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THE STRUCTURE AND STEREOCHEMISTRY OF ATRACTYLIGENIN

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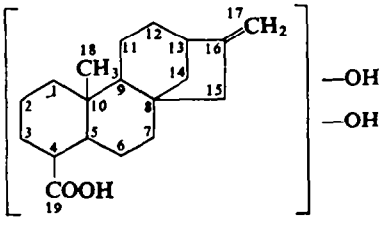
Abstract—The structure of atractyligenin $C_{19}H_{28}O_4$, the nor-diterpenoidic aglycone of atractyloside $C_{30}H_{44}O_{16}S_2K_2$ has been substantiated as Ia. The absolute configuration shown in Ia proves it to be a derivative of (−)kaurene.

PREVIOUS research[1] on *atractyligenin* $C_{19}H_{28}O_4$, the aglycone of atractyloside $C_{30}H_{44}O_{16}S_2K_2$, a toxic glucoside contained in the root of *Atractylis gummifera* L., had only resulted in the assignment of a partial structure to this diterpenoid.



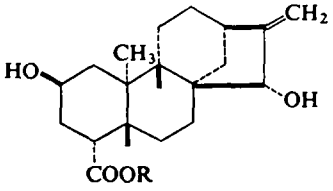
The position of the two secondary OH groups was still uncertain, and the stereochemistry of this substance required elucidation. Further investigations partially summarized in recent short papers[2, 3] and details now reported on the NMR and ORD

[1] T. Ajello, F. Piozzi, A. Quilico and V. Sprio, *Gazz. Chim. Ital.* **93**, 867 (1963) and bibliography therein reported.

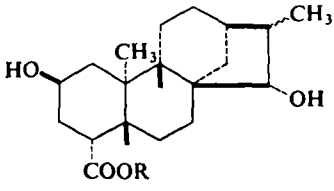
[2] F. Piozzi, A. Quilico, T. Ajello, V. Sprio and A. Melera, *Tetrahedron Letters* 1829 (1965).

[3] F. Piozzi, A. Quilico, R. Mondelli, T. Ajello, V. Sprio and A. Melera, *La Chimica e l'Industria, Milano* **48**, 371 (1966).

measurements as well as new chemical evidence have resulted in the complete elucidation of the structure and absolute configuration of atractyligenin, as shown in formula Ia.



Ia R = H
Ib R = Me



IIa R = H
IIb R = Me

The NMR spectra of *atractyligenin methyl ester* (Ib) and *hydroatractyligenin methyl ester* (IIb) confirm the presence in both substances of a single tertiary Me group; the NMR spectrum of IIb shows in addition a secondary Me group arising from the hydrogenation of the exocyclic methylene of Ib. The two protons of $\diagdown C{=}CH_2$ appear as two fairly broad signals at 5·08 δ and 5·24 δ, at lower fields than normally found for the exocyclic methylene of tetracyclic terpenes of the phyllocladene and kaurene type, all of which give broadened signals at about 4·70–4·80 δ.[4,5]

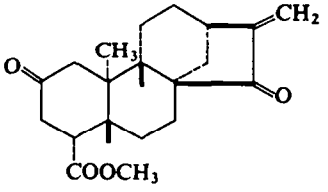
In the NMR spectra of Ia and IIb a multiple signal arising from the proton $\diagdown CH$—OH appears. This is formed by a triplet of triplets, indicating that this proton is axial and is coupled with two axial protons and two equatorial protons located on two adjacent carbon atoms. There is only one position in the atractyligenin and hydroatractyligenin skeleton that fulfills this requirement, that is position C-2; we can, therefore, conclude that one of the secondary OH groups is placed at C-2, and that its configuration is equatorial. Chemical evidence later discussed in this paper confirms this assignation.

The proton of the second $\diagdown CH$—OH group appears as a slightly broadened singlet in the NMR spectrum of Ib and as a doublet in that of IIb. This fact, together with the shift of the signal towards higher fields which can be observed for IIb, indicates that the second OH group of Ib is located in the neighbourhood of the $\diagdown C{=}CH_2$ double bond, presumably at C-15. This conclusion is strongly supported by the UV spectrum of *diketo-atractyligenin methyl ester* (III), which exhibits the characteristic absorption of α,β-unsaturated ketones (λ_{max} 234 mμ; $\epsilon = 7700$). In its NMR spectrum the two protons of the exocyclic methylene appear as two triplets centered at 5·53 and 5·98 δ with J = 1 c/s due to the coupling with the allylic proton at C-13 and to geminal coupling. The strong downfield shift is attributable to the deshielding effect of the neighbouring keto group at C-15.

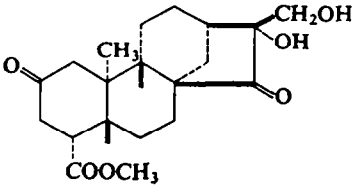
[4] L. H. Briggs, B. F. Cain, R. C. Cambie, B. R. Davis, P. S. Rutledge and J. K. Wilmshurst, *J. Chem. Soc.* 1345 (1963).

[5] G. Hugel, L. Lods, J. M. Mellor, D. W. Theobald and G. Ourisson, *Bull. Soc. Chim.* 2882, 2888 (1965).

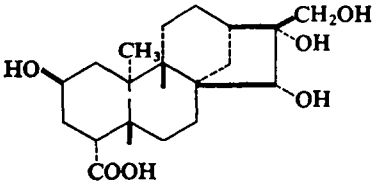
Hydroxylation of the double bond of diketo-atractyligenin methyl ester (III) affords the *diketo-diol* (IV). Oxidation of atractyligenin (Ia) with performic acid followed by alkaline hydrolysis yields the tetrol (V) already described. The presence in



III

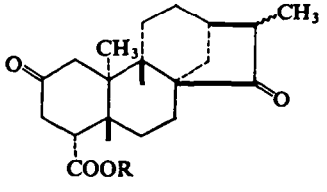


IV

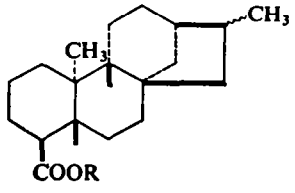


V

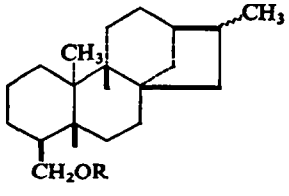
V of three vicinal hydroxyls at C-15, C-16 and C-17, is demonstrated by the consumption of two molecules of periodic acid on oxidation with this reagent. The C-4 carbon atom bearing the carboxy group of atractyligenin is secondary in accordance with the following reactions. Chromic acid oxidation of hydroatractyligenin (IIa) followed by esterification with CH_2N_2, as well as direct oxidation of its methyl ester (IIb), gives *diketo-hydroatractyligenin methyl ester* (VIb);[6] Huang-Minlon reduction of VIb affords *atractylanic acid* (VIIa) which on reduction with LAH gives 19-*hydroxy-atractylane* (VIIIa). The NMR spectrum of the *acetyl derivative* (VIIIb) shows an eight signals pattern at 3·40–4·20 δ due to the AB part of an ABX system arising from the two



VIa R=H
VIb R=Me



VIIa R=H
VIIb R=Me

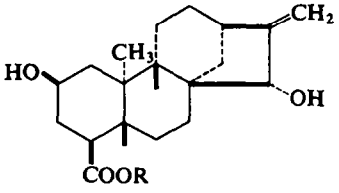


VIIIa R=H
VIIIb R=Ac

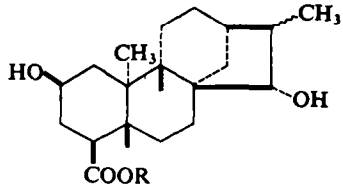
[6] This product was also formed on catalytic hydrogenation of diketoatractyligenin methyl ester (III)

oxymethylene protons at C-19 coupled with the proton at C-4 and VIIIb, therefore, has an $\diagdown$CH—CH_2OAc group.

