A Novel Approach for Mannich-Type Bases Having a Terminal Olefin: Zinc Triflate and Water-Promoted Cyclization/C−N Bond Cleavage Process

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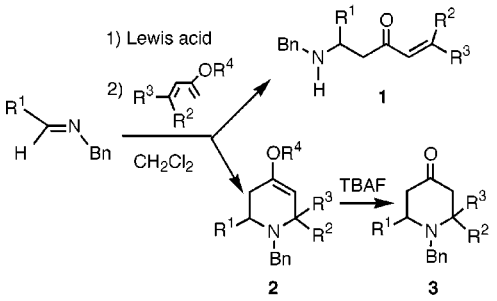
β-Aminoketones are important building blocks for the synthesis of biologically attractive compounds.[1] One of the most direct and powerful synthetic strategies for construction of them is the Mannich[1,2] or a very recently developed Mannich-type reaction[3] which has broadened the potential usefulness of this widely known nucleophilic addition to aldimines.[4] However, general preparation of pharmaceutically attractive β-aminoketones having a terminal olefin **1**[5] by the reaction of aldimines with dienes bearing an enol ether moiety has not been reported yet because the [4 + 2] type cycloaddition generally proceeds to give cycloadducts **2** (Scheme 1).[6,7] While the isolation of **1** has been reported, substituents of aldimines or dienes must be chosen carefully,[8,9] or a mixture of **1** and cycloadducts is obtained.[10] In addition, other synthetic examples are complicated or not general, namely, (1) six steps from diethyl acetonylacetamidomalonate,[5a] (2) palladium(II)-assisted coupling process under severe temperature-controlled conditions,[11] (3) hydrolysis of 6-vinyl-5,6-dihydro-4*H*-1,3-oxazine which was formed by Diels−Alder reaction of 2-methoxy-1,3-butadiene with chloral acetylimine as a heterodiene.[12] Here we report the first efficient Lewis acid system for general preparation of the Mannich-type bases having a terminal olefin **1** which cannot be prepared by widely known Mannich or Mannich-type reactions. In the reaction of aldimines with 2-silyloxy-1,3-butadienes described herein, zinc triflate and water act as a Lewis acid for cycloaddition, to cleave the C−N bond of cycloadduct **2** and to protect from unnecessary and facile intramolecular Michael addition in situ.

Scheme 1



1a-3a : R^1 = Ph, R^2 = H, R^3 = Ph, R^4 = TMS

In our initial studies, we examined the reaction of benzaldimine with 4-phenyl-2-trimethylsilyloxy-1,3-butadiene (1.2 equiv to aldimine) in the presence of Lewis acid in dichloromethane (Scheme 1).[13] The reaction without water gave only cycloadduct **2a**[14] even when various Lewis acids were used (Table 1, entries 1−8). We also tried to trap the Mannich-type base **1a** by the reaction in the presence of TMSOTf at −20 °C for 30 min, but only the mixture of cycloadduct **2a** and the aldimine was detected in the ^{1}H NMR spectrum of the crude products (entry 3). Fortunately, the use of water (2 equiv)[15] and zinc triflate (2 equiv) as a Lewis acid afforded the corresponding Mannich-type base **1a** in 84% yield after

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(13) The reaction without water was carried out under similar conditions as described in Experimental Section.

(14) Though the cycloadduct **2** was detected in the ^{1}H NMR spectrum of the crude products, **2** was converted to piperidone **3** to confirm the isolated yield of the cycloadduct as shown in Scheme 1 because purification of **2** by column chromatography gave the mixture of **2** and desilylated product **3**. The desilylation of **2** was carried out with 1 equiv of TBAF in THF at room temperature for 1 h (similar procedure as we described before, see ref 7c). **3a** was completely characterized in ref 7d.

(15) The use of 1.2−3 equiv of water did not largely affect the yields.

