NOVEL RING TRANSFORMATION REACTIONS OF XANTHINE DERIVATIVES

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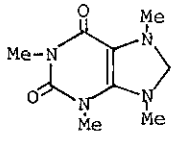
Novel ring transformation reactions of xanthine derivatives were investigated.

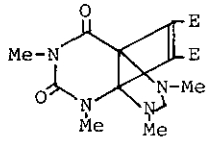
[1] Preparation of 1,3,7,9-Tetraalkyl-8,9-dihydroxanthines 1,3,7,9-Tetraalkylxanthinium perchlorates were prepared by known procedures[1] and quantitatively converted to the corresponding 1,3,7,9-tetraalkyl-8,9-dihydroxanthines by reduction with $NaBH_4$ in water.

[2] Reactions of 1,3,7,9-Tetraalkyl-8,9-dihydroxanthines with Dimethyl Acetylenedicarboxylate (DMAD) The reaction of 1,3,7,9-tetramethyl-8,9-dihydroxanthine (I) with DMAD in CH_3CN gave a propellane type compound, 4,5,8,9-tetrahydro-4,5-(dimethoxycarbonyletheno)-1,3,7,9-tetramethylxanthine (II). This reaction may proceed by an ionic cycloaddition of DMAD to an enamine moiety of I.

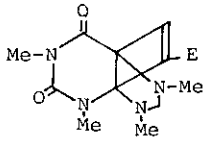
[3] Reactions of 1,3,7,9-Tetraalkyl-8,9-dihydroxanthines with Methyl Propiolate The reaction of I with methyl propiolate in CH_3CN gave a propellane type compound, 4,5,8,9-tetrahydro-4,5-(11-methoxycarbonyletheno)-1,3,7,9-tetramethylxanthine (III) and a ring expanded compound, 4,5-dihydro-3-methoxycarbonyl-1,5,6,8-tetramethyl-7,9-dioxopyrimido[4,5-b]1H-1,5-diazepine (IV). The Structure of IV was determined by the NOE measurement. The mechanism of this reaction may be explained as follows: When methyl propiolate reacts on C_5 of I, which has two reaction sites, C_5 and N_7, the reaction proceeds by a cyclization route to an enamine moiety of I to give III. In contrast, when methyl propiolate attacks N_7, the reaction occurs through an iminium salt intermediate to give IV. In the presence of Lewis acids or water, this reaction gave other compounds. Reactions of I with other various electrophiles are also discussed.



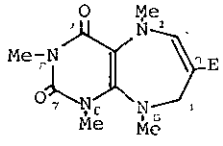
I



II



III



IV

(E = COOMe)

1) S.M.Hecht, B.L.Adams, and J.W.Kozarich, J.Org.Chem., 41, 2303 (1976). A.V.El'tsov and Kh.L.Muravich-Alexander, Tetrahedron Lett., 1968, 739.