Constituents of *Solidago* Species. Part V.[1] Non-acidic Diterpenoids from *Solidago gigantea* var. *serotina*

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Eight new furan-containing diterpenoids from *Solidago gigantea* Ait. var. *serotina* (Kuntze) Cronqu., are formulated as **1***c*–*g*, **2**, **3***a*, and **4***a* on the basis of chemical and spectroscopic evidence and by correlation with solidagoic acid A of previously defined constitution and stereochemistry. The structure (**5***a*) of a ninth related compound is tentatively assigned. The allylic oxidation of some of these new diterpenoids and related compounds with the chromium trioxide – pyridine complex is reported. In the course of this investigation of formal total synthesis of compound Y from *Leonotis leonurus* was achieved.

On propose les formules **1***c*–**1***g*, **2**, **3***a* et **4***a* pour huit nouveaux diterpénoïdes contenant du furanne qui ont été isolés de *Soligado gigantea* Ait. var. *serotina* (Kuntze) Cronqu.; ces conclusions sont basées sur des preuves chimiques et spectroscopiques et aussi par corrélation avec l'acid solidagoïque A dont la constitution et la stéréochimie ont été définies précédemment. La structure **5***a* est proposée pour un neuvième composé relié aux précédents. On rapporte aussi les résultats obtenus lors de l'oxydation allylique de quelques-uns de ces diterpénoïdes et composés apparentés par le complexe CrO_3 : pyridine. Au cours de cette étude une synthèse totale formelle du composé Y isolé de Leonotis leonurus a été réussie.
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In the preceding paper (1) we have summarized the evidence which allows the assignment of constitution and relative stereochemistry[3] to solidagoic acids A (**1***a*) and B (**1***b*), constituents of the ethyl acetate soluble extractive of the roots of *Solidago gigantea* Ait. var. *serotina* (Kuntze) Cronqu. The present paper is devoted to nine furan-containing diterpenoids which have been isolated from neutral fractions of the same extract. The complex mixture containing these compounds was separated initially by chromatography over silica gel, final purification of each being achieved by preparative t.l.c. The presence of a β-substituted furan ring in all nine diterpenoids was indicated by their reaction with Ehrlich's reagent and the presence of signals arising from this moiety in their i.r. (ν_{max} near 1500 and 870 cm^{-1}), n.m.r. (near τ 2.65, 2.75, and 3.65; 1H each), and mass (*m/e* 81 and 95) spectra. It thus appeared probable that these compounds and the solidagoic acids have an identical carbon skeleton and indeed it has been possible to interrelate eight of the neutral constituents with the two acids. On this and additional chemical and spectroscopic evidence, firm assignments of constitution and relative stereochemistry can be made for the eight (**1***c*–*g*, **2**, **3***a*, and **4***a*). A structure (**5***a*) is advanced for the ninth primarily on spectroscopic grounds. The absolute configuration assigned to these compounds rests on their correlation with acid A and is therefore only tentative. The compounds will be discussed in the following order of increasing chromatographic polarity on silica gel (ethyl acetate – light petroleum mixtures as eluant).

Compound I

The least polar constituent was the oily aldehyde **1***c*, $[\alpha]_D$ −164°. Peaks at 2690 and 1722 cm^{-1}, typical of an aldehyde function, are clearly visible in its i.r. spectrum while the —C*H*O proton resonates at τ 0.54 (s). Other resonances which may be readily assigned are those of an olefinic proton (τ 4.28, m) and three methyl groups, one tertiary (τ 9.22, 3H, s), one secondary (τ 9.22, 3H, d, J = 6 Hz), and the

[1]For Part IV see ref. 1 and for the preliminary account of this work ref. 2.

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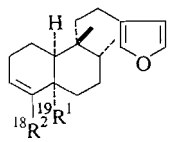
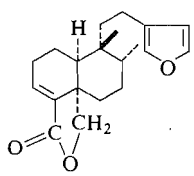
[3]The absolute configuration advanced must be viewed as only tentative.



1

a $R^1 = CO_2H$; $R^2 = CH_3$
b $R^1 = CO_2H$; $R^2 = CH_2OAng$
c $R^1 = CHO$; $R^2 = CH_3$
d $R^1 = R^2 = CHO$
e $R^1 = CH_2OH$; $R^2 = CH_3$
f $R^1 = CH_3$; $R^2 = CH_2OH$
g $R^1 = R^2 = CH_2OH$
h $R^1 = R^2 = CH_2OAc$
i $R^1 = CHO$; $R^2 = CH_2OAc$
j $R^1 = CH_3$; $R^2 = CH_2OAc$
k $R^1 = R^2 = CH_3$
l $R^1 = CHDOAc$; $R^2 = CH_2OAc$
m $R^1 = CH_2OH$; $R^2 = CH_2OAc$
n $R^1 = CH_2OAc$; $R^2 = CH_2OH$
o $R^1 = CO_2Me$; $R^2 = CH_3$
p $R^1 = CH_2OAc$; $R^2 = CH_3$
q $R^1 = CH_2OAc$; $R^2 = CHO$
r $R^1 = CHO$; $R^2 = CH_2OAc$



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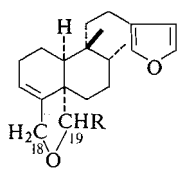
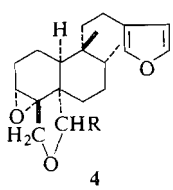


3

a R = OH
b R = OAc
c R = H



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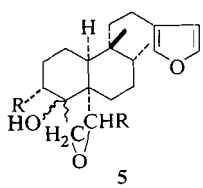
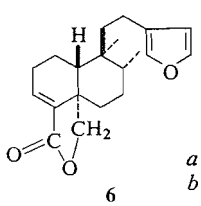
b R = OAc



5

a R = OH
b R = OAc



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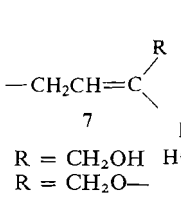

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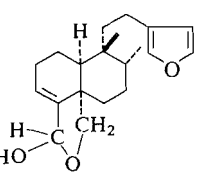
a R = CH_2OH
b R = CH_2O—



8

other on an olefinic bond (τ 8.58, 3H, d, J = 2 Hz). These data suggested that this compound is identical with the aldehyde prepared (1) from solidagoic acid A (**1***a*) via the alcohol (**1***e*) and this was verified by direct comparison of the two samples.

Compound II

The next constituent (**2**), m.p. 92–95°, $[\alpha]_D$ +12°, could be readily formulated as a γ-lactone because of the strong carbonyl absorption at 1772 cm^{-1} in the i.r. The presence of a double bond in conjugation with the carbonyl group was deduced from the intensity (ε 18 000) of a u.v. maximum at 210 nm and from the chemical shift value and multiplicity of a resonance attributable to an olefinic proton. This proton resonates as a triplet at τ 3.35, showing only vicinal coupling to the C-2 methylene group and significantly no allylic coupling. This was confirmed by a nuclear double resonance experiment in which irradiation of a broad triplet at τ 7.77 (2 H-2) caused that of the olefinic proton to collapse to a sharp singlet. Double irradiation also located H-8, since with H_2 at τ 8.37 the doublet at τ 9.10 (secondary methyl) collapsed to a singlet. Also assignable in the n.m.r. spectrum are resonances arising from a tertiary methyl group (τ 8.97, 3H, s) and the methylene group in the lactone ring (τ 5.56 and 6.20, both 1H, both d, J = 9 Hz), an *isolated* AB system. Assuming this lactone to have the same skeleton as the aldehyde discussed above, these spectroscopic data indicate the formulation **2**. Confirmation of this conclusion was obtained by its reduction with lithium aluminum hydride to the diol **1***g*. This compound and the derived diacetate (**1***h*) were identical with the corresponding samples prepared (1) from solidagoic acid B (**1***b*). It should be noted that although the lactone described here has the same gross structure as that (**6**) isolated (3) from *Dodonaea* species, they differ in stereochemistry at C-9 and -10.

Compound III

The third component, m.p. 103–105°, $[\alpha]_D$ −49°, was readily assigned the structure **1***d*, the presence of two aldehyde groups being immediately recognized from the n.m.r. singlets at τ −0.17 and 0.89. The chemical shift of the former reflects the allylic nature of the proton involved. Support for our conclusions concerning the structure of this compound came from its i.r. absorption at 1720 (isolated aldehyde) and 1690

cm^{-1} ($\alpha\beta$-unsaturated aldehyde). Reduction of this dialdehyde with lithium aluminum hydride and then acetylation of the resulting diol added final confirmation of the constitution and stereochemistry (as **1***d*), the products again being identical with those prepared from solidagoic acid B.

