# 1,2-Disubstituted Alkenes as Migratory Insertion Participants in Zn(II)-Promoted Metalloamination/Cyclization of N,N-Dimethylhydrazinoalkenes

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Ⓢ *Supporting Information*

ABSTRACT: Diethylzinc-mediated metalloamination/cyclization of unsaturated N,N-dimethylhydrazines has been extended to the use of 1,2-disubstituted alkenes as N−Zn migratory insertion acceptors. Representative 2-arylethenes and vinylcyclopropanes readily serve as reaction participants in metalloamination/cyclization−allylation cascades.
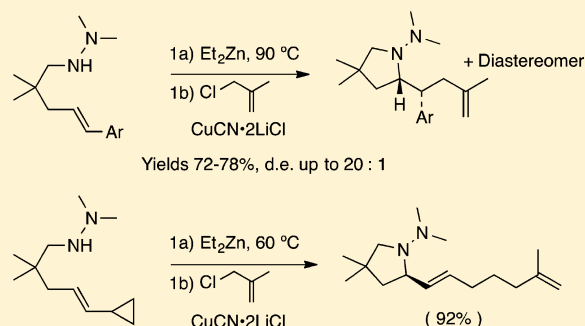
Classical intramolecular hydroamination[1] of unsaturated carbon−carbon bonds constitutes an efficient and atom-economical method for the synthesis of nitrogenous hetero-cycles. By definition, this process results in the simple delivery of a hydrogen atom to the terminus of the carbon-based addend. In contrast, *metalloamination*/cyclization leads to consecutive N−C/C−metal bond formation, wherein the C−M bond can subsequently be parlayed into new functionality. Examples of the latter cascade reaction which involve the catalytic utilization of organometallic intermediates derived from Pd(II),[2−4] Cu(II),[5] Ir(III),[6] Au(I),[7] Rh(III),[8] or the stoichiometric use of Ti(IV)[9] or Zn(II)[10] intermediates have appeared.[11] The majority of *catalytic* metalloamination/cyclizations involve organometallic or free-radical intermediates that are fleeting in nature and are, therefore, synthetically limited in the ultimate C−M bond functionalization step. We have previously reported that N,N-dimethylhydrazinoalkenes bearing monosubstituted alkenes undergo facile metalloamination/cyclization mediated by diethylzinc. Subsequent allylation or acylation of the newly formed C−Zn bond, in situ, efficiently provided the corresponding pyrrolidines or piperidines, respectively.[12] We now show that suitable 1,2-disubstituted alkenes can serve as migratory insertion N−Zn acceptors in this process.

The dimethylhydrazinoalkene substrates that were used in this study were prepared in a manner analogous to the routes we reported previously.[12] Specifically, alkylation of the allylic chlorides 1a and 1c with the lithioimine 2a followed by immediate hydrolysis (H₂C₂O₄) and dimethylhydrazone formation (Me₂NNH₂) furnished 3a and 3c. Alternatively, alkylation of 1b with lithioisobutyronitrile 2b gave nitrile 4, which upon reduction (DIBAL-H) and subsequent condensa-tion of the crude aldehyde with Me₂NNH₂ provided 3b.

Reduction of the dimethylhydrazones (NaBH₃CN, H⁺) ultimately secured the substrate dimethylhydrazinoalkenes 5a−c (Scheme 1).

Cyclization Studies. We have previously shown that various 2-arylethenyl substituents serve as viable participants in hydroamination/cyclizations of primary alkenes catalyzed by

**Scheme 1. Synthesis of Dimethylhydrazines**
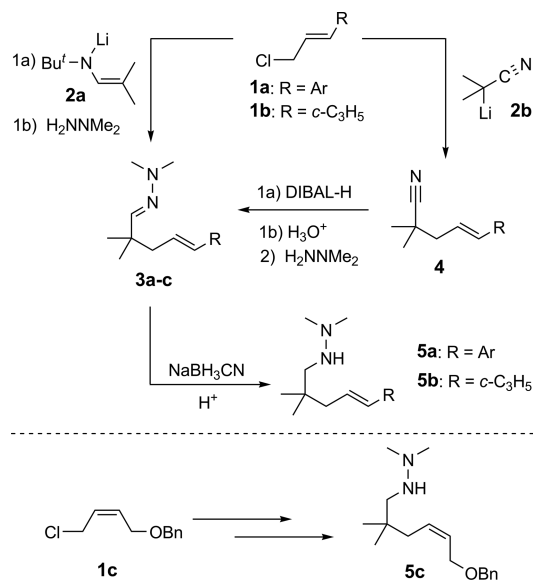
complexes of the group 3 metals.[13] We therefore began the present investigation by examining the metalloamination/cyclization of dimethylhydrazinoalkenes bearing this substituent type. It was readily determined that migratory insertion acceptors in this category are well suited for Zn(II)-mediated metalloamination–allylation, with the stereochemical outcome being very strongly governed by the influence of the electronegativity of substituents at the 2-position. For example, allylative cyclization of the simple phenyl-bearing hydrazine **5a** [(1a) Et$_2$Zn (1.0 equiv), (1b) CuCN·2LiCl,[14] 1-chloro-2-methyl-2-propene (1.2 equiv)] provided the diastereomeric dimethylhydrazines **6a$_a$** and **6a$_s$** as a 1:3 mixture in 79% isolated yield. The stereochemical assignment for the major diastereomer **6a$_s$** is based on the substantial aromatic shielding effect observed for its 4β-methyl substituent (0.52 ppm) compared to the 4β-methyl (0.93 ppm) present in **6a$_a$**. The corresponding 2-chloro derivative **5a$_{Cl}$** was considerably more selective in its cyclization–allylation, favoring diastereomer **6a$_{Cla}$** over **6a$_{Cls}$** (72%, de = 10:1). Moreover, analogous treatment of the 2-fluoro-bearing substrate **5a$_F$** provided superb stereoselectivity, giving **6a$_{Fa}$** (78%, de >20:1, Scheme 2). The origin of this surprising stereoselectivity enhancement is under current investigation.

