165. *The Alkylation of Mercaptobenzothiazole.*

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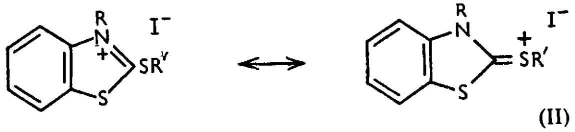
Further alkylation of the isomeric *N*- and *S*-alkyl derivatives of mercaptobenzothiazoles has been investigated, and spectral data used to establish the structure of the products. The formation of anomalous products can be explained by the thermal dissociation of the salts. The structure and spectra of the corresponding acid salts of 2-alkylthiobenzothiazoles are discussed.

Direct alkylation of mercaptobenzothiazole leads to alkylthiobenzothiazoles;[1] the isomeric *N*-alkyl derivatives are prepared less directly. Both types of compound give salts on further alkylation with alkyl iodide or alkyl sulphate. The product from ethyl iodide and 2-methylthiobenzothiazole has been reported[2] to be identical with that formed from methyl iodide and 2-ethylthiobenzothiazole; Fry and Kendall[3] suggested that in both cases the product was 3-methyl-2-methylthiobenzothiazolium iodide which was isolated from the mixture of all possible products of transalkylation of 2-alkylthiobenzothiazole with the salt initially formed. The evidence available was largely that of melting points, notoriously unreliable with these compounds, and analyses of crude products. To obtain more precise results infrared and ultraviolet spectra of the products have been examined and correlated; the results have in part confirmed and also extended those reported previously.



(I) (II)

The mode of formation and the close similarity of the ultraviolet spectra (Table 1) strongly suggest that the salts are *NS*-dialkyl compounds (I). This is confirmed by the existence of only one dimethyl iodide and only one diethyl iodide but of two ethylmethyl iodides. To account for the formation of anomalous products it has been suggested[4] that the initial product of the addition of alkyl iodide to 2-alkylthiobenzothiazoles is the sulphonium salt, (Benzothiazolyl)RR'S^+ I^-, which undergoes carbonium-ion rearrangement; similar intermediates have been postulated for the halogen-catalysed isomerisation of 2-alkylthiobenzothiazoles to the thermodynamically more stable *N*-alkyl isomers.[5]

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[1] Hunter, *J.*, 1930, 123; Reed, Robertson, and Sexton, *J.*, 1939, 473.
[2] Sexton, *J.*, 1939, 470.
[3] Fry and Kendall, *J.*, 1951, 1716.
[4] Davies and Sexton, *J.*, 1942, 304; Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502.
[5] Moore and Waight, *J.*, 1952, 4237.

The isolation of distinct salts [(I; R = Me, R′ = Et) and (I; R = Et, R′ = Me)] from 2-ethylthio- and 2-methylthio-benzothiazole, respectively, by using the appropriate alkyl iodide and a short reaction time excludes such intervention. The primary product is apparently formed by alkylation at the free hetero-atom. The mixtures, obtained from attempts to raise the yield of these salts by longer heating, may accordingly be ascribed to some further reaction of the primary product. Thus when a longer reaction time (*e.g.*, the conditions used by Beilenson and Hamer [6]) is used, in both cases the product isolated by by the normal method is the *NS*-dimethyl iodide (see Experimental).

TABLE 1. *Ultraviolet absorption spectra.*

Benzothiazole	λ(mμ)	—	256	285	294	—	—
	log ε	—	3·76	3·22	3·13	—	—
2-Thiobenzothiazoline	λ(mμ)	[235]	[252]	[282]	—	—	320
	log ε	4·12	3·82	3·34	—	—	4·43
3-Methyl-2-thiobenzothiazoline	λ(mμ)	241	[255]	[283]	—	—	324
	log ε	4·12	3·82	3·41	—	—	4·41
3-Ethyl-2-thiobenzothiazoline	λ(mμ)	242	[255]	[283]	—	—	324
	log ε	4·47	4·1	3·2	—	—	4·7
2-Methylthiobenzothiazole	λ(mμ)	244	—	278	288	299	—
	log ε	3·94	—	4·1	4·03	3·92	—
2-Ethylthiobenzothiazole	λ(mμ)	[245]	—	280	[290]	302	—
	log ϵ	3·9	—	4·06	4·0	3·9	—
3-Methyl-2-methylthiobenzothiazolium iodide	λ(mμ)	—	257	—	—	306	—
	log ε	—	3·85	—	—	4·18	—
3-Ethyl-2-methylthiobenzothiazolium iodide	λ(mμ)	—	258	—	—	308	—
	log ε	—	3·85	—	—	4·14	—
2-Ethylthio-3-methylbenzothiazolium iodide	λ(mμ)	—	258	—	—	305	—
	log ε	—	3·78	—	—	4·1	—
3-Ethyl-2-ethylthiobenzothiazolium iodide	λ(mμ)	—	258	—	—	307	—
	log ε	—	3·75	—	—	4·03	—

Figures in [square] brackets refer to points of inflexion.

