

THE STRUCTURE OF ISOREINECKIAGENIN, REINECKIAGENIN AND ISOCARNEAGENIN

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DURING recent years, the steroidal components of Reineckia Carnea KUNTH have been investigated by our group.^{1,2,3} We now wish to report the results of the structural investigation of three new sapogenins isolated from the extract together with convallamarogenin (Va)^{4,*} and isorhodeasapogenin (IX).^{5,**} Table 1 shows the physical constants of these sapogenins.

¹ K. Takeda, T. Okanishi and A. Shimaoka, Yakugaku Zasshi 75, 560 (1955).

² T. Okanishi and A. Shimaoka, Ann. Rept. Shionogi Research Lab. 10, 1391 (1960).

³ K. Takeda, T. Okanishi, K. Sasaki and A. Shimaoka, Chem. Pharm. Bull. (Japan) 9, 631 (1961); K. Sasaki, Ibid. 9, 684, 693 (1961).

⁴ R. Tschesche, H. Schwarz and G. Snatzke, Chem. Ber. 94, 1699 (1961).

⁵ K. Morita, Bull. Chem. Soc. Japan 32, 791, 794 (1959).

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Table 1

	m.p.	$[\alpha]_D$	Rf value
Compound A (isoreineckiagenin, Ia)	240- 2°	-65.7°	0.58
" B (reineckiagenin, IIa)	278-80°	-70.6°	0.55
" C (isocarneagenin, XIIa)	242- 4°	-63.4°	0.55
(carneagenin,* XIII)	262- 4°	-71.6°	0.55)

* synthesized

The new saponins compound A and compound B, both corresponded to the empirical formula $C_{27}H_{44}O_8$.

Compound A, isoreineckiagenin (Ia) afforded a diacetate (Ib, $C_{29}H_{48}O_8$, colourless needles, m.p. 202-4°, $[\alpha]_D$ -87.0°) on acetylation with acetic anhydride-pyridine at room temperature, but a triacetate (Ic, $C_{31}H_{50}O_8$, colourless prisms, m.p. 133-5°, $[\alpha]_D$ -74.0°) was obtained together with the diacetate (Ib) on acetylation at 90-100°.

Under the same conditions, compound B, reineckiagenin (IIa) gave a diacetate (IIb, $C_{29}H_{48}O_8$, colourless needles, m.p. 198-200°, $[\alpha]_D$ -82.0°) and a triacetate (IIc, $C_{31}H_{50}O_8$, colourless plates, m.p. 195-8°, $[\alpha]_D$ -68.8°). Therefore, it is evident that isoreineckiagenin (Ia) and reineckiagenin (IIa) possess three hydroxyl groups, and their third hydroxyl group may be a tertiary one.

The infra-red spectra of Ia and IIa showed that the characteristic bands⁶ of the E- and F-rings had undergone a considerable change, but that they might belong to the 25D and 25L series⁷ respectively.

When Ib and IIb were dehydrated with phosphorus oxychloride in

⁶ R. N. Jones, J. Amer. Chem. Soc. **75**, 158 (1953).

⁷ M. E. Wall, C. R. Eddy, M. L. Meelenman and M. E. Klump, Anal. Chem. **24**, 1337 (1952).

pyridine, both gave III ($C_{27}H_{46}O_6$, colourless needles, m.p. 178-81°) and IV ($C_{27}H_{44}O_6$, colourless needles, m.p. 108-12°/143-5°).

