The Chemistry of Pseudomonic Acid. Part 3.[1] The Rearrangement of Pseudomonic Acid A in Acid and Basic Solution

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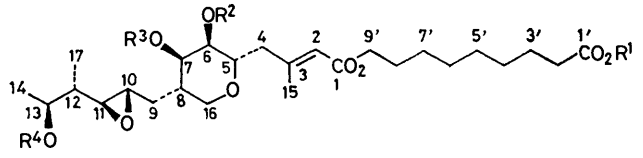
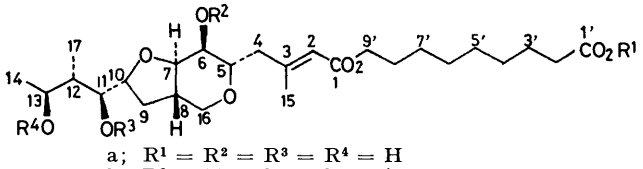
The acid and base catalysed rearrangement products of pseudomonic acid A (1a), derived from (1a) by intramolecular opening of the epoxide ring, have been shown to possess the *trans*-fused bicyclic structures (2a) and (3a). Structural assignments were made on the basis of the spectroscopic and chemical properties of (2a) and (3a) and their derivatives and confirmed by *X*-ray analysis. In strongly basic solution intramolecular rearrangement of (1a) was accompanied by the loss of the nonanoate ester side chain and formation of (12a) and (13a).

THE major metabolite responsible for the antibacterial properties of culture filtrates of *Pseudomonas fluorescens* (NCTC 10586) has been designated pseudomonic acid A (1a).[2,3] Chain and Mellows observed that the antibacterial activity of pseudomonic acid A in solution was dependent on the pH.[4] Activity was retained within



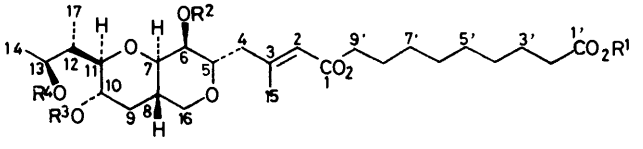
a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = Me$, $R^2 = R^3 = R^4 = H$
c; $R^1 = Me$, $R^2,R^3 = >CMe_2$, $R^4 = H$
d; $R^1 = Me$, $R^2 = R^3 = R^4 = Bz$

the range pH 4—9 ,but was gradually lost outside these limits. On one occasion they observed complete loss of antibacterial activity, together with the formation of a new substance, when the pH of a fermentation extract



a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = Me$, $R^2 = R^3 = R^4 = H$
c; $R^1 = Me$, $R^2 = H$, $R^3,R^4 = >CMe_2$

containing pseudomonic acid A inadvertently fell below 4 for 48 h. This new substance, isomeric with pseudomonic acid A, was isolated as its methyl ester and assigned gross structure (2b), rather than (3b), on the basis of its spectroscopic and chemical properties.[2]



a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = Me$, $R^2 = R^3 = R^4 = H$
c; $R^1 = Me$, $R^2 = H$, $R^3,R^4 = >CMe_2$

In view of our interest in pseudomonic acid A (1a), a novel antibiotic, we have investigated more fully its chemical instability to acid and alkali. A solution of (1a) was acidified with hydrochloric acid and the reaction monitored by silica thin-layer chromatography. Unfortunately this failed to distinguish the reaction products from the starting material since only a single spot was observed during the course of the reaction. Use of reverse-phase high-pressure liquid chromatography (h.p.l.c.) using a C-18 μ-Bondapak column eluted with aqueous methanolic ammonium acetate buffer proved more informative. The gradual disappearance of the pseudomonic acid A peak was accompanied by the appearance of two new peaks, poorly resolved, and with shorter retention times than that of the starting material.

When an aqueous solution of pseudomonic acid A was made alkaline (pH 11.0) with sodium hydroxide and monitored as above by h.p.l.c., loss of the pseudomonic acid A peak again occurred together with the formation of two new peaks, with identical R_F values to those observed under acidic conditions. However, the relative heights of the new peaks were different in the two experiments. Moreover additional changes occurred in the basic solution containing (1a) which were attributed to hydrolysis of the allylic ester bond with loss of 9-hydroxynonanoic acid.

The products from the acid treatment of pseudomonic acid A were converted into their methyl esters with methyl iodide and potassium carbonate in dry acetone, and separated by careful silica chromatography. The major component, I, had an R_F of 0.47 on silica whereas the minor component, II, had an R_F of 0.43 identical to that of methyl pseudomonate A (1b). Compound II was found to correspond chromatographically and spectroscopically to the acid rearranged product obtained by Chain and Mellows as described above.† Esters I and II were distinguished from each other and from (1b) by normal phase h.p.l.c. (see Figure 1). It was later found to be convenient to prepare I and II directly from methyl pseudomonate A (1b) by treatment of an aqueous methanolic solution of (1b) with hydrochloric acid.

The methyl esters I and II were shown by accurate mass measurements to be isomeric with methyl pseudomonate A (1b), $C_{27}H_{46}O_9$. Both I and II retained the α,β-unsaturated ester function present in (1b) as indicated by their i.r. spectra, $\nu_{max.}$ 1 710 and 1 650 cm^{-1}, and u.v. spectra, I ($\lambda_{max.}$ 223 nm, ε = 14 300) and II

† We thank Dr Mellows for kindly providing us with a sample of his acid-rearranged product.

($\lambda_{max.}$ 222 nm, $\varepsilon = 9\,800$). The ^{1}H n.m.r. spectra of I and II confirmed the presence of the unsaturated ester group, vinylic proton at δ 5.65, vinylic methyl at δ 2.15 and the nonanoate ester side chain, methylene envelope at δ 1.3. A notable difference in the ^{1}H n.m.r. spectra of I and II compared with that of methyl pseudomonate A (1b) was the absence in I and II of the epoxide protons present at δ 2.5—2.8 in (1b). This clearly indicated the involvement of the epoxide group in the rearrangement. The ^{13}C n.m.r. spectra of I and II confirmed the loss of

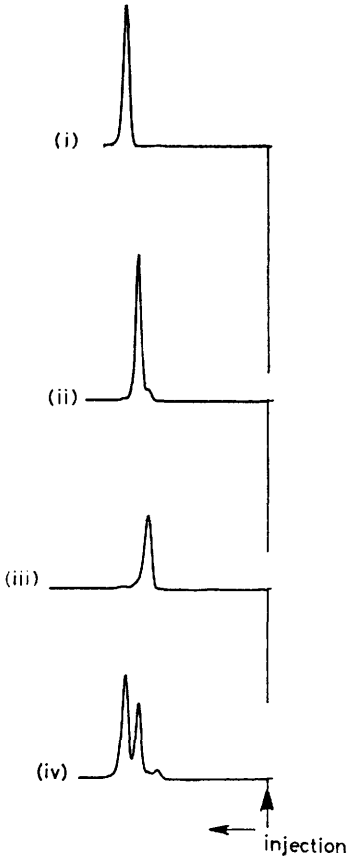
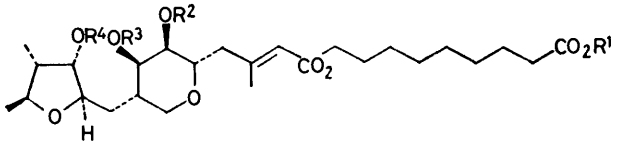


FIGURE 1 Waters Associates μ-Porasil (silica) column eluted with acetonitrile (containing 2% water) at 1 ml/min (chart speed 2 mm/min). The eluant was monitored at $\lambda_{max.}$ 230 nm. (i) Isomer I (2b). (ii) Isomer II (3b). (iii) Methyl pseudomonate (1b). (iv) The mixture of I and II after acidic treatment of (1b)

the epoxide ring evident from the absence of the epoxide carbon signals observed at δ 55.5 and 61.2 in (1b). The complexity of the remaining features of the ^{1}H n.m.r. and ^{13}C n.m.r. spectra of I and II, except for the indication of the presence of two secondary methyl groups, made further structural assignments difficult.

