Abstract: Lithiated allylic phosphonates undergo efficient olefination reactions with a variety of aldehydes in the presence of HMPA to give terminal 1,3-dienes with high selectivity for the E-isomer. This method is general and procedurally simple.

Key words: aldehydes, alkenation, phosphorus, Wittig reactions, ylides

We recently described the Lewis acid-catalyzed cycloisomerization of tetraenones via 4+3 trapping of the Nazarov oxyallyl intermediate. This methodology called for the efficient preparation of 1,4-dien-3-ones bearing penultimate 1,3-diene moieties. Our studies required the dienal the efficient preparation of 1,4-dien-3-ones bearing penultimate 1,3-diene moieties. Our studies required the dienal...
tive to reaction time and order of addition. Under the optimal conditions, phosphonate 5a was treated with BuLi at -78 °C, then after 15 min, a mixture of aldehyde 2 and HMPA (2.4 equiv) was added and the reaction mixture was allowed to warm to room temperature. Deviation from this procedure led to greatly reduced yields of 4a, with the remainder of the material isolated as a complex mixture of phosphorus-containing products. Other bases (e.g., KOBu-t, NaH, LDA) gave poor yields (<20%), and omission of HMPA gave only traces of 4a. Substitution of N,N,N′-dimethylpropyleneurea (DMPU) for HMPA led to somewhat lower yields as well (56%). There is ample evidence for the lithiation of phosphonates such as 5a by BuLi in the absence of HMPA, and for addition of the resulting phosphoryl-stabilized allyl anion to aldehydes and other electrophiles. However, the presence of HMPA is clearly essential in this case, presumably due to its perturbation of the aggregation state of the intermediate organolithium species.

The optimum conditions used with 2 were applied to several other aldehydes, and the results were compared with those from analogous literature examples utilizing the Yamamoto procedure (Table). In general, dienes 4 were obtained in comparable yields and with higher E-selectivity. Moreover, the method can be easily adapted to the preparation of substituted dienes, as illustrated by the use of diethyl methallylphosphonate (5b). In these cases, the E-selectivity was uniformly excellent: any (Z)-diene formed was present in quantities below the limits of detection using 1H NMR.

The original impetus for this study was the need for an efficient route to dienals such as 1. In fact, aqueous hydrolysis of 4a furnished 1 in 93% yield, and its homologue 4b gave dienal 6 in comparable yield (Scheme 3). Thus, this methodology permits access to the versatile dienals 1 and 6 in 3 steps and 60% or 52% overall yields, respectively, from cyclohexene or cycloheptene. In a more general sense, this study describes a convenient method for terminal diene synthesis, using readily available aldehydes and allylphophonates, which proceeds with high E-selectivity.

### Table: Terminal Diene Synthesis via Allylphosphonates 5a and 5b

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Phosphonate</th>
<th>Yield (%)</th>
<th>E:Z value</th>
<th>Yamamoto Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(MeO)2CH(CH3)2</td>
<td>5a</td>
<td>72</td>
<td>20:1</td>
<td>70%, 6:1</td>
</tr>
<tr>
<td>2</td>
<td>(MeO)2CH(CH3)3</td>
<td>5a</td>
<td>69</td>
<td>16:1</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>(MeO)2CH(CH3)4</td>
<td>5a</td>
<td>62</td>
<td>18:1</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>THPO(CH2)4</td>
<td>5a</td>
<td>65</td>
<td>20:1</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>5a</td>
<td>60</td>
<td>40:1</td>
<td>79%, 19:1</td>
</tr>
<tr>
<td>6</td>
<td>CH3(CH2)3</td>
<td>5a</td>
<td>66</td>
<td>20:1</td>
<td>88%, 19:1</td>
</tr>
<tr>
<td>7</td>
<td>c-C6H11</td>
<td>5a</td>
<td>76</td>
<td>15:1</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>(MeO)2CH(CH3)4</td>
<td>5b</td>
<td>65</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>(MeO)2CH(CH3)5</td>
<td>5b</td>
<td>69</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>THPO(CH2)4</td>
<td>5b</td>
<td>63</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>Ph</td>
<td>5b</td>
<td>57</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>CH3(CH2)3</td>
<td>5b</td>
<td>71</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>c-C6H11</td>
<td>5b</td>
<td>75</td>
<td>&gt;98:2</td>
<td>-</td>
</tr>
</tbody>
</table>

