STANDARD SESQUITERPENIC LACTONES FOR STRUCTURAL CORRELATIONS; STEREOISOMERIC (6*R*, 7*S*, 10*S*, 11*S*)-10-HYDROXYGUAIAN-6,12-OLIDES AND RELATED (6*R*, 7*S*)-GUAIENOLIDES*

K. VOKÁČ and Z. SAMEK

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10, Prague 6

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The absolute configuration of six stereoisomeric (6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguiaian-6,12-olides was determined on the basis of PMR spectral studies and by direct correlation of their dehydration products with the derivatives of α-santonin. Further the mechanism of elimination of the hydroxyl at $C_{(10)}$ in 10-hydroxyguaianolides and some stereochemical aspects of artabsin hydrogenation are also discussed. The results obtained show that in the case of the double bond hydrogenation in the presence of electron donors in allylic position — oxygen atoms of hydroxyls or ether oxygen atoms of the lactone ring — the hydrogenation is very stereoselective and it is directed by the configuration of the allylic centre.

A series of difficulties met with during the determination of the stereochemistry of native sesquiterpenic lactones by means of chemical spectral methods arises from the fact that up to now reliably defined sets of stereoisomers of single skeletal types do not exist. This is especially true of the basic homobicyclic skeletons and their secoanalogs which contain 5–7 chiral centres and may exist, in principle, in the full number of 32–128 stereoisomers. Present experience shows that the biogenesis of sesquiterpenic lactones is appreciably stereoselective and that it rules to a certain extent the systematic occurrence of a series of chiral centres which always have a certain absolute configuration.

Non-selective biogenesis of lactones leading to a simultaneous formation of enantiomers was described by Ourisson and coworkers[1]. The appreciable conformational selectivity of the biogenesis may also lead to characteristic configurational sequences of vicinal chiral centres of homocyclic systems[2]. For rapid and relatively reliable orientation in the majority of configurational relationships a series of empirical rules of CD (refs[2,3]) and PMR (refs[4–9]) may be used. The problem of the stereochemistry of single native substances is mostly reduced to 1–3 centres of chirality. Nevertheless, in view of the possibility of enantiomerism and the empirical character of the interpre-

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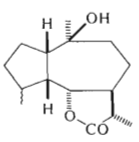
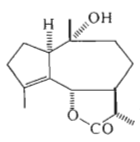
tations of physical measurements the problem of stereoisomery still remains to its full extent. An objective solution of the structural problem still cannot be forwarded without a direct confrontation of isotropic and anisotropic properties of substances with a defined stereoisomery. Therefore it seems useful to concentrate the possibilities of preparative chemistry and physical methods in order to create the necessary experimental basic data.

The first experiments were done in a series of guaian-6,12-olides. In this type of substances the present chemical correlations were mainly based on the work of Barton and coworkers[10], where, however, only a few 3-oxo derivatives of isophoto-α-santonin lactone and isophotoartemisin were defined.

The structure of guaian-6,12-olides comprises 7 chiral centres, $C_{(1)}$, $C_{(4)}$, $C_{(5)}$, $C_{(6)}$, $C_{(7)}$, $C_{(10)}$ and $C_{(11)}$ and allows for the existence of 128 isomers. For practical purposes of identification the half of this number suffices, *i.e.* 64, isomers with a fixed configuration at $C_{(7)}$. These may be further classified into subgroups of 32 *cis*- and *trans*-lactones and to subgroups with invertible centres $HOC_{(i)}—CH_3$ ($i = 4, 10, 11$) and $CH_3—C_{(11)}—H$, and non-invertible centres $CH_3—C_{(i)}—H$ ($i = 4, 10$). The interconversion of substances from various subgroups may take



VI, („a") $4\alpha—CH_3$
XI, („ß") $4\beta—CH_3$



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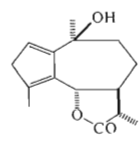
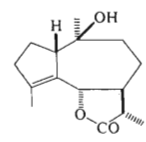
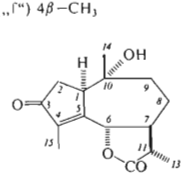


II



XII



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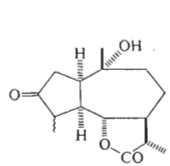
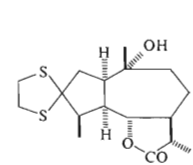


XIII, $4\alpha—CH_3$
XIV, $4\beta—CH_3$



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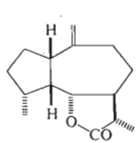
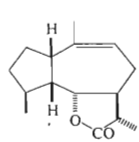
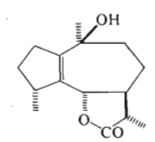


XXII



XXIII



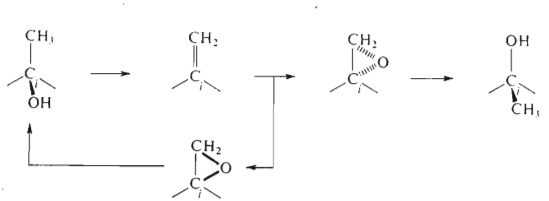
XXIV

place either by direct equilibration (in the case of $C_{(11)}$) or according to Scheme 1 (ref.[11]) in the case of $C_{(4)}$ and $C_{(10)}$.

The aim of this communication is the definition of the group of stereoisomeric (6*R*, 7*S*)-10-hydroxyguaian-6,12-olides with two invertible centres, $C_{(10)}$ and $C_{(11)}$, derived by direct hydrogenation of isophoto-α-santonin lactone (*I*) and artabsin (*II*).

In connection with the solution of the absolute configuration of artabsin (*II*) we described[11] the preparation of two stereosiomeric (10*R*)-10-hydroxyguaian-6,12-olides *III* and *IV* by hydrogenation of isophoto-α-santonin lactone (*I*) and 3-deoxo-isophoto--α-santonin lactone (*V*), and six stereoisomeric (10*S*)-10-hydroxyguaian-6,12-olides *VI*–*XI* (tetrahydroartabsins "a"–"f") by hydrogenation of artabsin (*II*) and dihydroartabsin (*XII*) on Adams catalyst in acetic acid. The structure of isomer *III* was determined[11] by direct correlation with 4α-methyldihydroxyisophoto-α-santonin lactone (*XIII*) the stereo structure of which was determined by X-ray analysis[12]. On inversion of the centrum $C_{(10)}$ in *III* (Scheme 1) tetrahydroartabsin "b" (*VII*) was prepared which proved that substance *II* belonged as well as all tetrahydroartabsins among (10*S*)-10-hydroxyguaian-6,12-olides. The absolute configuration of the isomer *IV* was derived[11] on the basis of PMR spectra and the mechanism of hydrogenation, and its correctness was now also proved by direct correlation with 4β-methyldihydroisophoto-α-santonin lactone (*XIV*) *via* thioketal *XV*. The absolute configuration of the remaining five tetrahydroartabsins *VI*, *VIII*–*XI* was determined by correlation of (10*R*)-guaianolides *III* and *IV* and (10*S*)-guaianolides *VI*–*XI* *via* the products of elimination of 10-hydroxy groups under standard conditions with thionyl chloride in pyridine (Scheme 2), as well as by correlation of their PMR spectra.

