Acknowledgment. We thank The National Institutes of Health (Grant CA 30065) for their generous financial support. We also thank the BSRG Committee for partial support from BSRG Grant SO7BR07157 awarded by the Biomedical Research Support Grant Program, Dr. Richard Heppner of the Laramie Energy Technology Center for determining mass spectra, The National Science Foundation (Grant CHE-8026553) for funds to purchase a JEOL 270-MHz NMR spectrometer, and Drs. J. J. Partridge, Jr., W. G. Salmond, and R. Chorvat for various authentic samples.

Registry No. 4, 55064-27-2; **6** (R = CH_3), 84051-40-1; **6** (R = C_4H_9), 84029-11-8; **6** (R = C_6H_5), 78905-13-2; **7**, 35961-41-2; **8**, 84056-75-7; **10**, 84056-76-8; **11**, 84051-41-2; **11** (methylsulfinyl derivative), 84051-42-3; **11** (methylsulfonyl derivative), 84051-43-4; **11** (desulfurized dienol), 84051-44-5; **12**, 55064-27-2; i (R = CH_3, R_2' = $(CH_2)_{11}$), 84051-45-6; i (R = C_4H_9, R_2' = $(CH_2)_{11}$), 84051-46-7; i (R = C_6H_5, R_2' = $(CH_2)_{11}$), 83862-54-8; i (R = C_6H_5, R_2' = 3β-tetrahydropyranyloxy-preg-5-en-20-yl), 79409-72-6; i (R = C_6H_5, R_2' = 6β-methoxy-3α,5α-cyclopregnan-20-yl), 84051-47-8; i (R = C_6H_5, R_2' = 3β-methoxy-5-pregnen-20-yl), 83862-55-9; ii (R, R″ = CH_3, R_2' = $(CH_2)_{11}$), 84051-48-9; ii (R = C_4H_9, R_2' = $(CH_2)_{11}$, R″ = CH_3), 84051-49-0; ii (R = C_6H_5, R_2' = $(CH_2)_{11}$, R″ = CH_3), 84051-50-3; ii (R = C_6H_5, R_2' = 3β-tetrahydropyranyloxypreg-5-en-20-yl, R″ = CH_3), 84051-51-4; ii (R = C_6H_5, R_2' = 3β-tetrahydropyranyloxypreg-5-en-20-yl, R″ = C_2H_5), 84056-77-9; ii (R = C_6H_5, R_2' = 6β-methoxy-3α,5α-cyclopregnan-20-yl, R″ = CH_3), 84051-52-5; ii (R = C_6H_5, R_2' = 3β-methoxy-5-pregnen-20-yl, R″ = CH_3), 84051-53-6; iii (R = CH_3, R_2' = $(CH_2)_{11}$, R″ = CH_3, R‴ = H), 84051-54-7; iii (R = C_6H_5, R_2' = 3β-tetrahydropyranyloxy-preg-5-en-20-yl, R″ = CH_3, R‴ = H), 84051-55-8; iii (R = C_6H_5, R_2' = 3β-methoxy-5-pregnen-20-yl, R″ = CH_3, R‴ = H), 84051-56-9; iii (R = C_6H_5, R_2' = 3β-methoxy-5-pregnen-20-yl, R‴, R‴ = CH_3), 84056-97-3; iii (R = C_6H_5, R_2' = 3β-methoxy-5-pregen-20-yl, R″ = CH_3, R‴ = C_2H_5), 84051-57-0; $NiCl_2$, 7718-54-9; cyclododecanone, 830-13-7; 6β-methoxy-3α,5α-cyclopregnan-20-one, 32249-55-1; 3β-methoxy-5-pregnen-20-one, 511-26-2; 3-pentanone, 96-22-0; acetone, 67-64-1.

Total Synthesis of (+)-Methyl Pseudomonate C from Carbohydrates

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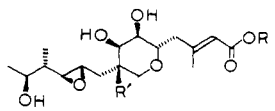
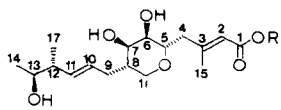
Pseudomonic acids A (**1a**), B (**1b**), and C (**1c**) are members



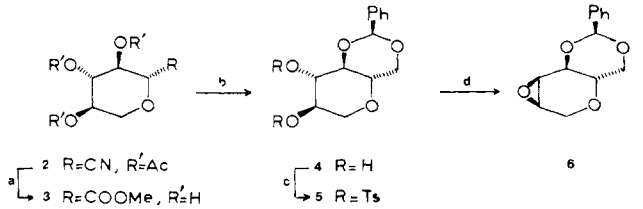
1a R = $(CH_2)_8COOH$, R′ = H
1b R = $(CH_2)_8COOH$, R′ = OH



