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DBP YLIDES: WITTIG REAGENTS FOR SYNTHESIS OF E-ALKENES FROM ALDEHYDES

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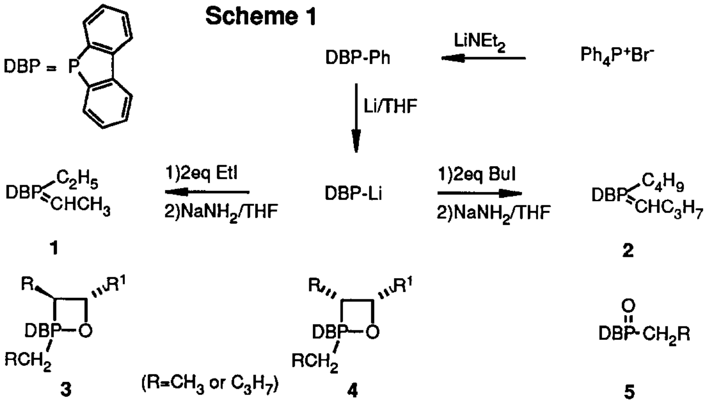
Summary. Phosphorus ylides based on the dibenzophosphole (DBP) ring system convert aldehydes into trans-disubstituted oxaphosphetanes with good to excellent selectivity. Decomposition at 70-110° affords alkenes with E:Z ratios from 6:1 to > 100:1.

The Wittig reaction of Ph_3P=CHR with aldehydes R'CHO is often the method of choice for synthesis of alkenes with high selectivity for the Z isomer (usually, >90%; >99% if R' is teriary alkyl).[1] We now report a comparably selective Wittig synthesis of E-alkenes from aldehydes using ylides based on the dibenzophosphole (DBP) ring system. Salt-free DBP ethylide 1 or butylide 2 can be made in THF ($NaNH_2$ method)[2] from phosphonium salts which are available from commercial Ph_4P^+ Br^- as shown in Scheme 1.[3] The ylides have high Wittig reactivity in the initial addition step with aldehydes at -78°, but the resulting oxaphosphetanes are resistant to olefin formation. Their stability probably results from the ca. 94° bond angle enforced by long C-P bonds in the phosphole ring.[4] This factor stabilizes pentacoordinate phosphorus in oxaphosphetanes 3 and 4(phosphole spanning apical-basal sites) and destabilizes the tetrahedral ylide 1 or the phosphine oxide 5. Prolonged heating at 70 °C (5-10 hours) or ca. 30 min. at 110°C is required to induce cycloreversion to 5 and the alkene.[5] Experimentally, this is best done in sealed tubes (THF as solvent), but it is also possible to use higher boiling ethers such as diglyme in ordinary apparatus with careful control to maintain inert conditions. As summarized in Table 1, the procedure affords alkenes with exceptional E-selectivity, ranging from 6:1 for benzaldehyde to a remarkable 124:1 in the case of an α-branched aldehyde (entry f). The optimum experiment involves butylidene DBP ylide 2, but the results with ethylidene analogs are similar and fall consistently in the synthetically useful range, especially with enolizable aldehydes.

Initially, we suspected that the E-selectivity observed with DBP ylides may result from equilibration[6,7] at the stage of the unusually stable oxaphosphetanes 3 and 4. However, isomeric oxaphosphetanes 3c and 4c synthesized independently from epoxides 6 and 7 (Scheme 2)[8,9] decomposed with >99% retention of stereochemistry. Also, the Wittig reaction of entry "a", Table 1, could be studied directly by high field ^{31}P NMR.[10] Major (-64.6 ppm) and a minor (-62.2 ppm) pentavalent phosphorus signals were observed in the characteristic

