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Stereoselective [2,3] sigmatropic rearrangement of acyclic allylic phosphinites

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Received (in Cambridge, UK) 4th November 2003, Accepted 4th December 2003
First published as an Advance Article on the web 5th January 2004

The [2,3] sigmatropic rearrangement of open-chain allylic phosphinites was found to proceed with high stereoselectivity, allowing the preparation of chiral (*E*) allylic phosphine oxides and aminophosphine oxides with 99% *ee* and a perfect transfer of the chiral information.

Chiral phosphines and diphosphines are important ligands for the performance of asymmetric metal catalyses.[1] The stereoselective synthesis of chiral phosphines has attracted much attention.[2] Recently, we have shown that cyclic allylic phosphinites undergo highly stereoselective [2,3] sigmatropic rearrangements,[3] affording chiral phosphines and diphosphines which are suitable ligands for the performance of Rh(I)-catalyzed asymmetric hydrogenations[4] and hydroborations.[5] Although this rearrangement is known to be highly enantioselective using chiral phosphorus centers,[6] the transfer of chirality in the carbon backbone of an open-chain system has not been studied. Much work has also been reported on the rearrangement of propargylic phosphinites,[7] but the stereochemical course of this rearrangement has not been addressed. Herein, we wish to report applications of this sigmatropic rearrangement for the preparation of chiral acyclic phosphine oxides (bearing an α-quaternary center) as well as chiral aminophosphine oxides.

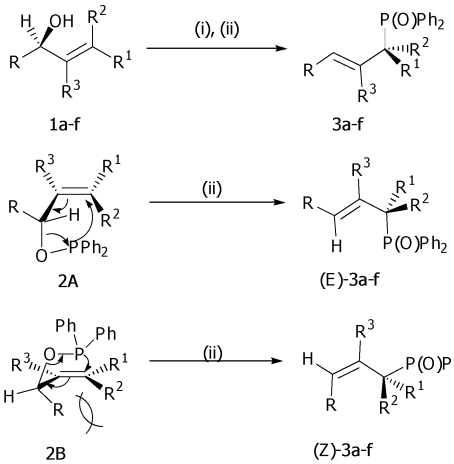
We first prepared a range of allylic alcohols of type **1** using standard methods[8] in order to study the influence of the substituents on the stereoselectivity of the rearrangement. The treatment of the alcohols **1** with Ph_2PCl (1 equiv.) in the presence of DMAP (1 equiv.) in Et_2O (rt, 0.5 h) provided quantitatively the corresponding allylic phosphinites **2a–f**. The heating of these phosphinites at 80 °C for 3–20 h provided the (*E*) and (*Z*) allylic phosphine oxides **3a–f** with good to excellent stereoselectivity (Table 1 and Scheme 1).

In contrast to cyclic allylic phosphinites, the acyclic phosphinites **2a–f** can adopt two conformations suitable for the [2,3] sigmatropic rearrangement (**2A** and **2B**). In the case of **2A**, there is a moderate steric interaction between the allylic hydrogen atom and the substituent R^1, resulting in a weak 1,3-allylic strain.[9] On the other hand, the second conformation **2B** that we can envision for the sigmatropic rearrangement shows a strong interaction between the

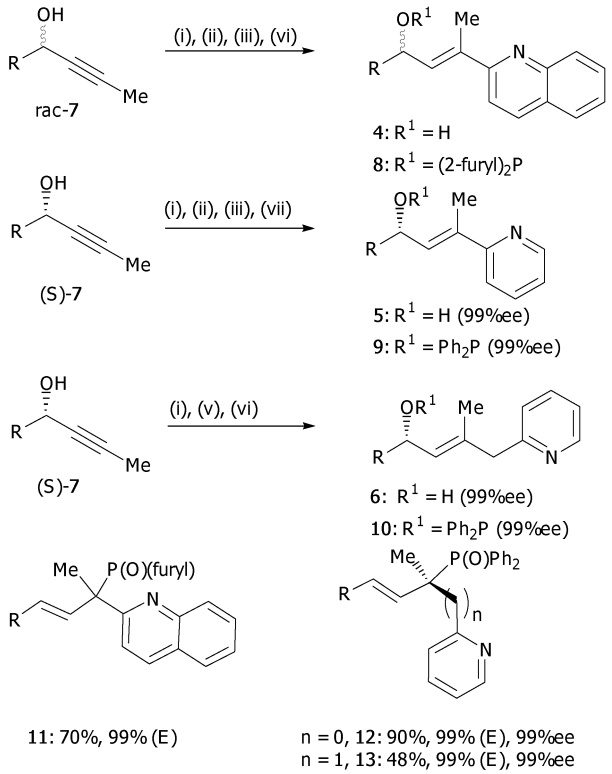
Table 1 Influence of the substituents on the stereoselectivity

Entry	Alcohol	R^1	R^2	R^3	Product[a]	*E* : *Z*[b]	Yield (%)[c]
1	**1a**	Me	H	H	**3a**	97 : 3	75
2	**1b**	Bu	H	H	**3b**	96 : 4	60
3	**1c**	Me	H	Me	**3c**	95 : 5	50
4	**1d**	2-pyr	H	H	**3d**	85 : 15	50
5	**1e**	H	Me	H	**3e**	> 99 : 1	50
6	**1f**	Bu	Me	H	**3f**	> 99 : 1	50

[a] R = CH_2–CH_2–(1-naphthyl). [b] Determined by ^{31}P NMR. [c] Isolated yield of analytically pure products.

