0,0-Dimethylacrylophenones: BF3.Et2O-POCl3 catalysed acylation of phenols using 0,0-dimethylacrylic acid

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Boron trifluoride etherate - phosphoryl chloride reagent is a useful reagent for the condensation between phenols and 0,0-dimethylacrylic acid. The main products are acrylophenones. But surprisingly hydroquinone gives mono and diacrylates.

Preparation and evaluation of substituted 2,2-dimethylchromenes is receiving the attention of many chemists and agrochemists as potential compounds showing antijuvenile hormone (AJH) activities in insects. As a consequence of this attractive bioactivity, several methods for their synthesis have been reported. The most straightforward of these procedures is the condensation of phenols with 0,0-dimethylacrylic acid (DMAA) in the presence of an acid catalyst (HF3, SbCl5, BF3.C6H5NO2, ZnCl2-POCl3, CH3SOOH-POCl3, PPAP4, AlCl3-POCl3, TFA) to afford 2,2-dimethylchromanones which by reduction and dehydration are readily converted to chromenes. 2-Hydroxy-0,0-dimethylacrylophenones are the intermediates in this sequence. During the last ten years a number of hydroxy(methoxy) acrylophenones have been identified as natural products co-occurring with chromanones9,10. Though the biological role of these acrylophenones is not yet known, their role as plant defence compounds against insects has been indicated11. The synthesis of acrylophenones is, therefore, of interest. 2-Hydroxyacrylophenones are not obtainable during acid-catalysed condensation between dimethylacrylic acid and a phenol, the chief product is 2,2-dimethylchromanone, and also by ring opening of chromanones12. In an effort towards developing a method for the synthesis of phenolic acrylophenones, we investigated a milder Friedel-Crafts catalyst BF3.Et2O in combination with POCl3 as acylating agent13. An equimolar quantity of dimethylacrylic acid and the phenol was added to a reagent comprising two fold excess of phosphoryl chloride and four fold excess of BF3.Et2O and stirred at room temperature for 6-8 hr. The reaction was worked up in the usual manner and products were isolated. The condensation reactions were carried out at 50-60°C where the reaction was too slow at room temperature. Identification of the products was based on comparison with reference samples, literature data, spectra and chemical tests. The results are shown in Table 1.

The reagent comprising of BF3.Et2O - POCl3 is most efficient for the condensation between reactive phenols (e.g. resorcinol, phloroglucinol) and DMAA, the chief product being acrylophenone. 2,2-Dimethylchromanones were isolated as minor compounds in some cases. Other possible products such as dihydrocoumarin, indanone were not formed. Surprisingly, phenol gave the acrylate ester 9 (10%) as the only product. Orcinol gave the acrylophenone 4 as the only isolable product. Methyl ethers were less reactive as compared to free phenols. Demethylation of 2-methoxy group in 2-methoxycoumarone was observed as a side reaction which was often noted in many cases. The reagent system was not applicable to substrates like hydroxyacetophenone, hydroxybenzoic acid and hydroxybenzoates. Saturated acids like phenylacetic acid, 3-methylbutyric acid, 3-phenoxypropionic acid (intramolecular cyclisation) did not react.

The condensation between resorcinol and cinnamic acid was briefly examined and the results are interesting. The reaction between resorcinol and unsubstituted cinnamic acid gave 2',4'-dihydroxycoumarone10 (45%) but 4-methoxycinnamic acid gave exclusively 7-hydroxy-4-(4'-methoxyphenyl)-3,4-dihydrocoumarin 11 (90%)14. In a similar manner reaction between 0-methylcinnamic acid gave 2',4'-dihydroxy-0-methylchalcone12 (85%) (Scheme 1). Similar re-
### Table I—Reaction of phenols with DMAA using BF₃·Et₂O-POCl₃

<table>
<thead>
<tr>
<th>Phenol/Methyl ether</th>
<th>Reaction period (hr)</th>
<th>Product (compd No.)</th>
<th>Ref.</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resorcinol</td>
<td>5</td>
<td>1-(2,4-(OH)₂phenyl)-3-Me-2-butenone-1 1</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>Pyrogallol</td>
<td>6</td>
<td>1-(2,3,4-(OH)₃phenyl)-3-Me-2-butenone-1 2</td>
<td>18</td>
<td>75</td>
</tr>
<tr>
<td>Phloroglucinol</td>
<td>5</td>
<td>5,7-(OH)₂-2,2-(Me)₂-chromanone 3</td>
<td>18</td>
<td>90</td>
</tr>
<tr>
<td>Orcinol</td>
<td>4</td>
<td>1-(2,4-(OH)₂-6-(Me)phenyl)-3-Me-2-butenone-1 4</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>1,3-(OMe)₂-benzene</td>
<td>24</td>
<td>1-(2-OH)-4-(OME)phenyl)-3-Me-2-butenone-1 5i</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>1,2,4-(OMe)₃-benzene</td>
<td>24</td>
<td>1-(2-OH)-4,5-(OME)₂phenyl)-3-Me-2-butenone-1 6i</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>1,2,3,5-(OMe)₄-benzene</td>
<td>24</td>
<td>1-(2,3,4,6-(OME)₄phenyl)-3-Me-2-butenone-1 7i</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>3,4,5-(OMe)₃-phenol</td>
<td>12</td>
<td>1-(2-OH)-3,4,5-(OME)₃phenyl)-3-Me-2-butenone-1 8</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>

(a) Room temperature, 25 °C; (b) 50-60 °C; (c) Yield refers to isolated yield.

