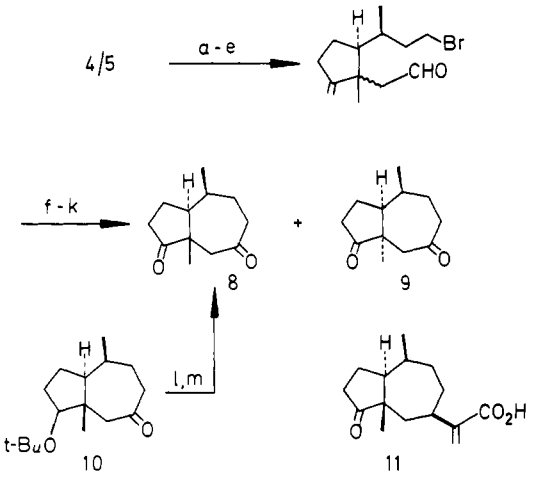
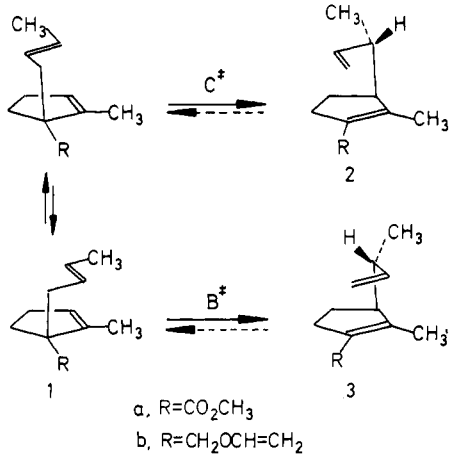
Scheme I[a]



[a] (a) $HC(OCH_3)_3$, CH_3OH, *p*-TsOH; (b) $(sia)_2BH$; H_2O_2, NaOH;[10] (c) MsCl, Et_3N;[11] (d) LiBr, acetone; (e) H_3O^+; (f) KCN, HOAc, C_2H_5OH; (g) $CH_2{=}CHOC_2H_5$, *p*-TsOH; (h) LDA, THF;[12] (i) H_3O^+; (j) KOH, CH_3OH; (k) O_3; (l) CF_3CO_2H; (m) $CrO_3 \cdot C_5H_5N \cdot HCl$.[13]

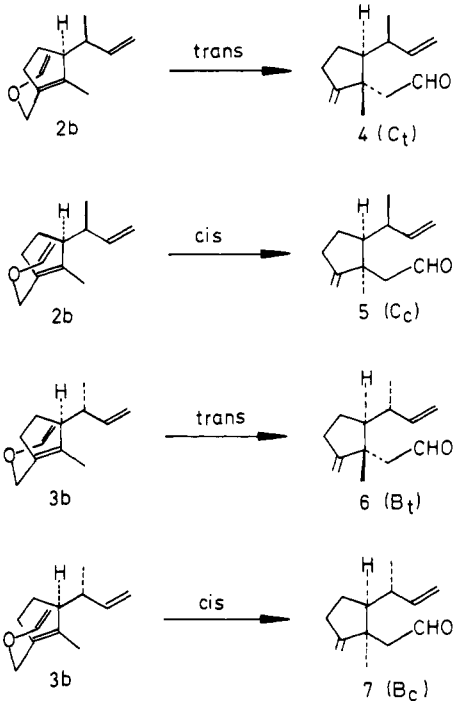
Scheme II



Thus, the lowest energy reaction pathway for the Cope rearrangement of **1b** proceeds through a chairlike transition state to produce **2b** (Scheme II) followed by Claisen rearrangement on the less hindered α face of the five-membered ring, giving rise to **4** (C_t),[7] having the butenyl and acetaldehyde chains in a trans arrangement (Scheme III).