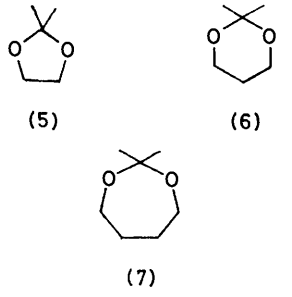
At this point three structures were considered for the acid and base catalysed rearrangement products I and II. Structures (2b) and (3b) would arise by intramolecular rear attack of the 7-hydroxy-group of (1a) on the epoxide ring carbons C-10 and C-11 respectively. Structure (4b) on the other hand would involve intramolecular ring opening at C-10 by attack of the C(13)-hydroxy. We were able to eliminate (4b) as a possible structure by converting I and II into their acetonide derivatives, $C_{30}H_{48}O_9$, with 2,2-dimethoxypropane and toluene-*p*-sulphonic acid, and comparing the ^{13}C n.m.r. spectra of the acetonides with those of model compounds.

The literature suggests 1,2-, 1,3-, and 1,4-diols equally readily form acetonide derivatives. The 1,3-diol (2b),

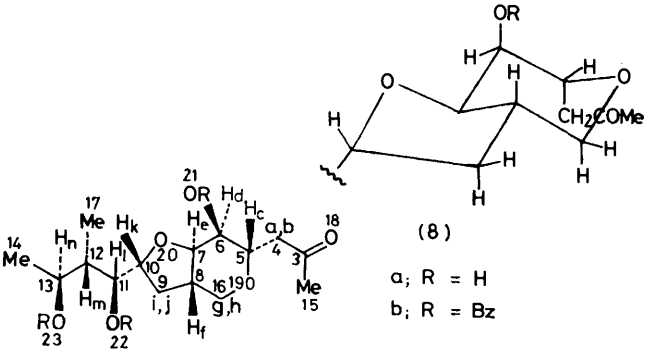


a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = Me$, $R^2 = R^3 = R^4 = H$

the 1,4-diol (3b), and the 1,2-diol (4b) would be expected, therefore, to form such derivatives. The ^{13}C chemical shifts of the quaternary carbons in the acetonides derived from isomers I and II occurred at δ 97.5 and δ 100.2 respectively. The quaternary carbon in the acetonide (1c) of the 1,2-diol, methyl pseudomonate A (1b), occurred at δ 108.9. This suggested that isomers I and II did not incorporate a 1,2-diol system thereby eliminating (4b) as a possible structure. Confirmatory



evidence that the shift of the quaternary acetonide carbon in the ^{13}C n.m.r. spectrum was indeed indicative of the size of the acetonide containing ring, came from a study of the 5-, 6-, and 7-membered acetonides (5),[5] (6),[6] and (7)[7] prepared from their respective diols. Comparison of the ^{13}C chemical shifts of the quaternary acetonide carbons as shown in Table 1 suggested that the acetonide from isomer I was incorporated in a 6-membered ring and hence was tentatively assigned



structure (2c), whereas the acetonide from isomer II was contained in a 7-membered ring and, therefore, corresponded to structure (3c). This led to structures

(2b) and (3b) being provisionally assigned to isomers I and II respectively. As far as we are aware this is the first time that the ring size of acetonides has been

TABLE 1

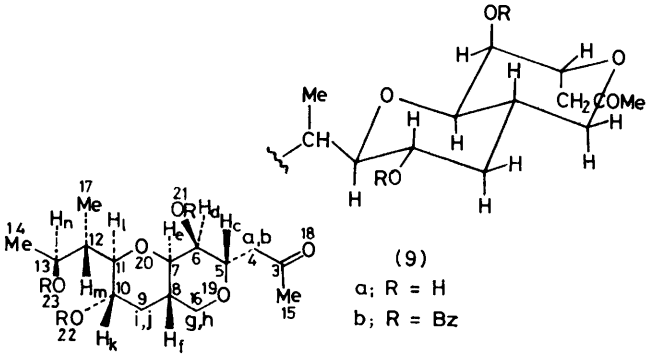
Comparison of the ^{13}C n.m.r. chemical shift of the quaternary acetonide carbon in (1c), (2c), (3c), (5), (6), and (7)

Compound	δ_C (p.p.m.) from $SiMe_4$ ($CDCl_3$) of quaternary acetonide carbon	
(5)	108.5	s *
(1c)	108.9	s
(6)	97.7	s
(2c)	97.5	s
(7)	100.9	s
(3c)	100.2	s

* Denotes singlet.

distinguished on the basis of the carbon shift of the quaternary acetonide carbon.

In order to provide derivatives of isomers I or II



(9)
a; R = H
b; R = Bz

hopefully more amenable to proton n.m.r. analysis, the crystalline methyl ketone (8a), $C_{15}H_{20}O_6$, m.p. 114—115 °C, $[\alpha]_D$ +5.8°, was obtained by ozonolysis of isomer I followed by reductive work up with trimethyl phosphite. Treatment of (8a) with benzoyl chloride in pyridine afforded the oily tribenzoate (8b), $C_{36}H_{38}O_9$, $[\alpha]_D$ +67°. Similarly isomer II afforded the crystalline methyl ketone (9a), $C_{15}H_{26}O_6$, m.p. 114—114.5 °C, $[\alpha]_D$ +25°, and the corresponding tribenzoate (9b) as a foam $C_{36}H_{38}O_9$, $[\alpha]_D$ +50°.

TABLE 2

220 MHz ^1H n.m.r. assignments for compound (8b)

H in 8b	δ_H in p.p.m. from $SiMe_4$ ($CDCl_3$)	Multiplicity	Coupling constants (Hz)
Me-17	1.12	d	$*J_{m,\ Me\text{-}17}$ 7
Me-14	1.35	d	$*J_{n,\ Me\text{-}14}$ 6
H_f	1.70	complex m	$J_{e,f}$ 11; $*J_{f,g}$ 5; $*J_{f,h}$ 10
Me-15	2.07	s	
H_j	2.12	complex m	
H_a	2.17	4 lines,	$*J_{a,b}$ 17; $*J_{a,c}$ 5
H_m	2.42	complex m	$*J_{l,m}$ 6; $*J_{m,n}$ 6
H_b	2.45	4 lines,	$*J_{b,c}$ 10
H_i	*ca.* 2.4	complex m	
H_h	3.44	4 lines,	$*J_{g,h}$ 10
H_e	3.47	4 lines	$*J_{d,e}$ <2
H_g	4.04	4 lines	$*J_{f,g}$ 5
H_k	4.47	8 lines	$*J_{k,l}$ 6
H_c	4.57	8 lines	$*J_{c,d}$ *ca.* 1
H_d	5.22	4 lines	
H_n	5.37	8 lines	
H_l	5.53	3 lines	$*J_{l,m}$ 6
Aromatic protons	7.5—8.1	Complex; 3 benzoate groups.	

