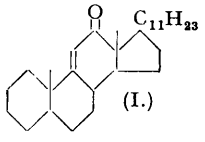
332. *Triterpenoids. Part III.* cyclo*Artenone, a Triterpenoid Ketone.*

By D. H. R. Barton.

The crystalline ketone from the fruit of *Artocarpus integrifolia* has been shown to be triterpenoid rather than steroid in character. Its formula has been established as $C_{30}H_{48}O$. By reduction with sodium and *n*-propanol the ketone has been converted into the corresponding alcohol, fully characterised by derivatives. A number of further transformation products has been prepared. The presence of an *iso*propylidene group in a side chain, and of a *cyclo*propane ring, has been demonstrated by both chemical and physical methods. The name *cyclo*artenone is proposed for the ketone, and *cyclo*artenol for the corresponding alcohol.

The non-volatile alcoholic fraction from the non-saponifiable matter of the fruit of *A. integrifolia* has been found to contain the triterpenoid alcohols *cyclo*artenol and butyrospermol.

In an extensive series of investigations Nath and his collaborators (Nath, *Z. physiol. Chem.*, 1937, **247**, 9; 1937, **249**, 71; *Science and Culture*, 1937, **3**, 297; Nath and Mukherjee, *J. Indian Chem. Soc.*, 1939, **16**, 229; Nath and Sen Gupta, *Indian J. Med. Res.*, 1939, **27**, 171; Nath and Chakraborty, *J. Indian Chem. Soc.*, 1945, **22**, 19; Nath, Chowdhury, and Uddin, *ibid.*, 1946, **23**, 245; see also Banerjee and Bhattacharyya, *Science and Culture*, 1938, **4**, 60; *Z. Krist.*, 1939, **100**, 420; Balakrishna and Seshadri, *Proc. Indian Acad. Sci.*, 1947, **26**, *A*, 46, 203; 1948, **27**, *A*, 409) have reported on a ketone contained in the non-saponifiable matter of the latex from the fruits of *Artocarpus integrifolia*. According to Nath this compound, for which he has proposed the name artostenone, is an αβ-unsaturated steroidal ketone, $C_{30}H_{50}O$, of the constitution (I).



(I.)

Our attention was first directed to this ketone by the fact that the rotation reported by Nath ($[\alpha]_D$ +24° in chloroform) was at variance with the value to be expected ($[\alpha]_D$ about +85° in $CHCl_3$).* Furthermore we were unable to accept the chemical evidence adduced by Nath as indicative of a steroid formulation. It seemed to us that artostenone might well be triterpenoid in character. The evidence reported below may be construed as confirming our criticisms of Nath's work and, for reasons that will become clear from the sequel, we have renamed the ketone cyclo*artenone*.†

A. integrifolia is common in Ceylon and we were able to obtain a supply of the latex-bearing core of the fruit through the courtesy of Dr. A. R. Lowe, Principal Research Officer of the Government Industrial Research Laboratory. The processing of this material (see Experimental) yielded crystalline *cyclo*artenone, m. p. 109°, $[\alpha]_D$ +24° (in chloroform). The physical data are in excellent agreement with those reported by Nath, but the yield of ketone was much superior (Nath, 25·6 g. from 525 fruit; this investigation, 4·95 g. from 3 fruit). Whereas Nath considered that *cyclo*artenone had the molecular formula $C_{30}H_{50}O$, all our analytical data (especially the values for hydrogen) for this compound and its derivatives indicate a $C_{30}H_{48}O$ formulation (see Table II).

Although Nath has reported degradative evidence which might be construed as proof of αβ-unsaturation in *cyclo*artenone, this is contraindicated by both physical and chemical data. *cyclo*Artenone showed $\lambda_{max.}$ 284—289 mμ. ($\varepsilon_{max.}$ 260) in the ultra-violet with no high-intensity absorption above 220 mμ. This is characteristic of a ketone grouping *isolated* from an ethylenic double bond. Furthermore, the infra-red spectrum of *cyclo*artenone (Fig. 1) showed a maximum at 5·85 μ. in carbon disulphide, a value characteristic of a *saturated* ketone grouping in a six-membered ring (compare R. Norman Jones *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 2024). The infra-red spectrum of *cyclo*artenone showed weak absorption near 12 μ. (Fig. 1) which could be

* The rotation is calculated in the following way. All the fundamental steroid hydrocarbons have molecular rotations between 0° and +100° (Barton and Klyne, *Chem. and Ind.*, 1948, 755); changes in the saturated side chain do not cause large changes in the molecular rotation. If a mean of +50° is taken for the molecular rotation of Nath's artostane and +310° is added for the introduction of the 9(11)-en-12-one chromophore (Barton and Klyne, *loc. cit.*) the calculated molecular rotation for artostenone becomes about +360°.

† This name was kindly suggested to us by the Editor.—D.H.R.B.

interpreted (see Barton and Brooks, *J.*, 1951, 257) as indicating the grouping $-CH{=}C<$. The ultra-violet absorption spectrum, which showed $\lambda_{max.}$ 199 mμ. ($\varepsilon_{max.}$ 3,560) (see Experimental), confirmed the presence of a triply substituted ethylenic linkage.*

Reduction of *cyclo*artenone by sodium and boiling *n*-propanol afforded *cyclo*artenol, $C_{30}H_{50}O$, characterised as the acetate and benzoate. Catalytic hydrogenation of *cyclo*artenyl acetate proceeded smoothly to furnish *cyclo*artanyl acetate, hydrolysed to *cyclo*artanol, $C_{30}H_{52}O$, which was further characterised as the benzoate. The changes in molecular rotation (see

FIG. 1.

