The Chemistry of Pseudomonic Acid. Part 5.[1] Structure and Chemistry of Pseudomonic Acid C. *X*-Ray Crystal Structure of Ethyl Monate C

J. Peter Clayton
Beecham Pharmaceuticals, Research Division, Brockham Park, Betchworth, Surrey RH3 7AJ
Peter J. O'Hanlon and Norman H. Rogers *
Beecham Pharmaceuticals, Research Division, Walton Oaks, Dorking Road, Tadworth, Surrey KT20 7NT
Trevor J. King
Department of Chemistry, The University of Nottingham, University Park, Nottingham NG7 2RD

A third and minor antibiotic component, designated pseudomonic acid C (1a),[2] has been isolated from cultures of the strain *Pseudomonas fluorescens* NCIB 10586 which produced the structurally related pseudomonic acid A (2a) and B (3). The structure and stereochemistry of the acid (1a) have been confirmed by single-crystal *X*-ray analysis of the derived ethyl monate C (1f). Pseudomonic acid A has been converted stereospecifically into pseudomonic acid C in high yield. The epoxidation and the acid- and base-stability of pseudomonic acid C have been studied.

Pseudomonas fluorescens NCIB 10586, the bacterium which produces the antibiotics pseudomonic acid A (2a)[3-5] and pseudomonic acid B (3),[6] also produces a third and related antibiotic, pseudomonic acid C.[2] The presence of pseudomonic acid C in culture filtrates of *Pseudomonas fluorescens* was observed by reverse-phase high performance liquid chromatography (h.p.l.c.). Pseudomonic acid C was less polar than pseudomonic acids A and B and the proportions of these metabolites in the culture medium were A : B : C 93 : 5 : 2.

Pseudomonic acid C was isolated as its crystalline methyl ester (1b). It was evident from spectral data that the structure of the ester (1b) differed from that of methyl pseudomonate A (2b) by having a C(10)=C(11) double bond in place of a *trans* epoxide moiety. The acid was therefore assigned structure (1a).

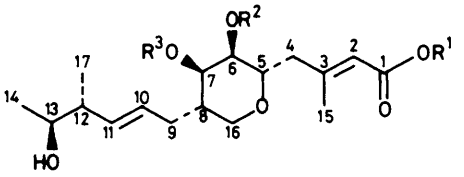
The 10,11-double bond was assigned the *E*-configuration from the 90 MHz n.m.r. spectrum of the acetonide derivative (1c), prepared from the diol (1b) by reaction with 2,2-dimethoxypropane and toluene-*p*-sulphonic acid. The addition of Eu(fod)$_3$ † (1.15 equiv.) afforded a sufficient chemical-shift difference between the 10- and 11-H for a measurement of the coupling constant $J_{10,11}$ (15.1 Hz) which confirmed the *E* geometry of the double bond.

Treatment of pseudomonic acid C (1a) or its methyl ester (1b) with aqueous sodium hydroxide at room temperature overnight afforded, after work-up, monic acid C (1d) in 74% yield. Under these conditions the nucleus of pseudomonic acid A (2a) undergoes rearrangement, in addition to hydrolysis, to produce the bicyclic products (4) and (5).[7,8] At pH 1.0 pseudomonic acid C (1a) is stable, with no loss of antibacterial activity, whilst in contrast pseudomonic acid A (2a) rearranges within 30 min.[8] However, in the hydrolysis (NaOH–MeOH) of compound (1a), varying quantities of a bicyclic by-product (6a) were obtained depending on reaction conditions. This product, after treatment with diazomethane, was isolated as its oily methyl ester (6b). The i.r. spectrum and the lack of u.v. absorption of this ester confirmed the absence of an α,β-unsaturated ester moiety. The structure and epimeric nature of the product was confirmed by its ^{1}H- and ^{13}C-n.m.r. spectra. In one reaction in which pseudomonic acid C (1a) was hydrolysed with excess of sodium hydroxide in aqueous methanol at temperatures ≤ 100 °C for 4 h, three products were observed. After work-up of the reaction mixture and treatment of the acidic products with diazomethane, three methyl esters were separated by column chromatography. Methyl monate C (1e), methyl isomonate C (7a), and the bicyclic rearrangement product (6b) were isolated in 21, 29, and 16% yield, respectively. The intermediate bicyclic product (6b) arises from intramolecular Michael attack of the C(6) hydroxy-group on the acrylate ester function in compound (1a), a favoured *5-exo-trig* process,[9] followed by cleavage of the nonanoic acid side-chain and subsequent isolation as the methyl ester (6b). In the equilibrium reaction, retro-Michael cleavage of the bicyclic ring prior to hydrolysis of the nonanoate ester must account for the formation of the isomeric acrylic ester (7a). When monic acid C (1d) was treated under identical conditions to those described above, neither isomerisation nor bicyclic-product formation was observed, thus confirming the proposed mechanism which requires the ester function to be present. The resulting monic acid C (1d) as its sodium salt was converted into its crystalline ethyl ester (1f) with ethyl iodide in *N*,*N*-dimethylformamide (DMF) containing a trace of hexamethylphosphoric triamide (HMPA).

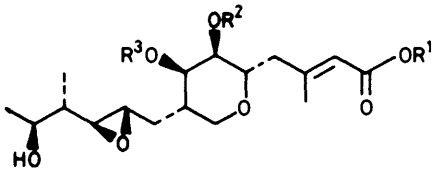
Unequivocal confirmation of the structure and stereochemistry of the 10,11-double bond in pseudomonic acid C (1a) was achieved by *X*-ray analysis of the crystalline ethyl monate C (1f). [Methyl pseudomonate C (1b), like methyl pseudomonate A (2b),[7] although crystalline was unsuitable for *X*-ray analysis.] Fractional atomic co-ordinates and bond-lengths and -angles for compound (1f) are given in Tables 1—3, and the conformation in the crystal lattice is illustrated in a perspective drawing (Figure). The stereochemistry depicted was inferred from that of pseudomonic acid A, since A-series derivatives can be de-epoxidised stereospecifically into C-series derivatives.

Since only small quantities of pseudomonic acid C (1a) can be obtained from fermentations of *Pseudomonas fluorescens*, a high yielding and stereospecific method for the conversion of readily available pseudomonic acid A (2a) or monic acid A (2d) into the corresponding C-series compounds was desirable. Early studies[2] have shown that compound (2b) can be deoxygenated to afford methyl pseudomonate C (1b) by potassium selenocyanate[10] in refluxing aqueous

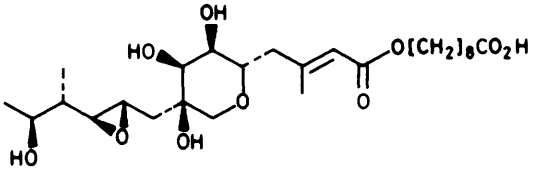
† Eu(fod)$_3$ = europium tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionate).



