with stirring under nitrogen to a suspension of sodium amide (0.54 g, 13.7 mmol) in 70 mL of tetrahydrofuran. The yellow mixture was stirred for 4 h. A solution of ketone **6** (0.5 g, 3.3 mmol) in 5 mL of tetrahydrofuran was added dropwise to the yellow reaction mixture, which was then stirred under nitrogen for 14 h. The reaction mixture was heated under reflux for an additional 2 h to obtain a clear light brown solution. It was then cooled and evaporated under reduced pressure. Water (10 mL) was added to the residue, and the mixture was extracted with dichloromethane (2 × 25 mL). The combined organic phases were extracted with 5% hydrochloric acid (2 × 10 mL). The aqueous phase was then basified with potassium carbonate and extracted with dichloromethane (2 × 20 mL). The combined organic phases were washed with saturated sodium chloride solution, dried, filtered, and evaporated to give 0.4 g (64%) of a 3:2 mixture of the isomers of **8**. The ^{1}H NMR spectrum of the mixture showed peaks at δ 3.87, 2.88, 2.42 (s), and 1.84 (d) in addition to the peaks listed below for the major isomer. The ratio of isomers was determined by integration of the spectrum. The isomers were separated by column chromatography on silica gel (hexane/acetone, 1:1): TLC (hexane/acetone, 1:1) R_f 0.41 (major), 0.37 (minor); ^{1}H NMR (major isomer) δ 4.28 (1 H, d), 3.3 (1 H, m), 2.43 (3 H, s), 2.03–2.6 (4 H, m), 1.85 (3 H, d), 1.4–1.8 (6 H, m); ^{13}C NMR δ 165.64, 119.77, 101.21, 69.52, 65.09, 40.94, 34.27, 32.13, 30.19, 27.38, 21.99, 16.30. IR: 2927.8, 2878.6, 2804.4 2206.4, 1616 cm^{-1}; MS, *m/e* 190, 175, 147, 134, 119, 108, 96, 91, 82, 55, 42.

Anal. Calcd for $C_{12}H_{18}N_2$: C, 75.74; H, 9.54; N, 14.72. Found: C, 75.81; H, 9.55; N, 14.67.

Camphorsulfonate-*d* salt: mp 219–220 °C.

Anal. Calcd for $C_{22}H_{34}N_2O_4S$: C, 62.53; H, 8.11; N, 6.63. S, 7.59. Found: C, 62.54; H, 7.99; N, 6.67; S, 7.66.

2-Acetyl-9-methyl-9-azabicyclo[4.2.1]non-2-ene (1b) (*N*-Methylanatoxin-*a*). *n*-Butyllithium in hexane (1 mL of 1.5 M solution, 1.57 mmol) was added dropwise to a solution of diisopropylamine (0.15 g, 1.5 mmol) in 10 mL of tetrahydrofuran. The solution was stirred under nitrogen for 2 h at 0 °C. Compound **8** (0.21 g, 1.1 mmol) in 40% hexamethylphosphoric amide and tetrahydrofuran was added to the lithium diisopropylamide solution at −78 °C. Oxygen gas was bubbled into the solution for 40 min. The reaction was stirred for 0.5 h before it was quenched with 8 mL of 1 M sodium sulfite. The mixture was stirred for an additional 1 h at 25 °C. The reaction mixture was diluted with 20 mL of 20% dichloromethane and ether and then washed with 40 mL of 1 M NaOH. The organic phase was washed with saturated sodium chloride solution (20 mL), dried, filtered, and evaporated to give the crude product.

The crude product was added to a solution containing excess *d*-10-camphorsulfonic acid-d_{10} in isopropyl alcohol. The solution was stirred briefly and evaporated to give the camphorsulfonate salt. Flash column chromatography (methanol/acetone/hexane/diethylamine, 4:4:1:0.1) allowed purification of the camphorsulfonate salt. The pure dried salt was then converted to the free base, *N*-methylanatoxin-*a*.

An aqueous solution of the salt was basified with potassium carbonate and extracted with dichloromethane. The organic layer was washed with saturated sodium chloride solution, dried and evaporated to give 0.084 g (42.7%) of pure *N*-methylanatoxin-*a*.

N-Methylanatoxin-*a* camphorsulfonate salt: TLC (methanol/acetone/hexane, 4:5:1), R_f 0.11; ^{1}H NMR (*N*-methylanatoxin-*a*) δ 6.91 (1 H, dd), 4.43 (1 H, d), 3.38 (1 H, m), 2.25 (3 H, s), 2.28 (3 H, s), 1.85–2.5 (5 H, m), 1.32–1.7 (3 H, m); ^{13}C NMR δ 198.98, 148.77, 142.75, 63.11, 58.63, 36.70, 31.38, 28.38, 25.87, 25.44, 24.83; IR 2929.1, 2880.4, 1659.6, 1630.9 cm^{-1}; MS, *m/e* 179, 164, 150, 136, 122, 108, 96, 82, 57, 43.

Registry No. (±)-**1a**, 85514-42-7; (±)-**1b**, 70470-06-3; (±)-**1b**·camphorsulfonic acid-d_{10}, 100514-09-8; **3a**, 37996-41-1; **3b**, 56258-84-5; **4b**, 100514-10-1; **5**, 63989-32-2; (±)-**6**, 70423-78-8; (±)-(*Z*)-**8**, 100514-06-5; (±)-(*E*)-**8**, 100514-07-6; (±)-(*E*)-**8**·camphorsulfonic acid-d_{10}, 100514-08-7; (±)-(*Z*)-**8**·camphorsulfonic acid-d_{10}, 100514-11-2; diethyl (1-cyanoethyl)phosphonate, 29668-61-9.

A Highly Convergent Total Synthesis of (+)-Compactin

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An intramolecular Diels–Alder approach to the construction of (+)-compactin is described. Alkylation of the lithium enolate of (acetylmethylene)triphenylphosphorane with the tosylate of allenic alcohol **15** affords phosphorane **16**, which condenses with aldehyde **6** (prepared from tri-*O*-acetyl-D-glucal) to afford enone **3**. Intramolecular Diels–Alder reaction, reduction with lithium tri-*sec*-butylborohydride, and acylation with (*S*)-(+)-2-methylbutyric anhydride yields a chromatographically separable mixture of diastereomers; conversion to compactin was accomplished by acid hydrolysis followed by oxidation.

The isolation of compactin (also known as ML-236 B) in 1976[1,2] and the demonstration that this material is a potent inhibitor of sterol biosynthesis, both in vitro and in vivo,[3,4] have led to extensive investigations of approaches to the total synthesis of **1** and related compounds.[5] In addition, considerable attention has been focused on defining the structural features of compactin necessary for potent activity as an inhibitor of HMG-CoA reductase (the enzyme which mediates the rate-limiting step in sterol biosynthesis) and also upon clarifying the mechanism of inhibition.[6,7] We record herein our studies on the con-

(1) Endo, A.; Kuroda, M.; Tsujita, Y. *J. Antibiot.* **1976**, *29*, 1346.
(2) Brown, A. G.; Smale, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1165.
(3) (a) Endo, A.; Kuroda, M.; Tsujita, Y. *J. Antibiot.* **1976**, *29*, 1346. (b) Endo, A. *J. Antibiot.* **1979**, *32*, 852. (c) Endo, A.; Kuroda, M.; Tanzawa, K. *FEBS Lett.* **1976**, *72*, 323. (d) Kaneko, I.; Shimada, Y. H.; Endo, A. *Eur. J. Biochem.* **1978**, *87*, 313. (e) Betteridge, D. J.; Galton, D. J.; Krone, W.; Reckless, J. P. D. *Lancet* **1978**, *2*, 1342.
(4) (a) Endo, A.; Tsujita, Y.; Kuroda, M. *J. Biochem.* **1977**, *77*, 31. (b) Tsujita, Y.; Kuroda, M.; Tarzama, K.; Kitano, N.; Endo, A. *Atherosclerosis (Shannon, Irel.)* **1979**, *32*, 307. (c) Kuroda, M.; Tsujita, Y.; Tanzawa, K.; Endo, A. *Lipids* **1979**, *14*, 585. (d) Yamamoto, A.; Sudu, H.; Endo, A. *Atherosclerosis (Shannon, Irel.)* **1980**, *35*, 259.
(5) For previous total syntheses of compactin, note: (a) Wang, N. Y.; Hsu, C. T.; Sih, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6358. (b) Hirama, M.; Uei, M. *Ibid.* **1982**, *104*, 6538. (c) Grieco, P. A.; Zella, R. E.; Lis, R.; Finn, J. *J. Am. Chem. Soc.* **1983**, *105*, 1403. (d) Girota, N. N.; Wendler, N. L. *Tetrahedron Lett.* **1983**, *23*, 5501; (e) **1983**, *24*, 3687. (f) Girota, N. N.; Reamer, R. H.; Wender, N. L. *Ibid.* **1984**, *25*, 5371. (g) Rosen, T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 3731.
(6) Nakamura, C. E.; Abeles, R. H. *Biochemistry* **1985**, *24*, 1364.

