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Rhodium(III)-Catalyzed Three-Component 1,2-Diamination of Unactivated Terminal Alkenes

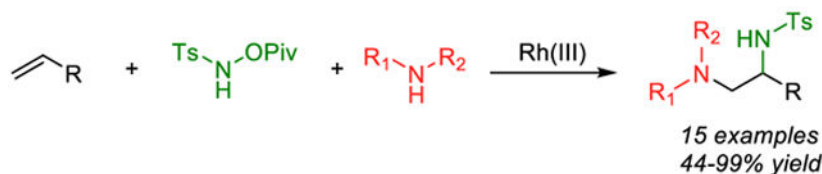
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Abstract

We report a three-component diamination of simple unactivated alkenes using an electrophilic nitrene source and amine nucleophiles. The reaction provides rapid access to 1,2-vicinal diamines from terminal alkenes through a one-pot protocol. The transformation proceeds smoothly with excellent tolerance for a broad array of primary and secondary amines, affording the desired product with good yield and regioselectivity. The mechanism is proposed to proceed through a Rh(III)-catalyzed aziridination of alkenes with subsequent ring opening by primary or secondary amines.

Graphical Abstract



Keywords

alkene diamination; Rh(III)-catalysis; One-pot synthesis; nitrene

The 1,2-vicinal diamine is a prevalent structural motif in natural products and pharmaceuticals. Moreover, they are commonly utilized as ligands on various metal complexes to catalyze essential organic transformations.¹ Owing to the high demand, the development of efficient synthetic strategies for the synthesis of 1,2-diamines has been actively pursued. Several notable synthetic approaches exist including aza-Henry reaction,² Mannich reaction between α -amino-compounds and imines,³ and the addition of nucleophile into α -amino imines.⁴ Among the potential synthetic precursors for the synthesis of vicinal amines, alkenes are ideal – they are ubiquitous feedstock materials, and

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Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

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Dedicated to Professor Mark Lautens on the occasion of his 70th birthday

unreactive functionality that is well tolerated in other transformations. Thus, the simultaneous addition of two nitrogen functionalities to the alkene double bond is a straightforward and useful way to access 1,2-vicinal diamines (Scheme 1). However, aside from some prominent successes,^{5,6} transition-metal-catalyzed 1,2-diamination of alkenes is significantly underdeveloped compared to the much better established dihydroxylation and aminohydroxylation of alkenes. Presumably, this is because 1,2-diamines are generally good ligands and can act as a chelating ligand for the metal complex.

Alternatively, the nucleophilic ring opening of aziridines by amines is an efficient strategy to access diamines from readily available starting materials.⁷ Recently, we reported a Rh(III)-catalyzed formal [4+1] approach to pyrrolidines from simple unactivated terminal alkenes and nitrene sources.⁸ Mechanistic investigations led us to propose a Rh-catalyzed intermolecular aziridination with subsequent ring expansion by triflic acid for the synthesis of 5-membered saturated *N*-heterocycle.

Motivated by the fact that aziridine formation is highly efficient in this system, we envisioned that this intermediate can be utilized for the one-pot synthesis of vicinal diamines in the presence of exogenous nitrogen nucleophiles. In order to test this idea, we added morpholine (**2a**) as amine nucleophile after the initial aziridination of 1-hexene (**1a**) and 4-methyl-*N*-(pivaloyloxy)benzenesulfonamide (Ts-NH-OPiv) in the presence of a catalytic amount of Cs₂CO₃ (0.1 equiv.) and [Ind*RhCl₂]₂ catalyst (2.5 mol%) in HFIP.

Preliminary results showed that when 2 equiv. of morpholine was added and stirred at room temperature and 40 °C, desired diamination products were formed as a single regioisomer albeit low yield (entry 1, 2). Increasing reaction temperature to 80 °C further improved the reaction yield to 63% (entry 3). Since we observed unreacted aziridine on workup, longer reaction time and higher concentration were applied to complete the reaction, and the yield of **3aa** improved to 87% when the reaction was conducted at 80 °C for 16 hours in 0.2 M of HFIP (entry 6). Lewis acid-promoted aziridine ring opening by amines is well-known;⁷ however, adding AgSbF₆ together with morpholine after aziridination gives a lower yield of **3aa** (entry 4). Finally, a quantitative yield of the desired product is observed at 0.2 M with 3 equiv. of morpholine (entry 7). Having optimized the reaction conditions, we next sought to explore the scope of this methodology. First, various commercially available primary and secondary amines were examined using 1-hexene as an alkene coupling partner (Scheme 2). Cyclic secondary amines such as pyrrolidine (**2b**) and piperidine (**2c**) provide diamination products with good yield (**3ab**, **3ac**). Bicyclic 1,2,3,4-tetrahydroisoquinoline (**2d**) also works well as a nucleophile giving 65% of corresponding 1,2-diamine (**3ad**). The reaction with dibutyl amine also delivers 1,2-vicinal diamine product with good yield (**3ae**). The reaction also proceeds smoothly with primary amines, giving desired products (**3af** - **3ai**) in good yield. When aniline (**2h**) and 4-methoxyaniline (**2i**) are used as a nucleophile, the minor regioisomer is also observed in small amounts. Hydrazine-type nucleophile (1-aminopyrrolidine) was also tested but only trace amount of desired product was observed.

