Cyclizations of Substituted Benzylidene-3-alkenylamines: Synthesis of the Tricyclic Core of the Martinellines

Kristine E. Frank† and Jeffrey Aubé*

Department of Medicinal Chemistry, University of Kansas, Lawrence, Kansas 66045-2506

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The martinellines (**1** and **2**) are natural products that possess both interesting biological activity and chemical structure. During the investigation of a hetero Diels−Alder route to these molecules, alternate Lewis acid-dependent cyclizations of (2′-amino-*N*′-*tert*-butoxycarbonyl-5′-chlorobenzylidene)-3-butenylamine (**10**) were observed. The reaction of a variety of imines with TMSOTf or $TiCl_4$ led to the formation of different heterocycles including iminodibenzo[*b,f*][1,5]diazocines, hexahydropyrido[1,2-*c*]quinazolin-6-ones, tetrahydropyrrolo[1,2-*c*]quinazolin-5-ones, 2-arylpiperidines, and 2-arylpyrrolidines. Tetrahydropyrrolo[1,2-*c*]quinazolin-5-one **54**, obtained via this new methodology, was used as an intermediate in the synthesis of the tricyclic ring system (**65**) of the martinellines.

Preparations from the root bark of *Martinella* species have been used by Amazon Indian tribes for the treatment of a variety of eye ailments including conjunctivitis.[1] Fractionation of an ethanolic extract of *Martinella iquitosensis* root bark by workers at Merck led to the isolation of martinelline (**1**) and martinellic acid (**2**) (Figure 1). These compounds showed modest activity as bradykinin receptor antagonists, which could contribute to the antiinflammatory effect of the root bark preparations. Additionally, martinelline demonstrated antagonist activity at histaminergic, α-adrenergic, and muscarinic receptors as well as weak antibacterial activity, which could further contribute to the efficacy of the folkloric preparations.

The martinellines are interesting from a chemical standpoint due to the pyrroloquinoline ring system, which had not been previously detected in a natural product.[1] Several groups have recently published synthetic approaches to the tricyclic core of these natural products, but the total synthesis of **1** or **2** has not yet been achieved.[2] Our initial retrosynthetic analysis revolved around an intramolecular Diels−Alder reaction of an *o*-quinone methide imide (*o*-azaxylene) formed in situ from an imine (Scheme 1). This material could conceivably arise from the deprotonation of the aniline or via Lewis acid activation of same. The appeal of this disconnection was that it would set all three stereocenters of the martinellines in one step. The relative stereochemistry at C-2 and C-2a would be controlled by the double bond geometry of the dienophile and it was proposed that the 5,6-fused ring system would prefer to be cis, which would set the desired relative stereochemistry at C-2a and C-5a. Although numerous examples of Diels−Alder reactions of *o*-quinone imides[3] or *o*-quinone methides[4] with terminal amido substitution exist, only a single example of a species containing nitrogen atoms at both positions has been reported.[5,6]

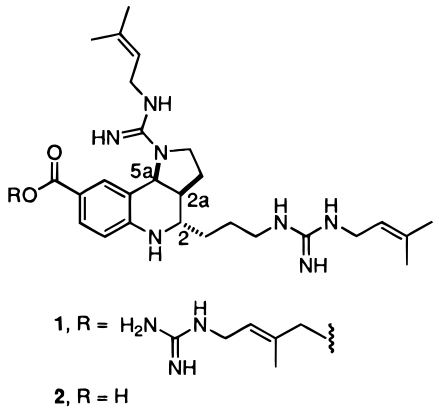
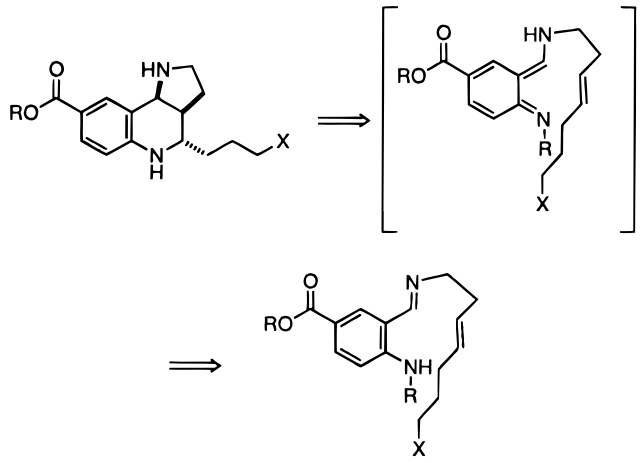


Figure 1. Martinellines and their numbering system.

Scheme 1



Results and Discussion

Model Reactions. A model imine was prepared to study the proposed Diels−Alder reaction. A para-

* To whom correspondence should be addressed. Tel: 1.785.864.4496. Fax: 1.785.864.5326. E-mail: jaube@ukans.edu.

† Current Address: Pharmacia & Upjohn, 7254-209-619, 301 Henreitta Street, Kalamazoo, MI 49007.

(1) Witherup, K. M.; Ransom, R. W.; Graham, A. C.; Bernard, A. M.; Salvatore, M. J.; Lumma, W. C.; Anderson, P. S.; Pitzenberger, S. M.; Varga, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 6682−6685.

(2) (a) Gurjar, M. K.; Pal, S.; Rao, A. V. R. *Heterocycles* **1997**, *45*, 231−234. (b) Ho, T. C. T.; Jones, K. *Tetrahedron* **1997**, *53*, 8287−8294. (c) Hadden, M.; Stevenson, P. J. *Tetrahedron Lett.* **1999**, *40*, 1215−1218. (d) Lovely, C. J.; Mahmud, H. *Tetrahedron Lett.* **1999**, *40*, 2079−2082. (e) Batey, R. A.; Simoncic, P. D.; Lin, D.; Smyj, R. P.; Lough, A. J. *Chem. Commun.* **1999**, 651−652. (f) Snider, B. B.; Ahn, Y.; Foxman, B. M. *Tetrahedron Lett.* **1999**, *40*, 3339−3342.

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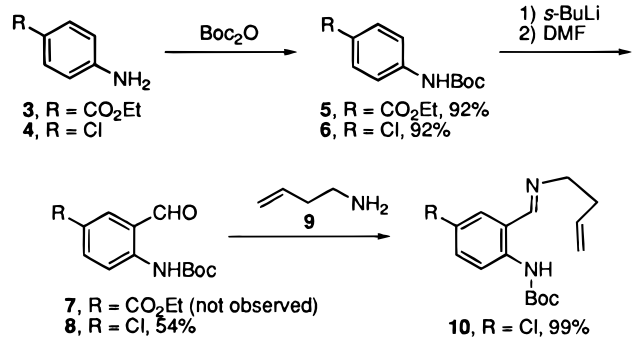
Scheme 2



substituted aniline (**3** or **4**) was protected as the *tert*-butyl carbamate (**5** or **6**) in order to direct ortho-lithiation with *sec*-butyllithium (Scheme 2). When ethyl *p*-aminobenzoate (**3**) was used as the starting material the *o*-lithiation was unsuccessful. Thus, *p*-chloroaniline (**4**) was used to rapidly enter into an appropriately substituted aldehyde (**8**) for the model system. The reduction of 3-butenenitrile with lithium aluminum hydride gave amine **9**, which was condensed with aldehyde **8** to give imine **10**.

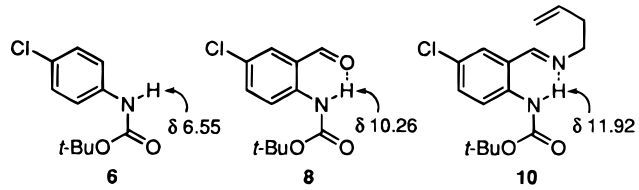
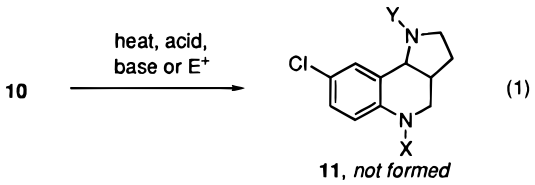


Figure 2. ^{1}H NMR evidence for intramolecular hydrogen bonding.

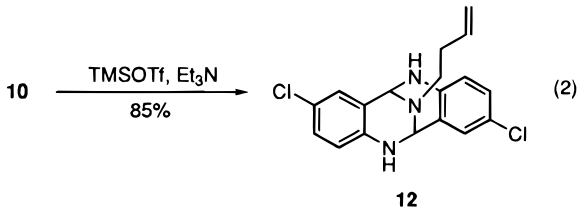
The Diels−Alder adduct (**11**) was not observed under a variety of reaction conditions including heat, acid, and base (eq 1). Also unsuccessful were attempts to activate the imine using a variety of electrophiles including acetic anhydride, methylchloroformate, 2,2,2-trichloroethylchloroformate, chlorotrimethylsilane, methyl iodide, boron trifluoride diethyl etherate, and ytterbium triflate.



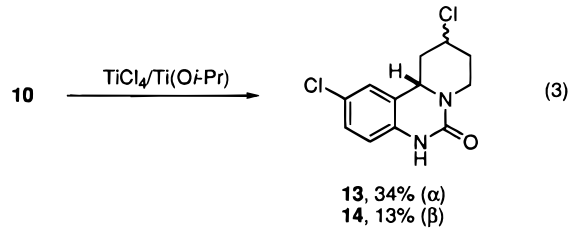
(1)

The inability to externally activate the imine may be due to intramolecular hydrogen bonding as shown in Figure 2. This hypothesis is supported by the observations that the ^{1}H NMR signal of the aniline hydrogen shifts significantly downfield when **6** is formylated at the ortho position (**8**), and shifts even further downfield after imine formation (**10**). If this hydrogen bond is indeed responsible for the lack of electrophile activation at the imine nitrogen lone pair (and therefore lack of diene formation), then use of an alternate aniline protecting group might ultimately permit [4 + 2] cyclization. In light of other developments, however, this tactic was not pursued.

Although **11** was not formed in any of the reactions of imine **10**, two alternate products were observed. The reaction of **10** with TMSOTf in the presence of triethylamine gave iminodibenzo[*b*,*f*][1,5]diazocine **12** in 85% yield (eq 2). The reaction of **10** with $TiCl_4$/$Ti(OiPr)_4$ gave hexahydropyrido[1,2-*c*]quinazolin-6-ones **13** and **14**, in a total of 47% yield (eq 3). The Lewis acid-dependent formation of both heterocycles from imine **10** warranted further investigation.[6]



(2)



(3)

The iminodibenzo[*b*,*f*][1,5]diazocine ring system has been observed in a variety of reactions involving *o*-aminobenzaldehydes.[7] Recent reports have described the preparation of this ring system from the reaction of primary amines with the iminophosphorane derived from 2-azidobenzaldehyde.[8] In the present case, **12** probably arises from the pseudodimerization of the deprotected[9] aniline derived from imine **10** (Scheme 3).

The formation of the hexahydropyrido[1,2-*c*]quinazolin-6-one ring system was interesting primarily because it appeared to occur via an imine−olefin cyclization with an unusual acyl iminium intermediate (Scheme 4). This intermediate may close directly as shown but may also involve an isocyanate intermediate. Chloride addition could occur along with C−C bond formation to give the isomer shown. Alternatively, nonstereospecific trapping of an initially formed cation could account for the formation of both stereoisomers.

