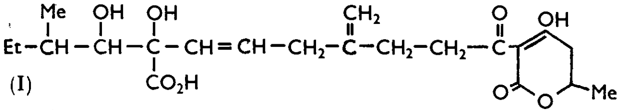
334. *Alternaric Acid. Part III.*[1] *Structure.*

By J. R. Bartels-Keith.

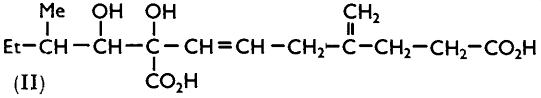
Alternaric acid is shown to be 12-(5,6-dihydro-4-hydroxy-6-methyl-2-oxopyran-3-yl)-4,5-dihydroxy-3-methyl-9-methylene-12-oxododec-6-ene-5-carboxylic acid (I).

Previous studies have shown that alternaric acid contains a carboxyl group and a β-dicarbonyl grouping[2] and is oxidised by alkaline hydrogen peroxide to 7,8-dihydroxy-9-methyl-3-methyleneundec-5-ene-1,7-dicarboxylic acid[1] (II). Evidence is here presented that alternaric acid has structure (I).

It was further shown in the earlier work[2] that alternaric acid gave carbon dioxide on acid hydrolysis and acetone (1 mol.) on alkaline hydrolysis. Repetition of this work shows that acetaldehyde (0·5 mol.) is also formed on alkaline hydrolysis. The ready formation of both acetone (1 mol.) and acetaldehyde under these conditions is best explained by the presence of the grouping (III). The presence of a tricarbonylmethane system is indicated by the orange ferric reaction of alternaric acid and its derivatives, as well as by their ultraviolet absorption spectra in acid and in alkaline media which recall the behaviour[3] of 2-formyl-5,5-dimethylcyclohexane-1,3-dione (cf. IV) but are inconsistent with the presence of a simple β-dicarbonyl function. The enol (IV) shows a band at 235 mμ in the presence of acid, whereas under these conditions alternaric acid and its derivatives absorb near

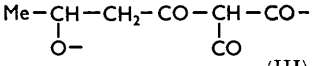


(I)



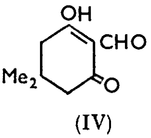
$$\mathrm{Et-\overset{Me}{CH}-\overset{OH}{CH}-\underset{CO_2H}{\overset{OH}{C}}-CH{=}CH-CH_2-\overset{CH_2}{\overset{\|}{C}}-CH_2-CH_2-CO_2H}$$

(II)

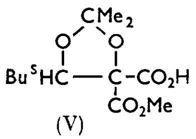


$$\mathrm{Me-\underset{O-}{CH}-CH_2-CO-\underset{CO}{CH}-CO-}$$

(III)



(IV)



(V)

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[1] Part II, Bartels-Keith, *J.*, 1960, 860.
[2] Grove, *J.*, 1952, 4056.
[3] Akehurst and Bartels-Keith, *J.*, 1957, 4798.

210 mμ, suggesting the presence of an ester or lactone group in the tricarbonylmethane system.

Ozonolysis of the acid (II) gave formaldehyde, lævulic acid, and succinic acid.[1] Alternaric acid on ozonolysis under similar conditions also gave formaldehyde and lævulic acid, together with other products which complicated the isolation of succinic acid. Esterification of the total acidic ozonolysis products followed by gas–liquid chromatography of the volatile methyl esters gave methyl oxalate, methyl lævulate, methyl succinate, and methyl (−)-β-hydroxybutyrate. Formation of the last ester affords additional evidence for the presence of the grouping (III).

Alternaric acid is readily cleaved by periodic acid and gives a positive reaction with potassium triacetoxyosmiate,[4] indicating that the glycol system of the acid (II) is present also in alternaric acid. The ozonolysis results for alternaric acid further indicate the presence of a terminal methylene group located as in the acid (II), and it follows that one or both of the carboxyl groups of the latter are derived from the points of attachment of the grouping (III) to the carbon chain of the acid (II).

