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Routes to *N*,*N*′-Unsymmetrically Substituted 1,3-Diketimines

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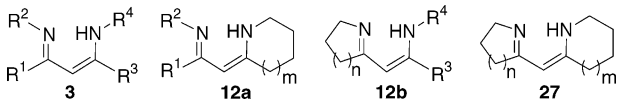


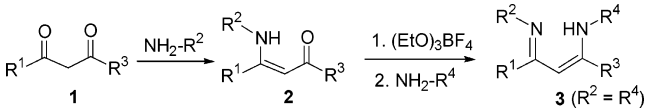
A series of novel *N*,*N*′-unsymmetrically substituted 1,3-diketimines (**3**, **12**, and **27**) have been synthesized from the reaction of exocyclic enaminoketones **8** with amines or metalloenamines (from **13** or **14**) with imidoyl thioether **25** or **26**.

Introduction

Highly conductive and inexpensive copper is believed to be the metal of choice for integrated circuit interconnects of the future. The development of a suitable volatile precursor for chemical vapor deposition (CVD)[1] or atomic layer deposition (ALD)[2] of thin metallic films of copper is expected to revolutionize the manufacturing of such electronic devices as semiconductor microchips and flat panel displays. 1,3-Diketones,[3] 1,3-ketoenamines,[4] and 1,3-diketimines[5] have been widely used as bidentate chelating ligands for volatile metal complexes. Currently, the most widely tested volatile precursor for Cu metal deposition is hexafluoroacetylacetonato(trimethylsilylethylene)copper(I), Cupraselect.[6]

In addition to Cu, Cupraselect is composed of C, H, Si, O, and F. In the modern industry of microelectronics, however, it is increasingly recognized that the presence of oxygen or halogens in the precursor may be detrimental to the desired performance, including device efficiency.[7] Therefore, oxygen- and halogen-free 1,3-diketimine ligands are preferred over 1,3-diketones and 1,3-ketoenamines, particularly for metal complex precursors for microchip interconnect layers. While efficient synthetic methods have been developed for numerous 1,3-diketones and their monoimino derivatives, 1,3-diketimines remain extremely rare. A few symmetrically substituted 1,3-diketimines have already been prepared and tested as suitable ligands for metal complexes with desired material properties.[8] In contrast, no efficient synthetic approach has been reported for most desired *N*,*N*′-unsymmetrically substituted 1,3-diketimines that are expected to produce Cu precursors of enhanced volatility. The great demand for unsymmetrical 1,3-diketimines prompted us to explore synthetic routes to these highly valuable yet inaccessible compounds. In this paper, we report the first general and efficient synthetic method for the preparation of *N*,*N*′-unsymmetrically substituted 1,3-diketimines to meet the stringent industrial requirements for their volatile copper chelates.

SCHEME 1. McGeachin's Route to *N*,*N*′-Symmetrically Substituted 1,3-Diketimines



Results and Discussion

As stated in the Introduction, our goal was to develop the first general and efficient method for the synthesis of *N*,*N*′-unsymmetrically substituted 1,3-diketimines. Symmetrical 1,3-diketimines **3** ($R^2 = R^4$) are synthesized

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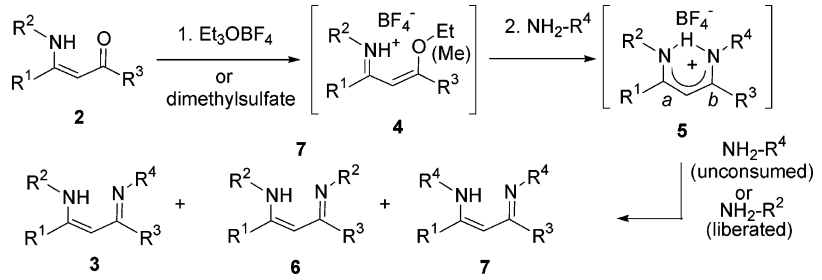
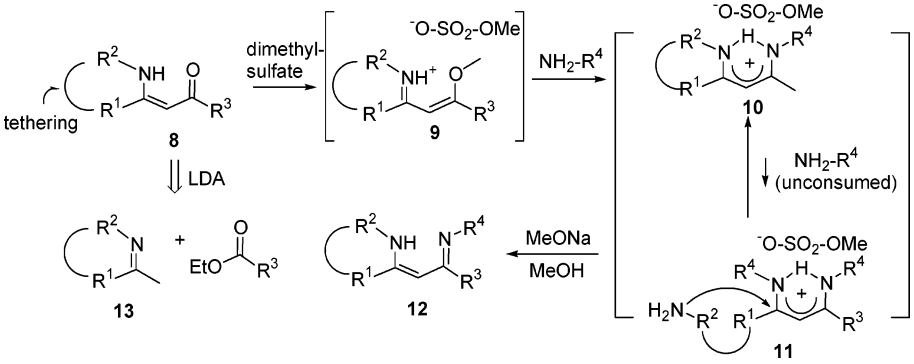
SCHEME 2. Formation of a 1,3-Diketimine Mixture When $R^2 \neq R^4$



SCHEME 3. Cyclic Ketimine Leading to a Single Unsymmetrical 1,3-Diketimine



by following McGeachin's protocol (Scheme 1)[9] from 1,3-diketones **1** to first make enaminoketones **2**, which are then alkylated with a strong electrophile such as a trialkyloxonium salt, and finally aminated.

