H, 10.16. Found: C, 60.47; H, 10.31. Relevant ^{1}H NMR data: δ 4.08 (dd, 1 H, J = 2.0, 3.0 Hz), 3.88 (dd, 1 H, J = 2.3, 10.0 Hz), 3.59 (dd, 1 H, J = 2.0, 3.0 Hz), 2.49 (dt, 1 H, J = 7.0, 10.0 Hz).

Synthesis of Emithioketal 33. This product was obtained from **32a** in two steps involving selective hydrolysis of the thioester function (MeONa in MeOH, 0 °C, 2 h) and PTSA-catalyzed reaction with freshly distilled benzaldehyde in THF as solvent (15 h, rt). Compound **33** was an oil that was purified by flash chromatography with a 80:20 hexanes/Et_2O mixture as eluant. Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.58; H, 7.71. Relevant ^{1}H NMR data: δ 6.08 (s, 1 H), 4.14 (dd, 1 H, J = 2.0, 12.0 Hz), 3.30 (dd, 1 H, J = 3.1, 5.4 Hz).

Lewis Acid-Promoted 3-Aza-Cope Rearrangement of *N*-Alkyl-*N*-allylenamines

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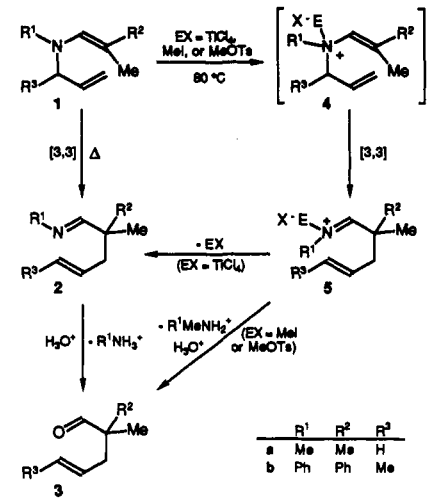
The 3-aza-Cope rearrangement of the *N*-alkyl-*N*-allylenamines derived from isobutyraldehyde, which proceeds thermally at 250 °C, has been accelerated by a variety of electrophilic reagents to give γ,δ-unsaturated imines. Protic acids, such as HCl (0.5 equiv), and the Lewis acidic reagents $TiCl_4$ (0.1–0.2 equiv), $Et_2O{\cdot}BF_3$ (0.5 equiv), and $AlMe_3$ (1.0 equiv) produced complete [3,3] rearrangement of substrates at 111 °C. By increasing the Lewis acidity of the aluminum reagents, this transformation was achieved at 50 °C with $ClAlMe_2$, Cl_2AlMe, and methylaluminum bis(2,6-diphenylphenoxide). Reaction conditions were studied initially by GLC analysis of the *N*-isobutyl derivative. These optimum conditions were then used to obtain isolated yields of 59–99% for rearrangement and in situ $LiAlH_4$ reduction of the analogous *N*-methylcyclohexyl substrate to the corresponding δ,ε-unsaturated amine. Substrates derived from 2-phenylpropanal, *n*-butanal, cyclohexanone, and cyclopentanone were used to examine the general effectiveness of HCl, $TiCl_4$, and $AlMe_3$ as reagents for acceleration of the [3,3] rearrangement. The most versatile and efficient reagent for promoting this reaction, $AlMe_3$, produced overall yields of 83–96% for the two-step rearrangement and reduction of these substrates.

Introduction

The [3,3] sigmatropic shift of allyl vinyl ethers, the Claisen rearrangement, has had significant impact on the regio- and stereochemically controlled formation of carbon–carbon bonds, and mechanistic studies of this rearrangement have provided important insight into these and related pericyclic processes.[1] While the analogous 3-aza-Cope rearrangement of allylenamine substrates has many of the same advantages, there are intrinsic properties of this nitrogen system that provide for some unique synthetic opportunities (**1** to **2**, Scheme I). Included in these features are the higher *E*–*Z* control of enamine geometry, which presents a valuable alternative to the less selective enol ether formation,[1g] and the availability of optically active allylamines from amino acid sources.[2] A rather intriguing feature of this substrate is the presence of an asymmetric heteroatom at the 3-position, a property which the allyl vinyl ether substrates lack.[3]

Scheme I



Despite the attractive possibilities of this reaction, the 3-aza-Cope rearrangement has been of limited synthetic utility due, in part, to the elevated temperatures required for thermally induced rearrangement, 250 °C for **1a** to **2a** and 205 °C for **1b** to **2b**.[4] In order to overcome these limitations, a number of methods for accelerating this rearrangement have appeared involving manipulation of the electron density of the atoms in the six-membered transition state. An increase in electron density at the enamine functionality through the use of *N*-allylketene *N*,*O*-acetals produced rearrangement at 180–190 °C, a significant decrease from the 250 °C required for the corresponding enamines.[3,5] A similar [3,3] rearrangement occurred for a substrate with a dialkylamine substituent,

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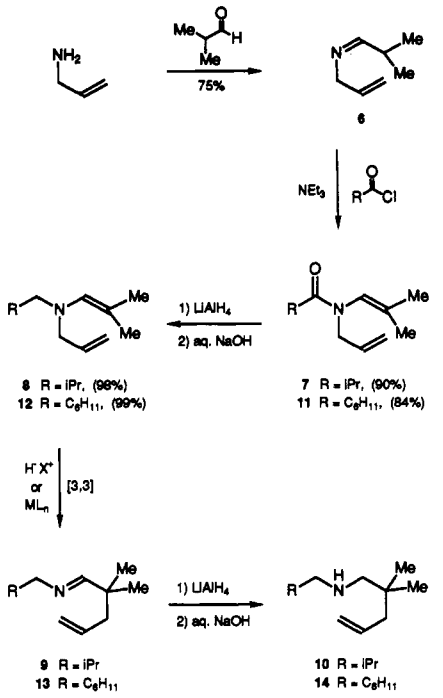
an *N*-alkylketene *N,N*-acetal, at 200 °C.[5a] Increasing electron density at the enamine by formation of the *N*-allylamide enolates further reduced the temperature required for rearrangement to 135 °C.[6]

Other methods of promoting the 3-aza-Cope rearrangement through charge-accelerated processes have included reducing the electron density on the nitrogen. The effectiveness of this approach is apparent from the slightly lower reaction temperature required for the less Lewis basic aniline derivative **1b** (205 °C) than for the rearrangement of **1a** (Scheme I).[4] Further reduction in the electron density at nitrogen, by forming a cationic quaternary nitrogen center, has produced rearrangement at a temperature as low as 80 °C. The quaternary ammonium intermediate **4a** has been accessed by methylation of **1a** as shown in Scheme I,[7] and a modification of the methylation procedure, methylation of an *N*-allylimine followed by the addition of a base, has been found to produce rearrangement at 25 °C.[8] A more common route to **4** has been the allylation of *N,N*-dialkylenamines.[9] Unfortunately, symmetrical allyl groups must be used to avoid problems associated with N- versus C-allylation in this method. Another type of route has been reported that used conjugate addition of a tertiary amine to ethyl propiolate to form the cationic nitrogen species.[10] In most of these cases in which the tetraalkyl ammonium species was generated, product isolation was limited to hydrolysis of the iminium ion **5** to the corresponding aldehyde **3**, the same product accessible through Claisen rearrangement.

