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A VERSATILE AND CONCISE ROUTE TO FUNCTIONALLY SUBSTITUTED γ-BUTYRO-LACTONES AND SPIRO- γ-BUTYROLACTONES (LACTONE ANNELATION)

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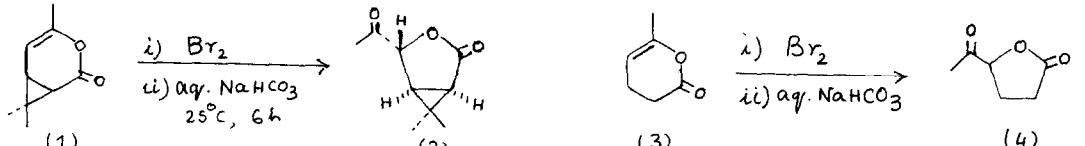
Summary : A novel route to the synthesis of functionally substituted γ-butyro-lactones and spiro- γ-butyrolactones, from six-membered cyclic enol-esters, is described.

The preparation of spiro- γ-lactones has been the focus of recent interest[1]. However, only a few studies, e.g. a recent one by Trost *et al*[2], have dealt with the synthesis of functionally substituted spiro- γ-lactones. The usefulness of these compounds was further demonstrated in the synthesis of natural products[3].

In connection with our work on the development of novel routes to (1R, Cis)-synthetic pyrethroids, an important class of potent insecticides, we discovered a novel route to functionally substituted γ-lactones via six-membered cyclic enol-esters through a sequence comprising halogen addition to the double bond and subsequent halo-lactonization. We wish to report in this communication the generality of this approach towards the synthesis of various functionalised γ-lactones and spiro-γ-lactone.

Thus, the reaction of enol-ester (1), $[\alpha]_D^{25}$ -100° (C 2, $CHCl_3$) with bromine in CCl_4 at 0° C yielded after aqueous work up (1R, Cis)- γ-lactone (2)[4], m.p. 63-4° C, $[\alpha]_D^{25}$ -48.5° (C 1, EtOH), in quantitative yield.

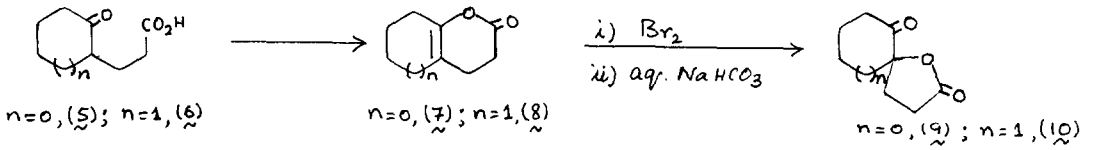


(1) (2) (3) (4)

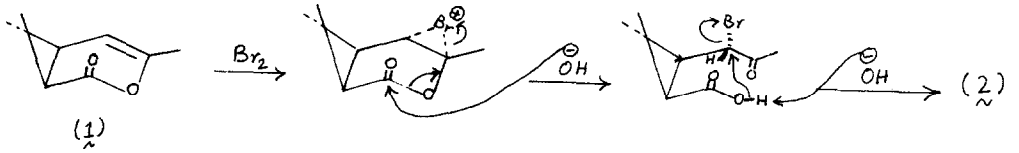
Similarly, 6-methyl-3,4-dihydro-pyran-2-one(3), obtainable from readily available 4-acetylbutyric acid, yielded 5-acetyl-tetrahydro-2-(3H)-furanone(4) in 80% isolated yield. This lactone (4) which is a constituent of the aroma of wine[5], can therefore be synthesized[5] in one step from a commercially available starting material.

It is further observed that the suitably substituted bicyclic enol-esters (7) and (8), readily obtained from the corresponding acids (5) and (6), respectively[6],

undergo similar reaction to afford the spiro-γ-lactones (9)[7] (m.p. 104-5° C) and (10)[7] (m.p. 49-50° C) in isolated yields of 79% and 81% respectively.



The formation of γ-lactone from the cyclic enol-ester is explained as follows :



The usefulness of this approach for other synthetic transformations is currently being explored.

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7. The compounds have been fully characterized by spectral analysis.
   (9); IR ($CHCl_3$), ν, 1795 CM^{-1} and 1770 CM^{-1}; NMR ($CDCl_3$), δ, 1.75-3.0 (m, 10H); MS (70 e.v.), M^+ 154 (19), 126 (20), 98 (100), 70 (20), 56 (48), 42 (40);
   (10); IR ($CHCl_3$), ν, 1780 CM^{-1} and 1725 CM^{-1}; NMR ($CDCl_3$), δ, 2.5-2.9 (m, 4H), 1.5-2.5 (m, 8H); MS (70 e.v.), M^+ 168 (15), 124 (35), 111 (100), 98 (40), 83 (17), 67 (15), 56 (24), 55 (42), 41 (27), 39 (36).

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