[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Nitroso Compounds. II. The Reduction of Certain Derivatives of α-Nitrosoisobutyric Acid to the Corresponding Azoxy Compounds

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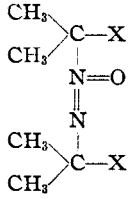
In the first paper of this series it was shown that, when bimolecular methyl α-nitrosoisopropyl ketone was treated with stannous chloride, the nitroso group was not reduced to the amino group but to hydrazine.[1] An intermediate reduction product was isolated whose molecular composition and chemical behavior corresponded to 2-azoxy-2-methyl-3-butanone and to it this structure was assigned tentatively.

The reduction of two α-nitroso acid derivatives has therefore been investigated, namely, the nitrile and ester of 2-methyl-2-nitrosopropionic acid. The present paper records the results of this work.

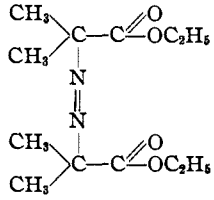
Discussion of Results

When 2-methyl-2-nitrosopropionitrile is reduced at room temperature with stannous chloride and hydrochloric acid, a crystalline compound, insoluble in dilute acid, is obtained. This compound has the chemical composition and molecular weight of 2-methyl-2-azoxypropionitrile (Ia) and this structure is provisionally assigned to it.

When ethyl 2-methyl-2-nitrosopropionate is reduced with stannous chloride and hydrochloric acid at 50–55°, it gives a quite stable oily liquid which may be distilled with steam or under reduced pressure. Analyses and molecular weight determinations correspond to the empirical formula $C_{12}H_{22}O_5N_2$ of the azoxy ester (Ib). It is stable toward boiling water as shown by the fact that after boiling in water for one and one-half hours, it was not appreciably decomposed.



(I) (a) X = CN, (b) X = $CO_2C_2H_5$, (c) X = CO_2H



(II)

This same compound may also be prepared more easily and with better yields by the oxidation of ethyl 2-methyl-2-azopropionate,[2] (II), with perhydrol, according to the method followed by Jolles,[3] in oxidizing aromatic azo compounds to azoxy compounds. It therefore seems reasonably certain that the compound is ethyl 2-methyl-2-azoxypropionate (Ib).

When the 2-methyl-2-azoxypropionitrile prepared by the reduction of the nitrosonitrile is treated with dry hydrogen chloride in ethyl alcohol, esterification occurs and upon dilution with water ethyl 2-methyl-2-azoxypropionate is obtained. This is strong evidence for the structure already assigned to the nitrile.

Ethyl 2-methyl-2-azoxypropionate is easily saponified by boiling with dilute sodium hydroxide. After cooling the boiling solution and acidifying, the almost pure 2-methyl-2-azoxypropionic acid precipitates as a white crystalline solid. It is easily decomposed when warmed.

Inasmuch as Thiele and Heuser[2] have prepared the hydrazo and azo compounds corresponding to the above azoxy ester and nitrile, the series of possible dimolecular reduction intermediates between the nitroso compound and the amine, as in the case of aromatic compounds, is now complete. However, it has not yet been possible to isolate the azo or hydrazo compounds from the products of reduction of the azoxy acid derivatives. The corresponding diazonium salts or diazo compounds analogous to those in the aromatic series still remain unknown.

The instability of the azoxy acid is not strange when it is remembered that α-azoisobutyric acid is too unstable to isolate[2] and loses one mole of carbon dioxide immediately it is liberated from its salt although α-hydrazoisobutyric acid is relatively stable[2] when warmed.

Experimental

2-Methyl-2-azoxypropionitrile.—Fifty grams (0.225 mole) of crystallized stannous chloride was dissolved in 114 cc. of concentrated hydrochloric acid. The temperature was held at 20–25° and 29.4 g. (0.15 mole) of bimolecular 2-methyl-2-nitrosopropionitrile[4] was added with violent stirring. The solution, after stirring for three hours, had turned blue and had a slight turbidity which was not

(1) Aston, Menard and Mayberry, THIS JOURNAL, **54**, 1592 (1932)
(2) Thiele and Heuser, *Ann.*, **290**, 1 (1896).
(3) Jolles, *Gazz. chim. ital.*, **61**, 543 (1931).
(4) Piloty, *Ber.*, **31**, 1878 (1898).

removed by filtration. It was then poured into 500 cc. of cold water and the turbid solution placed in the refrigerator to crystallize. In three or four days white hair-like crystals of 2-methyl-2-azoxypropionitrile had replaced the turbidity. The compound is insoluble in water and dilute hydrochloric acid, difficultly soluble in ligroin, very soluble in ether, ethanol, methanol and benzene. Recrystallized from ethanol and water, it melted at 37°; yield 4.8 g. (18% of the theoretical).

Anal. Calcd. for $C_5H_{12}ON_4$: C, 53.33; H, 6.67; N, 31.11. Found: C, 53.17, 53.16; H, 6.38, 6.47; N (Dumas), 31.00. *Mol. wt.* from freezing point lowering in benzene: calcd. 180; found 184.

Other experiments using amounts of reducing agent varying from the calculated to five times the calculated showed no increase in yield.

