National Institutes of Health (Grant CA 17918; also, Grant RRO 2388-01 to support the purchase of the AM-500 NMR system).

Registry No. **6**, 80737-85-5; **7**, 80737-87-7; **8**, 83076-81-7; **9**, 109890-65-5; **10**, 109890-66-6; **11**, 109890-67-7; **12**, 109890-68-8; **13**, 109890-69-9; **14**, 109890-70-2; **15**, 109890-71-3; **16**, 3699-66-9; (*E*)-**17**, 109890-72-4; (*Z*)-**17**, 109890-79-1; **18**, 109890-73-5; **19**, 109890-74-6; **20**, 109890-75-7; **21**, 109890-76-8; **22**, 109957-49-5; **23**, 109890-77-9; **25**, 109890-78-0; 2-(*tert*-butyldimethylsiloxy)-butadiene, 80738-05-2; acetophenone, 98-86-2; 1-phenylethanol, 98-85-1; methyl (triphenylphosphoranylidene)acetate, 2605-67-6.

Stereoselective Syntheses of *cis*-2-Alkyl-6-methylpiperidines

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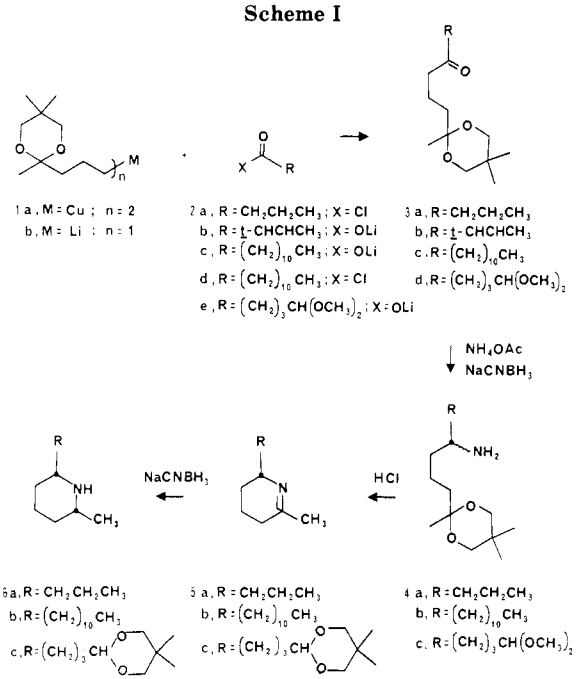
Syntheses in the pine alkaloid family, the fire ant venom series, and continued studies in the *Poranthera* species are presented. Reaction of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal or the corresponding dialkylcuprate compound with carboxylic acid derivatives gives selectively protected 1,5-dicarbonyl compounds. After reductive amination of the newly formed ketone function, acidic hydrolysis of the cyclic ketal gives 6-alkyl-2-methyl-3,4,5,6-tetrahydropyridines. Stereoselective reduction of the imine function affords cis-2,6-disubstituted piperidines. Examples of this approach include syntheses of dihydropinidine from *Pinus sabiniana* and the fire ant venoms *cis*-2-methyl-6-undecylpiperidine and 2-methyl-6-undecyl-3,4,5,6-tetrahydropyridine from *Solenopis geminata* and *S. xyloni*. A preliminary report on an approach to porantherilidine, from *Poranthera corymbosa*, is described.

Introduction

Part of the research in these laboratories has been concerned with the stereochemical course of nucleophilic addition to tetrahydropyridinium ions. In the cases studied,[1] the product formed in a stereospecific manner is a substituted piperidine molecule. Previous reports from these laboratories have described a general method of synthesis of 2,3-disubstituted piperidines by the annulation of Δ^2-tetrahydropyridines, with methyl vinyl ketone.[2] The aim here is to develop methodology for the synthesis of 2,6-disubstituted piperidines. As usual, the main objectives are efficient skeletal construction and stereochemically controlled bond formations. Moreover, any general methodology should be sufficiently flexible to permit analogue development. Interest in these molecules is intense because, in addition to providing an entry to the piperidine alkaloids, the N-substituted alkyl and acyl derivatives have a broad spectrum of useful properties. Alkaloids with the 2,6-disubstituted piperidine ring structure have been detected in certain members of the pine and fire ant species. *Pinus sabiniana* yields 2,6-dimethylpiperidine, pinidine, and dihydropinidine, **6a**. Substantial amounts of pinidine have also been detected in *P. jeffreyi* and *P. torreyana*.[3] Related alkaloids have been found in other plants[4] and also in the Myrmicinae ants belonging to subgenus *Solenopsis* of the genus *Solenopsis*. Known for their particularly potent stings, the term fire ant has been given to the four main North American forms *Solenopsis*; *S. invicta* = *saevissima*, *S. richteri* = *saevissima*, *S xyloni*, and *S geminata*. The latter two types are indigenous to the southern U.S.A. The former two groups, consisting of two subspecies referred to as red and black, have been imported into this country from South America as cargo stowaways.[5]

Cyclization procedures and the reduction of pyridines are the two most widely applied methods of preparing the parent 2,6-disubstituted piperidine ring structure.[6] Several clever adaptations have been applied to the synthesis of the pine and fire ant alkaloids.[7] Herein we report our efforts directed toward the syntheses of these types of molecules. Furthermore, as part of our continued interest in general methods for the stereospecific total synthesis of natural products, preliminary results on the application

Scheme I



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of this methodology to the *Poranthera corymbosa* alkaloids are described.

Results and Discussion

For a first application we focused on a synthesis of dihydropinidine, **6a**. As shown in Scheme I, reaction of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal (**1a**) in the presence of copper(I) iodide with butyryl chloride furnished the selectively protected 1,5-dicarbonyl equivalent **3a** in 91% yield. Condensation of the carbonyl function of **3a** with ammonium acetate in methanol under reductive conditions[8] afforded amine–ketal **4a** in 78% after flash chromatography. Hydrolysis of the ketal function of **4a** gave the ring-closed 2,6-disubstituted imine derivative **5a** in 83% yield. Reduction of the imine functionality with sodium cyanoborohydride at pH 5.3 and basic extractive workup with ether gave a solution of the free base. Treatment with anhydrous hydrochloric acid precipitated the amine salt. After a single recrystallization (±)-dihydropinidine hydrochloride was obtained in 81% yield. The overall yield for the four-step process in 58%. As described in the Experimental Section, this approach lends itself well to a procedure that does not require extensive purification or chromatography after each step. The material so obtained was recrystallized to give the pure material in 35% yield overall.

