599. *Organic Sulphur Compounds. Part II.* The Condensation of Benzothiazole-2-sulphenamide with Carbonyl Compounds.*

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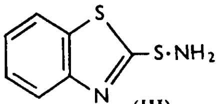
Under basic conditions the condensation between benzothiazole-2-sulphenamide and carbonyl compounds gives high yields of *S*-2-benzothiazolyl thio-oximes. The infrared and ultraviolet spectra of these compounds are reported and discussed.

The reaction between sulphenamides (I) and carbonyl compounds to give thio-oximes (II) was first demonstrated by Zincke and his co-workers.[1] The scope of the reaction was extended to non-aromatic sulphenamides by Vörlander and Mittag [2] who reported similar reactions using triphenylmethanesulphenamide. Apart from a patent claim [3] that *N*-substituted sulphenamides and ketones give low yields of products of unknown structure, the condensation appears not to have been investigated subsequently. The present work was designed to extend the scope of the reaction, to define the conditions under which it proceeds, and to find whether the products were useful for characterising carbonyl compounds or for protecting the carbonyl group.

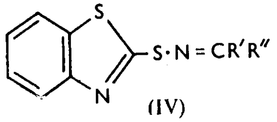
Benzothiazole-2-sulphenamide (III) is readily accessible and stable. It was conveniently prepared from 2-mercaptobenzothiazole by a modification of Carr, Smith, and Alliger's [4] method. When benzaldehyde was heated in alcoholic solution with the sulphenamide the product (IV; R = H, R' = Ph), which was formed in good yield, was contaminated by a considerable amount of benzothiazolyl disulphide. Sulphenamides are known [5] to be decomposed by acids into disulphides and it may well be that part of the benzothiazolyl disulphide resulted from the action of benzoic acid, present as a contaminant in the aldehyde.

(I) $R\cdot S\cdot NH_2$

(II) $R\cdot S\cdot N=CR'R''$



(III)



(IV)

$Me\cdot S\cdot CR=NR$ (V)

A condensation of this type should be catalysed by a base, which would simultaneously neutralise any undesirable acids. Weak bases such as sodium and potassium acetates and bicarbonates had little effect. For benzaldehyde as the carbonyl component it was found that sodium or potassium carbonate induced a rapid reaction which gave a clean product. By using potassium carbonate as the catalyst it was possible to prepare derivatives of a wide variety of aromatic aldehydes.

None of the required products was obtained under these conditions with either ketones or aliphatic aldehydes. These demanded the presence of a more potent base. By adding a few drops of 2N-alkali to the alcoholic solution of the reagents, derivatives of several aliphatic aldehydes and ketones were prepared. It was not, even with such a catalyst, possible to prepare derivatives of aromatic ketones or of certain branched-chain aliphatic ketones.

The potential usefulness of the sulphenamide group in the protection of a carbonyl group was demonstrated with the benzylidene compound. Stable under neutral and

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* Part I, *J.*, 1956, 4245.

[1] Zincke and Farr, *Annalen*, 1912, **391**, 57; Zincke and Lenhardt, *ibid.*, 1913, **400**, 2; Zincke and Röse, *ibid.*, 1914, **406**, 103; Zincke and Baeumer, *ibid.*, 1918, **416**, 86.

[2] Vorländer and Mittag, *Ber.*, 1919, **52**, 413.

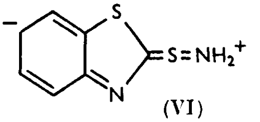
[3] U.S.P., 2,581,936.

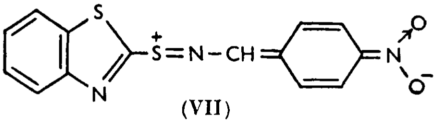
[4] Carr, Smith, and Alliger, *J. Org. Chem.*, 1949, **14**, 921.

