Bull Soc Chim Fr (1995) 132, 95-113

Praseodymium NMR-shift reagents for carboxylic acids and their carboxylates : synthesis, X-ray structure and applications

Nicole Platzer[b*], Henri Rudler[a*], Cecilio Alvarez[d], Latifa Barkaoui[b], Bernard Denise[a], Nicole Goasdoué[b], Marie-Noëlle Rager[b], Jacqueline Vaissermann[c], Jean-Claude Daran[c]

[a] *Laboratoire de Chimie organique et organométallique, URA 408,*
[b] *Laboratoire de Chimie structurale*
[c] *Laboratoire de Chimie des Métaux de Transition, URA 608,*
4, place Jussieu, 75252 Paris Cedex 5, France
[d] *Instituto de Química-Unam, circuito exterior, Ciudad Universitaria, Mexico, DF 04510 Coyoacan*

(received 12 September 1994, accepted 24 November 1994)

Summary – The compound $(Pr(tpip)_3$ **1**, tris(tetraphenylimidodiphosphinato)praseodymium, was obtained from $PrCl_3 \cdot 6H_2O$ and tpipK in aqueous medium free from any external ligand, and characterized by X-ray crystallography. Recrystallization of **1** from acetone solution gave $Pr(tpip)_3(CH_3COCH_3)$ **3**. Under the same conditions $DyCl_3 \cdot 6H_2O$ gave $Dy(tpip)_3$ **2**. $Pr(tpip)_3$ induces important upfield shifts in the ^1H NMR spectra of carboxylic acids, as a result of the formation of labile $Pr(tpip)_3(RCOOH)$ adducts. It can thus be used for the straightforward simplification and analysis of the ^1H NMR spectra of carboxylic acids. Attempts to isolate $Pr(tpip)_3(AcOH)$ only gave small amounts of $Pr(tpip)_3(H_2O)$ **4**. However, in the case of chloropropionic acid, the adduct $Pr(tpip)_3(CH_3CHClCOOH)_2$ **5** could be isolated and fully characterized by X-ray crystallography. $Pr(tpip)_3$ reacts instantaneously with potassium or ammonium carboxylates to give, upon exchange of one tpip ligand followed by dimerization, the dinuclear complexes $Pr_2(tpip)_4(RCOO)_2$ **6** in which tpip acts both as chelating and bridging ligands, whereas the carboxylate groups act as tridentate bridging-chelating ligands. These new complexes have been fully characterized by X-ray analysis in the case of citronelic and 3-hydroxybutyric acids. The ^1H NMR spectra of such complexes disclose very important high-field shifts for the protons associated with the carboxylate groups. Moreover, in the case of chiral acids, the achiral $Pr(tpip)_3$ reagent can be used, in association with carboxylates to determine their optical purity by means of the formation of diastereoisomeric dinuclear complexes which can be differentiated by ^1H NMR spectroscopy. Applications of these new reagents will be provided.

praseodymium complexes / NMR / carboxylic acids / carboxylates / optical purity

Introduction

Since Hinckley's first report on lanthanide shift reagents [1], the field has experienced tremendous growth. The β-diketonato lanthanide (III) reagents are extensively used for the study of substrates containing basic groups [2-4]. They were supplemented by the dinuclear silver (I)/lanthanide (III) β-diketonato shift reagents in the case of weakly nucleophilic substrates [5-7].

Unfortunately almost all of these reagents are destroyed by acidic compounds [8]. Acidic substrates can thus only be studied using less efficient lanthanide salts provided they have an acceptable solubility in polar solvents [9-11].

We have recently reported preliminary communications on the development of new lanthanide-containing NMR shift reagents among which the tris(tetraphenylimidodiphosphinato)praseodymium chelate $Pr(tpip)_3$ has been shown to be very effective for the study of carboxylic acids, phenols and carboxylates [12-14]. X-ray analyses have allowed the solid-state characterization of a 1:1 adduct, formed by tris(tetraphenylimidodiphosphinato)lanthanum $La(tpip)_3$ with ethyl acetate [12], and of a new dinuclear dicarboxylate complex, the [tetrakis(tetraphenylimidodiphosphinato)] [di (3-phenylpropionato)]dipraseodymium [14].

New compounds corresponding to these two types of structures have now been obtained and characterized : the 1:1 adducts formed by water or acetone with $Pr(tpip)_3$; the 2:1 adduct formed by 2-chloropropionic acid with $Pr(tpip)_3$; and two dinuclear adducts, the [tetrakis(tetraphenylimidodiphosphinato)] [di(citronellato)] dipraseodymium and the [tetrakis(tetraphenylimidodiphosphinato)] [di(3-hydroxybutanoato)] dipraseodymium complexes. The crystallographic data for these compounds will be presented in this paper in addition to those of the free chelates $Pr(tpip)_3$ and $Dy(tpip)_3$.

The somewhat surprising results obtained from solid-state analysis led us to use ^1H and ^{13}P NMR to study the species formed in apolar solvents from the new

* Correspondence and reprints

reagents and carboxylic acids or their carboxylates. A series of reagents obtained with different lanthanide cations was also evaluated. Various applications of the new reagents will be presented.

Synthesis of the lanthanide complexes Ln(tpip)$_3$

Although some of the lanthanide complexes Ln(tpip)$_3$ (Ln = La, Pr, Nd, Er) [15] had already been synthesized and described, no direct evidence for their anhydrous nature had been obtained so far. We therefore synthesized Pr(tpip)$_3$, Dy(tpip)$_3$ and Eu(tpip)$_3$ for their evaluation as shift reagents, as well as Gd(tpip)$_3$, as a relaxation reagent for ^{13}C NMR spectroscopy. Crystals of Pr(tpip)$_3$ and Dy(tpip)$_3$ were obtained from hexane/dichloromethane or chloroform solutions. ORTEP views of these two compounds appear in figures 1 and 2, whereas the bond distances and angles can be found in the supplementary material.

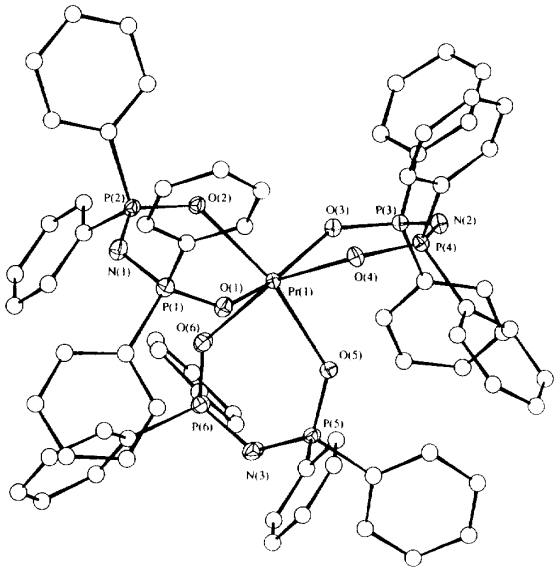

Fig 1. ORTEP drawing of complex **1**. Ellipsoids are shown at the 50% probability level. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.353 (3), Pr(1)-O(2) 2.377 (3), Pr(1)-O(3) 2.370 (3), Pr(1)-O(4) 2.364 (3), Pr(1)-O(5) 2.354 (3), Pr(1)-O(6) 2.343 (4), O(2)-Pr(1)-O(1) 80.5 (1), O(3)-Pr(1)-O(4) 80.1 (1), O(5)-Pr(1)-O(6) 77.6 (1).

Unlike anhydrous Ln(thd)$_3$ (thd = tetramethyl heptanedionato), which exists as dimers in the solid state [16], Pr(tpip)$_3$ **1** and Dy(tpip)$_3$ **2** consist of discrete entities. The coordination polyhedron around the metals is a distorted octahedron of six oxygens from three chelated tpip groups, with average Pr-O and Dy-O distances of 2.360 and 2.263 Å respectively.

$$LnCl_3, 6H_2O + 3TPIPK \xrightarrow{H_2O} Ln(TPIP)_3 + 3KCl \quad \text{(eq 1)}$$

1 Ln = Pr
2 Ln = Dy

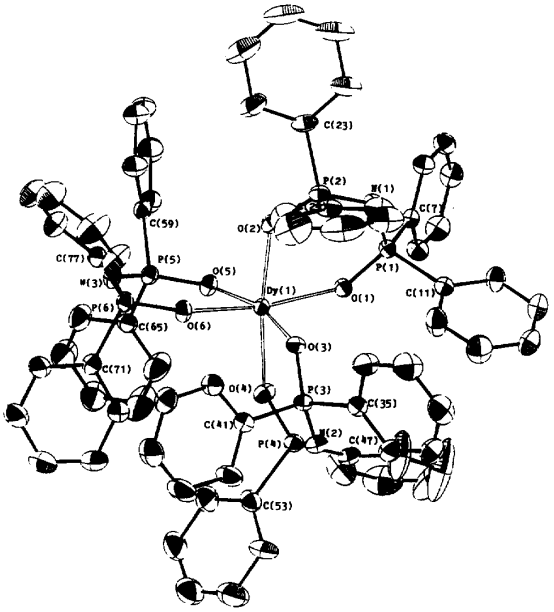

Fig 2. ORTEP drawing of complex **2**. Ellipsoids are shown at the 50% probability level. Important bond lengths (Å) and bond angles (°) : Dy(1)-O(1) 2.251 (2), Dy(1)-O(2) 2.261 (3), Dy(1)-O(3) 2.279 (2), Dy(1)-O(4) 2.286 (3), Dy(1)-O(5) 2.247 (2), Dy(1)-O(6) 2.253 (2), O(2)-Dy(1)-O(1) 81.53.

When the recrystallization was carried out in acetone/hexane, then the heptacoordinated complex Pr(tpip)$_3$(CH_3COCH_3) **3** was isolated.

$$Pr(TPIP)_3 + CH_3COCH_3 \longrightarrow Pr(TPIP)_3(CH_3COCH_3) \quad \text{(eq 2)}$$

3

Its structure was determined by X-ray analysis (fig 3). It is a capped trigonal prism, in which the capping oxygen is the acetone carbonyl oxygen. The acetone-oxygen O(7) lies at a longer distance from the metal (Pr-O(7) = 2.613 Å) than the chelated oxygens from the tpip ligands (Pr-O mean value : 2.384 Å). Similar observations were made for the Pr(tpip)$_3$(H_2O) complex **4**, which was obtained from the residue of the reaction of Pr(tpip)$_3$ with AcOH. In this case (fig 4), Pr-O(7) at 2.64 (2) Å is again longer than the mean value of the Pr-O distances of the tpip ligands.

^1H and ^{31}P NMR

The chelates were studied in apolar solvents, usually $CDCl_3$. Whatever the nature of lanthanide cation used to prepare the chelate, all the phenyl groups were equivalent and the protons gave rise to two (or three) broad signals in the range 7-8 ppm. A single resonance is also obtained for all the phosphorus atoms. The signal is shifted to low field with respect to the signal of the free ligand upon formation of the chelate. Its position varies strongly with the lanthanide cation (see table I). The shift is by far greater for the dysprosium chelate.

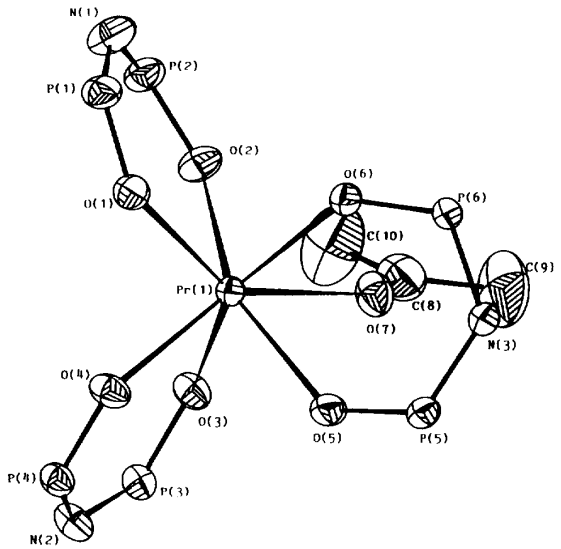

Fig 3. ORTEP drawing of complex **3**. Ellipsoids are shown at the 50% probability level. Phenyl groups omitted for clarity. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.399 (3), Pr(1)-O(2) 2.362 (3), Pr(1)-O(7) 2.613 (3), C(8)-O(7) 1.205 (7), O(2)-Pr(1)-O(1) 77.83 (9), C(8)-O(7)-Pr(1) 145.1 (4).