Examination of the conditions leading to transalkylation showed that the *S*-alkyl group in the *NS*-dialkyl iodides could be replaced by heating them with alkyl iodide. Further, an alkylating action entirely analogous to that of the alkyl iodides is shown by the salts themselves: inaddit ion to *N*-alkylation [3] of free 2-alkylthiobenzothiazoles *S*-alkylation of *N*-alkyl thiones, and *S*-alkyl exchange between mixtures of salts occur. However, when an attempt was made to equilibrate a mixture of the two *NS*-ethyl-methyl iodides in an open flask the product contained no salt but was a mixture of the two *N*-alkyl thiones. While the pure salts were stable to prolonged heating in sealed tubes, when heated in open vessels they gave quantitative yields of the appropriate thione and alkyl iodide was liberated; to this may be attributed the alkylating action previously [3] associated with the salts themselves. Production of mixtures of salts may be expected to follow from re-alkylation of the thione to a salt which will in general differ from that formed initially until a state of dynamic equilibrium is reached. Such a mechanism may also operate in the isomerisation, catalysed by alkyl halide, of 2-alkylthiobenzothiazoles to the *N*-alkyl thiones.

Mixtures were not formed in the other preparations of the *NS*-ethyl-methyl salts investigated and in each case the product was that expected. The homogeneity of the salts formed from alkyl sulphates can be ascribed to the mild reaction conditions. The stability of the *N*-alkyl group makes the salts formed by direct alkylation of the *N*-alkyl thiones insensitive to subsequent reaction. In these alkylations methylation was easier than ethylation.

Spectral Measurements.—The ultraviolet spectra (Table 1) of the dialkylated salts are similar. Bands at 257 and 306 mμ can be assigned to benzene and thioamide absorption

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[6] Beilenson and Hamer, *J.*, 1939, 143.

respectively;[7, 8] similar bands are shown by many 2-thio-substituted benzothiazoles.[9] A long-wavelength band at 325 mμ is due to the conjugated thione group and is completely lacking in the spectra of the salts. The most important contributions to the structure of the salts probably arise from the benzothiazolium (I) rather than the sulphonium (II) form.

The infrared spectra of the salts are generally similar in form. Groups of bands common to many derivatives of benzothiazole are derived from the aromatic nucleus: C⁚C stretching (1455—1470, 1592—1608 cm.$^{-1}$), C·H deformation (743—767 cm.$^{-1}$), 1 : 2-disubstituted benzene (1013—1030, 1050—1060 cm.$^{-1}$), aromatic–nitrogen stretching (1307—1330 cm.$^{-1}$), and aromatic–sulphur stretching frequencies (703—709 cm.$^{-1}$). The assignment of a band at 1495 cm.$^{-1}$ in the spectrum of mercaptobenzothiazole to the N·C⁚S group[10] seems of doubtful validity; a corresponding band is found in the spectra of the *NS*-dialkyl salts (1502—1511 cm.$^{-1}$) but is absent from that of the *N*-alkyl thiones. The frequencies of bands in the range 700—1000 cm.$^{-1}$ are given in Table 2; this region was the most valuable for characterising the salts.

