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Free radical-mediated vinyl amination: a mild, general pyrrolidinyl enamine synthesis

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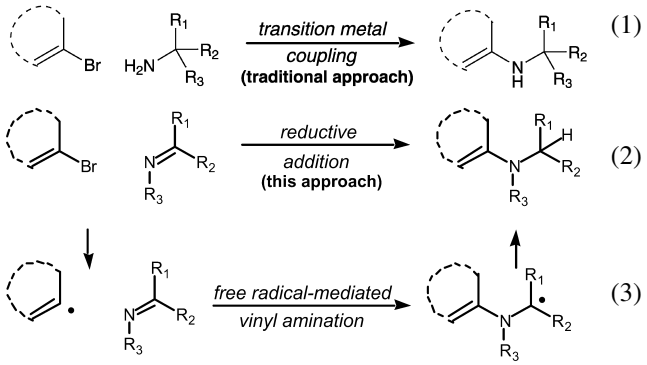
Abstract—The complete scope of free radical-mediated vinyl amination is described, using 5-*exo*-trig cyclizations of vinyl radicals to the nitrogen of azomethines. The focus is primarily on *N*,*N*-dialkyl enamines since their nucleophilicity renders them the most challenging enamines to synthesize using redox conditions. These studies establish several encouraging precedents for the broader application of this strategy.

1. Introduction

The vinyl–nitrogen bond is a fundamental structural building block ubiquitous within organic chemistry. When part of an aromatic system, a substantial degree of stability is imparted. However, in the absence of any resonance stabilization for the olefin and nitrogen, a highly reactive enamine results. These intermediates have often been deployed in organic synthesis as enolate equivalents that are neutral, yet still potently nucleophilic.[1,2]

The vast majority of enamine syntheses are thermodynamically-driven, often condensative processes.[3] Methods that can provide kinetic control, either formally or

vinyl amination: strategies



otherwise, include metallocene-catalyzed alkyne hydroamination,[4] Tebbe olefination of lactams,[5] and pyrolysis of cyclopropyl ketimines.[6] Vinyl amination[7] using an olefin donor and an amine was reported only recently by Barluenga[8] using the palladium catalyst systems popularized by Hartwig and Buchwald.[9]

Our examination of this problem begins not from the view in which the nitrogen–hydrogen σ bond of the amine is activated (Eq. (1)), thereby necessitating the use of a base, but instead by activation of a nitrogen–carbon π bond (Eq. (2)). Our first solution was the addition of aryl (carbon) radicals to an azomethine (Eq. (3)), a transformation first documented by Takano[10] and Warkentin[11,12] but improved and generalized by us.[13] A typical requirement for regioselective carbon–nitrogen bond formation is the use of a ketimine bearing at least one radical-stabilizing substituent as the azomethine acceptor.[14] Our attention toward pyrrolidinyl enamines stems from their pervasiveness in alkaloid natural products. By coupling the development of a new method to direct the formation of nucleophilic enamines with the pyrrolidine motif, we offer a powerful platform from which alkaloids containing a pyrrolidine subunit may be accessed.[15,16]

Our approach to vinyl amination is by some measure an extension of free radical-mediated aryl amination. Yet, a closer examination of the process reveals significant new issues that render this proposition non-trivial. For example, the products of vinyl amination are *N*,*N*-dialkyl enamines that are not resonance stabilized and consequently more nucleophilic and reactive than aminoaryl products resulting from aryl amination. Furthermore, vinyl radicals invert rapidly and cannot cyclize when in the *trans*-form (relationship between the radical and β-alkyl). However, both stereoisomers are reactive toward hydrogen atom transfer from stannane. Finally, although 5-membered

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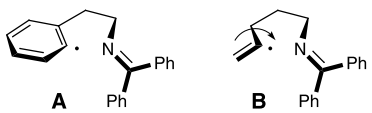
heterocyclic rings were again targeted, an additional degree of freedom is introduced in many of the substrates examined (c.f. **A**–**B**). Fortunately, the studies described below demonstrated that none of these issues were ultimately obstructive.



2. Synthesis of the cyclization precursors

Cyclization precursors **1**–**10** were targeted for synthesis to carefully evaluate the relative importance of conformational and stereoelectronic effects. 1- and 2-bromopropene derivatives **1**–**4** were readily prepared from 3-aminopropanol (**11**) (Scheme 1). Protection of amine **11** as its phthalimide and subsequent oxidation with the Dess–Martin periodinane provided aldehyde **12** in 42% overall yield. Use of the Smithers reagent[17] derived from dibromomethane transformed the aldehyde to terminal vinyl bromide **13** as a 4:1 mixture of *Z*/*E* isomers in 49% yield. The imide could then be deprotected using hydrazine hydrate to liberate amine **1** in 71% yield. Similarly, the Smithers reagent derived from 1,1-dibromoethane enabled access to the 2-bromopropene derivative **2** as a 4:1 mixture of *Z*/*E* stereoisomers. It is significant to note that these low molecular weight amines are often both water soluble and volatile, thereby, demanding strict attention to the handling procedures outlined. Although no convenient point to separate the olefin stereoisomers was found, it was of little consequence since the intermediate vinyl radicals produced during cyclization readily epimerize.

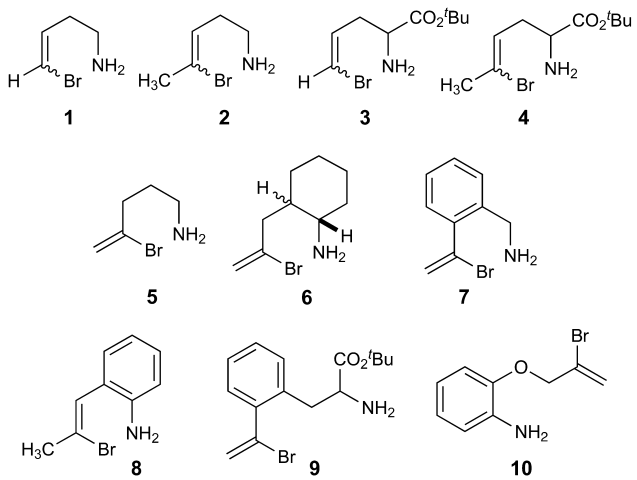
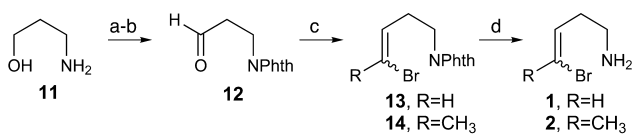
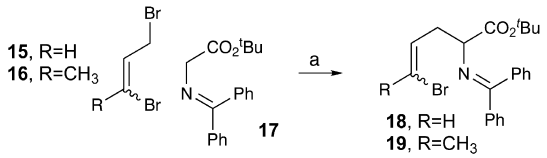


Chart 1.



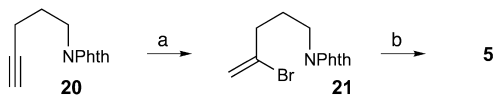
Scheme 1. *Reagents and conditions*: (a) phthalic abhydride, DMAP, 12°C (64%); (b) Dess–Martin periodinane, CH_2Cl_2 (65%); (c) Ph_3PCRBr_2, ^{n}BuLi, THF, −78°C (**13**, 49%; **14** 39%); (d) NH_2NH_2, CH_3OH, 65°C (**1**, 71%; **2**, 92%).

α-Amino acid derivatives **3**–**4** were prepared from the corresponding bromopropene and bromobutene derivatives using phase transfer-catalyzed alkylation of glycine *tert*-butyl ester **17**.[18] The amine (**3**) (Scheme 2) could be retrieved after hydrolysis of the ketimine, but direct use of the benzophenone imine provided a desirable level of brevity for the synthesis of the derived proline derivatives.



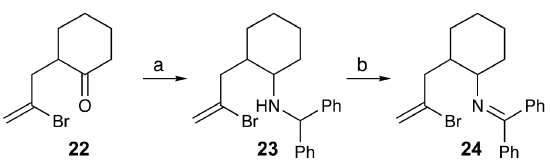
Scheme 2. *Reagents and conditions*: (a) NaOH, $BnEt_3NCl$, H_2O–CH_2Cl_2 (**18**, 80%; **19**, 96%).

Phthalimide **20** was prepared from 5-chloro-1-pentyne according to the Marks protocol (Scheme 3).[4] Bromoboration and subsequent treatment with protic acid returned the α-olefin **21**. Removal of the phthalimide with hydrazine hydrate provided the desired, highly hygroscopic amine **5**.



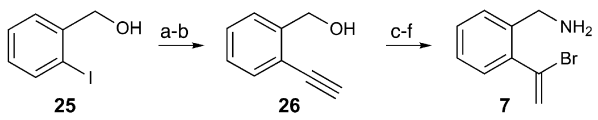
Scheme 3. *Reagents and conditions*: (a) BBr_3, CH_2Cl_2, −78°C, then AcOH, hexanes, △ (81%); (b) NH_2NH_2, CH_3OH, 65°C (97%).

The benzophenone imine of **6** could be directly accessed as described in Scheme 4. Both stereoisomers were synthesized from cyclohexanone **22**.[19] Imine formation from diphenylmethyl amine and reduction provided secondary amine **23** in 50% yield for the two steps. Use of the Honek protocol[20] for DDQ oxidation to the corresponding imine provided **24** in 78% yield. *cis*-**24** and *trans*-**24** were separable on neutral alumina. Relative stereochemical assignments are based on NOE measurements on the derived cyclization products (vide infra).