* Confirmed by spin decoupling.

TABLE 3

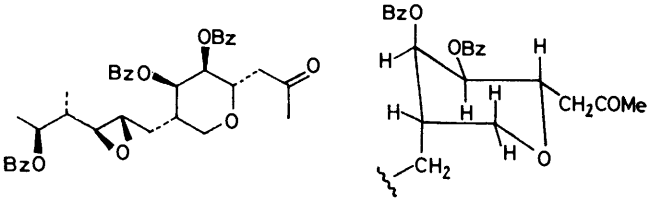
220 MHz ^1H n.m.r. assignments for compound (9b)

H in 9b	δ_H in p.p.m. from $SiMe_4$ ($CDCl_3$)	Multiplicity	Coupling constants (Hz)
Me-17	0.62	d	$*J_{m,Me\text{-}17}$ 7
Me-14	1.38	d	$*J_{n,Me\text{-}14}$ 6
H_f	1.38	complex m	$J_{f,g}$ <2; $J_{f,h}$ 10; $J_{e,f}$ 11
H_m	2.08	m	$*J_{l,m}$ <2; $*J_{m,n}$ 7
Me-15	2.21	s	
H_i, H_j	2.3—2.4	complex m	$*J_{i,k\text{ and }j,k}$ 5 and 10
H_a, H_b	2.6—3.0	8 lines;	$*J_{a,b}$ 16; $J_{a,c}$ 5; $*J_{b,c}$ 11
H_h	3.38	6 lines	$J_{g,h}$ 10
H_e	3.45	4 lines	$J_{d,e}$ <2
H_g	3.72	4 lines	
H_l	3.79	4 lines	$*J_{k,l}$ 10
H_c	4.71	8 lines	$*J_{c,d}$ *ca.* 1
H_k	5.06	6 lines	
H_n	5.18	8 lines	
H_d	5.25	4 lines	
Aromatic protons	7.5—8.1	Complex; 3 benzoate groups	

* Confirmed by spin decoupling.

The 220 MHz ^1H n.m.r. spectra of the tribenzoates (8b) and (9b) were obtained and extensive spin–spin decoupling experiments carried out. This enabled each of the proton signals to be assigned as indicated in Table 2 for (8b) and Table 3 for (9b). The various coupling constants are also shown. The crucial evidence that permitted structure (8b) to be assigned to the tribenzoate derived from I and (9b) to that derived from II was obtained from decoupling of H_m. Proton H_m was itself identified at δ 2.42 in (8b) and δ 2.08 in (9b) by irradiating Me-17. When H_m was irradiated two of the three easily identifiable downfield protons attached to carbons carrying benzoate groups simplified in the one case, whereas in the other tribenzoate, derived from isomer II, only one such proton was affected. These experiments therefore gave strong support for isomer I being structure (2b) and II having structure (3b).

The stereochemistry depicted in structures (2), (3), (4), (8), and (9) is based on the known absolute stereochemistry of pseudomonic acid (1a) itself.[3] The ^1H n.m.r. data presented for (8b) and (9b) in Tables 2 and 3 are entirely in agreement with the assigned structures and, as shown by Dreiding models, the values of the coupling constants of the ring protons are indicative of the rigid



(10)

trans-fused bicyclic structures depicted. It is of interest to note that the acetonyl-substituted perhydropyran ring in (8b) and (9b) adopts a chair conformation opposite to that observed for the ketone tribenzoate (10) derived from pseudomonic acid A (1a).[2] This is evident from the 1 Hz coupling constant between H_c and H_d in (8b) and (9b), indicating that these protons are equatorially disposed, compared with the corresponding value of 10 Hz in (10) reflecting an axial relationship of H_c and H_d.

Final and unequivocal confirmation of the structures of the rearrangement products I (2b) and II (3b) was achieved by *X*-ray analysis of their corresponding crystalline methyl ketones, (8a) and (9a) respectively, prepared as described above. Bond lengths and angles are given in Figures 2 and 3 and the conformation in the crystal lattice illustrated by means of the perspective drawings in Figures 4 and 5. The absolute stereochemistry depicted was inferred from that of pseudomonic acid A. It will be observed that the conformations adopted by (8a) and (9a) in the crystal lattice

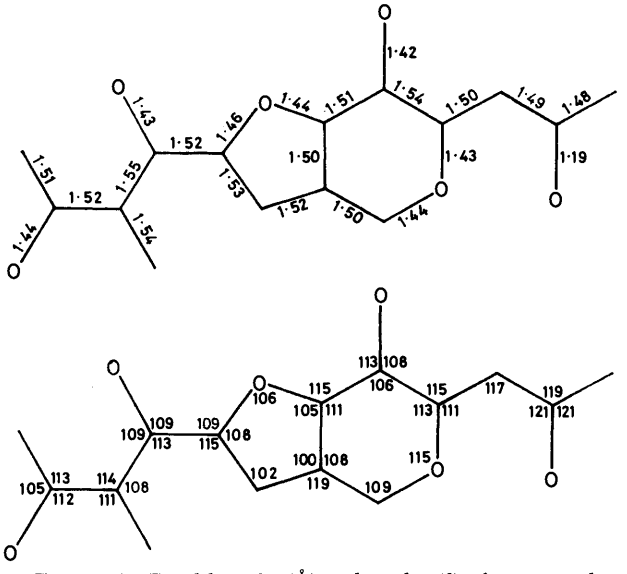


FIGURE 2 Bond lengths (Å) and angles (°) of compound (8a)

parallel those determined for the tribenzoates (8b) and (9b) in solution from ^{1}H n.m.r. measurements. The results of the *X*-ray analyses therefore confirm the deductions made from spectroscopic and chemical evidence that the two major rearrangement products formed when pseudomonic acid A (1a) is subjected to acidic or alkaline solution are the compounds (2a), 9-{4-[1*S*,6*R*-8*R*-(1*S*,3*S*-dihydroxy-2*S*-methylbutyl)-5*S*-hydroxy-3,7-dioxabicyclo[4.3.0]nonan-4*S*-yl]-3-methylbut-2(*E*)-enoyloxy}nonanoic acid and (3a), 9-{4-[1*R*,6*S*-4*S*,10*S*-dihydroxy-3*R*-(2*S*-hydroxy-1*S*-methylpropyl)-2,8-dioxabicyclo[4.4.0]decan-9*S*-yl]-3-methylbut-2(*E*)-enoyloxy}nonanoic acid. It is also apparent that the acid-rearrangement product obtained by Chain and Mellows, referred to earlier, and said by them to have structure (2a) is correctly formulated as (3a).

