Tetrahedron Letters No.28, pp. 1859-1866, 1964. Pergamon Press Ltd.
Printed in Great Britain.

CONSTITUENTS OF ERYTHROXYLON MONOGYNUM ROXB.

II. ERYTHROXYDIOLS X AND Y. TWO NOVEL SKELETAL TYPES OF DITERPENOIDS

J. D. Connolly[+], R. McCrindle, R. D. H. Murray and K. H. Overton
Chemistry Department, The University, Glasgow

A. Melera
Varian AG, Zürich, Switzerland

(Received 25 May 1964)

This communication is concerned with the constitution and stereochemistry of three isomeric diols, erythroxydiols X, Y and Z, which we have isolated from the light petroleum extractive of the trunk wood of E. monogynum.

Separation was conveniently effected by chromatography on silver nitrate-silica gel of the mixture of derived acetonides. The physical constants of the three diols and their acetonides are listed in the Table.

TABLE

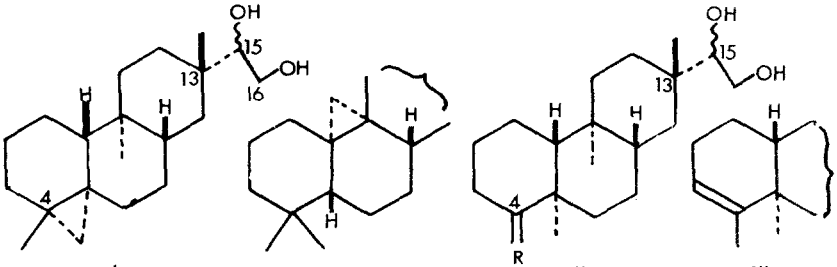
	Diol		Acetonide	
	m.p.	$[\alpha]_D^*$	m.p.	$[\alpha]_D^*$
X	124 - 6°	+ 12°	89 - 90°	+14°
Y	144 - 6°	+ 87°	109 - 110°	-23°
Z	136 - 8°	- 35°	108 - 110°	-22°
P			142 - 4°	+31°
Q			111 - 3°	-17°

* in $CHCl_3$

[+] I.C.I. Postdoctoral Fellow, 1963-1964.

In addition there were isolated (as the acetonides) two minor constituents, the triol P and the triol monoacetate Q, which are also briefly discussed.

Elementary analysis of the two major diols X (I) and Y (II; R= CH_2) and their derivatives, and the mass spectrometric molecular weights of their acetonides indicated the composition $C_{20}H_{34}O_2$. Whereas diol Y clearly contains



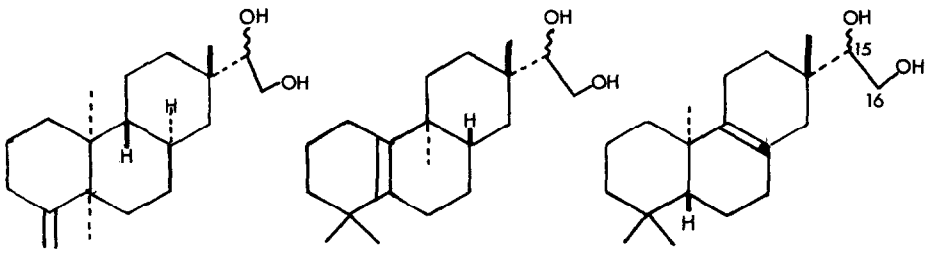
I Ia II III

one vinylidene group as its only element of unsaturation [$\epsilon_{200\ m\mu}$ 3500, $\epsilon_{210\ m\mu}$ 175, $\epsilon_{220\ m\mu}$ 0; ν_{max}^{Nujol} 905 cm^{-1}; 2H singlet at τ 5.5; dihydro-Y transparent above 210 mμ and T.N.M. -ve], the diol X contains instead a cyclopropane ring [two 1H doublets at τ 9.46 and 9.88 (J, 4.5 c.p.s.)]. Diol Y is thus tricyclic, diol X tetracyclic.

