On Pyrazino[d, d']ditropone and its Derivatives

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It is already known that 2, 5-diaminotroponimine reacts with formic acid and nitrous acid forming 1, 3-diazaazulene or 1,2,3-triazaazulene derivatives respectively[1,2].

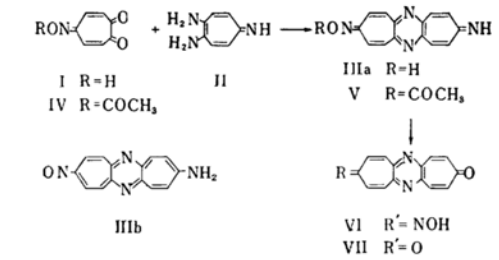
If one considers the facile condensation of 5-nitrosotropolone with 1, 2-diamine to form a troponeoxime with the heterocyclic system[3-6], it is expected that the formation of a new 7-6-7 hetrocyclic system in which N-atoms are located in a six-membered ring by application of 2, 5-diaminotroponimine, will make a tautomer of 4,5-diaminotroponimine.

An account of the attempt to synthesize such a 7-6-7 membered ring system is reported herein.

Heating of 5-nitrosotropolone (I)[7] in methanol afforded brown crystals, m. p. over 300°C, $C_{14}H_{11}ON_4Cl$, very easily with dihydrochloride of 2, 5-diaminotroponimine (II)[1]. Neutralization of the aqueous solution of these crystals with sodium hydrogencarbonate gave brown powder III, m. p. over 300°C, $C_{14}H_{10}ON_4$, indicating the former crystals to be monohydrochloride of III. III is insoluble in various organic solvents and recrystallized with difficulty. Ultraviolet spectra of III in acidic and alkaline media show a little shift to longer wavelength region compared with that in methanol.

The structural confirmation of III came from alkaline permanganate oxidation, in which pyrazine tetracarboxylic acid dihydrate, m. p. 205°C[8], was obtained. Its tetramethyl ester obtained by the reaction with diazomethane showed no depression of melting point on admixture with authentic tetramethyl pyrazinetetracarboxylate, m. p. 182°C, obtained by methylation of pyrazinetetracarboxylic acid, the latter being synthesized by oxidation of quinoxalotroponeoxime[3]. Therefore, together with its analytical value and the following reactions, it is clear that III is pyrazino [d, d']-ditroponemonoiminemonooxime.

Attempted acetylation of III with acetic anhydride led to the formation of a black substance. However, acetate V was obtained by the reaction of acetate IV[3] of 5-nitrosotropolone with II.



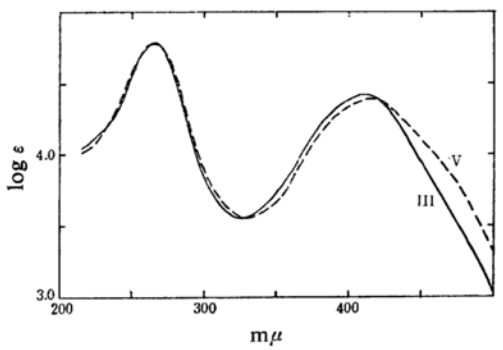


Fig. 1. Ultraviolet absorption spectra of III and V in methanol.

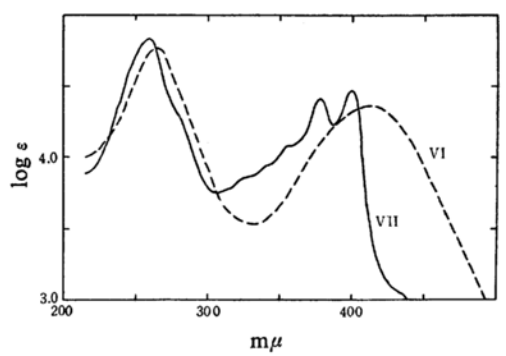


Fig. 2. Ultraviolet absorption spectra of VI and VII in methanol.

