84. Chemical Degradation of Sarverogenin, Proof for the Presence of the Steroid Carbon Skeleton

Glycosides and Aglycones, 335th Communication[1])

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(21.V.87)

Chemical degradation of sarverogenin (**1**) to several bile-acid derivatives of known structures is described. This is a proof that **1** contains the normal tetracyclic steroid skeleton, and that the structure suggested for **1** by *Fuhrer et al.* [3] on the basis of spectral data is correct.

Introduction. – Sarverogenin (**1**) [2] is the sugar-free portion of many plant glycosides present particularly in different African *Strophanthus* species (*Apocynaceae* [2c] [3]). After earlier attempts to elucidate the structure, and in particular the trials to place the unknown function of the last O-atom as epoxy group in 7,16α [4], 9,16α- [8], or other [7b] positions, the final structure **1** as 7,8β-epoxy-3β,11α,14β-trihydroxy-12-oxo-5β-cardenolide has been proposed by *Fuhrer et al.* [3] for sarverogenin on the basis of spectral data, mainly ^{1}H-NMR spectra. This result can, however, only be accepted as full proof of the structure, if the assumption, that sarverogenin contains the normal tetracyclic steroid skeleton, is correct. The probability that this is true was rather high for many reasons, *e.g.* the biological activity of the parent glycosides [7a]. However, a rigid chemical proof by transformation of sarverogenin (**1**) into a product of known structure containing the steroid skeleton was not available. Formula **1** was also not accepted by *Taylor* (in lit. 1970), because the signal at δ = 3.88 ppm for di-*O*-acetyl-sarverogenin (**2**) assigned to the H_α–C(17) [3] is at so much lower field than the analogous signal for digitoxigenin, reported at δ = 2.55 ppm [5]. We found, however, that the shift to low field in **2** is due to the deshielding effect of the 12-oxo group which is very close to the H_α–C(17). The corresponding signal in digoxigenone (= 14β-hydroxy-3,12-dioxo-5β(H)-cardenolid) was observed [6] at δ = 4,18 ppm, *i.e.* at a very similar position to that in **2**.

The following reactions (see *Charts I–V*) provide the proof that sarverogenin contains the tetracyclic steroid skeleton, by transforming it into relais compounds[2]) derived from

[1]) 334th Communication: [1].

[1a]) In commemoration of Dr. *André Lardon* (born 5.II.1907) who performed the experimental work, which forms the basis of this communication and was achieved during two years of his long illness (*Parkinson*'s desease). His courage allowed him to continue to work at the bench which he refused to leave in spite of his diminished mobility. Sadly he passed away on January 28, 1984.

[2]) Compounds obtained from sarverogenin and also from steroids of known structure, *e.g.* cholic acid, digitoxigenin *etc.*

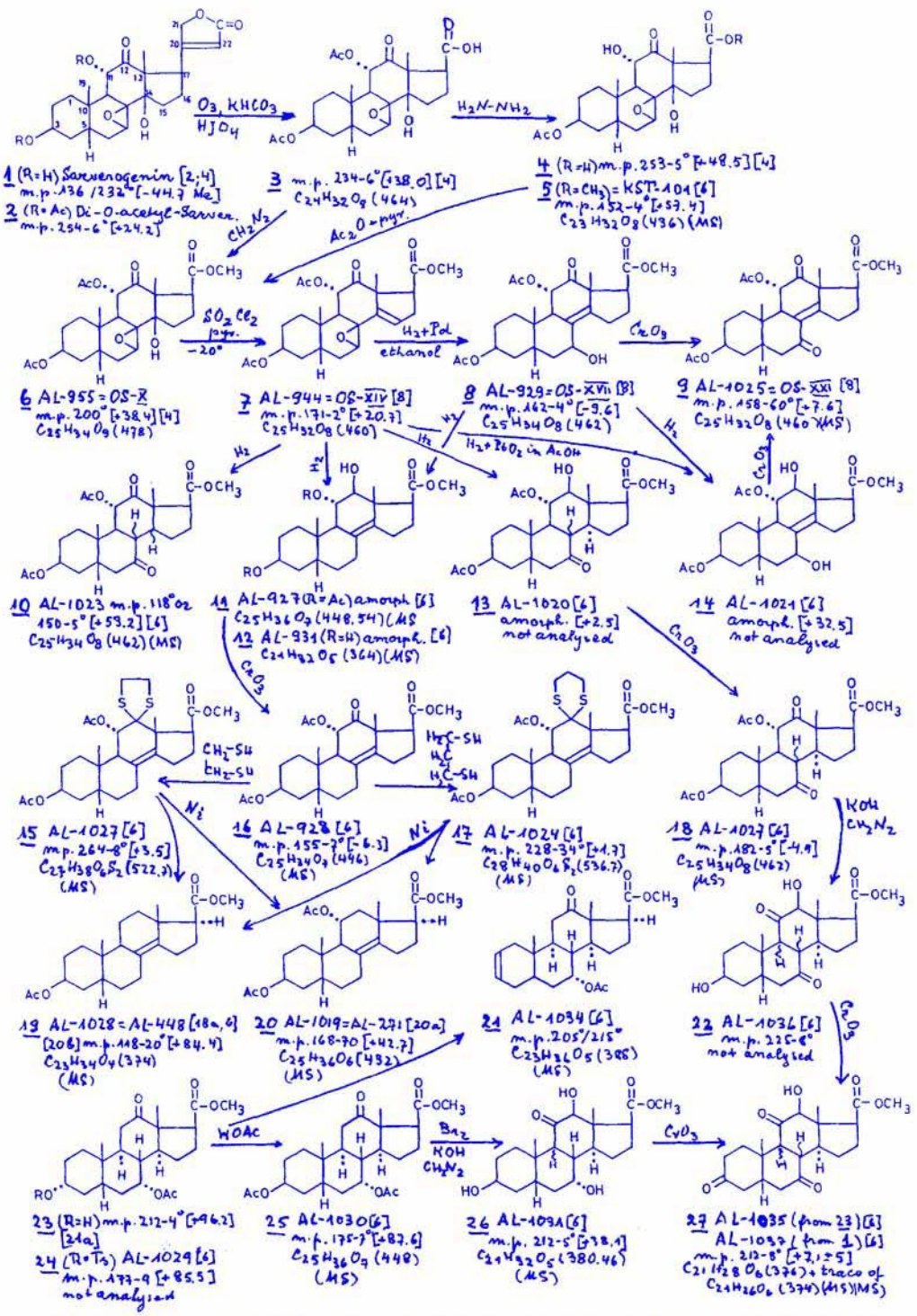

Chart I. The figures in long angular brackets give the optical rotation $[\alpha]_D$, without further indication in $CHCl_3$, Me = methanol. Ac = $CH_3-C(=O)-$; Tosyl = Ts = para-$H_3C-C_6H_4-S(=O)_2-$; (MS) means that a mass spectrum was recorded.

compounds of established structures. They also give additional structural proofs for most of the intermediates. The compounds **3**, **4**, **5** (still amorphous) of *Chart I* have already been described by *Taylor* [4] but formulated with a five-membered epoxy ring. The compound **5** was first obtained crystalline by *K. Stöckel* and is described in *Exper Part.* Compounds **7**, **8**, and **9** were first described by *Schindler* [8] who also suggested different tentative structures. Particular care was taken to assure that no arrangements [9–11] occurred during elimination reactions.

Degradations *via* Ester 5 Started by Elimination of the 14β-Hydroxy Group *(Chart I)*. – Degradation of Di-*O*-acetylsarmentogenin (**2**) [2] with the ozone-perjodate method [12] gave the known etianic acid (**3**) [4], originally formulated [4] with a five-membered epoxy ring. The ^{1}H-NMR spectrum *(Fig. 1)* of its methyl ester is in good agreement with our structure **6**, and the signal of the H_α–C(7) at 3.5 ppm (a *d* with J = 5.8 Hz) is clearly visible. As pointed out by *Schindler* [8], this ester is, like sarverogenin (**1**) itself [4], unusually stable under acidic conditions [4] [7b], but elimination of H_2O with $SOCl_2$ in pyridine [13–15] proceeds smoothly at 0° with formation of the unsaturated ester **7**, tentatively formulated by *Schindler* [8] also with a five-membered epoxide ring. Ob-

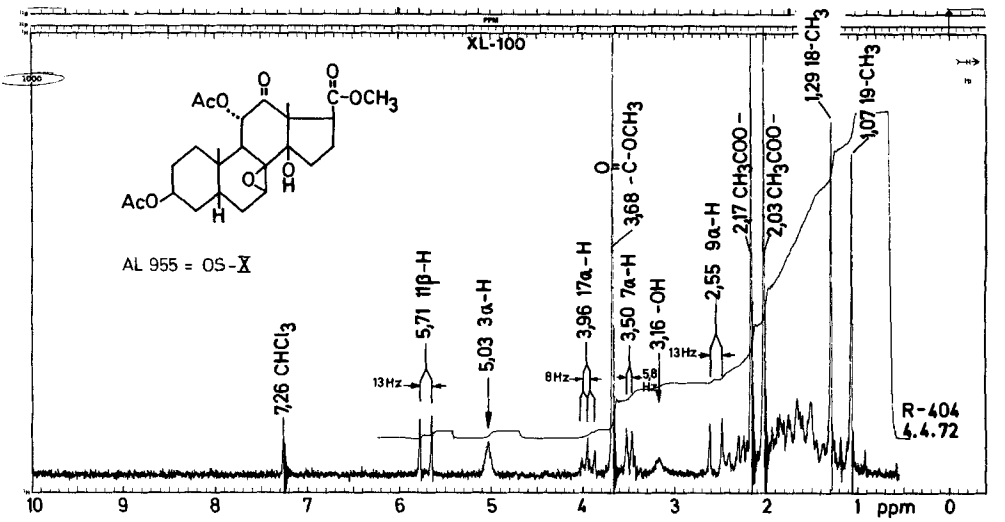

Fig. 1. *^{1}H-NMR Spectrum of* **6** *(AL-955) from Sarverogenin.* The signals of the H_α–C(7) (δ = 3.5 ppm, *d*, J = 5.8 Hz) of the H_α–C(17) (at δ = 3.96 ppm, *t*), and the diaxial coupling (J = 13 Hz) of the H_α–C(9) with the H_β–C(11) (δ centered at 2.55 and 5.71 ppm) are shown.

viously, no rearrangement has occurred during the elimination. In the ^{1}H-NMR spectrum of the ester **7**, the signal of the H_α–C(7) of the oxirane ring at *ca.* 3.48 ppm is clearly visible and also the new signal of the H–C(15) at *ca.* 4.5 ppm (not present in *Fig. 1*). Hydrogenation of **7** under mild conditions (Pd in EtOH) leads, obviously under 1,4-addition, to the unsaturated ester **8**, first prepared also by *Schindler* [8] but tentatively formulated with an α-OH group at C(15). It is better compatible with the 7β-position as given in formula **8**, as shown in the following reactions (see below). Dehydrogenation of **8** with CrO_3, also

described already by *Schindler* [8], yields the dioxo-ester **9**. Its IR absorption spectrum is given in *Fig. 9*. This ester exhibitis selective UV absorption with $\lambda_{max}^{alc.} = 252$ mμ ($\log\varepsilon = 3.98$) [8], indicating a *cisoid*-α,β-unsaturated oxo group. *Barton et al.* [16] found the maximum at 255 mμ ($\varepsilon = 8400$) for this chromophore (compound XXVI in their publication). The acetylated keto group at 11,12-position in **9** contributes only little absorption in this region (compound **6** has a band at 283 mμ ($\log\varepsilon = 1{,}66$) [8]), producing (probably together with another low-intensity band) a slight shoulder around 280–290 mμ in the spectrum of **9**, but obviously responsible for a small hypsochromic shift. *Fieser* [15] reported $\lambda_{max}^{alc.} = 261.5$ mμ ($\log\varepsilon = 3.98$) for 3β-acetoxy-7-oxo-8(14)-cholestene, and *Sigg et al.* [18a] found 260 mμ ($\log\varepsilon = 4.0$) and a second low-intensity band at 318 mμ ($\log\varepsilon = 1.99$) for 7-oxo-5β(H)-8(14)-etienic-acid methylester. The ^{1}H-NMR spectrum *(Fig. 2)* is in agreement with structure **9**.

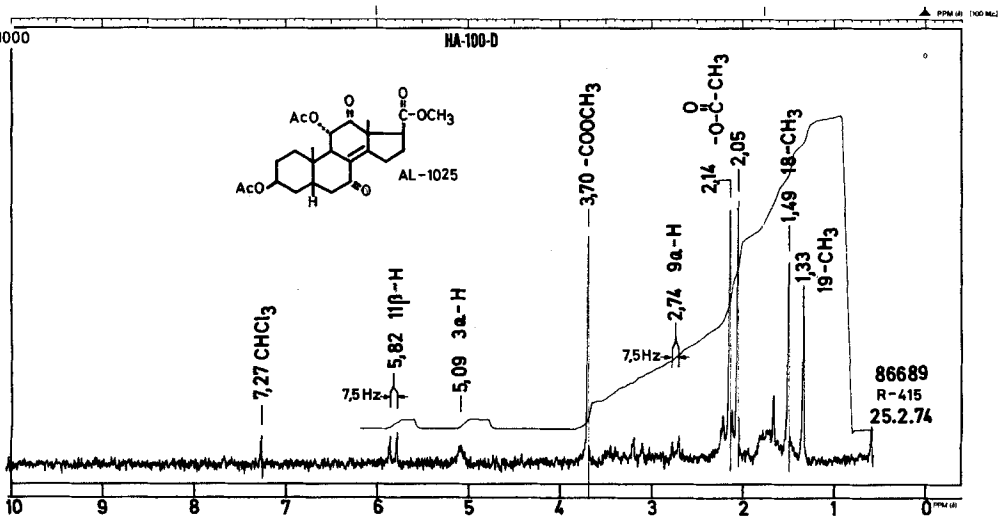

Fig. 2. *^{1}H-NMR Spectrum of* **9** *(AL-1025 = OS-21) from Sarverogenin*

Hydrogenation of the hydroxy-ketone **8** under more vigorous conditions, *i.e.* with Pt in AcOH, gave, with partial hydrogenolysis of the OH group at C(7), a mixture containing mainly the two amorphous compounds **11** and **14** which could be separated by chromatography. The MS of **11** ($M = 448$) was in agreement with the empirical formula $C_{25}H_{36}O_7$. According to IR spectrum, no oxo group but an OH group was present. The β-position of the latter at C(12) can be deduced from the ^{1}H-NMR spectrum *(Fig. 3)*. Saponification of **11** and re-methylation gave the amorphous trihydroxy-ester **12**. Dehydrogenation of **11** with CrO_3 gave the crystalline oxo-ester **16** which showed no OH absorption in the IR but selective absorption in the UV spectrum (EtOH) with $\lambda_{max} \approx 260$ μm ($\log\varepsilon = 2.2$) indicative of a β,γ-unsaturated oxo group. The ester **14** showed in the IR also no oxo group but OH absorption. After dehydrogenation with excess CrO_3, it gave the dioxo-ester **9**, obtained in the same way from **8**. When **7** was directly hydroge-

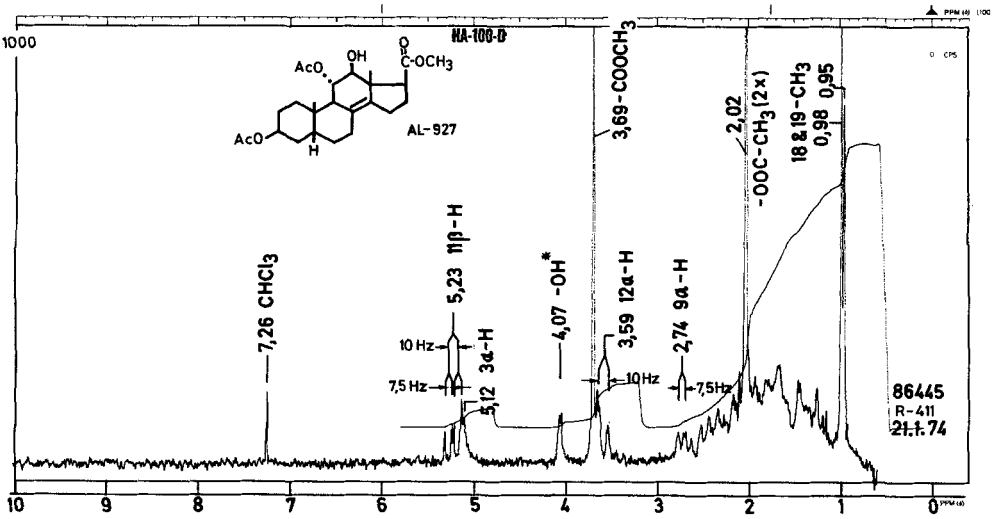

Fig. 3. *^{1}H-NMR Spectrum of* **11** *(AL-927) from Sarverogenin*

nated under vigorous conditions (Pt in AcOH), we obtained, besides **11** and **14**, two more compounds, **10** and **13**. Compound **10** was a saturated dione, showing no OH absorption in the IR, while **13** (amorphous, perhaps not quite pure), after oxidation with CrO_3, gave a crystalline dione **18** isomeric with **10**. Configurations at C(8) and at C(14) are not established in **10**, while it is uncertain only at C(8) in **18** (see below).

The formation of the four compounds **10**, **11**, **13**, and **14** *via* **8** can be rationalized as follows. We assume that, in spite of great excess of H_2, small amounts of O_2 on contact with Pt may allow formation of some **9** from **8** by partial dehydrogenation. In **9**, the double bond is activated by the conjugated oxo group and can be hydrogenated to **10**. In this compound, both oxo groups are again strongly hindered. We have not checked, whether it is possible to get **13** from **10** by hydrogenation, or whether **9** is first reduced to the 12β-hydroxy compound and subsequently hydrogenated to **13**, in which the oxo group is again strongly hindered. Formation of **11** is obviously the main reaction by hydrogenolysis of the 7-OH group in allylic position. Once this is eliminated, the C(8)=C(14) bond is known to become resistant to hydrogenation even under vigorous conditions ([20a] and former lit. given there). On the other hand, this double bond makes the 12-oxo group reactive and susceptible to reduction with Pt + H_2 in AcOH under formation of **11** and **14**, both of which were amorphous.

The two esters **11** and **13** could be transformed into two bile-acid derivatives of known structure as follows: compound **11** was oxidized with CrO_3 to the crystalline, unsaturated oxo-ester **16**. Its UV spectrum (cyclohexane) [20a] showed high-intensity absorption in the low-wave region (technique, see [20a]) with λ_{max} = 205 mμ (log ε = 4.0) indicative of a fully substituted C(8)=C(14) bond and a lower-intensity band at *ca.* 260 mμ (log ε = 2.2) compatible with a β,γ-unsaturated oxo group and a shoulder at *ca.* 289 mμ (log ε = 2.02). The 12-oxo group, quite unreactive in the 14β-OH compounds **1**, **6** *etc.*, containing a saturated C-ring, becomes reactive in **16** as the double bond reduces steric hindrance and

strain. This allowed us to use *Hauptman*'s method [17] to eliminate the ketonic oxygen. We tried two varieties both of which worked. Reaction of **16** with ethandithiol gave the dithiolane **15**, while propane-1,3-dithiol produced the dithiane **17**. Both products crystallized well; their MS are given in *Figs. 12* and *13*. After desulfuration with *Raney*-Ni under partial hydrogenolysis of the AcO group at C(11), a mixture **19**/**20** was obtained, separable by chromatography. The yield *via* **15** was slightly better. The ester **19** (prep. *AL-1028*) was, according to physical data and mixed m.p., identical with the authentic material obtained first as *HPS-XXVIII* [18a, b] from tanghinigenin [19] (the incorrect formula with C(8)=C(9) bond [18a] was later corrected for C(8)=C(14) bond [18b]). The ester **19** was also obtained from digitoxigenin [18b] [20b] and the structure of such a preparation *(AL-448)* unequivocally proved [20b] to have the C(8)=C(14) bond. *Fig. 10* shows the comparison of the IR of the two preparations, corresponding in every detail.

The second ester **20** (prep. *AL-1019*) could, in a similar way, be identified with authentic material (prep. *AL-271*) obtained by degradation of sarmentogenin [20a]. Isolation of **19** and **20** is clear evidence for the presence of the 5β-steroid skeleton in sarverogenin (**1**) and also for the presence of the two OH groups in 3β- and 11α-positions.

Additional Reactions to Show the Presence of Oxygen in 7- and 12-Positions. – The amorphous saturated ester **13**, obtained as by-product in the hydrogenation of **7** could be transformed into the relais compound **27** as follows: dehydrogenation of **13** with CrO_3 gave the crystalline dioxo-ester **18** in which the probably labile configuration [21] at C(8) is unknown. As we were not able to get suitable starting material to synthesize **18**, we transformed it by alkaline saponification and re-methylation into a crystalline 11,7-dioxo-ester of the putative structure **22**. It is well known [10] that the bile-acid derivatives with a ketol group in 11,12-position are isomerized by warming in KOH solution to a mixture of all four possible isomers in which the 11-oxo-12β-hydroxy-configuration (*Marker-Lawson* structure) predominates [10]. Although this may not always be true [22], we assume that the two oxo groups really are in 7- and 11-positions as given in formula **22**. Even if the OH group at C(12) should be α-orientated (as in *Tobias*' compound [22]), it would not devaluate the further result. In an effort to synthesize **22** from the ester **23** [21c] with established structure, obtained from cholic acid, the 3α-OH group in **23** was first epimerized by acetolysis of the tosylate **24**. Apart from the expected unsaturated by-product **21**, the desired 3β-acetoxy-ester **25** was obtained. By bromination and subsequent treatment with hot KOH solution and re-methylation with CH_2N_2, it was transformed into a trihydroxy-oxo-ester, which we believe to have the thermodynamically favored structure **26** (see below). As not sufficient material was available to search for suitable conditions for selective dehydrogenation of the 7α-OH group in **26** to produce the desired **22**, we subjected both **22** and **26** to dehydrogenation with CrO_3 under relatively mild conditions in which the OH group at C(12) is not, or only slowly oxidized. The so-obtained crystalline relais compound **27** from both sources was not quite pure and contained obviously in both cases a little 3,7,11,12-tetraone as impurity, visible as a weak peak at m/z 374 in the EI-MS of both preparations. According to m.p., mixed m.p., and fragmentation patterns in the MS, the two preparations *AL-1075* (from cholic acid) and *AL-1037* (from sarverogenin) were identical. The configuration of the compound **27** at C(8) and C(9) is not established, but it seems reasonable to assume that, during equilibra-

tion in hot alkaline solution (**25**→**26** and **18**→**22**), the same thermodynamically favored structure at these two centers has been formed. We, therefore, accept the formation of **27** on both pathways (in spite of its not perfect purity and incertainty about configuration at C(8) and C(9)) as additional proof for the presence of the steroid nucleus in sarverogenin **1** and also for the presence of oxygen in the positions 3,7,11, and 12 in this cardenolide.

Opening of the Oxirane Ring and Reactions *via* the 11,12-Dione 37 *(Chart II)*. – Treatment of **6** with HBr, probably by diaxial opening [23] [24] of the oxirane ring, yields the crystalline 7α-bromo compound **28**. The reaction is reversible and with HCl a similar 7α-chloro compound **29** is obtained, as encountered in the analogous reaction of tanghinigenin [19]. Reduction of **28** with Zn in AcOH produced the 8β,14β-diol **30**. Its ^{1}H-NMR spectrum is given in *Fig. 4*. This diol **30**, with $SOCl_2$ in pyridine (*Darzens* reagent [13]), gave the thionyl ester **31**, *i.e.* did *not* cause the normal H_2O elimination similar to the change of **6** to **7**. Such behaviour is typical for steroids possessing two OH groups close together on the same side of the ring system [25a–e] and in particular also for 8β,14β-diols [25d].

