Further elution gave the *trans*-dialkylpiperidine as a dark viscous oil: 0.012 g (3.8%); TLC R_f (10% Et_2NH/petroleum ether) = 0.41; ^1H NMR (δ) 0.90 (m, 6 H), 1.10–1.55 (m, 14 H), 1.55–1.95 (m, 5 H), 2.49–2.65 (m, 1 H), 2.76–2.97 (m, 2 H), 3.00–3.55 (br s, dilution dependent, 2 H), 3.59–3.76 (m, 1 H); ^{13}C NMR (δ) d: 14.2, 14.2, 36.6, 60.3, 69.3; u: 19.7, 22.9, 24.7, 28.2, 34.0, 37.7, 38.0, 39.8, 42.8, 51.5; IR (cm^{-1}) 3300, 2960, 2937, 2862, 2811, 1468, 1446, 1377, 1135; MS (*m/z*) 241 (M^+, 2), 240 (1), 212 (2), 198 (100), 180 (24), 166 (4), 140 (15), 126 (4), 112 (16).

(*R*,*R*,*R*)-(−)-Indolizidine 223AB (4). Dehydrative cyclization was accomplished using the method of Orahovats.[13] Thus, Et_3N (0.082 mL, 0.58 mmol), CCl_4 (0.056 mL, 0.58 mmol), and CH_3CN (0.4 mL) were added to a stirred mixture of *cis*-piperidine 17 (0.109 g, 0.450 mmol) and triphenylphosphine (0.153 g, 0.585 mmol) at 0 °C. After 5 min the cooling bath was removed. After 14 h the mixture was chromatographed directly (eluting with 110 mL of NH_4OH/Et_2O/pentane in a ratio of 1/12/87) to give indolizidine 223AB 4 as a yellow oil: 0.0849 g (85%); TLC R_f (10% Et_2NH/petroleum ether) = 0.54; $[\alpha]_D$ −99° (*c* 0.96, *n*-pentane). Bulb-to-bulb distillation of 0.0283 g (≈70 °C, 0.5 mmHg) gave a clear oil: 0.0251 g (76% from 17); $[\alpha]_D$ −102° (*c* 1.1, *n*-hexane) (lit.[5] $[\alpha]_D$ −101° (*c* 2.3, *n*-hexane)); ^1H NMR (δ) 0.87–0.98 (m, 6 H), 0.98–1.07 (m, 4 H), 1.07–1.38 (m, 6 H), 1.38–1.56 (m, 4 H), 1.56–1.98 (m, 6 H), 2.28–2.48 (m, 2 H), 3.27–3.34 (t, J = 7.4 Hz, 1 H); ^{13}C NMR (δ) d: 14.3, 14.7, 56.8, 58.7, 59.2; u: 19.1, 23.1, 24.8, 25.2, 26.5, 29.3, 30.2, 31.1, 32.5, 36.0; IR (cm^{-1}) 2959, 2931, 2861, 2798, 1581, 1553, 1455, 1384, 1342, 1236, 1096, 1004; MS (*m/z*) 223 (M^+, 2), 222 (3), 181 (12), 180 (100), 178 (3), 167 (12), 166 (94), 164 (2), 152 (3), 150 (3), 124 (10), 122 (8), 108 (18). These data (^1H, ^{13}C NMR, TLC) were identical with those recorded by us for natural material.

Acknowledgment. We thank CRDEC/Aberdeen and the Center for Catalytic Science and Technology of the University of Delaware for support of this work.

Supplementary Material Available: ^{13}C spectra for compounds 4, 6, 9–17 (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Zirconium-Mediated Reactions of Alkylpyrazines and Alkynes. Synthesis of Highly Substituted Alkylpyrazines

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Received May 28, 1992

Sequential one-pot addition of alkylpyrazines, alkynes, and a proton source to a solution of $Cp_2Zr(Me)(THF)^+$ (1) in CH_2Cl_2 at room temperature affords (*E*)-alkenyl-substituted alkylpyrazines **2–10** in excellent yields. The regio- and stereoselectively observed in these reactions is similar to those observed previously for related early transition metal-mediated reactions and is ascribed to steric and Si electronic effects. Conventional synthetic organic manipulation of the alkenylpyrazines provides easy access to a variety of highly substituted alkylpyrazines including tri- and tetrasubstituted alkylpyrazines **13**, **17–20**, dibromoalkylpyrazine **14**, bromoalkylpyrazine **15**, and epoxyalkylpyrazine **16**.

Introduction

Alkylpyrazines have been recognized as flavor components in foods,[1] as pheromones in various insect species,[2] and as versatile synthetic intermediates.[3] In the past, condensation reactions[3a] and nucleophilic addition of alkyllithium reagents[4] were commonly employed for the preparation of alkylpyrazines. These methods suffer from poor yields resulting from incomplete conversions/side reactions and exhibit poor regioselectivity in the preparation of unsymmetrically substituted pyrazines. More recently, synthetic methods based on electrocyclization reactions[5] and transition metal-mediated reactions[6] have been described. Herein we describe a facile zirconium-mediated reaction of alkylpyrazines and alkynes which offers a simple route to alkenyl-substituted alkylpyrazines. Conventional synthetic organic manipulations of these alkenylpyrazines provide access to a variety of highly substituted alkylpyrazines.

As a part of our ongoing efforts to develop synthetic organic applications of cationic $Cp_2Zr(R)(L)^+$ complexes,[7,8] we recently reported that complex $Cp_2Zr(CH_3)(THF)^+$ (1) reacts with pyridines under mild conditions via C–H ac-

(1) (a) Maga, J. A. Pyrazines in Foods. An Update. In *CRC Critical Reviews In Food Science And Nutrition*; Furia, T. E., Ed.; CRC: Boca Raton, FL, 1982; Vol. 16, pp 1–48. (b) Borphy, J. J.; Cavill, G. W. K. *Heterocycles* **1980**, *14*, 477. (c) Seeman, J. I.; Ennis, D. M.; Secor, H. V.; Clawson, L.; Palen, J. *Chem. Senses* **1989**, *14*, 395 and references therein.

(2) (a) Fales, H. M.; Blum, M. S.; Southwick, E. W.; Williams, D. L.; Roller, P. P.; Don, A. W. *Tetrahedron* **1988**, *44*, 5045. (b) Tecle, B.; Sun, C. M.; Borphy, J. J.; Toia, R. F. *J. Chem. Ecol.* **1987**, *13*, 1811. (c) Wheeler, J. W.; Avery, J.; Olubajo, O.; Shamim, M. T.; Storm, C. B. *Tetrahedron* **1982**, *38*, 1939 and references therein.

(3) (a) Barlin, G. B. *The Chemistry of Heterocyclic Compounds*; Wiley: New York, 1982; Vol. 41. (b) Hasegawa, M.; Katsumata, T.; Ito, Y.; Saigo, K.; Iitaka, Y. *Macromolecules* **1988**, *21*, 3134.

(4) Klein, B.; Spoerri, P. E. *J. Am. Chem. Soc.* **1951**, *73*, 2949. (b) Klein, B.; Spoerri, P. E. *J. Am. Chem. Soc.* **1950**, *72*, 1844. (c) Wheeler, J. W.; Blum, M. S. *Science* **1973**, *182*, 501. (d) Rizzi, G. P. *J. Org. Chem.* **1968**, *33*, 1333. (e) Schwaiger, W.; Ward, J. P. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 513. Strong base induced metalation/electrophilic addition reactions have been employed for elaboration of alkyl side chains of pyrazines, see: (f) Wheeler, J. W.; Avery, J.; Olubajo, O.; Shamim, M. T.; Storm, C. B.; Duffield, R. M. *Tetrahedron* **1982**, *38*, 1939.

(5) Buchi, G.; Galindo, J. *J. Org. Chem.* **1991**, *56*, 2605.

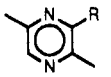
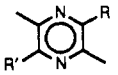
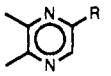
(6) (a) Chen, W.; Zhang, J.; Hu, M.; Wang, X. *Synthesis* **1990**, 701. (b) Akita, Y.; Noguchi, T.; Sugimoto, M.; Akihiro, O. *J. Heterocycl. Chem.* **1986**, *23*, 1481 and references therein.

