Asymmetric Synthesis of a Constituent of Iris Essential Oil by Homoenolate Alkylation of a Chiral Bicyclic Lactam

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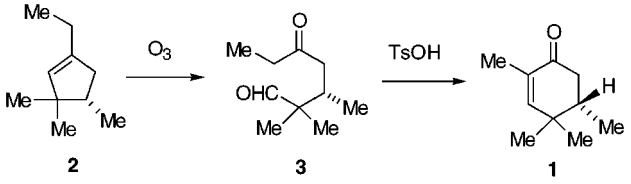
Recently, we reported the preparation of an α-cyano enamine **B** from a chiral bicyclic lactam, **A**, which, when metalated, underwent stereoselective alkylation at the γ-carbon to produce **C** (Scheme 1).[1] Hydrolysis of the alkylated cyano enamine revealed the lactam carbonyl, and subsequent reduction and auxiliary cleavage provided enantiopure 5-substituted cyclohexenones **D**. As an extension of this homoenolate-equivalent alkylation strategy, (*S*)-(−)-2,4,4,5-tetramethylcyclohexenone (**1**) was chosen as a suitable target for total synthesis. The (*R*)-

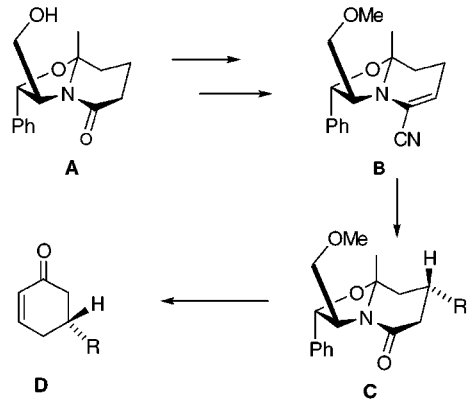


(+)-enone was isolated from the essential oil of iris rhizomes and first characterized fully by Garnero and Joulain in 1981.[2] Enantioselective syntheses of both (+)-**1** and (−)-**1** were carried out by Chapuis in 1993 utilizing pinene derivatives.[3] Ozonolysis of cyclopentene **2** afforded keto aldehyde **3**, which was subjected to acid-catalyzed aldol condensation to provide the chiral, nonracemic natural product **1**.

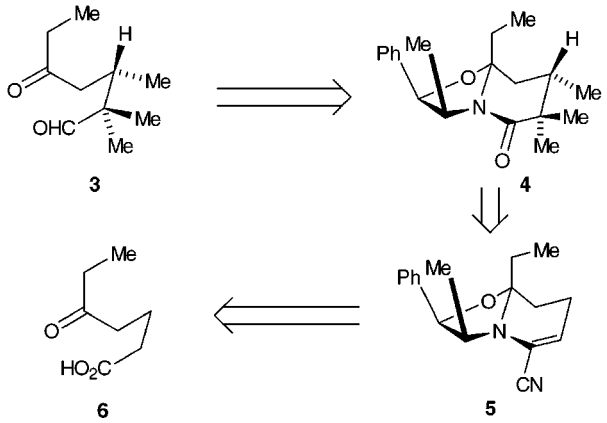
It was envisioned that Chapuis' chiral, optically active intermediate keto aldehyde **3** could be obtained by the standard partial reduction and acid-mediated hydrolysis of trimethylated bicyclic lactam **4**. The single tertiary stereocenter would be installed through the *endo*-selective alkylation of α-cyano enamine **5**,[1] followed by α,α-dimethylation of the lactam obtained after hydrolysis.

The required keto acid **6** was prepared in a two-step process beginning with the addition of 4-carbomethoxybutanoyl chloride to a solution of ethylmagnesium bromide in THF at −78 °C, resulting in chemoselective conversion of the acid chloride to the ketone.[4] Hydrolysis of the resultant keto ester to the acid **6** proceeded in excellent overall yield (90% over two steps). Cyclodehydration of the crude keto acid **6** with (−)-(1*R*,2*S*)-*nor*-ephedrine yielded bicyclic lactam **7** as a 3:1 mixture of angular ethyl epimers (determined by ^{1}H NMR) that were

