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Alkynyliodonium Salts in Organic Synthesis. Development of a Unified Strategy for the Syntheses of (−)-Agelastatin A and (−)-Agelastatin B

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The total syntheses of natural agelastatin A and agelastatin B were accomplished via a strategy that utilized an alkynyliodonium salt → alkylidenecarbene → cyclopentene transformation to convert a relatively simple amino alcohol derivative to the functionalized core of the agelastatin system. Subsequent manipulations delivered debromoagelastatin, which served as a precursor to both agelastatin A and agelastatin B. Alkylidenecarbene insertion chemoselectivity issues were explored en route to the final targets.

The agelastatins comprise a small group of tetracyclic, brominated metabolites isolated from the alcoholic extracts of several axinellid sponges.[1] Their structural elucidation rests on extensive NMR, molecular modeling, and exciton coupling studies. The structural and relative stereochemical assignments of agelastatin A (**1**) were confirmed by total synthesis of the racemate.[2] The similarity in skeletal connectivity between the agelastatins and the axillenid congener oroidin (**5**) sparked a biosynthesis hypothesis linking the two structures, although no data which address this point have been forthcoming.[1a,e] Agelastatin A displays significant cytotoxicity against both the L1210 and KB tumor cell lines as well as notable activity against a doxorubicin-resistant L1210 leukemia strain.[1d] In vivo activity in mice inoculated with L1210 leukemia cells was recorded, but only upon repeated intraperitoneal injection.[1d] A limited number of structural analogues available through semisynthesis from **1** were examined in similar in vitro assays. The upshot of these structure−activity investigations was that cytotoxicity dropped precipitously upon any structural modification. Thus, there appears to be very precise structural requirements for inducing cytotoxicity in these assays. No molecular-level biological mechanism-of-action has been proposed to rationalize how this particular constellation of H-bonding functionality exerts its effects, but it is interesting to note that the C(1) bromide in **1** is readily replaced with hydride upon treatment with $LiAlH_4$ with no concurrent reduction of the aminal moiety.[1c] This result is suggestive of an unexpectedly high level of electrophilicity at C(1), which in conjunction with latent electrophilicity at C(9a) as revealed by the synthesis studies (vide infra) might support the contention that agelastatin A functions as a novel type of bis alkylating agent in vivo.

Agelastatin A cannot be completely purified from its congener agelastatin B (**2**) when isolated from the sponge, and derivatization through trimethylation at N(5), N(6) and the tertiary alcohol was required to effect separation and full characterization. This problem of acquiring clean samples of (−)-**1** and (−)-**2** can be rectified by total chemical synthesis, and a full accounting of our efforts in this area follows.[3] The total synthesis of agelastatin A and agelastatin B in enantiomerically pure form described herein confirms the absolute stereochemical assignment and, for the first time, provides pure samples of both compounds for further biological evaluation.

Our interest in the polycyclic agelastatin core grew from continuing studies designed to exploit the rich chemistry of alkynyliodonium salts[4] in complex molecule synthesis. Alkynyliodonium salts serve as convenient precursors to highly reactive alkylidenecarbenes, which themselves offer many opportunities for bond formation with normally refractory substrates.[5] One characteristic reaction of these carbenes involves insertion into an otherwise unactivated C−H bond five atoms removed from the carbenic center to furnish functionalized cyclopentenes. The similarity between the cyclopentene product **8** and the cyclopentane core of the agelastatins provided the motivation for pursuing this strategy, as

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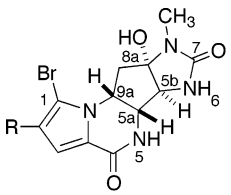
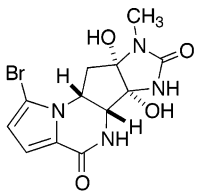
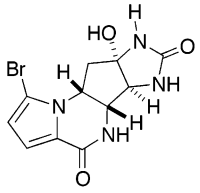


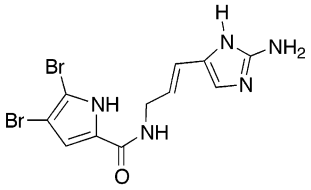
1 R = H agelastatin A
2 R = Br agelastatin B



3 agelastatin C



4 agelastatin D



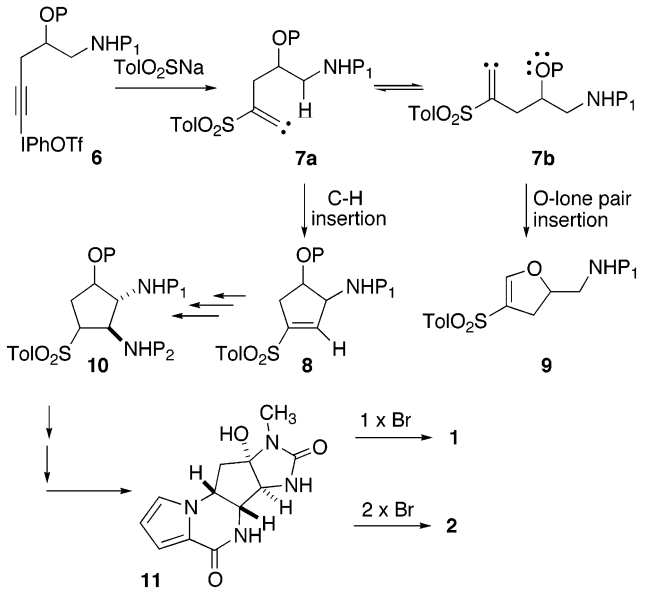
5 oroidin

detailed in Scheme 1. However, this approach to the agelastatins was not without its risks. Alkylidenecarbene **7** is faced with a choice: 1,5 C−H insertion to deliver the desired cyclopentene product **8**, or formal oxygen/lone-pair insertion to provide the dihydrofuran **9** via a putative ylide intermediate.[6] Both of these reaction channels have been described, and the only example where they were in direct competition (:NBOC vs C−H) does not provide support for the desired 1,5 C−H insertion pathway.[7] Therefore, further data on alkylidenecarbene insertion chemoselectivity was required, and the systematic study pursued in support of the agelastatin synthesis work provides insight into the electronic factors which influence this competition. The choice of sulfinate as the triggering nucleophile in the key cyclization sequence was made in light of the downstream needs to activate both C(5a) and C(9a) for sequential nucleophilic (e.g., amine) additions. Thus, the alkenyl sulfone moiety in **8** satisfies the former requirement, whereas the latter strategic need can be met when the sulfone serves as a leaving group in chemistry evolving from intermediate **10**. Finally, a desire to synthesize both the monobromide agelastatin A and the dibromide agelastatin B prompted a careful evaluation of both the timing and the means for bromide incorporation into the agelastatin tetracyclic core. The later in the synthesis sequence that the divergence to either agelastatin A or agelastatin B occurs, the more efficient the overall route. The logical extension of this strategy would delay pyrrole bromination until the final step, assuming that selective mono- and dibromination of a debromoagelastatin precursor could be achieved. There is scant precedent for this selectivity, and earlier work on agelastatin synthesis resorted to use of a TMS directing group to enforce regioselective bromination at C(1).[2] Nevertheless, this question appeared worthy of further study, and so development of selective debromoagelastatin bromination sequences was built into the design strategy.

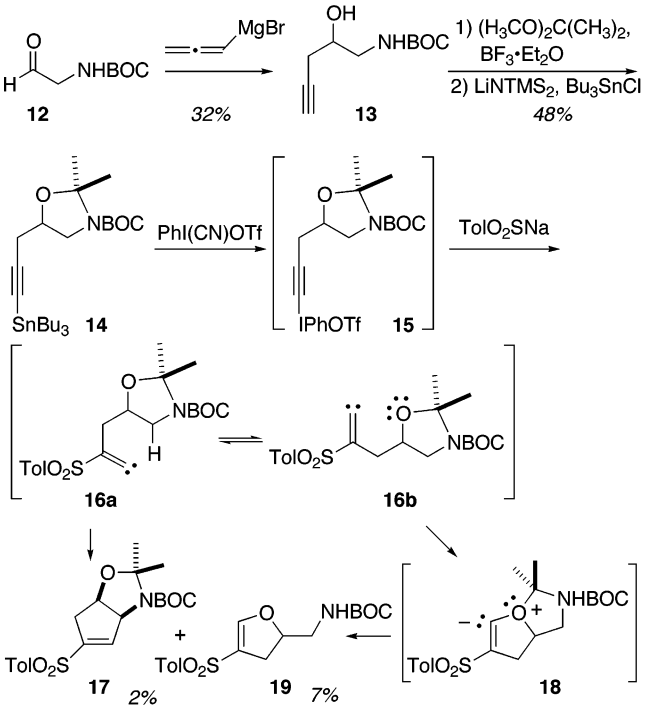
Results and Discussion

The initial approach to a functionalized alkynyliodonium salt of the type **6** commenced with combination of

SCHEME 1



SCHEME 2



an allenic Grignard reagent with the freshly prepared aldehyde **12** to furnish the hydroxycarbamate **13** in modest yield, Scheme 2. No allene-containing products were observed. Acetonide formation proceeded smoothly from **13**, and alkyne stannylation delivered the precursor **14** to the central iodonium salt intermediate. The conversion of alkynylstannane **14** into the unisolated alkynyliodonium salt **15** proceeded through treatment with Stang's reagent, PhI(CN)OTf.[8] The crude alkynyliodonium salt was washed with hexane at −40 °C to remove tin residues and then rapidly cannulated as a solution in DME into a suspension of $TolO_2SNa$ in refluxing DME.

(6) (a) Feldman, K. S.; Wrobleski, M. L. *Org. Lett.* **2000**, *2*, 2603−2605. (b) Feldman, K. S.; Wrobleski, M. L. *J. Org. Chem.* **2000**, *65*, 8659−8668.

(7) Feldman, K. S.; Mingo, P. A.; Hawkins, P. C. D. *Heterocycles* **1999**, *51*, 1283−1294.

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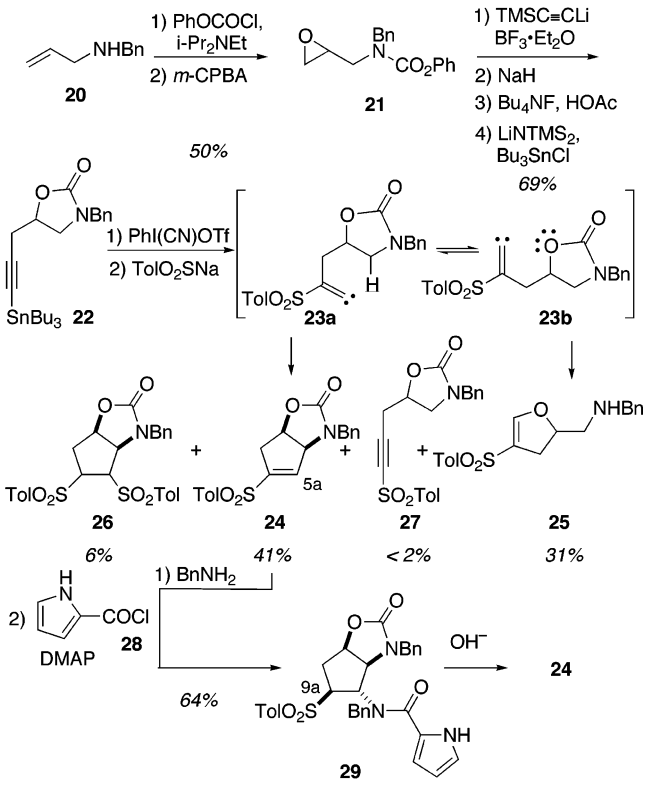
SCHEME 3



Two cyclized products were isolated in only symbolic amounts following extensive chromatography. Although very little cyclized material was recovered, the ~3:1 preference for the oxygen/lone pair insertion product **19** over the C−H insertion product **17** is consistent with the expectations generated by the C−H vs :NBOC example[7] alluded to earlier. Little effort was made to improve these results, as the particular set of reaction conditions (solvent, temperature, concentration, reagent ratio) determined to be optimal for related reactions was used here.[9] The remainder of the reaction product(s) defied either purification or characterization. Rather, a more productive approach might involve redesigning the substrate.

Toward this end, the *N*-benzyl oxazolidinone alkynylstannane **22** was targeted next, Scheme 3. The electron-withdrawing character of the carbonyl in **22** raises the possibility that the offending oxygen lone pair in **23** would no longer be so readily available for capture by the intermediate alkylidenecarbene. The synthesis of this alkyne employed a slight variation of the chemistry used for alkyne attachment in **14**. Acetylide anion addition to an epoxycarbamate **21** furnished the intact oxazolidinone system in much higher yield than the allenyl Grignard-based sequence of Scheme 2. Again, exposure of alkynylstannane **22** to Stang's reagent, followed by rapid addition of the cold alkynyliodonium salt solution to refluxing DME containing $TolO_2SNa$, led to isolation of a suite of cyclized products **24** −**26** along with a small amount of an alkyne-bearing product **27**. On the assumption that the bis sulfone **26** is derived from **24** and excess sulfinate anion, the overall yield of C−H insertion product, 48%, is 1.5 times that of the formal oxygen/lone-pair insertion product **25**. Alkyne **27** results from a third option available to the alkylidenecarbene, 1,2-sulfone shift.[10] The preponderance of C−H insertion product rather than formal oxygen/lone-pair insertion product presumably reflects the diminished electron availability at oxygen in **23** compared to **16**, as discussed above. Thus, by the simple expedient of replacing an acetonide protecting group with a more electron demanding carbonyl, the reaction has benefited by significant improvements in yield and chemoselectivity. Continuation of this approach to the agelastatins required the stereoselective *N*-attachment of a pyrrole carboxamide unit at C(5a). This transformation proceeded readily via initial conjugate addition of benzylamine to the activated alkene in **24** followed by acylation of the resultant secondary amine with acid chloride **28**.[2a] The stereochemical outcome of amine addition plausibly stems from the considerable steric bias that attends the rigid bicyclo[3.3.0]octane framework. Although of no consequence in the agelastatin effort, the C(9a) sulfonyl in **29** emerged as a single diastereomer, the selectivity again a likely consequence of preferred anion protonation on the accessible convex face of the bicyclic ring system. The stereochemical assignment of **29** is based on comparison of the ^{1}H NMR spectrum of the precursor amine addition product with the ^{1}H NMR spectrum of **43c** (vide infra), a compound whose stereochemical assignment rests on the nOe enhancements shown in Scheme 6. Unfortunately, this agelastatin route bogged down with intermediate **29**, as all efforts to effect oxazolidinone hydrolysis led to destruction of this compound. In some instances, the formal *β*-elimination product **24** could be identified in the product mixture.