The McGeachin methodology, however, cannot be extended to the synthesis of *N*,*N*′-unsymmetrically substituted 1,3-diketimines. When $R^2 \neq R^4$ (Scheme 2), the reaction always produces a mixture of all three possible diketimines **3**, **6**, and **7**, which are nearly impossible to separate.[10]

As shown in Scheme 2, the initially generated unsymmetrical 1,3-diketiminium salt **5** can undergo nucleophilic attack by the still present NH_2R^4 on both a and b carbon atoms, liberating NH_2R^2 and NH_2R,[4] respectively. The NH_2R^2 thus produced can also act as a nucleophile toward both a and b electrophilic centers. As result, a mixture of all three possible diketimines **3**, **6**, and **7** is produced. To prevent this exchange and hence maintain the desired unsymmetry for the 1,3-diketimine product, we reasoned that tethering R^1 and R^2 together (compound **8**) should suppress the liberation of NH_2R^2. This way, only the *N*,*N*′-unsymmetrically substituted 1,3-diketimine **12** would be produced (Scheme 3). As long as NH_2R^2 is tethered to R^1, the equilibrium between **10** and **11** is expected to favor **10** (intra- vs intermolecular substitution), leading to the desired unsymmetrical diketimine **12**.

The starting materials, endocyclic ketimines **13**, were synthesized from their lactam derivatives[11] or via the sequential reaction of the corresponding saturated amine with *N*-chlorosuccinimide, followed by treatment with KOH.[12] Ketimines **13** were then treated with the ester derivative in the presence of LDA to afford **8** (Scheme 3). Activation of this exocylcic enaminoketone **8** with dimethyl sulfate (or Meerwein salt) furnished **9**. Treatment of **9** with primary amines afforded unsymmetrical cyclic 1,3-diketimines **12** in up to 90% overall isolated yield (Table 1).

TABLE 1. *N*,*N*′-Unsymmetrically Substituted 1,3-Diketimines

compd	R^1	R^2	R^3	R^4	method	yield (%)
3-1	CH_3	*i*-Bu	CH_3	CH_3	Scheme 10	53[a]
12a-1	CH_3	*i*-Bu	$m = 0$		Scheme 10	66[a]
12b-1	$n = 1$		CH_3	*n*-Bu	Scheme 3	75[b]
12b-2	$n = 1$		CH_3	*n*-Pr	Scheme 3	87[b]
12b-3	$n = 1$		CH_3	CH_3CH_2	Scheme 3	90[b]
12b-4	$n = 1$		CH_3	CH_3	Scheme 3	76[b]
12b-5	$n = 1$		CH_3	H	Scheme 3	72[b]
12b-6	$n = 2$		CH_3	CH_3	Scheme 3	69[b]
27-1	$n = 2$		$m = 0$		Scheme 10	84[a]
27-2[c]	$n = 1$		$m = 0$		Scheme 10	79[a]

[a] Yield from compound **13** or **14**. [b] Yield from compound **8**. [c] A symmetrical dicyclic diketimine can also be synthesized by this route.

We also considered using nitrilium ions as a starting material for noncyclic 1,3-diketimines, as shown in Scheme 4. The reaction of lithiated **14** with nitrilinium ion **15** or **16** would lead to 1,3-diketimine **17** (Scheme 4). The starting nitrilium ion **15** or **16** could be easily generated by reacting a nitrile with Meerwein salt,[13] or with an alkyl chloride in the presence of $SbCl_5$.[14] However, extensive gelation was observed upon addition of *N*-isopropylacetonitrilium hexachloroantimonate (**16**) to lithiated **14** in THF. That prompted us to attempt the reaction of ketimne **14** (R^1 = Me, R^2 = *i*-Pr) with *N*-methylacetonitrilium tetrafluoroborate (**15**). This strat-

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(11) Hua, D. H.; Miao, S. W.; Bharathi, S. N.; Katsuhira, T.; Bravo, A. A. *J. Org. Chem*. **1990**, *55*, 3682
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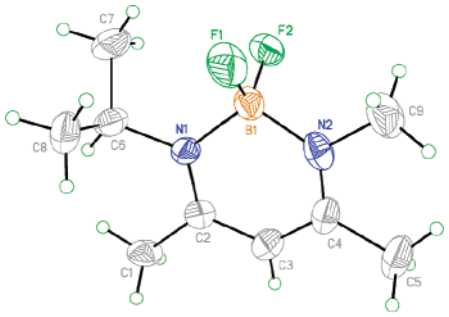
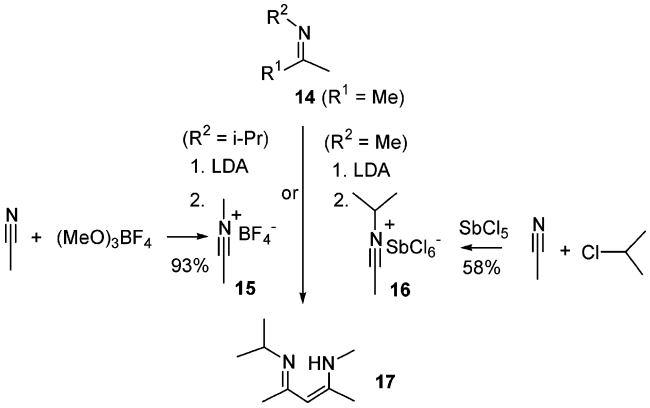
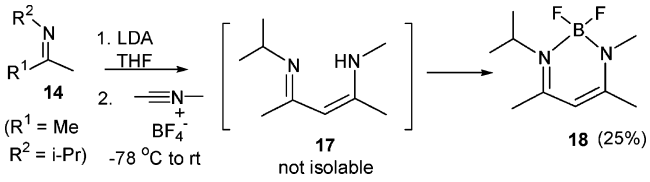


