Multicomponent Reactions Involving 2-Methyleneaziridines: Rapid Synthesis of 1,3-Disubstituted Propanones

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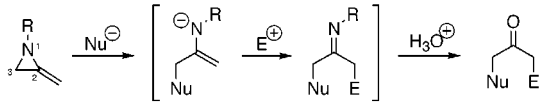
Ring opening of 1-alkyl-2-methyleneaziridines **1** or **2** is accomplished with organocopper reagents (R_2CuLi or RMgX/CuI) in the presence of boron trifluoride diethyl etherate giving 1-substituted propan-2-ones **3**−**9** in 42−88% yield. Ring opening with RMgCl/CuI in the absence of the Lewis acid allows further alkylation of the metalloenamine (metalated imine) intermediate in a regiocontrolled manner. The sequential formation of two new intermolecular carbon−carbon bonds in this reaction provides a rapid entry into a variety of 1,3-disubstituted propan-2-ones, including **11** and **14**−**23**. The scope and mechanism of this multicomponent reaction (MCR) has been assessed. It is established that this MCR tolerates alkyl, aryl, and benzylic Grignard reagents and a wide range of electrophiles, including alkyl iodides, bromides, and tosylates, as well as epoxides and aldehydes. In addition, *gem*-dimethyl substitution on the exocyclic double bond of the 2-methyleneaziridine is tolerated. This MCR has been applied to the one-pot synthesis of (*Z*)-6-heneicosen-11-one, **25**, an important sex attractant of the Tussock moth. Using 3-deuterio-1-(1-phenylethyl)-2-methyleneaziridine, **26**, we determined that this MCR occurs predominantly by direct ring opening at the sp^3-hybridized aziridine carbon atom (C-3).

Introduction

Multicomponent reactions (MCRs) are emerging as important tools for the efficient synthesis of a wide variety of organic molecules.[1] Such reactions offer a number of practical, environmental, and economic advantages over more traditional approaches to the construction of complex molecular architectures. While numerous MCRs have been devised, relatively few processes that result in the formation of two or more intermolecular carbon−carbon bonds are known. As part of a program centered on the development of new synthetic methods based on the highly strained yet readily accessible 2-methyleneaziridine ring system,[2] we wondered whether these heterocycles could be used to develop a novel and potentially general MCR leading to the construction of two new carbon−carbon bonds. The idea was to open a 2-methyleneaziridine with a nucleophile to produce a transient metalloenamine (metalated imine) that might be further C-alkylated with an electrophile to yield a 1,3-disubstituted propanone after imine hydrolysis (Scheme 1). This method is attractive as considerable variation in this MCR can be imagined.

Scheme 1



Most obviously, the structure of the nucleophile and the electrophile could be changed to make a wide range of 1,3-disubstituted propanones. Furthermore, 2-methyleneaziridines bearing substitutents at C-3[3] or on the exocyclic double bond are known;[4] thus, further substituents could conceivably be incorporated at C-1 or C-3 of the ketone products by opening more highly substituted derivatives. Additionally, by reduction of the intermediate imine, access to the corresponding amines might be possible, further increasing the utility of this MCR.[5]

If two carbon−carbon bonds are to be produced in the MCR depicted in Scheme 1, an organometallic reagent must be employed as the nucleophilic component. Since 2-methyleneaziridines bearing electron-withdrawing groups (EWGs) on the nitrogen are not readily accessible,[6] this necessitates ring opening of an essentially unactivated aziridine (R ≠ EWG). Few examples of organometallic ring-opening reactions of unactivated

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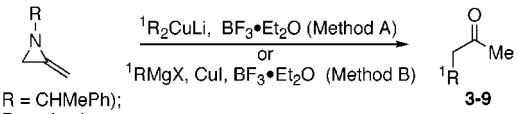
aziridines are known,[7] although we anticipated that the increased ring strain energy of 2-methyleneaziridine compared to aziridine (12−13 kcal/mol; HF/6-31G*)[8] might work to our advantage. A few ring-opening reactions of 2-methyleneaziridines have been reported previously.[9−11,2c,e,3a] Of most relevance, Quast has proposed that the decomposition of 3-lithio-1-*tert*-butyl-2-methyleneaziridine involves nucleophilic ring opening of 1-*tert*-butyl-2-methyleneaziridine by this organolithium species with concurrent carbon−carbon bond formation.[3a] In light of these observations, we felt that opening of a 2-methyleneaziridine with a suitable organometallic reagent should be feasible, allowing for the realization of the MCR depicted in Scheme 1. In this article, we describe in detail our observations concerning the ring-opening reactions of 2-methyleneaziridines with organocopper reagents and the use of this MCR strategy to make a wide variety of 1,3-disubstituted propanones.[12]

Results and Discussion

The most convenient and efficient method for the synthesis of 2-methyleneaziridines involves ring closure of the corresponding *N*-(2-bromoallyl)alkylamines with sodium amide in liquid ammonia.[9,13,14] 1-(1-Phenylethyl)-2-methyleneaziridine **1**[2a] and 1-cyclohexyl-2-methyleneaziridine **2**[2e] used extensively in this study were made in good yields by this method. As the first step toward realizing the proposed MCR, we examined conditions for effecting simple opening of the 2-methyleneaziridine ring with simultaneous carbon−carbon bond formation. Since Ganem has shown that *N*-alkylated aziridines can be ring opened with Gilman-type cuprates in the presence of BF_3·Et_2O,[15] we anticipated that these conditions might effect ring opening of 2-methyleneaziridines. Treatment of methyleneaziridine (±)-**1** with dibutyl copper lithium (1.5 equiv) and BF_3·Et_2O (1.5 equiv) in THF (−78 → −10 °C) and subsequent hydrolysis furnished heptan-2-one **3** in 42% isolated yield after bulb-to-bulb distillation (Table 1, entry 1). In fact, this transformation can be accomplished more conveniently, and in higher yield, using butylmagnesium chloride in the presence of BF_3·Et_2O and a catalytic amount of copper(I) iodide (5 mol %) in THF (−30 → 0 °C) over 1 h (Table 1, entry 2). The modest isolated yields of heptan-2-one **3** obtained in these two reactions are largely due to its volatility, as the chemical conversion is good as judged by GC analysis. Further studies using the RMgX/BF_3·Et_2O/CuI method (Method B) established that it is quite general, and a variety of methyl ketones **3**−**9** can be made in moderate to good yields (Table 1). Similar yields were obtained using

Table 1. Copper-Catalyzed Ring Opening of 2-Methyleneaziridines in the Presence of Boron Trifluoride Diethyl Etherate

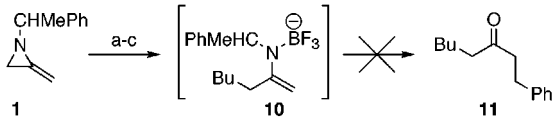


1 (R = CHMePh); **2** (R = *c*-hex) **3-9**

entry	aziridine	method	R^1	product (%)
1	**1**	A	$-(CH_2)_3CH_3$	**3** (42{73[a]})
2	**1**	B	$-(CH_2)_3CH_3$	**3** (56{90[a]})
3	**1**	B	$-(CH_2)_7CH_3$	**4** (82)
4	**1**	B	$-Ph$	**5** (65)
5	**1**	B	$-CH_2Ph$	**6** (70)
6	**1**	B	−cyclohexyl	**7** (49)
7	**1**	B	$-C_6H_4OMe$	**8** (60)
8	**1**	B	$-(CH_2)_6CH{=}CH_2$	**9** (88)
9	**2**	B	$-(CH_2)_7CH_3$	**4** (85)

[a] GC yield determined using nonane as the internal standard.