The lability of *N*-BOC oxazolidinones to hydrolysis[11] suggested that an *N*-BOC analogue of **22**, the oxazolidinone **33** (Scheme 4), might overcome the difficulties experienced with the former species. In addition, the presumably enhanced electron demand of the oxazolidinone carbonyl in the *N*-BOC derivative compared to the *N*-Bn system **23** may provide a more substantial bias toward 1,5 C−H insertion over formal oxygen/lone-pair insertion within the intermediate alkylidenecarbene. The synthesis of alkynylstannane **33** proceeded uneventfully from allyl carbamate **30** utilizing chemistry developed with **22**. Buchwald's tin-for-silicon exchange procedure[12] (**32** → **33**) was necessitated by the insolubility of the free alkyne in solvents compatible with anionic stannylation chemistry. The key iodination/cyclization sequence with **33** delivered the desired cyclopentene **35** in comparable yield to the *N*-Bn case **24**, although the ratio of byproducts was markedly different. No formal oxygen/lone-pair insertion product could be detected, either in the crude

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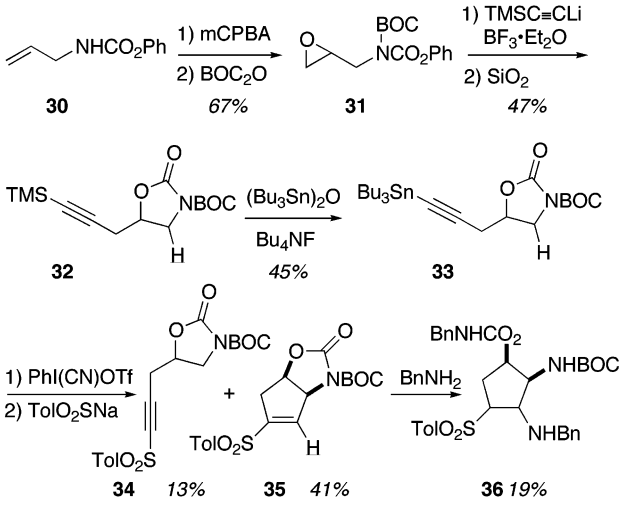
(11) (a) Ishizuka, T.; Kunieda, T. *Tetrahedron Lett.* **1987**, *28*, 4185−4188. (b) Flynn, D. L.; Zelle, R. E.; Grieco, P. A. *J. Org. Chem.* **1983**, *48*, 2424−2426.

(12) Warner, B. P.; Buchwald, S. L. *J. Org. Chem.* **1994**, *59*, 5822−5823.

SCHEME 4

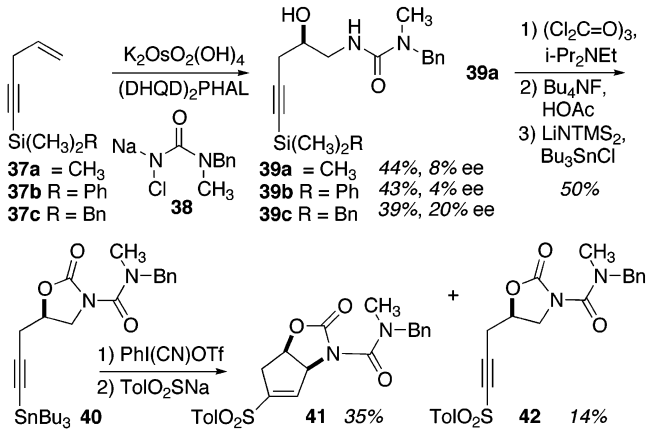


reaction mixture or upon extensive chromatography. However, the 1,2-sulfone shift product **34** now was formed to a significant extent. One interpretation of these observations might cite the BOC's role in engaging the nitrogen's lone pair in resonance, thereby biasing the competition between N and O for the oxazolidinone's carbonyl toward oxygen. In this scenario, the oxygen's lone pair would be less available to the alkylidenecarbene than in the related carbene **23**, leading to a diminution, or in this case a complete suppression, of reaction at oxygen. A tradeoff, however, can be seen in the increased formation of the 1,2-sulfone shift product **34**. The hydrogen targeted for insertion by the alkylidenecarbene (cf. H, **33**) is now attached to an arguably more electron deficient carbon compared to the similar H in **23** as a consequence of the adjacent *N*-BOC (vs *N*-Bn in **23**). Therefore, the rate of insertion of the inherently electrophilic alkylidenecarbene[13] into the C-H of **33** is likely to be decreased compared to **23**, and the normally slower 1,2-sulfone shift becomes more prominent. Ochiai has shown that varying the electron demand of the sulfonyl group does not appreciably influence the partitioning of an alkylidenecarbene between 1,5 C−H insertion and 1,2-sulfone shift,[10] and so this encroaching competition with the desired reaction channel cannot be easily suppressed.

Ultimately, this route ran afoul of the very oxazolidinone carbonyl lability upon which it was founded. Attempted benzylamine conjugate addition to the alkene of **35** was complicated by concurrent attack of the amine nucleophile at the carbonyl. The double addition product carbamate **36** was isolated in poor yield, and all efforts to steer the addition to the alkene were ineffective. Thus, a plausibly less activating N-substituent was required. An *N*-urea, such as *N*-CON(CH_3)CH_2Ar, seemed like a logical choice in that it should serve the dual function of diminishing the electrophilicity of the oxazolidinone carbonyl while at the same time firmly refocusing the route toward the *N*-methyl urea-containing target, agelastatin A.

The synthesis of the urea bearing cyclization substrate **40** follows a different strategy compared to the previous

SCHEME 5



efforts, Scheme 5. Recent advances in osmium-mediated asymmetric amido alcohol synthesis could foster a promising approach for controlling the absolute stereochemistry in **40**, provided that the heretofore unexplored urea reagent **38** functions similarly to the precedented amide or carbamate analogues.[14] Exposure of enynes **37a**−**c** to the conditions recommended by Sharpless furnished the hydroxy urea products **39a**−**c**, respectively, with complete control of regiochemistry in the desired sense. Unfortunately, no useful levels of asymmetric induction were achieved with these systems. Modest enantioselectivity resulted from use of the $(DHQD)_2$PHAL ligand, and use of the $(DHQD)_2$AQN and $(DHQD)_2$PYR alternatives was even less fruitful. The phenyl- and benzylsilyl entries **37b** and **37c**, respectively, were examined under the premise that the aryl residues might provide an additional complementary binding element for the cleft formed by the chiral ligand.[15] The poor ee values leave it unclear as to whether this expectation was met. Conversion of the urea alcohol **39a** into the corresponding stannylated alkyne **40** proceeded smoothly utilizing methodology developed earlier. The derived alkynyliodonium salt combined with sulfinate nucleophile to furnish the expected cyclopentene **41** along with sulfonylalkyne **42**, again with no trace of a formal oxygen/lone-pair insertion product. The yields of the two products were similar to those observed with the *N*-BOC substrate **33**, indicating that the electronic influence of the urea group upon alkylidenecarbene partitioning was not demonstrably different than that of the BOC moiety.

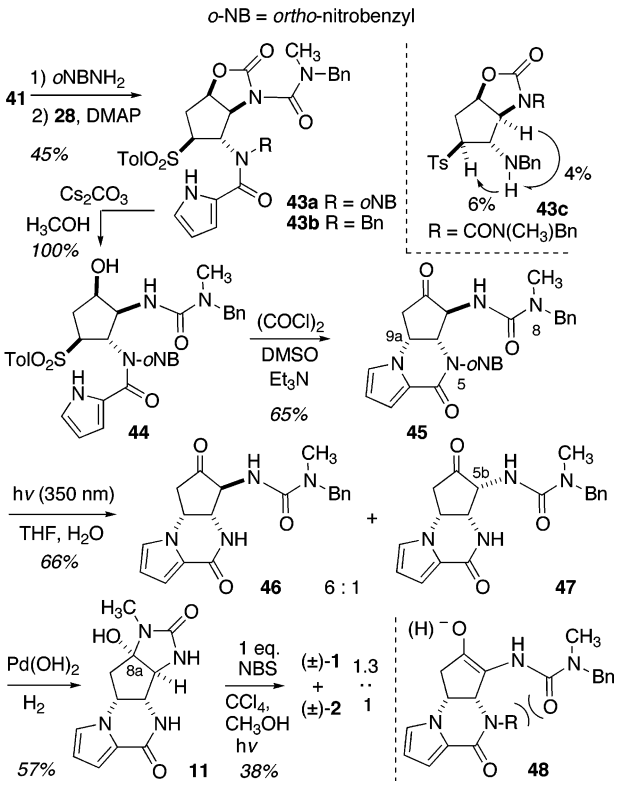
The question of paramount interest at this juncture involved the site of nucleophilic attack upon addition of a benzylamine to the urea-containing bicyclic **41**. It was gratifying to observe that only the product of alkene addition was detected upon exposure of **41** to *o*-nitrobenzylamine (*o*NB-amine), Scheme 6. The resultant secondary amine could be acylated with **28** to deliver the required C(5a) pyrrole carboxamide unit without any interference from chemistry at the oxazolidinone carbonyl. The choice of the *o*NB-amine was in response to

(13) Gilbert, J. C.; Giamalva, D. H. *J. Org. Chem.* **1992**, *57*, 4185−4188.

(14) (a) Reddy, K. L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1998**, *120*, 1207−1217. (b) Bruncko, M.; Schlingloff, G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **1997**, *36*, 1483−1486. (c) Rudolph, J.; Sennhenn, P. C.; Vlaar, C. P.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *25*, 2810−2813.

(15) Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 10805−10816.

SCHEME 6



difficulties encountered upon attempted deprotection of the simpler benzylamine analogue near the end of the route, vide infra. This benzylamine analogue **43b** was formed from **41** in overall 42% yield without rupture of the oxazolidinone ring. The stereochemical assignment shown in **43a** is based upon comparison of its ^{1}H NMR spectrum with that of **43b**, whose stereochemical assignment rests on interpretation of the nOe effects shown in Scheme 6, structure **43c**. Fortunately, the susceptibility of the oxazolidinone carbonyl to nucleophilic attack was not diminished below the point of usefulness by the urea moiety, as simple treatment of **43a** with Cs_2CO_3/CH_3OH effected clean hydrolysis of the heterocyclic ring without any concomitant loss of the pyrrole carboxamide moiety.

Acquisition of the cyclopentanol **44** sets up the second key cyclization reaction of the synthesis. Exposure of this alcohol to Swern oxidation conditions initiates a sequence of events that most plausibly includes oxidation of the alcohol to an unobserved cyclopentanone, β-elimination of sulfinate to furnish an intermediate cyclopentenone, and finally cyclization of the pendant pyrrole's nitrogen into the β-position (C(9a)) of this putative enone to deliver the intact agelastatin tricycle **45** as the sole characterizable reaction product. Evidence for the intermediacy of the cyclopentenone was gleaned by subjecting cyclopentanol **44** to oxidation under nonbasic conditions (Dess–Martin). Signals consistent with the putative cyclopentenone were detected in the ^{1}H NMR spectrum of the crude oxidation mixture, and addition of excess Et_3N to this mixture afforded cyclized product **45** in 48% overall yield. Cyclization of a similar enone provided the pivotal N(9)–C(9a) connection in earlier agelastatin work as well.[2]

Three further operations were necessary to complete the syntheses of (±)-agelastatins A/B via this route: two N-deprotections and the concluding pyrrole bromination discussed earlier. The N(5) *o*NB protecting group was removed under strictly neutral conditions by irradiation at 350 nm. Despite the neutrality of the reaction medium, a small amount of the C(5b) epimer **47** was formed. It is possible that incipient A^{1,2} strain in an intermediate **48** (R = *o*NB) discourages enolization and therefore maintains the stereochemical integrity at C(5b) in **45**, but the presence of a sterically undemanding proton in **48** (R = H) more readily permits this enolization. In any event, the inseparable mixture **46**/**47** was subjected to hydrogenolytic debenzylation conditions to yield (±)-debromoagelastatin (**11**), which was now separable from its C(5b)/C(8a) diastereomer derived from **47**. Attempted hydrogenolysis of a N(5)-benzyl analogue of **45** led only to cleavage of the N(8) benzyl unit, a result that necessitated the reroute through the N(5) *o*NB series. A few scouting experiments designed to probe bromination selectivity with **11** revealed that the ratio of agelastatin A to agelastatin B was quite solvent dependent. In pure CCl_4, the sparingly soluble **11** was brought into solution by monobromination, and (±)-**1** in now much higher concentration underwent further bromination to give a preponderance of the dibrominated product (±)-agelastatin B (**2**) (ca. 3:1). Incorporation of some methanol in the reaction medium rendered **11** much more soluble, and under these conditions, a slight preference for formation of the monobromide product (±)-agelastatin A (**1**) was observed (ca. 1.3:1). No further effort was expended on optimizing this step in the racemic series, as material in hand was limited, and by this time an enantioselective route that provided substantial quantities of (−)-**11** had been developed along parallel lines, as described next.

The asymmetric synthesis of both (−)-agelastatin A (**1**) and (−)-agelastatin B (**2**) benefited from the lessons learned during the exploration of the racemic series. One point of departure, the use of *o*NB protection for both N(5) and N(9), offers the dual advantages of (1) consolidation of the late-stage deprotection operations and (2) skirting an epimerizable intermediate analogous to **46**. The route starts with the known alkynyloxirane **49**,[16] which is readily available in two steps from (*R*)-epichlorohydrin.[17] Introduction of N(6) employs azide and the reductive cyclization conditions of Vilarrasa[18] to deliver the oxazolidinone **50** in good yield. An ^{1}H NMR assay of enantiomeric purity using the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol[19] revealed that **50** was formed in 94% ee, a value linked to the ee of the starting (*R*)-epichlorohydrin. N-Acylation of **50** with *o*NB-protected *N*-methylcarbamoyl chloride followed by the usual Si-to-Sn alkyne terminus transformation afforded the oxidative cyclization precursor **51**. By analogy to the related *N*-Bn substrate **40**, treatment of **51** with Stang's reagent and then $TolO_2SNa$ in refluxing DME provided the C–H insertion product **53** in ~27% yield along with 41% of the 1,2-sulfone shift product **52**. Optimization studies of this key transformation probed the influence of solvent

