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STRUCTURES OF TRITERPENES FROM *DRYOBALANOPS AROMATICA**

H. T. CHEUNG† and C. S. WONG

Department of Chemistry, University of Hong Kong, Hong Kong

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Abstract—Further constituents of *Dryobalanops aromatica* resin include oleanolic acid acetate, hedragonic acid, and dryobalanonoloic acid, shown to be 20(*S*)-20-hydroxydammar-24-en-3-on-21-oic acid. Also isolated (in the form of 3,23-*O*-isopropylidene derivatives) were methyl 11-oxoasiatate and dryobalanolide, shown to be 2α,3β,23-trihydroxyursa-11-en-13β,28-olide. The structural and possible biogenetic relationship between the 17 triterpenes so far isolated from the resin is discussed.

INTRODUCTION

THE DIPTEROCARPACEAE are a family of resin-bearing trees found in the Indo-Malayan region. In a recent survey, Bisset *et al.*[3] studied the distribution of sesqui- and tri-terpenoid constituents of resins of over 50 spp. from 6 genera. Notable among the observations made was the occurrence of dammarane triterpenes in all spp. studied. In earlier parts of this series,[2] we reported the isolation from *Dryobalanops aromatica* Gaertn.f. resin of four dammarane triterpenes‡ and eight pentacyclic triterpenes of the ursane, oleanane and lupane groups. Later work has resulted in the further isolation of several triterpene constituents, and we give below details of work establishing the structures of these compounds. We also take the opportunity to review the results of work on this resin, and to comment on the structural and possible biogenetic relationship between the triterpene constituents isolated.

RESULTS AND DISCUSSION

In our earlier separation of triterpenes, the acid components were first converted to the methyl esters.[2] From the least polar materials we have now isolated (in addition to methyl oleanolate acetate) a nor-triterpene, methyl hedragonate (methyl 24-nor-olean-12-en-3-on-28-oate) (I),[5] and a new triterpene (V) named methyl dryobalanonolate. From the most polar materials have been obtained two compounds shown to be related to asiatic acid (see below).

* Part III in the series "Constituents of Dipterocarpaceae Resins". Parts of this work have been communicated.[1]

† Present address: Department of Pharmacy, University of Sydney, Sydney, Australia. Work partly carried out at the University of Malaya.

‡ Dammarane triterpenes of an unidentified *Dryobalanops* species were also studied by Hirose *et al.*[4]

[1] H. T. CHEUNG and L. TÖKES, *Tetrahedron Letters* 4363 (1968); H. T. CHEUNG, C. S. WONG and T. C. YAN, *ibid.* 5077 (1969).

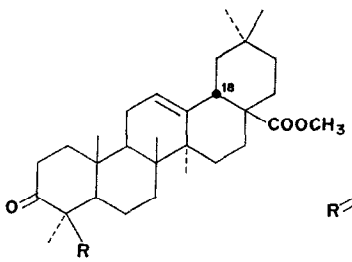
[2] H. T. CHEUNG and M. C. FENG, *J. Chem. Soc.* C, 1047 (1968); H. T. CHEUNG, *ibid.* 2686 (1968).

[3] M. A. DIAZ, G. OURISSON and N. G. BISSET, *Phytochem.* 5, 855 (1966); N. G. BISSET, M. A. DIAZ, C. EHRET, G. OURISSON, M. PALMADE, F. PATIL, P. PESNELLE and J. STREITH, *ibid.* 865 (1966); N. BISSET, M. A. DIAZ-PARRA, C. EHRET and G. OURISSON, *ibid.* 6, 1395 (1967).

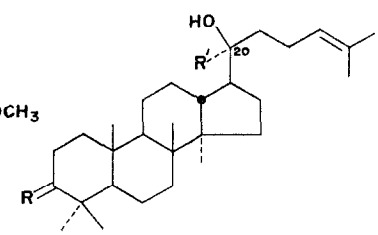
[4] Y. HIROSE, T. YANAGAWA, Y. SAYAMA, T. IGARASHI and T. NAKATSUKA, *J. Japan Wood Res. Soc.* 14, 36 (1968); Y. HIROSE, T. YANAGAWA and T. NAKATSUKA, *ibid.* 59 (1968); T. YANAGAWA, Y. HIROSE and T. NAKATSUKA, *ibid.* 440 (1968).

The nor-triterpene methyl ester, $C_{30}H_{46}O_3$ (MS), showed spectral data (see Experimental, Table 4) suggestive of a structure similar to methyl oleanonate (II) but having only one methyl group at position 4. Direct comparison established its identity with methyl hedragonate (I)[5] obtained by Barton and de Mayo[6] by a reversed aldol-reaction on hederagenin methyl ester. In view of the known occurrence of hederagenin in the resin,[2] the isolation of methyl hedragonate is not unexpected.