(7) For general chemistry of $Cp_2Zr(R)(L)^+$ and related complexes, see: (a) Jordan, R. F.; Dasher, W. E.; Echols, S. F. *J. Am. Chem. Soc.* **1986**, *108*, 1718. (b) Jordan, R. F.; Bajgur, C. S.; Willet, R.; Scott, B. *J. Am. Chem. Soc.* **1986**, *108*, 7410. (c) Jordan, R. F.; LaPointe, R. E.; Bajgur, C. S.; Echols, S. F.; Willett, R. *J. Am. Chem. Soc.* **1987**, *109*, 4111. (d) Jordan, R. F.; Bajgur, C. S.; Dasher, W. E.; Rheingold, A. L. *Organometallics* **1987**, *6*, 1041. (e) Jordan, R. F.; LaPointe, R. E.; Bradley, P. K.; Baenziger, N. C. *Organometallics* **1989**, *8*, 2892. (f) Jordan, R. F.; Bradley, P. K.; Baenziger, N. C.; LaPointe, R. E. *J. Am. Chem. Soc.* **1990**, *112*, 1289. (g) Jordan, R. F.; LaPointe, R. E.; Baenziger, N. C.; Hinch, G. D. *Organometallics* **1990**, *9*, 1539. (h) Borkowsky, S. L.; Jordan, R. F.; Hinch, G. D. *Organometallics* **1991**, *10*, 1268.

(8) For reviews, see: (a) Jordan, R. F. *Adv. Organomet. Chem.* **1991**, *32*, 325. (b) Jordan, R. F.; Bradley, P. K.; LaPointe, R. E.; Taylor, D. F. *New J. Chem.* **1990**, *14*, 505.

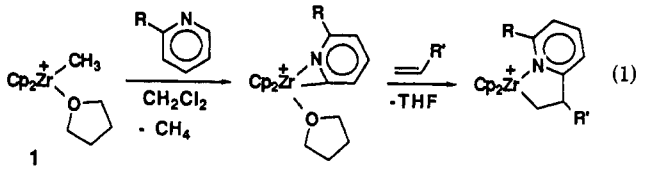
0022-3263/92/1957-5994$03.00/0

Table I. $Cp_2Zr(Me)(THF)^+$-Mediated Reaction of Pyrazines and Alkynes[a]

entry	starting material	alkyne	product	yield (%)[b]
				
1	2,5-dimethylpyrazine	1-pentyne	R = (*E*)-CH=CH(CH$_2$)$_2$CH$_3$ (**2**)	83
2	2,5-dimethylpyrazine	(trimethylsilyl)acetylene	R = (*E*)-CH=CHSi(CH$_3$)$_3$ (**3**)	89
3	2,5-dimethylpyrazine	1-(trimethylsilyl)propyne	R = (*E*)-C(Me)=CHSi(CH$_3$)$_3$ (**4**)	87
				
4[c]	2,5-dimethylpyrazine	1-(trimethylsilyl)propyne	R = R′ = (*E*)-C(Me)=CHSi(CH$_3$)$_3$ (**5**)	61
5	**4**	1-(trimethylsilyl)propyne	R = R′ = (*E*)-C(Me)=CHSi(CH$_3$)$_3$ (**5**)	89
6	**2**	1-pentyne	R = R′ = (*E*)-CH=CH(CH$_2$)$_2$CH$_3$ (**6**)	92
7	**2**	(trimethylsilyl)acetylene	R = (*E*)-CH=CH(CH$_2$)$_2$CH$_3$, R′ = (*E*)-CH=CHSi(CH$_3$)$_3$ (**7**)	86
				
8	2,3-dimethylpyrazine	1-pentyne	R = (*E*)-CH=CH(CH$_2$)$_2$CH$_3$ (**8**)	86
9	2,3-dimethylpyrazine	(trimethylsilyl)acetylene	R = (*E*)-CH=CHSi(CH$_3$)$_3$ (**9**)	85
10	2,3-dimethylpyrazine	1-(trimethylsilyl)propyne	R = (*E*)-C(Me)=CHSi(CH$_3$)$_3$ (**10**)	81

[a] Unless indicated otherwise a 1:1 molar ratio of $Cp_2Zr(Me)(THF)^+$ and the starting pyrazine were used. [b] Isolated yields. Products purified by column chromatography on alumina. [c] $Cp_2Zr(Me)(THF)^+$ and the starting pyrazine used in a 1:0.5 molar ratio, respectively.

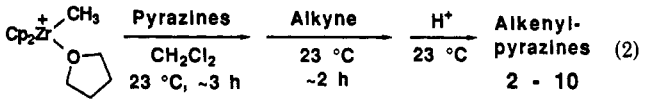
tivation/CH_4 elimination to yield $Cp_2Zr(\eta^2\text{-}N,C\text{-pyridyl})(L)^+$ complexes (eq 1). These reactive three-membered azazirconacycles readily insert unsaturated substrates to afford ring-expanded azazirconacycles (eq 1).[9,10] This chemistry forms the basis for the regio- and stereoselective synthesis of alkenyl-substituted alkylpyrazines.



1 (1)

Results and Discussion

Sequential one-pot addition of alkylpyrazines, alkynes, and a proton source to a solution of $Cp_2Zr(Me)(THF)^+$[11] (**1**) in CH_2Cl_2 affords (*E*)-alkenyl-substituted alkylpyrazines in excellent yields (eq 2 and Table I). Thus,



1 (2)

the reaction of 2,5-dimethylpyrazine with terminal alkynes such as 1-pentyne and (trimethylsilyl)acetylene in the presence of 1.0 equiv of **1** affords the (*E*)-alkenylpyrazines **2** and **3**, respectively, in good yields (entries 1 and 2, Table I). The coupling patterns observed in the ^{1}H NMR spectra of **2** and **3** are consistent with the assigned regiochemistry. In particular, the ^{1}H NMR spectra of **2** and **3** exhibit $^3J_{C\text{-}H}$ = ca. 15–19 Hz for the vinyl-H's, which establishes the (*E*)-alkenyl geometry. The reaction of 2,5-dimethylpyrazine with 1-(trimethylsilyl)propyne in presence of 1.0 equiv of **1** affords the (*E*)-alkenylpyrazine **4**, in which the $SiMe_3$ substituent is located on the carbon β to the pyrazine ring (entry 3, Table I). The ^{1}H NMR spectrum of **4** exhibits a quartet at δ 5.60 and a doublet at δ 2.15 for the vinyl-H and vinyl-CH_3, respectively. The observed coupling constants ($^4J_{H\text{-}H}$ = 1.2 Hz) establishes that the vinyl-CH_3 and the vinyl-H are vicinal. The dialkenyl-substituted pyrazine **5** is produced in 61% yield from the reaction of 2,5-dimethylpyrazine and 1-(trimethylsilyl)-propyne in the presence of 0.5 equiv of **1** (entry 4, Table I). Alternatively **5** is obtained in 89% yield from the reaction of the trisubstituted pyrazine **4** with 1-(trimethylsilyl)propyne in presence of 1.0 equiv of **1** (entry 5, Table I). The ^{1}H NMR spectrum of **5** exhibits a quartet ($^4J_{H\text{-}H}$ = 1.0 Hz) at δ 5.61 for the two equivalent vinyl-H's, a singlet at δ 2.47 for the two equivalent py-CH_3's, and a doublet ($^4J_{H\text{-}H}$ = 1.0 Hz) at δ 2.16 for the two equivalent vinyl-CH_3's. Conspicuously absent from the ^{1}H NMR spectrum of **5** is the py-H resonance which is observed in the ^{1}H NMR spectrum of the related monoalkenyl analogue **4**. Similarly, the tetrasubstituted dialkenylpyrazines **6** and **7** are obtained from the reaction of trisubstituted pyrazine **2** with 1-pentyne and (trimethylsilyl)acetylene, respectively, in the presence of 1.0 equiv of complex **1** (entries 6 and 7, Table I). Analogous cationic Zr-mediated reactions involving 2,3-dimethylpyrazine and 1-pentyne, (trimethylsilyl)acetylene, and 1-(trimethylsilyl)propyne afford alkenylpyrazines **8**, **9**, and **10**, respectively, in high yields (entries 8–10, Table I). NMR and mass spectroscopic data for **8–10** are similar to those for **2–4** and are consistent with the assigned structures. No other regio- or stereoisomeric alkenyl-substituted alkylpyrazines were detected in any of the above reactions. The (*E*)-alkenyl geometry for **3**, **5–7**, and **9** is assigned by analogy to **2**, **4**, **8** and **10** and on the basis of the known chemistry of cationic $Cp_2Zr(pyridyl)^+$ complexes.[9,10]