The structure of the minor component **5** was established by deliberately generating Cope products derived from a boatlike transition state. To this end, ester **1a** was thermolyzed to produce a 60:40 equilibrium mixture of **1a**/(**2a** + **3a**). The ratio **2a**/**3a** was shown to decrease with time at a given temperature (266 °C, 0.5 h, 93:7; 263 °C, 2 h, 82:18; 266 °C, 4 h, 75:25; 235 °C, 6 h, 95:5) as witnessed by the increase of the high-field methyl doublet (270 MHz) at δ 0.83 (**3a**) relative to its counterpart at δ 1.06 (**2a**). A mixture of esters **1a**/(**2a** + **3a**) (60:40) was converted by successive $LiAlH_4$ reduction and vinylation to a mixture of vinyl ethers **1b**[8] (60%) and **2b** + **3b** (40%). A VPC collected sample of **2b** + **3b** (**2b**/**3b** = 79:21) was thermolyzed at 180 °C (14 h)[9] to effect Claisen rearrangement, providing an

Scheme III



NMR (270 MHz) detectable mixture of three aldehydes in a ratio of 67:14:19 (integration of aldehyde protons). While the first two of these aldehydes were assignable to the previously observed thermolysis products **4** (C_t) and **5** (C_c), the third component [NMR (270 MHz) δ 9.64 (dd, J = 4, 2 Hz, CHO, singlet upon irradiation of CH_2CHO), 1.02 (s, R_3CCH_3), 0.99 (d, J = 7 Hz, R_2CHCH_3)] was ascribable to **6** (B_t), arising from **3b**. Therefore, the minor component of the Cope–Claisen rearrangement of **1b** must arise from a chairlike Cope rearrangement and a Claisen rearrangement cis to the butenyl side chain as represented in **5** (C_c).

If the rate of the Cope–Claisen rearrangement of **1b** were appreciable at 180 °C, the extrapolated (ln **4**/**5** vs. $1/T$) ratio **4**/**5** would be 88:12. If it is assumed that the same selectivity applies for the formation of **6** and **7** from **3b**, then the relative distribution of products should be **4** (C_t):**5** (C_c):**6** (B_t):**7** (B_c) or 70% (88 × 79):9% (12 × 79):18% (88 × 21):3% (12 × 21). The ratio **4**/**5**/**6** is in good agreement with the observed values. The component **7** (B_c) could not be detected.

Acknowledgment. This research was supported by a grant from the National Cancer Institute, National Institutes of Health (CA16432). The 270-MHz NMR spectrometer is supported by Grant CHE-7916210 from the Chemistry Division of the National Science Foundation.

(7) This designation refers to the transition states required to form **4**. Thus, "C" refers to the chairlike transition state of the Cope rearrangement while the subscript "t" indicates trans arrangement of the acetaldehyde and butenyl groups in the product of the Claisen rearrangement.
(8) The *Z* isomer of **1b** was not detected.
(9) Thermolysis of a mixture of **2b** + **3b** (**2b**/**3b** = 82:18) for 3 h at 180 °C indicated 38% conversion to products **4**, **5**, and **6** with no sign of retro-Cope product **1b**.
(10) Brown, H. C.; Liotta, R.; Scouten, C. G. *J. Am. Chem. Soc.* **1976**, *98*, 5297.
(11) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.
(12) Stork, G.; Maldonado, L. *J. Am. Chem. Soc.* **1971**, *93*, 5286.
(13) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

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Received June 13, 1980

Total Synthesis of Pseudomonic Acid C: Application of the Alkoxyselenation Reaction in Organic Synthesis

Sir:

Pseudomonic acids A (**1a**) and B (**1b**) are antimicrobially active acidic substances produced by a strain of *Pseudomonas fluorescens* (NCIB 10586). The patent literature abounds with reports of the good activity in vitro of the major metabolite **1a** against

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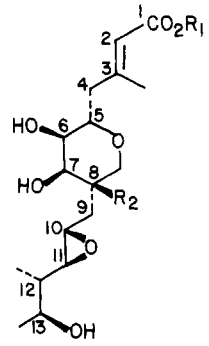
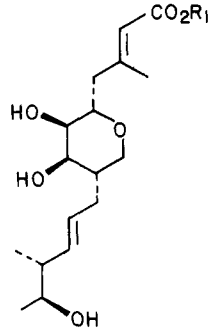


1a $R_1 = (CH_2)_8CO_2H$; $R_2 = H$
1b $R_1 = (CH_2)_8CO_2H$; $R_2 = OH$
1c $R_1 = (CH_2)_8CO_2Me$; $R_2 = H$
1d $R_1 = C_2H_5$; $R_2 = H$