Methyl dryobalanonolate,* $C_{31}H_{50}O_4$, contains hydroxyl (ν_m 3470, 1165 cm^{-1}), carbomethoxyl (ν_m 1740 cm^{-1}; 3-H NMR signal at δ 3·7), keto (ν_m 1705 cm^{-1}), and tri-substituted olefinic functions (ν_m 1605, 840 cm^{-1}; 1-H multiplet near δ 5·05). The hydroxyl group is tertiary since it did not react with acetic anhydride in cold pyridine, and since no signal due to >CH—OH was found in the NMR spectrum. The high-field region of the 60 MHz NMR spectrum was similar in three aspects to that of dipterocarpol (hydroxydammarenone-II) (III) and of dryobalanone (IV) which are dammarane 3-ketones known to occur in the same resin.[2] Firstly, the complex signals due to two protons near δ 2·4 were remarkably



(I) R = H
(II) R = CH_3



(III) R = O ; R′ = CH_3
(IV) R = O ; R′ = CH_2OH
(V) R = O ; R′ = $COOCH_3$
(VI) R = H, β-OH ; R′ = CH_2OH
(VII) R = H, β-OH ; R′ = $COOCH_3$

similar in shape to those due to the methylene protons α to the 3-keto group in dipterocarpol and dryobalanone. Secondly, there were two peaks at δ 1·55 and 1·65 due to methyl groups on double bonds. Finally and most significantly, there were five distinct and unsplit peaks, each due to one angular methyl group, the frequencies of which correspond nearly

TABLE 1. NMR FREQUENCIES OF METHYL GROUPS (Hz)*

	4α-Me	4β-Me	10β-Me	8β-Me	14α-Me	20-Me
Dipterocarpol (III)	65·5	63	57·5	60·5	54	69·5
Dryobalanone (IV)	65	62·5	57	60	53	—
Methyl dryobalanonolate (V)	64	62	56	59	51	—

* Relative to $SiMe_4$ as measured in $CDCl_3$ at 60 MHz.

exactly to those in dryobalanone, and to five of the six in dipterocarpol (Table 1). It had been shown[2] that the sixth and the least-shielded angular methyl group (on C-20) in dipterocarpol is replaced in dryobalanone by a hydroxylmethyl group. It is likely that in methyl dryobalanonolate, this group is replaced by a carbomethoxyl group (see V).

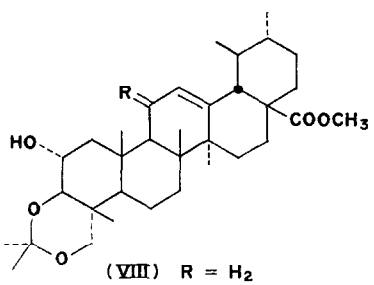
* *Note added in proof.* Since our preliminary communication,[1] the isolation from *Dipterocarpus pilosus* of a compound given the same structure was reported (A. S. GUPTA and SUKH DEV, *Tetrahedron* **27**, 823 (1971)).

[5] W. A. JACOBS and E. A. GUSTUS, *J. Biol. Chem.* **69**, 641 (1926).
[6] D. H. R. BARTON and P. DE MAYO, *J. Chem. Soc.* 887 (1954).

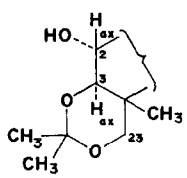
To confirm, methyl dryobalanonolate was correlated chemically with dryobalanone (IV). Thus methyl dryobalanonolate on treatment with sodium borohydride yielded the 3β-alcohol (VII), ν_m 3510, 3450, 1730 cm^{-1}. This product upon reaction with lithium aluminium hydride gave dryobalanol (VI) which was identical to an authentic sample obtained[2] by borohydride reduction of dryobalanone.

Asiatic acid (XVI) is one of the most abundant constituents of the resin. In our work, crude methyl asiatate was purified by conversion to the 3,23-*O*-isopropylidene derivative ('acetonide') followed by chromatography over alumina. In addition to methyl 3,23-*O*-isopropylidene-asiatate (VIII),[2] we isolated two minor acetonides which turned out to be oxygenated derivatives of asiatic acid.