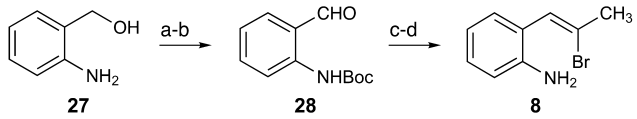
Scheme 4. *Reagents and conditions*: (a) (i) Ph_2CHNH_2, 4 Å MS, C_6H_6, (ii) $NaBH_4$ (*cis*/*trans*=3:1, 50%); (b) (i) DDQ, CH_2Cl_2, 55°C (78%), (ii) chromatography (neutral Al_2O_3).

Vinyl bromide **7** was formed from *ortho*-iodobenzyl alcohol in six steps by first using a Sonagashira coupling with trimethylsilyl acetylene (Scheme 5). Subsequent alkyne deprotection, treatment with carbon tetrabromide/triphenylphosphine, and bromination with boron tribromide led to an intermediate benzyl halide with adequate efficiency (72% yield). This halide was then transformed to the required amine (**7**) via a straightforward Gabriel amine synthesis.



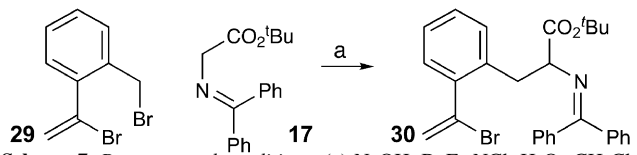
Scheme 5. *Reagents and conditions*: (a) TMS–C≡C–H, $(Ph_3P)_4Pd$, CuI, TEA, 50°C (quant); (b) K_2CO_3, CH_3OH (quant); (c) Ph_3P, CBr_4, 2,6-lutidine (93%); (d) (i) BBr_3, CH_2Cl_2, −78°C, (ii) AcOH, hexanes, 60°C (72%); (e) KPhth, DMF, 60°C (43%); (f) NH_2NH_2, CH_3OH (84%).

Synthesis of aniline **8** (Scheme 6) commenced from *ortho*-aminobenzyl alcohol by *tert*-butoxycarbonyl (Boc) protection and oxidation to benzaldehyde derivative **28** with the Dess–Martin reagent (48% overall). Wittig olefination using the Smithers reagent provided amine **8** after Boc deprotection with trifluoroacetic acid.



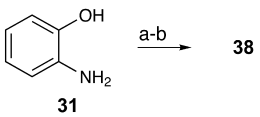
Scheme 6. *Reagents and conditions*: (a) Boc_2O, THF (92%); (b) Dess–Martin periodinane, CH_2Cl_2 (52%); (c) $Ph_3PCBr_2(CH_3)$, ^nBuLi, THF, −78°C (44%); (d) TFA, CH_2Cl_2 (64%).

Two substrates were targeted as 6-*exo*-cyclization substrate variants. The first of these, ketimine **30** was formed directly via the glycine Schiff base alkylation protocol (Scheme 7). Treatment of **17** with aqueous alkali and the benzylic bromide synthesized en route to **7** provided the desired benzophenone ketimine (**30**) in 63% yield.



Scheme 7. *Reagents and conditions*: (a) NaOH, $BnEt_3NCl$, H_2O–CH_2Cl_2 (63%).

The benzophenone imine of **10** (ketimine **38**) was prepared concisely from *ortho*-hydroxy aniline in 86% yield as depicted in Scheme 8.



Scheme 8. *Reagents and conditions*: (a) Ph_2C=NH, 4 Å MS, C_6H_6 (91%); (b) NaH, 2-bromoallyl bromide, THF (95%).

3. Free radical-mediated vinyl amination

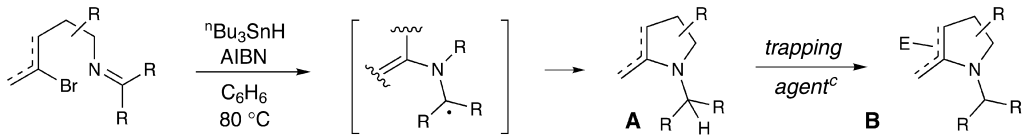
Our protocol for vinyl amination involves the traditional generation of a vinyl radical using tri-*n*-butylstannane/AIBN and its regioselective addition to the nitrogen of a ketimine.[15] Generally speaking, both acetophenone and benzophenone ketimines work equally well in the context of the cyclization. However, each offers unique practical attributes. Acetophenone imines are formed via condensation of the amine with acetophenone, facilitated by activated (at 400°C) 4 Å MS at room temperature. Although the resulting imine is not sufficiently inert toward chromatography, the condensations are clean transformations, and excess acetophenone can be removed slowly by application of a high vacuum. In cases where acetophenone imine is slow to form (for either steric or electronic reasons), or a symmetrical ketimine is desired, transimination with benzophenone imine is the method of choice. The benzophenone ketimines that result can be chromatographed on neutral alumina. It is particularly critical to remove benzophenone, as it effectively halts the desired free radical amination process.

The ketimine derivatives of amines **1**–**10** described in Chart 1 were individually optimized for vinyl radical addition to the azomethine nitrogen (Eq. (4), Table 1). Ketimines of **1**–**2** are analogous to the aryl aminations described previously, yet they possess an additional degree of freedom by virtue of the epimerizable vinyl radical intermediate: when the radical is *trans* to the alkyl chain, intermolecular hydrogen atom transfer is the only possible direct functionalization. Notwithstanding, ketimines **32** and **18**, which present little bias for either the *Z*- or *E*-vinyl radical configurations, cleanly cyclized to their corresponding enamines. Despite the reluctance of **39a** to react cleanly with any acylating agent, it was clear from ^1H NMR analysis that formation of **39a** was quite selective. Again, volatility of the the Δ^2-pyrroline was evident throughout the optimization process. In cases where enamine volatility is a concern, care must be exercised to maintain a closed refluxing benzene reaction mixture. Formation of the analogous but less volatile vinylogous amide **41b** in 54% yield (Table 1, entry 3) supports this contention. The near identical behavior of ketimines **33** and **19** (Table 1, entries 2 and 4) compared to their counterparts **32** and **18** (Table 1, entries 1 and 3) suggests that the vinyl radical is indeed epimerizing faster than cyclization. This result also underscores an important advantage to free radical-mediated amination in that mixtures of vinyl halide stereoisomers can be used. Cyclizations of **33** and **19** uniformly produced exocyclic enamines **40a** and **42a**, respectively, instead of the expected endocyclic isomers. When these transformations were executed in refluxing C_6D_6 so as to allow periodic monitoring of the reaction, no spectroscopic evidence for the endocyclic enamine was observed. Although the endocyclic isomer must be the first intermediate, it is apparently quick to isomerize.[21]

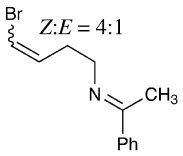
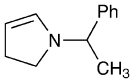
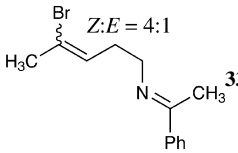
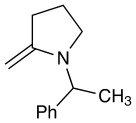
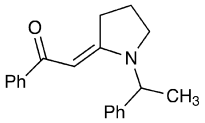
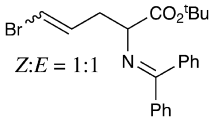
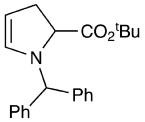
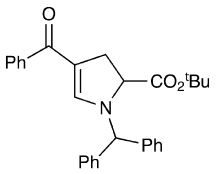
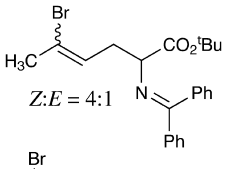
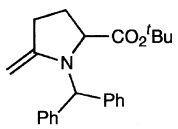
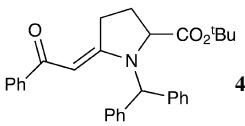
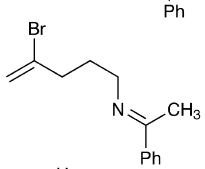
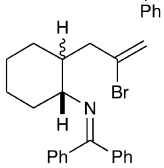
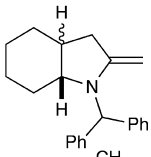
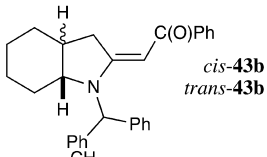
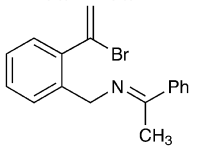
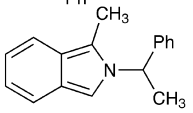
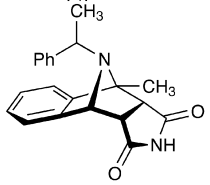
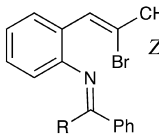
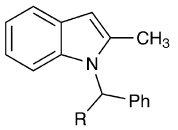
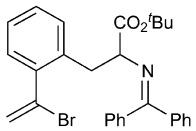
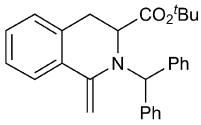
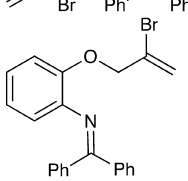
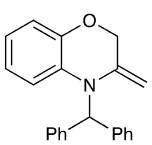
Following several trial cyclizations of ketimine **34** that lead to uniformly low yields, the reaction was effected in C_6D_6 in a sealed J-Young tube in order to monitor the reaction. Once again, selective formation of the desired enamine was evident, with little or no formation of the reduced vinyl radical (comparison with an authentic sample). This example is the most conformationally mobile example we have cyclized successfully. A 36% yield over three steps (condensation, cyclization, benzoylation) could be reproduced consistently, suggesting that amounts of the intermediate enamine are again lost to the headspace of the refluxing benzene solution during cyclization.

