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Efficient intramolecular hydroamination of aminoalkynes catalyzed by a zirconium(IV) complex

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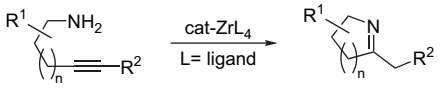
Abstract

The neutral zirconium(IV) bis(thiophosphinic amidate) complex was demonstrated to be an effective precatalyst for 5-*exo*-, 6-*exo*-, and 7-*exo-dig* intramolecular hydroamination of aminoalkynes, producing the cyclic imines in excellent yields (92–98%).

Keywords: Aminoalkyne; Catalysis; Cyclization; Hydroamination; Zirconium

1. Introduction

Transition metal-catalyzed intramolecular hydroamination of aminoalkynes has been recognized as an effective method for the synthesis of nitrogen-containing heterocyclic compounds.[1] A variety of metallocenes as well as nonmetallocene complexes of the group 3 metals have been developed as efficient catalysts in hydroamination of aminoalkenes, aminoalkynes, and aminoallenes.[2] Recently, there have been several reports describing inter- and intramolecular hydroamination of these compounds with the group 4 metals.[3] However, these procedures suffer from some disadvantages such as inconvenient preparation and instability of the catalysts and limited substrate scope. Therefore, there is still a strong need for a highly efficient catalytic synthesis of azacycles common to naturally occurring alkaloids through hydroamination. We have previously described that chelating bis(thiophosphinic amidate) complexes of the group 3 metals (particularly Y and Nd) are powerful catalysts for intramolecular hydroamination of aminoalkenes.[2j] Very recently, we reported that a neutral zirconium(IV) complex was an effective precatalyst for intramolecular hydroamination of aminoalkenes and aminoallenes to give cyclic amines in good to excellent yields.[4] In continuation of our studies directed toward the development of efficient group 4 metal-catalyzed-hydroamination of aminoalkynes, we now report the realization of this goal with zirconium complex (Scheme 1).



Scheme 1. Zirconium-catalyzed intramolecular hydroamination of aminoalkynes.

2. Results and discussion

The catalytic activity of several group 3 and 4 metal complexes in Scheme 2 was first examined in the hydroamination of 5-phenyl-4-pentynyl-1-amine (**1**) and 5-decynyl-1-amine (**2**) and the results are summarized in Table 1. $TiCl(NMe_2)_3$ gave the desired product in 91% yield (by NMR in benzene-d_6) at 75 °C for 17 h (entry 1). However, $Ti(NMe_2)_4$ required

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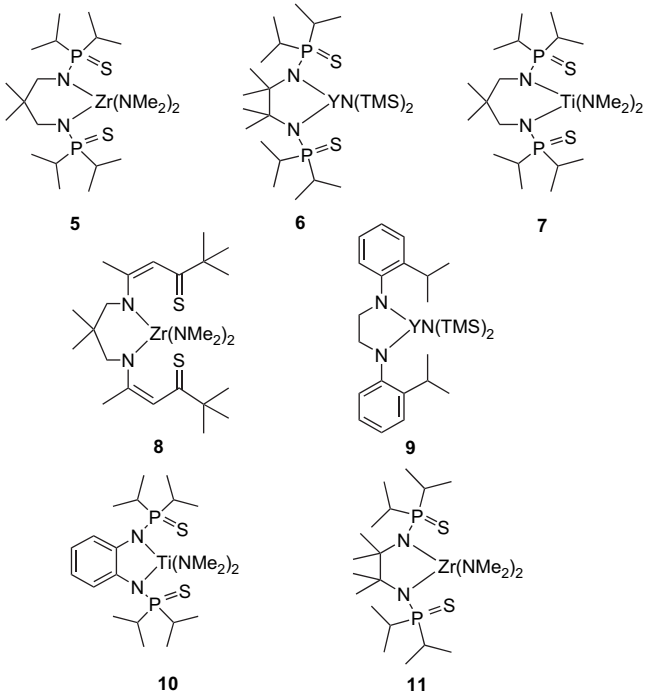
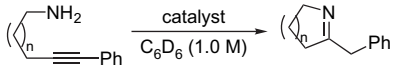


Scheme 2. Representative group 3 and 4 complexes.

