Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.26; H, 5.74; N, 11.59.

All other nitrones were prepared similarly; the results are summarized in Table I.

TABLE I

PREPARATION OF NITRONES (9)

Reactants	Product	Mp, °C	Lit. mp, °C	Yield, %
5a + 6a[d]	9a	119–122	126–127[a]	29
5a + 6b[d]	9b	158–158.5	162[b]	32
5a + 6c[d]	9c	166–168	171[b]	35
5a + 6d[d]	9d	148.5–149	150[b]	54
5c + 6a[e]	9g	148.5–150	151–152[c]	39

[a] Beilstein's "Handbuch der Organischen Chemie," 4th ed, Vol. 15, Springer Verlag, Berlin, 1932, p 8. [b] Reference 2. [c] Reference 4. [d] 2:1 molar excess of 6. [e] Equimolar amounts of reactants employed.

In addition, these nitrones were prepared independently by condensation of aryl hydroxylamines with imidate esters as previously described.[4]

p-Bromoformanilide (10, R′ = Br). Method A.—A solution of 4.28 g (0.04 mol) of nitrosobenzene and 3.66 g (0.02 mol) of "methylene-p-bromoaniline" (6e) in 150 ml of chloroform was allowed to stand in the dark at room temperature. After 1 day, tlc examination of the reaction mixture revealed the presence of the nitrone 9c. After 4 days, the reaction mixture was evaporated to dryness and the residue recrystallized from benzene to give 2.05 g (52%) of tan crystals of 10 (R = Br), identical with an authentic sample prepared independently.[25] The presence of azoxybenzene in the reaction mixture was confirmed by vpc.

Method B.—A mixture of 1.46 g (0.005 mol) of the nitrone 9c, 0.54 g (0.005 mol) of nitrosobenzene, and 50 ml of chloroform was allowed to stand at room temperature in the dark for 5 days. Evaporation of the reaction mixture and recrystallization of the residue from benzene gave 0.28 g (28%) of tan crystals of p-bromoformanilide, identical with the material prepared by method A above. Again, azoxybenzene was present in the crude reaction mixture, as determined by vpc.

Other substituted formanilides (10) were prepared analogously; the results are summarized in Table II.

TABLE II

PREPARATION OF PARA-SUBSTITUTED FORMANILIDES (10)

Reactants	Product	Yield, %
2 5a + 6a	10, R = H	a
2 5a + 6b	10, R = Cl	49
5a + 9b	10, R = Cl	38
2 5a + 6c	10, R = CH_3	a
5a + 9d	10, R = CH_3	a
5a + 9e	10, R = OCH_3	a

[a] Product identified by vpc but not isolated.

Registry No.—**9e**, 27396-35-6; **9f**, 27396-36-7.

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(25) L. F. Fieser and J. F. Jones in "Organic Syntheses," Collect. Vol. III, E. C. Horning, Ed., Wiley, New York, N. Y., 1955, p 590.

Study of the Michael and Mannich Reactions with Benzothiazole-2-thiol[1a]

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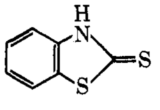
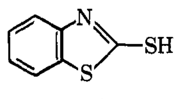
Received May 7, 1970

The reaction of the anion of benzothiazole-2-thiol (MBT) with activated olefins in the presence of sodium hydride with Michael reaction acceptors produced 3-substituted benzothiazoline-2-thiones. Similarly, the Mannich reaction of MBT anion with formaldehyde and primary or secondary amines produced the N- (or 3-) substituted benzothiazoline-2-thiones. Possible mechanisms and supporting nmr, ir, and uv data are discussed. The N substitution of MBT anion is discussed within the framework of the oxibase scale which can predict the condition for formation of N products or S products from this ambident anion.

The object of the present investigation was to study the Michael and Mannich reactions of the ambident anion of benzothiazoline-2-thione (I), the so-called 2-mercaptobenzothiazole or MBT of the rubber industry, with various activated vinyl compounds as well as with formaldehyde and various amines. Harman,[1b,2] studying the reaction of organic mercaptans such as I with acrylonitrile, formulated the MBT addition product as an S-substituted benzothiazole-2-thiol derivative. We have now found that the correct structure is the N derivative. Likewise we have shown that the Michael reaction products with activated carbon–carbon double bonds such as methyl vinyl ketone, phenyl vinyl ketone, 2-vinylpyridine, 4-vinylpyridine, divinyl sulfone (which produces a diadduct), and 2-nitro-1-butene, are all N-substituted benzothiazoline-2-thione derivatives.