The exclusive formation of the above rearrangement products (2a) and (3a) and the distinctive absence of formation of (4a) can be rationalized by Baldwin's

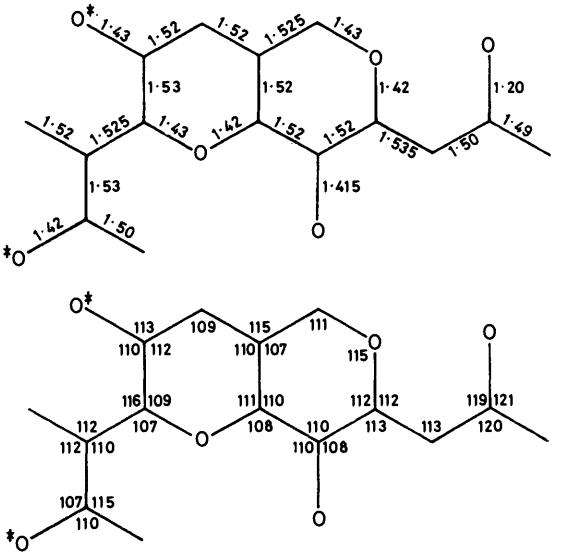


FIGURE 3 Bond lengths (Å) and angles (°) of compound (9a)

Rules of Ring Closure.[8] If the epoxide is regarded as approximating to a trigonal system, formation of (2a) is an example of a 5-*exo-trig* process and formation of (3a) is a 6-*endo-trig* process, both of which are favoured. Most interestingly formation of (4a) would involve attack by the C-13 hydroxy-group in a 5-*endo-trig* process which is disfavoured and indeed this product is not observed.

In a previous paper we described our attempts to prepare monic acid A (11a) by treatment of pseudomonic acid A (1a) with an excess of sodium hydroxide.[1] Two major acidic products were obtained in this reaction neither of which corresponded to monic acid A (11a). The two products were isolated as their oily methyl esters by silica chromatography and were found to be isomeric with methyl monate A (11b). The major product (R_F 0.40) can now be formulated as (12b) and the minor one (R_F 0.34) as (13b) by analogy with isomers

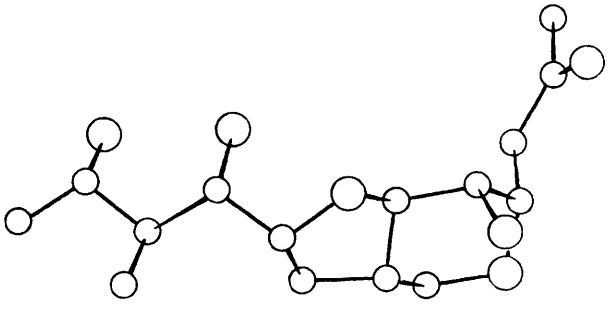


FIGURE 4 Perspective drawing of the ketone (8a)

(2b) and (3b) derived from pseudomonic acid A. Structures (12b) and (13b) were supported by the spectroscopic data, especially the excellent correlations observed between the ^{13}C chemical shifts of compounds (2b) and

(12b) and between compounds (3b) and (13b) illustrated in Table 4.

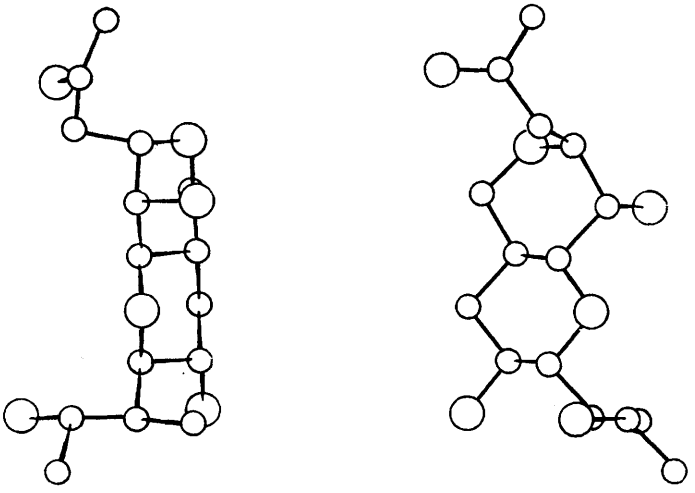
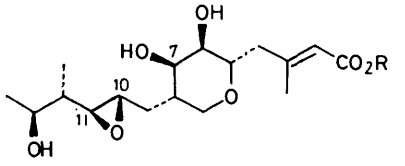


FIGURE 5 Perspective drawings of the ketone (9)

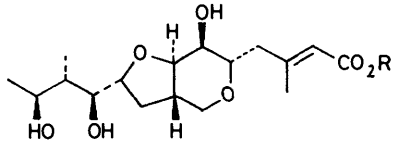
Finally we attempted quantitatively to compare the rates of intramolecular rearrangement and the ratios of the isomeric products formed. In order to avoid hydrolysis of the allylic ester function we utilised monic acid A



(11)

a; R = H

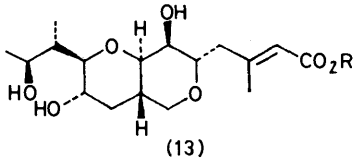
b; R = Me



(12)

a; R = H

b; R = Me



(13)

a; R = H

b; R = Me

(11a) for these studies. Aqueous solutions of (11a) were adjusted to pH 1.0 and 13.0 and examined at room temperature by reverse-phase h.p.l.c. The acidic solution completely rearranged in less than 30 min to a 1.6 : 1. However, the alkaline solution changed more slowly with only 30% rearrangement after 30 min with mixture of compounds (12a) and (13a) in the ratio of a ratio of (12a) to (13a) of 3.5 : 1. After 18 h the reaction was complete with a final ratio of (12a) to (13a) of 3.7 : 1. When the isolated pure esters (12b) and (13b) were separately subjected to the same acidic and alkaline conditions of the rearrangement reaction no interconversion of these two isomeric compounds, as determined by reverse-phase h.p.l.c., occurred. Therefore, the rearranged acids (12a) and (13a) are derived from monic acid A (11a) by two competing mechanisms, in which the relative rates of intramolecular rear attack of

TABLE 4

Comparison of ^{13}C n.m.r. spectra of the esters (2b) and (12b) and (3b) and (13b) *

Carbon †	(2b)	(12b)	(3b)	(13b)	Multiplicity
1′	174.3		174.4		s
1	166.5	166.6	166.5	166.5	s
3	155.3	156.6	155.2	155.5	s
2	118.3	117.6	118.3	117.9	d
	81.1	80.9	82.2	82.2	d
	80.5	80.4	76.3	76.1	d
	77.2	77.0	75.3	75.5	d
	76.6	76.4	70.1	70.2	d
	72.0	72.0	69.1	69.3	d
	69.0	68.8	66.3	66.5	d
	65.8	65.7	64.3	64.3	t
9′	63.9		64.0		t
OMe	51.4	50.9	51.4	51.0	q
	42.2	42.0	39.8	40.1	d
	41.5	41.3	39.8	40.1	t
	36.2	36.2	32.9	34.7	d
2′	34.1		34.1		t
4′,5′,6′	29.0		29.0		t
8′	28.7		28.7		t
9	26.7	26.5	34.6	33.0	t
7′	26.0		25.9		t
3′	24.9		24.9		t
14	21.0	20.9	22.0	22.2	q
15	18.5	18.5	18.4	18.3	q
17	12.7	12.6	10.7	10.8	q

* P.p.m. to low field of Me_4Si; solvent $CDCl_3$. † Carbon assignments made by reference to T. C. Feline, R. B. Jones, G. Mellows, and L. Phillips, *J.C.S. Perkin I*, 1977, 309.

the 7-hydroxy-group on the epoxide carbons C-10 and C-11 are dependent on the conditions used.

