703. *Infrared Spectra of Some 2-Thiohydantoins: the Nature of the " Thioureide " Band.*

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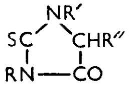
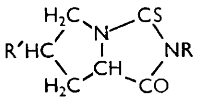
The infrared spectra of a series of 2-thiohydantoins, including 1- and 3-monoalkyl and 1 : 3-dialkyl derivatives, have been measured over the range 2500—800 cm.$^{-1}$. The " thioureide " band, which is present in the spectra of compounds having no NH group, is not entirely due to a δNH vibration, although it is postulated that coupling between δNH and νCN modes may occur in suitable cases.

Randall, Fowler, Fuson, and Dangl [1] have attributed a strong band (" thioureide ") in the infrared spectra of compounds containing the $>N{-}C({=}S){-}$ system to a νCN frequency modified by resonance of the type $>N{-}C({=}S){-} \longleftrightarrow N{-}C^{+}({-}S^{-}){-}$. Bellamy [2] cautiously accepts this assignment. Chatt, Duncanson, and Venanzi,[3] however, have assigned this band to a major contribution of the canonical form $>N^{+}{=}C({-}S^{-}){-}$ in the case of dithiocarbamates. The position of the band in the infrared spectrum is regarded as a manifestation of the bond order of the CN linkage. On the other hand, Mecke and Mecke [4] have studied the spectra of a number of cyclic thiolactams and thioureas and have concluded that the thioureide band is due to a δNH frequency comparable with the amide II band in primary and secondary amides and peptides. In addition, Hadži [5] has observed strong bands at 1523—1536 cm.$^{-1}$ in the spectra of thiobenzanilide, *N*-methyl(thiofuramide) and thiofuranilide, and these are attributed essentially to δNH modes. The evidence advanced includes (i) weakening or disappearance of the band after deuteration, (ii) a shift to lower frequencies in the liquid state [4] or in solution [5] compared with solid samples in pressed discs of potassium bromide, behaviour which is claimed to be more characteristic of a deformation than a stretching mode, and (iii) absence of the band in *N*-methyl(thiofuranilide).[5] In addition, Ramachandran, Epp, and McConnell,[6] who also attribute the thioureide band to a δNH frequency, report that it is absent from the spectra of 3-phenylpyrrolidino-(1′ : 2′-1 : 5)-2-thiohydantoin (II; R = Ph, R′ = H) and its 4′-hydroxy-derivative (II; R = Ph, R′ = OH). We notice, however, from the diagrams published by Hadži [5] and Ramachandran *et al.*[6] that compounds containing fully substituted nitrogen atoms absorb strongly at about 1450 cm.$^{-1}$. We believe that these bands, which are probably too strong to be confused with δCH modes, are modified thioureide bands as described below.


(I)


(II)

Several other compounds possessing the $>N{-}C({=}S){-}$ system, in which the nitrogen atom is tertiary, absorb strongly in the infrared region under consideration. Thus, thioureide bands are present in the spectra of (i) *NNN′N′*-tetramethylthiourea [7] at 1508 cm.$^{-1}$, (ii)

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[1] Randall, Fowler, Fuson, and Dangl, " Infrared Determination of Organic Structures," D. van Nostrand Co. Inc., New York, 1949, p. 5.

[2] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 294.

[3] Chatt, Duncanson, and Venanzi, *Suomen Kem.*, 1956, **29**, *B*, 75.

[4] Mecke and Mecke, *Chem. Ber.*, 1956, **89**, 343; Mecke, Mecke, and Lüttringhaus, *ibid.*, 1957, **90**, 975.

[5] Hadži, *J.*, 1957, 847.

[6] Ramachandran, Epp, and McConnell, *Analyt. Chem.*, 1955, **27**, 1734.

[7] Ettlinger, *J. Amer. Chem. Soc.*, 1950, **72**, 4699.

N-thioacetylpiperidine [8] at 1504 cm.$^{-1}$, (iii) salts and complexes of *NN*-dialkyldithiocarbamic acids [3, 9] and methyl *NN*-dimethyldithiocarbamate [3] at 1480—1544 cm.$^{-1}$, and (iv) *NNN'N'*-tetra-alkylthiuram sulphides [9] and disulphides [3, 9] at 1504—1514 cm.$^{-1}$. We have confirmed the observations on *NNN'N'*-tetramethylthiuram disulphide and *NNN'N'*-tetramethylthiourea. In addition, we have examined the infrared spectra of a number of 1 : 3-dialkyl-2-thiohydantoins, and in every case a strong thioureide band was present. Since the amide II band is absent from the spectra of all *NN*-dialkylamides so far examined,[10] it seems illogical to press the analogy of this band with the thioureide band too far.

