Tetrahedron Letters No.19, pp. 2109-2113, 1966. Pergamon Press Ltd.
Printed in Great Britain.

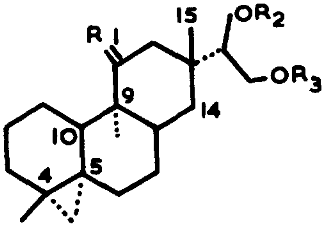
CONSTITUENTS OF ERYTHROXYLON MONOGYNUM ROXB.

III. ERYTHROXYTRIOLS P AND Q.

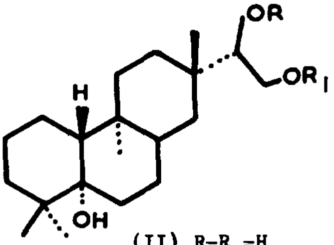
J.D. Connolly, D.M. Gunn, R. McCrindle,
R.D.H. Murray and K.H. Overton.
Department of Chemistry,
The University of Glasgow, Glasgow, W.2.

(Received 17 March 1966)

We have previously described (1) isolation from the trunk wood of E. monogynum of derivatives of the triols P and Q and suggested tentative structures for them. We now present evidence that triol Q is to be formulated as (I) and triol P as (II).



(I) $R_1 = \alpha OH, H;\ R_2 = R_3 = H$
(III) $R_1 = \alpha OH, H;\ R_2 + R_3 = >C(CH_3)_2$
(IV) $R_1 = O;\ R_2 + R_3 = >C(CH_3)_2$
(V) $R_1 = H_2;\ R_2 + R_3 = >C(CH_3)_2$
(VI) $R_1 = \alpha OAc, H;\ R_2 + R_3 = >C(CH_3)_2$
(VII) $R_1 = \beta OAc, H;\ R_2 + R_3 = >C(CH_3)_2$
(VIII) $R_1 = \beta OH, H;\ R_2 + R_3 = >C(CH_3)_2$

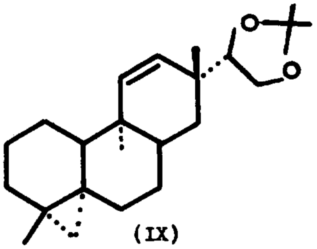


(II) $R = R_1 = H$
(IIa) $R + R_1 = >C(CH_3)_2$

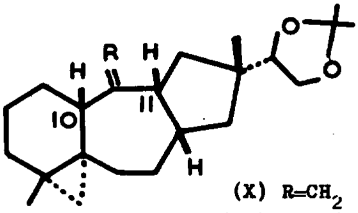
Oxidation of triol Q acetonide [QA] (III), $C_{23}H_{38}O_3$, m.p. 115–116°, $[\alpha]_D$ + 5°, with the Sarrett reagent affords the corresponding ketone (IV), $C_{23}H_{36}O_3$, m.p. 92–93°, $[\alpha]_D$ + 124°, and this on Wolff-Kishner reduction is transformed into diol X-acetonide (V) (2) as the sole product. Triol Q is therefore diol X with an additional secondary hydroxyl group.

As previously indicated (1) the n.m.r. spectrum (1H, τ5·07, quartet, J = 10; 6 c.p.s.) of QA-acetate (VI) suggests an equatorial acetate. The spectrum of the epimeric acetate (VII), m.p. 119–121°, $[\alpha]_D$ + 34°, [derived from the borohydride reduction product (VIII) m.p. 113–115°, $[\alpha]_D$ + 36°, of ketone (IV)](1H, τ5·12, triplet, $W^{1/2}$9 c.p.s. (3)) suggests an axial acetate. Both spectra indicate that the nuclear hydroxyl group of triol Q has only two hydrogens on adjacent carbon(s). Base-catalysed deuterium exchange of the ketone (IV) confirms this (16% d_o, 61% d_1, 12% d_2, 0% d_3, after 96 hrs., at 60° in $NaOD/D_2O$ - dioxan) and its n.m.r. spectrum demonstrates that both α-hydrogens are attached to the <u>same</u> carbon atom: one proton centred at τ7·08 (doublet, J = 13 c.p.s.) is coupled to one geminal proton (n.m.d.r. at 100 Mc/s.) at τ8·23. Since both doublets exhibit only very minor secondary couplings (with H-14 and H-15 ?) there cannot be hydrogen on adjacent carbon. On deuterium exchange the proton at τ7·08 (probably equatorial) is replaced first. Stereoselective deuterium exchange of ketones under basic conditions has been previously observed (4).

