

## A New Route to Trienals using 2-Substituted 2*H*-Pyran-based Wittig Reagents

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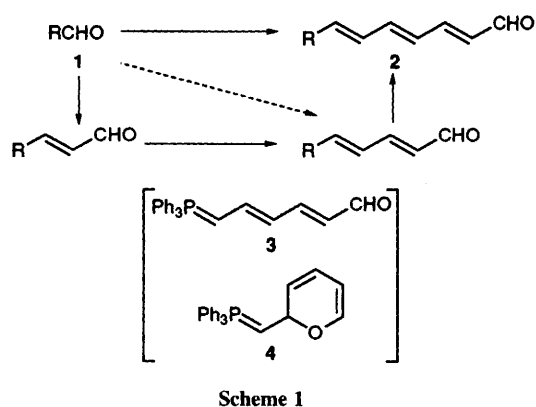
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A procedure is presented which allows the six-carbon homologation of aldehydes to give the corresponding trienals *via* the likely intermediacy of the novel 2-triphenylphosphoranylidenemethyl-2*H*-pyran; application of this methodology to a short synthesis of the marine alarm pheromone, navenone B, is also described.

There is continuing interest in the development of new procedures for the preparation of polyunsaturated aldehydes in view of their versatility in the synthesis of natural products such as leukotrienes, polyene antibiotics, pheromones and other bioactive compounds.<sup>1-6</sup> We have recently described procedures for the stereoselective preparation of *E,E*-<sup>1</sup> and *Z,E*-dienals<sup>2</sup> and, in an extension of this work, required a procedure for the six-carbon homologation of aldehydes **1** into trienals **2**, as shown in Scheme 1. This transformation could, in principle, be carried out by a series of two-carbon homologation reactions<sup>3</sup> or by sequential four + two/two + four homologations.<sup>4</sup> Previous attempts to effect a six-carbon homologation (**1** → **2**) were unsuccessful although homologation to the corresponding ethyl ester was possible *via* use of a Wadsworth-Emmons phosphonate reagent.<sup>5</sup>

The requisite Wittig reagent **3** is apparently unavailable but we wondered if 2-triphenylphosphoranylidenemethyl-2*H*-pyran **4** could be prepared and, if so, whether it could be employed to effect the required six-carbon homologation. This approach might be expected to give reasonable efficiency since the aldehyde is protected during the reaction and only revealed when the 2*H*-pyran undergoes electrocyclic ring opening (**7** → **8**, Scheme 2). The initial trienal **8** would be expected to have the *2Z,4E*-stereochemistry, although we envisaged that isomerisation to the all-*trans*-isomer **9** would be facile.<sup>1,3,4</sup> In view of our interest in organometallic additions to pyrylium salts,<sup>2</sup> we decided to investigate the possibility that reagent **4** could be formed from the C-2 addition of methylenetriphenylphosphorane to pyrylium tetrafluoroborate **5**<sup>7</sup> followed by deprotonation of the resulting adduct **6**.‡

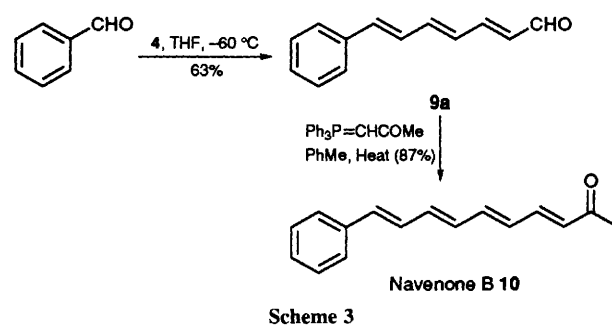
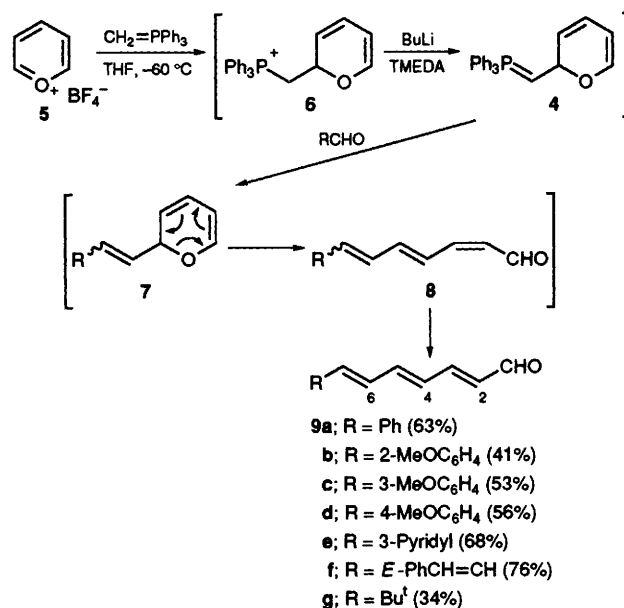
The success of this approach is shown in Scheme 2. Methylenetriphenylphosphorane was generated in tetrahydrofuran (THF) at -60 °C. Addition of the Wittig reagent to a suspension of pyrylium tetrafluoroborate **5** in THF followed, after four hours, by the addition of butyllithium generated a dark red solution of the presumed phosphorane



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‡ The reaction of substituted pyrylium salts with Wittig reagents in order to prepare carbocyclic aromatic compounds has been reported previously.<sup>8</sup>

4.‡ A range of aldehydes were added to this reagent and after a low-temperature aq. NH<sub>4</sub>Cl quench, trienals **9** were isolated. This procedure gave fair to good yields of trienals **9** from aromatic aldehydes, cinnamaldehyde (giving *E,E,E*-tetraenal **9f**) and pivaldehyde. Aliphatic aldehydes, nonenal and nonadienal did not undergo the required homologation, possibly owing to deprotonation. The attempted preparation of a hexaenal by homologation of trienal **9a** also failed, possibly because of its low reactivity. The trienals were formed as single isomers according to high field <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. They were assigned the all-*trans*-stereochemistry **9** on the basis of coupling constants (*e.g.* for **9a**, *J*<sub>2,3</sub> = 15.6 Hz, *J*<sub>4,5</sub> = 14.2 Hz, *J*<sub>6,7</sub> = 14.2 Hz), the characteristic<sup>1,2</sup> chemical shifts of the formyl protons ( $\delta$  *ca.* 9.5–9.6) and comparison of physical data with known compounds (*e.g.* **9a**, m.p. 115.5–116 °C, lit.<sup>6</sup> m.p. 116.5–118 °C). Isomerisation of the expected *2Z,4E*-dienals **8** presumably occurs during work-up.



§ Attempts to isolate phosphorane **3** by warming pyran **4** were unsuccessful.

The value of this methodology is illustrated by an extremely short synthesis of navenone B **10**, the trail-breaking alarm pheromone of the sea slug *Navanax inermis*<sup>6</sup> (Scheme 3). Benzaldehyde was homologated to give trienal **9a** in 63% yield. The synthesis was completed by a, previously described,<sup>6</sup> second Wittig reaction giving the natural product **10** in 87% yield (m.p. 137–140 °C, lit.<sup>6</sup> m.p. 145 °C) with consistent<sup>6</sup> <sup>1</sup>H NMR data.

We are currently optimising this route to polyenals as well as investigating modifications which allow the methodology (i) to be extended to aliphatic aldehydes, and (ii) to be utilised for the preparation of the *cis*-isomers **8**.¶||

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¶ Attempts to use other Wittig reagents, e.g. ethylenetriphenylphosphorane, proved unsuccessful.

|| All new compounds gave consistent spectral and analytical/mass spectrometric data.

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