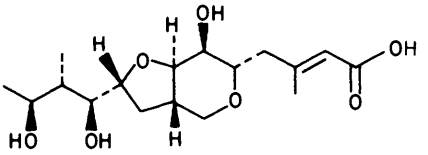
(1) a; $R^1 = [CH_2]_8CO_2H$, $R^2 = R^3 = H$
b; $R^1 = [CH_2]_8CO_2Me$, $R^2 = R^3 = H$
c; $R^1 = [CH_2]_8CO_2Me$, $R^2R^3 =$ 
d; $R^1 = R^2 = R^3 = H$
e; $R^1 = Me$, $R^2 = R^3 = H$
f; $R^1 = Et$, $R^2 = R^3 = H$
g; $R^1 = [CH_2]_8CO_2H$, $R^2R^3 =$ 
h; $R^1 = Et$, $R^2R^3 =$ 



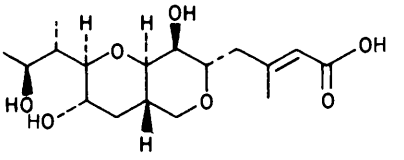
(2) a; $R^1 = [CH_2]_8CO_2H$, $R^2 = R^3 = H$
b; $R^1 = [CH_2]_8CO_2Me$, $R^2 = R^3 = H$
c; $R^1 = [CH_2]_8CO_2H$, $R^2R^3 =$ 
d; $R^1 = R^2 = R^3 = H$
e; $R^1 = Me$, $R^2 = R^3 = H$
f; $R^1 = Et$, $R^2 = R^3 = H$



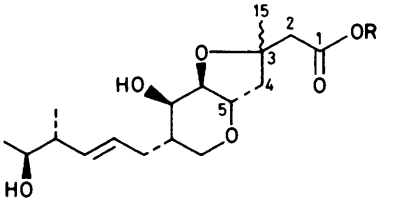
(3)



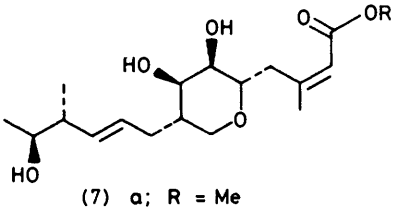
(4)



(5)



(6) a; R = H
b; R = Me



(7) a; R = Me
b; R = $[CH_2]_8CO_2Me$

methanol, but seven days were required and a yield of only 10% of (1b) was obtained. Side reactions, including rearrangement of the starting material (2b), contributed to the poor yield. Many of the published procedures for converting epoxides into olefins, particularly those which are stereospecific,[11–17] have been examined with little or no success. However, Kozikowski and his co-workers [18] have successfully deoxygenated an authentic sample of compound (2f) using a low-valent tungsten chloride in tetrahydrofuran (THF) [12] to give the ester (1f) stereospecifically. The potassium selenocyanate procedure remained the more favourable in our hands and, therefore, a detailed examination of the method in order to improve yields and eliminate undesirable side reactions was undertaken.

A variety of higher boiling aqueous primary, secondary, and tertiary alcohols were initially examined. A higher yield in the conversion of the epoxide (2b) into its olefin (1b) using potassium selenocyanate in methoxyethanol–water (9 : 1), compared with the original conditions of methanol–water (9 : 1), was observed, but the formation of methyl isopseudomonate C (7b) and methoxyethyl esters was also observed. Isomerisation and transesterification was avoided, however, by using either 2-ethylbutan-1-ol or 1,1-dimethylpropan-1-ol (both in a 9 : 1 admixture with water) and the yield of deoxygenated product in each case was >50% after the mixture had been heated under reflux for 2 d. These reaction conditions were sufficiently severe as to effect intramolecular rearrangement [8] of the starting material (2b) at a rate almost comparable with that of the deoxygenation reaction. Protection of the glycol system as the acetonide was found to be necessary to avoid this problem.

The potassium salt of the acetonide (2c) was treated with potassium selenocyanate in 1,1-dimethylpropan-1-ol–water (9 : 1) and the mixture was heated under reflux for 2 d. The acetonide group was quantitatively removed from the resultant product (1g) in 80% aqueous acetic acid and the pseudomonic acid C (1a) was isolated in 58% overall yield. Similarly, monic acid C (1d) was obtained from monic acid A (2d) in 72% yield.

Re-epoxidation of C-series compounds can result in the production of two epimeric epoxides, one of which corres-

Table 1. Fractional atomic co-ordinates (× 10^4) with standard deviations in parentheses

Atom [a]	x/a	y/b	z/c
C(1)	7 403(2)	4 416(12)	7 304(5)
C(2)	6 956(2)	4 782(10)	6 328(5)
C(3)	6 854(2)	6 332(9)	5 690(4)
C(4)	6 378(2)	6 522(8)	4 685(4)
C(5)	6 085(1)	4 722(8)	4 280(3)
C(6)	5 571(1)	5 097(8)	3 407(3)
C(7)	5 321(1)	3 228(8)	2 931(3)
C(8)	5 695(1)	1 973(8)	2 408(3)
C(9)	5 785(1)	2 676(8)	1 174(3)
C(10)	6 008(1)	1 216(8)	461(3)
C(11)	5 744(1)	264(8)	−453(3)
C(12)	5 948(2)	−1 319(8)	−1 112(3)
C(13)	5 852(1)	−978(9)	−2 498(3)
C(14)	6 098(2)	803(11)	−2 843(3)
C(15)	7 174(2)	8 059(11)	5 886(7)
C(16)	6 200(2)	1 806(8)	3 334(3)
C(17)	5 717(3)	−3 173(10)	−822(5)
C(18)	7 872(3)	1 909(22)	8 544(9)
C(19)	7 708(4)	326(11)	9 286(9)
O(1)	7 711(2)	5 534(10)	7 825(4)
O(5)	6 412(1)	3 620(7)	3 671(2)
O(6)	5 231(1)	6 093(9)	4 025(3)
O(7)	5 167(1)	2 262(8)	3 934(3)
O(13)	5 310(1)	−906(9)	−2 973(3)
O(18)	7 435(2)	2 629(10)	7 600(6)

[a] Crystallographic numbering scheme.

