methane is obtained. It has been reported that the product was a mixture of the di- and tribromo compounds.[1] This conclusion came solely from the fact that the elemental analysis of the crude reaction product was between the values for di- and tribromonitromethane, and could easily be misleading.

An intermediate may be isolated if the reaction mixture is cooled and acidified after ten minutes' heating. This intermediate, whose empirical formula is $C_2H_2Br_2N_2O_3$, was thought to be α,α-dibromo-α-nitroacetamide.[1] The infrared spectrum of this compound has intense absorption at 2.93, 3.17, 5.90, and 6.35 microns which is characteristic of secondary amides.[2] Therefore, it is most likely N,α-dibromonitroacetamide. When this compound is refluxed in water, dibromonitromethane is obtained and the aqueous solution is acidic and contains ammonia and bromide ion.

The reaction occurs in two steps:

$$O_2N{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}NH_2 + 2OBr^- \longrightarrow O_2NCHBr{-}\overset{\overset{O}{\|}}{C}{-}NHBr + 2OH^- \quad (I)$$

$$O_2NCHBr{-}\overset{\overset{O}{\|}}{C}{-}NHBr + H_2O \longrightarrow O_2NCHBr_2 + CO_2 + NH_3 \quad (II)$$

Step II is a further example of the rearrangement observed when α-haloamides are treated with hypobromite.[3] Since the reaction will occur in water initially free of bromide ion it is an indication that the rearrangement of the N-bromoamide is intramolecular as postulated by Haszeldine.[4]

The reaction was tried in acidic, neutral, and basic solution, both at room temperature and 100° but under none of these conditions could nitroacetamide be converted to nitromethylamine.

EXPERIMENTAL

Ethyl nitroacetate. This compound was prepared by the method of Rodionov and its physical constants agreed with those reported.[5]

Ammonium ethyl acinitroacetate. Into 6 g. of ethyl nitroacetate in 50 ml. of anhydrous ether, cooled in Dry Ice, was bubbled anhydrous ammonia. A pasty precipitate formed immediately. It was recrystallized from 95% ethanol to give 3.2 g. (57%) of ammonium ethyl acinitroacetate with m.p. 86–88° with decomposition.

Anal. Calcd. for $C_4H_{10}N_2O_4$: C, 32.00; H, 6.67; N, 18.68. Found: C, 31.76; H, 6.51; N, 18.61.

An aqueous solution of the compound gives a red color with ferric chloride solution, but no precipitate with silver nitrate solution, as had been reported.[1]

Ammonium acinitroacetamide. A solution of 3 g. of ammonium ethyl acinitroacetate in 45 ml. of absolute ethanol saturated with ammonia was heated in a sealed tube at 100° for 1.25 hr. The solid initially present quickly dissolved, and soon after glistening plates began to precipitate from the solution. The tube was cooled and the crystals collected to yield 1.5 g. (70%) of ammonium acinitroacetamide with m.p. 117–119° with decomposition.

Anal. Calcd. for $C_2H_7N_3O_3$: C, 19.81; H, 5.79; N, 34.75. Found: C, 19.87; H, 5.63; N, 34.58.

The compound gives a red color with ferric chloride solution and no precipitate with silver nitrate solution. Although the properties are different from those previously reported;[6] m.p. 152°, precipitate with silver nitrate solution; the present assignment is probably correct since nitroacetamide, m.p. 99–100°, is obtained upon acidification and extraction with ether.[7]

N,α-dibromonitroacetamide. To an aqueous solution of 2.42 g. (0.02 mole) of ammonium acinitroacetamide was added 0.80 g. (0.02 mole) of sodium hydroxide and the solution warmed to expel ammonia. After addition of 0.04 mole of hypobromite solution the mixture was warmed for 10 min., cooled, acidified, filtered, and the precipitate recrystallized from chloroform to give 2.9 g. (55%) of N,α-dibromonitroacetamide with m.p. 113–114°.

Anal. Calcd. for $C_2H_2Br_2N_2O_3$: C, 9.17; H, 0.77; N, 10.70; Br, 61.03. Found: C, 9.42; H, 0.87; N, 10.82; Br, 61.00.

Dibromonitromethane. 5.2 g. of N,α-dibromonitroacetamide was refluxed in 30 ml. of water for 2 hr. The organic layer was separated, dried over calcium chloride, and vacuum distilled to give 2.6 g. (61%) of dibromonitromethane, b.p. 44–45° (0.7 mm.) and n_D^{25} 1.5757.

Anal. Calcd. for $CHBr_2NO_2$: C, 5.49; H, 0.46; N, 6.40; Br. 73.06. Found: C, 5.46; H, 0.50; N, 6.15; Br, 73.27.

Department of Chemistry
Cornell University
Ithaca, N. Y.

