Anal. Calcd for $C_8H_{12}S_2$: C, 55.76; H, 7.02; S, 37.22; mol wt, 172.316. Found: C, 55.35; H, 6.72; S, 37.72; mol wt, 172 (mass spectrum, molecular ion).

Reaction of Tetramethylene Sulfoxide with Acetyl Bromide.—To a solution of 5.2 g (0.05 mol) of tetramethylene sulfoxide in 100 ml of carbon tetrachloride was added with stirring an equimolar quantity of acetyl bromide at 0°; 1-bromothiophanium bromide deposited out of solution and was identified by nmr spectrometry.

Reaction of Tetramethylene Sulfoxide with Acetyl Chloride.—To a solution of 5.2 g (0.05 mol) of tetramethylene sulfoxide in 100 ml of methylene chloride was added with stirring an equimolar quantity of acetyl chloride at ambient temperature. After addition of the acetyl chloride was complete, the temperature was raised and kept at 40–50° until all hydrogen chloride evolution ceased. Then 4 g (0.125 mol) of methanol was added followed by 7.0 g (0.09 mol) of pyridine in small portions, and the mixture was stirred overnight.

With acetyl bromide, when carbon tetrachloride was employed as the solvent, bromothiophanium bromide was deposited out of solution. Analysis by mixed injection of the crude reaction mixture was by vpc as previously described.

Registry No.—Thiophane, 110-01-0; 1,1-dideuterio-1,4-dichlorobutane, 39495-73-3; 1,1-dideuterio-1,4-dihydroxybutane, 39495-74-4; thionyl chloride, 7719-09-7; α,α-dideuteriothiophane, 39495-75-5; α-acetoxythiophane, 1608-66-8; tetramethylene sulfoxide, 1600-44-8; 2-(2-thiophanyl)-2,3-dihydrothiophene, 39495-77-7.

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Quaternization of Thiazoles

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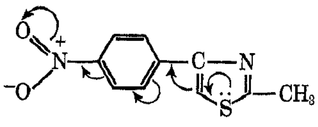
Different thiazoles have been prepared and their rate of quaternization with methyl iodide studied by the conductance method. The lower reactivity of quinaldine (**10**) over 2-methylbenzothiazole (**5**) has been explained on the basis of the β value of sulfur atom and the vinyl group. A charge transfer complex has been proposed to explain the rate retardation effect of an amino group, which otherwise should have accelerated the rate. The pK_a values of these thiazoles have been calculated by employing Edward's equation. The rate of quaternization in a series of isomeric alcohols has been investigated.

Quaternization has been a subject of interest since the days of Menschutkin.[1] The quaternization kinetics of heterocyclic bases like pyridine[2] and tetrahydroquinoline[3] have been investigated, but thiazoles have not been utilized for such studies. The quaternary salts of these thiazoles have been used by Rout, *et al.*,[4] for the synthesis of various dyes. The relative basicities of these thiazoles have been evaluated with the aid of Brooker's deviation factor.[5]

Results and Discussion

Thiazoles react with methyl iodide to form a quaternary salt. The rate data, Arrhenius parameters, and entropy of activation values are given in Table I. The reactivity of different 4-aryl substituted 2-methylthiazoles conform to the order **1** > **2** > **3** > **4**. This order of reactivity of different substituents is justifiable, since they oppose the main resonance of the sulfur atom with the thiazole ring[6] (I). The order of reactivity of other bases is **12** > **11** > **10** > **5** > **7** > **9** > **6** > **8**. The compounds **5**, **10**, and **11** belong to the same series of even alternant hydrocarbons. Quinaldine reacts more slowly than lepidine, possibly owing to the ortho effect. At 80°, the k values (extrapolated) are reversed, presumably owing to the loss of steric effect and the operation of the polar effects alone. Quinaldine reacts *ca.* four times slower than 2-methylbenzothiazole in agreement with the observation that the β value of sulfur is 25% lower than that of a vinyl group.[7]



I

The greater rate of reactivity of **1** over **8** is surprising, since an amino group would (1) increase the negative charge density around nitrogen in the reactant state and (2) stabilize the transition state. This decrease in rate may be due to the existence of an equilibrium between loose contact pairs and a charge trans-

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(1) M. Menschutkin, *Z. Phys. Chem.*, **5**, 589 (1890).

