

MAGNETIC ANISOTROPIES AND ELECTRIC FIELD EFFECTS  
FOR THE HYDROXYL, AMINO, CHLORO AND BROMO GROUPS

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Previous reports on the origin of proton chemical shifts which arise on the introduction of a C-X bond (X is =O, C≡N, OH or Cl) into a molecule, have invoked either magnetic anisotropy alone<sup>1-8</sup> or have concluded<sup>9</sup> that only the electric dipole is important. Recent calculations<sup>10</sup> on C-Cl and C-F bonds have claimed to combine both effects in one, deriving apparent group anisotropies.

Using the general approach outlined in previous publications<sup>11-13</sup> we wish to report the derivation of the "apparent group" magnetic and electric field parameters for the hydroxyl, amino, chloro and bromo groups.

For the hydroxyl and amino substituents, a freely rotating model was assumed axially symmetric with respect to the C-N and C-O bonds<sup>9</sup>. The C-Cl and C-Br bonds were assigned conical symmetry.

The position of the electric and induced magnetic dipoles was taken as coincident and our calculations investigated the effects of varying this position along the internuclear bond. The diamagnetic anisotropy of the displaced C-H bond was also assigned various values between zero and  $7.54 \cdot 10^{-30} \text{ cm}^3/\text{molecule}$  (12).

5 $\alpha$  androstane was used as a standard and equations set up using the C-19 and C-18

chemical shifts in a series of mono-substituted-5 $\alpha$ -androstanes : these were solved by the method of least squares. The chemical shifts of the amino, chloro and bromo steroids were measured in deuterocyclohexane while those of the androstanols were measured in deuteriochloroform.

#### Hydroxy and Amino Groups

Initial calculations indicated discrepancies between observed and calculated shifts for substituents on a carbon atom vicinal to the methyl group such as 17 $\beta$ /18 methyl. Anomalous shifts of this kind have been previously noted and explanations proffered in terms of solvent cage distortion<sup>9, 18</sup>. Because such shifts cannot be explained solely in terms of diamagnetic anisotropy and electrostatic effects however, they were excluded from the final calculations.

The 11 $\alpha$  substituted androstanes were likewise excluded because of the possibility of intermolecular hydrogen binding with the 1 $\beta$  proton and their departure from a freely rotating situation.

Table 1 shows the values of magnetic anisotropy and electric field parameters derived from fourteen hydroxy and amino androstanes.

These values were used to recalculate the shifts for the C-18 and C-19 methyl groups when for the monosubstituted hydroxy androstanes calculated and observed shifts all agreed within  $\pm 1.5$  Hz\*, and for the amino androstanes, all but one agreed within  $\pm 3$  Hz. Further it was shown that the observed shifts are predicted less satisfactorily by using either the magnetic anisotropy or electric field effects alone. When both are used however, the electric contribution is either greater than or equal to the magnetic contribution.

#### Chloro and Bromo Groups

Because of the anomalous nature of the C-19 signal in 5 $\alpha$  halo steroids (cf. ref. 9) such examples were omitted from final calculations.

For C-Cl and C-Br bonds, the use of both magnetic and electric effects would appear to offer little overall advantage as opposed to use of the electric field alone since in neither case is magnetic anisotropy the controlling factor, the major contribution coming

\* All frequency values are quoted with respect to the field at 100 MHz.

from the electric field effect.

For such calculations the value of the electric shielding constant is shown in Table I (A). When these values are used to calculate chemical shifts for the C-18 and C-19 methyl groups of the twelve mono-chloro androstanes, all but three of twenty-two calculated values agree within ( $\pm$ ) 3 Hz of the observed value. Similar agreement is observed for the eleven mono-bromo androstanes.

One notable exception to this view is those cases (2 $\beta$ , 4 $\beta$ , 6 $\beta$ /19) where a 1,3 syn-diaxial relationship exists and where observed shifts are of the order of -30Hz. In such cases, magnetic and electric effects must both be invoked in order to explain the observed values : for this the relevant constants are as in Table 1 (B).

Because of such examples in the steroids as well as in other rigid cyclic systems, we deem it prudent to include both magnetic and electric effects in any calculations of chemical shifts.

