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CONFORMATIONAL STUDIES. XVI. NONCHAIR POPULATIONS OF 2-*t*-BUTYL-5-METHYL-1,4-CYCLOHEXANEDIOLS AND *TRANS*-2-*t*-BUTYL-*TRANS*-5-METHYLCYCLOHEXANOL.[1]

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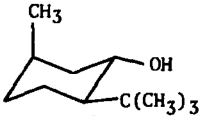
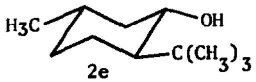
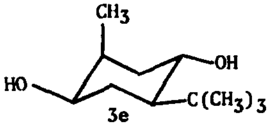
In their study of 2,5-dialkylcyclohexanols, Feltkamp and Franklin[3] found that *trans*-2-*t*-butyl-*trans*-5-methylcyclohexanol (1) unexpectedly gave a C-1 proton nmr band width smaller by 2.5 Hz than that of its *trans*-*cis* epimer (2). In interpretation of this result, they considered two possibilities. Either the ring of chair conformation 1e is deformed by its axial methyl group, or 1e must be present in solution in rapid equilibrium with significant populations of other conformations having C-1 proton nmr band widths smaller than that of 1e. They felt that the latter possibility was "extremely unlikely." We report here results of an nmr study of 2-*t*-butyl-5-methyl-1,4-cyclohexanediols (3 - 6) which brought us to the opposite conclusion; ring deformation is not a major factor, but conformations other than chair 1e must be populated significantly (>10%) for 1. Clearly, the strong *t*-butyl-hydroxyl gauche interaction[4,5] plus the two 1:3 diaxial methyl-hydrogen interactions destabilize chair 1e relative to other conformations of 1 in which these interactions may be relieved.



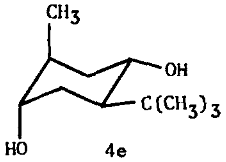
1e



2e

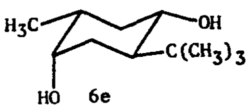


3e



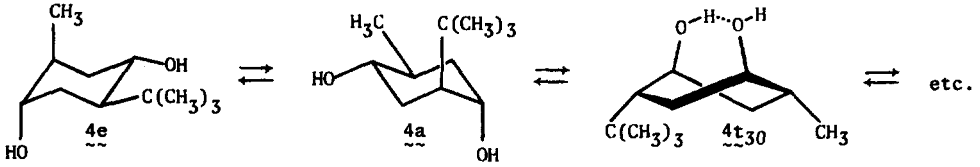
4e

5e



6e

We have prepared diols 3 - 6, the C-4 hydroxyl derivatives of 1 and 2. Because the structural difference between diols 3 and 4 is a subtle one, the large difference in their conformational properties is most remarkable. Introduction of an equatorial hydroxyl group at C-4 of 1e (to give 3) stabilizes the equatorial chair conformation (3e) and/or destabilizes its competitors to the extent that no evidence for detectible populations of other conformations of 3 was obtained. However, introduction of an axial hydroxyl group at C-4 of 1e (to give 4) destabilizes the equatorial chair conformation (4e) and/or stabilizes its competitors to the extent that substantial populations of other conformations of 4 were detected by nmr and infrared spectroscopy. Indeed, the population of chair 4e must be less than 66%.



The reported[3] C-1 proton nmr band widths of 1 and 2, 20.5 and 23.0 Hz respectively, may be compared to the values found for diols 3, 24.2 Hz; 4, 17.8 Hz; 5, 23.5 Hz; and 6, 24.3 Hz. Only the values of 1 and 4 deviate from the range 23.0 - 24.3 Hz, the band width range actually expected[3] for the equatorial chair conformations, 1e - 6e. These band width comparisons show clearly that neither 1 nor 4 is conformationally homogeneous.

Conclusive evidence for presence of significant populations of nonchair conformations of diol 4 has been obtained. Infrared spectra of 0.001 and 0.0025 M carbon tetrachloride *solutions of diol 4 show a broad absorption peak at 3513 cm^{-1} attributable to hydroxyl groups* the hydrogen atoms of which are intramolecularly hydrogen bonded in nonchair conformations such as $4t_{30}$, illustrated above, with an estimated population of 7 - 14%.[6] All other hydroxyl groups in the solution contribute to an unsymmetrical absorption peak at 3622 cm^{-1}. The hydrogen bonded conformations may comprise a small fraction of the total nonchair population of diol 4. This point was explored further by nmr spectroscopy.

Whereas diol 3-3,3,4,5-d_4 in methanol-d_4 showed negligible temperature dependence of the C-1 proton nmr band width, diol 4-3,3,4,5-d_4 in methanol-d_4 showed a 3.4 Hz decrease in band width as the temperature was raised from -30° to 86° (Table). Thus, the population of chair 4e decreased with increasing temperature. Vicinal coupling constants for the *deuterium-substituted derivatives of diols 3 - 5 are given in the Table.*[7]

Assuming that the configuration of the hydroxyl group at C-4 does not affect the vicinal coupling constants involving the C-1 proton of 3 and 4, and assuming that chair 3e is the only conformation significantly populated for diol 3, one could equate the coupling constants and band width observed for 3-3,3,4,5-d_4 (Table) with those expected for chair 4e-3,3,4,5-d_4.