Table 2. Bond lengths (Å) with standard deviations in parentheses

C(1)-C(2)	1.463(7)	C(8)-C(9)	1.531(5)
C(1)-O(1)	1.202(7)	C(8)-C(16)	1.522(5)
C(1)-O(18)	1.311(9)	C(9)-C(10)	1.496(6)
C(2)-C(3)	1.312(7)	C(10)-C(11)	1.308(5)
C(3)-C(4)	1.518(6)	C(11)-C(12)	1.501(6)
C(3)-C(15)	1.480(7)	C(12)-C(13)	1.544(5)
C(4)-C(5)	1.516(5)	C(12)-C(17)	1.511(7)
C(5)-C(6)	1.531(5)	C(13)-C(14)	1.505(8)
C(5)-O(5)	1.430(4)	C(13)-O(13)	1.422(5)
C(6)-C(7)	1.531(6)	C(16)-O(5)	1.425(5)
C(6)-O(6)	1.420(5)	C(18)-C(19)	1.510(13)
C(7)-C(8)	1.526(5)	C(18)-O(18)	1.493(9)
C(7)-O(7)	1.440(5)		

sponds to the A-series derivative and the other to its epimer (8). Treatment of the tris(trimethylsilyl)-protected alcohols, (1b) and (1e) with *m*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane afforded, after de-protection and work-up, an epimeric mixture of epoxides. In both examples separation of the epimers was not achieved, but by analytical h.p.l.c. the ratios (2b) : (8a) and (2e) : (8b) were both found to be 1 : 2. The ^{1}H- and ^{13}C-n.m.r. spectra indicated an epimeric mixture of products in the ratio indicated by h.p.l.c. The epoxide carbons of methyl pseudomonate A (2b) give rise to signals at δ_C 56.5 [C(10)] and 61.0 p.p.m. [C(11)], whilst those of the isomer (8a) occur at δ_C 58.9 [C(10)] and 62.6 p.p.m. [C(11)]. Some stereoselectivity was observed in this reaction in favour of the unnatural epoxides which were found to have no antibacterial activity. No stereoselectivity was observed when the unprotected triol (1b) was treated with either *m*-CPBA or t-butyl hydroperoxide in the presence of vanadyl acetylacetonate [VO(acac)$_2$]. However, Kozikowski and his co-workers [18] have shown that by protecting the glycol (1f) as its benzylidene acetal (1h), t-BuOOH in the presence of VO(acac)$_2$ affords a 3 : 1 mixture of compounds (2f) : (8c) after de-protection.

Table 3. Bond angles (°) with standard deviations in parentheses

O(1)-C(1)-C(2)	127.8(6)	C(7)-C(8)-C(9)	112.3(3)
O(1)-C(1)-O(18)	120.8(6)	C(7)-C(8)-C(16)	109.0(3)
C(2)-C(1)-O(18)	111.4(5)	C(9)-C(8)-C(16)	112.0(3)
C(1)-C(2)-C(3)	127.3(5)	C(8)-C(9)-C(10)	113.6(3)
C(2)-C(3)-C(4)	122.1(4)	C(9)-C(10)-C(11)	125.0(3)
C(2)-C(3)-C(15)	124.4(4)	C(10)-C(11)-C(12)	125.9(3)
C(4)-C(3)-C(15)	113.5(5)	C(11)-C(12)-C(13)	111.9(3)
C(3)-C(4)-C(5)	116.4(4)	C(11)-C(12)-C(17)	110.6(4)
C(4)-C(5)-C(6)	112.2(3)	C(13)-C(12)-C(17)	111.1(4)
C(4)-C(5)-O(5)	106.8(3)	C(12)-C(13)-C(14)	113.3(4)
C(6)-C(5)-O(5)	109.2(3)	C(12)-C(13)-O(13)	109.7(3)
C(5)-C(6)-C(7)	109.7(3)	C(14)-C(13)-O(13)	108.9(4)
C(5)-C(6)-O(6)	109.6(3)	C(8)-C(16)-O(5)	110.7(3)
C(7)-C(6)-O(6)	109.6(3)	C(5)-O(5)-C(16)	112.4(3)
C(6)-C(7)-C(8)	112.1(3)	C(1)-O(18)-C(18)	121.0(7)
C(6)-C(7)-O(7)	107.9(3)	O(18)-C(18)-C(19)	112.5(6)
C(8)-C(7)-O(7)	108.7(3)		

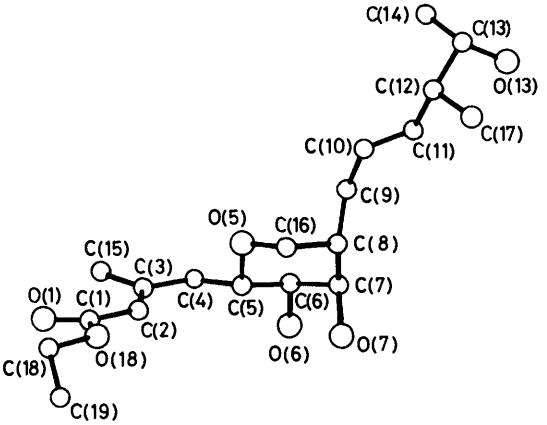
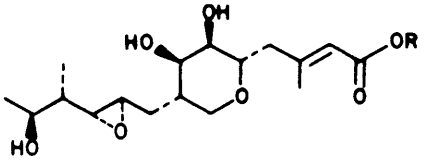


Figure. Crystal structure of ethyl monate C (1f) showing crystallographic numbering scheme



(8) a; R = $[CH_2]_8CO_2Me$
b; R = Me
c; R = Et

Experimental

M.p.s were determined on a Büchi apparatus and are uncorrected. Mass spectra were obtained at 70 eV using a VG 70-70F instrument operating at 8 kV. ^{1}H N.m.r. data were recorded at 90 MHz on a Perkin-Elmer R32 instrument and ^{13}C measurements were obtained using a Varian CFT 20 spectrometer; all n.m.r. data were recorded at ambient temperatures with tetramethylsilane as internal standard. The numbering system used for assigning the chemical shifts is that shown in formula (1). Column chromatography was carried out on Merck Kieselgel H (type 60). R_F Values refer to analytical thin-layer chromatography (t.l.c.) which was performed on pre-coated Merck Kieselgel 60 F_{254}. The analytical plates were developed with chloroform–methanol

(9 : 1 or 3 : 1 v/v) and the components were visualized by either u.v. light or charring with sulphuric acid. 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 unless otherwise stated. Both t.l.c. and h.p.l.c. were performed routinely on all compounds. Dichloromethane was distilled from phosphorus pentaoxide. THF and DMF were dried over calcium hydride and freshly distilled immediately before use.