- Isolated yields.
- Ratios were determined by 1H NMR integration unless otherwise specified.
- From this work.
- Ratios determined by GC analysis.
- See Ref. 12

### Scheme 3

All air or moisture sensitive reactions were carried out in oven dried (120 °C) or flame dried glassware under N2, unless otherwise noted. Reactive liquids were transferred by syringe and were added into the reaction flask through rubber septa. Et2O and THF were freshly distilled from sodium-benzophenone ketyl. Purchased reagents were used as received unless otherwise indicated. 1H NMR and 13C NMR spectra were recorded on a Varian Unity-300, Varian XL-300 (1H, 300 MHz; 13C, 75 MHz) or Varian VXR-500 (1H, 500 MHz; 13C, 125 MHz) spectrometer. IR spectra were measured with a Mattson FTIR 3000 infrared spectrometer. Mass spec-
tra were determined on a Finnigan Mat 95 high resolution gas chromatograph/mass spectrometer with Finnigan Mat ICIS II operating system. GC analyses of product E/Z ratios were determined on a Hewlett-Packard 5890 Series II Gas Chromatograph equipped with a 30 m × 0.30 mm HP-5 capillary column and a flame ionization detector.

**Terminal (E)-Dienes ; General Procedure**

To a solution of diethyl allylphosphonate (5a, 1.55 g, 6.0 mmol) or diethyl (2-methylallyl) phosphonate (5b, 1.15 g, 6.0 mmol) in anhyd THF (15 mL) was added dropwise BuLi (2.5 M in hexanes, 2.4 mL, 6.0 mmol) at –78 °C. After stirring for 15 min, a solution of the aldehyde (see below for individual cases) (5.0 mmol) in HMPTA (1.21 mL, 12 mmol) was added dropwise via cannula. The resulting solution was stirred for 2 h at –78 °C, and then allowed to warm to r.t. Stirring was continued for an additional 12 h at r.t. before quenching with sat. aq NH₄Cl solution. The mixture was extracted with EtO (3 × 15 mL). The combined organic phases were washed with brine (30 mL), dried (MgSO₄) and concentrated to afford the crude product. Purification by flash chromatography (EtOAc–hexanes) gave the desired dienes (Table).

**E)-9,9-Dimethylocta-1,3,diene (4a)**

The diene was prepared from lithiated 5a and 6,6-dimethylhexanal (2) according to the general procedure and was obtained as a colorless oil in 69% yield (E/Z = 20:1, determined by integration of ¹H NMR signals of H-2); Rf 0.36 (19 EtOAc–hexanes). IR (film): 3086, 2988, 2857, 1651 cm⁻¹.

**IR (film):** 3086, 2988, 2857, 1651 cm⁻¹.

**HRMS:** m/z calcd for C₈H₆O (M⁺ – OCH₃) 180.1515; found 180.1525.

**E)-8-(2-Tetrahydroxypropyloxy)-octa-1,3,diene**

The diene was prepared from 5a and 5-(2-tetrahydroxypropyloxy)pentanal according to the general procedure and was obtained as a colorless oil in 65% yield (E/Z = 20:1, determined by integration of ¹H NMR signals of H-2); Rf 0.48 (1.9 EtOAc–hexanes).

**IR (film):** 3004, 2941, 1651, 1601 cm⁻¹.

**HRMS:** m/z calcd for C₁₉H₁₆O₄ (M⁺ – 2 × OCH₂) 338.1008; found 338.1006.

**E)-1-Phenylbuta-1,3-diene**

The diene was prepared from lithiated 5a and benzaldehyde according to the general procedure and was obtained as a colorless oil in 60% yield (E/Z = 40:1, determined by GC); Rf 0.85 (hexanes).

