Synthesis of Optically Active Butenolides via Chromium Alkoxycarbene Complexes: Total Synthesis of (+)-Tetrahydrocerulenin and Two Butenolides from the Marine Sponge *Plakortis lita*

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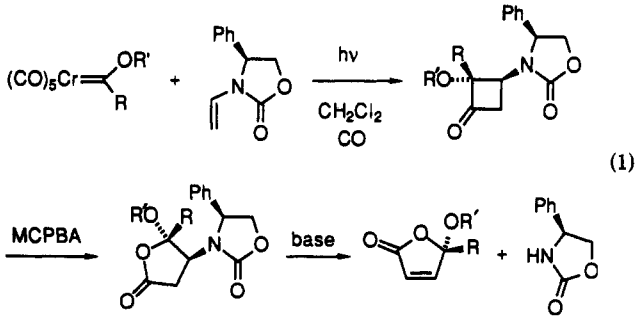
Optically active butenolides were synthesized from the corresponding cyclobutanones, derived from the photolysis of chromium alkoxycarbene complexes and optically active ene–carbamates. The cyclobutanones were oxidized (Baeyer–Villiger) to the corresponding lactones, and subsequent base-induced elimination of the β-oxazolidinone ring provided optically active butenolides efficiently. The butenolides were utilized in the syntheses of (+)-tetrahydrocerulenin and two marine natural products.

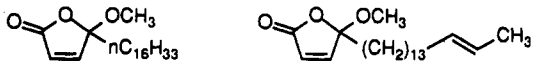
Introduction

Recently, an efficient synthesis of optically active cyclobutanones by the photochemical reaction of chromium alkoxycarbene complexes with optically active ene–carbamates was reported from these laboratories.[1] These underwent clean Baeyer–Villiger oxidation to the corresponding butyrolactone which, in the presence of base, tended to undergo an elimination of the oxazolidinone group to give the optically active butenolide (eq 1).



(1)

Butenolides are an interesting class of compounds, both because of their intrinsic reactivity, which has been utilized in the synthesis of more complex organic compounds,[2] and because of their occurrence in nature.[3] For example, optically active butenolides (−)-1 and (−)-2 were recently isolated from the marine sponge *Plakortis lita*[4] and their structure derived from spectroscopic data. Their absolute configurations were not assigned. Because the chemistry in eq 1 permits the facile synthesis of these kinds of compounds with known absolute configuration, syntheses of 1 and 2 were undertaken.

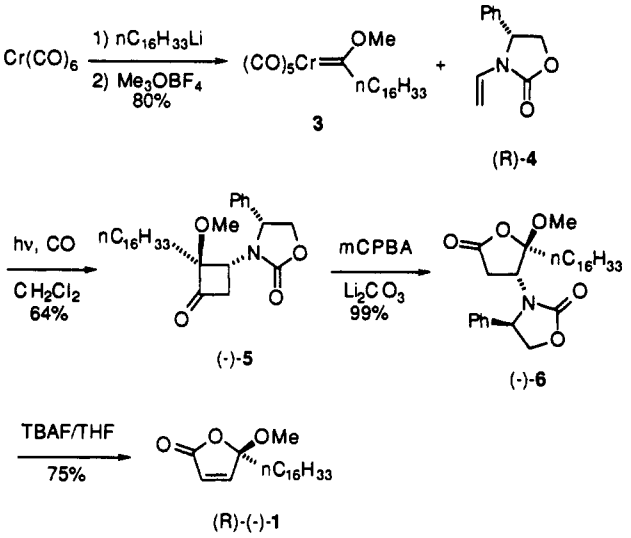


(-)-1 (-)-2

Results and Discussion

Synthesis of (−)-1 was achieved in a straightforward manner (Scheme I). The required *n*-hexadecylcarbene complex 3 was prepared in 80% yield from chromium hexacarbonyl and *n*-hexadecyllithium. Previous experience had shown that butenolides derived from (*S*)-ene–carbamates usually had positive rotations, and those from the *R* enantiomer had negative rotations. Thus, photolysis of 3 with (*R*)-ene–carbamate 4 gave (−)-cyclobutanone 5 in 64% isolated yield, with a de of ≥97% for the crude material (the other diastereoisomer could not be detected by ^{1}H-NMR spectroscopy). Baeyer–Villiger oxidation (*m*-CPBA/Li_2CO_3) followed by elimination (TBAF/THF/0 °C) gave butenolide (−)-1 in 48% overall yield from ene–carbamate 4 (38% overall yield from chromium hexacarbonyl). The enantiomeric excess of synthetic (−)-1 was determined to be >95% by ^{1}H-NMR spectroscopy using chiral shift reagents (see Experimental Section) under conditions which gave base-line separation of the enantiomers in a racemic mixture synthesized as in Scheme I using a racemic analog of 4.

Scheme I



A comparison of the physical data for (−)-1 from natural sources[4] and synthetic (−)-1 is instructive. Both had negative signs of rotation, $[\alpha]_D$ = −13.9° for isolated material[4] and −32.4° for synthetic material, indicating that

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(1) Hegedus, L. S.; Bates, R. W.; Söderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923.

(2) For examples, see: (a) Feringa, B. L.; de Lange, B.; Jansen, J. F. G. A.; de Jong, J. C.; Lubben, M.; Faber, W.; Schudde, E. P. *Pure Appl. Chem.* **1992**, *64*, 1865. (b) Hanessian, S. *Aldrichimica Acta* **1989**, *22*, 3.

(3) (a) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (b) Newaz, S. S. *Aldrichimica Acta* **1977**, *10*, 64.

(4) De Guzman, F. S.; Schmitz, F. J. *J. Nat. Prod.* **1990**, *53*, 926.

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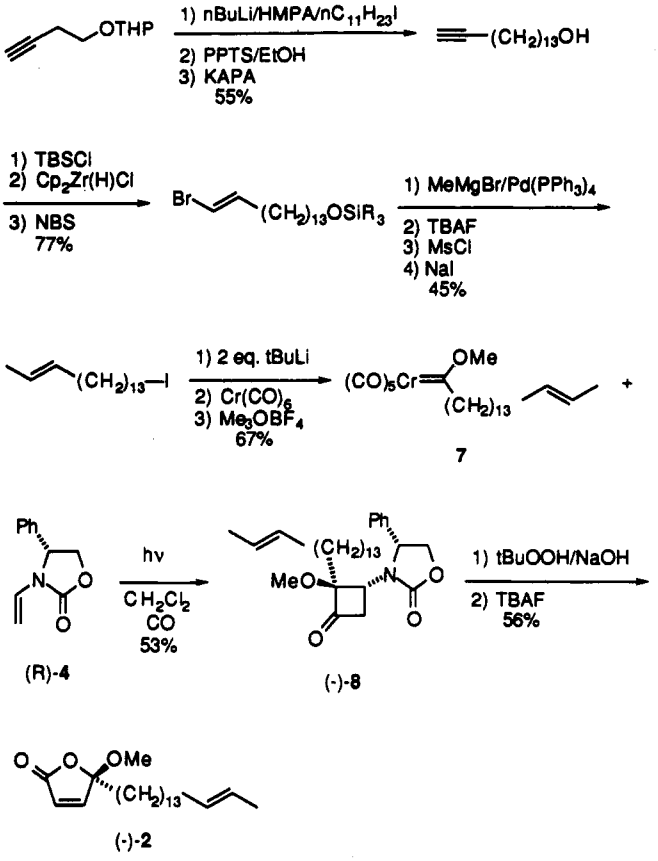
Scheme II

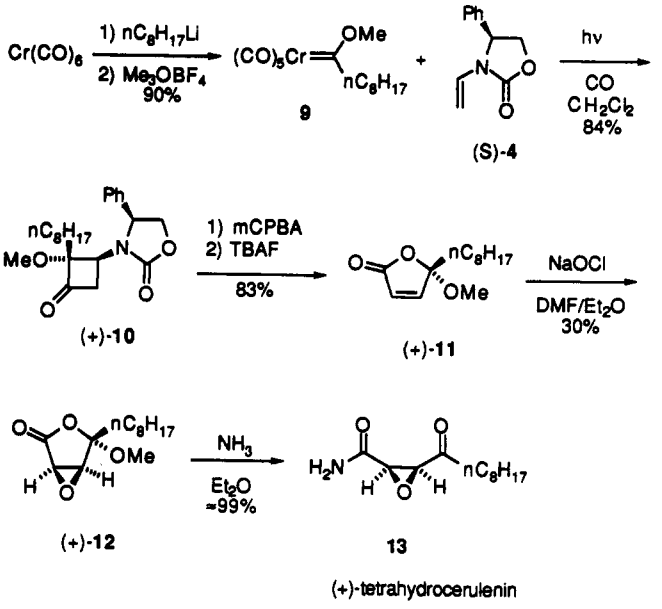


they both had the same absolute configuration, but that natural material was probably impure. This synthesis allows the assignment of absolute configuration of (−)-**1** as *R*, since the absolute configuration of the photochemical cycloaddition between chromium carbene complexes and ene–carbamates was previously established by X-ray crystallography.[1] The ^{1}H-NMR spectra of natural and synthetic material were identical.[5] Because of the small amounts of natural material available (≈4 mg), the signals for the quaternary and carbonyl carbons in the ^{13}C-NMR spectrum were very weak and difficult to assign. The corresponding spectrum of synthetic material showed complete correspondence with natural material for all other carbons, as well as strong signals at δ 111.3 (vs the reported 101.0) for the quaternary carbon and δ 170.0 (vs 153.5) for the carbonyl carbon.

