4-(Dimethylamino)pyridine as a Catalyst for Carbon Acylation. 2. Control of Carbon vs. Oxygen Acylation in Benzofuranones

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3-Phenylbenzofuranone (1), when deprotonated with sodium hydride and treated with excess chloroformates, generally affords products arising from oxygen acylation (enol carbonates 4). Such molecules, when treated with a catalytic quantity of 4-(dimethylamino)pyridine (DMAP, 6) in halogenated solvents, rearrange to the carbon-acylated isomers 3. These migrations are proposed to involve the intermediate of a carbonylated (dimethylamino)pyridinium species (10), which transfers the ester functionality from oxygen to carbon. Inclusion of DMAP in the acylation reaction mixture, however, leads to direct carbon acylation. Thus, complete regiocontrolled acylation of these substrates is attainable.

Introduction

A long-standing challenge in organic synthetic chemistry involves the regioselective acylation of enolate anions, and a large amount of work has been devoted to the exploration of conditions designed to effect preferential carbon or oxygen acylation. In general, carbon acylation is favored by acid chlorides (vs. anhydrides), divalent counterions (vs. alkali metals), diethyl ether as solvent (vs. dimethoxyethane), low temperature, and inverse addition of enolate to acid chloride. However, although these guidelines are useful for many molecules, the regioselectivity of enolate acylation is known to be extremely substrate-dependent, and it is known that with certain substrates, O-acylation competes or even predominates despite the use of conditions conducive to reaction at carbon. In particular, delocalized enolates, such as those derived from malonates and similar compounds, diacly acetic acid esters, etc., tend toward oxygen acylation as a consequence of the greater electron density on that atom. This kinetic acylation often affords the O-acylated isomer as the sole isolable product, despite utilization of the above-mentioned techniques that typically aid in guiding the incoming electrophile to carbon. On the other hand, even highly carbon-selective acylation reactions are frequently contaminated with the oxygen-functionalized isomer, often posing serious separation problems and always reducing reaction yields.

We recently reported a novel oxygen-to-carbon ester migration in the benzofuranone ring system mediated by 4-(dimethylamino)pyridine (DMAP). Enol carbonates derived from oxygen acylation with alkyl chloroformates were found to rearrange quantitatively to the corresponding carbon-acylated isomers upon treatment with a catalytic amount of DMAP: the conversion is accompanied by a transient, very deep blue coloration. Since that time, we have embarked upon a project aimed at probing the mechanism and extending the scope of this potentially very useful reaction. Benzofuranones comprise an important class of natural products with a wide spectrum of biological activity, and so are frequent synthetic targets. Thus, they have been the focus of our attention to

Reference 2a, pp 783-785.


date, and we herein report the details of this investigation.

Results and Discussion

This unique reaction was discovered during a synthetic program aimed at the preparation of various compounds for testing as potential antineoplastic agents. Our specific target compound was the ester lactone 3b, which we initially envisioned as the product of treating the enolate derived from 3-phenylbenzofuranone (1) with excess ethyl chloroformate. In fact, only the enol carbonate 4b arising from kinetic oxygen acylation was isolated, although a more polar trace impurity, later identified as the desired carbon-acylated isomer 3b, was detectable via thin-layer chromatography. Many reaction parameters, as outlined in the Introduction, were manipulated in an attempt to affect this propensity for oxygen acylation. Although in some cases the proportion of carbon-acylated product was raised to approximately 20-30%, we sought to define conditions wherein formation of the desired ester lactone was the predominant reaction pathway. These attempts all met with failure.

We were therefore delighted to discover that exposure of enol carbonate 4b in dichloromethane solution to a catalytic amount of DMAP resulted in the instantaneous production of an indigo blue/purple coloration which spontaneously disappeared within a few minutes; workup revealed that a quantitative rearrangement to the desired isomer 3b had occurred. These observations are summarized in Scheme I.

