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Brief Communication

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

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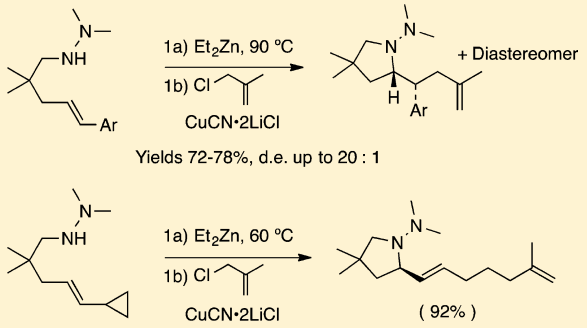
Supporting Information

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.

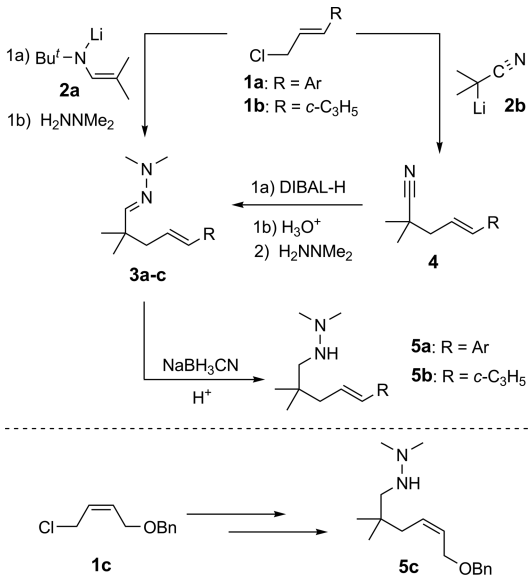


Classical intramolecular hydroamination[1] of unsaturated carbon−carbon bonds constitutes an efficient and atom-economical method for the synthesis of nitrogenous heterocycles. By definition, this process results in the simple delivery of a hydrogen atom to the terminus of the carbon-based addend. In 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 ($H_2C_2O_4$) and dimethylhydrazone formation (Me_2NNH_2) furnished **3a** and **3c**. Alternatively, alkylation of **1b** with lithioisobutyronitrile **2b** gave nitrile **4**, which upon reduction (DIBAL-H) and subsequent condensation of the crude aldehyde with Me_2NNH_2 provided **3b**. Reduction of the dimethylhydrazones ($NaBH_3CN$, 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



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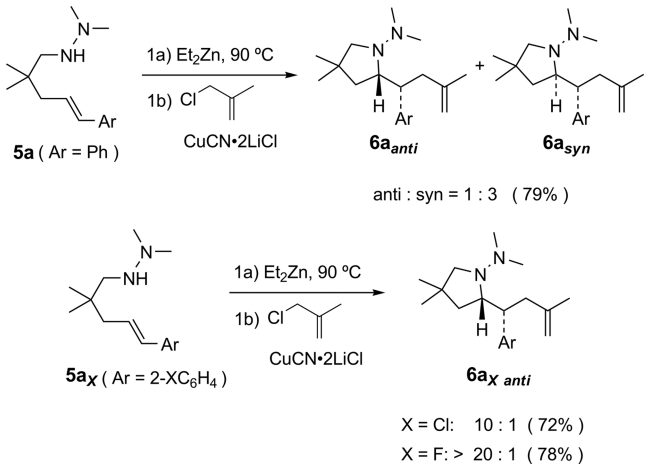
complexes of the group 3 metals.[13] We therefore began the present investigation by examining the metalloamination/cyclization of dimethylhydrazinoalkenes bearing this substituent type. It was readily determined that migratory insertion acceptors in this category are well suited for Zn(II)-mediated 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_2Zn (1.0 equiv), (1b) CuCN·2LiCl,[14] 1-chloro-2-methyl-2-propene (1.2 equiv)] provided the diastereomeric dimethylhydrazines $\mathbf{6a}_a$ and $\mathbf{6a}_s$ as a 1:3 mixture in 79% isolated yield. The stereochemical assignment for the major diastereomer $\mathbf{6a}_s$ 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 $\mathbf{6a}_a$. The corresponding 2-chloro derivative $\mathbf{5a}_{Cl}$ was considerably more selective in its cyclization−allylation, favoring diastereomer $\mathbf{6a}_{Cla}$ over $\mathbf{6a}_{Cls}$ (72%, de = 10:1). Moreover, analogous treatment of the 2-fluoro-bearing substrate $\mathbf{5a}_F$ provided superb stereoselectivity, giving $\mathbf{6a}_{Fa}$ (78%, de >20:1, Scheme 2). The origin of this surprising stereoselectivity enhancement is under current investigation.

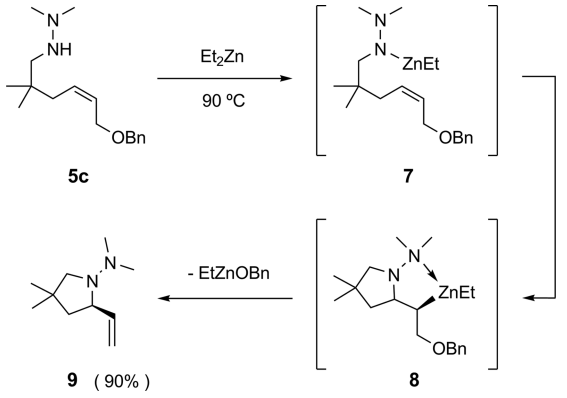
Scheme 2. Cyclization−Allylation of Dimethylhydrazines 5a



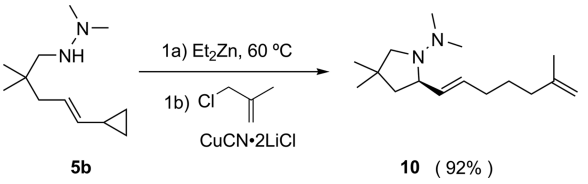
In an effort to elucidate the functional group compatibility of metalloamination/cyclization, the *cis*-allylic ether bearing dimethylhydrazinoalkene **5c** was *N*-metalated with diethylzinc at 90 °C. Under these conditions, *cis* → *trans* isomerization of the alkene occurred rapidly *prior to the 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

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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_4Cl(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_2O (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_2Cl_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-dimethylhydrazone (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_2Cl_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_2O (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_2O (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_2Cl_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_2O (20 mL), and filtered through a plug of Celite, washing with Et_2O (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 $C_{17}H_{26}N_2O$ [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_4Cl (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

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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 $NaBH_3CN$ (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 $NaBH_3CN$ (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, $^1J_{C-F}$ = 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 $NaBH_3CN$ (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 $NaBH_3CN$ (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 $C_{17}H_{28}N_2O$ [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_4Cl (satd) and NH_3/H_2O (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_4Cl (satd) and NH_3/H_2O (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,

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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*,4,4-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%). ^1H 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.

^1H 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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