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Stereoselective Preparation of Phosphine Oxides *via* a 2,3-Sigmatropic Shift of Allylic Diphenylphosphinites

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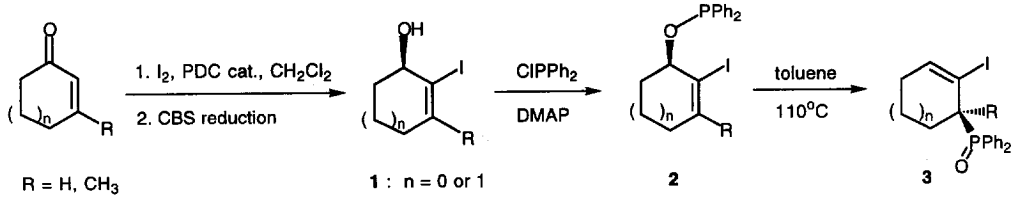
Abstract

The thermic rearrangement of various chiral or racemic allylic diphenylphosphinites to allylic phosphine oxides has been applied for the preparation of several chiral diphosphine oxides of interest for asymmetric catalysis.

The design and the preparation of chiral phosphines and diphosphines for asymmetric catalysis is an active area of research [1]. Herein, we wish to report a new approach to chiral and racemic functionalized phosphine oxides starting from readily available chiral allylic alcohols of type **1** using the [2,3] sigmatropic rearrangement of allylic diphenylphosphinites of type **2** [2] (Scheme 1). To the best of our knowledge, this rearrangement (Arbuzov rearrangement) has never been applied to chiral cyclic systems.



Scheme 1

The 2-iodoallylic alcohols **1a-d** were prepared in a two-step sequence from the corresponding commercially available 2-cyclohexenones or 2-cyclopentenones. The enones were treated with iodine (1.1 to 1.4 equiv) in the presence of catalytic amounts of pyridinium dichromate (0.3 equiv) in dichloromethane for 6 to 24 h, affording 2-iodoenones in good yields [3]. The 2-iodoenones were reduced by the CBS method [4] with methyl-oxazaborolidine as catalyst (10-15 mol %) and $BH_3.Me_2S$ (0.6 equiv) in THF affording the desired 2-iodoallylic alcohols **1a-d**. The enantiomeric excesses were in a range of 95% to 99% without recrystallization. The reaction of these chiral allylic alcohols with chlorodiphenylphosphine (1.05 equiv) in the presence of DMAP (1.05 equiv) in toluene furnished the intermediate phosphinites which were heated under reflux overnight. The phosphine oxides **3a**, **3b** and **3c** were isolated in good yield (Table 1). Of particular interest is the rearrangement of the phosphinite derived from the 3-substituted cyclohexenol **1c**. It furnished the phosphine oxide **3c** in 77% yield bearing a chiral quaternary center. In the case of **1d** the rearrangement failed (Scheme 1 and Table 1).

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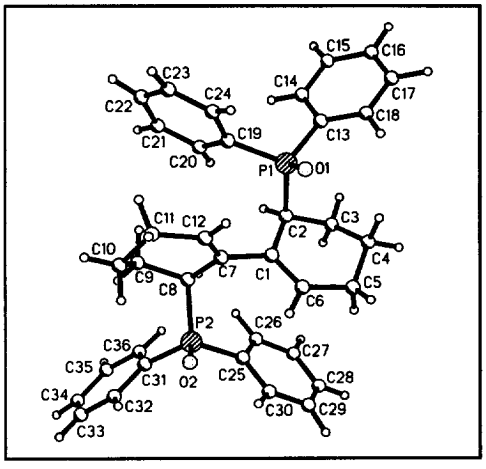
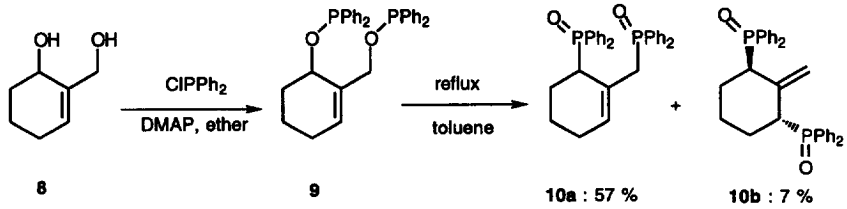
The [2,3] sigmatropic rearrangement was also performed on more elaborated systems. Thus, optically pure 1,4-diols **4a** and **4b** were obtained by reductive nickel catalyzed homocoupling reaction [5] from the alcohols **1a** and **1b** in 42% and 49% yield respectively (Zn (1 equiv), Bu_4NI (0.4 to 0.6 equiv), $NiCl_2(PPh_3)_2$ (0.2 to 0.3 equiv) in THF).