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Table 1. Reaction of Aldimine with Silyloxydiene in CH_2Cl_2 in the Presence of Lewis Acid

entry	Lewis acid	conditions	yield of **1a** (%)[a]	yield of **3a** (%)[a,b]
1	TMSOTf[c]	rt, 1 h	0	97
2	TMSOTf[c]	0 °C 1 h	0	95
3	TMSOTf[c]	−20 °C 30 min	0	20
4	$TiCl_4$[c]	0 °C 1 h	0	79
5	$Sn(OTf)_2$[c]	rt, 1 h	0	59
6	Et_2AlCl[c]	rt, 1 h	0	64
7	$BF_3{\cdot}Et_2O$[c]	rt, 4 h	0	95
8	$Zn(OTf)_2$[c]	rt, 3 h	0	80
9	$Zn(OTf)_2$[d] + H_2O[d]	rt, 5 h	84	0
10	$ZnCl_2$[d] + H_2O[d]	rt, 5 h	30	0
11	$Sc(OTf)_3$[d] + H_2O[d]	rt, 5 h	80	0

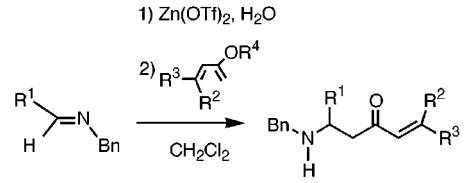
[a] Isolated yield after chromatography. [b] Yields after conversion of **2a** to **3a** by with TBAF, see ref 14. Detection of acyclic produce **1a** by ^{1}H NMR was done before desilylation procedure. [c] 1 equiv to aldimine. [d] 2 equiv to aldimine.

5 h at room temperature (entry 9). Surprisingly, no cyclic products (**2a** and **3a**) were detected by 500 MHz ^{1}H NMR. Large amounts of water (>100 equiv to the aldimine) in the reaction decomposed the product presumably due to the instability of **1a** having *sec*-amine and α,β-unsaturated ketone moieties. The use of $Sc(OTf)_3$ and water also afforded **1a** in high yield (entry 11), but attempts to use other Lewis acids such as $Ti(O\textit{i}\text{-}Pr)_4$ or TMSOTf with water gave only decomposed products. The reaction with $BF_3{\cdot}Et_2O$ and water gave both desilylated product **3a** and Mannich-type base **1a** in a ratio of 16:84 by ^{1}H NMR analysis. We also tried to use a catalytic amount of zinc triflate or $Sc(OTf)_3$ (0.1 equiv) with water (0.1 equiv), but cycloadduct **2a** and a small amount of **1a** were detected by ^{1}H NMR. The reaction of pure **1a** with 1 equiv of TMSOTf in dichloromethane at room temperature completely gave piperidone **3a** (see Experimental Section); however, intramolecular Michael addition of **1a** with zinc triflate and water did not occur in situ probably because the acidity of the solution or coordination of nitrogen atom of acyclic product **1a** to the zinc reagent might protect from further Michael addition.

Various aldimines underwent the reaction under similar conditions using zinc triflate and water as in Scheme 1 (Table 2). Substituted benzaldimines bearing an electron-donating (R^1 = *o*-methoxyphenyl in entry 1) or electron-withdrawing (R^1 = *o*-chlorophenyl, *p*-chlorophenyl in entries 5 and 6) substituent on the aromatic ring were converted to the corresponding Mannich-type bases **1** in high yields. To our surprise, the aldimine bearing an alkyl substituent at α-position also reacted with the silyloxydiene under the similar conditions (entry 8). The use of *tert*-butyldimethylsilyloxybutadiene also gave the Mannich-type base after 12h (entry 9). Attempts to react with 2-silyloxy-1,3-butadiene gave only piperidone; however, good to excellent yields of the Mannich-type bases were obtained from the reaction with 4,4-dimethyl-2-trimethylsilyloxy-1,3-butadiene under similar conditions (entries 10−14). All reactions proceed under extremely mild reaction conditions!

