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Comparative Reactivity of Different Types of Stable Cyclic and Acyclic Mono- and Diamino Carbenes with Simple Organic Substrates

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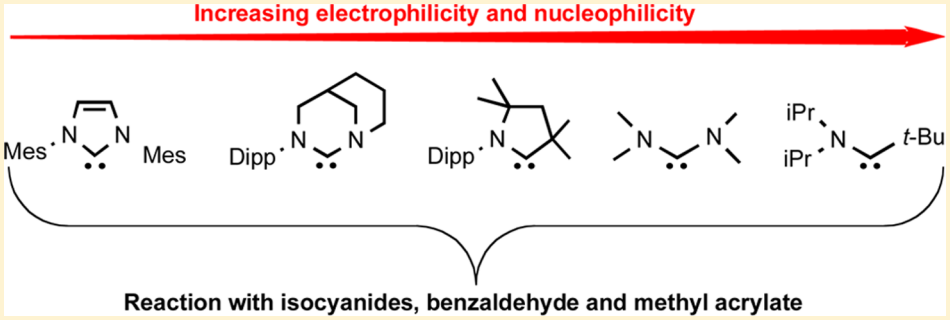
Supporting Information



ABSTRACT: A series of stable carbenes, featuring a broad range of electronic properties, were reacted with simple organic substrates. The *N*,*N*-dimesityl imidazolylidene (NHC) does not react with isocyanides, whereas anti-Bredt di(amino)carbene (pyr-NHC), cyclic (alkyl)(amino)carbene (CAAC), acyclic di(amino)carbene (ADAC), and acyclic (alkyl)(amino)carbene (AAAC) give rise to the corresponding ketenimines. NHCs are known to promote the benzoin condensation, and we found that the CAAC, pyr-NHC, and ADAC react with benzaldehyde to give the ketone tautomer of the Breslow intermediate, whereas the AAAC first gives the corresponding epoxide and ultimately the Breslow intermediate, which can be isolated. Addition of excess benzaldehyde to the latter does not lead to benzoin but to a stable 1,3-dioxolane. Depending on the electronic properties of carbenes, different products are also obtained with methyl acrylate as a substrate. The critical role of the carbene electrophilicity on the outcome of reactions is discussed.

INTRODUCTION

Closed-shell singlet carbenes possess a lone pair of electrons and an accessible vacant orbital, making them both Lewis acids and bases, which confer their extreme reactivity.[1] Since the discovery of the first stable singlet carbenes in the late 1980s and early 1990s,[2] it has been well-established that this reactivity can be tamed by introducing π-donor substituents, which can make up for the electron deficiency of the carbene center, as illustrated by carbenes **a**−**e** (Figure 1).[3] The different substitution and structural patterns result in carbenes with different electronic properties. Placing one of the nitrogen atoms of a classical N-heterocyclic carbene (NHC)[4] in the bridgehead position of a bicyclic scaffold, as shown in the anti-Bredt NHC **b**,[5] precludes its π-donation thereby enhancing the π-accepting properties of the carbene center. This structural modification has no significant effect on the nucleophilicity of **b**, compared to classical NHCs, since this property is linked to the σ-effect of the carbene substituents. In contrast, the replacement of a σ-electron-withdrawing and π-donating amino substituent of imidazol-2-ylidene **a**, by a σ-electron-donating and non-π-donating alkyl group, results in the more electrophilic, but also more nucleophilic, cyclic (alkyl)(amino)carbene (CAAC) **c**.[6] Acyclic carbenes **d**[7] and **e**[8] are more nucleophilic than their cyclic counterparts **a** and **c** since the wider carbene bond angle decreases the s-character of the lone pair;[9] concomitantly, they are more electrophilic due to the free rotation of the amino group. Several spectroscopic and electrochemical data confirmed that the electrophilicity[10] and nucleophilicity[11,12] of carbenes **a**−**e** increase in the order **a** < **b** < **c** < **d** < **e**. The influence of the electronic properties of these carbenes on their ligand properties and on the catalytic activity of the corresponding transition metal complexes has been extensively studied.[10−13] In marked contrast, no comparative studies on the reactivity of different stable amino carbenes with simple organic substrates have been reported.[14] Herein we discuss the outcome of the reactions of carbenes **a**−**e** with alkyl isocyanides, benzaldehyde, and methyl acrylate.

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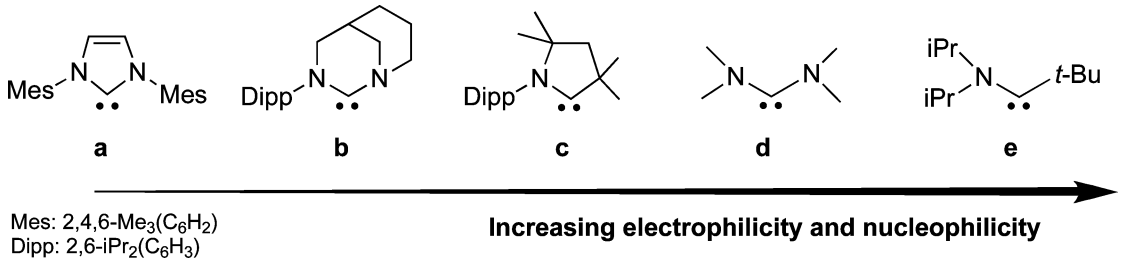

Figure 1. Carbenes **a**–**e** ranked according to their electrophilicity and nucleophilicity.

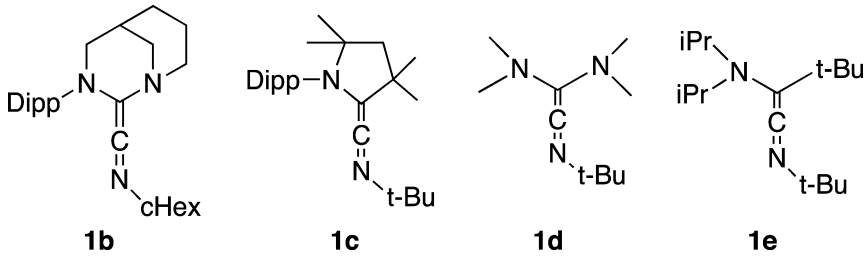

Figure 2. Adducts of carbenes **b**–**e** with isocyanides (no reaction observed with NHC **a**).