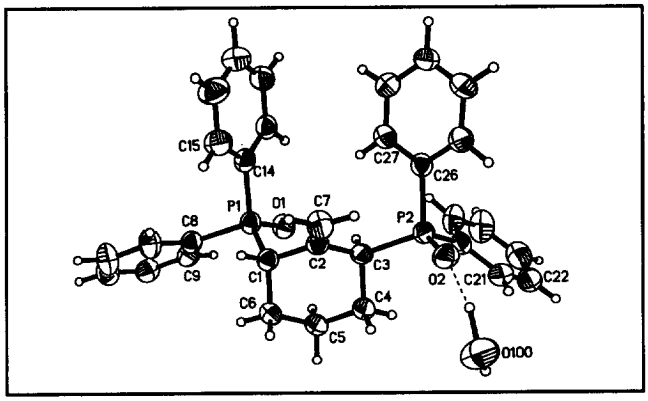
The double rearrangement of the corresponding biphosphinites afforded the biphosphine oxides **5a** and **5b** in 86% and 65% yield. In these cases, the formation of the biphosphinites had to be performed in ether and the chlorohydrate of DMAP had to be filtrated before the rearrangement. The absence of **meso-5a** in the crude reaction mixture confirms that these [2,3] sigmatropic rearrangements occur with complete retention of the stereochemical information. The stereochemistry of **5a** was confirmed by X-ray structure (Figure 1) [8].

Figure 1. X-ray Structure of **5a**

By using an unsaturated racemic 1,3-diol like **8** [6], two biphosphine oxides **10a** and **10b** are expected. The reaction of **8** with $ClPPh_2$ (2.1 equiv) and DMAP (2.1 equiv) in ether (20°C, 1h) provided the *bis*-phosphinite **9** which after filtration and heating under reflux in toluene for 16h underwent a double [2,3] sigmatropic rearrangement. It afforded the products **10a** and **10b** in a 88:12 ratio. After purification by flash chromatography, **10a** and **10b** were isolated in 57% and 7% yield (Scheme 2).



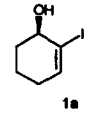
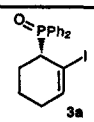
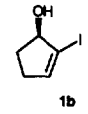
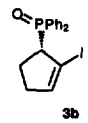
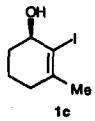
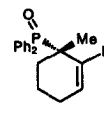
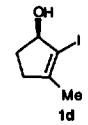
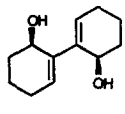
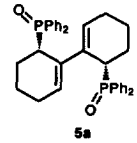
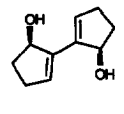
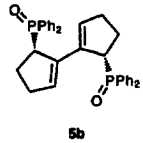
Scheme 2



The product-ratio between **10a** and **10b** indicates that the exocyclic rearrangement is favored over the endocyclic rearrangement. The obtained X-ray structure of **10b** confirms the *trans*-conformation between the diphenylphosphinoyl groups (Figure 2) [8]. No **meso-10b** was detectable by ^{31}P NMR on the crude reaction mixture.

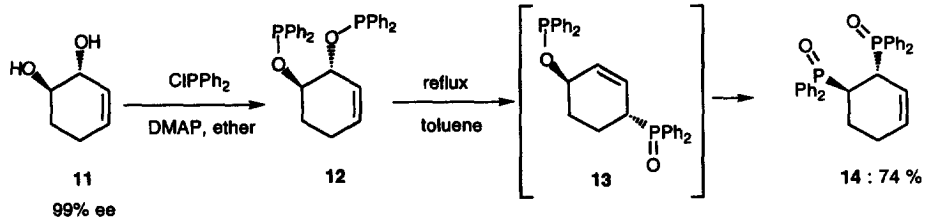
Figure 2. X-ray Structure of **10b**

Table 1. Chiral phosphine oxides or diphosphine oxides obtained by a [2,3]-sigmatropic rearrangement of phosphinites or diphosphinites prepared from enantiomerically enriched allylic alcohols **1a-d** or *bis*-allylic diols **4a-b**.