Neisseria gonorrhoeae, *Haemophilus influenzae*, and most *Mycoplasma* species.[1] Pseudomonic acid A does not show cross-resistance with other commonly used antibiotics and is effective against multiple strains of *S. aureus*.[2]

The structure of **1a** was established by NMR, mass spectral, and degradative studies of its methyl ester and various derivatives.[3] X-ray analysis of a derivative prepared from the ozonolysis product of methyl pseudomonate A (**1c**) has confirmed this structural assignment and also provided the absolute stereochemistry.[4] The pseudomonic acids are not readily classified on a structural basis with any of the known antibiotic groups. The nearest relatives of **1** are the polycyclic polyether monocarboxylic acids such as nigericin, monensin, and alborixin, compounds that function as antibiotics by influencing cation transport across membranes.

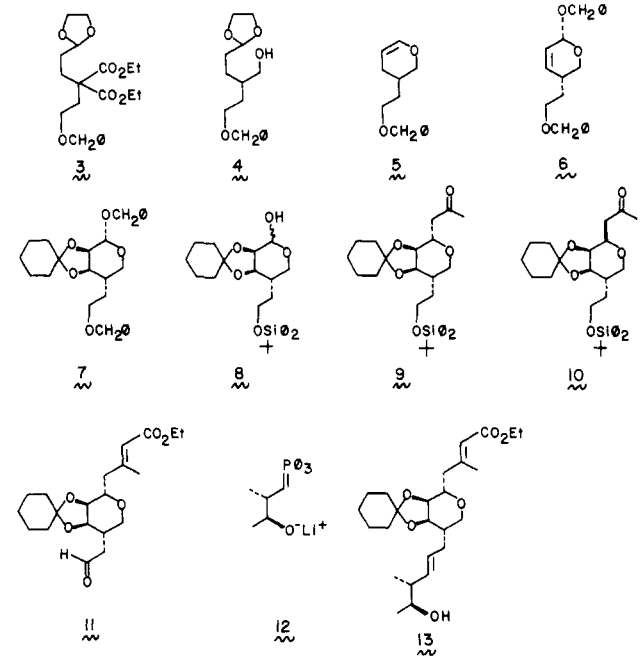
Very recently, the isolation and structural characterization of the third member of this novel class of antibiotics have been disclosed.[5] This compound, which has been designated pseudomonic acid C (**2a**), lacks the epoxide oxygen present in the other



2a $R_1 = (CH_2)_8CO_2H$
2b $R_1 = (CH_2)_8CO_2Me$
2c $R_1 = C_2H_5$

two metabolites. Because of this structural difference, pseudomonic acid C retains its biological activity under both mild acid and alkaline conditions, conditions under which pseudomonic acid A rearranges with total loss of antibiotic activity. Unequivocal proof of the structure of **2a** has been obtained by the stereospecific conversion of methyl pseudomonate A (**1c**) into methyl pseudomonate C (**2b**).

We now report a total synthesis strategy for assembling pseudomonic acid C. Our synthesis of this special "*C*-glycoside" is based on the anticipated stereoselective alkoxyselenation of the key 3,4-dihydro-2*H*-pyran **5** and the predicted emergence of **9**



as the kinetic product from the Wittig reaction of **8** with acetylmethylenetriphenylphosphorane.[6] While several operationally different approaches were investigated for the construction of the dihydropyran **5**, the most efficient scheme developed to date consists of sequentially alkylating diethyl malonate with β-bromopropionaldehyde ethylene acetal[7] and β-iodoethyl benzyl ether[8] (78% overall). Hydrolysis of the disubstituted diester **3** to the corresponding diacid, followed by decarboxylation and borane reduction, affords **4**. Acidic cleavage of the ethylene acetal yields an unstable cyclic hemiacetal (92% overall from **3**) which is immediately dehydrated in 83% yield to **5** by treatment with a large excess of methanesulfonyl chloride (4 equiv) and triethylamine (8 equiv) in methylene chloride.[9] Benzyloxyselenation of this dihydropyran (phenylselenenyl chloride, benzyl alcohol, triethylamine in THF at room temperature) affords a 2.5:1 mixture (76%) of the chromatographically separable stereoisomers.[10] Oxidation of the major selenide to selenoxide (sodium metaperiodate, sodium bicarbonate, $MeOH/H_2O$) followed by syn elimination (refluxing CCl_4 in the presence of calcium carbonate) yields the *cis*-2-benzyloxy-5,6-dihydro-2*H*-pyran **6** in nearly quantitative yield.[11] Stereospecific vicinal hydroxylation[12] of this intermediate followed by protection of the diol as the cyclohexylidene ketal gives **7** in 95% overall yield. Hydrogenolysis of the benzyl groups (10% Pd/C, ethanol, 92%) and selective protection of the primary alcohol by silylation (*tert*-butyldiphenylsilyl chloride, imidazole, DMF) yield **8** (α/β anomer 85:15)