As we already described earlier[11], *III* gives on elimination $\Delta^{1(10)}$-guaienolide *XVI* and $\Delta^{10(14)}$-guaienolide *XVIII*, while from tetrahydroartabsin "b" (*VII*) only *XVI* is formed quantitatively. An analogous pair is *IV*, giving $\Delta^{1(10)}$-guaienolide *XVII* and $\Delta^{10(14)}$-guaienolide *XIX*, and tetrahydroartabsin "c" (*VIII*) which again gives *XVII* quantitatively. Hence, tetrahydroartabsin "c" must be the $C_{(4)}$-epimer of tetrahydroartabsin "b", *i.e.* (1*R*, 4*S*, 5*S*, 6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguiaian-6,12-olide (*VIII*). Tetrahydroartabsin "e" (*X*) behaves analogously to *III* and *IV*, giving both $\Delta^{1(10)}$-



SCHEME 1

-guaienolide *XVI* (similarly to *III* and *VII*) and $\Delta^{10(14)}$-guaienolide *XX*, and so does tetrahydroartabsin "d" (*IX*) which affords both $\Delta^{1(10)}$-guaienolide *XVII*, similarly to *IV* and *VIII*, and $\Delta^{10(14)}$-guaienolide *XXI*. Hence, tetrahydroartabsin "e" must be the $C_{(1)}$-epimer of tetrahydroartabsin "b", *i.e.* (1*S*, 4*R*, 5*S*, 6*R*, 7*S*, 10*S*, 11*S*)-10--hydroxyguaian-6,12-olide (*X*) and tetrahydroartabsin "d" must be the $C_{(1)}$-epimer of tetrahydroartabsin "c" (*VIII*) and the $C_{(4)}$-epimer of tetrahydroartabsin "e" (*X*) *i.e.* (1*S*, 4*S*, 5*S*, 6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguaian-6,12-olide (*IX*).

By this correlation, *via* 5αH-guaienolides, all four possible 5αH-epimers were determined and the remaining two tetrahydroartabsins "a" (*VI*) and "f" (*XI*) must therefore have 5βH-configuration; they differ only in the configuration at the centres $C_{(1)}$ and $C_{(4)}$. In these cases elimination took place so that $\Delta^{10(14)}$-guaienolide *XXII* was formed quantitatively from *VI* and $\Delta^{9(10)}$-guaienolide *XXIII* from *IX*, so that the character of the diastereoisomeric relationships of these two tetrahydroartabsins could not be determined in this way directly. Further conslusions followed from the analysis of the possibilities of the conditions of *syn-anti* elimination from the point of view of more probable conformations of (6*R*, 7*S*)-10-hydroxyguaian-6,12-olides. The possible conformations of the homobicyclic system derived from Dreiding models are represented schematically in Fig. 1*A* – 1*D* as Newman projections of five characteristic fragments, namely for the case of 5αH, 1αH; 5αH, 1βH; 5βH, 1βH, and 5βH, 1αH (in all instances for the 4*R*, 10*S*-diastereomer). From the study of the relationships ring size versus reaction rate in *syn-anti* eliminations of cycloalkanes[13] it is known that *trans*-cycloalkenes arise predominantly by *syn*-elimination, while *cis*-cycloalkenes are formed by *anti*-eliminations. In our case we have to do with a seven-membered ring with only two possibilities of elimination to *cis*-endocyclic bonds on fragments $C_{(1)}$—$C_{(10)}$ and $C_{(9)}$—$C_{(10)}$, and therefore it can be supposed that the observed distribution of the endocyclic double bonds in the products of elimination will reflect primarily the sterical conditions for the *anti*-process, *anti*-periplanar conformation of the bonds $C_{(1)}$—H and $C_{(10)}$—OH, and $C_{(10)}$—OH and $C_{(9)}$—H. As another factor the optimum positions of the endocyclic double bonds must be considered from the point of view of optimum conformations of $\Delta^{1(10)}$- and $\Delta^{9(10)}$-guaienolides (Fig. 2 and Table I) because it must be admitted that in view of the possibility of a H-shift the final double bond position need not, in principle, always correspond to optimum conditions of *anti*-elimination on the appropriate fragment. On the other hand even without regard to the *syn*- or *anti*-elimination mechanism an optimum course may be expected according to the Franck–Condon principle at smallest conformational differences of the starting and the final products. In the case of (6*R*, 7*S*)--10-hydroxyguaian-6,12-olides the conformational disposition for optimum sterical condition of *anti*-elimination may be expected a *priori* on the $C_{(1)}$—$C_{(10)}$ bond in the case of the diastereoisomers 1αH, 10βOH and 1βH, 10αOH, as it is also shown in Newman projections in Fig. 1*A* – *D*. The above mentioned results of the eliminations of 5αH-isomers (Scheme 2) also confirm in principle the dominant role of the

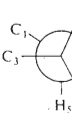
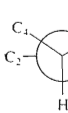
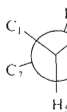
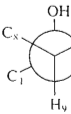
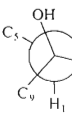
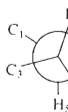
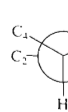
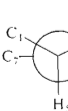
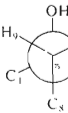
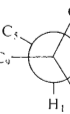
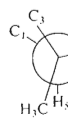
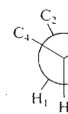
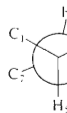
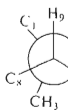
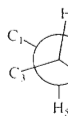
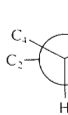
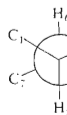
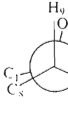
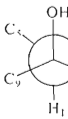
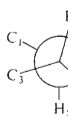
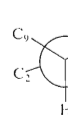
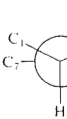
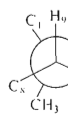
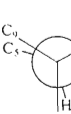
C_4-C_5	C_5-C_1	C_5-C_6	C_9-C_{10}	$C_{10}-C_1$
				
C_8-chair-like		$H_6 \ldots O-H$ 2,5 Å		
				
C_1-boat-like		$H_6 \ldots O-H$ 3,8 Å		
				
C_5-chair-like (C_1-chair)		$H_6 \ldots O-H \sim 5$ Å		
				
C_6-boat-like		$H_6 \ldots O-H$ 2,6 Å		
				
C_9-boat-like		$H_6 \ldots O-H$ 4,6 Å		

FIG. 1A

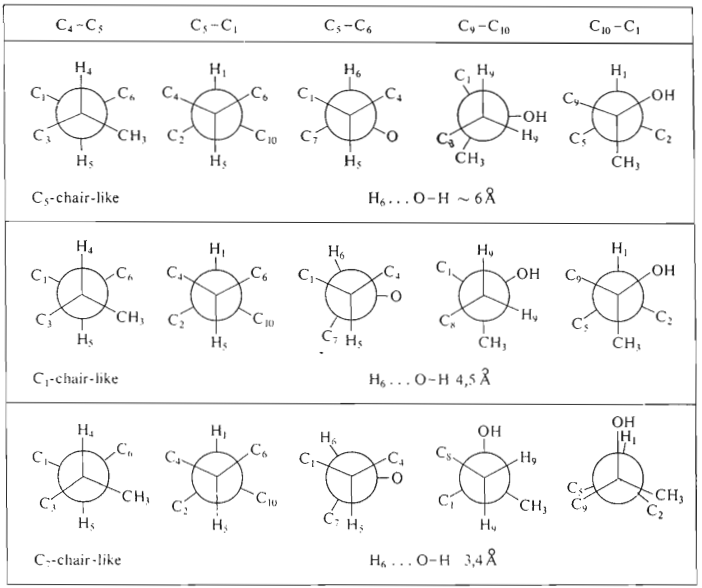


FIG. 1*B*

anti-process. In the case of 1αH, 5αH-isomers (Fig. 1*A*) none of the possible conformations of *endo*-cycloalkenes (Table I) is directly contained in the conformation set of hydroxy derivatives and hence a pseudorotation between the two extremes must be considered, *i.e.* the C_8-chair-like and C_5-chair-like conformations of the seven-

FIG. 1

Schematic Prepresentation of Conformational Possibilities of 6β-H,7α-H,-10-Hydroxyguaian--6,12-olides by Means of Newman Projections, of Some Fragments Derived from Dreiding Models.

