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AN EFFICIENT SYNTHESIS OF 2-HYDROXYPHENYLPHOSPHONATES

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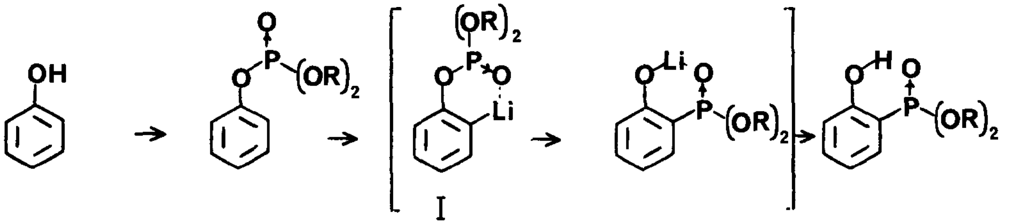
Abstract: The high yield conversion of phenols into diethyl 2-hydroxyphenylphosphonates via base catalyzed rearrangement of diethyl phenyl phosphates has been achieved.

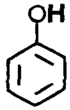
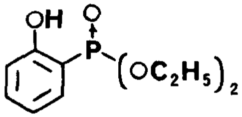
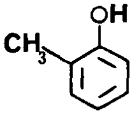
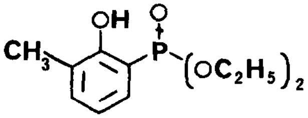
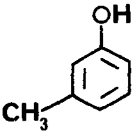
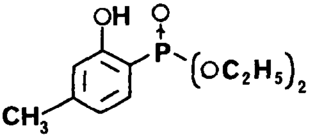
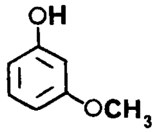
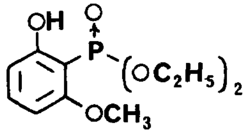
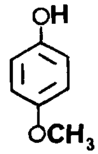
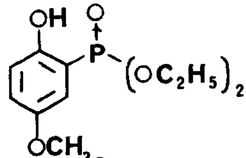
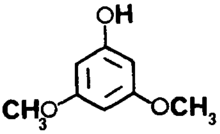
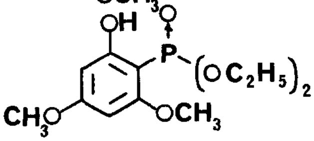
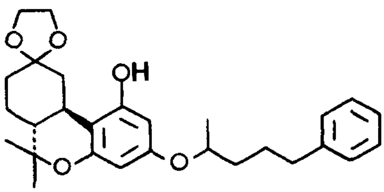
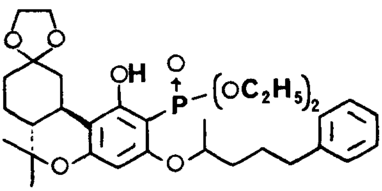
The preparation of esters of 2-hydroxyphenylphosphonates has previously been achieved by the light-induced reaction between aryl iodides and phosphites.[1,2] 2-Hydroxyphenylphosphonic acids have also been prepared from 2-aminophenylphosphonic acids.[3] This communication reports a new, efficient conversion of phenols into 2-hydroxyphenylphosphonates as outlined below.



Phosphate esters of substituted phenols are readily obtained in high yield upon reaction of the phenol with a phosphonate diester, carbon tetrachloride and triethylamine.[4] Reaction of the aryl phosphate esters with a strong base such as lithium diisopropylamide in tetrahydrofuran or potassium amide in liquid ammonia-tetrahydrofuran produces excellent yields (Table 1) of 2-hydroxyphenylphosphonates. The reaction mechanism is explained as proceeding via an intramolecular collapse of an intermediate I. Only one isomer is formed in each case mentioned, and that one correlates with ease of metallation at the position ortho to the phosphate group.

A typical procedure is as follows: To a -78°C solution of 4.83 ml (0.0345 mole) of diisopropylamine in 50 ml of tetrahydrofuran is slowly added 14.4 ml (0.0345 mole) of 2.4M n-butyllithium in hexane. The solution of lithium diisopropylamide is stirred 15 min at -78°C, and then a solution of 10.0 g (0.0345 mole) of diethyl 3,5-dimethoxyphenyl phosphate in 50 ml of tetrahydrofuran is slowly added. The reaction is stirred 15 min longer at -78°C and 30 min at 0°C yielding a white slurry. The reaction is added to 300 ml saturated ammonium chloride and 300 ml ether. The ether extract is dried over magnesium sulfate and evaporated to an oil. Distillation of the crude oil yields 9.33 g (93%) of diethyl 2,4-dimethoxy-6-hydroxyphosphonate ($bp_{0.05}$ 117-121°C).

TABLE 1

Substrate	Product[5]	Yield (%)	BP (torr)
		93	92-97(0.05)
		87	97-101(0.06)
		92	97-102(0.05)
		95	118-122(0.04)
		95	117-121(0.05)
		93	137-141(0.05)
		78	Viscous Oil

References:

1. R. Obrycki and C. E. Griffin, J. Org. Chem., 33, 632 (1968).
2. K. Issleib and R. Vollmer, Z. Chem., 18, 451 (1978).
3. G. O. Doak and L. D. Freedman, J. Amer. Chem. Soc., 74, 753 (1952).
4. G. W. Kenner and N. R. Williams, J. Chem. Soc., 522 (1955).
5. All products and intermediates have been characterized by pmr, ir and ms.

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