Scheme 1



Scheme 2 R^1=C(CH$_3$)$_2$CH$_2$Ph

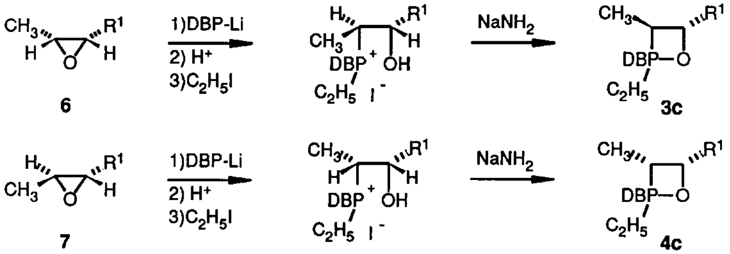


Table 1. Olefin from R'CHO + DBP Ylides (THF, sealed tubes unless otherwise noted)

entry	ylide	R'	E:Z	Yield	entry	ylide	R'	E:Z	Yield
a	1	CH_2CH_2Ph	19:1	83%[a]	g	1	$PhCH_2$	23:1	66%[a]
b	2	CH_2CH_2Ph	>20:1	66%[b,c]	h	2	$PhCH_2$	10:1	64%[a]
c	1	$PhCH_2C(Me)_2$	9:1	62%[a]	i	1	cyclo-C_6H_{11}	32:1	92%[a]
d	2	$PhCH_2C(Me)_2$	12:1	82%[b]	j	2	cyclo-C_6H_{11}	84:1	97%[a]
e	1	$C_9H_{19}CH(Me)$	81:1	78%[b]	k	2	Ph	6:1	75%[a]
f	2	$C_9H_{19}CH(Me)$	124:1	91%[b]	l	2	PhCH(Me)	32:1	84%[b]

a) Yield by glpc vs. internal standard, b) isolated yield after chromatography, c) diglyme solution, open system under N_2.

oxaphosphetane region in a ratio of 94:6 (-30 °C). After heating at 110 °C (30 min), the final olefin ratio (95:5 E:Z) was in agreement with the oxaphosphetane ratio (3a:4a) observed at low temperatures by NMR. The observed E-olefin selectivity in these examples is therefore attributed to kinetically favored formation of trans-disubstituted oxaphosphetanes 3. A discussion of the origins of this selectivity is deferred to a full paper, but the effect results from a subtle interplay of 1,2 and 1,3 interactions and is specific to the P-alkyl DBP ylides.[4b] Non-constrained ylides with the same electronic environment at phosphorus (for example, $Ph_2EtP{=}CHCH_3$) are marginally trans-selective with unbranched aldehydes, but cis selective with R'CHO were R' is tertiary alkyl.[7b]

The DBP derivatives 1 and 2 have the highest kinetic trans selectivity among the currently known non-stabilized, salt-free ylides. It should be noted that somewhat longer but still practical routes for E-alkene synthesis from aldehydes are available,[11] and that isomerization of the conventional Wittig intermediates with strong base (Schlosser modification)[12] is useful in certain systems. Due to their higher cost, the DBP ylides will be convenient in those cases where the aldehyde is the limiting reagent, and where the ylide α-substituent is relatively simple. Further refinements in the phosphorus substitution pattern for optimal E-olefin selectivity are under investigation.

Acknowledgement

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5. Typical procedure:
Dry phosphonium salt and sufficient purified THF (dist. from Na/Ph_2CO) to make a ca. 0.1 M solution were placed in a 40 mL centrifuge tube under nitrogen (septum; syringe techniques) together with a large excess (2-3 equiv) of $NaNH_2$ (Aldrich). The mixture was stirred magnetically for 2 hrs at room temperature. Nitrogen needles were then removed, the septum holes were protected with silicone grease, and the red supernatant was clarified by centrifugation. The supernatant solution was transferred by cannula under nitrogen pressure into a round bottom flask at -78 ° and a THF solution of the aldehyde (0.7 eq) was added dropwise. After 5 min, the mixture was transferred by cannula(N_2) into a thick walled tube suitable for sealing. The liquid was cooled (-78 °) under vacuum, the tube was sealed, and then heated 30 min at 110 °C to decompose the oxaphosphetanes. Conventional aqueous/pentane workup gave the olefin products.

6. Equilibration (partial) in oxaphosphetanes derived from salt-free, nonstabilized ylides + aliphatic R'CHO is exceedingly rare. The only known examples involve tertiary R' and the P-trialkyl substituted ylides $Bu_3P{=}CHC_3H_7$[7a] and $Et_3P{=}CHCH_3$.[7b]

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9. ^{31}P NMR: 3c, -64.1 ppm; 4c, -65.5 ppm, -23 °C, THF.

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