[5] Moore and Johnson, *J. Amer. Chem. Soc.*, 1935, **57**, 1517; 1936, **58**, 1091; Zincke and Eismayer, *Ber.*, 1918, **51**, 751.

alkaline conditions it was decomposed by dilute hydrochloric acid to give an almost quantitative yield of benzaldehyde.

Infrared Spectra.—The bands ascribed to the C=N stretching mode in those thio-oximes which contain no system capable of entering into conjugation with the π-electrons in this bond fall within the narrow range 1618—1622 cm.$^{-1}$. An exception is the derivative from *cyclo*pentanone in which the band appears at 1629 cm.$^{-1}$, although the *cyclo*hexanone derivative absorbs at 1622 cm.$^{-1}$. A similar distinction exists [6] in the infrared spectrum of the five- and six-membered cyclic ketones themselves. Conjugation with the C=N group causes a considerable band shift, *e.g.*, the benzylidene derivative (IV; R = Ph, R′ = H) shows a twinned peak at 1597 and 1572 cm.$^{-1}$.


(VI)


(VII)

The frequency range, 1640—1690 cm.$^{-1}$, normally associated [7] with the C=N stretching mode has been defined by a study of oximes, imines, and many derivatives examined in connection with penicillin.[7, 8] These frequencies are significantly higher than those observed in the thio-oximes. However, Goulden [9] has observed related frequencies in other compounds in which a sulphur atom is linked directly to a carbon–nitrogen double bond, *e.g.*, for the compound (V) he finds the appropriate band at 1622 cm.$^{-1}$ (R = Me) and at 1611 cm.$^{-1}$ (R = Ph). There can be little doubt that there is considerable interaction between the sulphur atom and the π-orbitals of the carbon–nitrogen double bond. This interaction is far more significant than any which may exist between similar bonds and nitrogen or oxygen atoms despite the presumably more efficient overlap which might be expected to occur in these cases. The effect of the sulphur substituent may be ascribed

Ultraviolet absorption spectra.

Benzothiazole derivative	λ (mμ) [a]	log ε	λ (mμ) [a]	log ε	λ (mμ) [a]	log ε	λ (mμ)	log ε	λ (mμ)	log ε	λ (mμ)	log ϵ	λ (mμ)	log ϵ
Benzothiazole	216	4·38	256	3·76			285	3·22	294	3·13				
2-Methylthio-	224	4·32	[244]	3·94	280	4·1	[289]	4·03	299	3·92				
-2-sulphenamide	225	4·24	[240]	3·94	280	4·05	290	3·99	300	3·91				
Substituted sulphenamide (IV)														
R R′														
H Me	229	4·41	—	—	[286]	4·23	294	4·24	303	4·19				
H Pr^i	231	4·37	—	—	[285]	4·20	295	4·21	303	4·19				
Me Me	230	4·19	—	—	[286]	4·08	295	4·09	305	4·05				
Me Et	230	4·38	—	—	[286]	4·26	295	4·27	306	4·24				
$[CH_2]_4$	231	4·39	—	—	—	—	295	4·3	306	4·22				
$[CH_2]_5$	231	4·35	—	—	—	—	295	4·24	303	4·22				
H Ph	230	4·28	250	4·19	—	—	290	3·98	300	4·0	330	4·24		
H Ph·CH=CH [b]							287	4·18	[300]	4·15	355	4·27		
H *p*-MeO·C_6H_4	225	4·37	255	4·1	270	4·23	290	4·12	302	4·16	335	4·27		
H *o*-NO_2·C_6H_4	[240]	4·33	[260]	4·21	270	4·21					325	4·16	[350]	3·9
H *m*-NO_2·C_6H_4	225	4·32	240	4·29	[270]	4·15					335	4·08		
H *p*-NO_2·C_6H_4 [b]					275	4·41							380	4·28

[a] Data in brackets refer to points of inflexion. [b] These spectra were measured on $CHCl_3$ solutions, all other spectra from MeOH solutions.

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[6] Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956.

[7] Randall, Fowler, Fuson, and Dangl, " Infra-red Determinations of Organic Structure," Van Nostrand Co. Ltd., New York, 1949, p. 5; Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 226.

