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ANALYSIS OF DIAMINE STEREOISOMERS FROM PROTON PARAMAGNETIC SHIFTS

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We wish to report an easy method of determining the stereoisomeric composition of bis(4-aminocyclohexyl)methane (BACM, Fig. 1a) with NMR, using the paramagnetic shift reagent tris(dipivalomethanato)europium $[Eu(dpm)_3]$ (1-6).

A 100 or 220 MHz NMR spectrum of a mixture of BACM stereoisomers - cis-cis (cc), cis-trans (ct) and trans-trans (tt) - gives the overall ratio trans/cis. In transsubstituted rings the proton H(4) is in the axial position and absorbs at δ = 2.49 ppm (triplet of triplets); in the cis-substituted rings the proton H(4) largely occupies the equatorial position and absorbs at 2.93 ppm (quintet with 3 Hz spacings). All other protons give signals between 0.9 and 1.8 ppm. After addition of $Eu(dpm)_3$ to the solution of BACM in CCl_4, for instance 1 mole per mole of diamine, the spectrum shows a large number of signals between 5 and 23 ppm. Interpretation, however, is quite difficult. For the assignment of the signals, tt- and ct-BACM (purity: 99% and 94% respectively) have been prepared by recrystallization and subsequent hydrolysis of the di-trifluoroacetamide of BACM isomeric mixtures. The low concentration of cc-BACM, not exceeding 9% in our isomeric mixture, prohibited its isolation.

The 100 MHz spectrum of tt-BACM in CCl_4 has been recorded with increasing amounts of $Eu(dpm)_3$, up to the molar ratio Eu/BACM = 1.14. The chemical shifts as a function of the amount of $Eu(dpm)_3$ are presented in Fig. 3. The spectrum for Eu/BACM = 0.91 is presented in Fig. 1c; the proton assigments shown are based on observed signal intensities and splitting patterns, and on the information, reported in the literature (1-6), that the induced shift decreases with increasing distance between a proton and the complexed functional group.

The equatorial protons H(2)-e and H(3)-e give doublet signals (J = 12 Hz) and the axial protons H(2)-a and H(3)-a give quartets (J = 12 Hz). The triplets G (J = 12 Hz) and N (J = 6 Hz) come from H(1)-a and the bridge protons, respectively. At low europium concentrations signals G and K coincide, at high concentrations (Fig. 1c) signals K and L coincide, while line broadening is considerable.

For ct-BACM a spectrum and the shift dependencies are presented in Figs. 1b and 2. The assignment has been made partly by comparison with the tt-spectra. The signal A_c of H(4)-cis, being a quintet with 3 Hz spacings at Eu/BACM = 0, is still a narrow one at higher europium concentrations. Apparently, the amino group in a cis-substituted ring still favours the axial position, and complexing with $Eu(dpm)_3$ does not seem to influence the conformation very much. Signals A_c and A_t coincide at lower europium concentrations, but diverge at higher concentrations, A_c being more downfield again. A possible explanation of this phenomenon is the more favourable complexing of the equatorial amino function (trans) at lower europium concentrations. In a proton decoupling experiment, irradiation of resonance C simplifies signal D into a doublet (J = 10 Hz), revealing that C (highfield part) comes from H(3)-e-cis and D from H(3)-a-cis. Irradiation of the resonances H and J (coinciding at low europium concentration) changes E into a doublet (J = 10 Hz), indicating that E represents H(2)-a-cis. It is clear from the signal intensities that signals F and J are the resonances of the protons H(1) in ct-BACM. We suggest that F comes from H(1)-a-trans. In a 220 MHz spectrum of BACM, containing 78% ct and 22% tt, the signals F, G and J are observed separately at Eu/BACM = 1.2. Here F is more shifted than G. Also the signal KL of the protons H(2)-trans is more shifted for ct- than for tt-isomer (this follows from relative intensities). Apparently, the protons H(1)-trans and H(2)-trans are more affected in ct- than in tt-BACM by the addition of $Eu(dpm)_3$. This difference is in agreement with a shorter distance between the protons mentioned and the axial amino function (cis) in ct-isomer, as demonstrated in Dreiding models. In addition, the triplet M (6 Hz spacings) of the ct-bridge protons is shifted more downfield than triplet N of the tt-bridge protons, and can be distinguished from KL at higher europium concentrations.