Many methods for the addition of alkenes to iminium species have been developed for the formation of a variety of heterocycles.[10] A key feature in a number of applications of such olefin cyclizations is the use of a silyl group to direct the ring closure via stabilization of the develop-

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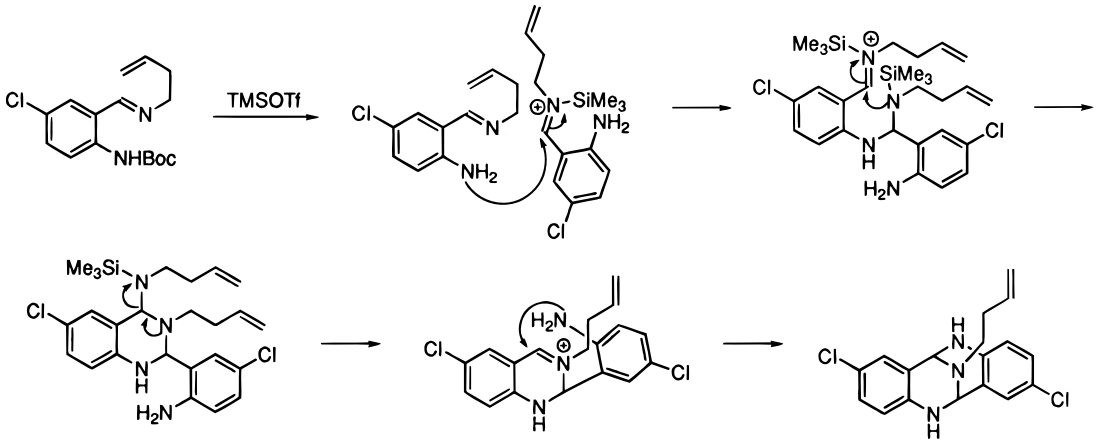
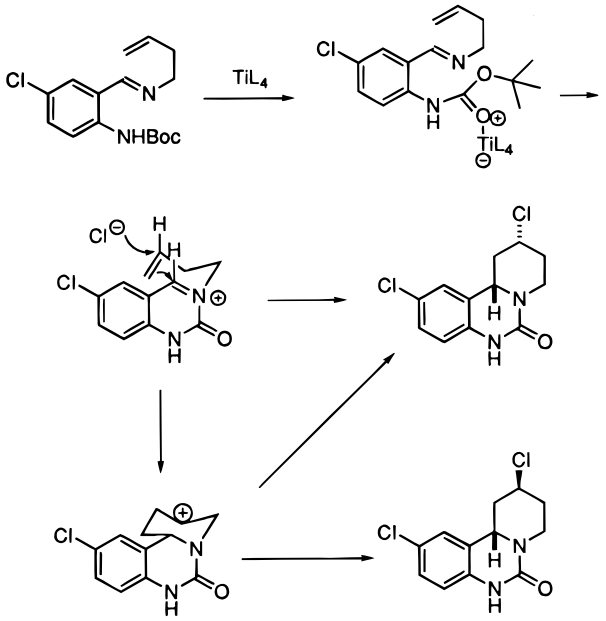
Scheme 3



Scheme 4



ing β-carbocation. The use of a silyl directing group in quinazolinone formation merited exploration for its potential application toward the formation of the pyrroloquinolone ring system.

A number of additional imines were prepared to explore the formation of iminodibenzo[*b*,*f*][1,5]diazocines, hexahydropyrido[1,2-*c*]quinazolin-6-ones, and related heterocycles (Table 1). Imine **25** was formed via condensation of aldehyde **8** with amine **15**. Imines **26**−**31** were formed from reaction of the corresponding aldehyde with amine **9**. The preparation of imines **32**−**36** required allyl silanes **21** and **24**, which were themselves prepared from known precursors (Scheme 5). Thus, alcohols **19**[11] and **22**[12] were converted to the corresponding azides (**21** and **24**, respectively) via mesylation followed by azide displacement. In a one-pot Staudinger/aza-Wittig reaction, each azide was reacted with triphenylphosphine to form the corresponding iminophosphorane prior to the addition of an aldehyde to give imines **32**−**36**. These reactions afforded imines in high yields, which were used without further purification.

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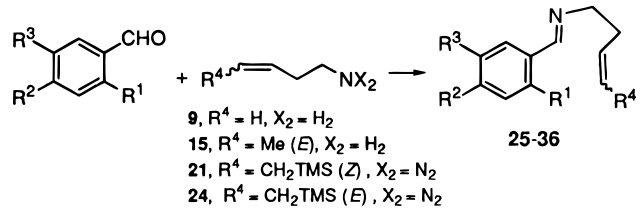
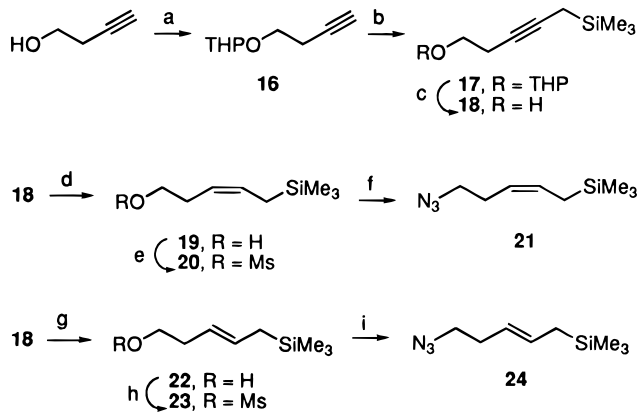
Table 1. Formation of Imines 25−36



entry	R^1	R^2	R^3	alkene	imine
1	NHBoc	H	Cl	**15**	**25**
2	NHBoc	H	H	**9**	**26**
3	H	H	H	**9**	**27**
4	H	OMe	H	**9**	**28**
5	H	NO_2	H	**9**	**29**
6	H	CO_2Me	H	**9**	**30**
7	NO_2	H	Cl	**9**	**31**
8	NHBoc	H	Cl	**21**	**32**
9	NHBoc	H	Cl	**24**	**33**
10	NH_2	H	Cl	**21**	**34**
11	NO_2	H	Cl	**21**	**35**
12	NHPiv	H	Cl	**21**	**36**

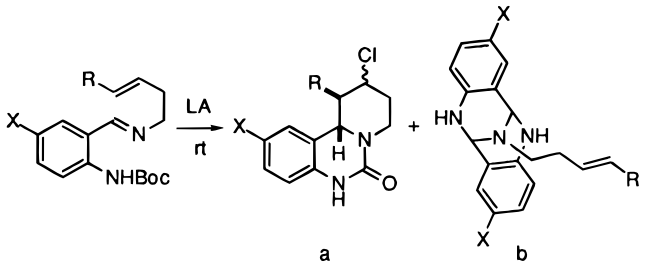
Scheme 5[a]



[a] Reaction conditions: (a) DHP, *p*-TsOH, 88%; (b) *n*-BuLi, then $TMSCH_2OTf$ or $TMSCH_2I$, 50−81%; (c) MeOH, *p*-TsOH, 84%; (d) H_2, Lindlar's catalyst, quinoline, 90%; (e) MsCl, Et_3N, 97%; (f) NaN_3, 91%; (g) LAH, 61%; (h) MsCl, Et_3N, 95%; (f) NaN_3, 91%.

The first set of imines (**10**, **25**, and **26**) were investigated for their differential reactivity with a variety of Lewis acids (Table 2). The reaction of TMSOTf with either imine **10** or **25** gave iminodibenzo[*b*,*f*][1,5]diazocine **12** or **37**, respectively (entries 1 and 4). The absence of triethylamine lowered the yield of this transformation

Table 2. Lewis Acid-Promoted Cyclization of Imines 10, 25, and 26



					product(s)	
entry	imine	R	X	Lewis acid	**a** (yield, %)[a]	**b** (yield, %)
1	**10**	H	Cl	TMSOTf	*b*	**12** (61)
2	**10**			$TiCl_4$	**13** (35−42)	**12** (ca. 13)
3	**10**			$Ti(OiPr)_4$	*b*	*b*
4	**25**	CH_3	Cl	TMSOTf	*b*	**37** (64)
5	**25**			$TiCl_4$	**38** (40)	**37** (30)
6	**26**	H	H	$TiCl_4$	**39** (65)[c]	*b*

[a] Formed as a >9:1 ratio of α/β chloride epimers (based on ^{1}H NMR). [b] Not isolated. [c] Reaction run in refluxing CH_2Cl_2.

(cf. entry 1 vs eq 2). The reaction of these imines with $TiCl_4$ led to varying mixtures of iminodibenzo[*b*,*f*][1,5]-diazocines and hexahydropyrido[1,2-*c*]quinazolin-6-ones (entries 2, 5, and 6). However, in contrast to the results with $TiCl_4$/$Ti(OiPr)_4$ (eq 3), the hexahydropyrido[1,2-*c*]-quinazolin-6-one diastereomeric ratio was >9:1. This suggests that the lower Cl^- concentration in the mixed Lewis acid system may favor stepwise addition (Scheme 4). Additionally, treatment of imine **10** with $Ti(OiPr)_4$ alone did not promote either reaction pathway (entry 3).

Imines **27**−**31** allowed for exploration of the imine−olefin reaction in the absence of urea formation (Table 3). This series of reactions was carried out at CH_2Cl_2 reflux for 72 h. This increased reaction time and temperature was needed for product formation. Although some product (**40**−**44**) was obtained from each of these examples, none approached efficiencies consistent with synthetic utility. Neither starting material nor other products could be cleanly isolated from these low-yielding cases. On the other hand, those examples containing an *o*-NHBoc substituent gave consistently higher yields and cleaner products, observations that are consistent with the mechanism for the examples involving acyl iminium ion formation prior to attack by the olefin as shown in Scheme 4. Interestingly, the stereochemistry of the piperidine products depended upon the electronic nature of the aromatic ring, with trans products preferred from Ar = Ph and for electron-rich aromatics. As the electronic-withdrawing character of the aromatic ring was increased, the amount of cis isomer went up. The trans isomer favored in the former cases might arise from a transition structure in which the aryl group occupies a pseudoaxial orientation to avoid steric interactions with the titanium presumably bound to the nitrogen atom (Figure 3). The cis isomers could result from an increasing incursion of a stepwise process, possibly involving a ring flip of the initially formed carbocation adduct. These points were not further examined due to the relatively poor yields of these processes.

The final set of imines investigated contained the allyl silane substituent (Table 4). The *cis*-allyl silane gave a higher yield and higher diastereomeric ratio than the *trans*-allyl silane (entries 1 and 2). In the case of the unprotected aniline, an imine−olefin reaction was not seen, instead iminodibenzo[*b*,*f*][1,5]diazocine **46** was formed (entry 3). Once again, imine−olefin cyclizations in the absence of urea formation gave lower yields (entries 4 and 5). Also, both pyrrolidine products (**47** and **48**) appeared to be unstable on silica gel and were therefore not obtained cleanly.

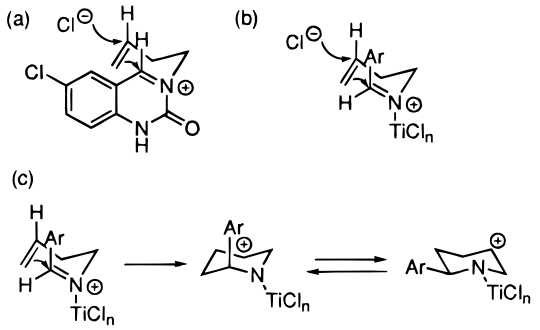
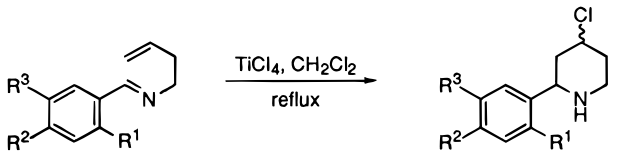


Figure 3. Comparison of possible transition structures for cyclization reactions: synchronous cyclization/trapping cases resulting from (a) carbamate activation or (b) Lewis acid activation, or (c) stepwise cyclization followed by trapping via conformationally mobile intermediates (trapping step not shown; however, see Scheme 4 for an analogous example).

Table 3. $TiCl_4$-Promoted Cyclization Reactions of Imines 27−31

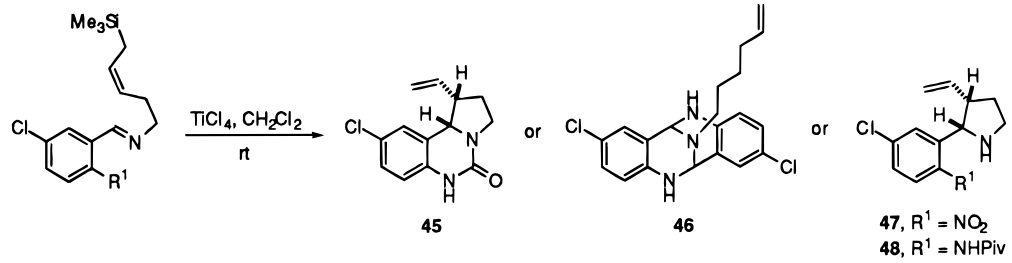


entry	imine	R_1	R_2	R_3	product	yield (%)	trans/cis[a]
1	**27**	H	H	H	**40**	25	19:1
2	**28**	H	OCH_3	H	**41**	18	9:1
3	**29**	H	NO_2	H	**42**	31	1:3
4	**30**	H	CO_2CH_3	H	**43**	52	7:3
5	**31**	NO_2	H	Cl	**44**	≤21[b]	1:19

[a] Based on ^{1}H NMR integration. [b] Product impure.

