



## Phosphazene bases and the anionic oxy-Cope rearrangement

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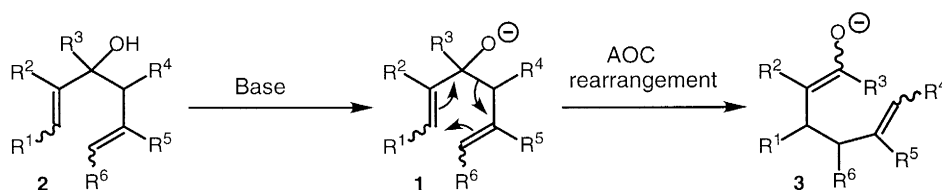
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### Abstract

Compounds containing a 1,5-hexadien-3-ol system undergo anionic oxy-Cope rearrangement when treated with the phosphazene super-base,  $P_4$ -*t*-Bu. The [3,3] sigmatropic rearrangement occurs in hexane as well as in THF. The weaker phosphazene base,  $P_2$ -Et fails to induce rearrangement. This is the first example of the use of a metal-free base to induce anionic oxy-Cope rearrangement. © 2000 Elsevier Science Ltd. All rights reserved.

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The anionic oxy-Cope (AOC) rearrangement<sup>1</sup> is the [3,3] sigmatropic rearrangement of an alkoxide **1** generated from a 1,5-dien-3-ol **2** to give an enolate **3** (Scheme 1). The alkoxide **1** rearranges  $10^{10}$  to  $10^{17}$  times faster than alcohol **2** due to weakening of the C(3)–C(4) bond in the ground state by *n*-donation from the oxyanion. The *n*-donation is greatest and the rearrangement fastest when the oxyanion is completely naked; consequently, potassium salts rearrange faster than sodium salts, which rearrange faster than lithium salts.<sup>2</sup> Crown ethers and polar aprotic solvents are often used to reduce association between the oxyanion and the cation. However, metal-free bases have never been used for this reaction.



Scheme 1.

The phosphazene super-bases **4** and **5**,<sup>3</sup> developed by Reinhard Schwesinger, are extremely strong, uncharged, metal-free bases (Fig. 1). We here report that  $P_4$ -*t*-Bu **4** completely deprotonates alcohol **2** to give alkoxide **1** and a huge ‘soft’ cation, which is known<sup>3</sup> to have its positive charge delocalised over a volume of ca. 500 Å<sup>3</sup>, and that this alkoxide is sufficiently naked to undergo AOC rearrangement.

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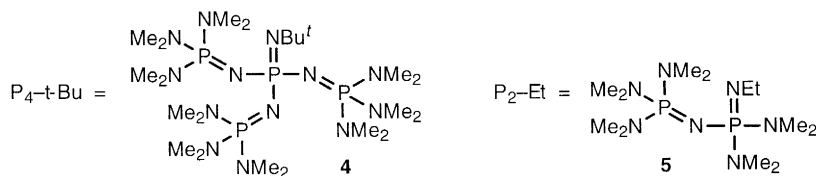
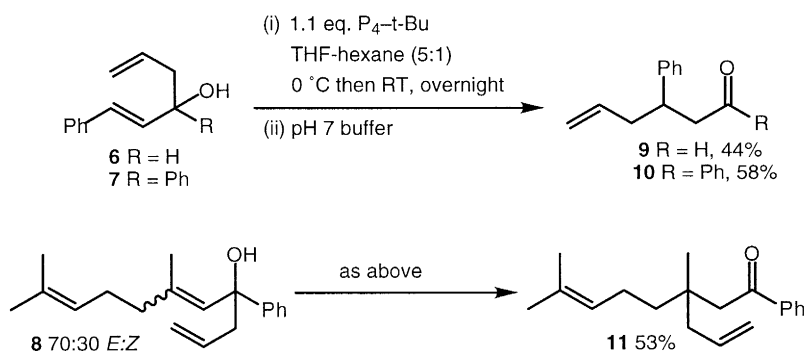


Fig. 1.

In our optimised procedure (see below), a THF solution of alcohol **6**, **7**, or **8** was added to  $P_4$ -*t*-Bu **4** in THF–hexane at low temperature (Scheme 2). Any precipitates dissolved during the slow warming to room temperature. Rearrangement occurred at room temperature and quenching with phosphate buffer gave the ketone **9**, **10** or **11** as essentially the only product visible in the  $^1\text{H}$  NMR spectrum of the crude mixture. When the alcohol **6**, **7**, or **8** was added to a solution of the base **4** at room temperature, the reaction was not clean. Furthermore, if the 1 M solution of  $P_4$ -*t*-Bu **4** in hexane was added by syringe to the cooled alcohol, the base crystallised in the needle blocking it. Interestingly, alcohol **6** also rearranged in pure hexane (0.5 M), and side-products could be minimised by adding the alcohol to  $P_4$ -*t*-Bu **4** at  $0^\circ\text{C}$  (the base precipitates at lower temperature).



Scheme 2.

Alcohols **6–8** were recovered unchanged when phosphazene  $P_2$ -Et **5** was used instead of  $P_4$ -*t*-Bu **4**.

Potassium hydride, which is generally supplied as a dispersion in mineral oil and is insoluble in organic solvents, is the base most commonly used for AOC rearrangements.  $P_4$ -*t*-Bu **4** is soluble in organic solvents and is available (Fluka) as an easy to handle 1 M solution in hexane; consequently, we expect that phosphazene base **4** will be widely used for AOC rearrangements.

Standard procedure: Dry THF (0.8 ml) was added to a stirred solution of phosphazene base  $P_4$ -*t*-Bu **4** (700  $\mu\text{L}$  of a 1 M solution in hexane *ex* Fluka, 700  $\mu\text{mol}$ , 1.07 equiv.) under argon, and the solution was cooled to  $-78^\circ\text{C}$ . A solution of alcohol **7** (164 mg, 655  $\mu\text{mol}$ , 1 equiv.) in dry THF (1 ml) was added dropwise over 10 min and any residue in the syringe was washed out with more dry THF (1 ml). After 30 min, the pale yellow solution was allowed to warm to  $0^\circ\text{C}$  over 2 h 40 min. The mixture was stirred for 17 h at room temperature and then injected into the vortex of rapidly stirring pH 7 phosphate buffer (5 ml). The mixture was extracted into diethyl ether (4 $\times$ 5 ml) and the combined extracts were washed with brine (5 ml), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated under vacuum. The residue was chromatographed on silica [20 g, dichloromethane–hexane (0.5:1 then 1:1)] to give the pure ketone **10** (95 mg, 58%) as crystals.

## Acknowledgements

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