0.12 mmol) was added, and the solution was brought to reflux for 1 h. After being cooled to room temperature, the reaction mixture was partitioned between water (2 mL) and ether (5 mL). The aqueous phase was extracted with ether, and the combined organic layers were washed with brine, dried, and concentrated. Purification by MPLC on Florisil (elution with 25% ethyl acetate in petroleum ether) gave 22 mg (78%) of **40** and its isomer **41** (ratio 4:1) as an oil: IR (neat, cm^{-1}) 2950, 2920, 2850, 1740, 1450, 1375, 1260, 1100; ^1H NMR (300 MHz, C_6D_6) δ 5.70-5.68 (m, 1 H), 5.58-5.57 (m, 1 H), 5.33-5.31 (m, 1 H), 2.77 (m, 1 H), 2.49-2.24 (m, 2 H), 2.12-1.71 (series of m, 13 H), 1.59-1.29 (series of m, 13 H), 0.89-0.81 (m, 6 H), 0.77-0.71 (m, 6 H); MS m/z (M^+) calcd 218.1670, obsd 218.1683.

(3a*R,5*S**,5a*R**,7*S**,8a*S**,8b*S**)-5-(*tert*-Butyldimethylsiloxy)-6-ethyldecahydro-7-methyl-*as*-indacen-3(2*H*)-one (42).** Alcohol **12** (130.4 mg, 0.55 mmol) and imidazole (150 mg, 2.2 mmol) were dissolved in 2.5 mL of dimethylformamide under argon. *tert*-Butyldimethylsilyl triflate (0.22 mL, 1.1 mmol) was added dropwise, and the solution was stirred at 25 °C for 1 h. A second equivalent of the triflate was added to the reaction mixture was stirring for 1 h before it was quenched with saturated sodium bicarbonate solution (1.5 mL). Water (1.5 mL) was added, and the solution was extracted with ether. The combined organic layers were washed with brine and dried prior to concentration. Purification by MPLC on silica gel (elution with 8% ethyl acetate in petroleum ether) gave 184.4 mg (95.4%) of **42** as a white solid: mp 46-48 °C (crystallized on standing at 0 °C); IR (neat, cm^{-1}) 2960, 2930, 2860, 1740, 1460, 1410, 1380, 1360, 1255, 1090, 1060, 840, 770; ^1H NMR (300 MHz, C_6D_6) δ 3.53-3.51 (m, 1 H), 2.08-1.99 (m, 2 H), 1.92-1.24 (series of m, 14 H), 0.98 (s, 9 H), 0.92 (t, J = 7.3 Hz, 3 H), 0.79 (d, J = 7.1 Hz, 3 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 217.49, 70.45, 49.70, 47.53, 45.31. 40.35, 37.82, 37.60, 35.79, 33.22, 29.66, 26.39, 26.16 (3C), 22.65, 18.30, 15.96, 13.29, -4.19, -4.67; MS m/z (M^+) calcd 335.2406, obsd 335.2434.

Acknowledgment. We are grateful to the National Institutes of Health for their financial support of this work (Grant No. GM-28468), Ruth Hsu for the X-ray crystallographic analysis, and Dwight Macdonald for yield improvements at several stages.

Supplementary Material Available: Tables listing the experimental X-ray diffraction data, bond distances, bond angles, least-squares planes, positional parameters, and refined temperature factor expressions for **25**-OPNB (12 pages). Ordering information is given on any current masthead page.

Total Synthesis of (+)-Ikarugamycin. 2. Elaboration of the Macrocyclic Lactam and Tetramic Acid Substructures and Complete Assembly of the Antibiotic

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Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received April 27, 1990*

Abstract: The antibiotic ikarugamycin (**5**) has been synthesized in a triply convergent and enantioselective manner. The previously prepared ketone **1** was first converted to acetylenic ester **2**, an intermediate in which all eight of the stereogenic centers present in the carbotricyclic segment of **5** have been set in their proper absolute configuration. Very high levels of kinetic resolution were achieved during 1,4-addition of vinylmagnesium bromide to aldimine **9**. Following coupling of **2** to the ornithine segment **20**, the aldehyde group was unmasked and condensation was effected with phosphonate **23**. After arrival at **3**, the acyl ketene was liberated thermally and macrocyclization occurred smoothly. The total synthesis was completed by partial hydrogenation of the triple bond, dehydrative removal of the hydroxyl group in ring B, Dieckmann cyclization to form the tetramic acid, and deblocking of the amide nitrogen. The spectral properties of the synthetic material were identical with those of the natural product.

In the preceding paper,[2] we developed a concise, stereocontrolled approach to **1**, a tricyclic ketone which was intended to become the decahydro-*as*-indacene subunit of ikarugamycin (**5**).[3] The appendage of functionalized sidechains onto ring C as in **2** was expected to proceed with the proper stereoselectivity by analogy to the established behavior of related linear triquinane systems.[4] The reactive centers present in **2** were to be selected in order to permit convenient introduction of the ornithine segment (see **3**) as well as those additional trigonal carbons that would ultimately allow for construction of the macrocyclic lactam as in **4**. The final issues at this stage of inception were to involve dehydrative removal of water to set the cyclohexene double bond[2] and Dieckmann cyclization to generate the tetramic acid ring system.[5]

Several additional tactical issues central to the projected synthesis in Scheme I derive from precedent developed by others in other contexts. The impact of this prior art on the retrosynthetic analysis will be made known at appropriate points below. This full account of our total synthesis of (+)-ikarugamycin elaborates upon findings announced in preliminary form[6] alongside a communication by Boeckman and co-workers in which an alternate route to the same antibiotic was described.[7] In both undertakings, the complex target was approached in a manner that delayed to the final stages the assembly of its sensitive and highly polar acyl tetramic acid unit in order to avoid the difficulties in manipulation and purification often associated with this class of compounds.

(1) NSERC Postdoctoral Fellow, 1987-1989.

(2) Paquette, L. A.; Romine, J. L.; Lin, H.-S.; Wright, J. *J. Am. Chem. Soc*, preceding paper in this issue.

(3) (a) Jomon, K.; Kuroda, Y.; Ajisaka, M.; Sakai, H. *J. Antibiot.* **1972**, *25*, 271. (b) Ito, S.; Hirata, Y. *Tetrahedron Lett.* **1972**, *1181*; 1185; 2257. (c) Ito, S.; Hirata, Y. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 227,1813.

(4) (a) Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41; **1984**, *119*, 1. (b) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry*; Springer-Verlag: Berlin, 1987.

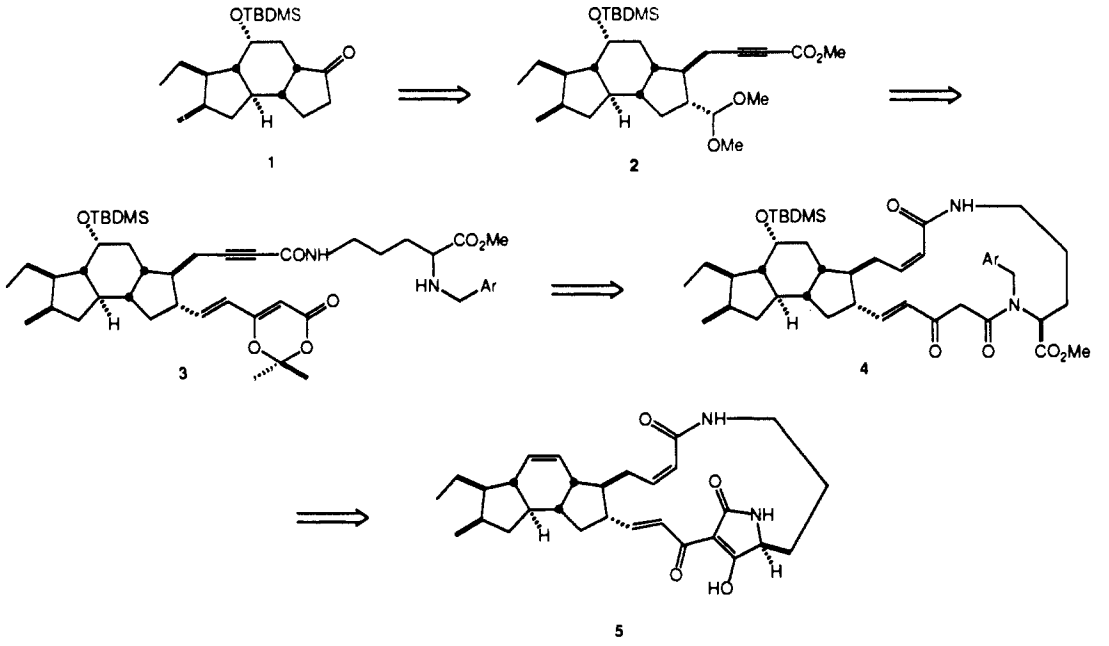
(5) See, for example: (a) Bloomer, J. L.; Kappler, F. E. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1485. (b) Boeckman, R. K., Jr.; Perni, R. B. *J. Org. Chem.* **1986**, *51*, 5486. (c) Ley, S. V.; Smith, S. C.; Woodward, P. R. *Tetrahedron Lett.* **1988**, *29*, 5829.

(6) Paquette, L. A.; Macdonald, D.; Anderson, L. G.; Wright, J. *J. Am. Chem. Soc.* **1989**, *111*, 8037.

