relationship between this genus and *Alstonia*, which has recently been reported to contain reserpine.[3]

Paper chromatographic examination[4] of the methanolic extract of the ground roots gave evidence for the presence of at least twelve alkaloids. The behavior of four of the spots so closely resembled that of similar spots from authentic samples of reserpine, rescinnamine, deserpidine, and ajmaline, that these alkaloids may be presumed to be present in the plant. Judging from this chromatogram, the amount of reserpine and rescinnamine in the root sample were about the same while the other alkaloids were present in much smaller quantities.

By using a slight modification of the technique of Hochstein, *et al.*,[4] the presence of reserpine was confirmed by the isolation of 0.007% of the alkaloid. Further isolation studies were not carried out.

Similar chromatography of the more basic alkaloids derived from the acetic acid fraction showed that only minor amounts of ajmaline were present and that it was accompanied by three other unidentified substances.

EXPERIMENTAL

Root extraction. A sample of about 500 g. of air dried *Tonduzia longifolia* (A.DC.) Mgf. root was ground in a rotary cutter until it passed through a $^1/_8$ inch screen. A 100-g. aliquot of this material (6.5% moisture) was refluxed for one hour with 600 ml. of methanol, filtered, and the residue then was twice washed with 200-ml. portions of boiling solvent. The combined extracts were concentrated *in vacuo* to dryness and yielded 4.4 g. of brown oil.

Separation of the alkaloids. The above residue (4-g. portion) was dissolved in 10 ml. of methanol and 20 ml. of 5% aqueous acetic acid was added. The mixture then was extracted with two 25-ml. portions of hexane which were discarded. The acetic acid solution then was extracted with four 25-ml. portions of chloroform. The combined extracts were washed with dilute ammonium hydroxide and water, dried, and the solvent was removed *in vacuo*. This weakly basic fraction was used for the isolation of reserpine.

The acetic acid solution was paper chromatographed using system (B). Four spots resulted—one of which was identified as ajmaline.

Isolation of reserpine. The weakly basic fraction mentioned above was triturated with ether and the ether-insoluble material was dissolved in the minimum of methanol. On standing, 7.0 mg. (0.007%) of reserpine crystallized from solution and was identified by melting point and paper chromatography.

The methanol mother liquor was concentrated to dryness and paper chromatographed. Seven alkaloidal spots separated, three of which could be identified in the usual way as reserpine, deserpidine, and rescinnamine. It is evident that the roots contained more reserpine than was actually isolated.

Chromatographic procedure. The systems used were those already described:[4] (A) benzene-cyclohexane (1:1) on formamide-impregnated Whatman No. 1 paper, and (B) benzene-chloroform (1:1) on similar paper. The alkaloidal spots were located by their fluorescence under ultraviolet light. The identification of the spots was made by a comparison of the spots produced by known samples of the alkaloids when concurrently run with the mixture. Table I gives the R_f values found in this work for the alkaloids used in the systems indicated.

TABLE I

R_f VALUES FOR ALKALOIDS

Alkaloids	Systems (A)	Systems (B)
Ajmaline	0.00	0.15
Deserpidine	.50	.9
Rescinnamine	.26	.9
Reserpine	.35	.9

Acknowledgment. We are greatly indebted to Dr. Jorge Léon and Dr. L. R. Holdridge of the Instituto Interamericano de Ciencias Agrícolas, Turrialba, Costa Rica for the *Tonduzia longifolia* (A.DC.) Mgf. roots used in this work. Our thanks are also due to Prof. R. E. Woodson, Jr., Washington University, St. Louis, Missouri, for the botanical verification of the material.

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Preparation of Polymethylene *bis*-(1- or 3-nitro-2-thiopseudourea)[1]

LAWRENCE FISHBEIN AND J. A. GALLAGHAN

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An earlier paper by the authors[2] described the preparation of 2-alkyl-1(or 3)-nitro-2-thiopseudourea, (N-nitro-S-methyl pseudothiourea) and its use, primarily, in the preparation of mono-substituted derivatives of nitroguanidine. It was of interest to this laboratory to extend this type of synthesis to the possible preparation of analogous reactive reagents which would be useful in the facile preparation of *bis*-(3-nitroguanidines). In the present paper, the syntheses of the corresponding polymethylene *bis*-(1- or 3-nitro-2-thiopseudourea) derivatives are described, as shown in the sequence of reactions on chart I.

The final products were characterized by reaction with alkane diamines to yield *bis*-(3-nitroguanidine) alkanes and the corresponding alkane dithiols.

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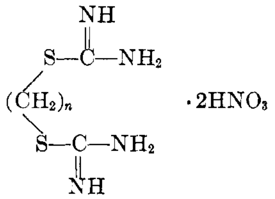
[1] Published with permission of the Bureau of Ordnance, Navy Department. The opinions and conclusions are those of the authors.