TABLE

NMR C-1 PROTON BAND WIDTHS AND VICINAL COUPLING CONSTANTS FOR DIOLS 3 - 6.[a]

		Coupling Constants, Hz			Band Width, Hz	
Diol	T, °C	J_{AX}	J_{BX}	J_{CX}	W_{Calcd}[b]	W_{Obs}[c]
3-3,3,4,5-d_4	33°	4.4	11.0	10.2	25.6	25.4[d]
4-3,3,4,5-d_4	86°	3.9	7.0	6.7	17.6	17.7
	41°	3.9	7.6	7.2	18.7	18.8
	-11°	3.8	8.4	8.0	20.2	20.2
	-30°	3.9	8.9	8.4	21.2	21.1
5-3,3,4,5-d_4[e]	33°	4.2	10.9	9.9	25.0	24.9
6-3,3,4,5-d_4	33°	-	-	-	-	25.6

[a] The 3,3,4,5-d_4 derivatives of diols 3 - 6 were studied in methanol-d_4 solution at 100MHz with irradiation of deuterium.[9]

[b] The calculated band width, W_{Calcd}, is $J_{AX} + J_{BX} + J_{CX}$.

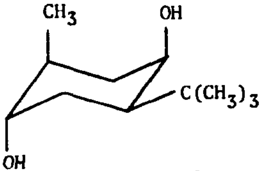
[c] Observed band widths are measured to better than 0.2 Hz, and appear to be 1.0 - 1.4 Hz larger for the 3,3,4,5-d_4 derivatives listed here than for the corresponding d_0 diols given earlier in the text.

[d] The observed band width was essentially independent of temperature for 3-3,3,4,5-d_4: W_{Obs} = 25.3 Hz at 61°; 25.7 Hz at -40°.

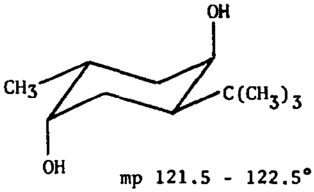
[e] In pyridine plus deuterium oxide.

At 41° for 4-3,3,4,5-d_4, $W_{Obs} = N_eW_e + (1-N_e)W_x = 18.8$ Hz, where N_e is the mole fraction of chair 4e-3,3,4,5-d_4, W_e = 25.4 Hz (taken equal to W_{Obs} for 3-3,3,4,5-d_4), and W_x is the weighted average band width of all other conformations present. Since $W_x > 6$ Hz (the minimum band width expected for any conformation of 4-3,3,4,5-d_4), solving for N_e gives: $N_e < 0.66$. Therefore, at 41° in methanol-d_4 solution, the population of chair conformation 4e-3,3,4,5-d_4 must be less than 66%. The trans vicinal coupling constants, J_{BX} and J_{CX} (Table), taken individually, support a comparable limit. A more detailed analysis[2] suggests the following chair populations: 50 ± 10% of 4e, and 12 ± 10% of 4a (the remainder, 38 ± 20%, being the total nonchair population of 4 under these conditions).

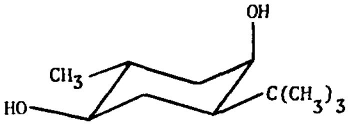
All eight racemic 2-t-butyl-5-methyl-1,4-cyclohexanediols have been prepared and characterized.[2] Configurations have been established.[2] Only the all *cis*-isomer, mp 99 - 100°, has been reported previously.[6] In addition to diol **3**, mp 130 - 131.5°, diol **4**, mp 128.5 - 129°, diol **5**, mp 184.5°, and diol **6**, mp 175 - 175.5°, shown above, the three other new isomeric diols are shown below.



mp 93 - 95°



mp 121.5 - 122.5°



mp 156.5 - 157°

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5. R. D. Stolow, A. A. Gallo, and James L. Marini, *Tetrahedron Lett.*, 4655 (1969).
6. Compare R. D. Stolow, P. M. McDonagh, and M. M. Bonaventura, *J. Am. Chem. Soc.*, **86**, 2165 (1964).
7. The values reported as "coupling constants" in ref. 3 are actually *splittings*. In his review of ref. 3 (ref. 8, pp. 294-295), Booth has made this point explicitly.[8] Comparison of "coupling constants" from ref. 3 with those given in the Table would be invalid.
8. H. Booth, in *Progress in Nuclear Magnetic Resonance Spectroscopy*, Vol. 5 (editors J. W. Emsley, J. Feeney and L. H. Sutcliffe), Pergamon Press, Oxford (1969), presents a comprehensive review (through May 1967) of applications of nmr to conformational analysis of cyclic compounds.
9. See footnote 13 in ref. 4.