Clow [11] determined the diamagnetic susceptibilities of a series of thioureas and concluded that the structure tended to the extreme form $(>N)_2C{:}S$ as the degree of substitution of the nitrogen atoms was increased. Hence, if the thioureide band results from a νCN mode, it would be expected to shift to lower frequencies as the degree of substitution is increased and the contribution of $\overset{\delta+}{C}\text{–}N$ or $C\text{=}\overset{\delta+}{N}$ to the structure decreases. There are some examples in the literature. *NNN'*-Trimethylthiourea [7] absorbs at 1550 and *NNN'N'*-tetramethylthiourea [7] at 1508 cm.$^{-1}$; *N*-*n*-butyl(thioacetamide) [8] has a peak at 1542 and *N*-thioacetylpiperidine [8] at 1504 cm.$^{-1}$; *NN'*-dimethylthiuram disulphide [3] has a band at 1530 cm.$^{-1}$ with a shoulder at 1545 cm.$^{-1}$ while the corresponding peak for *NNN'N'*-tetramethylthiuram disulphide [3, 9] is variously given as 1504 and 1514 cm.$^{-1}$; the ferric complexes of of *N*-ethyl- and *NN*-diethyl-dithiocarbamic acid [3] have bands at 1520 and 1496 cm.$^{-1}$ respectively. We now find that pyrrolidino(1' : 2'-1 : 5)-2-thiohydantoin (II; R = R' = H) has maximal absorption at 1508 and the 3-methyl derivative (II; R = Me, R' = H) at 1458 cm.$^{-1}$. More generally in the thiohydantoin series, those compounds which are unsubstituted at $N_{(1)}$ and $N_{(3)}$ absorb at 1545—1562 cm.$^{-1}$; with a substituent at either $N_{(1)}$ or $N_{(3)}$ (I; R or R' = H respectively), the band shifts to 1508—1539 cm.$^{-1}$, while with both positions blocked, the peak appears at 1458—1523 cm.$^{-1}$. Increase of size of substituent appears to enhance the size of shift.

Although Hadži [5] and Mecke and Mecke [4] claim that deuteration leads to disappearance of the thioureide band, we notice from their published spectra that a strong band usually appears at a slightly lower frequency. We have observed a corresponding shift following the deuteration of *N*-alkyl-2-thiohydantoins. 1-Methyl-2-thiohydantoin absorbs strongly at 1539, whereas the $N_{(3)}$-D-derivative has a peak at 1524 cm.$^{-1}$. Similarly, the peak at 1530 cm.$^{-1}$ in the spectrum of 3-ethyl-2-thiohydantoin is replaced by a peak at 1480 and shoulder at 1506 cm.$^{-1}$ after deuteration. In both cases, peaks near 1080 cm.$^{-1}$, which appear after deuteration, are probably due to δND modes.[5]

The above results lead us to the view that the thioureide band results from the coupling of a stretching frequency of a CN bond, modified by resonance as suggested by Randall *et al.*[1] or Chatt *et al.*,[3] with a δNH mode, the latter having the higher frequency. When the hydrogen is replaced by deuterium or an alkyl group, there is no possibility of coupling, and the band shifts to a lower frequency characteristic of the νCN mode alone. Hence, although the thioureide band may be partly dependent on the presence of an NH group for its position, it is not a diagnostic test.

In contrast to this assignment, Mecke and Mecke [4] and Hadži [5] have attributed bands at lower frequencies to νCN modes. While it is not possible at present to decide finally between these possibilities, some comments may be made concerning the interpretations due to these workers. (i) Hadži has examined only four thioamides, the spectra of which are very complex owing largely to the presence of aromatic and heterocyclic rings. (ii) The assignment of a band at 1330—1375 cm.$^{-1}$ to a νCN mode in these compounds may be

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[8] Marvel, Radzitzky, and Brader, *J. Amer. Chem. Soc.*, 1955, **77**, 5997.

[9] Mann, *Trans. Inst. Rubber Ind.*, 1951, **27**, 232.

[10] Richards and Thompson, *J.*, 1947, 1248; Thompson, Brattain, Randall, and Rasmussen, "Chemistry of Penicillin," Princeton Univ. Press, Princeton, New Jersey, 1949, p. 388.

