TABLE IV

w_2	ϵ_{12}	v_{12}			
0.00168	2.238	0.97593	$\epsilon_1 = 2.212$	$\beta = 0.48$	$R_D = 53.8$
0.00331	2.260	0.97520	$v_1 = 0.9768$	$p_2^0 = 2.5105$	$P_\mu^0 = 448.9$
0.00561	2.292	0.97412	$\alpha = 14.33$	M = 200.3	$\mu = 4.65$ D

TABLE V

w_2	ϵ_{12}	v_{12}			
0.00150	2.246	0.97636	$\epsilon_1 = 2.212$	$\beta = 0.29$	$R_D = 54.5$
0.00281	2.281	0.97596	$v_1 = 0.9768$	$p_2^0 = 3.8381$	$P_\mu^0 = 768.0$
0.00488	2.324	0.97537	$\alpha = 22.04$	M = 214.3	$\mu = 6.08$ D

physical measurements carried out in the course of this work. In particular we wish to thank Mr. E. Townley for the ultraviolet spectra, Mr. J. McGlotten for the *p*Ka and dipole moment data, Mr. R. Wayne for the determination and interpretation of infrared spectra, and Mr. E. Connor for microanalyses. Microanalyses were also performed by Galbraith Laboratories, Knoxville, Tennessee.

BLOOMFIELD, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

The Cyclization of *N*-Alkenylthionamides to Thiazolines and Dihydrothiazines

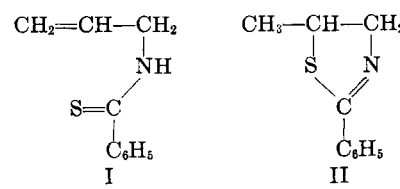
PETER A. S. SMITH AND JOHN M. SULLIVAN[1]

Received June 23, 1960

A group of *N*-alkenylbenzthionamides and acetthionamides have been prepared from the corresponding isothiocyanates and Grignard reagents. Allylic *N*-alkenylthionamides cyclize when treated with acidic catalysts such as aluminum chloride, but not with benzoyl peroxide. The position of cyclization follows the Markovnikov rule with an apparent slight preference for thiazolines over dihydrothiazines when other factors are equal.

In the course of the wartime penicillin project, one of us found that *N*-allyldicarboethoxyacetthionamide could be cyclized to a thiazoline ring.[2] It was the object of the present work to learn something of the nature of the reaction and to determine whether the cyclization of allylthionamides might have any generality. If so, an efficient synthetic route might become available, since allylic isothiocyanates are readily available, and thionamides can be prepared by the addition of Grignard reagents to them.[3]

N-Allylbenzthionamide (I) was chosen as an uncomplicated model. Cyclization to 2-phenyl-5-methyl-2-thiazoline (II) was effected by a variety of acidic catalytic agents, such as zinc chloride, boron fluoride, and sulfuric acid; aluminum chloride in nitrobenzene was the most effective, giving II in 47% yield. In contrast, benzoyl peroxide did not produce detectable cyclization. The assignment of structure II to the cyclization product, instead of the isomeric dihydrothiazine structure, is supported by the agreement of the melting point of its picrate with that reported for 2-phenyl-5-methyl-2-thiazoline picrate prepared in a different way, but more direct proof that cyclization had taken place at the β-rather than the γ-carbon was obtained by hydrolyzing II to 1-aminopropan-2-thiol, isolated and identified as the hydrochloride of the corresponding disulfide.



