ON TERPENES. CCXV.* ABSOLUTE CONFIGURATION OF ARTABSIN

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The authors proved that artabsin has the absolute configuration 6(*S*),7(*S*),10(*S*),11(*S*)-10-hydroxyguai-1,4-dien-6,12-olide. The proof is based on correlation with a derivative of α-santonin.

In one of the preceding papers of this series[1,2] we described the revision of the structure of artabsin (*I*) and determined its stereochemistry with the exception of the arrangement at $C_{(10)}$. When deriving the configuration of the centers $C_{(6)}$, $C_{(7)}$, and $C_{(11)}$ we based out considerations on the correlation of artabsin with isophotosantonin lactone (*II*), *via* guai-1(10)-en-6,12-olide (*III*), which was described earlier by Suchý and coworkers[3], and the validity of which was not affected by the new structure of artabsin. We now carried out this correlation in a different way, *i.e. via* the tetrahydro derivatives of artabsin; by doing this we were able to prove the partial stereo structure and to determine the configuration of the remaining centre at $C_{(10)}$. The course of the correlation is represented in Scheme 1. The basic idea was the isolation of all products of hydrogenation of *I*, *i.e.* all tetrahydro derivatives, and their comparison with two corresponding hydroguaianolides (*IV* and *V*) prepared stereoselectively from 4α-methyl-5α-H- and 4β-methyl-5α-H-dihydroisophoto-α-santonin lactone (*VI*) and (*VII*) (refs[4,5]). Substances *IV* and *V* were chosen because the absolute stereostructure of *VI* (according to Cahn–Ingold–Prelog notation (1(*R*),4(*S*), 5(*R*),6(*R*),7(*S*),10(*R*),11(*S*)-dihydroisophotosantonin lactone) has been determined by X-ray analysis of its 2-bromo derivative[4], and also because the $C_{(4)}$-epimeric substances could be expected among the tetrahydro derivatives of artabsin in view of the possible hydrogenation mechanisms.

Hydrogenation of artabsin on platinum oxide in acetic acid gave in addition to the three earlier described[6] tetrahydroartabsins "a", "b", and "c", three additional tetrahydroartabsins, indicated by letters "d", "e", "f". The structure of all six tetrahydroartabsins *VIIIa – VIIIf* was corroborated by IR, mass, and PMR spectra. The isomer of m.p. 131°C, described by Suchý and coworkers[3], indicated earlier as tetrahydroartabsin "d" could not be isolated, but we demonstrated by studying

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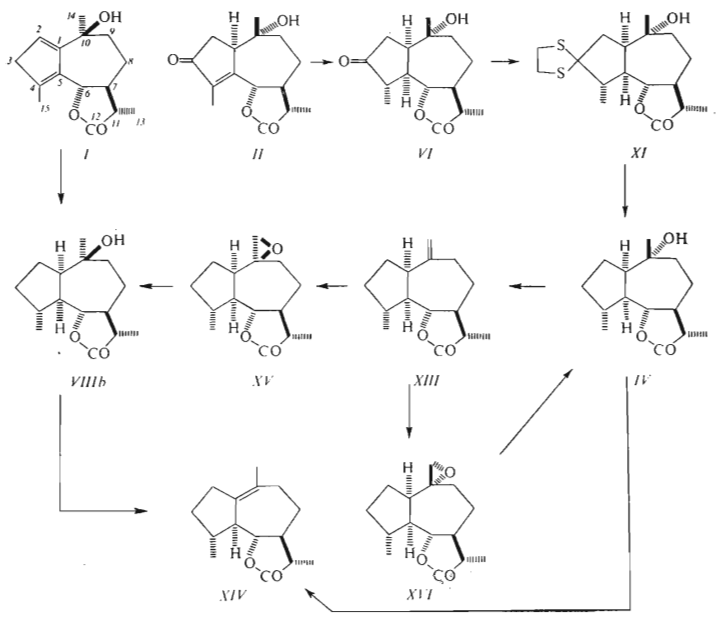
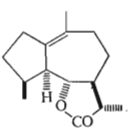
an authentic sample that this substance was identical with dihydroartabsin *IX* described earlier[2,6]. The remaining two tetrahydroartabsins (from eight possible ones could not be isolated even after hydrogenation of dihydroartabsin *IX*, which gave only tetrahydroartabsins "a", "b", "d", and "f".

