The Dominant Role of Electric Field and the Questionable Role of Anisotropy Effects of Single-Bond Substituents in ^{1}H NMR Shifts. Shielding Mechanisms of and Steric Distortions in Some Monosubstituted Steroids

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^{1}H NMR shifts of 19-methyl protons in cholestanes bearing halo and hydroxy substituents in 3- and 5-positions are reported, compared with 2-, 4-, and 6-substituted steroids, and analyzed for the relevant shielding mechanisms. Linear electric-field effects correctly predict sign and magnitude of observed shift increments as well as the substantial differences between 3α- and 3β-substituted compounds; substituents situated closer to the observed nuclei show deviations ascribed to through-bond effects. Except for the oxo substituent, no correlation is found with anisotropy effects calculated from literature Δχ values. On the basis of MM1 force field minimized structures, steric distortions as van der Waals effects and sterically induced charge polarizations are investigated and are found to be negligible with the exception of the 3-oxo steroid. Shifts of the protons at C3 and those of some 17-substituted estr-4-ene derivatives are also reported.

Introduction to Methods and Earlier Work

Although anisotropy and electrical-field effects are invoked in countless publications for the rationalization of proton shifts, even a semiempirical basis for the application of these concepts still presents serious difficulties, in particular with regard to the effects of C–X single bonds.[1] The differentiation of shielding mechanisms is easier with long-range substituent effects on NMR shifts, which, besides holding promise for the recognition of charge-density variations,[2] are an important tool for deriving molecular structures from shifts. Thus the exchange of substituents in steroids leads to characteristic changes of the angular methyl proton shifts. After the early work of Zürcher,[3a] the corresponding shift increments have been found to be consistent and additive in many compounds.[4]

The origin of the observed shielding variations[5] has been sought mainly in magnetic anisotropy contributions σ_{an}, as given by the McConnell equation (eq 1), and in linear

$$\sigma_{an} = \Delta\chi(1 - \cos^2\theta)/3r^3 \quad (1)$$

electric-field effects σ_{el}, as quantified by Buckingham (eq 2). The differential dependence of σ_{an} and σ_{el} on geometry

$$\sigma_{el} = kq_xP_{CY}l_{CY}^{-1}r^{-2} = \text{constant } E_Z \quad (2)$$

factors involving r^{-3} or r^{-2}, susceptibility Δχ, and charge q values from different sources together with shift observations in steroids have been used for estimating σ_{an} and σ_{el}. For C–X single bonds, Zürcher[3a] concluded that electrical-field effects dominate,[3b] whereas for multiple bonds he[3a] and ApSimon et al.[6] arrived at larger anisotropy contributions.[7] It is difficult to assess the validity of earlier calculations which were partially published in preliminary form only. The approximation of actual C–X dipoles by single-point charges[3,6,7] can lead to errors, particularly at shorter intramolecular distances. In some investigations, the considerable variation in C–X dipole length has been neglected.[3,6,7] The location of both the pole and the point of field action on a polarized bond has been treated arbitrarily or has been searched for by variation to consistency of experimental and calculated shifts.[3,6,7] By use of similar procedures, polarity and/or Δχ of the C–H bond displaced by the C–X bond has been either neglected or varied. The calculational variations mentioned above can lead to a large number of possible σ_{an} and σ_{el} combinations. The discrepancies of up to 500% between reported Δχ values (Table 1)[40] indicate the difficulties involved particularly with σ_{an} calculations.[1,7a,8]

In the present paper, linear electric-field effects are calculated for proton shifts in steroids on the basis of a procedure and parametrization which succeeded in rationalizing some long-range substituent effects on ^{13}C NMR shifts.[9-11] Anisotropy contributions, which are known to play only a minor role in carbon shielding,[12] are investigated by using literature Δχ values (Table 1).[40] Steric perturbations, which have been recognized on a quantitative basis for ^{13}C shifts,[13,14] but, to our knowledge,

