

NITROXIDES XLIX : STEROIDAL NITROXIDES

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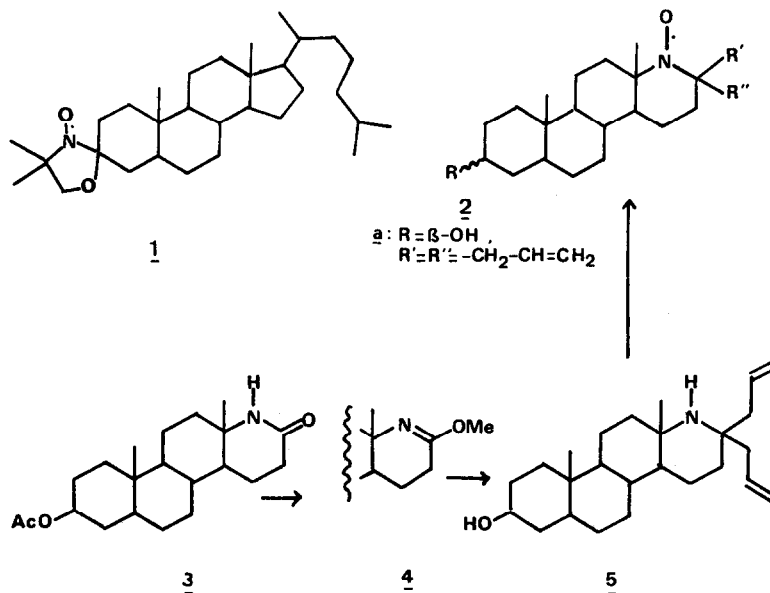
The first steroidal nitroxide 1 used as spin label has been synthesised by Keana (1) starting from 5 α -cholestan-3-one. In this free radical, the nitroxide group NO is included in an oxazolinic ring external to the steroidal skeleton on Carbon-3. We have started a study of the spectral and chemical properties of steroidal nitroxides (formula 2) in which the NO group is included in the skeleton. In this case, the nitrogen 2p_y-orbital axis is approximatively perpendicular to the average plane of the molecule. Furthermore, in 2, the C-3 position remains free and is now available for introduction of various functional groups on rings A and B. This may lead to labelled analogues of natural steroids.

We report here the synthesis of the free radical 2a (R = β -OH ; R' = R'' = CH₂-CH=CH₂). Dimethylsulfate (2) reacts with isoandrololactam acetate 3 (3) in boiling benzene solution and gives O-methyl isoandrololactim acetate 4 (56% yield ; i. r. (nujol) [1735 (CO), 1675 cm⁻¹ (C=N)] ; n. m. r. (CDCl₃) [τ 9.17 (Me 19), 9.05 (Me 18), 7.97 (CH₃CO₂), 6.38 (OMe), 5.27 ppm (H_{3 α)]). Allyl magnesium bromide in ether (4) reacts with the lactim ether 4, leading to the amine 5 (28% yield ; i. r. (pure film) [3300 (OH and NH), 3050 (ν _{CH} olef.), 1640 (C=C), 995 and 910 cm⁻¹ (δ _{CH} out of plane)] ; n. m. r. (CDCl₃) [τ 9.22 (Me 19), 8.88 (Me 18), 7.65 (OH + NH), 6.42 (H_{3 α)], 5 - 4.80 - 4.17 ppm (allylic protons)]. Amine 5 (1 eq.) oxidized by m-chloro-perbenzoic acid (4 eq.) leads to the nitroxide 2a * (45 % yield ; M = 386.3051, C₂₅H₄₀NO₂ requires 386.3058 ; i. r. (film)}}

(*) It must be noticed that in the oxidation conditions of amine 5, the two allylic chains have not been epoxidized.

[3350 (OH), 3030 (ν_{CH} olef.), 1640 (C=C), 995 and 912 cm^{-1} (δ_{CH} out of plane)]; e. p. r. (CH_2Cl_2), a 3 line-spectrum $a_{\text{N}} = 15.35$ Oe). Nitroxide 2a is optically active. Circular dichroism of this nitroxide chromophore (5) will be reported in the full paper.

Further work on steroidal nitroxides is now in progress, including modifications in rings A and B, and functionalization of potential side chains R' or R'' (2).



References

- (1) J. F. W. Keana, S. B. Keana and D. Beetham, J. Amer. Chem. Soc., 1967, 89, 3055.
- (2) cf. O. Cervinka, Chem. Listy, 1958, 52, 1145.
- (3) R. Anliker, J. Wohlfahrt and H. Heusser, Helv. Chem. Acta, 1955, 38, 1404.
- (4) cf. R. Lukes and M. Cerny, Coll. Czechoslov. Chem. Commun., 1961, 26, 2886.
- (5) Y. Brunel, H. Lemaire and A. Rassat, Bull. Soc. chim. Fr., 1964, p. 1895.