330. *The Nonadrides. Part II.*[1] *The Constitutions of Glauconic and Glaucanic Acids*

By D. H. R. Barton, L. M. Jackman, L. Rodriguez-Hahn, and J. K. Sutherland

New pyrolytic, reductive, and hydrolytic reactions of glauconic acid have been studied and interpreted in terms of the established constitution. The structure of glauconin, one of the major pyrolysis products of glauconic acid, has been confirmed by synthesis.

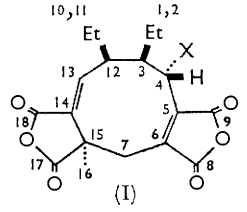
The earlier work on glauconic acid (I; X = OH), and the deduction of the structure, have been described.[1,2] We present now a concise account of our new experimental work on this interesting medium-ring compound. The reactions can be roughly classified as pyrolytic, reductive, hydrolytic, and oxidative. The last named will be presented[3] in connection with the determination of the absolute configuration.

In the structure determination the reductive reactions were by far the most informative. The zinc dust–acetic acid reduction of (I; X = OH) to the lactone (II) and of (I; X = OAc) to glaucanic acid (I; X = H) has been discussed.[1] Similar reduction of the ketone (I; X,H = O) takes yet another course. This ketone was prepared by chromium trioxide–acetone oxidation[4] of glauconic acid, and although it could not be reduced back to glauconic acid, there is little doubt, from its spectra and further transformations, that it has the given structure. Zinc dust–acetic acid reduction of the ketone gave two C_{17}-compounds. The first, $C_{17}H_{22}O_6$ (III; R = H), contained the intact itaconic anhydride unit, identified from its spectra [$\lambda_{max.}$ 225—228 mμ (ε 8600); $\nu_{max.}$ 1830 and 1770 cm.$^{-1}$; 16-Me 8·59 τ, 13-vinyl H as a doublet at 3·08 τ (J = 10 c./sec.)]; these values are characteristic of this unit, and are found in all compounds of this series containing it. As ultraviolet models, 1- and 2-dehydrocyclohexane-1,2-dicarboxylic acid anhydrides, having $\lambda_{max.}$ 250 mμ (ε 3500) and 223 (7600), respectively, in cyclohexane, were used. For the compound (III; R = H) the infrared spectrum suggested, besides the anhydride unit, the presence of a ketone and of a carboxylic acid group; a monomethyl ester was prepared having the required spectrum.

The second product (IV; R = H), $C_{17}H_{24}O_7$, was a tricarboxylic keto-acid from which a trimethyl ester could be prepared. The ultraviolet spectrum showed the absence of double bonds, so that the compound must be bicyclic, and a band at 1740 cm.$^{-1}$ placed the keto-group in a five-membered ring. Sublimation of the acid gave a succinic anhydride, suggesting that two of the carboxyls were *cis*-1,2.

[1] Part I, D. H. R. Barton and J. K. Sutherland, preceding Paper.
[2] J. E. Baldwin, D. H. R. Barton, J. L. Bloomer, L. M. Jackman, L. Rodriguez-Hahn, and J. K. Sutherland, *Experientia*, 1962, **18**, 345.
[3] Part III, D. H. R. Barton, L. D. S. Godinho, and J. K. Sutherland, following Paper.
[4] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J.*, 1946, 39.

In the formation of the tricarboxylic acid (IV; R = H) a new ring is created and the itaconic anhydride grouping of (I; X,H = O) is destroyed. Since this type of reaction does not occur in the absence of the keto-group the simplest explanation is that an internal Michael reaction [5] has taken place in the ene-1,4-dione type reduction of (I; X,H = O). The loss of the 9-carboxyl may be synchronous with, or follow, the cyclisation [see (V)], but it cannot precede it since (III; R = H) does not cyclise under the reaction conditions.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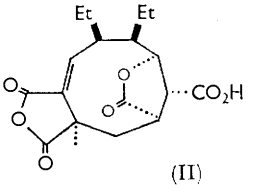
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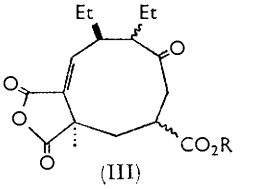
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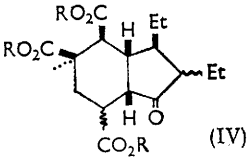
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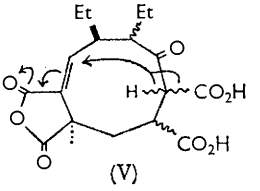
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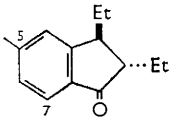
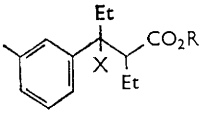