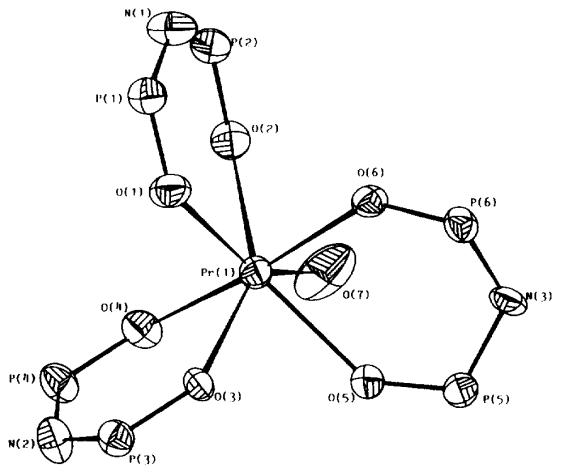

Fig 4. ORTEP drawing of complex **4**. Ellipsoids are shown at the 50% probability level. Phenyl groups omitted for clarity. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.36 (1), Pr(1)-O(2) 2.39 (1), Pr(1)-O(7) 2.64 (2), O(2)-Pr(1)-O(1) 77.5 (3), O(7)-Pr(1)-O(2) 66.7 (4).

The carboxylic acids adducts

All attempts to isolate adducts between $Pr(tpip)_3$ and simple carboxylic acids failed. However, reaction of a mixture of $Pr(tpip)_3$ and a slight excess of 2-chloropropionic acid in chloroform, and slow evaporation of the solvent led to crystals of a new complex in 55% yield, the elemental analysis and ^1H NMR spectrum of

Table I. ^{31}P NMR data for some lanthanide chelates (ppm) with respect to external H_3PO_4 (85%).

Species	$(tpip)^-K^{+(a)}$	$Pr(tpip)_3$	$Dy(tpip)_3$	$Eu(tpip)_3$
δ (ppm)	16.42	29.76	147.00	38.08

[a] Solvent : $CDCl_3$ except for the free ligand (D_2O).

which were in agreement with structure **5**, a 1:2 adduct between $Pr(tpip)_3$ and the acid.

$$Pr(TPIP)_3 + 2\ CH_3CHClCOOH \longrightarrow Pr(TPIP)_3\ (CH_3CHClCOOH)_2 \quad \text{(eq 3)}$$

5

This could be confirmed by an X-ray diffraction study; the ORTEP projection of **5** appears in figure 5. The coordination polyhedron around the praseodymium ion consists of a square antiprismatic arrangement of eight oxygens for the octacoordinated units. Although in the related $M(acac)_3(H_2O)_2$ complexes the two water molecules occupy the adjacent positions on the square face [17], the two oxygen atoms of the coordinated carboxylates in **5** are located on different square faces. It is also worthwhile mentioning the lengthening of the Pr-O bonds of the tpip ligands *trans* to the coordinated carboxylic oxygens (2.55 vs 2.35 Å).

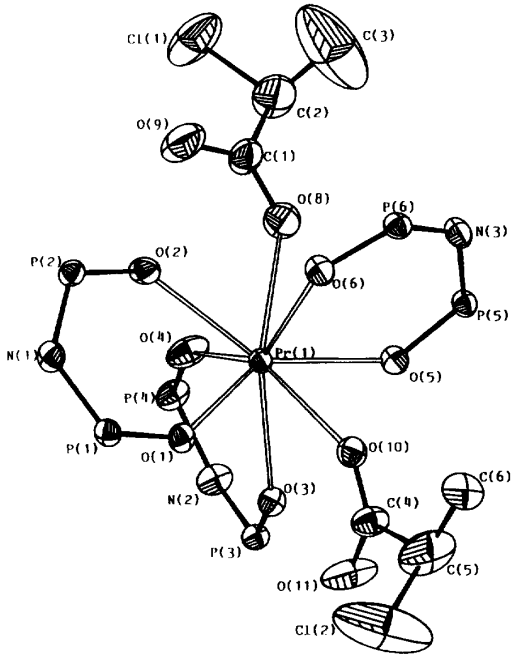

Fig 5. ORTEP drawing of complex **5**. Ellipsoids are shown at the 50% probability level. Phenyl groups omitted for clarity. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.350 (5), Pr(1)-O(2) 2.520 (5), Pr(1)-O(3) 2.554 (4), Pr(1)-O(4) 2.332 (5), Pr(1)-O(5) 2.390 (5), Pr(1)-O(6) 2.360 (5), Pr(1)-O(8) 2.662 (6), C(1)-O(8) 1.22 (1), C(1)-O(9) 1.26 (1), O(2)-Pr(1)-O(1) 75.1 (1), C(1)-O(8)-Pr(1) 136.2 (6).

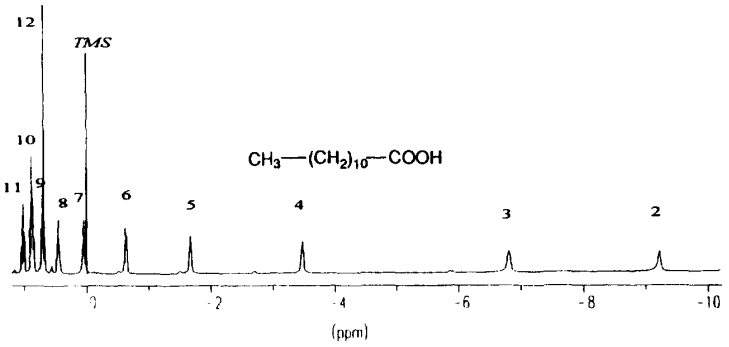

Fig 6. Spectrum recorded for an equimolar mixture of lauric acid and $Pr(tpip)_3$ in $CDCl_3$.

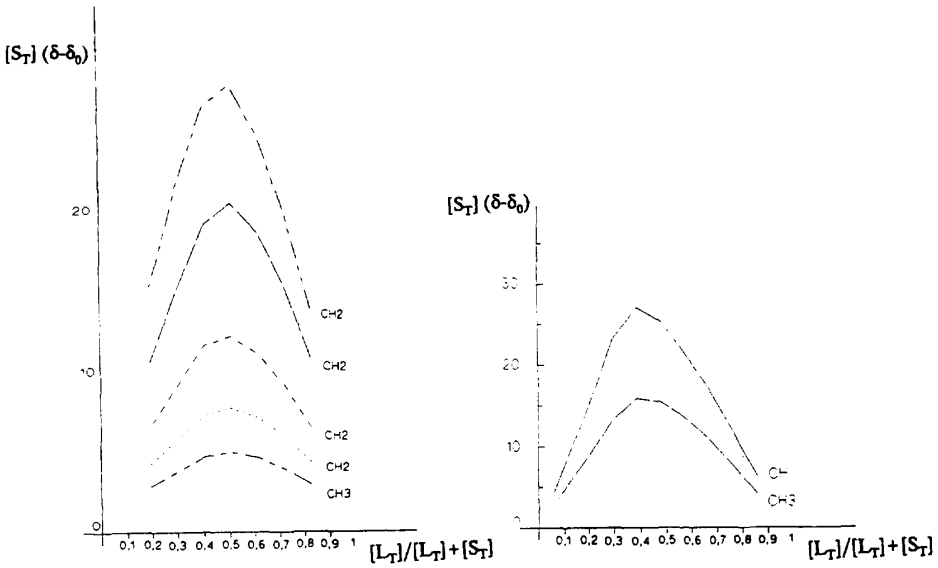

Fig 7. Job's plots for the determination of the stoichiometric composition of the complexes formed between $Pr(tpip)_3$ and caproic or 2-chloropropionic acids.

NMR studies of species in solution

• *^1H NMR*

Progressive addition of the chelate $Pr(tpip)_3$ to a solution of a carboxylic acid, eg lauric acid, induced shielding of the resonances and led to a completely resolved spectrum as shown in figure 6. For an equimolar mixture of the substrate and the reagent, the most shielded protons, in the α position with respect to the carboxylic group, were shifted by *ca* 11 ppm. Similar shielding were attained for the α protons of various carboxylic acids such as 2-(2-thienyl)propionic acid, 5-norbornene-2-carboxylic acid and 2-chloropropionic acid. In the last case, it is noteworthy that the shifts were significantly smaller when crystals of the 1:2 adduct were dissolved in $CDCl_3$ due to the lower molar ratio [reagent]/[substrate]. The binding ability of the various acids was thus very similar.

Addition of small amounts of the reagent $Pr(tpip)_3$ to caproic acid spread out all the ^1H resonances. It was then possible to use Job's method [18] to determine the stoichiometry of the adduct. The induced shifts $(\delta - \delta_0)$ were measured using mixtures in which the sum of the concentrations of the chelate $[L_T]$ and the substrate $[S_T]$ was kept constant. As shown in figure 7, the curves $[S_T][\delta - \delta_0] = f([L_T]/[S_T] + [L_T])$ drawn for the various protons exhibited clear maxima for the value 0.5 of the fractional amount of the added reagent demonstrating that a 1:1 adduct was formed in solution. In the case of 2-chloropropionic acid, the maxima were shifted toward a lower value of the fractional ratio of the reagent, *ca* 0.43, showing that both 1:1 and 1:2 adducts were present in solution.

In mixtures of linear fatty acids containing at least seven carbons, the resonances originating from the methylene protons situated at the same position with respect to the carboxylic group collapse into single signals, whatever the molar ratio [chelate]/[substrate]. Small differences were observed only for the first terms in the series of linear carboxylic acids. The relevant data

are given in the supplementary material of this paper. It might be deduced that the formation of a 1:1 adduct occurs in all cases and that the binding constants of the various linear carboxylic acids to the chelate $Pr(tpip)_3$ might be considered as equal. The binding constant and the shifts induced for the protons of the 1:1 complex were determined in the case of caproic acid by use of Armitage's method [19, 20]. The binding constant was $K = 70$ mol L^{-1} and the induced shifts were 18.7, 12.4, 7.3, 5.0 and 2.7 ppm starting from the α protons.

In order to gain information on the origin of the shifts, the effects of two reagents $Pr(tpip)_3$ and $Eu(tpip)_3$, which induce shifts in opposite directions [21], were compared using lauric acid as the substrate. Although the shifts induced by $Eu(tpip)_3$ were smaller in magnitude, the ratio of the shifts induced by the two reagents remained identical within experimental error for all the protons but those of the methylene at C-2 for which small discrepancies appeared. Furthermore, for each reagent, it was observed that the relative induced shifts were almost independent of the [chelate]/[substrate] molar ratio as well as of the concentration of the substrate if the protons at C-2 were disregarded.

Taken together, these observations prove that the shifts are determined by a single mechanism, the pseudo-contact one, for all the protons but those in α position with respect to the carboxylic site. In this last case, a contact mechanism might also contribute to the shifts. In all studies it will thus be advisable to normalize the induced shifts with respect to those observed, *eg* at the β position of the carboxylic site.

• *^{31}P NMR*

Further insight into the behavior of the different species in solution might be gained by observation of the ^{31}P nucleus. Upon complexation of a chelate with a carboxylic acid, a single resonance was observed for all the phosphorus atoms. The moderate shift of the ^{31}P resonance to low field with respect to the resonance of the free chelate in the $Pr(tpip)_3$-carboxylic acid complexes was equal to 6.8 ppm for equivalent molar concentrations of lauric acid and chelate. The data are given in the supplementary material. The shift was smaller when bulky substituents were situated in close proximity to the carboxylic acid.

Upon addition of lauric acid to $Dy(tpip)_3$, the ^{31}P resonance was scarcely shifted (1 ppm for an equimolar ratio [substrate]/[chelate]). The shift to upfield for the $Eu(tpip)_3$ complex ($\sim$ 8.1 ppm for an equimolar ratio) was similar in magnitude to that observed for the $Pr(tpip)_3$ complex. It is noteworthy that the shifts for the phosphorus atoms were opposite to the direction of the shifts for the protons of the organic ligand.

The above observations show that a rapid exchange occurs on the NMR time-scale between the free and complexed species. The effective symmetry of the complex needed for the interpretation of the induced shifts by means of the McConnell Robertson equation is thus attained [22] :

$$\delta\upsilon_i = \frac{K[L]}{K[L]+1}\Delta\upsilon_i$$

where $\delta\upsilon_i$ is the shift observed for nucleus i, $\Delta\upsilon_i$ is the induced shift in the 1:1 adduct, K the binding constant, and [L] the concentration of the free chelate in the solution.