Butenolide (−)-**2** was synthesized in a similar fashion (Scheme II), but the unsaturated side-chain precursor had to be synthesized by conventional methodology, as well. The overall yield was 20% from chromium hexacarbonyl. Comparison of the physical properties of synthetic (−)-**2** with that derived from natural sources again showed a specific rotation of the same sign, indicating the correct absolute configuration for this compound to be *R*, but with a higher value for synthetic material (−31.9° vs −13.7°). The ^{1}H-NMR spectra were identical, and the ^{13}C-NMR spectrum of synthetic material again differed from that reported for natural material by having clearly assignable peaks for the quaternary carbon (δ 111.3 vs 101.5) and the carbonyl carbon (δ 170.0 vs 153.5). These two carbon signals were, again, very difficult to distinguish from baseline noise for the ^{13}C spectrum of natural material.[5]

(5) We thank Professor Schmitz for providing copies of spectra for compounds **1** and **2**.

Scheme III



A number of years ago, Nozoe[6] had reported a racemic synthesis[7] of the antibiotic (+)-tetrahydrocerulenin[8] (**13**) using racemic butenolide (±)-**11** as a key intermediate. Since the chemistry developed in Schemes I and II is well-suited to this target, the synthesis of (+)-tetrahydrocerulenin was undertaken (Scheme III). Since **13** has the opposite absolute configuration from butenolides **1** and **2**, the (S)-ene–carbamate **4** was the required starting material. Butenolide **11** was obtained with ≥95% ee as determined by ^{1}H-NMR chiral shift studies, under conditions which gave base-line separation of enantiomers for racemic material. As reported by Nozoe,[6] epoxidations of **11** were highly stereoselective (only a single diastereoisomer could be detected in the ^{1}H-NMR spectrum of the crude material) but proceeded in poor yield (30% in our hands, 40% reported). Treatment of epoxy lactone (+)-**12** with ammonia in ether gave (+)-tetrahydrocerulenin (**13**) in virtually quantitative yield. The physical data for synthetic **13** were identical in all respects to those reported for (+)-tetrahydrocerulenin.[6-8] This five-step synthesis in overall 19% yield is very direct, and the overall yield is comparable to the other reported syntheses,[8] notwithstanding the problematic epoxidation step.

Experimental Section

General Procedures. Optical rotations were obtained at a wavelength of 589 nm (Na D line) in a 1.0-dm cell with a total volume of 1 mL. Specific rotation ($[\alpha]_D$) is reported in degrees per decimeter at 25 °C and the concentration (*c*) given in grams per 100 mL in the specified solvent.

(6) Ohta, T.; Tsuchiyama, H.; Nozoe, S. *Heterocycles* **1986**, *24*, 1137.

(7) For other syntheses of (±)-tetrahydrocerulenin, see: (a) Jakubowski, A. A.; Guziec, F. S., Jr.; Tishler, M. *Tetrahedron Lett.* **1977**, 2399. (b) Jakubowski, A. A.; Guziec, F. S., Jr.; Sigiura, M.; Tam, C. C.; Omura, S. *J. Org. Chem.* **1982**, *47*, 1221. (c) Sestrick, M. R.; Miller, M.; Hegedus, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 4079.

(8) For syntheses of (+)-tetrahydrocerulenin, see: (a) Ohrui, H.; Emoto, S. *Tetrahedron Lett.* **1978**, 2095 (nine steps, 29% overall yield from previously synthesized intermediate (no yield)). (b) Pougny, J. R.; Sinaÿ, P. *Tetrahedron Lett.* **1978**, 3301 (seven steps, 29% from previously synthesized intermediate (no yield)). (c) Vigneron, J. P.; Blanchard, J. M. *Tetrahedron Lett.* **1980**, *21*, 1739 (no yields reported). (d) Yoda, H.; Katagiri, T.; Takabe, K. *Tetrahedron Lett.* **1991**, *32*, 6771 (nine steps, 22%). (e) Morisaki, N.; Funabashi, H.; Furukawa, J.; Shimazawa, R.; Kanematsu, A.; Ando, T.; Okuda, S.; Iwasaki, S. *Chem. Pharm. Bull.* **1992**, *40*, 2945 (10 steps, 3%).

The photoreactions were carried out using a 450-W 7825 medium-pressure Hg lamp immersed in a Pyrex well and Ace pressure tubes equipped with a pressure head capable of withstanding 150 psi.

Flash chromatography was performed on ICN Silitech (32–63 μm, 60 Å). Radial layer chromatography was performed using plates with silica gel 60 PF_{254} (with gypsum, EM Science).

[(Methoxy)(octyl)carbene]pentacarbonylchromium(0) **9**,[7c] [(ethoxy)(methyl)carbene]pentacarbonylchromium(0),[9] and (±)-*syn*-diphenylethanolamine[10] were prepared according to the published methods. The hexadecyl iodide was made from the bromide (Aldrich) via halogen exchange (NaI/acetone).

[(Methoxy)(hexadecyl)carbene]pentacarbonylchromium(0) (3).[19] A 100-mL Airless flask equipped with a stir bar was flame dried and filled with argon. Hexadecyl iodide (1.57 mL, 5 mmol) and Et_2O (50 mL) were placed into the flask. The flask was cooled to −20 °C (ethylene glycol/CO_2) at which time the iodide precipitated. At −20 °C, *t*-BuLi (6 mL, 1.7 M in pentane) was added quickly to the flask. The resulting faint yellow solution was stirred at −20 °C (0.5 h) and then warmed to 25 °C. The mixture was stirred at 25 °C (1 h). The lithium reagent was added via a cannula to an Airless flask containing $Cr(CO)_6$ (1.1 g, 5 mmol) and Et_2O (20 mL). The brown solution was stirred at 25 °C (18 h). The solvent was removed under reduced pressure, and the brown residue was taken up in H_2O (60 mL). Me_3OBF_4 was added until the solution was acidic (pH = 2). The mixture was extracted with hexanes (4 × 100 mL). The combined hexane layers were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave an orange oil. Purification via flash chromatography (hexanes, SiO_2) gave 1.84 g (80%) of **3** as an orange solid: ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, *J* = 6.4 Hz, CH_3), 1.23 (bs, 26 H, CH_2), 1.49 (m, 2 H, CH_2), 3.27 (m, 2 H, Cr=CCH_2), 4.74 (s, 3 H, OCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.12 (CH_3), 22.69, 26.33, 29.26, 29.36, 29.41, 29.59, 29.68, 31.94, 63.15 (Cr=CCH_2), 67.57 (OCH_3), 216.44 (cis CO), 223.18 (trans CO), 363.78 (Cr=C); IR (film) δ 2062, 1938 (CO) cm^{-1}.

