

o-Nitrotoluene and benzaldehyde gave 1-phenyl-2-(*o*-nitrophenyl)ethanol (7, X=Y=H) which was oxidized by concentrated nitric acid in the presence of chloroform. *o*-Nitrobenzyl phenyl ketone (8, X=Y=H) was obtained in 98 % yield (m.p. 75–77°, IR (KBr): 3100, 2910, 1690, 1620, 1600, 1580, 1520, 1450, 1410, 1360, 1290, 1210, 1005, 995, 790, 730, 700, 690, 675 cm⁻¹).

Catalytic reduction of 8 gave 2-phenylindole in 85 % yield (m.p. 187–188°, lit.⁸ 186°).

Our results thus show two useful routes to substituted indoles; one to indoles substituted in the benzene ring and unsubstituted in the pyrrol ring, and one to indoles with an aryl group in the 2-position.

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The Conformation of a *gem*-Dimethyl-substituted Cycloheptene

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In a previous paper¹ the synthesis of a cycloheptene derivative, 2-carboxy-3,3,6,6-tetramethyl-cycloheptene is described. Variable-temperature NMR-spectra are now obtained of this compound, with a coalescence temperature as high as –40° in 100 MHz NMR.

In Fig. 1 the ¹H NMR-spectra of 2-carboxy-3,3,6,6-tetramethyl-cycloheptene in CDCl₃ at 35°, –41°, and –66° and in CHFCl₂ at –85° are shown.

The absorption for the *gem*-dimethyl protons at lowest field changes gradually into two sharp lines at low temperature, the other methyl signal is broad, but is not resolved at –85°C. The difference in chemical shift between the two methylene protons alpha to the double bond is ca. 50 Hz, their geminal coupling constant 14 Hz. The vicinal coupling, to the olefinic proton, of the methylene proton at lowest field is 7 Hz, the other is uncertain because of overlapping of lines from the other methylenes in the ring.

The triplet of the olefinic proton is not fully resolved at –66°, at –85° the signal is hidden by the signals of the proton in the solvent.

The free energy of activation for the exchange process was calculated² resulting in $\Delta G^\ddagger = 12.2$ kcal/mol.

The infrared spectra were taken of the crystalline solid in KBr and in CS₂ solution. IR-absorption bands at 1730 and 3510 cm⁻¹ showed that the solution contained some monomeric acid together with the hydrogen-bonded dimer. Otherwise, the spectra of the two phases were alike which indicate that the cycloheptene skeleton takes the same conformation in solution as in the crystal, and that there is only one conformer in the solution.

The compound melted at 130° and no solid-solid transition was observed by differential calorimetry. The entropy and enthalpy of fusion were $\Delta S = 23.9$ cal/mol deg. and $\Delta H = 9.7$ kcal/mol.

As a result of independent calculations Favini *et al.*³ found the chair and Allinger *et al.*⁴ the boat to be the lowest energy form of cycloheptene. From NMR-data most investigators find the chair conformation in cycloheptene derivatives.^{5,6} In 20 different benzocycloheptene derivatives, described by Kabuss *et al.*⁷ including one with substituents in 3 and 6 positions analogous to our compound, only one conformer occurred in the low temperature NMR-spectra, presumably that of the chair form. Grunwald and Price⁸ found two conformers by low temperature NMR of 3,3,6,6-

