Proton-coupled Carbon-13 Nuclear Magnetic Resonance Spectra from Individual Carbon Sites in a Molecule: the Rotameric Equilibrium in Menthone

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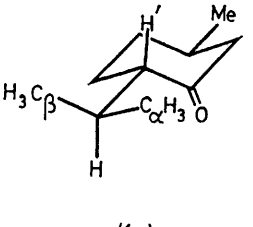
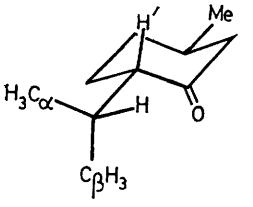
Summary Vicinal carbon–proton coupling constants have been measured for menthone by a new technique and show that the most stable rotamer is (**1a**) rather than (**1b**).

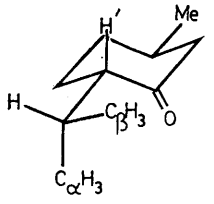
THE relative stabilities of the rotamers (**1a**—**c**) of menthone (**1**) and analogous 2(*eq*)-isopropylcyclohexanones have been the subject of considerable debate.[1–5] Low temperature circular dichroism in steroid analogues[1,3] and lanthanide induced shifts in ^{1}H n.m.r. spectra[5] suggest that (**1b**) is more stable than (**1a**) but the opposite conclusion has been inferred from an analysis of conformational equilibria in alkylcyclohexanones.[2,4] Rotamer (**1c**) and other chair or twist conformers are not expected to make a significant contribution at room temperature.[1–5] This Communication describes the use of a new technique in Fourier transform n.m.r. spectroscopy in determining the relative stabilities of (**1a**) and (**1b**).



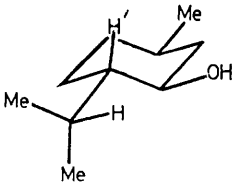
(1a)



(1b)



(1c)



(2)

The C–H coupling constants for the methyl carbons C_α and C_β of the isopropyl group in (**1**) will be the weighted average of those for the three rotamers (**1a**—**c**), but only the vicinal (three bond) couplings to the 2(*ax*)-proton of the ring, $^3J_{C-H}$, will depend on the rotameric equilibrium. These couplings are expected to be relatively small when the methyl group is *gauche* to the ring proton [Me_α in (**1a**) and (**1b**), and Me_β in (**1a**) and (**1c**)], and large when the methyl group is *trans* to the ring proton [Me_α in (**1c**) and Me_β in (**1b**)]. The proton-coupled ^{13}C n.m.r. spectrum of menthone (see Figure) is too crowded for easy analysis; the new method,[6] however, allows the normal coupled spectrum to be decomposed into a set of independent partial spectra or subspectra, one for each resonance in the decoupled spectrum.

In a conventional Fourier transform n.m.r. experiment, a spectrum is obtained by transforming the free induction decay (FID) following a strong nonselective radiofrequency pulse. The spectrum may be modified by using selective excitation,[7] in which the form of a train of radiofrequency pulses is used to control the range of resonance frequencies to be excited. The new experiment combines selective excitation and gated decoupling:[8] one line in the decoupled spectrum is excited selectively, but the proton decoupler is switched off before acquisition of an FID. Transformation of this FID results in a subspectrum which is the multiplet corresponding to one line in the decoupled spectrum, in most cases to one carbon site in a molecule; the superposition of a complete set of such subspectra is the normal proton-coupled spectrum.

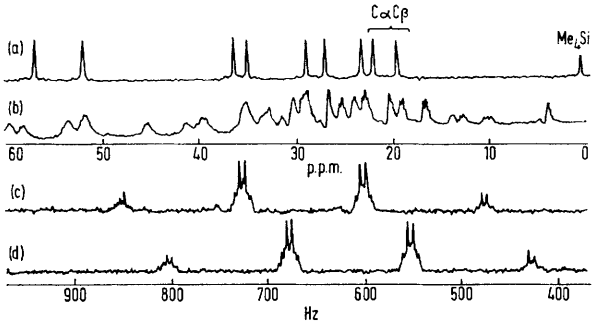


FIGURE. Carbon-13 n.m.r. spectra and subspectra for menthone (**1**) containing $CDCl_3$ (20% v/v) and $SiMe_4$ (5% v/v): (a) proton-decoupled and (b) proton-coupled spectra, and (c) and (d) proton-coupled subspectra for isopropyl methyls C_α and C_β (the assignment of C_α and C_β is uncertain).

The two isopropyl methyl multiplets are dominated by a large coupling to the three directly bonded protons. The fine structure of each component of these quartets is caused by a two bond coupling to the isopropyl methine proton H″ and three bond couplings to the axial proton on C-2 of the ring and to the protons of the other methyl group. The Figure shows the proton-decoupled (a) and -coupled (b) ^{13}C n.m.r. spectra of menthone, together with the proton-coupled subspectra (c) and (d) (expanded) resulting from selective excitation of C_α and C_β.

The fine structure of the two multiplets in (c) and (d) is indistinguishable; first order analysis gives a value of 2·5 ± 0·5 Hz for the coupling to the axial ring proton H′. The equality and magnitude of the couplings from the two methyls to H′ point strongly to the predominance of rotamer (**1a**) rather than (**1b**) or (**1c**). Fortunately menthol [(**2**); the hydroxy-group ensures that the dominant rotamer, analogous to (**1b**), is that depicted] provides an excellent model for ^3J(C–H′) in (**1b**). The isopropyl methyls

in (**2**) give rise to two quartets, one similar to (c) and (d) and the other a poorly resolved quintet of quartets, showing that the *trans* coupling $^3J(C–H') = 5{\cdot}0 \pm 1$ Hz is considerably larger than the *gauche* ($2{\cdot}5 \pm 0{\cdot}5$ Hz), as expected. The results obtained show a clear preference for rotamer (**1a**) in menthone, which is at least 4 kJ mol^{-1} more stable than rotamer (**1b**), in agreement with Cotterill and Robinson.[2,4]

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