Constituents of *Solidago* Species. Part IV.[1] Solidagoic Acids A and B, Diterpenoids from *Solidago gigantea* var. *serotina*

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Solidagoic acids A and B, two new diterpenoids from *Solidago gigantea* Ait. var. *serotina* (Kuntze) Cronqu., are formulated (absolute configuration tentative) as **1***a* and *b* on the basis of chemical, spectroscopic, and optical evidence.

On propose les formules **1***a* et **1***b* pour les acides solidagoïques A et B, deux nouveaux diterpénoides isolés de *Solidago gigantea* Ait. var. *serotina* (Kuntze) Cronqu. Ces structures pour lesquelles les configurations absolues ne sont pas définitives sont attribuées en se basant sur des preuves chimiques spectroscopiques et optiques. [Traduit par le journal]

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In the course of our studies on the constituents of *Solidago* species, we have obtained (1) from the roots of *S. gigantea* Ait. var. *serotina* (Kuntze) Cronqu.[3] several new diterpenoids. In the present paper we discuss the constitution and stereochemistry of two of them, solidagoic acids A (**1***a*) and B (**1***b*).

The chloroform soluble fraction of an ethyl acetate extract of dried root material was examined by t.l.c. and found to contain a large number of furanoid compounds which were detected by their color reaction with Ehrlich's reagent. Column chromatography of this material over alumina and elution with chloroform – light petroleum furnished nine neutral diterpenoids, which form the subject of the following article. Two acidic compounds, solidagoic acids A and B, were then recovered by elution with ethyl acetate – acetic acid and separated by rechromatography, this time over silica gel.

Solidagoic Acid A

The less polar acid, A, m.p. 169–171°, was isolated in approximately 0.6% yield, based on the weight of dried roots. Analytical and mass spectral data indicated that the compound has the molecular formula $C_{20}H_{28}O_3$. Its i.r. absorption at 875 cm^{-1} taken in conjunction with three narrow multiplets at τ 2.75, 2.94, and 3.82 in its n.m.r. spectrum indicated the presence of a β-substituted furan ring. This probably constitutes part of a furano-ethyl side chain since its mass spectrum has a prominent ion at *m/e* 189 (M – 95; cleavage of C_9—C_{11} bond). The broad absorption band between 3100 and 3600 cm^{-1} in the i.r. confirmed that the remaining oxygen atoms are present in a carboxyl group, as had been deduced from its chromatographic behavior. In the n.m.r. spectrum an olefinic proton and a methyl group attached to a double bond give rise to an unresolved multiplet ($w_{1/2}$ = 11 Hz) at τ 4.45 and a broad singlet at 8.48 respectively, while a three proton singlet at τ 9.02 and a doublet at 9.11 (J = 6 Hz) can be attributed to two additional methyl groups, the former tertiary, the latter secondary. The results presented above indicated the possibility that solidagoic acid A has a clerodane-type skeleton (**2**), one of the tertiary methyl groups in **2** being replaced by a carboxyl group. The n.m.r. spectra of several simple derivatives of the acid added support to this proposal. Thus in the alcohol (**1***c*) and the acetate (**1***d*) the —CH_2O— protons appear as AB quartets (J = 11 Hz) centered at τ 6.47 and

[1]For Part III see ref. 4.

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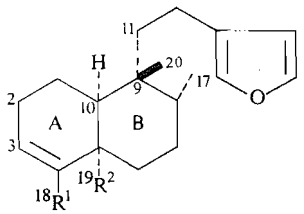
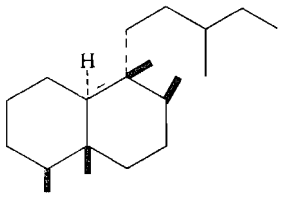
[3]Dr. C. Jeffrey, Royal Botanic Gardens, Kew, U.K. kindly identified this taxon and has retained the specimens supplied as vouchers. In our preliminary communication this taxon was referred to by the presently unacceptable name, *S. serotina* Ait.



1

a $R^1 = CH_3$; $R^2 = CO_2H$
b $R^1 = CH_2OAng$; $R^2 = CO_2H$
c $R^1 = CH_3$; $R^2 = CH_2OH$
d $R^1 = CH_3$; $R^2 = CH_2OAc$
e $R^1 = CH_3$; $R^2 = CHO$
f $R^1 = R^2 = CH_3$
g $R^1 = CH_3$; $R^2 = CO_2Me$
h $R^1 = R^2 = CH_2OH$
i $R^1 = R^2 = CH_2OAc$
j $R^1 = CH_2OAng$; $R^2 = CO_2Me$
k $R^1 = CH_2OAc$; $R^2 = CH_2OH$
l $R^1 = CH_2OH$; $R^2 = CH_2OAc$



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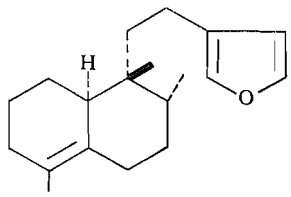

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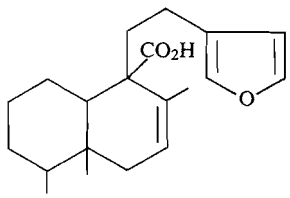

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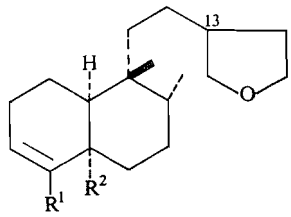
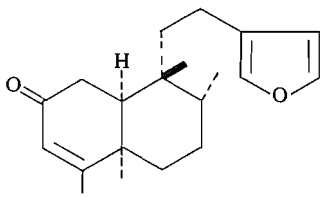


C-13 epimeric mixture

5

a $R^1 = CH_3$; $R^2 = CHO$
b $R^1 = R^2 = CH_3$
c $R^1 = CH_3$; $R^2 = CO_2Me$
d $R^1 = CH_3$; $R^2 = CH_2OAc$
e $R^1 = CH_3$; $R_2 = CH_2OH$
f $R^1 = R^2 = CH_2OH$
g $R^1 = R^2 = CH_2OAc$



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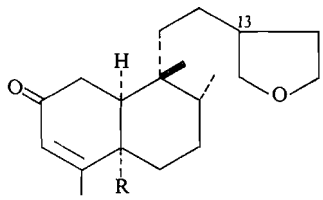


C-13 epimeric mixture

7

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

5.96 respectively, while in the related aldehyde (**1***e*) the aldehydic proton resonates as a sharp singlet at τ 0.54. Significantly, none of these protons shows evidence of vicinal spin–spin coupling indicating that these functional groups are indeed attached to a quaternary carbon atom.

Further evidence for a clerodane-type skeleton came from the discovery that the olefinic bond is βγ to the carboxyl group. When acid A (**1***a*) was heated at 270° under N_2 for 20 min, it decarboxylated and furnished the olefin (**3**), which retains a resonance at τ 8.35 attributable to a methyl on a double bond but no resonance from an olefinic proton. Surprisingly, this nor-olefin (**3**) was the only product recovered from treatment of the alcohol (**1***c*) with chloroacetic anhydride in refluxing pyridine. In this case its formation presumably involves a reaction of the retro-Prins type. At this stage acid A could be tentatively assigned either the gross structure **1***a* (no stereochemistry) or the alternative **4**. The latter, which is unlikely on biogenetic grounds, was eliminated from consideration on the basis of the following evidence.

Huang–Minlon reduction of the aldehyde (**1***e*) and of its tetrahydro analog (**5***a*) afforded **1***f* and **5***b* respectively. Oxidation of these and of

the tetrahydro derivative (**5***c*) of methyl solidagoate (**1***g*) with the Sarett reagent slowly produced the enones **6**, **7***a*, and **7***b*, all of which exhibit resonances attributable to a methylene group α to the ketone at about τ 7.5. Significantly, in each case, the multiplets appear to constitute[4] the AB part of an ABX system. Indeed, when the n.m.r. spectrum of the alcohol (**1***c*) was recorded in the presence of tris(dipivalomethanato)europium the resonance of the proton giving rise to the X part in the enones separated out and appeared as a fairly narrow triplet. Therefore this proton (H-10) has probably no further vicinal neighbors. These results, and the observation that catalytic hydrogenation of **7***a* afforded a ketone (**8***a*), the i.r. absorption of which at 1720 cm^{-1} is compatible with its formulation as a cyclohexanone, allows the part structure **9** to be written for acid A with reasonable assurance. Bearing in mind biogenetic considerations and the presence of a β-furanoethyl side chain, a secondary and a tertiary methyl group, this can be expanded to **1***a* (no stereochemistry). The results reported below concerning the stereochemistry of acid A place this assignment of structure beyond reasonable doubt.