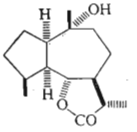
Hydrogenation of isophoto-α-santonin lactone (*II*) on palladium on charcoal in ethanol always gave only 4α-methyl-dihydroisophoto-α-santonin lactone (*VI*),* m.p. 152–152·5°C as the main product in contrast to the published results[7]. As a by-product we isolated a small amount of a substance $C_{15}H_{22}O_3$, (*X*) m.p. 148–150°C which displayed in its IR spectrum characteristic bands of a γ-lactone (1173 and 1762 cm^{-1}) and a hydroxy group (3590 cm^{-1}). This was in agreement with the PMR spectrum (Table I) which contained a signal of proton $H_{(6)}$ as a broad doublet at 4·64 p.p.m. ($J_{6,7} \approx 11$ Hz) and a broad singlet of methyl on a double bond at 1·84 p.p.m. On the basis of these facts the substance has the structure *X*. However, ac-



SCHEME 1



III



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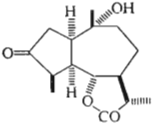
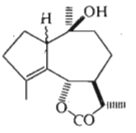
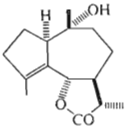


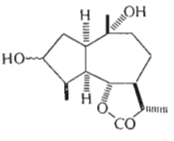
VII



IX



X



XII

cording to spectral characteristics and the melting point it was not identical with dihydroartabsin *IX*. Ketone *VI* was converted to ethylenethioketal *XI* which was then desulfurised with Raney nickel to give hydroxyguaianolide *IV*.

Hydrogenation of lactone *II* was also carried out on platinum oxide in acetic acid. Substance $C_{15}H_{24}O_4$, m.p. 154–155·5°C, was isolated as the main product. According to its IR spectrum (γ-lactone at 1175 and 1760 cm^{-1}; hydroxyl at 3600 cm^{-1}) and PMR spectrum (Table I) it has the structure *XII*. By oxidation of substance *XII* with chromium trioxide in pyridine we obtained a compound which according to spectral data and the mixture melting point was identical with 4β-methyldihydroisophoto-α-santonin lactone (*VII*).* In addition to substance *XII* we also isolated two isomeric hydroxyguaianolides in small amount. Their composition was $C_{15}H_{24}O_3$ (*m/e* 252). According to infrared and mass spectral data and PMR spectra, as well as according to mixture melting point one of them was identical with hydroxyguaianolide *IV*. The second hydroxyguaianolide, of m.p. 125·5–127·5°C, displayed a signal of proton $H_{(6)}$ in its PMR spectrum (Table I) as a broadened triplet at 4·11 p.p.m. (with splitting $J_{5,6} \cong J_{6,7} \cong 9{\cdot}5$ Hz). The magnitude of this splitting indicates a *trans* configuration of protons $H_{(6)}$, and $H_{(5)}$, and $H_{(6)}$, and $H_{(7)}$, similarly as in other derivatives of isophotosantonin lactone with 5α-H (Table I). Hence, it could be supposed that this substance is probably the $C_{(4)}$-epimer of substance *IV*, *i.e.* substance *V*.

* Prof. G. Jommi, University of Milan, arrived at the same result. He could obtain ketone *VII* only after hydrogenation in autoclave (personal communication). However, we did not employ this method because we succeeded in the preparation of the $C_{(4)}$-epimer of the substance *IV* by direct hydrogenation of compound *II*.

