³¹P N.M.R. Nonequivalence of Diastereoisomeric O,O-Dialkyl Phosphorodithioates

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The enantiomeric excess of chiral alcohols can be obtained from the ratio of integrations of ³¹P n.m.r. absorptions of diastereoisomeric *O*,*O*-dialkyl dithioates (**3**, X = S) derived therefrom; ³¹P n.m.r. nonequivalence of L-cinchonidine salts of (**3**) was also observed.

Recently we reported new methods for determination of the enantiomeric excess (e.e.) of chiral alcohols,^{1,2} thiols,^{2,3} amino acid esters, and primary amines.⁴ The principle involved is the ³¹P n.m.r. analysis of diastereoisomeric



Scheme 1.* indicates configuration at chiral centres, only one enantiomer of (RR, SS)-pair shown.

phosphorus derivatives of these compounds using PCl₃ (for alcohols) or MePXCl₂ (X = O or S) as derivatizing agents. Consequently no auxiliary chiral compound is necessary in order to determine the e.e. by this method. In the case of phosphonates (1), derived from racemic alcohols, a mixture of a (\pm) -pair and two meso-isomers is formed, as is illustrated for di-(s-butyl) phosphonate (2) (Scheme 1). When a non-pseudochiral phosphorus atom is present, as in (3), only a (\pm) -pair and one meso-isomer are expected (Scheme 1). In general this stereochemical feature would be of advantage in e.e. determinations as only two ³¹P n.m.r. signals will be present for racemic compounds.^{1,3} Phosphates $(3, X = O, R = Bu^s)$ show only one absorption at -0.16 p.p.m. (CDCl₃). It is remarkable that despite the high symmetry at phosphorus, ³¹P n.m.r. non-equivalence for diastereoisomeric (\pm and meso) O,O-di-(s-butyl) hydrogen phosphorodithioate (4) (Figure 1) is observed. In accordance with expectation two singlets (50:50 ratio) for (\pm) - and meso-(4) ($\Delta\delta$ 6.6 Hz) and a single absorption for (S,S)-(4) are found.

Various chiral alcohols were converted into phosphorodithioic derivatives by stirring at 20 °C a CDCl₃ solution of 2 equiv. of the alcohol and 1 equiv. of O,O-diphenyldithioic acid⁵ (5) as a thiophosphorylating agent (Scheme 2). Figure 1(d) shows the ³¹P n.m.r. spectrum of (7) derived from racemic menthol (6) following this procedure. These results indicate that (5) can be used as an alternative reagent for determination of the e.e. of chiral alcohols, although chemical shift differences are generally smaller for the meso- and (\pm) -pair of these phosphorus derivatives.^{2,4} Furthermore we found that it is possible to discriminate between the meso- and (\pm) -phosphorodithioic acids using chiral tertiary amines. The (-)-cinchonidine salts of (4) and (7) clearly give ^{31}P n.m.r. nonequivalence only for one of the phosphorodithioic isomers (Figure 1). The low field ³¹P n.m.r. absorption of acids (4) and (7) can therefore be assigned to the (RR,SS)-pair. These diastereoisomeric salts belong to dynamic diastereoisomeric systems⁶ and their n.m.r. nonequivalence critically depends



Figure 1. ³¹P N.m.r. spectra at 80.988 MHz [CDCl₃, Nicolet NT-200, 85% H₃PO₄ (δ 0.0 p.p.m.) as external standard]: (a) (4) derived from racemic s-butyl alcohol; (b) (-)-cinchonidine salt of racemic (4); (c) (7) derived from (-)-menthol; (d) (7) derived from racemic menthol; (e) (-)-cinchonidine salt of racemic (7).

on solvent, and amine structure and concentration. So far we have observed this phenomenon only using racemic phosphorodithioic acids with chiral tertiary amines in $CDCl_3$.

As far as we know our results demonstrate for the first time ³¹P n.m.r. nonequivalence of diastereoisomeric salts of



thiophosphates non-chiral at phosphorus.^{7,8} These observations might also be useful in elucidating the role of the prochiral phosphorus atom as a potential chiral binding site in phospholipids.⁹

Received, 19th December 1986; Com. 1800

References

- 1 B. L. Feringa, A. Smaardijk, and H. Wynberg, J. Am. Chem. Soc., 1985, 107, 4798.
- 2 B. L. Feringa, A. Smaardijk, H. Wynberg, B. Strijtveen, and R. M. Kellogg, *Tetrahedron Lett.*, 1986, **27**, 997.
- 3 B. Strijtveen, B. L. Feringa, and R. M. Kellogg, *Tetrahedron*, 1987, 43, 123.
- 4 B. L. Feringa, B. Strijtveen, and R. M. Kellogg, J. Org. Chem., 1986, 51, 5484.
- J. Lefferts, K. C. Molloy, J. J. Zuckerman, I. Haiduc, C. Guta, and C. Ruse, *Inorg. Chem.*, 1980, **19**, 1662.
 'Asymmetric Synthesis,' ed. J. D. Morrison, Academic Press, New
- 6 'Asymmetric Synthesis,' ed. J. D. Morrison, Academic Press, New York, vol. 1, 1982; A. Horeau and J. P. Guette, C.R. Acad. Sci., Ser. C., 1968, 276, 257.
- 7 M. Mikolajczyk, J. Omelánczuk, M. Leitloff, J. Drabowicz, A. Ejchart, and J. Jurczak, J. Am. Chem. Soc., 1978, 100, 7003.
- 8 The phosphorus atom in (3) does not constitute a chiral centre; for a recent discussion, see: K. Mislow and J. Siegel, J. Am. Chem. Soc., 1984, 106, 3319.
- 9 M. D. Tsai, R. T. Jiang, and K. Bruzik, J. Am. Chem. Soc., 1983, 105, 2478.