Although imine **34** underwent pseudodimerization in the presence of $TiCl_4$, it was worthy of further study because the aniline hydrogens showed no evidence of hydrogen bonding to the imine nitrogen (2H at δ 6.39 in the ^{1}H NMR). When trichloroacetic anhydride (TCAA) was used in an attempt to activate the imine to initiate diene formation, two different heterocycles were observed depending on the amount of TCAA present. When 1.1 equiv of TCAA was used, the product was not readily identified by spectroscopic methods. Instead, it was necessary to prepare imine **49** which underwent cyclization with TCAA to give a product (**50**) that was unambiguously identified by X-ray crystallography (Scheme 6). Spectral comparisons with **50** allowed for the identification of urea **52** as the product of the reaction shown in Scheme 7. When this reaction was run at lower temperatures (83 °C), it was possible to isolate imine **51** which could then be carried on to urea **52** upon heating at 130 °C. These results further support the intermediacy of an acyl iminium ion in the previously described imine-olefin cyclizations. However, in this case, the acyl iminium ion intermediate is trapped by the trichloromethyl group liberated from the amide intermediate (**51**) upon urea formation.

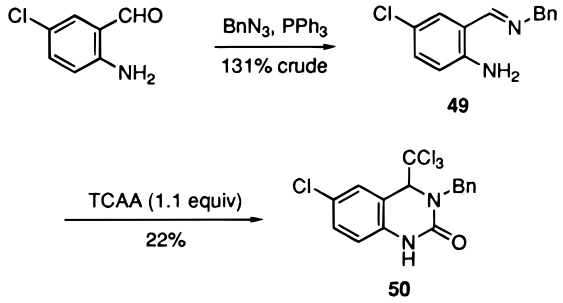
Table 4. $TiCl_4$-Promoted Cyclization Reactions of Imines 32−36



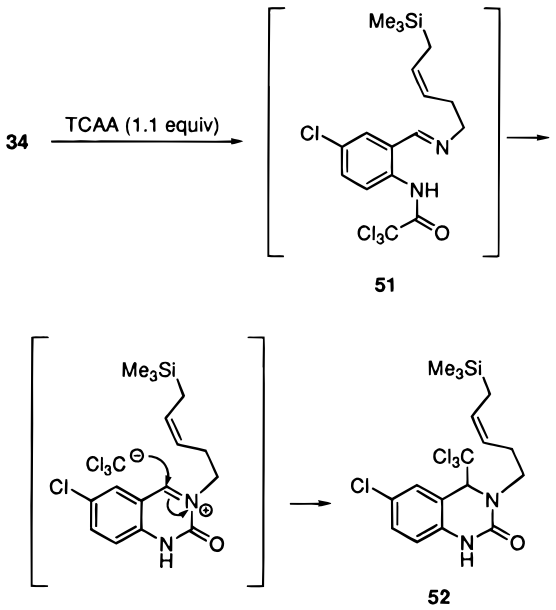
entry	imine	R_1	alkene geometry	product	yield (%)	diastereomeric ratio[a]
1	**32**	NHBoc	Z	**45**	62−75	19:1
2	**33**	NHBoc	E	**45**	55	3:1
3	**34**	NH_2	Z	**46**	39	*b*
4	**35**	NO_2	Z	**47**	≤23[c]	*d*
5	**36**	NHPiv	Z	**48**	≤31[c]	17:3

[a] Based on ^{1}H NMR integration. [b] Not applicable. [c] Product impure. [d] Not determined.

Scheme 6

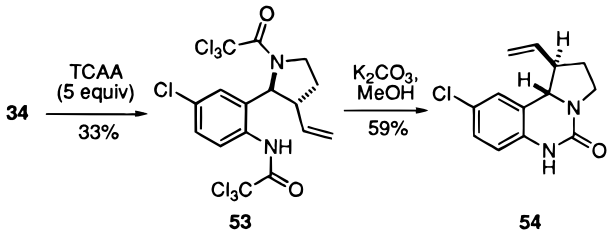


Scheme 7

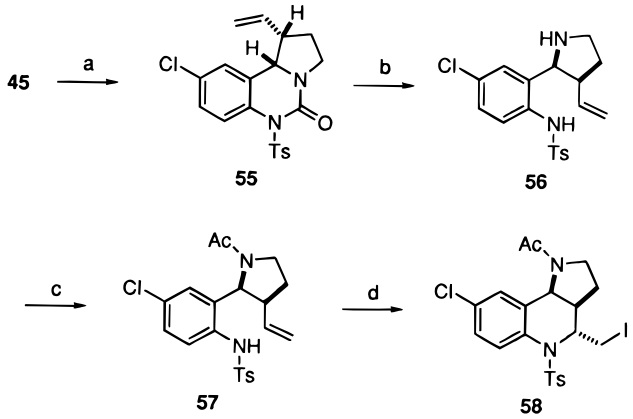


Having seen that the first equivalent of TCAA reacted with the aniline nitrogen and that higher temperatures (>83 °C) were needed for amide **51** to react further, an excess of TCAA (5 equiv) was used at room temperature in an attempt to activate the imine prior to urea formation. Apparently the excess TCAA successfully activated the imine, since imine-olefin product **53** was formed (Scheme 8). This product was identified as the trans diastereomer when basic hydrolysis led to the formation of urea **54**, previously seen as the minor product of the cyclization of imines **32** and **33** (Table 4).

Scheme 8



Scheme 9[a]

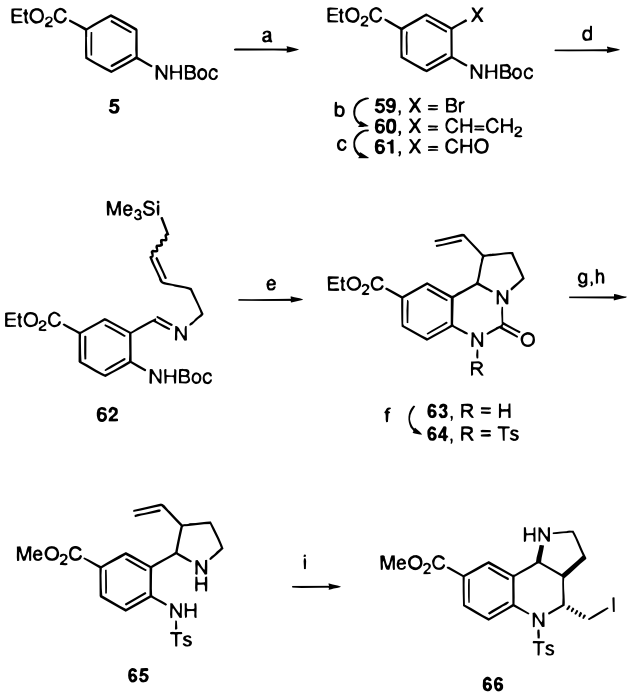


[a] Reaction conditions: (a) NaH, TsCl, 90%; (b) 50% aq NaOH, 65%; (c) AcCl, DMAP, Pyr, 85%; (d) I_2, 84%.

Application to the Synthesis of the Martinelline Ring System. Imine−olefin product **45**, obtained in up to 75% yield from imine **32**, was seen as a useful intermediate in martinelline synthesis due to the cis relationship of the pyrrolidine substituents. The urea moiety in **45** was hydrolyzed by activation with *p*-toluenesulfonyl chloride followed by NaOH treatment to give pyrrolidine **56** (Scheme 9). After acylation of the pyrrolidine nitrogen, iodoamidation gave pyrroloquinoline **58**. The tricyclic core of martinelline was thus obtained with complete control over relative stereochemistry, as established by an X-ray crystallographic analysis of pyrroloquinoline **58**.

A similar sequence was also carried out in a series including the carbomethoxy group present in the natural product (Scheme 10). Aldehyde **61** was formed from carbamate **5** in three steps and 66% overall yield. In these experiments, a ca. 2:1 mixture of *cis*- and *trans*-alkene

Scheme 10[a]



[a] Reaction conditions: (a) Br_2, HOAc, 100%; (b) *n*-Bu_3Sn-($CH{=}CH_2$), $(Ph_3P)_4Pd$, 85%; (c) O_3, then DMS, 78%; (d) **21/24**, PPh_3, 100−123% (crude); (e) $TiCl_4$, 80%; (f) NaH, TsCl, 91%; (g) 50% aq NaOH, (h) H_2SO_4, MeOH, 57% over two steps, (i) I_2, 44%.

isomers (**21/24**) was used in the synthesis of **62**. The cyclization of imine **62** gave urea **63** as an inseparable mixture of diastereomers (17:3, cis/trans). Tosylation of urea **63** gave **64**, which was subjected to basic hydrolysis conditions. Hydrolysis of the ester accompanied urea hydrolysis; thus, re-esterification was required prior to the iodoamination reaction which gave pyrroloquinoline **66** (isolated as a single diastereomer).

Summary

A variety of interesting heterocycles can be formed from the Lewis acid-mediated cyclizations of imines. In respect to the martinellines, the in situ formation of an acyl iminium ion aided in imine−olefin cyclization yield and diastereoselectivity, while the use of an allyl silane directed ring closure for pyrrolidine formation. In another key step, haloamidation gave the tricyclic core ring system. This advanced intermediate is suitably functionalized for the elongation of the C-2 side chain and further elaboration to form the martinellines.

Experimental Section

General methods have been published.[13]

Materials. Except where noted, all starting materials were purchased from Aldrich, Fluka, Fisher, Lancaster, or TCI chemical companies and used as received. The following known compounds were prepared by literature procedures: ethyl 4-(*N*-*tert*-butoxycarbonyl)aminobenzoate (**5**),[14] *N*-*tert*-butoxycarbonyl-4-chloroaniline (**6**),[15] 3-buten-1-amine (**9**),[16] *N*-*tert*-butoxycarbonylaniline,[15] 2-amino-*N*-*tert*-butoxycarbonylbenzaldehyde,[17] 2-aminobenzaldehyde.[18] Known compounds prepared by modified procedures have been included in the supplemental information: 4-[(tetrahydropyran-2-yl)oxy]-1-butyne (**16**), 5-[(tetrahydropyran-2-yl)oxy]-1-(trimethylsilyl)-2-pentyne (**17**), 5-(trimethylsilyl)-3-pentyn-1-ol (**18**), (*Z*)-5-(trimethylsilyl)-3-penten-1-ol (**19**), (*Z*)-1-methanesulfonyloxy-5-(trimethylsilyl)-3-pentene (**20**), (*E*)-5-(trimethylsilyl)-3-penten-1-ol (**22**), (*E*)-1-methanesulfonyloxy-5-(trimethylsilyl)-3-pentene (**23**), *N*-(4-chlorophenyl)-2,2-dimethylpropionamide, and *N*-(4-chloro-2-formylphenyl)-2,2-dimethylpropionamide.

2-Amino-*N*-*tert*-butoxycarbonyl-5-chlorobenzaldehyde (8). To a solution of **6**[15] (3.00 g, 13.2 mmol) in THF (20.0 mL) at −78 °C under argon was added *s*-BuLi (1.3 M in cyclohexane, 25.0 mL, 32.5 mmol) dropwise over 5 min. The reaction was stirred for 15 min at −78 °C and then at −20 °C for 3.5 h. DMF was added, and the reaction was stirred at −20 °C for 1 h. The reaction mixture was partitioned between H_2O and Et_2O (50 mL each). The layers were separated, and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (19:1) to give 1.82 g of **8** (54%) as white plates: mp 115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 9H), 7.46 (dd, J = 9.1, 2.5 Hz, 1H), 7.54 (d, J = 2.5 Hz, 1H), 8.41 (d, J = 9.1 Hz, 1H), 9.80 (s, 1H), 10.26 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 28.1, 81.2, 119.9, 122.0, 126.4, 134.8, 135.6, 140.2, 152.5, 193.6; IR (KBr) 3370, 2980, 1715 cm^{-1}; MS (CI) m/z 256 (M^+ + H), 217, 156, 127, 57; HRMS calcd for $C_{12}H_{15}NO_3Cl$ 256.0740, found 256.0754.

(2′-Amino-*N*′-*tert*-butoxycarbonyl-5′-chlorobenzylidene)-3-butenylamine (10). A mixture of **8** (0.50 g, 2.0 mmol) and **9**[16] (0.28 g, 3.9 mmol) was heated to 90 °C for 1 h. The reaction was then cooled to room temperature, and the excess amine was removed under reduced pressure to give 0.60 g (99%) of crude imine as a pale yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 9H), 2.46 (m, 2H), 3.70 (td, J = 6.6, 1.1 Hz, 2H), 5.04−5.18 (m, 2H), 5.95 (m, 1H), 7.25 (d, J = 2.5 Hz, 1H), 7.29 (dd, J = 8.9, 2.5 Hz, 1H), 8.24 (s, 1H), 8.36 (d, J = 8.9 Hz, 1H), 11.92 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.3, 35.6, 60.6, 80.1, 116.5, 119.5, 121.4, 125.8, 130.9, 132.2, 135.9, 139.3, 153.4, 162.6; IR (KBr) 2980, 1710 cm^{-1}; MS (CI) m/z 309 (M^+ + H), 253, 235, 208, 167, 57; HRMS calcd for $C_{16}H_{22}N_2O_2Cl$ 309.1370, found 309.1372.