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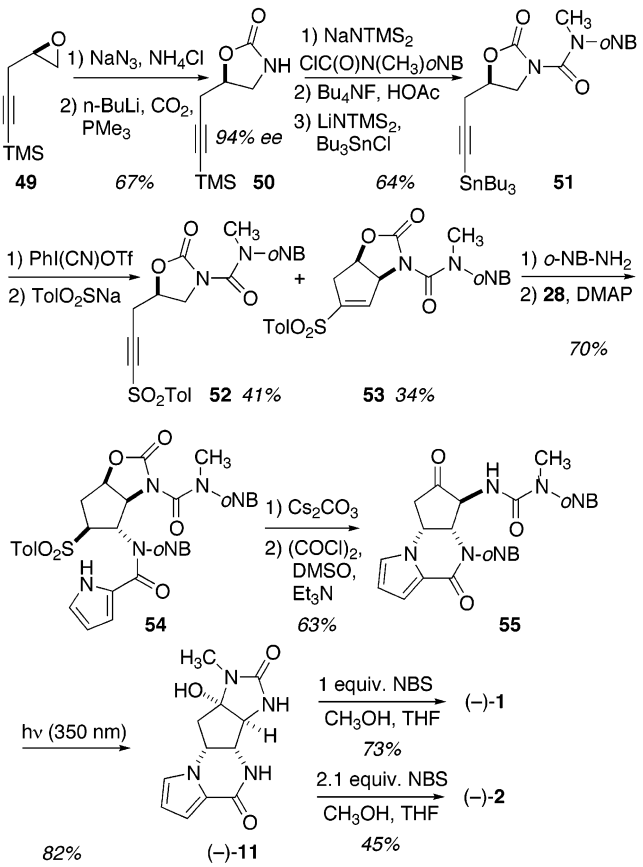
(THF, DME, 1,4-dioxane), temperature (25→85 °C), reagent ratio (**51**:$TolO_2SNa$ = 1:0.9 to 1:1.1), and substrate concentration (0.10→0.01 M) on overall product yield. The optimum conditions emerging from these studies converged on DME solvent at 65 °C with 1.0 equiv of $TolO_2SNa$ per alkyne at 0.05 M. Under this regime, the yield of the desired bicycle **53** rose to 34% with 41% of the alkynyl sulfone **52** formed as well. Although this yield was rather disappointing, the brevity of the route ensured that enough material was available to complete the synthesis studies. Conjugate addition of *o*NB-amine to the electron-deficient alkene of **53** proceeded without interference from the oxazolidinone carbonyl as expected, and acylation of the resulting secondary amine with **28** furnished the bicycle **54** bearing a pendant pyrrole carboxamide moiety. Both oxazolidinone hydrolysis and oxidation/cyclization under Swern's conditions did not deviate from the course followed by the simpler *N*-Bn species **43a**, and the tricycle **55** was formed in good overall yield. The value of incorporating an *o*NB protecting group at N(7) in **55** is expressed in the next step, the photochemical cleavage of both nitrogen protecting groups. An epimerization-sensitive intermediate similar to **46**, if formed at all, only has fleeting existence en route to the cyclized aminal unit of the product debromoagelastatin (−)-**11**. Once the cyclopentanone carbonyl is engaged as the aminal, epimerization at C(5b) is no longer possible. More exacting bromination studies with diastereomerically homogeneous (−)-**11** revealed that in a polar reaction medium, electrophilic pyrrole bromination can indeed deliver (−)-agelastatin A (**1**) in good yield with no more than 4% of an agelastatin B contamination. Use of an excess of NBS under otherwise identical conditions afforded the dibromide product (−)-agelastatin B (**2**) as a clean sample. The synthetic sample of (−)-**1** displayed ^{1}H NMR, mass spectral, and TLC behavior identical with those of an authentic sample provided by Dr. D'Ambrosio of the Università di Trento, and ^{13}C NMR and optical rotation data that matched those published. The spectral data for synthetic agelastatin B were congruent with those published for the natural material. In summary, the utility of alkynyliodonium salts in complex natural products synthesis has been demonstrated for the first time. Total syntheses of the tetracyclic marine alkaloids agelastatin A and agelastatin B were completed in both racemic and enantioselective form. The key alkynyliodonium salt-based cyclization formed the central, highly functionalized cyclopentane core of the target molecules from which further functional group manipulation afforded the natural products.

Experimental Section

Moisture- and oxygen-sensitive reactions were carried out in flame-dried glassware under an argon atmosphere. Tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl under an argon atmosphere immediately before use. Toluene, benzene, and dichloromethane (CH_2Cl_2) were distilled from calcium hydride (CaH_2) under an argon atmosphere immediately before use. Purification of products via flash chromatography[20] was performed with 32−63 μm silica gel and the solvent systems indicated. Hexanes, ethyl acetate (EtOAc), CH_2Cl_2, and Et_2O used in flash chromatography were distilled from CaH_2 prior to use. Deactivated silica gel was prepared by treatment of the silica with 5% triethylamine in hexanes solution prior to use.

SCHEME 7



Melting points are uncorrected. Low- and high-resolution mass spectra were obtained according to the specified technique and were performed by the University of Texas, Austin, TX and the Pennsylvania State University, University Park, PA. Combustion analyses were performed by Midwest Microlabs, Indianapolis, IN. Copies of ^{1}H and ^{13}C NMR spectra are supplied in the Supporting Information for those compounds without combustion analyses.

General Procedure A: Ureahydroxylation of Pentenynes 37a−c. *N*-Benzyl-*N*-methylurea (3 equiv vs alkene **37**) was suspended in *n*-propanol (0.25 M). Sodium hydroxide (3 equiv vs alkene **37**) was dissolved in water (0.41 M); 95% of this hydroxide solution was added to dissolve the urea, and the solution was cooled in an ice−water bath. Freshly prepared *tert*-butylhypochlorite[21] (3 equiv vs alkene **37**) was added. The mixture was stirred at 4 °C for 1.5 h, and then the $(DHQD)_2$-PHAL ligand (10 mol %) dissolved in *n*-PrOH (0.031 M) and the silylpent-4-en-1-ynes **37a**−**c**[22] were added, followed by potassium osmate dihydrate (5 mol %) freshly dissolved in the remaining hydroxide solution. The mixture was warmed with the ice bath overnight to room temperature. The reaction was diluted with saturated aqueous Na_2SO_3. The aqueous layer was washed with 2 × EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified via flash chromatography on silica gel with the indicated solvent system to yield urea alcohols **39a**−**c**. Enantioselectivities were deter-

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mined with the Chiralcel OD and OD-H HPLC columns with 5% *i*-PrOH/hexanes as eluent.

General Procedure B: Pyrrole Carboxamide Formation. Pyrrole-2-carboxylic acid (10 equiv vs amine) was suspended in dry benzene (0.2 M), and oxalyl chloride (20 equiv) was added. One drop of DMF was added, leading to immediate gas evolution. The mixture was stirred until all solids were dissolved (2 h). The solution was concentrated with use of an aspirator equipped with a $CaCl_2$-filled drying tube and then under high vacuum to afford a white solid. This solid was dissolved in dry CH_2Cl_2 (0.8 M) and distilled pyridine (20 equiv) was added with immediate formation of a yellow precipitate. The secondary amine was dissolved in dry CH_2Cl_2 (0.04 M) and added to the pyrrole-2-carboxylic acid chloride solution. 4-(Dimethylamino)pyridine (0.1 equiv) then was added and the mixture was stirred at room temperature for 2 d. The yellow suspension was diluted with CH_2Cl_2 and poured into ice cold 1 M H_3PO_4. The organic layer was washed with brine and the aqueous layers were extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to furnish the crude amide. This crude residue was purified via flash chromatography with the indicated solvents.

General Procedure C: Swern Oxidation of Cyclopentanols. Dimethyl sulfoxide (2.4 equiv) was dissolved in CH_2Cl_2 (3.5 M) and cooled to −78 °C. Oxalyl chloride (1.2 equiv) was added dropwise, and the resulting solution was stirred at −78 °C for 10 min and room temperature for 3 min, and then recooled to −78 °C. The cyclopentanol was added dropwise as a solution in CH_2Cl_2 (0.12 M). The mixture was stirred at −78 °C for 2 h, and then Et_3N (10 equiv) was added dropwise. This mixture was stirred at −78 °C for 10 min, and then at room temperature overnight. Saturated aqueous NH_4Cl was poured into the reaction mixture, and the organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified via flash chromatography with the indicated solvents.

***tert*-Butyl-*N*-(2-hydroxypent-4-ynyl)carbamate (13).** Magnesium turnings (6.0 g, 250 mmol) were flame dried under vacuum, suspended in 100 mL of Et_2O, and treated with $HgCl_2$ (246 mg, 0.9 mmol). The mixture was stirred at room temperature for 30 min then cooled to 4 °C, and propargyl bromide (1.5 mL of an 80% solution in toluene, 14 mmol) was added. The mixture was stirred for 14 min at room temperature and a rise in temperature was observed. The solution was maintained at 4 °C and the remainder of the propargyl bromide (20.5 mL, 198 mmol total) was added dropwise. The mixture was stirred at 0 °C for an additional 1 h, and then the mixture was transferred via cannula to a flask cooled to −42 °C. *N*-Boc glycinal (**12**)[23] (8.7 g, 55 mmol) in 18 mL of dry Et_2O was added dropwise over 20 min. The reaction mixture was warmed to 8 °C for 5 h and then poured into a cold saturated NH_4Cl solution, producing vigorous bubbling. The aqueous layer was extracted with 3 × 10 mL of Et_2O. The organic layers were combined and dried over Na_2SO_4, filtered, and concentrated in vacuo, and the residue was purified via flash chromatography on silica gel (30−40% EtOAc/hexanes as eluent) to yield 3.56 g of **13** (32%) as a colorless oil. IR ($CDCl_3$) 3598, 3458, 3308, 1709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.95 (br s, 1H), 3.86 (m, 1H), 3.39 (br d, J = 13.1 Hz), 3.18 (m, 1H), 2.38 (m, 2H), 2.14 (m, 1H), 1.42 (s, 9H); CIMS *m*/*z* (rel intensity) 200 (MH^+, 9); HRMS Calcd for $C_{10}H_{18}NO_3$ 200.1287, found 200.1287.

Oxazolidine 14. Alcohol **13** (106 mg, 0.53 mmol) was dissolved in 1.9 mL of acetone, and 2,2-dimethoxypropane (0.58 mL, 4.7 mmol) was added followed by 1 drop of $BF_3{\cdot}Et_2O$. The mixture was stirred at room temperature for 130 min and then concentrated in vacuo. The yellow oil was dissolved in CH_2Cl_2 and washed with aqueous $NaHCO_3$. The aqueous layer was extracted with 3 × 5 mL of CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and filtered through a short pad of silica gel (20% EtOAc/hexanes as eluent) to yield 75 mg of an acetonide product (59%). IR ($CDCl_3$) 3309, 2124, 1696 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 4.22 (m, 1H), 3.76 (m, 1H), 3.26 (m, 1H), 2.57 (ddd, J = 16.7, 5.0, 2.6 Hz, 1H), 2.46 (ddd, J = 16.7, 6.9, 2.5 Hz, 1H), 2.04 (br s, 1H), 1.57 (s, 3H), 1.51 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$, amide rotomers) δ 152.0, 151.8, 94.1, 93.6, 80.1, 79.5, 79.2, 77.2, 71.7, 70.4, 50.2, 28.4, 28.3, 27.1, 26.1, 25.4, 24.5, 23.2; CIMS *m*/*z* (rel intensity) 240 (MH^+, 18).

This alkyne (66 mg, 0.28 mmol) was dissolved in 0.55 mL of dry THF then cooled to −78 °C, and LiHMDS (0.28 mL of a 1 M solution in THF, 0.28 mmol) was added over 30 min. The mixture was stirred at −78 °C for 35 min, and then tributyltin chloride (75 μL, 0.28 mmol) in 0.3 mL of dry THF was added dropwise. The mixture was stirred at −78 °C for 45 min and then brought to room temperature for 2.5 h. After concentrating in vacuo, the residue was purified via flash chromatography on deactivated silica gel (4% EtOAc/hexanes as eluent) to yield 120 mg of **14** (81%) as a colorless oil. IR ($CDCl_3$) 2150, 1692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (m, 1H), 3.74 (m, 1H), 3.29 (m, 1H), 2.66 (dd, J = 16.7, 4.5 Hz, 1H), 2.49 (dd, J = 16.7, 7.8 Hz, 1H), 1.7−1.4 (m, 12H), 1.47 (s, 9H), 14−1.2 (m, 6H), 1.1−0.8 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 105.5, 94.1, 84.7, 79.5, 72.4, 50.4, 28.8 (J_{C-Sn} = 11.4 Hz), 28.4, 26.9 (J_{C-Sn} = 29.5 Hz), 26.2, 25.5, 24.8, 13.7, 10.9 ($J^{13C-117Sn}$ = 183.3 Hz and $J^{13C-119Sn}$ = 191.8 Hz); CIMS *m*/*z* (rel intensity) 530 (MH^+, 100); HRMS Calcd. for $C_{25}H_{48}NO_3{}^{118}Sn^+$ 530.2661, found 530.2669.

Cyclopentene 17. Alkynylstannane **14** (0.12 g, 0.23 mmol) was dissolved in 3 mL of dry CH_2Cl_2 then cooled to −42 °C, and PhI(CN)OTf (84 mg, 0.22 mmol) was added in one portion. The mixture was stirred at −42 °C for 2 h, and then half of this solution was transferred via cannula to a flame-dried flask and concentrated in vacuo with an aspirator and drying tube at −42 °C. The residue was dissolved in 1.5 mL of dry DME prechilled to −42 °C. The mixture was cooled to −78 °C, and sodium *p*-toluenesulfinate (20 mg, 0.11 mmol) was added in one portion. The mixture was stirred at −78 °C for 5 min and then brought to reflux and held there for 15 min, cooled to room temperature, and concentrated in vacuo. The crude mixture was purified via flash chromatography on silica gel (20−30% EtOAc/hexanes as eluent) to yield a mixture of products. Resubjection of this mixture to flash chromatography (32% EtOAc/hexanes as eluent) yielded an inseparable mixture of 5.2 mg of **17** (2%) with small amounts of several byproducts and 2.6 mg of **19** (7%) as a white solid.

17: IR (C_6D_6) 1705 cm^{-1}; ^1H NMR (300 MHz, d_6-acetone) δ 7.77 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 6.59 (d, J = 1.3 Hz, 1H), 4.93 (d, J = 5.5 Hz, 1H), 4.80 (apparent t, J = 5.4 Hz, 1H), 2.84 (m, 1H), 2.48 (m, 1H), 2.44 (s, 3H), 1.48 (s, 9H), 1.40 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, d_6-acetone) δ 145.9, 139.3, 130.8, 128.9, 128.5, 94.8, 77.7, 72.9, 67.3, 53.4, 48.8, 37.4, 28.5, 27.0, 24.1, 21.5; CIMS *m*/*z* (rel intensity) 394 (MH^+, 2).

19: IR (C_6D_6) 3432, 1720 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.78 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 7.35 (s, 1H), 6.21 (s, 1H), 5.01 (m, 1H), 3.29 (m, 2H), 2.84 (m, 1H), 2.57 (ddd, J = 14.3, 7.6, 1.8 Hz, 1H), 2.47 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, d_6-acetone) δ 156.5, 144.7, 139.5, 130.7, 127.9, 118.2, 104.0, 86.1, 79.0, 44.5, 31.2, 28.5, 21.4; CIMS *m*/*z* (rel intensity) 254 ($[M - Boc + H_2]^+$, 100).

Oxirane 21. Pyridine (7.3 mL, 90 mmol) and phenylchloroformate (6.3 mL, 50 mmol) were successively added to allylbenzylamine (6.6 g, 45 mmol) in 100 mL of CH_2Cl_2 at 0 °C over 10 min. The resulting mixture was allowed to stir at 0 °C for 1 h then at room temperature for 2 h. The reaction mixture was diluted with 10 mL of H_2O. The phases were separated and the organic layer was washed with 25 mL of brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to provide 13.9 g of an orange oil. Purification of this crude

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material on silica gel (15% Et_2O/hexanes to 25% Et_2O/hexanes as eluent) afforded 11.13 g (93%) of the allyl carbamate as a colorless oil. IR (film) 1724, 1714 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$, amide rotomers) δ 7.5−7.3 (m, 7H), 7.3−7.0 (m, 3H), 5.85 (m, 1H), 5.25 (m, 2H), 4.63/4.56 (each s, 1H), 3.98/3.96 (each s, 2H); ^{13}C NMR (90 MHz, $CDCl_3$, amide rotomers) δ 155.1, 154.6, 151.4, 137.2, 132.9, 132.8, 129.2, 128.6, 128.2, 127.5, 125.2, 121.7, 118.0, 117.1, 50.0, 49.7, 49.3, 48.8; CIMS *m/z* (rel intensity) 268 (MH^+, 100). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.71. Found: C, 76.53; H, 6.59.

m-CPBA (60%, 17.8 g, 62 mmol) was added to the allyl carbamate (8.4 g, 31 mmol) in 250 mL of CH_2Cl_2 at 0 °C in three portions over 15 min. After 5 h, an additional amount of 60% *m*-CPBA (8.9 g, 32 mmol) was added and the solution was allowed to stir for 12 h. The reaction mixture was diluted carefully with saturated sodium bisulfite solution and then saturated $NaHCO_3$ solution was added. The phases were separated and the organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to provide 7.9 g of a yellow oil. Purification of the crude material on silica gel (15% EtOAc/hexanes to 20% EtOAc/hexanes as eluent) afforded 6.52 g (74%) of **21** as a colorless oil. IR (film) 1730, 1714 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$, amide rotomers) δ 7.6−7.4 (m, 7H), 7.3−7.1 (m, 3H), 4.9−4.6 (m, 2H), 3.8−3.6 (m, 1H), 3.3−3.0 (m, 2H) superimposed by 3.2−3.1 (m, 1H), 2.77 (apparent t, J = 4.1 Hz, 1H), 2.52 (d, J = 4.6 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$, amide rotomers) δ 154.9, 151.2, 137.2, 137.1, 129.3, 128.7, 128.3, 127.6, 127.4, 125.4, 121.6, 51.7, 50.5, 50.4, 49.2, 48.5, 45.3, 45.1; CIMS *m/z* (rel intensity) 284 (MH^+, 100). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05. Found: C, 71.67; H, 5.64.