Table 1
Optimization of intramolecular hydroamination of aminoalkynes[a]



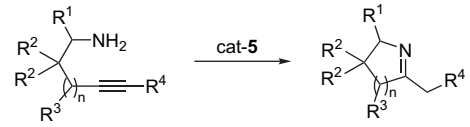
1 (n= 1), **2** (n= 2) **3** (n= 1), **4** (n= 2)

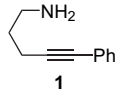
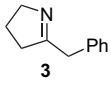
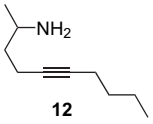
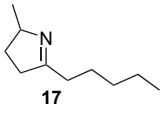
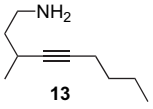
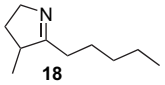
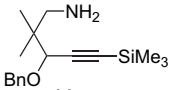
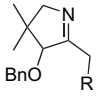
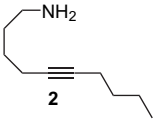
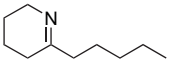
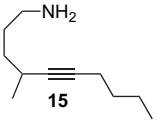
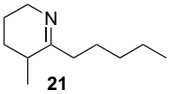
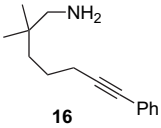
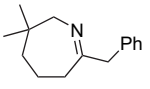
Entry	*n*	Catalyst	Temp (°C)	Time (h)	Yield[b] (%)
1	2	$TiCl(NMe_2)_3$	75	17	91
2	2	$Ti(NMe_2)_4$	75	58	87
3	2	$Zr(NMe_2)_4$	75	24	0
4	2	$Zr(NMe_2)_4$	125	24	86
5	2	**5**	75	5.5	95
6	2	**6**	75	21	0
7	2	**6**	100	30	0
8	2	**7**	75	43	73
9	2	**8**	125	41	0
10	1	**5**	60	1.5	95
11	1	**9**	60	9	94
12	1	**10**	60	9	0
13	1	**10**	125	9	95
14	1	**11**	60	9	91
15	1	$Y[N(TMS)_2]_3$	60	80	96

[a] Reactions were carried out in the presence of 5 mol % of catalyst in benzene-d_6.
[b] NMR yields based on *p*-xylene as an internal standard.

a longer reaction time (75 °C, 58 h) to produce the cyclic imine (**4**) in 87% yield (entry 2). Although reaction of aminoalkyne **2** with 5 mol % of $Zr(NMe_2)_4$ did not proceed at 75 °C for 24 h (entry 3), compound **4** was obtained in 86% yield at 125 °C after 24 h (entry 4), indicating that reactivity of $TiCl(NMe_2)_3$ and $Ti(NMe_2)_4$ in hydroamination is better than $Zr(NMe_2)_4$. With these results, a variety of precatalysts generated in situ from the direct metalation of several 1,2- or 1,3-diamino proligands with titanium, zirconium, or yittrium complexes were applied to intramolecular hydroamination. Of the catalytic systems examined, the best results were obtained with 5 mol % of catalyst **5** in benzene-d_6 at 75 °C for 5.5 h, producing the desired product in 95% yield (entry 5). Although the use of catalysts **6** and **8** did not provide the cyclic compound (entries 6, 7, and 9), 5 mol % of catalyst **7** afforded compound **4** in 73% yield at 75 °C for 43 h (entry 8). Treatment of **1** with 5 mol % of **5** gave rise to the cyclic imine **3** in 95% yield through 5-*exo-dig* intramolecular hydroamination (entry 10). The hydroamination of **1** was also examined using $Y[N(TMS)_2]_3$, **9**, **10**, and **11**. When aminoalkyne **1** was treated with 5 mol % of $Y[N(TMS)_2]_3$ at 60 °C for 80 h, the desired product **3** was produced in 96% yield (entry 15). Although the hydroamination of **1** using catalysts **9**, **10**, and **11** gave the cyclic imine **3** in 94%, 95% and 91% yields,