(6*R,12*S**)-2,8-Dichloro-13-(but-3-enyl)-6,12-iminodibenzo[*b*,*f*][1,5]-5,6,11,12-tetrahydrodiazocine (12).** To a solution of **10** (0.10 g, 0.32 mmol) in chlorobenzene (3.0 mL) at 0 °C was added TMSOTf (0.10 mL, 0.52 mmol) dropwise. The reaction was allowed to warm to room temperature over 1 h, and then triethylamine (0.09 mL, 0.65 mmol) was added. After 4 h, the reaction was quenched with saturated aqueous NH_4Cl (0.5 mL). The reaction was diluted with CH_2Cl_2 and then washed with saturated aqueous NaCl (5 mL), dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (4:1) to give 47.9 mg (81%) of a white foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (m, 2H), 2.54 (m, 1H), 2.75 (m, 1H), 4.57 (br s, 1H), 4.90 (s, 2H), 5.01−5.11 (m, 2H), 5.81 (m, 1H), 6.52 (d, J = 8.5 Hz, 2H), 7.00 (dd, J = 8.5, 2.4 Hz, 2H), 7.04 (d, J = 2.3 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 32.2, 49.3, 65.5, 116.2, 117.4, 123.3, 125.1, 127.7, 128.6, 135.9, 139.2; IR (film) 3390, 2930, 2840 cm^{-1}; MS (CI) m/z 346 (M^+ + H), 304, 290, 209, 72; HRMS calcd for $C_{18}H_{18}Cl_2N_3$ 346.0878, found 346.0882.

$TiCl_4$/Ti(OiPr)$_4$-Promoted Imine−Olefin Cyclization of 10. To a solution of Ti(OiPr)$_4$ (1.2 mL, 4.0 mmol) in CH_2Cl_2 (45 mL) at room temperature was added $TiCl_4$ (0.44 mL, 4.0 mmol). After 10 min, the solution was cooled to −78 °C. Then,

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(16) Sato, T.; Nakamura, N.; Ikeda, K.; Okada, M.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2399−2407.
(17) Muchowski, J. M.; Venuti, M. C. *J. Org. Chem.* **1980**, *45*, 4798−4801.
(18) Horner, J. K.; Henry, D. W. *J. Med. Chem.* **1968**, *11*, 946−949.

a solution of **10** (0.25 g, 0.81 mmol) in CH_2Cl_2 (5 mL) was added, and the reaction was warmed to room temperature. After 6 h, the reaction was quenched with 10% aqueous NaOH (50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were then dried (Na_2SO_4), decanted, and concentrated under reduced pressure. Repeated silica gel chromatography with EtOAc/hexanes/2% Et_2NH (30/19/1) gave 76 mg (34%) of **13** and 29 mg (13%) of **14**.

(10*R,11a*S**)-2,10-Dichloro-5,8,9,10,11,11a-hexahydropyrido[1,2-*c*]quinazolin-6-one (13):** yellow solid; mp 240−241.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86 (qd, J = 12.3, 4.5 Hz, 1H), 1.97 (dd, J = 4.5, 12.0 Hz, 1H), 2.23 (m, 1H), 2.41 (m, 1H), 2.69 (td, J = 13.6, 2.5 Hz, 1H), 4.11 (tt, J = 11.8, 4.4 Hz, 1H), 4.47 (dd, J = 11.8, 2.3 Hz, 1H), 4.68 (dq, J = 13.9, 2.3 Hz, 1H), 6.66 (d, J = 8.5 Hz, 1H), 7.02 (d, J = 2.1 Hz, 1H), 7.14 (dd, J = 8.5, 2.2 Hz, 1H), 8.23 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 35.4, 43.2, 44.2, 55.7, 57.5, 115.3, 120.9, 125.4, 127.1, 128.7, 134.3, 152.3; IR (KBr) 3180, 2280, 1655 cm^{-1}; MS (EI) m/z 270 (M^+ + H), 235, 181, 55; HRMS calcd for $C_{12}H_{13}Cl_2N_2O$ 271.0405, found 271.0395. Anal. Calcd for $C_{12}H_{12}Cl_2N_2O$: C, 53.16; H, 4.46; N, 10.33. Found: C, 52.99; H, 4.20; N, 10.00.

(10*R,11a*R**)-2,10-Dichloro-5,8,9,10,11,11a-hexahydropyrido[1,2-*c*]quinazolin-6-one (14):** white solid; mp 242.5−243 °C; ^{1}H NMR (400 MHz, *d*-DMSO) δ 1.79 (d, J = 14.5 Hz, 1H), 1.96 (m, 1H), 2.08 (m, 2H), 3.02 (td, J = 12.7, 2.2 Hz, 1H), 4.21 (dd, J = 13.6, 2.8 Hz, 1H), 4.79 (br s, 1H), 4.86 (dd, J = 10.0, 4.1 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 7.17 (m, 2H), 9.49 (s, 1H); ^{13}C NMR (100.6 MHz, *d*-acetone) δ 31.6, 37.6, 40.1, 51.9, 58.5, 115.0, 121.7, 124.8, 125.3, 128.1, 135.7, 151.6; IR (KBr) 3180, 1660 cm^{-1}; MS (CI) m/z 271 (M^+ + H), 235, 181, 74; HRMS calcd for $C_{12}H_{13}Cl_2N_2O$ 271.0405, found 271.0379.

(*Z*)-5-Azido-1-(trimethylsilyl)-2-pentene (21). To a solution of **20**[11] (3.20 g, 13.5 mmol) in DMF (50.0 mL) at room temperature was added sodium azide (3.52 g, 54.1 mmol). The reaction was heated to 110 °C over 45 min. The reaction was cooled to room temperature and partitioned between H_2O and Et_2O (50 mL each). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with saturated aqueous NaCl (100 mL), dried (Na_2SO_4), decanted, and concentrated under reduced pressure at room temperature. The crude product was purified by silica gel chromatography with pentane/Et_2O (9:1) to give 2.25 g (91%) of a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 9H), 1.50 (d, J = 8.9 Hz, 2H), 2.31 (m, 2H), 3.26 (d, J = 7.2 Hz, 2H), 5.25 (m, 1H), 5.55 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ −1.8, 18.8, 26.8, 51.2, 122.2, 128.9; IR (film) 3005, 2080 cm^{-1}; MS (CI) m/z 184 (M^+ + H), 156, 90, 73; HRMS calcd for $C_8H_{18}N_3Si$ 184.1270, found 184.1283.

(*E*)-5-Azido-1-(trimethylsilyl)-2-pentene (24). To a solution of **23**[12] (0.65 g, 2.7 mmol) in DMF (10 mL) at room temperature was added sodium azide (0.71 g, 11 mmol). The reaction was heated to 110 °C over 1 h. The reaction was cooled to room temperature and partitioned between H_2O and Et_2O (10 mL each). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with saturated aqueous NaCl (20 mL), dried (Na_2SO_4), decanted, and concentrated under reduced pressure at room temperature. The crude product was purified by silica gel chromatography with pentane/Et_2O (19:1) to give 0.45 g (91%) of a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 9H), 1.44 (d, J = 8.2 Hz, 2H), 2.28 (m, 2H), 3.24 (t, J = 7.0 Hz, 2H), 5.22 (m, 1H), 5.54 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −2.1, 22.9, 32.3, 51.5, 123.8, 130.0; IR (film) 2940, 2080 cm^{-1}; MS (CI) m/z 184 (M^+ + H), 156, 90, 73; HRMS calcd for $C_8H_{18}N_3Si$ 184.1270, found 184.1252.

(*E*)-3-Penten-1-amine (15). Prepared based on literature procedure.[16] The crude product was purified by distillation: bp 93−95 °C; colorless liquid, 3.25 g (62%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (m, 3H), 1.99 (q, J = 6.7 Hz, 2H), 2.57 (t, J = 6.6 Hz, 2H), 4.61 (s, 2H), 5.23 (m, 2H), 5.39 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 17.7, 36.5, 41.4, 127.0, 128.3; IR (film) 3400 (br), 2920 cm^{-1}; MS (CI) m/z 86 (M^+ + H), 69; HRMS calcd for $C_5H_{12}N$ 86.0970, found 86.0963.

(2′-Amino-*N*′-*tert*-butoxycarbonyl-5′-chlorobenzylidene)-*trans*-3-pentenylamine (25). A mixture of **8** (0.50 g, 2.0 mmol) and **15** (0.33 g, 3.9 mmol) was heated to 90 °C for 1.5 h. The reaction was then cooled to room temperature, and the excess amine was removed under reduced pressure to give 0.63 g of crude imine as a pale yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (s, 9H), 1.66 (d, J = 4.9 Hz, 3H), 2.38 (q, J = 6.5 Hz, 2H), 3.61 (m, 2H), 5.52 (m, 2H), 7.23 (d, J = 2.5 Hz, 1H), 7.28 (dd, J = 9.0, 2.5 Hz, 1H), 8.21 (s, 1H), 8.36 (d, J = 9.0 Hz, 1H), 11.91 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.0, 28.3, 34.2, 61.2, 80.1, 119.5, 121.5, 125.7, 127.1, 128.2, 130.8, 132.2, 139.3, 152.4, 162.5; IR (KBr) 2970, 1705, 1635 cm^{-1}; MS (CI) m/z 323 (M^+ + H), 267, 249, 167, 57; HRMS calcd for $C_{17}H_{24}N_2O_2Cl$ 323.1526, found 323.1509.

General Procedure for the Synthesis of Imines with Amine 9. A mixture of the aldehyde (0.10−0.50 g) and **9** (1.5 equiv) was heated to 90 °C for 2 h. The reaction was then cooled to room temperature, and the excess amine was removed under reduced pressure to give the crude imine, which was used without further purification.

3-Butenyl-(2′-amino-*N*′-*tert*-butoxycarbonylbenzylidene)amine (26). Prepared by the general procedure: yellow oil, 0.12 g; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (s, 9H), 2.47 (m, 2H), 3.68 (m, 2H), 5.05−5.18 (m, 2H), 5.96 (m, 1H), 7.00 (m, 1H), 7.27 (dd, J = 7.6, 1.5 Hz, 1H), 7.34 (m, 1H), 8.31 (s, 1H), 8.39 (d, J = 8.4 Hz, 1H), 12.01 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 28.4, 35.4, 60.6, 79.7, 116.3, 118.0, 120.2, 120.9, 131.2, 133.0, 136.2, 140.8, 153.6, 163.9; IR (film) 3400 (br) 3060, 1710, 1625 cm^{-1}; MS (CI) m/z 275 (M^+ + H), 219, 201, 174, 133, 57; HRMS calcd for $C_{16}H_{23}N_2O_2$ 275.1760, found 275.1765.

(*N*′-*tert*-Butoxycarbonyl-2′-amino-5′-chlorobenzylidene)-[(*Z*)-5-(trimethylsilyl)-3-pentenyl]amine (32). A solution of **21** (0.51 g, 2.8 mmol) and triphenylphosphine (0.76 g, 2.9 mmol) in THF (5.0 mL) was stirred at room temperature for 2 h. Next, **8** (0.71 g, 2.8 mmol) was added, and the reaction was heated at reflux for 16 h. The reaction was then cooled to room temperature, concentrated under reduced pressure, triturated with ether, filtered through Florisil, and concentrated under reduced pressure to give 1.12 g of a crude yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 9H), 1.52 (s, 1H), 2.39 (q, J = 6.8 Hz, 2H), 3.63 (t, J = 6.4 Hz, 2H), 5.42 (m, 1H), 5.49 (m, 1H), 7.24 (d, J = 2.4 Hz, 1H), 7.29 (dd, J = 8.9, 2.4 Hz, 1H), 8.23 (s, 1H), 8.37 (d, J = 8.9 Hz, 1H), 12.00 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −1.86, 18.6, 28.2, 28.6, 61.0, 79.8, 119.3, 121.3, 123.8, 125.6, 127.4, 130.7, 132.1, 139.3, 153.3, 162.3; IR (film) 2990, 1710, 1625 cm^{-1}; MS (CI) m/z 395 (M^+ + H), 339, 321, 167, 73, 57; HRMS calcd for $C_{20}H_{32}ClN_2O_2Si$ 395.1922, found 395.1939.