Alkynylstannane 22. A 2.5 M solution of *n*-BuLi in hexane (16 mL, 39 mmol) was added to trimethylsilylacetylene (5.5 mL, 39 mmol) in 92 mL of THF at −78 °C over 25 min. After 15 min, $BF_3{\cdot}Et_2O$ (4.9 mL, 39 mmol) was added over 5 min. The reaction mixture was allowed to stir at −78°C for 20 min before the addition of a solution of the epoxide (7.4 g, 26 mmol) in 40 mL of THF over 25 min. After 1 h at −78 °C, the mixture was poured into 20 mL of saturated NH_4Cl solution and diluted with 150 mL of EtOAc. The phases were separated and the organic layer was washed with 40 mL of brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford 11.4 g of an orange oil. Purification of the crude product by flash chromatography on silica gel (15% EtOAc/hexanes, 20% EtOAc/hexanes, to 25% EtOAc/hexanes as eluent) afforded 9.54 g (96%) of the expected homopropargyl alcohol as a light yellow oil. IR (film) 2175, 1715 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$, amide rotomers) δ 7.5−7.3 (m, 7H), 7.3−7.1 (m, 3H), 4.8−4.6 (m, 2H), 4.06 (br s, 1H), 3.53 (m, 2H), 2.48 (apparent t, J = 5.2 Hz, 2H), 0.15 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$, amide rotomers) δ 156.6, 155.2, 151.2, 151.1, 137.2, 137.0, 129.3, 128.7, 128.2, 127.7, 127.4, 125.5, 125.3, 121.6, 102.5, 101.8, 88.2, 87.7, 69.8, 68.6, 52.5, 52.4, 51.7, 51.0, 26.5, 0.0; CIMS *m/z* (rel intensity) 382 (MH^+, 24). Anal. Calcd for $C_{22}H_{27}NO_3Si$: C, 69.26; H, 7.13. Found: C, 69.09; H, 6.84.

A 60% dispersion of sodium hydride (0.97 g, 24 mmol) was added in three portions over 15 min to this homopropargyl alcohol (9.3 g, 24 mmol) in 200 mL of THF at 0 °C. After 1 h at 0 °C, the mixture was diluted with 40 mL of H_2O and extracted with 200 mL of EtOAc. The phases were separated and the organic layer was washed with 5 × 50 mL of cold 1 N NaOH solution, 2 × 50 mL of H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford 7.0 g of the oxazolidinone product as a white solid (100%). Mp 73−74 °C; IR (film) 2178, 1760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5H), 4.59 (m, 1H), 4.54 (d, J = 15.1 Hz, 1H), 4.34 (d, J = 14.7 Hz, 1H), 3.52 (apparent t, J = 9.0 Hz, 1H), 3.29 (dd, J = 9.0, 6.0 Hz, 1H), 2.7−2.5 (m, 2H), 0.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 135.7, 129.0, 128.2, 128.1, 99.4, 88.5, 70.9, 48.4, 48.3, 26.0, 0.0; CIMS *m/z* (rel intensity) 288 (MH^+, 100). Anal. Calcd for $C_{16}H_{21}NO_2Si$: C, 66.85; H, 7.36. Found: C, 66.56; H, 7.35.

Glacial acetic acid (2.1 mL, 36 mmol) and a 1.0 M THF solution of Bu_4NF (36 mL, 36 mmol) were added to this oxazolidinone derivative (7.0 g, 24 mmol) in 60 mL of THF. After 6 h, the mixture was diluted with 20 mL of H_2O and extracted with 150 mL of Et_2O. The phases were separated and the organic layer was washed with two 20-mL portions of H_2O and 20 mL of brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a yellow oil. Purification of the crude product by flash chromatography on silica gel (35% EtOAc/hexanes, 40% EtOAc/hexanes, to 50% EtOAc/hexanes as eluent) afforded 4.74 g (92%) of the terminal alkyne product as a colorless oil. IR (film) 3288, 2122, 1749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5H), 4.60 (m, 1H), 4.47 (d, J = 14.7 Hz, 1H), 4.39 (d, J = 14.7 Hz, 1H), 3.54 (apparent t, J = 9.0 Hz, 1H), 3.28 (dd, J = 9.0, 6.0 Hz, 1H), 2.67−2.51 (m, 2H), 1.97 (t, J = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 135.6, 128.8, 128.2, 128.0, 77.3, 71.5, 70.4, 48.3, 48.2, 24.7; CIMS *m/z* (rel intensity) 216 (MH^+, 100). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.43; H, 6.26.

A 1.0 M solution of LiHMDS in THF (21.4 mL, 21.4 mmol) was added to this terminal alkyne (4.6 g, 21.4 mmol) in 45 mL of THF at −78 °C over 1 h. The reaction mixture was allowed to stir at −78 °C for 1.5 h before the addition of tributyltin chloride (5.8 mL, 21.4 mmol). The solution was allowed to warm to ambient temperature and stir for 2.5 h. The mixture was diluted with 20 mL of saturated NH_4Cl solution and extracted with 200 mL of Et_2O. The phases were separated and the organic layer was washed with 50 mL of brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford 11.5 g of the stannylated alkyne **22** as a yellow oil. Purification of the crude product on silica gel (20% EtOAc/hexanes to 25% EtOAc/hexanes as eluent) afforded 8.53 g (81%) of **22** as a pale yellow oil. IR (film) 2154, 1765 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.07 (s 5H), 4.30 (d, J = 14.7 Hz, 1H), 4.02 (d, J = 14.7 Hz, 1H), 3.94 (m, 1H), 2.82 (dd, J = 10.5, 8.6 Hz, 1H), 2.80 (dd, J = 12.1, 8.7 Hz, 1H), 2.3−2.2 (m, 2H), 1.7−1.5 (m, 6H), 1.4−1.2 (m, 6H), 1.0−0.8 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 135.7, 128.8, 128.1, 128.0, 103.3, 86.3, 71.3, 48.5, 48.3, 28.8 ($J_{C-^{119}Sn}$ = 11.6 Hz), 26.9 ($J_{C-^{119}Sn}$ = 29.1 Hz), 26.3, 13.7, 11.0 ($J_{C-^{119}Sn}$ = 191.1 Hz, $J_{C-^{117}Sn}$ = 183.1 Hz). APCIMS *m/z* (rel intensity) 506 (Sn^{120}) (MH^+, 80); APCI-HRMS Calcd for $C_{25}H_{40}NO_2{}^{120}Sn$ 506.2086, found 506.2056.

Cyclopentene 24. Cyano(phenyl)iodonium triflate (0.11 g, 0.29 mmol) was added to a −42 °C solution of the alkynylstannane **22** (0.15 g, 0.29 mmol) in 3.5 mL of CH_2Cl_2. After 1 h, the solvent was removed in vacuo at −42 °C and the white residue was used immediately (assuming quantitative yield). This alkynyl(phenyl)iodonium triflate (0.15 g, 0.29 mmol) in 18 mL of THF prechilled to −42 °C was added via cannula to a refluxing suspension of anhydrous $TolO_2SNa$ (52 mg, 0.29 mmol) in 1.1 mL of THF. An additional 1 mL of THF was used to rinse over any residual iodonium salt. The yellow suspension was held at reflux for 30 min and then stirred at room temperature for 10 min. The reaction mixture was poured into brine and extracted with 50 mL of EtOAc. The organic layer was washed with brine, dried over Na2SO4, filtered, and concentrated in vacuo to afford 0.14 g of a yellow oil. Purification of the crude material by flash chromatography on deactivated silica gel (30% EtOAc/hexanes, 40% EtOAc/hexanes, to 50% EtOAc/hexanes as eluent) afforded 44 mg (41%) of the 1,5 C−H insertion product **24** as a white solid, 31 mg (31%) of the formal oxygen/lone-pair insertion product **25**, and 9 mg (6%) of the (bis)sulfone/conjugate addition product **26**.

24: mp 124 °C; IR (film) 1747 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.4−7.2 (m, 7H), 6.33 (s, 1H), 5.11 (apparent t, J = 6.8 Hz, 1H), 4.61 (d, J = 15.0 Hz, 1H), 4.57 (d, J = 7.7 Hz, 1H), 4.30 (d, J = 15.0 Hz, 1H), 3.03 (dd, J = 18.2, 6.8 Hz, 1H), 2.79 (d, J = 17.8 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 157.6, 147.7, 145.6, 135.5, 134.8, 134.7, 130.2, 129.1, 128.5, 128.3, 76.0, 64.3, 47.6, 37.9,

21.7; CIMS *m/z* (rel intensity) 370 (MH^+, 100); CI-HRMS Calcd for $C_{20}H_{20}NO_4S$ 370.1113, found 370.1108.

25: IR (film) 3468 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.55 (s, 1H), 7.4−7.2 (m, 7H), 4.37 (d, J = 15.1 Hz, 1H), 4.29 (d, J = 15.1 Hz, 1H), 4.11 (br s, 1H), 3.02 (d, J = 12.6 Hz, 1H), 2.93 (dd, J = 12.8, 3.3 Hz, 1H), 2.42 (m, 4H), 2.20 (dd, J = 15.6, 4.0 Hz, 1H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 142.7, 139.2, 136.0, 129.5, 128.9, 128.2, 127.6, 126.9, 98.9, 62.4, 59.8, 50.8, 28.6, 21.9. FABMS *m/z* (rel intensity) 370 (MH^+, 2).

Pyrrole Carboxamide 29. Benzylamine (0.32 mL, 2.9 mmol) was added to the bicyclic cyclopentene **24** (0.18 g, 0.49 mmol) in 5 mL of absolute EtOH. After 24 h at reflux, the reaction mixture was cooled and concentrated in vacuo to afford an oil. Purification of the crude product by flash chromatography on silica gel (50% EtOAc/hexanes, 60% EtOAc/hexanes, to 70% EtOAc/hexanes as eluent) afforded 0.19 g (81%) of the secondary amine product as a white solid. Mp 138 °C; IR (film) 3322, 1748 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.56 (d, J = 8.3 Hz, 2H), 7.2−6.9 (m, 11H), 6.73 (d, J = 7.9 Hz, 1H), 4.83 (d, J = 15.4 Hz, 1H), 3.98 (dd, J = 15.8, 7.1 Hz, 1H), 3.90 (d, J = 15.8 Hz, 1H), 3.81 (dd, J = 7.5, 3.4 Hz, 1H), 3.5−3.2 (m, 3H), 2.83 (d(apparent)t, J = 10.6, 7.4 Hz, 1H), 2.14 (ddd, J = 17.4, 10.6, 6.8 Hz, 1H), 1.87 (s, 3H), 1.8−1.6 (m, 1H), 1.40 (br s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 157.0, 144.7, 139.9, 136.6, 136.1, 130.0, 129.0, 128.9, 128.7, 128.5, 128.2, 127.9, 127.5, 74.5, 65.9, 64.6, 63.9, 51.1, 46.4, 34.7, 21.2; CIMS *m/z* (rel intensity) 477 (MH^+, 100). Anal. Calcd for $C_{27}H_{28}N_2O_4S$: C, 68.05; H, 5.92. Found: C, 68.35; H, 5.94.

Following general procedure B, this secondary amine (31 mg, 0.065 mmol) was acylated with **28**. The crude product was purified by flash chromatography on silica gel (45% EtOAc/hexanes, 50% EtOAc/hexanes, to 60% EtOAc/hexanes as eluent) to afford 28 mg (76%) of amide **29** as a white solid. Mp 206−207 °C; IR (film) 3354, 1755 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 9.35 (br s, 1H), 7.74 (d, J = 8.2 Hz, 2H), 7.4−7.1 (m, 11H), 6.95 (t, J = 1.8 Hz, 1H), 6.9−6.8 (m, 2H), 6.52 (br s, 1H), 6.19 (dd, J = 6.4, 2.7 Hz, 1H), 5.4−5.2 (m, 2H), 4.65 (d, J = 17.3 Hz, 1H), 4.39 (d, J = 8.2 Hz, 1H), 4.27 (d, J = 16.4 Hz, 1H), 4.16 (br s, 1H), 4.00 (ddd, J = 10.5, 6.8, 4.1 Hz, 1H), 3.40 (d, J = 16.4 Hz, 1H), 2.87 (ddd, J = 17.8, 9.8, 8.0 Hz, 1H), 2.46 (s, 3H), 2.32 (ddd, J = 15.1, 6.4, 4.1 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 163.3, 157.0, 145.5, 136.0, 135.3, 134.2, 130.2, 129.4, 128.8, 128.5, 128.3, 127.5, 127.4, 127.2, 123.5, 122.2, 113.3, 110.8, 79.1, 70.7, 68.1, 65.3, 54.3, 45.7, 37.4, 21.7; CIMS *m/z* (rel intensity) 570 (MH^+, 100); CI-HRMS Calcd for $C_{32}H_{32}N_3O_5S$ 570.2063, found 570.2057.

Oxirane 31. Phenyl-*N*-allylcarbamate (**30**)[24] (3.0 g, 17 mmol) was dissolved in 430 mL of CH_2Cl_2 and cooled to 4 °C. *m*-CPBA (77%, 5.9 g, 26 mmol) was added in one portion. After 2 min, the solution was warmed to room temperature and held there with stirring for 60 h. The mixture was poured into 300 mL of ice cold 10% Na_2SO_3. The organic layer was washed with 3 × 300 mL of saturated $NaHCO_3$, water, and then brine, dried over Na_2SO_4, and filtered, and the residue was concentrated in vacuo to yield 3.3 g of the oxirane product (100%) as a yellow oil. IR ($CHCl_3$) 1732 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.36 (apparent t, J = 7.9 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H), 7.12 (d, J = 7.7 Hz, 2H), 3.70 (d(apparent)t, J = 14.7, 3.1 Hz, 1H), 3.31 (d(apparent)t, J = 14.7, 5.7 Hz, 1H), 3.18 (m, 1H), 2.83 (apparent t, J = 4.2 Hz, 1H), 2.67 (apparent t, J = 3.2 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 154.8, 150.8, 129.3, 125.4, 121.5, 50.5, 45.1, 42.4; ESMS *m/z* (rel intensity) 194 (MH^+, 100).

