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Published in:
Journal of the Chemical Society, Chemical Communications

DOI:
[10.1039/c39870000695](https://doi.org/10.1039/c39870000695)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
1987

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Feringa, B. (1987). 31P N.M.R. Nonequivalence of Diastereoisomeric O,O-Dialkyl Phosphorodithioates. *Journal of the Chemical Society, Chemical Communications*, 27(9). <https://doi.org/10.1039/c39870000695>

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^{31}P 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 ^{31}P n.m.r. absorptions of diastereoisomeric *O,O*-dialkyl dithioates (**3**, $\text{X} = \text{S}$) derived therefrom; ^{31}P 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 ^{31}P 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 PCl_3 (for alcohols) or MePXCl_2 ($\text{X} = \text{O}$ 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-pseudo-chiral 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 ^{31}P n.m.r. signals will be present for racemic compounds.^{1,3} Phosphates (**3**, $\text{X} = \text{O}$, $\text{R} = \text{Bu}^s$) show only one absorption at -0.16 p.p.m. (CDCl_3). It is remarkable that despite the high symmetry at phosphorus, ^{31}P 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*)-(b) are found.

Various chiral alcohols were converted into phosphorodithioic derivatives by stirring at 20°C a CDCl_3 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 ^{31}P 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 ^{31}P 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. ^{31}P N.m.r. spectra at 80.988 MHz [CDCl_3 , Nicolet NT-200, 85% H_3PO_4 (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 ^{31}P 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

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