893. *Aliphatic Acids. Part IV.*[1] *Addition of Thiocyanogen and the Preparation of Epithio-acids.*

By J. F. McGhie, W. A. Ross, F. J. Julietti, and B. E. Grimwood.

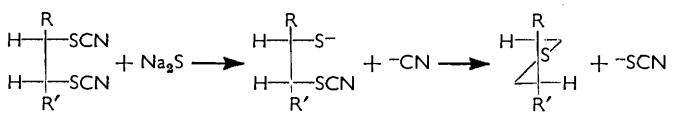
An improved procedure for addition of thiocyanogen to olefinic acids is described. The constitution of the compound obtained by the alkaline hydrolysis of *erythro*-9,10-dithiocyanato-octadecanoic acid is established as *trans*-9,10-epithio-octadecanoic acid. The general nature of the reaction has been investigated, and new methods developed for the preparation of epithio-acids.

Since the investigation of the addition of thiocyanogen to olefins by Kaufmann and Liepe,[2] three workers [3,4] have reported on this reaction with olefinic acids. We have developed a modified procedure involving anhydrous conditions, and have investigated the addition to a number of *cis*- and *trans*-olefinic acids, obtaining improved yields (*ca.* 80%) of the products. Our finding that *trans*-acids afforded crystalline products, whilst *cis*-mono-olefinic acids gave oily dithiocyanato-acids is in agreement with previous reports.[3,4]

From the known pseudohalogen nature of thiocyanogen, it would be expected to afford additive compounds by *trans*-addition, as do halogens themselves. Thus *cis*-olefinic acids will give *threo*-, and *trans*-olefinic acids *erythro*-dithiocyanato-acids. This assumption is supported by comparing the *erythro*- and the *threo*-dithiocyanato-acids with the corresponding dibromides:[5] in all cases the *erythro*-isomer has the higher melting point.

Kaufmann [6] and Wood [7] have reviewed the reactions, uses, and analysis of organic thiocyanates. Quantitative estimation of the thiocyanate group is usually carried out by the method of Panchenko and Smirnov.[8] This involves reaction of the thiocyanate with an excess of alcoholic sodium sulphide, followed by precipitation of thiocyanate as silver thiocyanate, and a subsequent Volhard titration. In the course of the estimation of the thiocyanogen groups in *erythro*-9,10-dithiocyanato-octadecanoic acid (I) a compound, $C_{18}H_{34}O_2S$, of m. p. 63—64° was isolated; this proved to have far-reaching importance in our investigation.

Delépine and Jaffeux [9] were the first to report the preparation of episulphides by the action of sodium sulphide on either vicinal halogeno-thiocyanates or dithiocyanates. Accordingly we formulate the compound in question as *trans*-9,10-epithio-octadecanoic acid (II), its formation being as shown.



R = $CH_3[CH_2]_7$–; R′ = –$[CH_2]_7CO_2H$.

This reaction was of general application, *erythro*- and *threo*-1,2-dithiocyanato-acids being converted into *trans*- and *cis*-epithio-acids, respectively, in yields of about 60% (see Table 2).

[1] Part III, *J.*, 1962, 3108.
[2] Kaufmann and Liepe, *Ber.*, 1923, **56**, 2514.
[3] Kimura, *Chem. Umschau*, 1930, **37**, 72.
[4] Kaufmann, *Chem. Umschau*, 1930, **37**, 113; Holde, *ibid.*, p. 173.
[5] Cramp, Thesis, London 1958; Holde and Gorgas, *Angew. Chem.*, 1926, **39**, 1443; Lewkowitsch, "Chemical Technology and Analysis of Oils, Fats, and Waxes," Macmillan and Co., London, 1921, Vol. I, p. 580; Holt, *Ber.*, 1891, **24**, 4120.
[6] Kaufmann, *Angew. Chem.*, 1941, **54**, 195; "Newer Preparative Methods of Organic Chemistry," Interscience Publ., Inc., New York, 1948, p. 369.
[7] Wood, *Org. Reactions*, 1946, **3**, 251.
[8] Panchenko and Smirnov, *J. Gen. Chem.* (*U.S.S.R.*), 1932, **2**, 193.
[9] Delépine and Jaffeux, *Compt. rend.*, 1921, **172**, 158.

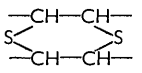
TABLE 1.

Melting points of related acids.