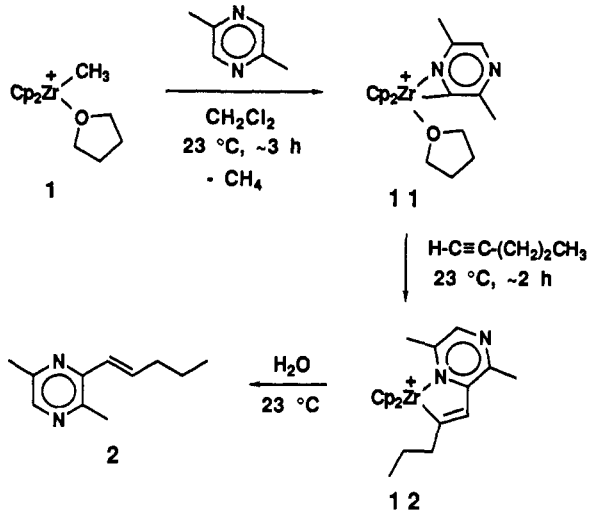
Reaction Mechanism. The Zr-mediated reaction of pyrazines and alkynes leading to **2–10** (entries 1–3, 5–10, Table I) proceeds via sequential ortho C–H activation and alkyne insertion analogous to eq 1. The synthesis of **2** was studied in detail (Scheme I). The cationic complex $Cp_2Zr(Me)(THF)^+$ (**1**) reacts with 2,5-dimethylpyrazine via ligand substitution and C–H activation/CH_4 elimination to afford the $Cp_2Zr(\eta^2\text{-}N,C\text{-3,6-dimethylpyrazin-2-yl})(THF)^+$ (**11**) (Scheme I).[9a] Treatment of **11** with 1-pentyne affords the five-membered unsaturated metallacycle **12** exclusively, in which the alkyne substituent is located on the carbon α to zirconium (Scheme I). The ^{1}H NMR spectrum of **12** exhibits a resonance at δ 6.83 for the vi-

(9) (a) Guram, A. S.; Jordan, R. F. *Organometallics* **1990**, *9*, 2116. (b) Guram, A. S.; Jordan, R. F. *Organometallics* **1990**, *9*, 2190. (c) Guram, A. S.; Jordan, R. F.; Taylor, D. F. *J. Am. Chem. Soc.* **1991**, *113*, 1833. (d) Guram, A. S.; Jordan, R. F. *Organometallics* **1991**, *10*, 3470.

(10) For related catalytic C–H activation/insertion chemistry of $Cp_2Zr(R)(L)^+$ complexes, see: (a) Jordan, R. F.; Taylor, D. F.; Baenziger, N. C. *J. Am. Chem. Soc.* **1989**, *111*, 778. (b) Jordan, R. F.; Taylor, D. F.; Baenziger, N. C. *Organometallics* **1990**, *9*, 1546.

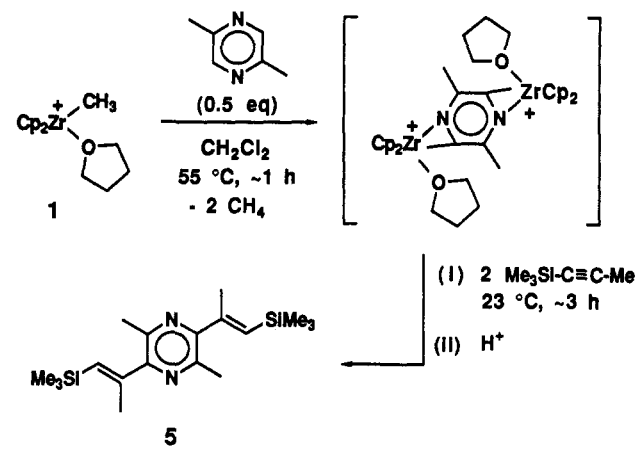
(11) The counterion is BPh_4^-.

Scheme I



nyl-H, a Cp resonance, and the expected pattern for the aromatic-H and the aliphatic side chains. One of the py CH_3 resonances (δ 1.44, 2.62) is significantly upfield shifted from that of the parent heterocycle **2** (δ 2.50 and 2.45), consistent with N-coordination. Similar upfield shifts have been noted previously for related cationic pyridine complexes.[9c,d,10] The ^{13}C NMR spectrum of **12** exhibits a low-field quaternary carbon resonance at δ 233.3 for Zr*C*-(*n*-Pr)=CH (assignment confirmed by DEPT), consistent with the assigned regiochemistry. The regiochemistry of alkyne insertion is similar to that observed previously for related Cp_2Zr(pyridyl)(THF)$^+$, Cp_2Zr(benzyne), and related complexes and is rationalized on the basis of steric effects.[9d,12] Hydrolysis of **12** proceeds with retention of configuration to afford (*E*)-3,6-dimethyl-2-(1-pentenyl)-pyrazine, **2**. For reactions involving $SiMe_3$-substituted alkynes, five-membered unsaturated metallacycles in which the $SiMe_3$ substituent is located α to zirconium are exclusively formed,[13] and hydrolysis affords alkenylpyrazines **3–5**, **7**, **9**, and **10** in which the $SiMe_3$ group is located on the carbon β to the pyrazine ring. Analogous regioselectivity is observed for related insertion/coupling reactions of Si-substituted alkynes at early transition metal centers and is rationalized on basis of steric and Si electronic effects.[9d,12b,c,14,15]

Scheme II



The formation of tetrasubstituted pyrazine **5** from the reaction of 2,5-dimethylpyrazine and 1-(trimethylsilyl)-propyne in the presence of 0.5 equiv of **1** (entry 4, Table I) probably proceeds via the mechanism shown in Scheme II. Initial double metalation of 2,5-dimethylpyrazine at 55 °C in CH_2Cl_2 affords the bis-metallacyclic intermediate as an insoluble solid. Treatment of this intermediate with (trimethylsilyl)propyne and a proton source affords **5**.

The alkenylpyrazines obtained from the Zr-mediated reaction of alkylpyrazines and alkynes are versatile synthetic intermediates and provide easy access to a variety of highly substituted alkylpyrazines (Scheme III). Catalytic hydrogenation (Pd/C, ~3 atm of H_2) of **2** affords the trialkylpyrazine **13** cleanly and quantitatively. **2** reacts efficiently with Br_2 to afford the dibromo compound **14** and with HBr to give the monobromo compound **15**. Treatment of **2** with MCPBA affords the epoxide **16** in good yield. Pyrazines **13–16** are unambiguously characterized by NMR and mass spectroscopy. Conspicuously absent from the ^1H NMR spectrum of **13–16** are the resonances for the vinyl-H's of the parent pyrazine **2**. The ^1H NMR spectrum of **15** exhibits a pair of doublet of doublets at δ 3.36 and 3.23 for py-CH_2 and a multiplet at δ 4.61 for py-CH_2CHBr, which establishes that Br is located on the carbon β to the pyrazine ring. The other regioisomer in which Br is located on the α carbon is also formed in trace amounts.

The saturated alkylpyrazines **17–19** (Table II) are obtained in quantitative yield from the catalytic Pd/C hydrogenation of the corresponding unsaturated alkylpyrazines and are unambiguously characterized by NMR and mass spectroscopy. Catalytic hydrogenation (Pd/C, ~3 atm of H_2) of **5** afforded a 1/0.8 mixture of diastereomeric saturated alkylpyrazines **20a** and **20b**, which were not separated (Table II). The ^1H NMR spectrum of the mixture **20a** and **20b** exhibited nearly overlapping resonances; however the GC retention times and the mass spectra are distinctly different for the two diastereomers.

Summary

Sequential one-pot addition of alkylpyrazines, alkynes, and a proton source to a solution of $Cp_2Zr(Me)(THF)^+$ (**1**) affords (*E*)-alkenyl-substituted alkylpyrazines in high yields. The (*E*)-alkenyl stereoselectivity results from cis insertion of the alkyne into the Zr–C bond of the Cp_2Zr-(η^2-*N*,*C*-pyrazinyl)(THF)$^+$ intermediate. Reactions involving terminal alkynes afford products in which the alkyne substituent is located on the alkenyl carbon β to the pyrazine ring. Similarly, reactions involving Me_3Si-substituted alkynes afford products in which the Me_3Si substituent is located on the β-alkenyl carbon. This re-

(12) (a) Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047. (b) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486. (c) Buchwald, S. L.; Fang, Q. *J. Org. Chem.* **1989**, *54*, 2793. (d) Buchwald, S. L.; Lum, R. T.; Fisher, R. T.; Davis, W. M. *J. Am. Chem. Soc.* **1989**, *111*, 9113. (e) McDade, C.; Bercaw, J. E. *J. Organomet. Chem.* **1985**, *279*, 281.

