

Stereoselective Addition of Phenols to Dimethyl Acetylenedicarboxylate adsorbed on Alumina

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Although phenols react with dimethyl acetylenedicarboxylate (DMAD) to give a mixture of both *cis*- and *trans*-addition products, the reaction with DMAD adsorbed on alumina gives *cis*-addition products stereoselectively.

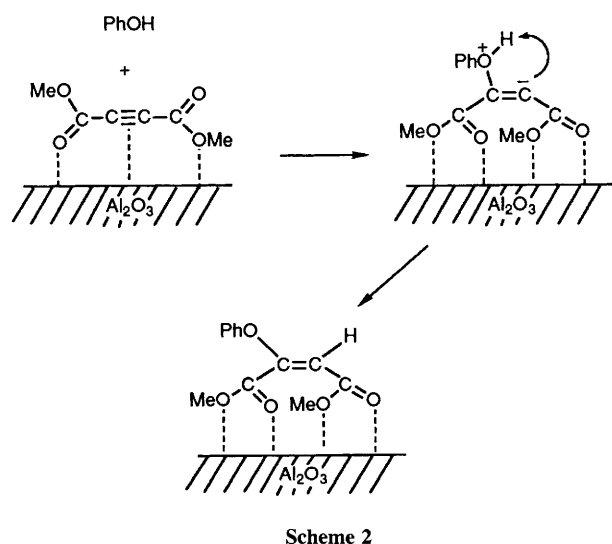
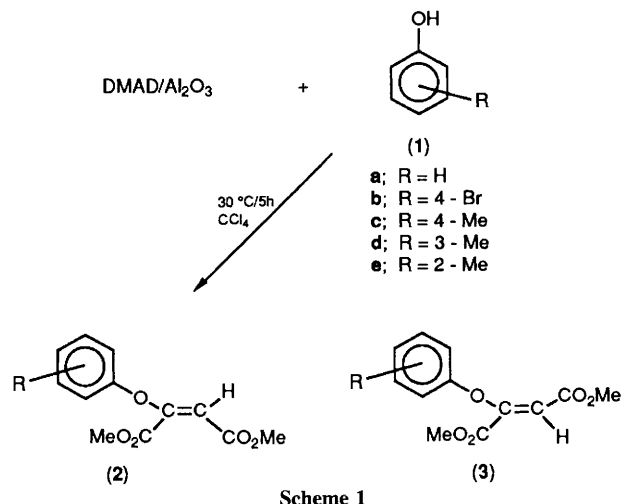
Significant improvement in regioselectivity has been achieved for a variety of organic reactions by adsorption of substrates onto the surface of inorganic solids.¹ However, few examples of stereoselective control using substrates adsorbed on inorganic solids have been reported.²

Nucleophiles, such as amines,³ phenols,⁴ and thiols⁵ add to dimethyl acetylenedicarboxylate (DMAD) either directly or in the presence of a base to give 1:1 adducts. Phenols react with DMAD in the presence of potassium carbonate to give a mixture of both *cis*- and *trans*-addition products. The ratio of

Table 1. Addition of phenols to DMAD adsorbed on alumina.

Phenols	Yield/% of (2) ^a
(1a)	5 ^b [(2a)/(3a) 37/63]
(1a)	15 ^c [(2a)/(3a) 41/59]
(1a)	91 (2a)
(1b)	87 (2b)
(1c)	84 (2c)
(1d)	83 (2d)
(1e)	91 (2e)

^a Isolated yield. ^b Without alumina. ^c DMAD and alumina.



these isomers is dependent on the size of the attacking nucleophile, the solvent, and the reaction conditions. We have found that phenols react with DMAD adsorbed on neutral alumina in the absence of a base to give stereoselectively the *cis*-addition products in high yields.⁶

The reaction of phenol with DMAD was carried out in carbon tetrachloride at 30 °C for 5 h and gave a 5% yield of a mixture of phenoxymaleate (2a) and phenoxyfumarate (3a), consisting of 37% (2a) and 63% (3a) (detected by NMR spectroscopy). In contrast, a similar reaction where DMAD was first coated onto neutral alumina produced (2a) in 91% yield. Compound (3a) was not detected. Substituted phenols also reacted with DMAD adsorbed on neutral alumina to give the corresponding maleates (2a) in high yields.

In a typical experiment, to a solution of DMAD (8 mmol) in dichloromethane (50 ml) was added neutral alumina (Woelm N-Super 1, 20 g) at room temperature. After removal of the solvent from the mixture using a rotary evaporator at 40 °C under reduced pressure, the resulting alumina-supported DMAD (DMAD/Al₂O₃) was further dried *in vacuo* (3 mmHg) at 40 °C for 1 h. Phenol (8 mmol) was added to a suspension of DMAD/Al₂O₃ in carbon tetrachloride (60 ml). The mixture was stirred vigorously at 30 °C for 5 h. The product mixture was filtered, and the solid washed with dimethylformamide (DMF). The washings were diluted with water and extracted using ether. The filtrate and the ether extract were combined, concentrated under reduced pressure, and the products obtained were analysed by GLC and NMR spectroscopy.

When DMAD and alumina were merely mixed in carbon tetrachloride, and then phenol was added to the mixture, the stereoselectivity was not observed. Empirical testing of four supports (alumina, silica gel, molecular sieve, Kieselguhr) revealed that only alumina has an effect on the stereoselectivity. The yield of (2) obtained from the reaction in a variety of solvents, *e.g.*, chloroform, acetonitrile, and dioxane, is about the same as in carbon tetrachloride. The rate of this reaction and the ratio of the product isomers were approximately solvent independent suggesting that the reaction occurs on the surface of alumina and that the DMAD is strongly adsorbed.

These observations suggest that adsorption of organic compounds onto inorganic supports could provide a way of controlling stereoselectivity.

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