![Scheme I](attachment:image.png)

The reagents BF₃·Et₂O and POCl₃ individually are ineffective compared to the combined reagent. The mechanism of the reaction catalysed by BF₃·Et₂O-POCl₃ is not clear. The active acylating species may...
be RCO.OPOCl₂. There is a possibility of Fries migration of a preformed phenolic ester.

**Hydroquinone-DMAA condensations**

The condensation between DMAA and hydroquinone is of particular interest and deserves special mention because (i) acrylophenone 13 is a natural product isolated from *Nama Johnstonii*¹⁶, (ii) the reaction was little investigated. Fries rearrangement of the bis-dimethylacrylate to the dihydroxyacrylophenone 13 has been reported unsuccessful¹⁷ (AlCl₃, CS₂, Δ). Subsequently, the acrylophenone was prepared by Friedel-Crafts reaction between hydroquinone dimethyl ether and acryloyl chloride followed by demethylation. This, perhaps, is the only reported synthesis of 2,5-dihydroxy-β,β-dimethylacrylophenone¹⁷.

In the present study, the direct condensation between 1,4-dihydroxybenzene and DMAA was investigated using (i) BF₃·Et₂O-POCl₃, (ii) TFA and (iii) ZnCl₂-POCl₃. The reagents (i) and (ii) gave a mixture of products consisting of the monoester 14 and the diester 15 in 70% and 5% yields respectively. They were separated by column chromatography. The structure of the products were readily established by IR, ¹H NMR and MS spectra and chemical tests and also by comparison with an authentic sample in the case of the diester 15 (pyridine-β,β-dimethylacryloyl chloride). The reaction using ZnCl₂-POCl₃ gave along with the esters 14 and 15, one more product in 15% yield. Its structure was established as 4,4,9,9-tetramethyl-3, 4, 8, 9-tetrahydro-2H,7H-benzo[1,2-b : 5,4-b']dipyran-2,7-dione 16. Neither the 6-hydroxy-2,2-dimethylchromanone nor the acrylophenone was formed (Scheme II).

Ester formation seems to be the preferred reaction in the case of hydroquinone and also with other hydroquinones (unpublished work).

**Experimental Section**

**General.** Melting points were taken in open capillaries in a sulphuric acid bath. IR spectra were recorded in KBr on a Shimadzu IR-435 spectrophotometer. ¹H NMR on a Hitachi R-699 FT NMR (60 MHz), ¹³C NMR spectra on a Varian XL-300 (75 MHz) spectrophotometer in CDCl₃ using TMS as internal standard. Mass spectra were recorded on a Jeol JMX-DX 300 (70 eV) spectrometer. Column chromatography was carried out over silica gel (60-120 mesh). BF₃·Et₂O was distilled over CaH₂. POCl₃ was used as supplied (E. Merck). Anhydrous zinc chloride was fused before use.

**General procedure.** POCl₃ (0.1 mole) and BF₃·Et₂O (0.2 mole) were mixed at 0°C. DMAA (0.05 mole) was then added to it and the mixture stirred for

![Scheme II](image-url)
coumarin, 11: mp 178-79°C (ethanol); IR: 3.0 (d, 2H, H, and H$_2$) 3.9 (s, 3H, OCH$_3$). 4.1 (t, unsym., H$_3$, H$_2$). 6.3-6.7 (6, 7H, Ar-H) ppm; MS: m/z 270 (M$^+$, 100%), 252 (10) 242 (100), 213 (68), 198 (46), 197 (100), 184 (28), 163 (19), 128 (30), 121 (18), 107 (15), 91 (13), 85 (7), 77 (18), 57 (16).

2',4'-Dihydroxy-$eta$-methylchalcone, 12: Yellow oil; IR (film): 3415, 3110, 2875, 1361, 1575 cm$^{-1}$. 1H NMR: δ 1.95 (s, 3H, CH$_3$), 4.63-6.56 (m, 7H, C-3', C-5' and Ar-H) ppm; MS: m/z 274 (M$^+$, 13%), 192 (12), 149 (5), 110 (6), 111 (7), 83 (100), 71 (16), 55 (28).

Phenyl 1,4-bis-(3-methylbut-2-enolate), 14: mp 113-14°C (ethanol) (II$^+$, mp 115°C). IR: 3000, 1740, 1655, 1518, 1450 cm$^{-1}$. 1H NMR: δ 1.85 (s, 6H, 2 x CH$_3$), 2.09 (s, 6H, 2 x CH$_2$), 5.70 (m, 2H, 2 x CH = CMe$_2$), 6.9 (s, 4H, Ar-H) ppm; MS: m/z 274 (M$^+$, 13%), 192 (12), 149 (5), 110 (6), 111 (7), 83 (100), 71 (16), 55 (28).

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References

5. (c) Sekhover F, Jaszberenyi J C & Sekhover, Heterocycles, 27, 1988, 2595.
6. (c) Sekhover F, Jaszberenyi J C, Heterocycles, 38, 1994, 2099.
13 To the best of our knowledge the application of BF₃·Et₂O·POCl₃ as an acylation catalyst has not been reported.