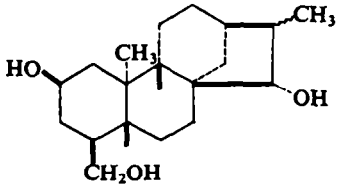
The p*K* MCS value of atractylanic acid (VIIa) is 7·53 which is close to that expected for an equatorial secondary carboxy group at C-4.[7] Since the NMR spectra of atractyligenin methyl ester (Ib) and hydroatractyligenin methyl ester (IIb) show signals for an equatorial proton at C-4, it must be concluded that, during the drastic conditions required by the Huang-Minlon reduction, the original axial carboxy group has epimerized to equatorial. This is confirmed by the fact that on prolonged refluxing with KOH in ethylene glycol both atractyligenin (Ia) and hydroatractyligenin (IIa) are converted into the corresponding 4-*epiatractyligenin* (IXa) and 4-*epihydroatractyligenin* (Xa) containing an equatorial carboxy group.



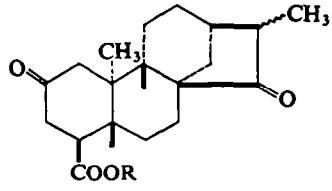
IXa R = H
IXb R = Me



Xa R = H
Xb R = Me



XI



XIIa R = H
XIIb R = Me

Reduction of 4-epihydroatractyligenin methyl ester (Xb) with LAH gives 4-*epihydroatractyltriol* (XI); chromic acid oxidation in acetone of Xa produces a 4-*epidiketohydroatractyligenin* (XIIa) which, on Huang-Minlon reduction, gives the same atractylanic acid (VIIa) mentioned above.

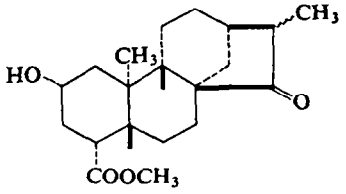
The reciprocal position and the stereochemical relationships of the two substituents of ring A in atractyligenin are further demonstrated by the catalytic reduction (PtO_2) of diketohydroatractyligenin methyl ester (VIb), which yields 15-*ketohydroatractyligenin methyl ester* (XIII). The OH group of XIII resulting from the reduction of the ketonic function of C-2 is now axial, as appears from the analysis of NMR data reported in the Experimental.

Moreover, on passing XIII over alumina, *γ-lactone* (XIV) is obtained, which obviously can be formed only if the OH at C-2 and the carbomethoxy group at C-4 are both axial.

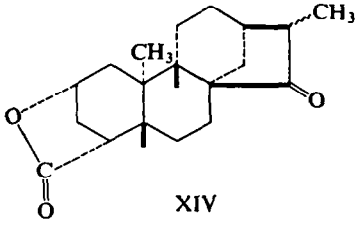
Further information on the structure and stereochemistry of atractyligenin has been provided by the study of its bromo derivatives. Oxidation of 2-*acetyl-atractyligenin*

[7] C. Pascual and W. Simon, *Helv. Chim. Acta* 47, 683 (1964).

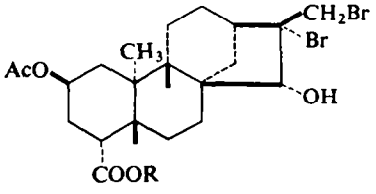
methyl ester dibromide (XVb) with Jones' reagent affords *2-acetyl-15-ketoatractyligenin methyl ester dibromide* (XVI) which exhibits a positive Cotton effect. Treatment of XVa with zinc dust and alkali yields *isoatractyligenin* (XVIIa), whereas dehydrohalogenation of the former with ethanolic KOH gives *16-bromoatractyligenin* (XVIIIa)



XIII



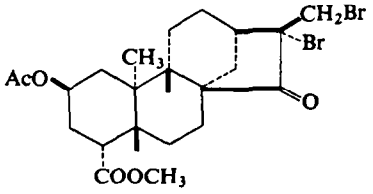
XIV



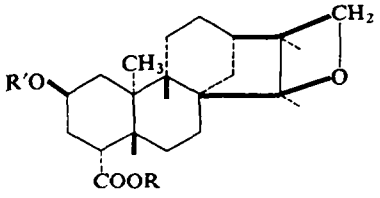
XV

which, by further action of zinc and alkali, is also converted into isoatractyligenin (XVIIa). Both these substances contain an oxetane ring, as demonstrated by the characteristic absorption bands of their IR spectra (bands at about 1200 and 960 cm^{-1}) and the analysis of their NMR spectra (Experimental).

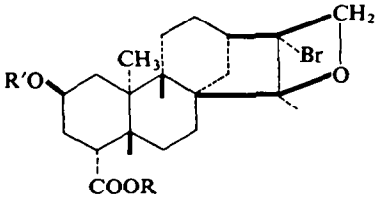
Isoatractyligenin methyl ester (XVIIb) and 16-bromoisoatractyligenin methyl ester



XVI

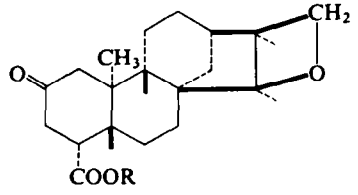


XVIIa R=H R′=H
XVIIb R=Me R′=H
XVIIc R=H R′=Ac
XVIId R=Me R′=Ac

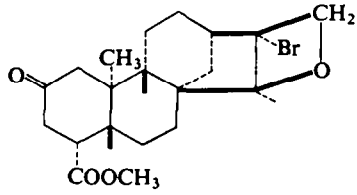


XVIIIa R=H R′=H
XVIIIb R=Me R′=H
XVIIIc R=H R′=Ac
XVIIId R=Me R′=Ac

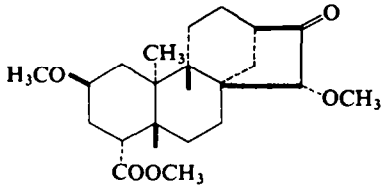
(XVIIIb) on chromic acid oxidation of the hydroxyl groups at C-2 produce the corresponding *monoketones* XIXb and XX), both of which exhibit strongly negative Cotton effects ($[\alpha]_{309} = -1910°$ and $[\alpha]_{310} = -1370°$ respectively). This indicates an antipodal *trans*-junction for rings A and B of atractyligenin, with 10α-Me and 5β-H as in (−)kaurene.