1. cyclo*Artenone in* CS_2. 2. cyclo*Artenone in* $CHCl_3$.

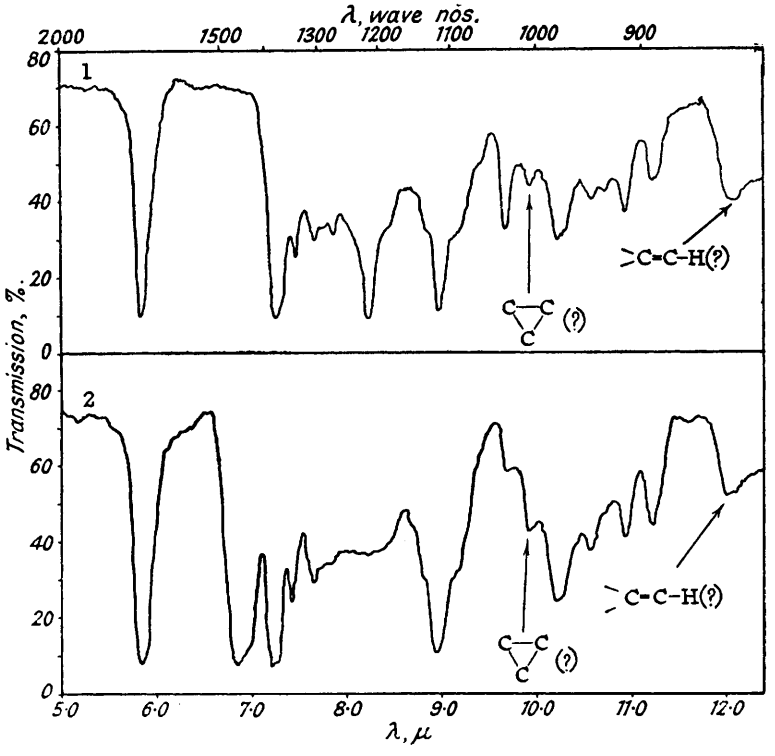


Table I) on acetylation and benzoylation of *cyclo*artenol and *cyclo*artanol are comparable with those recorded for triterpenoids rather than steroids (Barton and Jones, *J.*, 1944, 659; Barton, *J.*, 1946, 1116; Heilbron, Jones, and Robins, *J.*, 1949, 444).

The easily hydrogenated ethylenic linkage was further characterised by the preparation of *cyclo*artenyl benzoate dibromide. It was shown to be present as an *iso*propylidene grouping

TABLE I.

	$[M]_D$.				Differences.		
Compound.	Alcohol.	Acetate.	Benzoate.	Ketone.	Δ_1.	Δ_2.	Δ_3.
*cyclo*Artenol	+204°	+272°	+345°	+102°	+68°	+141°	−102°
*cyclo*Artanol	+193	+268	+351	—	+75	+158	—
α- and β-Amyrin group	—	—	—	—	+6	+145	+60
Lupeol–betulin group	—	—	—	—	+70	+200	+140
Butyrospermol	−51	+51	+180	−170	+102	+231	−119
Dihydrobutyrospermol	−60	+56	+164	−182	+116	+224	−122

* The characterisation of the degree of substitution of ethylenic linkages in the steroid and triterpenoid series by a study of their apparent absorption spectra in the 195—215-mμ. region was initiated at the University of Manchester (Bladon, Henbest, Koch, and Woods, forthcoming paper; cf. Bateman and Koch, *J.*, 1944, 600). We thank Drs. Henbest and Koch for informing us of this valuable technique before its general publication.

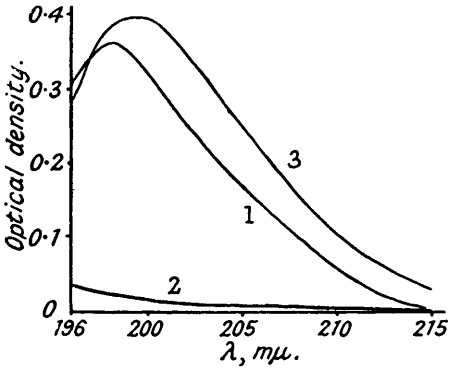
in the following way. *cyclo*Artenyl benzoate reacted smoothly with osmium tetroxide to give, after reductive fission of the osmate, dihydroxy*cyclo*artanyl benzoate, split by lead tetra-acetate into acetone and benzoyloxytrisnor*cyclo*artanal. The latter was not isolated in a state of purity but was oxidised further by silver oxide to trisnor*cyclo*artanoloic acid benzoate, characterised as the methyl ester. This ester was readily hydrolysed by boiling 1% ethanolic potassium hydroxide. The experiments prove the presence of a side chain $-CH{:}CMe_2$ and make it very probable that this can be expanded to $-CH_2{\cdot}CH{:}CMe_2$.

