N, 7·0; S, 8·2. $C_{25}H_{26}N_2S$ requires C, 77·7; H, 6·8; N, 7·3; S, 8·3%),

[9] B. Helferich, P. E. Speidel, and W. Toeldte, *Ber.*, 1923, **56**, 766.

accompanied by unchanged triphenylmethyl isothiocyanate (17%); N-(N'-*triphenylmethylthiocarbamoyl*)*morpholine* (39%), m. p. 150—152° (from acetone), or (68%), m. p. 150—153° (from cold methylene chloride–ether, 1 : 2) (Found: C, 74·3; H, 6·3; N, 7·6; S, 8·6. $C_{24}H_{24}N_2OS$ requires C, 74·2; H, 6·2; N, 7·2; S, 8·3%), accompanied by unchanged triphenylmethyl isothiocyanate. Under the same conditions, aniline gave *N*-phenyltriphenylmethylamine [2] (~60%). The derivatives from diethylamine, di-n-butylamine, pyrrolidine, piperidine, and morpholine all decomposed after being melted, leaving triphenylmethyl isothiocyanate, identical (infrared spectrum) with an authentic sample. The derivatives from diethylamine and morpholine decomposed when recrystallisation from ethanol was attempted, giving mainly triphenylmethyl ethyl ether and some triphenylmethanol.

Reactions with Primary or Secondary Amines at the Boiling Point.—Mixtures with the compositions given above were refluxed for 1 hr. Isopropylamine (at 33—35°), n-butylamine (at 76—78°), and pyrrolidine (at 87—88°) gave the same thiourea derivatives as at room temperature, in yields (recrystallised products) of 90, 75, and 82%, respectively. Diethylamine (at 54—56°) gave a lower yield of adduct (30%), with unchanged isothiocyanate. Cyclohexylamine (at 132—134°) gave unidentified solids, and di-n-butylamine (at 156—159°) gave an oil. Piperidine (at 104—106°) gave *N*-triphenylmethylpiperidine (65%), m. p. and mixed m. p. 156—159° (from ethanol) (lit.,[10] 153°). Morpholine (at 126—130°) gave dimorphic N-*triphenylmethylmorpholine* (79%), m. p. 178—180° and 187—189° (from ethanol) (Found: C, 83·7; H, 6·9; N, 4·5. $C_{23}H_{23}NO$ requires C, 83·9; H, 7·0; N, 4·3%). Only in the last two cases was thiocyanate ion found in the aqueous layer. *N*-(*N'*-triphenylmethylthiocarbamoyl)morpholine (in boiling morpholine for 1 hr.) gave *N*-triphenylmethylmorpholine (73%), m. p. and mixed m. p. 178—180° and 187—189° (from ethanol).

Reduction by Tertiary Amines.—A solution of triphenylmethyl isothiocyanate (2 mmoles) in redistilled tertiary amine (5 ml.) was refluxed for varying periods, excess of amine was removed under reduced pressure, and triphenylmethane was isolated by chromatography on silica or alumina. From triethylamine (at 88—89°) only unchanged isothiocyanate (95%) was obtained after 12 hr., but this was accompanied by a trace of triphenylmethane (1%) after 24 hr. From tri-n-propylamine (at 155—156°), triphenylmethane was obtained, after 3 or 6 hr., in yields of 62 and 89%, respectively, accompanied by unchanged isothiocyanate, a trace of triphenylmethanol, and oils. From tri-n-butylamine (at 211—213°), triphenylmethane was obtained in yields of 95—97%, together with gums, after heating for periods of 3—24 hr. From *NN*-diethylaniline (at 214—216°), triphenylmethane was obtained, after 3 or 6 hr., in yields of 89 and 93%, respectively, together with gums. The isothiocyanate was recovered almost quantitatively from refluxing solutions of pyridine or its homologues.

Triphenylmethylamine.—Gaseous ammonia was passed through a refluxing solution of triphenylmethyl isothiocyanate (2 mmoles) in methyl cyanide (50 ml.) for 1 hr. Dilution with water and extraction with methylene chloride afforded triphenylmethylamine (81%), m. p. and mixed m. p. 104—106° (from light petroleum) (lit., 103°; [11a] 105° [11b]) The aqueous layer, treated with nitric acid and silver nitrate, yielded silver thiocyanate (97%). The amine was also obtained from ammonia and triphenylmethyl bromide in refluxing benzene, but the isothiocyanate was unchanged under these conditions.

N-*Triphenylmethylacetamide.*—A solution of triphenylmethyl isothiocyanate (2 mmoles) and acetamide (10 mmoles) in phenyl cyanide (25 ml.) was refluxed for 3 hr., solvent was removed under reduced pressure, water added, and the product isolated by extraction with methylene chloride. Trituration with cold ether removed unchanged isothiocyanate (62% recovery after recrystallisation from acetone) and left *N*-triphenylmethylacetamide (16%), m. p. and mixed m. p. 212—214° (from hot ether) (lit.,[12] 214°). The isothiocyanate was unchanged when the reaction was attempted similarly in methyl cyanide, but triphenylmethyl bromide gave *N*-triphenylmethylacetamide (55%) under these conditions.

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[12] H. Brederick and E. Reif, *Chem. Ber.*, 1948, **81**, 426.