923. *The Chemistry of Extractives from Hardwoods. Part XXX.* The Constitution of Katonic Acid, a Triterpene from* Sandoricum indicum.†

By F. E. King and J. W. W. Morgan.

Katonic acid has been shown to be 3α-hydroxyolean-12-en-29-oic acid by its conversion into β-amyrene, epi-β-amyrin, and 30-nor-β-amyra-9(11),13(18)-diene-12,19-dione. Acetylation of katonic acid by acetic anhydride and perchloric acid gives an anomalous product which has tentatively been assigned the constitution (III; R = Ac).

A minor extractive, indicic acid, is an ester of katonic acid in which the 3-hydroxyl group is combined with an unidentified triterpene acid.

Sandoricum indicum (family *Meliaceae*) is found in the forests of Burma, Siam, and the East Indies, where the timber, katon, is used locally for cart- and boat-building. The red-brown heartwood contains terpenaceous material which can be extracted from the shredded wood with boiling light petroleum. The white solid deposited from the cold solution consists essentially of a new triterpene, katonic acid (0·36—0·91% of the wood), and a small amount (0·04%) of a second triterpene, indicic acid. The main petroleum-soluble extract is divisible into steam-volatile oil (3·0%) and an acidic resin (2·0%), but these fractions have not yet been examined.

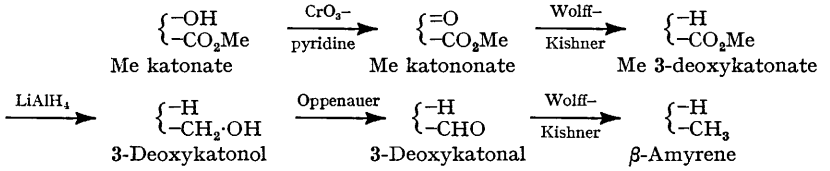
Katonic acid, m. p. 285—287°, $[\alpha]_D$ +47°, has the molecular formula $C_{30}H_{48}O_3$, and responds to the Liebermann–Burchard and the Tschugaeff test. It dissolves in aqueous-ethanolic sodium hydroxide, and the presence of a carboxyl group is confirmed by the ready formation of a methyl ester under Fischer–Speier conditions, thereby also demonstrating its unhindered nature. Likewise, the acid can be regenerated from the methyl ester under mild conditions of alkaline hydrolysis. Katonic acid and its methyl ester each form a monoacetate, establishing the presence of the remaining oxygen as an alcoholic hydroxyl group. Derivatives of katonic acid impart a yellow colour to tetranitromethane, but there is no evidence of conjugation in the ultraviolet absorption spectrum; the end absorption corresponds to that of a trisubstituted double bond.[1] Katonic acid and its derivatives are unaffected, however, by catalytic hydrogenation and by perphthalic acid.

* Part XXIX, preceding paper.

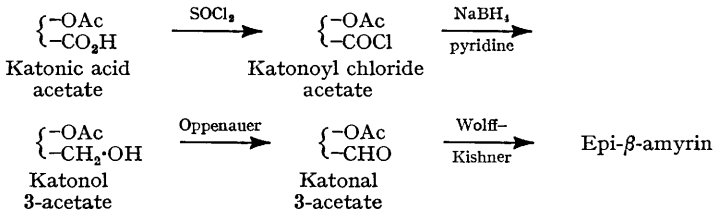
† Presented in a summarised form at the Chemical Society Symposium "Recent Advances in Terpenoid Chemistry," Glasgow, July 1957.

[1] Bladon, Henbest, and Wood, *J.*, 1952, 2737.

The carbon skeleton of katonic acid was established by the annexed series of reactions which resulted in the formation of β-amyrene, confirmed by comparison with an authentic specimen. The location of the hydroxyl group at position 3 was inferred from the positive



Zimmermann reaction given by methyl katononate,[2] and the large negative shift in molecular rotation occurring on acetylation (Δ_1 — 148°) indicated that it was oriented axially, an inference supported by bands at 1068s, 1037w, and 992s cm.$^{-1}$ in the infrared spectrum of katonic acid.[3] Further, reduction of methyl katononate by sodium borohydride affords an epimer. The unusual axial configuration of the hydroxyl group was evident also from the dehydration of methyl katonate by phosphorus pentachloride without ring contraction to methyl dehydrodeoxykatonate,[4] as was shown by its hydrogenation to methyl deoxykatonate. Final confirmation of the situation of the hydroxyl group was obtained by establishing a relation with epi-β-amyrin as in the annexed scheme.



The easy esterification of katonic acid, now related to the β-amyrin group of triterpenes, indicates that the carboxyl is at position 4 or 20. However, the former position can be rejected since katononic acid does not display the ready decarboxylation of a β-keto-acid; moreover, both methyl olean-12-en-23-oate and olean-12-en-24-oate are known [5] and are different from methyl 3-deoxykatonate.

Proof that the carboxyl group is indeed attached at position 20 was obtained by oxidation of methyl epikatonate acetate with selenium dioxide. The resulting dienedione was saponified and concommitantly decarboxylated to give the nor-β-amyradienedione (I) identical with that obtained similarly from methyl 11-deoxo-18β-glycyrrhetate acetate.[6] However, from a comparison of corresponding derivatives of epikatonic and 11-deoxo-18β-glycyrrhetic acid (Table) it is clear that the carboxyl group has opposite configurations in the two series of compounds. Since in 18β-glycyrrhetic acid it has the β-axial configuration,[7] in katonic acid the carboxyl group must be α-equatorial and this accords with its ease of esterification. Katonic acid is therefore 3α-hydroxyolean-12-en-29-oic acid (II; R = H).