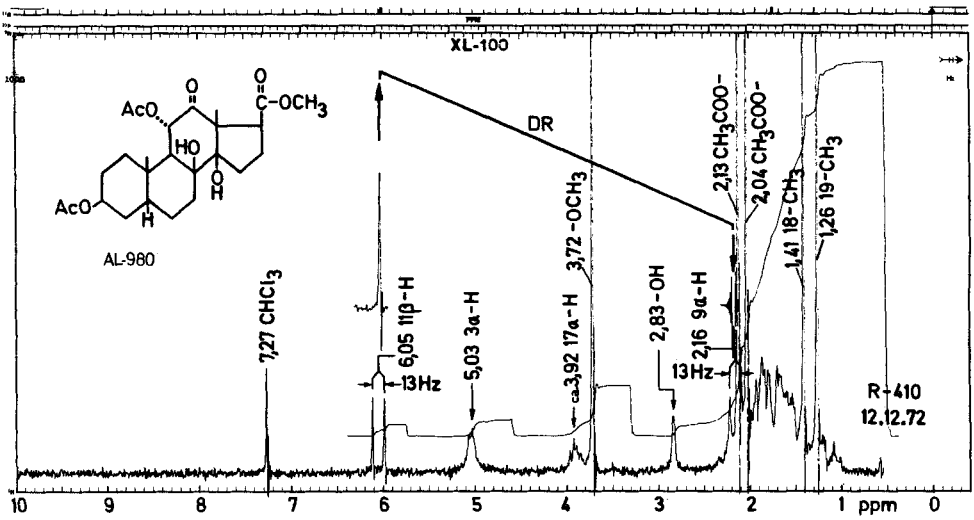

Fig. 4. *^{1}H-NMR Spectrum of* **30** *(AL-980) from Sarverogenin* (**30**) *(AL-980)*

Warming substance **6** with HCOOH gave the 7α-formyloxy-ester **33**. We base the 7α-assignment on the *Fürst-Plattner* rule [23] [24] for the formation of *trans*-diaxial derivatives by opening of oxirane rings. Formula **33** is well compatible with the ^{1}H-NMR *(Fig. 5)*. A crystalline by-product **32** was not further investigated. Selective saponification of the HCOO group in **33** was readily achieved with slightly moist Al_2O_3 yielding the crystalline trihydroxy-ester **34**. The same product in lower yield and less pure could also be obtained directly from **6** by warming with aqueous H_2SO_4 in MeOH. Its acetylation product **35** on treatment with $SOCl_2$ in pyridine again gave a cyclic thionyl ester **36**, indicative of the 8β,14β-position of the two not acetylated OH groups.

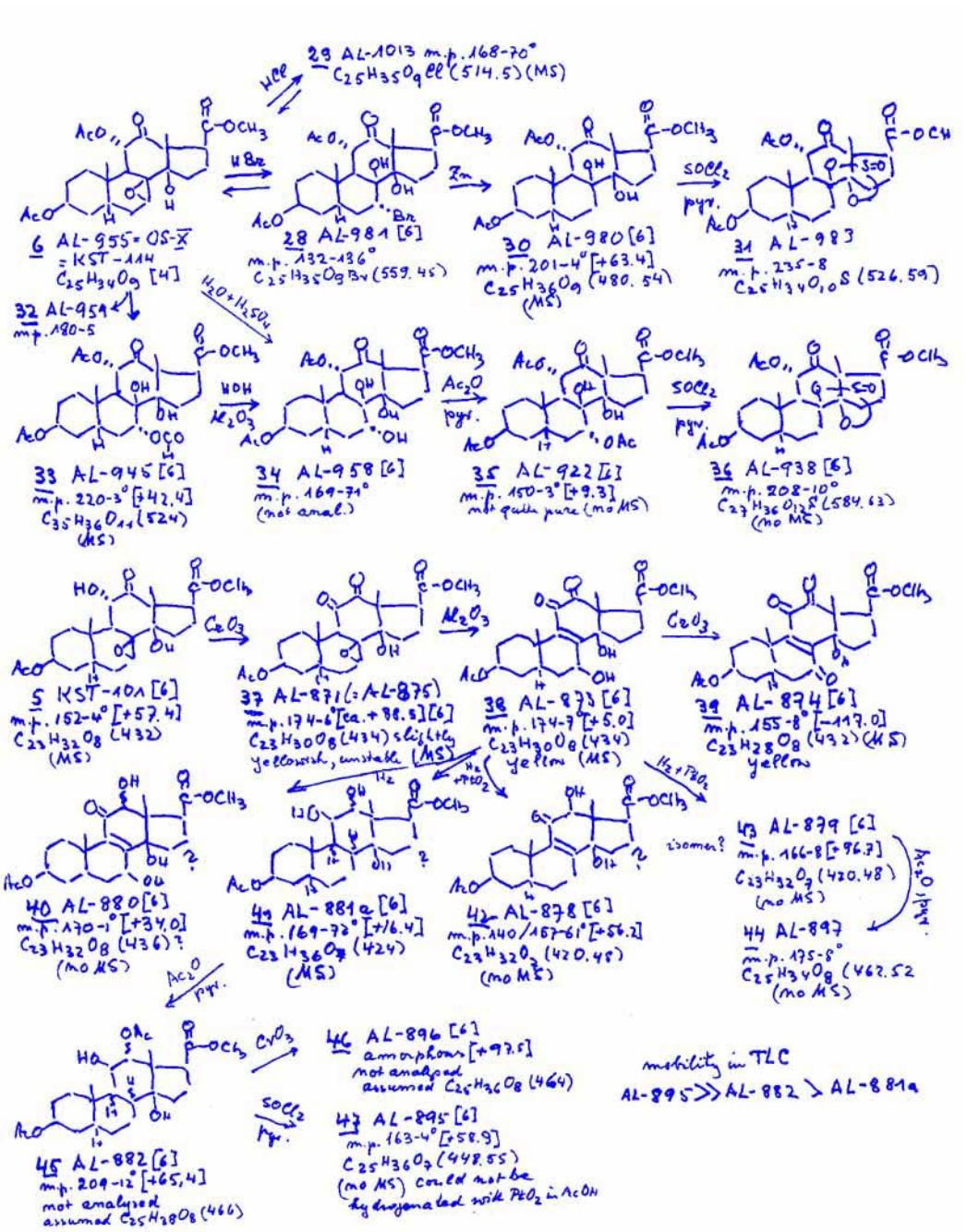

Chart II. Opening of oxiran ring and reactions via 11,12-diketone.

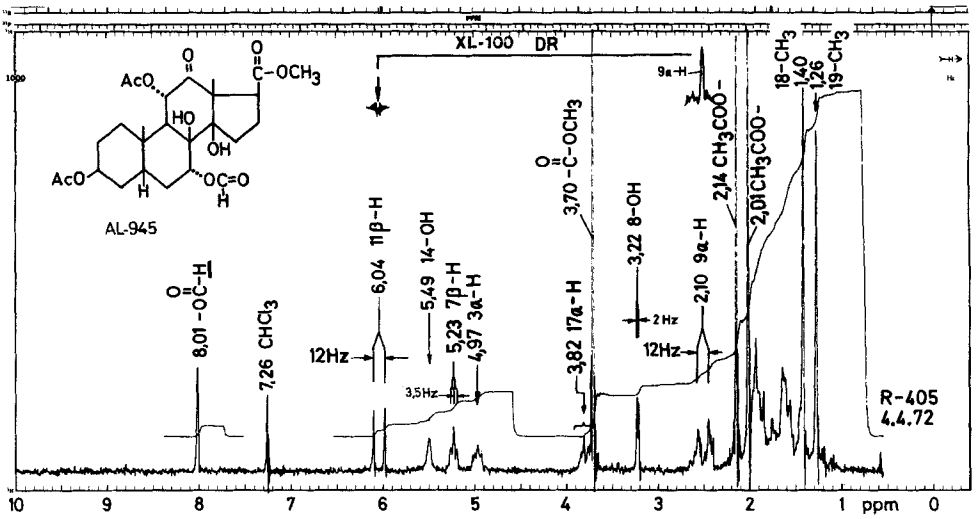

Fig. 5. *^{1}H-NMR Spectrum of* **33** *(AL-945) from Sarverogenin*

Another series of reactions typical for sarverogenin derivatives with free 11- and 12-oxo groups [7b] was started with the mono-*O*-acetyl-ester **5**. Careful chromic-acid oxidation gave the 11,12-dione **37** showing characteristic low-intensity absorption in the UV with two maxima at 284 mμ (log ε = 1.88) and at *ca.* 390 mμ (log ε = 1.36), the latter just reaching the VIS region and giving a faintly yellowish color to **37**. Such absorption is typical for aliphatic α,β-diones [26] [27] and 11,12-dioxo-steroids [7] [26] [28]. The latter are also relatively stable and do not enolize spontaneously as do monocyclic *ortho*-diones [26]. On contact with Al_2O_3, however, **37** did isomerize, producing the yellow, unsaturated diketone **38** showing high-intensity absorption in the low-wave region of the UV with a maximum at 199 mμ (log ε = 3.892) or below, and a second band at 277 mμ (log ε = 3.646), and a further flat absorption around 400 mμ reaching the VIS region. Dehydrogenation of **38** with CrO_3 gave the yellow trione **39** in which the maxima are shifted to 214 mμ (log ε = 3.6) and 264 (log ε = 3.84) with a shoulder at *ca.* 350 mμ (log ε = 3.48), and further absorption in the VIS region around 440 mμ. The same chromophoric system in a,b,c,d-tetraoxo-polyporenic-acid methylester (m.p. 142°) was reported [7b] to show these maxima at 282.5 mμ (log ε = 3.86), 365 mμ (log ε = 1.78), and at 460 mμ (log ε = 1.35), and 9,7,11,12-tetraoxo-8-lanostene (m.p. 154°) gave a nearly identical curve [7b]. Hydrogenation of **38** with PtO_2 in AcOH gave a complicated mixture from which four crystalline compounds **40**, **41**, **42**, and **43** were isolated. The reaction has obviously followed a similar way as described for **7** and **8**. We assume that, in one part of material, the double bond has first been hydrogenated with formation of **41** and other saturated products, while in another part of **38** only reduction of the oxo groups and hydrogenolysis had occurred. The structure of these compounds has not been examined in detail, but the empirical formula of **41** has been verified by MS.

The sequence **5**→**37** corresponds to the reversible transformation by CrO_3 or Cu^{II}-acetate of the three isomeric glycosides; intermedioside, inertoside, and leptoside

(of which intermedioside contains sarverogenin as sugar-free component), to a common oxidation product chryseoside [7b]. This can be reduced again with NaHg to a mixture of the three original glycosides. In this way, it was shown that these three glycosides differed from each other onyl in position and spacial isomerism of the 11,12-ketol groups. Reactions corresponding to **37**→**38**→**39** were also first observed for chryseoside [7b].

Degradation of 5 *via* the Mesylate 4b to Relais Compounds 19 *(AL-1047)*, 61 *(AL-1094)*, 63 *(AL-1092)*, and 64 *(AL-1061)* (*Chart III*). – Treatment of **5** with MsCl gave the mesylate **48** and this with $SOCl_2$/pyridine the unstable compound **49**. Hydrogenation of the latter with PtO_2 in AcOH gave a mixture probably similar to that which had been obtained from **7** *(Chart I)*. From this mixture, two crystalline compounds **50** and **52** could be isolated. We assume that the first step in the hydrogenation is again formation of the 7-hydroxy-$\Delta^{8(14)}$-compound (analogous to **8**, *Chart I*) which, by hydrogenolysis of the 7-OH group and reduction of the 12-oxo group, yielded **50**, while **52** could be formed *via* the 7-oxo-$\Delta^{8(14)}$-compound (analogous to **9**, *Chart I*) by first hydrogenation of the activated double bond with subsequent hydrogenation of the 7-oxo group. This would explain the 7α-orientation of the OH group in **52** (deduced from the ^{1}H-NMR of **56** (see below)). Both mesylates **50** and **52** could further be transformed into useful relais compounds as follows.

trans-Positions (both axial) of the two H-atoms in **50** at C(11) and C(12) can be deduced from the ^{1}H-NMR [6]. Contact of this mesylate **50** with Al_2O_3 produced the epoxide **51** (^{1}H-NMR spectrum, *Fig. 5*) which, by hydrogenation with PtO_2 in AcOH, gave a mixture **54**/**19** which could be separated. The latter (**19** = *AL-1047*) was identical with compound *AL-1028 (Chart I)* and authentic material *(AL-448)* from digitoxygenin [18b] [20]. Compound **54** was also oxidized to **57** with CrO_3 in acetone [48]. This is a simple method to produce β,γ-unsaturated ketones from homo-allylic alcohols which, with CrO_3 in AcOH, often give other products [49]. We originally intended to isomerize

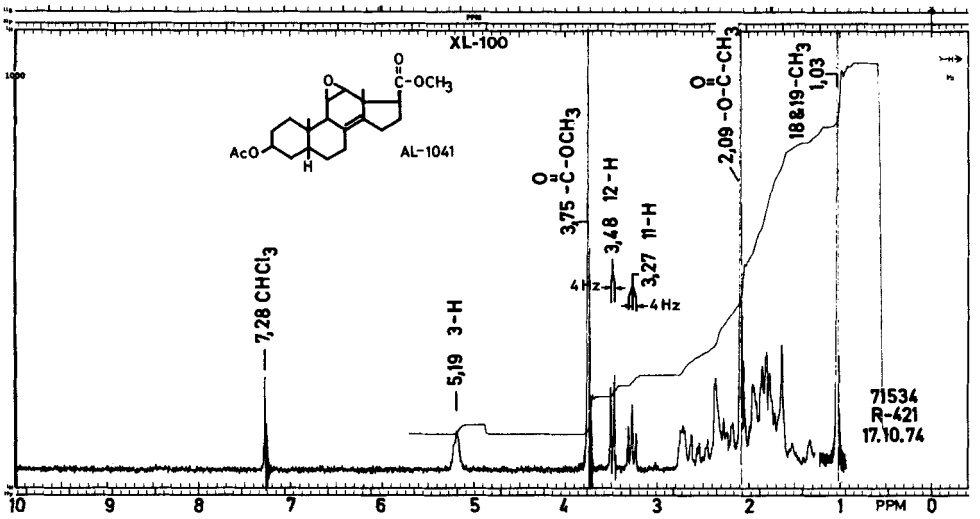

Fig. 6. *^{1}H-NMR Spectrum of* **51** *(AL-1041) from Sarverogenin*

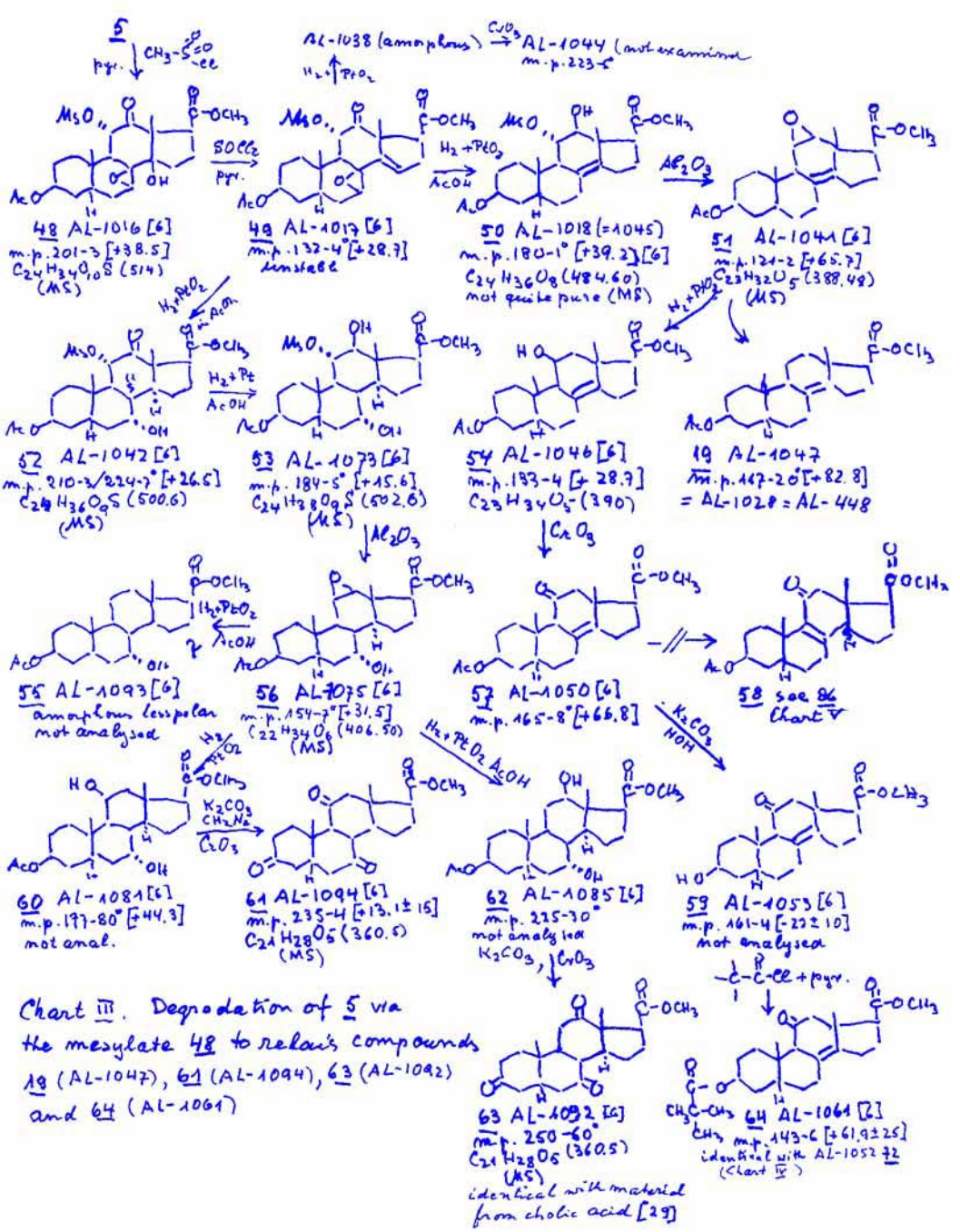

Chart III. Degradation of 5 via the mesylate 48 to relais compounds 19 (AL-1047), 61 (AL-1094), 63 (AL-1092) and 64 (AL-1061)

57, by boiling it with HCOOH, to the α,β-unsaturated ketone **58** but had to renounce due to lack of material. Compound **58** (see **86**, *Chart V*) has nevertheless been prepared from sarmentogenin of established structure. During this work, it was realized that the isomerization of **57** to **58** with HCOOH is possible, but it is not a simple process and gives low yield. We, therefore, saponified **57** to the hydroxy-ester **59** and esterified it with trimethylacetyl chloride to the relais compound **64** *(AL-1061)*. It was identical with material from sarmentogenin (see **72**, *Chart IV*).

Compound **52**, after prolonged hydrogenation with PtO_2 in AcOH, could be further reduced to **53** which, on contact with Al_2O_3, gave the epoxide **56**. On hydrogenation with PtO_2 in AcOH, this epoxide gave a mixture from which, apart from some amorphous less polar material (perhaps **55**), two obviously isomeric crystalline diols **60** and **62** could be isolated. Both were saponified with K_2CO_3, and the crude triols (after remethylation) were oxidized to the crystalline trioxo compounds **61** and **63**. The latter was identical with the known 3,7,12-trioxo-5β-etianic-acid methylester prepared from cholic acid [29]. Synthesis of the other relais compound also from cholic acid is described in *Chart IV*. The identification of **61** and **63** give further proof for the presence of the steroid nucleus in sarverogenin and give independent evidence of the presence of oxygen in the positions 3,7,11, and 12.

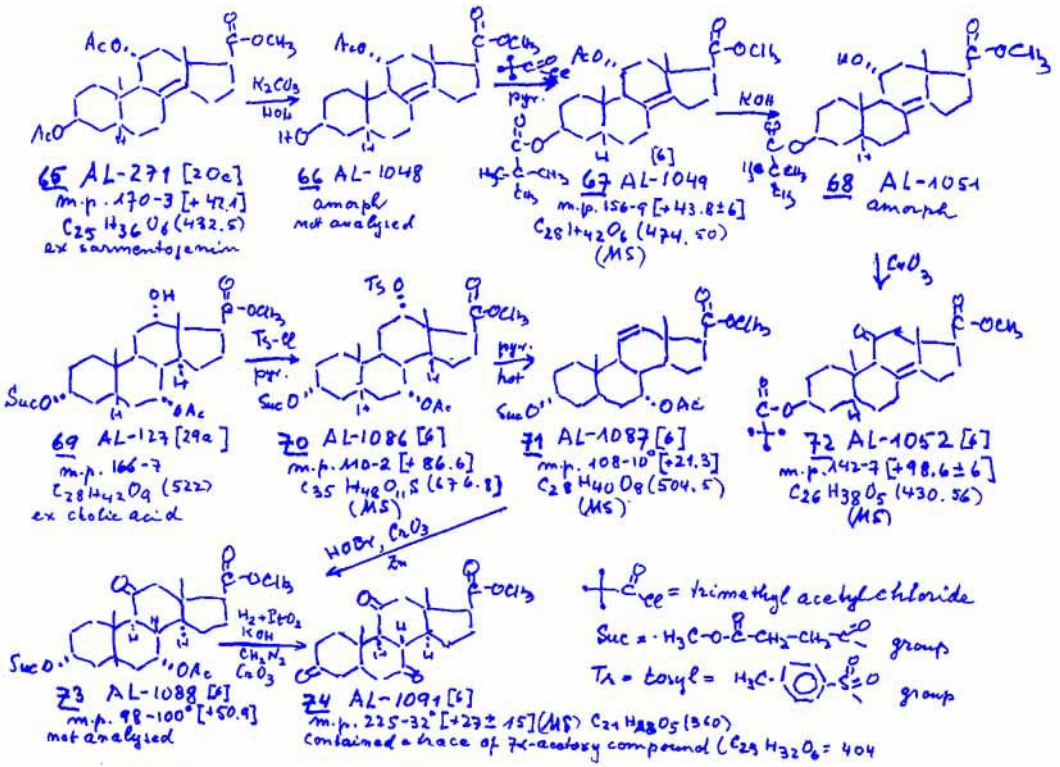

Chart IV. Synthesis of relais compounds 72 (AL-1052 from sarmentogenin) and 74 (AL-1091 from cholic acid)

Synthesis of the Relais Compounds 72 *(AL-1052)* from Sarmentogenin and of 74 *(AL-1091)* from Cholic Acid *(Chart IV)*. – The ester **65** with established structure was prepared from sarmentogenin [20a]. Partial saponification with K_2CO_3 gave the 11-mono-*O*-acetyl derivative **66** which was esterified with trimethylacetic acid to **67**. Partial saponification with KOH in MeOH gave the amorphous **68** which, with CrO_3 in acetone [48], gave the crystalline oxo-ester **72** *(AL-1052)*, identical with **64** (= *AL-1061*, *Chart III*) from sarverogenin. The precise optical rotation of **64** cannot be given, as the estimation had to be done with 0.67 mg of material.

For the synthesis of relais compound **7** *(AL-1091)*, we could start from **69** prepared from cholic acid [29]. Tosylation of ester **69** gave **70** and heating with pyridine the ester **71**. Introduction of the 11-oxo group was performed by addition of HOBr, oxidation with CrO_3 and subsequent reductive elimination of the Br (in 12-position) [31a] [6][3]) gave the desired 11-oxo compound **73**. After katalytic hydrogenation (to avoid isomerization at C(9) in the next reaction), the crude 11β-hydroxy-ester was saponified with KOH, acidic parts of the saponification product re-methylated with CH_2N_2, and the crude 3β,7α,11β-trihydroxy-ester oxidized with chromic acid to yield the desired crystalline 3,7,11-trioxo-ester **74** (prep. *AL-1091*). According to MS, the analytical sample contained a trace of a by-product with *m/z* 404 (probably the 7α-acetoxy-ester), but otherwise the spectrum was practically identical with **60** *(AL-1094)* from sarverogenin.

Formation of the Lactone 76 to Give Additional Proof for the 14β-Position of the OH Group and Some Reactions with 76 *(Chart V)*. – Treatment of the acid **3** with Ac_2O in pyridine gave, apart from a by-product (**75**, *AL-975*, not further examined), the crystal-

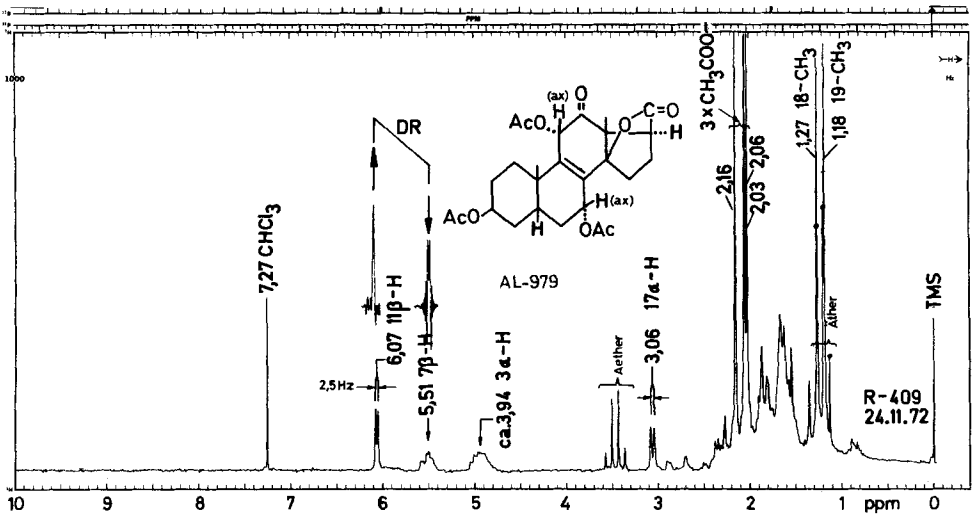

Fig. 7. *^{1}H-NMR Spectrum of* **78** *(AL-979) from Sarverogenin*

[3]) The OH group in [31a] is still incorrectly formulated as 11α as other groups in the C and D Ring. Corrections see *Carlisle* and *Crawfoot* [32]; *Gallagher* and *Long* [33] and *Sorkin* and *Reichstein* [34].