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Investigations in Heterocycles. II. Unsymmetrical Ureas, Thioureas and Related Thiazolines

George deStevens, Heino A. Luts, and Angelina Halamandaris

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In the past few years several papers[1–3] have appeared on the use of thioureas as effective chemotherapeutic agents for the treatment of tubercular infections in experimental animals. Our recent work[4,5] on cycloalkeno[*d*]thiazolin-2-ones suggested

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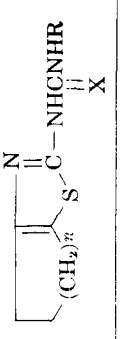
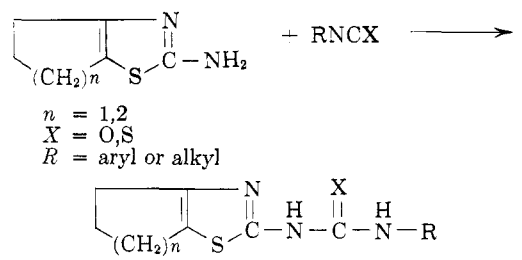
TABLE I



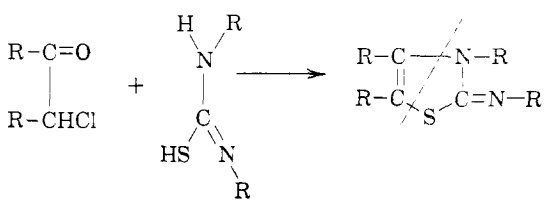
R	n	X	M.P., °C.	Yield, %	Empirical Formula	Analysis, % Calculated C	H	S	Cl	Found C	H	S	Cl
CH_3	2	S	218–220	33	$C_9H_{10}N_3S_2$	48.18	4.48			47.96	4.76		
p-ClC_6H_4	1	S	202–203	20	$C_{13}H_{12}ClN_3S_2$	50.39	3.90			50.33	3.96		
								(N)				(N)	
p-ClC_6H_4	2	S	217–218	32	$C_{14}H_{13}ClN_3S_2$			13.02	10.98			12.80	11.29
2,5-$Cl_2C_6H_3$	2	S	264	55	$C_{14}H_{13}Cl_2N_3S_2$	46.92	3.66		19.78	47.13	3.44		19.48
								(N)				(N)	
p-$(CH_3)_2N—C_6H_4$	2	S	230–232	62	$C_{16}H_{20}N_4S_2$	57.79	6.06	16.88		57.61	6.29	16.82	
p-*i*-$(CH_3)_2CH—O—C_6H_4$	2	S	190	30	$C_{18}H_{23}N_3OS_2$	59.46	6.41	17.74		59.39	6.55	18.00	
o-ClC_6H_4	2	O	210	57	$C_{14}H_{14}ClN_3OS$	54.62	4.57		11.52	54.47	4.75		11.51
2,5-$Cl_2C_6H_3$	2	O	264	68	$C_{14}H_{13}Cl_2N_3OS$	49.13	3.80		20.25	49.42	4.15		20.56
o-$C_2H_5OC_6H_4$	2	O	233–235	35	$C_{16}H_{19}N_3O_2S$	60.54	6.03	10.10		60.55	6.20	10.09	
o-$CH_3—C_6H_4$	2	O	320–322	43	$C_{15}H_{17}N_3OS$	62.69	5.96	11.16		62.67	5.86	11.45	
Naphthyl	2	O	264–265	40	$C_{18}H_{17}N_3OS$	66.90	5.28	10.26		66.97	5.58	10.26	

the use of related 2-aminothiazoles for the preparation of unsymmetrical ureas and thioureas. The diverse methods of preparation of these compounds have been outlined in a comprehensive review by Schroeder.[6] The procedure incorporated herein is simply the condensation of a 2-amino-4,5-substituted thiazole (2-amino-5,6-dihydro-4H cyclopentathiazole and 2-amino-4,5,6,7-tetrahydrobenzothiazole[7]) with alkyl and aryl isocyanates and isothiocyanates. The general reaction is formulated as follows:



The analytical data for the corresponding products are outlined in Table I.

During the course of our studies on anti-tubercular agents, Dr. Mizzoni[8] of our Chemical Research Laboratories postulated that the incorporation of the thiourea moiety into a heterocyclic system may lead to effective chemotherapeutics for the treatment of tuberculosis. Such a heterocycle would be the 2-iminothiazolines. The accompanying structure, in which the broken line delineates the pseudoform of a thiourea, illustrates this principle. Several of Mizzoni's compounds, in fact, showed good activity against tuberculosis in experimental animals. We have applied this concept in our studies on thiazoles fused to alicyclic systems. α-Chlorocyclopentanone and α-chlorocyclohexanone were condensed with the thioureas. In the course of our study it was found that 2-bromotetralone was a very reactive intermediate and lended itself very readily for this type of condensation. Consequently, several 8,9-dihydro-β-naphthothiazolines were prepared also for testing. The analytical data for the resulting heterocyclic compounds are presented in Table II and Table III.