In order to facilitate comparison with other triterpenoid compounds *cyclo*artenone was reduced by the Wolff–Kishner method to the corresponding hydrocarbon *cyclo*artene, $C_{30}H_{50}$, readily hydrogenated to *cyclo*artane, $C_{30}H_{52}$.

*cyclo*Artenol and related compounds containing the *iso*propylidene grouping referred to above gave strong yellow colours with tetranitromethane. *cyclo*Artanol and its derivatives, on the other hand, gave only pale yellow colours. At first this was attributed to a strongly sterically hindered ethylenic linkage, but the following facts seem to preclude this. *cyclo*-Artanyl acetate was resistant to selenium dioxide and chromic acid; it failed to react with perbenzoic acid and even with hot peracetic acid under conditions adequate for attack on the double bond of α-amyrin benzoate (Picard, Sharples, and Spring, *J.*, 1939, 1045). Whilst *cyclo*artenol and its acetate showed absorption maxima at 198 mμ., *cyclo*artanol, *cyclo*artanyl acetate, and *cyclo*-artane exhibited *no selective absorption* in the ultra-violet even in the 195—210-mμ. range (see Fig. 2).

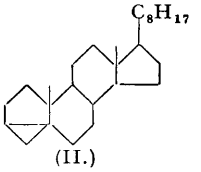
FIG. 2.

1. cyclo*Artenyl acetate* (*c*, 0·0067%).
2. cyclo*Artanyl acetate* (*c*, 0·014%).
3. *Artenyl acetate* (*c*, 0·0052%).

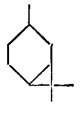


These facts appear to be best explained by the presence of a *cyclo*propane ring in *cyclo*-artenone and its derivatives. The following chemical and physical evidence supports this conclusion. On treatment with dry hydrogen chloride in chloroform *cyclo*artanyl benzoate was isomerised to artenyl benzoate, hydrolysis of which furnished artenol further characterised as the acetate. The last was also prepared by similar isomerisation of *cyclo*artanyl acetate. Artenol and its derivatives gave strong yellow colours with tetranitromethane and the presence of an ethylenic double bond thus indicated was confirmed by treating artenyl benzoate with perbenzoic acid, to give the corresponding oxide, and artenyl acetate with perhydrol–acetic acid to furnish artenyl acetate oxide. The acetate oxide showed no selective absorption in the 280—290-mμ. region. Hydrogenation of artenyl acetate gave artanyl acetate $C_{32}H_{56}O_2$, which, like the oxides mentioned above, was saturated to tetranitromethane. This chemical evidence for the presence of a double bond in artenol was confirmed by the absorption spectra of the alcohol and its acetate: both showed maxima at 199·5 mμ. indicative of a triply substituted double bond (Fig. 2). In agreement, the infra-red absorption spectrum of the alcohol showed a weak maximum near 12 μ.

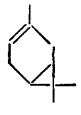
Derfer, Pickett, and Boord (*J. Amer. Chem. Soc.*, 1949, **71**, 2482) have studied the infra-red absorption spectra of a number of alkyl-substituted *cyclo*propane derivatives and have concluded that the *cyclo*propane ring is characterised by an intense band at 9·8—10·0 μ. In agreement, we find that *i*-cholestane (3 : 5-*cyclo*cholestane) (II) shows strong absorption (Fig. 3) at 9·9 μ.



(II.)



(III.)



(IV.)

The presence of a band near 10 μ. in *cyclo*artenone and *cyclo*artanyl acetate is also apparent (Figs. 1 and 4 respectively) although somewhat masked by more intense neighbouring absorption bands not present in *i*-cholestane. The assignment of this band to a *cyclo*propane ring would seem to be confirmed by the spectrum of artenol (Fig. 5), where there is no maximum

at 10 μ. The *cyclo*propane band of carane (III) and of car-3-ene (IV) is similarly flanked by neighbouring bands of greater intensity (Plíva and Herout, *Coll. Czech. Chem. Comm.*, 1950, **15**, 160).

It is of interest that even carefully purified *i*-cholestane gives a pale yellow colour with tetranitromethane and we do not believe that the weakly positive response to this test given by *cyclo*artanol derivatives can be construed as evidence against the presence of a *cyclo*propane ring. *i*-Cholestane, like the *cyclo*artanol derivatives, shows no selective absorption in the ultra-violet in the 195—210-mμ. region.

That the *cyclo*propane ring of *cyclo*artenone was not in the βγ-position with respect to the *iso*propylidene group was rendered probable by the following evidence. Treatment of *cyclo*artenyl acetate with hydrogen chloride in chloroform solution afforded artadienyl acetate hydrochloride from which artadienol, characterised as the benzoate, was obtained by alkaline hydrolysis. The crude artadienol showed no selective butadienyl absorption in the ultra-violet.

It is to be concluded that *cyclo*artenol is a new triterpenoid alcohol containing one double bond in a side chain *iso*propylidene group and five rings, one of them a *cyclo*propane ring. This is the first record of a triterpenoid compound containing the latter grouping. None of the *cyclo*artenone derivatives described in this paper appears to be identical with any other compound described in the literature.

FIG. 3.
i-*Cholestane in* CS_2.