Scheme 2. Cyclization–Allylation of Dimethylhydrazines 5a
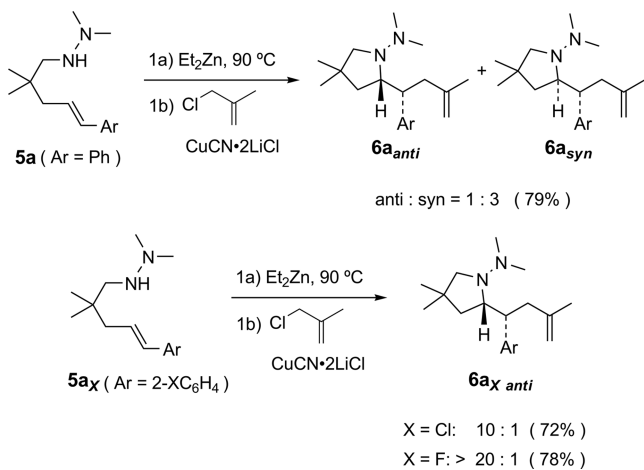
In an effort to elucidate the functional group compatibility of metalloamination/cyclization, the *cis*-allylic ether bearing dimethylhydrazinoalkene **5c** was N-metalated with diethylzinc at 90 °C. Under these conditions, *cis* → *trans* isomerization of the alkene occurred rapidly *prior to the metalloamination event*. In addition, β-elimination of the benzyloxy substituent proved unavoidable, leading to the direct formation of pyrrolidine **9** in 90% isolated yield after only 4 h (Scheme 3).

The utilization of vinylcyclopropanes as cyclization participants was subsequently investigated with the expectation that cyclopropane C–C bond scission would provide a considerable driving force for ring closure. It is therefore of considerable interest that the vinylcyclopropane-bearing substrate **5b** underwent *exceptionally* facile cyclization with concomitant cleavage of the cyclopropane ring to give the corresponding allylation product **10** in excellent (92%) yield (Scheme 4). *It should be emphasized that the vinylcyclopropane "acceptor" is by far the most reactive of the disubstituted alkenes that we have examined to date.*

Scheme 3. Cyclization–Elimination of Dimethylhydrazine 5c
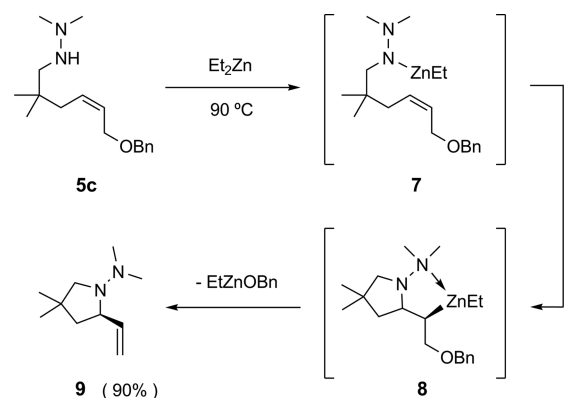
Scheme 4. Cyclization–Allylation of Dimethylhydrazine 5b
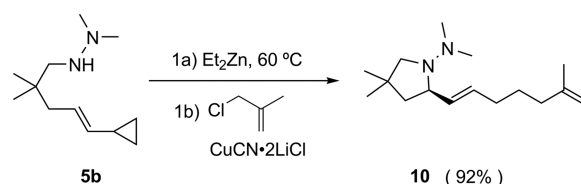
In conclusion, diethylzinc-mediated metalloamination/cyclization–allylation has been extended to encompass the utilization of 1,2-disubstituted alkenes as migratory insertion participants. Highly diastereoselective (de >20:1) C–N/C–C difunctionalization in the 2-arylethane series is observed where aryl is a 2-fluorophenyl substituent. The vinylcyclopropane substituent confers high reactivity toward metalloamination with concomitant scission of the cyclopropane ring. Intramolecular metalloamination involving a 3-(benzyloxy)-1(Z)-propenyl substituent proceeds with initial *cis* → *trans* isomerization followed by terminal elimination of EtZnOBn.