This oxirane (100 mg, 0.52 mmol) was dissolved in 5 mL of dry THF. Triethylamine (87 μL, 0.62 mmol) followed by 4-DMAP (13 mg, 0.1 mmol) mixed with di-*tert*-butyl dicarbonate (147 mg, 0.67 mmol) were added. The orange solution was stirred at room temperature for 18 h. The solution was concentrated in vacuo and the residue was purified via flash chromatography on silica gel (20% EtOAc/hexanes as eluent) to yield 102 mg of **31** (67%) as a yellow oil. IR ($CDCl_3$) 1797, 1750, 1709 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.37 (t, J = 7.9, Hz, 2H), 7.24 (m, 1H), 7.16 (m, 2H), 4.04 (dd, J = 14.7, 4.6 Hz, 1H), 3.93 (dd, J = 14.7, 4.6 Hz, 1H), 3.24 (dd, J = 4.1, 2.6 Hz, 1H), 2.80 (apparent t, J = 4.4 Hz, 1H), 2.67 (dd, J = 4.9, 2.6 Hz, 1H), 1.54 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 152.4, 151.7, 150.6, 129.3, 125.9, 121.3, 83.7, 49.7, 47.6, 45.7, 27.8; ESIMS *m/z* (rel intensity) 294 (MH^+, 59).

Oxazolidinone 32. Trimethylsilylacetylene (2.12 mL, 15 mmol) was dissolved in 20 mL of THF, and the mixture was cooled to −78 °C. *n*-Butyllithium (6 mL of a 2.5 M solution in hexanes, 15 mmol) was added over 18 min. This mixture was stirred at −78 °C for 15 min, and then boron trifluoride etherate (1.9 mL, 15 mmol) was added over 6 min. This mixture was stirred at −78 °C for 20 min and then epoxide **31** (2.94 g, 10 mmol) was added as a solution in 10 mL of THF over 20 min. This mixture was stirred at −78 °C for 2.5 h, saturated NH_4Cl was added to the solution, and the mixture was allowed to warm to room temperature. The mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and adsorbed onto silica gel. The crude product was purified via flash chromatography on silica gel (18%, 25%, then 50% EtOAc, hexanes as eluent) to yield 1.75 g of the crude oxazolidinone which was recrystallized from 20 mL of Et_2O and 150 mL of hexanes to yield pure **32** (1.41 g, 47%) as a white solid. Mp 116−117 °C; IR ($CDCl_3$) 3692, 3604, 2181, 1816, 1720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.60 (m, 1H), 4.03 (dd, J = 10.4, 8.6 Hz, 1H), 3.81 (dd, J = 10.4, 5.8 Hz, 1H), 2.66 (d, J = 5.6 Hz, 2H), 1.54 (s, 9H), 0.14 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 151.5, 149.5, 98.6, 89.2, 83.9, 70.1, 47.6, 28.1, 26.1, −0.1; APCIMS *m/z* (rel intensity) 320 ($[MNa]^+$, 9). Anal. Calcd for $C_{14}H_{23}NO_4Si$: C, 56.54; H, 7.79. Found: C, 56.40; H, 7.84.

Stannylalkyne 33. Oxazolidinone **32** (600 mg, 2.0 mmol) was dissolved in 5.3 mL of dry THF, and then bis(tributyltin) oxide (0.54 mL, 1 mmol) and Bu_4NF (42 μL of a 1 M solution of Bu_4NF in THF, 0.4 mmol) were added. The flask was sealed and heated to 60 °C for 4 h. Bu_4NF (10 μL of a 1 M solution of Bu_4NF in THF, 0.1 mmol) was added and the mixture was heated for an additional 50 min. The solution was concentrated in vacuo, and the residue was purified via flash chromatography with deactivated silica gel (12−20% EtOAc/hexanes as eluent) to yield 0.47 g of **33** (45%) as a colorless oil. IR ($CDCl_3$) 2153, 1821, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.59 (apparent tdd, J = 10.7, 6.3, 4.4 Hz, 1H), 4.03 (dd, J = 10.4, 8.4 Hz, 1H), 3.85 (dd, J = 10.4, 6.3 Hz, 1H), 2.77 (ddd, J = 16.7, 9.2, 4.7 Hz, 1H), 2.63 (dd, J = 16.7, 8.0 Hz, 1H), 1.6−1.4 (m, 6H), 1.56 (s, 9H), 1.3−1.2 (m, 6H), 1.1−0.8 (m, 15H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 151.2, 149.1, 102.2 (J_{C-Sn} = 29.5 Hz), 86.7, 83.3, 70.3, 47.4, 28.6 (J_{C-Sn} = 11.6 Hz), 27.7, 26.6 (J_{C-Sn} = 29.6 Hz), 25.8, 13.4, 10.7 ($J^{13}C-^{117}Sn$ = 183.0 Hz and $J^{13}C-^{119}Sn$ = 191.4 Hz); ESIMS *m/z* (rel intensity) 533 ($[M + Na]^+$, 32); HRMS Calcd for $C_{23}H_{41}NO_4{}^{118}Sn$ 516.2140, found 516.2133.

Cyclopentene 35. Alkynylstannane **33** (1.21 g, 2.35 mmol) was dissolved in 28 mL of dry CH_2Cl_2 then cooled to −50 °C, and PhI(CN)OTf (883 mg, 2.33 mmol) was added in one portion. The mixture was stirred at −42 °C for 2 h, and then concentrated in vacuo at −42 °C at aspirator pressure through a drying tube. The residue was dissolved in 9.4 mL of dry DME prechilled to −42 °C and poured into a refluxing suspension of $TolO_2SNa$ (427 mg, 2.35 mmol) in 22 mL of dry DME. The mixture was held at reflux for 15 min, cooled to room temperature, and concentrated in vacuo. The crude mixture was purified via flash chromatography on silica gel (40−50% EtOAc/hexanes as eluent) to yield 365 mg of **35** (41%) and 116 mg of alkyne **34** (13%) as white solids. A sample of **35** was recrystallized from 3:5 $CHCl_3$/hexanes for characterization.

35: mp 145 °C (decomposes with gas evolution); IR ($CDCl_3$) 3690, 3607, 1818, 1723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 6.64 (d, J =

(24) Patonay, T.; Patonay-Peli, E.; Mogyorodi, F. *Synth. Commun.* **1990**, *20*, 2865−2885.

1.6 Hz, 1H), 5.20 (d, $J = 7.2$ Hz, 1H), 5.10 (apparent t, $J = 6.7$ Hz, 1H), 3.01 (ddd, $J = 18.0$, 6.4, 2.3 Hz, 1H), 2.77 (d, $J = 18.0$ Hz, 1H), 2.43 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 148.4, 147.6, 145.6, 134.9, 134.4, 130.2, 128.2, 84.7, 75.1, 64.0, 37.5, 27.8, 21.6; APCIMS *m/z* (rel intensity) 397 ($[M + H_3O]^+$, 3). Anal. Calcd for $C_{18}H_{21}NO_6S$: C, 56.98; H 5.58. Found: C, 56.80; H, 5.56.

34: IR (CCl_4) 2213, 1805 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, $J = 8.4$ Hz, 2H), 7.36 (d, $J = 8.4$, Hz, 2H), 4.65 (m, 1H), 4.06 (dd, $J = 10.9$, 10.2 Hz, 1H), 3.70 (dd, $J = 10.9$, 5.5 Hz, 1H), 2.82 (m, 2H), 2.46 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 150.9, 149.2, 146.0, 138.4, 130.3, 127.7, 88.4, 84.7, 81.5, 69.1, 47.8, 28.2, 25.3, 22.0; APCIMS *m/z* (rel intensity) 402 (MNa^+, 3).

Cyclopentylcarbamate 36. Cyclopentene **35** (107 mg, 0.28 mmol) was suspended in 3.8 mL of absolute EtOH and benzylamine (159 μL, 1.8 mmol) was added. The mixture was heated at reflux for 3 h. Additional benzylamine (42 μL, 0.5 mmol) was added and the mixture was held at reflux for an additional 16 h. The brown solution was cooled to room temperature and concentrated in vacuo, and the residue was purified via flash chromatography on silica gel (40−50% EtOAc/hexanes as eluent) to yield **36** (26.5 mg, 19%) as a yellow solid. Mp 154−158 °C; IR (C_6D_6) 3681, 3424, 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 60 °C) δ 7.69 (d, $J = 7.8$ Hz, 2H), 7.4−7.2 (m, 12H), 5.08 (m, 1H), 5.02 (m, 1H), 4.35 (m, 2H), 4.12 (m, 1H), 3.81 (m, 2H), 3.65 (m, 1H), 3.51 (m, 1H), 2.4−2.0 (m, 6H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 60 °C) δ 155.6, 155.4, 144.9, 135.8, 130.0, 129.5, 128.8, 128.73, 128.68, 128.4, 128.0, 127.6, 127.2, 126.1, 80.2, 73.4, 65.5, 62.5, 58.3, 50.7, 45.4, 30.7, 28.4, 21.5; APCIMS *m/z* (rel intensity) 594 (MH^+, 100).

Hydroxy Urea 39a. Following general procedure A, pentenyne **37a**[22a] (55 mg, 0.40 mmol) and urea **38** were combined. Purification of the crude reaction product by flash chromatography on silica gel (1% MeOH, 19% Et_2O, CH_2Cl_2 as eluent) yielded 56 mg of hydroxy urea **39a** (44%, 8% ee) as a yellow oil. Enantiomeric excess was determined by chiral HPLC with a Chiralcel OD-H column (5% ^{i}PrOH/hexanes at 1 mL/min), detecting at $\lambda = 205$ nm. Retention times were 20.25 and 26.84 min for the two enantiomers. IR ($CHCl_3$) 2181, 1775, 1679 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3−7.0 (m, 5H), 5.34 (t, $J = 5.5$ Hz, 1H), 4.80 (br s, 1H), 4.45 (s, 2H), 3.82 (m, 1H), 3.5 (ddd, $J = 14.1$, 6.0, 2.8 Hz, 1H), 3.26 (ddd, $J = 14.1$, 6.9, 5.4 Hz, 1H), 2.82 (s, 3H), 2.43 (dd, $J = 16.9$, 5.9 Hz, 1H), 2.34 (dd, $J = 16.9$, 7.1 Hz, 1H), 0.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 137.5, 128.7, 127.3, 127.2, 103.2, 86.9, 70.3, 52.2, 46.1, 34.3, 26.1, 0.1; ESMS *m/z* (rel intensity) 319 (MH^+, 100).

Hydroxy Urea 39b. Ethynyldimethylphenylsilane[22b] (10.4 g, 65 mmol) was added rapidly dropwise to ethylmagnesium bromide (78 mL as a 1 M solution in THF, 78 mmol) in 10 mL of THF. This mixture was heated at 50 °C for 1 h then cooled to room temperature, and CuBr (93 mg, 0.65 mmol) was added. Allyl bromide (8.4 mL, 98 mmol) was added over 1 h, and the exotherm raised the temperature to about 62 °C. The mixture was heated at 55 °C for 1.5 h, and then saturated NH_4Cl, Et_2O, and water were added. The organic layer was washed with water and brine, and the aqueous layers were washed twice with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to provide 13.6 g of a yellow liquid. This crude product was distilled at 61 °C/0.03 Torr to yield 12.4 g of **37b** (95%) as a colorless liquid. IR (KBr plates) 2177 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.7−7.5 (m, 2H), 7.4−7.3 (m, 3H), 5.89 (ddt, $J = 17.0$, 10.0, 5.1 Hz, 1H), 5.42 (dq, $J = 17.0$, 1.8 Hz, 1H), 5.21 (dq, $J = 10.0$, 1.8 Hz, 1H), 3.12 (dt, 5.2, 1.8 Hz, 1H), 0.50 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 137.4, 133.6, 131.9, 129.3, 127.8, 116.4, 105.3, 85.0, 24.2, −0.7; EIMS *m/z* (rel intensity) 200 (M^+, 22).

Following general procedure A, pentenyne **37b** (93 mg, 0.46 mmol) and urea **38** were combined. Urea alcohol **39b** was isolated after flash chromatography on silica gel (50−60% EtOAc/hexanes as eluent) as 75 mg of a yellow oil (43%, 4% ee). Enantiomeric excess was determined by chiral HPLC with a Chiralcel OD-H column (5% ^{i}PrOH/hexanes as eluent at 1 mL/min), detecting at $\lambda = 205$ nm. Retention times were 33.10 and 44.20 min for the two enantiomers. IR ($CDCl_3$) 3475, 3314, 2174 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.59 (m, 2H), 7.4−7.1 (m, 8H), 5.03 (t, $J = 5.6$ Hz, 1H), 4.57 (s, 1H), 4.45 (s, 2H), 3.86 (m, 1H), 3.53 (ddd, $J = 14.3$, 6.1, 2.8 Hz, 1H), 3.30 (ddd, $J = 14.3$, 6.7, 5.4 Hz, 1H), 2.82 (s, 3H), 2.50 (dd, $J = 16.9$, 5.9 Hz, 1H), 2.41 (dd, $J = 16.9$, 7.4 Hz, 1H), 0.38 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.7, 137.3, 137.1, 133.5, 129.3, 128.6, 127.8, 127.3, 127.1, 105.0, 85.0, 70.5, 52.2, 46.0, 34.3, 26.1, −0.9; ESMS *m/z* (rel intensity) 381 (MH^+, 100).

Hydroxy Urea 39c. Benzyldimethylchlorosilane (10.9 g, 59 mmol) was added rapidly dropwise to ethynylmagnesium bromide (130 mL of a 0.5 M solution in THF, 65 mmol). The brown solution was heated at reflux for 18 h and cooled to 4 °C for 20 min, then water and Et_2O were added. The organic layer was washed with water and brine. The aqueous layers were washed twice with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by distillation at 99 °C/22 Torr to yield benzylethynyldimethylsilane (8.8 g, 86%) as a colorless liquid. IR (KBr plates) 2034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 2H), 7.1−7.0 (m, 3H), 2.38 (s, 1H), 2.21 (s, 2H), 0.14 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.3, 128.2, 124.5, 94.4, 88.5, 25.9, −2.3. Anal. Calcd for $C_{11}H_{14}Si$: C, 75.79; H, 8.10. Found: C, 75.48; H, 8.33.

This silane (8.0 g, 46 mmol) was added rapidly dropwise to ethylmagnesium bromide (55 mL of a 1 M solution in THF, 55 mmol). This mixture was heated at 50 °C for 1 h then cooled to room temperature, and CuBr (66 mg, 0.46 mmol) was added. Allyl bromide (6.0 mL, 69 mmol) was added over 1 h, and the exotherm raised the temperature to 55 °C. The mixture was heated at 55 °C for 1.5 h, and then saturated NH_4Cl, water, and Et_2O were added. The organic layer was washed with water and brine, and the aqueous layers were washed twice with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a yellow liquid. This liquid was distilled at 58−60 °C/0.05 Torr to yield 9.3 g of **37c** (95%) as a colorless liquid. IR (KBr plates) 2176 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.20 (m, 2H), 7.1−7.0 (m, 3H), 5.79 (ddt, $J = 17.0$, 10.0, 5.1 Hz, 1H), 5.30 (d(apparent)q, $J = 17.0$, 1.7 Hz, 1H), 5.12 (d(apparent)q, $J = 10.0$, 1.7 Hz, 1H), 2.99 (dt, $J = 5.2$, 1.8 Hz, 2H), 2.19 (s, 2H), 0.12 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.1, 131.9, 128.4, 128.1, 124.2, 116.3, 104.8, 85.5, 26.4, 24.1, −2.0; EIMS *m/z* (rel intensity) 214 (M^+, 10). Anal. Calcd for $C_{14}H_{18}Si$: C; 78.44, H; 8.46. Found: C; 78.44, H; 8.52.