Next, we tested the synthetic utility of this method with a variety of terminal unactivated alkene substrates (Scheme 3). Allyl cyclohexane and 2-allyladamantane are successfully converted to the corresponding diamination products in good yield (**3ba**, **3ca**). A variety of

functional groups such as phenyl (**3da**), *tert*-butyldiphenylsilyl protected alcohol (**3ea**), ethyl ester (**3fa**), and protected amine (**3ga**) are all well tolerated, giving the desired 1,2-diamination product in good yield.

Based on our previous work⁸ and aziridine ring opening precedent,⁷ we propose the following mechanism for the reaction. First, [Ind*RhCl₂]₂ catalyst metalates Ts-NH-OPiv to generate Rh complex **II**, which undergoes Rh-nitrene formation to yield intermediate **III**. Subsequent aziridination with an unactivated alkene coupling partner (**1a**) would give aziridine intermediate with the regeneration of active Rh(III) catalyst. Alternatively, the alkene coupling partner (**1a**) can coordinate with Rh complex **II** and undergoes alkene migratory insertion to form complex **IV**. Subsequent C-N bond formation and N-O bond cleavage would generate aziridine intermediate. Nucleophilic attack of primary and/or secondary amines to sterically less hindered terminal carbon of aziridine produces diamination products at elevated temperature.

In summary, we demonstrate the one-pot synthesis of vicinal diamines from readily available α -olefins through Rh(III)-catalyzed aziridination and subsequent nucleophilic attack by exogenous amines. The reaction exhibits broad functional group tolerance with good yield and regioselectivity.

The experimental section has no title; please leave this line here.

HFIP, Cs₂CO₃ and **1a**, **1b**, **1d**, **1f**, **2a-2i** were purchased from Sigma Aldrich and used without further purification. **1c**,⁸ **1e**,⁹ **1g**¹⁰ and [Ind*RhCl₂]₂ catalyst¹¹ were synthesized following literature procedures. ¹H and ¹³C NMR spectra were collected at ambient temperature on Bruker 400 MHz and Bruker Avance III 500 MHz spectrometers. Regioisomeric ratios were measured by integration of ¹H NMR spectra of product mixtures prior to purification. Low resolution mass spectra were recorded on a Waters Acquity UPLC-MS or Agilent 5977B GC/MS. Infrared spectra were collected on a Perkin Elmer Spectrum Two FT-IR Spectrometer. Melting point were measured by Stanford Research System MPA160 melting point apparatus.

General Procedures

To a 1 dram vial, [Ind*RhCl₂]₂ (0.0025 mmol, 2.5 mol%), Ts-NH-OPiv (0.13 mmol, 1.3 equiv) and Cs₂CO₃ (0.01 mmol, 0.1 equiv) were measured and dissolved in HFIP (0.2 M) and stirred 16 hours at 22 °C. Then, amine (0.3 mmol, 3 equiv) was added to the vial and heated to 80 °C and stirred for additional 16 hours. The mixture was concentrated under reduced pressure and the crude material was purified by flash chromatography either manually on SiliCycle® SilicaFlash® P60 (230-400 mesh) silica gel or automatically using a Teledyne Isco Lumen CombiFlash with RediSep Rf Disposable Flash columns.

4-methyl-*N*-(1-morpholinohexan-2-yl)benzenesulfonamide (**3aa**)

Yield: 20.4 mg, 98%, yellow oil.

R_f = 0.35 (EA/Hex 1:1).

^1H NMR (500 MHz, CDCl_3) δ 7.76 (m, 2H), 7.29 (m, 2H), 3.53 – 3.44 (m, 4H), 3.13 – 3.04 (m, 1H), 2.41 (s, 3H), 2.24 (d, J = 7.4 Hz, 2H), 2.21 – 2.12 (m, 1H), 2.11 – 2.03 (m, 1H), 2.07 (dt, J = 11.0, 4.3 Hz, 2H), 1.67 (ddd, J = 14.4, 9.6, 4.6 Hz, 1H), 1.53 (dddd, J = 14.0, 11.2, 7.3, 4.1 Hz, 1H), 1.29 – 1.18 (m, 3H), 1.17 – 1.08 (m, 1H), 0.84 (t, J = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.5, 137.2, 129.7, 127.4, 66.8, 61.1, 53.3, 50.0, 33.1, 26.9, 22.8, 21.6, 14.1.

IR (CDCl_3 , cm^{-1}) ν 3272, 2954, 2928, 2858, 1598, 1453, 1329, 1302, 1159, 1115, 1092, 815, 665, 550.

LRMS (ESI) m/z [$\text{C}_{17}\text{H}_{29}\text{N}_2\text{O}_3\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 341.2, found 341.1.

4-methyl-*N*-(1-(pyrrolidin-1-yl)hexan-2-yl)benzenesulfonamide (3ab)

Yield: 25.2 mg, 78%, pale-yellow oil.

