

### 399. *Acyl Isothiocyanates. Part IV.\* The Reaction between Acetaldehyde Ammonia and some Isothiocyanates.*

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The products of the reaction between acetaldehyde ammonia and alkoxy-carbonyl isothiocyanates, claimed by Dixon and Taylor<sup>1</sup> to be *NN'*-ethylidenethioureas (I), are found to be 1,1-di[alkoxycarbonyl(thioureido)]ethanes (III). Acetaldehyde ammonia and phenyl isothiocyanate, however, afforded perhydro-4,6-dimethyl-1-phenyl-2-thio-1,3,5-triazine (V), as suggested by Dixon.<sup>2</sup> The mechanisms of these reactions are briefly discussed.

DIXON and TAYLOR<sup>1</sup> studied the reaction between acetaldehyde ammonia and several acyl isothiocyanates. The *NN'*-ethylidenethiourea structure (I) was ascribed to the products, partly on analytical grounds, and partly from consideration of the products of hydrolysis. We felt that this structure was erroneous for several reasons, not the least being the discovery by Lund<sup>3</sup> that acetaldehyde ammonia is the trihydrate of perhydro-2,4,6-trimethyl-1,3,5-triazine (II), a suggestion made long ago by Delépine.<sup>4</sup> Methoxy- and ethoxy-carbonyl isothiocyanates with acetaldehyde ammonia gave crystalline products, which had m. p.s almost identical with those quoted by Dixon and Taylor,<sup>1</sup> and thus appeared to be the same compounds. We were unable, however, to reproduce the sulphur and nitrogen analyses reported by these workers; our results led conclusively to the empirical formulæ  $C_4H_7O_2N_2S$  and  $C_5H_9O_2N_2S$ , respectively. Confirmation was forthcoming from potentiometric titration with tetrabutylammonium hydroxide in dry pyridine. Cryoscopic determination of molecular weights in urethane solution, however, revealed that the molecular formulæ were  $C_8H_{14}O_4N_4S_2$  and  $C_{10}H_{18}O_4N_4S_2$ . These results strongly suggested that the compounds were 1,1-di[alkoxycarbonyl(thioureido)]ethanes (III; R = Me or Et). Further, their ultraviolet absorption spectra (Table) closely resembled those of methyl and ethyl thioallophanates and *N*-cyclohexylthioallophanates, with the exception that the extinction coefficients were approximately double, a result which is explained by the presence of two identical, isolated chromophores.

#### *Ultraviolet absorption data in 95% ethanol.*

Compound	$\lambda$ (m $\mu$ ) and $\epsilon$ (in parentheses)		
(III; R = Me) .....	259(29,500)	233(6700)	
(III; R = Et) .....	259(29,500)	233(6300)	
(IV; R = Me) .....	262(15,000)	227(300)	
(IV; R = Et) .....	262(16,800)	227(400)	
Methyl <i>N</i> -cyclohexylthioallophanate .....	262(15,300)	233(1200)	212(13,000)
Ethyl <i>N</i> -cyclohexylthioallophanate .....	262(14,100)	232(3100)	213(13,900)

Examination of the infrared spectra of the compounds (III) afforded additional evidence of structure. The presence of two  $\nu$ NH bands is compatible with the structure (III) but not with that proposed by Dixon and Taylor.<sup>1</sup> A single  $\nu$ C:O band appeared at 1724  $cm^{-1}$  in chloroform but two peaks were observed in the spectra of Nujol mulls of both compounds. The significance of this is not clear, especially since the additional peak was at a frequency higher than 1724  $cm^{-1}$  for the methyl derivative and lower than 1724  $cm^{-1}$  for the ethyl homologue. Strong absorption at 1523—1535  $cm^{-1}$  is assigned

\* Part III, *J.*, 1959, 2286.

<sup>1</sup> Dixon and Taylor, *J.*, 1916, **109**, 1244.

<sup>2</sup> (a) Dixon, *J.*, 1888, **53**, 411; (b) *Idem*, *J.*, 1892, **61**, 509.

