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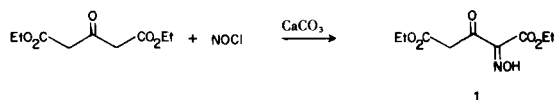
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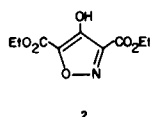
The reaction of diethyl acetonedicarboxylate with greater than two equivalents of nitrosyl chloride or the reaction of diethyl isonitrosoacetonedicarboxylate with one equivalent of nitrosyl chloride gave diethyl 4-hydroxyisoxazole-3,5-dicarboxylate in quantitative yield. Mechanistic possibilities are discussed.

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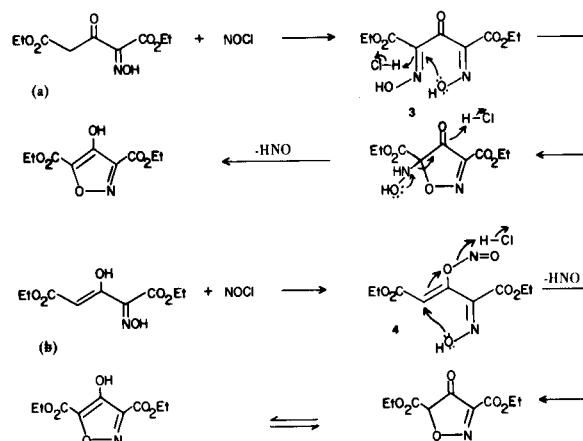
In connection with our work on the syntheses of medicinal agents, we would like to report an interesting side reaction from the treatment of diethyl acetonedicarboxylate with nitrosyl chloride. Alekseeva, *et al.* (1), have reported the preparation of diethyl isonitrosoacetonedicarboxylate (**1**) by the treatment of diethyl acetonedicarboxylate with nitrosyl chloride in the presence of calcium carbonate.



In their procedure they used more than a 100% excess of nitrosyl chloride, which was then removed by distillation into a cold trap. In our hands, on a smaller scale, little of **1** was obtained, but instead a white crystalline compound was recovered which was identified by nmr, ir, ms, and combustion analysis as diethyl 4-hydroxyisoxazole-3,5-dicarboxylate (**2**).



Compound **2** was first reported in 1891 by von Pechmann (2) as the product of the reaction of diethyl acetonedicarboxylate with isoamyl nitrite. It has also been prepared by the reaction of diethyl  $\alpha$ -bromoacetonedicarboxylate with sodium nitrite (3) and silver nitrite (4). We found that compound **2** was obtained either by the reaction of excess nitrosyl chloride with diethyl acetonedicarboxylate in the presence of one equivalent of calcium carbonate or by the reaction of **1** with one equivalent of nitrosyl chloride and calcium carbonate. Since hydrogen chloride gas is generated in the reaction, we tested to see if the cyclization was promoted by the second equivalent of nitrosyl chloride or simply by hydrogen chloride in the presence of air. Treatment of **1** with hydrogen chloride under the same conditions which produced **2** with nitrosyl chloride gave no reaction. Two possible mechanisms for the formation of **2** are shown below.



Under a variety of conditions, we were unable to isolate either of the proposed intermediates (**3** or **4**). Intermediate **3** seems plausible in light of the formation of **1**; precedence for intermediate **4**, however, is found in the known reaction of alcohols with nitrosyl chloride to yield nitroso compounds.

## EXPERIMENTAL

Melting points were taken on a Hoover-Thomas Uni-melt apparatus and are uncorrected. Nmr spectra were recorded on a Hitachi-Perkin-Elmer R-20B 60 MHz spectrometer and ir spectra were obtained on a Perkin-Elmer 283 spectrophotometer.

Diethyl Isonitrosoacetonedicarboxylate (**1**).

Into a dry 3-necked flask outfitted with a magnetic stirring bar, a thermometer and gas inlet and outlet tubes was added calcium carbonate (4.9 g., 49 mmoles), diethyl acetonedicarboxylate (11.4 ml., 63 mmoles) and anhydrous ether (40 ml.). The reaction mixture was cooled to 10–15°, then nitrosyl chloride (5 g., 75 mmoles) was slowly bubbled in with stirring. After stirring at 15° for 15 minutes, the excess nitrosyl chloride was removed by connecting the outlet tube to a trap immersed in dry ice-acetone. After 1 hour, additional calcium carbonate (0.8 g., 8 mmoles) was added and stirring was continued at room temperature for an hour. The thick reaction mixture was filtered and the salts washed with ether. Evaporation of the ether gave a pale yellow oil (12 g., 83%) which by nmr analysis, was a 95:5 mixture of **1** and starting material.

Diethyl 4-Hydroxyisoxazole-3,5-dicarboxylate (**2**).

## Method A.

The same procedure employed to prepare **1** was followed except 12 g. (181 mmoles) of nitrosyl chloride was used and purified as in Method B.

#### Method B.

In the same set-up used for the preparation of **1** was added diethylisonitrosoacetonedicarboxylate (4.6 g., 20 mmoles), calcium carbonate (1.8 g., 18 mmoles) and anhydrous ether (25 ml.). After cooling to 15°, nitrosyl chloride (1.5 g., 23 mmoles) was added. After work-up as for **1**, a pale yellow solid (4.5 g., 98%) was obtained. Recrystallization from ether-petroleum ether gave long white needle clusters, m.p. 100-100.5° (lit. (2) m.p. 104-105°); nmr (deuteriochloroform):  $\delta$  1.43 (t, 3H), 1.46 (t, 3H), 4.47 (q, 2H), 4.52 (q, 2H), 6.3-6.7 (broad s, 1H); ir (potassium bromide): 3360, 1735, 1695, 1318, 1225, 1190, 1175, 1025  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_9\text{H}_{11}\text{NO}_6$ : C, 47.15; H, 4.84; N, 6.11.

Found: C, 47.40; H, 4.78; N, 6.24.

#### Acknowledgment.

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#### REFERENCES AND NOTES

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