R_f = 0.16 (DCM:MeOH 19:1).

^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.43 (s, 1H), 3.01 (ddt, J = 9.4, 7.3, 4.6 Hz, 1H), 2.51 (dd, J = 12.3, 9.6 Hz, 1H), 2.41 (s, 3H), 2.32 – 2.21 (m, 3H), 2.16 (td, J = 8.2, 4.4 Hz, 2H), 1.75 – 1.56 (m, 5H), 1.51 (dddd, J = 14.2, 11.3, 7.2, 4.2 Hz, 1H), 1.31 – 1.02 (m, 3H), 0.83 (t, J = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.3, 137.3, 129.6, 127.4, 58.3, 54.0, 52.3, 33.2, 27.0, 23.7, 22.8, 21.7, 14.1.

IR (CDCl_3 , cm^{-1}) ν 3287, 2958, 2928, 1382, 1320, 1159, 1093, 909, 731, 660, 549.

LRMS (ESI) m/z [$\text{C}_{17}\text{H}_{28}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 325.2, found 325.2.

4-methyl-*N*-(1-(piperidin-1-yl)hexan-2-yl)benzenesulfonamide (3ac)

Yield: 24.8 mg, 73%, yellow oil.

R_f = 0.27 (EA/Hex 1:1).

^1H NMR (400 MHz, CDCl_3) δ 7.80 – 7.71 (m, 2H), 7.33 – 7.25 (m, 2H), 3.07 (ddt, J = 10.3, 8.2, 4.2 Hz, 1H), 2.41 (s, 3H), 2.28 (dd, J = 12.7, 10.3 Hz, 1H), 2.19 (dd, J = 12.6, 4.7 Hz, 1H), 2.15 – 2.04 (m, 3H), 1.70 (ddt, J = 10.2, 8.8, 4.1 Hz, 1H), 1.56 – 1.46 (m, 1H), 1.45 – 1.32 (m, 6H), 1.32 – 1.16 (m, 6H), 1.15 – 1.05 (m, 1H), 0.84 (t, J = 7.1 Hz, 3H).

^{13}C NMR [101 MHz, CDCl_3] δ 143.2, 137.3, 129.6, 127.4, 60.9, 54.2, 50.1, 38.7, 33.2, 27.3, 26.9, 25.7, 24.1, 22.8, 21.6, 14.1.

IR (CDCl_3 , cm^{-1}) ν 2930, 2859, 1709, 1597, 1553, 1455, 1404, 1332, 1160, 1093, 664, 550.

LRMS (ESI) m/z [$\text{C}_{18}\text{H}_{31}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 339.2, found 339.1.

N-(1-(3,4-dihydroisoquinolin-2(1H)-yl)hexan-2-yl)-4-methylbenzenesulfonamide (3ad)

Yield: 25 mg, 65%, yellow solid.

R_f = 0.65 (EA/Hex 1:1).

M.P. = 94 - 98 (°C)

^1H NMR (500 MHz, CDCl_3) δ 7.73 – 7.67 (m, 2H), 7.22 – 7.17 (m, 2H), 7.17 – 7.04 (m, 3H), 6.78 – 6.73 (m, 1H), 3.28 (d, J = 14.8 Hz, 1H), 3.23 – 3.11 (m, 2H), 2.85 – 2.76 (m, 1H), 2.69 (dt, J = 16.4, 5.4 Hz, 1H), 2.57 (dt, J = 11.2, 5.5 Hz, 1H), 2.50 (ddd, J = 15.3, 8.0, 4.3 Hz, 1H), 2.47 – 2.41 (m, 2H), 2.41 (s, 3H), 1.80 – 1.71 (m, 1H), 1.64 – 1.54 (m, 1H), 1.35 – 1.14 (m, 4H), 0.87 (t, J = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.3, 137.0, 134.0, 129.7, 128.7, 127.3, 126.6, 126.4, 125.7, 60.7, 55.5, 51.1, 50.6, 33.2, 29.1, 27.2, 27.0, 22.9, 21.7, 14.1.

IR (CDCl_3 , cm^{-1}) ν 3276, 2954, 2926, 2867, 1598, 1454, 1328, 1160, 1093, 903, 813, 741, 666, 550.

LRMS (ESI) m/z [$\text{C}_{22}\text{H}_{31}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 387.2, found 387.2.

N-(1-(dibutylamino)hexan-2-yl)-4-methylbenzenesulfonamide (3ae)

Yield: 26.4 mg, 69%, pale-yellow oil.

R_f = 0.31 (DCM:MeOH 19:1).

^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.39 (s, 1H), 2.99 (tt, J = 9.2, 4.6 Hz, 1H), 2.40 (s, 3H), 2.37 – 2.04 (m, 6H), 1.68 (dtd, J = 12.5, 7.2, 6.4, 3.3 Hz, 1H), 1.52 (dddd, J = 14.0, 11.4, 7.3, 4.1, Hz, 1H), 1.34 – 1.18 (m, 6H), 1.13 (m, 6H), 0.90 – 0.80 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.3, 137.3, 129.6, 127.5, 57.2, 53.5, 51.1, 32.8, 28.7, 26.9, 22.9, 21.6, 20.7, 14.2, 14.2.

