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SYNTHESIS AND (NON-CHAIR) CONFORMATION OF SOME $3\alpha,7\alpha$-DISUBSTITUTED BICYCLO[3.3.1.]NONANES

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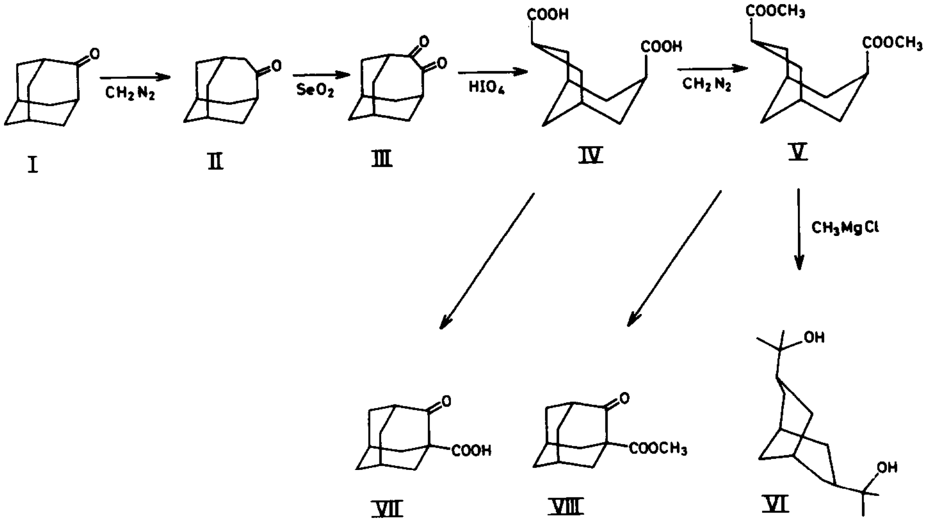
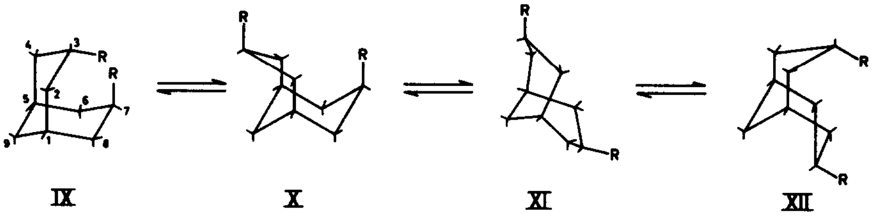
Recent developments have made homoadamantane derivatives readily accessible[1-3]. Cleavage of these compounds would seem a convenient route to $3\alpha,7\alpha$-disubstituted bicyclo[3.3.1]nonanes. As an example we have studied the oxidative cleavage of 4-homoadamantanone (II), which compound was prepared from adamantanone (I) and diazomethane as described by Black and Gill[1]. Compound II was oxidized with selenium dioxide into 4,5-homoadamantanedione (III)[2]. Further oxidation by heating III at 70° with periodic acid in dioxane-water (3:1) for 70 h furnished in 85% yield $3\alpha,7\alpha$-bicyclo[3.3.1]nonanedicarboxylic acid (IV); m.p. 180.5-181°.

The dicarboxylic acid IV was converted with diazomethane into the corresponding dimethyl ester V. Various attempts to epimerize IV or V failed because ring closure towards 2-oxoadamantanecarboxylic acid (VII) or its methyl ester (VIII) occurred quantitatively. Treatment of V with a solution of methylmagnesium chloride in THF afforded $3\alpha,7\alpha$-bis-2-(2-hydroxypropyl)bicyclo-[3.3.1]nonane (VI) in 80% yield; m.p. 106-107°.