Table 1. Formation and Structure of Model Ketenimines 1a′–e′

Carbene	Ketenimine[a]	ΔH^{298K} (kcal.mol^{-1})	ΔG^{298K} (kcal.mol^{-1})	C1-C2 (pm)	C1-C2-N1 (°)	HOMO[b]
a'	1a'	-5.1	+5.6	139.8	134.7	
b'	1b'	-28.4	-16.6	132.8	171.6	
c'	1c'	-36.5	-24.7	131.9	175.3	
d'	1d'	-28.9	-17.1	132.7	174.0	
e'	1e'	-42.2	-30.3	132.7	170.0	

[a]B3LYP/6-31g* level of theory. [b]With isovalue at 0.08 su.

RESULTS AND DISCUSSION

Reaction of Carbenes a–e with Isocyanides. It is already known that carbon monoxide does not react with NHC **a**,[15] while it reacts with more electrophilic carbenes such as **b**–**e**.[16,17] However, with the exception of sterically hindered CAACs and carbene **e**, the corresponding ketene was not observed because it reacts further with a second molecule of carbene. Isocyanides and CO are isoelectronic but the former are less π-accepting and more sterically hindered. Consequently, we reasoned that the reaction of isocyanides with carbenes should lead to stable ketenimines.[18] Not surprisingly, *tert*-butyl or *c*-hexyl isocyanide does not react with NHC **a**, but cleanly add to carbene **b**–**e**, leading to the expected ketenimines **1b**–**e** (Figure 2). The main spectroscopic features of **1b**–**e** are the very low-field ^{13}C NMR chemical shift of the central ketenimine carbon (δ 194–209 ppm) and the intense infrared absorption at 1980–2000 cm^{-1} (C═N stretching vibration).

As shown in Table 1, DFT calculations[19] are in line with these experimental results. The reaction of methyl isocyanide with the model NHC **a**′ was found to be exothermic by only −5.1 kcal·mol^{-1}, and due to the entropic cost, the process is predicted to be endergonic by +5.6 kcal·mol^{-1} at 298 K. In

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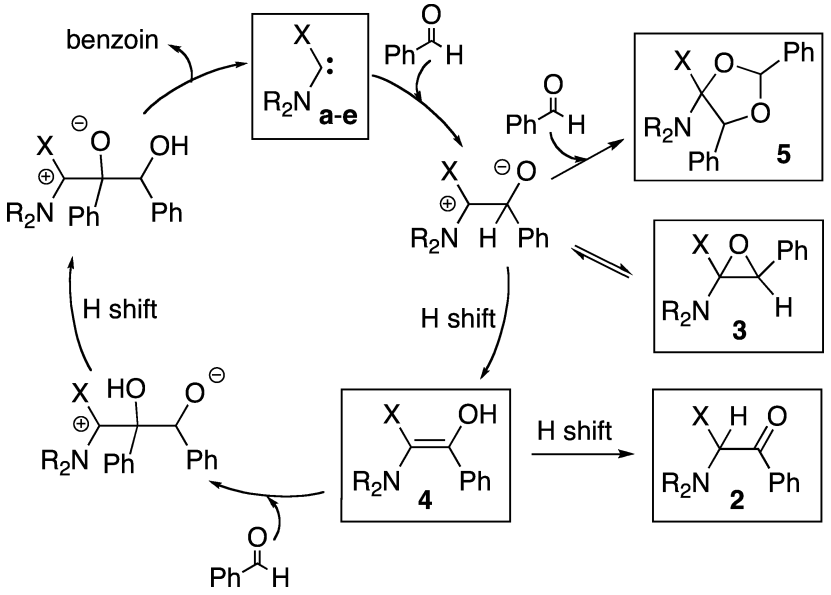
Scheme 1. Mechanism for the Catalytic Benzoin Condensation (Carbene a) and Formation of Compounds 2−5 from Carbenes b−e



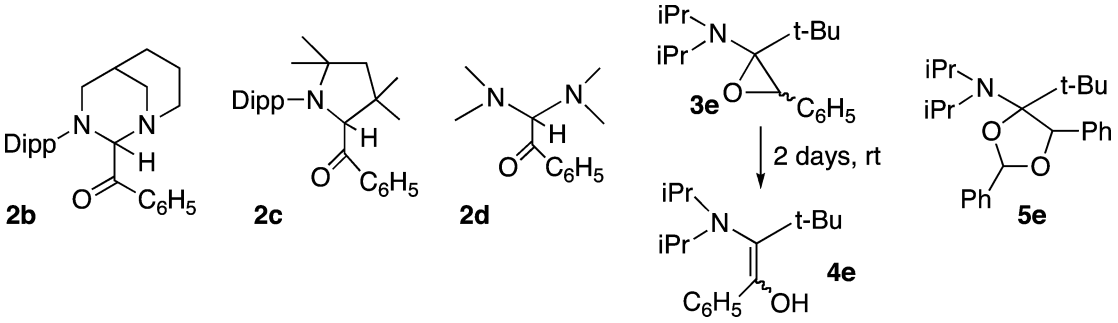


Figure 3. Products from the reaction of carbenes **b**−**e** with benzaldehyde; NHC **a** is known to catalyze the benzoin condensation.

accordance with previous calculations,[18a] we found that the hypothetical adduct **1a**′ has a pronounced bent geometry (C1−C2−N1: 134.7°) with a long C1−C2 bond (140 pm). The HOMO features a C2-centered sp^2-hybridized orbital with a negligible coefficient on C1. As a result, **1a**′ is better described as a zwitterionic compound, in which the π-system connecting C1 and C2 is highly polarized. In contrast, the additions of the more electrophilic carbenes **b**′−**e**′ are thermodynamically favored, and the ΔG value decreases as the electrophilicity of the carbene increases (ΔG from −16 to −30 kcal·mol^{-1}). Moreover, ketenimines **1b**′−**e**′ have a near-linear geometry (C1−C2−N1 > 170°), with a typical short C1═C2 double bond (131−133 pm). Their HOMO reflects the destabilizing effect of the +M amino group(s), as it is an antibonding combination of the π-system of the C1═C2 double bond with the lone pair orbital of the amino substituent(s). Note that this destabilizing effect is much less important in the case of the ketenimine derived from acyclic carbenes (**d**′, **e**′) compared to the cyclic analogues (**a**′, **c**′) because **1d**′ and **e**′ can adopt conformations that minimize the interaction of the amino lone pair with the π-system of the ketenimine.