(1) For recent examples and leading references see J. B. Lambert and J. E. Goldstein, *J. Am. Chem. Soc.*, **99**, 5689 (1977).
(2) D. G. Farnum, *Adv. Phys. Org. Chem.*, **11**, 123 (1975).
(3) (a) R. F. Zürcher in "Progress in NMR Spectroscopy", Vol. 2, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Eds., Pergamon Press, Oxford, 1967, p 205. (b) For similar conclusions see J. A. ApSimon, H. Beierbeck, and D. K. Todd, *Can. J. Chem.*, **50**, 2351 (1972).
(4) W. Arnold. W. Meister and G. Englert, *Helv. Chim. Acta*, **57**, 1559 (1974).
(5) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, Oxford, 1969, p 61ff.
(6) For C=O bonds: (a) J. W. ApSimon, P. V. Demarco, D. W. Mathieson, W. G. Craig, A. Karim, L. Saunders, and W. B. Whalley, *Tetrahedron*, **26**, 119 (1970); (b) J. W. ApSimon and H. Beierbeck, *Can. J. Chem.*, **49**, 1328 (1971). For C–C bonds: (c) J. W. ApSimon, W. G. Craig, P. V. Demarco, D. W. Mathieson, L. Saunders, and W. B. Whalley, *Tetrahedron*, **23**, 2357 (1967).
(7) For similar approaches see, e.g., (a) J. Horner and D. Callaghan, *J. Chem. Soc. A*, 518 (1968); (b) A. K. Davis, D. W. Mathieson, P. D. Nicklin, J. R. Bell, and K. J. Toyne, *Tetrahedron Lett.*, 413 (1973).
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(9) H.-J. Schneider, W. Gschwendtner, and U. Buchheit, *J. Magn. Res.*, **26**, 175 (1977).
(10) H.-J. Schneider and W. Freitag, *J. Am. Chem. Soc.*, **99**, 8363 (1977).
(11) H.-J. Schneider, W. Freitag, W. Gschwendtner, and G. Maldener, *J. Magn. Res.*, **36**, 273 (1979).
(12) See, e.g., (a) G. J. Martin, M. L. Martin, and S. Odiot, *Org. Magn. Reson.*, **7**, 2 (1975); (b) G. E. Maciel, *Top. Carbon-13 NMR Spectrosc.*, 1, 53 (1974); (c) G. Miyajima and K. Nishimoto, *Org. Magn. Reson.*, **6**, 313 (1974); (d) H.-J. Schneider and V. Hoppen, *J. Org. Chem.*, **43**, 3866 (1978).
(13) H.-J. Schneider and E. F. Weigand, *J. Am. Chem. Soc.*, **99**, 8362 (1977).

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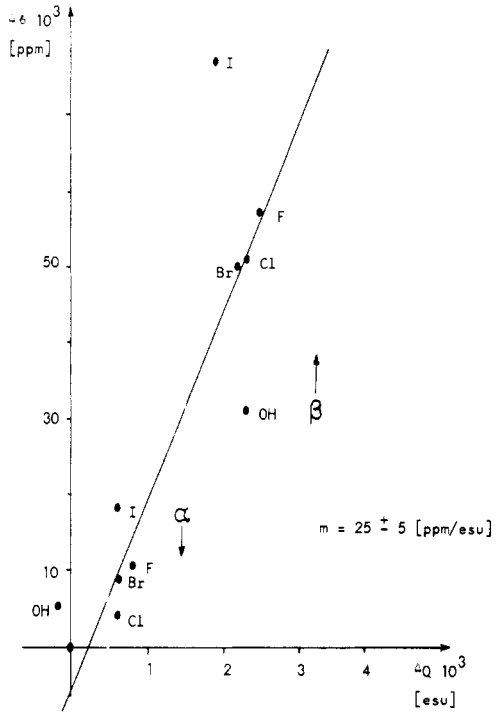


Figure 1.

Table II. Observed and Calculated Shielding Increments on 19-Me Protons in 3-X-Cholestanes[a]

3β-X	Δδ obsd[b]	Δδ el[c]	Δδ an[d]
F	0.057	0.045	0.002
Cl	0.051	0.041	−0.005
Br	0.050	0.039	−0.014
I	0.077	0.034	−0.023
OH	0.031[g]	0.041	0.001
Me	−0.017		
3α-X			
F	0.005	0.014	−0.039
Cl	0.004	0.011	−0.060
Br	0.009	0.011	−0.075
I	0.018	0.011	−0.103
OH	−0.002[g]	0.009	−0.041
Me	−0.003		
3=O[f]	0.233[h]	0.039	0.201
			0.137
	0.037[e,h]		0.026[e]
			0.018[e]