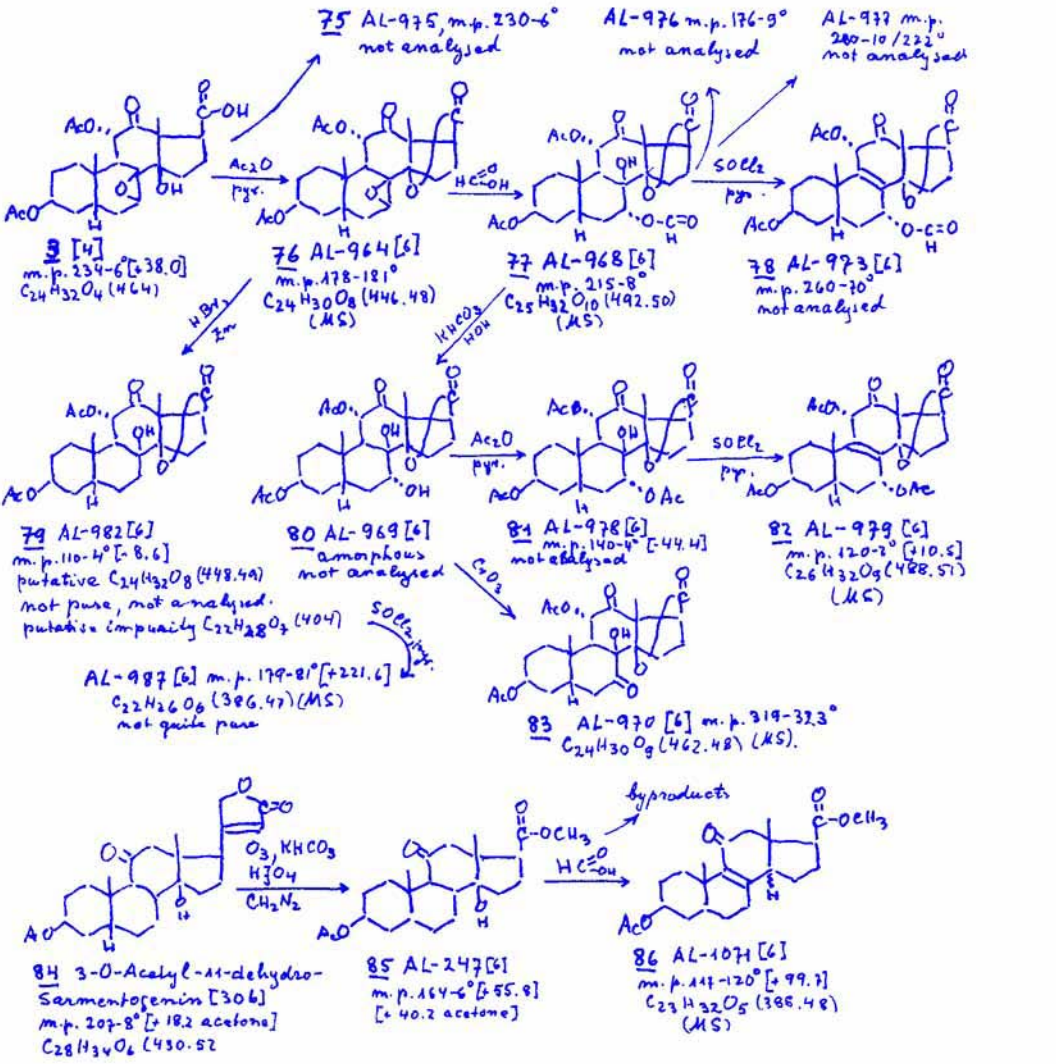

Chart V. Lactone (17→14) formation and opening of the oxiran ring in the lactone. Synthesis of 86 (AL-1071) as putative relais compound but not obtained (as 58) from 57 (Chart III, AL-1050)

line lactone **76**. Its IR spectrum in CCl_4 shows no band in the OH-stretching region but three strong bands in the C=O region at $\lambda = 5.52$ μ (indicative of a five-membered lactone), at 5.67 μ (Ac group) and 5.75 (hexacyclic ketone). Formation of stable lactones is typical for 14β-hydroxy-etianic acids [35]. Reductive cleavage of the oxirane ring in **76** by addition of HBr and reduction of the crude 7α-bromo compound with Zn gave the hydroxy-lactone **79** (not quite pure) which, by treatment with $SOCl_2$ in pyridine, gave (in poor yield) a crystalline lactone *AL-987* ($C_{22}H_{26}O_6$), obviously originating from an impurity (perhaps $C_{22}H_{28}O_7$, corresponding to partially saponified **76**) present in the crude lactone **79**. Treatment of **76** with HCOOH gave the 7α-formyloxy derivative **77** which, after treatment with $SOCl_2$ in pyridine, gave (apart from two by-products *AL-976* and *AL-977*), the compound **78**, which was unstable and was not further investigated. Saponification of **77** with $KHCO_3$ in aqueous MeOH gave the amorphous **80** which, by acetylation, produced the crystalline **81**. With $SOCl_2$ in pyridine, this was transformed into **82**. The ^{1}H-NMR spectrum *(Fig. 7)* is in agreement with the structure. Chromic-acid oxidation of **80** gave the 7,12-dioxolactone **83**.

These additional reactions, as formulated in *Charts II–V*, give further support of nearly every detail in the formula **1** *(Chart I)* of sarverogenin.

We wish to express our gratitude to the following persons: Mr. *K. Aegerter* (Inst. für Org. Chemie, Universität Basel) for recording IR and UV spectra and inscription of *Figs. 8–13*, Mrs. *D. Ammann* for typing the experimental part, Dr. *J. v. Euw* for help at the bench, Dr. *H. Fuhrer* and *A. Borer* (Physics Laboratory of *Ciba-Geigy* AG, Basel) for recording NMR spectra and Dr. *H. Fuhrer* in particular for his help in interpretation and the ^{13}C-NMR spectrum of the epoxy-ester **56**, Prof. *E. Heilbronner* (Inst. für Physikalische Chemie, Universität Basel) for organizing the publication of this article, Dr. *H. Hürzeler* (Physics Laboratory of Ciba-Geigy) for recording the MS and his help in their interpretation, Prof. *W. Morgan* (London) for his kind help in correcting the manuscript, Mrs. *M. Stenz* for typing the theoretical part, Dr. *K. Stöckel* (formerly research assistant at Inst. für Org. Chemie, Universität Basel) for inscription of *Figs. 1–7*, Mr. *E. Thommen* (formerly microanalyst at Inst. für Org. Chemie, Universität Basel) for performing the microanalysis. Our particular thanks go to the *Direction of the Research Department* of *Ciba-Geigy*, Basel, for their permission to Dr. *Fuhrer* and Dr. *Hürzeler* to perform the mentioned spectra for us.

Experimental Part

General. All m.p. were taken on the *Kofler* hot-stage microscope and are corrected by calibration with standard compounds of precisely known m.p. Optical rotation was measured on a *Schmidt & Hensch polarimeter No. 11791* (visual) and *Perkin-Elmer 141 polarimeter* (photoelectric). Samples for combustion analyses were dried at 0.01 Torr over P_2O_5 at 20° for 24 h. Analyses were performed by *E. Thommen* on a *Perkin-Elmer* CHN analyser *No. 240* with amounts of 1.2–1.5 mg. Thin-layer chromatography (TLC) was performed on glass plates layered with SiO_2 (*Art. 7741, Kieselgel HF 254 + 366*, Type *66, für Dünnschichtchromatographie Merck*), activated at 105° for 30 min. Spots were visualized under UV lamp and by spraying with 15% TsOH in EtOH and subsequent heating to 100–120°. UV spectra (λ_{max} [nm] (log ε)) were recorded by Mr. *K. Aegerter* on an *Unicam-SP-500* spectrophotometer, in the short-wave region (200–210 nm) in a 1-mm cell using the technique described in [20a].

IR were also recorded by Mr. *K. Aegerter* in a grating double-beam *Perkin-Elmer* IR spectrophotometer model *125*. ^{1}H-NMR spectra were recorded by *Dr. H. Fuhrer* and *Mr. A. Borer*, Physics Laboratory *Ciba-Geigy Ltd.*, Basel, on a *Varian* spectrograph, model *HA-100* (100 MHz); the signals with asterisk (*), assigned to OH groups, disappear after shaking with D_2O. Chemical shifts are in δ values based on Tetramethylsilane (TMS) ($\delta = 0$ ppm). EI-mass-spectra (MS) were recorded under the direction of Dr. *H. Hürzeler*, Physics Laboratory, *Ciba-Geigy Ltd.*, Basel, on a *Varian CH-7* mass spectrometer with direct inlet system at 70 eV. Metastable ions are indicated as *m**. Interpretation of the MS (rel. int. [%] in parentheses) (see *Chart VI*) is tentative in analogy to established fragmentation patterns by EI in steroids [38–41] and for cardenolides, and etianic-acid derivatives in

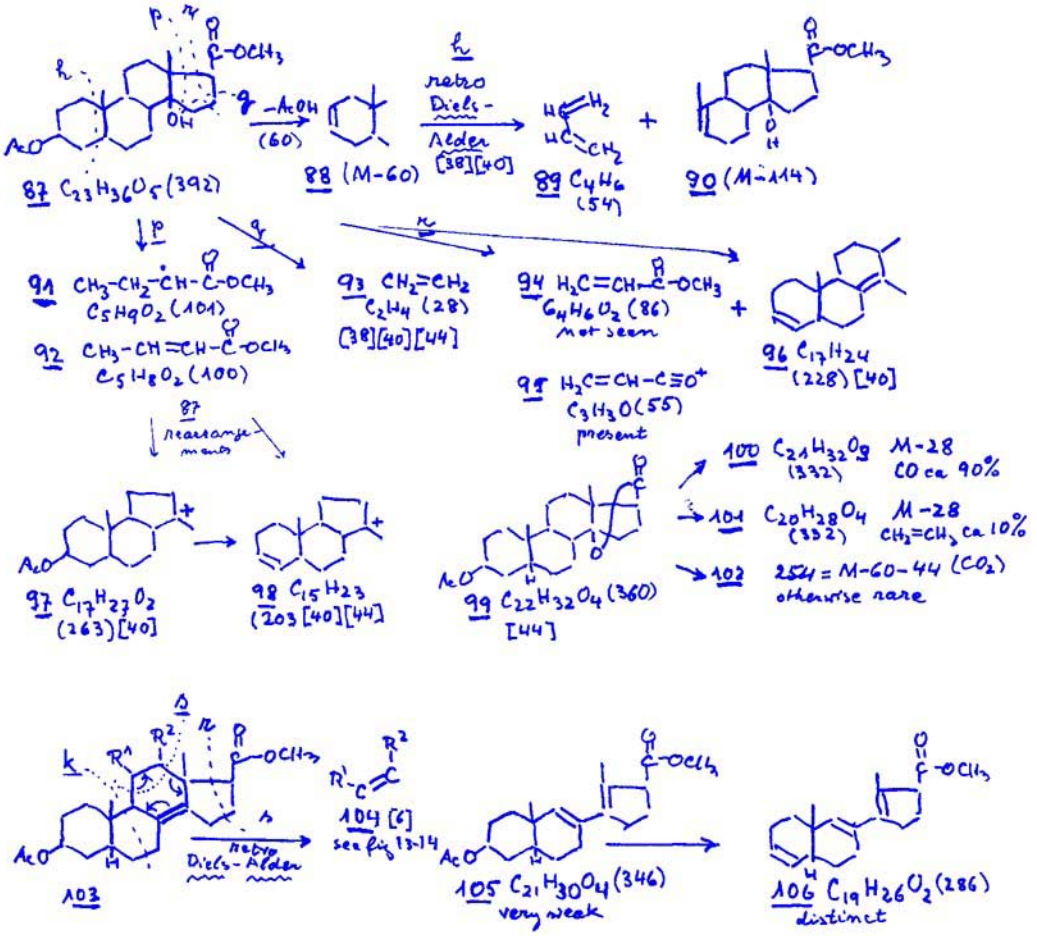

Chart VI. Main fractionation patterns in EI mass spectra of 3β-Acetoxy-14β-hydroxy-5β-H-etianic acid methylester 87 [38][40][44], its lactone 99 [44] and Δ 8:14 derivatives 103 [6].

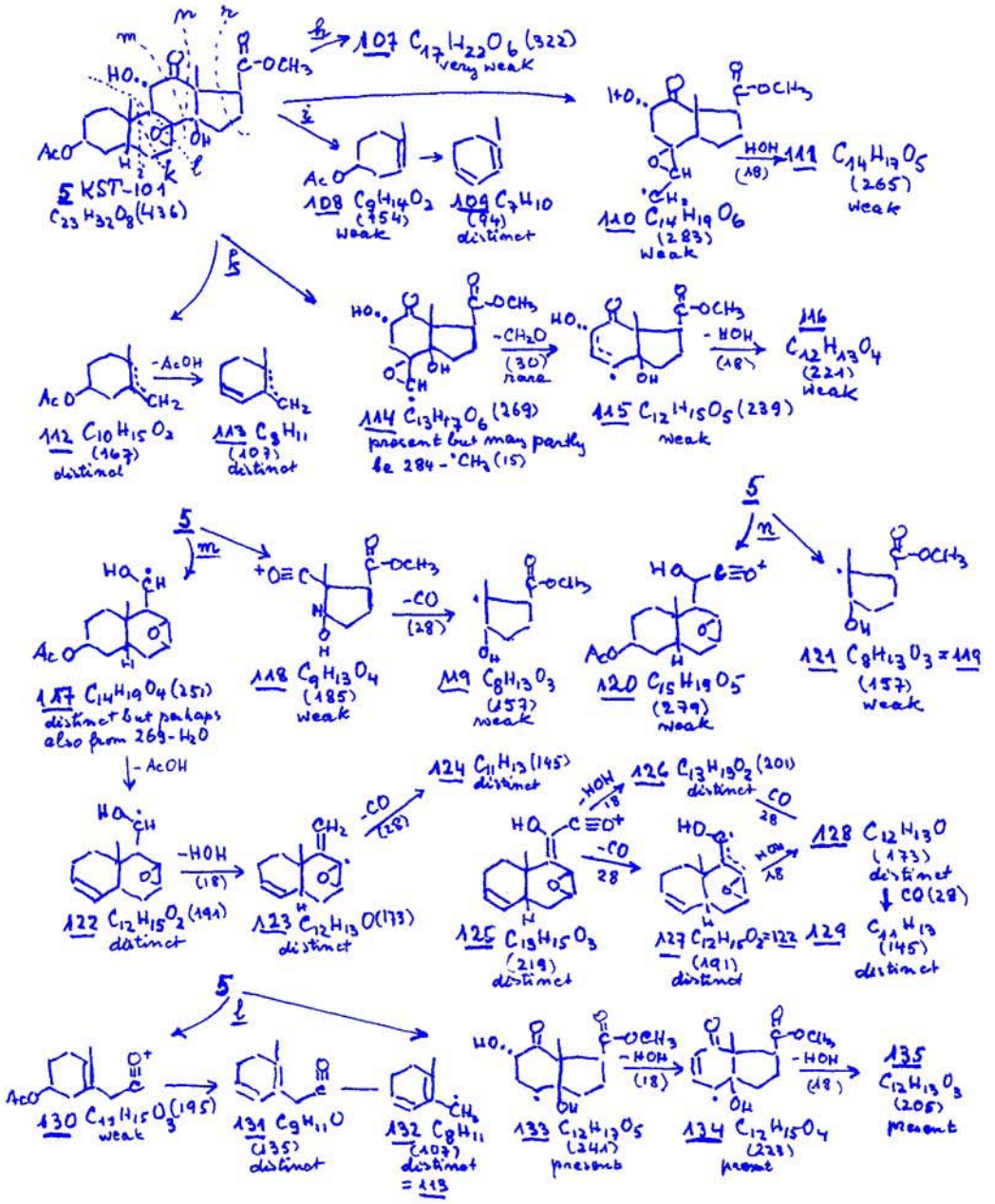

Chart VII. Attempt for a detailed analysis of observed fragments in the MS of 5

particular [42–44]. Normal loss of small units like 15 (CH_3), 18 (H_2O), 28 (CO or C_2H_4), 31 (OCH_3), 42 ($H_2C{=}C{=}O$), 60 (AcOH) is most frequent. In the spectrum of 3β-Acetoxy-14β-hydroxy-5β(H)-etianic-acid methylester (**87**) [38] [40], the first loss of 28 is $CH_2{=}CH_2$ [38] [40] [44], while in the lactone (**99**), it is mainly CO [44]. In the latter, also the loss of CO_2 (44) was observed [44], an otherwise relatively rare reaction. Special fragmentation patterns (not always explained in detail) can occur along *Pathways h,i,k,l,m,n,p,q,r*, and *s* depending on substituents. In **87**, the *Pathways h,p*, and *q* are distinct [44], while *Pathway s* is often observed in $\Delta^{8(14)}$-steroids (see *Fig. 13*). For the MS of compound **5**, an attempt was made to analyze many fragments, and tentative formulae for those are given in *Chart VII*. Their composition could not be checked by high resolution, but is mainly based on analogy to the MS of anodendroside-A [45]. The structure of this compound is most similar to that of sarverogenin (**1**), containing (most probably) only an additional C(16)=C(17) bond. A great number of fragments in the MS of anodendioride-A have been analyzed by high-resolution MS. In most of the other MS reported in this paper, only the peaks of the highest mass units are mentioned to prove the molecular composition.

3,12-Dioxo-14β-hydroxy-5β(H)-cardenolid (= Digoxigenone [35] [36], *AL-917)*. Colorless needles from Et_2O/pentane, m.p. 267–270°. ^{1}H-NMR (*R-396*): 1.19, 1.21 (*2s*, CH_3(18), CH_3(19)); 2.50* (*s*, OH); 4.19 (*dt*, H–C(17), collapsing to *t* after irr. of H–C(22) at 6.0); 4.96 (*d*, CH_2(21), collapsing to *d* (J = 4) after irr. of H–C(22) at 6.0).

3β-Acetoxy-7,8β-epoxy-12α,14β-dihydroxy-12-oxo-5β(H)-etianic-acid Methylester (**5**; *KST-101*). Prepared from the acid **4** in $CHCl_3$ with CH_2N_2 in Et_2O, gave colorless crystals from acetone/Et_2O, washed with Et_2O/pentane. M.p. 152–154°. $[\alpha]_D^{26} = +57.4° \pm 3°$ (c = 0.55, $CHCl_3$). IR: *Fig. 8*. MS: 436 (M), 418 ($M - H_2O$), 405 ($M - 31$(= OCH_3)), 400 ($M - 2\ H_2O$), 390 (418 – 28 (= CO or C_2H_4)), 387 (418 – 31(= OCH_3)), 386 (418 – 32(= CH_3OH), 376 (M – 60 (= AcOH)), 369 (400 – 31), 358 (376 – 18), 345 (405 – 60 or 376 – 31), 344 (376 – 32), 343 (358 – 15 (= CH_3)), 340 (358 – 18), 330 (358 – 28), 329 (387 – 58 (= vinyl-alcohol C (11–12)), 327 (345 – 18 or 358 – 31), 326 (344 – 18 or 358 – 32), 322 (M – 114 (= **107**)), 317 (345 – 28), 316 (344 – 28), 315 (330 – 15 or 343 – 28), 312 (330 – 18 or 340 – 28), 308 (326 – 18), 302 (330 – 28), 301 (316 – 15 or 329 – 28), 299 (327 – 28 or 330 – 31), 298 (326 – 28 or 330 – 32), 297 (312 – 15 or 329 – 32), 285 (316 – 31 or 317 – 32), 284 (302 – 18 or 316 – 32), 283 (**110**), 279 (**120**), 271 (229 – 28), 270 (285 – 15 or 298 – 28), 269 (114 and 284 – 15), 265 (**111**), 251 (**117** or 269 – 18), 241 (133). Anal. calc. for $C_{23}H_{32}O_8$ (436.48): C 63.28, H 7.39; found: C 63.32, H 7.46.

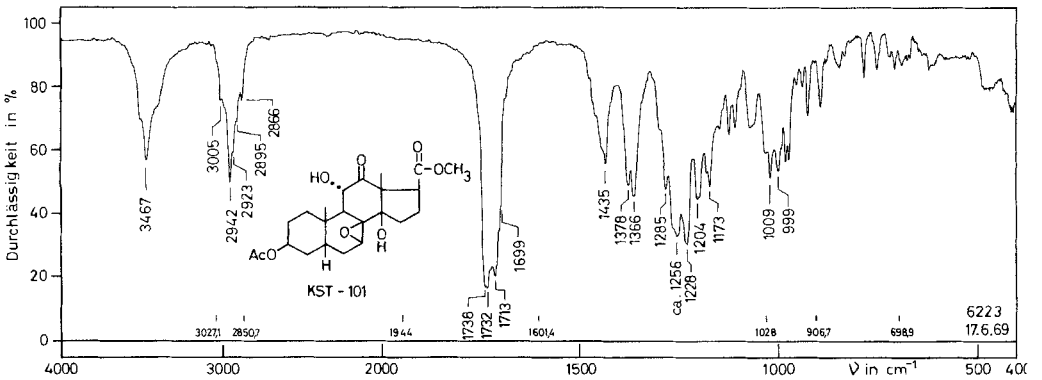

Fig. 8. *IR Spectrum of* **5** (*KST-101*; m.p. 152–4°. 0.70 mg, solid in *ca.* 300 mg KBR)

Acetylation of 20 mg of **5** with Ac_2O in pyridine gave ester **6**, m.p. 199–201°, mixed m.p. with authentic **6** without depression.

3β,11α-Diacetoxy-7,8β-epoxy-14β-hydroxy-12-oxo-5β(H)-etianic-acid Methylester (**6**; [4], *AL-955*). Acid **3** (200 mg) was dissolved in 5 ml of $CHCl_3$ and CH_2N_2 soln. in Et_2O added until the yellow color persisted. After standing ½ h, the solvent was evaporated *in vacuo*. Crystallization from aceton/Et_2O/pentane gave colorless crystals. M.p. 199–201°. IR (CH_2Cl_2): 2.83*w* (OH); *ca.* 5.80 (CO not resolved) *etc.* IR (KBr): 3.35*m*, 3.40*s*, 3.48*m* (*CH*), 5.72 (Ac), 5.79 (ester with H-bonding), 5.82 (oxo); many sharp and *s* bands up to 25. ^{1}H-NMR: *Fig. 1*.

3β,11α-Diacetoxy-7,8β-epoxy-12-oxo-5β(H)-14(15)-etienic-acid Methylester (**7** [8], *AL-944*). To the ester **5** (500 mg), m.p. 198–200°, dissolved under exclusion of moisture in 5 ml of abs. pyridine, cooled to 0°, 0.5 ml of $SOCl_2$ was added dropwise and left 16 h at 0° and 1 h at 20°. After addition of crushed ice, it was extracted with $CHCl_3/Et_2O$ 1:3. The org. layer was washed at 0° with dil. HCl and Na_2CO_3 soln., dried (Na_2SO_4), and evaporated. The crude product (475 mg) gave 354 mg of crystals; m.p. 166–168° from Et_2O/pentane. The material from the mother liquor, after chromatography (SiO_2), gave another 56 mg of similar crystals (total 410 mg). Recrystallization gave the anal. sample, m.p. 170–171°. UV (EtOH): 287 (2.179), 295 (2.132). IR (CH_2Cl_2): no band in OH region. IR (KBr): 3.329*w* (H–C(7)); 3.35*w*, 3.38*m*; 5.69*s*; 5.75 (not resolved; Ac, ester); 5.78 (keto); other *s* bands at 6.95, 7.28 (Ac), 8.12*vs* (Ac), 9.78*s*. ^{1}H-NMR (*R-400*): 1.18 (*s*, CH_3(19)); 1.42 (*s*, CH_3(18)); 2.02 (*s*, Ac); 2.17 (*s*, Ac); 2.45 (*d*, J = 13, H_α–C(9) overlapping with 2.45 (*d*, *q* H–C(16))); 2.96 (*d*, *q*, H–C(16)); 3.48 (*d*, J = 5.7, H_α–C(7)); 3.70 (*s*, MeO); 3.78 (*t*, H = 9, H_α–C(17)); 5.04 (br. *d*, H_α–C(3)); 5.49 (*d*, J = 13. H_β–C(11)).

3β,11α-Diacetoxy-7β-hydroxy-12-oxo-5β(H)-8(14)-etienic-acid Methylester (**8**; *AL-929* = OS-XVII [8]; formulated there with 7α-OH). Ester **7** (281 mg) in 10 ml of katalytically pure EtOH and 150 mg of 5% Pd on carbon [37] were shaken under H_2. After 30 min, absorption stopped, the soln. filtered, and evaporated *in vacuo*. The residue was dissolved in a little benzene/Et_2O, filtered over 20 mg of SiO_2, and the clear soln. evaporated *in vacuo*. The product (281 mg) was twice crystallized from Et_2O/pentane: 202 mg of *AL-929* as colorless needles. M.p. 162–164°. The material from the mother liquor, after chromatography, gave 13 mg additional crystals of the same m.p. *Schindler* [8] reported 169–170.5° for his *OS-XVII* but 161–163° for another sample. UV (EtOH; in 1-mm cell [20a]): 203.5 (4.03; fully substituted C(8)=C(14) bond [20a]), 280 (2.12; β,γ-unsaturated oxo group). IR (CH_2Cl_2): 2.78*m* (OH), 5.78*vs* (CO region, not well resolved).

