The Chemistry of Extractives from Hardwoods. Part XXIII. The Isolation of a New Triterpene (Terminolic Acid) from* Terminalia ivorensis.

By F. E. King, T. J. King, and J. M. Ross.

[Reprint Order No. 5983.]

By the successive extraction of idigbo, a hardwood derived from *Terminalia ivorensis*, with light petroleum, ether, and ethanol, " β "-sitosterol, a new triterpene (terminolic acid), $C_{30}H_{48}O_6$, and ellagic acid have been isolated. Terminolic acid, a pentacyclic tertiary monocarboxylic acid containing one double bond and four hydroxyl groups, of which two are adjacent, is a member of the β-amyrin–oleanolic acid series.

The West African tree *Terminalia ivorensis* yields a commercial timber known as idigbo or black afara. The colour of the heartwood varies from pale yellow to red-brown and the alternative name, which refers to the appearance of the bark, is intended to distinguish it from white afara or limba, the wood of a related species, *Terminalia superba*. Idigbo is resistant to wood-rotting fungi and finds many constructional uses but has the undesirable property of developing yellow stains in contact with dilute alkalis including soap solutions. The description which follows gives details of the first chemical investigation of the extraneous constituents of the wood.

Boiling light petroleum removed a small quantity (0·3%) of a viscous oil. This slowly deposited a crystalline solid which was identified as " β "-sitosterol. Further extraction with boiling ether produced an amorphous powder which separated from the hot solvent and was obtained crystalline after some preliminary purification, by repeated dissolution in acetone or more conveniently through the sparingly soluble sodium salt. The product, a new triterpene $C_{30}H_{48}O_6$, hereafter called terminolic acid, in some cases constituted approximately 1·5% of the wood.

A large amount of amorphous solid was extracted by ethanol, and crystallisation of the portion insoluble in acetic acid yielded ellagic acid. It is to this constituent that the yellow staining of the wood by alkalis is due. Ellagic acid has been found in other *Terminalia* species, *e.g.*, the fruit of *T. chebula* (Perkin and Nierenstein, *J.*, 1905, **87**, 1412) and the wood of *T. arjuna* (King, King, and Ross, *J.*, 1954, 3995).

Terminolic acid is only weakly acidic, being virtually insoluble in sodium hydrogen carbonate solution, and with aqueous sodium hydroxide above 0·5N its solubility is inhibited by the formation of the sodium salt. Treatment with diazomethane or with sodium hydroxide–methyl sulphate gave the ester, methyl terminolate, $C_{31}H_{50}O_6$. The hindered character of the carboxyl group was evident from its inertness to Fischer–Speier conditions of esterification, and from the inability of its esters to be hydrolysed under normal conditions. The acid resisted reduction by catalytic and chemical methods, and gave only a very weak yellow colour with tetranitromethane, but the coloration was more pronounced with the ester and acetate. The presence of a double bond was proved by quantitative oxidation with monoperphthalic acid, analysis of the product agreeing with the addition of one atom of oxygen. From this evidence in conjunction with the molecular formula it may be concluded that terminolic acid is pentacyclic. The infra-red absorption of methyl terminolate (bands at 800 to 850 cm.$^{-1}$ and weak shoulder at 1640—1670 cm.$^{-1}$) was indicative of a trisubstituted olefinic bond (cf. Jeger, Ruzicka, *et al.*, *Helv. Chim. Acta*, 1950, **33**, 672, 687, 711, 1050; Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402). Its situation with respect to the carboxyl group was evident from the formation with bromine in acetic acid of a highly crystalline bromo-lactone, thus denoting a βγ- or γδ-unsaturated acid, analogy with other triterpene acids and the infra-red observations just mentioned favouring the latter possibility. The susceptibility of the compound to per-acid oxidation and the easy formation of the bromo-lactone place terminolic acid in the β-amyrin–oleanolic acid group of pentacyclic triterpenes.

---

* Part XXII, *J.*, 1955, 1117.

Analyses of the acid and methyl ester acetates, which were obtained crystalline only after considerable manipulation, proved the remaining four oxygen atoms to be present as hydroxyl groups.

