mixture of *trans*-**3f** and *trans*-**4f** [61 mg, 23%; $[\alpha]^{25}_D$ -44.4° (*c* 1.22, $CHCl_3$)], and **5f** (130 mg, 49%).

5f: colorless oil, isolated as a 2:1 mixture of diastereomers; ^1H NMR ($CDCl_3$) δ 1.6–2.68 (m, 10 H), 3.0 and 3.29 (s, 3 H), 2.8–3.82 (m, 4 H), 3.85–4.15 (m, 1 H), 5.3–5.5 and 5.6–5.75 (m, exchangeable with D_2O, 1 H), 6.1–6.28 and 6.28–6.4 (m, 1 H), 7.12–7.36 (m, 3 H), 7.36–7.5 (m, 2 H); $[\alpha]^{22}_D$ -15.0° (*c* 0.99, $CHCl_3$); IR (film) 3470, 3050, 3010, 2920, 2870, 1625, 1590 cm^{-1}; chemical ionization mass spectrum, *m/z* (relative intensity) 316 (M^+ + 1, 96), 298 (100). Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99. Found: C, 72.32; H, 8.12.

(3a*S*,4*S*)-4,5,6,7-Tetrahydro-4-phenyl-2,1-benzisoxazol-3(3a*H*)-one (8) and 4,5,6,7-Tetrahydro-4-phenyl-2,1-benzisoxazolin-3(1*H*)-one (9). A 5:1 mixture of *trans*-**3f** and *trans*-**4f** (51 mg, 0.16 mmol), hydroxylamine hydrochloride (11.1 mg, 0.16 mmol), and potassium hydroxide (17.9 mg, 0.32 mmol) in 95% ethanol (5 mL) were stirred at room temperature for 48 h. The mixture was concentrated at reduced pressure, and water (5 mL) and methylene chloride (20 mL) were added. The organic phase was washed with brine and dried over magnesium sulfate. Concentration at reduced pressure and flash chromatography (silica gel, ethyl acetate/hexane (1:1)) afforded a 1:1 mixture of **8** and **9** (28 mg, 81%): ^1H NMR ($CDCl_3$) δ 1.5–1.88 (m, 3 H), 2.0–2.55 (m, 3 H), 2.78–2.94 and 3.75–3.85 (m, 2 H), 3.35 (d, *J* = 11.8 Hz, 0.65 H), 7.1–7.45 (m, 5 H); $[\alpha]^{24}_D$ -10.5° (*c* 0.55, $CHCl_3$); IR (film) 3100, 2950, 2860, 1700, 1600 cm^{-1}; chemical ionization mass spectrum, *m/z* (relative intensity) 216 (M^+ + 1, 100), 198 (6). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.46; H, 6.02.

(4*R*/*S*)-1-Methyl-4,5,6,7-tetrahydro-4-phenyl-2,1-benzisoxazolin-3-one (10d). Sodium hydride (48 mg, 0.2 mmol) was added to a mixture of **8** and **9** (25.8 mg, 0.12 mmol) in THF (5 mL). After the mixture was stirred at room temperature for 1 h, methyl iodide (36 μL, 0.58 mmol) was added and the mixture was stirred for an additional 12 h. Water (2 mL) was added, and the aqueous phase was washed with methylene chloride (10 mL). The organic phase was washed with brine and dried over magnesium sulfate. Concentration at reduced pressure and flash chromatography (silica gel, ethyl acetate/hexane (1:1)) afforded **10d** (10 mg, 38%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 1.7–1.88 (m, 3 H), 1.9–2.14 (m, 1 H), 2.3–2.6 (m, 2 H), 3.28 (s, 3 H), 3.81–3.86 (m, 1 H), 7.1–7.36 (m, 5 H); IR (film) 3020, 2930, 2850, 1730, 1620 cm^{-1}; chemical ionization mass spectrum, *m/z* (relative intensity) 230 (M^+ + 1, 100). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.16; H, 6.74.

A mixture (1:2) of *trans*-**3f** and *trans*-**4f** (150 mg, 0.47 mmol) was converted to **10d** by treatment with *N*-methylhydroxylamine as described for **10a**. The product, a colorless oil, was obtained with 28.9% ee (Chiracel OJ HPLC column, hexane/ethanol (1:1), 1.0 mL/min, 40 °C; retention times (+)-**10d** 6.65 min, (-)-**10d** 9.07 min);[14] $[\alpha]^{22}_D$ +15.5 (*c* 1.69, $CHCl_3$).

A chromatographically homogeneous sample of *trans*-**3f** (96 mg, 0.3 mmol) was converted to (4*S*)-**10d** by treatment with *N*-methylhydroxylamine in 91% yield as described for **10a**: mp 95–7 °C; $[\alpha]^{24}_D$ -56.3° (*c* 1.20, $CHCl_3$). The product was obtained with 98.7% ee as determined by the chiral HPLC analysis.[14]

(3*R*)-3-Phenylcyclohexanone (11). A stirred solution of (4*S*)-**10d** (82 mg, 0.36 mmol, 98.7% ee) in THF (5 mL) was cooled to -78 °C, and then ammonia (15 mL) was added. Lithium (7 mg, 1 mmol) was added, and the mixture was allowed to warm to -33 °C and then was refluxed for 1 h. Ammonium chloride was added, and the mixture was partitioned between water (5 mL) and methylene chloride (20 mL). The organic phase was washed with brine and dried over magnesium sulfate. Concentration at reduced pressure and flash chromatography (silica gel, ethyl acetate/hexane (1:1)) afforded **11** (38 mg, 61%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 1.55–2.0 (m, 2 H), 2.0–2.22 (m, 2 H), 2.25–2.7 (m, 4 H), 2.85–3.15 (m, 1 H), 7.05–7.42 (m, 5 H); $[\alpha]^{22}_D$ +20.5° (*c* 0.58, $CHCl_3$),[11] IR (film) 3050, 3020, 2920, 2850, 1705 cm^{-1}; chemical ionization mass spectrum, *m/z* (relative intensity) 175 (M^+ + 1, 100). Chiral HPLC comparisons of this material to racemic **11** confirmed the enantiomeric purity determined for (4*S*)-**10d** (98.7% ee).

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Supplementary Material Available: Experimental procedures and structures for compounds **11a**, **11b**, **12a**, **12b**, **14**, **15**, **16**, and **17** and tables of characterization data for products of organometallic addition to **2b**, crystal data, atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, and hydrogen atom coordinates and isotropic thermal parameters (12 pages). Ordering information is given on any current masthead page.

(14) We thank Dr. Hisao Nishimura and Daicel, Inc., for assistance with HPLC analyses.

Asymmetric Syntheses of 1,6-Dialkyl-1,4-cyclohexadiene Derivatives

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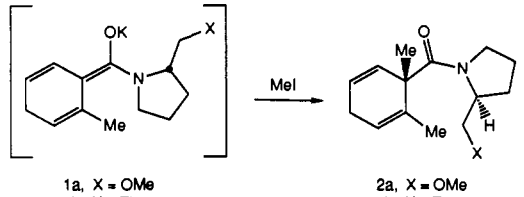
Contribution from the Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590. *Received January 4, 1991*

Abstract: Ortho-lithiation–alkylation of tertiary benzamide **3** provides a series of 2-substituted chiral benzamides **3a–g** (Scheme I). Birch reduction of **3a–j** followed by alkylation of the resulting chiral amide enolate with MeI at -78 °C gives 1,6-dialkyl-1,4-cyclohexadiene derivatives **4a–j** with excellent diastereoselectivities (Table I). Applications of this asymmetric synthesis are illustrated by conversions of **4g** to enantiomerically pure bicyclic lactone **9** and octalone **11** (Scheme III) and **4j** to hexahydro-9-anthracenone **14** (Scheme IV).

We have described the generation of enolate **1a** by potassium in ammonia reduction of the chiral benzamide **3** and alkylation of **1a** with methyl iodide to give the 1,4-cyclohexadiene **2a** in 90% isolated yield with a diastereoisomeric excess (de) of >98%.[1]



1a, X = OMe
b, X = Et

2a, X = OMe
b, X = Et

Enolate **1b**, prepared to test the importance of internal chelation arguments, gave **2b** with only slightly reduced de. The assignment of a specific configuration to enolate **1a** rested on circumstantial evidence rather than definitive spectroscopic data. Enolate configuration **1a** places the vinyl methyl substituent distant from the large, solvated alkoxide substituent. Aggregation of the enolate also probably increases the effective size of the alkoxide relative to the substituents on the nitrogen atom.

