Anti Eliminations of Horner–Wittig Intermediates

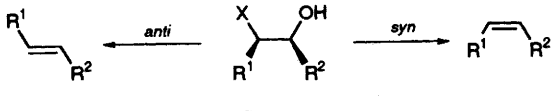
Nicholas J. Lawrence* and Faiz Muhammad

Department of Chemistry, UMIST, PO Box 88, Manchester, UK M60 1QD

Erythro phosphinyl alcohols **3** and the *threo* isomers **4** give (*E*)- and (*Z*)-alkenes, respectively, by an *anti* elimination in contrast to the *syn* Horner–Wittig elimination of the corresponding phosphinoyl alcohols.

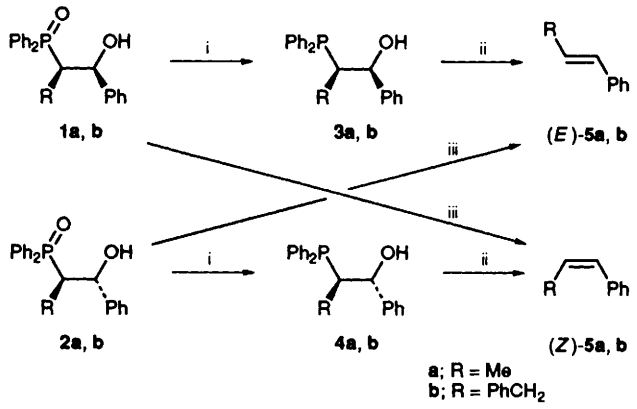
Alcohols bearing an adjacent functional group X that allows for both *syn* and *anti* elimination to the corresponding (*E*)- and (*Z*)-alkene are versatile synthetic intermediates *e.g.* X = carboxyl;[1] silyl;[2] dimesitylboron[3] (Scheme 1). Notably lacking from this class are phosphinoyl alcohols where X = R_2PO, or indeed any other phosphorus group. We herein report our endeavours to rectify this.

Our search for an *anti* elimination of 1,2-phosphinoyl alcohols, intermediates of the Horner–Wittig reaction,[4] was prompted by a need to make tri- and tetra-substituted carbon–carbon double bonds. In such cases the reaction is complicated by a tendency of the alkoxide to undergo a reverse aldol type reaction, expelling the α-phosphinoyl anion, rather than the desire *syn* elimination. We reasoned that this would not be a problem if we could find acidic conditions for the elimination. We used the methods of Warren and coworkers[5] to synthesize a range of *erythro* 1,2-phosphinoyl alcohols **1a**, **b** and *threo* isomers **2a**, **b** of defined stereochemistry, which were reduced to the corresponding phosphines **3a**, **b** and **4a**, **b** with cerium(III) chloride modified lithium aluminium hydride.[6] Only in one case did we isolate the phosphine preferring to use them crude, thereby avoiding any chance of reoxidation to the starting material. When **3a** was treated with hydrogen peroxide the phosphine oxide **1a** was obtained exclusively, indicating that the initial reduction was stereospecific, as expected. When the phosphinyl alcohols were treated with phosphorus trichloride we obtained alkenes resulting from an *anti* elimination† (Scheme 2 and Table 1). The *erythro* alcohols **3a**, **b** give selectively (*E*)-alkenes, while the *threo* alcohols **4a**, **b** give (*Z*)-alkenes *via*



Scheme 1

† To a solution of the crude phosphinyl alcohol (1 mmol) **3** or **4** and triethylamine (5 mmol) in dry dichloromethane (5 cm^3) was added dropwise phosphorus trichloride (1.15 mmol) at 0 °C. The mixture was stirred for 3 h at room temp. Standard aqueous work up gave crude alkene which was purified by column chromatography (SiO_2).