Configuration of the methyl at $C_{(4)}$ and hydroxyl at $C_{(10)}$ is chosen as 4α and 10β. For the definition of regular conformations of the seven-membered ring see Fig. 2. *A:* cases with 1α-H and 5α-H; *B:* cases with 1β-H and 5α-H; *C:* cases with 1β-H amd 5β-H; *D:* cases with 1α-H and 5β-H.

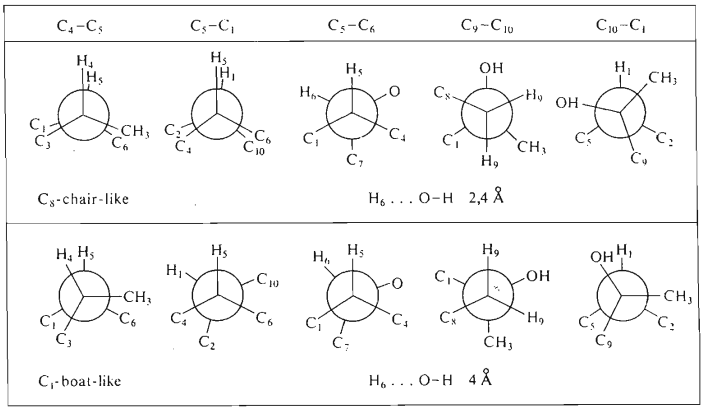

C4–C5
C5–C1
C5–C6
C9–C10
C10–C1
C8-chair-like
H6 . . . O–H 2,4 Å
C1-boat-like
H6 . . . O–H 4 Å

FIG. 1C

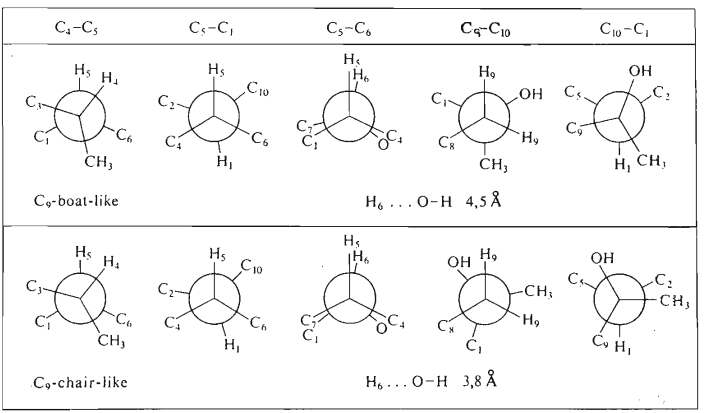
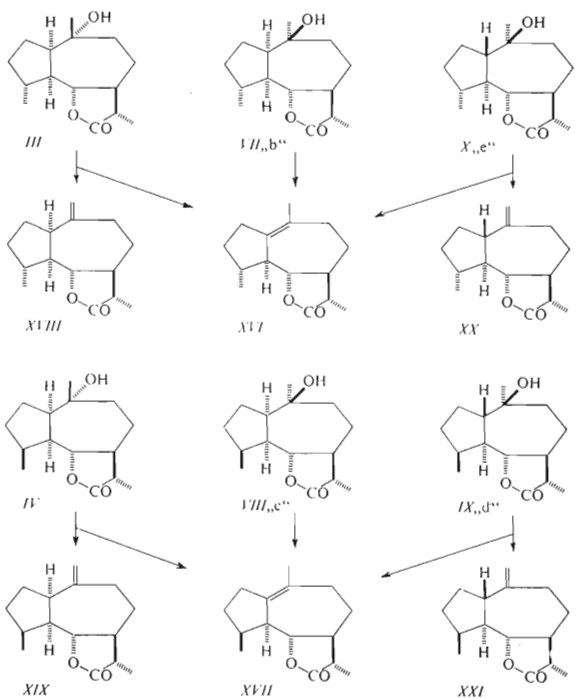

C4–C5
C5–C1
C5–C6
C9–C10
C10–C1
C9-boat-like
H6 . . . O–H 4,5 Å
C9-chair-like
H6 . . . O–H 3,8 Å

FIG. 1D

membered ring. This pseudorotation takes place *via* C_1-boat-like and C_6-boat-like conformations which are optimum for the formation of $\Delta^{1(10)}$- and $\Delta^{9(10)}$-double bonds (Fig. 2). In the case of 10βOH (*VII* and *VIII*) conditions of *anti*-elimination at $C_{(1)}$—$C_{(10)}$ are achieved practically within the whole conformational range, while the conditions of *anti*-elimination at $C_{(10)}$—$C_{(9)}$ deteriorate (they are optimum only in the C_8-chair-like conformation). The quantitative formation of $\Delta^{1(10)}$-cyckloalkenes is also in agreement with this. In the case of 10αOH (*III* and *IV*) optimum conditions of *anti*-elimination at the $C_{(1)}$—$C_{(10)}$ bond are never realised. On the other hand the



SCHEME 2

formation of $\Delta^{1(10)}$-cycloalkenes is not quantitative and is either a consequence of *syn*-elimination or of an H-shift. The same situation exists also in the case of 1βH, 5αH, 10βOH-isomers (*IX* and *X*) (Fig. 1*B*). Here too only the conditions for *syn*-elimination at $C_{(1)}$—$C_{(10)}$ can exist. Further in this case pseudorotation comprises also C_7-chair-like conformation which is simultaneously the optimum conformation of 5αH-guai-1(10)-en-6,12-olides. In spite of this a quantitative formation of $\Delta^{1(10)}$-cycloalkenes was not observed in this case either.

This consistency of the quantitative occurrence of $\Delta^{1(10)}$-cycloalkenes in the products of elimination of 5αH-derivatives and of the conditions of *anti*-elimination at the $C_{(1)}$—$C_{(10)}$ bond permits the supposition that tetrahydroartabsins ..a" (*VI*) and "f" (*XI*) in which the formation of $\Delta^{1(10)}$-olefins was in no case observed do not have an a priori disposition for *anti*-elimination at $C_{(1)}$—$C_{(10)}$ and hence a configurational sequence 1αH, 10βOH either. As shown in Fig. 1*D* in the case of 1αH, 5βH, 10βOH-isomers two conformations of the seven-membered ring are possible, *i.e.* C_9-boat-like and C_9-chair-like, in which in both cases conditions for *anti*-elimination at $C_{(1)}$—$C_{(10)}$ exist. In addition to this the C_9-boat-like conformation is simultaneously the optimum conformation for the formation of 5βH-guai-1(10)-en-6,12-olides (Table I). Tetrahydroartabsins "a" (*VI*) and "f" may therefore be assigned as probable only the configuration 1βH, 5βH, and these substances can also be considered as $C_{(4)}$-epimers.

A more detailed interpretation of the observed results of the elimination of the 10-hydroxy group cannot be given at the present stage. The question of the formation of the exomethylene double bond $\Delta^{10(14)}$ is of special interest, because it seems that a disposition to this formation exists in all instances; however, it was not always observed. It is probable that the bimolecular elimination process will take place more easily *via* the sequence of rigid or pseudorigid transition states than *via* the sequence of dynamical states with a short medium time of existence, as for example in the case of the methyl group CH_3—C—OH.

TABLE I

Conformational Possibilities of $\Delta^{1(10)}$- and $\Delta^{9(10)}$-Guaien-6,12-olides According to Dreiding Models

Olefin	Configuration		Conformation of 7-ring[a]
	H_1	H_5	
$\Delta^{1(10)}$	—	α	C_7-chair
	—	β	C_9-boat
$\Delta^{9(10)}$	α	α	C_6-boat
	α	β	C_1-boat
	β	α	C_6-chair
	β	β	C_6-boat

[a] For the definition of the seven-membered ring conformations see Fig. 2.

