APPLICATION OF TRIS(DIPIVALOMETHANATO)EUROPIUM(III) PMR SHIFT REAGENT TO 4-AZA-HOMOADAMANTAN-5-ONE AND 4-AZA-1,1-BISHOMOADAMANTAN-5-ONE[1]

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The pmr spectra of compounds in the title were found to be analyzable with the aid of a pmr shift reagent, $Eu(dpm)_3$. The shift value of each proton was discussed from the characteristic europium shift parameter $\underline{S}$ value.

The results supported a complex formation between $Eu(dpm)_3$ and the lactams on the amide oxygen side rather than the nitrogen, and also untwisted forms of these ring systems as for -NHCO- and -NHCOCH$_2$- moieties.

Since the reports[2,3] on the paramagnetic shift induced by tris(dipivalomethanato)europium(III), $Eu(dpm)_3$, in organic compounds, many shift reagents have been applied to structure determinations of organic molecules. However, studies concerning lactam functions seem to be quite few and only fragmentary[4] compared to extensive ones on other functions,[5] particularly on alcohols[6,7] and ketones.[8,9] Now we wish to report our results of application of $Eu(dpm)_3$
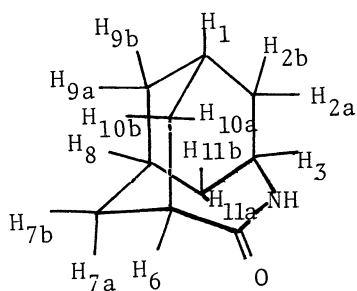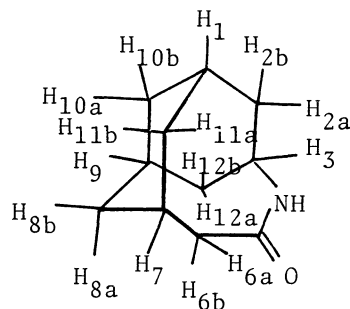


I                                                    II

to the pmr analysis of 4-azahomoadamantan-5-one (4-azatricyclo[4.3.1.1$^{3,8}$]undecan-5-one) (I)[10] and 4-aza-1,1-bishomoadamantan-5-one (4-azatricyclo[5.3.1.1$^{3,9}$]-dodecan-5-one) (II).[11]

The original pmr spectrum of I (CDCl$_3$, 60 MHz, 25°) was poorly resolved and only three signals due to NH, H$_3$, and H$_6$ appeared together with a broad multiplet due to all other protons. However, the addition of Eu(dpm)$_3$ induced a good separation and the spectrum [Eu(dpm)$_3$/I = 0.470] revealed signals at δ 12.07 (s, 1H, NH), 9.42 (s, 1H, H$_6$), 5.21 (d, $\underline{J}$=13.2 Hz, 2H, H$_{7a}$ and H$_{10a}$), 4.36 (s, 1H, H$_3$ ), 4.02 (d of t, $\underline{J}$=13.2 and 5.0 Hz, 2H, H$_{7b}$ and H$_{10b}$), 3.37 (d, $\underline{J}$=12.6 Hz, 2H, H$_{2a}$ and H$_{11a}$), 3.36 (s, 2H, H$_1$ and H$_8$), 2.96 (d, $\underline{J}$=13.0 Hz, 2H, H$_{9a}$ and H$_{9b}$), and 2.86 (d, $\underline{J}$=12.6 Hz, 2H, H$_{2b}$ and H$_{11b}$).

The changes in the chemical shift values on addition of Eu(dpm)$_3$ were directly plotted against the molar ratio of Eu(dpm)$_3$ to I affording respective linear lines assignable to the particular hydrogens as shown in Figure 1a. The so-called europium shift parameter $\underline{S}$ values were calculated from the slopes of the lines and are summarized in Table 1.

The similar application of Eu(dpm)$_3$ shift reagent to II was proved to be useful also. The original spectrum showed only poorly resolved signals at δ 7.52 (broad s, 1H, NH), 3.56 (s, 1H, H$_3$), 2.60 (d, $\underline{J}$=3.6 Hz, 2H, H$_{6a}$ and H$_{6b}$) and 2.4-1.4 (m, 13H, other protons). The spectrum in the presence of the shift reagent [Eu(dpm)$_3$/II = 0.512], however, revealed better resolved signals at δ 13.98 (broad s, 1H, NH), 10.75 (d, $\underline{J}$=3.6 Hz, 2H, H$_{6a}$ and H$_{6b}$), 4.54 and 4.34 ( overlapped s, 2H, H$_7$ and H$_3$), 4.12 (d, $\underline{J}$=13.8 Hz, 2H, H$_{8a}$ and H$_{11a}$), 3.64 (d, $\underline{J}$= 13.8 Hz, 2H, H$_{8b}$ and H$_{11b}$), 3.57 (d, $\underline{J}$=13.2 Hz, 2H, H$_{2a}$ and H$_{12a}$), 2.98 (d, $\underline{J}$= 13.2 Hz, 2H, H$_{2b}$ and H$_{12b}$), 2.97 (s, 2H, H$_1$ and H$_9$), and 2.40 (s, 2H, H$_{10a}$ and H$_{10b}$). The plot of the chemical shift value against the molar ratio of Eu(dpm)$_3$ afforded also respective linear lines (Figure 1b) and the calculated $\underline{S}$ values are summarized in Table 1.