The use of non-carbon electrophiles, in the form of Lewis acid catalysts, have been explored as well.[11] Although Lewis acid catalysis of the Claisen rearrangement has been studied extensively,[11,12] only one method of promoting the aliphatic 3-aza-Cope sigmatropic rearrangement has been reported. In this case, the use of 0.25 equiv of $TiCl_4$ promoted transformation of **1b** to **2b** at 80 °C.[13] Complexation of the enamine to the Lewis acid, generating an electron-deficient nitrogen center, has been suggested to produce this rate enhancement. However, this in situ carbonyl condensation and rearrangement procedure was less effective for straight-chain aldehydes (20–30%) and was unsuccessful for ketones. A recent report by Bailey has extended the use of $TiCl_4$ to obtain asymmetric induction as high as 90% ee for substrates where R^1NH_2 was (*R*)-(+)-α-methylbenzylamine.[14] In each case, this methodology has been limited to the use of enamines formed from 2-substituted aldehydes.[15]

Our own research interests have focused on the use of the aliphatic 3-aza-Cope rearrangement in organic synthesis. In order to develop this method into a useful synthetic carbon–carbon bond-forming reaction, we found it necessary to determine which of a variety of catalysts would promote the rearrangement of **1** to **2** most efficiently. The generality of the electrophilic reagents was investigated for a variety of enamine substrates prepared from the aldehydes 2-methylpropanal, 2-phenylpropanal, and *n*-butanal and from the ketones cyclohexanone and cyclopentanone. Hydride reduction of imine **2** would then provide a route to the corresponding δ,ε-unsaturated amine, which has found creative use in the formation of nitrogen heterocycles.[16]

Scheme II



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Results and Discussion

Substrate Preparation. Determination of the ability of Lewis acid catalysts to accelerate the 3-aza-Cope rearrangement required the preparation of two *N*-allyl-*N*-alkylenamine substrates (Scheme II). For the purposes of optimizing reaction conditions by capillary gas chromatrography (GLC), **8** was ideal for analysis of the reaction progress and product formation. However, the product of rearrangement and reduction, **10**, proved to be somewhat volatile, and the use of substrate **12** was preferable to facilitate the process of obtaining optimum isolated yields for the δ,ϵ-unsaturated amine.

Synthesis of **8** and **12** was accomplished from allylamine through the route illustrated in Scheme II. Imine formation from the reaction of allylamine with isobutyraldehyde gave **6** in 75% yield, and subsequent reaction of **6** with isobutyryl chloride and NEt_3 produced a 90% yield of reported.[17] Reduction of enamide **7** with $LiAlH_4$ gave **8** as the only product in 98% distilled yield. In the same manner, compound **11** was prepared by reaction of **6** with cyclohexanecarbonyl chloride in 84% yield or, if the reaction mixture containing **6** was acylated without prior isolation of the imine, **11** was isolated in 68% yield in two steps from allylamine. Reduction of enamide **11** with $LiAlH_4$ produced a 99% yield of the desired enamine **12**. Substrates **15**, **18**, **21**, and **24** (eqs 1 and 2), which vary in enamine substituent pattern, were prepared by the same route from the corresponding carbonyl compound as previously reported.[17]

Rearrangement Promoted by Proton Sources. Catalysis of the [3,3] rearrangement by protic acids was first observed during the preparation of **8** through a more established route for enamine formation.[17] Heating *N*-allyl-*N*-isobutylamine and isobutyraldehyde in the presence of 0.0025 equiv of *p*-toluenesulfonic acid, with azeotropic removal of H_2O, produced the corresponding enamine **8**. If the enamine condensation reaction mixture was heated to reflux in benzene (80 °C), the reaction was found to give **8** in 80% yield as the only product. However, with the use of toluene to azeotrope the water (111 °C), the rearrangement product **9** was formed from **8** to an extent of 10–15% over the course of 72 h. In order to enhance the conversion to **9**, increased amounts of a stronger acid were required.[18]

HCl as the proton source produced efficient transformation of **8** to **9**, and conditions of the reaction were optimized by GLC analysis (Table I). This acid-promoted rearrangement required only 0.3 equiv of HCl for complete conversion to **9** within 6 h in refluxing toluene.[19] The use of 0.5 equiv of HCl produced a slight increase in yield, optimized at 82%, but further increase in the amount of catalyst to 0.8 equiv of HCl offered no synthetic advantage. Complete conversion was achieved at a lower temperature (80 °C) with 0.5 equiv of HCl, but the yield was significantly reduced. Product isolation by in situ reduction of the imine with $LiAlH_4$ gave the corresponding amine **10** in 81% yield.[20] Rearrangement and reduction of the less volatile **12** under the same conditions produced a slightly improved 85% isolated yield of **14**.[21]

Table I. Catalytic Acceleration of the 3-Aza-Cope Rearrangement[a]

reagent	equiv	time/temp (h/°C)	yields (%) GLC[b]	yields (%) isolated[c]
HCl	0.3	6/111	70	
	0.5	3/111	82	85
	0.5	6/80	64	
	0.8	6/111	82	
$TiCl_4$	0.1	24/111	83	73[d]
	0.3	24/111	64	
	0.5	24/111	56	
	0.5	24/80[e]	8	
$(ArO)_2TiCl_2$	0.5	24/111	80	71
	0.5	48/111	87	
$Et_2O{\cdot}BF_3$	0.5	24/80[f]	59	
	0.5	24/111	82	59
	1.0	9/111	75	
	1.5	5/111	70	
$SnCl_4$	0.1	48/111[g]	14	
$ZnCl_2$	1.0	12/111	86	
	1.0	24/111	74	

[a] All reactions were run 0.2 M in toluene. [b] Rearrangement of **8** to **9** was performed on a 1.0 mmol scale. Yields were determined by capillary gas chromatographic (GLC) analysis of the quenched reaction mixture (10% w/v MeONa/MeOH) using internal standards and correcting for detector response (ref 19). Values were based on reacted substrate. [c] Isolated yield of **14** after rearrangement of **12** (5 mmol) followed by in situ reduction of **13**. [d] 0.2 equiv of catalyst required on 5.0 mmol scale. [e] 18% conversion. [f] 97% conversion. [g] 84% conversion.

