^{31}P N.M.R. Nonequivalence of Diastereoisomeric *O,O*-Dialkyl Phosphorodithioates

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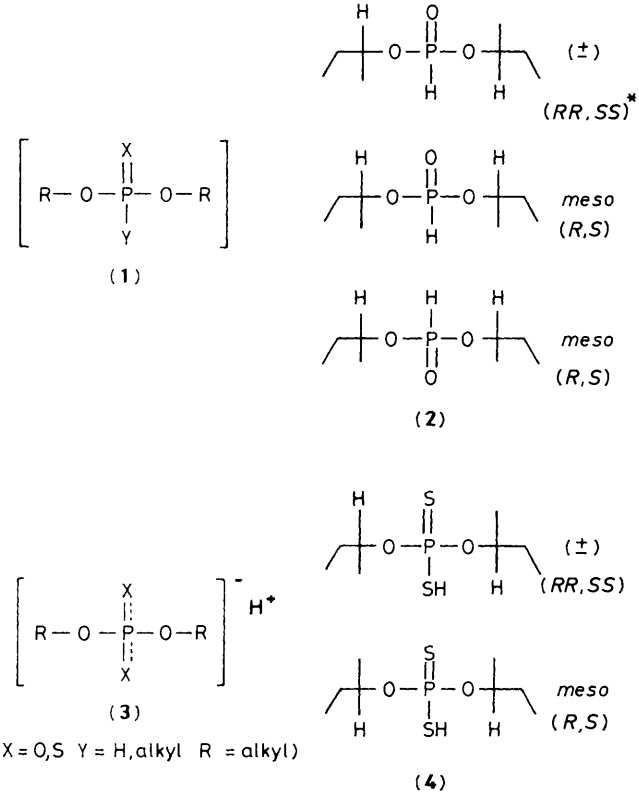
The enantiomeric excess of chiral alcohols can be obtained from the ratio of integrations of ^{31}P n.m.r. absorptions of diastereoisomeric *O,O*-dialkyl dithioates (**3**, X = S) derived therefrom; ^{31}P n.m.r. nonequivalence of L-cinchonidine salts of (**3**) was also observed.

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 phosphorus derivatives of these compounds using PCl_3 (for alcohols) or $MePXCl_2$ (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 (±)-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 (±)-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**, X = O, R = 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 (± and *meso*) *O,O*-di-(s-butyl) hydrogen phosphorodithioate (**4**) (Figure 1) is observed. In accordance with expectation two singlets (50 : 50 ratio) for (±)- and *meso*-(**4**) (Δδ 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 $CDCl_3$ solution of 2 equiv. of the alcohol and 1 equiv. of *O,O*-diphenyldithioic acid[5] (**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 (±)-pair of these phosphorus derivatives.[2,4] Furthermore we found that it is possible to discriminate between the *meso*- and (±)-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 systems[6] and their n.m.r. nonequivalence critically depends



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

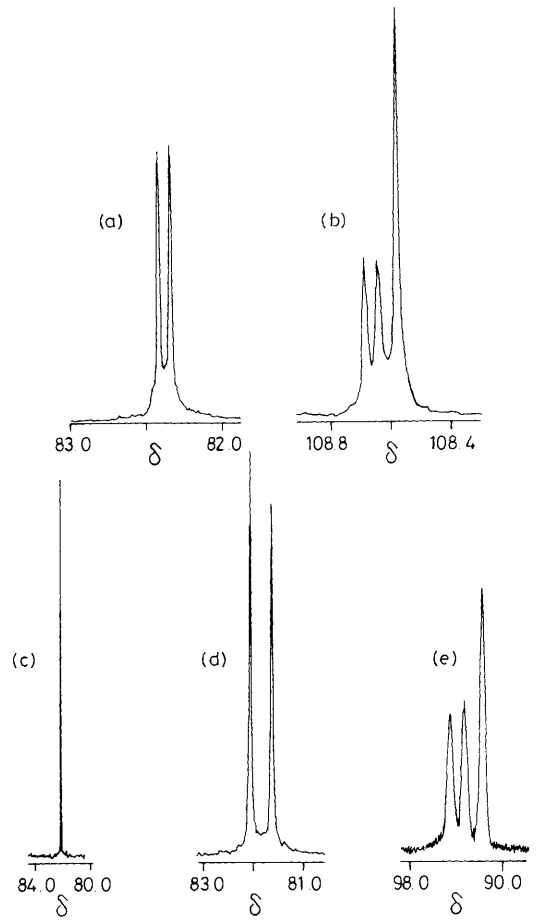
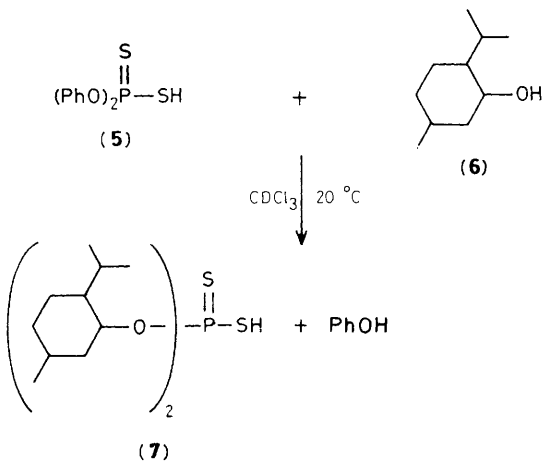


Figure 1. ^{31}P N.m.r. spectra at 80.988 MHz [$CDCl_3$, Nicolet NT-200, 85% H_3PO_4 (δ 0.0 p.p.m.) as external standard]: (a) (**4**) derived from racemic s-butyl alcohol; (b) (−)-cinchonidine salt of racemic (**4**); (c) (**7**) derived from (−)-menthol; (d) (**7**) derived from racemic menthol; (e) (−)-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



Scheme 2

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]

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