(1) Rogers, N. H. Ger. Offen. 2706548; *Chem. Abstr.* **1977**, *87*, 201313z. Isagai, K.; Ikeda, Y.; Matsuki, H. Jpn. Kokai 77 70083; *Chem. Abstr.* **1977**, *87*, 182603a. Barrow, K. D.; Mellows, G. Ger. Offen. 2227739, *Chem. Abstr.* **1973**, *83*, 96086s. Clayton, J. P.; Rogers, N. H. Ger. Offen. 2726618; *Chem. Abstr.* **1978**, *88*, 170351z.

(2) Sutherland, R.; Comber, K. R.; Mizen, L. W.; Slocombe, B.; Clayton, J. P. 16th ICAAC Meeting, Abstract 52, 1976.

(3) Chain, E. B.; Mellows, G. *J. Chem. Soc., Perkin Trans. 1* **1977**, 294.

(4) Alexander, R. G.; Clayton, J. P.; Luk, K.; Rogers, N. H.; King, T. J. *J. Chem. Soc., Perkin Trans. 1* **1978**, 561.

(5) Clayton, J. P.; O'Hanlon, P. J.; Rogers, N. H. *Tetrahedron Lett.* **1980**, 881.

(6) The Wittig process has found extensive application in the synthesis of *C*-glyco*furanosides*: Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensen, A. T.; Byran, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602.

(7) Büchi, G.; Wüest, H. *J. Org. Chem.* **1969**, *34*, 1122.

(8) Bennett, G. *J. Chem. Soc.* **1927**, *127*, 1277.

(9) A minor variation in this scheme which may lead to the production of **5** in chiral form consists of substituting Meyers' chiral oxazoline for the diethyl malonate: Meyers, A. I. *Acc. Chem. Res.* **1978**, *11*, 375.

(10) For an examination of the stereochemical course of the alkoxyselenation reaction as applied to other 3,4-dihydropyrans and a general experimental procedure for carrying it out, see: Kozikowski, A. P.; Sorgi, K. L.; Schmiesing, R. J. *J. Chem. Soc., Chem. Commun.* **1980**, 477.

(11) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22.

(12) Van Rheenan, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

which on Wittig reaction with acetylmethylenetriphenylphosphorane (CH_3CN, sealed tube, 170 °C, 10 h, 74%) provides the desired pyran isomer **9** as the major "kinetic product" in addition to the "thermodynamic" product **10** (ratio 2.5:1).[13]

For completion of the synthesis, two additional condensation reactions are carried out in order to elongate the top and bottom chains. Reaction of **9** first with the anion of ethyl diethylphosphonoacetate gives in 97% yield predominantly the α,β-unsaturated ester of *E* geometry contaminated with 20% of the corresponding *Z* isomer.[14] Separation of this mixture by medium-pressure liquid chromatography followed by desilylation (tetrabutylammonium fluoride, 90%) and oxidation (PCC, 76%) of the lower chain hydroxyl group yields aldehyde **11**. The stage is now set for introduction of the additional carbon atoms of the lower side chain by condensation with the ylide **12** derived from (3-hydroxy-2-methylbutyl)triphenylphosphonium iodide. This phosphonium salt is conveniently prepared from tiglic acid by a sequence involving (a) reduction of acid to alcohol through its mixed anhydride ($ClCO_2CH_3$, BH_4^-), (b) hydroboration/oxidation (BH_3·THF; NaOH, H_2O_2) of the olefin,[15] and (c) sequential conversion of the primary hydroxyl group to trimsylate, iodide, and then the phosphonium salt. In model studies, the ylide **12** reacts with benzaldehyde to provide, in accordance with the reported behavior of a related γ-oxido ylide,[16] a disubstituted olefin of predominantly *E* geometry (*E*/*Z* 85:15, 50%).

