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ACID INDUCED EMPIMERIZATION AND REARRANGEMENTS OF ARBORINOL, THE NOVEL TRITERPENE FROM GLYCOSMIS ARBOREA (ROXB.) DC[1].

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In connection with studies on some other triterpenes, it became necessary for us to ascertain the possibility of epimerization of the axial C_3-OH group under the condition of acetylation using glacial acetic acid : conc. sulphuric acid : water (50:1:1). Arborinol (I) and isoarborinol (II), the epimeric pair of triterpenes isolated from Glycosmis arborea in this laboratory[2] with their structures and stereochemistry well-established[3-5] being readily available were chosen for this investigation.

Arborinol was left for seven days (or fifteen days with the same result) in the aforesaid acid mixture at room temperature. The product was boiled with a mixture of benzene-chloroform (1:3) and the soluble and insoluble fractions were treated separately.

The soluble part showed five distinct spots in TLC over silica gel G using benzene : petroleum ether (7:3) as solvent system. The mixture was resolved through chromatography over neutral alumina (Brockmann, activity I) and the homogeneity was ascertained by TLC while identity of the components were established besides this method by m.p., m.m.p., IR and in some cases by mass spectrum.

In addition to the expected arborinol acetate as the major product and unconverted arborinol, we could separate isoarborinol, its acetate, and a new compound designated as isoarborenene-I, m.p. 187-90° as minor products by elution with varying proportions of benzene in petroleum ether.

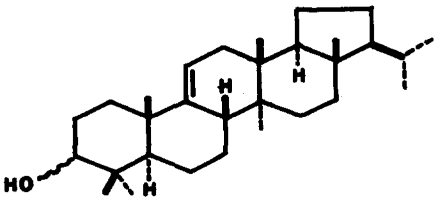
The conversion of arborinol to isoarborinol appears to be the first report of epimerization of the axial C_3-OH group of a triterpene to the more stable equatorial one under the condition used apparently through S_{N_1} mechanism[6].

The insoluble product, isoarborenene-II, could not be crystallized but was obtained pure from ethanol as amorphous solid, m.p. 220°, $[\alpha]_D$ + 100° (c = 0.5; py).

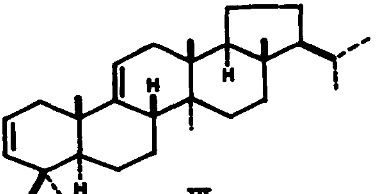
Both isoarborenene-I and isoarborenene-II showed molecular ion peak at m/e 408 corresponding to the formula $C_{30}H_{48}$, and an intense peak at m/e 393 ($M-CH_3$), the other important peaks in the mass spectra appeared at 326 (M-82), 255, 241 (M-167), 191. Evidently, both of them are dehydro compounds but none of them could be identical with the already known[3] Δ^{2}-arborene (III), m.p. 244-245°, a product of phosphorous pentachloride treatment on arborinol. The principal mass spectral peaks of III differ by one mass unit higher than those underlined. Obviously, both the dehydro compounds must be the double bond rearranged product of III with or without migration of methyl group(s).

The relative intensitites of the characteristic[7] ion peaks at M-167 and M-179 points to a $\Delta^{9(11)}$ or Δ^{8} rather than the Δ^{7} position of the double bond in both of them. The rearrangement of $\Delta^{9(11)}$-double bond to Δ^{8}, $\Delta^{13(18)}$ and Δ^{16}-positions with concomitant methyl migration under acidic condition has been shown[8] in davallic acid (IV) with 14β, 13α, 18β, 17α configuration where steric strain provides the conformational driving force. However, such 1:2 shift of the methyl groups consequent on the formation of carbonium ion at C_8 is prohibited in arborene series since Barton et al.[9] have shown that lanosterol system having the same 14α, 13β, 18α, and 17β configuration rearranges to isolanosterol (Δ^{7}) by migration of the Δ^{8}-double bond only.

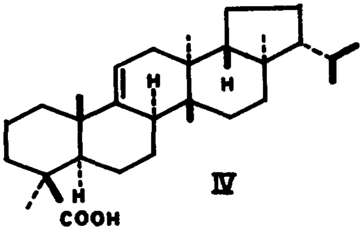
The structures of the two compounds can thus be accommodated in the



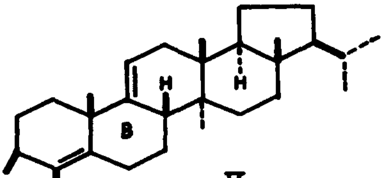
I. OH = α(a)
II. OH = β(e)



III



IV



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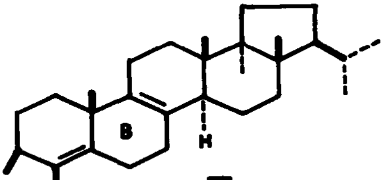
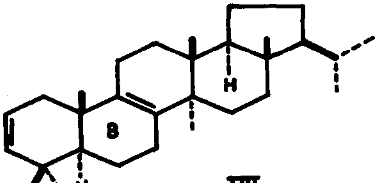