The *cis*-fused pyrrolidine **43b** was conveniently prepared in 64% overall yield via the free radical amination protocol (Table 1, entry 6). Similarly, the *trans* isomer (*trans*-**24**) cyclized without event, delivering the *trans*-fused

Table 1. 5-*exo*-Trig vinyl radical cyclizations to ketimine nitrogen[a]



(4)

Entry	Ketimine	Intermediate enamine[b] (**A**)	Isolated product (**B**)	Overall yield[c]/steps
1	 **32**	 **39a**		38[d,e]/2
2	 **33**	 **40a**	 **40b**	34[d]/3
3	 **18**	 **41a**	 **41b**	54/2
4	 **19**	 **42a**	 **42b**	68/2
5	 **34**	**40a**	**40b**	36[d]/3
6	 *cis*-**24**	 *cis*-**43a**	 *cis*-**43b**	64/2
7	*trans*-**24**	*trans*-**43a**	*trans*-**43b**	57/2
8	 **35**	 **44a**	 **44b**	31[f]/3
9	 R=CH_3 (**36**)	 **45**		64/2
10	R=Ph (**37**)	**46**		53/2
11	 **30**	 **47**		0
12	 **38**	 **48**		0

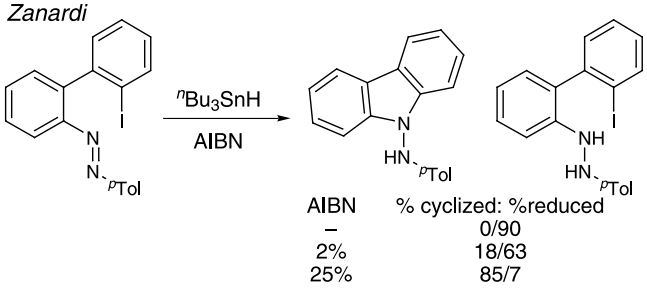
[a]See Ref. 15 for complete experimental details. [b]Observed by ^{1}H NMR. [c]Isolated yields from amine (2-3 steps depending on substrate) after trapping with PhCOCl (**39a**–**43a**), maleimide **44a**, or no trapping agent (**45**–**46**). [d]Enamines **39a**, **40a**, and **42a** are volatile. [e]Yield measured by ^{1}H NMR relative to HMDS as an internal standard. [f]A single diastereomer was observed and isolated after trapping.

indolizidine *trans*-**43b** in 57% yield for the two steps (Table 1, entry 7). Insofar as substituted cyclohexanones are readily prepared in enantiomerically pure form, this procedure constitutes a versatile platform from which to target indolizidine natural and unnatural products.

Ketimine **35** was expected to provide the exocyclic enamine by analogy to the preceding cyclizations. Interestingly, only isoindole **44a** was observed spectroscopically (^{1}H NMR) in the crude reaction mixture.[22] This isoindole could be retrieved after rapid flash chromatography, yet its purity was only marginally improved. As a result, the crude reaction mixture was instead treated with maleimide and placed in the freezer overnight. The precipitate that formed was then filtered, dried, and found to be analytically pure cycloadduct **44b**. Although the yield for these three steps is modest at best, it is significant to note both the mild conditions used to produce the isoindole, as well as the diastereomerically pure nature of the cycloadduct.

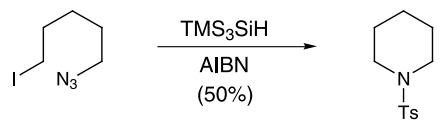
Our interest in the cyclization of ketimines **36**–**37** stemmed primarily from the possibility that these ketimines were the most likely, theoretically, to be reduced directly by stannane via either radical or non-radical pathways using reducing reaction conditions. Gratifyingly, no evidence for direct reduction to the corresponding secondary amines was obtained. Zanardi[23] and Kim[24] have demonstrated the utility of aryl diazo and alkyl azides, respectively, to serve as nitrogen sources for carbon radicals (Eqs. (5) and (6)).

Zanardi



(5)

Kim

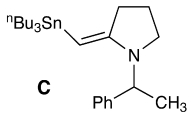


(6)

Yet both of these acceptors require either the use of aryl/alkyl iodides and/or tris(trimethylsilyl)silane to minimize products of direct reduction. Although we cannot exclude reversible addition/elimination of stannane to the ketimines studied here, it remains clear that the azomethine functional group offers this clear advantage over both azo and azide nitrogen sources for carbon radical amination.

Unfortunately, all attempts to effect 6-*exo* cyclization of a vinyl radical to ketimine nitrogen were unsuccessful. Two examples are shown in Table 1 (entries 11 and 12). Treatment of **30** with stannane and AIBN furnished only the product of direct reduction, presumably through intramolecular 1,5-hydrogen atom transfer if not intermolecularly from stannane. A second attempt utilized **38**, a substrate lacking the intramolecular hydrogen atom transfer pathway. Yet only complex product mixtures resulted.

The first demonstration that tandem bond-forming processes could be based on free radical mediated vinyl amination came in the form of a series of alkyne bisfunctionalization reactions. Although aminoacylation and aminothiolation of an alkyne were possible, only the aminostannation variant was efficient (Table 2). As expected, the nucleophilicity of the intermediate β-stannylenamine (**C**) was readily tapped by acylation,



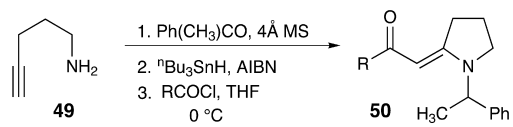
C

providing uniformly good yields (up to 60%) of vinylogous amides **50a**–**j** for the three steps (condensation, cyclization, acylation). Unfortunately, attempts to form the homologous azetidine and azirine ring systems using this tandem functionalization protocol resulted in only hydrostannation of the alkyne. Similarly, attempts to effect aminostannation on substrates analogous to **47** and **48** in which the vinyl bromide is replaced by a terminal alkyne were similarly fruitless.

4. Conclusions

The 5-*exo*-trig cyclizations of vinyl radicals to azomethine nitrogen described here provide a strategically innovative approach to the synthesis of highly nucleophilic *N*,*N*-dialkyl enamines. With only two exceptions, the expected kinetic enamine product was produced selectively and under mild, non-dehydrative conditions. At the present time, the cyclizations are generally limited to the formation of pyrrolidine derivatives, yet within this class there exists considerable generality in backbone construction. The examples described here also further demonstrate the efficiency with which carbon radicals can be added regioselectively to the nitrogen of an azomethine. Ryu has described the complementary regioselective 6-*endo*-trig

Table 2. Vinylogous amides from an alkyne hydrostannation/acylation sequence[a]



49 **50**

Entry	R	Compound	Yield (3 steps, %)[b]
1	Me	**50a**	51
2	Et	**50b**	54
3	^{i}Pr	**50c**	57
4	^{i}Bu	**50d**	53
5	Ph	**50e**	60
6	PhO	**50f**	49
7	MeO$_2$C	**50g**	36
8	CH$_3$C=CH	**50h**	28
9	ClCH$_2$	**50i**	54
10	ClCH$_2$CH$_2$	**50j**	27

[a] See Section 5 for complete details.
[b] Isolated yield after silica gel chromatography.

cyclization of a vinyl radical to azomethine carbon through the deployment of an aldimine instead of a ketimine.[25] This dramatic turnover in regioselection underscores the importance of steric effects in the control of regioselectivity.

5. Experimental

5.1. Data for compounds

5.1.1. 4-Bromo-but-3-enylamine (1). To a 0.1 M solution of phthalimide **13** (460 mg, 1.6 mmol) in methanol was added hydrazine hydrate (160 μL, 3.3 mmol). The mixture was refluxed for 1 h, during which a white precipitate formed. The reaction mixture was cooled to room temperature, concentrated, and diluted with ether. Filtration of the white solid through Celite and concentration gave the desired product (174 mg, 71%) as an inseparable 4:1 mixture of *E*/*Z* isomers; R_f=0.07 (20% EtOAc in hexanes); IR (film) 3345, 3263, 2932, 1654, 1624 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.25 (d, *J*=7.0 Hz, 1H), 6.10 (dt, *J*=7.3, 7.0 Hz, 1H), 2.77 (t, *J*=6.9 Hz, 2H), 2.32 (dt, *J*=6.9, 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 132.1, 110.2, 40.4, 33.3; HRMS (EI): exact mass calcd for C_4H_9BrN $[M+H]^+$, 151.9898. Found 151.9895.

5.1.2. 4-Bromo-pent-3-enylamine (2). To a 0.1 M solution of phthalimide **14** (256 mg, 0.87 mmol) in methanol was added hydrazine hydrate (85 μL, 1.8 mmol). The mixture was refluxed for 1 h resulting in the formation of a white precipitate. The reaction mixture was cooled to room temperature, concentrated and diluted with ether. Filtration of the white solid through Celite and concentration gave the desired amine (131.7 mg, 92%) as an inseparable 4:1 mixture of *Z*/*E* isomers, (*Z*)-isomer: R_f=0.05 (20% EtOAc/hexanes); IR (film) 3343, 1689, 1514, 1453, 1273, 1252, 1170 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.00 (qt, *J*=10.4, 2.0 Hz, 1H), 3.63 (td, *J*=9.2, 2.0 Hz, 2H), 2.94–2.88 (m, 2H), 2.41 (d, *J*=2.0 Hz, 3H), 1.43 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 129.8, 125.6, 41.5, 34.0, 29.1; HRMS (EI): exact mass calcd for $C_5H_{11}BrN$ $[M+H]^+$, 164.0075. Found 164.0078; (*E*)- isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddd, *J*=16.8, 7.6, 1.6 Hz, 1H), 2.91 (ddd, *J*=15.2, 8.8, 1.6 Hz, 2H), 2.98–2.87 (m, 2H), 2.46 (d, *J*=1.6 Hz, 3H), 1.43 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 126.5, 124.3, 41.2, 36.0, 29.1.