The conclusions drawn from chemical correlations could be further supported and completed by configurational analysis by means of the PMR spectra (characteristic parameters are summarised in Table II). From the present experimental material it follows that guaian-6,12-olides with the configurational sequence of 5αH, 6βH, 7αH in the PMR spectra usually display a characteristic signal of proton H_6 in the form of a first-order or second-order triplet or doublet of doublets in consequence of quasiequivalence of $J_{5,6} \approx J_{6.7} \approx 9-11$ Hz. This empirical fact also corresponds in principle to the theoretical views because the sterical conditions of the quasi-*anti*--periplanar interaction are approximately equal on fragments $C_{(5)}$—$C_{(6)}$ and $C_{(6)}$—$C_{(7)}$ even in the case of the above mentioned configurational guaianolidic sequence, without regard to the conformation of the molecule (Fig. 1*A*, 1*B*). Only the cases of pseudoguaianolidic sequence 5βH, 6βH, 7αH (Fig. 1*C*, 1*D*) are problematic when in the case of 1αH-isomers the occurrence of *syn*-periplanar $J_{5,6}$ is possible, the magnitude of which may be in principle comparable with the magnitude of the *anti*-periplanar interaction (C_9-chair-like conformation, Fig. 1*D*). In the case of 1βH (Fig. 1*C*), however, the selection is already possible a *priori* in view of the fundamental differences in dihedral angles $\Phi_{5,6}$ and $\Phi_{6,7}$, and hence also in the magnitude of $J_{5,6}$ and $J_{6,7}$ ($J_{5,6} < J_{6,7}$, $J_{5,6} < 8$ Hz). As follows from Table II a quasi--equivalence of $J_{5,6} \approx J_{6,7} \approx 9-11$ Hz was found for all 5αH-isomers in agreement with the preceding conclusions. Only in the case of tetrahydroartabsins ..a'' (*VI*) and ..f'' (*XI*) differing interactions were observed, *i.e.* $J_{5,6} \cong 5$ to 6 Hz and $J_{6,7} \cong 9-11$ Hz. These differences are in complete agreement with the sterical disposition of the *syn*--clinal coupling $J_{5,6}$ and quasi-*anti*-periplanar coupling $J_{6,7}$, which is possible, according to Dreiding models (Fig. 1*C*), only in the case of configuration 1βH, 5βH, in agreement with the preceding conclusions. The coupling constants $J_{5,6}$ found are listed in Table II in dependence on the configuration of $C_{(5)}$ and $C_{(6)}$.

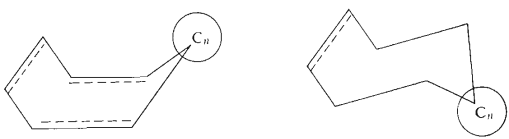


FIG. 2

Definition of Regular Conformations of the Seven-membered Ring

$C_{(n)}$ indicates the atom lying in the symmetry plane of the regular conformation. The possible position of the double bonds are indicated by dotted lines.

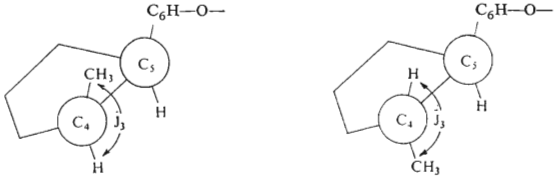
TABLE II

Characteristic Parameters of the PMR Spectra

Compound	Configuration			Chemical shifts[a]				Splittings[a]				Other data[a,b]			
	$H_{(1)}$	$H_{(4)}$	$H_{(5)}$	$H_{(6)}$	$H_{(13)}$	$H_{(14)}$	$H_{(15)}$	$J_{5,6}$	$J_{6,7}$	$J_{11,13}$[c]	$J_{4,15}$[c]	$H_{(4)}$	$H_{(5)}$	$H_{(7)}$	$H_{(11)}$
6βH, 7αH, 11βH-10-hydroxyguaian-6,12-olides															
III[d]	α	β	α	4·04	1·19	1·19	1.07	10·0	10·0	6·5	6·1	2·0	—	—	2·18
IV[d]	α	α	α	4·11	1·20	1·22	0·92	10·0	10·0	6·7	7·0	2·35	2·35	1·75	2·29
VII	α	β	α	4·46	1·18	1·22	1·12	9	9	6·9	5·8	1·8	1·65	1·65	2·1
VIII	α	α	α	4·48	1·20	1·22	0·94	9	9	6·8	6·9	2·25	2·1	1·65	2·2
X	β	β	α	3·81	1·17	1·20	1·11	9·5	9·5	6·6	6·3	2·0	1·65	1·65	2·0
IX	β	α	α	4·00	1·19	1·20	0·95	10·0	10·0	6·7	7·0	2·4	1·85	1·65	2·1
VI	β	β	β	4·91	1·21	1·29	1·05	6·0	10·5	6·5	7·35	2·3	2·94[e]	2·05	2·15
XI	β	α	β	4·91	1·21	1·26	1·09	5·0	9·0	6·55	5·9	1·75	2·2	1·65	2·15
6βH, 7αH, 11βH-guaien-6,12-olides															
XVI	—	β	α	3·59	1·21	1·71	1·17	9·4	9·4	6·7	5·8	—	—	—	—
XVII	—	α	α	3·71	1·21	1·71	0·91	10·0	10·0	6·7	6·7	2·55	—	—	2·2
XVIII	α	β	α	3·83	1·19	4·86[f]	1·13	9·5	9·5	6·9	6·4	1·95	—	—	2·1
XIX	α	α	α	4·02	1·22	4·98 4·93[g]	0·94	11	9	6·8	7·1	2·35	—	—	2·2
XX	β	β	α	3·73	1·19	4·96 4·85[g]	1·14	9	9	6·9	6·0	—	—	—	—
XXI	β	α	α	3·92	1·19	4·95 4·85[g]	0·97	10·5	9	6·9	7·0	2·4	—	—	2·2
XXII	β	β	β	4·22	1·21	4·80[h] 4·75	1·09	4·9	9·5	6·4	7·3	2·2	2·91[i]	2·2	2·2
XXIII	β	α	β	4·45	1·25	1·77[j]	1·11	5	9	6·7	6·1	2·0	2·5	2·5	2·2
XXIV[k]	—	β	—	5·20	1·21	1·36	1·04	—	9·5	6·85	6·8	3·02[e]	—	1·85	2·25

Another characteristic parameter is the magnitude of the average vicinal coupling of methyl group protons on $C_{(4)}$, $J_{4,15} = \bar{J}_3(CH_3—CH)$. As was shown recently[7] for the secondary methyl groups bound to the sp_3 carbon atom in the fragment $CH_3—CH—C—R$ the relation $\bar{J}_3(R,CH_3\text{-}syn\text{-periplanal}, syn\text{-clinal}) > \bar{J}_3(R,CH_3\text{-}anti\text{-periplanal}, anti\text{-clinal})$ applies under the supposition that their staggered conformation is more stable in relation to CH than the eclipsed conformation and that C—R is the dominant group perturbing the internal movement of the methyl group around the $CH_3—CH$ bond. This rule may be applied with advantage to the case of the $C_{(4)}$-methyl group in guaianolides for the $CH_3—C_{(4)}H/—C_{(3)}H_2—/——C_{(5)}H—C_{(6)}H—/C_{(7)}H/—O$ fragment, where the conformational analysis of the fragment $CH_3—C_{(4)}H$ may be carried out relatively to $C_{(5)}H—C_{(6)}H—O$. The corresponding rules in dependence on the absolute configuration of $C_{(5)}$ are represented schematically in Fig. 3.

