

A New Method for Carboxylating Active Methylene Groups with Carbon Dioxide

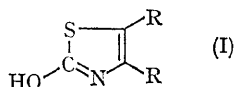
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THE chemical approach to the enzymatic carboxylation system has led recently¹ to the discovery that methylmagnesium carbonate is a very effective carboxylating agent for active methylene groups. The driving force appears to be the chelating power of magnesium for the product.

We now report a milder carboxylation process based on the use of alkaline salts of some aromatic or heterocyclic phenolic derivatives.

Nuclear reaction as in the Kolbe synthesis is prevented, when necessary, by substituting or deactivating the reactive positions, or by using compounds lacking hydrogen in such positions.



So far, the best results have been obtained with hydroxythiazole derivatives (I; R = alkyl) or with phenol. The sodium or potassium salts can be used as such or in the presence of organic media. When carbon dioxide is passed through the mixture containing the substrate to be carboxylated, a very

* Calculated from isolated benzoylacetic acid.

¹ M. Stiles, *J. Amer. Chem. Soc.*, 1959, **81**, 2598.

mild reaction takes place at room temperature and atmospheric pressure.

Using acetophenone (0.01 mole) in dimethylformamide with 0.04 mole of the potassium salt of (I; R = Me), or of phenol we obtained potassium benzoylacetate (0.006 mole).* The yield, based on converted acetophenone, is almost quantitative.

Cyclohexanone (0.01 mole) and 0.04 mole of the potassium salt of (I) or of phenol in dimethylformamide gave 0.004 mole of potassium cyclohexan-2-one-1,3-dicarboxylate and cyclohexan-2-one-1-carboxylate in the ratio 3 : 1.

Cyclohexanone (0.4 mole) and potassium phenate (0.08 mole) without dimethylformamide gave approximately 0.03 mole of cyclohexanone monocarboxylate and 0.004 mole of cyclohexanone dicarboxylate. Phenol or hydroxythiazoles are easily separated by conventional techniques and recycled.

The general mechanism of this reaction is being investigated. We thank Prof. A. Quilico for helpful discussions.

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