With acetic anhydride–pyridine katonic acid yields a normal crystalline acetate, probably *via* a syrupy mixed anhydride. With acetic anhydride–perchloric acid, however, a new product $C_{32}H_{48}O_3$, $[\alpha]_D$ —273°, $\lambda_{max.}$ 273 mμ (ε 8900), is obtained which contains an *O*-acetyl group and is non-acidic. The second compound is also formed by further treatment of katonic acid acetate with acetic anhydride–perchloric acid, but methyl katonate

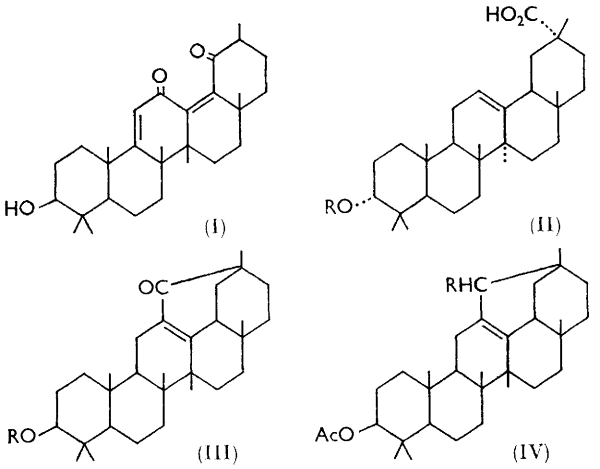
[2] Barton and de Mayo, *J.*, 1954, 887.
[3] Cole, *J.*, 1956, 4868.
[4] Barton, *Experientia*, 1950, **6**, 316.
[5] Vogel, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1951, **34**, 2321.
[6] Ruzicka and Jeger, *Helv. Chim. Acta*, 1942, **25**, 775.
[7] Beaton and Spring, *J.*, 1955, 3126.

		11-Deoxo-18β-glycyrrhetic acid	Epikatonic acid			11-Deoxo-18β-glycyrrhetic acid	Epikatonic acid
Me ester	m. p.	248° [a]	199—200°	Decarboxylated dienedione	m. p.	255—256·5°	256—257°
	$[\alpha]_D$	+108	+58		$[\alpha]_D$	−42	−40
Me ester acetate	m. p.	262—264	245—246		$\lambda_{max.}$ log ε	276—277 mμ 4·11	276—277 mμ 4·13
	$[\alpha]_D$	+120	+54				
Dienedione of Me ester acetate	m. p.	239—240	233—234	,, ,, acetate	m. p.	279—280° [b]	278—279·5
	$[\alpha]_D$	−69	−168				
	$\lambda_{max.}$ log ε	278—279 mμ 4·22	277 mμ 4·12				

[a] Ruzicka, Leuenberger, and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1271. [b] Ruzicka and Jeger, *ibid.*, 1942, **25**, 775.

gives a normal acetate with this reagent. The anomalous acetylation product is hydrolysed to a new compound, $C_{30}H_{46}O_2$, and is recovered from it by normal acetylation.

The new acetate appears to contain a ketonic carbonyl group, seemingly formed by cyclisation of the carboxyl as in (III; R = Ac). Examination of a molecular model shows that this ring closure can occur without affecting the configuration of either C/D or D/E ring junction but requires conformational changes with the result that ring D acquires the boat form whilst ring E assumes its original chair conformation. It is significant that 11-deoxo-18β-glycyrrhetic acid, on the other hand, in which the carboxyl group has the opposite β-axial conformation, simply undergoes normal acetylation. The infrared absorption of the new product at 1648 and 1635 $cm.^{-1}$ is somewhat low for a typical conjugated ketonic carbonyl, but the acetate-carbonyl absorption at 1728 $cm.^{-1}$ is normal. The ketonic group is sterically hindered and no carbonylic derivatives have been obtained. That it arises from the carboxyl group of katonic acid and not from an entering acetyl group is demonstrated by using propionic anhydride–perchloric acid as reagent; hydrolysis of the resulting propionate again yields the compound $C_{30}H_{46}O_2$ obtained *via* the anomalous acetate. Other experiments have established that catalytic amounts only of perchloric acid are required, thus showing that the reaction does not involve oxidation products. The necessity for a strongly ionising reagent (acetic anhydride–perchloric acid) suggests that the kation $(C_{29}H_{47}O)CO^+$, probably formed from mixed anhydride, is an essential intermediate.



An ambiguity exists in the occurrence of maximum ultraviolet absorption for the new ketone at 273 mμ, which is outside the normal limits of 225—252 mμ for an αβ-unsaturated ketone,[8] although for cyclopentylidenecyclopentanone $\lambda_{max.}$ 259 mμ has been recorded.[9]

[8] Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 76.
[9] French and Wiley, *J. Amer. Chem. Soc.*, 1949, **71**, 3702.

The observed value is in fact within the range 269—317 mμ recorded for dienones [10] although other triterpene dienones have maximum absorption at appreciably higher wavelengths than the katonic acid derivative (*e.g.*, methyl 18-dehydroglycyrrhetate acetate, $\lambda_{max.}$ 280 mμ: nor-β-amyra-12,17-dien-11-one acetate, $\lambda_{max.}$ 297 mμ). Nevertheless no purely chemical indication of a second olefinic bond has been obtained. Catalytic hydrogenation of the anomalous acetate results in the absorption of 2 mols., the keto-group being reduced to methylene. This is evident from the molecular formula of the product $C_{32}H_{50}O_2$ and the disappearance of infrared absorption at 1646 and 1635 cm.$^{-1}$. Ultraviolet absorption is maximal at 217 mμ (ε 5400) which again is intermediate between the normal absorption region for isolated and conjugated double bonds. Reduction with lithium aluminium hydride produces a diol with $\lambda_{max.}$ 223—224 mμ (ε 5200).