[a] In parts per million relative to X = H (0.777 ppm[h]). [b] Measured in 20–30% $CDCl_3$ solutions at 27 °C and 90 MHz. [c] Calcd. with eq 2 with k = 17.8 ppm/eu. [d] Calcd. with eq 1 and Δχ* literature values (see Table 1).[40] Observed and calculated shielding increments on 18-Me protons relative to X = H (0.647 ppm[h]). [f] $\Delta\delta_{an}$ calculations were carried out with two Δχ sets from Table 1, using ApSimon's equation.[6a,b] [g] J. C. Jacquesy, R. Jacquesy, J. Levisalles, J. P. Pete, and H. Rudler, *Bull. Soc. Chim. Fr.*, 2224 (1964). [h] Cf. D. Lavie, S. Greenfield, Y. Kashman, and E. Glotter, *Isr. J. Chem.*, 5, 151 (1967).

not yet for ^1H shielding variations, are studied with the aid of force-field calculations and subsequent estimations of van der Waals square electric-field effects[5] and sterically induced charge polarizations along C–H bonds.[13-16]

Table III. Increments in 5-X Cholestanes[a]

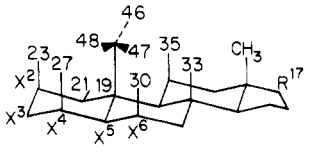
5α-X	Δδ obsd[b]	Δδ el[c]	Δδ an[d]
F[e]	0.156	0.082	−0.154
Cl	0.253	0.077	−0.200
Br	0.233	0.071	−0.232
OH	0.180[f]	0.073	−0.158
5β-X			
Cl	0.149	0.134	+0.135
Br	0.113	0.128	+0.158
OH	−0.013[f]	0.123	+0.101

[a] In parts per million relative to X = H (5α-H 0.777 ppm (footnote *h*, Table II); 5β-H 0.924 ppm). [b] Measured in 20–30% $CDCl_3$ solutions at 27 °C and 60 MHz. [c] See footnote *c*, Table II. [d] See footnote *d*, Table II. [e] Since 5α-fluorocholestane was not available, 3β-acetoxy-5α-fluorocholestane was measured relative to 3β-acetoxy-5α-cholestane (19-Me protons 0.821 ppm (footnote *h*, Table II)). [f] See footnote *h*, Table II.

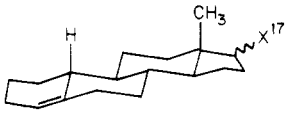
Since a large number of hetero substituents substantially increases the information on possible shielding mechanisms, we have prepared, by standard procedures, and measured data on cholestanes where only one substituent at a time is varied in the 3- or 5-position. For most substituents, both α and β configurations (**3α,β**; **5α,β**) were investigated and complemented by some literature data on 2-, 4-, and 6-substituted androstanes. In studying ^{13}C NMR shielding mechanisms, we have found a considerable dependence on refined molecular geometries.[14] Evaluation of $E_Z(\sigma_{el})$, with Dreiding models and manual operations, e.g., yielded a sensitivity of only 50 ppm/e[9] instead of 170 ppm/e, as obtained from calculations based on force field minimized structures with the aid of suitable computer programs.[11]

Results

Uncertain conformations render σ_{el} and σ_{an} calculations ambiguous. Thus we obtain with 17α-X-substituted estrenes, for X = Cl, a σ_{el} increment which, with k = 17.8 ppm/e in eq 1, leads to $\Delta\delta_{el}$ = +0.123 ppm, in fair accordance with $\Delta\delta_{obsd}$ = +0.084 ppm at 18-CH_3. For 17α, X = F, however, $\Delta\delta_{el}$ = +0.130, in contrast to $\Delta\delta_{obsd}$ = −0.060, is observed, which can be a consequence of a conformational change in the flexible[17] D ring. The calculated σ_{an} contributions for the 17α-Cl and -F compounds are also inconsistent (−0.132 and −0.186 ppm, respectively).