■ EXPERIMENTAL SECTION

General Remarks. Materials and Methods. Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. J. Young NMR experiments were performed under an argon atmosphere, using standard Schlenk line techniques, or in an argon-filled drybox. THF and diethyl ether were distilled from sodium/benzophenone ketyl under nitrogen. Dichloromethane, diisopropylamine, trifluoromethylbenzene, and toluene were distilled from CaH$_2$ under nitrogen. Benzene and *p*-xylene were distilled from potassium metal. All other materials were used as received from commercial sources. Thin-layer chromatography (TLC) employed 0.25 mm glass silica gel plates with UV indicator and were visualized with UV light (254 nm) or potassium permanganate staining. Flash chromatographic columns were hand-packed with silica gel 60 as a slurry in the initial elution solvent. Nuclear magnetic resonance (NMR) data were obtained at 300 or 500 MHz. Infrared spectra (IR) were obtained from a FTIR-4100. High-resolution mass spectra (HRMS) were obtained from TOF instrumentation. Infrared spectrum were recorded neat and are reported in cm^{-1}.

(E)-2,2-Dimethyl-5-phenylpent-4-enal-N,N-dimethylhydrazone (3a). A 50 mL round-bottomed flask equipped with a magnetic stirring bar, a reflux condenser, and an N$_2$ inlet was charged with (E)-2,2-dimethyl-5-phenylpent-4-enal[15] (3.66 g, 19.4 mmol), and benzene (15 mL) was subsequently added. The reactant mixture was cooled to 0 °C, and N,N-dimethylhydrazine (2.96 mL, 38.9 mmol) was added dropwise via syringe. The reactant mixture was heated to reflux for 12 h. After cooling, the resulting mixture was dried with MgSO$_4$ and filtered through a pad of Celite. The crude product was purified by bulb-to-bulb distillation (75 °C, 0.5 Torr) to afford 3.99 g (89%) of

the title compound as a clear oil. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.37 (d, J = 7.2 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 6.63 (s, 1H), 6.41 (d, J = 15.8 Hz, 1H), 6.26 (dt, J = 15.5, 7.7 Hz, 1H), 2.74 (s, 6H), 2.34 (d, J = 6.7 Hz, 2H), 1.14 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 146.3, 138.3, 132.6, 128.8, 127.8, 127.3, 126.4, 45.4, 43.8, 38.2, 26.5. IR (film): 3025, 2957, 2906, 2864, 2820, 2782, 1598, 1495, 1468, 1444, 1019, 966, 740, 693 cm^{-1}. HRMS (ESI): calcd for C$_{15}$H$_{22}$N$_2$ [M + H]$^+$ 231.1861, found 231.1883.

(E)-2-((E)-5-(2-Chlorophenyl)-2,2-dimethylpent-4-en-1-ylidene)-1,1-dimethylhydrazone (3a$_{Cl}$). A 50 mL round-bottom flask equipped with a magnetic stirring bar and an N$_2$ inlet was charged with diisopropylamine (0.981 mL, 7.00 mmol) followed by THF (10 mL). The resulting mixture was cooled to 0 °C, *n*-butyllithium (2.21 mL, 3.10 M in hexane) was added, and the solution was allowed to stir for 30 min at this temperature. A solution of *N*-tert-butyl-2-methylpropan-1-imine (0.890 g, 7.00 mmol) in THF (2 mL) was added dropwise via syringe, and the reaction mixture was warmed to room temperature. After 2 h, the resulting yellow solution was cooled to −78 °C, and (*E*)-1-chloro-2-(3-chloroprop-1-en-1-yl)benzene (1.40 g, 7.50 mmol) was added dropwise via syringe. The reaction mixture was allowed to warm to 23 °C and stirred at this temperature for 12 h. The resulting homogeneous solution was diluted with ether (25 mL) and quenched with NH$_4$Cl(aq) (10 mL). The organic layer was washed with brine (10 mL), dried with MgSO$_4$, and concentrated in vacuo. The crude imine was immediately dissolved in THF (15 mL), and a solution of oxalic acid (1.01 g, 8.00 mmol) in H$_2$O (5 mL) was added at room temperature. The reaction mixture was allowed to stir for 2 h and subsequently diluted with diethyl ether (25 mL). The organic layer was washed with brine (10 mL), dried with MgSO$_4$, and concentrated in vacuo. The crude aldehyde was then dissolved in CH$_2$Cl$_2$ (10 mL) followed by *N,N*-dimethylhydrazine (0.841 g, 14.00 mmol) and MgSO$_4$. The solution was allowed to stir for 4 h, filtered through a plug of Celite, and concentrated in vacuo. The crude hydrazone was purified by column chromatography (5% EtOAc/Hex) to give (*E*)-2-((*E*)-5-(2-chlorophenyl)-2,2-dimethylpent-4-en-1-ylidene)-1,1-dimethylhydrazine (1.13 g, 61%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.47 (dd, J = 7.8, 1.8 Hz, 1H), 7.31 (dd, J = 7.9, 1.4 Hz, 1H), 7.17 (td, J = 7.5, 1.4 Hz, 1H), 7.12 (td, J = 7.6, 1.8 Hz, 1H), 6.73 (d, J = 15.6 Hz, 1H), 6.57 (s, 1H), 6.19 (dt, J = 15.4, 7.6 Hz, 1H), 2.70 (s, 6H), 2.34 (dd, J = 7.5, 1.4 Hz, 2H), 1.10 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 145.5, 135.9, 132.5, 130.5, 129.5, 128.5, 127.8, 126.8, 126.6, 45.1, 43.40, 37.8, 26.2. IR (film): 2948, 2734, 1566, 1457, 1434, 1251, 1025, 751. HRMS (ESI): calcd for C$_{15}$H$_{22}$ClN$_2$ [M + H]$^+$ 265.1472, found 265.1457.