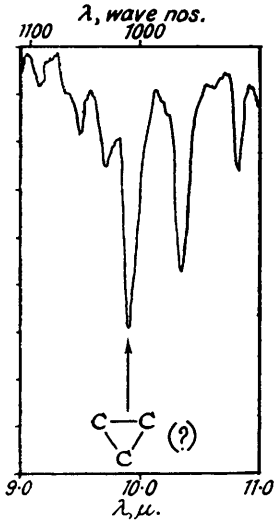


FIG. 4.
cyclo*Artanyl acetate in* CS_2.

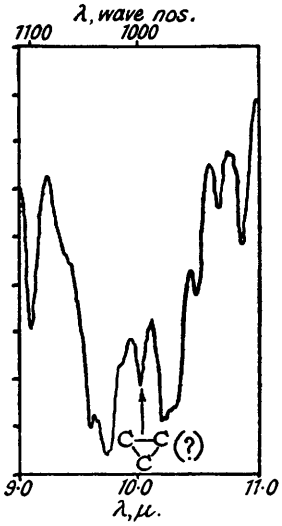
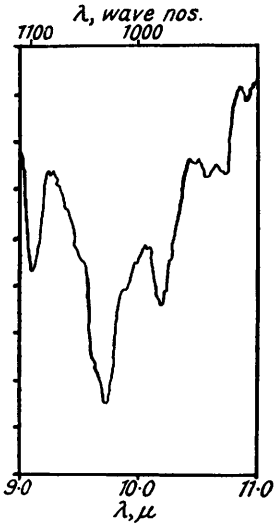


FIG. 5.
Artenol in CS_2.



It was clearly of interest to examine the non-volatile alcoholic fraction of the non-saponifiable matter, separated from *cyclo*artenone during the chromatographic fractionation of the latter. By acetylation and further chromatography the triterpenoid butyrospermyl acetate (characterised by conversion into the benzoate and the dihydro-acetate and by comparison of all three compounds with authentic specimens very kindly provided by Professor E. R. H. Jones, F.R.S., and Dr. T. G. Halsall) and *cyclo*artenyl acetate were isolated. It is possible that *cyclo*artenol and butyrospermol are related to each other, for the change in molecular rotation on oxidation of these two compounds to the corresponding ketones (Table I) is negative, an unusual feature in triterpenoid compounds (Barton and Jones, *loc. cit.*).

EXPERIMENTAL.

M. p.s are uncorrected. For rotation measurements all specimens were dried *in vacuo* at 20° below their m. p.s or at 110°, whichever was the lower temperature. All rotations were taken in chloroform solution; the values recorded have been approximated to the nearest degree. For the calculation of molecular rotations the specific rotations at $c = 2{\cdot}00$, or at the nearest concentration to this at which measurements were made, have been taken as the most suitable.

Ultra-violet absorption spectra were determined in absolute ethanol solution, using a Unicam Spectrophotometer, Model SP 500.

Unless specified to the contrary infra-red absorption spectra were determined using the Baird Associates (Cambridge, Mass.) self-recording double-beam instrument. We are indebted to Dr. Hans Heymann (Harvard) for most of the measurements recorded.

The standard chemical operations covered by the phrase, " in the usual way," were carried out as detailed in Part I of this series (Barton and Brooks, *J.*, 1951, 257).

Alkaline hydrolyses were effected by using several equivs. of potassium hydroxide and refluxing the reactants for 30—60 minutes in methanolic or dioxan–methanolic solution depending on the solubility requirements of the ester.

Light petroleum refers throughout to the fraction of b. p. 40—60°.

The analyses for new compounds, when not given in the text, are summarised in Table II.

TABLE II.

Substance.	Formula.	Found (%), C.	Found (%), H.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{48}O$, C.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{48}O$, H.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{50}O$, C.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{50}O$, H.
*cyclo*Artenone	$C_{30}H_{48}O$	84·8	11·3	84·85	11·4	84·45	11·8
*cyclo*Artenol	$C_{30}H_{50}O,\frac{1}{2}CH_3{\cdot}OH$	82·4	11·8	82·75	11·85	82·35	12·25
*cyclo*Artenyl acetate	$C_{32}H_{52}O_2$	82·15	11·1	82·0	11·2	81·65	11·55
*cyclo*Artenyl benzoate	$C_{37}H_{54}O_2$	83·25	10·15	83·7	10·2	83·4	10·6
*cyclo*Artenyl benzoate dibromide	$C_{37}H_{54}O_2Br_2$	64·7	7·8	64·35	7·85	64·15	8·15
*cyclo*Artanol	$C_{30}H_{52}O,\frac{1}{2}CH_3{\cdot}OH$	82·1	12·3	82·35	12·25	82·0	12·65
*cyclo*Artanyl acetate	$C_{32}H_{54}O_2$	81·5	11·45	81·65	11·55	81·3	11·9
*cyclo*Artanyl benzoate	$C_{37}H_{56}O_2$	83·2	10·6	83·4	10·6	83·1	10·95
Artenol	$C_{30}H_{52}O$	83·75	12·0	84·05	12·25	83·6	12·65
Artenyl acetate	$C_{32}H_{54}O_2$	81·85	11·7	81·65	11·55	81·3	11·9
Artanyl acetate	$C_{32}H_{56}O_2$	80·95	11·95	81·25	11·95	80·9	12·35
Artenyl benzoate	$C_{37}H_{56}O_2$	82·95	10·2	83·4	10·6	83·1	10·95
Artenyl acetate oxide	$C_{32}H_{54}O_3$	78·7	11·05	78·95	11·2	78·6	11·55
Artenyl benzoate oxide	$C_{37}H_{56}O_3$	80·55	10·4	80·95	10·3	80·65	10·65
Artadienyl acetate hydrochloride	$C_{32}H_{53}O_2Cl$	76·6	10·6	76·05	10·6	75·75	10·9
Artadienyl benzoate	$C_{37}H_{54}O_2$	83·2	10·15	83·7	10·2	83·4	10·6
*cyclo*Artene	$C_{30}H_{50}$	87·9	12·05	87·75	12·25	87·3	12·65
*cyclo*Artane	$C_{30}H_{52}$	87·5	12·45	87·3	12·65	86·9	13·15
Dihydroxy*cyclo*artanyl benzoate	$C_{37}H_{56}O_4$	78·8	9·9	78·65	10·0	78·4	10·35
Methyl trisnor*cyclo*artanoloate benzoate	$C_{35}H_{50}O_4$	78·3	9·05	78·55	9·45	78·25	9·8

