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ADDITION OF THIOCYANOGEN AND RELATED PSEUDOHALOGENS

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INTRODUCTION

The reaction of thiocyanogen with olefins was first examined by Kaufmann (1), who isolated a *vic*-dithiocyanate. Soon after this discovery, Kaufmann (2-4) applied the thiocyanogen addition reaction to the analysis of unsaturated oils and fats, the results of which he subsequently expressed as the Thiocyanogen Value (T.V.) or Number. The usefulness of this analytical method derived from the quantifiable difference between halogen and thiocyanogen in their addition to polyunsaturated fatty acids and esters. Compared to halogen's stoichiometric addition to most polyolefinic compounds, thiocyanogen added quantitatively to oleic acid, but to only one of two double bonds in linoleic and to two of three double bonds in linolenic acid. The Thiocyanogen Value, in conjunction with the Iodine Number, was widely adopted as the standard analytical procedure for determination of the relative composition of monoene, diene, and triene in natural fatty materials (5).

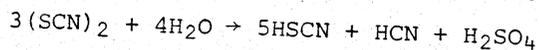
Following Kaufmann's pioneering work, several successive improvements in the procedure appeared (6-13). However, neither detailed studies of its empirical nature nor improvements in preparation and isolation of the reaction products were reported. The pseudohalogen (14,15) and ambident (16,17) characteristics of the thiocyanate group had been recognized and several reviews (17-20) have described thiocyanogen and its reactions with aromatic and olefinic compounds. However, thiocyanogen was not included in a general review (21) of halogens and halogenoids as electrophiles in stereochemical additions to olefins and acetylenes. This omission graphically underscored the need of in-depth studies of olefin thiocyanations to bring thiocyanogen chemistry within the general framework of halogenoid reactions.

Recently, there have been significant contributions to the clarification of the mechanism of reaction of olefin thiocyanogen reactions. Some applications of the reaction products in synthesis have also been made and will be briefly described. It is the aim of this report to update former reviews and discussions by elaborating upon the most recent developments.

THIOCYANOGEN PREPARATION

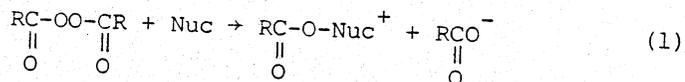
Thiocyanogen is generally prepared by addition of bromine to lead thiocyanate or other metal thiocyanates. Variation and improvements in preparative procedures and the chemistry and stability of thiocyanogen not presented in this report have been described in former reviews (13,18-20). Maxwell et al. (22) have noted that thiocyanogen prepared from "aged" lead thiocyanate produces large amounts of free radical addition products and should be avoided in preparations of stereospecific adducts.

Two new developments on the preparation of thiocyanogen have been reported that could simplify use of the reagent in some applications. Thiocyanogen was reported to be unstable in the presence of water, in which it undergoes rapid hydrolysis as shown in the following equation (18,20). However, it

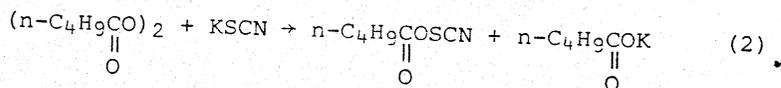


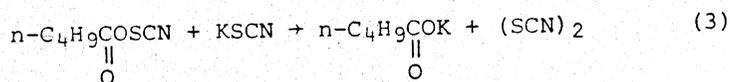
has now been demonstrated that thiocyanogen may be prepared in a two-phase system, such as water/toluene (23). As the thiocyanogen is generated, it is extracted into the hydrocarbon layer where it may be used without drying. Accordingly, sodium thiocyanate and chlorine may be used in place of silver or lead thiocyanate and bromine where anhydrous conditions are unimportant.

A reaction of ionic thiocyanate with diacyl peroxides offers another new method for the preparation of thiocyanogen (24). The reaction is based on the susceptibility of acyl peroxides to nucleophilic attack (eq. 1) and involvement of the acyloxy intermediate in competitive ionic and free radical reactions.



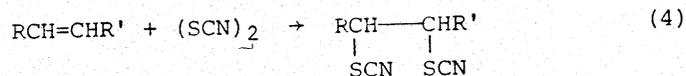
The reaction is a two-step process that is illustrated in the following two equations:





GENERAL CHARACTERISTICS OF THIOCYANATION

Kaufmann (1,18,25) prepared *vic*-dithiocyanate adducts I by reaction of thiocyanogen with representative types of unsaturated compounds (eq. 4). Adducts were obtained from



I

simple monounsaturated structures illustrated by ethylene, butylene, allyl alcohol, oleic acid, elaidic acid, erucic acid, brassidic acid, ricinelaidic acid, pinene, antipyrène, anethole, and safrole. Enolizable compounds such as acetoacetic ester, acetyldibenzoylmethane, ethyl α,β -diacetylsuccinate, and formylphenylacetic ester also added thiocyanogen. The dienes butadiene, 2,3-dimethylbutadiene and isoprene each added one molecule of thiocyanogen to give presumably 1,4-disubstituted products. Yields were high for butadiene (80%) but totaled less than 20% for each of the latter two dienes. Double bonds in the vicinity of electron-withdrawing groups were also reported as unreactive with the reagent so that under nonaccelerative conditions (*vide infra*) no addition products were obtained from styrene, stilbene, crotonic acid, fumaric acid, maleic acid, cinnamic acid or ester, and cinnamaldehyde.