Reaction of 2 equiv of this ylide (prepared by treating the phosphonium salt with 2 equiv of *n*-BuLi, −78 °C to room temperature, 1 h) with aldehyde **11** (−35 to −20 °C, 1 h, then 3 h, room temperature) followed by deprotection of the diol (50% aqueous acetic acid) produces, however, two major diastereomers in addition to two minor components. ^{1}H NMR (300 MHz) analysis of the two major products, which are easily separable by high-pressure liquid chromatography (high-pressure LC), reveals that one diastereomer contains a C_{10}–C_{11} double bond of *E* geometry and the other diastereomer a C_{10}–C_{11} double bond of *Z* geometry (*E*/*Z* ≃ 60:40).

In order to determine whether the major olefinic product of *E* geometry isolated from the Wittig mixture corresponds to the correct diastereomer, it was deemed necessary to deoxygenate an authentic sample of ethyl monate A (**1d**) kindly provided by Dr. Norman Rogers of Beecham Pharmaceuticals. Deoxygenation is carried out by first trimethylsilylating the hydroxy groups of **1d** and then treating this intermediate with low-valent tungsten chloride (from WCl_6 and 4 equiv of *n*-BuLi) in tetrahydrofuran.[17] Workup with aqueous acetic acid to effect desilylation generates an olefin which by ^{1}H NMR spectroscopy and high-pressure LC consists of >90% of the *E* isomer. This olefin is, in fact, identical with the synthetic material analyzed by 300-MHz ^{1}H NMR, thus leading us to assign structure **13** to the major product formed in the Wittig reaction.

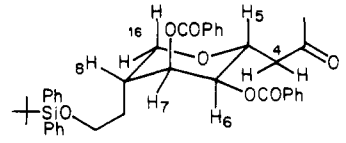
With ethyl monate C (**2c**) thus in hand, the synthesis of pseudomonic acid C is completed by saponifying **2c** with aqueous sodium hydroxide, isolating the sodium salt, and treating it with methyl 9-iodononanoate in DMF/HMPA.[18] The methyl pseudomonate C (**2b**) so generated is identical with the natural material obtained from Beecham Pharmaceuticals by TLC, ^{1}H NMR, IR, and mass spectrometry and can be converted to pseudomonic acid C by hydrolysis with potassium hydroxide/sodium bicarbonate in ethanol/THF. Since methyl pseudomonate A can be converted to pseudomonic acid A (trimethylsilylation followed by potassium hydroxide/sodium bicarbonate hydrolysis and acidic workup), the total synthesis of pseudomonic acid C does also constitute a formal total synthesis of pseudomonic acid A.[19]

In summary, the studies described herein define a "classical" malonic ester approach to the regiocontrolled construction of substituted dihydropyrans. The alkoxyselenation/syn elimination reaction is shown to provide an operationally simple alternative to the more conventional bromoalkoxylation/dehydrobromination reaction for effecting the conversion of 3,4-dihydro-2*H*-pyrans to 2-alkoxy-5,6-dihydro-2*H*-pyrans.[20] The use of the Wittig reaction in the transformation of **8** to **9** does, moreover, constitute one of the very few applications of this chemistry to the synthesis of *C*-glyco*pyranosides* and represents one of the first efforts to establish the stereochemical consequences of this reaction.[21]

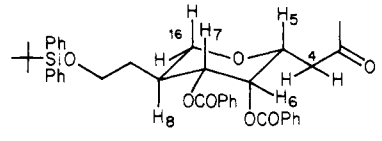
Alternatives to the last Wittig reaction (**11** → **13**) are now being investigated in an effort to improve the overall synthetic scheme.[22]