I II

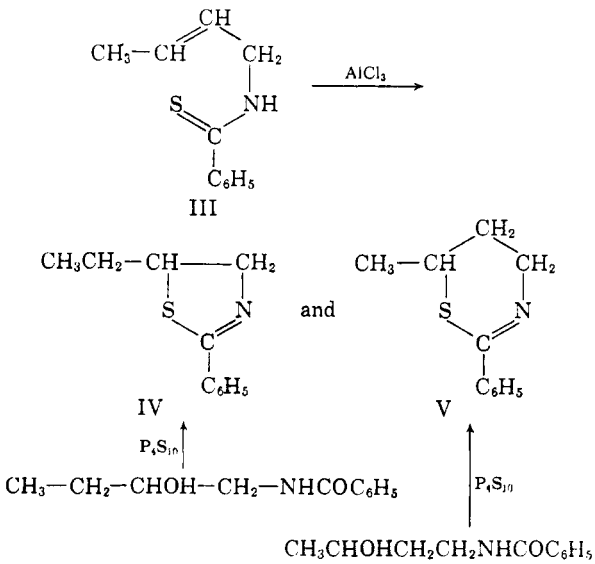
This cyclization is stoichiometrically identical to the intermolecular addition of mercaptans to olefins, and is readily conceived as a reaction of the enethiol tautomer of the thionamide. The

(1) From the doctoral thesis of J. M. S., Union Carbide Summer Fellow, 1957. Presented at the National Meeting, American Chemical Society, New York, September, 1960.

(2) *The Chemistry of Penicillin*, ed. by H. T. Clarke, Princeton University Press, Princeton, 1949, p. 470. [A similar reaction had been postulated previously, but not experimentally established as an intermediate stage in the acid-catalyzed condensation of phenols with allyl isothiocyanate: J. B. Niederl, W. F. Hart, and J. V. Scudi, *J. Am. Chem. Soc.*, **58**, 707 (1936); J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 3094 (1952)].

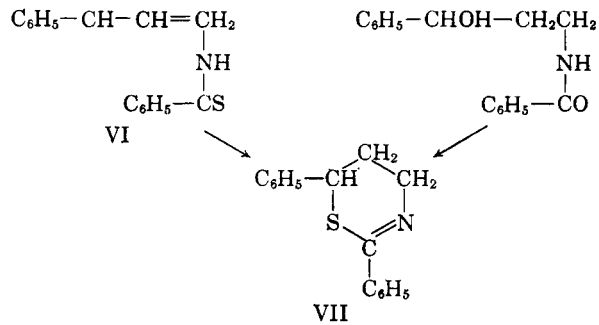
(3) M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, 1954, p. 1200.

intermolecular reaction does not require acid catalysts, however, and is promoted by light or benzoyl peroxide; addition takes place in the anti-Markovnikov position, as is to be expected of a free-radical reaction.[4,5] Our cyclization reaction therefore seemed, in contrast, to be an ionic addition of sulfur to an olefin. The evidence given by the position of cyclization is in this example ambiguous, however, since it might have been determined as much by a preference for forming a five-membered ring rather than a six-membered one, as by a preference for the formation of a carbonium ion at the more highly substituted β-carbon. Accordingly, we next investigated *N*-crotylbenzthionamide (III), in which the unsaturated carbon atoms are equally substituted. A mixture was produced in poor yield (20%), and separated by fractional distillation. The components were 2-phenyl-5-ethyl-2-thiazoline (IV) and 2-phenyl-6-methyl-5,6-dihydro-1,3,4-thiazine (V) in a ratio of between three and eight to one. This result is consistent with the concept of preferred cyclization to the most highly substituted carbon atom combined with a weak preference for five-membered ring formation; but, of course, certainty cannot be attached to such a conclusion in view of the low yields.



For identification, the thiazoline IV was prepared independently by treatment of *N*-(2-hydroxybutyl)benzamide with phosphorus pentasulfide; the samples were compared as their picrates. In a similar manner, V was prepared from *N*-(3-hydroxybutyl)benzamide.

When the stability of the carbonium ion at the γ-carbon was enhanced by phenyl substitution, as in *N*-cinnamylbenzthionamide (VI), cyclization appeared to occur there exclusively, to give the thiazine VII, although in low yield. This thiazine was identified through independent synthesis from *N*-(3-hydroxy - 3 - phenylpropyl)benzamide and phosphorus pentasulfide. The required 3-phenyl-3-hydroxypropylamine was obtained by the Curtius degradation applied to γ-phenyl-γ-butyrolactone through the hydrazide, azide, and 6-phenyltetrahydro-1,3-oxazin-2-one.