Table 2
Zirconium-catalyzed intramolecular hydroamination of aminoalkynes[a]



Entry	Aminoalkyne	Time (h)	Product	Yield[b] (%)
1	 **1**	1.5	 **3**	95 (91)[c]
2	 **12**	2.5	 **17**	98
3	 **13**	2.5	 **18**	93
4	 **14**	11	 **19** (R: $SiMe_3$) **20** (R: H)	96[d] 90[e]
5	 **2**	5.5	 **4**	95
6	 **15**	10	 **21**	92
7[f]	 **16**	7	 **22**	93

[a] Reactions were carried out in the presence of 5 mol % of catalyst **5** in benzene-d_6 at 75 °C.
[b] NMR yields based on *p*-xylene as an internal standard.
[c] Isolated yield (3.0 mmol scale). Reaction was carried out at 60 °C.
[d] NMR yield of **19**.
[e] Isolated yield of **20** after quenching with NaOH in methanol.
[f] The reaction was carried out at 100 °C.

respectively, a longer reaction time (9 h) was needed at 60 and 125 °C (entries 11–14). These results show that zirconium(IV) bis(thiophosphinic amidate) complex **5** is the best catalyst for the hydroamination of both aminoalkynes **1** and **2** in terms of yield and reaction time.

To demonstrate the efficiency and scope of the present method, we applied this catalyst **5** to intramolecular hydroamination of a variety of aminoalkynes. The results of this study are summarized in Table 2. Aminoalkyne **12** bearing a methyl group at carbon adjacent to nitrogen was smoothly cyclized to give **17** in 98% yield (75 °C, 2.5 h, entry 2). Subjecting **13** to 5 mol % of **5** provided the desired product **18** in 93% yield (75 °C, 2.5 h, entry 3). Reaction of **14** with 5 mol % of **5** produced compound **19** in 96% NMR yield (75 °C, 11 h, entry 4). The reaction mixture was quenched with methanolic NaOH, producing the protodesilylated compound **20** in 90% yield. Under the optimum conditions, 6-aminoalkyne **15** was readily cyclized to afford **21** in 92% yield through 6-*exo-dig* intramolecular hydroamination (entry 6). Encouraged by these results regarding the preparation of five- and six-membered cyclic imines through hydroamnation of 5- and 6-aminoalkyne, the intramolecular hydroamination of 7-aminoalkynes was subsequently examined. Exposure of 7-aminoalkyne **16** to catalyst **5** produced the seven-membered cyclic imine **22** in 93% yield (100 °C, 7 h) through 7-*exo-dig* intramolecular hydroamination (entry 7). Since the aminoalkynes **1** and **2**, which do not have substituents on carbon chain between amino and alkynyl group, gave the desired products **3** and **4** in excellent yields, the present method is not strongly reliant on the Thorpe–Ingold effect.

3. Conclusion

In conclusion, we have demonstrated that the neutral zirconium(IV) bis(thiophosphinic amidate) complex **5** generated in situ from the direct metalation of NPS ligand with $Zr(NMe_2)_4$ is a potent catalyst for intramolecular hydroamination of a variety of aminoalkynes. 5-*exo*-, 6-*exo*- and 7-*exo-dig* intramolecular hydroamination of aminoalkynes proceeded smoothly in all cases to produce the cyclic imines in excellent yields. No *endo*-cyclized products were formed in these reactions.