For all the functional groups considered here, the best agreement between observed and calculated shifts was noted when the coincident point dipoles were placed on the more electronegative atom, and when the diamagnetic anisotropy of the displaced C-H bond was zero; other recent reports<sup>14, 15</sup> would likewise suggest that the C-H bond be taken as isotropic.

Application of the above 'group factors' to steroidal positions not included in the original analysis of mono-substituted androstanes gave calculated shifts in good agreement with literature figures taken from polysubstituted examples.

The application of these parameters to chemical shift calculations may be illustrated by reference to the ethylene ketal of 5-Bromo-Pentacyclo [5.3.0.0<sup>2,5</sup>.0<sup>3,9</sup>.0<sup>4,8</sup>]decan-6-one (Table III). Successful calculations have also been carried out for the C-8 and C-9 (but not C-10) methyl groups in borneol and isoborneol and for certain proton shifts in arylcyclohexanols (Table II). In addition satisfactory results have been achieved for 1- and 2-Adamantyl halides and various halogenated bornane derivatives

Geometric factors were calculated from X-ray data<sup>16</sup> and all calculations were carried out on the ICL 1904 computer of the University of Bradford.

TABLE 1

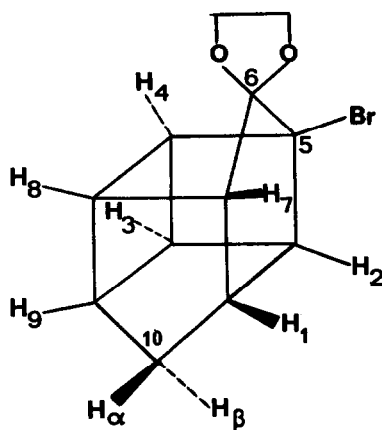
	Preferred position of dipole ( $\text{Å}^0$ ) distance from carbon atom.	Magnetic anisotropy $\text{cm}^3/\text{molecule}$	Electric field constant K $\text{cm}^3/\text{molecule}$
-NH <sub>2</sub>	1.47	$-5.59 \times 10^{-30}$	$-9.59 \times 10^{-30}$
-OH	1.42	$-5.48 \times 10^{-30}$	$-8.50 \times 10^{-30}$
C-Cl (A)	1.77	0	$-2.4 \times 10^{-30}$
C-Br	1.91	0	$-8.4 \times 10^{-30}$
C-Cl (B)	1.77	$-4.5 \times 10^{-30}$	$-8.9 \times 10^{-30}$
C-Br	1.91	$-4.0 \times 10^{-30}$	$-10.2 \times 10^{-30}$

TABLE II

	Observed resonance	Calc. (Hz) at 100 MHz	Obs. (Hz) at 100 MHz
Iso-borneol-bornane	C-9 methyl	-3.3	0.0
	C-8 methyl	-17.5	-19.0
Borneol-bornane	C-9 methyl	-2.2	-3.0
	C-8 methyl	-0.3	-3.0
Arylcyclohexanol- arylcyclohexane	Proton in 1-3 cis diaxial relationship with OH	-55.3	-65.3
	Proton in 1-4 trans diaxial relationship with OH	-5.2	-9.0

TABLE III

<u>PROTON</u>	<u>CALCULATED SHIFTS</u> Hz at 100 MHz	<u>OBSERVED SHIFTS</u> Hz at 100 MHz
H <sub>1</sub>	-9.3	-11.0
H <sub>2</sub>	-35.4	-28.5
H <sub>3</sub>	-16.6	-11.0
H <sub>4</sub>	-31.9	-28.5
H <sub>7</sub>	-13.4	+ 2.8 *
H <sub>8</sub>	-11.7	-28.5 *
H <sub>9</sub>	-8.7	-11.0
H <sub>10α</sub>	-7.4	-11.0
H <sub>10β</sub>	-3.1	- 6.5



\* Discrepancies in the case of H<sub>7</sub> and H<sub>8</sub> are similar to those noted <sup>17</sup> for the δ protons of 1-haloadamantanes and the D protons of the 2-substituted compounds.

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