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DEHYDRATION AND SOLVOLYSIS PRODUCTS FROM GLYCYRRHETIC ACID

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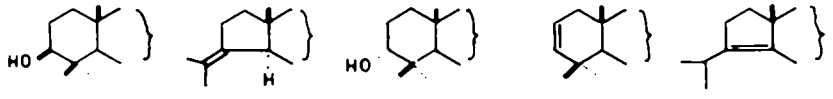
Abstract—Dehydration of methyl glycyrrhetate (VI) and β-amyrin with PCl_5 and with Fuller's earth afforded ring-A contracted products in which double bond migrations may occur. HI-induced dehydration of VI afforded a conjugated enonene 18α derivative. Solvolysis of VI sulphonate esters under a variety of conditions gave a number of ring-A contracted and uncontracted products in which the new ethenoid linkage was mostly confined to ring A.

DEHYDRATION[1] of triterpenoid alcohols may be accompanied by fundamental skeletal rearrangements. A classical reaction of the 3β (equatorial) alcohols (I) is their retropinacolic dehydration[2] with phosphorus pentachloride to give the ring-A contracted isopropylidene derivatives (II), a reaction which is favoured by the existing coplanarity of the involved centres.[3] On the other hand, the 3α (axial) alcohols (III) afford[4] by the same reagent non-contracted dehydration products (IV) formed by a conventional *trans* diaxial ionic elimination. The latter constitution also results[2c,5] from pyrolysis of 3β-benzoate esters in a thermal *cis* elimination.[6] Isomerization of II, in which the original 5α configuration is retained[3,7] is reported [2b,2d] to lead to the



I II III IV V

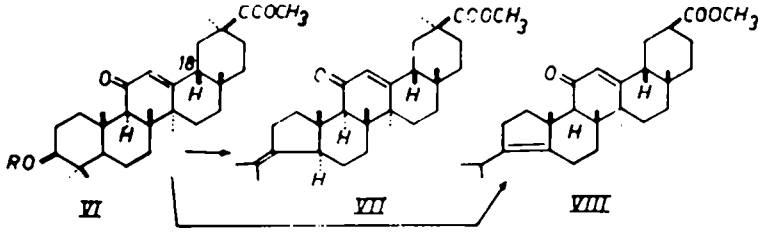
corresponding cyclopentene derivative (V). Such transformations are modelled in the analogous reactions of 2,2-dimethylcyclohexanol[8] and are accounted for

[1] O. Jeger, *Fortsch. Chem. Org. Naturstoffe* **7**, 1 (1950).
[2] [a] A. Vesterberg, *Ber. Dtsch. Chem. Ges.* **20**, 1242 (1887); K. A. Vesterberg and S. Westerlind, *Liebigs Ann.* **428**, 247 (1922); L. Ruzicka, H. Silbermann and M. Furter, *Helv. Chim. Acta* **15**, 482 (1932); L. Ruzicka, M. Montavon and O. Jeger, *Ibid.* **31**, 819 (1948); [b] G. G. Allan, F. S. Spring, R. Stevenson and W. S. Strachan, *J. Chem. Soc.* 3371 (1955); [c] A. Winterstein and G. Stein, *Liebigs Ann.* **502**, 223 (1933); [d] G. G. Allan, M. B. E. Fayez, F. S. Spring and R. Stevenson, *J. Chem. Soc.* 456 (1956).
[3] J.-F. Biellmann and G. Ourisson, *Bull. Soc. Chim. Fr.* 331 (1962).
[4] C. W. Shoppee and G. A. R. Johnston, *J. Chem. Soc.* 3261 (1961); G. Bancroft, Y. M. Y. Haddad and G. H. R. Summers, *Ibid.* 3295 (1961).
[5] H. Dieterle, H. Brass and F. Schaal, *Arch. Pharm.* **275**, 557 (1937).
[6] D. J. Cram, *Steric Effects in Organic Chemistry* (Edited by M. S. Newman) p. 304. Wiley, N.Y. (1956).
[7] J. F. Biellmann and G. Ourisson, *Bull. Soc. Chim. Fr.* 348 (1960).
[8] H. Meerwein, *Liebigs Ann.* **405**, 129 (1914).

stereochemically[9] and in conformational terms.[10] The recently reported[11] anomalous behaviour of methyl 3-epi-β-boswellate (a 3β alcohol), where no products of type II were obtained, seems to limit the generalizations outlined above to the 4,4-dimethyl products.