3β,11α-Diacetoxy-7,12-dioxo-5β(H)-etienic-acid Methylester (**9**; *AL-1025*; described as *OS-XXI* [8] with assumed 15-oxo group). Our sample gave colorless plates from Et_2O/pentane, m.p. 158–160°. UV: see [8]. IR: see *Fig. 9*. ^{1}H-NMR: see *Fig. 2*. MS (*Hü 15539*): 461 (*M* + H), 460 (*M*), 447 (trace?), 445 (*M* – $^{\cdot}CH_3$), 434 (trace?), 432 (*M* – 28), 430 (*M* – 30 (CH_2O) or 445 – 15), 429 (*M* – $^{\cdot}OCH_3$), 418 (*M* – $H_2C{=}C{=}O$), 417 (432 – 15), 400 (*M* – AcOH), 390 (418 – CO or C_2H_4), 385 (400 – $^{\cdot}CH_3$), 373 (432 – 59 ($^+O{\equiv}COH_3$)), 368 (400 – 32 (CH_3OH)),

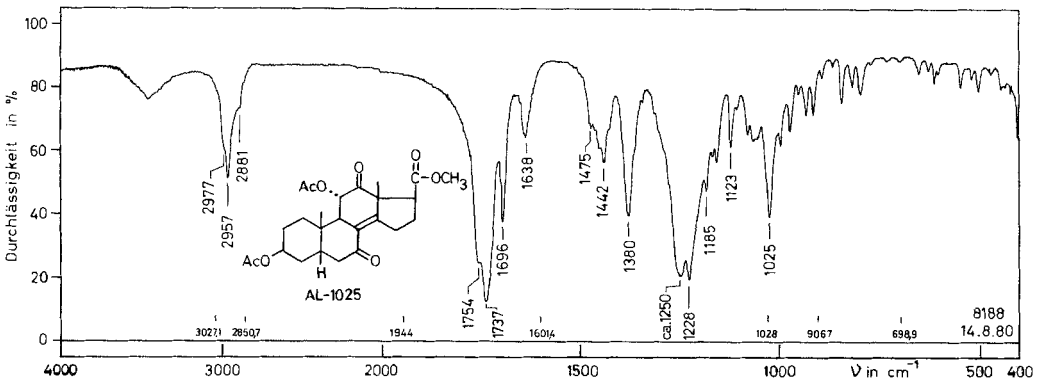

Fig. 9. *IR Spectrum of* **9** (*AL-1025*; 168°, 0.67 mg solid in *ca.* 300 mg KBr)

362 (390 – 28), 361 (390 – 29($HC{\equiv}O^+$); *m** calc. 361^2:390 = 334.16; found 334.5, perhaps partly 461 – 100 (CH_3–CO–O–CH=C=O, or CH_3–CH=CH–$COOCH_3$)); 353 (368 – 15), 341 (401 – 60), 340 (400 – 60; *m** calc. 340^2:400 = 289.00, found 289), 325 (340 – 15), 312 (340 – 28), 301 (361 – 60(AcOH or HCO–OCH_3)), 297 (312 – 15), 293 (461 – 168 (ring A + C(6)), 281 (341 – 60; *m** calc. 341^2:281 = 231.56, found 231.5), 280 (312 – 32 (CH_3OH) or 340 – 60), 253 (312 – 59 (OH_3–$C{\equiv}O^+$); *m** calc. 253^2:312 = 205.16, found 205), 235 (253 – 18), 225 (253 – 28), *etc.*

Hydrogenation of 7 with PtO_2 in AcOH and Isolation of 10, 11, 13, and 14. – Ester **7** (310 mg) and 150 mg of PtO_2 in 6 ml of AcOH were hydrogenated for 10 h, when absorption had stopped. Filtration and evaporation *in*

vacuo gave 310 mg of product which was chromatographed on 10 g of SiO_2; fractions were checked on TLC. *Fr. 2–5* eluted with benzene/Et_2O 9:1 gave 32 mg of crude **10** *(AL-1023)*, *Fr. 6–9* eluted with benzene/Et_2O 8:2 gave 137 mg of crude **11** *(AL-927)*, *Fr. 10–13* eluted with benzene/Et_2O 7:3 gave 49 mg of crude **13** *(AL-1020)*, and *Fr. 14–19* eluted with benzene/Et_2O 5:5 and pure Et_2O gave 35 mg of crude **14** *(AL-1021)*.

3β,11α-Diacetoxy-7,12-dioxo-5β,8ξ,14ξ(H)-etianic-acid Methylester (**10**; *AL-1023*). The crude product (32 mg), after re-chromatography on 4 g of SiO_2 (28 mg), gave 18 mg of crystals from Et_2O/pentane, which became opaque on heating, with m.p. 118–120°; occasionally a m.p. 150–158° was observed. $[\alpha]_D^{25} = +53.2 \pm 4°$ ($c = 0.50$, $CHCl_3$). UV (cyclohexane): 284 (1.745, oxo group). IR (CCl_4): no band in OH region, 5.72*s* (Ac, ester), 5.78*s* (ketone), *etc.* $C_{25}H_{34}O_8$ (462.52). MS: 462 (*M*), 447 (*M* – CH_3), 444 (*M* – H_2O), 431 (*M* – OCH_3), 420 (*M* – CH_2CO), 402 (*M* – AcOH), 374 (402 – C_2H_4 or CO), 360 (420 – AcOH), 342 (402 – 60), 314 (374 – 60), 286 (314 – 28), 252, *etc.*

3β,11α-Diacetoxy-12β-hydroxy-5β(H)-8(14)-etienic-acid Methylester (**11**; *AL-927*). This compound has so far not crystallized, but after re-chromatography, it was obviously relatively pure (see MS). Colorless glass, $[\alpha]_D^{21} = +37.3° \pm 3°$ ($c = 0.389$, $CHCl_3$). UV (cyclohexane): 200 (4.17; fully subst. C(8)=C(14) bond [20a]), 282.5 (2.36). IR: 2.71 (OH), 2.80–2.86 and 2.92 (OH, bonded), 5.78*s* (Ac, ester), *ca.* 5.86 (sh; Ac, bonded). ^{1}H-NMR (*R-411*): *Fig. 3*. $C_{25}H_{36}O_7$ (448.54) MS: 449 (*M* + H), 448 (*M*), 447 (*M* – H), 446, 417 (*M* – $^{\cdot}OCH_3$), 388 (*M* – AcOH), 373 (388 – $^{\cdot}CH_3$; *m** calc. 373^2:388 = 358.58, found 359), 339(?), 328 (388 – AcOH), 313 (373 – AcOH; *m** calc. 313^2:373 = 262.65, found 263), 205 (perhaps a fragment corresponding to *Pathway h* (*Chart VII*) embracing C(7)+ rings C + D (280 – AcOH – CH_3)).

3β,11α,12β-Trihydroxy-8(14)-etienic-acid Methylester (**12**; *AL-931*). Ester **11** (24 mg) in 6 ml of 3% KOH in MeOH was boiled under reflux for 3 h. After addition of 5 ml of H_2O, MeOH was removed *in vacuo*, the soln. acidified with HCl, and extracted with $CHCl_3$. The org. layer, after washing with H_2O and drying (Na_2SO_4), was evaporated *in vacuo*. The residue (18 mg) was dissolved in 0.5 ml of MeOH and treated with CH_2N_2 in Et_2O until the yellow color persisted. Evaporation *in vacuo*: 19 mg of **12** *(AL-931)* as amorphous glass. IR ($CHCl_3$): 2.73*w* (OH), 2.81–2.84*w* (br., OH, bonded), 2.91*w* (OH, bonded), 5.74 (ester), 5.88 (ester, bonded), *etc.* $C_{21}H_{32}O_5$ (364.46) MS: 364 (*M*), 346 (*M* – H_2O), 331 (346 – $^{\cdot}CH_3$), 328 (346 – H_2O), 313 (328 – $^{\cdot}CH_3$).

3β,11α-Diacetoxy-12β-hydroxy-7-oxo-5β,8ξ(H)-etianic-acid Methylester (**13**; *AL-1020*). The material (49) mg) did not crystallize, but, according to TLC, it was relatively homogenous (gave cryst. **18**). Colorless glass. $[\alpha]_D^{25} = +2.5° \pm 4°$ ($c = 0.557$, $CHCl_3$). UV (cyclohexane): no high-intensity absorption at 200 nm, 245.5 (3.0; perhaps impurity), and sh around 283. UV (EtOH): 250 (3.00), and sh at *ca.* 294 (~ 2.18).

3β,11α-Diacetoxy-7β,12β-dihydroxy-5β(H)-8(14)-etienic-acid Methylester (**14**; *AL-1021*). The material (85 mg) did not crystallize and obtained as colorless glass. $[\alpha]_D^{24} = +32.5° \pm 4°$ ($c = 0.354$, $CHCl_3$). UV(cyclohexane): 201 (3.97; fully subst. C(8)=C(14) bond), 245 (2.21), 280 (1.93; perhaps impurity). IR (CCl_4): 2.76*m* (OH), 2.81*m*, 2.9*m* (OH, bonded), 5.79*vs* (Ac, bonded), 5.85*m* (Ac and ester, bonded), 8.12*vs* (br., Ac), *etc.*

Oxidation of 14 to 9. – Ester **14** (80 mg) dissolved in 5 ml of acetone [48] was cooled to 0°, and 0.18 ml of *Kiliani*'s soln.[4]) were added dropwise under shaking. After 1 h at 0°, a soln. of 200 mg of NaOAc in 5 ml of H_2O+ ice was added, the acetone evaporated *in vacuo*, and the aq. suspension extracted with $CHCl_3/Et_2O$ 1:3. The washed and dried soln. gave, after evaporation *in vacuo*, 76 mg of crude product. Chromatography on 4 g of SiO_2 gave 60 mg of purified material, which, after crystallization from Et_2O/pentane, gave 50 mg of colorless platelets, m.p. 158–160°, according to TLC and mixed m.p., identical with material obtained from **8** and with *OS-XXI*. This is a proof for the structure of **14**.

Hydrogenation of Ester 8 Leading to the Isolation of 11 and 14. – Ester **8** (200 mg) was hydrogenated with 80 mg of PtO_2 in 5 ml of AcOH as decribed for **7**. The crude mixture (200 mg) was chromatographed on 8 g of Al_2O_3 and gave (from *Fr. 3–9*) 175 mg of **11** (*AL-927*; according to TLC identical with the above described material from **7**) and 6 mg of **14** (*AL-1021*; according to TLC identical with material from **7**).

3β,11α-Diacetoxy-12-oxo-5β(H)-8(14)-etienic-acid Methylester (**16**; *AL-928*). The crude ester **11** (175 mg *AL-927*) in 10 ml of acetone was cooled to 0°, 0.35 ml of *Kiliani's* mixture [4]) added and left 1 h at 0°. Workup as for **9** (from **14**) gave 167 mg of neutral product. From Et_2O/pentane, 90 mg of crystals, m.p. 154–157°, were obtained. The material from the mother liquor (87 mg) was re-oxidized with 0.2 ml of *Kiliani's* mixture and gave another 28 mg of cryst. **16**. From the amorphous residue (53 mg material from mother liquor), after chromatography, another

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[4]) 26.6 g CrO_3 dissolved in the cooled mixture of 40 ml water and 23 ml of conc. H_2SO_4, then filled up with water to 100 ml [49] (p. 1445).

8 mg of cryst. **16** were isolated. Total yield 126 mg. The anal. sample *AL-928* was obtained as colorless crystals. M.p. 155–157°. $[\alpha]_D^{26} = -6.3° \pm 5°$ ($c = 0.301$, $CHCl_3$). UV (cyclohexane): 205 (4.00); fully subst. C(8)=C(14) bond), *ca.* 260 (2.194), *ca.* 289 (2.02; ketone). IR(CH_2Cl_2): no OH band, 5.71 *vs* (ketone, Ac, ester, not resolved), 7.25*s* (Ac), 8.15*s* (Ac), 9.75*s*. ^{1}H-NMR: 1.16 (*s*, CH_3(19)); 1.42 (*s*, CH_3(18)); 2.05 (*s*. Ac), 2.14 (*s*, Ac); 3.05 (*d*, $J = 7.75$, H–C(9)), overlapping with 3.17 (*t*, $J = 9.5$, H–C(17)); 3.68 (*s*, CH_3 (ester)); 5.13 (*m*, H_α–C(3)); 5.65 (*d*, $J = 7.75$ H_β–C(11)) (*cf. Fig. 2* for **9**). $C_{35}H_{34}O_{29}$ (446.52). MS: 446 (*M*), 415 (*M* – $^{\cdot}OCH_3$), 402 (*M* – CO_2?), 397 (415–H_2O?) 386 (*M* – AcOH), 354 (386–CH_3OH; *m** calc. 354^2:386 = 324.65, found 325), 339 (354–$^{\cdot}CH_3$). Anal. calc. for $C_{25}H_{36}O_7 \cdot 1/2\ H_2O$: C 65.91, H 8.18; found: C 65.94, H 7.80.

3β,11α-Diacetoxy-7,12-dioxo-5β,8ξ(H)-etianic-acid Methylester (**18**; *AL-1026*). To ester **13** (*AL-1020*, amorphous, 62 mg) in 5 ml of acetone at 0°, 0.12 ml of *Kiliani's* mixture[4]) was added and, after shaking, left for 1 h at 0°. Another 0.1 ml of *Kiliani's* mixture added and this repeated four times at hourly intervals. Workup as described for **9** (from **14**) gave 50 mg of crude neutral product. After chromatography on 4 g of SiO_2, the *Fr.* eluted with benzene/Et_2O (34 mg) gave from Et_2O/pentane 22 mg of crystalline ester **18**, m.p. 176–184°, and after recrystallization 16 mg of anal. sample *AL-1026* as colorless prisms. M.p. 182–185°. $[\alpha]_D^{25} = -4.9° \pm 3°$ (c=0.325, $CHCl_3$). UV(EtOH): no high-intensity absorption, 251 (2.766). IR (CCl_4): no band in OH region, 5.70*s*, 5.79*vs* (Ac and ester), 5.81*s* (ketone), 7.23*s*, 8.0*vs*, 8.11*vs* (Ac), 9.76–9.80 (Ac). $C_{25}H_{34}O_8$ (462). MS: 462 (*M*), 447 (*M* – $^{\cdot}CH_3$), 434 (*M* – 28), 431 (*M* – $^{\cdot}OCH_3$), 402 (*M* – AcOH), 314 (374 – AcOH), 342.

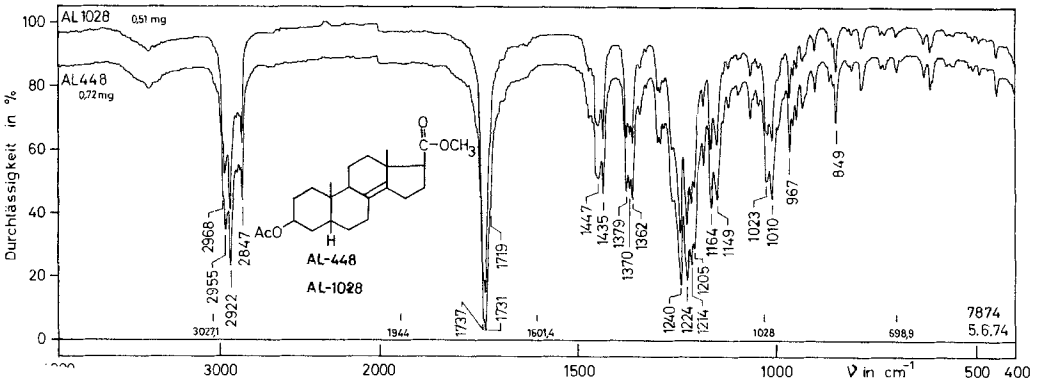


Fig. 10. *IR Spectrum of* **19** (*AL-448*; from digitoxigenin) *and* AL-1028 (from sarverogenin; *ca.* 5% displaced to lower transmittance, solid in *ca.* 300 mg KBr)

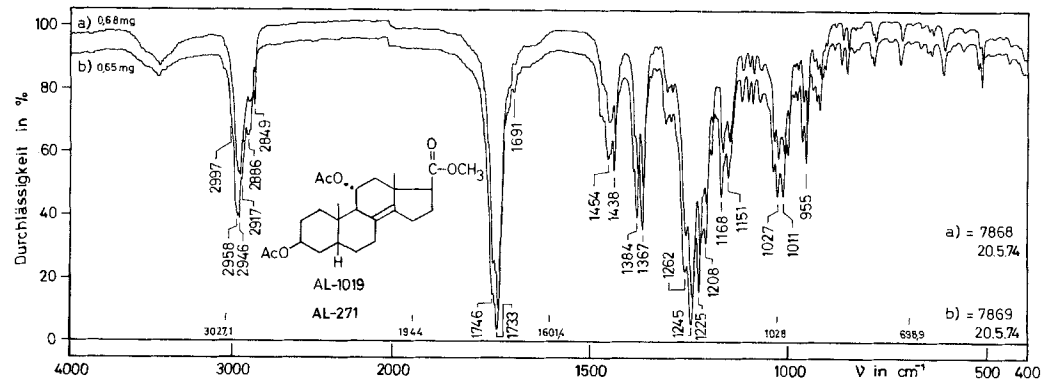


Fig. 11. *IR Spectrum of* **20** (*AL-199*; from sarverogenin) *and* AL-271 (from sarmentogenin; *ca.* 5% displaced to lower transmission, solid in *ca.* 300 mg KBr)

3β,12α-Diacetoxy-12,12-dithiolano-5β(H)-8(14)-etienic-acid Methylester (**15**; *AL-1027*). Compound **16** (69 mg) was dissolved in 2 ml of dry ethanedithiol, the soln. cooled to 0° and, with exclusion of moisture, a slow stream of dry HCl gas was bubbled through it. After standing 16 h at 5°, again HCl was passed at 0° for 3 h. Aq. Na_2CO_3 with ice and $CHCl_3/Et_2O$ 1:3 were added, the org. layer washed several times with 5% NaOH and H_2O, dried (Na_2SO_4), and evaporated. The product (84 mg) gave from Et_2O/pentane 30 mg of ester **15**. M.p. 245–260°. The material from the mother liquor (54 mg) and 25 mg of fresh ester **15** were together treated as above and gave another 17 mg of crystals. Recrystallization from Et_2O/pentane gave the anal. sample *AL-1027*. M.p. 264–268°, $[\alpha]_D^{25} = +3.5 \pm 3°$ (c=0.366, $CHCl_3$). $C_{27}H_{38}O_6S_2$ (522.71) which contained a trace of impurity of $C_{27}H_{36}O_7S_2$ (536). MS: *Fig. 12*.

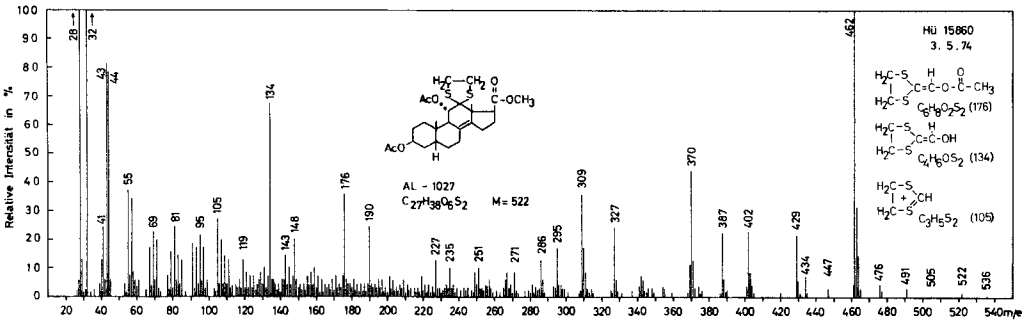


Fig. 12. *MS of* **15** (*AL-1027*; m.p. 264, from sarverogenin; tentative assignment: main compound $C_{27}H_{38}O_6S_2$ (522), 536 (trace impurity, $C_{27}H_{36}O_7S_2$), 522 (M), 505 (trace, 536 – OCH_3), 491 (M – OCH_3), 476 (trace, 536 – AcOH), 462 (M – AcOH), 447 (462 – CH_3), 434 (462 – 28; m* 408), 429 (462 – SH), 402 (462 – AcOH, m* 349.5), 387 (402 – CH_3 or 429 – CH_2=C=O), 370 (462 – $C_2H_4S_2$), 327 (387 – C_2H_4S or 387 – $COOCH_3$ – H), 309, 295, 286 (462 – $C_6H_8O_2S_2$), 176 ($C_6H_8O_2S_2$), 148 (176 – C_2H_4), 134 (176 – CH_2=C=O), 105 ($C_3H_5S_2$), 43 ($CH_3C{\equiv}O^+$), 32 (S), 28 (C_2H_4 and CO); fragment 176 ($C_6H_8O_2S_2$) corresponds to *retro-Diels-Alder* elimination of C(11)–C(12))

3β,12α-Diacetoxy-12,12-dithiano-5β(H)-8(14)-etienic-acid Methylester (**17**; *AL-1024*). Compound **16** (70 mg) in 2 ml of propane-1,3-dithiol were treated as for **15**. The crude product (73 mg) gave 27 mg of crystals. M.p. 220–228°. The anal. sample *AL-1024* showed m.p. 228–234°. $[\alpha]_D^{24} = +1.7° \pm 3°$ (c = 0.346, $CHCl_3$). $C_{28}H_{40}O_6S_2$ (536.74). MS: *Fig. 13*.

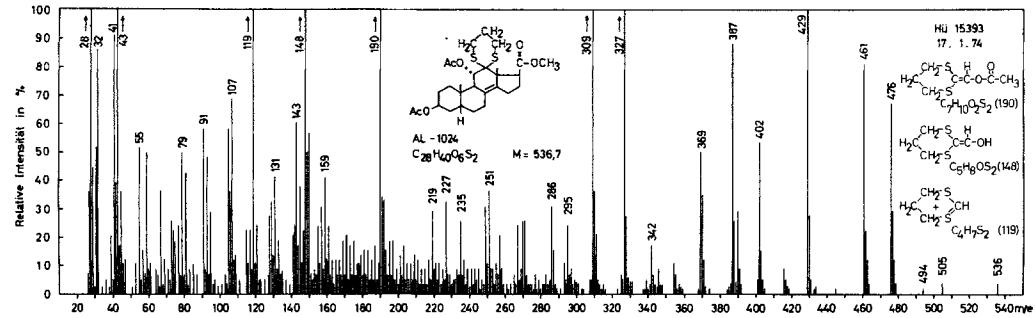


Fig. 13. *MS of* **17** (*AL-1024*; m.p. 228°, from sarverogenin; tentative assignment: 536 (M), 505 (M – OCH_3), 494 (M – CH_2=C=O), 476 (M – AcOH), 461 (476 – CH_3), 429 (476 – CH_2 – SH), 402 (476 – C_3H_6S), 387 (429 – 42, m* 349), 369 (429 – AcOH), 327 (387 – $COOCH_3$ – H or 387 – C_2H_4S), 309 (369 – $COOCH_3$ – H or 369 – C_2H_4S), 286 (476 – $C_7H_{10}O_2S_2$), 190 ($C_7H_{10}O_2S_2$), 148 (190 – CH_2=C=O, m* 115), 119 ($C_4H_7S_2^+$), 43 ($CH_3 - C{\equiv}O^+$), 32 (S), 28 (C_2H_4 and CO); fragment m/z 190 ($C_7H_{10}O_2S_2$) corresponds to *retro-Diels-Alder* elimination of C(11)–C(12))

3β-Acetoxy-5β(H)-8(14)-etienic-acid Methylester (**19**; *AL-1028*) *and 3β,11α-diacetoxy-5β(H)-8(14)-etienic-acid Methylester* (**20**; AL-1019) *from* **15**. Ester **15** (44 mg) and the *Raney*-Ni from 2 g of Al-Ni alloy suspended in 5 ml MeOH were shaken under H_2 for 16 h at 20°. The soln. was filtered, the residue washed with $CHCl_3$, and the soln. evaporated *in vacuo*. The residue dissolved in $CHCl_3/Et_2O$ 1:3 was washed with dil. HCl and Na_2CO_3, dried (Na_2SO_4), and evaporated. The crude product (33 mg) was united with a former batch (8 mg) and chromatographed on 4 g of SiO_2. The *Fr. 1* eluted with benzene/Et_2O (9 mg) gave from MeOH at −15° 4 mg of crystalline *AL-1028* (**19**), and the later fractions (13 mg) gave from MeOH at −15° 8 mg of cryst. *AL-1019* (**20**), m.p. 165–170°.