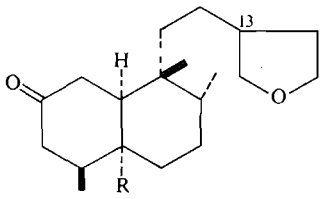
Solidagoic Acid B

The more polar acidic component, solidagoic acid B (**1***b*), m.p. 134–135°, analyzed for $C_{25}H_{34}O_5$, although its mass spectrum shows no peak higher than *m/e* 314, which thus probably corresponds to loss of a five carbon unit. An i.r. absorption band at 1695 cm^{-1} and characteristic (2) resonances at τ 3.96 (1H) and between 7.95 and 8.15 (6H) indicated the presence of an angelate ester. The remainder of the n.m.r. spectrum shows a marked similarity to that of acid A, suggesting a close relationship. Thus two methyl groups, one tertiary, the other secondary, give rise to a singlet at τ 8.97 and a doublet at 9.09 (J = 6 Hz) respectively while a multiplet at 4.02 ($w_{1/2}$ = 10 Hz) may be assigned to an olefinic proton. However, the resonance attributed to the olefinic methyl in acid A has been replaced by a two-proton singlet at τ 5.50, suggesting that in acid B this methyl has suffered oxygenation. The latter compound could then be formulated as **1***b* (no stereochemistry).

Certain nuclear magnetic double resonance and chemical experiments added substance to this conclusion. When the broad singlet at τ 5.50 (—CH_2—OAng) was irradiated the resonance of the olefinic proton at τ 4.02 was converted into a triplet (J_{obs} = 4 Hz). Irradiation at τ 7.93 (allylic protons, 2 H-2) also collapsed the multiplet at τ 4.02, this time to a broad singlet ($w_{1/2}$ = 4 Hz) and in addition sharpened ($w_{1/2}$ = 2.5 Hz) the singlet at τ 5.50. These experiments confirmed that the double bond bears on one end a proton and an allylic methylene and on the other a —CH_2—O— group. Moreover, pyrolysis of the acid at 320° in an evacuated tube afforded, in addition to an oily distillate, crystalline angelic acid (**10***a*), m.p. 45°, which was collected separately in a cold trap. Comparison of this material with an authentic sample of angelic acid was achieved by g.l.c. over 20% free fatty acid phase (FFAP) at 125°, the three isomeric acids, senecioic (**10***b*), tiglic (**10***c*), and angelic, being well separated on this free acid phase. The less volatile material from the above pyrolysis was seen from t.l.c. to consist of two compounds of very similar polarity which were separated only by repeated preparative t.l.c. The less polar component, $C_{20}H_{26}O_3$ (**11**), an oil, which was by far the more abundant, shows a strong absorption in the i.r. at 1778 cm^{-1}, indicative of a γ-lactone. The methylene protons in the lactone ring resonate as a pair of doublets at τ 5.31 and 5.60 (J = 12 Hz), the former being markedly broadened by long range coupling. The very minor component, m.p. 145–147°, on i.r. and mass spectral evidence only, is formulated tentatively as the isomeric lactone **12**. The formation of these lactones can be rationalized by suggesting attack of the carboxyl group at, in the former case the methylene group carrying the ester, in the latter C-3 with a concomitant rearrangement of the olefinic bond into the exocyclic position, each process involving expulsion of angelic acid.

A direct correlation of acids A and B was next sought and accomplished in the following manner. Reduction of the methyl ester of B with lithium aluminum hydride furnished the corresponding diol (**1***h*). Hydrogenation of the derived diacetate (**1***i*) in ethanol–triethylamine over 10% palladized charcoal afforded an acetate identical in all respects to that (**1***d*) previously prepared from A. A minor product from the hydrogenation was the tetrahydro derivative (**5***d*) of **1***d*. These experiments demonstrated that the sole difference in the two acids A and B lies in the nature of the function attached at C-4, in the

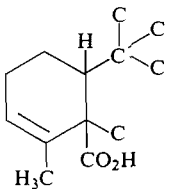
[4]This n.m.r. system is more fully discussed below under the heading stereochemistry.



C-13 epimeric mixture

8

a R = CH_3
b R = CO_2Me



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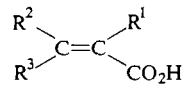
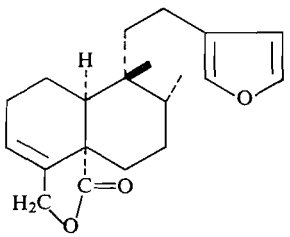
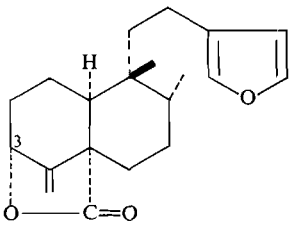


10

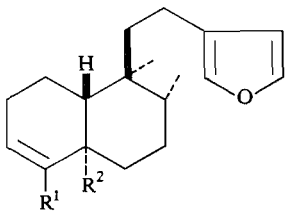
a $R^1 = R^3 = CH_3$; $R^2 = H$
b $R^2 = R^3 = CH_3$; $R^1 = H$
c $R^1 = R^2 = CH_3$; $R^3 = H$



11



12



13

a $R^1 = CO_2H$; $R^2 = CH_3$
b $R^1 = CH_3$; $R^2 = CH_3$
c $R^1 = CH_3$; $R^2 = CH_2OH$
d $R^1 = CH_3$; $R^2 = CHO$

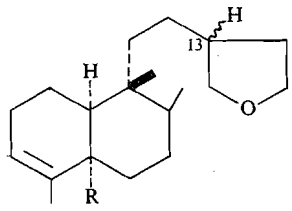
former this is a methyl group, in the latter, an allylic primary angelate ester.

Stereochemistry

The constitutions of acids A and B having been established with some certainty the major problem remaining involved the assignment of stereochemistry at the four asymmetric centers, C-5, -8, -9, and -10. At the outset, attempts were made to correlate **1***a* with hardwickiic acid (**13***a*, 3) in which rings A and B are *trans*-fused. With this intention, the furano-olefin (**1***f*) was prepared from acid A as described above and compared with the analogous compound (**13***b*, 4) from hardwickiic acid. Significant differences were observed in their n.m.r. spectra, for example in the chemical shifts of the resonances of the C-5, -8, and -9 methyl groups (τ 8.83, 9.08, and 8.92 respectively in the former and τ 9.00, 9.14, and 9.26 in the latter). If these two olefins have the same gross structure then they must differ in configuration at one or more centers. Indeed, results gradually accumulated which when taken *in toto* pointed unequivocally to the presence of the relatively rare *cis*-AB ring fusion[5] in acid A (**1***a*).

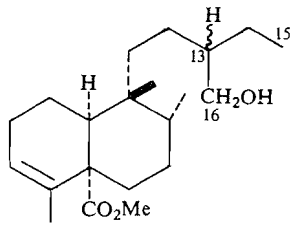
In this context, the first results which arrested our attention came from studies on the catalytic hydrogenation of **1***a*. Treatment with hydrogen in the presence of platinum oxide produced a mixture of products from which the two major constituents, the tetrahydroacids (**14***a* and *b*), were readily separated. The residue after methylation furnished two compounds (**15***a* and *b*) which had suffered hydrogenolytic cleavage of the furan ring. That these are epimers at C-13 rather than C-15/C-16 structural isomers follows (10) from the presence of an ill-resolved doublet ($w_{1/2}$ = 6 Hz) at τ 6.5 in the n.m.r. spectrum of both. The following aspects of this reaction were initially surprising. First, appreciable quantities of material in which the Δ^3 olefinic

[5]At the time the main bulk of this work was carried out only columbin (5) and its congeners were known to have this type of structure. Since then plathyterpol (6), tinophyllone (7), gutierolide (8), cistodiol, and the related diacid (9) have swollen this list.