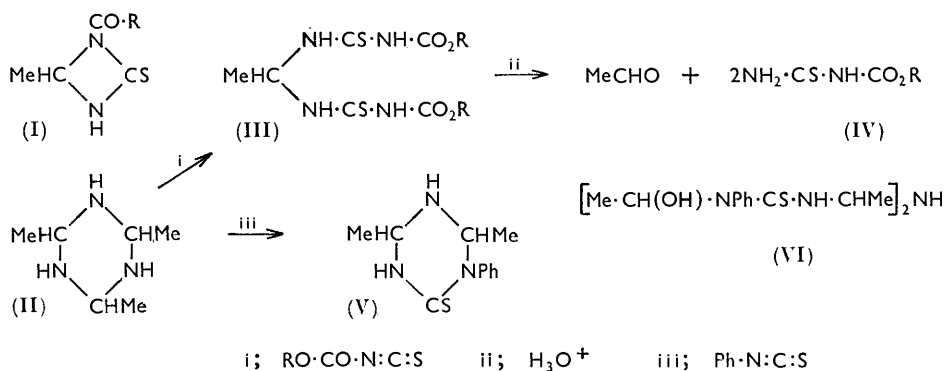
<sup>3</sup> Lund, *Acta Chem. Scand.*, 1958, **12**, 1768.

<sup>4</sup> Delépine, *Bull. Soc. chim. France*, 1898, **19**, 15.

to the "thioureide" band.<sup>5</sup> Fuller data for both compounds and for the thioallophanates and their *N*-cyclohexyl derivatives are included in the Experimental section.

Dixon and Taylor<sup>1</sup> reported that their compounds were hydrolysed by hot, dilute acid to acetaldehyde and the corresponding alkyl thioallophanate. This was regarded as confirmatory evidence for the structure (I; R = OMe or OEt). We have confirmed this observation qualitatively, but it should be noted that lability to acid might be expected for either structure. Quantitatively, however, we found that the yields of thioallophanates and acetaldehyde (isolated as the dimedone derivative) approximated to those required by structure (III). Dixon and Taylor<sup>1</sup> reported that the products from alkoxy-carbonyl isothiocyanates and acetaldehyde ammonia were hydrolysed by cold, strong alkali to inorganic thiocyanate. Earlier observations by these and other authors<sup>6</sup> had indicated that such lability was characteristic of *NN*-disubstituted thioureas, particularly when one substituent was an acyl group. This observation was therefore important evidence in favour of the structure proposed. Our compounds, however, were quite stable under these conditions, and it is possible that Dixon and Taylor obtained different products. Unfortunately, no further comparison was possible, but in view of the agreement of m. p.s. we believe that our compounds are the same as those isolated by Dixon and Taylor, but that the products of the latter were slightly impure. A trace of thiocyanate would have been sufficient to have given a pronounced reaction with ferric chloride.

Dixon also studied the reactions of acetaldehyde ammonia with acetyl isothiocyanate,<sup>1,2b</sup> and benzoyl isothiocyanate.<sup>2b</sup> Acetyl isothiocyanate afforded two compounds, to which the formulæ C<sub>5</sub>H<sub>8</sub>ON<sub>2</sub>S (I; R = Me) and C<sub>7</sub>H<sub>15</sub>O<sub>2</sub>N<sub>3</sub>S were ascribed, while benzoyl isothiocyanate yielded *N*-benzoylthiourea as the only identifiable product. We have not so far succeeded in isolating any crystalline material from these reactions, but, in