FIGURE 1. X-ray crystallography of difluoroboron diketiminate complex **18**.

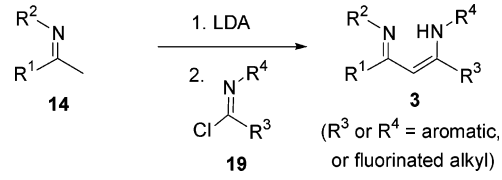
SCHEME 4. Possible Routes to Noncyclic Unsymmetrical 1,3-Diketimine



SCHEME 5. Formation of a Difluoroboron Diketiminate Complex



SCHEME 6. 1,3-Diketimine from the Reaction of Ketimine with Imidoyl Halide



egy did work. Unfortunately, the desired 1,3-diketimine **17** chelated the boron of the BF_4^- to produce stable complex **18** (Scheme 5), whose structure was confirmed by X-ray analysis (Figure 1).

To synthesize noncyclic *N,N′*-unsymmetrically substituted 1,3-diketimines, we tried an alternative way by employing the reaction of ketimine **14** and imidoyl halide **19**, as shown in Scheme 6. This reaction, however, appeared to be limited only to aromatic or fluorinated imidoyl halides (R^3 and R^4 = aryl or CF_3) which are sufficiently stable for isolation.[15] Nonfluorinated aliphatic unsymmetrical 1,3-diketimines **3** could not be synthesized via Scheme 6 because of poor stability of **19** with R^3 and R^4 = alkyl. For instance, amide **20** (R^3 = Me, R^4 = Et) did not afford isolable imidoyl halide **21** upon treatment with PCl_5, but rather a 1:1 mixture of **21** and **22** was believed to be formed, as suggested by the NMR data (Scheme 7). Upon standing, white crystals were deposited from the oily reaction mixture, which were collected and identified by X-ray analysis as salt **23** (Figure 2), the product of quantitative dimerization of **21** (Scheme 8).

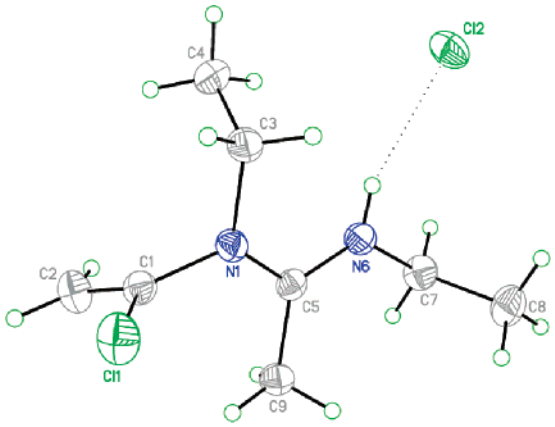


FIGURE 2. X-ray crystallography of dimerized salt **23**.

The reported[16] methods to prepare and isolate some nonfluorinated aliphatic imidoyl halides did not work in our hands. It is noteworthy that most nonfluorinated aliphatic imidoyl halides have only been generated in situ to be used for subsequent steps without isolation.[17] Our attempts to use the in situ generated nonfluorinated aliphatic imidoyl halides to prepare 1,3-diketimines as in Scheme 6 were unsuccessful, prompting us to find an alternative to this approach. To stabilize the electrophile, we considered leaving groups other than chloride. The initially tested imidoyl alkyl ether **24** appeared insufficiently reactive toward the lithiated enamine. We were pleased to find, however, that imidoyl alkyl thioether **25** exhibited sufficient reactivity for the synthesis of 1,3-diketimine (Scheme 9).

Indeed, by reacting imine **13** or **14** with imidoyl thioether **25** or **26**, we successfully prepared a series of *N,N′*-unsymmetrically substituted 1,3-diketimines, both cyclic and noncyclic, in 53−84% yield (Scheme 10 and Table 1). Imidoyl thioether electrophile **25** or **26** can be synthesized in high yield from numerous commercially available aliphatic amides via conversion to their thione derivatives,[18] followed by alkylation.[19]

All diketimines prepared in this work were purified by vacuum distillation to produce colorless, ^1H and ^{13}C NMR spectroscopically pure (>98%) oily liquid materials (for spectra, see the Supporting Information). It was noticed that the freshly distilled colorless products turn yellow within a few hours after purification, even if stored