I



IA

The fact that benzothiazoline-2-thione (I) also enters into a variety of Mannich reactions with formaldehyde and various aliphatic and aromatic amines or phenols to give N-substituted 3-alkylbenzothiazoline-2-thiones is not well known. This paper constitutes a correction for a number of such products incorrectly postulated as S-substituted compounds[3-9] reported in the older literature. The structural assignments of the few N-substituted products were made by Morton and Stubbs[10] based on the absorption at 320–325 mμ indicative of the (–N–(S=)C–S dithio carbamate) structure. These results were confirmed later by Koch[11] and Moore

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(1) (a) Presented in part before the Organic Chemistry Division of the American Chemical Society, Atlantic City, N. J., Sept 17, 1965; (b) M. W. Harman, *Ind. Eng. Chem.*, **29**, 205 (1937).

(2) M. W. Harman, U. S. Patents 1,951,052 (1934); 2,010,000 (1935); and 2,049,229 (1935).

(3) M. H. Zimmerman, U. S. Patent 1,960,197 (1934).

(4) W. J. S. Naunton, W. Baird, and H. M. Bunbury, *J. Soc. Chem. Ind. London Trans.*, **53**, 127 (1934); *Rubber Chem. Technol.*, **7**, 417 (1934).

(5) D. F. Twiss and F. A. Jones, *J. Soc. Chem. Ind. London Trans.*, **54**, 13 (1935).

(6) J. L. Kurlychek, U. S. Patent 2,358,402 (1944).

(7) M. Bogemann and E. Zauker, German Patent 575,114 (1933).

(8) C. Cokman, U. S. Patent 1,901,582 (Sept 13 1933).

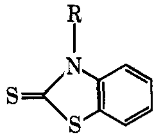
(9) R. Robinson, H. Bunbury, J. Davies, and W. J. S. Naunton, British Patent 377,253 (1944).

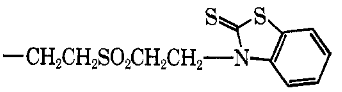
(10) R. A. Morton and A. L. Stubbs, *J. Chem. Soc.*, 1321 (1939).

(11) H. P. Koch, *ibid.*, 401 (1949).

TABLE I

MICHAEL REACTION PRODUCTS[c]



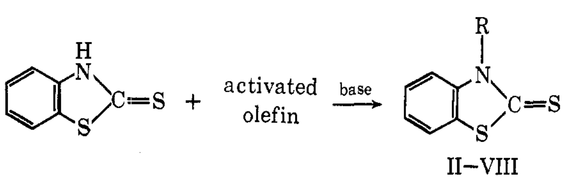
Products[c]	R	Solvent	Mp, °C	Yield, %	Ir data, μ	Uv data, mμ	Nmr (ppm)[a] AB type splitting (Figure 2) 4,5,6,7 aromatic protons
II	$-CH_2CH_2COCH_3$	THF	140–141	70–75	5.95, 9.20, 6.90	228, 240, 262, 320	7.0
III	$-CH_2CH_2COPh$	THF	144.5–145	95.0	5.86, 6.20, 9.30	. . ., 242, 260, 320	7.20
IV[b]	2-Pyridylethyl	THF	(1) 94–95 (2) 123–124	80.0	6.10, 9.30, 13.20	236, 258, 321	7.20
V[b]	4-Pyridylethyl	THF	(1) 141–142 (2) 159–160	80	6.10, 9.30, 13.20	235, 258, 321	7.21
VI	$-CH_2CH_2CH(NO_2)CH_3$	EtOH	89–90	85	6.45, 7.30, 9.10, 13.50	240, 255, 321	7.30
VII	$-CH_2CH_2CN$	EtOH	165–166	90	4.50, 6.20, 9.30	240, 154, 320	7.20
VIII		THF	215–216	50	6.70, 9.30, 8.30	240, 270, 320	7.40

[a] The AB type splitting, accompanied by some secondary splitting, we describe as the one envelope type (AB) as compared to the two envelope (A_2B_2). [b] Two crystalline modifications of each of the pyridyl compounds were observed. In each case, the low-melting modification was formed from the reaction mixture, and after melting and resolidification, then crystallized in the more stable, high melting modification. In each case, the low- and high-melting forms showed identical elementary analysis, which, coupled with identical uv, ir, and nmr spectra, indicated the absence of organic structural isomers. [c] Satisfactory analytical data were reported (±0.35%) for C, H, N, and S, Ed.

and Wright.[12] Stavroskaya and Kolosova[13] offered additional chemical evidence.

Discussion of Results

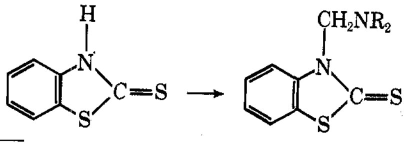
The reaction of benzothiazoline-2-thione (I) with compounds containing activated carbon–carbon double bonds proceeded readily at ambient temperature in tetrahydrofuran as a solvent using catalytic amounts of sodium hydride.



II–VIII

The products were isolated as white crystalline solids and characterized as indicated in Table I. The adducts from the 2- and 4-vinylpyridines gave two different solids for each starting material, identified as two crystal modifications of the same product in each case.