(13) ^1H NMR monitoring of several of these reactions reveals clean, quantitative, and regioselective formation of single unsaturated five-membered metallacycle in each case. The five-membered metallacycle $Cp_2Zr(\eta^2$-*N*,*C*-(C($SiMe_3$)=CCH_3(3,6-dimethylpyrazin-2-yl))$^+$ (**12a**) isolated from the reaction of **11** and 1-(trimethylsilyl)propyne was more thoroughly characterized. Spectroscopic data for **12a**. ^1H NMR (360 MHz, CD_2Cl_2): δ 8.16 (s, 1 H, py-H), 6.44 (br s, 1 H, Zr-C(R)=C(*H*)), 2.80 (s, 3 H, py-CH_3), 2.25 (s, 3 H, vinyl-CH_3), 1.39 (s, 3 H, py-CH_3), 0.22 (s, 9 H, Si(CH_3)$_3$). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 238.9 (Zr-C(R)=), 151.5 (py-C), 151.3 (py-C), 146.3 (py-C), 143.9 (py-C), 142.6 (Zr-C(*R*)=*C*(CH_3)), 116.7 (Cp), 27.2 (CH_3), 26.8 (CH_3), 19.8 (CH_3), 2.27 (Si(CH_3)$_3$). FTIR (KBr pellet): $\nu_{C=C}$ 1579.6 cm^{-1}.

(14) (a) Hyla-Kryspin, I.; Gleiter, R.; Kruger, C.; Zwettler, R.; Erker, G. *Organometallics* **1990**, *9*, 517. (b) Erker, G.; Zwettler, R.; Kruger, C.; Hyla-Kryspin, I.; Gleiter, R. *Organometallics* **1990**, *9*, 524. (c) Eisch, J. J.; Piotrowski, A. M.; Brownstein, S. K.; Gabe, E. J.; Lee, F. L. *J. Am. Chem. Soc.* **1985**, *107*, 7219. (d) Mattia, J.; Humphrey, M. B.; Rogers, R. D.; Atwood, J. L.; Rausch, M. D. *Inorg. Chem.* **1978**, *17*, 3257. (e) Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 108. (f) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788.

(15) (a) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870. (b) Alt, H. G.; Engelhardt, H. E.; Rausch, M. D.; Kool, L. B. *J. Am. Chem. Soc.* **1985**, *107*, 3717.

Scheme III

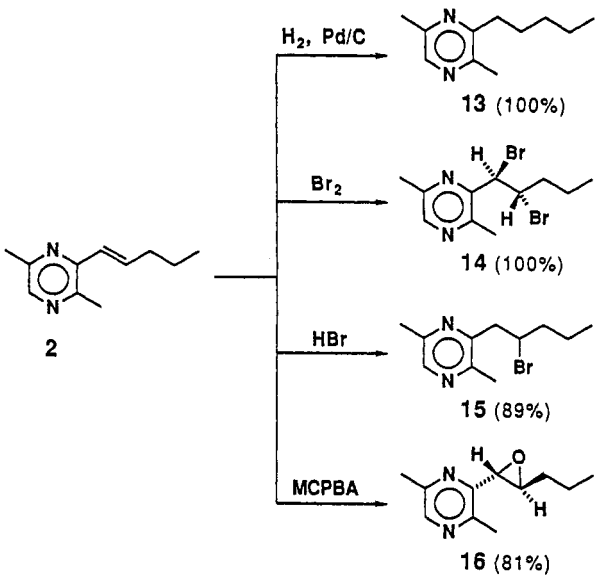
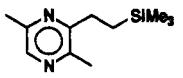
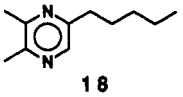
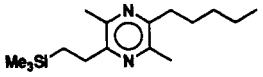
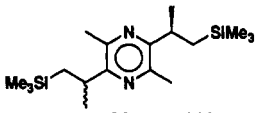


Table II. Catalytic (Pd/C) Hydrogenation of Alkenylpyrazines

starting material	product	yield (%)[a]
4	 17	100
8	 18	100
7	 19	100
5	 20a & 20b	100

[a] NMR yields.

gioselectivity is ascribed to steric and Si electronic effects in the insertion step as described previously.[9b,d] In the present study, we have cleaved the alkenylpyrazine ligands from the penultimate unsaturated five-membered azazirconacycles by hydrolysis. Presumably other electrophilic Zr–C cleavage reactions could also be used to obtain products with functionality at the β-alkenyl carbon.[16] The alkenylpyrazines are versatile intermediates for the synthesis of a variety of highly substituted alkylpyrazines including tri- and tetrasubstituted alkylpyrazines, bromoalkylpyrazines, dibromoalkylpyrazines, and epoxyalkylpyrazines. Thus Zr-mediated synthesis of alkenylpyrazines provides an attractive approach to highly substituted alkylpyrazines.[17]

Experimental Section

All manipulations were performed under nitrogen atmosphere or vacuum, using a Vacuum Atmospheres Drybox, Schlenk techniques, or a high-vacuum line. $ClCH_2CH_2Cl$ and CH_2Cl_2 were distilled from CaH_2. CD_2Cl_2 and $CDCl_3$ were purchased from MSD Isotopes and Aldrich Chemical Co., respectively, and distilled from P_2O_5. All solvents were stored in evacuated bulbs and vacuum transferred into reaction flasks or NMR tubes. 2,5- and 2,3-dimethylpyrazines, Pd/C, and MCPBA (50–60%) were purchased from Aldrich Chemical Co. The pyrazines were purified by distillation. Alkynes were purchased from Aldrich Chemical Co. or Petrach Systems Inc. and dried with molecular sieves. NMR spectra were recorded on 300- and 360-MHz spectrometers in sealed tubes. ^1H and ^{13}C chemical shifts are reported versus Me_4Si and were determined by reference to the residual ^1H and ^{13}C solvent peaks. The anion in all cases is BPh_4^-. All spectra of cationic complexes exhibited expected BPh_4^- resonances: ^1H NMR (CD_2Cl_2) δ 7.35 (m, 8 H), 7.05 (t, J = 7.4 Hz, 8 H), 6.90 (t, J = 7.4 Hz, 4 H); ^{13}C NMR (CD_2Cl_2) δ 163.5 (q, J = 49 Hz), 135.4, 125.7, 121.7. The IR $\nu_{C=C}$ absorbance of the alkenylpyrazines could not be unambiguously assigned in several cases due to their weak character. Complex $Cp_2Zr(Me)(THF)^+$ (1) was prepared as described in ref 7h. See ref 9a for synthesis and characterization data for $Cp_2Zr(\eta^2\text{-}(N,C)\text{-}3,6\text{-dimethylpyrazin-2-yl})(THF)^+$ (11).