In an attempt to extend this methodology to pinidine, we reacted commercially availabe methyl crotonate with lithium hydroxide in methanol and water to form the corresponding lithium carboxylate salt **2b**.[9] The salt was reacted with 1 equiv of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal at −25 °C. After extractive workup and chromatography, the desired protected enone **2b** was obtained in 12% yield. Additionally, a large quantity of starting material and smaller amounts of unidentified products were obtained. It is likely that deprotonation competes effectively with the addition reaction. As a consequence, the yield suffers. Rather than attempting to optimize this reaction or employ the cuprate–acid chloride procedure, we decided it would be more expeditious to proceed despite the low yield. Ketal enone **2b** was stirred with ammonium acetate and sodium cyanoborohydride in methanol to yield the completely saturated amine **4a**. This results was not entirely surprising because 1,4-reduction of the incipient dienamine gives an enamine which may be reduced, in turn, to the amine stage. As suspected, the use of lithium salts of α,β-unsaturated acids having active γ hydrogen atoms and α,β-unsaturated ketones in this procedure clearly presents complications. Use of the corresponding acid chloride and the alkyl cuprate compounds may solve this difficulty. Although the employment of selective reducing agents may help overcome 1,4-reduction, the approach to pinidine was abandoned.

The synthesis of the fire ant venoms 2-methyl-6-undecylpiperidine (**6b**) and 2-methyl-6-undecylpiperideine (**5b**) is shown in Scheme I. Addition of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal (**1b**) to a suspension of lithium laurylate (**2c**) gave the desired, selectively protected 1,5-dicarbonyl **3c** in low yield. Large amounts of the unreacted lithium salt were also recovered. Solubility was the major problem here. Therefore, we reacted the corresponding dialkylcuprate reagent **1a** with lauryl chloride (**2d**). After extractive workup and chromatography, ketone **3c** was obtained as a low melting crystalline solid in 89% yield. Reductive amination furnished the desired amine **4b** in 92% yield. Hydrolysis of the ketal function and cyclization gave the imine derivative **5b** in 87% yield after flash chromatography. The mass spectrum was in excellent agreement with the spectrum reported for the venom isolated from *S. geminata*.[5c] Characteristic fragments resulting from cleavage of the long alkyl side chain occur at m/e 96 and 97. The base peak at m/e 110 is due to proton abstraction from the side chain by the nitrogen atom, followed by migration of the C-6 hydrogen atom and rupture of the chain. Preparation of this proposed biosynthetic intermediate also provides access to solenopsin A.[7i] The cis-disubstituted compound **6b** found in the venom of the queens of each of the four major fire ant species was obtained after stereospecific reduction with sodium cyanoborohydride in 95% yield. A 68% overall yield was obtained for the sequence. The spectral properties recorded for **6b** were in agreement with the literature reports. The cis stereochemistry was confirmed by the presence of Bohlmann bands[10] in the infrared spectrum and a band at 1320 cm^{-1} that is absent in the trans isomer.[7f]

The *P. corymbosa* alkaloids present attractive synthetic targets.[11] The focus here describes an approach to porantherilidine. The structure, shown to be 1-[(6α-methylquinolizidin-4β-yl)methyl]butyl benzoate, was determined from X-ray diffraction data. Previously this molecule has been synthesized by routes featuring a cycloaddition of an olefin with an alkyl piperideine *N*-oxide.[12] In our approach, 5-lithio-2-pentanone 2,2-dimethylpropylene ketal again finds applicability to the preparation of a key cis-2,6-disubstituted piperidine. The required acylium ion synthon was prepared by the method of Lee and Stevens.[13] Basic hydrolysis provided the corresponding lithium salt, **2e**. Reaction of **1b** with a THF suspension of the lithium carboxylate salt gave the selectively protected ketone **3d** in 74% yield after chromatography. Reductive amination furnished the corresponding amine **4c** in 72% yield. Hydrolysis of the acetal and ketal functions, followed by adjusting the pH to 5.3, afforded the desired Δ^1-tetrahydropyridine **5c** in 93% yield. Under these reaction conditions the more substituted, thermo-

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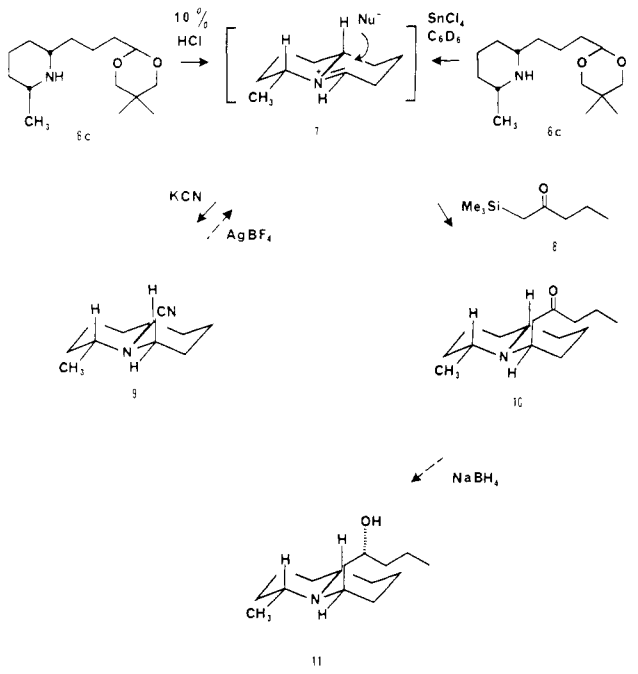
Scheme II



dynamically favored imine forms. Attesting to the stability of the cyclic acetal group at pH 5, the free aldehyde function is trapped by the liberated neopentanediol. Stereospecific reduction of the imine function gave the expected disubstituted piperidine **6c** in 82% yield. The cis stereochemistry was confirmed by the presence of Bohlmann bands (3000–2700 cm^{-1}) in the infrared spectrum. As a convenient alternative, key piperidine **6c** may be formed by a "one pot procedure" from amine **4c** in 70% yield (Experimental Section).