Reaction of Carbenes a−e with Benzaldehyde. NHCs such as **a**[20] are well-established organocatalysts for a variety of organic reactions,[21] such as the benzoin condensation. In such a reaction, the initial zwitterionic carbene−aldehyde adducts undergo a proton shift to afford amino enols (Scheme 1). The latter, known as Breslow intermediates,[22] are acyl anion equivalents and react with a second equivalent of aldehyde to yield, after a second proton shift, to the benzoin and regeneration of the carbene. In marked contrast, no evidence for benzoin condensation occurs with carbenes **b**−**e**, even with an excess of benzaldehyde (Figure 3). Instead, carbenes **b**−**d** cleanly react with benzaldehyde to afford ketones **2b**−**d**, which are the tautomers of the Breslow intermediates (77−95% yield). On the other hand, carbene **e** adds to benzaldehyde to yield epoxide **3e** as a mixture of two diastereomers (8:2 ratio; 81% yield). It is a very rare example of an amino-substituted epoxide,[23] and its stability is in line with the superior π-accepting properties of **e** over carbenes **a**−**d**. Although storable as a solid, **3e** undergoes a ring opening and a proton shift, giving rise to enol **4e**, within 2 days in solution at room temperature. Interestingly, when an excess of benzaldehyde was added to carbene **e**, dioxolane **5e** was isolated in 72% yield and characterized by NMR and X-ray crystallography. Thus, in contrast to the benzoin condensation in which a carbon acts as a nucleophile, the formation of **5e** implies the nucleophilic attack of the oxygen to the second molecule of benzaldehyde.

In the case of imidazolylidenes, such as **a**, 1,2,4-triazolylidenes, and thiazolinylidenes, which are active catalysts for the benzoin condensation, the corresponding Breslow intermediates are highly reactive and usually considered as elusive species. These compounds, as well as their keto forms and even

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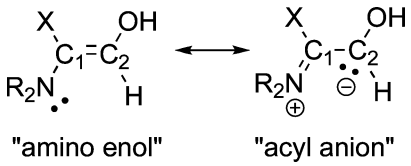
the spirodioxolanes, which are both resting forms of the Breslow intermediate, have only very recently been characterized.[24] The relative robustness of compounds **2b**−**d** and **3e**−**5e**, especially their reluctance to enter into the catalytic cycle of the benzoin condensation, is a consequence of the enhanced π-accepting properties of carbenes **b**−**e** compared to those of **a**. This statement is supported by simple DFT calculations, as shown in Table 2. The HOMO of the Breslow intermediate **4a′** is an antibonding combination of the π-system of the enol and the p orbital of the amino groups. The large and small coefficients on C2 and C1, respectively, clearly illustrate the "acyl anion" character of **4a′**. There is a good inverse correlation between the electrophilicity of the carbene and the nucleophilicity of the corresponding Breslow intermediate. When the electrophilicity of the carbene increases, the polarization of the C1═C2 double bond and the energy of the HOMO decrease (**4a′** > **4b′** > **4c′** ∼ **4d′** > **4e′**).

Table 2. Calculated Structure for Breslow Intermediates Stemming from the Reaction of Carbenes a′−e′ with H_2CO



Carbene	Breslow Intermediate[a]	C1-C2 (pm)	q(C1)[b]	q(C2)[b]	HOMO[c] (Energy in eV)
a'	4a'	136.0	+0.55	-0.12	(-3.65)
b'	4b'	135.1	+0.44	-0.06	(-4.25)
c'	4c'	134.4	+0.33	-0.06	(-4.61)
d'	4d'	134.9	+0.39	-0.03	(-4.64)
e'	4e'	134.7	+0.29	-0.01	(-4.76)

[a]B3LYP/6-31g* level of theory. [b]Mulliken charges. [c]With isovalue at 0.08 su.

Reaction of Carbenes a−e with Methyl Acrylate. In order to complete our study, we investigated the reaction of carbenes **a**−**e** with a Michael acceptor. Keeping in mind that classical NHCs, such as **a**, are known to induce the anionic polymerization of acrylates,[20,25] we performed a dropwise addition of a near-stoichiometric amount of methyl acrylate to a solution of carbene **a** in THF at −78 °C. ^{13}C, ^{1}H NMR, and mass spectrometry indicated the formation of the two isomeric 1:2 carbene−acrylate adducts **6a** and **7a** (Figure 4). Under the same experimental conditions, the reaction of carbenes **b**−**e** afforded compounds **8b**, **7c**, **9d**, and **10e**, **8e**, respectively.

The mechanism of formation of products **6**−**10** is presented in Scheme 2. The first step is always a 1,4-addition of nucleophilic aminocarbenes to methyl acrylate, leading to zwitterionic intermediates **I**. Similar to the reaction with benzaldehyde, the cyclized form **10e** of intermediate **I** was isolated in the case of the most electrophilic carbene (**e**) of the series.[8,26] After a week at room temperature, cyclopropane **10e** isomerizes into enamine **8e**. With the less electrophilic anti-Bredt diaminocarbene **b**, the cyclic form **10** is not observed, the enamine **8b** forms instantaneously. Using the even less electrophilic imidazolylidene **a**, the ene-diamine **8a** is not observed either as it readily reacts with a second equivalent of methyl acrylate to afford **6a**, via intermediate **III**. Note that no reaction occurs when an excess of methyl acrylate was added to **8e**,**b**. In the case of carbenes **a**, **c**, and **d**, the 1,3-zwitterionic intermediates **I** react with a second equivalent of methyl acrylate to form the 1,5-zwitterions **II**. With the more electrophilic carbene **d**, **II** undergoes a ring closure, affording cyclopentane derivative **9d**, whereas with carbenes **a** and **c**, a 1,4-proton shift leads to **7a**,**c**.

