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Detection of the enantiomers of P-stereogenic pentacoordinated phosphorus compounds: ^{31}P NMR of oxaphosphetes in optically active solvents

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Abstract

The enantiomers of spirocyclic oxaphosphetes possessing the sterically bulky 2,4,6-triisopropyl-phenyl group bound to the pentacoordinated phosphorus stereogenic centre could be distinguished in optically active amines as solvents.

Since 1,2-oxaphosphetanes are well-known intermediates in the Wittig reaction, a number of efforts have been made for their structural characterisation both in solution and in solid state.[1] Detailed NMR investigations have clearly shown that the most electronegative substituents (e.g. oxygen) prefer the apical position in a trigonal bipyramidal (*tbp*) structure and that the pentacoordinated phosphorus atom is in a dynamic condition due to the pseudorotations.[2] If there is one carbon stereogenic centre in the oxaphosphetane ring of the spirocyclic dibenzophosphole derivative that is a relatively rigid model, two diastereoisomers ($\mathbf{1_1}$ and $\mathbf{1_2}$) have been detected at −30°C.[3] The two isomers possess distinct ^{13}C chemical shifts and $^{1}J(^{31}\mathrm{P},\ ^{13}\mathrm{C})$, $^{2}J(^{31}\mathrm{P},\ ^{13}\mathrm{C})$ coupling constants, and can be transformed into each other by pseudorotations around the phosphorus atom of the dibenzophosphole moiety.[4]

To the best of our knowledge, no reference to the P-chirality of those compounds with five different substituents at the phosphorus atom **2** has been reported to date (Fig. 1).

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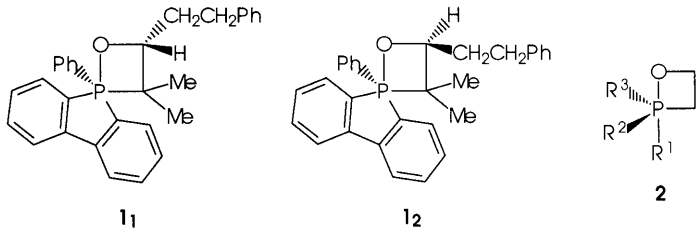
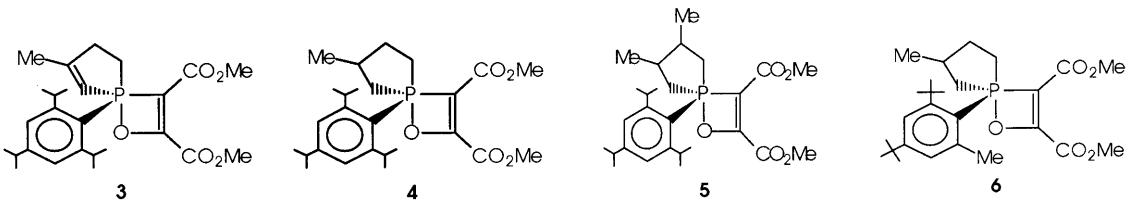


Figure 1.

This fact is rather surprising, since $PR_1R_2R_3R_4R_5$ ($R_1 \neq R_2 \neq R_3 \neq R_4 \neq R_5$) compounds of *tbp* structure are obviously P-stereogenic compounds. Contrary to the lack of mention of simple chiral phosphoranes, the chiral phosphines with a tetrahedral phosphorus atom have an enormously growing literature mainly due to the importance of chiral (among them P-stereogenic) phosphines in homogeneous catalysis.

On the basis of our recent synthetic results,[5,6] the P-stereogenicity of some simple spirocyclic oxaphosphete derivatives with sterically bulky 2,4,6-triisopropylphenyl- **3**–**5** or 2,4-di-*tert*-butyl-6-methylphenyl substituents **6** (Fig. 2) is discussed. Compounds **4**, **6** and **5** possess one and two carbon stereogenic centres, respectively, and due to the presence of a phosphorus stereogenic centre, they are mixtures of two ($\mathbf{4_1}$, $\mathbf{4_2}$; $\mathbf{6_1}$, $\mathbf{6_2}$) and three diastereoisomers ($\mathbf{5_1}$, $\mathbf{5_2}$, $\mathbf{5_3}$) (Fig. 2). It is noteworthy, that the diastereomers of spiro derivatives **4**–**6** were not found to interconvert at room temperature. Accordingly, **4**, **6** and **5** show two and three sharp singlets, respectively, in the $^{31}P\{^1H\}$ NMR in $CDCl_3$ (Table 1). At the same time, **3** containing only one P stereogenic centre gives a single peak in $^{31}P\{^1H\}$ NMR under the same conditions.



R_P/S_P

$R_C, R_P / S_C, S_P$
$S_C, R_P / R_C, S_P$

$R_C, R_C, R_P / S_C, S_C, S_P$
$S_C, S_C, R_P / R_C, R_C, S_P$
$S_C, R_C, R_P / R_C, S_C, S_P$

$R_C, R_P / S_C, S_P$
$S_C, R_P / R_C, S_P$

Figure 2.

Since all of our model compounds proved to be chemically stable both in alcohols and amines, readily available optically active compounds could be used as solvents. The P-stereogenicity of the above heterocycles was proved in a simple way by using optically active amines, such as (*R*)-(+)-α-methylbenzylamine (**MBA**), (*R*)-(+)-1-(1-naphthyl)ethylamine (**NEA**), and (*S*)-(−)-1-amino-2-(methoxymethyl)pyrrolidine (**AMP**) in the NMR experiments (Fig. 3).