1c R = $(CH_2)_8COOH$
1d R = $(CH_2)_8COOMe$
1e R = Et

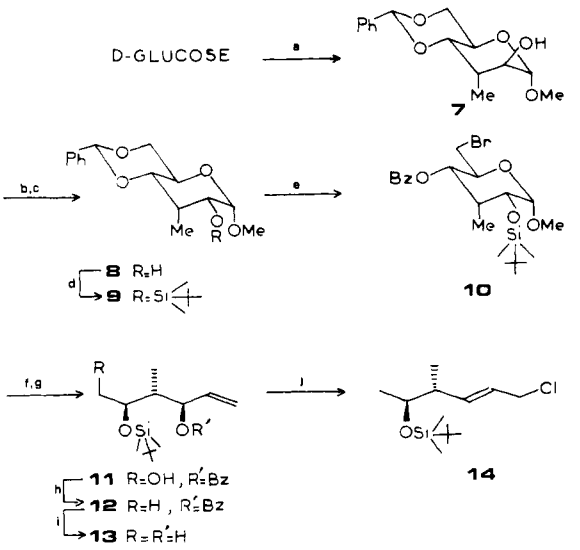
of a new group of metabolites with antimicrobial and antimycoplasmal activity, produced by submerged fermentations of a strain of *Pseudomonas fluorescens*.[1-3] The stability and the natural scarcity of pseudomonic acid C, which has been isolated[3] as its methyl ester **1d**, qualify it as an attractive synthetic target. We report the first enantiospecific total synthesis of **1d**, which makes use of carbohydrates as chiral templates. While this work was in progress, total syntheses of (±)-pseudomonic acid C emerged.[4,5]

Scheme I[a]



[a] Reagents: (a) (1) MeONa, (2) NaOH, (3) MeOH–HCl, 70%; (b) (1) $LiAlH_4$, (2) $PhCH(OMe)_2$, TsOH, 85%; (c) TsCl, pyridine, 70%; (d) MeONa, $CHCl_3$, room temperature, 24 h, quantitative.

Scheme II[a]



[a] Reagents: (a) Reference 24; (b) DCCI–DMSO–TFA–pyridine, room temperature, 2 h; (c) $LiAlH_4$, Et_2O, 0 °C, 30 min, 95% from **7**; (d) TBDMSCl, imidazole, DMF, room temperature, 12 h, 83%; (e) NBS, $BaCO_3$, CCl_4, 80 °C, 1.5 h, 75%; (f) acid washed Zn (100 equiv) 9:1 propanol–water (v/v), 80 °C, 30 min; (g) $NaBH_4$, EtOH, −35 °C, 30 min, 50% from **10**; (h) (1) TsCl, pyridine, room temperature, 12 h, (2) NaI, $H_3CC(O)C_2H_5$, 80 °C, 10 h, (3) $NaBH_4$, Me_2SO, room temperature, 12 h, 60%; (i) MeONa, MeOH, room temperature, quantitative; (j) $SOCl_2$, pyridine, 0 °C, 1.5 h, 88%.

Other synthetic efforts have been published,[6] giving evidence of the popularity of this target.

The crystalline cyanide **2**, readily available[7] from D-xylose, was converted into the ester **3**,[8] then into the acetal **4**. Tosylation of **4** produced **5**, which was next *quantitatively* converted into the epoxide **6**, as illustrated in Scheme I. No trace of the isomeric epoxide was present in the reaction mixture.[9]

Our approach was based on the idea that the rigid tricyclic epoxide **6** would probably undergo a regiospecific opening upon treatment with a suitable allylic anion, thus adorning the core with the left side appendage. With this idea in mind we then prepared the chiral chloride **14** from D-glucose, as shown in Scheme II. The key reaction of this sequence was the treatment of the bromide **10** with activated zinc,[10] generating an aldehyde which was reduced into the alcohol **11**.