Most of the studies related to such dehydration reactions were made with pentacyclic triterpenoids (such as α- and β-amyrins, oleanolic acid and allobetulin), tetracyclic triterpenoids (such as dipterocarpol) and 4,4-dimethylcholestanol derivatives. In many of these parent alcohols, the molecule was either saturated or contained the usual ethenoid linkage in ring C. We have examined the dehydration reactions of glycyrrhetic acid (as methyl ester) to see if the specific structural features of such molecules influence the course of the reaction.

Methyl glycyrrhetate (VI, R = H) was dehydrated with phosphorus pentachloride and afforded methyl A-neooleana-3,12-dien-11-on-30-oate (VII) in high yield. The NMR spectrum of the product contained signals[12] which could be assigned to the various angular Me groups (δ 0·83: 25 and 28; δ 1·15: 26 and 27; δ 1·35: 29) besides two singlets (δ 1·58 and 1·71) due to the two isopropylidene methyl groups. This



substance exhibited an unexpectedly positive Cotton effect in the circular dichroism.[13] It was surprising to find that VII was not responsive to the isomerizing action of trichloroacetic acid or even that of hydrogen chloride. The desired product, methyl A-neooleana-3(5),12-dien-11-on-30-oate (VIII), was, however, obtained by the direct treatment of VI (R = H) with activated Fuller's earth in boiling xylene. Under the same conditions 18α-oleanolic acid lactone was reported[14] to give an analogously constituted dehydration product. The proposed formulation VIII finds support in the NMR spectrum where the non-equivalence of the two isopropyl methyl groups—due to rotational isomerism giving rise to two more stable conformations of the side chain—produces[15] a quadruplet in the Me region at δ 0·89, 0·95, 1·00 and 1·07 with intensities corresponding to $\frac{1}{2}$ Me group for each. An analysis of this quadruplet gives a J_{H-Me} value of 7 c/s and a chemical shift difference between the two Me groups of 4 c/s. This phenomenon finds an exact analogy in the spectrum[15] of a

[9] D. H. R. Barton, *Experientia* **6**, 316 (1950); D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.* 1048 (1951); D. H. R. Barton, *Ibid.* 1027 (1953); D. H. R. Barton and R. C. Cookson, *Quart. Rev.* **10**, 44 (1956).

[10] D. H. R. Barton and G. A. Morrison, *Fortsch. Chem. Org. Naturstoffe* **19** (1961).

[11] G. G. Allan, *Chem. & Ind.* 1497 (1965).

[12] We are deeply indebted to Dr. J.-F. Biellmann (Insitut de Chemie, Strasbourg) for making the NMR measurements and signal assignments: cf. Ref. 15.

[13] We thank Dr. G. Snatzke (Bonn University) for making the CD measurements and for helpful discussions.

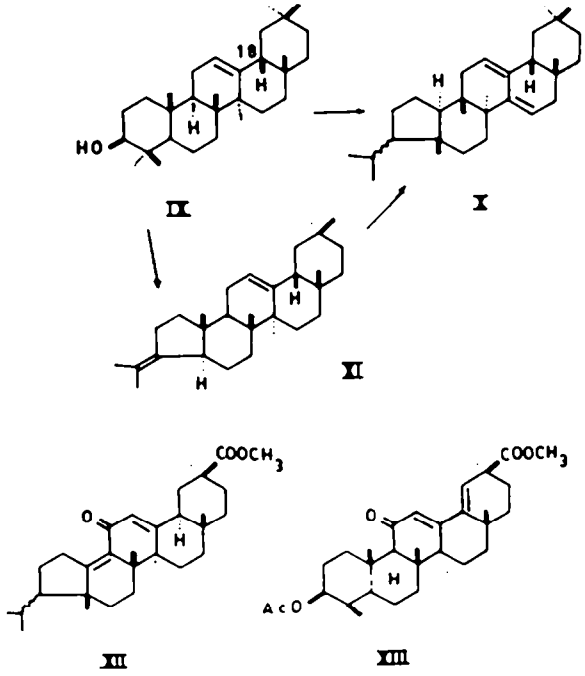
[14] L. Ruzicka, A. Rudowski, J. Norymberski and O. Jeger, *Helv. Chim. Acta* **29**, 210 (1946).