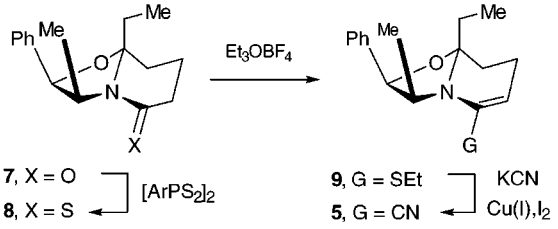
Scheme 1



separated by flash chromatography to yield **7** as a single diastereomer (64%). The separation of the epimers



proved to be difficult, and a second column was necessary to provide diastereomerically pure material. Thionation of **7** with the Belleau reagent[5] proceeded smoothly to provide thiolactam **8** in 84% yield. Conversion of **8** to the *N*,*S*-ketene acetal **9** by treatment with Meerwein's reagent[6] followed by cyanation with potassium cyanide in the presence of copper(I) iodide and catalytic iodine gave cyano enamine **5** in excellent overall yield (88%).[1]



It was anticipated that introduction of the γ-methyl group would proceed in a stereoselective fashion as before.[1] Thus, metalation of **5** with LiTMP at −78 °C in THF/HMPA, followed by quench with methyl iodide, afforded crude alkylated product that was not isolated

(1) Schwarz, J. B.; Meyers, A. I. *Tetrahedron* **1997**, *53*, 8795. For reviews of the chemistry of bicyclic lactams, see: Romo, D.; Meyers, A. I. *Tetrahedron* **1991**, *47*, 9503. Meyers, A. I.; Brengel, G. P. *J. Chem. Soc., Chem. Commun.* **1997**, 1.

(2) Isolation: (a) Naves, Y. R. *Helv. Chim. Acta* **1949**, *32*, 1351. (b) Naves, Y. R. *ibid.* **1949**, *32*, 2171. (c) Treibs, W. *Chem. Ber.* **1950**, *83*, 431. Structure determination: (d) Garnero, J.; Joulain, D. *Riv. Ital. E.P.P.O.S.* **1981**, *63*, 141.

(3) For an enantioselective synthesis of **1**, see: Chapuis, C.; Brauchli, R.; Thommen, W. *Helv. Chim. Acta* **1993**, *76*, 535.

(4) Eberle, M. K.; Kahle, G. G. *Tetrahedron Lett.* **1980**, *21*, 2303.

(5) Lajoie, G.; Lepine, F.; Maziak, L.; Belleau, B. *Tetrahedron Lett.* **1983**, *24*, 3815. For recent applications of chiral bicyclic thiolactams, see: Devine, P. N.; Meyers, A. I. *J. Am. Chem. Soc.* **1994**, *116*, 2633. Munchhof, M. J.; Meyers, A. I. *J. Am. Chem. Soc.* **1995**, *117*, 5399.

(6) Meerwein, H. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 1080.