5.1.3. 4-Bromo-pent-4-enylamine (5). A solution of phthalimide **21** (1.78 g, 6.1 mmol) and hydrazine monohydrate (0.588 mL, 12.1 mmol) in methanol (30 mL) was heated to 65°C for 1.5 h. The reaction mixture was cooled to room temperature, concentrated, and diluted with CH_2Cl_2. The solution was filtered to remove the white solid and concentrated to give the amine (972 mg, 97%) as a yellow liquid; R_f=0.05 (20% EtOAc in hexanes); IR (film) 3362, 2938, 1629, 1585, 1431 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.59 (s, 1H), 5.40 (s, 1H), 2.73 (t, *J*=7.0 Hz, 2H), 2.48 (t, *J*=7.5 Hz, 2H), 1.71 (quint, *J*=7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 134.4, 116.9, 41.2, 39.1, 32.1; HRMS (CI): exact mass calcd for $C_5H_{11}BrN$ $[M+H]^+$, 166.0054. Found 166.0049.

5.1.4. 2-(1-Bromo-vinyl)-benzylamine (7). Alcohol **26** (1.9 g, 14.4 mmol), CBr_4 (8.61 g, 26.1 mmol), and 2,6-lutidine (8.2 mL, 70.4 mmol) were combined in cold (5°C) dichloromethane (40 mL) and treated dropwise with a solution of PPh_3 (7.64 g, 29.1 mmol) in dichloromethane (10 mL). The mixture was stirred for 12 h prior to concentration, addition of ether, and removal of $POPh_3$ by filtration through Celite. The solution was washed with 1N HCl, dried, and concentrated. The residual yellow oil was purified by flash chromatography (neutral alumina, 5% ethyl acetate in hexanes) to give the bromide as a yellow oil (2.6 g, 93%), R_f=0.66 (SiO_2, 40% CH_2Cl_2/hexanes); IR (film) 3292, 2109, 1488 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J*=7.5, 1.2 Hz, 1H), 7.47 (dd, *J*=7.8, 1.1 Hz, 1H), 7.36 (dt, *J*=7.5, 1.5 Hz, 1H), 7.29 (dt, *J*=7.5, 1.4 Hz, 1H), 4.71 (s, 2H), 3.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 167.9, 140.1, 133.5, 130.0, 129.6, 128.7, 83.1, 80.9, 31.8; HRMS (EI): exact mass calcd for C_9H_7Br $[M]^+$, 193.9731. Found 193.9731. A cold (−78°C) dichloromethane solution (20 mL) of *ortho*-ethynyl-benzyl bromide (1.0 g, 5 mmol) was treated with boron tribromide (5 mL, 1 M in CH_2Cl_2) dropwise over 45 min. The solution was warmed to room temperature and stirred for 45 min prior to the addition of water and the final 10 min stirring period. Following concentration, the crude oil was diluted with hexanes (70 mL) and acetic acid (5.5 mL), and the solution was refluxed for 3 h. The reaction mixture was cooled, washed with water, dried and concentrated. Flash chromatography (neutral alumina, 100% hexanes, then 10% dichloromethane in hexanes) furnished the targeted vinyl bromide (990 mg, 72%) as a yellow oil; R_f=0.33 (100% hexanes); IR (film) 1630 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J*=7.6, 1.9 Hz, 1H), 7.37–7.32 (m, 3H), 6.01 (d, *J*=1.7 Hz, 1H), 5.99 (d, *J*=1.7 Hz, 1H), 4.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 140.5, 135.1, 131.2, 130.0, 129.7, 128.9, 122.8, 107.2, 31.0; HRMS (EI): exact mass calcd for $C_9H_7Br_2$ $[M]^+$, 273.8993. Found 273.8996. A solution of the bromide (2.5 g, 9.1 mmol) and potassium phthalimide (4.2 g, 22.7 mmol) in DMF (40 mL) was warmed (60°C) for 12 h. The mixture was cooled, concentrated in vacuo, diluted with CH_2Cl_2, and filtered. The filtrate was concentrated, and the product purified by chromatography (neutral alumina, 5% ethyl acetate in hexanes) to give the desired product as a white solid (1.3 g, 43% yield); R_f=0.73 (30% EtOAc/hexanes); IR (film) 3059, 1983, 1770, 1721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J*=5.4, 3.1 Hz, 2H), 7.74 (dd, *J*=8.5, 3.1 Hz, 2H), 7.34–7.31 (m, 1H), 7.26 (dd, *J*=4.9, 3.9 Hz, 2H), 7.20 (dd, *J*=3.9, 3.9 Hz, 1H), 6.01 (d, *J*=1.5 Hz, 1H), 5.95 (d, *J*=1.5 Hz, 1H), 5.05 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.3, 139.9, 134.4, 133.7, 132.3, 129.6, 129.5, 127.8, 127.5, 127.3, 123.7, 122.7, 39.2; HRMS (EI): exact mass calcd for $C_{17}H_{12}BrNO_2$ $[M]^+$, 341.0051. Found 341.0037. A solution of the phthalimide (273 mg, 0.86 mmol) and hydrazine monohydrate (85.6 mg, 1.71 mmol) in methanol (6 mL) was warmed (60°C) for 12 h. The solvent was then removed under vacuum, and the residue was treated with ether and filtered through Celite. Concentration of the filtrate gave analytically pure amine (153 mg, 84%) as a yellow oil; R_f=0.18 (30% EtOAc/hexanes); IR (film) 3371, 3288, 3062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J*=7.4 Hz, 1H), 7.34 (ddd, *J*=8.7, 7.0, 1.9 Hz, 1H), 7.26 (dd, *J*=5.3, 1.6 Hz, 1H), 7.24

(ddd, J=7.8, 7.8, 1.3 Hz, 1H), 5.90 (d, J=1.6 Hz, 1H), 5.79 (d, J=1.6 Hz, 1H), 4.00 (s, 2H), 1.86–1.79 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 140.9, 139.6, 135.1, 129.6, 129.4, 128.28, 127.0, 121.7, 44.9; HRMS (EI): exact mass calcd for $C_9H_{11}N$ $[M+H]^+$, 212.0075. Found 211.9889.

5.1.5. 2-(2-Bromo-propenyl)-phenylamine (8). Smithers' salt, $Ph_3PC(CH_3)Br_2$ (6.99 g, 13.3 mmol) was warmed in a round-bottom flask under vacuum for 10 min. After the flask was flushed with nitrogen, THF (100 mL) was added, the resulting suspension was cooled to −78°C, and ^{n}BuLi added (4.25 mL, 2.5 M in hexanes, 10.6 mmol) over a 5 min period. The dark red–brown solution was stirred 2 h prior to addition of aldehyde **28** (1.18 g, 5.3 mmol). The solution was stirred for 12 h, diluted with water, and extracted with ether. The combined organic layers were dried and concentrated, and the orange oily residue was purified by flash chromatography (SiO_2, 10% ethyl acetate in hexanes) to furnish the Z-vinyl bromide (>95:5) as a yellow oil (725 mg, 44%); R_f=0.60 (20% EtOAc/ hexanes); IR (film) 3429, 2978, 1731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J=7.0 Hz, 1H), 7.39–7.28 (m, 2H), 7.08 (dd, J=7.4, 7.4 Hz, 1H), 6.64 (s, 1H), 6.39 (s, 1H), 2.56 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 153.0, 135.8, 134.1, 133.9, 129.9, 124.8, 123.2, 80.9, 30.0, 28.6; HRMS (EI): exact mass calcd for $C_{14}H_{19}BrNO_2$ $[M+H]^+$, 312.0582. Found 312.0606. To a solution of protected amine (714 mg, 2.3 mmol) in CH_2Cl_2 (40 mL) was added trifluoroacetic acid (2 mL) at 0°C. The solution was warmed to room temperature over 6 h, washed with 1 M NaOH, dried and concentrated to an oil that was purified by flash chromatography (SiO_2, 10% ethyl acetate in hexanes) to furnish the aniline as a yellow oil (308 mg, 64%); R_f=0.22 (10% EtOAc/hexanes); IR (film) 3452, 3372, 3026 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J=6.4 Hz, 1H), 7.14 (ddd, J=7.5, 7.5, 1.2 Hz, 1H), 6.80 (ddd, J=7.5, 7.5, 0.9 Hz, 1H), 6.73 (dd, J=7.9, 0.7 Hz, 1H), 6.61 (s, 1H), 2.53 (d, J=1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 143.9, 130.1, 129.0, 126.0, 125.3, 123.2, 118.5, 115.7, 30.0; HRMS (EI): exact mass calcd for $C_9H_{11}BrN$ $[M+H]^+$, 210.9997. Found 210.9995. Anal. calcd for $C_9H_{10}BrN$: C, 50.97; H, 4.75; N, 6.60. Found: C, 51.19; H, 4.80; N, 6.43.

