





was treated with 204 mg. of 2,4-dinitrophenylhydrazine in 30 ml. of 2 *N* hydrochloric acid and 10 ml. of methanol. The resulting 2,4-dinitrophenylhydrazone was removed by extraction with benzene and purified by chromatography through a deactivated alumina column.<sup>6</sup> Further purification was achieved by chromatography on a silicic acid-Celite (2:1) column.<sup>7</sup> The main fraction, eluted with 5% ether in petroleum ether, yielded 60 mg. of product, which was recrystallized three times from *n*-heptane to give 6.8 mg. of orange crystals, m.p. 45–48°. An additional 16 mg. of crystals, m.p. 45–51°, was obtained similarly from the mother liquor.

*Anal.* Calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>: C, 53.05; H, 6.16; N, 19.04. Found: C, 53.37; H, 6.42; N, 18.87.

**Ozonolysis of Streptimidone (Ia).**—Ozone was passed through a solution of 866 mg. (2.95 mmoles) of crystalline streptimidone in 20 ml. of ethyl acetate (distilled three times from 2,4-dinitrophenylhydrazine) at –80° for 45 minutes. The blue color of ozone appeared after 5 minutes of ozonization. The ethyl acetate solution was concentrated *in vacuo* to approximately 10 ml., then mixed with 10 ml. of methanol, 1 g. of ferrous sulfate and 175 ml. of water. The mixture was steam distilled (525 ml. of distillate) into a 2 *N* hydrochloric acid solution saturated with 2,4-dinitrophenylhydrazine (DNP mixture).

The precipitate from the DNP mixture was filtered, washed with methanol and dried to give 67 mg. (5.2%) of a rust colored precipitate, which was crystallized first from dimethylformamide–water and then from dimethylformamide to give 31 mg. (2.4%) of pyruvaldehyde bis-2,4-dinitrophenylhydrazone, identified by comparison with an authentic sample (no mixed melting point depression; identical ultraviolet and infrared spectra).

(6) Alcoa F-20 alumina was adjusted to pH 5 with dilute sulfuric acid and then dried for 4 hours at 200°.

(7) B. E. Gordon, F. Wopat, Jr., H. D. Burnham and L. C. Jones, Jr., *Anal. Chem.*, **23**, 1754 (1951).

(8) M. C. Chiang [*J. Chinese Chem. Soc.*, **18**, 65 (1951); cf. C. A., **46**, 4472 (1952)] reported 45–47° as the melting range of 4-methyl-2-hexanone 2,4-dinitrophenylhydrazone.

*Anal.* Calcd. for C<sub>16</sub>H<sub>12</sub>N<sub>8</sub>O<sub>8</sub>: C, 41.67; H, 2.80; N, 25.92. Found: C, 41.68; H, 2.70; N, 26.11.

The filtrate and washings from the DNP mixture were extracted with chloroform. The extract was evaporated to dryness *in vacuo*, and a benzene solution of the residue was percolated through a deactivated alumina<sup>8</sup> column to remove 2,4-dinitrophenylhydrazine. Evaporation of the effluent to dryness yielded 137 mg. of crystals, which was recrystallized from methanol to give 75 mg. (12.1%) of formaldehyde 2,4-dinitrophenylhydrazone, m.p. 158–163°, identified by its infrared spectrum and by paper chromatography, using *n*-heptane saturated with methanol.<sup>9</sup> Paper chromatography showed that the mother liquor from above contained an additional 53 mg. of formaldehyde 2,4-DNP (8.5%) and 9 mg. of acetaldehyde 2,4-DNP (1.4%).

As a control experiment, employing completely identical isolation procedures, ozonolysis of the C-9 ketone from dihydrostreptimidone (streptimidone with one olefinic linkage catalytically reduced<sup>1</sup>) yielded methyl ethyl ketone (39%) as the major product.

The reagent grade ethyl acetate used in the isolation procedures in some of the previously reported ozonolysis experiments<sup>1</sup> was shaken with 2 *N* hydrochloric acid saturated with 2,4-dinitrophenylhydrazine. The weight of the resulting methyl ethyl ketone 2,4-dinitrophenylhydrazone isolated indicated that the ethyl acetate contained methyl ethyl ketone at approximately 40 μg./ml. Thus, in the ozonolysis experiments of the present investigation, meticulous removal of any ketones and aldehydes from all solvents was performed, by repeated distillation from solid 2,4-dinitrophenylhydrazine.

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(9) D. F. Meigh, *Nature*, **170**, 379 (1952).

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## Investigations in Heterocycles. X.<sup>1</sup> The Synthesis of Tetrahydro-1,3-benzodiazepines, a New Heterocyclic System

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A method has been developed for the preparation of 3-substituted-1,2,4,5-tetrahydro-1,3-benzodiazepines. The structure of these compounds has been rigorously proved by means of chemical transformations and spectral data.

Within the past decade the synthesis of seven-membered ring compounds containing two nitrogen atoms has attracted considerable attention. Ried<sup>2</sup> and co-workers have enlarged significantly upon the early findings of Thiele<sup>3</sup> and Steinmig concerning the synthesis of 2,4-disubstituted-1H-1,5-benzodiazepines (I), whereas the preparation of 1-ethyl-4-(3-tropanyl)-tetrahydro-1H-1,4-benzodiazepine (II) and its derivatives has been the subject of a report by Archer, *et al.*<sup>4</sup>

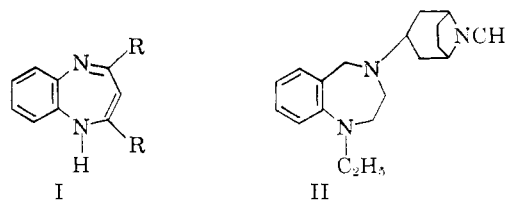
Finally, another member of this group, 1-H-1,3-benzodiazepine, has recently been described only in derivative form by Plieninger<sup>5</sup> and Nogradi.

(1) For part IX in this series see G. deStevens, A. Halamandaris, P. Wenk and L. Dorfman, *J. Am. Chem. Soc.*, **81**, 6292 (1959).

(2) W. Ried and A. Draibach, *Chem. Ber.*, **92**, 949 (1959); W. Ried and E. Torinus, *ibid.*, **92**, 2902 (1959).

(3) J. Thiele and G. Steimmig, *ibid.*, **40**, 955 (1907).

(4) S. Archer, J. R. Lewis, M. J. Unser, J. O. Hoppe and H. Lape, *J. Am. Chem. Soc.*, **79**, 5783 (1957).



They have found that the autoxidation of the lactone β-(*o*-acetamidophenyl)-α-amino-γ-hydroxycrotonic acid (III) gives rise to the lactone of 5-hydroxymethyl-2-methyl-1H-1,3-benzodiazepine-4-carboxylic acid (IV).

Our interest in seven-membered heterocycles of the 1,3-benzodiazepine class was confined to the study of the completely saturated system, 1,2,4,5-tetrahydro-3-methyl-1,3-benzodiazepine (V) and its analogs.

(5) H. Plieninger and I. Nogradi, *Ber.*, **88**, 1965 (1955).