Tris(tetraphenylimidodiphosphinato)praseodymium: a Powerful Tool for the Analysis of Fatty Acids by ^{1}H N.M.R. Spectroscopy

C. Alvarez,[a] N. Goasdoue,[b] N. Platzer,*[b] I. Rodriguez,[a] and H. Rudler*[c]

[a] *Instituto de Quimica, Universidad Nacional Autonoma de Mexico, Circuito Exterior, Cuidad Universitaria, Coyoacan 04510, Mexico D.F.*

[b] *Laboratoire de Chimie Organique Structurale, UA 455, Université Pierre et Marie Curie, T74 4 place Jussieu, 75252 Paris Cedex 5, France*

[c] *Laboratoire de Chimie Organique, UA 408, Université Pierre et Marie Curie, T44–45 4 place Jussieu, 75252 Paris Cedex 5, France*

The shifts induced by tris(tetraphenylimidodiphosphinato)praseodymium in the ^{1}H n.m.r. spectra of fatty acids have led us to resolve completely the signals of lauric acid, analyse a mixture of four saturated fatty acids, and characterize unsaturated acids, *e.g.* arachidonic acid, by determining the position and the configuration of the double bonds, and the preferred conformation of the backbone.

New lanthanide shift reagents have recently been described.[1] Replacement of the usual β-diketonato ligands by tetraphenylimidodiphosphinato ligands results in a marked increase in stability in aqueous and acid media. The aim of the present communication is to outline the use of the most effective of them, tris(tetraphenylimidodiphosphinato)-praseodymium [Pr(tpip)$_3$], as a powerful tool for the characterization of saturated and unsaturated fatty acids by ^{1}H n.m.r. spectroscopy.

Figure 1 shows the ^{1}H n.m.r. spectra obtained for lauric acid, alone and in the presence of the amount of Pr(tpip)$_3$ which produces complete resolution of the different signals. The quantitative interpretation of the induced shifts is easy. First, it can be shown by use of Job's method[2] that 1:1 association occurs between a carboxylic acid, *e.g.* caproic acid, and the chelate Pr(tpip)$_3$. Secondly the shifts appear to be determined by a single dominant mechanism, the pseudocontact one, for all the protons but those at C-2. Indeed the relative induced shifts, following the addition of increasing amounts of the reagent, are found to be almost independent of the chelate/substrate ratio as well as of the overall concentration of the carboxylic acid if the protons at C-2 are disregarded. Finally Eu(tpip)$_3$ induces shifts smaller in magnitude and opposite in direction than those with Pr(tpip)$_3$ but the relative shifts remain very similar with both reagents.[3] As a result the shifts induced by Pr(tpip)$_3$ obey the simple relation (1), where $\delta\nu$ is the observed induced shift, $\Delta\nu$ the induced shift corresponding to the 1:1 adduct species, K the binding constant, and L the concentration of the free chelate. The relative effects of Pr(tpip)$_3$ $R_{ij} = \delta\nu_i/\delta\nu_j = \Delta\nu_i/\Delta\nu_j$ reported in

Table 1. Relative shifts caused by $Pr(tpip)_3$ in the ^1H n.m.r. spectra of saturated and unsaturated acid, normalised relative to 3-H.

Proton	Lauric	Mixture[a]	Acid Oleic	Linoleic	Arachidonic
2	1.47	1.39	1.41	1.49	1.42
3	1	1	1	1	1
4	0.57	0.56	0.57	0.57	0.54
5	0.35	0.34	0.35	0.35	**0.38**[c]
6	0.22	0.22	0.22	0.22	**0.19**
7	0.14	0.14	0.13	0.13	0.23
8	0.091	0.092	0.088	0.086	**0.17**
9	0.061	0.061	**0.065**	**0.065**	**0.092**
10	0.042	0.040	**0.039**	**0.044**	0.10
11	0.026	0.025	0.043	0.040	**0.085**
12	0.020	0.022 (L)[b]	0.022	**0.038**	**0.052**
13				**0.020**	0.063
14		0.01_2 (M)[b]		0.023	**0.052**
15			0.02	0.020	**0.033**
16		0.006_1 (P)[b]		~0.02	0.042
17					
18		0.003_3 (S)[b]	0.01_0[b]	0.01_1[b]	0.03
19					
20					0.02_5[b]

[a] Equimolar mixture of lauric (L), myristic (M), palmitic (P), and stearic (S) acid. [b] Methyl group shifts. [c] Ethylenic proton shifts are in bold type.

