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STERIC INHIBITION OF THE ROTATION OF THE PHENYL GROUPS IN 2,6-DIMETHYL-1-PHENYLCYCLOHEXANOL AND DENDROCREPINE DETECTED BY MEANS OF CARBON-13 NUCLEAR MAGNETIC RESONANCE

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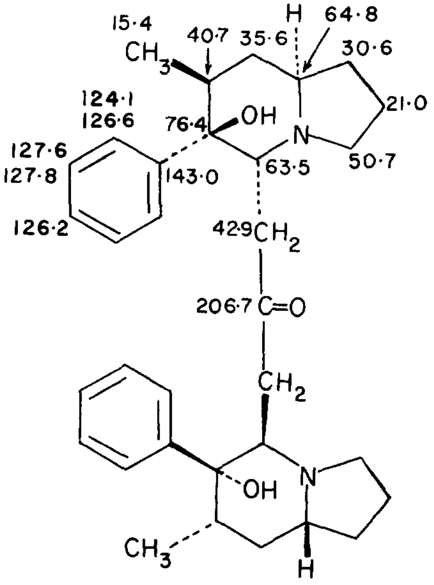
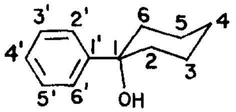
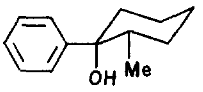
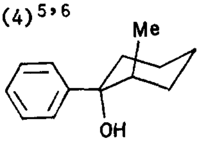
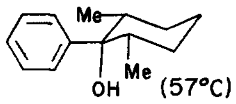
In the course of an investigation on the biosynthesis of the alkaloids of the orchid *Dendrobium crepidatum* Lindl. we examined the ^{13}C NMR spectrum of dendrocrepine (1).[2,3] The chemical shifts (ppm from Me$_4$Si in CDCl$_3$) indicated on formula 1, were assigned by off-resonance decoupling, and by comparison with the spectra of indolizidine and methylpiperidines.[4] To our surprise, the phenyl groups gave rise to six resonances. An examination of space-filling models indicated that the non-equivalence of the two ortho and two meta positions could be due to lack of rotation of the phenyl groups. We have thus examined the ^{13}C NMR spectra of a series of 1-phenylcyclohexanols to determine whether this is a general phenomenon of sterically crowded phenyl groups attached to a saturated six membered ring. The spectra, determined in CDCl$_3$ at 25°, are recorded in Table I. It is assumed that the phenyl group in all these compounds adopts an equitorial position. Chemical shifts in the cyclohexane ring can then be assigned based on the well known substituent effects of axial and equitorial methyl groups in cyclohexanes[8] and cyclohexanols.[9] The chemical shifts of the ortho, meta, and para positions of the phenyl groups were assigned by comparison with α,α-dimethylbenzyl alcohol.[10] The



1 Dendrocrepine

Table I. Chemical Shifts of 1-Phenylcyclohexanols (ppm from Me_4Si in $CDCl_3$)

Carbon No	1-Phenylcyclohexanol (2) 	2-c-Methyl-1-phenylcyclohexanol (3)[5,6] 	2-t-Methyl-1-phenylcyclohexanol (4)[5,6] 	2-c-Methyl-6-c-methyl-1-phenylcyclohexanol (5)[7] 
1	73.0	75.7	75.4	78.2
2	38.7	41.1	39.5	41.8
3	22.1	30.4	28.6	30.6
4	25.5	26.2	19.8	26.2
5	22.1	22.0	21.8	30.6
6	38.7	40.0	31.3	41.8
Me		15.5	15.8	15.7
1'	149.3	148.3	148.4	146.8
2',6'	124.4	124.5	125.7	125.2
3',5'	127.9	127.8	128.1	128.0
4'	126.4	125.9	126.8	126.1

spectra of 1-phenylcyclohexanol (2) and the cis and trans-2-methyl-1-phenylcyclohexanols (3) and (4) were unexceptional between 25° and -60°C, four resonances due to the aromatic carbons being observed, indicating free rotation of the phenyl group in these compounds. However, the spectrum of 2,6-dimethyl-1-phenylcyclohexanol (5) was atypical in the aromatic region, and was found to be dramatically temperature dependent. Figure 1 illustrates that region of the spectrum where the ortho, meta, and para carbons of the phenyl group resonate. At -51°C five resonances are clearly observed. By analogy with the aromatic resonances in the other phenylcyclohexanols, the two resonances (12.9 Hz separation) at 127.9 ppm are assigned to the meta carbons. The single resonance at 125.9 ppm (essentially temperature independent) is the para carbon, and the two resonances (41 Hz separation) at 124.9 ppm arise from the two ortho carbons. As the temperature is raised the peaks due to the meta and ortho carbons broaden. At 0°C one ortho carbon resonates at 124.0 ppm while the other ortho carbon is coincident with the para resonance. The coalescence point is reached at 36°C. At 57°C the ortho carbons appear as a broad resonance at 125.2 ppm. The chemical shifts of the aliphatic carbons and C-1' did not change significantly over the -51° to +57°C temperature range, indicating that