Identification of AL-1028 (**19**). The crystals (4 mg) were united with a second batch (5 mg) and recrystallization from Et_2O/pentane gave 3.5 mg of anal. sample of m.p. 118–120°. $[\alpha]_D^{25} = +83.0° \pm 5°$ ($c = 0.265$, $CHCl_3$), the mixed m.p. with authentic material *AL-448* from digitoxigenin [20] gave no depression. According to MS, the sample still contained a trace of putative $C_{23}H_{32}O_5$(388) as impurity. MS: 388 (trace), 374 (*M*), 359 (*M* − $^{\cdot}CH_3$), 343 (*M* − $^{\cdot}OCH_3$), 328 (trace, 388 − AcOH), 314 (374 − AcOH; *m** calc. 314^2:374 = 263.63, found, 264), 299 (314 − $^{\cdot}CH_3$; *m** calc. 299^2:314 = 284,72, found 285), 239, 213 (299 − 86 (**94** in *Chart VI*), 206 ($C_{13}H_{18}O_2$ CH_2(7) + rings C + D)), 147. Authentic material *AL-448* (without trace of impurity) gave, except of this, a virtually identical MS. The IR spectra (*Fig. 10*) were indistinguishable.

Identification of AL-1019 (**20**). The anal. sample crystallized from Et_2O/pentane had m.p. 167–170°, $[\alpha]_D^{25} = +41.1° \pm 5°$ ($c = 0.277$ in $CHCl_3$), the mixed m.p. with authentic material (*AL-271* from sarmentogenin [20a]) gave no depression. $C_{25}H_{36}O_6$ (432.55). MS: no $M^{+\cdot}$, 403 (0.3, 432-29 (HC≡O^+)), 388 (2, *M* − 44 (CO_2 or CH_3CHO), 386 (0.3, *M* − 46 (1.3%?)), 357 (5, 372 − 15 ($^{\cdot}CH_3$)), 354 (0.5, 372 − 18), 341 (1.2, 372 − 31 ($^{\cdot}OCH_3$)), 330 (1, 372 − 42 (CO or CH_2=CH_2)), 312 (48, 372 − 60; *m** calc. 312^2:372 = 261.68, found 262) 297 (100, 312 − 15), 281 (5, 312 − 31), 271 (6.6?), 269 (4.5, 297 − 28), 265 (28, 297 − 32), 258 (60, 312 − 54 (*retro-Diels-Alder*), 237 (50, 265 − 28 or 297 − 60), 226 (66, 312 − 86 (**94**) or vinyl acetate from C(11-12)), 211 (100, 226 − 15), 189 (28), 145 (40), 129 (38), 107 (30), 105 (28), methyltropylium ion), 81 (31, tropylium ion), 87 (31), 79 (23), 67 (20), 55 (22, CH_2=CH−C≡O^+), 43 (89, CH_3−C≡O^+), 32 (62), 28 (89). The authentic material *AL-271* (from sarmentogenin [20a]) contained a trace of impurity giving a peak at *m/z* 448 (1% intensity, perhaps $C_{25}H_{36}O_7$, probably the 8,14-epoxide from which it was prepared [20a]) but gave otherwise a virtually identical MS: The IR spectra (*Fig. 11*) were indistinguishable.

3β,12α-Dihydroxy-7,11-dioxo-5β,8ξ,9ξ(H)-etianic-acid Methylester (**22**; *A-1036*). Ester **18** (12 mg) in 4 ml of 5% KOH in MeOH were boiled under reflux for 1 h. After addition of 1 ml of H_2O, MeOH was removed *in vacuo*, the aq. soln. acidified with HCl, and extracted with $CHCl_3/Et_2O$ 1:3. The washed and dried org. layer, after removing solvent *in vacuo*, gave 9.5 mg of residue, which was then methylated with CH_2N_s in Et_2O. Crystallization from acetone/Et_2O gave 2.5 mg of **22** as colorless needles. M.p. 225–228°.

12β-Hydroxy-3,7,11-trioxo-5β,8ξ,9ξ(H)-etianic-acid Methylester (**27**; *AL-1037*) *from* **22**. Ester **22** (9 mg; crystals + material from mother liquor) was dissolved in 2 ml of acetone, cooled to 0°, and, after addition of 0.15 ml of *Kiliani's* mixture[4]), left 20 min at 0°. Workup as described for **9** gave 7.5 mg of crude, partly crystalline product. After chromatography on 2 g of SiO_2, 2.5 mg of *AL-1037* were obtained as colorless needles. M.p. 210–220°. According to MS, *AL-1037* was still a mixture; apart from a trace impurity, it contained some 3,7,11,12-tetraoxo-ester ($C_{21}H_{26}O_6$=374). The main constituent was $C_{21}H_{28}O_6$ (376) (**27**). MS (approximate intensities in relation to *m/z* 330 (100%)): 502 (1), 442 (0.5) (impurities), 377 (6, *M* + H), 376 (3, *M*), 374 (1.6, tetraoxo, M_2), 368 (2, impurity), 348 (16, *M* − CO or C_2H_4), 345 (45, *M* − OCH_3), 330 (100, 348 − H_2O; *m** calc. 330^2:348 = 312.93, found 312), 316 (40, 348 − CH_3OH), 298 (25, 316 − H_2O, *m** 281.03), 208, 180.

7α-Acetoxy-3α-tosyloxy-12-oxo-5β(H)-etianic-acid Methylester (**24**; *AL-1029*). Ester **23** (211 mg; m.p. 212–219° [21a]) and 350 mg of TsCl, both dried at 0.1 Torr and 40° for 2 h, were dissolved in 4 ml of abs. pyridine and left in the dark under exclusion of moisture 60 h at 20°. After addition of 1 g of ice, it was left for 1 h at 20° to hydrolize excess of TsCl. Extraction with $CHCl_3/Et_2O$ 1:3, washing with dil. HCl, Na_2CO_3 and H_2O, drying, and evaporating gave 274 mg of crude product, from Et_2O/pentane: 253 mg colorless needles, m.p. 177–179°. $[\alpha]_D^{26} = +85.5°$ (c=0.467, $CHCl_3$).

3β,7α-Diacetoxy-12-oxo-5β(H)-etianic-acid Methylester (**25**; *AL-1030*) *and By-products* **21** (*AL-1034*) *and* AL-1032 *from* **24**. Water-free K-acetate (550 mg) were liquified with 0.31 ml of H_2O by warming, mixed with 1.6 ml of Ac_2O the soln. of 260 mg of **24** in 7.5 ml of warm DMF added, and the mixture kept at 110–115° for 7 h. After cooling, H_2O was added and the product extracted with $CHCl_3/Et_2O$ 1:3. Washing with dil. HCl, Na_2CO_2, and H_2O, drying, and evaporation gave 180 mg of crude mixture. It was chromatographed on 8 g of SiO_2. *Fr. 3–5* (eluted with benzene/Et_2O 9:1): 21 mg of crude ester **21** (*AL-1034*). The *Fr. 6–9* (eluted with benzene/Et_2O 9:1 and 8:2): 84 mg of eluate and from Et_2O/pentane 71 mg of **25** (*AL-1030*), m.p. 173–174°. The *Fr. 11–12* (eluted with fresh Et_2O): 65 mg of eluate and from acetone/Et_2O *AL-1032* as fine needles. M.p. 216–218° (not further investigated).

Putative 7α-Acetoxy-12-oxo-5β(H)-2(3)-etienic-acid Methylester (**21**; *AL-1034*). After recrystallization from Et_2O/pentane, we obtained long needles, m.p. 215–219°. $[\alpha]_D^{27} = +93.2 \pm 5°$ ($c = 0.279$, $CHCl_3$). $C_{23}H_{23}O_5$ (388.48).

MS: 389 (8, M + H), 388 (10, M), 373 (20, $M - {}^{\cdot}CH_3$), 357 (100, $M - {}^{\cdot}OCH_3$ (31)), 346 (76, M – 42), 328 (48, 346 – H_2O), 314 (14, 346 – CH_3OH), 296 (28, 328 – CH_3OH; m^* calc. 296^2:328 = 267.12, found 267), 274 (100, 328 – 54(C_4H_6 *retro-Diels-Alder*)), 167 (100), 105 (50).

3β,7α-Diacetoxy-12-oxo-5β(H)-etianic-acid Methylester (**25**; *AL-1030*). The anal. sample was obtained from Et_2O/pentane as thick needles, m.p. 175–177°. $[\alpha]_D^{24}$ = +87.6° (c = 0.593, $CHCl_3$). $C_{25}H_{36}O_7$ (448.54). MS: 449 (0.4, M + H), 448 (0.5, M), 433 (3.3, $M - {}^{\cdot}CH_3$), 417 (7.2, $M - {}^{\cdot}OCH_3$), 388 (7.2, M – AcOH), 373 (7.2, 388 – ${}^{\cdot}CH_3$), 357 (7.8, 388 – ${}^{\cdot}OCH_3$), 341 (2.6, 356 – ${}^{\cdot}CH_3$), 328 (100, 388 – AcOH; m^* calc. 328^2:388 = 277.20, found 277), 313 (19, 328 – ${}^{\cdot}CH_3$), 310 (100, 328 – H_2O; m^* calc. 310^2:328 = 292.99, found 293), 296 (26, 328 – CH_3OH; m^* calc. 296^2:328 = 267.12, found 267), 281 (14, 296 – ${}^{\cdot}CH_3$), 274 (31, 328-54 (*retro-Diels-Alder*)), 268 (296 – CO).

Putative 3β,7α,12β-Trihydroxy-11-oxo-5β(H)-etianic-acid Methylester (**26**; *AL-1036*). Ester **25** (58 mg, *AL-1030*) was dissolved in 2 ml of AcOH, 0.005 ml of 33% dry HBr in AcOH and 3 times 8 mg of Br_2 were added. The first two portions lost their color after 8–10 min; after the third addition, the soln. still remained slightly brown after 1 h. It was diluted with $CHCl_3/Et_2O$ 1:3 washed at 0° as usual, dried, and evaporated *in vacuo*. The amorphous product (69 mg) was mixed with 2 ml of 10% KOH in MeOH and boiled under reflux for 1 h. Processing as for **22** gave 48 mg of crude acid which was methylated with CH_2N_2 in $CHCl_3/Et_2O$. Crystallization from acetone/Et_2O gave 31 mg of *AL-1031* (**26**) of m.p. 208–212°. The anal. sample consisted of colorless grains, m.p. 212–215°. $[\alpha]_D^{25}$ = 38.1° ± 5° (c = 0.271, $CHCl_3$). $C_{21}H_{38}O_6$ (380.46). MS: 394 (1, impurity), 380 (100, M), 365 (3, $M - {}^{\cdot}CH_3$), 362 (16, $M - H_2O$), 349 (3, $M - {}^{\cdot}OCH_3$), 334 (32, 362 – CO or C_2H_4), 316 (41, 334 – H_2O), 288 (47, 316 – CO or C_2H_4), 225 (57, *Pathway 1*) in *Chart VII*: rings C + D ($C_{12}H_{17}O_4$)), 208 (80), 193 (22, 225 – CH_3OH).

12β-Hydroxy-3,7,11-trioxo-5β,8ξ,9ξ(H)-etianic-acid Methylester (**27**; *AL-1035*) *from Cholic Acid* via **26**. To **26** (50 mg, *AL-1031*) dissolved in 3 ml of acetone at 0°, 0.6 ml *Kiliani*'s mixture (containing 78 mg CrO_3) were added and kept 20 min. at 0°. Processing as usual gave 43 mg of neutral product. Crystallization from acetone/Et_2O gave 10 mg of **27**. M.p. 212–215°. The material from the mother liquor (33 mg) was chromatographed on 2 g of SiO_2. The *Fr. 1* eluted with benzene/Et_2O up to 20% of Et_2O gave 9 mg of solid which yielded needles from acetone/Et_2O, m.p. 243–248°, which according to TLC and mixed m.p. were identical with 3,7,12-trioxo-5β(H)-etianic-acid methylester (**62**) [29], a product obviously derived from unbrominated **25** in the reaction sequence. The following fractions (eluted with benzene/Et_2O 7:3) gave 12 mg of solids, and from these 9 mg of more **27** as crystals, m.p. 210–218°. The anal. sample *AL-1035* consisted of long needles, m.p. 212–216°. $[\alpha]_D^{17}$ = +7.1° ± 5° (c = 0.231, $CHCl_3$). The mixed m.p. with *AL-1037* (material from sarverogenin) gave no depression, and the TLC showed the same mobility. UV (EtOH): no high-intensity absorption, 273 (2.134, oxo groups). IR ($CHCl_3$): 2.87*w* (br., OH), 5.81*vs* (br., oxo groups, ester not resolved). According to MS (see below), the main constituent of *AL-1035* was $C_{21}H_{28}O_6$ (376.43) (**27**), but it also contained some 3,7,11,12-tetraoxo-ester ($C_{21}H_{26}O_6$ = 374 = M_2) and a little 3,7,12-trioxo-ester **62** ($C_{21}H_{28}O_5$ = 360 = M_3) mentioned above. MS: 377 (4.5, M + H), 376 (3, M), 374 (10, M_2), 360 (25, **62**, M_3), 348 (20, M – CO or C_2H_4), 345 (45, $M - CH_3$), 330 (100, 348 – H_2O; m^* calc. 312.93, found 313), 316 (40, 348 – CH_3OH), 298 (316 – H_2O; m^* calc. 281.03, found 281), 208, 190, *etc.* Aside of the weak peak at m/z 360 (=M_3), the spectrum was virtually identical (including all small peaks not mentioned here) with the MS of *AL-1037* (**27** from sarverogenin).

Compounds Presented in *Chart II.* – *3β,11α-Diacetoxy-7α-bromo-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid Methylester* (**28**; *AL-981*). To the Ester **6** (103 mg) in 1 ml of abs. $CHCl_3$ and 4 ml of dry AcOH, 1 ml 30% HBr/AcOH at 0° was added and left 10 min at 0°. After addition of $CHCl_3/Et_2O$ 1:3, it was washed at 0° with NaOAc soln. and H_2O, dried, and evaporated *in vacuo*. The residue (117 mg) gave 100 mg of crystalline **28**, from Et_2O pentane, m.p. 132–136°. Anal. calc. for $C_{25}H_{35}BrO_9$ (559.45): Br 14.28; found: Br 13.83.

3β,11α-Diacetoxy-7α-chloro-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid Methylester (**29**; *AL-1013*). Prepared as **28** but with dry HCl gas passing the soln. in $CHCl_3$/AcOH. Colorless crystals were obtained from Et_2O/pentane, m.p. 168–170°. IR(KBr): 2.81*w* (OH), 2.86*m* (OH), 2.94 – 7m (br., OH, bonded), 5.71*s* (CO of Ac), 5.76*s* (CO of Ac), 5.89*s* (CO of ester, bonded), 7.27*m*, 8.05*vs* (Ac), 9.75*m*, *etc.* $C_{25}H_{35}O_9Cl$(514). MS: 514 (9, with Cl, M), 496 (0.3 with Cl, $M - H_2O$), 478 (8, no Cl, M – HCl), 472 (5, with Cl, $M - CH_2 = C = O$), 460 (4, no Cl, 478 – 18), 454 (9, with Cl, 472 – 18 or M – 60), 447 (6, no Cl, 478 – ${}^{\cdot}OCH_3$), 436 (5, with Cl (?), 454 – 18 or 478 – 42), 418 (25, no Cl, 478 – 60), 412 (7, with Cl, 454 – 42 or 472 – 60), 401 (13, no Cl, 418 – ${}^{\cdot}OH$ or 436 – Cl(35)), 400 (17, no Cl, 418 – 18), 394 (14, no Cl, 454 – 60 or 412 – 18 (?)), 390 (12, no Cl, 418 – 28), 376 (9, 394 – 18), 372 (10, 390 – 18), 368 (7, 412 – CO_2(44)), 359 (11, Cl possible, M + H – 156 (ring C) (?)), 358 (27, no Cl, 418 – 60 or 514 – 156 (?)), 341 (11, Cl possible, 359 – 18), 340 (24, 358 – 18), 330 (15, 358 – 28), 312 (14, 330 – 18), 298 (13, Cl not excluded, 340 – 42 or 358 – 60 or 454 – 156), 284 (9, 312 – 28), 281 (15, 312 – ${}^{\cdot}OCH_3$ (31), 264 (24, 312 – 28), 263 (100, 298 – 35?), 214 (43), 203 (60, 263 – 60; m^* calc. 203^2:263 = 156.69, found 157), 156 (100 $C_8H_{12}O_3$ (ring C)), 97 (102), 93 (40), 79 (45), 55 (40, $CH_2 = CH - C{\equiv}O^+$), 43 (90, $CH_3 - C{\equiv}O^+$), 41 (40), 36 (24, HCl).

3β,11α-Diacetoxy-8β,14β-dihydroxy-12-oxoetianic-acid Methylester (**30**, *AL-980*). To 358 mg of **28** in 5 ml AcOH, 400 mg of NaOAc and 400 mg of Zn dust were added and shaken at 20° for 1 h. The suspension was diluted with $CHCl_3/Et_2O$ 1:3, filtered, the filtrate washed with ice – H_2O, dil. HCl, Na_2CO_3 soln. and H_2O, dried (Na_2SO_4), and evaporated *in vacuo*. The product (279 mg) was a mixture and chromotographed on 10 g of SiO_2. *Fr. 6–10* (eluted with benzene/Et_2O 9:1): 84 mg of crude eluate yielding 66 mg of crystalline **30** of m.p. 195–201°. *Fr. 11–15* (eluted with benzene/Et_2O 8:2 and 7:3; total 152 mg) gave from Et_2O/pentane 113 mg of crystalline **6**, m.p. 190–195°. The anal. sample of **30** (*AL-980*) had m.p. 201–203°. $[\alpha]_D^{25} = -63.4° \pm 3°$ ($C = 0.497$, $CHCl_3$). UV (EtOH): 283 (1.72). ^{1}H-NMR: *Fig. 4*. $C_{25}H_{36}O_9$ (480.54). MS: 481 (M + H), 480 (M), 463 (462 + H), 462 ($M - H_2O$), 445 (463 – H_2O), 431 (462 – OCH_3), 420 (480 – AcOH), 402 (420 – H_2O), 360 (420 – AcOH), 342 (360 – H_2O), 264 (420 – 156 (ring D, $C_8H_{12}O_3$; m^* calc. $264^2:420 = 165.94$, found 166), 256, 214, 204 (264 – AcOH; m^* calc. $204^2:264 = 157.63$, found 157.5), 156 ($C_8H_{12}O_7$ (ring D)), 108 (*vs.*).

3β,11α-Diacetoxy-12-oxo-8β,14β-thionylenedioxy-etianic-acid Methylester (**31**; *AL-983*). To 15 mg of **30** in 0.3 ml of abs. pyridine, 0.05 ml $SOCl_2$ were added at 0° and left 4 h at 5°. Usual workup gave 15.5 mg of neutral product, and from Et_2O 12 mg of crystalline **31**, m.p. 235–238°. Anal. calc. for $C_{25}H_{34}O_{10}S$ (526.59): S 6.09; found: 5.94.

3β,11α-Diacetoxy-7α-formyloxy-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid Methylester (**33**; *AL-945*) *and By-product* **32** (*AL-956*). Ester **6** (60 mg) in 2 ml of HCOOH was warmed to 80° for 1 h and then boiled under reflux for a further h. Workup with ice, H_2O, and $CHCl_3/Et_2O$ 1:3, washing at 0° gave 66 mg of neutral product, and from Et_2O/48 mg of crystalline **33**, m.p. 220–223°. The 18 mg of amorphous foam from the mother liquor were united with 38 mg of similar material from a second batch (total 56 mg) and chromatographed on 4 g of SiO_2. *Fr. 2–3* (eluted with benzene and benzene/Et_2O 9:1) gave 5 mg of crystalline **32** (*AL-959*), m.p. 180–185°. *Fr. 4–6* gave some more **33**.

Compound **32** *(AL-959, By-product)* M.p. 180–185°. UV (EtOH): 284 (1.840 ketone), no high-intensity maximum about 200 nm. Not further investigated.

Compound **33** (*AL-945*). M.p. 220–223°. $[\alpha]_D^{27} = +42.4 \pm 3°$ ($c = 0.542$, $CHCl_3$). UV (EtOH): 280 (1.64). IR (CH_2Cl_2): 2.82*w* (sharp, OH), 2.92–3.01*w* (br. OH, bonded), 5.73*s* (Ac not bonded), 5.81*vs* (ester, formyl, Ac bonded), 5.87*s* (ketone), 7.35*s* (Ac), 8.15*vs* (Ac), 8.51 and 8.58*vs* (formyl), 9.81*s*. ^{1}H-NMR: *Fig. 5*. $C_{25}H_{36}O_{11}$ (524.55). MS: 525 (0.6, M + H), 524 (16, M), 510 (0.05, 525 – $^{\cdot}CH_3$(15)), 507 (0.17, 525 – H_2O(18)), 506 (0.15, M – 18), 496 (0.16, M – CO or $CH_2 = CH_2$ (28)), 482 (30, $M - H_2C = C = O$(42); m^* calc. $482^2:524 = 443.37$, found 443), 478 (0.8, M – HCOOH (46)), 475 (0.3), 464 (5, M – AcOH (60)), 461 (0.5, 478 – $^{\cdot}OH$ (17)), 460 (0.3, 478 – 18), 447 (18, 464 – 17), 446 (16, 464 – 18), 433 (0.3, 461 – 18), 432 (0.3, 460 – 18), 429 (0.7, 447 – 18), 422 (35, 464 – 42), 419 (35, 447 – 28), 418 (10, 464 – 46), 404 (6.2, 464 – 60), 401 (2.2, 447 – 46), 400 (2.8, 446 – 46), 390 (5, 418 – 28), 387 (2.5, 418 – $^{\cdot}OCH_3$(31), 386 (2.8, 418 – CH_3OH (32)), 372 (2.5, 418 – 46 or 400 – 28 or 390 – 18), 369 (1.5, 400 – 31), 358 (12, 418 – 60 or 404 – 46), 343 (1.7, 358 – 15), 340 (3.8, 358 – 18), 330 (3.8, 358 – 28), 327 (3.2), 308 (3.8), 263 (112), 203 (62), 156 (98, ring D), 97 (75), 93 (20), 79 (28), 55 (15, $CH_2{=}CH{-}C{\equiv}O^+$), 43 (75, $CH_3{-}C{\equiv}O^+$).

3β,11α-Diacetoxy-7α,8β,14β-trihydroxy-12-oxo-5β(H)-etianic-acid Methylester (**34**; *AL-958*). Ester **33** (40 mg) in benzene/Et_2O 1:1 was poured on a column of 4 g of Al_2O_3 (activity II) and left for 8 h at 20°. Elution with $CHCl_3$ gave 35 mg of eluate which yielded 21 mg of crystals, m.p. 160–170°. The anal. sample showed m.p. 169–171° (not further investigated).

3β,7α,11α-Triacetoxy-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid Methylester (**35**; *AL-922*). Ester **34** (25 mg, *AL-958*) in 0.4 of abs. pyridine and 0.2 ml Ac_2O were kept 14 h at 20° and warmed to 70° during 4 h. Addition of $CHCl_3/Et_2O$ 1:3, ice and H_2O, washing the org. layer with dil. HCl, Na_2CO_3 soln., and H_2O gave 27 mg of neutral product, m.p. 150–153°. The same product could be obtained in poor yield from **6** (300 mg) in 12 ml dioxane + 3 ml 40% H_2SO_4/H_2O (*w*/*w*) 4 days at 38°. Addition of ice/H_2O, extraction with $CHCl_3$, washing with H_2O, drying, and evaporation *in vacuo* gave 222 mg of crude product (mixture). It was treated with CH_2N_2 in Et_2O and then acetylated with Ac_2O in pyridine. Chromatography on 8 g of SiO_2 gave 123 mg of foam (crude **35**) from *Fr. 3–6* (eluted with benzene/Et_2O 85:15) and 100 mg of **6** from further *Fr.* eluted with Et_2O. After re-chromatography of the foam, 33 mg of crystalline **35** were obtained, m.p. 150–153° (*AL-922*). $[\alpha]_D^{25} = +9.3° \pm 5°$ ($c = 0.183$, $CHCl_3$). It may have been not quite pure.

3β,7α,11α-Triacetoxy-8β,14β-thionylenedioxy-12-oxo-5β(H)-etianic-acid Methylester (**36**; Al-938). To 40 mg of **35** in 0.4 ml abs. pyridine, 0.1 ml of $SOCl_2$ was added and kept at 0° for 3 h. Processing as for **31** gave 40 mg of crude product, and from Et_2O 24 mg of crystals, m.p. 208–210°. UV (EtOH): no high-intensity absorption. Anal. calc. for $C_{27}H_{36}O_{12}S$(584.63): C 55.46, H 6.21, S 5.48; found: C 55.51, H 6.58, S 5.67.

