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An Unusual Double 4σ-Bond Long-range Coupling in 3α-Methyl-5α-androst-1-ene 3β,19-Oxide

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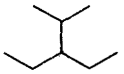
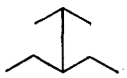
Summary The n.m.r. examination of 3α-methyl-5α-androst-1-ene 3β,19-oxide (2) revealed simultaneous long-range coupling by the two nonequivalent protons of the C-19 methylene group.

MEINWALD and LEWIS,[1] and Anet[2] were the first to report long-range coupling through 4σ-bonds. Since that time, several groups of investigators[3] have observed proton–proton coupling through 4σ-bonds, mainly in bridged bicyclic compounds. An M or W arrangement of the 4σ-bonds appears to be the stereochemical requirement of this type of coupling.[3] Moreover, 4σ-bond coupling constants ($J_{4\sigma}$) usually lie in the range 0—2 Hz, with the exception of some bridged bicyclic compounds in which larger $J_{4\sigma}$ have sometimes been observed.[3]

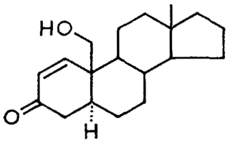

(5a)


(5b)

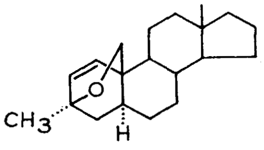
We report the easy formation of the unsaturated steroidal ether (2), which constitutes a remarkable example of a molecule in which *both protons of the same methylene group* give rise to two long-range couplings through 4σ-bonds.

Reaction of 19-hydroxy-5α-androst-1-en-3-one (1; m.p. 178—179°; $[\alpha]_D$ + 22°)[4]‡ with methylmagnesium iodide, followed by brief acid treatment, afforded 3α-methyl-5α-androst-1-ene 3β,19-oxide (2; m.p. 87—88°; $[\alpha]_D$ + 128°). Structure (2), in which ring A exists in the quasi-boat conformation, is suggested for this substance on the basis of absence of i.r. absorption in the regions of 3500 and 1660—1750 cm^{-1}, as well as absence of u.v. absorption maximum above 220 nm. Its mass spectrum shows the major peak at m/e 256, which corresponds to (M — CH_2O^+).

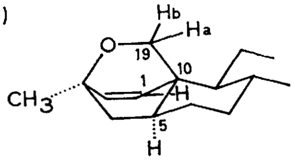
The 100MHz n.m.r. spectrum of the 3β,19-oxido-steroid (2) is in good agreement with the suggested structure. The 17-methyl and 3-methyl protons appear, respectively, at 0·68 and 1·30 p.p.m. The 10-methylene group (C-19) shows an AB pattern: δ_{19a} 4·095, δ_{19b} 3·229 p.p.m. ($J_{19a-19b}$ 8·2 Hz). Moreover, both 19a-H and 19b-H present an additional 4σ-bond coupling; *i.e.* one C-19 proton (19a) interacts with 1-H (J_{1-19a} ⩽0·5 Hz), and the other C-19 proton (19b) is coupled with 5-H (J_{5-19b} ⩽1 Hz), [see formula (3)].



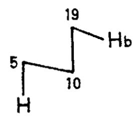
(1)



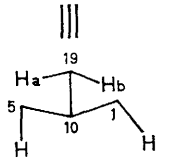
(2)

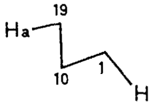


(3)

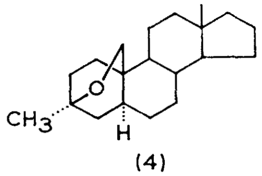


(3b)





(3a)



(4)

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‡ Satisfactory elemental analyses were obtained for the new compounds.

The olefinic protons at C-1 and C-2 also show an AB system centred at 6·22 p.p.m.: δ_1 6·311, δ_2 6·138 p.p.m. (J_{1-2} 8·2 Hz). Due to long-range coupling between the protons at positions 1 and 19a, the signal corresponding to A (1-H) is broader than that of B (2-H).

These assignments for the spin–spin coupling interactions were tested through double-resonance experiments. When 1-H was saturated with an external field, at 6·3 p.p.m., the 4·1 p.p.m. doublet sharpened. Likewise, irradiation of 5-H at 1·62 p.p.m. sharpened the doublet at 3·2 p.p.m.

An examination of the geometry of these 4 σ-bond systems with molecular models, revealed that the required M spatial arrangement exists between both 1-H and 19a-H [see (3a)], as well as 5-H and 19b-H [see (3b), leading to a configuration of type (5a) or (5b) responsible for this double long-range coupling.

The substantial difference observed between the chemical shifts of both C-19 protons (*ca.* 87 Hz) is attributed to the fact that 19b-H falls into the shielding cone of the Δ^1-double bond. This was confirmed by catalytic hydrogenation (PtO_2–MeOH) of the Δ^1-oxide (2) to the saturated 3β,19-oxide (4; m.p. 65—66°; $[\alpha]_D - 47°$), 0·65 (18-H), 1·03 p.p.m. (3-Me), in which the C-19 methylene now presents an ABX pattern: δ_{19a} 4·04 and δ_{19b} 3·74 p.p.m. ($J_{19a-19b}$ 9·0; $J_{5\alpha-19b} \leqslant 0·5$; $J_{1\alpha-19a}$ 3·0 Hz), assigned to the 4σ-bond coupling between 1α-H and 19a-H.

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