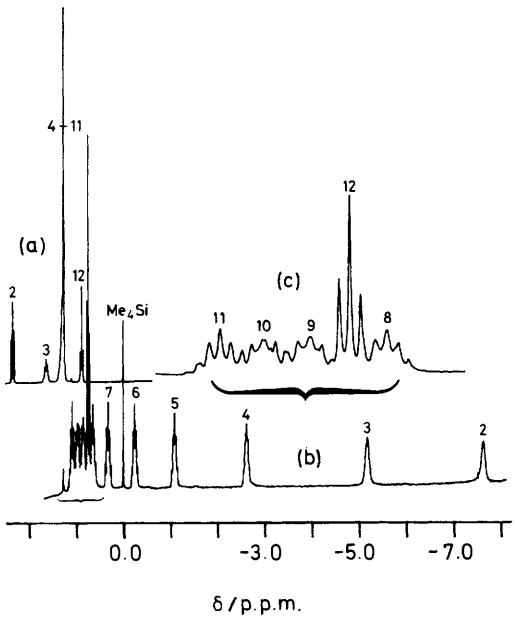

Figure 1. ^1H N.m.r. spectrum of 0.1 M lauric acid in $CDCl_3$ with (a) no shift reagent; (b) 0.057 M $Pr(tpip)_3$; (c) an expansion of the region of spectrum (b) between δ 0.5 and 1.5.

Table 1 for several fatty acids were obtained by normalising the induced shifts with regard to the protons at C-3.

$$\delta\nu = \Delta\nu\, KL/(KL + 1) \qquad (1)$$

Figure 2 shows the spectra obtained for a mixture of four saturated acids: lauric, myristic, palmitic, and stearic. In the absence of reagent the signals originating from the different acids are undiscernible. Through the use of $Pr(tpip)_3$ it is possible to spread out the spectrum and to obtain distinct

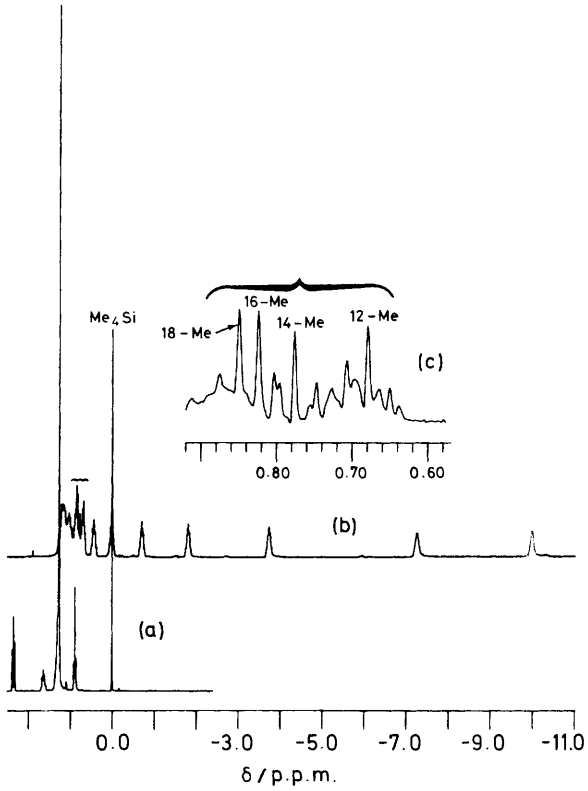

Figure 2. ^1H N.m.r. spectrum of a mixture of lauric, myristic, palmitic, and stearic acids (total concentration 0.1 M) with (a) no shift reagent; (b) 0.1 M $Pr(tpip)_3$; (c) an expansion of that region of spectrum (b) including the methyl groups.