3β-Acetoxy-7,8β-epoxy-11,12-dioxo-14β-hydroxy-5β(H)-etianic-acid Methylester (**37**; *AL-871*). To 720 mg of **5** in 4 ml of AcOH, 10 ml of a 2% CrO_3 soln. in AcOH were added at 5° in 8 portions every 5–10 min under shaking

and then left for another 2 h at 10°. Dilution with ice and H_2O and workup with $CHCl_3/Et_2O$ 1:3 at low temp. gave 685 mg of crude neutral product, and from Et_2O/pentane 476 mg of pale yellowish (nearly colorless) crystals): **37**, m.p. 174–176°. $[\alpha]_D^{26} = +88.3° \pm 3°$ ($c = 0.412$, $CHCl_3$). UV (EtOH): 284 (1.880), 390 (1.36). MS: 434 (*M*), 416 (*M* – H_2O; *m** calc. $416^2:434 = 398.75$, found 399), 406 (*M* – 28 CO or C_2H_4), 401 (*M* – H_2O – $^{\cdot}CH_3$), 388 (*M* – H_2O – 28), 385 (416 – $^{\cdot}OCH_3$), 384 (416 – $HOCH_3$), 374 (*M* – AcOH), 370 (388 – H_2O), 356 (416 – AcOH), 342 (384 – CH_2=C=O), 328 (vs, 388 – AcOH), 313 (328 – CH_3), 310 (328 – H_2O), 296 (328 – $HOCH_3$), 274 (328 – 54 (C_4H_6, *retro-Diels-Alder* of C(1–4))), 269 (vs), 258, 250 ($C_{14}H_{18}O_4$ rings A + B + O=C(11)). Isomerization to **38** cannot be excluded during (or prior) to recording of the spectrum. Anal. calc. for $C_{23}H_{30}O_8$ (434.47): C 63.58, H 6.96; found: C 63.54, H 6.93.

3β-Acetoxy-7β,14β-dihydroxy-11,12-dioxo-5β(H)-8(9)-etienic-acid Methylester (**38**; *AL-873*). Crude crystals of **37**, (460 mg), m.p. 163–175° (still containing some unoxidized ester **5**), dissolved in benzene $CHCl_3$ 4:1 were poured on a column of 15 g of Al_2O_3 (*Merck*, activity II–III) and left for 20 min. Elution with $CHCl_3$ furnished 410 mg of eluate which gave 304 mg of crystals (*AL-873*) from Et_2O/pentane, m.p. 174–176°. The material from the mother liquor (110 mg) gave after chromatography 67 mg of crystalline **5** and 20 more mg of **38**. The anal. sample (*AL-873*) was obtained as thick yellow prisma, m.p. 174–176°. $[\alpha]_D^{25} = +5.0° \pm 2°$ ($c = 0.653$, $CHCl_3$). UV (EtOH): 200 (3.92), 310 (1.97, flat, reaching into visible region). IR (KBr): 2.85 (sharp), 2.975*s* (br.), 3.33, 3.42, 5.70 (tooth), 5.79 (tooth), 5.82vs, 5.86, 6.94*m*, 7.25*s*, 7.90vs, 8.08vs, 8.30*s*, 9.65*s*, 9.98*s*. $C_{28}H_{30}O_8$ (434.42). MS: 434 (*M*), 416 (*M* – H_2O), 414 (*w*, impurity), 406 (*M* – 28=CO or C_2H_4), 401 (*M* – H_2O–$^{\cdot}CH_3$), 388 (*M* – H_2O – 28), 385 (416 – $^{\cdot}OCH_3$), 384 (416 – $HOCH_3$), 374 (*M* – AcOH), 370 (388 – H_2O), 356 (416 – AcOH), 342 (384 – HC=C=O), 328 (vs, (388 – AcOH)), 313 (328 – CH_3), 310 (328 – H_2O), 296 (vs, (328 – $HOCH_3$), 274 (328 – 54 (C_4H_6; *retro-Diels-Alder* of C(1–4))), 269 (vs), 258, 250 ($C_{14}H_{18}O_4$: rings A + B + O=C(11)). Apart from the small peak at *m/z* 414 (impurity) this spectrum was very similar to the MS of compound **37**. Anal. calc. for $C_{23}H_{30}O_8$ (434.47): C 63.58, H 6.96; found: C 63.43, H 6.93.

3β-Acetoxy-14β-hydroxy-7,11,12-trioxo-8(9)-etienic-acid Methylester (**39**, *AL-879*). Ester **38** (46 mg) was dissolved in 0.5 ml of AcOH and at 5° 1.3 ml of 2% CrO_3/AcOH soln. added under shaking in 5 portions during 1 h. After keeping 16 h at 5°, it was worked up as described for **37**. The crude neutral product (30 mg) gave 21 mg of yellow crystals from Et_2O/pentane, m.p. 155–158°. $[\alpha]_D^{26} = -117.0° \pm 3°$ ($c = 0.528$, $CHCl_3$); UV (EtOH): 206–220 (3.598, neatly flat), 264 (3.842), and a sh at *ca.* 350 (2.148) with absorption extending to the VIS region. The preparation still contained a small amount of unoxidized **38**. MS: 434 (*w*, impurity **38**). 432 (*M*), 416 (*w*, 434 – H_2O), 414 (*M* – H_2O), 404 (*M* – 28 (CO or C_2H_4)), 400 (*M* – $HOCH_3$), 386 (404 – H_2O), 372 (432 – AcOH), 344 (404 – AcOH or 372 – 28), 326 (344 – H_2O), 312 (344 – $HOCH_3$), 298 (326 – 28), 284 (344 – AcOH or 312–CO), 272 (326 – 54, *retro-Diels-Alder* of C(1–4)), 267 (*m*), 257 (*s*), *etc.*. Anal. calc. for $C_{23}H_{28}O_8$) 432.45): C 63.88, H 6.53; found: C 63.63, H 6.51.

Hydrogenation of 38 Leading to 40, 41, 42, and 43. – Ester **38** (152 mg) of m.p. 174–176° was hydrogenated in 4 ml of AcOH with 140 mg of PtO_2 during 14 h, absorption had ceased before. Filtration and evaporation gave 153 mg of product. According to TLC, it was a mixture containing 4 main products in the order of increasing polarity: **42**, **43**, **40**, **41** and, in addition, small amounts of more polar material. Approximate R_f values on SiO_2 plates (ascending with AcOEt/cyclohexane 1:1): **42** (0.82); **43** (0.79); **40** (0.55); **41** (0.49).

The mixture (153 mg) was chromatographed on 8 g of SiO_2. *Fr. 1–3* (20 mg, eluted with benzene and benzene/Et_2O 9:1) gave from a trace of Et_2O/pentane (at 0°) 8 mg of **42** as needles of double m.p. 140/157–161°. *Fr. 4–6* (30 mg, eluted with benzene/Et_2O 85:15) gave from Et_2O/pentane 10 mg of **43** in leaflets, m.p. 166–168°. *Fr. 7* (5 mg) was a mixture. *Fr. 8–14* (35 mg, eluted with benzene/Et_2O 80:20, 70:30, and 60:40) gave from Et_2O/pentane 12 mg of **40** as colorless grains, m.p. 170–172°. *Fr. 15* (7 mg) was a mixture. *Fr. 16–18* (40 mg, eluted with benzene/Et_2O 1:1) contained **41** and could for a long time not be crystallized. Some crystals were finally obtained from a little CS_2 after standing 16 h at 0°. With these for nucleation, better crystals (leaflets) could be obtained, m.p. 169–182°. Further *Fr.* (total 25 mg) containing 3–4 more polar compounds were eluted with Et_2O, $CHCl_3$, and $CHCl_3$/MeOH.

More of the mentioned 4 compounds were isolated after hydrogenation of a second batch (525 mg) of **38** with re-chromatography of material from mother liquors.

Putative 3β-Acetoxy-7β,12β,14β-trihydroxy-11-oxo-5β(H)-8(9)-etienic-acid Methylester (**40**; *AL-880*). Colorless grains from Et_2O/pentane, m.p. 170–172°. $[\alpha]_D^{24} = +34.0°$ ($c = 0.350$, $CHCl_3$). UV (EtOH) 244 (3.826; α,β-unsaturated ketone). IR (film on KBr): 2.69*s* (OH), 5.74*s* (Ac, ester), 5.92 (unsat. ketone). Anal. calc. for $C_{23}H_{32}O_8$ (436.48): C 63.28, H 7.39; found: C 62.99, H 7.36.

Putative 3β-Acetoxy-11β,12,14β-trihydroxy-5β,8ξ,9ξ(H)-etianic-acid Methylester (**41**; *AL-881a*). Colorless platelets from Et_2O/pentane, m.p. 169–172°. $[\alpha]_D^{16} = +16{,}4° \pm 4°$ ($c = 0.359$, $CHCl_3$). UV (EtOH): sh *ca.* 256 (1.98) and ca. 281 (1.16), perhaps impurity, no-high intensity band. IR (CH_2Cl_2): 2.77, 2.82 (*OH* 7), 2.97–2.98

(OH, bonded), 5.80*vs* (CO bonded), 5.90 (tooth). MS: 424 (*M*), 409 (*M* – $^{\cdot}CH_3$), 406 (*M* – H_2O), 396 (*M* – C_2H_4), 378 (*M* – H_2O–C_2H_4), 374 (406 – CH_3OH), 364 (*M* – AcOH), 346 (*M* – AcOH–H_2O), 328 (*M* – AcOH–ZH_2O), 314 (346 – CH_3OH), 310 (364 – CH_2–CH=CH–CH_2 (**54**), *retro-Diels-Alder* of C(1–4) or *M* – AcOH – $3H_2O$), 296 (314 – H_2O; *m** calc. 296^2:314 = 279.03, found 280).

Putative 3β,12ξ-Diacetoxy-11β,14β-dihydroxy-5β,8ξ,9ξ(H)-etianic-acid Methylester (**45**; *AL-882*). Compound **41** (55 mg) was acetylated in 0.2 ml of abs. pyridine and 0.1 ml of Ac_2O 10 h at 20° and 5 h at 70°. The crude product (63 mg) gave 42 mg of **45** (*AL-882*) as colorless crystals from Et_2O/pentane, m.p. 209–212°. $[\alpha]_D^{23}$ = +66.4° (*c* = 0.379, $CHCl_3$). Not analyzed. IR (CCl_4): 2.75, 2.85, 3.38*m*, 3.425*m*, 5.78*vs*, 6.97*m*, 7.31*s*, 8.05*vs*, 8.20 (tooth), 8.62*m*, 9.82*s*..

Putative 3β,12ξ-Diacetoxy-11β-hydroxy-5β,8ξ,9ξ(H)-14(15)-etianic-acid Methylester (?) (**47**; *AL-895*). Treatment of 25 mg of **45** in 0.2 ml of abs. pyridine with 0.3 ml of $SOCl_2$ as described for **7** gave 25 mg of crude product and from Et_2O/pentane 14 mg of **47**, m.p. 163–164°. $[\alpha]_D^{26}$ = +58.9° ± 4° (*c* = 0.365, $CHCl_3$). UV (cyclohexane): *ca.* 208 (4.45), probably disturbed by some impurity. IR (CCl_4): 2.89*w*, (wide; OH bonded), 5.76*vs* (Ac, ester), 7.92*m*, 8.05*vs*, 9.68*s*. IR (KBr): 3.32 w (sharp), 3.39*m*, 3.45*w* (sharp), 5.76, 5.78, 6.75*w*, 6.96*m*, 7.32s, 7.95*vs*, 8.51*m*, 9.75*s*, 11.2*m*. Anal. calc. for $C_{25}H_{36}O_7$ (448.55): C 66.93, H 8.09; found: C 66.97, H 7.91. This compound **47** (*AL-895*) was not changed by hydrogenation with PtO_2, in AcOH, and not oxidized, or very slowly, with CrO_3 in AcOH. In the TLC, **45** runs quicker than **41** and **47**, much faster than **45**.

On the other hand, **45** is converted by CrO_3 in AcOH to **46** (*AL-896*), amorphous, $[\alpha]_D^{25}$ = +97.5° ± 3° (*c* = 0.521, $CHCl_3$). (Not analyzed, perhaps 3β,12ξ-diacetoxy-14β-hydroxy-11-oxo-ester (?).) IR (CCl_4): 2.89 (wide, OH, bonded), 5.75*s*, (Ac, ester), 7.32*vs*, 8.06*vs*, 9.72*s*, compatible with OH, AcO, keto, and ester group.

Putative 3β-Acetoxy-12ξ,14β-dihydroxy-11-oxo-5β(H)-8(9)-etienic-acid Methylester (?) (**42**; *AL-878*). Colorless needles from Et_2O/pentane, double m.p. 140/157–161°. $[\alpha]_D^{25}$ = +57.2° ± 4° (*c* = 0.39, $CHCl_3$). UV (EtOH): 282 (4.002), indicative for *double* unsaturated ketone. IR (KBr): 2.95, 5.76, 5.86, 6.03, 6.19, 6.95*s*, 7.30*s*, 7.90*s*, 8.05*vs*, 8.36*s*, 8.46*s*, 9.82*vs*. Anal. calc. for $C_{23}H_{32}O_7$ (420.48): C 65.69, H 7.67; found: C 65.73, H 7.73.

Putative 3β-Acetoxy-12ξ,14β-dihydroxy-11-oxo-5β(H)-8(14)-etienic-acid Methylester (?, not formulated on *Chart II*; **43**; *AL-879*). Colorless platelets from Et_2O/pentane, m.p. 166–168°. $[\alpha]_D^{24}$ = +96.7° ± 6° (*c* = 0.31, $CHCl_3$). UV (EtOH): 247 (3.86), and 297 (1.93), compatible with α,β-unsaturated ketone. IR(KBr): 2.79*w*, 3.49*m*, 5.79*vs*, 5.98*s*, 6.24*w*, 7.25*s*, 7.90*s*, 8.02*s*, 8.63*m*, 9.79. Anal. calc. for $C_{23}H_{32}O_7$ (420.48): C 65.69, H 7.67; found: C 65.88, H 7.76.

Putative 3β,12-Diacetoxy-14β-hydroxy-11-oxo-5β(H)-8(14)-etienic-acid Methylester (?, not formulated on *Chart II*; **44**; *AL-897*). Crude amorphous **43** (37 mg) was acetylated in 0.2 ml of abs. pyridine and 0.1 ml of Ac_2O 16 h at 20° and 4 h at 70°. The product (42 mg) after chromatography on 1 g of SiO_2 gave 13 mg crystalline **44** from Et_2O/pentane, m.p. 175–178°. UV (EtOH): 246.5 (3.183), and a flat second one at *ca.* 299–307 (1.73–1.73). Anal. calc. for $C_{25}H_{34}O_8$ (462.5): C 64.91, H 7.41; found: C 64.92, H 7.69.

Compounds Presented in *Chart III.* – *3β-Acetoxy-7,8β-epoxy-14β-hydroxy-11α-mesyloxy-12-oxo-5β(H)-etianic-acid Methylester* (**48**; *AL-1016*). To 216 mg of **5** in 3 ml of abs. pyridine, 0.2 ml CH_3SO_2Cl were added at 0°, and the mixture kept with exclusion of moisture 16 h at 22°. After addition of 0.5 g of ice, the mixture was kept for 1 h at 20° to hydrolize the excess of MsCl. Extraction with $CHCl_3/Et_2O$, washing with dil. HCl, Na_2CO_3, and H_2O, drying, and evaporation gave 260 mg of neutral product. This gave 196 mg of crystalline **48** from Et_2O/pentane. The anal. sample had m.p. 201–203°. $[\alpha]_D^{26}$ = +38.8° ± 3° (*c* = 0.535, $CHCl_3$). $C_{24}H_{34}O_{10}S_2$ (514.58). MS: 529 (trace of impurity) 515 (*M* + 1), 514 (*M*), 497 (*M* – $^{\cdot}OH$), 483 (*M* – OCH_3), 482 (*M* – $HOCH_3$), 465 (497 – $HOCH_3$), 454 (*M* – AcOH), 437 (454 – $^{\cdot}OH$), 436 (454 – H_2O), 435 (*M* – SO_2CH_3), 418 (*vs*, *M* – CH_3SO_2OH (96)), 400 (418 – H_2O), 375 (435 – AcOH), 358 (*vs*, *M* – 156 ($C_8H_{12}O_3$, ring D or/and 418 – AcOH), 357 (358 – H or 375 – H_2O), 340 (*vs*, 358 – H_2O), 329, 325, 312 (340–28), 297 (329 – CH_3OH or 325 – 28), 281 (437 – 156 (ring C)), 269, 253, 237, 221, 213, 203, 191, 183 (237 – 54 (CH_2–CH=CH–CH_2), C(1–4) *retro-Diels-Alder* or 269 – 86 ($C_4H_6O_4$ = C(16, 17, 20)), 175, 167 (253 – 86 ($C_4H_6O_4$)), 163, 97 (CH_3SO_2OH + H), 93, 91, 79 ($CH_3SO_2^+$), 43 (*vs*, CH_3–C≡O$^+$).

3β-Acetoxy-7,8β-epoxy-11α-mesyloxy-12-oxo-5β(H)-14(15)-etienic-acid Methylester (**49**; *AL-1017*). To 346 mg **48** in ml of abs. pyridine, 0.3 ml of $SOCl_2$ were added at 0° and kept under exclusion of moisture 16 h at 5° and 1 h at 20°. Workup with ice-H_2O and $CHCl_3/Et_2O$ 1:3 at 0°, washing with dil. HCl and Na_2CO_3, and evaporation *in vacuo* gave 324 mg of crude product giving colorless crystals, m.p. 132–134°. $[\alpha]_D^{25}$ = +28.7° (*c* = 0.435, $CHCl_3$). The product is not stable and had to be hydrogenated immediately. A small sample kept 1 day at 20° was already yellow and melted at 128–134°.

Hydrogenation of 49 with PtO_2 in AcOH to 50 and 52. – The crude **49** (320 mg, m.p. 128–134°) was hydrogenated in 3 ml of AcOH with 100 mg of PtO_2. Filtration, *etc.* gave 322 mg of mixture which was chromatographed on 9 g of SiO_2. *Fr. 3–4* (59 mg, eluted with benzene/Et_2O 8:2) gave from Et_2O/pentane 25 mg of

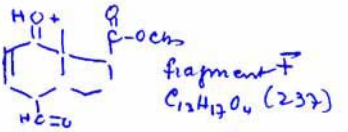
50 (*AL-1018*) as colorless prisms, m.p. 179–180°. *Fr. 5–6* (20 mg, eluted with benzene/Et_2O 8:2 and 6:4) were a mixture *Fr. 7–9* (46 mg, eluted with benzene/Et_2O 1:1 and pure Et_2O) gave from acetone/Et_2O 30 mg of crystalline **52** (*AL-1042*), m.p. 210–213°. The *Fr. 10–11* (132 mg, eluted with Et_2O/$CHCl_3$ 8:2) contained a more polar compound *AL-1038* which did not crystallize but gave with CrO_3 a crystalline oxidation product *AL-1044*, m.p. 223–5° from acetone/Et_2O. UV (EtOH): 235 (3.766) and 254 (3.785), indicating α,β-unsaturated ketone or two conjugated bonds. In a second experiment, the hydrogenation of 291 mg of crude **49** gave after chromatography 10 mg of a low-polarity product (*Fr. 2*), which furnished from Et_2O a few crystals, m.p. 198–200°; not further examined. The main products were 157 mg of crude **50** yielding 119 mg of pure crystals, m.p. 179–180°, and 51 mg of crude **52** yielding 33 mg of crystals, m.p. 208–213°. Only traces of more polar material (*AL-1038*) were obtained.

3β-Acetoxy-12β-hydroxy-11α-mesyloxy-5β(H)-8(14)-etienic-acid Methylester (**50**; *AL-1018*). Colorless prisms from Et_2O/pentane, m.p. 179–180°. $[\alpha]_D^{26} = +38.3° \pm 6°$ ($c = 0.285$, $CHCl_3$). IR(CH_2Cl_2): 2.76*w* (OH), 2.83*w* (wide, OH), 2.93–2.95 (wide, OH, bonded) 5.78*s* (Ac), 5.88*s* (ester, bonded), 8.54*s* (Ac), 9.29*s*, *etc.* IR (KBr): 2.82, 2.85 (OH), 2.95 (OH, bonded), 5.78*s* (Ac), 5.90*s* (ester, bonded), 7.32 (Ac), 7.42, 8.02, 8.14, (Ac), 8.42, 9.78*m*, 10.72*s*, 12.1*s*. ^{1}H-NMR: 0.99 (CH_3(18), CH_3(19)); 2.04 (CH_3O); 2.82 (*d*, $J \approx 7.5$, H_α–C(9)); *ca.* 3.70 (partly covered, *d*, $J \approx 7.5$, H_α–C(12)); 3.76 (*s*, CH_3 of ester); 4.93 (*dd*, $J = 9.5, 7.5$, H_β–C(11)); 5.17 (br. *s*, H_α–C(3)). According to MS, the prep. contained still a little **52**. $C_{24}H_{36}O_9S$ (500.6). *M* for **50** is $C_{24}H_{36}O_8S$ (484.60), MS:501 (0.3, **52** + 1 as impurity), 485 (1.1 *M* + H), 469 (0.7, *M* – CH_3), 453 (0.7, *M* – OCH_3), 441 (1.4, *M* – CH_3CO), 440 (1.1, 500 – 60, impurity), 422 (440 – H_2O), 409 (2, 469–AcOH), 388 (48, *M* – CH_3SO_3H; *m** 353.5), 370 (100, 388 – H_2O; *m** calc. 370^2:388 = 352.83, found 353.5), 355 (50, 370 – CH_3), 344 (20), 328 (40, 388 – AcOH), 313 (60, 328 – CH_3), 311 (70, 328 – OH) 310 (66, 328 – H_2O), 295 (100, 328 – CH_3–H_2O), 286 (16), 281 (16), 269 (29), 263 (9), 256 (20), 253 (36), 251 (100), 235 (90), 227 (29), 221 (26), 209 (25), 205 (62), 195 (40), 187 (30), 181 (40), 167 (57), 161, 159, 157, 155, 145, 143 (90), 133, 131, 129, 119, 117, 115, 107 (88), 105 (79), 96 (37, CH_3SO_3H), 95 (37), 93 (65), 91 (90), 79 (80), 77, 67, 59, 55, 43 (vs, CH_3–C≡O).

3β-Acetoxy-11,12β-epoxy-5β(H)-8(14)-etienic-acid Methylester (**51**; *AL-1041*). Compound **50** (251 mg, m.p. 178–181°) dissolved in benzene was soaked on a column of 15 g of Al_2O_3 (*Merck*, activity I according to *Brockman*) and left closed for 2 days. Elution with benzene/Et_2O 9:1 gave 111 mg of eluate. 3 days later another 50 mg were eluted and after 3 other days a final 15 mg. This material (total 176 mg) gave from Et_2O/pentane 160 mg of crystals, m.p. 115–120°. Recrystallization furnished the anal. sample *AL-1041* as colorless leaflets, m.p. 121–122°. $[\alpha]_D^{26} = +65.7° \pm 3°$ ($c = 0.514$, $CHCl_3$). UV (cyclohexane): 200 (4.059), fully substituted C(8)=C(14) bond. IR (KBr): 3.30*w*, 3.34, 3.96, 3.375, 3.39, 3.41, 3.46, 3.49, 3.50, 5.74, 5.77 (Ac, ester), 6.925*s*, 7.26*s* (Ac), 7.33*s*, 7.72*m*, 7.96*s*, 8.04*vs*, 8.15*s*, 8.30*m* (Ac), 8.37*s*, 8.56*m*, 9.8*s* (Ac). ^{1}H-NMR: *Fig. 6*. $C_{23}H_{32}O_5$ (388.48). MS: 388 (*M*), 373 (*M* – $^{\cdot}CH_3$), 370 (*M* – H_2O), 356 (*M* – CH_3OH), 328 (*s*, *M* – AcOH or/and 356 – CO) 313 (328 – $^{\cdot}CH_3$), 310 (328 – H_2O), 296 (328 – CH_3OH), 281 (296 – $^{\cdot}CH_3$), 268 (296 – CO), 253 (268 – $^{\cdot}CH_3$), 235, 227, 205 (*vs* rings C + D analogous to **135** in *Chart VII*), 189, 161, 145 (*vs*), 131, 119, 107 (*vs*, **113**, *Chart VII*), 91 (C_7H_7-tropylium ion[3]), 79, 67, 43 (CH_3–C≡O^+).

3β-Acetoxy-7α-hydroxy-11α-mesyloxy-12-oxo-5β,8ξ(H)-etianic-acid Methylester (**52**; *AL-1042*). The anal. sample showed first a double m.p. 210 – 3,/224 – 7°, but gave gross crystalline grains from acetone/Et_2O, m.p. 224–227°. $[\alpha]_D^{25} = +26.5°$ ($c = 0.474$, $CHCl_3$). Both forms showed the same rotation. UV (EtOH): no high-intensity absorption but λ_{max} rather flat, 281 (1.942). $C_{24}H_{36}O_9S$ (500.60). MS: 511 (*w*, impurity), 501 (*M*+H), 500 (*w*,*M*), 482 (*M* – H_2O), 469 (*vs*, *M* – $^{\cdot}OCH_3$), 441 (*s*, 469 – CO or 501 – AcOH), 440 (*vs*, *M* – CH_3OHCO or *M* – $HCOOCH_3$ or *M* – AcOH), 409 (469 – AcOH or 469 – CH_3OH–CO), 390, 386, 380, 370, 361, 354, 345 (441 – CH_3SO_3H), 344 (440 – CH_3SO_3H), 329 (344 – $^{\cdot}CH_3$), 326 (344 – H_2O), 315 311 (326 – $^{\cdot}CH_3$ or 329 – H_2O), 294, 251, 237, 208, 93 (*vs*), 81 (*vs*), 79 (*vs*), 43 (CH_3–C≡O^+). Anal. calc. for: S 6.40; found: S 6.27.