Fermentation of Pseudomonas fluorescens (*N.C.I.B. 10586*) *and Isolation of Methyl Pseudomonate C* (1b).—The bacterium was cultured on an agar slope and the culture was flooded with sterile water. A sample was added to a seed-stage medium containing Oxoid yeast (2.0% w/v), glucose (0.11), Na_2HPO_4 (0.26), and KH_2PO_4 (0.24). The culture was grown at 28 °C overnight and was used to inoculate a production-stage medium containing corn steep liquor (0.3% w/v), glucose (2.0), glycerol (0.5), $(NH_4)_2SO_4$ (0.2), $CaCO_3$ (0.4), KH_2PO_4 (0.04), Na_2HPO_4 (0.065), $MnCl_2·4H_2O$ (0.0003), KCl (0.05), $MgSO_4·7H_2O$ (0.0375), and silicone antifoam (P2000 1 drop/100 ml). The fermentation was carried out at 25 °C for 48 h after which time production was essentially complete. After removal of the cells by centrifugation, the supernatant was partitioned into ethyl acetate at pH 4. The ethyl acetate layer was extracted with aqueous sodium hydrogen carbonate. The aqueous extract was acidified to pH 4 and re-extracted with ethyl acetate. The organic extract was dried ($MgSO_4$) and evaporated to low volume. Diethyl ether was added and pseudomonic acid A (2a) was allowed to crystallise out. The mother liquor from the crystallisation was evaporated to dryness under reduced pressure. The residual oil was dissolved in 50% aqueous methanol, the pH was adjusted to 7 with aqueous sodium hydroxide, and the resulting solution was evaporated to dryness. The residual sodium salts were dissolved in DMF and the solution was stirred with methyl iodide at room temperature overnight. After removal of the solvent under reduced pressure the residue was partitioned between ethyl acetate and water and the organic layer was washed in turn with aqueous sodium hydrogen carbonate and brine. The organic solution was dried ($MgSO_4$) and evaporated to dryness to afford an oil from which some methyl pseudomonate A (2b) crystallised. The residual oil was chromatographed on silica with gradient elution with 0—4% methanol–chloroform. Fractions containing substantially pure methyl pseudomonate C (1b) [R_F 0.43, chloroform–methanol (9 : 1); methyl pseudomonate A (2b) R_F 0.39] were combined and rechromatographed on silica (gradient elution with 0—4% methanol–chloroform). Fractions containing pure *methyl pseudomonate C* (1b) were combined and evaporated to dryness to give an oil which crystallised with time, m.p. 47—49 °C; $\nu_{max.}$ ($CHCl_3$) 3 400, 1 720, 1 710, 1 650, 1 150, and 980 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 14 900); δ_H ($CDCl_3$) 5.72 (1 H, m, 2-H), 5.40 (total 2 H, m, 10- and 11-H), 4.05 (2 H, t, 9′-H_2)*, 3.65 (3 H, s, OMe), 2.18 (3 H, s, 15-H_3), 1.30 (total 12 H, m, $[CH_2]_6$), 1.13 (3 H, d, 17-H_3), and 0.98 (3 H, d, 14-H_3); δ_C ($CDCl_3$) 174.3 (s) [C(1′)], 166.8 (s) [C(1)], 156.8 (s) [C(3)], 134.5 (d) and 129.4 (d) [C-(10) and -(11)], 117.6 (d) [C(2)], 74.8 (d) [C(5)], 71.2 (d) [C(13)], 70.4 (d) [C(7)], 68.9 (d) [C(6)], 64.8 (t) [C(16)], 63.8 (t) [C(9′)], 51.4 (q) (OMe), 44.7 (d) [C(12)], 43.1 (t) [C(4)], 42.0 (d) [C(8)], 34.1 (t) [C(2′)], 32.4 (t) [C(9)], 29.1 (t) [C-(4′), -(5′), and -(6′)], 28.7 (t) [C(8′)], 26.0 (t) [C(7′)], 24.9 (t) [C(3′)], 20.4 (q) [C(14)], 19.1 (q) [C(15)], and 16.6 p.p.m. (q) [C(17)]; *m/z* (NH_3 c.i.) (relative intensity) 499 ($M^+ + 1$, 100%) (Found: C, 65.0; H, 9.5. $C_{27}H_{46}O_8$ requires C, 65.0; H, 9.3%).

Pseudomonic Acid C (1a).—A solution of methyl pseudomonate C (1b) (0.23 g) in DMF (25 ml) was diluted with 0.05M phosphate buffer (pH 7.2) (120 ml) and the mixture was stirred with bakers' yeast (6 g) overnight. The reaction mixture was filtered, the filtrate was evaporated to dryness, and the residue was dissolved in 1 : 1 ethyl acetate–water (100 ml). The organic layer was washed with water and the combined aqueous layers were adjusted to pH 3 (5M HCl) and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated under reduced pressure to yield an oil which was chromatographed on silica (8 g) using gradient elution with 0—6% methanol–chloroform as eluant. Fractions containing pure *pseudomonic acid C* (1a) were combined and evaporated to yield an oil (0.15 g, 67%); $\nu_{max.}$ ($CHCl_3$) 3 430, 1 710, 1 650, 1 220, 1 153, 1 110, 1 050, and 977 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 14 100); δ_H ($CDCl_3$) 5.69 (1 H, m, 2-H), 5.4 (total 2 H, m, 10- and 11-H), 4.65br (total 4 H, 6-, 7-, and 13-OH and CO_2H), 4.01 (2 H, t, 9′-H_2), 2.15 (3 H, s, 15-H_3), 1.12 (3-H, d, 17-H_3), and 0.96 (3 H, d, 14-H_3); δ_C* ($CDCl_3$) 178.1 [C(1′)], 166.9 [C(1)], 156.9 [C(3)], 134.5 and 129.5 [C-(10) and -(11)], 117.6 [C(2)], 74.9 [C(5)], 71.4 [C(13)], 70.4 [C(7)], 69.0 [C(6)], 64.9 [C(16)], 63.9 [C(9′)], 44.7 [C(12)], 43.0 [C(4)], 41.9 [C(8)], 34.0 [C(2′)], 32.4 [C(9)], 28.9 [C-(4′), -(5′), and -(6′)], 28.6 [C(8′)], 25.9 [C(7′)], 24.7 [C(3′)], 20.4 [C(14)], 19.2 [C(15)], and 16.7 p.p.m. [C(17)] (Found: C, 64.0; H, 9.3. $C_{26}H_{44}O_8$ requires C, 64.4; H, 9.2%).