The first minor acetonide, $C_{34}H_{52}O_6,H_2O$, is an $\alpha\beta$-unsaturated ketone, showing UV absorption maximum at 250 nm (ϵ 11 000), and IR absorption at 1670 and 1625 cm^{-1}. Other IR bands were assigned to hydroxyl (3520 cm^{-1}), ester (1730, 1200 cm^{-1}), ketal (several bands at 1055–1190 cm^{-1}), and isopropylidenedioxy groups (865 cm^{-1}).* The NMR spectrum showed a three-proton singlet at δ 3·6 due to a methyl ester, and a one-proton singlet at δ 5·6 which was assigned to an olefinic proton of the conjugated carbonyl



(VIII) R = H_2
(IX) R = O



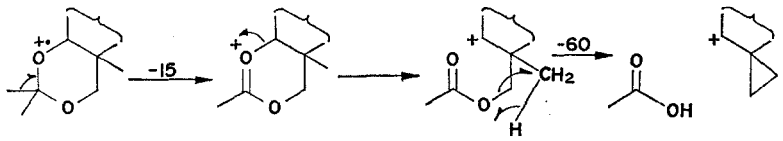
(X)

system. The 2α-hydroxy-3β,23-isopropylidenedioxy partial structure (X) was indicated by presence of signals similar to those found in methyl 3,23-*O*-isopropylidene-asiatate (VIII),[2] viz. a six-proton singlet at δ 1·45 (—O—C(CH$_3$)$_2$—O—), a two-proton singlet at δ 3·5 (C-23), and a one-proton unsymmetrical doublet (*J*, 10 Hz) near δ 3·3 (C-3). There were in addition resonances due to six *C*-methyl groups (δ 0·8–1·3) some of which showed second-order perturbation indicating the presence of secondary methyl group(s).[8]

The above spectral data and biogenetic considerations led us to consider a methyl 3,23-*O*-isopropylidene-11-oxoasiatate structure (IX) for the conjugated ketone. This was substantiated by examination of the mass spectrum. The molecular ion M$^+$ is at *m/e* 556, corresponding to a molecular formula of $C_{34}H_{52}O_6$. Fragments at M$^+$-15 and M$^+$-75 may be accounted for as due to fragmentation of an isopropylidenedioxy group in a six-membered ring as shown in Scheme 1.[9]

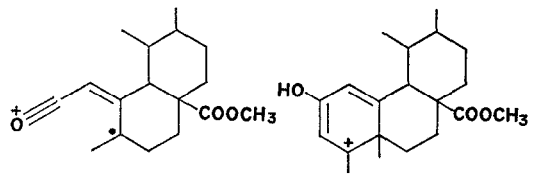
* This 865 cm^{-1} absorption was also shown by the 2,23-*O*-isopropylidene derivatives of methyl asiatate and of methyl asiatate 2-acetate.[2]

[7] H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.* **85**, 3688 (1963); J. Karlinger and C. Djerassi, *J. Org. Chem.* **31**, 1945 (1966).
[8] H. T. Cheung and D. G. Williamson, *Tetrahedron* **25**, 119 (1969); and references cited therein.
[9] J. A. McCloskey and M. J. McClelland, *J. Am. Chem. Soc.* **87**, 5090 (1965); R. E. Wolff, G. Wolff and J. A. McCloskey, *Tetrahedron* **22**, 3093 (1966).



SCHEME 1. FRAGMENTATION OF THE ISOPROPYLIDENEDIOXY GROUP.

The cleavage of pentacyclic triterpene 11-oxo-12-enes such as IX has been shown by Djerassi and co-workers[7] to occur at rings C and B leading to ions such as XI *a* and *b*. In the case of the conjugated ketone isolated, strong peaks are found at *m/e* 276 and 317 which correspond to ions *a* and *b* respectively. Other significant peaks are at *m/e* 257 and 217 due to *b*-$HCOOCH_3$ and *a*-$COOCH_3$ fragment ions respectively.



(XIa) *m/e* 276 (XIb) *m/e* 317

Correctness of the structure IX was established as follows. The conjugated ketone was treated with aqueous acid in ethanol to remove the isopropylidenedioxy group, and the resulting triol was acetylated to yield the triacetate. This product was found to be identical to methyl 11-oxoasiatate triacetate (XIII)[10] prepared by chromic acid oxidation of methyl asiatate triacetate (XVII). In compounds of the ursane series, the *cis* D/E ring junction with 18β-H is more stable than the *trans* one (18α), the latter being associated with two methyl groups at ring E in unfavourable axial configurations.[12] Methyl 11-oxoasiatate triacetate therefore has a 18β configuration. NMR evidence suggests that the same configuration is also possessed by methyl 3,23-*O*-isopropylidene-11-oxoasiatate from the resin, as shown in IX. Thus it was shown by Collins *et al.*[13] that in related compounds such as glycyrrhetinic acid, an allylic coupling between H-12 and H-18 (of *ca.* 1·3 Hz) was associated with a 18α configuration; no such coupling was detected for a 18β configuration. We do not find any detectable allylic coupling either for methyl 3,23-*O*-isopropylidene-11-oxoasiatate isolated, or for methyl 11-oxoasiatate triacetate.

From the manner of its isolation, the conjugated ketone IX undoubtedly exists in the resin as the corresponding acid triol, viz. 11-oxoasiatic acid (XIV). The latter compound and its methyl ester* are known[10,11] though not as plant constituents. Pentacyclic triterpene 11-ketones rarely occur naturally, known examples being glycyrrhetinic acid (olean-12-en-11-on-3β-ol-30-oic acid)[14] and neoilexonol (ursa-12-en-11-on-3β-ol).[15]

* Until our work, methyl 11-oxoasiatate (XII) could not be obtained crystalline (see Experimental).