IR (CDCl_3 , cm^{-1}) ν 3286, 2976, 2863, 1381, 1349, 1118, 1075, 916, 733, 662, 548.

LRMS (ESI) m/z [$\text{C}_{21}\text{H}_{38}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 383.3, found 383.3.

N-(1-(cyclopentylamino)hexan-2-yl)-4-methylbenzenesulfonamide (3af)

Yield: 28 mg, 83%, clear brown oil

R_f = 0.3 (DCM/MeOH 95:5)

^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 8.1$ Hz, 1H), 7.28 (d, $J = 8.1$ Hz, 1H), 3.16 (p, $J = 6.4$ Hz, 1H), 2.85 (p, $J = 6.5$ Hz, 1H), 2.49 (s, 1H), 2.48 (s, 1H), 2.41 (s, 2H), 1.76 – 1.55 (m, 2H), 1.53 – 1.33 (m, 2H), 1.23 – 1.09 (m, 3H), 0.79 (t, $J = 6.9$ Hz, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.3, 138.0, 129.7, 127.3, 59.6, 53.5, 50.9, 33.0, 32.9, 27.7, 24.0, 23.9, 22.6, 21.6, 14.0.

IR (CDCl_3 , cm^{-1}) ν 3278, 2953, 2930, 2862, 1598, 1454, 1325, 1157, 1092, 905, 814, 723.

LRMS (ESI) m/z [$\text{C}_{18}\text{H}_{31}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 339.2, found 339.2

4-methyl-*N*-(1-(pentylamino)hexan-2-yl)benzenesulfonamide (3ag)

Yield: 20 mg, 59%, beige solid.

$R_f = 0.2$ (DCM/MeOH 95:5)

M.P. = 59 – 63 ($^{\circ}\text{C}$)

^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 8.3$ Hz, 2H), 7.28 (d, $J = 8.0$ Hz, 2H), 3.20 – 3.10 (m, 1H), 2.49 – 2.45 (m, 2H), 2.42 (s, 3H), 2.40 – 2.26 (m, 2H), 1.52 – 1.37 (m, 2H), 1.36 – 1.26 (m, 4H), 1.24 – 1.12 (m, 6H), 0.89 (t, $J = 7.2$ Hz, 3H), 0.81 (t, $J = 6.8$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.3, 138.0, 129.7, 127.3, 53.3, 52.4, 49.8, 33.4, 29.9, 29.5, 27.6, 22.7, 22.6, 21.6, 14.2, 14.0.

IR (CDCl_3 , cm^{-1}) ν 3278, 2955, 2926, 2857, 1459, 1326, 1159, 1093, 814, 664.

LRMS (ESI) m/z [$\text{C}_{18}\text{H}_{31}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 341.2, found 341.2

4-methyl-*N*-(1-(phenylamino)hexan-2-yl)benzenesulfonamide (3ah)

Yield: 23.0 mg, 66%, 5.0:1 rr, yellow oil.

$R_f = 0.30$ (EA/Hex 1:4).

Major isomer: ^1H NMR [500 MHz, CDCl_3] δ 7.80 – 7.76 (m, 2H), 7.31 – 7.26 (m, 2H), 7.18 – 7.13 (m, 2H), 6.76 – 6.69 (m, 1H), 6.52 – 6.46 (m, 2H), 4.84 (d, $J = 7.9$ Hz, 1H), 3.45 – 3.36 (m, 1H), 3.17 (dd, $J = 12.9, 4.7$ Hz, 1H), 3.06 (dd, $J = 12.9, 7.3$ Hz, 1H), 2.44 (s, 3H), 1.55 – 1.47 (m, 1H), 1.45 – 1.38 (m, 1H), 1.22 – 1.06 (m, 4H), 0.79 (t, $J = 7.0$ Hz, 3H).

Major isomer: ^{13}C NMR (126 MHz, CDCl_3) δ 147.7, 143.5, 137.6, 129.7, 129.2, 127.2, 117.7, 112.9, 53.5, 48.1, 33.3, 27.6, 22.4, 21.5, 13.8.

IR (CDCl_3 , cm^{-1}) ν 3400, 3280, 2954, 2930, 2861, 1602, 1508, 1322, 1157, 1091, 749, 665, 550.

LRMS (ESI) m/z [$\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 347.2, found 347.1.

***N*-(1-((4-methoxyphenyl)amino)hexan-2-yl)-4-methylbenzenesulfonamide
(3ai)**

Yield: 22.0 mg, 58%, 7.0:1 rr, yellow oil.

$R_f = 0.77$ (EA/Hex 1:1).

Major isomer:

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.76 – 7.72 (m, 2H), 7.28 – 7.24 (m, 2H), 6.78 – 6.70 (m, 2H), 6.46 – 6.41 (m, 2H), 4.79 (d, $J = 7.8$ Hz, 1H), 3.74 (s, 4H), 3.40 – 3.32 (m, 1H), 3.09 (dd, $J = 12.8, 4.6$ Hz, 1H), 2.97 (dd, $J = 12.8, 7.2$ Hz, 1H), 2.42 (s, 3H), 1.53 – 1.33 (m, 2H), 1.28 – 1.20 (m, 1H), 1.20 – 1.02 (m, 4H), 0.77 (t, $J = 7.0$ Hz, 3H).