Pseudomonic acid C (1a) *from Pseudomonic Acid A* (2a).—Pseudomonic acid A (0.5 g) was dissolved in a mixture of 2,2-dimethoxypropane (20 ml) and ethyl acetate (20 ml) and toluene-*p*-sulphonic acid (a few crystals) was added. The solution was stirred for 1 h and was then washed with brine and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the residue, 6,7-*O*-isopropylidenepseudomonic acid A (2c), was dissolved in 50% aqueous methanol (20 ml) and converted into its potassium salt by the addition of potassium hydrogen carbonate (100 mg). The solution was evaporated to dryness under reduced pressure and the residue was redissolved in 1,1-dimethylpropan-1-ol–water (9 : 1; 15 ml). Potassium selenocyanate (0.432 g) was added and the mixture was heated under reflux for 2 d. The solution was filtered and the filtrate was evaporated to dryness. The residue was dissolved in water (20 ml) and the solution was layered with ethyl acetate (20 ml); the pH of the stirred mixture was adjusted to 2 by the addition of 5M HCl. The organic layer was separated and the aqueous layer was further extracted with ethyl acetate (3 × 20 ml). The combined extracts were dried ($MgSO_4$) and evaporated to afford the oily acetonide (1g) which was redissolved in 80% acetic acid (10 ml) and the solution was stirred overnight at room temperature. The mixture was then evaporated to dryness and the residual oily pseudomonic acid C was chromatographed on silica (10 g) with gradient elution using 0—6% methanol–chloroform as eluant. Fractions containing pure product were combined and evaporated to give pseudomonic acid C as an oil (0.28 g, 58% overall).

Methyl 6,7-O-*Isopropylidenepseudomonate C* (1c).—Methyl pseudomonate C (1b) (0.230 g) was dissolved in 2,2-dimethoxypropane (10 ml) containing one crystal of toluene-*p*-sulphonic acid. The solution was stirred at room temperature

* Primed numbers refer to the side chain R′ as follows:

1 9′ 8′ 7′ 6′ 5′ 4′ 3′ 2′ 1′
$-CO_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CO_2Me$

* Multiplicities as for (1b).

for 5 min and was then diluted with diethyl ether, washed in turn with aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated to dryness to give an oil (0.269 g) which was subjected to p.l.c. (preparative-layer chromatography) silica (20 × 20 × 0.2 cm) plates with chloroform–methanol (30 : 1) as developer; the major band was removed. The *acetonide* (1c) was obtained as an oil (0.160 g, 65%); $\nu_{max.}$ ($CHCl_3$) 3 450, 1 722, 1 643, and 1 220 cm^{-1}; $\lambda_{max.}$ (EtOH) 221 nm (ε 16 000); δ_H ($CDCl_3$) 5.73 (1 H, s, 2-H), 5.45 (total 2 H, m, 10- and 11-H), 4.05 (2 H, t, 9′-H_2), 3.63 (3 H, s, OMe), 2.18 (3 H, s, 15-H_3), 1.48 (3 H, s, acetonide Me), 1.33 (total 15 H, m, $[CH_2]_6$ and acetonide Me), 1.13 (3 H, d, 14-H_3), and 0.98 (3 H, d, 17-H_3); δ_C ($CDCl_3$) 174.2 (s) [C(1′)], 166.7 (s) [C(1)], 156.1 (s) [C(3)], 134.9 (d) and 129.2 (d) [C-(10) and -(11)], 117.8 (d) [C(2)], 108.7 (s) (CMe_2), 74.3 (d) [C(5)], 71.2 (d) [C(13)], 76.4 (d) and 75.6 (d) [C-(6) and -(7)], 66.5 (t) [C(16)], 63.8 (t) [C(9′)], 51.4 (q) (OMe), 44.7 (d) [C(12)], 44.1 (t) [C(4)], 36.9 (d) [C(8)], 34.1 (t) [C(2′)], 34.1 (t) [C(9)], 29.1 (t) [C-(4′), -(5′), and -(6′)], 28.8 (t) [C(8′)], 28.3 (q) and 26.3 (q) (CMe_2), 26.0 (t) [C(7′)], 24.9 (t) [C(3′)], 20.3 (q) [C(14)], 19.1 (q) [C(15) and 16.5 p.p.m. (q) [C(17)]; *m/z* (rel. int.) 523 ($M^+ - CH_3$, 6%) (Found: C, 66.8; H, 9.6. $C_{30}H_{50}O_8$ requires C, 66.9; H, 9.4%).

Monic acid C (1d).—(a) *From pseudomonic acid C* (1a). A solution of pseudomonic acid C (0.08 g) in 0.1M sodium hydroxide (20 ml) was stirred overnight at room temperature. After evaporation to low volume the solution was adjusted to pH 2 (5M HCl), saturated with sodium chloride, and extracted with ethyl acetate (3 × 25 ml). The combined extracts were dried ($MgSO_4$) and evaporated to dryness. The residue was chromatographed on silica (2 g) with gradient elution using 0—8% methanol–chloroform as eluant. Fractions containing pure product were combined to give, after work-up, *monic acid C* (0.04 g, 74%), m.p. 101—102 °C; $\nu_{max.}$ (KBr) 3 400, 1 692, 1 644, 1 238, and 975 cm^{-1}; $\lambda_{max.}$ (EtOH) 218 nm (ε 9 679); δ_H (CD_3OD) 0.97 (3 H, d, 17-H_3), 1.08 (3 H, d, 14-H_3), 2.13 (3 H, s, 15-H_3), 5.4 (total 2 H, m, 10- and 11-H), and 5.67 (1 H, s, 2-H); δ_C (CD_3OD) 170.2 [C(1)], 159.0 [C(3)], 135.8 and 129.7 [C-(10) and -(11)], 118.6 [C(2)], 76.2 [C(5)], 72.5 [C(7)], 71.6 [C(13)], 70.0 [C(6)], 65.8 [C(16)], 45.3 [C(12)], 44.1 [C(4)], 43.7 [C(8)], 33.7 [C(9)], 20.4 [C(14)], 19.3 [C(15)], and 16.7 p.p.m. [C(17)]; *m/z* (rel. int.) 284 ($M^+ - C_2H_4O$, 4%), 266 (13), 248 (2), 185 (12), and 167 (16) (Found: *m/z*, 284.1624. $C_{17}H_{28}O_6 - C_2H_4O$ requires *m/z* 284.1623) (Found: C, 61.8; H, 8.4. $C_{17}H_{28}O_6$ requires C, 62.2; H, 8.6%).