It was further checked that complexation of the carboxylic group is highly favored over that of any other functional group, *eg*, amine, alcohol, ester or ketone.

Comparison of different lanthanide cations

The europium chelate induces about six times smaller shifts than the praseodymium chelate. Furthermore the resonances of the protons of the phenyl groups of the ligands might overlap the substrate resonances. The dysprosium chelate poorly complexes carboxylic acids and the shifts in the upfield direction were not sufficient for practical use. The lack of any shift when the ytterbium chelate was used may indicate that it is incapable of forming the adducts. The smaller Yb(III) is expected to be more sensitive than Pr(III) to steric constraints and the tpip ligand has two bulky phenyl groups near each donor oxygen atom. $Pr(tpip)_3$ appeared as the most powerful reagent for the study of carboxylic acids.

Studies of carboxylates

In a preliminary communication [14], we described the synthesis and X-ray structure of a dinuclear complex **6** obtained from $Pr(tpip)_3$ and the potassium or ammonium salt of phenylpropionic acid. This reaction that occurred according to equation 4 is instantaneous and can be carried out and followed in a NMR tube.

$$2\ Pr(TPIP)_3 + 2\ RCOO^- \longrightarrow Pr_2(TPIP)_4\ (RCOO)_2 + 2\ TPIP^- \qquad \text{(eq 4)}$$

6

The same reaction has been carried out starting from (*R*)-(+)-citronellic acid or (+)-3-hydroxybutyric acid and gave the dinuclear complexes **7** or **8**, respectively, which were fully characterized by X-ray crystallography. ORTEP views of **7** and **8** appear in figures 8 and 9.

The striking feature of these new complexes is their dinuclear nature. The metal centers each bear a chelating (tpip) ligand, and are linked together by four bridging ligands : two tpip groups, and two carboxylate groups. Thus only one of the tpip groups on each metal center has been replaced by a carboxylate.

The discrete units consist of two pentagonal bipyramids with a common edge of two oxygen atoms originating from the two different carboxylate groups. The coordination sphere of each metal is completed in the plane by two oxygens of the chelating tpip ligand and by one oxygen from a carboxylate group. The axial groups are the oxygen atoms of two bridging tpip ligands. Interestingly enough, the bridging carboxylate groups act as tridentate ligands. One oxygen atom is bound to two metal centers and the two Pr(O) bond distances are only slightly different (Pr(1)-O(5) = 2.429 (4) Å, Pr′(1)-O(5) = 2.627 (4) Å).

Dinuclear carboxylates of trivalent rare earth have previously been synthesized from trivalent salts and ammonium carboxylates [23-25] (eq 5), and their structure established by X-ray diffraction studies. This was,

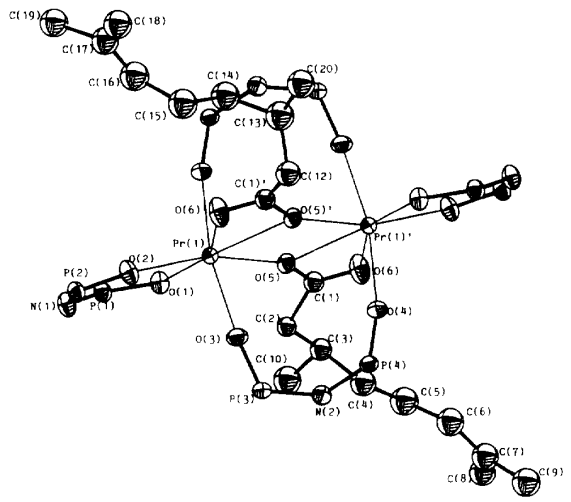

Fig 8. ORTEP drawing of complex **7**. Ellipsoids are shown at the 50% probability level. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.384 (4), Pr(1)-O(2) 2.357 (4), Pr(1)-O(3) 2.319 (4), Pr(1)-O(5) 2.429 (3), Pr(1)-O(5′) 2.627 (4), O(6)-C(1) 1.236 (7), O(5)-C(1) 1.264 (6), Pr(1)-O(5)-Pr(1′) 111.2 (1), O(5′)-Pr(1)-O(5) 68.8 (1).

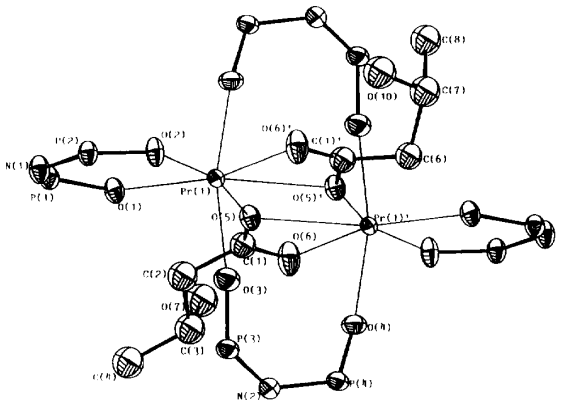

Fig 9. ORTEP drawing of complex **8**. Ellipsoids are shown at the 50% probability level. Important bond lengths (Å) and bond angles (°) : Pr(1)-O(1) 2.405 (8), Pr(1)-O(2) 2.321 (8), Pr(1)-O(5) 2.456 (8), Pr(1)-O(6′) 2.538 (9), Pr(1)-O(5)-Pr(1′) 111.3 (3).

for example, the case for the trinicotinates of Pr(III), La(III) and Sm(III) in which the nicotinate groups are coordinated to the metal through the carboxylate oxygens with four bridging and two chelating carboxylates. However, significant variations in the mode of coordination of the carboxylate groups, mainly due to the nature of the metal, appeared in these structures. Thus, in the case of La(III) and Sm(III), the dinuclear complexes contained only bidentate carboxylates (bridging and chelating). For Pr(III), however, one bridging nicotinate was best described as a tridentate ligand, since one oxygen atom was bound to two metal centers. One of these bonds was nevertheless much longer than the other (Pr(2)-O = 2.90 (2) Å, Pr(1)-O = 2.43 (2) Å) which raises questions about its existence.

$$Ln_2(SO_4)_3 + 6\ RCOO^- \longrightarrow Ln_2(RCOO)_6 + 3\ SO_4^{=} \qquad \text{(eq 5)}$$

NMR studies of species in solution

• *^1H NMR*

The changes produced by the reagent $Pr(tpip)_3$ in the NMR spectrum of a carboxylate were strikingly different from those observed for the carboxylic acids. Upon successive additions of $Pr(tpip)_3$ to a solution of the potassium salt of lauric acid, two distinct sets of resonances were observed : one nearly unshifted and one with shifts almost independent of the molar ratio [chelate]/[substrate]. The signals in the last series grew in intensity at the expense of the others until a stoichiometric ratio was achieved. No significant further shifts were observed upon new additions of the reagent. The data are given in the *Experimental section*. Similar sets of resonances appeared when an amine (diisopropylamine) was progressively added to a solution containing a carboxylic acid and the reagent, due to the *in situ* formation of the carboxylate. The spectra are well resolved. The upfield shifts are much greater than those observed for the stoichiometric mixture of lauric acid and $Pr(tpip)_3$ (fig 10).

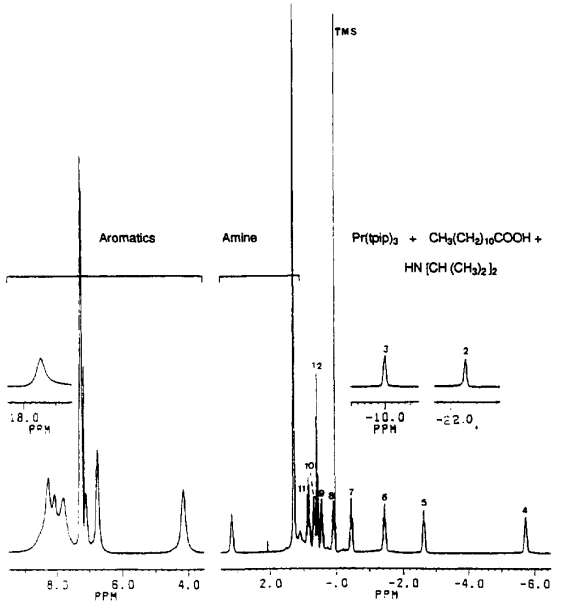

Fig 10. ^1H NMR spectrum obtained from $Pr_2(tpip)_4(CH_3(CH_2)_{10}COO)_2$ in $CDCl_3$.

It might be deduced from the above observations that rapid exchange on the NMR time-scale failed to occur between complexed and uncomplexed species when the substrate is a carboxylate. Nevertheless slow exchange can be probed by saturation-transfer experiments. In

mixtures containing the carboxylate adduct and either the free acid (lauric acid, diisopropylamine, $Pr(tpip)_3$ in 1:0.5:0.5, molar ratio) or the free carboxylate (lauric acid, diisopropylamine, $Pr(tpip)_3$ in 1:1:0.5 molar ratio) the protons at the sites C4 to C11 of the uncomplexed species gave a single broad signal. Saturation of this signal led to the partial saturation of the well-separated signals observed for the same sites 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 C4 to those at C11. The occurrence of slow exchange was also evident when solutions containing binuclear complexes formed with the isopropylammonium salts of lauric and propionic acid were mixed. Besides the signals originating from the two binuclear complexes, signals originating from a third mixed species involving one molecule of each substrate appeared. In the mixed complex, the shifts are slightly increased for the protons of the propionate and the opposite trend was observed for the protons of the laurate up to the seventh position. Complexation thus appeared slightly less favored for the bigger ligand probably due to steric effects. Data are given in the *Experimental section.*

• *^{31}P NMR*

The results obtained with carboxylates were strikingly different from those obtained for the acids. The complexes were either isolated (see *Experimental section*) or prepared directly in the NMR tube by addition of diisopropylamine to the solution containing the carboxylic acid and the chelate. The spectrum recorded upon dissolution of the crystals in $CDCl_3$ showed two resonances of equal intensity (table II). When the complex was prepared *in situ* in the NMR tube, a third narrower signal appeared with the same intensity as the other two. Its frequency did not significantly vary whatever the nature of the cation involved in the chelate and whatever the nature of the carboxylate. In the light of the previous results and the solid-state structure of the complexes formed between the carboxylates and $Pr(tpip)_3$, the narrow resonance that appears only when the complex is prepared in solution must arise from free ligands released when the complexation of the carboxylates occurs. The other two resonances clearly correspond to two different types of tpip ligands. Their positions depend primarily upon the nature of the lanthanide cation. In the cases of Pr and Eu it seems reasonable to assign the resonance which is the less shifted with respect to its position in complexes involving an acid to the ligand linked with a single cation. The other resonance, which is far more shifted to low field in the case of the praseodymium cation and to high field in the case of the europium cation, is then ascribed to the phosphorus atoms of the ligands between two metallic centers. As regards Dy, the resonance shifted to high field is tentatively assigned to the ligand linked with a single cation by comparison with Pr since in both cases the same direction is expected for the shifts.

The results obtained by ^1H and ^{31}P NMR studies provide overwhelming evidence for the existence of a new type of association in solution when carboxylates react with tris (tetraphenylimidodiphosphinato)lanthanide chelates. The spectral features are

Table II. ^{31}P NMR. Chemical shifts for the ^{31}P signals in the binuclear complexes (ppm) with respect to external H_3PO_4 (85%).

$Pr_2(tpip)_4$ $(laurate)_2$ [a]	$Eu_2(tpip)_4$ $(laurate)_2$ [a]	$Dy_2(tpip)_4$ $(laurate)_2$ [a]	$Pr_2(tpip)_4$ $(citronellate)_2$ [b]
11.35	11.32	11.45	
6.93	25.99	−185.13	8.52
134.06	−99.28	382.52	131.75

[a] The complex was prepared in situ.

[b] Crystals were dissolved in $CDCl_3$.

in accord with a binuclear structure similar to the solid-state structure. The unusual stability of the association in solution might result from the presence of the two bridging tetraphenylimidodiphosphinato ligands and from the involvment of the two carboxylate groups simultaneously bound to the two metallic centers.

