Tetrahedron Letters No.16, pp. 1069-1070, 1971. Pergamon Press. Printed in Great Britain.

A NOVEL SYNTHESIS OF MIXED ESTERS OF PHOSPHORIC ACID FROM ALKYL o-HYDROXYPHENYL HYDROGEN PHOSPHATES

J. Calderón and C. Cruz

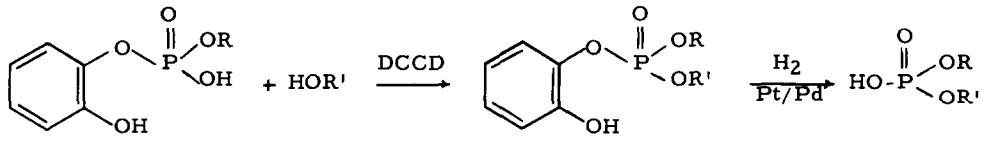
Instituto de Química Orgánica General (CSIC). Juan de la Cierva, 3. Madrid-6. Spain.

(Received in UK 15 March 1971; accepted for publication 19 March 1971)

The alkyl o-hydroxyphenyl hydrogen phosphates have been used as intermediates in the synthesis of alkyl dihydrogen phosphates. In this work we report its application in the synthesis of dialkyl hydrogen phosphates.

The alkyl o-hydroxyphenyl hydrogen phosphates can be prepared, in good yield, according to the following procedures: a) from o-phenylene phosphorochloridate and alcohols in the presence of a base (1, 2, 3); b) by reacting directly o-phenylene hydrogen phosphate and the alcohol (4) or in the presence of dicyclohexylcarbodiimide (5, 6) and c) by alcoholysis of alkyl o-phenylene phosphates (7). In each case the alkyl o-phenylene phosphate is obtained; hydrolysis of this substance yields the expected alkyl o-hydroxyphenyl hydrogen phosphates. In order to obtain the corresponding monoesters of phosphoric acid, the protecting o-hydroxyphenyl group is removed either by hydrogenolysis over PtO_2 (1, 2, 5, 7) or by oxidative phosphorylation (3).

The alkyl o-hydroxyphenyl hydrogen phosphates (I) react with alcohols in the presence of dicyclohexylcarbodiimide (DCCD) to give dialkyl o-hydroxyphenyl phosphates (II). The o-hydroxyphenyl group is cleaved by hydrogenolysis over a mixed Pt/Pd catalyst to obtain the dialkyl hydrogen phosphates (III) according with the following reaction scheme:



I II III

R, R' = alkyl

The alkyl o-hydroxyphenyl hydrogen phosphates prepared by the methods mentioned above are generally obtained in salt form. Once the cation is retained on Amberlite IR-120 (in H^+ form), the condensation with the alcohol is carried out in dry dioxane in the presence of dicyclohexylcarbodiimide. The dialkyl o-hydroxyphenyl phosphates are further purified by distillation under vacuum. The hydrogenolysis step is carried out under pressure slightly higher than atmospheric, and the corresponding dialkyl hydrogen phosphates are separed as the barium salts.

In this way, we have prepared: ethyl isopropyl-, n-butyl ethyl-, di-n-butyl-, n-butyl t-butyl-, butyl octyl-, and isopropyl octyl-hydrogen phosphates.

At present we are studying the preparation and isolation of new dialkyl o-hydroxyphenyl phosphates that cannot be distilled, with the aim of preparing phospholipids. So far we have succeded in preparing in good yield o-hydroxyphenyl phosphates of diglycerides.

References

1) M. Lora-Tamayo and J. Calderón, An. real soc. españ. Fís. Quím., 46-B, 475 (1950).

2) J. Calderón, An. real soc. españ. Fís. Quím., 53-B, 69 (1957).

3) T.A. Khwaja, C.B. Reese, and J.C.M. Stewart, J. Chem. Soc., 2092 (1970).

4) K. Nagasawa, Chem. and Pharm. Bull. (Japan), 7, 397 (1959).

5) M.A. Calama and J. Calderón, An. real soc. españ. Fís. Quím., 62-B, 1015 (1966).

6) M.A. Calama and J. Calderón, An. real soc. españ. Fís. Quím., in press.

7) J. Calderón and G. Moreno, An. real soc. españ. Fís. Quím., 56-B, 603 (1960).