We now report a significant extension of this methodology to a wide range of 2-substituted-benzamide analogues (**3a–j**), which

(1) Schultz, A. G.; Macielag, M.; Sundararaman, P.; Taveras, A. G.; Welch, M. *J. Am. Chem. Soc.* **1988**, *110*, 7828.

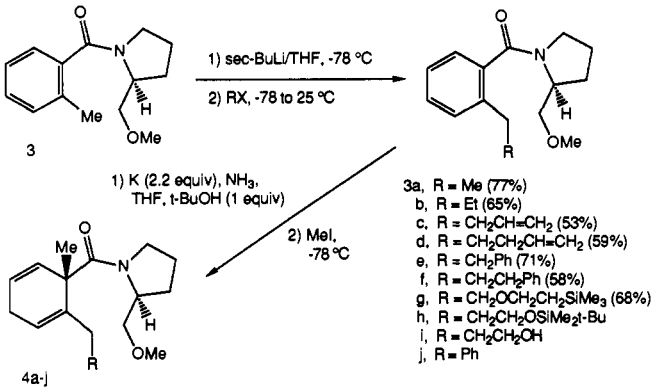
0002-7863/91/1513-4931$02.50/0

Table I. Stereoselectivities of Reductive Alkylations of Benzamides 3a–j

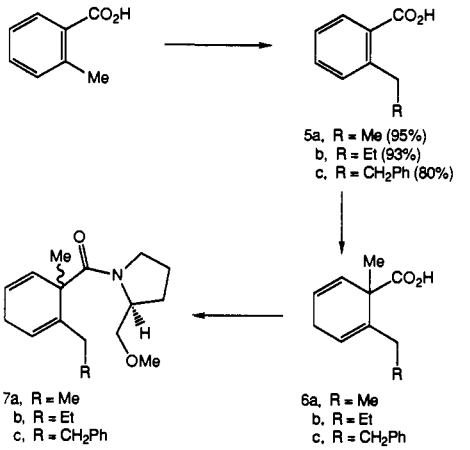
entry	product 4	% yield[a] (isolated)	diastereomer distribn (% de)[b]	GC retention time (min) major	GC retention time (min) minor
1	a, R = Me	66	25:1 (93)	23.2	24.6
2	b, R = Et	79	19:1 (90)	27.4	29.7
3	c, R = $CH_2CH{=}CH_2$	76	29:1 (93)	17.2	18.4
4	d, R = $CH_2CH_2CH{=}CH_2$	69	18:1 (90)	11.1	12.1
5	e, R = CH_2Ph	62	40:1 (95)	27.6	27.8
6	f, R = CH_2CH_2Ph	77	26:1 (93)	26.7	28.9
7	g, R = $CH_2OCH_2CH_2SiMe_3$	71	33:1 (94)	19.2	20.2
8	h, R = $CH_2CH_2OSiMe_2t$-Bu	88	53:1 (96)	16.3	18.0
9	i, R = CH_2CH_2OMe	79	42:1 (95)	27.4	29.2
10	j, R = Ph	69	48:1 (96)	18.6	19.8

[a] Yields have not been corrected for unreacted starting materials that can be recovered during chromatographic separation of the reaction mixtures. [b] Diastereomer distribution determined by GC analyses.

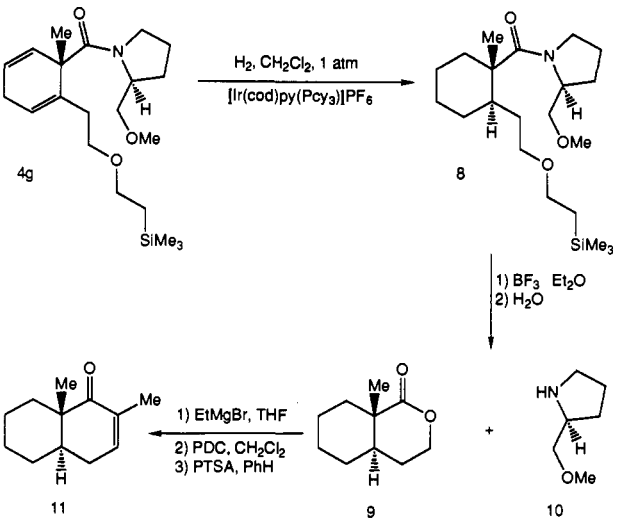
Scheme I



Scheme II



Scheme III



are prepared by benzylic substitution of **3**. Selected applications of the process demonstrate that this variant of chiral cyclohexane ring construction[2] will have broad scope. It is noteworthy that the sense of diastereoselection for analogues of enolate **1a** (i.e., those obtained from Birch reduction of **3a–j**) is the same as that previously observed for **1a**.

Results and Discussion

Preparation of Substrates for Reductive Alkylation. Ortholithiation of tertiary benzamide **3** provided a convenient route to 2-substituted chiral benzamides **3a–g** (Scheme I).[3a] The yields for this benzylic substitution were in the moderate to good range (yields given in parentheses refer to isolated products); alternatively, lithiation–alkylations of 2-methylbenzoic acid gave substituted benzoic acids **5a–c** in excellent yields.[3b] Benzamides **3h** and **3i** were obtained from **3c** by standard transformations (see the Experimental Section). The 2-benzylbenzamide **3j** was prepared from commercially available 2-benzylbenzoic acid.

Reductive Alkylations of Benzamides 3a–j. Birch reductions of **3a–j** were performed at −78 °C with potassium (2.2 equiv) in NH_3–THF with 1 equiv of *tert*-butyl alcohol. Methyl iodide was added, and after 1 h at −78 °C, ammonium chloride was added to the reaction mixture. Under these conditions, little if any reduction of unsaturated substituents on the benzamide ring was observed (e.g., **3c–f** and **3j**). Isolated yields of **4a–j** along with the percent de for each alkylation are reported in Table I. It should be noted that O-methylation of the 3′-hydroxypropyl side chain occurred on reductive alkylation of **3i**.

The hydroxyl group in **3i** provides an opportunity for internal chelation of the derived potassium enolate. This could have resulted in a change of enolate configuration and an inversion of the sense of alkylation diastereoselectivity.[4,5] However, this is not the case as determined by the conversion of **4h** to **4i** via (1) treatment of **4h** with 48% HF in acetonitrile and (2) methylation of the resulting primary alcohol (NaH/THF, MeI).

The diastereomer distribution from each reductive alkylation was determined by GC analysis. Mixtures of diastereomers **7a–7c** were prepared from racemic **6a–c** (Scheme II) to establish the validity of peak assignments. In all cases shown in Table I, the major diastereomer (e.g., **4a–j**) eluted before the minor diastereomer. This same order of elution was observed for **2a** (and its

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(3) (a) Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306. Date, M.; Watanabe, M.; Furukawa, S. *Chem. Pharm. Bull.* **1990**, *38*, 902. Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. (b) Coughlin, D. J.; Salomon, R. G. *J. Org. Chem.* **1979**, *44*, 3784. Thompson, R. C.; Kallmerten, J. *J. Org. Chem.* **1990**, *55*, 6076. For the lithiation of 2-methylbenzoic acid esters, see: Hauser, F. M.; Rhee, R. P.; Prasanna, S.; Weinreb, S. M.; Dodd, J. H. *Synthesis* 1980, 72.

(4) (a) Sonnet, P. E.; Heath, R. R. *J. Org. Chem.* **1980**, *45*, 3137. (b) Evans, D. E.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

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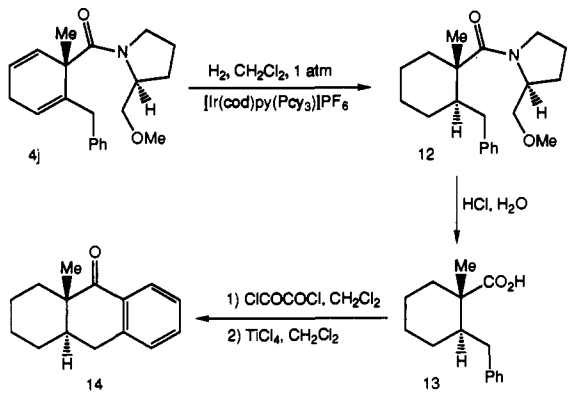
Scheme IV

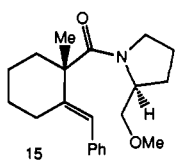


diastereomer) for which absolute configurations had been rigorously established.[1] Futhermore, the methoxyl resonances in ^1H NMR spectra of **7a–c** are clearly resolved, and as with **2a**, the methoxyl resonances from **4a,b** and **4e** are shifted downfield from methoxyl resonances attributed to the minor diastereomers.