Compounds IV, V, and VI were studied with the use of PMR spectroscopy. The possible conformations of 3α,7α-disubstituted bicyclo[3.3.1]nonanes are outlined below. Appleton et al[4] have shown that for methyl 3α-bicyclo[3.3.1]nonanecarboxylate the double chair conformation (IX) can



be populated to only a small extent. Consequently conformation IX may be discarded for the present systems, as is also obvious from an inspection of molecular models. Thus compounds IV-VI may be considered to exist as an equilibrium of the two equivalent rigid chair-boat conformations (X and XII) and the flexible double boat conformation (XI). Estimation of 1,3-diaxial interactions indicates that even when R is rather small, as in V, the conformation XI may play a role. Anyway when R becomes bulkier, the contribution of XI is expected to increase as a result of unfavorable 1,3-diaxial interactions in the chair-boat conformations X and XII, which are absent in the double twist-boat conformation XI.

The 100 MHz spectrum of compound VI (Fig. 1A) was too complex to allow for a first-order interpretation. Therefore spectra were recorded with increasing amounts of Eu(DPM)$_3$[5] until separation between the various multiplets was achieved. From this spectrum (Fig. 1B) chemical shifts and coupling constants were obtained by first-order analysis. More accurate data were obtained by computer iteration starting from these chemical shifts and coupling constants (see Table I). From a plot of the chemical shift of the methyl protons versus the shift of the various ring protons with increasing amounts of Eu(DPM)$_3$ (Fig. 2) the chemical shifts of the protons in the absence of Eu(DPM)$_3$ were extrapolated. Computer simulation, using these chemical shifts and the coupling constants from Table I, yielded a spectrum which was identical with the original one (Fig. 1A). Hence complexation with Eu(DPM)$_3$ had no observable influence on the conformation and the geometry. The splitting pattern of the signal of the 2α-, 4α-, 6α-, and 8α-protons can only be explained by a double twist-boat conformation. These protons are then geminally coupled (J= -12 Hz) to the corresponding β-protons, "trans diaxial" (J= 12 Hz) to the 3- and 7-protons, respectively, and only weakly (J= 2 Hz) to the 1- and 5-protons, respectively. The coupling

TABLE I

The coupling constants of compounds IV-VI in Hz (± 0.5 Hz)

	$J_{12\alpha}$	$J_{12\beta}$	J_{19}	$J_{2\alpha2\beta}$	$J_{2\alpha3}$	$J_{2\beta3}$
IV	3.0	7.0	3.0	-14.0	7.1	7.1
V	3.0	7.0	3.0	-14.0	7.1	7.1
VI	2.0	10.0	2.5	-12.0	12.0	6.0

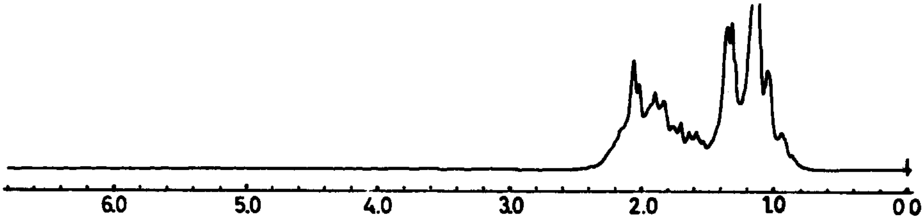


Fig. 1A. 100 MHz PMR spectrum of VI in $CDCl_3$ (δ-scale).

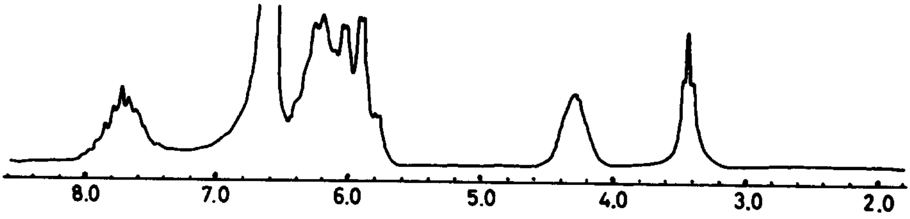


Fig. 1B. 100 MHz spectrum of 80 mg VI in 0.5 ml $CDCl_3$ and 80 mg $Eu(DPM)_3$.

