Tetrahedron Letters No.41, pp. 4363-4366, 1968. Pergamon Press. Printed in Great Britain.

OXYGENATED DERIVATIVES OF ASIATIC ACID FROM DRYOBALANOPS AROMATICA

H.T. Cheung* and L. Tökés

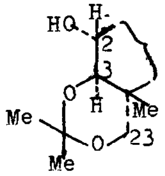
Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia and
Institute of Steroid Chemistry, Syntex Research†, Palo Alto, Calif., U.S.A.

(Received in Japan 18 June 1968; received in UK for publication 12 July 1968)

The isolation from the resin of Dryobalanops aromatica of eight pentacyclic and four dammarane triterpenes has been recorded recently (1,2). We report here the occurrence, as minor constituents, of 11-oxo-asiatic acid (II) and 2α,3β,23-trihydroxyursa-11-en-13β,28-olide (VI). These may be considered as oxygenated derivatives of asiatic acid (3), the major triterpene acid found in the resin (1).

Isolation of the minor constituents resulted from purification of crude methyl asiatate via the 3,23-O-isopropylidene ("acetonide") derivative. Chromatography of the crude acetonides yielded, besides methyl 3,23-O-isopropylidene-asiatate (XI)(1), two minor acetonides which are respectively an α,β-unsaturated ketone and a γ-lactone.

The conjugated ketone, $C_{34}H_{52}O_6,H_2O$ #, m.p. 253-255°, showed IR and UV absorption for hydroxy, ester, and conjugated carbonyl groups. NMR signals were found for one vinyl proton (τ 4.4) and one methyl ester (τ 6.4). Presence of a 2α-hydroxy-3β,23-O-isopropylidene system (A) was suggested by occurrence of signals similar to those found in methyl 3,23-O-isopropylidene-asiatate (XI)(1): a 2-H singlet at τ6.5 (C-23), a 1-H unsymmetrical doublet near τ6.7 (J_{ax-ax}=10 Hz)(C-3), and a 6-H singlet at τ 8.55 ($-O.C(CH_3)_2.O-$). Second



(A)

---

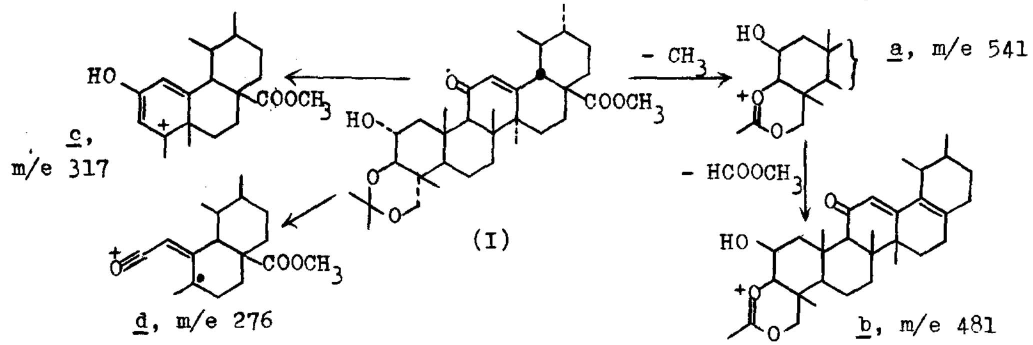
[*] To whom enquiries are to be directed.

[†] Contribution No. 344.

[#] All new crystalline compounds gave satisfactory elemental analyses. UV and NMR (60 MHz) spectra referred to EtOH and $CDCl_3$ solutions respectively. Mass spectra were recorded with an Atlas CH-4 instrument at 70 ev.