Major isomer:

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 152.5, 144.4, 142.0, 137.8, 129.8, 127.3, 114.9, 113.8, 55.9, 52.8, 50.1, 35.1, 27.7, 22.5, 20.2, 12.3.

IR (CDCl_3 , cm^{-1}) ν 3278, 2953, 2930, 2860, 1512, 1463, 1322, 1236, 1157, 1091, 1037, 903, 817, 725, 664.

LRMS (ESI) m/z [$\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_3\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 377.2, found 377.2.

***N*-(1-cyclohexyl-3-morpholinopropan-2-yl)-4-methylbenzenesulfonamide
(3ba)**

Yield: 26 mg, 71%, colorless oil

$R_f = 0.30$ (EA/Hex 6:4)

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.76 (d, $J = 8.2$ Hz, 2H), 7.30 (d, $J = 8.0$ Hz, 2H), 5.21 (bs, 1H), 3.54 – 3.45 (m, 4H), 3.15 (ddt, $J = 9.9, 8.1, 5.1$ Hz, 1H), 2.42 (s, 3H), 2.29 (dd, $J = 12.7, 5.0$ Hz, 1H), 2.22 – 2.15 (m, 3H), 2.07 (m, 2H), 1.76 – 1.48 (m, 4H), 1.34 – 1.07 (m, 5H), 0.95 – 0.79 (m, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 143.5, 137.2, 129.7, 127.4, 66.9, 61.9, 53.5, 48.1, 41.7, 34.0, 34.0, 33.1, 29.8, 26.5, 26.2, 21.6.

IR (CDCl_3 , cm^{-1}) ν 3273, 2921, 2851, 1598, 1448, 1327, 1160, 1117, 1072, 1009, 815.

LRMS (ESI) m/z [$\text{C}_{20}\text{H}_{33}\text{N}_2\text{O}_3\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 381.2, found 381.2

***N*-((1-adamantan-2-yl)-3-morpholinopropan-2-yl)-4-methylbenzenesulfonamide (3ca)**

Yield: 34 mg, 79%, colorless oil

$R_f = 0.4$ (EA/Hex 6:4)

^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.51 (t, J = 4.7 Hz, 4H), 3.10 (ddt, J = 9.8, 8.2, 5.0 Hz, 1H), 2.41 (s, 3H), 2.30 (dd, J = 12.7, 5.1 Hz, 1H), 2.26 – 2.15 (m, 3H), 2.10 (dt, J = 11.2, 4.6 Hz, 2H), 2.01 (ddd, J = 13.7, 8.3, 4.9 Hz, 1H), 1.91 (dd, J = 12.6, 2.8 Hz, 1H), 1.79 (tdt, J = 14.5, 5.4, 3.0 Hz, 5H), 1.70 (d, J = 3.3 Hz, 2H), 1.66 – 1.41 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.5, 137.2, 129.7, 127.4, 66.9, 61.8, 53.5, 48.7, 40.4, 39.2, 38.3, 37.1, 32.8, 31.6, 31.6, 31.5, 28.2, 28.0, 21.6.

IR (CDCl_3 , cm^{-1}) ν 3270, 2904, 2851, 1452, 1402, 1329, 1160, 1116, 1092, 906, 727.

LRMS (ESI) m/z [$\text{C}_{24}\text{H}_{37}\text{N}_2\text{O}_3\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 433.3, found 433.3

4-methyl-*N*-(1-morpholino-3-phenylpropan-2-yl)benzenesulfonamide (3da)

Yield: 16.4 mg, 44%, yellow oil.

R_f = 0.36 (EA/Hex 1:1).

^1H NMR [500 MHz, CDCl_3] δ 7.86 – 7.74 (m, 2H), 7.33 – 7.29 (m, 2H), 7.28 – 7.23 [m, 2H), 7.23 – 7.18 (m, 1H), 7.17 – 7.11 (m, 2H), 3.51 – 3.40 (m, 4H), 3.34 – 3.24 (m, 1H), 3.17 (dd, J = 13.7, 3.8 Hz, 1H), 2.79 (dd, J = 13.7, 8.1, Hz, 1H), 2.42 (s, 3H), 2.24 – 2.13 (m, 2H), 2.13 – 2.02 (m, 2H), 2.02 – 1.92 (m, 2H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.67, 137.06, 136.76, 129.83, 129.80, 128.53, 127.39, 126.70, 66.80, 60.39, 53.15, 50.95, 39.72, 21.64. ff

IR (CDCl_3 , cm^{-1}) ν 3261, 3060, 3027, 2922, 2854, 2814, 1598, 1453, 1332, 1160, 1115, 1089, 702, 665, 551.

LRMS (ESI) m/z [$\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_3\text{S}$] $^+$ ($[\text{M}+\text{H}]^+$) calculated 375.2, found 375.2.