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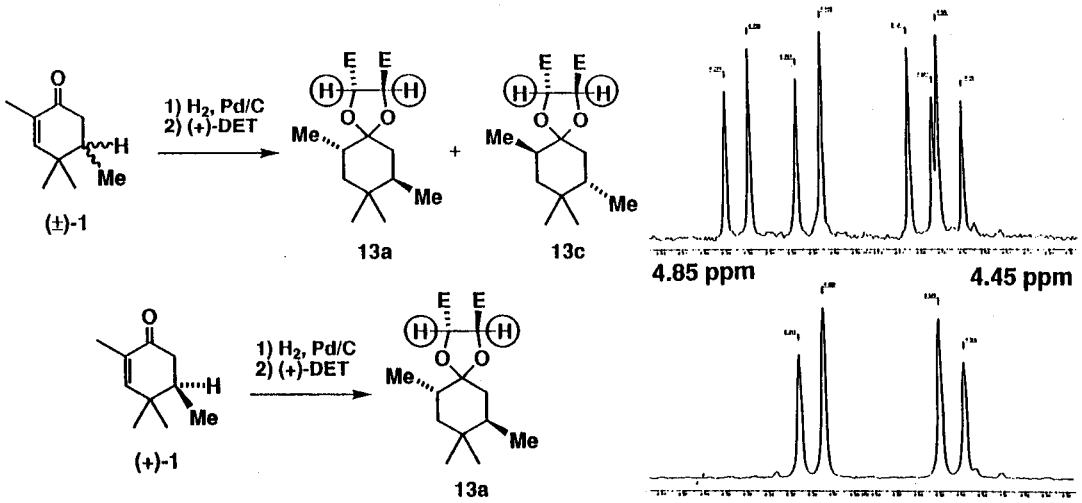
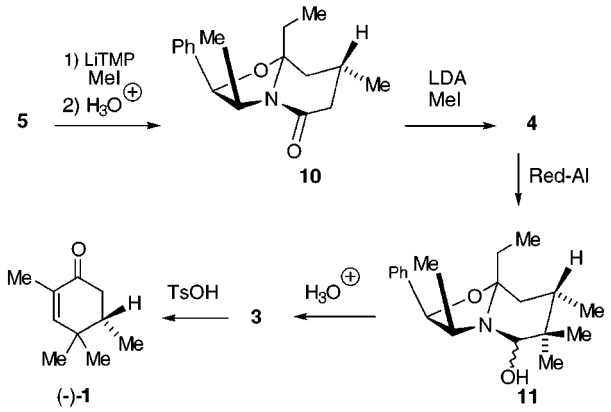
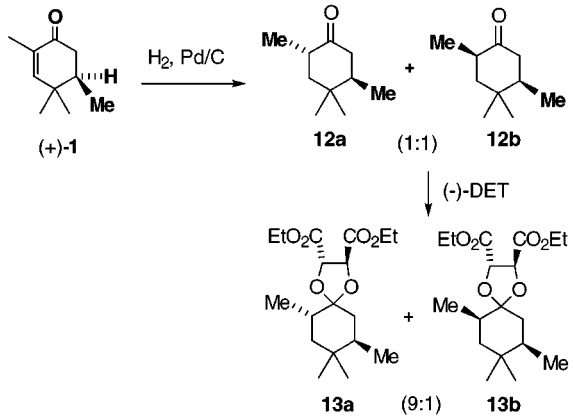
Scheme 2



but directly subjected to hydrolysis (1 N HCl, THF/H_2O) and flash chromatography. As expected, lactam **10** was obtained as a single diastereomer in 59% yield, containing the sole stereocenter present in the natural product **1**. Introduction of the α,α-*gem*-dimethyl moiety proceeded uneventfully with excess LDA and methyl iodide leading to **4**. Partial reduction of **4** with Red-Al (THF, 0 °C) smoothly gave the carbinolamine **11** as a single diastereomer in nearly quantitative yield. The stereochemistry of the newly formed hydroxyl group was of no consequence and thus not determined. Hydrolysis (tetrabutylammonium dihydrogen phosphate, EtOH−H_2O, reflux) furnished the keto aldehyde **3**. Interestingly, aldol cyclization of **3** was not promoted by base (KOH/EtOH, THF), and therefore the acid-catalyzed procedure previously reported[3] (*p*-TsOH, cyclohexane, reflux) was employed, producing (*S*)-(−)-2,4,4,5-tetramethylcyclohex-2-enone (**1**) in 72% overall yield from **4**.



The synthetic product matched well to the natural material in most respects (NMR, IR, MS). However, the optical rotations were found to vary by a large margin. Thus, (−)-**1** obtained above showed $[\alpha]^{23}_D$ −44.9 (*c* 2.00, $CHCl_3$); the product from isolation[2d] was reported as $[\alpha]^{23}_D$ +11.0 (*c* 4.0, $CHCl_3$), and the Chapuis[3] product exhibited $[\alpha]^{23}_D$ −62.4 (*c* 5.38, $CHCl_3$). Furthermore, (+)-**1** was also prepared from (+)-(1*S*,2*R*)-*nor*-ephedrine using the identical scheme, and the optical rotation was very close in magnitude to (−)-**1** ($[\alpha]^{23}_D$ +40.7, *c* 2.82, $CHCl_3$). To verify that no racemization of the stereocenter occurred during the reduction/hydrolysis procedure, the enone (+)-**1** was subjected to hydrogenation (Pd/C, EtOAc), resulting in a 1:1 mixture of cyclohexanone diastereomers **12a** and **12b** at the newly formed α-methyl stereocenter. Ketalization with (−)-diethyl tartrate in refluxing toluene catalyzed by *p*-TsOH resulted in formation of two tartrate diastereomers **13a** and **13b** in a 9:1 ratio by GC.[7] The racemic natural product (±)-**1** was also synthesized by a procedure adapted from the isolation paper.[2d] Hydrogenation of (±)-**1** followed by ketalization with (−)-diethyl tartrate provided two major compounds in a 1:1 ratio as determined by GLC. These were presumed to be *trans*-2,5-dimethyl ketals **13a** and **13c**. The minor products from ketalization of the cyclohexanones derived from both (+)-**1** and (±)-**1** were likely the *cis*-2,5-dimethyl ketals. The assignments were based on work by Chapuis, who demonstrated that the equilibrium ratio (NaOEt) of *trans*-**12a** and *cis*-**12b** was 9:1 (Scheme 2).[3] Proof of the assignments was obtained via GLC analysis of the 9:1 ketal mixture derived from (+)-**1** and the 1:1 mixture of **13a** and **13c** from (±)-**1**, which showed that no **13c** was present in the 9:1 mixture. This was