4. Experimental

4.1. General

Infrared spectra were recorded on a Perkin–Elmer model 1600 FT-IR. ^{1}H NMR spectra were recorded on a Bruker AVANCE DPX-300 (300 MHz) or AVANCE DPX-500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million from TMS with the residual protic solvent resonance as the internal standard (chloroform: 7.27, benzene: 7.16). ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX-300 (75 MHz) or AVANCE DPX-500 (125 MHz) spectrometer. Chemical shifts were reported in parts per million from TMS with the solvent as an internal standard ($CDCl_3$: 77.23). High-resolution mass spectra were recorded on an Autospec M363 series (Micromass). All experiments were carried out under an argon atmosphere. Organozirconium complexes were manipulated under an argon atmosphere in a glove box. Benzene was distilled from sodium. Zirconium(IV) bis(thiophosphinic amidate) complex (**5**) was prepared from the reaction of $Zr(NMe_2)_4$ with *N*,*N*′-bis(*p*,*p*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (NPS ligand).[4]

4.2. Typical procedure for intramolecular hydroaminations of aminoalkynes using catalyst 5

In an argon-filled glove box, $Zr(NMe_2)_4$ (20 μl, 0.02 mmol, 1.0 M solution in benzene-d_6) and *N*,*N*′-bis(*p*,*p*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (7.97 mg, 0.02 mmol) in benzene-d_6 (0.4 mL) were introduced sequentially into a J. Young NMR tube.[5] The reaction mixture was stirred at 25 °C for 10 min until ligand exchange was judged complete by the disappearance of the $Zr(NMe_2)_4$ resonance in the ^{1}H NMR spectrum with concomitant production of Me_2NH. The appropriate aminoalkyne (0.4 mmol) and *p*-xylene (10 μl, 0.08 mmol) as an internal standard were added to the resulting solution and the reaction mixture was subsequently heated at 75 or 100 °C in an oil bath to achieve hydroamination. The reaction mixture was treated with 10 drops of methanolic NaOH (5%), stirred for 0.5 h at room temperature, concentrated in vacuo, and filtered the crude compound through silica gel to afford pure imines.

4.2.1. Spectral data

*4.2.1.1. 5-Phenyl-4-pentynyl-1-amine (**1**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38–7.37 (m, 2H, Ph), 7.27–7.26 (m, 3H, Ph), 2.87 (t, *J*=6.8 Hz, 2H, CH_2NH_2), 2.48 (t, *J*=7.0 Hz, 2H, $CH_2{\equiv}C$), 1.74 (q, *J*=6.9 Hz, 2H, $CH_2CH_2CH_2$), 1.32 (br, 2H, NH_2). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 131.7, 128.4, 127.8, 124.1, 89.8, 81.1, 41.5, 32.7, 17.1. IR (film) 3298, 3056, 2938, 2866, 2228, 1598, 1570, 1560, 1490, 1442, 756, 692 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{13}N$ (M^+), 159.1048; found, 159.1043.

*4.2.1.2. 5-Decynyl-1-amine (**2**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.67 (t, 2H, *J*=6.5 Hz, CH_2NH_2), 2.15–2.10 (m, 4H, $CH_2C{\equiv}CCH_2$), 1.51–1.45 (m, 4H, $NH_2CH_2CH_2CH_2$), 1.45–1.32 (m, 4H, $C{\equiv}CCH_2CH_2CH_2$), 1.08 (br, 2H, NH_2), 0.87 (t, *J*=7.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 80.6, 79.9, 42.0, 33.2, 31.4, 26.6, 22.1, 18.8, 18.6, 13.8. IR (film) 3338, 2958, 2934, 2862, 2158, 1570, 1488, 1466, 1434, 1382, 1328 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1516.

*4.2.1.3. 1-Methyl-4-nonynyl-1-amine (**12**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.02 (sex, 1H, *J*=6.3 Hz, $CHNH_2$), 2.24–2.21 (m, 2H, $CH_2C{\equiv}C$), 2.16–2.12 (m, 2H, $C{\equiv}CCH_2$), 1.56–1.45 (m, 4H, $C{\equiv}CCH_2CH_2CH_2$), 1.43–1.35 (m, 4H, $CHCH_2$, NH_2), 1.08 (d, *J*=6.5 Hz, 3H, NH_2CHCH_3), 0.90 (t, *J*=7.5 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 80.8, 79.7, 46.3, 39.2, 31.4, 23.9, 22.2, 18.6, 16.1, 13.8. IR (film) 3300, 2950–2850, 1590, 1460, 1370, 825 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1519.