(b) *From monic acid A* (2d). Monic acid A (3.44 g) was dissolved in a mixture of 2,2-dimethoxypropane (30 ml) and ethyl acetate (30 ml) and a few crystals of toluene-*p*-sulphonic acid were added. After 1 h the solution was diluted with ethyl acetate, washed with brine, and then dried ($MgSO_4$). The solvent was removed under reduced pressure and the residual acetonide was dissolved in 50% aqueous methanol (40 ml) and the solution was treated with potassium hydrogen carbonate (1.0 g). The solution was evaporated to dryness, potassium selenocyanate (4.32 g) and 1,1-dimethylpropan-1-ol–water (9 : 1; 150 ml) were added, and the mixture was refluxed for 42 h and filtered. The filtrate was diluted with ethyl acetate and extracted with water (4 × 25 ml). The combined aqueous extracts were acidified (pH 2; 5M HCl) and re-extracted with ethyl acetate (4 × 25 ml); the extracts were dried ($MgSO_4$). The solvent was removed under reduced pressure and the residual oil was dissolved in 80% acetic acid (100 ml). The solution was left overnight at room temperature and was then evaporated to dryness; the crude product was chromatographed on silica (50 g) using gradient elution with 0—10% methanol–chloroform as eluant. The fractions containing pure product were combined and evaporated to yield monic acid C (1d) (2.57 g, 72%).

Alkaline Hydrolysis of Pseudomonic Acid C (1a).—To a solution of pseudomonic acid C (1a) (140 mg) in methanol (10 ml) were added water (7 ml) and 1M sodium hydroxide (1.6 ml). The solution was heated on a steam-bath for 4 h and was then cooled and the pH was adjusted to 1.5 with 1M HCl. The mixture was saturated with sodium chloride and extracted with ethyl acetate (5 × 15 ml). The extracts were dried ($MgSO_4$) and treated with excess of diazomethane. Removal of the solvent under reduced pressure afforded a mixture of methyl esters which was chromatographed on silica (5 g) using gradient elution with 0—2% methanol–chloroform as eluant. The first component to be eluted was identified as an oily mixture of isomers (6b) (15 mg, 16%); $\nu_{max.}$ ($CHCl_3$) 3 400 and 1 740 cm^{-1}; $\lambda_{max.}$ (EtOH) <210 nm; δ_H ($CDCl_3$) 0.98 (3 H, d, 17-H_3), 1.13 (3 H, d, 14-H_3), 1.37 and 1.46 (each 3 H, 2 × s, 15-H_3), 2.52 and 2.65 (each 2 H, 2 × s, 2-H_2), 3.66 (3 H, s, OMe), and 5.43 (total 2 H, m, 10- and 11-H); δ_C ($CDCl_3$) 170.8 [C(1)], 134.8 and 129.7 [C-(10) and -(11)], 80.2, 77.9 and 77.4, 73.0 and 72.8, 68.6 and 68.3, and 67.7 and 67.3 [C-(3), -(5), -(6), -(7), and -(16)], 71.1 [C(13)], 51.8 and 51.5 (OMe), 46.7, 41.3, and 40.6 and 40.7 [C-(2), -(4), and -(8)], 44.8 [C(12)], 33.9 and 33.8 [C(9)], 28.7 and 28.5 [C(15)], 20.3 [C(14)], and 16.6 p.p.m. [C(17)]; *m/z* (rel. int.) 342 (M^+, 12%), 324 (15), 298 (29), and 280 (17) (Found: M^+, 342.2062. $C_{18}H_{30}O_6$ requires *M*, 342.2041).

The second component to be eluted was identified as *methyl isomonate C* (7a) (28 mg, 29%); $\nu_{max.}$ ($CHCl_3$) 3 400, 1 720, and 1 645 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 8 380); δ_H ($CDCl_3$) 0.97 (3 H, d, 17-H_3), 1.13 (3 H, d, 14-H_3), 2.01 (3 H, d, 15-H_3), 3.68 (3 H, s, OMe), 5.44 (total 2 H, m, 10- and 11-H), and 5.82 (1 H, s, 2-H); δ_C ($CDCl_3$) 173.0 [C(1)], 159.8 [C(3)], 134.6 and 129.6 [C-(10) and -(11)], 117.2 [C(2)], 76.5 [C(5)], 71.1 [C(13)], 70.1 [C(7)], 67.5 [C(6)], 65.0 [C(16)], 51.5 (OMe), 44.8 [C(12)], 40.9 [C(8)], 35.6 [C(4)], 32.4 [C(9)], 27.2 [C(15)], 20.3 [C(14)], and 16.5 p.p.m. [C(17)]; *m/z* (rel. int.) 342 (M^+, 2%), 324 (6), 298 (31), 280 (9), 266 (18), 169 (44), and 111 (100) (Found: M^+, 342.2031. $C_{18}H_{30}O_6$ requires *M*, 342.2041).

The third component was identified as *methyl monate C* (1e) (20 mg, 21%); $\nu_{max.}$ ($CDCl_3$) 3 500, 1 710, 1 650, 1 440, and 1 150 cm^{-1}; $\lambda_{max.}$ (EtOH) 221 nm (ε 12 000); δ_H ($CDCl_3$) 0.97 (3 H, d, 17-H_3), 1.14 (3 H, d, 14-H_3), 2.18 (3 H, s, 15-H_3), 3.62 (3 H, s, OMe), 5.4 (total 2 H, m, 10- and 11-H), and 5.72 (1 H, m, 2-H); δ_C ($CDCl_3$) 167.2 [C(1)], 157.4 [C(3)], 134.4 and 129.3 [C-(10) and -(11)], 117.1 [C(2)], 74.8 [C(5)], 71.3 [C(13)], 70.3 [C(7)], 68.9 [C(6)], 64.9 [C(16)], 50.9 (OMe), 44.6 [C(12)], 43.0 [C(4)], 41.9 [C(8)], 32.4 [C(9)], 20.4 [C(14)], 19.2 [C(15)], and 16.6 p.p.m. [C(17)]; *m/z* (NH_3 c.i.) (rel. int.) 360 (MNH_4^+, 22%) and 343 (MH^+, 100).

Ethyl Monate C (1f).—Monic acid C (1d) (0.328 g) was dissolved in 50% aqueous methanol and converted into its sodium salt by the addition of sodium hydrogen carbonate (0.081 g). The solution was evaporated to dryness and dissolved in a mixture of DMF (20 ml) and HMPA (few drops) and ethyl iodide (0.4 ml) was added. After being stirred at room temperature overnight the solution was evaporated to dryness under reduced pressure and the residue was partitioned between ethyl acetate (20 ml) and brine (20 ml). After separation of the organic phase, the aqueous layer was further extracted with ethyl acetate (20 ml) and the combined organic phases were dried ($MgSO_4$). After removal of the solvent under reduced pressure the residual oil was chromatographed on silica (5 g) using gradient elution with 0—6% methanol–chloroform as eluant. Fractions containing pure product were