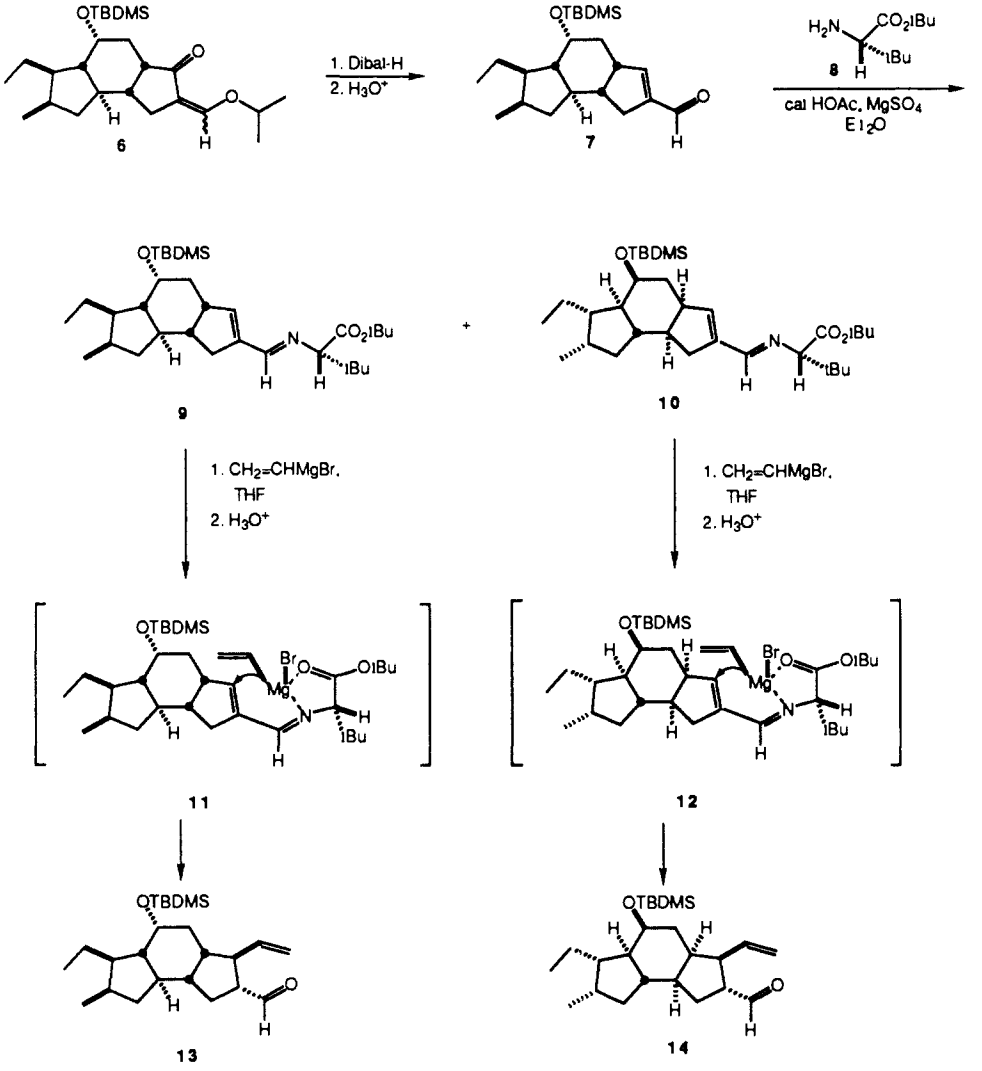
(7) Boeckman, R. K., Jr.; Weidner, C. H.; Perni, R. B.; Napier, J. J. *J. Am. Chem. Soc.* **1989**, *111*, 8036.

0002-7863/90/1512-9292$02.50/0

Scheme I



Scheme II

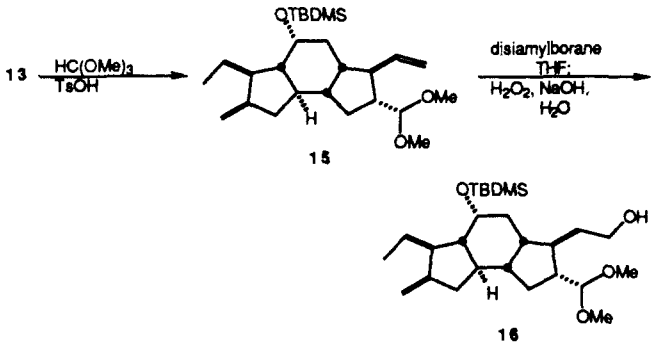


Results and Discussion

Initial Pendant Group Attachment and Kinetic Resolution Studies. Vinylogous ester **6** was conveniently available in a one-pot procedure involving the formylation of **1** and direct in situ O alkylation of the resultant enolate anion with isopropyl iodide[8] (Scheme II). The regiospecificity of this one-carbon homologation follows, of course, from the mechanistic demands of the Claisen condensation.[9] Hydride reduction and acid hydrolysis of **6** made

(8) Johnson, W. S.; Posvic, H. *J. Am. Chem. Soc.* **1947**, *69*, 1361.

Scheme III

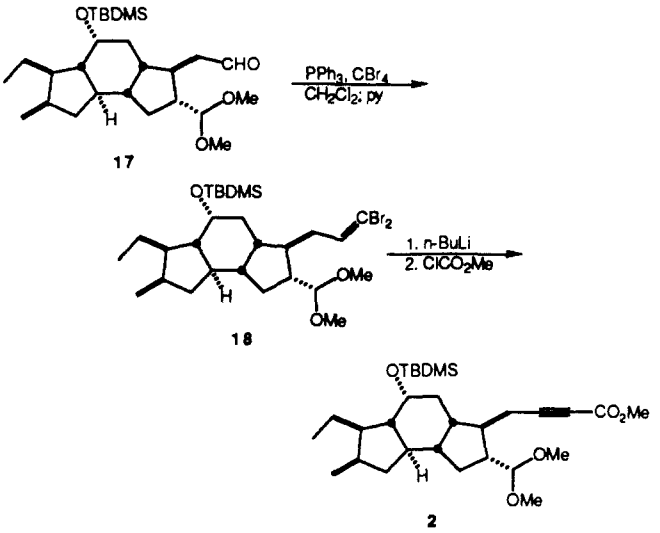


available the α,β-unsaturated aldehyde **7**, thereby setting the stage for application of Koga's elegant noncatalytic asymmetric 1,4-conjugate addition chemistry.[10] In order to test the potential usefulness of this procedure in the present context, racemic **7** was condensed with L-*tert*-leucine *tert*-butyl ester (**8**). As expected, an inseparable 1:1 mixture of the diastereomeric aldimines **9** and **10** resulted.

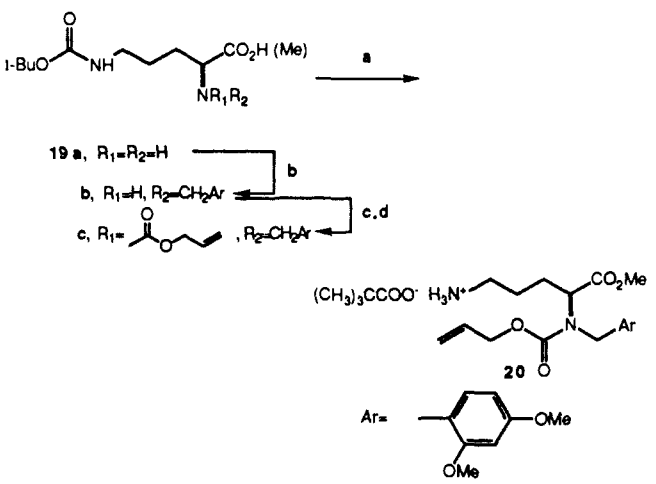
The bidentate chelating ability of such α-amino acid esters toward Grignard reagents is recognized to fix the nitrogen and oxygen atoms in a manner where reasonable conformational rigidity results.[10,11] As a consequence, the large α-*tert*-butyl substituent acts by virtue of its relative steric bulk to drive carbon–carbon bond formation to the opposite face of the complex. In view of the absolute configuration of **8**, our intent to add vinylmagnesium bromide translates into enforced delivery of the vinyl group in the manner pictured in **11** and **12**. However, these diastereomers constitute a "matched" and "mismatched" pair. Where **11** is concerned, the vinyl group is to be guided onto the sterically less-congested β-face of the decahydro-*as*-framework and little impedance to the 1,4-addition should be experienced. On the other hand, the competing process for β-introduction of the vinyl group in **12** should be kinetically disfavored by the concave topography in the vicinity of the α,β-double bond. The major uncertainty associated with this tactic was the extent to which steric factors present in "mismatched" diastereomer **12** would preclude ultimate conversion to **14**. We remain unaware of any related attempt to capitalize upon steric compression within the original aldehyde to override the controlling elements present in the amino acid auxiliary.

In the event, dropwise treatment of >5 mol equiv of vinylmagnesium bromide to a cold (−36 °C) tetrahydrofuran solution of the **11**/**12** mixture followed by a 10% aqueous citric acid quench at 0 °C gave rise to a difficultly separable 83:17 mixture of **13** and **14** (^{1}H NMR analysis). With proper allowance for the quantity of **7** recovered, the efficiency of the vinylation was 48‰ and the actual yield of the desired **13** was 22%. In order to ascertain the level of enantiomeric purity of **13**, the **13**/**14** mixture was directly ketalized, hydroborated, and subjected to chromatographic purification. At this point, major alcohol **16** (Scheme III) was easily obtained free of its diastereomer in excellent yield (84% for the two steps). The optical purity of the initially isolated crystalline product, $[\alpha]^{25}_D$ −45.1°, was established through conversion to its Mosher ester[12] to be 91% ee. Two recrystallizations of **16** from petroleum ether resulted in an increase in $[\alpha]^{25}_D$ to −48.9° corresponding to 98% ee. Further recrystallization provided enantiomerically pure material, $[\alpha]^{25}_D$ −49.7°.

Scheme IV



Scheme V[a]



[a] (a) HCOOH, 10 °C, 3 h; $(CH_3)_3COOH$; (b) ArCHO, $NaBH_3CN$, MeOH; (c) $ClCO_2CH_2CH{=}CH_2$, $NaHCO_3$, dioxane, H_2O; MeOH; H_3O^+; (d) CH_2N_2.

The synthesis was continued with alcohol of 98% ee quality to insure against possible complications from diastereomer formation. With **16** in hand, all eight of the stereogenic centers present in the carbotricyclic segment of ikarugamycin had been set in their proper absolute configuration.

In order to take advantage of the known ease of conversion of aliphatic aldehydes to homologated acetylenic esters,[13] **16** was oxidized to **17** with PCC under buffered conditions and transformed into dibromoolefin **18** by reaction with carbon tetrabromide and triphenylphosphine in dichloromethane (Scheme IV). The conversion to **2** was brought about by reaction with *n*-butyllithium in tetrahydrofuran at −78 °C for 35 min and at 25 °C for 20 min, followed by capture of the lithium acetylide with methyl chloroformate. This chain lengthening, realized with exceptional efficiency (84% overall), advanced matters to where amide bond construction had next to be dealt with.

To this end, the appropriately functionalized ornithine segment was assembled by converting the known[13a] δ-*N*-*t*-Boc protected amino acid **19a** to the fully protected derivative **19c** (Scheme V). The δ-amino group in **19c** could best be chemoselectively unmasked by exposure to formic acid at 10 °C. This route to **20** provides for efficient differential blocking of the α-amino substituent. Removal of the allyl carbamate was destined to occur prior to manipulation of the 2,4-dimethoxybenzyl functionality.

(9) House, H. O. *Modern Synthetic Reactions*, Second Edition; W. A. Benjamin, Inc.: Menlo Park, CA, 1972; Chapter 11.