Rearrangement by Metal Halides. The use of $TiCl_4$, which has been reported to promote rearrangement in similar systems,[13] was examined as a means of promoting the transformation of **8** to **9** under a variety of conditions.[22] Carbon–carbon bond formation was found to proceed within 24 h in refluxing toluene with as little as 0.1 equiv of Lewis acid. Increasing the quantity of $TiCl_4$ still produced a single volatile product, but caused a decrease in yield presumably through enhanced substrate oligomerization. At a lower reaction temperature of 80 °C, 0.5 equiv of this Lewis acid only produced 18% conversion to **9** within 24 h. On a larger reaction scale, 0.2 equiv of $TiCl_4$ was typically required to achieve complete conversion to imine product.[23] Catalysis of the rearrangement of **8** to **9** with 0.2 equiv of $TiCl_4$, followed by in situ reduction of the resulting imine with $LiAlH_4$, produced **10** in 71% isolated yield.[20] Similarly, transformation of **12** to **14** was accomplished in 73% yield. Steric and electronic modification of the titanium catalyst, by the exchange of ligands to form bis(2,6-diphenylphenoxy)$TiCl_2$,[24] promoted rear-

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(18) Weaker acid catalysts, such as phenol or 2,6-diphenylphenol (0.5 equiv), produced only minor amounts of **9** at 111 °C during consumption of **8** under a variety of reaction conditions.

(19) Reaction mixtures were quenched with a 10% w/v solution of NaOMe/MeOH for analysis by GLC. Under the quenching conditions, loss of **8** or **9** was not observed even after an extended period of time (24 h).

(20) In the case of the more volatile compound **10**, an excess of aqueous HCl was added, and the solution was concentrated under reduced pressure. The residue was treated with 15% aqueous NaOH to a pH of 14, the amine was extracted with 3 × 50 mL portions of Et_2O, and the organic layers were dried ($MgSO_4$) prior to distillation.

(21) For transformations with some of the electrophilic reagents containing halogens (HCl, $ClAlMe_2$, and Cl_2AlMe), GLC yields were lower than isolated yields in some cases due possibly to ammonium chloride salt formation prior to analysis.

(22) Because hydrolysis of $TiCl_4$ could produce up to 4 equiv of HCl, which was also found to promote rearrangement, the $TiCl_4$ was distilled prior to use and rigorous measures were taken to exclude oxygen and water from the reaction mixtures. In each case, the characteristics of the $TiCl_4$-catalyzed rearrangements were very different from those of the HCl reactions.

(23) The addition of $TiCl_4$ to the enamine produced an oil on the sides of the flask, which could be a mixture of the salts corresponding to **4** and **5**. The increased amount of catalyst required to get complete conversion of **8** to **9** could be due to the decreased surface area/volume ratio of the reaction vessel as the reaction is scaled up. As a result, the surface area of the oily intermediate was decreased, and the reaction slowed.

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Table II. Studies of [3,3] Rearrangement Promoted by Aluminum Reagents[a]

reagent	equiv	time/temp (h/°C)	yields (%) GLC[b]	yields (%) isolated[c]
$AlMe_3$	0.5	24/111	100	
	1.0	12/111	100	99
	1.5	6/111	100	
	1.5	24/80	100	
$ClAlMe_2$	0.2	24/111	50[d]	
	0.5	24/80	71[e]	
	1.0	24/25	54	
	1.0	24/40	67	
	1.0	24/50	88	91
	1.0	9/60	83	
	1.0	5/80	96	96
Cl_2AlMe	1.0	24/50	79	87
	1.0	12/80	91	84
$(ArO)_2AlMe$	1.0	24/40	87	80
	1.0	12/60	84	
Cl_3Al	1.0	24/50	36	
	1.0	24/80	63	

[a] All reactions were run 0.2 M in toluene. [b] Rearrangement of 8 to 9 was performed on a 1.0 mmol scale. Yields were determined by capillary gas chromatographic (GLC) analysis of the quenched reaction mixture (10% w/v MeONa/MeOH) using internal standards are correcting for detector response (ref 19). Values were based on reacted substrate. [c] Isolated yield of 14 after rearrangement of 12 (5 mmol) followed by in situ reduction of 13. [d] 19% conversion to product. [e] 60% conversion to product.

rangement of 8 to 9 at 111 °C in 87% yield by GLC analysis. Rearrangement of 12 to 13, followed by reduction with $LiAlH_4$, gave 14 in 71% isolated yield with use of this catalyst.

Although there has been one report in which BF_3 was used as a catalyst for formation of an *N*-allyl *N*,*N*-ketene acetal at 30 °C, there was no evidence for charge accelerated rearrangement under the reaction conditions.[25] However, rearrangement of substrate 8 was promoted by $Et_2O{\cdot}BF_3$ at a higher temperature of 111 °C. For complete conversion to 9 within 24 h, a minimum of 0.5 equiv of catalyst was required, and increasing quantities of $Et_2O{\cdot}BF_3$ gave progressively decreasing yields. At a milder temperature of 80 °C, conversion to 9 by using 0.5 equiv of $Et_2O{\cdot}BF_3$ was only 97% complete after 24 h with a somewhat lower yield of 59%. With use of the optimum conditions, transformations of 12 to 14 was achieved in 59% isolated yield. Rearrangement promoted by $ZnCl_2$, one of the most effective catalysts reported for the rearrangement of allylaniline substrates,[11a] produced less selective transformation of 8 to 9. When 1.0 equiv of the Lewis acid was used, rearrangement required 12 h to reach completion with 86% GLC yield of 9, but 8–15% of an unidentified side product was unavoidably generated in the process. Further exposure to the reaction conditions caused degradation of 9 over the course of time.

Rearrangement by Organoaluminum Complexes. As found for the Claisen rearrangement, complexes of aluminum were the most effective catalysts for the 3-aza-Cope rearrangement.[12] Acceleration of the 3-aza-Cope rearrangement with aluminum reagents also paralleled that of the Claisen rearrangement in that stoichiometric amounts of the complexes were necessary to produce complete transformation of 8 to 9. For example, the use of 0.5 equiv of $AlMe_3$ at 111 °C produced 59% conversion of 8 to 9 after 6 h, but the reaction only progressed to 68% conversion after an additional 18 h (Table II). Increasing the initial amount of Lewis acid to 1.0 equiv, produced complete transformation within 12 h at 111 °C in 100% GLC yield. Under these optimum conditions, the rearrangement and reduction of 8 produced 10 in 95% yield,[20] and the same transformation with 12 gave a 99% isolated yield of 14. Complete conversion to product was also achieved at a temperature as low as 80 °C within 24 h, but required the use of 1.5 equiv of $AlMe_3$. Although the Claisen rearrangement of allyl vinyl ethers with $AlMe_3$ was found to result in addition of a methyl group to the resulting aldehyde, addition of a methyl group to the imines 9 or 13 was not observed after the analogous 3-aza-Cope transformation.[26]

Table III. Yields of the 3-Aza-Cope Rearrangement/Reduction as a Function of Reagent and Enamine Substitution Pattern[a]

substrate	product	reagent (equiv) HCl (0.5)	reagent (equiv) $TiCl_4$ (0.2)	reagent (equiv) $AlMe_3$ (1.0)
8	10	81	71	95
12	14	85	73	99
15[b]	17	77	88	92
18	20	0	0	84
21	23	99	92	96
24	26	10[c]	3[c]	83

[a] Isolated yields of reactions performed 0.2 M in refluxing toluene followed by treatment with $LiAlH_4$. [b] *E*:*Z* = 86:14. [c] Purified yields (ref 29).