Following general procedure A, pentenyne **37c** (91 mg, 0.42 mmol) and urea **38** were combined. Urea alcohol **39c** was isolated after flash chromatography on silica gel (50−60% EtOAc/hexanes as eluent) as 64 mg of a colorless oil (39%, 20% ee). Enantiomeric excess was determined by chiral HPLC with a Chiralcel OD-H column (5% ^{i}PrOH/hexanes as eluent at 1 mL/min), detecting at $\lambda = 205$ nm. Retention times were 39.00 and 43.70 min for the two enantiomers. IR ($CDCl_3$) 3475, 3318, 1629 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.4−7.1 (m, 7H), 7.1−7.0 (m, 3H), 4.90 (br s, 1H), 4.48 (s, 2H), 3.85 (m, 2H), 3.44 (d, $J = 13.2$ Hz, 1H), 3.24 (m, 1H), 2.87 (s, 3H), 2.45 (dd, $J = 16.9$, 5.9 Hz, 1H), 2.34 (dd, $J = 16.9$, 7.4 Hz, 1H), 2.16 (s, 2H), 0.12 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.7, 139.1, 137.4, 128.7, 128.3, 128.0, 127.4, 127.1, 124.2, 104.5, 85.4, 70.6, 52.2, 45.9, 34.4, 26.2, 26.0, −2.0; ESIMS *m/z* (rel intensity) 417 (MNa^+, 100).

Stannylalkyne 40. Urea alcohol **39a** (5.6 g, 17 mmol) was dissolved in 174 mL of dry THF. Diisopropylethylamine (10 mL, 58 mmol) and triphosgene (5.69 g, 19 mmol) were added, and the reaction mixture was stirred for 20 min under a partial aspirator vacuum such that there was mild bubbling of the solution. Saturated $NaHCO_3$ was poured into the reaction mixture and the resulting solution was extracted with EtOAc. The organic layer was washed with water and then brine, dried

over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified via flash chromatography on silica gel (30−40% EtOAc/hexanes as eluent) to furnish 4.4 g of the oxazolidinone product (73%) as a yellow oil. IR ($CHCl_3$) 2181, 1775, 1679 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5H), 4.68 (m, 1H), 4.60 (s, 2H), 4.07 (dd, J = 9.8, 8.1 Hz, 1H), 3.87 (dd, J = 9.9, 6.5 Hz, 1H), 2.96 (s, 3H), 2.75 (dd, J = 16.9, 4.8 Hz, 1H), 2.64 (dd, J = 16.9, 7.5 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (90 MHz, C_6D_6) δ 154.0, 153.3, 137.2, 128.8, 128.1, 127.6, 100.2, 88.4, 71.6, 53.2, 48.1, 35.8, 25.4, −0.1; APCIMS m/z (rel intensity) 345 (MH^+, 100). Anal. Calcd for $C_{18}H_{24}N_2O_3Si$: C, 62.76; H, 7.02. Found: C, 62.67; H, 7.12.

This oxazolidinone (680 mg, 1.97 mmol) was dissolved in 2 mL of THF, and glacial acetic acid (172 μL, 3 mmol) followed by Bu_4NF (3 mL as a 1 M solution in THF, 3 mmol) were added. The reaction was complete by TLC after 4 h at room temperature. The solution was poured into saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude dark yellow oil (612 mg) was purified via flash chromatography on silica gel (40−50% EtOAc/hexanes as eluent) to furnish 427 mg of the terminal alkyne (80%). IR ($CHCl_3$) 3307, 1776, 1679 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5H), 4.71 (m, 1H), 4.63 (d, J = 15.4 Hz, 1H), 4.57 (d, J = 15.3 Hz, 1H), 4.10 (dd, J = 9.9, 8.0 Hz, 1H), 3.84 (dd, J = 9.9, 6.3 Hz, 1H), 2.96 (s, 3H), 2.66 (m, 2H), 2.04 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 153.4, 136.4, 128.8, 127.84, 127.78, 77.1, 72.1, 71.8, 53.4, 48.4, 36.1, 24.3; ESIMS m/z (rel intensity) 295 (MNa^+, 100). Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92. Found: C, 65.94; H, 6.00.

This terminal alkyne (427 mg, 1.57 mmol) was dissolved in 3 mL of dry THF and cooled to −78 °C, then LiHMDS (1.54 mL as a 1 M solution in THF, 1.54 mmol) was added via syringe pump over 30 min. Tributyltin chloride (0.47 mL, 1.73 mmol) was dissolved in 1 mL of THF to prevent freezing and added over 10 min via syringe pump 5 min after completing the LiHMDS addition. The reaction solution was warmed to room temperature over 1 h, stirred at room temperature 1 h, and then was concentrated in vacuo. Purification of the residue via flash chromatography on silica gel (1% Et_3N/CH_2Cl_2 as eluent) afforded 759 mg of **40** (86%) as a colorless oil. IR ($CHCl_3$) 2153, 1774, 1679 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 7.4−6.9 (m, 5H), 4.45 (d, J = 15.2 Hz, 1H), 4.40 (d, J = 15.2 Hz, 1H), 3.94 (m, 1H), 3.69 (dd, J = 9.6, 6.7 Hz, 1H), 3.54 (apparent t, J = 8.8 Hz, 1H), 2.71 (s, 3H), 2.20 (dd, J = 17.2, 6.3 Hz, 1H), 2.13 (dd, J = 17.2, 5.1 Hz, 1H), 1.61 (m, 6H), 1.35 (m, 6H), 0.93 (m, 15H); ^{13}C NMR (90 MHz, C_6D_6) δ 154.1, 153.4, 137.2, 128.8, 128.1, 127.6, 103.9, 86.4, 72.0, 53.1, 48.2, 35.8, 29.2 (J_{C-Sn} = 11.5 Hz), 27.3 (J_{C-Sn} = 29 Hz), 35.6, 13.8, 11.2 (J_{C-Sn} = 183.0 Hz); ESIMS m/z (rel intensity) 563 (MH^+, 9); HRMS Calcd for $C_{27}H_{43}N_2O_3{}^{118}Sn^+$ 563.2295, found 563.2292.

Cyclopentene 41. Urea alkynylstannane **40** (5.36 g, 9.54 mmol) was dissolved in 96 mL of dry CH_2Cl_2 and cooled to −42 °C. PhI(CN)OTf (3.58 g, 9.44 mmol) was added in one portion, the solution was stirred at −42 °C for 1 h, and then the mixture was concentrated in vacuo at −42 °C. The white solid iodonium salt (~9.4 mmol) was dissolved in 38 mL of dry DME that was prechilled to −42 °C. The flask was briefly removed from the cold bath to warm and dissolve residual solids, and the solution was poured rapidly into a refluxing suspension of $TolO_2SNa$ (1.7 g, 9.6 mmol) in 153 mL of DME. This mixture turned clear yellow immediately after addition. The reaction mixture was held at reflux for 5 min, cooled to room temperature, and concentrated in vacuo. Purification of the residue via flash chromatography on silica gel (40−60% EtOAc/hexanes as eluent) afforded 1.43 g of **41** (35%) and 565 mg of **42** (14%), both as off-white solids.

41: mp 131−132 °C; IR (CCl_4) 1791, 1685 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.4−7.1 (m, 7H), 6.89 (apparent q, J = 1.8 Hz, 1H), 5.19 (d(apparent)q, J = 7.1, 1.3 Hz, 1H), 5.12 (td, J = 6.6, 1.1 Hz, 1H), 4.57 (d, J = 15.3 Hz, 1H), 4.52 (d, J = 15.3 Hz, 1H), 2.98 (dddd, J = 17.9, 6.1, 2.3, 1.0 Hz, 1H), 2.90 (s, 3H), 2.86 (d(apparent)q, J = 17.9, 1.7 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 153.0, 152.0, 147.1, 145.5, 136.4, 136.1, 134.9, 130.2, 128.8, 128.3, 127.7, 127.6, 77.2, 65.1, 53.5, 37.1, 36.3, 21.6; APCIMS m/z (rel intensity) 427 (MH^+, 98). Anal. Calcd for $C_{22}H_{22}N_2O_5S$: C, 61.96; H 5.20. Found: C, 61.78; H, 5.22.

42: IR ($CDCl_3$) 2213, 1790, 1682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.7−7.1 (m, 7H), 4.74 (m, 1H), 4.59 (s, 2H), 4.11 (apparent t, J = 9.0 Hz, 1H), 3.70 (dd, J = 10.0, 6.2 Hz, 1H), 2.97 (s, 3H), 2.84 (m, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3, 152.6, 145.6, 138.0, 136.0, 129.9, 128.5, 127.5, 127.2, 102.9, 88.9, 80.8, 70.4, 53.1, 48.0, 36.0, 24.5, 21.5; ESMS m/z (rel intensity) 427 (MH^+, 100).

Pyrrole Carboxamide 43a. Cyclopentene **41** (0.60 g, 1.4 mmol) and 2-nitrobenzylamine (426 mg, 2.8 mmol) were added to 14 mL of ethanol, and the mixture was heated at reflux for 15 h. Additional 2-nitrobenzylamine (444 mg, 2.9 mmol) in 5.1 mL of EtOH was added. The mixture was held at reflux an additional 2 d. The crude mixture was concentrated in vacuo and then purified via flash chromatography on silica gel (30−34% $EtOAc/CH_2Cl_2$ as eluent) to yield 657 mg of the secondary amine (81%) as an orange solid. Mp 82−84 °C; IR ($CHCl_3$) 1780, 1678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 60 °C) δ 7.89 (dd, J = 8.1, 1.2 Hz, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.6−7.3 (m, 8H), 7.21 (d, J = 8.1 Hz, 2H), 5.05 (dd, J = 13.9, 7.2 Hz, 1H), 4.78 (d, J = 7.8 Hz, 1H), 4.62 (br s, 1H), 4.16 (d, J = 14.1 Hz, 1H), 3.96 (d, J = 14.1 Hz, 1H), 3.62 (d, J = 4.4 Hz, 1H), 3.42 (m, 1H), 2.95 (s, 3H), 2.56 (m, 1H), 2.4−2.2 (m, 4H), 1.95 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 152.9, 149.1, 145.5, 136.3, 134.4, 134.3, 133.4, 131.8, 130.2, 128.8, 128.6, 128.4, 127.9, 127.7, 125.1, 77.4, 68.8, 66.2, 64.1, 53.2 (br), 48.8, 36.2 (br), 33.8, 21.7; ESMS m/z (rel intensity) 601 (MNa^+, 100). Anal. Calcd for $C_{29}H_{30}N_4O_7S$: C, 60.19; H 5.23. Found: C, 60.26; H, 5.16.

Following general procedure B, this secondary amine (317 mg, 0.55 mmol) was acylated with **28** and purified via flash chromatography on silica gel (50−60% EtOAc/hexanes as eluent) to yield 207 mg of **43a** (56%) as a white solid. Mp 109−111 °C; IR ($CDCl_3$) 3450, 1775, 1678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 60 °C) δ 9.48 (br s, 1H), 8.18 (dd, J = 8.1, 0.9 Hz, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.75 (t, J = 7.3 Hz, 1H), 7.68 (dd, J = 3.1, 1.5 Hz, 1H), 7.59 (m, 2H), 7.47 (t, J = 7.7 Hz, 1H), 7.33 (dd, J = 3.6, 1.5 Hz, 1H), 7.3−7.0 (m, 6H), 6.9−6.8 (m, 3H), 6.44 (t, J = 3.4 Hz, 1H), 6.08 (m, 2H), 5.53 (m, 2H), 5.37 (d, J = 7.8 Hz, 1H), 4.75 (br s, 2H), 4.38 (d, J = 15.1 Hz, 1H), 4.00 (m, 1H), 3.89 (s, 1H), 3.01 (m, 1H), 2.91 (s, 3H), 2.51 (br d, J = 14.0 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 60 °C) δ 164.3, 153.1, 152.8, 147.4, 145.7, 136.1, 134.7, 134.2, 131.6, 129.9, 129.3, 128.4, 128.3, 127.22, 127.16, 125.3, 123.3, 122.9, 122.7, 113.0, 110.3, 80.5, 71.1, 68.2, 67.5, 53.1, 36.6, 35.2, 21.3; ESIMS m/z (rel intensity) 672 (MH^+, 100); ES-HRMS Calcd for $C_{34}H_{34}N_5O_8S$ 672.2128, found 672.2109.

Cyclopentanol 44. Oxazolidinone **43a** (259 mg, 0.38 mmol) was dissolved in 2.9 mL of dry MeOH and 0.9 mL of dry CH_2Cl_2. Cesium carbonate (74 mg, 0.23 mmol) was added and the mixture was stirred at room temperature overnight. The mixture was treated with citric acid monohydrate (192 mg, 0.91 mmol) and diluted with water and EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude mixture was purified via flash chromatography on silica gel (4% $MeOH/CH_2Cl_2$ as eluent) to yield 200 mg of **44** (81%) as a pale yellow solid. Mp 214−215 °C; IR ($CHCl_3$) 3603, 3451, 1734 cm^{-1}; ^1H NMR (300 MHz, MeOD, 60 °C) δ 8.01 (dd, J = 8.0, 1.5 Hz, 1H), 7.70 (d, J = 8.3 Hz, 2H), 7.57 (dd, J = 7.0, 1.6 Hz, 1H), 7.4−7.0 (m, 10H), 6.88 (dd, J = 2.6, 1.3 Hz, 1H), 6.15 (br s, 1H), 6.01 (dd, J = 3.7, 2.6 Hz, 1H), 5.12 (d, J = 18.9 Hz, 1H), 4.97 (br s, 1H), 4.78 (d, J = 18.9 Hz, 1H), 4.68 (br s, 1H), 4.36 (m, 3H), 4.12 (d(apparent)t, J = 7.3, 2.2 Hz, 1H), 2.69 (s, 3H), 2.49 (ddd, J = 15.3, 10.4, 5.2 Hz, 1H), 2.35 (s, 3H), 2.17 (ddd, J = 15.1, 5.3, 2.3 Hz, 1H); ^{13}C NMR (75 MHz, MeOD, 60 °C) δ 162.3, 157.8, 147.9, 145.5, 137.8, 134.4, 133.4, 133.0, 130.1, 129.8,

128.5 (2 overlapping signals), 127.9, 127.6, 127.2, 124.8, 124.1, 122.0, 112.9, 110.2, 71.0, 66.1, 65.0, 58.2, 52.3, 51.8, 34.0, 33.1, 21.4; ESMS *m/z* (rel intensity) 646 (MH^+, 100); ES-HRMS Calcd for $C_{33}H_{36}N_5O_7S$ 646.2335, found 646.2275; Anal. Calcd for $C_{33}H_{35}N_5O_7S$: C, 61.38; H, 5.46. Found: C, 61.24; H, 5.46.