(*N*′-*tert*-Butoxycarbonyl-2′-amino-5′-chlorobenzylidene)-[(*E*)-5-(trimethylsilyl)-3-pentenyl]amine (33). A solution of **24** (0.25 g, 1.4 mmol) and triphenylphosphine (0.36 g, 1.4 mmol) in THF (3.0 mL) was stirred at room temperature for 2.5 h. Next, **8** was added, and the reaction was heated at reflux for 18 h. The reaction was then cooled to room temperature, concentrated under reduced pressure, triturated with ether, filtered through Florisil, and concentrated under reduced pressure to give 0.57 g of a crude yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.03 (s, 9H), 1.44 (d, J = 8.1 Hz, 2H), 1.56 (s, 9H), 2.43 (q, J = 6.7 Hz, 2H), 3.64 (t, J = 6.7 Hz, 2H), 5.31 (m, 1H), 5.52 (m, 1H), 7.32 (m, 1H), 8.23 (s, 1H), 8.39 (d, J = 9.0 Hz, 1H), 11.98 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −2.1, 22.8, 28.2, 34.4, 61.8, 80.0, 119.5, 121.5, 125.4, 125.7, 128.7, 130.8, 132.1, 139.3, 153.4, 162.4; IR (film) 2960, 1710, 1630 cm^{-1}; MS (CI) m/z 395 (M^+ + H), 339, 263; HRMS calcd for $C_{20}H_{32}ClN_2O_2Si$ 395.1921, found 395.1949.

(2′-Amino-5′-chlorobenzylidene)-[(*Z*)-5-(trimethylsilyl)-3-pentenyl]amine (34). A solution of **21** (1.41 g, 7.71 mmol) and triphenylphosphine (2.02 g, 7.71 mmol) in THF (50 mL) was stirred at room temperature for 4 h. Next, 2-amino-5-chlorobenzaldehyde[18] was added and the reaction was heated at reflux for 16 h. The reaction was then cooled to room

temperature, concentrated under reduced pressure, triturated with ether, filtered through Florisil, and concentrated under reduced pressure to give 3.09 g of a crude dark yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H), 1.49 (d, J = 8.4 Hz, 2H), 2.37 (q, J = 7.1 Hz, 2H), 3.58 (td, J = 7.1, 1.0 Hz, 2H), 5.32 (m, 1H), 5.49 (m, 1H), 6.39 (br s, 2H), 6.59 (d, J = 8.6 Hz, 1H), 7.07 (dd, J = 8.6, 2.4 Hz, 1H), 7.16 (d, J = 2.4 Hz, 1H), 8.25 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −1.8, 18.6, 29.1, 61.5, 116.7, 124.2, 127.2, 128.4, 128.5, 130.3, 132.1, 146.9, 162.5; IR (film) 3460, 3250, 3005, 1630 cm^{-1}; MS (CI) m/z 295 (M^+ + H), 279, 263, 167, 73; HRMS calcd for $C_{15}H_{24}ClN_2Si$ 295.1397, found 295.1410.

$TiCl_4$-Promoted Imine−Olefin Cyclization of 10. To a solution of **10** (0.10 g, 0.32 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added $TiCl_4$ (0.14 mL, 1.3 mmol). The reaction was allowed to warm slowly to room temperature. After 24 h, the reaction was quenched with 10% aqueous NaOH (5 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (2:1 to 1:3) to give 31.1 mg (35%) of **13** and 7.4 mg (13%) of **12**.

(6*R,12*S**)-2,8-Dichloro-13-((*E*)-pent-3-enyl)-6,12-iminodibenzo[*b*,*f*][1,5]-5,6,11,12-tetrahydrodiazocine (37).** To a solution of **25** (0.10 g, 0.31 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C was added TMSOTf (0.09 mL, 0.47 mmol). The reaction was allowed to warm slowly to room temperature. After 3 h, the reaction was quenched with 10% aqueous NaOH (5 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (3:1) to give 36 mg (64%) of a tan foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (d, J = 5.9 Hz, 3H), 2.29 (m, 2H), 2.47 (m, 1H), 2.69 (m, 1H), 4.57 (br s, 2H), 4.89 (s, 2H), 5.40 (m, 1H), 5.48 (m, 1H), 6.51 (d, J = 8.5 Hz, 2H), 6.99 (dd, J = 8.5, 2.3 Hz, 2H), 7.03 (d, J = 2.3 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 17.9, 31.0, 49.9, 65.5, 117.3, 123.2, 125.1, 126.7, 127.6, 128.2, 128.5, 139.2; IR (KBr) 3390, 2920, 1600 cm^{-1}; MS (CI) m/z 360 (M^+ + H), 49; HRMS calcd for $C_{19}H_{20}Cl_2N_3$ 360.1034, found 360.1023. Anal. Calcd for $C_{19}H_{19}Cl_2N_3$: C, 63.34; H, 5.32; N, 11.66. Found: C, 62.88; H, 5.59; N, 11.15.

(10*R,11*R**,11a*S**)-2,10-Dichloro-5,8,9,10,11,11a-hexahydro-11-methylpyrido[1,2-*c*]quinazolin-6-one (38).** To a solution of **25** (0.10 g, 0.31 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C was added $TiCl_4$ (0.14 mL, 1.3 mmol). The reaction was allowed to warm slowly to room temperature. After 24 h, the reaction was quenched with 10% aqueous NaOH (5 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (2:1) to give 23 mg (40%) of **38** as a tan foam and 26 mg (30%) of **37** a tan solid. An analytical sample of **38** was crystallized from EtOH/CH_3CN: colorless prisms; mp 245−246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, J = 6.5 Hz, 3H), 1.91 (m, 1H), 2.13 (qd, J = 12.6, 4.7 Hz, 1H), 2.25 (m, 1H), 2.77 (td, J = 13.1, 2.6 Hz, 1H), 3.80 (td, J = 10.6, 4.8 Hz, 1H), 3.94 (d, J = 10.5 Hz, 1H), 4.51 (m, 1H), 6.69 (d, J = 8.5 Hz, 1H), 7.02 (d, 2.0 Hz, 1H), 7.19 (dd, J = 8.5, 2.0 Hz, 1H), 7.95 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.4, 35.3, 44.1, 44.3, 63.6, 64.1, 115.4, 119.7, 126.4, 127.6, 128.8, 135.1, 154.0; IR (KBr) 3180, 3070, 1645 cm^{-1}; MS (CI) m/z 285 (M^+ + H), 249, 181, 85; Anal. Calcd for $C_{13}H_{14}Cl_2N_2O$: C, 54.75; H, 4.95; N, 9.82. Found: C, 55.02; H, 5.04; N, 9.56. X-ray data for this compound are available in the Supporting Information.

General Procedure for Imine−Olefin Cyclizations of Imines. To a solution of the imine (0.10 g) in CH_2Cl_2 (10 mL) at room temperature was added $TiCl_4$ (5.0 equiv). The reaction was heated at reflux for 72 h and then cooled to room temperature. The reaction was quenched by slow addition of 10% aqueous NaOH (10 mL) and was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were then dried (Na_2SO_4), decanted, and concentrated under reduced pressure to give cyclized product after silica gel chromatography.

(10*R,11a*S**)- and (10*R**,11a*R**)-2-Chloro-5,8,9,10,11,11a-hexahydropyrido[1,2-*c*]quinazolin-6-one (39).** Prepared by the general procedure except the reaction was run for 24 h. The crude product was purified by silica gel chromatography with EtOAc/hexanes (1:1) to give 0.056 g (65%) of a white solid as a 19:1 mixture of diastereomers, based on ^{1}H NMR integration, mp 214−214.5 °C dec. Major isomer, (10*R**,11a*S**)-**39**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (qd, J = 12.4, 4.5 Hz, 1H), 1.98 (q, J = 12.4 Hz, 1H), 2.22 (m, 1H), 2.42 (m, 1H), 2.70 (td, J = 13.5, 2.3 Hz, 1H), 4.13 (tt, J = 11.8, 4.3 Hz, 1H), 4.51 (dd, J = 11.7, 2.1 Hz, 1H), 4.69 (dq, J = 13.7, 2.1 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 7.5 Hz, 1H), 7.18 (t, J = 7.7 Hz, 1H), 7.68 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 35.5, 43.2, 44.4, 56.1, 57.9, 114.0, 119.4, 122.2, 125.3, 128.7, 135.6, 152.6; IR (film) 3165, 3015, 1640 cm^{-1}; MS (CI) m/z 237 (M^+ + H), 201, 147; HRMS calcd for $C_{12}H_{14}ClN_2O$ 237.0794, found 237.0812. Minor isomer, (10*R**,11a*R**)-**39** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (m, 1H), 3.27 (m, 1H), 5.04 (m, 1H).

(2*R,4*S**)- and (2*R**,4*R**)-4-Chloro-2-phenylpiperidine (40).** Prepared by the general procedure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.030 g (25%) of a pale yellow solid as a 94:6 mixture of diastereomers, based on ^{1}H NMR integration, mp 58−59 °C. Major isomer, (2*R**,4*S**)-**40**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (br s, 1H), 1.97 (m, 2H), 2.07 (m, 2H), 3.02 (dq, J = 11.9, 2.6 Hz, 1H), 3.32 (td, J = 11.9, 2.7 Hz, 1H), 4.16 (dd, J = 10.9, 2.5 Hz, 1H), 4.62 (t, J = 3.0 Hz, 1H), 7.25 (m, 1H), 7.32 (m, 2H), 7.37 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 33.5, 41.3, 42.1, 55.3, 58.2, 126.7, 127.3, 128.5, 144.0; IR (film) 3440 (br), 3240, 2930 cm^{-1}; MS (CI) m/z 196 (M^+ + H), 160, 131, 118, 91; HRMS calcd for $C_{11}H_{15}ClN$ 195.0893, found 196.0909. Minor isomer, (2*R**,4*R**)-**40** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (m, 1H), 2.34 (m, 1H), 2.82 (m, 1H), 3.22 (m, 1H), 3.61 (m, 1H), 4.03 (m, 1H).

(2*R,4*S**)- and (2*R**,4*R**)-4-Chloro-2-(4′-methoxyphenyl)piperidine (41).** Prepared by the general procedure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.022 g (18%) of a pale yellow solid as a 9:1 mixture of diastereomers, based on ^{1}H NMR integration, mp 71−74 °C. Major isomer, (2*R**,4*S**)-**41**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75−2.34 (m, 5H), 3.30 (dt, J = 11.7, 2.7 Hz, 1H), 3.32 (td, J = 11.7, 2.7 Hz, 1H), 3.79 (s, 3H), 4.11 (dd, J = 10.2, 2.7 Hz, 1H), 4.61 (t, J = 2.7 Hz, 1H), 6.85 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 33.3, 41.3, 41.9, 54.7, 55.3, 58.1, 113.8, 127.7, 127.9, 158.9; IR (KBr) 3420 (br), 3305, 2935 cm^{-1}; MS (CI) m/z 226 (M^+ + H), 190, 161; HRMS calcd for $C_{12}H_{17}ClNO$ 226.0998, found 226.0985. Minor isomer, (2*R**,4*R**)-**41** (diagnostic peaks only): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.21 (m, 1H), 3.58 (m, 1H), 4.00 (m, 1H).

(2*R,4*S**)- and (2*R**,4*R**)-4-Chloro-2-(4′-nitrophenyl)-piperidine (42).** Prepared by the general procedure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.037 g (31%) of a light orange solid as a 3:1 mixture of diastereomers, based on ^{1}H NMR integration: mp 77−80 °C. Major isomer, (2*R**,4*S**)-**42**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77 (q, J = 11.8 Hz, 1H), 1.85 (m, 2H), 2.23 (m, 1H), 2.31 (m, 1H), 2.83 (td, J = 12.3, 2.4 Hz, 1H), 3.28 (dq, J = 12.2, 2.7 Hz, 1H), 3.79 (dd, J = 11.3, 2.1 Hz, 1H), 4.02 (m, 1H), 7.56 (m, 2H), 8.18 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 37.0, 45.6, 46.6, 57.4, 61.3, 124.3, 127.9, 151.1; IR (film) 3300 cm^{-1}; MS (CI) m/z 241 (M^+ + H), 205; HRMS calcd for $C_{11}H_{14}ClN_2O_2$ 241.0744, found 241.0753. Minor isomer, (2*R**,4*R**)-**42** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (m, 1H), 2.07 (m, 2H), 3.06 (m, 1H), 3.36 (dd, J = 11.9, 2.8 Hz, 1H), 4.30 (dd, J = 11.1, 2.1 Hz, 1H), 4.62 (t, J = 2.8 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 33.6, 41.4, 42.7, 55.3, 57.9, 124.2, 128.0, 147.7, 152.1.