Methyl terminolate tetra-acetate is oxidised by selenium dioxide to a substance which though non-crystalline is substantially the 11 : 13(18)-dehydro-derivative since its ultra-violet absorption closely resembles that of similar triterpenes, *e.g.*, dehydro-oleanolic acid (Barton and Holness, *J.*, 1952, 78). More vigorous oxidation with this reagent gave the 10 : 13-diene-12 : 19-dione, similarly identified by its light absorption, thus affording further support for the relation of terminolic acid to the β-amyrin series.

The reaction of terminolic bromo-lactone with methanolic potassium hydroxide led to the β-epoxide (see King, King, and Ross, *loc. cit.*). However, this suffered partial rearrangement when crystallised and so could not be obtained pure; it was converted by the action of hydrogen chloride in chloroform into the methyl dihydro-12-oxo-ester. The mono-perphthalic acid oxidation product of methyl terminolate on the other hand, as with that of methyl oleanolate acetate (Picard and Spring, *J.*, 1940, 1389), consists of the stable α-epoxide. A comparison of the infra-red spectra of the α-epoxide and the saturated ketone confirms their respective structures, the epoxide exhibiting a single carbonyl peak at 1712 cm.$^{-1}$, due to the ester grouping, whereas the dihydro-oxo-ester has a broad peak at 1685 cm.$^{-1}$, with a shoulder at 1715 cm.$^{-1}$ (determinations with suspensions in Nujol owing to the insolubility of the compounds in carbon tetrachloride). The authors thank Dr. G. D. Meakins, University of Manchester, for these measurements which were undertaken through the kindness of Professor E. R. H. Jones, F.R.S. When the epoxide is treated with hot acetic and hydrochloric acids it yields the methyl dihydro-oxo-ester tetra-acetate identical with that obtained from acetylation of the saturated ketone and by the action of hot acetic acid–hydrogen peroxide on methyl terminolate tetra-acetate. Hydrolysis of the actate yields methyl dihydro-12-oxoterminolate. The marked negative shift in specific rotation when passing from methyl terminolate (+40°) to the dihydro-12-oxo-ester (−45°) is similar to that for the change of methyl arjunolate (+68°) to methyl dihydro-12-oxoarjunolate (−30).*

Attempts to oxidise terminolic acid to keto-compounds, and thence by reduction to relate them to known triterpenes, failed to yield any crystalline oxidation products. With sodium periodate an amorphous product was obtained which gave a precipitate with 2 : 4-dinitrophenylhydrazine solution, thus disclosing the presence of a 1 : 2-glycol unit; a quantitative determination in which it was ascertained that only one molecule of the oxidising agent was required proved the glycol unit to be isolated from the remaining hydroxyl groups.

As with the corresponding derivative of arjunolic acid (Part XVIII), reductive fission of the product obtained in the lead tetra-acetate oxidation of terminolic bromo-lactone took place without the evolution of carbon dioxide. Hence it is apparent that the α-glycol cannot be adjacent to the carboxyl group where it would give rise on oxidation to a β-carbonylic acid. Its location is, in fact, by this observation restricted to ring A or B. Further experiments, to be reported shortly, confirm the expectation based on the botanical relationship of the respective species that the new triterpene is a hydroxyarjunolic acid.

EXPERIMENTAL

Specimens for analysis, except where otherwise indicated, were dried at 120°/0·1 mm. for 2 hr. Alcoholic solutions were used for measurements of ultra-violet absorption spectra and chloroform for the optical rotations (determined at room temperature).

Extraction of Terminalia ivorensis *Heartwood.*—The botanical origin of commercial idigbo used in the research was kindly verified by Mr. B. J. Rendle, D.S.I.R. Forest Products Research Laboratory. Continuous extraction of the coarsely powdered wood (3·5 kg.) with boiling light petroleum (b. p. 60—80°) for 18 hr. afforded a red-brown viscous oil (10—12 g., 0·3%). Crystalline solid which gradually separated was removed from the oil with boiling methanol. By repeated crystallisation from methanol " β "-sitosterol (1 g.) was obtained as plates, m. p. 136—137°, $[\alpha]_D$ −34° (*c*, 2·03), and its acetate had m. p. 124—125°, $[\alpha]_D$ −38° (*c*, 1·13) (Found : C,

---

* The specific rotation of methyl dihydro-12-oxoarjunolate was misprinted as +30° in *J.*, 1954, 4000.