Tricyclic Cyclopentanone 45. Following general procedure C, cyclopentanol **44** (124 mg, 0.19 mmol) was oxidized and cyclized, and the resulting solid was purified to yield 62 mg of **45** (67%) as a yellow solid. Mp 110−114 °C; IR ($CHCl_3$) 3687, 1764, 1719, 1651 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.1, 1.2 Hz, 1H), 7.55 (dt, J = 7.5, 1.1 Hz, 1H), 7.4−7.3 (m, 2H), 7.3−7.1 (m, 5H), 6.90 (dd, J = 3.9, 1.5 Hz, 1H), 6.76 (dd, J = 2.6, 1.5 Hz, 1H), 6.39 (d, J = 6.6 Hz, 1H), 6.25 (dd, J = 3.9, 2.7 Hz, 1H), 5.64 (d, J = 16.8 Hz, 1H), 4.9−4.8 (m, 3H), 4.43 (s, 2H), 3.54 (dd, J = 9.1, 6.8 Hz, 1H), 3.18 (dd, J = 18.6, 5.5 Hz, 1H), 3.04 (d, J = 18.4 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 207.3, 158.5, 157.5, 148.6, 137.2, 133.8, 133.1, 129.3, 128.9, 128.5, 127.5, 127.2, 125.3, 123.6, 122.5, 115.8, 111.8, 61.8, 60.1, 52.2, 51.3, 46.8, 42.3, 34.4; APCIMS *m/z* (rel intensity) 488.3 (MH^+, 100).

Tricyclic Cyclopentanones 46/47. Cyclopentanone **45** (60 mg, 0.12 mmol) was dissolved in 19.3 mL of THF and 3.4 mL of water. The solution was dispersed with glass beads and suspended in a Rayonet photochemical reactor with 350-nm bulbs, then the mixture was irradiated for 6 h. The mixture was then filtered and the beads were washed with EtOAc and water. The organic layer was washed with brine, dried over Na_2SO_4, filtered, concentrated in vacuo, and purified via preparatory plate chromatography (5% MeOH, CH_2Cl_2 as eluent) to yield **46** and its C(5b) epimer **47** (42 mg, 96%) in a 3.2:1 ratio. IR ($CDCl_3$) 3689, 3419, 1762, 1661, 1552, 1514 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$ for the major product **46**) δ 7.5−7.0 (m, 6H), 6.78 (dd, J = 2.6, 1.4 Hz, 1H), 6.30 (dd, J = 3.9, 2.7 Hz, 1H), 4.81 (d, J = 15.5 Hz, 1H), 4.50 (m, 1H), 4.31 (br s, 1H), 4.05 (d, J = 15.9 Hz, 1H), 3.29 (br s, 1H), 3.16 (dd, J = 18.6, 6.0 Hz, 1H), 2.95 (d, J = 18.6 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ for the major product **46**) δ 207.0, 160.1, 157.5, 137.3, 128.7, 128.5, 127.4, 127.1, 122.9, 115.2, 111.6, 62.2, 55.7, 54.5, 51.8, 50.5, 42.3, 34.0; APCIMS *m/z* (rel intensity) 375.2 (MNa^+, 100), 353.2 (MH^+, 76).

(±)-Debromoagelastatin A (11). A mixture of cyclopentanones **46**/**47** (90 mg, ∼0.22 mmol of **46**) was dissolved in 2.5 mL of dry THF, and palladium hydroxide on carbon (dried, 53 mg) was added. The mixture was stirred under a balloon of hydrogen gas for 16 h, and then the mixture was loaded directly onto two 1 mm thick silica gel prep plates and developed with 18% MeOH/EtOAc to yield 34 mg of **11** (57%) as a white solid, [partially mixed at low R_f with C(5b)-epidebromoagelastatin A (12 mg)]. IR (CH_2Cl_2) 3284, 1716, 1671 cm^{-1}; ^1H NMR (360 MHz, CD_3OD) 7.02 (dd, J = 2.6, 1.5 Hz, 1H), 6.88 (dd, J = 3.9, 1.5 Hz, 1H), 6.22 (dd, J = 3.9, 2.6 Hz, 1H), 4.64 (dt, J = 9.9, 5.8 Hz, 1H), 4.00 (dd, J = 6.1, 1.5 Hz, 1H), 3.80 (d, J = 1.3 Hz, 1H), 2.79 (s, 3H), 2.61 (dd, J = 13.3, 6.4 Hz, 1H), 2.27 (dd, J = 13.3, 10.3 Hz, 1H); ^{13}C NMR (90 MHz, CD_3OD) δ 162.2, 161.5, 125.7, 123.0, 115.6 (d, J = 22.3 Hz), 111.2, 96.0, 68.1, 63.0, 55.8, 41.8, 24.4; ESMS *m/z* (rel intensity) 285 (MNa^+, 24).

(±)-Agelastatin A (1) and (±)-Agelastatin B (2). Debromoagelastatin A (**11**) (6.9 mg, 26 μmol) was suspended in 1.0 mL of THF and 1.0 mL of CH_3OH, and NBS (4.7 mg, 26 μmol) was added. The suspension was stirred at room temperature under irradiation from a 500 W halogen spotlight and a 250 W GE infrared heat lamp for 1 h, at which time the mixture was concentrated in vacuo. ^1H NMR analysis of the crude reaction mixture indicated a ca. 1.3:1 mixture of (±)-**1** to (±)-**2**. This mixture was purified via prep plate chromatography (24% EtOH/CH_2Cl_2) to yield 3.8 mg of (±)-**1** and (±)-**2** in a 1.1:1 ratio (38%).

1: IR (CH_2Cl_2) 1724, 1673 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 6.90 (d, J = 4.1 Hz, 1H), 6.32 (d, J = 4.1 Hz, 1H), 4.59 (d(apparent)t, J = 11.6, 6.0 Hz, 1H), 4.07 (d, J = 5.7 Hz, 1H), 3.88 (s, 1H), 2.80 (s, 3H), 2.64 (dd, J = 13.2, 6.6 Hz, 1H), 2.09 (apparent t, J = 12.6 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 161.4, 161.1, 124.1, 116.0, 113.8, 107.2, 95.7, 67.4, 62.2, 54.4, 40.0, 24.2. ESMS *m/z* (rel intensity) 285.1 (MNa^+, 24), 245.1 (M − OH, 100).

2: IR (CH_2Cl_2) 1722, 1678 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 6.96 (s, 1H), 4.60 (d(apparent)t, J = 11.8, 6.0 Hz, 1H), 4.11 (d, J = 5.5 Hz, 1H), 3.88 (s, 1H), 2.81 (s, 3H), 2.68 (dd, J = 13.1, 6.5 Hz, 1H), 2.12 (apparent t, J = 12.6 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 161.4, 159.6, 117.0, 111.0, 108.6, 101.8, 95.6, 67.6, 62.1, 55.5, 40.0, 24.2; APCIMS *m/z* (rel intensity) 421 (MH^-, 84).

(8a*R*)-Oxazolidinone 50. A flask equipped with an overhead stirrer was charged with alkynyl epoxide **49**[16] (9.7 g, 63 mmol), sodium azide (20.5 g, 315 mmol), ammonium chloride (17 g, 310 mmol), and 630 mL of 95% ethanol. The white suspension was stirred at room temperature for 39 h. The mixture was diluted with 400 mL of EtOAc then filtered, and the filtrate was concentrated in vacuo. The resulting white solid was dissolved with 250 mL of EtOAc and 250 mL of H_2O. The aqueous layer was washed with 2 × 75 mL of EtOAc, and the organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to give 11.9 g of (4*R*)-5-azido-4-hydroxy-1-(trimethylsilyl)pent-1-yne (84%) as a yellow oil. ^1H NMR (360 MHz, $CDCl_3$) δ 3.97 (br s, 1H), 3.48 (dd, J = 12.8, 3.8 Hz, 1H), 3.40 (dd, J = 12.8, 6.9 Hz, 1H), 2.50 (m, 2H), 2.28 (br s, 1H), 0.16 (s, 9H). The crude azide was dissolved in 530 mL of dry THF and, after cooling to −78 °C, *n*-butyllithium (5.3 mL of a 2.5 M solution of *n*-BuLi in hexanes, 13 mmol) was added dropwise. After 10 min, dry ice was allowed to sublime through drierite into the solution for 40 min, and then trimethylphosphine (74 mL of a 1 M solution in THF, 74 mmol) was added. The solution was stirred at −78 °C for 20 min, and then the bath was removed and the mixture warmed gradually with vigorous bubbling to room temperature. The mixture was stirred under a balloon pressure of 1 atm of carbon dioxide at room temperature for 4 h. Phosphate buffer (pH 7.0, 250 mL) was poured into the reaction mixture which then was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 10.6 g of a yellow tacky solid. 160 mg of this residue was purified via flash chromatography on silica gel (70 to 75% EtOAc/hexanes as eluent) to yield 126 mg of (*R*)-**50** (67% from epoxide **49**) as a white solid. An analytical sample was sublimed at 100 °C/0.1 Torr. $[\alpha]^{20}_D$ −58.8° (*c* 1.0, $CHCl_3$); mp 70−71 °C; IR ($CDCl_3$) 3469, 2180, 1765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (br s, 1H), 4.74 (apparent tdd, J = 8.2, 6.0, 4.9 Hz, 1H), 3.74 (apparent t, J = 8.6 Hz, 1H), 3.50 (dd, J = 8.7, 6.1 Hz, 1H), 2.73 (dd, J = 16.8, 4.9 Hz, 1H), 2.65 (dd, J = 16.8, 7.6 Hz, 1H), 0.15 (s, 9H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.9, 99.4, 88.1, 73.9, 44.8, 25.8, −0.3; APCMS *m/z* (rel intensity) 198 (MH^+, 100). Anal. Calcd for $C_9H_{15}NO_2Si$: C, 54.79; H, 7.66. Found: C, 54.46; H, 7.60.

(8a*R*)-Stannylalkyne 51. Crude oxazolidinone **50** (9.4 g, 42 mmol, purity 87%) was dissolved in 430 mL of dry THF, and the solution was cooled to −78 °C. Lithium hexamethyldisilazide (42 mL as a 1 M solution in THF, 42 mmol) was added over 30 min. The mixture was stirred at −78 °C for 2 h, and then methyl (2-nitrobenzyl)carbamoyl chloride[25] (12 g, 54 mmol) was transferred via cannula as a solution in 100 mL of dry THF. The mixture was warmed with the bath for 6 h to room temperature, and then the bath was removed and the solution was stirred at room temperature overnight. The solution was cooled in an ice−water bath and then diluted with 500 mL of 1 M HCl. The organic layer was washed with water and brine. The aqueous layers were extracted with 400 mL of EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 19 g of an orange gum. A 280-mg portion of this gum was purified via flash

(25) Yoakim, C.; Ogilvie, W. W.; Cameron, D. R.; Chabot, C.; Guse, I.; Haché, B.; Naud, J.; O'Meara, J. A.; Plante, R.; Déziel, R. *J. Med. Chem.* **1998**, *41*, 2882−2891.

chromatography on silica gel (36−40% EtOAc/hexanes as eluent) to yield 206 mg (87%) of oxazolidinone urea as a yellow gum. $[\alpha]^{20}_D$ −29.0° (*c* 1.0, $CHCl_3$); IR ($CDCl_3$) 2181, 1774, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 60 °C) δ 8.04 (d, J = 7.9 Hz, 1H), 7.7−7.5 (m, 2H), 7.43 (t, J = 7.4 Hz, 1H), 5.04 (d, J = 17.2 Hz, 1H), 4.97 (d, J = 17.1 Hz, 1H), 4.71 (m, 1H), 4.08 (dd, J = 9.9, 8.0 Hz, 1H), 3.90 (dd, J = 9.9, 6.6 Hz, 1H), 3.05 (s, 3H), 2.77 (dd, J = 17.0, 4.9 Hz, 1H), 2.68 (dd, J = 17.0, 7.3 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 153.3, 147.9, 133.9, 131.9, 128.1 (2 overlapping signals), 125.0, 98.6, 88.7, 72.0, 50.9, 48.0, 37.2, 25.3, −0.3; APCMS *m*/*z* (rel intensity) 390 (MH^+, 100). Anal. Calcd for $C_{18}H_{23}N_3O_5Si$: C, 55.51; H, 5.95. Found: C, 55.63; H, 5.92.

The crude oxazolidinone urea from above (18.9 g, 36 mmol) was dissolved in 70.5 mL of dry THF. Acetic acid (4.05 mL, 70.7 mmol) and Bu_4NF (70.5 mL of a 1 M solution in THF, 70.5 mmol) were added. The mixture was stirred at room temperature for 6 h. Saturated $NaHCO_3$ and EtOAc were added to the reaction mixture. The organic layer was washed with 1 M H_3PO_4 and then brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The orange gum was purified via flash chromatography on silica gel (46−50% EtOAc/hexanes as eluent) to yield 10.9 g of the terminal alkyne (97%) as a yellow tacky solid. IR ($CDCl_3$) 3308, 1775, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.2 Hz, 1H), 7.67 (d, J = 4.6 Hz, 1H), 7.46 (m, 2H), 5.03 (s, 2H), 4.78 (m, 1H), 4.14 (dd, J = 9.9, 8.0 Hz, 1H), 3.90 (dd, J = 9.9, 6.4 Hz, 1H), 3.07 (s, 3H), 2.73 (dd, J = 5.7, 2.7 Hz, 2H), 2.10 (t, J = 2.7 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 153.9, 153.3, 147.9, 133.9, 131.8, 128.1 (2 overlapping signals), 125.0, 76.8, 71.9, 71.8, 51.0, 48.0, 37.2, 23.9; APIMS *m*/*z* (rel intensity) 318 (MH^+, 100).

The alkyne from above (1.6 g, 5.0 mmol) was dissolved in 10 mL of dry THF then cooled to −78 °C, and LiHMDS (5 mL as a 1 M solution in THF, 5 mmol) was added over 30 min. The mixture was stirred at −78 °C for 30 min, and then tributyltin chloride (1.41 mL, 5.2 mmol) dissolved in 3 mL of dry THF was added. The mixture was allowed to warm with the bath to room temperature overnight. Saturated NH_4Cl and EtOAc were added to the reaction mixture. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The orange oil was purified via flash chromatography with deactivated silica gel (40% EtOAc/hexanes as eluent) to yield 2.3 g of the alkynylstannane **51** (76%) as a viscous yellow oil. $[\alpha]^{20}_D$ −29.8° (*c* 1.0, $CHCl_3$); IR (CCl_4) 2154, 1782, 1690 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 8.08 (d, J = 8.2 Hz, 1H), 7.65 (m, 2H), 7.46 (t, J = 7.3 Hz, 1H), 5.03 (s, 2H), 4.74 (m, 1H), 4.10 (dd, J = 10.0, 7.8 Hz, 1H), 3.94 (dd, J = 9.9, 6.7 Hz, 1H), 3.08 (s, 3H), 2.83 (dd, J = 16.7, 4.7 Hz, 1H), 2.72 (dd, J = 16.7, 8.0 Hz, 1H), 1.6−1.4 (m, 6H), 1.3−1.1 (m, 6H), 1.1−0.8 (m, 6H), 0.90 (m, 9H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 154.2, 153.7, 148.2, 134.1, 132.1, 128.6, 128.3, 125.3, 102.5, 87.2, 72.7, 51.2, 48.5, 37.5 (br), 28.8 (J_{C-Sn} = 11.5 Hz), 26.9 (J_{C-Sn} = 30.2 Hz), 25.7, 13.6, 11.0 ($J_{C-^{119}Sn}$ = 191.4 Hz, $J_{C-^{117}Sn}$ = 182.9 Hz); ESMS *m*/*z* (rel intensity) 608 (M^+, 100); HRMS Calcd for $C_{27}H_{41}N_3O_5{}^{116}Sn^+$ 606.2147, found 606.2153. Anal. Calcd for $C_{27}H_{41}N_3O_5Sn$: C, 53.48; H, 6.82; N, 6.93. Found: C, 53.47; H, 6.72; N, 7.15.

