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Phosphorylation of Phenols with Diethyl Chlorophosphonate on the Surface of Magnesia†

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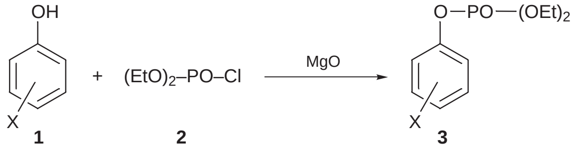
Phosphorylation of phenols with diethyl chlorophosphonate on the surface of magnesia is an easy, rapid, safe and high-yielding reaction.

Surface-mediated solid phase reactions are of growing interest[1] because of their ease of set up and work-up, mild reaction conditions, rate of the reaction, selectivity, high yields, lack of solvent and the low cost of the reactions in comparison with their homogeneous counterparts. As part of our efforts to explore[2] the novel utilities of surface-mediated reactions, here we report a new method for the phosphorylation of phenols. The synthesis of phosphate esters is an important objective in organic synthesis, since they have found wide use in the preparation of biologically active molecules[3] as well as in the reduction of phenols to aromatic hydrocarbons.[4] Mixed phosphonate esters have been prepared by several methods;[5–8] one of the best involves the reaction of a dialkyl phosphite with an alcohol or phenol in the presence of triethyl amine in carbon tetrachloride.[9,10] Other variations have been reported,[11–13] including phase transfer and use of trialkylphosphites with molecular iodine.[13] Recently, phosphorylation of phenols with diethyl cyanophosphonate in the presence of triethylamine at 0 °C has been reported.[14] We describe here a new and easy method for the phosphorylation of phenols **1** with diethyl chlorophosphonate **2** on a magnesia surface without solvent (Scheme 1). We have found that the reaction of a phenol with 1.2 equivalents of diethyl chlorophosphonate in the presence of 1.5 equivalents of magnesia was complete within 1 h. The overall yields of these reactions are given in Table 1.



Scheme 1

As shown in Table 1, *o*-, *m*-, *p*-substituted phenols with diethyl chlorophosphonate in the presence of magnesia afford the desired products in excellent yields. These results clearly show that the reactions seem to be faster with higher yields when the aromatic part of the phenol molecules carry electron-withdrawing groups. The reaction also proceeded with high yields for α- and β-naphthols (products **3i**, **3j**).

Acidic, neutral, and basic alumina are not as effective as magnesia and usually give low yields of the corresponding esters.

Simple work-up, low consumption of solvent, fast reaction rates, mild reaction condition, good yields, and selectivity of the reaction make this method an attractive and a useful contribution to the present methodologies.[15]

Experimental

General.—All chemicals were commercial products and distilled or recrystallized before use. IR spectra were measured using a Bruker Vector 22 spectrometer. ^{1}H NMR spectra were recorded on a Bruker Avance DPX 250 MHz instrument. Mass spectra were obtained on GC-MS Shimadzu GP 1000 spectrometer.

General Procedure for the Phosphorylation of Phenols with Diethyl Chlorophosphate on the Surface of Magnesia.—Magnesia (0.3 g) was added to a mixture of diethyl chlorophosphonate (0.86 ml, 0.006 mol) and the phenol (0.005 mol). This mixture was stirred at room temperature or 60 °C for 0.25–1 h (Table 1). The solid mixture was washed with dichloromethane (4 × 25). The solution was then washed with a dilute NaOH solution and a saturated sodium chloride solution and dried over $MgSO_4$. After evaporating of solvent, the crude product was isolated in a pure state by distillation *in vacuo* in 85–95% yield.

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Table 1 Phosphorylation of phenols with diethyl chlorophosphonate in the presence of magnesia

Product	Ar	*t*/h	Yield[a] (%)	Product	Ar	*t*/h	Yield[a] (%)
3a	Ph	1[b]	87	**3f**	2,4-$Cl_2C_6H_3$	0.5	90
3b	*o*-ClC_6H_4	0.5	90	**3g**	*m*-MeC_6H_4	1[b]	85
3c	*p*-MeC_6H_4	0.75[b]	88	**3h**	*o*-$O_2NC_6H_4$	0.5	88
3d	*p*-$O_2NC_6H_4$	0.25	95	**3i**	α-$C_{10}H_7$	1[b]	85
3e	*m*-BrC_6H_4	0.5	90	**3j**	β-$C_{10}H_7$	1[b]	85

[a] Isolated yield. [b] Reaction carried out at 60 °C.

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15 All products gave satisfactory spectral data in accord with the assigned structures. *E.g.* for **3g** δ_H($CDCl_3$, TMS): 1.15–1.30 (2t, 6H, 2-OCH_2CH_3), 2.31 (s, 3H), 3.90–4.65 (2q, 4H, 2-OCH_2CH_3), 7.13–7.33 (m, 4H); IR (neat): ν 1608 (Ar), 1278 ($P{=}O$), 1032, 966 cm^{-1} (P–O–Et).