also demonstrated by the ^1H NMR spectrum (Scheme 2). Since **13c** would only be present in the ketal sample from (+)-**1** if the sample was not optically pure, the synthetic sample of (+)-**1** obtained from bicyclic lactam **4** in all

(7) Tartrate ketals have previously been used to determine ee's of chiral cyclohexanones: Rossiter, B. E.; Eguchi, M.; Miao, G.; Swingle, N. M.; Hernandez, A. E.; Vickers, D.; Fluckiger, E.; Patterson, R. G.; Reddy, K. V. *Tetrahedron* **1993**, *49*, 965. The tartrate ketals from (+)-**1** and (±)-**1** were prepared by the method described in ref 1.

likelihood was no less than 95% optically pure. It is indeed possible that the naturally occurring enone **1** isolated from iris rhizomes exists as a mixture of enantiomers, thus accounting for the smaller magnitude of optical rotation.

Experimental Section

Thin-layer chromatography (TLC) and flash chromatography were performed with E. Merck or Amicon Matrix silica gel (230−400 mesh). All reagents were purchased from Aldrich. All nonaqueous reactions were conducted under an argon atmosphere in flame-dried apparatus. Tetrahydrofuran was distilled from sodium−benzophenone ketyl under argon atmosphere prior to use. HMPA was distilled from calcium hydride under reduced pressure prior to use. Methyl iodide was passed through a plug of basic Al_2O_3 prior to use.

Methyl 5-Oxoheptanoate. To 25.0 mL of stirred THF was added ethylmagnesium bromide (1.0 M solution in THF, 15.2 mL, 15.2 mmol). The solution was cooled to −78 °C, and 4-carbomethoxybutanoyl chloride (Aldrich, 2.10 mL, 15.2 mmol) was added dropwise at such a rate that the temperature of the mixture did not exceed −70 °C. The mixture was allowed to warm slowly to ambient temperature over 12 h and then quenched with saturated NH_4Cl (aq, 15 mL). Water (10 mL) was added to dissolve the solids, and the phases were separated. The aqueous phase was extracted with ether (2 × 30 mL), and the combined organic phases dried ($MgSO_4$) and concentrated to yield 2.35 g (98%) of keto ester as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7.3 Hz, 3H), 1.84 (quint, J = 7.2 Hz, 2H), 2.26−2.45 (m, 4H), 3.61 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 7.60, 18.77, 32.90, 35.73, 40.89, 51.34, 173.44, 210.45; IR (neat) 1736, 1715 cm^{-1}.

5-Oxoheptanoic Acid 6. To the crude keto ester (2.35 g, 14.9 mmol) were added methanol (50 mL) and 20% KOH (aq, 50 mL). The mixture was stirred at ambient temperature for 4 h, poured into a separatory funnel, and washed with ether (100 mL). The phases were separated, and the aqueous phase was acidified to pH 2 with concentrated HCl (exotherm). The solution was allowed to cool to ambient temperature and extracted with ether (2 × 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated to yield 1.98 g (92%) of **6** as a yellow oil that solidified upon standing: mp 42−44 °C (lit.[8] mp 39.1−41.4 °C); ^{1}H NMR ($CDCl_3$) δ 1.01 (t, J = 7.3 Hz, 3H), 1.86 (quint, J = 7.2 Hz, 1H), 2.32−2.49 (m, 7H), 11.3 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 7.62, 18.48, 32.91, 35.80, 40.79, 179.15, 210.92; IR (neat) 1734, 1709 cm^{-1}. Physical and spectral properties matched well with those described previously.[8]