DMAP is well-established in synthetic chemistry as an extremely useful "hyper-nucleophilic" acylation catalyst, and thus is routinely employed to accelerate the acylation of oxygen, nitrogen, and other nucleophilic atoms. However, its potential utility in carbanion acylation reactions is essentially unexplored.

Our examination of this intriguing transformation indicates the rearrangement to be completely general in the benzofuranone system for ester functionalities introduced via chloroformates. For these molecules, with only one exception, oxygen acylation was the predominant reaction when carried out under all tested conditions; however, each resulting enol carbonate 4 isomerized rapidly to the carbon-acylated isomer 3 when treated with DMAP. In order to maximize the potential synthetic utility of the reaction, however, we also deemed it important to ascertain whether it was in fact necessary to effect such an isomerization as a separate step or if inclusion of DMAP in the acylation reaction mixture would lead directly to carbon acylation via a one-pot procedure. Our ultimate aim was, if the latter scenario were feasible, to develop conditions that would produce exclusive oxygen acylation (e.g., polar aprotic solvent, alkali metal cation), since the resulting enol carbonates are useful synthetic intermediates in their own right, but that would exhibit a complete reversal of regioselectivity upon inclusion of (dimethylamino)pyridine.

We were thus extremely gratified to discover that not only can carbon acylation be effected in a single step by simply incorporating DMAP into a reaction mixture, which alone promotes nearly exclusive oxygen acylation, but the chemical yield is higher than that obtained for the two-step process. The increase in chemical yield for these conversions was not particularly surprising in view of the reputation for enhancing most typical acylation reactions currently enjoyed by DMAP and its derivatives.

The general reaction sequences that comprised the current study are outlined in Scheme II. In all cases, both the one-step and two-step conversions were examined. The primary goals of this aspect of the investigation were to compare the efficiency of the two sequences in producing carbon-acylated products, to verify that the rearrangement reaction as a separate manipulation was viable for all substrates, and to determine if the blue color characteristic of alkyl ester migrations was a general phenomenon and would thus provide some insight into the mechanistic course of the migratory process.

3-Phenylbenzofuranone (1) was deprotonated with sodium hydride in dimethylformamide (DMF), according to a literature procedure. For the two-step reactions, the green-brown enolate was treated directly with an excess of the appropriate chloroformate. Following aqueous workup, the resulting enol carbonate 4 was purified via distillation and/or recrystallization and fully characterized. Dissolution in dichloromethane followed by treatment with DMAP effected the oxygen-to-carbon ester transfer reaction. The rearrangements were routinely monitored by TLC, the carbon-acylated compound being significantly more polar than the enol carbonate isomer. In some cases, reaction progress was followed by using NMR spectroscopy by carrying out the rearrangement in an NMR tube with deuteriochloroform as the solvent and recording the spectrum at short intervals. The methyl derivative 4a provided the clearest profile, as the time required for reaction completion could be accurately determined by observing the simultaneous disappearance of the enol carbonate methyl group (3.80 ppm) and appearance of the ester methyl group (3.72 ppm). FT-IR spectrophotometry also provided unambiguous differentiation of carbon- vs. oxygen-acylated products. The enol carbonates 4 typically exhibited a single characteristic carbonyl stretching band at ca. 1900 cm⁻¹, while the corresponding carbon-acylated isomers 3 exhibited two peaks at ca. 1815 (corresponding to the benzofuranone carbonyl) and 1745 (arising from the ester functionality) cm⁻¹. The single-step procedures entailed adding a catalytic amount of DMAP to the above enolate solution prior treatment with the chloroformate. Significantly, for the substrates exhibiting the transitory blue color upon rearrangement during a separate step (which was observed for all but one), a blue color was also visible at this point in spite of the brownish turbidity of

References cited therein.

(a) NaH, DMF, 25 °C; (b) CICO₂R; (c) DMAP, CH₃Cl₂, 25 °C; (d) DMAP.