[15] J.-M. Lehn, *Bull. Soc. Chim. Fr.* 1832 (1962).

similarly constituted isopropylcyclopentene derivative in the dammarane series. The Me group signals at δ 0·85, 1·10, 1·15, 1·21 and 1·30 in this spectrum are attributable to the C-28, C-25, C-27, C-26 and C-29 groups respectively. In both compounds VII and VIII the configuration of the C-18 hydrogen atom is assumed[2d] to remain unchanged (β).

It was thought that the effect of Fuller's earth might reasonably lead to isomerization of VII to VIII. However, such treatment of VII afforded yet another dehydration product (A) of undecided nature, m.p. 235–238°, $[\alpha]_D$ +162·6°, in which the UV spectrum indicated the presence of an isolated $\alpha\beta$-unsaturated ketonic chromophore. The NMR spectrum contains a pattern of C-Me groups different from that of VII along with signals from two vinylic protons at δ 5·38 and 5·63 (doublet).

This remarkable effect of Fuller's earth as a non-ionic dehydrating agent was observed to lead to a different course of isomerization in β-amyrin (IX). This reaction gave a dehydration product which was strongly laevo-rotatory, $[\alpha]_D$ −135·8°, and exhibited maximal absorption in the UV light at 240 mμ (ϵ = 16,000). These properties favour its formulation as 5,8α,9β-trimethyl-10α-novoleana-12,14-diene (X) which is a structural analogue of "1-α-amyradiene"[2b] and may therefore be a stereoisomer of "1-β-amyradiene".[2d] The latter compound was given[2d] an undecided configuration at C-18, but in view of its preparation by a circuitous route involving HI-treatment it may well possess an α-oriented hydrogen atom at this centre in contrast to X which in all probability has a *cis*-locking of rings D and E. We have also obtained compound X by a Fuller's earth-induced isomerization of A-neooleana-3,12-diene[2d] (XI). Allan *et al.*[2d] attributed the failure of β-amyrin to directly undergo this "backbone"[16] type of transformation to the instability in acid media of the *cis*

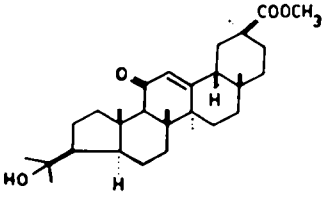


[16] W. Laird, F. S. Spring and R. Stevenson, *J. Amer. Chem. Soc.* **82**, 4108 (1960).

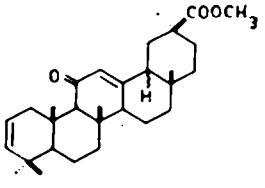
D/E-ring fusion in the oleanane series. The preparation of X directly from β-amyrin using Fuller's earth, therefore, represents a novel method for effecting such remarkable dehydration-rearrangement regardless of the stereochemistry at C-18. In the use of this non-ionic reagent, the possibility of inversion at C-18 is prevented and X, therefore, retains the original configuration.

A change in the stereochemistry at this labile centre to the more stable α-configuration under ionic conditions is particularly favoured by the presence of a 12-en-11-one system as in glycyrrhetic acid. Thus treatment of VI acetate (R = Ac) with boiling hydriodic acid–acetic acid mixture gave methyl 5,8,14-trimethyl-18α-novoleana-9(10),12-dien-11-on-30-oate (XII) in which the angular Me group migration was limited to that attached to C-10. This compound shows maximal absorption at 205, 254 and 286 mμ (ϵ = 5100, 11,600 and 10,000) as expected[3d] for a cisoid-transoid conjugated enonene. A support of the assigned 18α configuration in XII was obtained by its preparation by a similar treatment from methyl 18α-glycyrrhetate acetate[17] and from methyl 3β-acetoxyoleana-12,18-dien-11-on-30-oate[18] (XIII) where the reduction of the terminal ethylenic linkage occurred to give an 18α hydrogen atom. In the circular dichrograms, XII exhibited a negative while XIII a positive Cotton effect.