Bicyclic Lactam 7. The crude keto acid **6** (1.98 g, 13.7 mmol) and (−)-(1*R*,2*S*)-*nor*-ephedrine (2.30 g, 15.2 mmol) were taken up in toluene (76 mL) and heated at reflux with azeotropic removal of water for 12 h, cooled, and concentrated. Flash chromatography (twice) of the residue (1:1 hexanes−ethyl acetate) provided 2.29 g (64%) of the lactam **7** as a pale yellow oil: $[\alpha]^{23}_D$ −49.5 (*c* 1.60, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.84 (d, J = 7.0 Hz, 3H), 1.09 (t, J = 7.5 Hz, 3H), 1.52−1.98 (m, 5H), 2.21 (ddd, J = 2.4, 5.4, 8.0 Hz, 1H), 2.44 (m, 2H), 4.70 (quint, J = 6.7 Hz, 1H), 5.09 (d, J = 5.8 Hz, 1H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.75, 14.97, 16.14, 28.53, 29.31, 32.05, 54.67, 78.99, 94.94, 126.08, 127.69, 128.28, 136.64, 169.02; IR (neat) 1649 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16. Found: C, 73.99; H, 8.21.

Thiolactam 8. To a stirred solution of lactam **7** (1.67 g, 6.44 mmol) in 32.0 mL of toluene was added Belleau's reagent[5] (1.79 g, 3.86 mmol). The mixture was heated to reflux for 1 h, cooled, and concentrated onto silica gel. Flash chromatography of the residue (4:1, hexanes: ethyl acetate) afforded 1.48 g (84%) of thiolactam **8** as a colorless crystalline solid: mp 173−175 °C; $[\alpha]^{23}_D$ +45.9 (*c* 1.64, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.97 (d, J = 6.0 Hz, 3H), 1.11 (t, J = 7.5 Hz, 3H), 1.71−2.02 (m, 5H), 2.21 (m, 1H), 2.80 (m, 1H), 3.20 (m, 1H), 5.21 (m, 2H), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.62, 13.72, 15.21, 28.40, 30.91, 37.95, 61.42, 77.78, 96.76, 126.05, 127.97, 128.38, 135.64, 197.37; IR (neat) 1466 cm^{-1}.

(8) Utaka, M.; Watabu, H.; Takeda, A. *J. Org. Chem.* **1987**, *52*, 4363.

***N,S*−Ketene Acetal 9.** To a stirred solution of thiolactam **8** (1.59 g, 5.77 mmol) in 30 mL of CH_2Cl_2 was added triethyloxonium tetrafluoroborate[6] (1.4 M solution in CH_2Cl_2, 5.36 mL, 7.51 mmol). The solution was heated at reflux for 1 h, cooled, poured into saturated $NaHCO_3$ (aq, 50 mL), and shaken. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (30 mL). The combined organic phases were dried (K_2CO_3) and concentrated to yield 1.75 g (100%) of *N,S*-ketene acetal **9** as a colorless cloudy oil: ^{1}H NMR ($CDCl_3$) δ 0.81 (d, J = 6.7 Hz, 3H), 1.04 (t, J = 7.4 Hz, 3H), 1.22 (t, J = 7.3 Hz, 3H), 1.68 (q, J = 7.5 Hz, 2H), 1.78 (m, 2H), 2.06−2.23 (m, 2H), 2.54 (m, 1H), 2.80 (m, 1H), 4.00 (quint, J = 6.6 Hz, 1H), 4.92 (m, 1H), 5.28 (d, J = 5.4 Hz, 1H), 7.28 (m, 5H).