(VI)

The carbon skeleton shown in (IV; R = H) has been proved by dehydrogenation. When the acid (IV; R = H) was heated in a sealed tube at 290° for 24 hr. with 20% palladised charcoal the crude optically inactive indanone (VI) was formed. This showed a methyl peak at 7·58 τ, in agreement with that for 5-methylindanone at 7·60.[6] The indanone was characterised as its optically inactive 2,4-dinitrophenylhydrazone, and its structure was proved by synthesis.[7] Ethyl *m*-tolyl ketone [8] in a Reformatsky reaction with ethyl α-bromobutyrate and zinc gave the hydroxy-ester (VII; X = OH, R = Et) which was dehydrated to the cinnamic ester, reduced to (VII; X = H, R = Et), and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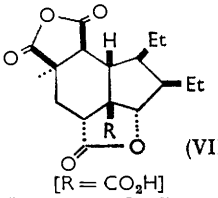
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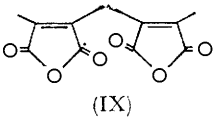
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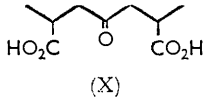
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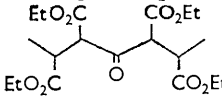
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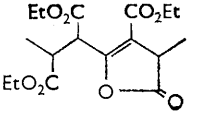

(XII)

hydrolysed to the acid (VII; X = H, R = H). Cyclisation of the acid with polyphosphoric acid gave a mixture of the 5- and 7-methyl-2,3-diethylindanones, with a slight preponderance of the 7-methyl isomer as judged by the aromatic methyl absorptions at 7·58 and 7·41 τ, respectively. (7-Methylindanone absorbs at 7·46 τ the methyl being shielded by the carbonyl group.[6]) On preparing the 2,4-dinitrophenylhydrazones a sharp-melting complex was obtained with a slight preponderance of the 5-isomer (methyl absorptions at 7·58 and 7·27 τ were assigned by analogy to the ketones, the 7-methyl at 7·27 τ being deshielded by the C=N- group). From the mother-liquors the pure 2,4-dinitrophenylhydrazone of the 7-methyl isomer could be isolated. The mixture of isomeric 2,4-dinitrophenylhydrazones

[5] E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, 1959, **10**, 179.
[6] J. A. Elvidge and R. G. Foster, *J.*, 1963, 590.
[7] J. A. Barltrop, R. M. Acheson, P. G. Philpott, K. E. MacPhee, and J. S. Hunt, *J.*, 1956, 2928.
[8] O. Wallach and M. Reutschler, *Annalen*, 1908, **360**, 61.

was resolved by preparative thin-layer chromatography on silica gel, and that of the 5-methyl isomer (Me at 7·58 τ) was identical with the dinitrophenylhydrazone from degradation of the natural material.

A similar transannular cyclisation occurred when the acid chloride of the dihydroglauconic acid (II) was heated at 200°. Sublimation of the product gave (VIII) ($\nu_{max.}$ 1860, 1785, and 1740 cm.$^{-1}$). The monomethyl ester showed ε(220 mμ) 810, which established that the isomer contained no double bond and was, therefore, bicyclic. The stereochemistry assigned to the newly created centres in dihydroglauconic acid and its saturated isomer has not been proved but is based on mechanistic considerations.

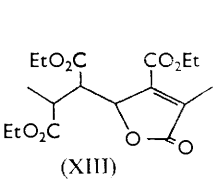
The most striking earlier reaction [1,2] was the pyrolytic fission of glauconic acid to αβ-diethylacraldehyde and glauconin (IX). As discussed already [1,2] the degradative evidence was in favour of formulation (IX). We have confirmed this by a synthesis which is essentially a reversal of the hydrolytic degradation of glauconin to the acid (X). The tetraester (XI), which had been prepared by the alkylation of acetonedicarboxylic ester by ethyl α-bromopropionate,[9] was heated under reflux in benzene in the presence of methanesulphonic acid with azeotropic removal of water and ethanol, to give a mixture of enol- and αβ-unsaturated-γ-lactones. The esters (XII) and (XIII), as well as other double-bond isomers, must be present but the main constituent is the enol-lactone (intensity of the infrared band). Neither acid nor base catalysis altered the composition of the mixture. Alkaline hydrolysis of the mixture gave mainly the acid (X) (presumably derived from hydrolysis of the enol-lactones), or, when the hydrolysate was refluxed with acetic anhydride, the spiro-dilactone derived from (X). However, on each occasion a small yield of glauconin was obtained, probably from hydrolysis of (XIII), followed by elimination of water and double-bond migration.