Scheme 2[a]



1 **10** **11**

[a] Reagents and conditions: (a) BuMgCl, CuI (5 mol %), BF_3·Et_2O, THF, −30 → 0 °C, 1 h; (b) $PhCH_2Cl$, room temperature, 20 h; (c) aq HCl, room temperature, 2 h.

N-cyclohexyl-2-methyleneaziridine **2** (entry 3 cf entry 9). The use of other N-substituents has not been examined at this point in time. Notably, in the absence of either the BF_3·Et_2O or the CuI, ring opening does not occur to any great extent at −30 °C. If just the CuI is omitted, and the reaction mixture is warmed to 0 °C over 1 h, then ring opening is observed, albeit in much lower yield. For example, in experiments performed in parallel, undecan-2-one **4** was formed in 67% isolated yield with added CuI (5 mol %) and in just 17% yield with no added CuI.

Encouraged by our initial results, we set about trying to realize the MCR depicted in Scheme 1. However, attempts to alkylate the presumed metalloenamine intermediate produced by ring opening of methyleneaziridine **1** with RMgX/BF_3·Et_2O/CuI were completely unsuccessful. Introduction of an electrophile such as benzyl chloride into the vessel prior to aqueous (aq) hydrolysis did not result in the formation of the expected 1-phenyloctan-3-one **11**. Similar experiments performed using more reactive electrophiles (e.g., MeI or $PhCH_2Br$) or employing additives such as DMPU also failed to promote the alkylation step. To account for this lack of reactivity, we suggest that the stable boron "ate" complex **10** is formed (Scheme 2).

To substantiate this proposal, we sought to ascertain if a metalloenamine generated by the traditional method of imine deprotonation[16] would also be deactivated by the presence of BF_3·Et_2O. Treatment of heptan-2-one *tert*-butylimine **12**[17] with EtMgBr and then benzyl chloride yielded an inseparable mixture of ketones **11** and **13** in an unoptimized 51% yield after acidic hydrolysis. ^1H NMR and GC analysis indicated that **13** was predominant (**11**:**13** = 2:3) (Scheme 3). Significantly, when BF_3·

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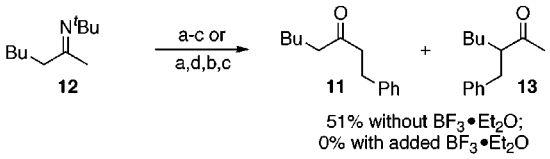
Scheme 3[a]



[a] Reagents and conditions: (a) EtMgBr, THF, reflux, 18 h; (b) $PhCH_2Cl$, reflux, 20 h; (c) aq HCl, reflux, 2 h; (d) $BF_3{\cdot}Et_2O$ (1.5 equiv), 15 min.

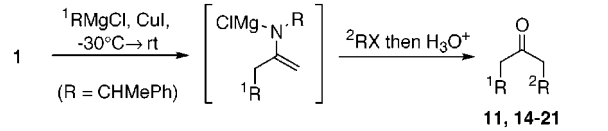
Et_2O (1.5 equiv) was added to the reaction prior to addition of benzyl chloride, **11** and **13** could not be observed by either ^1H NMR or GC-MS analysis. Thus, we conclude that $BF_3{\cdot}Et_2O$ efficiently suppresses the reactivity of metalloenamines, a finding consistent with our earlier failed attempts to achieve a MCR (Scheme 2).

On the basis of these initial findings, we concluded that it would be necessary to effect opening of 2-methyleneaziridines with organometallic reagents in the absence of an added Lewis acid. After further experimentation, we determined that the ring opening could be effectively achieved using just the Grignard reagent in the presence of CuI (20 mol %) by warming the mixture to room temperature and stirring for an extended period (24 h) prior to introduction of the electrophile. Using these conditions, treatment of methyleneaziridine **1** with BuMgCl and then $PhCH_2Cl$ yielded alkylated ketone **11** in 70% isolated yield after imine hydrolysis and silica gel chromatography (Table 2, entry 1). Significantly, the formation of **11** occurs in a highly regiocontrolled fashion, and no trace of 3-benzyl-heptan-2-one **13** could be detected in the crude reaction mixture by GC analysis. This finding reveals one important advantage of our MCR over the traditional approach to metalloenamines by way of imine deprotonation. In this latter method, even by careful choice of the reaction conditions, it is not always possible to achieve complete regiocontrol in the deprotonation of unsymmetrical imines.[18,19] At this juncture, it is worth noting that other copper(I) salts, namely, CuBr, $CuBr{\cdot}SMe_2$, CuCN, and CuI/Cu (1:3), can be used to effect ring opening of **1** in the presence of BuMgCl. However, none of these catalysts are as effective as CuI.

If the MCR proceeds through a genuine metalloenamine intermediate, one would expect a wide variety of electrophiles (e.g., alkyl halides, epoxides, aldehydes, and nitriles) to be effective as traps.[16] Indeed, a variety of R−X reagents (X = Cl, Br, I, or OTs) have been used successfully (Table 2). Using 3-chloro-1-iodopropane (entry 10), we observed only displacement of the more reactive iodide leading to the chloroketone product, **21**. Furthermore, a variety of Grignard reagents can be employed. Moderate to good yields of products were obtained in all cases, and the method provides a flexible and concise approach to a variety of 1,3-disubstituted propanones, namely, **14**−**21**.

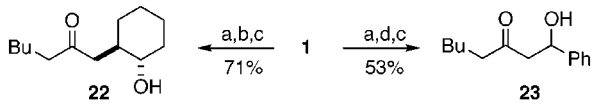
Other types of electrophiles can be used in this MCR beyond simple alkyl halides. Opening of **1** with BuMgCl

Table 2. Three-Component Coupling Reactions of 2-Methyleneaziridine 1 Using RX as the Electrophile (X = halogen or OTs)



entry	R^1	^{2}RX	product (%)
1	*n*-C_4H_9	$PhCH_2Cl$	**11** (70)
2	*n*-C_8H_{17}	$H_2C{=}CHCH_2Br$	**14** (80)
3	*n*-C_8H_{17}	$H_2C{=}CHCH_2CH_2OTs$	**15** (67)
4	$PhCH_2$	4-$MeC_6H_4CH_2Cl$	**16** (80)
5	$PhCH_2$	$PhCH_2Cl$	**17** (66)
6	*n*-C_4H_9	$TBDMSOCH_2CH_2CH_2Br$	**18** (58)
7	*n*-C_4H_9	$TBDMSOCH_2CH_2CH_2I$	**18** (65)
8	*c*-hex	$PhCH_2Cl$	**19** (57)
9	Ph	$H_2C{=}CHCH_2Br$	**20** (52)
10	Et	$ClCH_2CH_2CH_2I$	**21** (74)

Scheme 4[a]



[a] Reagents and conditions: (a) BuMgCl, CuI, THF, room temperature, 24 h; (b) cyclohexene oxide, −78 °C → room temperature, 18 h; (c) aq AcOH, hexane, 2 h, room temperature; (d) PhCHO, 40 °C, 2 h.