With **6c** in hand, we turned our attention to synthesizing the requisite five-carbon enol equivalent. In a method similar to that of Kishi and co-workers,[14] we reacted the Grignard reagent, prepared in 95% from (chloromethyl)-trimethylsilane,[15] with butyryl chloride in the presence of copper(I) iodide. After basic workup and distillation we obtained 1-(trimethylsilyl)-2-pentanone (**8**) in 83% yield.

The stage was now set to form the final carbon–carbon bond of the porantherilidine ring skeleton. With carefully controlled cleavage of the acetal function and formation of the immonium ion **7**, we should be able to introduce the five-carbon appendage in a stereospecific manner. Since the immonium ion is in equilibrium with the corresponding unsubstituted enamine tautomer, we must avoid basic conditions to prevent the insidious dimerization reaction noted for molecules of this type.[16] Also, under strongly acidic conditions the silyl enol ether will surely be cleaved before nucleophilic addition can occur. Therefore, we had at least two alternatives. The first was to cleave the acetal function with a Lewis acid thus forming, on condensation, the cyclic immonium ion. Addition of the α-silyl ketone in the presence of the Lewis acid should then unleash the active nucleophile (Scheme II).[14]

The second possibility was to hydrolyze the acetal with aqueous hydrochloric acid in the presence of potassium cyanide. In this manner the unsubstituted immonium ion may be trapped as the cyano amine. After isolation and purification, the required immonium ion may be regenerated by using nonaqueous conditions with silver tetrafluoroborate.[7c] Subsequent addition of the β-keto silane should effect the desired stereospecific nucleophilic addition and establish the porantherilidine ring skeleton.

At this time we have not optimized the yield or fully characterized cyano amine **9**. Preliminary data indicates that it forms. The 200-MHz proton spectrum obtained is suggestive of this formulation. Also, the mass spectrum has characteristic fragments at m/e 178 (parent), 163 (base peak, $M^+ - CH_3$), and 151 ($M^+ - HCN$). Furthermore, the high resolution mass spectrum was in agreement with the exact mass calculated for $C_{11}H_{18}N$.

For the Lewis acid catalyzed approach, treatment of a benzene-d_6 or an acetonitrile-d_3 solution of the amino acetal **6c** with tin(IV) chloride followed by the addition of an excess of the β-keto silane gave, after basic workup and chromatography, a small amount of basic, ketone-containing compound (IR), having a ^1H NMR spectrum not inconsistent with the one expected for the bicyclic keto amine **10**. Furthermore, the mass spectrum of this compound has fragments at m/e 222 and 152 which possibly correspond to cleavage of a methyl group and the oxopentyl side chain of a quinolizidine ring.

Reduction of the so formed bicyclic keto amine with sodium borohydride is expected to give a mixture of porantherilidine and epiporantherilidine alcohols. Both of these alcohols may be converted to porantherilidine.[12]

Conclusions

Our synthesis of (±)-dihydropinidine proceeds in 58% overall yield, which compares favorably with the highest yield reported in the literature. Also, the starting materials are readily obtainable and inexpensive. Use of carboxylic acids (or acid chlorides) is a particularly noteable advantage of this method since a large number of analogues may be prepared. While the overall yield is lower, the sequence not involving chromatography is an added convenience.

Use of this methodology has been successfully applied to a convenient preparation of two of the fire ant venoms. This procedure provides a means to introduce the long side chains common to the ant venoms in a high yield process. A high yield route to 2-methyl-6-undecylpiperdideine may facilitate the examination of the proposed enzymatic system responsible for the formation of the trans isomer found in the imported fire ant.

Although circumstances not related to the chemistry described here have prevented us from completing a synthesis of porantherilidine at this time, we have a high degree of confidence in the eventual success of continued pursuits along these lines. Overall, we have shown how 2-alkyl-6-methylpiperidines can be formed in a stereoselective, high yield process. As described, the reaction of a carbonyl-protected organometallic reagent with a carboxylic acid derivative provides an attractive alternative to the Michael reaction for preparing selectively protected 1,5-dicarbonyl compounds. By the choice of suitably protected organometallic reagents other than the one described here one may be able to prepare a variety of differentially appended 2,6-piperidines. Consequently this strategy may find continued application in alkaloid syntheses.

Experimental Section

General Comments. Melting and boiling points are uncor-

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rected. Infrared spectra were recorded on a Beckman 4210 spectrophotometer. Proton nuclear magnetic resonance (NMR) spectra were obtained on a Bruker WP 200 FT or a AM 500 FT instrument operating at 200.133 and 500.135 MHz, respectively. Chemical shifts are reported as parts per million (ppm) downfield from tetramethylsilane in δ units. Coupling constants are in hertz (Hz). NMR data are reported in this order: chemical shift; multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad); numer of protons; coupling constants. Except as indicated, either deuteriochloroform or carbon tetrachloride with 5% added deuteriobenzene was used as solvents. Carbon NMR spectra were recorded on the Bruker instruments operating at 50.320 and 125.759 MHz. Peak positions are in ppm when using deuteriochloroform, carbon tetrachloride, or deuteriobenzene with assigned values of 77.0, 96.0, or 128.0, respectively, as internal standards. High resolution mass spectral (MS) data were collected on an AEI-MS9 instrument. Fragmentation data are reported as *m/e* (relative intensity). Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI.