Ethyl 2-Methyl-2-azoxypropionate.—One hundred and twelve grams (0.500 mole) of crystallized stannous chloride was dissolved in 209 cc. of concentrated hydrochloric acid and warmed to 50–55°; 29 g. (0.100 mole) of bimolecular ethyl 2-methyl-2-nitrosopropionate[5] was then added during twenty minutes with stirring. The solution was stirred for ten minutes longer, holding the temperature between the same limits, and then poured into one liter of cold water. Solid sodium bicarbonate was added until the solution was neutral, and the solution steam distilled until no more oil came over. This required about five hours. The distillate was then extracted with ether, the solution dried with sodium sulfate, the ether removed by distillation and the residue distilled under reduced pressure: b. p. 142–144° at 12 mm.; yield of ethyl 2-methyl-2-azoxypropionate, 11.5 g. (42% of the theoretical), n_D^{20} 1.4404, d_4^{20} 1.0500.

Anal. Calcd. for $C_{12}H_{22}O_5N_2$: C, 52.55; H, 8.04; N, 10.21. Found: C, 52.60; H, 8.25; N, 10.34, 10.40. *Mol. wt.* from the freezing point lowering in benzene: calcd. 274; found 257.

A reduction duplicating the above conditions but at 20–25° was tried but after stirring for three hours, 96% of unreduced ester was recovered. Insolubility of the nitroso ester in the reducing medium was shown not to be the only reason for the lack of reaction by adding 100 cc. of ethanol, which rendered the nitroso ester completely soluble in the reducing medium. The temperature was held as before, at 20–25°; 86% of the unreacted ester was recovered from this run after three hours.

Ethyl 2-Methyl-2-azoxypropionate from Ethyl 2-Methyl-2-azopropionate.—Using the general directions followed by Jolles[3] for the oxidation of aromatic azo compounds with perhydrol, ethyl 2-methyl-2-azopropionate[2] was oxidized to ethyl 2-methyl-2-azoxypropionate. Eighteen grams of ethyl 2-methyl-2-azopropionate was dissolved in 200 cc. of glacial acetic acid and 50 cc. of perhydrol was added with shaking. The mixture was held at 40–43° for twenty-four hours, after which it was poured into one liter of cold water. The solution became milky at once and upon standing a short time a heavy oil separated. The oil was extracted with ether, the ether solution neutralized with sodium bicarbonate solution, separated, washed with water, dried with sodium sulfate and the ether removed by distillation. The residue was then fractionated under reduced pressure; yield of azoxy ester 14.7 g. (77% of the theoretical), b. p. 136–138° at 8 mm., n_D^{20} 1.4406, d_4^{20} 1.0500.

Anal. Calcd. for $C_{12}H_{22}O_5N_2$: C, 52.55; H, 8.04. Found: (micro analysis), C, 52.70, 52.91; H, 8.58, 8.56.

Ethyl 2-Methyl-2-azoxypropionate from 2-Methyl-2-azoxypropionitrile.—Four and one-half grams of 2-methyl-2-azoxypropionitrile was dissolved in 40 cc. of absolute ethanol and dry hydrogen chloride passed in until the solution was saturated. After standing overnight in the refrigerator the solution was diluted with 100 cc. of cold water, neutralized with sodium bicarbonate and steam distilled. The distillate was extracted with ether, the ether solution dried with sodium sulfate and then fractionated, that boiling above 80° being fractionated under reduced pressure; yield of ethyl 2-methyl-2-azoxypropionate, 3.5 g. (55.5% of the theoretical), b. p. 155–157° at 20 mm., n_D^{20} 1.4404, d_4^{20} 1.0503.

2-Methyl-2-azoxypropionic Acid.—Three grams of ethyl 2-methyl-2-azoxypropionate was added to 45 cc. of water and 3 cc. of 40% sodium hydroxide (twice the calculated quantity). The solution was then refluxed for forty-five minutes, cooled and acidified with hydrochloric acid. A white solid precipitated. This was nearly pure 2-methyl-2-azoxypropionic acid; yield of nearly pure acid 1.9 g. (79.8% of the theoretical) of m. p. 128–129°. A small sample recrystallized very quickly from boiling water melted sharply at 128.5°. As this acid decomposes very rapidly at the boiling point of water, it is necessary to cool the boiling solution very rapidly.

Anal. Calcd. for $C_8H_{14}O_5N_2(C_6H_{12}ON_2(COOH)_2)$: C, 44.02; H, 6.42; N, 12.84; neut. eq., 109. Found: (micro) C, 44.32; H, 6.59; N (Dumas), 12.07; neut. eq., 108.7.

Summary

1. 2-Methyl-2-azoxypropionitrile has been prepared for the first time by the reduction of 2-methyl-2-nitrosopropionitrile with stannous chloride and hydrochloric acid.

2. Ethyl 2-methyl-2-azoxypropionate has been prepared for the first time (a) by the reduction of ethyl 2-methyl-2-nitrosopropionate, (b) by the oxidation of ethyl 2-methyl-2-azopropionate with perhydrol and (c) by the esterification of 2-methyl-2-azoxypropionitrile.

3. 2-Methyl-2-azoxypropionic acid has been prepared for the first time by the hydrolysis of the corresponding ethyl ester.

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(5) Piloty and Schwerin, *Ber.*, **34**, 1867 (1901).