cholestanes 2 to 6α,β-X (R^{17} = C_8H_{17})



estrenes 17α, X = H, Cl, F

With the geometrically well-defined 3α- and 3β-cholestanes (**3α,β**), we find that the through-space effect E_Z (eq 2) of the C3–X dipole predicts the observed 19-CH_3 ^1H NMR shift within the errors to be expected (Figure 1, Table II). The least-squares regression yields a sensitivity of 25 ± 5 ppm/e, which is well in the theoretical[2] range of 17.8 ppm/e. Deviations for the OH substituents can

(14) H.-J. Schneider, W. Gschwendtner, and E. F. Weigand, *J. Am. Chem. Soc.*, **101**, 7195 (1979).
(15) B. V. Cheney, *J. Am. Chem. Soc.*, **90**, 5386 (1968).
(16) D. M. Grant and B. V. Cheney, *J. Am. Chem. Soc.*, **89**, 5315 (1967).
(17) B. Fuchs, *Top. Stereochem.*, **10**, 52ff (1978).

Table IV. Increments Caused by 2α-X and 6α-X Substituents on 19-Me Protons[a]

2α-X	$\Delta\delta_{obsd}$[b]	$\Delta\delta_{el}$[c]	$\Delta\delta_{an}$[d]
Cl	0.094[4]	0.054	−0.144
Br	0.075[4]	0.051	−0.176
OH	0.087[4]	0.054	−0.103
6α-X			
F	0.025[4]	0.064	
Cl	0.035[4]	0.059	
OH	−0.007[4]	0.059	

[a] In parts per million relative to X = H. [b] Values from the literature references indicated. [c] See footnote c, Table II. [d] See footnote d, Table II.

be due to uncertain rotamers of this group. Calculation of the C–X anisotropy contribution σ_{an} (eq 2) with literature $\Delta\chi$ values (Table 1)[40] leads to shift increments $\Delta\delta_{an}$ (Table II), which are by far too large, particular for the 3α substituents, which the E_Z theory correctly predicts to produce only very small effects. If one were to adjust $\Delta\chi$ so as to fit the observed values with the necessary inclusion of σ_{el}, one would end up, e.g., for X = I, with $\Delta\chi \simeq +40 \times 10^{-30}$ cm^3/molecule instead of -26.6×10^{-30} cm^3/molecule.

Similarly misleading shifts are predicted by σ_{an} with 5α-cholestanes (**5α**), whereas σ_{el} at least leads to $\Delta\delta$ increments of correct sign and order of magnitude (Table III). The consistently too small $\Delta\delta_{el}$ values can be enhanced by through-bond electric effects of the substituents closer to the observed nuclei. The necessary electron-density accumulation at Cβ (C10) by back-donation from the lone pairs at X is also indicated by ^{13}C shifts observations.[10]

5β-Substituents approach the observed nuclei so closely that the van der Waals square electric effect could be expected to deshield additionally the C19 protons. Thus, by use of eq 3[18] and the scaling obtained from other

$$E^2 = 3P_{C\text{-}X}I_X r^{-6} \quad (3)$$

studies,[10] the C19 ^{13}C signal should be deshielded by 0.182 ppm for X = Cl and 0.228 ppm for X = Br. There is no comparable scaling factor available to us for ^{1}H shifts, but surprisingly the calculated *linear* field values, other than σ_{an} (Table III), fit the experimental numbers very well.

For the **2α-X** and **6α-X** compounds, we obtain again an acceptable range on the basis of σ_{el} whereas σ_{an} carries wrong signs (Table IV). The smaller shifts for 6α substituents, however, which by symmetry should produce the same effect as 2α-X,[3] are not predicted by E_Z. The origin of this deviation remains obscure, since force-field calculations of other equatorial-substituted ring compounds[13,14] indicate no significant geometry difference between the 2α and 6α series.

In all the calculations, the effect of the displaced C–H dipole was substracted from the effect of C–X. Table 5[40] shows that the C–H $\Delta\delta_{el}$ and $\Delta\delta_{an}$ values are so large that to neglect them would lead to gross errors.

Steric distortions may be expected to alter the geometry factors for eq 1 and 2 and to introduce additional shielding mechanisms, particularly for large substituents in axial positions. Thus introduction of CH_3 in **3α** leads to flattening of the A ring and, e.g., to a closer approach of the 2β and 4β hydrogens toward 19-CH_3. Yet the resulting change in the square electric-field effect (eq 3) was calculated to only −0.003 ppm for the ^{13}C shift of 19-CH_3.