followed by quenching with cyclohexene oxide yielded γ-hydroxyketone **22** in 71% yield as a single diastereomer after imine hydrolysis (Scheme 4). We presume that trans opening of the epoxide occurs, leading to **22**, although we have not unambiguously confirmed this stereochemical assignment. Using benzaldehyde as the electrophile, we obtained β-hydroxyketone **23** in 53% yield. As this reaction generates a new asymmetric center, we wanted to establish if any useful levels of asymmetric induction could be obtained using an enantiopure 2-methyleneaziridine. In fact, β-hydroxyketone **23** produced from (*S*)-**1**[2a] displayed only modest enantiomeric enrichment (21% ee), as determined using chiral HPLC analysis (see Experimental Section). This low level of asymmetric induction is consistent with studies by Sugasawa and Toyoda,[20] who obtained 3-hydroxy-3-(4-nitrophenyl)-1-phenyl-propan-1-one in 19% ee using a similar "aldol-type" condensation of a metalloenamine controlled by an (*S*)-1-phenylethyl group on nitrogen. Thus, we conclude that useful levels of asymmetric induction at a remote stereocenter are not possible. However, we have observed excellent levels of stereocontrol (90% de) in related MCRs when the newly formed asymmetric center is much closer to the chiral nitrogen substituent.[5]

In a simple application of this MCR, we have devised a very short synthesis of (*Z*)-6-heneicosen-11-one, an important sex pheromone of the Tussock moth.[21] Treatment of (±)-**1** with nonylmagnesium chloride and copper(I) iodide in THF at room temperature and then tosylate **24**[22] (made in 88% yield from commercially available (*Z*)-

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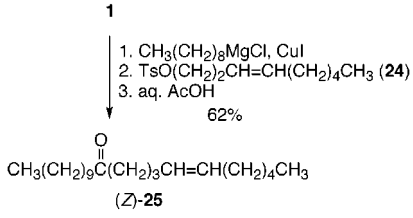
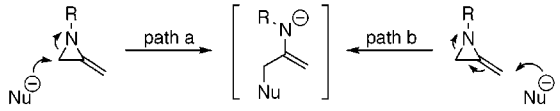
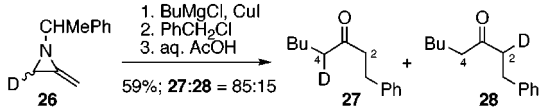
Scheme 5



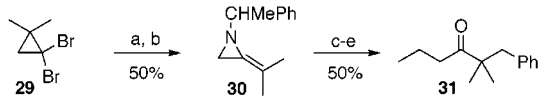
Scheme 6



Scheme 7



Scheme 8[a]



[a] Reagents and conditions: (a) $H_2NCHMePh$, 1,2-dichlorobenzene, 150 °C; (b) $NaNH_2$, NH_3; (c) CuI, EtMgCl, THF, 24 h, room temperature; (d) BnBr, 40 °C, 18 h; (e) aq HCl, 40 °C, 2 h.

3-nonen-1-ol) gave **25** in 62% yield (Scheme 5). (*Z*)-6-heneicosen-11-one **25** produced by this MCR displayed physical and spectroscopic data in very good agreement with published values (see Experimental Section).[23] In this example, MPLC was required to facilitate separation of **25** from (*Z*)-octadec-6-ene, produced as a result of direct coupling of $CH_3(CH_2)_8MgCl$ with **24**, and from octadecane, presumably a byproduct of Grignard formation. Direct reaction of the Grignard with the electrophile is a problem in these MCRs, although in most instances, this contaminant can conveniently be removed using simple flash chromatography. This side reaction arises because the MCRs are performed using excess Grignard reagent (2.5−3.0 molar equiv). To date, attempts to reduce the amount of Grignard to suppress this competing process have simply resulted in lower yields of the ketone product being isolated.

Work to investigate the mechanism of the aziridine ring-opening reaction has been undertaken. In principle, the intermediate metalloenamine produced in these MCRs could be generated by direct opening of the aziridine ring at the sp^3-hybridized carbon (Scheme 6, path a), or alternatively, by attack at the exocyclic alkene carbon by means of a "conjugate-type" process (Scheme 6, path b). In the context of 2-methyleneaziridine opening by alkyl chloroformates, we have previously established that ring opening occurs exclusively by direct opening (i.e., path a).[2c,e] However, in the metalloenamine chemistry described herein, where copper(I) salts are present, we felt that conjugate-type opening could not be discounted.

To help elucidate the mechanism of opening, we prepared C-3 deuterated methyleneaziridine **26** according to the published method by lithiation of **1** using *sec*-butyllithium followed by quenching with CD_3OD.[2e] Deuterium incorporation was confirmed by mass spectrometry {MH^+ = 161 (100%)}, and by reduction in the integral for the aziridine hydrogens. Both diastereomers of **26** were produced in a 3:1 ratio as judged by integration of the remaining aziridine signals at 2.11 ppm (0.75H) and 2.01 ppm (0.25H). Subjection of **26** to the standard MCR protocol using BuMgCl and $PhCH_2Cl$ yielded an inseparable mixture of deuterated ketones **27** and **28** in an 85:15 ratio. This conclusion was made on the basis of the following pieces of spectroscopic data. The presence of deuterium in the ketone product mixture was readily established by mass spectrometry {$M + NH_4^+$ = 223 (100%)}. In the ^{13}C NMR spectrum, the carbon at 43.0 ppm moved slightly upfield to 42.7 ppm and was observed as a triplet as a result of coupling to deuterium (J = 19.2 Hz). $^1H-^1H$ and $^1H-^{13}C$ correlation spectroscopy using nondeuterated ketone **11** enabled this carbon to be unambiguously assigned as C-4. Analysis of the ^1H NMR also indicated that the majority of the deuterium was located at C-4. The methylene signal at 2.41−2.32 ppm (H-4) integrated to just 1.15H, whereas that at 2.77−2.68 ppm (H-2) integrated to 1.85H. Consistent with this observation, the ^2H NMR revealed two broad singlets centered at 2.69 and 2.34 ppm in a 15:85 ratio. From this experiment, it is clear that ring opening of methyleneaziridine **1** by Grignard reagents in the presence of CuI occurs predominantly by direct attack at C-3 of the aziridine ring (Scheme 6, path a). The formation of **28** might indicate that the conjugate-type process (Scheme 6, path b) is occurring as a minor reaction pathway in these copper-catalyzed MCRs, although other mechanistic explanations for the formation of this product cannot be fully discounted.[24]

To further substantiate these mechanistic findings, we decided to examine if a methyleneaziridine bearing a *gem*-dimethyl group on the exocyclic double bond would participate in this MCR. (±)-Isopropylideneaziridine **30** was easily made in two steps from 1,1-dibromo-2,2-dimethylcyclopropane **29**[25] and (±)-1-phenylethylamine along similar lines to other known isopropylidineaziridines (Scheme 8).[4a−c] Treatment of **30** with EtMgCl and benzyl bromide gave ketone **31** in an unoptimized 50% yield after acidic hydrolysis. The formation of **31** is completely consistent with our mechanistic findings (vide supra). In this instance, none of the corresponding product derived from Grignard attack on the exocyclic double bond (Scheme 6, path b) was observed. This example establishes, for the first time, that highly substituted metalloenamines can be generated using this methodology.

(23) For previous syntheses of (*Z*)-6-heneicosen-11-one, see: (a) Smith, R. G.; Daves, G. D., Jr.; Daterman, G. E. *J. Org. Chem.* **1975**, *40*, 1593. (b) Mori, K.; Uchida, M.; Matsui, M. *Tetrahedron* **1977**, *33*, 385. (c) Konda, K.; Murahashi, S.-I. *Tetrahedron Lett.* **1979**, 1237. (d) Wang, K. K.; Chu, K.-H. *J. Org. Chem.* **1984**, *49*, 5175. (e) Ballini, R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1419. (f) Stowell, J. C.; Polito, M. A. *J. Org. Chem.* **1992**, *57*, 4560. (g) White, J.; Whiteley, C. G. *Synthesis* **1993**, 1141 and references therein.