Once the structures of the products of pyrolysis had been established we investigated the reaction further. Attempts to stop the reaction at its intermediate stages or to detect the intermediates failed. However, when glauconic acid acetate (I; X = OAc) was heated under the same conditions (refluxing diglyme) an isomer (XIV) was isolated. Its infrared spectrum showed that there had been no change in the functional groups present, but the ultraviolet and n.m.r. spectra showed that their environments had changed considerably. In particular the inflection at 260 mμ due to the maleic anhydride residue and the characteristic n.m.r. absorption of the vinyl proton and quaternary methyl group of the itaconic anhydride residue had disappeared. There were now present two vinyl protons, at 3·26 and 3·95 τ, each split as a doublet (J = 1 c./sec.). The hydrogen next to the acetoxyl was a doublet at 5·09 τ (J = 8 c./sec.). The two vinyl protons were present in a methylene group since ozonolysis gave formaldehyde. These facts, coupled with the probable course of the pyrolysis of glauconic acid, suggested that the acetate had rearranged to (XV; X = OAc), followed by another rearrangement (arrows) to give (XIV). In agreement with this structure (XIV) was catalytically reduced to a bicyclic dihydro-compound [ε(220 mμ) 300; $\nu_{max.}$ 1850, 1780, and 1715 cm.$^{-1}$]. Alkaline hydrolysis of the dihydro-compound gave a lactone hydrate (XVI) which titrated as a tricarboxylic acid and was not originally present in the hydrolytic reaction product. Sublimation of the lactone gave the bisanhydride (XVII).

When the tetrahydropyranyl ether of glauconic acid (I; X = OH) was pyrolysed, yet another series of complicated rearrangements took place and a compound (XVIII; R = H), $C_{18}H_{20}O_7$, was isolated along with some glauconin (IX). The derived monomethyl ester (XVIII; R = Me) showed anhydride and ester absorption, the 1780 cm.$^{-1}$ band being particularly strong and probably masking a γ-lactone absorption. The ultraviolet spectrum [$\lambda_{max.}$ 253 (ε 3500)] indicated that the only chromophore present was a maleic anhydride residue. The n.m.r. spectrum was most instructive, showing an unsplit methyl group on a double bond at 7·80 τ, an ethylidene group with a methyl doublet at 7·90, and a vinyl proton quartet at 4·01 (J = 7·5 c./sec.). In addition, the hydrogen assigned to C-4

[9] H. Sutter and N. Wijkman, *Annalen*, 1935, **519**, 97.

appeared as a singlet at 4·85 and that assigned to C-13 as a doublet at 6·58 (J = 12 c./sec.). The remainder of the spectrum is consistent with this structure. We envisage the ether first rearranging to the usual intermediate (XV; X = *O*-tetrahydropyranyl) which then eliminates hydroxypyran to form (XIX); a homodiene rearrangement [10] follows, to give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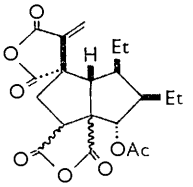
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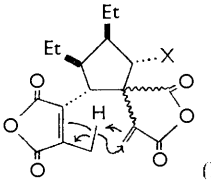
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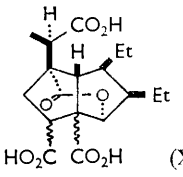
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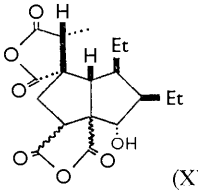
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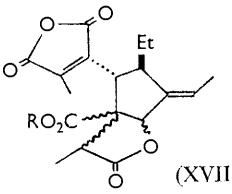
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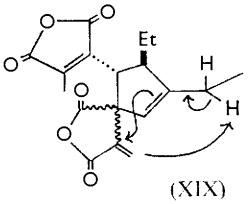
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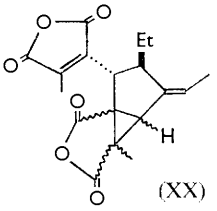
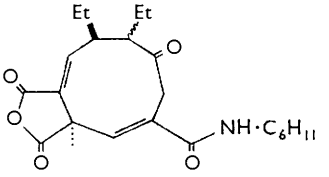

(XX)


(XXI)

the cyclopropane (XX), and finally the anhydride is hydrated and the cyclopropane ring is opened to form the γ-lactone.

Hydrolysis as a method of degradation of glauconic acid derivatives was largely unsuccessful. However, on heating glauconic acid ketone under reflux in benzene with cyclohexylcarbamic acid the amide (XXI) was obtained. The n.m.r. spectrum had the typical quaternary methyl at 8·44 and vinyl proton at 3·08 τ (J = 10 c./sec.). In addition, there was an additional vinyl proton as a singlet at 3·44. The spectra support formulation (XXI), rather than the isomeric structure with the ethylenic linkage in its original position.