(E)-2-((E)-5-(2-Fluorophenyl)-2,2-dimethylpent-4-en-1-ylidene)-1,1-dimethylhydrazone (3a$_F$). The title compound was synthesized by the general procedure for hydrazone 3a$_{Cl}$ utilizing *N*-(tert-butyl)-2-methylpropan-1-imine (1.00 g, 7.86 mmol) and (*E*)-1-(3-chloroprop-1-en-1-yl)-2-fluorobenzene (1.48 g, 8.65 mmol). The crude hydrazone was purified by column chromatography (5% EtOAc/Hex) to give (*E*)-2-((*E*)-5-(2-fluorophenyl)-2,2-dimethylpent-4-en-1-ylidene)-1,1-dimethylhydrazine (1.13 g, 59%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.41 (td, J = 7.7, 1.8 Hz, 1H), 7.14 (ddd, J = 7.3, 5.4, 1.9 Hz, 1H), 7.05 (td, J = 7.5, 1.2 Hz, 1H), 6.99 (ddd, J = 10.9, 8.1, 1.2 Hz, 1H), 6.58 (s, 1H), 6.52 (d, J = 16.0 Hz, 1H), 6.29 (dt, J = 16.0, 7.5 Hz, 1H), 2.70 (s, 6H), 2.33 (dd, J = 7.5, 1.3 Hz, 2H), 1.10 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 159.9 (d, 1JC-F = 247.8), 145.6, 130.2, 128.1, 128.0, 127.1, 124.5, 123.9, 115.7, 115.5, 45.4, 43.4, 37.8, 26.1. IR (film): 3040, 2957, 2922, 2864, 2782, 1486, 1468, 1229, 1020, 970, 753 cm^{-1}. HRMS (ESI): calcd for C$_{15}$H$_{21}$FN$_2$ [M + H]$^+$ 249.1768, found 249.1746.

(E)-2-((E)-5-Cyclopropyl-2,2-dimethylpent-4-en-1-ylidene)-1,1-dimethylhydrazone (3b). A 100 mL multineck round-bottomed flask, equipped with a magnetic stirrer, addition funnel, and rubber septum, was flame-dried under vacuum and then backfilled with a nitrogen atmosphere. The flask was charged with nitrile 4 (1.0 g, 6.7 mmol) and dry CH$_2$Cl$_2$ (25 mL) and then cooled to −78 °C for the dropwise addition of DIBAL-H (13.4 mL, 13.4 mmol, 1.0 M in hexanes) via the addition funnel. The solution was allowed to stir at −78 °C for 1 h and then slowly warmed to 23 °C over 3 h. Once the reaction was

complete, the solution was chilled to 0 °C, quenched with methanol (5 mL), and diluted with Et$_2$O (20 mL), and 1.0 M HCl was slowly added until all of the precipitate was dissolved. The biphasic solution was separated, and the aqueous layer was extracted with Et$_2$O (2 × 20 mL). The organic layers were combined, washed with brine (30 mL), dried over MgSO$_4$, and concentrated in vacuo. The crude aldehyde was transferred into a 50 mL round-bottomed flask, equipped with a magnetic stirrer, and redissolved in dry CH$_2$Cl$_2$ (25 mL). A small amount of MgSO$_4$ was added to the solution prior to the dropwise addition of *N,N*-dimethylhydrazine (1.02 mL, 13.4 mmol) via syringe. The reaction mixture was stirred for 2 h at 23 °C, diluted with dry Et$_2$O (20 mL), and filtered through a plug of Celite, washing with Et$_2$O (3 × 15 mL). The solution was concentrated in vacuo and purified via Kugelrohr distillation (75 °C at 1.0 Torr) from CaH$_2$ to provide the title compound (1.20 g, 92%) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 6.52 (s, 1H), 5.45 (dt, J = 14.9, 7.4 Hz, 1H), 4.98−4.87 (m, 1H), 2.73−2.60 (m, 6H), 2.11−1.94 (m, 2H), 1.32 (dt, J = 9.0, 4.5 Hz, 1H), 0.99 (d, J = 8.1 Hz, 6H), 0.65−0.57 (m, 2H), 0.30−0.23 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 146.7, 136.6, 124.0, 44.6, 43.5, 37.4, 25.7, 24.6, 13.5, 6.4. IR (film): 3001, 2956, 2864, 1468, 1443, 1249, 1019, 963, 810, 587, 526 cm^{-1}. HRMS (ESI): calcd for C$_{12}$H$_{22}$N$_2$ [M + H]$^+$ 195.1862, found 195.1883.