TABLE 2. *Infrared spectra (band frequencies in cm.$^{-1}$).*

2-Thiobenzothiazoline	1000(w)	—	—	938(w)	869(w)	851(w)	—
3-Methyl-2-thiobenzothiazoline	—	966(s)	—	928(m)	—	—	823(w)
3-Ethyl-2-thiobenzothiazoline	997(s)	—	—	935(w)	919(m)	849(m)	833(w)
2-Methylthiobenzothiazole	1009(s)	974(w)	961(m)	928(w)	904(w)	855(w)	—
2-Ethylthiobenzothiazole	995(s)	971(w)	—	931(w)	—	849(w)	—
3-Methyl-2-methylthiobenzothiazolium iodide	—	976(m)	952(w)	—	893(w)	851(w)	816(m)
3-Ethyl-2-methylthiobenzothiazolium iodide	988(m)	976(m)	957(w)	927(w)	—	857(w)	—
2-Ethylthio-3-methylbenzothiazolium iodide	994(m)	966(w)	—	—	—	—	818(m)
3-Ethyl-2-ethylthiobenzothiazolium iodide	—	976(w)	—	929(w)	—	—	840(w)
2-Methylthiobenzothiazolium iodide	988(m)	973(m)	952(w)	—	869(w)	855(w)	—
2-Ethylthiobenzothiazolium iodide	996(m)	977(w)	952(w)	—	—	859(w)	812(m)
2-Ethylthiobenzothiazolium perchlorate	994(w)	—	952(w)	923(w)	—	862(w)	—

2-Thiobenzothiazoline	—	—	751(s)	—	719(m)	707(w)
3-Methyl-2-thiobenzothiazoline	—	—	749(s)	—	717(m)	709(w)
3-Ethyl-2-thiobenzothiazoline	779(m)	—	743(s)	—	718(m)	709(w)
2-Methylthiobenzothiazole	—	765(s)	758(s)	727(m)	722(m)	707(w)
2-Ethylthiobenzothiazole	—	—	754(s)	728(s)	—	705(w)
3-Methyl-2-methylthiobenzothiazolium iodide	—	—	756(s)	—	—	712(m)
3-Ethyl-2-methylthiobenzothiazolium iodide	786(m)	767(s)	—	—	720(m)	715(w)
2-Ethylthio-3-methylbenzothiazolium iodide	796(w)	762(s)	—	—	—	715(m)
3-Ethyl-2-ethylthiobenzothiazolium iodide	789(w)	768(s)	759(m)	—	724(w)	711(w)
2-Methylthiobenzothiazolium iodide	778(m)	—	752(s)	—	721(w)	707(w)
2-Ethylthiobenzothiazolium iodide	—	—	757(s)	—	722(w)	707(w)
2-Ethylthiobenzothiazolium perchlorate	—	—	762(s)	—	720(m)	711(w)

Spectra and Structure of the Acid Salts of 2-Alkylthiobenzothiazoles.—2-Alkylthiobenzothiazoles react with hydriodic acid to give crystalline salts whose spectral characterisation presents several points of interest. Attempts to measure the ultraviolet spectra in solution in alcohol or acetic acid led only to the spectra of the free bases. Attempts to measure the ultraviolet spectrum of 2-ethylthiobenzothiazolium perchlorate gave similar results in alcohol but in 0·1N-perchloric acid in acetic acid the spectrum ($\lambda_{max.}$ 311 mμ, log ε 3·95) was closely similar to those of the dialkyl salts. The infrared spectrum of the perchlorate showed many of the bands found in the spectra of the *NS*-dialkyl salts (Table 2); in addition a new band at 3096 cm.$^{-1}$ (in Nujol) was observed in a position appropriate to an N^+·H stretching frequency.[11] The perchlorate can thus be regarded as structurally analogous to the *NS*-dialkylated compounds. The spectra of the hydriodides in the

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[7] Morton and Stubbs, *J.*, 1939, 1321.
[8] Cerniani and Passerini, *J.*, 1954, 2261.
[9] Barltrop and Morgan, *J.*, 1957, 3072.
[10] Mann, *Trans. Inst. Rubber Ind.*, 1951, **27**, 232.
[11] Thompson, Nicholson, and Short, *Discuss. Faraday Soc.*, 1950, **9**, 222.

single-bond stretching region differ markedly from that of the perchlorate though they show a general similarity over the rest of the spectrum. The weak N$^+$·H stretching band is missing and is replaced by a strong broad band at 2674 and 2551 cm.$^{-1}$ in the methylthio- and ethylthio-salts, respectively. This region is associated with the S·H stretching frequency but it is highly improbable that a sulphonium salt would give rise to bands of such intensity. Bands in this region are also found in the spectra of amino-[12] and amido-acids where they have been attributed to overtone or combination bands.[13] Closer analogies are provided by triethylammonium halides, all four of which show bands at 2540 cm.$^{-1}$ differing only in their fine structure,[14] and by pyridinium chloride (though not the iodide) which has a similar band at 2450 cm.$^{-1}$. These bands have been assigned[14] to a strong N$^+$–H···X$^-$ hydrogen bond. A band at 2577 cm.$^{-1}$ in the spectrum of *o*-phenylenediamine perchlorate is of interest since the perchlorate ion is not normally hydrogen bonded; the band may be attributed to intramolecular hydrogen bonding and a similar explanation may account for the band found in the spectra of amino-acids. Accordingly, in the spectra of 2-alkylthiobenzothiazolium iodides the band may be assigned to an N$^+$·H vibration and these salts can be given structures analogous to those of the *NS*-dialkyl iodides. Further support was provided by the spectra of the hydriodides in dioxan (none of the usual liquids was a solvent for these salts) in which a band at 3378 cm.$^{-1}$ is indicated.