This rule was already used in the preceding communication[11] for the determination of the configuration of the $C_{(4)}$-methyl group of the isomer *IV* and its validity may now be demonstrated on all 5αH-isomers in which the configuration of the $C_{(4)}$-methyl group has been determined for the couples of $C_{(4)}$-epimeric 10-hydroxy-



5α-H-guaian-6,12-olides: $J_3(\alpha\text{-}CH_3) < J_3(\beta\text{-}CH_3)$
5β-H-guaian-6,12-olides: $J_3(\alpha\text{-}CH_3) < J_3(\beta\text{-}CH_3)$

FIG. 3

Rule for the Determination of Absolute Configuration of the Methyl Group at $C_{(4)}$ in Guaien-6,12-olides from the Magnitude of the Average Vicinal Interaction $J_3 = {}^3J(CH_3—C—H) = J_{4,15}$

[a] Measured on a Varian HA-100 instrument, solvent deuteriochloroform, internal standard tetramethylsilane (TMS), chemical shifts in δ(TMS)-scale, splittings in Hz; [b] approximate values of chemical shifts from decoupling experiments (if not otherwise stated); [c] counter measurements on 50 Hz sweep-width-chart; [d] data given for comparison (ref.[11]); [e] multiplet, $J_{5,4} = 8{\cdot}0$, $J_{5,1} = 11{\cdot}2$, $J_{5,6} = 6{\cdot}0$ (tentative assignment of $J_{5,4}$ and $J_{5,1}$); [f] relative intensity 2H; [g] broadened singlets; [h] doublets, ${}^2J = 2{\cdot}4$, ${}^4J_{14'1} \neq 0$ ($H_{14'}$ (upfield proton signal), H_1 : 3·15; [i] multiplet, $J_{5,6} = 4{\cdot}9$, $J_{4,5} = 8{\cdot}5$, $J_{5,1} = 11{\cdot}5$ (tentative assignment of $J_{5,1}$ and $J_{5,4}$); [j] H_9 : 5·23; [k] 10β-OH-$\Delta^{1(5)}$-guaien-6,12-olide, other data : H_2,$H_{2'}$: 2·65—2·3, $J_{6,2}$ and $J_{6,2'} \neq 0$; [l] multiplet, $J_{4,6} \neq 0$.

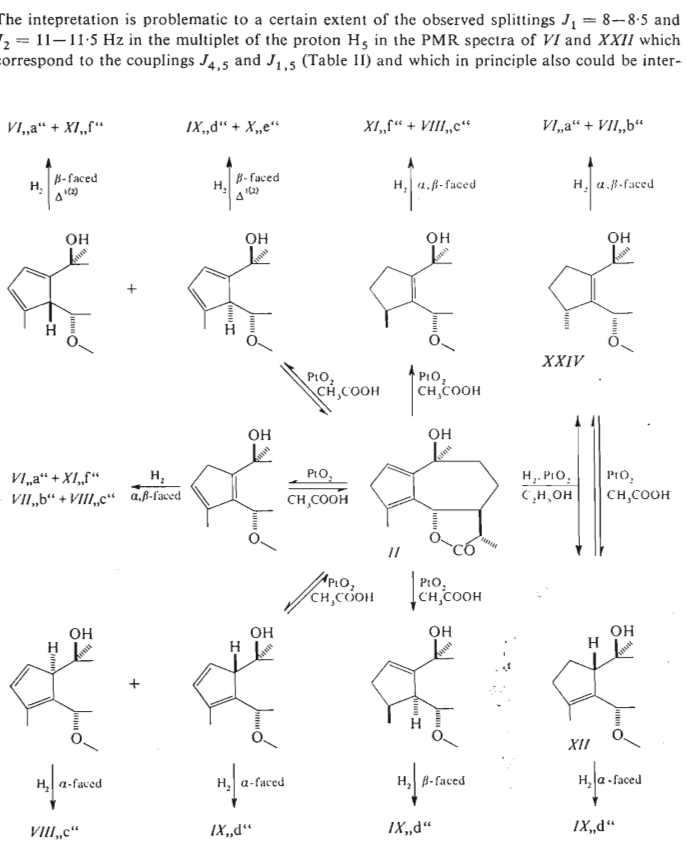
guaianolides in Table II. The validity of this rule is also demonstrated by PMR spectra of $C_{(4)}$-epimeric 5αH-$\Delta^{1(10)}$- and 5αH-$\Delta^{10(14)}$-olefins in Table II. On application of this rule to 5βH-guaianolides *VI* and *XI* absolute configuration of the C_4-methyl (Fig. 3) may be deduced, *i.e.* 4α-methyl for tetrahydroartabsin ..a" (*VI*) and 4β-methyl for tetrahydroartabsin "f" (*XI*). Therefore tetrahydroartabsin "a" (*VI*) may be considered as a $C_{(5)}$-epimer of tetrahydroartabsin "e" (*X*), *i.e.* (1*S*, 4*R*, 5*R*, 6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguaian-6,12-olide, and tetrahydroartabsin "f" (*XI*) as a $C_{(5)}$-epimer of tetrahydroartabsin "d", *i.e.* (1*S*, 4*S*, 5*R*, 6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguaian-6,12-olide.

As is further evident from Table II the systematic relation for the vicinal couplings of the $C_{(4)}$-methyl group protons is simultaneously accompanied by a systematic relation of the chemical shifts δH_{15} while it applies that $C_{(4)}$-epimer with a large coupling constant J_3 (CH_3—CH) = $= J_{4,15}$ has the H_{15} signal at a higher field, *i.e.* $\delta H_{15}(\alpha\text{-}CH_3, \alpha\text{-}H_5) > \delta H_{15}(\beta\text{-}CH_3, \alpha\text{-}H_5)$ and *vice versa* for 5β H-guaianolides. This relation of the chemical shifts is especially well fulfilled in 5β H-derivatives where the difference $\Delta_{\alpha,\beta} = \delta_\alpha - \delta_\beta$ is of the order of 0·15—0·20 p.p.m.. In the case of 5β H-derivatives *VI* and *XI* this relation is also fulfilled, but nonetheless the difference of chemical shifts between the αCH_3 and βCH_3 is small in this case. The stereochemical reason for this relation is not quite evident so far. A similar variation of the chemical shifts was also observed in the case of CH_3—C_{11}—H ref.[8]).

The stereochemical assignment of tetrahydroartabsins "a" (*VI*) and "f" (*XI*) may be further supported by the interpretation of the chemical shifts of protons H_6. The signal of this proton usually lies in the region about 4 p.p.m. (in $CDCl_3$) and one of the significant effects which may in the case of 10-hydroxyguaian-6,12-olides condition the variation of its chemical shift is the transannular Van der Waals effect of the 10-hydroxy group. This effect conditions the paramagnitic contribution to the chemical shift, and as follows from Table II the chemical shifts H_6 might reflect it in the cases of tetrahydroartabsins "b" (*VII*) and "c" (*VIII*) and δH_6 = 4·46—4·48 p.p.m., and especially in the cases of tetrahydroartabsins "a" (*VI*) and "f" (*XI*) with δH_6 = 4·91 p.p.m. Significant Van der Waals contributions larger than 0·1 p.p.m. may be expected[9] at O...H distances smaller than 3 Å. As follows from the measurement of the distance $C_{(10)}$—O...H_6 on Dreiding models for single conformations (in Fig. 1*A*—1*D*) a sterical disposition to such an effect on proton H_6 exists exactly in the cases of 1αH, 5αH, 10βOH-guaian-6,12-olides *VII* and *VIII* only. In the cases of 1βH, 5βH, 10βOH-guaian-6,12-olides it exists in such configurational arrangement as was assigned earlier independently from other points of view to tetrahydroartabsins "a" (*VI*) and "f" (*XI*). The presence of the Van der Waals effect was also demonstrated by measuring the acylation effects on the H_6 protons signal in the cases of tetrahydroartabsin "b" (*VII*) and "a" (*VI*) with the utilisation of the *in situ* acylation of the 10-OH group with trichloroacetyl isocyanate (TAI-method[14–16], for the use of the TAI-method for the study of the Van der Waals effect see ref.[2]). The diamagnetic shifts obtained $\Delta\delta H_6(TAC) = \delta H_6(C_{(10)}\text{—OH}) - \delta H_6(C_{(10)}\text{—OTAC}) = + 0{\cdot}18$

p.p.m. for *VII* and +0·32 p.p.m. for *VI* (in $CDCl_3$, TAC = $CCl_3CONHCO$—) correspond to the Van der Waals effect on 2·0–2·5 Å distances (ref.[9]), and these distances are consistent with the C_8-chair-like conformation of the seven-membered ring for the case of 1αH, 5αH, 10βOH ($C_{(10)}$—O...H_6 = 2·5 Å, Fig. 1*A*) and C_8-chair-like conformation in the case of 1βH, 5βH, 10βOH ($C_{(10)}$—O...H_6 = 2·5 Å, Fig. 1*C*).

