Acylation of 5-Isoxazolylalkyl Carbanions: Synthesis of Bis- and Tris-isoxazole Compounds

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Summary Bis- and tris-isoxazole compounds have been prepared from 3,5-dimethylisoxazole.

In order to develop synthetic units for the preparation of various natural products whose biogenetic pathways may be explained by the β-polyketomethylene theory,[1] we have used isoxazoles as the equivalents of β-dicarbonyl compounds.

The carbanion (Ia)[2] was treated with the ethylene acetal of ethyl acetoacetate in THF–hexane at −78°, yielding the 5-acyl derivative (II) (55%). This gave the bis-isoxazole compound (III), b.p. 117—121° (1 mm) after oximation and acidic hydrolysis (98%).

Compound (III) was treated with lithium di-isopropylamide, to form a carbanion on the 5-methyl carbon, and was then converted into the tris-isoxazole (IV), m.p. 76—77°, as for (III).

Benzoylation of the anion of (III) with methyl benzoate gave the 5-benzoylmethyl derivative (V) (76%) m.p. 125—126°, accompanied by a small amount of (VI) m.p. 102—104°.

Although 3,5-diethyl-4-methylisoxazole[3] formed the carbanion (Ib) slowly when BuLi was used, this difficulty was overcome by the use of lithium di-isopropylamide or lithium diethylamide.[4] Condensation of (Ib) with methyl 2-(3-ethyl-4-methyl-5-isoxazolyl)propionate, prepared by carbonation followed by esterification of (Ib), gave the ketone (VIIb), as an oil. Similarly, (Ia) reacted with methyl 3-methoxyisoxazole-5-acetate[5] to furnish the ketone (VIIc), m.p. 65—66°. This compound is regarded as an equivalent of the β-penta-acetate (VIII)

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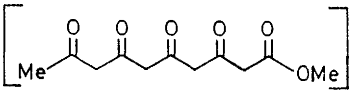
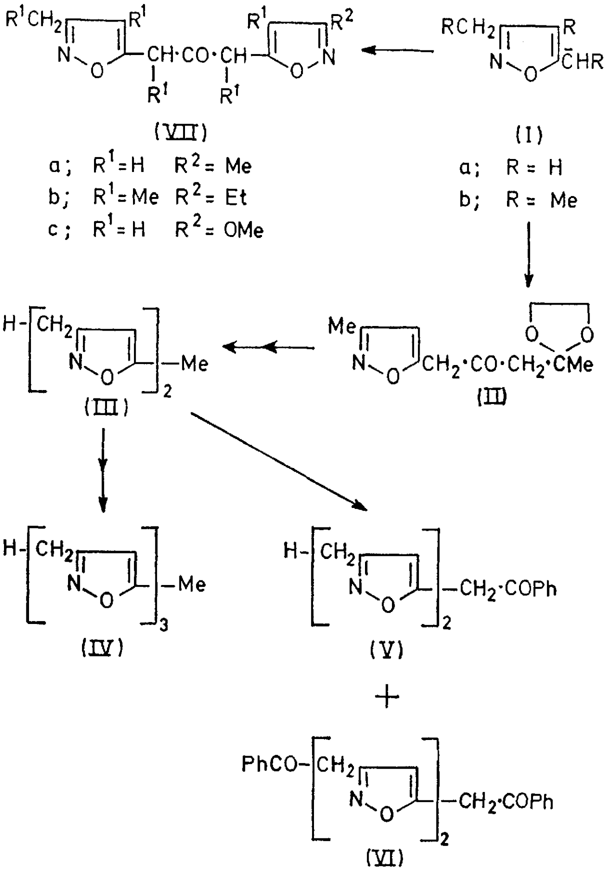


(VIII)



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