(2) E. M. Kosower, *J. Amer. Chem. Soc.*, **80**, 3267 (1958).

(3) J. Wolford, G. Toth, G. Bernathi, and J. Kobor, *Tetrahedron Lett.*, **43**, 43, 4019 (1971).

(4) (a) P. K. Misra, B. K. Patnaik, and M. K. Rout, *J. Indian Chem. Soc.*, **36**, 35 (1959); (b) B. K. Sabata, B. K. Patnaik, and M. K. Rout, *ibid.*, **37**, 613 (1960); (c) K. Mukherjee, R. C. Parida, A. Nayak, and M. K. Rout, *ibid.*, **47**, 1121 (1970); (d) P. B. Tripathy and M. K. Rout, *J. Indian Chem. Soc.*, **39**, 103 (1962); (e) B. K. Sabata, B. K. Patnaik, and M. K. Rout, *ibid.*, **38**, 679 (1970); **47**, 1121 (1970); (f) D. C. Pati and M. K. Rout, *ibid.*, **45**, 425 (1968); (g) K. Mukherjee, C. S. Panda, S. Misra, G. B. Behera, and M. K. Rout, *ibid.*, **47**, 323 (1970).

(5) L. G. S. Brooker, S. G. De nt,D. W. Heseltine, and E. VanLare, *J. Amer. Chem. Soc.*, **75**, 4335 (1953).

(6) A. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," The Queens College, Oxford, 1967.

(7) A. Streitweiser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1962, p 127.

TABLE I

VALUES OF RATE CONSTANTS, ARRHENIUS PARAMETERS, ENTROPY OF ACTIVATION, n, E_n, AND H VALUES OF THE HETEROCYCLIC BASES IN THEIR QUATERNIZATION REACTION WITH METHYL IODIDE IN NITROBENZENE

Compd no.	Compd	$k \times 10^4$, sec^{-1}					E, kcal/mol	Log PZ	$-\Delta S^{\ddagger}$, eu	n	E_n	H	pK_a
		50°	55°	60°	65°	80°[a]							
1	4-Phenyl-2-methylthiazole	3.84	6.21	10.30	15.91	40.62	20.32	10.14	14.3	3.69	1.076	4.40	2.66
2	4-(*m*-Nitrophenyl)-2-methylthiazole	1.75	3.20	3.84	5.75		17.00	7.66	23.8				
3	4-(*p*-Chlorophenyl)-2-methylthiazole	1.72	2.30	2.90	4.37		11.60	4.02	40.6				
4	4-(*p*-Nitrophenyl)-2-methylthiazole	1.28	1.77	2.30	3.22		13.30	5.03	35.9				
5	2-Methylbenzothiazole	2.26	2.88	4.72	6.41	13.76	14.90	6.36	25.2	3.35	0.98	4.0	2.26
6	2-Methylbenzoxazole	1.53	2.16	3.00	4.60	9.30	15.71	6.73	32.7	3.23	0.94	2.53	0.79
7	6-Amino-2-methylbenzothiazole	1.92	2.56	3.20	3.84	5.35	12.10	4.39	34.3	3.25	0.95	3.86	2.12
8	2-Amino-4-phenylthiazole	0.96	1.28	1.84	2.99	4.02	18.83	8.63	19.4	3.06	0.89	3.60	1.86
9	2-Methyl-4,5-diphenylthiazole	1.61	2.30	3.70	7.67	9.92	26.80	14.21	−6.2	2.97	0.87	3.46	1.72
10	Quinaldine[b]	1.59	2.69	5.37	8.07	99.68	21.63	10.45	6.4	3.96	1.15	4.80	3.06
11	Lepidine[b]	4.03	6.35	8.53	9.69	89.86	15.00	7.02	26.8	3.93	1.14	4.66	2.92
12	2-Methylbenzimidazole	4.69	6.83	9.56	10.90	63.62	9.41	3.36	43.6	3.83	1.12	4.53	2.79

[a] Extrapolated values. [b] Data are at 35, 40, 45, and 50°, respectively.