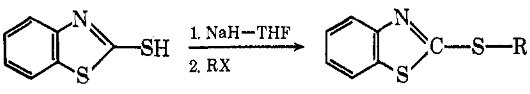
Similarly, the reactions of benzothiazoline-2-thione (I) with primary and secondary amines in anhydrous ether produced the amine salts of compound I in quantitative yield. When these salts were dissolved in water and allowed to react with formaldehyde at ambient temperatures, the corresponding Mannich reaction products were formed in high yields (eq 2).



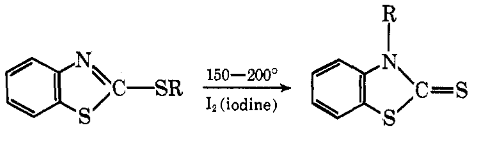
(2)

The Michael as well as the Mannich reaction products (Tables I and II) all showed among other absorptions a distinct band at 320–325 mμ in the ultraviolet. This intense band was assigned to the π → π* transition of the nonbonding ($3p^2$) electron pair of the sulfur atom and the other π electron of the heterocyclic ring. The infrared absorption at 1074 cm^{-1} (medium) was assigned to the thione (C=S) vibrational frequency.

The 3-alkylbenzothiazoline-2-thiones (see eq 4) were prepared from the corresponding 2-alkylthiobenzothiazoles, which in turn were prepared by modification of the procedures of Moore[14] and Sexton;[15] see Table III. The 2-alkylthiobenzothiazoles were prepared by nucleophilic displacement on the corresponding alkyl halides using sodium hydride in tetrahydrofuran (eq 3). These were rearranged thermally to the 3-alkylbenzothiazoline-2-thione in accordance with eq 4.



(3)



(4)

Examination of the nmr spectra of all the described products, II–XXIV resulted in the discovery of characteristic differences in the nature of the aromatic protons

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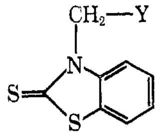
(12) C. G. Moore and E. S. Wright, J. Chem. Soc., 4237 (1952).

(13) V. I. Stavroskaya and M. O. Kolosova, Zh. Obshch. Khim., **30**, 711 (1960).

(14) C. G. Moore, J. Chem. Soc., 4237 (1952).

(15) W. A. Sexton, ibid., 470 (1939).

TABLE II
MANNICH REACTION PRODUCTS[c]



Products[c]	Y	Solvent	Mp, °C	Yield, %	Ir data, μ	Uv data, mμ	Nmr data AB type splitting (Figure 2) 4,5,6,7 aromatic protons
IX	Piperidino[a]	Water	159–161	73.4	6.20, 9.30, 13.40, 14.20	244, 258, 320	7.0[b]
X	Pyrrolidino	Water	122–125	80.3	6.20, 9.28, 13.40, 14.20	245, 252, 320	7.10
XI	Benzylamino	Water	128–130	75.6	6.20, 9.36, 13.40, 14.20	230, 258, 325	7.40
XII	*N*,*N*-Diethylamino[a]	Water	88–89	80.5	6.35, 9.38, 13.80, 14.50	240, 260, 322	7.80
XIII	Cyclohexylamino[a]	Water	157–158	88.0	6.40, 9.40, 13.70, 14.59	245, 265, 325	7.60
XIV	Morpholino[a]	Water	149–150	79.0	6.32, 9.42, 13.69, 14.60	240, 260, 320	7.50

[a] These compounds were reported in the literature, see ref 13. [b] The AB type of splitting, accompanied by some secondary splitting, we describe as the one envelope type (AB) as compared to the two envelope (A_2B_2). [c] Satisfactory analytical data were reported (±0.35%) for C, H, N, and S, Ed.

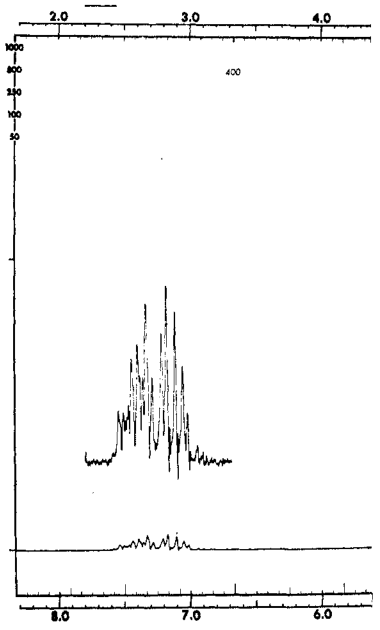


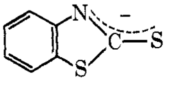
Figure 1.

on the benzene rings for the two classes of the derivatives of various benzothiazoles and similar aromatic heterocyclic compounds. In the S-alkyl esters of benzothiazole-2-thiol (XV–XX), the heterocyclic ring is aromatic and in conjugation with the benzene ring. The ring current in the heterocyclic ring causes a change in the electronic environment, different for the 5 and 6 protons. Hence, the resonance peaks from the four aromatic protons are split into two distinct envelopes of several lines, each representing two protons close together or sometimes overlapping, resembling a somewhat off-symmetrical A_2B_2 type splitting, Figure 1.