The copper-catalyzed[11] (CuI) ring opening of epoxide **6** with Grignard reagent derived from **14** (2 equiv, THF, −30 °C, 10 min)

(1) Alexander, R. G.; Clayton, J. P.; Luk, K.; Rogers, N. H.; King, T. J. *J. Chem. Soc., Perkin Trans. 1* **1978**, 561.
(2) Chain, E. B.; Mellows, G. *J. Chem. Soc., Perkin Trans. 1* **1977**, 318.
(3) Clayton, J. P.; O'Hanlon, P. J.; Rogers, N. H. *Tetrahedron Lett.* **1980**, *21*, 881.
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(6) (a) Raphael, R. A.; Stibbard, J. H. A.; Tidbury, R. *Tetrahedron Lett.* **1982**, *23*, 2407. (b) Fleet, G. W. J.; Gough, M. J. *Ibid.* **1982**, *23*, 4509.
(7) Helferich, B.; Ost, W. *Ber. Dtsch. Chem. Ges.* **1962**, *95*, 2612.
(8) Satisfactory NMR and analytical data (combustion and/or mass spectral analyses) have been obtained for all compounds. The complete data will appear in a full paper.
(9) Unambiguous stereostructural assignments of the epoxide **6** are reported in the supplementary material.
(10) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990. Nakane, M.; Hutchinson, C. R.; Gollman, H. *Tetrahedron Lett.* **1980**, *21*, 1213.
(11) Huyn, C.; Derguini-Boumechal, F.; Linstrumelle, G. *Tetrahedron Lett.* **1979**, *20*, 1503.

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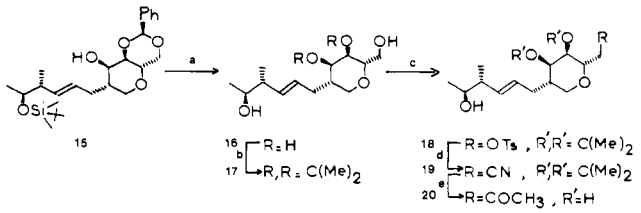
Scheme III[a]



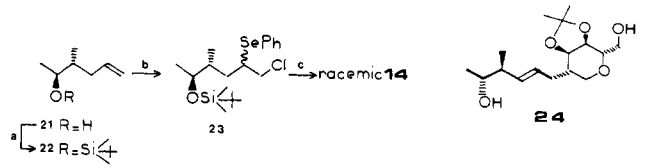
[a] Reagents: (a) 4:1 dioxane-1 N HCl, (v/v) room temperature, 6 h, 97%; (b) acetone, 0.5% H_2SO_4, molecular sieve 4 Å, room temperature, 20 min, 77%; (c) 1.1 equiv of TsCl, Et_3N, DMAP, CH_2Cl_2, room temperature, 1.5 h, 96%; (d) KCN, HMPT, crown ether (18-crown-6), room temperature, 12 h, 94.5%; (e) $AlMe_3$, $Ni(acac)_2$, PhMe, 0 °C, 6 h, then (a), 84%.

afforded the expected product **15** in 43% yield. This reaction is characterized by the regiospecificity of the nucleophilic ring opening of the epoxide, the regiospecific formation, from the allylic Grignard reagent, of the "normal", i.e., "nonrearranged" addition product, and finally the formation of a *E* double bond,[12] these last two features being critical and far from obvious.[13] Acid hydrolysis of **15** gave the polyol **16**, which then converted into the acetonide derivative **17**[14] (Scheme III).

The use of the costly chiral chloride **14** can be averted by that of the racemic form, prepared in three steps from the easily available alcohol **21**,[13a,15] taking up an idea introduced by Raucher[16] (Scheme IV). Entry of the racemic chloride **14** into the previously described methodology finally gave two stereoisomers (ratio 1:1) separable on a silica gel column (3:1 toluene–acetone, v/v): **17**, fully identical with the compound previously prepared, and **24**.

Selective tosylation of **17** afforded **18**; treatment with potassium cyanide produced **19**. After extensive experimentation, the ketone **20** was obtained in 84% yield upon treatment of the cyanide **19** with trimethylaluminum in the presence of $Ni(acac)_2$,[17] followed by acid hydrolysis.[18] Elongation of the right side chain was essentially performed along lines already described.[4,19] Silylation of the ketone **20** (BSA,CH_3CN, room temperature, 12 h), reaction with the anion of ethyl diethylphosphonoacetate (dioxane, room

Scheme IV[a]



[a] Reagents: (a) TBDMSCl, imidazole, DMF, room temperature, 30 min, 96%; (b) PhSeCl, CCl_4, 0 °C, 15 min; (c) H_2O_2, pyridine, 0 °C, 20 min, then room temperature, 3 h, 72% from **22**.

temperature, 12 h), and desilylation (4:1 dioxane–1 NHCl, v/v, room temperature, 10 min) gave predominantly ethyl monate C (**1e**;[21] 82.4%), easily separated from the *Z* isomer (12.2% yield) on a silica gel column (13:1 CH_2Cl_2–MeOH, v/v). Saponification of the ester **1e** (aqueous 1 N NaOH, 30 equiv, room temperature, 1 h, then 65 °C, 5 min) and treatment of the isolated sodium salt with methyl 9-iodononanoate[22] (DMF, room temperature, 3 h) produced methyl pseudomonate C (**1d**), identical with the natural substance isolated by the Beecham group (TLC in various solvents, optical rotation, ^1H and ^{13}C NMR).