Although small $\Delta\delta$ values have been obtained, the enantiomers of **3** were clearly resolved both in **AMP** and **MBA** (Table 1). Enantiomeric separation ($\Delta\delta$) values of similar order of magnitude have been obtained in most cases for at least a part of the two or three diastereoisomers of **4** and **5**, respectively (Table 1). According to our knowledge, no prece-

Table 1
$^{31}P\{^{1}H\}$ NMR data of **3–6** in $CDCl_3$ and optically active solvents[a]

Oxaphosphete	Solvent	δ (ppm)	$\Delta\delta$ (ppm)[b]
3	$CDCl_3$	39.505	
4	$CDCl_3$	32.918 (**4$_1$**)	
		32.274 (**4$_2$**)	
5	$CDCl_3$	32.519 (**5$_1$**)	
		29.080 (**5$_2$**)	
		23.931 (**5$_3$**)	
6	$CDCl_3$	39.955 (**6$_1$**)	
		39.764 (**6$_2$**)	
3	(*R*)-(+)-**MBA**	39.364; 39.376	0.012
3	(*S*)-(–)-**AMP**	41.881; 41.876	0.005
4	(*R*)-(+)-**MBA**	32.764; 32.758 (**4$_1$**)	0.006
		32.279; 32.266 (**4$_2$**)	0.013
4	(*R*)-(+)-**NEA**	34.513 (**4$_1$**)	0
		34.199 (**4$_2$**)	0[c]
4	(*S*)-(–)-**AMP**	35.510; 35.517 (**4$_1$**)	0.007
		34.929 (**4$_2$**)	0
5	(*R*)-(+)-**MBA**	32.456 (**5$_1$**)	0
		29.158 (**5$_2$**)	0
		24.002; 23.999 (**5$_3$**)	0.003
6	(*R*)-(+)-**MBA**	40.930 (**6$_1$**)	0
		40.625 (**6$_2$**)	0[c]

[a] 7–10 mg oxaphosphete was dissolved in 0.7 ml solvent; ^{31}P NMR spectra were taken at 161.9 MHz at room temperature on a Varian Inova 400 instrument. Spectra are referred to 85% H_3PO_4 as external standard. Samples were locked to D_2O in an insert tube.

[b] $\Delta\delta$ stands for the 'enantiomeric shift difference' observed in optically active solvents.

[c] Although the strong broadening of the singlet has been observed, no separation of the signals of enantiomers has been reached.

dence for the detection of a P-stereogenic pentacoordinate phosphorus species has been described. (It is worth noting that the optically active alcohol (*S*)-(–)-2-methyl-1-butanol proved to be inefficient in all cases.[7])

The fact that no enantiomeric separation has been reported for chiral phosphoranes and oxaphosphetanes/oxaphosphetes previously might be explained by fast pseudorotation around the pentacoordinated phosphorus atom. The interconversion of enantiomers (e.g. in case of type **2** compounds) is rapid as the barriers leading to strain-free intermediate are relatively low.[8] In optically active solvents the equal contribution from the equilibrating pseudorotamers (fast on the NMR timescale) leads to the observation of average chemical shifts. However, in the case of oxaphosphetes **3–5**, the fast interconversion of the possible enantiomers is hindered by the rigid spiro-fusion with an unsaturation in the oxaphosphetane ring and by the presence of the sterically demanding 2,4,6-trialkylphenyl substituent as was shown by the experiments above.

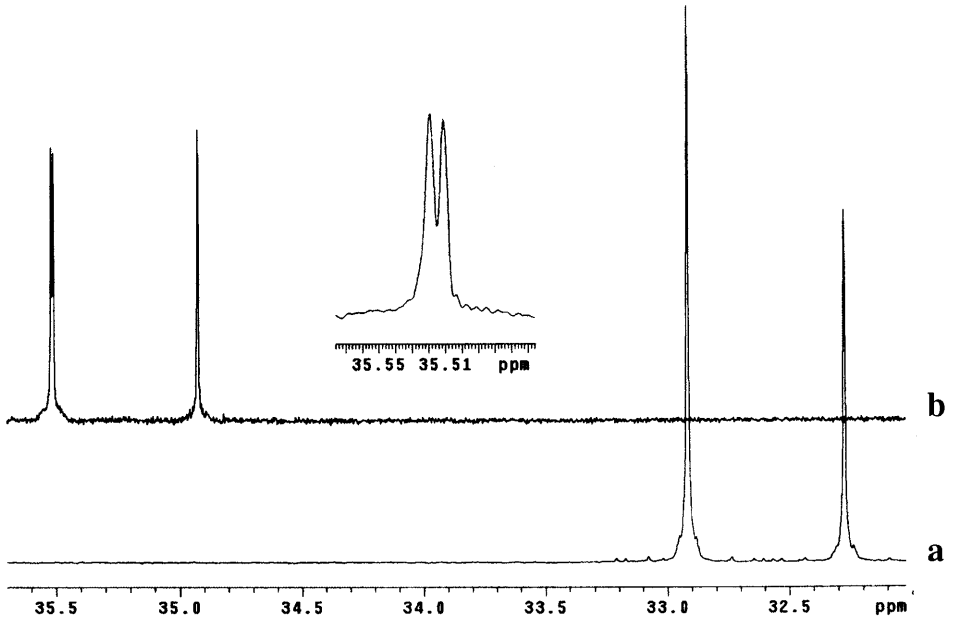


Figure 3. The ^{31}P NMR spectra of **4** (a) in $CDCl_3$ at 25°C and (b) in **AMP** at 30°C

Acknowledgements

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7. Similarly, the above-mentioned optically active amines and alcohols caused only a line-broadening of the phosphete signals in the ^1H NMR spectra when they were used as chiral additives in equimolar amount to phosphetes in $CDCl_3$. The application of further chiral solvating agents in ^1H NMR is in progress.
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