The ultraviolet absorption of the reduced compounds is in agreement with the presence of a conjugated cyclopropane system, but this possibility can be excluded since neither the anomalous acetate nor its catalytic reduction product showed additive reactions with hydrogen chloride. The reduction product, however, underwent isomeric change with this reagent to a substance showing end absorption consistent with presence of an isolated trisubstituted double bond. If, therefore, expression (III; R = Ac) is accepted for the ketone acetate, the product of catalytic hydrogenation becomes (IV; R = H), and that from lithium aluminium hydride reduction (IV; R = OH).

Present in crude katonic acid and separated by its low solubility in chloroform was a second crystalline product, indicic acid (average yield 0·04% of the wood), m. p. 254—255°, $[\alpha]_D$ +70°. A tetranitromethane test was negative but unsaturation was revealed by ultraviolet end absorption. Evidence for the carboxyl group was the slow formation of a methyl ester in boiling 3% methanolic hydrogen chloride. The spectrum of methyl indicate in the 3400—3600 cm.$^{-1}$ region has no absorption characteristic of hydroxyl, so that indicic acid does not contain a free alcoholic group; nor does it respond to carbonyl reagents.

The formula originally attributed to indicic acid, *i.e.*, $C_{30}H_{46}O_3$, was revised to $C_{60}H_{92}O_6$ when as a result of mild alkaline hydrolysis it was decomposed into katonic acid and a further triterpene, $C_{30}H_{46}O_4$, m. p. 304—306° (Liebermann–Burchard colour magenta; tetranitromethane test negative). Full identification of the new triterpene has not been possible, but it has the properties of a dicarboxylic acid. Thus, diazomethane, or long treatment with 3% methanol–hydrogen chloride, produced a neutral dimethyl ester, m. p. 135—136°, while less prolonged reaction led to an acid monomethyl ester, m. p. 228—229°, from which the neutral ester was obtained by further methylation. The ultraviolet absorption of the normal ester is indicative of a tri- or even tetra-substituted double bond. Indicic acid has, therefore, the partial structure (II; R = $C_{30}H_{45}O_3$) but owing to insufficiency of material characterisation of the residue $C_{30}H_{45}O_3$ remains incomplete.

Experimental

Unless otherwise stated, specific rotations are given for ~1% solutions in $CHCl_3$ at room temperature, ultraviolet absorption spectra of ethanolic solutions were measured on a Unicam S.P. 500 spectrophotometer, and analytical specimens were dried at 150—160° in a vacuum. Light petroleum was of b. p. 60—80°.

Extraction of Sandoricum indicum *Heartwood.*—Yields varied for different samples of timber but a typical extraction is given. The finely shredded heartwood (7·15 kg.) was extracted for 18 hr. with boiling light petroleum, giving a white solid (112 g.) suspended in a green (sometimes red) petroleum solution. The filtered petroleum solution was evaporated to a syrup (365 g.) which was separated into a steam-volatile oil (220 g.) and a non-volatile resin (145 g.). The white solid dissolved almost completely in chloroform, leaving an insoluble residue (14·2 g.)

[10] Evans and Gillam, *J.*, 1945, 432.

which was a mixture of wood chips and crude indicic acid. The chloroform-soluble part (90·5 g.) was dissolved in 2·5 l. of methanol; the solution, on concentration to 1 l. and cooling, deposited stout needles of katonic acid, m. p. 277—278° (44 g.).

Katonic Acid.—Repeated crystallisation of the crude crystals from methanol gave pure *katonic acid*, m. p. 285—287° (vac.), $[\alpha]_D$ +47° (Found, for a sample dried at room temperature: C, 76·2; H, 10·8. $C_{30}H_{48}O_3,CH_3{\cdot}OH$ requires C, 76·2; H, 10·7. Found, after drying at 160° in a vacuum: C, 79·3; H, 10·6; wt. loss, 7·5. $C_{30}H_{48}O_3$ requires C, 79·0; H, 10·6; wt. loss, 6·7%), ε_{210} 3740, ε_{220} 705. The compound was insoluble in aqueous sodium hydroxide; a portion (1—2 mg.) was dissolved in ethanol, and sufficient water just to cause precipitation was added: addition of one drop of aqueous sodium hydroxide redissolved the precipitate. A magenta colour is produced in the Liebermann–Burchard test, and with Tschugaeff's reagent an initial pink colour changes rapidly to orange and then reddish-brown. No colour is produced with tetranitromethane.

A suspension of katonic acid (0·5 g.) in 3% methanolic hydrogen chloride (10 ml.) was boiled under reflux for 4 hr. during which the solid dissolved. On cooling, stout needles of *methyl katonate* (0·38 g.), m. p. 189—190°, $[\alpha]_D$ +47° (Found: C, 79·3; H, 10·8. $C_{31}H_{50}O_3$ requires C, 79·0; H, 10·6%), which gave a yellow colour with tetranitromethane were obtained. The *acetate*, m. p. 201—202°, $[\alpha]_D$ +14° (Found: C, 77·4; H, 10·1; OAc, 8·4. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·3; OAc, 8·4%), was obtained by the action of acetic anhydride and pyridine on the ester.

A solution of methyl katonate (0·2 g.) in 1% ethanolic potassium hydroxide (50 ml.) was boiled for 3 hr. and then poured into water (150 ml.) and chloroform (50 ml.). The resultant emulsion was broken by sodium chloride, giving a white solid insoluble in either layer. This solid and the separated aqueous layer were acidified, and the product was extracted into chloroform which on evaporation gave crystals of katonic acid (0·14 g., 72%), m. p. and mixed m. p. 284—285° (vac.).