*4.2.1.4. 3-Methyl-4-nonynyl-1-amine (**13**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.83–2.76 (m, CH_2NH_2), 2.49–2.45 (m, 1H, $CHC{\equiv}C$), 2.15 (td, J=6.87, 2.07 Hz, 2H, $C{\equiv}CCH_2$), 1.53–1.46 (m, 4H, $NH_2CH_2CH_2$, NH_2), 1.45–1.33 (m, 4H, $C{\equiv}CCH_2CH_2CH_2$), 1.15 (d, J=6.89 Hz, 3H, $CHCH_3$), 0.90 (t, J=7.11 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 84.1, 80.8, 41.2, 40.4, 31.3, 23.6, 21.9, 21.7, 18.4, 13.6. IR (film) 3353, 2958, 2934, 2859, 2158, 1488, 1382 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1515.

*4.2.1.5. 3-Benzyloxy-2,2-dimethyl-5-trimethylsilyl-4-pentynyl-1-amine (**14**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35 (d, J=4.5 Hz, 4H, Ph), 7.31–7.28 (m, 1H, Ph), 4.83 (d, J=12.0 Hz, 1H, CH_2Ph), 4.47 (d, J=12.0 Hz, 1H, CH_2Ph), 3.87 (s, 1H, $CHOCH_2$), 2.89 (d, J=13.0 Hz, 1H, $CHHNH_2$), 2.67 (d, J=13.0 Hz, 1H, $CHHNH_2$), 1.63 (br, 1H, NH_2), 1.03 (s, 3H, $(CH_3)_2C$), 1.01 (s, 3H, $(CH_3)_2C$), 0.21 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.3, 128.5, 128.2, 127.8, 103.4, 92.5, 75.6, 71.0, 50.1, 39.6, 22.2, 21.5, 0.2. IR (film) 3396, 3064, 2957, 2887, 2167, 1652, 1608, 1496, 1454, 1386, 1249, 1069, 840, 759, 697 cm^{-1}. HRMS (EI): calcd for $C_{17}H_{27}NOSi$ (M^+), 289.1862; found, 289.1864.

*4.2.1.6. 4-Methyl-5-decynyl-1-amine (**15**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.67–2.60 (m, 2H, CH_2NH_2), 2.34–2.31 (m, 1H, $C{\equiv}CCHCH_3$), 2.09 (td, J=6.5, 2.0 Hz, 2H, $CHC{\equiv}CCH_2$), 1.57–1.48 (m, 1H, CH_2CHCH_3), 1.48–1.46 (m, 1H, CH_2CHCH_3), 1.44–1.29 (m, 6H, $NH_2CH_2CH_2$, $C{\equiv}CCH_2CH_2CH_2$), 1.24 (br, 1H, NH_2), 1.08 (d, J=7.0 Hz, $CH_3CHC{\equiv}C$), 0.84 (t, J=7.0 Hz, 3H, $CH_2CH_2CH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 84.6, 80.6, 42.2, 34.7, 31.8, 31.4, 26.0, 22.0, 21.7, 18.5, 13.7. IR (film) 3366, 3296, 2933, 2862, 2152, 1608, 1587, 1455, 1388, 1095, 845, 784 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{21}N$ (M^+), 167.1674; found, 167.1675.

*4.2.1.7. 2,2-Dimethyl-7-phenyl-6-heptynyl-1-amine (**16**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41 (dd, J=7.75, 2.0 Hz, 2H, Ph), 7.30–7.25 (m, 3H, Ph), 2.46 (s, 2H, CH_2NH_2), 2.39 (t, J=7.0 Hz, 2H, $CH_2{\equiv}C$), 1.59–1.53 (m, 2H, CH_2CH_2), 1.37–1.33 (m, 2H, CH_2CH_2), 1.18 (br, 2H, NH_2), 0.87 (s, 6H, $(CH_3)_2C$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 131.5, 128.1, 127.4, 124.0, 90.2, 80.7, 52.7, 38.7, 34.3, 24.7, 23.6, 20.2. IR (film) 3346, 3067, 2936, 2864, 2232, 1560, 1542, 1490, 756 cm^{-1}. HRMS (EI): calcd for $C_{15}H_{21}N$ (M^+), 215.1674; found, 215.1671.

