# A New Method for the Determination of the Enantiomeric Purity of Carboxylic Acids: Reaction of Carboxylates with Tris(tetraphenylimidodiphosphinato)praseodymium and *X*-Ray Structure of a Dinuclear Dicarboxylato Adduct

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Tris(tetraphenylimidodiphosphinato)praseodymium reacts with ammonium or potassium salts of carboxylic acids to give dinuclear dicarboxylato complexes, the structure of which has been established and which can be used for the determination of the enantiomeric purity of carboxylic acids.

Very recently,[1,2] we described the use of new lanthanide shift reagents for the characterization of fatty acids by n.m.r. The aim of the present Communication is to show that carboxylates (potassium or ammonium salts) also react well with tris(tetraphenylimidodiphosphinato)praseodymium [Pr(tpip)$_3$] to form a new type of complex, the structure of which was elucidated by *X*-ray analysis. As regards n.m.r. spectroscopy, the chemical shift dispersion of the $^1$H signals is far greater than for the corresponding carboxylic acids. Furthermore, in contrast with the usual behaviour of complexes involving shift reagents, the adducts formed between Pr(tpip)$_3$ and carboxylates do not undergo fast exchange with the free species on the n.m.r. time scale. Finally, owing to the dinuclear character of the complexes, which contain two carboxylate ligands, diastereoisomers are formed when racemic salts are used. The new achiral reagent is likely to allow a simple determination of the enantiomeric purity of chiral carboxylic acids *via* their carboxylates.

Thus, the interaction of Pr(tpip)$_3$ with a series of carboxylates leads to new adducts, the n.m.r. data of which are collected in Table 1. For the purpose of comparison, the observed chemical shifts for the 1 : 1 mixture of Pr(tpip)$_3$ with 3-phenylpropionic and 2-phenylbutyric acids (0.1 mol dm$^{-3}$) are also reported. The difference in the nature of the complexes formed by carboxylates and acids is illustrated on the one hand by the enhancement of the induced shifts when the salts are used, and on the other hand, by the occurrence of two sets of resonances for racemic carboxylates instead of one set of resonances for racemic acids. The similarity of the shifts observed for the two counter ions (ammonium and potassium) indicates clearly that the same adducts are formed in both cases. This was confirmed by carrying out both reactions on a preparative scale. Thus, the reaction of Pr(tpip)$_3$ with the potassium salt of 3-phenylpropionic acid in tetrahydrofuran (THF) gave a white solid after evaporation of the solvent. The $^1$H n.m.r. spectrum of this compound was identical to the

**Table 1.** $^1$H N.m.r. data (with respect to tetramethylsilane) for the complexes formed by the interaction of [Pr(tpip)$_3$] with various carboxylic acids and their carboxylates.

| Acid | | Lauric | 3-Phenylpropionic | | | 2-Phenylbutyric | | 2-Methylbutyric |
|---|---|---|---|---|---|---|---|---|
| Counter ion | | $R_2NH_2^+$ | $H^+$ | $K^+$ | $R_2NH_2^+$ | $H^+$ | $R_2NH_2^+$ | $R_2NH_2^+$ |
| Solvent | | $CDCl_3$[a] | | $CDCl_3$ | | $CDCl_3$ | $CD_2Cl_2$[b,c] | $C_6D_6$[b,c] |
| H-2 | | δ−23.36 | −10.30 | −23.60 | −24.86 | −7.70 | −29.93 *m*<br>−27.97 *d, l* | −21.78 *d, l*<br>−21.78 *m* |
| H-3 | | −10.37 | −6.31 | −10.80 | −11.38 | −6.80 | −14.24 *d, l*<br>−13.33 *m*<br>−7.56 *d, l*<br>−7.24 *m* | −9.71 *d, l*<br>−9.71 *m*<br>−8.45 *d, l*<br>−8.85 *m* |
| H-4 | | −5.97 | | | | −3.48 | −5.82 *d, l*<br>−5.64 *m* | −4.55 *d, l*<br>−4.74 *m* |
| H-5 | | −2.78 | | | | | | |
| H-6 | | −1.56 | | | | | | |
| H-7 | | −0.55 | | | | | | |
| H-8 | | 0.03 | | | | | | |
| H-9 | | 0.39 | | | | | | |
| H-10 | | 0.63 | | | | | | |
| H-11 | | ~0.85 | | | | | | |
| H-12 | | 0.55 | | | | | | |
| H of Ph | *o* | | 3.24 | 0.97 | 0.74 | 0.29 | −5.16 *d, l*<br>−6.08 *m* | |
| | *m* | | 5.71 | 4.53 | 4.42 | 4.92 | 3.42 *d, l*<br>3.01 *m* | |
| | *p* | | 5.94 | 5.02 | 4.46 | 5.46 | 4.48 *d, l*<br>4.19 *m* | |
| 2-$CH_3$ | | | | | | | | −8.85 *m*<br>−9.08 *d, l* |

[a] The shifts are very similar for the potassium salt. [b] *d, l* = *SS/RR* diastereoisomers, *m* = *SR* diastereoisomers. [c] The signals of the *d, l* diastereoisomers were ascribed by the use of the *S*-(+)-enantiomers of 2-methylbutyric and *S*-(+)-2-phenylbutyric acids.

