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PROTON MAGNETIC RESONANCE SPECTRA OF CHIRAL PHOSPHORUS ESTERS : CHEMICAL SHIFT NON-EQUIVALENCE OF ENANTIOMERS INDUCED BY OPTICALLY ACTIVE PHOSPHINOTHIOIC ACIDS

Martin J.P. Harger

Department of Chemistry, The University, Leicester LE1 7RH

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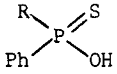
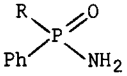
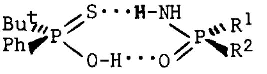
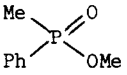
The optically active phosphinothioic acids (+)-(R)-(1) and (-)-(S)-(2) can induce non-equivalence of enantiomers in the p.m.r. spectra of chiral phosphinic amides such as (3) and (4).[1] These amides contain hydrogen-bond donor (N-H) and acceptor (P=O) groups and may associate with an optically active acid to give rapidly-exchanging diastereoisomeric complexes such as (5) and (6). While useful for measuring enantiomer ratios in samples of chiral phosphinic amides, the phosphinothioic acids (R)-(1) and (S)-(2) would be of limited value if they were able to induce enantiomer non-equivalence only in compounds having both donor and acceptor hydrogen-bonding sites. We now show that this restriction is not present.


1 ; R = Bu^t
2 ; R = Me


3 ; R = Bu^t
4 ; R = Me


5 ; R^1 = Me, R^2 = Ph
6 ; R^1 = Ph, R^2 = Me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The 100 MHz p.m.r. spectrum of racemic methyl methylphenylphosphinate (7) in CCl_4 includes a doublet (J_{PH} 11.5 Hz) at δ 3.55 due to the P-OMe group. Addition of 0.5 molar equivalents of (R)-(1), $[\alpha]_D$ +28.1° (MeOH), causes this signal to separate into two doublets (δ 3.59 and 3.55) of equal intensity, 4.2 Hz apart. With 1.0 equivalents of (R)-(1), the separation between the OMe resonances is increased to 7.0 Hz but further addition of the optically active acid has relatively little effect. The pure (-)-(S) enantiomer of (7) displays only one OMe signal (δ 3.55) in the presence of (R)-(1), whereas other non-racemic samples give two signals of unequal intensity, with that due to the (S)-enantiomer being at higher field. For each sample of (7) the enantiomer composition implied by the relative intensities (peak heights) of the two OMe signals agrees well with the ratio estimated from the optical rotation:

$[\alpha]_D$ (PhH) of MePhP(O)OMe	-57.8°	-51.7°	-37.3°	-25.8°	-13.4°	0.0°	+11.2°
% (-) Enantiomer[2]	99.8	94.6	82.2	72.2	61.6	50.0	40.3
% Highfield enantiomer[3]	≥99.4	93.9	82.3	72.4	61.9	50.3	41.1

The acid (S)-(2), $[\alpha]_D$ -22.3° (MeOH), also induces non-equivalence of the enantiomers of ester (7), but now it is the lowfield OMe resonance that is associated with the (S)-enantiomer and the separation between the signals [$\Delta\delta$ 5.4 Hz with 1.0 equivalents of (2)] is somewhat less than with acid (1).

TABLE. 100 MHz P.m.r. spectra of phosphorus esters. Chemical shift non-equivalence ($\Delta\delta$) of enantiomers induced by added optically active phosphinothioic acids.[a]

	$\underline{\text{Me}}\text{PhP(O)OC}\underline{\text{Me}}_3$		$\underline{\text{Me}}\text{PhP(O)OPh}$	$\underline{\text{Me}}\text{PhP(O)S}\underline{\text{Me}}$		$\underline{\text{Me}}\text{PhP(O)SPh}$
Added (R)-(1) $\Delta\delta$/Hz	0.5	5.8	6.9	2.9	6.0	6.3
Added (S)-(2) $\Delta\delta$/Hz	1.2	4.2	5.1	2.4	5.2	4.0

	$\underline{\text{Me}}\text{CH}_2\text{PhP(O)O}\underline{\text{Me}}$		$\underline{\text{Me}}_2\text{CHPhP(O)O}\underline{\text{Me}}$		$\underline{\text{Me}}_3\text{CPhP(O)O}\underline{\text{Me}}$		$\underline{\text{Me}}_3\text{CPhP(O)S}\underline{\text{Me}}$	
Added (R)-(1) $\Delta\delta$/Hz		5.8	$\sim$5	3.7	1.8	0	5.0	4.4
Added (S)-(2) $\Delta\delta$/Hz	0	4.6	4.0	2.0	1.0	1.1	3.6	4.8

[a] In CCl_4 at 27°C; [ester]=[acid] = 0.12 M

The results in the Table show that optically active phosphinothioic acids can induce substantial chemical shift non-equivalence in a variety of other phosphorus esters. While it seems probable that hydrogen bonding between the phosphoryl group of the ester (acceptor) and the hydroxyl group of the acid (donor) gives rise to diastereoisomeric complexes, the precise geometry of these species is unclear. The O (or S) atom of the alkoxyl (or thioalkoxyl) group in the ester may also be involved in complexing with the acid, but a second hydrogen-bond acceptor site is apparently not essential: in the presence of 1.0 equivalents of (R)-(1), t-butylmethylphenylphosphine oxide displays enantiomer non-equivalence in both the methyl ($\Delta\delta$ 6.1 Hz) and t-butyl ($\Delta\delta$ 4.8 Hz) signals. The importance of the phosphoryl group is emphasised by the failure of the thiophosphoryl esters MePhP(S)OMe, MePhP(S)OPh, and $Bu^tPhP(S)OMe$ to exhibit enantiomer non-equivalence in the presence of (R)-(1).

Use of optically active phosphinothioic acids offers an attractive alternative to optically active solvents[4] and lanthanide shift reagents[5,6] for measuring ratios of enantiomers in phosphoryl compounds by p.m.r. spectroscopy. They do not cause broadening of signals in the spectrum, only small amounts (8-16 mg) are required, and samples can be easily recovered.

Acknowledgement I thank Professor S. Trippett for samples of some of the compounds examined.

References and Footnotes

1. M.J.P. Harger, *J.C.S. Perkin II*, 1978, in the press.
2. Based on $[\alpha]_D$ -58.0° (PhH) for optically pure (-) MePhP(O)OMe. This value is marginally greater than previous estimates (K.E. DeBruin and D.E. Perrin, *J. Org. Chem.*, 1975, 40, 1523 ; see also ref.6).
3. P.m.r. spectra recorded with [MePhP(O)OMe] = 0.20 M and [(+)-(R)-(1)] = 0.16 M; $\Delta\delta_{OMe}$ = 6.0 Hz at 100 MHz.
4. R.A. Lewis, K. Naumann, K.E. DeBruin, and K. Mislow, *Chem. Comm.*, 1969, 1010; W.H. Pirkle, S.D. Beare, and R.L. Muntz, *J. Amer. Chem. Soc.*, 1969, 91, 4575.
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6. M.J.P. Harger, *J.C.S. Perkin I*, 1977, 2057.