Compound IV

The next component, an oil, $[\alpha]_D$ −38°, shows hydroxyl absorption in the i.r. at 3630 cm^{-1}, while in its n.m.r. spectrum two carbinyl protons form an AB quartet at τ 6.37 and 6.51 (J = 11 Hz). In addition, a proton and methyl group attached to an olefinic bond give rise to signals at τ 4.29 and 8.33 respectively. These data suggested formulation of the compound as **1***e* and direct comparison with a sample of the primary alcohol derived from solidagoic acid A confirmed this.

Compound V

Compound V, $[\alpha]_D$ −45°, also failed to crystallize. Its spectral properties appeared to indicate that it is an isomer of compound IV. In the i.r. it lacks carbonyl absorption but a peak at 3620 cm^{-1} reveals the presence of a hydroxyl group. Resonances in its n.m.r. spectrum at τ 9.15 (d, J = 6 Hz), 8.82 (s) and 8.97 (s) can be assigned to a secondary and two tertiary methyl groups, while a multiplet at τ 4.26 (1H) and broad singlet at τ 5.84 (2H) arise from one olefinic and two carbinyl protons respectively. The chemical shift of this last resonance is indicative of the allylic nature of the primary alcohol group. A tentative assignment of structure, **1***f*, can be made on the basis of the above evidence and it gains support from a series of spin–decoupling experiments. Irradiation at τ 7.95 (2 H-2) caused collapse of the multiplet at τ 4.26 (H-3) to a broad singlet and significant sharpening of the singlet at τ 5.84 (2 H-18). In addition, this last signal appeared as a doublet (J = 1.5 Hz) upon irradiation at the olefinic proton (τ 4.26) and conversely with H_2 at τ 5.84 the multiplet at τ 4.26 simplified to a triplet (J_{obs} = 4 Hz). These results suggest the part structure **7***a* which is accommodated in the postulated structure, **1***f*. Our initial attempts to confirm this structural assignment involved preparation of **1***f* from solidagoic acid B (**1***b*) via the diol (**1***g*) and the derived aldehydo-acetate (**1***i*), but conversion of the aldehyde group into a methyl group could not be effected (see below). Correlation of **1***f* with a compound of known constitution was achieved as follows. The derived acetate (**1***j*) when hydrogenated in ethanol–triethylamine over palladized charcoal (1) afforded the furanoolefin (**1***k*) and its tetrahydro- and hexahydroderivatives. The first of these (**1***k*) was identical with the compound prepared previously (1) from solidagoic acid A.

Compound VI

The n.m.r. spectrum of the next component, an oil, $[\alpha]_D$ −30° shows a marked similarity to those of the less polar compounds discussed above. The resonances at τ 4.52 (1 H, m), 9.03 (3H, s), and 9.15 (3H, d, J = 6 Hz) are assignable to an olefinic proton and two methyl groups, the former tertiary, the latter secondary. The n.m.r. spectrum also reveals the presence of a hemiacetal ring. This gives rise to a multiplet at τ 6.65 (—O*H*) which is lost upon exchange with D_2O and two broad singlets, one from —C*H*(OH)O— at τ 4.58, the other from —CH_2O— at τ 5.79. If one considers only structures related to those discussed above for this compound then two possibilities arise, **3***a* and **8**. Certain double resonance experiments demonstrated that the former formulation is preferable. Upon irradiation in turn at τ 4.52 (H-3) and 7.90 (2 H-2) the broad singlet at 5.79 (2 H-18) collapsed to an ill-resolved doublet ($w_{1/2}$ = 5 Hz) and a clean doublet (J = 3 Hz) respectively. These results lead to the part structure **7***b* and then to **3***a*. The coupling of the hydroxyl proton to H-19 was demonstrated by irradiating at τ 6.65 whereupon the resonance at τ 4.58 became a very sharp singlet.

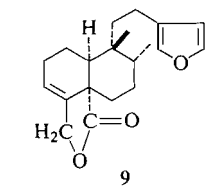
The presence of a cyclic hemiacetal moiety in compound VI was also indicated chemically. Acetylation of this compound furnished **3***b* from which the parent was readily regenerated by chromatography over neutral alumina. Although all attempts to oxidize **3***a* to the corresponding lactone (**9**) (1) failed, correlation with a known compound was achieved by treating it with sodium borohydride. The resulting diol (**1***g*) and the derived diacetate were identical with those prepared previously. Further confirmation of the orientation of the hemiacetal ring was obtained from an examination of the n.m.r. spectrum of the deuterated diacetate, **1***l*, prepared from **3***a* by reduction with lithium aluminum deuteride and acetylation of the product. This spectrum was nearly identical to that

of the simple diacetate except that the methylene resonance at *higher field* (τ 6.01) in the latter has been replaced by a signal that integrates for only one proton. An unexpected conversion of the diol (**1***g*) into **3***a* was achieved as follows. In the course of attempts to reduce the aldehyde group in **1***i* to a methyl group, it was treated with hydrazine hydrate in methanol at 20° but none of the desired hydrazone was obtained. However, the only isolable product was identical with the hemiacetal of natural provenance.

Compound VII

Compound VII (**4***a*), $[\alpha]_D$ −47° was isolated as an oil which slowly solidified at −5° but melted at *ca.* 18°. In keeping with its chromatographic polarity it shows evidence of hydroxylic absorption in the i.r. at 3600 and 3400 cm^{-1}. The deduction was made that this group forms part of a hemiacetal ring because of the presence in its n.m.r. spectrum of a singlet at τ 4.49 (H-19) and an AB quartet centered at τ 6.11 (J = 10 Hz, 2 H-18) and since the derived acetate (**4***b*) was readily transformed back to **4***a* by alumina. A structural difference between this compound and those discussed above was clearly evident in its n.m.r. spectrum. Thus, the multiplet at *ca.* τ 4.4 arising from the olefinic proton is absent and replaced by a singlet at τ 6.71, a chemical shift value indicative of a proton attached to an epoxide ring. Treatment of **4***a* with sodium borohydride furnished the diol (**10**) in which the epoxide ring remained intact. It appeared likely that compound VII is the epoxy analog of compound VI, but all attempts to convert the latter into the former with *m*-chloroperbenzoic acid, in various solvents, led either to the recovery of substrate or to non-furanoid products. However, the validity of our structural assignment was demonstrated as follows.

Reduction of **4***a* with lithium aluminum hydride gave the triol **11***a* which was then transformed into the hydroxy-diacetate **11***b*. This compound absorbs in the i.r. at 3590 (hydroxyl) and 1745 (acetate carbonyl) cm^{-1}, while in its n.m.r. spectrum resonances at τ 5.63 (q, J = 13 Hz) and 5.83 (broad s) can be assigned to two functional groups of the type $-CH_2OAc$. The failure of the third hydroxyl group to acetylate and the lack of a resonance attributable to a carbinyl proton in the n.m.r. spectrum of **11***b* was taken to indicate the tertiary nature of the hydroxyl group. Treatment of **11***b* with phosphoryl chloride in pyridine gave mainly one product, the known diacetate **1***h*. These reactions allowed compound VII to be formulated as either **4***a* or **12**. To solve this residual problem the above sequence of reactions (**4***a* → **1***h*) was repeated substituting lithium aluminum deuteride for the corresponding hydride. The mass



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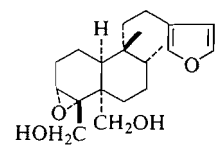

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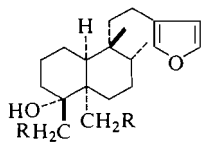
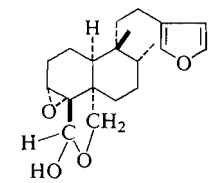


11

a R = OH
b R = OAc



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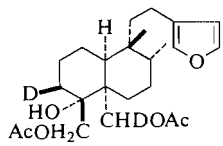

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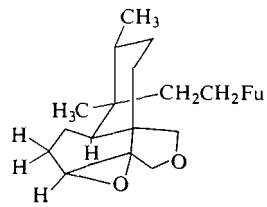

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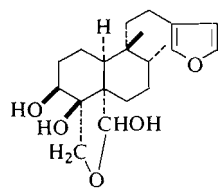

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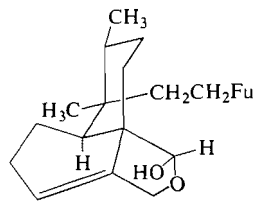

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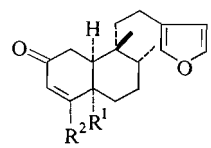


17

a $R^1 = R^2 = CH_3$
b $R^1 = CO_2Me$; $R^2 = CH_3$
c $R^1 = CH_2OAc$; $R^2 = CH_3$
d $R^1 = CHO$; $R^2 = CH_3$
e $R^1 = R^2 = CH_2OAC$

spectrum of the resulting hydroxy-diacetate (**13**) revealed the presence of two deuterium atoms as anticipated, while in its n.m.r. spectrum the two-proton singlet at τ 5.83 is still present but the quartet centered at τ 5.63 (in **11***b*) has been replaced by a one-proton singlet at τ 5.35. This reflects the stereospecificity of the reductive opening of the hemiacetal ring. Dehydration as described above yielded the monodeutero-diacetate (**1***l*) prepared previously from compound VI, confirming that both compounds have the hemiacetal ring attached in the same fashion. This second reaction sequence also enables assignments to be made for the resonances between τ 5 and 6 in the n.m.r. spectrum of the hydroxy-diacetate **11***b*. The singlet at τ 5.83 derives from the methylene group of the C-18 acetate function, shifting downfield to τ 5.43 on dehydration since it is now allylic, while the quartet at τ 5.63 from the C-19 methylene shifts upfield to 6.01 and becomes a singlet. The epoxide ring is assigned to α-orientation on the following grounds. First, the narrowness ($w_{1/2}$ = 3 Hz) of the signal arising from the proton attached to the epoxide ring in **4***a* suggests (4) the stereochemical situation **14**. Second, *trans*-diaxial opening (5) of the epoxide in **14** with lithium aluminum hydride would lead to a tertiary alcohol, as is observed. Third, **11***a* has been prepared from **1***g* by a route (see below) which would be expected to introduce the tertiary hydroxyl on the α-face of the molecule.