3,6-Dimethyl-2-(1-pentenyl)pyrazine (2). To a slurry of 1 (41 mg, 0.065 mmol) in CH_2Cl_2 (0.5 mL) was added 2,5-dimethylpyrazine (7 mg, 0.065 mmol). The mixture was stirred at 23 °C for 15 min, resulting in a clear solution. After the solution was stirred for 2 h at 23 °C, 1-pentyne (5.5 mg, 0.081 mmol) was added, and the stirring continued for an additional 2.5 h. A drop of distilled H_2O was added, and the heterogeneous mixture was stirred for 15 min at 23 °C during which the organic phase became colorless. Column chromatography on alumina using 8:1 pentane/CH_2Cl_2 and CH_2Cl_2 as eluents and subsequent removal of solvents afforded 2 (9.5 mg, 83%) as a pale yellow oil. In a scale-up of the above preparation, 244 mg (88%) of 2 was isolated (1, 1 g; 2,5-dimethylpyrazine, 170 mg; 1-pentyne, 125 mg). ^1H NMR (300 MHz, CD_2Cl_2): δ 8.10 (s, 1 H, py-H), 6.93 (dt, $^3J_{H-H}$ = 15.2, $^3J_{H-H}$ = 7.1 Hz, 1 H, py-CH=C*H*CH_2), 6.59 (dt, $^3J_{H-H}$ = 15.2, $^4J_{H-H}$ = 1.5 Hz, 1 H, py-C*H*=CHCH_2), 2.50 (s, 3 H, Me), 2.45 (s, 3 H, Me), 2.27 (qd, $^3J_{H-H}$ = 7.3, $^4J_{H-H}$ = 1.5 Hz, 2 H, =CHCH_2CH_2), 1.54 (sextet, $^3J_{H-H}$ = 7.4 Hz, 2 H, $CH_2CH_2CH_3$), 0.97 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_2CH_3). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 150.6 (py-C), 148.2 (py-C), 147.3 (py-C), 141.6 (py-C), 139.0 (alkenyl-C), 125.5 (alkenyl-C), 35.6, 30.1, 22.6, 21.3, 14.0 (CH_2CH_3). FTIR (NaCl film): $\nu_{C=C}$ 1649.1 cm^{-1}. MS (EI, 70 eV): m/e 177 (4), 176 (58) [molecular ion], 162 (10), 161 (100), 159 (6), 148 (10), 147 (54), 146 (32), 145 (14), 134 (9), 133 (64), 131 (5), 122 (17), 80 (4), 79 (4), 78 (4), 77 (9). HRMS (EI) for $C_{11}H_{16}N_2$: calcd 176.1313, obsd 176.1302.

3,6-Dimethyl-2-(1-(trimethylsilyl)ethen-2-yl)pyrazine (3). Compound 3 was isolated in 87% yield (9.5 mg) as a pale yellow oil from the one-pot stepwise reaction of 1 (33 mg, 0.053 mmol) with 2,5-diethylpyrazine (6 mg, 0.056 mmol), 1-(trimethylsilyl)-acetylene (6 mg, 0.061 mmol), and H_2O (1 drop). The procedure described for the preparation of 2 was used here. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.17 (s, 1 H, py-H), 7.25 (d, $^3J_{H-H}$ = 18.5 Hz, 1 H, alkenyl-H), 7.12 (d, $^3J_{H-H}$ = 18.5 Hz, 1 H, alkenyl-H), 2.56 (s, 3 H, Me), 2.48 (s, 3 H, Me), 0.19 (s, 9 H, $SiMe_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 151.0 (py-C), 148.1 (py-C), 147.6 (py-C), 142.6 (py-C), 138.6 (alkenyl-C), 138.5 (alkenyl-C), 21.4 (CH_3), 21.2 (CH_3), −1.3 ($Si(CH_3)_3$). MS (EI, 70 eV): m/e 207 (2), 206 (7) [molecular ion], 205 (3), 193 (4), 192 (13), 191 (100), 176 (2), 175 (2), 161 (3), 133 (6). HRMS (EI) for $C_{11}H_{18}N_2Si$: calcd 206.1239, obsd 206.1237.

3,6-Dimethyl-2-(1-(trimethylsilyl)propen-2-yl)pyrazine (4). Compound 4 was isolated in 89% yield (9.1 mg) as a yellow oil from the one-pot stepwise reaction of 1 (29 mg, 0.046 mmol) with 2,5-diethylprazine (5 mg, 0.046 mmol), 1-(trimethylsilyl)propyne (7 mg, 0.063 mmol), and H_2O (1 drop). The procedure described for the preparation of 2 was used here. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.17 (s, 1 H, py-H), 5.60 (q, $^4J_{H-H}$ = 1.2 Hz, 1 H, C(Me)=C*H*$SiMe_3$), 2.48 (s, 3 H, Me), 2.46 (s, 3 H, Me), 2.15 (d, $^4J_{H-H}$ = 1.2 Hz, 3 H, C(*Me*)=), 0.22 (s, 9 H, $SiMe_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 157.2 (py-C), 151.7 (py-C), 149.8 (py-C), 147.3 (py-C), 141.6 (alkenyl-C), 132.1 (alkenyl-C), 22.3 (CH_3), 21.6 (CH_3), 21.2 (CH_3), −0.14 ($Si(CH_3)_3$). MS (EI, 70 eV): m/e 221 (1), 220 (7) [molecular ion], 207 (3), 206 (14), 205 (100), 203 (1), 191 (1), 190 (2), 189 (2), 175 (3), 165 (1), 161 (1), 148 (2), 147 (23), 145

(16) (a) Schwartz, J.; Labinger, J. A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 333. (b) Negishi, E.; Takahashi, T. *Aldrichchim. Acta* **1985**, *18*, 31. (c) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1.

(17) Under the conditions described in the Experimental Section, pyrazine itself does not undergo orthometalation by 1. This lack of reactivity is ascribed to the absence of ortho substituents which have been shown to promote orthometalation, see ref 9a.

(2), 135 (2), 107 (1), 73 (8), 84 (2), 83 (1), 80 (1), 77 (1), 58 (1). HRMS (EI) for $C_{11}H_{16}N_2$: calcd 220.1396, obsd 220.1410.

3,6-Dimethyl-2,5-bis(1-(trimethylsilyl)propen-2-yl)-pyrazine (5). A solution of 1 (35 mg, 0.056 mmol) and 2,5-dimethylpyrazine (3 mg, 0.028 mmol) in $ClCH_2CH_2Cl$ (0.5 mL) was heated at 50 °C for 1 h to afford an insoluble light yellow solid. 1-(Trimethylsilyl)propyne was added, and the reaction mixture was stirred at 23 °C for 3 h. To the resultant clear yellow solution was added HCl (1 N, 1 drop), and the heterogeneous mixture was stirred for 15 min during which the organic phase became colorless. Column chromatography on alumina using 8:1 pentane–CH_2Cl_2 and CH_2Cl_2 as eluents and subsequent removal of solvent gave 5 (5.7 mg, 61%) as an off-white solid.

Alternatively, compound 5 was isolated in 89% yield (6.0 mg) as an off-white solid from the one-pot stepwise reaction of 1 (13 mg, 0.021 mmol) with 3 (4.5 mg, 0.020 mmol), 1-(trimethylsilyl)propyne (~4 mg, 0.035 mmol) and HCl (1 N, 1 drop). The procedure described for the preparation of 2 was used here. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 5.61 (q, $^4J_{H-H}$ = 1.0 Hz, 2 H, alkenyl-H's), 2.47 (s, 6 H, py-Me), 2.16 (q, $^4J_{H-H}$ = 1.0 Hz, 6 H, alkenyl-CH_3's), 0.22 (s, 18 H, $Si(CH_3)_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 155.0 (py-C), 151.7 (py-C), 145.8 (alkenyl-C), 131.9 (alkenyl-C), 22.2 (CH_3), 21.6 (CH_3), –0.2 ($Si(CH_3)_3$). MS (EI, 70 eV): *m/e* 333 (1), 332 (4) [molecular ion], 319 (9), 318 (28), 317 (100), 261 (3), 260 (9), 259 (42), 245 (7), 244 (9), 243 (18), 229 (9), 227 (2), 213 (2), 151 (8), 97 (6), 73 (20), 59 (4). HRMS (EI) for $C_{18}H_{32}N_2Si_2$: calcd 332.2104, obsd 332.2133.

3,6-Dimethyl-2,5-di(1-pentenyl)pyrazine (6). A solution of 1 (13 mg, 0.021 mmol) and 2-(1-pentenyl)-3,6-dimethylpyrazine (2) (3 mg, 0.017 mmol) in CH_2Cl_2 (0.5 mL) was stirred at 23 °C for 24 h. 1-Pentyne (1.5 mg, 0.022 mmol) was added via vacuum transfer at –196 °C, and the yellow solution was stirred at 23 °C for 2 h. A drop of distilled H_2O was added, and the heterogeneous mixture was stirred at 23 °C for 15 min during which the organic phase became colorless. Column chromatography on alumina using pentane and CH_2Cl_2 as eluents, and subsequent removal of solvent gave 6 (3.8 mg, 92%) as an off-white solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 6.88 (dt, $^3J_{H-H}$ = 15.2, $^3J_{H-H}$ = 7.2 Hz, 1 H, py-CH=C*H*CH_2), 6.57 (dt, $^3J_{H-H}$ = 15.2, $^4J_{H-H}$ = 1.5 Hz, 1 H, py-C*H*=$CHCH_2$), 2.50 (s, 6 H, Me), 2.26 (qd, $^3J_{H-H}$ = 7.3, $^4J_{H-H}$ = 1.5 Hz, 2 H, =$CHCH_2CH_2$), 1.53 (sextet, $^3J_{H-H}$ = 7.4 Hz, 2 H, $CH_2CH_2CH_3$), 0.97 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_2CH_3). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 147.1 (py-C), 146.2 (py-C), 137.8 (alkenyl-C), 125.5 (alkenyl-C), 35.7, 22.8 (py-CH_3), 21.4, 14.0 (CH_2CH_3). MS (EI, 70 eV): *m/e* 245 (15), 244 (85) [molecular ion], 243 (5), 230 (17), 229 (100), 216 (11), 215 (61), 202 (9), 201 (48), 200 (5), 199 (19), 190 (23), 189 (6), 187 (8), 186 (8), 185 (39), 184 (15), 183 (9), 173 (11), 171 (16), 170 (8), 169 (5), 161 (13), 160 (6), 159 (10), 132 (5), 92 (5), 91 (15), 79 (11), 78 (7), 77 (25), 66 (8), 65 (9), 53 (8), 51 (5), 42 (5), 41 (7), 39 (7).