(24) In unpublished findings, we have established that 2-aminoallyl cations can be generated from 2-methyleneaziridines in the presence of Lewis acids. Thus, the formation of **28** might be explained by the formation of a 2-amino-1-deuterio-allyl cation from **26** under the MCR conditions. This cation would be expected to undergo attack by BuMgCl with equal propensity at C-1 and C-3, ultimately leading to the formation of quantities of both **27** and **28**.

(25) Skattebol, L. *Acta Chem. Scand.* **1963**, *17*, 1683 and references therein.

Conclusion

In summary, we have devised a new regiocontrolled approach to metalloenamines via carbon−carbon bond formation that complements the original route to these carbanions introduced by Stork[26] and by Wittig.[27] Quenching of these intermediates with a variety of electrophiles provides a very direct entry into 1,3-disubstituted ketones. We believe this new type of MCR will find further applications in organic synthesis, and studies in this area are ongoing in our laboratories.

Experimental Section

General. All experiments were performed under an inert atmosphere in oven-dried glassware. Copper(I) iodide was purified prior to use.[28] Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. All other solvents and reagents were purified by standard protocols. Petroleum ether refers to that boiling in the range of 40−60 °C. Chromatography was performed on Fisher Matrex 60 silica gel. Other general details have been reported previously.[2e]

Ring Opening of 2-Methyleneaziridine (1 or 2) with RMgX/CuI in the Presence of Boron Trifluoride Diethyl Etherate (General Method 1). Copper(I) iodide (5 mol %) in a round-bottomed flask was heated under vacuum and then purged with nitrogen (three cycles were performed). Freshly distilled THF (2−4 mL) was added and the mixture cooled to −30 °C whereupon the Grignard reagent (3.0 molar equiv) was added. After stirring for 10 min, boron trifluoride diethyl etherate (1.5 molar equiv) was added dropwise. Methyleneaziridine **1**[2a] or **2**[2e] in THF (1−2 mL) was added and the mixture allowed to warm slowly to 0 °C over a 1 h period. Aqueous NH_4Cl (4 mL) was added and the mixture allowed to warm to room temperature and stirred for 1 h. The aqueous phase was extracted with diethyl ether (3 × 5 mL), and the combined organic fractions were washed with 0.1 M aq HCl (3 × 15 mL) and brine (3 × 15 mL) and dried ($MgSO_4$). Removal of the solvent and purification gave the title compounds.

Heptan-2-one, 3. To CuI (18 mg, 0.095 mmol), BuMgCl (2.0 M in THF, 2.83 mL, 5.66 mmol), and $BF_3{\cdot}Et_2O$ (0.36 mL, 2.84 mmol) in THF (4 mL) was added **1** (300 mg, 1.88 mmol) in THF (2 mL) according to General Method 1. Workup followed by bulb-to-bulb distillation (50 °C/water pump) afforded **3** (120 mg, 56%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) 2.41 (2H, t, J = 7.6 Hz), 2.13 (3H, s), 1.63−1.52 (2H, m), 1.38−1.20 (4H, m), 0.89 (3H, t, J = 6.8 Hz). This and other data were identical with those of a commercial sample of heptan-2-one.

Undecan-2-one, 4 from 1. To CuI (6 mg, 0.032 mmol), octylMgCl (2.0 M in THF, 0.95 mL, 1.90 mmol), and $BF_3{\cdot}Et_2O$ (0.12 mL, 0.95 mmol) in THF (2 mL) was added **1** (100 mg, 0.63 mmol) in THF (1 mL) according to General Method 1. Workup followed by bulb-to-bulb distillation (100 °C/water pump) afforded **4** (88 mg, 82%) as a colorless liquid: IR (film) 2925, 1718 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 2.41 (2H, t, J = 7.8 Hz), 2.12 (3H, s), 1.58−1.48 (2H, m), 1.32−1.15 (12H, m), 0.87 (3H, t, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 209.5, 43.8, 31.9, 29.9, 29.7, 29.4, 29.3, 29.2, 23.9, 22.7, 14.1; MS (CI) m/z 188 (M + NH_4^+); HRMS calcd for $C_{11}H_{26}NO$ 188.2014, found 188.2016.

Undecan-2-one, 4 from 2. To CuI (7 mg, 0.037 mmol), octylMgCl (2.0 M in THF, 1.09 mL, 2.18 mmol), and $BF_3{\cdot}Et_2O$ (0.14 mL, 1.10 mmol) in THF (2 mL) was added **2** (100 mg, 0.73 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5% EtOAc in petroleum ether) afforded **4** (105 mg, 85%) as a colorless liquid (data as described above).

1-Phenyl-propan-2-one, 5. To CuI (12 mg, 0.063 mmol), PhMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), and $BF_3{\cdot}Et_2O$ (0.24 mL, 1.89 mmol) in THF (2 mL) was added **1** (200 mg, 1.26 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5% EtOAc in petroleum ether) afforded **5** (110 mg, 65%) as a yellow oil: IR (film) 3023, 1721, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.42−7.20 (5H, m), 3.73 (2H, s), 2.18 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 206.5, 134.3, 129.4, 128.8, 127.1, 51.0, 29.3; MS (CI) m/z 152 (M + NH_4^+); HRMS calcd for $C_9H_{14}NO$ 152.1075, found 152.1075.

4-Phenyl-butan-2-one, 6. To CuI (6 mg, 0.032 mmol), $PhCH_2MgCl$ (2.0 M in THF, 0.94 mL, 1.88 mmol), and $BF_3{\cdot}Et_2O$ (0.12 mL, 0.95 mmol) in THF (2 mL) was added **1** (100 mg, 0.63 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5% EtOAc in petroleum ether) afforded **6** (65 mg, 70%) as a yellow oil: IR (film) 3023, 1713, 1600 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.35−7.10 (5H, m), 2.95−2.89 (2H, m), 2.82−2.75 (2H, m), 2.16 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 207.9, 140.9, 128.4, 128.2, 126.0, 45.1, 30.0, 29.6; MS (CI) m/z 166 (M + NH_4^+); HRMS calcd for $C_{10}H_{12}ONa$ 171.0786, found 171.0784.

1-Cyclohexyl-propan-2-one, 7. To CuI (12 mg, 0.063 mmol), cyclohexylMgCl (2.0 M in Et_2O, 1.89 mL, 3.78 mmol), and $BF_3{\cdot}Et_2O$ (0.24 mL, 1.89 mmol) in THF (2 mL) was added **1** (200 mg, 1.26 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5% EtOAc in petroleum ether) afforded **7** (87 mg, 49%) as a yellow oil: IR (film) 2926, 1713, 1353 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 2.30 (2H, d, J = 6.9 Hz), 2.14 (3H, s), 1.90−1.78 (1H, m) 1.74−1.60 (5H, m), 1.36−1.05 (3H, m), 1.02−0.85 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) 209.2, 51.6, 33.9, 33.2, 30.6, 26.2, 26.1; MS (CI) m/z 158 (M + NH_4^+); HRMS calcd for $C_9H_{20}NO$ 158.1545, found 158.1546.