CONCLUSION

From this comparative study, it can be concluded that the reactivity of imidazol-2-ylidenes, which are by far the most popular carbenes, is not representative for the whole range of stable carbenes that are available. The reactions observed with very simple organic substrates illustrate the importance of the electrophilicity of stable singlet carbenes, a property that is almost irrelevant in the case of classical NHCs, such imidazol-2-

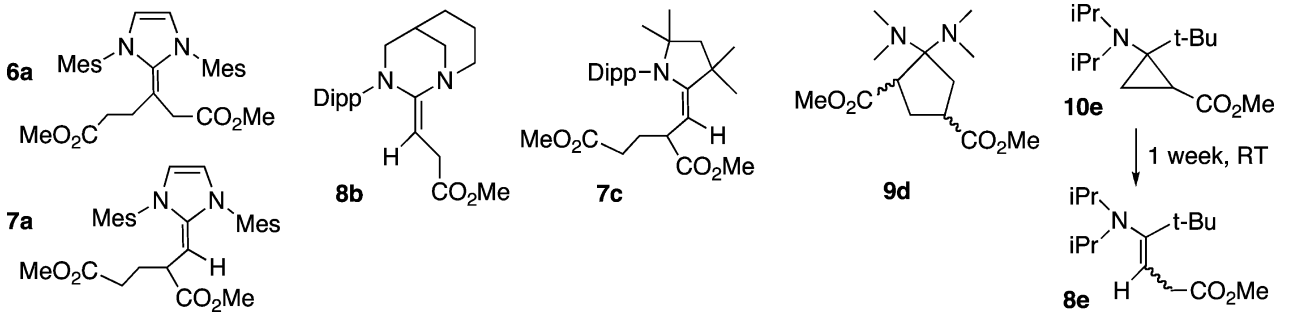


Figure 4. Products from the reaction of carbenes **a**−**e** with methyl acrylate.

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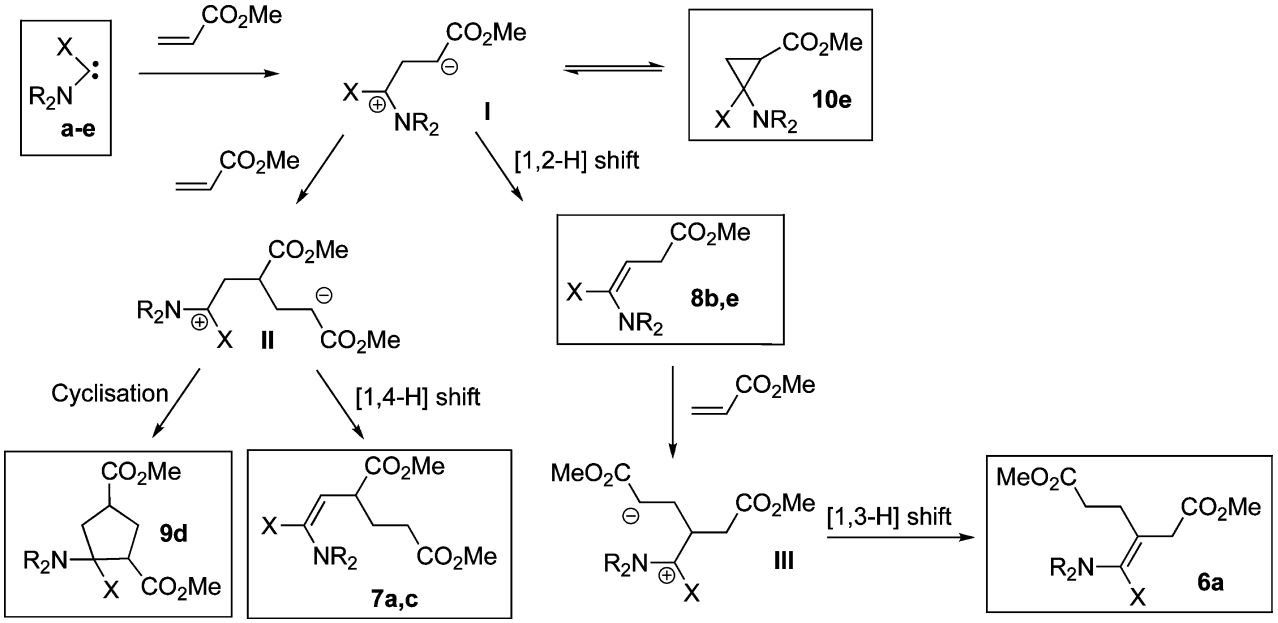
Scheme 2. Mechanism for the Formation of Compounds 6−10



ylidenes and imidazolin-2-ylidenes. These results should encourage the organometallic community not to restrict itself to NHCs but to broaden the range of carbenes they use as ligands. The recent isolation of two-coordinate neutral zinc,[27] manganese,[28] and gold[29] complexes, thanks to electrophilic carbene ligands, is a nice illustration of this statement.

EXPERIMENTAL SECTION

General. All manipulations were performed under an inert atmosphere of argon using standard Schlenk techniques. Dry, oxygen-free solvents were employed. ^{1}H and ^{13}C NMR spectra were recorded on Varian Inova 300, 400, and 500 MHz or Bruker Avance 300 MHz spectrometers. Carbenes **a**−**e** were synthesized according to literature procedures.[5−8,30] Note that carbene **d** was synthesized according to Alder et al. by addition of an excess of TMPLi (1.2 equiv) to the corresponding conjugate acid salt, and **d** was used in situ, with no further purification, because of its rapid dimerization. Commercially available *tert*-butyl isocyanide, benzaldehyde, and methylacrylate were dried over $MgSO_4$ and freshly distilled under inert atmosphere.