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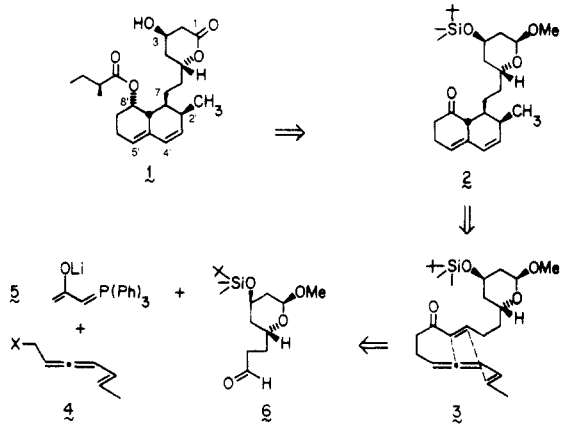
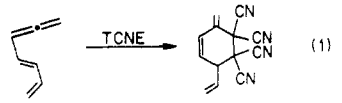
Scheme I. Retrosynthetic Analysis of (+)-Compactin



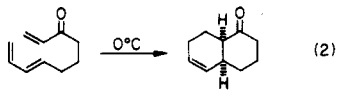
struction of this material, which have culminated in the development of a reasonably direct total synthesis of (+)-compactin. Our retrosynthetic analysis of (+)-compactin is summarized in Scheme I.

Synthetic Analysis

This approach to the total synthesis of compactin (note Scheme I) centered on recognition of the hexahydronaphthalene moiety as being potentially accessible via an intramolecular Diels–Alder reaction. Although very little relevant literature on *intra*molecular [4 + 2] cycloadditions utilizing vinylallenes as the diene component was available at the time we began our work, reports of bimolecular cycloadditions utilizing vinylallenes suggested that, as might be expected, they were considerably more reactive than simple butadienes. For example, compound **7**, which is both a vinylallene and a 1-substituted butadiene, was reported[8] to react with tetracyanoethylene (TCNE) to afford a single [4 + 2] cycloadduct **8**, in which the vinylallene moiety underwent preferential cycloaddition. Also



(1)



(2)

of interest in this regard was the report that substrate **9** underwent facile intramolecular [4 + 2] cycloaddition at 0 °C to afford **10**.[9] Although considerably lower reactivity for **3** could be expected as a result of β-substitution and due to the requirement (vide supra) of an exo transition state, it did appear that the requisite cycloaddition was feasible.

In this context, both acylation of the $C_{8'}$ hydroxyl and establishment of the correct stereochemistry at $C_{8'}$ by reduction of the corresponding ketone were known operations from work at Merck.[10] Thus, intramolecular [4 + 2] cycloaddition with an enone as dienophile also appeared feasible with respect to the requisite subsequent transformations of the β–γ unsaturated ketone which would result from such a process. However, there were obvious concerns with the intermediacy of such a material under the conditions of the Diels–Alder reaction, since isomerization to the presumably more stable conjugated enone seemed a reasonable possibility.

The expected stereochemistry of the cycloaddition was also a matter of crucial concern. Although the transition state expected for such a cycloaddition process is very difficult to represent on paper, examination of molecular models clearly revealed that, with the trans enone required to fix relative stereochemistry at $C_{1'}$ and $C_{9'}$, only an exo cycloaddition was possible. Endo geometries for approach of diene and dienophile in this system could only be achieved at the expense of conjugation (ca. 90° dihedral angle) between the C=O and C=C of the enone moiety. The apparent requirement for an exo transition state then translates to a requirement for a *trans*-vinyl moiety in the vinylallene component to obtain the desired stereochemistry for the methyl substituent at $C_{2'}$. This state of affairs, from the standpoint of such an approach to the total synthesis of compactin, is actually very fortunate. That is, if an endo cycloaddition were predicted, a *cis*-vinyl unit would be required, and such an intramolecular Diels–Alder approach would in fact have been precluded by the very facile 1,5-hydrogen migrations known to occur in such systems.[11]

The final issues with respect to this analysis concern construction of the "lactone portion" of the molecule and the assembly of the subunits indicated in Scheme I. The β-hydroxyvalerolactone moiety of compactin appeared potentially vulnerable to β-elimination under the expected conditions of intramolecular [4 + 2] cycloaddition, therefore we chose to carry this subunit through the crucial Diels–Alder reaction at a lower oxidation state, with the lactone carbonyl protected as an acetal. However, the nature of the route selected to (+)-compactin, which involves the coupling of an optically pure lactone moiety with a racemic (yet chiral) vinylallene unit, was destined to produce a mixture of two diastereomers, in which one diastereomer would possess the correct relative and absolute configuration at all centers, while the other would be antipodal with respect to $C_{1'}$, $C_{2'}$, $C_{8'}$, and $C_{9'}$. Clearly, an epimeric mixture at the "anomeric center" in the protected lactone portion of the molecule would unduly complicate such an approach, by producing four diastereomers rather than two. Since our primary interest was in the [4 + 2] cycloaddition to construct the hexahydronaphthalene portion of the molecule, we selected an approach to the masked lactone moiety[12] which controlled the disposition of the "anomeric" alkoxy group. A modified version of the route reported by Falck[12b] and the Sandoz group[12g,h] was used for the construction of this subunit of the molecule.

(7) (a) Ferres, H.; Hatton, I. K.; Jennings, L. J. A.; Tyrrell, A. W. R. *Tetrahedron Lett.* **1983**, *24*, 3769. (b) Nguyen, T.-G.; Gerbing, K.; Eggerer, H. *Z. Physiol. Chem.* **1984**, *365*, 1. (c) Stokker, G. E.; Hoffman, W. F.; Alberts, A. W.; Cragoe, E. J. Jr.; Deana, A. A.; Gilfillan, J. L.; Huff, J. W.; Novello, F. C.; Prugh, J. D.; Smith, R. L.; Willard, A. K. *J. Med. Chem.* **1985**, *28*, 347.

(8) Bross, H.; Schneider, R.; Hopf, H. *Tetrahedron Lett.* **1979**, 2121.

(9) Gras, J. L.; Bertrand, M. *Tetrahedron Lett.* **1979**, 4549.

(10) Personal communication to G.E.K. from Professor C. H. Heathcock.

(11) See: Chandraratna, R. A. S.; Bayerque, A. L.; Okamura, W. H. *J. Am. Chem. Soc.* **1983**, *105*, 3589 and references therein.