Reaction of glauconic acid ketone with freshly distilled cyclohexylamine under the same conditions gave an imide, $C_{27}H_{38}N_2O_5$, which is not formed from the amide (XXI) and was not investigated further.

Experimental

Melting points were taken on a Kofler block. Unless otherwise specified, optical rotations were measured in chloroform, ultraviolet spectra in ethanol, and infrared spectra in Nujol. N.m.r. spectra were taken at 20° on ~10% w/v solutions in deuterochloroform (unless stated otherwise) with tetramethylsilane as internal standard.

Glauconic Acid and Known Derivatives.—The following compounds were prepared by literature procedures [1,2] and had constants in good agreement with those of the earlier workers. Crystallisation solvents were as specified in the literature.

Glauconic acid, m. p. 202—203°, had $[\alpha]_D$ +33° (*c* 1·02), $\lambda_{max.}$ 223 mμ (ε 10,500), inflection near 260 mμ, $\nu_{max.}$ 3510, 1830, 1770, 1670 cm.$^{-1}$. Its acetate, m. p. 172—173°, had $[\alpha]_D$ +35° (*c* 1·00), $\lambda_{max.}$ 220 mμ (ε 10,600), $\nu_{max.}$ 1835, 1770, 1740 cm.$^{-1}$.

Dihydroglauconic acid, m. p. 230°, had $[\alpha]_D$ +57° (*c* 1·01), $\lambda_{max.}$ 230 mμ (ε 8000), $\nu_{max.}$ 1835, 1770, 1720 cm.$^{-1}$. Its monomethyl ester, m. p. 202—204°, had $[\alpha]_D$ +34° (*c* 1·21), $\lambda_{max.}$ 232 mμ (ε 8550), $\nu_{max.}$ 1840, 1780, 1740 cm.$^{-1}$, and its derived trimethyl ester, an oil, had ε(215 mμ) 10,000, $\nu_{max.}$ 1775, 1745 cm.$^{-1}$.

[10] A. Habich, R. Bamer, R. M. Roberts, and H. Schmid, *Helv. Chim. Acta*, 1962, **45**, 1943.

Glauconin, m. p. 169—170°, had $[\alpha] \pm 0°$, $\lambda_{max.}$ 250 mμ (ε 10,200 in cyclohexane), $\nu_{max.}$ 1825, 1775 cm.$^{-1}$.

Glaucanic acid, m. p. 186°, had $[\alpha]_D$ +185° (*c* 1·05), $\lambda_{max.}$ 220 mμ (ε 10,700), inflection at 250 mμ, $\nu_{max.}$ 1840, 1775 cm.$^{-1}$.

Glauconic Acid m-*Iodobenzoate*.—Glauconic acid (362 mg.) in pyridine (5 ml.) was treated with *m*-iodobenzoyl chloride (313 mg.) for 3 hr. at room temperature, to give the *product*, m. p. 194—195° (from acetone–ether), $[\alpha]_D$ +89° (*c* 0·64), $\nu_{max.}$ 1840, 1770, 1725 cm.$^{-1}$ (Found: C, 51·9; H, 4·3; I, 21·85. $C_{25}H_{26}IO_8$ requires C, 51·95; H, 4·0; I, 21·95%).

Zinc Dust Reduction of Glauconic Acid Acetate.—The acetate (1·0 g.; carefully purified), in glacial acetic acid (8 ml.), was heated under reflux with zinc dust (2·5 g.; AnalaR) for 7 hr. The excess of zinc was filtered off and the acetic acid removed *in vacuo*. Addition of dilute hydrochloric acid (2N), extraction with chloroform, and chromatography over silica gel (60 g.) (elution with benzene) gave glaucanic acid (82 mg.) (m. p., mixed m. p., and infrared spectrum).

Glauconic Acid Ketone.—Glauconic acid (1·5 g.) in acetone (25 ml.; AnalaR) was titrated [4] with 8N-chromic acid (from 17·5 g. of chromium trioxide in 50 ml. of water and 14·8 ml. of concentrated sulphuric acid). When no more oxidising agent was consumed the mixture was poured into water, solid sodium pyrosulphite added, and the solution extracted with chloroform. The extract was washed with water, dried, and concentrated to give an oil, which solidified on trituration with ether. The *ketone* (944 mg.) had m. p. 174—176° (decomp.) (from acetone–ether), $[\alpha]_D$ +45° (*c* 0·56), $\lambda_{max.}$ 220 mμ (ε 10,000), $\nu_{max.}$ 1830, 1770, 1695 cm.$^{-1}$, $\nu_{max.}$ ($CHCl_3$) 1830, 1770, 1715 cm.$^{-1}$ (Found: C, 62·75; H, 5·35. $C_{18}H_{18}O_7$ requires C, 62·4; H, 5·25%).