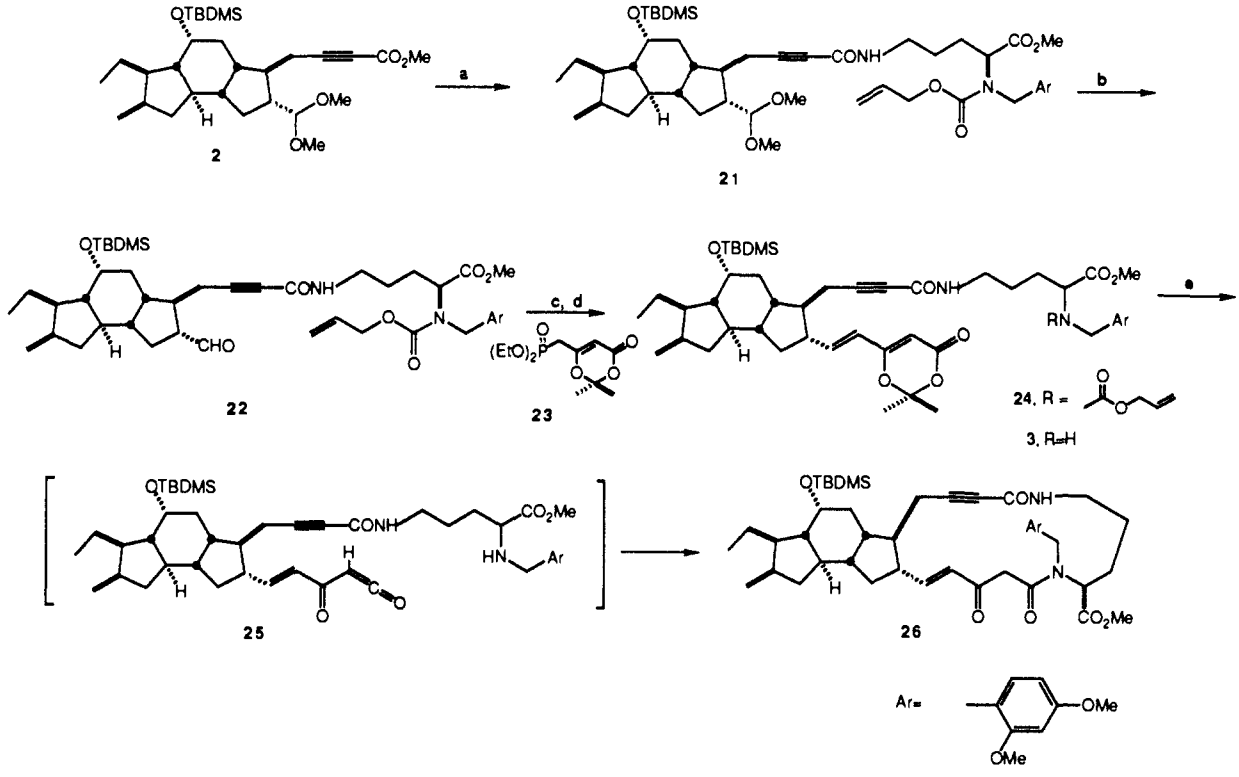
(10) (a) Hashimoto, S.; Yamada, S.; Koga, K. *J. Am. Chem. Soc.* **1976**, *98*, 7450. (b) Hashimoto, S.; Kogen, H.; Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1979**, 3009. (c) For a recent review of this field, consult the following: Tomioka, K.; Koga, K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Part A, Chapter 7.

(11) (a) Yamada, S.; Hashimoto, S. *Chem. Lett.* **1976**, 921. (b) Hashimoto, S.; Komeshima, N.; Yamada, S.; Koga, K. *Tetrahedron Lett.* **1977**, 2907. (c) Hashimoto, S.; Yamada, S.; Koga, K. *Chem. Pharm. Bull. Jpn.* **1979**, *27*, 771.

(12) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(13) (a) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769. See also: (b) Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1974**, 705. (c) Cha, J. K.; Cooke, P. J. *Tetrahedron Lett.* **1987**, *28*, 5473.

Scheme VI[a]



[a](a) K_2CO_3, MeOH, H_2O; 2,4,6-$(CH_3)_3PhSO_2Cl$, THF; DMAP, **20**; (b) acetone, (TsOH); (c) $KN(TMS)_2$, **23**, THF; (d) $Pd(PPh_3)_4$, PPh_3, HOAc, THF; (e) toluene, 110 °C, 4 h.

Selection of the latter was predicated on existing claims of its suitability for, and ease of removal from, tetramic acid nuclei[14] and the purported stability of 5 to these deblocking conditions.[15]

Having completed the preparation of **20**, we anticipated subsequent construction of pivotal intermediate **3** to be straightforward. This premise appeared especially true given the feasibility studies earlier documented.[5] The approach was initiated by hydrolysis of **2** with potassium carbonate in aqueous methanol, activation of the carboxylic acid by conversion to a mixed carboxylic-sulfonic anhydride with mesitylenesulfonyl chloride, and in situ condensation with **20** in the presence of 4-(dimethylamino)pyridine (Scheme VI). Once amide bond formation had been accomplished (46% from **2**), the aldehyde functionality was unmasked by transketalization of **21** with dry acetone. These anhydrous conditions were made necessary in order to bypass concomitant deblocking of the silyl ether.

Condensation of **22** with phosphonate **23**[16] proceeded fully as expected. In contrast, initial efforts to achieve cleavage of the allyl carbamate residue in **24** by means of $(Ph_3P)_4Pd$[17] were unsuccessful. The problem appeared to reside in the fact that the liberated allylamine was proceeding to attack the reaction product nucleophilicity. Once this was recognized, it proved an easy matter to deter this side reaction by having an appropriate amount of acetic acid present in the tetrahydrofuran from the outset for neutralization purposes. Under these circumstances, **3** was isolated as a clear glass in 71% yield (67% conversion).

The crucial macrocyclization was realized by heating dilute solutions of **3** in toluene for 4 h. As hoped, the extensive representation of digonal and trigonal centers in the electrophilic[18] acyl ketene **25** so generated greatly facilitated the desired intramolecular trapping. The 94% efficiency with which **26** was formed is particularly notable.

With the macrocyclization successfully accomplished, the next step was to semisaturate the acetylenic triple bond. The Lindlar method proved satisfactory for this purpose (76% of **4**, Scheme VII), although great care was required in monitoring the progress of reaction. Our experience has been that the catalyst system becomes more reactive with time as a color change from brown to black is observed. Accordingly, overreduction occurred if the hydrogenation process was not duly interrupted after 1 equiv of hydrogen had been adsorbed.

Subsequent desilylation in anticipation of the requisite dehydration was easily accomplished in 86% yield with dilute solutions of 48% hydrofluoric acid in acetonitrile. Although **27** was indeed amenable to conversion to **28** when exposed to the Burgess reagent[19] in warm benzene in accord with our prototype studies,[2,20] the yield was only marginally acceptable (36%). This is because at least two competing reactions operate concurrently. A small amount of the trisubstituted double isomer of **28** was isolated, suggesting that S_Ni behavior was being exhibited by the system in a modest way. In addition, ^1H NMR spectroscopy of impure byproducts provided indication that chemistry of a less well-defined nature was occurring between the inner salt and functional groups on the macrocyclic ring. Modification of the reaction solvent and temperature might have improved matters, but the short supply of material precluded studies of this type. Conceivably, somewhat larger scale reactions would be more suited to enhanced efficiency.

To complete the synthesis, **28** was cyclized by Dieckmann condensation with KO-*tert*-Bu in *tert*-butyl alcohol at room temperature. Fully aware of the disastrous potential for base-promoted racemization at the chiral center residing in close proximity, we allowed the ring closure to proceed for only 10 min. This rapid treatment afforded **29** as a product homogeneous by TLC in 66%

(14) (a) Schlessinger, R. H.; Bebernitz, G. R.; Lin, P.; Poss, A. J. *J. Am. Chem. Soc.* **1985**, *107*, 1777. (b) DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. *Ibid.* **1985**, *107*, 5219. (c) Bryan, D. B.; Hall, R. F.; Holden, K. G.; Huffman, W. F.; Gleason, J. G. *Ibid.* **1977**, *99*, 2353.

(15) See footnote 19 of ref 13c.

(16) (a) Boeckman, R. K., Jr.; Thomas, A. J. *J. Org. Chem.* **1982**, *47*, 2823. (b) Boeckman, R. K., Jr.; Perni, R. B.; McDonald, J. E.; Thomas, A. J. *Org. Synth.* **1987**, *66*, 194.

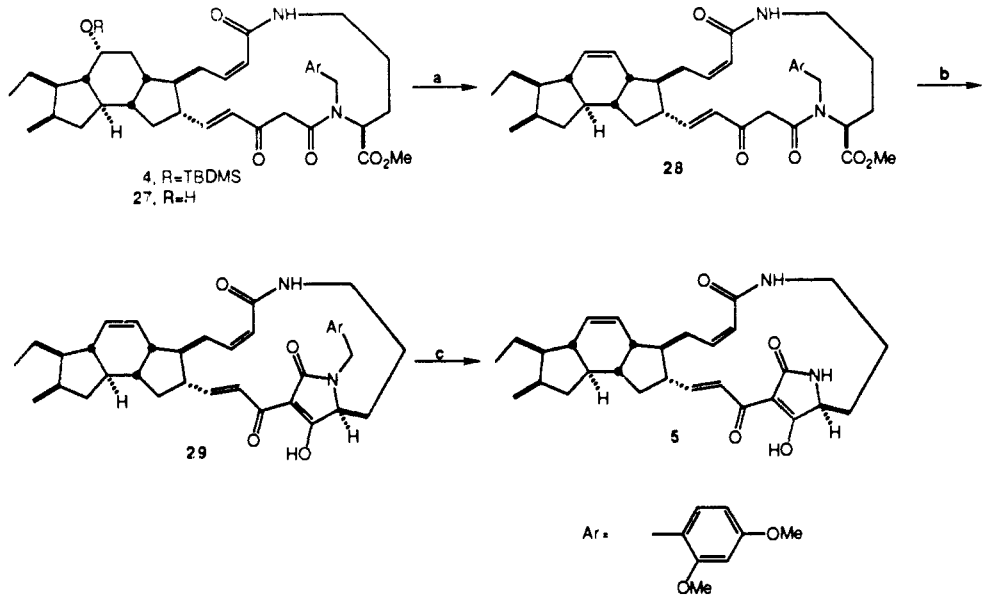
(17) Jeffrey, P. D.; McCombie, S. W. *J. Org. Chem.* **1982**, *47*, 587.