Additional experiments were done to gain more mechanistic information of this unusual reaction. Interestingly, when the reaction of benzaldimine with the 4-phenyl-2-silyloxy-1,3-butadiene in the presence of zinc triflate and water was quenched at 1 h, both cycloadduct **2a** and the Mannich-type base **1a** were detected in a ratio of 25:75 by ^{1}H NMR spectrum of the crude products. Isolated cycloadduct **2a**, which was prepared from cycloaddition

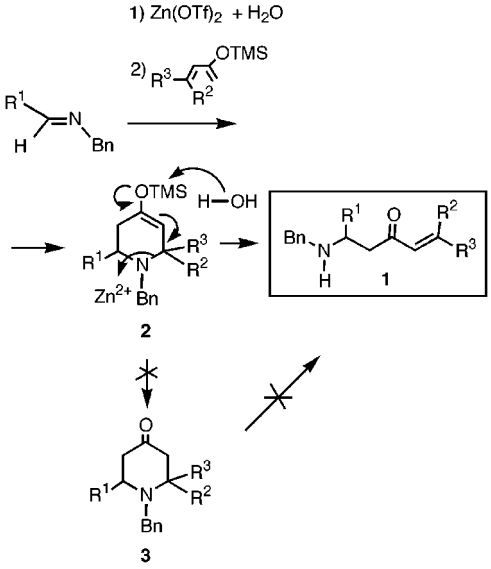
Table 2. Reaction of Aldimines with Silyloxydienes in CH_2Cl_2 in the Presence of Zinc Triflate and Water



entry	R^1	R^2	R^3	R^4	conditions	product	yield (%)[a]
1	*o*-MeOPh	H	Ph	TMS	rt, 5 h	**1b**	92
2	*o*-tolyl	H	Ph	TMS	rt, 5 h	**1c**	80
3	*m*-tolyl	H	Ph	TMS	rt, 5 h	**1d**	90
4	*p*-tolyl	H	Ph	TMS	rt, 5 h	**1e**	85
5	*o*-ClPh	H	Ph	TMS	rt, 5 h	**1f**	93
6	*p*-ClPh	H	Ph	TMS	rt, 5 h	**1g**	71
7	2-furyl	H	Ph	TMS	rt, 5 h	**1h**	85
8	*i*-Pr	H	Ph	TMS	rt, 5 h	**1l**	78
9	Ph	H	Ph	TMS	rt, 12 h	**1a**	74
10	Ph	Me	Me	TMS	rt, 5 h	**1j**	76
11	*o*-MeOPh	Me	Me	TMS	rt, 5 h	**1k**	63
12	*p*-ClPh	Me	Me	TMS	rt, 5 h	**1l**	85
13	2-furyl	Me	Me	TMS	rt, 5 h	**1m**	41
14	*i*-Pr	Me	Me	TMS	rt, 5 h	**1n**	53

[a] Isolated yield after chromatography.

Scheme 2



of aldimine with silyloxydiene in the presence of TMSOTf,[13] was also converted to **1a** in the presence of zinc triflate and water (see Experimental Section), indicating that the Mannich-type base **1a** was formed by way of cycloadduct **2a** (Scheme 2). Thus, the novel Lewis acid system has two effective functions in situ: (1) activation of aldimines as a Lewis acid for cycloaddition; (2) effective carbon−nitrogen cleavage and protection from further Michael addition. Pure piperidone **3a** (completely characterized in ref 7d), which was obtained by reaction of **2a** with TBAF, was not converted to the Mannich-type base **1a** with zinc triflate and water (see Experimental Section). We also tried C−N cleavage of the cycloadduct **2a** with aqueous HCl (10%), CF_3SO_3H (2 equiv to aldimine), or aqueous NaOH (10%) in dichloromethane at room temperature for 30 min, but piperidone **3a**, the mixture of **1a**, **2a**, and **3a**, or decomposed products were obtained, respectively. The carbon−nitrogen cleavage of cycloadduct **2** in this reaction system was highly effective compared to that by these methods.