Methyl Katononate.— A solution of methyl katonate (0·7 g.) in pyridine (7 ml.) was added to a suspension of the complex prepared by dissolving chromic acid (0·7 g.) in pyridine (7 ml.);[11] the mixture was kept at room temperature overnight, then diluted with water and extracted with ether. Evaporation of the ethereal solution (after washing with acid, base, and water) gave a solid which by two recrystallisations from methanol gave iridescent plates of *methyl katononate* (0·47 g.), m. p. 157—158°, $[\alpha]_D$ +80° (Found: C, 79·7; H, 10·7. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%). The compound gave a positive Zimmermann test [2] and a *2,4-dinitrophenylhydrazone*, m. p. 213—214° (Found: C, 68·3; H, 8·0; N, 9·0. $C_{37}H_{52}O_6N_4$ requires C, 68·5; H, 8·1; N, 8·6%), $\lambda_{max.}$ 367 mμ (ε 26,000 in $CHCl_3$).

Methyl 3-Deoxykatonate.—Methyl katononate (0·5 g.), 90% hydrazine hydrate (1·5 ml.) and potassium hydroxide (1·5 g.) in ethylene glycol (15 ml.) were boiled under reflux for 1·5 hr. Distillate was then removed until the vapour temperature reached 180°, and boiling was continued for another 3 hr. The product was diluted with water, then acidified, and the solid was collected in ether. The white solid obtained on evaporation was boiled for 1·5 hr. with 3% methanolic hydrogen chloride (50 ml.). Plates of *methyl 3-deoxykatonate* (0·39 g.), m. p. 166—167°, $[\alpha]_D$ +66° (Found: C, 81·9; H, 11·3. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·3%), requiring no further purification, were deposited from the solution.

3-Deoxykatonol.—Methyl 3-deoxykatonate (0·8 g.) in dry ether (25 ml.) was added dropwise to a boiling 0·32M-solution of lithium aluminium hydride in ether (33 ml.), and boiling was continued for 6 hr. Excess of hydride was decomposed by dropwise addition of methanol, then the mixture was diluted with water and acidified and the product extracted by ether. Recrystallisation of the solid from methanol gave needles of *3-deoxykatonol* (0·65 g.), m. p. 167—168°, $[\alpha]_D$ +90° (Found: C, 84·7; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

3-Deoxykatonal.—A solution of 3-deoxykatonol (2 g.) and *p*-benzoquinone (6 g.) in toluene (200 ml.) was concentrated to 160 ml., aluminium t-butoxide (2 g.) was added, and the mixture was boiled for 3 hr. Excess of quinone was removed by steam-distillation and the product was extracted by ether. The ether solution, after having been washed with dilute sodium hydroxide, yielded a white solid (1·4 g.) which was purified by passing it in light petroleum solution through a column of alumina and recrystallising the eluted solid four times from ethanol. Pure *3-deoxykatonal* has m. p. 165—166° (with evolution of a gas; tube inserted

[11] Poos, Arth, Beyler, and Sarrett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

10° below m. p.), $[\alpha]_D$ +101° (Found: C, 84·5; H, 11·5. $C_{30}H_{48}O$ requires C, 84·7; H, 11·4%), and gives a 2,4-*dinitrophenylhydrazone*, m. p. 200—202° (Found: C, 71·6; H, 8·6; N, 9·6. $C_{36}H_{52}O_4N_4$ requires C, 71·5; H, 8·7; N, 9·3%), $\lambda_{max.}$ 360—361 mμ (ε 24,400 in $CHCl_3$).

β-*Amyrene*.—The reduction of 3-deoxykatonal (0·5 g.) was carried out as described for methyl katononate. The product was recrystallised from ethanol–light petroleum and gave an unidentified compound (0·08 g.), decomp. >250°, and β-amyrene (0·25 g.), m. p. 159°, $[\alpha]_D$ +96° (Found: C, 87·4; H, 12·4. Calc. for $C_{30}H_{50}$: C, 87·7; H, 12·3%). The latter compound depressed the m. p. of the starting compound, but did not depress that of authentic β-amyrene, m. p. 161—162°, kindly supplied by Professor E. R. H. Jones and Dr. T. G. Halsall.

Action of Phosphorus Pentachloride on Methyl Katonate.—Phosphorus pentachloride (1 g.) was added to a solution of methyl katonate (1 g.) in light petroleum (100 ml.) at room temperature and after 100 min. the mixture was heated under reflux for 1 hr. The cooled petroleum solution was washed with water, dried, and passed through a column of alumina. The eluted product, recrystallised from light petroleum, was *methyl dehydro-3-deoxykatonate*, m. p. 158—159°, $[\alpha]_D$ +107° (Found: C, 82·3; H, 10·6. $C_{31}H_{48}O_2$ requires C, 82·2; H, 10·7%).

Reduction of this compound by hydrogen over a platinum catalyst in glacial acetic acid gave methyl 3-deoxykatonate, m. p. and mixed m. p. 166—167°, $[\alpha]_D$ +65°.

Katonic Acid Acetate.—Katonic acid (10 g.) in pyridine (100 ml.) containing acetic anhydride (20 ml.) was boiled for 1 hr. The solid obtained by pouring the mixture into water was triturated with aqueous ammonia for ~30 min., then filtered off and stirred with dilute hydrochloric acid. The product was washed with water and recrystallised from light petroleum, to give blades of *katonic acid acetate* (6·5 g.), m. p. 221—223°, $[\alpha]_D$ +18° (Found: C, 76·9; H, 10·0. $C_{32}H_{50}O_4$ requires C, 77·0; H, 10·1%), ε_{210} 3800, ε_{220} 800.