The cyclization of allylic thionamides was found to proceed as readily with acetthionamides as with benzthionamides. *N*-Allyl- (IX), *N*-(β-methallyl)- (X) and *N*-(α-methallyl)acetthionamide (XI) gave respectively 2,5-dimethyl-2-thiazoline (48%), 2,5,5-trimethyl-2-thiazoline(46%), and 2,4,5-trimethyl-2-trimethyl-2-thiazoline (46%).

A structural situation not permitting formation of the thiazoline ring is presented by *N*-(3-butenyl)-benzthionamide (VIII). Cyclization gave only a small conversion to isolable product, which was identified as 2-phenyl-6-methyl-5,6-dihydro-1,3,4-thiazine by comparison with an authentic sample.

EXPERIMENTAL[6]

Isothiocyanates. Allyl isothiocyanate is commercially available; 3-butenyl,[7] crotyl,[7] and β-methallyl[8] isothiocyanates were prepared according to published methods. α-Methallyl isothiocyanate, b.p. 51–57°/22 mm. (reported[9] b.p. 70–72°/34 mm.) was prepared from crotyl chloride and sodium thiocyanate, through crotyl thiocyanate, according to the procedure used by Bruson and Eastes[8] for β-methallyl isothiocyanate. Cinnamyl isothiocyanate, b.p. 120–127°/1 mm. (reported[10] b.p. 162°/12 mm.) was prepared in 54% yield by the Kaluza reaction according to the general directions of Moore and Crossley,[11] and less satisfactorily by the isomerization of cinnamyl thiocyanate.[12]

N-(Hydroxyalkyl)benzamides. These compounds, with the exception of 3-hydroxy-3-phenylpropylamine, whose prep-

(4) F. G. Bordwell and W. A. Hewett, *J. Am. Chem. Soc.*, **79**, 3493 (1957).

(5) S. J. Cristol and G. D. Brindell, *J. Am. Chem. Soc.*, **76**, 5699 (1954).

(6) Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting and boiling points are uncorrected.

(7) M. G. Ettlinger and J. E. Hodgkins, *J. Am. Chem. Soc.*, **77**, 1834 (1955).

(8) H. A. Bruson and J. W. Eastes, *J. Am. Chem. Soc.*, **59**, 2011 (1937).

(9) A. Kjaer, K. Rubinstein, and K. A. Jensen, *Acta Chem. Scand.*, **7**, 518 (1953).

(10) E. Bergmann, *J. Chem. Soc.*, 1361 (1935).

(11) M. L. Moore and F. S. Crossley, *Org. Syntheses*, **Coll. Vol. III**, John Wiley and Sons, New York, 1955, p. 599.

(12) P. A. S. Smith and D. W. Emerson, *J. Am. Chem. Soc.*, **82**, 3076 (1960).

aration follows, were prepared by benzoylating the known amino alcohols, mostly commercially available, in the presence of saturated aqueous potassium carbonate, and showed physical constants in agreement with published values. Two compounds were previously unreported. *N-(2-Hydroxybutyl)benzamide* formed colorless crystals, m.p. 106.5–108° (from benzene).

Anal. Calcd. for $C_{11}H_{15}NO$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.34; H, 7.80; N, 7.33.

N-(3-Hydroxybutyl)benzamide was obtained as a viscous oil, b.p. 174–180°/0.5 mm.; it could not be induced to crystallize, but its infrared spectrum showed the absorptions to be expected of a hydroxy amide structure.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.35; H, 7.90; N, 7.34.