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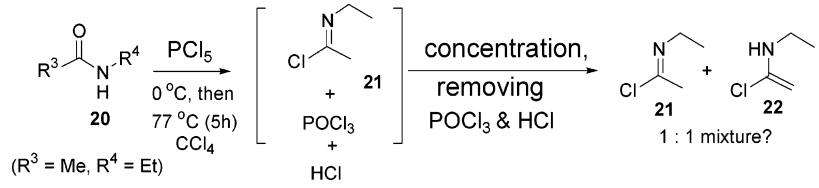
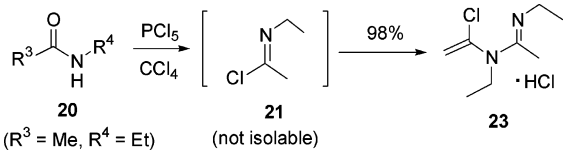
(19) (a) Cambie, R. C.; Chambers, D.; Rutledge, P. S.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 40. (b) Casadei, M. A.; Rienzo, B. D. *Synth. Commun.* **1983**, *13*, 753.

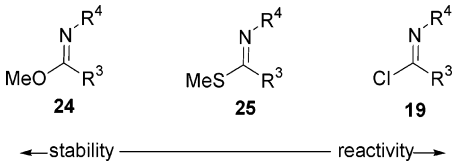
SCHEME 7. Reaction of *N*-Ethylacetamide with PCl_5



SCHEME 8. Quantitative Dimerization of Aliphatic Imidoyl Chloride



SCHEME 9. Comparison of Stability and Reactivity from Imidoyl Derivatives



under nitrogen in a glovebox. Although due to the poor stability satisfactory elemental analysis data could not be obtained, all of the new 1,3-diketimines were successfully characterized by HRMS. Purification by column chromatography on silica gel is impossible, resulting in immediate decomposition of the diketimines. These compounds should be used immediately after their preparation and purification.

Conclusion

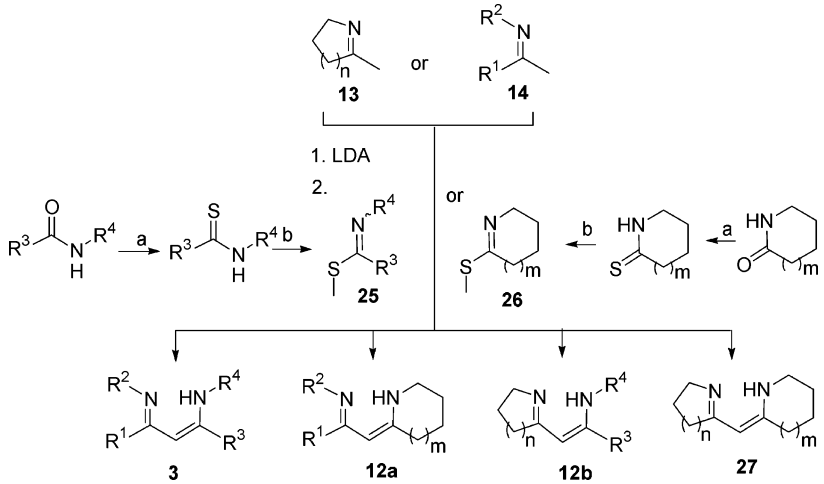
In conclusion, we have developed the first general methods for the synthesis of novel *N*,*N*′-unsymmetrically substituted 1,3-diketimines. One of the methods is limited to the preparation of only cyclic compounds, whereas the other method can afford both cyclic and acyclic unsymmetrical diketimines. The products are low molecular weight ligands for highly desired oxygen- and halogen-free metal precursors of enhanced volatility for copper CVD and/or ALD processes. Studies toward the synthesis of such metal complex precursors and their use are currently under way in our laboratories. Results of these studies will be published separately.

Experimental Section

General Methods. Unless otherwise indicated, all reactions were run under an inert atmosphere of nitrogen using dry solvents stored over 3 Å molecular sieves. Commercial reagents were used as received. All of the 1,3-diketimnes prepared are acid sensitive, and thus were purified by vacuum distillation rather than silica gel column chromatography. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, and calibrated using a solvent peak as an internal reference.

((1*Z*,3*E*)-4-Aza-1,3,6-trimethylhepta-1.3-dienyl)methylamine (3-1) from the Reaction of 14 (R^1 = Me, R^2 = Isobutyl) with 25 (R^3 = R^4 = Me). To a solution of diisopropylamine (10.29 g, 101.8 mmol, 2.1 equiv) in THF (200 mL) was added *n*-BuLi (35.2 mL, 101.8 mmol, 2.1 equiv, 2.89 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −10 °C for another 30 min. Then *N*-isopropylideneisobutylamine **14** (7.13 g, 63 mmol, 1.3 equiv) solution in THF (20 mL) was added dropwise to the mixture at −10 °C. After the mixture was stirred for 40 min at the same temperature, methyl *N*-methylthioacetimidate **25** (R^3 = R^4 = Me) (5 g, 48.45 mmol) solution in THF (15 mL) was added to the mixture dropwise at −10 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (30 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, pentane (100 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by vacuum distillation (35 °C, 72 mTorr) to afford compound **3-1** (4.3 g,

SCHEME 10. Routes to Diverse *N*,*N*′-Unsymmetrically Substituted 1,3-diketimines[a]



[a] Reagents and conditions: (a) Lawesson's reagent or P_4S_{10} (88−89%); see ref 18; (b) MeI or $(MeO)_3BF_4$ (92−98%); see ref 19.