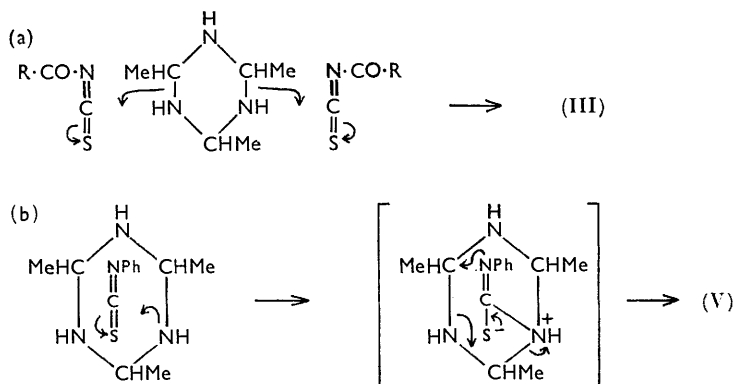
view of the results with alkoxy-carbonyl isothiocyanates, the compound (I; R = Me) must be regarded with suspicion. Dixon<sup>2</sup> also made an extensive study of the reaction of alkyl and aryl isothiocyanates with aldehyde ammonia derivatives. He concluded that all the products were derivatives of perhydro-2-thio-1,3,5-triazine. Thus, phenyl isothiocyanate and acetaldehyde ammonia gave perhydro-4,6-dimethyl-1-phenyl-2-thio-1,3,5-triazine (V). Earlier, Schiff<sup>7</sup> suggested the open-chain structure (VI) for this compound. Repetition of this work has enabled us to confirm the structure suggested by Dixon. Apart from analytical data, the infrared spectrum contained no bands definitely assignable to  $\nu_{\text{OH}}$  vibrations, as would be expected from Schiff's formula. We do not agree, however, with the mechanism suggested by Dixon for the reaction. We suggest that the reactions

<sup>5</sup> Elmore, *J.*, 1958, 3489 (and references cited therein).

<sup>6</sup> Hegershoff, *Ber.*, 1899, 32, 3649; Wheeler, *Amer. Chem. J.*, 1902, 27, 270; Dixon and Hawthorne, *J.*, 1907, 92, 122; Dixon and Taylor, *J.*, 1908, 93, 18.

<sup>7</sup> Schiff, *Ber.*, 1876, 9, 565.

of alkoxy-carbonyl and phenyl isothiocyanates with acetaldehyde ammonia proceed according to the mechanisms summarised below:



Presumably, the greater basicity of the nitrogen atom in PhN= in the intermediate of scheme (b), compared with that in R·CO·N= in scheme (a), favours nucleophilic attack at C<sub>(2)</sub>.

#### EXPERIMENTAL

Ultraviolet absorption spectra were measured on a Carey recording spectrophotometer, model 14. Infrared spectra were measured on a Perkin-Elmer spectrophotometer, model 21, a sodium chloride prism being used, with the sample as a Nujol mull or dissolved in hexachlorobutadiene. Carbonyl bands were also located in some cases with the sample dissolved in chloroform. Equivalents were determined by potentiometric titration against tetrabutylammonium hydroxide in pyridine. Molecular weights were determined cryoscopically in urethane.

1,1-Di[methoxycarbonyl(thioureido)]ethane (III; R = Me).—A mixture of methyl chloroformate (9.85 g.) and potassium thiocyanate (10.4 g.) in dry acetone (100 c.c.) was heated under reflux for 15 min. To the cooled and filtered solution was added a solution of acetaldehyde ammonia (6.1 g.) in acetone (100 c.c.). After several hours at 0°, the product (2.99 g.) was crystallised from ethanol, and then had m. p. 187.5–188.0° (Dixon and Taylor<sup>1</sup> report m. p. 187.5°) (Found: C, 32.7; H, 4.9; N, 18.9; S, 21.8%; Equiv., 148; *M*, 272. C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>N<sub>4</sub>S<sub>2</sub> requires C, 32.6; H, 4.8; N, 19.0; S, 21.8%; Equiv., 147; *M*, 294) The infrared spectrum had the following bands: 3220 (νNH), 3170 (νNH), 3030 (νCH), 1736 and 1726 in Nujol but 1724 in chloroform (νC=O), 1523 (thioureide), 1449 (δCH), 1380 (C–Me), 1303, 1264, 1244, 1210, 1163, 1130, 1098, 1034, 966, 935, 803, 773, 744, and 722 cm.<sup>-1</sup>. This compound (294 mg., 0.001 mole) was heated in 2*N*-sulphuric acid (13 c.c.) for 4 hr. under a warm-jacketed reflux condenser. A slow stream of nitrogen carried acetaldehyde into a saturated solution of dimedone in 10% aqueous ethanol. Several hours after completion of the reaction, the dimedone derivative (244 mg., 0.0008 mole) was collected; it had m. p. and mixed m. p. 140.0–140.5°. Starting material dissolved during the reaction, and methyl thioallophanate (168 mg., 0.00125 mole) crystallised from the cooled hydrolysate. After recrystallisation from water, it had m. p. and mixed m. p. 165.0–165.5° (decomp.). Identity was confirmed by comparison of infrared spectra, which had the following bands: 3310 (νNH), 3290 (νNH), 3240 (νNH), 3170 (νNH), 2955 (νCH), 2860 (νCH), 2710, 1717 (νC=O), 1615 (δNH), 1607 (δNH), 1527 (thioureide), 1447, 1224, 1097, 995, 951, 824, 774, and 718 cm.<sup>-1</sup>.