N-(6-((*tert*-butyldiphenylsilyl)oxy)-1-morpholinohexan-2-yl)-4-methylbenzenesulfonamide (3ea)

Yield: 47.1 mg, 79%, colorless oil.

R_f = 0.40 (EA/Hex 2:3).

^1H NMR (500 MHz, CDCl_3) δ 7.81 – 7.75 (m, 2H), 7.72 – 7.64 (m, 4H), 7.48 – 7.37 (m, 6H), 7.33 – 7.26 (m, 2H), 5.28 (s, 1H), 3.70 – 3.59 (m, 2H), 3.58 – 3.47 (m, 4H), 3.11 (qd, J = 7.4, 4.1 Hz, 1H), 2.42 (s, 3H), 2.25 (d, J = 7.3 Hz, 2H), 2.22 – 2.14 (m, 2H), 2.14 – 2.05 (m, 2H), 1.77 – 1.68 (m, 1H), 1.60 – 1.48 (m, 3H), 1.41 – 1.27 (m, 2H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 143.4, 137.0, 135.6, 134.0, 129.6, 127.6, 127.2, 66.7, 63.6, 60.9, 53.2, 49.9, 33.0, 32.5, 26.9, 21.5, 21.0, 19.3.

IR (CDCl_3 , cm^{-1}) ν 3267, 2930, 2857, 1427, 1330, 1160, 1109, 1093, 816, 703, 550, 504.

LRMS (ESI) m/z $[C_{33}H_{47}N_2O_4SSi]^+$ ($[M+H]^+$) calculated 595.3, found 595.3.

ethyl 6-((4-methylphenyl)sulfonamido)-7-morpholinoheptanoate (3fa)

Yield: 32.5 mg, 79%, yellow oil.

R_f = 0.43 (DCM:MeOH 19:1).

1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.50 (dt, J = 12.3, 6.1 Hz, 4H), 3.09 (qd, J = 7.1, 4.6 Hz, 1H), 2.42 (s, 3H), 2.29 – 2.21 (m, 4H), 2.11 (m, 4H), 1.74 – 1.50 (m, 4H), 1.35 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.21 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 143.5, 137.0, 129.7, 127.3, 66.7, 60.9, 60.3, 53.3, 49.7, 34.1, 32.9, 24.9, 24.1, 21.6, 14.3.

IR ($CDCl_3$, cm^{-1}) ν 3268, 2930, 2858, 1729, 1329, 1302, 1158, 1116, 1092, 666, 551.

LRMS (ESI) m/z $[C_{20}H_{32}N_2O_5S]^+$ ($[M+H]^+$) calculated 413.2, found 413.2.

N-(6-(1,3-dioxoisindolin-2-yl)-1-morpholinohexan-2-yl)-4-methylbenzenesulfonamide (3ga)

Yield: 42.0 mg, 86%, yellow oil.

R_f = 0.25 (EA/Hex 2:1).

1H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.79 – 7.71 (m, 4H), 7.32 – 7.27 (m, 2H), 5.13 (brs, 1H), 3.70 – 3.60 (m, 2H), 3.56 – 3.46 (m, 4H), 3.17 – 3.08 (m, 1H), 2.42 (s, 3H), 2.28 – 2.14 (m, 4H), 2.14 – 2.05 (m, 2H), 1.76 – 1.67 (m, 1H), 1.66 – 1.56 (m, 3H), 1.40 – 1.20 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 143.4, 137.1, 133.9, 132.1, 129.6, 127.2, 123.2, 66.7, 61.0, 53.2, 49.7, 37.6, 32.6, 28.5, 21.8, 21.5.

IR ($CDCl_3$, cm^{-1}) ν 3274, 2938, 2859, 2814, 1708, 1397, 1331, 1159, 1116, 721.

LRMS (ESI) m/z $[C_{25}H_{32}N_3O_5S]^+$ ($[M+H]^+$) calculated 486.2, found 486.1.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Information

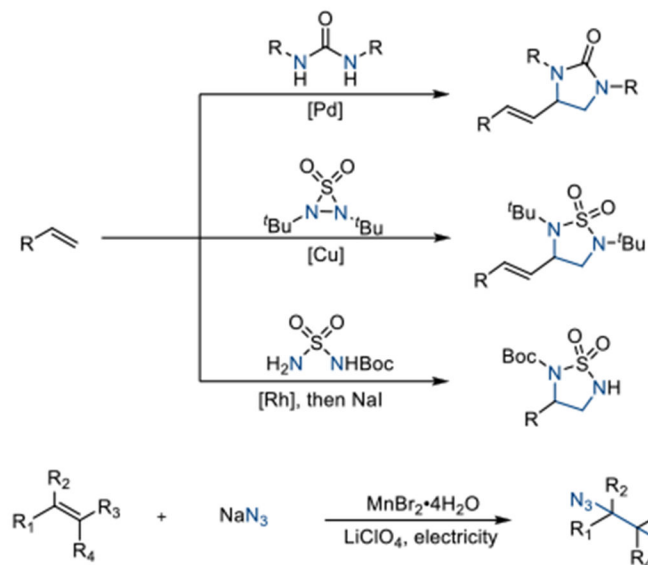
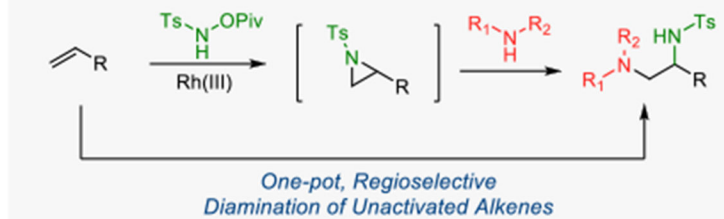
We thank the National Institute of General Medical Sciences (NIGMS, Grant No. GM80442) for support.