*4.2.1.8. 6-Pentyl-2,3,4,5-tetrahydropyridine (**4**).* Subjecting 5-decynyl-1-amine (61.3 mg, 0.4 mmol) to 5 mol % **5** under the general procedure provided the cyclic imine **4** (58.2 mg, 95%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.48 (t, J=6.5 Hz, 2H, CH_2N), 2.08–2.03 (m, 4H, $CH_2C{=}N$, $N{=}CCH_2$), 1.62–1.57 (m, 2H, $CH_2CH_2C{=}N$), 1.51–1.43 (m, 4H, CH_2CH_2N, CCH_2CH_2), 1.28–1.21 (m, 4H, $CH_2CH_2CH_3$), 0.87 (t, J=6.75 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.3, 49.2, 41.2, 31.8, 29.1, 26.3, 22.6, 22.0, 19.7, 14.1. IR (film) 2958, 2934, 2860, 1660 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1519.

*4.2.1.9. 2-Methyl-5-pentyl-3,4-dihydro-2H-pyrrole (**17**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.04–3.99 (m, 1H, CHN), 2.57–2.50 (m, 1H, $CH_2C{=}N$), 2.45–2.40 (m, 1H, $CH_2C{=}N$), 2.30 (t, J=7.75 Hz, $N{=}CCH_2$), 2.10–2.03 (m, 1H, $NCHCH_2$), 1,60–1.54 (m, 2H, $CCH_2CH_2CH_2$), 1.39–1.28 (m, 5H, $CCH_2CH_2CH_2CH_2$, $NCHCH_2$), 1.27 (d, J=7.0 Hz, 3H, $CHCH_3$), 0.89 (t, J=7.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.4, 67.8, 37.5, 34.1, 31.9, 30.9, 26.5, 22.7, 22.3, 14.2. IR (film) 2950, 2920, 2860, 1620, 1425, 1410, 1360 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1516.

*4.2.1.10. 4-Methyl-5-pentyl-3,4-dihydro-2H-pyrrole (**18**).* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.82–3.76 (m, 1H, CH_2N), 3.66–3.59 (m, 1H, CH_2N), 2.78–2.68 (m, 1H, $CHC{=}N$), 2.35–2.18 (m, 2H, $N{=}CCH_2$), 2.15–2.07 (m, 1H, NCH_2CH_2), 1.67–1.56 (m, 2H, $NCHCH_2$), 1.48–1.41 (m, 1H, NCH_2CH_2), 1.32 (br m, 2H, $CCH_2CH_2CH_2CH_2$), 1.22 (td, J=5.02, 1.09 Hz, 2H, $CCH_2CH_2CH_2CH_2$), 1.17 (td, J=5.58, 1.03 Hz, 2H, $CCH_2CH_2CH_2CH_2$), 1.11 (dd, J=7.13, 1.34 Hz, 3H, $CHCH_3$), 0.89 (t, J=6.10 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 58.8, 44.4, 32.2, 32.1, 31.69, 26.3, 22.9, 17.8, 14.4. IR (film) 2950, 2928, 2860, 1622 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{19}N$ (M^+), 153.1517; found, 153.1515.

*4.2.1.11. 4-Benzyloxy-3,3,5-trimethyl-3,4-dihydro-2H-pyrrole (**20**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38 (d, 2H, J=4.0 Hz, Ph), 7.34–7.31 (m, 1H, Ph), 4.75 (d, J=12.0 Hz, 1H, CH_2Ph), 4.60 (d, J=12.0 Hz, 1H, CH_2Ph), 3.98 (s, 1H, $CHOBn$), 3.55 (d, J=14.5 Hz, 1H, CH_2N), 3.37 (d, J=14.5 Hz, 1H, CH_2N), 2.03 (s, 3H, CCH_3), 1.17 (s, 3H, $C(CH_3)_2$), 1.03 (s, 3H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.2, 138.3, 128.7, 128.1, 128.1, 92.8, 73.8, 71.9, 42.8, 26.7, 21.6, 18.0. IR (film) 3334, 2981, 2361, 1626, 1481, 1377, 1309, 754, 730 cm^{-1}. HRMS (CI): calcd for $C_{14}H_{20}NO$ (M+1), 218.1544; found, 218.1534.