(E)-2-((Z)-6-(Benzyloxy)-2,2-dimethylhex-4-en-1-ylidene)-1,1-dimethylhydrazone (3c). The title compound was synthesized by the general method of hydrazone 3a$_{Cl}$ utilizing *N*-tert-butyl-2-methylpropan-1-imine (1.09 g, 8.60 mmol) and (*Z*)-(((4-bromobut-2-en-1-yl)oxy)methyl)benzene (2.29 g, 9.50 mmol) to yield (*E*)-2-((*Z*)-6-(benzyloxy)-2,2-dimethylhex-4-en-1-ylidene)-1,1-dimethylhydrazone (1.58 g, 67%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.33 (d, J = 4.3 Hz, 4H), 7.29−7.25 (m, 1H), 6.49 (s, 1H), 5.71−5.57 (m, 2H), 4.49 (s, 2H), 4.06 (d, J = 6.1 Hz, 2H), 2.67 (s, 6H), 2.13 (d, J = 7.3 Hz, 2H), 1.03 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 145.3, 138.4, 131.2, 129.8, 129.0, 128.3, 127.9, 127.8, 127.5, 72.2, 66.0, 43.3, 39.1, 37.6, 26.0. IR (film): 2956, 2926, 2853, 1468, 1444, 1098, 1072, 1026, 1010, 735, 698 cm^{-1}. HRMS (ESI): calcd for C$_{17}$H$_{26}$N$_2$O [M + H]$^+$ 275.2124, found 275.2115.

(E)-5-Cyclopropyl-2,2-dimethylpent-4-enenitrile (4). A 50 mL round-bottomed flask equipped with a magnetic stirring bar and an N$_2$ inlet was charged with diisopropylamine (0.920 g, 9.09 mmol) and THF (25 mL). The reaction mixture was cooled to 0 °C, and *n*-butyllithium (3.03 mL, 3.0M, 9.09 mmol) was added dropwise via syringe. The resulting solution was allowed to stir at this temperature for 30 min and then cooled to −78 °C, isobutyronitrile (0.621 g, 9.00 mmol) was added dropwise via syringe, and the reaction mixture was stirred for an additional 2 h at this temperature. A solution of (*E*)-(3-chloroprop-1-en-1-yl)cyclopropane (1.19 g, 10.2 mmol) in THF (2 mL) was added all at once, and the reaction mixture was allowed to slowly warm to 23 °C over 3 h. The reaction was quenched with aqueous NH$_4$Cl (5 mL) and diluted with diethyl ether (25 mL). The organic layer was washed with brine (10 mL), dried with MgSO$_4$, and concentrated in vacuo. The crude nitrile was purified by column chromatography (5−15% EtOAc/Hex) to yield the title compound (1.52 g, 87%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.60−5.51 (m, 1H), 5.12 (ddt, J = 15.1, 8.6, 1.3 Hz, 1H), 2.20 (dd, J = 7.4, 1.2 Hz, 2H), 1.44−1.38 (m, 1H), 1.32 (s, 6H), 0.76−0.67 (m, 2H), 0.38 (dt, J = 6.4, 4.4 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 139.6, 125.0, 120.9, 43.8, 32.6, 26.1, 13.5, 6.7. IR (film): 3005, 2987, 2933, 2234, 1662, 1468, 1459, 1021, 966. HRMS (ESI): calcd for C$_{10}$H$_{15}$N [M + H]$^+$ 150.1283, found 150.1289.

(E)-2-((E)-(2,2-Dimethyl-5-phenylpent-4-en-1-yl)-1,1-dimethylhydrazine (5a). A 100 mL round-bottomed flask equipped with a magnetic stirring bar and an N$_2$ inlet was charged with hydrazone 3a (0.60g, 2.60 mmol), and methanol (30 mL) was subsequently added. Sodium cyanoborohydride (0.18g, 2.87 mmol) was added in one portion, and the solution was titrated with HCl/MeOH (methyl orange indicator, 20% v/v) until a light red color persisted. The reactant mixture was stirred for 30 min, and the volatiles were removed in vacuo. The crude salt was neutralized with aqueous NaOH (25% w/v) to a pH of 11 and the crude product extracted with diethyl ether (3 × 10 mL). The organic layer was dried with MgSO$_4$, filtered through a

pad of Celite, and concentrated in vacuo. The crude product was purfied by bulb to bulb distillation (75−80 °C, 0.5 Torr) to afford 0.52 g (85%) of the title compound. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.42 (d, J = 7.2 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 6.52 (d, J = 15.7 Hz, 1H), 6.43 (dt, J = 15.7, 7.5 Hz, 1H), 2.66 (s, 2H), 2.36 (s, 6H), 2.29 (d, J = 7.5 Hz, 2H), 1.78 (s, 1H), 1.07 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 138.6, 132.8, 128.9, 128.0, 127.3, 126.6, 59.2, 47.9, 44.3, 35.3, 26.2. IR (film): 3197, 3025, 2949, 2835, 2764, 1494, 1474, 1448, 966, 692 HRMS (ESI): calcd for C$_{15}$H$_{24}$N$_2$ [M + H]$^+$ 233.2018, found 233.2045.