Ketenimine 1b. Cyclohexyl isocyanide (52 mg, 0.47 mmol) was added dropwise to a THF solution (2 mL) of **b** (0.46 mmol) at −78 °C. After 1 h, the solution was warmed to room temperature. The volatiles were removed under vacuum, and the product was extracted with hexane. The solvent was evaporated, and **1b** was obtained as a 1:1 mixture of two diastereomers (135 mg; 75% yield). ^{1}H NMR (500 MHz, C_6D_6): δ = 0.94 (m, 1 H), 1.1 (m, 5 H), 1.3−1.4 (m, 12 H), 1.5−1.6 (m, 6 H), 1.8 (br, 3 H), 2.4 (br, 1 H), 2.8 (m, 1 H), 3.0 (m, 1 H), 3.3 (m, 2 H), 3.4 (m, 1 H), 5.6−5.7 (m, 3 H), 3.9 (br, 1 H), 7.1−7.3 (br, 3 H). ^{13}C NMR (125 MHz, C_6D_6): δ = 17.6 (CH_2), 19.3 (CH_2), 21.2 (CH_3), 21.3 (CH_3), 21.6 (CH_3), 21.7 (CH_3), 22.18 (CH_2), 22.2 (CH_2), 22.24 (CH_2), 22.30 (CH_3), 22.34 (CH_3), 22.60 (CH_3), 22.64 (CH_3), 23.33 (CH_2), 23.35 (CH_2), 25.80 (CH), 25.82 (CH), 25.9 (CH), 26.40 (CH), 26.42 (CH), 26.65 (CH), 28.60 (CH_2), 29.2 (CH_2), 30.8 (CH_2), 31.07 (CH_2), 31.1 (CH_2), 48.1 (CH_2), 50.7 (CH_2), 51.4 (CH_2), 52.4 (CH_2), 53.0 (CH_2), 56.6 (CH_2), 63.3 (CH), 64.2 (CH), 111.4 (NCN), 114.9 (NCN), 120.9 (CH_{aro}), 121.7 (CH_{aro}), 121.8 (CH_{aro}), 122.9 (CH_{aro}), 125.2 (CH_{aro}), 125.6 (CH_{aro}), 138.7 (C_{aro}), 139.0 (C_{aro}), 144.7 (C_{aro}), 145.1 (C_{aro}), 147.4 (C_{aro}), 148.1 (C_{aro}), 208.1 (CN), 216.5 (CN) ppm. IR (benzene): $\nu_{(CN)}$ 2013 cm^{-1}. HRMS (FAB) $[M + H]^+$ calcd for $C_{26}H_{40}N_3$, 394.3217; found, 394.3201.

Ketenimine 1c. *t*-Butyl isocyanide (0.08 mL, 0.7 mmol) was added dropwise to a THF solution (5 mL) of **c** (0.5 mmol) at −78 °C. The solution was warmed to room temperature and stirred for 2 h. After evaporation of the solvent and extraction with hexane (10 mL), **1c** was isolated as a yellow oil (0.16 g, 90%). ^{1}H NMR (300 MHz, C_6D_6): δ = 7.21−7.27 (m, 3 H), 3.76 (sept, J = 6.8 Hz, 1 H), 3.43 (sept, J = 6.7 Hz, 1 H), 2.03 (d, J = 12.3 Hz, 1 H), 1.89 (d, J = 12.3 Hz, 1 H), 1.60 (d, J = 6.7 Hz, 3 H), 1.57 (s, 3 H), 1.44 (s, 6 H), 1.40 (d, J = 7.1 Hz, 6 H), 1.35 (d, J = 6.5 Hz, 3 H), 1.19 (s, 9 H), 1.16 (s, 3 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 209.2 (C), 151.7 (C), 150.7 (C), 137.2 (C), 128.1 (CH), 125.1 (CH), 124.3 (CH), 112.5 (C), 64.5 (C), 59.1 (C), 56.7 (CH_2), 40.0 (C), 34.0 (CH), 30.6 (CH_3), 30.4 (CH), 29.3 (CH_3), 29.0 (CH_3), 28.5 (CH_3), 26.8 (CH_3), 25.9 (CH_3), 25.6 (CH_3), 25.2 (CH_3) ppm. IR (CH_2Cl_2): $\nu_{(CN)}$ 1982 cm^{-1}. HRMS (ESI-TOF) $[M + H]^+$ calcd for $C_{25}H_{41}N_2$, 369.2364; found, 369.2373.

Ketenimine 1d. A THF solution (15 mL) of **d** (7.0 mmol) was prepared in situ from the corresponding amidinium salt and lithium 2,2,6,6-tetramethylpiperidine. The solution was stirred at −78 °C, and *t*-butyl isocyanide (1.19 mL, 10.4 mmol) was added dropwise. The solution was warmed to room temperature over 2 h. After evaporation of the solvent and extraction with hexane (15 mL), a yellow oil was isolated, which essentially consisted of a 1:1 mixture of **1d** and tetramethylpiperidine (1.4 g, 65%). ^{1}H NMR (300 MHz, C_6D_6): δ = 2.34 (s, 12 H), 1.18 (s, 9 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 202.1 (C), 118.8 (C), 58.6 (C), 42.7 (CH_3), 30.5 (CH_3) ppm. IR (CH_2Cl_2): $\nu_{(CN)}$ 1981 cm^{-1}.

Ketenimine 1e. *t*-Butyl isocyanide (0.50 mL, 4.4 mmol) was added dropwise at −78 °C to a THF solution (10 mL) of **e** (0.50 g, 2.9 mmol). Then the solution was warmed to room temperature over 1 h. After evaporation of the solvent and extraction with hexane (10 mL), **1e** was isolated as a yellow oil (0.59 g, 80%). ^{1}H NMR (300 MHz, C_6D_6): δ = 3.16 (sept, J = 6.6 Hz, 2 H), 1.23 (s, 9 H), 1.14 (d, J = 6.6 Hz, 12 H), 1.13 (s, 9 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 193.6 (C), 94.6 (C), 58.2 (C), 53.0 (CH), 33.7 (C), 30.6 (CH_3), 30.4 (CH_3), 24.0−22.0 (br s, CH_3) ppm. IR (CH_2Cl_2): $\nu_{(CN)}$ 1981 cm^{-1}. HRMS (ESI-TOF) $[M + H]^+$ calcd for $C_{16}H_{33}N_2$, 253.2638; found, 253.2644.

Ketone 2b. Benzaldehyde (0.05 mL, 0.47 mmol) was added dropwise at −78 °C to a THF solution (10 mL) of **b** (0.5 mmol). The solution was warmed to room temperature over 1 h. After evaporation of the solvent and extraction with benzene (2 × 10 mL), **2b** was isolated as a red oil (150 mg, 82%). ^{1}H NMR (300 MHz, C_6D_6): δ = 8.0 (m, 1 H), 7.25−6.80 (m, 7 H), 6.52 (s, 1 H), 4.64 (m, 1 H), 3.69

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(dd, J = 9 and 4 Hz, 1 H), 3.29 (br d, J = 12 Hz, 1 H), 3.23 (br d, J = 13 Hz, 1 H), 3.04−2.87 (m, 3 H), 2.62 (m, 2 H), 1.81 (d, J = 7 Hz, 3 H), 1.32 (d, J = 7 Hz, 3 H), 1.30−1.15 (m, 4H), 1.15 (d, J = 7 Hz, 3 H), 0.94 (d, J = 7 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 193.3 (C), 151.1 (C), 147.0 (C), 144.2 (C), 136.4 (C), 132.4 (CH), 129.1 (CH), 126.9 (CH), 125.0 (CH), 124.6 (CH), 80.3 (CH), 58.6 (CH_2), 55.4 (CH_2), 49.2 (CH_2), 30.4 (CH), 29.5 (CH), 28.7 (CH), 28.4 (CH_2), 25.9 (CH_3), 24.1 (CH_3), 23.9 (CH_3), 23.5 (CH_3), 22.3 (CH_2) ppm. HRMS (FAB) $[M + Na]^+$ calcd for $C_{26}H_{34}N_2ONa$ 413.2569; found, 413.2558.