Methyl alternarate with acetone in the presence of sulphuric acid gave an unstable liquid isopropylidene derivative which retains the enolic chromophore of alternaric acid, as shown by its ultraviolet absorption in acid and alkaline media, its infrared absorption spectrum, and its characteristic colour reactions with ferric chloride and cupric acetate. Oxidation with potassium permanganate in acetone gave the half-ester (V), originally obtained [1] on similar oxidation of the isopropylidene derivative of the ester of acid (II). It follows that the ester group of (V) is derived from the carboxyl group of alternaric acid, and therefore that the terminal carboxyl group of acid (II) represents the sole point of attachment of the grouping (III) in alternaric acid. This conclusion can be accommodated only by structure (I), which moreover explains the acid-hydrolysis of alternaric acid since the chromophore may be regarded as the ring-homologue of an acyltetronic acid.

The infrared absorption spectra of alternaric acid and its derivatives all show a band near 1710 cm.$^{-1}$ consistent with the presence of a conjugated ester or δ-lactone grouping. Further, sodium hydrogen alternarate shows infrared absorption characteristic of the carboxylate ion, together with a band at 1714 cm.$^{-1}$ which must therefore arise solely from the unbonded carbonyl group of the tricarbonylmethane system. Since alternaric acid contains no alkoxyl group [2] but retains all the structural features of acid (II), these findings confirm the presence of the δ-lactone ring.

EXPERIMENTAL

M. p.s are corrected. Unless otherwise stated, ultraviolet absorption spectra were determined for ethanol solutions with a Unicam S.P. 500 spectrophotometer, and infrared absorption spectra refer to Nujol mulls.

Sodium Hydrogen Alternarate.—0·0985N-Sodium hydroxide (2·65 ml.; 1 equiv.) was added to alternaric acid (107 mg.), and the mixture evaporated at room temperature *in vacuo*. The residue was dissolved in hot ethanol, and the solvent displaced with ethyl acetate until further addition of the latter caused turbidity. Evaporation of the solution gave *sodium hydrogen alternarate*, m. p. 156—158·5° (decomp.) (97 mg.) (Found: C, 58·4; H, 6·9; Na, 5·4%; equiv., 436. $C_{21}H_{29}O_8Na$ requires C, 58·3; H, 6·8; Na, 5·3%; *M*, 432·5), $\lambda_{max.}$ 210, 274 mμ (ε 12,560, 10,700), $\nu_{max.}$ 3345, 1714, 1614, 1596, and 1559 cm.$^{-1}$. The salt gave a yellow colour with ferric chloride in aqueous methanol, and a blue precipitate, partly soluble in chloroform, when shaken with aqueous cupric acetate.

Condensation of Methyl Alternarate with Acetone.—A solution of concentrated sulphuric acid (0·20 ml.) in acetone (20 ml.) was added to methyl alternarate (395 mg.) in acetone (20 ml.). After 18 hr. powdered sodium hydrogen carbonate (685 mg.) was added with shaking and the mixture left for 2 hr. The suspension was then cooled to 0°, and shaken with ether (80 ml.) and water (25 ml.), and the aqueous layer was further extracted with ether (20 ml.). The combined ethereal extracts were washed with 25% aqueous sodium chloride and evaporated, giving an

[4] Criegee, Marchand, and Wannowins, *Annalen*, 1942, **550**, 99.