All solvents were of, at least, reagent grade quality. Further purification and drying employed standard methods.[17] For the manipulation of reaction mixtures involving air-sensitive compounds,[18] standard Schlenkware was flame-dried in vacuo and filled with argon. Anhydrous solvents were transferred via oven-dried cannula or syringes. Thin layer chromatography (TLC) was carried out on EM 60 PF 254 silica gel plates or EM 150 F-254 precoated aluminum oxide plates. Silica gel for flash chromatography[19] was EM Kieselgel 60 (230–400 mesh ASTM). Fractions obtained from chromatography were monitored by TLC. Components were visualized by UV light, iodine vapor, and molybdophosphoric acid. Nitrogenous bases were distinguished by spraying with aqueous cobalt(II) chloride–ammonium thiocyanate solutions.[20]

2,6-Nonanedione 2-(2,2-Dimethylpropylene ketal) (3a). A stirred ether solution (50 mL) of butyryl chloride (3.52 g, 3.42 mL, 33.0 mmol) under nitrogen was cooled to −78 °C. The dialkylcuprate **1a** (33.0 mmol, 95.0 mL of a 0.35 M THF solution of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal[11e] and copper(I) iodide, 3.05 g, 16.0 mmol), precooled to −25 °C, was added over 20 min. The reaction was quenched by adding small portions (20 mL) to saturated Na_2CO_3 (20 mL), with vigorous stirring at 0 °C after 30 min. The aqueous layer was extracted with ether (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and then concentrated in vacuo. The resultant oil (12.31 g) was subjected to flash chromatography (silica gel, 25% ethyl acetate–hexane) to yield pure material (3.56 g, 14.57 mmol, 91.2%): bp 70–75 °C at 0.02 mmHg; IR (neat liquid) 2960, 2950, 2870, 1710, 1460, 1375, 1225, 1095 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 3.42 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 3.29 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 2.26 (m, 4 H), 1.56–1.41 (m, 6 H), 1.23 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.76 (m, 6 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) 210, 98.7, 70.3 (double intensity), 44.6, 42.7, 37.5, 29.9, 22.8, 22.4, 20.1, 17.8, 17.2, 13.7; mass spectrum, (M^+) 243 (11.4), 242 (0.3), 228 (3.4), 227 (15.8), 157 (8.3), 141 (5.1), 129 (100), 113 (28.4), 85 (16.0), 69 (10.9). Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.42; H, 10.74. Found: C, 69.33; H, 10.80.

6-Amino-2-nonanone 2,2-Dimethylpropylene Ketal (4a). A methanol solution (15 mL) of ketone ketal **3a** (1.00 g, 4.13 mmol) was stirred with 4A molecular sieves (0.780 g) as ammonium acetate (3.18 g, 41.3 mmol) was added. After the addition of sodium cyanoborohydride (0.251 g, 4.13 mmol), the reaction mixture was stirred 24 h at room temperature under a nitrogen atmosphere. The reaction mixture was filtered, concentrated on a rotary evaporator, diluted with water (2 mL), basified with 15% NaOH, and extracted with ether (3 × 50 mL). The combined organic layers were dried (K_2CO_3), filtered, and then concentrated in vacuo. Flash chromatography (silica gel, 5% triethylamine–ethyl acetate) gave amino ketal **4a** as a colorless oil (785 mg, 3.23 mmol, 78.2%): bp 140–145 °C (oven temperature) at 0.04 mmHg; IR (neat liquid) 3360, 3300, 2960, 2870, 1600, 1460, 1375, 1255, 1212, 1100, 1042 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 3.50 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 3.37 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 2.66 (m, 1 H, NC*H*), 1.64–1.56 (m, 2 H), 1.42–1.35 (m, 4 H), 1.31 (s, 3 H, CH_3), 1.28–1.10 (m, 6 H), 0.97 (s, 3 H, CH_3), 0.89–0.85 (m, 3 H, CH_3), 0.84 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 98.9, 70.4 (double intensity), 50.9, 43.6, 40.3 (double intensity, two carbons not resolved), 32.0, 22.8, 22.7, 20.4, 20.1, 19.3, 13.9; high resolution mass spectrum, calcd for $C_{14}H_{29}NO_2$ 243.2198, found 243.2201; mass spectrum, (M^+) 243 (0.6), 228 (15.6), 226 (12.1), 200 (30.5), 156 (15.8), 129 (90.1), 98 (40.0), 96 (36.8), 86 (12.6), 72 (100). Anal. Calcd for $C_{14}H_{29}NO_2$: C, 69.13; H, 11.93, N, 5.76. Found: C, 69.16; H, 12.03; N, 5.62.

2-Methyl-6-propyl-3,4,5,6-tetrahydropyridine (5a). Amino ketal **4a** (0.480 g, 1.97 mmol) was stirred with THF (3 mL) and 10% HCl (3 mL) under a nitrogen atmosphere for 1 h. At the end of this time the reaction mixture was made basic with 15% NaOH and then extracted with ether (3 × 10 mL). The combined ether extracts were dried (K_2CO_3), filtered, and concentrated in vacuo. The resultant oil was purified by flash chromatography (silica gel, 9:1 hexane–ethyl acetate with 5% triethylamine added) to give the imine as an unstable yellow oil (0.288 g, 1.64 mmol, 83.3%): IR ($CDCl_3$) 2970, 2940, 2880, 1660, 1610, 1445 1375, 1320 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 3.80 (m, 1 H, NC*H*), 2.80 (br m, 2 H, $NCCH_3CH_2$), 2.13–1.01 (m, 11 H), 0.98 (t, J = 7.0 Hz, 3 H, CH_3); high resolution mass spectrum, calcd for $C_9H_{17}N$ 139.1361, found 139.1352; mass spectrum (M^+) 139 (6.7), 110 (42.8), 97 (55.4), 96 (60.0), 82 (35.2), 68 (23.7), 55 (41.6), 42 (95.0), 41 (100), 35 (56.7).