Applications. Many of the reductive alkylation products listed in Table I should have value as annelation substrates. This point is illustrated with **4g** (Scheme III) and **4j** (Scheme IV). Amide-directed olefin hydrogenation[6] of **4g** with the homogeneous catalyst/solvent system [Ir(cod)py(PCy$_3$)]PF$_6$/CH_2Cl_2[7] gave **8** in 98% yield. An efficient protocol for removal of the chiral auxiliary involves treatment of **8** with BF_3·Et_2O in benzene at room temperature[8] followed by addition of water. Extractive workup (ethyl acetate/10% HCl) provided the crystalline lactone **9** in 82% yield and the opportunity for recovery of the chiral auxiliary **10** (see the Experimental Section). The recovered chiral auxiliary was recycled to benzamide **3** by treatment of **10** with 2-methylbenzoyl chloride in CH_2Cl_2 in the presence of triethylamine.

Lactone **9** was determined to have enantiomeric purity >98% by a chiral shift reagent ^1H NMR experiment. A sample of racemic **9** was prepared from the achiral, pyrrolidine-derived analogue of benzamide **3g** (see the supplementary material) to facilitate the analysis. Thus, chiral lactone **9** is available in essentially enantiomerically pure form in 57% overall yield from benzamide **3g**. It is expected that lactone **9** and simple analogues will have wide application in natural products synthesis. An application to octalone synthesis is shown in Scheme III; e.g., the conversion of **9** to **11** in 81% overall yield.

Hydrogenation of **4j** with the Ir catalyst system gave **12** in 89% isolated yield (Scheme IV). A mixture of **12** and styrene derivative **15** was obtained in one experiment with low catalyst loading. As expected,[6] the isomerized olefin **15** underwent what appeared to be a completely stereoselective hydrogenation with 4 mol % of the Ir catalyst to give **12** in 97% yield.



Treatment of **12** with hydrochloric acid at reflux for 7 h provided the carboxylic acid **13** in 95% yield. Obviously, substrates more sensitive to strong acid than **12** will have to be cleaved by more elaborate procedures; such methods have been described.[1] Conversion of **13** to the acid chloride and cyclization with $TiCl_4$ in CH_2Cl_2 gave the enantiomerically pure *trans*-hexahydro-9-anthracenone **14**.[9] It should be possible to carry out a second stereoselective reductive alkylation of the benzoyl group in **14** as has been previously demonstrated for preparations of hydrofluoren-9-ones and hydrophenanthren-9-ones.[10]

Conclusion

It has been shown that reductive alkylations of chiral benzamides **3** and **3a–j** occur with excellent stereoselectivities. This process coupled with amide-directed olefin hydrogenation enables the preparation of trans-fused octalones of high enantiomeric purity; e.g., **11** and **14**. Although the present study has featured alkylations only with methyl iodide, prior experience[2] suggests that comparable or higher diastereoselectivities will be obtained with more highly functionalized alkylation reagents.

Experimental Section

General Procedure. ^1H NMR spectra were recorded at 200 MHz employing chloroform as an internal standard. Chemical ionization mass spectra were obtained on a Hewlett-Packard 5987A GC–MS system (isobutane). Analytical GC analyses were performed on a Hewlett-Packard 5710A gas chromatograph with a flame ionization detector (300 °C) fitted with a 3% OV-17 6-ft standard diameter column (gas pressures: N_2, 40 psi; air, 24 psi; H_2, 24 psi). Peak areas were measured with a HP-3380A integrator. Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI. Melting points are uncorrected. Thin-layer chromatography was performed with Merck Kieselgel 60 F-254 precoated glass plates. Baker silica gel (40-μm average particle size) was utilized for flash chromatography. When appropriate, reactions were performed under an atmosphere of nitrogen with flame-dried glassware. Tetrahydrofuran (THF) was distilled over sodium and benzophenone under nitrogen. The concentrations of organolithium reagents were determined prior to use.[11]

Procedure for Preparation of [2′-(Methoxymethyl)pyrrolidinyl]benzamides: (*S*)-2-Ethyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3a). To a solution of **3** (0.233 g, 0.001 mol) in THF (30 mL) at −78 °C was added *sec*-BuLi (1.3 M solution in cyclohexane, 0.846 mL, 1.1 equiv) over a 2-min period. The resulting maroon solution was stirred at −78 °C for 45 min, and then methyl iodide (0.2 mL, 3 equiv) was added. After being stirred at room temperature for 8 h, the reaction was quenched with a 10% solution of hydrochloric acid. Most of the organic solvents were removed at reduced pressure. The residue was diluted with water and then extracted twice with chloroform. The combined organic layers were washed with a saturated solution of sodium bicarbonate and brine and then dried over magnesium sulfate. Concentration at reduced pressure and flash chromatography (hexanes/ethyl acetate (1:1)) afforded 0.189 g (77%) of **3a**: ^1H NMR ($CDCl_3$) δ 7.36–7.18 (m, 4 H), 4.46–4.41 (m, 1 H), 3.71–3.68 (d, 2 H, J = 5.07 Hz), 3.42 (s, 3 H), 3.2–3.0 (m, 2 H), 2.8–2.5 (m, 2 H), 2.1–1.7 (m, 4 H), 1.28–1.2 (t, 3 H, J = 7.6 Hz); IR (film) 3010, 2980, 2890, 1620 cm^{-1}; MS, m/z (relative intensity) 248 (M^+ + 1, 60), 215 (95), 202 (100). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56. Found: C, 72.21; H, 8.26.

In a separate experiment, **3** ($[\alpha]^{26}_D$ −55.8 (c 0.025, CH_2Cl_2)) was treated with *sec*-BuLi as described but the solution of the benzylic anion was quenched with NH_4Cl/H_2O at −78 °C. Workup gave recovered **3** in almost quantitative yield; $[\alpha]^{27}_D$ −58.1 (c 0.026, CH_2Cl_2).

(*S*)-2-Propyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3b). Flash chromatography (hexanes/ethyl acetate (3:2)) gave **3b** (0.169 g, 65%): oil; ^1H NMR ($CDCl_3$) δ 7.31–7.15 (m, 4 H), 4.5–4.4 (m, 1 H), 3.8–3.62 (m, 2 H), 3.47 (s, 3 H), 3.25–3.05 (m, 2 H), 2.74–2.5 (m, 2 H), 2.18–1.6 (m, 6 H), 1.01–0.93 (t, 3 H, J = 7.6 Hz); IR (film) 3015, 2980, 2890, 1620 cm^{-1}; MS, m/z (relative intensity) 262 (M^+ + 1, 25) 229 (100), 216 (95). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87. Found: C, 73.24; H, 8.67.

(*S*)-2-Butenyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3c). Flash chromatography (hexanes/ethyl acetate (1:1)) gave **3c** (2.88 g, 53%): oil; ^1H NMR ($CDCl_3$) δ 7.32–7.15 (m, 4 H), 5.88–5.73 (m, 1 H), 5.04–4.89 (m, 2 H), 4.48–4.30 (m, 1 H), 3.71–3.57 (m, 2 H), 3.36 (s, 3 H), 3.2–3.0 (m, 2 H), 2.8–2.55 (m, 2 H), 2.45–2.30 (m, 2 H), 2.1–1.67 (m, 2 H); IR (film) 3090, 2950, 2940, 1620 cm^{-1}; MS, m/z (relative intensity) 274 (M^+ + 1, 100), 228 (5). Anal. Calcd for

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(8) The primary alcohol obtained by cleavage of the (trimethylsilyl)ethyl group in **8** can be isolated in 94% yield at this stage by rapid extractive workup (ethyl acetate/aqueous $NaHCO_3$).
(9) *rac*-**14** and (+)-**14** are literature compounds, but a rotation for (+)-**14** was not reported. ^1H NMR spectral data for (−)-**14** prepared in this study agree with those reported for *rac*-**14**. See: Hagishita, S.; Kuriyama, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3216.
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(11) Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

$C_{17}H_{23}NO_2$: C, 74.69; H, 8.48. Found: C, 74.66; H, 8.53.