Comparison of different lanthanide cations

Two different types of tetraphenylimidodiphosphinato ligands are present, and so the many resonances of the phenyl protons are spread over a large range of chemical shifts, essentially 6.4 to 9 ppm, with two extra signals around 4.1 and 17.4 ppm. As a consequence, the complexation with the europium chelate which results in downfield shifts is generally not suitable for the study of carboxylates. The ytterbium chelate does not appear to react with carboxylates since no shifts are observed. Surprising results were obtained for the chelate $Dy(tpip)_3$, which induced only limited shifts in the spectra of carboxylic acids. The binuclear species was easily formed and the shifts of the resonances of the carboxylate protons were an order of magnitude higher than for the praseodymium complexes. It must be noticed that the detection of the more shifted protons is difficult with the available spectrometers. Table III lists a comparison of the shifts for the protons of the laurate substrate in the binuclear Pr and Dy complexes. It is worth noting that when the relative shifts are normalized with respect to the shifts of the 3-CH_2 protons,

Table III. Comparison of the binuclear complexes [tetrakis(tetraphenylimidodiphosphinato)][di(laurato)]dipraseodymium and [tetra(tetraphenylimidodiphosphinato)][di(laurato)]didysprosium.

	Pure acid	Pr complex			Dy complex		
Sites	δo [a]	δ [b]	$\Delta\delta$ [c]	Ri/3 [d]	δ	$\Delta\delta$	Ri/3
2	2.35	−22.95	25.3	2.14	−256.7	259.1	2.31
3	1.63	−10.2	11.8	1	−110.3	111.9	1.0
4		−5.87	7.13	0.60	−68.3	69.53	0.62
5		−2.7	3.96	0.33	−34.6	35.86	0.32
6		−1.5	2.76	0.23	−24.38	25.64	0.23
7	1.26	−0.51	1.77	0.15	−15.42	16.68	0.15
8		0.07	1.18	0.10	−10.35	11.61	0.10
9		0.4	0.86	0.07	−7.23	8.49	0.07
10		0.64	0.62	0.05	−4.83	6.09	0.05
11		0.88	0.38	0.03	−3.25	4.51	0.04
12	0.88	0.45	0.43	0.036	−2.39	3.27	0.03

[a] chemical shift for the carboxylate, [b] chemical shift for the binuclear complex, [c] induced shift, [d] induced shift normalized with respect to the protons at C-3.

Table IV. Characterization of linear saturated and unsaturated carboxylic acids : chemical shift for selected protons of the pure acid in $CDCl_3$ solution (ppm) and relative shifts, R, normalized with respect to the shift of the methyl group of decanoic acid in presence of $Pr(tpip)_3$.

Compound	Me group		8-CH_2		11-CH_2		14-CH_2		17-CH_2	
	δ	R	δ	R	δ	R	δ	R	δ	R
C10	0.88	1								
C12	0.88	0.52	1.28	2.15	1.29	0.78				
C14	0.88	0.28	±0.03	±0.06	±0.04	±0.10				
C16	0.88	0.15_4								
C18	0.88	0.085								
Z Δ9-C16 : 1	0.88_4	0.39	2.01	2.09	2.01	1.03_9				
E-Δ9-C16 : 1	0.88	0.29	1.96_4	2.08	1.96_4	0.69_9				
Z-Δ9-C18 : 1	0.88	0.24_4	2.01_2	2.07	2.01	0.98				
Z. Z-Δ9-Δ12-C18 : 2	0.88_9	0.42	2.04_9	2.07	2.77	1.00	2.04_9	0.60		
Z. Z. Z-Δ9. Δ12. Δ15-C18 : 3	0.97_5	0.50	2.06_2	2.06	2.81	1.02	2.81	0.62	2.07_7	0.54

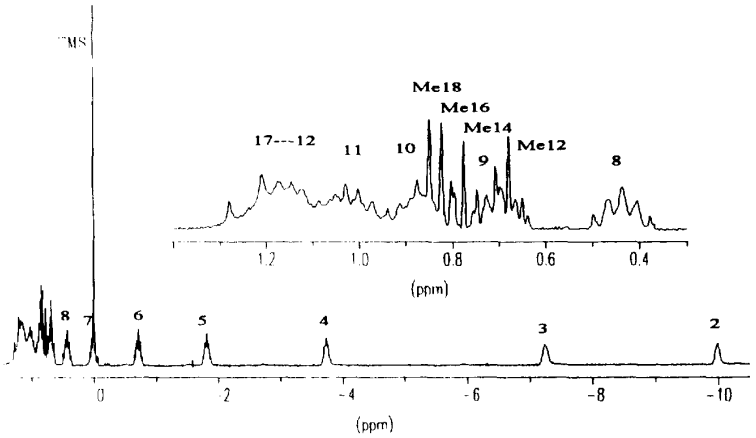

Fig 11. Spectrum of a mixture of C-18, C-16, C-14 and C-12 carboxylic acids in the presence of $Pr(tpip)_3$.

they are very similar for the two complexes except for the 2-CH_2 protons. It might be anticipated that the shifts originate mainly from the pseudo-contact mechanism in the binuclear complexes. For the nuclei that lie in close proximity to the carboxylate groups nevertheless other mechanisms might be important. Finally, for the study of carboxylates, the best reagent is generally $Pr(tpip)_3$.

Applications

Analysis of mixtures of fatty acids

In the ^1H NMR spectra of saturated fatty acids, only a few resonances are resolved corresponding to the protons in α and β positions with respect to the carboxylic group and to the methyl group. In unsaturated fatty acids, the ethylenic protons, the methylene protons between two double bonds and the methylene protons α to a double bond coalesce into three broad signals preventing the determination of the position of the double bonds and that of the configuration. Spreading out these spectra by the use of $Pr(tpip)_3$ allows the resolution of many signals.

Saturated carboxylic acids adopt the same extended conformation of the chain in solution. As a result, in mixtures of fatty acids the signals of methylene protons equally remote from the carboxylic group overlap. Fortunately, the signals of the methyl groups which are unequally remote from the carboxylic site gave well-resolved signals. An easy way to determine the constituents in such mixtures is to add a small amount of a known carboxylic acid and to measure the ratio between the shifts observed for the different methyl groups and that of the methyl group in this reference. Decanoic acid $CH_3(CH_2)_8COOH$ is well suited for this purpose since the signal of its methyl protons does not overlap any other signal. The relative shifts measured for the C18, C16, C14 and C12 carboxylic acids are collected in table IV and the expanded spectrum of a mixture of these acids is shown in figure 11.

As regards unsaturated acids, we have previously shown that all the resonances of arachidonic acid are well resolved after complexation with $Pr(tpip)_3$ [13]. The same result is achieved for linoleic acid (Δ9, Δ12, Δ15, C18) despite the fact that the first double bond is more remote from the carboxylic group. Except for a few methylene groups, the resonances of less unsaturated acids, such as linoleic acid (Δ9, Δ12, C18), the *Z* and *E* isomers of hexadec-9-enoic acid (Δ9, C16) and oleic acid (Δ9, C18) are also resolved.

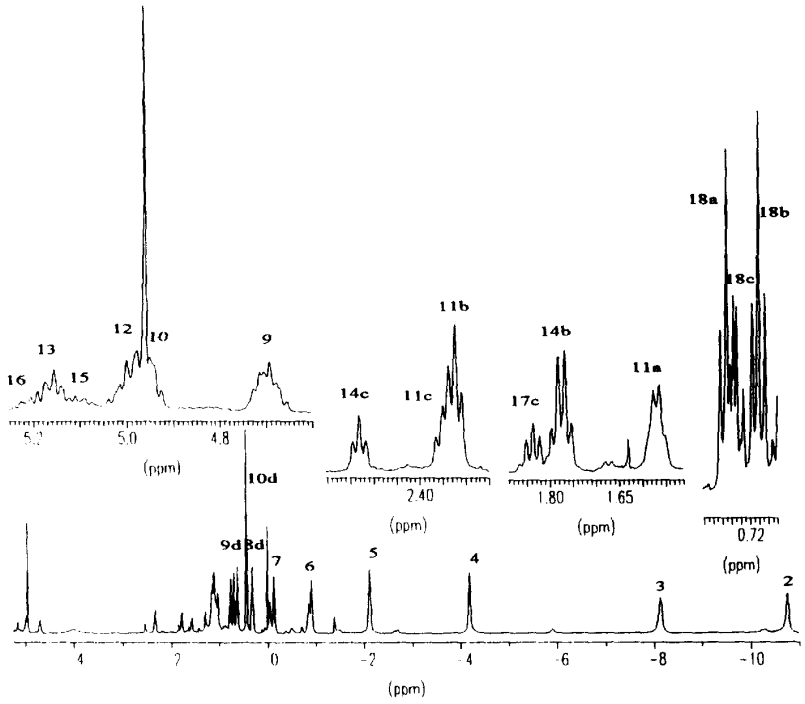

Fig 12. Typical patterns observed for a mixture of a) oleic (Δ9 C18), b) linoleic (Δ9 Δ12 C18) and c) linolenic (Δ9 Δ12 Δ15 C18) acids in presence of $Pr(tpip)_3$, d) decanoic acid was added as a reference.

The spreading of the ethylenic protons enables the measurement of the coupling constants and thus provides information on the configuration. Furthermore, due to the bending of the chain in the *Z* isomer, it was observed that the signal of the protons situated after the double bond, in particular the easily identified 11-CH_2 and CH_3, were more shifted in the *Z* isomer than in the *E* isomer of Δ9, C16 acids.

Another interesting feature is that the shifts of the resonances of the methylene groups α to a double bond or situated between two double bonds are spread according to their position within the chain. Due to the bending of the chain according to the number of double bonds of the unsaturated acids, protons otherwise situated in the same position are differentiated. The quantification of the three acids might be obtained by measuring the intensities of characteristic signals.

Finally, in mixtures of saturated and unsaturated acids the signals of the methylene groups of the unsaturated acids overlap those of the saturated acid up to the γ position with respect to the first double bond. The signals originating from methylene groups in the α or β position to the first double bond appear to low field with respect to those of the methylene equally remote form the carboxylic group in the saturated acid. The observation of the position for which the splitting occurs thus allows us to specify the position of the first double bond.

Figure 12 shows the typical patterns observed for a mixture of the three (Δ9, Δ12, Δ15, C18), (Δ9, Δ12, C18) and (Δ9, C18) acids. As in the case of saturated acids, the induced shifts of the characteristic signals were referenced to the shift of the methyl group in decanoic acid $CH_3(CH_2)_8COOH$. The pertinent data are collected in table IV.

Study of diastereomers

Transesterification and spaltrohr distillation of the preen-gland wax of domestic goose followed by hydrolysis led to (2*R*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyl undecanoic and decanoic acids [26]. Complexation with $Pr(tpip)_3$ provides an easy way to probe the occurrence of racemization at the α carbon. Figure 13 shows the well-resolved spectrum of (2*R*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyl undecanoic acid in the presence of 1.3 equivalents of the reagent. For this chiral molecule strong diastereotopic effects are observed for the protons of all the methylene groups. Figure 14 shows the spectrum obtained for a sample of (2*R*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyl decanoic acid partially racemized at C2. Most signals originating from the two diastereomers are fairly well separated in particular those of all the methyl groups. The extent of racemization is easily measured. It is noteworthy that strong variations of the relative shifts are observed for the various sites. In particular the methyl groups at C-2 and C-4 are more shifted when the configuration at C-2 is *S* and the reverse is true for the methyl groups at C-6, C-8 and C-10. These observations most likely reflect highly preferred conformations of the two species in solution. A preliminary study has shown that the bonds C-1, C-2 and C-3, C-4 are antiparallel in the 2*S*,4*R*,6*R*,8*R* isomer and gauche in the 2*R*,4*R*,6*R*,8*R* isomer. Thus in the first case steric

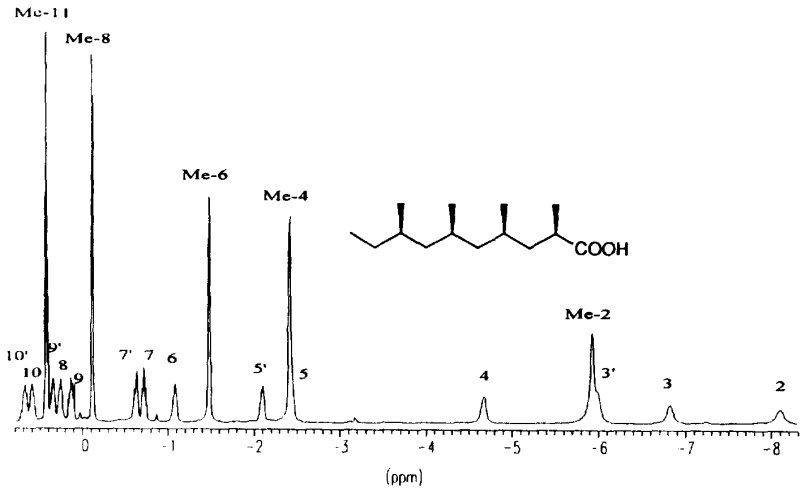

Fig 13. Spectrum recorded for (2*R*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyl undecanoic acid in the presence of 1.3 equivalents of $Pr(tpip)_3$.