TABLE II

QUATERNIZATION OF 2-METHYL-4-PHENYLTHIAZOLE WITH CH_3I IN DIFFERENT SOLVENTS

Solvent	$k \times 10^4$, sec^{-1}				E, kcal/mol	Log PZ	$-\Delta S^{\ddagger}$, eu
	50°	55°	60°	65°			
Nitrobenzene	3.84	6.21	10.3	15.91	20.32	10.14	14.3
n-Butyl alcohol	2.68	5.18	7.3		23.00	11.88	4.3
sec-Butyl alcohol	1.84	3.00	6.00	9.59	23.57	12.10	3.3
tert-Butyl alcohol	0.84	1.28	1.53	2.99	19.50	9.00	17.50
Isobutyl alcohol	1.53	3.00	5.00	8.40	24.60	13.45	−2.8

fer complex.[8] This also can be a plausible explanation for the reduced reactivity of **7** over **5**. The values $k_5/k_7 = 1.2$ and $k_1/k_8 = 4.0$ may possibly be due to the steric effect arising out of charge transfer complex formation at the neighboring amino group in **8**.

A phenyl group at position 5 in the thiazole ring retards the rate of reaction of 4-phenyl-2-methylthiazole. The presence of the benzene ring at both the 4 and 5 positions of the thiazole ring produces strain on the molecule; as a result the benzene rings at position 4 become noncoplanar, decreasing thereby the interaction of the 4-phenyl group with the ring.[9]

The value of n, the nucleophilic constant of the Swain–Scott equation,[10] has been evaluated with $S_{CH_3I} = 1.4$[11] and log k_0 (hydrolysis of methyl iodide) = 8.4432.[12] The E_n values of the Edwards equation[13] have been obtained for different thiazoles. With these E_n values and values for $\alpha = 4.5$ and $\beta = 0.075$ for methyl iodide,[14] the pK_a values of these thiazoles have been calculated. All these data are presented in Table I. The order of basicity thus obtained agrees with the order derived by Rout, *et al.*, from the absorption spectra of the unsymmetrical cyanines.[4]

The reactivity of 4-phenyl-2-methylthiazole (**1**) in different pure solvents follows the order nitrobenzene > *n*-butyl alcohol > *sec*-butyl alcohol = isobutyl alcohol > *tert*-butyl alcohol (Table II). The trend in reactivity in different isomeric alcohols is quite interesting. The entropy of activation values for *n*-, iso-, and *sec*-butyl alcohols are very near to each other (+2 to −5 eu) whereas that in *tert*-butyl alcohol is −17.5 eu. The boiling point and density data of all these alcohols indicate *tert*-butyl alcohol to be less H bonded and so less ordered.[15] The solubility of all these alcohols in water,[16] however, indicates the greater capacity of the *tert*-butyl alcohol to form an intermolecular H bond over the rest. The polar transition state, therefore, is solvated to a greater extent in *tert*-butyl alcohol. These tendencies have possibly contributed to such a large negative entropy of activation.

Experimental Section

The purity of the compounds used in the kinetic study was checked on a silica gel G tlc plate. The following compounds were obtained from Schudart and Co.: 2 methylbenzothiazole, bp 242° (lit.[17] bp 240°); 2-methylbenzimidazole, recrystallized from water, mp 175° (lit.[18] mp 176°); 2-methylbenzoxazole, bp 202.3° [lit.[19] bp 204° (760 mm)]; quinaldine, bp 245–247° (lit.[20] bp 257°); 2-methyl-6-aminobenzothiazole, mp 129° (lit.[21] mp 126°).

The thiazoles (**1–4**, **9**) were prepared from appropriately substituted phenacyl bromides and thioacetamide by the method of Hantzsch.[22] The compounds are 2-methyl-4-phenylthiazole, mp 66° (lit.[22] mp 67°); 2-methyl-4-(*m*-nitrophenyl)thiazole, mp 104°; 2-methyl-4-(*p*-chlorophenyl)thiazole, mp 110°; 2-methyl-4-(*p*-nitrophenyl)thiazole, mp 147° (lit.[23] mp 145°); 2 methyl-4,5-diphenylthiazole, mp 110°.

