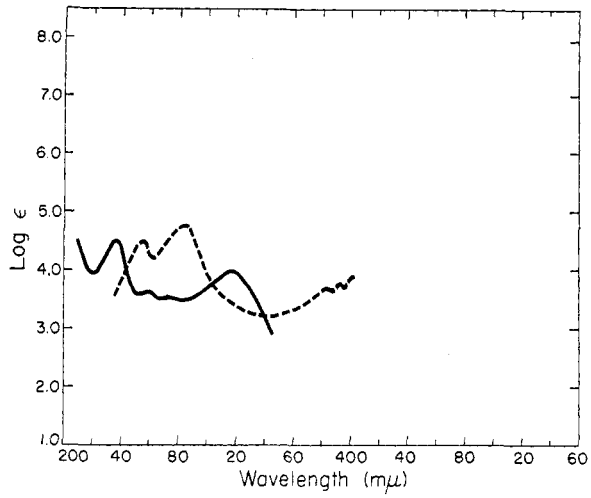

Fig. 2.—2,3-Dimethylquinoxaline ---· in dioxane; 6,11-*endo*succinic anhydride benzo[*b*]phenazine——.

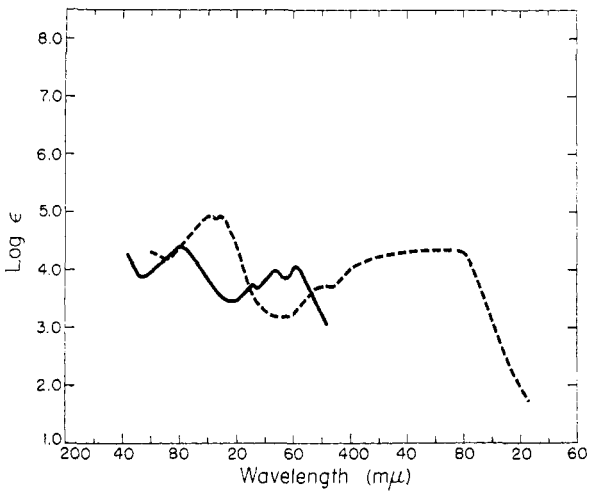

Fig. 3.—Dibenzo[*a,i*]phenazine ---, in dimethyformamide; 8,13-*endo*succinic anhydride dibenzo[*a,i*]phenazine ——, in dioxane.

TABLE III

SPECTRAL DATA FOR THE DIELS-ALDER ADDUCTS OF BENZO[*b*]PHENAZINE AND OF DIBENZO[*a,i*]PHENAZINE

Compound No.	λ(mμ)	log ε	λ(mμ)	log ε	λ(mμ)	log ε
II	238	4.51			318	4.00
IIc	245	4.43	279	4.18	318	4.04
					332	3.99
					468	2.30
					500	2.20
VII			282	4.43	332	3.75
					348	4.02
					365	4.10
VIIa	225	4.67	289	4.43	332	3.75
					348	4.02
					365	4.10

able solvent, giving a yield of purified product of the order of 80 to 90%.

Method B. Benzenesulfinic Acid Added to Phenazines.—A solution of 0.1 mole of the phenazine and 0.11 mole of benzenesulfinic acid sodium salt in 200 ml. of acetic acid was refluxed until the bright red solution had turned yellow, *i.e.*, about 0.5–1 hr. The reaction mixture was cooled, and the product was collected by filtration and purified by crystallization; yield, 84–89%.

Method C. Addition of Arylamines to Benzo[*b*]phenazine.—A mixture of benzo[*b*]phenazine[10] (2 g.) and an equal weight of the arylamine in 15 ml. of acetic acid was heated on the steam bath for 1 hr. After the mixture had cooled, the product was collected and crystallized from dimethylformamide and alcohol; yield, 60–70%.

Benzo[*b*]phenazine-6,11-*endo*diethylsuccinate (IIa).—A solution of 5 g. of I in 25 ml. of diethyl maleate was refluxed for 3 hr. Ligroin was added to the cold solution. The product separated and was crystallized from toluene–ligroin; yield, 4.3 g.

Method D. Oxidation of Dihydrophenazines to Phenazines.—The dihydrophenazine was dissolved in a minimum amount of warm pyridine and added to an equal weight of cupric acetate dihydrate dissolved in warm pyridine. The combined solutions were warmed on the steam bath while air was passed in for 0.5 hr. The reaction mixture was cooled and then flooded with methanol. The solid was isolated by filtration, washed well with water, then methanol, and dried. The product was then recrystallized from the appropriate solvent.