Compound VIII

The neutral compound penultimate in polarity was the diol (**1***g*), m.p. 60–63°, $[\alpha]_D$ −46°, into which several of the compounds discussed above have been converted. The functional groups in **1***g* were readily inferred from its i.r. and n.m.r. data and those of the derived monoacetates (**1***m* and *n*) and diacetate (**1***h*), while chemical transformations clearly defined the spatial relationship of the two primary hydroxyl groups. In the first of these reactions, the diol was converted into a cyclic ether by treatment with *p*-bromobenzenesulfonyl chloride in pyridine (6). Its formulation as **3***c* followed from its very low polarity on t.l.c. and from spectral evidence. In the i.r. it lacks both carbonyl and hydroxyl absorption while its mass spectrum has the molecular ion at *m/e* 300 ($C_{20}H_{28}O_2$). In its n.m.r. spectrum the ethereal methylene groups resonate as two AB quartets, one centered at τ 5.85 (2 H-18) the other at 6.28 (2 H-19). A second important transformation involved the oxidation of the diol with the Sarett reagent. Under mild conditions (see below) the major product was significantly a γ-lactone (ν_{max} 1772 cm^{-1}), thus providing additional confirmation of the disposition of the two hydroxylic groups. This lactone (**2**) m.p. 89–90°, was in fact shown by direct comparison to be identical to compound II. Unambiguous proof of the structure of the diol **1***g* was obtained by hydrogenation (1) of the derived diacetate in ethanol containing triethylamine over palladized charcoal. The resulting monoacetate (**1***p*) was identical with that prepared from solidagoic acid A (1) of well-defined structure.

Compound IX

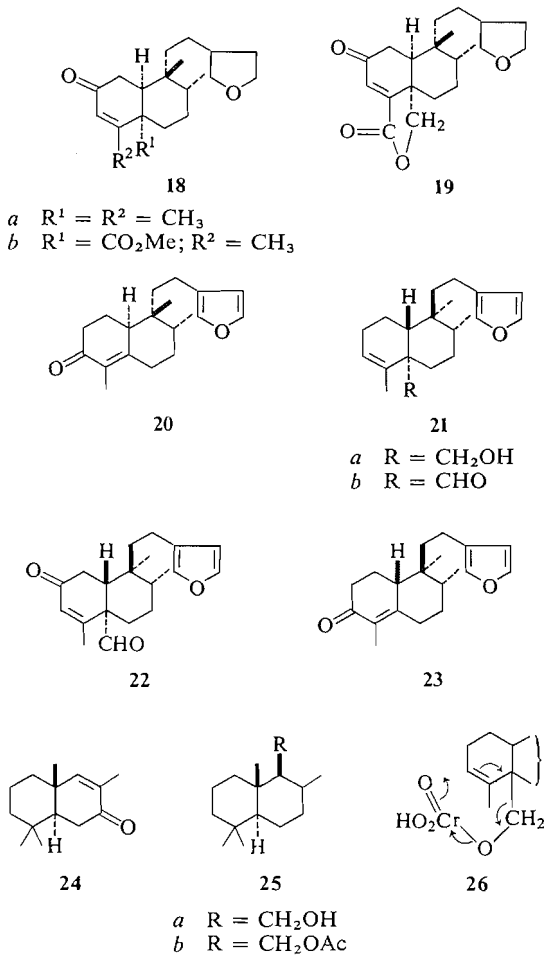
The most polar of these neutral furanoid compounds (**5***a*), m.p. 135–137°, $[\alpha]_D$ −18° has no resonances attributable to olefinic protons in its n.m.r. spectrum. However, it does have a multiplet at τ 4.50 which can be assigned to HO—C*H*—O— in a hemiacetal ring. Additional lines which form a complex pattern between τ 5.6 and 6.6 although presumably arising from protons of the type >C*H*—O— were of little diagnostic value. However, the n.m.r. spectrum of the derived hydroxy-diacetate (**5***b*) proved more informative. Thus the methine proton (H-19) of the hemiacetal acetate has shifted downfield and appears as a singlet at τ 3.28 while the ethereal methylene protons (2 H-18) are now clearly visible as an AB quartet centered at τ 5.88. A broadened triplet at τ 5.18 (J = 6 Hz) can be assigned to the methine of a secondary acetate group. The multiplicity and value of the observed coupling constant for this proton indicate that if it is attached to a cyclohexane ring, it is probably axial and vicinally related to two protons. Bearing in mind the above spectral evidence and the structures of the other diterpenoids in this plant the plausible structure (**5***a*) can be advanced for compound IX. In an attempt to relate this compound to one of known structure the hemiacetal **3***a* was treated with osmium tetroxide. However, the resulting triol was not identical with the natural product. The formulation of this new triol as **15** rests on the narrowness of the resonance from H-3 ($w_{1/2}$ = 6 Hz, τ 6.33). Presumably the presence of the hemiacetal ring has induced the decalin system

to adopt the conformation **16** in which, although both faces of the olefinic bond are open to attack, the β would probably be preferred if the C-19 hydroxyl group is α-orientated.

Oxidations with the Chromium Trioxide – Pyridine Complex

Of major importance in our arguments concerning the structure and stereochemistry of solidagoic acids A and B (1), and by extension the related neutral diterpenoids of natural provenance, have been n.m.r. and c.d. studies on the αβ-unsaturated ketones **17***a*, **18***a*, **18***b*, and **19**. A key step in the formation of **17***a* was the introduction of the C-2 ketone using the chromium trioxide – pyridine complex at 20°, conditions which minimize oxidative attack on the furan ring. In the course of our structural studies the reactions of other derivatives of solidagoic acid A and its congeners with this complex were examined and in addition the investigation was extended to related compounds for two reasons. First, compounds containing the enone substitution pattern in **17***a*, but with a *trans*-fused decalin system, were required as models for our n.m.r. work (1). Second, at the time the major portion of the work described in this section was completed[4] (7), only one report of an allylic oxidation with the Sarett reagent existed (9) and the reaction appeared to have enough intrinsic interest to warrant study. It should be noted, that in general, these reactions were carried out using concentrations of chromium trioxide in pyridine of the order of 100 mg/ml.

Oxidation of the methyl ester **1***o* and the acetate **1***p* for 18 days afforded the enones **17***b* and *c* (56 and 50% respectively, based on substrate consumed). The alcohol **1***e* in only 12 h gave (1) the aldehyde **1***c* (67%), the enone-aldehyde **17***d* (3%) and the nor-enone **20** (5%). Maingayol (**21***a*) (10) reacted (1) similarly and furnished **21***b*, **22**, and **23**. The formation of these nor-enones and of **24** from drimenol (**25***a*) (11) might involve a mechanism of the type **26** (arrows) or equivalent intermolecular process. The diacetate **1***h*, as anticipated, was converted into the enone **17***e* (*ca.* 50%) during 17 days. The parent diol (**1***g*) was subjected to oxidation for 14 h under two distinct sets of conditions, namely, with a chromium trioxide – pyridine concentration of first, 250 mg/ml, and second, 2.5 mg/ml. In the former case the major product was the enone-lactone **27** (60%), the minor being the lactone **2** (15%). In the latter oxidation the lactone **2** (74%) was the only isolable product. Our attention was next directed to the two monoacetates **1***m* and *n* (1). The latter with chromium trioxide in pyridine (25 mg/ml) during 14 h smoothly formed the aldehyde **1***q* (74%). The other monoacetate (**1***m*) during 12 h was converted with the complex at a concentration of 2.5 mg chromium trioxide per milliliter of pyridine into the aldehydo-acetate **1***r* (*ca.* 100%)

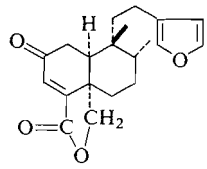


[4]However, soon thereafter a paper was published (8) concerning the oxidation of 17 olefins with the isolated chromium trioxide – pyridine complex in methylene chloride. In this medium similar results to those reported here were obtained, but the reaction times involved were significantly shorter. Probable mechanisms for the reaction are outlined in this paper (8) and no further discussion is required here.