3,6-Dimethyl-2-(1-(trimethylsilyl)ethen-2-yl)-5-(1-pentenyl)pyrazine (7). A solution of 1 (33 mg, 0.053 mmol) and 2 (7.6 mg, 0.043 mmol) in CD_2Cl_2 (0.4 mL) was stirred at 23 °C for 30 min. 1-(Trimethylsilyl)acetylene (5.5 mg, 0.056 mmol) was added via vacuum transfer at –196 °C, and the yellow solution was stirred at 23 °C for 15 min. A drop of distilled H_2O was added, and the heterogeneous mixture was stirred at 23 °C for 8 h during which the organic phase became colorless. Column chromatography on alumina using pentane and CH_2Cl_2 as eluents and subsequent removal of solvent gave 7 (10.5 mg, 89%) as an off-white solid. ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.20 (d, $^3J_{H-H}$ = 18.6 Hz, 1 H, alkenyl-H), 7.08 (d, $^3J_{H-H}$ = 18.6 Hz, 1 H, alkenyl-H), 6.91 (dt, $^3J_{H-H}$ = 15.3 Hz, $^3J_{H-H}$ = 7.1 Hz, 1 H, py-CH=C*H*CH_2), 6.57 (dt, $^3J_{H-H}$ = 15.3 Hz, $^4J_{H-H}$ = 1.5 Hz, 1 H, py-C*H*=$CHCH_2$), 2.57 (s, 3 H, py-CH_3), 2.54 (s, 3 H, py-CH_3), 2.26 (qd, $^3J_{H-H}$ = 7.6, $^4J_{H-H}$ = 1.5 Hz, 2 H, =$CHCH_2CH_2$), 1.53 (sextet, $^3J_{H-H}$ = 7.4 Hz, 2 H, $CH_2CH_2CH_3$), 0.96 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_2CH_3), 0.17 (s, 9 H, $Si(CH_3)_3$). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 147.6 (py-C), 147.2 (py-C), 146.9 (py-C), 145.3 (py-C), 138.5 (alkenyl-C), 138.1 (alkenyl-C), 137.0 (alkenyl-C), 125.0 (alkenyl-C), 35.4, 22.2, 21.4, 21.2, 13.9 (CH_2CH_3), –1.3 ($Si(CH_3)_3$). FTIR (NaCl film): $\nu_{C=C}$ 1652.8, 1646.5 cm^{-1}. MS (EI, 70 eV): *m/e* 275 (2), 274 (10) [molecular ion], 261 (6), 260 (22), 259 (100), 245 (4), 231 (7), 230 (7), 229 (29), 217 (4), 215 (8), 207 (7), 210 (16), 199 (1), 171 (4), 97 (4), 77 (5), 73 (11), 59 (7), 44 (4), 36 (6), 32 (40). HRMS (EI) for $C_{16}H_{26}N_2Si$: calcd 274.1859, obsd 274.1861.

5,6-Dimethyl-2-(1-pentenyl)pyrazine (8). To a slurry of 1 (60 mg, 0.096 mmol) in CH_2Cl_2 (0.5 mL) was added 2,3-dimethylpyrazine (10.2 mg, 0.095 mmol) via syringe. The mixture was heated at 50 °C for 10 min, resulting in a clear solution. 1-Pentyne (8.4 mg, 0.124 mmol) was added, and the resulting yellow solution was stirred at 23 °C for 1 h. HCl (1 N, 1 drop) was added, and the heterogeneous mixture was stirred at 23 °C for 30 min during which the organic phase became colorless. Column chromatography on alumina using pentane and CH_2Cl_2 as eluents afforded 8 (14.3 mg, 86%) as a yellow oil. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 8.17 (s, 1 H, py-H), 6.77 (dt, $^3J_{H-H}$ = 15.7, $^3J_{H-H}$ = 7.0 Hz, 1 H, py-CH=C*H*CH_2), 6.41 (dt, $^3J_{H-H}$ = 15.7, $^3J_{H-H}$ = 1.5 Hz, 1 H, py-C*H*=$CHCH_2$), 2.47 (s, 3 H, Me), 2.46 (s, 3 H, Me), 2.24 (qd, $^3J_{H-H}$ = 7.3, $^4J_{H-H}$ = 1.5 Hz, 2 H, =$CHCH_2CH_2$), 1.52 (sextet, $^3J_{H-H}$ = 7.4 Hz, 2 H, $CH_2CH_2CH_3$), 0.96 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_2CH_3). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 151.8 (py-C), 150.4 (py-C), 148.4 (py-C), 139.3 (py-C), 136.6 (alkenyl-C), 127.1 (alkenyl-C), 35.4, 22.6, 22.3, 21.9, 13.9. MS (EI, 70 eV): *m/e* 177 (7), 176 (78) [molecular ion], 162 (10), 161 (100), 159 (9), 148 (15), 147 (73), 146 (24), 145 (10), 135 (6), 134 (16), 133 (3), 132 (10), 131 (5), 122 (19), 93 (4), 91 (4), 65 (9), 53 (5), 52 (6), 40 (18). HRMS (EI) for $C_{11}H_{16}N_2$: calcd 176.1313, obsd 176.1303.

3,6-Dimethyl-2-(1-(trimethylsilyl)ethen-2-yl)pyrazine (9). Compound 9 was isolated in 85% yield (9.8 mg) as a pale yellow oil from the one-pot stepwise reaction of 1 (35 mg, 0.056 mmol) with 2,3-diethylprazine (6 mg, 0.056 mmol), 1-(trimethylsilyl)-acetylene (6.5 mg, 0.066 mmol), and H_2O (1 drop). The procedure described for the preparation of 8 was used here. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 8.27 (s, 1 H, py-H), 7.07 (d, $^3J_{H-H}$ = 19.0 Hz, 1 H, alkenyl-H), 6.91 (d, $^3J_{H-H}$ = 19.0 Hz, 1 H, alkenyl-H), 2.50 (s, 3 H, Me), 2.49 (s, 3 H, Me), 0.18 (s, 9 H, $SiMe_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 152.1 (py-C), 151.6 (py-C), 148.0 (py-C), 140.6 (py-C), 139.9 (alkenyl-C), 135.7 (alkenyl-C), 22.3 (Me), 22.1 (Me), –1.4 ($SiMe_3$). MS (EI, 70 eV): *m/e* 207 (2), 206 (8) [molecular ion], 205 (7), 193 (4), 192 (17), 191 (100), 161 (4), 59 (3). HRMS (EI) for $C_{11}H_{18}N_2Si$: calcd 206.1239, obsd 206.1218.

5,6-Dimethyl-2-(1-(trimethylsilyl)propen-2-yl)pyrazine (10). Compound 10 was isolated in 81% yield (18.2 mg) as a pale yellow oil from the one-pot stepwise reaction of 1 (64 mg, 0.102 mmol) with 2,3-dimethylprazine (11 mg, 0.102 mmol), 1-(trimethylsilyl)propyne (15 mg, 0.134 mmol), and HCl (1 N, 1 drop). The procedure described for the preparation of 8 was used here. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 8.44 (s, 1 H, py-H), 6.54 (br s, 1 H, C(Me)=C*H*$SiMe_3$), 2.50 (s, 3 H, Me), 2.49 (s, 3 H, Me), 2.25 (d, $^4J_{H-H}$ = 1.2 Hz, 3 H, C(*Me*)=), 0.22 (s, 9 H, $SiMe_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 151.7 (py-C), 150.9 (py-C), 150.8 (py-C), 148.9 (py-C), 138.0 (alkenyl-C), 130.9 (alkenyl-C), 22.3 (Me), 21.9 (Me), 19.3 (Me), –0.07 ($SiMe_3$). MS (EI, 70 eV): *m/e* 221 (0.3), 220 (1) [molecular ion], 219 (2), 207 (3), 206 (13), 205 (100), 203 (1), 191 (1), 190 (2), 189 (1), 175 (4), 165 (2), 161 (2), 147 (6), 135 (2), 84 (1), 83 (3), 73 (5), 59 (1). HRMS (EI) for $C_{11}H_{16}N_2$: calcd 220.1396, obsd 220.1401.