Dihydropinidine Hydrochloride (6a). Tetrahydropyridine **5a** (325 mg, 2.34 mmol) was stirred under nitrogen with a citrate–phosphate buffer (3 mL) and THF (3 mL). Sodium cyanoborohydride was added (147 mg, 2.34 mmol) and the mixture was stirred for 24 h at room temperature. The reaction mixture was filtered, made basic with 15% NaOH, filtered, and then extracted with ether (3 × 10 mL). The dried (K_2CO_3) ether extracts were acidified with ethereal HCl (5 N) to precipitate the amine hydrochloride. The crystals were collected then dried in vacuum (mp 200–205 °C). The crude product was recrystallized from 2:1 ethyl acetate–ethanol to give dihydropinidine hydrochloride (337 mg, 1.90 mmol, 81.1%). Alternatively, 50 mL of dry ether was added to butyryl chloride (3.52 g, 33 mmol). After the solution was cooled to −78 °C under nitrogen, the cuprate reagent prepared from 5-lithio-2-pentanone 2,2-dimethylpropylene ketal (0.35 M in 50% benzene–pentane, 95 mL, 33.2 mmol) and copper(I) iodide (3.05 g, 16.0 mmol at 0 °C) was added by cannula to the stirred solution over 15 min. The mixture was warmed to −25 °C for 15 min and then to 0 °C at which time the reaction was quenched (saturated $NaHCO_3$). The layers were separated. The aqueous layer was extracted with ether, dried (Na_2SO_4), filtered, and concentrated in vacuo to give a yellow oil. The oil was dissolved in methanol (100 mL). Ammonium acetate (12.32 g, 160 mmol), sodium cyanoborohydride (1.00 g, 16.0 mmol), and 3A molecular sieves were added. The reaction mixture was stirred overnight. Subsequently, the mixture was filtered and concentrated in vacuo. The residue was dissolved in water (5 mL), made basic with 20% sodium hydroxide, and extracted with ether. The combined extracts were dried (Na_2CO_3), filtered, and concentrated in vacuo. The resultant oil was stirred with 10% HCl for 1 h. The pH was adjusted to 5.3 with 40% sodium hydroxide and a citrate–phosphate buffer. Sodium cyanoborohydride was added (1.00 g, 16.0 mmol) and the reaction mixture was stirred overnight. Subsequently, the mixture was treated as above to yield crude dihydropinidine. The oil was dissolved in a small amount of ether (15 mL) and anhydrous HCl (5 N in ether) was added to precipitate the hydrochloride salt (mp 200–205 °C). Two recrystallizations from 2:1 ethyl acetate–ethanol gave purer material (1.00 g, 5.63 mmol, 35.2%): mp 207–210 °C (lit.[7a] mp 215–220 °C); IR ($CDCl_3$) 3660, 3400, 2960, 2875, 2840, 2790, 2760, 1590, 1435, 1100, 1015 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 9.40 (br, 1 H, N*H*), 9.10 (br, 1 H, N*H*), 3.08 (m, 1 H, NC*H*), 2.94 (m, 1 H NC*H*), 2.07 (m, 1 H), 1.96–1.60 (m, 5 H), 1.55 (d, J = 6.2 Hz, 3 H, CH_3), 1.51–1.18 (m, 4 H), 0.89 (t, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) 58.0, 54.2, 35.0, 30.4, 27.2, 22.7, 19.2, 18.5, 13.5; high

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resolution mass spectrum, calcd for $C_9H_{19}N$ (M^+ – HCl) 141.1545, found 141.1508; mass spectrum, (M^+ – HCl) 141 (6.5), 140 (13.7), 126 (40.3), 98 (46.5), 97 (100), 70 (56.7), 56 (59.0), 55 (61.2), 43 (72.0), 41 (61.3).

***trans*-2-Nonene-4,8-dione 8-(2,2-Dimethylpropylene ketal) (3b).** A flask was charged with methyl crotonate (1.80 g, 18.0 mmol) and lithium hydroxide monohydrate (0.755 g, 18.0 mmol). Water (5 mL) and methanol (15 mL) were added. The mixture, originally at 0 °C, was warmed to room temperature overnight with stirring. After this period the reaction volatiles were removed in vacuo. The residue was suspended in THF (10 mL) and cooled (–25 °C) as a pentane solution of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal (0.50 M, 36.0 mL, 18.0 mmol) was added by cannula over 10 min. The reaction mixture was stirred overnight under nitrogen as the temperature was allowed to rise to ambient. After the usual workup, the resultant oil (4.7 g) was subjected to flash chromatography (silica gel, 10% ethyl acetate–hexane) to yield ketal enone **3b** as a colorless oil (0.550 g, 2.29 mmol, 12.7%): IR (neat liquid) 2960, 2870, 1670, 1635, 1445, 1395, 1375, 1120, 1190 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 6.85 (dq J = 16, 6.8 Hz, 1 H, CH_3CH), 6.12 (dd, J = 16, 1.7 Hz, 1 H, $COCH$), 3.54 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 3.43 ($^1/_2$ AB q, J = Hz, 2 H, OCH_2), 2.56 (t, J = 7 Hz, 2 H, $COCH_2$), 1.89 (dd, J = 6.8, 1.7 Hz, 3 H, $CHCH_3$), 1.76 (m, 4 H, CH_2), 1.37 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.89 (s, 3 H CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 200.4, 142.4, 132.0, 98.9, 70.35 (double intensity), 39.9, 37.4, 29.9, 22.8, 22.5, 20.3, 18.3, 18.2; high resolution mass spectrum, calcd for $C_{13}H_{21}O_3$ (M^+ – CH_3) 225.1491, found 225.1480; mass spectrum, (M^+) 240 (2.1), 226 (20.1), 225 (72.0), 155 (36.9), 129 (68.1), 97 (14.9), 85 (10.7), 69 (100), 56 (16.8), 55 (20.8). Anal. Calcd for $C_{14}H_{24}O_3$: C, 70.00; H, 10.00. Found: C, 69.88; H, 10.05.

6-Amino-2-nonanone 2,2-Dimethylpropylene Ketal (4a) (from 3b). Enone ketal **3b** (125 mg, 0.520 mmol) was dissolved in methanol (5 mL). Ammonium acetate (400 mg, 5.20 mmol), 3A molecular sieves (50 mg), and sodium cyanoborohydride (33.0 mg, 0.520 mmol) were added. The mixture was stirred overnight. After the usual workup, the resultant oil was subjected to flash chromatography (silica gel, 5% triethylamine–ethyl acetate) to yield 6-amino-2-nonanone 2,2-dimethylpropylene ketal (97.4 mg, 0.401 mmol, 77.1%). The TLC and spectral characteristics of the material obtained in this manner were identical with those reported above.