4-Hydroxy-4-phenylbutyryl hydrazide. γ-Phenyl-γ-butyrolactone[13] (16.2 g., 0.1 mole) prepared by sodium borohydride reduction of β-benzoylpropionic acid, was refluxed for 12 hr. with 3.2 g. (0.1 mole) of hydrazine. Upon cooling, the hydrazide precipitated; the yield of crude material, m.p. 118–128°, was 85%. A small amount was recrystallized three times from a mixture of benzene and ethanol for an analytical sample, m.p. 124.5–126°.

Anal. Calcd. for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27; N, 14.42. Found: C, 61.84; H, 7.30; N, 14.59.

6-Phenyltetrahydro-1,3-oxazin-2-one. γ-Hydroxy-γ-phenylbutyryl hydrazide (5.2 g., 0.027 mole) was dissolved in 200 ml. of water which contained 1.4 ml. (0.025 mole) of sulfuric acid. This solution was stirred at −5° with 70 ml. of ether while 1.83 g. (0.027 mole) of sodium nitrite, dissolved in 75 ml. of water, was added over a 0.5-hr. period. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether layers were dried, an equal amount of benzene was added, and the solution was refluxed for 12 hr. During this time, 6-phenyltetrahydro-1,3-oxazin-2-one separated in a ring of beautiful, white, analytically pure crystals around the surface of the liquid; weight 2.4 g. (50%), m.p. 180–181°.

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.89; H, 6.30; N, 7.77.

An additional 0.7 g. of crude product, m.p. 170–178°, was obtained by evaporation of the mother liquors.

3-Hydroxy-3-phenypropylamine oxalate. A solution of 2.4 g. (0.0135 mole) of 6-phenyltetrahydro-1,3-oxazine-2-one and 7 g. of 85% potassium hydroxide in 20 ml. of ethanol was refluxed for 20 hr. The mixture was then poured into water and carefully acidified to *p*H 2; carbon dioxide was evolved. The acidified solution was extracted with ether to remove nonbasic impurities and was then made basic and extracted successively with ether and benzene. The combined extracts were dried and evaporated, leaving 1.2 g. of yellowish oil with an amine-like odor. Davies and Powell[14] report 3-hydroxy-3-phenylpropylamine to be a solid, m.p. 63.5–64.5°. The impure amino alcohol was converted to its oxalate by precipitation from ether with ethereal oxalic acid and recrystallized from aqueous ethanol; weight 0.6 g., m.p. 190–194°. A second recrystallization gave an analytical sample, m.p. 194–195°.

Anal. Calcd. for $C_{20}H_{28}N_2O_6$: C, 61.21; H, 7.19; N, 7.14. Found: C, 61.27; H, 7.22; N, 7.09.

Another form of the oxalate can also be obtained with m.p. 148–150°.

N-Alkenylthionamides. These compounds were prepared by the reaction of Grignard reagents with alkenyl isothiocyanates. The results are summarized in Table I. The following example is typical of the procedure followed.

N-Crotylbenzthionamide. trans-Crotyl isothiocyanate[7] (17 g., 0.15 mole) was added dropwise to a stirred ether solution of 0.2 mole of phenylmagnesium bromide. When the reaction subsided, refluxing was maintained for 0.5 hr. The Grignard complex was hydrolyzed with aqueous ammonium chloride. Removal of solvent from the ether layer and distillation of the residue gave 21 g. (73%) of *N*-crotylbenzthionamide, b.p. 156–157°/0.9 mm. (Analytical data are in Table I.)

TABLE I

THIONAMIDES PREPARED FROM ISOTHIOCYANATES
RNCS + R'MgX → RNHCSR'

No.	R	R'	M.P. °, or B.P. °/mm.	Yield, %
III	$CH_3CH{=}CHCH_2$	C_6H_5	156–157/0.9	73[a]
VI	$C_6H_5CH{=}CHCH_2$	C_6H_5	88–89	62[b]
VIII	$CH_2{=}CHCH_2CH_2$	C_6H_5	137–145/0.4	42
IX	$CH_2{=}CHCH_2$	CH_3	87/0.4[c]	52
X	$CH_2{=}CHCHCH_3$	CH_3	90–98/1	46[d]
XI	$CH_2{=}C(CH_3)CH_2$	CH_3	98–103/0.3	67[e]