VI



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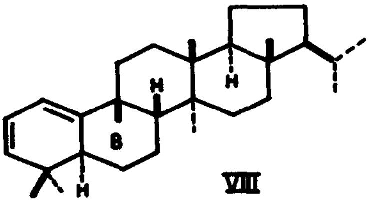

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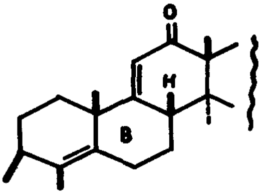
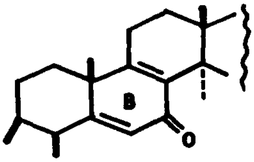
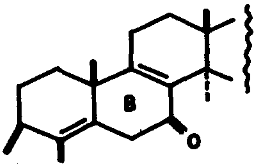


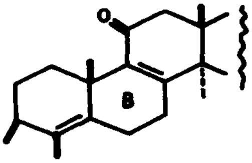
IX



X



XI



XII

expressions (V-VII) although the possibility of (VIII) can not be ruled out.

Both the compounds were subjected to oxidation with chromic acid in acetic acid under conditions[10] which would furnish $\alpha:\beta$-unsaturated mono- and di- ketodihydrolanosteryl acetate from the corresponding dihydro compound. Isoarborenene-I afforded a single product exhibiting UV absorption maximum at 242 mμ (chloroform) compatible with $\Delta^{9(11)}$-12-one (IX). Since arborinol (I) furnishes a 12-keto compound under similar condition, isoarborenene-I has been assigned structure V* supported by its NMR spectrum which clearly shows the presence of only one vinyl proton[3]. Isoarborenene-II, on the other hand, afforded three different ketones which could be isolated pure through preparative TLC in quantities sufficient for UV measurements. The ketones showed one λmax each at 240 (ε = 5,380), 253 and 256 mμ (ethanol) compatible respectively with IX or $\Delta^{5,8}$-diene-7-one (X), Δ^{8}-7-one (XI) and Δ^{8}-11-one (XII) structures. Obviously, the expected trans-enedione that would absorb at 270 mμ was not formed. Structure IX cannot represent the ketone, m.p. 241-242°, absorbing at 240 mμ from this compound because it should then be identical with the ketone from isoarborenene-I contrary to the evidence from TLC. The formation of the same ketone cannot also be explained on the basis of structure VII, the mass spectral fragmentation pattern of which would be expected to be similar to that of Δ^{2}-arborene (III). Structure VIII for isoarborenene-II is least likely since it cannot explain the formation of three ketones. We are thus left with VI as the most rational structure for isoarborenene-II. Unfortunately, no useful information could be derived from NMR spectrum due to its poor solubility.

The assigned structures of isoarborenene-I (V) and isoarborenene-II (VI) are further supported by the identical fragmentation pattern in the mass spectra indicating similar environment in ring A. Moreover, the intensities

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* The compound, m.p. 207-208° reported[3] from the mother liquor of Δ^{2}-arborene (III) may be identical with isoarborenene-I.

of ion peaks of lower mass units of isoarborenene-I have been found to be almost the same as in all other compounds with $\Delta^{9(11)}$-double bond in the series whereas in isoarborenene-II corresponding peaks are far less intense. It is interesting to note that while the diagnostic peak of arborene system at M-85 arises out of decomposition of ring E[7], the rupture of ring A with or without rearrangement of a hydrogen atom (corresponding to peaks at M-81 and M-82 respectively for Δ^2-arborene and isoarborenenes) appears to be characteristic of the dehydro compounds.

It may be noted here that isoarborinol (II) having the equatorial (β) C_3-OH group under the same acetylation condition yielded the corresponding acetate as the only transformation product.

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REFERENCES

1. Part XVI. Studies on Indian Medicinal Plants. Part XV. S. C. Pakrashi and E. Ali, Tetrahedron Letters No. 23, 2143 (1967).
2. S. C. Pakrashi and S. K. Roy, J. Sci. Industr. Res. (India) B20, 186 (1961); S. C. Pakrashi, S. K. Roy and J. Bhattacharyya, J. Indian Chem. Soc. 41, 651 (1964).
3. H. Vorbrüggen, S. C. Pakrashi and C. Djerassi, Liebigs. Ann. 668, 57 (1963).
4. O. Kennard, L. Riva di Sanseverino, C. Djerassi and E. Vorbrüggen, Tetrahedron Letters No. 39, 3433 (1965).
5. O. Kennard, L. Riva di Sanseverino and J.B. Rollett, Tetrahedron 23, 131 (1967).

6. A. Fischer, M. J. Hardman, M. P. Hartshorn and D. N. Kirk, Tetrahedron 23, 1647 (1967).

7. H. Budzikiewicz, J. M. Wilson and C. Djerassi, J. Amer. Chem. Soc. 85, 3688 (1963).

8. K. Nakanishi, Y. Y. Lin, H. Kakisawa, H. Y. Hsu and H. C. Hsiu, Tetrahedron Letters No. 22, 1451 (1963).

9. D. H. R. Barton, J. F. McGhie, M. K. Prodhan and S. A. Knight, J. Chem. Soc. 876 (1955).

10. L. Ruzicka, E. Rey and A. C. Muhr, Helv. Chim. Acta 27, 472 (1944).