Cyano Enamine 5. To a stirred solution of *N,S*-ketene acetal **9** (1.75 g, 5.77 mmol) in 40 mL of THF were added potassium cyanide (0.56 g, 8.66 mmol), copper(I) iodide (1.65 g, 8.66 mmol), and iodine (73 mg, 0.29 mmol). The mixture was heated to reflux for 12 h, cooled to ambient temperature, and concentrated to ca. 5 mL. The residue was diluted with 5 mL of hexanes−ethyl acetate (8:1) and loaded onto a 5 × 4 cm plug of basic alumina. Elution with hexanes−ethyl acetate (8:1) provided 1.41 g (91% from thiolactam **8**) of cyano enamine **5** as a pale yellow oil. The crude cyano enamine was suitable for alkylation. Analytically pure material was obtained by flash chromatography (8:1 hexanes−ethyl acetate): $[\alpha]^{23}_D$ +79.3 (*c* 1.63, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.85 (d, J = 6.7 Hz, 3H), 1.04 (t, J = 7.5 Hz, 3H), 1.65 (m, 3H), 1.91 (m, 1H), 2.13 (m, 1H), 2.30 (m, 1H), 3.85 (quint, J = 6.6 Hz, 1H), 5.27 (d, J = 6.2 Hz, 1H), 5.47 (m, 1H), 7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 7.36, 18.25, 21.98, 26.21, 30.00, 60.52, 78.59, 94.13, 115.00, 116.35, 118.93, 126.29, 127.71, 128.26, 136.74; IR (neat) 2223, 1617 cm^{-1}. Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51. Found: C, 75.95; H, 7.58.

***β*-Methyl Lactam 10.** To a stirred solution of 2,2,6,6-tetramethylpiperidine (1.33 mL, 7.88 mmol) in 20.0 mL of THF at −78 °C was added *n*-butyllithium (1.89 M solution in hexanes, 4.17 mL, 7.88 mmol) followed by HMPA (1.37 mL, 7.88 mmol). The solution was stirred for 5 min at −78 °C, warmed to 0 °C, stirred for 15 min, anhd then cooled to −78 °C, at which time cyano enamine **5** (1.41 g, 5.25 mmol) in 7.0 mL of THF was added dropwise over 5 min. The solution was stirred at −78 °C for 20 min, and methyl iodide (0.65 mL, 10.5 mmol) was added dropwise over 5 min, stirred for 1 h at −78 °C, and quenched with saturated $NaHCO_3$ (aqueous 15 mL). The mixture was diluted with ether (15 mL), water was added to dissolve the solids (15 mL), and the phases were separated. The aqueous phase was extracted with ether (2 × 25 mL), and the combined organic phases were dried (K_2CO_3) and concentrated to a red oil. To the crude cyano enamine were added THF (50 mL) and 1 N HCl (aq, 50 mL) and the mixture stirred at ambient temperature for 6 h. The THF was evaporated, the residue was extracted with ether (3 × 50 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (1:1 hexanes−ethyl acetate) provided 0.84 g (59%) of *β*-methyl lactam **10** as a pale yellow oil: $[\alpha]^{23}_D$ −72.8 (*c* 1.93, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.85 (d, J = 7.0 Hz, 3H), 1.06 (d, J = 5.9 Hz, 3H), 1.09 (t, J = 7.6 Hz, 3H), 1.27 (app t, J = 12.1 Hz, 1H), 1.75−2.07 (m, 4H), 2.25 (dd, J = 4.5, 12.7 Hz, 1H), 2.67 (app q, J = 10.8 Hz, 1H), 4.70 (quint, J = 6.8 Hz, 1H), 5.09 (d, J = 5.9 Hz, 1H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.80, 16.26, 22.78, 22.96, 32.94, 37.96, 38.42, 54.79, 79.28, 94.89, 126.08, 127.67, 128.28, 136.77, 169.06; IR (neat) 1652 cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48. Found: C, 74.80; H, 8.57.

***α,α,β*-Trimethyl Lactam 4.** To a stirred solution of diisopropylamine (0.53 mL, 3.79 mmol) in 6.0 mL of THF at 0 °C was added *n*-butyllithium (2.15 M solution in hexanes, 1.72 mL, 3.70 mmol). The solution was stirred for 15 min at 0 °C and then cooled to −78 °C, at which time lactam **10** (0.51 g, 1.85 mmol) in 3.5 mL of THF was added dropwise over 3 min. Stirring was continued at −78 °C for 30 min, and methyl iodide (0.35 mL, 5.54 mmol) was added in one portion. After being stirred for 15 min at −78 °C, the solution was warmed to ambient temperature and stirred for 15 min. The mixture was quenched with saturated NH_4Cl (aq, 10 mL), and the phases were separated. The aqueous phase was extracted with ether (15 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated to 0.58 g of an orange oil containing a mixture