(12) For previous approaches to the lactone portion of compactin, note: (a) Prugh, J. D.; Deaha, A. A. *Tetrahedron Lett.* **1982**, *23*, 281. (b) Yang, Y. L.; Falck, J. R. *Ibid.* **1982**, *23*, 4305. (c) Majewski, J.; Clive, D. L. J.; Anderson, P. C. *Ibid.* **1984**, *25*, 2901. (d) Rosen, T.; Taschner, M. J.; Heathcock, C. H. *J. Org. Chem.* **1984**, *49*, 3994. (e) Danishefsky, S.; Kerwin, S. F.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358. (f) Danishefsky, S.; Kobayashi, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 1981. (g) Wareing, J. R.; Fuller, C. E.; Kathawala, F. G. *Abstracts of Papers*, 185th National Meeting of the American Chemical Society, Seattle, March, 1983; American Chemical Society: Washington, DC, 1983; ORGNII. (h) Wareing, J. R.; Fuller, C. E.; Jewell, C. F., Jr.; Kathawala, F. G. *Abstracts*, 5th International Conference on Organic Synthesis, Frieburg i. Br., Federal Republic of Germany, August, 1984; p 201. (i) Kozikowski, A. P.; Li, C.-S. *J. Org. Chem.* **1985**, *59*, 778.

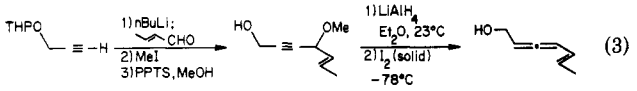
Thus tri-*O*-acetyl-D-glucal was employed as starting material for the "lactone portion" of compactin.

Two final comments regarding this analysis are in order. First of all, it should be noted that our approach to the union of the "top" and "bottom" halves of compactin relies on a totally unexceptional Wittig reaction with aldehyde **6**. A latent version of **6** was expected to be easily accessible via free radical allylation of an appropriate glucose-derived precursor, thus obviating the potential difficulties associated with "two-electron" approaches to construction of the C_6–C_7 bond (i.e., chain extension of glucose at C_6). During the course of our work, numerous problems associated with such approaches have been reported.[5f]

Second, the main benefits from the present approach derive from its high level of convergence. Thus, such an intramolecular Diels–Alder approach allows for especially direct disconnections for the assembly of simple fragments by sequential alkylation and Wittig processes, as outlined in Scheme I. The successful realization of this strategy is detailed below.

Results

Construction of the Vinylallene Segment. Although numerous approaches to the synthesis of allenes have been recorded, none were appropriate for the construction of the requisite vinylallene **15**.[13] A process previously developed in these laboratories in response to this problem was utilized,[14] as shown in eq 3.

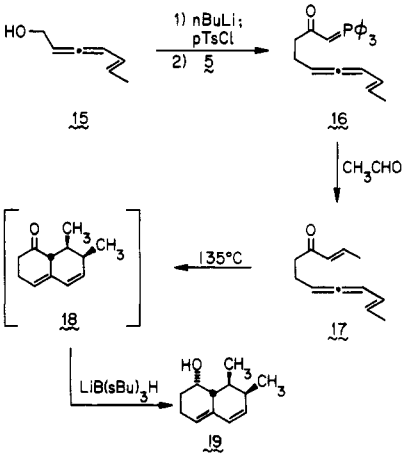


(3)

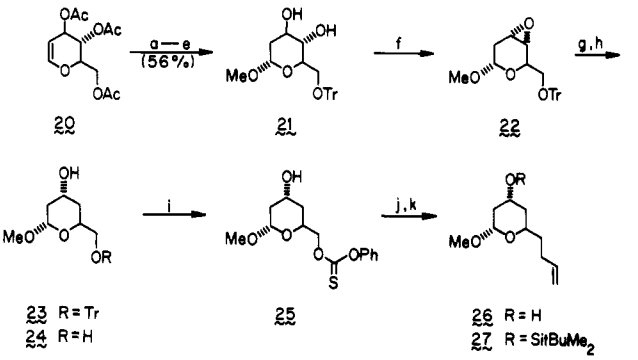
13 14 15

Conversion of **15** to a substrate suitable for deployment in alkylation reactions with the known Cooke dianion **5** proved unexpectedly difficult. For example, conversion of allenic alcohol **15** to the corresponding chloride could be accomplished in only ~50% isolated yield by the Meyers procedure,[15] and, unfortunately, this material proved to be an unstable intermediate that could not be stored. Moreover, the chloride proved to be a very poor reagent for the requisite alkylation process, as only very poor (ca. 20%) yields could be realized for reaction of the chloride derived from **15** with the Cooke dianion **5**.

Scheme II



Scheme III. Preparation of the Lactone Portion[a]

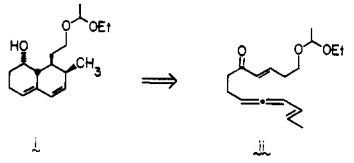


[a] (a) NaOMe, MeOH; (b) $Hg(OAc)_2$, MeOH; (c) NaCl; (d) $NaBH_4$; (e) $(Ph)_3CCl$, pyr; (f) NaH, $ArSO_2Cl$; (g) $LiAlH_4$; (h) Li, NH_3 (liquid); (i) PhOCSCl, pyr; (j) $CH_2{=}CHCH_2SnBu_3$, $h\nu$; (k) *t*-$BuSiMe_2Cl$, imidazole, DMF.

Far better results were realized via in situ activation. Thus, deprotonation of allenic alcohol **15** (1.0 equiv of *n*-BuLi, THF, −78 °C), addition of 1.0 equiv of tosyl chloride, and warming to 0 °C generated the corresponding tosylate, which was transferred via cannula to a solution of Cooke's dianion[16] which was maintained at 0 °C. Warming to 23 °C over 1 h and conventional extractive workup afforded phosphorane **16** in 75% yield. This material proved rather difficult to characterize spectroscopically, as it gave a very broad and poorly resolved NMR spectrum. However, a satisfactory C, H combustion analysis was obtained, and full characterization was conveniently achieved by reaction with acetaldehyde, followed by spectral and combustion analysis of the expected Wittig product **17**. (Note Scheme II.)

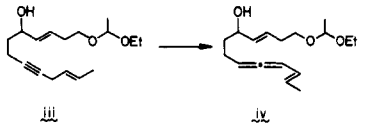
This readily available material provided an initial substrate for investigation of the intramolecular Diels–Alder process. It was found that reasonably high temperatures were required for this intramolecular cycloaddition to proceed at a convenient rate. Heating **17** at 135 °C in toluene, in the presence of BHT as a polymerization inhibitor, did in fact lead smoothly to the production of a new substance (presumably **18**) which was immediately reduced with lithium tri-*sec*-butylborohydride. Isolation of the material so produced afforded a single compound in 84% yield. No evidence of double bond isomerization was found. Thus, **19** displayed only two methyl doublets in its high-field NMR spectrum, and the downfield region (5–6 ppm) of the NMR spectrum was essentially identical

(13) During the course of our work, a formal total synthesis of compactin appeared which utilized the intramolecular Diels–Alder approach discussed herein for the construction of i from ii. In this case, however,



i ii

the vinyl allene moiety was obtained by base-catalyzed isomerization of enyne iii, which gave ca. 50% of iv along with conjugated enynes and unreacted starting material. This mixture was then processed by oxi-



iii iv

dation, thermolysis, and reduction to give i in ~30% yield: Deutsch, E. A.; Snider, B. B. *J. Org. Chem.* **1982**, *47*, 2682.

(14) Keck, G. E.; Webb, R. R. *Tetrahedron Lett.* **1982**, *23*, 3051.

(15) Meyers, A. I.; Collington, E. W. *J. Org. Chem.* **1971**, *36*, 3044.

(16) Cooke, M. P.; Burman, D. L. *J. Org. Chem.* **1982**, *47*, 4955.

with that of compactin. Thus, strong evidence was in hand that construction of compactin itself by such an approach was a viable possibility. With these results available, attention was turned to the synthesis of the lactone portion of the molecule.