(18) W. T. Raynes, A. D. Buckingham, and H. J. Bernstein, *J. Chem. Phys.*, **36**, 3481 (1962).

Table VIII. ^{1}H NMR Shifts[a] and Half-Height Widths[b] ($W_{1/2}$) of H3 in 3-X-Cholestanes and H17 in 17-X-Estr-4-enes[c]

3β-X	H3	$W_{1/2}$	3α-X	H3	$W_{1/2}$
F	4.45	25	F	4.77	7
Cl	3.86	22	Cl	4.48[e]	7
Br	4.00	21	Br	4.68[e]	8
I	4.16	21	I	4.94[e]	7
OH	3.50[d]	22	OH	4.07[d]	7
17β-X	**H17**	**$W_{1/2}$**	**17α-X**	**H17**	**$W_{1/2}$**
			F	4.53	8
			Cl	4.07	9
OH	3.68	18	OH	3.76	8
OTs	4.31	18	OTs	4.55	8.5

[a] In parts per million relative to internal Me_4Si. [b] In Hertz. [c] Measured in 20–30% $CDCl_3$ solutions at 27 °C and at 90 MHz. [d] C. R. Narayana and K. N. Tyer, *Tetrahedron Lett.*, 3741 (1965). [e] H. Loiber and E. Zbiral, *Helv. Chim. Acta*, **59**, 2100 (1976).

This is the result of six single interactions, which mostly tend to cancel each other (see Table 6).[40] Similarly for the oxo substituent in position 3, an A-ring flattening and E^2 change amounting to −0.082 ppm (summation over seven single interactions, Table 6)[40] in ^{13}C shielding of 19-CH_3 was obtained. Here we also calculated the change in "Grant–Cheney" forces on the C–H bonds of 19-CH_3 (14 single interactions, see Table 7),[40] using the modified eq 4.[13] The corresponding shielding is −2.4 ppm for ^{13}C and

$$F = 0.6952 \times 10^{-5}\left(\frac{18\epsilon}{r^*}\right)\left[\left(\frac{r^*}{r}\right)^{10} - \left(\frac{r^*}{r}\right)^{7}\right]\cos\theta \quad (4)$$

0.050 ppm for ^{1}H.

Other than for the C–X single bonds discussed so far, σ_{an} reaches sizeable values for the C=O double bond.[3,6a,b] Here we obtain increments consistent with the large observed effect if σ_{el}, σ_{an}, *and* the steric F contribution given above are taken into consideration (Table II). That anisotropy effects of the carbonyl group are responsible for very long distance shielding effects is shown by the increment of the 3-oxo group on the 18-CH_3 ^{1}H shifts, which is correctly predicted by the calculated $\Delta\delta_{an}$ (see Table II).

Chemical shifts and half-height widths of the functional H3 protons in 3α,β (Table VIII) show the usual dependence on substituent electronegativity and orientation. The δ values are generally larger than those reported for cyclohexanes[5] by 0.20 ± 0.02 ppm for axial and by 0.1 to 0.2 ppm for equatorial protons, which can be partially due to different solvent and temperature effects.

Conclusions

The polarization of C–H bonds by the electrostatic field effect E_Z of a C–X dipole correctly predicts the range of observed long-range shielding on the basis of ~20 ppm/e, including the marked differences between α and β positions. The observed effects increase in comparison to the calculated increments with increasing proximity of the substituents to the observed nuclei, e.g., from 20% for 3β to ~40% for 2α/4α to ~100–200% in excess for 5α substituents. This can qualitatively be attributed to the increasing action of inductive through-bond effects, but *not* to anisotropy effects, which in most cases would predict wrong signs and orders of magnitude.

The results consequently prohibit any attempts to estimate $\Delta\chi$ values or to adjust the calculational procedure for anisotropy contributions of C–X single bonds. Only for the carbonyl group does σ_{an} represent a considerable portion of the observed effect.

Steric distortions, as calculated on the basis of force field minimized structures, like van der Waals E^2 effects and sterically induced charge polarizations, will contribute to a minor degree even for the 3α-methyl steroids; in the ketone they amount to ~20% of the observed effect.