[10] J. POLONSKY *Bull. Soc. chim. France* 649 (1952); J. POLONSKY and J. ZYLBER, *ibid.* 1586 (1961); and references cited therein.

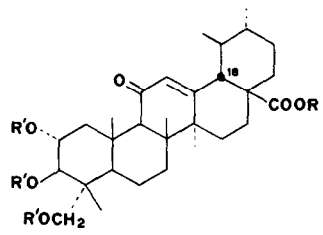
[11] P. BOITEAU and M. CHANEZ, *Diss. Pharm.* **15**, 189 (1963).

[12] D. H. R. BARTON and J. J. HOLNESS, *J. Chem. Soc.* 78 (1952); E. J. COREY and J. J. URSPRUNG, *J. Am. Chem. Soc.* **78**, 183 (1956).

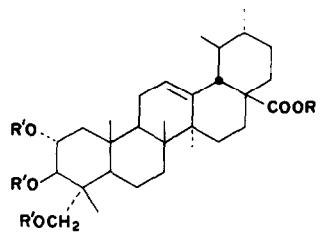
[13] D. J. COLLINS, J. J. HOBBS and S. STERNHELL, *Austral. J. Chem.* **16**, 1030 (1963).

[14] *Elsevier's Encyclopaedia of Organic Chemistry*, Vol. 14, p. 526, Elsevier, New York and Amsterdam (1940); Vol. 14 Supplement, p. 939 S (1952).

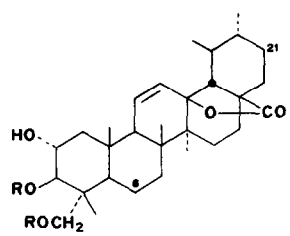
[15] K. YAGISHITA and M. NISHIMURA, *Agric. Biol. Chem. Tokyo* **25**, 517, 844 (1961).



(XII) R = CH_3 ; R' = H
(XIII) R = CH_3; R' = Ac
(XIV) R = H ; R' = H
(XV) R = H , R' = Ac



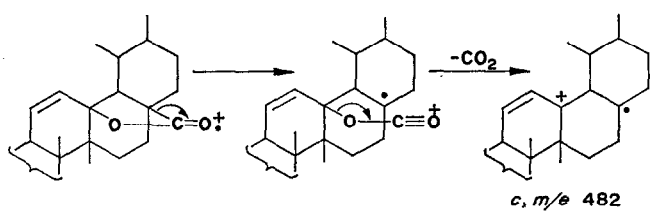
(XVI) R = R' = H
(XVII) R = CH_3, R' = Ac.



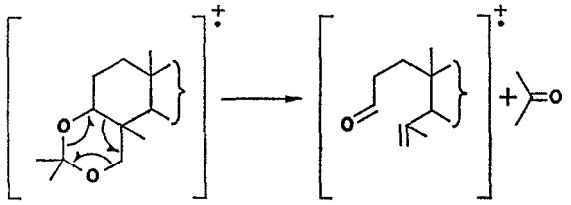
(XVIII) R = H
(XIX) RR = $-C(CH_3)_2-$

The second acetonide separated from the resin (see above), $C_{33}H_{50}O_5$, is named dryobalanolide acetonide. It showed IR absorption at 1765 cm^{-1} characteristic of a γ-lactone; other IR bands were found at 3580 (hydroxyl), 1205, 1135, 1115, 1065, 1045 (hydroxyl and ketal), and 865 (isopropylidenedioxy) cm^{-1}. Only end-absorption was observed in the UV. The NMR spectrum showed signals indicative of the presence of the 2α-hydroxy-3β,23-isopropylidenedioxy system X (see above). An AB quartet was found centered at δ 5·8 with J_{AB} = 11 Hz, and $\delta_B - \delta_A$ = 24 Hz; signals of the higher-field half of the quartet were further split, with J = 3 Hz. These signals could be assigned to an ethylenic system of the type: >CH—CH=CH—C<. Finally, resonances for about six *C*-methyl groups were found in the region δ 0·9–1·2; the occurrence of second-order perturbation suggested that some of the *C*-methyl groups are secondary.[8]

