Vinylphosphonium Salt Mediated Reaction between Alkyl Propiolates and Aminophenols or Hydroxyphenols

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Abstract: Addition of catechol to methyl propiolate or ethyl phenylpropiolate in the presence of Ph3P leads to methyl 2-(1,3-benzodioxol-2-yl)acetate or 3-(1-phenylmethylidene)-1,4-benzodioxin-2-one. 2-Aminophenols react with alkyl propiolates in the presence of Ph3P to produce a nearly 1:1 mixture of 3-methyl-2H-1,4-benzoxazin-2-one derivatives and methyl (E)-3-(2-aminophenoxy)-2-propenoates.

Keywords: alkyl propiolates, triphenylphosphine, hydroxyphenol, aminophenol, benzodioxol, 2H-1,4-benzoxazin-2-one, O-vinylation

Vinyl ethers of alcohols and phenols are well established monomers, building blocks and auxiliaries in organic synthesis, steadily expanding their scope of application.1–3 The O-alkylated phenols have numerous industrial applications, particularly in the production of dyes and agrochemicals.3–6 Recently, we described7 a convenient method for preparation of alkyl 2-arylacrylates and alkyl 3-aryloxypropenoates by nucleophilic conjugate addition of phenols to alkyl propiolates in the presence of triphenylphosphine (Ph3P). In this paper, we wish to extend that methodology using bifunctional reagents such as aminophenols and hydroxyphenols.

The reaction of catechol (2) with methyl propiolate (1) in the presence of Ph3P was carried out in dichloromethane. The colorless oil separated from the reaction mixture was identified as methyl 2-(1,3-benzodioxol-2-yl)acetate (3; Scheme 1).

Scheme 1

A possible mechanism for this transformation is proposed in Scheme 2. It is conceivable that the initial event is the formation of 1,3-dipolar intermediate 4 from Ph3P and the acetylenic compound, which is subsequently protonated by 2.7–10 Nucleophilic attack of the oxygen atom of the conjugate base of 2 on the vinylphosphonium cation 5 then produces the 1,3-dipolar intermediate 6, which is converted to 3, by elimination of Ph3P and cyclization (see Scheme 2).

When the same reaction was carried out with ethyl phenylpropiolate (7), 3-(1-phenylmethylidene)-1,4-benzodioxin-2-one 8 was obtained (Scheme 3).

The plausible mechanism proposed for formation of product 8 is similar to that shown in Scheme 2, except for the addition of the conjugate base of 2 to the vinylphosphonium cation, which leads to ylide 9. The intermediate 9 is converted to the 1,3-dipolar species 10 by [1,3]-H+ shift. Next, intermediate 10 is converted to 8 via the vinyl ether 11 by elimination of Ph3P and ethanol (see Scheme 4).

The reaction of 2-aminophenol (12) with 1 in the presence of Ph3P was carried out in dichloromethane. Two products were isolated from the reaction mixture and identified as...
3-methyl-2H-1,4-benzoxazin-2-one (13a) and methyl (E)-3-(2-aminophenoxy)-2-propenoate (14a; see Table 1).

A plausible mechanism for the formation of products 13a and 14a is shown in Scheme 5. The reaction starts from addition of Ph₃P to the electron-deficient acetylenic ester to form the zwitterionic intermediate 4, which is either subsequently protonated by the OH-acid 12 to produce vinylphosphonium cation 5a, or loses a methoxy group to give 5b. Then, addition of conjugate base of the OH-acid 12 to 5a or 5b produces 13a or 14a in nearly 1:1 ratio. Similar pathways can be proposed for formation of 13b–f and 14b–f.

The structures of compounds 13a–f and 14a–f were determined on the basis of their elemental analyses, mass spectra, ¹H and ¹³C NMR and IR spectroscopic data. Observation of two characteristic doublets with ³J_HH of about 12 Hz in the ¹H NMR spectra of 14a–f is consistent with O-vinylation of the aromatic ring and formation of alkyl (E)-aryloxy propenoates (14a–f). The ¹³C NMR spectra of 13a–f and 14a–f show distinct resonances in agreement with the proposed structures.

Under the same reaction conditions given for catechol, two products were isolated from the reaction mixture of resorcinol or hydroquinone with alkyl propiolates in the presence of Ph₃P (see Table 2). When 3- or 4-aminophenol...
nol was treated with ethyl propiolate in the presence of Ph₃P only the O-vinylation products were obtained (Table 2).

The presented reactions provide simple entries to the synthesis of methyl 2-(1,3-benzodioxol-2-yl)acetate (3), 3-alkyl-2H-1,4-benzoxazin-2-one derivatives 13a–f, and alkyl (E)-3-(aminophenoxy)-2-propenoates 14a–f, 27, and 28 of potential synthetic interest.

Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were measured on a Shimadzu IR-460 spectrometer. ¹H NMR and ¹³C NMR spectra were measured with a Bruker DRX-500 Avance instrument with CDCl₃ as solvent at 500.1 MHz and 125.7 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Alkyl propiolates, hydroxyphenols, aminophenols, and Ph₃P were obtained from Fluka and were used without further purification.

Preparation of Compounds 3, 8, 13, and 14; General Procedure
To a stirred solution of the phenol derivative (2 mmol) and the alkyl propiolate (2 mmol) in CH₂Cl₂ (10 mL) was added dropwise at –10 °C over 10 min Ph₃P (2 mmol). The reaction mixture was then allowed to warm to r.t. and stand for 24 h. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography (Merck 230–400 mesh) using n-hexane–EtOAc (4:1) as eluent to give the product.

**Table 1** Reaction of Alkyl Propiolates with 2-Aminophenols in the Presence of Triphenylphosphine

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aminophenol</th>
<th>Alkyl propiolate</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![NH2]</td>
<td>![CO2Me]</td>
<td>![13a(50%)] ![14a(40%)]</td>
</tr>
<tr>
<td>2</td>
<td>![OH NH2]</td>
<td>![CO2Et]</td>
<td>![13b(75%)] ![14b(40%)]</td>
</tr>
<tr>
<td>3</td>
<td>![Cl OH NH2]</td>
<td>![CO2Et]</td>
<td>![13c(40%)] ![14c(45%)]</td>
</tr>
<tr>
<td>4</td>
<td>![OH]</td>
<td>![CO2Et]</td>
<td>![13d(70%)] ![14d(30%)]</td>
</tr>
<tr>
<td>5</td>
<td>![OH]</td>
<td>![CO2Et]</td>
<td>![13e(55%)] ![14e(40%)]</td>
</tr>
<tr>
<td>6</td>
<td>![OH]</td>
<td>![CO2Et]</td>
<td>![13f(65%)] ![14f(50%)]</td>
</tr>
</tbody>
</table>

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Table 2. O-Vinylation of Resorcinol, Hydroquinone, 1,3-Diaminobenzene, and 1,4-Diaminobenzene with Alkyl Propiolates in the Presence of Triphenylphosphine

<table>
<thead>
<tr>
<th>Entry</th>
<th>Hydroxyphenol</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>22</td>
</tr>
</tbody>
</table>

MS: \( m/z \) (%) = 239 (3) [M+ + 1], 238 (8) [M+], 210 (9), 147 (21), 132 (37), 130 (40), 91 (100), 44 (52).

3-Methyl-2H-1,4-benzoxazine-2-one (13a)
Yield: 0.16 g (50%); white solid; mp 97–98 °C.
IR (KBr): 1718 (C=O), 1087 (CO) cm–1.
\(^1\)H NMR: \( d = 2.60 \) (s, 3 H, CH₃), 7.31 (d, \( J_{HH} = 8.2 \) Hz, 1 H, CH), 7.37 (t, \( J_{HH} = 7.2 \) Hz, 1 H, CH), 7.50 (t, \( J_{HH} = 7.2 \) Hz, 1 H, CH), 7.70 (d, \( J_{HH} = 7.4 \) Hz, 1 H, CH).
\(^1\)C NMR: \( d = 21.3 \) (CH₃), 116.4 (CH), 125.4 (CH), 128.6 (CH), 131.1 (CH), 132.0 (CN), 146.6 (CO), 153.2 (N=C), 155.1 (C=O).

MS: \( m/z \) (%) = 162 (3) [M+ + 1], 161 (6) [M+], 146 (50), 120 (5), 118 (20), 76 (15).
Anal. Calcd for C₉H₇NO₂ (161.2): C, 67.08; H, 4.38; N, 8.69. Found: C, 67.00; H, 4.50; N, 8.73.

3-Benzyl-2H-1,4-benzoxazin-2-one (13b)
Yield: 0.34 g (75%); pale yellow solid; mp 116–118 °C.
IR (KBr): 1732 (C=O), 1052 cm–1.
\(^1\)H NMR: \( d = 4.20 \) (s, 2 H, CH₂), 7.25 (d, \( J_{HH} = 8.1 \) Hz, 1 H, CH₂), 7.31 (d, \( J_{HH} = 7.8 \) Hz, 1 H, CH), 7.34 (d, \( J_{HH} = 7.8 \) Hz, 1 H, CH), 7.40–7.47 (m, 4 H, 4 × CH), 7.74 (dd, \( J_{HH} = 7.9 \) Hz, \( J_{HH} = 1.3 \) Hz, 1 H, CH).
\(^1\)C NMR: \( d = 40.6 \) (CH₂), 125.4 (CH), 127.1 (CH), 128.6 (CH), 129.1 (CH), 129.6 (CH), 130.8 (CH), 131.3 (CH), 132.3 (C), 135.5 (C), 146.6 (C), 152.8 (C), 156.3 (C=O).