(16) Prepared via a modification of the procedure outlined in ref 11a.


the reaction mixture. The obvious conclusion is that the same reactive intermediate is functioning here as in the rearrangement portion of our two-step procedure. This point will be addressed in more detail shortly.

The results of these experiments are summarized in Table I. With one exception, all of the chlorofromates tested gave essentially exclusive oxygen acylation when DMAP was not employed. The corresponding C-acylated isomers were detectable via TLC; however, attempts to employ NMR analysis to quantify the isomer ratio failed due to the extremely minute amounts of carbon-acylated material formed. Vinyl chlorofromate (entry 9) was anomalous in that nearly exclusive carbon acylation occurred directly without the intervention of DMAP catalysis, although a trace of enol carbonate was visible upon TLC analysis. The identity of the impurity as the O-acylated isomer 4f was surmised from the observation that treatment of the product mixture in dichloromethane solution with DMAP caused the disappearance of the trace spot on TLC with an accompanying marked increase in resolution of the infrared and NMR spectra.

The rearrangement reactions typically required less than 2 min, and in no case could residual enol carbonate be detected. Interestingly, the appearance of color during these reactions was not a prerequisite for success. The enol carbonate formed by using phenyl chlorofromate developed no color at all when treated with DMAP, although the reaction proceeded to completion in a timeframe consistent with our other rearrangements.

The possible identity of the transient species responsible for the blue color observed in the majority of these rearrangements is intriguing. Acylation reactions employing acid chlorides (5, X = Cl) or anhydrides (5, X = O₂CR) and catalyzed by DMAP (as well as by pyridine or other derivatives such as the commercially available 4-pyrrolidinopyridine) are known to proceed via acylation of the pyridine ring in 6 to afford a highly reactive pyridinium species (e.g., 7), as outlined in Scheme III. The entity then undergoes facile nucleophilic attack (8 = O, S, N, etc.), affording the acylated product 9 and regenerating the catalyst.

We propose that a similar species is operative in our rearrangement reaction; the overall sequence of events is depicted in Scheme IV. Although oxygen acylation (affording enol carbonate 4) is kinetically favored as a consequence of the greater electron density on and thus greater nucleophilicity of that atom, equilibrating conditions should favor carbon functionalization due to the greater exothermcity associated with the formation of a carbon–carbon bond (the conjugative stability typically associated with $\beta$-diesters is obviated by the presence of the 3-phenyl substituent in the current cases). Nucleophilic attack by DMAP (6) on the enol carbonate 4 carbonyl group would afford the acylated pyridinium ion 10, expelling the highly delocalized 3-phenylbenzofuranone enolate anion 2 in the process. Subsequent attack by the enolate carbon atom (cf. structure 2b) would afford the carbon-functionalized isomer 3.

The characteristic coloration is rationalized as follows. From our experiments, we know that the enolate 2 derived from 3-phenylbenzofuranone is greenish. Since 1-(ethoxy)carbonyl)-4-(dimethylamino)pyridinium chloride (10, R = Et) is known to be colorless, the obvious implication is that the deep blue color observed during the rearrangement reaction must be due to an interaction between these two entities, probably through the formation of a charge-transfer (or donor-acceptor) complex. Such complexes between electron-rich and electron-deficient aromatic systems are well-precedented.

Interestingly, the free radical generated via thermolysis of the dimer of 1 (2,2'-dioxo-3,3'-diphenyl-2,2',3,3'-tetrahydrobenz[i]furan-3-yl, 11) is also deep blue. How-

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Table I. Chemical Yields for Scheme II, Including a Comparison of the Efficiency of the One-Step vs. Two-Step Carbon Acylation Reactions

