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 $J_7^{gem} = 14$ 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 $J_{17} = 7$ 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-data[11] 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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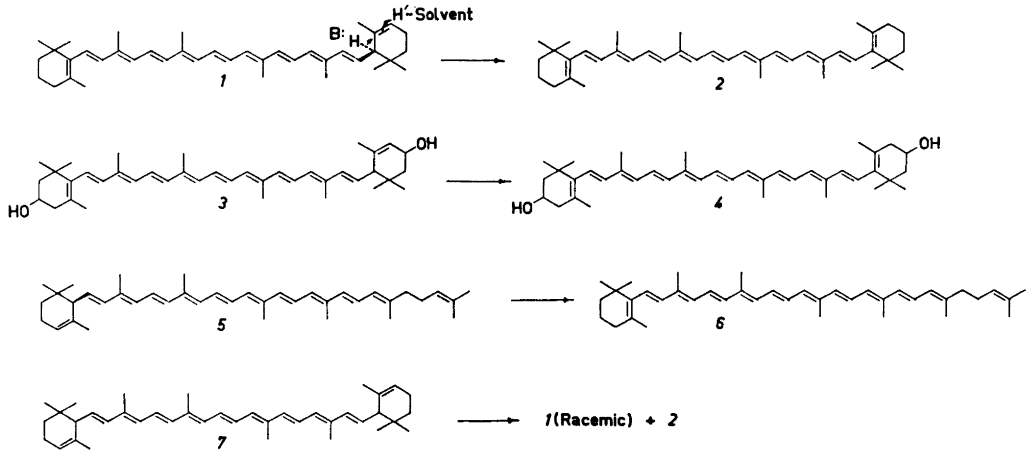
More than 25 years ago Karrer and Jucker[1] reported the base catalyzed isomerization of α-carotene (*1*, β,ε-carotene by new nomenclature,[2] stereochemistry subsequently assigned[3]) by prolonged treatment with NaOEt/EtOH in benzene at elevated temperature. Extensive decolorization of the carotene occurred and from 30 mg of α-carotene (*1*) a small amount of β-carotene (*2*, β,β-carotene[2]) was isolated. The same authors reported the sodium ethoxide catalyzed isomerization of lutein (*3*, β,ε-carotene-3,3′-diol[2]) to zeaxanthin (*4*, β,β-carotene-3,3′-diol,[2] Scheme 1). More recently, Kargl and Quackenbush[4] reported the isomerization of δ-carotene (*5*, ε,ψ-carotene,[2] stereochemistry later assigned[5]) to γ-carotene (*6*, β,ψ-carotene[2]) by the procedure described by Karrer and Jucker.[1]



Scheme 1.

Attempts to utilize this procedure for the small scale (0.2 – 1.0 mg) isomerization of α-carotene (*1*) to β-carotene (*2*) or ε-carotene (*7*, ε,ε-carotene [2]) to α-carotene (*1*) and β-carotene (*2*) failed. Buchecker *et al.*[6] reported similar difficulties during attempts to isomerize lutein (*3*) to zeaxanthin (*4*). A modified base catalyzed isomerization was developed to allow small scale conversions of α-type (ε by new nomenclature [2]) end groups to β-type end groups.

Treatment of synthetic, racemic ε-carotene (*7*, 0.125 mg) with KOH/MeOH (20 %, 0.5 ml), benzene (0.5 ml) and anhydrous dimethyl sulfoxide (DMSO, 2 ml) in a sealed tube under an atmosphere of nitrogen at 118°C for 15 – 30 min gave, after the usual extractive isolation and chromatography, α-carotene (*1*, racemic, 16 – 28 %) and β-carotene (*2*, 16 – 21 %). Total pigment recovery including unreacted ε-carotene (*7*) was 51 – 68 %. The composition and total pigment recovery depended on reaction time. Shorter reaction times yielded higher pigment recovery, higher conversion to α-carotene (*1*) and lower conversion to β-carotene (*2*). Increased reaction times resulted in higher conversion to β-carotene but lower total pigment recovery. When NaOEt, KOEt, or *t*-BuOK were used as base the carotene was completely degraded in 10 min.

Attempted isomerization of lutein (*3*) to zeaxanthin (*4*) using the above optimum conditions failed. However, when a solution of lutein (*3*, 1.0 mg), KOMe/MeOH (5 %, 0.5 ml) and DMSO (2 ml) in a sealed tube under N_2 was heated at 118°C for 20 min, zeaxanthin was formed in 10 – 15 % yield. Stereochemical aspects of this reaction are treated separately.[7]

Instruments used were those commonly employed in this laboratory.[8] Identity of all products of the isomerization study was established by electronic absorption spectroscopy, mass spectrometry and chromatography including co-chromatography with authentic specimens. α-Carotene (*1*), β-carotene (*2*), and ε-carotene (*3*) were separated on Al_2O_3 plates developed with petroleum ether, ethyl ether (95 + 5). Lutein (*3*) and zeaxanthin (*4*) were separated on plates prepared from MgO, $Ca(OH)_2$, kieselgel G, $CaSO_4$ and H_2O (9 + 12 + 30 + 3 + 93) activated for 1 h at 100°C; developed with acetone-petroleum ether-isopropanol (20 + 77 + 3).

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