[$Cp_2Zr(\eta^2$-(*N*,*C*)-(C($CH_2CH_2CH_3$)=CH(3,6-dimethylpyrazinyl)][BPh_4] (12). To a slurry of 1 (1.098 g, 1.751 mol) in CH_2Cl_2 (0.5 mL) was added 2,5-dimethylpyrazine (172 mg, 1.593 mol). The mixture was stirred at 23 °C for 15 min resulting in a clear solution. After the solution was stirred for 2 h at 23 °C, 1-pentyne (142 mg, 2.101 mol) was added, and the stirring was continued for an additional 2.5 h. The reaction solution was then filtered through a glass wool plug. Hexane (~10 mL) was added to the filtrate to induce slow precipitation of the product. The product was isolated by filtration, washed with hexane (3 × 10 mL), and dried in vacuo to give 12 (1.066 g, 91%) as a yellow solid. The isolated sample contained 0.25 equivalent CH_2Cl_2 which is accounted for in the isolated yield. This sample was used for NMR/IR spectroscopic studies and elemental analysis. Alternatively, treatment of complex 11 (46 mg, 0.065 mmol) with 1-pentyne (5.5 mg, 0.081 mmol) affords complex 12 (~100% yield by NMR). ^{1}H NMR (360 MHz, CD_2Cl_2): δ 8.06 (s, 1 H, py-H), 6.83 (br s, 1 H, Zr-C(R)=C(*H*)), 2.62 (s, 3 H, py-CH_3), 2.26 (t, $^3J_{H-H}$ = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 1.59 (sextet, $^3J_{H-H}$ = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 1.44 (s, 3 H, py-CH_3), 1.04 (t, $^3J_{H-H}$ = 7.3 Hz, 3 H, CH_2CH_3). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 233.3 (Zr-C(R)=), 151.6 (py-C), 148.8 (py-C), 146.8 (py-C), 141.4 (py-C), 120.2 (Zr-C(R)=*C*(H)), 116.3 (Cp), 44.1 ($CH_2CH_2CH_3$), 22.1 (Me), 21.8 (Me), 18.5 ($CH_2CH_2CH_3$), 14.2 ($CH_2CH_2CH_3$). FTIR (KBr pellet):

$\nu_{C=C}$ 1578.4 cm^{-1}. Anal. Calcd for $C_{45}H_{45}BN_2Zr \cdot 0.25CH_2Cl_2$: C, 73.72; H, 6.22; N, 3.79. Obsd: C, 73.97; H, 6.17; N, 3.67.

3,6-Dimethyl-2-pentylpyrazine (13). Compound **13** was isolated in 100% yield (by NMR) from the reaction of **2** (2.7 mg, 0.015 mmol) with H_2 (~3 atm) in presence of catalytic amount of Pd/C. The procedure described for the preparation of **17** (vide infra) was used here. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.09 (s, 1 H, py-H), 2.68 (t, $^3J_{H-H}$ = 7.7 Hz, 2 H, py-CH_2), 2.46 (s, 3 H, Me), 2.45 (s, 3 H, Me), 1.68 (m, 2 H), 1.33 (m, 4 H), 0.89 (t, $^3J_{H-H}$ = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 155.1 (py-C), 150.3 (py-C), 148.8 (py-C), 140.8 (py-C), 35.1, 32.2, 28.5, 22.9, 21.3, 21.1 14.2. MS (EI, 70 eV): *m/e* molecular ion peak absent, 163 (3) [M - 15], 149 (8), 136 (3), 135 (13), 123 (8), 122 (100), 121 (14), 107 (3), 81 (3), 80 (7), 66 (3), 54 (4), 53 (10), 52 (4), 44 (28), 42 (15), 41 (10), 40 (25).

3,6-Dimethyl-2-(1-(1,2-dibromopentyl))pyrazine (14). To a solution of **2** (7 mg, 0.040 mmol) in $CHCl_3$ (0.5 mL) was added a Br_2 (1 M solution in $CHCl_3$, 0.12 mL, 0.12 mmol) at 0 °C. The solution was stirred for 5 min and warmed up to 23 °C. Removal of the solvent and excess Br_2 under vacuum gave **14** (~13 mg, ~100%) as a pale yellow solid. Compound **14** decomposes slowly. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.27 (s, 1 H, py-H), 5.34 (d, $^3J_{H-H}$ = 1.6 Hz, 1 H, pyC*H*(Br)), 5.02 (m, 1 H, py-CH(Br)C*H*(Br)), 2.60 (s, 3 H, Me), 2.54 (s, 3 H, Me), 2.46 (m, 1 H), 2.01 (m, 1 H), 1.75 (m, 1 H), 1.57 (m, 1 H), 1.03 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_3). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 152.2 (py-C), 152.0 (py-C), 147.6 (py-C), 142.9 (py-C), 56.1 (py-CH(Br)), 51.8 (py-CH(Br)*C*H(Br)), 38.9, 21.3, 20.7, 20.4, 13.6. MS (EI, 70 eV): *m/e* molecular ion peak absent, 257 (30) [M(338) - Br(81)], 255 (31) [M(334) - Br(79)], 176 (57), 175 (93), 161 (100), 159 (10), 148 (16), 147 (68), 146 (61), 145 (19), 133 (49), 132 (14), 122 (25), 80 (12), 79 (10), 77 (16), 53 (11).

3,6-Dimethyl-2-(2-bromopentyl)pyrazine (15). HBr was bubbled through a solution of **2** (4.4 mg, 0.025 mmol) in Et_2O (0.5 mL) at 0 °C for 10 min. The slurry was filtered through a $MgSO_4$ plug (2 cm). Concentration of the filtrate under vacuum gave **15** (5.7 mg, 89%) as a colorless oil. The regioisomer 3,6-dimethyl-2-(1-bromopentyl)pyrazine (**15'**) was also formed in trace amounts. Compound **15** decomposes slowly. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.18 (s, 1 H, py-H), 4.61 (m, 1 H, py-CH_2C*H*(Br)), 3.36 (dd, $^2J_{H-H}$ = 14.9 Hz, $^3J_{H-H}$ = 8.8 Hz, 1 H, py-CH_2), 3.23 (dd, $^2J_{H-H}$ = 14.9 Hz, $^3J_{H-H}$ = 5.2 Hz, 1 H, py-CH_2), 2.52 (s, 3 H, Me), 2.46 (s, 3 H, Me), 1.92 (m, 1 H), 1.66 (m, 1 H), 1.54 (m, 1 H), 0.95 (t, $^3J_{H-H}$ = 7.3 Hz, 3 H, CH_3). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 151.6 (py-C), 150.7 (py-C), 149.3 (py-C), 141.7 (py-C), 56.3, 43.7, 41.4, 30.1, 21.6, 21.2, 13.5.