3β-Acetoxy-7α,12β-dihydroxy-11α-mesyloxy-5β,8ξ(H)-etianic-acid Methylester (**53**; *AL-1073*). Ester **52** (90 mg) was hydrogenated in 3 ml of AcOH with 80 mg of PtO_2 3 days. Absorption of H_2 was rather slow. Workup as above gave 90 mg of crude **53** and from acetone/Et_2O 67 mg of colorless crystals. The anal. sample *AL-1073* formed grains, m.p. 184–185° (with decomposition). $[\alpha]_D^{26} = +15.5° \pm 3°$ ($c = 0.373$, $CHCl_3$). $C_{24}H_{32}O_9S$ (502.61). MS: 406 (*M* – 96 (CH_3SO_3H)), 388 (406 – H_2O), 346 (406 – AcOH), 328 (346 – H_2O), 310 (328 – H_2O), 295 (310 – CH_3), 237 (fragment F), 205 (F – CH_3OH)



Hydrogenation of the Epoxide 51 and Isolation of 54 and 19. – Epoxy-ester **51** (70 mg) in 3 ml of AcOH were hydrogenated with 70 mg of PtO_2 for 2 days. The absorption of H_2 was slow. The product (68 mg) was chromatographed on 4 g of Sio_2. The *Fr. 4–8* (17 mg, eluted with benzene/Et_2O 95:5 and 9:1) gave 4.5 mg of crystalline **19** (*AL-1047*), m.p. 117–120°. *Fr. 9–10* (27.5 mg, eluted with benzene/Et_2O 9:1 and 9:2) were a mixture containing also some **51**. The *Fr. 11–13* (25 mg, eluted with benzene/Et_2O 9:2 and 1:1) gave 20 mg of crystalline **54**, (*AL-1046*) from Et_2O/pentane. Elution with pure Et_2O gave 13 mg.

3α-Acetoxy-11β-hydroxy-5β(H)-8(14)-etienic-acid Methylester (**54**; *AL-1046*). The anal. sample was obtained from Et_2O/pentane as colorless grains, m.p. 133–134°. $[\alpha]_D^{25}$ = +28.7° (*c* = 0.574, $CHCl_3$). UV(cyclohexane): 201 (4.055), corresponding to fully substituted C(8)=C(14) bond. $C_{23}H_{34}O_5$ (390.50). MS: 390 (*M*), 372 (*M* – H_2O; *m** 372^2:390 calc. 354.83, found 355.5), 358 (*M* – CH_3OH), 357 (372 – $^{\cdot}CH_3$; *m** calc. 342.60, found 343), 330 (372 – CH_3OH or *M* – AcOH), 315 (330 – $^{\cdot}CH_3$), 312 (330 – H_2O; *m** calc. 294.98, found 295 and 372 – AcOH; *m** calc. 261.68, found 262), 297 (312 – $^{\cdot}CH_3$), 353, 206, 205, 204, 157, 145, 105, 91, 79, 67, 55, 43 ($CH_3 - C{\equiv}O^+$).

3β-Acetoxy-5β(H)-8(14)-etienic-acid Methylester (**19**; *AL-1047*) *from* **51**. The anal. sample showed m.p. 117–120°. $[\alpha]_D^{25}$ = +82.8°±5° (*c* = 0.227, $CHCl_3$). According to TLC and mixed m.p., it was identical with *AL-1028* (*Chart 1*) and *AL-448* from digitoxigenin [20].

3β-Acetoxy-11,12β-epoxy-7α-hydroxy-5β(H)-etianic-acid Methylester (**56**; *AL-1075*). Ester **53** (95 mg, m.p. 183–5°) was dissolved in 0.5 ml of $CHCl_3$, 2 ml of benzene added, the soln. poured on to a column of 10 g of Al_2O_3 (*Merck*, activity I–II), remaining traces rinsed with benzene/$CHCl_3$ 1:4, and the column left closed for 10 days at 25°. Elution with benzene/$CHCl_3$ 4:1 gave 27 mg of eluate (crude **56**). Elution with pure $CHCl_3$ and $CHCl_3$/MeOH 9:1 gave 50.5 mg of eluate which was a mixture containing still a little **53**. Crystallization of the crude **56** from Et_2O/pentane gave *AL-1075*, m.p. 154–157°. $[\alpha]_D^{25}$ = +31.5±5° (*c* = 0.222, $CHCl_3$). UV (EtOH): no high-intensity absorption. IR ($CHCl_3$): 2.64*w*, 2.71*w*, 2.96*m* (all sharp OH), 2.83, 2.93 (br., flat, OH, bonded), 5.78*s* (Ac, ester), 6.96, 7.25*m* (Ac). IR (KBr): 2.81*m* (sharp, OH), 3.34, 3.35, 3.37, 3.38, 3.48, 3.46 (CH), 5.75*s* (Ac, ester), 5.81*s* (Ac, ester, bonded), 7.01*m*, 7.25*m*, 8.4*s*, 8.62*s*, 9.8*s* (Ac). ^{1}H-NMR: 0.790 (*s*, CH_3(18)); 1.14 (*s*, CH_3(19)); 2.07 (*s*, CH_3 of acetyl); 3.17 (*dd*, *J* = 3.8, 2.8, H_α–C(11)); 3.24 (*d*, *J* = 3.8, H_α–C(12)); 3.73 (*s*, CH_3 of ester); 3.95 (*d*, with wide base, H_β–C(7)); 5.06 (*m*, H_α–C(8)); position of angular Me groups calc. [47] CH_3(18): ground value = 0.692 + increments for 17β-$COOCH_3$ = −0.050,11,12β-epoxy = 0.125, 7α-OH = 0.008, 3β-OAc = 0.008 total calc. 0.783, found 0.790; CH_3(19): ground value = 0.925 + increments for 17β-$COOCH_3$ = −0.008,11,12β-epoxy = 0.175,7α-OH = 0.008, 3β-OAc = 0.058, total calc. 1.142, found 1.14). ^{13}C-NMR (25.5 MHz; numbers of C-atoms, in brackets chemical shifts in ppm): C(1) (30.9); C(2) (25.2); C(3) (70.4); C(4) (33.9); C(5) (37.1); C(6) (34.0); C(7) (68.7); C(8) (34.5); C(9) (36.4); C(10) (34.7); C(11) (50.7); C(12) (54.0); C(13) (43.3); C(14) (49.7); C(15) (23.8); C(16) (22.0); C(17) (56.4); C(18) (12.0); C(19) (24.9); C(20) (173.8), C(21) (methoxy, 51.6); C(22) (C = O, Ac, 170.2); C(23) (CH_3 – Ac, 21.5). The values for C(8) and C(9) are in agreement with H_β–C(8) and H_α–C(9) orientation for a 5β(H)-steroid. The 7α-OH group shifts the resonance of C(9) and C(14) for *ca.* 7 ppm to higher field. For an analogous 5β(H),14α(H)-steroid without the 7α-OH, the resonance of C(9) would be expected at *ca.* 43.5 ppm and the C(14) resonance at *ca.* 56.7 ppm. $C_{23}H_{34}O_6$ (406.50). MS: 406 (*M*), 391 (*M* – $^{\cdot}CH_3$), 388 (*M* – H_2O), 375 (*M* – $^{\cdot}OCH_3$), 359 (388 – CHO(?)); 356 (388 – CH_3OH), 347 (*M* – $CH_3O-C{\equiv}O^+$), 346 (*M* – AcOH), 328 (388 – AcOH or 346 – H_2O), 313 (328 – $^{\cdot}CH_3$), 300 (328 – CO or C_2H_4), 299 (328 – $^{\cdot}CHO$ or $^{\cdot}C_2H_5$(?)), 295 (300 – $^{\cdot}CH_3$), 269 (300 – $^{\cdot}OCH_3$), 251 (269 – H_2O), 209, 195, 179, 177, 161, 159, 149, 147, 145, 135, 133, 131, 121, 116, 105, 99, 79, 67, 55, 43.

3β-Acetoxy-11-oxo-5β(H)-8(14)-etienic-acid Methylester (**57**; *AL-1050*). To 44 mg of **54**, m.p. 130–134°, in 2 ml of acetone, 0.2 ml of *Kiliani*'s mixture were added at 0° and kept for 5 min. Addition of ice *etc.* (see **9** from **14**) gave 42 mg of neutral product. Crystallization from Et_2O/pentane gave 39 mg of **57** as colorless thick needles, m.p. 165–168°. $[\alpha]_D^{26}$ = +66.8° (*c* = 0.317, $CHCl_3$). UV (EtOH): 203 (4.052 fully substituted C(8) = C(14) bond), 275 (2.23; β,γ-unsaturated ketone).

3β-Hydroxy-11-oxo-5β(H)-8(14)-etienic-acid Methylester (**59**; *AL-1053*). To 14 mg of **57** (second quality m.p. 140–150°) in 6 ml of MeOH, the soln. of 30 mg of K_2CO_3 in 2 ml of H_2O was added and shaken for 6 days. Evaporation of MeOH *in vacuo*, extraction with Et_2O, *etc.* gave 12.5 mg of neutral product, which was chromatographed on 1 g of SiO_2. The *Fr. 1–6* (eluted with benzene/Et_2O 95:5 and 9:10) gave 3.6 mg of amorphous material. *Fr. 8–11* (6 mg, eluted with benzene/Et_2O 4:1 and 1:1) gave crystalline **59** (*AL-1053*), m.p. 161–164°. $[\alpha]_D^{25}$ = −22.0° ± 10° (*c* = 0.136, $CHCl_3$). *Fr. 12–14* (eluted with pure Et_2O and $CHCl_3$) gave 2.8 mg of amorphous material.

Hydrogenation of the Epoxy-ester 56 Leading to the Isolation of 60 and 62. – Epoxy-ester **56** (17.5 mg, second quality) in 1 ml of AcOH was hydrogenated with 60 mg of PtO_2 for 2 days. Filtration and evaporation *in vacuo* gave

18 mg of crude product which was chromatographed on 4 g of SiO_2. *Fr. 3–5* (3.9 mg eluted with benzene/Et_2O 9:1) was *AL-1093* (by-product **55**, amorphous). *Fr. 6* (1.5 mg eluted with benzene/Et_2O) was amorphous. Acetylation of these 1.5 mg gave no crystals. Saponification with hot KOH in MeOH and remethylation gave 2 mg of amorphous product. This was oxidized with CrO_3, but no crystals could be obtained after chromatography. *Fr. 7–10* (4.3 mg, eluted with benzene/Et_2O 4:1 and 7:3) gave 3.4 mg of crude crystalline **60** (*AL-1081*), m.p. 170–177° from Et_2O/pentane. *Fr. 11* (1.1 mg, eluted with benzene/Et_2O 1:1) gave no crystals, and after saponification (KOH), remethylation, and oxidation no pure material was obtained. *Fr. 12–14* (7.4 mg eluted with pure Et_2O) gave from Et_2O 3 mg of crystalline **62** (*AL-1085*), m.p. 210–220°.

3β-Acetoxy-7α,11β-dihydroxy-5β(H)-etianic-acid Methylester (**60**; *AL-1081*). Recrystallization from Et_2O gave colorless crystals, m.p. 177–180°. $[\alpha]_D^{26} = +44.3° \pm 5°$ ($c = 0.278$, $CHCl_3$).

3,7,11-Trioxo-5β(H)-etianic-acid Methylester (**61**; *AL-1094*). To 4.2 mg of crude crystals of **60** in 1.5 ml of MeOH, the soln. of 100 mg of K_2CO_3 in 0.5 ml of H_2O was added and boiled under reflux 4 h. Elimination of the MeOH *in vacuo*, acidification with HCl, extraction with $CHCl_3$, and remethylation with CH_2N_2 in Et_2O gave 4 mg of crude neutral product. It was dissolved in 0.2 ml of AcOH, and slowly 0.25 ml 2% CrO_3/AcOH soln. added in 3 portions. The mixture was kept 16 h at 22°. After addition of 3 drops of MeOH and standing for another h, the workup gave 3.8 mg of crude neutral product. It was chromatographed on 2 g of SiO_2. *Fr. 1–9* (2.4 mg, eluted with benzene/Et_2O 9:1) gave 1.2 mg of crystalline **60**. Recrystallization from acetone/pentane gave the anal. sample *AL-1094*, m.p. 235–242°. $[\alpha]_D^{26} = +13.1° \pm 15°$ ($c = 0.085$, $CHCl_3$). $C_{21}H_{28}O_5$ (346.44). MS: 360 (*M*), 345 (*M* – $^{\cdot}CH$; *m** calc. $345^2:360 = 330.62$, found 331), 342 (*M* – H_2O; *m**, calc. $342^2:360 = 325.21$, found 325), 332 (*M* – $^{\cdot}OCH_3$), 328 (*w*, *M* – CH_3OH), 300 (328 – CO), 209, 195, 177, 149, 109, 108, 93, 81, 67, 55.

3β-Acetoxy-7α,12β-dihydroxy-5β(H)-etianic-acid Methylester (**62**; *AL-1085*). After recrystallization the m.p. was 225–230°.

3,7,12-Trioxo-5β(H)-etianic Methylester (**63**; *AL-1092*) *from* **62.** Crude ester **62** (4.8 mg) in 1.5 ml of MeOH was mixed with 50 mg of K_2CO_3 in 0.25 ml of H_2O and boiled under reflux for 2 h. After removing MeOH *in vacuo*, the aq. suspension was acidified with HCl and extracted with $CHCl_3/Et_2O$ 1:3. After addition of CH_2N_2 in Et_2O until the yellow color persisted for ½ h, the washed soln. was evaporated. The crude product (4.5 mg) was dissolved in 0.1 ml of AcOH and oxidized with 0.2 ml of 2% CrO_3/AcOH soln. as described for **61**. The crude product (3.5 mg) was chromatographed on 2 g of SiO_2. *Fr. 6* (eluted with benzene/Et_2O 7:3) gave from Et_2O/pentane opaque grains, m.p. 250–260°, with transformation in fine needles. $C_{21}H_{28}O_5$ (360.43). MS: 360 (*M*), 345 (*M* – $^{\cdot}CH_3$), 342 (*M* – H_2O; *m** calc. $342^2:360 = 324.9$, found 325), 329 (*M* – $^{\cdot}OCH_3$), 328 (*M* – CH_3OH), 313 (328 – $^{\cdot}CH_3$; *m** calc. $313^2:328 = 298.69$ found 299), 310 (328 – H_2O), 300 (328 – CO), 285 (300 – $^{\cdot}CH_3$), 282 (300 – H_2O) 259, 250 (282 – H_2O), 232 (250 – H_2O), 221 (*M* – 140 (ring D) +H), 218 (*M* – 142 (ring A + C(6–7)), 203 (221–H_2O), 192 (*M* – 168 (ring D + C(12))), 182, 175, 161 (300–140 (ring D) +H), 150(*s*), 137, 127, 121, 109, 93, 91, 81, 67, 59, 55, 41, 28. According to TLC and mixed m.p. (no depression) identical with authentic material [29], while the mixed m.p. with ester **61** gave a depression. Unfortunately, due to lack of material, no rotation could be measured and no further proof for identity was possible to exclude isomers [21b].

11-Oxo-3β-(trimethylacetoxy)-5β(H)-8(14)-etienic-acid Methylester (**64**; *AL-1061*). To 6 mg of crude crystalline **59** (*AL-1053*) in 0.2 ml of abs. pyridine, 30 mg of trimethylacetyl chloride were added at 0° and left 16 h at 25°. After addition of *ca.* 0.2 g of ice and standing for 1 h, it was worked up with Et_2O to give 7 mg of neutral product. From Et_2O/pentane, 1 mg of crystalline **64** (*AL-1061*) could be secured, m.p. 142–147°. $[\alpha]_D^{21} = +61.9° \pm 25°$ ($c = 0.068$, $CHCl_3$). It had the same mobility in TLC as **72** (*AL-1052*) from sarmentogenin (see *Chart IV*). Due to lack of material, no final identification was possible.

Preparation of Relais Compounds 72 (*AL-1052*) and 74 (*AL-1091*) (*Chart IV*). – *11α-Acetoxy-3β-hydroxy-5β(H)-8(14)-etienic-acid Methylester* (**66**; *AL-1048*). Ester **65** (95 mg, *AL-271*) [20a] of m.p. 166–170° in 15 ml of MeOH was mixed with 70 mg of K_2CO_3 in 3 ml of H_2O and shaken for 3 days at 20°. Usual workup gave 85 mg of neutral product which was chromatographed on 5 g of SiO_2. *Fr. 4–5* (20 mg eluted with benzene/Et_2O 9:1) were starting material **65**. *Fr. 4–9* (eluted with benzene/Et_2O 9:1 and 85:15) were mixtures containing some 3β-acetoxy-11α-hydroxy-ester. *Fr. 10–15* (36 mg, eluted with benzene/Et_2O 4:1 and pure Et_2O) were essentially ester **66** but did not crystallize. *Fr. 16–17* (5 mg, eluted with $CHCl_3$ and $CHCl_3$/5% MeOH), contained mainly the dihydroxy-ester.

11α-Acetoxy-3β-(trimethylacetoxy)-5β(H)-8(14)-etienic-acid Methylester (**67**; *AL-1049*). To the 36 mg of crude, amorphous **66** in 0.8 of abs. pyridine, 0.2 ml of trimethylacetyl chlorid were added at 0° and then left at 25° for 16 h. After addition of 0.1 g of ice, the mixture was left for 1 h again. Workup gave 45 mg of crude product. From MeOH at –15°, 12 mg of crystals, m.p. 154–158°, were secured. Chromatography of the amorphous material from the mother liquor gave 18 mg more. Recrystallization from pentane gave colorless prism, m.p. 156–159°. $[\alpha]_D^{25} = +43.8° \pm 3°$ ($c = 0.388$, $CHCl_3$). UV (EtOH): 199.5 (4.063) corresponding to the fully substituted

C(8)=C(14) bond, and 252 (2.121). $C_{28}H_{42}O_6$ (474.61). According to the MS, it contained some impurity (perhaps $C_{28}H_{40}O_7 = M_2 = 488$). MS: 488 ($M_2$), 428 ($M_2$ – $AcOH_7$), 474 (M not visible), 443 ($M - {}^{\cdot}OCH_3$), 414 (M – AcOH), 399 (414 – ${}^{\cdot}CH_3$), 383 (414 – ${}^{\cdot}OCH_3$), 373, 355 (383 – CO) 312 (414 – 102 (trimethylacetic acid); m^* calc. $312^2:414 = 235.13$, found 235.5), 297 (312 – ${}^{\cdot}CH_3$), 281 (312 – ${}^{\cdot}OCH_3$), 265 (297 – CH_3OH), 258 (312 – 54(C(1–4)) from *retro-Diels-Alder*; m^* calc. $258^2:312 = 213.35$, found 213.5), 237 (265 – CO), 226 (258 – CH_3OH), 215, 216(*s*), 189, 57.

11α-Hydroxy-3β-(trimethylacetoxy)-5β(H)-8(14)-etienic-acid Methylester (**68**; *AL-1051*). To a soln. of 150 mg KOH in 10 ml of MeOH, 35 mg of **67** (*AL-1049*) were added and kept 2 days at 25°. The mixture was just acidified with aq. HCl, MeOH partly removed *in vacuo*, and the suspension extracted with $CHCl_3/Et_2O$. After addition of CH_2N_2 in Et_2O, the soln. was kept for 30 min, washed, dried, and evaporated. The crude mixture (27 mg) was chromatographed on 1 g of SiO_2. The first *Fractions* gave 6 mg of starting material *AL-1049*, from the *Fr. 4–8*, 16 mg of amorphous but according to TLC relatively pure **68** (*AL-1051*) was obtained.

11-Oxo-3β-(trimethylacetoxy)-8(4)-etienic-acid Methylester (**72**; *AL-1052*) *from* **68** (*ex sarmentogenin*). The 16 mg of **68** were dissolved in 1 ml of acetone and 0.08 ml of *Kiliani*'s mixture added at 0°, and left for 5 min. Usual workup gave 16 mg of crude product. This gave 4 mg of crystals, m.p. 140–145°. Another 6 mg were secured from the material from the mother liquor. Recrystallization from pentane gave colorless prisms, m.p. 143–146°. $[\alpha]_D^{25} = +98.6° \pm 6°$ ($c = 0.306$, $CHCl_3$). UV (cyclohexane): 196 (4.60). $C_{26}H_{38}O_5$ (430.56). MS: 430 (M), 399 ($M - {}^{\cdot}OCH_3$), 388 ($M - H_2C{=}O(42)$, *retro-Diels-Alder of* C(11-12)), 328 ($M - 102 = (CH_3)_3C{-}COOH$), 313 (328 – CH_3), 310 (328 – H_2O), 297 (328 – ${}^{\cdot}OCH_3$), 295 (313 – H_2O), 276, 253 (295 – 42), 222 (276 – 54, *retro-Diels-Alder* of C(1–4)), 209, 107, 52, 41.

7α-Acetoxy-3α-(methoxysuccinyloxy)-12α-tosyloxy-5β(H)-etianic-acid Methylester (**70**; *AL-1086*). Ester **69** [29a] (72 mg) and 300 mg of TsCl, both dried at 0.1 Torr at 40° for 2 h, were dissolved in 1 ml of abs. pyridine and left a week at 35°. After addition of 0.1 g of ice, the soln. was left for 16 h at 20° to hydrolize excess of TsCl. Workup with Et_2O gave 78 mg of crude product which was chromatographed on 4 g of SiO_2. The *Fr.* eluted with benzene/Et_2O and pure Et_2O (43 mg) gave from Et_2O/pentane crystalline **70**, m.p. 110–112°. The later *Fr.* eluted with $CHCl_3$ gave 22 mg of **69**. The anal. sample of **70** (*AL-1086*) showed m.p. 108–111°. $[\alpha]_D^{27} = +21.3° \pm 4°$ ($c = 0.481$ in $CHCl_3$). $C_{35}H_{48}O_{11}S$ (676.80). MS: M (not visible), 645 ($M - {}^{\cdot}OCH_3$), 544 (M – 132 ($CH_3O{-}CO{-}CH_2CH_2{-}COOH$), 512 (544 – CH_3OH), 505 (M – 141 ($CH_3{-}C_6H_4{-}SO_3^-$)), 484 (544–AcOH), 445 (505–AcOH), 444 (M – 142 – AcOH), 429 (444 – ${}^{\cdot}CH_3$), 412 (444 – CH_3OH), 385 (444 – $COOCH_3$, 59), 372, 313, 312, 297, 258, 253, 237, 203, 172 ($CH_3{-}C_6H_4{-}SO_3H$), 157, 145, 115 ($CH_3{-}OCO{-}CH_2{-}CH_2{-}C{\equiv}O^+$), 91.

7α-Acetoxy-3α-(methoxysuccinyloxy)-5β(H)-11(12)-etienic-acid Methylester (**71**; *AL-1087*). Tosylester **70** (85 mg, m.p. 110–112°) in 1 ml of abs. pyridine was sealed *in vacuo* in a bomb tube and heated in boiling xylene (*ca.* 120°) for 15 h. Usual workup gave 67 mg of crude product which was chromatographed on 4 g of SiO_2. *Fr. 5–9* (eluted with benzene/Et_2O 85:15) gave 36.5 mg of crude **71**. From *Fr. 10–15* (eluted with benzene/Et_2O 4:1 and 1:1), 25,5 mg of **70** were recovered. The pure **71** was obtained from Et_2O/pentane in colorless needles, m.p. 108–110°. $[\alpha]_D^{27} = +21.3° \pm 3°$ ($c = 0.481$, $CHCl_3$). ^{1}H-NMR: 0.72 (*s*, CH_3(18)); 0.89 (*s*, CH_3(19)); 1.62 (*s*, H_2O); 2.08 (*s*, CH_3 of acetyl); 2.61 (*s*, $COCH_2CH_2CO$); 3.19 (*s*, $CH_3O{-}C{=}O$); 3.70 (*s*, $CH_3O{-}C{=}O$); 4.64 (*m*, H_β–C(3)); 5.00 (br. *s*, H_β–C(7)); 5.50 (*dd*, $J = 10.3, 2$, H–C(11)); 6.21 (*dd*, $J = 10.3, 2.4$, H–C(12)). $C_{28}H_{40}O_8$ (504). MS: M (504, not visible), 473 ($M - {}^{\cdot}OCH_3$), 444 ($M - CH_3OH{-}CO$ or M – AcOH), 429 (444 – ${}^{\cdot}CH_3$), 412 (444 – CH_3OH), 373 (372 + H), 372 (M – 132 ($CH_3O{-}CO{-}CH_2CH_2{-}COOH$)), 357 (372 – ${}^{\cdot}CH_3$), 330 (372 – $CH_2{=}C{=}O$ (42)), 313 (373 – AcOH), 312 (372 – AcOH), 297 (312 – ${}^{\cdot}CH_3$; m^* calc. $297^2:312 = 282.72$, found 283), 258 (312 – C_4H_6 (*retro-Diels-Alder* of C(1–4))), 253 (312 – $CO{-}{}^{\cdot}OCH_3$), 237 (397 – 60), 226 (258 – CH_3OH), 215 (237 – CO), 211 (226 – ${}^{\cdot}CH_3$), 203, 197, 157, 131, 129, 115 ($CH_3O{-}CO{-}CH_2{-}CH_2{-}C{\equiv}O^+$), 105, 91, 87 (105 – H_2O), 79, 59, 55, 43 ($CH_3C{\equiv}O^+$).