Reference

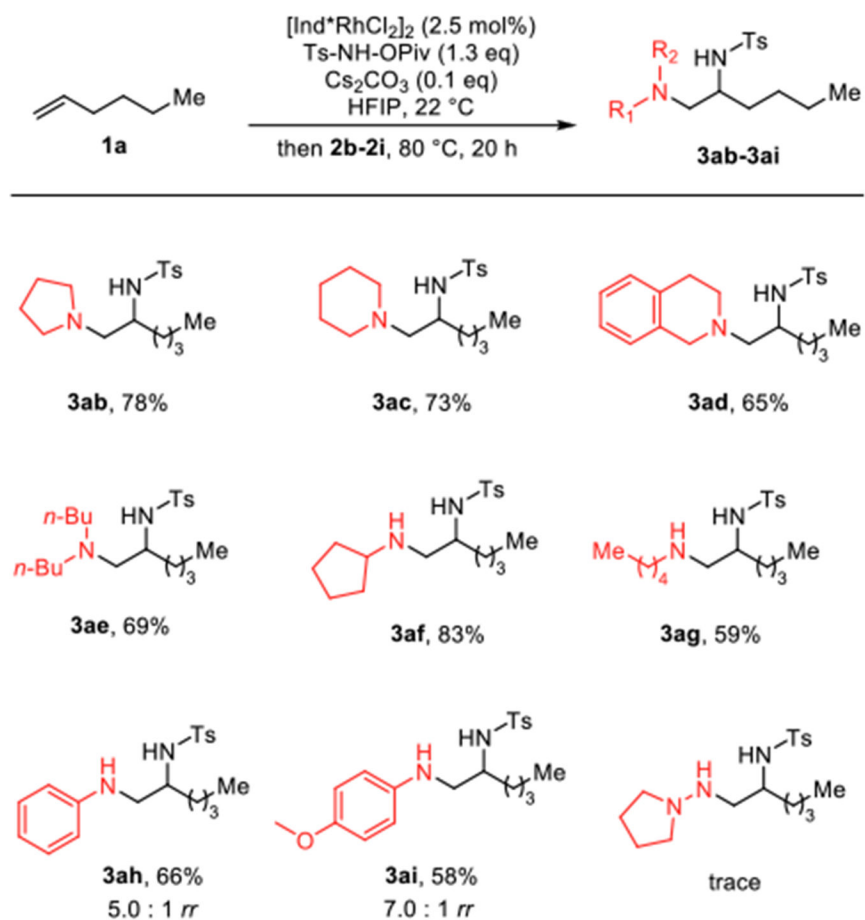
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Previous Work

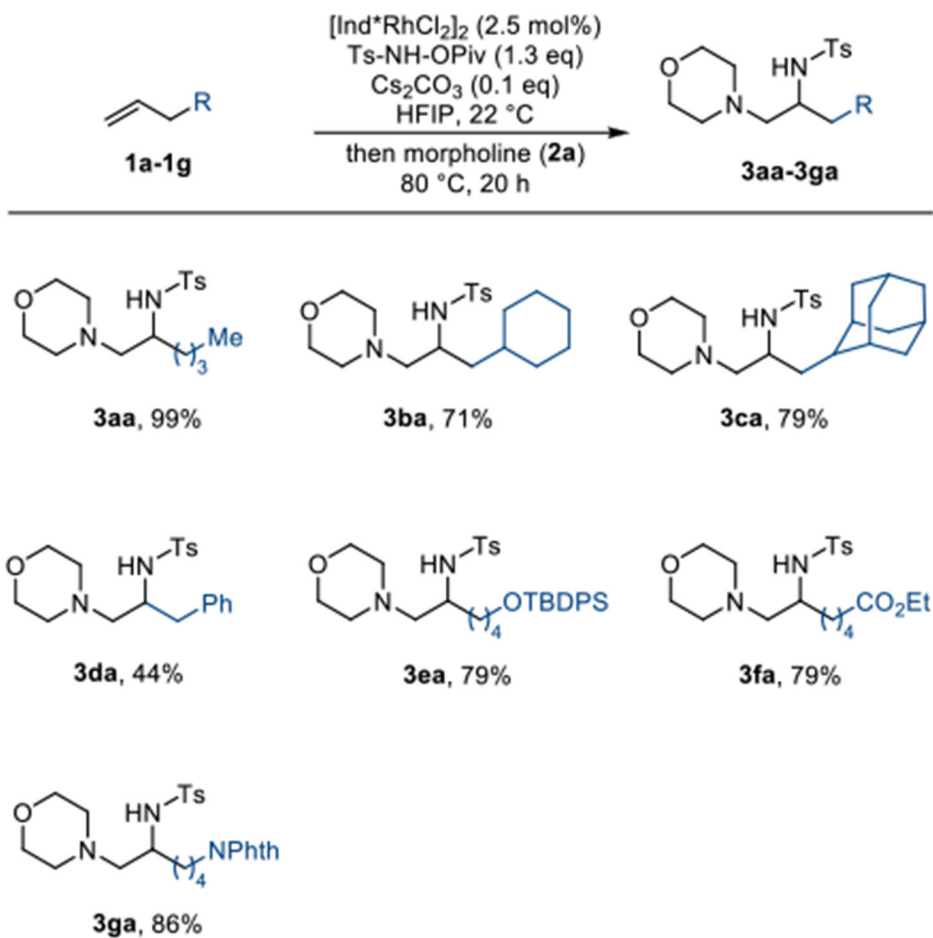
Transition-metal catalyzed diamination of alkenes