1-(4-Methoxyphenyl)-propan-2-one, 8. To CuI (12 mg, 0.063 mmol), anisylMgBr (0.5 M in THF, 7.56 mL, 3.78 mmol), and $BF_3{\cdot}Et_2O$ (0.24 mL, 1.89 mmol) in THF (2 mL) was added **1** (200 mg, 1.26 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5−10% EtOAc in petroleum ether) afforded **8** (124 mg, 60%) as a yellow oil: IR (film) 1706, 1511 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.14 (2H, d, J = 8.5 Hz), 6.89 (2H, d, J = 8.5 Hz), 3.82 (3H, s), 3.66 (2H, s), 2.16 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 207.0, 158.7, 130.4, 126.3, 114.2, 55.3, 50.1, 29.2; MS (CI) m/z 182 (M + NH_4^+); HRMS calcd for $C_{10}H_{12}NaO_2$ 187.0735, found 187.0736.

Undec-10-en-2-one, 9. To CuI (6 mg, 0.030 mmol), 7-octenylMgBr (0.44 M, 4.0 mL, 1.76 mmol) (made by refluxing 8-bromo-1-octene (1.0 g, 5.23 mmol) and magnesium turnings (0.13 g, 5.35 mmol) in THF (12 mL) for 1 h), and $BF_3{\cdot}Et_2O$ (0.11 mL, 0.87 mmol) in THF (2 mL) was added **1** (95 mg, 0.60 mmol) in THF (1 mL) according to General Method 1. Workup followed by column chromatography (2.5% EtOAc in petroleum ether) afforded **9** (89 mg, 88%) as a colorless oil: IR (film) 2921, 1713, 1637 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 5.89−5.76 (1H, m), 5.04−4.93 (2H, m), 2.43 (2H, t, J = 7.4 Hz), 2.15 (3H, s), 2.09−2.01 (2H, m), 1.62−1.52 (2H, m), 1.45−1.23 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) 209.5, 139.1, 114.2, 43.8, 33.8, 29.9, 29.2, 29.1, 28.94, 28.85, 23.8; MS (CI) m/z 186 (M + NH_4^+); HRMS calcd for $C_{11}H_{20}NaO$ 191.1412, found 191.1412.

Ring Opening of 1 with Bu_2CuLi in the Presence of Boron Trifluoride Diethyl Etherate. CuI (180 mg, 0.95 mmol) in a round-bottomed flask was heated under vacuum and then purged with nitrogen (three cycles were performed). Freshly distilled THF (2 mL) was added and the mixture cooled to −40 °C. Butyllithium (2.5 M in hexanes, 0.75 mL, 1.88 mmol) was added dropwise and the mixture stirred for 10 min. After the mixture was cooled to −78 °C, boron trifluoride diethyl etherate (0.12 mL, 0.95 mmol) was added dropwise. Methyleneaziridine **1** (100 mg, 0.63 mmol) in THF (1 mL) was added and the mixture stirred at −78 °C for 1 h. Saturated NH_4Cl solution (2 mL) was added and the solution allowed to warm to room temperature over 1 h. The layers were sepa-

(26) Stork, G.; Dowd, S. R. *J. Am. Chem. Soc.* **1963**, *85*, 2178.
(27) Wittig, G.; Frommeld, H. D.; Suchanek, P. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 683.
(28) Linstrumelle, G.; Krieger, J. K.; Whitesides, G. M. *Org. Synth.* **1976**, *55*, 103 and references therein.

rated, and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with 0.1 M HCl (3 × 15 mL) and water (3 × 15 mL) and then dried ($MgSO_4$). Careful removal of the solvent under reduced pressure on a rotary evaporator using an ice/water bath, followed by bulb-to-bulb distillation (50 °C/ca. 20 mmHg), gave **3** (30 mg, 42%) as a colorless liquid.

Alkylation of Imine 12 in the Absence and in the Presence of Boron Trifluoride Diethyl Etherate. To a three-necked flask equipped with a reflux condenser was added EtMgBr (1.0 M in THF, 4.73 mL, 4.73 mmol). Imine **12**[17] (800 mg, 4.73 mmol) in THF (1 mL) was added dropwise and the reaction mixture refluxed overnight. After the mixture was cooled to room temperature, benzyl chloride (0.54 mL, 4.69 mmol) was added dropwise, and the reaction mixture was refluxed for 20 h. The mixture was allowed to cool; 10% HCl (3 mL) was added and the mixture refluxed for 2 h. The layers were separated, and the organic phase was washed with 5% HCl (5 mL) and brine (4 × 10 mL) and dried ($MgSO_4$); the solvent was removed under reduced pressure. Kugelrohr distillation (150 °C/0.5 mmHg) afforded a 3:2 mixture of **13** and **11** (495 mg, 51%), which were inseparable by column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) 7.30−7.17 (5H, m), 2.92−2.65 (3.4H, m), 2.37 (0.8H, t, J = 7.6 Hz), 2.05 (1.8H, s), 1.70−1.40 (2H, m), 1.35−1.15 (4H, m), 0.92 and 0.88 (3H, overlapping t, J = 6.8 Hz). GC-MS **13** (7.3 min) 204 (M^+), 189 ($M^+ - Me$); **11** (8.1 min) 204 (M^+), 148 ($M^+ - C_4H_8$). Addition of BF_3·Et_2O (1.5 molar equiv) at room temperature with stirring for 15 min prior to addition of the benzyl chloride suppresses the formation of **11** and **13**.

Procedure for MCR (General Method 2). Copper(I) iodide (48 mg, 0.252 mmol) in a round-bottomed flask was heated under vacuum and then purged with nitrogen (three cycles were performed). Freshly distilled THF (4 mL) was added and the mixture cooled to −30 °C whereupon the Grignard reagent (2.5−3.0 molar equiv) was added. After the mixture was stirred for 10 min, **1** (1.0 molar equiv) in THF (2 mL) was added. The mixture was allowed to warm to room temperature and stirred for 24 h. The flask was then cooled to 0 °C and the electrophile (1.1−2.0 molar equiv) added dropwise. A reflux condenser was fitted and the reaction mixture heated at 40 °C for 2 h, allowed to cool to room temperature, and stirred overnight. Workup using either method A or B (see below) followed by purification gave the title compounds. *Workup A:* 10% aq HCl (2−3 mL) was added and the mixture heated to 50 °C for 2 h. After the mixture was cooled to room temperature, solid NaCl was added, and the mixture was extracted with diethyl ether, washed with 0.5 M aq HCl (2 × 15 mL), aq NH_4Cl (2 × 20 mL), aq $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. *Workup B:* 1 M acetic acid (2−3 mL) was added with hexane (2−3 mL), and the reaction was stirred at room temperature for 2 h. The mixture was extracted with diethyl ether and washed with aq NH_4Cl (2 × 20 mL), aq $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure.

1-Phenyloctan-3-one, 11. BuMgCl (2.0 M in THF, 0.94 mL, 1.88 mmol), **1** (100 mg, 0.63 mmol), and benzyl chloride (79 μL, 0.69 mmol) were reacted according to General Method 2 on half of the normal scale. Consequently, the THF volumes were halved, as was the amount of copper(I) iodide (24 mg, 0.126 mmol) used. Workup A followed by chromatography (2.5% EtOAc in hexane) gave **11** (90 mg, 70%) as a yellow oil: IR (film) 2931, 1713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.32−7.19 (5H, m), 2.95−2.90 (2H, m), 2.78−2.73 (2H, m), 2.40 (2H, t, J = 7.4 Hz), 1.64−1.53 (2H, m), 1.39−1.20 (4H, m), 0.90 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 210.5 (s), 141.2 (s), 128.5 (d), 128.3 (d), 126.1 (d), 44.3 (t), 43.0 (t), 31.4 (t), 29.8 (t), 23.5 (t), 22.5 (t), 13.9 (q); MS (EI) m/z 222 ($M + NH_4^+$); HRMS calcd for $C_{14}H_{24}NO$ 222.1858, found 222.1856.