81·3; H, 11·5. Calc. for $C_{31}H_{52}O_3$: C, 81·6; H, 11·4%). Other derivatives were the benzoate, m. p. and mixed m. p. 145—146° (Found: C, 82·8; H, 10·4. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5%) and *p*-nitrobenzoate, m. p. 181—182° (Found: C, 76·5; H, 9·0. Calc. for $C_{36}H_{53}O_4N$: C, 76·7; H, 9·5%), which likewise closely resembled published descriptions, summarised, for example, in *J.*, 1953, 1193.

The wood was next treated with boiling ether, 18 hours sufficing for complete removal of the extractable triterpene, part of which separated as a free-flowing amorphous cream powder (maximum yield 50—55 g., 1·5%). The amount of this extractive varied from specimen to specimen of the wood and in some was almost nil.

Finally, the wood was exhaustively extracted with boiling ethanol and the solution concentrated to 1 l. The solid which was then deposited was crystallised from pyridine and yielded ellagic acid (19·5 g.). After further crystallisation from pyridine (charcoal) it separated in pale yellow needles, m. p. >360° (Found: C, 55·4; H, 2·2. Calc. for $C_{14}H_6O_8$: C, 55·6; H, 2·0%): max. at 255 (log ε, 4·69) and 365 mμ (log ε, 4·07). The tetra-acetate, cream coloured leaflets from acetic anhydride, had m. p. 340—343° (Perkin and Nierenstein, *loc. cit.*, give 343—346°). The tetramethyl ether, plates, m. p. 343—344°, from acetic anhydride, was prepared with diazomethane in methanol–ether (Goldschmidt, *Monatsh.*, 1905, **26**, 1139) (Found: C, 59·8; H, 3·7. Calc. for $C_{18}H_{14}O_8$: C, 60·3; H, 3·9%), unchanged ellagic acid being removed with a little boiling pyridine. Complete evaporation of the alcohol gave a brown powder (547 g.) from which a further quantity of ellagic acid (4·2 g./50 g.) was isolated by treatment with dioxan (2 c.c./g.).

Terminolic Acid.—(*a*) The amorphous product obtained by ether-extraction was digested with acetic acid (2 c.c./g.) at 70° and the solution filtered from the residue of ellagic acid. The addition of water to the filtrate precipitated the dissolved solid which was dried and extracted in batches (20 g.) (Soxhlet) with acetone (125 c.c.). With the appearance of solid from the solution the solvent was changed, the process being repeated until only weakly coloured solutions were obtained. Concentration of these solutions gave crystalline *terminolic acid* (7 g.) which separated from acetone in minute prisms, m. p. 335—336°. The repeatedly crystallised analytical specimen had m. p. 347°, $[\alpha]_D$ +42° (*c*, 0·11 in EtOH) (Found: C, 71·2, 71·2, 71·6; H, 9·3, 9·4, 9·6; active H, 0·76%; equiv. 510, 498. $C_{30}H_{48}O_6$ requires C, 71·4; H, 9·5; 5 active H, 0·99%; equiv., 504).

(*b*) Later extractions were performed without previous treatment with light petroleum; for example, the whole product extracted from 7 kg. of wood was dissolved in boiling methanol (700 c.c.), and the solution filtered and made weakly alkaline with concentrated aqueous sodium hydroxide. When the sodium ellagate which separated in the cold had been removed, the solution was diluted with water to 1500 c.c. and treated with excess of sodium hydroxide. By concentrating the solution on a steam-bath until a test portion crystallised on cooling, terminolic acid was isolated as the sodium salt, obtained as colourless silky needles by recrystallisation from the aqueous methanolic alkali, fairly soluble in alcohol but only sparingly in dilute aqueous sodium hydroxide (yields 20—60 g.).

With cold concentrated sulphuric acid the triterpene exhibits a yellow colour slowly changing to violet; in the Liebermann–Burchard test it reacts pink, changing to red-brown, and the colour sequence with Tschugaieff's acetyl chloride–zinc chloride reagent is orange—deep-red—brown. Terminolic acid is freely soluble in both hot and cold acetic acid, dioxan, pyridine and 2-ethoxyethanol; it dissolves sparingly in acetone and the simple alcohols.