(*S*)-2-Pentenyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3d). Flash chromatography (hexanes/ethyl acetate (1:1)) gave **3d** (0.17 g, 59%): oil; ^{1}H NMR ($CDCl_3$) δ 7.38–7.14 (m, 4 H), 5.94–5.72 (m, 1 H), 5.1–4.9 (m, 2 H), 4.51–4.89 (m, 1 H), 3.8–3.6 (m, 2 H), 3.41 (s, 3 H), 3.2–3.01 (m, 2 H), 2.8–2.5 (m, 2 H), 2.2–1.6 (m, 8 H); IR (film) 3050, 2980, 2890, 1620 cm^{-1}; MS, *m/z* (relative intensity) 288 (M^+ + 1, 100) 242 (5), 131 (5). Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77. Found: C, 75.08; H, 8.79.

(*S*)-2-(2″-Phenylethyl)-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3e). Flash chromatography (hexanes/ethyl acetate (1:1)) gave **3e** (0.23 g, 71%): oil; ^{1}H NMR ($CDCl_3$) δ 7.32–7.19 (m, 9 H), 4.5–4.41 (m, 1 H), 3.75–3.65 (m, 2 H), 3.39 (s, 3 H), 3.17–2.9 (m, 6 H), 2.1–1.7 (m, 4 H); MS, *m/z* (relative intensity) 324 (M^+ + 1, 100). Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79. Found: C, 77.99; H, 7.64.

(*S*)-2-(3-Phenylpropyl)-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3f). Flash chromatography (hexanes/ethyl acetate (1:1)) gave **3f** (0.841 g, 58%): oil; ^{1}H NMR ($CDCl_3$) δ 7.35–7.1 (m, 9 H), 4.51–4.4 (m, 1 H), 3.64–3.62 (d, 2 H, *J* = 4.6 Hz), 3.39 (s, 3 H), 3.14–3.0 (m, 2 H), 2.9–2.57 (m, 4 H), 1.98–1.66 (m, 6 H); IR (film) 3040, 2980, 1625 cm^{-1}; MS, *m/z* (relative intensity) 338 (M^+ + 1, 100). Anal. Calcd for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06. Found: C, 77.94; H, 7.90.

(*S*)-2-[2-[(Trimethylsilyl)ethoxy]ethyl]-1-[[2′-(methoxymethyl)-pyrrolidinyl]carbonyl]benzene (3g). Flash chromatography (hexanes/ethyl acetate (2:3)) gave **3g** (5.36 g, 68%): gold-tinted oil; ^{1}H NMR ($CDCl_3$) δ 7.4–7.1 (m, 4 H), 4.6–4.51 (m, 1 H), 3.9–3.6 (m, 7 H), 3.4–3.0 (m, 6 H), 2.25–1.78 (m, 4 H), 1.17–1.02 (t, 2 H, *J* = 7.5 Hz), 0.1 (s, 9 H); IR (film) 3050, 2990, 2890, 1620 cm^{-1}; MS, *m/z* (relative intensity) 364 (M^+ + 1, 100), 336 (10). Anal. Calcd for $C_{20}H_{33}NO_3Si$: C, 66.07; H, 9.15. Found: C, 66.03; H, 9.47.

(*S*)-2-[3-[(*tert*-butyldimethylsilyl)oxy]propyl]-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3h). To a solution of **3i** in dimethylformamide (3 mL) were added imidazole (1.98 g, 3.0 equiv) and *tert*-butyldimethylsilyl chloride (2.2 g, 2.0 equiv). The mixture was stirred for 12 h, water added, and the mixture extracted with ethyl acetate (3 × 15 mL). The combined organic layers were washed successively with 10% hydrochloric acid solution (4 × 5 mL), saturated aqueous sodium bicarbonate (10 mL), and brine and then dried over magnesium sulfate. Evaporation of the solvent under reduced pressure and flash chromatography (hexanes/ethyl acetate (2:1)) afforded **3h** (2.3 g, 81%): oil; ^{1}H NMR ($CDCl_3$) δ 7.37–7.15 (m, 4 H), 4.61–4.5 (m, 1 H), 3.73–3.6 (m, 4 H), 3.45 (s, 3 H), 3.23–3.05 (m, 2 H), 2.82–2.6 (m, 2 H), 2.15–1.7 (m, 6 H), 0.9 (s, 9 H), 0.15 (s, 6 H); IR (film) 3050, 2980, 1625 cm^{-1}; MS, *m/z* (relative intensity), 392 (M^+ + 1, 100), 334 (15), 264 (30), 142 (20). Anal. Calcd for $C_{22}H_{37}NO_3Si$: C, 67.47; H, 9.52. Found: C, 67.54; H, 9.66.

(*S*)-2-(3-Hydroxypropyl)-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3i). Ozone was passed into a solution of **3c** (2.0 g, 0.0073 mol) in methanol (20 mL) and methylene chloride (60 mL) cooled to −78 °C. The light blue solution was purged with nitrogen until the solution became colorless. Sodium borohydride (1.11 g, 3.0 equiv) was added at −78 °C, the cooling bath was removed, and the reaction mixture was stirred at room temperature overnight. Brine was added, and the organic phase was dried with anhydrous magnesium sulfate. Concentration at reduced pressure provided **3i**, which was used without further purification: oil; ^{1}H NMR ($CDCl_3$) δ 7.42–7.2 (m, 4 H), 4.52–4.40 (m, 1 H), 3.9–3.6 (m, 2 H), 3.52–3.47 (t, 2 H, *J* = 5.08 Hz), 3.43 (s, 3 H), 3.26–3.03 (m, 2 H), 2.78–2.71 (t, 2 H, *J* = 5.08 Hz) superimposed on 2.88–2.6 (br s, 1 H), 2.15–1.67 (m, 6 H); IR (film) 3400, 1625 cm^{-1}. Anal. Calcd for $C_{16}H_{22}NO_3$: C, 69.29; H, 8.36. Found: C, 68.98; H, 8.42.

(*S*)-2-Benzyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (3j): prepared by methods described previously[1] from 2-benzylbenzoic acid (86%): oil; ^{1}H NMR ($CDCl_3$) (mixture of rotational isomers) δ 7.4–7.1 (m, 9 H), 4.33–4.26 (m, 2 H), 4.09–3.91 (m, 1 H), 3.69–3.60 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.6 Hz), 3.59–3.48 (dd, 1 H, *J* = 9.2 Hz, *J* = 6.3 Hz), 3.44 (s, 3 H), 3.04–2.91 (m, 1 H), 1.95–1.6 (m, 4 H); IR (film) 3025, 3015, 2985, 2920, 2885, 1630, 1600, 1395, 1010, 740, 700 cm^{-1}; MS, *m/z* (relative intensity) 310 (M^+ + 1, 100), 195 (5). Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49. Found: C, 77.49; H, 7.37.

Procedure for Preparation of 2-Substituted-benzoic Acids. 2-Ethylbenzoic Acid (5a). To a solution of 2-methylbenzoic acid (1.0 g, 0.0074 mol) in THF (100 mL) at −78 °C was added *sec*-BuLi (1.19 M in cyclohexane, 13.5 mL, 2.2 equiv) over a 2-min period. The resulting orange-red solution was stirred at −78 °C for 1 h, and then MeI (3.3 mL, 7 equiv) was added. After the mixture was stirred at room temperature for 4 h, it was quenched slowly with concentrated hydrochloric acid. The organic solvents were removed under reduced pressure, the residue was diluted with water and extracted three times with diethyl ether. The combined organic layers were washed with water and brine and then dried over magnesium sulfate. Evaporation under reduced pressure provided a colorless solid (mp 56–58 °C). Recrystallization from hexanes/diethyl ether gave 1.05 g (95%) of **5a**: mp 61 °C (lit.[12] mp 68 °C); ^{1}H NMR ($CDCl_3$) δ 8.05–8.01 (d, 1 H, *J* = 7.8 Hz), 7.54–7.45 (dt, 1 H, *J* = 7.8 Hz, *J* = 1.5 Hz), 7.32–7.24 (m, 2 H), 3.12–3.01 (qt, 2 H, *J* = 7.4 Hz), 1.3–1.23 (t, 3 H, *J* = 7.4 Hz); IR ($CHCl_3$) 3350–2400 (br), 1710 cm^{-1}. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.94; H, 6.62.