The configuration of the $C_{(4)}$-methyl in substance *V* is also supported by the relation found between the average values of the vicinal interaction of methyl protons in the PMR spectra of substances *IV* and *V* ($J_{4,15}$ (*IV*) = 6·1 Hz < $J_{4,15}$ (*V*) = = 7·0 Hz) which is in agreement with the general rule for vicinal interactions on sp_3-fragments of CH_3—CH—C′—H′ type $J(CH_3,H'$-*syn*-clinal, *syn*-periplanar) < < $J(CH_3),H'$-*anti*-clinal, *anti*-periplanar)[8] (for another example of this rule see substances *VI* and *VII* in Table I and ref.[9,10]). Furthermore, the absolute configuration of substance *V* may be supported by the results of the hydrogenation of substance *X* which was also carried out in acetic acid on platinum oxide, and which in contrast to the results of hydrogenation of dihydroartabsin *IX* gave substance *V* as the main product and substance *IV* as the only minor component. In view of the fact that under the same conditions of hydrogenation of substance *II* substance *XII* is formed as the main product, with the absolute configuration of hydrogen atoms 4α, 5α, and 1α (as was proved by oxidation of diollactone *XII* to hydroxyketolactone *VII*) – *i.e.* a normal product of 1,2-addition-, it can be assumed that in the case of hydrogenation of substance *X* compound *V* also arises by a normal *cis*-addition on the double bond $\Delta^{4(5)}$ and that it has identical configurations on centres $C_{(4)}$, $C_{(5)}$, and $C_{(1)}$ as substance *XII*. On the other hand substance *IV* may arise from intermediates formed by H-shift in triades $C_{(3)}$—$C_{(4)}$—$C_{(5)}$ or $C_{(4)}$—$C_{(5)}$—$C_{(6)}$ or $C_{(4)}$—$C_{(5)}$—$C_{(1)}$. The number of corresponding products of hydrogenation indicates that the participation of the centre $C_{(1)}$ is least probable.

However, we did not carry out a direct correlation of substance *V* with ketone *VII*, as we originally intended, because it was found that just as substance *X* was not identical with dihydroartabsin *IX*, substances *IV* and *V* were not identical with any of the six isolated tetrahydroartabsins either. It could be assumed that in the case of the validity of the stereochemistry at $C_{(6)}$, $C_{(7)}$, and $C_{(11)}$ inferred earlier, the configuration of the centre $C_{(10)}$ in artabsin and its derivatives must be opposite to that in guaianolides derived from isophotosantonin lactone, as we were able to prove this assumption by the inversion of the configuration of the centre $C_{(10)}$ in compound *IV* the problem of absolute configuration of substance *V* in direct connection with the absolute configuration of artabsin lost its importance, and therefore it will be solved later.

The configuration inversion at $C_{(10)}$ in substance *IV* was carried out in the following manner (Scheme 1): Dehydration of substance *IV* with thionyl chloride in pyridine gave two isomeric guaienolides of elemental composition $C_{15}H_{22}O_2$ (*m/e* 234) which according to IR and PMR spectra (Table I) have the structure *XIII* and *XIV*. By epoxidation of substance *XIII* with perphthalic acid we further obtained two stereoisomeric epoxides *XV* (m.p. 111–112·5°C) and *XVI* (m.p. 101–102°C). Hydrogenation of epoxide *XV* on palladium on strontium carbonate in ethyl acetate[11] gave a substance (in quantitative yield) which was identical with tetrahydroartabsin "b" (*VIIIb*) according to spectral data and mixture melting point. However, we were unable to open the epoxide *XVI* in this manner, but hydrogenation on palladium

* We thank professor G. Jommi, University of Milan, for the authentic sample.