The Synthesis of 2-Substituted Imino-3-amino-4-thiazolidones

V. BON AND M. TIŠLER

Department of Chemistry, University of Ljubljana, Ljubljana, Yugoslavia

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Although 4-substituted thiosemicarbazides react with ethyl monochloroacetate or other derivatives of monochloroacetic acid to produce 1,3,4,-thiadiazine derivatives, their reaction in presence of sodium acetate furnishes 2-substituted imino-3-amino-4-thiazolidones. This structure was established by different reactions and chemical transformation to the known 2-phenylimino-4-thiazolidone.

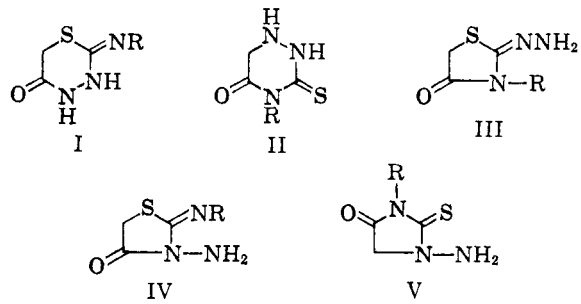
The known reactions of monochloroacetic acid or its derivatives with thiosemicarbazide, 4-substituted thiosemicarbazides or thiosemicarbazones follow two different paths. 1,3,4-Thiadiazine derivatives were obtained from 4-methyl- or 4-ethylthiosemicarbazide and monochloroacetic acid[1] in the presence of sodium acetate or with ethyl monochloroacetate[2] and some other substituted thiosemicarbazides. A compound of this type was claimed to be obtained when treating thiosemicarbazide with

(1) P. Chabrier and E. Cattelain, *Bull. soc. chim. France*, 48 (1950).
(2) P. K. Bose and B. K. Nandi, *J. Indian Chem. Soc.*, **7**, 961 (1930).

chloroacetyl chloride[3] or with chloroacetamide.[4] On the other hand, thiosemicarbazones of aldehydes and ketones behave differently towards monochloroacetic acid or its ester, giving rise to a five-membered heterocycle, *e.g.* derivatives of 2-hydrazino-4-thiazolidone.[1,5]

In this paper we describe the formation of hitherto unknown 2-substituted imino-3-amino-4-thiazolidones from the corresponding 4-substituted thiosemicarbazides and ethyl monochloroacetate in the presence of sodium acetate. Furthermore, we observed the formation of a new heterocyclic compound, $C_{20}H_{22}N_8O_4S_3$, m.p. 306°, instead of a 1,3,4-thiadiazine derivative,[2] when monochloroacetic acid, its ester, or amide reacted with 4-phenylthiosemicarbazide in the absence of sodium acetate. This compound was obtained also from the corresponding thiazolidone (IV. R = C_6H_5) after refluxing with 0.1 *N* hydrochloric acid.

Interaction between 4-substituted thiosemicarbazides and ethyl monochloroacetate could afford, in principle, the following cyclization products (or tautomeric forms):

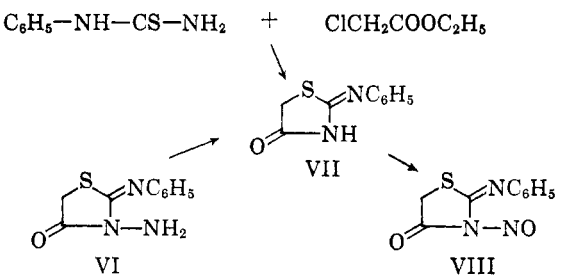


I II III

IV V

To establish unequivocally the structure of our new compounds, we performed different reactions with the product, obtained from 4-phenylthiosemicarbazide and ethyl monochloroacetate in the presence of sodium acetate. This compound (VI) gave a negative test for the presence of a mercapto or thioketo group (iodine–azide reaction[6]) and did not react with mercuric oxide, thus excluding the structures II and V. Furthermore, no evidence was obtained for the presence of a hydrazino group with the aid of common tests,[7,8] thus excluding the structure III or an uncyclized product. However, the compound reacted with benzaldehyde and formed also an isopropylidene derivative with acetone. The isopropylidene derivative was not identical with the product, obtained from acetone 4-phenylthiosemicarbazone and ethyl monochloroacetate[9] thus excluding definitely the possibility of the structure III. The phenyl compound was found fairly unstable against acid or alkaline reagents. With 0.1 *N* sodium hydroxide or 2 *N* hydrochloric acid the molecule is decomposed on heating, but with 0.1 *N* hydrochloric acid a high-melting substance (m.p. 306°) was obtained and this could be synthesized from 4-phenylthiosemicarbazide and ethyl monochloroacetate in the absence of sodium acetate. Acetylation of VI with acetic anhydride afforded a diacetyl product.