XIXa R = H
XIXb R = Me



XX



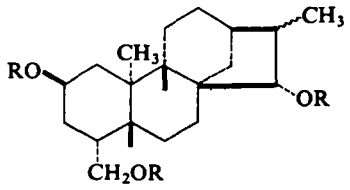
XXI

Atractyligenin, therefore, has the absolute configuration of (−)kaurene. This is urther corroborated by the negative Cotton effect of the monoketone at C-15 (XIII) and the positive Cotton effect of the *norketone* (XXI) formed on ozonolysis of atractyligenin methyl ester–dimethyl ether, indicating a ββ-configuration for C-15 and C-16. The configuration of the secondary OH group at C-15 results from the study of the triols obtained by reduction of the carboxylic function of atractyligenin (Ia) and hydroatractyligenin (IIa). *Hydroatractylitriol* (XXIIa), formed on reduction with LAH of IIa, has the 2β-OH group equatorial; in the NMR spectrum of its *triacetate* (XXIIb) the proton at C-15 appears as a doublet centered at 4·60 δ with J = 3·5 c/s. Reduction with LAH of diketohydroatractyligenin methyl ester (VIb) affords a *stereohydroatractylitriol* (XXIIIa) in which the OH group at C-2 is α-axial; the NMR spectrum of its *triacetate* (XXIIIb) shows the proton at C-15 as a doublet centered at 4·75 δ with J = 11 c/s, This increment of the coupling constant is accompanied by a strong shift towards higher fields of the signal of the secondary Me group at C-16, indicating that in XXIIIa the configuration of the OH at C-15 is inverted in respect to XXIIa. Since it is known[8] that the LAH reduction of a C-15 keto group in the (−)kaurene series always produces a 15β-OH, it can be inferred that the C-15 OH present in atractyligenin has the α-configuration.

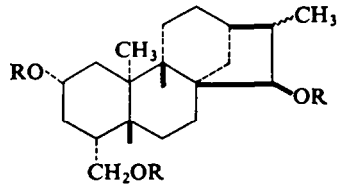
The configuration 15α-OH is also supported by the relatively high stability of *atractylitriol* (XXIV) towards acidic reagents: it is known that only the (−)kaurene derivatives with 15β-OH readily undergo the allylic rearrangement yielding the ketone at C-15, whereas derivatives with 15α-OH do not rearrange. Actually, atractyltriol (XXIV) resists the action of methanolic HCl and no ketonic compound could be

[8] L. H. Briggs, R. C. Cambie and P. S. Rutledge, *J. Chem. Soc.* 5374 (1963); C. Djerassi, C. R. Smith A. E. Lippmann, S. K. Figdor and J. Herran., *J. Amer. Chem. Soc.* 77, 4801 (1955).

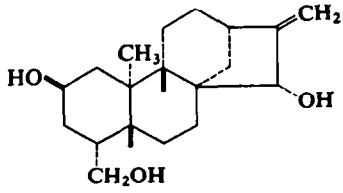
detected among the scanty by-products of the reaction. Reduction with LAH of diketo-atractyligenin methyl ester (III) affords *stereoatractyltriol* (XXV) possessing 2α-OH and 15β-OH configuration, converted by hydrogenation into stereohydroatractyltriol (XXIIIa). On treatment with methanolic HCl stereoatractylitriol (XXV) yields 15-*ketodiol* (XXVI) (IR band at 1735 cm^{-1}, CO in five-membered ring) which exhibits a negative Cotton effect.



XXIIa R=H
XXIIb R=Ac

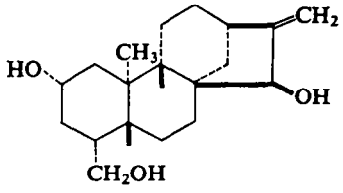


XXIIIa R=H
XXIIIb R=Ac

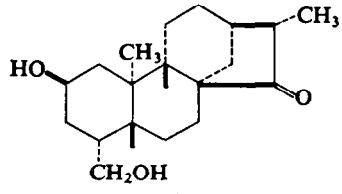


XXIV

The configuration of 15α-OH has, therefore, been determined and atractyligenin is assigned the absolute configuration shown in Ia.



XXV



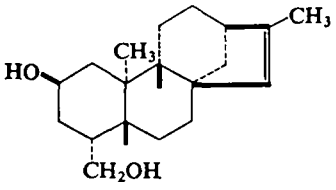
XXVI

Concerning the configuration of the secondary Me group at C-16 of hydroatractyligenin and its derivatives, TLC of IIb and VPC of diketohydroatractyligenin methyl ester (VIb) indicate that both products are mixtures of two epimers in the approximate ratios 80–85% to 20–15%. Attempts to isolate the pure epimers by fractional crystallization or gas chromatography were unsuccessful, although appreciable enrichment of one form was observed. Since alkaline treatment of diketohydroatractyligenin (VIa) results in a strong enrichment (up to 60%) in the originally less abundant epimer, this should represent the thermodynamically more stable 16α-CH_3 epimer; consequently, the 16β-CH_3 configuration should be assigned to the more abundant epimer.[9]

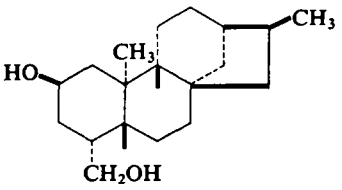
The allylic character of the OH group at C-15 in atractyligenin and its derivatives is confirmed by the partial hydrogenolysis which accompanies the reduction with sodium

[9] Catalytic hydrogenation of (−)kaurene gives mainly (−)kaurane with 16β-Me configuration.[4] Many derivatives of (−)kaurene present the same behaviour.

and ethanol of atractylitriol (XXIV) and atractyligenin methyl ester (Ib). Chromatographic separation over silica gel of the reaction mixture resulting from the reduction of Ib or XXIV affords *atractylendiol* (XXVII) which contains an endocyclic double bond, and is easily converted by catalytic hydrogenation into *atractylandiol* (XXVIII).

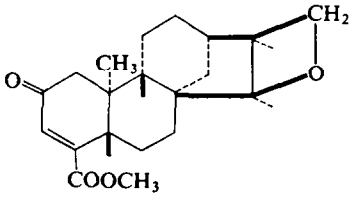


XXVII

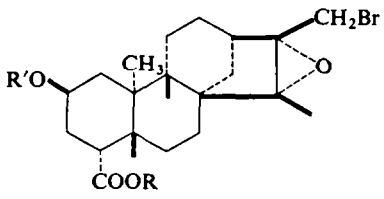


XXVIII

The chemical evidence in support of a C-2 OH group in atractyligenin involves bromination of 2-ketoisoatractyligenin methyl ester (XIXb) followed by dehydrohalogenation with collidine yielding a product which has the spectrochemical behaviour of an α,β-unsaturated ketone and α,β-unsaturated ester (XXIX). Its IR spectrum shows bands at 1682 cm^{-1} (α,β-unsaturated ketone) and 1720 cm^{-1} (α,β-unsaturated ester), and its UV spectrum has two maxima at 236 mμ ($\epsilon = 7700$) and 206 mμ ($\epsilon = 14{,}000$), respectively, the former disappearing after reduction with $NaBH_4$. Reduction of XXIX over C–Pd regenerates 2-ketoisoatractyligenin methyl ester (XIXb).



