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PERACID OXIDATION OF O-ALKYL IMINO-ESTERS OF HEXANOLACTAM

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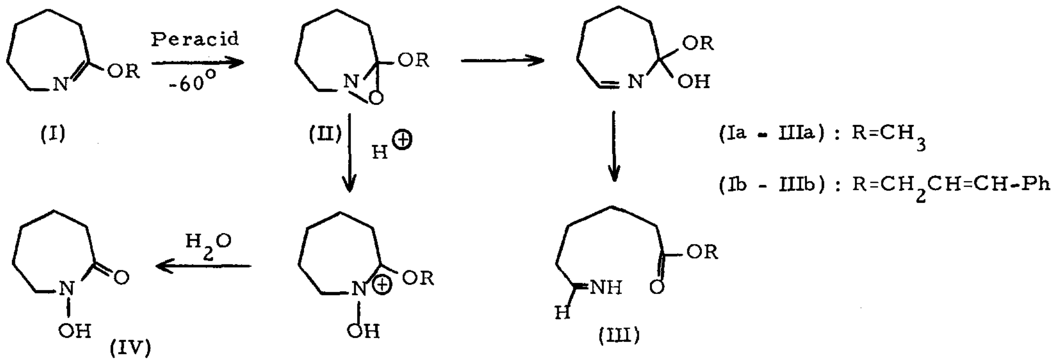
Cyclic hydroxamic acids[1] are of synthetic interest because of their presence in important classes of natural products and there is a need for new synthetic methods. For instance, no case of a direct N-hydroxylation of an aliphatic amide or lactam has been recorded in the literature. We now report the conversion of a lactam to a cyclic hydroxamic acid in only two steps, via a related iminoester.

Reaction of O-methylhexanolactim (Ia) with m-chloroperbenzoic acid in methylene chloride at -60° yielded N-hydroxyhexanolactam[2] (IV) in 3% yield, the hexahydro-1,3,5-triazine trimer[3] of methyl 6-iminohexanoate (IIIa) (isolated as methyl 6-oxohexanoate 2',4'-dinitrophenylhydrazone[4] in 11% yield) and a secondary oxidation product, methyl 6-nitrosohexanoate, isolated as the dimer, m.p. 49° (10% yield), $(C_7H_{13}NO_3)_2$, m/e 129 (M/2-NO). Chromatography of the crude nitroso dimer resulted in its conversion into methyl 5-cyanopentanoate[5] which was obtained in similar overall yield (11%). When the same reaction was carried out in the presence of excess anhydrous potassium carbonate, the oxazirane (IIa)$^+$, b.p. 110-120°/0.27 mm, (17% yield) m/e 143 (M), was isolated. It was slowly converted in acid-free solution ($CDCl_3$) at 0° to the above imine trimer in spectroscopically quantitative yield.

In an attempt to improve the yield of hydroxamic acid (IV), peracid oxidation of O-cinnamylhexanolactim (Ib)[6] was investigated. Reaction in the absence of potassium carbonate afforded the hydroxamic acid (IV), which was isolated in 13% yield. In the presence of anhydrous potassium carbonate exclusive ring cleavage resulted in the formation of cinnamyl 6-iminohexanoate (IIIb), isolated as a trimer (a hexahydro-1, 3, 5-triazine) in 66% yield, whose structure was confirmed by conversion to methyl 6-oxohexanoate 2', 4'-dinitrophenylhydrazone[4]. The oxazirane (IIb) could not be isolated.

It would appear that the cinnamyloxy group is better able than the methoxyl group to stabilize the carbonium ion which would arise from cleavage of the carbon-oxygen bond in the oxazirane ring. This reasoning is in accord with the general behaviour of oxaziranes on hydrolysis with acid[3,7].

Oxidation of O-methylpentanolactim in the absence of potassium carbonate gave N-hydroxypentanolactam[2] in 10% yield. Attempts are being made to improve the yield of hydroxamic acid, by oxidation of iminoesters derived from different alcohols.



+ Satisfactory i. r. and H n.m.r. (CDCl$_3$; 60MHz) spectroscopic data were obtained for all compounds described.

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