As expected, increasing the Lewis acidity of the aluminum catalyst produced conversion of 8 to 9 with reduced reaction times or at lower reaction temperatures (Table II). By the use of 1.0 equiv of $ClAlMe_2$ at 80 °C, the reaction was complete within 5 h in 96% yield by GLC analysis. With the use of these conditions for rearrangement of 12 and subsequent reduction of 13 gave a 96% yield of the corresponding secondary amine.[21] Complete conversion of 12 to 13 also was achieved within 24 h at a temperature of 50 °C in 88% yield by GLC. This reaction temperature represents an overall decrease of 200 °C from the conditions necessary for thermal rearrangement! As was discussed for $AlMe_3$, $ClAlMe_2$ also was required in stoichiometric amounts. Rearrangement of 8 at 111 °C with 0.2 equiv of catalyst was only 19% complete after 24 h. The use of 0.5 equiv of Lewis acid at 80 °C gave a 57% conversion to 9 in 3 h, but the reaction advanced to only 60% conversion after an additional 21 h. Further increase of the aluminum Lewis acidity, by the use of Cl_2AlMe, produced results similar to those observed for $ClAlMe_2$. At 80 °C, a 91% GLC yield of 8 to 9 was obtained, and the reaction of 12 under these same conditions gave an 84% isolated yield of 14. Comparable yields were obtained at 50 °C.

An aluminum catalyst of similar oxidation state, methylaluminum bis(2,6-diphenylphenoxide),[12h] was also a very efficient catalyst for facilitating the 3-aza-Cope rearrangement. Rearrangement of 8 to 9 using this catalyst was complete within 24 h at 25 °C to give a 59% yield, and a yield of 87% was obtained by promoting the reaction at 40 °C. Similarly, the rearrangement and reduction of 12 under these conditions produced an 80% yield of 14. To

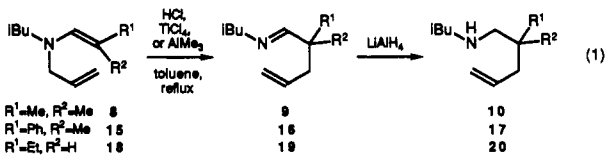
(25) Ficini, J.; Barbara, C. *Tetrahedron Lett.* **1966**, 6425.

(26) The preparation of the product of methyl addition to 9, *N*-(2-methyl-1-propyl)-*N*-(1,2,2-trimethylpent-5-en-1-yl)amine, was performed by the addition of methylmagnesium bromide to 9 followed by aqueous workup.

complete the methyl- and chloro-substituted series of aluminum Lewis acids, Cl_3Al was used as a catalyst for the transformation of **8** to **9**. This catalyst produced significantly lower yields of product under the same rearrangement conditions as those used for Cl_2AlMe.

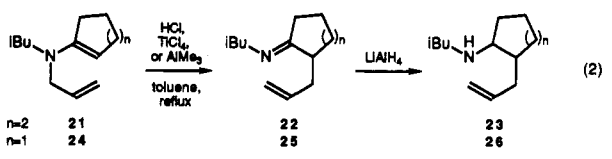
Variation of Enamine Substitution. In order to determine the versatility of the different types of reagents (protic acids, metal halides, and organoaluminum species) on various substrates, three representative reagents were studied. These reagents, HCl, $TiCl_4$, and $AlMe_3$, were each used to promote rearrangement of substrates **15**, **18**, **21**, and **24**, which all differed in enamine substitution pattern. The results are shown in Table III.

The 3-aza-Cope rearrangement of the aldehyde enamines was highly dependent on both the enamine substituent pattern and the type of electrophile used. With the traditionally successful geminally disubstituted enamine substrates,[7,9] such as **8** and **12**, rearrangement and subsequent reduction gave good yields of **10** and **14**, as previously discussed. The substrate derived from 2-phenylpropanal, **15**, gave similar results (eq 1). Rearrangement of **15** to **16** followed by $LiAlH_4$ reduction produced isolated yields which ranged from 77% to 92% for the three reagents. Substrate **18**, with only one alkyl substituent on the nucleophilic enamine carbon, was much more sensitive toward these reaction conditions. Treatment with HCl (0.5 or 1.0 equiv) or $TiCl_4$ (0.1 to 1.0 equiv) under a variety of conditions produced complete degradation of **18** to oligomeric products. In contrast, treatment of **18** with $AlMe_3$ resulted in rearrangement to **19** as the only volatile product, and reductive workup gave an 84% isolated yield of **20**.



(1)

The properties of the carbonyl compound had an enormous effect on the success of the acceleration of the 3-aza-Cope rearrangement for the ketone-derived substrates. The transformation of **21** to **22** proceeded quantitatively with each electrophilic reagent used, and reduction of the intermediate imine with $LiAlH_4$ gave **23** as a 90:10 mixture of diastereomers (eq 2).[27] For each reagent, isolated yields of greater than 92% were obtained. However, the results obtained for rearrangement and reduction of **24** were poor with the use of HCl or $TiCl_4$. Rearrangement with HCl for lengthy reaction times, followed by reduction with $LiAlH_4$, resulted in a mixture of unreacted **24** (9%), *N*-isobutyl-*N*-allylcyclopentylamine (**27**, 36%),[28] and **26** (10%) as the only distillable products.[29]



(2)

The reaction with $TiCl_4$ resulted in a similar mixture of **24** (11%), **27** (26%), and **26** (3%), and the use of an alternate catalyst, $Et_2O{\cdot}BF_3$ (0.5 equiv), gave a somewhat improved mixture of **27** (11%) and **26** (43%). As was found for **18**, the other substrate sensitive to HCl and $TiCl_4$ conditions, a stoichiometric amount of $AlMe_3$ successfully promoted the 3-aza-Cope rearrangement of **24**. Carbon–carbon bond formation and imine reduction produced an 83% yield of **26** as a 90:10 mixture of diastereomers.[27]

There are several features that made $AlMe_3$ a rather unique reagent for the acceleration of the 3-aza-Cope rearrangement. The most apparent difference was that $AlMe_3$ must be used in stoichiometric quantities for 3-aza-Cope rearrangement to reach completion. These observations suggest that the aluminum reagent formed a complex with the nitrogen of the imine product (**5**) that was not easily recycled to form the complex with substrate **4**. Although requiring 1.0 equiv of $AlMe_3$ places a limitation on this methodology, this same affinity for nitrogen may be directly related to the effectiveness of this reagent. As has been demonstrated, enamine substrates which were more subject to electrophilic attack at carbon, such as **18** and **24**, react through alternate pathways with HCl and $TiCl_4$.[30] However, the differing properties of the Lewis acid/base interaction of the aluminum with the enamines made this reagent much more compatable with sensitive enamine substrates. As a result, $AlMe_3$ was a versatile and efficient reagent for carbon–carbon bond formation through the charge-accelerated 3-aza-Cope rearrangement with all substrates tested.