1,1-Di[ethoxycarbonyl(thioureido)]ethane (III; R = Et).—A mixture of ethyl chloroformate (21.7 g.) and potassium thiocyanate (20.8 g.) in dry acetone (100 c.c.) was heated under reflux for 15 min. To the cooled, filtered solution was added a solution of acetaldehyde ammonia (12.2 g.) in acetone (200 c.c.). Next day, water (600 c.c.) was added, and the solution was left at 0°. The ethane (8.55 g.) had m. p. 153.5–154.5° after recrystallisation from ethanol (Dixon and Taylor<sup>1</sup> report m. p. 152–153°) (Found: C, 37.2; H, 5.7; N, 17.8; S, 19.3%; Equiv., 159; *M*, 323. C<sub>10</sub>H<sub>18</sub>O<sub>4</sub>N<sub>4</sub>S<sub>2</sub> requires C, 37.3; H, 5.6; N, 17.4; S, 19.9%; Equiv., 161; *M*,

322). The infrared spectrum had the following bands: 3280 ( $\nu$ NH), 3180 ( $\nu$ NH), 2990 ( $\nu$ CH), 2740, 1727, and 1696 in Nujol but 1724 in chloroform ( $\nu$ C=O), 1535 (thioureide), 1450 ( $\delta$ CH), 1386 (C-Me), 1334, 1303, 1262, 1239, 1206, 1142, 1098, 1035, 948, 890, 877, 773, and 725  $\text{cm}^{-1}$ . This compound (644 mg., 0.002 mole), heated in 2N-sulphuric acid (25 c.c.) under reflux as described above, afforded the dimedone derivative (200 mg., 0.00065 mole) of acetaldehyde, m. p. and mixed m. p. 139.5—140°, and ethyl thioallophanate (450 mg., 0.00304 mole), m. p. and mixed m. p. 139.5—140° after two recrystallisations from water. Identity was confirmed by comparison of infrared spectra, which had the following bands: 3340 ( $\nu$ NH), 3250 ( $\nu$ NH), 3170 ( $\nu$ NH), 2990 ( $\nu$ CH), 2720, 2210, 2110, 1897, 1702 ( $\nu$ C=O), 1617 ( $\delta$ NH), 1540 (thioureide), 1477, 1463, 1446, 1403, 1376, 1313, 1270, 1221, 1114, 1100, 1017, 997, 893, 764, and 727  $\text{cm}^{-1}$ .

*Methyl N-Cyclohexylthioallophanate.*—A mixture of methyl chloroformate (9.45 g.) and potassium thiocyanate (10.7 g.) in dry acetone was heated under reflux for 15 min. Cyclohexylamine (9.9 g.) was added slowly with cooling, and the mixture was left for 2 hr. It was poured into ice-water (1500 c.c.), and the *product* (8.0 g.) was collected and twice recrystallised from ethanol (charcoal); it then had m. p. 124—125° (Found: C, 50.3; H, 7.6; N, 13.0%; *Equiv.*, 213.  $\text{C}_9\text{H}_{16}\text{O}_2\text{N}_2\text{S}$  requires C, 50.0; H, 7.5; N, 13.0%; *Equiv.*, 216). The infrared spectrum had the following bands: 3410 ( $\nu$ NH), 3225 ( $\nu$ NH), 2930 ( $\nu$ CH), 2850 ( $\nu$ CH), 1720 ( $\nu$ C=O), 1546 (thioureide), 1532, 1450, 1434, 1404, 1354, 1343, 1302, 1272, 1260, 1241, 1198, 1174, 1152, 1115, 1075, 1032, 988, 945, 891, 822, 768, 725, and 692  $\text{cm}^{-1}$ .