EXPERIMENTAL

M.p.s were determined on a Büchi apparatus and are uncorrected. Mass spectra were obtained at 70 eV using an A.E.I. MS9 instrument operating at 8 kV. ^{1}H N.m.r. spectra were recorded at 90 MHz on a Perkin-Elmer R 32 instrument and ^{13}C measurements using a Varian CFT 20 spectrometer. Both ^{1}H and ^{13}C n.m.r. spectra were recorded at ambient temperatures with $SiMe_4$ as internal standard. Column chromatography was carried out on Merck Kieselgel H (type 60). Analytical (t.l.c.) and preparative thin layer chromatography were performed on pre-coated Merck Kieselgel 60 F_{254}. The analytical plates were eluted with chloroform–methanol 9 : 1 (v/v) unless otherwise stated and the components visualized by either u.v. light or charring with sulphuric acid. High pressure liquid chromatography (h.p.l.c.) was performed on a Waters Associates instrument using a C_{18} μ-Bondapak, reverse-phase column with ammonium acetate–water–methanol buffer solutions as eluant, and a μ-Porasil (silica), normal-phase column with acetonitrile (containing 2% water) as eluant the components being detected by u.v. spectroscopy at λ 230 nm (see Figure 1). *NN*-Dimethylformamide (DMF) was distilled *in vacuo* from calcium hydride and stored over regenerated Linde 4A molecular sieves.

The Preparation of Methyl 9-(4-{1S,6R,8R-(1S,3S-*Dihydroxy*-2S-*methylbutyl*)-5S-*hydroxy*-3,7-*dioxabicyclo*[4.3.0]-*nonan*-4S-*yl*}-3-*methylbut*-2(E)-*enoyloxy*)*nonanoate, Isomer I*, (2b), *and Methyl* 9-(4-{1R,6S-4S,10S-*Dihydroxy*-3R-(2S-*hydroxy*-1S-*methylpropyl*)-2,8-*dioxabicyclo*[4.4.0]*decan*-9S-*yl*}-3-*methylbut*-2(E)-*enoyloxy*)*nonanoate, Isomer II*, (3b) *by Acid-catalysed Rearrangement of* (1a) *or* (1b).—A solution of pseudomonic acid (1a) (1 g) in methanol (10 ml) and 1M-hydrochloric acid (10 ml) was stirred at room temperature for 30—40 min. The methanol was removed under reduced pressure and the resulting oil extracted into ethyl acetate. The organic layer was washed with brine, dried ($MgSO_4$), and evaporated to give an oily mixture of the acids, (2a) and (3a). The latter was dissolved in dry acetone and anhydrous potassium carbonate (3 g) and methyl iodide (2 ml) were added. The mixture was stirred overnight at room temperature and evaporated to dryness. The residue was partitioned between ethyl acetate and water. The organic layer was separated, washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to give an oily mixture of the methyl esters, (2b) and (3b) (0.955 g) in the ratio of 1.4 : 1 respectively (by normal-phase h.p.l.c.). When a solution of methyl pseudomonate (1b) (5 g) in methanol (50 ml) and 1M-hydrochloric acid (50 ml) was stirred at room temperature for 30—40 min, an identical mixture of (2b) and (3b) (4.75 g) was obtained after work-up. The combined mixture from the two experiments was chromatographed on silica (200 g) with a gradient of chloroform to 6% methanol–chloroform as eluant. *Isomer I* (2b) (R_F = 0.47) was isolated as a white crystalline solid (3.44 g), m.p. 60—61 °C, $[\alpha]_D^{22}$ −2.8° (*c* 1.0, $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 400, 2 980, 2 850, 1 730, 1 710, and 1 650 cm^{-1}; $\lambda_{max.}$ (EtOH) 223 nm (ε 14 300), δ_H ($CDCl_3$) 5.65 (1 H, m, C2-*H*), 3.60 (3 H, s, OCH_3), 2.15 (3 H, s, C15-CH_3), 1.30 (10 H, m, CH_2 envelope), 1.15 (3 H, d, C14-CH_3), and 0.81 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) see Table 4 (Found: C, 62.90; H, 8.99%; $M^{+\cdot}$, 514.314 080. $C_{27}H_{46}O_9$ requires C, 63.00; H, 9.03%; $M^{+\cdot}$, 514.314 158). The more-polar *isomer II* (3b) (R_F = 0.43) was obtained as an oil (1.50 g), $[\alpha]_D^{22}$ −9.1° (*c* 1.0, $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 3 450, 2 950, 2 850, 1 730, 1 710, and 1 650 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 9 800); δ_H ($CDCl_3$) 5.66 (1 H, m, C2-*H*), 3.60 (3 H, s, OCH_3), 2.16 (3 H, s, C15-CH_3), 1.30 (10 H, m, CH_2 envelope), 1.20 (3 H, d, C14-CH_3), and 0.94 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) see Table 4 (Found: $M^{+\cdot}$, 514.314 580. $C_{27}H_{46}O_9$ requires $M^{+\cdot}$, 514.314 158).

Acetonide (2c).—A solution of isomer I (2b) (0.285 g) in 2,2-dimethoxypropane containing 1 crystal of toluene-*p*-sulphonic acid was stirred at room temperature for 5 min. The reaction mixture was diluted with ether, washed with sodium hydrogencarbonate solution and brine and then dried ($MgSO_4$) and evaporated to leave an oil. Preparative layer chromatography with chloroform–methanol (30 : 1) as eluant afforded the pure *acetonide* (2c) (R_F = 0.38) as an oil (0.178 g), $[\alpha]_D^{20}$ −2.6° (*c* 1.0, $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 3 500, 2 950, 1 730, 1 710, 1 650, 1 460, 1 440, and 1 390 cm^{-1}; $\lambda_{max.}$ (EtOH) 223 nm (ε 13 900); δ_H ($CDCl_3$) 5.65 (1 H, m, C2-*H*), 3.60 (3 H, s, OCH_3), 2.16 (3 H, s, C15-CH_3), 1.45 [2 × 3 H, s, (CH_3)$_2$C], 1.30 (10 H, m, CH_2 envelope), 1.14 (3 H, d, C14-CH_3), and 0.83 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) 173.9 (C1′), 166.1 (C1), 155.3 (C3), 117.9 (C2), 97.5 (>C<O,O), 79.6 (d), 79.3 (d), 76.2 (d), 75.5 (d), 70.1 (d), 68.7 (d), 65.6 (t), 63.5 (C9′), 51.1 (OCH_3), 41.2 (t), 37.6 (d), 35.8 (d), 33.8 (C2′), 29.9 (q), 28.8 (C4′, C5′, and C6′), 28.5 (C8′), 26.8 (C9), 25.7 (C7′), 24.6 (C3′), 19.5 [C4 and one (CH_3)$_2$C], 18.1 (C15), and 12.1 (C17) (Found: $M^{+\cdot}$, 554.345 99. $C_{30}H_{50}O_9$ requires $M^{+\cdot}$, 554.345 45).