TABLE I
Characteristic Parameters of PMR Spectra

Compound[a]	$H_{(6)}$[b]	$H_{(13)}$[c]	$H_{(14)}$	$H_{(15)}$[b]	Other protons[d]
II[e]	4·81 bd $J_{6,7} = 9·5$ $J_{6,15} = 1·6$	1·25 d (6·5)	0·94 s	1·86[f] $J_{15,6} = 1·6$ $J_{15,1} = 2·1$	$H_{(11)}$: 2·31 $H_{(1)}$: 3·23 bm $H_{(2)}$: 2·54 (2 H)[h]
III[g]	3·71 t (10)	1·21 d (6·7)	1·71 bs	0·91 d (6·7)	$H_{(4)}$: 2·53 $H_{(11)}$: 2·20
IV	4·04 t (10)	1·19 d (6·5)	1·19 s	1·07 d (6·1)	$H_{(4)}$: 2·0 $H_{(11)}$: 2·20
V	4·10 bt (10)	1·20 d (6·7)	1·22 s	0·92 d (7·0)	$H_{(4)}$: 2·27 $H_{(11)}$: 2·18
VI	4·11 bt (9)	1·25 d[l] (6·4)	1·17 s	1·21 d[l,i] (7·0)	$H_{(4)}$; 2·31 $H_{(11)}$: 2·21
VII	3·96 t (10)	1·22 d[i] (6·3)	1·25 s	1·23 d[i] (7·5)	—
VIIIb[g]	4·46 bt (10)	1·18 d[i] (6·9)	1·22 s	1·12 d[i] (5·8)	$H_{(4)}$: 1·87 $H_{(11)}$: 2·16

[a] Varian HA-100; solvent deuteriochloroform; first-order analysis; multiplicity indicated as follows: b broadened signals, s singlet, d doublet, t triplet, dd doublet of doublets, m unresolved multiplet; chemical shifts are given in δ (TMS)-scale, splittings in parentheses; internal standard tetramethylsilane (unless stated otherwise); concentration uncertain (<20 mg/0·5 ml). [b] Splittings from 500 Hz sweep-width chart; broadening of $H_{(6)}$-triplets due to second-order effects. [c] Splittings from 50 Hz sweep-width chart. [d] Approximate positions of $H_{(4)}$ and $H_{(11)}$ from INDOR- or tickling-experiments. [e] Internal standard hexamethyldisiloxane (HMDS); $\delta_{(HMDS)} = 0·06$ p.p.m. [f] Couplings confirmed by DR-experiments. [g] Compound *III* prepared from *VIIIc*. [h] AB-part of an ABX-system with degenerate low-field subspectrum; average position of both subspectra. [i] Overlapping methyl signals; coupling constants uncertain. [j] Measured with small addition of hexadeuteriodimethyl sulfoxide. [k] Intensity 2 H; $W_{1/2} \approx 5$ Hz. [l] Tentative assignment based on the correlation with other compounds of the Table. [m] $^2J = 4·3$; low-field proton $^4J = 1·3$ and high-field one $^4J = 0·65$.

on charcoal in ethyl acetate gave a substance identical with the starting hydroxyguaianolide *IV* (according to spectral data and mixture melting point). Hence the absolute configuration expressed by formula *XVI* may be assigned to epoxide of m.p. 101 to

TABLE I
(*Continued*)

Compound[a]	$H_{(6)}$[b]	$H_{(13)}$[c]	$H_{(14)}$	$H_{(15)}$[c]	Other protons[d]
X	4·64 bd $J_{6,7} = 11$ $J_{6,15} \neq 0$	1·21 d (6·6)	0·99 s	1·84[f] $J_{15,6} \neq 0$ $J_{15,1} \neq 0$	$H_{(1)}$: 3·10 bm
XI	4·10 t (9·5)	1·22 d (6·6)	1·22 s	1·25 d[i] (6·2)	S-$(CH_2)_2$-S : 3·27 s (4 H)
XII[i]	4·26 bt (9·5)	1·16 d[i] (6·7)	1·19 s	0·92 d (6·8)	$H_{(3)}$: 4·10 bm
XIII	3·83 t (10)	1·19 d[i] (6·9)	4·86 m[k]	1·13 d[i] (6·4)	$H_{(1)}$: 2·79 $H_{(4)}$: 1·95 $H_{(11)}$: 2·12
XIV	3·59 t (9·5)	1·19 d (6·8)	1·71 bs	1·15 d (5·9)	$H_{(4)}$: 2·17 $H_{(11)}$: 2·17
XV	4·19 bt (9)	1·22 d (6·8)	2·74 d 2·42 d $^2J = 4·95$[c]	1·13 d (6·1)	—
XVI	4·00 t (9·5)	1·22 d (6·8)	2·75 dd[m,c] 2·53 dd[m,c]	1·12 d (5·9)	—