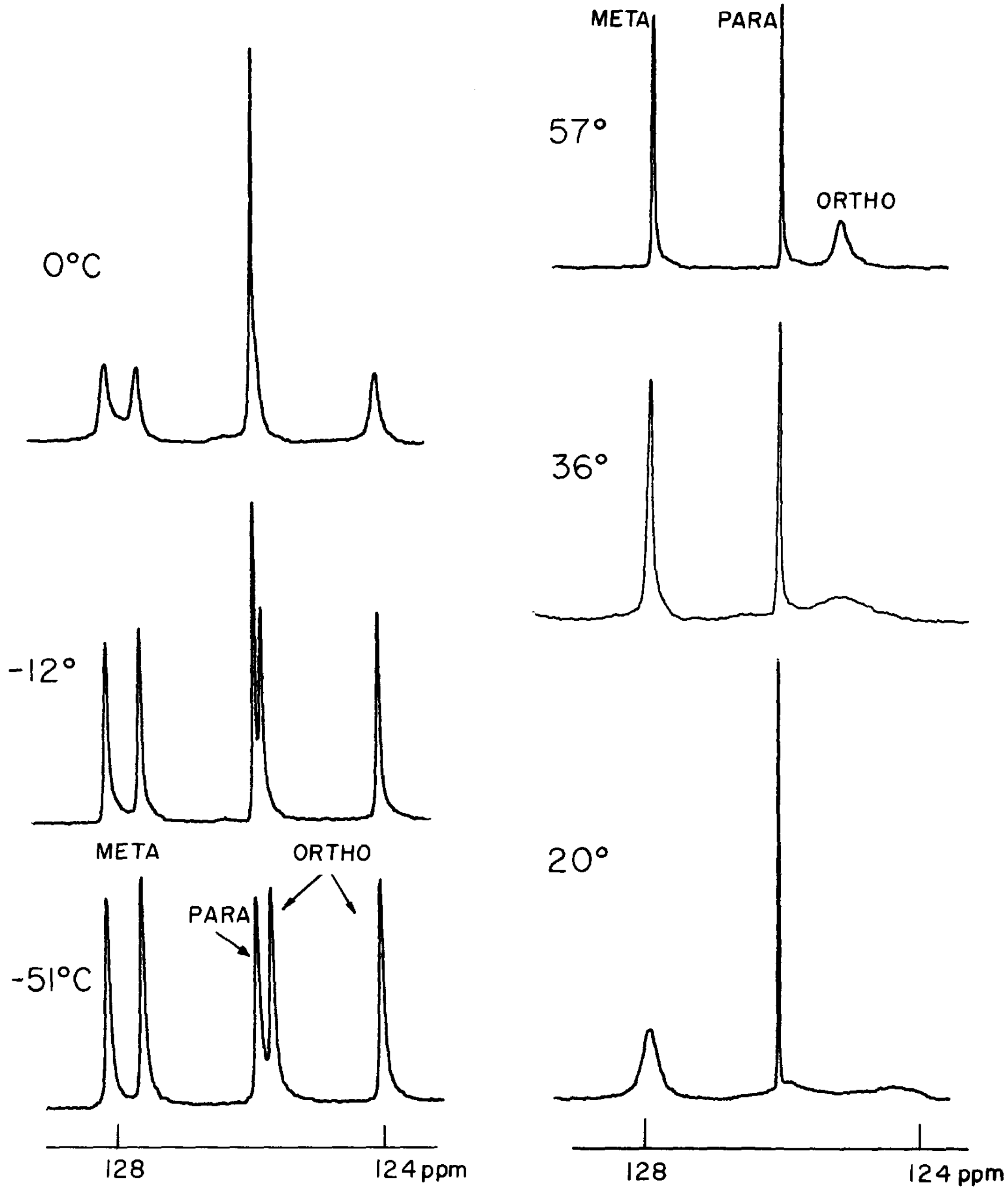
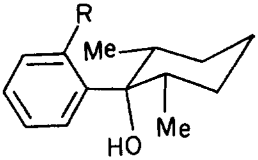
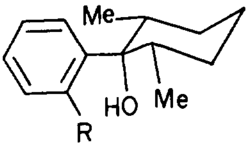


Figure 1. The variable temperature ^{13}C NMR spectrum (aromatic region) of 2-*c*-methyl-6-*c*-methyl-1-phenylcyclohexanol (300 mg in 2 ml of $CDCl_3$ in a 12 mm tube). Spectra were determined on a Varian XL-100/15 spectrometer. The spectral window was 2000 Hz, giving a digital resolution of 1 Hz. No line broadening was applied.

there was no change in the conformation of the cyclohexane ring. These results clearly demonstrate that the phenyl group in 2,6-dimethyl-1-phenylcyclohexanol is sterically inhibited from undergoing free rotation below 0°C. Line shape analysis[11] was carried out on these temperature dependent spectra, and the free energy of activation ($\Delta G^{\ddagger}$) for rotation of the phenyl group in (5) was found to be 15.2 kcal/mol.

When the ^{13}C NMR spectrum of dendrocrepine was determined at +57°C the six phenyl resonances were reduced to four at 143.1 (1'), 127.8 (meta), 126.3 (para), and 125.9 (ortho) ppm, indicating that the phenyl groups in this alkaloid are also free to rotate at this higher temperature. We believe that it will be possible to prepare stable rotational isomers of the type illustrated below.[12]





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References and Notes

1. Contribution No. 160 from this Laboratory. This paper is dedicated to Professor D. H. R. Barton on the occasion of his 60th birthday, September 8, 1978.
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