Methyl Terminolate.—Diazomethane in ether was added to a suspension of the purified acid in methanol and after 2 hr. the solvents were evaporated. The residue was recrystallised from methanol, to give *methyl terminolate* (80—90%), m. p. 160—170°, also obtained in high yield by shaking the acid or the sodium salt with methyl sulphate and excess of 1% methanolic sodium hydroxide. The ester crystallised in prisms, m. p. (slow heating) 165—168°, $[\alpha]_D$ +40° (*c*, 0·78) (Found, after drying at 150° *in vacuo*: C, 71·8; H, 9·6; OMe, 7·2. $C_{31}H_{50}O_6$ requires C, 71·8; H, 9·65; OMe, 6·0%). The ester was unattacked when heated under reflux with 10% alcoholic potassium hydroxide for 4 hr. *Ethyl terminolate*, prepared with ethyl sulphate and 1% alcoholic sodium hydroxide, crystallised from ethanol in plates, m. p. 164—165°, $[\alpha]_D$ +41° (*c*, 1·06) (Found, after drying at 150° *in vacuo*: C, 72·2; H, 10·1; OEt, 8·5. $C_{32}H_{52}O_6$ requires C, 72·2; H, 9·8; OEt, 8·5%).

p-*Nitrobenzyl terminolate*, obtained by refluxing the acid with 0·5% alcoholic sodium hydroxide and *p*-nitrobenzyl bromide for 1 hr., crystallised from ethanol in prisms, m. p. 242° (Found: C, 69·4; H, 8·0; N, 2·3. $C_{37}H_{53}O_8N$ requires C, 69·5; H, 8·3; N, 2·2%).

To an ethanol solution (25 c.c.) of methyl terminolate (0·1 g.) aqueous sodium metaperiodate

(2 c.c.; 0·363M) was added. Titration of an aliquot in the usual way after 3 hr. indicated the oxidation of one α-glycol unit (Found: 0·97 and 1·09). No further appreciable oxidation had occurred after 24 hr.

Terminolic Acid Tetra-acetate.—The usual procedures, including chromatography of light petroleum–benzene solutions on alumina, failed to effect crystallisation of the amorphous products obtained with the common acetylating agents. That formed from acetic anhydride–perchloric acid was distilled at 260—290°/10^{-5} mm. and dissolved in hot *cyclo*hexane, and after collection from the cold solution appeared to be the *tetra-acetate* (Found: C, 67·8; H, 8·4; OAc, 22·8. $C_{38}H_{56}O_{10}$ requires C, 67·9; H, 8·3; 4OAc, 25·6%). Chromatography by absorption on acid-washed alumina in light petroleum–benzene (4 : 1) and elution with benzene eventually gave the crystalline actate in low yield as leaflets, m. p. 217° (from methanol), $[\alpha]_D$ −12·5° (*c*, 0·36) (Found: C, 67·9; H, 8·3%). The sparing solubility of both acetate and its saponification product in the alcoholic alkaline reagent may account for the low OAc value.

Methyl Terminolate Tetra-acetate.—Acetylation (acetic anhydride–pyridine at room temperature overnight) of pure methyl terminolate yielded an amorphous product which could be obtained crystalline by absorption on acid-washed alumina from benzene solution followed by elution with the same solvent. The *ester tetra-acetate* separated from methanol in leaflets, m. p. after drying *ca.* 187—189° (Found: C, 68·0; H, 8·15; OMe, 5·6; OAc, 22·9. $C_{39}H_{58}O_{10}$ requires C, 68·2; H, 8·4; OMe, 4·5; 4OAc, 25%).

Oxidation of Methyl Terminolate Tetra-acetate with Selenium Dioxide.—(*a*) A solution of methyl terminolate tetra-acetate (0·97 g.) in acetic acid (50 c.c.) containing sublimed selenium dioxide (0·45 g.) was heated under reflux for 15 hr. After filtration from selenium, the solution was evaporated under diminished pressure, and the residue dissolved in ether which was then washed with aqueous sodium hydrogen carbonate and water and evaporated. The amber gummy residue (0·96 g.), dissolved in benzene and filtered through alumina, gave 0·88 g. of non-crystalline eluate. This was dissolved in benzene (2 c.c.), and the solution diluted to 25 c.c. with light petroleum (b. p. 60—80°). Chromatography on alumina (Grade H, 25 g.) gave the following fractions: 1, eluant 1220 c.c. of 1 : 3 light petroleum–benzene, 235 mg.; 2, eluant 600 c.c., of ether, 160 mg.; 3, eluant 800 c.c., of methanol, 110 mg. The fractions separated from acetone as amorphous solids with the following light absorption: 1, max. 243, 250·5, 260 mμ (log ε, 4·37, 4·42, 4·23); 3, max. 242, 250·5, 259·5 mμ (log ε, 4·23, 4·40, 4·15). Dehydro-oleanolic acid (Barton and Holness, *J.*, 1952, 78) has max. 242, 252, 261 mμ (log ε, 4·41, 4·46, 4·28).