Zinc Dust Reduction of Glauconic Acid Ketone.—Glauconic acid ketone (4 g.) in acetic acid (100 ml.) was heated under reflux with zinc dust (20 g.; AnalaR) for 24 hr. After filtration the acetic acid was removed *in vacuo*, and water and a few drops of conc. hydrochloric acid added to the residue. The mixture was extracted with ethyl acetate and the extract concentrated to give an oil (3·7 g.). This oil, in benzene, was chromatographed on silica gel (B.D.H.; 400 g.). Elution with benzene–ether (9 : 1) gave the *monocyclic acid* (III; R = H) (540 mg.), m. p. 170—180° (from chloroform–n-hexane), $[\alpha]_D$ +8° (*c* 1·0), $\lambda_{max.}$ 225—228 mμ (ε 8690), $\nu_{max.}$ ($CHCl_3$) 1830, 1770, 1715, 1700 cm.$^{-1}$ (Found: C, 62·95; H, 6·8. $C_{17}H_{22}O_6$ requires C, 63·35; H, 6·9%). The *monomethyl ester* (diazomethane) had m. p. 115—117° (from ether–n-hexane), $[\alpha]_D \pm 0°$ (*c* 1·0), $\lambda_{max.}$ 225 mμ (ε 8300), $\nu_{max.}$ ($CHCl_3$) 1830, 1770, 1725, 1700 cm.$^{-1}$ (Found: C, 64·5; H, 7·25. $C_{18}H_{24}O_6$ requires C, 64·25; H, 7·2%). The acid (III; R = H) was recovered quantitatively when subjected to the original conditions of reduction.

Elution of the column (see above) with ether gave the *tricarboxylic acid* (IV; R = H) (1·3 g.), m. p. 169—170° (from ethyl acetate–n-hexane or from acetonitrile), $[\alpha]_D$ −90° (*c* 1·0 in acetone), ε(220 mμ) 485, $\nu_{max.}$ 1742, 1709 cm.$^{-1}$ (Found: C, 60·45; H, 7·3%. Equiv., 113. $C_{17}H_{24}O_7$ requires C, 60·0; H, 7·1%; Equiv., 113). The *trimethyl ester* (IV; R = Me) (diazomethane) had m. p. 104—107° (from ether–n-hexane), $[\alpha]_D$ −101° (*c* 1·0), ε(220 mμ) 500, $\nu_{max.}$ ($CHCl_3$) 1730 cm.$^{-1}$ (Found: C, 63·05; H, 8·05. $C_{20}H_{30}O_7$ requires C, 62·8; H, 7·9%). On sublimation at 160°/10^{-5} mm. the tricarboxylic acid (IV; R = H) gave an *anhydride acid*, m. p. 168—170° (from ether–light petroleum), $[\alpha]_D$ −59° (*c* 1·1), ε(220 mμ) 410, $\nu_{max.}$ 1840, 1770, 1730, 1700 cm.$^{-1}$ (Found: C, 64·05; H, 7·3. $C_{17}H_{22}O_6$ requires C, 63·35; H, 6·9%).

Dehydrogenation of the Tricarboxylic Acid (IV; R = H).—The acid (IV; R = H) (260 mg.) was heated with 20% palladised charcoal (70 mg.) in an evacuated tube at 290° for 24 hr. The residue was extracted with ethyl acetate, the extract filtered, washed with aqueous sodium hydrogen carbonate, and evaporated *in vacuo* to an oil. The latter, after distillation at 100°/0·05 mm., in benzene was filtered (50 mg.) through alumina. The product had $[\alpha]_D \pm 0°$, $\lambda_{max.}$ 208, 255, 277 mμ (ε 17,800, 8500, 2100), $\nu_{max.}$ 1700, 1610 cm.$^{-1}$, and gave a 2,4-*dinitrophenylhydrazone*, m. p. 166—168° (from chloroform–ethanol), $\lambda_{max.}$ ($CHCl_3$) 395 mμ (ε 33,700) (Found: C, 63·0; H, 6·05; N, 14·75. $C_{20}H_{22}N_4O_4$ requires C, 62·8; H, 5·8; N, 14·65%). The oily ketone was recovered unchanged after heating with triethylamine in ethanol at 100° for 3 hr.