Experimental and Computational Details

Compounds 3α- and 3β-fluoro-5α-cholestane,[19] 3β-chloro-5α-cholestane,[20] 3α-chloro-5α-cholestane,[21] 3β-bromo-5α-cholestane,[22] 3α-bromo-5α-cholestane,[19] 5α-cholestan-3β-ol,[23] 5α-cholestan-3α-ol,[19] 5α-cholestan-3-one,[24] 5α-cholestane,[22] 3β-acetoxy-5α-fluorocholestane,[25] 3β-acetoxycholestane,[19] 5α- and 5β-chlorocholestane,[26] 5α- and 5β-bromocholestane,[27] cholestan-5α-ol,[28] cholestan-5β-ol,[29] and 5β-cholestane[30] were prepared according to the literature references indicated. The structures of these and all new compounds were checked by ^{13}C and ^1H NMR spectroscopy.

3α,β-Iodo-5αH-cholestane. 3β-(Tosyloxy)cholestane (1 mmol) was dissolved in 2 mL of a methyl ethyl ketone/2-propanol mixture (1:1) and stirred under reflux with 10 mmol of potassium iodide for 4 days. After workup with ether and water, the reaction product contained 70% 3β-iodocholestane, 24% 3α-iodocholestane, and 6% cholest-2-ene (by ^1H and ^{13}C NMR) and was used without further purification.

3α,β-Methyl-5αH-cholestane. 3-Methylene-5αH-cholestane[31] (1 g) was hydrogenated in a mixture of 15 mL of cyclohexane and 10 mL of acetic acid over Adams platinum catalyst at room temperature and 1.5 atm. The reaction product obtained in 83% yield after standard workup contained 80% of the 3α-methyl and 20% of the 3β-methyl steroid (by ^{13}C NMR).

17α-Fluoroestr-4-ene. 17β-(Tosyloxy)estr-4-ene[32] (1 mmol) was heated to 80 °C for 1 day with 6 mmol of tetraethylammonium fluoride in 1 mL of *N*-methylpyrrolidone.[33] After workup with ether and water, 68% crude product (mp 72–85 °C) was obtained which contained 90% 17α-fluoroestrene and 10% olefinic by-products.

17α-Chloroestr-4-ene was obtained in 74% yield similarly to the procedure described above by heating tetraethylammonium chloride with the tosylate at 100 °C for 4 h.

17α-Acetoxyestr-4-ene. The 17β-tosylate was treated as described above with tetraethylammonium acetate at 80 °C for 3 days, yielding 76% of the inverted acetate, mp 61–65 °C.

17α-Hydroxyestr-4-ene was obtained by alkaline saponification of the acetoxy compound (82%, mp 122–126 °C).

17α- and 17β-(Tosyloxy)estr-4-enes were obtained from the hydroxy steroids with tosyl chloride in pyridine in 70–75% yield (α-OTs, mp 125–130 °C; β-OTs, mp 82–84 °C) after recrystallization from ethanol–methanol.

^1H NMR spectra were measured at 90 MHz on a Bruker WH 90/BNC-12 in the PFT mode and at 60 MHz on a Varian EM-360 in the CW mode, respectively. Force-field calculations were carried out with the Allinger MM1 program[34] for the following compounds: 17β-isopropylandrostane with 3α-X = H and CH_3 as a model for steric distortion and E^2 calculations for **3α-Me**; 5α-androstane and androstan-3-one for E^2, F, σ_{el}, and σ_{an} calculations.

Geometries for the **2α**-X and **6α**-X compounds were obtained by attaching the X groups to the minimized androstane conformation, using the standard C–X bond length.[35] Conformations of **5α**-X derivatives were minimized for X = H and F; other halo substituents were attached as described above.

5β-X geometries were simulated by formal displacement of the C4–C5 bond in 17β-isopropyl-5α-androstane by a C–X bond. **17α**-X conformations were obtained from minimized 17α-fluoroestr-4-ene (D ring in twist form) by exchanging the C17–X bonds.

3α,β-X geometries (except X = Me, see above) were obtained by attaching hydrogens to a published X-ray structure of 3β-hydroxy-5α-androstan-17-one[36] and displacing the corresponding C3–X bonds.

