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# STEREOCHEMICAL ASPECTS OF PROTON CHEMICAL SHIFTS. II

# THE INFLUENCE OF THE HYDROXYL SUBSTITUENT ON THE CHEMICAL SHIFT OF THE RING PROTONS IN CYCLOHEXANE DERIVATIVES.

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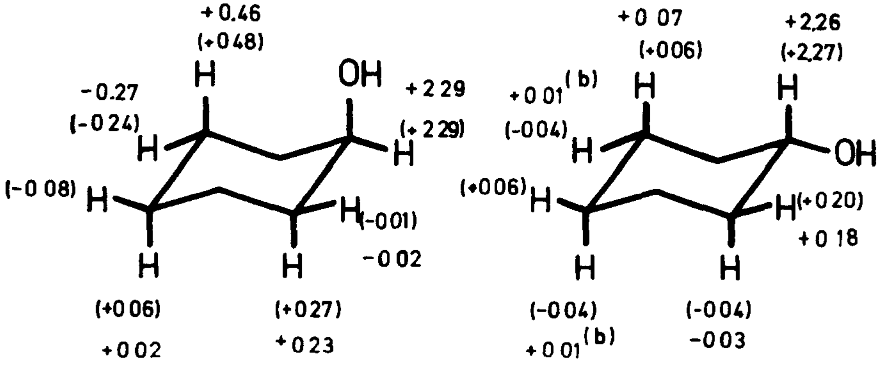
Recently we have published (1) the influence of methyl substitution on the chemical shift of the ring protons in cyclohexane derivatives, and now wish to report on our preliminary findings related with hydroxyl substitution. Some shift increments have been reported (2) and shift values may be found for partially deuterated cyclohexanols (2a,3), but inspection of these literature data reveals several discrepancies. In our continuous effort to obtain reliable shift increments we have studied 300 MHz spectra of the isomeric 3-Me, 4-Me and 4-t-Bu cyclohexanols, and were able to extract from the $^1$H NMR spectra (4) precise chemical shifts of almost all of the ring protons. By comparison with the shift values observed (1) in the parent alkylcyclohexanes the OH-shift increments were obtained as depicted in chart 1.



(a) Values between brackets: Me-cyclohexanols, others for 4-t-Bu-cyclohexanols. (b) Deduced from a broad degenerate multiplet of the 4a and 3a protons in trans-4-t.butylcyclohexanol.

Besides the practical impact for structural assignments, the observed increments merit two major comments.

1. Increments for vicinal protons *cis* related to a substituent are comparable, ($\Delta$OH $\sim$ 0.0 ppm), but an equatorial-equatorial arrangement deshields the ring protons by 0.2 ppm. These facts parallel the behaviour for methyl substitution (1), where also the *cis* protons undergo the same influence no matter the orientation of the methylgroup ($\Delta$Me $\sim$ -0.3 ppm), but the equatorial protons are displaced to lower field by an equatorial methyl group ($\Delta$Me $\sim$ 0.0 ppm ). We believe that in each instance the observed increment in the *cis*-case is the normal value. It is indeed the predicted value for a gauche (ca. 60°) relationship both in the methyl and the hydroxyl case. This prediction is based on an interpolation between the eclipsed and clinal position (ca. 120°) as observed in the $-CH_2-CHX-$ fragment of substituted acenaphtenes (5). In 1-methyl-adamantane introduction of this methyl group causes a 0.3 ppm shielding of the $\beta$ protons (6). These data clearly show that the anomaly is to be identified with the equatorial-equatorial case.

2. There is a remarkable shielding effect by an axial substituent (OH see Chart 1; Me see ref. 1) on the *equatorial* $\gamma$-proton when its geminal partner (the "synaxial" $\gamma$-proton) is deshielded in the known way (7b). Contrary to the well documented "steric compression" effect (van der Waals deshielding) of the latter, the shielding of the equatorial ring proton has not been recognised generally. Although the effect has been noted in some halfcage compounds (7a), in N-*t*-Bu-aziridines (7b), in 1,3-dioxanes (8) and in Me- (1), or MeO-substituted *c*.hexanes (9), it has, to the best of our knowledge, never been invoked in any chemical shift calculation. It might well be that this is "..the specific effect, that is being omitted in the calculation", Allinger (10) mentions in his paper. In any way, all of the models used up to now (11), only reproduce a proton deshielding by an included van der Waals term.

In a recent publication, Remijnse et al. (12) explain the anomalous behaviour of ring protons vicinal to methyl groups by an "unideality" of the chair. Ring distortion in terms of an altered C-C bond anisotropy contribution has been invoked (13) as being the origin of the anomaly, but as pointed out earlier (8b) small deviations of about 5° can hardly explain shift differences up to 0.3 ppm. The same argument holds for the angular dependent chemical shift contribution introduced by Fay et al. (5). It should be noted in this context, that introduction of even a t.Bu group, that is known to provoke minor distortion in the opposite side of the ring (14), does not alter the anomalous effects, observed in methyl substituted cases (Chart 1).

As a conclusion, equatorial protons in cyclohexanes, substituted in a vicinal position by a variety of groups, are approximately 0.25-0.30 ppm more deshielded than expected, an effect that is not explained by any existing chemical shift theory Also the shielding of the $\gamma$-equatorial ring proton as caused by an axial substituent deserves more attention. With respect to the latter, the $\gamma$-shielding effect (15) in $^{13}$C-NMR spectroscopy is certainly noteworthy.

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