3,6-Dimethyl-2-(1,2-epoxypent-1-yl)pyrazine (16). To a solution of **2** (9 mg, 0.051 mmol) in CH_2Cl_2 (0.5 mL) was added MCPBA (~1.5 equiv) at 23 °C. The reaction solution was allowed to stand at 45 °C for 4 h and then poured into 1 N NaOH solution (0.5 mL). The two-phase mixture was vigorously stirred for 1 min, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 0.5 mL). The combined organic fractions were dried with $MgSO_4$ and filtered. The fitrate was concentrated in vacuo, and the residue was column chromatographed on alumina using CH_2Cl_2 and then EtOAc as eluents. Concentration of the EtOAc fraction in vacuo gave **16** (7.9 mg, 81%) as a colorless oil. The isolated sample contained trace amounts of EtOAc. ^1H NMR (300 MHz, CD_2Cl_2): δ 7.94 (s, 1 H, py-H), 3.79 (d, $^3J_{H-H}$ = 2.0 Hz, 1 H, py-C*H*), 3.35 (m, 1 H, py-CH(O)C*H*), 2.50 (s, 3 H, Me), 2.40 (s, 3 H, Me), 1.68 (m, 2 H, $CH_3CH_2CH_2$), 1.55 (m, 2 H, $CH_3CH_2CH_2$), 1.00 (t, $^3J_{H-H}$ = 7.3 Hz, 3 H, CH_3). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 153.8 (py-C), 152.6 (py-C), 141.0 (py-C), 131.6 (py-C), 60.1 (py-*C*H(O)), 55.8 (py-CH(O)*C*H), 34.2, 21.5, 19.7, 14.1, 11.5. MS (EI, 70 eV): *m/e* 192 (6) [molecular ion], 191 (6), 180 (5), 179 (6), 177 (12), 176 (50), 175 (12), 165 (7), 164 (9), 163 (10), 162 (15), 161 (100) [base peak], 159 (8), 150 (9), 149 (50), 148 (21), 147 (48), 146 (35), 145 (14), 138 (8), 136 (7), 135 (33), 134 (12), 133 (57), 132 (13), 131 (8), 123 (8), 122 (55), 121 (24), 120 (8), 119 (8), 108 (26), 107 (31), 104 (7), 96 (7), 94 (8), 91 (8), 81 (10), 80 (19), 79 (10), 78 (11), 77 (16), 67 (8), 66 (13). HRMS (EI) for $C_{11}H_{15}N_2O$: calcd 192.1259, obsd 192.1237.

3,6-Dimethyl-2-((trimethylsilyl)ethyl)pyrazine (17). A slurry of **4** (5 mg, 0.024 mmol) and Pd/C (cat., ~0.5 mg) in CH_2Cl_2 was charged with H_2 (~3 atm) and stirred at 23 °C for 2 h. The slurry was filtered through a $MgSO_4$ plug (2 cm). Concentration of the filtrate under vacuum gave **17** (~5 mg, ~100%) as a colorless oil. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.09 (s, 1 H, py-H), 2.73 (m, 2 H, py-CH_2), 2.47 (s, 3 H, Me), 2.43 (s, 3 H, Me), 0.88 (m, 2 H, CH_2SiMe$_3$), 0.05 (s, 9 H, $SiMe_3$). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 156.9 (py-C), 150.3 (py-C), 148.5 (py-C), 140.8 (py-C), 132.1, 29.8, 21.2, 21.1, 15.6, -1.8 ($SiMe_3$). MS (EI, 70 eV): *m/e* 209 (3), 208 (16) [molecular ion], 195 (4), 194 (17), 193 (100), 191 (9), 180 (2), 179 (12), 177 (3), 165 (4), 161 (3), 136 (10), 135 (94), 133 (8), 107 (4), 97 (3), 84 (6), 80 (5), 75 (2), 74 (4), 73 (49), 72 (2), 67 (3), 66 (3), 65 (2), 59 (13), 58 (6), 55 (3), 54 (3), 45 (9), 44 (4), 43 (8), 42 (9), 40 (8).

5,6-Dimethyl-2-pentylpyrazine (18). Compound **18** was isolated in ca. 100% yield (3.1 mg) from the reaction of **8** (3 mg, 0.017 mmol) with H_2 (~3 atm) in presence of catalytic amount of Pd/C. The procedure described for the preparation of **17** was used here. ^1H NMR (300 MHz, CD_2Cl_2): δ 8.09 (s, 1 H, py-H), 2.68 (t, $^3J_{H-H}$ = 7.7 Hz, 2 H, py-CH_2), 2.46 (s, 3 H, Me), 2.45 (s, 3 H, Me), 1.68 (m, 2 H), 1.33 (m, 4 H), 0.89 (t, $^3J_{H-H}$ = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (90 MHz, CD_2Cl_2): δ 154.3 (py-C), 151.6 (py-C), 149.6 (py-C), 140.7 (py-C), 35.3, 31.9, 29.7, 22.9, 22.2, 21.7, 14.1. MS (EI, 70 eV): *m/e* 178 (3) [molecular ion], 163 (2), 149 (11), 136 (3), 135 (23), 123 (10), 122 (100), 80 (4), 40 (11). HRMS (EI) for $C_{11}H_{18}N_2$: calcd 178.1470, obsd 178.1477.

3,6-Dimethyl-2-((trimethylsilyl)ethyl)-5-pentylpyrazine (19). Compound **19** was isolated in ca. 100% yield (by ^1H NMR) from the reaction of **7** (2.2 mg, 0.008 mmol) with H_2 (~3 atm) in presence of catalytic amount of Pd/C. The procedure described for the preparation of **17** was used here. ^1H NMR (360 MHz, CD_2Cl_2): δ 2.69 (m, 4 H, py-CH_2's), 2.44 (s, 3 H, py-CH_3), 2.43 (s, 3 H, py-CH_3), 1.61 (m, 2 H), 1.35 (m, 4 H), 0.90 (overlapping multiplet and triplet, 5 H, CH_2CH_3 and CH_2Si), 0.03 (s, 9 H, $Si(CH_3)_3$). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 153.8 (py-C), 151.9 (py-C), 148.0 (py-C), 147.7 (py-C), 34.9, 32.2, 29.3, 28.8, 23.0, 21.2, 21.1, 15.8, 14.2, -1.72 ($Si(CH_3)_3$). HRMS (EI) for $C_{16}H_{30}N_2Si$: calcd 278.2178, obsd 278.2177.

3,6-Dimethyl-2,5-bis(3-(trimethylsilyl)prop-2-yl)pyrazine (20a and 20b, Diastereomeric Mixture). Compounds **20a** and **20b** were isolated in 100% yield (by ^1H NMR) as a ~1:0.8 mixture of diastereomers from the reaction of **5** (3.7 mg, 0.011 mmol) with H_2 (~3 atm) in presence of catalytic amount of Pd/C. The procedure described for the preparation of **17** was used here. ^1H NMR (360 MHz, CD_2Cl_2): for major isomer **20a**, δ 3.16 (sextet, $^3J_{H-H}$ = 6.7 Hz, 2 H, py-CH(CH_3)'s), 2.47 (s, 6 H, py-CH_3's), 1.23 (obscured by py-CH_3's, 2 H, CH(H)$SiMe_3$'s), 1.21 (d, $^3J_{H-H}$ = 6.7 Hz, 6 H, py-CH(CH_3)'s), 0.84 (t, $^3J_{H-H}$ = 6.7 Hz, 2 H, CH(H)-$SiMe_3$'s), -0.13 (s, 9 H, $Si(CH_3)_3$). ^1H NMR (360 MHz, CD_2Cl_2): for minor isomer **20b**, δ 3.16 (obscured by **20a**, 2 H, py-CH(CH_3)'s), 2.49 (s, 6 H, py-CH_3's), 1.22 (d, $^3J_{H-H}$ = 6.7 Hz, 6 H, py-CH(CH_3)'s), 1.21 (obscured by py-CH_3's, 2 H, CH(H)$SiMe_3$'s), 0.79 (t, $^3J_{H-H}$ = 6.7 Hz, 2 H, CH(H)$SiMe_3$'s), -0.13 (s, 9 H, $Si(CH_3)_3$). MS (EI, 70 eV): for major isomer **20a**, *m/e* 336 (10) [molecular ion], 322 (8), 321 (29), 264 (22), *263* (*100*), 221 (9), 219 (7), 217 (7), 73 (64), 59 (9), 45 (12), 44 (14), 40 (9). MS (EI, 70 eV): for minor isomer **20b**, *m/e* 336 (7) [molecular ion], 322 (6), 321 (21), 264 (18), 263 (82), 233 (8), 221 (9), 219 (7), 217 (7), 175 (5), *73* (*100*), 59 (14), 45 (21), 44 (22), 40 (20). HRMS (EI) for $C_{18}H_{36}N_2Si$: calcd 336.2417, obsd 336.2418.

Acknowledgment. This work was supported by the National Science Foundation (CHE9022700) and the Volkswagen-Stiftung. NMR spectra were obtained in the University of Iowa Highfield NMR Facility. R.F.J. gratefully acknowledges a Sloan Foundation Research Fellowship (1989–91) and Union Carbide Research Innovation Awards (1989,90).

Supplementary Material Available: ^1H NMR spectra of compounds **2–10** and **12–20** (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.