Acetonide (3c).—A solution of the isomer II (3b) (0.50 g) in 2,2-dimethoxy-propane containing 1 crystal of toluene-*p*-sulphonic acid was stirred at room temperature for 5 min. The reaction was worked up as for (2c). The resulting oily mixture was chromatographed twice on preparative layer plates to yield the pure *acetonide* (3c) as an oil (0.112 g); $\nu_{max.}$ ($CHCl_3$) 3 580, 2 950, 2 850, 1 740, 1 720, and 1 650 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 13 900); δ_H ($CDCl_3$) 5.66 (1 H, m, C2-*H*), 3.61 (3 H, s, OCH_3), 2.19 (3 H, s, C15-CH_3), 1.3 [*ca.* 16 H, CH_2 envelope and (CH_3)$_2$C], 1.15 (3 H, d, C14-CH_3), and 0.82 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) 174.2 (C1′), 166.4 (C1), 155.2 (C3), 118.3 (C2), 100.2 (>C<O,O), 86.5 (d), 76.9 (d), 76.2 (d), 69.1 (d), 68.3 (d), 68.2 (d), 64.5 (t), 63.9 (C9′), 51.4 (OCH_3), 45.5, 40.2, 33.1 (C9), 34.1 (C2′), 32.7 (t), 29.1 (C4′, C5′, and C6′), 28.7 (C8′), 26.0 (C7′), 25.1 and 24.4 [(CH_3)$_2$C], 25.0 (C3′), 20.3 (C14), 18.4 (C15), and 15.2 (C17) (Found: $M^{+\cdot}$ 554.344 860. $C_{30}H_{50}O_9$ requires $M^{+\cdot}$ 554.345 456).

2,2-*Dimethyl*-1,2-*dioxolan* (5).[5]—Ethylene glycol (56 ml) was dissolved in dry acetone (100 ml) and concentrated sulphuric acid (1 ml). Anhydrous sodium sulphate (40 g) was added and the mixture stirred at room temperature for 4—5 h. The reaction mixture was poured into an excess of sodium hydrogen carbonate solution and extracted with ether; the extract was washed with brine and dried (Na_2SO_4). The ether solution was concentrated and the residue distilled to give 2,2-dimethyl-1,2-dioxolan (5) as a colourless liquid (8.12 g), b.p. 92—94 °C (lit.,[5] b.p. 92.5—92.7 °C), δ_H ($CDCl_3$) 3.95 [4 H, s, O(CH_2)$_2$O] and 1.38 [6 H, s, (CH_3)$_2$C]; δ_C ($CDCl_3$) 108.5 (>C<O,O), 64.6 [O(CH_2)$_2$O], and 25.7 [(CH_3)$_2$C].

2,2-*Dimethyl*-1,3-*dioxan* (6).—A solution of propane-1,3-diol (14.5 ml), 2,2-dimethoxypropane (20.8 g), and toluene-*p*-sulphonic acid (5—10 mg) in benzene (60 ml) was distilled and the azeotrope of methanol–benzene (b.p. 58 °C) collected. The temperature gradually rose to a steady 80 °C (benzene). The benzene solution was cooled, washed with sodium hydrogen carbonate solution and brine, and then dried (Na_2SO_4). The dry benzene solution was distilled and the 2,2-dimethoxy-1,3-dioxan (6) (8 ml) collected at b.p. 122—124 °C, n_D^{20} 1.368 (lit.,[6] b.p. 123—125 °C; $n_D^{16.5}$ 1.425); $\nu_{max.}$ (film) 2 950, 1 380, 1 370, 1 250, 1 200, and 1 100 cm^{-1}; δ_H ($CDCl_3$) 3.83 (4 H, t, $CH_2O \times 2$), 1.63 (2 H, quintuplet), $CH_2CH_2CH_2$), and 1.39 [6 H, s, $(CH_3)_2C$]; δ_C ($CDCl_3$) 97.7 ($>C<^{O}_{O}$), 59.9 ($CH_2O \times 2$), 25.8 (CH_2), and 24.3 [$(CH_3)_2C$] (Found: C, 62.4; H, 10.7. $C_6H_{12}O_2$ requires C, 62.02; H, 10.43%).

2,2-*Dimethoxy*-1,4-*dioxepan* (7).[7]—A solution of butane-1,4-diol (18 g), 2,2-dimethoxypropane (20.8 g), and toluene-*p*-sulphonic acid (5—10 mg) in benzene (60 ml) was refluxed and the azeotrope collected. The reaction was carried out and worked up exactly as for the previous compound (6). The fraction distilling at 124—125 °C was collected and re-distilled to give 2,2-dimethyl-1,4-dioxepan (7) (10 ml), b.p. 124—125 °C, n_D^{20} 1.373 (lit.,[7] b.p. 136—137°, n_D^{25} 1.425), $\nu_{max.}$ (film) 2 950, 1 380, 1 230, 1 210, 1 090, 1 060, and 1 040 cm^{-1}; δ_H ($CDCl_3$) 3.62 (4 H, t, $CH_2O \times 2$), 1.66 [4 H, m, $(CH_2)_2$], and 1.30 [6 H, s, $(CH_3)_2C$]; δ_C ($CDCl_3$) 100.9 ($>C<^{O}_{O}$), 62.1 ($CH_2O \times 2$), 29.9 [$(CH_2)_2$], and 25.1 [$(CH_3)_2C$] (Found: C, 64.8; H, 10.55. $C_7H_{14}O_2$ requires C, 64.56; H, 10.86%).

1S,6R-8R-(1S,3S-*Dihydroxy*-2S-*methylbutyl*)-5S-*hydroxy*-3,7-*dioxabicyclo*[4.3.0]*nonan*-4S-*ylacetone* (8a).—Ozonised oxygen was bubbled through a solution of isomer I (2b) (0.542 g) in methanol (20 ml) containing 5 drops of pyridine at −80 °C for 0.5 h when a blue colour developed. The excess of ozone was blown off with dry nitrogen at −80 °C. Triethyl phosphite (97%, 0.19 ml) was added and the mixture allowed to reach room temperature. The solvent was removed under reduced pressure and the oily residue chromatographed on silica (15 g) with a gradient of methanol–chloroform (0—5%) as eluant. The desired *ketone* (8a) was obtained as crystalline solid (0.380 g), m.p. 114—115 °C (prisms from ethyl acetate, m.p. 117.5—118.5 °C), $[\alpha]_D^{20}$ +5.78° (*c* 1.0, MeOH), $\nu_{max.}$ (Nujol) 3 500, 3 450, 2 950, 2 850, 1 710, 1 460, and 1 380 cm^{-1}; δ_H (CD_3OD) 2.16 (3 H, s, CH_3CO), 1.13 (3 H, d, C14-CH_3), and 1.85 (3 H, d, C17-CH_3); δ_C (CD_3OD) 208.7 (C3), 81.7 (d), 81.2 (d), 76.9 (2 × C, d), 70.6 (d), 70.1 (d), 67.1 (t), 43.8 (d), 44.8 (t), 37.4 (d), 30.2 (C15), 28.2 (t), 19.5 (C14), and 11.6 (C17) (Found: C, 59.75; H, 8.5. $C_{15}H_{26}O_6$ requires C, 59.57; H, 8.68%).