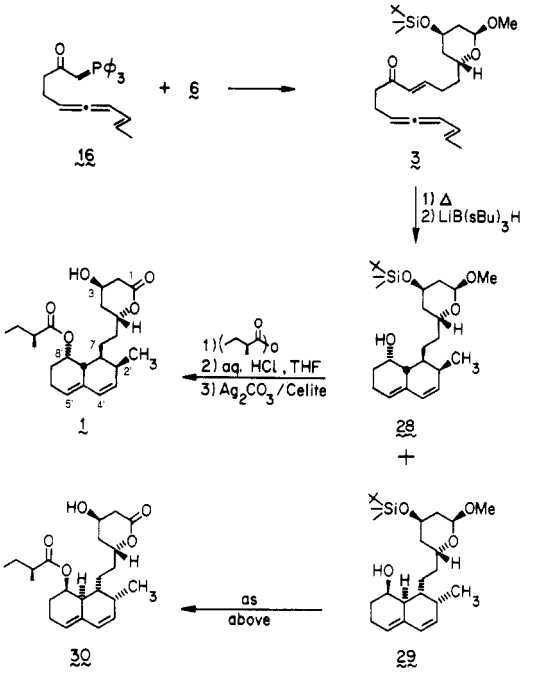
Synthesis of Aldehyde 6. This particular portion of compactin presents a formidable challenge, which is, at first glance, far from obvious. Despite intensive investigation,[12] no really satisfactory route to the lactone portion of compactin is presently known. As previously described in our retrosynthetic analysis, we chose to utilize a known route from tri-*O*-acetyl-D-glucal for the preparation of intermediate **6**, modified such that stereochemical integrity at the anomeric center was maintained.

The initial stages of this route utilize chemistry first described by Corey[17] in his total synthesis of *N*-methylmaysanine. Thus, conversion of commercially available tri-*O*-acetyl-D-glucal to the trityl ether **21** is readily accomplished in four steps without purification of intermediates, as shown in Scheme III and detailed in the Experimental Section. Conversion of this material to epoxide **22**, also as described by Corey, followed by lithium aluminum hydride reduction, yields alcohol **23**.[12b,d,g,h] At this point, removal of the trityl ether at C_6, without disturbing stereochemistry at the anomeric center, was required. The method (CF_3CO_2H) previously employed by Falck[12b] to effect this transformation was reported to be accomplished by anomerization. Attempts to cleave the trityl ether by hydrogenolysis proved capricious, particularly when "scale-up" (from ca. 100 mg to 1–3 g) was attempted. Thus, dissolving metal reduction, along the lines previously described by Grieco,[5c] was employed. Reduction of **23** with lithium in liquid ammonia, with THF as cosolvent, proceeded cleanly to give **24** in 90% isolated yield after appropriate workup.

For the final elaboration to **27**, free radical (or "one-electron") chain extension[18] at C_6 was required. As a precursor for the requisite carbon-centered radical, a mixed thiocarbonate was employed, since the relatively low reactivity of phenyl chlorothiocarbonate toward alcohols allowed for selective acylation at the primary hydroxyl in diol **24**. Thus, treatment of **24** with 1.0 equiv of phenyl chlorothiocarbonate in pyridine at 0 °C, followed by warming to room temperature, gave **25** in 87% yield after purification by column chromatography. Reaction of the mixed thiocarbonate with allyltri-*n*-butylstannane then proceeded uneventfully, and protection of the sole remaining hydroxyl group as its *tert*-butyldimethylsilyl ether was easily accomplished under the standard[19] conditions, to afford **27** in 82% overall yield from **25**.

Linking of Subunits and Conversion to Compactin. With the key pieces required for construction of compactin in hand and with the results gleaned from previous model studies in mind, the convergent assembly of **15**, **5**, and **6** proceeded without incident. Thus, Wittig reaction of **16** (prepared as previously described) with aldehyde **6** (freshly prepared by ozonolysis of **27** in CH_2Cl_2, followed by workup with dimethyl sulfide[20]) proceeded cleanly, although considerably more sluggishly then expected, to give **3** in 74% yield after purification by chromatography over silica gel. It should be noted that this material must be produced as a 1:1 mixture of diastereomers if starting materials are consumed.

Scheme IV



Intramolecular Diels–Alder reaction of this substance was, perhaps not surprisingly, somewhat more sluggish than in our model studies. However, heating **3** (ca. 0.05 M in toluene containing BHT) in a reasonable Dumas tube at 140 °C for 1.25 h effected clean consumption of starting material to give a new product, presumably **2**. Due to the potential lability of **2** and the previously discussed diastereomer problem, this material was immediately reduced with Li–Selectride as previously described, and the resulting mixture of alcohols was acylated with (*S*)-2-methylbutyric anhydride to afford (84% overall from **3**) a mixture of diastereomers **28** and **29**.

Separation of the diastereomeric adducts from the Diels–Alder reaction could in principle have been accomplished at any of several stages; in practice, separation was most readily achieved after acylation of the mixture of alcohols with (*S*)-(+)-2-methylbutyric anhydride. The diastereomers proved readily separable (TLC, R_f 0.33 and 0.43, three elutions with 10% THF–hexanes) at this point, although the relative stereochemistry of the two products was totally unknown. Thus each was processed for ultimate comparison with natural material. Hydrolysis of both the methyl glycoside and the *tert*-butyldimethylsilyl ether, using conditions (2:5 10% HCl–THF; 45 °C) previously developed by Grieco[5c] was followed by oxidation with Fetizons reagent (silver carbonate on Celite) to give the desired β-hydroxyl lactones **1** and **30** in 77% yield (Scheme IV). Not unexpectedly, the high-field ^1H NMR spectra of **1** and **30** were very similar and an assignment using this information alone would be quite difficult. However, one of the materials (derived from the methyl glycoside of R_f 0.33) gave an optical rotation of $[\alpha]_D$ +271°, while $[\alpha]_D$ for the other isomer was +100°. Natural compactin, measured under the same conditions on the same instrument, gave $[\alpha]_D$ +280°. Thus it is clear that the material derived from the lower R_f isomer in fact possesses the configuration of the natural substance at all centers, while the higher R_f material is antipodal at $C_{1'}$, $C_{2'}$, $C_{8'}$, and $C_{9'}$. Moreover, the material with $[\alpha]_D$ +271° also had the same melting point, chromatographic mobility, and 300-MHz ^1H NMR spectrum as (+)-compactin, and the richly detailed 75-MHz

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^{13}C NMR spectra (all 23 carbons observed) were superimposable.

Experimental Section

General Procedures. Melting points were recorded on a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories and acceptable values are reported to a ±0.4% tolerance. All yields reported are isolated yields of material judged homogeneous by TLC and NMR spectroscopy unless otherwise specified. In addition to standard Schlenk techniques, all glassware was oven-dried, and for air-sensitive reactions, solvents, reagents, etc. were introduced into the reaction vessels via syringe through serum caps under an atmosphere of argon. All photochemical work was accomplished by using a 450-W Hanovia Hg lamp Model 679A36 (Ace Glass Inc. PZ678) with a Pyrex filter. All temperatures are reported in °C and all pressures are reported in mmHg. All solvents were distilled and/or dried prior to use by standard methods. Diethyl ether, tetrahydrofuran, and toluene were distilled from sodium benzophenone ketyl under argon. Hexanes, ethyl acetate, diisopropylamine, pyridine, HMPA, dioxane, and triethylamine were distilled from CaH_2. Methylene chloride and 1,2-dichloroethane were distilled from P_2O_5. Infrared spectra were obtained on neat liquids or thin films on NaCl plates with a Beckman Acculab 3 IR spectrometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter at 589 nm in the indicated solvent. The abbreviations s, m, w, and br reported in IR data stand for strong, medium, weak, and broad, respectively.

Thin-layer chromatography was performed on Merck 25-mm glass silica gel plates; visualization of developed plates was by fluorescence quenching and staining with 12-phosphomolybdic acid or Dragendorff's reagent. Column chromatography utilized Merck or Davison silica gel (60–200 mesh). MPLC refers to medium-pressure liquid chromatography and utilizes Altex columns with silica gel 60 (0.040–0.063 mm) and an Altex preparative UV detector and FMI lab pump operated between 10 and 60 psi. HPLC refers to high-pressure liquid chromatography, which was performed on a Varian Vista 5000 with the indicated columns. VPC analysis utilized a Varian 2100 with glass columns or a Varian 3400 interfaced with a Varian Vista Series 402 computer–printer–plotter with the indicated columns. Pipet chromatography refers to disposable Pasteur pipets slurry packed with silica gel (60–200 mesh) in hexanes.