The acid chloride was prepared by the action of thionyl chloride on the acetate. Recrystallisation from light petroleum gave *katonoyl chloride acetate*, m. p. 172—174°, $[\alpha]_D$ +17° (*c* 0·8 in C_6H_6) (Found: C, 74·2; H, 9·6; Cl, 6·5. $C_{32}H_{49}O_3Cl$ requires C, 74·4; H, 9·6; Cl, 6·9%).

Katonol 3-Acetate.—The above acid chloride (1·67 g.) in pyridine (15 ml.) was added to a solution of sodium borohydride (0·3 g.) in pyridine (10 ml.), and the mixture was kept at room temperature for 2 hr. The resulting gel was stirred into dilute hydrochloric acid, leaving a white precipitate which was collected and boiled with alcohol (25 ml.) for 16 hr. Evaporation of the alcohol left a syrup which when stirred under light petroleum gave a white solid (0·76 g.). The evaporated petroleum mother-liquor was boiled for another 17 hr. with alcohol, and another 0·35 g. of the white solid was obtained. The combined solids, in ether, were chromatographed on alumina, thus giving *katonol 3-acetate* (0·5 g.) which after two recrystallisations from light petroleum had m. p. 207—208°, $[\alpha]_D$ +40° (Found: C, 79·5; H, 11·1. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

Epi-β-amyrin.—Oppenauer oxidation as described for the preparation of 3-deoxykatonal was used to oxidise katonol 3-acetate (0·6 g.) to *katonal 3-acetate* (0·25 g.), m. p. 162—163° (with evolution of a gas), $[\alpha]_D$ +42°. The aldehyde was purified by chromatography on alumina in light petroleum solution and subsequent recrystallisation from ethanol, and was characterised as the 2,4-*dinitrophenylhydrazone*, m. p. 240—241° (Found: C, 69·0; H, 8·3; N, 8·6. $C_{38}H_{54}O_6N_4$ requires C, 68·8; H, 8·2; N, 8·5%).

Wolff–Kishner reduction of the aldehyde (0·144 g.) under the conditions outlined for the preparation of methyl 3-deoxykatonate gave a product which was chromatographed on alumina in ether–light petroleum (1 : 1). Elution with ether gave crystals of epi-β-amyrin (0·06 g.), m. p. 225—226·5°, $[\alpha]_D$ +77° (Found: C, 84·8; H, 11·9. Calc. for $C_{30}H_{50}O$: C, 84·5; H, 11·8%). Ruzicka and Wirz [12] give m. p. 225°, $[\alpha]_D$ +73°, for this compound, and the m. p. of the sample obtained in the present work was undepressed on admixture with an authentic sample kindly provided by Dr. W. Klyne.

Methyl Epikatonate.—Sodium borohydride (0·15 g.) in methanol (20 ml.) was added to a solution of methyl katononate (0·5 g.) in methanol (100 ml.), and the mixture was kept at room temperature for 20 hr. Evaporation of the solution gave a residue which was boiled with 3% methanolic hydrogen chloride (25 ml.) for another 16 hr. The filtered solution, on cooling, deposited plates of *methyl epikatonate* (0·35 g.), m. p. 199—200°, $[\alpha]_D$ +58° (Found: C, 79·1; H, 10·5. $C_{31}H_{50}O_3$ requires C, 79·0; H, 10·6%). The *acetate*, m. p. 245—246°, $[\alpha]_D$ +54°

[12] Ruzicka and Wirz, *Helv. Chim. Acta*, 1941, **24**, 248.

(Found: C, 77·1; H, 10·2. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·3%), was prepared by the action of acetic anhydride in pyridine on the ester.

Oxidation of Methyl Epikatonate Acetate, Methyl 11-*Deoxo*-18β-*glycyrrhetate Acetate, and Methyl Katonate Acetate by Selenium Dioxide.*—Methyl epikatonate acetate (0·6 g.) and selenium dioxide (0·6 g.) in glacial acetic acid (30 ml.) were boiled for 24 hr. The resultant solution was filtered and evaporated to a solid, which in ether solution was washed with aqueous sodium hydrogen carbonate. The solid thus obtained was chromatographed on alumina in ether, giving in the first fractions a solid which after three recrystallisations from methanol gave colourless needles (9 mg.), m. p. 229°, $\lambda_{max.}$ 241,249, and 258·5 mμ characteristic of the 11,13(18)-diene. Subsequent fractions gave needles of the 9(11),13(18)-*diene*-12,19-*dione* from methyl epikatonate acetate (0·28 g.), m. p. 233—234°, $[\alpha]_D$ −168° (Found: C, 73·2; H, 8·5. $C_{33}H_{46}O_6$ requires C, 73·5; H, 8·6%), $\lambda_{max.}$ 277 mμ (ε 13,200).

Methyl 11-deoxo-18β-glycyrrhetate acetate (m. p. 262—264°) under similar conditions gave the 9(11),13(18)-diene-12,19-dione, m. p. 239—240° $[\alpha]_D$ −69°, $\lambda_{max.}$ 278—279 mμ (ε 16,700). Ruzicka and Jeger [6] give m. p. 236—237°, $[\alpha]_D$ −73°, $\lambda_{max.}$ 280 mμ (ε 15,800), for this compound.