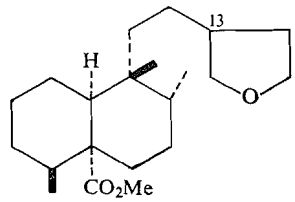
14

a R = CO_2H; 13*S*
b R = CO_2H; 13*R*
c R = CO_2Me; 13*S*
d R = CH_2OH; 13*S*
e R = CO_2Me; 13*R*



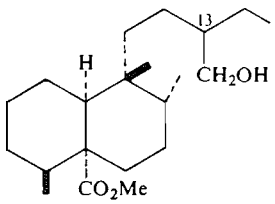
15

a 13*R*
b 13*S*

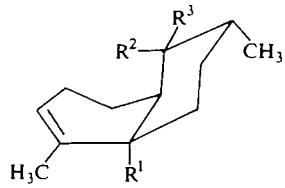


16 13*S*

bond had been saturated were absent. Indeed, the methyl ester **14***c* of the less polar tetrahydro acid (**14***a*) and **15***a* only very slowly gave products (**16** and **17**) of hydrogenation of the double bond under the same conditions. The unreactivity of the olefin in this reaction and towards osmium tetroxide, diborane, and *m*-chloroperbenzoic acid (see Experimental) contrasts with the behavior of related compounds (4, 11). The only configurational and conformational assignment for acid A which seemed to explain this situation is the *cis*-fused system **18***a* (or enantiomer) in which one face of the olefinic bond is shielded by the carboxyl group and the other by either the C-9 methyl or C-9 side chain. Second, **14***a* and *b* were very readily separated by chromatography even though they are simply C-13 epimers. This led us to suspect interaction of the tetrahydrofuran moiety with the carboxyl group in the less polar acid and this was confirmed spectroscopically. At high dilution **14***a* shows two strong carbonyl bands in the i.r. at 1729 (intramolecular hydrogen bond) and 1692 (dimer) cm^{-1} while **14***b* has only one band at 1692 and a weak shoulder at 1729 cm^{-1}. It appeared unlikely that a difference of configuration at C-13 could directly affect the conformations of rings A and/or B and lead to a difference in the tendencies of the carboxylic groups in **14***a* and *b* to hydrogen bond to the olefinic bond. Thus the peaks at 1729 cm^{-1} presumably result from hydrogen bonding of the carboxyl to the ethereal oxygen in the side chain. The ν(CO) is considerably lower than that predicted (12, 13) for species with the carboxylic hydroxyl involved in hydrogen bonding intramolecularly to an oxygen atom other than the carboxylic carbonyl. However, the value observed in the present case is very close to that obtained for ν(CO) when the i.r. spectra of **14***a* and *b* are recorded in carbon tetrachloride in the presence of tetrahydrofuran. In both only one band was observed (1724 cm^{-1}) and attributable to free and bonded hydroxyl groups (the latter band being much more intense especially for **15***a*), $\Delta\nu_{OH}$ about 100 cm^{-1}, and peaks in the carbonyl region at 1725 and 1712 (less intense) cm^{-1}. This last absorption can be assigned to a conformer in which the hydroxyl is bonded to the ester carbonyl, a situation in which ν(CO) is known to decrease (13). However, to explain the relative intensities of the hydroxyl and carbonyl bands in even approximate terms the presence of a further hydrogen bonded species, —OH...O—C—, must be proposed. In this ν(CO) should be similar to that of



17 13*R*



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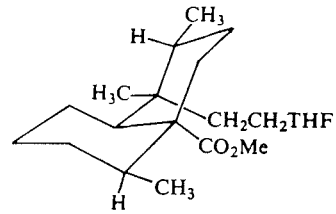
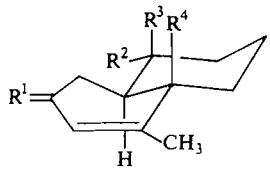


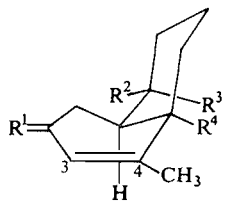
19

a $R^1 = CO_2H$; $R^2 + R^3 = CH_3 + CH_2CH_2Fu$
b $R^1 = CO_2Me$; $R^2 = CH_3$; $R^3 = CH_2CH_2THF$



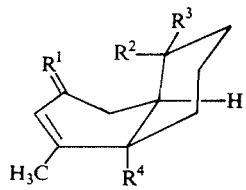
20

a $R^1 = O$



21

a $R^1 = O$
b $R^1 = O$; 3,4-dihydro



22

a $R^1 = O$
b $R^1 = H_2$

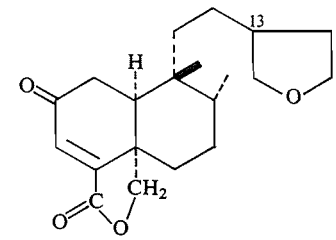
non-bonded conformers (13). The tentative assignment of relative stereochemistry at C-13 to **15***a* and *b* is again based on a study of molecular models. These results appeared to indicate clearly the presence in **1***a* of an A–B *cis*-ring fusion *and* a *cis*-relationship of the carboxyl and furanoethyl side chain.

Further results reinforced these stereochemical conclusions. The acid strength ($pK_{MCS}^* = 8.14$, (14)) of **1***a* corresponds (15) much more closely to that for an angular carboxyl group in a *cis*- rather than a *trans*-fused decalin system. In addition, the relative stereochemistry proposed above would explain the marked difference in reactivity of **14***c* and **16** towards lithium aluminum hydride. Thus in refluxing ether reduction of the former to **14***d* was complete in 4 h while under identical conditions the latter was essentially unchanged. Catalytic hydrogenation of **14***c* in conformation **18***b* would be expected to proceed on the face of the molecule remote from the shielding influence of the C-9 methyl group. The product (**16**) would be expected to flip into the other possible chair–chair conformation (**19**) because of the severe steric interaction between the C-4 and -9 methyl groups. In **18***b* the methoxycarbonyl group is relatively unencumbered and open to attack by lithium aluminum hydride, while in **19** this is not the case.

In the early stages of the investigation it was felt that the n.m.r. spin–spin coupling constants of H-10 to 2 H-1 in derivatives of acid A might serve to distinguish among the various possibilities of mode of A-B ring fusion and ring conformation. With respect to relative stereochemistry three *distinct*[6] possibilities exist, namely, a *trans*-fused decalin (**20**) or a *cis*-fused decalin in either conformation **21** or **22**. In the first two, H-10 is axial to ring A and should show one axial–axial and one axial–equatorial coupling. Recently, as mentioned above, it has been possible in one instance to discern the resonance due to H-10. When spectra of **1***c* were recorded in the presence of gradually increasing concentrations of tris(dipivalomethanato)europium a multiplet separated out downfield from the remaining methylene and methine resonances. In several of these it forms a well-defined, though broadened, triplet presumably because the 2 C-1 protons have become accidentally equivalent. The spacings (5 Hz) observed would then represent an average of the two true coupling constants. Nonetheless, this strongly indicates the stereochemical situation **22***b* for

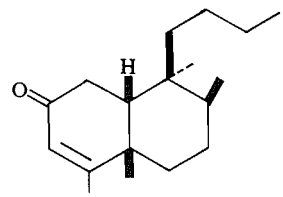
[6]Related conformations with ring A in flattened chair, boat, or twist-boat conformations will be discussed where appropriate.

this compound, in accord with the conclusions reached above. Our original approach to determine the couplings of H-10 involved a study of the resonances arising from the C-1 protons. Readily available for this purpose was the enone **23**, which was formed from diol **1***h* by catalytic hydrogenation of the furan ring and then oxidation (16) with the Sarett reagent. In **23** the C-2 carbonyl effects a downfield shift of the resonances of the two C-1 protons, while the complicating signals of 2 H-12 are shifted upfield by saturation of the furan ring. In deuterobenzene–deuterochloroform (85:15) the C-1 protons are accidentally equivalent and resonate as a clean doublet (splitting 9 Hz) at τ 7.96 while in deuterobenzene alone they form a multiplet with three strong lines at about τ 8. Analysis of this as the AB part of an ABX system gave values for J_{AX} (3.75 Hz) and J_{BX} (14.25 Hz). The magnitude of these coupling constants revealed that the compound has either the *trans*-AB ring fusion or the *cis*-fusion in conformation **21***a*. Other results suggested choice of the latter, conformation **21***a* being preferred to **22***a* in this case probably because the constraint imposed by closure of the lactone ring is less in the former. To investigate the role, if any, of the lactone ring in determining the conformational preference in **23**, the n.m.r. spectra of the enones **6** and **7***a* were recorded for solutions in carbon tetrachloride, benzene, and various mixtures of these. By this means the resonances attributable to 2 H-1 were located for both. In each, the coupling constants of these two protons (A and B) to H-10 (X) were calculated as $J_{AX} = 8.25$ and $J_{BX} = 0.75$ Hz. These results clearly indicated that the compounds should not be formulated as **20***a* or **21***a*. Left for consideration are the ring A *classical* half-boat analogs of **20***a* and **21***a*, which might have coupling constants of this order of magnitude, and **22***a* or related half-boat or twist analogs. Of these, a situation close to **22***a*, but with ring A in a flattened half-boat, is considered to be the favored conformation[7] on the basis of three pieces of evidence. First, of the various possibilities described above this best explains (17) the magnitude of the coupling constants under discussion, the H-1 equatorial/H-10, H-1 axial/H-10 dihedral angles being *ca.* 75 and 45° respectively. Second, in this



C-13 epimeric mixture

23



24

conformation the C-9 methyl group now protrudes over the olefinic bond and should be shielded by it (18). Indeed, in other compounds in this series, this methyl typically produces a resonance at about τ 8.95 but in these enones at about 9.15. Third, the magnitudes of the shifts induced by benzene on the C-4, -5, and -9 methyl groups of **6** and **7***a* accord with the values expected (19) for this conformation. At this stage the relative stereochemistry of acid A at C-5, -9, and -10 could be written with confidence as in **1***a*. Further support for this assignment came from a comparison of the n.m.r. spectrum of **6** with plathyterpenone (**24**) the constitution and relative stereochemistry of which have been rigidly defined (20). In either $CDCl_3$ or C_6D_6 the resonances attributed to 2 H-1, H-3, C-4 CH_3, C-5 CH_3, C-8 CH_3, and C-9 CH_3 are nearly identical in shape and value of chemical shift for both compounds.[8] On this basis the stereochemistry at C-8 is assigned as in **1***a*.