In summary, we have developed the novel Lewis acid system for synthesis of the Mannich-type bases having a terminal olefin. On the basis of the proposed mechanism, carbon−nitrogen bond cleavage containing a tertiary or quaternary carbon was achieved efficiently in the reaction. We are currently investigating the application of the Lewis acid system, and the results will be reported shortly.

Experimental Section

^{1}H NMR (at 400 or 500 MHz) spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard. Dichloromethane was purified with standard reagents[16] and distilled from CaH_2 before use.

Typical Procedure for Preparation of Mannich-Type Bases (1). To a stirred solution of zinc triflate (0.36 g, 1 mmol) and water (0.018 mL, 1 mmol) in dichloromethane (3 mL) were added 0.5 mmol of aldimine and 0.6 mmol of silyloxydiene at room temperature. The solution was stirred at room temperature for 5 h, quenched with aqueous $NaHCO_3$, and extracted with dichloromethane. The organic layers were dried over $MgSO_4$, and the solvent was evaporated. The crude product was purified by short flash column chromatography (Merck silica gel 60, hexane/CH_3CO_2Et = 3/1). If necessary, further purification was carried out by HPLC (JAI LC908, 1,2-dichloroethane). The chromatographic purification should be performed as quickly as possible because cyclization or decomposition of **1** might occur on silica gel in some cases. The Mannich-type bases **1** are not stable at room temperature for a long period (>8 h) after aqueous $NaHCO_3$ workup but can be stored below −15 °C with slightly decomposition.

***N*-Benzyl-4-trimethylsilyloxy-2,6-diphenyl-3,4-didehydropiperidine (2a).** 2,6-Trans isomer (purified by recrystallization from dichloromethane/*n*-hexane): colorless crystals; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.30 (s, 9 H), 2.48 (dd, 1 H, J = 16.9, 5.3 Hz), 2.54 (dd, 1 H, J = 16.9, 8.7 Hz), 3.37 (d, 1 H, J = 13.5 Hz), 3.47 (d, 1 H, J = 13.5 Hz), 4.08 (dd, 1 H, J = 8.7, 5.3 Hz), 4.27 (s, 1 H), 5.11 (s, 1 H), 7.19−7.42 (m, 15H). Since this product was not stable at room temperature for a long period or under chromatographic conditions (see ref 14), conversion with TBAF was carried out to give the corresponding piperidone **3a** which was characterized as described before.[7d] 2,6-Cis isomer (colorless oil) was not separated from the crude mixture, but its NMR spectrum exhibits characteristic singlet at 4.70 ppm.

5-Benzylamino-1,5-diphenyl-1-penten-3-one (1a): starting from corresponding imine (0.09 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 144 mg (84% yield) of **1a**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (dd, 1H, J = 16.6, 4.6 Hz), 3.08 (dd, 1H, J = 16.6, 8.8 Hz), 3.57 (d, 1H, J = 13.2 Hz), 3.65 (d, 1H, J = 13.2 Hz), 4.26 (dd, 1H, J = 8.8, 4.6 Hz), 6.65 (d, 1H, J = 16.1 Hz), 7.21−7.51 (m, 16H). HRMS-FAB (M^+): calcd for $C_{24}H_{23}NO$ 341.1780, found 341.1773.

5-Benzylamino-5-(2-methoxyphenyl)-1-phenyl-1-penten-3-one (1b): starting from corresponding imine (0.10 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 171 mg (92% yield) of **1b**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.93 (dd, 1H, J = 16.9, 4.2 Hz), 3.01 (dd, 1H, J = 16.9, 8.8 Hz), 3.56 (d, 1H, J = 13.2 Hz), 3.66 (d, 1H, J = 13.2 Hz), 4.54 (dd, 1H, J = 8.8, 4.2 Hz), 6.66 (d, 1H, J = 17.6 Hz), 7.16−7.68 (m, 15H). HRMS-FAB (M^+): calcd for $C_{25}H_{25}NO_2$ 371.1885, found 371.1898.