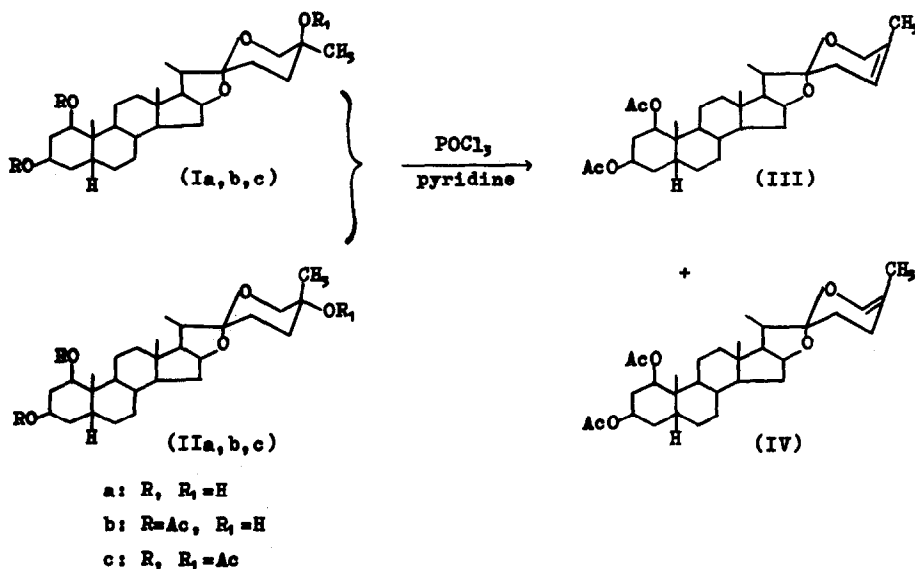


Chart 1

The NMR spectra^{***} of III and IV show a signal at 8.42 τ and at 8.45 τ respectively, corresponding to a methyl group on a double bond; and one proton on the double bond in III gives rise to a signal centered at 4.60 τ whereas that in IV appears as a signal at 3.94 τ , corresponding to a proton attached to a carbon atom which holds an oxygen atom.

From the above-mentioned results, it may be concluded that the tertiary hydroxyl groups of Ia and IIa cannot be situated at any other position save C-25. In order to further confirm the structures of Ia and IIa, these compounds were synthesized from convallamarogenin (Va).

As shown in chart 2, the carbonyl compound (VII, $C_{27}H_{44}O_7$, colour-

^{***} Spectra were taken on deuterated chloroform solutions with a Varian A-60 NMR Spectrometer.

less prisms, m.p. 177-8°, $[\alpha]_D -106.4^\circ$) was obtained by oxidation of convallamarogenin diacetate (Vb) with osmium tetroxide followed by lead tetracetate oxidation. Reaction of VII with methylmagnesium iodide gave reineckiagenin (IIa) and a small amount of isoreineckiagenin (Ia), as expected. Moreover, oxidation of convallamarogenin (Va) with monopero-phthalic acid gave two isomeric epoxides, $C_{27}H_{42}O_3$ (X, colourless needles, m.p. 230-2°, $[\alpha]_D -68.7^\circ$ and XI, colourless needles, m.p. 282-3°, $[\alpha]_D -53.3^\circ$). On treatment of the two isomeric epoxides with lithium aluminum hydride, Ia was obtained from X and IIa from XI. From these results, the constitutions of isoreineckiagenin (Ia) and reineckiagenin (IIa) have been established as 5 β -spirostane-1 β ,3 β ,25-triols.

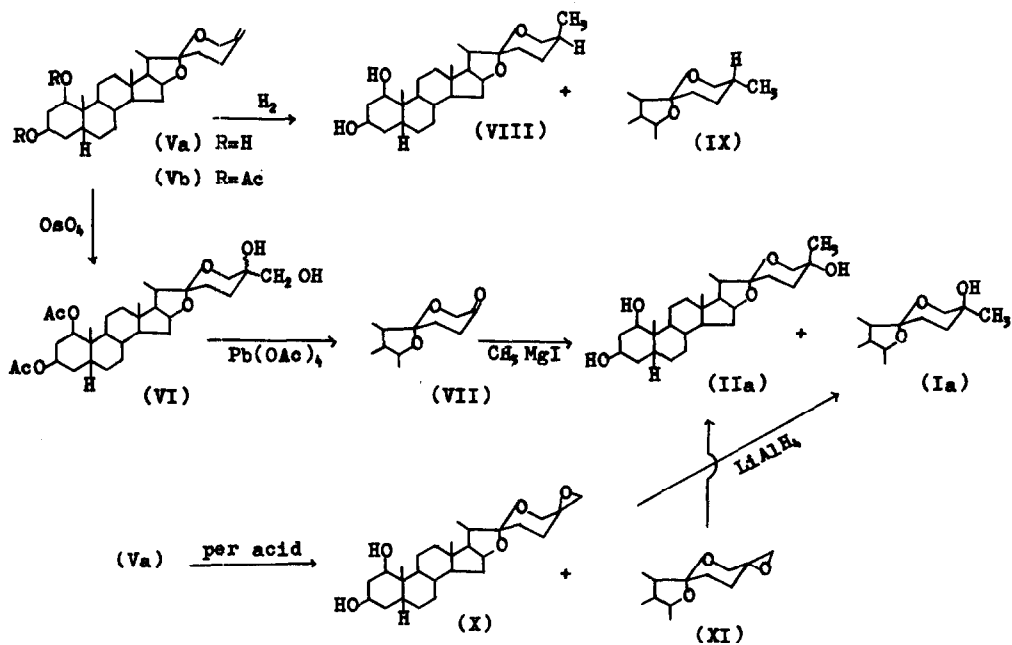


Chart 2

As to the configuration of the C-25 hydroxyl group, the infra-red spectrum of isoreineckiagenin diacetate (Ib) showed an absorption band at 3594 cm^{-1} corresponding to the intramolecular hydrogen bond, whereas that of reineckiagenin diacetate (IIb) showed an absorption band at 3610 cm^{-1} corresponding to the free hydroxyl group.⁸ These facts well support the above-mentioned presumption that Ia and IIa belong to 25D and 25L series respectively.