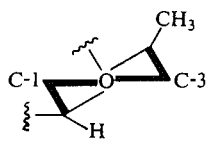
The absolute configuration of acids A and B remains for discussion. Since **6** and **24** appear to have the same relative stereochemistry and conformation of the ring system, a comparison was made of their Cotton effects. Both showed negative Cotton effects for the $n \rightarrow \pi^*$ transition, the former in c.d., the latter (20) in o.r.d., measurements. Thus plathyterpenone and acids

[7]This of course may represent an "average" of several contributing forms.

[8]We are grateful to Professor T. J. King for supplying the n.m.r. spectra and o.r.d. curve of plathyterpenone.

A and B have identical stereochemistry at C-5, -8, -9, and -10. The absolute configuration of plathyterpenone has been assigned (20) as in **24** on the basis of o.r.d. measurements. However, if the conformation deduced above for **6** on the basis of n.m.r. results is indeed preferred, then ring A is in a flattened boat and these compounds on the basis of their Cotton effects should be assigned (21) the *opposite* absolute configuration to that presently accepted for plathyterpenone. Since the deduction of absolute configurations from the Cotton effects of αβ-unsaturated ketones is known (21) to be fraught with difficulties, c.d. measurements were performed on **8***a* and *b*, prepared by catalytic hydrogenation of **7***a* and *b*. The relative stereochemistry at C-4 in **8***a* and *b* would be expected to be that shown, on the basis of their mode of formation and arguments analogous to those applied above to **16**.

Conformational analysis of these compounds appears to suggest that they should adopt conformation **21***b*. On this assumption and on the basis of the octant rule (22) the observed positive c.d. would lead to the assignment of absolute configuration *identical* to that published for plathyterpenone. However, precedent (23) warns that in *cis*-2-decalones related twist-forms although of minor abundance may play a decisive role in the Cotton effect. In the present instance a form of the type **25** might well



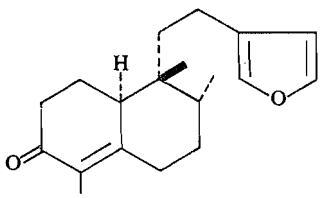
25

contribute to the conformational equilibrium and dictate the sign of the c.d., in which case the absolute configuration is *opposite* to that published for plathyterpenone. In a further attempt to resolve the problem, the two norenones **26** and **27** were prepared (16) by oxidation of **1***c* and maingayol (**13***c*, (14)), a compound of known absolute configuration, respectively. It seems probable that in both, C-10 would retain its original stereochemistry. The negative c.d. observed for **27** accords with that expected (24) for a ring B chair/ring A half-chair conformation, with C-9 pseudo-equatorial to the latter ring. The c.d. measured for **26** was opposite in sign and would appear to indicate that this compound and **27** have opposite configurations at C-10, if ring A has the same conformation in both. It appears unlikely that the difference in relative stereochemistry at C-8 could lead to marked changes in the conformation of ring A especially in the absence of a methyl group at C-10 (24). However, conclusions based on the above type of evidence for the absolute configuration of acids A and B, and by extension plathyterpol, can only be regarded as tentative although on balance it would appear that they should be formulated as shown in **1***a* and *b*.

At various stages in these studies, attempts were made to prepare heavy atom derivatives suitable for X-ray crystallographic examination, originally with the purpose of elucidating the relative stereochemistries, but more recently the absolute configuration. So far no suitable compounds have been obtained. Various heavy metal salts of acid A and the iodoacetate and *p*-iodobenzoate of **1***c* all failed to crystallize satisfactorily. Treatment of acid A with bromine in dioxan produced a complex mixture from which the bromofuran (**28***a*), dibromofuran (**28***b*), and butenolide (**29**) were isolated. The former two, although crystalline, again proved unsuitable for X-ray studies, in one case (**28***a*) because of poor crystalline form, in the other (**28***b*), because the data collected were insufficient and of poor quality.

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). G.l.c. was carried out with a Varian Aerograph 1200 gas chromatograph using a stainless steel column (1/8 in. × 5 ft packed with 3% SE-30) and nitrogen as carrier gas with a flow rate of 25 ml/min except for angelic, senecioic, and tiglic acids. These were separated on a Pye "Argon" gas chromatograph at 125° with a gas flow rate of 60 ml/min using a glass column (1/8 in. × 4 ft) packed with 20% FFAP. Light petroleum was of b.p. 40–60°. Microanalyses were by Miss F. Cowan, Glasgow. High resolution mass spectra were run on an AEI MS 902 instrument equipped with a PDP 8 computer at the N.T.H., Trondheim by one of us (T.A.). I.r. solution spectra were recorded in carbon tetrachloride on a Unicam SP100 Mark II or Perkin–Elmer 225 or 257 or Beckman IR12 spectrophotometer, u.v. spectra in ethanol on a Unicam S.P. 800 spectrophotometer and circular dichroism curves 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



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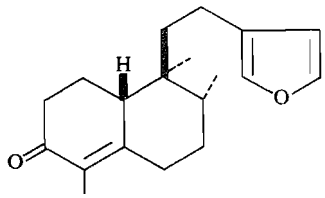

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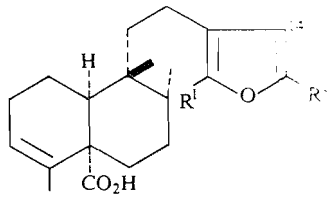
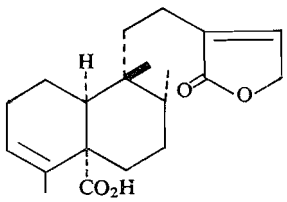


28

a R^1 = Br; R^2 = H
b R^1 = R^2 = Br



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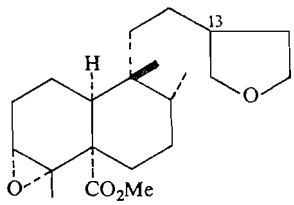
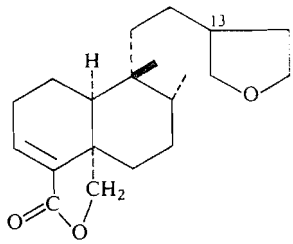


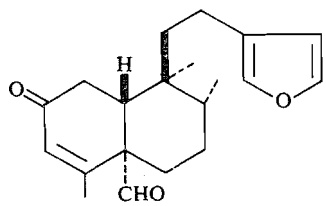
C-13 epimeric mixture

30



C-13 epimeric mixture

31



32

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 CH7 or A.E.I. MS9 or MS12 instrument.

Isolation of Solidagoic Acids A and B

Finely ground, dried roots of *Solidago gigantea* var. *serotina* (500 g) were extracted for 24 h with ethyl acetate in a Soxhlet apparatus. Evaporation of the solvent afforded the crude extract (27 g) which on t.l.c. showed 11 major components when sprayed with the Ehrlich reagent. The chloroform soluble portion (24 g) of this extract was chromatographed over alumina (Grade III; neutral; 2 kg) using as eluting solvent light petroleum – chloroform mixtures. Non-acidic constituents were isolated from the various fractions (see Part V, ref. 16). After elution with chloroform–methanol (19:1) the acidic components were recovered with ethyl acetate – acetic acid (4:1). These were separated by column chromatography over silica gel. Elution with ether – light petroleum (1:9) afforded solidagoic acid A (**1***a*, 3.1 g) which crystallized as large plates from ethyl acetate – light petroleum and had m.p. 169–171°; $[\alpha]_D$ −58° (*c*, 0.9); ν_{max} 1743 (w) and 1695 (s) cm^{-1} (0.008 *M*); 1741 (vw), 1722 (s), and 1695 (m) cm^{-1} in presence of tetrahydrofuran (0.3 *M*); τ 4.45 (m, 1 H-3, $w_{1/2}$ = 11 Hz), 8.48 (s, 3 H-18), 9.02 (s, 3 H-20) and 9.11 (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, 75.75; H, 8.58.

Elution with ether – light petroleum (1:4) afforded solidagoic acid B (**1***b*, 371 mg) which on crystallization from ethyl acetate – light petroleum formed needles, m.p. 134–135°; $[\alpha]_D$ −28° (*c*, 0.7; $CHCl_3$); ν_{max} 3600, 3100, 1720, 1695, 875 cm^{-1}; λ_{max} 221 nm (ε 6000); τ 3.96, 7.95–8.15 (1H and 6H respectively; angelate proton and methyl groups), 4.02 (m, 1 H-3), 5.50 (s, 2 H-18), 8.97 (s, 3 H-20) and 9.09 (d, 3 H-17, *J* = 6 Hz); *m/e* 314 (M − 100).