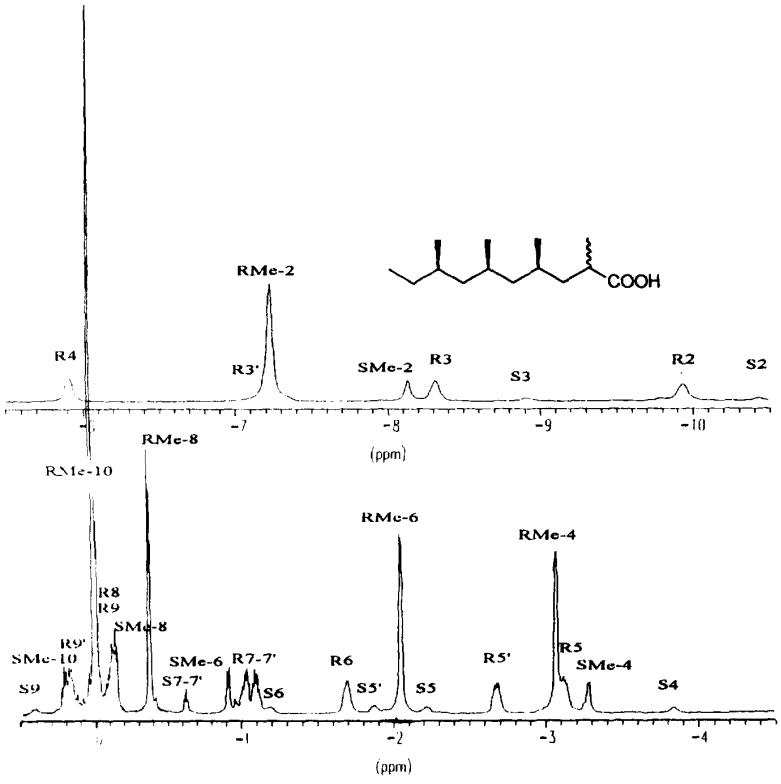

Fig 14. Spectrum obtained for a mixture of (2*R*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyldecanoic acid (major compound, signals labelled *R*) and (2*S*,4*R*,6*R*,8*R*)-2,4,6,8-tetramethyldecanoic acid (minor compound, signals labelled *S*).

interactions are minimized for the carboxylic group and bonding to the reagent is easier. In contrast, due to the extended conformation of the first part of the chain, the sites at the end of the chain are more remote from the praseodymium atom.

Studies of chiral carboxylates

Due to the duplication of the substrate in the binuclear species, diastereomeric complexes DL (*RR*/*SS*)

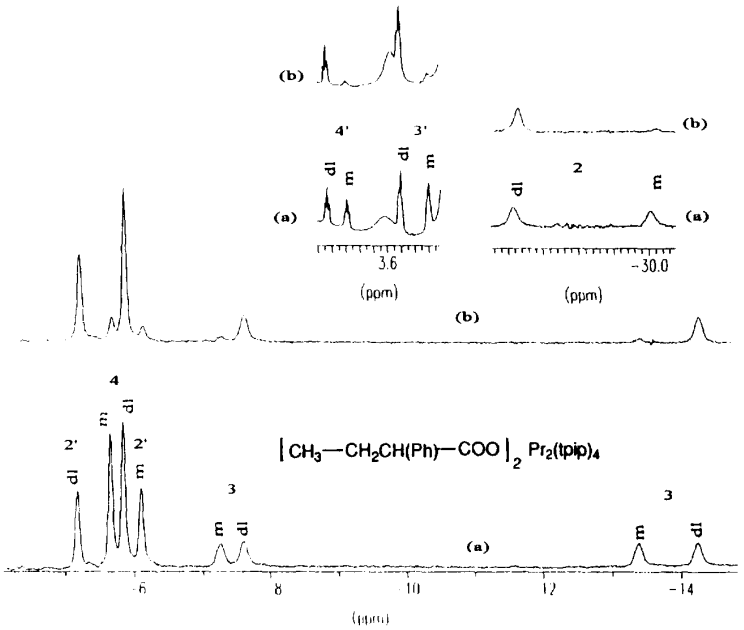

Fig 15. Spectra recorded for the binuclear [tetrakis(tetraphenylimidodiphosphinato)][di(2-phenylbutanoato)]dipraseodymium complexes : a) diastereomeric species, DL and *meso*, obtained from the racemic mixture of the *R,S* 2-phenylbutanoic acid, b) DL species obtained from the *R* 2-phenylbutanoic acid.

and *meso* (*RS/SR*) are formed with racemic chiral carboxylates. They are expected to produce different resonance signals since the exchange is slow on the NMR time-scale. If so, important potential applications of the formation of the binuclear complexes would be : 1) the control of the optical purity; and 2) the determination of the enantiomeric excess (ee).

The ability of chiral compounds to form pairs of diastereomers through proper duplication of the chiral part of the molecule, *eg*, the formation of anhydrides from carboxylic acids, or by reaction with a compound of known chirality has been used for this purpose [27]. The main problem encountered in this field was, besides the need to prepare the diastereomers, the difficulty of obtaining well-separated pairs of resolved signals in the NMR spectra.

The formation of dinuclear dicarboxylato complexes occurs directly by adding the reagent to a carboxylate dissolved in $CDCl_3$. When the substrate is a carboxylic acid, the addition of the reagent only needs to be followed by the addition of an equivalent of diisopropylamine.

A preliminary study [14] has shown that the diastereomeric complexes of 2-phenylbutanoate exhibit a shift difference of about 2 ppm for the α proton. All the other protons gave distinct resonances and the smallest shift difference was only 0.2 ppm for the methyl group. The spectrum is presented in figure 15.

Numerous examples have been studied in order to determine the conditions required to observe large degrees of enantiomeric resolution.

The separation between the resonances of the proton in the diastereomeric complexes of 2-(thiophen-2-yl)propionate is slightly less than in the case of 2-phenylbutanoate, about 1.4 ppm, while the shift to high field is intrinsically greater. Figure 16 allows the comparison of the spectra recorded for the DL complex and for the mixture of the DL and *meso* complexes.

From a practical point of view, this method can be applied in the determination of the optical purity of the commercially important antiinflammatory agent Naproxen, which in 1990 was the only non-stereoidal antiinflammatory drug on the market in an enantiomerically pure form; the (*S*)-enantiomer is 28 times more active than its (*R*)-enantiomer. The partial ^1H NMR spectrum of the dinuclear complex obtained from the optically active compound (*S,S*) is displayed on figure 17a, with signals for the α-proton at δ -29.94 ppm, for the α-methyl at δ -10.16 ppm, and for two aromatic protons, at δ -4.90 and 3.49 ppm. The NMR spectrum of the complexes obtained from the racemic form appears in figure 17b. The separation of the signals for the (D,L) and (*meso*) pairs is large for the α-protons ($\Delta\delta$ = 1.62 ppm) and smaller for the α-methyl ($\Delta\delta$ = 0.10 ppm) and the two aromatic protons ($\Delta\delta$ = 0.12 and 0.42 ppm).

In the complexes of 2-methylbutanoate, which is chiral due to small differences (Et vs Me), a smaller but significant separation occurs for each methyl group (-10.29 (DL) and -10.16 ppm (*meso*) for the methyl group at C-2; -5.02 (DL) and -5.15 ppm (*meso*) for the more remote 4-methyl group). One of the geminal protons at C-3 gives also distinct resonances (-9.4 (DL) and -9.85 (*meso*) ppm). The resonances of the second proton were not resolved (DL and *meso* -11.40 ppm). All the signals are less shifted to high field than for the two preceding examples.

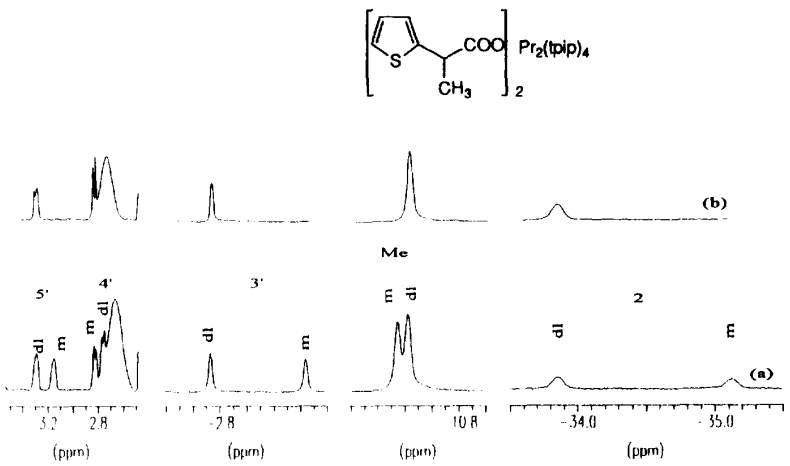

Fig 16. Spectra recorded for the binuclear [tetrakis(tetraphenylimidodiphosphinato)] di[2-(thiophen-2-yl)propionato] dipraseodymium complexes : a) diastereomeric species, DL and *meso*, obtained from the racemic mixture of the *R,S* 2-(thiophen-2-yl)-propionic acid; b) DL species obtained from the *R* 2-(thiophen-2-yl)-propionic acid.

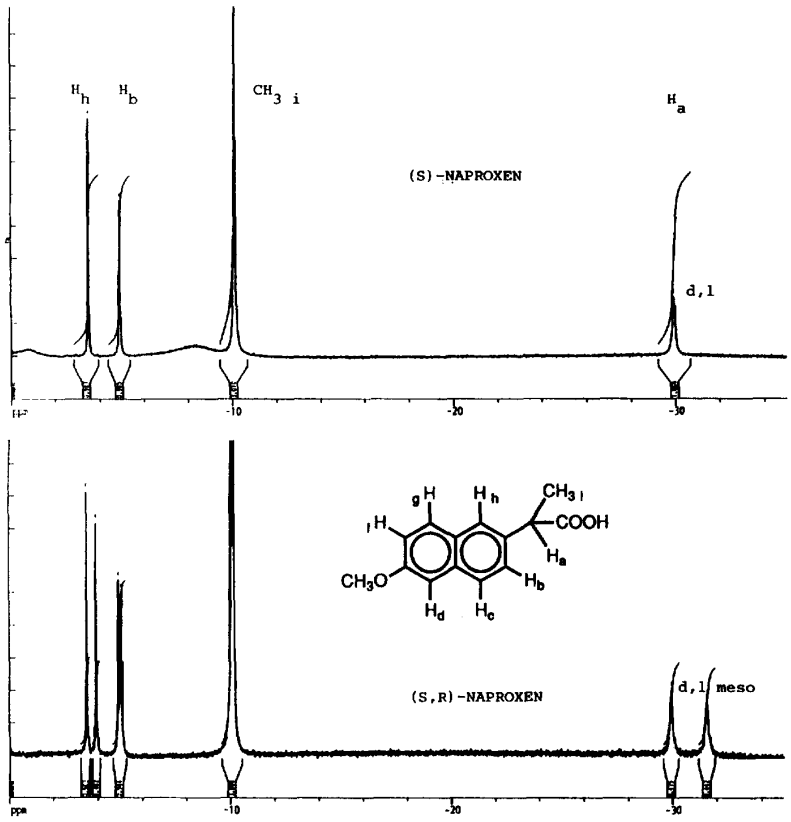

Fig 17. Spectra recorded for the binuclear complexes obtained a) from (*S*)-Naproxen and b) from the racemic mixture of Naproxen.