5.1.6. 3-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-propional-dehyde (12). A mixture of 3-aminopropan-1-ol (2.25 g, 30 mmol) (**11**), phthalic anhydride (4.44 g, 30 mmol), and DMAP (402 mg, 3.0 mmol) were refluxed at 120°C for 2 h. The mixture was then cooled to room temperature, diluted with CH_2Cl_2 and washed with water. The crude residue was dried and concentrated to give a thick paste that was purified by column chromatography (silica gel, 30% ethyl acetate in hexanes) to give the desired product (3.94 g, 64%) as a white solid, mp 73–75°C; R_f=0.22 (40% EtOAc/hexanes); IR (film) 3464, 2949, 1710, 1649, 1399 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.84 (m, 2H), 7.76–7.72 (m, 2H), 4.13 (t, J=6.2 Hz, 2H), 3.82 (t, J=6.9 Hz, 2H), 2.05 (quint, J=6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.5, 134.2, 132.2, 123.5, 62.1, 35.3, 27.7; HRMS (EI): exact mass calcd for $C_{11}H_{11}NO_3$ $[M]^+$, 205.0739. Found 205.0737. To a cooled (0°C) mixture of alcohol (0.52 g, 2.5 mmol) in CH_2Cl_2 (7 mL) was added Dess–Martin periodinane (1.08 g, 2.5 mmol). The mixture was warmed to room temperature and stirred for 20 min prior to washing with satd aq $Na_2S_2O_3$. The crude product was dried, concentrated and purified by flash chromotography (silica gel, 30% ethyl acetate in hexanes) to furnish a white solid (0.33 g, 65%), mp 119–121°C; R_f=0.30 (30% EtOAc/ hexanes); IR (film) 3080, 2950, 1710, 1614, 1370 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.83 (dd, J=5.4, 3.1 Hz, 2H), 7.71 (dd, J=5.4, 3.1 Hz, 2H), 4.02 (t, J=7 Hz, 2H), 2.86 (dt, J=6.8, 1.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) ppm 199.7, 168.3, 134.4, 132.2, 123.6, 42.6, 31.9; HRMS (EI): exact mass calcd for $C_{11}H_9NO_3$ $[M]^+$, 203.0582. Found 203.05845.

5.1.7. 2-(4-Bromo-but-3-enyl)-isoindole-1,3-dione (13). To a cooled (−78°C) suspension of Ph_3PCHBr_2 (3.73 g, 7.2 mmol) in THF (30 mmol) was added ^{n}BuLi (4.1 mL, 1.8 M in hexanes) dropwise. The solution was stirred for 2 h, after which a solution of aldehyde **12** (734 mg, 3.6 mmol) in THF (10 mL) was added and the reaction mixture was stirred for 2 h. The mixture was warmed to room temperature, quenched with water and extracted with diethyl ether. The crude product was dried, concentrated, and purified by flash chromatography (silica gel, 20% ethyl acetate in hexanes) to give the vinyl bromide as a light orange oil (496 mg, 49%); R_f=0.12 (10% EtOAc/hexanes); IR (film) 2941, 2336, 1773, 1711, 1396 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.83 (m, 2H), 7.71–7.70 (m, 2H), 6.22 (d, J=7.1 Hz, 1H), 6.14 (dt, J=13.3, 6.8 Hz, 1H), 3.81 (t, J=6.8 Hz, 2H), 2.61 (ddd, J=13.7, 6.8, 1.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 134.7, 134.2, 131.0, 123.5, 110.9, 36.3, 32.2, 29.4; HRMS (EI): exact mass calcd for $C_{12}H_9NO_2$ $[M-H]^+$, 279.9796. Found 279.9787.

5.1.8. 2-(4-Bromo-pent-3-enyl)-isoindole-1,3-dione (14). To a cooled (−78°C) suspension of $Ph_3PC(CH_3)Br_2$ (5.77 g, 11 mmol) in THF (30 mL) was added ^{n}BuLi (6.8 mL, 1.6 M in hexanes) dropwise. To this solution was added a solution of the aldehyde **12** (1.11 g, 5.5 mmol) in THF (10 mL) and the reaction mixture was stirred for 4 h. The mixture was warmed to room temperature, quenched with water and extracted with diethyl ether. The crude product was dried, concentrated, and purified by flash column chromatography to gave the vinyl bromides as an inseparable 4:1 mixture of Z/Eisomers (636 mg, 39%); (E)-isomer: R_f=0.32 (20% EtOAc/hexanes); IR (film) 1771, 1710, 1612, 1437, 1396, 1355, 1186, 1063 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J=5.4, 3.0 Hz, 2H), 7.70 (dd, J=5.5, 3.1 Hz, 2H), 5.64 (ddd, J=7.8, 7.8, 1.5 Hz, 1H), 3.75 (t, J=6.8 Hz, 2H), 2.52 (ddd, J=6.9, 6.1, 0.8 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.5, 134.1, 132.3, 127.8, 125.1, 123.4, 36.6, 31.1, 29.1; HRMS (CI): exact mass calcd for $C_{13}H_{12}NO_2$ $[M]^+$, 293.0051. Found 293.0050. (Z)-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J=5.4, 3.0 Hz, 2H), 7.70 (dd, J=5.5, 3.1 Hz, 2H), 5.84 (ddd, J=7.8, 7.8, 1.2 Hz, 1H), 3.71 (t, J=7.2 Hz, 2H), 2.40 (dd, J=7.8, 7.5 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.4, 134.3, 132.2, 127.8, 125.4, 123.5, 36.9, 31.1, 28.8.

5.1.9. 2-(Benzhydrylidene-amino)-5-bromo-pent-4-enoic acid *tert*-butyl ester (18). To a solution of Schiff base **17** (383 mg, 1.30 mmol) in CH_2Cl_2 (3 mL) was added sodium hydroxide (1.04 g, 26.0 mmol) in water (1.5 mL), and benzyltriethylammonium chloride (59.1 mg, 260 mmol).

1,3-Dibromopropene (156 μL, 1.56 mmol, 1:1 *Z*/*E*) was added, and the reaction mixture was stirred for 20 min and then diluted with ether. The layers were separated, the aqueous layer was extracted with ether, and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude oil was purified by flash chromatography (neutral alumina, 10% CH_2Cl_2 in hexanes) to give a yellow oil (430 mg, 80%) as an inseparable mixture (1:1) of *Z*/*E* olefin stereroisomers: R_f=0.58 (10% EtOAc/hexanes); IR (film) 3292, 3058, 1619 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (ddd, *J*=7.0, 3.4, 1.5 Hz, 2H), 7.48–7.44 (m, 3H), 7.42–7.38 (m, 1H), 7.36 (dd, *J*=7.5, 3.5 Hz, 2H), 7.19 (dt, *J*=7.1, 1.7 Hz, 2H), 6.22 (ddd, *J*=12.5, 12.5, 6.7 Hz, 1H), 6.10 (d, *J*=3.1 Hz, 1H), 4.10 (dd, *J*=6.8, 5.5 Hz, 0.5H), 4.00 (dd, *J*=7.0, 5.9 Hz, 0.5H), 2.86–2.77 (m, 0.5H), 2.76–2.70 (m, 0.5H), 2.64–2.60 (m, 1H), 1.47 (s, 4.5H), 1.46 (s, 4.5H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 171.8, 171.0, 170.7, 170.5, 139.8, 139.7, 136.7, 136.6, 134.4, 131.3, 130.64, 130.57, 129.06, 129.13, 128.9, 128.7, 128.31, 128.26, 128.05, 120.12, 107.1, 109.8, 64.8, 65.4, 37.1, 34.3; HRMS (EI): exact mass calcd for $C_{22}H_{24}BrNO_2$ $[M]^+$, 413.0990. Found 413.0987.

5.1.10. 2-(Benzhydrylidene-amino)-5-bromo-hex-4-enoic acid *tert*-butyl ester (19). To a solution of Schiff base **17** (200 mg, 0.68 mmol) in CH_2Cl_2 (2 mL) was added sodium hydroxide (542 mg, 14 mmol) in water (1.1 mL), and benzyltriethylammonium chloride (30.9 mg, 0.14 mmol). 1,3-Dibromopropene[26] (229 μL, 2.0 mmol, 1:1 *Z*/*E*) was added, and the reaction mixture was warmed to room temperature, stirred for 12 h, and then diluted with ether. The layers were separated, the aqueous layer was extracted with ether, and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude oil was purified by flash chromatography (neutral alumina, 4% ethyl acetate in hexanes) to give the product as a yellow oil (280 mg, 96%). The product was an inseparable mixture of *Z*/*E* isomers (1:4); *E* isomer: R_f=0.55 (5% EtOAc/hexanes); IR (film) 3058, 2976, 1729, 1620 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J*=7.8, 1.6 Hz, 2H), 7.49–7.45 (m, 4H), 7.36 (dd, *J*=7.5, 1.6 Hz, 2H), 7.22 (dd, *J*=7.8, 1.6 Hz, 2H), 5.74 (ddd, *J*=7.9, 7.9, 1.2 Hz, 1H), 4.01 (dd, *J*=7.6, 5.4 Hz, 1H), 2.62 (dd, *J*=7.8, 7.8 Hz, 1H), 2.60 (dd, *J*=7.2, 2.8 Hz, 1H), 2.20 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 170.8, 139.6, 136.7, 132.7, 130.6, 130.3, 129.1, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 122.0, 81.5, 65.6, 33.7, 28.3, 23.8; HRMS (CI): exact mass calcd for $C_{23}H_{27}BrNO_2$ $[M+H]^+$, 428.1125. Found 428.1234; *Z* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J*=7.8, 1.6 Hz, 2H), 7.49–7.45 (m, 4H), 7.36 (dd, *J*=7.5, 1.6 Hz, 2H), 7.22 (dd, *J*=7.8, 1.6 Hz, 2H), 5.74 (ddd, *J*=7.9, 7.9, 1.2 Hz, 1H), 3.96 (dd, *J*=7.8, 5.4 Hz, 1H), 2.67–2.58 (m, 2H), 2.20 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 170.8, 139.6, 136.7, 132.7, 130.6, 130.3, 129.1, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 122.0, 81.5, 65.6, 31.9, 28.3, 22.9.

