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AN EMPIRICAL CORRELATION OF NMR CHEMICAL SHIFTS AND CONFORMATIONS IN ETHERS AND AMINES

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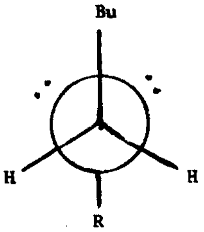
In 1967, Goldberg, Lam and Davis[1] reported an unexpected upfield shift for the methylene hydrogens of neopentyl groups adjacent to ether or amine heteroatoms. In 1969 Tani and Oguni[2] reported a similar unexpected upfield shift for the similar neopentyl type tertiary hydrogen in poly(t-butylethylene oxide). We have now prepared several monomeric and dimeric units of this polymer and have observed the same unexpected upfield shift for neopentyl ether hydrogens;[3] but not for the corresponding neopentyl-like alcohols.

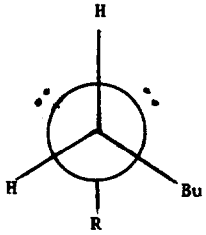
We[4] and Tani and Oguni[2] have ascribed the unusual nmr spectra of the two crystalline poly(t-butylethylene oxides) to highly preferred conformations at the C-C polymer chain bond.

We now wish to suggest that the "neopentyl ether shift" is due to steric factors producing preferred conformations at the C-O bond in neopentyl ethers and the C-N bond in neopentyl amines. It is possible to estimate the magnitude of the observed shifts by (a) postulating that an unshared electron pair in a skew relationship to an α-H produces an nmr chemical shift of 1.7 ppm, and (b) assuming reasonable conformational equilibria.

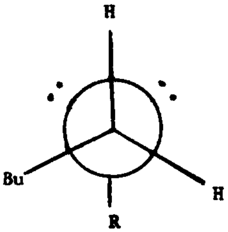
Consider first the conformational relationships at the C-O bond in neopentyl alcohol or ether.



A



B

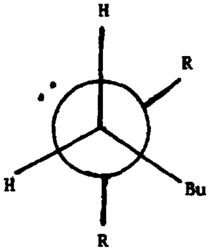


C

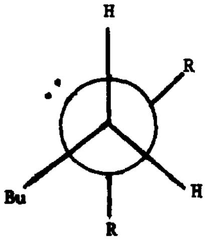
For free rotation at the C-O bond (i.e., for R = H or Bu ≠ t-Bu), both hydrogens in A would be shifted downfield from the normal methylene position (δ 1.2 ppm) by 1.7 ppm to δ 2.90 ppm, whereas in B and C one hydrogen would be skew to <u>two</u> adjacent electron pairs and shifted downfield by 3.4 ppm to δ 4.6 ppm or an average for the two hydrogens of δ 3.75 ppm. The average then for conformations A, B and C would be $(2.9 + 3.75 + 3.75)/3 = \delta\ 3.47$ ppm. This value is in good agreement with the δ 3.4 ppm observed for most methylene groups adjacent to oxygen in unhindered open chain alcohols and ethers.

When Bu = t-Bu and R = alkyl, hindrance in conformations B and C would favor conformation A, δ 2.90 ppm, in good agreement with the observed position for neopentyl ethers of 2.95 - 3.00 ppm.[1,2,3] In cyclic ethers, in which a carbon ring joins R to Bu, conformation A is excluded so the time-averaged chemical shift would be expected to be δ 3.75 ppm, in agreement with 3.63 for THF and 3.83 for 1,3-dioxanes.[5]

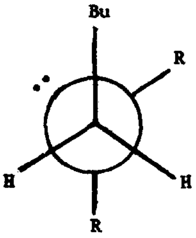
The three classical conformations at a C-N bond are indicated below.



A'



B'



C'

In conformation A' both hydrogens are skew to the unshared pair on nitrogen and would be shifted downfield from δ 1.2 ppm by 1.7 ppm to δ 2.9 ppm while for B' and C' only one hydrogen is shifted downfield so the average would be δ 2.05 ppm. The average for equal population of conformations A', B' and C' would be δ 2.33 ppm, which is a bit low for the observed value of δ 2.5 - 2.55 ppm in unhindered open chain tertiary amines. Better agreement would be based on the postulate that for unhindered amines, A' is preferred over B' or C' by a factor of 2 (calculated δ 2.48 ppm). For primary amines, with R = H and Bu a primary alkyl group, the observed shift of δ 2.65 - 2.70 ppm[6] would be consistent with an even greater preference (5:1) for conformation A', calculated δ 2.66 ppm.[7] The factor promoting conformation A' cannot be steric; perhaps it results from an attraction of hydrogens on carbon for the unshared pair on nitrogen.

For hindered amines, i.e. Bu = t-Bu and R = alkyl, the observed δ 2.01 ppm[1] is accurately predicted by excluding A', calculated δ 2.05 ppm.

The case of cyclic amines is complicated by the controversial question of the preferred configuration at nitrogen, i.e., R_{eq} vs R_{ax}.

In R_{eq}, H_{ax} is trans to the unshared pair and would have no chemical shift whereas in R_{ax}, both hydrogens are skew to nitrogen and would be expected to appear at δ 2.9 ppm. An indiscriminate equilibrium would then predict δ 2.48 ppm. The observed value of δ 2.26 ppm for N-methyl piperidine[8] would be in better accord with a three-to-one preference for the conformation with R_{eq} (calculated δ 2.26 ppm). For R = H, the observed value for piperidine, δ 2.67 ppm,[8] would indicate a three-to-one preference for the configuration R_{ax}; calculated δ 2.69 ppm. Thus our rule is in accord with the view that CH_3 > unshared pair > H,[9] rather than the order CH_3 > H > unshared pair.[10]

For a nitrogen heterocycle of fixed configuration at N, triethylene diamine (1,4-diazabicyclo-(2,2,2)octane), with a geometry corresponding to R_{ax}, the observed value of δ 2.85 ppm is in good agreement with calculated (δ 2.9 ppm).

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