(18) (a) Hyatt, J. A.; Feldman, P. L.; Clemens, R. J. *J. Org. Chem.* **1984**, *49*, 5105. (b) Clemens, R. J.; Hyatt, J. A. *Ibid.* **1985**, *50*, 2431.

(19) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *26*, 38.

(20) Paquette, L. A.; Romine, J. L.; Lin, H.-S. *Tetrahedron Lett.* **1987**, *28*, 31.

Scheme VII[a]



[a] (a) $CH_3OC(O)NSO_2NEt_3$, C_6H_5, Δ; (b) *t*-BuOK (1 equiv), *t*-BuOH; (c) CF_3CO_2H, 62 °C, 10 min.

yield. To our surprise, however, subsequent removal of the 2,4-dimethoxybenzyl group in **29** was not readily accomplished. Realization of the final step was achieved only after an extensive search for the proper deprotection protocol. Any departure from the reaction conditions ultimately found effective (CF_3COOH, 62 °C, 10 min) gave ill-defined materials. The identity of the crystalline solid so produced as (+)-ikarugamycin (**5**) was confirmed by careful comparison of its high-field (300 MHz) and UV spectroscopic properties as well as TLC mobility and optical rotation with that of an authentic sample of the natural antibiotic provided by Professor Boeckman.

It is relevant and perhaps useful to call attention to the high affinity of macrocyclic lactams **4** and **26–29** for the encapsulation of sodium ion. Washings of organic solutions of any of these materials with brine or other Na^+X^- solution is adequate to generate complexes which are exceedingly difficult to dissociate into their components. The same phenomenon surfaces when these lactams are chromatographed on silica gel. This adsorbent must therefore be avoided in all purifications. Biosil A constitutes a serviceable alternative.[21]

The total synthesis described above makes (+)-ikarugamycin available in 25 steps (0.11% overall yield) from racemic 7,7-dimethoxy-2-norbornen-5-one, demonstrates the synthetic potential of Koga's 1,4-asymmetric conjugate addition process, and confirms the absolute stereochemical assignment previously advanced for (+)-**5** by Ito and Hirata.[3c]

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 1320 spectrophotometer. ^1H NMR spectra were recorded at 300 MHz and the ^{13}C NMR data obtained at either 75 or 20 MHz as indicated. Mass spectra were measured on a Kratos MS-30 instrument by Mr. Dick Weisenberger at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All MPLC separations were conducted on Merck Lobar columns (Lichroprep Si-60) with the help of a Fluid Metering INC pump and a Waters Associates Model R403 differential refractometer detector. The Biosil A was 200–400 mesh. All reactions were performed under an inert atmosphere (nitrogen or argon) unless otherwise indicated. Solvents were reagent grade and dried prior to use.

(3a*R,5*S**,5a*R**,7*S**,8a*S**,8b*S**)-5-(*tert*-Butyldimethylsiloxy)-6-ethyldecahydro-2-(isopropoxymethylidene)-7-methyl-*as*-indacen-3-(2*H*)-one (6).** A magnetically stirred solution of potassium hexamethyldisilazide (39 mL of 0.5 M in toluene, 19 mmol) in dry tetrahydrofuran (60 mL) was blanketed with nitrogen and treated dropwise with ketone **1** (3.37 g, 9.64 mmol) in the same solvent (20 mL) during 6 min. After 1 h at −78 °C, ethyl formate (1.70 mL, 21 mmol) was introduced dropwise. Stirring was continued at −78 °C for 25 min, after which the temperature was allowed to warm slowly to 25 °C. After 3 h, the reaction mixture was cooled to 0 °C, treated sequentially with HMPA (40 mL) and 2-iodopropane (1.90 mL, 19 mmol), and stirred at room temperature for 11 h. Following partitioning between ether (200 mL) and water (300 mL), the aqueous phase was extracted with ether, and the combined organic layers were dried and evaporated to give **6** (3.16 g, 78%) as a yellow oil consisting of a mixture of isomers which was customarily used without further purification.

In a smaller scale reaction (500 mg of **1**), the products were separated and purified by MPLC on Florisil (elution with 10% ethyl acetate in petroleum ether). The *E*/*Z* distribution was 15:1 and the total weight of the pure isomers was 399 mg (67%).

For the *E* isomer: colorless oil; IR (neat, cm^{-1}) 1710, 1640; ^1H NMR (300 MHz, C_6D_6) δ 7.55 (s, 1 H), 3.67–3.58 (m, 2 H), 2.66–2.61 (m, 2 H), 2.46–2.43 (m, 1 H), 2.15–1.98 (m, 3 H), 1.89–1.80 (m, 1 H), 1.75–1.66 (m, 2 H), 1.49–1.32 (m, 6 H), 1.12 (s, 9 H), 1.10–1.00 (m, 2 H), 0.99 (d, *J* = 6.2 Hz, 6 H), 0.86 (d, *J* = 7.1 Hz, 3 H), 0.23 (s, 3 H), 0.20 (s, 3 H); MS *m*/*z* (M^+ − *t*-Bu) calcd 363.2356, obsd 363.2314. For the *Z* isomer: colorless oil; IR (neat, cm^{-1}) 1710, 1630; ^1H NMR (300 MHz, C_6D_6) δ 7.15 (s, 1 H), 4.03–4.00 (m, 1 H), 3.53–3.45 (m, 2 H), 2.92–2.85 (m, 1 H), 2.5–1.5 (series of m, 5 H), 1.40–1.10 (m, 5 H), 1.00–0.70 (m, 8 H), 0.95 (s, 9 H), 0.78 (d, *J* = 7.1 Hz, 6 H), 0.06 (s, 6 H); HS *m*/*z* (M^+ − *t*-Bu) calcd 363.2356, obsd 363.2338.

***tert*-Butyl (2*S*)-2-[[[(3a*R**,5*S**,5a*R**,6*S**,7*S**,8a*S**,8b*R**)-5-(*tert*-Butyldimethylsiloxy)-6-ethyl-1,3a,4,5,5a,6,7,8,8a,8b-decahydro-7-methyl-*as*-indacen-2-yl]methylene]amino]-3,3-dimethylbutyrate (9) and Its Diastereomer (10).** A hexane solution of diisobutylaluminum hydride (30.0 mL of 1.0 M, 30.0 mmol) was added dropwise during 12 min to a precooled (−78 °C) solution of unpurified **6** (as obtained above, 14.3 mmol) in dry methylene chloride (120 mL) under a nitrogen atmosphere. After being stirred for 2 h at −78 °C, the mixture was poured into cold (0 °C) 30% hydrochloric acid (75 mL) and well agitated for 3 h at 25 °C. The usual extractive workup furnished a yellow oil that was purified by HPLC (silica gel, elution with 4% ethyl acetate in petroleum ether) to give 2.5 g (48% overall from **1**) of **7** as a faintly yellow oil: IR (neat, cm^{-1}) 2960, 2930, 2860, 1680, 1460, 1375, 1255, 1175, 1090, 1005, 860, 835, 775; ^1H NMR (300 MHz, C_6D_6) δ 9.67 (s, 1 H), 6.00 (s, 1 H), 3.44–3.37 (m, 1 H), 2.51–2.43 (m, 2 H), 2.29–2.24 (m, 1 H), 2.06–1.97 (m, 1 H), 1.75–1.65 (m, 3 H), 1.62–1.49 (m, 2 H), 1.39–1.16 (m, 5 H), 0.99 (s, 9 H), 0.95 (t, *J* = 7.3 Hz, 3 H), 1.78 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 190.17, 156.45, 145.03, 71.61, 50.31, 48.27, 43.87, 39.99, 39.68, 38.40, 34.25, 34.14, 33.18, 25.84, 22.30, 17.93, 15.10, 12.86, −4.07, −4.55; MS *m*/*z* (M^+ − *t*-Bu) calcd 305.1936, obsd 305.1945. Anal. Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.71; H, 10.44.

The *tert*-butyl ester of L-*tert*-leucine (1.07 mL, 5.20 mmol) was added to a solution of enal **7** (1.72 g, 4.74 mmol) in anhydrous ether (30 mL) containing magnesium sulfate (10 g, 83 mmol) at 25 °C under nitrogen. Acetic acid (13 μL, 0.23 mmol) was introduced, and stirring was con-

(21) Hirsch, J.; Ahrens, E. H., Jr. *J. Biol. Chem.* **1958**, *233*, 311.

tinued for 18 h. At this point, an additional 2 g (17 mmol) of magnesium sulfate was added, and stirring was maintained for an additional 2 h. The mixture was filtered through Celite and evaporated to leave the 1:1 mixture of α,β-unsaturated imines **9** and **10** as a pale yellow oil: ^{1}H NMR (300 MHz, C_6D_6) δ 8.01 (s, 0.5 H), 7.99 (s, 0.5 H), 5.80 (m, 1 H), 3.61 (s, 0.5 H), 3.58 (s, 0.5 H), 3.45 (m, 1 H), 2.95–2.45 (series of m, 3 H), 2.10–1.55 (series of m, 4 H), 1.39 (s, 4.5 H), 1.37 (s, 4.5 H), 1.182 (s, 4.5 H), 1.180 (s, 4.5 H), 1.02 (s, 4.5 H), 1.01 (s, 4.5 H), 1.50–0.75 (series of m, 12 H), 0.11 (s, 1.5 H), 0.10 (s, 3 H), 0.09 (s, 1.5 H); MS *m/z* (M^+) calcd 530.4029, obsd 530.4039. This material was used directly without further handling.

(2*R*,3*R*,3a*R*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsilyoxy)-6-ethyldodecahydro-7-methyl-3-vinyl-*as*-indacene-2-carboxaldehyde (13). The imine mixture was taken up in dry tetrahydrofuran (80 mL) under nitrogen, and this solution was cooled to −36 °C while being stirred and treated dropwise with vinylmagnesium bromide (15.0 mL of 1 M in tetrahydrofuran, 15.0 mmol) below −32 °C. After being stirred for an added 25 min, the yellow homogeneous solution was poured into cold (0 °C) 10% citric acid (180 m) during 10 s with vigorous agitation. A small amount of ether was used to complete the transfer. After 3 h of stirring at 25 °C, the product was extracted into ether, and the combined organic phases were washed with water, saturated sodium bicarbonate solution, and brine prior to drying. Solvent evaporation followed by MPLC purification of the residue (silica gel, elution with 3% ethyl acetate in petroleum ether) gave a 5:1 mixture of diastereomers **13** and **14** (541 mg, 29%) and recovered enal **7** (930 mg, 54%). For pure **13** obtained by MPLC on silica gel (elution with 4% ethyl acetate in petroleum ether): IR (neat, cm^{-1}) 1725; ^{1}H NMR (300 MHz, C_6D_6) δ 9.38 (d, J = 2.6 Hz, 1 H), 5.52 (m, 1 H), 4.96–4.92 (m, 2 H), 3.48 (m, 1 H), 2.37–2.20 (m, 2 H), 2.10–2.00 (m, 1 H), 1.80–0.75 (series of m, 16 H), 1.01 (s, 9 H), 0.85 (d, J = 7.1 Hz, 3 H), 0.10 (s, 3 H), 0.09 (s, 3 H); MS *m/z* (M^+ − *t*-Bu) calcd 333.2250, obsd 333.2276.

