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SYNTHETIC STUDIES IN STEROIDAL ALKALOIDS AND SAPOGENINS II. SYNTHESIS OF KRYPTOGENIN AND DIOSGENIN

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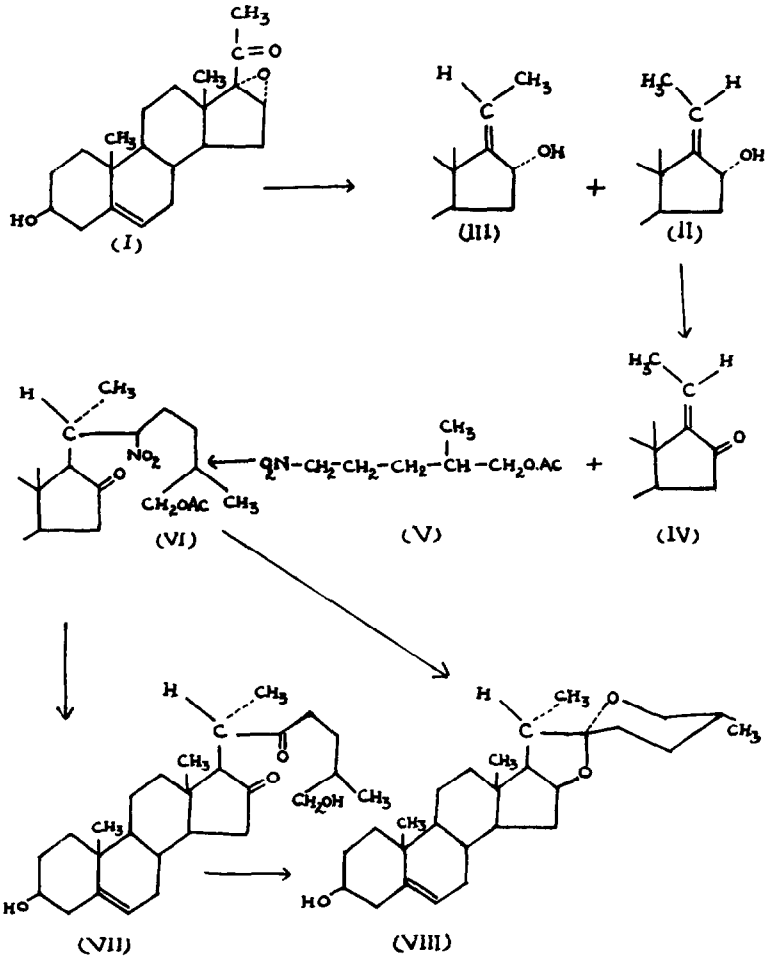
In continuation of our earlier communication[1,2] concerning development of a common route to steroidal alkaloids and sapogenins we now report formal total[3] synthesis of kryptogenin and diosgenin.

Reaction of epoxide I with hydrazine hydrate[4] gave after chromatography on alumina, a material melting at 183-184°. Careful thin layer chromatography showed it to be a mixture of cis (II, ca.80%) and trans(III) isomers. It was oxidised with maganese dioxide and chromatographed on acid-washed alumina to obtain pure cis-ketone IV ($C_{21}H_{30}O_2$, m.p. 171-172°, $[\alpha]_D$-208°, C-20 hydrogen multiplet centred at 3.5 τ) and pure trans-alcohol V ($C_{21}H_{32}O_2$, m.p. 218-219°, $[\alpha]_D$ - 74°).

The nitro acetate V ($C_8H_{15}NO_4$, b.p. 110-111°/1 mm., $[\alpha]_D$ + 3.6°) was synthesised[1] from partially resolved[5] 2-allyl propionic acid ($[\alpha]_D$ - 5.3° corresponding to more than 80% acid of R configuration) in six steps. It is assumed


(I)
(III)
(II)
(IV)
(V)
(VI)
(VII)
(VIII)

to have the same optical purity as the starting acid.

Michael addition of the nitro acetate V to the cis-ketone IV and crystallisation of the adduct afforded VI ($C_{29}H_{45}O_6N$, m.p. 229-230°, $[\alpha]_D$ - 157°, ν_{max}^{KBr} 1740, 1530 cm^{-1}) in 40% yield. The purity of this material was not thoroughly investigated but thin layer chromatography indicated it to be one diasteriomer. It was subjected to a Nef reaction. Chromatography of the product on neutral alumina and crystallisation from ethyl acetate furnished pure diketone VII (20%) which corresponded to kryptogenin (physical constants including I.R.)

This diketone can be selectively reduced[6] to diosgenin for which, however, a direct synthesis has been developed by us. When the nitro ketone VI was refluxed with excess sodium borohydride in ethanol and the mixture acidified diosgenin (VIII) was formed in excellent yield. Apparently in this one operation reduction, Nef reaction and cyclisation had all proceeded. The material obtained after a single crystallisation was found identical with natural diosgenin (mixed m.p. 204-205°, superimposable I.R. and same R_f value).

For spirostanes Mazur, Danieli and Sondheimer[6] also have developed an elegant approach. The present route however, is considerably shorter and is stereoselective. This method is also easily amenable to elaboration of

sapogenins with additional functions in ring F. We are also studying conversion of intermediates of the type VIII to solanum alkaloids. It is interesting to note that the amino triols obtained on reduction of these nitro ketones could be common biogenetic intermediates[7] for steroidal sapogenins and alkaloids.

REFERENCES

1. S.V.Kessar and A.L. Rampal, Chemistry & Industry, 1957 (1963) should be considered part I of this series.
2. Some of these results were first presented in the international symposium on steroidal and indole alkaloids held from 14th to 18th September, 1965 at Smolenice, Czechoslovakia.
3. Total synthesis of dehydropregnenolone which is our starting material is known. H.Cardwell, J.Cornforth, S.Duff, H.Holtermann and R.Robinson, J.Chem.Soc., 361 (1953).
4. Huang-Minlon and Chung-Tungshun, Tetrahedron Letters, 666 (1961); R.Sciaky and F.Facciano, Gazz.Chim.Ital., 93, 1014 (1963); W.R. Benn and R.M.Dodson, J.Org.Chem., 29, 1142 (1964).
5. G.Stallberg, Acta.Chem.Scand., 11, 1430 (1957).

6. Y.Mazur, N.Danieli and F.Sondheimer, J.Amer.Chem.Soc., 82, 5889 (1960).

7. Tschesche, Fortschr. Chem. Org. Naturstoffe (Wein), 12, 131 (1955).