Summary

Acceleration of the 3-aza-Cope rearrangement of the *N*-alkyl-*N*-allylenamines derived from isobutyraldehyde was accomplished at temperatures as low as 25 °C, which represents a decrease in reaction temperature of greater than 200 °C from that of the thermal rearrangement. A variety of catalysts, including protic acids (HCl), transition-metal halides ($TiCl_4$, BF_3, $ZnCl_2$), and organometallic reagents ($X_nAlMe_{(3-n)}$), effectively promoted rearrangement of the *N*-alkyl-*N*-allylenamine to the corresponding imine. Each type of electrophilic reagent demonstrated different stoichiometry requirements, from 0.1 to 1.0 equiv, for complete conversion of substrate to product. Reduction of the intermediate imine, without prior isolation, gave **14** in 59 to 99% isolated yields for the two-step process from **12**. The substitution pattern of the enamine substrates was critical to successful 3-aza-Cope rearrangement by HCl and $TiCl_4$, but $AlMe_3$ produced efficient product formation with even the most sensitive enamine substrates.

Experimental Section

General Methods. All reactions were carried out performing standard inert atmosphere techniques to exclude moisture and oxygen, and reactions were performed under an atmosphere of either nitrogen or argon. Benzene, toluene, tetrahydrofuran (THF), and Et_2O were distilled from sodium/benzophenone immediately prior to use. Triethylamine was heated at reflux over calcium hydride for a minimum of 12 h and then distilled immediately prior to use. Solutions of HCl (1.0 M in Et_2O), $LiAlH_4$ (1.0 M in THF), and Cl_2AlMe (1.0 M in hexanes) were obtained from Aldrich Chemical Co. Solutions of $AlMe_3$ and $ClAlMe_2$ (1.0 M in toluene) were prepared from neat organoaluminum compounds obtained from Aldrich Chemical Co. Cyclohexanecarbonyl chlorides, isobutyryl chloride, allyl amine, $TiCl_4$, and $Et_2O{\cdot}BF_3$ were distilled prior to use. Additions were made with gas tight

(27) The use of other hydride reducing agents to achieve greater selectivity is currently being investigated.

(28) Tertiary amine **18** was prepared through an independent route. *N*-allylcyclopentylamine was made by $LiAlH_4$ reduction of the imine formed from allylamine and cyclopentanone. Reaction with 2-methylpropanoyl chloride and NEt_3 gave the corresponding secondary amide, which was reduced to **18** with $LiAlH_4$.

(29) A mixture of products was obtained by distillation (40–44% mass recovery), and the individual yields were calculated on the contribution of each compound to this purified product mixture.

(30) For discussions of N- versus C-protonation of enamines, see: (a) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975. (b) Hinman, R. L. *Tetrahedron* **1968**, *24*, 185, and references therein.

syringes or via cannula transfer under nitrogen. Unless specified, concentration of solutions after workup was performed on a Büchi rotary evaporator.

Gas chromatographic (GLC) analyses were carried out on a Perkin-Elmer 8500 instrument with a 50 m RSL-200 capillary column (5% methyl phenyl silicone), an FID detector at a 220 °C injector temperature, and a 300 °C detector temperature. Helium gas pressure was set at 15 psi with a flow rate of 2 mL/min. NMR spectra were obtained on Varian Gemini 300 or VRX-300 spectrometers with $CDCl_3$ as solvent. Data are reported as follows: chemical shift relative to residual $CHCl_3$ (7.24 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet), integration, and coupling. Infrared spectra were recorded on a Nicolet 42 FT-IR instrument.

***N*-Allylisobutylideneamine (6).** Allylamine (3.54 g, 62 mmol) was added to a flask containing 100 mL of Et_2O and 14 g of 4-Å molecular sieves. Over the period of 10 min, isobutyraldehyde (4.47 g, 62 mmol) was added dropwise at 25 °C. After being stirred at ambient temperature overnight, the solution was filtered and the remaining solids were washed with two 50-mL portions of Et_2O. The mixture then was distilled under nitrogen at atmospheric pressure to give **6** (5.13 g, 46.0 mmol) in 75% yield (bp 112–114 °C): ^1H NMR (300 MHz) ($CDCl_3$) δ 1.05 (d, 6 H, J = 6.9 Hz), 2.42 (dsept, 1 H, J = 4.9, 6.9 Hz), 3.95 (d, 2 H, J = 5.6 Hz), 5.05 (dd, 1 H, J = 1.8, 10.3 Hz), 5.10 (dd, 1 H, J = 1.8, 17.2 Hz), 5.93 (ddt, 1 H, J = 10.3, 17.2, 5.6 Hz), 7.51 (d, 1 H, J = 4.9 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 19.3, 34.1, 63.2, 115.5, 136.1, 170.9; IR (neat) 3083, 3013, 2967, 2932, 2874, 2824, 2674, 1466, 1456, 1437, 1366, 1103, 1019, 995, 916 cm^{-1}.

Synthesis of 7 by Acylation of 6. To 50 mL of dry THF were added **6** (3.34 g, 30 mmol) and NEt_3 (3.54 g, 33 mmol). The solution was cooled to 0 °C, and isobutyryl chloride (3.50 g, 33 mmol) in 20 mL of THF was added dropwise over a 30-min period. After being heated at reflux for 1.5 h, the solution was cooled to ambieng temperature and filtered through a pad of silica on a glass frit, and the solids were washed with two portions of Et_2O. The solvents were removed under reduced pressure, and the crude oil was purified by flash column chromatography (silica, 230–400 mesh; eluent 50:50 Et_2O–petroleum ether). The solvents were evaporated, and the enamide was isolated via Kugelrohr distillation under vacuum to give **7** (4.88 g, 27 mmol) in 90% yield (bp 55–65 °C (<1 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 1.02 (d, 6 H, J = 6.8 Hz), 1.57 (s, 3 H), 1.70 (s, 3 H), 2.65 (sept, 1 H, J = 6.8 Hz), 3.89 (d, 2 H, J = 6.2 Hz), 5.04 (dd, 1 H, J = 1.6, 11.3 Hz), 5.06 (dd, 1 H, J = 1.6, 16.0 Hz), 5.74 (ddt, 1 H, J = 11.3, 16.0, 6.2 Hz), 5.85 (s, 1 H); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 17.3, 18.8, 21.5, 30.9, 50.0, 116.9, 123.5, 133.4, 135.9, 177.7; IR (neat) 3083, 2975, 2936, 2876, 1653, 1472, 1404, 1242, 1208, 1092, 993, 920 cm^{-1}. Anal. Calcd for $C_7H_{15}N$: C, 74.27; H, 13.36; N, 12.37. Found: C, 74.43; H, 13.69; N, 12.21.