Anal. Calcd. for $C_{25}H_{34}O_5$: C, 72.43, H, 8.27. Found: C, 72.40, H, 8.55.

Methyl Esters of Acids A and B

The methyl esters were prepared by treatment of the acids in ether with ethereal diazomethane for 5 min. Ester A (**1***g*), an oil, after distillation at 100–105°/0.01 mm had $[\alpha]_D$ −67° (*c*, 1.0); ν_{max} 1728 and 878 cm^{-1}; τ 4.51 (m, 1 H-3, $w_{1/2}$ = 9 Hz), 6.47 (s, 3H, —OCH_3), 8.47 (broad s, 3 H-18), 8.97 (s, 3 H-20) and 9.10 (d, 3 H-17, *J* = 6 Hz).

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.60; H, 9.25.

The oily ester B (**1***j*), purified by preparative t.l.c. (ethyl acetate – light petroleum, 3:17) and then distillation at 110–120°/0.005 mm, had $[\alpha]_D$ −25° (*c*, 0.95; $CHCl_3$); ν_{max} 1728 cm^{-1}; τ 3.97 (m, angelate H), 4.09 (m, 1 H-3), 5.63 (s, 2 H-18), 6.52 (s, 3H, —O*CH*$_3$), 9.05 (s, 3 H-20) and 9.19 (d, 3 H-17, J = 6 Hz); *m/e* 428 (M).

Anal. Calcd. for $C_{26}H_{36}O_5$: C, 72.86; H, 8.47. Found: C, 73.32; H, 8.49.

Reduction of Methyl Ester with Lithium Aluminum Hydride

The methyl ester (**1***g*), (1.58 g) was treated in dry refluxing tetrahydrofuran (50 ml) with excess lithium aluminum hydride for 72 h. Work-up gave the crude alcohol (**1***c*, 1.50 g) which failed to crystallize and was distilled at 115–120°/0.01 mm. The resulting oil had $[\alpha]_D$ −38° (*c*, 1.0); ν_{max} 3630 and 875 cm^{-1}; τ 2.74, 2.82, 3.78 (all m, 1 H each, furan protons), 4.35 (m, 1 H-3), 6.47 (ABq, 2 H-19, J = 11 Hz), 8.33 (broad s, 3 H-18), 8.91 (s, 3 H-20) and 9.10 (d, 3 H-17, J = 6 Hz); with 0.21 *M* ratio of Eu(DPM)$_3$ to **1***c*, τ 1.55 (very broad ABq, 2 H-19, J = 11 Hz), 2.77, 2.90, 3.67 (all m, furan protons), 3.43 (m, 1 H-3), 5.4 (broadened t, 1 H-10, J_{obs} = 5 Hz), 7.32 (broad s, 3 H-18), 8.18 (s, 3 H-20), 8.44 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.57; H, 10.11.

The Acetate **1***d*

The alcohol (**1***c*, 50 mg) in dry pyridine (2 ml) was treated at 20° for 14 h with acetic anhydride (2 ml). The oily acetate obtained on work-up was purified by preparative t.l.c. (benzene) and then distillation *in vacuo*. It had $[\alpha]_D$ −60° (c, 0.8); ν_{max} 1740, 1235, 872 cm^{-1}; τ 4.26 (m, 1 H-3), 5.96 (q, 2 H-19, J = 12 Hz), 8.00 (s, 3 H, —OCO*CH*$_3$), 8.35 (broad s, 3 H-18), 8.91 (s, 3 H-20) and 9.10 (d, 3 H-17, J = 6 Hz); *m/e* 344 (M).

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.70, H, 9.36. Found: C, 76.99; H, 9.54.

Decarboxylation of Acid A

Solidagoic acid A (**1***a*, 72 mg) was heated at 270° under N_2 for 20 min and the product distilled out at that temperature *in vacuo*. The resulting oil was redistilled at 110–120°/0.005 mm and afforded the furano–olefin **3** (45 mg) which had $[\alpha]_D$ −33° (*c*, 1.0); τ 8.35 (s, 3 H-18), 8.98 (d, 3 H-17, J = 6 Hz), and 9.1 (s, 3H-20); *m/e* 272 (M).

Anal. Calcd. for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.57; H, 10.19.

When the alcohol (**1***c*, 125 mg) was treated with excess chloroacetic anhydride in refluxing pyridine for 5 days and the mixture resulting from work-up separated by preparative t.l.c. (light petroleum – ethyl acetate, 19:1) this same furano-olefin (**3**, 24 mg) and substrate (43 mg) were obtained.

Oxidation of Alcohol **1***c*

The alcohol (**1***c*, 725 mg) in dry pyridine (10 ml) was treated at 20° for 14 h with chromium trioxide (800 mg). The crude material obtained (782 mg) consisted of three major components, which were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:9). The least polar component, the aldehyde (**1***e*) had $[\alpha]_D$ −161° (*c*, 0.85); ν_{max} 2690, 1722 and 872 cm^{-1}; τ 0.54 (s, 1 H-19), 4.28 (m, 1 H-3), 8.57 (d, 3 H-18, J = 2 Hz), 9.00 (s, 3 H-20) and 9.18 (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, 79.90; H, 9.38.

The compound of intermediate polarity, the nor-enone (**26**, 35 mg) was obtained as an oil and after distillation (160°/0.02 mm) had $[\alpha]_D$ −100° (*c*, 0.7); ν_{max} 1675 and 872 cm^{-1}; λ_{max} (ethanol) 257 nm (ε 13 000); λ_{max} (chloroform) 252 nm (ε 14 500); c.d. (ethanol) $[\theta]_{314}$ +8000 and $[\theta]_{257}$ −37 000; c.d. (chloroform) $[\theta]_{326}$ +7000 and $[\theta]_{250}$ −39 000; τ 8.27 (d, 3 H-18, J = 2 Hz), 8.90 (d, 3 H-17, J = 7 Hz) and 9.06 (s, 3 H-20); *m/e* 286 (M).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.58; H, 9.15.

The most polar of the major components was the aldehydo-enone (**7***c*, 25 mg) which was purified further by distillation at 140°/0.03 mm. It had $[\alpha]_D$ −197° (*c*, 0.86); ν_{max} 2700, 1730, 1680 and 873 cm^{-1}; λ_{max} 243 nm (ε 7000); τ 0.43 (s, 1 H-19), 4.09 (s, 1 H-3), 8.29 (s, 3 H-18), 9.04 (s, 3 H-20), and 9.16 (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, 76.48; H, 8.40.

*Catalytic Hydrogenation of Methyl Ester A (***1***g)*

Methyl ester A (**1***g*, 380 mg) in absolute ethanol (40 ml) was hydrogenated for 25 min over Adams catalyst (200 mg). Removal of the catalyst and solvent afforded an oil (390 mg) consisting (t.l.c.) of one major and several minor components. Separation of these by preparative t.l.c. (ethyl acetate – light petroleum, 1:3) afforded the oily tetrahydro-methyl ester (**5***c*, mixture of epimers at C-13, 215 mg) which was further purified for analysis by distillation at 130°/0.04 mm. It had ν_{max} 1728 cm^{-1}; τ 4.56 (m, 1 H-3) and 6.33 (s, 3H, —O*CH*$_3$).

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.62; H, 10.47.

The Alcohol **5***e*

Reduction of the tetrahydro-methyl ester (**5***c*, 60 mg) with excess lithium aluminum hydride in refluxing ether for 14 h and work-up afforded the oily alcohol (**5***e*, 57 mg) which after distillation at 140°/0.02 mm had $[\alpha]_D$ −16° (*c*, 1.2, $CHCl_3$); τ 4.42 (m, 1 H-3), 6.56 (q, 2 H-19, J = 12 Hz), 8.36 (broad s, 3 H-18), 8.99 (s, 3 H-20) and 9.14 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.52; H, 11.28.

The Aldehyde **5***a*

The above alcohol (**5***e*, 23 mg) in dry pyridine (2 ml) was treated at 20° for 15 h with chromium trioxide (100 mg). Work-up and preparative t.l.c. (ethyl acetate – light petroleum, 1:4) of the product yielded the aldehyde (**5***a*, 17 mg). Distillation *in vacuo* afforded a colorless oil, $[\alpha]_D$ −88° (*c*, 1.2, $CHCl_3$); ν_{max} 1723 cm^{-1}; τ 0.76 (d, 1 H-19, separation 2 Hz) and 4.36 (m, 1 H-3); *m/e* 304 (M).

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.92; H, 11.05.

Huang–Minlon Reduction of Aldehydes **1***e and* **5***a*

Aldehyde **1***e* (50 mg) in ethylene glycol (2 ml) was treated at 95° for 48 h with 100% hydrazine hydrate (3 ml).