(*S*)-Phenylglycinol. $NaBH_4$ (7.5 g, 198 mmol) and THF (200 mL) were placed into a 3-neck round-bottom flask equipped with an addition funnel (under argon). The mixture was cooled to 0 °C, and $BF_3{\cdot}Et_2O$ (50 mL, 387 mmol) was added via the addition funnel to the mixture at 0 °C. After the addition was complete, (*S*)-phenylglycine (15.0 g, 99 mmol) was added in several portions to the white slurry at 0 °C. The mixture was warmed to 25 °C and stirred at that temperature (15 h). MeOH was added to quench the excess $NaBH_4$. The solution was concentrated under reduced pressure to remove the THF, and the resulting white slurry was stirred at 25 °C (10 h) with 20% NaOH (400 mL). The aqueous solution was extracted with $CHCl_3$ (5 × 100 mL), and the combined $CHCl_3$ layers were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave 11.0 g (81%) of (*S*)-phenylglycinol as a white solid. Spectroscopic data were identical with reported values.[11]

(*R*)-Phenylglycinol. The above procedure for the reduction of (*S*)-phenylglycinol was followed. (*R*)-Phenylglycine (15.0 g, 99.2 mmol), $NaBH_4$ (7.5 g, 198.4 mmol), and $BF_3{\cdot}Et_2O$ (50 mL, 397 mmol) gave 9.11 g (67%) of (*R*)-phenylglycinol as a white solid. Spectroscopic data were identical with reported values.[12]

3-Vinyl-(*S*)-4-phenyl-2-oxazolidinone (4). The procedure previously reported was modified to accommodate the scale-up of this reaction. [(Ethoxy)(methyl)carbene]pentacarbonylchromium(0) (1.95 g, 7.36 mmol) and (*S*)-phenylglycinol (1.0 g, 7.36 mmol) in DMF (30 mL) were placed into a 100-mL round-bottom flask, and the mixture was stirred at 25 °C under argon (3 h). The reaction mixture was partitioned between Et_2O (50 mL) and H_2O (50 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL). The combined Et_2O layers were washed with H_2O (2 × 50 mL) and brine (50 mL). The Et_2O layer was dried over $MgSO_4$. Filtration (silica gel) and concentration under reduced pressure gave the aminocarbene complex as a thick yellow oil. Two 100-mL airless flasks were flame dried and filled with argon. NaH/oil dispersion (50 wt %) (353 mg each, 14.7 mmol) was added to each flask. The oil was washed away with hexanes (3 × 5 mL). Diphenyl carbonate (1.58 g, 7.36 mmol) and THF (10 mL) was placed into one flask, and THF (10 mL) was placed into the other flask. The aminocarbene complex was taken up in THF (20 mL) and added to the flask containing NaH/THF via a cannula at 25 °C. After $H_{2(g)}$ evolution ceased (10 min), the faint red solution was added to the diphenyl carbonate/THF/NaH mixture via a cannula at 25 °C. The resulting deep red mixture was stirred at 25 °C (13.5 h). Air was bubbled through the mixture upon which time the mixture became green. The green mixture was concentrated under reduced pressure to remove the THF. The green residue was taken up in hexanes/EtOAc (1/1, 100 mL), and the solution was filtered through silica gel to afford a yellow solution. The solution was washed with 2 N NaOH (2 × 50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried over $MgSO_4$. The organic layer was filtered and diluted to 350 mL with hexanes/EtOAc (1/1). The solution was saturated with air and was placed into a light box equipped with six 20-W Vitalite fluorescent lamps (24 h). Every 6–8 h, the solution was filtered to remove the brown precipitate. The solvent was removed to give a clear oil. Purification via flash chromatography (1/1 hexanes/EtOAc, SiO_2) gave 1.08 g (78%, from the alkoxycarbene complex) of (*S*)-**4** as a white solid. Spectroscopic data were identical with reported values.[13]

3-Vinyl-(*R*)-4-phenyl-2-oxazolidinone (4). (*R*)-**4** was prepared in a similar manner as described above using [(ethoxy)(methyl)carbene]pentacarbonylchromium(0) (4.6 g, 17.4 mmol), (*R*)-phenylglycinol (2.39 g, 17.4 mmol), NaH/oil dispersion (50 wt %) (1.67 g, 34.8 mmol), and diphenyl carbonate (3.73 g, 17.4 mmol). This gave 2.52 g (77%) of (*R*)-**4** as a white solid. Spectroscopic data were identical with reported values.[13]

(±)-*syn*-4,5-Diphenyl-3-vinyl-2-oxazolidinone (4). (±)-**4** was prepared in a similar manner as described above using [(ethoxy)(methyl)carbene]pentacarbonylchromium(0) (4.3 g, 16.3 mmol), (±)-*syn*-diphenylethanolamine (3.47 g, 16.3 mmol), NaH/oil dispersion (50 wt %) (1.56 g, 32.7 mmol), and diphenyl carbonate (3.49 g, 16.3 mmol). Purification via recrystallization (hexanes/Et_2O) gave 3.03 g (70%) of (±)-**4** as a white solid. Spectroscopic data were identical with reported values.[13]

General Procedure for the Photoreaction of Chromium Carbene Complexes and Ene–Carbamates To Produce Cyclobutanones. The reported procedure was modified to increase the yield of this reaction.[1] The chromium carbene complex (1.5–2.0 equiv) and ene–carbamate (1 equiv) in degassed CH_2Cl_2 were placed in an Ace pressure tube. The pressure tube was charged to 60–90 psi CO (3 cycles) and irradiated at 25 °C (10–20 h). The solvent was removed under reduced pressure, and the $Cr(CO)_6$ was recovered via sublimation (50 °C, 0.1 mmHg). The crude cyclobutanone was purified via flash or radial chromatography.

General Procedures for the Baeyer–Villiger Oxidation of the Cyclobutanones to the Corresponding γ-Lactones. Procedure A. The cyclobutanone (1 equiv), *m*-CPBA (1–2 equiv), and Li_2CO_3 (0.3 equiv) in CH_2Cl_2 were stirred at 25 °C (10–24 h). The reaction mixture was washed with 10% $Na_2S_2O_3$-(aq) and saturated $NaHCO_{3(aq)}$ and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave essentially the pure lactone. The lactone was purified by flash or radial chromatography.

Procedure B.[14] The cyclobutanone was taken up in THF, and the mixture was cooled to 0 °C. *t*-BuOOH (4 equiv of a 3.0 M solution) and 2 N $NaOH_{(aq)}$ (2 equiv) were added at 0 °C, and the mixture was stirred at 0 °C for 0.5 h. The reaction mixture was partitioned between EtOAc and 10% $Na_2S_2O_{3(aq)}$. The aqueous layer was extracted with EtOAc. The combined EtOAc layers were washed with brine and dried over Na_2SO_4. Filtration and concentration gave the crude lactone. The lactone was purified by flash chromatography.

(9) Darensbourg, M. Y.; Darensbourg, D. J. *Inorg. Chem.* **1970**, *9*, 32.
(10) Weijlard, J.; Pfister, K.; Swanezy, E. F.; Robinson, C. A.; Tishler, M. *J. Am. Chem. Soc.* **1951**, *73*, 1216.
(11) Imwinkelried, R.; Hegedus, L. S. *Organometallics* **1988**, *7*, 702.
(12) Tseng, C. C.; Terashima, S.; Yamada, S.-I. *Chem. Pharm. Bull.* **1977**, *25*, 166.
(13) Montgomery, J.; Wieber, G. M.; Hegedus, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 6255.
(14) Grieco, P. A.; Oguri, T.; Wang, C.-L. J.; Williams, E. *J. Org. Chem.* **1977**, *42*, 4113.

General Procedure for the Conversion of γ-Lactones to Butenolides. The γ-lactone was taken up in THF and cooled to 0 °C. TBAF (1.2–2 equiv) was added to the mixture at 0 °C, and the mixture was stirred at 0 °C until no more starting material was evident by TLC (approximately 1 h). The reaction mixture was partitioned between EtOAc and saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted with EtOAc. The combined EtOAc layers were washed with brine and dried over $MgSO_4$ or Na_2SO_4. Filtration and concentration of the mixture gave the crude butenolide. The butenolide was purified by flash or radial chromatography.

(−)-Cyclobutanone (5). [(Methoxy)(hexadecyl)carbene]pentacarbonylchromium(0) (**3**) (1.3 g, 2.83 mmol) and (*R*)-ene–carbamate **4** (382 mg, 2.02 mmol) in CH_2Cl_2 (50 mL) were allowed to react according to the general photoreaction procedure (11.5 h). Purification via flash chromatography (5/1, 3/1, 1/1 hexanes/EtOAc, SiO_2) gave 626 mg (64%) of (−)-**5** as a white solid, mp = 74–75 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J* = 6.5 Hz, CH_3), 1.24 (bs, 28 H, CH_2), 1.85 (m, 2 H, CH_2), 2.52 (dd, 1 H, *J* = 10.1, 17.9 Hz, CH_2C=O), 3.15 (s, 3 H, OCH_3), 3.22 (dd, 1 H, *J* = 9.4, 17.9 Hz, CH_2C=O), 4.19 (dd, 1 H, *J* = 10.1, 17.9 Hz, OCH_2), 4.34 (t, 1 H, *J* = 9.8 Hz, CHN), 4.67 (t, 1 H, *J* = 8.6 Hz, OCH_2), 4.87 (dd, 1 H, *J* = 4.9, 8.5 Hz, PhC*H*N), 7.26, 7.39 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.08 (CH_3), 22.65, 23.06, 29.32, 29.48, 29.52, 29.65, 29.81, 29.94, 31.88, 42.58 (CH_2), 47.31 (CHN), 52.42 (OCH_3), 61.58 (PhCHN), 70.05 (OCH_2), 98.77 (*C*(OCH_3)(CH_2)), 126.39, 129.36, 129.53 (Ar), 138.72 (Ar ipso), 157.84 (carbamate C=O), 205.71 (cyclobutanone C=O); IR (film) ν 1780, 1739 cm^{-1}; $[\alpha]_D$ = −40.0° (*c* = 0.55, CH_2Cl_2). Anal. Calcd for $C_{30}H_{47}NO_4$: C, 74.19; H, 9.75; N, 2.88. Found: C, 74.26; H, 9.66; N, 2.98.