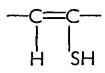
Acid	Epithio-acid *cis*	Epithio-acid *trans*	Epoxy-acid *cis*	Epoxy-acid *trans*
Octadec-6-enoic	74·5—75·5°	78—79°	60—61°	67—68°
Octadec-9-enoic	58—58·5	63—64	59·5	55·5
Docos-13-enoic	61—62	69—70	63·5	70·0

The melting points of this series of *cis*- and *trans*-epithio-acids are as given in Table 1, the melting points of the corresponding epoxy-acids being included for comparison.

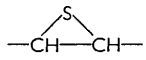
Kaufmann [10] isolated a compound of m. p. 63—64° on treating the dithiocyanato-acid (I) with alcoholic alkali. To this compound there has been assigned a dithian [10] (III), a mercapto- [11] (IV), and an epithio-structure [12] (V). Kaufmann proposed the dithian formulation as a result of molecular-weight determinations that indicated not only the compound of m. p. 63—64° but also its precursor (I) as being bimolecular. Since our compound of m. p. 63—64° was identical with Kaufmann's in a mixed-melting-point determination and in spectral properties, we repeated the molecular-weight determinations.



(III)

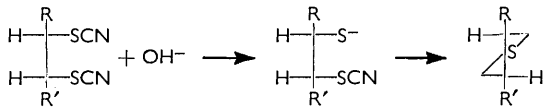


(IV)



(V)

In agreement with Kimura,[3] we found that the acid (I) was unimolecular and, in contrast to Kaufmann, we also found the compound of m. p. 63—64° to be unimolecular. These results have been confirmed independently by both Mr. F. H. Oliver and Mr. R. H. Doggett, A.R.I.C. We feel that Kaufmann's results may be due to his erroneously assuming the cryscopic constant for camphor to be 50, instead of the more usual value of 35.



(I) (II)

We then observed that the action of alkali on vicinal dithiocyanato-acids was a general method for the preparation of epithio-acids, the yields being *ca.* 60%, somewhat higher than when sodium sulphide is used. The mechanism of the reaction is similar to that proposed above for the reaction involving sodium sulphide. It is similar to that proposed by Mousseron *et al.*[13] for the formation of epithiocyclohexane from 1,2-dithiocyanatocyclohexane with lithium aluminium hydride, and that of Siegel and Rosenblatt [14] for the conversion of ethylene dithiocyanate into thiiran by aqueous-alcoholic potassium hydroxide.

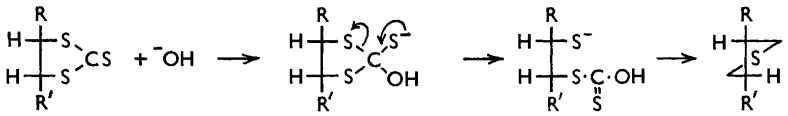
Kaufmann [10] mentioned that *threo*-9,10-dithiocyanato-octadecanoic acid also afforded the sulphide (II). This is incorrect, the product having m. p. 58—59·5°, which, although close to, is not identical with, that of compound (II). The non-identity of the two substances is in accordance with our mechanistic scheme, *erythro*- and *threo*-dithiocyanato-acids affording *trans*- and *cis*-epithio-acids, respectively.

To support our view that the thiiran ring is present in the compounds described above, we investigated known methods for the preparation of compounds containing this feature.

[10] Kaufmann, *Ber.*, 1937, **70**, 2519.
[11] Salchow, *Kautschuk*, 1937, **13**, 119.
[12] Salchow, *Kautschuk*, 1938, **14**, 12.
[13] Mousseron, Jacquier, Mousseron-Canet, and Zagdoun, *Bull. Soc. chim. France*, 1952, **19**, 1042.
[14] Siegel and Rosenblatt, *J. Amer. Chem. Soc.*, 1958, **80**, 1753.

trans-9,10-Epoxyoctadecanoic acid failed to react with thiourea [15] or thiocyanate ion.[16] However, suitable modification of Wagner-Jauregg's method [17] gave *trans*-9,10-epithio-octadecanoic acid, although in variable yield (15—40%),* identical with our and Kaufmann's compound.

