Excellent *Z*-Selective Olefin Formation Using Pentacoordinate Spirophosphoranes and Aldehydes. Wittig Type Reaction via Hexacoordinate Intermediates

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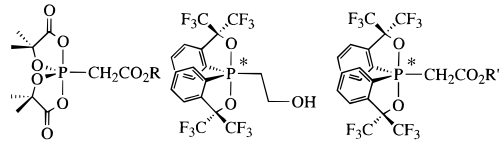
Recent interest in hexacoordinate phosphorus species has risen, since their involvement has been implied in various reactions dealing not only with pentacoordinate but also with tetracoordinate phosphorus compounds.[1] However, synthetic application of pentacoordinate phosphorus utilizing the hexacoordinate state has been limited. Recently, Evans, Jr., et al. have shown that the 10-P-5[2] phosphoranes **1** are capable of undergoing the Wittig reaction[3] and have observed hexacoordinate species in the reaction mixture at low temperatures with the olefin forming step being the rate-determining step.[4] During



1 **2** **3** R'=(-)-menthyl

our successful effort to prepare the first example of a stereochemically rigid enantiomeric pair of pentacoordinate phosphoranes (**2**) bearing asymmetry only upon the phosphorus atom by reductive removal of the ester moiety in **3**,[5a,b] we had also observed hexacoordinate phosphates.[6] This hinted at the possibility of effecting the Wittig reaction using 10-P-5 phosphoranes and prompted us to examine phosphoranes **4**. Thus, we have found that the reaction with aldehydes actually does proceed and that the olefins are obtained with excellent *Z*-selectivity even at 0 °C. As that for stabilized ylides, the method for stereoselective *Z*-olefin synthesis has been limited only to the use of Still's reagent[7] or the recently reported diphenyl phosphonoacetate at low temperatures.[8]

The phosphoranes **4Aa**−**c** were prepared from the P−H phosphorane[9] by alkylation with the corresponding haloacetic esters in the presence of 1,8-diazabicyclo[5.4.0.]undec-7-ene (DBU).[5] Compounds **4A** can be treated with water and subjected to chromatography without noticeable amounts of decomposition.[10] Treatment of **4A** with base followed by benzaldehyde furnished cinnamic esters **6a** with high *Z*-selectivity along with oxidophosphorane **7A**−M^+ ($M^+ = Li^+$, Na^+, K^+) (for $M^+ = H^+$: ^{31}P NMR ($CDCl_3$) δ −14.6),[9a] also a stable compound, even though the reactions were carried out at 0 °C to room temperature (Scheme 1).[11] Isomeric ring-opened **8A**−M^+ was not detected at all and most of **7A**−M^+ could be separated by filtration before quenching the reaction with water. A countercation effect was found to exist at 0 °C in THF as the ratio (*Z*-**6a**:*E*-**6a**) was 72:28 for the lithium, 96:4 for the sodium, and 98:2 for the potassium enolates, respectively. Temperature dependence on the ratio was subtle in THF for both the potassium enolate (99:1 at −20 °C; 98:2 at 0 °C, 97:3 at room temperature) and the lithium enolate (75:25 at −45 °C; 72:28 at 0 °C). The effect of solvent polarity was found to be small for the potassium enolate at 0 °C (98:2 in THF; 97:3 in Et_2O; 95:5 in toluene). The steric effect of the alkoxy group was also negligible in THF at 0 °C [98:2 for **5Aa**−K^+ (R = Et); 97:3 for **5Ac**−K^+ (R = *t*-Bu)].

The reaction of **4Aa** was examined with a variety of aromatic and aliphatic aldehydes employing *t*-BuOK as base in THF. The yields of olefins **6** were high (73−83%), and the *Z*-selectivities were excellent (*Z*:*E* = 96:4 to 98:2, Table 1).[12] It is remarkable that excellent *Z*-selectivity was attained easily at temperatures (0 °C to room temperature) much higher than those necessary for the two *Z*-selective reagents mentioned above and that even alkyl aldehydes carrying secondary or tertiary carbons adjacent to the carbonyl group also showed high selectivity.[7,8,13]

A competitive deprotonation reaction with $(EtO)_2P(O)CH_2CO_2Et$ revealed that **4Aa** was at least three pK_a units less acidic than the phosphonate.[14] This implies that the reverse aldol reaction which produces the carbanion and aldehyde is thermodynamically less favorable and thus must be relatively slow.[15] A competitive reaction with a mixture of benzaldehyde and *p*-tolualdehyde showed benzaldehyde to be clearly more reactive, thus indicating that the reaction ρ value is positive. Since the ρ value of the olefin forming step in the Wittig reaction is