The final proof of the structure was presented through the reaction of VI with nitrous acid, used successfully for deamination on other types of heterocycles.[10] There were obtained two substances, one with m.p. 177° and the second with m.p. 226°. The first was found identical with the known 2-phenylimino-4-thiazolidone (VII), prepared from phenylthiourea and ethyl monochloroacetate,[11] and the second substance as its N-nitroso derivative (VIII).



VI VII VIII

The infrared spectrum of VI, determined as a mull in Nujol, shows bands at 3289 and 3226 cm.$^{-1}$ (N—H) as well a band which is characteristic of the carbonyl group in the 1704-cm.$^{-1}$ region, thus excluding the possible enolic form. The position of the last mentioned absorption band is consistent with that of γ-lactams, near 1700 cm.$^{-1}$.[12]

Experimental[13]

2-Phenylimino-3-amino-4-thiazolidone (VI).—A mixture of 4-phenylthiosemicarbazide (2 g.) and sodium acetate trihydrate (3.5 g.) in ethanol (35 ml.) was heated with an equimolar amount (1.46 g.) of ethyl monochloroacetate on a water bath for 1 hr. After cooling, the product was precipitated on addition of water. The colorless crystals were separated and recrystallized from aqueous ethanol; m.p. 119°; yield 8%.

Anal. Calcd. for $C_9H_9N_3OS$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.10; H, 4.44; N, 19.96.

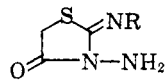
In ethanol λ_{max} 2700 Å., ϵ 8300. The infrared spectrum had bands at 3289, 3226, and 1704 cm.$^{-1}$ for N—H and C=O, respectively.

The benzylidene derivative was prepared in the usual way and after recrystallization from aqueous ethanol melted at 169°.

(3) J. Klosa, *Arch. Pharm.*, **287**, 12 (1954).
(4) U.S. Patent 2,534,087; *Chem. Abstr.*, **45**, 2714 (1951).
(5) F. J. Wilson and R. Burns, *J. Chem. Soc.*, 870 (1922).
(6) F. Feigl, "Spot tests," Vol. II, Organic Applications, Elsevier Publishing Co., Amsterdam, 1954, p. 164.
(7) S. Siggia and L. J. Lohr, *Anal. Chem.*, **21**, 1202 (1949).
(8) F. Feigl, V. Anger, and O. Frehden, *Mikrochemie*, **15**, 181 (1934).
(9) H. W. Stephen and F. J. Wilson, *J. Chem. Soc.*, 2531 (1926).
(10) C. F. Kröger, E. Tenor, and H. Beyer, *Ann.*, **643**, 121 (1961).
(11) P. J. Meyer, *Ber.*, **10**, 1965 (1877).
(12) L. J. Bellamy, "The Infrared spectra of Complex Molecules," J. Wiley, New York, N. Y., 1960, p. 214.
(13) All melting points were taken on a Kofler heating micro stage. Infrared spectra were determined with a Perkin-Elmer Model 21 spectrophotometer and sodium chloride optics.

TABLE I

2-SUBSTITUTED IMINO-3-AMINO-4-THIAZOLIDONES



Compound no.	R	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
1	*o*-Tolyl	91	$C_{10}H_{11}N_3OS$	54.29	5.01	19.00	54.07	5.14	19.07
2	*p*-Tolyl	82	$C_{10}H_{11}N_3OS$	54.29	5.01	19.00	54.11	5.12	18.73
3	*o*-Methoxyphenyl	140	$C_{10}H_{11}N_3O_2S$	50.63	4.67	17.72	50.51	4.90	17.69
4	*p*-Methoxyphenyl	148	$C_{10}H_{11}N_3O_2S$	50.63	4.67	17.72	50.40	4.85	17.51
5	*m*-Chlorophenyl	96	$C_9H_8N_3OSCl$	44.72	3.33	17.38	44.65	3.11	17.27
6	*p*-Chlorophenyl	118	$C_9H_8N_3OSCl$	44.72	3.33	17.38	44.60	3.44	17.43
7	*p*-Bromophenyl	154	$C_9H_8N_3OSBr$	37.77	2.82	14.68	38.05	3.04	14.85
8	Cyclohexyl	125	$C_9H_{15}N_3OS$	50.69	7.09	19.71	50.52	7.07	19.81

Anal. Calcd. for $C_{16}H_{13}N_3OS$: C, 65.08; H, 4.44; N, 14.23. Found: C, 65.20; H, 4.65; N, 14.16.