Reduction of 7 to 8. To a flask containing $LiAlH_4$ (2.51 g, 66 mmol) was added 300 mL of Et_2O, and the suspension was cooled to 0 °C. Amide **7** (10.87 g, 60 mmol) in 30 mL of Et_2O was added dropwise over a 45-min period. The solution was warmed to room temperature and stirred for 6 h. After the solution was cooled to 0 °C, the reaction was quenched by addition of 2.5 mL of H_2O, followed by 2.5 mL of 15% aqueous NaOH, and then again by 7.5 mL of H_2O. The solution was stirred for 1.5 h and then dried with K_2CO_3. The solids were removed by filtration, and the solvent was removed under reduced pressure. Enamine **8** was isolated via Kugelrohr distillation (bp 54–55 °C (8 mmHg), 9.84 g, 98% yield): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.83 (d, 6 H, J = 6.6 Hz), 1.58 (d, 3 H, J = 1.3 Hz), 1.58 (tsept, 1 H, J = 7.3, 6.6 Hz), 1.65 (d, 3 H, J = 1.3 Hz), 2.25 (d, 2 H, J = 7.3 Hz), 3.15 (dt, 2 H, J = 1.6, 1.6, 6.2 Hz), 5.02 (ddt, 1 H, J = 2.0, 10.2, 1.6 Hz), 5.08 (ddt, 1 H, J = 2.0, 17.2, 1.6 Hz), 5.22 (qq, 1 H, J = 1.3, 1.3 Hz), 5.81 (ddt, 1 H, J = 10.2, 17.2, 6.2 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 17.4, 20.4, 22.0, 27.4, 59.6, 63.1, 115.9, 122.8, 135.8, 136.9; IR (neat) 3081, 3009, 2955, 2926, 2870, 2803, 1676, 1644, 1468, 1449, 1377, 1337, 1194, 1117, 1101, 995, 916 cm^{-1}.

General Procedure for Rearrangement of 8 to 9. All flasks used in rearrangement studies were heated under vacuum for 20–30 min and then purged with argon for 10 min. A solution containing **8** (0.167 g, 1 mmol), *o*-xylene (0.121 mL, 1 mmol, internal GLC standard), and 5 mL of toluene was cooled to −78 °C. After an initial gas chromatograph was taken, the Lewis acid reagents (see Tables I and II for equiv) were added at −78 °C or the HCl was added at 0 °C or the HCl was added at 0 °C. For Cl_3Al and $(ArO)_2AlMe$ accelerated reactions, a solution of **8** was added to the catalyst in 25 mL of toluene via cannula at −78 °C. All aliquots for analysis were removed from the reaction vessel via cannula, quenched in Et_2O with 10% w/v solution of NaOMe in MeOH, and dried over Na_2SO_4 or K_2CO_3 prior to GLC analysis.

Preparation of 11 by Acylation of 6. Imine **6** (2.44 g, 22 mmol) and NEt_3 (3.69 mL, 26.4 mmol) were taken up in 150 mL of THF and cooled to 0 °C. Cyclohexanecarbonyl chloride (3.50 g, 24 mmol) in 35 mL of THF was added dropwise over a 2-h period. The reaction was allowed to warm to room temperature during the addition and then was brought to reflux for 2.5 h. After the solution was cooled to ambient temperature, solids were removed by filtration through a pad of silica on a glass frit and then washed with two portions of Et_2O. The solvents were removed via rotary evaporation, and the remaining oil was purified by column chromatography (silica, 230–400 mesh; eluent 30:70 Et_2O–petroleum ether) and isolated via Kugelrohr distillation to give **11** (75–100 °C, (<1 mmHg), 3.35 g, 69% yield): ^1H NMR (300 MHz) ($CDCl_3$) δ 1.21 (m, 4 H), 1.43 (m 2 H), 1.61 (m, 4 H), 1.60 (s, 3 H), 1.75 (s, 3 H), 2.38 (m, 1 H), 3.96 (d, 1 H, J = 6.2 Hz), 5.02 (d, 1 H, J = 11.5 Hz), 5.04 (d, 1 H, J = 15.8 Hz), 5.72 (ddt, 1 H, J = 11.5, 15.8, 6.2 Hz), 5.82 (s, 1 H). ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 17.6, 21.8, 25.7, 28.9, 41.5, 50.0, 116.7, 123.3, 133.3, 135.9, 176.0. IR (neat) 3101, 2930, 2855, 1653, 1451, 1427, 1342, 1256, 1206, 1123, 990, 918, 895, 831 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.54; H, 10.28; N, 7.72.

Two-Step Synthesis of 11 from Allylamine. Allylamine (2.20 g, 30.0 mmol) and isobutyraldehyde (1.74 g, 30.0 mmol) were taken up in 85 mL of benzene. A Dean-Stark trap was fitted on the apparatus, and the solution was heated to reflux to azeotropically remove the resulting water. After being heated 19–22 h, the water was removed, 4-Å molecular sieves were added to the Dean-Stark trap, and reflux was continued for 2 h. The solution was cooled to ambient temperature, and NEt_3 (3.03 g, 30.0 mmol) and cyclohexanecarbonyl chloride (4.40 g, 30.0 mmol) were added, sequentially, and then heated at reflux for 3 h. After benzene was removed under reduced pressure, the crude oil was purified by flash column chromatography (silica, 230–400 mesh; eluent 30:70 Et_2O–petroleum ether). The solvents were evaporated, and the enamide was distilled under vacuum to give 4.53 g of **11** (20.5 mmol, 68% yield). Spectroscopic data was identical to that reported for the product obtained by acylation of isolated **6**.