XXIX



XXXa R = H R' = H
XXXb R = H R' = Ac
XXXc R = Me R' = Ac

The oxetane ring of isoatractyligenin (XVIIa) and related compounds (XVIIIa, XIXa and XX), probably has the $\beta\beta$-configuration adopted in formula (XVIIa). This assignation is based on the assumption that in atractyligenin dibromide monoacetate (XVa) the bromo methyl group at C-16 has a β-configuration[10] and nucleophilic attack at C-15 by the $-CH_2Br$ at C-16 would lead to structure XVII.

Treatment of atractyligenin (Ia) with bromine and alkali gives, as stated, a *monobromo derivative* (XXXa); as shown by the NMR spectrum of its *monoacetate methyl ester* (XXXc) (Experimental), this compound contains an epoxide ring. Taking into account the fact that in the parent compound Ia the OH group at C-15 has the α-configuration, it is likely that the epoxide ring formed by nucleophilic attack at C-16 has the $\alpha\alpha$-configuration, as shown in formula XXXa. By prolonged refluxing with zinc dust and KOH the epoxybromo derivative (XXXa) regenerates atractyligenin (Ia).

[10] Addition reactions on the C-16–C-17 double bond of (−)kaurene backbone are believed to take place from the less hindered α-side.

EXPERIMENTAL PART

M.ps determined in capillary tubes are corrected. IR and UV spectra were recorded on spectrophotometers Perkin–Elmer Infracord 137 (nujol mull) resp. Beckman DK-2 (EtOH soln). NMR spectra were recorded on Varian HR-60, A-60 and HR-100 spectrometers, in $CDCl_3$ soln with TMS as internal standard: the chemical shifts are given in δ units from TMS and are taken to be positive in the direction of decreasing magnetic field.

$[\alpha]_D$ measurements were performed in EtOH soln on Perkin–Elmer 141 polarimeter. ORD determinations were recorded at the Institute of Organic Chemistry, University of Rome (by the courtesy of Prof. L. Panizzi) and at the Research Laboratories Lepetit, Milan (by the courtesy of Dr. G. G. Gallo) on Rudolph spectropolarimeters.

TLC was run on chromatoplates of silica gel G Merck. For preparative chromatography on column, silica gel Merck (< 0·08 mm) and neutral aluminium oxide Woelm were employed.

Atractyligenin methyl ester (Ib)

Atractyligenin (Ia), m.p. 189° (pseudo m.p. ~154°), $[\alpha]_D = -146°$, when treated with CH_2N_2 gave a methyl ester m.p. 158°–159° (beautiful plates from cyclohexane–AcOEt 3:1). IR spectrum: 3600 and 3300 cm^{-1} (OH), 1725 cm^{-1} (COOR), 1664 cm^{-1} (C=C), 907 cm^{-1} (>C=CH_2). NMR spectrum (at 100 Mc): s. at 0·92 δ (t-Me), s. at 3·68 δ ($COOCH_3$), broad signal at 3·86 δ (C-15 proton), broad signals at 2·71 δ (allylic proton on C-13) and 2·66 δ (equatorial proton on C-4), triplet of triplets at 4·23 δ ($J_{ax-ax}=10$ c/s, $J_{ax-eq}=4$ c/s: axial proton on C-2), two broad signals at 5·08 and 5·24 δ (exocyclic methylene on C-16).

Hydroatractyligenin methyl ester (IIb)

This was prepared[1] by catalytic hydrogenation of Ib on Pd–C or by CH_2N_2 treatment of IIa, m.p. 236°–237°, $[\alpha]_D = -95°$. The amorphous, uncrystallizable methyl ester was a mixture of 16β-Me and 16α-Me epimers in the approximate ratio 80–85% to 15–20%. IR spectrum: 3350 cm^{-1} (OH), 1730 cm^{-1} (COOR). NMR spectrum (at 100 Mc): s. at 0·90 δ (t-Me), d. at 1·14 δ ($J=7·5$ c/s: sec-Me), triplet of doublets at 2·66 δ ($J_{ax-eq}=5$ c/s, $J_{eq-eq}=2$ c/s: equatorial proton on C-4), broad doublet at 3·25 δ ($J=3·5$ c/s: C-15 proton), triplet of triplets at 4·25 δ ($J_{ax-ax}=10$ c/s, $J_{ax-eq}=4$ c/s: axial proton on C-2): by double irradiation at 2·16 δ this last signal changes into a triplet with $J=10$ c/s.

Diketoatractyligenin methyl ester (III)

This was prepared[1] by Jones' oxidation of atractyligenin methyl ester: m.p. 159°–160°, $[\alpha]_D = -216°$, after chromatography on Al_2O_3 act. 1 (eluent hexane–AcOEt 9:1) and crystallization from MeOH. IR spectrum: 1735 cm^{-1} (C_5-ring CO), 1715 cm^{-1} (COOR and C_6-ring CO), 1650 cm^{-1} (C=C), 876 cm^{-1} (>C=CH_2). UV spectrum: λ_{max} 234 mμ, $\epsilon=7700$ (α-monosubstituted α,β-unsaturated ketone).[11] NMR spectrum (at 100 Mc): s. at 0·98 δ (t-Me), signal at 2·75 δ (allylic proton on C-13), two triplets at 5·33 and 5·98 δ ($J=1$ c/s: exocyclic methylene protons, coupled with C-13 allylic proton and strongly deshielded by the C-15 keto group).

OsO_4 *Hydroxylation of diketoatractyligenin methyl ester*

Diketo-diol IV. Diketoatractyligenin methyl ester (mg 310) was dissolved in 100 ml anhyd. ether, then OsO_4 (250 mg) and pyridine (1 ml) were added and formation of a brown ppt. was observed. After 24 hr, 25 ml EtOH and a soln of $Na_2S_2O_5$ (2 g) in water (12 ml) was added, and the mixture refluxed 4 hr on a water bath. The ethereal layer was separated and yielded a solid residue which was chromatographed on Al_2O_3 act. 2; fractions eluted with AcOEt were neglected, fractions eluted with AcOEt–MeOH (4:1) gave rosettes of white needles, m.p. 191° (from cyclohexane–AcOEt). On TLC (eluent AcOEt–MeOH, 99:1) a single spot, $R_f=0·30$. (Found: C, 65·54; H, 7·73. $C_{20}H_{28}O_6$ requires: C, 65·91; H, 7·74%.) IR spectrum: 3400 and 3330 cm^{-1} (OH), 1740 cm^{-1} (C_5-ring CO), 1715 cm^{-1} (COOR and C_6-ring CO).

[11] Compare the UV values given by K. Wiesner, R. Armstrong, M. F. Bartlett and J. A. Edwards, *J. Amer. Chem. Soc.* **76**, 6068 (1954), for an identical structure in garryine.

Tetrol V

This was prepared by performic acid oxidation of the diacetyl derivative of atractyligenin and subsequent hydrolysis at 0° with aqueous KOH.[1] Almost the same yield of tetrol was obtained by analogous treatment of atractyligenin. When subjected to periodic acid oxidation, V requires 1·85 moles HIO_4: *formaldehyde* was evolved (identified as 2,4-dinitrophenylhydrazone, m.p. 166° also when mixed with sure specimen).

