New Conformational Effect: Predominance of the Axial Conformation in Spiro[5.2]octan-4-ol Derivatives

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Summary A new conformational effect, the predominance of the axial conformation in 4-methoxy- and 4-acetoxy-derivatives of spiro[5.2]octane, is reported, and its origin is discussed in terms of orbital interaction together with charge transfer and steric repulsion.

The preference for equatorial rather than axial substituents in six-membered rings is a basic concept in conformational analysis. Exceptions to this preference are usually explained in terms of 'conformational effects,'[1] the 'anomeric' effect being the most typical,[1–3] showing a preference for axial rather than equatorial conformations in structures of type (**1**). It has been suggested recently that a charge-transfer interaction donating electrons from a lone pair *p*-orbital of the heteroatom into the σ^*-antibonding C–Y orbital [see (**2**)] gives rise to the anomeric effect.[1–3]

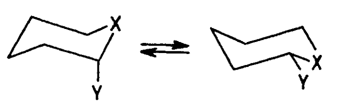
This concept may be generalized and we report here a new and unusual case of axial predominance of substituents at C-4 in derivatives of spiro[5.2]octane (**3**), in which the heteroatom X in structures (**1**) and (**2**) is replaced by the cyclopropane ring. The cyclopropane ring has two degenerate orbitals of *e*-type symmetry (HOMO's), one of which, e_A, is suitably placed for interaction with the adjacent axial σ^*-orbital, as in structure (**2**). The stabilisation of neighbouring electron-deficient centres by the cyclopropane ring in the bisected conformation is well documented.[4]

With this in mind we have determined the positions of conformational equilibria for the series of model spiro-compounds (**4**) and (**5**), and the dimethyl compounds (**6**) for reference, by measurement of the widths of the outermost peaks of the ^1H n.m.r. signals due to H_X in the ABX systems, as has been used previously for systems of type (**1**).[5] The position of the conformational equilibria was found from the Eliel equation: $^3J_{HH} = \sum_i n_i J_i$, using $J_{aa} = 11$, J_{ae} 3·0, and J_{ee} 2·5 Hz as standard coupling constants. These data are shown in the Table. The ^1H n.m.r. spectrum of (**4a**) at −80 °C (CS_2; 160 MHz) contains peaks due to both conformers; *eq*-H_Y gives a narrow singlet with a width at half-height ($W_{\frac{1}{2}}$) of 5·5 Hz and *ax*-H_Y gives an unresolved broad multiplet (at lower field compared with *eq*-H_Y) with $W_{\frac{1}{2}}$ 16 Hz. Integration shows the presence of 87 ± 3% of the conformer with the OAc group axial.

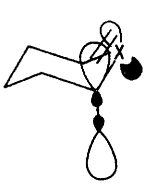
TABLE. ^1H N.m.r. (80 MHz) and conformational equilibrium data for compounds of type (**4**), (**5**), and (**6**).

	% of axial conformation		
Compound	CCl_4	C_6H_6	CD_3CN
(**4a**)	89	—	82
(**4b**)	80	75	80
(**3c**)	51[a]	—	—
(**4d**)	61	59	—
(**5a**)	43[b]	38	41
(**5b**)	48	43	46
(**6a**)	—	14	—
(**6b**)	19	—	—
(**6c**)	11[a]	—	—

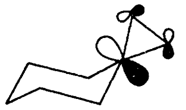
[a] At 294 MHz. [b] At 100 MHz.



(1A) (1B)



(2)



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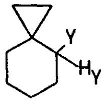

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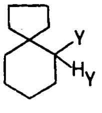
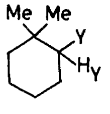
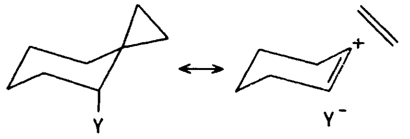


(5)

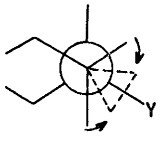


(6)

a; Y = OAc
b; Y = OMe
c; Y = $OSiMe_2$
d; Y = OH



(7A) (7B)



(8)

The results in the Table are interesting. The most important conclusion is the existence of a new conformational effect, *i.e.* the marked increase in the content of the axial conformation for the spiro-compounds (**4**) compared with the reference compounds (**6**). We refer to this effect as the 'fish-tail' effect [see (**7A**)]. Two features of this effect can be deduced from the Table. Firstly, the position of the equilibrium changes slightly with solvent polarity, no clear-cut trend being observed, however. An analogous dependence has been found for the anomeric derivatives of 1,4-dioxan,[6] 1,4-oxathian,[7] and their benzo-analogues.[8] Secondly, the proportion of axial isomer (**1A**) decreases with decreasing substituent electronegativity [*cf.* (**4a**), (**4b**) and (**4c**)]. We suggest two explanations for the origin of this effect. The first is the orbital interaction of type (**2**) already discussed, which can be best represented in terms of no-bond resonance, structures (**7**). Secondly, the effect may, at least in part, be due to an increase in the steric *gauche* repulsion in the equatorial form (**1B**), see structure (**8**). The content of the axial form (**1A**) for the spiro-compounds (**5**) is also slightly increased compared with (**6**). However comparison equilibrium data for (**4a**), (**4b**), and (**4c**), taking into account the steric bulk and the electronegativity of the substituents indicates that steric repulsion is of relatively minor importance. In conclusion we emphasize that this effect cannot be explained in terms of the concept of dipole–dipole (electrostatic) interactions, which has been widely applied to the anomeric effect.

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