Entry	Allylic alcohols of type **1** or **4**	%*ee* [a]	$[\alpha]_D^{20}$ [b]	Product of type **3** or **5**	Yield (%)d	$[\alpha]_D^{20}$ [b]
1	 **1a**	95 (*R*)	+ 60.6 (1.06)	 **3a**	86 (*S*)	- 99.3 (1.42)
2	 **1b**	96 (*R*)	+ 31.9 (1.37)	 **3b**	77 (*S*)	- 25.2 (1.30)
3	 **1c**	99 (*R*)	+ 84.0 (1.86)	 **3c**	80 (*S*)	+ 52.0 (1.21)
4	 **1d**	95 (*R*)	+35.1 (1.81)	decomposition	-	-
5	 **4a**	100 (*R*, *R*)	+ 243.0 (1.07)	 **5a**	86 (*S*, *S*)	-143.1 (1.03)
6	 **4b**	100 (*R*, *R*)	- 65.4 (1.01)[c]	 **5b**	65 (*S*, *S*)	- 69.1 (1.33)

[a]The enantiomeric excesses were determined by chiral HPLC (Chiralcel OD or OJ columns). [b]Optical rotation; the concentrations of **1a-d**, **3a-c**, **4a** and **5a-b** in $CHCl_3$ are given in parenthesis. [c]In MeOH. [d]Isolated yields of analytically pure products.

Similarly, the optically pure unsaturated 1,2-diol **11** ((*1R*, *2R*) *trans* cyclohex-3-en-1,2-diol) [7] was converted to the corresponding biphosphinite **12**. After filtration on silicagel, heating of **12** in toluene for 42 h at reflux furnished the chiral *trans* 1,2-diphosphine oxide **14** ($[\alpha]_D$ -68.7 (*c* 1.23, $CHCl_3$)) in 74% yield via the intermediate **13** (Scheme 3).



Scheme 3

In summary, we have described a stereoselective preparation of monophosphine oxides, 1,2-*bis*-phosphine oxides, 1,3-*bis*-phosphine oxides and 1,4-*bis*-phosphine oxides starting from readily available chiral or racemic allylic alcohols. The preparation of new ligands from these phosphine oxides and their application in asymmetric catalysis is currently being investigated [9].

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[7] The preparation of the optically pure diol **11** will be reported in further article. The enantiomeric excess was determined by chiral GC analysis of the corresponding diacetate on cyclodextrin column. $[\alpha]_D$ -22.3 (*c* 1.21, $CHCl_3$). For the preparation of the racemic diol see: Posternak, T.; Friedli, H. *Helv. Chim. Acta* **1953**, *36*, 251-256.

[8] X-Rays analysis were performed by measuring intensity data on a Enraf-Nonius CAD-4 diffractometer using graphite-monochromated Cu Kα radiation and the ω scan technique up to θ = 65° for compound **5a** and θ = 70° for compound **10b**. Lists of atomic coordinates, bond distances, bond angles, torsional angles have been deposited at the Cambridge Crystallographic Data Center (12 Union Road, Cambridge CB2 1EZ, UK). Deposition numbers of **5a** and **10b** are CCDC 118281 and CCDC 118282.

[9]**Typical Procedures**

Method A: A 250-mL-flask under argon equipped with a magnetic stirrer and a reflux condenser is charged with (*R*)-2-iodo cyclohexenol (3.36 g, 15 mmol), DMAP (1.93 g, 15.8 mmol, 1.05 eq) and toluene (80 mL freshly distilled over sodium). To this homogeneous solution is added dropwise pure chlorodiphenylphosphine (2.85 mL, 3.49 g, 15.8 mmol, 1.05 eq). The resulting suspension is stirred at rt for 1 h and then heated to reflux for 16 h. The mixture is cooled to rt, diluted with CH_2Cl_2 and ether and washed successively with a 10 % solution of HCl, water and brine. The organic phase is dried over $MgSO_4$, filtrated and the solvents evaporated *in vacuo*. The crude compound is purified by chromatography over silica gel (CH_2Cl_2/Et_2O 1:1) yielding pure **3a** as a colorless crystalline solid (5.25 g, 86 %; mp = 193-195 °C). The same procedure is applied for phosphine oxides **3b** and **3c**.

Method B: A 100-mL-flask under argon equipped with a magnetic stirrer is charged with (1*R*, 1'*R*)2,2-bicyclohexenol (157 mg, 0.808 mmol), DMAP (218 mg, 1.78 mmol, 2.2 eq) and ether (15 mL freshly distilled over sodium). To the homogeneous solution, pure chlorodiphenylphosphine (0.31 mL, 0.375 g, 2.1 eq, 1.70 mmol) is added dropwise. The resulting suspension is stirred at rt for 1 h, filtrated under argon over Celite and washed twice with ether. The etheral solution is evaporated under reduced pressure and the resulting solid biphosphinite is diluted in toluene (30 mL freshly distilled over sodium). The resulting solution is refluxed under argon for 20 h and then cooled to rt. The work-up corresponds to the procedure A. The crude compound is purified by column chromatography (Et_2O/CH_2Cl_2/MeOH 60/40/0 to 60/40/5) yielding **5a** as a colorless crystalline solid (396 mg, 86 %; mp = 270-274 °C with decomposition).