Tris(nitroxymethyl)methylamine and tris(nitroxymethyl)nitrosomethane

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Previously unknown tris(nitroxymethyl)methylamine has been synthesised as the free base by nitration of tris(hydroxymethyl)-methylamine with nitryl fluoride; by oxidation of tris(nitroxymethyl)methylamine with sodium nitrite in aqueous nitric acid, tris(nitroxymethyl)nitrosomethane, the first representative of aliphatic nitrates containing a nitroso-group, is prepared for the first time.

Nitrates of polyatomic alcohols are widely used in medicine for the treatment of cardio-vascular diseases.[1–3] In the search for novel compounds exhibiting broad cardiological activity, functionally substituted nitrates of polyatomic alcohols containing primary amino or nitroso groups are of particular interest. To date, no aliphatic compounds, which incorporate both nitroxy and primary amino groups or nitroxy and nitroso groups attached to neighbouring carbon atoms, have been described. Here we synthesise tris(nitroxymethyl)methylamine **1** and tris(nitroxymethyl)nitrosomethane **2**. Syntheses of the nitrate of **1** that involve either nitric acid[4] or its solutions in dichloromethane[5] have been reported. Attempts to isolate compound **1** as the free amine by neutralising the nitrate were unsuccessful. This was due to the fact that neutralisation of this salt with alkali metal carbonates or hydroxides or with ammonia occurs ambiguously and is accompanied by the formation of side products thus yielding a complex mixture of nitrogen-containing compounds. At the same time, it is the free amine rather than its salt that is needed for synthetic purposes. We found that the amine **1** can be obtained by bubbling nitryl fluoride through a solution of tris(hydroxymethyl)methyl-amine in anhydrous MeCN.

$$H_2NC(CH_2OH)_3 \xrightarrow[0 \text{ to } -5^\circ C]{FNO_2} H_2NC(CH_2ONO_2)_3$$

1 (48%)

After dilution of the reaction mixture with water, **1** was isolated by extraction with dichloromethane as a colourless crystalline solid, mp 103–104 °C (decomp.). Found (%): C, 18.67; H, 3.04; N, 21.80. $C_4H_8N_4O_9$. Calc. (%): C, 18.75; H, 3.15; N, 21.80. IR, ν/cm^{-1}: 867 (O–NO_2), 1015 and 1060 (C–O), 1289 and 1655 (ONO_2), 2930 and 3030 (CH_2), 3290 (NH_2). ^{1}H NMR ([$^2H_6$]acetone): 5.1 (s, 6 H, CH_2); 3.9 (s, 2 H, NH_2).

Reactions of primary aliphatic amines with FNO_2 have been reported. In these studies, however, amines were either nitrated to give primary nitramines[6] or converted into nitrates containing the same number of carbon atoms.[7] In our procedure, the amino group remains unaffected, which allows the synthesis of compound **1**. Thus, we were first to obtain an aliphatic compound, simultaneously incorporating a primary amino and nitroxy groups at neighbouring carbon atoms.

Oxidation of the amine **1** with sodium nitrite in aqueous nitric acid (equimolar with respect to **1**) has led to the first representative of organic nitrates containing a nitroso group.

$$\mathbf{1} \xrightarrow[H_2O]{HNO_3,\ NaNO_2} ONC(CH_2ONO_2)_3$$

2

The nitrosation of primary amines normally[8] affords alcohols *via* intermediate nitrosoamine, which eliminates nitrogen. However, in our case, the reaction follows a different pathway, which results in the formation of the previously unknown compound **2** together with other products. Compound **1** can be converted to **2** over a wide temperature range (0–50 °C); however, the highest yield of **2** (27%) was achieved at 0–5 °C. Compound **2** is isolated during the reaction as an oil, which is separated from the aqueous phase and dissolved in chloroform. When this mixture was kept in a refrigerator, compound **2** precipitated as white crystals, mp 72.5–74 °C. Found (%): C, 17.53; H, 2.43; N, 20.63. $C_4H_6N_4O_{10}$. Calc. (%): C, 17.77; H, 2.22; N, 20.74. IR (KBr pellets), ν/cm^{-1}: 863 (O–NO_2), 1001 (C–O), 1289 and 1646 (ONO_2), 1244 and 1574 (N=O). ^{1}H NMR ([$^2H_3$]acetonitrile) 5.08 (s, 6 H, CH_2). UV-VIS (acetone): two bands due to the n→π* transition were observed, λ_{max} 676 and 328 nm, which is typical of the C–N=O group.

Compound **2** can be stored at 0–15 °C for long periods; chloroalkane solutions of **2** are blue.

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