1) T. Nozoe, M. Sato, S. Ito, K. Matsui and T. Matsuda, *Proc. Japan Acad.*, **29**, 565 (1953).
2) T. Nozoe, S. Ito and K. Matsui, ibid., **30**, 313 (1954).
3) T. Nozoe, M. Sato and T. Matsuda, *Sci. Repts. Tohoku Univ., First Ser.*, **37**, 407 (1953).
4) T. Nozoe, S. Ito, S. Suzuki and K. Hiraga, *Proc. Japan Acad.*, **32**, 344 (1956).
5) S. Ito, *Sci. Repts. Tohoku Univ., First Ser.*, **42**, 236 (1958).
6) S. Ito, ibid., **43**, 247 (1959).
7) T. Nozoe, S. Seto, H. Takeda and T. Sato, ibid., **35**, 274 (1952).
8) F. D. Chattaway and W. G. Humphrey, *J. Chem. Soc.*, **1929**, 645.

From the similarity of the ultraviolet spectra of III and V shown in Fig. 1, compound III is assumed to have the structure IIIa rather than its tautomeric form IIIb.

Although III and V are easily soluble in aqueous alkali, acidification of these solutions with acetic acid afforded not the original substance but the same needles VI, m. p. 266°C, $C_{14}H_9O_2N_3$, from both III and V. The infrared spectrum of VI shows peaks at 3250 (O-H), at 1627 (C=O) and at 1585 cm^{-1} (C=C). VI gives carbonyl derivatives such as oxime and 2, 4-dinitrophenylhydrazone. These results indicate VI to be pyrazino[d, d']ditroponemonoxime, which is produced by hydrolysis of the acetyl group and or imino group in V or III.

The reaction of benzoate[3] of 5-nitrosotropolone and II afforded dark brown crystals. Although these crystals were unstable for further purification, VI was obtained by treatment of these crystals with alkaline.

Heating of III or VI in formic acid in the presence of copper carbonate[5,9] gave pyrazino-[d, d']ditropone (VII), peaks of infrared spectrum at 1635 (C=O) and at 1598 cm^{-1} (C=C), in poor yield. The ultraviolet spectrum of VII (Fig. 2) exhibits the characteristic fine structure compared with III and VI. This kind of fine structure has been observed in the case of quinoxalotropone or pyrazinotropone[5,6]. While being stable to acid, VII is unstable to alkali and gradually turns to brown in alkaline solution.

Experimental*

Pyrazino[d, d']ditroponemonoiminemonoxime (III.)—A solution of 900 mg. of I and 1.1 g. of dihydrochloride of II dissolved in 40 ml. of methanol was refluxed for twenty minutes and brownish orange crystals separated out. After cooling, 1.3 g. of the crystals, m. p. over 300°C, were obtained by filtration. These crystals are positive to the halogen test and are insoluble in various organic solvents. Recrystallization of the crystals was carried out from a large amount of dilute hydrochloric acid.

Found: C, 58.55; H, 3.66; N, 18.93. Calcd. for $C_{14}H_{10}ON_4 \cdot HCl$: C, 58.64; H, 3.88; N, 19.54%.

Neutralization of these crystals dissolved in a large amount of water with aqueous sodium hydrogencarbonate gave brown powder III, m. p. over 300°C. Attempted recrystallization of III from various solvents was in vain.

Found: C, 66.98; H, 4.10; N, 22.10. Calcd. for $C_{14}H_{10}ON_4$: C, 67.19; H, 4.03; N, 22.39%.

Picrate; red needles, m. p. over 300°C, turn to black from about 225°C.

Found: C, 50.21; H, 3.00; N, 20.50. Calcd. for $C_{20}H_{13}O_8N_7$: C, 50.11; H, 2.73; N, 20.45%.

Oxidation of III.—To a solution of 500 mg. of III and 400 mg. of potassium hydroxide dissolved in 40 ml. of water, a solution of 5g. of potassium permanganate dissolved in 250 ml. of water was added at 80°C in a period of 6 hr. The excess of potassium permanganate was killed by a few drops of methanol and the resulting manganese dioxide was filtered. Manganese dioxide was washed with hot water thoroughly, and the combined solution of filtrate and washing was concentrated to about 15 ml., and was acidified with dilute hydrochloric acid affording colorless crystals, 230 mg. Recrystallization of the crystals from hydrochloric acid gave pyrazinetetracarboxylic acid as colorless plates, m. p. 205°C (decomp.).