of mono- and dimethylated lactams. The crude product was resubjected to the above alkylation conditions to effect complete dimethylation to **4**. Flash chromatography of the residue (2:1 hexanes−ethyl acetate) furnished 0.49 g (88%) of lactam **4** as colorless crystals: mp 129−130 °C; $[\alpha]^{23}_D$ −78.3 (*c* 1.36, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (d, J = 7.1 Hz, 3H), 0.99 (d, J = 6.9 Hz, 3H), 1.10 (s, 3H), 1.10 (t, J = 7.4 Hz, 3H), 1.24 (s, 3H), 1.46 (app t, J = 13.0 Hz, 1H), 1.81−2.01 (m, 3H), 2.05 (dd, J = 2.4, 10.7 Hz, 1H), 4.73 (quint, J = 6.5 Hz, 1H), 5.07 (d, J = 6.2 Hz, 1H) 7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.97, 16.49, 16.56, 21.35, 25.82, 33.87, 33.96, 35.18, 41.80, 55.76, 79.82, 93.80, 126.10, 127.58, 128.27, 137.37, 175.66; IR (neat) 1643 cm^{-1}.

Carbinolamine 11. To a stirred solution of lactam **4** (0.33 g, 1.10 mmol) in 15.0 mL of THF at 0 °C was added Red-Al (3.4 M solution in toluene, 0.64 mL, 2.19 mmol) dropwise. The mixture was allowed to warm slowly to ambient temperature and stirred 12 h. The reaction was quenched by dropwise addition of methanol (2 mL) and concentrated. The residue was dissolved in 1:1 hexanes− ether (30 mL), washed with 10% NaOH (aq, 30 mL), water (30 mL), and brine (30 mL), dried ($MgSO_4$), and concentrated to provide 0.33 g (99%) of carbinolamine **11** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.65 (d, J = 6.6 Hz, 3H), 0.87 (d, *J* 6.9 Hz, 3H), 0.95 (s, 3H), 0.99 (s, 3H), 1.01 (t, J = 7.3 Hz, 3H), 1.21 (s, 1H), 1.53 (dd, J = 3.9, 13.4 Hz, 1H), 1.65 (app t, J = 13.2 Hz, 1H), 1.86 (m, 2H), 2.04 (m, 1H), 3.61 (quint, J = 6.6 Hz, 1H), 4.36 (s, 1H), 5.27 (d, J = 6.7 Hz, 1H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.35, 15.70, 18.61, 20.05, 24.66, 30.94, 33.30, 37.37, 37.56, 61.30, 77.57, 90.57, 93.54, 126.39, 127.16, 127.94, 138.25; IR (neat) 3455 cm^{-1}.

(*S*)-2,4,4,5-Tetramethylcyclohexenone (1). To a stirred solution of the crude carbinolamine **11** (0.33 g, 1.09 mmol) in 22.0 mL of absolute EtOH was added tetrabutylammonium dihydrogen phosphate (1.0 M solution in water, 22.0 mL, 22.0 mmol), and the mixture was heated to reflux for 24 h, cooled, and extracted with ether (3 × 30 mL). The combined organic phases were washed with water (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated. The crude keto aldehyde **3** was taken up in 20 mL of cyclohexane, *p*-toluenesulfonic acid monohydrate (10 mg, 0.05 mmol) was added, and the mixture was heated to reflux with azeotropic removal of water for 6 h. The mixture was cooled, washed with saturated $NaHCO_3$ (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated (with caution owing to product volatility). Flash chromatography of the residue (6:1 pentane−ether) provided 0.12 g (72% from lactam **4**) of cyclohexenone **1** as a colorless oil: $[\alpha]^{23}_D$ −44.9 (*c* 2.00, $CHCl_3$) [lit.[2d] $[\alpha]^{23}_D$ +11.0 (*c* 4.0, $CHCl_3$), lit.[3] $[\alpha]^{23}_D$ −62.4 (*c* 5.38, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 0.93, (d, J = 6.9 Hz, 3H), 0.94 (s, 3H), 1.09 (s, 3H), 1.72 (s, 3H), 1.92−2.04 (m, 1H), 2.16−2.36 (m, 2H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 15.61, 15.75, 20.13, 28.00, 36.12, 38.56, 42.43, 132.32, 156.36, 200.37; IR (neat) 1670 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{16}O(M^+)$ 152.2101, found 152.1199. Spectral and physical data matched closely in all respects to those published previously.[3]

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for all compounds (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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