5.1.11. 2-(4-Bromo-pent-4-enyl)-isoindole-1,3-dione (21). To a cold (−78°C) solution of alkyne **20** (3.14 g, 14.7 mmol) in CH_2Cl_2 (12 mL) was added boron tribromide (14.7 mL, 1.0 M in CH_2Cl_2) dropwise 20 min. The solution was warmed to room temperature and stirred for an additional 45 min prior to the addition of water (10 mL). Following extraction with CH_2Cl_2 and concentration, the orange/yellow oil was diluted with hexanes (50 mL) and acetic acid (3 mL) and the suspension was refluxed for 3 h. The reaction mixture was cooled, neutralized with sodium bicarbonate, and washed with brine. The crude product was dried, concentrated, and purified by flash chromatography (SiO_2, 5% ethyl acetate in hexanes) to give the vinyl bromide (3.5 g, 81%) as a clear oil; R_f=0.20 (5% EtOAc in hexanes); IR (film) 3465, 3060, 2939, 1770, 1710, 1629, 1467, 1396, 1371 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J*=5.5, 3.1 Hz, 2H), 7.74 (dd, *J*=5.4, 3.0 Hz, 2H), 5.66 (s, 1H), 5.44 (s, 1H), 3.74 (t, *J*=7.1 Hz, 2H), 2.51 (t, *J*=7.3 Hz, 2H), 1.99 (quint, *J*=7.4 Hz, 2H); ^{13}C NMR (ppm) (100 MHz, $CDCl_3$) 168.6, 134.2, 133.1, 132.3, 123.5, 117.7, 39.0, 37.1, 27.2; HRMS (CI): exact mass calcd for $C_{13}H_{13}BrNO_2$ $[M+H]^+$, 296.0109. Found 296.0108.

5.1.12. Benzhydryl-[2-(2-bromo-allyl)-cyclohexyl]-amine (23). A solution of ketone **22**[19] (0.981 g, 4.5 mmol), diphenylmethyl amine (794 μL, 4.6 mmol), and benzene (5 mL) was stirred with 4 Å molecular sieves at 80°C for 24 h. The crude mixture was then cooled, filtered through Celite, and concentrated to an orange oil (1.48 g, 85%); IR (film) 3060, 1710, 1629 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.40 (m, 4H), 7.36–7.20 (m, 6H), 5.64 (s, 1H), 5.48 (s, 1H), 5.24 (s, 1H), 3.06–2.94 (m, 2H), 2.74–2.01 (m, 4H), 1.94–1.57 (m, 3H), 1.33–1.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 172.8, 145.9, 134.6, 128.8, 128.6, 127.73, 127.67, 127.23, 127.19, 119.0, 60.0, 48.6, 42.5, 41.4, 33.2, 28.2, 25.4; HRMS (EI): exact mass calcd for $C_{22}H_{24}BrN$ $[M]^+$, 381.1092. Found 381.1109. To a solution of this imine (1.01 g, 2.6 mmol) in chilled methanol (16 mL) was added sodium borohydride (101 mg, 2.6 mmol). The solution was stirred for 15 min, then warmed to room temperature for an additional 2 h. The solution was quenched with satd aq NH_4Cl and extracted with CH_2Cl_2. The organic layers were combined, dried with Na_2SO_4, and concentrated. Flash chromatography (SiO_2, 7% ethyl acetate in hexanes) provided the product as an orange oil (602.2 mg, 59%) and an inseparable mixture of *cis*/*trans* diastereomers (3:1); R_f=0.57 (10% EtOAc/hexanes); IR (film) 3330, 3060, 3025, 2926, 2853, 1628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.41 (m, 3H), 7.32–7.28 (m, 5H), 7.25–7.20 (m, 2H), 5.55 (s, 1H), 5.42 (s, 1H), 4.97 (s, 1H), 2.71 (m, 1H), 2.61 (d, *J*=4.6 Hz, 1H), 2.57 (d, *J*=9.3 Hz, 1H), 2.07–2.04 (m, 1H), 1.74–1.73 (m, 2H), 1.56–1.50 (m, 2H), 1.43–1.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 145.2, 144.4, 134.9, 128.8, 128.7, 128.0, 127.7, 127.5, 127.3, 118.0, 63.8, 53.7, 45.5, 42.2, 28.8, 26.4, 25.9, 22.4; HRMS (EI): exact mass calcd for $C_{22}H_{25}BrN$ $[M-H]^+$, 382.1170. Found 382.1170.

5.1.13. Benzhydrylidene-[2-(2-bromo-allyl)-cyclohexyl]-amine (24). Using the Honek protocol, a mixture of amine **23** (198 mg, 0.5 mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquininone (119 mg, 0.5 mmol) and benzene (10 mL) was stirred at 60°C for 45 min, then cooled to room temperature. The solvent was removed under vacuum and the residue was chromatographed (neutral alumina, 3% dichloromethane in hexanes) to give the ketimine as a colorless oil (153.7 mg, 78%). This mixture of *cis*/*trans* diastereomers (3:1) was separated by flash chromatography; *cis*-diastereomer: R_f=0.65 (Al_2O_3, 5% EtOAc/hexanes); IR

(film) 3059, 1626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J=6.6, 1.3 Hz, 2H), 7.48–7.42 (m, 3H), 7.38–7.32 (m, 3H), 7.15 (dd, J=6.0, 1.7 Hz, 2H), 5.51 (s, 1H), 5.38 (s, 1H), 3.48 (m, 1H), 2.34 (ddd, J=14.1, 14.1, 3.6 Hz, 1H), 2.31 (ddd, J=14.5, 14.5, 8.1 Hz, 1H), 1.93–1.82 (m, 4H), 1.68–1.63 (m, 1H), 1.58–1.50 (m, 2H), 1.44–1.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.9, 140.5, 137.4, 134.4, 129.9, 128.6, 128.3, 128.2, 128.0, 117.8, 60.0, 45.0, 40.2, 33.9, 26.3, 25.8, 21.7; HRMS (EI): exact mass calcd for $C_{22}H_{24}BrN$ $[M]^+$, 380.1013. Found 380.1030; *trans*-diastereomer: R_f=0.53 (Al_2O_3, 5% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J=7.8, 1.6 Hz, 2H), 7.47–7.42 (m, 3H), 7.37–7.30 (m, 3H), 7.12 (dd, J=7.8, 1.9 Hz, 2H), 5.47 (s, 1H), 5.39 (s, 1H), 2.90 (ddd, J=9.9, 9.8, 4.3 Hz, 1H), 2.61 (dd, J=14.1, 3.1 Hz, 1H), 2.13–2.05 (m, 1H), 1.86 (dd, J=13.4, 2.4 Hz, 1H), 1.78–1.61 (m, 4H), 1.36–1.26 (m, 2H), 1.19–1.10 (m, 1H), 0.70 (dddd, J=13.0, 13.0, 13.0, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 167.1, 140.3, 137.7, 133.9, 130.0, 128.72, 128.67, 128.4, 128.3, 127.8, 117.8, 66.0, 46.1, 41.9, 34.1, 29.4, 25.8, 24.9.

5.1.14. (2-Ethynyl-phenyl)-methanol (26). A solution of trimethylsilyl acetylene (2.82 mL, 20 mmol) and *ortho*-iodobenzyl alcohol (2.33 g, 10 mmol) in triethylamine (150 mL) was degassed using the freeze-pump-thaw method and added to a flask containing $Pd(PPh_3)_4$ (150 mg, 196 μmol). The mixture was warmed to 40°C for 5 h. The solvent was removed in vacuo, and the residue was rinsed over a Celite pad with Et_2O. The organic washes were concentrated to give an orange–yellow oil (2.0 g, 100%), R_f=0.16 (40% CH_2Cl_2/hexanes); IR (film) 3310, 3262, 2106 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, J=7.5, 0.8 Hz, 1H), 7.42 (d, J=7.5 Hz, 1H), 7.33 (dt, J=6.5, 1.2 Hz, 1H), 7.23 (dd, J=7.5, 1.1 Hz, 1H), 4.82 (d, J=5.5 Hz, 2H), 2.70 (t, J=5.5 Hz, 1H), 0.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 143.8, 132.6, 129.2, 127.9, 127.8, 121.2, 102.3, 99.9, 63.9, 0.03; HRMS (EI): exact mass calcd for $C_{12}H_{16}OSi$ $[M]^+$, 204.0970. Found 204.0979. The alcohol (2.0 g, 9.9 mmol) and potassium carbonate (691 mg, 5 mmol) in methanol (60 mL) was stirred for 3 h. The solvent was removed, satd aq NH_4Cl was added, and the resulting mixture was extracted with ether. The organic layers were combined, washed with water and brine, dried, and concentrated to an analytically pure yellow solid (1.3 g, 100%), mp 64–66°C; R_f=0.25 (SiO_2, 60% CH_2Cl_2/hexanes); IR (film) 3313, 3262, 2101, 1963 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J=7.6 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.37 (dd, J=7.6, 7.4 Hz, 1H), 7.26 (dd, J=7.5, 7.4 Hz, 1H), 4.83 (s, 2H), 3.35 (s, 1H), 1.28 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 143.5, 133.1, 129.5, 127.6, 127.5, 120.4, 82.2, 63.9, 30.0; HRMS (EI): exact mass calcd for C_9H_8O $[M]^+$, 132.0575. Found 132.0580.