1R,6S-4S,10S-*Dihydroxy*-3R-(2S-*hydroxy*-1S-*methylpropyl*)-2,8-*dioxabicyclo*[4.4.0]*decan*-9S-*ylacetone* (9a).—Ozonised oxygen was bubbled through a solution of isomer II (3b) (1.06 g) in methanol (60 ml) containing 5 drops of pyridine at −80 °C for 0.5 h. After removal of the excess of ozone, triethyl phosphite (0.42 ml) was added and the reaction mixture worked up and chromatographed on silica (30 g) as for the previous compound (8a). The desired *ketone* (9a) was obtained as a crystalline solid (0.339 g), m.p. 113—114° [prisms from ethyl acetate, m.p. 114—115 °C; depression of mixed m.p. to 90—120 °C with (8a)], $[\alpha]_D^{20}$ +25.0° (*c* 1.0 $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 3 400, 2 950, 2 850, 1 710, 1 350, 1 100, and 1 050 cm^{-1}; δ_H ($CDCl_3$) 4.45 (1 H, m, C5-*H*), 2.16 (3 H, s, CH_3CO), 1.23 (3 H, d, C14-CH_3), and 0.95 (3 H, s, C17-CH_3); δ_C ($CDCl_3$) 206.3 (C3), 82.1 (d), 76.8 (d), 74.9 (d), 70.0 (d), 69.0 (d), 66.1 (d), 64.7 (t), 43.4 (t), 39.9 (d), 34.6 (t), 32.9 (d), 30.0 (C15), 21.9 (C14), and 10.6 (C17) (Found: C, 59.27; H, 8.4%; $M^{+\cdot}$, 302.172 960. $C_{15}H_{26}O_6$ requires C, 59.57; H, 8.68%; $M^{+\cdot}$, 302.172 924).

The Tribenzoate (8b).—The ketone (8a) (0.150 g) was dissolved in a preformed solution of pyridine (6 ml) and benzoyl chloride (2 ml) and the solution stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure and poured into an excess of sodium hydrogen carbonate solution; the mixture was then extracted with ether. The ether extract was washed with sodium hydrogen carbonate solution and brine and then dried ($MgSO_4$) and evaporated under reduced pressure to give an oil, which was chromatographed on preparative layer plates with 30% methanol–chloroform as eluant. The desired *tribenzoate* (8b) was obtained as an oil (0.351 g), which, after trituration with light petroleum (b.p. 40—60 °C) and drying, afforded (8b) as white foam, $[\alpha]_D^{20}$ +67° (*c* 1.0, $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 2 950, 2 850, 1 720, 1 710, 1 610, 1 580, and 1 460 cm^{-1}; δ_H ($CDCl_3$) see Table 2; δ_C ($CDCl_3$) 204.2 (C3), 165.8 (Ph*C*O), 165.7 (2 × Ph*C*O), 144.4—125.9 (aromatic carbons), 78.1, 78.0, 76.0, 72.7, 71.9, 70.8, 65.8, 43.4, 39.8, 37.4, 29.8 (C15), 29.7, 16.4 (C14), and 11.3 (C17) Found: C, 70.1; H, 6.55. $C_{36}H_{38}O_9$ requires C, 70.33; H, 6.24%).

The Tribenzoate (9b).—The ketone (9a) (0.250 g) was dissolved in a preformed solution of pyridine (6 ml) and benzoyl chloride (2 ml) and the solution stirred overnight at room temperature. The reaction was worked up in the same manner as for (8b). Preparative layer chromatography, with chloroform as eluant afforded pure *tribenzoate* (9b) (R_F = 0.2) as a white foam (0.761 g), $[\alpha]_D^{20}$ +50.0° (*c* 1.0, $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 2 950, 2 850, 1 710 (broad), 1 600, 1 590, and 1 450 cm^{-1}; δ_H ($CDCl_3$) see Table 3; δ_C ($CDCl_3$) 204.4 (C3), 165.8 (2 × Ph*C*O), 165.5 (Ph*C*O), 138.3—128.4 (aromatic carbons), 79.1 (d), 75.4 (d), 73.4 (d), 73.3 (d), 70.6 (d), 68.3 (d), 64.4 (t), 43.3 (t), 38.2 (d), 33.9 (d), 31.2 (t), 29.5 (C15), 17.9 (C14), and 8.6 (C17) (Found: $M^{+\cdot}$, 614.251 000. $C_{36}H_{38}O_9$ requires $M^{+\cdot}$, 614.251 561. Found: C, 70.17; H, 6.24. $C_{36}H_{38}O_9$ requires C, 70.33; H, 6.24%).

The Preparation of Methyl 4-{1S,6R-8R-(1S,3S-*dihydroxy*-2S-*methylbutyl*)-5S-*hydroxy*-3,7-*dioxabicyclo*[4.3.0]*nonan*-4S-*yl*}-3-*methylbut*-2(E)-*enoate* (12b) *and Methyl* 4-{1R,6S-4S,10S-*Dihydroxy*-3R-(2S-*hydroxy*-1S-*methylpropyl*)-2,8-*dioxabicyclo*[4.4.0]*decan*-9S-*yl*}-3-*methylbut*-2(E)-*enoate* (13b) *by Alkali Treatment of* (1a).—Pseudomonic acid (1.0 g) was dissolved in an excess of 1M-sodium hydroxide solution (6 ml) and the solution stirred at room temperature. Samples taken at intervals of 2 h were examined by reverse-phase h.p.l.c. and the reaction was complete after 20 h with two products formed in the ratio 3.3 : 1 [(12a) and (13a) respectively]. The mixture was neutralized to pH 7.0 with 1M-hydrochloric acid, evaporated to complete dryness under reduced pressure and finally dried *in vacuo* over phosphorus pentoxide. The residue was dissolved in *NN*-dimethylformamide (10 ml). Methyl iodide (5 ml) was added and the solution stirred overnight at room temperature. The reaction mixture was evaporated to dryness *in vacuo* and the residue partitioned between ethyl acetate and water. The organic layer was separated, washed with brine, dried ($MgSO_4$), and evaporated to give an oily

mixture of esters. The latter was chromatographed on silica (20 g) with a gradient of methanol–chloroform (0—4%) as eluant. The first and major fraction to be eluted was the *ester* (12b) (R_F = 0.40) as an oil (0.539 g), $[\alpha]_D$ +4.7° (*c* 1.0, $CHCl_3$), $\nu_{max.}$ 3 400, 2 950, 2 850, 1 710, 1 650, 1 420, and 1 150 cm^{-1}; $\lambda_{max.}$ (EtOH) 221 nm (ε 11 000); δ_H ($CDCl_3$) 5.65 (1 H, m, C2-*H*), 3.64 (3 H, s, OCH_3), 2.17 (3 H, s, C15-CH_3), 1.16 (3 H, d, C14-CH_3), and 0.80 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) see Table 4; *m/e* (relative intensity) 358 ($M^{+\cdot}$, 1.1), 256 ($M^{+\cdot} - C_5H_{10}O_2$, 12.3), 227 ($M^{+\cdot} - H_2O - C_6H_9O_2$, 16.0), 141 (13.7), 111 (34.6), 97 (30.7), and 83 (100) (Found: C, 60.05; H, 8.65. $C_{18}H_{30}O_7$ requires C, 60.30; H, 8.45%). The minor and more-polar *ester* (13b) (R_F = 0.34) was also obtained as oil (0.010 g), $[\alpha]_D$ −11.6° (*c* 1.0, $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 400, 2 950, 2 850, 1 710, 1 440, and 1 160 cm^{-1}; $\lambda_{max.}$ (EtOH) 221 nm (ε 8 830); δ_H 5.65 (1 H, m, C2-*H*), 3.65 (3 H, s, OCH_3), 2.16 (3 H, s, C15-CH_3), 1.20 (3 H, d, C14-CH_3), and 0.94 (3 H, d, C17-CH_3); δ_C ($CDCl_3$) see Table 4 (Found: $M^{+\cdot}$, 358.198 57. $C_{18}H_{30}O_7$ requires $M^{+\cdot}$, 358.199 13).