102°C, and that expressed by formula *XV* to the second epoxide of m.p. 111 – 112·5°C (the inversion of configuration at $C_{(1)}$ during the epoxidation of the unsaturated lactone *XIII* may be considered as very improbable). Therefore, tetrahydroartabsin "b" must have the absolute stereostructure of 1(*R*),4(*R*),5(*S*),6(*R*),7(*S*),10(*S*),11(*S*)-10-hydroxyguai-6,12-olide (*VIIIb*) and artabsin the absolute stereostructure of 6(*S*), 7(*S*),10(*S*),11(*S*)-10-hydroxyguai-1,4-dien-6,12-olide (*I*). In accordance with formula *VIIIb* tetrahydroartabsin "b" afforded (in contrast to substance *IV*) on dehydration with thionyl chloride in pyridine substance *XIV* in quantitative yield. The determination of the absolute configuration of other tetrahydroartabsins as well as all other presently unidentified derivatives of artabsin and isophotosantonin lactone which were prepared during the investigation of artabsin, will be the object of a subsequent paper in this series.

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. The PMR spectra were recorded on a Varian HA-100 apparatus.

Hydrogenation of Artabsin (*I*)

Artabsin (2·5 g) was hydrogenated in acetic acid (20 ml) in the presence of platinum oxide (0·5 g) at normal pressure and at room temperature. The hydrogenation products (2·5 g) were isolated in the usual manner and then separated by chromatography on 250 g of silica gel containing 15% of water. *Tetrahydroartabsin* VIIIc: Fractions 67—87 (20 ml each) eluted with light petroleum–ether mixture (6 : 4) gave 240 mg of residue, m.p. 135·5—136°C (ethyl acetate–hexane), which according to its melting point and mixture melting point and IR spectra was identical with authentic[4] isomer "c". *Tetrahydroartabsin* VIIIb: Fractions 90—102 (20 ml each) were also eluted with a light petroleum–ether mixture, containing 40% of ether. After evaporation they gave a substance (230 mg), m.p. 160·5—161°C (ethyl acetate–hexane), identical according to its melting point, mixture melting point, and IR spectrum with the authentic isomer "b". *Tetrahydroartabsin* VIIIa: Fractions 144—205 (20 ml each) were obtained on elution with a mixture of light petroleum and ether (1 : 1). After evaporation they afforded 1 100 mg of a substance which after crystallisation weighed 800 mg and melted at 107·5—108·5°C (benzene–hexane), and which was identical according to its melting point and mixture melting point and IR spectra with the authentic[4] isomer "a". *Tetrahydroartabsin* VIIId: Fractions 219—235 (elution with light petroleum–ether 45 : 55) gave 45 mg of a substance melting at 146—147. 5°C (ethyl acetate–hexane). Its IR spectrum contained bands characteristic of γ-lactone at 1 175 cm^{-1} and 1 767 cm^{-1} and a band at 3 595 cm^{-1} characteristic of the hydroxy group. Molecular mass determined by mass spectroscopy was 252 which corresponds to the composition $C_{15}H_{24}O_3$. ORD (*c* = 0·09; methanol: 25°C): $[\Phi]_{400}$ 251°, $[\Phi]_{300}$ 502°, $[\Phi]_{250}$ 1 334°, $[\Phi]_{232}$ 2 625°, $[\Phi]_{215}$ 0°, $[\Phi]_{208}$ —723°, $[\Phi]_{204}$ 0°. *Tetrahydroartabsin* VIIIe: Fractions 246—285 (20 ml each), which were eluted with a mixture of light petroleum and ether (4 : 6), gave after evaporation 140 mg of a substance melting at 93—94°C (benzene–hexane) the IR spectrum of which contained a γ-lactone band at 1 178 and 1 767 cm^{-1} and a hydroxyl band at 3 595 cm^{-1}. Molecular mass, determined by mass spectrography was 252, corresponding to the composition $C_{15}H_{24}O_3$; $[\alpha]_D^{20}$ —14·8° (*c* 3·4, chloroform). *Tetrahydroartabsin* VIIIf: Fractions 135—143 and the mother liquors after the crystallisation of isomer "a" (totally 330 mg) were rechromatographed on 40 g of silica gel containing 15% of water, taking light petroleum–ether mixture (6 : 4) as eluent. Fractions 102—130 (5 ml each) gave a substance (55 mg) which melted at 102—104°C, the IR spectra of which contained bands of γ-lactone group at 1 190 and 1 758 cm^{-1} and a band of hydroxy group at 3 590 cm^{-1}. The molecular mass, 252 (determined by mass spectrometry) corresponds to the composition $C_{15}H_{24}O_3$; ORD (*c* 0·075, methanol, 26°C): $[\Phi]_{400}$ —340°, $[\Phi]_{300}$ —578°, $[\Phi]_{275}$ —680°, $[\Phi]_{250}$ —714°, $[\Phi]_{233}$ —374°, $[\Phi]_{225}$ —1 020°, $[\Phi]_{215}$ —2 780°.