2-Amino-4-phenylthiazole was prepared by the condensation

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(8) Inone and Kato [H. Inone and Y. Kato, *Tetrahedron*, **28**, 527 (1972)] have observed such an equilibrium between aniline and nitrobenzene. Behera, *et al.*, have also proposed a charge transfer complex between *O*-phenylenediamine and nitrobenzene [G. B. Behera, R. C. Acharya, and M. K. Rout, *J. Indian Chem. Soc.*, **48**, 917 (1971)].

(9) E. D. Sych and A. I. Kripianov, *Chem. Abstr.*, **57**, 9834 (1962).

(10) C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, **75**, 151 (1963).

(11) R. G. Pearson, H. Sobel, and J. Songstead, *ibid.*, **90**, 319 (1968).

(12) S. S. Radhakrishna Murti and G. P. Panigrahi, *J. Indian Chem. Soc.*, **46**, 320 (1969).

(13) J. O. Edwards, *J. Amer. Chem. Soc.*, **76**, 1540 (1954).

(14) R. E. Davis, "Survey of Progress in Chemistry," A. Scott, Ed., Academic Press, New York, N. Y., 1964.

(15) F. Franks and D. T. G. Ives, *Quart. Rev. Chem. Soc.*, **20**, 1 (1966).

(16) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Longmans Green and Co., London, 1956, p 1046.

(17) J. Fraser and F. M. Hammer, *J. Chem. Soc.*, 507 (1936).

(18) M. A. Phillips, *ibid.*, 2395 (1928).

(19) W. Theilacher, *J. Prakt. Chem.*, **153**, 54 (1939).

(20) J. T. Hackman and J. P. Wibant, *Recl. Trav. Chim. Pays-Bas*, **62**, 237 (1943).

(21) K. Fries and A. Wolter, *Justus Liebigs Ann. Chem.*, **527**, 60 (1936).

(22) A. Hantzsch, *ibid.*, **250**, 269 (1889).

(23) E. D. Sych, *Chem. Abstr.*, **54**, 5619*f* (1948).

of phenacyl bromide and thiourea by the method of Hurd, *et al.*[24] The compound melted at 148° (lit.[23] mp 147°).

The solvents used were of AnalaR B. D. H. variety. They had the following characteristics: nitrobenzene, bp 210–211°; *sec*-butyl alcohol, bp 99°; *n*-butyl alcohol, bp 118°; *tert*-butyl alcohol, bp 83°.

Kinetic Measurements.—The rate of reaction of the thiazoles with methyl iodide was studied in nitrobenzene at different temperatures in a thermostat (±0.1°) by monitoring the change in electrical conductivity with a Phillips model conductivity bridge at 1000 Hz. The platinum electrodes of the conductivity cell were coated with platinum black. Pseudo-first-order kinetics were maintained during the course of a kinetic run where [thiazole] was 0.01 *M* and [CH$_3$I] was 0.2 *M* (20-fold excess). Pseudo-first-order rate plots of log $R_t/R_t - R_\infty$ *vs.* time, where R_t and R_∞ are the electrical resistances at time *t* and at infinite time, respectively, were linear. The pseudo-first-order rate constants were calculated from the slopes of these linear plots and were reproducible to within ±0.2 units.

Registry No.—**1**, 1826-16-0; **2**, 39541-91-8; **3**, 24840-75-3; **4**, 33102-81-7; **5**, 120-75-2; **6**, 95-21-6; **7**, 2941-62-0; **8**, 2010-06-2; **9**, 3755-83-7; **10**, 91-63-4; **11**, 491-35-0; **12**, 615-15-6; methyl iodide, 74-88-4.

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(24) C. D. Hurd and H. L. Herhrmeister, *J. Amer. Chem. Soc.*, **71**, 4007 (1949).