Mass spectral fragmentation data were measured on a VG Micromass 7070 instrument in the electron impact (EI) or chemical ionization (CI) modes. High-resolution (+)-FAB analysis was performed on a Varian (Finnigan) MAT 731 instrument at 6 keV utilizing Xe^0 affluent and a peak matched against glycerol cluster ions. Samples reluctant to display $[M{\cdot}H^+]$, $[M{\cdot}gly]^+$, etc. were doped with NaCl.

^1H NMR data were recorded on a Varian EM-390 (90 MHz) or a Varian SC-300 (300 MHz) instrument in the indicated deuterated solvent. ^{13}C NMR data utilized a Varian FT-80 instrument (20 MHz) or a Varian SC-300 (75 MHz). Chemical shifts are reported in ppm relative to the internal standard Me_4Si. The abbreviations s, d, t, q, p, etc. stand for the resonance multiplicities singlet, doublet, triplet, quartet, pentuplet, etc.

Methyl 2-Deoxy-6-(triphenylmethyl)-α-D-glucopyranoside (21). This material was prepared according to the procedure of Corey.[17] Into a 1-L flask equipped with a mechanical stirrer were added tri-*O*-acetyl-D-glucal (89.3942 g, 0.328 mol) and 600 mL of anhydrous methanol. To the resulting homogeneous solution was added sodium methoxide (0.8267 g, 16.4 mmol) as a solid followed by stirring at 25 °C. After 2 h, TLC indicated complete hydrolysis to an unsaturated triol having R_f 0.10 (50% THF/hexanes). The solution was treated with mercuric acetate (109.87 g, 0.345 mmol) as a solid to effect methoxy mercuration (3 h, 25 °C). The intermediate mercuration product was obtained as a white crystalline solid after concentration of the reaction mixture and filtration. The mercuration product thus obtained was dissolved into 500 mL of anhydrous methanol and reacted with sodium chloride (26.857 g, 0.460 mol) at 25 °C for 15 min to produce the corresponding chloromercurial. The reaction mixture was cooled to 0 °C and treated with sodium borohydride (12.749 g, 0.337 mol) for 30 min. Analytical TLC after this time indicated formation of a new substance having R_f 0.28 (15% MeOH/$CHCl_3$). Concentration in vacuo provided a residue, which was suspended in ethyl acetate and treated with a slight excess of 12 M HCl and then with excess solid sodium bicarbonate. Filtration thorough Celite and concentration in vacuo provided the crude methyl 2-deoxy-α-D-glucopyranoside which was dried in vacuo (2.1 mm, 100 °C, 5 h). The thoroughly dried triol was treated with trityl chloride (54.164 g, 0.94 mol) in ca. 400 mL of anhydrous pyridine for 18 h, to provide after extractive workup, the crude diol trityl ether, R_f 0.67 (15% MeOH/$CHCl_3$). Recrystallization from methylene chloride/hexanes (2:1) provided 76.7 g (56%) of the title compound: mp 139–141 °C; 90-MHz ^1H NMR ($CDCl_3$) δ 7.25 (m, 15 H), 4.70 (m, 1 H), 3.4 (m, 2 H), 3.3 (m, 3 H), 3.25 (s, 3 H), 1.90 (m, 2 H); IR 3485 cm^{-1} (br), 3050 (s), 3020 (m), 2910 (m), 2820 (w), 1595 (m), 1485 (s), 1440 (s), 1005 (s), 755 (s), 730 (m), 695 (s), 630 (s); mass spectrum (EI), *m/z* (relative intensity) 381 (0.2), 260 (2.1), 243 (9.4), 183 (9.6), 165 (9.4), 154 (2.6), 105 (13.1), 79 (100.0), 77 (86.3), 52 (68.0), 51 (31.3).

Methyl 2-Deoxy-3,4-epoxy-6-(triphenylmethyl)-α-D-3-*allo*-glucopyranoside (22). This material was prepared according to the procedure of Corey.[17] Into a 1-L flask under argon was added methyl 2-deoxy-6-(triphenylmethyl)-α-D-glucopyranoside (48.4368 g, 0.115 mol) followed by HMPA (180 mL). The resulting solution was cooled to 0 °C and treated with sodium hydride (22.1251 g, 0.461 mol) followed by warming to 25 °C for 2 h. The reaction mixture was diluted with 180 mL of THF and cooled to −23 °C. Treatment in one portion with 1-[(2,4,6-triisopropylphenyl)sulfonyl]imidazole (42.3963 g, 0.126 mol) as a THF solution, and reaction over 3 h while warming to 0 °C provided the crude epoxide, R_f 0.50 (35% THF/hexanes), after filtration through Celite and extractive isolation. Recrystallization from ether/hexanes (1:1) provided the title compound (39.7 g, 86%) as a white crystalline solid: mp 100 °C; 90-MHz ^1H NMR ($CDCl_3$) δ 7.40 (m, 6 H), 7.20 (m, 9 H), 4.65 (t, *J* = 4.0 Hz, 1 H), 4.10 (t, *J* = 5.5 Hz, 1 H), 3.60 (m, 1 H), 3.3 (m, 1 H), 3.25 (s, 3 H), 3.15 (m, 2 H), 2.1 (m, 2 H); IR (NaCl film) 3045 cm^{-1} (s), 2910 (s), 2820 (m), 1955 (m), 1890 (m), 1810 (m), 1730 (w), 1590 (s), 1440 (s), 1340 (s), 920 (s), 890 (s), 850 (s), 800 (s), 750 (s), 700 (s), 625 (s); mass spectrum (EI), *m/z* (relative intensity) 355 (0.2), 260 (8.3), 244 (37.5), 243 (100.0), 242 (26.0), 202 (94.3), 165 (78.1), 105 (58.9), 84 (25.0).

Methyl 2,4-Dideoxy-6-(triphenylmethyl)-α-D-allopyranoside (23). This material was prepared according to the procedure of Grieco.[5c] Into a 1-L flask under argon was added lithium tetrahydroaluminate (2.081 g, 54.8 mmol) followed by ca. 200 mL of anhydrous diethyl ether. The solution was cooled to −15 °C, and a diethyl ether solution of methyl-D-2-deoxy-3-*allo*-3,4-epoxy-6-(triphenylmethyl)-α-D-3-*allo*-glucopyranoside (22.0466 g, 54.8 mmol in ca. 400 mL) was added dropwise over 2 h. TLC analysis after this time indicated complete starting material consumption and the presence of a new product having R_f 0.35 (35% THF/hexanes). The reaction mixture was quenched with a 1:1 mixture of sodium sulfate decahydrate and Celite. Filtration through Celite, followed by evaporation of the filtrate, provided a clear viscous oil (21.03 g, 95%). Crystallization from absolute ethanol provided an analytical sample of the title compound: mp 67 °C; 90-MHz ^1H NMR ($CDCl_3$) δ 7.4 (m, 6 H), 7.2 (m, 9 H), 4.85 (s, 1 H), 4.09 (m, 2 H), 3.4 (s, 3 H), 3.1 (m, 4 H), 1.7 (m, 5 H); IR (NaCl film) 3440 cm^{-1} (br), 3045 (m), 3020 (m), 2910 (s), 2820 (m), 1950 (w), 1720 (m), 1590 (m), 840 (m), 750 (s), 700 (s), 645 (s), 630 (s); mass spectrum (EI) *m/z* (relative intensity) 404 $[M^+]$ (0.8), 274 (6.9), 260 (10.1), 244 (41.3), 243 (100.0), 242 (35.9), 241 (37.1), 183 (32.5), 165 (97.6), 105 (60.5), 77 (34.5), 69 (28.6).