Hydrogenation of Dihydroartabsin *IX*

Dihydroartabsin[2] (50 mg) was hydrogenated on platinum oxide (10 mg) in acetic acid (2 ml). Hydrogenation products isolated in the usual manner were chromatographed on 15 g of silica gel containing 15% of water (eluent: light petroleum containing 40% of ether; fractions 3 ml each). Fractions 21—24 gave a substance (5 mg), m.p. 160—162°C (ethyl acetate–hexane), identical according to its R_F value, PMR and IR spectra, and mixture melting point with tetrahydroartabsin "b". Fractions 35—37 gave a substance (3 mg), m.p. 95—102°C, identical according to the same criteria with tetrahydroartabsin "f". Fractions 41—52 afforded 21 mg of substance melting at 107·5—108·5°C (ethyl acetate–hexane) identical according to the above

criteria with tetrahydroartabsin "a". Fractions 58—81 gave a substance (14 mg), m.p. 144—146°C (ethyl acetate–hexane) identical according to R_F, IR and PMR spectra and mixture melting point with tetrahydroartabsin "d".

Hydroxyguaienolide *X* and Lactone *VI*

The products of hydrogenation of isophoto-α-santonin lactone *II* (5 g) (on palladium in ethanol[5]) were chromatographed on 300 g od silica gel containing 15% of water. Fractions 76—108 (20 ml each) were obtained on elution with a light petroleum–ether mixture (4 : 6) After evaporation of the solvent substance *X* (280 mg) was obtained, m.p. 148—150°C (ethyl acetate–hexane) the IR spectrum of which displayed bands of γ-lactone grouping (1 173 and 1 762 cm^{-1}) and a band of a hydroxy group (3 590 cm^{-1}). The molecular mass determined from the mass spectrum was 250 corresponding to the composition $C_{15}H_{22}O_3$; $[\alpha]_D^{20}$ 120·5° (*c* 1·95, chloroform). Fractions 306—420 (20 ml each) were obtained by elution with ether. Their dry residue (3·4 g of substance *VI*) had m.p. 152—152·5°C (benzene–hexane). The IR spectrum of this substance contained bands characteristic of a γ-lactone (at 1 168 and 1 762 cm^{-1}), a carbonyl on a five-membered ring (1 730 cm^{-1}), and a hydroxy group (3 590 cm^{-1}). The molecular mass, 266 (from mass spectrum), corresponds to the elemental composition $C_{15}H_{22}O_4$; $[\alpha]_D^{20}$ 39·2 (*c* 2·5, chloroform).