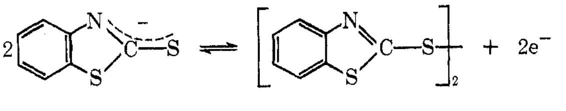
Thus, the 4,7 protons of compounds XV–XX, which are highly deshielded by the heterocyclic ring current, form the downfield envelope. The degree of deshielding in the benzothiazole system depends on the density of the circulating current from the heterocyclic ring. Since the sulfur and nitrogen atoms of the heterocyclic thiazole ring cannot produce identical environments for the adjacent protons on the benzene ring, it is highly improbable for the two envelopes to be perfectly symmetrical. Still, elements of symmetry can be seen. Analogy is made with the nmr spectra of aromatic protons of α,α'- and β,β'-substituted naphthalene derivatives[16] where for similar reasons, two perfectly symmetrical envelopes are formed.

On the other hand, the N- or 3-substituted derivatives of benzothiazoline-2-thione, II–XIV and XXI–XXIV including the 3-alkyl esters as well as the Michael and Mannich reaction products, even including compound I, all showed a single envelope for the four aromatic protons, resembling an AB type splitting in which the chemical shift, δ, of the 4,7 protons *vs.* that of the 5,6 protons, is much smaller than the *J* values (splitting constants), Figure 2.

Application of the Oxibase Scale to Rationalize the Production of N-Substituted Products.—The anion of MBT can be formulated as follows



in which two nucleophilic sites, either nitrogen or sulfur, can be easily identified. The sulfur atom is the most easily oxidized site as treatment of MBT^- with mild oxidants produce the disulfide in a half-cell reaction

 (5)

$$E = \epsilon^\circ + 2.60\ V = 2.23V$$

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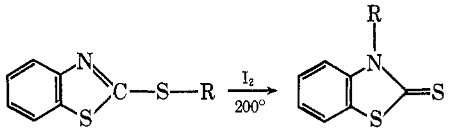
[16] See J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, p 147.

TABLE III

2-ALKYLTHIOBENZOTHIAZOLES AND 3-ALKYLBENZOTHIAZOLINE-2-THIONES



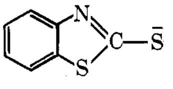
Products	R	Mp or bp (mm), C°	Solvent	Yield, %	Ir data, μ	Uv data, mμ	Nmr data A_2B_2 type (Figure 1) 4,7 protons, ppm	5,6 protons, ppm	AB type of splitting (Figure 2) 4,5,6,7 protons, ppm
				2-Substituted Thiobenzothiazoles[a,c]					
XV	CH_3–[a]	48–49 133–135 (0.5)	THF	93	6.20, 13.30, 14.20	244, 275, 289, 298	7.80	7.50	
XVI	$CH_3CH_2CH_2$–[a]	168–175 (15)	THF	81	6.23, 13.34, 14.20	246, 278, 289, 298	7.69	7.50	
XVII	$(CH_3)_2CH$–[a]	110–115 (0.5)	THF	79	6.10, 13.30, 14.24	245, 277, 286, 298	7.70	7.50	
XVIII	$CH_3(CH_2)_3$–[a]	145–146 (1)	THF	80	6.0, 13.30, 14.24	244, 275, 287, 298	7.70	7.50	
XIX	$(CH_3)_2CHCH_2CH_2$–	125–128 (0.5)	THF	73	6.10, 13.30, 14.24	242, 280, 285, 301	7.80	7.50	
XX	$CH_3CH_2\underset{\underset{CH_3}{\vert}}{C}HCH_2$–	139–140 (0.5)	THF	70	6.20, 13.30, 14.24	240, 279, 284, 298	7.80	7.50	
				3-Substitituted Benzothiazoline-2-thiones[b,c]					
XXI	CH_3–[b]	90–91	None	71.5	6.20, 9.30, 14.20	225, 281, 298, 320			7.0
XXII	$CH_3CH_2CH_2$–[b]	74–75	None	65.0	6.10, 9.30, 14.30	298, 281, 290, 321			7.10
XXIII	$(CH_3)_2\underset{\underset{R}{\vert}}{C}$–[b]	66–67	None	53.0	6.20, 9.30, 14.30	245, 278, 298, 320			7.40
XXIV	$CH_3(CH_2)_3$–		None	45.0	6.05, 9.41, 14.30	245, 278, 300, 320			6.9

[a] Some of the compounds were reported in literature ref 15. [b] Some of the compounds were reported in literature ref 15. [c] Satisfactory analytical data were reported (±0.35%) for C, H, N, and S, Ed.