Diketohydroatractyligenin (VIa)

In 100 ml of hot acetone, 1 g hydroatractyligenin was dissolved, Jones' reagent was added till a yellow colour persisted (about 2 ml) and the soln was poured into 500 ml water. Ether extraction afforded a vitreous residue which crystallized from AcOEt and after drying *in vacuo* resulted in white, hard prisms, m.p. 236°, $[\alpha]_D = -160°$. (Found: C, 71·98; H, 8·21. $C_{19}H_{26}O_4$ requires: C, 71·67; H, 8·23%.) IR spectrum: 1740 cm^{-1} (C_5-ring CO), 1715 cm^{-1} (COOH and C_6-ring CO). By treatment with CH_2N_2, the *methyl ester* (VIb) was obtained as crystals (from EtOH) m.p. 185°–186°, no depression when mixed with the product obtained by analogous oxidation of hydroatractyligenin methyl ester; IR spectra, $[\alpha]_D$, R_f on TLC were identical.

Diketohydroatractyligenin methyl ester (VIb)

This was prepared by Jones' oxidation of hydroatractyligenin methyl ester;[1] $[\alpha]_D$ varied from −155° to −163° according to samples, as the product was a mixture of 16β-Me and 16α-Me epimers, the m.p. also varied from 179°–180° to 190°–192°. NMR spectrum (at 60 Mc): s. at 0·95 δ (t-Me), d. at 1·10 δ ($J = 7·5$ c/s: sec-Me), s. at 3·68 δ ($COOCH_3$). Analytical gas chromatography (Wilkens Aerograph HyFI A-600 instrument, flame ionization detector; 5′ × ⅛″ column packed with 20% SE-30 on Chromosorb W 60/80, temp 220°, carrier gas N_2 1·2 atm): two peaks after 22′ 15″ and 24′ 30″ ($T_R = 1·1$) in the ratio 15–25% to 75–85% according to the samples.

Basic equilibration of diketohydroatractyligenin (VIa)

A sample of VIa was methylated by CH_2N_2 to VIb: GLC indicated the occurrence of two epimers, 16α-Me (14%) and 16β-Me (86%). Another sample of the same VIa (mg 500) and KOH (2 g) was dissolved in 20 ml EtOH and refluxed for 12 hr; the soln was evaporated to dryness under red. press., the residue taken up in water and the soln acidified. The resulting product was methylated with CH_2N_2 and subjected to GLC yielding 16α-Me (62%) and 16β-Me (38%) epimers; after crystallization from EtOH, m.p. 193°–195°; GLC revealed no appreciable change in the ratio of the two epimers.

Atractylanic acid (VIIa)

This was prepared by Huang-Minlon reduction of VIb[1] and after crystallization from AcOEt had m.p. 205°–206°, $[\alpha]_D = -67°$. pK^*_{MCS} determination[12]. Found, 7·53; calc. 7·69 for a sec. equatorial carboxy group on C-4. With CH_2N_2 the acid afforded a *methyl ester* (VIIb) as greasy crystals, m.p. 60°. NMR spectrum (at 60 Mc): d. at 0·90 δ (sec-Me), s. at 0·95 δ (t-Me), s. at 3·65 δ ($COOCH_3$), no signal at 2·66 δ for the equatorial proton on C-4. Analytical gas chromatography (see under diketohydroatractyligenin methyl ester, same conditions except temp 250°): two peaks after 25′ 20″ and 27′ ($T_R = 1·07$) in the ratio 80% to 20%.

19-*Hydroxyatractylane* (VIIIa)

Atractylanic acid (mg 200) was reduced with LAH in ethereal soln. A white product was obtained and crystallized from aqueous MeOH as silky needles, m.p. 99°. (Found: C, 82·43; H, 11·50. $C_{19}H_{32}O$ requires: C, 82·54; H, 11·66%.) IR spectrum: 3350 cm^{-1} (OH), no carbonyl band. With pyridine–Ac_2O the substance gave an oily *acetyl derivative* (VIIIb), b.p. 180° under 1 mm Hg; IR spectrum: 1745 cm^{-1} (AcO, C=O stretching), 1240 cm^{-1} (AcO, C—O stretching), no OH band. NMR spectrum (at 60 Mc): s. at 0·95 δ (t-Me), d. at 0·90 δ ($J = 5$ c/s: sec-Me), s. at 1·97 δ (CH_3COO), eight-lines pattern at 3·40–4·20 δ (AB part of an ABX system: $J_{AB} = 10$ c/s, $J_{AX} = 6$ c/s, $J_{BX} = 3·5$ c/s: CH—CH_2OAc group).

[12] By the courtesy of Dr. W. Simon, E.T.H., Zürich.

4-Epiatractyligenin (IXa)

In 100 ml ethylene glycol, 2·5 g atractyligenin methyl ester and 5 g KOH was refluxed for 6 hr and the soln then poured into 400 ml water and acidified with H_2SO_4. The ppt was collected and crystallized from AcOEt as white needles (2·2 g), m.p. 240°–242°, $[\alpha]_D = -74°$. (Found: C, 70·99; H, 9·00. $C_{19}H_{28}O_4$ requires: C, 71·22; H, 8·81%). IR spectrum: 3350 cm^{-1} (OH), 1680 cm^{-1} (COOH), 1650 cm^{-1} (C=C), 895 cm^{-1} (>C=CH_2). 4-Epiatractyligenin was also obtained as a by-product in the prep. of atractylitriol by Na–EtOH reduction of atractyligenin methyl ester. By ozonolysis at room temp in AcOH soln, 4-epiatractyligenin yielded 0·75 moles *formaldehyde*, collected and weighed as 2,4-dinitrophenylhydrazone (m.p. 165°, no depression admix.). In EtOH soln on Pd–C, 4-epiatractyligenin absorbed 0·97 moles H_2, and yielded *4-epihydroatractyligenin*, m.p. 274°–276°, IR spectra superimposable. With CH_2N_2 4-epiatractyligenin yielded an oily *methyl ester* (IXb) which solidified but the crystals, m.p. 146°–148°, were very soluble in every solvent; the product was a single substance on TLC (AcOEt–MeOH 99:1; R_f=0·45). IR spectrum: 3350 cm^{-1} (OH), 1735 cm^{-1} (COOR), 1650 cm^{-1} (sh, C=C), 904 cm^{-1} (>C=CH_2). NMR spectrum (at 100 Mc): s, at 1·00 δ (t-Me), s, at 3·67 δ ($COOCH_3$), broad signal at 2·75 δ (allylic proton on C-13), broad signal at 3·82 δ (C-15 proton), unresolved m. at 3·80–3·90 δ (axial proton on C-2), two broad signals at 5·08 and 5·22 δ (exocyclic methylene).

4-Epihydroatractyligenin (Xa)

This was prepared by the procedure described for 4-epiatractyligenin; it crystallized from AcOEt with some difficulty (highest value of m.p. 276°), $[\alpha]_D = -24°$. (Found: C, 71·01; H, 9·38. $C_{19}H_{30}O_4$ requires: C, 70·77; H, 9·38%.) IR spectrum: 3550 and 3250 cm^{-1} (OH), 1690 cm^{-1} (COOH). By treatment with CH_2N_2 it gave an oily *methyl ester* (Xb) which hardened into uncrystallizable crusts, m.p. 106°–108°. IR spectrum: 3350 cm^{-1} (OH), 1730 cm^{-1} (COOR). NMR spectrum (at 100 Mc): s. at 0·98 δ (t-Me), d. at 1·12 δ (J=7 c/s: sec-Me), broad doublet at 3·35 δ (J=4 c/s: C-15 proton), s. at 3·67 δ ($COOCH_3$), unresolved m. at 3·85 δ (axial proton on C-2).