Ethylene Thioketal *XI* and Hydroxyguaienolide *IV*

To a solution of lactone *VI* (3·0 g) in acetic acid (20 ml) ethanedithiol (0·8 g) and *p*-toluenesulfonic acid (0·8 g) were added and the mixture was left to stand at room temperature for 5 hours. It was then poured onto ice and extracted with ethyl acetate; the isolated neutral fraction gave on crystallisation from ethyl acetate ethylene thioketal *XI* (3·9 g), m.p. 233·5—234°C, the IR spectrum of which displayed maxima characteristic of γ-lactones (1 165 and 1 764 cm^{-1}) and of hydroxy group (3 580 cm^{-1}). Its mass, 342 (from mass spectrum) corresponds to the composition C_{17}. $.H_{26}O_3S_2$; $[\alpha]_D^{20}$ ±0° (*c* 2·6, chloroform). *Desulfuration*: Ethylene thioketal *XI* (3·8 g) was desulfurized with excess Raney nickel in boiling dioxan for 1 hour. From the reaction mixture crystalline compound *IV* (1·9 g) was isolated as the sole product, m.p. 85—86°C (benzene–hexane) the IR spectrum of which contained bands typical of γ-lactone (1 189 and 1 765 cm^{-1}) and of hydroxy group (3 590 cm^{-1}). Its mass (252, from mass spectral data) corresponds to the composition $C_{15}H_{24}O_3$; $[\alpha]_D^{20}$ —22·0° (*c* 3·8, chloroform).

Hydrogenation of Isophoto-α-santonin Lactone (*II*)

Lactone *II* (2 g) was hydrogenated in acetic acid (10 ml) in the presence of platinum oxide (0·4 g). The reaction product was chromatographed on 200 g of silica gel containing 13% of water. Fractions 47—58 (15 ml each) were obtained on elution with a light petroleum–ether mixture (1 : 1). After concentration they afforded a crystalline compound (25 mg), m.p. 84—87°C (ethyl acetate–hexane), which melted undepressed on admixture with hydroxyguaianolide *IV*. Both substances also had identical R_F values and PMR spectra. Fractions 59—70 (15 ml each) were obtained after elution with light petroleum–ether 1 : 1 and they contained substance *V* (220 mg), 125·5—127·5°C (ethyl acetate–hexane) the IR spectrum of which showed bands at 1 188 and 1 764 cm^{-1} characteristic of a γ-lactone grouping, and a band at 3 590 cm^{-1} due to a hydroxy group. The mass of this substance was 252 (from the mass spectrum), corresponding to the composition $C_{15}H_{24}O_3$. ORD (*c* 0·12, methanol, 26°C): $[\Phi]_{400}$ 84·8°, $[\Phi]_{300}$ 275·5°, $[\Phi]_{250}$ 869°, $[\Phi]_{231}$ 2014°, $[\Phi]_{225}$ 1526°, $[\Phi]_{216}$ 0°, $[\Phi]_{210}$ —890. Fractions 344—415 (15 ml each) were obtained by elution with ether containing 10% of ethyl acetate and they afforded diollactone *XII*

(1·0 g), m.p. 154—155°C (ethanol). Its IR spectrum contained bands at 1175 and 1760 cm^{-1} due to a γ-lactone group, and at 3600 cm^{-1}, due to a hydroxyl. For $C_{15}H_{24}O_4$ (268·3) calculated: 67·15% C, 9·01% H, 0·75% H act.; found: 67·17% C, 8·86% H, 0·74% H act.

4β-Methyl-dihydroisophoto-α-santonin Lactone (*VII*)

Diollactone *XII* (350 mg) was oxidised with chromium trioxide (350 mg) in pyridine in the usual manner. The obtained hydroxyketo lactone *VII* (240 mg) was crystallised from a mixture of ethyl acetate and hexane; m.p. 136—142°C, undepressed on admixture of lactone *VII*. The IR spectrum contained bands due to a γ-lactone grouping (1182 and 1765 cm^{-1}), to a carbonyl in a five-membered ring (1739 cm^{-1}), and to a hydroxyl (3595 cm^{-1}).

Hydrogenation of Hydroxyguaienolide *X*

Hydroxyguaienolide *X* (130 mg) was hydrogenated on platinum oxide (30 mg) in acetic acid (5 ml). Hydrogenation products isolated in the usual manner were separated chromatographically on 25 g of silica gel containing 13% of water (fractions 2 ml each; eluent light petroleum with 45% of ether). Fractions 130—151 gave a substance (5 mg), m.p. 86—88°C (benzene–hexane) identical according to its R_F value, IR and PMR spectra, and mixture melting point with hydroxyguaianolide *IV*. Fractions 164—208 afforded 90 mg of a substance melting at 126·5—128°C (benzene–hexane) which was identical according to the same criteria as above with hydroxyguaianolide *V*.