The results of the biological testing of these compounds will be presented elsewhere.

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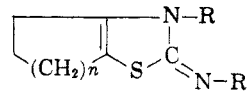
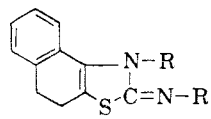
TABLE II



R	n	M.P., °C.	Yield, %	Empirical Formula	Analysis, % Calculated N	Calculated S	Found N	Found S
C_2H_5	1	157	32	$C_{10}H_{16}N_2S\cdot HCl$	12.57	14.38	12.82	14.37
C_2H_5	2	145–147	70	$C_{11}H_{18}N_2S\cdot HCl$	11.35	13.00	11.48	13.26
Cyclohexyl	1	188–190	46	$C_{19}H_{28}N_2S\cdot HCl$	7.98	9.18	8.02	9.00
Cyclohexyl	2	184–186	75	$C_{20}H_{30}N_2S\cdot HCl$	7.65	8.73	7.44	8.56
p-C_3H_7O—C_6H_4	2	104–106	15	$C_{25}H_{30}N_2O_2S$	6.63	7.58	6.64	7.80
p-$iC_5H_{11}O$—C_6H_4	2	124–125	30	$C_{29}H_{33}N_2O_2S\cdot HCl$	5.44	6.23	5.80	6.00

TABLE III



R	M.P., °C.	Yield, %	Empirical Formula	Analysis, % Calculated N	Calculated S	Found N	Found S
Cyclohexyl	108–109	38	$C_{23}H_{28}N_2S$	7.65	8.76	7.50	8.99
p-$C_3H_7OC_6H_4$	220–223	30	$C_{29}H_{30}N_2O_2S\cdot HBr$	5.09	5.83	5.04	5.79
p-$iC_5H_{11}OC_6H_4$	234–235	45	$C_{33}H_{38}N_2O_2S\cdot HBr$	4.62	5.28	4.70	5.07
p-C_4H_9—C_6H_4	223–225	44	$C_{31}H_{34}N_2S\cdot HBr$	5.12	5.87	5.03	5.88

EXPERIMENTAL[9]

Preparation of intermediates. α-Chlorocyclopentanone and α-chlorocyclohexanone were prepared according to the procedure outlined by Kötz,[10] and 2-bromotetralone was prepared according to Wilds.[11] The substituted arylisocyanates and isothiocyanates were prepared by well known methods.[6]

Condensation of 2-amino-4,5-cyclic substituted thiazoles with arylisocyanates and arylisothiocyanates. General procedure. An equivalent amount of arylisocyanate or isothiocyanate was added to the 2-aminothiazole dissolved in 10 times its volume of dry benzene. A vigorous reaction usually occurred leading to copious precipitation of the product. The reaction mixture, after refluxing for a period of time, was filtered, washed with benzene, and recrystallized from ethanol. In preparing the ureas, it was found that only 1 to 2 hr. reflux was necessary, whereas the condensation between the 2-aminothiazoles and the arylisothiocyanates proceeded at a much slower rate, requiring from 12 to 24 hr. of reflux.

Condensation of α-haloketones with symmetrical thioureas. General procedure. The products of this condensation are presented in Tables II and III. For the sake of clarity, the details for the preparation of 3-p-butylphenyl-2-p-butylphenylimino-8,9-dihydro-β-naphthothiazoline hydrobromide will be described. The other compounds in these tables are prepared in similar fashion.

A mixture of 17.0 g. (0.05 mole) of 1,4-bis(p-butylphenyl)-2-thiourea, 11.3 g. (0.05 mole) of 2-bromotetralone, and 200 ml. of absolute ethyl alcohol was refluxed for 6 hr. The clear solution was evaporated to one-tenth its volume and then 300 ml. of dry ether was added with vigorous stirring. After chilling overnight, the fine white powder was collected on a Büchner funnel and washed well with ether. Analytically pure material was obtained by dissolving the powder in a minimum amount of absolute ethyl alcohol and precipitating the product through the addition of ether.

Acknowledgments. We would like to express our gratitude to Mr. Louis Dorfman and his associates for the microanalytical data.

RESEARCH DEPARTMENT
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SUMMIT, N. J.

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Vinyl Derivatives of the Metals. VII. Preparation of Organotin Esters by Cleavage of Vinyltin Compounds[1,2]

ARNOLD SAITOW, EUGENE G. ROCHOW, AND DIETMAR SEYFERTH[3]

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A large variety of methods has been applied to the preparation of the now commercially useful organotin esters. The oldest, most frequently used and most widely applicable procedure involves the

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(3) Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Mass.