4-Epihydroatractylitriol (XI)

This was obtained by LAH reduction of Xb in ethereal soln. The product crystallized from benzene–EtOH as white prisms, m.p. 204°, $[\alpha]_D = -11°$. (Found: C, 73·85; H, 10·30. $C_{19}H_{32}O_3$ requires: C, 73·98; H, 10·46%.) IR spectrum: 3250 cm^{-1} (OH).

4-Epidiketohydroatractyligenin (XIIa)

A soln of 1·2 g 4-epihydroatractyligenin in 300 ml hot acetone was treated with Jones' reagent and yielded a product which after crystallization (twice) from AcOEt had m.p. 208°–209°, $[\alpha]_D = -84°$. (Found: C, 72·02; H, 8·23. $C_{19}H_{26}O_4$ requires: C, 71·67; H, 8·23%.) IR spectrum: 1740 cm^{-1} (C_5-ring CO), 1715 cm^{-1} (COOH and C_6-ring CO). By treatment with CH_2N_2 the *methyl ester* (XIIb) was obtained, m.p. 138°–139° from EtOH. (Found: C, 72·02; H, 8·41. $C_{20}H_{28}O_4$ requires: C, 72·26; H, 8·49%.) IR spectrum: 1740–1720 cm^{-1} broad (COOR and CO). A sample of the methyl ester (mg 600) was subjected to Huang-Minlon reduction (99% hydrazine hydrate, 10 ml; diethylene glycol, 20 ml; anhydrous ethanol, 10 ml): *atractylanic acid* (VIIa) was isolated, m.p. 205° and was identical with the product obtained by Huang-Minlon reduction of VIb: IR spectra were superimposable, no depression at mixed m.p.

Catalytic hydrogenation of VIb

15-*Ketohydroatractyligenin methyl ester* (XIII) *and transformation into γ-lactone* (XIV). The hydrogenation in AcOH soln on PtO_2 absorbed 1 mole H_2 slowly. The product crystallized from MeOH: m.p. 172°, $[\alpha]_D = -200°$. NMR spectrum (at 60 Mc): s. at 1·20 δ (t-Me), d. at 1·03 δ (J=7 c/s: sec-Me), s. at 3·73 δ ($COOCH_3$), m. at 4·10 δ (line width $W_{1/2}$=10 c/s: equatorial proton on C-2). ORD: negative Cotton effect with $[\alpha]_{323} = -1150°$. The substance gave a *mono acetyl derivative* m.p. 106°; transformable again into (VIb) by Jones' oxidation; after LAH reduction *stereo-hydroatractylitriol* was formed. According to these results, the substance has the structure XIII of 15-keto-hydroatractyligenin methyl ester. When eluted with benzene through Al_2O_3 act. 1, XIII cyclized yielding quantitatively XIV, m.p. 228° (from MeOH). (Found: C, 75·60; H, 8·69. $C_{19}H_{26}O_3$ requires: C, 75·46; H, 8·67%.)

IR spectrum: 1770 cm^{-1} (γ-lactone), 1733 cm^{-1} (C_5-ring CO). NMR spectrum (at 60 Mc): d. at 1·03 δ ($J = 6·5$ c/s: sec-Me), s. at 1·32 δ (t-Me), m. at 4·87 δ (equatorial proton on C-2, line width $W_{1/2} = 12$ cps), no signal for $COOCH_3$.

2-Acetyl-15-ketoatractyligenin dibromide methyl ester (XVI)

This was obtained from XVa by Jones' oxidation of XVb[1] and the ORD determination gave a positive Cotton effect with $[\alpha]_{340} = +1450°$.

Isoatractyligenin (XVIIa)

Isoatractyligenin $C_{19}H_{28}O_4$ was obtained[1] by Zn and alkali treatment of XVa or by analogous treatment of XVIIIa, as white crystals from AcOEt, m.p. 232°, $[\alpha]_D = -115°$. The substance did not take up H on catalysts; it contains only one OH and a carboxy group, while the fourth O atom forms a cyclic ether bond. *Isoatractyligenin methyl ester* (XVIIb) is amorphous, uncrystallizable. *Isoatractyligenin monoacetyl derivative* (XVIIc) has m.p. 228° (from AcOEt). *Isoatractyligenin methyl ester monoacetyl derivative* (XVIId) has m.p. 151° (from MeOH). The IR spectra reveal the presence of an oxetane ring: 1190 and 950 cm^{-1} for XVIIa, 1205 and 975 cm^{-1} for XVIIb, 1185 and 980 cm^{-1} for XVIIc, 1200 and 965 cm^{-1} for XVIId.[13] The NMR spectrum of XVIId at 100 Mc: s. at 1·00 δ (t-Me), s. at 2·03 δ (CH_3COO), s. at 3·71 δ ($COOCH_3$), quartet at 4·77 δ ($J_{AB} = 6·2$ c/s, $J_{AX} = 7·8$ c/s; H_A proton on C-17), quartet at 4·11 δ ($J_{AB} = 6·2$ c/s, $J_{BX} = 4·5$ c/s: H_B proton on C-17), d. at 4·51 δ ($J_{CX} = 4·8$ c/s: H_C proton on C-15), triplet of triplets at 5·38 δ (axial proton on C-2). By irradiation at 2·80 δ of the H_X proton on C-16, the quartet at 4·77 δ changed into a d. ($J_{AB} = 6·2$ c/s), the quartet at 4·11 δ into a d. ($J_{AB} = 6·2$ c/s), the d. at 4·51 δ into a s. By irradiation of H_B at 4·11 δ, the quartet of H_A at 4·77 δ changed into a d. ($J_{AX} = 7·8$ c/s).

16-Bromoisoatractyligenin (XVIIIa)

This was obtained by treatment of XVa with aqueous-ethanolic KOH as white needles, m.p. 218°–219° (from chf), $[\alpha]_D = -98°$. IR spectrum: 3400 cm^{-1} (OH), 1700 cm^{-1} (COOH), 1210 and 971 cm^{-1} (oxetane ring). The substance did not take up H on catalysts. With CH_2N_2 it gave a *methyl ester* (XVIIIb) as white crystalline felt, m.p. 187°–188° (from ethyl ether). IR spectrum: 3300 cm^{-1} (OH), 1740 cm^{-1} (COOR), 1190 and 975 cm^{-1} (oxetane ring). NMR spectrum of XVIIIb at 100 Mc: s. at 0·92 δ (t-Me), s. at 3·67 δ ($COOCH_3$), m. at 4·24 δ (axial proton on C-2), triplet of doublets at 2·67 δ (equatorial proton on C-4), AB quartet at 4·72 and 5·02 δ ($J = 7·3$ c/s: methylenic protons at C-17) d. at 4·58 δ ($^4J = 1·9$ c/s: C-15 proton, long-range coupled with C-13 proton, that must be *cis* to the first). By irradiation at 2·30 δ of C-13 proton, the d. at 4·58 δ simplified into a sharp s.

