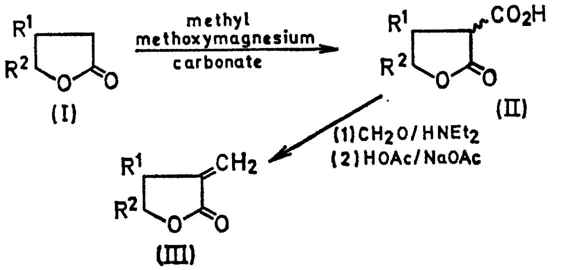
A New Method for the Synthesis of α-Methylenebutyrolactones

By J. MARTIN, P. C. WATTS, and FRANCIS JOHNSON*

(*The Dow Chemical Company, Eastern Research Laboratory, Wayland, Massachusetts* 01778)

Summary Methyl methoxymagnesium carbonate (Stiles' reagent) carboxylates butyrolactones in very high yield, and, with a new application of the Cope condensation for the introduction of the methylene group, permits the synthesis of α-methylenebutyrolactones in good overall yield.

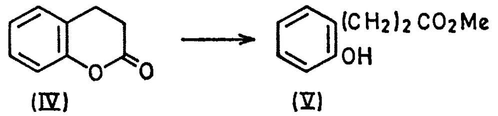
MANY natural products, which have been the object of synthetic research in recent years, contain a butyrolactone with an α-methylene group. Despite considerable work, the methods[1-3] used for the introduction of the methylene function were unsatisfactory.

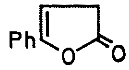


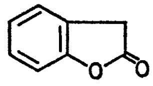
We have found that the α-methylene function can be introduced in two quite simple steps—carboxylation of (I) with Stiles' reagent,[4] methyl methoxymagnesium carbonate, to produce the acid (II), then brief treatment of the latter first with a mixture of aqueous formaldehyde and diethylamine, followed by a separate treatment of the crude product with sodium acetate in acetic acid.† The first step requires 6—7 hr. and gives excellent yields of the acids, in all cases tried so far. The second sequence can be accomplished in less than 30 min. and in almost all cases examined yields are about 50%. A number of products‡ made by these procedures are shown in the Table.

Lactone (I)	% Yield of carboxylic acid (II)	% Yield of α-methylene lactone (III)
R^1=H; R^2 = Ph	92	49
R^1=H; R^2 = C_4H_9	98	62
R^1=H; R^2 = C_6H_{13}	98	68
R^1=CH_2·CON=C_5H_8; R^2=C_8H_{17}	72·6	48

The carboxylation step, however, does not appear applicable to six-membered ring lactones, as when valerolactone was treated with methyl methoxymagnesium carbonate no acidic products could be isolated. Dihydrocoumarin (IV) gave as the only acidic material, the ring-opened product (V). On the other hand, both (VI) and (VII) gave acidic products when treated with Stiles' reagent, but these largely decomposed during the isolation procedure.




(VI)


(VII)

(*Received, October 9th,* 1969; *Com.* 1520.)

---

† The methyleneation of (II) can be accomplished by combining all of these reagents in one solution but except for one case the yields are consistently lower.

‡ Suitable elemental analyses have been obtained for all of the new materials listed.

[1] E. E. van Tamelen and S. R. Bach, *J. Amer. Chem. Soc.*, 1955, **77**, 4683; 1958, **80**, 3079.

[2] J. A. Marshall and N. Cohen, *Tetrahedron Letters*, 1964, 1997; *J. Org. Chem.*, 1965, **30**, 3475.

[3] H. Minato and I. Horibe, *Chem. Comm.*, 1965, 531.

[4] H. L. Finkbeiner and M. Stiles, *J. Amer. Chem. Soc.*, 1963, **85**, 616.