2-Propylbenzoic Acid (5b). **5b** was obtained as a yellow-tinted oil: 93%; lit.[13] mp 58 °C; ^{1}H NMR ($CDCl_3$) δ 8.05–8.01 (d, 1 H, *J* = 7.7 Hz), 7.5–7.43 (t, 1 H, *J* = 7.6 Hz), 7.31–7.24 (m, 2 H), 3.05–2.97 (t, 2 H, *J* = 7.6 Hz), 1.72–1.6 (sextet, 2 H, *J* = 7.6 Hz), 0.98–0.92 (t, 3 H, *J* = 7.6 Hz). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.13; H, 7.37. Found: C, 72.91; H, 7.49.

2-(2′-Phenylethyl)benzoic Acid (5c). Methylene chloride extraction and flash chromatography (ethyl acetate) provided **5c**: 80%; mp 128–130 °C (lit.[13] mp 130–131.5 °C); ^{1}H NMR ($CDCl_3$) δ 8.24–8.19 (dd, 1 H, *J* = 7.8 Hz, *J* = 1.3 Hz), 7.61–7.28 (m, 8 H), 3.49–3.41 (dt, 2 H, *J* = 6.4 Hz, *J* = 1.2 Hz), 3.10–3.02 (dt, 2 H, *J* = 6.4 Hz, *J* = 1.2 Hz).

Procedure for the Preparation of 1-Substituted-6-(pyrrolidinylcarbonyl)-6-methyl-1,4-cyclohexadienes. (2′*S*,6*S*)-1-Ethyl-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4a). A solution of **3a** (0.39 g, 0.0016 mol) in THF (8 mL) was cooled to −78 °C, and ammonia (80 mL) and *tert*-butyl alcohol (1 equiv) were added. Potassium (0.142 g, 2.3 equiv) was added to the stirred solution in small pieces. Methyl iodide (0.5 mL, 5 equiv) was added, and the resulting yellow solution was stirred for 1 h at −78 °C. After the addition of NH_4Cl (0.5 g), the ammonia was allowed to evaporate and water (10 mL) was added. The mixture was extracted with methylene chloride (3 × 20 mL). The combined organic layers were washed successively with a 10% hydrochloric acid solution, saturated aqueous sodium bicarbonate, and brine. After the mixture was dried over $MgSO_4$, the solvent was removed under reduced pressure: GC analysis, 145 °C for 2 min, then 1 °C/min to 270 °C; see Table I for analytical data; ^{1}H NMR (C_6D_6) δ 5.80–5.72 (dt, 1 H, *J* = 10 Hz, *J* = 1 Hz), 5.68–5.57 (m, 1 H), 5.45–5.36 (m, 1 H), 4.7–4.52 (m, 1 H), 3.79–3.73 (dd, 1 H, *J* = 9 Hz, *J* = 3.2 Hz), 3.66–3.59 (dd, 1 H, *J* = 9 Hz, *J* = 6.4 Hz), 3.51–3.44 (m, 2 H), 3.26 (s, 3 H), 2.8–2.35 (m, 2 H), 2.4–1.3 (m, 6 H), 1.8 (s, 3 H), 1.13–1.04 (t, 3 H, *J* = 7.2 Hz) (only one diastereomer was detected). Flash chromatography (hexanes/ethyl acetate (1:1)) afforded 0.275 g (66%) of **4a** as a yellow-tinted oil: ^{1}H NMR ($CDCl_3$) δ 5.81–5.76 (m, 1 H), 5.59–5.53 (m, 2 H), 4.42–4.3 (m, 1 H), 3.67–3.57 (dd, 1 H, *J* = 9.3 Hz, *J* = 3.2 Hz), 3.53–3.31 (m, 3 H), 3.37 (s, 3 H), 2.9–2.71 (m, 2 H), 2.22–2.07 (m, 1 H), 1.97–1.58 (m, 5 H), 1.36 (s, 3 H), 1.08–1.01 (t, *J* = 7.3 Hz); IR (film) 2980, 2880, 1630 cm^{-1}; MS, *m/z* (relative intensity) 264 (M^+ + 1, 100), 142 (25). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57. Found: C, 72.87; H, 9.44.

(2′*S*,6*S*)-1-Propyl-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4b): GC analysis, 145 °C for 2 min, then 1 °C/min to 270 °C; ^{1}H NMR (C_6D_6) 5.78–5.35 (dt, 1 H, *J* = 10 Hz, *J* = 1 Hz), 5.67–5.61 (m, 1 H), 5.44 (m, 1 H), 4.6 (m, 1 H), 3.78–3.72 (dd, 1 H, *J* = 9.2 Hz, *J* = 3.3 Hz), 3.68–3.59 (dd, 1 H, *J* = 9.2 Hz, *J* = 6.4 Hz), 3.58–3.4 (m, 2 H), 3.26 (s, 3 H), 2.72–2.4 (m, 2 H), 2.31–1.4 (m, 8 H), 1.8 (s, 3 H), 1.11–1.0 (t, 3 H, minor diastereomer, *J* = 7.2 Hz), 1.0–0.93 (t, 3 H, major diastereomer, *J* = 7.2 Hz). Flash chromatography (hexanes/ethyl acetate (1:1)) afforded 0.569 g (79%) of **4b** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.79–5.73 (dt, 1 H, *J* = 6.5 Hz, *J* = 1.3 Hz), 5.57–5.55 (m, 2 H), 4.31–4.28 (m, 1 H), 3.64–3.57 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.5–3.3 (m, 3 H), 3.36 (s, 3 H), 2.86–2.58 (m, 2 H), 2.1–1.61 (m, 6 H), 1.56–1.32 (m, 2 H), 1.34 (s, 3 H), 0.95–0.88 (t, 3 H, *J* = 7.2 Hz); IR (film) 2980, 2885, 1635 cm^{-1}; MS, *m/z* (relative intensity) 278 (M^+ + 1, 100), 142 (20). Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81. Found: C, 73.71; H, 9.80.

(2′*S*,6*S*)-1-Butenyl-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4c): GC analysis, 170 °C for 2 min, then 1 °C/min to 300 °C; ^{1}H NMR (C_6D_6) δ 5.93–5.59 (m, 3 H), 5.42 (m, 1 H), 5.19–5.04 (m, 2 H), 4.6–4.56 (m, 1 H), 3.77–3.45 (m, 4 H), 3.26 (s, 3 H), 2.71–2.11 (m, 6 H), 1.97–1.42 (m, 4 H), 1.77 (s, 3 H); only one diastereomer was detected. Flash chromatography (hexanes/ethyl acetate (2:1)) afforded 0.16 g (76%) of **4c** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.77–5.72 (m, 2 H), 5.55–5.49 (m, 2 H), 5.05–4.91 (m, 2 H), 4.31–4.20 (m, 1 H), 3.61–3.55 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.5–3.25 (m, 3 H), 3.34 (s, 3 H), 2.85–2.58 (m, 2 H), 2.3–2.07 (m, 4 H), 2.0–1.65 (m, 6 H), 1.33 (s, 3 H); IR (film) 3025, 2990, 2925, 2820, 1630 cm^{-1}; MS, *m/z* (relative intensity) 290 (M^+ + 1, 100), 142 (25). Anal.

(12) Gabriel, S.; Michael, A. *Chem. Ber.* **1877**, *10*, 2199.
(13) Gabriel, S.; Michael, A. *Chem. Ber.* **1878**, *11*, 1007.

Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40. Found: C, 74.58; H, 9.34.

(2′*S*,6*S*)-1-Pentenyl-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4d): GC analysis, 190 °C for 2 min, then 2 °C/min to 320 °C); ^{1}H NMR (C_6D_6) δ 6.01–5.62 (m, 3 H), 5.49–5.4 (m, 1 H), 5.22–5.04 (m, 2 H), 4.7–4.55 (m, 1 H), 3.78–3.71 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.69–3.61 (dd, 1 H, *J* = 9.4 Hz, *J* = 6.4 Hz), 3.59–3.41 (m, 2 H), 3.26 (s, 3 H); only one diastereomer was detected. Flash chromatography (hexanes/ethyl acetate (2:1)) afforded 0.075 g (69%) of **4d** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.86–5.76 (m, 2 H), 5.61–5.54 (m, 2 H), 5.09–4.96 (m, 2 H), 4.39–4.25 (m, 1 H), 3.67–3.61 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.5–3.34 (m, 3 H), 3.39 (s, 3 H), 2.92–2.63 (m, 2 H), 2.2–2.01 (m, 4 H), 1.96–1.46 (m, 6 H), 1.39 (s, 3 H); IR (film) 3080, 2980, 2925, 1625 cm^{-1}; MS, *m/z* (relative intensity) 304 (M^+ + 1, 100), 144 (35), 142 (65), 116 (25). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.20; H, 9.63. Found: C, 75.32; H, 9.51.

