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COMPONENTS OF *CROTON OBLONGIFOLIUS*—III

CONSTITUTION OF OBLONGIFOLIC ACID

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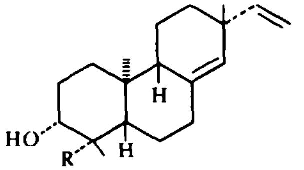
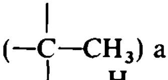
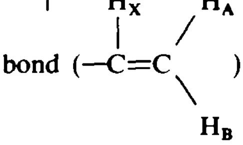
Abstract—Chemical and spectral studies of the major diterpene acid component of the bark of *Croton oblongifolius*, $C_{20}H_{30}O_2$, and its conversion products (derivatives) have shown that it belongs to the pimarane group with the carboxyl in the 4-position (axial) and with the double bonds at Δ 7 and 15-positions and its stereochemistry is opposite that of isopimaric acid. It is therefore formulated as (+) isopimara-7 (8), 15-diene-19-oic acid.

IN THE earlier communications[1,2*] the constitution of two new diterpenic alcohols, oblongifoliol (I) and deoxyoblongifoliol (Ia) obtained from the bark of *Croton oblongifolius* (Euphorbiaceae) were discussed. They were obtained from the neutral fraction of the combined light petroleum (60–80°) and acetone extracts. The acidic fraction gave by column chromatography four crystalline compounds, A, B, C and D. This paper deals with the constitution of compound A.



I:R = CH_2OH
Ia:R = CH_3

Compound A, $C_{20}H_{30}O_2$ (M^+302), was obtained as colourless crystals, m.p. 151–152°, and was dextro-rotatory: it gave a red colour in the Liebermann–Burchard and a yellow colour in TNM tests indicating it to be an unsaturated diterpene. It does not absorb in the UV region; its IR spectrum (Nujol) has peaks at 1695 cm^{-1} (carboxyl), 1642, 980 and 911 cm^{-1} (monosubstituted double bond), 879, 855, 838 and 823 cm^{-1} (trisubstituted double bond). Its NMR spectrum has signals for three tertiary methyls  $(-\overset{|}{\underset{|}{C}}-CH_3)$ at δ 0·80, 0·87 and 1·25, three protons on a monosubstituted double bond  $(-\overset{\overset{H_X}{|}}{C}=C\begin{smallmatrix}H_A\\ H_B\end{smallmatrix})$ at δ 4·77–6·08 exhibiting a characteristic ABX pattern with coupling constants J_{AB} 1·5 c/s, J_{AX} 10 c/s and J_{BX} 17·7 c/s and for a proton on a tri-

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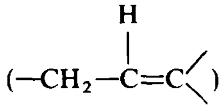
[*] References 1 and 2 are treated as part I and II of this series.

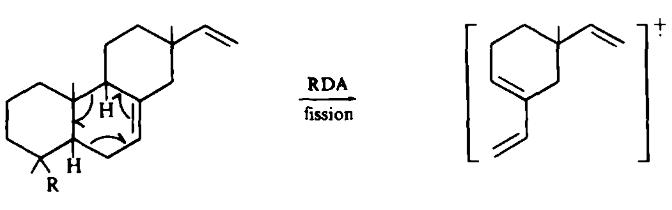
substituted double bond in the system  $(\text{—CH}_2\text{—}\overset{\overset{\text{H}}{|}}{\text{C}}\text{=C}\langle)$ at δ 5·40 as a triplet. The mass spectrum shows the presence of a carboxyl function by a prominent peak at *m/e* 257 (32 %) due to the loss of 45 units (—COOH) from the molecular ion. Compound A reacted with diazomethane forming an oily ester and has been named *oblongifolic acid*.

Reduction of its methyl ester with LAH yielded a dextrorotatory alcohol, $C_{20}H_{32}O$ as colourless needles, m.p. 81–82°. By tosylation and subsequent LAH reduction this alcohol could be converted into an oily hydrocarbon which could not be studied fully owing to poor yield.

The NMR spectral pattern of the acid and its derivatives (Table 1) shows that it is a pimarane type.[3] The position and orientation of the carboxyl function were determined as follows. The methyl ester [II] underwent hydrolysis only under drastic conditions indicating that the carboxyl function is axially oriented. This was supported by its IR spectrum which has characteristic peaks[4] at 1232, 1190 and 1149 cm^{-1} for axial orientation of the ester group, and also by NMR spectra of the corresponding alcohol (III) and its acetate (IV).[5] The methylene protons of the alcohol $(\text{—C}\underline{\text{H}}_2\text{OH})$ appear as a quartet centred at δ 3·73 and those of the acetate $(\text{—C}\underline{\text{H}}_2\text{OAc})$ appear as a quartet centred at δ 4·20. The above IR and NMR spectral data are in agreement with the carboxyl function being at C_4.