*4.2.1.12. 5-Methyl-6-pentyl-2,3,4,5-tetrahydropyridine (**21**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.58–3.50 (m, 2H, CH_2N), 2.26–2.16 (m, 3H, $CH_2C{=}N$, $N{=}CCHCH_3$), 1.80–1.74 (m, 1H, $CH_2CHC{=}N$), 1.66–1.59 (m, 1H, $CH_2CH{-}C{=}N$), 1.56–1.46 (m, 3H, $CH_2CH_2C{=}N$, NCH_2CH_2), 1.45–1.40 (m, 1H, NCH_2CH_2), 1.35–1.25 (m, 4H, $CH_2CH_2CH_3$), 1.13 (d, J=7.5 Hz, $CHCH_3$), 0.89 (t, J=7.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 49.6, 38.4, 32.9, 32.0, 28.3, 26.6, 22.7, 20.0, 18.8, 14.1. IR (film) 2955, 2930, 2864, 1663 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{21}N$ (M^+), 167.1674; found, 167.1676.

*4.2.1.13. 7-Benzyl-3,3-dimethyl-3,4,5,6-tetrahydro-2H-azepine (**22**).* ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.30–7.25 (m, 4H, Ph), 7.22–7.20 (m, 1H, Ph), 3.55 (s, 2H, CH_2Ph), 3.40 (s, 2H, CH_2N), 2.24 (t, J=5.75 Hz, 2H, $CH_2C{=}N$), 1.40 (t, J=6.0 Hz, 2H, $(CH_3)_2CCH_2$), 1.20–1.14 (m, 2H, $CH_2CH_2CH_2$), 0.88 (s, 6H, $(CH_3)_2C$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.8, 137.1, 129.4, 128.6, 126.9, 61.9, 49.7, 44.4, 32.1, 27.3, 19.5, 16.3. IR (film) 3100–2860, 1680, 1485 cm^{-1}. HRMS (EI): calcd for $C_{15}H_{21}N$ (M^+), 215.1674; found, 215.1668.

4.3. Preparative synthesis of 3,4-dihydro-5-benzyl-2H-pyrrole (**3**)

$Zr(NMe_2)_4$ (150.0 μl, 0.15 mmol, 1.0 M solution in benzene-d_6) was added to a solution of *N*,*N*′-bis(*p*,*p*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (59.79 mg, 0.15 mmol) in benzene (3 mL) under an argon atmosphere. The homogeneous reaction mixture was stirred at 25 °C for 10 min. After 5-phenyl-4-pentynyl-1-amine (**1**) (477.7 mg, 3.0 mmol) was added to the reaction mixture, it was heated to 75 °C for 1.5 h to complete hydroamination. The reaction mixture was cooled and treated with 10 drops of methanolic NaOH (5%), and then stirred for 0.5 h at room temperature and concentrated in vacuo. The residue was subjected to flash chromatography on silica gel using $MeOH/CH_2Cl_2$=1:15 to furnish the title compound (406.0 mg, 85%) as a colorless oil. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.33–7.30 (m, 2H, Ph), 7.25–7.22 (m, 3H, Ph), 3.84 (t, J=6.0 Hz, 2H, CH_2NH_2), 3.69 (s, 2H, CH_2Ph), 2.40 (t, J=8.0 Hz, 2H, $CH_2CH_2CH_2$), 1.84 (quintet, J=8.0 Hz, 2H, $CH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.1, 137.2, 129.2, 128.8, 126.8, 61.1, 40.9, 36.7, 22.8. IR (film) 3100–2850, 1604, 1496 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{13}N$ (M^+), 159.1048; found, 159.1046.