<table>
<thead>
<tr>
<th>entry</th>
<th>chloro-</th>
<th>1 → 4</th>
<th>overall yield</th>
<th>two-step</th>
<th>one-step</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (a)</td>
<td>methyl</td>
<td>77.8</td>
<td>85.7</td>
<td>67.9</td>
<td>72.7</td>
</tr>
<tr>
<td>2 (b)</td>
<td>ethyl</td>
<td>89.0</td>
<td>90.0</td>
<td>80.1</td>
<td>88.3</td>
</tr>
<tr>
<td>3 (c)</td>
<td>n-propyl</td>
<td>87.5</td>
<td>83.0</td>
<td>72.6</td>
<td>76.5</td>
</tr>
<tr>
<td>4 (d)</td>
<td>n-butyl</td>
<td>74.9</td>
<td>96.0</td>
<td>71.9</td>
<td>76.3</td>
</tr>
<tr>
<td>5 (e)</td>
<td>sec-butyl</td>
<td>88.2</td>
<td>91.3</td>
<td>80.5</td>
<td>92.2</td>
</tr>
<tr>
<td>6 (f)</td>
<td>benzyl</td>
<td>85.2</td>
<td>86.4</td>
<td>73.6</td>
<td>81.3</td>
</tr>
<tr>
<td>7 (g)</td>
<td>phenyl</td>
<td>64.0</td>
<td>89.5'</td>
<td>29.5</td>
<td>79.4</td>
</tr>
<tr>
<td>8 (h)</td>
<td>allyl</td>
<td>94.0</td>
<td>63.5</td>
<td>60.0</td>
<td>74.8</td>
</tr>
<tr>
<td>9 (i)</td>
<td>vinyl</td>
<td>d</td>
<td>d</td>
<td>d</td>
<td>55.0</td>
</tr>
</tbody>
</table>

All yields refer to purified material. Accompanied by blue coloration except where noted. Rearrangement was colorless. Direct carbon acylation was observed.

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Table II. Solvent Dependency of the DMAP-Mediated Rearrangement of Enol Carbonate 4a to 3a

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Dielectric Constant&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reaction Time (min)</th>
<th>Reaction Color</th>
<th>Precipitate Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>dimethylformamide</td>
<td>37</td>
<td>2.00</td>
<td>deep purple</td>
<td>no ppt</td>
</tr>
<tr>
<td>dichloromethane</td>
<td>9.1</td>
<td>1.00</td>
<td>purple</td>
<td>no ppt</td>
</tr>
<tr>
<td>chloroform</td>
<td>4.8</td>
<td>0.50</td>
<td>purple</td>
<td>no ppt</td>
</tr>
<tr>
<td>diethyl ether</td>
<td>4.5</td>
<td>no reaction&lt;sup&gt;b&lt;/sup&gt;</td>
<td>purple</td>
<td>no reaction&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>hexane</td>
<td>1.9</td>
<td>no reaction&lt;sup&gt;b&lt;/sup&gt;</td>
<td>purple</td>
<td>no reaction&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>b</sup>Colorless supernatant.

ever, the intermediacy of any free radical species in the 4 to 3 rearrangement reactions is doubtful in light of the proven involvement of DMAP and the accompanying lack of any literature documentation for its utilization in radical reactions.<sup>23,24</sup> Additionally, no CIDNP effects were encountered in the experiments wherein the rearrangement reactions were monitored via nuclear magnetic resonance.<sup>25</sup> The intermediacy of a polar donor-acceptor ion pair is also supported by the marked solvent-dependence of the rearrangement. Solutions of methyl enol carbonate 4a were prepared in several solvents (10% w/v) and treated with a catalytic amount (ca. 10 mol %) of DMAP. Reactions were followed by disappearance of the blue color, while TLC was employed to verify reaction completion. The results are outlined in Table II and indicate an interesting trend. The halogenated solvents performed most satisfactorily, with chloroform allowing a substantially faster rearrangement than the more polar dichloromethane. Dimethylformamide slowed the reaction considerably, consistent with solvation and thus partial separation of the ion pair (although evidently insufficient to negate the charge-transfer phenomenon). Examination of nonpolar solvents relatively incapable of maintaining ionic species in solution (diethyl ether, hexane) provided the most conclusive evidence. In both cases, addition of DMAP resulted in the precipitation of a purple, highly crystalline material, with the supernatant liquid remaining clear and colorless. Intrigued that this precipitate might consist of the actual ion pair 2-10<sup>26</sup> (Scheme IV), we combined equimolar amounts of enol carbonate 4a and DMAP in hexane and isolated the precipitated material under anhydrous conditions. Dissolution of the crystals in chloroform afforded a deep blue solution that quickly decolorized and was found to contain solely the carbonacylated isomer 3a (in addition to DMAP). This precipitate proved to be extraordinarily air-sensitive; attempts at rigorous analysis are in progress and will be reported elsewhere when complete.