signals at least for the protons of the nine first methylene groups but, for each position, the signals originating from the different acids still merge into one another. Further addition of one component of the acid mixture does not lead to additional resonances or to any change in the ratio of induced shifts. These results prove that the equilibrium constants for complex formation are almost identical for all the saturated carboxylic acids. Fortunately, the signals of the terminal methyl groups which lie at different positions in the aliphatic chain of the various acids are clearly separated. The discrimination is still preserved if the overall concentration is as low as 10^{-4} M.

Consequently the number of signals originating from the terminal methyl groups and the relative values of the induced shifts *vs.* the protons at C-3 or, better, *vs.* the induced shift observed for the methyl protons of a known acid added as a standard, will allow the full characterization of an unknown mixture of saturated acids.

As regards unsaturated acids, owing to the similar environment of the ethylenic protons neither the position nor the configuration of the substituents can be determined from the ^1H n.m.r. spectrum of the pure acid. However, after spreading out the spectrum by addition of $Pr(tpip)_3$ both characteristics are easily obtained. Figure 3 shows the spectra recorded for arachidonic acid. The fine structure for the ethylenic protons is well preserved and through selective irradiation of the methylene groups situated in between the double bonds, coupling constants of *ca.* 11 Hz were measured in agreement with the *cis*-configuration of all double bonds.

In contrast with the monotonic decrease of relative shifts along the chain in saturated acid, it is noteworthy that the relative shifts of the methylene protons situated in between

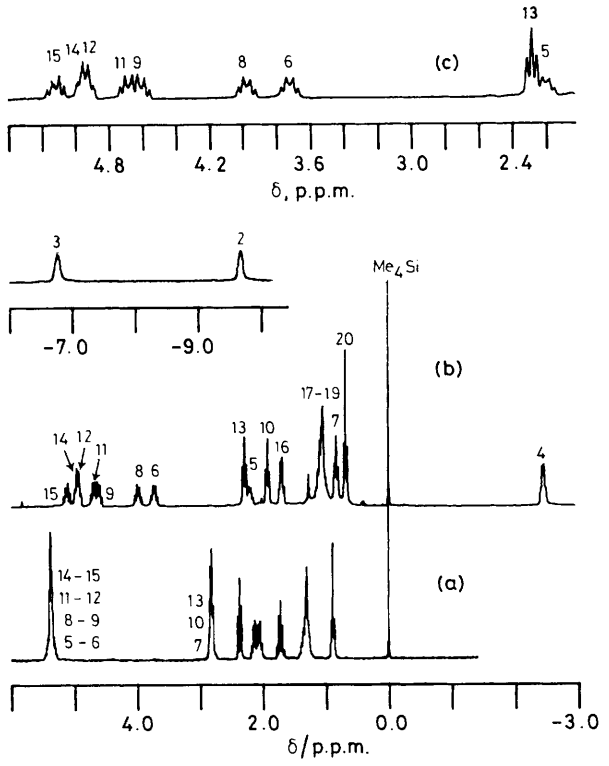

Figure 3. ^{1}H N.m.r. spectrum of ~0.05 M arachidonic acid in $CDCl_3$ with (a) no shift reagent; (b) ~0.05 M $Pr(tpip)_3$; (c) an expansion of that region of spectrum (b) including the ethylenic protons.

two double bonds is greater than those of both adjacent ethylenic protons. Furthermore the relative shift for the protons at C-18 is ten times that measured for the same position in stearic acid. The arachidonic acid exhibits in $CDCl_3$ solution more bending in its chain than oleic acid or linoleic acid. The results are in fair agreement with a conformation previously described for methyl arachidonate.[4]

The applications of the chelate $Pr(tpip)_3$ which may be envisaged, include the determination of the position and rate of deuterium incorporation in labelled samples of fatty acids and the characterization of various functionalities along the chain.

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