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(10) Selected data of phosphoranes (elemental analyses of all compounds are within 0.4% of calculated values). **4Aa**: mp 91−92 °C; ^{31}P NMR ($CDCl_3$) −27.0. **4Ab**: mp 113−114 °C; ^{31}P NMR ($CDCl_3$) −27.3. **4Ac**: mp 133−135 °C; ^{31}P NMR ($CDCl_3$) −26.3.

(11) Typical reaction conditions are given for the reaction of PhCHO. To a THF solution (5 mL) of phosphorane **4Aa** (505 mg, 0.839 mmol) was added a THF solution (3 mL) of *t*-BuOK (90 mg, 0.80 mmol) at 0 °C under an inert atmosphere. After 30 min of stirring, PhCHO (80 mg, 0.75 mmol) in THF (3 mL) was added to the yellowish solution. After 3 h of stirring, the reaction mixture was filtered through Celite to remove most of the precipitate (**7**−K^+), and then the reaction was quenched with water. Extraction with Et_2O followed by usual workup and chromatographic treatment (benzene−SiO_2) gave ethyl cinnamate (**6**, 108 mg) in 82% yield (*Z*:*E* = 98:2 determined by 400 MHz ^{1}H NMR).

(12) All olefins from alkyl aldehydes, PhCHO, and *p*-$NO_2C_6H_4CHO$ exhibited ca. 11−12% NOE signal enhancement between the two *cis*-vinylic protons.

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(14) Treatment of a 1:1 mixture of **4Aa** and ethyl phosphonate with 0.9 equiv (to one reagent) of *t*-BuOK lead to deprotonation of only the latter at the detection limit of 1% (−log{[deprotonated **4Aa**][$(EtO)_2POCH_2CO_2Et$]}/{[**4Aa**][$(EtO)_2POCH^-CO_2Et$]} = ca. 3).

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(16) The reaction of ca. 1:1 mixture of benzaldehyde (σ_p = 0) and *p*-tolualdehyde (σ_p = −0.17) with 1 equiv (to one aldehyde) of phosphorane resulted in a 25:75 mixture of aldehydes and a 78:22 mixture of ethyl cinnamate and ethyl *p*-methylcinnamate. This gives an approximation of ca. 5 times higher reactivity for benzaldehyde.

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Scheme 1

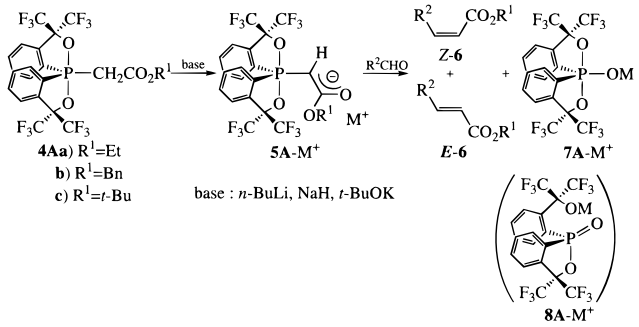


Table 1. Reactions of **4Aa** with Aldehydes at 0 °C Using *t*-BuOK as Base[a]

entry	aldehyde	yield (%)	*Z*:*E*[b]	*Z*:*E*[c]
1	C_6H_5CHO	82	98:2	2:98(60)
2	*p*-$MeOC_6H_4CHO$	76	97:3	2:>98(27)
3	*p*-$O_2NC_6H_4CHO$	83	96:4	13:87(40)
4	*o*-$O_2NC_6H_4CHO$	77	98:2	28:72(42)
5	$PhCH_2CH_2CHO$	73	>98:2	
6[d]	PhMeCHCHO	79	>98:2	
7[d,e]	*t*-BuCHO	75	>98:2	