combined and evaporated to yield the *ethyl ester* (1f) (0.242 g, 68%), m.p. 96.5—97.5 °C; $\nu_{max.}$ ($CHCl_3$) 3 420, 1 710, 1 645, and 980 cm^{-1}; $\lambda_{max.}$ (EtOH) 222 nm (ε 11 600); δ_H ($CDCl_3$) 0.99 (3 H, d, 17-H_3), 1.14 (3 H, d, 14-H_3), 1.27 (3 H, t, OCH_2Me), 2.20 (3 H, d, 15-H_3), 4.13 (2 H, q, OCH_2Me), 5.44 (total 2 H, m, 10- and 11-H), and 5.76 (1 H, m, 2-H); δ_C ($CDCl_3$) 166.9 [C(1)], 157.0 [C(3)], 134.4 and 129.3 [C-(10) and -(11)], 117.5 [C(2)], 74.8 [C(5)], 71.3 [C(13)], 70.3 [C(7)], 68.9 [C(6)], 64.9 [C(16)], 59.6 (OCH_2Me), 44.6 [C(12)], 43.1 [C(4)], 42.0 [C(8)], 32.4 [C(9)], 20.4 [C(14)], 19.2 [C(15)], 16.6 [C(17)], and 14.3 p.p.m. (OCH_2CH_3) (Found: C, 64.2; H, 9.3. $C_{19}H_{32}O_6$ requires C, 64.0; H, 9.1%).

Epoxidation of Methyl Pseudomonate C (1b).—A solution of methyl pseudomonate C (0.498 g) in THF (5 ml) was treated with *N,O*-bis(trimethylsilyl)acetamide (0.816 ml) at 0 °C. The solution was stirred at room temperature for 2 h and was then evaporated to dryness and the residue was dried at 55 °C/1 mmHg for 1 h. The resulting tris(trimethylsilyl) ether was dissolved in dichloromethane (5 ml) and the solution was cooled to 0 °C. *m*-Chloroperbenzoic acid (0.193 g) was added to the solution which was subsequently stirred at 0 °C for 0.5 h, and for 2 h at room temperature. Saturated aqueous sodium hydrogen carbonate (15 ml) was added to the reaction mixture, followed by extraction with ethyl acetate (5 × 20 ml). The extracts were combined, washed with brine, dried ($MgSO_4$), and evaporated to dryness to afford a residual oil which was chromatographed on silica (10 g) using gradient elution with 0—6% methanol–chloroform as eluant. Fractions containing the epoxides [R_F 0.39, $CHCl_3$–MeOH (9 : 1)] were combined and evaporated to dryness to yield a mixture of the epimeric epoxides (8a) and (2b) (0.24 g, 47%) in a 2 : 1 ratio; [h.p.l.c., using a Waters Associates μ-porasil column with acetonitrile (containing 2% water)–dichloromethane (3 : 7) as eluant]; $\lambda_{max.}$ (both epimers) (EtOH) 219 nm (ε 14 750); δ_H (mixture) (CD_3OD) 0.95 (each 3 H, 2 × d, 17-H_3), 1.17 (each 3 H, 2 × d, 14-H_3), 2.17 (3 H, d, 15-H_3), 3.63 (3 H, s, OMe), 4.06 (2 H, t, 9′-H_2), and 5.73 (1 H, s, 2-H); δ_C *major isomer* (8a) (CD_3OD) 175.4 [C(1′)], 167.9 [C(1)], 158.6 [C(3)], 118.0 [C(2)], 75.9 [C(5)], 71.5 [C(13)], 70.4 [C(7)], 69.6 [C(6)], 65.6 [C(16)], 64.5 [C(9′)], 62.6 [C(11)], 58.9 [C(10)], 51.8 (OMe), 44.2 [C(4) and -(12)], 41.0 [C(8)], 34.5 [C(2′)], 32.7 [C(9)], 29.9 [C-(4′), -(5′), and -(6′)], 29.5 [C(8′)], 26.7 [C(7′)], 25.7 [C(3′)], 21.2 [C(14)], 19.2 [C(15)], and 13.2 p.p.m. [C(17)]; *minor isomer* (2b) (CD_3OD) 175.4 [C(1′)], 167.9 [C(1)], 158.6 [C(3)], 118.0 [C(2)], 75.9 [C(5)], 71.3 [C(13)], 70.4 [C(7)], 69.6 [C(6)], 66.1 [C(16)], 65.5 [C(9′)], 61.0 [C(11)], 56.5 [C(10)], 51.8 (OMe), 43.8 [C(12)], 43.4 [C(4)], 41.2 [C(8)], 34.5 [C(2′)], 32.7 [C(9)], 29.9 [C-(4′), -(5′), and -(6′)], 29.5 [C(8′)], 26.7 [C(7′)], 25.7 [C(3′)], 20.3 [C(14)], 19.2 [C(15)], and 12.2 p.p.m. [C(17)]; *m/z* (both isomers) (rel. int.) 514 (M^+, 1%), 496 (2), 478 (3), 465 (2), 452 (2), 412 (4), 327 (7), 270 (25), and 227 (100) (Found: M^+, 514.3104. $C_{27}H_{46}O_9$ requires *M*, 514.3142).

Epoxidation of Methyl Monate C (1e).—A solution of methyl monate C (0.1 g) in THF (2 ml) was treated with *N,O*-bis(trimethylsilyl)acetamide (0.196 g) at 0 °C. The solution was stirred at room temperature for 2 h and was then evaporated to dryness under reduced pressure. The residue was dried at 55 °C and 1 mmHg for 2 h. The tris(trimethylsilyl) ether was dissolved in dichloromethane (2 ml), *m*-chloroperbenzoic acid (0.056 g) was added, and the mixture was stirred at 0 °C for 0.5 h and then at room temperature for 2 h. Saturated aqueous sodium hydrogen carbonate was then added to the reaction mixture and the product was extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$), and evaporated to dryness to yield an epimeric mixture of epoxides (8b) and (2e) (60 mg, 57%) in a 2 : 1 ratio. [h.p.l.c. using a Waters Associates μ-Porasil column with acetonitrile (containing 2% water)–dichloromethane (3 : 7) as eluant]; $\nu_{max.}$ (both epimers) ($CHCl_3$) 3 400, 1 718, and 1 646 cm^{-1}; $\lambda_{max.}$ (both epimers) (EtOH) 219 nm (ε 12 500); δ_H (mixture) (CD_3OD) 0.95 (each 3 H, 2 × d, 17-H_3), 1.18 (each 3 H, 2 × d, 14-H_3), 2.16 (3 H, d, 15-H_3), 3.64 (3 H, s, OMe), and 5.75 (1 H, s, 2-H); δ_C *major isomer* (8b) (CD_3OD) 168.7 [C(1)], 159.3 [C(3)], 117.9 [C(2)], 76.2 [C(5)], 71.8 [C(13)], 70.7 [C(7)], 69.9 [C(6)], 65.9 [C(16)], 63.0 [C(11)], 59.3 [C(10)], 51.2 (OMe), 44.6 [C(12)], 44.0 [C(4)], 41.3 [C(8)], 33.0 [C(9)], 21.5 [C(14)], 19.3 [C(15)], and 13.3 p.p.m. [C(17)]; *minor isomer* (2e) (CD_3OD) 168.7 [C(1)], 159.3 [C(3)], 117.9 [C(2)], 76.2 [C(5)], 71.6 [C(13)], 70.7 [C(7)], 69.9 [C(6)], 66.4 [C(16)], 61.3 [C(11)], 56.9 [C(10)], 51.2 (OMe), 43.8 [C(4)], 43.7 [C(12)], 41.6 [C(8)], 33.0 [C(9)], 20.4 [C(14)], 19.3 [C(15)], and 12.3 p.p.m. [C(17)]; *m/z* (both isomers) (rel. int.) 358 (M^+, 1%), 327 (3), 264 (6), 227 (63), and 111 (84) (Found: M^+, 358.1986. $C_{18}H_{30}O_7$ requires *M*, 358.1990).