5.1.15. (2-Formyl-phenyl)-carbamic acid *tert*-butyl ester (28). A THF solution (45 mL) of 2-aminobenzyl alcohol (2.01 g, 16.3 mmol) and di-*tert*-butyl carbonate (3.7 g, 16.9 mmol) was stirred at 25°C for 12 h. The solvent was removed by vacuum and the residue purified by flash chromatography (SiO_2, 30% ethyl acetate in hexanes) to give the carbamate as a yellow oil (3.3 g, 92%). R_f=0.48 (40% EtOAc/hexanes); IR (film) 3358, 2979, 1729, 1703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J=8.1 Hz, 1H), 7.72 (br s, 1H), 7.29 (ddd, J=8.7, 8.7, 1.3 Hz, 1H), 7.13 (dd, J=7.5, 1.2 Hz, 1H), 7.00 (ddd, J=7.4, 7.4, 0.8 Hz, 1H), 4.61 (d, J=2.8 Hz, 2H), 2.90 (br s, 1H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 153.8, 138.1, 129.5, 129.24, 129.16, 123.4, 121.4, 80.7, 64.3, 28.6; HRMS (EI): exact mass calcd for $C_{12}H_{17}NO_3$ $[M]^+$, 223.1208. Found 223.1206. Anal. calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.26; H, 7.72; N, 6.20. The benzyl alcohol (1.17 g, 5.2 mmol) in cold CH_2Cl_2 (35 mL) was treated with the Dess–Martin periodinane (3.41 g, 8.0 mmol). The mixture was stirred at 0°C for 20 min, then at room temperature for 30 min prior to a series of washes with satd aq $Na_2S_2O_3$, $NaHCO_3$, and H_2O. The organic layer was dried, the solvent was removed, and the residue was chromatographed (SiO_2, 10% ethyl acetate in hexanes) to give the aldehyde as a pale yellow solid (605 mg, 52%), mp 57–58°C; R_f=0.52 (20% EtOAc/hexanes); IR (film) 3291, 2980, 1732, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.39 (br s, 1H), 9.91 (s, 1H), 8.47 (d, J=8.5 Hz, 1H), 7.64 (dd, J=7.7, 1.6 Hz, 1H), 7.58 (ddd, J=7.7, 7.7, 1.6 Hz, 1H), 7.14 (ddd, J=7.5, 7.5, 0.9 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 195.3, 153.1, 142.0, 136.3, 136.2, 121.7, 121.4, 118.5, 81.2, 28.5; HRMS (EI): exact mass calcd for $C_{12}H_{16}NO_3$ $[M+H]^+$, 221.1052. Found 221.1045. Anal. calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.35; H, 6.73; N, 6.30.

5.1.16. 2-(Benzhydrylidene-amino)-3-[2-(1-bromo-vinyl)-phenyl]-propionic acid *tert*-butyl ester (30). To a solution of Schiff base **17** (50.0 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was added NaOH (140.2 mg), 3.5 mmol), Et_3BnNCl (9.1 mg, 0.40 mmol) and H_2O (1 mL). The biphasic mixture was stirred for several minutes prior to addition of dibromide **29** (47.2 mg, 0.17 mmol). The mixture was stirred for 6 h, then diluted with CH_2Cl_2 and separated. The organic layer was washed with H_2O, dried and concentrated to a yellow oil that was purified by flash chromatography (neutral alumina, 5% ethyl acetate in hexanes) to furnish the product as a colorless oil (52.3 mg, 63%); R_f=0.33 (Al_2O_3, 10% EtOAc/hexanes); IR (film) 3059, 1733, 1625 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J=8.5 Hz, 2H), 7.35–7.33 (m, 1H), 7.28 (dd, J=6.1, 5.8 Hz, 4H), 7.24–7.20 (m, 4H), 7.15–7.09 (m, 3H), 5.56 (s, 1H), 5.00 (s, 1H), 4.19 (dd, J=9.8, 3.7 Hz, 1H), 3.49 (dd, J=13.7, 3.7 Hz, 1H), 3.20 (dd, J=13.4, 9.8 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 171.1, 170.5, 141.0, 139.7, 136.6, 136.0, 132.7, 132.0, 130.4, 130.3, 129.4, 129.0, 128.7, 128.5, 128.4, 128.3, 128.2, 127.9, 126.6, 121.8, 81.3, 67.2, 36.9, 28.3; HRMS (EI): exact mass calcd for $C_{28}H_{28}BrNO_2$ $[M]^+$, 489.1303. Found 489.1316.

5.1.17. 1-[2-((1*E*-1-aza-2,2-diphenylvinyl)phenoxy)]-2-bromoprop-2-ene (38). A mixture of *ortho*-aminophenol (445 mg, 4.08 mmol) and benzophenone imine (739 mg, 4.08 mmol) in benzene (70 mL) was refluxed for 24 h under a steady flow of nitrogen. The solvent was removed in vacuo to give the analytically pure ketimine as a colorless oil (1.00 g, 91%). R_f=0.25 (5% EtOAc/hexanes); IR (film) 3460, 2980, 2116, 1672, 1291 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=7.1 Hz, 2H), 7.60 (d, J=7.1 Hz, 1H), 7.52 (dd, J=7.4, 4.2 Hz, 1H), 7.46–7.40 (m, 4H), 7.22 (dd, J=7.6, 1.3 Hz, 2H), 6.98 (d, J=4.0 Hz, 2H), 6.50 (ddd, J=8.4, 4.0, 0.7 Hz, 1H), 6.23 (d, J=7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 168.7, 151.9, 140.0, 136.6, 136.0,

132.8, 131.3, 130.6, 130.3, 129.7, 129.5, 129.3, 128.8, 128.6, 128.5, 127.0, 120.7, 119.4, 114.8; HRMS (EI): exact mass calcd for $C_{19}H_{15}NO$ $[M]^+$, 273.1154. Found 273.1162. To a suspension of sodium hydride (33.2 mg, 1.39 mmol) in THF (5.6 mL) at −10°C was added, while stirring vigorously, a solution of the imino phenol (315 mg, 1.15 mmol) and 2,3-dibromopropene (143 μL, 1.38 mmol) in THF (5.6 mL). After 10 min the mixture was warmed to room temperature and stirred for and additional 12 h. The reddish brown solution was then quenched with H_2O (0.3 mL), concentrated, redissolved in CH_2Cl_2 (15 mL) and washed with H_2O. The resulting product was dried (Na_2SO_4), concentrated and purified by flash chromatography (SiO_2, 10% ethyl acetate in hexanes) to furnish the product as a reddish brown oil (428 mg, 95%). R_f=0.48 (10% EtOAc/hexanes); IR (film) 3058, 2912, 1955, 1882, 1627, 1481 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J*=8.2, 1.2 Hz, 2H), 7.75 (dd, *J*=8.6, 1.5 Hz, 1H), 7.57 (tt, *J*=7.3, 2.5 Hz, 2H), 7.46 (dd, *J*=8.0, 0.7 Hz, 4H), 7.38 (t, *J*=7.6 Hz, 1H), 7.22 (t, *J*=7.0 Hz, 2H), 6.83 (dtd, *J*=22.9, 8.2, 1.5 Hz, 1H), 6.69 (dt, *J*=6.4, 1.6 Hz, 1H), 5.80 (dd, *J*=3.7, 1.5 Hz, 1H), 5.52 (dd, *J*=3.7, 1.5 Hz, 1H), 4.46 (t, *J*=1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 167.8, 137.8, 132.6, 131.0, 130.3, 129.6, 129.0, 128.5, 128.4, 127.9, 124.4, 121.9, 117.3, 113.9, 70.4; HRMS (EI): exact mass calcd for $C_{22}H_{18}BrNO$ $[M]^+$, 391.0572. Found 391.0585.

5.2. General procedure for ketimine condensations

A rapidly stirred benzene solution of the amine (0.5 M), ketone (0.5 M), and 4 Å MS (1:1 w/w) was stirred at 25°C until complete conversion was achieved, as evidenced by ^1H NMR. The mixture was filtered through a pad of Celite and washed with Et_2O or benzene. The solvent was removed in vacuo to give the analytically pure ketimine which was used immediately. The same procedure was used when the benzophenone ketimine was desired, except benzophenone imine[27] was used in place of the ketone.

5.3. Representative procedure for radical cyclizations[28]

5.3.1. *tert*-Butyl-1-(diphenylmethyl)-5-methylenepyrrolidine-2-carboxylate (42b). To a solution of **19** (43 mg, 100 μmol) and $^nBu_3SnH$ (59.5 μL, 221 μmol) in hot (85°C) benzene (9.2 mL) was added a solution of AIBN (13.2 mg, 80.4 μmol) in benzene (0.8 mL) over 4 h. Thirty minutes into the addition period, an additional amount of $^nBu_3SnH$ (59.5 μL, 221 μmol) was added to the reaction mixture. The solution was refluxed for 1 h following complete AIBN addition and cooled to room temperature. The intermediate enamine could be observed by ^1H NMR spectroscopy after solvent removal. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.20 (m, 10H), 5.62 (s, 1H), 3.84 (dd, *J*=8.7, 1.3 Hz, 1H), 3.59 (s, 1H), 3.26 (s, 1H), 2.78 (ddd, *J*=7.9, 3.7, 1.9 Hz, 1H), 2.59 (dd, *J*=14.2, 7.1 Hz, 1H), 1.83 (dd, *J*=12.5, 8.2 Hz, 1H), 1.75 (s, 9H). The crude benzene solution was cooled to 5 °C and treated with triethylamine (140 μL, 1 mmol) and benzoyl chloride (60 μL, 500 μmol). The solution was allowed to warm to room temperature over 2 h. The solvent was removed and the residue subjected to flash chromatography (SiO_2, 22% ethyl acetate in hexanes) to furnish the vinylogous amide as a white solid (31.6 mg, 69%), mp 51–53°C; R_f=0.18 (20% EtOAc/hexanes); IR (film) 3063, 1729, 1631 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J*=7.1, 1.5 Hz, 2H), 7.42–7.40 (m, 1H), 7.39 (d, *J*=7.9 Hz, 2H), 7.36–7.30 (m, 6H), 7.28 (d, *J*=7.2 Hz, 2H), 7.23 (d, *J*=7.4 Hz, 2H), 5.95 (s, 1H), 5.68 (s, 1H), 4.11 (dd, *J*=9.3, 1.3 Hz, 1H), 3.78 (dd, *J*=18.2, 8.7 Hz, 1H), 3.25 (td, *J*=9.5, 9.3 Hz, 1H), 2.35 (ddt, *J*=12.9, 11.1, 9.3 Hz, 1H), 2.07 (dd, *J*=12.8, 8.8 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 188.7, 171.4, 166.5, 141.8, 139.6, 138.3, 130.7, 130.5, 130.3, 129.1, 128.9, 128.4, 128.2, 127.9, 127.8, 127.5, 92.0, 81.9, 65.7, 64.8, 32.4, 28.0; HRMS (CI, CH_4): exact mass calcd for $C_{30}H_{31}NO_3$ $[M]^+$, 453.2304. Found 453.2288.