Ketone 2c. Benzaldehyde (0.1 mL, 1.0 mmol) was added dropwise at −78 °C to a THF solution (10 mL) of **c** (0.9 mmol). Then the solution was warmed to room temperature over 1 h. After evaporation of the solvent and extraction with hexane (10 mL), **2c** was isolated as a yellow solid (0.33 g, 95%). ^{1}H NMR (300 MHz, C_6D_6): δ = 7.94−7.98 (m, 2 H), 7.04−7.32 (m, 6 H), 5.48 (s, 1 H), 4.82 (sept, J = 6.7 Hz, 1 H), 3.51 (sept, J = 6.7 Hz, 1 H), 2.13 (d, J = 12.3 Hz, 1 H), 1.91 (d, J = 12.3 Hz, 1 H), 1.77 (s, 3 H), 1.58 (d, J = 6.7 Hz, 3 H), 1.50 (d, J = 6.7 Hz, 3 H), 1.41 (d, J = 6.7 Hz, 3 H), 1.40 (d, J = 6.7 Hz, 3 H), 1.35 (s, 3 H), 1.19 (s, 3 H), 1.14 (s, 3 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 201.9 (C), 153.8 (C), 149.7 (C), 140.9 (C), 139.6 (C), 132.8 (CH), 129.0 (CH), 128.8 (CH), 127.6 (CH), 125.6 (CH), 125.0 (CH), 79.0 (CH), 63.8 (C), 59.4 (CH_2), 41.8 (C), 32.4 (CH), 32.2 (CH), 29.0 (CH_3), 28.7 (CH_3), 28.4 (CH_3), 28.0 (CH_3), 27.0 (CH_3), 26.7 (CH_3), 26.1 (CH_3), 25.0 (CH_3) ppm. HRMS (EI) $[M - H]^+$ calcd for $C_{27}H_{36}NO$ 390.2796; found, 390.2804.

Ketone 2d. Benzaldehyde (0.84 mL, 8.3 mmol) was added dropwise at −78 °C to a THF solution (20 mL) of **d** (7.5 mmol). Then the solution was warmed to room temperature and stirred for 2 h. After evaporation of the solvent, the residue was extracted with hexane (20 mL). This solution was kept at −20 °C overnight, and **2d** precipitated as a beige solid (1.20 g, 77%). ^{1}H NMR (300 MHz, C_6D_6): δ = 8.13 (m, 2 H), 7.05−7.16 (m, 3 H), 3.91 (s, 1 H), 2.25 (s, 12 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 196.1 (C), 139.8 (C), 133.0 (CH), 129.4 (CH), 129.0 (CH), 88.7 (CH), 41.5 (CH_3) ppm. HRMS (EI) $[M - H]^+$ calcd for $C_{12}H_{17}N_2O$ 205.1341; found, 205.1340.

Epoxide 3e. Benzaldehyde (0.08 mL, 0.7 mmol) was added dropwise at −78 °C to a solution of **e** (0.7 mmol) in THF (5 mL). Then the solution was warmed to room temperature over 1 h. After evaporation of the solvent and extraction with hexane (10 mL), **3e** was isolated as a mixture of two diastereomers (80/20) as a yellow oil (0.17 g, 81%). Major diastereomer. ^{1}H NMR (C_6D_6, 300 MHz): δ = 7.37−7.40 (m, 2 H), 7.00−7.13 (m, 3 H), 3.88 (m, 1 H), 3.46 (m, 1 H), 2.90 (m, 1 H), 1.09 (s, 9 H), 1.04−1.30 (m, 12 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 137.9 (C), 128.6 (CH), 128.2 (CH), 127.7 (CH), 86.3 (C), 63.0 (CH), 53.2 (CH), 50.4 (CH), 39.7 (C), 28.5 (CH_3), 24.9 (CH_3) ppm. Minor diastereomer. ^{1}H NMR (C_6D_6, 300 MHz): δ = 7.37−7.40 (m, 2 H), 7.00−7.13 (m, 3 H), 4.11 (1 H), 3.27 (m, 2 H), 0.92 (s, 9 H), 0.81 (d, J = 6.3 Hz, 12 H) ppm. ^{13}C NMR (C_6D_6, 75 MHz): δ = 138.3 (C), 128.6 (CH), 127.7 (CH), 127.4 (CH), 84.3 (C), 65.7 (CH), 55.2 (CH), 49.3 (CH), 39.2 (C), 29.1 (CH_3), 26.4 (CH_3), 26.0 (CH_3) ppm. HRMS (ESI-TOF) $[M + H]^+$ calcd for $C_{18}H_{30}NO$, 276.2322; found, 276.2323.

Enol 4e. A C_6D_6 solution (0.5 mL) of epoxide **3e** (100 mg) was kept at room temperature in a NMR tube, and according to ^{1}H and ^{13}C NMR spectroscopy, the enol derivative **4e** was quantitatively formed within 48 h. ^{1}H NMR (300 MHz, C_6D_6): δ = 8.07 (s, 1 H), 7.28−7.32 (m, 2 H), 7.00−7.09 (m, 3 H), 3.29 (sept, J = 6.3 Hz, 2 H), 1.04 (d, J = 6.3 Hz, 12 H), 0.95 (s, 9 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 153.8 (C), 139.1 (C), 130.6 (CH), 128.4 (CH), 128.3 (CH), 124.6 (C), 49.6 (CH), 36.7 (C), 33.0 (CH_3), 23.2 (CH_3), 23.0 (CH_3) ppm.