The literature contains several examples of solvolysis reactions performed with the sulphonate esters of 4,4-dimethyl-steroid and triterpenoid alcohols. The nature of the products, which are frequently more than one in a single reaction, depends largely on the precise reaction conditions and nature of reagents used. Thus a variety of ring-A contracted and non-contracted products, sometimes with Me group migrations, were reported. The configuration of the C-3 esterified OH function appears to be important in deciding the course of reaction.[4] Solvolysis of methyl glycyrrhetate 3β-methanesulphonate (VI, R = Ms) by heating in aqueous dioxan with calcium carbonate at 80° for 18 hr gave a complex mixture from which two pure products were isolated. One was identified as the isopropylidene derivative VII and the other was a tertiary alcohol for which structure XIV is assigned. The latter compound possesses the expected properties for such constitution besides a negative Cotton effect in circular dichroism and was readily dehydrated with phosphorus oxychloride in pyridine to VII. The assigned configurations of the isopropanol side chain and at C-5 follow from the evidence given[3,7] for analogously constituted products. When solvolysis was performed under more drastic conditions (refluxing for 24 hr), only a trace of XIV was detected and two products were isolated of which one was identified as VII. The other dehydration product, m.p. 236–239°, $[\alpha]_D$ +270·2°, is formulated as methyl 18ξ-oleana-2,12-dien-11-on-30-oate (XV). This constitution is based on the fact that the NMR spectra of this compound and its



XIV



XV

[17] J. M. Beaton and F. S. Spring, *J. Chem. Soc.* 3126 (1955).
[18] G. A. R. Kon and W. C. J. Ross, *J. Chem. Soc.* 741 (1942).

C-18 epimer XVI, m.p. 241–244°, $[\alpha]_D$ +246°, *vide infra*, are almost identical with respect to location and distribution of the Me group signals and in the presence of two vinyl protons (C-2 and C-3) in addition to that at C-12. The two isomers, however, are distinctly different in their location on silver nitrate-impregnated silica gel chromatoplates.[19] In fact this technique was helpful in distinguishing all the other dehydration products in this series despite their close structural relationship and nonpolar nature. The results of these two solvolysis experiments demonstrate the influence of the experimental conditions on the final reaction products. Products analogously constituted as XV and XVI have previously been reported to result from the sulphonate esters of ursane,[20] oleanane[20,21] and 4,4-dimethylcholestane[3,7,22,23] derivatives upon treatment with organic base, with basic or acid alumina and upon solvolysis in aqueous dioxan. The latter reaction is also reported to give products corresponding in constitution to VII[3,7], VIII[3,7,22] and XIV[3,7,22] from 4,4-dimethylcholestan-3β-yl methanesulphonate.

Both products XV and XVI were found to result, along with trace amounts of compound A and another one also of undecided nature (B, see later), from methyl glycyrrhetate (VI, R = H) directly by the action of phosphorus oxychloride in pyridine. Such reaction performed with 4,4-dimethylcholestan-3β-ol is known[23] to yield the analogously constituted 4,4-dimethylcholest-2-ene along with 3α-methyl-4-methylenecholestane which results by molecular rearrangement. Also, methyl oleanolate affords[24] by the same treatment a single product formulated as methyl oleana-2,12-dien-28-oate. We find a support for the constitutions XV and XVI in their formation, along with VIII, by pyrolysis of methyl glycyrrhetate benzoate (VI, R = Bz). It is remarkable in this connection to note the ability of the C-18 hydrogen atom to epimerise under thermal conditions.