The isopropylidene derivative was prepared by refluxing the above compound (VI, 0.8 g.) in 5 ml. of ethanol and 3.5 ml. of acetone on a water bath for 3 hr. The reaction mixture was diluted with water and the precipitated product was recrystallized from aqueous ethanol, m.p. 93°.

Anal. Calcd. for: $C_{12}H_{13}N_3OS$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.00; H, 5.15; N, 17.07.

The infrared spectrum revealed no absorption bands characteristic for N—H group, but at 1709 cm.$^{-1}$ (assignable to C=O group).

The diacetyl derivative was prepared in the usual way and after recrystallization from water melted at 93°.

Anal. Calcd. for $C_{13}H_{13}N_3O_3S$: C, 53.61; H, 4.50; N, 14.43. Found: C, 53.87; H, 4.32; N, 14.58.

The infrared spectrum showed no N—H absorption bands, but a band at 1724 cm.$^{-1}$, assignable so C=O group.

Other thiazolidones were prepared in a similar way (yields 4–20%) and are listed in Table I together with their melting points and analytical data. All compounds gave negative iodine–azide tests.[6]

Reaction of VI with Nitrous Acid.—Compound VI (2.3 g.) was dissolved in hydrochloric acid (15 ml. of 2 *N*) with gentle heating and the solution cooled to 0° and then a solution of sodium nitrite (0.7 g. in 10 ml. of water) was added. Immediately a pale brown product separated and was filtered off. From the filtrate, after standing 5 hr. at room temperature, another product separated. The first compound was recrystallized from aqueous ethanol and was found identical with an authentic specimen of 2-phenyli-4-thiazolidone (VII), prepared from phenylthiourea and ethyl monochloroacetate according Meyer,[11] m.p. and mixed m.p. 177°.

Anal. Calcd. for $C_9H_8N_2OS$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.12; H, 4.54; N, 14.65.

The second substance was recrystallized from ethanol and some water added, m.p. 226°. It was found identical with the product, prepared through nitrosation of 2-phenylimino-4-thiazolidone (VII) and thus represents the N-nitroso compound (VIII).

Anal. Calcd. for $C_9H_7N_3O_2S$: C, 48.87; H, 3.19; N, 19.00. Found: C, 49.05; H, 3.65; N, 19.00.

All attempts to reduce the nitroso compound back into the 3-amino compound (VI) were unsuccessful.

Reaction of 4-Substituted Thiosemicarbazides with Monochloroacetic Acid or Its Derivatives in the Absence of Sodium Acetate. General Procedure.—A mixture of 4-substituted thiosemicarbazide (2.0 g.) and the equivalent amount of ethyl monochloroacetate in ethanol (30 ml.) was refluxed on water bath for 1 hr. A precipitate, which was formed during the reaction, was collected and washed well with hot ethanol. All compounds obtained were practically insoluble in common organic solvents.

From 4-methylthiosemicarbazide the 2-methylimino-3,4-dihydro-1,3,4,2*H*-thiadiazin-5(6*H*)-one, m.p. 284°, was obtained, previously prepared by Chabrier and Cattelain[1] (m.p. 284°) and Bose and Nandi[2] (m.p. 282°).

Anal. Calcd. for $C_4H_7N_3OS$: C, 33.10; H, 4.86. Found: C, 33.31; H, 4.90.

Infrared spectrum: bands at 3333, 3247 cm.$^{-1}$ (N—H) and 1706 cm.$^{-1}$ (C=O).

4-Phenylthiosemicarbazide afforded not a thiadiazine derivative as proposed in the work of Bose and Nandi (m.p. 184°),[2] but a compound with m.p. 306°, practically insoluble in common organic solvents; yield 26%. The substance was purified by recrystallization from N,N-dimethylformamide and gave a negative iodine–azide reaction.

Anal. Calcd. for $C_{20}H_{22}N_8O_4S_3$: C, 44.93; H, 4.15; N, 20.96; S, 18.00; mol. wt., 534.6. Found: C, 44.96; H, 4.36; N, 21.19; S, 17.76; mol. wt. (Rast), 553, 568.

Infrared spectrum: bands at 3300, 3226, cm.$^{-1}$(N—H) and 1724 cm.$^{-1}$ (C=O).

The same compound was obtained if in the reaction ethyl monochloroacetate was substituted for monochloroacetic acid or chloroacetamide.

Acknowledgment.—The authors are indebted to Dr. S. Detoni for the infrared data used in this work.