

DOES THE BOAT-LIKE CONFORMER EXIST FOR
1,8,8-TRIMETHYLBICYCLO[3.2.1]OCTAN-3-ONE?¹

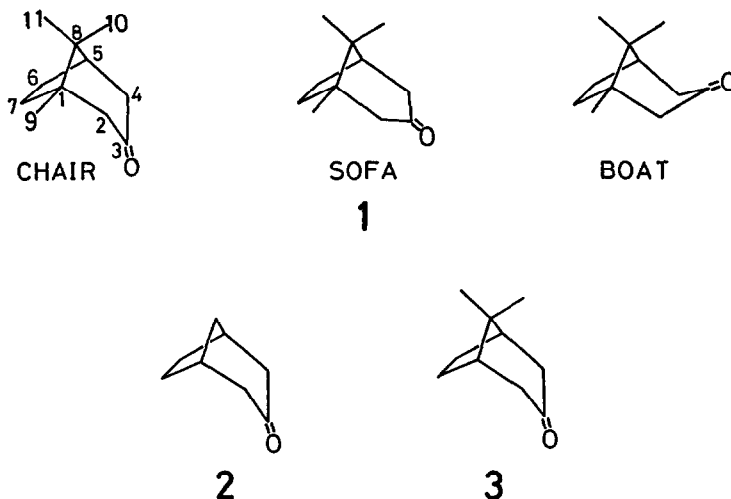
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Abstract: Neither molecular mechanics (MM2 and MM2') nor molecular orbital (MNDO and *ab initio*) calculations confirmed the existence of a boat-like conformer for the title compound, recently proposed to exist up to 20% in hydrocarbon solvents based on the CD spectra.

Recently, Lightner *et al.*⁴ observed remarkably large temperature-dependence in the CD spectra of a compound, which they described as (+)-(1*S*,5*R*)-1,8,8-trimethylbicyclo[3.2.1]octan-3-one **1**, in hydrocarbon solvents. Assuming a two-conformer equilibrium, they obtained a conformational energy difference of 0.74 kcal/mol. Chair and boat-like (sofa or boat) conformers have been suggested for the major and minor components, respectively.⁴

One would wonder how a methyl group can be accommodated in the small space between C₈ and the carbonyl group of these *non-chair* conformations. We describe below the results of our computational studies which exclude the existence of such conformation of **1**.



We first used the molecular mechanics technique.⁵ In order to check the possibility of twisted conformers,⁶ extensive portions of torsional energy surface of 1 were covered using the two-bond driver option.⁷ Even for the parent structure, bicyclo[3.2.1]octan-3-one 2, the existence of sofa or boat conformer is doubtful. Whereas Fournier^{8,9} reported successful minimization of 2 in his molecular mechanics studies, both MM2¹⁰ and the recently modified version (MM2')^{11,12} failed to give any minimum in the sofa/boat region of the energy surface except for a significant loss of slope. In these cases, dihedral angles $C_8-C_1-C_2-C_3$ and $C_3-C_4-C_5-C_8$, were simultaneously driven, and the chair conformation was the only well-defined energy minimum.

Because of the negative result with 2, it was not surprising to have found no minimum at all in the sofa/boat region of torsional energy surface of 1 when the same pair of bonds as in 2 were driven (Figure 1a). Again, the chair was the only minimum. This Figure also reveals that skeletal twisting of 1 and 2 does not give any advantage in terms of the total steric energy.

The cyclohexane ring in chair-2 is flattened out near C_3 and puckered in the opposite part due to the anti-reflex effect^{9,16} caused by the bridging over C_1 and C_5 : $C_2-C_3-C_4-C_5$ 38.7° , $C_1-C_8-C_5$ 100.3° by MM2'. This feature is maintained in chair-1 (corresponding angles are 35.0 and 98.8°). Because of these deformations, the axial-methyl group lies closer to carbonyl carbon than in the usual chair form. The calculated methyl $H...C_3$ nonbonded distance (2.98 \AA by MM2') is almost equal to the sum of van der Waals radii of hydrogen