[2] Fishbein and Gallaghan, *J. Am. Chem. Soc.*, **76**, 1877 (1954).

TABLE I

2,2′-POLYMETHYLENE *bis*-(2-THIOPSEUDOURONIUM NITRATES)

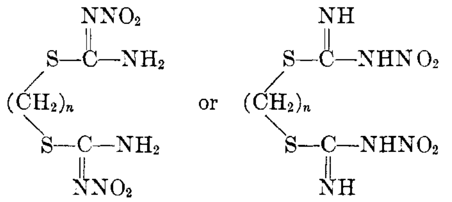


		Yield, % method			Analyses					
	M.p., °C.				Carbon, %		Hydrogen, %		Nitrogen %	
n	uncorr.	A[a]	B[b]	Formula	Calc'd	Found	Calc'd	Found	Calc'd	Found
2	223–225	—	75.0	$C_4H_{12}N_6O_6S_2$	15.79	15.63	3.94	3.71	27.63	28.05
3	144–146	—	70.0	$C_5H_{14}N_6O_6S_2$	18.86	18.63	4.44	4.61	26.44	26.33
4	174–176	45.3	50.5	$C_6H_{16}N_6O_6S_2$	21.68	21.53	4.62	4.80	25.36	25.41
5	134–136	55.0	76.3	$C_7H_{18}N_6O_6S_2$	24.27	24.21	5.21	5.05	24.27	23.95
10	127–129	—	80.5	$C_{12}H_{28}N_6O_6S_2$	34.61	34.44	6.73	6.91	20.11	19.89

[a] Nitrate salt prepared by procedure of Lane.[5] [b] Nitrate salt prepared by procedure of Fishbein and Gallaghan.[2]

TABLE II

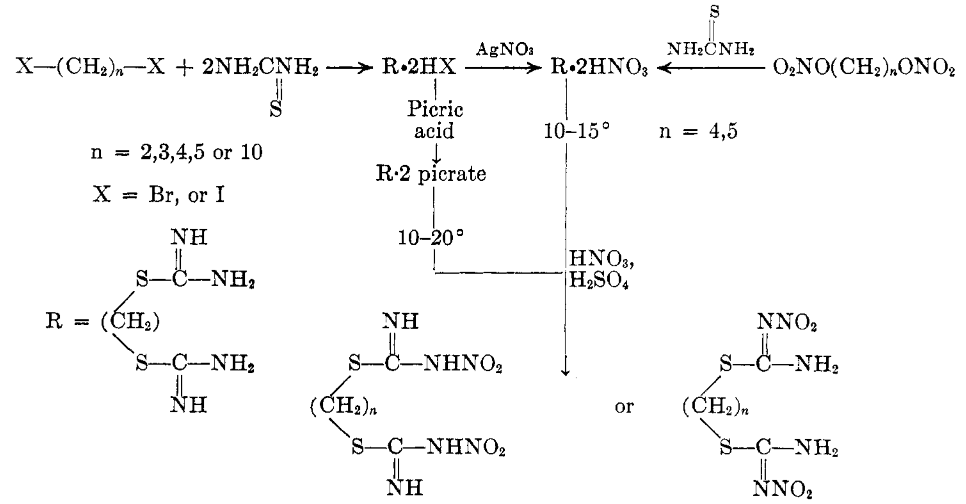
2,2′-POLYMETHYLENE *bis*-(1- OR 3-NITRO-2-THIOPSEUDOUREAS)



		Yield, % method			Analyses					
	M.p., °C.				Carbon, %		Hydrogen, %		Nitrogen, %	
n	uncorr.	A[a]	B[b]	Formula	Calc'd	Found	Calc'd	Found	Calc'd	Found
2	224–226	78.2	82.4	$C_4H_8N_6O_4S_2$	17.83	18.18	2.97	3.16	31.32	31.09
3	185–186	73.7	75.0	$C_5H_{10}N_6O_4S_2$	21.23	20.85	3.54	3.32	29.79	29.31
4	216–218	75.3	78.6	$C_6H_{12}N_6O_4S_2$	24.33	24.77	4.05	4.15	28.39	28.05
5	165–166	56.2	80.0	$C_7H_{14}N_6O_4S_2$	27.09	27.35	4.51	4.68	27.15	26.93
10	145–149	73.1	81.0	$C_{12}H_{24}N_6O_4S_2$	37.89	37.69	6.32	6.19	22.10	22.07

[a] Method A. Nitration of the corresponding picrate salt. [b] Method B. Nitration of the corresponding nitrate salt.

