Application of LIS Reagents in Determining the Stereochemistry of the 7-Phenyl-2-oxabicyclo[4.1.0]heptanes

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Stereochemical assignments are made for the *endo*- and *exo*-7-phenyl-2-oxabicyclo[4.1.0]heptanes by analysis of their europium doped nmr spectra.

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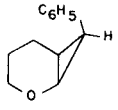
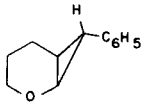
Davis and Willcott [1] have made structural assignments to rigid organic molecules by analyzing the lanthanide-induced shifts observed in their nmr spectra. We wish to extend the application of their method to semi-rigid molecules for the purpose of assigning their stereochemistry. The compounds studied were the *endo*- and *exo*-7-phenyl-2-oxabicyclo[4.1.0]heptanes, Ia and Ib respectively. Stereochemical assignments were made by comparing indices obtained from the serial-dilution method of Shapiro [2] to indices calculated for the *endo* and *exo* isomers using the McConnell-Robertson equation [3].



Ia



Ib

X-Ray coordinate data of several bicyclo[4.1.0] compounds have shown the six-membered ring to have all atoms in the same plane except atom number three, which projects in the opposite direction as atom number seven [4,5]. As a first approximation, which in the final analysis proved satisfactory, we selected this conformation for the six-membered ring in the molecular models constructed for the *endo* and *exo* isomers from which coordinate data was obtained, even though it was realized that the conformation of a compound need not be the same in the solid and liquid states. The phenyl ring was then attached so as to produce the *endo* model. Holding the coordinates of the bicyclic ring fixed, we then obtained phenyl hydrogen positions corresponding to incremental phenyl rotations about the C7-C8 bond. At each incremental phenyl position a number of sets of indices were calculated by varying the lanthanide position. An agreement factor was calculated comparing the experimental indices of Ia to the calculated values at each position of the phenyl ring.

The conformation yielding the best agreement between the experimental and calculated indices, while still making "chemical sense," finds the phenyl ring orientation 54° counterclockwise from the plane defined by C1, C7 and C8, looking down the C7-C8 bond. This is nearly parallel to the bridgehead bond and furnishes an agreement factor of 2.87. Repeating the calculations with the phenyl ring attached in the *exo* configuration furnishes 7.31 as the best agreement factor. The phenyl ring orientation was 148° counterclockwise from the plane defined by C1, C7 and C8, looking down the C7-C8 bond. The "R factor ratio test" was performed on this data for the one-dimensional hypothesis: the *exo* configuration agrees as well with the experimental data as does the *endo* configuration. An examination of the significance points for a system possessing ten degrees of freedom [6] shows that the *exo* structure can be rejected at the 0.5% level if the ratio of the *exo/endo* agreement factor exceeds 1.511. The observed R-factor ratio is 7.31/2.87 = 2.55. Thus, of the two stereoisomers possible for 7-phenyl-2-oxabicyclo[4.1.0]heptane, the *endo* configuration can be assigned to Ia at the 99.5% confidence level. Similarly, analysis of the *exo* configuration furnishes an agreement factor of 2.72 for the *exo* coordinates with a phenyl ring rotation of 110° counterclockwise from the plane defined by C1, C7 and C8, looking down the C7-C8 bond. At a phenyl ring rotation of 44° counterclockwise from the plane defined by C1, C7 and C8, looking down the C7-C8 bond, an agreement factor of 4.38 was found for the *endo* coordinates. The R-factor ratio test was performed on this data for the one-dimensional hypothesis: the *endo* configuration agrees as well with the experimental data as does the *exo* configuration. The observed R-factor ratio is 4.38/2.72 = 1.61, which exceeds 1.511, allowing the *endo* structure to be rejected at the 0.5% level. Thus, the *exo* configuration could be assigned to Ib at the 99.5% confidence level. Results obtained using this method were in agreement with those obtained for these compounds using other methods, including X-ray analysis.

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