5-Benzylamino-5-(2-methylphenyl)-1-phenyl-1-penten-3-one (1c): starting from corresponding imine (0.10 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 142 mg (80% yield) of **1c**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.84 (dd, 1H, J = 16.6, 3.9 Hz), 2.88 (dd, 1H, J = 16.6, 8.8 Hz), 3.49 (d, 1H, J = 13.2 Hz), 3.60 (d, 1H, J = 13.2 Hz), 4.47 (dd, 1H, J = 8.8, 3.9 Hz), 6.59 (d, 1H, J = 16.4 Hz), 7.09−7.59 (m, 15H). HRMS-FAB $(M + H)^+$: calcd for $C_{25}H_{26}NO$ 356.2014, found 356.2007.

5-Benzylamino-5-(3-methylphenyl)-1-phenyl-1-penten-3-one (1d): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 159 mg (90% yield) of **1d**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.99 (dd, 1H, J = 16.9, 4.4 Hz), 3.08 (dd, 1H, J = 16.9, 9.0 Hz), 3.57 (d, 1H, J = 13.2 Hz), 3.66 (d, 1H, J = 13.2 Hz), 4.22 (dd, 1H, J = 9.0, 4.4 Hz), 6.66 (d, 1H, J = 16.1 Hz), 7.06−7.51 (m, 15H). HRMS-FAB $(M + H)^+$: calcd for $C_{25}H_{26}NO$ 356.2014, found 356.2015.

5-Benzylamino-5-(4-methylphenyl)-1-phenyl-1-penten-3-one (1e): starting from corresponding imine (0.10 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 151 mg (85% yield) of **1e**: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.87 (dd, 1H, J = 16.4, 4.4 Hz), 2.95 (dd, 1H, J = 16.4, 8.7 Hz), 3.46 (d, 1H, J = 13.2 Hz), 3.55 (d, 1H, J = 13.2 Hz), 4.12 (dd, 1H, J = 8.7, 4.4 Hz), 6.54 (d, 1H, J = 16.2 Hz), 7.14−7.50 (m, 15H). HRMS-FAB $(M + H)^+$: calcd for $C_{25}H_{26}NO$ 356.2014, found 356.2012.

5-Benzylamino-5-(2-chlorophenyl)-1-phenyl-1-penten-3-one (1f): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 174 mg (93% yield) of **1f**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (dd, 1H, J = 16.4, 9.3 Hz), 3.11 (dd, 1H, J = 16.4, 3.7 Hz), 3.59 (d, 1H, J = 12.9 Hz), 3.65 (d, 1H, J = 12.9 Hz), 4.73 (dd, 1H, J = 9.3, 3.7 Hz), 6.69 (d, 1H, J = 16.1 Hz), 7.21−7.74 (m, 15H). HRMS-FAB $(M + H)^+$: calcd for $C_{24}H_{23}NOCl$ 376.1468, found 376.1455.

5-Benzylamino-5-(4-chlorophenyl)-1-phenyl-1-penten-3-one (1g): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 133 mg (71% yield) of **1g**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 (dd, 1H, J = 16.6, 4.4 Hz), 3.04 (dd, 1H, J = 16.6, 8.5 Hz), 3.54 (d, 1H, J = 13.2 Hz), 3.62 (d, 1H, J = 13.2 Hz), 4.23 (dd, 1H, J = 8.5, 4.4 Hz), 6.64 (d, 1H, J = 16.1 Hz), 7.12−7.52 (m, 15H). HRMS-FAB (M^+): calcd for $C_{25}H_{22}NOCl$ 375.1390, found 375.1374.