CHART I



EXPERIMENTAL

2,2′-Polymethylene bis-(2-thiopseudouronium halides). The various 2,2′-alkylene *bis*-(2-thiopseudouronium halides) were prepared according to the procedure of Yale,[3] utilizing thiourea and the appropriate polymethylene dihalide, and have been previously reported.[4]

2,2′-Polymethylene bis-(2-thiopseudouronium nitrate). Method A. The nitrate salts were prepared from the corresponding isolated, and purified halide salts, by the procedure of Fishbein and Gallaghan[2] utilizing an aqueous solution of silver nitrate. The physical properties of the nitrate salt derivatives are shown in Table I.

Method B. The 2,2′-polymethylene *bis*-(2-thiopseudouronium nitrate) derivatives were prepared according to the method of Lane[5] by reacting thiourea with the corresponding polymethylene dinitrate.

2,2′-Polymethylene bis-(2-thiopseudouronium picrate). The picrate salts were prepared by heating the respective 2,2′-polymethylene *bis*-(2-thiopseudouronium halide) salt with a saturated alcoholic solution of picric acid, the technique being essentially that described by Cheronis.[6] The picrate salt derivatives were recrystallized from 60% ethanol and have been previously reported.[7]

Preparation of 2,2′-polymethylene bis-(1- or 3-nitro-2-thiopseudourea). Method A. Nitration of the nitrate salt. 2,2′-Decamethylene *bis*-(2-thiopseudouronium nitrate) (1.0 g., 0.0024 mole) was added with stirring to 3.5 ml. of concentrated sulfuric acid at 0-5° until the sample dissolved. To this mixture was added 1.7 ml. of fuming nitric acid (98%) at 0-10°. The temperature was allowed to rise to 17°, after which time the mixture was drowned in 15 g. of ice yielding 0.74 g. (81%) of product melting at 139-143°. One crystallization from acetone-alcohol (1:1) raised the m.p. to 145-147°.

Method B. Nitration of the picrate salt. 2,2′-Pentamethylene *bis*-(2-thiopseudouronium picrate) (2 g., 0.0028 mole) was made into a slurry by adding 6 g. of concentrated sulfuric acid at 10-20°; 2 ml. of fuming nitric acid (99%) then was added with stirring. The mixture was allowed to stand at 25° overnight, after which time the slurry was filtered through a sintered glass funnel. Repeated washings, with ether, (5 × 40 ml.), after the removal of the mixed acid filtrate, leached out the picric acid (1.2 g.) and left 0.2 g. of compound on the crucible. The mixed-acid filtrate was treated with 100 ml. of anhydrous ether-alcohol (1:1) causing the precipitation of an additional 0.3 g. of solid product. A total of 0.5 g. (56.2%) of product was collected melting at 145-155°. The crystallization from acetone-alcohol (1:1) raised the m.p. to 164-166°. A mixture melting point with a sample of 2,2′-pentamethylene *bis*-(1- or 3-nitro-2-thiopseudourea) was not depressed. The syntheses of the other 2,2′-polymethylene *bis*-(1- or 3-nitro-2-thiopseudourea) derivatives (Table II) were accomplished utilizing both Methods A and B as described above.

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Reactions of Long-Chain Amines. VI. Preparation of Thioureas*

JOHN G. ERICKSON

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A general method of preparing monosubstituted ureas consists of heating the corresponding amine with urea.[1] The similar reaction, that of amines with thiourea, has not been reported as a means of preparing N-monosubstituted thioureas.[2] We have found, however, that it may be conveniently used to prepare N-alkylthioureas from primary long-chain aliphatic amines. Previously, the only route to these thioureas lay through reactions of alkyl isothiocyanates with ammonia.[3-7]

In the present procedure, the amine is heated with an excess of thiourea for a short time at approximately the melting point of thiourea. To avoid decomposition of the alkylthiourea, long reaction times are avoided.

We have also prepared a number of 1,3-disubstituted thioureas by reactions of long-chain amines with alkyl and aryl isothiocyanates. In addition, the preparation of a 1,3-dialkylthiourea from a long-chain amine and carbon disulfide is described.[8]

Yields and properties of all of these products are summarized in Table I.

EXPERIMENTAL

Reagents. The preparation of the long-chain amines has been described.[9] The isothiocyanates were commercial products.

Preparation of alkylthioureas from amine and thiourea (*Method A*). A mixture of the primary long-chain amine (one mole) and thiourea (two moles) is stirred and heated at 170-180° for 10-15 minutes. As soon as the mixture becomes homogeneous it is cooled rapidly. Recrystallization from benzene, Skellysolve C, or isopropyl alcohol yields the monoalkylthiourea.

From amine and isothiocyanate (*Method B*). A 10% excess of alkyl or aryl isothiocyanate is added at 25° to a solution of the amine in benzene or toluene. Filtration and recrystallization from benzene yields the pure disubstituted thiourea.

From amine and carbon disulfide (*Method C*). Carbon disulfide (one mole) is added in portions to a solution of the

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* Paper No. 185, Journal Series, General Mills, Inc., Research Dept.

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