Possible structures for dryobalanolide acetonide are XIX and its analogues with the double-bond at alternative positions 6 or 21. A choice in favour of XIX came from the following observation. In an attempt to remove the *O*-isopropylidene group with mild acid, intractable materials were obtained. The lactone ring was thus unstable to acids, as would be expected if the ether oxygen atom were allylic (XIX). Confirmation was obtained by examination of the mass spectrum. The molecular ion M^+ occurred at *m/e* 526, corresponding to the molecular formula $C_{33}H_{50}O_5$. By far the strongest peak in the spectrum was due to an ion at *m/e* 482. According to high resolution analysis, this corresponded to the loss of CO_2 from M^+ and, in the case of structure XIX, the formation of a stable allylic ion *c* (Scheme 2). No such allylic ion could be formed if alternative structures with a double-bond at 6 or at 21 were adopted for dryobalanolide. As before (see Scheme 1) fragmentation of the isopropylidenedioxy system yielded ions M^+-15 and M^+-75. In addition another cleavage pattern of this moiety was observed in these compounds, viz. the loss of the elements of acetone from M^+ (and from M^+-44 in XIX), which may be represented as shown in Scheme 3.



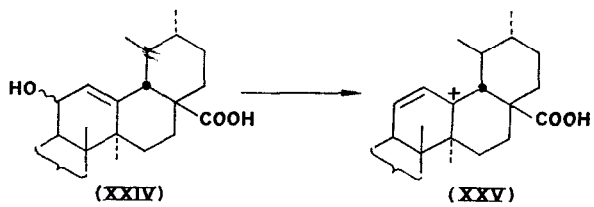
SCHEME 2. FRAGMENTATION OF XIX.



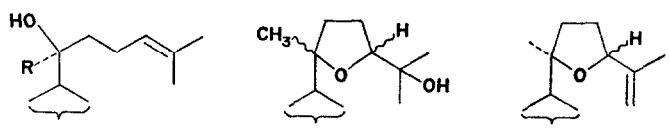
SCHEME 3. FRAGMENTATION OF THE ISOPROPYLIDENEDIOXY GROUP.

While hitherto not reported to occur naturally, 11-en-13β,28-olide of the ursane series such as that represented by dryobalanolide (XVIII) is not unknown. As long ago as 1940, Huzii and Osumi[16] reduced 11-oxoursolic acid (XX) with sodium and ethanol and obtained a 'dehydroursolic acid lactone'. An 11-en-13β,28-olide structure XXI was later assigned to the lactone by Barton and his co-workers.[17] A simple confirmation of the structure proposed for dryobalanolide acetonide would come from a partial synthesis from asiatic acid, in which use is made of the above described reaction. 11-Oxoasiatic acid triacetate (XV)[10] was reduced with sodium and ethanol. The resulting triol lactone XVIII, without isolation, was then converted to the 3,23-*O*-isopropylidene derivative XIX, which turned out to be identical with dryobalanolide acetonide.

Barton *et al.*[17] assigned a β-configuration to the C-18 hydrogen of the dehydroursolic lactone (XXI) of Huzii and Osumi. This example is being followed in our structure XVIII



(XXIV) (XXV)



(XXVI) (XXVII) (XXVIII)

for the corresponding lactone of the asiatic acid series. During the sodium and ethanol reduction of the 11-ketone, epimerization at position 18 to give the less stable trans C/D junction[12] was not expected to occur.

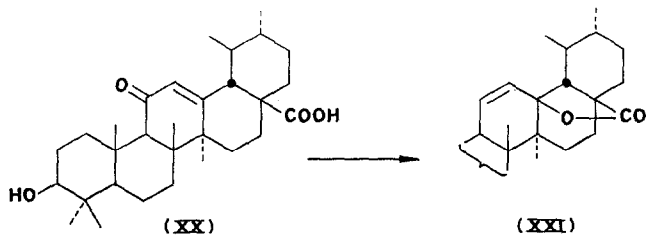
Some *oleanane* triterpenes structurally related to the 11-en-13β,28-olide XVIII have been reported to occur naturally. Thus 12-hydroxyoleanolic acid lactone (XXII)[18] is a 'hydrated' analogue, while saikogenins E (XXIII), F, and G[19] with a 13β,28-oxide link may be considered as being in a less oxygenated state. To our knowledge, however, no similar 13β,28-bridge has been known to exist in a naturally occurring *ursane* triterpene.

The possible genesis of the 11-en-13β,28-olide system in dryobalanolide is of some

[16] K. HUZII and S. OSUMI, *J. Pharm. Soc. Japan* **60**, 117, 291 (1940).
[17] D. H. R. BARTON, H. T. CHEUNG, P. J. L. DANIELS, K. G. LEWIS and J. F. MCGHIE, *J. Chem. Soc.* 5163 (1962).
[18] T. G. HALSALL and R. T. APLIN, *Fortschr. Chem. Org. Naturstoffe* **22**, p. 174 (1964).
[19] T. KUBOTA and H. HINOH, *Tetrahedron* **24**, 675 (1968).

interest. The most obvious consideration is that dryobalanolide is derived from a 11-hydroxy compound XXIV by lactonization through an intermediate such as XXV. Such a process was more likely to have occurred during the isolation procedure[2] than in the plant.