(−)-Lactone (6). Cyclobutanone (−)-**5** (300 mg, 0.62 mmol), *m*-CPBA (160 mg, 0.74 mmol), and Li_2CO_3 (14 mg, 0.2 mmol) in CH_2Cl_2 (50 mL) were subjected to Baeyer–Villiger procedure A (11 h). This gave 309 mg (99%) of (−)-**6** as a white solid, mp = 92–93 °C; ^{1}H NMR (300 MHz, C_6D_6) δ 0.91 (t, 3 H, *J* = 7.7 Hz, CH_3), 1.30 (bs, 28 H, CH_2), 1.45 (m, 2 H, CH_2), 1.64 (d, 1 H, *J* = 18.2 Hz, CH_2C=O), 2.05 (m, 2 H, CH_2), 2.32 (dd, 1 H, *J* = 8.1, 18.2 Hz, CH_2C=O), 2.94 (s, 3 H, OCH_3), 3.44 (dd, 1 H, *J* = 2.4, 8.8 Hz, OCH_2), 3.75 (t, 1 H, *J* = 8.5 Hz, OCH_2), 4.08 (dd, 1 H, *J* = 2.4, 8.2 Hz, PhC*H*N), 4.72 (d, 1 H, *J* = 7.8 Hz, CHN), 6.95, 7.02 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, C_6D_6) δ 14.33 (CH_3), 22.49, 23.08, 29.67, 29.80, 29.88, 29.97, 30.11, 30.17, 31.98, 32.30 (CH_2), 49.40 (CH_3), 56.79, 57.89 (CH), 70.53 (OCH_2), 112.05 (*C*(OCH_3)(CH_2)), 126.43, 129.22, 129.57 (Ar), 140.98 (Ar ipso), 157.64 (carbamate C=O), 173.21 (lactone C=O); IR (film) ν 1799, 1739 (C=O) cm^{-1}; $[\alpha]_D$ = −34.7° (*c* = 0.6, CH_2Cl_2). Anal. Calcd for $C_{30}H_{47}NO_5$: C, 71.82; H, 9.44; N, 2.79. Found: C, 71.55; H, 9.29; N, 2.75.

(−)-Butenolide (1).[4] Lactone (−)-**6** (150 mg, 0.30 mmol) and TBAF (0.36 mL, 1.0 M in THF, 0.36 mmol) in THF (20 mL) were subjected to the butenolide general procedure. Purification via radial chromatography (4/1/1 hexanes/Et_2O/CH_2Cl_2, 1 mm SiO_2) gave 76 mg (75%) of (−)-**1** as a white solid, mp = 69 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, CH_3), 1.23 (bs, 28 H, CH_2), 1.90 (m, 2 H, CH_2), 3.20 (s, 3 H, OCH_3), 6.19 (d, 1 H, *J* = 5.7 Hz, =CH), 7.10 (d, 1 H, *J* = 5.7 Hz, =CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.10 (CH_3), 22.67, 23.27, 29.35, 29.47, 29.66, 31.91, 36.98 (CH_2), 51.11 (OCH_3), 111.28 (*C*(OCH_3)(CH_2)), 124.75 (=CH), 153.53 (=CH), 169.98 (C=O); IR (film) ν 1762 (C=O) cm^{-1}; $[\alpha]_D$ = −32.4° (*c* = 0.5, CH_2Cl_2). Anal. Calcd for $C_{21}H_{38}O_3$: C, 74.51; H, 11.31. Found: C, 74.67; H, 11.15.

(±)-Cyclobutanone (5). [(Methoxy)(hexadecanyl)carbene]-pentacarbonylchromium(0) (**3**) (304 mg, 0.66 mmol) and (±)-*syn*-diphenyl ene–carbamate (100 mg, 0.38 mmol) in CH_2Cl_2 (50 mL) were allowed to react according to the general photoreaction procedure (18.5 h). Purification via radial chromatography (8/1/0.5 hexanes/CH_2Cl_2/EtOAc, 2 mm SiO_2) gave 90 mg (42%) of (±)-**5** as a white solid, mp = 104–105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, *J* = 6.4 Hz, CH_3), 1.24 (bs, 28 H, CH_2), 1.73 (m, 1 H, CH_2), 2.03 (m, 1 H, CH_2), 2.44 (dd, 1 H, *J* = 10.1, 18.0 Hz, CH_2C=O), 2.78 (dd, 1 H, *J* = 9.3, 17.9 Hz, CH_2C=O), 3.40 (s, 3 H, OCH_3), 4.63 (t, 1 H, *J* = 9.7 Hz, CHN), 5.03 (d, 1 H, *J* = 7.5 Hz), 5.89 (d, 1 H, *J* = 7.4 Hz), 6.80, 7.00, 7.10 (m, 10 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.10 (CH_3), 22.67, 23.08, 29.35, 29.46, 29.57, 29.64, 29.69, 30.06, 31.91, 43.68 (CH_2), 47.53 (CHN), 52.69 (OCH_3), 65.99, 80.24, 98.69 (*C*(OCH_3)(CH_2)), 126.12, 126.98, 127.98, 128.26, 128.67 (Ar), 133.44, 134.73 (Ar ipso), 158.23 (carbamate C=O), 205.25 (cyclobutanone C=O); IR (film) ν 1780, 1734 (C=O) cm^{-1}. Anal. Calcd for $C_{36}H_{51}NO_4$: C, 76.97; H, 9.15; N, 2.49. Found: C, 76.77; H, 8.98; N, 2.44.

(±)-Lactone 6. Cyclobutanone (±)-**5** (90 mg, 0.16 mmol), *m*-CPBA (45 mg, 0.19 mmol), and Li_2CO_3 (10 mg, 0.05 mmol) in CH_2Cl_2 (20 mL) were subjected to Baeyer–Villiger procedure A (12.5 h). This gave 92 mg (99%) of (±)-**6** as a white solid, mp = 76–77 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, *J* = 6.4 Hz, CH_3), 1.21 (bs, 28 H, CH_2), 1.75 (m, 1 H, CH_2), 1.94 (d, 1 H, *J* = 18.1 Hz, CH_2C=O), 2.25 (m, 1 H, CH_2), 2.76 (dd, 1 H, *J* = 8.0, 18.2 Hz, CH_2C=O), 3.33 (s, 3 H, OCH_3), 4.79 (d, 1 H, *J* = 7.3 Hz, CH), 4.88 (d, 1 H, *J* = 7.5 Hz, CHN), 5.78 (d, 1 H, *J* = 7.2 Hz, CH), 6.90, 7.10 (m, 10 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.07 (CH_3), 22.18, 22.64, 29.27, 29.30, 29.47, 29.63, 29.85, 31.87, 32.07 (CH_2), 50.03 (OCH_3), 56.29, 63.05, 80.98 (CH), 112.66 (*C*(OCH_3)(CH_2)), 125.83, 127.93, 128.08, 128.67, 128.99 (Ar), 132.87, 135.35 (Ar ipso), 157.59 (carbamate C=O), 173.94 (lactone C=O); IR (film) ν 1798, 1748 (C=O) cm^{-1}. Anal. Calcd for $C_{36}H_{51}NO_5$: C, 74.83; H, 8.90; N, 2.42. Found: C, 74.71; H, 8.73; N, 2.43.

(±)-Butenolide 1. Lactone (±)-**6** (92 mg, 0.16 mmol) and TBAF (0.24 mL, 1.0 M in THF, 0.24 mmol) in THF (25 mL) were subjected to the butenolide general procedure. Purification via flash chromatography (3/1 hexanes/EtOAc, SiO_2) gave 40 mg (74%) of (±)-**1** as a white solid. Spectroscopic data were identical with the above values.

Chiral Shift Study of (±)-1 and (−)-1. (±)-**1** and (−)-**1** (7 mg) were separately combined with (+)-Eu(hfc)$_3$ (7 mg, 30 mol %) and $CDCl_3$ (0.7 mL). ^{1}H NMR analysis of the (±)-**1** sample indicated a split of the methoxy signals (4.1 ppm). The (−)-**1** sample contained only one methoxy signal which indicated an ee ≥ 95% for the butenolide.

