Pergamon

Tetrahedron Letters, Vol. 38, No. 44, pp. 7753-7756, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10069-7

The Stereospecific Olefin Formation Reaction of 10-P-5 β-Hydroxy-α,β-diphenylethylphosphoranes

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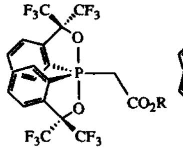
Abstract: Deprotonation of P-H spirophosphorane **4** bearing Martin ligands with *n*-BuLi followed by reaction with *trans*-stilbene oxide gave a pair of *anti*-β-hydroxy-α,β-diphenylethylspirophosphoranes **5**-*S*p**R***S** and **5**-*S*p**S***R**, whereas treatment with *cis*-stilbene oxide yielded *syn*-β-hydroxy-α,β-diphenylethylspirophosphoranes **5**-*S*p**S***S**. The remaining diastereomer **5**-*S*p**R***R** was obtained selectively by α-benzoylation of benzylspirophosphorane **3** followed by reduction with $LiBH_4$. Deprotonation of the diastereomers with *t*-BuOK or *t*-BuONa lead to the stereospecific formation of stilbenes. The *anti* diastereomers gave *cis*-stilbene (*Z*:*E*=99:1) and the *syn* diastereomers furnished *trans*-stilbene (*Z*:*E*=1:99).

The effectiveness and versatility of the Wittig reaction and its modifications in organic synthesis are well established.[1] We have recently developed a novel method of producing olefins bearing an alkoxycarbonyl group with high Z-selectivity by utilizing the enolate from 10-P-5[2] phosphorane **1**, which could be classified as a stabilized ylide.[3] In order to prove the intermediacy of hexacoordinate species in the reaction, we prepared β-hydroxyethylphosphorane **2** which does not carry an α-substituent. In the event, we have found that **2** quantitatively gives hexacoordinate species even at ambient temperatures upon deprotonation.[4] However, this compound did not give the expected olefin upon heating.[5] Thus, we have extended our studies to an intermediary case, i. e., diastereomeric β-hydroxyethylphosphoranes **5** carrying an α-phenyl group. Only in the case of modified Wittig reagents have there been successes in obtaining Z-olefins with high[6] or excellent[7] selectivities in the Wittig reaction. The use of phosphines (Horner reagents) and phosphonates (Wadsworth-Emmons reagents) have proved less successful. Studies on β-hydroxyethylphosphine oxides[8] and phosphonates,[9] which share the common feature with **5** of being anionic as the reactive species, have revealed that deprotonation led to either large sums of the benzyl compound or *E*-olefins as a consequence of C-C bond cleavage, thereby accounting for the low Z-selectivity. We have found that the deprotonation reaction of 10-P-5 β-hydroxy-α,β-diphenylethylspirophosphoranes leads to stereospecific formation of stilbenes in contrast to these conventional anionic reagents.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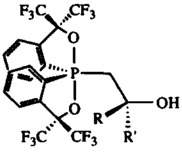
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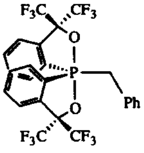
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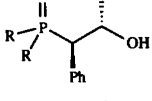
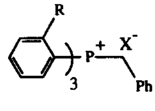
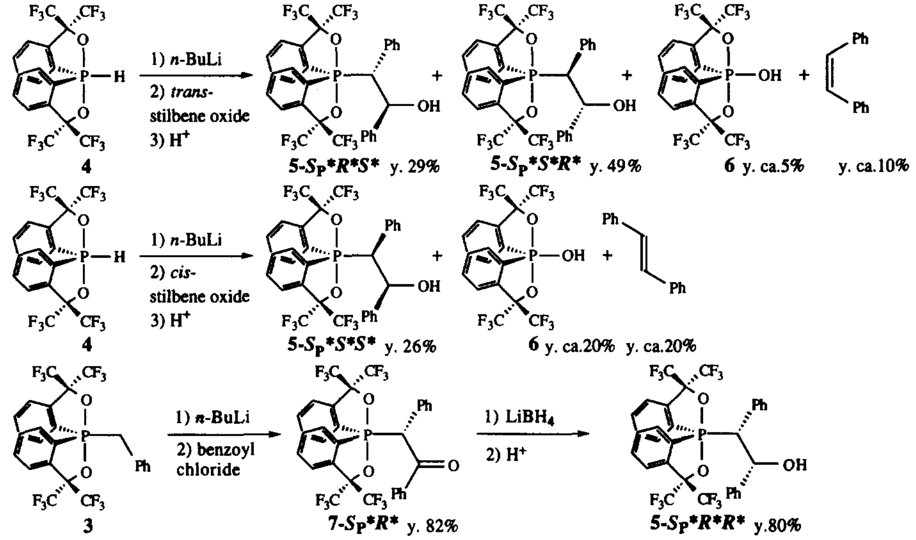

R=Ph, MeO


R=MeOCH₂O, X=Br
R=H, X=I

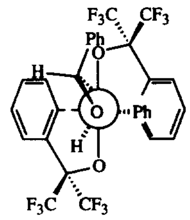
The preparation of the diastereomeric β-hydroxyethylphosphoranes was carried out by treating P-H phosphorane **4**[10,11] with *n*-BuLi followed by treatment with stilbene oxide at room temperature in THF.