Potassium hydroxide (100 mg) was added and the temperature of the mixture allowed to rise to 210° and remain there for 13 h under N_2. After cooling, the solution was acidified and then extracted with ethyl acetate. The product was purified by preparative t.l.c. (ethyl acetate – light petroleum, 1:9) and distillation. The resulting furano-olefin (**1***f*, 24 mg) was obtained as an oil and had $[\alpha]_D$ −19° (*c*, 1.0); ν_{max} 872 cm^{-1}; τ 4.67 (m, 1 H-3), 8.36 (broad s, 3 H-18), 8.83 (s, 3 H-19), 8.92 (s, 3 H-20) and 9.08 (d, 3 H-17, J = 6 Hz); *m/e* 286 (M).

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.82; H, 10.75.

An identical procedure converted **5***a* (125 mg) into the oily tetrahydrofuran (**5***b*, 58 mg) which had τ (deuterochloroform) 4.70 (m, 1 H-3), 8.36 (broad s, 3 H-18), 8.85 (s, 3 H-19), 9.00 (s, 3 H-20), 9.14 (d, 3 H-17, J = 6 Hz).

Mol. Wt. Calcd. for $C_{20}H_{34}O$: 290.2610. Found: (high resolution mass spectrometry): 290.2609.

Oxidation of the Furano-olefin (1f) with the Chromium Trioxide – Pyridine Complex

The furano-olefin (**1***f*, 68 mg) in pyridine (4 ml) was added to chromium trioxide (75 mg) in pyridine (1 ml), and stirred at 20° for 18 days. The resulting mixture was treated with ethanol (1 ml) for 15 min and then diluted with water (20 ml). Extraction with ethyl acetate, followed by preparative t.l.c. (ethyl acetate – light petroleum) afforded, in addition to unreacted **1***f* (26 mg), the enone **6** (17 mg) which was distilled at 175°/0.2 mm. The resulting low melting solid had ν_{max} 1665 cm^{-1}; λ_{max} 247 nm (ε 7500); τ (carbon tetrachloride) 4.21 (broad s, 1 H-3, $w_{1/2}$ = 4 Hz), 7.45 (3 lines, 2 H-1), 8.05 (d, 3 H-18, J = 1 Hz), 8.73 (s, 3 H-19), 8.98 (d, 3 H-17, J = 7 Hz), and 9.10 (s, 3 H-20); τ (benzene) 4.10 (broad s, 1 H-3), 7.45 (d, 2 H-1, J_{obs} = 4.5 Hz), 8.49 (d, 3 H-18, J = 1 Hz), 9.12 (s, 3 H-19), 8.19 (s, 3 H-20) and 9.25 (d, 3 H-17, J = 7 Hz); c.d. (ethanol) $[\theta]_{328}$ −3000 and $[\theta]_{247}$ +2000; c.d. (chloroform) $[\theta]_{335}$ −2300.

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

Oxidation of the Ester (5c) with Chromium Trioxide – Acetic Acid

Chromium trioxide (195 mg) was added to the ester (**5***c*, 252 mg) in acetic acid (20 ml) and water (1 ml). After stirring at 20° for 1 h, ethanol (50 ml) was added and then the solvent removed *in vacuo*. The residue was dissolved in ether–brine and the ether layer washed with saturated aqueous bicarbonate and brine. Evaporation of the solvent gave an oil (265 mg). The two major constituents of this complex mixture were separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:1). The less polar constituent, the epoxy-ester (**30**, 54 mg) was further purified by preparative t.l.c. (ethyl acetate – chloroform, 1:10) and then distillation *in vacuo*. It had ν_{max} (liquid film) 1720 cm^{-1}; τ 6.37 (s, 3H, $-OCH_3$), 7.06 (m, 1 H-3, $w_{1/2}$ = 4 Hz), 8.97 (s, 3 H-18), 9.21 (s, 3 H-20) and 9.22 (d, 3 H-17, J = 6 Hz).

Mol. Wt. Calcd. for $C_{21}H_{34}O_4$: 350.2457. Found (high resolution mass spectrometry): 350.2456.

The more polar component, the enone-ester (**7***b*, 43 mg) was isolated as an oil and gave one peak on g.l.c. (250°, retention time 6 min). After distillation *in vacuo* it had ν_{max} (liquid film) 1725 and 1670 cm^{-1}; λ_{max} 237 nm; τ 4.24 (broad s, 1 H-3, $w_{1/2}$ = 2.5 Hz), 6.30 (s, 3H, $-OCH_3$), 8.27 (d, 3 H-18, J = 1.5 Hz), 9.11 (s, 3 H-20), and 9.13 (d, 3 H-17, J = 7 Hz).

Mol. Wt. Calcd. for $C_{21}H_{32}O_4$: 348.2301. Found (high resolution mass spectrometry): 348.2303.

Oxidation of the Olefin 5b with Chromium Trioxide – Acetic Acid

Oxidation of the tetrahydrofurano-olefin (**5***b*, 275 mg) with chromium trioxide (275 mg) in acetic acid (20 ml) and water (1 ml) as above afforded an oil (200 mg). Separation of the very complex mixture by preparative t.l.c. (ethyl acetate – light petroleum, 1:3, run thrice) furnished the oily enone (**7***a*, 29 mg) which gave one peak on g.l.c. (230°, retention time 7 min) and after distillation *in vacuo* had ν_{max} 246 nm (ε 8500); τ (carbon tetrachloride) 4.20 (broad s, 1 H-3, $w_{1/2}$ = 3 Hz), 7.46 (3 lines, 2 H-1), 8.06 (d, 3 H-18, J = 1.5 Hz), 8.72 (s, 3 H-19), 9.04 (d, 3 H-17, J = 6.5 Hz) and τ 9.17 (s, 3 H-20); τ (carbon tetrachloride – benzene, 1:1) 7.50 (d, 2 H-1, J_{obs} = 4.5 Hz), 8.34 (d, 3 H-18, J = 1.5 Hz), 8.97 (s, 3 H-19), 9.22 (d, 3 H-17, J = 7 Hz), and 9.24 (s, 3 H-20).

Mol. Wt. Calcd. for $C_{20}H_{32}O_2$: 304.2402. Found (high resolution mass spectrometry): 304.2404.

The Keto-ester 8b

The enone-ester (**7***b*, 63 mg) in 95% ethanol (50 ml) was shaken in a low pressure hydrogenator with hydrogen (33 p.s.i.) over palladized charcoal (5%, 80 mg) for 5 h. Removal of catalyst and solvent left an oil which was submitted to preparative t.l.c. (ethyl acetate – light petroleum, 1:3, run four times). The major, and least polar, component of the mixture was the oily keto-ester (**8***b*, 24 mg) which gave one peak on g.l.c. (250°, retention time 5.3 min) and had ν_{max} 1735 cm^{-1}; τ 6.35 (s, 3H, $-OCH_3$) and 9.20 (broad s, 9H, $3CH_3$); c.d. (ethanol) $[\theta]_{305}$ −45 and $[\theta]_{273}$ +190.

Mol. Wt. Calcd. for $C_{21}H_{34}O_4$: 350.2457. Found (high resolution mass spectrometry): 350.2459.

The Ketone 8a

Hydrogenation of the enone (**7***a*, 43 mg) as described immediately above afforded an oil which showed one major product on t.l.c. Preparative t.l.c. (ethyl acetate – light petroleum, 1:10) afforded the ketone (**8***a*, 22 mg) as an oil, which showed one peak on g.l.c. (230°, retention time 7 min) and had ν_{max} 1720 cm^{-1} (liquid film 1715 cm^{-1}); τ (carbon tetrachloride) 8.78 (s, 3 H-19), 9.03 (d, 3 H-18, J = 7 Hz), 9.10 (s, 3 H-20), and 9.13 (d, 3 H-17, J = 6 Hz); τ (benzene – carbon tetrachloride, 1:1) 8.99 (s, 3 H-19), 9.25 (d, 3 H-18, J = 7 Hz), 9.29 (d, 3 H-17, J = 6 Hz) and 9.30 (s, 3 H-20); c.d. (ethanol) $[\theta]_{283}$ +375.

Mol. Wt. Calcd. for $C_{20}H_{34}O_2$: 306.2559. Found (high resolution mass spectrometry): 306.2557.

Pyrolysis of Acid B (1b)

Acid B (**1***b*, 75 mg) was heated at 300° for 5 min in an evacuated tube. A few crystals of angelic acid, m.p. 45° (sealed tube), collected on a cooled part of the tube. This material was identified by g.l.c. over 20% FFAP at 125°, angelic, senecioic, and tiglic acids being well separated under these conditions, having retention times of 26, 28, and 35 min respectively. The less volatile distillate (49 mg) consisted (t.l.c.) of two products and starting material. The unreacted acid B was removed by filtration through

a short column of neutral alumina and the products were then separated by preparative t.l.c. (ethyl acetate – light petroleum, 1:19). The more abundant lactone (**11**, 20 mg) after distillation *in vacuo* had $[\alpha]_D$ −66° (*c*, 1.4); ν_{max} 1778 and 872 cm^{-1}; τ 4.41 (m, 1 H-3), 5.45 (ABq, 2 H-18, J = 12 Hz), 8.96 (s, 3 H-20), and 9.13 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40, H, 8.34. Found: C, 76.34; H, 8.48.