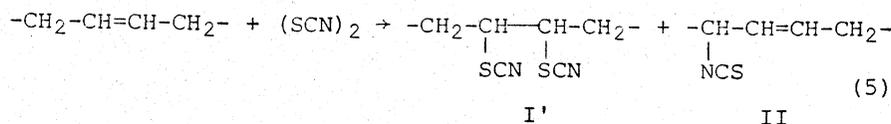
The above results gave preliminary evidence of the dependence of thiocyanation rate on double bond position. Thiocyanogen reacts either ionically by heterolytic scission

(dark reaction) $(\text{NCS}^{\delta+}-\text{SCN}^{\delta-})$ or by a free radical pathway via

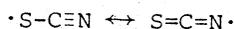
homolytic scission $(\text{NCS}\cdot\cdot\text{SCN})$ (light induced reaction) of the S-S bond. Addition of thiocyanogen is slow under ionic conditions but is accelerated photolytically (1,25-27). Although thiocyanogen is light-sensitive and decomposes in the course of light-induced addition, yields of products remain high. For example, ethylene added traces of thiocyanogen in a dark reaction over a period of nine days in contrast to complete addition in sunlight in two hours (27). Similarly, stilbene and styrene, though unreactive in the dark, were found to be reactive toward thiocyanogen under free-radical conditions (27).

Bacon and coworkers (28) found that light or peroxide promoted free-radical reactions of thiocyanogen may give allylic isothiocyanate as a coproduct with dithiocyanate

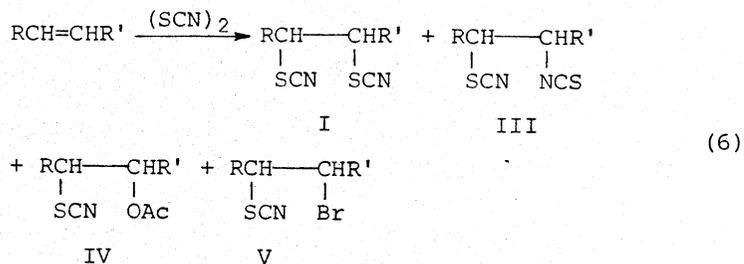
adducts (eq. 5). The relative amounts of substitution and addition products formed were found to be dependent on olefinic structure. Cyclohexene, for example, yielded types I' and II (eq. 5) in approximately equal amounts, 1-methyl cyclohexene produced largely type II, and 1-octene was converted almost exclusively to the addition product I'. These reactions



indicated homolytic scission of thiocyanogen to give a thiocyanate free radical as the mediating species. The ambident character of the radical is depicted as a resonance-stabilized structure:



In contrast to the free radical pathway formulated by eq. 5, the complex behavior of thiocyanogen in ionic additions (dark reactions) was discovered only within the past decade when compounds such as the nonsymmetrical α -isothiocyanato- β -thiocyanate adducts III (eq. 6) were isolated as reaction



trans olefin \rightarrow *erythro* (*meso*) (Ia, IIIa, IVa, Va)
cis olefin \rightarrow *threo* (*dl*) (Ib, IIIb, IVb, Vb)

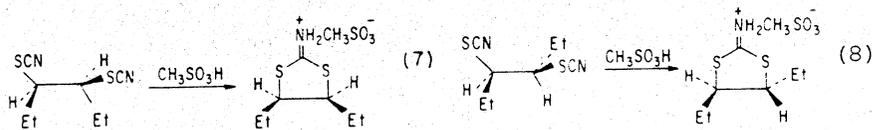
coproducts (29-31). The isothiocyanate isomer was obtained from reactions carried out in either nonpolar (29,30) or polar (29,31) solvents. In acetic acid solution, thiocyanation gave a mixture of four compounds I, III-V (eq. 6) (31). Adduct I was the primary product ($\sim 80\%$) accompanied by its isomeric adduct III as a minor coproduct ($\sim 10\%$). Solvent participation resulted in formation of adduct IV. Adduct V was derived by reaction with bromothiocyanogen and probably lead bromide, which are present as contaminants in the thiocyanogen reagent. The pure isomeric adducts I and III were easily distinguished from each other by characteristic differences in their infrared spectra. The dithiocyanates I display a single sharp absorption band for the thiocyanate group at

2170 cm^{-1} , while the spectrum for adduct III shows a medium broad band for the isothiocyanate group at 2100 cm^{-1} along with the 2170 cm^{-1} thiocyanate absorption.

STEREOCHEMISTRY AND MECHANISMS

The stereochemistry of ionic addition to *cis* and *trans* olefinic acids was first clearly proposed by McGhie and co-workers (32). Earlier workers had observed that *trans*-olefinic acids afforded crystalline dithiocyanato-acids whereas the products from *cis*-olefinic acids were oily and noncrystallizable (33,34). McGhie's stereochemical assignments of *vic*-dithiocyanate adducts were based on the premise of thiocyanogen's analogous behavior to halogen addition, *i.e.*, the expectation of the *threo* adduct from *cis*-olefin and *erythro* adduct from *trans*-olefin. Interpretation of analogous behavior, however, must be tempered with caution, since McGhie's hypothesis of the reaction's stereochemistry involved melting point relationships between thiocyanates and epoxides that were largely, though not completely, in accord. It has since become evident from the analysis of many types of electrophilic additions that the stereochemistry of reaction products depends upon the nature of the reagent, the structure of the olefin, and the reaction conditions employed (21). Establishing the stereochemical structures of isomeric pairs therefore necessitates definitive methods of preparation and analysis.