Rearrangement of Monic Acid A (11a).—(i) *Acidic conditions.* Monic acid A (11a) (10 mg) was dissolved in dilute hydrochloric acid (pH 1.0) (5 ml) at room temperature. Samples taken at time 0, 0.5, 1, 2, and 18 h were examined by reverse-phase h.p.l.c. for the formation of (12a) and (13a). Complete rearrangement to these acids had occurred in less than 0.5 h with a ratio of (12a) to (13a) of 1.6 : 1.

(ii) *Alkaline conditions.* Monic acid A (11a) (10 mg) was dissolved in 0.1M-sodium hydroxide solution (pH 13.0) (5 ml). Samples taken at time 1 and 18 h were examined by reverse-phase h.p.l.c. Incomplete reaction was observed at 1 h but by 18 h the formation of (12a) and (13a) in a ratio of 3.7 : 1 was complete.

Crystal Structure Determinations.—Crystal data. For (8a): $C_{15}H_{26}O_6$, M = 302.4, monoclinic, a = 8.825(2), b = 9.218(2), c = 10.708(3) Å, β = 115.6(1)°, U = 785.6 Å^3, D_c = 1.28, D_m = 1.27 g cm^3, $F(000)$ = 328. Space group $P2_1$, Mo-K_α radiation (graphite monochromator) λ = 0.710 69 Å, μ = 1.05 cm^{-1}.

For (9a): $C_{15}H_{26}O_6$, M = 302.4, monoclinic a = 8.386(2), b = 7.127(2), c = 14.393(3) Å, β = 90.8(1)°, U = 860.1 Å^3, D_c = 1.17, D_m = 1.17 g cm^3, Z = 2, $F(000)$ = 328. Space group $P2_1$, Mo-K_α radiation (graphite monochromator) λ = 0.710 69 Å, μ = 0.96 cm^{-1}.

In both cases the crystal parameters were initially found from oscillation and Weissenberg photographs and were then refined by least-squares from the setting angles of 23 reflections measured on a Hilger–Watt four-circle diffractometer. Reflections were measured for θ ≤ 25° (ω–2θ scan mode), reflections were deemed observed and were used in the refinement if $I \geqslant 3\sigma I$. Lorentz and polarisation corrections, but not absorption corrections were made. In the case of (8a), 1 015 from 1 484 reflections were observed and for (9a), 1 341 from 1 632 were observed.

Both structures were solved by MULTAN [9] (although not without some difficulty) and refined by full-matrix least-squares. Oxygen atoms were identified from isotropic temperature factors, bond lengths, and hydrogen substitution. Hydrogen atoms were located from a difference map and were then included in calculated (where possible) fixed positions. At convergence, with non-hydrogen atoms treated anisotropically the maximum shift/standard deviation was, for (8a), 0.05 and for (9a) 0.02. The R values were 4.9% (8a) and 4.6% (9a) and the ranges of the standard deviations of bond lengths and angles for parameters not involving hydrogen, were (8a) (0.007—0.01 Å and 0.41—0.69°) and (9a) (0.004—0.007 Å and 0.24—0.43°).

Tables 5 and 6 list the fractional co-ordinates for the ketones (8a) and (9a). Figures 2 and 3 show bond lengths and angles and Figures 4 and 5 are perspective drawings of the two molecules. The configurations are inferred from that known for pseudomonic acid A.[3] The conformations would not appear to have any remarkable features.

TABLE 5

Fractional co-ordinates for (8a) (× 10^4) with standard deviations in parentheses

Atom	*x/a*	*y/b*	*z/c*
C(3)	10 602(8)	8 307(8)	189(8)
C(4)	10 844(8)	7 597(8)	1 506(7)
C(5)	10 320(8)	8 432(7)	2 460(6)
C(6)	8 409(7)	8 550(7)	1 978(5)
C(7)	7 843(7)	7 101(8)	2 282(5)
C(8)	8 761(8)	6 735(8)	3 796(6)
C(9)	7 770(8)	5 415(8)	3 860(6)
C(10)	5 980(8)	5 839(8)	2 858(8)
C(11)	4 925(7)	4 615(8)	1 940(6)
C(12)	4 953(7)	3 232(8)	2 774(6)
C(13)	4 187(7)	1 902(8)	1 874(6)
C(14)	4 172(9)	584(8)	2 707(8)
C(15)	11 196(12)	7 549(9)	−729(10)
C(16)	10 585(8)	6 572(9)	4 136(7)
C(17)	4 031(11)	3 580(10)	3 669(8)
O(18)	9 894(9)	9 445(8)	−142(7)
O(19)	11 197(5)	7 925(7)	3 855(5)
O(20)	6 094(5)	7 007	1 986(4)
O(21)	8 113(5)	9 705(6)	2 718(4)
O(22)	5 557(5)	4 254(6)	956(5)
O(23)	5 132(6)	1 468(6)	1 130(4)

TABLE 6

Fractional co-ordinates for (9a) (× 10^4) with standard deviations in parentheses

Atom	*x/a*	*y/b*	*z/c*
C(3)	−4 132(5)	8 196(8)	9 490(3)
C(4)	−2 645(4)	7 694(7)	9 057(3)
C(5)	−1 225(4)	8 979(7)	9 395(3)
C(6)	234(4)	8 623(6)	8 886(2)
C(7)	−15(4)	9 469(6)	7 908(2)
C(8)	−403(4)	11 548(6)	7 966(3)
C(9)	−531(5)	12 409(6)	6 994(3)
C(10)	997(4)	11 989(6)	6 565(2)
C(11)	1 295(4)	9 877(6)	6 545(2)
C(12)	2 814(5)	9 268(7)	6 140(2)
C(13)	2 906(5)	7 125(7)	6 103(3)
C(14)	4 370(8)	6 374(10)	5 727(5)
C(15)	−4 050(6)	8 399(9)	10 522(4)
C(16)	−1 911(5)	11 720(7)	8 457(3)
C(17)	4 316(5)	10 109(8)	6 681(3)
O(18)	−5 380(4)	8 322(8)	8 992(3)
O(19)	−1 673(3)	10 905(6)	9 371(2)
O(20)	1 409(2)	9 172	7 483(1)
O(21)	1 574(3)	9 464(5)	9 418(2)
O(22)	990(3)	12 767(5)	5 649(2)
O(23)	1 506(4)	6 502(5)	5 536(2)

In (8a) there are short intermolecular distances between O(23) and O(22), thus O(23) is 2.61 and 2.89 Å from O(22) in two different adjacent molecules. However, the hydrogen atoms found in the difference map to be attached to these oxygens lie some way from the O–O line (O–H–O angles 148° and 121°) so there must be some doubt as to the existence of genuine hydrogen bonds in this compound. In (9a), however, there does appear to be an intermolecular hydrogen bond joining O(22) and O(23) the O–O distance being 2.69 Å and the O–H–O angle being 176°.

Apart from MULTAN, crystallographic computations

were done using the Oxford ' CRYSTALS ' package,[10] and the drawings were prepared using PLUTO.[11] The thermal parameters for the ketones (8a) and (9a) and listings of the observed and calculated structure factors are available in Supplementary Publication No. 22399 (27 pp.).*

We thank Professor R. Ramage, U.M.I.S.T., Professor R. A. Raphael, University of Cambridge, and Dr. G. Mellows, Imperial College, for their helpful discussions during the course of this work.

[8/738 *Received*, 20*th April*, 1978]

* For details of the Supplementary Publication Scheme see Notice to Authors No. 7, *J.C.S. Perkin I*, 1977, Index issue.

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