It is appropriate to review at this stage the present state of knowledge regarding the triterpene constituents of *Dryobalanops* spp.[2–4] These constituents fall into two main



(XX) (XXI)

(XXII) (XXIII)

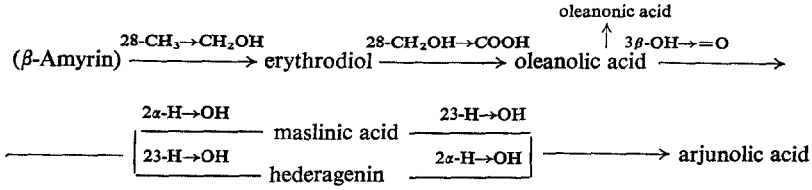
divisions, viz. the dammarane, and the pentacyclic triterpenes. The twelve pentacyclic compounds from *D. aromatica* (Table 2) show marked regularities in their structural features. Thus within each sub-group, ursane, oleanane or lupane, the pentacyclic constituents differ from each other in the degree of oxidation at positions 2, 3, 11, 23 and 28. By analogy with steroid biogenesis, such oxidative modifications are generally assumed to result from secondary reactions which occur after the formation of the parent substances

TABLE 2. PENTACYCLIC TRITERPENES FROM *Dryobalanops aromatica*

Skeleton	Compound	Nature of C-28	Substituents at positions 2α	23	11	Other Structural Features	Ref.
Oleanane	Erythrodiol	CH_2OH	—	—	—		2
	Oleanolic acid	COOH	—	—	—		2
	Oleanolic acid acetate	COOH	—	—	—	3-acetate	–
	Oleanonic acid	COOH	—	—	—	3-oxo	2
	Hedragonic acid	COOH	—	—	—	3-oxo-24-nor	–
	Maslinic acid	COOH	OH	—	—		2
	Hederagenin	COOH	—	OH	—		2
	Arjunolic acid	COOH	OH	OH	—		2
Ursane	Asiatic acid	COOH	OH	OH	—		2
	11-Hydroxy-asiatic acid (or equivalent)*	COOH	OH	OH	OH		–
	11-Oxoasiatic acid	COOH	OH	OH	=O		–
Lupane	Alphitolic acid	COOH	OH	—	—		2

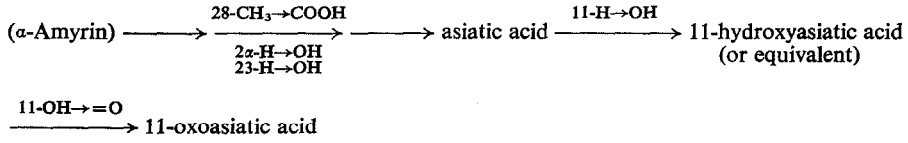
* Constituent actually isolated (dryobalanolide) was likely to be derived from 11-hydroxyasiatic acid (see text).

(in this case, α-amyrin, β-amyrin, and lupeol). It would appear that in this particular plant, if reductive processes were not important, secondary oxidation might proceed by successive attacks at the following positions and in the order: 28, 28 again, 2α (or 23), then 23 (or 2α), 11, and finally 11 again. Such plausible genesis of the oleanane constituents is shown in Scheme 4.



SCHEME 4. GENESIS OF OLEANANE CONSTITUENTS IN *D. aromatica*.

In the ursane series, the oxidative process leads to asiatic acid, the first of the series to be isolated. Further oxidation then occurs at C-11 in two steps (Scheme 5). Alphitolic acid, with oxygenation at 28 and 2α, is the only lupane triterpene isolated.



SCHEME 5. GENESIS OF URSANE CONSTITUENTS IN *D. aromatica*.

TABLE 3. DAMMARANE TRITERPENES OF *Dryobalanops* spp.

Compound	C-3 Substituent	Side-chain	Plant	Ref.
Dammarendiol-II	β-OH	(XXVI), R=CH_3	*D. aromatica*	2
Dipterocarpol (IV)	=O	(XXVI), R=CH_3	*D. aromatica*	2, 3
(Hydroxydammarenone-II)			*D. spp.*	4
Dryobalanone (V)	=O	(XXVI), R=CH_2OH	*D. aromatica*	2
			D. spp.	4
Dryobalanol (VII)	β-OH	(XXVI), R=CH_2OH	*D. spp.*	4
Dryobalanonolic acid	=O	(XXVI), R=COOH	*D. aromatica*	—
Ocotillol-II	β-OH	(XXVII), β-CH_3	*D. aromatica*	2
Ocotillol-I	β-OH	(XXVII), α-CH_3	*D. spp.*	4
Ocotillone-I and -II	=O	(XXVII)	*D. oblongifolia*	3
			D. spp.	4
Futabanone	=O	(XXVIII)	*D. spp.*	4

The five dammarane triterpenes we isolated,[2] as well as those obtained by other workers[3,4] from the same or different *Dryobalanops* spp., differ from each other in the nature of the side-chain, and in the degree of oxidation at C-3 (Table 3). A regular oxidation pattern as apparently found for the pentacyclic consistuents is not discerned for the dammarane triterpenes.