**IR (film):** 3086, 2930, 1601 cm⁻¹.

**HRMS:** m/z calcd for C₁₀H₁₀ (M⁺ – OCH₃) 152.1280; found 152.1280.

**E)-10,10-Dimethyloctadeca-1,3,diene (4b)**

The diene was prepared from lithiated 5a and 7,7-dimethyloctanal according to the general procedure and was obtained as a colorless oil in 69% yield (E/Z = 16:1, determined by integration of ¹H NMR signals of H-2); Rf 0.35 (19 EtOAc–hexanes). IR (film): 3086, 2981, 2858, 1650, 1602 cm⁻¹.

**HRMS:** m/z calcd for C₁₀H₁₀ (M⁺ – OCH₃) 152.1280; found 152.1280.

**E)-11,11-Dimethyloctadeca-1,3,diene**

The diene was prepared from lithiated 5a and 8,8-dimethyloctanal according to the general procedure and was obtained as a colorless oil in 62% yield (E/Z = 18:1, determined by integration of ¹H NMR signals of H-2); Rf 0.38 (19 EtOAc–hexanes). IR (film): 3088, 2956, 1650, 1603 cm⁻¹.

**HRMS:** m/z calcd for C₁₀H₁₀ (M⁺ – OCH₃) 152.1280; found 152.1280.

**E)-1-Cyclohexylbuta-1,3-diene**

The diene was prepared from lithiated 5a and decanal according to the general procedure and was obtained as a colorless oil in 66% yield (E/Z = 20:1, determined by integration of ¹H NMR signals of H-2); Rf 0.88 (hexanes).

**IR (film):** 3088, 2958, 1635, 1642 cm⁻¹.

**HRMS:** m/z calcd for C₁₀H₁₀ (M⁺ – OCH₃) 152.1280; found 152.1280.

**E)-1-Cyclohexylbuta-1,3-diene**

The diene was prepared from lithiated 5a and cyclohexane-carboxaldehyde according to the general procedure and was obtained as a colorless oil in 76% yield (E/Z = 15:1 by GC); Rf 0.90 (hexanes).

**IR (film):** 3038, 2927, 1650, 1603 cm⁻¹.

**HRMS:** m/z calcd for C₁₀H₁₀ (M⁺ – OCH₃) 152.1280; found 152.1280.

**E)-1-Cyclohexylbuta-1,3-diene**

The diene was prepared from lithiated 5a and cyclohexane-carboxaldehyde according to the general procedure and was obtained as a colorless oil in 76% yield (E/Z = 15:1 by GC); Rf 0.90 (hexanes).
(E)-9,9-Dimethoxy-2-methylnona-1,3-diene
The diene was prepared from lithiated 5b and 6,6-dimethoxyhexanal according to the general procedure and was obtained as a colorless oil in 65% yield (single isomer by 1H NMR); Rf 0.39 (1:9 EtOAc–hexanes).

IR (film): 3082, 2950, 1609, 1456, 1382, 1128, 1076, 964 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 6.14 (d, 1 H, J = 15.7 Hz), 5.64 (dt, 1 H, J = 15.6, 7.0 Hz), 4.85 (s, 2 H), 4.35 (t, 1 H, J = 5.9 Hz), 3.31 (s, 6 H), 2.09 (q, 2 H, J = 6.7 Hz), 1.83 (br s, 3 H), 1.65–1.56 (m, 2 H), 1.49–1.30 (m, 4 H).

13C NMR (75 MHz, CDCl₃): δ = 142.34, 133.14, 130.82, 114.47, 104.64, 52.80, 32.85, 32.54, 29.46, 24.41, 18.91.


(E)-11,11-Dimethoxy-2-methylundeca-1,3-diene
The diene was prepared from lithiated 5b and 8,8-dimethoxyoctanal according to the general procedure and was obtained as a colorless oil in 69% yield (single isomer by 1H NMR); Rf 0.42 (1:9 EtOAc–hexanes).

IR (film): 3081, 2987, 1608 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 6.12 (d, 1 H, J = 15.6 Hz), 5.64 (dt, 1 H, J = 15.6, 7.0 Hz), 4.85 (s, 2 H), 4.35 (t, 1 H, J = 5.9 Hz), 3.31 (s, 6 H), 2.09 (q, 2 H, J = 6.7 Hz), 1.83 (s, 3 H), 1.62–1.56 (m, 2 H), 1.44–1.28 (m, 8 H).