The oxidation potential of this oxidative dimerization potential has been estimated to be −0.37 V (American convention) in water at 25° by O'Connor.[17] Relative to water, the oxibase scale E value is 2.23 V. The high E value of MBT^- can be explained within molecular orbital theory by noting that the highest filled molecular orbital on the sulfur is quite large (large coefficient of the atomic orbital) and that its energy is high.

Thus the electrons are easily removed by an oxidant. Secondly, the charge density on the sulfur atom in the MBT^- is quite low, on the basis of Hückel π electron theory.

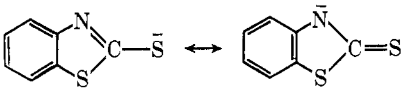
In terms of the oxibase scale[18–21] the result is that the E value of the S^- is high and the H value, defined as $H = pK_a + 1.74$, is small.



E_{S^-} high

H_{S^-} small

The nitrogen anion, on the other hand, has a larger charge density than the sulfur anion, thus indicating that the nitrogen is a stronger base toward a proton. The H_{N^-} is therefore larger than H_{S^-}, a fact well attested by the observation that MBT exists in the thion form (eq 6).[22–24]



(6)

The orbital on nitrogen which would serve as the source of the nucleophilic electrons is smaller and of lower energy. Thus E_{N^-} is low compared to E_{S^-}.

Attack of a H.—The proton in solution[25] has an α of 0.00 and a β of 1.00; therefore one observes an N–H attack.

$$\log K_{S^-}/K_{N^-} = 1.00[H_{S^-} - H_{N^-}]$$

$$\log K_{S^-}/K_{N^-} < 0 \text{ since } H_{N^-} > H_{S^-}$$

Attack on CH_3I.—Methyl iodide is an α reagent (α = 2.95 while β = −0.003). To a good approximation the methylation is controlled by the E term and S methylation results.

$$\log K_S/K_{N^-} = 2.96[E_S - E_{N^-}] + 0.003[H_{S^-} - H_{N^-}]$$

$$\log K_S/K_N > 0 \text{ because } E_{S^-} > E_{N^-} \text{ and } H_{N^-} > H_{S^-}$$

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[17] J. O'Connor, Ph.D. Thesis, Purdue University, June 1969.

[18] R. E. Davis in "Survey of Progress in Chemistry," A. Scott, Ed., Academic Press, New York, N. Y., 1964, pp 189–238.

[19] R. E. Davis, R. Nehring, W. J. Blume, and C. R. Chuang, *J. Amer. Chem. Soc.*, **91**, 91 (1969).

[20] R. E. Davis, S. P. Molnar, and R. Nehring, *ibid.*, **91**, 97 (1969).

[21] R. E. Davis, H. Nakshbendi, and A. Ohno, *J. Org. Chem.*, **31**, 2702 (1966).

[22] B. Stanovnik and M. Tisler, *Vestn. Sloven. Kem. Drust.*, **10**, 1 (1963).

[23] B. Ellis and P. J. F. Griffiths, *Spectrochim. Acta*, **22**, 2005 (1966).

[24] R. A. Morton and A. L. Stubbs, *J. Chem. Soc.*, 1321 (1939).

[25] J. O. Edwards, *J. Amer. Chem. Soc.*, **76**, 1540 (1954).

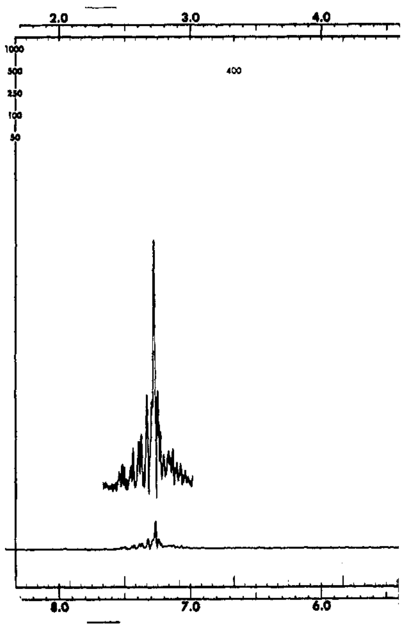


Figure 2.

The oxibase scale also predicts that the amount of N methylation would increase relative to S methylation with the series CH_3I, CH_3Br, CH_3Cl, and CH_3OTs.

Attack on Benzoyl Chloride.—Benzoyl chloride[26] is an α reagent ($\alpha = 3.5$ and $\beta = 0.01$). The α value is large because the lowest unfilled acceptor orbital is of low energy while the β value is low because of the reduced amount of positive charge on the carbonyl carbon caused by the electronic effects of the benzene ring.

$$\log K_{S^-}/K_{N^-} = 3.5[E_{S^-} - E_{N^-}] + 0.01[H_{S^-} - H_{N^-}]$$
$$\cong 3.5[E_{S^-} - E_{N^-}] \gg 0$$

Thus, the result is –S–(O=)C–Ph.