Tetradec-1-en-5-one, 14. OctylMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and allyl bromide (218 μL, 2.52 mmol) were reacted according to General Method 2. Workup B followed by chromatography (2.5% EtOAc in hexane) gave **14** (211 mg, 80%) as a yellow oil: IR (film) 1710, 1597 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 5.86−5.75 (1H, m), 5.05−4.96 (2H, m), 2.50 (2H, t, J = 8.0 Hz), 2.39 (2H, t, J = 8.0), 2.35−2.29 (2H, m), 1.58−1.50 (4H, m), 1.31−1.20 (10H, m), 0.88 (3H, t, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 211.5 (s), 138.2 (d), 116.1 (t), 43.9 (t), 42.7 (t), 32.8 (t), 30.4 (t), 30.3 (t), 30.2 (t), 28.7 (t), 24.8 (t), 23.6 (t), 15.0 (q); two carbons coincident; MS (EI) m/z 210 (M^+) 155; HRMS calcd for $C_{14}H_{26}O$ 210.1984, found 210.1982. Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46%. Found C, 79.67; H, 12.51%.

Pentadec-1-en-6-one, 15. OctylMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and 3-butenyl *p*-toluenesulfonate[29] (610 mg, 2.52 mmol) were reacted according to General Method 2. Workup B followed by chromatography (2.5% EtOAc in hexane) gave **15** (190 mg, 67%) as a yellow oil: IR (film) 2915, 1710, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 5.80−5.73 (1H, m), 5.04−4.95 (2H, m), 2.40 (2H, t, J = 8.0 Hz), 2.38 (2H, t, J = 8.0 Hz), 2.08−2.02 (2H, m), 1.67 (2H, pentet, J = 7.2 Hz), 1.60−1.50 (2H, m), 1.35−1.20 (12H, m), 0.88 (3H, t, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 211.7 (s), 138.4 (d), 115.5 (t), 43.3 (t), 42.3 (t), 33.5 (t), 32.3 (t), 29.83 (t), 29.81 (t), 29.7 (t), 24.3 (t), 23.2 (t), 23.1 (t), 14.5 (q) two carbons coincident; MS (EI) m/z 224 (M^+) 155 ($M^+ - C_5H_9$); HRMS calcd for $C_{15}H_{28}O$ 224.2140, found 224.2138. Anal. Calcd. for $C_{15}H_{28}O$: C, 80.29; H, 12.58%. Found C, 80.18; H, 12.34%.

1-Phenyl-5-*p*-tolyl-pentan-3-one, 16. $PhCH_2MgCl$ (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and 4-methylbenzyl chloride (334 μL, 2.52 mmol) were reacted according to General Method 2. Workup A followed by chromatography (2.5% EtOAc in hexane) gave **16** (254 mg, 80%) as a yellow oil: IR (film) 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.28−7.02 (9H, m), 2.90−2.82 (4H, m), 2.71−2.66 (4H, m), 2.30 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) 209.6 (s), 141.5 (s), 138.3 (s), 136.0 (s), 129.6 (d), 128.9 (d), 128.7 (d), 128.6 (d), 126.5 (d), 45.1 (t), 44.9 (t), 30.1 (t), 29.7 (t), 21.4 (q); MS (EI) m/z 252 (M^+), 105; HRMS calcd for $C_{18}H_{20}O$ 252.1514, found 252.1503. Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99%. Found C, 85.60; H, 7.96%.

1,5-Diphenyl-pentan-3-one, 17. $PhCH_2MgCl$ (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and benzyl chloride (218 μL, 1.89 mmol) were reacted according to General Method 2. Workup A followed by chromatography (2.5% EtOAc in hexane) gave **17** (197 mg, 66%) as a yellow oil: IR (film) 2928, 1710, 1464 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.28−7.14 (10H, m), 2.88 (4H, t, J = 7.6 Hz), 2.70 (4H, t, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 209.5 (s), 141.4 (s), 128.9 (d), 128.7 (d), 126.5 (d), 44.9 (t), 30.1 (t); MS (EI) m/z 238 (M^+) 133, 105, 91; HRMS calcd for $C_{17}H_{18}O$ 238.1358, found 238.1357.

1-(*tert*-Butyldimethylsilyloxy)-decan-5-one 18 Using 1-(*tert*-Butyldimethylsilyloxy)-3-bromopropane. BuMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and 1-(*tert*-butyldimethylsilyloxy)-3-bromopropane (584 μL, 2.52 mmol) were reacted according to General Method 2. Workup A followed by chromatography (2.5% EtOAc in hexane) gave **18** (211 mg, 58%) as a yellow oil: IR (film) 2922, 1710, 1099, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 3.56 (2H, t, J = 6.0 Hz), 2.36 (4H, 2 overlapping t), 1.62−1.42 (6H, m), 1.32−1.18 (4H, m), 0.86 (12H, overlapping t and s), 0.00 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) 211.8 (s), 63.2 (t), 43.1 (t), 42.9 (t), 32.7 (t), 31.8 (t), 26.3 (q), 24.0 (t), 22.9 (t), 20.7 (t), 18.7 (s), 14.3 (q), −4.9 (q); MS (EI) m/z 229 ($M^+ - {}^t$Bu); HRMS calcd for $C_{12}H_{25}O_2Si$ 229.1623, found 229.1592. Anal. Calcd for $C_{16}H_{34}O_2Si$: C, 67.07; H, 11.96%. Found C, 67.13; H, 11.80%.

1-(*tert*-Butyldimethylsilyloxy)-decan-5-one 18 Using 1-(*tert*-Butyldimethylsilyloxy)-3-iodopropane. BuMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and 1-(*tert*-butyldimethylsilyloxy)-3-iodopropane[30] (757 mg, 2.52 mmol) were reacted according to General Method 2. Workup A followed by chromatography (2.5% EtOAc in hexane) gave **18** (237 mg, 65%) as a yellow oil (data as described above).

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1-Cyclohexyl-4-phenyl-butan-2-one, 19. Cyclohexylmagnesium chloride (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and benzyl chloride (290 μL, 2.52 mmol) were reacted according to General Method 2. Workup B followed by chromatography (2.5% EtOAc in hexane) gave **19** (164 mg, 57%) as a yellow oil: IR (neat) 2919, 1716, 1445 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.30−7.17 (5H, m), 2.89 (2H, t, J = 7.6 Hz), 2.71 (2H, t, J = 7.6 Hz), 2.26 (2H, d, J = 6.9 Hz), 1.90−1.73 (1H, m), 1.70−1.55 (5H, m), 1.28−1.17 (2H, m), 1.16−1.05 (1H, m), 0.95−0.80 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 210.0 (s), 141.2 (s), 128.5 (d), 128.3 (d), 126.0 (d), 50.8 (t), 44.9 (t), 33.9 (d), 33.2 (t), 29.7 (t), 26.2 (t), 26.1 (t); MS (CI) m/z 231 (MH^+), 148; HRMS calcd for $C_{16}H_{23}O$ 231.1749, found 231.1743.