Extraction of cyclo*Artenone from the Fruit of* A. integrifolia.—The inner, latex-containing cores of three large ripe fruit had been sealed, with addition of some chloroform, in tinned cans. The following procedure was adopted for the extraction of the *cyclo*artenone. The cores were milled thoroughly in a Waring Blender with addition of chloroform, and the resulting pulp was left overnight. The chloroform was removed by filtration and the pulp washed with more chloroform. The chloroform was removed *in vacuo* and the gummy residue was saponified by refluxing it with 25 g. of potassium hydroxide in 250 ml. each of methanol and benzene for 2 hours on the steam-bath. The benzene and methanol were then removed *in vacuo* and the non-saponifiable matter was extracted from the residue in the usual way. This procedure furnished a brown gum, which was chromatographed over a large column of alumina (Merck) with the results indicated below. All fractions, were 200 ml. in volume and, after evaporation, were set side for one month at room temperature.

Fraction no.	Eluent.*	Eluate.	Fraction no.	Eluent.*	Eluate.
1—2	1 : 1 Pet.-C_6H_6	Gum	11	C_6H_6	Gum
3—4	,, ,,	Cryst. (large fractions)	12	9 : 1 C_6H_6–Et_2O	Gum
5—7	,, ,,	Cryst.	13	4 : 1 ,,	Gum
8	,, ,,	Cryst. (small fraction)	14	1 : 1 ,,	Gum (small fraction)
9—10	C_6H_6 ,,	Partly cryst.	15	1 : 1 Et_2O–MeOH	Partly cryst. (small fraction)

* Pet. = light petroleum.

Fractions 3—8 were combined and rechromatographed in the same way. The results are indicated below.

Fraction no.	Eluent.	Eluate.
16	200 ml. Pet.	Gum (small fraction)
17	200 ml. ,,	Gum, cryst. on storage
18—22	200 ml. ,,	All small cryst. fractions
23—24	400 ml. 1 : 9 C_6H_6–Pet.	Larger cryst. fractions
25—26	400 ml. 1 : 4 ,,	Large cryst. fractions
27	400 ml. 1 : 1 ,,	Small fraction : cryst.
28	400 ml. C_6H_6	Trace, not cryst.
29	400 ml. 1 : 19 Et_2O–C_6H_6	Small fraction; slowly cryst.
30—31	400 ml. 1 : 9 ,,	Larger fractions; slowly cryst.
32	400 ml. 1 : 1 Et_2O–MeOH	Viscous gum

Fractions 18—24 were recrystallised once from benzene–methanol to give 2·65 g. of pure *cyclo*artenone, m. p. 109°, $[\alpha]_D$ +24° (*c*, 3·39), $[M]_D$ +102°, $\lambda_{max.}$ 199 mμ., $\varepsilon_{max.}$ = 3560, ε_{215} = 780

(*c*, 0·004), $\lambda_{max.}$ 284—289 mμ., $\varepsilon_{max.}$ = 260. Fractions 23 and 24, combined and recrystallised once from benzene–methanol, gave 2·3 g. of *cyclo*artenone, m. p. 105°. Pure *cyclo*artenone showed a yellow colour, changing through orange with a green fluorescence to red, in the Liebermann–Burchard reaction. It gave a yellow colour with tetranitromethane.

Fractions 17 and 27 were combined and converted into crude *cyclo*artenyl acetate (see below). Subsequent recrystallisation of the crude acetate furnished 0·6 g. of pure acetate.