The deviation of proportionality, observed in Figs. 2 and 3 at Eu/BACM $>$ 0.8, can very well be explained by assuming a complexing of europium with two amino functions similar to that in $Eu(dpm)_3$. 2pyridine (1). This octavalent coordination, being predominant at lower

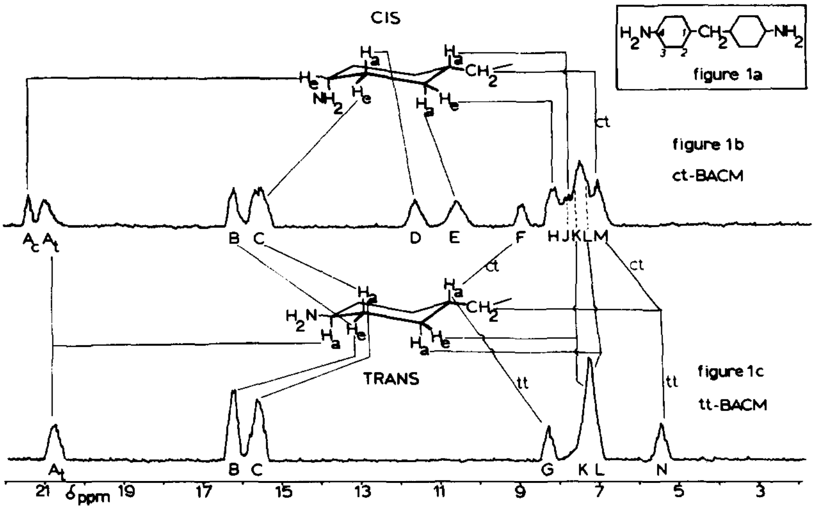

Fig. 1

100 MHz spectra of BACM in CCl_4 with added $Eu(dpm)_3$ at 25°C.; δ in ppm from TMS.

(b) : ct-BACM; Eu/BACM = 0.92 (c) : tt-BACM; Eu/BACM = 0.91

europium concentrations, is supposed to be in equilibrium with the heptavalent coordination, in which europium is complexed with only one amino group.

From NMR spectra of BACM isomeric mixtures with a well-chosen concentration of $Eu(dpm)_3$ we can now determine the isomeric composition. The percentage tt is calculable from the intensity of signal N. The ct- and cc-percentages then follow from the overall ratio cis/trans (A_c/A_t, normal NMR spectrum). The percentage ct can also be obtained directly from the intensity of signal F, whereby the presence of cc-BACM in an isomeric mixture does not interfere.

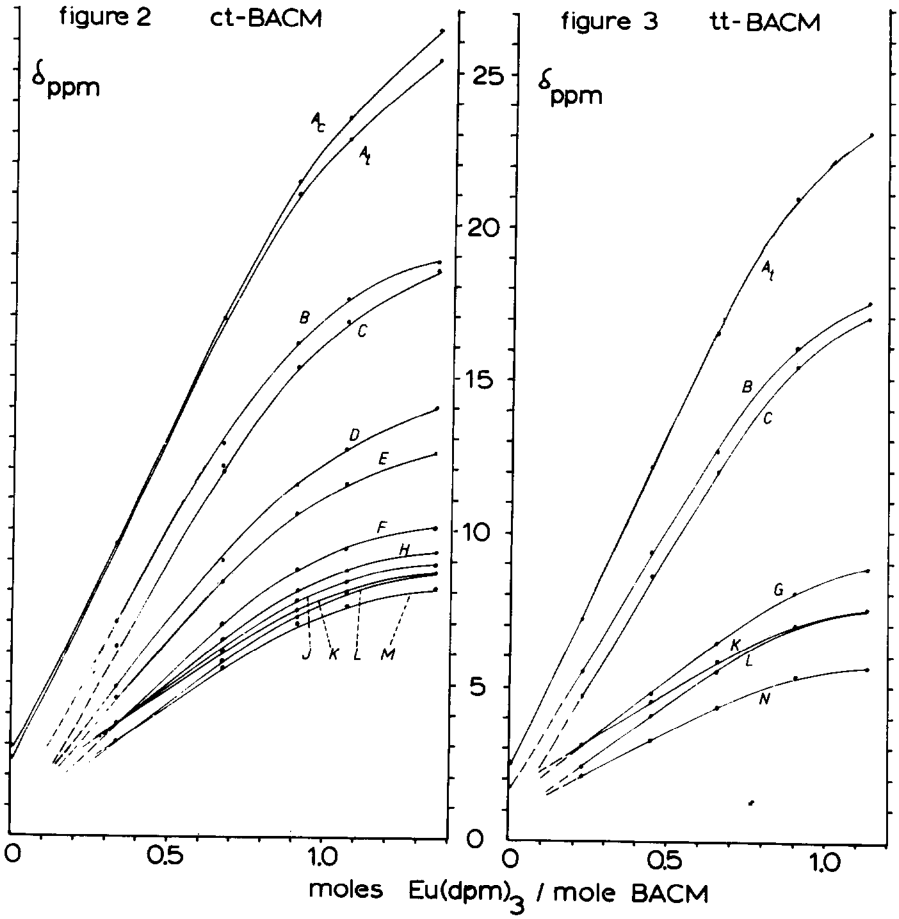

Fig. 2 and 3

Chemical shifts as a function of added Eu(dpm)$_3$ to 1.10^{-4} moles BACM in 0.5 ml CCl_4.

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