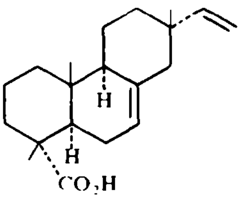
The positions of the double bonds were fixed as follows. The monosubstituted double bond indicated by IR and NMR spectra was confirmed by the liberation of formaldehyde during ozonolysis. It can be only at C_{13} of the pimarane skeleton, its splitting pattern being similar to that of methyl sandaracopimarate and methyl isopimarate.[6] The trisubstituted double bond may be at C_5–C_6, C_7–C_8 or C_9–C_{11}. The position C_9–C_{11} can be ruled out on biogenetic considerations of pimarane type of resin acids.[7] Oblongifolic acid did not undergo decarboxylation when heated above its m.p. showing that the double bond is not in the C_5–C_6 position. Thus it can be only at C_7–C_8. This conclusion is supported by the appearance of a singlet at δ 1·95 for C_{14} protons as in the case of isopimaric acid.

The mass spectrum of oblongifolic acid provides full support for these structural features. The molecular ion peak at *m/e* 302 is also the base peak; the other prominent peaks are given in Table 2. The peaks M-45 and M-61 support the presence of a C_4 carboxyl.[8] The peak at *m/e* 148 (23 %) is characteristic of a number of diterpenic compounds having a C_7–C_8 double bond and is formed by a facile RDA fission involving this double bond[8, 9] as shown.

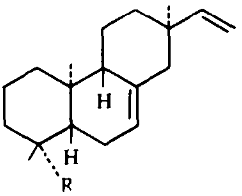


m/e 148 (23 %)

The spectra of oblongifolic acid and its derivatives exhibit a close similarity with the spectra of isopimaric acid and its derivatives.[3, 6, 7, 10, 11] The mass spectral agreement is given in Table 2. The points of differences are: (1) the orientation of the carboxylic function leading to the difference in the NMR and (2) the opposite rotation.[12] This indicates that oblongifolic acid and isopimaric acid have opposite stereochemistry at all the asymmetric centres and the relationship is just the same as between (−) pimaric acid and (+) pimaric acid.[13] Hence oblongifolic acid should be formulated as (+) isopimara-7(8), 15-dien-19-oic acid.



Isopimaric acid



Oblongifolic acid

I:R = CO_2H
II:R = CO_2CH_3
III:R = CH_2OH
IV:R = CH_2OAc

There is close similarity in the chemical shift and splitting pattern of the protons on the double bonds of oblongifoliol, deoxyoblongifoliol and oblongifolic acid. It is therefore now suggested that the ring double bond for oblongifoliol[1] and deoxyoblongifoliol[2] may not be at 8,14 as reported earlier but be at 7,8.

TABLE 1. NMR DATA OF OBLONGIFOLIC ACID DERIVATIVES
δ values

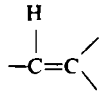
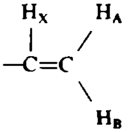
Compound	$-\overset{\vert}{\underset{\vert}{C}}-CH_3$	A	B	X	J_{AB}	J_{AX}	J_{BX}		
									
Ester (II)	0·70 (3H) 0·87 (3H) 1·20 (3H)	4·84,	4·89,	5·83;	1·5,	10·0,	17·5 c/s	5·38 (1H)	3·65 $(-CO_2C\underline{H}_3)$
Alcohol (III)	0·87 (6H) 0·97 (3H)	4·87,	4·93,	5·86;	1·8,	10·0,	17·5 c/s	5·38 (1H)	
Acetate (IV)	0·87 (6H) 0·95 (3H)	4·86,	4·91,	5·85;	1·5,	10·0,	17·8 c/s	5·37 (1H)	2·03 $(-CH_2OCOC\underline{H}_3)$

TABLE 2. MASS SPECTRAL VALUES OF OBLONGIFOLIC ACID (A) AND METHYL ISOPIMARATE (B)[11]

Compound	*m/e* values											
(A)		302	287	273	257	241	201	148	133	119	105	91
(B)	316	301	287	273	257	241	201	148	133	119	105	91

EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken using a Perkin–Elmer spectrophotometer. NMR spectra were determined in $CDCl_3$ on a Varian A-60 spectrometer using TMS as an internal standard. Light petroleum refers to the fraction b.p. 60–80°. All specific rotations were taken in $CHCl_3$. Oblongifolic acid and its derivatives show peaks for a monosubstituted double bond at 1642, 980 and 911 cm^{-1} and a trisubstituted double bond at 879, 855, 838 and 823 cm^{-1}.