EXPERIMENTAL

M.ps. were uncorrected. Unless otherwise stated, UV, NMR, and IR spectra referred to EtOH and $CDCl_3$ solutions and Nujol mull respectively. MS were recorded at 70 eV. Identities were established through m.m.p. determination, and comparison of IR spectra.

Isolation of triterpenes. The crude triterpene acids (400 g) from the resin of *Dryobalanops aromatica*[2] were separated into Et_2O-soluble and Et_2O-insoluble fractions. The former was converted to the methyl esters by treatment with an excess of CH_2N_2 in Et_2O. On chromatography over alumina, the crude methyl esters (48 g) were separated into the following, listed in the order of elution: (a) methyl oleanolate acetate (60 mg), m.p. 222–224°; (b) methyl oleanonate (II) (2·8 g), m.p. 179–180°; (c) methyl hedragonate (I) (230 mg), m.p. 203–204° (lit.[6] 203–205°) (Found: C, 79·6; H, 10·4. Calc. for $C_{30}H_{46}O_3$: C, 79·8; H, 9·9%), identical to an authentic sample,[6] provided by Professor D. H. R. Barton; (d) methyl dryobalanonolate (V) (7·0 g), crystallizing as plates from CH_2Cl_2–MeOH, m.p. 148–149° (Found: C, 76·6; H, 10·4. $C_{31}H_{50}O_4$ requires: C, 76·5; H, 10·4%); for IR and NMR data see text. A sample treated with Ac_2O in dry pyridine at room temperature was recovered unchanged.

	NMR FREQUENCIES OF METHYL GROUPS (Hz)*						MS (*m/e*)							
	C-23	C-24	C-25	C-26	C-27	C-29/ C-30								
Methyl oleanonate† (II)	65·5	63·5	63·5	47·5	69	54,56	468	453	409	262	249	203	189	133
Methyl hedragonate (I)	60‡	—	67	48	67	54,56	454	439	395	262	249	203	189	133

* Relative to $SiMe_4$ as measured in $CDCl_3$ at 60 MHz. † For assignments see Refs. 8 and 7. ‡ Doublet (J 7 Hz) shown by double resonance.

Conversion of methyl dryobalanonolate (V) *to dryobalanol* (VI). Methyl dryobalanonolate (218 mg) was treated with $NaBH_4$ (0·5 g) in MeOH at room temp. After acidification, the mixture was worked up to yield *methyl 20(S)-dammar-24-en-3β,20-diol-21-carboxylate* (VII) (170 mg) forming needles from CH_2Cl_2–MeOH, m.p. 113–114°, ν_m 3510, 3450 and 1730 cm^{-1}; NMR: δ 5·0 (1H), 3·7 (3H), 3·15 (1H) (X of ABX, $J_{AX} + J_{BX}$ = 16 Hz), 1·7 (3H), 1·6 (3H), 0·8–1·0 (15H).

To the diol VIII (191 mg) in dry Et_2O was added $LiAlH_4$ and the mixture was refluxed for 5 hr. On working up, there was obtained dryobalanol (VI) (147 mg), m.p. 128–129° (from CH_2Cl_2–MeOH) or 104–107° (from Et_2O–light petroleum) (lit.[2] 106–108°), identical to an authentic sample obtained by $NaBH_4$ reduction of dryobalanone.[2]

Purification ofmethyl asiatate and isolation of minor constituents. Impure methyl asiatate[2] (39 g) in acetone (600 ml) was stirred with anhydrous $CuSO_4$ (12 g) for 48 hr. Dilute $NaHCO_3$ was added and the mixture was extracted with $CHCl_3$. Crude 'acetonide' obtained from the $CHCl_3$ solution was chromatographed over basic alumina to yield the following, listed in the order of elution: (a) methyl 3,23-*O*-isopropylidene asiatate[2] (VIII) (31 g), m.p. 211–213°; (b) 3,23-*O*-isopropylidene-2α,3β,23-trihydroxyursa-11-en-13β,28-olide (XIX) (dryobalanolide acetonide) (0·80 g) forming needles from Et_2O–MeOH, m.p. 278–280°, UV: ε = 3600 at 210 nm; for IR, NMR and MS data see text. (Found: C, 75·5; H, 9·2. $C_{33}H_{50}O_5$ requires: C, 75·2; H, 9·6%); (c) methyl 3,23-*O*-isopropylidene-11-oxoasiatate (IX) (0·20 g) forming needles from MeOH, m.p. 253–255°, λ_{max} 250 nm (ε 11 000); for IR, NMR and MS data see text. (Found: C, 70·9; H, 9·8. $C_{34}H_{52}O_6,H_2O$ requires: C, 71·0; H, 9·5%.)