5.4. General procedure for β-stannyl enamine acylations

The crude β-stannyl enamine was dissolved in tetrahydrofuran and cooled to 0°C. To this 0.1 M solution, an acid chloride (1 equiv.) was added dropwise. After 30 min, the solvent was removed to afford the acylated enamine product. The crude mixture was then diluted with diethyl ether and stirred at room temperature while a saturated solution of KF was added. The mixture was allowed to stir for 4–6 h. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to afford the crude product, which was purified by flash column chromatography on silica gel.

5.4.1. 1-[1-(Phenylethyl)pyrrolidin-2-ylidene]butan-2-one (50b). Following the general procedure, to the β-stannyl enamine (0.841 g, 1.77 mmol) in cold THF (0°C) propionyl chloride (0.163 g, 1.77 mmol) were added and stirred for 30 min to give the vinylogous amide in 54% yield of a clear oil. R_f=0.42 (10% acetone/CH_2Cl_2); IR (film) 3060, 3029, 2973, 2874, 1641, 1545, 1482, 1418, 1290, 1199, 1137, 1028, 958, 895, 759, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.23 (m, 5H), 5.22 (s, 1H), 4.97 (q, *J*=6.9 Hz, 1H), 3.43–3.29 (m, 2H), 3.22 (ddd, *J*=16.9, 8.1, 8.1 Hz, 1H), 3.10 (ddd, *J*=8.5, 8.5, 5.2 Hz, 1H), 2.31 (q, *J*=7.5 Hz, 2H), 1.99–1.81 (m, 2H), 1.58 (d, *J*=6.9 Hz, 3H), 1.08 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 198.3, 165.2, 140.3, 128.9, 127.8, 126.8, 89.3, 53.1, 47.1, 36.6, 33.8, 21.1, 17.0, 10.1; HRMS (EI): exact mass calcd for $C_{16}H_{21}NO$ $[M]^+$ 243.1623. Found 243.1624.

5.4.2. 3-Methyl-1-[1-(1-phenylethyl)pyrrolidin-2-ylidene]butan-2-one (50c). Following the general procedure, to the β-stannyl enamine (0.858 g, 1.81 mmol) in cold THF (0°C) iosbutyryl chloride (0.191 g, 1.81 mmol) were added and stirred for 30 min to give the vinylogous amide in 57% yield of a yellow oil. R_f=0.48 (10% acetone/CH_2Cl_2); IR (film) 3050, 2963, 2932, 2867, 1641, 1543, 1482, 1290, 1177, 1077, 990, 841, 772, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.24 (m, 5H), 5.22 (s, 1H), 4.97 (q, *J*=6.9 Hz, 1H), 3.42–3.30 (m, 2H), 3.24 (ddd, *J*=16.8, 7.8, 7.8 Hz, 1H), 3.11 (ddd, *J*=9.8, 8.3, 5.2 Hz, 1H) 2.49 (septet, *J*=6.8 Hz, 1H), 1.99–1.81 (m, 2H), 1.59 (d, *J*=6.9 Hz, 3H), 1.08 (d, *J*=6.8 Hz, 3H) 1.06 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 201.8, 165.7, 140.4, 128.9, 127.8, 126.8, 88.5, 53.2, 47.2, 41.1, 33.9, 21.1, 20.1,

20.0, 17.0; HRMS (CI): exact mass calcd for $C_{17}H_{23}NO$ $[M]^+$ 257.1780. Found 257. 1783.

5.4.3. 2-Oxo-3-[1-(1-phenylethyl)pyrrolidin-2-ylidene]-propionic acid methyl ester (50g). Following the general procedure, to the β-stannyl enamine (0.985 g, 2.06 mmol) in cold THF (0°C) methyl chlorooxoacetate (0.19 mL, 2.06 mmol) were added and stirred for 30 min to give the vinylogous amide in 36% yield of an off white solid, mp 75–76.5°C; R_f=0.40 (100% ethyl acetate); IR (film) 3000, 2948, 1719, 1627, 1542, 1454, 1296, 1199, 1113, 1001, 787, 765, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.25 (m, 5H), 6.08 (s, 1H), 5.19 (q, J=6.9 Hz, 1H), 3.82 (s, 3H), 3.64–3.40 (m, 2H), 3.34 (ddd, J=16.4, 7.9, 7.9 Hz, 1H), 3.15 (ddd, J=10.6, 8.4, 5.5 Hz, 1H), 2.02–1.88 (m, 2H), 1.63 (d, J=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 176.8, 170.3, 166.0, 139.0, 129.1, 126.9, 86.5, 53.8, 52.6, 48.0, 34.8, 20.5, 16.6; HRMS (CI): exact mass calcd for $C_{16}H_{19}NO_3$ $[M]^+$ 273.1365. Found 273.1356.

5.4.4. 1-[1-(1-Phenylethyl)pyrrolidin-2-ylidene]pent-3-en-2-one (50h). Following the general procedure, to the β-stannyl enamine (0.301 g, 0.629 mmol) in cold THF (0°C) crotonyl chloride (0.104 g, 0.629 mmol) were added and stirred for 30 min to give the vinylogous amide in 28% of a yellow oil. R_f=0.15 (40% ethyl acetate/hexanes); IR (film) 2974, 2933, 1661, 1607, 1538, 1481, 1291, 1137, 1082, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.24 (m, 5H), 6.71 (dq, J=15.3, 7.1 Hz, 1H), 6.14 (d, J=15.3 Hz, 1H), 5.27 (s, 1H), 5.02 (q, J=6.9 Hz, 1H), 3.51–3.42 (m, 1H), 3.39–3.26 (m, 2H), 3.15–3.09 (m, 1H), 1.99–1.86 (m, 2H), 1.82 (d, J=6.9 Hz, 3H), 1.60 (d, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 186.4, 166.7, 140.2, 136.2, 134.6, 128.9, 127.9, 126.8, 90.4, 53.3, 47.4, 34.2, 21.1, 18.1, 17.0; HRMS (CI): exact mass calcd for $C_{17}H_{21}NO$ $[M]^+$ 255.1623. Found 255.1613.

5.4.5. 1-Chloro-3-[1-phenylethyl)pyrrolidin-2-ylidene]-propan-2-one (50i). Following the general procedure, to the β-stannyl enamine (0.147 g, 0.31 mmol) in cold THF (0°C) 2-chloroethynyl chloride (24 μL, 0.31 mmol) were added and stirred for 30 min to give the vinylogous amide of a light yellow oil. R_f=0.68 (20% acetone/CH_2Cl_2); IR (film) 3060, 3029, 2978, 2938, 2877, 1629, 1582, 1481, 1454, 1417, 1314, 1295, 1205, 1176, 1001, 759, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.42 (m, 5H), 5.55 (s, 1H), 5.04 (q, J=6.9 Hz, 1H), 3.97 (s, 2H), 3.44–3.36 (m, 2H), 3.25 (ddd, J=16.6, 8.1, 8.1 Hz, 1H), 3.16 (ddd, J=10.2, 8.5, 5.3 Hz, 1H), 2.08–1.84 (m, 2H), 1.61 (d, J=6.9 Hz, 3H); ^{13}C NMR (ppm) (100 MHz, $CDCl_3$) ppm 188.0, 168.0, 139.6, 129.0, 128.1, 126.8, 86.0, 53.6, 48.8, 47.8, 34.3, 20.7, 16.9; HRMS (CI): exact mass calcd for $C_{15}H_{18}ClNO$ $[M]^+$ 263.1077. Found 263.1079.

5.4.6. 4-Chloro-1-[1-(phenylethyl)pyrrolidin-2-ylidene]-butan-2-one (50j). Following the general procedure, to the β-stannyl enamine (0.645 g, 1.35 mmol) in cold THF (0°C) 3-chloropropionyl chloride (0.172 g, 1.35 mmol) were added and stirred for 30 min to give the vinylogous amide in light yellow oil. R_f=0.71 (20% acetone/CH_2Cl_2); IR (film) 3040, 2975, 2876, 1634, 1540, 1481, 1495, 1452, 1293, 1177, 1048, 993, 758, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 5H), 5.19 (s, 1H), 4.98 (q, J=6.9 Hz, 1H), 3.86–3.76 (m, 2H), 3.44–3.33 (m, 2H), 3.24 (ddd, J=16.8, 8.0, 8.0 Hz, 1H), 3.13 (ddd, J=8.4, 8.4, 5.1 Hz, 1H), 2.77 (dd, J=6.9, 6.9 Hz, 2H), 2.07–1.85 (m, 2H), 1.60 (d, J=6.9 Hz, 3H); ^{13}C NMR (ppm) (100 MHz, $CDCl_3$) 192.4, 166.3, 140.0, 129.0, 127.9, 126.8, 89.7, 53.4, 47.4, 45.9, 41.2, 34.1, 20.9, 17.0; HRMS (CI): exact mass calcd for $C_{16}HClNO$ $[M]^+$ 277.1233. Found 277.1230.

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