(2′*S*,6*S*)-1-(2-Phenylethyl)-6-methyl-6-[[2′-(methoxymethyl)-pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4e): GC analysis, 190 °C for 2 min, then 2 °C/min to 320 °C; the minor diastereomer could not be detected; ^{1}H NMR (C_6D_6) δ 7.41–7.13 (m, 5 H), 5.71–4.94 (m, 3 H), 4.63–4.51 (m, 1 H), 3.81–3.62 (m, 2 H), 3.5–3.42 (t, 2 H, *J* = 7.1 Hz), 3.29 (s, 3 H), 2.88–2.74 (t, 2 H, *J* = 7.3 Hz), 2.73–2.34 (m, 4 H), 1.95–1.39 (m, 4 H), 1.79 (s, 3 H). Flash chromatography (hexanes/ethyl acetate (2:1)) afforded 0.13 g (62%) of **4e** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36–7.2 (m, 5 H), 5.84–5.78 (m, 1 H), 5.68–5.65 (m, 1 H), 5.61–5.56 (m, 1 H), 4.41–4.26 (m, 1 H), 3.67–3.61 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.51–3.35 (m, 3 H), 3.39 (s, 3 H), 2.95–2.67 (m, 4 H), 2.51–2.34 (m, 1 H), 2.26–2.04 (m, 1 H), 1.95–1.64 (m, 4 H), 1.41 (s, 3 H); IR (film) 3025, 2980, 2925, 2890, 1630 cm^{-1}; MS, *m/z* (relative intensity) 340 (M^+ + 1, 10), 144 (100), 116 (10). Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61. Found: C, 77.87; H, 8.56.

(2′*S*,6*S*)-1-(3-Phenylpropyl)-6-methyl-6-[[2′-(methoxymethyl)-pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4f): GC analysis, 200 °C for 2 min, then 1 °C/min to 350 °C; ^{1}H NMR (C_6D_6) δ 7.4–7.11 (m, 5 H), 5.78–5.95 (m, 2 H), 5.43–5.35 (m, 1 H), 4.51–4.66 (m, 1 H), 3.79–3.73 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.67–3.59 (dd, 1 H, *J* = 9.4 Hz, *J* = 6.4 Hz), 3.5–3.41 (m, 2 H), 3.26 (s, 3 H), 2.71–2.4 (m, 6 H), 2.39–1.31 (m, 6 H), 1.77 (s, 3 H); only one diastereomer was detected. Flash chromatography (hexanes/ethyl acetate (2:1)) afforded 0.16 g (77%) of **4f** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36–7.17 (m, 5 H), 5.82–5.76 (m, 1 H), 5.61–5.55 (m, 2 H), 4.35–4.21 (m, 1 H), 3.67–3.61 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.3 Hz), 3.47–3.38 (m, 3 H), 3.39 (s, 3 H), 2.91–2.62 (m, 4 H), 2.25–1.61 (m, 8 H), 1.39 (s, 3 H); IR (film) 3065, 3020, 2980, 2935, 2890, 1630 cm^{-1}; MS, *m/z* (relative intensity) 354 (M^+ + 1, 94), 144 (100), 142 (45), 116 (12), 91 (5). Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.83. Found: C, 78.02; H, 9.02.

(2′*S*,6*S*)-1-[2-[(Trimethylsilyl)ethoxy]ethyl]-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4g): GC analysis, 190 °C for 2 min, then 2 °C/min to 320 °C. Birch reduction of **3g** on a 5-g scale followed by flash chromatography (hexanes/ethyl acetate (2:1)) afforded **4g** (3.67 g, 71%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 5.79–5.73 (m, 1 H), 5.6–5.51 (m, 2 H), 4.37–4.24 (m, 1 H), 3.59–3.29 (m, 11 H), 2.88–2.60 (m, 2 H), 2.4–2.05 (m, 2 H), 1.95–1.65 (m, 4 H), 1.35 (s, 3 H), 0.97–0.88 (t, 2 H, *J* = 9.1 Hz), 0.019 (s, 9 H); IR (film) 2980, 2870, 1630, 1400, 1380, 1250, 1100 cm^{-1}; MS, *m/z* (relative intensity) 380 (M^+ + 1, 100), 352 (5), 262 (5), 144 (35), 142 (40). Anal. Calcd for $C_{21}H_{37}NO_3Si$: C, 66.45; H, 9.83. Found: C, 66.46; H, 9.82.

(2′*S*,6*S*)-1-[3-[(*tert*-Butyldimethylsilyl)oxy]propyl]-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4h). Addition of potassium during the Birch reduction process was performed at −33 °C due to the insolubility of the substrate at −78 °C. After all the metal was added, the blue solution was cooled to −78 °C. Alkylation and workup were performed as described above to give **4h** as a yellow-tinted oil (0.193 g, 93%): GC analysis, 210 °C for 2 min, then 1 °C/min to 330 °C; ^{1}H NMR (C_6D_6) δ 5.75–5.73 (m, 1 H), 5.67–5.6 (m, 1 H), 5.53–5.42 (m, 1 H), 4.71–4.55 (m, 1 H), 3.82–3.43 (m, 6 H), 3.26 (s, 3 H), 2.73–2.39 (m, 2 H), 2.41–2.09 (m, 2 H), 2.06–1.34 (m, 6 H), 1.78 (s, 3 H), 1.10 (s, 9 H), 0.02 (s, 3 H); ^{1}H NMR ($CDCl_3$) δ 5.79–5.71 (dt, 1 H, *J* = 9.6 Hz, *J* = 1.0 Hz), 5.56–5.49 (m, 2 H), 4.37–4.23 (m, 1 H), 3.63–3.51 (m, 4 H), 3.49–3.25 (m, 2 H), 3.35 (s, 3 H), 2.86–2.61 (m, 2 H), 2.2–1.6 (m, 8 H), 1.34 (s, 3 H), 0.87 (s, 9 H), 0.01 (s, 3 H). A combustion analysis was obtained on a derivative, **4i**.

(2′*S*,6*S*)-1-(3-Methoxypropyl)-6-methyl-6-[[2′-(methoxymethyl)-pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4i): GC analysis, 170 °C for 2 min, then 1 °C/min to 220 °C. Flash chromatography (hexanes/ethyl acetate (1:1)) afforded 0.131 g (79%) of **4i** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.79–5.71 (dt, 1 H, *J* = 9.6 Hz, *J* = 1.0 Hz), 5.57–5.48 (m, 2 H), 4.36–4.2 (m, 1 H), 3.63–3.54 (dd, 1 H, *J* = 9.3 Hz, *J* = 3.1 Hz), 3.42–3.25 (m, 5 H), 3.36 (s, 3 H), 3.35 (s, 3 H), 2.76–2.59 (m, 1 H), 2.16–1.62 (m, 8 H), 1.35 (s, 3 H); IR (film) 2920, 1625, 1115 cm^{-1}; MS, *m/z* (relative intensity) 308 (M^+ + 1, 50), 276 (5), 165 (35), 144 (100), 142 (30). Anal. Calcd for $C_{18}H_{29}NO_3$: C, 70.32; H, 9.51. Found: C, 70.06; H, 9.47.

(2′*S*,6*S*)-1-Benzyl-6-methyl-6-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (4j): GC analysis, 200 °C for 2 min, then 1 °C/min to 320 °C. Flash chromatography (hexanes/ethyl acetate (3:2)) provided 0.450 g (69%) of **4j** as a clear oil. A lower fraction (0.089 g) contained starting material along with an undetermined component (14%): GC analysis (same conditions) t_R(min) 21.1 (unknown), 21.8 (**3j**); ^{1}H NMR ($CDCl_3$) δ 7.39–7.12 (m, 5 H), 5.76–5.71 (m, 1 H), 5.56–5.50 (dt, 1 H, *J* = 9.5 Hz, *J* = 0.5 Hz), 5.32–5.30 (m, 1 H), 4.15–4.11 (m, 1 H), 3.61–3.54 (dd, 1 H, *J* = 9.4 Hz, *J* = 3.4 Hz), 3.41–3.26 (m, 4 H), 3.31 (s, 3 H), 3.15–3.07 (d, 1 H, *J* = 15 Hz), 2.72–2.67 (m, 2 H), 1.79–1.48 (m, 4 H), 1.44 (s, 3 H); IR (film) 3010, 2985, 2930, 2890, 2810, 1625, 1400, 1380, 1240, 1100 cm^{-1}; MS, *m/z* (relative intensity) 326 (M^+ + 1, 100), 285 (5), 144 (90), 142 (75). Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36. Found: C, 77.52; H, 8.16.