(*b*) The ester acetate (0·5 g.) and excess (0·5 g.) of selenium dioxide were heated in boiling acetic acid for 24 hr. The product, freed from selenium and acetic acid, was dissolved in benzene, and the solution washed with aqueous sodium hydrogen carbonate. Chromatography on alumina and elution with benzene removed the 11 : 13(18)-diene, and further elution with ether yielded an uncrystallisable product (100 mg.) which however possessed the light absorption of a 10 : 13-diene-12 : 19-dione, *viz.*, $\lambda_{max.}$ 276 mμ (ε 11,300). Ruzicka, Jeger, and Winter (*Helv. Chim. Acta*, 1943, **26**, 265) found $\lambda_{max.}$ 275 mμ (ε 12,500) for the diene-dione from methyl oleanolate acetate.

Terminolic Bromo-lactone.—To a stirred solution of terminolic acid (2 g.) and sodium acetate (8 g.) in acetic acid (90 c.c.), 3% bromine–acetic acid (50 c.c.) was added during ½ hr. After a further ½ hr. the mixture was poured into water containing sodium thiosulphate (4 g.), and the precipitate collected, washed with aqueous sodium hydrogen carbonate and water, and dried. The *bromo-lactone* crystallised from methanol in leaflets (1·6 g.), m. p. 232° (decomp.), $[\alpha]_D$ +32° (*c*, 0·87) (Found: C, 61·7; H, 8·0; Br, 12·5. $C_{30}H_{47}O_6Br$ requires C, 61·7; H, 8·1; Br, 13·6%).

*Methyl Dihydro-*12*-oxoterminolate.*—The bromo-lactone (2·3 g.) was refluxed with 3% methanolic potassium hydroxide (50 c.c.) for 1 hr. and diluted with water until crystallisation began. The resulting β-epoxide (1·4 g.) crystallised from aqueous methanol in needles, m. p. *ca.* 250° which became indefinite on further crystallisation. A solution of the epoxide in chloroform (25 c.c.), treated with a stream of hydrogen chloride, gave *methyl dihydro-*12*-oxoterminolate* which was isolated by evaporation of the solvent. Crystallised from methanol it formed rectangular tablets (1·1 g.) exhibiting a dual m. p., *ca.* 200—205° and 317—321°, $[\alpha]_D$ −45° (*c*, 0·93) (Found, in a specimen dried at 150°/0·1 mm.: C, 70·0; H, 9·5. $C_{31}H_{50}O_7$ requires C, 69·6; H, 9·4%).

Acetylation of the dihydro-oxo-ester (0·5 g.) by refluxing acetic anhydride (3 c.c.) and pyridine (1 c.c.) for 1·5 hr. yielded *methyl dihydro-*12*-oxoterminolate tetra-acetate* which readily crystallised from methanol in long, fine needles, m. p. 284—285°, $[\alpha]_D$ −39° (*c*, 0·44) (Found:

C, 66·9; H, 8·2. $C_{39}H_{58}O_{11}$ requires C, 66·7; H, 8·3%); light absorption, $\lambda_{max.}$ 286 mμ (ε 40). The acetate was also obtained (yield 70%) by oxidation of methyl terminolate tetra-acetate with hot acetic acid–hydrogen peroxide for 2 hr.

Methyl 12 : 13-*Epoxyterminolate.*—A solution of methyl terminolate (0·985 g.) in ether (20 c.c.) was mixed with ethereal monoperphthalic acid (5 c.c.; 0·5N), and the mixture maintained at 0—2°. Portions removed after 1, 2, 6, and 18 days showed a consumption of 0·58, 0·66, 0·97, and 1·03 mols. respectively of the per-acid.