5-Benzylamino-5-(2-furyl)-1-phenyl-1-penten-3-one (1h): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 141 mg (85% yield) of **1h**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (dd, 1H, J = 16.4, 5.6 Hz), 2.98 (dd, 1H, J = 16.4, 7.8 Hz), 3.42 (d, 1H, J = 13.2 Hz), 3.55 (d, 1H, J = 13.2 Hz), 4.13 (dd, 1H, J = 7.8, 5.6 Hz), 6.02−6.03 (m, 1H), 6.11−6.13 (m, 1H), 6.47 (d, 1H, J = 16.4 Hz), 7.01−7.41 (m, 12H). HRMS-FAB $(M + H)^+$: calcd for $C_{22}H_{22}NO_2$ 332.1650, found 332.1659.

5-Benzylamino-6-methyl-1-phenyl-1-hepten-3-one (1i): starting from corresponding imine (0.11 mL, 0.5 mmol) with diene (0.13 mL, 0.6 mmol) to afford 120 mg (78% yield) of **1i**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, 6H, J = 6.8 Hz), 1.87−1.92 (m, 1H), 2.56−2.68 (m, 2H), 3.00−3.03 (m, 1H), 3.70 (d, 1H, J = 12.7 Hz), 3.75 (d, 1H, J = 12.7 Hz), 6.69 (d, 1H, J = 16.1 Hz), 7.14−7.51 (m, 11H). HRMS-FAB $(M + H)^+$: calcd for $C_{21}H_{26}NO$ 308.2014, found 308.2006.

6-Benzylamino-2-methyl-6-phenyl-2-hexen-4-one (1j): starting from corresponding imine (0.09 mL, 0.5 mmol) with diene (0.11 mL, 0.6 mmol) to afford 112 mg (76% yield) of **1j**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (s, 3H), 2.39 (s, 3H), 2.72 (dd, 1H, J = 16.6, 4.4 Hz), 2.82 (dd, 1H, J = 16.6, 8.8 Hz), 3.54 (d, 1H, J = 13.2 Hz), 3.61 (d, 1H, J = 13.2 Hz), 4.17 (dd, 1H, J = 8.8, 4.4 Hz), 5.97 (s, 1H), 7.22−7.59 (m, 10H). HRMS-FAB $(M + H)^+$: calcd for $C_{20}H_{24}NO$ 294.1858, found 294.1857.

6-Benzylamino-6-(2-methoxyphenyl)-2-methyl-2-hexen-4-one (1k): starting from corresponding imine (0.10 mL, 0.5 mmol) with diene (0.11 mL, 0.6 mmol) to afford 101 mg (63% yield) of **1k**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (s, 3H), 2.12 (s, 3H), 2.82−2.88 (m, 2H), 3.57 (d, 1H, J = 13.2 Hz), 3.66 (d, 1H, J = 13.2 Hz), 3.82 (s, 3H), 4.40−4.50 (m, 1H), 6.02 (s, 1H), 7.22−7.47 (m, 9H). HRMS-FAB $(M + H)^+$: calcd for $C_{21}H_{26}NO_2$ 324.1963, found 324.1978.

6-Benzylamino-6-(4-chlorophenyl)-2-methyl-2-hexen-4-one (1l): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.11 mL, 0.6 mmol) to afford 140 mg (85% yield) of **1l**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (s, 3H), 2.12 (s, 3H), 2.68 (dd, 1H, J = 16.6, 4.3 Hz), 2.78 (dd, 1H, J = 16.6, 8.8 Hz), 3.52 (d, 1H, J = 13.2 Hz), 3.58 (d, 1H, J = 13.2 Hz), 4.14 (dd, 1H, J = 8.8, 4.3 Hz), 5.96 (s, 1H), 7.20−7.34 (m, 9H). HRMS-FAB $(M + H)^+$: calcd for $C_{20}H_{23}NOCl$ 328.1468, found 328.1457.