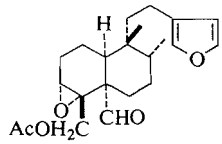
and unexpectedly at a concentration of 100 mg/ml into the corresponding epoxide **28** (68%). This epoxide on reduction with lithium aluminum hydride furnished the known triol **11***a*. Formation of an epoxide by chromium(VI) oxidation of an alkene, although a well-known (1, 12, 13) reaction under acidic conditions, is a novel reaction in pyridine solution. The orientation of the epoxide ring in **28** is assigned as α for two reasons. First, in the substrate the β-face of the A ring is probably (1) shielded by the C-9 methyl group. Second, it seems likely that even in pyridine solution, the initial step in the reaction would involve formation of the chromate ester of the primary alcohol at C-5 followed by transfer (13) of an oxygen atom from this ester to the double bond, *i.e.* from the α-side.

As models in our n.m.r. and c.d. studies on the stereochemistry of solidagoic acid A (1), we required compounds of the general type **29** or enantiomer. In view of the results reported above, the diacetate **30***a* from confertifolin (**31**) (14) was treated with chromium trioxide in pyridine (100 mg/ml) for 18 days and afforded, as anticipated, the enone **32***a* (81%). For this compound the relevant coupling constants, H-5/H-6 equatorial and H-5/H-6-axial, were calculated as $J = 3.5$ and 13.5 Hz respectively. When the diol **30***b* was oxidized under similar conditions but for a shorter time (14 h), three products were isolated, the β,β′-disubstituted furan (**33**) (40%), confertifolin (**31**, 22%), and isodrimenin (**34** (14), 25%). The reaction can be envisaged as proceeding through the two possible hydroxyaldehydes to the corresponding hemiacetals and thence by dehydration to the furan or oxidation to the lactones. The oxidation of drimenyl acetate (**25***b*) was examined next. In this case the only product isolated was the enone **32***b* (67%) in which the double bond had migrated into the $\Delta^{8,9}$ position. Earlier workers had reported (15) the isolation of the enone-acid **32***c*, albeit in very low yield, from the products of oxidation of drimenol (**25***a*) with the Sarett reagent. A mechanism which would explain the formation of these isomeric enones has been proposed recently (9). Oxidation of the furanoolefin (**35***a*) (16) gave the expected enone (**35***b*) which showed a negative Cotton effect for the $n \rightarrow \pi^*$ transition.

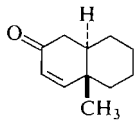
Oxidation of cholesteryl acetate (**36***a*) for 14 days afforded the 7-keto derivative (**36***b*, 33%). It is noteworthy that in this case the yield



27



28



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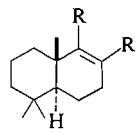
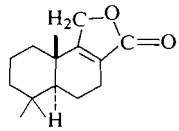
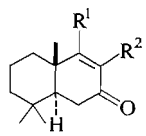


30

a R = CH_2OAc
b R = CH_2OH

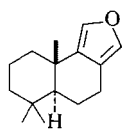


31

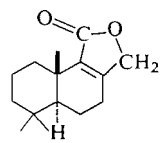


32

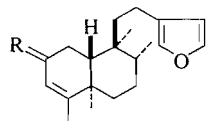
a $R^1 = R^2 = CH_2OAc$
b $R^1 = CH_2OAc$; $R^2 = CH_3$
c $R^1 = CO_2H$; $R^2 = CH_3$



33



34

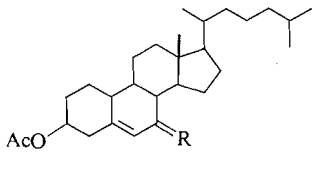


35

a R = H_2
b R = O

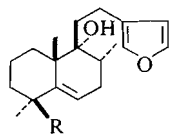
is inferior to that from oxidation by either the chromium trioxide – pyridine complex in methylene chloride (74%) (9) or *t*-butylchromate (60%) (17). Finally, the oxidation of two derivatives of marrubiin (18) was studied. The ester **37***a* during 10 days formed the enone **38***a* (81%) while **37***b* in just less than 1 week gave **38***b* (70%) and over 25 days the corresponding product **39** (12%) which has suffered cleavage of the furan ring. Direct comparison showed that the enone **38***b* is identical to compound Y[5] from *Leonotis*

[5]Dr. D. E. A. Rivett kindly supplied a sample of this compound.



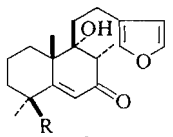
36

a R = H_2
b R = O



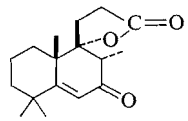
37

a R = CO_2Me
b R = CH_3
c R = CH_2OH
d R = CH_2OAc

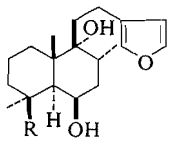


38

a R = CO_2Me
b R = CH_3
c R = CHO

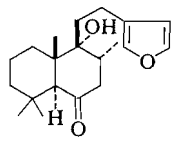


39



40

a R = CO_2Me
b R = CH_3



41

leonurus (19). Since marrubiin has been synthesized (20), this conversion of marrubiin into compound Y constitutes a formal total synthesis of the latter.

Experimental

Melting points are uncorrected and were determined on a Kofler hot-stage apparatus. Specific rotations refer to solutions in ethanol unless otherwise stated. Woelm Grade I alumina, deactivated to the appropriate grade according to Brockmann, was used for chromatography. For analytical and preparative t.l.c., chromatoplates were spread with Kieselgel G (Merck). Light petroleum was of b.p. 40–60°. Microanalyses were by Miss F. Cowan, Glasgow. High resolution mass spectra were run at the N.T.H, Trondheim, by Dr. T. Anthonsen. I.r. solution spectra were recorded in carbon tetrachloride on a Perkin–Elmer 225 or 257 or Beckmann I.R.12 spectrophotometer, u.v. spectra in ethanol on a Unicam S.P.800 spectrophotometer and the circular dichroism curve on a Cary 61 spectropolarimeter. P.m.r. spectra were run on a Perkin–Elmer R-10 or Varian Associates A-60A or HA 100 spectrometer in carbon tetrachloride, unless otherwise stated, using approximately 0.3 *M* solutions and tetramethylsilane as internal standard. Mass spectra were run on a Varian Associates CH 7 or A.E.I. MS9 or MS12 instrument.

Isolation Procedure

The chloroform soluble portion (24 g) of an extract (1) of *Solidago gigantea* var. *serotina* was chromatographed over alumina (Grade III; neutral; 2 kg) using as eluting solvent light petroleum – chloroform mixtures. Compounds were isolated from the various fractions by preparative t.l.c. and then either crystallization or distillation *in vacuo*.

Fraction A (4.3g), eluted with chloroform – light petroleum (1:19) was a complex mixture (t.l.c.) of non-polar compounds which was not investigated further. Fraction B (923 mg) was eluted with chloroform – light petroleum (1:9) and contained compound I, the oily aldehyde **1***c* (471 mg) as the major constituent. It had $[\alpha]_D$ −164° (*c*, 0.9) and was identical (i.r., n.m.r., and t.l.c.) to the aldehyde prepared (1) from solidagoic acid A. Fraction C (1.3 g), eluted with chloroform – light petroleum (1:4), furnished compounds II and III. The first of these, the lactone **2** (311 mg) formed needles from light petroleum and had m.p. 92–95°, $[\alpha]_D$ +12° (*c*, 0.65); ν_{max} 1772 and 874 cm^{-1}; λ_{max} 210 nm (ε 18 000); τ 3.35 (t, 1 H-3, J_{obs} = 3 Hz), 5.56 (d, 1 H-19, *J* = 9 Hz), 6.20 (d, 1 H-19, *J* = 9 Hz), 8.97 (s, 3 H-20) and 9.10 (d, 3 H-17, *J* = 6 Hz); *m/e* 314 (M).

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.44; H, 8.41.

Compound III, the dialdehyde **1***d* (472 mg), crystallized from ethyl acetate – light petroleum as needles, m.p. 103–105°, $[\alpha]_D$ −49° (*c*, 0.7); ν_{max} 1720, 1690 and 878 cm^{-1}; τ −0.17 (s, 1 H-18), 0.89 (s, 1 H-19), 3.16 (t, 1 H-3, J_{obs} = 4 Hz), 9.04 (s, 3 H-20) and 9.15 (d, 3 H-17, *J* = 6 Hz) *m/e* 314 (M).

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.52; H, 8.43.