MS: \( m/z \) (%) = 238 (6) [M+ + 1], 237 (8) [M+], 146 (51), 91 (100), 44 (12).
Anal. Calcd for C₁₅H₁₁NO₂ (237.2): C, 75.94; H, 4.67; N, 5.90. Found: C, 76.00; H, 4.50; N, 5.75.

6-Chloro-3-methyl-2H-1,4-benzoxazin-2-one (13c)
Yield: 0.14 g (40%); yellow oil.
IR (KBr): 1732 (C=O), 1218, 1115 cm–1.
\(^1\)H NMR: \( d = 2.44 \) (s, 3 H, CH₃), 7.05 (s, 1 H, CH), 7.13 (d, \( J_{HH} = 8.1 \) Hz, 1 H, CH), 7.55 (d, \( J_{HH} = 8.1 \) Hz, 1 H, CH).
\(^1\)C NMR: \( d = 21.5 \) (CH₃), 116.4 (CH), 126.4 (CH), 128.1 (CH), 128.5 (CCl), 130.8 (CH), 131.3 (CH), 132.3 (C), 135.5 (C), 152.8 (C), 156.3 (C=O).

MS: \( m/z \) (%) = 196 (7) [M+], 181 (23), 168 (34), 141 (63), 55 (100).
Anal. Calcd for C₉H₆ClNO₂ (195.6): C, 55.26; H, 3.09; N, 7.16. Found: C, 55.21; H, 3.00; N, 7.25.

7-Chloro-3-methyl-2H-1,4-benzoxazin-2-one (13d)
Yield: 0.26 g (70%); yellow solid; mp 55 °C.
IR (KBr): 1728 (C=O), 1187, 1113 cm–1.
\(^1\)H NMR: \( d = 2.56 \) (s, 3 H, CH₃), 7.30 (d, \( J_{HH} = 5.0 \) Hz, 1 H, CH), 7.33 (s, 1 H, CH), 7.71 (d, \( J_{HH} = 5.0 \) Hz, 1 H, CH).
\(^1\)C NMR: \( d = 29.7 \) (CH₃), 116.7 (CH), 125.9 (CH), 129.5 (CH), 132.2 (C), 132.3 (C), 133.6 (C), 133.8 (C), 155.1 (C=O).

MS: \( m/z \) (%) = 196 (9) [M+], 181 (27), 168 (41), 141 (53), 55 (100).
Anal. Calcd for C₉H₇ClNO₂ (195.6): C, 55.26; H, 3.09; N, 7.16. Found: C, 55.21; H, 3.10; N, 7.34.

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3.6-Dimethyl-2H-1,4-benzoxazine-2-one (13e)

Yield: 0.18 g (55%); yellow crystal; mp 139–143 °C

IR (KBr): 1725 (C=O), 1095 (CO) cm⁻¹.

1H NMR: δ = 2.42 (s, 3 H, CH3), 2.55 (s, 3 H, CH3), 7.16 (d, JHH = 8.2 Hz, 1 H, CH), 7.26 (d, JHH = 8.2 Hz, 1 H, CH), 7.32 (s, 1 H, CH).

13C NMR: δ = 20.8 (CH2), 21.3 (CH2), 115.9 (CH), 131.4 (CH), 153.5 (CH), 137.1 (C), 137.2 (C), 144.5 (C), 153.5 (C), 154.9 (CO).

MS: m/z (%) = 176 (5) [M⁺ + 1], 175 (8) [M⁺], 160 (31), 120 (70), 91 (100), 55 (72).


1.18.7 (CH), 118.8 (CH), 125.9 (CH), 137.5 (C), 143.7 (C), 159.7 (CH), 169.8 (C=O).

MS: m/z (%) = 242 (9) [M⁺], 227 (16), 213 (31), 197 (70), 169 (64), 142 (100), 100 (52), 73 (21), 29 (15).

Anal. Calcd for C10H11NO3: 172.17; C, 54.6; H, 5.6; N, 5.8. Found: C, 54.6; H, 5.5; N, 5.16.

Ethyl (E)-3-Amino-5-chlorophenoxy-2-propenoate (14d)

Yield: 0.14 g (30%); yellow oil.

IR (KBr): 3267 (NH), 1119 (CO), 1699 (C=O) cm⁻¹.