(E)-2-(5-(2-Chlorophenyl)-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (5a$_{Cl}$). The title compound was synthesized by the general reduction procedure of **5a** utilizing hydrazone **3a$_{Cl}$** (0.794 g, 3.00 mmol) and NaBH$_3$CN (0.375 g, 6.00 mmol) to yield (E)-2-(5-(2-chlorophenyl)-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (0.640 g, 80%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.41 (td, J = 7.7, 1.8 Hz, 1H), 7.13 (tdd, J = 7.2, 5.1, 1.8 Hz, 1H), 7.04 (td, J = 7.5, 1.3 Hz, 1H), 6.98 (ddd, J = 10.9, 8.1, 1.3 Hz, 1H), 6.52 (d, J = 15.9 Hz, 1H), 6.31 (dt, J = 15.6, 7.6 Hz, 1H), 2.58 (s, 2H), 2.45−2.38 (m, 6H), 2.16 (dd, J = 7.6, 1.3 Hz, 2H), 1.92 (s, 1H), 0.92 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 130.5, 128.0, 127.9, 127.1, 124.3, 123.9, 115.7, 115.5, 58.7, 47.8, 44.2, 34.6, 25.8. IR (film): 2950, 2832, 1489, 1223, 979, 741 cm^{-1}. HRMS (ESI): calcd for C$_{15}$H$_{23}$ClN$_2$ [M + H]$^+$ 266.1550, found 266.1562.

(E)-2-(5-(2-Fluorophenyl)-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (5a$_F$). The title compound was synthesized by the general reduction procedure of **5a** utilizing hydrazone **3a$_F$** (0.751 g, 3.00 mmol) and NaBH$_3$CN (0.375 g, 6.00 mmol) to yield (E)-2-(5-(2-fluorophenyl)-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (0.668 g, 89%) as a clear oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.41 (td, J = 7.7, 1.8 Hz, 1H), 7.13 (tdd, J = 7.2, 5.1, 1.8 Hz, 1H), 7.04 (td, J = 7.5, 1.3 Hz, 1H), 6.98 (ddd, J = 10.9, 8.1, 1.3 Hz, 1H), 6.52 (d, J = 15.9 Hz, 1H), 6.31 (dt, J = 15.6, 7.6 Hz, 1H), 2.58 (s, 2H), 2.45−2.38 (m, 6H), 2.16 (dd, J = 7.6, 1.3 Hz, 2H), 1.92 (s, 1H), 0.92 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 159.9 (d, [1]J$_{C−F}$ = 248.1), 130.5, 128.0, 127.9, 127.1, 124.3, 123.9, 115.7, 115.5, 58.7, 47.8, 44.2, 34.6, 25.8. IR (film): 2952, 2837, 1486, 1455, 1229, 970, 753 cm^{-1}. HRMS (ESI): calcd for C$_{15}$H$_{23}$FN$_2$ [M + H]$^+$ 251.1924, found 251.1912.

(E)-2-(5-Cyclopropyl-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (5b). The title compound was synthesized by the general reduction procedure of hydrazine **5a** utilizing hydrazone **3b** (0.988 g, 5.00 mmol) and NaBH$_3$CN (0.628 g, 10.0 mmol) to yield (E)-2-(5-cyclopropyl-2,2-dimethylpent-4-en-1-yl)-1,1-dimethylhydrazine (0.746 g, 76%) as a clear liquid. ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.45 (dt, J = 15.1, 7.5 Hz, 1H), 4.92 (dd, J = 15.1, 8.4 Hz, 1H), 2.48 (s, 2H), 2.36 (s, 6H), 1.84 (s, 2H), 1.30 (qt, J = 8.4, 4.8 Hz, 1H), 0.82 (s, 6H), 0.65−0.54 (m, 2H), 0.26 (dt, J = 6.3, 4.2 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 136.2, 124.3, 58.5, 47.7, 43.3, 34.0, 25.6, 24.6, 13.5, 6.3. IR (film): 3017, 2921, 2722, 1423, 1402, 1319, 1021, 953, 818, 635, 562 cm^{-1}. HRMS (ESI): calcd for C$_{12}$H$_{24}$N$_2$ [M + H]$^+$ 197.2018, found 197.2033.