(2*R,4*S**)- and (2*R**,4*R**)-4-Chloro-2-(4′-carbomethoxyphenyl)piperidine (43).** Prepared by the general procedure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.062 g (52%) of a light orange solid as a 7:3 mixture of diastereomers, based on ^{1}H NMR integration, mp 58.5−61 °C. Major isomer, (2*R**,4*S**)-**43**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (m, 2H), 1.95 (m, 2H),

2.06 (m, 2H), 3.03 (m, 1H), 3.32 (td, J = 11.9, 2.7 Hz, 1H), 3.90 (s, 3H), 4.22 (dd, J = 11.0, 2.2 Hz, 1H), 4.61 (t, J = 2.9 Hz, 1H), 7.44 (m, 2H), 7.99 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 33.3, 41.0, 42.1, 51.9, 55.0, 57.8, 126.6, 129.1, 129.7, 149.3, 166.8; IR (film) 3400 (br), 3300, 2930, 1695 cm^{-1}; MS (CI) m/z 254 (M^+ + H), 218; HRMS calcd for $C_{13}H_{17}ClNO_2$ 254.0948, found 254.0948. Minor isomer, (2*R**,4*R**)-**43** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (m, 1H), 2.30 (m, 1H), 2.81 (td, J = 12.3, 2.4 Hz, 1H), 3.26 (m, 1H), 3.70 (dd, J = 11.2, 2.1 Hz, 1H), 4.01 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 36.7, 45.1, 46.2, 52.0, 57.3, 61.2, 126.5, 129.3, 129.8, 148.4, 166.7.

(2*R,4*S**)- and (2*R**,4*R**)-4-Chloro-2-(5′-chloro-2′-nitrophenyl)piperidine (44).** Prepared by the general procedure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.025 g (21%) of a yellow oil as an approximately 9:1 mixture of product to impurity which may include the minor diastereomer, based on ^{1}H NMR integration: ^{1}H NMR (500 MHz, $CDCl_3$, minor impurities present) δ 1.77 (q, J = 11.7 Hz, 1H), 1.89 (qd, J = 12.4, 4.4 Hz, 1H), 2.24 (m, 2H), 2.50 (m, 1H), 2.82 (td, J = 12.3, 2.3 Hz, 1H), 3.25 (m, 1H), 4.01 (m, 1H), 4.17 (dd, J = 11.0, 2.2 Hz, 1H), 7.37 (dd, J = 8.7, 2.2 Hz, 1H), 7.79 (d, J = 8.7 Hz, 1H), 7.92 (d, J = 2.2 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 36.4, 44.0, 46.1, 55.7, 56.4, 125.8, 128.5, 129.1, 139.6, 140.0, 147.0; IR (film) 3300, 3080 cm^{-1}; MS (CI) m/z 275 (M^+ + H); HRMS calcd for $C_{11}H_{13}Cl_2N_2O_2$ 275.0354, found 275.0333.

(1*R,10b*R**)-9-Chloro-1-ethenyl-2,3,6,10b-tetrahydro-1*H*-pyrrolo[1,2-*c*]quinazolin-5-one (45).** To a solution of **32** (0.50 g, ca. 1.3 mmol) in CH_2Cl_2 (50 mL) at room temperature was added $TiCl_4$ (0.70 mL, 6.4 mmol). The reaction was quenched after 18.5 h with 10% aqueous NaOH (50 mL) and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.23 g (75%) of a pale yellow solid as a 19:1 mixture of diastereomers, based on ^{1}H NMR. This solid was crystallized from acetone/H_2O or CH_2Cl_2/CH_3CN to get an analytical sample of **45**. Colorless or light yellow prisms, respectively: mp 213.5−215 °C (after crystallization from CH_2Cl_2/CH_3CN); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (ddd, J = 12.6, 8.0, 1.3 Hz, 1H), 2.23 (m, 1H), 3.24 (m, 1H), 3.57 (m, 1H), 3.75 (m, 1H), 4.81 (d, J = 4.6 Hz, 1H), 5.07−5.19 (m, 2H), 5.59 (m, 1H), 6.61 (d, J = 8.5 Hz, 1H), 6.94 (s, 1H), 7.13 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 29.4, 43.0, 45.6, 61.4, 115.3, 117.5, 119.8, 126.4, 126.7, 128.1, 135.6, 136.3, 153.1; IR (KBr) 3270, 3065 cm^{-1}; MS (CI) m/z 249 (M^+ + H), 194, 165. Anal. Calcd for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.82; H, 5.40; N, 11.24. X-ray data for this compound are available in the Supporting Information.

(6*R,12*S**)-2,8-Dichloro-13-(pent-4-enyl)-6,12-iminodibenzo[*b*,*f*][1,5]-5,6,11,12-tetrahydrodiazocine (46).** To a solution of **34** (0.25 g, ca. 0.62 mmol) in CH_2Cl_2 at room temperature was added $TiCl_4$ (0.34 mL, 3.1 mmol). The reaction was quenched with 10% aqueous NaOH (10 mL) after 16 h and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (4:1) to give 43.4 mg (39%) of a white foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 (m, 2H), 2.09 (dd, J = 14.2, 7.2 Hz, 2H), 2.46 (m, 1H), 2.67 (m, 1H), 4.56 (br s, 2H), 4.87 (s, 2H), 4.94−5.03 (m, 2H), 5.79 (m, 1H), 6.51 (d, J = 8.5 Hz, 2H), 6.99 (dd, J = 8.5, 2.4 Hz, 2H), 7.03 (d, J = 2.3 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.8, 31.3, 49.3, 65.5, 114.9, 117.3, 123.2, 125.2, 127.6, 128.5, 138.1, 139.3; IR (film) 3400, 2930, 2850 cm^{-1}; MS (CI) m/z 360 (M^+ + H), 304, 290, 206, 84; HRMS calcd for $C_{19}H_{20}Cl_2N_3$ 360.1034, found 360.1014. Anal. Calcd for $C_{19}H_{19}Cl_2N_3$: C, 63.34; H, 5.32; N, 11.66. Found: C, 63.32; H, 4.87; N, 11.28.

(2*R,3*R**)- and (2*R**,3*S**)-2-(5′-Chloro-2′-nitrophenyl)-3-ethenylpyrrolidine (47).** To a solution of **35** (0.20 g, ca. 0.54 mmol) in CH_2Cl_2 (20 mL) was added $TiCl_4$ (0.27 mL, 2.5 mmol). The reaction was quenched after 24 h with 10% aqueous NaOH (20 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 33 mg (23%) of a brown oil as a 19:1 mixture of product to impurity which may include the minor diastereomer, based on ^{1}H NMR integration: ^{1}H NMR (300 MHz, $CDCl_3$, minor impurities present) δ 1.80 (m, 1H), 2.05 (m, 1H), 2.16 (br s, 1H), 2.57 (m, 1H), 3.21 (m, 2H), 4.68 (d, J = 7.0 Hz, 1H), 4.94 (m, 1H), 4.99 (m, 1H), 5.81 (m, 1H), 7.31 (dd, J = 8.7, 2.4 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.87 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 32.2, 46.0, 52.7, 62.0, 115.6, 125.7, 127.6, 129.1, 138.6 (2 carbons), 139.3, 141.7; IR (film) 3060 cm^{-1}; MS (CI) m/z 253 (M^+ + H), 239; HRMS calcd for $C_{12}H_{14}ClN_2O_2$ 253.0744, found 253.0766. Minor isomer (diagnostic peaks only): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 (m, 2H), 5.20 (m, 1H), 7.12 (m, 1H), 7.47 (m, 1H).

(2′*R,3′*R**)- and (2′*R**,3′*S**)-*N*-[4′-Chloro-2′-(3″-ethenylpyrrolidin-2″-yl)phenyl]-2,2-dimethylpropionamide (48).** To a solution of **36** (0.10 g, ca. 0.23 mmol) in CH_2Cl_2 (10 mL) was added $TiCl_4$ (0.15 mL, 1.4 mmol). The reaction was heated at reflux for 24 h, then quenched with 10% aqueous NaOH (10 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 22 mg (31%) of a brown oil as a 17:3 mixture of diastereomers, based on ^{1}H NMR integration. Major isomer, (2′*R**,3′*R**)-**48**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 1.90 (m, 1H), 2.18 (m, 1H), 3.15 (dd, J = 13.3, 6.4 Hz, 1H), 3.68 (td, J = 9.3, 2.8 Hz, 1H), 3.84 (m, 1H), 4.89 (d, J = 4.8 Hz, 1H), 5.06 (d, J = 10.4 Hz, 1H), 5.13 (d, J = 16.6 Hz, 1H), 5.73 (m, 1H), 6.79 (m, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.05 (dd, J = 8.4, 2.5 Hz, 1H). Minor isomer, (2′*R**,3′*S**)-**48** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.68 (m, 1H), 3.04 (m, 1H), 3.63 (m, 1H), 4.12 (m, 1H), 4.40 (d, J = 8.6 Hz, 1H), 5.22 (d, J = 10.2 Hz, 1H), 5.36 (d, J = 17.2 Hz, 1H), 5.96 (m, 1H), 7.01 (s, 1H), 7.12 (m, 1H), 7.18 (m, 1H). This compound was not characterized further.

(2*R,3*S**)-2-(5′-Chloro-2′-(2,2,2-trichloroacetyl)aminophenyl)-1-(2,2,2-trichloroacetyl)-3-ethenylpyrrolidine (53).** To a solution of **34** (0.10 g, ca. 0.30 mmol) in CH_3CN (5.0 mL) was added trichloroacetic anhydride (0.27 mL, 1.5 mmol). After 16.5 h, the reaction mixture was diluted with Et_2O (15 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 5 mL). The organic layer was dried (Na_2SO_4), decanted, and concentrated under reduced pressure. Silica gel chromatography with hexanes/EtOAc (15:1) gave impure product (67 mg) which was crystallized from acetone/hexane to give 50 mg (33%) of waxy colorless prisms: mp 200.5−202 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.98 (m, 1H), 2.36 (m, 1H0, 3.04 (m, 1H), 3.95 (td, J = 11.4, 5.4 Hz, 1H), 4.52 (ddd, J = 11.4, 7.2, 1.8 Hz, 1H), 4.84 (d, J = 8.1 Hz, 1H), 5.00−5.09 (m, 2H), 5.72 (m, 1H), 7.27 (d, J = 2.4 Hz, 1H), 7.35 (dd, J = 8.4, 2.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 9.48 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 32.3, 50.2, 51.1, 63.3, 92.6, 92.7, 117.6, 126.6, 127.4, 129.0, 133.2, 133.3, 135.3, 135.9, 160.1, 160.6; IR (KBr) 3310 (br), 2970, 1700, 1650 cm^{-1}; MS (CI) m/z 518 (M^+ + NH_4), 511 (M^+ + H), 479, 367, 117, 96; HRMS calcd for $C_{16}H_{13}Cl_7N_2O_2$ 510.8875, found 510.8862.

(1*R,10b*S**)-9-Chloro-1-ethenyl-2,3,6,10b-tetrahydro-1*H*-pyrrolo[1,2-*c*]quinazolin-5-one (54).** To a solution of **53** (0.050 g, 0.097 mmol) in MeOH (3 mL) was added a solution of K_2CO_3 (0.5 g, 3.6 mmol) in H_2O (2 mL). The reaction was heated at reflux for 20 h, then cooled to room temperature and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 14 mg (59%) of light yellow flakes: mp 213−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (m, 1H), 2.21 (m, 1H), 2.97 (m, 1H), 3.63 (dd, J = 9.7, 5.2 Hz, 1H), 4.43 (d, J = 9.6 Hz, 1H), 5.31 (d, J = 10.3 Hz, 1H), 5.38 (d, J = 17.1 Hz, 1H), 5.95 (m, 1H), 6.69 (d, J = 8.5 Hz, 1H), 7.12 (dd, J = 8.5, 1.7 Hz, 1H), 7.35 (d, J = 1.2 Hz, 1H), 7.90 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 30.9, 43.5, 49.8, 60.3, 114.8, 117.9, 123.2, 124.6, 127.0, 128.3, 135.9, 138.1,

152.8; IR (film) 3430, 3190, 3080, 1670 cm^{-1}; MS (CI) *m*/*z* 249 ($M^+ + H$), 194, 165. Anal. Calcd for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.42; H, 5.42; N, 10.95.