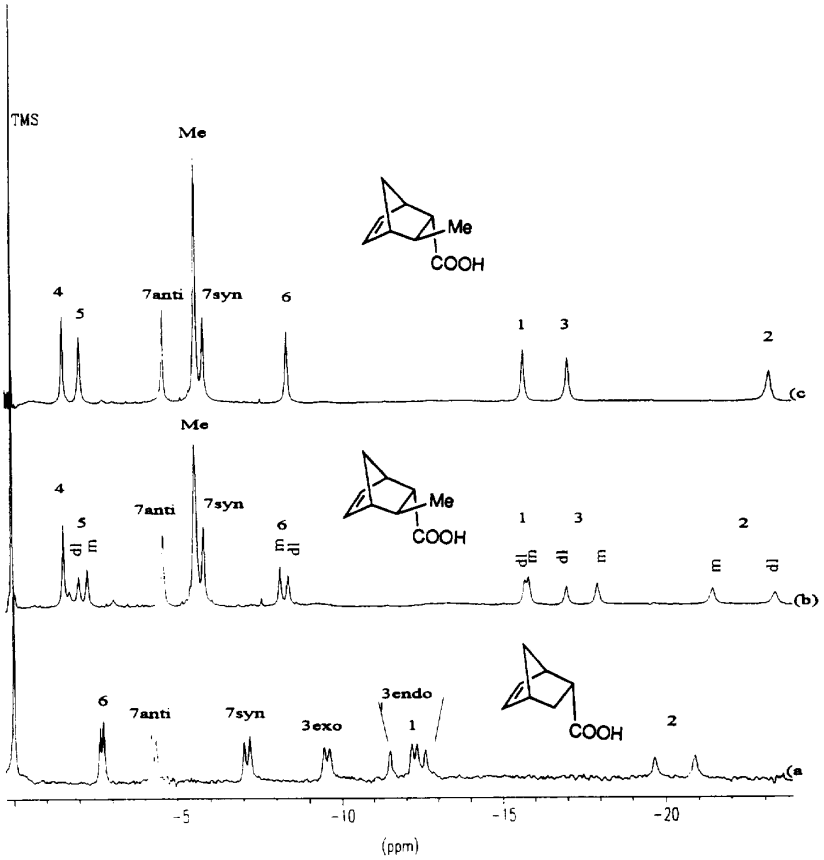

Fig 18. Spectra of binuclear complexes : a) diastereomeric species, DL and *meso*, obtained from the racemic mixture of bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, b) diastereomeric species, DL and *meso*, obtained from the racemic mixture of the 3-methylbicyclo[2.2.1]hept-5-ene-2-carboxylic acid, c) DL species obtained from the same acid.

Finally, the stereomers of complexes obtained from substrates that are chiral due to the replacement of one hydrogen by deuterium were not significantly distinguished.

From the above examples, it is clear that the sense of the nonequivalence within a pair of diastereomers is not necessarily the same for all the protons since reversals might be observed in each case, *eg*, δH_2 DL > δH_2 *meso* but δH_3 *meso* > δH_3 DL in 2-phenylbutanoate complexes, δH_2 DL > δH_2 *meso* but δCH_3 *meso* > δCH_3 DL in 2-(thiophen-2-yl)propionate complexes, or $\delta 2$-CH_3 *meso* > $\delta 2$-CH_3 DL but $\delta 4$-CH_3 DL > $\delta 4$-CH_3 *meso* in 2-methylbutanoate complexes. Furthermore the spectral nonequivalence of the diastereotopic nuclei, *eg*, the methylenic protons at C-3 in 2-phenylbutanoate or 2-methylbutanoate, is considerably enhanced in the binuclear complexes. These results suggest that the geometry of the diastereomeric complexes is substantially distinct and that the nuclei reside in very different spatial environments.

When the carboxylic group is directly linked to a rigid skeleton, steric effects are most likely expected to play an important role. The binuclear species are nevertheless easily formed. Thus the complexes of bicyclo[2.2.1]hept-5-ene-2-carboxylate and 3-methylbicyclo[2.2.1]hept-5-ene-2-carboxylate [28] with the carboxylate group in the *endo* position in both cases and the methyl group in the *exo* position were compared (fig 18). In the first case the differentiation was observed for all the protons of the diastereomers; in the second the signals remain unresolved for H-4, the bridgehead protons H-7, H-7′ and the methyl group, which are the more remote sites with respect to the carboxylate group. The other protons gave resolved signals.

Even the chiral iron tricarbonyl complex of hexa-2,4-dienoic acid leads to the formation of complexes which show strong diastereomeric effects for the ethylenic protons H-4, H-5 and for the terminal methyl group. In contrast, the signals of the protons in close proximity to the carboxylate are slightly separated (H-3) or remain unresolved (H-2) (fig 19).

This method is also applicable in the cases where the chiral centers are not in the α position with respect to the carboxylic group. Thus in the complexes of 3-phenylbutanoate or citronellate, in which the chiral center lies in the β position, well-separated pairs of signals were still observed for most protons.

In 5-(1,2-dithiolan-3-yl)pentanoic acid (thioctic acid) the tertiary chiral carbon is five bonds from the carboxylic group. The labile complex formed by addition of the chelate $Pr(tpip)_3$ to the acid shows well-resolved signals. Diastereotopic effects are significant for the pro-

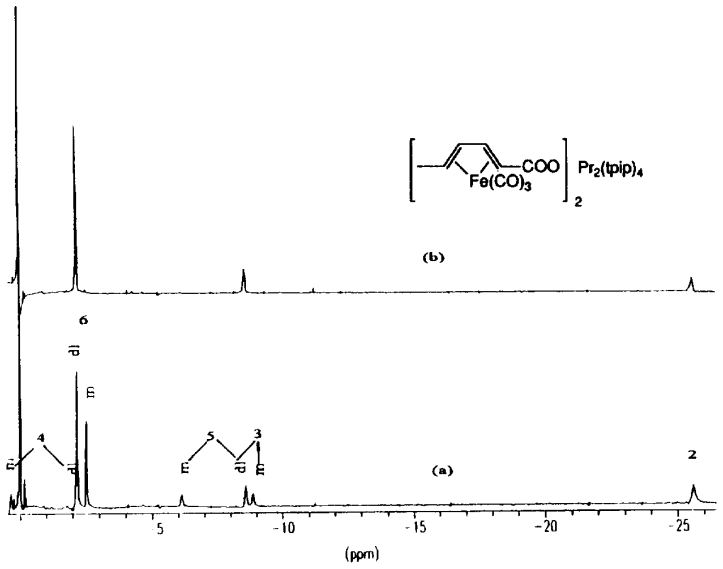

Fig 19. Spectra recorded for the binuclear complexes obtained from a) the racemic mixture of the chiral iron tricarbonyl complex of hexa-2,4-dienoic acid and b) a pure enantiomer of the chiral iron tricarbonyl complex of hexa-2,4-dienoic acid.

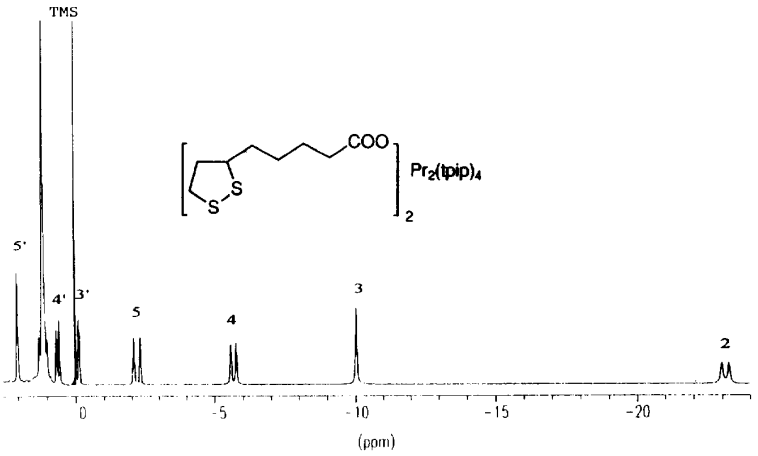

Fig 20. Spectra recorded for the binuclear complexes obtained from the racemic mixture of *R,S*-thioctic acid.

tons of the intracyclic methylene groups and within the chain for the protons of the methylene groups in the α and β positions with respect to the chiral center. In contrast, diastereotopic effects do not appear for the methylene groups more remote from the chiral centre, *ie* the groups at C-3 and C-2. Upon formation of the binuclear complexes, the protons at C-3 remained undifferentiated but two distinct signals appeared for the methylene group at C-2 in the α position with respect to the carboxylic group, one for each diastereomeric binuclear complex. The spectrum is shown in fig 20.

The following example will show a case where two chiral centers are present. The 2-(5-{1-[(*tert*-butoxycarbonyl)amino]-2-methylpropyl}thiophen-2-yl) propionic acid bears one chiral center in the α position and a second five bonds from the carboxylic group. Six diastereomeric binuclear species might be expected in ratio 1:2:1, 1:2:1 for the carboxylate complexes. As shown in figure 21, the six signals were distinguished for the α proton, and partially resolved for the proton H-3′ of the thienyl ring.

The above example has shown that the presence of a second functional group remote from the carboxylic group did not prevent the formation of the binuclear species. It has been checked that it remains true when functional groups such as $-O-CO-CH_3$ or $-OH$ are present in the β position with respect to the carboxylate. It is noteworthy that the ^1H NMR spectrum of the binuclear complex **7** formed from (*R*)-3-hydroxybutanoate showed strong shielding for all the protons, in particular for the hydroxyl proton. This is in fair agreement with the position determined for the hydroxylic oxygen atom in the solid-state structure described above (OH −27.6, H2,2′ −29.2 and 27.1, H-3 −10.7 and CH_3 −8.0 ppm).

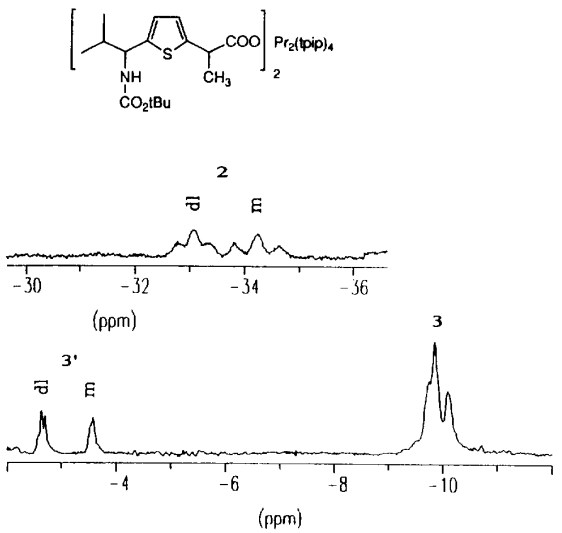

Fig 21. Partial spectrum recorded for the binuclear stereomeric species obtained from 2-(5-{1-[(*tert*-butoxycarbonyl) amino]-2-methylpropyl}thiophen-2-yl)propionic acid.

Mixed binuclear complexes

It has been shown above that mixed species are formed whenever two different carboxylates are simultaneously opposed to $Pr(tpip)_3$. It was interesting to use a very dissymmetric compound such as 2-chloropropionate as the first carboxylate. When the second is a linear saturated carboxylate, diastereotopic effects appear for the protons of each methylene group up to at least the fifth position.

From this observation it might be inferred that enantiomers in which the chirality results from the replacement of one hydrogen by deuterium might give distinct mixed species. Effectively, the signals of the protons of the mixed species formed by (*S*)-2-chloropropionate and racemic 2-^{2}H,12-phenyldodecanoate are clearly separated, as shown in figure 22. The signals have been identified by comparison with the signals obtained for the mixed species involving either the (*R*) or (*S*) 2-^{2}H,12-phenyldodecanoate. The equilibrium might be displaced towards the formation of the mixed species by the use of a large excess of (*S*) 2-chloropropionate. The two signals originating from the pure (*S*)-2-chloropropionate dinuclear complex are situated at −38 and −9.8 ppm.

The formation of mixed species involving (*S*)-2-chloropropionate might also be useful when the second carboxylate bears a chiral carbon remote from the functional group. Effectively, thioctic acid was used to check that the separation of the protons was greater between the diastereomeric mixed species than between the dithioctic diastereomers. Other signals might be useful to distinguish the mixed diastereomers, *eg*, the signals of the proton H-2 or those of the methyl protons of the (*S*)-2-chloropropionate unit (fig 23).