Attack on Acetyl Compounds.—Data are available[27] from which α and β values can be computed on $CH_3C(=O)O^-$ as an acetylating agent: $\alpha = 0.70$; $\beta = 0.46$. The value of β is the dominate term (β range up to 1.0 for H^+) and the acetylation is controlled by the βH term.

$$\log K_{S^-}/K_{N^-} = 0.70[E_{S^-} - E_{N^-}] + 0.46[H_{S^-} - H_{N^-}]$$

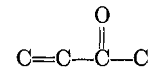
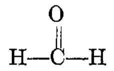
The first term is small and the second term is negative; therefore the result is $N(O{=})CCH_3$.

The foregoing discussions should show the power of the oxibase scale to predict ambident anion reactivities.

As predicted by the oxibase scale, our experiments showed that the reaction of MBT with benzoyl chloride gave the S-substituted thio ester S(O=)CPh, whereas the reaction with acetyl chloride gave the N-substituted amide, $N(O{=})CCH_3$. The physical data obtained by ir, nmr, and uv supported the structural assignments. The thio ester, S(O=)CPh, showed a strong absorption at 5.92 μ in the ir spectrum characteristic of thio esters, whereas the amide, $N(O{=})CCH_3$, showed a strong absorption band at 6.20 μ indicative of amide absorption. The nmr spectrum of the benzoyl derivative of MBT gave the usual pattern of the A_2B_2 type absorption showing the double envelope pattern, indicative of S substitution. However, the acetyl derivative showed the usual AB type pattern at 7.30 ppm, indicative of N substitution. Similarly the $CH_3(O{=})CN$ methyl group appeared at 2.70 ppm, at lower field than the $CH_3(O{=})CS$ methyl group which appeared at 2.40 ppm downfield from TMS.

Thus the experimental facts indeed support the predictions based on the oxibase scale, that benzoylation proceeds on the sulfur to give the S-substituted benzothiazole while the acetylation gives the N-substituted benzothiazoline-2-thione.

Let us now consider the addition of a nucleophile to an unsaturated ketone, such as methyl vinyl ketone, or to an aldehyde, such as formaldehyde, in the Mannich and Michael reactions.

Methyl vinyl ketone	 $C{=}C{-}\overset{\overset{O}{\|}}{C}{-}C$	α	low
Formaldehyde	 $H{-}\overset{\overset{O}{\|}}{C}{-}H$	β	high

The structural analogies between these compounds and acetylation agents for the introduction of the acetyl group are at once obvious, and in contrast to the case of the introduction of the benzoyl group. That is, whereas the presence of the benzene ring reduces the amount of the positive charge on the carbonyl carbon (high α) of the benzoyl, the methyl and ethylenic groups and protons exert an opposite influence on the carbon in formaldehyde and methyl vinyl ketone. Hence, these aliphatic carbonyl substrates have low α values, and, correspondingly, relatively high β values. Examination of the literature shows that Mannich and Michael additives are fast with strong bases (*e.g.*, toward protons with the highest α values) and slow with poor bases (*e.g.*, toward I^-), in spite of the fact that the attacking species are "good" nucleophiles in the sense that they have high E values toward carbon.

In the present case, the attacking ambident MBT anion offers two choices, S^- with high E_S and low H_S as against N^- with low E_{N^-} and high H_{N^-}. As with the acetylating reagents, the substrate species exhibit a low α and high β. Hence, in the equation derived from oxibase scale considerations

$$\log K_{S^-}/K_{N^-} = \alpha[E_{S^-} - E_{N^-}] + \beta[H_{S^-} - H_{N^-}]$$

the high value of H_{N^-} makes the second term negative, while a low E_{N^-} makes the first term small; therefore K_{N^-} is larger than K_{S^-}, the N^- anion wins out in the competition, and the N-substituted benzothiazoline-2-thiones are the products observed.

Attempts were made to isolate the S-substituted Michael addition products by interrupting the reaction at various times before completion; however, only N-substituted products were prepared and no S-substituted products could be isolated at any time during the reaction.

Experimental Section

General Procedure for the Michael Reaction Products.—The Michael reaction adducts generally were prepared by adding the freshly distilled activated olefinic compounds to a cooled solution of benzothiazole-2-thiol in tetrahydrofuran containing a catalytic amount of sodium hydride. The resulting solution was then heated for 48 hr at 40-45°. The products isolated from solution were solids which were purified by recrystallization from suitable

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[26] R. E. Davis, "Organosulfur Chemistry," M. J. Janssen, Ed., Interscience, New York, N. Y., 1967, pp 311-328. (Data taken from Table 18.1 except for b.)