Fractions D, E, and F were all eluted with chloroform – light petroleum (1:1). The first of these, fraction D (928 mg), contained two major components. Compound IV, the alcohol **1***e* (38 mg), had $[\alpha]_D$ −38° (*c*, 0.9) and was identical (n.m.r. and t.l.c.) to the alcohol prepared (1) from solidagoic acid A. Compound V, the alcohol **1***f* (671 mg), had $[\alpha]_D$ −45° (*c*, 0.6); ν_{max} 3620, 3400 and 875 cm^{-1}; τ 4.26 (m, 1 H-3; $w_{1/2}$ = 8 Hz), 5.84 (s, 2 H-18), 7.80 (s, —O*H*), 8.82, 8.97 (both s, 3 H-19 and 3 H-20), and 9.15 (d, 3 H-17, *J* = 6 Hz); *m/e* 302 (M).

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.30; H, 9.94.

Fraction E (4.3 g) contained compound VI, the hemiacetal **3***a* (1.7 g), and a sterol (220 mg) which crystallized from ethyl acetate – light petroleum as needles, m.p. 161–163°; ν_{max} 3600 cm^{-1}; *m/e* 412 ($C_{29}H_{48}O$). The hemiacetal had $[\alpha]_D$ −30° (*c*, 1.1; chloroform); ν_{max} 3600, 3390 and 872 cm^{-1}; τ 4.52 (m, 1 H-3, $w_{1/2}$ = 10 Hz), 4.58 (broad s, 1 H-19), 5.79 (broad s, 2 H-18, $w_{1/2}$ = 7 Hz), 6.65 (m, —O*H*), 9.03 (s, 3 H-20) and 9.15 (d, 3 H-17, *J* = 6 Hz); *m/e* = 316 (M).

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.91; H, 9.03.

The derived oily acetate (**3***b*), ν_{max} 1740 and 882 cm^{-1}, τ 3.68 (s, 1 H-19), 4.44 (m, 1 H-3) and 5.72 (m, 2 H-18, $w_{1/2}$ = 12 Hz), on chromatography over alumina (Grade III, neutral) was reconverted into the parent hemiacetal. Fraction F (3.2g) furnished compound VII, the epoxy-hemiacetal **4***a* (1.9g), which solidified on cooling and had m.p. *ca.* 18°; $[\alpha]_D$ −47° (*c*, 0.8); ν_{max} 3600, 3400, and 872 cm^{-1}; τ 4.49 (s, 1 H-19), 6.00 (d, 1 H-18, *J* = 10 Hz), 6.22 (d, 1 H-18, *J* = 10 Hz), 6.71 (s, 1 H-3, $w_{1/2}$ = 3 Hz), 7.03 (m, —O*H*), 9.12 (s, 3 H-20), and 9.19 (d, 3 H-17, *J* = 6 Hz); *m/e* 332 (M).

Anal. Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.33; H, 8.64.

Its acetate (**4***b*), τ 3.62 (s, 1 H-19), 6.10 (d, 1 H-18, J = 10 Hz), 6.18 (d, 1 H-18, J = 10 Hz), 6.71 (s, 1 H-3), 8.17 (s, 3H, —OCOCH_3), 9.13 (s, 3 H-20), and 9.20 (d, 3 H-17, J = 6 Hz), was transformed back to the parent hemiacetal on chromatography over alumina.

Fraction G (2.9 g), eluted with chloroform, afforded compound VIII the diol **1***g* (2.6 g), m.p. 60–63°, $[\alpha]_D$ −46° (*c*, 0.9), which was identical to the diol prepared (1) from solidagoic acid B. Fraction H (509 mg) was eluted with methanol–chloroform (1:19) and yielded compound IX, the dihydroxy-hemiacetal **5***a* (284 mg), which on crystallization from ether – light petroleum had m.p. 135–137°; $[\alpha]_D$ −18° (*c*, 0.95); ν_{max} 3425 and 875 cm^{-1}; τ 4.50 (m, 1 H-19, $w_{1/2}$ = 10 Hz), 9.03 (s, 3 H-20) and 9.15 (d, 3 H-17, J = 6 Hz); *m/e* 350 (M).

Anal. Calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.42; H, 8.89.

The derived diacetate **5***b* had n.m.r. signals at τ 3.28 (s, 1 H-19), 5.18 (t, 1 H-3, J_{obs} = 6 Hz), 5.74 (d, 1 H-18, J = 10 Hz), 6.03 (d, 1 H-18, J = 10 Hz), 7.89, 8.02 (both s, 2—OCOCH_3), 8.98 (s, 3 H-20) and 9.18 (d, 3 H-17, J = 6 Hz).

Reduction of the Lactone **2** *with Lithium Aluminum Hydride*

The lactone **2** (17 mg) was treated with a very large excess of lithium aluminum hydride in refluxing dry ether for 14 h. Work-up afforded an oil (16 mg) which was submitted to preparative t.l.c. (ethyl acetate – light petroleum, 2:3). The major component (11 mg) on crystallization from ethyl acetate – light petroleum had m.p. 57–61°, $[\alpha]_D$ −50° (*c*, 1.1) and was identical (t.l.c. and n.m.r.) to the diol (**1***g*) of natural provenance (see above).

Reduction of the Dialdehyde **1***d* *with Lithium Aluminum Hydride*

The dialdehyde (24 mg) when reduced for 2 h as above gave on work-up and purification the known diol **1***g* (13 mg), m.p. 58–61°, $[\alpha]_D$ −51° (*c*, 1.3).

Conversion of the Alcohol **1***f* *into the Furano-olefin* **1***k*

The alcohol **1***f* (100 mg) in dry pyridine (2 ml) was treated at 20° for 15 h with acetic anhydride (1 ml). The crude product, the acetate **1***j* (98 mg), was purified by preparative t.l.c. (chloroform) and distillation *in vacuo*. It was obtained as an oil $[\alpha]_D$ −34° (*c*, 1.4); ν_{max} 1740, 1230, and 878 cm^{-1}; τ 4.34 (m, 1 H-3), 5.55 (s, 2 H-18), 8.05 (s, 3H, —OCOCH_3), 8.82, 8.93 (both s, 3 H-19 and 3 H-20), and 9.10 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.95; H, 9.34.

Hydrogenation of this acetate (50 mg) in ethanol (25 ml) containing triethylamine (5 ml) over 10% palladized charcoal for 5 min afforded a mixture (t.l.c.) of two products. These were separated by preparative t.l.c. (light petroleum), the less polar being the major component. This compound was the furano-olefin **1***k* (31 mg) which after distillation *in vacuo* had $[\alpha]_D$ −21° (*c*, 1.1) and was identical (i.r., n.m.r., t.l.c.) to the furano-olefin prepared (1) from solidagoic acid A. The minor component was the tetrahydrofuran-olefin on mass spectrometric evidence, *m/e* 290 (M).

In a separate experiment the above acetate (**1***j*, 45 mg) was hydrogenated in ethanol containing triethylamine over palladized charcoal for 40 min. Work-up gave mainly one compound which was purified by preparative t.l.c. (ethyl acetate – light petroleum, 1:19) and distillation at 100°/0.05 mm. The resulting oil (28 mg) was the hexahydro derivative of **1***k* and had $[\alpha]_D$ −7° (*c*, 0.7, chloroform); *m/e* 292 (M).

Anal. Calcd. for $C_{20}H_{36}O$: C, 82.12; H, 12.40. Found: C, 81.95; H, 12.23.

Reduction of the Hemiacetal **3***a*

(*i*) The hemiacetal **3***a* (60 mg) in absolute ethanol (5 ml) was treated at 20° for 15 h with a large excess of sodium borohydride. The solution was diluted with water and extracted with ethyl acetate. The product was essentially pure (t.l.c.) diol **1***g* (54 mg) which on crystallization from ethyl acetate – light petroleum had m.p. 60–61°; $[\alpha]_D$ −52° (*c*, 1.2).

(*ii*) The hemiacetal **3***a* (50 mg) was heated with excess lithium aluminum deuteride in refluxing dry ether for 14 h. The deuterodiol (47 mg) obtained after work-up was acetylated with acetic anhydride – pyridine and afforded the corresponding deuterodiacetate (**1***l*, 39 mg). In its n.m.r. spectrum it exhibited resonances at τ 4.06 (m, 1 H-3), 5.43 (s, 2 H-18), 6.01 (s, 1 H-19), 7.98 (s, 6H, 2—OCOCH_3), 8.93 (s, 3 H-20), and 9.08 (d, 3 H-17, J = 6 Hz); *m/e* 403 (M).