(1*R,10b*R**)-9-Chloro-6-*p*-toluenesulfonyl-1-ethenyl-2,3,6,10b-tetrahydro-1*H*-pyrrolo[1,2-*c*]quinazolin-5-one (55).** To a solution of **45** (4.00 g, 16.1 mmol) in THF (400 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 2.00 g, 50.0 mmol). After 1 h, *p*-toluenesulfonyl chloride (3.40 g, 17.8 mmol) was added, and the reaction was allowed to warm to room temperature while stirring for an additional 15 h. The reaction was then quenched with saturated aqueous NH_4Cl (100 mL) and extracted with EtOAc (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (1:1) to give 5.80 g (90%) of a dark yellow solid. An analytical sample was prepared by crystallization from CH_3CN/CH_2Cl_2. Dark tan cubes: mp 184−184.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (m, 1H), 2.24 (m, 1H), 2.45 (s, 3H), 3.33 (m, 1H), 3.52 (td, J = 11.5, 7.1 Hz, 1H), 3.74 (m, 1H), 4.71 (d, J = 4.8 Hz, 1H), 5.11 (dd, J = 11.1, 1.2 Hz, 1H), 5.22 (dd, J = 17.1, 1.2 Hz, 1H), 5.37 (m, 1H), 7.02 (d, J = 1.3 Hz, 1H), 7.23 (dd, J = 8.8, 2.0 Hz, 1H), 7.37 (m, 3H), 8.10 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.6, 30.6, 44.3, 45.2, 59.5, 118.4, 122.4, 127.2, 127.7, 128.1, 128.3, 129.7, 130.5, 134.1, 134.9, 137.5, 144.7, 149.4; IR (KBr) 2960 cm^{-1}; MS (CI) *m*/*z* 403 ($M^+ + H$); HRMS calcd for $C_{20}H_{20}ClN_2O_3S$ 403.0883, found 403.0861.

(2*R,3*R**)-2-(5′-Chloro-2′-*p*-toluenesulfonylaminophenyl)-3-ethenylpyrrolidine (56).** A solution of **55** (5.80 g, 14.4 mmol) in THF/MeOH/50% aqueous NaOH (3:2:1, 150 mL) was heated at reflux for 96 h. The reaction was cooled to 0 °C, acidified to pH ∼1 with 10% HCl, and extracted with CH_2Cl_2 (5 × 200 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with CH_2Cl_2/MeOH/$EtNH_2$ (97:2:1) to give 3.52 g (65%) of a tan solid: mp 61−62.5 °C, mp (HCl salt) 222−225 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (m, 1H), 2.09 (m, 1H), 2.39 (s, 3H), 2.95 (m, 1H), 3.05 (dt, J = 9.9, 7.6 Hz, 1H), 3.34 (m, 1H), 4.37 (m, 1H), 4.61 (dd, J = 10.1, 1.6 Hz, 1H), 4.76 (d, J = 16.9 Hz, 1H), 5.27 (dt, J = 16.9, 9.7 Hz, 1H), 6.87 (d, J = 2.4 Hz, 1H), 7.04 (dd, J = 8.8, 2.4 Hz, 1H), 7.25 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.5, 32.0, 45.4, 48.5, 66.2, 116.3, 119.0, 127.0, 127.4, 127.6, 127.8, 129.4, 129.6, 137.0, 137.5, 137.7, 143.4; IR (film) 3320, 3070, 1475 cm^{-1}; MS (CI) *m*/*z* 377 ($M^+ + H$), 221, 167; HRMS calcd for $C_{19}H_{22}ClN_2O_2S$ 377.1090, found 377.1112.

(2*R,3*R**)-1-Acetyl-2-(5′-chloro-2′-*p*-toluenesulfonylaminophenyl)-3-ethenylpyrrolidine (57).** To a solution of **56** (0.50 g, 1.3 mmol) in CH_2Cl_2 (5.0 mL) at room temperature was added DMAP (16 mg, 0.13 mmol), pyridine (0.16 mL, 2.0 mmol), and acetyl chloride (0.14 mL, 2.0 mmol). After 3 h, saturated aqueous $NaHCO_3$ (5 mL) was added, and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.48 g (85%) of a pale yellow solid as a 3:2 mixture of rotamers, based on ^{1}H NMR integration: mp 67.5−69 °C; Major rotamer: ^{1}H NMR (400 MHz, *d*-DMSO) δ 1.54 (s, 3H), 1.70 (m, 1H), 1.86 (m, 1H), 2.36 (s, 3H), 3.27 (m, 1H), 3.41 (m, 1H), 3.72 (m, 1H), 4.82 (d, J = 10.5 Hz, 1H), 4.95 (m, 1H), 5.34 (m, 1H), 5.61 (d, J = 8.0 Hz, 1H), 6.74 (d, J = 8.7 Hz, 1H), 6.91 (d, J = 2.4 Hz, 1H), 7.18 (dd, J = 8.6, 2.4 Hz, 1H), 7.38 (m, 2H), 7.63 (d, J = 8.2 Hz, 2H), 9.48 (s, 1H); ^{13}C NMR (125.7 MHz, *d*-DMSO) δ 21.0, 22.0, 26.4, 45.5, 47.1, 59.2, 116.6, 126.5, 127.0, 127.8, 129.8, 130.9, 133.3, 135.5, 135.8, 136.8, 138.4, 143.6, 168.8; IR (KBr) 3060, 2950 cm^{-1}; MS (CI) *m*/*z* 419 ($M^+ + H$), 263; HRMS calcd for $C_{21}H_{24}ClN_2O_3S$ 419.1196, found 419.1203. Minor rotamer: ^{1}H NMR (400 MHz, *d*-DMSO) δ 1.98 (s, 3H), 2.01 (m, 2H), 2.34 (s, 3H), 3.05 (m, 1H), 3.58 (m, 1H), 3.84 (m, 1H), 4.76 (d, J = 10.4, 1H), 4.89 (m, 1H), 5.10 (m, 1H), 5.29 (m, 1H), 6.94 (d, J = 2.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 1H), 7.14 (dd, J = 8.7, 2.4 Hz, 1H), 7.35 (m, 2H), 7.71 (d, J = 8.2 Hz, 2H), 9.79 (s, 1H); ^{13}C NMR (125.7 MHz, *d*-DMSO) δ 20.9, 22.4, 28.6, 45.0, 46.6, 57.2, 116.1, 123.9, 126.6, 126.9, 127.1, 127.2, 128.9, 129.7, 134.1, 135.2, 137.1, 143.3, 168.9.

(3a*R,4*R**,9b*S**)-1-Acetyl-8-chloro-4-(iodomethyl)-5-*p*-toluenesulfonyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline (58).** To a solution of **57** (0.10 g, 0.24 mmol) in CH_3CN (5.0 mL) at room temperature was added I_2 (0.61 g, 2.4 mmol). The reaction was heated at reflux for 24 h and then cooled to room temperature and diluted with Et_2O (20 mL). The resulting solution was washed with saturated $NaHCO_3$ (5 mL), 10% aqueous $Na_2S_2O_3$ (3 × 10 mL), and saturated aqueous NaCl (10 mL). The organic layer was dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 0.11 g (84%) of a yellow solid. An analytical sample was crystallized from CH_2Cl_2/CH_3CN: thick colorless prisms; mp 189.5−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (m, 1H), 2.09 (s, 3H), 2.15 (m, 1H), 2.44 (s, 3H), 3.01 (m, 1H), 3.11 (t, J = 10.4 Hz, 1H), 3.26 (dd, J = 10.3, 5.2 Hz, 1H), 3.50 (m, 2H), 4.84 (m, 1H), 5.43 (d, J = 7.8 Hz, 1H), 7.11 (dd, J = 9.0, 2.5 Hz, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 9.0 Hz, 1H), 7.83 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 5.1, 21.5, 22.5, 28.1, 38.0, 46.7, 52.0, 57.7, 121.7, 127.1, 128.4, 128.8, 129.9, 130.0, 131.5, 132.0, 137.5, 144.5, 171.1; IR (KBr) 3440 (br), 3130, 3015, 1625 cm^{-1}; MS (CI) *m*/*z* 545 ($M^+ + H$), 375, 263, 249, 219, 112, 91, 65, 43; Anal. Calcd for $C_{21}H_{22}ClIN_2O_3S$: C, 46.29; H, 4.07; N, 5.14. Found: C, 46.08; H, 4.23; N, 5.44. X-ray data for this compound are available in the Supporting Information.

Ethyl 3-Bromo-4-(*N*-*tert*-butoxycarbonyl)aminobenzoate (59). Bromine (12.0 mL, 233 mmol) was added dropwise to a solution of **5**[14] (35.0 g, 132 mmol), sodium acetate (43.0 g, 524 mmol), and acetic acid (700 mL). After 41 h, the reaction was cooled to 0 °C, 50% aqueous NaOH (600 mL) was added slowly, and the mixture was extracted with EtOAc (3 × 500 mL). The combined organic layers were washed with 10% aqueous NaOH (2 × 150 mL) and saturated aqueous NaCl (150 mL), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (4:1) to give 45.9 g (100%) of a pale pink solid: mp 82.5−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, J = 7.1 Hz, 3H), 1.56 (s, 9H), 4.36 (q, J = 7.1 Hz, 2H), 7.22 (br s, 1H), 7.95 (dd, J = 8.7, 1.9 Hz, 1H), 8.19 (d, J = 1.9 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.3, 28.2, 61.1, 81.8, 111.3, 118.4, 125.5, 129.8, 133.6, 140.2, 151.8, 165.1; IR (KBr) 3380, 2960, 1720, 1690 cm^{-1}; MS (CI) *m*/*z* 344 ($M^+ + H$), 305, 288, 243, 224, 198, 57. Anal. Calcd for $C_{14}H_{18}BrNO_4$: C, 48.55; H, 5.27; N, 4.07. Found: C, 48.63; H, 5.18; N, 3.82.

Ethyl 4-(*N*-*tert*-Butoxycarbonyl)amino-3-ethenylbenzoate (60). A solution of **59** (7.50 g, 21.8 mmol) and 2,6-di-*tert*-butyl-4-methylphenol (50 mg) in toluene (50 mL) was deoxygenated with argon. The flask and reflux condenser were covered with aluminum foil. Next, $(Ph_3P)_4Pd$ (1.25 g, 1.08 mmol) and tributyl(vinyl)tin (9.00 mL, 30.8 mmol) were added, and the mixture was heated at reflux for 24 h. The reaction was then cooled to room temperature, filtered through a short pad of silica gel and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (9:1) to give 5.40 g (85%) of a thick pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, J = 7.1 Hz, 3H), 1.53 (s, 9H), 4.36 (q, J = 7.1 Hz, 2H), 5.52 (dd, J = 11.0, 1.0 Hz, 1H), 5.73 (dd, J = 17.3, 1.0 Hz, 1H), 6.66 (br s, 1H), 6.77 (dd, J = 17.3, 11.0 Hz, 1H), 7.93 (dd, J = 8.6, 1.9 Hz, 1H), 8.02 (d, J = 1.9 Hz, 1H), 8.06 (d, J = 8.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.4, 28.3, 60.8, 81.3, 119.1, 119.8, 125.0, 127.5, 128.9, 130.0, 131.4, 139.3, 152.3, 166.3; IR (film) 3320 (br), 2960, 1720 (sh), 1695 cm^{-1}; MS (CI) *m*/*z* 292 ($M^+ + H$), 236,191, 57. Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.81; H, 7.33; N, 4.53.

Ethyl 4-(*N*-*tert*-Butoxycarbonyl)amino-3-formylbenzoate (61). Alkene **60** (4.00 g, 13.7 mmol) was dissolved in CH_2Cl_2, cooled to −78 °C, and then ozone was bubbled through the solution until it turned blue (ca. 30 min). The reaction was

quenched with DMS (2.0 mL), allowed to warm to room temperature, and then was concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (5:1) to give 3.13 g (78%) as a white solid: mp 100.5−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, J = 7.1 Hz, 3H), 1.55 (s, 9H), 4.40 (q, J = 7.1 Hz, 2H), 8.20 (dd, J = 8.9, 1.7 Hz, 1H), 8.34 (d, J = 1.8 Hz, 1H), 8.55 (d, J = 8.9 Hz, 1H), 9.96 (s, 1H), 10.60 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.3, 28.2, 61.2, 81.3, 117.9, 120.5, 123.6, 136.7, 137.9, 145.3, 152.4, 165.1, 194.6; IR (KBr) 3250, 2985, 1715, 1695 cm^{-1}; MS (CI) m/z 294 (M^+ + H), 255, 238, 194, 57. Anal. Calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.78. Found: C, 61.45; H, 6.83; N, 4.80.