[a] *Anal.* Calcd. for $C_{11}H_{13}NS$: C, 69.07; H, 6.85; N, 7.32. Found: C, 69.31; H, 7.06; N, 7.19. [b] *Anal.* Calcd. for $C_{16}H_{15}NS$: C, 75.84; H, 5.97; N, 5.53. Found: C, 75.54; H, 6.26; N, 5.38. [c] Sachs and Loevy[14] report b.p. 135–136°/17 mm. [d] *Anal.* Calcd. for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84. Found: C, 55.78; H, 8.58; N, 10.93. [e] *Anal.* Calcd. for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84. Found: C, 55.54; H, 8.34; N, 11.02.

Cyclization of N-alkenylthionamides to 2-thiazolines and/or 5,6-dihydro-1,3,4-thiazines. The cyclizations were brought about by heating the thionamides with anhydrous aluminum chloride, with minor variations among the examples. The results are summarized in Table II. The following example is typical of the procedure used.

2-Phenyl-5-methyl-2-thiazoline. Anhydrous aluminum chloride (33 g., 0.25 mole) was added directly to 44.3 g. (0.25 mole) of *N*-allylbenzthionamide[15] and the mixture was stirred. Much heat was evolved and a solid cake soon formed. Nitrobenzene was added to dissolve the cake and the mixture was held at 125° for 2 hr. Excess 25% sodium hydroxide solution was added to the cooled mixture, which was then stirred for 0.5 hr., and extracted with ether. The ether layer was extracted with 10% hydrochloric acid, and the acid layer was neutralized with excess 10% sodium hydroxide solution and extracted with ether. After removal of solvent from the dried ether extracts and distillation of the residue, 21 g. (47%) of 2-phenyl-5-methyl-2-thiazoline, was obtained, b.p. 148–150°/18 mm., or 86–91°/1 mm. A Kuhn-Roth C-methyl determination showed 0.72 equiv. per mole. (Other analytical data are in Table II.)

A similar experiment using zinc chloride in place of aluminum chloride and 12 hr. of heating gave a 31% yield. In another experiment where boron trifluoride etherate was used as the catalyst, with heating at 105° for 12 hr. in a sealed tube, the yield was 35%. In an experiment where benzoyl peroxide was the only catalytic agent, no basic products of any kind could be detected, and the thionamide remained apparently unchanged.

Hydrolysis of 2-phenyl-5-methylthiazoline. A solution of 5.5 g. of 2-phenyl-5-methyl-2-thiazoline in 25 ml. of concentrated hydrochloric acid was heated at 175° for 5 hr. in a sealed tube. The cooled reaction mixture deposited 2.2 g. (58%) of benzoic acid, which was removed by filtration. The filtrate was extracted with ether, and the aqueous layer was made strongly basic with 10% sodium hydroxide and extracted with ether in order to remove unchanged thiazoline. The aqueous layer was then acidified and the amino mercaptan salt was converted to the amino disulfide salt by adding iodine-potassium iodide solution until the iodine color persisted. Then the mixture was made basic

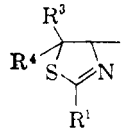
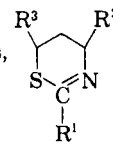
(13) R. R. Russell and C. A. Vander Werf, *J. Am. Chem. Soc.*, 69, 12 (1947).

(14) R. E. Davies and G. Powell, *J. Am. Chem. Soc.*, 67, 1466 (1945).

(15) F. Sachs and H. Loevy, *Ber.*, 37, 874 (1904).