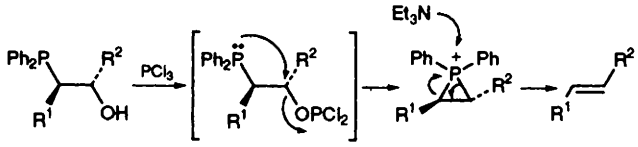
Scheme 2 *Reagents and conditions*: i, $LiAlH_4$, $CeCl_3$, tetrahydrofuran, room temp., 2 h; ii, PCl_3, NEt_3, CH_2Cl_2, room temp., 2 h; iii, NaH, DMF, 50 °C, 2 h

Table 1

Alkene	Starting phosphinyl or phosphinoyl alcohol	$E:Z^a$	Yield (%)
(*E*)-**5a**	**3a**	>95 : 5	32
(*E*)-**5a**	**2a**	>99 : 1 (ref. 4)	81
(*Z*)-**5a**	**4a**	7 : 93	43
(*Z*)-**5a**	**1a**	4 : 96 (ref 4)	75
(*E*)-**5b**	**3b**	>95 : 5	56
(*E*)-**5b**	**2b**	>95 : 5	97
(*Z*)-**5b**	**4b**	10 : 90	50
(*E*)-**5b**	**1b**	>95 : 5	99

[a] As measured by 200/300 MHz NMR integration.

an *anti* elimination. Our method compliments the base induced *syn* elimination and in some cases offers distinct advantages. For example, when **1b** was treated with sodium hydride in dimethylformamide (DMF) to our surprise the *trans* alkene (*E*)-**5b** was obtained. It would seem that (*Z*)-**5b**, the expected product, is configurationally unstable under these basic conditions, even when only 1 equiv. of sodium hydride is used.[7] Treatment of (*Z*)-**5b** with sodium diphenylphosphinate, the basic by-product from the elimination, had no effect upon the *Z*:*E* ratio. The likelihood that **1b** is converted into the *threo* isomer **2b**, prior to elimination, is small since alkyldiphenylphosphine oxides of this type are stable. It is only when the anion of the phosphine oxide is stable (for example, when it is benzylic)[8] and the alkene sterically compressed that loss of stereospecificity is observed.



Scheme 3

Whatever the reason for this odd behaviour we were able to make the *cis* alkene by elimination of the phosphinyl alcohol **4b**, which gave (*Z*)-**5b** with high *anti* selectivity. We rationalise the *anti* stereochemistry of our new reaction by invoking loss of phosphorus from an *epi*-phosphonium ion that is formed by displacement of the oxyphosphorus group by the diphenylphosphinyl group. A similar mechanism involving *epi*-selenonium[9] and *epi*-sulfonium[10] ions has been suggested for the *anti* elimination of 1,2-selenyl alcohols and 1,2-sulfinyl alcohols.

We are currently extending this new method for making alkenes and investigating the nature of the mechanism and will report the findings at a later date. We thank the Pakistan Government for a scholarship (F. M.).

Received, 6th May 1993; Com. 3/02606J

References

1 *Anti* eliminations: S. Hara, H. Taguchi, H. Yamamoto and H. Nozaki, *Tetrahedron Lett.*, 1975, 1545; J. Mulzer and G. Brüntrup, *Tetrahedron Lett.*, 1979, 1909; *syn* eliminations: W. Adam, J. Baeza and J.-C. Liu, *J. Am. Chem. Soc.*, 1972, **94**, 2000; M. U. S. Sultanbawa, *Tetrahedron Lett.*, 1968, 4569; T. Tanzawa and J. Schwartz, *Organometallics*, 1990, **9**, 3026.
2 P. F. Hudrlik and D. Peterson, *J. Am. Chem. Soc.*, 1975, **97**, 1464; D. J. Ager, *Org. React.* (*N.Y.*), 1990, **38**, 1.
3 A. Pelter, D. Buss and E. Colclough, *J. Chem. Soc., Chem. Commun.*, 1987, 297.
4 L. Horner, H. Hoffmann and H. G. Wippel, *Chem. Ber.*, 1958, **91**, 61.
5 *Erythro* selective: A. D. Buss and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2307; *threo* selective: A. D. Buss, R. Mason and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 5293; A. D. Buss and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 3931.
6 T. Imamoto, T. Takeyama and T. Kusumoto, *Chem. Lett.*, 1985, 1491; we will report the results of the use of this reagent system at a later date.
7 G. Buche and D. R. Martens, *Tetrahedron Lett.*, 1976, 3657.
8 A. D. Buss, S. Warren, J. S. Leake and G. Whitham, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2215.
9 J. Rémion and A. Krief, *Tetrahedron Lett.*, 1976, 3743.
10 J. N. Denis, W. Dumont and A. Krief, *Tetrahedron Lett.*, 1979, 4111.