(Z)-2-(6-(Benzyloxy)-2,2-dimethylhex-4-en-1-yl)-1,1-dimethylhydrazine (5c). The title compound was synthesized by the general reduction method of hydrazine **5a** utilizing hydrazone **3c** (1.00 g, 3.64 mmol) and NaBH$_3$CN (0.458 g, 7.29 mmol) to yield (Z)-2-(6-(benzyloxy)-2,2-dimethylhex-4-en-1-yl)-1,1-dimethylhydrazine (0.916 g, 91%) as a clear oil. ^{1}H NMR (500 MHz, DMSO): δ 7.33 (q, J = 3.9, 2.9 Hz, 4H), 7.26 (ddd, J = 7.3, 4.9, 2.3 Hz, 1H), 5.72−5.60 (m, 2H), 4.50 (s, 2H), 4.07 (d, J = 5.8 Hz, 2H), 2.51 (s, 2H), 2.38 (s, 6H), 1.99 (d, J = 7.0 Hz, 2H), 1.86 (s, 1H), 0.86 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 138.4, 130.1, 128.3, 127.9, 127.8, 127.5, 127.5, 72.2, 65.9, 58.6, 47.7, 37.7, 34.4, 25.6. IR (film): 2956, 2926, 2853, 1468, 1444, 1098, 1072, 1026, 1010, 735, 698 cm^{-1}. HRMS (ESI): calcd for C$_{17}$H$_{28}$N$_2$O [M + H]$^+$ 277.2281, found 277.2276.

Synthesis of Cyclic Hydrazines. General Procedure for CuCN-Mediated Allylation of Metalloamination Intermediates. In an argon-filled glovebox, ZnEt$_2$ in p-xylene (50 μL, 2.0 M, 0.10 mmol) and toluene or (trifluoromethyl)benzene (0.5 mL) were introduced into a J. Young NMR tube equipped with a Teflon screw cap, and hydrazinoalkene (**5a−c**) (0.10 mmol) was subsequently

added. The reactant mixture was heated in a 90 °C oil bath until metalloamination was complete (90% by ^{1}H NMR, p-xylene as internal standard). The volatiles were removed in vacuo, and THF (0.5 mL) was introduced to the J. Young tube in an argon-filled drybox followed by the addition of a solution of CuCN·2LiCl in THF[14] (150 μL, 1.0 M, 0.15 mmol). After 5 min, methallyl chloride (10.9 mg, 0.12 mmol)] was added, and the reactant mixture was kept at 23 °C for 2 h (or until the reaction was complete 95% ^{1}H NMR). The Teflon screw cap was removed, the reactant mixture was transferred to a 10 mL test tube and diluted with diethyl ether (2.0 mL), and an aqueous solution of NH$_4$Cl (satd) and NH$_3$/H$_2$O (1:1 v/v, 2 mL) was subsequently added. The resulting suspension was vigorously stirred for 10 min until the aqueous layer developed a deep blue color. The organic layer was removed and washed with a second portion of NH$_4$Cl (satd) and NH$_3$/H$_2$O (1:1 v/v, 2 mL) followed by brine (2 mL) and dried with MgSO$_4$. The ether solution was then transferred to a 10 mL round-bottomed flask equipped with a magnetic stirring bar and a N$_2$ inlet and cooled to 0 °C. Trifluoroacetic acid (13.7 mg, 0.12 mmol) was added dropwise via a gastight syringe, and the reactant mixture was allowed to stir for 1 h. The volatiles were removed in vacuo, and the resultant viscous oil was triturated with pentane (3 × 1 mL) to afford the trifluoroacetate salts **6**.

N,N,4,4-Tetramethyl-2-(3-methyl-1-phenylbut-3-en-1-yl)-pyrrolidin-1-amine (6a). The title compound was isolated as a clear oil (free base) (22.6 mg, 79%). ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.27−7.22 (m, 2H), 7.21−7.17 (m, 2H), 7.17−7.13 (m, 1H), 4.70−4.61 (m, 1.5H), 3.39 (tt, J = 8.0, 3.6, 1H), 2.97 (td, J = 8.2, 4.3, 0.8H), 2.67 (d, J = 14.5, 0.3H), 2.61 (d, J = 8.0, 0.3H), 2.52 (dd, J = 14.3, 7.8, 0.8H), 2.44−2.40 (m, 1.5H), 2.37 (s, 6H), 2.34−2.30 (m, 1H), 1.69 (s, 2.2H), 1.65 (s, 0.8H), 1.28 (dd, J = 12.5, 8.9, 1H), 1.19−1.13 (m, 1H), 1.08 (s, 1H), 0.93 (s, 1H), 0.92 (s, 2H), 0.52 (s, 2H). ^{13}C NMR (126 MHz, CDCl$_3$): δ = 144.6, 129.9, 128.6, 127.9, 127.0, 125.7, 125.6, 111.5, 65.6, 63.4, 53.6, 52.8, 43.3, 43.2, 40.5, 39.8, 39.6, 38.7, 38.3, 34.9, 33.5, 30.6, 29.3, 29.2, 29.0, 22.7, 22.3. IR (film): 2938, 2863, 2812, 1452, 1181, 700, cm^{-1}. HRMS (ESI): calcd for C$_{19}$H$_{31}$N$_2$ [M + H]$^+$ 287.2487, found 287.2566.