The observed orders of magnitude in the $\underline{S}$ values for both I and II systems indicate clearly that the complex formation is favored at the amide oxygen side rather than the nitrogen side despite of the fact that I involves a basic nitrogen (the formation of I hydrochloride),[10] since the $\underline{S}$ value is known to be correlated with the spatial distance between the hydrogen nucleus and the complexed europium atom.[2-4,12] Furthermore, above results suggest an untwisted form of these ring

systems as for -NHCO- and -NHCOCH$_2$- moieties.[13]   The larger vicinal coupling

constant for H$_{7b}$ (H$_{10b}$) than that for H$_{7a}$ (H$_{10a}$) suggests a flattened chair-form

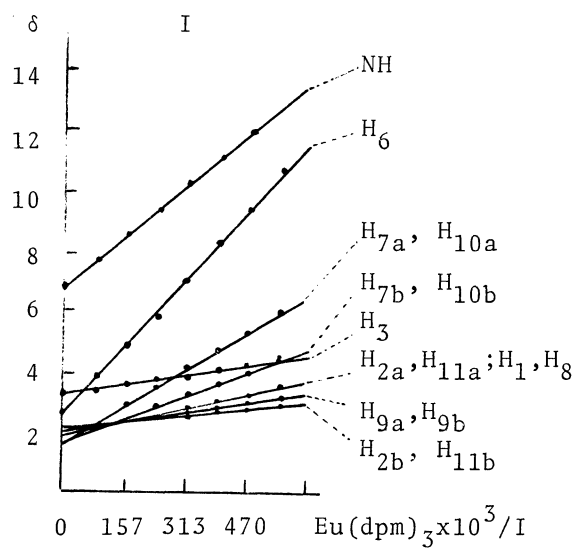of the cyclohexane rings in I, and a similar situation is also expectable in II.[14]
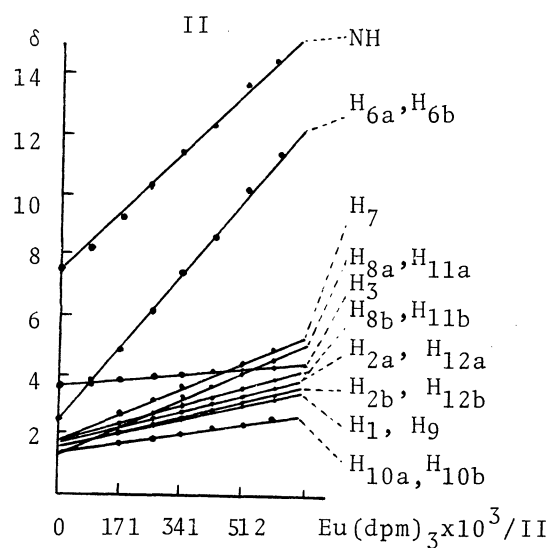


Figure 1a.                                      Figure 1b.

TABLE 1.    The Europium Shift Parameter S Values for Lactams I and II

| Hydrogen for I | S | Hydrogen for II | S |
|---|---|---|---|
| H$_1$, H$_8$ | 3.28 | H$_1$, H$_9$ | 1.24 |
| H$_{2a}$, H$_{11a}$ | 3.28 | H$_{2a}$, H$_{12a}$ | 3.90 |
| H$_{2b}$, H$_{11b}$ | 2.03 | H$_{2b}$, H$_{12b}$ | 2.61 |
| H$_3$ | 2.28 | H$_3$ | 1.54 |
| H$_{7a}$, H$_{10a}$ | 7.96 | H$_{6a}$, H$_{6b}$ | 13.8 |
| H$_{7b}$, H$_{10b}$ | 5.36 | H$_7$ | 4.89 |
| H$_6$ | 14.6 | H$_{8a}$, H$_{11a}$ | 5.34 |
| H$_{9a}$, H$_{9b}$ | 2.41 | H$_{8b}$, H$_{11b}$ | 4.27 |
|  |  | H$_{10a}$, H$_{10b}$ | 1.64 |

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4) For examples of upfield shift reported for an anilide and a lactam, see T. H. Siddall, III, Chem. Commun., 452 (1971);   P. H. Mazzochi, H. J. Tamburin, and G. R. Miller, Tetrahedron Lett., 1819 (1971).

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12) The $\underline{S}$-$\underline{r}^{-3}$ relationship is not yet examined since the exact position of the complexed europium atom is difficult to estimate, though the $\underline{S}$-$\underline{r}'^{-2}$ relationship obtained by using the distance $\underline{r}'$ between the center of hydrogen and that of oxygen of 4-homoadamanten-5-ol on a Fieser molecular model seems to be practically useful for prediction of the shift values.   The use of internal proton standard method for I and II is not appropriate for the lack of a common suitable proton as the standard and the preparation of derivatives of I and II suitable for application of this method is in progress; cf. D. R. Kelsey, J. Amer. Chem. Soc., 94, 1764 (1972).

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