The failure of standard methods to afford the sulphide (II) led us to explore other routes for the conversion of epoxy- into epithio-acids. We have developed what appears to be a general method for the preparation of episulphides. Potassium methyl xanthate readily reacts with epoxides, to give cyclic trithiocarbonates, and the latter on alkaline hydrolysis are known to give vicinal dithiols in poor yield.[18] Iqbal and Owen [19] showed that enhanced yields may be obtained by reductive hydrolysis with lithium aluminium hydride. Our results suggested that the predominant reaction was formation, not of dithiol, but of the episulphide, by the route illustrated. This proved to be the case. A number of long-chain epoxy-acids were converted by potassium methyl xanthate into the trithiocarbonates,[20] these reacting with alkali to give the expected epithio-acids in yields of 50—60%. No evidence of dithiol formation was observed, and by this procedure *cis*- and *trans*-epoxy-acids may be converted into the *cis*- and *trans*-epithio-acids, respectively. These results explain the poor yields of dithiols obtained by alkaline hydrolysis of simple trithiocarbonates. Preliminary experiments to support this showed that ethylene trithiocarbonate with alkali gave polymeric " ethylene sulphide," m. p. 108—109°. This must have arisen by polymerisation of the intermediate thiiran. We shall report this work in detail later.



Delépine and Jaffeux [9] obtained simple thiirans, not only from vicinal dithiocyanates, but also from halogeno-thiocyanates. Angus *et al.*[21] have described the preparation of thiocyanogen chloride and its reaction with simple olefins. We have found that thiocyanogen chloride reacts with olefinic acids to give the expected addition products. These proved to be uncrystallisable oils, but they were smoothly converted by alkaline hydrolysis into the expected epithio-acids in 42—60% yields. Since addition of thiocyanogen chloride to the olefinic bond would be expected to follow the same course as that of thiocyanogen, *cis*- and *trans*-olefinic acids should afford the *cis*- and *trans*-epithio-acids, respectively. This is the case.

TABLE 2.

	Method 1		Method 2		Method 3		Method 4	
Acid	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
6,7-Epithio-octadecanoic ...	64	53	63	66	56	75	48	51
9,10-Epithio-octadecanoic...	51	51	51	63	68	68	41	54
13,14-Epithiodocosanoic ...	61	74	62	74	72	78	49	54

Method: 1, $Na_2S,9H_2O$ and dithiocyanato-acid. 2, KOH and dithiocyanato-acid. 3, From trithiocarbonate. 4, From olefin *via* chloro-thiocyanate.

Table 2 shows the yields (%) from the various methods used for the preparation of the epithio-acids.

* *Added in proof:* Since this paper was submitted, consistent yields of 90% have been obtained by this method by Mr. G. Swift working in these laboratories.

[15] Culvenor, Davies, and Pausacker, *J.*, 1946, 1050.
[16] van Tamelen, *J. Amer. Chem. Soc.*, 1951, **71**, 3444.
[17] Wagner-Jauregg, *Annalen*, 1949, **561**, 87.
[18] Frassetti, *Ber.*, 1905, **38**, 488; Culvenor and Davies, *Austral. J. Sci. Res.*, 1948, **1**, *A*, 236.
[19] Iqbal and Owen, *J.*, 1960, 1030.
[20] McGhie, Ross, Julietti, and Grimwood, unpublished work; cf. Culvenor, Davies, and Pausacker, *J.*, 1946, 1050.
[21] Angus, Bacon, and Guy, *Chem. and Ind.*, 1955, 564; Angus and Bacon, *J.*, 1958, 774.

The *cis*- and *trans*-epithio-acids obtained in this investigation showed characteristic infrared absorption at 16·43 and 16·63 μ, respectively, and these measurements have been used to identify and distinguish between pairs of isomers.

The compound of m. p. 64·6° first obtained by Rankoff [22] as a minor product in the elaidinisation is *trans*-9,10-epithio-octadecanoic acid, as suspected by Kaufmann;[10] this identity was confirmed by a comparison with an authentic specimen prepared by Rankoff's method.

Experimental

M. p.s were taken on the Kofler block. Infrared spectra were taken for Nujol mulls, unless stated to the contrary. Microanalyses were by Miss J. Cuckney and her associates, Imperial College of Science and Technology, London. Light petroleum refers to the fraction of b. p. 40—60°, unless otherwise stated.

Addition of Thiocyanogen to Mono-olefinic Acids.—A vigorously stirred suspension of pure lead thiocyanate (dried over P_2O_5 in the dark *in vacuo*) in anhydrous acetic acid (150 ml.) was treated with dry bromine (1·6 g.) and left until colourless. [Anhydrous acetic acid was prepared by heating under reflux acetic acid with acetic anhydride (5% by weight) for 4 hr.] To the stirred suspension was then added the olefinic acid (0·01 mole) and stirring was continued for 8 hr. Next day the mixture was filtered and poured into water (500 ml.). With the *trans*-acids crystals were slowly formed, which were filtered off and recrystallised from light petroleum. With *cis*-acids, the product was extracted with ether, washed free from acetic acid, and dried ($MgSO_4$). Removal of the ether afforded the dithiocyanates as viscous oils. Quantities up to 0·1 mole have been treated by this method without appreciable loss in yield.