Ethyl α-*Ethyl*-β-*hydroxy*-β-(m-*tolyl*)*valerate*.—A small portion from ethyl *m*-tolyl ketone (12·6 g.) and ethyl α-bromobutyrate (18 g.) in dry benzene (100 ml.) was added to zinc (7 g.) in dry benzene (20 ml.). After initiation of the reaction by refluxing and stirring, the remainder of the benzene solution was added dropwise during 1 hr. (gentle reflux). After refluxing and stirring for a further 1 hr. the mixture was cooled and dilute sulphuric acid added. The layers were separated and the aqueous phase extracted with ether. The combined organic extracts

were washed with saturated sodium hydrogen carbonate solution and water, and dried. Concentration gave an oil which was twice distilled to give the *ester* (14·9 g.), b. p. 112—114°/0·8 mm., n_D^{20} 1·4945, $\nu_{max.}$ 3550, 1710 cm.$^{-1}$ (Found: C, 73·3; H, 9·15; OEt, 16·65. $C_{16}H_{24}O_3$ requires C, 72·7; H, 9·15; 1 OEt, 17·0%).

Ethyl α-Ethyl-β-(m-tolyl)pent-2-enoate.—The crude product from the previous reaction (16·6 g.) in dry benzene (100 ml.) containing phosphorous pentoxide (11·5 g.) was refluxed for 3 hr. The benzene was decanted, the residue washed with benzene, and the combined solutions dried (K_2CO_3). After concentration of the solution, the oil remaining was distilled, to give the *unsaturated ester* (9·2 g.), b. p. 122—128°/2 mm., n_D^{20} 1·5050, $\nu_{max.}$ 1724 cm.$^{-1}$ (Found: C,79·05; H, 9·35. $C_{16}H_{22}O_2$ requires C, 78·0; H, 9·0%).

α-Ethyl-β-(m-tolyl)valeric Acid.—The unsaturated ester (see above) (5·2 g.) in acetic acid (100 ml.) was hydrogenated over 10% palladised charcoal (500 mg.) (1 mol. uptake). The resulting *dihydro-ester* (VII; X = H) (4·24 g.) had b. p. 110—112°/1·5 mm., n_D^{20} 1·4880, $\lambda_{max.}$ (cyclohexane) 265, 273 mμ (ε 530, 530) (Found: C, 78·0; H, 9·9. $C_{16}H_{24}O_2$ requires C, 77·35; H, 9·75%). This ester (4·22 g.) in 50% aqueous ethanol (100 ml.) containing potassium hydroxide (10 g.) was heated under reflux overnight. Separation of the acidic fraction gave α-ethyl-β-(*m*-tolyl)valeric acid (3·1 g.), b. p. 146°/1·5 mm., n_D^{20} 1·5042, $\lambda_{max.}$ (cyclohexane) 260, 273 mμ (ε 410, 390), $\nu_{max.}$ 3000—2500, 1710 cm.$^{-1}$.

5- and 7-Methyl-2,3-diethylindanone.—The acid (IV; R = H) (550 mg.) in ether (1 ml.) was added to 80% phosphoric acid (8 ml.) and phosphorus pentoxide (12 g.) (previously heated for 2 hr. on a steam-bath to give a clear solution) and heated at 100° for 3 hr. with occasional stirring. The cooled solution was poured on to ice and the aqueous phase extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution and water, dried, the solvent evaporated, and the residue distilled, b. p. 100°/1 mm. (360 mg.), $\nu_{max.}$ 1700 cm.$^{-1}$. The n.m.r. spectrum showed it to be a mixture of the 5- and 7-methyl compounds (7·58 and 7·41 τ) with a slight preponderance of the latter. On preparing the 2,4-dinitrophenylhydrazones a sharp melting mixture, m. p. 152—153° (from chloroform–ethanol), was formed. It could be resolved into two 2,4-dinitrophenylhydrazones by preparative thin-layer chromatography on Silica Gel G using repeated elution with chloroform–cyclohexane (1 : 20). The less mobile band was extracted with chloroform. Crystallisation of the product from chloroform–ethanol gave the 2,4-dinitrophenylhydrazone of 5-methyl-2,3-diethylindanone, m. p. 166—168°, identical (mixed m. p. and infrared spectrum) with the 2,4-dinitrophenylhydrazone of the dehydrogenation product of the acid (IV; R = H). The 2,4-dinitrophenylhydrazone of 7-methyl-2,3-diethylindanone, had m. p. 174—180° (from chloroform–ethanol).