Guaienolides *XIII* and *XIV*

Hydroxyguaianolide *IV* (1·8 g) was dehydrated with thionyl chloride (2·5 g) in pyridine (25 ml) at 0°C for 24 hours. The reaction mixture was worked up in the conventional manner to give an oily product (1·7 g). This was chromatographed on 150 g of silica gel impregnated with silver nitrate. Fractions 47—72 (20 ml each) were eluted with light petroleum containing 10% of ether and afforded crystalline guaienolide *XIV* (700 mg), m.p. 75—76°C (hexane). Its IR spectrum contained bands at 1178 and 1756 cm^{-1} due to a γ-lactone group; molecular mass 234 (from mass spectrum) corresponds to elemental composition $C_{15}H_{22}O_2$; $[\alpha]_D^{20}$ —31·2 (*c* 3·2, chloroform). Fractions 90—165 (20 ml each) were obtained by elution with light petroleum containing 15% of ether. After evaporation they afforded guaienolide *XIII* (600 mg), m.p. 45—48° (pentane); the IR spectrum contained maxima at 1175 and 1755 cm^{-1} characteristic of γ-lactone, and at 898 and 1637 cm^{-1} due to the corresponding exomethylene group. Molecular mass was 234 (mass spectrum), corresponding to the composition $C_{15}H_{22}O_2$.

Epoxides *XV* and *XVI*

Guaienolide *XIII* (500 mg) was epoxidated in an ethereal solution with perphthalic acid (800 mg) by standing for one day at 0°. The neutral fraction of the reaction mixture was chromatographed on 60 g of silica gel containing 15% of water. Fractions 41—73 (10 ml each) were eluted with light petroleum–ether (8 : 2) mixture to give epoxide *XV* (280 mg), m.p. 111—112·5°C (ether–hexane). Molecular mass 250 (from mass spectrum) corresponds to the composition $C_{15}H_{22}O_3$; $[\alpha]_D^{20}$ 8·1° (*c* 2·6, chloroform). Fractions 108—134 (10 ml each) eluted with light petroleum containing 30% of ether gave epoxide *XVI* (170 mg), m.p. 101—102°C (ether–hexane). Molecular mass 250 (from mass spectrum) coresponds to the composition $C_{15}H_{22}O_3$; $[\alpha]_D^{20}$ 1·3° (*c* 2·7, chloroform). *Epoxide* XVI (75 mg) was hydrogenated on 100 mg of 10% palladium on charcoal in ethyl acetate (3 ml)(ref.[8]). The hydrogenation products were chromatographed on 20 g of silica gel containing 15% of water. Fractions 96—102 (3 ml each), eluted with light petroleum–ether

mixture 1 : 1 gave a substance (11 mg), m.p. 83—87°C (ethyl acetate–hexane) the R_f value of which was identical with hydroxy guaianolide *IV* with which it melted undepressed. *Epoxide* XV (120 mg) was hydrogenated on 110 mg of 5% palladium on strontium carbonate in ethyl acetate (4 ml). The obtained product *VIIIb* (110 mg) was crystallised from a mixture of ethyl acetate and hexane; m.p. 161·5°C, undepressed on admixture with tetrahydroartabsin "b", The substances also had identical IR and PMR spectra; $[\alpha]_D^{20}$ —12·4° (*c* 2·7, chloroform).

Guaienolide *XIV* from Hydroxyguaianolide (*VIIIb*)

Hydroxyguaianolide *VIIIb* (150 mg) was dehydrated with thionyl chloride (300 mg) in pyridine (2 ml) at 0°C for 24 hours. The reaction mixture was worked up in the conventional manner to give a substance (130 mg), m.p. 75—76°C (hexane), identical according to its R_f value, IR spectrum and mixture melting point with guaianolide *XIV*.

Elemental analyses were carried out in our analytical department under the direction of Dr J. Horáček, the IR spectra were measured by Mrs K. Matoušková and Mrs S. Holubová under the direction of Dr J. Smolíková, and the mass spectra were measured by Mrs M. Vokáčová under the direction of Dr L. Dolejš. Our thanks are due to all those mentioned.

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