Acknowledgment. This work was supported by the National Institutes of Health through Grant AI-16138. We are indebted to the National Science Foundation Grant CHE-79-05-185 for providing funds to purchase the 300-MHz Bruker NMR spectrometer used in these studies. The 250- and 600-MHz NMR spectra were obtained on instrumentation at the Mellon Institute maintained by NIH Grant RR-00292 to the Mellon–Pitt–Carnegie

(13) Equilibration does occur under these reaction conditions. This was evidenced by resubjecting pure **9** to these conditions and observing its nearly complete conversion to **10**. For a discussion of the stereochemistry of the Wittig reaction in a related system, see ref 6. The assignment of structure to these Wittig products can be made by examination of the 250-MHz ^{1}H NMR spectra of the corresponding benzoates I and II. The chemical shifts and coupling constants of I are, moreover, closely in line with those reported for the degradation product of pseudomonic acid A, 3,4-bis(benzoyloxy)-5-(5-benzoyloxy-2,3-epoxy-4-methylhexyl)tetrahydropyran-2-ylacetone (ref 2).



I



II

I: IR 1720 (br) cm^{-1}; 250-MHz ^{1}H NMR (CCl_4) δ 8.16–7.13 (m, 20 H), 5.58 (t, 1 H, *J* = 3.2 Hz, H-7), 5.04 (dd, 1 H, *J* = 10, 3 Hz, H-6), 4.40 (oct, 1 H, *J* = 9.6, 8.3, 3.7 Hz, H-5), 3.97 (dd, 1 H, *J* = 11.9, 2.3 Hz, H-16 equatorial), 3.80 (m, 3 H), 3.64 (d, 1 H, *J* = 11.6 Hz, H-16 axial), 2.60 (dd, 1 H, *J* = 16, 8.5 Hz, H-4), 2.44 (dd, 1 H, *J* = 15.5, 4 Hz, H-4), 2.24 (m, 1 H), 2.05 (s, 3 H), 1.33–0.78 (m, 2 H), 1.04 (s, 9 H). II: IR 1720 (br) cm^{-1}; 250-MHz ^{1}H NMR (CCl_4) δ 8.16–7.06 (m, 20 H), 5.44 (d, 1 H, *J* = 3 Hz, H-6), 5.09 (dd, 1 H, *J* = 11, 3 Hz, H-7), 4.15 (oct, 1 H, *J* = 8, 4.2, 1 Hz, H-5), 4.13 (dd, 1 H, *J* = 11.3, 4.6 Hz, H-16 equatorial), 3.65 (m, 3 H), 3.33 (t, 1 H, *J* = 11.3 Hz, H-16 axial), 2.68 (dd, 1 H, *J* = 16.8, 7.8 Hz, H-4), 2.38 (dd, 1 H, *J* = 16.8, 4.2 Hz, H-4), 2.07 (s, 3 H), 1.73 (m, 1 H), 1.33–0.77 (m, 2 H), 1.02 (s, 9 H).

(14) A similar ratio of isomers has been obtained in the preparation of ethyl monate A from the ozonolysis product of pseudomonic acid A. See: Clayton, J. P.; Luk, K.; Rogers, N. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 308.

(15) Dolby, L. J.; Meneghini, F. A.; Koizumi, T. *J. Org. Chem.* **1968**, *33*, 3060.

(16) Salmond, W. G.; Berta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 790.

(17) Sharpless, K. B.; Umbreit, M. A.; Nieh, M. T.; Flood, T. C. *J. Am. Chem. Soc.* **1972**, *94*, 6538.

(18) A similar transformation has been performed by the Beecham group. See ref 14.

(19) Protection of the hydroxyl groups of methyl pseudomonate C (**2b**) as their trimethylsilyl ethers followed by epoxidation with MCPBA and deprotection has been shown to afford a high-pressure LC separable mixture of methyl pseudomonate A (**1c**) plus its isomer in a 1:2 ratio (ref 5). We have found that reaction of **2b** with MCPBA/$NaHCO_3$ in methylene chloride for 1 day at −15 °C gives **1c** plus its isomer in a 1:1 ratio. When ethyl monate C is epoxidized by using VO(acac)$_2$/*t*-BuOOH in methylene chloride at 0 °C for 2 days, a 1.5:1 mixture of ethyl monate A (**1d**) and its isomer results. If the cis-diol group of **2c** is protected as its benzylidene acetal, the VO(acac)$_2$/*t*-BuOOH system affords a 3:1 mixture of **1d** and its isomer. These and other epoxidation studies will be discussed in detail in the full paper.