The intepretation is problematic to a certain extent of the observed splittings J_1 = 8—8·5 and J_2 = 11—11·5 Hz in the multiplet of the proton H_5 in the PMR spectra of *VI* and *XXII* which correspond to the couplings $J_{4,5}$ and $J_{1,5}$ (Table II) and which in principle also could be inter-



SCHEME 3

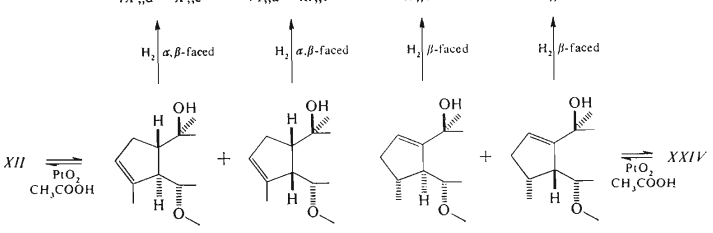
preted in the sense of 1α H, 5βH configuration. However, in principle the large splitting constant 11—11·5 Hz may correspond to a *syn*-periplanar interaction which when in C_8-chair-like conformation *VI* and *XXII* (Fig. 1*C*) may occur — according to Dreiding models — both on the $C_{(4)}$—$C_{(5)}$ and the $C_{(1)}$—$C_{(5)}$ fragment. Present theoretical and experimental material[16] indicates that for the values of *syn*-periplanar interaction in sp^3-sp^3-fragments the values ranging from 10—13 Hz may be expected. In the Table II the splitting of 11—11·5 Hz was assigned tentatively to the $J_{1,5}$ interaction which would correspond to the $C_{(3)}$-envelope-like conformation of the five-membered ring with $\phi_{4,5} \neq 0$.

From the complete number of (6*R*, 7*S*, 10*S*, 11*S*)-10-hydroxyguaian-6,12-olides which may form totally 8 stereoisomers we succeeded in preparing and defining 6 isomers only. The remaining two $C_{(4)}$-epimers with the 1αH, 5βH-configuration could not be prepared by hydrogenation. Up to now we have described the hydrogenation[11] of artabsin (*II*) and dihydroartabsin (*XII*). In the first case we were able to identify the six described tetrahydroartabsins *VI*—*XI* in the reaction mixture. In the second case we identified only four tetrahydroartabsins, *i.e.* "a" (*VI*), "b" (*VII*), "d" (*IX*) and "f" (*XI*).

In the preceding communication [11] the absolute configuration of dihydroartabsin *XII* was not determined. Under the supposition that the main products of hydrogenation of *XII* — tetrahydroartabsins "a" (*VI*) and "d" (*IX*) — may be considered as the products of *cis*-addition of hydrogen, dihydroartabsin *XII* may now be defined as (1*S*, 6*S*, 7*S*, 10*S*, 11*S*)-10-hydroxyguai-4-en-6,12-olide. We now repeated again the partial hydrogenation of artabsin (*II*) but we obtained as a new 10-hydroxy-6,12--olide only dihydroartabsin *XXIV* with a tetrasubstituted double bond $\Delta^{1(5)}$ as a product of 1,4-addition. In an orienting experiment we hydrogenated a small amount of *XXIV*; again we obtained the already known tetrahydroartabsins, *i.e.* as the main products tetrahydroartabsin "a" (*VI*) and "b" (*VII*), and as the minor product tetrahydroartabsin "e" (*X*). Under the supposition that *VI* and *VII* may be considered as products of *cis*-addition of hydrogen, the absolute configuration of *XXIV* may then be defined as (4*R*, 6*S*, 7*S*, 10*S*, 11*S*)-10-hydroxy-1(5)-en-6,12-olide. The supposition of the relationship of the main product *vs* 1,2-*cis*-addition during the hydrogenation of the double bonds in mono-olefins *XII* and *XXIV* may be considered as rational although the number of products as well as their stereochemistry indicates a simultaneous participation of the H-shift. This is also confirmed by the formerly described[11] case of hydrogenation of substance *V* where hydroxyguaianolide *IV* is formed as the main product, which is also deducible as the product of *cis*-addition of hydrogen, and the product of the H-shift *III* is a minor product. In this connection the question arises why druring the hydrogenation of artabsin (*II*) (and in view of the existence of the H-shift) two of the possible steroisomers are not formed (or are formed only in untraceable amount) as is also the case in hydrogenation of *XII* and *XXIV*, *i.e.* those $C_{(4)}$-epimers which have the configuration 1αH and 5βH.

Present results of hydrogenations clearly indicate the stereoselectivity of the hydro-

genation process, which in the case of artabsin (*II*) means that the 1,2-*cis*-addition of hydrogen to the double bonds could not have taken place from both sides, because only in this manner the *trans*-annelated derivatives with the configuration 1αH, 5βH could have arisen. This means that the *cis*-addition on the double bond $\Delta^{4(5)}$ could not have taken place from the β-side (β-faced) and the *cis*-addition on the $\Delta^{1(2)}$ bond from the α-side (α-faced). For a rational explanation of this phenomenon a formal agreement of the observed directions of the addition of hydrogen and the absolute configuration of the allylic oxygen functions on $C_{(6)}$ and $C_{(10)}$ is suitable, which, from the point of view of hydrogenation as a heterogeneous catalysis, assumes a realistic aspect. Earlier views on the course of this process originated from the supposition of the formation of an adsorbed molecular layer of the H-acceptor on the catalyst surface on which atomisation of the molecular hydrogen takes place simultaneously. Further it should be assumed that the addition of the atomic hydrogen also takes place from that side of the H-acceptor by which it was oriented to the catalyst at the moment of hydrogen atomisation. Finally, it must be admitted that in the case of a selective orientation of the H-acceptor to the catalyst a selective addition must also take place. Hence, the crucial question is on which side the H-acceptor will be adsorbed onto the catalyst surface. The orientation of the H-acceptor can be determined either by sterical requirements or by the affinity of the surrounding atoms of groups to the catalyst. In our case C–O bonds are in the direct vicinity of the double bonds, and that in cyclic molecules with a planar distribution of atoms in which the formation of selectively oriented molecular layers may be assumed. The stereoselective course of hydrogenation, in the case of a dominat role of the allylic grouping, is represented schematically in Fig. 4. Using these directive effects all earlier hydrogenation experiments with artabsin (*II*) (Scheme 3), dihydroartabsin *XII* and dihydroartabsin *XXIV* (Scheme 4)) may be interpreted rationally. Admitting an optional cyclic shift of the double bonds in a five-membered ring, the directive effect of the $\alpha C_{(6)}$–O-bond is



SCHEME 4

the condition for the α-faced addition in the case of the double bonds $\Delta^{4(5)}$ and $\Delta^{1(5)}$, and the directive effect of the $\beta C_{(10)}$—O-bond is the condition for the β-faced addition in the case of the $\Delta^{1(2)}$ and $\Delta^{1(5)}$ double bonds. Bifacial addition is only possible in the case of the $\Delta^{1(5)}$ double bond.