1-Phenyl-hex-5-en-2-one, 20. PhMgCl (2.0 M in THF, 1.89 mL, 3.78 mmol), **1** (200 mg, 1.26 mmol), and allyl bromide (218 μL, 2.52 mmol) were reacted according to General Method 2. Workup B followed by chromatography (2.5% EtOAc in petroleum ether) gave **20** (114 mg, 52%) as a pale yellow oil: IR (film) 3032, 2919, 1716, 1644, 1496 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35−7.20 (5H, m), 5.80−5.72 (1H, m), 5.02−4.94 (2H, m), 3.70 (2H, s), 2.58 (2H, t, J = 7.4 Hz), 2.34−2.25 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 207.6 (s), 137.0 (d), 134.2 (s), 129.4 (d), 128.7 (d), 127.0 (d), 115.3 (t), 50.2 (t), 41.0 (t), 27.7 (t); MS (CI) m/z 192 ($M + NH_4^+$) 175 (MH^+); HRMS calcd for $C_{12}H_{18}NO$ 192.1388, found 192.1386.

1-Chloro-octan-5-one, 21. EtMgCl (2.0 M in THF, 1.58 mL, 3.16 mmol), **1** (200 mg, 1.26 mmol), and 1-chloro-3-iodopropane (203 μL, 1.89 mmol) were reacted according to General Method 2. Workup B followed by chromatography (2.5% EtOAc in petroleum ether) gave **21** (151 mg, 74%) as a yellow oil: IR (film) 2960, 1701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 3.53 (2H, t, J = 6.3 Hz), 2.43 (2H, t, J = 6.9 Hz), 2.38 (2H, t, J = 7.3 Hz), 1.82−1.68 (4H, m), 1.63−1.55 (2H, m), 0.91 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 210.6 (s), 44.73 (t), 44.70 (t), 41.7 (t), 32.0 (t), 21.0 (t), 17.3 (t), 13.8 (q); MS (CI), m/z 182 and 180 ($M + NH_4^+$); HRMS calcd for $C_8H_{19}NO^{35}Cl$ 180.1155, found 180.1157.

(1′*S,2′*R**)-1-(2-Hydroxycyclohexyl)-heptan-2-one, 22.** BuMgCl (2.0 M in THF, 1.58 mL, 3.16 mmol), **1** (200 mg, 1.26 mmol), and cyclohexene oxide (254 μL, 2.51 mmol) were reacted according to General Method 2 with minor modifications. The electrophile was added at −78 °C and the mixture warmed to room temperature and stirred for 18 h prior to workup. Workup B followed by chromatography (10% ethyl acetate in petroleum ether) gave **22** (190 mg, 71%) as a pale yellow oil: IR (film) 3416, 2925, 1706 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 3.17−3.05 (1H, m), 2.74 (1H, dd, J = 16.6, 6.3 Hz), 2.50−2.35 (2H, m), 2.28 (1H, dd, J = 16.6, 5.8 Hz), 2.07 (1H, bs), 2.04−1.95 (1H, m), 1.85−1.65 (3H, m), 1.63−1.54 (3H, m), 1.35−1.15 (7H, m), 1.05−0.95 (1H, m), 0.88 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 212.8 (s), 75.4 (d), 47.5 (t), 43.5 (t), 41.4 (d), 36.1 (t), 32.0 (t), 31.4 (t), 25.5 (t), 24.9 (t), 23.5 (t), 22.5 (t), 13.9 (q); MS (CI) m/z 230 ($M + NH_4^+$), 213 (MH^+), 195 ($MH^+ - H_2O$); HRMS calcd for $C_{13}H_{25}O_2$ 213.1854, found 213.1854. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39%. Found C, 73.29; H, 11.73%.

1-Hydroxy-1-phenyl-octan-3-one, 23. BuMgCl (2.0 M in THF, 1.58 mL, 3.16 mmol), **1** (200 mg, 1.26 mmol), and benzaldehyde (192 μL, 1.89 mmol) were reacted according to General Method 2. Workup B followed by chromatography (10% EtOAc in petroleum ether) gave **23** (147 mg, 53%) as a yellow oil: IR (film) 3633−3300, 2928, 2867, 1703, 1450 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.37−7.26 (5H, m), 5.15 (1H, dd, J = 8.8, 3.6 Hz), 3.42 (1H, bs), 2.85 (1H, dd, J = 17.2, 8.8 Hz), 2.78 (1H, dd, J = 17.2, 3.6 Hz), 2.42 (2H, t, J = 7.4 Hz), 1.62−1.54 (2H, m), 1.33−1.20 (4H, m), 0.89 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 211.8 (s), 142.8 (s), 128.5 (d), 127.6 (d), 125.6 (d), 70.0 (d), 51.0 (t), 43.7 (t), 31.3 (t), 23.2 (t), 22.4 (t), 13.9 (q); MS (EI) m/z 220 (M^+) 149 ($M^+ - C_5H_{11}$); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1464. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%. Found C, 76.10; H, 9.33%. The enantiomers of **23** can be resolved by HPLC on a Diacel OD column (1% IPA in hexanes; 0.7 mL/min; λ = 220 nm): 23.2 and 24.6 min. Using (*S*)-**1**[2a] in this procedure gave **23** in 21% ee {23.2 min (major) and 24.6 min (minor)}.

(*Z*)-6-Heneicosen-11-one, 25.[21,23] Nonylmagnesium chloride in THF (1.0 M, 3.78 mL, 3.78 mmol), prepared by refluxing 1-chlorononane (1.87 mL, 10.0 mmol) and magnesium turnings (255 mg, 10.5 mmol) in THF (10 mL) for 2 h, **1** (200 mg, 1.26 mmol), and 3-*cis*-nonen-1-yl-*p*-toluenesulfonate **24** (746 mg, 2.52 mmol) were reacted according to General Method 2. Workup B followed by medium-pressure liquid chromatography (MPLC) on a Merck LiChroprep Si60 column (2% EtOAc in petroleum ether) gave **25** (242 mg, 62%) as a colorless oil: n_D^{25} 1.4560 (lit. 1.4541[23b]); IR (neat) 2919, 1716, 1460 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 5.41−5.37 (1H, m), 5.34−5.28 (1H, m), 2.41−2.36 (4H, m), 2.06−1.97 (4H, m), 1.67−1.61 (2H, m), 1.61−1.54 (2H, m), 1.36−1.21 (20H, m), 0.91−0.86 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 211.3 (s), 131.0 (d), 128.7 (d), 42.8 (t), 42.1 (t), 31.9 (t), 31.5 (t), 29.5 (t), 29.45 (t), 29.39 (t), 29.36 (t), 29.27 (t), 27.2 (t), 26.6 (t), 23.9 (t), 23.8 (t), 22.6 (t), 22.5 (t), 14.04 (q), 14.00 (q) two carbons coincident; MS (CI) m/z 326 ($M + NH_4^+$), 309 (MH^+); HRMS calcd for $C_{21}H_{44}NO$ 326.3423, found 326.3419. Anal. Calcd for $C_{21}H_{40}O$: C, 81.75; H, 13.07%. Found C, 81.79; H, 13.41%.

3-*cis*-Nonen-1-yl-*p*-toluenesulfonate, 24.[22] To a stirred solution of *cis*-3-nonen-1-ol (2.9 mL, 17.2 mmol) in anhydrous pyridine (50 mL) at 0 °C was added *p*-toluenesulfonyl chloride (6.62 g, 34.7 mmol). The reaction was stirred at 0 °C for 90 min and then allowed to stand at 0 °C for 23 h. The mixture was poured into cold HCl (1.4 mL, 1.5 M). After extraction with diethyl ether, the organic layer was dried ($MgSO_4$) and the solvent removed in vacuo. Column chromatography (20% EtOAc in petroleum ether) gave **24** (4.50 g, 88%) as a colorless liquid: IR (film) 2925, 1598, 1178 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.79 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.3 Hz), 5.52−5.44 (1H, m), 5.25−5.18 (1H, m), 3.99 (2H, t, J = 7.0 Hz), 2.44 (3H, s), 2.44−2.36 (2H, m), 1.97−1.92 (2H, m), 1.31−1.18 (6H, m), 0.87 (3H, t, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 144.7 (s), 134.0 (d), 133.1 (s), 129.8 (d), 127.9 (d), 122.6 (d), 69.8 (t), 31.4 (t), 29.1 (t), 27.2 (t), 27.1 (t), 22.5 (t), 21.6 (q), 14.0 (q); MS (CI) m/z 314 ($M + NH_4^+$); HRMS calcd for $C_{16}H_{28}NO_3S$ 314.1790, found 314.1791.