The above examples demonstrate that the optical purity might be probed safely for many asymmetric carboxylates (or carboxylic acids). If the chiral center is

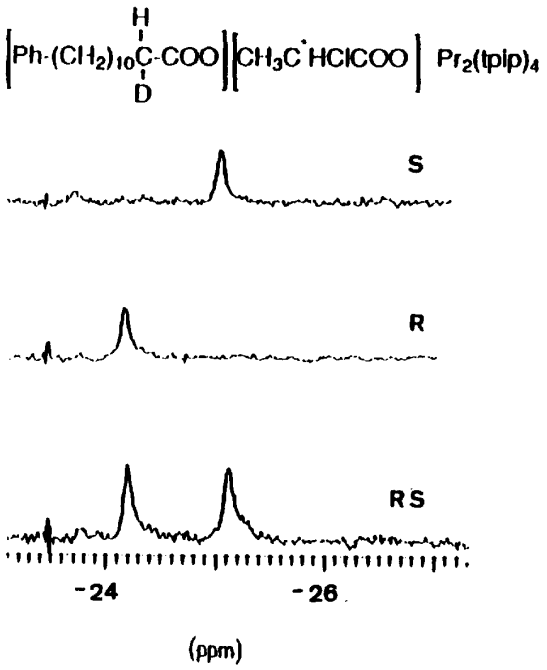

Fig 22. Partial spectrum recorded for the mixed binuclear complexes formed by *S*-2-chloropropionate and 2-^{2}H.12-phenyldodecanoate : a) *R,S* 2-^{2}H.12-phenyldodecanoate; b) and c) *R* and *S* 2-^{2}H.12-phenyldodecanoate, respectively.

remote by more than five bonds from the functional group, it would be advisable to control the separation of the signals originating from the diastereomers by use of a racemic sample. This method was used for the determination of the optical purity of various compounds [28, 29].

Enantiomeric excess

An important application of the formation of the binuclear complexes is the determination of the enantiomeric excess in mixtures of enantiomers. We have shown that the formation of binuclear dicarboxylate complexes or mixed binuclear 2-chloropropionate-carboxylate complexes results in unusually large degrees of enantiomeric resolution. High accuracy is then expected for the determination of the enantiomeric excess since it depends on the precision of the integration of the peaks obtained for the diastereomeric species.

Quantitative studies were made for several chiral salts (mixtures of known enantiomeric excess were prepared by weight). Table V compares the ratio of the two diastereomers calculated from the enantiomeric excess and measured by integration of several pairs of signals of citronellate complexes. Similar data for 2-methylbutyrate and 2-phenylbutyrate are given in the supplementary material. The agreement in the two series of values shows that there is no significant asymmetric induction in the formation of the diastereomers.

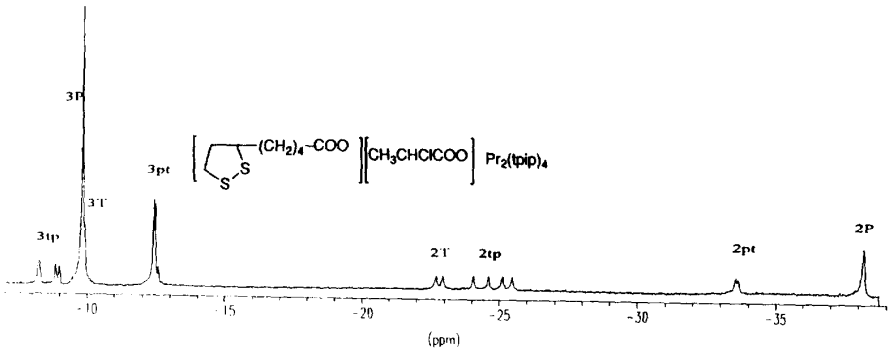

Fig 23. Spectrum of the mixed binuclear complex involving 2-chloropropionate and thioctate carboxylates. Due to the presence of an excess of 2-chloropropionate, signals corresponding to pure di(2-chloropropionate)binuclear complex are present.

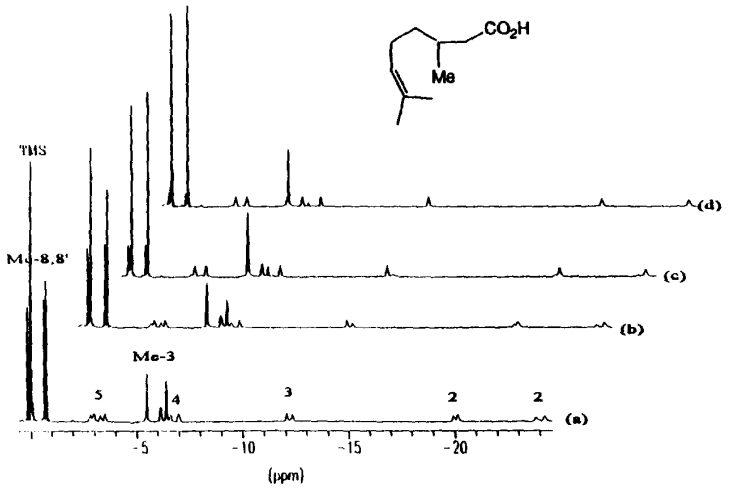

Fig 24. Spectra recorded for the binuclear complexes formed by use of mixtures of *R* and *S* citronellic acid with various enantiomeric excess : a) 7.7% b) 40% c) 85% d) 95%.

Table V. Quantitative study of the formation of the binuclear complexes of citronellate. Comparison of the measured DL/*meso* ratio to the theoretical value calculated from the enantiomeric excess.

ee %	DL/*meso* calculated	DL/*meso* measured*
98	44.45	44.25
95	18.21	17.81
85	6.19	6.37
70	2.90	2.92
58	2.00	2.04
48	1.59	1.61
40	1.37	1.38
29.8	1.19	1.19
21.5	1.09	1.11
10	1.02	1.03
7.7	1.01	1.01

* The result is the mean of the integrations of several signals.

While it must be emphasized that the uncertainty in the determination of the quantitative ratio of the two diastereomeric species increases when the enantiomeric excess is high, due to the difficulty in comparing signals of very different intensities, it is noteworthy that the qualitative detection of a very small amount of one diastereomer in presence of the other remains very easy. Figure 24 shows the spectra recorded for the binuclear complexes obtained from mixtures of (*R*) and (*S*) citronellic acid with various ee's. Furthermore, synthetic mixtures of citronellic acid have been used to show that the presence of the minor antipode is still detected when the ee reaches 99%.

Conclusion

New lanthanide chelates involving the tetraphenylimidodiphosphinato ligand have been synthesized, crystallized, and studied by X-ray analysis. They were shown to react very selectively with carboxylic acids to form labile complexes in apolar solvents. Tris(tetraphenylimidodiphosphinato)praseodymium is a powerful NMR reagent for the study of carboxylic acids. Applications currently in progress are the analysis of complex mixtures of saturated and unsaturated

fatty acids of natural origin, the differentiation of diastereomeric acids, and an approach to the conformational behavior of unsaturated acids. The new reagents were also shown to be a valuable aid in the complete assignment of the ^1H spectra of polycyclic carboxylic acids, *eg*, oleanolic acid.

A new type of binuclear complexes involving two praseodymium cations, four tpip ligands and two carboxylate ligands were isolated and their structure deduced from X-ray analysis. A thorough understanding of the nature of the binuclear complexes in solution was obtained. The formation of the dinuclear dicarboxylato adducts was used to probe the optical purity of chiral carboxylic acids as well as to measure the enantiomeric excess in mixtures of enantiomers. In cases where the direct method failed, *eg*, when the chirality results from the lone replacement of a hydrogen atom by a deuterium, the difficulty was overcome by promoting the formation of mixed diastereomeric complexes involving the deuteriated chiral acids and one pure enantiomer of 2-chloropropionic acid.

Experimental section

General

The NMR spectra were recorded on Bruker AM 500 and WM 250 spectrometers. The proton spectra are reported relative to tetramethylsilane. They were obtained at 500.13 MHz with 32 K data points over about 11 kHz spectral width for the labile complexes formed by carboxylic acids with the tris(tetraphenylimidodiphosphinato) chelates of various lanthanide cations and over 30 kHz spectral width for the binuclear [tetrakis(tetraphenylimidodiphosphinato)] [di(carboxylato)]dipraseodymium complexes. For the dysprosium complexes the largest available 50 kHz spectral width was used and the fractional region of the spectrum were successively detected. The ^{31}P spectra are reported with respect to external H_3PO_4 (85%). They were obtained at 101.25 MHz with 32 K data points over spectral width from 4 kHz for praseodymium or europium chelates to 40 kHz for dysprosium chelate. The solvent was $CDCl_3$. It should be mentioned that CD_2Cl_2 or C_6D_6 may also be used.

Preparation of Ln(tpip)$_3$ complexes

The Ln(III) complexes (Ln = Pr, Dy, Gd) were prepared by the addition of stoichiometric amounts (1:3) of the aqueous solution of the lanthanide chloride to an aqueous solution of the potassium salt of the ligand tpip. A precipitate formed almost immediately. This was collected over a filter, washed with water several times and dried under vacuum.

- *Pr(tpip)$_3$* **1**

Yield, 78%.

Anal calc for $C_{72}H_{60}O_6N_3P_6Pr$: C, 62.20; H, 4.32; N, 3.02; Pr, 10.15. Found : C, 61.67; H, 4.27; N, 3.00; Pr, 9.91.

- *Dy(tpip)$_3$* **2**

Yield, 75%.

Anal calc for $C_{72}H_{60}O_6N_3P_6Dy$: C, 61.25; H, 4.25; N, 2.98. Found : C, 61.14; H, 4.24; N, 3.03.

- *Gd(tpip)$_3$*

Yield, 77%.

Anal calc for $C_{72}H_{60}O_6N_3P_6Gd$: C, 61.49; H, 4.27; N, 2.99. Found : C, 61.37; H, 4.24; N, 2.97.

The main characteristics of the various lanthanide chelates are given below :

Chelates	Color	^1H NMR δ (ppm)			F°C
		o	*m*	*p*	
Pr(tpip)$_3$	pale-green	8.0	7.1	7.2	250
Eu(tpip)$_3$	white	3.5	7.0	7.2	290
Dy(tpip)$_3$	white	7.4	6.5		>260
Nd(tpip)$_3$	purple	7.9	7.1	7.3	273
Yb(tpip)$_3$	pale-yellow	7.6	7.2		>300

The chemical shifts of the protons upon dissolution of the crystals of the [tetrakis(tetraphenylimidodiphosphinato)] [di(laurato)]dipraseodymium (counter ion K^+) in $CDCl_3$ are : H-2 −22.8; H-3 −10.2; H-4 −6.0; H-5 −2.8; H-6 −1.6; H-7 −0.6; H-8 0.05; H-9 0.39; H-10 0.63; H-11 0.86; H-12 0.56 ppm.

The chemical shifts (δ ppm) of the resonances of the mixed binuclear species involving the carboxylates of lauric and propionic acid are compared below with the resonances of the binuclear species involving one type of carboxylate only (data in parentheses) : Laurate protons : H-2 −23.06 (−23.18), H-3 −10.05 (−10.27), H-4 −5.78 (−5.91), H-5 −2.64 (−2.72), H-6 −1.45 (−1.51), H-7 −0.49 (−0.51), H-8 0.05 (0.05), H-9 0.42 (0.42), H-10 0.66 (0.66), H-11 0.82 (0.82), H-12 0.55 (0.55); Propionate protons : H-2 −23.73 (−23.53), H-3 −11.12 (−10.87).

- *Pr(tpip)$_3$(CH$_3$CHClCOOH)$_2$* **5**

It was obtained from Pr(tpip)$_3$ (0.27 g, 0.0002 mol) in chloroform, and chloropropionic acid (0.00023 mol). Slow evaporation of the solvent gave long needles (55%, 0.15 g) which were collected.

Anal calc for $C_{78}H_{70}O_{10}N_3P_6Cl_2Pr$: C, 58.28; H, 4.35; N, 2.61. Found : C, 58.01; H, 4.24; N, 2.73.

- *Pr$_2$(tpip)$_4$(C$_{10}$H$_{17}$O$_2$)$_2$* **7**

Potassium citronellate in THF, was added to a solution of Pr(tpip)$_3$ in the same solvent. After stirring for 1 h, the solvent was evaporated in vacuum, and the residue taken up in a mixture of methylene chloride/hexane. After cooling at −10°C, crystals suitable for an X-ray analysis were obtained.

Anal calc for $C_{116}H_{114}O_{12}N_4P_8Pr_2$: C, 60.73; H, 4.97; N, 2.44. Found : C, 60.94; H, 4.98; N, 2.45.

- *Pr$_2$(tpip)$_4$(C$_9$H$_9$O$_2$)$_2$* **8**

This complex was obtained under the same conditions from 2-phenylpropionic acid and Pr(tpip)$_3$.

Anal calc for $C_{114}H_{98}O_{12}N_4P_8Pr_2$: C, 60.10; H, 4.30; N, 2.46. Found : C, 58.55; H, 4.40; N, 2.52.