Extraction of Croton oblongifolius *bark* (*acid A, B, C and D*). The dried, powdered bark (2 kg × 4) was extracted 3 times with boiling light petroleum and then three times with boiling acetone. On TLC both extracts gave identical spots. The two extracts were therefore concentrated and combined, taken up in ether and extracted with 10% Na_2CO_3 aq five times. The combined Na_2CO_3 soln was again extracted with ether, acidified with HCl acid and then extracted with ether. This ether extract was concentrated and the oily residue (30 g) dried and adsorbed on silica gel and chromatographed. The column was eluted successively with light petroleum, benzene and chloroform. The following compounds were isolated: light petroleum: benzene (4:1) eluted compound A (0·3 g), (1:1) compound B (0·05 g) and (1:3) compound C (0·35 g); benzene: chloroform (1:1) eluted compound D (0·03 g). All compounds except compound B were found to be terpenic in nature. Compound A (oblongifolic acid) crystallised from MeOH as colourless crystals m.p. 151–152°, $[\alpha]_D^{19.5}$ + 11·03 (*c*. 2·8). (Found: C, 79·1; H, 9·7. $C_{20}H_{30}O_2$ requires: C, 79·5; H, 9·9%).

Ozonolysis of oblongifolic acid. A soln of 0·1 g of the acid in 15 ml of EtOAc was treated at 0° with a stream of ozonised O_2 (3% ozone) for 2 hr. The solvent was evaporated *in vacuo* and the residue distilled with steam after the addition of 20 mg Zn dust. The distillate gave a purple colour with chromotropic acid indicating the liberation of CH_2O.

Dihydro oblongifolic acid. A soln of oblongifolic acid (0·15 g) in EtOAc (25 ml) was hydrogenated in the presence of 10% Pd-C (0·2 g) for 2 hr. The catalyst was filtered off, the solvent removed *in vacuo* and the residue crystallised from MeOH yielding colourless needles, m.p. 141–142°. It gave a yellow colour with TNM. Its IR spectrum did not have peaks at 1642, 980 and 911 cm^{-1} indicating saturation of the vinylic double bond. It showed peaks for carboxyl (1695 cm^{-1}) and a trisubstituted double bond. The ORD and CD curves were recorded using Model ORD/UV.5 and show the plain negative ORD and positive CD curves. (Found: C, 78·5; H, 10·8. $C_{20}H_{32}O_2$ requires: C, 78·9; H, 10·5%).

Methyl oblongifoliate. A suspension of oblongifolic acid (0·5 g) in ether (10 ml) was treated with ethereal diazomethane. After keeping for 24 hr the solvent was removed and the residue passed through a column of silica gel. Elution with light petroleum: benzene (9:1) gave an oily ester. Its IR spectrum (thin film) has peaks for the ester (1750, 1232, 1190 and 1149 cm^{-1}) besides the monosubstituted and the trisubstituted double bonds.

Saponification of methyl oblongifoliate. Methyl oblongifoliate (0·1 g) was refluxed for 10 hr with KOH (2 g) in MeOH (10 ml). It did not undergo hydrolysis and the ester was recovered unchanged. Then the ester was refluxed with KOH (2 g) in ethylene glycol (10 ml) for 6 hr. The soln was diluted with water and extracted with ether to remove neutral products, acidified with cold HCl and the acid product extracted with ether. The ether soln was dried (Na_2SO_4) and evaporated to give the acid which crystallised and compared well with oblongifolic acid.

Conversion of methyl oblongifoliate into the alcohol. A soln of methyl oblongifoliate (0·4 g) in dry THF (20 ml) was added to a suspension of LAH (2 g) in dry THF (20 ml). The mixture was refluxed with stirring for 6 hr and decomposed with 1:1 EtOAc and water, acidified with ice cold HCl and extracted with ether. The ether soln was dried (Na_2SO_4) and evaporated to yield the alcohol. It crystallised from MeOH as needles, m.p. 81–82°, $[\alpha]_D^{19.5}$ + 41·2 (*c* 1·8). Its IR spectrum (KBr) has peaks for OH (3636 and 1081 cm^{-1}), besides the monosubstituted and trisubstituted double bonds. (Found: C, 82·8; H, 10·9. $C_{20}H_{32}O$ requires: C, 83·3; H, 11·1%).

Acetylation of the alcohol. Acetylation of the alcohol (0·1 g) by the pyridine (0·5 ml) and Ac_2O (2 ml) method gave the acetate, m.p. 41–42°, $[\alpha]_D^{28.5}$ + 12·16 (*c* 3·6). (Found: C, 79·5; H, 10·0. $C_{22}H_{34}O_2$ requires: C, 80·0; H, 10·3%).

Tosylation of the alcohol. The alcohol (0·2 g) was tosylated using pyridine (3 ml) and *p*-toluenesulphonyl chloride (0·4 g). The tosylate crystallised from light petroleum as stout needles, m.p. 87–88°. (Found: C, 72·9; H, 8·7. $C_{27}H_{38}SO_3$ requires: C, 73·3; H, 8·6%).

Conversion of the tosylate into hydrocarbon. A soln of the tosylate (0·10 g) in dry THF (10 ml) was added to a suspension of LAH (0·4 g) in dry THF (10 ml). The mixture was refluxed with stirring for 8 hr and then worked up as in experiment 6. The product was chromatographed over silica gel in light petroleum. The earlier fractions of light petroleum gave the oily hydrocarbon. The IR spectrum has peaks for monosubstituted and trisubstituted double bonds.

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