(2*R*,3*R*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsilyoxy)-6-ethyldodecahydro-7-methyl-3-vinyl-*as*-indacene-2-carboxaldehyde Dimethyl Acetal (15). A solution of the 5:1 mixture of aldehydes (541 mg, 1.39 mmol) in trimethyl orthoformate (5 mL) was treated with *p*-toluenesulfonic acid monohydrate (8 mg). Stirring was continued for 30 min at 25 °C prior to neutralization with saturated sodium bicarbonate solution. The usual extractive workup gave crude **15** (600 mg, 99%), which was normally used without additional purification. A small amount of **15** was isolated in pure form (MPLC on silica gel, elution with 4% ethyl acetate in petroleum ether) as a colorless oil: IR (neat, cm^{-1}) 3080, 1640; ^{1}H NMR (300 MHz, C_6D_6) δ 5.74 (ddd, J = 17.7, 10.2, 8.4 Hz, 1 H), 5.08 (dd, J = 17.7, 2.0 Hz, 1 H), 5.00 (dd, J = 10.2, 2.0 Hz, 1 H), 4.20 (d, J = 5.7 Hz, 1 H), 3.55 (m, 1 H), 3.20 (s, 3 H), 3.17 (s, 3 H), 2.29–0.79 (series of m, 19 H), 1.02 (s, 9 H), 0.86 (d, J = 7.0 Hz, 3 H), 0.119 (s, 3 H), 0.116 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 142.62, 113.53, 107.86, 73.53, 54.03, 53.50, 53.26, 51.23, 49.07, 48.13, 40.77, 40.10, 39.85, 36.96, 33.56, 33.13, 26.29, 22.73, 18.28, 16.00, 13.28, −3.58, −4.25; MS *m/z* (M^+ − *t*-Bu) calcd 379.2668, obsd 379.2703.

(2*R*,3*R*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsilyoxy)-6-ethyldodecahydro-3-(2-hydroxyethyl)-7-methyl-*as*-indacene-2-carboxaldehyde Dimethyl Acetal (16). Disiamylborane was prepared by the dropwise addition of 2-methyl-2-butene (5.0 mL, 48 mmol) to the borane–tetrahydrofuran complex (20 mL of 1.2 M in tetrahydrfuran) at 0 °C under nitrogen. Stirring was continued for 3 h after which titration with ethylene glycol and measurement of the hydrogen evolution indicated 1.0 N. This solution was stored in the freezer and titrated prior to use. The disiamylborane solution (4.0 mL of 0.69 N in tetrahydrofuran, 2.8 mmol) was added to crude acetal **15** (600 mg) in dry tetrahydrofuran (8 mL) at 0 °C under nitrogen. Stirring was continued for 40 min after which ethanol (9 mL), 3 M sodium hydroxide solution (5.5 mL), and 30% hydrogen peroxide (5.5 mL) were introduced in sequence. After the mixture had been stirred at 25 °C for 10 h, extractive workup with ether was undertaken. Purification of the crude product by MPLC (silica gel, elution with 35% ethyl acetate in petroleum ether) gave alcohol **16** (465 mg, 74%) and its diastereomer (96 mg, 15%).

The optical activity of **16** at this stage, $[\alpha]^{25}_D$ −45.1° (*c* 10.0, ether), was determined by the Mosher ester method to be 91% ee. Two recrystallizations of this material from petroleum ether gave colorless crystals: mp 82–83 °C; $[\alpha]^{25}_D$ −48.9° (98% ee); 330 mg (52%). Further recrystallizations to constant α gave colorless prisms: mp 82–83 °C, $[\alpha]^{25}_D$ −49.7° (*c* 9.8, ether); IR (KBr, cm^{-1}) 3600–3200; ^{1}H NMR (300 MHz, C_6D_6) δ 4.10 (d, J = 7.8 Hz, 1 H), 3.68 (m, 2 H), 3.45 (m, 1 H), 2.052 (s, 3 H), 2.048 (s, 3 H), 2.40–0.75 (series of m, 22 H), 1.04 (s, 9 H), 0.94 (d, J = 7.3 Hz, 3 H), 0.130 (s, 3 H), 0.126 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 109.17, 72.56, 61.04, 54.78, 51.82, 50.17, 47.87, 46.44, 45.04, 43.25, 40.02, 39.71, 39.12, 38.53, 33.79, 33.12, 26.27, 22.39, 18.23, 16.71, 13.44, −3.44, −4.28; MS *m/z* (M^+ − CH_3OH) calcd 365.2513, obsd 365.2573. Anal. Calcd for $C_{26}H_{50}O_4Si$: C, 68.67; H, 11.08. Found: C, 68.64; H, 11.07.

Methyl (2*R*,3*R*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsiloxy)-6-ethyl-2-formyldodecahydro-7-methyl-*as*-indacene-3-tetrolate 2-(Dimethyl acetal) (2). A stirred mixture of pyridinium chlorochromate (380 mg, 1.77 mmol) and sodium acetate (290 mg, 3.54 mmol) in dry dichloromethane (13 mL) was cooled to 0 °C and treated dropwise with a solution of alcohol **16** (330 mg, 0.726 mmol) in the same solvent (8 mL) during 2 min. Stirring was maintained for 2 h at 0 °C and for 2 h at 25 °C. The brown mixture was diluted with ether (50 mL) and filtered through Florisil (5 g, elution with ether). Flash chromatographic purification (silica gel, elution with 10% ethyl acetate in petroleum ether) furnished 290 mg (89%) of **17** and 8.8 mg (3%) of unreacted alcohol. For **17**: clear, colorless oil; IR (neat, cm^{-1}) 2700, 1726; ^{1}H NMR (300 MHz, C_6D_6) δ 9.49 (t, J = 1.9 Hz, 1 H), 4.05 (d, J = 7.1 Hz, 1 H), 3.44 (m, 1 H), 3.08 (s, 3 H), 3.07 (s, 3 H), 2.39–2.31 (m, 1 H), 2.25–0.75 (series of m, 20 H), 1.03 (s, 9 H), 0.89 (d, J = 7.0 Hz, 3 H), 0.14 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 200.84, 108.61, 72.80, 65.87, 54.47, 51.70, 50.60, 49.75, 48.36, 47.35, 43.19, 42.69, 39.85, 39.54, 37.79, 33.92, 33.28, 26.22, 22.52, 18.27, 16.31, 15.57, 13.34, −3.62, −4.34; MS *m/z* (M^+ − *t*-$BuCH_3OH$) calcd 363.2355, obsd 363.2329; $[\alpha]^{25}_D$ −27.0° (*c* 0.11, ether) for 98% ee material.

Carbon tetrabromide (420 mg, 1.3 mmol) dissolved in methylene chloride (3 mL) was added dropwise to a solution of triphenylphosphine (680 mg, 2.5 mmol) in the same solvent (18 mL) at 0 °C under nitrogen. The bright yellow solution was stirred for 15 min prior to the dropwise addition of **17** (294 mg, 0.648 mmol) in methylene chloride (4 mL). The reaction mixture was stirred for an additional 15 min, at which point pyridine (0.31 mL, 3.8 mmol) was added to deter possible acetal cleavage during subsequent processing. Extractive workup with ether following quenching with saturated sodium bicarbonate solution provided a residual gum that was triturated several times with petroleum ether to remove most of the triphenylphosphine oxide. Final purification was achieved by chromatography on TLC mesh silica gel (4 g, elution with 4% ethyl acetate in petroleum ether), and **18** (395 mg, 100%) was obtained as a clear colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 6.37 (t, J = 7.3 Hz, 1 H), 4.05 (d, J = 6.7 Hz, 1 H), 3.46 (m, 1 H), 3.13 (s, 3 H), 3.10 (s, 3 H), 2.27–2.02 (series of m, 4 H), 1.84–1.71 (m, 5 H), 1.62–1.59 (m, 3 H), 1.48–1.25 (m, 6 H), 1.04 (s, 9 H), 1.01 (t, J = 7.5 Hz, 3 H), 0.89 (d, J = 7.1 Hz, 3 H), 0.16 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 138.64, 108.65, 89.02, 72.86, 54.57, 52.06, 50.57, 48.40, 47.22, 46.56, 42.43, 39.86, 39.81, 39.78, 38.31, 33.77, 33.28, 26.24, 22.54, 18.28, 16.33, 13.36, −3.57, −4.28; MS *m/z* (M^+ − *t*-Bu) calcd 551.0988, obsd 551.1001; $[\alpha]^{25}_D$ −13.5° (*c* 0.12, ether) for 98% ee material.

n-Butyllithium (0.91 mL of 1.6 M in hexanes, 1.46 mmol) was added dropwise to **18** (395 mg, 0.694 mmol) in dry tetrahydrofuran (2.2 mL) at −78 °C under nitrogen. After 35 min of stirring at −78 °C, the temperature was raised to 25 °C for 20 min. The reaction mixture was then recooled to −78 °C, at which point methyl chloroformate (113 μL, 1.46 mmol) was introduced dropwise. After an additional 40 min at −78 °C, the mixture was allowed to warm to 10 °C during 1 h. The addition of saturated sodium bicarbonate solution was followed by extractive workup with ether and MPLC purification on silica gel. Elution with 10% ethyl acetate in petroleum ether afforded 310 mg (94%) of **2** and 5.5 mg (2%) of the terminal acetylene. For **2**: clear colorless oil; IR (neat, cm^{-1}) 2240, 1718; ^{1}H NMR (300 MHz, C_6D_6) δ 4.06 (d, J = 2.1 Hz, 1 H), 3.50 (m, 1 H), 3.28 (s, 3 H), 3.12 (s, 1 H), 3.09 (s, 1 H), 2.40 (dd, J = 17.3, 4.6 Hz, 1 H), 2.30 (dd, J = 17.3, 6.8 Hz, 1 H), 2.15 (m, 1 H), 2.05–1.60 (series of m, 8 H), 1.50–1.25 (m, 2 H), 0.15 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 154.05, 108.62, 88.68, 74.56, 72.47, 54.32, 52.14, 51.82, 50.63, 48.12, 46.20, 45.97, 42.16, 39.81, 39.73, 37.52, 33.83, 26.20, 23.18, 22.52, 18.23, 16.32, 13.36, −3.79, −4.37; MS *m/z* (M^+ − *t*-Bu) calcd 449.2723, obsd 449.2713; $[\alpha]^{25}_D$ −6.4° (*c* 0.12, ether) for material of 98% ee. Anal. Calcd for $C_{29}H_{50}O_5Si$: C, 68.73; H, 9.94. Found: C, 69.02; H, 9.95.