**This Work**

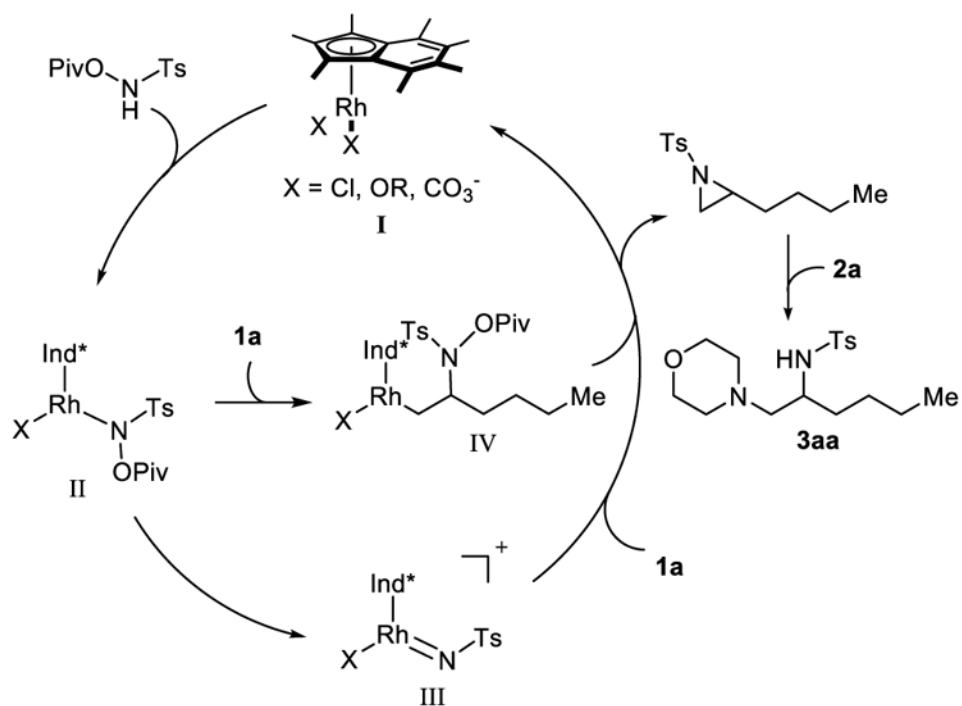
Scheme 1.
Transition metal-catalyzed alkene diaminations

**Scheme 2.**

Amine Nucleophile Substrate Scope ^a Determined by ¹H NMR analysis of unpurified reaction mixture



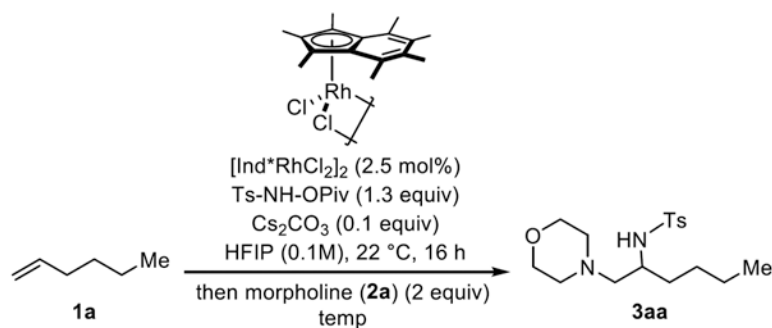
Scheme 3.
Terminal Alkene Substrate Scope



Scheme 4.
Proposed Mechanism

Table 1

Optimization Table



entry	conc. (M)	morpholine (equiv)	temp.(°C)	reaction time (h)	yield (%) ^a
1	0.1	2	22	8	< 5
2	0.1	2	40	8	19
3	0.1	2	80	8	63
4 ^b	0.1	2	80	8	28
5	0.1	2	80	20	78
6	0.2	2	80	20	87
7	0.2	3	80	24	99

^aDetermined by ¹H NMR analysis of unpurified reaction mixture

^bAgSbF₆ (1 equiv.) was added.