TABLE II

CYCLIZATION OF *N*-ALKENYLTHIONAMIDES TO

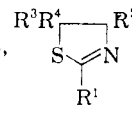
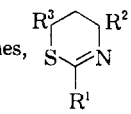
2-Thiazolines,  , and Dihydrothiazines, 

Thionamide No.	R^1	R^2	R^3	R^4	M.P. °, or B.P. °/Mm.	Yield, %	Picrate, M.P. °
I	C_6H_5	H	CH_3	H	148–150/18[a]	47	158–160[b]
III	C_6H_5	H	C_2H_5	H	88–90/0.2[c]	12	131–132[c]
	C_6H_5	H	CH_3	[d]	112–119/0.3[c]	1.5	162.5–164.5[c]
VI	C_6H_5	H	C_6H_5	[d]	86.5–87.5[e]	19	160–162[f]
VIII	C_6H_5	H	CH_3	[d]			164–165.5[c]
IX	CH_3	H	CH_3	H	48/22[g]	48	
X	CH_3	CH_3	CH_3	H	55–56/25[h]	46	170–172[i]
XI	CH_3	H	CH_3	CH_3	52/25[j]	46	150–154[k]

[a] *Anal.* Calcd. for $C_{10}H_{11}NS$: C, 67.75; H, 6.26; N, 7.90. Found: C, 67.76; H, 6.31; N, 7.94. [b] Reported picrate m.p. 156–157°; chloroplatinate, m.p. 179° [A. Salomon, *Ber.*, 26, 1321 (1893)]; nitro derivative, m.p. 70.5–71.5° (R. Adams and S. H. Babcock, *J. Am. Chem. Soc.*, 59, 2260 (1937)). Found: Chloroplatinate, m.p. 184–186° dec.; nitro derivative, m.p. 67–69°. [c] See Table III for analyses. 2-Phenyl-6-methyl-5,6-dihydro-1,3,4-thiazine was obtained from both thionamide III and VIII. Thionamide (III) also produced 7% of an intermediate fraction, b.p. 90–112°/0.3 mm., presumably a mixture of thiazoline and dihydrothiazine. The ratio of thiazoline to dihydrothiazine is 8:1 if the composition of this fraction is ignored; it is still 3:1 if the intermediate fraction is a 1:1 mixture, the most unfavorable possibility to be expected. [d] Dihydrothiazine, no R^4. [e] *Anal.* Calcd. for $C_{16}H_{15}NS$: C, 75.84; H, 5.97; N, 5.53. Found: C, 75.67; H, 5.86; N, 5.47. [f] *Anal.* Calcd. for $C_{22}H_{18}N_4O_7S$: C, 54.77; H, 3.76; N, 11.61; S, 6.65. Found: C, 54.67; H, 3.92; N, 11.71; S, 6.54. [g] Reported, b.p. 152°: S. Gabriel and C. F. von Hirsch, *Ber.*, 29, 2609 (1896). [h] *Anal.* Calcd. for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84. Found: C, 55.95; H, 8.79; N, 10.70. [i] *Anal.* Calcd. for $C_{12}H_{14}N_4O_7S$: C, 40.22; H, 3.94; N, 15.63. Found: C, 40.21; H, 4.09; N, 15.77. [j] B.p. 152°/760 mm. *Anal.* Calcd. for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84. Found: C, 55.64; H, 8.42; N, 10.86. [k] *Anal.* Calcd. for $C_{12}H_{14}N_4O_7S$: C, 40.22; H, 3.94; N, 15.63. Found: C, 40.28; H, 4.06; N, 15.74.