### Conclusion

In summary, we have developed a new method for regioselective acylation in the benzofuranone ring system. Whereas conventional acylation techniques afford mainly oxygen-functionalized products, exposure of these mate-

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<sup>24</sup> A referee has suggested that the blue color could be due to an equilibrium mixture of the pyridinium cation/enolate anion salt and a radical pair formed by the complete transfer of an electron from the anion to the cation. This possibility will be considered as our investigation into the phenomenon continues.

<sup>25</sup> The absence of a CIDNP effect does not conclusively rule out free-radical involvement, but such cases are very unusual. See: Glarum, S. H. In Chemically Induced Magnetic Polarization; Lepley, A. R., Closs, G. L., Eds.; John Wiley and Sons: New York, 1973.

<sup>26</sup> Such molecular complexes have been isolated previously. See: Prout, C. K.; Wright, J. D. Angew. Chem., Int. Ed. Engl. 1968, 7, 659.

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### Experimental Section

All reactions were carried out under an atmosphere of nitrogen, unless otherwise specified. Glassware was routinely oven-dried at 120 °C for a minimum of 4 h and then was assembled under a nitrogen stream. Anhydrous solvents were obtained by distillation, immediately prior to use, from sodium benzophenone ketyl (tetrahydrofuran), barium oxide (disopropylamine, dimethylformamide), or sodium (toluene). Infrared spectra were obtained on a Nicolet Model 20 DXB Fourier transform or a Perkin-Elmer Model 70 spectrophotometer; absorption maxima are reported in wavenumbers (cm<sup>-1</sup>) and, in the case of the latter instrument, were standardized by reference to the 1601-cm<sup>-1</sup> peak of polystyrene. Proton nuclear magnetic resonance spectra were recorded on a Varian T-60 instrument. All samples were measured as solutions in deuteriochloroform (CDCl<sub>3</sub>) or dimethyl-d<sub>6</sub> sulfoxide (DMSO). Chemical shifts are reported downfield from tetramethylsilane (TMS) in parts per million of the specified solvent as eluent; visualization was effected by either ultraviolet light or by charring with phosphomolybdic acid. Preparative column chromatography employed Merck silica gel 60 (230–400-mesh ASTM). Combustion microanalyses were performed by Galbraith Laboratories, Knoxville, TN.

### General Procedure for O-Acylation of 3-Phenylbenzofuranone

To a 50-mL, three-necked flask, fitted with a magnetic stirring bar, rubber septum, thermometer, and nitrogen inlet, was charged 0.8 g (27 mmol) of sodium hydride (80% dispersion in oil) that was washed with three 5-mL portions of hexane. A 13-mL portion of dimethylformamide (DMF) was cooled with stirring and cooling in an ice bath. To the stirring suspension was added 4.2 g (20 mmol) of 3-phenylbenzofuranone in small portions at 20–30 °C as foaming allowed. The slurry was stirred for 90 min, becoming turbid and green, and a chloroformate (22 mmol) was added over a period of several minutes. The heterogeneous mixture was stirred overnight at room temperature and poured into 200 mL of water, and the mixture was thoroughly extracted with ether. The consolidated extracts were washed with water and brine, dried over anhydrous magnesium sulfate, and filtered, and the filtrate was concentrated in vacuo. The products were distilled to remove nonvolatile impurities but were not rigorously purified prior to rearrangement.