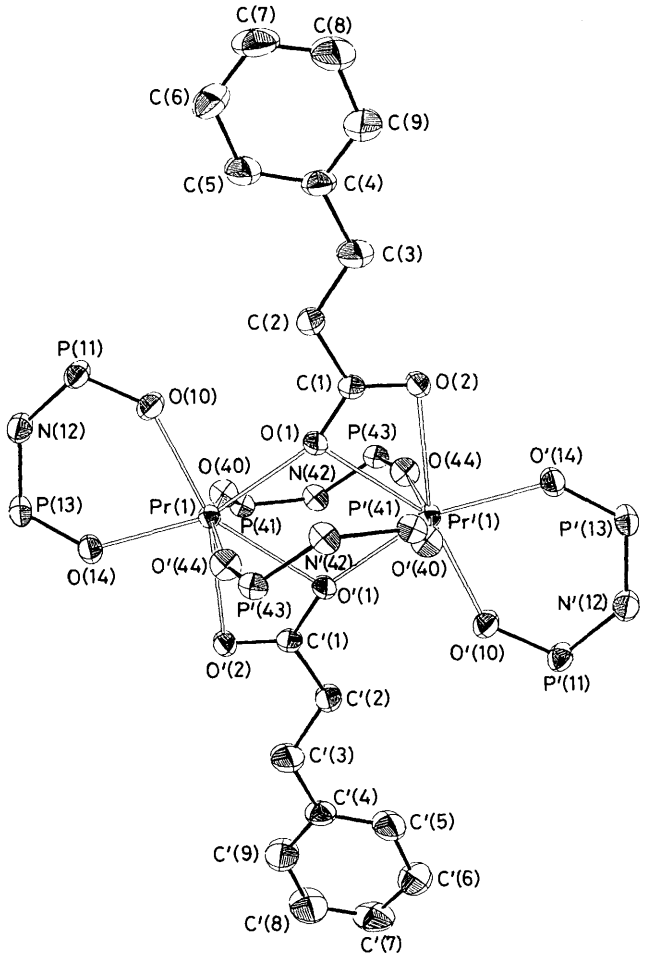


**Figure 1.** ORTEP view of the tetrakis(tetraphenylimidodiphosphinato)di(3-phenylpropionato)dipraseodymium complex; important bond lengths (Å): Pr(1)–Pr'(1) 4.1200(1), Pr(1)–O(1) 2.427(7), Pr(1)–O'(2) 2.548(7), Pr(1)–O'(1) 2.594(7), O(1)–C(1) 1.27(1), C(1)–O(2) 1.24(1); important bond angles (°): O(1)–Pr(1)–O'(1) 69.8(3), O'(2)–Pr(1)–O'(1) 50.2(2), Pr(1)–O(1)–Pr'(1) 110.2(3), O(2)–C(1)–O(2) 120.8(9).

spectrum obtained by mixing the di-isopropylammonium salt with $Pr(tpip)_3$ in $CDCl_3$.

Recrystallization from MeOH : $CH_2Cl_2$ gave crystals of the new complex (m.p. > 260 °C) suitable for an *X*-ray analysis.† An ORTEP view is shown in Figure 2, the phenyl groups of the ligands being omitted for the sake of simplicity. It appears that the new complex is a centrosymmetric dinuclear complex of praseodymium in which the metal centres are held together

† *Crystal data:* $C_{114}H_{98}P_8N_4O_{12}Pr_2$, $M$ = 2246.6, monoclinic, space group $P2_1/n$, $a$ = 16.978(2), $b$ = 20.948(2), $c$ = 17.306(2) Å, β = 115.36(1)°, $D_c$ = 1.34 g cm$^{-3}$, $Z$ = 2.9541 data collected at room temperature on a Nonius CADA diffractometer. No absorption correction was applied (flat Ψ scan). Anomalous dispersion terms and a correction for secondary extinction were applied. The structure was solved by standard Patterson–Fourier techniques and refined by least squares using anisotropic thermal parameters for all non-hydrogen atoms. H atoms were placed in calculated positions. 7214 Reflections with $I > 3\sigma(I)$ were used to solve and refine the structure to $R$ = 0.053 and $R_w$ = 0.089. 624 Least squares parameters. The programs used were CRYSTALS and ORTEP-2. The large discrepancy observed between $R$ and $R_w$ is related to a disorder problem involving a mixture of MeOH and $CH_2Cl_2$ solvent molecules. It has not yet been solved. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