Also, both methyl oleana-2,12-dien-11-on-30-oates (XV and XVI) were found to result from methyl glycyrrhetate toluene-*p*-sulphonate (VI, R = Ts) by different treatments. Thus reaction with sodium iodide in acetone solution under pressure afforded a mixture of products from which XVI and product A were isolated together with some XV which was detected on the chromatoplates. Acetolysis of the same ester, however, gave XV along with a dehydration product of unsettled constitution (B), m.p. 216–218°, $[\alpha]_D$ +239·5°, and traces of VII and VIII. The UV spectrum of compound B indicates an isolated $\alpha\beta$-unsaturated ketone grouping and the NMR spectrum reveals a close relationship to XV and XVI in proton and Me group contents. These reactions, involving expulsion of the sulphonic acid, reveal the capacity of the conditions used to induce a retropinacolic rearrangement as well as an independant 2,3-*cis* elimination.

EXPERIMENTAL

M.ps are uncorrected. Optical rotations were measured in chf unless otherwise stated. UV spectra: in EtOH soln using a Carl Zeiss M4QIII instrument. NMR spectra:[19] in $CDCl_3$ with TMS as a

[19] J. W. Copius-Peereboom, *Z. Anal. Chem.* **205**, 325 (1964); also cf. Ref. 20.
[20] F. Kohen, B. K. Patnaik and R. Stevenson, *J. Org. Chem.* **29**, 2710 (1964).
[21] C. Djerassi, D. B. Thomas, A. L. Livingston and C. R. Thompson, *J. Amer. Chem. Soc.* **79**, 5292 (1957).
[22] F. Kohen and R. Stevenson, *J. Org. Chem.* **30**, 2268 (1965).
[23] J. Levisalles, J. C. N. Ma and J. P. Pete, *Bull. Soc. Chim. Fr.* 1126 (1963); A. L. Combier, J. Levisalles, J. P. Pete and H. Rudler, *Ibid.* 1689 (1963).

standard using a Varian 60 mc instrument. CD measurements[18] were made with a Roussel-Jouan dichrograph in dioxan at 20°, 2 cm path length.

Thin-layer chromatography. A slurry of silica gel G (Merck) (3 g) in a 10% $AgNO_3$aq (15 ml) was applied to glass plates followed by drying at 120° for 2 hr. The chromatoplates were developed with CH_2Cl_2–AcOEt–AcOH (25:1:0·5) as solvent system and the spots were revealed by the chlorosulphonic acid–AcOH (1:3) spray reagent.

Methyl glycyrrhetate 3β-methanesulphonate (VI, R = Ms)

A soln of methyl glycyrrhetate (400 mg) in dry pyridine (2·5 ml) was treated with methanesulphonyl chloride (1 ml) and the mixture left to stand overnight. After adding excess water, the product (286 mg) was isolated in the usual manner and crystallized from abs EtOH to give plates, m.p. 169–170° (dec), $[\alpha]_D$ +134·5°. (Found: C, 67·94; H, 8·74; S, 5·72. $C_{33}H_{50}O_6S$ requires: C, 68·29; H, 8·96; S, 5·80%.)

Methyl glycyrrhetate 3β-toluene-p-sulphonate (VI, R = Ts)

A soln of methyl glycyrrhetate (400 mg) in dry pyridine (2 ml) was treated with toluene-*p*-sulphonyl chloride (400 mg). After standing overnight and working up in the usual manner, the product (350 mg) was crystallized from abs EtOH to give fine needles, m.p. 159–160° (dec), $[\alpha]_D$ +119°. (Found: C, 71·86; H, 8·48; S, 4·90. $C_{39}H_{54}O_6S$ requires: C, 71·96; H, 8·36; S, 4·93%.)