TABLE III

CYCLIZATION OF β- OR *N*-HYDROXYALKYLBENZAMIDES TO

Thiazolines,  , or Dihydrothiazines, 

R^1	R^2	R^3	R^4	M.P. °, or B.P. °/Mm.	Yield, %	Picrate, M.P. °	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
C_6H_5	H	CH_3	H	146–149/18[a]	30	153–155[a]						
C_6H_5	H	H	[b]	124/1.5[c]	8.5	181–182.5	47.29	3.47	13.79	47.39	3.65	13.88
C_6H_5	H	C_2H_5	H	106–109/1[d]	60	131–132	48.57	3.84	13.33	48.72	3.89	13.52
C_6H_5	H	C_6H_5	[b]	86–88[a]	40	157.5–159.5[a]						
C_6H_5	H	CH_3	[b]	122–123/1.5[e]	44	162.5–164.5	48.57	3.84	13.33	48.64	3.86	13.46

[a] See Table II. [b] Dihydrothiazine, no R^4. [c] M.p. 44–46° [reported m.p. 44–45° by G. Pinkus, *Ber.*, 26, 1077 (1893)]. [d] Anal. Calcd. for $C_{11}H_{13}NS$: C, 69.06; H, 6.85; N, 7.32. Found: C, 68.86; H, 6.72; N, 7.40. [e] *Anal.* Calcd. for $C_{11}H_{13}NS$: C, 69.06; H, 6.85; N, 7.32. Found: C, 68.88; H, 6.80; N, 7.52.

and subjected to continuous ether extraction for 2 hr. The ether was dried and saturated with dry hydrogen chloride to precipitate β-aminoisopropyl disulfide [2,2′-dithiobis-(propylamine)] dihydrochloride. After two recrystallizations from absolute alcohol it melted at 222–222.5° (reported[16] m.p. 213–214°), undepressed by a sample prepared from 2-mercapto-5-methyl-2-thiazoline (*vide infra*).

Anal. Calcd. for $C_6H_{18}N_2S_2Cl_2$: C, 28.45; H, 7.16; N, 11.06; S, 25.32; Cl, 28.00. Found: C, 28.53; H, 7.25; N, 10.94; S, 25.21; Cl, 27.84.

2-Mercapto-5-methyl-2-thiazoline. This substance was prepared by the reaction of 1-amino-2-bromopropane hydrobromide[17] with carbon disulfide in basic solution according to the procedure of Hirsch.[18] The product melted at 93–95°, although Hirsch reported 82°.

Anal. Calcd. for $C_4H_7NS_2$: C, 36.06; H, 5.30; N, 10.51. Found: C, 36.34, 36.25; H, 5.22, 5.28; N, 10.56, 10.47.

β-Aminoisopropyl disulfide [2,2′-dithiobis(propylamine)] hydrochloride. A 3.4-g. sample of 2-mercapto-5-methyl-2-thiazoline was hydrolyzed by the same procedure as that used in the hydrolysis of 2-phenyl-5-methyl-2-thiazoline except that the removal of benzoic acid was not necessary.

(16) S. Gabriel and E. Leupold, *Ber.*, 31, 2832 (1898).

(17) M. T. Leffler and R. Adams, *J. Am. Chem. Soc.*, 59, 2252 (1937).

(18) P. Hirsch, *Ber.*, 23, 964 (1890).

It gave 1.1 g. (33%) of crude β-aminoisopropyl disulfide dihydrochloride, m.p. 202–210°. After recrystallization from ethanol, it melted at 223.5–226°.

Cyclization of N-(hydroxyalkyl)benzamides to 2-thiazolines or 5,6-dihydro-1,3,4-thiazines. These preparations were carried out by heating the amides with phosphorus pentasulfide; the results are summarized in Table III. The following example is typical of the procedure used.

2-Phenyl-5-methyl-2-thiazoline from N-(2-hydroxypropyl)-benzamide. A mixture of 16 g. of *N*-(2-hydroxypropyl)-benzamide,[18] 10 g. of phosphorus pentasulfide, and 250 ml. of toluene was refluxed for 12 hr. The toluene was decanted from a gummy residue which remained in the flask. The residue was warmed on a steam bath with 10% sodium hydroxide solution. The basic solution was extracted with ether and the ether layer was combined with the toluene and extracted with 10% hydrochloric acid. The acid extracts were neutralized and extracted with ether. After drying of the ether solution, removal of solvent, and distillation of the residual oil, 4.8 g. (30%) of 2-phenyl-5-methyl-2-thiazoline was obtained; b.p. 146–149°/18 mm. The picrate prepared from this sample had m.p. 153–155°, undepressed when mixed with the product obtained from *N*-allylbenzthionamide.

