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A Chiral Phosphorous Derivatizing Agent for the Determination of the Enantiomeric Excess of Chiral Alcohols, Amines by ^{31}P NMR

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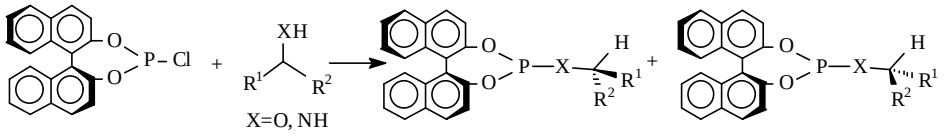
Abstract: A chiral phosphorous derivatizing agent prepared from PCl_3 and (S)-BINOL was described. It is used to determine the enantiomeric excess of chiral alcohols and amines by ^{31}P NMR.

Keywords: Chiral phosphorous, derivation, chiral alcohols, chiral amines, enantiomeric excess, asymmetric induction.

The suitable chiral derivatizing agent (CDA) is the essential factor for the determination of the optical purity of the enantiomeric substances by NMR method. Among different kinds of CDAs, the chiral phosphorous derivatizing agents[1] have become very popular.

In this paper, we report a simple and highly efficient ^{31}P NMR method for the ee determination of chiral alcohols and amines, based on the phosphorous CDA **1**[2].



1 **2** **3A** **3B**

The potential of asymmetric induction is the most important character of CDAs. We chose several racemic and enantiomerically enriched alcohols or amines as the reaction substrates. The results were summarized in **Table 1**.

As shown in **Table 1**, the kinetic discrimination for the aromatic alcohols (entry **3a**~**3g**) was not observed. Moreover, the value of $\Delta\delta$ (5.10~8.38 ppm) is larger than those obtained by using other reported phosphorous CDAs[3,4,5,6], which ranged from 0.10 ppm to 1.40 ppm.

For the chiral aliphatic alcohols, great asymmetric induction was observed (entry **3h**~**3j**). Interestingly, the values of $\Delta\delta$ decreased from 0.44 ppm to 0.10 ppm with increase the space hindrance. Further more the separation of peaks in ^{31}P NMR were incomplete (entry **3j**). As chiral amines were concerned, the primary amines can react

with the CDA (entry **3k**), but not for the secondary amines.

Table 1 ^{31}P-NMR diastereomeric shift difference of **3A** and **3B** obtained from reagent **1** and **2** [a]

No.	Compound **2**			^{31}P δ (ppm)		Δδ(ppm)	
	R^1	R^2	X	**3A**	**3B**		Ratio [f]
3a	Ph	Me	O	148.66,	141.78	6.88	50:50
3b	Ph	Et	O	151.11,	142.85	8.26	49:51
3c	Ph	CH_2Cl	O	150.60,	142.22	8.38	49:51
3d	2-Cl-Ph	Me	O	147.62,	139.70	7.92	50:50
3e	*p*-NO_2-Ph	Me	O	144.15,	139.05	5.10	48:52
3f	*m*-Cl-Ph	Me	O	147.73,	139.51	8.22	48.5:51.5
3g	*o*-Br-Ph	Me	O	139.46,	146.04	6.58	48.5:51.5
3h	Et	Me	O	148.54,	148.10	0.44	46:54
3i	*n*-C_7H_{15}	Me	O	148.41,	148.00	0.41	40:60
3j	*t*-Bu	Me	O	152.63,	152.73	0.10	—[b]
3k	Ph	Me	NH	151.37,	152.43	1.06	47:53
3l[c]	Ph	Me	NH	151.36		—	100:0
3m[d]	Ph	CN	O	138.39,	132.82	5.57	86.5:13.5
3n[e]	Ph	Me	O	142.00,	148.80	6.80	45.5:54.5

a. recorded in $CDCl_3$(200M Hz), using 85% H_3PO_4 as an external standard; b. no good base-line separation; c. L-1-phenylethylamine was used; d. 70% enantiomeric excess determined by polarimetry; 68% ee determined by HPLC; e. 8.8% enantiomeric excess determined by polarimetry; f. ^{31}P NMR integral ratio of **3A** and **3B**.

Moreover, the outcomes obtained by the CDA **1** were compared with the results determined by polarimetry (**3l**~**3n**), they were in good agreement each other.

In conclusion, CDA **1** is a very efficient agent for the ee determination of chiral aromatic alcohols and amines. The possibility of determination of ee values for other chiral amines, amino acid esters and chiral thiols with CDA **1** is under investigation.

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