Structural assignments of adducts I and III were definitively confirmed by NMR (31,35). The method was applied to the stereochemical geometries of the 3,4-dithiocyanate adducts derived from *cis*- and *trans*-hexenes as representative models of adducts I and similarly to the 3-isothiocyanato-4-thiocyanate isomers in representation of adducts III. Because of symmetry in *erythro*- and *threo*-*vic*-dithiocyanates, differentiation of their geometries was elusive. The uncertainty of assignments was finally resolved by cyclization of the *erythro* and *threo* adducts which led to their *cis*- and *trans*-1,3-dithiolane-2-imino salts of methanesulfonic acid, VI and VII (eq. 7 and 8), respectively (see Heterocycles).



erythro Ia

cis VI

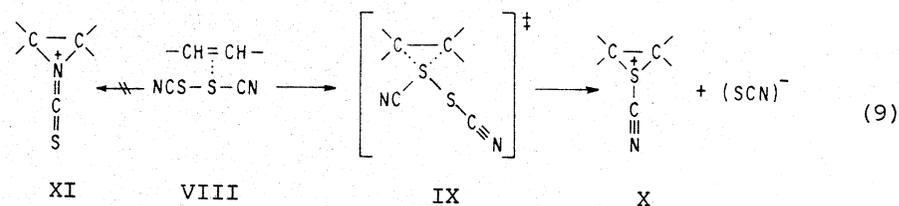
threo Ib

trans VII

The stereochemical structures of *erythro*- and *threo*-3,4-dithiocyanatohexanes were confirmed by examination of the chemical

shifts and ^{13}C satellite spectra of VI and VII, respectively. Cyclization of adduct I does not engage participation of the precursor's C-S bonds at the point of carbon attachment in the alkane chain. Chemical shifts of the *cis*- and *trans*-dithiolaneimino salts VI and VII were compared with published assignments for known cyclic analogues, which established their stereochemical assignments. Through these relationships the assignments of the corresponding dithiocyanates (I) were derived. In each example the chemical shift of *vic*-methine protons of the *trans* isomers appear ~ 0.2 ppm upfield relative to *cis* isomers, a difference noted for many *cis-trans* isomeric pairs of planar three-to-five membered cyclic compounds (36). The stereochemical assignment for the *cis* cyclic isomer confirmed the stereochemistry of the precursor *erythro* adduct Ia, and similarly the *trans* stereochemistry of the alternate cyclic isomer confirmed the identity of the *threo* dithiocyanate Ib. Configuration of the *cis* and *trans*-dithiolane structures VI and VII was further verified through analysis of the corresponding natural abundance ^{13}C proton satellites (35). These data definitively supported McGhie's assignments (32) for *threo* and *erythro* structures of *vic*-dithiocyanate adducts. Unlike the *vic*-dithiocyanate adducts, Ia and Ib, asymmetry in the isomeric 3-isothiocyanato-4-thiocyanatohexanes and in the *vic*-dithiocyanates from β -methylstyrene enabled direct conformational analysis of their stereochemistry (35).

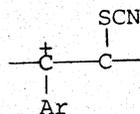
A mechanism for ionic thiocyanogen addition to aliphatic olefins was proposed by Guy *et al.* (29) to involve a three-membered cation, the S-cyanoepisulfonium ion X (eq. 9), as the reaction intermediate. A representation of the episulfonium ion transition state, analogously proposed for the



interaction of other types of sulfur reagents with π -electrons (37), gains strong support from the existence of stable episulfonium salts (38,39). The initial interaction between thiocyanogen and olefin may be postulated to be a contact charge-transfer VIII that subsequently reorganizes to a π -complex transition state IX (31), which then proceeds to the episulfonium ion intermediate X (eq. 9). *Trans* addition to X by reactive nucleophilic species present in solution, *i.e.*, the ambident anion ($\bar{\text{S}}-\text{C}\equiv\text{N} \leftrightarrow \text{S}=\text{C}=\bar{\text{N}}$), acid solvent, and competitive anions like Br, accounts for the ancillary products (eq.

6) and stereochemical specificity. The absence of diisothiocyanate adduct products eliminated an aziridinium ion type of structure XI from mechanistic considerations (eq. 9).

Guy et al. (29,40) observed a difference in the thiocyanation mechanism for aliphatic and aromatic alkenes on the basis of careful product analysis. Aliphatic alkenes reacted stereospecifically *trans* and nonregiospecifically: *cis*- and *trans*-RCH=CHR' gave *rac*- and *meso*-RCH(SCN)CH(SCN)R' plus *threo*- and *erythro*-RCH(SCN)CH(NCS)R', respectively; RCH=CH₂ gave RCH(NCS)CH₂SCN, RCH(SCN)CH₂NCS and RCH(SCN)CH₂SCN. Addition to aryl alkenes was nonstereospecific (*trans*-stereoselective) and yielded Markownikoff oriented *vic*-isothiocyanatothiocyanate isomers. For example, where Y=SCN or NCS, *trans*-1-phenylpropene gave *threo*- and *erythro*-C₆H₅CHYCH(SCN)CH₃; indene gave *cis*- and *trans*-1-Y-thiocyanate derivatives; styrene gave C₆H₅CHYCH₂SCN. The products from the two types of olefins were attributed to differences in the nature of the transition state. Product specificity from aliphatic olefins was derived from a cyclic structure analogous to intermediate X. For aryl olefins, the formation of an open carbonium ion was proposed to arise from the greater stabilizing effect of the aryl substituent over an alkyl analogue; this would explain the nonstereospecific Markownikoff addition.



SOLVENT AND CATALYST EFFECTS

The course of ionic thiocyanogen addition to olefins is strongly influenced by such factors as solvent polarity, the thiocyanogen/olefin ratio, and the presence in solution of free radicals and heavy metals (22). These parameters determine not only the stereochemistry of the products but also the relative formation of adducts I and III and the overall conversions (Table I). Thiocyanate adduct IV can originate only in acetic acid solutions. In benzene, chloroform, methylene chloride, or acetonitrile, but not in acetic acid, thiocyanogen was observed to add both homolytically and heterolytically under presumed non-free-radical conditions (22). The free radical indirect reaction accompanied heterolytic addition even in the dark, with the resultant indiscriminate distribution of nonstereoselective isomeric adducts. Inclusion of inhibitor (29), for example 2,6-di-*tert*-butyl-4-methylphenol (22), suppressed the free radical component accompanying the heterolytic additions. Although unwanted

TABLE I

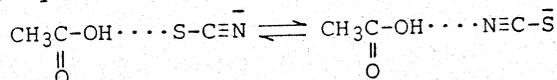
THIOCYANATION OF *trans*-3-HEXENES IN BENZENE: PARAMETER EFFECTS ON PRODUCT COMPOSITION AND YIELDS^a