Since methyl pseudomonate C can be converted to pseudomonic acids A[23] and C,[5] the present work also constitutes formal total synthesis of pseudomonic acids A and C.

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Supplementary Material Available: Spectral information and physical constants for key substances (6 pages). Ordering information is given on any current masthead page.

(12) Tiny amounts of *Z* isomer ($E/Z > 25$) were easily removed by silica gel chromatography in the subsequent steps.

(13) For discussions on these features, see: (a) Felkin, H.; Frajerman, C.; Roussi, G. *Bull. Soc. Chim. Fr.* **1970**, 3704. (b) Glaze, W. H.; Duncan, D. P.; Berry, D. J. *J. Org. Chem.* **1977**, *42*, 694. (c) Linstrumelle, G.; Lorne, R.; Dang, H. P. *Tetrahedron Lett.* **1978**, 4069. For a recent discussion on the η^1 structure ("σ compound") of allylic Grignard compounds, see: Schlosser, M.; Stähle, M. *Angew. Chem., Int. Ed. Engl.* **1980**, 487.

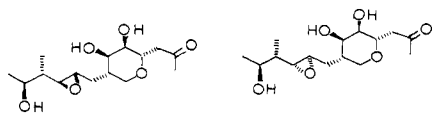
(14) The trans geometry of the C-10, C-11 double bond was clearly established[3] from the ^1H NMR spectrum of the ketal **17** in $CDCl_3$ after addition of 1 equiv of $Eu(fod)_3$, which induces a sufficient separation in the chemical shifts between H-10 and H-11 to enable measurement of the coupling constant, $J_{10,11} = 16$ Hz.

(15) cis-Epoxybutane was prepared according to Pasto and Lumbo: Pasto, D. J.; Lumbo, C. C. *J. Org. Chem.* **1965**, *30*, 1271.

(16) Raucher, S. *Tetrahedron Lett.* **1977**, 3909.

(17) Bagnell, L.; Jeffery, E. A.; Meisters, A.; Mole, T. *Aust. J. Chem.* **1974**, *27*, 2577.

(18) Epoxidation of **20** with MCPBA (CH_2Cl_2, room temperature, 1.5 h) afforded a product (80% yield) that was chromatographically identical (TLC in various solvents) with the ketone obtained from pseudomonic acid A.[19] However, as shown by GLC, this was a mixture of i and ii in a ratio of about 2:3. This ratio was confirmed by ^{13}C NMR, where all the signals belonging to the synthetic sample i were fully identical with those of the sample derived from the natural antibiotic. After GLC (capillary column, CP SIL 5, 25 m × 0.25 mm, 210 °C) the mass spectra of both TMS synthetic and provided samples were identical. Epoxidation with TBHP–$VO(acac)_2$[20] did not significantly enhance production of the isomer i (1:1 ratio).



(19) Clayton, J. P.; Luk, K.; Rogers, N. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 308.

(20) Sharpless, K. P.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

(21) Identical with a sample provided by the Beecham group.

(22) Methyl 9-iodononanoate was prepared from the monomethyl ester of azelaic acid (a, $SOCl_2$; b, $NaBH_4$, dioxane; c, NIS, PPh_3, CH_2Cl_2).

(23) Kozikowski, A. P.; Schmiesing, R. J.; Sorgi, K. L. *Tetrahedron Lett.* **1981**, *22*, 2059.

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Vinylcyclopropene Triplet Rearrangement Mechanisms: Mechanistic and Exploratory Organic Photochemistry[1,2]

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In previous studies on vinylcyclopropene photochemistry considerable attention has been focused on the rearrangements deriving from the triplet excited state.[3-6] We now have evidence excluding two especially reasonable reaction mechanisms and establishing a mechanism previously thought to have only minor significance. This single mechanism accounts for all of the known triplet cyclopropene to cyclopentadiene rearrangements.

Thus, our earlier work[3,5,6] considered several triplet mechanisms outlined in Scheme I. Mechanism B involved a triplet three-ring opening to afford a carbene which then rearranged to cyclo-

(1) This is Paper 138 of our photochemical series.

(2) (a) For Paper 137 note: Zimmerman, H. E. *Chimia* **1982**, *36*, 423-428. (b) For Paper 136 see: Zimmerman, H. E. *Acc. Chem. Res.* **1982**, *15*, 312-317.

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