Methyl 2,4-Dideoxy-α-D-allopyranoside (24). Methyl 2,4-dideoxy-6-(triphenylmethyl)-α-D-allopyranoside was detritylated according to the method of Grieco,[5c] with the exception that lithium was employed. Extractive isolation and chromatographic purification provided the diol as a clear oil (90%): R_f 0.11 (35% THF/hexanes); $[\alpha]^{25}_D$ +73.37° (*c* 0.0225, CH_2Cl_2); 300-MHz ^1H NMR ($CDCl_3$) δ 4.89 (d, *J* = 3.3 Hz, 1 H), 4.11 (m, 2 H), 3.68 (m, 1 H), 3.58 (dd, *J* = 11.7, 6.2 Hz, 1 H), 3.41 (s, 3 H), 1.98 (br s, 1 H), 1.85 (m, 4 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 99.5, 65.8, 64.4, 64.0, 55.3, 35.1, 33.8; mass spectrum (CI, CH_4), *m/z* (relative intensity) 163 [M + 1] (1.3), 145 (2.2), 131 (100.0), 113 (92.7), 87 (26.0), 71 (42.2), 59 (13.7), 29 (123.2); IR (neat) 3420 cm^{-1} (br),

2920 (s), 2830 (m), 2240 (w), 1420 (s), 1365 (s), 1185 (s), 1045 (s), 920 (s), 875 (m), 840 (m), 775 (m), 730 (s). Anal. Calcd for $C_7H_{14}O_4$: C, 51.65; H, 8.64. Found: C, 51.22; H, 8.74.

Methyl 2,4-Dideoxy-(5*R*)-6-(phenoxythioxomethyl)-α-D-allopyranose (25). Methyl 2,4-dideoxy-α-D-allopyranose (0.8825 g, 5.4 mmol) was diluted with 15 mL of pyridine and then cooled to 0 °C under argon. Phenyl chlorothioformate (0.9874 g, 5.7 mmol) was then added via syringe in one portion. After addition the reaction mixture was brought slowly to 25 °C by the dissipation of the cold bath, and then stirred for an additional 1 h. After this time, TLC analysis revealed the consumption of the starting diol and the formation of a less polar UV active spot with R_f 0.37 (35% THF/hexanes). The reaction mixture was diluted with ether, washed with an equal volume of water, dried (Na_2SO_4), and azeotroped with toluene to afford an oil. Chromatography over silica gel eluting with 5% THF/hexanes provided 1.1659 g (87%) of product as an oil after combining fractions of pure material: $[\alpha]^{25}_D$ +56.66° (*c* 0.0412, CH_2Cl_2); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.65 (m, 2 H), 7.35 (m, 1 H), 7.17 (m, 2 H), 4.91 (d, *J* = 3.3 Hz, 1 H), 4.61 (m, 3 H), 4.19 (m, 1 H), 3.39 (s, 3 H), 1.80 (m, 4 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 195.7, 153.7, 130.0, 127.0, 122.3, 99.6, 76.5, 63.8, 61.5, 55.5, 34.9, 34.1; IR (NaCl plates) 3530 cm^{-1} (br), 3020 (w), 2930 (s), 2830 (w), 1590 (m), 1490 (s), 1290 (s), 1205 (s), 920 (s), 840 (s), 770 (s), 730 (s), 690 (s); mass spectrum (CI, CH_4), *m/z* (relative intensity) 249 [M + 1] (6.5), 223 (9.5), 144 (4.8), 127 (19.6), 126 (12.4), 113 (8.1), 93 (100.0), 92 (30.3), 91 (28.8), 29 (53.1). Anal. Calcd for $C_{14}H_{18}O_5S$: C, 56.37; H, 6.04. Found: C, 55.99; H, 6.21.

Methyl 2,4,6-Trideoxy-3(*R*)-(*tert*-butyldimethylsiloxy)-(5*R*)-6-(2-propenyl)-α-D-allopyranose (27). Methyl 2,4-dideoxy-6-(phenoxythioxomethyl)-α-D-allopyranose (0.4947 g, 1.9 mmol) was combined with allyltri-*n*-butylstannane (0.9881 g, 2.9 mmol) and then diluted with 2 mL of toluene in a Pyrex tube. The mixture was degassed with argon and irradiated through a Pyrex filter for 7 h. After this time analytical TLC indicated consumption of starting materials and the presence of a non-UV-active spot, which became UV-active upon heating, at R_f 0.44 (35% THF/hexanes). The contents of the tube were concentrated in vacuo and chromatographed over silica gel to afford a crude alcohol, which was immediately silylated with *tert*-butyldimethylchlorosilane (DMF/imidazole/23 °C).[19] Extractive workup (diethyl ether) provided the crude silyl ether, which was purified by chromatography over silica gel (elution with 2.5% THF/hexanes) to afford 0.4674 g (82%) of pure material: $[\alpha]^{25}_D$ +57.67° (*c* 0.1148, CH_2Cl_2); 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.80 (m, 1 H), 4.95 (m, 2 H), 4.65 (dd, *J* = 4.3, 2.9 Hz, 1 H), 4.01 (m, 2 H), 3.8 (s, 3 H), 2.13 (m, 2 H), 1.52 (m, 6 H), 0.84 (s, 9 H), −0.02 (s, 3 H), −0.04 (s, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 138.9 (d), 114.9 (t), 98.5 (d), 64.1 (d), 63.9 (d), 55.0 (q), 39.2 (t), 37.1 (t), 34.9 (t), 30.0 (t), 26.2 (q), 25.8 (s), −4.7 (q), −4.9 (q); mass spectrum (CI, CH_4), *m/z* (relative intensity) 299 (3.1), 269 (100.00), 243 (15.0), 211 (14.2), 137 (37.8), 119 (22.9), 57.1 (10.2), 41 (1.9). Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 64.00; H, 10.66. Found: C, 64.14; H, 10.64.

(±)-2,3,5-Heptatrien-1-ol (15). This material was prepared according to the method of Keck.[14] Into a 1-L flask under argon were added lithium tetrahydroaluminate (8.267 g, 0.217 mol) and 200 mL of anhydrous diethyl ether. To the resulting suspension a diethyl ether solution of 4-methoxy-5-hepten-2-yn-1-ol (7.6346 g, 54.5 mmol in 200 mL) was added dropwise over 1 h at 25 °C. After addition the solution was cooled to −78 °C and treated with iodine (41.468 g, 0.163 mol) as the solid in three portions. After gas evolution had ceased, TLC analysis indicated complete starting material consumption and the formation of an intensely UV-active substance having R_f 0.40 (35% THF/hexanes). The reaction mixture was quenched by the dropwise addition of methanol at −78 °C. Extractive isolation (1:1 ether/CH_2Cl_2) followed by concentration in vacuo afforded a crude residue, which was purified by chromatography over silica gel, eluting with 10% THF/hexanes. Fractions containing pure material were combined to yield 4.678 g (78.1%) of material as a clear oil. An analytical sample had the following physical and spectral properties: bp 55–65 °C (0.1 mm); 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.88 (m, 2 H), 5.64 (m, 1 H), 5.44 (m, 1 H), 4.08 (dd, *J* = 6.3, 2.2 Hz, 2 H), 3.87 (br, s 1 H), 1.72 (dt, *J* = 6.4, 0.7 Hz, 3 H); 20-MHz ^{13}C NMR ($CDCl_3$) δ 212.7 (s), 135.1 (d), 133.3 (d), 102.9 (d), 100.0 (d), 67.6 (t), 25.2 (q); IR (neat) 3320 cm^{-1} (br), 3010 (m), 2920 (s), 2870 (s), 1940 (s), 1440 (m), 1230 (m), 1065 (s), 1010 (s), 965 (s), 925 (m), 870 (m), 805 (w), 735 (m).