R in NCS R Et-CH-CH-Et	Filtered				
	Unfiltered No inhib ^b	No inhib ^b	15% inhib ^b 2.4 mol (SCN)	15% in- hib ^{b,c,d} 10% iron	No inhib ^b hv
	<u>trans-Hexene^f Products</u>				
Et-CH=CH- $\overset{\text{NCS}}{\underset{ }{\text{CH}}}$ CH ₃ ^e					
-Br	10.2				60.1
-NCS (e)	25.8	55.0	65.8	3.4	3.8
-NCS (t)	12.5	8.1	1.9		2.7
-SCN (e)	32.2	30.8	30.9	92.9	19.3
-SCN (t)	19.3	6.1	1.4	3.7	14.1
Yield ^g	55.3	50.9	58.2	82.8	68.4

^aFrom Maxwell *et al.* (22). ^bThiocyanations carried out in the ratio 1.2 mol (SCN)₂/1.0 mol olefin. ^c2,6-Di-*tert*-butyl-4-methylphenol. ^dpowdered iron as catalyst. ^eProduct is primarily *trans*-CH₃CH₂CH=CHCH(NCS)CH₃. ^fYield and product distribution were similar for *cis*-3-hexene. ^gTotal isolated yield of thiocyanated products.

isomeric products were not totally suppressed, the presence of free radical inhibitor restricted their formation to below 3% of the products. The homolytic reaction, however, did not proceed in acetic acid even under photoinitiated conditions.

Solvents exhibit marked differences in their influence on thiocyanations. Formation of the *vic*-dithiocyanate adduct in acetic acid is attributed to predominant hydrogen bonding by the acid solvent at the nitrogen atom of the ambident thiocyanate ion, as is shown in the following equilibrium. Attack on X (eq. 9) by the nonsolvated ends of the ambident nucleo-



phile leads to stereochemically pure products of the isomeric mixture I and III. In aprotic solvents, in contrast to acetic acid, the relative formation of adducts I and III depends upon the dielectric constant of the medium (Table II). Solvents of low dielectric constant, such as benzene, lead to formation of the isothiocyanatothiocyanate adduct III as the predominant product (~65%).

An explanation for the solvent effect was proposed (22) in accordance with Pearson's Hard Soft Acid Base (HSAB) concept (41-43). The large polarizable sulfur atom with charge dispersed over a large surface is designated a "soft base" compared to the nitrogen atom, a "hard base" bearing a greater charge to size ratio. Hard base-hard acid interactions were predicted to be charge controlled and to depend primarily on ionic interaction of the reagents. Soft base-soft acid interactions are termed frontier controlled in reactions having low electronegativity and are enhanced by high polarizability and low solution energies of the reactants. Association of ions and ion pairs is stronger in solvents of low dielectric constant ϵ than in polar solvents. A nonpolar aromatic solvent such as benzene can solvate the soft sulfur atom of thiocyanogen or thiocyanate anion in a charge-transfer interaction leading principally to a charge controlled nitrogen attack of the episulfonium cation. As ϵ increased in the order $\text{C}_6\text{H}_6 < \text{CHCl}_3 < \text{CH}_2\text{Cl}_2 < \text{CH}_3\text{CN}$, the product distribution (and therefore the relative rates) increased in favor of sulfur attack (Table II). A dipolar aprotic solvent like acetonitrile may associate with thiocyanate anion by dipolar alignment. In the following pictorial representation of one possible interaction,

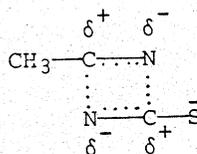


TABLE II

Change in Product Ratio with Increasing Dielectric Constant^a

Solvent	ϵ	III/I
Benzene	2.3	2.15
CHCl ₃	4.8	1.47
CH ₂ Cl ₂	8.9	1.14
CH ₃ CN	37.5	0.46

^aThe results represent the average obtained from the separate thiocyanations of *cis*- and *trans*-3-hexene (22).

TABLE III

Half-lives of Catalyzed and Noncatalyzed Thiocyanogen Additions to Hexenes^{a,b}

Olefin	Catalyst	Half life at 25 C
<i>cis</i> -3-Hexene	None	11 hr
	Fe(SCN) ₃	<15 min ^c
<i>trans</i> -3-Hexene	None	44 hr
	Fe(SCN) ₃	<15 min ^c
	Fe ^o ^d	<15 min ^c

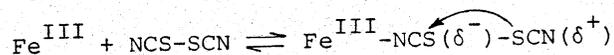
^aFrom Maxwell and Silbert (45). ^bReactions in benzene in the ratio of 1.2 mmol (SCN)₂/1.0 mmol olefin carried out in the dark. ^cReactions complete in 15 min. ^dIron powder.

the sulfur is negatively polarized by solvation for nucleophilic attack on the intermediate cation.

Another variable in this reaction, leading to changes in product outcome, is the ability of transition metals to influence the reaction pathway. Kaufmann and Thomas (44) had proposed in their early work the use of iron as a Friedel-Crafts catalyst for nuclear thiocyanation of an aromatic ring. Reaction between iron and thiocyanogen coats the metal with a film of black ferric thiocyanate, which is the active catalyst. Guy et al. (29) reported the qualitative observation that iron powder also catalyzed the addition of thiocyanogen to olefins to give a marked increase in dithiocyanate yields. Quantitative determinations with iron metal and ferric thiocyanate were undertaken by Maxwell et al. (22) who showed the nearly exclusive formation of dithiocyanate adduct I in benzene solution, compared to approximately 35% I and 65% III in catalyst-free reactions (Table I). The catalyzed rates of addition to *cis*- and *trans*-3-hexenes were at least 180 and 45 times faster,

respectively, than noncatalyzed reactions (45) (Table III). Other thiocyanates of row 1 transition metals (Ti to Cu inclusive) also demonstrated catalysis in both polar and nonpolar solvents (Table IV) (46). Only vanadium in benzene solution was as effective as iron, and cobalt was nearly so, for the stereospecific formation of the dithiocyanate adduct. The other transition metals, except manganese, were stereoselective for producing I, but isomer III was also substantially produced in benzene or acetonitrile solutions. A comparative examination of Mn, Fe, and Co metal powders to determine the relative effectiveness of metals flanking Fe in atomic numbers also showed iron to be the most efficient.