The nature of the diol function was revealed as follows. Diol X (I) forms both a monoacetate, m.p. 116-118°, and a diacetate, m.p. 106-107°. The latter has in its N.M.R. spectrum an ABX system [A 5.56, B 6.02, X 5.08 τ; J_{AB} 11, J_{AX} 3, J_{BX} 9 c.p.s.], which clearly defines the diol as a primary--secondary vicinal glycol, the adjacent carbon atom being fully substituted. This is supported by the derived keto-acetate (I; 15-ketone, 16-acetate), m.p. 95-96°; 104-106°, whose N.M.R. spectrum lacks protons on carbon adjacent to carbonyl alone. A paramagnetic shift in this compound of 15 cycles for one methyl group

suggests that this is attached to C-13.

The ABX system in Y diacetate is virtually superimposable on that of X diacetate, suggesting identity of the diol functions and location of the structurally dissimilar elements at a remote part of the molecule. The nature and environment of the diol suggests its location on a pimarane skeleton at C-15 and C-16 as in darutigenol (2). On this basis the vinylidene group of diol Y is best accommodated at C-4 of a rearranged pimarane skeleton (as II; R= CH_2), and this is supported by (i) ozonolysis of diol Y acetonide (3H singlets at τ 9.19, 9.12, and 8.94) to the nor-ketone (II; R=O), m.p. 138-140°, $\nu_{max}^{CCl_4}$ 1710 (cyclohexanone), 1420 (CH_2 next CO) cm^{-1}; 3H singlets at τ 9.19, 9.15, 8.89; absence of 2H singlet at τ 5.5) and (ii) isomerisation of Y acetonide to the acetonide of the naturally occurring diol Z (III) [$\epsilon_{207\ m\mu\ (max)}$ 2900, $\epsilon_{210\ m\mu}$ 2010, $\epsilon_{220\ m\mu}$ 1000, 1H multiplet at τ 4.85 (vinyl H)*. A possible alternative structure (IIa) for diol Y [on the biogenetic precedent of thelepogine (3)] is excluded by its interconversion with rosenonolactone (see later).



IIa IV V

---

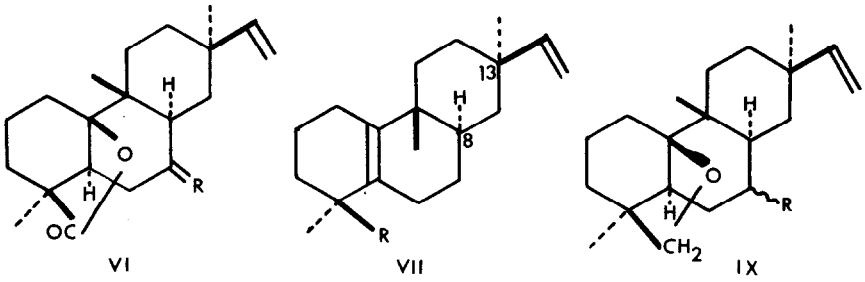
* It has very recently come to our notice (4) that the rearranged pimaradiene structure (II) is found in dolabradiene (II antipode; 13β Me?; Δ^{15}) from Thujopsis dolabrata and that this has been confirmed by a total synthesis.

The close structural relationship between diols X and Y was underlined by the following experiments. Treatment of either X or Y acetonide in dry chloroformic hydrogen chloride at 20° for 0.5 hr. led to a mixture of acetonides, from which the same three major products were isolated in each case: (i) diol Y acetonide; (ii) diol Z acetonide; $[\alpha]_D$ (from both X and Y) - 22°, and (iii) the new acetonide (IV; acetonide) m.p. 108-110° $[\alpha]_D$ - 83°, [$\epsilon_{200\ m\mu}$ 5250, $\epsilon_{210\ m\mu}$ 2800, $\epsilon_{220\ m\mu}$ 700, no N.M.R. signals below τ 6.0; T.N.M. +ve]. That this is not the alternative olefin (V) follows from (i) the number of allylic protons in the N.M.R. spectrum which is clearly four and not six, (ii) direct comparison of the derived $\Delta^{5(10),15}$ diene (enantio-VII; R= Me, see later) with $\Delta^{8(9)}$ pimaradiene (5) (enantio-V; Δ^{15}) from which it differed in its G.L.C. and N.M.R. properties and (iii) synthesis of the diene (VII; R= Me) from rosenonolactone (see below).