oil (433 mg.). A solution of the product in light petroleum (5 ml.; b. p. 60—80°) was filtered to remove a trace of polymeric material, and the filtrate evaporated in a stream of nitrogen. Distillation of the residue at 115°/5 × 10^{-5} mm. (path length 1 cm.) gave *methyl* OO-*isopropylidenealternarate* (338 mg.) as a viscous oil (Found: C, 65·0; H, 7·9; OMe, 8·2. $C_{25}H_{36}O_8$ requires C, 64·6; H, 7·8; OMe, 6·7%), $[\alpha]_D^{25}$ −5·2° (*c* 3·68 in EtOH), $\lambda_{max.}$ (in hexane) 274 mμ (ε 9880), $\lambda_{max.}$ (in 0·1N-NaOH) 250, ~270 mμ (ε 15,120, 12,640), $\nu_{max.}$ (film) 3700—3260w, 1715s, 1639m, 1563s, and 1538 (shoulder) cm.$^{-1}$, $\nu_{max.}$ (in CCl_4) 1730s cm.$^{-1}$. The compound was sparingly soluble in water but dissolved slowly in aqueous sodium hydrogen carbonate, and was miscible with the common organic solvents. It gave an orange colour with methanolic ferric chloride, and a blue-violet chloroform-soluble copper complex with aqueous cupric acetate.

Permanganate Oxidation of Methyl OO-*Isopropylidenealternarate*.—The ester (333 mg.) in acetone (15 ml.) was treated portionwise with powdered potassium permanganate (1·71 g.) during 2 hr. at 22° (cooling). After a further 0·5 hr. the mixture was decolorised with aqueous sulphurous acid at 5—10° and rapidly extracted with ether (3 × 20 ml.). The combined ethereal extracts were washed with 9% aqueous sodium hydrogen carbonate (9 × 5 ml.), and the combined aqueous washings were acidified with 3N-sulphuric acid and rapidly extracted with ether (3 × 20 ml.). The combined ethereal extracts when washed with water and evaporated gave methyl hydrogen 2,2-dimethyl-5-s-butyl-1,3-dioxolan-4,4-dicarboxylate (V) (153 mg.), identified by its infrared absorption spectrum. The *S*-benzylthiouronium salt had m. p. 146—146·5° (75 mg., 25%), identical (mixed m. p. and infrared absorption spectrum) with a specimen obtained earlier.[1]

Ozonolysis of Alternaric Acid.—(*a*) Ozonised oxygen was passed through a solution of alternaric acid (202 mg.) in methyl acetate (12 ml.) at −50° for 23 min. The mixture was diluted with water and distilled to small bulk, and the distillate (100 ml.) added to 0·25% aqueous dimedone (100 ml.). After 6 days, isolation gave a derivative, m. p. 180—186° (119 mg.). Recrystallisation from methanol gave formaldehyde dimethone, m. p. 187—189° (106 mg., 0·74 mol.), identical (mixed m. p. and infrared absorption spectrum) with a synthetic specimen.

The residue from the foregoing distillation was continuously extracted with ether for 22 hr. Evaporation of this extract gave a product (170 mg.) which partly dissolved in methylene chloride leaving a solid (30 mg.) which could not be purified further but contained succinic acid as indicated by its infrared absorption spectrum. Treatment of the methylene chloride-soluble fraction with hot methanolic 2,4-dinitrophenylhydrazine hydrochloride gave a product from which was obtained methyl lævulate 2,4-dinitrophenylhydrazone (52 mg., 34%), identical (mixed m. p. and infrared absorption spectrum) with a synthetic specimen.

(*b*) Ozonised oxygen was passed through a solution of alternaric acid (1·010 g.) in methyl acetate (60 ml.) at −50° for 1·8 hr. Evaporation at 0° under reduced pressure gave a syrupy ozonide which was decomposed with water and left overnight at 0°. The product was made alkaline with 9% aqueous sodium hydrogen carbonate (20 ml.), washed with ether, acidified, and continuously extracted with ether for 22 hr. Evaporation of the extracts gave a mixture of acids (1·111 g.) which was treated with an excess of ethereal diazomethane. The mixture of esters (1·098 g.) so obtained was distilled at 24—67°/0·015 mm. into a trap at −80°. Gas–liquid chromatography of the distillate (756 mg.) gave methyl oxalate, methyl (−)-β-hydroxybutyrate, methyl lævulate, and methyl succinate, identified by comparison of their retention volumes and infrared absorption spectra with those of synthetic specimens. The results are summarised in the Table. The unidentified product was apparently unstable on the column, as were several minor products of large retention volume which were not further investigated.