53%) as a colorless oil: ^{1}H NMR (500 MHz, C_6D_6) δ 11.41 (s, br, 1H), 4.62 (s, 1H), 2.94 (d, 2H, J = 6.6 Hz), 2.82 (s, 3H), 1.77 (m, 1H), 1.71 (s, 3H), 1.66 (s, 3H), 0.94 (d, 6H, J = 6.4 Hz); ^{13}C NMR (125 MHz, C_6D_6) δ 161.9, 159.8, 95.1, 54.6, 33.4, 30.4, 20.7, 19.4, 18.9; HRMS (EI) *m/z* calcd for $C_{10}H_{10}N_2$ 168.1626, found 168.1623.

(1*Z*)-1-(1-Pyrrolin-2-yl)prop-1-en-2-ol (8a) (−(R^{1}R^2)− = −(CH$_2$)$_3$−, R^3 = Me) from the Reaction of 2-Methyl-1-pyrroline 13 with Ethyl Acetate. To a solution of diisopropylamine (22.2 g, 219 mmol, 2.1 equiv) in THF (200 mL) was added *n*-BuLi (75.9 mL, 219 mmol, 2.1 equiv, 2.89 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −5 °C for another 30 min. Then 2-methyl-1-pyrroline **13** (11.3 g, 136 mmol, 1.3 equiv) solution in THF (10 mL) was added dropwise to the mixture at −5 °C. After the mixture was stirred for 30 min at the same temperature, ethyl acetate (9.2 g, 104 mmol) solution in THF (5 mL) was added to the mixture dropwise at −5 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (80 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, ether (100 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by column chromatography (30% ethyl acetate in hexane) to afford compound **8a** (11 g, 84%) as a solid: mp 58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (s, br, 1H), 5.08 (s, 1H), 3.53 (t, 2H, J = 7.1 Hz), 2.56 (t, 2H, J = 8.2 Hz), 1.99 (s, 3H), 1.94 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 195.2, 167.8, 90.3, 47.7, 32.6, 29.0, 21.5; HRMS (EI) *m/z* calcd for $C_7H_{11}NO$ 125.0841, found 125.0842.

(1*Z*)-1-(3,4,5,6-Tetrahydropyrid-2-yl)prop-1-en-2-ol (8b) (−(R^{1}R^2)− = −(CH$_2$)$_4$−, R^3 = Me) from the Reaction of 2-Methyl-3,4,5,6-tetrahydropyridine 13 with Ethyl Acetate. To a solution of diisopropylamine (10.1 g, 99.8 mmol, 2.1 equiv) in THF (200 mL) was added *n*-BuLi (34.5 mL, 99.8 mmol, 2.1 equiv, 2.89 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −5 °C for another 30 min. Then 2-methyl-3,4,5,6-tetrahydropyridine **13** (6 g, 61.7 mmol, 1.3 equiv) solution in THF (10 mL) was added dropwise to the mixture at −5 °C. After the mixture was stirred for 30 min at the same temperature, ethyl acetate (4.2 g, 47.5 mmol) solution in THF (5 mL) was added to the mixture dropwise at −5 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (80 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, ether (100 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by column chromatography (30% ethyl acetate in hexane) to afford compound **8b** (3.97 g, 60%) as a liquid: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 11.01 (s, br, 1H), 4.86 (s, 1H), 3.30 (t, 2H, J = 6.1 Hz), 2.33 (t, 2H, J = 6.4 Hz), 1.91 (s, 3H), 1.79 (m, 2H), 1.75 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 194.1, 164.4, 93.5, 41.6, 28.8, 28.7, 22.8, 19.8; HRMS (EI) *m/z* calcd for $C_8H_{13}NO$ 139.0997, found 139.0995.

((1*Z*)-1-Methyl-2-(1-pyrrolin-2-yl)vinyl)(2-methylpropyl)-amine (12a-1) from the Reaction of 14 (R^1 = Me, R^2 = Isobutyl) with 26 (*m* = 0). To a solution of diisopropylamine (10.29 g, 101.8 mmol, 2.1 equiv) in THF (200 mL) was added *n*-BuLi (46.3 mL, 101.8 mmol, 2.1 equiv, 2.2 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −10 °C for another 30 min. Then *N*-isopropylideneisobutylamine **14** (7.13 g, 63 mmol, 1.3 equiv) solution in THF (20 mL) was added dropwise to the mixture at −10 °C. After the mixture was stirred for 40 min at the same temperature, lactim thioether **26** (*m* = 0) (5.58 g, 48.45 mmol) solution in THF (15 mL) was added to the mixture dropwise at −10 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (20 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, pentane (120 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by vacuum distillation (54 °C, 102 mTorr) to afford compound **12a-1** (5.8 g, 66%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s, br, 1H), 4.54 (s, 1H), 3.82 (t, 2H, J = 7.1 Hz), 2.98 (d, 2H, J = 6.7 Hz), 2.46 (t, 2H, J = 8.0 Hz), 1.90 (s, 3H), 1.77−1.69 (m, 3H), 0.92 (d, 6H, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 154.4, 87.3, 60.1, 51.0, 37.7, 29.6, 22.4, 20.0, 19.1; HRMS (EI) *m/z* calcd for $C_{11}H_{20}N_2$ 180.1626, found 180.1633.