Methyl A-neooleana-3,12-dien-11-on-30-oate (VII)

Methyl glycyrrhetate (500 mg) was added portionwise to a suspension of PCl_5 (320 mg) in pet. ether (60–80°, 4 ml) and the mixture was shaken for 40 min. After the usual workup, the product (300 mg) was crystallized from acetone as fine needles (R_f 0·85), m.p. 218–221°, $[\alpha]_D$ +212·3°. (UV: max at 250 mμ, ε 11,400; CD (λ, $\Delta\varepsilon$): 375 (+0·30), 359·5 (+0·52), 346 (+0·50), 333 (+0·30), 274 (+0·10), 269 (+0·16). NMR signals at δ 0·83, 1·15, 1·35, 1·58, 1·71 (Me groups), 3·70 (OMe group) and 5·73 (vinyl proton). (Found: C, 79·52; H, 10·00; mol.wt. 466 by mass spectroscopy. $C_{31}H_{46}O_3$ requires: C, 79·78; H, 9·94%; mol.wt. 466.)

Methyl A-neooleana-3(5),12-dien-11-on-30-oate (VIII)

Methyl glycyrrhetate (800 mg) was dissolved in dry xylene (25 ml) and refluxed with activated Fuller's earth (3·5 g) for 3 hr. More Fuller's earth (3·5 g) was added and the reaction was followed on chromatoplates until the starting material completely disappeared after a further ½ hr reflux. The crude product (750 mg), isolated by the usual workup, was purified by chromatography on alumina and elution with hexane–benzene (1:1) to give 380 mg of VIII (R_f 0·75), m.p. 180–182°, $[\alpha]_D$ +206·2°. (UV: max at 247 mμ, ε 13,200.) NMR signals at δ 0·85, 1·10, 1·15, 1·21, 1·30 (Me groups C-28, C-25, C-27, C-26 and C-29 respectively), 0·89, 0·95, 1·00, 1·07 (non-equiv isopropyl Me groups), 3·71 (OMe group) and 5·77 (vinyl proton). (Found: C, 79·58; H, 9·89. $C_{31}H_{44}O_3$ requires: C, 79·78; H, 9·94%.)

Compound A. The isopropylidene derivative (VII, 0·21 g) was dissolved in xylene (dry, 15 ml) and refluxed with activated Fuller's earth (4·5 g) for 3 hr. More Fuller's earth (4·5 g) was added and reflux was continued for ½ hr. After the usual workup, the product (200 mg) was repeatedly crystallized from MeOH to give crystalline plates (R_f 0·73) m.p. 235–238°, $[\alpha]_D$ +162·6°. (UV: max at 245 mμ, ε 11,500.) NMR signals at δ 0·76, 0·96, 1·19, 1·25, 1·36, 1·57, 1·72 (Me groups), 3·69 (OMe group), 5·38 and doublet at 5·63 (vinyl protons). (Found: C, 79·80; H, 10·01. $C_{31}H_{44}O_3$ requires: C, 79·78; H, 9·94%.)

Treatment of VII with trichloroacetic acid in chf at room temp for 1 hr or with a sat soln of HCl in CH_2Cl_2 at 10° for 2 hr followed by the usual workup, gave unchanged material.

5,8α,9β-*Trimethyl-10α-novoleana-12,14-diene* (X)

(a) A soln of β-amyrin (500 mg) in xylene (20 ml) was refluxed with activated Fuller's earth (4·8 g) for 3 hr. After another addition of the reagent (4·8 g) and a further reflux period of ½ hr, the product (490 mg) was isolated as usual. Crystallization from acetone–MeOH gave fine needles, m.p. 144–147°, $[\alpha]_D$ −135·8° (UV: max at 240 mμ, ε 16,000). (Found: C, 87·63; H, 11·66. $C_{30}H_{46}$ requires: C, 88·16; H, 11·84%.)

(b) The same treatment of XI[16] (270 mg) with Fuller's earth afforded a crude product (250 mg) which crystallized from acetone–MeOH as fine needles, m.p. 145–149° underpressed by the previous preparation of X (identical IR spectra).