Alkaline Hydrolysis of Alternaric Acid.—Alternaric acid (1·03 g.) was heated under reflux with N-sodium hydroxide (20 ml.), the system being closed by a bubbler containing water. After 1 hr. the mixture was cooled, adjusted to pH 9, and steam-distilled. The distillate was washed with ether to remove an oil, and the aqueous layer combined with the contents of the bubbler and added to 0·2% aqueous dimedone (500 ml.). After 4 days the product was collected (m. p. 135—136°; 382 mg.). Recrystallisation from light petroleum (b. p. 60—80°) gave acetaldehyde dimedone (357 mg.), m. p. and mixed m. p. 137—138°. The aqueous filtrate from the foregoing derivative was distilled to half bulk, giving a distillate which yielded a 2,4-dinitrophenylhydrazone, m. p. 117—121° (186 mg.). Repeated recrystallisation from ethanol and from light petroleum (b. p. 60—80°) gave acetone 2,4-dinitrophenylhydrazone (42 mg.), m. p. and mixed m. p. 123—125°.

Estimation of Acetone produced on Alkaline Hydrolysis of Alternaric Acid.—Samples of

Gas–liquid chromatography of methyl esters derived from ozonolysis of alternaric acid.

	Relative retention volumes at 129° [a]		Separation at 141° [b]	
	From ozonolysis	Synthetic	Recovery (mg.)	Yield (%)
Me_2 oxalate	0·57	0·568	10·9	5·2
Me (−)-β-hydroxybutyrate [c]	0·92	0·910	24·2	11·5
Unidentified	1 37	—	0·7	—
Me lævulate	1·69	1·67	116·4	50·2
Me_2 succinate	1·95	1·93	29·5	11·3

[a] Column: 88·0 × 0·5 cm. of dinonyl sebacate [5] (28·6%) on Celite 545. Nitrogen, 10·5 ml./min.; inlet pressure, 244 mm.; outlet pressure, 34 mm. Thermal conductivity detector. Retention volumes were measured from the air peak and expressed relative to the retention volume of cyclohexanol as an internal standard. [b] The mixed esters (548 mg.) were chromatographed on a column (366 × 1·5 cm.) of the same static phase. Nitrogen, 103 ml./min.; inlet pressure 912 mm.; outlet pressure 753 mm. [c] $[\alpha]_D^{25}$ −18° (*c* 1·04 in EtOH).

alternaric acid (~100 mg.) were added to 7% aqueous cupric sulphate pentahydrate (5 ml.) and 6N-sodium hydroxide (5 ml.) containing 35% of sodium potassium tartrate, and the mixture was steam-distilled for 1 hr., the distillate being collected under N-sodium hydroxide (20 ml.). 5% Aqueous silver nitrate (3 ml.) and 6% hydrogen peroxide (3 drops) were added to the distillate with shaking. After 30 min., the precipitate was separated and washed with water (15 ml.), and the acetone in the filtrate and washings was determined volumetrically by Messinger's method.[6] Alternaric acid (89·8, 105·5, 89·4, and 92·4 mg.) gave acetone (0·98, 0·90, 1·04, and 1·11 mol., respectively). Under similar conditions the copper complex of acetylacetone gave 1·96 mols. of acetone. Preliminary investigations showed that acetaldehyde did not interfere in this procedure.

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[5] Haslam and Jeffs, *J. Appl. Chem.*, 1957, **7**, 24.

[6] See Scott, " Standard Methods of Chemical Analysis," D. van Nostrand Co., Inc., New York, 5th edn., Vol. II, p. 2136; Goodwin, *J. Amer. Chem. Soc.*, 1920, **42**, 39.