When half the above amount of selenium dioxide was used, the oxidation of methyl katonate acetate by the above procedure gave the 11,13(18)-*diene*, m. p. 159—160°, $[\alpha]_D$ −188° (Found: C, 77·6; H, 9·9. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·9%), $\lambda_{max.}$ 241, 249, and 259 mμ (ε 29,300, 33,600, and 22,100), and the 9(11),13(18)-*diene*-12,19-*dione*, m. p. 201—202°, $[\alpha]_D$ −209° (Found: C, 73·5; H, 8·5. $C_{33}H_{46}O_6$ requires C, 73·5; H, 8·6%), $\lambda_{max.}$ 279 mμ (ε 12,600).

Alkaline Hydrolysis of the Dienediones of Methyl Epikatonate Acetate, Methyl 11-*Deoxo*-18β-*glycyrrhetate Acetate, and Methyl Katonate Acetate.*—The dienedione from methyl epikatonate acetate (0·2 g.) in 5% ethanolic potassium hydroxide (4 ml.) was heated under reflux for 3 hr. The product obtained by pouring the mixture into water was dissolved in chloroform, and the chloroform solution was washed with aqueous sodium hydroxide. Evaporation of the chloroform solution gave a white solid (0·1 g.) which after four recrystallisations from aqueous acetone gave 30-nor-β-amyra-9(11),13(18)-diene-12,19-dione (0·04 g.), m. p. 256—257°, $[\alpha]_D$ −40° (Found: C, 79·4; H, 9·8. $C_{29}H_{42}O_3$ requires C, 79·4; H, 9·7%), $\lambda_{max.}$ 276—277 mμ (ε 13,600). An authentic sample of the compound, whose preparation is described below, did not depress the m. p. of the above compound and the two had identical infrared spectra. The combined mother-liquors were evaporated and the residue was chromatographed on alumina in ether. Elution by 100 : 1 ether–methanol gave an impure sample of nor-β-amyradienedione (0·04 g.), m. p. 237—250° (after one recrystallisation from aqueous acetone). This was acetylated by acetic anhydride in pyridine, two recrystallisations of the product from aqueous acetone and one from ethanol–light petroleum serving to give the acetate (0·011 g.), m. p. 278—279·5°.

The dienedione from methyl 11-deoxo-18β-glycyrrhetate acetate (0·3 g.) was boiled for 16 hr. with 10% methanolic potassium hydroxide (7·5 ml.). The mixture was diluted with water and extracted with ether, giving a solid (0·068 g.) which after two recrystallisations from aqueous acetone was 30-nor-β-amyra-9(11),13(18)-diene-12,19-dione, m. p. 255—256·5°, $[\alpha]_D$ −42°, $\lambda_{max.}$ 276—277 mμ (ε 13,000). This compound had been obtained by Ruzicka and Jeger [6] who give m. p. 255—256°, $[\alpha]_D$ −36°, $\lambda_{max.}$ 280 mμ (ε 15,800) (acetate, m. p. 279—280°).

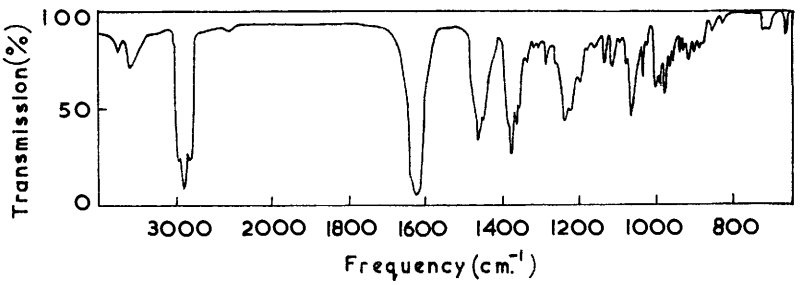
Similar alkaline hydrolysis of the dienedione of methyl katonate acetate gave 30-nor-epi-β-amyra-9(11),13(18)-diene-12,19-dione, m. p. 286—288°, $[\alpha]_D$ −42° (Found: C, 79·4; H, 9·8. $C_{29}H_{42}O_3$ requires C, 79·4; H, 9·7%), $\lambda_{max.}$ 278 mμ (ε 11,200).

Anomalous Acetate.—Katonic acid (10 g.) was dissolved in acetic anhydride (150 ml.) containing 70% perchloric acid (0·5 ml.) by occasional shaking. The mixture was kept at room temperature overnight and then decomposed with water. The product was collected, dried, decolorised by passage in ether through a short column of alumina, and recrystallised from ethanol as colourless needles of the anomalous *acetate* (6·5 g.), m. p. 238—239°, $[\alpha]_D$ −273° [Found: C, 79·75; H, 10·05%; *M* (Rast), 450. $C_{32}H_{48}O_3$ requires C, 79·9; H, 10·1%; *M*, 480], $\lambda_{max.}$ 273 mμ (ε 8900), $\nu_{max.}$ (in CCl_4) 1725, 1646, and 1635 $cm.^{-1}$. The compound is insoluble in aqueous-ethanolic sodium hydroxide and gives a yellow colour with tetranitromethane but no colour in the Liebermann–Burchard test; it failed to give an oxime or a 2,4-dinitrophenylhydrazone, and it did not give a Zimmermann reaction. After having been boiled for 19 hr. with selenium dioxide in acetic acid the compound was unchanged.

Hydrolysis of the acetate by 3% methanolic hydrogen chloride or by 10% ethanolic potassium hydroxide gave a deacetylated *compound*, m. p. 303—305° (decomp.), $[\alpha]_D$ −289° (Found:

C, 82·4; H, 10·2. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·5%), $\lambda_{max.}$ 274 mμ (ε 9000) (infrared spectrum shown), which was reconverted into the anomalous acetate by the action of acetic anhydride in pyridine.