(20) Sweet, F.; Brown, R. K. *Can. J. Chem.* **1968**, *46*, 2283.

(21) For another recent investigation of the Wittig reaction in the preparation of α- and β-*C*-glycopyranosides, see: Fraser-Ried, B.; Dawe, R. D.; Tulshian, D. B. *Can. J. Chem.* **1979**, *57*, 1746.

(22) All new compounds reported in this work gave satisfactory spectral and analytical data or correct high-resolution mass spectral values for the molecular ion.

(23) Fellow of the Alfred P. Sloan Foundation, 1978–1980.

Corporation. We thank Alexander Vasilakis for his assistance in preparing some of the starting materials.

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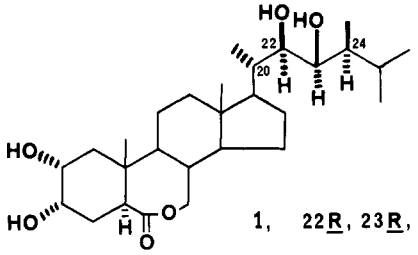
Received June 5, 1980

Stereoselective Synthesis of Brassinolide: A Plant Growth Promoting Steroidal Lactone

Sir:

The structure and stereochemistry of brassinolide (**1**) were determined[1] recently by X-ray crystallography, after isolation of



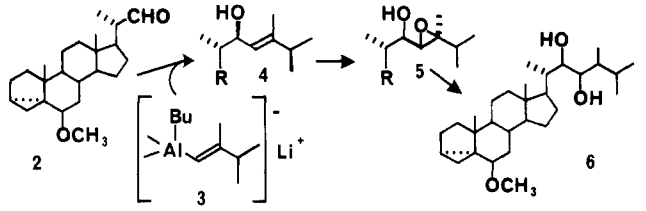
1, 22R, 23R, 24S

4 mg from 40 kg of bee-collected pollen of *Brassica napus* L. (rape). Brassinolide promotes cell division, cell elongation, and plant growth. For high activity, both the B-ring lactone and the configuration at C-24 were found[2] to be important. The novel biological activity and the scarcity of this natural product stimulated our work in which we report the first synthesis of brassinolide.

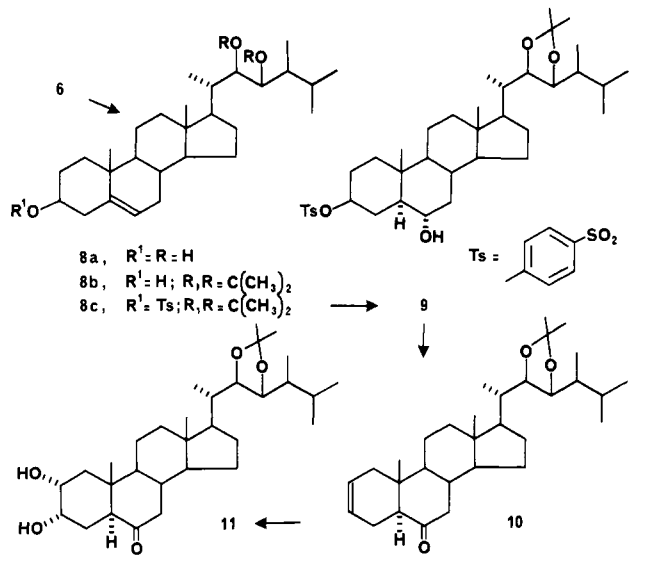
Our plan for construction of the dihydroxy side chain generates four contiguous asymmetric centers by using stigmasterol's chiral C-20 to generate asymmetry first at C-22, which in turn controls the stereochemistry of C-23 and C-24 during hydroxyl-directed epoxidation of **4**. Inversion of configuration at C-24 upon anti-Markovnikov reduction of epoxide **5** completes the three-step synthesis of the side chain. An alternative direct hydroboration-oxidation of the *Z* isomer of **4** to glycol **6** was expected to offer less stereochemical control. The choice of first elaborating the side chain and then the nucleus requires only one protecting group in the 11 steps to brassinolide from the 3,5-cyclo steroidal aldehyde **2** (prepared easily[3-5] from stigmasterol).