Acetal 5e. Benzaldehyde (0.21 mL, 2.1 mmol) was added dropwise at −78 °C to a solution of carbene **e** (0.7 mmol) in THF (10 mL). The solution was warmed to room temperature over 1 h. After evaporation of the solvent and extraction with hexane (10 mL), **5e** was isolated as an oily residue (0.19 g, 72%). Colorless crystals were obtained in a hexane solution at −20 °C. mp: 110−112 °C. ^{1}H NMR (300 MHz, C_6D_6): δ = 7.63−7.71 (m, 4 H), 6.94−7.13 (m, 6 H), 6.20 (s, 1 H), 5.25 (s, 1 H), 3.47 (sept, J = 6.6 Hz, 2 H), 1.14 (d, J = 6.6 Hz, 6 H), 1.12 (d, J = 6.6 Hz, 6 H), 0.85 (s, 9 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 139.5 (C), 138.6 (C), 129.2 (CH), 129.0 (CH), 128.6 (CH), 128.4 (CH), 127.0 (CH), 105.2 (C), 101.3 (CH), 92.1 (CH), 47.7 (CH), 43.2 (C), 28.3 (CH_3), 26.3 (CH_3), 26.0 (CH_3) ppm. HRMS (ESI-TOF) $[M + H]^+$ calcd for $C_{25}H_{36}NO_2$, 382.2741; found, 382.2746.

Reaction of Methyl Acrylate with Carbene a. Methyl acrylate (0.29 mL, 3.4 mmol) was added dropwise at −78 °C to a solution of **a** (2.3 mmol) in THF (5 mL). The solution was warmed to room temperature and stirred for 2 h. After evaporation of the solvent and extraction with hexane (10 mL), a 1:1 mixture of the two isomers **6a** and **7a** was obtained as a yellow oil (0.79 g, 72%). ^{1}H NMR (300 MHz, C_6D_6): δ = 6.81 (s, 1 H), 6.78 (s, 1 H), 6.76 (s, 2 H), 6.75 (s, 1 H), 6.74 (s, 1 H), 6.72 (s, 2 H), 5.65 (d, J = 2.5 Hz, 1 H), 5.59 (d, J = 2.5 Hz, 1 H), 5.55 (d, J = 2.5 Hz, 1 H), 5.53 (d, J = 2.5 Hz, 1 H), 3.28 (m, 1 H), 3.25 (s, 3 H), 3.24 (s, 3 H), 3.23 (s, 3 H), 3.16 (s, 3 H), 2.72 (d, J = 11.0 Hz, 1 H), 2.68 (s, 2 H), 2.56 (m, 1 H), 1.50−2.41 (m, 7 H), 2.39 (s, 3 H), 2.36 (s, 6 H), 2.29 (s, 3 H), 2.28 (s, 6 H), 2.23 (s, 3 H), 2.20 (s, 3 H), 2.11 (s, 3 H), 2.10 (s, 3 H), 2.08 (s, 6 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 176.3 (C), 173.9 (C), 173.9 (C), 173.5 (C), 144.5 (C), 144.0 (C), 138.5 (C), 138.4 (C), 138.2 (C), 138.0 (C), 137.8 (C), 137.7 (C), 137.6 (C), 137.5 (C), 137.4 (C), 137.3 (C), 136.2 (C), 134.7 (C), 130.2 (CH), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.6 (CH), 116.7 (CH), 116.6 (CH), 114.6 (CH), 114.3 (CH), 68.3 (C), 60.5 (CH), 51.0 (CH_3), 50.9 (CH_3), 50.7 (CH_3), 50.6 (CH_3), 41.0 (CH), 35.1 (CH), 34.0 (CH_2), 32.6 (CH_2), 30.9 (CH_2), 27.6 (CH_2), 21.2 (CH_3), 21.1 (CH_3), 18.4 (CH_3), 18.3 (CH_3), 18.2 (CH_3) ppm. HRMS (EI) $[M]^+$ calcd for $C_{29}H_{36}N_2O_4$, 476.2675; found, 476.2673.

Reaction of Methyl Acrylate with Carbene b. Methyl acrylate (40 mg, 0.46 mmol) was added at −78 °C to a solution of carbene **b** (0.46 mmol) in THF (7 mL). The mixture was stirred 30 min at −78 °C, and an additional hour at room temperature. The solvent was removed under vacuum, and the residue was extracted with pentane. The volatiles were removed under vacuum, affording **8b** as a red waxy oil (110 mg, 65%). ^{1}H NMR (125 MHz, C_6D_6): δ = 7.34−7.19 (m, 3 H), 3.52 (m, 2 H), 3.40 (s, 3 H), 3.45−3.28 (m, 7 H), 2.86 (dt, J = 13 and 3 Hz, 1 H), 2.75 (d, J = 13 Hz, 1 H), 2.14 (m, 1 H), 1.69 (m, 1 H), 1.58 (m, 1 H), 1.48 (d, J = 7 Hz, 3 H), 1.41 (d, J = 7 Hz, 3 H), 1.40−1.20 (m, 1 H), 1.39 (d, J = 7 Hz, 3 H), 1.33 (d, J = 7 Hz, 3 H), 1.07 (dd, J = 7 and 3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 173.9 (C), 152.1 (C), 148.9 (C), 147.1 (C), 140.9 (C), 128.1 (CH), 125.2 (CH), 124.8 (CH), 79.0 (CH_3), 55.4 (CH_2), 54.9 (CH_2), 50.5 (CH_2), 32.1 (CH_2), 31.7 (CH_2), 29.0 (CH), 28.4 (CH), 28.3 (CH), 24.7 (CH_3), 24.6(CH_3), 24.2 (CH_3), 21.0 (CH_2). IR (THF) ν: 1737 (CO_{ester}) and 1637 ($C{=}C_{enamine}$) cm^{-1}. HRMS (FAB) $[M + Na]^+$ calcd for $C_{23}H_{34}N_2O_2Na$, 393.2518; found, 393.2520.