2-(1-(2-Chlorophenyl)-3-methylbut-3-en-1-yl)-N,N,4,4-tetramethylpyrrolidin-1-amine (6a$_{Cl}$). The title compound was isolated as a mixture of diastereomers (1:10) (free base) (23.1 mg, 72%). ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.27 (ddd, J = 13.7, 8.2, 1.7 Hz, 2H), 7.15 (td, J = 7.5, 1.4 Hz, 1H), 7.09−7.00 (m, 1H), 4.49 (s, 1H), 4.39 (s, 1H), 3.59 (ddd, J = 11.7, 7.5, 4.0 Hz, 1H), 3.02 (dt, J = 14.1, 5.4 Hz, 2H), 2.58 (d, J = 8.5 Hz, 1H), 2.52 (d, J = 8.4 Hz, 1H), 2.40 (s, 1H), 2.31 (s, 6H), 1.66 (s, 3H), 1.30−1.26 (m, 1H), 1.25−1.22 (m, 1H), 1.07 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 144.8, 142.1, 134.7, 129.6, 129.16 126.5, 126.1, 111.2, 64.9, 53.2, 42.9, 40.8, 39.8, 34.5, 29.3, 28.7, 22.5. IR (film): 2952, 2865, 2844, 1472, 1441, 1025, 884, 750 cm^{-1}. HRMS (ESI): calcd for C$_{19}$H$_{29}$ClN$_2$ [M + H]$^+$ 321.2098, found 321.2101.

2-(1-(2-Fluorophenyl)-3-methylbut-3-en-1-yl)-4,4-N,N-tetramethylpyrrolidin-1-amine (6a$_F$). The title compound was isolated as a clear oil (free base) (23.7 mg, 78%). ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.17 (td, J = 7.5, 1.8 Hz, 1H), 7.11 (tdd, J = 7.3, 5.1, 1.8 Hz, 1H), 7.01 (td, J = 7.5, 1.3 Hz, 1H), 6.94 (ddd, J = 10.9, 8.1, 1.3 Hz, 1H), 4.55 (d, J = 10.8 Hz, 2H), 3.50 (dd, J = 10.6, 5.7 Hz, 1H), 3.10−2.98 (m, 1H), 2.76 (dd, J = 14.4, 5.8 Hz, 1H), 2.52−2.38 (m, 3H), 2.39−2.29 (m, 6H), 1.65 (s, 3H), 1.34 (dd, J = 12.8, 8.7 Hz, 1H), 1.27−1.19 (m, 1H), 0.93 (s, 3H), 0.77 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 161.5 (d, 1JC-F = 244.1), 144.6, 131.2, 129.9, 127.1, 123.1, 115.1, 115.0, 111.3, 64.0, 53.0, 41.1, 40.4, 39.8, 34.1, 29.2, 28.9, 22.2. IR (film): 3072, 2950, 2865, 2770, 1648, 1582, 1489, 1453, 1222, 886, 754 cm^{-1}. HRMS (ESI): calcd for C$_{19}$H$_{30}$FN$_2$ [M + H]$^+$ 305.2394, found 305.2357.

N,N,4,4-Tetramethyl-2-vinylpyrrolidin-1-amine (9). The title compound was isolated as a clear oil (TFA salt) 25.4 mg (90%). ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.84 (ddd, J = 17.2, 10.2, 8.4 Hz, 1H), 5.36−5.22 (m, 2H), 3.81 (q, J = 8.3 Hz, 1H), 3.16 (d, J = 8.8 Hz, 1H), 2.95 (s, 6H), 2.81 (d, J = 8.8 Hz, 1H), 1.92 (dd, J = 13.1, 8.0 Hz, 1H), 1.62 (dd, J = 13.1, 8.5 Hz, 1H), 1.16 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 136.2, 119.8, 64.9, 60.9, 45.0, 42.0, 35.0, 29.1,

28.5. IR (film): 2966, 2876, 1781, 1670, 1200, 1164, 796, 704 cm^{-1}. HRMS (ESI): calcd for $C_{10}H_{20}N_2$ [M + H]$^+$ 169.1705, found 169.1731.

(E)-N,N,4-Tetramethyl-2-(6-methylhepta-1,6-dien-1-yl)-pyrrolidin-1-amine (10). The title compound was isolated as a clear oil (TFA salt) 33.5 mg (92%). ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.79–5.70 (m, 1H), 5.48 (dd, J = 15.4, 8.6 Hz, 1H), 4.70–4.65 (m, 1H), 4.65–4.60 (m, 1H), 3.83–3.73 (m, 1H), 3.18 (d, J = 9.1 Hz, 1H), 2.90 (d, J = 5.1 Hz, 6H), 2.79 (d, J = 9.1 Hz, 1H), 2.06–1.95 (m, 4H), 1.87 (dd, J = 13.1, 7.5 Hz, 1H), 1.71–1.66 (m, 3H), 1.66–1.60 (m, 2H), 1.52–1.45 (m, 2H), 1.16 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 145.3, 137.0, 127.2, 110.1, 64.9, 60.2, 45.1, 41.6, 37.2, 34.7, 31.6, 29.2, 28.8, 26.5, 22.2. IR (film): 2966, 2936, 2873, 1780, 1670, 1652, 1463, 1202, 1168, 704 cm^{-1}. HRMS (ESI): calcd for $C_{16}H_{30}N_2$ [M + H]$^+$ 251.2120, found 251.2163.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01328.

^{1}H and ^{13}C NMR spectra for all newly synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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