Origin of the 27-Methylene Group of the Steroidal Sapogenin Convallamarogenin

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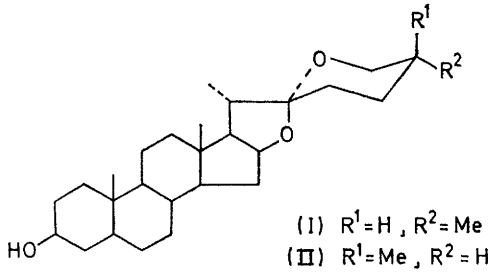
Summary In convallamarogenin biosynthesized in *Convallaria majalis* the 27-methylene group is derived from C-2 of mevalonic acid.

TAMM *et al.*[1] have showed that in *Digitalis lanata* the equatorial 27-methyl group of tigogenin (I), a steroidal "iso"-sapogenin (25 *R*), is derived from C-2 of mevalonic acid (MVA), and C-26, bearing the oxygen function, is derived from C-3′.

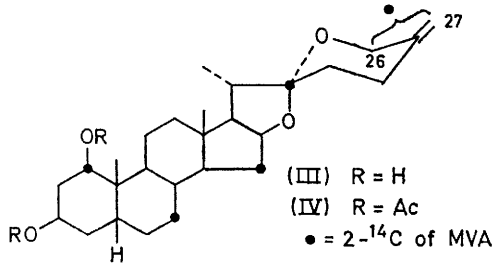
It was suggested[2] that the biogenesis of the "neo"-sapogenins (25 *S*), *e.g.* (II), involves the oxidation of the terminal methyl group of cholesterol coming from C-2 of MVA, the biological interconversion between "neo"- and "iso"-sapogenins having been excluded.

We report on the origin of C-27 in the biosynthesis of convallamarogenin (III), a member of a third class of steroidal sapogenins in which a 25(27) double bond is present.

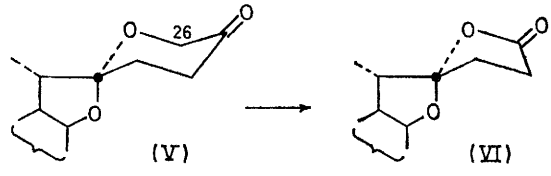
We administered [2-^{14}C]MVA to *Convallaria majalis* and obtained convallamarogenin (III) labelled with ^{14}C in positions 1, 7, 15, 22, and 26 (or 27). After four weeks the radioactive sapogenin fraction was extracted and acetylated.[3] 1,3-Diacetylconvallamarogenin (IV) was isolated, purified by t.l.c. and t.l.c.–$AgNO_3$, and diluted with carrier material. This was oxidized with osmium tetroxide and the osmate ester decomposed with hydrogen sulphide to give a mixture of isomeric diols. The axial[4] diol was separated from its isomer by t.l.c. and treated with the stoicheiometric amount of sodium periodate to yield the ketone (V) and formaldehyde (recovered as the dimedone derivative), corresponding to C-27 of convallamarogenin.



(I) R^1=H, R^2=Me
(II) R^1=Me, R^2=H



(III) R = H
(IV) R = Ac
• = 2-^{14}C of MVA



(V) (VI)

The ketone (V) and formaldehyde showed values of molar radioactivity close to those calculated (83·2 and 16·5%, respectively, of the starting convallamarogenin). To confirm these data, the ketone (V) was treated with an excess of $NaIO_4$ in a sealed tube at 100° for 1 h, to give the lactone (VI) (m.p. 210—212°; ν_{max} = 1770, 1730 cm^{-1}; M^+ = 502) with the same molar activity as the starting ketone, and nonradioactive formaldehyde (recovered as the dimedone derivative).

These results indicate that the exocyclic methylene group (C-27) of convallamarogenin is derived from C-2 of MVA.

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[1] R. Joly and Ch. Tamm, *Tetrahedron Letters*, 1967, 3535.
[2] R. D. Bennett, E. Heftmann, and R. Joly, *Phytochemistry*, 1970, **9**, 349.
[3] R. Tschesche, H. Schwarz, and G. Snatzke, *Chem. Ber.*, 1961, **94**, 1699.
[4] K. Takeda, T. Okanishi, H. Minato, and A. Shimaoka, *Tetrahedron*, 1963, **19**, 759.