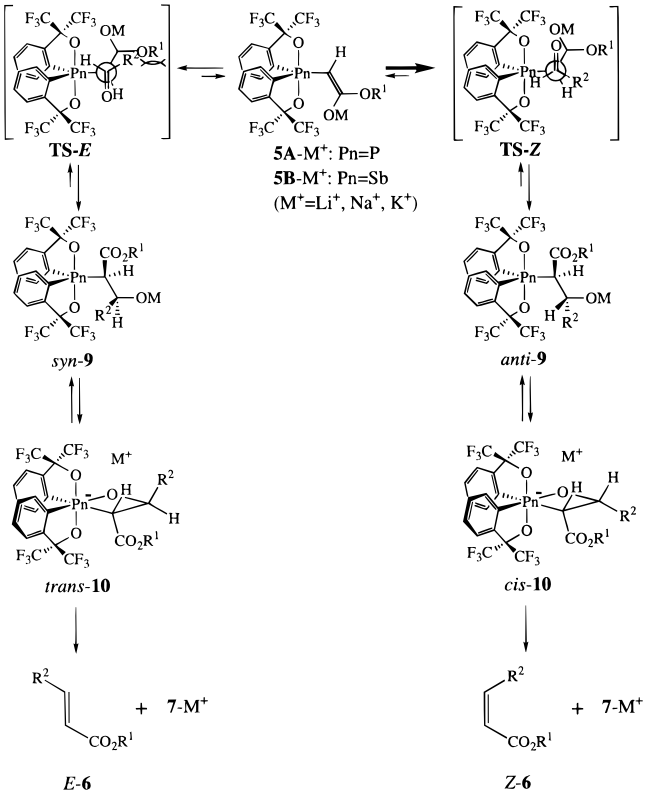
[a] Reaction time was set at 3 h and not optimized. [b] Ratios were determined by ^1H NMR (400 MHz). [c] Selectivity of the corresponding 10-Sb-5 reagent using LDA as base with the total yield in parenthesis. [d] The reaction mixture was allowed to warm to room temperature and was stirred overnight. [e] **4Ab** was used instead of **4Aa**.

known to be negative,[17] it follows that the rate-determining step is the nucleophilic addition of the enolate to the aldehyde. This is consistent with our unsuccessful attempts to observe intermediates in the reaction by NMR or by low-temperature quenching experiments. These results are reasonable since such intermediates cannot be observed for stabilized ylides other than for specially designed model compounds.[18]

Thus, the mechanism of this reaction can be summarized as follows (Scheme 2). The steric hindrance effected by the *gem*-bis(trifluoromethyl) moiety results in the almost exclusive kinetic formation of *anti*-**9A** as opposed to *syn*-**9A**. This is also consistent with the fact that **5A** does not react with ketones. This process is followed by ring closure to form a 12-P-6 hexacoordinate species in which the bonds are expected to be weakened by attaining higher coordination. The ring opening of the bidentate used by Evans allows the stabilization of both the enolate and the adduct leading to facile equilibration, whereas the Martin ligand is conformationally fixed by the aryl group and the *gem*-dimethyl effect thereby lowering possibilities of retro aldol reaction to occur. Hence, by employing the present phosphorane **4A**, *Z*-olefins bearing an electron-withdrawing group are furnished almost exclusively even at 0 °C to room temperature.

In order to show the generality of the role of hexacoordinate intermediates, we prepared the corresponding antimony compounds **4B** and examined the Wittig reaction with aromatic

Scheme 2



aldehydes (Table 1). It was necessary to use 2 equiv of lithium diisopropylamide (LDA) as base to maximize the yields and the yields of **6** were lower (27−60%) than those for **4A**. Aliphatic aldehydes did not give the expected olefins even when 1 equiv of LDA was used. Surprisingly, the stereoselectivity was reversed and *E*-olefins were obtained predominantly (*Z*:*E* = 28:72 to <2:>98). The higher *E* ratio with aromatic aldehydes carrying electron-donating groups reflects the slower rate in formation of the corresponding electron-rich olefins compared with that of electron-deficient olefins from the hexacoordinate intermediates. This implies the possibility for reverse aldol reaction to occur for the adducts of the stiborane.[19]

Further investigation on the mechanism of this reaction and examination of the scope of 10-P-5 phosphoranes as Wittig reagents are in process.

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Supporting Information Available: Experimental procedures and spectroscopic data for phosphoranes **4Aa**−**c** and reaction products (4 pages). See any current masthead page for ordering and Internet access instructions.

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(19) The reason why 2 equiv of LDA is optimal for antimony compounds **4B** is not clear. Lower amounts of base lead to lower *E*-selectivity and thus higher *Z*-selectivity, although the differences were small (i.e., *Z*:*E* = 12:88 (1 equiv of LDA) and 6:94 (2 equiv of LDA)).