[27] W. P. Jencks and J. Carriuolo, *J. Amer. Chem. Soc.*, **82**, 1778 (1960).

solvents. Specific examples are detailed below including some special cases where the activated olefinic compounds were prepared *in situ*. See Tables I–III.

3-(3-Oxobutyl)benzothiazoline-2-thione (II).—A solution of benzothiazole-2-thiol (I) (17.0 g, 0.101 mol) in 200 ml of anhydrous tetrahydrofuran and 50 mg of sodium hydride contained in a 58.1% oil dispersion was cooled to 5° and methyl vinyl ketone (8.0 g, 0.114 mol) was added over a period of 15 min. The reaction mixture was stirred for 48 hr at 40–45°. Concentrating the solvent to half its volume by evaporation under reduced pressure followed by cooling to −78° resulted in 17.5 g, 70–72% yield, of crude crystalline product, II, mp 138–140°. Two recrystallizations from isopropyl ether gave analytically pure II: mp 140.0–140.5°; $\lambda_{\text{max}}^{\text{Nujol}}$ 5.85 (C=O), 6.30 (C=C), and 9.30 μ (C=S).

Anal. Calcd for $C_{11}H_{11}NOS_2$: C, 55.76; H, 4.67; N, 5.90. Found: C, 55.50; H, 4.83; N, 5.86.

The oxime of compound II was prepared in the usual manner.[28] A 90% yield of the product was obtained after recrystallization from absolute ethanol, mp 149–150°.

Anal. Calcd for $C_{11}H_{12}N_2OS_2$: C, 52.35; H, 4.79; N, 11.10; S, 25.41. Found: C, 51.85; H, 4.84; N, 11.08; S, 25.44.

3-(2-Benzoylethyl)benzothiazoline-2-thione (III).—Into a 500-ml round bottom flask were placed 95% ethanol (200 ml), compound I (16.70 g, 0.10 mol), and sodium hydride (4.10 g, 0.10 mol, contained in a commercial 58.1% dispersion in oil). To this cooled solution was added dropwise 50 ml of an ethanol solution of β-chloropropiophenone (16.8 g, 0.10 mol). The reaction mixture was heated to 40–45° for 48 hr. After filtration of the sodium chloride, the reaction mixture was cooled to −78° and filtered, resulting in 27.10 g, 90% yield, of white, crystalline product, III, mp 140–145°. Recrystallization from ethanol produced analytically pure material: mp 144.5–145°; $\lambda_{\text{max}}^{\text{Nujol}}$ 5.85 (C=O), 6.20 (C=C), and 9.30 μ (C=S).

Anal. Calcd for $C_{16}H_{13}NOS_2$: C, 64.21; H, 4.35; N, 4.68; S, 21.40. Found: C, 64.22; H, 4.39; N, 4.70; S, 21.59.

Bis[2-(2-benzothiazolinethion-3-yl)ethyl] Sulfone (VIII).—To a solution of compound I (16.70 g, 0.10 mol) in 200 ml of anhydrous tetrahydrofuran was added 50 mg of sodium hydride contained in a 58.1% dispersion in oil. After cooling to 5°, freshly distilled divinyl sulfone (11.8 g, 0.10 mol) was added slowly with stirring. The reaction mixture was heated to 40–45°, with stirring for 48 hr. Cooling to −78° and filtration resulted in 22.0 g (50% yield) of crude compound VIII, mp 214–216°. Recrystallization from isopropyl ether produced analytically pure material: mp 215–216°; $\lambda_{\text{max}}^{\text{Nujol}}$ 6.20 (C=C), 9.30 (C=S), and 8.30 μ (SO_2).

Anal. Calcd for $C_{18}H_{16}N_2O_2S_5$: C, 47.76; H, 3.56; N, 6.19; S, 35.42. Found: C, 47.63; H, 3.56; N, 5.97; S, 35.62.

3-(2-Nitrobutyl)benzothiazoline-2-thione (VI).—To compound I (16.70 g, 0.10 mol) dissolved in 100 ml of ethanol were added sodium hydride (4.10 g, 0.10 mol, contained in 58.1% oil dispersion) and then, dropwise, freshly distilled 2-nitro-*n*-butyl acetate[29] (16.10 g, 0.10 mol). The reaction mixture was heated with stirring 48 hr at 40–45°. Acidification with 10% hydrochloric acid and cooling to −78° and filtration produced 20.99 g, 83% yield, of white, crystalline, crude VI, mp 88–90°. Recrystallization from isopropyl ether resulted in analytically pure material: mp 89.5–90°; $\lambda_{\text{max}}^{\text{Nujol}}$ 6.45 and 7.30 (NO_2), 9.10 (thione), 13.50, and 14.20 μ (aromatic).