By this procedure (on 0·01-molar scale) octadec-*trans*-6-enoic acid afforded erythro-6,7-*dithiocyanato-octadecanoic acid* (3·0 g.), m. p. 43—43·5° (Found: C, 60·8; H, 8·6; N, 7·0; S, 15·9. $C_{20}H_{34}N_2O_2S_2$ requires C, 60·3; H, 8·5; N, 7·0; S, 16·1%). Octadec-*trans*-9-enoic acid gave *erythro*-9,10-dithiocyanato-octadecanoic acid (3·0 g.), m. p. 79—80°; docos-*trans*-13-enoic acid gave *erythro*-13,14-dithiocyanatodocosanoic acid (3·4 g.), m. p. 57—58°.

Action of Sodium Sulphide on the Dithiocyanato-acids.—The dithiocyanato-acid (5 g.) in ethanol (75 ml.) was heated for 30 min. under reflux with a solution of sodium sulphide nonahydrate (19 g.) in ethanol (180 ml.). The mixture was cooled, diluted with water, acidified with 2N-sulphuric acid, and heated until evolution of hydrogen sulphide ceased. The product obtained by ether-extraction crystallised from light petroleum (b. p. 60—80°), to give the episulphide. *erythro*-6,7-Dithiocyanato-octadecanoic acid gave trans-6,7-*epithio-octadecanoic acid* (2·1 g.), m. p. 78—79° (Found: C, 68·7; H, 10·85; S, 10·2. $C_{18}H_{34}O_2S$ requires C, 68·8; H, 10·9; S, 10·2%); *erythro*-9,10-dithiocyanato-octadecanoic acid yielded trans-9,10-*epithio-octadecanoic acid* (2·0 g.), m. p. 63—64° (Found: C, 68·8; H, 10·8; S, 10·2%); *threo*-6,7-dithiocyanato-octadecanoic acid afforded cis-6,7-*epithio-octadecanoic acid* (2·5 g.), m. p. 74—75° (Found: C, 68·6; H, 11·1; S, 10·4%); *threo*-9,10-dithiocyanato-octadecanoic acid yielded cis-9,10-*epithio-octadecanoic acid* (2·0 g.), m. p. 58·5—59·5° (Found: C, 68·7; H, 10·7; S, 10·2%); *erythro*-13,14-dithiocyanatodocosanoic acid afforded trans-13,14-*epithiodocosanoic acid* (3·0 g.), m. p. 69—70° (Found: C, 71·4; H, 11·4; S, 8·7. $C_{22}H_{42}O_2S$ requires C, 71·3; H, 11·4; S, 8·7%); *threo*-13,14-dithiocyanatodocosanoic acid afforded cis-13,14-*epithiodocosanoic acid* (2·5 g.), m. p. 61—62° (Found: C, 71·4; H, 11·7; S, 8·7%).

Reaction of Dithiocyanato-acids with Potassium Hydroxide.—The dithiocyanato-acid (5 g.) was heated under reflux for 30 min. with 0·5N-alcoholic potassium hydroxide (150 ml.). The solution was cooled, diluted with water, and acidified with 10% hydrochloric acid. The product was filtered off, dried azeotropically with benzene, and crystallised from light petroleum (b. p. 60—80°), to give the episulphide. By this procedure the *erythro*-6,7-, -9,10-, and -13,14-dithiocyanato-acids afforded 2·6 g., 2·5 g., and 3·0 g. of the respective *trans*-epithio-acids. Similarly the *threo*-6,7-, -9,10-, and -13,14-dithiocyanato-acids yielded 2·5 g., 2·0 g., and 2·5 g. of the respective *cis*-epithio-acids.

Conversion of trans-9,10-*Epoxyoctadecanoic Acid into* trans-9,10-*Epithio-octadecanoic Acid by Thiocyanic Acid.*—Potassium thiocyanate (7·5 g.) in water (20 ml.) in a separatory funnel (500 ml.) was diluted by addition of ice (200 g.) and shaken with ether (20 ml.). Syrupy

[22] Rankoff, *Ber.*, 1931, **64**, 619.

phosphoric acid (5·5 ml.) was added slowly with intermittent shaking. The aqueous layer was removed, and the ethereal solution was washed twice with ice–water. To this ethereal solution of thiocyanic acid was added a solution of *trans*-9,10-epoxyoctadecanoic acid (5 g.) in ether (5 ml.). After 3 days at 0° the ether was removed on the steam-bath, and the residue was heated for a further 10 min. The product was an oil but showed infrared bands indicating the presence of OH and SCN groups.