Infrared spectrum of deacetylated anomalous acetate, in chloroform.



When katonic acid acetate was treated with the acetylating agent under similar conditions (one-tenth of the above scale), the anomalous acetate, m. p. 237—239°, was obtained in the same yield, but when acetic acid was used in place of acetic anhydride katonic acid acetate, m. p. and mixed m. p. 221—223°, was recovered unchanged.

Preparation of the Anomalous Acetate using a Controlled Quantity of Perchloric Acid.—Katonic acid (2 g., 4·1 mmoles) was dissolved in acetic anhydride (5 ml.) containing 70% perchloric acid (0·017 ml., 0·2 mmole) and kept at room temperature for 4 days before being digested with water. A solution of the solid product in 1 : 1 ether–light petroleum was purified on an alumina column, giving 1·64 g. of a solid, m. p. 225—230°. Repeated recrystallisation from ethanol gave pure anomalous acetate (0·79 g., 1·65 mmoles), m. p. 238—239°.

Anomalous Propionate.—A solution of katonic acid (2 g.) in propionic anhydride (30 ml.) containing perchloric acid (0·1 ml.) was kept at room temperature for 22 hr., then decomposed with water at 60—70°. The solid obtained was recrystallised from light petroleum or ethanol, to give the anomalous *propionate* (1·3 g.), m. p. 223—225°, $[\alpha]_D$ −258° (Found: C, 80·4; H, 10·1. $C_{33}H_{50}O_3$ requires C, 80·1; H, 10·2%), $\lambda_{max.}$ 273 mμ (ε 9300).

Hydrolysis of the anomalous propionate (0·5 g.) by boiling 10% ethanolic potassium hydroxide (15 ml.) for 2 hr. gave suspended crystals which were completely precipitated by water and recrystallised from ethanol as blades (0·32 g.), m. p. 298—300° (decomp.) undepressed when mixed with the deacetylated anomalous acetate; the two compounds had identical infrared spectra. Acetylation of the hydrolysis product by acetic anhydride in pyridine gave the anomalous acetate, m. p. 239·5—240°, identified with an authentic sample by mixed m. p. and coincident infrared spectra.

Action of Acetic Anhydride and Perchloric Acid on Methyl Katonate and 11-*Deoxo*-18β-*glycyrrhetic Acid.*—Powdered methyl katonate (1 g.) was shaken with acetic anhydride (15 ml.) containing 70% perchloric acid (0·1 ml.) at room temperature for 2 hr. The solid was filtered off and recrystallised from methanol, to give methyl katonate acetate (0·42 g.), m. p. and mixed m. p. 202—203°. The solid obtained by decomposing the anhydride solution with water was chromatographed on alumina in light petroleum; elution with 1 : 9 ether–light petroleum gave a white solid which after recrystallisation from methanol was identified as methyl katonate acetate (0·11 g.). Further elution with ether gave a brown syrup (0·12 g.). After a 16 hours' reaction methyl katonate acetate (0·29 g.) was recovered but no other products were obtained.

11-Deoxo-18β-glycyrrhetic acid (90 mg.) was stirred with the above acetylation mixture (1·5 ml.) and kept at room temperature for 17 hr. The solid obtained on decomposition of the mixture with water recrystallised from ethanol as needles of the mixed *acetic* 3-O-*acetyl*-11-*deoxo*-18β-*glycyrrhetic anhydride* (50 mg.), m. p. 355—356° (vac.), $[\alpha]_D$ +112° (Found: C, 75·6; H, 9·6. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%), ε_{210} 2940, ε_{220} 480.

Decomposition of the mixed anhydride by dilute aqueous ammonia in aqueous ethanol at room temperature gave 11-deoxo-18β-glycyrrhetic acid acetate, which crystallised from ethanol as leaflets, m. p. 310—311° (Found: C, 77·3; H, 10·2. Calc. for $C_{32}H_{50}O_4$: C, 77·0; H, 10·1%). Ruzicka and Marxer [13] give m. p. 309—310°, $[\alpha]_D$ +115·8°.

[13] Ruzicka and Marxer, *Helv. Chim. Acta*, **1939**, **22**, 195.

Reduction of the Anomalous Acetate.—(a) *By lithium aluminium hydride.* A solution of the anomalous acetate (0·5 g.) in ether (30 ml.) was added cautiously to a stirred, refluxing 0·2M-solution of lithium aluminium hydride in ether (40 ml.), and the mixture was boiled for 16 hr. Excess of hydride was decomposed by dropwise addition of methanol, and the product was isolated in ether in the usual way. The white solid obtained crystallised from ether–light petroleum as needles (0·25 g.) which recrystallised from ether as prisms of the *diol*, m. p. 206—210°, $[\alpha]_D$ −121° (Found: C, 82·1; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·7; H, 11·0), $\lambda_{max.}$ 223—224 mμ (ε 5200).

(b) *By hydrogen.* Reduction of the anomalous acetate (1 g.) in acetic acid (25 ml.) over a platinum catalyst (from 110 mg. of platinum oxide) required 103 c.c. of hydrogen (N.T.P.) (theor. for C:O, 93 c.c.). Recrystallisation of the product from ethanol gave long needles of the reduced anomalous *acetate* (0·87 g.), m. p. 202—206°, $[\alpha]_D$ −129° (Found: C, 82·5; H, 10·8. $C_{32}H_{50}O_2$ requires C, 82·4; H, 10·8%), $\lambda_{max.}$ 217 mμ (ε 5400), which gave a reddish-brown colour with tetranitromethane but resisted further hydrogenation and was unaffected by perphthalic acid in ether at 0°.