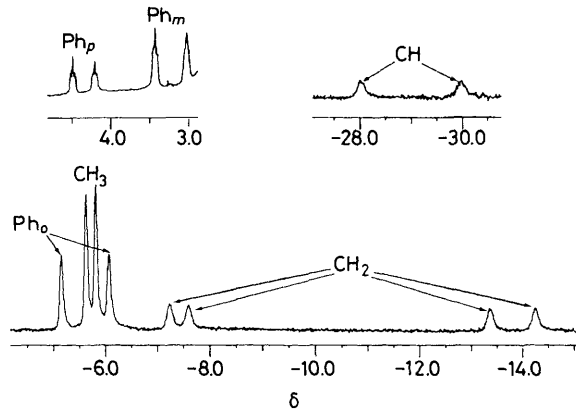


**Figure 2.** $^1$H N.m.r. spectrum of the two diastereoisomers obtained from racemic 2-phenylbutyric acid (solvent $CD_2Cl_2$).

**Table 2.** 2-Methylbutyrate: $[Pr(tpip)_3]$ complexes: comparison of calculated and measured ratio of diastereoisomeric species.

| Enantiomeric excess (e.e.) /%[a] | Calculated ratio *SS, RR*/*SR* (*d, l*/*m*) | Integrated ratio of n.m.r. signals at δ −4.55/−4.74[b] | Integrated ratio of n.m.r. signals at −8.45 / −9.08 / −8.85[c] |
|---|---|---|---|
| 9 | 1.02 | 1.00 | 1.02 |
| 29 | 1.19 | 1.17 | 1.19 |
| 66 | 2.53 | 2.50 | 2.58 |
| 86.8[d] | 7.14 | 8.3 | 6.2 |

[a] By weight. [b] 4-Me signals. [c] Due to overlap of the signals originating from the 2-Me group and from one of the protons at C-3 in the *SR* species the sum of the two signals was used in each case. [d] Qualitative detection of the minor isomer can easily be done with much greater optical purity.

both by the two carboxylato groups, acting as tridentate ligands, and by two bridging tpip ligands; only one tpip ligand remains on each metal centre as a bidentate ligand.

As in known mononuclear complexes, the carboxylato ligands are bound in a symmetric way to the same metal centre, the two C–O bond lengths being equivalent. However, in contrast to other dinuclear carboxylato complexes[3] the presence of the two bridging tpip ligands brings the metal centres in close proximity so as to allow an interaction of one oxygen atom linked to Pr(1) with Pr'(1), the bridging O(1) being asymmetrically bound to the two metal centres with Pr(1)–O(1) = 2.427(7) Å and Pr'(1)–O(1) = 2.594(7) Å. The net result of the reaction is thus the exchange of one tpip ligand by the carboxylato group followed by the coupling of two monomeric units and rearrangement of the ligands.

The particular structure of these adducts explains the n.m.r. results. Due to the dinuclear structure of these adducts and to the bridging nature of the ligands, the carboxylato ligand is held firmly in the adduct and fast exchange with free species no longer occurs. Nevertheless, slow exchange still takes place as can be seen by a saturation transfer experiment. When lauric acid, di-isopropylamine, and $Pr(tpip)_3$ were used in a 1 : 1 : 0.5 ratio, two sets of signals pertaining to the adduct and the free carboxylate were observed. In particular, the protons at sites C(4) to C(11) in the free carboxylate gave rise to a unique signal, the saturation of which led to the partial saturation of the well separated signals observed for the same protons in the adduct. As a result of the competition between

the relaxation effect of the paramagnetic cation and the saturation transfer, the effectiveness of the last process increases from the protons at C(4) to those at C(11).

The pronounced covalent character of the bonding between the carboxylate and the praseodymium and the presence of the two metal centres can explain the surprisingly high field resonances of the nuclei close to the carboxylato group. As far as the resonances of the protons associated with the tpip ligands are concerned, six signals in a 2 : 2 : 1 : 1 : 2 : 2 ratio are observed, one of them being shifted to low field (*ca.* 20 p.p.m.) and one to high field (*ca.* 4 p.p.m.).

When a racemic carboxylate is used, in agreement with the presence of two carboxylate ligands in the complex, the two diastereoisomeric complexes give distinct sets of signals. The remarkable separation of the resonances is shown for the salt of 2-phenylbutyric acid in Figure 2. It is noteworthy that the low field $^1$H n.m.r. signal due to the tpip ligands is also split. As stated earlier,[4,5,6] the use of an achiral reagent might provide a simple method for the enantiomeric excess determination of carboxylic acids. Thus, the acid dissolved in the deuteriated solvent ($CD_2Cl_2$ or $C_6D_6$) is simply converted, in the n.m.r. tube, to the carboxylate by adding an equivalent of an amine. Addition of $Pr(tpip)_3$ then produces an immediate and complete transformation of the carboxylate into the diastereoisomeric complexes. Furthermore, by the use of weighed mixtures of racemic 2-methylbutyric acid and (+)-2-methylbutyric acid, the formation of the complexes occurs without deviation from the statistical ratios. The results are reported in Table 2.

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