Reaction with *trans*-stilbene oxide yielded a pair of *anti* diastereomers, **5-$S_P^*R^*S^*$** [δ_P ($CDCl_3$) -23.5; y. 29%][12] and **5-$S_P^*S^*R^*$** [δ_P ($CDCl_3$) -21.9, y. 49%], along with *cis*-stilbene (ca. 10%) and P-OH (ca. 5 %) phosphorane **6**, which are products of overreaction. The relative stereochemistry of **5-$S_P^*R^*S^*$** could be determined by X-ray structural analysis.[13] On the other hand, reaction of **4** with *cis*-stilbene oxide gave only one *syn* diastereomer, **5-$S_P^*S^*S^*$** [δ_P ($CDCl_3$) -19.3, y. 26%] of which relative stereochemistry could be determined by chemical correlation (vide infra), together with *trans*-stilbene (y. ca. 20%) and **6** (y. ca. 20%). Since the phosphoranide is expected to have essentially trigonal bipyramid character,[14] the selectivity can be rationalized by assuming that the orientation of the epoxide has the most bulky phenyl group[15] in the equatorial plane and the next bulky alkyl group *gauche* in the open space between the apical and equatorial bonds as in model **A** (vide infra; viewed from O→C→P direction). Heating (*t*-butyltoluene, 190 °C, 11 days) of **5-$S_P^*S^*S^*$** lead to a mixture (5:2) of **5-$S_P^*S^*S^*$** and **5-$S_P^*R^*R^*$** [δ_P ($CDCl_3$) -19.1], the remaining diastereomer, by epimerization of the phosphorus atom. No decomposition to stilbene and **6** or to benzaldehyde and **3** could be observed during this reaction, thus indicating the high thermal stability of the β-hydroxyethylphosphoranes.

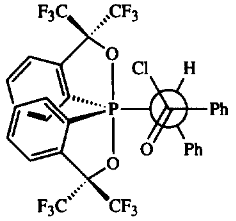


Since **5-$S_P^*R^*R^*$** could not be obtained in a satisfactory manner, an alternate method was sought. The reaction of **3** with *n*-BuLi followed by treatment with benzoyl chloride resulted in the exclusive formation of a carbonyl compound **7-$S_P^*R^*$** [δ_P ($CDCl_3$) -25.2, y. 82%]. The relative stereochemistry of this compound could also be determined by X-ray structural analysis.[13] The reduction of this compound with $LiBH_4$ was also found to be stereoselective, giving only **5-$S_P^*R^*R^*$** (y. 80%). Since the reduction of **7-$S_P^*R^*$** could only result in the formation of **5-$S_P^*R^*R^*$** and/or **5-$S_P^*R^*S^*$** of which the latter had already been established by X-ray analysis, the relative stereochemistry of all four isomers of **5** could be certified.

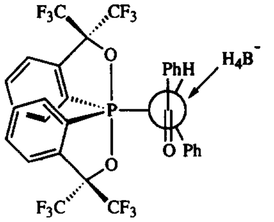
The stereoselective formation of **7** can be rationalized by assuming model **B**, in which *gauche* interactions are minimized since the order in substituent size is Ph>Cl>O. The stereochemistry of reduction of **7** with $LiBH_4$ is consistent with usual Felkin-Anh selectivity as shown in **C**.