3-Methyl-2-thiobenzothiazoline has been reported[15] to give a chloroplatinate. No signs of salt formation could be detected when the *N*-alkyl thiones or mercaptobenzothiazole itself was treated with acids; their spectra remained unchanged even in perchloric–acetic acid.

EXPERIMENTAL

2-*Alkylthiobenzothiazoles*.—2-Methylthiobenzothiazole, b. p. 116°/0·5 mm., m. p. 49° [hydriodide, m. p. 179—181° (decomp.)], and 2-ethylthiobenzothiazole, b. p. 114°/1 mm., m. p. 26° [hydriodide, m. p. 149—150° (decomp.) (Found: C, 33·3; H, 3·4. Calc. for $C_9H_{10}NS_2I$: C, 33·4; H, 3·1%), *perchlorate*, m. p. 137—138° (Found: C, 34·2; H, 3·2. $C_9H_{10}O_4NS_2Cl$ requires: C, 34·4; H, 3·3%)], were prepared from mercaptobenzothiazole.[1]

3-*Alkyl*-2-*thiobenzothiazoline*.—3-Methyl-2-thiobenzothiazoline, b. p. 156°/0·5 mm., m. p. 96°, and 3-ethyl-2-thiobenzothiazoline, m. p. 79·5—80·5°, were prepared from *NS*-dimethyl and -diethyl sulphates, respectively.[2]

3-*Alkyl*-2-*alkylthiobenzothiazolium Iodides*.—(*a*) The *NS*-dimethyl iodide, m. p. 146—147° (decomp.), was prepared from methyl iodide or methyl sulphate–potassium iodide[2] and both 2-methylthiobenzothiazole and 3-methyl-2-thiobenzothiazoline (Found: C, 33·9; H, 2·9. Calc. for $C_9H_{10}NS_2I$: C, 33·4; H, 3·1%). (*b*) *NS*-Diethyl iodide, m. p. 119·5—120·5° (decomp.) was obtained by four entirely analogous preparations (Found: C, 37·6; H, 4·4. Calc. for $C_{11}H_{14}NS_2I$: C, 37·6; H, 4·4%). (*c*) Methylation of the *N*-ethyl thione or the action of ethyl sulphate–potassium iodide on 2-methylthiobenzothiazole led to 3-ethyl-2-methylthiobenzothiazolium iodide, m. p. 132—134° (decomp.) (Found: C, 35·5; H, 3·5; N, 4·2. Calc. for $C_{10}H_{12}NS_2I$: C, 35·6; H, 3·6; N, 4·2%), which was decomposed by sodium sulphide to the *N*-ethyl thione and methanethiol (mercury derivative,[16] m. p. 173°). (*d*) 2-Ethylthio-3-methylbenzothiazolium iodide, m. p. 137—138° (decomp.), was prepared by three methods entirely analogous to those described above (*c*) (Found: C, 35·3; H, 3·6%); with sodium sulphide it gave *N*-methyl-thione and ethanethiol (mercury derivative,[17] m. p. 75°).

Action of Methyl Iodide on 2-*Ethylthiobenzothiazole*.—(*a*) Ethylthiobenzothiazole (2·3 g.) when refluxed with methyl iodide (2·3 g.) for 2 hr. gave a mixture which after two crystallisations from methanol left the *NS*-dimethyl iodide, m. p. 143—145° (decomp.), mixed m. p. 144—145°

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[12] Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949.

[13] Fuson, Josien, and Powell, *J. Amer. Chem. Soc.*, 1952, **74**, 1.

[14] Lord and Merrifield, *J. Chem. Phys.*, 1953, **21**, 166.

[15] Mohlau and Klopfer, *Ber.*, 1898, **31**, 3164.

[16] Klason, *Ber.*, 1887, **20**, 3410.

[17] *Idem, J. prakt. Chem.*, 1877, **15**, 205.