Methyl asiatate and methyl asiatate triacetate (XVII)). Methyl 3,23-*O*-isopropylidene asiatate[2] was treated with aqueous acid to give methyl asiatate in 88% yield. Treatment of the latter compound with Ac_2O in pyridine afforded in 89% yield methyl asiatate triacetate (XVII), an amorphous solid[10], $\nu_m^{CCl_4}$ 1745, 1255, 1244 cm^{-1}.

Methyl 11-oxoasiatate triacetate (XIII). (a) Methyl asiatate triacetate (570 mg) in HOAc (3·5 ml) and Ac_2O (1·0 ml) was heated with CrO_3 (0·34 g) and anhydrous NaOAc (0·50 g) at 60–70° for 6 hr. On working up, methyl 11-oxoasiatate triacetate (XIII) (485 mg, 83%) was obtained, m.p. 268–269° (lit.[10] 258–260°), λ_{max} 251 nm (ε 12 000); $\nu_m^{CHCl_3}$ 1735, 1660, 1620, 1230, 1044 cm^{-1}. (Found: C, 69·1; H, 8·9. Calc. for $C_{37}H_{54}O_9$: C, 69·1; H, 8·5%). (b) Methyl 3,23-*O*-isopropylidene-11-oxoasiatate (IX) (12 mg) isolated from *Dryobalanops aromatica* resin (above) was refluxed in a mixture of 2 N HCl (0·2 ml) and EtOH (1 ml) for 30 min. The resulting crude triol XII was treated with Ac_2O in pyridine, yielding methyl 11-oxoasiatate triacetate (XIII)(6 mg), m.p. 265–266°, identical to an authentic sample (above).

Methyl 11-*oxoasiatate* (XII). Methyl 11-oxoasiatate triacetate (XIII) (79 mg) was refluxed for 3 hr in a mixture of EtOH (1·5 ml) and 2 N KOH (0·5 ml). Methyl 11-oxoasiatate (XII) was obtained as prisms of monohydrate (36 mg) from benzene-light petroleum (saturated with H_2O), m.p. 184–186° (lit.[10] amorphous), λ_{max} 250 nm (ϵ 11 000). (Found: C, 69·8; H, 9·1. $C_{31}H_{48}O_6$, H_2O requires: C, 69·6; H, 9·4%). It could be reconverted to the triacetate XIII on acetylation with Ac_2O and pyridine.

11-*Oxoasiatic acid triacetate* (XV). Asiatic acid (XVI), prepared from methyl asiatate by hydrolysis with KOH in diethylene glycol at 160°, was acetylated to give amorphous[10] asiatic acid triacetate, $\nu_m^{CHCl_3}$ 1735, 1695, 1230 cm^{-1}. The latter compound (600 mg) was treated with CrO_3 (0·30 g) and anhydrous NaOAc (3·5 ml) and Ac_2O (1 ml) at 65–75° for 4 hr. On working up at pH 7 and on crystallization from ether were obtained needles of 11-oxoasiatic acid triacetate (XV) (250 mg) m.p. 284–286° (lit.[10] 270–275°), λ_{max} 254 nm (ϵ 11 000), ν_m^{Nujol} 1745, 1720, 1660, 1635, 1240 cm^{-1}.

Reduction of 11-*oxoasiatic acid triacetate* (XV) *and acetonide formation.* To 11-oxoasiatate triacetate (70 mg) in absolute EtOH (5 ml) under reflux was added Na until the rate of dissolution was very slow. Aqueous HCl was added with cooling until just acidic. Extraction with $CHCl_3$ yielded a gum which was dissolved in acetone (10 ml), and stirred with anhydrous $CuSO_4$ (0·5 g) overnight. $CuSO_4$ was removed by filtration, and the filtrate added to N Na_2CO_3. Upon removal of acetone *in vacuo* and extraction with $CHCl_3$, one obtained, after usual work-up, needles of 3,23-*O*-isopropylidene-2α,3β,23-trihydroxyurs-11-en-13β, 28-olide (XIX) (20 mg), identical to dryobalanolide acetonide.

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The NMR spectra of steroids are generally complex because of the presence of a large number of aliphatic and alicyclic methylene groups. Nevertheless, Shoolery and Rogers[1] in their classical study of the NMR spectra of steroids showed that the three proton signals of the methyl groups due to the equivalence of the protons were the most pronounced and sharpest peak in the spectra and were above the background of methylene and methine protons in the region of 0·5–1·5δ. They showed that the substituents as well as stereochemical and conformational changes can have a pronounced effect on the chemical shift of these methyl groups, and in so doing demonstrated the practical application of NMR spectro-