Reduction of 11 to 12. Enamide **11** (4.71 g, 21.0 mmol) in 40 mL of Et_2O was added dropwise to a suspension of $LiAlH_4$ (0.89 g, 23.0 mmol) in 300 mL of Et_2O at 0 °C over a 1-h period. The reaction mixture was warmed to room temperature and then stirred for 5 h. The $LiAlH_4$ was quenched at 0 °C through slow addition of 0.9 mL of H_2O, 0.9 mL of 15% NaOH, and then 2.7 mL of H_2O. After being stirred for 1 h, the solids were removed by filtration, and the solvents were removed via rotary evaporation to give an oil. The oil was isolated via Kugelrohr distillation to give 4.15 g of **12** (70–80 °C (5 mmHg), 95% yield): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.83 (m, 2 H), 1.15 (m 4 H), 1.30 (m, 1 H), 1.59 (s, 1 H), 1.65 (s, 3 H), 1.75 (s, 3 H), 2.30 (d, 2 H, J = 7.2 Hz), 3.14 (d, 2 H, J = 6.1 Hz), 5.02 (dd, 1 H, J = 10.2, 2.0 Hz), 5.09 (dd, 1 H, J = 17.3, 2.0 Hz), 5.22 (s, 1 H), 5.81 (ddt, 1 H, J = 17.3, 10.2, 6.1). ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 17.6, 22.3, 26.2, 26.9, 31.6, 37.1, 59.6, 61.9, 115.7, 122.0, 135.7, 136.8; IR (neat) 3091, 2923, 2851, 2797, 1650, 1600, 1449, 1374, 1337, 1283, 1263, 1178, 1123, 993, 9163, 843 cm^{-1}.

Representative Procedure for Charge-Accelerated 3-Aza-Cope Rearrangement and Reductive Workup (12 to 14). All flasks used in rearrangement studies were heated under vacuum for 20–30 min and purged with argon for 10 min. The electrophilic reagents (see Tables I and II for equiv) were added to a solution containing **12** (1.04 g, 5.0 mmol) in 25 mL of toluene to give a final concentration of 0.2 M of **12**. Lewis acids were added at −78 °C, and HCl was added at 0 °C. For Cl_3Al and $(ArO)_2AlMe$ accelerated reactions, a solution of **12** was added to the catalyst in 25 mL of toluene via cannula at −78 °C. The reaction mixture was heated until complete conversion of **12** to **13** had occurred

(see Tables I and II for temperatures and reaction times). Following rearrangement, the reaction was placed in an ice bath, and 5.5 mL of 1.0 M $LiAlH_4$ solution was added.[31] After 3 h, the reduction was quenched at 0 °C through slow addition of 0.2 mL of H_2O, 0.2 mL of 15% NaOH, and then 0.6 mL of H_2O. The solids were removed by filtration through sodium sulfate on a glass frit. Solvents were removed by rotary evaporation and the oil was isolated via Kugelrohr distillation to give **14**.

14: (bp 70–80 °C (<1 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.89 (s, 6 H), 1.31 (m 4 H), 1.40 (m, 1 H), 1.72 (m, 6 H), 1.96 (d, 2 H, J = 7.5 Hz), 2.28 (s, 2 H), 2.37 (d, 2 H, J = 6.8 Hz), 4.97 (d, 1 H, J = 16.6 Hz), 4.98 (d, 1 H, J = 12.2 Hz), 5.78 (ddt, 1 H, J = 16.6, 12.2, 7.5 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 25.5, 26.1, 26.8, 31.4, 37.6, 44.7, 57.8, 60.5, 116.6, 135.7; IR (neat) 3350, 3074, 2923, 2853, 2807, 2753, 1639, 1462, 1447, 1364, 1127, 995, 913 cm^{-1}. Anal. Calcd for $C_{14}H_{27}N$: C, 80.31; H, 13.00; N, 6.70. Found: C, 79.00; H, 12.49; N, 6.85.

10: (bp 50–60 °C (8 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.85 (s, 6 H), 0.86 (d, 6 H, J = 6.6 Hz), 0.87 (bs, 1 H), 1.71 (tsept, 1 H, J = 6.9, 6.6 Hz), 1.98 (d, 2 H, J = 7.5 Hz), 2.29 (s, 2 H), 2.35 (d, 2 H, J = 6.9 Hz), 4.99 (m, 2 H), 5.79 (ddt, 1 H, J = 9.2, 17.9, 7.5 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 20.6, 25.5, 27.9, 34.4, 44.7, 59.1, 60.3, 116.6, 135.7; IR (neat) 3359, 3077, 3005, 2957, 2872, 2811, 1640, 1466, 1385, 1364, 1121, 995, 912 cm^{-1}. Anal. Calcd for $C_{11}H_{23}N$: C, 78.04; H, 13.69; N, 8.27. Found: C, 77.64; H, 13.87; N, 7.68.

17: (bp 60–70 °C (<1 mmHg): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.75 (d, 3 H, J = 6.6 Hz), 0.77 (d, 3 H, J = 6.6 Hz), 0.88 (bs, 1 H), 1.34 (s, 3 H), 1.63 (tsept, 1 H, J = 6.8, 6.6 Hz), 2.29 (dd, 1 H, J = 11.8, 6.8 Hz), 2.32 (dd, 1 H, J = 11.8, 6.8 Hz), 2.35 (dd, 1 H, J = 7.6, 13.8 Hz), 2.52 (dd, 1 H, J = 6.6, 13.8 Hz), 2.63 (d, 1 H, J = 11.5 Hz), 2.80 (d, 1 H, J = 11.5 Hz), 4.94 (d, 1 H, J = 10.0 Hz), 4.99 (d, 1 H, J = 17.1 Hz), 5.57 (dddd, 1 H, J = 10.0, 17.1, 7.6, 6.6 Hz), 7.25 (m, 5 H); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 20.2, 23.2, 27.6, 41.7, 45.0, 58.6, 60.6, 117.2, 126.0, 126.7, 128.4, 135.3, 146.5; IR (neat) 3337, 3061, 3025, 2957, 2928, 2872, 2811, 1640, 1601, 1497, 1466, 1447, 1379, 1123, 959 cm^{-1}. Anal. Calcd for $C_{16}H_{25}N$: C, 83.06; H, 10.89; N, 6.05. Found: C, 82.73; H, 10.93; N, 6.08.

20: (bp 70–80 °C (8 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.85 (t, 3 H, J = 7.4 Hz), 0.85 (d, 6 H, J = 6.6 Hz), 1.29 (m, 2 H), 1.48 (ddq, 1 H, J = 6.4, 6.4, 7.4 Hz), 1.50 (ddq, 1 H, J = 6.4, 7.4 Hz), 1.69 (tsept, 1 H, J = 6.7, 6.6 Hz), 2.04 (dddd, 2 H, J = 1.3, 1.3, 6.1, 7.2 Hz), 2.34 (d, 2 H, J = 6.7 Hz), 2.44 (d, 1 H, J = 6.4 Hz), 2.45 (d, 1 H, J = 6.4 Hz), 4.95 (ddt, 1 H, J = 1.1, 10.0, 1.3 Hz), 4.99 (ddt, 1 H, J = 1.1, 17.2, 1.3 Hz), 5.76 (ddt, 1 H, J = 10.0, 17.2, 7.2 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 10.8, 20.4, 24.3, 28.0, 36.3, 39.3, 53.0, 58.3, 115.8, 137.5; IR (neat) 3418, 3079, 2959, 2928, 2874, 2813, 1640, 1466, 1381, 1366, 1125, 995, 911 cm^{-1}. Anal. Calcd for $C_{11}H_{23}N$: C, 78.04; H, 13.69; N, 8.27. Found: C, 77.65; H, 13.66; N, 8.25.