**Carboxylic acid, methyl 3-phenylbenzofur-2-yl ester (4a)**

This ester was prepared from methyl chloroformate and was isolated in 77% yield following bulb-to-bulb distillation (145–150 °C/0.05 mm) as a viscous, clear, colorless oil: IR (neat) 2970, 1800, 1650, 1475, 1220, 1200 cm<sup>-1</sup>; NMR (CDCl<sub>3</sub>) 8 8.00–7.20 (m, 9 H, Ar H), 3.80 (s, 3 H, CH<sub>3</sub>); TLC (silica gel; CH<sub>2</sub>Cl<sub>2</sub>) R<sub>f</sub> 0.66.

**Carboxylic acid, ethyl 3-phenylbenzofur-2-yl ester (4b)**

This ester was prepared from ethyl chloroformate and was isolated in 89.0% yield following bulb-to-bulb distillation (115–125 °C/0.02 mm) as a viscous, clear, colorless oil: IR (neat) 2972, 1795, 1755, 1642, 1481, 1204, 1199 cm<sup>-1</sup>; NMR (CDCl<sub>3</sub>) 8 8.00–7.20 (m, 9 H, Ar H), 3.90 (q, 2 H, -OCH<sub>2</sub>-), 2.48 (t, 3 H, CH<sub>3</sub>); TLC (silica gel; CH<sub>2</sub>Cl<sub>2</sub>) R<sub>f</sub> 0.76.

**Carboxylic acid, n-propyl 3-phenylbenzofur-2-yl ester (4c)**

This ester was prepared from propyl chloroformate and was isolated in 87.5% yield following bulb-to-bulb distillation (120–128 °C/0.02 mm) as a viscous, clear, light yellow oil: IR (neat) 2970, 1800, 1650, 1575, 1473, 1202, 1199 cm<sup>-1</sup>; NMR (CDCl<sub>3</sub>) 8 8.05–7.13 (m, 9 H, Ar H), 3.95 (t, 2 H, -OCH<sub>2</sub>-), 1.15 (m, 2 H, -CH<sub>2</sub>-), 0.83 (t, 3 H, CH<sub>3</sub>); TLC (silica gel; CH<sub>2</sub>Cl<sub>2</sub>) R<sub>f</sub> 0.66.
Carbonic acid, n-butyl 3-phenylbenzofur-2-yl ester (4d) was prepared from n-butyl chloroformate and was isolated in 74.9% yield following bulb-to-bulb distillation (152–141 °C/0.03 mm) as a viscous, clear, colorless oil: IR (neat) 2970, 1800, 1600, 1518, 1485, 1380 cm⁻¹; NMR (CDCl₃) δ 8.00–7.20 (m, 9 H, Ar H), 5.29 (s, 2 H, -CH₂), 4.15 (t, 2 H, -OCH₂), 2.00–1.40 (m, 4 H, -CH₂CH₂-), 1.05 (t, 3 H, CH₃); TLC (silica gel; CH₂Cl₂) Rₖ 0.68.

Carbonic acid, sec-butyl 3-phenylbenzofur-2-yl ester (4e) was prepared from sec-butyl chloroformate and was isolated in 85.2% yield following bulb-to-bulb distillation (190–196 °C/0.08 mm) as a viscous, clear, colorless oil: IR (neat) 2970, 1805, 1379 cm⁻¹; NMR (CDCl₃) δ 8.00–7.20 (m, 9 H, Ar H), 5.30 (s, 2 H, -CH₂), 2.24–1.65 (m, 1 H, CHMe₂), 1.11 (d, 6 H, CH₃); TLC (silica gel; CH₂Cl₂) Rₖ 0.74.