From this point of view all stereoisomers may be formed exept those with 1αH, 5βH configuration. From Scheme 4 it also clearly follows why in no case tetrahydroartabsin "c" (*VIII*) should be formed on hydrogenation of dihydroartabsins *XII* and *XXIV*, which was also observed to be so. This isomer can be formed only on hydrogenation of artabsin (*II*), and that either *via* an α-faced 1,4-addition or on hydrogenation of some of "isoartabsins" formed by a cyclic shift of the double bonds (Scheme 3). In this connection the fact is interesting that on partial hydrogenation of artabsin (*II*) on Adams catalyst in ethanol only dihydroartabsins *XII* and *XXIV* were obtained, *i.e.* both of them the products of a β-faced 1,2- and 1,4-addition. This phenomenon may be explained by the fact that a directive effect of the 10β-group

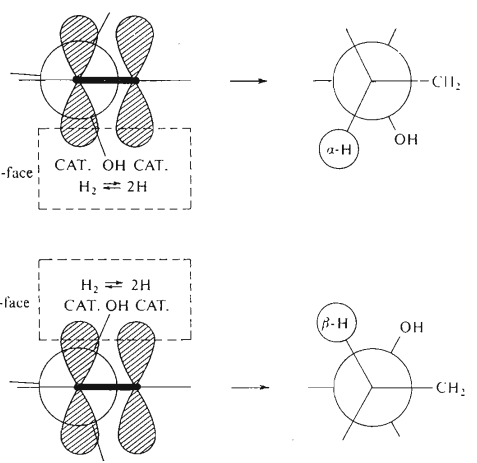


FIG. 4

Schematic Representation of the Directive Effect of Electron Donors in Allylic Position on the Stereoselective Course of the Heterogeneous Catalytic Hydrogenation of Double Bonds

Dotted lines show the area of a simultaneous co-ordination of π-electrons of the double bond and of free electron pairs of the allylic donor on the catalyst (cat.).

as the centre of maximum activity dominates in ethanol, while during hydrogenation of artabsin on PtO_2 in acetic acid the affinity of the hydroxy group is paralysed by intermolecular interactions with the carboxyl group, in consequence of which the directive effect of the $\alpha C_{(6)}$—O-bond increases in importance. Under these conditions a bifacial 1,4-addition also may take place under formation of tetrahydroartabsin "c" (*VIII*). An especially suggestive example of directive effects is the hydrogenation[11] of isophoto-α-santonin lactone (*I*) and deoxoisophoto-α-santonin lactone *V* where in agreement with the postulated rules only C_4-epimeric stereoisomers with the 1αH, 5αH configuration are formed under all conditions, because in this case both allylic directive effects are coincident with α-faced addition.

The preparation of the two remaining stereoisomers, as well as the confirmation of the postulated hypotheses, are still the subject of experimental work. None the less, the set of data on six stereoisomers may be already considered as utilisable, because the remaining two $C_{(4)}$-epimers with 1αH, 5βH configuration may be easily eliminated and defined individually by PMR-spectroscopy.

EXPERIMENTAL

The melting points were measured on a Kofler block and they were not corrected. The PMR spectra were recorded on a Varian HA-100 machine. The ORD curves were measured on a ORD/UV-5 Japan Spectroscopic Co. apparatus in methanol at 25°C, concentration 0·06—0·09 g/100 ml.

Hydroxyguaianolides *III* and *IV* from Dihydroisophoto-α-santonin lactones *XIII* and *XIV*

The products of hydrogenation[11] of isophoto-α-santonin lactone (2 g), containing according to PMR spectrum a mixture of both $C_{(4)}$-epimers of dihydroisophoto-α-santonin lactone *XIII* and *XIV*, were converted in view of the instability of the 4β-methyl isomer directly in crude state and in the conventional manner[11] to ethylene thioketals. The reaction mixture was then chromatographed on 140 g of silica gel containing 13% of water. Using a benzene–ethyl acetate mixture (1 : 1) both thioketals (2 g) were eluted. Their mixture was desulfurated with Raney nickel (10 g) in boiling dioxan for 4 hours. The products were chromatographed on 350 g of silica gel containing 13% of water. Fractions 330—390 (10 ml each), eluted with light petroleum–ether (1 : 1) gave on evaporation substance *III* (0·6 g), m.p. 86°C (ethyl acetate–hexane), identical according to its R_F value, IR spectrum, and mixture melting point with authentic 4α-methylhydroxyguaianolide[11]. Fractions 431—465, eluted with light petroleum–ether (4 : 6) afforded on evaporation a substance (0·3 g) of m.p. 115—117°C (ethyl acetate–hexane) of the composition $C_{15}H_{22}O_3$ (according to high-resolution mass spectrum). Its IR spectrum contained an absorption band typical of a γ-lactone (at 1760 cm^{-1}) and a band of a hydroxyl group at 3590 cm^{-1}. Fractions 481—510, eluted with the same mixture, afforded substance *IV* (0·15 g), m.p. 125—127°C (ethyl acetate–hexane), identical according to its R_F value, IR spectrum, and mixture melting point with authentic 4β-methylhydroxyguaianolide[11].

Hydroxyguaianolide (*III*). ORD: $[\Phi]_{300}$ −249°, $[\Phi]_{250}$ −62°, $[\Phi]_{249}$ 0, $[\Phi]_{233}$ 684°, $[\Phi]_{235}$ 0, $[\Phi]_{220}$ −1027°.

Tetrahydroartabsin "a" (VI) (ref.[11]). ORD: $[\Phi]_{300}$ −1117°, $[\Phi]_{249}$ −1755°, $[\Phi]_{235-242}$ −1627°, $[\Phi]_{225}$ −3150°.

Tetrahydroartabsin "b" (VII) (ref.[11]). ORD: $[\Phi]_{300}$ −190°, $[\Phi]_{250}$ −54°, $[\Phi]_{249}$ 0, $[\Phi]_{232}$ 598°, $[\Phi]_{224}$ 0, $[\Phi]_{220}$ −789°.

Tetrahydroartabsin "c" (VIII) (ref.[11]). ORD: $[\Phi]_{350}$ 196°, $[\Phi]_{300}$ 274°, $[\Phi]_{250}$ 862°, $[\Phi]_{233}$ 1960°, $[\Phi]_{219}$ 0.

Tetrahydroartabsin "e" (X) (ref.[11]). ORD: $[\Phi]_{350}$ −213°, $[\Phi]_{300}$ −248°, $[\Phi]_{253}$ 0, $[\Phi]_{250}$ 71°, $[\Phi]_{233}$ 852°, $[\Phi]_{225}$ 0, $[\Phi]_{220}$ −1136°.

Guaienolides *XVI* and *XX* from Tetrahydroartabsin "e" (*X*)

Tetrahydroartabsin "e" (*X*; 0·2 g) was dehydrated with thionyl chloride (0·3 g) in pyridine (3·5 ml) at 0°C for 24 hours. The reaction mixture was worked up in the conventional manner and the neutral fraction was chromatographed on 35 g of silica gel containing 13% of water. Fractions 33—45 (7 ml each) were eluted with a mixture of light petroleum and ether (95 : 5) and they afforded after evaporation guaienolide *XVI* (70 mg), m.p. 71—74°C (hexane), identical according to its mixture melting point, IR and PMR spectra with $\Delta^{1(10)}$-guaienolide obtained on dehydration of hydroxyguaienolides *III* and *VII* (ref.[11]). Fractions 108—126 gave an oily guaienolide *XX* (60 mg) of molecular weight 234 (from mass spectrum), corresponding to the composition $C_{15}H_{22}O_2$. Its IR spectrum displayed a band of a γ-lactone at 1762 cm^{-1} and bands at 898 and 1640 cm^{-1} characteristic of exomethylene group.