A

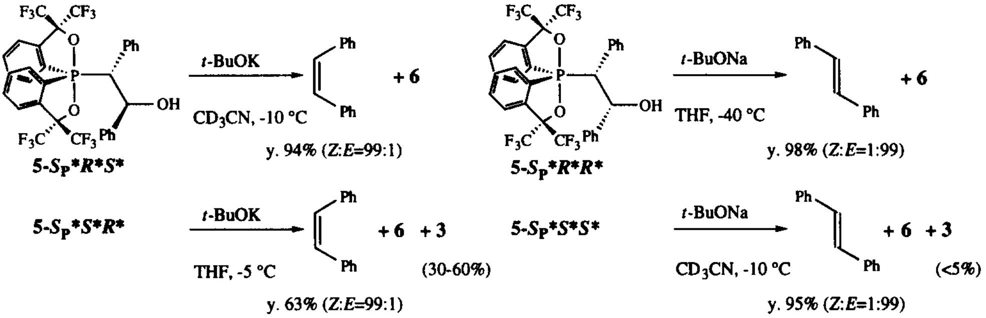


B

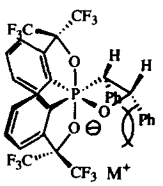


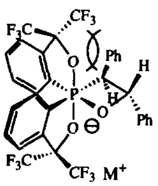
C

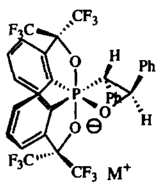
The olefination reaction upon deprotonation using Li^+-base was rather slow and complex. However reaction with K^+- or Na^+-base was rapid and stereospecific. The reactions of $\mathbf{5\text{-}}S_P{*}R{*}S{*}$ and $\mathbf{5\text{-}}S_P{*}R{*}R{*}$ proceeded stereospecifically and quantitatively to give *cis* and *trans* stilbenes, respectively with *syn* elimination (99:1). The reactions of $\mathbf{5\text{-}}S_P{*}S{*}R{*}$ and $\mathbf{5\text{-}}S_P{*}S{*}S{*}$ also gave the same exclusive *cis-trans* ratios. However, $\mathbf{5\text{-}}S_P{*}S{*}R{*}$ gave significant amounts (30-60%) of retro aldol product **3** while $\mathbf{5\text{-}}S_P{*}S{*}S{*}$ afforded only a small amount (<5%) of **3**. These results implied that there was a difference in the olefination rates due to steric hindrance in the transition state, and that solvent cage recombination was negligible in this system. The latter is endorsed by the fact that the α-proton of **3** cannot be deprotonated to give a benzyl anion by *t*-BuOK.

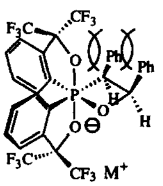


Although hexacoordinate species could not be observed upon deprotonation with *n*-BuLi at ambient temperatures with any of the diastereomers, $\mathbf{5\text{-}}S_P{*}R{*}S{*}\text{-}Na^+$ was observed in equilibrium with a hexacoordinate species [δ_P (THF) -110(br)](1:1) at -60 °C, and $\mathbf{5\text{-}}S_P{*}R{*}R{*}\text{-}Na^+$ was found to be completely converted to hexacoordinate species [δ_P (THF) -112]. The ratio for the former did not change upon progression of reaction, indicating that equilibration is fast. The observation of hexacoordinate species and the participation of retro-aldol can be rationalized by comparing the stereochemistry of plausible hexacoordinate intermediates derived from the β-hydroxide anions of **5**. As the drawings show, the 1,2-interaction between the α-phenyl group and the bidentate trifluoromethyl group is large in $\mathbf{8\text{-}}S_P{*}S{*}R{*}$ and $\mathbf{8\text{-}}S_P{*}S{*}S{*}$, thus making it difficult for them to observe the presence of hexacoordination. As for $\mathbf{8\text{-}}S_P{*}R{*}S{*}$, although 1,2-diphenyl interaction could be unfavorable for hexacoordination, the fact the hexacoordinate species is actually observed indicates that it is less effective than the above 1,2-interaction. Rather it seems that this same interaction helps the olefin formation as a buttress effect, i. e., a relief of steric hindrance is gained by the decomposition.


8-S_P*R*S*


8-S_P*S*S*


8-S_P*R*R*


8-S_P*S*R*

In conclusion, we have shown that the olefination reaction of β-hydroxy-α,β-diphenylethylspirophosphoranes by deprotonation proceeds stereospecifically in contrast to ordinary phosphoryl based anionic Wittig reagents and that hexacoordinate intermediates are involved. This provides evidence that the reversibility, i. e., retro aldol, of carbonyl adducts of α-anions of phosphoranes bearing Martin ligands is generally negligible once hexacoordinate intermediates are formed, as previously assumed.[3]

References and Footnotes

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12. All diastereomers of **5** and **7** gave correct elemental analysis (within 0.4%) and reasonable spectra. Mp: 5-Sp*R*S* (203.5-204.5 °C, dec); 5-Sp*S*R* (200.5-201.5 °C, dec); 5-Sp*R*R* (165-165.5 °C, dec); 5-Sp*S*S* (196-197 °C, dec); 7-Sp*R* (160-161 °C, dec); 7-Sp*S* (189-190 °C, dec).
13. Details of the X-ray analysis will be reported later in a full account.
14. The X-ray structure of a stiboranide differing only in the pnictogen atom suggests TBP character. See: Akiba, K.-y.; Nakata, H.; Yamamoto, Y.; Kojima, S. *Chem. Lett.* **1992**, 1559-1562.
15. The characteristic angular relationship of substituents within the epoxide would make this Ph group the most bulky in a ring opening reaction involving in-line attack of the P nucleophile.

(*Received in Japan* 16 *June* 1997; *accepted* 1 *September* 1997)