Anal. Calcd for $C_{11}H_{12}N_2O_2S_2$: C, 49.23; H, 4.51; N, 10.44; S, 23.89. Found: C, 48.80; H, 4.72; N, 9.95; S, 23.66.

Procedure for the Synthesis of the 2-Alkylthiobenzothiazoles.—The 2-alkylthiobenzothiazoles were prepared by addition of the appropriate alkyl halide, with stirring, to a solution of the sodium salt of benzothiazole-2-thiol prepared from compound I and sodium hydride in tetrahydrofuran under reflux. The reaction was usually completed in 2–3 hr. After completion, the reaction mixture was filtered, the filtrate was distilled to remove the solvent, and the products were isolated as liquids by vacuum distillation. This is similar to the previous method[15] except that a cleaner reaction was obtained by the use of sodium hydride in tetrahydrofuran solvent.

2-*n*-Butylthiobenzothiazole (XVIII).—To a solution of compound I (50.1 g, 0.30 mol) in anhydrous tetrahydrofuran was added sodium hydride (7.20 g, 0.30 mol) with constant stirring. While heating to a gentle reflux, *n*-butyl bromide (48 g, 0.35 mol) was added dropwise. The reaction was then cooled to room temperature and filtered. The solvent was removed by distillation and the resulting oil was washed with distilled water and dried. Distillation under reduced pressure gave a clear liquid, yield 80%, bp 145–146° (1 mm).

Anal. Calcd for $C_{11}H_{13}NS_2$: C, 59.13; H, 5.86; S, 28.71. Found: C, 58.98; H, 5.76; S, 29.12.

Procedure for the Synthesis of 3-Alkylbenzothiazoline-2-thiones.—The 3-alkylbenzothiazoline-2-thiones were prepared by rearrangement of the 2-alkylthiobenzothiazoles in the presence of catalytic amounts of iodine[15] without solvent at 200–250°. Yields of the 3-alkylbenzothiazoline-2-thiones decreased with the length of the alkyl group, and alkyl groups above isopropyl produced liquids which were purified by distillation *in vacuo*.

3-Methylbenzothiazoline-2-thione (XXI).—Into a 50-ml round bottom flask equipped with thermometer and condenser were placed 2-methylthiobenzothiazole (9.0 g, 0.05 mol) and 0.50 g of iodine. The mixture was heated to 200–250° and the temperature was maintained for 6–8 hr. Cooling and washing with 10% hydrochloric acid produced 6.47 g, 71.5% yield, of yellowish solid, mp 85–90°. Recrystallization from ethanol gave mp 90.0–90.5° (lit.[15] mp 90–91°).

Procedure for the Preparation of Mannich Reaction Products.—The Mannich reaction products were prepared from the corresponding substituted ammonium salts of compound I and formaldehyde at room temperature in aqueous solution. The ammonium salts were prepared by adding the desired amine to a solution of compound I in ether. The crystalline salt was filtered, washed with ether, dried, and dissolved in water. Aqueous formaldehyde (40%) was added in excess to form the Mannich reaction products of compound I in excellent yields.

3-Pyrrolidinomethyl-2-benzothiazoline-2-thione (X).—To a solution of compound I (16.7 g, 0.10 mol) in 800 ml of anhydrous ether was added pyrrolidine (7.10 g, 0.1 mol). The salt precipitated immediately and was filtered, washed with ether, and dried. The salt was formed in quantitative yield. (A solution was prepared by dissolving 23.6 g (0.10 mol) of this salt in 200 ml of distilled water). To this solution was added with stirring 30 ml of 40% formaldehyde. A white solid formed immediately, which was collected and dried, 20.0 g, 80% yield, mp 122–125°. Recrystallization from acetone gave analytically pure material, mp 124–125°.

Anal. Calcd for $C_{12}H_{14}N_2S_2$: C, 57.54; H, 5.42; N, 11.19; S, 25.62. Found: C, 57.40; H, 5.63; N, 11.09; S, 26.08.

Registry No.—IA, 149-30-4; II, 27410-83-9; oxime of II, 27410-84-0; III, 27410-85-1; IV, 5525-04-2; V, 27410-87-3; VI, 27410-88-4; VII, 27410-89-5; VIII, 20752-60-7; IX, 6957-11-5; X, 23124-36-9; XI, 27410-38-4; XII, 22075-92-9; XIII, 27410-40-8; XIV, 27410-41-9; XV, 615-22-5; XVI, 27410-43-1; XVII, 27410-44-2; XVIII, 2314-17-2; XIX, 27410-46-4; XX, 27371-67-1; XXI, 2254-94-6; XXII, 27410-48-6; XXIII, 27410-49-7; XXIV, 21261-91-6.

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(28) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, Wiley, New York, N. Y., 1964, p 254.

(29) H. Feuer and R. Miller, *J. Org. Chem.*, **26**, 1348 (1961).