Fractions 11—14 were combined with fractions 29—32 and worked up further as detailed below.

cyclo*Artenol.*—*cyclo*Artenone (1·6 g.) in *n*-propyl alcohol (100 ml.) was treated with sodium under reflux until saturated. The reaction mixture was diluted with water and extracted with ether. Evaporation of the ether and addition of methanol furnished cyclo*artenol*, recrystallised from chloroform–methanol in clumps of needles, m. p. 85—92° (decomp.) after sintering at 80°, $[\alpha]_D$ +48° (*c*, 5·03), $[M]_D$ +204°, $\lambda_{max.}$ 198 mμ., $\varepsilon_{max.}$ = 3,200 (*c*, 0·0094). It was not possible to raise the m. p. of *cyclo*artenol to that (106—107°) recorded by Nath (*Z. physiol. Chem.*, 1937, **247**, 17) for a (not analysed) specimen of the same compound.

cyclo*Artenyl Acetate.*—This was prepared by acetylation of *cyclo*artenol in pyridine with acetic anhydride at room temperature (24 hours) or at steam-bath temp. (30 minutes). The *acetate*, worked up in the usual way and recrystallised from chloroform–methanol in small plates, had m. p. 122·5—123·5°, $[\alpha]_D$ +58° (*c*, 5·34), $[M]_D$ +272°, $\lambda_{max.}$ 198 mμ., $\varepsilon_{max.}$ = 2,540, ε_{215} = 700 (*c*, 0·0067).

cyclo*Artenyl Benzoate.*—*cyclo*Artenol, in pyridine solution, was treated with benzoyl chloride at room temperature for 48 hours. The reaction mixture was worked up in the usual way. Crystallisation from chloroform–methanol furnished cyclo*artenyl benzoate* in long needles, m. p. 129—130°, $[\alpha]_D$ +65° (*c*, 5·50), $[M]_D$ +345°.

cyclo*Artenyl Benzoate Dibromide.*—*cyclo*Artenol benzoate in chloroform solution was treated at room temperature with a dilute solution of bromine in the same solvent until bromine was no longer absorbed. Washing with aqueous sodium hydrogen carbonate, evaporation *in vacuo*, and recrystallisation of the residue from chloroform–methanol afforded cyclo*artenyl benzoate dibromide*, m. p. 182—183° (decomp.) (taken rapidly) (Found: Br, 24·1. $C_{37}H_{54}O_2Br_2$ requires Br, 23·2%). With tetranitromethane the dibromide gave a pale yellow colour.

cyclo*Artanyl Acetate.*—*cyclo*Artenyl acetate (500 mg.) in glacial acetic acid (100 ml.) was hydrogenated using a platinum catalyst for 2 hours. Working up in the usual way and recrystallisation from chloroform–methanol afforded beautiful long needles of cyclo*artanyl acetate*, m. p. 132—133°, $[\alpha]_D$ +57° (*c*, 5·31), $[M]_D$ +268°, which had no selective absorption in the 195—300-mμ. range. The acetate gave a pale yellow colour with tetranitromethane. It was recovered unchanged in almost quantitative yield (*a*) on treatment with a ten-fold excess of perbenzoic acid at 5° for 15 days, (*b*) on treatment with perhydrol–acetic acid on the steam-bath according to the directions of Picard, Sharples, and Spring (*J.*, 1939, 1045) for α-amyrin benzoate, and (*c*) on refluxing with selenium dioxide (½ its wt.) in acetic acid for 12 hours. On chromic acid oxidation (½ its wt. of CrO_3) in acetic acid, at temperatures from 70° to 90° and reaction times from 0·5 to 1·5 hours *cyclo*artanyl acetate was, for the main part, recovered unchanged. In each experiment chromatographic fractionation was carried out but, apart from unchanged starting material, the reaction products were gummy and intractable. There was no indication of the formation of a yellow ene-1 : 4-dione, such as results from the oxidation of dihydrolanosteryl acetate or dihydroeuphyl acetate.

cyclo*Artanol.*—Alkaline hydrolysis of *cyclo*artanyl acetate in the usual way afforded cyclo*artanol*, recrystallised from aqueous methanol, m. p. 99—101° (decomp.), $[\alpha]_D$ +45° (*c*, 3·59), $[M]_D$ +193°, which had no selective absorption in the ultra-violet. *cyclo*Artanol gave a pale yellow colour with tetranitromethane.

Benzoate. *cyclo*Artanol was treated as for *cyclo*artenol (see above) to give the benzoate which, recrystallised from chloroform–methanol, had m. p. 137—138° to a cloudy melt clearing sharply at 148—149°, $[\alpha]_D$ +66° (*c*, 4·62), $[M]_D$ +351°. There was a beautiful and intense play of colours from the m. p. to the clearing point. *cyclo*Artanyl benzoate gave a pale yellow colour with tetranitromethane.

Artenyl Benzoate.—*cyclo*Artanyl benzoate (200 mg.) in dry chloroform (20 ml.) was treated at room temperature with a vigorous stream of hydrogen chloride for 30 minutes. The chloroform was removed *in vacuo* and the residue recrystallised from chloroform–methanol to furnish *artenyl benzoate*, m. p. 197—198°, $[\alpha]_D$ +78° (*c*, 3·05). Treatment of 200 mg. of this benzoate (2nd crop) with twice the theoretical amount of perbenzoic acid in chloroform solution at 0° for 2 days gave *artenyl benzoate oxide*; recrystallised from chloroform–methanol, this had m. p. 205—208° (decomp.), $[\alpha]_D$ +54° (*c*, 1·79). The former benzoate gave a strong yellow colour with tetranitromethane, but with the latter the test was negative.

