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Communications

A Bridged Tetrahydrophosphole Ylide Derived from 9-Phenylphosphabicyclo[4.2.1]nonane: A Reagent for *E*-Selective Wittig Reactions

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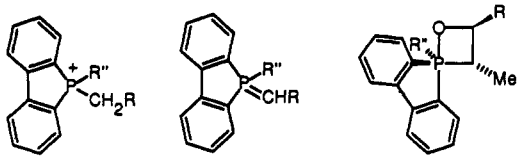
Summary: The bicyclic ylide **4** reacts with aldehydes to afford the *E*-alkenes. Selectivity is 94–6% *E* for unbranched aldehydes, but the selectivity decreases with increasing α-branching. Ylide **4** is the first *E*-selective, nonstabilized ylide that allows efficient utilization of the P-alkyl substituent.

A recent report from our laboratory describes the dibenzophosphole ("DBP") ylides **2a** as reagents for the conversion of aldehydes into *E*-alkenes.[1] Product ratios are generally better than 90:10 *E*/*Z* (Table I, column 1) and can exceed 100:1 *E*/*Z* for α-branched aldehydes, depending on the ylide substituent. However, the DBP ylides have some disadvantages. Only one of the two identical P-alkyl substituents in the precursor phosphonium salt **1** is utilized in the Wittig reaction. An inert group R″ at phosphorus would solve this problem, but so far our attempts to vary R″ have resulted in lower *E*-selectivity. For example, (Ph)DBP=$CHCH_3$ (**2b**, R″ = Ph, R = CH_3) affords a 1:1 *E*/*Z* mixture with $PhCH_2CH_2CHO$. Another problem with the DBP ylides is that the intermediate oxaphosphetanes **3** must be heated to induce conversion to the alkenes, a transformation that is best performed using sealed tube techniques at >100 °C. Because of these disadvantages, the DBP ylide method for *E*-alkene synthesis is not competitive with the Julia procedure (sulfone anion addition, followed by reductive elimination with sodium amalgam)[2] for coupling aldehydes with valuable alkylidene fragments.

Table I. Comparison of *Z*/*E* Selectivities in the Wittig Reaction of EtDBP=$CHCH_3$ and PhBTP=$CHCH_3$ with Aldehydes[a]

R′CHO	EtDBP=$CHCH_3$	PhBTP=$CHCH_3$
n-$C_6H_{13}CHO$		4:96 (76%)
$PhCH_2CH_2CHO$	5:95 (83%)[b]	5:95 (78%)
R″$CH(Me)CH_2CHO$[c]		4:96 (83%)
c-$C_6H_{11}CHO$	1:99 (97%)	6:94 (76%)
PhCH(Me)CHO	3:97 (84%)[b]	5:95 (80%)
$PhCH_2C(Me)_2CHO$	8:92 (82%)[b]	20:80 (84%)
TrNHCH(Me)CHO[d]		10:90 (91%)

[a] A 0.1 M solution of the ylide was generated with 0.89 M KHMDS in THF. The aldehyde was added dropwise at −78 °C, the cooling bath was removed, and the mixture was stirred 2 h at rt. Isolated yields are reported, and *Z*/*E* ratios are based on NMR assay. [b] Reference 1. [c] R″ = $CH_2CH_2CH{=}CMe_2$. [d] Reference 12.



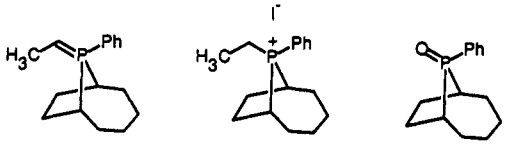
1a R″ = CH_2R b R″ = Ph 2a R″ = CH_2R b R″ = Ph 3

In an attempt to find a Wittig alternative to the Julia method, we have surveyed other 5-membered ring phosphorus environments. This investigation has encountered an *E*-selective ylide **4** (BTP=$CHCH_3$; the abbreviation "BTP" refers to the bridged tetrahydrophosphole ring system). The new reagent is improved relative to the DBP ylides **2a** in two respects: (1) **4** contains an inert *P*-phenyl substituent, and (2) oxaphosphetane intermediates generated from **4** decompose at room temperature. Representative Wittig reactions of **4** with straight-chain or

(1) Vedejs, E.; Marth, C. *Tetrahedron Lett.* **1987**, *28*, 3445.
(2) Julia, M.; Paris, J.-M. *Tetrahedron Lett.* **1973**, *14*, 4833. See also: Kocienski, P. J.; Lythgoe, B.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1045.
(3) Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694.