*Ethyl N-Cyclohexylthioallophanate.*—A mixture of ethyl chloroformate (10.8 g.) and potassium thiocyanate (10.7 g.) in dry acetone (100 c.c.) was heated under reflux for 15 min. Cyclohexylamine (9.9 g.) was added slowly with cooling, and the mixture was left for 2 hr. and filtered. Concentration under reduced pressure gave a gum which was shaken with water, and the suspension was extracted with three portions of ethyl acetate. The dried extracts ( $\text{Na}_2\text{SO}_4$ ) were evaporated to an oil which crystallised after cooling and being scratched. Recrystallised from ethanol and then from aqueous ethanol, the *product* (13.0 g.) melted indefinitely between 63° and 67° depending on the rate of heating (Found: C, 52.1; H, 7.8; N, 12.2%; *Equiv.*, 248.  $\text{C}_{10}\text{H}_{18}\text{O}_2\text{N}_2\text{S}$  requires C, 52.1; H, 7.9; N, 12.2%; *Equiv.*, 230). The infrared spectrum had bands: 3410 ( $\nu$ NH), 3240 ( $\nu$ NH), 2940 ( $\nu$ CH), 2860 ( $\nu$ CH), 1723 ( $\nu$ C=O), 1547 (thioureide), 1454, 1408, 1387, 1347, 1305, 1253, 1236, 1203, 1185, 1173, 1150, 1115, 1096, 1039, 974, 887, 846, 820, 772, 754, and 684  $\text{cm}^{-1}$ .

*Perhydro-4,6-dimethyl-1-phenyl-2-thio-1,3,5-triazine (V).*—A solution of acetaldehyde ammonia (3.05 g.) in acetone (50 c.c.) was treated with phenyl isothiocyanate (6.76 g.). Considerable heat was evolved, and crystals rapidly separated. After 1 hr. at 0°, the *product* (4.1 g.) was crystallised from acetonitrile; it then had m. p. 160.5—161.0° (Dixon<sup>2</sup> reports m. p. 148—149° after recrystallisation from ethanol; we found that the m. p. was lowered to *ca.* 150° by this treatment) (Found: C, 60.0; H, 6.9; N, 19.1.  $\text{C}_{11}\text{H}_{15}\text{N}_3\text{S}$  requires C, 59.6; H, 6.8; N, 19.0%). Apart from a shoulder at 236  $\text{m}\mu$  ( $\epsilon$  12,400), the ultraviolet spectrum was featureless down to 210  $\text{m}\mu$ . The infrared spectrum had bands: 3275 ( $\nu$ NH), 3185 ( $\nu$ NH), 3065 ( $\nu$ C<sub>ar</sub>H), 2990 ( $\nu$ CH), 2945 ( $\nu$ CH), 1598 (aromatic ring), 1530 (thioureide), 1498 (aromatic ring), 1483, 1449 ( $\delta$ CH), 1373 (C-Me), 1333, 1308, 1273, 1228, 1156, 1130, 1107, 1074, 1062, 1028, 1003, 972, 930, 910, 895, 865, 800, 755, and 693  $\text{cm}^{-1}$ .

We thank Professor Sir Alexander Todd, F.R.S., for laboratory facilities. Some of this work was carried out during the tenure (by J. R. O.) of a Senior D.S.I.R. Fellowship. We are also grateful to Imperial Chemical Industries Limited for financial assistance.

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[Received, August 5th, 1959.]