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THE STRUCTURE OF NEORUSCOGENIN

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A recent communication from France[1] presents convincing infrared and chemical evidence that one of the sapogenins isolated from Ruscus aculeatus L., neoruscogenin, differs from ruscogenin, a companion substance, by possessing an additional double bond exocylic to ring F. Since the former had been described as simply the C-25 epimer of the latter[2] by the discoverers of these sapogenins, and since other workers [3,4] in the field implicitly accepted that assignment, we should like to submit the following physical evidence which bears out the more recent structure.

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1 J. Robert, R. Vaupré and G. Poiget, Compt. rend. 3187 (1960).

2 C. Sannié and H. Lapin, Bull. soc. chim. 1237(1957).

3 D. Burn, B. Ellis and V. Petrow, J. Chem.Soc. 795 (1958).

4 A. L. Nussbaum, F.E. Carlon, D. Gould, E.P. Oliveto, E.B. Hershberg, M.L. Gilmore and W. Charney, J. Amer. Chem. Soc. 81, 5230 (1959)

A comparison (Table I) of the nuclear magnetic resonance spectra (fig. 1) of the diacetates of ruscogenin and neoruscogenin clearly shows (a) the appearance of a distinct new band in the vinylic proton region for neoruscogenin diacetate, (b) shift of a peak assigned to the C_{27}-protons adjacent to oxygen in ring F [5] in that sapogenin, as compared to ruscogenin diacetate, and (c) the absence of a band in neoruscogenin diacetate assigned to the C_{28}-protons in ruscogenin diacetate. These observations find a ready explanation in the proposed new structure[1].

Ruscogenin has been converted to the corresponding $\Delta^{1,4}$-dien-one, and the latter was shown to be identical[4] with the dehydrogenation product from diosgenone, $\Delta^{1,4}$-20α, 22β, 25 D-spirostadien-3-one [6]. On the other hand, Burn, Ellis and Petrow [3] carried out a like series of reactions on a presumed 1:1 mixture of ruscogenin and neoruscogenin but did not isolate the 25 D isomer ascribable to ruscogenin.

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[5] Private communication from Dr. J.F. Shoolery, Varian Associates. We should like to thank Dr. Shoolery for an enlightening discussion of the NMR spectrum of ruscogenin diacetate which he kindly measured for us some three years ago.

[6] For sapogenin nomenclature, see ref. 8.

TABLE I

Comparison of Corresponding NMR Bands of the Diacetates of Ruscogenin and Neoruscogenin

Rusco	Neorusco	Assignment	Comment
63	70.5	Proton at C_6	7
-	100.0	Δ 25(27)	Not present in Rusco
105 (low multiplet)	110	C_1,C_3,C_{16} [8]	
	122.5 132.0 144.0	C_{26}	Note shift
150	-	C_{26}	
209	209.5	Acetate Me protons	
226	-	C_{27} Me	Not present in Neorusco
244	243.5	C_{19}	9
259	258	C_{18}	

[7] This signal accurs at a rather low field as compared to a large number of Δ^5-steroids; see J.N. Shoolery and M.T. Rogers, J. Amer. Chem. Soc. 80, 5121 (1958). It is believed to be caused by an effect the 1β-acetyl substituent has on the normal polarization of the Δ^5 double bond. This effect will be discussed elsewhere.

[8] The proton at C_{16} is assigned to this peak, in addition to the protons of the two carbons substituted by equatorial acetates, as the result of peak area measurements and comparison of these spectra with those of diosgenin acetate, 1β,3β-diacetoxy-Δ^5-pregnen-20-one, and pregnenolone acetate.

[9] This represents a small shift from the normal position for C_{19}-angular methyl which is thought to be cause again by the proximity of the 1β-acetate (see previous ref.) Incidentally, this confirms the stereochemistry already proved by chemical means by W.R. Benn, F. Colton and R. Pappo, J. Amer. Chem. Soc. 79, 3920 (1957).

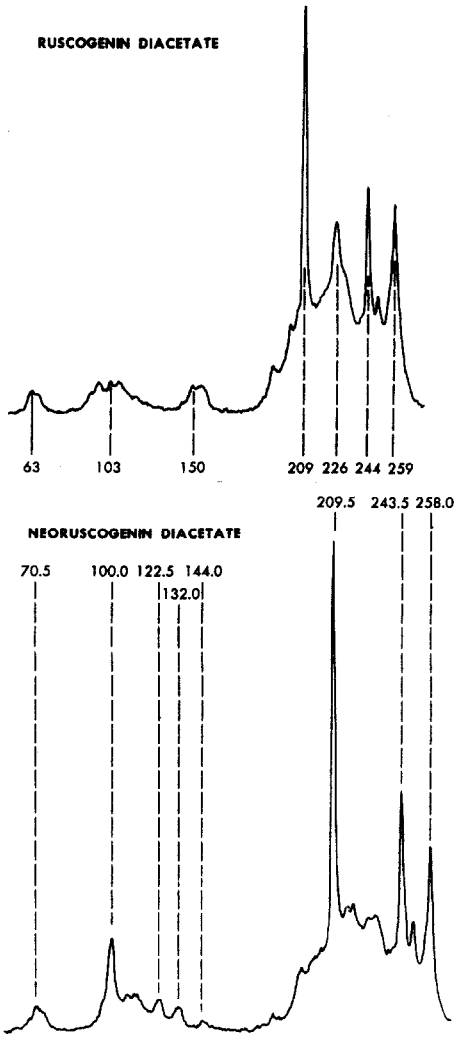

Fig 1

NMR Spectra of the Diacetates of Ruscogenin and Neoruscogenin.

The spectra were measured in deuterochloroform solution. A chloroform capillary is used as arbitrary reference zero. Signal at 40 mega-cycles/sec., chemical shift in cycles/sec.

They concluded that they had in hand $\Delta^{1,4}$-20α, 22β, 25 L-spirostadien-3-one, the corresponding "normal" isomer derived from neoruscogenin. If their premise is correct, this structure should now be changed to $\Delta^{1,4,25(27)}$-20α, 22β-spirostatrien-3-one.

Both the English authors [3] and the Schering group [4] had observed that neoruscogenin underwent the Marker pseudo-reaction more readily than did ruscogenin. This was ascribed [10] to steric decompression as discussed by Wall and Serota [11]. It is clear that this driving force can be only partly operative in the case at hand.

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10 See footnote 21, ref. 4

11 M. E. Wall and S. Serota, J. Amer.Chem.Soc. 79, 6481 (1957).