Conversion of Silyl Ether 4h to Methyl Ether 4i. In a Teflon vial **4h** (0.18 g, 0.46 mmol) was dissolved in acetonitrile (10 mL), and 48% aqueous hydrofluoric acid (1 mL) was added. After 30 min solid sodium bicarbonate and then water was added, and the mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over magnesium sulfate and then evaporated under reduced pressure to give the alcohol as a clear, colorless oil (0.12 g, 94%). The alcohol was dissolved in THF (1 mL), and sodium hydride (0.033 g, 3 equiv) was added. After 5 min, methyl iodide (0.086 mL, 3 equiv) was added. The mixture was stirred overnight at room temperature, quenched with a 10% solution of aqueous hydrochloric acid, and extracted with ethyl acetate (4 × 15 mL). The combined organic layers were washed with brine and dried over magnesium sulfate. Evaporation under reduced pressure provided 0.106 g (82%) of **4i** as a colorless oil: ^{1}H NMR spectra ($CDCl_3$ and C_6D_6) were identical with those obtained from the product of reductive alkylation of **3i**; GC analysis, 170 °C for 2 min, then 1 °C/min to 300 °C.

(1*S*,2*S*,2′*S*)-2-[2-[(Trimethylsilyl)ethoxy]ethyl]-1-methyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]cyclohexane (8). A solution of **4g** (2.07 g, 0.0054 mol) in dry methylene chloride (50 mL) containing $[Ir(cod)(py)PCy_3]PF_6$ (0.17 g, 4 mol %) was stirred under an atmosphere of hydrogen at room temperature for 10 h. Evaporation of the solvent under reduced pressure and flash chromatography of the residue (diethyl ether) gave **8** (2.03 g, 98%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 4.47–4.3 (m, 1 H), 3.73–3.70 (m, 1 H), 3.6–3.29 (m, 11 H), 2.3–2.1 (m, 1 H), 2.05–1.1 (m, 14 H), 1.17 (s, 3 H), 0.95–0.87 (t, 2 H, *J* = 9.1 Hz), 0.00 (s, 9 H); IR (film) 2940, 2890, 1620, 1465, 1380, 1250, 1110, 850, 830 cm^{-1}; MS, *m/z* (relative intensity) 384 (M^+ + 1, 100), 266 (15), 241 (12), 170 (15), 142 (5), 123 (2). Anal. Calcd for $C_{21}H_{41}NO_3Si$: C, 65.75; H, 10.77. Found: C, 65.97; H, 10.87.

Lactonization of 8 and Recovery of the Chiral Auxiliary. (4a*S*,8a*S*)-8a-Methyl-3,4,4a,5,6,7,8,8a-octahydro-1*H*-2-benzopyran-1-one (9). A solution of **8** (2.0 g, 0.0052 mol) and BF_3·OEt_2 (1.28 mL, 2 equiv) in benzene (20 mL) was vigorously stirred under nitrogen for 24 h at room temperature. Water (3 mL) was added, and vigorous stirring was continued for 20 h. The mixture was diluted with ethyl acetate (100 mL) and extracted three times with 10% hydrochloric acid. The combined aqueous layers were saved. The organic phase was washed successively with aqueous saturated sodium bicarbonate and brine and then filtered through silica gel over a layer of magnesium sulfate. Evaporation of the solvents under reduced pressure provided **9** (0.714 g, 82%) as a colorless solid, mp 42–43 °C. An analytical sample was recrystallized from hexane/ether: mp 44.5–46 °C; ^{1}H NMR ($CDCl_3$) δ 4.48–4.2 (m, 2 H), 2.1–1.25 (m, 9 H), 1.2 (s, 3 H); IR ($CHCl_3$) 2980, 2880, 1735, 1400 cm^{-1}; $[\alpha]^{25}_D$ +25.65° (*c* 0.0122, CH_2Cl_2); MS, *m/z* (relative intensity) 169 (M^+ + 1, 100). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.39; H, 9.73.

The enantiomeric purity of **9** was determined by observation of the ^{1}H NMR (200-MHz) spectrum in the presence of the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]praseodymium(III). Addition of 30 mol % $Pr(hfc)_3$ to a solution of racemic **9** in $CDCl_3$ caused the singlet at δ 1.2 (methyl group) to separate into two equivalent singlets at δ 0.64 and 0.68. Under the same conditions, nonracemic **9** gave one singlet at δ 0.69.

The aqueous layer was made basic (pH 12) with KOH pellets, then stirred for 6 h at room temperature, and extracted with methylene chloride (4 × 30 mL). The combined organic layers were filtered through anhydrous potassium carbonate, and most of the solvent was removed by distillation through a Vigreux column. Triethylamine (1.8 mL, 2.5 equiv) was added, and the solution was cooled to 0°C. 2-Methylbenzoyl chloride (0.884 g, 1 equiv) dissolved in methylene chloride (10 mL) was added over 5 min. The resulting mixture was stirred at room temperature for 7 h and then diluted with methylene chloride (50

mL). The mixture was washed with 10% hydrochloric acid (3 × 20 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL) and was then dried over magnesium sulfate. Evaporation of the solvent under reduced pressure and flash chromatography on silica gel (hexanes/ethyl acetate (1:1)) provided 0.51 g (42%) of **1a**.

(2*S*,8*S*)-2,8a-Dimethyl-1,4,4a,5,6,7,8,8a-octahydro-naphthalene-1-one (11). To a stirred solution of the lactone **9** (0.15 g, 0.89 mmol) in THF (5 mL) at −45 °C was added ethylmagnesium bromide (1.19 mL, 2.18 M solution in THF). The resulting solution was stirred at −45 °C for 2.5 h and then quenched with 10% hydrochloric acid. After being warmed to room temperature, the mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with aqueous saturated sodium bicarbonate and brine and dried over magnesium sulfate. Evaporation of the solvents under reduced pressure afforded a yellow oil. A ^1H NMR ($CDCl_3$) spectrum indicated a mixture of the expected keto alcohol and its cyclic hemiketal (~1:2). Flash chromatography (hexanes/ether (5:1)) provided two fractions. First fraction: R_f 0.75, predominantly the keto alcohol (0.075 g, 43%); ^1H NMR ($CDCl_3$) δ 3.64–3.5 (m, 2 H), 2.72–2.61 (qt, 2 H, J = 7.2 Hz), 2.2–1.1 (m, 12 H), 1.2 (s, 3 H), 0.97–0.9 (t, 3 H, J = 7.2 Hz); IR (film) 3300 (w, br), 2965, 2880, 1705, 1450, 1380, 1140, 1100 cm^{-1}; MS, m/z (relative intensity) 199 (M^+ + 1, 40), 181 (100), 109 (10). Second fraction: R_f 0.3, predominantly the cyclic hemiketal (0.089 g, 50%); ^1H NMR ($CDCl_3$) δ 3.65–3.56 (t, 2 H, J = 6.1 Hz), 2.62–2.48 (m, 2 H, J = 7.2 Hz, J = 1.6 Hz), 2.17–1.9 (m, 2 H), 1.8–0.9 (m, 10 H), 1.15 (s, 3 H), 1.1–1.0 (t, 3 H, J = 7.2 Hz); IR (film) 3400 (br), 2970, 2980, 1695 (w), 1450, 1380, 1090, 1060; MS, m/z (relative intensity) 199 (M^+ + 1, 95), 181 (100), 169 (5), 109 (15), 96 (10).