16-Bromoisoatractyligenin monoacetyl derivative (XVIIIc)

This was obtained by pyridine–Ac_2O treatment and had m.p. 229°–230° from MeOH. (Found: C, 57·57; H, 6·58; Br, 18·85; CH_3CO, 9·78. $C_{21}H_{29}O_5Br$ requires: C, 57·15; H, 6·62; Br, 18·11; CH_3CO, 9·75%.) IR spectrum: 1735 cm^{-1} (AcO, C=O stretching), 1705 cm^{-1} (COOH), 1240 cm^{-1} (AcO, C—O stretching), 1220 and 972 cm^{-1} (oxetane ring). *16-Bromoisoatractyligenin monoacetyl derivative methyl ester* (XVIIId) had m.p. 123° from ethyl ether.

Transformation of 16-bromoisoatractyligenin into isoatractyligenin

Compound XVIIIa (200 mg) and KOH (1·5 g) was dissolved in water (10 ml); Zn dust (600 mg) was added portionwise to the boiling soln during 3 hr. After filtering off and washing the excess Zn, the soln was acidified and extracted with ether, yielding a white residue which crystallized from AcOEt: m.p. 230°, no depression when mixed with isoatractyligenin, IR spectra superimposable.

2-Ketoisoatractyligenin (XIXa)

Isoatractyligenin (320 mg) was dissolved in acetone (30 ml) and treated with Jones' reagent (~0·4 ml) yielding white crystals from the ethereal extract; m.p. 235°–236°, $[\alpha]_D = -135°$. (Found: C, 72·09; H, 8·24. $C_{19}H_{26}O_4$ requires: C, 71·67; H, 8·23%.) IR spectrum: 1715^{-1} (COOH and C_6-ring CO), 1190 and 965 cm^{-1} (oxetane ring). The *methyl ester* (XIXb) was obtained by CH_2N_2 treatment and had

[13] G. M. Barrow and S. Searles, *J. Amer. Chem. Soc.* **75**, 1175 (1953); P. Yates and A. G. Szabo, *Tetrahedron Letters* 485 (1965).

been prepared[1] by Jones' oxidation of isoatractyligenin methyl ester: m.p. 168°, $[\alpha]_D = -135°$.[14] IR spectrum: 1725 cm^{-1} broad (COOR and C_6-ring CO), 1190 and 975 cm^{-1} (oxetane ring). ORD: negative Cotton effect with $[\alpha]_{309} = -1910°$.

2-Keto-16-bromoisoatractyligenin methyl ester (XX)

16-Bromoisoatractyligenin methyl ester (300 mg) was dissolved in acetone (20 ml) and oxidized with Jones' reagent. After pouring into 150 ml water, a ppt was formed which crystallized from MeOH as fine needles, m.p. 206°–207°. (Found: C, 58·23; H, 6·62; Br, 19·72. $C_{20}H_{27}O_4Br$ requires: C, 58·41; H, 6·62; Br, 19·43%.) IR spectrum: 1739 cm^{-1} (COOR), 1721 cm^{-1} (C_6-ring CO), 1025 and 977 cm^{-1} (oxetane ring). ORD: negative Cotton effect with $[\alpha]_{310} = -1370°$.

Methyl ester–dimethyl ether–norketone (XXI)

As previously described,[1] the product shows on ORD determination a positive Cotton effect, with $[\alpha]_{350} = +884°$.

Hydroatractylitriol (XXIIa)

This was best obtained by LAH reduction of hydroatractyligenin or its methyl ester in ethereal soln[1] and crystallized from benzene–EtOH as white prisms, m.p. 252°, $[\alpha]_D = -58°$. It formed a *triacetyl derivative* (XXIIb) on treatment with pyridine–Ac_2O. This was amorphous, uncrystallizable, as it was exceedingly soluble in every solvent, but was purified by chromatography on silica gel (eluent benzene–AcOEt 1:3): on TLC (eluent hexane–AcOEt 60:40) single spot, $R_f = 0{\cdot}64$. NMR spectrum of XXIIb at 60 Mc: s. at 1·05 δ (t-Me), d. at 1·10 δ (J = 6·5 c/s: sec-Me), signals at 2·0–2·1 δ (3 × CH_3COO), complex system at 3·80–4·30 δ (CH_2OAc on C-4), d. at 4·60 δ (J = 3·5 c/s: C-15 proton), m. at 5·10 δ (line width $W_{1/2} = 25$ c/s: axial proton on C-2). The complex system at 3·80–4·30 δ represents the AB part of an ABX system: by irradiation at 2·17 δ of the C-4 proton, the pattern changed into a quartet with J = 10·5 c/s. The d. at 4·60 δ was decoupled by irradiation at 2·08 δ of the C-16 proton.

Stereohydroatractylitriol (XXIIIa)

This was obtained by LAH reduction of VIb in ethereal soln and crystallized from benzene–EtOH, m.p. 242°, $[\alpha]_D = -113°$. The *triacetyl derivative* (XXIIIb), prepared by reaction with Ac_2O–pyridine was purified by chromatography on silica gel (eluent benzene–AcOEt 1:3): the substance was oily and did not solidify; on TLC (eluent hexane–AcOEt 60:40) single spot, $R_f = 0{\cdot}62$. IR spectrum: no OH band, 1724 and 1235 cm^{-1} (AcO, C=O and C—O stretching). NMR spectrum of XXIIIb at 100 Mc: d. at 0·82 δ (J = 7·5 c/s: sec-Me), s. at 1·20 δ (t-Me), complex system at 4·0–4·6 δ (CH_2OAc on C-4), d. at 4·75 δ (J = 11 c/s: C-15 proton), m. at 5·10 δ (line width $W_{1/2} = 9$ c/s: equatorial proton on C-2).

Atractylitriol (XXIV)

This was best prepared by Na and EtOH reduction of atractyligenin methyl ester.[1] The procedure was improved as follows: the alkaline soln, in which reduction was performed, was refluxed 4 hr, then evaporated to dryness under reduced press. and treated with water and extracted with ether until the whole ppt had been removed. From the aqueous alkaline soln remarkable quantities of *4-epiatractyligenin* were obtained on acidification; from the etheral extract a large residue was obtained: this was chromatographed on silica gel (10 g every 100 mg of product; eluent AcOEt, 50 ml fractions): fractions 6–11 gave *atractylendiol*, while fractions 12–18 yielded pure *atractylitriol*. The substance was crystallized from benzene–EtOH as white prisms, m.p. 217°, $[\alpha]_D = -101°$;[15] on TLC (eluent AcOEt–MeOH 95:5) $R_f = 0{\cdot}22$. IR spectrum: 3350 cm^{-1} (OH), 1650 cm^{-1} (C=C), 903 cm^{-1} ($\rangle C{=}CH_2$). The prep. of atractylitriol by LAH reduction of atractyligenin or atractyligenin methyl ester must be avoided because hydroatractylitriol is chiefly obtained.

Stereoatractylitriol (XXV)

The LAH reduction of III (ether–THF 1:1 soln, 48 hr reflux) yielded a residue from the organic layer, which crystallized from benzene–EtOH as hard crystals, m.p. 216°–218°, $[\alpha]_D = -103°$. (Found:

[14] In the previous communication,[1] m.p. 148°–149° was reported, that has been raised to 168° by many repeated crystallizations.

