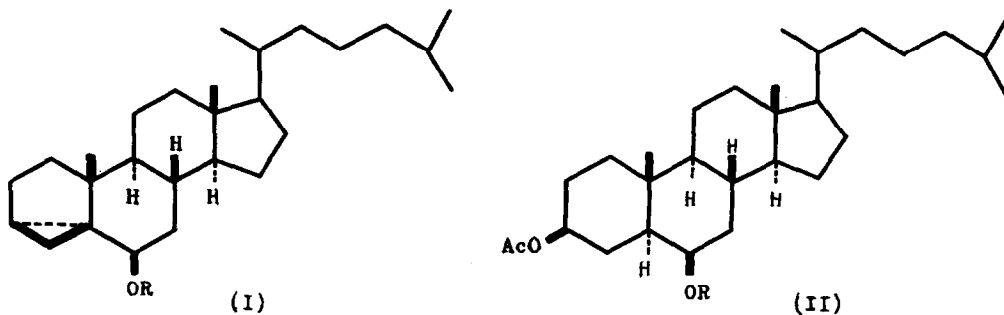


RELATIONSHIP BETWEEN NMR DESHIELDING EFFECTS AND NITRITE
PHOTOLYSIS IN $3\alpha,5\alpha$ -CYCLOCHOLESTANE- 6β -OL (1)

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The conformation of ring B of the *i*-steroids has been the subject of recent work (2) and it was deduced, on the basis of the n.m.r. spectral studies of the C-6 protons of the C-6 epimeric 6-hydroxy-17-ethylenedioxy- $3\alpha,5\alpha$ -cycloandrostanes and the derivatives, that the conformation of ring B of $3\alpha,5\alpha$ -cyclosteroids must adopt a chair form (3). If ring B of *i*-steroids possesses a chair conformation in which 6β -OH and 19-methyl are in the 1,3-diaxial relationship, the nitrite should potentially undergo the Barton reaction (4) and this must afford direct chemical evidence for the conformation of ring B.



i-Cholesterol (5) (I; R=H) was smoothly nitrosated to the stable nitrite (I; R=NO) (m.p. 74-76°) by the usual method. Contrary to our expectation, photolysis of this nitrite in benzene and subsequent separation by preparative thin

layer chromatography afforded only *i*-cholestanone (15%) and *i*-cholesterol (52%), respectively. No 19-oximino derivative was formed as proved by thin layer chromatography. In a similar study *epi-i*-cholesterol nitrite (glass), on photolysis in benzene, gave *i*-cholestanone (23%) and *epi-i*-cholesterol (38%), as was expected. Observation of the photolysis of *i*-cholesterol nitrite was in sharp contrast with the reported results on the photolyses of nitrites of 3 β -acetoxycholestan-6 β -ol (II; R=H) (oxime, 61%) (4) and the related compound (oxime, 55%) (6).

The 1,3-diaxial relationship between C-6 substituents and C-19 methyl would be reflected in the value of the deshielding effect in the n.m.r. spectrum, which is due to the magnetic anisotropy, the polar effect of the relevant groups and others (7). Therefore, we obtained chemical shift values of C-19 protons of various 6-substituted 3 α ,5 α -cyclocholestanes including the hitherto undescribed 6 β -cyano-3 α ,5 α -cyclocholestane (8) and the deshielding effects for C-19 protons of 6 α - and 6 β -substituents, taking 3 α ,5 α -cyclocholestane (9) as standard, and compared them with the corresponding values of the normal steroids. These values are tabulated below.

TABLE I

Chemical Shifts of C-19 Methyl Protons in 6-Substituted 3 α ,5 α -Cyclocholestanes and Effects of Some 6-Substituents on C-19 Protons

Compound	19-H (τ)	$\Delta\tau^*$ (ppm)
3 α ,5 α -cyclocholestane	9.093	-----
6 β -OH	8.968	0.125
6 α -OH	9.080	0.013
6 β -OAc	9.000	0.093
6 α -OAc	9.028	0.065
6 β -ONO	9.080	0.013
6 α -ONO	8.943	0.150
6-Oxo	8.960	0.133
6 β -C \equiv N	8.850	0.243

* A positive value denotes a downfield shift caused by a substituent. The spectra were recorded in CDCl₃ at 60Mc.

It is evident that the deshielding effects by 6 α -acetoxyl* and 6 α -hydroxyl substituents are significantly smaller than those by 6 β -substituents. Thus, these observed effects are consistent with the accepted configuration of the *i*-steroids. It is noteworthy that the reverse is true for 6 α - and 6 β -C-NO substituents. We have confirmed (10) that in 22,27-imino-17,23-oxidojervan skeleton, the relative deshielding effects between 11 α and 11 β -C-NO groups on C-19 protons are similarly reversed when compared with the relationships in 11 α - and 11 β -hydroxyl or acetoxyl substituents. (0.08 for the β -epimer and 0.17 for the α -epimer, respectively.)

In a pair of 3 α ,5 α -cyclocholestan-6-ol nitrites, conformational unambiguity might still be questioned since in these nitrites changes in the conformation from chair to boat form might be favored. In the n.m.r. spectrum of the β -nitrite a single proton resonance due to C-6 proton occurred at 5.04 τ as triplet with $J_{ae} \approx J_{ee} = 2.7$ cps. This spin-spin coupling pattern indicates that the proton at C-6 must be equatorial (2). In the α -nitrite the corresponding proton resonance occurred at 4.29 τ as quartet with $J_{aa} = 11.9$ and $J_{ea} = 4.4$ cps. These coupling constants require that the proton at C-6 be axial (2). These results exclude a possibility of boat conformation of B ring in these nitrites.

TABLE I indicates that the observed effects of 6 β -hydroxyl and 6 β -acetoxyl groups in 3 α ,5 α -cyclosteroid are to deshield the C-19 protons by 0.125 and 0.093 p.p.m. respectively and these values are appreciably less than those in the normal steroids for which the values 0.225 and 0.183 p.p.m. were reported respectively (11). This relationship also holds for 6 β -cyano group (0.283 p.p.m. for the normal steroids) (12). It is of interest that this phenomenon is parallel to the difference of the results of the photolyses between the normal steroids and the *i*-steroid. The value for 6 β -hydroxyl above in the normal steroid is comparable with the reported values (11) of the deshielding effects by 11 β -hydroxyl group on C-18 and C-19 methyl protons of normal steroids (0.258 and 0.242 p.p.m., respectively) in which the photolysis of the nitrite leads to

* It has generally been found that the difference between α - and β -acetoxyl groups in the substituent effects on the relevant methyl was smaller than that in hydroxyl group. Reference 7a. p. 20.

the formation of the oximino derivatives in both C-19 and C-18 methyls (13). Moreover, we have found (14) that the deshielding effect of the 11 β -hydroxyl on the C-18 methyl proton signal in 22,27-imino-17,23-oxidojervan skeleton is only 0.11 p.p.m. whereas it is 0.295 p.p.m. for the C-19 methyl which is exclusively attacked by 11 β -alkoxy radical.

All these results imply not only the close relationship between the nitrite photolysis and the effect of substituents but also that ring B of i-cholesterol is somewhat deformed, although it is a chair form. This also emphasizes the importance of the rigid conformational requirements for hydrogen abstraction in the Barton reaction.

It should be noted that various ramified reactions (15) could not be observed in the present photolyses of nitrites in which a β carbon of nitrite ester was in cyclopropane moiety.

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