[8] Thompson, Brattain, Randall, and Rasmussen, " The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 382; Lieber, Levering, and Patterson, *Analyt. Chem.*, 1951, **23**, 1594; Randall *et al.*, ref. 7.

[9] Goulden, *J.*, 1953, 997.

to the greater polarisability of sulphur. It may be noted that no band of comparable intensity occurs in this region in the spectrum of the parent benzothiazole system.

Ultraviolet Spectra.—An examination of the spectrum of 2-methylthiobenzothiazole has enabled us to confirm the results of previous investigations [10] and to show that spectrally it is indistinguishable from benzothiazole-2-sulphenamide. Similar are the spectra of a series of di(benzothiazolyl)methanes [11] but the spectrum of di(benzothiazolyl) disulphide is completely different.

In the spectrum of benzothiazole, the bands at 256, 285, and 294 mμ are ascribed [10] to benzene, benzo-, and thioamide absorption respectively. Analogous bands are found in 2-methylthiobenzothiazole and in benzothiazole-2-sulphenamide. Koch [12] has suggested that a fifth band appearing in the spectrum of the 2-thio-substituted compounds, at 280 mμ, may be due to conjugation involving the exocyclic sulphur atom as electron-donor.

The spectra of the sulphenamide derivatives of saturated aliphatic carbonyl compounds are closely similar. They all show three of the typical bands, at 230, 295, and 304 mμ, with a fourth (at 285 mμ) as a barely detectable inflexion. The band near 240 mμ is not recognisable. Thus the spectra of this series of compounds are essentially similar to that of the parent sulphenamide differing significantly only in the intensity of the absorption. The spectra of the derivatives prepared from unsaturated and aromatic aldehydes show an order considerably more anarchic but the spectral pattern shown by these compounds at the shorter wavelengths is similar to that of the saturated derivatives. The characteristic benzenoid and benzo-absorptions are present with increased intensity. Additionally, there appears in these spectra a new band at longer wavelengths, the position and intensity of which depends largely on the substituent in the aromatic ring.

It is well established [13] that a sulphur atom adjacent to an unsaturated system can cause a significant bathochromic shift in the position of the absorption maximum. Koch [12, 14] has suggested that the sulphur atom can conjugate as a donor with an unsaturated system R·S·C:C. This point has recently been emphasised by Bordwell and Boutan [15] who demonstrated that bivalent sulphur will only engage in conjugation when it can act as an electron-donor. Koch's further suggestion that a sulphur atom can link two otherwise conjugated systems through an unshared pair of electrons has been discounted [16] and it seems probable that only in cyclic systems can sufficient overlap exist to make this significant. The results reported here support these conclusions, for we find that the spectrum of benzothiazole-2-sulphenamide in which the effect of contributions from structures such as (VI) might be expected if the sulphur atom could exert a linking action is in fact almost identical with that of 2-methylthiobenzothiazole in which such contributions would be insignificant. Similarly, it is clear that in the alkylidenesulphenamides the imine and the benzothiazole chromophore are virtually insulated from each other.

These points are further exemplified by the substituted benzylidenesulphenamides. The long-wavelength bands of the corresponding aldoximes lie at comparable wavelengths, *e.g.*, for *o*-, *m*-, and *p*-nitrobenzaldoximes $\lambda_{max.} = 250$, 252, and 302 mμ respectively. The long-wavelength bands of the nitrobenzylidenesulphenamides lie at somewhat longer wavelengths, owing to bathochromic effect of the sulphur atom, and are clearly due to the isolated chromophore S·N:CHAr. Furthermore, the effect of substitution on the positions of these bands finds a ready interpretation in the donor conjugation of the sulphur atom, for we observe that the benzylidene- and *p*-methoxybenzylidene-sulphenamides have almost identical spectra, whereas, because of the participation of structures such as (VII),

