Selective Reduction of 2,2′,4,4′-Tetranitrobiphenyl

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In connection with our research a series of diamines was desired. Since 2,2′,4,4′-tetranitrobiphenyl (I) could be easily prepared by the nitration of biphenyl,[2] the selective reduction of this tetranitro compound was studied. Of the possible selective reagents, alcoholic sodium sulfide appeared to be the most convenient to use with polyamines. Since sodium sulfide selectively reduced the 2-nitro group in 2,4-dinitrotoluene to produce 2-amino-4-nitrotoluene while stannous chloride selectively reduced the 4-nitro group,[3] it was of particular interest to determine which nitro groups in this tetranitro derivative would be reduced. A modification of the method of Hodgson and Birtwell,[4] in which the polynitro compound is reduced in a methanolic solution of sodium sulfide and sodium bicarbonate, was used. Under these conditions 2,2′,4,4′-tetranitrobiphenyl (I) was selectively reduced to 2,2′-dinitrobenzidine (II) in 62% yield. This reduction is particularly significant since the sodium sulfide reagent never had been successfully used to reduce selectively a tetranitro compound,[5] although Hodgson, Ward, and Whitehurst[6] selectively reduced 1,3,6,8-tetranitronaphthalene with stannous chloride.

The structure of the 2,2′-dinitrobenzidine (II) was proved by an independent synthesis. Nitration of benzidine by the method of Tauber[7] gave a 57% yield of II. Acetylation of both samples of II with acetic anhydride produced an 81% yield of identical samples of *N,N′*-diacetyl-2,2′-dinitrobenzidine (III).

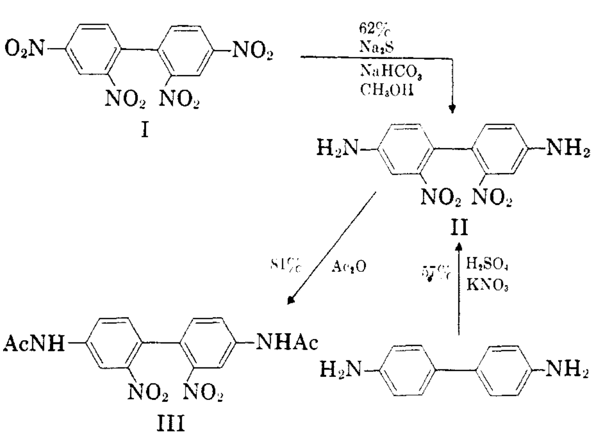
EXPERIMENTAL

2,2′-Dinitrobenzidine (II). *A. By selective reduction of 2,2′,4,4′-tetranitrobiphenyl* (I). The 2,2′,4,4′-tetranitrobiphenyl (I), m.p. 163–164° (reported[8] m.p. 163°), was prepared in 83% yield by the method of Huntress[2] in which biphenyl was nitrated with a mixture of concentrated nitric acid and sulfuric acid. To a solution of 67 g. (0.2 mole) of 2,2′,4,4′-tetranitrobiphenyl (I) in 2500 ml. of boiling methanol contained in a 5-liter, three-necked flask, equipped with a condenser, a stirrer, and a dropping-funnel, was added over a period of 1 hour a warm solution of 152 g. of sodium sulfide and 48 g. of sodium bicarbonate in 400 ml. of water. The presence of a large excess of sodium sulfide was avoided throughout the reaction by the periodic test of the solution with ferrous sulfate paper. The reaction mixture was cooled, and the resulting precipitate was removed by filtration. Concentration of the filtrate gave an additional crop of diamine. The combined crude material was recrystallized from ethanol to produce 34 g. (62%) of 2,2′-dinitrobenzidine (II), m.p. 212–214° (reported[7] m.p. 214°).

A mixture of 5 g. (0.018 mole) of II and 50 ml. of acetic anhydride was heated under reflux for 24 hours and the resulting product was recrystallized from acetic acid to yield 5.2 g. (81%) of *N,N′*-diacetyl-2,2′-dinitrobenzidine, m.p. 292–293° (dec.) [reported[9] m.p. 290° (dec.)].

B. From benzidine. In accordance with the procedure of Tauber,[7] benzidine was nitrated with potassium nitrate and sulfuric acid to yield 2,2′-dinitrobenzidine, m.p. 212–214°. A mixture melting point determination with the sample of II from the selective reduction showed no depression.

This sample of II was also acetylated with acetic anhydride to yield *N,N′*-diacetyl-2,2′-dinitrobenzidine (III), m.p. 292–293° (dec.), which did not depress the melting point of the sample of III prepared as described above.



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(2) Huntress, U. S. Patent 1,870,627 (1932) [*Chem. Abstr.*, **26**, 5579 (1932)].

(3) Anschutz and Heusler, *Ber.*, **19**, 2161 (1886).

(4) Hodgson and Birtwell, *J. Chem. Soc.*, 75 (1944).

(5) Wills, *Ber.*, **28**, 379 (1895).

(6) Hodgson, Ward, and Whitehurst, *J. Chem. Soc.*, 454 (1945)

(7) Tauber, *Ber.*, **23**, 795 (1890).

(8) Ullmann and Bielecki, *Ber.*, **34**, 2177 (1901).

(9) Cain and May, *J. Chem. Soc.*, **97**, 724 (1910).

Rauwolfia Alkaloids. XXIV.[1] Note on the Alkaloids of *Tonduzia Longifolia* (A.DC.) Mgf.

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During the course of our investigations on the reserpine content of various plants, we had occasion to examine the roots of *Tonduzia longifolia* (A.DC.) Mgf. obtained from Costa Rica. This small tree belonging to the Apocynacous family was of especial interest because of the close botanical

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(1) For previous paper, see Huebner, *Chemistry & Industry (London)*, 1186 (1955).

(2) Deceased October 24, 1955.

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)	(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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(3) Curtis, Handley, and Somers, *Chemistry & Industry (London)*, 1598 (1955); Crow and Greet, *Australian J. Chem.*, **8**, 461 (1955).

(4) Hochstein, Murai, and Boegemann, *J. Am. Chem. Soc.*, **77**, 3551 (1955).

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

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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).