((1*Z*)-1-Methyl-2-(1-pyrrolin-2-yl)vinyl)butylamine (12b-1) from the Reaction of 8a with Butylamine. Enaminoketone **8a** (5 g, 39.9 mmol) was treated with dimethyl sulfate (5.04 g, 39.9 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with THF (40 mL), followed by addition of butylamine (3.8 g, 51.9 mmol, 1.3 equiv). The resultant mixture was stirred overnight at room temperature, and then the mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (2.16 g, 39.9 mmol) solution in MeOH (30 mL). After the mixture was stirred at room temperature for 30 min, it was concentrated under reduced pressure. Pentane (100 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (44 °C, 45 mTorr), afforded compound **12b-1** (5.4 g, 75%) as a liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, br, 1H), 4.53 (s, 1H), 3.84 (t, 2H, J = 7.2 Hz), 3.17 (t, 2H, J = 7.1 Hz), 2.46 (t, 2H, J = 8.1 Hz), 1.91 (s, 3H), 1.72 (m, 2H), 1.53 (m, 2H), 1.37 (m, 2H), 0.91 (t, 3H, J = 8.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 154.0, 87.3, 59.8, 42.8, 37.6, 32.9, 22.2, 20.1, 18.6, 13.7; HRMS (EI) *m/z* calcd for $C_{11}H_{20}N_2$ 180.1626, found 180.1633.

((1*Z*)-1-Methyl-2-(1-pyrrolin-2-yl)vinyl)propylamine (12b-2) from the Reaction of 8a with Propylamine. Enaminoketone **8a** (5 g, 39.9 mmol) was treated with dimethyl sulfate (5.04 g, 39.9 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with THF (40 mL), followed by addition of propylamine (3.1 g, 51.9 mmol, 1.3 equiv). The resultant mixture was stirred overnight at room temperature, and then the mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (2.16 g, 39.9 mmol) solution in MeOH (30 mL). After the mixture was stirred at room temperature for 30 min, it was concentrated under reduced pressure. Pentane (100 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (37 °C, 68 mTorr), afforded compound **12b-2** (5.7 g, 87%) as a liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, br, 1H), 4.56 (s, 1H), 3.84 (t, 2H, J = 7.4 Hz), 3.14 (t, 2H, J = 7.1 Hz), 2.46 (2, 2H, J = 8.1 Hz), 1.91 (s, 3H), 1.72 (m, 2H), 1.56 (m, 2H), 0.94 (t, 3H, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 154.3, 87.6, 60.0, 45.0, 37.8, 23.9, 22.2, 19.0, 11.6; HRMS (EI) *m/z* calcd for $C_{10}H_{18}N_2$ 166.1470, found 166.1475.

((1*Z*)-1-Methyl-2-(1-pyrrolin-2-yl)vinyl)ethylamine (12b-3) from the Reaction of 8a with Ethylamine. Enaminoketone **8a** (5 g, 39.9 mmol) was treated with dimethyl sulfate (5.04 g, 39.9 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with THF (50 mL), followed by addition of ethylamine solution (26 mL, 51.9 mmol, 1.3 equiv, 2.0 M in THF). The resultant mixture was stirred overnight at room temperature, and then the mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (2.16 g, 39.9 mmol) solution in MeOH (20 mL). After the mixture was stirred at

room temperature for 30 min, it was concentrated under reduced pressure. Pentane (100 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (37 °C, 50 mTorr), afforded compound **12b-3** (5.6 g, 90%) as a liquid: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 9.71 (s, br, 1H), 4.54 (s, 1H), 3.81 (t, 2H, J = 7.3 Hz), 3.23 (q, 2H, J = 7.3 Hz), 2.45 (m, 2H), 1.93 (s, 3H), 1.71 (m, 2H), 1.18 (t, 3H, J = 7.3 Hz); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 174.2, 154.8, 87.9, 60.6, 38.1, 37.9, 22.8, 19.2, 16.3; HRMS (EI) *m/z* calcd for $C_9H_{16}N_2$ 152.1313, found 159.1319.

((1*Z*)-1-Methyl-2-(1-pyrrolin-2-yl)vinyl)methylamine (12b-4) from the Reaction of 8a with Methylamine. Enaminoketone **8a** (5 g, 39.9 mmol) was treated with dimethyl sulfate (5.04 g, 39.9 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with THF (50 mL), followed by addition of methylamine solution (26 mL, 51.9 mmol, 1.3 equiv, 2.0 M in THF). The resultant mixture was stirred overnight at room temperature, and then the mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (2.16 g, 39.9 mmol) solution in MeOH (20 mL). After the mixture was stirred at room temperature for 30 min, it was concentrated under reduced pressure. Pentane (100 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (32 °C, 50 mTorr), afforded compound **12b-4** (4.2 g, 76%) as a liquid: ^{1}H NMR (500 MHz, C_6D_6) δ 10.28 (s, br, 1H), 4.67 (s, 1H), 3.93 (t, 2H, J = 7.3 Hz), 2.40 (s, 3H), 2.38 (t, 2H, J = 7.9 Hz), 1.61 (s, 3H), 1.55 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.3, 154.8, 88.1, 60.4, 38.0, 28.9, 22.7, 18.5; HRMS (EI) *m/z* calcd for $C_8H_{14}N_2$ 138.1157, found 138.1155.