1H NMR: δ = 1.28 (t, JHH = 7.4 Hz, 3 H, CH3), 4.31 (q, JHH = 7.4 Hz, 2 H, CH2), 5.49 (s, JHH = 12.1 Hz, 1 H, CH), 6.66 (d, JHH = 7.9 Hz, 1 H, CH), 6.67 (d, JHH = 5.4 Hz, 1 H, CH), 6.94 (s, 1 H, CH), 7.69 (d, JHH = 12.1 Hz, 1 H, CH).

13C NMR: δ = 134.3 (CH2), 60.5 (CH2), 102.5 (CH), 117.1 (CH), 122.8 (CH), 136.1 (CCl), 142.7 (CN), 152.0 (CO), 158.8 (CO), 167.9 (C=O).

MS: m/z (%) = 242 (7) [M⁺], 227 (31), 213 (22), 197 (65), 169 (69), 142 (100), 100 (64), 73 (27), 29 (18).

Anal. Calcd for C10H11NO3: 172.17; C, 54.6; H, 5.0; N, 5.8. Found: C, 54.6; H, 5.0; N, 5.47.

Ethyl (E)-3-(2-Amino-4-methylphenoxy)-2-propenoate (14e)

Yield: 0.16 g (40%); yellow oil.

IR (KBr): 3267 (NH), 1119 (CO), 1699 (C=O) cm⁻¹.

1H NMR: δ = 1.28 (t, JHH = 7.2 Hz, 3 H, CH3), 2.24 (s, 3 H, CH3), 4.16 (q, JHH = 7.2 Hz, 2 H, CH2), 3.86 (br s, 2 H, NH2), 5.46 (d, JHH = 12.1 Hz, 1 H, CH), 6.53 (d, JHH = 7.8 Hz, 1 H, CH), 6.59 (s, 1 H, CH), 6.81 (d, JHH = 7.8 Hz, 1 H, CH), 7.72 (d, JHH = 12.2 Hz, 1 H, CH).

13C NMR: δ = 114.3 (CH2), 29.7 (CH), 60.3 (CH), 101.2 (CH), 117.2 (CH), 118.7 (CH), 119.4 (CH), 135.4 (C), 137.1 (C), 140.1 (C), 160.1 (CH), 167.2 (CO).

MS: m/z (%) = 221 (7) [M⁺], 192 (41), 149 (29), 130 (12), 121 (72), 109 (39), 91 (100).


Ethyl (E)-3-(2-Amino-5-chlorophenoxy)-2-propenoate (14f)

Yield: 0.12 g (30%); yellow oil.

IR (KBr): 3260 (NH), 1697 (C=O), 1633, 1587, 1669 (C=O) cm⁻¹.

1H NMR: δ = 1.27 (t, JHH = 7.1 Hz, 3 H, CH3), 2.24 (s, 3 H, CH3), 4.14 (q, JHH = 7.1 Hz, 2 H, CH2), 5.49 (d, JHH = 12.2 Hz, 1 H, CH), 6.68 (d, JHH = 7.9 Hz, 1 H, CH), 6.75 (s, 1 H, CH), 6.8 (d, JHH = 7.9 Hz, 1 H, CH), 7.7 (d, JHH = 12.2 Hz, 1 H, CH).

13C NMR: δ = 14.0 (CH2), 20.4 (CH2), 60.0 (CH), 101.4 (CH), 116.6 (CH), 119.2 (CH), 126.4 (CH), 128.5 (C), 134.7 (C), 142.7 (C), 159.8 (CH), 167.2 (CO).

MS: m/z (%) = 221 (6) [M⁺], 192 (34), 148 (42), 130 (21), 121 (70), 100 (46), 91 (100).

Anal. Calcd for C10H11NO3: 221.2; C, 65.14; H, 6.83; N, 6.33. Found: C, 65.24; H, 6.73; N, 6.25.
Preparation of Compounds 23–28; General Procedure

To a solution of the hydroxyphenol (2 mmol) and the alkylic propiolate (4 mmol) in CH₂Cl₂ (10 mL) was added dropwise at −10 °C over 10 min a solution of Ph₃P (4 mmol) in CH₂Cl₂ (5 mL). The reaction mixture was allowed to warm to r.t. and stand for 24 h. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography (Merck 230–400 mesh) using n-hexane–EtOAc (4:1) as eluent to give the product.

Methyl (E)-3-(3-Methoxy-3-oxo-1-propenyl)oxy)phenoxo(2-propenoate (23)

Yield: 0.26 g (50%); colorless oil.

IR (KBr): 3365 (OH), 1676 (C=O), 1114 (CO) cm⁻¹.

Anal. Calcd for C₁₄H₁₄O₆ (278.3): C, 60.43; H, 5.07. Found: C, 60.5 (21), 31 (18).

References


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