The HSAB concept provides an explanation of the catalytic effect of the heavy metals, which is exemplified by iron salts. Ferric thiocyanate is a metal coordinating complexing agent in solution (47). The presence of the soluble ferric thiocyanate salt in thiocyanogen-olefin additions induces rate enhancement, specific isomer formation, and stereochemical specificity. The nature of the thiocyanogen-ferric ion interaction may be understood by the following considerations. (a) *Rate enhancement* arises from polarization of the symmetric thiocyanogen molecule via ferric complexation, e.g., leading



to rapid formation of cation X (eq. 9). (b) *Isomer specificity in the product (adduct I) arises by coordination of the ferric ion (hard acid) with the nitrogen terminus (hard base) of thiocyanate (47) that leaves the sulfur terminus (soft base) free for nucleophilic attack on the intermediate X.* (c) *Stereochemical specificity (trans addition to cation X) then results from the considerable rate enhancement that precludes free rotation of an open-bonded cationic structure of the type $\text{R}_1\text{R}_2\text{C}^+-\text{C}(\text{SCN})\text{R}_3\text{R}_4$.*

The HSAB concept provided an explanation of an unexpected phenomenon observed for thiocyanations carried out in the presence of the insoluble lead salts retained after generation of thiocyanogen (22) (Table I). The adducts obtained in benzene for thiocyanations performed in this manner were non-stereospecific mixtures of adducts I, III, and V, of which I predominated over the expected isomer III. Lead-nitrogen interactions between lead salt and thiocyanogen would account for the change in selectivity. It was further found that thiocyanogen prepared from aged lead thiocyanate stored several months under refrigeration gave indiscriminating mixtures of adducts compared to reactions from freshly prepared lead thiocyanate. This is not clearly understood but is believed to involve a free radical process with participation of decomposed lead thiocyanate (22).

TABLE IV

Thiocyanation of *trans*-3-Hexene: Effect of Transition Metal Catalysts and Solvents on Product Composition and Conversion (46)

Cation	Solvent	erythro		threo		Conversion (%)
		† SCN	† NCS	† SCN	† NCS	
None	Benzene	31	66	2	1	58
	CH ₃ CN	69	31			36
Ti ⁺⁴	Benzene	90	9	1		82
	CH ₃ CN	90	8	2		46
V ⁺³	Benzene	99.6		0.4		90
	CH ₃ CN	96	4			40
Cr ⁺³	Benzene	63	34	2	~0.5	47
	CH ₃ CN	70	29	~0.5		29
Mn ⁺²	Benzene	47	49	3	2	49
	CH ₃ CN	75	25	~0.5		48
Fe ⁺³	Benzene	99.7	0.1	0.2		93
	CH ₃ CN	96	4	<1		44
Co ⁺³	Benzene	96	3	1		85
	CH ₃ CN	95	5			10
Ni ⁺²	Benzene	81	19	<1		57
	CH ₃ CN	89	11			48
Cu ⁺²	Benzene	72	28			53
	CH ₃ CN	77	23			40

ELECTROPHILIC CHARACTERISTICS OF ADDITIONS TO OLEFINIC ACIDS AND ESTERS

Olefin thiocyanation is an electrophilic reaction. It is therefore subject to the same factors that influence other electrophilic reactions, such as peracid epoxidations (48), *i.e.*, the rate is dependent on the number and nature of substituents attached to or in the vicinity of the double bond (DB). Several thiocyanation studies support this concordance on rates, *i.e.*, internal DB > terminal DB, the latter requiring photoactivation (30); *cis* > *trans* (49,50); sterically unhindered DB > sterically hindered DB (49); and inertness of double bond bearing electronegative substituents (29). The effects of the carboxyl group on rates of electrophilic additions to double bonds situated at different positions in a carbon chain have been established for epoxidations and should be applicable to thiocyanations (51-54).

Accordingly, Maxwell and Silbert (45) examined the heterolytic thiocyanations of monounsaturated acids and esters to delineate the foregoing relationships of electrophilic reac-

TABLE V

The Catalytic Effect of $\text{Fe}(\text{SCN})_3$ on Thiocyanogen Addition to Unsaturated Compounds in Benzene (45)

R = H, CH ₃	% Thiocyanogen addition ^a			
	Control ^{b,c}		Fe(SCN) ₃ ^d	
	H	CH ₃	H	CH ₃
CH ₃ (CH ₂) ₂ CH=CHCO ₂ R	0	0	~1	8
CH ₃ CH ₂ CH=CHCH ₂ CO ₂ R	0	0	4	28
CH ₃ CH=CH(CH ₂) ₂ CO ₂ R		13 ^e		90
CH ₃ (CH ₂) ₁₁ CH=CH(CH ₂) ₃ CO ₂ R		43 ^e		90
CH ₃ (CH ₂) ₁₀ CH=CH(CH ₂) ₄ CO ₂ R (<i>cis</i>)	70	70	90	90
CH ₃ (CH ₂) ₇ CH=CH(CH ₂) ₇ CO ₂ R (<i>cis</i>)	60	58	90	91
CH ₃ CH ₂ CH=CHCH ₂ R (<i>cis</i>)		72		90
CH ₃ (CH ₂) ₇ CH=CH(CH ₂) ₇ CO ₂ R (<i>trans</i>)	50	50	85	85
CH ₃ CH ₂ CH=CHCH ₂ R (<i>trans</i>)		50		83
CH ₂ =CH(CH ₂) ₈ CO ₂ R		~2		100
CH ₃ (CH ₂) ₄ CH=CHCH ₂ CH=CH(CH ₂) ₇ CO ₂ R		53		86
CH ₃ CH ₂ CH=CHCH ₂ CH=CHCH ₂ CH=CH(CH ₂) ₇ CO ₂ R		37		84