X-ray structure determinations

Crystallographic data and other pertinent information concerning every compound are summarized in table VI. Corrections were made for Lorentz, polarization and absorption effects.

All structures were solved by standard Patterson-Fourier techniques. Computations were performed by using Crystals [30] adapted on a Microvax-II computer. Form factors and corrections for anomalous dispersion were from ref [31]. For each compound, the number and the choice of the refined parameters depended upon the number of available reflections and the specific problems encountered. Except in the case of compound **1**, phenyl atoms were calculated and introduced in the final refinement as fixed contributors.

Table VI. Crystallographic data for complexes **1**, **2**, **3**, **4**, **5**, **7** and **8**.

Compound	**1**	**2**	**3**	**4**	**5**	**7**	**8**
Crystals Parameters							
fw	1 508.6	1 432	1 456.3	1 417	1 604	2 284	2 296
Crystal system	monoclinic	triclinic	triclinic	monoclinic	triclinic	triclinic	triclinic
Space group	$P\ 2_1/c$	$P\ \bar{1}$	$P\ \bar{1}$	$P\ 2_1/a$	$P\ \bar{1}$	$P\ \bar{1}$	$P\ \bar{1}$
a, Å	13.966	13.349 (2)	10.901 (3)	26.598 (9)	13.555 (4)	14.481 (2)	13.944 (2)
b, Å	24.482 (4)	14.160 (2)	13.754 (2)	10.885 (10)	13.716 (6)	14.594 (3)	14.519 (3)
c, Å	21.238 (4)	21.492 (3)	24.148 (4)	24.892 (5)	24.232 (9)	15.109 (2)	15.305 (4)
α, deg		72.21 (1)	87.43 (1)		73.94 (4)	105.30 (1)	106.58 (2)
β, deg	104.68 (2)	83.12 (1)	89.14 (2)	96.93 (3)	88.45 (3)	102.08 (1)	106.40 (2)
γ, deg		63.07 (1)	79.33 (2)		61.05 (3)	109.57 (1)	103.98 (1)
V, Å^3	7 025 (31)	3 448 (23)	3 554 (14)	7 154 (32)	3 757 (95)	2 742 (30)	2 668 (33)
Z	4	2	2	4	2	1	1
ρ, g cm^{-3}	1.43	1.37	1.36	1.36	1.42	1.38	1.43
μ (Mo-K$_\alpha$), cm^{-1}	9.92	15.4	8.68	9.14	9	10.5	10.8
Data collection							
Diffractometer	CAD4	CAD4	CAD4	PW1100	CAD4	CAD4	CAD4
Monochromator	graphite	graphite	graphite	graphite	graphite	graphite	graphite
Radiation	Mo-K$_\alpha$	Mo-K$_\alpha$	Mo-K$_\alpha$	Mo-K$_\alpha$	Mo-K$_\alpha$	Mo-K$_\alpha$	Mo-K$_\alpha$
Scan type	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
Scan range θ, deg	0.8 + 0.34 tan θ	1.2 + 0.34 tan θ	1.2 + 0.34 tan θ	0.9 + 0.34 tan θ	1.2 + 0.34 tan θ	1.2 + 0.34 tan θ	1.2 + 0.34 tan θ
2θ range, deg	2 – 56	3 – 50	3 – 56	4 – 40	2 – 50	2 – 56	3 – 50
Reflctn collected	16 924	11 986	17 120	5 018	13 201	10 232	9 388
Reflctn used (I > 3σ(I))	11 226	9 741	12 083	3 209	9 876	8 295	3 399
Refinement							
R	0.047	0.038	0.048	0.071	0.056	0.046	0.056
R_w^*	0.049	0.049	0.057	0.072	0.063	0.051	0.063
Abs corr**	DIFABS	DIFABS	DIFABS	DIFABS	DIFABS	DIFABS	DIFABS
min/max abs	0.76/1.17	0.84/1.17	0.75/1.29	0.97/1.02	0.97/1.0	0.88/1.18	0.91/1.14
second extinct param	0.38 10^{-4}	0.46 10^{-4}	no	no	no	1.18 10^{-4}	no
weighting scheme	unit weight	unit weight	Chebyschev***	Chebyshev	unit weight	unit weight	unit weight
coeff Ar			6.63; 0.13; 5.30	1.72; −0.17; 1.12			
ls parameters	996	807	834	309	902	38	368

Compound **1** : $C_{72}H_{60}O_6N_3P_6Pr$, $CHCl_3$
Compound **2** : $C_{72}H_{60}O_6N_3P_6Dy$, $(C_6H_{14})_{0.25}$
Compound **3** : $C_{75}H_{66}O_7N_3P_6Pr$, $(H_2O)_{0.5}$
Compound **4** : $C_{72}H_{62}O_7N_3P_6Pr$, $(CH_2Cl_2)_{0.7}$
Compound **5** : $C_{78}H_{70}O_{10}N_3P_6Cl_2Pr$
Compound **7** : $C_{116}H_{114}O_{12}N_4P_8Pr_2$
Compound **8** : $C_{104}H_{94}O_{14}N_4P_8Pr_2$, $(C_4H_8O)_2$
* $R_w = [\Sigma\ w\ (Fo - Fc)^2/\Sigma\ w\ Fo^2]^{1/2}$
** DIFABS : Walker N, Stuart D, *Acta Cryst*, 1983, A39, 159
*** E Prince, *Mathematical Techniques in Crystallography*, Springer Verlag, Berlin, 1982. Weighting scheme $w = w'[1-(\Delta F/6\sigma(F)^2]^2$, with $w' = 1/\Sigma^n$ Ar Tr(X), where n is the number of coefficients, Ar, for a Chebyshev series, for which X is F_c/F_c (max).

- *Compound* **1**

All non-hydrogen atoms were refined anisotropically, except the C and Cl atoms of the solvent molecule ($CHCl_3$), which were left isotropic. H atoms were located on successive difference Fourier maps and their coordinates were refined with an overall refinable isotropic thermal parameter.

- *Compound* **2**

All non-hydrogen atoms were refined anisotropically, except the C atoms of the solvent molecule (hexane). Restraints on bond lengths and bond angles were applied to refine this solvent molecule, which appears around the inversion center and only with half occupation factor.

- *Compound* **3**

All non-hydrogen atoms were refined anisotropically, except the O atoms of the solvent molecule (H_2O), which was refined with half occupation factor.

- *Compound* **4**

According to the few available reflections, only Pr, P, O and N atoms were anisotropically refined, while phenyl groups were isotropically refined as rigid groups. The isotropic refinement of the C and Cl atoms of the solvent molecule (CH_2Cl_2) led to an approximate value 0.7 of the occupation factor.

• *Compound* **5**
All non-hydrogen atoms were anisotropically refined. Restraints were applied to the $CH_3CHClCOO$ groups.

• *Compound* **7** *and* **8**
Some difficulties in the refinements arised from the high pseudo-symmetry of these molecules. For both compounds, the non-centrosymmetry is only due to the presence of an asymmetric carbon in the $C_{10}H_7O_2$ and $C_4H_7O_3$ chains. The $[Pr_2(C_{24}H_{20}O_2NP_2)_4]$ core was best refined in the $P\bar{1}$ space group. The refinement of the whole molecule in the genuine $P\bar{1}$ space group then led to strong correlations. This problem was overcome by use of the "link" and "combine" options of Crystals. The "link" option allows the "core" to remain centrosymmetric, and the "combine" option allows the two chains to keep their real configuration.
For both compounds, only the Pr, P, O and N atoms of the "core" were anisotropically refined. All C atoms were left isotropic as well as the C atoms of the asymmetric chains. For compound **8**, a solvent molecule (tetrahydrofuran) was also isotropically refined.

Acknowledgment

It is made to Dr M Mohr, Gesellschaft für Biotechnologische Forschung mbH, Braunschweig (Germany), to Dr Boland, University of Karlsruhe (Germany), to Dr A Guzmán, Synthex SA Cuernavaca (Mexico), to Dr R Grée, University of Rennes and Dr C Malen, Paris for providing us with samples of optically active and labeled carboxylic acids, to Centre National de la Recherche Scientifique, CONACYT (Mexico) and Commission des Communautés Européennes (DGSRD, ISC Programme, Bruxelles) for financial support.

Supplementary material available

X-ray characterization data for complexes **1, 2, 3, 4, 5, 7** and **8** including tables of distances and angles, fractional atomic coordinates, thermal parameters (tables S1-S32); calculated and observed structure factors (188 pages); NMR data of various carboxylic acids (tables S33-S36 and figures S1 and S2). Supplementary material data have been deposited with the British Library, Document Supply Center at Boston Spa, Wetherby, West Yorkshire, UK, as supplementary publication N° SUP 90368 and is available on request from the Document Supply Center.

References

1 Hinkley CC, *J Am Chem Soc* (1969) 91, 5160
2 Reuben J, *Prog Nucl Magn Reson Spectrosc* (1973) 9, 1
3 Hofer O, in *Topics in Stereochem*, Allinger NL, Eliel EL, Eds, Wiley, New York (1976), vol 9, p 111
4 Inazaki F, Tatsno M, *Prog Nucl Magn Reson Spectrosc* (1980) 14, 67
5 Wenzel TJ, Bettes TC, Sadlowski JE, Sievers RE, *J Am Chem Soc* (1980) 102, 5903
6 Wenzel TJ, Sievers RE, *Anal Chem* (1981) 53, 393
7 Wenzel TJ, Sievers RE, *Anal Chem* (1982) 54, 1602
8 Sanders JKM, Williams DH, *J Chem Soc, Chem Commun* (1970) 422
9 Hart FA, Mosse GP, Stainforth ML, *Tetrahedron Lett* (1971) 3389
10 Davoust D, Rebuffat S, Girand M, Molho D, *CR Acad Sci Paris* (1975) 232, 236
11 Davoust D, Rebuffat S, Molho D, Platzer N, Basselier JJ, *Tetrahedron Lett* (1976) 2825
12 Rodriguez I, Alvarez C, Gomez-Lara J, Toscano RA, Platzer N, Mulheim C, Rudler H, *J Chem Soc, Chem Commun* (1987) 1502
13 Alvarez C, Goasdoue N, Platzer N, Rodriguez I, Rudler H, *J Chem Soc, Chem Commun* (1988) 1002
14 Alvarez C, Barkaoui L, Goasdoue N, Daran JC, Platzer N, Rudler H, Vaissermann J, *J Chem Soc, Chem Commun* (1989) 1507
15 Rodriguez I, Alvarez C, Gomez-Lara J, Soriano-Garcia R, Toscano RA, *Lanthanide-Actinide Res* (1986) 1, 253
16 Erasmus CS, Boeyers JCA, *Acta Cryst* (1970) B26, 1843
17 Sinha SP, in *Structure and Bonding*; Dünitz JD, Ed, Springer, Berlin, 1976, vol 25, p 69
18 Job P, *Ann Chim* (1928) 9, 113
19 Armitage IM, Dunsmore G, Hall LD, Marshall AG,
a) *J Chem Soc, Chem Commun* (1971) 1281
b) *Can J Chem* (1972) 50, 2119
20 Gibb VG, Armitage IM, Hall LD, Marshall AG, *J Am Chem Soc* (1972) 94, 8919
21 Horrocks W Dew Jr, Sipe III JP, *J Am Chem Soc* (1971) 93, 6800
22 Mac Connell HM, Robertson RE, *J Chem Phys* (1958) 29, 1361
23 Aslanos LA, Abdul'Miner IK, Poraikoshits MA, *J Struct Chem* (1972) 13, 437
24 Moom JW, Glick MD, Baker Jr WA, *J Am Chem Soc* (1972) 94, 1858
25 Drew MGB, in *Progress in Inorg Chem*, Lippard JJ Ed, Wiley, New York, 1977, Vol 23, p 67
26 Morr M, Wray V, Fortkamp J, Schmid DR, *Liebigs Ann Chem* (1992) 433
27 Vigneron JP, Dhaenens M, Horeau A, *Tetrahedron Lett* (1973) 29, 1055
28 Kouklovsky C, Puoilhès A, Langlois Y, *J Am Chem Soc* (1990) 112, 6672
29 Melnyk O, Stéphane E, Pourcelot G, Cresson P, *Tetrahedron Lett* (1992) 48, 841
30 Watkins DJ, Carruthers JR, Betteridge PW, *Crystals User Guide*; Chemical Crystallography Laboratory, University of Oxford : Oxford, England, 1986
31 *International Tables for X-ray Crystallography*, Kynoch Press, Birmingham, UK, 1974, vol IV