Hydroxylation of the Hemiacetal **3***a*

The hemiacetal **3***a* (450 mg) was treated with osmium tetroxide (500 mg) in dry ether for 4 days. The reaction was worked-up with hydrogen sulfide gas, precipitated sulfides being filtered off. The crude product (430 mg) consisted (t.l.c.) of two components which were separated by preparative t.l.c. (chloroform–methanol, 19:1). The less polar (350 mg) was unreacted hemiacetal while the more polar, minor, product (40 mg) was the triol **15**, which could not be induced to crystallize. It had ν_{max} 3500 and 880 cm^{-1}; τ 4.51 (m, 1 H-19), 5.18 (m, 1H, —O*H*; lost on D_2O exchange), 5.56 (s, 1 *H*, —O*H*; lost on D_2O exchange), 6.14 (s, 2 H-18), 6.33 (s, 1 H-3, $w_{1/2}$ = 6 Hz after D_2O exchange), 6.82 (m, 1H, —O*H*; lost on D_2O exchange), 9.01 (s, 3 H-20) and 9.18 (d, 3 H-17, J = 6 Hz); *m/e* 350 (M).

Treatment of Acetoxy-aldehyde **1***i* *with Hydrazine Hydrate*

The acetoxy-aldehyde **1***i* (50 mg) in methanol (5 ml) was treated at 20° for 15 h with hydrazine hydrate (3 ml). Work-up afforded an oil (47 mg) from which the major product (32 mg) was recovered by preparative t.l.c. (chloroform). It had $[\alpha]_D$ −74° (*c*, 1.1) and was identical (n.m.r., i.r., and t.l.c.) with the hemiacetal (**3***a*) of natural provenance.

Attempted Epoxidation of the Hemiacetal **3***a*

Reaction of the hemiacetal **3***a* (15 mg) with *m*-chloroperbenzoic acid (20 mg) in chloroform (5 ml) at 20° for 90 min and work-up by filtration through a short column of neutral alumina afforded essentially pure (t.l.c.) starting material (13 mg). The reaction was repeated this time for 15 h. The products were a complex mixture (t.l.c., Ehrlich, and sulfuric acid staining) of non-furanoid compounds and starting material. Similar results were obtained when carbon tetrachloride or benzene was used as solvent.

Attempted Oxidation of the Hemiacetal 3a

(*i*) The hemiacetal **3***a* (10 mg) in ether was stirred at 20° for 16 h with activated manganese dioxide. Removal of the reagent and solvent afforded pure (t.l.c.) starting material (8 mg). This experiment was repeated using various grades of manganese dioxide but in all cases the result was similar.

(*ii*) Treatment of the hemiacetal (10 mg) at 20° with excess of the Sarett reagent for 6 h also yielded only starting material (10 mg).

Formation of the Epoxy-diol 10

A large excess of sodium borohydride was added to a solution of the epoxy-hemiacetal **4***a* (50 mg) in ethanol (10 ml) and the mixture allowed to remain at 20° for 15 h. Work-up afforded an oil (47 mg) which contained one major component. This compound, the epoxy-diol **10**, was purified by preparative t.l.c. (ethyl acetate – light petroleum, 1:1) and then distillation at 150°/0.04 mm. The resulting oil had $[\alpha]_D$ −6° (*c*, 1.5); ν_{max} 3630, 3380, and 875 cm^{-1}; τ 9.03 (s, 3 H-20) and 9.20 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.89; H, 9.12.

The corresponding acetate had $[\alpha]_D$ −11° (*c*, 0.6); ν_{max} 1745, 1235, and 875 cm^{-1}; τ 5.57 (d, 1 H-18, J = 12 Hz), 5.85 (d, 1 H-19, J = 7 Hz), 5.94 (d, 1 H-19, J = 7 Hz), 6.08 (d, 1 H-18, J = 12 Hz), 6.89 (d, 1 H-3, J = 3 Hz), 7.97, 7.99 (both s, 3H each, 2 —OCOCH_3), 8.97 (s, 3 H-20), and 9.14 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{24}H_{34}O_6$: C, 68.86; H, 8.19. Found: C, 69.04; H, 8.39.

Conversion of the Epoxy-hemiacetal 4a into the Diacetates 1h and l

(*i*) Treatment of the epoxy-hemiacetal **4***a* (50 mg) in refluxing dry tetrahydrofuran with excess lithium aluminum hydride for 15 h gave a product (43 mg) which consisted of two components of similar, high, polarity. These were separated by preparative t.l.c. (ethyl acetate – light petroleum, 3:1). The major, less polar component, the triol **11***a* (21 mg) was an oil which after distillation at 180°/0.1 mm had $[\alpha]_D$ −22° (*c*, 0.75); ν_{max} 3420 and 880 cm^{-1}.

Anal. Calcd. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59. Found: C, 71.33; H, 9.60.

This triol (50 mg) was acetylated and gave the hydroxy-diacetate **11***b* (46 mg), an oil which was distilled at 75°/0.01 mm and had $[\alpha]_D$ −13° (*c*, 1.0); ν_{max} 3590, 3480, 1745, 1240, and 875 cm^{-1}; τ 5.35 (d, 1 H-19, J = 13 Hz), 5.83 (s, 2 H-18), 5.91 (d, 1 H-19, J = 13 Hz), 8.00, 8.13 (both s 3 H each, 2 —OCOCH_3), 9.07 (s, 3 H-20) and 9.18 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{24}H_{36}O_6$: C, 68.54; H, 8.63. Found: C, 68.74; H, 8.86.

The hydroxy-diacetate **11***b* (15 mg) was heated at 80° with redistilled phosphoryl chloride (0.5 ml) in dry pyridine (3 ml) for 3 h. The reaction mixture was poured onto crushed ice and extracted with ethyl acetate to afford the crude product (17 mg). This consisted (t.l.c.) of two components which were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:4). The major, more polar, component (10 mg) was the oily diacetate which had $[\alpha]_D$ −58° (*c*, 1.0) and was identical (n.m.r., t.l.c.) to that obtained previously by acetylation of the diol **1***g*.

(*ii*) The above sequence of reactions was repeated starting with epoxy-hemiacetal (50 mg) but substituting lithium aluminum deuteride for the hydride. The hydroxy-diacetate **13** had n.m.r. resonances at τ 5.35 (s, 1 H-19) and 5.83 (s, 2 H-18); *m/e* 422 (M). The diacetate **1***l* (17 mg) obtained by dehydration was identical (n.m.r., mass spectroscopy) to that prepared from **3***a*.

Formation of the Ether 3c

The diol **1***g* (50 mg) was heated for 15 h with *p*-bromobenzenesulfonyl chloride (150 mg) in refluxing dry pyridine (5 ml). Work-up afforded an oil (46 mg) from which the major product (32 mg) was obtained by preparative t.l.c. (ethyl acetate – light petroleum, 3:17). This ether **3***c* was distilled at 150°/0.03 mm and had $[\alpha]_D$ −30° (*c*, 0.65), ν_{max} 872 cm^{-1}; τ 4.57 (m, 1 H-3), 5.73 (broad d, 1 H-18, J = 11 Hz), 5.84 (d, 1 H-19, J = 8 Hz), 5.98 (broad d, 1 H-18, J = 11 Hz), 6.73 (d, 1 H-19, J = 8 Hz), 9.01 (s, 3 H-20) and 9.16 (d, 3 H-17, J = 6 Hz); *m/e* 300 (M).

Anal. Calcd. for $C_{20}H_{28}O_2$: C, 79.95, H, 9.39. Found: C, 79.88; H, 9.52.

Oxidation of Methyl Ester 1o

Oxidation of the ester **1***o* (152 mg) in dry pyridine (2 ml) with chromium trioxide (500 mg) at 20° for 18 days and work-up afforded an oil (172 mg). The two major components of this oil were obtained by preparative t.l.c. (ethyl acetate – light petroleum, 3:7). The less polar component (48 mg) was unreacted ester while the other was the enone-ester **17***b* (63 mg). It was purified further by distillation *in vacuo* and had ν_{max} 1725, 1675, and 882 cm^{-1}; τ 4.23 (s, 1 H-3), 6.50 (s, 3H, —OCH_3), 8.29 (d, 3 H-18, J = 1 Hz), 9.07 (s, 3 H-20) and 9.07 (d, 3 H-17, J = 6 Hz); *m/e* 344 (M).

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.26; H, 8.35.

Oxidation of Acetate 1p

The acetate **1***p* (40 mg) in dry pyridine (2 ml) was treated at 20° for 17 days with chromium trioxide (100 mg). The oil (38 mg) obtained on work-up was separated by preparative t.l.c. (ethyl acetate – light petroleum, 2:3) to afford unreacted **1***p* (17 mg) as the less polar component. The other component, the enone-acetate **17***c* (12 mg) was obtained as an oil which distilled at 140°/0.04 mm; $[\alpha]_D$ −88° (*c*, 0.08); ν_{max} 1740, 1670, and 872 cm^{-1}; τ 4.07 (s, 1 H-3), 5.84 (d, 1 H-19, J = 12 Hz), 6.18 (d, 1 H-19, J = 12 Hz), 8.00 (s, 3 H, —OCOCH_3), 8.28 (broad s, 3 H-18), 8.97 (d, 3 H-17, J = 6 Hz), and 9.08 (s, 3 H-20).