Rearrangement of the Reduced Anomalous Acetate.—Hydrogen chloride was bubbled through a solution of the reduced anomalous acetate (0·5 g.) in dry chloroform (40 ml.) for 45 min. The syrup obtained by removing the solvent under reduced pressure crystallised from methanol in needles. Recrystallisation from methanol gave the rearrangement *product* (0·38 g.), m. p. 196—197°, $[\alpha]_D$ +55° (Found: C, 82·4; H, 11·0. $C_{32}H_{50}O_2$ requires C, 82·4; H, 10·8%), ε_{210} 1370, ε_{220} 440, which gave a yellow colour with tetranitromethane but was unattacked by perphthalic acid in ether at 0°.

Hydrogenation of the compound (110 mg.) in acetic acid (10 ml.) over a platinum catalyst (from 40 mg. of platinum oxide) required 6·8 c.c. of hydrogen (N.T.P.) (theor. for one double bond 5·3 c.c.). The *product* crystallised from methanol in leaflets (81 mg.), m. p. 188·5—189·5°, $[\alpha]_D$ −8° (Found: C, 82·1; H, 11·2. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%), ε_{210} 270, ε_{220} 190, and gave no colour with tetranitromethane.

When the anomalous acetate was subjected to the action of hydrogen chloride in chloroform, it was recovered from the reaction mixture unchanged.

Indicic Acid.—The chloroform-insoluble solid (27 g. from approx. 10 extractions) which remained after removal of katonic acid, was leached with pyridine. The pyridine solution was filtered and evaporated to a crystalline residue that was washed with alcohol. The crude *indicic acid* (13 g.) thus obtained could be recrystallised from ethanol–chloroform but the analytical sample was recrystallised from a large volume of ethanol, forming fine needles, m. p. 254—255°, $[\alpha]_D$ +70° (*c* 0·8 in pyridine) (Found: C, 78·9; H, 10·0. $C_{60}H_{92}O_6$ requires C, 79·2; H, 10·2%), ε_{210} 8540, ε_{220} 1710 (ε values given for molecular weight 908 are consistent with the presence of two trisubstituted double bonds). The compound gives a magenta colour in the Liebermann–Burchard test, does not give a yellow colour with tetranitromethane, and dissolves in aqueous-ethanolic alkali. It is very sparingly soluble in chloroform, ethanol, methanol, acetic acid, and benzene.

Methyl Indicate.—Crude indicic acid (4 g.) in 3% methanolic hydrogen chloride (400 ml.) was boiled under reflux with stirring for 20 hr. The suspension was cooled to room temperature and filtered. The solid (3·7 g.) was extracted with boiling light petroleum which removed *methyl indicate* (1·92 g.). Recrystallised from ethanol, this had m. p. 190—191°, $[\alpha]_D$ +73° [Found: C, 79·1; H, 10·2%; *M* (Rast), 818. $C_{62}H_{96}O_6$ requires C, 79·4; H, 10·3%; *M*, 936].

Alkaline Hydrolysis of Indicic Acid.—Indicic acid (1·42 g.) was boiled with 10% ethanolic potassium hydroxide (25 ml.) for 5 hr. The cooled solution was diluted with water and acidified, and the precipitated solid was collected in ether. Evaporation of the ether extracts gave a yellow solid which was stirred with chloroform (50 ml.). The insoluble white solid (0·23 g.), together with that obtained (0·18 g.) by concentrating the chloroform solution, recrystallised from methanol as plates of an *acid* (0·30 g.), m. p. 304—306° (vac.), $[\alpha]_D$ +133° (*c* 0·9 in pyridine) (Found: C, 76·7; H, 10·2. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·9%). This compound did not give a colour with tetranitromethane but gave a magenta colour in the Liebermann–Burchard test.

The chloroform-soluble part of the reaction mixture was evaporated and the residue recrystallised from methanol as needles (0·47 g.), m. p. 280—282°, undepressed when mixed with katonic acid. The acetate and methyl ester of katonic acid obtained from this source have been prepared and compared with authentic samples.

Dimethyl Ester of the Acid $C_{30}H_{46}O_4$.—The acid (60 mg.) was boiled with 3% methanolic hydrogen chloride (2 ml.) for 18 hr. and the solution was then diluted with water, made alkaline with aqueous sodium hydroxide, and extracted with ether. The residue obtained on evaporation of the ether was chromatographed on alumina in light petroleum. Elution with 1 : 20 ether–light petroleum gave the *dimethyl ester* (37 mg.), m. p. 135—136°, $[\alpha]_D$ +122° [Found: C, 76·9; H, 10·2%; *M* (Rast), 468. $C_{32}H_{50}O_4$ requires C, 77·0; H, 10·1%; *M*, 498], ε_{210} 5150, ε_{220} 1065. The same compound was obtained by methylation of the acid by excess of diazomethane in ether.

Monomethyl Ester of the Acid $C_{30}H_{46}O_4$.—A suspension of the acid (90 mg.) was boiled with 3% methanolic hydrogen chloride for 1 hr. The product was obtained by pouring the solution into water and extracting it with ether. Evaporation of the ethereal extracts gave a colourless syrup which was crystallised from light petroleum as the *monomethyl ester* (35 mg.), m. p. 228—229° (vac.) (Found: C, 77·4; H, 10·4. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%). The compound dissolved in aqueous ethanolic alkali.

Further methylation of this product with diazomethane gave the dimethyl ester, m. p. and mixed m. p. 134—135°.

BRITISH CELANESE LTD., PUTTERIDGE BURY LABORATORIES,
nr. LUTON, BEDFORDSHIRE.

[*Received, April 4th*, 1960.]