^aReactions in benzene solution carried out in the dark for 22 hours in the ratio 1.2 mmol (SCN)₂/1.0 mmol double bond. ^bYields obtained in the absence of iron are the maximum observed regardless of amount of excess thiocyanogen used. ^cExcept where noted the product composition is approximately 65% *vic*-isothiocyanate thiocyanate adduct (III) and 35% *vic*-dithiocyanate adduct (I). ^dThe product from the Fe(SCN)₃ reaction is stereochemically pure *vic*-dithiocyanate. ^eThese compounds were not fully characterized; however IR and NMR established that they were not *vic*-dithiocyanates.

tions with thiocyanogen. Using iron catalysts for comparison with noncatalyzed reactions as control experiments, they also determined the application of iron catalysis to resistant double bonds (Table V). Because of electron deficiency of a double bond in the vicinity of a carboxyl group, thiocyanogen fails to add to Δ^2 and Δ^3 positions in acids and esters in noncatalyzed reactions. The electronegative effect of the carboxyl group was experienced by the double bond at least as far down the chain as the Δ^5 -position. The products from Δ^3 and Δ^4 acids in the noncatalyzed experiments were incompletely identified but were not the expected isomeric derivatives of types I and III. Iron had a pronounced catalytic effect by inducing minor but significant formation of the dithiocyanate adduct from the Δ^2 and Δ^3 esters. The Δ^2 and Δ^3 acids

were resistant, although they offered small amounts of identifiable adducts. Catalysis was completely effective at Δ^4 and beyond. The nearly unreactive terminal double bond in undecylenic ester in heterolytic thiocyanations was quantitatively converted to dithiocyanate by the catalyst. Linoleic and linolenic esters, which normally add only two and four thiocyanate groups, respectively, by nonstoichiometric addition, gave their corresponding tetrathiocyanate and hexathiocyanate derivatives in the presence of catalyst. These compounds were previously unavailable by noncatalyzed addition techniques.

The effects of geometry and position of the double bond on addition were further delineated in this work (45). The *cis* double bond in *cis*-3-hexene and in methyl oleate gave a higher yield of products than the *trans* double bond in *trans*-3-hexene and in methyl elaidate within the time span (22 hours) of the reaction. Addition to *cis*-3-hexene was four times more rapid than to *trans*-3-hexene (Table III). This determination agreed with the 3-5 fold *cis-trans* rate differences reported by Plisov and Lakizo (49,50) for a series of unsaturated acids and esters. The latter workers have determined rate constants for thiocyanogen additions - the only *k* values presently available - from which other detailed relationships were noted. For example, in a series of homologous esters Plisov and Lakizo observed lower rates for erucates (*cis* Δ^{14}) than oleates (*cis* Δ^9) and for brassidates (*trans* Δ^{14}) than elaidates (*trans* Δ^9). Within each geometric series, increasing size of the alcohol moiety diminished the rates. Differences in rates were attributed to (a) relative differences in degrees of hindrance about the double bond reaction center caused by the steric nature of groups linked to it and to (b) conformational interactions with the bulkiness and chain size of the alcohol moiety. For example, in the Δ^{14} series, the longer chain length extending between the double bond and the ester moiety entropically favors more conformational interactions with the double bond, leading to a resultant lowering in rates. Interactions in the unsaturated carboxylic acids differ from those observed for the esters: thiocyanation of erucic and brassidic acids was faster than that of the esters, whereas oleic and elaidic acids were slower than their carboxylic esters. Although the mutual inductive influence between the carboxyl and another functional group in the chain is rapidly attenuated by distance, there is spectroscopic evidence of spatial interaction at moderate ranges. For example, an intramolecular hydrogen bond has been detected in methyl 12-hydroxystearate but not in methyl 10-hydroxystearate, a consequence of greater segmental flexibility in the more distantly located 12-hydroxyl group (55). It should not be surprising, therefore, that con-

formational differences between the Δ^9 and Δ^{14} series of esters would pertain to thiocyanations. Nevertheless, these earlier kinetic determinations may not represent strict heterolytic additions but may contain the effects of concomitant homolytic reactions (22).

THIOCYANOGEN HALIDES

In addition to thiocyanogen, there are four known members of the mixed halogen-halogenoid family comprising thiocyanogen monohalides Cl-SCN, Br-SCN, I-SCN, and the thiocyanogen trichloride Cl₃SCN. Some physical measurements have been reported for the members of this series (17,20), but the compounds have received less attention than thiocyanogen. With the exception of Cl-SCN, few studies on the electrophilic addition of these pseudohalogens to olefins and none with emphasis on unsaturated acids or esters have appeared. A presentation of recently available work may stimulate interest in their reactions. Thiocyanogen trichloride, however, is excluded from this discussion owing to its recent review (20).