The keto alcohol (0.063 g, 0.3 mmol) was dissolved in methylene chloride (7 mL), and dry basic alumina (200 mg, activity grade 1) was added. Pyridinium dichromate (385 mg, 3 equiv) was added, and the slurry was stirred for 14 h at room temperature. Filtration and evaporation of the solvent under reduced pressure provided a brown oil. Flash chromatography (hexanes/ether (4:1)) provided the expected keto aldehyde as a clear oil (0.055 g, 89%): ^1H NMR ($CDCl_3$) δ 9.68–9.66 (m, 1 H), 2.55–2.4 (m, 2 H), 2.22–1.93 (m, 2 H), 1.67–1.15 (m, 9 H), 1.09 (s, 3 H), 1.04–1.0 (t, 3 H, J = 7.1 Hz); IR (film) 2990, 2980, 2920, 2880, 2710 (w), 1730, 1705, 1445, 1375, 1090 cm^{-1}; $[\alpha]^{23}_D$ −0.116° (c 0.0172, CH_2Cl_2); MS, m/z (relative intensity) 197 (M^+ + 1, 100), 96 (5). To a solution of the keto aldehyde (0.045 g, 0.23 mmol) in benzene (15 mL) was added p-toluenesulfonic acid monohydrate (0.040 g). The reaction mixture was stirred for 1 h at room temperature and at reflux temperature for 3 h, then cooled, and diluted with ether. Saturated aqueous sodium bicarbonate was added slowly, and after 5 min the organic phase was separated, washed with brine, and dried over magnesium sulfate. Evaporation of the solvents under reduced pressure and flash chromatography (hexanes/ether (8:1)) afforded **11** as a clear oil (0.040 g, 98%): ^1H NMR ($CDCl_3$) δ 6.65–6.55 (m, 1 H), 2.15–2.06 (m, 2 H), 1.98–1.15 (m, 9 H), 1.03 (s, 3 H); IR (film) 2925, 2860, 1680, 1440, 1370, 1350, 1015 cm^{-1}; $[\alpha]^{23}_D$ −67.62° (c 0.0042, CH_2Cl_2); MS, m/z (relative intensity) 179 (M^+ + 1, 100). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.17. Found: C, 80.64; H, 10.21

(1*S*,2*S*,2′*S*)-2-Benzyl-1-methyl-1-[[2′-(metboxymethyl)pyrrolidinyl]-carbonyl]cyclohexane (12) and (1*S*,2*S*,2′*S*)-2-Benzylidine-1-methyl-1-[[2′-(methoxymethyl)pyrrolidinyl]carbonyl]cyclohexane (15). A solution of **4j** (0.100 g, 0.3 mmol) in dry methylene chloride (10 mL) containing $[Ir(cod)(py)PCy_3]PF_6$ (0.020 g, 10 mol %) was stirred under an atmosphere of hydrogen at room temperature for 14 h. Evaporation of the solvent under reduced pressure and flash chromatography of the residue (hexanes/ethyl acetate (2:1)) provided **12** (0.090 g, 89%) as a clear oil: ^1H NMR ($CDCl_3$) δ 7.34–7.22 (m, 5 H), 4.6–4.4 (m, 1 H), 3.82–3.48 (m, 4 H), 3.39 (s, 3 H), 2.77–2.69 (dd, 1 H, J = 12.7 Hz, J = 2.2 Hz), 2.61–2.43 (m, 1 H), 2.15–1.15 (m, 9 H), 1.35 (s, 3 H); IR (film) 3080, 3060, 3020, 2990, 2920, 2880, 1625, 1445, 1390, 1370, 1240, 1190, 1110, 700 cm^{-1}; MS, m/z (relative intensity) 330 (M^+ + 1, 100), 187 (8), 142 (5). Anal. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48. Found: C, 76.38; H, 9.35.

In a separate experiment amide **4j** (0.157 g, 0.48 mmol) was stirred in methylene chloride (10 mL) with $[Ir(cod)(py)PCy_3]PF_6$ (0.014 g, 4 mol %) under an atmosphere of hydrogen for 10 h at room temperature. Evaporation of the solvent under reduced pressure provided a dark oil. ^1H NMR spectroscopy along with TLC analysis of the reaction mixture indicated the presence of two compounds (1.5:1). Flash chromatography (hexanes/ethyl acetate (4:1)) provided **12** (0.090 g, 57%, oil) and **15** (0.066 g, 42%, oil): ^1H NMR ($CDCl_3$) δ 7.35–7.1 (m, 5 H), 5.17–5.15 (m, 1 H), 4.39–4.34 (m, 1 H), 3.89–3.72 (m, 1 H), 3.65–3.58 (dd, 1 H, J = 9.3 Hz, J = 3.2 Hz), 3.48–3.26 (m, 3 H), 3.36 (s, 3 H), 3.03–2.96 (m, 1 H), 2.12–1.61 (m, 10 H), 1.45 (s, 3 H); IR (film) 3015, 2990, 2925, 2825, 1625, 1600 (sh), 1450, 1385, 1260, 1180, 1110, 735 cm^{-1}; MS, m/z (relative intensity) 328 (M^+ + 1, 100), 142 (10). Anal. Calcd for $C_{21}H_{29}NO_2$: C, 77.02; H, 8.93. Found: C, 76.87; H, 9.06.

A solution of **15** (0.048 g, 0.144 mmol) in methylene chloride (10 mL) containing $[Ir(cod)(pyr)PCy_3]PF_6$ (0.005 g, 4 mol %) was stirred under an atmosphere of hydrogen for 17 h. Evaporation of the solvent under reduced pressure and flash chromatography (hexanes/ethyl acetate (2:1)) provided **12** (0.012 g, 97%) as a clear oil.

(1*S*,2*S*,2′*S*)-2-Benzyl-1-methyl-1-cyclohexanecarboxylic acid (13). To **12** (0.045 g, 0.137 mmol) were added approximately 1 mL of water and 1 mL of concentrated hydrochloric acid. The mixture was heated at reflux temperature for 7 h. After being cooled to room temperature, the mixture was extracted with methylene chloride (3 × 20 mL) and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure and flash chromatography (hexanes/ethyl acetate (3:1)) provided **13** (0.030 g, 95%) as an oil: ^1H NMR ($CDCl_3$) δ 7.32–7.17 (m, 5 H), 2.71–2.66 (m, 1 H), 2.22–2.17 (m, 2 H), 1.87–1.37 (m, 7 H), 1.25 (s, 3 H), 1.15–1.11 (m, 2 H); IR (film) 3500–2300 (br), 1695, 1600, 1445, 1405, 1395, 1290, 1260, 1250, 1160, 1130, 950, 910, 740 cm^{-1}; MS, m/z (relative intensity) 233 (M^+ + 1, 100), 215 (18), 187 (30). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.54; H, 8.67. Found: C, 77.26; H, 8.84.

(4a*S*,9a*R*)-4a-Methyl-1,2,3,4,4a,9,9a,10-octahydro-10-anthraceneone (14). To a solution of **13** (0.025 g, 107 mmol) in dry methylene chloride (1 mL) was added oxalyl chloride (11 μL, 0.11 mmol), and the mixture was stirred overnight at room temperature. Evaporation of the solvent under reduced pressure provided a tan oil that was used without further purification. The acid chloride was dissolved in dry methylene chloride (0.5 mL), and the reaction vessel was flushed with nitrogen and cooled to 0 °C. Titanium tetrachloride (1 M in methylene chloride, 0.2 mL, 2 equiv) was added, and the reaction was stirred at 0 °C for 3 h. The ice bath was removed, ether (10 mL) was added, and then brine (3 mL) was added over 10 min. After the mixture was vigorously stirred for 30 min, the layers were separated. The aqueous phase was extracted with ether (2 × 15 mL), and the combined organic layers were dried over magnesium sulfate. Evaporation of the solvents under reduced pressure and flash chromatography (hexanes/ethyl acetate (20:1)) gave **14**[9] (0.011 g, 70%, oil): ^1H NMR ($CDCl_3$) δ 8.06–8.01 (dd, 1 H, J = 7.7 Hz, J = 1.3 Hz), 7.52–7.42 (dt, 1 H, J = 5.9 Hz, J = 1.5 Hz), 7.35–7.18 (m, 2 H), 2.9–2.72 (m, 2 H), 2.11–2.04 (m, 2 H), 1.86–1.2 (m, 7 H), 1.11 (s, 3 H); IR (film) 3080, 2920, 2860, 1680, 1605, 1445, 1370, 1300, 1280, 1260, 980 cm^{-1}; $[\alpha]^{24}_D$ −1.5°; $[\alpha]^{24}_{365}$ −168° (c 0.005, CH_2Cl_2); MS, m/z (relative intensity) 215 (M^+ + 1, 100), 118 (5). Anal. Calcd for $C_{15}H_{18}O$: C, 84.06; H, 8.46. Found: C, 83.89; H, 8.34.

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Supplementary Material Available: Experimental procedures for compounds discussed in the text but not described in the Experimental Section (4 pages). Ordering information is given on any current masthead page.