7α-Acetoxy-3α-(methoxysuccinyloxy)-11-oxo-5β(H)-etianic-acid Methylester (**73**; *AL-1088*). To 35 mg of **71** in 2 mg of acetone, the soln. of 50 mg of *N*-bromoacetamide in 0,8 ml of H_2O was added and the mixture left 2 days at 25°. After addition of 2 ml of H_2O, the acetone was removed *in vacuo* and the suspension extracted with $CHCl_3/Et_2O$ 1:3. The org. layer was washed with dil. Na_2CO_3 soln. and H_2O, dried (Na_2SO_4), and evaporated *in vacuo*. The product (42 mg) was dissolved in 1 ml of AcOH, and 0.5 ml 2% CrO_3/AcOH soln. added and left 6 h. Usual workup gave 35 mg of crude bromo-ketone which was dissolved in 2 ml of AcOH, 30 mg of Zn dust and 30 mg of NaOAc added and warmed with shaking for ½ h to 90°. After removing part of AcOH *in vacuo* at 40°, the suspension was mixed with $CHCl_3/Et_2O$, filtered, and the soln. washed with H_2O, Na_2CO_3 soln., and H_2O. Drying and evaporating gave 30 mg of crude product (mixture) which was chromatographed on 4 g of SiO_2. *Fr. 3* (3 mg eluted with benzene/Et_2O 4:1) was starting material **71**. The *Fr. 4* (3 mg) was a mixture, while *Fr. 5–6* (9 mg eluted with benzene/Et_2O 4:1 and 7:3) were crude 11-oxo-ester **73**. *Fr. 7* (2 mg, eluted with benzene/Et_2O 7:3) was again a

mixture containting **73**, while *Fr. 8–12* (total 9.9 mg, eluted with benzene/Et_2O 1:1 and pure Et_2O) gave more polar material (not examined). The *Fr. 4* and *7* after re-chromatography gave 2 mg more of **71** and 3 mg more of **73**. Crystallization from Et_2O/pentane gave **73** (*AL-1088*) as opaque grains, m.p. 95–100°. $[\alpha]_D^{25} = +50.9° \pm 5°$ ($c = 0.267$, $CHCl_3$).

3,7,11-Trioxo-5β(H)-etianic-acid Methylester (**74**; *AL-1091*). Ester **73** (11.4 mg) in 1 ml of AcOH was hydrogenated with 10 mg of PtO_2 16 h at 25°. The crude 11β-hydroxy-ester could not be crystallized. The whole product (11 mg) was boiled under reflux with 2 ml of 4% KOH in MeOH for 2 h. After addition of H_2O, acidification with dil. HCl, it was extracted with $CHCl_3/Et_2O$. The soln. was washed with H_2O, dried, and evaporated *in vacuo*. The residue (10.5 mg) was dissolved in 0.5 ml of $CHCl_3$, and CH_2N_2 in Et_2O added, until the yellow color persisted for 10 min. After evaporation *in vacuo*, the residue was dissolved in 0.5 ml of 2% CrO_3/AcOH added in small portions during 3 h and then left at 25° for 16 h. Workup as usual gave 5.5 mg of crude neutral product which was chromatographed on 2 g of SiO_2. The *Fr. 5–6* (3 mg, eluted with benzene/Et_2O 4:1) gave from acetone/Et_2O 1.6 mg of crystalline **74** (*AL-1091*), m.p. 225–232°. $[\alpha]_D^{24} = +27.7° \pm ca.\ 15°$ ($c = 0.036$, $CHCl_3$). According to MS, this preparation probably contained a little 7α-acetoxy-3,11-dioxo-ester $C_{23}H_{32}O_6$ (404) as impurity. MS: 404 (impurity), 389 (404 – $^{\cdot}CH_3$), 373 (404 – $^{\cdot}OCH_3$), 360 (*M*), 345 (360 – $^{\cdot}CH_3$), 344 (404 – AcOH), 342 (360 – H_2O; *m** calc. $342^2{:}360 = 324.90$, found 325), 332 (360 – $H_2C{=}C{=}O$), 329 (360 – $^{\cdot}OCH_3$), 328 (360 – $HOCH_3$), 317 (345 – CO), 316 (360 – CO_2? or 317–$HC{\equiv}O^+$(29), 314 (332 – H_2O), 313 (328 – $^{\cdot}CH_3$), 310 (328 – H_2O), 303, 300 (328–CO or 360 – AcOH), 290 (332 – $H_2C{=}C{=}O$), 285 (300 – $^{\cdot}CH_3$), 284 (328 – CO_2 or 313 – $HC{\equiv}O^+$), 274 (*M* – 86 ($C_4H_6O_2{=}C$ (16, 17, 20)), 259 (274 – $^{\cdot}CH_3$), 250, 235, 232 (250 – H_2O), 231 (259 – 28), 222 (250 – 28), 209, 205 (*M* – 154–H, 154 (rings A,B+C(11)), 195, 177 (195 – 18 or 209 – CH_3OH or 205 – CO), 161, 153, 149 (177 – CO), 147, 95, 93, 91, 55 ($CH_2{=}CH{-}C{\equiv}O^+$), 43 ($CH_3C{\equiv}O^+$), 41, 31($^{\cdot}OCH$), 29 ($HC{\equiv}O^+$).

Chemical Proof for Special Orientation of Carboxyl Group and Oxygen in 8- and 14-Positions (***Chart V***). – *3β,11α-Diacetoxy-7,8β-epoxy-14β-hydroxy-12-oxoetianic-acid-(20–14)-lactone* (**76**; *AL-964*) *and By-product* **75** (*AL-975*). Acid **3** (600 mg) in 3 ml of abs. pyridine and 2 ml of Ac_2O were heated to 100° for 8 h. After evaporation *in vacuo*, the mixture was dissolved in $CHCl_3/Et_2O$ 1:3, washed with dil. HCl and Na_2CO_3 soln. dried, and the product (574 mg) chromatographed on 6 g of SiO_2. The material eluted with benzene/Et_2O 4:1 gave 488 mg of cryst. **76** from Et_2O/pentane, m.p. 175–180°. The anal. sample showed m.p. 178–181°. IR (CCl_4): no band in OH region (2.5–3.5), 5.53 *vs* (γ-lactone), 5.67*s* and 5.75*vs* (Ac and ketone), 7.33*s* (Ac), 7.75*w*, 8.0*s*, 8.15*vs* (Ac), 9.75*s* (Ac), 9.92*s*. $C_{24}H_{30}O_8$ (446.48). MS: 447 (*M*+H), 429 (447 – H_2O), 404 (*M* – $H_2C{=}C{=}O$), 401 (429 – CO), 387 (447 – AcOH), 386 (*M* – AcOH), 371 (386 – $^{\cdot}CH_3$), 369 (386 – $^{\cdot}OH$), 368 (386 – H_2O), 358 (386 – CO), 344 (386 – $H_2C{=}C{=}O$), 343 (344 – H), 330 (358 – CO), 327 (387 – AcOH), 326 (386 – AcOH), 315 (330 – $^{\cdot}CH_3$), 311 (326 – $^{\cdot}CH_3$), 309 (326 – $^{\cdot}OH$), 308 (326 – H_2O), 302 (330 – CO), 299 (327 – CO), 298 (326 – CO), 283 (298 – $^{\cdot}CH_3$), 281 (298 – $^{\cdot}OH$), 280 (298 – H_2O), 274 (302 – 28), 271 (299 – CO or C_2H_4), 270 (298 – CO or C_2H_4), 243, 225, 221, 203, 147, 145, 135, 119, 107, 105, 95, 93, 91 (tropylium ion), 81, 79, 77, 67, 55 ($CH_2{=}CH{-}C{\equiv}O^+$), 53, 43 ($CH_3C{\equiv}O^+$), 41, 29 ($HC{\equiv}O^+$). In another experiment with 970 mg of **3**, a small amount (20 mg) of a slightly more polar by-product **75** (*AL-975*) was obtained as crystals, m.p. 230–236°, probably with opened epoxy ring. IR ($CHCl_3$): 2.71*w* and 2.84*m* (OH), 5.54*s* (γ-lactone), 5.71*vs* (Ac), 5.87*vs* (Ac and keto group bonded), 7.30*s* (Ac), 8 μ region covered.

3β,11α-Diacetoxy-7α-formyloxy-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid-(20–14)-lactone (**77**, *AL-968*). Lactone **76** (605 mg, m.p. 175–180°) was heated with 5 ml of HCOOH to 100° for 1 h. After evaporation *in vacuo*, the residue was dissolved in acetone, filtered over a little SiO_2, the filtrate concentrated *in vacuo*, and Et_2O added. After crystallization started, some pentane was added dropwise, this gave 294 mg of crystalline **77**, m.p. 215–218°. The material from the mother liquor (298 mg) was chromatographed on 8 g of SiO_2. *Fr. 1–4* (137 mg, eluted with benzene/Et_2O 9:1 and 4:1) gave from Et_2O/pentane another 81 mg of crystals. With benzene/Et_2O 1:1, Et_2O and $CHCl_3$ more polar material was eluted (not examined). The anal. sample *AL-968* showed m.p. 215–218°. IR ($CHCl_3$): 2.71, 2.81*w* (sharp, OH), 2.86–2.94*w* (br., OH bonded), 5.56*vs* (γ-lactone), 5.71, 5.79*vs* (formyl, Ac, ketone), 6.24*w*, 7.30*m* (Ac), 8.1–8.35*vs* (region covered by $CHCl_3$, includes Ac), 8.62*s* (formyl (!)), 9.75, 10.08. $C_{25}H_{32}O_{10}$ (492.50). MS: 492 (*w*, *M*), 475 (*M* – OH), 450 (*M* – $H_2C{=}C{=}O$), 447 (*M* + H–HCOOH (46)), 446 (*w*, *M* – HCOOH), 436 (*M* – $CH_2{=}CH{-}CHO$ (56)), 432 (*M* – AcOH), 414 (432 – H_2O), 404 (432 – CO), 390 (432 – $CH_2{=}C{=}O$), 386 (432 – HCOOH), 372 (432 – AcOH), 368 (386 – H_2O), 362 (390 – CO), 357 (372 – $^{\cdot}CH_3$), 344 (390 – HCOOH or 386 – $CH_2{=}C{=}O$), 327 (386 + H – AcOH), 326 (386 – AcOH or 344/H_2O), 316 (344 – CO), 311 (326 – $^{\cdot}CH_3$), 308 (326 – H_2O or 386 – AcOH), 298 (326 – CO or 316 – H_2O), 297, 293 (308 – $^{\cdot}CH_3$ or 311 – H_2O), 283 (311 – CO), 281 (298 – $^{\cdot}OH$), 280 (298 – H_2O or 308 – CO), 270 (298 – CO), 265 (280 – $^{\cdot}CH_3$), 263, 254, 252 (270 – H_2O or 280 – CO), 237 (252 – $^{\cdot}CH_3$), 225, 221(*s*), 211, 203 (221 – H_2O), 191,

175, 173, 163, 161, 153, 147, 145, 135, 121, 119, 109, 108, 107 (*s*; perhaps C_7H_7–C≡O^+ (ring D)), 106, 105, 97, 95, 94, 93, 91, 81, 79, 67, 43 ($CH_3C{\equiv}O^+$), 29 ($HC{\equiv}O^+$), 28 (CO).

3β,11α-Diacetoxy-7α-formyloxy-14β-hydroxy-12-oxo-5β(H)-8(9)-etienic-acid-(20–14)-lactone (**78**; *AL-973*) *and By-products* AL-976 *and* AL-977. To 108 mg of **77** (m.p. 215–218°) in 0.6 ml of abs. pyridine, 0.15 ml $SOCl_2$ were added at 0° and left protected from moisture for 1 h at 5°. Normal workup at low temp. gave 104 mg of neutral product which, according to TLC, was a mixture. It was united with 40 mg of similar material of a previous experiment. These 144 mg were chromatographed on 8 g of SiO_2.

Fr. 1–3 (6.8 mg, eluted with benzene/Et_2O 19:1) were discarded. *Fr. 4–6* (52 mg, eluted with benzene/Et_2O 9:1 and 4:1) gave from acetone/Et_2O 12 mg of crude crystals of *AL-976*, m.p. 170–179°. *Fr. 7–10* (25.5 mg, eluted with benzene/Et_2O 7:3 and 1:1) gave from acetone/Et_2O 6 mg of crystalline *AL-977*, m.p. 210–220°. The *Fr. 11–13* (14 mg, eluted with Et_2O and $CHCl_3$) gave from acetone/Et_2O 8 mg of crystalline. *AL-973*, m.p. 260–270°. UV (EtOH): 201 (3.918; fully subst. double bond), 282 (3.692; β,γ-unsaturated ketone), perhaps still a mixture.

Putative 3β,11α-Diacetoxy-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid-(20–14)-lactone (**79**; *AL-982*). Lactone **76** (70 mg, m.p. 175–180°) in 2 ml of $CHCl_3$ and 1 ml of AcOH were cooled to 0°, 0.1 mg of 30% HBr-AcOH soln. added and kept 5 min at 0°. Workup at low temp. as with **28** gave 80 mg of crude product which was dissolved in 2 ml of AcOH; 100 mg of Zn-dust and 100 mg of NaOAc were added and the mixture shaken for 1 h at 25°. Workup as with **31** gave 75 mg of crude product which was chromatographed on 4 g of SiO_2. *Fr. 3–5* (48 mg, eluted with benzene/Et_2O 9:1) gave from Et_2O/pentane 20 mg of crystalline **79** *(AL-982)*, m.p. 110–114°. $[\alpha]_D^{25} = -8.6°$ ($c = 0.232$, $CHCl_3$). The later fractions (25 mg, eluted with benzene/Et_2O 4:1) contained mainly **76**. The lactone **79**, after treatment with SOCl in pyridine, gave prep. *AL-987*.

Lactone AL-987 (not formulated in *Chart V*). The compound *AL-987* showed m.p. 179–182°. $[\alpha]_D^{25} = +22.1°$. UV (EtOH): 202 (3.762), 245 (3.554), 299 (4.10!). IR (CCl_4): no OH bands, 5.54*s* (γ-lactone), 5.63, 5.75*s* (Ac), 5.87*s*, 6.06*w* (unsat. ketone). According to MS, it was still a mixture but contained mainly a compound $C_{22}H_{26}O_6$ (386.43); also combustion fitted, calc. C 68.37, H 6.78; found C 68.35, H 6.67. It, therefore, cannot be derived from a compound of structure **79** by simple loss of H_2O, this would have the empirical formula $C_{24}H_{30}O_7$.

3β-11α-Diacetoxy-7α,8β,14β-trihydroxy-12-oxo-5β(H)-etianic-acid-(20–14)-lactone (**80**; *AL-969*). Lactone **72** (*AL-968*; 90 mg; m.p. 215–218°) were dissolved in 20 ml of MeOH, a soln. of 100 mg of $KHCO_3$ in 5 ml of H_2O was added and the mixture left at 25° for 16 h. Usual workup gave 89 mg of crude **80** as amorphous resin.

3β,7α,11α-Triacetoxy-8β,14β-dihydroxy-12-oxo-5β(H)-etianic-acid-20–14-lactone (**81**; *AL-978*). Lactone **80** (45 mg amorphous) was dissolved in 0.5 ml of abs. pyridine, 0.3 ml of Ac_2O added, kept 4 h at 25° and 2 h at 70°. Usual workup gave 43 mg of crude product. The first crystals, m.p. 136–140°, were obtained from a trace of MeOH at −15°. These allowed nucleation in recrystallization from Et_2O/pentane giving **81**, m.p. 140–144°. $[\alpha]_D^{25} = -44.4° \pm 2°$ ($c = 0.914$, $CHCl_3$).

3β,7α,11α-Triacetoxy-14β-hydroxy-12-oxo-5β(H)-8(9)-etienic-acid-(20–14)-lactone (**82**; *AL-979*). To 220 mg of crude **81** in 0.8 ml of abs. pyridine, 0.3 ml of $SOCl_2$ were added at 0° and kept for 1 h at 5°. Usual workup gave 188 mg of crude product, and from Et_2O/pentane 123 mg of crystalline **82**, m.p. 120–122°. $[\alpha]_D^{25} = +5.0° \pm 2°$ ($c = 0.508$, $CHCl_3$). According to spectra, this prep. still contained small amounts of impurities. UV (cyclohexane): 204.5 (3.942; fully subst. C(8) = C(9) bond in β,γ-position to the oxo group), 286 (1.932; oxo group). IR (CCl_4): 2.89*w* (v. br., OH perhaps also H_2O), 5.55 *vs* (γ-lactone), 5.70 and 5.76 *vs* (Ac and ketone), 6.81 and 6.90*m*, 7.30*vs* (Ac), 8.1 (region covered), 8.28*vs* (Ac). IR (KBr): 2.91*w* (v. br., OH or H_2O), 5.55*vs* (γ-lactone), 5.70 (sh), 5.76*vs* (Ac and ketone), 730*s* (Ac), 8.00–8.15, 8.25*vs* (Ac), 9.62, 9.85*vs* (Ac). The ^{1}H-NMR (see *Fig. 7*) shows coupling of H_β–C(7) with H_β–C(11). $C_{26}H_{32}O_9$ (488.51). MS: 489 (*vw*, *M*+1), 464 (*w*, impurity $C_{24}H_{32}O_9$?), 446 (488 − H_2C=C=O or 464 − H_2O), 445 (488 − $^{\cdot}COCH_3$?), 429 (489 − AcOH), 428 (488 − AcOH or 446 − H_2O), 411 (*w*, 429 − H_2O), 404 (*w*, 464 − CO or 446 − H_2C=C=O), 400 (*w*, 428 − CO), 386 (s, 446 − AcOH or 428 − H_2C=C=O), 371 (*w*, 386 − $^{\cdot}CH_3$), 368 (*m*, 386 − H_2O or 428 − AcOH), 358 (*w*, 386 − CO or C_2H_4), 344 (386 − H_2C=C=O), 326 (386 − AcOH; *m**: 326^2:386 calc. 275. 33 found 275.5), 316 (344 − CO or C_2H_4), 311 (326 − $^{\cdot}CH_3$), 308 (326 − H_2O), 298 (326 − CO or C_2H_4), 283 (298 − $^{\cdot}CH_3$), 280 (298 − H_2O), 270 (298 − CO or C_2H_4), 255 (270 − $^{\cdot}CH_3$), 252 (270 − H_2O), 237 (252 − $^{\cdot}CH_3$), 234 (252 − H_2O), 228 (270 − H_2C=C=O), 221, 211, 173, 153, 145, 129, 119, 115, 108, 107, 105, 93, 91, 79, 77, 67, 60, 55, 43 (CH_3 − C≡O^+). Anal. calc. for $C_{26}H_{32}O_9$ calc. C 63.92, H 6.60%; found: C 63.14, H 6.69%.

3β,11α-Diacetoxy-8β,14β-dihydroxy-7,12-dioxo-5β(H)-etianic-acid-(20–14)-lactone (**83**; *AL-970*). To 43 mg of **80** (*AL-969*, amorphous) in 0.3 ml of AcOH, 0.5 ml of 2% CrO_3/AcOH soln. was added dropwise under shaking, and finally left 30 min at 25°. After addition of 2 drops of MeOH and standing for another 30 min, the usual workup gave 38 mg of crude neutral product. This yielded from acetone/Et_2O 32 mg of **83** in colorless crystals, m.p. 319–323°. IR ($CHCl_3$): 2.7*vw*, 2.83*w* (OH), 5.56*s* (γ-lactone), 5.70*s* (Ac), 5.78*vs* (Ac and oxo groups partly bonded), 7.29*s* (Ac), the 8.0–8.4*vs* region covered by $CHCl_3$, 9.79 and 10.01*s* (Ac). $C_{24}H_{30}O_9$ (462.48). MS: 463

(M + H), 462 (M), 445 (M – ·OH), 420 (M – H_2C=C=O), 417 (w, 445 – CO or CH_2CH_2), 402 (M – AcOH; m*: 402^2:462 calc. 349.79 found 350), 384 (402 – H_2O; m*: 484^2:402 calc. 366.81 found 367), 374 (402 – CO or C_2H_4), 360 (402 – H_2C=C=O; m*: 360^2:402 calc. 322.39 found 322.5), 342 (402 – AcOH; m*: 342^2:402 calc. 290.96 found 291), 332 (460 – CO or C_2H_4), 324 (342 – H_2O), 317 (332 – ·CH_3), 314 (342 – CO or C_2H_4 or 332 – H_2O), 306 (324 – H_2O), 296 (314 – H_2O or 324 – CO or C_2H_4), 286 (314 – CO or C_2H_4), 271 (286 – ·CH_3), 268 (286 – H_2O), 264 (324 – AcOH or 306 – H_2C=C=O), 258 (286 – CO or C_2H_4), 241 (ev. 296 – 55 (CH_2=CH–C≡O^+) from C (16, 17, 20)), 229, 213, 189, 179, 161, 153, 135, 125, 119, 108, 97, 93, 91, 81, 79, 77, 71, 67, 61, 55 (CH_2=CH–C≡O^+), 43 (CH_3–C≡O), 41, 29 (H–C≡O^+).

3β-Acetoxy-14β-hydroxy-11-oxo-5β(H)-etianic-acid Methylester (**85**; *AL-247*). Compound **84** (300 mg; m.p. 207 – 8°) [30b] was treated with O_3, Zn, $KHCO_3$, HIO_4, as described in [12] for 3-*O*-Acetyl-digitoxigenin and gave 200 mg of crude acid which was treated with CH_2N_2. The neutral product (200 mg) gave 100 mg of crystals from Et_2O/pentane, m.p. 160–165°. Additional 20 mg were obtained by chromatography from the amorphous residues. The anal. sample crystallized from Et_2O/pentane had m.p. 164–166°. $[\alpha]_D^{17}$ = +55.8° ± 2° (c = 1.146, $CHCl_3$) and $[\alpha]_D^{25}$ = +40.2° ± 2° (c = 0.807, acetone). Anal. calc. for $C_{23}H_{34}O_6$ (406.50): C 67.95, H 8.43; found: C 68.06, H 8.52.

3β-Acetoxy-11-oxo-5β(H)-8(9)-etienic-acid Methylester (**86**; *AL-1071*). Ester **85** (100 mg; m.p. 163–166°) was boiled under reflux with 3 ml of HCOOH for 6 h. To saponify formiates, the crude product (99 mg, UV (MeOH): 248 (3.798)) was dissolved in 10 ml of MeOH, a soln. of 200 mg of $KHCO_3$ in 5 ml of H_2O added, and the mixture shaken for 16 h at 25°. Usual workup (with Et_2O) gave 89 mg of neutral product which was chromatographed on 4 g of SiO_2. *Fr. 2–4* (21.5 mg, eluted with benzene/Et_2O 9:1) did not crystallize. *Fr. 5–6* (20 mg, eluted with benzene/Et_2O 3:1) gave 10 mg of **86** (*AL-1071*) in crystals, m.p. 119–120°. The later *Fr. 7–16* (eluted with benzene/Et_2O 6:4, 1:1, and pure Et_2O) gave 34 mg of amorphous material which, even after acetylation and chromatography, gave only 2 mg of additional crystals of **86**. The anal. sample showed m.p. 117–120°. $[\alpha]_D^{25}$ = +99.7° ± 15° (c = 0.051, $CHCl_3$). UV (EtOH): 248.5 (4.104; α,β- unsaturated ketone). $C_{23}H_{32}O_5$ (388.48). MS: 402 (0.3, impurity $C_{24}H_{34}O_5$?), 389 (28, M + H), 388 (10, M), 374 (0.1, 389 – 15 (·CH_3)), 373 (0.3, 388 – 15), 371 (0.05, 388 – 17 (OH)), 370 (0.05, 388 – 18), 357 (14, M – 31 (·OCH_3)), 356 (0.9, M – 32 ($HOCH_3$)), 346 (0.3, M – 42 (H_2C=C=O)), 345 (0.3, M – 43 (CH_3–C≡O^+)), 344 (0.4, M – 44 (CO_2)? or 373 – 29 (HC≡O^+)), 343 (0.2, 373 – 30 (CH_2O) or 358 – 15), 342 (0.7, 357 – 15), 329 (389 – 60 (AcOH)), 328 (41, M – 60; m*: calc. 328^2:388 = 277.78, found 277.5).

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