

A Novel Oxygen-to-Carbon Ester Migration catalysed by 4-(*N,N*-Dimethylamino)pyridine in the Benzofuranone Ring System

T. Howard Black,* Steven M. Arrivo, Jeffry S. Schumm, and John M. Knobloch

Department of Chemistry, Eastern Illinois University, Charleston, Illinois 61920, U.S.A.

4-(*N,N*-Dimethylamino)pyridine (DMAP) promotes the quantitative rearrangement of benzofuranone-derived enol carbonates to the corresponding carbon-acylated isomers.

Regioselective carbon acylation of enolates, especially those highly delocalized, is often a difficult task in synthetic chemistry, since the kinetically-formed oxygen-acylated product usually predominates.¹ We now report a novel method for carbon acylation in the benzofuranone system, which involves a quantitative rearrangement of the initially-formed enol carbonate to its carbon-acylated isomer, catalysed by 4-(*N,N*-dimethylamino)pyridine (DMAP).

The benzofuranones possess a wide spectrum of pharmacological activity² and so are frequent synthetic targets.³ In the course of a project aimed at the synthesis of potential

antineoplastic agents, we were faced with the preparation of (**1**; R = Et), a 3,3-disubstituted 2(3*H*)-benzofuranone derivative. Accordingly, 3-phenyl-2(3*H*)-benzofuranone (**2**) was prepared *via* a literature procedure,^{3a} deprotonated with

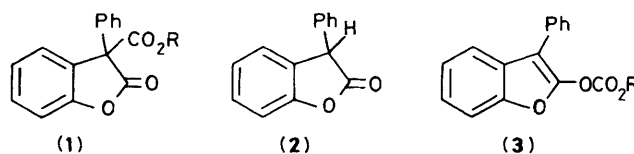


Table 1.^a

(2)	NaH-DMF, ROCOCl	(3)	DMAP, CH ₂ Cl ₂	(1)
	% Yield ^b of (3)		% Yield ^{b,d} of (1)	
R		B.p./°C ^c		M.p./°C
Me	77.6	143—150	87.5	68—70
Et	89.0	187—189	90.0	72—73
Pr ⁿ	87.5	185—187	83.0	89—90
Bu ⁿ	74.9	175—179	87.9	154—156(b.p.) ^c

^a All compounds exhibited appropriate spectral characteristics and gave satisfactory C,H combustion analyses. ^b Yields represent purified compounds. ^c All boiling points were obtained at 0.8 Torr. ^d Yields of crude product were approximately quantitative.

sodium hydride in dimethylformamide (DMF),⁴ and the resulting green-brown enolate treated with an excess of ethyl chloroformate. N.m.r. analysis revealed a mixture comprised almost entirely of enol carbonate (3; R = Et), arising from O-acylation.

Variation of many reaction conditions (solvent, temperature, reagent stoichiometry)⁵ did not affect the propensity for oxygen acylation. However, addition of a catalytic amount of DMAP⁶ to a methylene chloride solution of (3) caused a *quantitative rearrangement* to give the desired C-acylated ester (1). The migration, which was not exothermic, required only two minutes and was easily monitored by the intense deep-blue colouration accompanying the reaction.

Examination of several other alkyl chloroformates has thus far revealed this reaction to be general. The results are summarized in Table 1. In a typical reaction, a 10% solution (50 ml) of pure enol carbonate in methylene chloride is treated with *ca.* 20 mg of DMAP, instantly causing the characteristic deep-blue colour. After 1—2 minutes, the colour fades, indicating completion. Workup entails merely washing with 1% hydrochloric acid to remove catalyst followed by solvent removal. A single distillation or recrystallization affords the product in analytical purity.

Although dimethylaminopyridine is a commonly used catalyst for a wide variety of acylation reactions,⁶ its potential

for carbon acylation is essentially unexplored.⁷ The catalytic activity of DMAP is known to involve an acylated pyridinium intermediate;⁸ this is likely to be operative in the present case as well. It is noteworthy that inclusion of DMAP in the acylation reaction mixture causes direct carbon functionalization to (1); thus, either oxygen or carbon acylation is possible in a single step.

We thank Dr. William Szabo for valuable assistance at the inception of this project, and the Council on Faculty Research of Eastern Illinois University for partial financial support.

Received, 15th May 1986; Com. 654

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