((1*Z*)-1-(1-pyrrolin-2-yl)pro-1-en-2-ylamine (12b-5) from the reaction of 8a with Ammonia. Enaminoketone **8a** (10 g, 79.9 mmol) was treated with dimethyl sulfate (10.1 g, 79.9 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with CH_2Cl_2 (50 mL), followed by bubbling of ammonia gas through the solution for 3 h at room temperature. The resultant mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (4.31 g, 79.9 mmol) solution in MeOH (50 mL). After the mixture was stirred at room temperature for 30 min, it was concentrated under reduced pressure. Pentane (100 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (39 °C, 110 mTorr), afforded compound **12b-5** (7.1 g, 72%) as a liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (s, br, 2H), 4.62 (s, 1H), 3.87 (t, 2H, J = 7.1 Hz), 2.48 (t, 2H, J = 8.1 Hz), 1.89 (s, 3H), 1.75 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 174.2, 152.4, 89.3, 60.7, 38.5, 22.5, 22.2; HRMS (EI) *m/z* calcd for $C_7H_{12}N_2$ 124.1000, found 124.1003.

((1*Z*)-1-Methyl-2-(3,4,5,6-tetrahydropyrid-2-yl)vinyl)-methylamine (12b-6) from the Reaction of 8b with Methylamine. Enaminoketone **8b** (2 g, 14.4 mmol) was treated with dimethyl sulfate (1.81 g, 14.4 mmol) without solvent, giving a viscous mixture after being stirred for 4 h at room temperature. After being allowed to stand overnight, the solidified mixture was treated with THF (20 mL), followed by addition of methylamine solution (9.3 mL, 18.7 mmol, 1.3 equiv, 2.0 M in THF). The resultant mixture was stirred overnight at room temperature, and then the mixture was concentrated under reduced pressure, followed by addition of sodium methoxide (0.77 g, 14.4 mmol) solution in MeOH (20 mL). After the mixture was stirred at room temperature for 30 min, it was concentrated under reduced pressure. Pentane (60 mL) was added to the residue, and then the insoluble material was filtered. Concentration of the filtrate under reduced pressure, followed by vacuum distillation (39 °C, 60 mTorr), afforded compound **12b-6** (1.5 g, 69%) as a liquid: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 10.2 (s, br, 1H), 4.34 (s, 1H), 3.49 (t, 2H, J = 5.8 Hz), 2.88 (s, 3H), 2.16 (t, 2H, J = 6.6 Hz), 1.85 (s, 3H), 1.64 (m, 2H), 1.60 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 165.6, 157.0, 93.1, 47.0, 30.9, 30.5, 23.3, 20.8, 19.0; HRMS (EI) *m/z* calcd for $C_9H_{16}N_2$ 152.1313, found 152.1314.

Difluoroboron [((1*Z*,3*E*)-4-Aza-1,3,5-trimethylhexa-1,3-dienyl)methylaminate] (18) from *N*-(Isopropylidene)-isopropylamine 14 (R^1 = Me, R^2 = *i*-Pr). To a solution of *N*-(isopropylidene)isopropylamine **14** (R^1 = Me, R^2 = *i*-Pr) (5 g, 50.42 mmol) in THF (200 mL) was added *t*-BuLi (30 mL, 50.42 mmol, 1.7 M) dropwise at −78 °C. After the mixture was stirred for 40 min at −78 °C, nitrilium salt 15 (7.21 g, 50.42 mmol) was added to the mixture as a solid under nitrogen. The reaction mixture was stirred at −78 °C for 6 h and then stirred overnight as the temperature was allowed to gradually rise to room temperature. After removal of the solvent under reduced pressure, hexane (150 mL) was added to the residue. The mixture was filtered, and then the cold filtrate afforded a precipitated yellow solid, which was collected (1.94 g, 25%) by filtration: mp 71 °C; ^{1}H NMR (500 MHz, C_6D_6) δ 4.45 (s, 1H), 3.71 (m, 1H), 2.76 (s, 3H), 1.53 (s, 3H), 1.43 (dt, 6H, J = 1.4, 6.8 Hz), 1.28 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 162.3, 161.3, 94.9, 50.0, 31.4, 23.0, 20.5, 19.0; HRMS (EI) *m/z* calcd for $C_9H_{17}BF_2N_2$ 202.1453, found 202.1448. Anal. Calcd for $C_9H_{17}BF_2N_2$: C, 53.50; H, 8.48; N, 13.86. Found: C, 53.78; H, 8.32; N, 13.79.