0022-3263/93/1958-1985$04.00/0

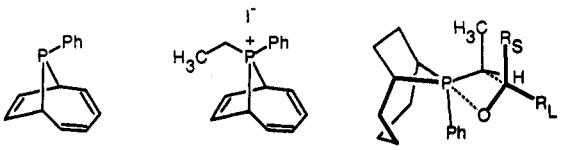
α-mono-substituted aliphatic aldehydes (Table I, column 2) proceed with the same 94–96% *E*-selectivity as in the analogous EtDBP=$CHCH_3$ experiments (Table I, column 1).[1] In the α,α-disubstituted aldehyde reaction, the BTP ylide reacts with significantly lower *E*-selectivity than does **2a**. However, an alternative is already available for the nonenolizable aldehyde using the relatively inexpensive reagent $(Me_2N)_3P{=}CHCH_3$.[4]



4 5 6

The BTP ylide **4** can be made from the phosphonium salt **5** using the standard KHMDS/THF procedure.[3,4] In contrast to the DBP ylide reactions,[1] no special precautions or techniques are required beyond those necessary with any nonstabilized ylide. Workup and product purification are also simplified because the phosphine oxide byproduct **6** can be removed from the organic phase by partitioning between hexane and water.

The synthesis of **5** was achieved starting from the known bicyclic phosphine **7**,[5a] followed by conversion to the salt **8**[6] with ethyl iodide and catalytic hydrogenation over 10% Pd/C (96% **5** isolated, overall yield). No previous example of the hydrogenation of an allylic phosphonium salt could be found in the literature. Evidently, hydrogenolysis of the allylic C–P bond is not a problem. The stereochemistry of **7** has previously been assigned from NMR evidence.[5] We have therefore confirmed that **5** has the indicated structure by X-ray crystallography (Figure 1).



7 8 9

Stereoselectivity in kinetically controlled Wittig reactions has been attributed to a delicate balance between 1,2- and 1,3-interactions in the developing 4-membered ring.[7] In the DBP series, the combination of a planar 5-membered ring and a compressed endocyclic C–P–C bond angle[8] of ca. 95° reduces the 1,3-interaction component. These factors are believed to favor the formation of the trans-disubstituted oxaphosphetane.[7] Judging from the geometry shown in Figure 1, the BTP phosphorus environment is quite different by comparison with the DBP ylide because the 5-membered ring is in an envelope

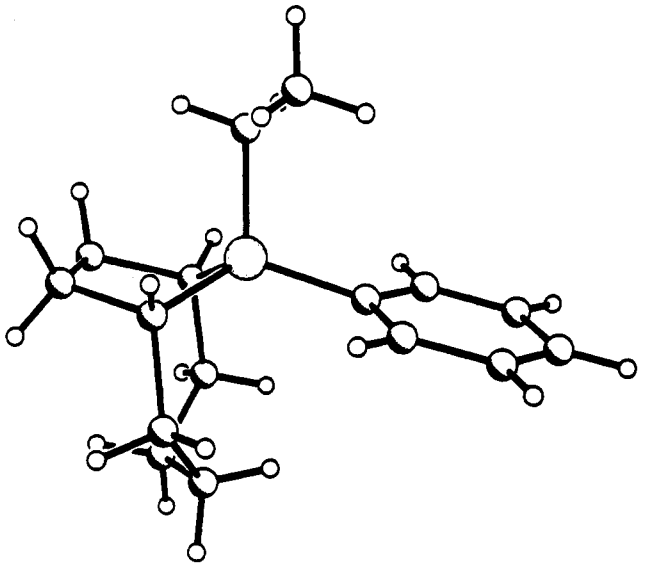


Figure 1. Crystal structure of **5**. The author has deposited atomic coordinates for **5** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

conformation with phosphorus at the "flap". Hypothetical transition states that minimize 1,3-interactions are still possible, such as the 4-center geometry **9**, but further mechanistic discussion would be premature.

Since the starting phosphine **7** is prepared from the relatively expensive cyclooctatetraene,[5] BTP ylides such as **4** will not be competitive with **2a** as reagents for the synthesis of simple *E*-alkenes. Some of the conventional $Ph_3P{=}CHR$ ylides also provide practical access to *E*-alkenes (Schlosser β-oxido ylide method; Salmond γ-oxido ylide; Maryanoff carboxylate ylide, etc.).[9,10] On the other hand, analogs of **4** should be useful in situations where a valuable alkylidene group must be coupled with an aldehyde. More general applications of the BTP ylide technology will require an inexpensive source of the 9-phosphabicyclo-[4.2.1]nonane skeleton.[11] Studies directed toward this goal are under way.

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Supplementary Material Available: Experimental procedures (preparation of **4**, **5**, and **8**) (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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