Reaction of Methyl Acrylate with Carbene c. Methyl acrylate (0.08 mL, 0.9 mmol) was added dropwise at −78 °C to a solution of **c** (0.6 mmol) in THF (5 mL). The solution was warmed to room temperature and stirred for 2 h. After evaporation of the solvent, extraction with hexane (10 mL), and purification on silica gel (1:1 mixture of ethyl acetate and hexane as eluent). **7c** was isolated as a colorless oil (0.18 g, 65%). ^{1}H NMR (300 MHz, C_6D_6): δ = 7.09−7.21 (m, 3 H), 3.69 (m, 1 H), 3.33 (d, J = 11.9 Hz, 1 H), 3.30 (s, 6 H), 3.15 (sept, J = 6.8 Hz, 2 H), 2.27 (m, 2 H), 2.00 (m, 1 H), 1.85 (m, 1 H), 1.77 (s, 2 H), 1.60 (s, 3 H), 1.45 (s, 3H, CH_3), 1.24 (d, J = 6.8 Hz, 3 H), 1.22 (d, J = 6.8 Hz, 3 H), 1.20 (d, J = 6.8 Hz, 3 H), 1.17 (d, J = 6.8 Hz, 3 H), 1.03 (s, 3 H), 1.01 (s, 3 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 175.3 (C), 173.5 (C), 157.9 (C), 150.8 (C), 150.7 (C), 134.4 (C), 128.8 (CH), 125.2 (CH), 125.1 (CH), 88.9 (CH), 62.9 (C), 57.5 (CH_2), 51.3 (CH_3), 51.2 (CH_3), 43.4 (CH), 41.6 (C), 32.2 (CH_2), 31.8 (CH_3), 30.8 (CH_3), 30.3 (CH_2), 30.2 (CH_3), 29.7 (CH_3), 28.9 (CH), 27.2 (CH_3), 26.5 (CH_3), 24.3 (CH_3), 24.2 (CH_3) ppm. HRMS (EI) $[M]^+$ calcd for $C_{28}H_{43}NO_4$, 457.3192; found, 457.3176.

Reaction of Methyl Acrylate with Carbene d. Methyl acrylate (1.06 mL, 11.8 mmol) was added dropwise at −78 °C to a solution of **d** (7.8 mmol) in THF (20 mL). Then the solution was warmed to room temperature and stirred for 2 h. After evaporation of the solvent

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and extraction with hexane (20 mL), a mixture containing **9d** (2 diastereomers in a 3:2 ratio) and tetramethylpiperidine was obtained as a yellow oil (1.56 g). Cyclopentanes **9d** were spectroscopically characterized without further purification. Major diastereomer. ^{1}H NMR (500 MHz, C_6D_6): δ = 3.38 (s, 6 H), 2.36 (s, 6 H), 2.23 (s, 6 H), 1.92−3.00 (m, 6 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 175.1 (C), 173.9 (C), 89.5 (C), 51.5 (CH_3), 51.4 (CH_3), 47.7 (CH), 41.6 (CH), 41.0 (CH_3), 39.5 (CH_3), 33.7 (CH_2), 32.3 (CH_2) ppm. Minor diastereomer. ^{1}H NMR (300 MHz): δ = 3.44 (s, 6 H), 2.49 (s, 6 H), 2.29 (s, 6 H), 1.92−3.00 (m, 6 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 175.5 (C), 174.8 (C), 88.2 (C), 51.4 (CH_3), 51.2 (CH_3), 50.3 (CH), 41.8 (CH_3), 41.3 (CH), 39.7 (CH_3), 35.7 (CH_2), 29.8 (CH_2) ppm. HRMS (EI) $[M]^+$ calcd for $C_{13}H_{24}N_2O_4$, 272.1736; found, 272.1732.

Reaction of Methyl Acrylate with Carbene e. Methyl acrylate (0.15 g, 1,74 mmol) was added at −78 °C to a THF solution (5 mL) of carbene **e** (0.27 g, 1.58 mmol). The solution was warmed to room temperature and stirred for 30 min. The solvent was removed under vacuum, and after extraction with hexane, **10e** was isolated as a white powder (0.345 g, 85%). mp: 75−77 °C. ^{1}H NMR (300 MHz, C_6D_6): δ = 0.87 (s, 9H), 1.10 (m, 1H), 1.12 (d, J = 6.5 Hz, 3 H), 1.24 (t, J = 6.0 Hz, 6H), 1.33 (d, J = 7.0 Hz, 3H), 1.69 (dd, J = 7.0 and 8.0 Hz, 1H), 1.88 (dd, J = 5.5 and 7.0 Hz, 1H), 3.13 (sept, J = 7.0 Hz, 1H), 3.2 (sept, J = 6.5 Hz, 1H), 3.47 (s, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ = 20.7 (CH_2), 25.5, 26.6, 26.7, 27.1 (CH_3), 27.3 (CH), 29.2 (CH_3), 38.6 (C), 51.7 (CH_3), 53.8 (CH), 54.2 (CH), 65.5 (C), 172.3 (C) ppm. HRMS (ESI-TOF) $[M + H]^+$ calcd for $C_{15}H_{30}NO_2$, 256.2271; found, 256.2272.

Rearrangement of cyclopropane **10e** was monitored by NMR spectroscopy at room temperature. The enamine **8e** was quantitatively formed within a week as a mixture of two isomers (85/15). Major isomer. ^{1}H NMR (300 MHz, C_6D_6): δ = 5.42 (t, J = 7.5 Hz, 1 H), 3.36 (s, 3 H), 3.17 (d, J = 7.5 Hz, 2 H), 3.08 (sept, J = 6.5 Hz, 2 H), 1.14 (s, 9 H), 1.06 (d, J = 6.5 Hz, 12 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 172.2 (C), 156.5 (C), 118.6 (CH), 51.6 (CH_3), 50.7 (CH), 36.8 (C), 34.9 (CH_2), 31.1 (CH_3), 22.5 (CH_3) ppm. Minor isomer. ^{1}H NMR (300 MHz, C_6D_6): δ = 5.77 (t, J = 7.5 Hz, 1 H), 3.37 (s, 3 H), 3.22 (sept, J = 6.5 Hz, 2 H), 3.10 (d, J = 7.5 Hz, 2 H), 1.11 (s, 9 H), 1.02 (d, J = 6.5 Hz, 12 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 172.5 (C), 157.6 (C), 119.3 (CH), 51.6 (CH_3), 50.7 (CH), 38.5 (C), 35.5 (CH_2), 32.4 (CH_3), 24.0 (CH_3) ppm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra; Cartesian coordinates and absolute energies for all optimized geometries. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(12) The Tolman electronic parameter (TEP) of a carbene is a measure of its overall donor properties, which are a convolution of its nucleophilicity and electrophilicity. According to the TEP values, **2** is a superior overall donor than **1**. As **2** is also more electrophilic, it is therefore more nucleophilic than **1**. Similarly, we can infer that **4** is more nucleophilic than **3**. As nucleophilicity also increases when replacing an amino substituent by an alkyl group, the nucleophilicity follows the order **1** < **2** < **3** < **4** < **5**.

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