Linear electric-field effects (eq 2) were calculated with a program (FELDEFFEKT[11,37]) which accepts Cartesian coordinates. Electron charges of the C–X dipoles were taken from the literature[10] except for the carbonyl dipole, where the charges were calculated from the dipole moment (2.4 D[38]). θ and r values for F calculations (eq 4) were obtained from the program MOLGEOMETRY.[39] All other calculations, based on geometries described above, were carried out by using conventional vector addition. Van der Waals E^2 effects (eq 2) were estimated by taking the X end of the fluctuating C–X bond for r calculation, which leads to some exaggeration of E^2. Only for the **5β**-X E^2 evaluation was the center[10] of the C–X bond used. The effects on the three 19-methyl protons were calculated on the basis of the staggered conformation obtained by force-field minimization and averaged afterward for comparison to experimental shifts.

Registry No. 3α-Fluoro-5α-cholestane, 3856-83-5; 3β-fluoro-5α-cholestane, 3824-61-1; 3β-chloro-5α-cholestane, 1474-58-4; 3α-chloro-5α-cholestane, 5847-30-3; 3β-bromo-5α-cholestane, 51154-61-1; 3α-bromo-5α-cholestane, 2309-03-7; 5α-cholestan-3β-ol, 80-97-7; 5α-cholestan-3α-ol, 516-95-0; 3β-acetoxy-5α-fluorocholestane, 3800-94-0; 5α-cholestan-3-one, 566-88-1; 3β-acetoxy-5α-cholestane, 1255-88-5; 5β-bromocholestane, 74098-15-0; 5α-chlorocholestane, 56114-17-1; cholestan-5α-ol, 910-19-0; 5β-chlorocholestane, 74098-16-1; cholestan-5β-ol, 20220-17-1; 5α-bromocholestane, 74098-17-2; 3-methylene-5αH-cholestane, 1173-33-7; 3α-iodo-5αH-cholestane, 29108-97-2; 3β-iodo-5αH-cholestane, 20853-75-2; 3α-methyl-5αH-cholestane, 74164-13-9; 3β-methyl-5αH-cholestane, 38544-61-5; 17α-fluoroestr-4-ene, 63840-69-7; 17α-chloroestr-4-ene, 63840-70-0; 17α-acetoxyestr-4-ene, 74098-18-3; 17α-hydroxyestr-4-ene, 63902-35-2; 17α-(tosyloxy)estr-4-ene, 74098-19-4; 17β-hydroxyestr-4-ene, 3646-30-8; 17β-(tosyloxy)estr-4-ene, 61319-71-9; 17β-isopropylandrostane, 5737-19-9; 17β-isopropyl-3α-methyl-5α-androstane, 74098-20-7; 3α-methyl-5α-androstane, 66169-32-2; 5α-androstan-3-one, 1224-95-9; 2α-chloro-5α-cholestane, 4405-84-9; 2α-bromo-5α-cholestane, 74098-21-8; 5α-cholestan-2α-ol, 570-66-1; 6α-fluoro-5α-cholestane, 74098-22-9; 6α-chloro-5α-cholestane, 58321-91-8; 5α-cholestane-6α-ol, 19043-45-9; 5α-androstane, 438-22-2; 5α-bromo-17β-isopropylandrostane, 74098-23-0; 17β-isopropyl-5αH-androstan-3β-ol, 7780-55-4; 3β-(tosyloxy)cholestane, 3381-52-0.

Supplementary Material Available: Magnetic susceptibility values $\Delta\chi$ from literature data (Table 1), $\Delta\delta_{el}$ and $\Delta\delta_{an}$ increments on angular CH_3 ^1H NMR shifts for C–H bonds (Table 5), square electric field effect contributions (Table 6), sterical force contributions F (Table 7), internal coordinates for 17β-isopropylandrostane and differences in 3α-X and 5α-X derivatives from force-field calculations, and Cartesian coordinates for 17β-isopropyl-3αH-androstane and 5αH-androstan-3-one (8 pages). Ordering information is given on any current masthead page.

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(39) Program MOLGEOMETRY, made available to us by Dr. R. Hoge, Fachrichtung Kristallographie, Universität des Saarlandes.
(40) See the supplementary material.