Ring Opening of Deuterated Methyleneaziridine 26. BuMgCl (2.0 M in THF, 0.94 mL, 1.88 mmol), **26**[2e] (100 mg, 0.62 mmol), and benzyl chloride (109 μL, 0.95 mmol) were reacted according to General Method 2 on half of the normal scale. Consequently, the THF volumes were halved, as was the amount of copper(I) iodide (24 mg, 0.126 mmol). Workup B followed by chromatography (2.5% EtOAc in petroleum ether) gave **27** and **28** (75 mg, 59%) in a 85:15 ratio as determined by NMR spectroscopy: IR (film) 2925, 1711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.30−7.12 (5H, m), 2.92−2.87 (2H, m), 2.77−2.68 (1.85H, m), 2.41−2.32 (1.15H, m), 1.58−1.52 (2H, m), 1.31−1.15 (4H, m), 0.88 (3H, t, J = 6.9 Hz); ^{2}H NMR (61 MHz, CCl_4) 2.69 (0.15D, br s), 2.34 (0.85D, br s); ^{13}C NMR (75 MHz, $CDCl_3$) 42.7 (t, J = 19.2 Hz, C-4), otherwise identical to that of **11**; MS (CI) m/z 223 ($M + NH_4^+$), 206 (MH^+); HRMS calcd for $C_{14}H_{20}DO$ 206.1655, found 206.1655.

(±)-*N*-(2-Bromo-3-methyl-2-butenyl)-1-phenylethylamine, 32. To 1,1-dibromo-2,2-dimethyl-cyclopropane **29**[25] (2.00 g, 8.77 mmol) in 1,2-dichlorobenzene (15 mL) was added (±)-1-phenylethylamine (2.5 mL, 19.39 mmol), and the mixture was heated for 72 h at 150 °C. After the mixture was cooled, petroleum ether (20 mL) was added and the mixture filtered and washed with additional petroleum ether (20 mL). The solvent was removed by rotary evaporation followed by Kugelrohr distillation (60 °C/15 mmHg). Column chromatography (5% EtOAc in petroleum ether) using silica pretreated with triethylamine gave **32** (1.35 g, 57%) as a yellow oil: IR (film) 3334, 2960, 1445 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.36−7.22 (5H, m), 3.75 (1H, q, J = 6.6 Hz), 3.43 (1H, d, J = 14.4 Hz), 3.34 (1H, d, J = 14.4 Hz), 1.91 (1H, bs, NH), 1.88 (3H, s), 1.55 (3H, s), 1.35 (3H, d, J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 145.1 (s), 133.4 (s), 128.4 (d), 127.0 (d), 126.9 (d), 121.7 (s), 55.8 (d), 51.1 (t), 25.5 (q), 24.8 (q), 20.5 (q); MS (EI) m/z 269 and 267 (M^+), 254 and 252 (M^+ − Me); HRMS calcd for $C_{13}H_{18}N^{79}Br$ 267.0623, found 267.0620.

(±)-2-Isopropylidene-1-(1-phenylethyl)-aziridine, 30. To a three-necked flask fitted with a dry ice condenser and

gas inlet was added sodium amide (7.89 g, 202 mmol, 30 equiv), and the system was purged with calcium chloride dried ammonia. Ammonia (ca. 75 mL) was condensed into the flask, and then **32** (1.80 g, 6.74 mmol) was added dropwise. After 30 min, diethyl ether (10 mL) was added, followed by water (10 mL) dropwise (CAUTION). After the ammonia had evaporated, water (10 mL) and diethyl ether (10 mL) were added and the mixture was stirred for 5 min. The organic phase was separated and the aqueous phase extracted with diethyl ether (3 × 10 mL). The organic extracts were washed successively with 10% NaOH solution (2 × 10 mL), 0.1 M acetic acid (10 mL), sodium hydrogen carbonate (10 mL), water (10 mL), and finally brine (10 mL). The organic extracts were dried ($MgSO_4$), and the solvent was removed under reduced pressure. Kugelrohr distillation (100 °C/1 mmHg) gave **30** (1.11 g, 88%) as a clear, colorless oil: IR (film) 3027, 2966, 2925, 1793, 1450 cm^{-1}; ^1H NMR (400 MHz, d_6-DMSO at 80 °C) 7.36−7.20 (5H, m), 3.00 (1H, q, J = 6.6 Hz), 2.00 (1H, s), 1.91 (1H, s), 1.67 (3H, s), 1.38 (3H, d, J = 6.6 Hz), 1.36 (3H, br s);^{13}C NMR (100 MHz, d_6-DMSO at 80 °C) 145.3 (s), 128.6 (d), 127.3 (d), 125.2 (s), 102.1 (s), 67.5 (d), 29.5 (t), 23.6 (q), 21.0 (q), 19.4 (q) two carbons coincident; MS (FI) m/z 187 (M^+); HRMS calcd for $C_{13}H_{17}N$ 187.1361, found 187.1366.

2,2-Dimethyl-1-phenyl-hexan-3-one, 31. Copper(I) iodide (41 mg, 0.215 mmol) was heated under vacuum in a round-bottomed flask then purged with nitrogen (three cycles were performed). Freshly distilled THF (4 mL) was added and the mixture cooled to −30 °C whereupon EtMgCl in THF (2.0 M, 1.34 mL, 2.68 mmol) was added. After the mixture was stirred for 10 min, **30** (200 mg, 1.07 mmol) in THF (2 mL) was added. The mixture was allowed to warm to room temperature and stirred for 24 h. The flask was then cooled to 0 °C and benzyl bromide (255 μL, 2.14 mmol) added dropwise. A reflux condenser was fitted and the reaction mixture heated at 40 °C for 18 h. After the mixture was cooled, 2 M aq HCl (3 mL) was added, and the solution was heated at 40 °C for 2 h. Upon cooling, the mixture was extracted with diethyl ether (20 mL) and the combined organic extracts were washed successively with aq NH_4Cl (2 × 20 mL), aq $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. Column chromatography on silica (2.5% EtOAc in petroleum ether) gave **31** (110 mg, 50%) as a pale yellow oil: IR (film) 3017, 2960, 1696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.30−7.20 (3H, m), 7.10−7.07 (2H, m), 2.81 (2H, s), 2.38 (2H, t, J = 7.2 Hz), 1.58 (2H, sextet, J = 7.2 Hz), 1.12 (6H, s), 0.89 (3H, t, J = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 215.6 (s), 138.0 (s), 130.3 (d), 128.0 (d), 126.3 (d), 48.3 (s), 45.4 (t), 39.9 (t), 24.3 (q), 17.1 (t), 13.8 (q); MS (FI) m/z 204 (M^+); HRMS calcd for $C_{14}H_{20}O$ 204.1514, found 204.1516.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **4**−**9**, **11**, **14**−**25**, and **30**−**32** and ^1H and ^2H NMR spectra for **27**/**28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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