The simple relationship which these experiments indicate between diols X and Y then leads to the most probable alternatives (I) or (Ia) for X. Of these we regard (I) as preferable on the grounds that the mass spectra of the acetonides of X (I) and Y (II) are indistinguishable. The mass spectra of cycloartanyl and lanost-8(9)-enyl acetates (6) also show identical fragmentation patterns but there are minor differences in the relative intensities of certain peaks.

The constitution of Y and its congeners was confirmed by conversion of rosenonolactone (VI; R= O) and the ene-diol (IV) into the antipodal dienes (respectively VII and antipode; R= Me), which additionally defines the stereochemistry

at C-8* and C-13 and the absolute configuration of erythroxydiols X and Y.



VI VII IX

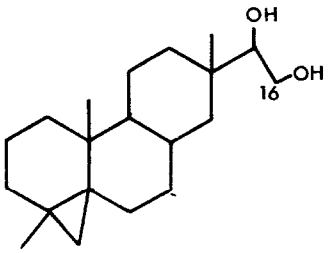
The triol (VIII), obtained from rosenonolactone (VI; R= O) with lithium aluminium hydride was converted into the ether toluene-p-sulphonate (IX; R= OTs) and then by further reduction into the ether (IX; R= H) m.p. 49-51° (8) which was also obtained from desoxyrosenonolactone* (VI; R= H_2). The ether (IX; R= H) was smoothly transformed by ethanolic hydrochloric acid into the dienol (VII; R= CH_2OH), m.p. 116-118° (8). Oxidation to the aldehyde (VII; R= CHO), conversion into the thioketal and desulphurisation with Raney nickel in acetone led to the diene (VII; R= Me), $[\alpha]_D$ - 116°, which was identical in I.R., U.V., N.M.R., mass spectrum, T.L.C. and G.L.C. (on three different columns) properties but of opposite rotation when compared with the diene $[\alpha]_D$ + 110°, obtained by Corey's procedure (9) from the isomerisation product (IV), m.p. 125-8° of diol Y. The diols X and Y are thus antipodally related to rosenonolactone and hence directly to

---

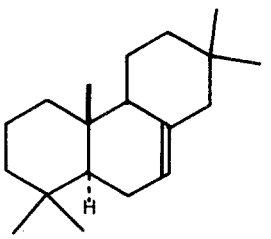
* The configuration at C-8 in desoxyrosenonolactone, although not rigidly proved, may on biogenetic grounds be assumed to be as in rosololactone (7).

the stachenols of E. monogynum.*

Very recently Soman and Sukh Dev have reported (12) their studies on devadarool from E. monogynum which from its physical constants appears to be identical with our diol X from the same source. We do not regard as compelling the evidence adduced by these authors for their preferred structure (Ia antipode, 8ξ, 13ξ, 15ξ; there is no evidence for the absolute configuration adopted). While we would readily concur that acid treatment of the 16-nor hydrocarbon based on the alternative structure (X) would not be expected to afford the same products as (XI), this merely eliminates the biogenetically less probable structure (X) for



X



XI

diol X, while actually supporting our (I). Moreover, we have found the relative intensities of the bands at 1360 and 1380 cm^{-1} in the I.R. an unreliable criterion

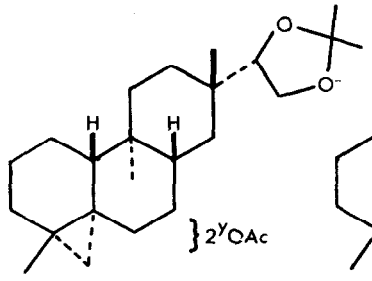
---

* In a recent paper by Kapadi and Sukh Dev (10), 10β-Me stereochemistry is assigned to monogynol from E. monogynum, clearly identical from its physical constants with our alcohol A (1). This error arises from comparison by the Indian authors of the derived saturated hydrocarbon of low (-3.9°) $[\alpha]_D$ with beyerane. Comparison, instead (1), of the unsaturated (Δ^{15}) hydrocarbon, $[\alpha]_D + 39^{\circ}$, with stachene [Δ^{15}--beyerene; $[\alpha]_D + 39^{\circ}$], clearly reveals their configurational identity. This is confirmed by a recent synthesis of alcohol A from isosteviol (11).

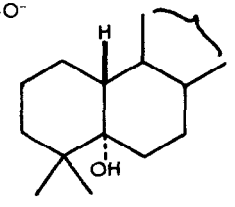
for the number of gem-dimethyl groups present. Details of this will appear in our full publication.