(decomp.), whose spectrum was identical with that of an authentic specimen (Found: C, 33·8; H, 3·4%). Degradation of the salt with sodium sulphide gave the *N*-methyl thione and methanethiol. (*b*) A mixture of the same reagents was heated for 30 min. Two crystallisations (from methanol) of the crude product gave 2-ethylthio-3-methylbenzothiazolium iodide, m. p. 134—136° (decomp.); its identity was confirmed by the infrared spectrum.

Action of Ethyl Iodide on 2-Methylthiobenzothiazole.—(*a*) This reaction [6] gave the *NS*-dimethyl iodide, m. p. 144—145° (decomp.). (*b*) When the reaction time was only 1 hr. a small yield of 3-ethyl-2-methylthiobenzothiazolium iodide, m. p. 132—134° (decomp.) (from methanol), was obtained; its identity was confirmed by the infrared spectrum.

Action of Heat on the Salts.—(*a*) 3-Ethyl-2-methylthiobenzothiazolium iodide was recovered after being heated in a sealed tube at 100° for 22 hr. 2-Ethylthio-3-methylbenzothiazolium iodide was similarly stable under these conditions. (*b*) A mixture of these salts (200 mg. of each) was heated in a sealed tube at 100° for 18 hr. From the product the *NS*-dimethyl iodide, m. p. 145—146° (decomp.), was isolated. (*c*) A similar mixture of salts was heated at 100° for 18 hr. under an air condenser closed only by a drying tube. The mixture of products, m. p. 58—67°, was completely soluble in benzene; in methanol it showed $\lambda_{max.}$ 325 mμ (log ε 4·8). (*d*) Each salt (150 mg.) was heated separately at 100°/10 mm. for 18 hr. to give a quantitative yield of the corresponding thione. The volatile product from the decomposition of the *NS*-dimethyl iodide was washed with pyridine; evaporation of excess of pyridine left pyridine methiodide, m. p. 116° (decomp.).

Action of Alkyl Iodide on the Salts.—2-Ethylthio-3-methylbenzothiazolium iodide (1 g.) was heated in a sealed tube at 100° for 18 hr. with methyl iodide (0·15 c.c.). The residue was washed with ether to leave the *NS*-dimethyl iodide, m. p. 144—145° (decomp.). 3-Ethyl-2-methylthiobenzothiazolium iodide, m. p. 132—134° (decomp.), was obtained similarly from the *NS*-diethyl iodide.

Action of the Salts on Alkyl Derivatives of Mercaptobenzothiazole.—(*a*) The *NS*-dimethyl iodide (1 g.) was heated in a sealed tube with 2-methylthiobenzothiazole (5 g.) at 100° for 18 hr. to give the *N*-methyl thione [3] (1·5 g.), m. p. 96°. The *NS*-dimethyl iodide (500 mg.), m. p. 145—146° (decomp.), was recovered. (*b*) 3-Ethyl-2-methylthiobenzothiazolium iodide (400 m.g.) was allowed to equilibrate with the *N*-methyl thione (300 mg.) for 18 hr. at 100°. The product was washed with benzene (2 × 5 c.c.); the residue was the *NS*-dimethyl iodide, m. p. 145—146° (decomp.). The benzene washings contained a mixture of thiones ($\lambda_{max.}$ 327 mμ) which was fractionated into the *N*-methyl thione, m. p. 91°, and the *N*-ethyl thione, m. p. 80°. Similar results were obtained when the *NS*-diethyl iodide was heated with the *N*-methyl thione.

Hydrolysis of 2-Alkylthiobenzothiazolium Iodides.—An attempt was made to decompose 2-ethylthio- and 2-methylthio-benzothiazolium iodides with sodium sulphide. In each case hydrolysis of the salt was complete before the reagent was added to the warm aqueous solution; the parent base was recovered quantitatively.

Spectra.—Ultraviolet spectra were measured in methanol unless otherwise stated on a Beckman D.U. and a Unicam S.P. 500 spectrometer. Infrared spectra were measured on a Perkin-Elmer self-recording instrument; specimens were prepared as mulls with Nujol or discs with potassium chloride.

This work was performed during the tenure of a Civil Service Senior Research Fellowship. The author thanks the Chief Scientist, Ministry of Supply, for permission to publish these results, Mr. J. Hatcher and Mr. F. Hastings for the infrared spectra, and Mr. F. E. Charlton for some analyses.

CHEMICAL DEFENCE EXPERIMENTAL ESTABLISHMENT,
PORTON, WILTSHIRE.

[*Received, September 9th*, 1957.]