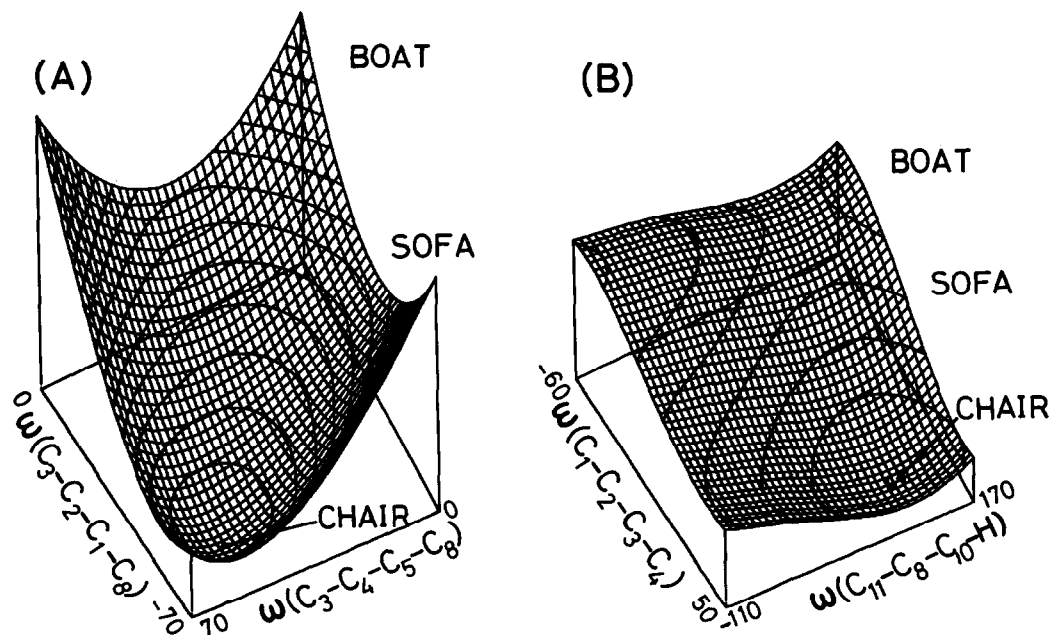


Figure 1. Torsional energy surfaces of 1. Contour lines are given at an interval of 1 kcal/mol. Dihedral angles are given in degrees.

(1.20 Å) and carbon (1.75 Å).¹⁷ Clearly, this space is barely enough to accommodate a methyl group and must be too small to do the same in sofa or boat conformation.

In chair-1, the local conformation at the dimethyl bridge involves perfect staggering like in n-propane with the consequence that one of methyl protons points itself straight toward C₃. This feature is maintained along the valley from chair towards boat in the torsional energy surface (Figure 1a). In order to seek the possibility of a boat-like energy minimum having distorted dimethyl bridge conformation, the two-bond driver calculations were repeated using dihedral angles C₁-C₂-C₃-C₄ and C₁₁-C₈-C₁₀-H as variables. Although a saddle point appeared in the boat region for a crush conformation (Figure 1b), this point is more than 3 kcal/mol higher than chair, and can by no means be considered as an evidence for the new conformer.

Molecular mechanics calculations sometimes fail to reproduce proximity effects¹⁸ which had not been taken into account at the time of parameterization of potential functions.^{5,19} In the case of **1**, a possibility of an attractive interaction of the type C-H...C, for which a remote precedence exists,¹⁷ may not be excluded between H₁₀ and the carbonyl carbon.

This last possibility was studied by MNDO and ab initio molecular orbital methods. MNDO²⁰ calculation of **1** was started from a boat conformation, which was subjected to the Fletcher-Powell geometry optimization including all structural parameters: we ended up with the chair form. Ab initio calculations were carried out on a smaller model structure **3** with the GAUSSIAN80 program package using STO-3G basis set.^{21,22} Geometry was optimized by the Murtaugh-Sargent technique, keeping C_s symmetry restriction and allowing all independent structural parameters of nonhydrogen atoms to relax. Standard geometries involving hydrogen atoms were not changed. Again, starting from a boat-3, we ended up with the chair. It is interesting to note that the methyl proton...carbonyl carbon distances obtained from these calculations, 2.80 (MNDO) and 2.68 (STO-3G) Å, are considerably shorter than that expected from van der Waals radii (vide supra) and probably indicate small attractive interaction.

In the present study, both molecular mechanics and molecular orbital methods gave the same conclusion: chair is the only energy minimum for **1**. Then how should Lightner's interesting observations be rationalized? The only explanation seems to be the temperature-dependent solvation which has been found to affect CD spectra even when nonpolar solvents are employed.²³

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