Tetrahydro-2-(3-butynyloxy)-2*H*-pyran. 3-Butyn-1-ol (5.7 mL, 75 mmol), dihydropyran (7.5 mL, 82.5 mmol), and CH_2Cl_2 (50 mL) were placed into a dry 100-mL round-bottom flask. The flask was cooled to 0 °C, and TsOH monohydrate (20 mg) was added to the mixture at 0 °C. The mixture was warmed to 25 °C and stirred at that temperature (2 h). The reaction mixture was washed with saturated $NaHCO_{3(aq)}$. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 layers were dried over $MgSO_4$. Filtration and concentration under reduced pressure gave a yellow oil. Purification via vacuum distillation gave 10.2 g (88%) of the THP-protected alkynol as a colorless oil, bp = 50–52 °C (0.4 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5–1.7 (m, 6 H, CH_2), 1.95 (t, 1 H, *J* = 2.7 Hz, CCH), 2.47 (dt, 1 H, *J* = 2.6, 7.1 Hz, $CCCH_2$), 3.4–3.6 (m, 2 H, OCH_2), 3.8–4.0 (m, 2 H, OCH_2), 4.63 (t, 1 H, *J* = 3.0 Hz, *H*C(OR)$_2$CH$_2$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.95, 19.54, 25.08, 30.14 (CH_2), 61.59, 65.11 (OCH_2), 68.98 (*C*CH), 80.97 (*C*CH), 98.22 (*C*(OR)$_2$R).

3-Pentadecyn-1-ol.[15] A 200-mL flask was flame dried and filled with argon. The THP-protected alkyne (7.40 g, 48 mmol), HMPA (14 mL), and THF (40 mL) were placed into the flask under argon. The flask was cooled to −40 °C (CH_3CN/CO_2), and *n*-BuLi (30 mL, 1.6 M in hexanes) was added dropwise to the mixture at −40 °C over 10 min. The resulting orange mixture was stirred at −40 °C (0.5 h). 1-Iodoundecane (11.3 g, 40 mmol) was added to the mixture at −40 °C. The reaction mixture was allowed to slowly warm to 25 °C and was stirred at that temperature (16 h). The reaction mixture was partitioned between hexanes and H_2O. The aqueous layer was extracted with two portions of hexanes. The combined hexane layers were washed with brine and dried over $MgSO_4$. Filtration and concentration gave the crude homologated THP-protected alcohol as a yellow oil. This material was used without any further purification. The crude material was taken up in EtOH (250 mL), and PPTS (500 mg) was added. The mixture was heated at 55 °C (15 h). The mixture was concentrated under reduced pressure, and the crude solid was taken up in Et_2O. The mixture was washed with saturated $NaHCO_{3(aq)}$. The aqueous layer was extracted with two portions of Et_2O. The combined Et_2O layers were washed with brine and dried over $MgSO_4$. Filtration and

(15) Schwarz, M.; Waters, R. M. *Synthesis* **1972**, 567.

concentration under reduced pressure gave the crude alcohol as a yellow solid. Purification via recrystallization (hexanes/Et_2O) gave 6.73 g (75%) of the alcohol as a white solid, mp = 34–35 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, 3 H, CH_3), 1.21 (bs, 18 H, CH_2), 1.45 (m, 2 H, CH_2), 2.10 (m, 3 H, OCH_2, OH), 2.37 (m, 2 H, CH_2), 3.62 (t, 2 H, J = 6.3 Hz, OCH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.03 (CH_3), 18.67, 22.62, 23.09, 28.85, 28.95, 29.10, 29.28, 29.48, 29.57, 31.86 (CH_2), 61.30 (OCH_2), 76.22, 82.59 (CC); IR (film) ν 3196 (OH) cm^{-1}. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.10; H, 12.38.

14-Pentadecyn-1-ol. This compound was made via isomerization of the previous product.[16] A 50-mL Airless flask was flame dried and filled with argon. KH (6 g, 35 wt % in oil) was weighed out and placed into the flask. The KH was washed with pentane (4 × 15 mL) and was dried by blowing argon over the washed KH. 1,3-Diaminopropane (30 mL) was added to the KH at 25 °C under argon. $H_{2(g)}$ evolution was noted, and the slurry was stirred at 25 °C (1 h). The alkynol (2.27 g, 10.1 mmol) in THF (5 mL) was added to the flask at 25 °C. The red mixture was stirred at that temperature (2 h). The reaction was quenched with H_2O (30 mL) at 0 °C. The reaction mixture was extracted with EtOAc (3 × 50 mL). The combined EtOAc layers were washed with brine and dried over $MgSO_4$. Filtration and concentration gave a brown residue. Purification via sublimation (115 °C, 0.3 mmHg) gave 1.66 g (73%) of the isomerized alkynol as a waxy solid: ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (bs, 18 H, CH_2), 1.51 (m, 4 H, CH_2), 1.91 (t, 1 H, J = 2.7 Hz, CCH), 2.16 (dt, 2 H, J = 2.6, 6.9 Hz, $CCCH_2$), 3.26 (t, 2 H, J = 6.6 Hz, OCH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.34, 25.70, 28.44, 28.70, 29.06, 29.39, 29.44, 29.55, 32.73 (CH_2), 62.92 (OCH_2), 67.99, 84.73 (CC); IR (film) ν 3285 (CCH).

1-(*tert*-Butyldimethylsiloxy)-14-pentadecyne. The above alcohol (1.3 g, 5.8 mmol), imidazole (790 mg, 11.6 mmol), and DMF (50 mL) were placed into a 100-mL round-bottom flask. TBDMSCl (1.31 g, 8.7 mmol) in DMF (10 mL) was added to the flask at 25 °C, and the reaction mixture was stirred at that temperature (13.5 h). The reaction mixture was partitioned between H_2O (100 mL) and hexanes (100 mL). The aqueous layer was extracted with hexanes (50 mL). The combined hexane layers were dried over $MgSO_4$. Filtration and concentration under reduced pressure gave the crude TBDMS ether. Purification via flash chromatography (9/1 hexanes/EtOAc, SiO_2) gave 1.86 g (95%) of the protected alcohol as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 6 H, $Si(CH_3)_2$), 0.87 (s, 9 H, $SiC(CH_3)_3$), 1.24 (bs, 18 H, CH_2), 1.50 (m, 4 H, CH_2), 1.91 (t, 1 H, J = 2.6 Hz, CCH), 2.15 (dt, 2 H, J = 2.6, 6.9 Hz, $CCCH_2$), 3.57 (t, 2 H, 7.3 Hz, OCH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −5.26 ($Si(CH_3)_2$), 18.40 ($SiC(CH_3)_3$), 25.81 (CH_2), 25.99 ($SiC(CH_3)_3$), 28.51, 28.77, 29.12, 29.45, 29.51, 29.62, 32.90 (CH_2), 63.33 (OCH_2), 68.02, 84.76 (CC).

(*E*)-1-Bromo-15-(*tert*-butyldimethylsiloxy)-1-pentadecene.[17] A 50-mL airless flask was flame dried and filled with argon. Cp_2ZrCl_2 (1.38 g, 4.73 mmol) and THF (20 mL) were placed in the flask. Super-Hydride–LiHBEt$_3$ (4.7 mL, 1.0 M in THF) was added dropwise to the flask at 25 °C. The solution was stirred at that temperature for 1 h. The above alkyne (800 mg, 2.36 mmol) in THF (5 mL) was added to the flask at 25 °C. The yellow solution was stirred at that temperature for 20 min. NBS (842 mg, 4.73 mmol) was added to the flask at 25 °C, and the cloudy mixture was stirred at that temperature for 15 min. The reaction mixture was partitioned between hexanes/EtOAc (9/1, 30 mL) and saturated $NaHCO_{3(aq)}$ (50 mL). The aqueous layer was extracted with hexanes/EtOAc (9/1, 2 × 30 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. Filtration (Celite/SiO_2) and concentration under reduced pressure gave a yellow oil. Purification via flash chromatography (9/1 hexanes/EtOAc, SiO_2) gave 798 mg (81%) of the vinyl bromide as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 6 H, $Si(CH_3)_2$), 0.87 (s, 9 H, $SiC(CH_3)_3$), 1.24 (bs, 18 H, CH_2), 1.5 (m, 2 H, CH_2), 2.00 (m, 2 H, CH_2), 3.58 (t, 2 H, J = 6.6 Hz, OCH_2), 5.98 (dt, 1 H, J = 1.2, 13.5 Hz, =CH), 6.15 (dt, 1 H, J = 7.2, 13.5 Hz, =CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −5.26 ($Si(CH_3)_2$), 18.37 ($SiC(CH_3)_3$), 25.81 (CH_2), 25.98 ($SiC(CH_3)_3$), 28.61, 28.96, 29.37, 29.45, 29.54, 29.63, 32.90, 32.94 (CH_2), 63.32 (OCH_2), 103.99, 138.27 (C=C).