Methyl 5,8,14-trimethyl-18α-novoleane-9(10),12-dien-11-on-30-oate (XII)

(a) A soln of methyl glycyrrhetate acetate (1·73 g) in AcOH (180 ml) was refluxed with HI (54 ml) for 16–18 hr. The product (1·44 g) was treated with charcoal and crystallized from chf–MeOH–acetone to give needles, m.p. 315–317°, $[\alpha]_D$ +6·86 (pyridine). (UV: 3 max at 205 mμ, ε 5100; 254 mμ, ε 11,600 and 286 mμ, ε 10,000; CD (λ, Δε): 388 (−0·90), 371 (−1·51), 356 (−1·26), 340 (−0·71). (Found: C, 79·82; H, 9·72; mol.wt. 466 by mass spectroscopy. $C_{31}H_{46}O_3$ requires: C, 79·78; H, 9·94%; mol.wt. 466.)

(b) The same treatement of methyl 18α-glycyrrhetate[17] (100 mg) with HI (10 ml) was carried out to give 90 mg of a crude product which, after crystallization, proved identical with the previous preparation of XII, m.p. and mixed m.p. 308–313° (identical IR spectra).

(c) The same treatment of XIII[18] (100 mg) as above gave a crude product (83 mg) which was also shown to be identical with XII, m.p. and mixed m.p. 309–313° (identical IR spectra). CD of compound XIII (λ, Δε): 366 (+0·14), 348 (+0·10), 310 (+0·28), 270 (+14·03).

Solvolysis of methyl glycyrrhetate methanesulphonate (VI, R = Ms)

(a) A soln of the methanesulphonate (300 mg) in aqueous dioxan (1:1, 90 ml) containing $CaCO_3$ (300 mg) was heated at 80° for 18 hr. The solvent was evaporated and the remaining solid was dissolved in AcOH (15 ml) and excess water then added. A small amount of the crude product (270 mg), obtained after the usual workup, was shaken briefly with alumina in benzene–chf soln and shown on the chromatoplates to contain XIV, VII (R_f 0·02 and 0·85, respectively). The two constituents were resolved by column chromatography of the crude product on alumina, whereby VII was obtained by elution with pet. ether–benzene (1:1) as needles (120 mg), m.p. 215–218° (undepressed, IR spectra identical). Elution with benzene–ether (1:1) gave XIV which crystallized from aqueous acetone as needles (80 mg), m.p. 280–281°, $[\alpha]_D$ +145·9. (UV: max at 248 mμ, ε 13,000; CD (λ, Δε): 367 (−0·30), 353 (−0·60), 339·5 (−0·66), 328 (−0·36), 269·5 (+0·20), 253 (+7·40); IR: OH absorption at 3335 cm^{-1} in Nujol). (Found: C, 76·89; H, 9·66. $C_{31}H_{48}O_4$ requires: C, 76·81; H, 9·98%.)

(b) The solvolysis of methyl glycyrrhetate methanesulphonate (300 mg) was conducted as described above but under reflux for 24 hr. The crude product (250 mg) was inspected on the chromatoplates to reveal the presence of 2 comps (R_f 0·02, 0·61 and 0·85) identified by direct comparison as XIV, XV and VII. From a column chromatography on alumina, VII (110 mg, m.p. and mixed m.p. 215–218°, identical IR spectra) was eluted with hexane–benzene (1:1). The end fractions of the same solvent mixture gave XV (20 mg) which crystallized from chf–MeOH, m.p. 236–239°, $[\alpha]_D$ +270·2°. (UV: max at 247 mμ, ε 8200). NMR signals at δ 0·80 (C-28 Me), 0·90, 0·95 (C-23 and C-24 Me), 1·13 (C-25 C-26 and C-27 Me), 1·34 (C-29 Me), 3·68 (OMe group), 5·38 5·42 and 5·70 (vinyl protons). (Found: C, 80·09; H, 9·94. $C_{31}H_{46}O_3$ requires: C, 79·78; H, 9·94%.)

Treatment of XIV (10 mg) with $POCl_3$ (1 ml) in pyridine (1 ml) sol at 100° for 2 hr gave a crude product which was shown on the chromatoplates to consist essentially of one spot (R_f 0·85) identical with that due to VII by direct comparison.