Synthesis of Glauconin.—The keto-ester (XI) (24 g.) in benzene (250 ml.) and methanesulphonic acid (redistilled; 20 ml.) was heated under reflux for 48 hr. (azeotropic removal of water). After pouring into water the aqueous layer was extracted with ether. The combined organic layers were washed with aqueous sodium hydrogen carbonate and water. Drying, removal of the solvent, and distillation *in vacuo* gave the mixed γ-lactones (17·95 g.), b. p. 110—120°/10^{-6} mm., n_D^{20} 1·4692, $\lambda_{max.}$ 228 mμ (ε 11,000), $\lambda_{max.}$ 285 (16,400 in N-sodium hydroxide), $\nu_{max.}$ 1805, 1773, 1730 cm.$^{-1}$ (Found: C, 56·9; H, 6·25. $C_{17}H_{24}O_8$ requires C, 57·3; H, 6·8%).

The γ-lactone mixture (10 g.) in aqueous sodium hydroxide (2N; 100 ml.) was heated on a steam-bath for 3 hr. under nitrogen. Acidification with 2N-sulphuric acid and continuous extraction with ether for 2 days gave an oil (5·92 g.) which was heated under reflux with acetyl chloride (50 ml.) for 30 min. After removal of the excess of acetyl chloride *in vacuo* the residue in chloroform was repeatedly extracted with saturated aqueous sodium hydrogen carbonate. The combined extracts were acidified with 2N-sulphuric acid and continuously extracted with chloroform. Removal of the solvent gave, on trituration with ether, glauconin (25 mg.) (m. p., mixed m. p., ultraviolet, and infrared spectra).

Isoglauconic Acid Acetate (with J. L. Bloomer).—Glauconic acid acetate (266 mg.) was heated under reflux in diglyme (2 ml.) under nitrogen for 20 hr. The solvent was removed *in vacuo* and the residue triturated with ether to yield the *isoglauconic acid acetate* (50 mg.), m. p. 257° (from acetone), $[\alpha]_D$ −5° (*c* 1·36), $\lambda_{max.}$ 220 mμ (ε 10,500), $\nu_{max.}$ 1840, 1750, 1720 cm.$^{-1}$ (Found: C, 61·75; H, 5·7. $C_{20}H_{22}O_8$ requires C, 61·55; H, 5·7%). Ozonolysis in ethylene chloride at −14° followed by reductive (zinc dust) work-up gave 53% of formaldehyde (dimedone derivative). The acetate (643 mg.) in glacial acetic acid (50 ml.) was hydrogenated over 10% palladised charcoal (53 mg.). After the uptake of 1 mol. of hydrogen the catalyst was filtered off and the solvent removed, to give *dihydroisoglauconic acid acetate* (237 mg.), m. p. 195—202°

(from acetone–chloroform), $[\alpha]_D$ −104° (*c* 0·52), ε(210 mμ) 300, $\nu_{max.}$ 1850, 1780, 1715 cm^{-1}. (Found: C, 61·35; H, 6·2. $C_{20}H_{24}O_8$ requires C, 61·2; H, 6·15%).

Hydrolysis of Dihydroisoglauconic Acid Acetate (with J. L. Bloomer).—The dihydro-compound (236 mg.) was heated on a steam-bath with 2·5N-sodium hydroxide (2 ml.) until all the solid dissolved, and then set aside at room temperature for 15 hr. Concentrated hydrochloric acid was added, and the precipitated solid (85 mg.) filtered off, m. p. 134—136°, $\nu_{max.}$ 1720, 1700, 1690 $cm.^{-1}$. This material, heated under a vacuum at 70°, gave an *anhydride*, m. p. 145—155°, $[\alpha]_D$ −58° (*c* 0·52 in ethanol), $\nu_{max.}$ 1855, 1780, 1703 $cm.^{-1}$. Satisfactory analytical results could not be obtained. However, when the hydrolysate was crystallised from ethyl acetate a *lactone hydrate* was formed, m. p. 197—203°, $[\alpha]_D$ −53° (*c* 0·65), $\nu_{max.}$ 1740, 1690 $cm.^{-1}$ (Found: C, 55·95; H, 6·7%; Equiv., 123. $C_{18}H_{26}O_9$ requires C, 55·95; H, 6·8%; Equiv., ($3CO_2H$) 129). Sublimation of this lactone gave an *anhydride*, m. p. 134—145°, $[\alpha]_D$ −53° (*c* 0·3), $\nu_{max.}$ 1850, 1780 $cm.^{-1}$ (Found: C, 61·4; H, 6·2. $C_{18}H_{22}O_7$ requires C, 61·7; H, 6·35%).

Glauconic Acid Tetrahydropyranyl Ether.—Glauconic acid (110 mg.) was set aside overnight with dihydropyran (3 ml.) containing 2 drops of 10N-hydrochloric acid. Dilution with water, chloroform extraction, and concentration of the extract yielded an oil which on dilution with light petroleum gave the *ether* (110 mg.), m. p. 196° (decomp.) (from acetone) (Found: C, 63·8; H, 6·8. $C_{23}H_{28}O_8$ requires C, 63·9; H, 6·55%). The ether was hydrolysed to starting material by a mixture of acetic acid, hydrochloric acid, and water at 100°.