THIOCYANOGEN MONOCHLORIDE

Guy and Pearson (56-58) have recently reported results of their addition of thiocyanogen monochloride to a variety of aliphatic and aryl alkenes. Their studies of thiocyanogen chloride addition to aliphatic olefins supports a mechanism analogous to that of thiocyanogen, i.e., formation of an intermediate or transition state cyanoepisulfonium ion X followed by anion (chloride) attack. The products of the reaction are α -chloro- β -thiocyanates in nonpolar solvents and additionally α -acetoxy- β -thiocyanates in acetic acid. The reaction with aliphatic alkenes is stereospecifically *trans* but the regiospecificity depends on the alkene structure (56,58). The major difference Guy and Pearson noted between thiocyanogen and thiocyanogen chloride additions to olefins is the enhanced reactivity of the latter reagent, which is attributed to polarization of the molecule in the manner



Cl-SCN

Heterolytic addition to *trans*-stilbene is nonstereospecific (*trans*-stereoselective) but *cis*- and *trans*-stilbene give different product ratios in acetic acid (Table VI), indicating that the two olefins are not involved in a common intermediate (57,58). The product ratios are also influenced by solvent, as shown in Table VI. The rate of addition decreases with decreasing solvating power of the solvent. The presence of electronegative groups (*trans*-4,4'-dinitrostilbene)

TABLE VI

Solvent Effect of Addition of Thiocyanogen Chloride to Stilbenes (57)

Stilbene	Solvent	Relative reaction rate	Isomer ratios	
			T-Cl:E-Cl ^a	T-OAc:E-OAc ^b
<i>cis</i>	AcOH	40	75:25	88:12
<i>trans</i>	AcOH	13	46:54	10:90
<i>trans</i>	CH ₂ Cl ₂	10	28:72	
<i>trans</i>	CHCl ₃	4	8:92	
<i>trans</i>	C ₆ H ₆	1	37:63	

^aT-Cl = *threo*-1-chloro-1,2-diphenyl-2-thiocyanate; E-Cl = *erythro*-1-chloro-1,2-diphenyl-2-thiocyanate. ^bT-OAc = *threo*-1-acetoxy-1,2-diphenyl-2-thiocyanate; E-OAc = *erythro*-1-acetoxy-1,2-diphenyl-2-thiocyanate.

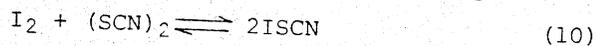
or steric factors (tetraphenylethylene) inhibits addition. Further structural and mechanistic details of the reaction with arylalkenes were discussed by Guy and Pearson (57,58).

THIOCYANOGEN BROMIDE

No work has been reported on the addition reaction of thiocyanogen bromide to olefins. It is anticipated that its chemistry in electrophilic reactions would be similar to its cogener thiocyanogen chloride, since polarization of both reagents associates negative charge with the halogen atom (59). Investigators have reported the presence of a dynamic equilibrium between bromine and thiocyanogen in solution (60) [Br₂ + (SCN)₂ ⇌ 2BrSCN], although the formation of BrSCN is less favorable than the formation of ClSCN in its corresponding equilibrium. The presence of all three components resulting from this equilibrium would contribute to a complex mixture of products in olefin additions. Minor amounts of *vic*-bromothiocyanates have been isolated from thiocyanogen additions where this reagent was generated by bromine displacement of metal thiocyanates (22,31).

IODINE THIOCYANATE

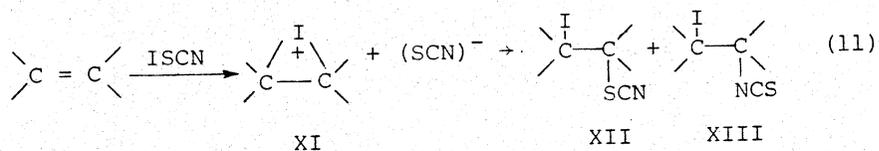
This reagent has not been prepared in pure form but arises in solution via the following equilibrium (eq. 10).



The reagent has been readily generated in organic solvents from metal thiocyanates, namely, from iodine (I) chloride/KSCN,

iodine/thallium (I) thiocyanate, or iodine/KSCN (61). Interestingly, it has now been generated in an aqueous medium from $I_2/KSCN$ with a phase transfer reagent for *in situ* reactions in biphasic solvent systems (62).

Because of similarities in the ionization potentials of both I and SCN, investigators have predicted that bonding in the molecule should be represented as the polarized form $I(\delta^+) - SCN(\delta^-)$, in contrast to the opposite polarization in the other members of the thiocyanogen series (12). This electrochemical correspondence, as well as the nature of its addition reactions to be described in this section, supports its designation as iodine thiocyanate rather than thiocyanogen iodide. Electrophilic addition would accordingly be expected to give rise to an iodonium ion (XI) as the cyclic cationic intermediate or transition state and then proceed to give two products, the *vic*-iodothiocyanate (XII) and *vic*-iodoisothiocyanate (XIII) (eq. 11). Hinshaw (63), for instance, added



iodine thiocyanate to olefins as another route to episulfides (see eq. 12), though the intermediate *vic*-iodothiocyanate XII was not isolated and the isomer XIII was not suspected. In earlier studies Raby and Mesnard (64,65) added iodine thiocyanate to a variety of aliphatic olefins but identifications of the products were based only on titrations and elemental analyses. Neither of these studies provided mechanistic information.

Woodgate and coworkers (61) examined the addition of ISCN to several aryl alkenes, cyclohexene, and an unsaturated steroid (cyclohexene analog). Addition to 2-phenylpropene in polar solvents, namely, CHCl_3 -sulfolane mixtures in various ratios (CHCl_3 -dimethylsulfoxide and CHCl_3 -hexamethylphosphoramide instead decreased crude yields), resulted in a complex mixture of nine products, most importantly in formation both of Markownikoff and anti-Markownikoff products of *vic*-iodoisothiocyanate XIII and *vic*-isothiocyanothiocyanate III adducts. Addition to cyclohexene in CHCl_3 -sulfolane (1:1) gave almost solely the *trans*-iodothiocyanate (XII) and a trace of *trans*-iodoisothiocyanate (XIII). The presence of thallium ion catalyzed predominant formation of the *vic*-iodoisothiocyanate adduct in a XIII:XII product ratio of 4:1. Since thallium is a soft acid (43), thallium-sulfur association of thiocyanate anion consequently polarizes the uncomplexed nitrogen terminus,

which is the reverse effect of ferric ion catalysis in thiocyanogen additions.