(±)-1-(Triphenylphosphoranylidene)-2-oxo-5,6,8-decatriene (16). Into an oven-dried 10-mL flask were added 2,3,5-heptatrien-1-ol (0.5221 g, 4.7 mmol) and 4 mL of THF, and the solution was cooled to −78 °C under argon. *n*-Butyllithium was added (4.9 mmol in *n*-hexanes) dropwise via syringe and the solution stirred at −78 °C for 15 min. The resulting alkoxide was then treated with a THF solution of tosyl chloride (0.9049 g, 4.7 mmol, 5 mL THF) followed by warming to 0 °C for 20 min. TLC analysis after this time indicated complete consumption of allenic alcohol and the formation of a faster running UV-active spot with R_f 0.49 (35% THF/hexanes). The homogeneous reaction mixture was then transferred via syringe and added dropwise to the β-oxido ylide prepared from (acetylmethylene)triphenylphosphorane (1.4212 g, 4.4 mmol) and *n*-butyllithium (4.4 mmol in *n*-hexanes) in THF (ca. 35 mL) at 0 °C according to the protocol of Cooke.[16] After addition, the reaction mixture was stirred at 0 °C for 1 h and at 0–25 °C for 2 h. TLC analysis after this time indicated near-complete consumption of the spot with R_f 0.49 and formation of an intense UV-active spot with R_f 0.07 (35% THF/hexanes). The reaction mixture was diluted with CH_2Cl_2 and quenched at 0 °C with water. The organic phase was washed with an equal volume each of saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated in vacuo to a burgundy oil. Rapid filtration through a bed of silica gel with ca. 200 mL of 5% THF/hexanes removed unreacted allenic tosylate. Further washing with $CHCl_3$ afforded a clear burgundy oil of the title compound (1.44 g, 3.5 mmol, 75% of theory): IR (neat, NaCl plates) 3045 cm^{-1} (w), 2960 (m), 1965 (w), 1530 (s), 1435 (s), 1390 (s), 1105 (m), 750 (s), 720 (s), 695 (s); mass spectrum [(+)-FAB(Xe^0)], *m/z* 413 ($MH_2{\cdot}H^+$), 411 ($M{\cdot}H^+$), 375, 331, 303, 262, 259, 243, 227, 99; (+)-FAB exact mass calcd for ($C_{28}H_{27}OP$) 411.1878, found 411.1895.

(±)-4-Oxo-2,7,8,10-dodecatetraene (17). To a $CHCl_3$ solution of (±)-1-(triphenylphosphoranylidene)-2-oxo-5,6,8-decatriene (300 mg, 0.733 mmol; in 3 mL) was added distilled acetaldehyde (0.2 mL, 3.66 mmol) at 27 °C and the mixture stirred for 10 min. TLC analysis of the crude reaction mixture indicated consumption of the starting phosphorane and production of triphenylphosphine oxide along with an intensely UV-active spot having R_f 0.63 (35% THF/hexanes). The crude reaction mixture was concentrated in vacuo and chromatographed over silica gel eluting with 2.5% THF/hexanes. Fractions containing pure material were combined to yield 0.114 g (0.65 mmol, 89%) of product as a clear oil having the following spectral characteristics: 90-MHz ^{1}H NMR ($CDCl_3$) δ 7.26 (dq, *J* = 16.5, 7 Hz, 1 H), 6.58 (d, *J* = 16.5 Hz, 1 H), 5.92 (m, 4 H), 3.08 (m, 2 H), 2.72 (m, 2 H), 2.35 (dd, *J* = 7, 2 Hz, 3 H), 2.21 (dd, *J* = 5, 2 Hz, 3 H); IR (neat, NaCl plates) 3020 cm^{-1} (m), 2920 (s), 1940 (m), 1695 (s), 1670 (s), 1630 (s), 1440 (s), 970 (s), 810 (w); mass spectrum (EI), *m/z* (relative intensity) 176 [M^+] (17.6), 119 (12.5), 105 (13.0), 91 (72.3), 69 (100.0), 41 (74.9), 28 (77.5).

(±)-1,2-Dimethyl-8-hydroxy-1,2,6,7,8,8(α/β)-hexahydronaphthalene (19). A toluene solution of (±)-4-oxo-2,7,8,10-dodecatetraene (0.038 g, 0.21 mmol, ca. 0.09 M) containing ca. 1% BHT was degassed by bubbling argon for 20 min and sealed in a Pyrex ampule. The ampule was heated at 135 °C for 45 min, whereupon analytical TLC revealed complete spot-to-spot conversion to a new, less polar, UV-active material at R_f 0.66 (3 × 10% THF/hexanes). The contents of the ampule were cooled to 0 °C and diluted with an equal volume of THF. Subsequent treatment of the reaction mixture with lithium tri-*sec*-butylborohydride (0.2029 g, 1.07 mmol) at 0 °C for 30 min afforded, after quenching with water and extractive isolation (CH_2Cl_2), a crude product with R_f 0.56 (35% THF/hexanes). Purification by chromatography over silica gel, eluting with 10% THF/hexanes, provided 0.031 g (0.17 mmol, 82.5%) of product as a clear oil: 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.94 (d, *J* = 9.8 Hz, 1 H), 5.74 (dd, *J* = 7.8, 5.7 Hz, 1 H), 5.55 (m, 1 H), 4.15 (m, 1 H), 2.21 (m, 3 H), 1.95 (m, 4 H), 1.31 (d, *J* = 7 Hz, 1 H), 1.08 (d, *J* = 6.0 Hz, 3 H), 0.91 (d, *J* = 7.0 Hz, 3 H); IR (NaCl plates) 3390 cm^{-1} (br), 2940 (m), 1680 (m), 1445 (m), 1030 (m), 910 (s), 850 (w), 730 (s), 650 (w); mass spectrum (EI), *m/z* 159 (19.6), 132 (22.1), 119 (23.3), 91 (39.8), 71 (100.0), 69 (40.0), 43 (106.6), 41 (105.8).

Methyl 2,4,6-Trideoxy-3(*R*)-(*tert*-butyldimethylsiloxy)-(5*R*)-6-(4-oxo-2,7,8,10-dodecatetraenyl)-α-D-allopyranoside

(6). Ozonolysis of methyl 2,4,6-trideoxy-3(*R*)-(*tert*-butyldimethylsiloxy)-(5*R*)-6-(2-propenyl)-α-D-allopyranoside in methanol afforded, after workup with dimethyl sulfide,[20] an intermediate aldehyde (0.037 g, 0.12 mmol) which was immediately reacted with (±)-1-(triphenylphosphoranylidene)-2-oxo-5,6,8-decatriene (0.065 g, 0.16 mmol) in ca. 2 mL of CH_2Cl_2. Reaction over an 18-h period produced an intensely UV-active spot at R_f 0.51 (3 × 10% THF/hexanes). The reaction mixture was concentrated in vacuo and chromatographed over silica gel by eluting with 10% THF/hexanes. Appropriate fractions were combined to yield 0.038 g (74%) of material as a clear oil. Rechromatography via MPLC provided an analytical sample of what appeared to be a single diastereomer having the following spectral characteristics: 300-MHz ^{1}H NMR ($CDCl_3$) δ 6.84 (d(t), J = 15.8, 7.2 Hz, 1 H), 6.10 (d, J = 15.8 Hz, 1 H), 5.76 (m, 2 H), 5.62 (m, 1 H), 5.59 (m, 1 H), 4.66 (dd, J = 4.4, 2.23 Hz, 1 H), 4.03 (m, 2 H), 3.28 (s, 3 H), 2.62–1.72 (m, 6 H), 1.55 (m, 9 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 206.7, 202.9, 200.0, 147.4, 130.8, 127.5, 127.4, 98.6, 95.1, 91.6, 64.0, 63.5, 55.0, 39.2, 38.9, 36.9, 34.2, 28.8, 25.8, 23.2, 18.1, −4.7, −4.9; IR (neat) 3020 cm^{-1} (w), 2920 (s), 2850 (s), 2220 (w), 1945 (w), 1720 (m), 1670 (m), 1630 (m), 1250 (s), 830 (s), 770 (s), 730 (s); mass spectrum (EI), m/z (relative intensity) 434 [M$^+$] (0.2), 324 (0.3), 270 (6.6), 167 (16.1), 138 (28.7), 110 (10.2), 97 (31.5), 96 (14.9), 85 (100.00), 74 (57.3), 69 (29.8), 55 (58.2).