Pyrolysis of Glauconic Acid Tetrahydropyranyl Ether.—The ether (1 g.) in mesitylene (25 ml.) was heated under reflux under nitrogen for 48 hr. After concentration *in vacuo* the gum obtained was chromatographed on silica gel (B.D.H.; 60 g.). Elution with benzene yielded glauconin (155 mg.). Elution with benzene–ether gave an *acid* (XVIII; R = H) (70 mg.), m. p. 186—188° [from ether–light petroleum (b. p. 60—80°)], $[\alpha]_D$ −73° (*c* 1·31), $\nu_{max.}$ 1840, 1780, 1720 $cm.^{-1}$ (Found: C, 62·35; H, 6·05. $C_{18}H_{20}O_7$ requires C, 62·05; H, 5·8%). The derived *ester* (XVIII; R = Me) (diazomethane) had m. p. 205—208° [from ether–light petroleum (b. p. 60—80°)], $[\alpha]_D$ −9° (*c* 1·13), $\lambda_{max.}$ 253 mμ (ε 3500 in cyclohexane), $\nu_{max.}$ 1830, 1780, 1735 $cm.^{-1}$ (Found: C, 63·45; H, 6·0. $C_{19}H_{22}O_7$ requires C, 62·95; H, 6·1%).

Reaction of Glauconic Acid Ketone with Cyclohexylamine.—The ketone (100 mg.) was heated under reflux for 2½ hr. in benzene (25 ml.) containing cyclohexylamine (1 ml.; freshly distilled from barium hydroxide). After cooling, the solution was washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water. After drying, concentration gave a gum which on trituration with acetone gave the *imide*, m. p. 195—197° [from chloroform–light petroleum (b. p. 60—80°)], $[\alpha]_D$ −28° (*c* 0·99), $\lambda_{max.}$ 226 mμ (ε 15,600), $\nu_{max.}$ 1755, 1700, 1630 $cm.^{-1}$ (Found: C, 69·1, 69·05; H, 8·45, 8·35; N, 5·95, 6·15. $C_{27}H_{38}N_2O_5$ requires C, 68·9; H, 8·15; N, 5·95%).

Reaction of Glauconic Acid Ketone with the Cyclohexylamine–Carbon Dioxide Adduct.—The ketone (120 mg.) in benzene (25 ml.) was heated under reflux for 3 hr. with the cyclohexylamine–carbon dioxide adduct (250 mg.) (prepared by mixing cyclohexylamine and solid CO_2). After cooling, the solution was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and dried. Concentration gave a solid (86 mg.) which was recrystallised from acetone–light petroleum (b. p. 60—80°) to give the *cyclohexylamide*, m. p. 178—179° (decomp.), $[\alpha]_D$ −26·4° (*c* 1·06), $\lambda_{max.}$ 218 mμ (ε 12,700), $\nu_{max.}$ 1830, 1775, 1690, 1670, 1650 $cm.^{-1}$ (Found: C, 68·85, 68·8; H, 7·85, 7·7; N, 3·4, 3·45. $C_{23}H_{31}NO_5$ requires C, 68·8; H, 7·8; N, 3·5%).

Pyrolysis of Dihydroglauconic Acid Chloride.—Dihydroglauconic acid (210 mg.) was set aside for 20 hr. with oxalyl chloride (3 ml.). Concentration yielded a solid which on trituration with ether gave the *acid chloride* (155 mg.). On warming with methanol it gave the methyl ester of dihydroglauconic acid. The acid chloride (98 mg.) was heated under nitrogen at 200° for ½ hr. The dark residue was sublimed at 200°/10^{-3} mm., to give the *acid* (VIII), m. p. 227—230° (from chloroform), $[\alpha]_D$ +5° (*c* 1·0), $\nu_{max.}$ 1860, 1785, 1740 $cm.^{-1}$ (Found: C, 61·8; H, 6·4. $C_{18}H_{22}O_7$ requires C, 61·7; H, 6·35%). With ethereal diazomethane it gave a *monomethyl ester*, m. p. 165—167° [from ether–light petroleum (b. p. 40—60°)], $[\alpha]_D$ +12° (*c* 0·9), ε(215 mμ) 810, $\nu_{max.}$ 1865, 1785, 1730 $cm.^{-1}$ (Found: C, 62·65; H, 6·4. $C_{19}H_{24}O_7$ requires C, 62·6; H, 6·65%).

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