Carbonic acid, benzyl 3-phenylbenzofur-2-yl ester (4f) was prepared from benzyl chloroformate and was isolated in 95.4% yield following bulb-to-bulb distillation (125–130 °C/0.05 mm) as a yellow solid: mp 89-90 °C; IR (neat) 1718, 1474, 1383, 1233, 1065 cm⁻¹; NMR (CDCl₃) δ 8.00–7.20 (m, 14 H, Ar H), 5.64 (m, 1 H, -CH=), 5.08 (m, 2 H, =CH₂), 4.56 (br d, 2 H, -OCH₂); TLC (silica gel; CH₂Cl₂) Rₖ 0.68.

Carbonic acid, allyl 3-phenylbenzofur-2-yl ester (4h) was prepared from allyl chloroformate and was isolated in 96.8% yield following bulb-to-bulb distillation (115–116 °C/0.03 mm) as a deep yellow oil: IR (neat) 1717, 1474, 1383, 1233, 1065 cm⁻¹; NMR (CDCl₃) δ 7.60–7.10 (m, 9 H, Ar H), 5.28 (m, 2 H, -CH₂), 4.61 (br d, 2 H, -OCH₂); TLC (silica gel; CH₂Cl₂) Rₖ 0.75.

Carbonic acid, 2,3-Dihydro-2-oxo-3-phenyl-3-benzofurancarboxylic acid, vinyl ester (3i) was prepared from allyl chloroformate and was isolated in 94.1% yield following bulb-to-bulb distillation (125–130 °C/0.02 mm) as a yellow oil: mp 63–64 °C; IR (KBr) 1818, 1745, 1646, 1615 cm⁻¹; NMR (CDCl₃) δ 8.00–7.20 (m, 9 H, Ar H), 4.95 (s, 2 H, -CH₂); TLC (silica gel; CH₂Cl₂) Rₖ 0.80.

Carbonic acid, phenyl 3-phenylbenzofur-2-yl ester (4g) was prepared from phenyl chloroformate and was isolated in 91.5% yield following bulb-to-bulb distillation (125–135 °C/0.40 mm) as a clear, colorless oil: IR (neat) 1811, 1798, 1744, 1380, 1220, 1066 cm⁻¹; NMR (CDCl₃) δ 8.02–7.21 (m, 9 H, Ar H), 4.12 (d, 2 H, OCH₂), 2.21–1.71 (m, 1 H, CHMe₂), 1.05 (d, 6 H, CH₃); TLC (silica gel; CH₂Cl₂) Rₖ 0.59. Anal. Calc'd for C₉H₈O₄: C, 71.92; H, 4.64.

Carbonic acid, butyl 3-phenylbenzofur-2-yl ester (4d) was prepared from allyl chloroformate and was isolated in 96.8% yield following bulb-to-bulb distillation (115–116 °C/0.03 mm) as a light orange oil: IR (neat) 1717, 1474, 1383, 1233, 1065 cm⁻¹; NMR (CDCl₃) δ 8.09–7.18 (m, 9 H, Ar H), 5.81 (m, 1 H, -CH=), 5.28 (m, 2 H, -CH₂), 4.61 (br d, 2 H, -OCH₂); TLC (silica gel; CH₂Cl₂) Rₖ 0.68.

Carbonic acid, 2,3-Dihydro-2-oxo-3-phenyl-3-benzofurancarboxylic acid, vinyl ester (3i) was isolated in 83.0% yield following bulb-to-bulb distillation (92–94 °C/0.05 mm) as a clear, colorless oil which solidified after standing for several days to a white, crystalline solid: mp 114–117 °C; IR (KBr) 1817, 1745, 1485, 1383, 1220, 1066 cm⁻¹; NMR (CDCl₃) δ 7.60–7.00 (m, 9 H, Ar H), 4.15 (t, 2 H, OCH₂), 1.32 (m, 4 H, CH₂CH₂), 0.88 (t, 3 H, CH₃); TLC (silica gel; CH₂Cl₂) Rₖ 0.77. Anal. Calc'd for C₉H₈O₄: C, 72.38; H, 5.44. Found: C, 72.39; H, 5.75.