δ-*N*-(*tert*-Butyloxycarbonyl)-L-ornithine (19a). Cupric carbonate (22.0 g, 0.100 mmol) was added portionwise to L-ornithine hydrochloride (16.9 g, 0.10 mol) in water (200 mL) at 90 °C. The deep blue solution was refluxed for 1 h and filtered through Celite that was subsequently rinsed with 400 mL of hot water. The filtrate was cooled to 22 °C, and sodium bicarbonate (16.8 g, 0.200 mmol) was introduced followed by the dropwise addition of $(t\text{-BuOCO})_2O$ (30 mL, 0.13 mol) in dioxane (240 mL) over 30 min. Stirring was continued for 14 h at 25 °C. The blue solid was separated by filtration and dried under vacuum to give 4.84 g of the copper complex, mp 244 °C dec with effervescence. The mother liquor was concentrated at 40–50 °C to a volume of 100 mL and cooled for 6 days at 0 °C after which a second crop was isolated (10.47 g, mp 244 °C dec). A third crop was similarly obtained (1.62 g, mp 238 °C dec). The total yield was 16.93 g (66%).

The copper complex (15.16 g, 29.7 mmol) was suspended in 2% aqueous acetic acid (360 mL) and methanol (120 mL) at 25 °C. Hy-

drogen sulfide gas was introduced below the surface while the solution was stirred for 30 min. Nitrogen was next purged through the mixture for 45 min. After filtration through Celite, the clear colorless filtrate was evaporated at 40 °C to give crude **19a** (11.8 g) as a light pink solid. Recrystallization from water gave three crops of colorless solid: (A) 4.08 g (30%), $[\alpha]^{25}_D$ +5.6° (*c* 1.3, 2 N NH_4OH) (lit[22] $[\alpha]^{23}_D$ +6.1 ± 1° in 2 N NH_4OH); (B) 2.95 g (21%), $[\alpha]^{25}_D$ +5.3° (*c* 1.2, 2 N NH_4OH); (C) 2.56 g (total yield 69%).

δ-*N*-(*tert*-Butyloxycarbonyl)-α-*N*-(2,4-dimethoxybenzyl)-L-ornithine (19b). Methanol (90 mL) was added to **19a** (3.0 g, 12.9 mmol) and 2,4-dimethoxybenzaldehyde (2.16 g, 13.0 mmol), and the mixture was stirred for 20 min. Sodium cyanoborohydride (990 mg, 15.8 mmol) was introduced, at which point a slight exotherm resulted and a heavy white precipitate formed after 1.5 h. After an additional 3 h of stirring, the reaction mixture was diluted with water (250 mL), stirred for 1 h at 25 °C, and cooled overnight at 0 °C. The white precipitate was isolated by filtration and dried in vacuo to give 4.31 g (87%) of **19b**. Recrystallization from methanol gave two crops: (A) 3.22 g (67%), $[\alpha]^{25}_D$ +10.5° (*c* 13.7, CH_3OH); (B) 0.53 g (11%), $[\alpha]^{25}_D$ +7.4° (*c* 10.0; CH_3OH). For **19b**: IR (KBr, cm^{-1}) 3600–3200 (br), 3100–2300 (br), 1710, 1615, 1590, 1510, 1460, 1390; ^1H NMR (300 MHz, DMSO-d_6) δ 7.24 (d, *J* = 8.3 Hz, 1 H), 6.80, (m, 1 H), 6.56 (d, *J* = 2.3 Hz, 1 H), 6.50 (dd, *J* = 8.3, 2.3 Hz, 1 H), 3.84 (d, *J* = 13.2 Hz, 1 H), 3.78 (s, 3 H), 2.75 (s, 3 H), 3.01 (t, *J* = 6.1 Hz, 1 H), 2.89 (d, *J* = 6.8 Hz, 1 H), 2.85 (d, *J* = 6.8 Hz, 1 H), 1.59 (m, 2 H), 1.44 (m, 2 H), 1.36 (s, 9 H); MS *m/z* for $C_9H_{13}NO_2$ calcd 167.0946, obsd 167.1002. Anal. Calcd for $C_{19}H_{30}N_2O_6 \cdot H_2O$: C, 56.99; H, 8.05. Found: C, 57.02; H, 7.65.

δ-*N*-(*tert*-Butyloxycarbonyl)-α-*N*-(2,4-dimethoxybenzyl)-L-ornithine (19c). A mixture of **19b** (1.50 g, 3.92 mmol) and sodium bicarbonate (5.3 g, 63 mmol) in water (53 mL) was stirred for 5 min. Dioxane (53 mL), was added, and the mixture was stirred a further 15 min before being cooled to 0 °C. Following the dropwise addition of allyl chloroformate (2.1 mL, 20 mmol), stirring was continued for 4 h. Methanol (130 mL) was introduced, and the temperature was raised to 25 °C for 3.5 h. Acidification with 10% hydrochloric acid followed by extractive workup with ether gave a clear viscous oil that was esterified with ethereal diazomethane at 0 °C to give 1.42 g (75%) of **19c**. MPLC of this material (silica gel, elution with 35% ethyl acetate in petroleum ether) gave **19c** (1.16 g, 61%) as a colorless oil: IR (neat, cm^{-1}) 3370, 1780, 1700, 1610, 1585; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.15 (m, 1 H), 6.44 (dd, *J* = 12.1, 2.2 Hz, 1 H), 6.42 (s, 1 H), 6.00–5.80 (m, 1 H), 5.28 (d, *J* = 17.2 Hz, 1 H), 5.20 (dd, *J* = 10.5, 1.1 Hz, 1 H), 4.63 (m, 2 H), 4.48 (m, 2 H), 4.50–4.10 (series of m, 2 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.59 (s, 3 H), 2.99 (m, 2 H), 2.05–1.55 (series of m, 4 H), 1.43 (s, 9 H); MS *m/z* (M^+ − *t*-Bu) calcd 423.1768, obsd 423.1775; $[\alpha]^{25}_D$ −27.8° (*c* 21.6, ether). Anal. Calcd for $C_{24}H_{36}N_2O_8$: C, 59.99; H, 7.55. Found: C, 59.88; H, 7.63.

Selective Deprotection of 19c. Formic acid (2.0 mL of 96%) was added to **19c** (208 mg, 0.432 mmol) at 10 °C under nitrogen, the mixture was stirred for 4.5 h, and the formic acid was evaporated in vacuo at 0 °C. Pivalic acid (44.2 mg, 0.432 mmol) was added to the residue followed by dilution with toluene (2 mL) and evaporation of this solvent. Additional toluene (2 mL) was again added and evaporatively removed to leave **20** as a viscous pale yellow oil. This material was utilized directly without further purification.

N^5-[4-[(2*R*,3*R*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsiloxy)-6-ethyl-2-formyldodecahydro-7-methyl-*as*-indacen-3-yl]-tetroloyl]-N^2-carboxy-N^2-(2,4-dimethoxybenzyl)-L-ornithine, N^2-Allyl Methyl Ester, 2-(Dimethyl acetal) (21). Potassium carbonate (33.4 mg, 0.242 mmol) in water (2.1 mL) was added to (111.6 mg, 0.220 mmol) of **2** in methanol (11 mL) at 25 °C. The slightly murky solution was heated at 43 °C for 4 h, then evaporated to dryness by repeated concentration and dilution with several portions of tetrahydrofuran (2 × 10 mL) and benzene (2 × 10 mL). In this way, the tendency of the potassium carboxylate solution to foam was minimized considerably. The potassium bicarbonate was removed by filtration through Celite of a benzene solution.

The glassy potassium carboxylate was taken up in dry tetrahydrofuran (1.5 mL) and added dropwise during 1 h to a solution of 2-mesitylenesulfonyl chloride (87 mg, 0.40 mmol) in tetrahydrofuran (1 mL) at 25 °C under nitrogen. During a subsequent 50 min of stirring, a white precipitate of potassium chloride appeared. A solution of **20** from above (0.432 mmol) in tetrahydrofuran (2.7 mL) was next introduced, to be followed 5 min later with 4-(dimethylamino)pyridine (106 mg, 0.869 mmol) in tetrahydrofuran (0.7 mL, dropwise over 25 min). After 16 h of stirring and extractive workup with ether, the crude product was purified by MPLC (silica gel, elution with 35% ethyl acetate in petroleum ether). There was isolated 86 mg (46% overall) of **21** as a colorless glass: IR (neat, cm^{-1}) 3340, 2240, 1740, 1700, 1650, 1610, 1590; ^1H NMR (300 MHz, C_6D_6) δ 7.65 (m, 0.4 H), 7.30 (m, 0.4 H), 7.30 (m, 0.6 H), 6.41 (m, 2 H), 5.78 (m, 1 H), 5.14 (d, *J* = 17.5 Hz, 1 H), 4.97 (d, *J* = 10.1 Hz, 1 H), 4.80 (m, 1 H), 4.67 (m, 1 H), 4.59 (m, 2 H), 4.39 (m, 0.6 H), 4.21 (m, 0.4 H), 4.14 (d, *J* = 7.0 Hz, 1 H), 3.54 (m, 1 H), 3.40 (s, 3 H), 3.34 (s, 3 H), 3.27 (s, 2 H), 3.25 (s, 1 H), 3.18 (s, 3 H), 3.15 (s, 3 H), 2.89 (m, 2 H), 2.42 (d, *J* = 5.6 Hz, 2 H), 2.20–1.96 (m, 6 H), 1.91–1.72 (m, 4 H), 1.53–1.24 (m, 9 H), 1.10–0.75 (m, 2 H), 1.04 (s, 9 H), 1.00 (t, *J* = 7.5 Hz, 3 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 0.17 (s, 3 H), 0.14 (s, 3 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 171.71, 161.12, 158.68, 156.44, 152.96, 133.50, 118.91, 117.14, 108.99, 104.76, 98.73, 85.07, 77.76, 72.55, 66.31, 59.98, 55.02, 54.59, 52.61, 51.56, 50.77, 48.13, 46.44, 46.16, 45.49, 42.14, 39.90, 39.33, 37.46, 33.85, 33.19, 26.74, 26.21, 23.25, 22.58, 18.24, 16.33, 13.37, −3.69, −4.33; MS *m/z* (M^+ − *t*-Bu) calcd 797.4410, obsd 797.4422; $[\alpha]^{25}_D$ −16.2° (*c* 56.9, ether). Anal. Calcd for $C_{47}H_{74}N_2O_{10}Si$: C, 66.01; H, 8.72. Found: C, 65.91; H, 8.67.