2,6-Heptadecanedione 2-(2,2-Dimethylpropylene ketal) (3c). Freshly distilled (bp 108–110 °C at 0.09 mmHg) lauroyl chloride (3.06 g, 3.24 mL, 14.0 mmol) and ether (40 mL) were cooled to –78 °C under argon. To the stirring solution was added a –25 °C solution of the dialkylcuprate reagent **1a** (prepared from 65.2 mL of a 0.46 M pentane solution of 5-lithio-2-pentanone 2,2-dimethlpropylene ketal and 2.67 g, 14.0 mmol of copper(I) iodide) by cannula over 15 min. After the addition was complete, the mixture was warmed to –15 °C and then to 0 °C over 45 min. The 0 °C solution was quenched by pouring the mixture into a rapidly stirring, saturated $NaHCO_3$ solution (100 mL) and worked up in the usual manner. The resultant oil was purified by flash chromatography (silica gel, 10% ethyl acetate–hexane) to give 2,6-heptadecanedione 2-(2,2-dimethylpropylene ketal) (**3c**) (2.21 g, 6.24 mmol, 89.2%) as a crystalline solid: mp 32–34 °C; bp 125 °C at 0.04 mmHg; IR (neat liquid) 2950, 2930, 2860, 1715, 1460, 1360, 1255, 1210, 1095, 1045 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 3.54 ($^1/_2$ AB q, J = 12 Hz, 2 H, OCH_2), 3.44 ($^1/_2$ AB q, J = 12 Hz, 2 H, OCH_2, 2.43 (t, 2 H, J = 6.9 Hz, $COCH_2$), 2.38 (t, J = 7.5 Hz, 2 H, $COCH_2$), 1.71 (m, 2 H), 1.68 (m, 1 H), 1.39 (s, 3 H, CH_3), 1.36–1.25 (m, 19 H), 1.00 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.88 (t, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 211.08, 98.60, 70.36, (double intensity), 42.78, 42.70, 37.54, 31.92, 29.94, 29.63, 29.50, 29.45, 29.35, 29.29, 23.89, 22.83, 22.79, 22.70, 22.52, 20.17, 17.92, 14.12; high resolution mass spectrum, calcd for $C_{22}H_{42}O_3$ 354.3134, found 354.3127; mass spectrum, (M^+) 354 (0.5), 340 (13.4), 339 (66.2), 270 (2.0), 269 (12.2), 130 (15.0), 129 (100), 128 (5.2), 110 (3.5), 69 (6.8), 43 (4.9). Anal. Calcd for $C_{22}H_{42}O_3$: C, 74.57; H, 11.86. Found: C, 74.61; H, 11.95.

6-Amino-2-heptadecanone 2,2-Dimethylpropylene Ketal (4b). A methanol (2 mL) solution of the ketone ketal **3c** (100 mg, 0.282 mmol) was stirred with 4A molecular sieves (50 mg) as ammonium acetate (217 mg, 2.82 mmol) was added. After the addition of sodium cyanoborohydride (17.7 mg, 0.282 mmol), the suspension was stirrred under nitrogen at room temperature for 4 h. After the usual workup and flash chromatography (silica gel, 5% triethylamine–ethyl acetate) amino ketal **4b** (92.1 mg, 0.259 mmol, 91.9%) was obtained a colorless oil: bp 145 °C at 0.04 mmHg; IR (CCl_4) 3490, 2965, 2935, 2870, 1625, 1460, 1375, 1125, 1095 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 3.55 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 3.43 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 2.70 (m, 1 H, NCH), 1.69 (m, 1 H), 1.53–1.43 (m, 5 H), 1.42 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 98.93, 70.35 (double intensity), 51.13, 38.3, 31.81, 29.94, 29.76, 29.62 (triple intensity, three peaks not resolved), 29.60, 29.31, 26.15, 22.78, 22.65, 22.47, 20.15, 19.99, 14.07 [Two carbons not observed due to coincidental overlap]; high resolution mass spectrum: calcd for $C_{21}H_{42}NO_2$ (M^+ – CH_3) 340.3217, found 340.3233; mass spectrum, (M^+) 355 (0.4), 340 (8.7), 268 (13.3), 200 (73.1), 184 (99.4), 129 (82.0), 114 (11.7), 96 (49.6), 56 (61.4), 43 (100). Anal. Calcd for $C_{22}H_{45}NO_2$: C, 74.37; H, 12.68; N, 3.94. Found: C, 74.28; H, 12.80; N, 4.02.

2-Methyl-6-undecyl-3,4,5,6-tetrahydropyridine (5b). Amino ketal **4b** (300.0 mg, 0.45 mmol) was stirred with 10% HCl (1 mL) and THF (5 mL) for 1 h. Following the usual extractive workup, the resultant oil (300 mg) was subjected to flash chromatography (silica gel, 9:1 hexane–ethyl acetate with 5% triethylamine added) to yield the imine derivative **5b** (185 mg, 0.737 mmol) in 87.2%: bp 120 °C at 0.05 mmHg; IR (neat liquid) 2935, 2860, 1655, 1460, 1370, 1180 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 3.23 (br m, 1 H, NCH), 2.09 (m, 2 H, $NC(CH_3)CH_2$), 1.91 (d, J = 1.5 Hz, 3 H, CH_3), 1.70 (m, 3 H), 1.43 (m, 1 H), 1.40–1.26 (m, 19 H), 1.11 (m, 1 H), 0.88 (t, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 166.82, 57.52, 37.52, 31.73, 30.10, 29.68, 29.54, 29.50, 29.48, 29.45, 29.16, 27.34, 26.65, 26.11, 22.49, 18.62, 13.91; high resolution mass spectrum, calcd for $C_{17}H_{33}N$ 251.2613, found 251.2610; mass spectrum, (M^+) 251 (33.5), 152 (31.9), 131 (11.0), 111 (25.4), 110 (100), 97 (97), 96 (51.4), 55 (26.5), 43 (17.2). Anal. Calcd for $C_{17}H_{33}N$: C, 81.27; H, 13.18; N, 5.58. Found: C, 81.01; H, 13.20; N, 5.49.

