SYNTHESIS OF 1,4-DIOXO-5,8-ENDOMETHYLENE-3,8,9,10-TETRAHYDROBENZ-2,3-OXAZINE FROM 3,6-ENDOMETHYLENE-1,2,3,6-TETRAHYDROPHTHALIC ANHYDRIDE

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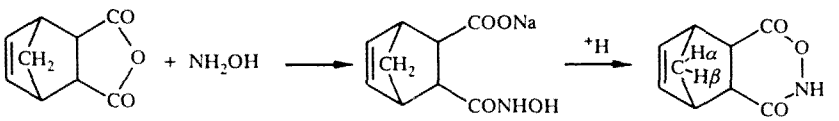
In contrast to derivatives of the 1,3- and 1,4-oxazines, the synthesis, properties and biological activity of derivatives of 1,2-oxazine have been little studied [1, 2]. One possible method to obtain these compounds is the Diels-Alder addition of dienes to nitroso compounds. Activation of nitroso compounds is by oxidation of the corresponding hydroxamic acids.

In this report we propose a new method for preparing derivatives of tetrahydrobenzoxazine by the reaction of 3,6-endomethylene-1,2,3,6-tetrahydrophthalic anhydride (endic anhydride) with hydroxylamine with subsequent acid work up as follows:



The intermediate compound — the sodium salt of a hydroxamic acid — gave a characteristic violet coloration with iron(III) chloride. The hydroxamic acid cyclized in acid medium to give a new compound — 1,4-dioxo-5,8-endomethylene-3,8,9,10-tetrahydrobenz-2,3-oxazine.

A solution prepared from hydroxylamine hydrochloride (3.88 g) and sodium (1.28 g) in methanol (22 cm^3) was added slowly with stirring to a cooled solution (ice–salt mixture) of 3,6-endomethylene-1,2,3,6-tetrahydrophthalic anhydride (7.38 g) in methanol (17 cm^3). A white precipitate which slowly deposited over 1 h (~20°C) was recrystallized from methanol to give sodium 2-carboxy-3,6-endomethylene-1,2,3,6-tetrahydrobenzoylhydroxamate (5.56 g, 56%), ^1H NMR spectrum: 5.78 (2 H, dd, CH=CH), 3.08 (2 H, m, CH-COO), 2.96 (2 H, m, CH), 1.58-1.37 ppm (2 H, m, CH_2).

A solution of this salt (2.5 g, 11.4 mmol) in water was acidified to pH 1-2 with hydrochloric acid (1 mol dm^{-3}). The solution was extracted with ethyl acetate (4 x 25 cm^3), the extract was dried with anhydrous sulfate and evaporated to a volume of 2 cm^3. White platelets of 1,4-dioxo-5,8-endomethylene-3,8,9,10-tetrahydrobenz-2,3-oxazine deposited (1.09 g, 53%), m.p. 160°C. ^1H NMR spectrum: 6.22 (2 H, dd, CH=CH), 3.52-3.43 (2 H, m, CHC=O), 3.31 (2 H, m, CH), 1.79 and 1.52 ppm (2 H, m, ^2J = 9.4 Hz, α-H and β-H).

Elemental analysis data agreed with calculated values.

REFERENCES

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