(*N*′-*tert*-Butoxycarbonyl-2′-amino-5′-carbethoxybenzylidene)-[(*Z*)-5-(trimethylsilyl)-3-pentenyl]amine (62). A solution of **21** (0.12 g, 0.65 mmol) and triphenylphosphine (0.17 g, 0.65 mmol) in THF (5.0 mL) was stirred at room temperature for 3 h. Next, **61** (0.19 g, 0.65 mmol) was added, and the reaction was heated at reflux for 20 h. The reaction was then cooled to room temperature, concentrated under reduced pressure, triturated with ether, filtered through Florisil, and concentrated under reduced pressure to give 0.35 g of a crude colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H), 1.39 (t, J = 7.0 Hz, 3H), 1.54 (s, 9H), 2.40 (q, J = 6.8 Hz, 2H), 3.64 (t, J = 6.7 Hz, 2H), 4.36 (q, J = 7.2 Hz, 1H), 5.42 (m, 1H), 5.50 (m, 1H), 8.00 (m, 2H), 8.37 (s, 1H), 8.46 (d, J = 9.3 Hz, 1H), 12.38 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −1.8, 14.4, 18.7, 28.3, 28.7, 60.8, 61.0, 80.3, 117.4, 119.6, 122.8, 123.9, 127.5, 132.4, 134.7, 144.7, 153.2, 163.1, 165.9; IR (film) 2960, 2940, 1715, 1700 cm^{-1}; MS (CI) m/z 433 (M^+ + H), 377, 279, 263, 208, 194, 183; HRMS calcd for $C_{23}H_{37}N_2O_4Si$ 433.2522, found 433.2526. This compound was used immediately in the next step without further purification.

(1*R,10b*R**)- and (1*R**,10b*S**)-9-Carbethoxy-1-ethenyl-2,3,6,10b-tetrahydro-1*H*-pyrrolo[1,2-*c*]quinazolin-5-one (63).** To a solution of **62** (9.13 g, ca. 21.1 mmol, as a ca. 2:1 mixture of *Z* and *E* isomers, based on ^{1}H NMR integration) in CH_2Cl_2 (500 mL) at room temperature was added $TiCl_4$ (12.0 mL, 109 mmol). After 18 h, 10% aqueous NaOH (500 mL) was added slowly, and the reaction mixture was extracted with CH_2Cl_2 (3 × 400 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:1) to give 4.83 g (80%) of a light yellow solid as a 17:3 mixture of diastereomers, based on ^{1}H NMR integration, mp 161−164 °C. Major isomer, (1*R**,10b*R**)-**63**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J = 7.1 Hz, 3H), 2.02 (m, 1H), 2.24 (m, 1H), 3.32 (m, 1H), 3.59 (m, 1H), 3.81 (m, 1H), 4.33 (q, J = 7.1 Hz, 2H), 4.87 (d, J = 4.6 Hz, 1H), 5.03 (d, J = 10.6 Hz, 1H), 5.16 (d, J = 17.2 Hz, 1H), 5.59 (m, 1H), 6.84 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H), 7.82 (dd, J = 8.3, 1.7 Hz, 1H), 9.33 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.3, 29.0, 43.1, 45.6, 60.7, 61.5, 113.8, 117.4, 117.8, 123.7, 128.7, 129.9, 135.6, 141.7, 153.0, 166.1; IR (KBr) 3180, 2960, 1685, 1660 cm^{-1}; MS (CI) m/z 287 (M^+ + H), 232. Anal. Calcd for $C_{16}H_{18}N_2O_3$: C, 67.12; H, 6.34; N, 9.78. Found: C, 67.09; H, 6.32; N, 9.55. Minor isomer, (1*R**,10b*S**)-**63** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.1 Hz, 3H), 1.91 (m, 1H), 3.00 (m, 1H), 3.67 (m, 1H), 4.32 (m, 2H), 4.47 (d, J = 9.6 Hz, 1H), 5.32 (d, J = 10.7 Hz, 1H), 5.40 (d, J = 17.1 Hz, 1H), 5.99 (m, 1H), 6.87 (d, J = 8.4 Hz, 1H), 7.85 (dd, J = 8.4, 1.7 Hz, 1H), 8.11 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.2, 30.6, 43.5, 50.1, 60.4, 60.6, 117.7, 121.0, 123.8, 126.3, 130.1, 138.3, 141.5, 153.3, 166.5.

(1*R,10b*R**)- and (1*R**,10b*S**)-9-Carbethoxy-6-*p*-toluenesulfonyl-1-ethenyl-2,3,6,10b-tetrahydro-1*H*-pyrrolo[1,2-*c*]quinazolin-5-one (64).** To a solution of **63** (2.0 g, 7.0 mmol) in THF (150 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 0.80 g, 20 mmol). After 45 min, *p*-toluenesulfonyl chloride (1.6 g, 8.4 mmol) was added and the reaction was allowed to warm to room temperature. After an additional 22 h, saturated aqueous NH_4Cl (100 mL) was added slowly and the reaction mixture was extracted with EtOAc (3 × 150 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with hexanes/EtOAc (2:1) to give 2.8 g (91%) of a yellow solid as a 17:3 mixture of diastereomers, based on ^{1}H NMR integration, mp 148.5−151.5 °C. Major isomer, (1*R**,10b*R**)-**64**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J = 7.1 Hz, 3H), 1.98 (dd, J = 12.6, 6.9 Hz, 1H), 2.25 (m, 1H), 2.46 (s, 3H), 3.44 (m, 1H), 3.54 (m, 1H), 3.79 (m, 1H), 4.36 (m, 1H), 4.81 (d, J = 4.7 Hz, 1H), 5.07 (d, J = 9.9 Hz, 1H), 5.25 (dd, J = 17.0, 1.3 Hz, 1H), 5.34 (m, 1H), 7.38 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.7 Hz, 1H), 7.75 (s, 1H), 7.94 (dd, J = 8.7, 1.1 Hz, 1H), 7.98 (m, 1H), 8.15 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1, 21.2, 30.2, 44.2, 45.1, 59.4, 60.9, 118.2, 120.4, 126.2, 126.6, 128.0, 128.7, 128.8, 129.3, 129.5, 134.8, 137.1, 139.0, 144.6, 148.9; IR (KBr) 2960, 2880, 1705 (sh), 1690 cm^{-1}; MS (CI) m/z 441 (M^+ + H). Anal. Calcd for $C_{23}H_{24}N_2O_5S$: C, 62.71; H, 5.49; N, 6.36. Found: C, 62.35; H, 5.72; N, 6.37. Minor isomer, (1*R**,10b*S**)-**64** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.05 (m, 1H), 3.38 (m, 1H), 3.82 (m, 1H), 4.50 (d, J = 9.6 Hz, 1H), 5.42 (m, 1H), 6.01 (m, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 8.19 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0, 21.4, 30.9, 44.6, 48.2, 59.0, 117.8, 120.2, 125.2, 126.1, 127.3, 128.1, 129.1, 130.2, 137.2, 139.2.

(2*R,3*R**)- and (2*R**,3*S**)-2-(5′-Carbomethoxy-2′-*p*-toluenesulfonylaminophenyl)-3-ethenylpyrrolidine (65).** A solution of **64** (2.50 g, 5.68 mmol) in THF/MeOH/50% aqueous NaOH (3:2:1, 120 mL) was heated at reflux for 67 h. The reaction was acidified to pH ∼1 with 10% HCl and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure to give 2.41 g of crude 2-(5′-carboxy-2′-*p*-toluenesulfonylaminophenyl)-3-ethenylpyrrolidine as a brown oil: IR (KBr) 3650−2300 (br), 3400, 3050, 1645 cm^{-1}; MS (CI) m/z 387 (M^+ + H), 259, 189; HRMS calcd for $C_{20}H_{23}N_2O_4S$ 387.1378, found 387.1375. To a solution of the crude acid (2.41 g) in MeOH (100 mL) was added concentrated H_2SO_4 (0.5 mL). The reaction was heated at reflux for 20 h, then cooled to room temperature and concentrated. To the resulting residue was added saturated aqueous $NaHCO_3$ (50 mL). This aqueous solution was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with CH_2Cl_2/MeOH (19:1) to give 1.31 g (57% over two steps) of a white foam as a 17:3 mixture of diastereomers, based on ^{1}H NMR integration. Major isomer, (2*R**,3*R**)-**65**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (m, 1H), 2.12 (m, 1H), 2.35 (s, 3H), 2.99 (m, 1H), 3.11 (m, 1H), 3.36 (m, 1H), 3.82 (s, 3H), 4.53 (m, 2H), 4.70 (m, 1H), 5.28 (m, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.7 Hz, 1H), 7.53 (d, J = 2.0 Hz, 1H), 7.69 (dd, J = 8.6, 2.0 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.4, 31.8, 45.1, 48.5, 51.8, 66.7, 116.3, 116.5, 122.9, 124.3, 126.8, 129.4, 129.5, 131.2, 136.5, 137.9, 143.2, 144.4, 166.6; IR (KBr) 3440 (br), 2930, 1690, 1590 cm^{-1}; MS (CI) m/z 401 (M^+ + H), 191; HRMS calcd for $C_{21}H_{25}N_2O_4S$ 401.1535, found 401.1559. Minor isomer, (2*R**,3*S**)-**65** (diagnostic peaks only): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74 (m, 1H), 2.16 (m, 1H), 2.34 (s, 3H), 3.18 (m, 1H), 3.29 (m, 1H), 3.82 (s, 3H), 4.46 (m, 1H), 4.85 (m, 1H), 5.52 (m, 1H), 7.21 (m, 1H), 7.48 (d, J = 2.0 Hz, 1H), 7.52 (m, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.76 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.4, 31.2, 44.2, 49.2, 51.9, 68.9, 116.9, 118.3, 123.4, 125.9, 126.7, 129.5, 129.7, 131.2, 137.1, 137.8, 143.4, 166.6.

(3a*R,4*R**,9b*S**)-8-Carbomethoxy-4-(iodomethyl)-5-*p*-toluenesulfonyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline (66).** To a solution of **65** (0.50 g, 1.2 mmol) in CH_3CN (30 mL) at room temperature was added iodine (3.0 g, 12 mmol). The reaction was heated at reflux for 21 h, then cooled to room temperature, and diluted with Et_2O (200 mL). The resulting solution was washed with saturated $NaHCO_3$ (20 mL) and 10% aqueous $Na_2S_2O_3$ (3 × 25 mL). The combined aqueous layers were extracted with Et_2O (50 mL). The combined organic layers were dried (Na_2SO_4), decanted, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography with EtOAc/hexanes (2:

1) to give 0.29 g (44%) of a beige foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (m, 1H), 2.20 (m, 1H), 2.42 (s, 3H), 2.77 (m, 2H), 2.92 (m, 1H), 3.06 (m, 2H), 3.90 (s, 3H), 4.17 (d, J = 8.7 Hz, 1H), 4.71 (m, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.6 Hz, 1H), 7.78 (d, J = 8.3 Hz, 2H), 7.87 (dd, J = 8.6, 2.1 Hz, 1H), 7.99 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 7.5, 21.6, 32.8, 43.0, 46.1, 52.1, 56.4, 61.2, 122.9, 127.0, 127.5, 129.6, 129.9, 131.4, 131.7, 136.9, 138.7, 144.6, 166.2; IR (KBr) 3410, 2930, 1700 cm^{-1}; MS (CI) m/z 527 (M^+ + H), 401, 342, 91; HRMS calcd for $C_{21}H_{24}IN_2O_4S$: 527.0501, found 527.0511.

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Supporting Information Available: Experimental procedures for compounds **16**−**22**, **23**, **27**−**31**, **35**, **36**, **40**−**44**, **49**−**52**, *N*-(4-chlorophenyl)-2,2-dimethyl-propionamide, and *N*-(4-chloro-2-formylphenyl)-2,2-dimethylpropionamide; X-ray data for compounds **38**, **45**, **50**, and **58**; and ^{1}H and ^{13}C NMR data for compounds **8**, **10**, **12**, **14**, **15**, **21**, **24**−**36**, **39**−**44**, **47**−**53**, **55**−**57**, **62**, **64,** and **65** (compounds **36** and **48** have ^{1}H data only). This material is available free of charge via the Internet at http://pubs.acs.org.

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