1-(*E*)-(*tert*-Butyldimethylsiloxy)-14-hexadecene.[18] The vinyl bromide (1.69 g, 4.03 mmol) and THF (40 mL) were placed into a dry 100-mL round-bottom flask. Pd[P(Ph)$_3$] (233 mg, 0.2 mmol) was added to the mixture at 25 °C. MeMgBr (1.6 mL, 3.0 M in Et_2O) was added dropwise at 25 °C, and the resulting yellow mixture stirred at that temperature (18 h). The reaction mixture was partitioned between saturated $NH_4Cl_{(aq)}$ and Et_2O. The aqueous layer was extracted with Et_2O. The combined Et_2O layers were washed with brine and dried over $MgSO_4$. Filtration and concentration gave a yellow oil. Purification via flash chromatography (9/1 hexanes/Et_2O, SiO_2) gave 853 mg (60%) of the alkenyl ether as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 6 H, $Si(CH_3)_2$), 0.89 (s, 9 H, $SiC(CH_3)_3$), 1.25 (bs, 18 H, CH_2), 1.50 (m, 2 H, CH_2), 1.62 (dd, 3 H, J = 4.0, 1.3 Hz, CH_3), 1.95 (m, 2 H, CH_2), 3.58 (t, 2 H, J = 6.5 Hz, OCH_2), 5.39 (m, 2 H, HC=CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −5.26 ($Si(CH_3)_2$), 17.91 (CH_3), 18.38 ($SiC(CH_3)_3$), 25.85 (CH_2), 26.00 ($SiC(CH_3)_3$), 29.25, 29.50, 29.59, 29.69, 32.65, 32.94 (CH_2), 63.33 (OCH_2), 124.48, 131.69 (C=C).

(*E*)-14-Hexadecen-1-ol. The TBDMS-protected alcohol (852 mg, 2.4 mmol) was taken up in THF (40 mL). TBAF (2.9 mL, 1.0 M in THF, 2.9 mmol) was added to the flask at 25 °C. The reaction was stirred at 25 °C until TLC indicated no more starting material (3 h). The reaction mixture was partitioned between saturated $NH_4Cl_{(aq)}$ and Et_2O. The aqueous layer was extracted with two portions of Et_2O. The combined Et_2O layers were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave a yellow solid. Purification via flash chromatography (3/1 hexanes/EtOAc, SiO_2) gave 509 mg (88%) of the alcohol as a white solid, mp = 35 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (bs, 18 H, CH_2), 1.55 (m, 2 H, CH_2), 1.61 (dt, J = 1.2, 4.7 Hz, CH_3), 1.95 (m, 2 H, CH_2), 3.61 (t, 2 H, J = 6.6 Hz, OCH_2), 5.38 (m, 2 H, HC=CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.89 (CH_3), 25.72, 29.19, 29.42, 29.52, 29.61, 32.59, 32.79 (CH_2), 63.04 (OCH_2), 124.48, 131.67 (C=C); IR (film) ν 3369 (OH) cm^{-1}. Anal. Calcd for $C_{16}H_{32}O$: C, 79.93; H, 13.41. Found: C, 80.15; H, 13.22.

(*E*)-1-Methanesulfonyl-14-hexadecene. The alcohol (496 mg, 2.07 mmol) and Et_3N (0.3 mL, 2.27 mmol) were dissolved in CH_2Cl_2 (15 mL). The mixture was cooled to 0 °C, and methanesulfonyl chloride (0.18 mL, 2.27 mmol) was added at that temperature. The mixture was warmed to 25 °C and stirred at that temperature (2 h). The mixture was diluted with CH_2Cl_2 (20 mL) and washed with saturated $NaHCO_{3(aq)}$. The CH_2Cl_2 layer was dried over $MgSO_4$. Filtration and concentration under reduced pressure gave 627 mg (95%) of the mesylate as a white solid: ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (bs, 18 H, CH_2), 1.61 (dt, 3 H, J = 1.2, 4.7 Hz, CH_3), 1.70 (m, 2 H, CH_2), 1.95 (m, 2 H, CH_2), 2.97 (s, 3 H, CH_3SO_3), 4.19 (t, 2 H, OCH_2), 5.38 (m, 2 H, HC=CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.87 (CH_3), 25.37, 28.99, 29.09, 29.16, 29.38, 29.47, 29.57, 32.56 (CH_2), 37.30 (CH_3SO_3), 70.18 (OCH_2), 124.46, 131.64 (C=C).

(*E*)-1-Iodo-14-hexadecene. The crude mesylate (627 mg, 1.97 mmol) and NaI (1.48 g, 9.86 mmol) were taken up in acetone (30 mL) and heated to 55 °C (20 h). The mixture was partitioned between hexanes and H_2O. The aqueous layer was extracted with hexanes, and the combined hexane layers were washed with 10% $Na_2S_2O_3$ and brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave 620 mg (90%) of the iodide as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (bs, 18 H, CH_2), 1.61 (dd, 3 H, J = 1.2, 3.5 Hz, CH_3), 1.75 (m, 2 H, CH_2), 1.90 (m, 2 H, CH_2), 3.15 (t, 2 H, J = 7.1 Hz, OCH_2), 5.38 (m, 2 H, HC=CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 7.07 (CH_2I), 17.90 (CH_3), 28.53, 29.18, 29.41, 29.52, 29.60, 30.49, 32.58, 33.55 (CH_2), 124.40, 131.59 (C=C).

Alkenylcarbene Complex 7.[19] A 10-mL airless flask was flame dried and filled with argon. The iodide (194 mg, 0.55 mmol) and Et_2O (15 mL) were placed into the flask. The flask was cooled to −78 °C at which time the iodide precipitated. *t*-BuLi

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(0.67 mL, 1.7 M in pentanes) was added to the mixture at −78 °C, and the mixture was stirred at that temperature (0.5 h). The reaction was warmed to 25 °C and stirred at that temperature (1 h). The anion solution was added via cannula to a 25-mL airless flask that contained $Cr(CO)_6$ (121 mg, 0.55 mmol) and Et_2O (10 mL). The yellow-brown mixture was stirred at 25 °C (13 h). The solvent was removed under reduced pressure. The brown residue was taken up in H_2O (10 mL), and Me_3OBF_4 was added until the solution was acidic (pH = 2). The mixture was extracted with Et_2O (3 × 30 mL), and the combined Et_2O layers were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave an orange oil. Purification via flash chromatography (9/1 hexanes/Et_2O, SiO_2) gave 168 mg (67%) of **7** as an orange oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (bs, 22 H, CH_2), 1.45 (m, 2 H, CH_2), 1.62 (d, 3 H, J = 6.2 Hz, CH_3), 1.95 (m, 2 H, CH_2), 3.27 (m, 2 H, =CCH_2), 4.74 (s, 3 H, OCH_3), 5.40 (m, 2 H, HC=CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.88 (CH_3), 26.33, 29.25, 29.41, 29.63, 32.61 (CH_2), 63.13 (OCH_3), 67.54 (CH_2), 124.49, 131.68 (C=C), 216.44 (cis CO), 223.16 (trans CO), 363.81 (Cr=C); IR (film) ν 2062, 1940 (CO) cm^{-1}.

(−)-Alkenylcyclobutanone 8. The alkenylcarbene complex **7** (314 mg, 0.69 mmol) and (*R*)-ene–carbamate **4** (87 mg, 0.46 mmol) in CH_2Cl_2 (10 mL) were allowed to react according to the general photoreaction procedure (19.5 h). Purification via flash chromatography (4/1, 2/1 hexanes/EtOAc, SiO_2) gave 36 mg of recovered ene–carbamate **4** and 117 mg (53%, 86% based on recovered ene–carbamate) of (−)-**8** as a white solid, mp = 70–71 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (bs, 22 H, CH_2), 1.40 (m, 1 H, CH_2), 1.57 (dd, 3 H, J = 1.2, 3.5 Hz, CH_3), 1.80 (m, 3 H, CH_2), 2.47 (dd, 1 H, J = 10.2, 17.9 Hz, CH_2C=O), 3.10 (s, 3 H, OCH_3), 3.17 (dd, 1 H, J = 9.4, 18.0 Hz, CH_2C=O), 4.14 (dd, 1 H, J = 4.9, 8.6 Hz, OCH_2), 4.29 (t, 1 H, J = 9.7 Hz, CHN), 4.62 (t, 1 H, J = 8.6 Hz, OCH_2), 4.83 (dd, 1 H, J = 4.9, 8.4 Hz, PhC*H*N), 5.34 (m, 2 H, HC=CH), 7.22, 7.36 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.88 (CH_3), 23.07, 29.17, 29.51, 29.60, 29.83, 29.95, 32.57 (CH_2), 42.60 (CH_2C=O), 47.34 (CH), 52.43 (OCH_3), 61.61 (CH), 70.06 (OCH_2), 99.80 ($C(OCH_3)(CH_2)$), 124.46, 126.40, 129.37, 129.54, 131.67 (Ar and C=C), 138.74 (Ar ipso), 157.84 (carbamate C=O), 205.69 (cyclobutanone C=O); IR (film) ν 1790, 1732 (C=O) cm^{-1}; $[\alpha]_D$ = −36.0° (c = 1.6, CH_2Cl_2). Anal. Calcd for $C_{30}H_{45}NO_4$: C, 74.50; H, 9.38; N, 2.90. Found: C, 74.64; H, 9.13; N, 2.78.