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.83; H, 8.52.

Oxidation of Diacetate 1h

The crude product (51 mg) obtained from oxidation of the diacetate **1***h* (50 mg) with chromium trioxide (120 mg) for 17 days at 20°, was submitted to preparative t.l.c. (ethyl acetate – light petroleum, 2:3). This furnished two components, starting material (18 mg) and the more polar enone-diacetate **17***e* (16 mg). The latter, an oil, after distillation at 150°/0.03 mm had ν_{max} 1753, 1675, 1220, and 875 cm^{-1}; τ 4.05 (s, 1 H-3), 5.28 (narrow m, 2 H-18), 5.86 (d, 1 H-19, J = 11 Hz), 6.13 (d, 1 H-19, J = 11 Hz), 7.91, 8.02 (both s, 3H each, 2 —OCOCH_3), 8.99 (d, 3 H-17, J = 7 Hz), and 9.12 (s, 3 H-20).

Anal. Calcd. for $C_{24}H_{32}O_6$: C, 69.21; H, 7.74. Found: C, 69.21; H, 7.72.

Oxidation of Diol 1g

(*i*) The diol **1***g* (50 mg) in dry pyridine (20 ml) was treated at 20° for 14 h with chromium trioxide (50 mg). The oily product (55 mg) resulting from work-up was purified by preparative t.l.c. (ethyl acetate – light petroleum, 1:19) and afforded as the sole product the lactone **2** (37 mg) which crystallized from ethyl acetate – light petroleum and had m.p. 89–90°, $[\alpha]_D$ +8° (*c*, 1.5). It was identical (m.p., mixed m.p., n.m.r., i.r., t.l.c.) with a sample of the naturally occurring lactone (see above).

(*ii*) The diol **1***g* (75 mg) in dry pyridine (2 ml) was treated at 20° for 14 h with a large excess of chromium trioxide (500 mg). The product consisted of two components (t.l.c.), the less polar of which corresponded to the lactone (**2**) obtained previously. Separation of the two compounds was effected by preparative t.l.c. and afforded **2** (11 mg) as the minor component. The more polar, major product (47 mg) the enone-lactone **27**, crystallized from ethyl acetate – light petroleum and had m.p. 148–149°; $[\alpha]_D$ −9° (*c*, 1.2); ν_{max} 1779, 1690, and 872 cm^{-1}; τ 3.56 (s, 1 H-3), 5.50 (d, 1 H-19, J = 8 Hz), 6.03 (d, 1 H-19, J = 8 Hz), 9.03 (s, 3 H-20), and 9.10 (d, 3 H-17, J = 6 Hz); *m/e* 328 (M).

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37. Found: C, 73.11; H, 7.23.

Oxidation of the Monoacetate 1n

The known (1) monoacetate **1***n* (50 mg) was oxidized in dry pyridine (2 ml) with chromium trioxide (50 mg) for 14 h. Work-up gave the crude product (52 mg) which consisted of two compounds (t.l.c.), the more polar being the much more abundant. This component, the acetoxy-aldehyde **1***q* (37 mg) was isolated by preparative t.l.c. (ethyl acetate – light petroleum 1:3). It was an oil which after distillation at 155°/0.025 mm had $[\alpha]_D$ −21° (*c*, 0.88); ν_{max} 2710, 1745, 1695, 1235 and 874 cm^{-1}; τ 0.73 (s, 1H-18), 3.29 (t, 1 H-3, J_{obs} = 4 Hz), 5.51 (d, 1 H-19, J = 12 Hz), 5.77 (d, 1 H-19, J = 12 Hz), 8.14 (s, 3H, —OCOCH_3), 8.97 (s, 3 H-20), and 9.16 (d, 3 H-17, J = 6 Hz); *m/e* 358 (M).

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: 73.70; H, 8.42.

Oxidation of Monoacetate 1m

(*i*) Oxidation of the known (I) monoacetate **1***m* (45 mg) with chromium trioxide (50 mg) in dry pyridine (20 ml) at 20° for 12 h and work-up afforded an oil (49 mg) which consisted of essentially one compound (t.l.c.). This compound, the acetoxy-aldehyde **1***r* was purified by preparative t.l.c. (chloroform – light petroleum, 4:1) and then distillation at 160°/0.04 mm. The resulting oil had $[\alpha]_D$ −89° (*c*, 0.8); ν_{max} 2690, 1745, 1725, 1230, and 878 cm^{-1}; τ 0.53 (s, 1 H-19), 4.03 (m, 1 H-3), 5.82 (s, 2 H-18), 8.08 (s, 3H, —OCOCH_3), 9.02 (s, 3 H-20), and 9.23 (d, 3 H-17, J = 6 Hz); *m/e* 358 (M).

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71, H, 8.44. Found: C, 73.86; H, 8.47.

(*ii*) When the monoacetate **1***m* (130 mg) was oxidized in dry pyridine (2 ml) at 20° for 12 h with a large excess of chromium trioxide (500 mg) the only product isolable, by preparative t.l.c. (chloroform – light petroleum, 1:9), was the aldehydo-epoxide **28** (90 mg). This was purified further by distillation at 150°/0.015 mm and the resulting oil had $[\alpha]_D$ +3° (*c*, 1.3); ν_{max} 2710, 1755, 1722, 1230, and 878 cm^{-1}; τ 0.05 (s, 1 H-19), 6.09 (d, 1 H-18, J = 12 Hz), 6.40 (d, 1 H-18, J = 12 Hz), 6.97 (s, 1 H-3, $w_{1/2}$ = 4 Hz), 8.04 (s, 3H, —OCOCH_3), 9.13 (s, 3 H-20), and 9.25 (d, 3 H-17, J = 6 Hz); *m/e* 374 (M).

Anal. Calcd. for $C_{22}H_{30}O_5$: C, 70.56; H, 8.08. Found: C, 70.21; H, 7.89.

Reduction of the Aldehydo-epoxide 28

Reduction of the aldehydo-epoxide **28** (60 mg) with excess lithium aluminum hydride in refluxing dry ether for 14 h afforded an oily mixture (t.l.c.) of products (57 mg) the less polar of which was the more abundant. This compound was isolated by preparative t.l.c. (methanol–chloroform, 3:97) and had $[\alpha]_D$ −27° (*c*, 0.91). It was identical (n.m.r., t.l.c.) with the triol **11***a* prepared from the epoxy-hemiacetal **4***a*. Acetylation furnished the hydroxy-diacetate **11***b* (35 mg), $[\alpha]_D$ −16° (*c*, 1.0) which was identical (t.l.c., n.m.r., i.r.) with a sample prepared from **4***a* (see above).

Oxidation of Diol 30b

Diol **30***b* was prepared by reduction of confertifolin[6] (**31**) (14) with lithium aluminum hydride and a sample (150 mg), m.p. 123°, was then treated with chromium trioxide (200 mg) in dry pyridine (2 ml) at 20° for 14 h. Work-up afforded a crude product which consisted (t.l.c.) essentially of three components. These were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:19). The major, and least polar, constituent was the furan **33** (57 mg) which after distillation *in vacuo* had ν_{max} 889 cm^{-1}; τ 2.93 (s, 1 H-11 and 1 H-12), 8.81, 9.08, and 9.10 (all s, 3H each, quaternary C—CH_3's).

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.40; H, 10.12.

The minor components were of similar polarity. The less polar of the two was isodrimenin (**34** (14), 37 mg), m.p. 125–127°, the identity of which was established by comparison (n.m.r., t.l.c., mixed m.p.) with an authentic sample. The more polar was confertifolin (**31** (14), 34 mg), m.p. 150–152°, the identity of which was also established by comparison (n.m.r., t.l.c., mixed m.p.) with an authentic sample.

Oxidation of Diacetate 30a

Acetylation of diol **30***b* (14) furnished the corresponding diacetate (**30***a*) as an oil which after distillation at 100°/0.05 mm had ν_{max} 1743 and 1225 cm^{-1}; τ 5.37, 5.40 (both s, 2 H-11 and 2 H-12), 7.93, 7.97 (both s, 3H each, 2 —OCOCH_3), 8.97, 9.03, and 9.10 (all s, 3H each quaternary C—CH_3's).

Anal. Calcd. for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 71.05; H, 9.55.

A portion (80 mg) of this diacetate was treated with chromium trioxide (200 mg) in dry pyridine (2 ml) at 20° for 16 days and afforded an oily product which contained two major components. These were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:3). The less polar component was substrate (23 mg) and the more polar the enone-diacetate **32***a* (47 mg) which was purified further by distillation *in vacuo*. The resulting oil had ν_{max} 1750, 1685, and 1230 cm^{-1}; τ 5.16 (s, 2 H-11 and 2

[6]We are grateful to Dr. K. H. Overton for suppling samples of confertifolin, isodrimenin, and drimenol.