Solvent-Dependency Studies. To a dry 10-mL test tube was added 100 mg (0.37 mmol) of carbonic acid, methyl 3-phenylbenzofur-2-yl ester (3a) along with 1.0 mL of the appropriate...
solvent; dissolution was effected by swirling. A 10-mg portion of DMAP was added and the test tube was shaken. The time necessary for complete dissolution of color was recorded and the appearance of any precipitate noted.

Isolation of the 2–10 Ion Pair. To a 50-mL, three-necked flask, fitted with a magnetic stirring bar, rubber septum, and nitrogen inlet, was charged 400 mg (1.50 mmol) of carbonic acid, methyl 3-phenylbenzofur-2-yl ester (4a) and 30 mL of hexane. To the stirring solution was added 185 mg (1.50 mmol) of 4-(dimethylamino)pyridine, resulting in the immediate precipitation of a purple, highly crystalline solid (the hexane supernatant remained clear and colorless). The hexane was removed via syringe while maintaining a nitrogen atmosphere, leaving 550 mg (94%) of the C-acylated isomer 3a. The clear, pale yellow solution was worked up in the general procedure for rearrangement reactions (see above) to afford 364 mg (94%) of 2,3-dihydro-2-oxo-3-phenyl-3-benzofurancarboxylic acid, methyl ester (3a), exhibiting identical physical and spectral characteristics as material prepared in earlier experiments.

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Stereoselective Synthesis of Vinylcyclopropanes via Palladium-Catalyzed Reactions

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Vinylcyclopropanes were synthesized in a stereocontrolled manner from 1-acetoxy-4-chloro-2-alkenes. A stereospecific palladium-catalyzed substitution of the chloro group by dimethyl malonate anion and subsequent palladium-catalyzed cyclization afforded the vinylcyclopropanes in about 70% overall yield. In the cyclization Pd(dppe)2, Pd(dba)2, dppe, or Pd(OAc)2/dppe was used as catalyst. The best result was obtained with Pd(OAc)2/dppe. It was found that the cyclization to vinylcyclopropane is reversible and under prolonged reaction time dienylmalonates are formed. This allows control of the relative stereochemistry between the cyclopropane ring and the double bond. In addition bicyclic vinylcyclopropanes are available by this approach.

Vinylcyclopropanes are a class of compounds that has attracted considerable interest among organic chemists. There are many naturally occurring vinyl cyclopropanes, e.g. carenes, sesquicarenes, sirenine, dictyopterenes, pyrethroids, etc. In addition, vinylcyclopropanes are important synthetic intermediates. As a consequence a number of methods for their preparation have been developed.4,6,4

One of us has recently developed a method for the preparation vinylcyclopropanes from 2-alkene-1,4-diol monoacetates utilizing palladium catalysis (eq 1).4 We would now like to extend this methodology by utilizing 1-acetoxy-4-chloro-2-alkenes as starting materials (eq 2).

This allows control of the relative stereochemistry between the cyclopropane ring and the double bond. In addition, bicyclic vinylcyclopropanes are available by this approach.

In the original approach (eq 1)4 the starting material was obtained either from hydrogenation of a 2-alkyne-1,4-diol or from condensation of an 1-alkyn-3-ol derivative with an aldehyde (or ketone) and subsequent hydrogenation. This, when both carbons bearing the oxygen atoms are chiral, a mixture of two diastereomers is formed. By the use of chloro acetates as starting materials (eq 3) this problem can be overcome. These chloro acetates are chiral, a mixture of two diastereomers is formed. By the use of chloro acetates as starting materials (eq 4) this problem can be overcome. These chloro acetates are prepared from the appropriate conjugated diene in a ste-