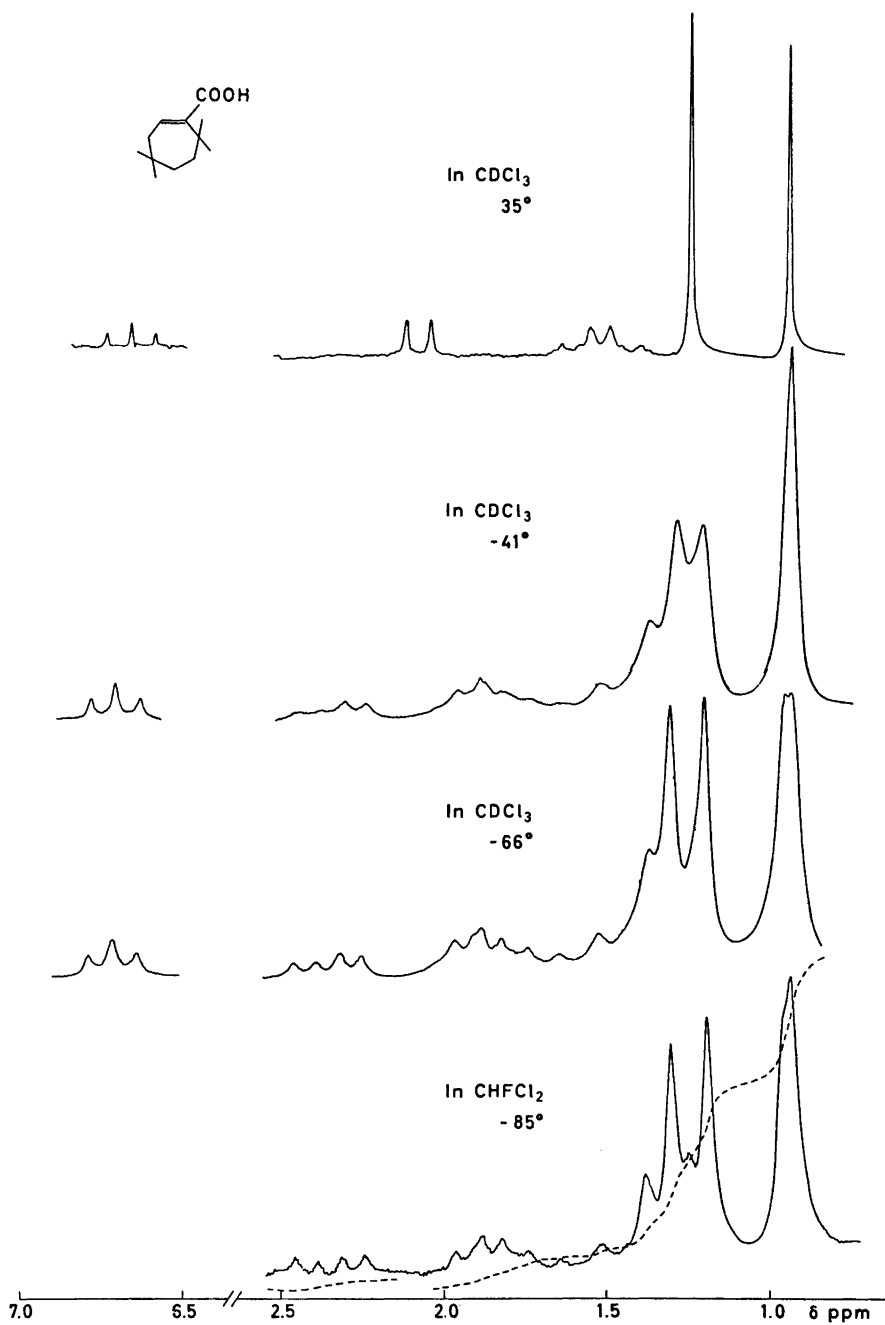


Fig. 1. Changes in the ^1H NMR-spectra of 2-carboxy-3,3,6,6-tetramethylcycloheptene at low temperatures.

tetramethylbenzocycloheptene, a conclusion based on new peaks arising in the methyl region by lowering the temperature. Our cycloheptene derivative has the *gem*-dimethyl groups in the same positions and new peaks arise in the low temperature spectra in lower part of the methyl region. This may be due to a second conformer but could also be explained by overlapping caused by the chemical shifts and the coupling of the methylenes in positions 4 and 5, which in the low temperature spectrum is extended over a region of at least 60 Hz. The fact that the infrared spectra show only one conformer in solution makes the last explanation the most probable and our assumption is that only one conformer is present.

From models it can be seen that the energetically possible forms of 2-carboxy-3,3,6,6-tetramethylcycloheptene are the two inverted chair forms and the two boat forms, however, only one of the two inverted twist boat forms. In the other the methyl-methyl interaction is too severe.

According to Favini *et al.*³ the dihedral angle, ω_7 , is the same in the chair and the boat forms of cycloheptene and = -72.2° . The π -contribution to the geminal coupling constant of the 7-protons in these two conformations should then be almost zero.⁹ Our observed value $J_{7,7^{gem}} = 14$ Hz is as expected for this size ring, (cyclohexane = 13 Hz) and the same as the value found for the 7-protons in benzo-cycloheptene = 14.1 Hz,⁶ which is found to take the chair conformation. The conclusion that may be drawn from the π -contribution to the coupling constant of the 7-protons is therefore that our cycloheptene derivative takes either the chair or the boat conformation.

The observed vicinal coupling constant $J_{1,7} = 7$ Hz is likewise in accordance with the dihedral angles of the chair and boat conformations and the corresponding theoretical values for allylic proton-proton coupling.¹⁰

The result of the analysis of the low-temperature NMR-spectra of 2-carboxy-3,3,6,6-tetramethylcycloheptene is therefore that the conformation is either the chair or the boat.

The inversion barrier in cycloheptene itself is calculated from NMR-data¹¹ at -160° to be 5.0 kcal/mol. The *gem*-dimethyl groups make it more difficult to find low-energy interconversion paths between the different forms, and this explains the considerably higher coalescence temperature, -40°C , and the corresponding higher barrier, 12.2 kcal/mol, in 2-carboxy-3,3,6,6-tetramethylcycloheptene.

The NMR-spectra were recorded with a Varian HA 100 15 D instrument. For the calorimetric measurements a Perkin-Elmer Differential Scanning Calorimeter IB was used.

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Isomerization of ϵ -Carotene to β -Carotene and of Lutein to Zeaxanthin

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More than 25 years ago Karrer and Jucker¹ reported the base catalyzed isomerization of α -carotene (*1*, β,ϵ -carotene by new nomenclature,² stereochemistry subsequently assigned³) by prolonged treatment with NaOEt/EtOH in benzene at elevated temperature. Extensive decolorization of the carotene occurred and from 30 mg of α -carotene (*1*) a small amount of β -carotene (*2*, β,β -carotene²) was isolated. The same authors reported the sodium ethoxide catalyzed isomerization of lutein (*3*, β,ϵ -carotene-3,3'-diol²) to zeaxanthin (*4*, β,β -carotene-3,3'-diol,² Scheme 1). More recently, Kargl and Quackenbush⁴ reported the isomerization of δ -carotene (*5*, ϵ,ψ -carotene,² stereochemistry later assigned⁵) to γ -carotene (*6*, β,ψ -carotene²) by the procedure described by Karrer and Jucker.¹