The NMR spectrum of isoreineckiagenin (Ia) showed a signal at 64 c.p.s. (8.93τ) and that of reineckiagenin (IIa) showed a signal at 76 c.p.s. (8.73τ) referred to tetramethylsilane, corresponding to the C-27 methyl group. The upward shift of the signal from 76 to 64 c.p.s. has been attributed to the change of the C-27 methyl group from axial to equatorial.⁹

Therefore, the C-27 methyl groups in isoreineckiagenin (Ia) and reineckiagenin (IIa) possess the equatorial (25D) and the axial configuration (25L), respectively.

Compound C, isocarneagenin (XIIa, $C_{27}H_{44}O_3$) afforded a triacetate (XIIb, $C_{30}H_{50}O_6$, colourless prisms, m.p. $215-8^\circ$, $[\alpha]_D -75.5^\circ$) on acetylation with acetic anhydride-pyridine at room temperature.

Since the infra-red spectrum of XIIa also showed that the characteristic bands of the E- and F-rings had undergone a marked change and XIIa was obtained together with convallamarogenin (Va), isoreineckiagenin (Ia) and reineckiagenin (IIa), it may be reasonable to suppose that the hydroxyl group of isocarneagenin (XIIa) is situated at C-27. Treatment

⁸ M. Mousseron-Canet, M. Mousseron and C. Levallois, Compt. rend. 253, 1386 (1961).

⁹ W. E. Rosen, J. B. Ziegler, A. C. Shabica and J. N. Shooley, J. Amer. Chem. Soc. 81, 1687 (1959).

of Va with diborane gave two isomeric triols, m.p. 242-4° (XIIa) and m.p. 262-4° (XIII) as shown in chart 3. The former was found to be identical with isocarneagenin by mixed melting point determination and comparison of infra-red spectra. Reduction of the monotosylate of isocarneagenin (XIIa) with lithium aluminum hydride gave isorhodeasapogenin (IX), thus the C-27 methylol group of XIIa should possess the equatorial configuration (25D) and its isomer (XIII) should be represented by the 25L formula. We wish to give the name "carneagenin" to this isomer (XIII).

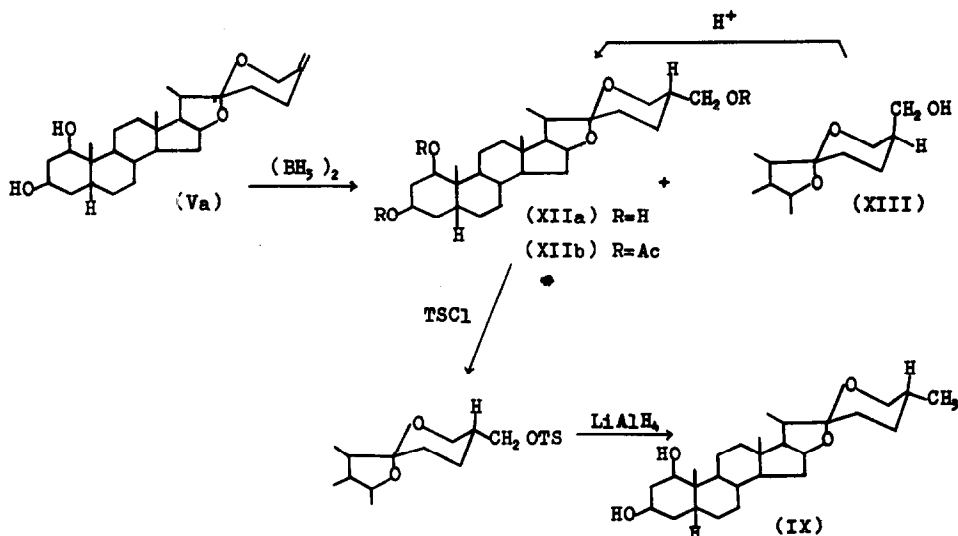


Chart 3

Carneagenin (XIII) was isomerized nearly quantitatively to isocarneagenin (XIIa) by dilute ethanolic hydrochloric acid at room temperature for one hr, that is, under extremely mild conditions as compared to the conditions required for isomerization of 25L to 25D sapogenin. Assuming that isomerization of carneagenin to isocarneagenin takes place on saponification of the saponins, there is a question as to whether

isocarneagenin is the naturally occurring sapogenin or not.

However, it is noteworthy that isoreineckiagenin, reineckiagenin and isocarneagenin are the only known steroidal sapogenins isolated from a plant source containing a hydroxyl group¹⁰ in the F-ring, and that isocarneagenin possesses a primary alcohol function at C-27.

¹⁰ M. J. Thompson, I. Scheer and E. Mosettig, J. Amer. Chem. Soc.
81, 5225, 5222 (1959).