13C NMR (125 MHz, CDCl₃): δ = 142.39, 132.95, 131.17, 114.34, 104.74, 52.81, 32.92, 32.68, 29.54, 29.52, 29.34, 24.76, 18.92.

(E)-8-(2-Tetrahydropyran-2-yl)-2-methylcta-1,3-diene
The diene was prepared from lithiated 5b and the corresponding aldehyde according to the general procedure and was obtained as a colorless oil in 63% yield (single isomer by 1H NMR); Rf 0.48 (1:9 EtOAc–hexanes).

IR (film): 3082, 2966, 1608 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 6.13 (d, 1 H, J = 15.6 Hz), 5.64 (dt, 1 H, J = 15.6, 7.0 Hz), 4.85 (s, 2 H), 4.57 (dd, 1 H, J = 4.4, 3.0 Hz), 3.90–3.84 (m, 1 H), 3.78–3.71 (m, 1 H), 3.53–3.47 (m, 1 H), 3.42–3.36 (m, 1 H), 2.14 (q, 2 H, J = 6.3 Hz), 1.83 (s, 3 H), 1.74–1.45 (m, 10 H).

13C NMR (125 MHz, CDCl₃): δ = 142.28, 133.21, 130.76, 114.45, 99.01, 67.60, 62.49, 32.73, 30.95, 29.49, 26.26, 25.69, 19.86, 18.87.

Anal. Calc for C₁₀H₁₆O: C, 74.95; H, 10.78. Found: C, 74.79; H, 10.63.

(E)-1-Phenyl-3-methylbuta-1,3-diene
The diene was prepared from 5b and benzaldehyde according to the general procedure and was obtained as a colorless oil in 57% yield (single isomer by 1H NMR); Rf 0.03 (1.9 EtOAc–hexanes).

IR (film): 3093, 2929, 2838, 1725, 1650, 1601 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 7.96 (t, 1 H, J = 1.8 Hz), 6.30 (dd, 1 H, J = 17.1, 10.2, 10.2 Hz), 6.00 (dd, 1 H, J = 15.1, 10.3 Hz), 5.62 (dt, 1 H, J = 15.1, 6.8 Hz), 5.05 (br d, 1 H, J = 17.0 Hz), 4.91 (br d, 1 H, J = 10.1 Hz), 2.39 (td, 1 H, J = 7.2, 1.8 Hz), 2.07 (br q, 2 H, J = 6.4 Hz), 1.66–1.55 (m, 2 H), 1.46–1.34 (m, 2 H).

13C NMR (125 MHz, CDCl₃): δ = 202.48, 137.17, 134.46, 131.48, 115.06, 43.73, 32.25, 28.65, 21.60.

(E)-Deca-7,9-dienal (6)
Aldehyde 6 was prepared from 4b by following the typical procedure for the preparation of 1 and was obtained as a colorless oil in 88% yield; Rf 0.34 (1:9 EtOAc–hexanes).

IR (film): 3093, 2929, 2838, 1725, 1650, 1601 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 9.76 (t, 1 H, J = 1.8 Hz), 6.30 (dd, 1 H, J = 17.0, 10.2, 10.2 Hz), 6.45 (br dd, 1 H, J = 15.1, 10.4 Hz), 5.68 (dt, 1 H, J = 15.1, 6.9 Hz), 5.08 (br d, 1 H, J = 16.9 Hz), 4.96 (br d, 1 H, J = 10.1 Hz), 2.42 (td, 2 H, J = 7.3, 1.8 Hz), 2.09 (br q, 2 H, J = 7.1 Hz), 1.64 (tt, 2 H, J = 7.5, 7.3 Hz), 1.46–1.30 (m, 4 H).

13C NMR (125 MHz, CDCl₃): δ = 202.90, 137.37, 135.13, 131.34, 115.04, 44.01, 32.45, 29.06, 28.84, 22.08.

HRMS: m/z calcd for C₁₀H₁₄O (M⁺): 152.1201; found 152.1209.

References