(−)-Alkenyl Lactone. Cyclobutanone (−)-**8** (45 mg, 0.093 mmol), *t*-BuOOH (0.12 mL, 3.0 M), and 2 N NaOH (0.093 mL) in THF (5 mL) were subjected to Baeyer–Villiger procedure B. Purification via flash chromatography (3/2 hexanes/EtOAc, SiO_2) gave 35 mg (76%) of (−)-alkenyl lactone as a white solid, mp = 76–77 °C: ^1H NMR (300 MHz, C_6D_6) δ 1.34 (bs, 22 H, CH_2), 1.22 (m, 5 H, C*H*HC=O, C*H*$_3$, C*H*H), 2.00 (m, 3 H, CH_2), 2.31 (dd, 1 H, J = 8.1, 18.1 Hz, CH_2C=O), 2.94 (s, 3 H, OCH_3), 3.43 (dd, 1 H, J = 2.5, 8.8 Hz, OCH_2), 3.73 (t, 1 H, J = 8.6 Hz, OCH_2), 4.06 (dd, 1 H, J = 2.5, 8.2 Hz, PhC*H*N), 4.73 (d, 1 H, J = 7.8 Hz, CHN), 5.44 (m, 2 H, HC=CH), 6.92, 7.02 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, C_6D_6) δ 18.09 (CH_3), 22.50, 29.63, 29.68, 29.92, 29.97, 30.02, 30.07, 30.12, 30.60, 32.01, 33.09 (CH_2), 47.42 (CH), 56.80, 57.95 (CH_3), 70.55 (OCH_2), 112.05 ($C(OCH_3)(CH_2)$), 124.82, 126.47, 126.71, 129.24, 129.59, 131.95 (Ar and C=C), 140.98 (Ar ipso), 157.63 (carbamate C=O), 173.18 (lactone C=O); IR (film) ν 1799, 1738 (C=O) cm^{-1}; $[\alpha]_D$ −30.1° (c = 1.7, CH_2Cl_2). Anal. Calcd for $C_{30}H_{45}NO_5$: C, 72.11; H, 9.08; N, 2.80. Found: C, 71.97; H, 8.86; N, 2.72.

(−)-Alkenyl Butenolide 2.[4] (−)-Alkenyl lactone (34 mg, 0.068 mmol) and TBAF (0.082 mL, 1.0 M in THF, 0.082 mmol) in THF (5 mL) were subjected to the butenolide general procedure. Purification via flash chromatography (3/1 hexanes/EtOAc, SiO_2) gave 17 mg (74%) of (−)-**2** as a white solid, mp = 52–53 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (bs, 22 H, CH_2), 1.62 (dt, 3 H, CH_3), 1.90 (m, 4 H, CH_2), 3.20 (s, 3 H, OCH_3), 5.39 (m, 2 H, HC=CH), 6.19 (d, 1 H, J = 5.7 Hz, =CH), 7.10 (d, 1 H, J = 5.7 Hz, =CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.91 (CH_3), 23.28, 29.20, 29.37, 29.49, 29.61, 32.60, 36.99 (CH_2), 51.12 (OCH_3), 111.28 ($C(OCH_3)(CH_2)$), 124.49, 124.75, 131.69, 153.53 (C=C), 169.98 (C=O); IR (film) ν 1764 (C=O) cm^{-1}; $[\alpha]_D$ = −31.9° (c = 0.8, CH_2Cl_2).

Chiral Shift Study of (−)-(2). Compound (−)-**2** (7 mg) and (+)-Eu(hfc)$_3$ (7 mg, 30 mol %) in $CDCl_3$ (0.7 mL) were combined and analyzed by ^1H NMR spectroscopy. Only one methoxy signal was seen which indicated an ee ≥ 95% for the butenolide.

(+)-Cyclobutanone 10. [(Methoxy)(octyl)carbene]chromium(0) (**9**) (3.5 g, 10 mmol) and (*S*)-ene–carbamate **4** (945 mg, 5 mmol) in CH_2Cl_2 (100 mL) were allowed to react according to the general photoreaction procedure (10 h). Purification via flash chromatography (3/1 hexanes/EtOAc, SiO_2) gave 1.58 g (84%) of (+)-**10** as a semisolid: ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, J = 6.9 Hz, CH_3), 1.25 (bs, 12 H, CH_2), 1.85 (m, 2 H, CH_2), 2.52 (dd, 1 H, J = 10.1, 17.9 Hz, CH_2C=O), 3.15 (s, 3 H, OCH_3), 3.22 (dd, 1 H, J = 9.4, 18.0 Hz, CH_2C=O), 4.19 (dd, 1 H, J = 4.9, 8.7 Hz, OCH_2), 4.34 (t, 1 H, J = 9.7 Hz, CHN), 4.67 (t, 1 H, J = 8.6 Hz, OCH_2), 4.88 (dd, 1 H, J = 4.9, 8.5 Hz, PhC*H*N), 7.25, 7.38 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.05 (CH_3), 22.58, 23.04, 29.14, 29.39, 29.77, 29.90, 31.76 (CH_2), 42.57 (CH_2C=O), 47.30 (CHN), 52.39 (OCH_3), 61.55 (PhCHN), 70.05 (OCH_2), 98.75 ($C(OCH_3)(CH_2)$), 126.38, 129.33, 129.50, 138.72 (Ar), 157.82 (carbamate C=O), 205.71 (cyclobutanone C=O); IR (film) ν 1783, 1738 (C=O) cm^{-1}; $[\alpha]_D$ = +47.0° (c = 0.053, CH_2Cl_2). Anal. Calcd for $C_{22}H_{31}NO_4$: C, 70.75; H, 8.37; N, 3.75. Found: C, 70.60; H, 8.24; N, 3.58.

(+)-Lactone. Cyclobutanone (+)-**10** (445 mg, 1.2 mmol), *m*-CPBA (510 mg, 2.4 mmol), and Li_2CO_3 (26 mg, 0.36 mmol) in CH_2Cl_2 (20 mL) were subjected to Baeyer–Villiger procedure A (17 h). This gave 428 mg (92%) of the (+)-lactone as a white solid. An analytical sample was obtained by filtration through basic Al_2O_3 (1/1 hexanes/EtOAc): ^1H NMR (300 MHz, C_6D_6) δ 0.94 (t, 3 H, J = 6.5 Hz, CH_3), 1.29 (bs, 11 H, CH_2), 1.45 (m, 1 H, CH_2), 1.62 (d, 1 H, J = 18.1 Hz, CH_2C=O), 1.67 (m, 1 H, CH_2), 2.01 (m, 1 H, CH_2), 2.31 (dd, 1 H, J = 8.1, 18.1 Hz, CH_2C=O), 2.93 (s, 3 H, OCH_3), 3.42 (dd, 1 H, J = 2.5, 8.8 Hz, OCH_2), 3.72 (t, 1 H, J = 8.5 Hz, OCH_2), 4.06 (dd, 1 H, J = 2.5, 8.2 Hz, PhC*H*N), 4.73 (d, 1 H, J = 8.0 Hz, CHN), 6.94, 7.00 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, C_6D_6) δ 14.34 (CH_3), 22.46, 23.04, 29.57, 29.88, 30.13, 31.99, 32.19 (CH_2), 49.40 (OCH_3), 56.78, 57.93, 70.52 (OCH_2), 112.04 ($C(OCH_3)(CH_2)$), 126.45, 129.23, 129.57 (Ar), 140.97 (Ar ipso), 157.61 (carbamate C=O), 173.19 (lactone C=O); IR (film) ν 1790, 1739 (C=O) cm^{-1}; $[\alpha]_D$ = +42.0° (c = 0.40, CH_2Cl_2). Anal. Calcd for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 67.61; H, 7.87; N, 3.56.