[11] Clow, *Trans. Faraday Soc.*, 1938, **34**, 457.

correct, but it would then be expected to arise from a C_{ar}–N bond,[12] as implied by Hadži.[5] It should, however, be pointed out that the νC=S frequency may appear here, as has been claimed in the case of thiocarbanilide.[13] Mecke and Mecke's [4] assignment of a band at ~1300 cm.$^{-1}$ in the spectra of cyclic thioamides and thioureas to a νCN mode has likewise been criticised recently by Lieber, Rao, Pillai, Ramachandran, and Hites,[14] who attribute this band to a νC=S vibration. It is also pertinent that Miyazawa, Shimanouchi, and Mizushima [15] concluded that a band at ~1300 cm.$^{-1}$ in the spectra of monosubstituted amides chiefly reflects δNH character. (iii) The argument [5] that bands at 1264 and 1280 cm.$^{-1}$ in the spectra of thiofuranilide and *N*-methylfuramide respectively are second νCN modes is weakened by the probability that at least one ν=C–O band attributable to

Infrared spectra (cm.$^{-1}$*) of 2-thiohydantoins in the solid state.* s = *strong;* m = *moderate;* w = *weak;* sh = *shoulder;* c = *complex band.*

2-Thiohydantoin	5-Ethyl	5-*iso*Propyl	3-Ethyl	Deuterated 3-ethyl	3-Ethyl-1-methyl	1 : 3-Diethyl
1796 sh	1762 s *b*	1754 s *b*	1746 s *b*	2393 s *f*	1738 s *b*	1744 s *b*
1725 s *b*	1562 s *a*	1558 s *a*	1530 s *a*	1746 s *b*	1520 s *a*	1702 sh
1545 s *a*	1475 w *c*	1486 w	1456 sh *c*	1506 sh	1449 m }	1514 s *a*
1430 m *c*	1416 s	1413 m	1435 m *e*	1480 s *a*	1435 m } *h*	1465 m }
1403 m	1396 sh	1395 m	1415 w	1450 sh	1400 s	1440 s } *h*
1385 sh	1332 m	1353 w	1383 w	1424 s	1371 s	1422 s
1304 s	1271 m	1338 w	1351 s	1390 sh	1356 sh	1390 sh
1214 w	1251 w	1292 m	1311 s	1376 s	1308 s	1372 s
1174 s	1217 m	1270 w	1270 s	1349 s	1253 m	1353 s
1161 s	1186 s	1209 w	1207 m	1288 m	1223 s	1328 s
1046 w	1113 w	1190 m	1175 w	1247 s	1194 w	1285 s
980 w	1061 w	1176 s	1115 s	1206 m	1138 m	1242 s
967 w	980 w	1138 w	1049 m	1170 w	1116 w	1223 s
893 m	925 m	1100 w	980 w	1136 m	1098 w	1186 w
	872 w	1067 w	948 m	1116 s	1088 w	1142 m
		1032 w		1082 w *g*	1066 w	1122 s
		983 w		1042 s	992 m	1106 m
		954 w		992 w	952 m	1074 m
		926 w		974 w	883 m	1012 m
		887 w		960 w		981 w
				947 w		953 m
				928 w		857 s
				912 w		
				898 m		
				850 w		
				839 m		

5-Methyl	5-*n*-Propyl	1-Methyl	Deuterated 1-methyl	1 : 3-Dimethyl
1744 s *b*	1744 s *b*	1735 s *b*	~2400 mc *f*	1744 s *b*
1553 s *a*	1553 s *a*	1539 s *a*	1730 s *b*	1633 w
1457 m *d*	1479 m *c*	1438 s *c*	1524 s *a*	1523 s *a*
1416 s	1458 w *e*	1400 s	1419 m	1462 m }
1398 s	1408 s	1349 s	1398 s	1449 m } *h*
1315 s	1395 sh	1296 m	1356 s	1430 m
1184 s	1333 m	1249 s	1322 sh	1390 s
1116 w	1324 m	1228 w	1251 m	1372 s
1092 m	1250 m	1189 s	1223 w	1353 sh
1044 m	1212 w	998 w	1189 m	1328 s
969 w	1179 s	968 w	1130 w }	1256 sh
927 m	1111 w	913 m	1088 w }	1246 s
825 m	1095 w		1075 w } *i*	1182 w
	1037 w		1068 w }	1135 m
	992 w		1015 w	1099 m
	959 m		1005 w	1055 m
	914 m		966 w	974 s
	892 m		939 m	869 m
	857 w		901 m	
			835 w	
			815 s	

Pyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin	
1749 s *b*	1172 m
1709 m	1151 s
1508 s *a*	1108 w
1470 m *c*	1054 m
1413 m	1018 w
1340 m	989 m
1312 w	912 w
1279 w	907 w
1255 m	891 w
1232 m	842 w

3-Methylpyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin	
1755 s *b*	1138 m
1458 s *a*	1090 w
1432 s *c*	1022 m
1334 s	989 m
1302 s	935 w
1247 w	914 w
1173 w	896 w

a Thioureide, *b* νC=O, *c* δCH_2, *d* $\nu C–CH_3$, *e* $\delta C–CH_3$, *f* νND, *g* δND, h δCH modes, *i* one of these bands is probably δND

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[12] Ref. 2, pp. 220—221.