[15] In the previous communication,[1] m.p. 199°–200° and $\alpha_D = -85°$ were reported. Present measurements were performed on samples repeatedly purified by chromatography on silica gel.

C, 74·69; H, 9·74. $C_{19}H_{30}O_3$ requires: C, 74·47; H, 9·87%.) IR spectrum: 3300–3200 cm^{-1} (OH), 1660 cm^{-1} (C=C), 892 cm^{-1} (>C=CH_2). By catalytic hydrogenation on Pd–C in EtOH soln, the substance absorbed 1·02 moles of H_2 and yielded *stereohydroatractylitriol* (XXIIIa), identified by m.p. and IR spectrum, both identical with the product obtained by LAH reduction of diketohydroatractyligenin methyl ester.

HCl *treatment of stereoatractylitriol:* 15-*Ketodiol* (XXVI)

A soln of 50 mg stereoatractylitriol in 10 ml MeOH and 0·5 ml conc. HCl was refluxed for 6 hr and then evaporated to dryness under reduced press. On TLC (eluent AcOEt–MeOH 95:5) the vitreous residue showed two strong spots, R_f=0·30 and R_f=0·24: the second one corresponded to that of stereoatractylitriol. The residue was chromatographed on silica gel (eluent AcOEt) and fractions corresponding to the first spot were collected: the product was crystallized from benzene–EtOH as hard druses, m.p. 157°–158°. (Found: C, 74·78; H, 9·81. $C_{19}H_{30}O_3$ requires: C, 74·47; H, 9·87%.) IR spectrum: 3300 cm^{-1} (OH), 1740 cm^{-1} (C_5-ring CO). ORD: negative Cotton effect with $[\alpha]_{317}=-1550°$.

Atractylendiol (XXVII)

This was obtained as a by-product in the prep. of atractylitriol and was isolated by chromatography on silica gel—eluent AcOEt. It crystallized from benzene–EtOH as thin platelets, m.p. 210°–212°; on TLC (eluent AcOEt–MeOH 95:5) R_f=0·34. (Found: C, 78·28; H, 10·28. $C_{19}H_{30}O_2$ requires: C, 78·57; H, 10·41%.). IR spectrum: 3300 cm^{-1} (OH), 1655 cm^{-1} (C=C), 813 cm^{-1} (trisubstituted double bond). NMR spectrum (at 60 Mc, pyridine–deuteroacetone soln): s. at 0·95 δ (t-Me), d. at 1·70 δ (J=1·5 c/s: allylic methyl), d. at 3·72 δ (J=7 c/s: CH_2OH on C-4), m. at 4·12 δ (axial proton on C-2), broad signal, $W_{1/2}$=4·5 c/s, at 5·10 δ (vinylic proton on C-15). The substance could also be obtained in good yield by treatment of XXIV with Na and EtOH, followed by chromatographic separation from partly unreacted atractylitriol. By catalytic hydrogenation (Pd–C, EtOH soln) the substance absorbed 1 mole H_2: the product, *atractylandiol* (XXVIII), had m.p. 205° (from benzene–EtOH). Found: C, 77·55; H, 10·94. $C_{19}H_{32}O_2$ requires: C, 78·03; H, 11·03. IR spectrum: 3300 cm^{-1} (OH), no double bond band. NMR spectrum (at 60 Mc, deuteropyridine soln): s. at 0·97 δ (t-Me), d. at 1·00 δ (sec-Me), d. at 3·92 δ with J=6·5 c/s (CH_2OH on C-4), m. at 4·30 δ (axial proton on C-2), no vinylic proton signal.

Bromination of 2-ketoisoatractyligenin methyl ester (XIXb) *and dehydrobromination to the α,β-unsaturated keto-ester* (XXIX)

Compound XIXb (130 mg) was dissolved in 0·8 ml AcOH and added to a soln of 75 mg Br in 0·7 ml AcOH; after 20 min the soln was poured into water and extracted with ether. The residue obtained (positive Beilstein test) was dissolved in 2 ml collidine: after 3 min refluxing, boiling was stopped and the mixture diluted with water which dissolved the white crystalline ppt. By ethereal extract (washed with HCl and water, dried and evaporated) yielded a small quantity of solid which crystallized from MeOH as little prisms (10 mg), m.p. 163°. (Found: C, 72·94; H, 7·85. $C_{20}H_{26}O_4$ requires: C, 72·70; H, 7·93%.) UV spectrum: λ_{max} 236 mμ, ε=7700 (β,β-disubstituted-α,β-unsaturated ketone), λ_{max} 206 mμ, ε=14,000 (α,β-unsaturated ester): added with $NaBH_4$, after 24 hr λ_{max} 236 mμ has disappeared while $_{max}$ 206 mμ was still present. IR spectrum: 1720 cm^{-1} (α,β-unsaturated ester), 1682 cm^{-1} (α,β-unsaturated ketone), 1180 and 977 cm^{-1} (oxetane ring). Structure XXIX is therefore attributed to the product. A small sample of XXIX gave on hydrogenation with Pd–C in EtOH a product m.p. 160°–162°, whose UV spectrum had no absorption maxima while its IR spectrum was superimposable on that of XIXb.

Treatment of atractyligenin with alkaline solution of bromine: Epoxybromo derivative (XXXa)

The procedure described[1] was improved by decreasing the quantity of the reagent: to a soln of atractyligenin (2 g) and KOH (0·6 g) in water (30 ml), a soln of 4·5 g KOH and 3 g Br in 25 ml water was added. The product was crystalline, $C_{19}H_{27}O_4Br$, m.p. 199°–200°, $[\alpha]_D=-99°$. The substance did not react with O_3. On actylation it gave a *mono acetyl derivative* (XXXb), m.p. 215° from aqueous EtOH. (Found: C, 56·55; H, 7·19; Br, 17·13; CH_3CO, 9·43. $C_{21}H_{29}O_5Br$ requires: C, 57·15; H, 6·62; Br, 18·11; CH_3CO, 9·75%.) On treatment of XXXb with CH_2N_2 the *monoacetyl derivative methyl ester*

(XXXc) was obtained as soft crusts, m.p. 149°–151°. NMR spectrum of XXXc at 60 Mc: s. at 0·95 δ (t-Me), s. at 2·00 δ (CH_3COO), s. at 3·68 δ ($COOCH_3$), s. at 2·84 δ (C-15 proton in epoxidic ring), AB quartet centered at 3·64 δ ($J_{AB}=11$ cps: CH_2Br protons).

Transformation of the epoxybromo derivative (XXXa) *into atractyligenin*

Compound XXXa (950 mg) and KOH (6 g) were dissolved in ethanol (8 ml) and water (25 ml). To the boiling soln, Zn dust (5 g) was added portionwise during 2 hr and then the soln was refluxed for 16 hr, diluted with water, extracted with ether (discarded), acidified and longwise extracted with ether. By concentration of the ether layer a product was obtained which was purified from aqueous EtOH, m.p. 188° (pseudo m.p. ~155°) also when mixed with atractyligenin: IR spectra are superimposable.