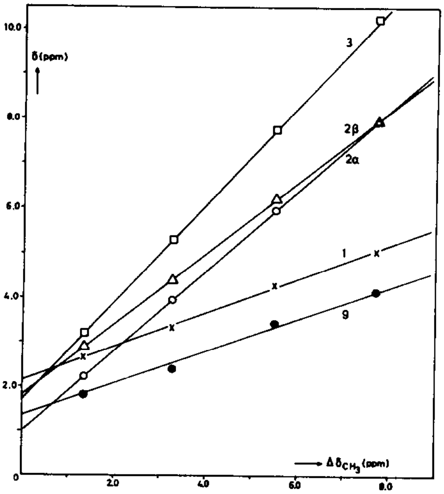


Fig. 2. The effect of $Eu(DPM)_3$ on the PMR of VI. The induced shift of the $C(CH_3)_2OH$-protons versus the chemical shifts of the ring protons.

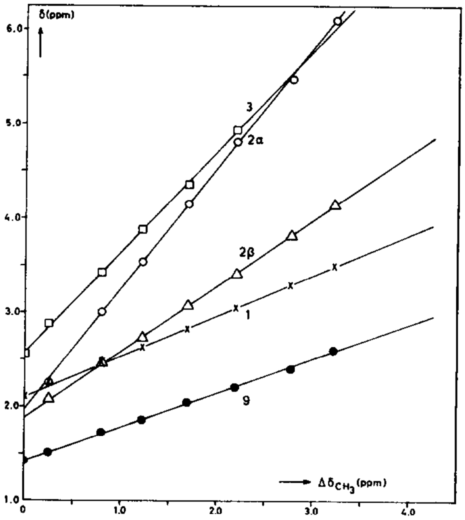


Fig. 3. The effect of $Eu(DPM)_3$ on the PMR spectrum of V. The induced shift of the $COOCH_3$-protons versus the chemical shifts of the ring protons.

constant $J_{2\beta3\beta}$ (6.0 Hz) has the same value as that found for the coupling between the corresponding 1- and 2-protons in cis-1,4-di-t-butylcyclohexane[6], which compound doubtless prefers the twist-boat conformation.

The 100 MHz PMR spectrum of compound V exhibits a sharp singlet for the protons of the two methoxycarbonyl functions, a quintet for the 3- and 7-protons (J= 7.1 Hz), and a triplet for the 9-protons (J= 3.0 Hz). The spectrum of IV is analogous to that of V. From spectra of V in the presence of various amounts of the paramagnetic shift reagent $Eu(DPM)_3$[5] all other coupling constants were derived (see Table I). The coupling constants were independent of the amount $Eu(DPM)_3$ added. Apparently the complexation with $Eu(DPM)_3$ had no observable influence on the conformation and geometry of V. As can be seen from Fig. 3, the influence of $Eu(DPM)_3$ on the 2α-protons is relatively large, showing that the distance of the Eu^{3+}-ion to these protons is rather small, especially in comparison with the 2β- and 3-protons[7]. Moreover substantial line broadening at low temperatures (-90°) shows that these compounds exist as an equilibrium of conformations. Both facts indicate that there is an important contribution of the chair-boat conformations (X and XII) to the conformational equilibrium. The values for the coupling constants between the 2-protons and the 3-proton (both 7.1 Hz), which cannot be explained by a double twist-boat conformation (compare compound VI), also seem to be in contradiction with the X-XII equilibrium, because then these couplings are expected to be 7-9 Hz ($J_{2\alpha3}$) and 3-5 ($J_{2\beta3}$). The flagpole interaction in the rigid boat parts and the 1,3-diaxial repulsion in the chair parts of the conformations X and XII, however, may cause such a flattening of both the chair and the boat that these couplings become of the same magnitude. Some other bicyclo[3.3.1]nonane derivatives are in preparation in order to verify this assumption.

Acknowledgement

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