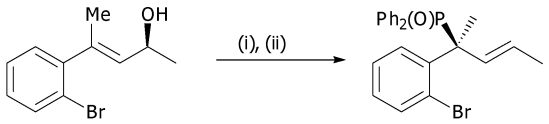


Scheme 1 *Reagents and conditions*: (i) PPh_2Cl (1 equiv.), DMAP (1 equiv.), Et_2O, rt, 0.5 h; (ii) toluene, 80 °C, 3 h.



Scheme 2 *Reagents and conditions*: (i) Bu_3SnH (1.5 equiv.), $PdCl_2(PPh_3)_2$ (0.05 equiv.), THF, rt, 0.5 h (70%); (ii) *n*-BuLi (2 equiv.), THF, −50 °C to rt, 1 h, then $ZnCl_2$ (2 equiv.), −50 °C to rt; (iii) 2-bromopyridine (3 equiv.), $Pd(PPh_3)_4$ (0.15 equiv.), THF, 65 °C, 48 h (50%); (iv) 2-TfO-quinoline (3 equiv.), $Pd(PPh_3)_4$ (0.15 equiv.), THF, 65 °C, 48 h (35%); (v) I_2 (1.1 equiv.), CH_2Cl_2, rt, (80%), then 2-pyridylmethylzinc chloride (3 equiv.), THF, 65 °C, 48 h (25%); (vi) DMAP (1 equiv.), $(2\text{-furyl})_2PCl$, Et_2O, rt, 0.5 h (95%); (vii) DMAP (1 equiv.), Ph_2PCl (1 equiv.), Et_2O, rt, 0.5 h (95%).

DOI: 10.1039/b313979d



14: 99%ee 15: 75%, >99%ee, >99% E

Scheme 3 *Reagents and conditions*: (i) PPh_2Cl (1 equiv.), DMAP (1 equiv.), Et_2O, rt, 0.5 h; (ii) toluene, 110 °C, 12 h.

substituents R and R^1. The sigmatropic rearrangement *via* **2A** leads to the (*E*)-allylic phosphine oxides **3** whereas the thermal reaction *via* **2B** furnishes predominantly the (*Z*)-allylic phosphine oxides **3**.

As can be seen from Table 1, the presence of a small substituent R^2 (R^2 = H; entries 1–4) led to lower *E* : *Z* ratios (85 : 15 to 97 : 3), whereas the phosphinites bearing a methyl group at this position (R^2 = Me) gave only the (*E*) products (*E*)-**3e** and (*E*)-**3f** in 50% yield (entries 5 and 6). The presence of a pyridine ring with a basic nitrogen was also possible (entry 4; R^1 = 2-pyr), however a lower *E* : *Z* ratio was observed. Nevertheless, we have applied this method to the preparation of three allylic alcohols **4–6** starting from the propargylic alcohol **7** (Scheme 2).[8]

Chiral propargylic alcohol (*S*)-**7**[10] was used (> 99% *ee*) for the preparation of the allylic alcohol **5** with 99% *ee*. All three alcohols were converted into the corresponding phosphinites **8–10** under standard conditions, using either chlorodiphenylphosphine or chlorodi(2-furyl)phosphine. The [2,3] sigmatropic shift was realized in the case of the 2-furyl substituted phosphinites **8** and **10** at 110 °C (3 h) and afforded only the (*E*)-allylic phosphine oxides **11** and **13** respectively in 70 and 48% yield (> 99% *E*), Scheme 2. In the case of the chiral phosphinite **9**, a smooth rearrangement occurred at 80 °C (3 h) and provided the desired aminophosphine oxide **12** in 90% yield (99% *ee*, > 99% *E*, Scheme 2).

Finally, we examined the rearrangement of the (*E*)-cinnamic alcohol derivative **14** which was prepared in 99% *ee*.[11] Its conversion to the corresponding phosphinite by the reaction with Ph_2PCl (1 equiv.) in the presence of DMAP (1 equiv.) in Et_2O was complete at rt within 0.5 h. Heating in toluene at reflux for 12 h furnished the desired allylic phosphine oxide **15** in 75% yield as a single stereoisomer (99% *ee*, > 99% *E*), Scheme 3.

The excellent transfer of the chirality observed in the preparation of the chiral aminophosphine oxide **13** and the allylic phosphine oxide **15** demonstrates the synthetic utility of this [2,3] sigmatropic rearrangement for the elaboration of new ligands for metal catalysis. Efforts in this direction are currently underway in our laboratories.[12]

We thank the Fonds der Chemischen Industrie for financial support. We also thank BASF AG (Ludwigshafen), Chemetall GmbH (Frankfurt) and Bayer Chemicals (Leverkusen) for the generous gift of chemicals.

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12 **Typical procedure**: An argon-flushed flask was charged with DMAP (1 mmol, 1 equiv.), an allylic alcohol (1 mmol, 1 equiv.) and Et_2O (5 mL). When a clear solution was obtained, neat chlorophosphine was added dropwise (1 mmol, 1 equiv.). A white precipitate was formed. It was stirred at rt for 30 min, then filtered through a short pad of dry silica gel. The solvents were evaporated *in vacuo* and toluene (5 mL) was added. The phosphinite was heated at the required temperature. The solvents were evaporated *in vacuo* and the residue was chromatographed (Et_2O–CH_2Cl_2, 1 : 1), leading to the pure phosphine oxide.
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