H-12), 7.95, 8.00 (both s, 3H each, 2 —OCOCH_3), 8.81, 9.06, and 9.08 (all s, 3H each, quaternary C—CH_3's); *m/e* 336 (M).

Anal. Calcd. for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 68.26; H, 8.47.

Oxidation of Drimenyl Acetate ***25b***

Drimenyl acetate (**25***b* (15), 70 mg) in dry pyridine (2 ml) was treated at 20° with chromium trioxide (200 mg) for 16 days. The oily product (77 mg) was separated into two components by preparative t.l.c. (ethyl acetate – light petroleum, 3:17). The less polar was starting material (23 mg). The more polar, the enone-acetate **32***b* (33 mg) was obtained as an oil which slowly crystallized at 0° and had m.p. 48–50°; ν_{max} 1745, 1677 and 1228 cm^{-1}; τ 5.27 (d, 1 H-11, J = 13 Hz), 5.29 (d, 1 H-11, J = 13 Hz), 7.97 (s, 3H, —OCOCH_3), 8.24 (s, 3 H-12), 8.91, 9.10, and 9.13 (all s, 3H each, quaternary C—CH_3's).

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.10; H, 9.40.

Oxidation of the Furano-olefin ***35a***

Treatment of the furano-olefin **35***a* (16, 50 mg) in dry pyridine (4 ml) with chromium trioxide (61 mg) at 20° for 4 weeks afforded an oil (45 mg) on work-up. This oil was separated into two components by preparative t.l.c. (ethyl acetate – light petroleum, 1:4). The less polar was unreacted furano-olefin (**35***a*, 24 mg). The other component was the oily enone **35***b* (16 mg) which was distilled *in vacuo* and had ν_{max} 1665 cm^{-1}; λ_{max} 239 nm (ε 10 500); c.d. in ethanol $[\theta]_{325}$ −4800 and $[\theta]_{241}$ +17 600; c.d. in chloroform $[\theta]_{331}$ −4500; τ 4.37 (q, 1 H-3, J = 1 Hz), 8.13 (d, 3 H-18, J = 1 Hz), 8.87 (s, 3 H-19), 9.12 (d, 3 H-17, J = 6 Hz), and 9.17 (s, 3 H-20).

Mol. Wt. Calcd. for $C_{20}H_{28}O_2$: 300.2089. Found (high resolution mass spectrometry): 300.2094.

Oxidation of Cholesteryl Acetate ***36a***

Cholesteryl acetate (**36***a*, 330 mg) in dry pyridine (10 ml) was treated with chromium trioxide (800 mg) at 20° for 14 days. The product (340 mg) when subjected to preparative t.l.c. (ethyl acetate – light petroleum, 3:17) gave two major fractions. The less polar was starting material (130 mg) and the other, the known (8) enone-acetate **36***b* (68 mg). It crystallized from light petroleum and had m.p. 154° (lit. value 161–163°); ν_{max} 1740 and 1682 cm^{-1}; τ 4.30 (s, 1 H-6) and 5.33 (m, 1 H-3, $w_{1/2}$ = 20 Hz).

Dehydration of Methyl Marrubiate ***40a***

Methyl marrubiate (**40***a*, 421 mg) in dry pyridine was treated at 20° for 7 days with toluene-*p*-sulfonyl chloride according to the method developed (21) by Burn and Rigby for the dehydration of marrubiic acid. Work-up afforded an oil (414 mg) which consisted essentially of only one compound, **37***a*. This was purified by preparative t.l.c. (chloroform) and distillation at 130°/0.02 mm. The resulting oil had ν_{max} 3650, 1772, and 882 cm^{-1}; τ 4.17 (t, 1 H-6, J_{obs} = 3 Hz), 6.37 (s, 3H, —OCH_3), 8.70 (s, 3H, quaternary C—CH_3), 9.00 (d, 3 H-17, J = 6 Hz), and 9.07 (s, 3H, quaternary C—CH_3).

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.61; H, 8.62.

This compound was further characterized by preparation of the corresponding primary alcohol (**37***c*) which was furnished by reduction of **37***b* with lithium aluminum hydride in refluxing ether. It was obtained as an oil, τ 4.38 (broad s, 1 H-6), 6.43 (d, 1 H-19, J = 11 Hz), 6.75 (d, 1 H-19, J = 11 Hz), 8.88, 8.92, (both s, 3H each, quaternary C—CH_3's) and 8.99 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.13; H, 9.27.

The corresponding acetate **37***d*, also an oil, had τ 4.29 (t, 1 H-6, J_{obs} = 3 Hz), 5.86 (d, 1 H-19, J = 11 Hz), 6.15 (d, 1 H-19, J = 11 Hz), 8.90 (s, 6H, quaternary C—CH_3's) and 9.00 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.15; H, 8.92.

Oxidation of the Olefinic-ester ***37a***

Oxidation of the ester **37***a* (750 mg) in dry pyridine (3 ml) with chromium trioxide (500 mg) at 20° for 10 days afforded an oily product (687 mg). This material was chromatographed over neutral alumina (grade III; 60 g). Early fractions containing unreacted **37***a* (320 mg) were eluted with ethyl acetate – light petroleum (1:19). The enone **38***a* (360 mg) was eluted next (ethyl acetate – light petroleum, 3:17) as an oil which had ν_{max} 1730, 1680, and 878 cm^{-1}; λ_{max} 241 nm (ε 12 000); τ 3.82 (sharp s, 1 H-6), 6.38 (s, 3 H, —OCH_3), 8.61 (s, 3 H quaternary C—CH_3) 8.73 (d, 3 H-17, J = 6 Hz), and 8.86 (s, 3H, quaternary C—CH_3). No satisfactory elemental analysis was obtained for this compound and it was characterized by preparation of **38***c*. Reduction of **38***a* with lithium aluminum hydride in refluxing ether gave a mixture (t.l.c.) of two triols (epimeric at C-7). This mixture was oxidized with the Sarett reagent and afforded **38***c*, an oil, which had ν_{max} 1720, 1670 and 882 cm^{-1}; λ_{max} 240 nm (ε 12 500); τ 0.79 (s, 1 H-19), 3.87 (sharp s, 1 H-6), 8.70 (d, 3 H-17, J = 7 Hz), 8.82 and 8.90 (both s, 3H each, quaternary C—CH_3's).

Anal. Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.65; H, 8.01.

Preparation of the Furano-olefin ***37b***

The known (5) ketone **41** (176 mg) was heated with excess lithium aluminum hydride in refluxing dry ether for 18 h. The product (182 mg) was chromatographed over neutral alumina (Grade III; 25 g), the major component, the axial alcohol **40***b* (88 mg), being eluted with ethyl acetate – light petroleum (1:9). This alcohol failed to crystallize and was purified by distillation at 155°/0.05 mm. It had ν_{max} 3610, 3390, and 865 cm^{-1}; τ 5.70 (m, 1 H-6, $w_{1/2}$ = 7 Hz), 8.75, 8.78, 9.02 (all s, 3H each, quaternary C—CH_3's), and 9.05 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.73; H, 10.03.

The diol **40***b* (66 mg) in dry pyridine (2 ml) was treated at 20° for 80 min with methane sulfonyl chloride (1 ml). The oil obtained (72 mg) was subjected to preparative t.l.c. (ethyl acetate – light petroleum, 1:19) and afforded the olefin **37***b* (57 mg) which was distilled *in vacuo*. The resulting oil had ν_{max} 3560 and 878 cm^{-1}; τ 4.36 (t, 1 H-6, J_{obs} = 3 Hz), 8.85, 8.88, and 8.90 (all s, 3H each, quaternary C—CH_3's), and 9.00 (d, 3 H-17, J = 6 Hz).

Mol. Wt. Calcd. for $C_{20}H_{30}O_2$: 302.2246. Found (high resolution mass spectrometry): 302.2250.

This olefin (50 mg) in dry pyridine (3 ml) was treated at 20° with chromium trioxide (100 mg) for 25 days. The crude product was submitted to preparative t.l.c. (chloro-

form) which furnished the only isolable product, the enone-lactone **39** (19), (7 mg). This material solidified after distillation *in vacuo* and had m.p. 128–134° and was identical (t.l.c., i.r., u.v., mass spectra) with a sample of **39** supplied by Dr. Rivett. A further sample (16 mg) of the olefin **37***b* was oxidized in dry pyridine (2 ml) with chromium trioxide (35 mg) for 5 days. The product contained (t.l.c.) essentially only two components. These were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:1). The less polar was starting material (3 mg) and the other, compound Y (**38***b*, (19), 8.5 mg) which crystallized from ethyl acetate – light petroleum. It had m.p. 110–114°, $[\alpha]_D$ −23° (*c*, 0.8), and was identical (mixed m.p. (110–114°), t.l.c., i.r., u.v.) with a sample of **38***b*, m.p. 112–114°, provided by Dr. Rivett.

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