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[10] Moreton and Stubbs, *J.*, 1939, 1321; Cerniani and Passerini, *J.*, 1954, 2261.
[11] Kiprianov, Yakovleva, and Rozum, *J. Gen. Chem.* (*U.S.S.R.*), 1952, **22**, 365.
[12] Koch, *J.*, 1949, 401.
[13] Fehnel and Carmack, *J. Amer. Chem. Soc.*, 1949, **71**, 84.
[14] Koch, *J.*, 1949, 387, 394.
[15] Bordwell and Boutan, *J. Amer. Chem. Soc.*, 1956, **78**, 854.
[16] Mangini and Passerini, *J.*, 1952, 1168.

o- and *p*-nitrobenzylidenesulphenamide absorb at longer wavelengths. Steric effects will partly neutralise the effect of the *o*-nitro-group.

EXPERIMENTAL

Benzothiazole-2-sulphenamide.—Simultaneous addition of a solution of 2-mercaptobenzothiazole (50 g.) in 1·1N-aqueous sodium hydroxide (225 c.c.) and a 6·5% solution of sodium hypochlorite (115 c.c.) to a cooled and vigorously stirred solution of ammonia (900 c.c.; *d* 0·88) under nitrogen, was regulated to be complete after 45 min. The product, a bulky solid, was collected and washed, using a centrifuge, until free from ammonia. The crude sulphenamide contained up to an equal weight of water from which the product was separated most readily by dissolving it in chloroform. The hot chloroform solution, when decanted from the aqueous layer, deposited on cooling, the sulphenamide (44·5 g.), m. p. 122—124° (Found: C, 46·1; H, 3·3. Calc. for $C_7H_6N_2S_2$: C, 46·1; H, 3·3%).

N-*Benzylidenebenzothiazole-2-sulphenamide.*—Benzaldehyde (4 c.c.) in ethanol (20 c.c.) was boiled under reflux with benzothiazole-2-sulphenamide (1 g.) for 30 min. The solution was concentrated and filtered hot; on cooling there were deposited pink needles (1·0 g.), m. p. 109—110°. Crystallisation from ligroin–benzene gave di(benzothiazolyl) disulphide, m. p. 175°; from the mother-liquor impure product, m. p. 109—111° was obtained. Repeated recrystallisations raised the m. p. to 113—117·5° (Found: C, 61·5, 61·6; H, 3·7, 3·7. $C_{14}H_{10}N_2S_2$ requires C, 62·2; H, 3·7%). Pure N-*benzylidenebenzothiazole-2-sulphenamide*, colourless needles, m. p. 112° was obtained by treating an ethanolic solution of the crude product with Norite (Found: C, 61·7; H, 3·8%). The infrared spectrum showed bands at 1597 (m) and 1572 (m) cm.$^{-1}$.

In approximate studies of the reaction conditions, sulphenamide (1 g.) was treated with benzaldehyde (0·5 g.) in boiling ethanol (5 c.c.) for various periods:

Time (hr.)	0·25	0·5	1·0	2·0
Yield (%)	48	72	87	97
M. p.	—	105°	107°	107°

Addition of potassium carbonate (1 g.) to the reaction mixture gave, after 15 minutes' boiling, a quantitative yield of product, m. p. 112°, free from disulphide. A similar result was obtained with sodium carbonate; addition of sodium or potassium acetate or hydrogen carbonate did not improve the yield.