23: (bp 40–50 °C (<1 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$, major diastereomer) δ 0.87, (d, 6 H, J = 6.6 Hz), 1.30 (m, 4 H), 1.50 (m, 4 H), 1.67 (m, 3 H), 1.95 (m, 1 H), 2.15 (m, 1 H), 2.26 (dd, 1 H, J = 6.8, 11.3 Hz), 2.38 (dd, 1 H, J = 6.8, 11.3 Hz), 2.59 (m, 1 H), 4.93 (ddt, 1 H, J = 1.1, 10.3, 1.4 Hz), 4.98 (ddt, 1 H, J = 1.1, 16.8, 1.4 Hz), 5.75 (ddt, 1 H, J = 10.3, 16.8, 6.7 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 20.6, 22.5, 23.0, 27.1, 28.4, 28.8, 33.4, 39.1, 55.4, 57.1, 115.3, 138.6; IR (neat) 3359, 3077, 2928, 2859, 2805, 1642, 1470, 1366, 1130, 1103, 993, 909 cm^{-1}. Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 80.16; H, 12.03; N, 7.47.

26: (bp 30–40 °C (<1 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$, major diastereomer) δ 0.86 (d, 6 H, J = 6.7 Hz), 1.43 (m, 3 H), 1.65 (m, 4 H), 1.90 (m, 2 H), 2.17 (m, 2 H), 2.27 (dd, 1 H, J = 6.9, 11.5 Hz), 2.39 (dd, 1 H, J = 6.6, 11.5 Hz), 2.96 (dt, 1 H, J = 5.8, 6.0 Hz), 4.94 (dd, 1 H, J = 1.2, 10.1 Hz), 5.00 (dd, 1 H, J = 1.2, 17.1 Hz), 5.79 (ddt, 1 H, J = 10.1, 17.1, 6.7 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 20.6, 21.0, 28.3, 30.7, 32.7, 41.9, 56.5, 61.5, 115.1, 138.7; IR (neat) 3349, 3077, 2955, 2870, 2011, 1642, 1470, 1387, 1366, 1138, 993, 911 cm^{-1}. Anal. Calcd for $C_{12}H_{23}N$: C, 79.49; H, 12.79; N, 7.72 Found: C, 79.17; H, 12.70; N, 7.68.

Preparation of *N*-Allyl-*N*-cyclopentylamine. Allylamine (5.71 g, 100 mmol), cyclopentanone (8.41 g, 100 mmol), and benzene (300 mL) were added to a flask fitted with a Dean-Stark trap, and the solution was then heated at reflux for 15 h. The water was drained from the trap, and 4-Å molecular sieves were added. Reflux was continued for 2 h more to remove the final traces of water from the reaction mixture. The benzene was removed by distillation, and the remaining oil was isolated via Kugelrohr distillation to give *N*-allylcyclopentylideneamine (8.09 g, 66 mmol) in 66% yield (50–70 °C (10–15 mmHg)).

To a suspension of 1.82 g (48 mmol) $LiAlH_4$ in 200 mL of Et_2O was added 4.93 g (40 mmol) of *N*-allylcyclopentylideneamine. The solution was stirred for 4 h at ambient temperature and was then quenched with 1.8 mL of H_2O, followed by 1.8 mL of 15% aqueous NaOH, and then by 5.4 mL of H_2O. After being stirred for 1 h, the solution was filtered to remove the aluminum salts and the solvent concentrated to an oil, which was distilled under vacuum to give *N*-allyl-*N*-cyclopentylamine (4.36 g, 35 mmol) in 87% yield (60–70 °C (15 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 1.28 (m, 2 H), 1.50 (m, 3 H), 1.64 (m, 2 H), 1.81 (m, 2 H), 3.06 (tt, 1 H, J = 6.7, 6.8 Hz), 3.20 (ddd, 2 H, J = 1.2, 1.2, 6.1 Hz), 5.03 (ddt, 1 H, J = 1.3, 10.2, 1.2 Hz), 5.12 (ddt, 1 H, J = 1.3, 17.1, 1.2 Hz), 5.89 (ddt, 1 H, J = 10.2, 17.1, 6.1 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 24.0, 33.1, 51.3, 59.2, 115.5, 137.2.

***N*-Allyl-*N*-isobutylcyclopentylamine (27).** To a solution of *N*-allyl-*N*-cyclopentylamine (3.76 g, 30 mmol) and triethylamine (3.33 g, 33 mmol) was added isobutyryl chloride (3.20 g, 30 mmol) dropwise. The solution was stirred at ambient temperature for 5 h and then filtered through a pad of silica. Removal of solvent produced an oil, which was isolated via Kugelrohr distillation to give *N*-allyl-*N*-cyclopentylisobutyramide (5.14 g, 26.4 mmol) in 88% yield (75–85 °C (<1 mmHg)).

To a suspension of $LiAlH_4$ (0.912 g, 24 mmol) in 100 mL of Et_2O was added *N*-allyl-*N*-cyclopentylisobutyramide (4.00 g, 20.4 mmol) in a dropwise manner. After addition was complete, the solution was stirred at ambient temperature for 2 h. The reaction was quenched by addition of 0.9 mL of H_2O, followed by 0.9 mL of 15% aqueous NaOH, followed by 2.7 mL of H_2O, and was then stirred for 1 h. After removal of solids by filtration, the solvent was removed and the resulting oil was isolated via Kugelrohr distillation to give **27** (3.27 g, 20.4 mmol) in quantitative yield (50–65 °C (4 mmHg)): ^1H NMR (300 MHz) ($CDCl_3$) δ 0.84 (d, 6 H, J = 6.6 Hz), 1.35 (m, 2 H), 1.45 (m, 2 H), 1.59 (m, 2 H), 1.70 (m, 3 H), 2.14 (d, 2 H, J = 7.1 Hz), 3.00 (tt, 1 H, J = 7.3, 7.4, Hz), 3.11 (ddd, 2 H, J = 1.9, 2.1, 6.4 Hz), 5.04 (ddt, 1 H, J = 1.6, 10.2, 2.1 Hz), 5.12 (ddt, 1 H, J = 1.7, 17.1, 1.9 Hz), 5.87 (ddt, 1 H, J = 10.2, 17.1, 6.4 Hz); ^{13}C NMR (75.5 MHz) ($CDCl_3$) δ 21.0, 24.1, 26.9, 29.2, 55.7, 59.5, 63.7, 116.1, 136.8. Anal. Calcd for $C_{12}H_{23}N$: C, 79.48; H, 12.79; N, 7.72. Found: C, 79.36; H, 12.79; N, 7.99.

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(31) In situ reduction of rearrangements catalyzed by $TiCl_4$ were performed at −78 °C to avoid reduction of the alkene functionality by titanium hydride species.