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References and notes

1. (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675; (b) Burling, S.; Field, L. D.; Messerle, B. A. *Organometallics* **2000**, *19*, 87; (c) Müller, T. E.; Grosche, M.; Herdtweck, E.; Pleier, A.-K.; Walter, E.; Yan, Y.-K. *Organometallics* **2000**, *19*, 170; (d) Vasen, D.; Salzer, A.; Gerhards, F.; Gais, H.-J.; Stürmer, R.; Bieler, N. H.; Togni, A. *Organometallics* **2000**, *19*, 539; (e) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546; (f) Haak, E.; Siebeneicher, H.; Doye, S. *Org. Lett.* **2000**, *2*, 1935; (g) Johnson, J. S.; Bergman, R. G. *J. Am. Chem. Soc.* **2001**, *123*, 2923; (h) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, *32*, 104; (i) Bytschkov, I.; Doye, S. *Eur. J. Org. Chem.* **2003**, 935; (j) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079.

2. (a) Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275; (b) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633; (c) Tian, S.; Arredondo, V. M.; Stern, C. L.; Marks, T. J. *Organometallics* **1999**, *18*, 4421; (d) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *Org. Lett.* **2001**, *3*, 3091; (e) Kim, Y. K.; Livinghouse, T.; Bercaw, T. E. *Tetrahedron Lett.* **2001**, *42*, 2933; (f) Kim, Y. K.; Livinghouse, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 3645; (g) Ryu, J.-S.; Li, G. Y.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 12584; (h) O'Shaughnessy, P. N.; Knight, P. D.; Morton, C.; Gillespie, K. M.; Scott, P. *Chem. Commun.* **2003**, 1770; (i) Gribkov, D. V.; Hulzsch, K. C.; Hampel, F. *Chem.—Eur. J.* **2003**, *9*, 4796; (j) Kim, Y. K.; Livinghouse, T.; Horino, Y. *J. Am. Chem. Soc.* **2003**, *125*, 9560; (k) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F.; Wagner, T. *Organometallics* **2004**, *23*, 2601; (l) Lauterwasser, F.; Hayes, P. G.; Brase, S.; Piers, W.; Schafer, L. L. *Organometallics* **2004**, *23*, 2234; (m) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *39*, 673; (n) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *J. Org. Chem.* **2004**, *69*, 1038; (o) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 4391; (p) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 1737; (q) Crimmin, M. R.; Casely, I. J.; Hill, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 2042.

3. (a) McGrane, P. L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992**, *114*, 5459; (b) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708; (c) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753; (d) Shi, Y.; Ciszewski, J. T.; Odom, A. L. *Organometallics* **2001**, *20*, 3967; (e) Ackermann, L.; Bergman, R. G. *Org. Lett.* **2002**, *4*, 1475; (f) Li, C.; Thomson, R. K.; Gillon, B.; Patrick, O.; Schafer, L. L. *Chem. Commun.* **2003**, 2462; (g) Doye, S. *Synlett* **2004**, 1653; (h) Hoover, J. M.; Petersen, J. R.; Pikul, J. H.; Johnson, A. R. *Organometallics* **2004**, *23*, 4614; (i) Odom, A. L. *J. Chem. Soc. Dalton Trans.* **2005**, 225.

4. (a) Kim, H.; Livinghouse, T.; Shim, J. H.; Lee, S. K.; Lee, P. H. *Adv. Synth. Catal.* **2006**, *348*, 701; (b) Kim, H.; Kim, Y. K.; Shim, J. H.; Kim, M.; Han, M.; Livinghouse, T.; Lee, P. H. *Adv. Synth. Catal.* **2006**, *348*, 2609; (c) Kim, H.; Livinghouse, T.; Seomoon, D.; Lee, P. H. *Bull. Korean Chem. Soc.* **2007**, *28*, 1127.

5. J. Young NMR tubes purchased from Aldrich or J. Young Ltd were used under refluxing conditions (75 °C or 100 °C) without any special precautions.