Tetrahedron Letters,Vol.25,No.11,pp 1141-1142,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

CHIRAL RELAXATION REAGENTS (CRR) IN ^{13}C NMR SPECTROSCOPY

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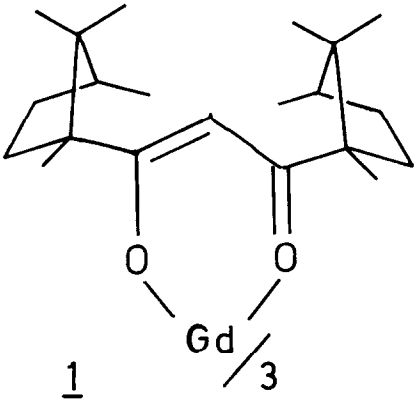
Summary: Enantiomers and chiral relaxation reagents (CRR) afford diastereomeric complexes, which differ clearly in their ^{13}C spin-lattice relaxation times.

Chiral lanthanide complexes and enantiomers are well known to form diastereomeric complexes in solution[1]; these complexes differ in their NMR parameters. For example, chiral shift reagents induce differences, $\Delta\Delta\delta$, in chemical shift, which allow a destinction of enantiomers e.g. via ^{1}H NMR. To our knowledge, the problem whether these diastereomeric complexes differ with respect to other NMR parameters, has not been investigated. It seemed obvious in this context to systematically study the spin-lattice relaxation times T_1 of enantiomers under the influence of relaxation reagents containing chiral ligands. To this end we have prepared the novel relaxation reagent[2] tris[d.d-dicampholylmethanato]gadolinium(III) [$Gd(dcm)_3$] 1 and report on its effects on the ^{13}C spin-lattice relaxation times of chiral compounds.



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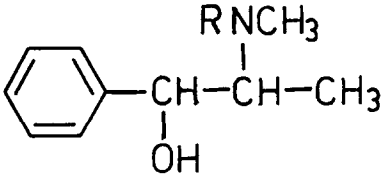

2 R=CH_3
3 R=H

Figure 1 shows ^{13}C inversion recovery spectra of (+) and (-)-methylephedrine[3] 2 (1.87 M in chloroform-d_1). Each sample was recorded under identical experimental conditions[4] and contained only 5 mg (3 x 10^{-3}M) of chiral relaxation reagent (CRR) $Gd(dcm)_3$ 1. The difference in relaxation times of the two enantiomers is dramatic. Whereas all carbon atoms of (+)-methylephedrine 2 show inverted signals, the signals of (-)-methylephedrine have relaxed extensively. Thus, the OH-substituted chiral carbon of (+)-methylephedrine exhibits a relaxation time, T_1 = 1.4 s, whereas the corresponding carbon of (-)-methylephedrine shows T_1 = 0.1 s.

For ephedrine we could show that the difference, $\Delta\Delta T_1$[5], of enantiomeric relaxation times depends on the concentration of the chiral relaxation reagent 1 (Figure 2).

Characteristically $\Delta\Delta T_1$ increases rapidly at low concentrations of 1 and decreases slowly at high concentrations of 1. Similar findings were obtained for 1-phenylethylamine and for N,N-dimethyl-1-phenylethylamine.

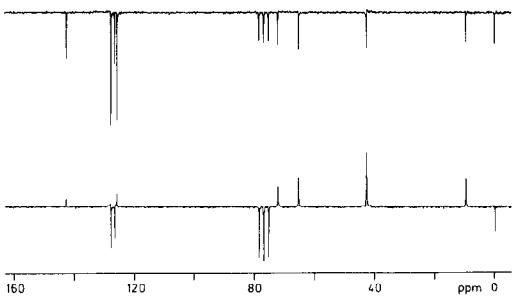

Figure 1. ^{13}C Inversion recovery spectra of 1.87M (+)methylephedrine (above) and 1.87 M (-)-methylephedrine (below) in chloroform-d_1 containing 3×10^{-3} M $_4$Gd(dcm)$_3$ (t_1 = 0.5 s; t_2 = 10 s, n = 100)[4].

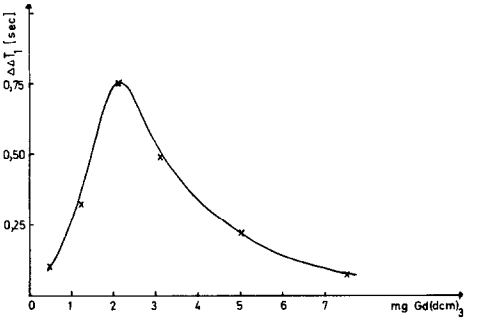

Figure 2. Difference of relaxation times, $\Delta\Delta T_1$, between (+) and (-)-ephedrine as a function of Gd(dcm)$_3$ concentration. Shown are values for the substituted aromatic carbon.

For controlling enantioselective syntheses and for checking enantiomeric purity it is extremely important to have efficient analytical probes. Our results show that chiral gadolinium relaxation reagents and enantiomers form diastereomeric complexes, the spin-lattice relaxation times of which may differ sharply. Thus the spin-lattice relaxation time T_1 - like the chemical shift δ - affords chiral information. Further investigations will show to what extent chiral relaxation, via ^{13}C NMR spectroscopy, can be developed into an analytical tool.

References and Notes

1 For recent reviews see: Reuben, J.; Elgavish, G.A. "Handbook on the Physics and Chemistry of Rare Earths". Gschneider, K.A.Jr., Eyring, L., Eds., Amsterdam 1979. Jardetzky, O.; Roberts, G.C.K. "NMR in Molecular Biology", Academic Press: New York, 1981.

2 McCreary, M.D.; Lewis, D.W.; Werneck, D.L.; Whitesides, G.M. J.Am.Chem.Soc. 96, 1038 (1974).

3 All compounds are commercially available or easily prepared. Optical rotation of enantiomers were identical with authentic samples.

4 Inversion recovery $(180^\circ - t_1 - 90^\circ - t_2)_n$ experiments were performed on a Bruker WP 80.

5 The term $\Delta\Delta T_1$ is chosen in analogy to the well known term $\Delta\Delta\delta$ for chiral shift differences.

(Received in Germany 27 December 1983)