The more polar lactone (**12**, 6 mg) crystallized from ethyl acetate – light petroleum and had m.p. 145–147°; ν_{max} 1785 cm^{-1}; *m/e* 314 (M).

*The Diol **1h***

Reduction of methyl ester B (**1*j***, 200 mg) in refluxing ether with lithium aluminum hydride gave the diol (**1*h***, 180 mg) which crystallized from ethyl acetate – light petroleum and had m.p. 61–62°; $[\alpha]_D$ −46° (*c*, 0.7); ν_{max} 3620, 3300, and 875 cm^{-1}; τ 4.11 (m, 1 H-3), 8.96 (s, 3 H-20), and 9.11 (d, 3 H-17, J = 6 Hz); *m/e* 318 (M).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.26; H, 9.30.

*Acetylation of Diol **1h***

The diol (**1*h***, 960 mg) in dry pyridine (20 ml) was treated with acetic anhydride (0.35 ml) at 20° for 2 h. Work-up afforded an oil (975 mg) which was separated into its components by preparative t.l.c. (ethyl acetate – light petroleum, 3:7). The least polar component (320 mg) was the oily diacetate (**1*i***) which after distillation *in vacuo* had $[\alpha]_D$ −44° (*c*, 1.7); ν_{max} 1745, 1238, and 875 cm^{-1}; τ 4.06 (m, 1 H-3), 5.43 (s, 2 H-18), 6.01 (s, 2 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* 402 (M).

Anal. Calcd. for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51. Found: C, 71.58; H, 8.72.

The next component, the monoacetate (**1*k***, 175 mg), was also an oil. After distillation at 120°/0.01 mm it had $[\alpha]_D$ −54° (*c*, 0.8); ν_{max} 3460, 1740, 1220, and 872 cm^{-1}; τ 4.08 (m, 1 H-3), 5.53 (q, 2 H-18, J = 12 Hz), 6.49 (q, 2 H-19; J = 12 Hz), 8.00 (s, 3H, —OCOCH_3), 8.94 (s, 3 H-20), and 9.12 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.20; H, 8.82.

The next component, the oily monoacetate **1*l*** (170 mg), after distillation at 150°/0.01 mm had ν_{max} 3580, 1745, 1230, and 878 cm^{-1}; τ 4.12 (m, 1 H-3), 5.50 (s, 2 H-18), 6.06 (s, 2 H-19), 8.03 (s, 3H, —OCOCH_3), 8.92 (s, 3 H-20) and 9.16 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.32; H, 8.73.

The final component was unreacted diol (**1*h***, 102 mg).

*Hydrogenolysis of Diacetate **1i***

The diacetate **1*i*** (60 mg) was hydrogenated in absolute ethanol (30 ml) containing triethylamine (5 ml) over 10% palladized charcoal for 40 min. Removal of catalyst and solvent afforded an oil which consisted (t.l.c.) essentially of two compounds. These were separated by preparative t.l.c. (benzene). The less polar product was the acetate **1*d*** (37 mg), identical (i.r., n.m.r., t.l.c., and $[\alpha]_D$) with the acetate prepared from acid A. The other product, the corresponding tetrahydro-acetate (**5*d***, 14 mg) after distillation at 150°/0.04 mm had $[\alpha]_D$ +28° (*c*, 1.2); ν_{max} 1740 and 1235 cm^{-1}; τ 4.50 (m, 1 H-3), 6.05 (s, 2 H-19), 8.01 (s, 3H, —OCOCH_3), 8.36 (broad s, 3 H-18), 8.97 (s, 3 H-20), and 9.12 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{22}H_{36}O_3$: C, 75.81; H, 10.41. Found: C, 75.86; H, 10.20.

*Hydrogenation of Acid A (**1a**)*

Acid A (403 mg) in absolute ethanol (20 ml) was shaken with hydrogen over Adams catalyst for 2.5 h. The product (427 mg) was submitted to preparative t.l.c. (chloroform, run thrice) and split into three fractions. The least polar fraction (73 mg) contained the oily tetrahydro-acid **14*a*** which distilled at 165–170°/0.02 mm and had ν_{max} 1729 and 1692 cm^{-1} (0.008 *M*); 1724 cm^{-1} in presence of tetrahydrofuran (0.95 *M*); τ 4.58 (m, 1 H-3), 8.47 (broad s, 3 H-18), 9.12 (s, 3 H-20), and 9.20 (broad s, 3 H-17).

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.75; H, 9.88.

The fraction (148 mg) of intermediate polarity contained the tetrahydro-acid **14*b*** which after sublimation at 155–165°/0.04 mm had m.p. 156–159°; ν_{max} 1692 and weak shoulder at 1729 cm^{-1} (0.007 *M*); 1724 cm^{-1} in presence of tetrahydrofuran (0.5 *M*); τ 4.58 (m, 1 H-3), 8.47 (broad s, 3 H-18), and 9.12 (broad s, 6H, 2CH_3).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.89; H, 10.14.

The final fraction (85 mg) ran as two poorly-resolved spots on t.l.c. (methanol–chloroform 1:9). The mixture was treated with diazomethane and the derived esters separated by preparative t.l.c. (chloroform, run twice). The less polar methyl ester (**15*a***, 52 mg) after distillation at 117–122°/0.05 mm was obtained as an oil ν_{max} 3642, 3554, 1725, and 1712 cm^{-1}; τ 4.58 (m, 1 H-3), 6.33 (s, 3H, —OCH_3), 6.55 (m, 2 H-16, $w_{1/2}$ = 6 Hz), 9.12 (s, 3 H-20) and 9.16 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.79; H, 10.71.

The more polar methyl ester (**15*b***, 15 mg) also was obtained as an oil and after distillation at 125–130°/0.04 mm it had ν_{max} 3644, 3544, 1725, and 1712 cm^{-1}; τ 4.58 (m, 1 H-3), 6.30 (s, 3H, —OCH_3) 6.55 (m, 2 H-16, $w_{1/2}$ = 6 Hz), and 9.15 (broad s, 6H, 2CH_3).

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.81; H, 10.85.

*Methyl Esters **14c** and **e***

The tetrahydro-acids (**14*a*** and ***b***) were treated with diazomethane and furnished the corresponding methyl esters. The ester (**14*c***) of the less polar acid (**14*a***) was distilled at 107–113°/0.06 mm. The oil obtained had ν_{max} 1728 cm^{-1}; τ 4.56 (m, 1 H-3), 6.33 (s, 3H, —OCH_3), 9.12 (s, 3 H-20), and 9.23 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.60; H, 10.44.

The ester (**14*e***) of the more polar acid (**14*b***) was also obtained as an oil. After distillation at 110–115°/0.02 mm it had ν_{max} 1728 cm^{-1}; τ 4.56 (m, 1 H-3), 6.32 (s, 3H, —OCH_3), 9.12 (s, 3 H-20), and 9.20 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.31; H, 10.27.

A mixture of **14*c*** and ***e*** ran as one spot on t.l.c. in all eluent mixtures examined.

*The Esters **16** and **17***

Ester **14*c*** (70 mg) in absolute ethanol (20 ml) was shaken with hydrogen over Adams catalyst (80 mg) for

28 h. Removal of catalyst and solvent left an oil which was subjected to preparative t.l.c. (ethyl acetate – light petroleum, 1:9, run twice). The less polar major constituent was the oily hexahydro-ester **16** (25 mg) which after distillation at 115–120°/0.1 mm had ν_{max} 1722 cm^{-1}; 6.36 (s, 3H, —OCH_3), 9.18 (s, 6H, 2CH_3), and 9.38 (d, 3H, CH_3, J = 6 Hz).

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 75.17; H, 10.77.

The more polar constituent was unreacted **14***c* (34 mg).

Hydroxy-ester **15***a* (23 mg) in absolute ethanol (10 ml) was shaken with hydrogen over Adams catalyst (50 ml) for 24 h. The residual oil after removal of catalyst and solvent was separated into its two major constituents by preparative t.l.c. (ethyl acetate – light petroleum, 1:9, run thrice). The less polar constituent, **17** (9 mg), was distilled at 105–112°/0.005 mm and the resulting oil had ν_{max} 3630, 3520, 1722, and 1710 cm^{-1}; τ 6.37 (s, 3H, —OCH_3), 6.50 (m, 2 H-16, $w_{1/2}$ = 6 Hz), 9.18 (s, 6H, 2CH_3), and 9.38 (d, 3H, CH_3, J = 6 Hz).