Guaienolides *XVII* and *XIX* from Hydroxyguaianolide *IV*

Hydroxyguaianolide *IV* (0·2 b) was dehydrated with thionyl chloride (0·4 g) in pyridine (4 ml). The neutral fraction of the mixture was chromatographed on 22 g of silica gel containing 13% of water. Fractions 59—70 (4 ml each), eluted with a mixture of light petroleum and ether (92 : 8), afforded guaienolide *XVII* (40 mg), m.p. 135—136°C (hexane). Molecular weight 234 (from mass spectrum) corresponds to the composition $C_{15}H_{22}O_2$. Its IR spectrum displays a band characteristic of a γ-lactone at 1780 cm^{-1}. Fractions 77—110 obtained on elution with a light petroleum–ether mixture (9 : 1) gave a non-crystalline guaienolide *XIX* (90 mg) of mol. weight 234 (from mass spectrum, also corresponding to the composition $C_{15}H_{22}O_2$. Its IR spectrum also contained bands for γ-lactone at 998, 1179 and 1781 cm^{-1}, further bands at 899, 1639 and 3080 cm^{-1}, characteristic of an exomethylene double bond.

Guaienolide *XVII* from Tetrahydroartabsin "c" (*VIII*)

Tetrahydroartabsin "c" (*VIII*; 0·3 g) was dehydrated with thionyl chloride (0·6 g) in pyridine. The neutral fraction was individual (190 mg), m.p. 135—136°C (hexane), identical according to its R_F value and IR and PMR spectra and mixture melting point with guaienolide *XVII*.

Guaienolide *XVII* and *XXI* from Tetrahydroartabsin "d" (*IX*)

Tetrahydroartabsin "d" (*IX*; 140 mg) was dehydrated with thionyl chloride (200 mg) in pyridine. The neufral fraction of the mixture was chromatographed on 34 g of silica gel (13% water). Fractions 50—77 (4 ml each), eluted with a mixture of light petroleum and ether (93 : 7), gave a product (40 mg) of m.p. 134—136°C (hexane), identical according to IR and PMR spectra and mixture melting point with guaienolide *XVII*. Fraction 76—90 afforded on rechromatography amorphous guaienolide *XXI* (30 mg), mol. weight 234 (from mass spectrum), corresponding to the composition $C_{15}H_{22}O_2$. Its IR spectrum displayed an absorption band of γ-lactone at 1760 cm^{-1} and bands typical of exomethylene group (at 898 and 1640 cm^{-1}).

Guaienolide *XXII* from Tetrahydroartabsin "a" (*VI*)

Tetrahydroartabsin "a" (*VI*; 0·5 g) was dehydrated with thionyl chloride (0·5 g) in pyridine. The neutral fraction of the reaction mixture was chromatographed on 35 g of silver nitrate impregnated with silica gel. Fractions 120—140 (10 ml each) which were eluted with a mixture of light petroleum and ether (92 : 8) afforded guaienolide *XXII* (0·2 g) of m.p. 52—54°C (hexane). Its molecular weight was 234 (from mass spectrum) and it corresponds to the composition $C_{15}H_{22}O_2$. Its IR spectrum contained absorption bands at 1755 cm^{-1} (γ-lactone) and 900 and 1635 cm^{-1} (exomethylene group).

Guaienolide *XXIII* from Tetrahydroartabsin "f" (*XI*)

Tetrahydroartabsin "f" (*XI*; 70 mg) was dehydrated with thionyl choride (0·1 g) in pyridine. The neutral fraction of the mixture was chromatographed on 10 g of silica gel impregnated with silver nitrate. Fractions 75—116 (4 ml each) were eluted with light petroleum–ether mixture (9 : 1), affording after evaporation of the solvent guaienolide *XXIII* (30 mg), m.p. 76—78°C (hexane), composition $C_{15}H_{22}O_2$ (molecular weight 234 from mass spectrum). The IR spectrum displayed absorption bands for γ-lactone at 1183 and 1760 cm^{-1}, and bands at 1632 and 3070 cm^{-1} characteristic of a trisubstituted double bond.

Dihydroartabsin *XXIV*

Artabsin (*II*; 0·75 g) was hydrogenated on platinum oxide (0·2 g) in ethanol (10 ml). The products were chromatographed on 140 g of silica gel with 13% of water. Fractions 69—78 (10 ml each) were eluted with benzene–ether (9 : 1) affording a substance (150 mg) of m.p. 133°C (benzene–hexane), identical according to R_F and IR spectrum with dihydroartabsin *XII* (ref.[12]). Fractions 79—105 (10 ml each), eluted with a mixture of benzene and ether (85 : 15), afforded on repeated chromatography amorphous dihydroartabsin *XXIV*. Its molecular mass was 250 (from mass spectrum), corresponding to the composition $C_{15}H_{22}O_3$. The IR spectrum displayed absorption bands for γ-lactone at 1168 and 1765 cm^{-1} and bands for the hydroxyl group at 3480 and 3590 cm^{-1}. ORD: $[\Phi]_{375}$ −468°, $[\Phi]_{350}$ −909°, $[\Phi]_{338}$ −1175°, $[\Phi]_{325}$ −798°, $[\Phi]_{313}$ 0, $[\Phi]_{300}$ 881°, $[\Phi]_{275}$ 1460°.

Hydrogenation: Dihydroartabsin *XXIV* (50 mg) was hydrogenated on platinum oxide (20 mg) in acetic acid (5 ml). The neutral products were chromatographed on 15 g of silica gel containing 13% of water. Fractions 33—48 (5 ml each), eluted with light petroleum–ether mixture (6 : 4) gave a substance (6 mg) of m.p. 159—161°C (ethyl acetate–hexane), identical according to R_F value and IR spectrum with tetrahydroartabsin "b" (*VII*) (ref.[11]). Fractions 74—91 were eluted with light petroleum–ether (1 : 1) affording after evaporation a substance (7 mg) of m.p. 103—106°C (ethyl acetate–hexane), identical according to its R_F value and the mass spectrum with tetrahydroartabsin "a" (*VI*). Fractions 106—127, eluted with light petroleum–ether (4 : 6), afforded a substance (3 mg), m.p. 87—91°C, identical according to its R_F value and IR spectrum with tetrahydroartabsin "e" (*X*).

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REFERENCES

1. Perold G. W., Muller J. C., Ourisson G.: Tetrahedron *28*, 5747 (1972).
2. Samek Z., Holub M., Vokáč K., Drożdż B., Jommi G., Gariboldi P., Corbella A.: This Journal *37*, 2611 (1972).
3. Stöcklin W., Waddell T. G., Geissman T. A.: Tetrahedron *26*, 2397 (1970).
4. Pinhey J. T., Sternhell S.: Australian J. Chem. *18*, 543 (1965).
5. Narayanan C. R., Venkatasubramanian N. K.: J. Org. Chem. *33*, 3156 (1968).
6. Samek Z.: Tetrahedron Letters *1970*, 671.
7. Samek Z.: Tetrahedron Letters *1971*, 1709.
8. Herz W., Aota K., Holub M., Samek Z.: J. Org. Chem. *35*, 2611 (1970).
9. Yoshioka H., Mabry T. J., Irwin M. A., Geissman T. A., Samek Z.: Tetrahedron *27*, 3317 (1971).
10. Barton D. H. R., Levisalles J. E. D., Pinhey J. T.: J. Chem. Soc. *1962*, 3472.
11. Vokáč K., Samek Z., Herout V., Šorm F.: This Journal *37*, 1186 (1972).
12. Asher J. D. M., Sim G. A.: J. Chem. Soc. *1965*, 1584.
13. Sicher J.: Angew. Chem. *84*, 177 (1972).
14. Goodlett V. W.: Anal. Chem. *37*, 431 (1965).
15. Trehan I. R., Monder C.: Tetrahedron Letters *1968*, 67.
16. Bystrov V. F.: Uspechi Chim. *41*, 512 (1972).

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