***cis*-2-Methyl-6-undecylpiperidine (6d).** Tetrahydropyridine **5b** (40.0 mg, 0.160 mmol) was stirred under nitrogen for 3 h with a citrate–phosphate buffer (1 mL, pH 5.3), THF (1 mL), and sodium cyanoborohydride (11.1 mg, 0.176 mmol). After workup, the resultant oil was subjected to flash chromatography (silica gel, 9:1 hexane–ethyl acetate with 5% added triethylamine) to give the cis-disubstituted piperidine **6b** (38.5 mg, 0.152 mmol) in 95.1% yield: bp 115 °C at 0.03 mmHg; IR (neat liquid) 2920, 2860, 2805, 2715, 1460, 1370, 1320, 1125, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 2.63 (m, 1 H NCH), 2.48 (m, 1 H, NCH), 1.75 (m, 1 H), 1.58 (m, 2 H), 1.36–1.23 (m, 22 H), 1.07 (d, J = 6.3 Hz, 3 H, CH_3), 1.03 (m, 2 H), 0.88 (t, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 57.30, 52.62, 37.63, 34.60, 32.44, 32.05, 29.99, 29.80, 29.76 (double intensity) 29.74, 29.48, 26.13, 25.04, 23.23, 22.80, 14.21; high resolution mass spectrum, calcd for $C_{17}H_{35}N$ 253.2769, found 253.2767; mass spectrum, (M^+) 253 (0.9), 252 (2.3), 238 (3.9), 99 (13.4), 98 (100), 96 (10.11), 83 (2.7), 81 (1.6), 71 (0.7), 70 (5.3), 69 (4.9), 57 (4.1), 55 (15.9), 43 (14.5), 41 (19.8). Anal. Calcd for $C_{17}H_{35}N$: C, 80.63; H, 13.83; N, 5.53. Found: C, 80.71; H, 13.72; N, 5.59.

1,1-Dimethoxy-5,9-decanedione 9-(2,2-Dimethylpropylene ketal) (3d). Methyl 5,5-dimethoxypentanoate (3.52 g, 20.0 mmol) was dissolved in methanol (30 mL) and water (10 mL). To the cooled (0 °C) solution was added LiOH (0.838 g, 20 mmol). The solution was stirred overnight while the flask was slowly warmed to room temperature. The volatiles were removed in vacuo. The cake was pulverized and then dried on the high vacuum line. The salt was suspended in THF (20 mL) as the mixture was cooled to –25 °C. A precooled (0 °C) pentane solution of 5-lithio-2-pentanone 2,2-dimethylpropylene ketal (0.40 M, 55.0 mL, 22.0 mmol) was added over 30 min by cannula to the stirred suspension. The mixture was stirred under nitrogen overnight as the reaction was allowed to warm to ambient temperature. After the usual workup, flash chromatography (silica gel, 75% hexane–ethyl acetate) furnished pure **3d** (4.59 g, 14.71 mmoles, 73.6%) as a colorless oil: bp 165 °C at 0.20 mmHg; IR (neat liquid) 3050, 3030, 2860, 2825, 1715, 1470, 1455, 1390, 1350, 1210, 1190, 1125, 1085 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 4.34 (t, J = 5.2 Hz, 1 H, $(CH_3O)_2CH$), 3.54 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 3.41 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 3.31 (s, 6 H, OCH_3), 2.43 (t, J = 6.7 Hz, 4 H, CH_2COCH_2), 1.78–1.56 (m, 8 H), 1.56 (s, 3 H, CH_3),

1.39 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 210.7, 104.5 (double intensity), 98.9, 70.5 (double intensity), 52.9, 42.9, 42.3, 37.7, 32.11, 30.1, 23.0, 22.6, 20.3, 19.0, 18.0; high resolution mass spectrum, calcd for $C_{17}H_{32}O_5$ 316.2249; found 316.2275; mass spectrum, (M^+) 316 (0.7), 302 (17.2), 301 (100), 285 (10.1), 284 (17.7), 253 (10.0), 129 (40.5), 75 (9.6), 71 (12.5). Anal. Calcd for $C_{17}H_{32}O_5$: C, 64.56; H, 10.13. Found: C, 64.39; H, 9.95.

5-Amino-1,1-dimethoxy-9-decanone 2,2-Dimethylpropylene Ketal (4c). Ketone **3d** (1.00 g, 3.16 mmol) was dissolved in methanol (15 mL). Molecular sieves (4A, 0.60 g) and ammonium acetate (2.46 g, 32.0 mmol) were added. After the addition of sodium cyanoborohydride (0.201 g, 3.2 mmol), the mixture was stirred under a nitrogen atmosphere at room temperature overnight. Subsequently, the suspension was filtered and subjected to basic extractive workup. Very pure material (0.770 g, 2.27 mmol, 71.8% yield) was obtained by flash chromatography (silica gel, 10% triethylamine–ethyl acetate): bp 160 °C at 0.20 mmHg; IR 3580, 3380, 3300, 2990, 2960, 2870, 1460, 1375, 1125, 1085 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 4.37 (t, J = 5.6 Hz, 1 H, $(CH_3O)_2CH$), 3.55 ($^1/_2$ AB q, J = 11.2 Hz, 2 H, OCH_2), 3.44 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 3.32 (s, 6 H, OCH_3), 2.71 (m, 1 H, NCH), 1.70–1.41 (m, 12 H), 1.36 (s, 3 H, CH_3), 1.33–1.26 (m, 2 H), 0.99 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 104.5 (double intensity), 98.9, 70.3 (double intensity), 52.7, 52.6, 51.1, 38.4, 37.7, 32.6, 29.9, 22.8, 22.5, 21.2, 20.1, 20.0; high resolution mass spectrum, calcd for $C_{16}H_{32}NO_4$ ($M^+ - CH_3$) 302.2323, found 302.2316; mass spectrum, (M^+) 302 (2.3), 200 (30.5), 129 (81.3), 114 (73.5), 96 (46.3), 82 (18.0), 75 (42.5) 71 (99.3), 69 (38.8), 56 (77.5), 43 (100). Anal. Calcd for $C_{17}H_{35}O_4N$: C, 64.35, H, 11.04; N, 4.42. Found: C, 64.43; H, 11.19; N, 4.36.