Artenol.—Alkaline hydrolysis of artenyl benzoate afforded *artenol*; recrystallised from chloroform–methanol, this had m. p. 152—154°, $[\alpha]_D$ +57° (*c*, 1·61), $\lambda_{max.}$ 199·5 mμ., $\varepsilon_{max.}$ = 4000, ε_{215} = 760 (*c*, 0·0082).

Acetate. (*a*) Artenol was acetylated with acetic anhydride in pyridine solution at room temperature overnight. Working up in the usual way and recrystallisation from chloroform–methanol gave the acetate in needles, m. p. 165—167°.

(*b*) *cyclo*Artanyl acetate (250 mg.) in dry chloroform (20 ml.) was treated with a vigorous stream of hydrogen chloride for 45 minutes. The chloroform was removed *in vacuo* and the residue recrystallised to give the same acetate, m. p. 165—167°, $[\alpha]_D$ +73° (*c*, 1·34), $\lambda_{max.}$ 199·5 mμ., $\varepsilon_{max.}$ = 3600, ε_{215} = 300 (*c*, 0·0052). Both artenol and its acetate gave strong yellow colours with tetranitromethane.

It was noted that, whilst artenol and its benzoate appeared to be homogeneous on crystallisation, acetylation of the alcohol gave an acetate which was purified only by repeated recrystallisation. It is possible therefore that artenol and its benzoate are contaminated with minor amounts of double-bond isomers not readily separable by crystallisation. Lack of material prevented a more extensive investigation of this phenomenon.

Treatment of artenyl acetate (2nd crop) with perhydrol–acetic acid on the steam-bath as in the procedure of Picard, Sharples, and Spring (*loc. cit.*) furnished *artenyl acetate oxide*; recrystallised from chloroform–methanol, this melted at 184—185°. It showed no selective absorption in the ultra-violet and gave no indication of a carbonyl band in the 280—290-mμ. region. The tetranitromethane test was negative.

Artanyl Acetate.—Artenyl acetate (10 mg.) in AnalaR acetic acid (20 ml.) and dry ether (10 ml.) was hydrogenated using a platinum catalyst (200 mg.) for 4 hours. Working up in the usual way afforded *artanyl acetate*, which recrystallised from methanol as matted needles, m. p. 148—149° (tetranitromethane test negative).

cyclo*Artene.*—*cyclo*Artenone (200 mg.) in anhydrous hydrazine (2 ml.) and absolute alcohol (6 ml.) containing dissolved sodium (250 mg.) was heated at 180° for 18 hours. Working up in the usual way and chromatography over alumina (Savory and Moore's standardised) afforded cyclo*artene*; recrystallised from methanol, this had m. p. 49—50° and $[\alpha]_D$ +59° (*c*, 0·88).

cyclo*Artane.*—*cyclo*Artene (30 mg.) in AnalaR acetic acid (20 ml.) and anhydrous ether (10 ml.) was hydrogenated using a platinum catalyst (100 mg.) for 2 hours. Working up in the usual way furnished cyclo*artane*; recrystallised from chloroform–methanol, this had m. p. 85—86° and $[\alpha]_D$ +59° (*c*, 1·48), but no selective absorption in the ultra-violet *cyclo*Artane gave a pale yellow colour with tetranitromethane.

Artadienyl Acetate Hydrochloride.—*cyclo*Artenyl acetate (200 mg.) in chloroform (25 ml.) was treated with gaseous hydrogen chloride at room temperature for 30 minutes. Removal of the solvent *in vacuo* and recrystallisation of the residue from chloroform–methanol gave *artadienyl acetate hydrochloride*, m. p. 170—172°, $[\alpha]_D$ +64° (*c*, 1·04).

This hydrochloride (100 mg.) was refluxed with excess of methanolic potassium hydroxide for 2·5 hours and the reaction product worked up in the usual way. Benzoylation (pyridine solution on the steam-bath for 30 minutes) and chromatography over alumina (Savory and Moore's standardised) gave *artadienyl benzoate* which, recrystallised from chloroform–methanol, had m. p. 185—187° and $[\alpha]_D$ +80° (*c*, 1·41).

Action of Osmium Tetroxide on cyclo*Artenyl Benzoate.*—*cyclo*Artenyl benzoate (610 mg.) in anhydrous ether (100 ml.) was treated with osmium tetroxide (900 mg.) dissolved in the same solvent (50 ml.) and kept for 5 days at room temperature. The ether was removed *in vacuo*, sodium sulphite (23 g.) in water (230 ml.) and ethanol (115 ml.) were added, and the whole was refluxed for 2 hours. The mixture was filtered hot and the filtrate diluted with water and extracted with ether. Evaporation of the ether afforded a solid which was purified by chromatography over alumina (Savory and Moore). Methanol–ether (1 : 19) eluted *dihydroxy*cyclo*artanyl benzoate*, which recrystallised from methanol as fine plates, m. p. 180—183° (decomp.), $[\alpha]_D$ +66° (*c*, 1·18). It gave a pale yellow colour with tetranitromethane.