Found: C, 32.72; H, 2.43; N, 9.81. Calcd. for $C_8H_4O_8N_2 \cdot 2H_2O$: C, 32.89; H, 2.76; N, 9.59%.

By the methylation reaction of 10 mg. of pyrazinetetracarboxylic acid with diazomethane, colorless needles, m. p. 181~182°C (from methanol-benzene) were obtained. This ester showed no depression of melting point on admixture with tetramethyl pyrazinetetracarboxylate obtained by another route.

Found: C, 46.32; H, 3.84; N, 8.92. Calcd. for $C_{12}H_{12}O_8N_2$: C, 46.16; H, 3.87; N, 8.97%.

Acetate V.—A solution of 200 mg. of acetate IV of 5-nitrosotropolone and 200mg. of dihydrochloride of II dissolved in 5 ml. of methanol was refluxed for 10 min., affording 300 mg. of red needles, which turn to black from around 250°C.

Found: C, 58.27; H, 3.77; N, 17.81. Calcd. for $C_{16}H_{12}O_2N_4 \cdot HCl$: C, 58.44; H, 3.98; N, 17.04%.

Neutralization of aqueous solution of the above crystals gave acetate V of III as brown powder, m. p. over 300°C.

Found: C, 65.60; H, 3.99; N, 19.07. Calcd. for $C_{16}H_{12}O_2N_4$: C, 65.75; H, 4.14; N, 19.17%.

Pyrazino[d, d']ditroponemonoxime (VI).—A solution of 100 mg. of hydrochloride of III dissolved in 1.5 ml. of 3 N sodium hydroxide solution was heated gently for 3 min. Ammonia gas evolved during this time. After allowing the solution to stand for 30 min. at room temperature, it was acidified with a few drops of acetic acid. Orange crystals, 70 mg., precipitated out were recrystallized from pyridine yielding, orange needles, m. p. 266°C (carbonize).

Found: C, 66.95; H, 3.77; N, 17.16. Calcd. for $C_{14}H_9O_2N_3$: C, 66.92; H, 3.61; N, 16.73%.

Oxime; red fine crystals (from pyridine), m. p. over 300°C.

Found: C, 63.79; H, 3.84; N, 20.62. Calcd. for $C_{14}H_{10}O_2N_4$: C, 63.15; H, 3.79; N, 21.04%.

2, 4-Dinitrophenylhydrazone; violet crystals, carbonize at about 265°C.

Found: C, 55.31; H, 3.24; N, 22.88. Calcd. for $C_{20}H_{13}O_5N_7$: C, 55.68; H, 3.04; N, 22.77%.

Pyrazino[d, d']ditropone (VII).—a) A mixture of 150 mg. of hydrochloride of III and 150 mg. of copper carbonate in 4.5 ml. of 80% formic acid was

9) R. Robinson, *Nature*, 173, 541 (1954).

* All the melting points were uncorrected. The microanalyses were carried out by Messrs. S. Oyama, S. Azumi and Miss A. Iwanaga, and I. R. spectra were measured with Perkin-Elmer Model 112 by a member of Professor Kinumaki's laboratory, Research Institute, Chemistry of Non-Aqueous Solution, Tohoku Univ., to whom the author's sincere acknowledgements are hereby extended.

heated at 80°C for 70 hr. The resulting brown precipitates were filtered affording 30 mg. of VI. By neutralization of the filtrate, 20 mg. of precipitates were obtained. Recrystallization from pyridine gave VII as gold-colored needles, m. p. 244~245°C (decomp.).

Found: C, 71.14; H, 3.43; N, 12.38. Calcd. for $C_{14}H_8O_2N_2$: C, 71.18; H, 3.41; N, 11.86%.

b) Three hundred milligrams of VI were heated at 75°C for 120 hr. with 300 mg. of copper carbonate and 10 ml. of 80% formic acid. After cooling, 150 mg. of undissolved VI was obtained. Neutralization of the filtrate with sodium hydrogencarbonate afforded 70 mg. of solid. Recrystallization from pyridine gave gold-colored needles VII, m. p. 244~245°C (decomp.).

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