2-Methyl-3,4,5,6-tetrahydropyridine-6-butanal 2,2-Dimethylpropylene Acetal (5d). A solution of the THF (1 mL), 10% HCl (1 mL), and amine **4c** (225 mg, 0.170 mmol) was stirred 1 h at room temperature and then the pH was adjusted to 5.3 with 40% NaOH and a citrate–phosphate buffer. The solution was stirred overnight. The oil resulting from extractive workup was subjected to flash chromatography (silica gel, 9:1 hexane–ethyl acetate with 5% added triethylamine) to give the imine (0.168 g, 0.644 mmol, 93.5%) as a colorless oil: IR (neat liquid) 3050, 2870, 2850, 1660, 1460, 1395, 1375, 1035, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 4.44 (t, J = 5.1 Hz, 1 H, $(RO)_2CH$), 3.59 ($^1/_2$ AB q, J = 11.3 Hz, 2 H, OCH_2), 3.42 ($^1/_2$ AB q, J = 11.3 Hz, 2 H, OCH_2), 3.24 (br, 1 H, NCH), 2.05 (m, 2 H), 1.91 (d, J = 1.8 Hz, 3 H, CH_3), 1.75–1.66 (m, 5 H), 1.55–1.51 (m, 3 H), 1.38 (m, 1 H), 1.19 (s, 3 H, CH_3), 1.13 (m, 1 H), 0.72 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 167.0, 102.1, 77.1 (double intensity), 57.40, 37.30, 34.80, 30.1, 30.0, 27.4, 26.6, 22.9, 21.7, 20.6, 18.6; high resolution mass spectrum, calcd for $C_{15}H_{27}NO_2$ 253.2081, found 253.2045; mass spectrum, (M^+) 253 (11.8), 238 (13.6), 167 (16.3), 111 (27.0), 110 (62.3), 97 (100), 96 (50.5), 69 (23.3), 41 (53.9).

***cis*-6-Methylpiperidine-2-butanal 2,2-Dimethylpropylene Acetal (6c).** Although **6c** could be prepared from the imine derivative **5c** in high yield (90%) by reduction with sodium cyanoborohydride, we found it more convenient to prepare the 2,6-disubstituted piperidine directly from **4c**. Amine **4c** (1.92 g, 6.01 mmol) was dissolved in THF (5 mL) and 10% HCl (5 mL). The solution was stirred for 1 h at room temperature under nitrogen, and then the pH was adjusted to 5.5 with 40% NaOH and a citrate–phosphate buffer. Sodium cyanoborohydride (0.377 g, 60.1 mmol) was added as a solid to the stirred solution. The reduction was allowed to proceed for 3 h. After the usual workup, flash chromatography (silica gel, 5% triethylamine–ethyl acetate) afforded **6c** (1.26 g, 4.96 mmol, 82.4%) as a colorless oil: bp 95 °C at 0.15 mmHg; IR (neat liquid) 3320, 2950, 2720, 1460, 1395, 1125, 1019 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) 4.34 (t, J = 4.9 Hz, 1 H, $(RO)_2CH$), 3.45 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 3.14 ($^1/_2$ AB q, J = 11 Hz, 2 H, OCH_2), 2.40 (m, 2 H, HCNCH), 1.80–1.18 (m, 11 H), 1.16 (s, 3 H, CH_3), 1.13–1.05 (m, 2 H), 0.94 (d, J = 6.5 Hz, 3 H, $NCHCH_3$), 0.33 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 99.21, 74.5 (double intensity), 54.4, 50.1, 32.8, 32.0, 30.2, 27.6, 27.5, 21.5, 20.3, 19.2, 18.9, 17.5; high resolution mass spectrum, calcd for $C_{15}H_{29}NO_2$ 255.2198, found 255.2181; mass spectrum, (M^+) 255 (8.2), 254 (11.2), 246 (60.1), 213 (15.6), 172 (14.7), 152 (29.7), 151 (72.8), 150 (12.07), 149 (10.3), 136 (30.5), 98 (100). Anal. Calcd for $C_{15}H_{29}NO_2$: C, 70.59; H, 11.39; N, 5.99. Found: C, 70.07; H, 10.87; N, 5.58.

1-(Trimethylsilyl)-2-pentanone (8). (Chloromethyl)trimethylsilane (3.05 g, 25.0 mmol) was added dropwise to magnesium (0.75 g, 25.0 mmol) and ether (20 mL), with stirring under a nitrogen atmosphere at room temperature. After the addition was complete (15 min), the mixture was stirred for an additional 15 min at room temperature. The precooled (−78 °C) solution was cannulated dropwise over 5 min into a suspension of copper(I) iodide (2.38 g, 12.5 mmol) and ether (50 mL at −78 °C) warmed to −25 °C for 15 min and then recooled to −78 °C. To the solution was added via cannula a solution of butyryl chloride (2.66 g, 25.0 mmol) in ether (5 mL). After 30 min at −78 °C, the solution was warmed to 0 °C for 30 min. The mixture was then quenched, subjected to extractive workup, and distilled. The α-silyl ketone (3.31 g, 20.8 mmol, 83.2%) was obtained as a colorless oil: bp 29–30 °C at 0.05 mmHg; IR ($CDCl_3$) 2980, 2975, 2905, 2890, 2225, 1680, 1409, 1300, 1255, 1190, 1135, 1060, 820 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 2.21 (t, J = 7.3 Hz, 2 H, $COCH_3$), 2.09 (s, 2 H, $COCH_2SiMe_3$), 1.46 (sextet, J = 7.3 Hz, 2 H, CH_2CH_3), 0.79 (t, J = 7.3 Hz, 2 H, CH_2CH_3), 0.00 (s, 9 H, $Si(CH_3)_3$; ^{13}C NMR 208, 45.9, 37.5, 17.0, 13.4, −1.50 (triple intensity); high resolution mass spectrum, calcd for $C_8H_{18}OSi$ 158.1127, found 158.1130; mass spectrum, (M^+) 158 (15.2), 143 (64.1), 130 (16.9), 116 (19.1), 115 (94.3), 75 (89.0), 73 (100), 59 (10.3), 45 (24.8), 43 (21.7). Anal. Calcd for $C_8H_{18}OSi$: C, 60.72; H, 11.38; Si, 17.76. Found: C, 60.64; H, 11.41; Si; 17.64.

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Registry No. **1b**, 108818-50-4; **3a**, 109531-97-7; **3b**, 109532-06-1; **3c**, 109532-00-5; **3d**, 109532-02-7; **4a**, 109531-98-8; **4b**, 109532-01-6; **4c**, 109532-03-8; **5a**, 109531-99-9; **5b**, 35285-61-1; **5c**, 109532-04-9; **6a**, 109583-97-3; **6a**·HCl, 109583-96-2; **6b**, 92619-72-2; **6c**, 109532-05-0; **8**, 60484-89-1; butyryl chloride, 141-75-3; methyl crotonate, 18707-60-3; lauroyl chloride, 112-16-3; methyl 5,5-dimethoxypentanoate, 23068-91-9; (chloromethyl)trimethylsilane, 2344-80-1.