The functional sequence $-\overset{|}{\underset{|}{C}}-CHOH-CH_2-\overset{|}{\underset{|}{C}}-$ can be fitted into the structure of erythroxydiol-X (V) only with the hydroxyl at either position 11 or 12. Not unexpectedly, the ketone (IV) does not condense with benzaldehyde and does not form a diosphenol, an ethylene ketal, an α-bromo- or α-acetoxy ketone under a variety of conditions. The secondary hydroxyl is placed at C-11 for the following reasons. Dehydration of the two epimeric alcohols (III) and (VIII) with thionyl chloride in cold pyridine gave in each case one major product.

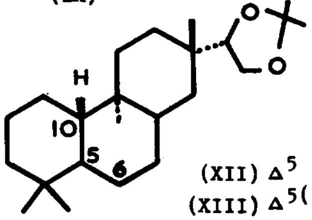


(IX)



(X) R=CH_2

(XI) R=O (configurations at C-10 and C-11 undefined)



(XII) Δ^5

(XIII) $\Delta^{5(10)}$

Thus the axial alcohol (VIII) afforded (75% by g.l.c.), the olefin (IX) $C_{23}H_{36}O_2$ [2H, AB quartet at τ4·07, 4·70; J = 10 c.p.s., with additional minor coupling (<1 c.p.s.) of the proton at τ4·70], which was isolated by preparative t.l.c., on silver nitrate-silica gel and furnished diol X-acetonide (V) on hydrogenation. The equatorial alcohol (III), under the same dehydrating conditions gave as major product (90% by g.l.c.) the olefin (X), $C_{23}H_{36}O_2$ [2H, doublet at τ5·16, 5·19, loss of one quaternary methyl]. Osmylation and cleavage with periodate of the resulting mixture of glycols afforded the nor-ketone (XI), $C_{22}H_{34}O_3$, m.p. 142-143°, $[\alpha]_D$ + 67°, $\nu_{max.}^{CHCl_3}$ 1696 cm^{-1}, which smoothly exchanged two protons for deuterium under basic conditions (11% d_o, 18% d_1, 71% d_2, 0% d_3 after 72 hrs., at

70° in NaOD / D_2O - dioxan).

Triol P [acetonide (PA), $C_{23}H_{38}O_3$, m.p. 142-143°, $[\alpha]_D$ + 31°] is formulated as (II) because of the properties previously summarised (1) and because of its behaviour on dehydration. Thus exposure of PA (IIa) to thionyl chloride in cold pyridine afforded a mixture of the olefin (XII), $C_{23}H_{38}O_2$, m.p. 85-86°, $[\alpha]_D$ - 29° (88%) and the previously obtained (2) isomer (XIII) (12%). Chloroformic hydrogen chloride at 20° converted (XII) into a mixture of (XII) (53%), (XIII) (34%) and two minor products. Assignment of the double bond in (XII) to position 5,6 rather than 1,10 rests on two properties resembling rimuene (5). Thus in the n.m.r. spectrum there is one high methyl signal at τ9·35 and in the mass spectrum the peak at m/e 136 (18%) arises from retro-Diels Alder fragmentation of ring B.

Sukh Dev and his colleagues have isolated (6) from E. monogynum hydroxydevadarool which is very probably erythroxytriol Q. These authors appear to concur with our preliminary suggestion (1) as to carbon skeleton. However, the reasoning whereby they place the nuclear secondary hydroxyl at C-7 is obscure.

The structural evidence for erythroxytriol Q and its conversion by two routes into erythroxydiol-X (V) constitutes the first chemical proof for location in this latter compound of a cyclopropane ring at position 4,5 and not at 9,10.

REFERENCES.

1. J.D. Connolly, R. McCrindle, R.D.H. Murray, K.H. Overton and A. Melera, Tetrahedron Letters, 1859 (1964).
2. J.D. Connolly, R. McCrindle, R.D.H. Murray, A.J. Renfrew, K.H. Overton and A. Melera, J. Chem. Soc. C., 268 (1966).
3. A. Hassner and C. Heathcock, J. Org. Chem., **29**, 1350 (1964).
4. A.F. Thomas and B. Willhalm, Tetrahedron Letters, 1309 (1965); J.M. Jerkunica, S. Borcic and D.E. Sunko, Tetrahedron Letters, 4465 (1965).
5. J.D. Connolly, R. McCrindle, R.D.H. Murray and K.H. Overton, J. Chem. Soc. C., 273 (1966).
6. R. Soman, Sukh Dev, R. Misra and R.C. Pandey, Tetrahedron Letters, 3767 (1964).