Anal. Calcd. for $C_{21}H_{38}O_3$: C, 74.51; H, 11.32. Found: C, 74.79; H, 11.26.

The more polar constituent was unreacted **15***a* (7 mg).

Attempted Hydroxylation, Hydroboration, Epoxidation of ***1a***, ***1d***, ***1g***

Acid A (**1***a*), its methyl ester (**1***g*), and the derived acetate (**1***d*) were recovered from treatment with (*a*) osmium tetroxide in ether for 20 h, (*b*) freshly distilled boron trifluoride etherate and lithium aluminum hydride for 2 h and then work-up with sodium hydroxide – hydrogen peroxide, (*c*) *m*-chloroperbenzoic acid in chloroform for 90 min. In each case extended reaction times led to destruction of the furan ring (n.m.r.).

Reduction of Ester ***14c***

The tetrahydro-ester (**14***c*, 113 mg) in dry refluxing ether was treated with excess lithium aluminum hydride for 4.5 h. Work-up gave the alcohol (**14***d*, 88 mg) as an oil which distilled at 120°/0.01 mm and was nearly identical (t.l.c., $[\alpha]_D$ and n.m.r.) with **5***e*.

The hexahydro-ester (**16**, 12 mg) was recovered essentially unchanged (n.m.r., t.l.c.) from attempted reduction with lithium aluminum hydride as above for 4 h.

Hydrogenation of Diol ***1h***

The diol (**1***h*, 325 mg) in absolute ethanol (35 ml) was hydrogenated over Adams catalyst (300 mg) for 2 h. Removal of catalyst and solvent afforded an oil (320 mg) which was seen from t.l.c. to consist of a complex mixture of compounds none of which contained a furan ring (Ehrlich's test). The major component, the tetrahydro-diol (**5***f*, 175 mg) was obtained by preparative t.l.c. (chloroform–methanol, 17:1). Distillation at 180°/0.035 mm gave an oil, $[\alpha]_D$ −47° (*c*, 0.77); ν_{max} 3620 and 3320 cm^{-1}; τ 4.22 (m, 1 H-3), 9.07 (s, 3 H-20), and 9.18 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.20; H, 10.80.

The corresponding diacetate (**5***g*) was also obtained as an oil by treatment of the diol with acetic anhydride – pyridine. After distillation at 175°/0.04 mm it had ν_{max} 1745 and 1235 cm^{-1}; τ 4.11 (m, 1 H-3), 5.49 (s, 2 H-18), 6.06 (s, 2 H-19), 8.00 (s, 6H, 2 —OCOCH_3), 8.99 (s, 3 H-20) and 9.10 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.66; H, 9.51.

Oxidation of Tetrahydro-diol ***5f***

The tetrahydro-diol (**5***f*, 102 mg) in dry pyridine (2 ml) was treated with chromium trioxide (500 mg) at 20° for 14 h. The products (98 mg) were separated by preparative t.l.c. (ethyl acetate – light petroleum, 3:17, run four times). Two major components were obtained. The less polar was the lactone **31** (27 mg) which on distillation at 155°/0.015 mm afforded an oil, $[\alpha]_D$ +26° (*c*, 1.1), ν_{max} 1775 cm^{-1}; τ 3.41 (t, 1 H-3, J_{obs} = 3 Hz), 9.11 (s, 3 H-20), and 9.18 (d, 3 H-17, J = 6 Hz).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.67; H, 9.47.

The more polar component, the oily enone-lactone **23** (43 mg), was distilled *in vacuo* and had $[\alpha]_D$ −4° (*c*, 0.9); ν_{max} 1783 and 1694 cm^{-1}; τ (carbon tetrachloride) 3.64 (s, 1 H-3), 5.57 (d, 1 H-19, J = 8 Hz), 6.12 (d, 1 H-19, J = 8 Hz), 7.72 (m, 2 H-1), 9.16 (s, 3 H-20), and 9.18 (d, 3 H-17, J = 6 Hz); τ (deuterobenzene–deuterochloroform, 85:15), 3.40 (s, 1 H-3), 5.58 (4 lines, 1 H-19), 6.61 (d, 1 H-19, J = 8 Hz), 7.92 and 8.02 (2 lines, 2 H-1), 9.48 (d, 3 H-17, J = 6 Hz), 9.62 (s, 3 H-20); τ (deuterobenzene) 3.36 (s, 1 H-3), 6.01 (4 lines, 1 H-19), 6.65 (d, 1 H-19, J = 8 Hz), 7.94, 8.02, and 8.05 (3 lines, 2 H-1), 9.50 (d, 3 H-17, J = 6 Hz), and 9.67 (s, 3 H-20); *m/e* 332 (M).

Anal. Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.03; H, 8 28.

*Oxidation of Maingayic Alcohol (****13c****)*

The alcohol[9] (**13***c*, 193 mg) in pyridine (10 ml) was added to chromium trioxide (415 mg) in pyridine (8 ml) and kept at 20° with stirring for 5 h. The resulting mixture was treated with methanol (1 ml) for 30 min and then diluted with water (20 ml). Extraction with ethyl acetate, followed by preparative t.l.c. (ethyl acetate – light petroleum, 1:7) afforded three compounds, described below in order of increasing polarity. The known (14) aldehyde (**13***d*, 108 mg) was obtained as an oil. The nor-enone (**27**, 25 mg), also an oil, was distilled *in vacuo* and had ν_{max} 1678 cm^{-1}; λ_{max} (ethanol) 257 nm (ε 13 000); c.d. (ethanol) $[\theta]_{314}$ −12 000 and $[\theta]_{257}$ +37 000; c.d. (chloroform) $[\theta]_{325}$ −9000 and $[\theta]_{250}$ +42 000; τ 8.22 (s, 3 H-18) 9.07 (d, 3 H-17, J = 6 Hz), and 9.33 (s, 3 H-20).

Mol. Wt. Calcd. for $C_{19}H_{26}O_2$: 286.1933. Found (high resolution mass spectrometry): 286.1931.

The aldehydo-enone (**32**, 17 mg), also an oil, was distilled *in vacuo* and had ν_{max} 1715 and 1675 cm^{-1}; λ_{max} 244 nm (ε 9500); τ 0.40 (s, 1 H-19), 3.98 (broad s, 1 H-3, $w_{1/2}$ = 2.5 Hz), 8.29 (d, 3 H-18, J = 1 Hz), 9.13 (d, 3 H-17, J = 6 Hz), and 9.27 (s, 3 H-20).

Mol. Wt. Calcd. for $C_{20}H_{26}O_3$: 314.1882. Found (high resolution mass spectrometry): 314.1880.

*Bromination of Acid A (****1a****)*

Acid A (**1***a*, 355 mg) was treated with bromine (0.15 ml) in dioxan (15 ml) at 0° for 3 h. Work-up afforded an oil which was subjected to preparative t.l.c. (light petroleum – ether, 1:3). By this means ten fractions were

[9]Kindly supplied by Dr. K. Kawazu, Okayama University, Japan.

obtained. The three major components were investigated (from bands 2, 3, and 7, numbered in order of increasing polarity). The least polar component of the three, the dibromide (**28***b*, 35 mg), on crystallization from ethyl acetate – light petroleum had m.p. 170–174° (dec.); τ 3.82 (s, 1 H-14), 4.50 (m, 1 H-3), 8.48 (broad s, 3 H-18), 8.98 (s, 3 H-20), and 9.12 (d, 3 H-17, $J = 6$ Hz); *m/e* 472, 474, 476 (M). The component of intermediate polarity, the monobromide (**28***a*, 14 mg), on crystallization from ethyl acetate – light petroleum had m.p. 173–178° (dec.); τ 2.78 (d, 1 H-15, $J = 2$ Hz), 3.80 (d, 1 H-14, $J = 2$ Hz), 4.47 (m, 1 H-3), 8.46 (broad s, 3 H-18), 8.97 (s, 3 H-20), and 9.14 (d, 3 H-17, $J = 6$ Hz); *m/e* 394, 396 (M). The most polar, the butenolide (**29**, 74 mg), was obtained as an oil and had n.m.r. signals at τ 2.83 (broad s, 1 H-14), 4.55 (m, 1 H-3), 5.25 (broad s, 2 H-15), 9.01 (s, 3 H-20), and 9.15 (d, 3 H-17, $J = 6$ Hz). Treatment with diazomethane afforded the oily methyl ester which was distilled *in vacuo* and had ν_{max} 1767 and 1727 cm^{-1}; τ 2.93 (t, 1 H-14, $J_{ob_s} = 1.5$ Hz), 4.58 (m, 1 H-3), 5.27 (m, 2 H-15), 6.51 (s, 3H, $-OCH_3$), 8.50 (broad s, 3 H-18), 9.02 (s, 3 H-20), and 9.16 (d, 3 H-17, $J = 6$ Hz).

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.70; H, 8.68.

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