((1*E*)-2-Aza-1-methylbut-1-enyl)(1-chlorovinyl)ethylamine Hydrochloride (23) from *N*-Ethylacetamide 20 (R^3 = Me, R^4 = Et). To a solution of PCl_5 (49 g, 235.5 mmol) in CCl_4 (100 mL) was added *N*-ethylacetamide **20** (R^3 = Me, R^4 = Et) (20.5 g, 235.3 mmol) solution in CCl_4 (100 mL) at 0 °C. After the mixture was stirred for 2 h at room temperature, it was refluxed for 5 h. After the mixture was cooled to room temperature under nitrogen, the mixture was concentrated under vacuum. The resultant viscous liquid was crystallized in toluene to afford compound **23** (24.3 g, 98%) as a solid, which can be further purified by recrystallization (toluene + methylene chloride): mp 110 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 11.60 (s, br, 1H), 5.66 (d, 1H, J = 2.5 Hz), 5.57 (d, 1H, J = 2.5 Hz), 4.04 (m, 2H), 3.56 (m, 2H), 2.38 (s, 3H), 1.27 (t, 3H, J = 7.2 Hz); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 162.9, 135.1, 119.8, 46.6, 40.7, 16.3, 14.8, 12.0. Anal. Calcd for $C_8H_{16}Cl_2N_2$: C, 45.51; H, 7.64; Cl, 33.58; N, 13.27. Found: C, 45.52; H, 7.42; Cl, 33.74; N, 13.29.

2-(Pyrrolidin-2-ylidenemethyl)-3,4,5,6-tetrahydropyridine (27−1) from the Reaction of 2-Methyl-3,4,5,6-tetrahydropyridine 13 (n = 2) with 26 (m = 0). To a solution of diisopropylamine (24 g, 237 mmol, 2.1 equiv) in THF (400 mL) was added *n*-BuLi (108 mL, 237 mmol, 2.1 equiv, 2.2 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −10 °C for another 30 min. Then 2-methyl-3,4,5,6-tetrahydropyridine **13** (n = 2) (14.3 g, 147 mmol, 1.3 equiv) solution in THF (20 mL) was added dropwise to the mixture at −10 °C. After the mixture was stirred for 40 min at the same temperature, lactim thioether **26** (m = 0) (13 g, 112.8 mmol) solution in THF (20 mL) was added to the mixture dropwise at −10 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (100 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, pentane (200 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by vacuum distillation (58 °C, 46 mTorr) to afford compound **27-1** (16 g, 86%) as an oil: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 9.08 (s, br, 1H), 4.49 (s, 1H), 3.78 (t, 2H, J = 7.1 Hz), 3.27 (t, 2H, J = 6.0 Hz), 2.46 (t, 2H, J = 7.9 Hz), 2.34 (t, 2H, J = 6.7 Hz), 1.73 (m, 2H), 1.67 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 173.9, 156.1, 87.0, 60.2, 42.0, 38.0, 29.6, 23.9, 22.8, 21.5; HRMS (EI) *m/z* calcd for $C_{10}H_{16}N_2$ 164.1313, found 164.1309.

2-(Pyrrolidin-2-ylidenemethyl)-1-pyrrolidine (27-2) from the Reaction of 2-Methyl-1-pyrroline 13 ($n = 1$) with 26 ($m = 0$). To a solution of diisopropylamine (11.1 g, 109.7 mmol, 2.1 equiv) in THF (200 mL) was added *n*-BuLi (38 mL, 109.7 mmol, 2.1 equiv, 2.89 M in hexane) dropwise at −78 °C. The mixture was stirred at −78 °C for 30 min and then stirred at −10 °C for another 30 min. Then 2-methyl-1-pyrroline **13** ($n = 1$) (5.65 g, 67.93 mmol, 1.3 equiv) solution in THF (10 mL) was added dropwise to the mixture at −10 °C. After the mixture was stirred for 40 min at the same temperature, lactim thioether **26** ($m = 0$) (6 g, 52.25 mmol) solution in THF (10 mL) was added to the mixture dropwise at −10 °C. The resultant mixture was stirred overnight as the temperature was allowed to gradually rise to room temperature. The reaction mixture was concentrated under reduced pressure, and then MeOH (50 mL) was slowly added to the residue. After removal of the solvent under reduced pressure, pentane (100 mL) was added to the residue. The mixture was filtered, and then the filtrate was concentrated under reduced pressure, followed by vacuum distillation (65 °C, 110 mTorr) to afford compound **27-2** (6.2 g, 79%) as an oil. The oil was solidified to give a white crystal: mp 32−33 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 9.09 (s, br, 1H), 4.65 (s, 1H), 3.63 (t, 2H, $J = 6.9$ Hz), 2.51 (t, 2H, $J = 7.9$ Hz), 1.85 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 167.2, 81.9, 53.7, 35.0, 23.4; HRMS (EI) *m/z* calcd for $C_9H_{14}N_2$ 150.1157, found 150.1163.

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Supporting Information Available: Crystallographic information files (CIFs) of compounds **18** and **23** and characterization data including ^{1}H and ^{13}C NMR spectra for compounds **3-1**, **8a** [$-(R^1R^2)- = -(CH_2)_3-$, R^3 = Me], **8b** [$-(R^1R^2)- = -(CH_2)_4-$, R^3 = Me], **12a-1**, **12b-1**, **12b-2**, **12b-3**, **12b-4**, **12b-5, 12b-6, 18**, **23**, **27−1**, and **27−2** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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