Reactions of 3-Carboxyacryloylhydrazines. II.[1] Acid-Induced Rearrangement of Isomaleimides

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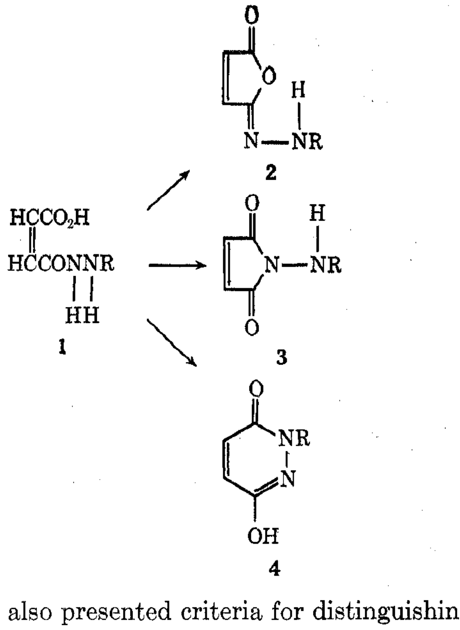
3-Carboxyacryloyl derivatives of several nitrophenylhydrazines undergo cyclization in acetic anhydride to the corresponding aminoisomaleimides. The latter in acid solutions rearrange to aminomaleimides or pyridazinones. Contrary to reports in the literature, these aminomaleimides do not rearrange to pyridazinones in acid media but are recovered unchanged.

Recently, Rubinstein, Skarbek, and Feuer[1] have discussed conditions under which 3-carboxyacryloylhydrazines **1** undergo cyclization to aminoisomaleimides **2**, aminomaleimides **3**, or pyridazinones **4** (eq 1).



(1)

They have also presented criteria for distinguishing between these structures.

In 1968, Baloniak[2] reported that the dehydration with acetic anhydride of various nitrophenyl-2-(3-carboxyacryloyl)hydrazines **1** led to the corresponding nitrophenylaminomaleimides **3**. It was further reported that these compounds were converted to pyridazinones **4** on treatment with sulfuric acid or with a mixture of sulfuric and acetic acids.[2-8]

These results, as well as previous reports in the literature[9,10] on ring formation and rearrangement, seemed incongruous when examined by the newly established criteria[1] and other recent work.[11,12] In light of the many discrepancies, it seemed important to reexamine the formation and interconversion of the various ring compounds formed by cyclization of **1** in acid solutions, and to reconcile the results obtained by previous workers.[2-10]

Results

Various aminoisomaleimide derivatives **2a–f** were prepared from the corresponding 3-carboxyacryloylhydrazines on treatment with acetic anhydride or thionyl chloride.[1] On treatment with acetic acid *N*-acetylaminoisomaleimide (**2a**), *N*-benzenesulfonylaminoisomaleimide (**2b**), 1-(2-nitrophenyl)aminoisomaleimide (**2c**), and 1-(2,4-dinitrophenyl)aminoisomaleimide (**2f**) rearranged to the corresponding aminomaleimides **3**. However, 1-(3-nitrophenyl)aminoisomaleimide (**2d**) was converted to the pyridazinone **4d**, while 1-(4-nitro-

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(1) H. Rubinstein, J. Skarbek, and H. Feuer, *J. Org. Chem.*, **36**, 3372 (1971).

(2) S. Baloniak, *Rocz. Chem.*, **42**, 1231 (1968).

(3) S. Baloniak, Abstracts, Third International Congress of Heterocyclic Chemistry, Sendai, Japan, 1971, p 323.

(4) S. Baloniak, *Rocz. Chem.*, **43**, 1187 (1969).

(5) S. Baloniak, *ibid.*, **42**, 1867 (1968).

(6) S. Baloniak, *ibid.*, **43**, 315 (1969).

(7) S. Baloniak and U. Wrzeciono, *ibid.*, **45**, 567 (1971).

(8) S. Baloniak and A. Mroczkiewicz, *ibid.*, **45**, 659 (1971).

(9) H. Feuer and H. Rubinstein, *J. Amer. Chem. Soc.*, **80**, 5873 (1958).

(10) H. Feuer and J. Asunskis, *J. Org. Chem.*, **27**, 4684 (1962).

(11) E. Hedaya, R. L. Hinman, and S. Theodoropulos, *ibid.*, **31**, 1311 (1966).

(12) A. Le Berre, J. Godin, and R. Garreau, *C. R. Acad. Sci., Ser. C*, **265**, 570 (1967).