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Preparation of Diphenylmethyl Esters by Oxone® Oxidation of Benzophenone Hydrazone

Massimo Curini,* Ornelio Rosati and Emanuela Pisani

Istituto di Chimica Organica, Facoltà di Farmacia, Università degli Studi, Via del Liceo, I-06123 Perugia Italy

Walter Cabri,* Stefano Brusco and Massimiliano Riscazzi

Bristol Myers Squibb, Chemical Development, Via del Murillo Km 2.800, I-04010 Sermoneta (LT) Italy

Abstract: Oxone® was found to be an efficient oxidizing reagent of benzophenone hydrazone for the preparation of diphenylmethyl esters (benzhydryl, Dpm).

Diphenylmethyl esters (benzhydryl, Dpm) have been used in synthetic organic chemistry as protecting groups of carboxylic acids because of their facile removal by hydrogenolysis or mild acid hydrolysis.[1] The use of Dpm derivatives is well documented in the synthesis of sensitive compounds such as α-amino acids[1a,2] or penicillins and cephalosporins.[3]

This protecting group has been introduced by interaction of carboxylic acids with diphenylmethyl phosphates,[2b,2d] diphenyldiazomethane generated by oxidation of benzophenone hydrazone[2c,3] or by reaction of silver carboxylates with diphenylmethyl chloride.[1a]

We have now found that Oxone® supported on wet Al_2O_3[4] can be successfully used as a benzophenone hydrazone oxidizing agent in the preparation of Dpm-esters. The reaction proceeds smoothly at 0° C by adding Oxone/Al_2O_3 to a mixture of the carboxylic acid, benzophenone hydrazone and a catalytic amount of iodine.[5]

In table I, we report the synthesis of Dpm-esters, starting from simple acids, *N*-protected *α*- and *β*-amino acids, and *β*-lactam derivatives. The yields obtained using our procedure are comparable or better with respect to those reported for similar transformations and the reaction system proved to be compatible with the presence of sensitive groups. This simple procedure can be easily carried out on large scale because of facile removal of the oxidation system by simple filtration.

Summing up, the Oxone/ Al_2O_3 reagent is cheap, easy to handle and the described method is of general applicability.

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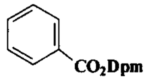
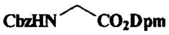
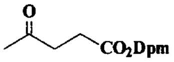
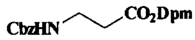
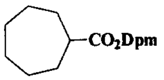
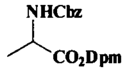
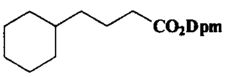
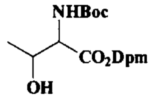
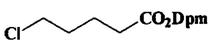
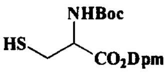
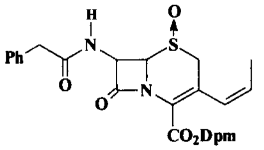
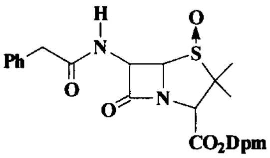
Table 1. Diphenylmethyl (Dpm) Esters Prepared.[a]

	Time (h)	Yield (%)[b]		Time (h)	Yield (%)[b]
	5	90		10	82
	5	75		6	81
	10	70		5	83
	10	75		3	89
	10	73		2.5	66
	3	85		4	95

[a] Satisfactory IR and ^{1}H-NMR data were obtained. [b] Yield refers to the pure isolate product.

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4. For the preparation of wet Alumina see: Greeenhalgh, R. P. *Synlett* **1992**, 235-236.
5. **Experimental procedure:** to a solution of starting material (2 mmol) in dichloromethane (10 ml) benzophenone hydrazone (3.2 mmol) was added at 0° C. After addition of 1% (w/w) iodine in dichloromethane solution (0.1 ml) a mixture of wet Alumina (2.28 g) and Oxone® (3 mmol) (previously mixed) was added during 30' (the reaction was exothermic). Stirring was continued for the appropriate time (see table). The reaction mixture was then filtered and the solvent was removed under vacuum. The crude was purified by crystallization or chromatography.

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