N^5-[4-[(2*R*,3*R*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsiloxy)-6-ethyl-2-formyldodecahydro-7-methyl-*as*-indacen-3-yl]-tetroloyl]-N^2-carboxy-N^2-(2,4-dimethoxybenzoyl)-L-ornithine, N^2-Allyl Methyl Ester (22). *p*-Toluenesulfonic acid monohydrate (12 mg) was added to a solution of **21** (225 mg, 0.263 mmol) in dry acetone (20 mL, distilled from K_2CO_3) at 25 °C under nitrogen. After 3 h of stirring, saturated aqueous sodium bicarbonate solution was introduced, and the product was extracted into ethyl acetate. The combined organic phases were dried and concentrated, and the residue was chromatographed on TLC grade silica gel (elution with 35% ethyl acetate in petroleum ether) to give **22** (196 mg, 92%) as a clear glass: IR (neat, cm^{-1}) 3340, 2710, 2240, 1740, 1700, 1650, 1610, 1590; ^1H NMR (300 MHz, C_6D_6) δ 9.35 (s, 1 H), 7.41 (m, 1 H), 6.42 (d, *J* = 2.0 Hz, 1 H), 6.42 (m, 1 H), 5.77 (m, 1 H), 5.48 (m, 1 H), 5.15 (d, *J* = 12.1 Hz, 1 H), 4.98 (d, *J* = 10.2 Hz, 1 H), 4.79 (m, 1 H), 4.68 (m, 1 H), 4.59 (m, 2 H), 4.42 (m, 1 H), 3.44 (m, 1 H), 3.40 (s, 3 H), 3.34 (s, 3 H), 3.28 (s, 3 H), 2.97 (m, 2 H), 2.35–0.80 (series of m, 24 H), 1.02 (s, 9 H), 0.98 (t, *J* = 7.3 Hz, 3 H), 0.84 (d, *J* = 7.1 Hz, 1 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 202.60, 171.71, 161.05, 158.68, 156.44, 152.89, 133.52, 118.80, 117.14, 104.82, 98.69, 83.73, 78.42, 72.36, 66.30, 59.97, 56.30, 55.09, 51.62, 50.74, 48.33, 45.51, 44.97, 42.60, 40.49, 39.59, 39.37, 35.75, 33.25, 31.93, 27.45, 26.74, 26.16, 22.58, 22.29, 18.17, 16.03, 13.24, −3.82, −4.34; MS *m/z* (M^+ − *t*-Bu) calcd 751.3990, obsd 751.3970; $[\alpha]^{25}_D$ −11.3° (*c* 4.2, ether).

N^5-[4-[(2*S*,3*S*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsiloxy)-2-[(*E*)-2-(2,2-dimethyl-4-oxo-*m*-dioxin-6-yl)vinyl]-6-ethyldodecahydro-7-methyl-*as*-indacen-3-yl]tetroloyl]-N^2-(2,4-dimethoxybenzyl)-L-ornithine N^2-Allyl Methyl Ester (24). A cold (−78 °C) solution of phosphonate **23** (116 mg, 0.418 mmol) in anhydrous tetrahydrofuran (5 mL) was treated while under nitrogen with potassium hexamethyldisilazide (0.835 mL of 0.5 M in toluene, 0.418 mmol). This mixture was stirred at −78 °C for 5 min and at 0 °C for 20 min. Aldehyde **22** (194 mg, 0.240 mmol) in dry tetrahydrofuran (7 mL) was introduced dropwise over 7 min. After an additional 30 min at 0 °C, the reaction mixture was allowed to warm to 25 °C over 8 h. Addition of saturated aqueous NH_4Cl solution, extractive workup with ether, and purification on a column of TLC grade silica gel (4 g, elution with 40% ethyl acetate in petroleum ether) gave **24** (198 mg, 88%) as a clear glass: IR (neat, cm^{-1}) 3340, 2240, 1728–1705, 1650, 1613, 1590; ^1H NMR (300 MHz, C_6D_6) δ 7.34–7.26 (m, 1 H), 6.41 (d, *J* = 2.0 Hz, 1 H), 6.41 (m, 1 H), 6.36 (dd, *J* = 15.5, 8.9 Hz, 1 H), 5.77 (m, 1 H), 5.70 (d, *J* = 16.0 Hz, 1 H), 5.28 (s, 1 H), 5.26 (m, 1 H), 5.15 (d, *J* = 16.8 Hz, 1 H), 4.98 (d, *J* = 10.7 Hz, 1 H), 4.80 (m, 1 H), 4.67 (m, 1 H), 4.60 (m, 2 H), 4.37 (m, 1 H), 3.50 (m, 1 H), 3.39 (s, 3 H), 3.33 (s, 3 H), 3.29 (br s, 3 H), 2.94 (m, 2 H), 2.25–0.80 (series of m, 19 H), 2.06 (d, *J* = 5.3 Hz, 2 H), 1.42 (s, 3 H), 1.38 (s, 3 H), 1.04 (s, 9 H), 1.01 (t, *J* = 7.3 Hz, 3 H), 0.87 (d, *J* = 7.2 Hz, 3 H), 0.16 (s, 3 H), 0.14 (s, 3 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 171.78, 162.84, 161.12, 160.86, 158.75, 156.47, 152.83, 144.13, 133.50, 131.23, 123.19, 118.85, 117.20, 106.14, 104.82, 98.76, 94.82, 83.42, 78.49, 73.41, 66.37, 60.00, 55.05, 51.62, 51.36, 49.84, 49.65, 49.12, 48.08, 45.58, 42.41, 41.15, 40.10, 30.75, 39.43, 39.03, 37.13, 33.52, 26.70, 26.22, 25.09, 24.84, 22.79, 20.94, 18.24, 15.81, 13.18, −3.62, −4.21; MS (FAB) (M^+ − *t*-Bu) calcd 875.452, obsd 875.520; $[\alpha]^{25}_D$ −58.2° (*c* 6.7, ether).

N^5-[4-[(2*S*,3*S*,3a*S*,5*R*,5a*S*,6*R*,7*R*,8a*R*,8b*S*)-5-(*tert*-Butyldimethylsiloxy)-2-[(*E*)-2-(2,2-dimethyl-4-oxo-*m*-dioxin-6-yl)vinyl]-6-ethyldodecahydro-7-methyl-*as*-indacen-3-yl]tetroloyl]-N^2-(2,4-dimethoxybenzyl)-L-ornithine Methyl Ester (3). A solution of **24** (196 mg, 0.210 mmol) and acetic acid (37 μL, 0.65 mmol) in tetrahydrofuran (6 mL) was treated with tetrakis(triphenylphosphine)palladium(0) (8 mg, 0.006 mmol) and triphenylphosphine (8 mg, 0.03 mmol) in tetrahydrofuran (1 mL) at 25 °C under nitrogen. The solution was kept in the absence of light for 4 h, then partitioned between 10% sodium hydroxide (12 mL) and ether (70 mL) at 0 °C. Extractive workup was followed by puri-

(22) Tesser, G. I.; Schwyzer, R. *Helv. Chim. Acta* **1966**, *49*, 1013.

fication on a column of TLC grade silica gel (4 g, elution with 80% ethyl acetate in petroleum ether) to give 64 mg (33%) of recovered **24** and 94 mg (71% based on recovered **24**) of **3** as a clear glass: IR (neat, cm^{-1}) 3320, 2240, 1728, 1650, 1610, 1590; ^1H NMR (300 MHz, $CDCl_3$) δ 7.10 (d, J = 8.9 Hz, 1 H), 6.63–6.55 (m, 1 H), 6.44–6.36 (m, 3 H), 5.90 (d, J = 15.5 Hz, 1 H), 5.25 (s, 1 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.73–3.64 (m, 4 H), 3.50–3.35 (m, 1 H), 3.31–3.23 (m, 4 H), 2.52–2.25 (m, 4 H), 2.25–1.15 (series of m, 32 H), 0.90–0.83 (m, 8 H), 0.06 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 175.34, 162.70, 160.83, 160.72, 159.14, 152.75, 144.06, 130.67, 123.15, 121.02, 106.14, 104.43, 99.04, 94.88, 83.16, 78.75, 73.42, 60.73, 55.02, 51.35, 51.16, 49.84, 49.12, 48.07, 47.28, 42.40, 41.15, 40.09, 39.21, 39.02, 37.13, 33.52, 31.08, 26.21, 25.09, 24.83, 22.79, 18.24, 15.80, 13.17, −3.62, −4.21; MS (FAB) m/z (M^+ + 1) calcd 849.501, obsd 849.50; $[\alpha]^{25}_D$ −53–3° (c 3.3, ether).

Methyl (2*R*,3*R*,3a*S*,4*R*,5a*S*,5b*S*,14*S*,19*E*,20a*S*,21a*S*,21b*R*)-4-(*tert*-Butyldimethylsiloxy)-7,8-didehydro-15-(2,4-dimethoxybenzyl)-3-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,15,16,17,18,20a,21,21a,21b-docosahydro-2-methyl-9,16,18-trioxo-1*H*-*as*-indaceno[3,2-*k*][1,6]-diazacycloheptadecine-14-carboxylate (26). A solution of **3** (136 mg, 0.160 mmol) in toluene (150 mL) was added dropwise over 1.5 h to refluxing toluene (300 mL) under nitrogen. Heating was continued for an additional 2.5 h, followed by evaporation of the toluene and purification on a column of Biosil A (4 g, elution with 60% ethyl acetate in petroleum ether). There was obtained 119 mg (94%) of **26** as a clear glass: IR (neat, cm^{-1}) 3320, 2230, 1738, 1650–1610, 1585; ^1H NMR (300 MHz, $CDCl_3$) δ 7.13 (t, J = 9.0 Hz, 0.6 H), 7.05 (t, J = 6.2 Hz, 0.4 H), 6.46–6.32 (m, 3 H), 4.47–4.30 (m, 2 H), 4.28–4.13 (m, 1 H), 3.87–3.63 (m, 8 H), 3.54 (s, 3 H), 3.45–3.16 (m, 2 H), 2.61–2.17 (m, 2 H), 2.15–0.90 (series of m, 22 H), 0.93–0.80 (m, 16 H), 0.047 (s, 3 H), 0.040 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 194.50, 170.59, 168.21, 161.08, 153.56, 132.17, 132.04, 130.00, 128.56, 128.40, 128.21, 115.96, 103.89, 98.58, 84.82, 72.73, 57.51, 55.40, 52.03, 50.64, 50.05, 48.97, 48.65, 47.44, 43.59, 40.60, 39.80, 39.28, 39.13, 38.11, 33.12, 29.67, 26.36, 26.93, 24.59, 22.56, 22.38, 22.22, 17.97, 15.68, 12.85, −3.86, −4.48; MS (FAB) m/z (M^+ − 1) calcd 791.460, obsd 791.45; $[\alpha]^{25}_D$ +31.3° (c 0.19, ether).