N-o-*Nitrobenzylidenebenzothiazole-2-sulphenamide.*—The sulphenamide (0·5 g.) was heated for 30 min. with *o*-nitrobenzaldehyde (0·5 g.) in ethanol (15 c.c.) in the presence of potassium carbonate (1 g.). Yellow needles crystallised from the cooled solution. Recrystallisation gave N-o-*nitrobenzylidenebenzothiazole-2-sulphenamide*, m. p. 124°, from ethanol (Found: C, 53·2; H, 3·1. $C_{14}H_9O_2N_3S_2$ requires C, 53·3; H, 2·9%). Similarly prepared were N-m-, yellow needles, m. p. 178—181° (from ethylene chloride) (Found: C, 52·7; H, 2·9%), and N-p-*nitrobenzylidene*-, yellow needles, m. p. 214—215° (decomp.) (from chloroform) (Found: C, 53·7; H, 3·0%), N-p-*anisylidene*-, colourless needles, m. p. 104° (from ethanol) (Found: C, 59·6; H, 3·8. $C_{15}H_{12}ON_2S_2$ requires C, 60·0; H, 4·1%), and N-*cinnamylidene-benzothiazole-2-sulphenamide*, yellow needles, m. p. 131—133° (from ethanol) (Found: C, 64·3; H, 4·1. $C_{16}H_{12}N_2S_2$ requires C, 64·9; H, 4·1%).

The same method applied to acetophenone, *tert.*-butyl methyl ketone, butyraldehyde, and acetone gave only small yields of disulphide.

N-iso*Propylidenebenzothiazole-2-sulphenamide.*—Sulphenamide (0·5 g.) was heated for 30 min. with acetone (2 c.c.) in ethanol containing 3 drops of 2N-aqueous sodium hydroxide. On cooling, there were deposited colourless crystals of N-iso*propylidenebenzothiazole-2-sulphenamide*, m. p. 131° (from ethanol) (Found: C, 54·4; H, 4·5. $C_{10}H_{10}N_2S_2$ requires C, 54·1; H, 4·5%), ν 1620 (m) cm.$^{-1}$.

N-sec.-*Butylidene*-, m. p. 80° (from ethanol) (Found: C, 55·3; H, 5·3. $C_{11}H_{12}N_2S_2$ requires C, 55·9; H, 5·1%), infrared spectrum showed a band at ν 1622 (m) cm.$^{-1}$; N-cyclo*pentylidene*-, m. p. 131° (m. p. mixed with the derivative from acetone 91—103°) (from ethanol) (Found: C, 57·4; H, 5·0. $C_{12}H_{12}N_2S_2$ requires C, 58·0; H, 4·9%), ν 1629 (m) cm.$^{-1}$; N-cyclo*hexylidene*-, colourless needles, m. p. 106—107° (from ethanol) (Found: C, 59·3; H, 5·4. $C_{13}H_{14}N_2S_2$ requires C, 59·5; H, 5·3%), ν 1622 (m) cm.$^{-1}$; N-*ethylidene*-, colourless needles, m. p. 86° (from ethanol) (Found: C, 51·7; H, 3·9. $C_9H_8N_2S_2$ requires C, 51·9; H, 3·8%), ν 1618 (m) cm.$^{-1}$, and N-iso*butylidene-benzothiazole-2-sulphenamide*, colourless needles, m. p. 55—56° (from ethanol) (Found: C, 55·6; H, 5·3. $C_{11}H_{12}N_2S_2$ requires C, 55·9; H, 5·1%), ν 1618 (m) cm.$^{-1}$, were prepared similarly.

By this method, no product was obtained from diethyl ketone, methyl *iso*propyl ketone, acetophenone, or benzophenone. Small amounts of disulphide were formed.

Acid Hydrolysis of Benzylidenebenzothiazole-2-sulphenamide.—The sulphenamide (135 mg.), in warm ethanol (2·0 c.c.), was treated with concentrated hydrochloric acid (25 mm.^{3}). Di-(2-benzothiazolyl) disulphide was rapidly precipitated. The mixture was diluted with water and the disulphide (80 mg., 96%) was collected and washed with a little 50% aqueous ethanol. Addition of acidified 2 : 4-dinitrophenylhydrazine solution to the filtrate gave benzaldehyde dinitrophenylhydrazone (120 mg.), m. p. 235°.

Spectral Measurements.—Infrared spectra were measured on a Perkin-Elmer recording spectrophotometer, on mulls in Nujol. Ultraviolet spectra were determined on Beckman DU and Unicam S.P. 500 spectrometers for MeOH solutions unless otherwise stated.

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