(16) Perrin, D. D.; Armarego, W. L. *Purification of Laboratory Chemicals*; Pergamon: New York, 1988.

6-Benzylamino-6-(2-furyl)-2-methyl-2-hexen-4-one (1m): starting from corresponding imine (0.08 mL, 0.5 mmol) with diene (0.11 mL, 0.6 mmol) to afford 58 mg (41% yield) of **1m** (HPLC purification was carried out): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86 (s, 3H), 2.13 (s, 3H), 2.85 (dd, 1H, J = 16.6, 5.6 Hz), 2.93 (dd, 1H, J = 16.6, 8.1 Hz), 3.60 (d, 1H, J = 12.9 Hz), 3.72 (d, 1H, J = 12.9 Hz), 4.25 (dd, 1H, J = 8.1, 5.6 Hz), 6.00−6.01 (m, 1H), 6.19 (d, 1H, J = 3.2 Hz), 6.32 (dd, 1H, J = 3.2, 1.7 Hz), 7.21−7.40 (m, 6H). HRMS-FAB (M^+): calcd for $C_{18}H_{21}NO_2$ 283.1572, found 283.1581.

6-Benzylamino-2,7-dimethyl-2-octen-4-one (1n): starting from corresponding imine (0.11 mL, 0.5 mmol) with diene (0.11 mL, 0.6 mmol) to afford 69 mg (53% yield) of **1n** (HPLC purification was carried out): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, 6H, J = 6.8 Hz), 1.88 (s, 3H), 1.90−1.95 (m, 1H), 2.14 (s, 3H), 2.45 (dd, 1H, J = 16.1, 8.1 Hz), 2.53 (dd, 1H, J = 16.1, 3.2 Hz), 2.97−3.01 (m, 1H), 3.75 (d, 1H, J = 13.2 Hz), 3.79 (d, 1H, J = 13.2 Hz), 6.08 (s, 1H), 7.21−7.33 (m, 5H). HRMS-FAB ($M + H)^+$: calcd for $C_{17}H_{26}NO$ 260.2014, found 260.2018.

Reaction of 1a in the Presence of TMSOTf. To a stirred solution of **1a** (86 mg, 0.25 mmol) in dichloromethane (2 mL) was added 0.25 mmol of trimethylsilyl triflate at room temperature. The solution was stirred at room temperature for 0.5 h, quenched with aqueous $NaHCO_3$, and extracted with dichloromethane. The organic layers were dried over $MgSO_4$, and the solvent was evaporated. The crude product was purified by flash column chromatography (Merck silica gel 60, hexane/CH_3CO_2-Et = 2/1) to yield 65 mg (76% isolated yield) of piperidone **3a**.

Reaction of 2a in the Presence of Zinc Triflate and Water. The solution of **2a** (61 mg, 0.15 mmol), zinc triflate (0.11 g, 0.3 mmol), and water (0.005 mL, 0.3 mmol) in dichloromethane (2 mL) was stirred at room temperature for 3 h. The mixture was quenched with aqueous $NaHCO_3$ and extracted with dichloromethane. The organic layers were dried over $MgSO_4$, and the solvent was evaporated. The crude product was purified by short flash column chromatography (Merck silica gel 60, hexane/CH_3CO_2Et = 3/1) to yield 41 mg (80% isolated yield) of **1a**.

Reaction of 3a in the Presence of Zinc Triflate and Water. The solution of **3a** (90 mg, 0.26 mmol), zinc triflate (0.28 g, 0.78 mmol), and water (0.014 mL, 0.78 mmol) in dichloromethane (4 mL) was stirred at room temperature for 5 h. The mixture was quenched with aqueous $NaHCO_3$ and extracted with dichloromethane. The organic layers were dried over $MgSO_4$, and the solvent was evaporated. Only the piperidone **3a** was observed by 500 MHz ^{1}H NMR.

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Supporting Information Available: ^{1}H NMR spectra of **2a**, **3a**, and **1a**−**n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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