Methyl (2*R*,3*R*,3a*S*,4*R*,5a*R*,5b*S*,7*Z*,14*S*,19*E*,20a*S*,21a*S*,21b*R*)-4-(*tert*-Butyldimethylsiloxy)-15-(2,4-dimethoxybenzyl)-3-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,15,16,17,18,20a,21,21a,21b-docosahydro-2-methyl-9,16,18-trioxo-1*H*-*as*-indaceno[3,2-*k*][1,6]-diazacycloheptadecine-14-carboxylate (4). A solution of **26** (57 mg, 0.072 mmol) in ethyl acetate (5 mL) was saturated with hydrogen at 25 °C (by repeated evacuation of filling of the reaction flask). Palladium on barium sulfate (5%, 15 mg) was introduced, and the mixture was stirred vigorously under hydrogen for 4 min after which distilled quinoline (6 μL) was added. After a further 5 h of agitation, the catalyst was removed by filtration through Biosil A, and the filtrate was concentrated. The residue was purified by chromatography on Biosil A (2 g, 200–400 mesh, elution with 40% ethyl acetate in petroleum ether) to give 3 mg of recovered **26** and 45 mg (79%) of **4** (83% adjusted yield) as a white crystalline solid: mp 135–136 °C (from ether); ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J = 8.9 Hz, 1 H), 6.86 (dd, J = 15.5, 8.7 Hz, 1 H), 6.44 (m, 3 H), 6.25 (d, J = 15.5 Hz, 1 H), 5.92 (m, 1 H), 5.80 (s, 1 H), 5.71 (t, J = 5.2 Hz, 1 H), 5.68 (t, J = 5.7 Hz, 1 H), 4.62 (d, J = 16.3 Hz, 1 H), 4.38 (d, J = 16.3 Hz, 1 H), 4.15 (m, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.79 (m, 1 H), 3.65–3.39 (m, 3 H), 3.54 (s, 3 H), 3.18–3.13 (m, 1 H), 2.81–2.76 (m, 1 H), 2.63–2.51 (m, 1 H), 2.25–1.12 (series of m, 24 H), 0.59 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 192.64, 170.95, 167.50, 161.10, 153.58, 129.59, 126.23, 125.38, 115.89, 104.55, 103.82, 103.22, 99.21, 78.00, 72.64, 58.20, 57.17, 54.79, 53.68, 52.57, 51.26, 50.46, 50.13, 49.22, 48.17, 47.17, 46.76, 42.35, 42.09, 41.32, 40.77, 39.49, 39.00, 38.24, 37.73, 37.35, 36.53, 33.66, 32.69, 30.45, 29.67, 28.86, 27.85; MS (FAB) m/z (M^+ + 1) calcd 793.53, obsd 793.53; $[\alpha]^{25}_D$ −50.8° (c 0.19, ether). Anal. Calcd for $C_{45}H_{68}N_2O_8Si$: C, 68.15; H, 8.64. Found: C, 67.92; H, 8.64.

Methyl (2*R*,3*R*,3a*S*,4*R*,5a*R*,5b*S*,7*Z*,14*S*,19*E*,20a*S*,21a*R*,21b*R*)-15-(2,4-Dimethoxybenzyl)-3-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,15,16,17,18,20a,21,21a,21b-docosahydro-4-hydroxy-2-methyl-9,16,18-trioxo-1*H*-*as*-indacene[3,2-*k*][1,6]-diazacycloheptadecine-14-carboxylate (27). A solution of **4** (11.6 mg, 0.015 mmol) in acetonitrile (1.5 mL) was treated with 1 drop of 48% hydrofluoric acid at 25 °C. Stirring was maintained for 13 min at which point saturated aqueous sodium bicarbonate solution was introduced. The product was extracted into ethyl acetate and purified by chromatography on Biosil A (1 g, elution with ethyl acetate). There was isolated 8.4 mg (85%) of **27** as a clear glass; IR (neat, cm^{-1}) 3350, 1737, 1657, 1640–1610, 1587; ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (dd, J = 5.9, 2.5 Hz, 1 H), 6.86 (dd, J = 15.5, 8.6 Hz, 1 H), 6.46 (m, 3 H), 6.31 (m, 1 H), 6.00–5.91 (m, 1 H), 5.79–5.73 (m, 1 H), 5.66–5.62 (m, 1 H), 4.64 (d, J = 16.0 Hz, 1 H), 4.63–4.44 (m, 1 H), 4.38 (d, J = 16.0 Hz, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.79 (m, 1 H), 3.76–3.42 (m, 3 H), 3.54 (s, 3 H), 3.13–3.09 (m, 1 H), 2.87–2.73 (m, 1 H), 2.61–2.55 (m, 1 H), 2.36–1.03 (series of m, 20 H), 0.97–0.81 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 192.73, 170.96, 167.35, 158.81, 152.50, 139.80, 130.20, 127.80, 124.76, 103.86, 98.56, 73.36, 57.84, 55.40, 55.25, 51.97, 51.28, 50.76, 49.69, 49.19, 48.65, 47.96, 47.74, 42.07, 41.42, 40.54, 38.99, 38.61, 38.11, 37.74, 33.50, 29.68, 26.25, 26.66, 26.19, 25.95, 22.75, 22.44, 15.24, 12.85; MS (FAB) m/z (M^+ + 1) calcd 678.489, obsd 678.48; $[\alpha]^{25}_D$ −14.8° (c 0.07, ethyl acetate).

Dehydration of 27. Alcohol **27** (14.7 mg, 0.0217 mmol) and Burgess reagent (5.7 mg, 0.024 mmol) were dissolved in benzene at 25 °C under nitrogen. This solution was stirred for 30 min at 25 °C, during which time a white precipitate appeared. The temperature was slowly raised to 50 °C during 2 h and stirring was maintained at this temperature for 16 h. After cooling, the mixture was partitioned between water and ethyl acetate. Further extractive workup (with use of KCl to break emulsions) followed by chromatographic purification on Biosil A (1 g, gradient elution with 70% ethyl acetate in petroleum ether to pure ethyl acetate) returned 1.9 mg of **27** and gave 4.5 mg (36% adjusted yield) of **28** as a clear glass: IR (neat, cm^{-1}) 3340, 1738, 1640, 1612, 1588; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J = 13.0 Hz, 1 H), 6.87 (dd, J = 15.4, 8.9 Hz, 1 H), 6.45 (m, 3 H), 6.26 (d, J = 15.2 Hz, 1 H), 5.80 (m, 1 H), 5.60 (m, 1 H), 4.59 (d, J = 16.8 Hz, 1 H), 4.39 (d, J = 16.8 Hz, 1 H), 4.50–4.29 (m, 1 H), 3.81 (m, 6 H), 3.79–3.60 (m, 1 H), 3.54 (s, 6 H), 3.51–3.25 (m, 1 H), 3.18–3.08 (m, 1 H), 2.74–2.56 (m, 1 H), 2.44–2.28 (m, 1 H), 2.37–1.00 (series of m, 18 H), 0.91 (t, J = 7.4 Hz, 3 H), 0.85 (d, J = 7.1 H, 3 H); MS (FAB) m/z (M^+ + 1) calcd 661.379, obsd 661.34; $[\alpha]^{23}_D$ +41° (c 0.037 ethyl acetate).

(2*R*,3*R*,3a*S*,5a*R*,5b*S*,7*Z*,14*S*,19*E*,20a*S*,21a*R*,21b*R*)-3-Ethyl-2,3,3a,5a,5b,6,10,11,12,13,14,15,20a,21,21a,21b-hexadecahydro-22-hydroxy-2-methyl-14,17-metheno-17*H*-*as*-indaceno[3,2-*k*][1,6]-diazacycloheptadecine-9,16,18(1*H*)-trione (Ikarugamycin, 5). A 4.2 mg (6.4 × 10^{-3} mmol) sample of **28** was dissolved in 0.2 mL of a solution of potassium *tert*-butoxide in *tert*-butyl alcohol (9.8 mg or 87 × 10^{-3} mmol in 2 mL) at 25 °C under nitrogen. The reaction mixture was stirred for 10 min and quenched with 5% citric acid. Extractive workup followed by purification on Biosil A (0.5 g of 200–400 mesh, elution with 20% methanol in ethyl acetate) gave 2.7 mg (66%) of **29** as a white solid homogeneous to TLC that was directly deblocked.

A 3 mg (4.8 × 10^{-3} mmol) sample of **29** was dissolved in doubly distilled trifluoroacetic acid (0.2 mL) and heated at 62 °C under argon for 10 min. The reaction mixture was cooled to 25 °C and the CF_3CO-OH was removed under high vacuum. The yellow residue was twice triturated with benzene (3 mL) and again evaporated in vacuo. Purification by chromatography on Biosil A (0.5 g, elution with 9:1 chloroform–ethanol) gave ikarugamycin (0.3 mg, 20%), spectroscopically (UV, ^1H NMR) and chromatographically identical with an authentic sample. Material from five such runs was combined for the following spectral analyses: ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, J = 15.5 Hz, 1 H), 6.77 (dd, J = 15.5, 10.2 Hz, 1 H), 6.08 (dt, J = 2.7, 11.1 Hz, 1 H), 5.96 (d, J = 9.8 Hz, 1 H), 5.85–5.15 (m, 4 H), 3.91 (d, J = 3.4 Hz, 1 H), 3.72–3.66 (m, 1 H), 3.49 (ddd, J = 16.6, 10.7, 4.4 Hz, 1 H), 2.65–2.39 (m, 4 H), 2.33–2.17 (m, 1 H), 2.16–1.98 (m, 4 H), 1.87–1.82 (m, 1 H), 1.62–1.11 (series of m, 9 H), 0.97 (t, J = 13.0 Hz, 3 H), 0.89 (d, J = 7.1 Hz, 3 H), 0.71 (ddd, J = 18.6, 11.9, 6.7 Hz, 2 H); UV λ_{CH_3OH} 277 (ϵ 20 700), 327 nm (17 300); $[\alpha]^{25}_D$ +287 (c 0.12, THF).

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