A solution similarly obtained from 1·0 g. of the methyl ester was shaken with aqueous sodium hydrogen carbonate; removal of the solvent gave the *epoxide* which crystallised from methanol in elongated prisms, m. p. 175°, $[\alpha]_D$ +7·7° (*c*, 0·92) (Found, in a specimen dried at 150°/0·1 mm.: C, 69·7; H, 9·4; OMe, 6·6. $C_{31}H_{50}O_7$ requires C, 69·6; H, 9·4; OMe, 5·8%).

Isomerisation of the 12 : 13-*Epoxide to Methyl Dihydro*-12-*oxoterminolate Tetra-acetate.*—A solution of the epoxide (0·5 g.) in acetic acid (18 c.c.) was treated with 10% hydrochloric acid (0·5 c.c.), heated on a steam-bath for 8 hr., poured into water, and worked up in the usual way; the ester tetra-acetate crystallised from methanol (Norite) in silky needles, m. p. and mixed m. p. 281—283° (Found: C, 66·8; H, 8·8%).

Hydrolysis by refluxing 5% methanolic potash for 1·5 hr. gave the methyl dihydro-12-oxoterminolate in rectangular plates, m. p. 195° and 312—317°.

Methyl 12 : 13-*Epoxyterminolate Tetra-acetate.*—Methyl terminolate tetra-acetate (1·1 g.) in ether (20 c.c.) was treated with ethereal monoperphthalic acid (50 c.c.; 0·3N) and kept at 0—2° for 12 days. On working up in the usual way the acetylated *epoxy-ester* was obtained as a colourless solid (1·1 g.) which could not be crystallised (Found: C, 66·3; H, 8·0. $C_{39}H_{58}O_{11}$ requires C, 66·7; H, 8·3%).

Reduction of Terminolic Bromo-lactone.—(a) *With zinc powder in acetic acid.* The bromo-lactone (0·8 g.) in acetic acid was heated with zinc powder (5 g.) on a steam-bath for 2 hr. The liquid was then filtered and the product precipitated with water; crystallised from methanol it gave terminolic acid (0·56 g.), which after repeated crystallisation from methanol, and finally butanol, formed large prisms, m. p. 342—344° (Found: C, 71·8; H, 9·4%).

(b) *With sodium amalgam.* To an ethanolic solution (40 c.c.) of terminolic bromo-lactone (0·82 g.) were added 3% sodium amalgam (5 g.) and a few drops acetic acid. The mixture was refluxed on a steam-bath for 2 hr. and then worked up by pouring the solution into water and acidifying it. The acid, crystallised from methanol, had m. p. 338—339° (slight decomp.).

Oxidation of Terminolic Bromo-lactone with Lead Tetra-acetate.—A warm solution of lead tetra-acetate (*ca.* 6 g.) in acetic acid (125 c.c.) was added to the bromo-lactone (4·84 g.) in acetic acid (125 c.c.) (temperature of mixture, 32°). After 12·5 hr. at 20° the excess of reagent was destroyed with ethylene glycol, and the mixture poured into water. The dried precipitate separated from methanol in a semigelatinous state but the product (3·4 g.) eventually crystallised from methanol and on further crystallisation gave colourless needles, m. p. 216—217° (decomp.) (Found, in a specimen dried at 150°/0·1 mm.: C, 61·8; H, 7·8. $C_{30}H_{45}O_6Br$ requires C, 61·9; H, 7·7%).

A solution of the oxidation product (0·91 g.) in acetic acid (30 c.c.) was heated with zinc dust (6·0 g.) on a steam-bath. A stream of purified nitrogen was passed through the reaction vessel and thence into baryta water, but no carbon dioxide evolution was detected during reduction (2 hr.). The product precipitated by water was dissolved in ether and washed with aqueous sodium hydrogen carbonate and then with 1% aqueous sodium hydroxide. The sodium hydroxide-soluble fraction (0·5 g.) separated from methanol in an amorphous condition.

One of the authors (J. M. R.) thanks the Department of Scientific and Industrial Research for a Maintenance Allowance.

THE UNIVERSITY, NOTTINGHAM.

[*Received, December 20th, 1954.*]