Preparation of Diastereomers 28 and 29. Vinylallene **3** (0.1027 g, 0.23 mmol) was dissolved in 5 mL of toluene and placed in a resealable Dumas tube along with 25 mg of BHT. The mixture was thoroughly degassed with argon for 20 min, sealed, and thermolyzed at 140 °C for 1.25 h. Analytical TLC after this time indicated complete consumption of starting material and the formation of two UV-active products at R_f 0.65 and 0.57 (5 × 10% THF/hexanes). The reaction mixture was diluted with 5 mL of THF and cooled to 0 °C. Treatment with lithium tri-*sec*-butylborohydride (0.46 mmol, 30 min, 0 °C) afforded, after aqueous workup, two spots with R_f 0.50 and 0.39 (3 × 10% THF/hexanes). Acylation of the crude reaction mixture with (*S*)-(+)-2-methylbutyric anhydride (0.69 mmol, 0.1283 g) according to the procedure of Grieco[5c] (DMAP, 0.34 mmol, 0.0421 g; $N(Et)_3$, 0.92 mmol, 0.093 g; in CH_2Cl_2) provided after 38 h almost complete conversion to a mixture of UV-active diastereomers having R_f 0.43, 0.33 (3 × 10% THF/hexanes). Extractive isolation and chromatographic purification over silica gel by MPLC, eluting with a gradient of hexanes to 2.5% THF/hexanes, provided an analytical sample of each diastereomer (84% combined yield). The isomer with R_f 0.33 contains the correct absolute configuration present in the mevinic acids (vide supra). Isomer R_f 0.43: $[\alpha]^{25}_D$ −22.0° (*c* 0.0095, CH_2Cl_2); HPLC t_r 15.6 min [5μ Alltex silica gel column (4.6 mm × 25 cm) 2.5% THF/hexanes, 2 mL/min]; 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.94 (d, J = 9.9 Hz, 1 H), 5.72 (dd, J = 9.9, 5.5 Hz, 1 H), 5.52 (m, 1 H), 5.25 (m, 1 H), 4.62 (dd, J = 4.2, 2.9 Hz, 1 H), 3.99 (m, 2 H), 3.27 (s, 3 H), 2.15 (m, 2 H), 1.95 (m, 2 H), 1.30 (m, 17 H), 1.12 (d, J = 5.7 Hz, 3 H), 0.92 (m, 12 H), 0.11 (s, 3 H), 0.07 (s, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 177.0, 134.4, 133.5, 128.5, 123.8, 98.4, 67.8, 64.5, 64.1, 55.0, 41.6, 39.0, 37.6, 37.5, 37.0, 33.0, 31.0, 26.9, 26.2, 25.8, 24.1, 21.0, 18.1, 17.0, 13.9, 11.7, −4.7; IR (neat) 2940 cm^{-1} (s), 2880 (s), 2860 (s), 1730 (s), 1460 (s), 1250 (s), 1185 (s), 935 (m), 830 (s), 770 (s), 710 (w), 660 (w), 620 (w); mass spectrum (EI), m/z 522 (0.2), 520 [M$^+$] (0.5), 488 (7.2), 431 (2.0), 386 (4.8), 357 (46.7), 323 (15.6), 255 (39.8), 254 (33.3), 237 (28.4), 159 (76.2), 145 (61.0), 89 (50.0), 75 (100.0), 57 (83.4). Isomer R_f 0.33: $[\alpha]^{25}_D$ +53.63° (*c* 0.0031, CH_2Cl_2); HPLC, t_r 17.4 min [5μ Alltex silica gel column (4.6 mm × 25 cm) 2.5% THF/hexanes, 2 mL/min]; 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.93 (d, J = 9.9 Hz, 1 H), 5.70 (m, 1 H), 5.50 (m, 1 H), 5.37 (m, 1 H), 5.23 (m, 1 H), 4.60 (m, 2 H), 3.25 (s, 3 H), 2.15 (m, 2 H), 1.95 (m, 2 H), 1.30 (m, 17 H), 1.12 (d, J = 5.7 Hz, 3 H), 1.92 (m, 12 H), 0.11 (s, 3 H), 0.07 (s, 3 H); IR (neat) 2925 cm^{-1} (s), 2860 (s), 1730 (s), 1460 (s), 1250 (s), 1185 (s), 940 (m), 830 (s), 770 (s), 715 (m), 660 (m); mass spectrum (EI), m/z 520 [M$^+$] (0.1), 357 (7.0), 299 (5.1), 255 (7.0), 225 (43.1), 197 (19.3), 159 (33.0), 123 (100.0), 105 (42.4), 89 (44.6), 57 (65.2).

Synthetic (+)-Compactin. A solution of compound **28** (0.0085 g, 0.16 mmol) in 1.5 mL of a 3:5 10% HCl/THF solution was heated at 45–55 °C for 20 min in a sealed tube. Analytical TLC analysis at this time indicated nearly complete selective hydrolysis to a diol having R_f 0.10 (35% THF/hexanes). Extractive isolation (CH_2Cl_2) provided the crude intermediate lactols, which were immediately oxidized with Fetizon's reagent (Ag_2CO_3/Celite, toluene, 95 °C/2 h). Analytical TLC of the crude reaction mixture provided a UV-active material having R_f 0.15 (35% THF/hexanes) that cospotted identically with natural (+)-compactin. Filtration through a Celite wafer and subsequent pipet chromatography over silica gel eluting with 10% THF/hexanes provided the analytical sample, which crystallized upon standing (0.0049 g, 77%). The synthetic (+)-compactin thus obtained proved indistinguishable from natural (+)-compactin by comparison of the following physical properties and spectral data: mp 148 °C; $[\alpha]^{25}_D$ +271.00° (*c* 0.002, CH_2Cl_2); 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.98 (d, J = 9.8 Hz, 1 H), 5.73 (dd, J = 9.8, 5.8 Hz, 1 H), 5.56 (m, 1 H), 5.34 (m, 1 H), 4.46 (m, 1 H), 4.35 (m, 1 H), 2.70 (m, 3 H), 2.36 (m, 3 H), 2.14 (m, 3 H), 1.95 (m, 3 H), 1.68 (m, 4 H), 1.43 (m, 5 H), 1.12 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 7.2 Hz, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 177.6, 171.4, 134.0, 133.1, 128.6, 124.1, 76.7, 67.9, 62.7, 41.9, 38.7, 37.6, 37.0, 36.1, 33.1, 31.0, 26.8, 26.3, 24.1, 21.0, 17.0, 13.9, 11.8; IR (neat) 3510 cm^{-1} (s), 3010 (w), 2960 (s), 2930 (s), 2840 (m), 1740 (s), 1695 (s), 1230 (s), 1200 (s), 1175 (s), 1080 (m), 1050 (m), 820 (m); mass spectrum (EI), m/z (relative intensity) 390 [M$^+$] (0.2), 270 (5.4), 255 (2.8), 210 (4.1), 184 (43.0), 169 (14.9), 158 (37.2), 145 (88.5), 143 (100.0), 129 (37.3), 91 (27.9), 57 (56.5).

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The Structure and Chemistry of Paulomycin[1]

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The gross structures and absolute stereochemistry of paulomycins A and B have been demonstrated to be those indicated in **1a** and **1b** by spectral studies on **1a** and **1b** and on their degradation products and by identity of degradation products with known compounds as well as by X-ray crystallographic studies.

Paulomycin was originally isolated as a mixture of paulomycins A and B[2] related to senfolomycins[3] and proceomycins.[4] Subsequently paulomycin was reisolated[5] and found to have excellent antibacterial properties. It

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