[13] Jones, Kynaston, and Hales, *J.*, 1957, 614.

[14] Lieber, Rao, Pillai, Ramachandran, and Hites, *Canad. J. Chem.*, 1958, **36**, 801.

[15] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1956, **24**, 408.

the furan ring will arise hereabouts. (iv) Hadži [5] has suggested that bands, which appear after deuteration at 1497 cm.$^{-1}$ with thiofuranilide and thiofuramide, and at 1468 cm.$^{-1}$ with thiobenzanilide, result from the interaction of a skeletal mode with either the δNH or νCN vibrations. Contribution from a δNH mode should be unimportant in a compound which is extensively deuterated; the alternative suggestion only differs from that of the present author by invoking a skeletal vibration, for which there seems no evidence.

It is of interest to record that *N*-ethylthiocarbamoylglycine ethyl ester cyclised to 3-ethyl-2-thiohydantoin in ethanolic ammonia at room temperature as well as in hot acid: this recalls the behaviour of *N*-thiocarbamoylglycine ethyl ester.[16] *N*-Benzoylthiocarbamoylglycine ethyl ester and *N*-ethyl-, *N*-phenyl-, and *N*-acetyl-thiocarbamoylglycylglycine ethyl ester were unaffected by ethanolic ammonia.

EXPERIMENTAL

Infrared spectra were obtained on a Grubb–Parsons double-beam spectrometer with rock-salt prism; specimens were prepared in potassium bromide discs. To obtain deuterated samples, the relevant compounds were kept in deuterium oxide at 100° for about 1 hr. The products crystallised with unchanged m. p. when the solutions were cooled.

3-*Ethyl*-2-*thiohydantoin*.—(*a*) Ethyl *iso*thiocyanate (4·2 g.) and glycine ethyl ester (from 7 g. of hydrochloride) were allowed to react in benzene (25 c.c.) at room temperature for 1 hr. Removal of solvent left *N*-ethylthiocarbamoylglycine ethyl ester as an oil. A mixture of the latter (1 g.), ethanol (2·5 c.c.), and 2N-hydrochloric acid (2·5 c.c.) was heated under reflux for 2 hr. Evaporation afforded the product (0·25 g.), which had m. p. 140—141°, unchanged after recrystallisation from water. (Jeffreys [17] records m. p. 144°.)

(*b*) A solution of the above oil (1 g.) in ethanolic ammonia (10 c.c.) was kept at room temperature for 2 hr. Evaporation yielded the product (0·15 g.), which had m. p. 140—141° alone and in admixture with the above specimen.

3-*Ethyl*-1-*methyl*-2-*thiohydantoin*.—This compound (68%) was prepared from ethyl *iso*thiocyanate and sarcosine ethyl ester by method (*a*) above. Recrystallised from benzene–light petroleum (b. p. 60—80°), it had m. p. 68·5—69·5°. (Jeffreys [18] records m. p. 67°.)

3-*Methylpyrrolidino*(1′ : 2′-1 : 5)-2-*thiohydantoin*.—DL-Proline (1·15 g.) and methyl *iso*thiocyanate (0·78 g.) were allowed to interact in 25% aqueous dioxan (40 c.c.) maintained at pH 9·5 by a pH-stat. The solution was evaporated to 10 c.c., adjusted to pH 1, and heated at 100° for 1 hr. After storage at 0°, the *thiohydantoin* (1·21 g.) crystallised. Recrystallised from benzene–light petroleum (b. p. 60—80°), it had m. p. 51·5—52·0° (Found: C, 49·2; H, 6·0; N, 16·3. $C_7H_{10}ON_2S$ requires C, 49·4; H, 5·9; N, 16·5%).

N-*Ethylthiocarbamoylglycylglycine Ethyl Ester*.—This *ester* (84%) was obtained from the reaction between ethyl *iso*thiocyanate and glycylglycine ethyl ester in chloroform. Recrystallised from chloroform–light petroleum (b. p. 40—60°), it had m. p. 97—98° (Found: C, 44·1; H, 7·2; N, 16·9. $C_9H_{17}O_3N_3S$ requires C, 43·7; H, 6·9; N, 17·0%).

N-*Phenylthiocarbamoylglycylglycine Ethyl Ester*.—Prepared in the same way, this *compound* (85%) had m. p. 140—141° after recrystallisation from chloroform–light petroleum (b. p. 40—60°) (Found: C, 52·8; H, 5·9; N, 14·6. $C_{13}H_{17}O_3N_3S$ requires C, 52·8; H, 5·8; N, 14·2%).

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[16] Elmore, Toseland, and Tyrrell, *J.*, 1955, 4388.

[17] Jeffreys, *J.*, 1954, 2221.

[18] *Idem, ibid.*, p. 389.