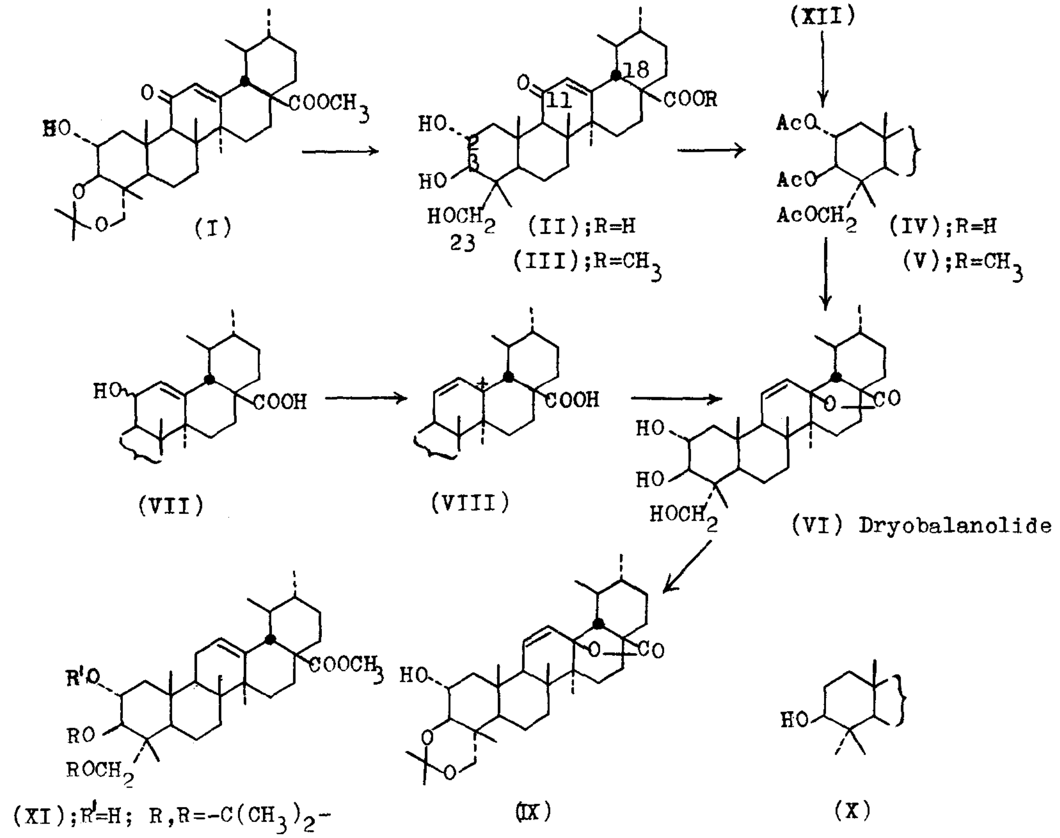
order perturbation in the methyl region indicates the presence of secondary methyl group(s).

Structure (I) for the ketone was considered, and was supported by the mass spectrum. The molecular ion M^+ is at m/e 556, corresponding to $C_{36}H_{52}O_6$. Peaks at M^+-15 and M^+-75 are accounted for by ions a and b. Ions c and d result from cleavage of the B or C ring of the 12-en-11-one (4). Other significant peaks are at m/e 257 and 217, due to c - $HCOOCH_3$ and d - $COOCH_3$.



Structure (I) was finally established by acid-catalysed removal of the O-isopropylidene group, and acetylation of the resulting triol (III)($C_{31}H_{48}O_6$,H_2O, m.p. 184-186°) to a triacetate which was identical with authentic methyl 11-oxo-asiatate triacetate (V)(3), m.p. 268-269°. The latter, which we prepared by chromic acid oxidation of methyl asiatate triacetate (XII)(3), should retain a 18β configuration which is the more stable one in ursane derivatives (5,6). As the formation of (V) from the naturally occurring 11-ketone (I) was not expected to be accompanied by epimerization at C-18, we prefer a 18β configuration for (I).

The second minor constituent, named dryobalanolide acetonide, $C_{33}H_{50}O_5$, m.p. 278-280°, showed IR bands for γ-lactone (1765 cm^{-1}) and hydroxy groups. In the NMR spectrum, centered at τ4.2, was found an AB quartet (J_{AB} = 11 Hz, $\delta_B - \delta_A$ = 24 Hz), the higher-field half of which was further split (J = 3 Hz). These signals were assigned to the system $-\overset{|}{C}H-CH=CH-\underset{|}{\overset{|}{C}}-$. Also found were resonances associated with the partial structure (A) and with secondary methyl group(s)(see above). The lactone ring was extremely unstable to acids, suggesting an allylic location of the lactone ether oxygen.