Dihydroxy*cyclo*artanyl benzoate (200 mg.) in AnalaR acetic acid (25 ml.) was treated with lead tetra-acetate (250 mg.) in the same solvent (25 ml.) at room temperature for 5 hours. The mixture was diluted with water (30 ml.) and distilled to half the volume. Treatment of the distillate in the usual way with 2 : 4-dinitrophenylhydrazine hydrochloride gave a yellow precipitate. After chromatography in benzene solution over alumina (Savory and Moore) this furnished acetone 2 : 4-dinitrophenylhydrazone (30 mg.); recrystallised from aqueous methanol, this had m. p. 125—126°, undepressed on admixture with an authentic specimen of the same m. p. (Found: C, 45·65; H, 4·2. Calc. for $C_9H_{10}O_4N_4$: C, 45·35; H, 4·25%).

The non-volatile products of the lead tetra-acetate oxidation crystallised as needles from the acetic acid mother-liquors on storage. Addition of water and ether, filtration, separation of the ethereal layer, and working up in the usual way afforded an acid fraction (insoluble potassium salt) and a larger neutral fraction. The latter was oxidised by silver oxide (Kuhn, Badstübner, and Grundmann, *Ber.*, 1936, **69**, 106), and the resulting acid fraction added to the first acid fraction. The combined acid fractions were methylated with diazomethane, and the resulting methyl ester was chromatographed over alumina (Savory and Moore). Elution with benzene afforded *methyl trisnor*cyclo*artanoloate benzoate* which, recrystallised from aqueous methanol, had m. p. 133—134°, $[\alpha]_D$ +65° (*c*, 1·47). The ester gave a pale yellow colour with tetranitromethane.

Methyl trisnor*cyclo*artanoloate benzoate (50 mg.) was refluxed with 1% absolute ethanolic potassium hydroxide (50 ml.) for 2 hours. The alcohol was removed *in vacuo*; the residue contained no neutral fraction.

Examination of the Alcohol Fraction from the Fruit of A. integrifolia.—Fractions 11—14 combined with fractions 29—32 of the chromatograms (see p. 1448) represented the alcohol fractions from the extract of *A. integrifolia*. They were combined and acetylated with pyridine–acetic anhydride on the water-bath for 1 hour. Working up in the usual way gave a very viscous mixture of acetates which did not solidify. The mixture was chromatographed over 400 g. of Savory and Moore alumina with the following results (each fraction crystallised once from chloroform–methanol before the m. p. was taken).

Fraction no.	Eluent.	Eluate.
1—4	400 ml. 9 : 1 Pet.–C_6H_6	Nothing
5	100 ml. 4 : 1 ,,	Solid; m. p. 96—100°
6	,, ,,	Solid, m. p. 116—123°
7	,, ,,	Solid, m. p. 134—136°
8	100 ml. 3 : 1 ,,	Cryst. easily, m. p. 112—115°
9	200 ml. 3 : 1 ,,	Cryst. very easily, m. p. 118—120°
10	,, ,,	Cryst. very easily; m. p. 118—120°
11	200 ml. 1 : 1 ,,	Cryst. very easily, m. p. 118—120°
12	200 ml. C_6H_6	Small amorphous fraction
13—16	800 ml. ,,	Traces only; oily

Recrystallisation of fraction 8 gave plates, m. p. 121—123°. These were combined with fractions 9, 10, and 11 (total wt. 1·35 g.) and recrystallised once from chloroform–methanol to give *cyclo*artenyl acetate, m. p. 122—123°, undepressed on admixture with the acetate (see above) obtained from *cyclo*artenone, $[\alpha]_D$ +58° (*c*, 3·00).

Recrystallised fraction 6 had m. p. 133—135°. It was combined with fraction 7 (total wt. 350 mg.) and recrystallised three times from chloroform–methanol, giving needles, m. p. 141—143°, $[\alpha]_D$ +14° (*c*, 3·21) (Found : C, 82·0; H, 11·35. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). There was no depression in m. p. on admixture with an authentic specimen of butyrospermyl acetate, m. p. 141—143°. Hydrogenation over a platinum catalyst in ether–acetic acid solution furnished a dihydro-acetate which, recrystallised from methanol, had m. p. 132—133° (Found : C, 81·8; H, 11·45. Calc. for $C_{32}H_{54}O_2$: C, 81·65; H, 11·55%). There was no depression in m. p. on admixture with an authentic specimen of dihydrobutyrospermyl acetate, m. p. 133—134°. Alkaline hydrolysis of the acetate isolated from *A. integrifolia* and benzoylation (pyridine–benzoyl chloride overnight) afforded the corresponding benzoate (from methanol), m. p. 128—130°, $[\alpha]_D$ +33° (*c*, 1·45), undepressed on admixture with an authentic specimen of dihydrobutyrospermyl benzoate, m. p. 130—132°.

i-*Cholestane*.—A reference specimen of this hydrocarbon was prepared from *i*-cholestenone by Schmid and Kägi's method (*Helv. Chim. Acta*, 1950, **33**, 1582). In spite of careful chromatographic fractionation and repeated recrystallisation from chloroform–methanol it always melted at 80—81°, had $[\alpha]_D$ +80° (*c*, 2·81), showed no selective absorption from 195 to 220 mμ. (*c*, 0·0113%), and gave a pale yellow colour with tetranitromethane of an intensity corresponding to that given by *cyclo*artanol and its derivatives retaining the unopened *cyclo*propane ring.

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