Stereoselective alkylation of aldehyde **2** with lithium butyldimethyl (*E*)-2,3-dimethylbutenylalanate[6] (**3**) gave in 46% yield, after chromatography on silica gel, the major 22*S*-allylic alcohol

Scheme I



Scheme II



4[7,8] [mp 127-129 °C; NMR ($CDCl_3$) δ 1.60 (d, J = 1.5 Hz, 3 H, H-28); monoacetate,[7,8] mp 113-114 °C] (Scheme I). In addition to traces of aldehyde **2**, the less polar 22*R* isomer of **4** was separated as a glass in 8% yield, indicating ca. 85:15 stereoselectivity, which compares favorably with alkenyllithium alkylations[5] of **2**.

Hydroxyl-directed epoxidation of **4** with *m*-chloroperbenzoic acid (CH_2Cl_2, 22 °C, 12 h) showed 95:5 stereoselectivity whereas *t*-BuOOH/$VO(acac)_2$ in toluene (0 °C, 3.5 h) gave an 85:15 ratio of the same epoxides, indicating a threo-selective conversion similar to those reported[9] for 2-methylpent-2-en-4-ol. Recrystallization gave pure epoxide **5**[7,8] [mp 98-99 °C; NMR ($CDCl_3$) δ 1.22 (s, 3 H, H-28), 2.77 (d, J = 7 Hz, 1 H, H-23), 3.54 (br d, J = 7 Hz, 1 H, H-22)] whose NMR coupling constant J = 7 Hz, for H-22 to H-23, and chemical shift of H-22 are consistent with those reported but are not definitive for threo epoxides.[10]

Completion of the side-chain synthesis by anti-Markovnikov reduction of **5** with inversion[11] at C-24 ($LiBH_4$, BH_3·THF; 50 °C, 20 h) showed 3:1 regioselectivity for formation of the vicinal glycol **6**[7] [mp 70-73 °C; ^{13}C NMR ($CDCl_3$) δ 10.3, 11.92, 12.14, 20.70, 20.90 (CH_3), 73.39, 74.80 (C-O)]. The minor 1,3-diol **7**[7,8] [mp 159.5-160 °C; NMR δ 1.19 (s, 3 H, H-28)] was separated initially by chromatography but does not form an acetonide, which simplified purification of crude reduction product **6** + **7**.

At this point, the close similarity of chemical shifts in the ^{13}C NMR spectrum of **6** with the relevant seven shifts of those reported[1] for brassinolide strongly supported[12] the assumed 22*R*,23*R*,24*S* configurations of **6**. Proof of the absence of racemization at C-20 came from $NaIO_4$ cleavage of diol **6** to give aldehyde **2**.

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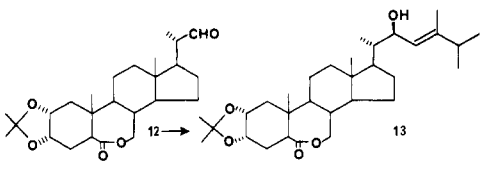
(6) Prepared from 3-methyl-1-butyne and trimethylaluminum with dicyclopentadienylzirconium dichloride catalysis, then butyllithium in hexane with the following procedure: Okukuda, N.; Negishi, E. *Tetrahedron Lett.* **1978**, 2357-2360. See also: VanHorn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252-2254. The alkylation reaction at 0 °C and then 22 °C for 14 h was initially 0.2 M in lithium reagent (1.5 equiv) in 30% ether/hexane. Similar alkenylations of aldehydes to form disubstituted alkenyl alcohols in 30-50% yield were reported by Newman, H. *Tetrahedron Lett.* **1971**, 4571-4572. The intermediate dimethyl[(*E*)-2,3-dimethylbutenyl]alane also alkylates aldehyde **12** to give **13** selectively in our alternate approach to the synthesis of **1**, which is in progress.



(7) This compound showed IR, NMR, electron impact, and/or chemical ionization mass spectral data fully compatible with the indicated structure.
(8) Elemental analyses for C, H within 0.3% of theory were obtained for this compound.
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