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Syntheses and Properties of Some *N*-Substituted Sulfamides

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Reactions of dialkylsulfamyl chlorides with ammonia or with aliphatic, aromatic, and heterocyclic amines have been employed to synthesize seventeen new *N*-substituted derivatives of sulfamide of the types $R_2NSO_2NH_2$, R_2NSO_2NHR, and $R_2NSO_2NR_2$. These compounds have been characterized in terms of analysis, melting or boiling point, refractive index, and infrared spectrum. Two intense absorption bands in the 1140–1145 cm.$^{-1}$ and 1320–1350 cm.$^{-1}$ regions are associated with S—O vibrations in the —SO_2— group. The compounds are either low-melting crystalline solids or high-boiling oily liquids. Certain of the solids show promise as derivatives for the characterization of amines.

Of the various known aquo-ammono sulfuric acids, sulfamide is of particular interest because of the many analogies, both formal and actual, between its chemistry and that of urea. Like urea, it is capable of forming derivatives in which alkyl or aryl groups are bonded to one or both of the nitrogen atoms. Such *N*-substituted derivatives may be of the types $RNHSO_2NH_2$, $RNHSO_2NHR$, $R_2NSO_2NH_2$, R_2NSO_2NHR, or $R_2NSO_2NR_2$, where the R-groups may be the same or different. Most of these classes are represented by a few known compounds,[1] but the total information available on them is limited. It has been of interest, therefore, to investigate in detail methods of synthesis and both chemical and physical properties for a number of such compounds.

All of these substances can be regarded as ammonolysis or aminolysis products of sulfuryl chloride. Their direct formation from sulfuryl chloride, however, is often complicated by lack of control or the production of polymeric products.[1] Sulfuryl chloride reacts readily with secondary aliphatic amines or saturated heterocyclic amines to yield disubstituted sulfamyl chlorides, R_2NSO_2Cl. From these by reaction with ammonia, primary, or secondary amines, compounds of the types $R_2NSO_2NH_2$, R_2NSO_2NHR, or $R_2NSO_2NR_2$, respectively, are more conveniently prepared than by any other procedure. Secondary aromatic amines, however, are apparently insufficiently basic to yield comparable sulfamyl chlorides and undergo preferential ring chlorination on treatment with sulfuryl chloride. Primary amines give a variety of products with sulfuryl chloride, but sulfamyl chlorides of the type $RNHSO_2Cl$ are apparently not among them.

The present communication is concerned with the ammonolysis and aminolysis products obtainable from diethyl and cyclopentamethylene sulfamyl chlorides as typical starting materials. These compounds were obtained either by treating the sulfamyl chloride with liquid ammonia or by refluxing in admixture with the appropriate amine in an inert solvent such as chloroform, benzene, or ether. Reactions with aliphatic amines were complete in twelve hours; those with aromatic amines required up to twenty-four hours.

The compounds prepared are listed in Table I, together with important data pertaining to their syntheses and properties. The tri- and tetra-substituted sulfamides are either colorless oils or white crystalline solids. They dissolve readily in the common organic solvents but are insoluble in cold water and only slightly soluble in boiling water. Recrystallization is best effected from *n*-heptane, carbon tetrachloride, or ether. The formation of characteristically and sharply melting compounds with many amines suggests that the sulfamyl chlorides may be useful reagents for the characterization of such amines.

No systematic investigation of the infrared spectra of the *N*-substituted sulfamides has been reported. The spectra of a number of related *N,N*-disubstituted sulfonamides contain strong bands, which have been ascribed,[2,3] respectively, to the

(1) L. F. Audrieth, M. Sveda, H. H. Sisler, and M. J. Butler, *Chem. Revs.*, 26, 49 (1940).