The residue was heated for 30 min. under reflux with 5% alcoholic potassium hydroxide (100 ml.). After cooling, the solution was acidified with 17% hydrochloric acid (50 ml.), and the solid which separated at 0° was removed and dissolved in ether. Fractional crystallisation from light petroleum gave, as the more soluble component, *trans*-9,10-epithio-octadecanoic acid. This recrystallised from aqueous acetone, giving the pure *trans*-episulphide (0·8 g.), m. p. 63—64° (Found: C, 68·8; H, 10·8; S, 10·2. Calc. for $C_{18}H_{34}O_2S$: C, 68·8; H, 11·0; S, 10·2%), identical with the product obtained by the two previous methods.

Preparation of Epithio-acids by Alkaline Hydrolysis of Cyclic Trithiocarbonates.—The trithiocarbonate (2 g.) was heated under reflux for 1 hr. with 0·5N-alcoholic potassium hydroxide (125 ml.), by which time the yellow colour of the trithiocarbonate had disappeared. After cooling, the solution was acidified with 10% hydrochloric acid and then diluted, and the product was isolated by ether-extraction. Crystallisation from light petroleum (b. p. 60—80°) gave the epithio-acid. In this manner *threo*-6,7-(thiocarbonyldithio)octadecanoic acid afforded *cis*-6,7-epithio-octadecanoic acid (0·9 g.), *threo*-9,10-(thiocarbonyldithio)octadecanoic acid gave *cis*-9,10-epithio-octadecanoic acid (1·1 g.), and *threo*-13,14-(thiocarbonyldithio)docosanoic acid gave *cis*-9,10-epithiodocosanoic acid (1·2 g.). The isomeric *erythro*-trithiocarbonates afforded *trans*-epithio-acids, namely, *trans*-6,7-epithio-octadecanoic (1·2 g.), *trans*-9,10-epithio-octadecanoic (1·1 g.), and *trans*-13,14-epithiodocosanoic acid (1·3 g.).

Episulphide Formation via the Chlorothiocyanate.—~0·15M-Thiocyanogen chloride was prepared as described by Bacon and Guy.[23] The olefinic acid (0·01 mole) was added to a solution of thiocyanogen chloride (10% excess). After 8 hr., the addition compounds were isolated in the usual way, as pale yellow, viscous oils. They were converted directly into the epithio-acids by heating them under reflux for 30 min. with 0·5N-alcoholic potassium hydroxide (125 ml.). Isolation of the products, as described for the dithiocyanato-acids, followed by crystallisation from light petroleum, gave the epithio-acids. Thus octadec-*cis*-6-enoic acid (2·8 g.) gave *cis*-6,7-epithio-octadecanoic acid (1·5 g.), octadec-*cis*-9-enoic acid gave *cis*-9,10-epithio-octadecanoic acid (1·3 g.), and docos-*cis*-13-enoic acid afforded *cis*-13,14-epithiodocosanoic acid (1·8 g.). The isomeric *trans*-acids gave slightly better yields: octadec-*trans*-6-enoic acid yielded *trans*-6,7-epithio-octadecanoic acid (1·6 g.), octadec-*trans*-9-enoic acid afforded *trans*-9,10-epithio-octadecanoic acid (1·7 g.), and docos-*trans*-13-enoic acid gave *trans*-13,14-epithiodocosanoic acid (2·0 g.).

Molecular-weight Determinations by Rast's Method.—*erythro*-9,10-Dithiocyanato-octadecanoic acid (1·24 mg.) in camphor (*K* 36·58; 11·29 mg.) gave a m. p. depression of 9° (Found: *M*, 410. Calc. for $C_{20}H_{34}N_2O_2S_2$: *M*, 398). Four further determinations gave an average value of 402. *trans*-9,10-Epithio-octadecanoic acid (0·953 mg.) in camphor (12·43 mg.) gave a m. p. depression of 8·6° (Found: *M*, 326. Calc. for $C_{18}H_{34}O_2S$: *M*, 314·5). The mean value of six determinations was 320.

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[23] Bacon and Guy, *J.*, 1960, 318.