Woodgate's results with aryl alkenes, which were stereochemically nonspecific, support an ionic pathway involving an open carbonium ion, which he suggested applied to other olefin types. However, this mechanism for aromatic alkenes cannot be generally extended to include aliphatic alkenes unless a common intermediate for both substrates has been established. Therefore, to clarify the mode of ionic addition to aliphatic alkenes, Maxwell and Silbert (66) examined the ISCN addition to *cis*- and *trans*-3-hexene in both benzene and acetic acid solutions. In benzene only two products, *vic*-iodoisothiocyanate (type XIII, eq. 11) (91%) and *vic*-isothiocyanatothiocyante (type III, eq. 6) (9%) adducts were obtained from each olefin by stereospecific *trans* addition of reagent. Formation of these two products from separate reaction pathways indicates the existence of an equilibrium (eq. 10) in benzene, strongly shifted to the right, but which still leaves substantial amounts of free thiocyanogen in solution. Consequently, thiocyanogen and iodine thiocyanate must compete in olefin addition. These results support the cyclic iodonium cationic structure XI as the intermediate for the ISCN addition product and the cyanoepisulfonium cation X as intermediate for the adduct from thiocyanogen. However, the more polarized ISCN would be expected to have a substantially higher addition rate to give a higher proportion of product than thiocyanogen. Interestingly, isothiocyanate products were the only isomeric species observed in benzene solution reactions. By comparison, thiocyanogen addition in benzene gave isothiocyanate adducts as the major but not sole isomeric products (Table I).

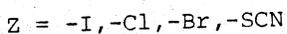
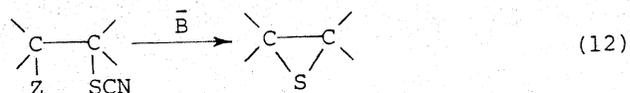
Results of ISCN experiments in acetic acid contrasted markedly with those obtained in benzene (59). The product profile was identical to that derived from thiocyanogen as expressed in eq. 6. No iodine-containing product was detected. These results, based on glc, IR, and NMR examination of the products, show that ISCN formation in the equilibrium (eq. 10) is largely precluded in acetic acid. This conclusion is at variance with reports by other investigators (64,65,67). Raby and Mesnard (65), on the basis of their rate determinations, proposed a formal ionic mechanism in which the iodonium ion (I^+) is the cationic species in acetic acid responsible for attack on a polarized double bond. Their mechanism appeared to represent a concerted reaction by I^+ and $(SCN)^-$ species. von Collin *et al.* (67) also reported rate data for a series of iodine thiocyanate-olefin reactions in acetic acid and benzene solutions. In neither Raby's nor von Collin's studies were the products of reaction isolated and identified, an omission that renders the kinetic data meaningless. In fact,

the rate determinations for reactions in acetic acid reflect instead the addition of thiocyanogen rather than of iodine thiocyanate.

HETEROCYCLES FROM THIOCYANATE ADDUCTS

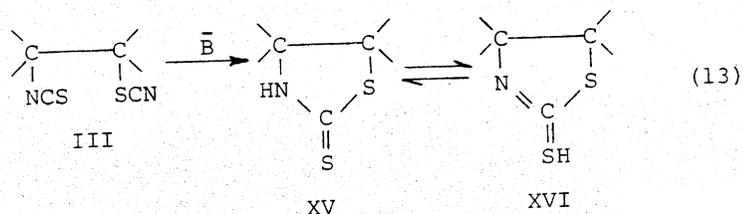
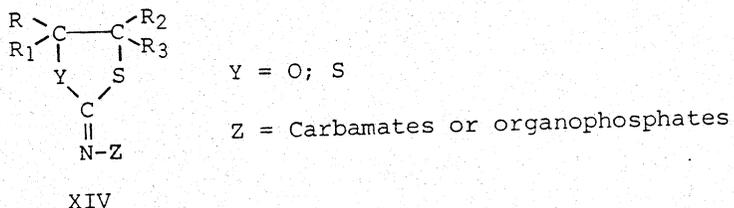
The ease of obtaining adducts by reaction of thiocyanogen or thiocyanogen halides with unsaturated compounds provides entry to several heterocyclic systems which may be incorporated into fatty acids.

Thiiranes are generated stereospecifically by base cyclization of *vic*-dithiocyanates I or α -halo- β -thiocyanates (eq. 12). The thiocyanate adducts offer an alternative to the



epoxides and α -hydroxy- β -halides, which are similarly converted to thiiranes by thiourea (68). Thiiranes have been prepared from long chain unsaturated acids and esters (68).

vic-Dithiocyanates are cyclized in methanesulfonic acid to 1,3-dithiolane-2-imine salts (eq. 7 and 8) (69). The free imines were not stable but were isolated as salts of methanesulfonic acid or as the hydrochloride salts prepared by ion exchange chromatography. Low molecular weight derivatives of the dithiolane and other related heterocyclic structures have insecticidal properties (70). Derivatives of these structural types from unsaturated fatty acids generalized by structure XIV offer new possibilities for research in their practical uses.



α -Isothiocyanato- β -thiocyanates III are base cyclized stereospecifically to the heterocyclic class of 4,5-thiazoline-2-thiones XV (71). The thiazoline-2-thiones tautomerize to derivatives of thiazolidine XVI.

SUMMARY AND CONCLUSIONS

Research carried out in the past decade has resolved many questions regarding the chemistry of thiocyanogen and the related pseudohalogens. Uppermost in this work have been the detailed investigations of products, rates, and mechanisms of olefin thiocyanations that have finally revealed the nature of the empiricism underlying these reactions. The influences of solvents and transition metals, particularly iron, on thiocyanogen's ambident addition pathway were invaluable in the clarification of mechanisms and in providing selective, quantitative, and rapid preparations of isomeric adducts. New adducts may now be prepared that offer the fatty acid chemist special opportunities in the synthesis of heterocyclic derivatives from the fatty acid adducts.

Finally, advances in the study of the chemistry of thiocyanogen chloride and iodine thiocyanate have given a more coherent picture of the similarities and differences encountered between all of the members of this chemical family.

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