The triol acetate Q, isolated* as the acetonide $C_{25}H_{40}O_4$, m.p. 111-113°, is tentatively formulated as (XII) on the following basis. The acetonide (τ 6-6.4, 3H) and cyclopropane (τ 9.47 and 9.85, 2H) regions of the N.M.R. spectrum are virtually identical with the corresponding regions of the acetonide X. The acetate function (ν_{max}^{Nujol} 1720, 1245 cm^{-1}; 3H singlet at τ 8.03) is secondary and probably equatorial (1H quartet centered at τ 5.07; J suggests axial H).

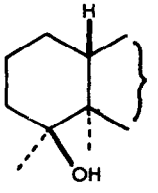
Triol P, isolated* as the acetonide $C_{23}H_{40}O_3$, m.p. 142-144°, probably contains the diol system of X and Y (characteristic multiplet in the acetonide at τ 6-6.4), one additional tertiary hydroxyl group ($\nu_{max}^{CCl_4}$ 3625 cm^{-1} in the acetonide; absence of -CHOH proton in the N.M.R.) and no unsaturation (T.N.M. -ve; transparent above 200 mμ). Constitution (XIII)is preferred to (XIV), since the N.M.R. spectrum (3H singlets at τ 8.98, 9.06, 9.10 and 9.13) does not contain the methyl signal at low field to be expected from (XIV).



XII



XIII



XIV

Biogenetically it is tempting to regard the cyclopropane ring spanning positions 4 and 5 in X and Q as a stabilised intermediate in the formation of Y from a normal pimarane precursor. Analogous rearranged carbon skeletons are of

---

* By Mr. D. M. Gunn of this department.

course well known in the bicyclic labdane series of diterpenoids [clerodin (13), cascarillin (14), columbin (15)] and the isolation of X may be significant in this connection. Of considerable interest also is the co-occurrence of the same tricyclic and tetracyclic carbon skeletons [dolabradiene and hibaene (4)] but of the antipodal series in Thujopsis dolabrata.

REFERENCES

1. Part I. R. D. H. Murray and R. McCrindle, Chem. and Ind., 500 (1964).
2. A. Diara, C. Asselineau, P. Laszlo and J. Pudles, Bull. Soc. Chim., (France), 99 (1963).
3. W. D. Crow, Austral. J. Chem., 15, 159 (1962); J. Fridrichsons and A. McL. Mathieson, Acta Cryst., 16, 206 (1963).
4. Y. Kitahara, A. Yoshikoshi and S. Oida, I.U.P.A.C. Symposium, Kyoto 1964; Abstracts, p. 39.
5. R. F. Church and R. E. Ireland, J. Org. Chem., 28, 17 (1963).
6. D. S. Irvine, J. A. Henry, and F. S. Spring, J. Chem. Soc., 1316 (1955).
7. A. I. Scott, S. A. Sutherland, D. W. Young, L. Guglielmetti, D. Arigoni and G. Sim, Proc. Chem. Soc., 19 (1964).
8. D. W. Young, Ph.D. Thesis, Glasgow 1963.
9. E. J. Corey and R. A. E. Winter, J. Amer. Chem. Soc., 85, 2677 (1963).
10. A. H. Kapadi and Sukh Dev, Tetrahedron Letters, 1171 (1964)
11. Private communication from Dr. J. R. Hanson, whom we cordially thank.
12. R. Soman and Sukh Dev, Tetrahedron Letters, 1181 (1964).
13. D.H.R. Barton, H. T. Cheung, A. D. Cross, L. M. Jackman and M. Martin-Smith, J. Chem. Soc., 5061 (1961); T. C. Paul, G. A. Sim, T. A. Hamor and J. M. Robertson, ibid., 4133 (1962).
14. J. M. Robertson, Proc. Chem. Soc. 235 (1963); D. E. Case, T. G. Halsall and A. W. Oxford, I.U.P.A.C. Symposium, Kyoto 1964, Abstracts, p. 54.
15. D. H. R. Barton and D. Elad, J. Chem. Soc., 2085 (1956); K. H. Overton, N. G. Weir, and A. Wylie, Proc. Chem. Soc., 211 (1961).