(5b*S*,8a*R*)-Cyclopentene 53. Stannylalkyne **51** (3.45 g, 5.7 mmol) was dissolved in 57 mL of dry CH_2Cl_2 then cooled to −42 °C, and PhI(CN)OTf (2.13 g, 5.6 mmol) was added in one portion. The mixture was stirred at −42 °C for 60 min, and then concentrated in vacuo at −42 °C. The crude alkynyliodonium salt was dissolved in 23 mL of dry DME at ∼0 °C, and then transferred via cannula to a refluxing suspension of $TolO_2SNa$ (998 mg, 5.6 mmol) in 89 mL of dry DME. The mixture immediately became a clear yellow solution that slowly darkened over 5 min at reflux. After cooling to −78 °C, the mixture was concentrated in vacuo, and the residue was purified via flash chromatography on silica gel (60% EtOAc/hexanes as eluent) to yield 900 mg of cyclopentene **53** (34%) as a yellow solid and 1.14 g of alkynyl sulfone **52** (41%) as a yellow solid.

53: $[\alpha]^{20}_D$ +137.8° (*c* 1.0, $CHCl_3$); mp 88−90 °C; IR ($CDCl_3$) 1776, 1682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.6, 1.1 Hz, 1H), 7.78 (d, J = 8.3 Hz, 2H), 7.7−7.5 (m, 2H), 7.47 (t, J = 7.6 Hz, 1H), 7.37 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 1.6 Hz, 1H), 5.27 (m, 2H), 5.07 (d, J = 17.1 Hz, 1H), 4.87 (d, J = 17.2 Hz, 1H), 3.1−2.8 (m, 5H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 152.1, 148.0, 147.0, 145.4, 136.1, 134.7, 133.9, 131.6, 130.1, 128.4 (2 overlapping signals), 128.2, 125.2, 77.3, 65.0, 51.3, 37.2 (br), 36.9, 21.5; ESMS *m*/*z* (rel intensity) 472 (MH^+, 2).

52: $[\alpha]^{20}_D$ +6.3° (*c* 1.0, $CHCl_3$); mp 114−117 °C; IR ($CDCl_3$) 2213, 1779, 1686, 1599 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.7−7.6 (m, 2H), 7.46 (td, J = 7.4, 2.1 Hz, 1H), 7.38 (d, J = 8.1 Hz, 2H), 5.04 (d, J = 17.2 Hz, 1H), 4.96 (d, J = 17.3 Hz, 1H), 4.81 (m, 1H), 4.16 (dd, J = 10.1, 8.2 Hz, 1H), 3.75 (dd, J = 10.1, 6.1 Hz, 1H), 3.05 (s, 3H), 2.92 (m, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 152.9, 148.1, 145.7, 138.1, 134.1, 131.8, 130.0, 128.3 (2 overlapping signals), 127.4, 125.2, 88.6, 81.0, 70.6, 51.2, 48.1, 37.6, 24.7, 21.7; ESI^+ MS *m*/*z* (rel intensity) 489.2 ($[M + H_2O]^+$, 100), 472.1 (MH^+, 13). Anal. Calcd for $C_{22}H_{21}N_3O_7S$: C, 56.04; H, 4.49; N, 8.91; S, 6.80. Found: C, 56.32; H, 4.63; N, 8.87; S, 6.82.

(5b*S*,8a*R*,5a*S*,9a*S*)-Pyrrole Carboxamide 54. Cyclopentene **53** (543 mg, 1.15 mmol) was suspended in 15.7 mL of absolute ethanol containing 2-nitrobenzylamine (877 mg, 5.76 mmol). The mixture was heated at reflux for 5 d. At that time, the solution was cooled to room temperature and then concentrated in vacuo. The residue was purified via flash chromatography with silica gel (60−65% EtOAc/hexanes as eluent) to yield 608 mg of pure secondary amine (85%) as a yellow solid. $[\alpha]^{20}_D$ +14.2° (*c* 1.0, $CHCl_3$); mp 80 °C ; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.1, Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.6−7.4 (m, 6H), 7.31 (d, J = 8.1 Hz, 2H), 5.33 (d, J = 18.1 Hz, 1H), 5.16 (dd, J = 13.2, 7.4 Hz, 1H), 4.82 (m, 2H), 4.78 (d, J = 16.3 Hz, 1H), 4.13 (d, J = 14.2 Hz, 1H), 3.94 (d, J = 14.2 Hz, 1H), 3.75 (d, J = 3.6 Hz, 1H), 3.50 (apparent td, J = 8.0, 4.2 Hz, 1H), 3.14 (s, 3H), 2.61, (m, 1H), 2.45 (m, 1H), 2.42 (s, 3H), 2.03 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 152.8, 148.7, 147.8, 145.2, 134.3, 134.04, 133.95, 133.0, 131.9, 131.4, 129.9, 128.1, 128.0, 125.1, 124.7, 122.2, 112.4, 77.6, 68.7, 65.8, 63.7, 51.0, 48.3, 37.4, 33.4, 21.4; APCMS *m*/*z* (rel intensity) 624 (MH^+, 38); HRMS Calcd for $C_{29}H_{30}N_5O_9S$ 624.1764, found 624.1744.

Pyrrole-2-carboxylic acid (564 mg, 5.0 mmol, 3 equiv) was suspended in 24.4 mL of dry benzene. Oxalyl chloride (885 μL, 10.1 mmol) and 2 drops of DMF were added. The mixture was stirred until a colorless solution was formed and gas evolution ceased (45 min). The mixture was concentrated, and the beige solid residue (**28**) was dissolved in 4.8 mL of dry 1,2-dichloroethane (DCE). The secondary *o*-nitrobenzylamine (1.06 g, 1.69 mmol) prepared above was dissolved in 12.2 mL of dry DCE. Pyridine (0.82 mL, 10.14 mmol) and 4-(dimethylamino)-pyridine (41 mg, 0.34 mmol) were added to the amine solution, and the mixture was slowly heated. The acid chloride **28** was added in 3 portions with 30-min intervals between additions when the amine mixture was at 30, 40, and 50 °C. The mixture was stirred between 45 and 55 °C for 2 days. The solution was diluted with CH_2Cl_2 and poured into saturated aqueous $NaHCO_3$. The organic layer was washed with 1 M H_3PO_4, saturated. $NaHCO_3$, and brine, filtered, and concentrated in vacuo. The residue was purified via flash chromatography (40, 45, and 50% EtOAc/hexanes as eluent) to provide 988 mg of amide **54** (82%) as a yellow-orange solid. $[\alpha]^{20}_D$ +15.5° (*c* 1.0, $CHCl_3$); mp 140−142 °C; IR ($CHCl_3$) 3451, 1772, 1681, 1610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 60 °C) δ 9.39 (s, 1H), 8.13 (dd, J = 8.1, 1.2 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.82 (dd, J = 7.9, 1.0 Hz, 1H), 7.72 (d, J = 8.1 Hz, 2H), 7.7−7.4 (m, 5H), 7.34 (d, J = 8.0 Hz, 2H), 6.91 (td, J = 2.7, 1.2 Hz, 1H), 6.16 (ddd, J = 3.8, 2.5, 1.3 Hz, 1H), 6.09 (dt, J = 3.9, 2.6 Hz, 1H), 5.6−5.4 (m, 2H), 5.29 (d, J = 8.0 Hz, 1H), 5.16 (d, J = 17.3 Hz, 1H), 5.05 (d, J = 19.1 Hz, 1H), 4.61 (d, J = 17.3 Hz, 1H),

4.00 (m, 2H), 3.09 (s, 3H), 2.97 (ddd, J = 16.4, 8.2, 7.1 Hz, 1H), 2.45 (s, 3H), 2.43 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ at 60 °C) δ 164.6, 153.6, 153.0, 148.4, 147.9, 145.8, 134.7, 134.6, 133.8, 132.1, 131.6, 130.2, 129.6, 128.6, 128.2, 128.0, 125.5, 125.1, 123.3, 122.7, 113.4, 110.8, 80.6, 71.2, 67.9, 67.4, 64.2, 53.2, 51.1, 37.3, 21.5; ESI$^+$ MS m/z (rel intensity) 717.2 (MH^+, 44).

(5b*S*,5a*S*,9a*R*)-Tricyclic Cyclopentanone 55. Amide **54** (130 mg, 0.18 mmol) was suspended in 3.6 mL of methanol at room temperature, and then Cs_2CO_3 (36 mg, 0.11 mmol) was added. The mixture was stirred at room temperature for 18 h. The clear orange solution was treated with citric acid monohydrate (91 mg, 0.43 mmol) and then diluted with water and CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 117 mg of the product cyclopentanol (94%) as a yellow-orange solid. $[\alpha]^{20}_D$ −2.9° (c 1.0, $CHCl_3$); mp 124−125 °C; IR ($CHCl_3$) 3635, 3446,1650 cm^{-1}; ^{1}H NMR (300 MHz, 10:1 MeOD/$CDCl_3$, 60 °C) δ 8.02 (dd, J = 7.8, 1.7 Hz, 1H), 7.96 (dd, J = 8.1, 1.3 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 7.4 Hz, 1H), 7.5−7.2 (m, 4H), 6.89 (dd, J = 2.6, 1.3 Hz, 1H), 6.17 (br s, 1H), 6.01 (dd, J = 3.8, 2.6 Hz, 1H), 5.77 (d, J = 8.8 Hz, 1H), 5.16 (d, J = 18.9 Hz, 1H), 4.97 (br s, 1H), 4.81 (d, J = 18.9 Hz, 1H), 4.78 (d, J = 17.7 Hz, 1H), 4.67 (br s, 1H), 4.64 (d, J = 17.7 Hz, 1H), 4.33 (br s, 1H), 4.14 (m, 1H), 2.78 (s, 3H), 2.45 (ddd, J = 15.3, 10.3, 5.2 Hz, 1H), 2.34 (s, 3H), 2.15 (ddd, J = 15.2, 5.1, 2.3 Hz, 1H); ^{13}C NMR (75 MHz, 10:1 MeOD/$CDCl_3$, 60 °C) δ 165.9, 159.6, 149.6, 149.2, 146.6, 136.2, 134.6, 134.5, 134.3, 134.1, 130.9, 130.3, 129.4, 129.2, 129.1, 128.9, 125.82, 125.76, 125.0, 123.1, 144.0, 110.5, 69.6, 64.7, 62.8, 58.9, 58.8, 50.8, 35.3, 33.6, 21.6; APCMS m/z (rel intensity) 691 (MH^+, 7); HRMS Calcd for $C_{33}H_{35}N_6O_9S$ 691.2186, found 691.2174.

Following general procedure C, this cyclopentanol (86 mg, 0.12 mmol) was oxidized and cyclized, and the resulting solid was purified (72−80% EtOAc/hexanes as eluent) to yield 40 mg of **55** (63%) as a yellow solid. $[\alpha]^{20}_D$ −31.4° (c 1.0, $CHCl_3$); mp 154−160 °C; IR ($CDCl_3$) 3531, 3461, 1765, 1652 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.64 (apparent t, J = 7.6 Hz, 2H), 7.48 (m, 2H), 7.35 (m, 2H), 7.02 (d, J = 5.8 Hz, 1H), 6.72 (s, 1H), 6.65 (d, J = 2.7 Hz, 1H), 6.17 (t, J = 3.0 Hz, 1H), 5.61 (d, J = 16.7 Hz, 1H), 5.0−4.7 (m, 5H), 3.37 (br s, 1H), 3.14 (dd, J = 18.6, 5.4 Hz, 1H), 3.00 (d, J = 18.6 Hz, 1H), 2.99 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 206.5, 158.4, 157.3, 148.4, 147.9, 134.1, 133.8, 133.5, 132.6, 129.2, 128.5, 127.9, 127.5, 125.2, 125.1, 122.8, 122.5, 115.5, 111.8, 61.5, 59.7, 51.1, 50.4, 46.5, 42.2, 35.2; ESI$^+$ MS m/z (rel intensity) 533.2 (MH^+, 100).

Detailed spectral data for (−)-**11**, (−)-**1**, and (−)-**2** can be found in the description of the racemic series earlier in the Experimental Section.

(−)-Debromoagelastatin A (11). Cyclopentanone **55** (13 mg, 25 μmol) was dissolved in 3.9 mL of THF, and 0.7 mL of water was added. The solution was dispersed with glass beads and suspended in a Rayonet photochemical reactor. Irradiation with 350-nm bulbs was continued for 6.5 h. The mixture was then filtered and the beads were washed with MeOH. The filtrate was concentrated in vacuo, and purified via silica gel preparatory plate chromatography (20% MeOH/EtOAc as the developing solvent) to yield 5.4 mg of (−)-**11** (82%) as a white solid. $[\alpha]^{20}_D$ −68.4° (c 0.5, CH_3OH); mp 244−245 °C.

(−)-Agelastatin A (1). (−)-Debromoagelastatin A (**11**) (5.7 mg, 22 μmol) was dissolved in 0.5 mL of CH_3OH and 1.0 mL of THF, and 2.1 mg of NBS (11 μmol, 0.5 equiv) was added. The solution was stirred at room temperature for 3 h, at which time a sample was removed, concentrated in vacuo, and assayed for conversion by ^{1}H NMR. The remainder of NBS required to complete 1 equiv was added (2.2 mg), and the mixture was stirred at room temperature overnight. The mixture was concentrated in vacuo, and the brown residue was purified via silica gel preparatory plate chromatography (14% MeOH/CH_2Cl_2 as developing solvent) to yield 5.1 mg of (−)-**1** (73%) as an off-white solid. ^{1}H NMR (300 MHz, MeOD) and TLC R_f matches an authentic sample of the natural product kindly supplied by Dr. D'Ambrosio: $[\alpha]^{20}_D$ −65.5° (c 0.5, CH_3OH).

(−)-Agelastatin B (2). (−)-Debromoagelastatin A (**11**) (25 mg, 95 μmol) was dissolved in 2.1 mL of MeOH and 4.2 mL of dry THF, and NBS (35.5 mg, 200 μmol, 2.1 equiv) was added. The solution was stirred at room temperature for 18 h. The mixture was concentrated in vacuo, and the yellow residue was purified via chromatography (10−15% MeOH/CH_2Cl_2) to yield (−)-**2** (17.8 mg, 45%) as an off-white solid. $[\alpha]^{20}_D$ −60.3° (c 0.5, MeOH); mp 220−221 °C dec.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for **1**, **2**, **11**, **14**, **17**, **19**, **22**, **24**, **25**, **29**, **31**, **33**, **34**, **36**, **39a-c**, **40**, **42**, **43a**, **45**, **53**, **54**, and **55**. This material is available free of charge via the Internet at http://pubs.acs.org.

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