Crystal Structure Determination of Compound (1f).—*Crystal data.* $C_{19}H_{32}O_6$, $M = 356.5$, monoclinic, $a = 26.278(3)$, $b = 7.105(2)$, $c = 11.205(2)$ Å, $\beta = 101.2(1)°$, $U = 2\,052.2$ Å^3, $D_c = 1.15$, $D_m = 1.14$ g cm^3, $F(000) = 776$. Space group *C*2, Mo—K_α radiation (graphite monochromator), $\lambda = 0.710\,69$ Å, $\mu = 0.41$ cm^{-1}.

Unfortunately, we were obliged to use a crystal which was much too large for accurate work, and so results of the highest quality were not expected.

The crystal parameters were initially found from oscillation and Weissenberg photographs and were refined by least-squares from the setting angles of 23 reflections measured on a Hilger–Watt Y290 four-circle diffractometer. Reflections were scanned for $\theta \leqslant 27.5°$ (ω–2θ scan mode) and, of the total of 2573 measured, 2190 had $I \geqslant 3\sigma I$ and were deemed observed and were used in the refinement. Lorentz and polarisation corrections, but not absorption corrections, were made.

The structure was determined by direct methods using MULTAN,[19] but was by no means straightforward, some six attempts under different conditions being made before a recognisable fragment of 16 atoms could be identified. Development of this fragment into the complete structure by Fourier methods gave no further problems. Final refinements were made by full-matrix least-squares with carbon and oxygen thermal parameters treated anisotropically and with hydrogen atoms included in fixed positions which were mainly calculated, but where this was not possible (*e.g.* in the group CH_3–C=C) the positions found from a difference map were used. One hydrogen atom, that on the hydroxy-group at C(6), could not be located and was omitted from the calculation. The discrimination between oxygen and carbon was based partly on chemical considerations and partly on the evidence of isotropic thermal parameters in calculations in which all atoms were treated as carbon.

A final *R*-value of 6.6% was obtained, which is satisfactory considering the size of the crystal used. Standard deviations of bond lengths not involving hydrogen atoms ranged from 0.004—0.013 Å, and of angles, from 0.27—0.67°.

Table 1 lists the fractional co-ordinates for compound (1f). Tables 2 and 3 show bond lengths and bond angles, respectively, and the Figure shows a perspective drawing of the molecule. The absolute configuration is inferred from that of pseudomonic acid A (2a),[5] from which the ester (1f) can be chemically derived.

Apart from MULTAN, crystallographic computations were carried out using the Oxford ' CRYSTALS ' package [20] and the drawings were prepared using PLUTO.[21] The thermal

parameters for compound (1f) and listings of the observed and calculated structure factors are available in Supplementary Publication No. SUP 23394 (19 pp.)*

Acknowledgements

We thank Mr J. Tyler and Mr G. Hill for technical assistance.

References

1 Part 4, S. Coulton, P. J. O'Hanlon, and N. H. Rogers, *J. Chem. Soc., Perkin Trans.* **1**, 1982, 729.
2 J. P. Clayton, P. J. O'Hanlon, and N. H. Rogers, *Tetrahedron Lett.*, 1980, **21**, 881.
3 A. T. Fuller, G. Mellows, M. Woolford, G. T. Banks, K. D. Barrow, and E. B. Chain, *Nature (London)*, 1971, **234**, 415.
4 E. B. Chain and G. Mellows, *J. Chem. Soc., Chem. Commun.*, 1974, 847; *J. Chem. Soc., Perkin Trans. 1*, 1977, 294.
5 R. G. Alexander, J. P. Clayton, K. Luk, and N. H. Rogers, *J. Chem. Soc., Perkin Trans. 1*, 1978, 561.
6 E. B. Chain and G. Mellows, *J. Chem. Soc., Perkin Trans. 1*, 1977, 318.
7 J. P. Clayton, K. Luk, and N. H. Rogers, *J. Chem. Soc., Perkin Trans. 1*, 1979, 308.
8 J. P. Clayton, R. S. Oliver, N. H. Rogers, and T. J. King, *J. Chem. Soc., Perkin Trans. 1*, 1979, 838.
9 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734, 736.
10 J. M. Behan, R. A. W. Johnson, and M. J. Wright, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1216.
11 G. Wittig and W. Haag, *Chem. Ber.*, 1955, **88**, 1654.
12 K. B. Sharpless, M. A. Umbreit, M. T. Nich, and T. C. Flood, *J. Am. Chem. Soc.*, 1972, **94**, 6538.
13 P. E. Sonnet and J. E. Oliver, *J. Org. Chem.*, 1976, **41**, 3279.
14 P. E. Sonnet, *J. Org. Chem.*, 1978, **43**, 1841.
15 D. J. Clive and C. V. Denyer, *J. Chem. Soc., Chem. Commun.*, 1973, 253.
16 S. M. Kupchan and M. Maruyama, *J. Org. Chem.*, 1971, **36**, 1187.
17 J. Rémion, W. Dumont, and A. Krief, *Tetrahedron Lett.*, 1976, 1383.
18 A. P. Kozikowski, R. J. Schmiesing, and K. L. Sorgi, *J. Am. Chem. Soc.*, 1980, **102**, 6580.
19 G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, 1971, **27**, 368.
20 W. R. Carruthers, personal communication.
21 W. D. S. Motherwell, Cambridge Data Centre, personal communication.

Received, 15*th February* 1982; *Paper* 2/279

* For details, see Notice to Authors No. 7, in *J. Chem. Soc., Perkin Trans. 1*, 1981, Index issue.