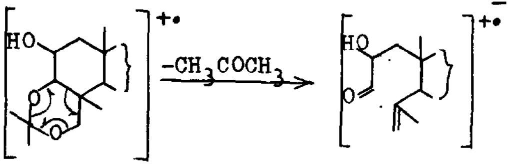


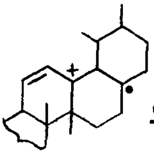
(XI);R'=H; R,R=-C(CH$_3$)$_2$-

(XII);R=R' =Ac

A structure which satisfies the above data is the 11-en-13β,28-olide (IX). This is related to the structure (X) given by Barton and coworkers (7) to a product obtained (8) on sodium and ethanol reduction of 11-oxo-ursolic acid. A partial synthesis from asiatic acid incorporating a similar reduction step would then lead to (IX). In the event, 11-oxo-asiatic acid triacetate (IV)(3) was so reduced, and the resulting triol lactone (VI) converted to the 3,23-O-isopropylidene derivative (IX). The latter proved to be identical with dryobalanolide acetonide.

The mass spectrum of dryobalanolide acetonide (IX) showed the molecular peak M^+ at m/e 526. The base peak, at M^+-44, corresponds to a loss of CO_2 and the formation of a stabilized allylic ion e. The radical site in e may gain further stabilization by forming a cyclopropyl or a conjugated diene derivative. Fragmentation of the O-isopropylidene moiety leads either to M^+-15 (see above) or to loss of acetone from M^+ and from e:





e, m/e 482

The 11-oxo-12-ene and 11-en-13β,28-olide units found in the minor constituents represent moieties uncommon in naturally occurring triterpenes. Occurrence of the former is exemplified by glycyrrhetic acid (9) and neo-ilexonol (10). Structural features related to the 11-en-13β,28-olide unit are found in 12-hydroxyoleanolic lactone (11) and in saikogenins E, F and G (12) with a 13β,28-oxide link.

Dryobalanolide (VI) could have been derived, in the plant or during isolation, from a 11-hydroxy compound (VII) by lactonization through an intermediate such as (VIII). The possible biogenetic relationship between the two minor constituents of the resin and the eight other pentacyclic triterpenes reported earlier (1,2) will be discussed in the full paper.

We thank Mr. M.C. Feng for participation in the isolation experiments, and Dr. D.H. Williamson of the University of Aberdeen for the NMR spectra.

References

1. H.T.Cheung and M.C.Feng, J.Chem.Soc. 1047(1968).
2. H.T.Cheung, Tetrahedron Letters 2807(1967); J.Chem.Soc. in press (1968).
3. J.Polonsky, Bull.Soc.Chim.France 649(1952); J.Polonsky and J.Zylber, ibid. 1586(1961), and references cited therein.
4. H.Budzikiewicz, J.M.Wilson, and C.Djerassi, J.Am.Chem.Soc. 85, 3688(1963).
5. D.H.R.Barton and N.J.Holness, J.Chem.Soc. 78(1952).
6. E.J.Corey and J.J.Ursprung, J.Am.Chem.Soc. 78, 83(1956).
7. D.H.R.Barton, H.T.Cheung, P.J.L.Daniels, K.G.Lewis, and J.F.McGhie, J.Chem.Soc. 5163 (1962).
8. K.Huzii and S.Osumi, J.Pharm.Soc.Japan 60, 117, 291 (1940); Chem.Abstr. 34, 7293 (1940).
9. Elsevier's Encyclopaedia of Organic Chemistry, Vol.14 p. 526, Elsevier, New York and Amsterdam (1940); Vol. 14 Supplement, p. 939 S(1952).
10. K.Yagishita and M.Nishimura, Agric.Biol.Chem.(Tokyo) 25, 517, 844 (1961).
11. T.G.Halsall and R.T.Aplin, Fortschr.Chem.Org.Naturstoffe 22, p.174 (1964)
12. T.Kubota and H.Hinoh, Tetrahedron 24, 675 (1968).