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

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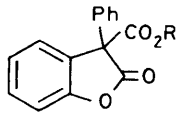
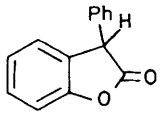
4-(*N,N*-Dimethylamino)pyridine (DMAP) promotes the quantitative rearrangement of benzofuranone-derived enol carbonates to the corresponding carbon-acylated isomers.

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).

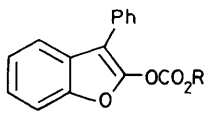
The benzofuranones possess a wide spectrum of pharmacological activity[2] and so are frequent synthetic targets.[3] In the course of a project aimed at the synthesis of potential antineoplastic agents, we were faced with the preparation of (**1**; R = Et), a 3,3-disubstituted 2(3*H*)-benzofuranone derivative. Accordingly, 3-phenyl-2(3*H*)-benzofuranone (**2**) was prepared *via* a literature procedure,[3a] deprotonated with



(1)



(2)



(3)

Table 1.[a]

(2)	NaH–DMF, ROCOCl	(3)	DMAP, CH_2Cl_2	(1)
R	% Yield[b] of (3)	B.p./°C[c]	% Yield[b,d] of (1)	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 stoicheiometry)[5] did not affect the propensity for oxygen acylation. However, addition of a catalytic amount of DMAP[6] 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.

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