Treatment of methyl glycyrrhetate with phosphorus oxychloride

A soln of methyl glycyrrhetate (5 mg) in pyridine (dry, 50 ml) was heated with $POCl_3$ (12 ml) at 100° for 2 hr and finally refluxed for 1 min. The product, (4·5 g) inspected on the chromatoplates, was found to contain 4 products (R_f 0·39, 0·61, 0·73 and 0·77) corresponding to XVI, XV, compound A and compound B, respectively. By column chromatography on alumina the product with R_f 0·39 (XVI) was eluted with benzene to give crystals (1·09 g) which were purified from MeOH–chf, m.p. 242–244°, $[\alpha]_D$ +246°. (UV: max at 248 mμ, ε 12,100; CD (λ, Δε): 370 (−0·10), 352 (−0·40), 337·5 (−0·42), 305·5 (−0·47), 240 (+11·56). NMR signals at δ 0·83 (C-28 Me), 0·91, 0·97 (C-23 and C-24 Me), 1·15 (C-25, C-26 and C-27 Me), 1·35 (C-29 Me), 3·69 (OMe group), 5·39, 5·43 and 5·70 (vinyl protons). (Found: C, 79·60; H, 9·93. $C_{31}H_{46}O_3$ requires: C, 79·78, 9·94%.)

Further elution with benzene gave the substance with R_f 0·61 (1·75 g) which was crystallized from chf–MeOH, m.p. and mixed m.p. with XV 236–239° (identical IR spectra).

Dehydration of methyl glycyrrhetate toluene-p-sulphonate (VI, R = Ts)

(a) A soln of the toluene-*p*-sulphonate (730 mg) in acetone (dry, 13 ml) containing NaI (1·46 g) was heated in a sealed tube at 100° for 5·5 hr. The reaction mixture was poured in dil $Na_2S_2O_3$aq and worked up as usual. The product (550 mg) was inspected on the chromatoplates and gave spots (R_f 0·39, 0·61 and 0·73) corresponding to compounds XVI, XV and A, respectively. By column chromatography of 200 mg of the crude mixture, XVI (130 mg) was removed with hexane–benzene (1:1), m.p. and mixed m.p. 241–244° (identical IR spectra) followed by compound A (50 mg), removed with the same solvent mixture, m.p. and mixed m.p. 235–238° (identical IR spectra).

(b) A soln of the toluene-*p*-sulphonate (1·7 g) in aqueous acetone (100 ml, 60% in water) was refluxed for 20 hr with AcOK (1·8 g). The mixture was evaporated under reduced press and the residue extracted with benzene and then inspected on the chromatoplates. This indicated the presence of 4 products (R_f 0·61, 0·75, 0·77 and 0·85) corresponding to XV, VIII, B and VII, respectively. By column chromatography on alumina XV (0·31 g) was eluted with hexane–benzene (1:1), m.p. and mixed m.p. 236–239° (identical IR spectra). The same solvent mixture removed in the late fractions compound B (0·19 g) which was recrystallized from chf–MeOH to give fine needles, m.p. 216–218°, $[\alpha]_D$ +239·5°. (UV: max at 247 mμ, ϵ 9000.) NMR signals at δ 0·84, 0·93, 0·98, 1·15, 1·36 (Me groups), 5·40, 5·45 and 5·72 (vinyl protons). (Found: C, 80·23; H, 9·94. $C_{31}H_{46}O_3$ requires: C, 79·78; H, 9·94%.)

Pyrolysis of methyl glycyrrhetate benzoate (VI, R = Bz)

A few mg of the benzoate (m.p. 316–318°) were heated at 360° for 1 hr in a N atm. The crude mixture was inspected on the chromatoplates where 3 spots (R_f 0·39, 0·61 and 0·75) were present corresponding to XVI, XV and VIII, respectively, by direct comparison.

Treatment of methyl glycyrrhetate methanesulphonate (VI, R = Ms) *with basic alumina*

A soln of the methanesulphonate (15 mg) in hexane was chromatographed on basic alumina (7 g). The hexane–benzene (1:1) eluate removed a small amount of a product identified with compound B, m.p. and mixed m.p. 216–218°. The mother liquors from this product were examined on the chromatoplates and found to contain XV (R_f 0·61) by direct comparison.