(+)-Butenolide 11. (+)-Lactone (200 mg, 0.51 mmol) and TBAF (0.62 mL, 1.0 M in THF, 0.62 mmol) in THF (40 mL) were subjected to the butenolide general procedure. Purification via radial chromatography (4/1/1 hexanes/Et_2O/CH_2Cl_2, 1 mm SiO_2) gave 104 mg (90%) of (+)-**11** as colorless needles, mp = 37–38 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, 3 H, J = 6.5 Hz, CH_3), 1.22 (bs, 12 H, CH_2), 1.84 (m, 2 H, CH_2), 3.18 (s, 3 H, OCH_3), 6.17 (d, 1 H, J = 5.7 Hz, =CH), 7.09 (d, 1 H, J = 5.7 Hz, =CH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.01 (CH_3), 22.56, 23.22, 29.06, 29.27, 29.44, 31.74, 36.95 (CH_2), 51.05 (OCH_3), 111.24 ($C(OCH_3)(CH_2)$), 124.70 (=CH), 153.53 (=CH), 169.94 (C=O); IR (film) ν 1770 (C=O) cm^{-1}; $[\alpha]_D$ = +43.0° (c = 1.1, CH_2Cl_2). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.14; H, 9.66. ^1H NMR spectroscopic data were identical with the reported values for (±)-**11**.[6]

(±)-Cyclobutanone 10. [(Methoxy)(octyl)carbene]pentacarbonylchromium(0) (**9**) (1.37 g, 3.94 mmol) and (±)-*syn*-diphenyl ene–carbamate (694 mg, 2.62 mmol) in CH_2Cl_2 (50 mL) were allowed to react according to the general photoreaction procedure (21 h). Purification via flash chromatography (3/1 hexanes/EtOAc, SiO_2) gave 888 mg (75%) of (±)-**10** as a white solid, mp = 178–179 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 6.3 Hz, CH_3), 1.27 (bs, 11 H, CH_2), 1.55 (m, 1 H, CH_2), 1.72 (m, 1 H, CH_2), 2.05 (m, 1 H, CH_2), 2.45 (dd, 1 H, J = 10.1, 17.9 Hz, CH_2C=O), 2.77 (dd, 1 H, J = 9.4, 18.0 Hz, CH_2C=O), 3.40 (s, 3 H, OCH_3), 4.63 (t, 1 H, J = 7.5 Hz, CHN), 5.03 (d, 1 H, J = 7.5 Hz), 5.89 (d, 1 H, J = 7.4 Hz), 6.82, 6.97, 7.10 (m, 10 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.11 (CH_3), 22.65, 23.07, 29.21, 29.44, 29.51, 30.05, 31.82 (CH_2), 43.68 (CH_2C=O), 47.52 (CHN), 52.69 (OCH_3), 65.98, 80.23, 98.68 ($C(OCH_3)(CH_2)$), 126.11, 126.98, 127.98, 128.26, 128.67 (Ar), 133.43, 134.72 (Ar ipso), 158.24 (carbamate C=O), 205.27 (cyclobutanone C=O); IR (film) ν 1780, 1738 (C=O) cm^{-1}. Anal. Calcd for $C_{28}H_{35}NO_4$: C, 74.80; H, 7.85; N, 3.12. Found: C, 74.60; H, 7.92; N, 3.04.

(±)-Lactone. Cyclobutanone (±)-**10** (660 mg, 1.47 mmol), *m*-CPBA (626 mg, 2.9 mmol), and Li_2CO_3 (33 mg, 0.44 mmol) in

CH_2Cl_2 (40 mL) were subjected to Baeyer–Villiger procedure A (12 h). Purification via flash chromatography (5/1/1 hexanes/Et_2O/CH_2Cl_2, SiO_2) gave 580 mg (85%) of (±)-lactone as a white solid, mp = 124–125 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, 3 H, CH_3), 1.2–1.5 (bs, 12 H, CH_2), 1.80 (m, 1 H, CH_2), 1.94 (d, 1 H, J = 18.2 Hz, CH_2C=O), 2.25 (m, 1 H, CH_2), 2.76 (dd, 1 H, J = 8.0, 18.2 Hz, CH_2C=O), 3.32 (s, 3 H, OCH_3), 4.81 (d, 1 H, J = 7.3 Hz, PhC*H*), 4.88 (d, 1 H, J = 7.4 Hz, CHN), 5.79 (d, 1 H, J = 7.2 Hz, PhC*H*), 6.8–7.1 (m, 10 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.01 (CH_3), 22.16, 22.54, 29.09, 29.21, 29.69, 29.83, 31.73, 32.04 (CH_2), 50.00 (OCH_3), 56.26, 63.01, 80.95 (CH), 112.63 ($C(OCH_3)(CH_2)$), 125.81, 127.89, 128.05, 128.63, 128.95 (Ar), 132.85, 135.32 (Ar ipso), 157.57 (carbamate C=O), 173.91 (lactone C=O); IR (film) ν 1798, 1748 (C=O) cm^{-1}. Anal. Calcd for $C_{28}H_{35}NO_5$: C, 72.23; H, 7.58; N, 3.01. Found: C, 71.98; H, 7.50; N, 2.96.

(±)-Butenolide 11. (±)-Lactone (200 mg, 0.43 mmol) and TBAF (0.52 mL, 1.0 M in THF, 0.52 mmol) in THF (25 mL) were subjected to the butenolide general procedure. Purification via radial chromatography (4/1/1 hexanes/Et_2O/CH_2Cl_2, 1 mm SiO_2) gave 89 mg (92%) of (±)-11 as a colorless oil. Spectroscopic data were identical with reported values.[6]

Chiral Shift Study of (±)-11 and (+)-11. (±)-11 and (+)-11 (14 mg) were separately combined with (+)-Eu(hfc)$_3$ (15 mg, 30 mol %) and $CDCl_3$ (0.7 mL). ^1H NMR analysis of the (±)-11 sample indicated a clean split of the methoxy signals (4.1 ppm). The (+)-11 sample contained only one methoxy signal which indicated an ee ≥ 95% for the butenolide.

Epoxy Lactone (+)-12. The procedure was followed as described by Nozoe and co-workers.[6] The butenolide (+)-11 (58 mg, 0.26 mmol) was taken up in Et_2O (10 mL)/DMF (10 mL), and the resulting mixture was cooled to 0 °C. NaOCl (0.4 mL, 10% aqueous solution) was added to the reaction mixture at 0 °C. The mixture was stirred at 0 °C (1 h). The reaction mixture was partitioned between 5% $Na_2S_2O_{3(aq)}$ and Et_2O. The aqueous layer was extracted with Et_2O twice. The combined Et_2O layers were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave a clear oil which was comprised of butenolide (+)-11 and epoxy lactone (+)-12. Purification via radial chromatography (15/1 hexanes/EtOAc, 1 mm SiO_2) gave (+)-12 and starting butenolide (+)-11. The recovered butenolide was resubjected to the reaction conditions. Upon purification, a total of 19 mg (30% of (+)-12 as a colorless oil was obtained: ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3 H, J = 6.2 Hz, CH_3), 1.25 (bs, 12 H, CH_2), 1.75 (m, 1 H, CH_2), 1.95 (m, 1 H, CH_2), 3.37 (s, 3 H, OCH_3), 3.76 (d, 1 H, J = 2.4 Hz, OCH), 3.92 (d, 1 H, J = 2.4 Hz, OCH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.03 (CH_3), 22.58, 23.14, 29.09, 29.30, 29.41, 30.63, 31.76 (CH_2), 49.79 (OCH), 50.34 (OCH_3), 57.11 (OCH), 108.07 ($C(OCH_3)(CH_2)$), 169.43 (C=O); IR (film) ν 1792 (C=O) cm^{-1}; $[\alpha]_D$ = +111° (c = 0.7, CH_2Cl_2). ^1H NMR spectroscopic data were identical with that reported for (±)-12.[6]

After purification of the epoxy lactone (+)-12, a second set of peaks was noted. These are due to the isomerization of the epoxy lactone (+)-12 to the linear keto ester epoxide. Stirring the epoxy lactone (+)-12 in MeOH for 10 h gave exclusively the open-chain isomer. This material could be transformed into (+)-tetrahydrocerulenin (13) also: ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3 H, CH_3), 1.24 (bs, 12 H, CH_2), 1.57 (m, 2 H, CH_2), 2.58 (ddd, 1 H, J = 6.6, 8.4, 17.9 Hz, CH_2C=O), 2.74 (ddd, 1 H, J = 6.6, 8.4, 17.9 Hz, CH_2C=O), 3.57 (d, 1 H, J = 4.9 Hz, OCH), 3.65 (d, 1 H, J = 4.9 Hz, OC*H*), 3.74 (s, 3 H, OCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.07 (CH_3), 22.62, 22.73, 29.06, 29.10, 29.32, 31.80, 40.39 (CH_2), 52.79, 52.99, 57.98 (OCH_3, OCH), 166.96 (ester C=O), 204.91 (ketone C=O).

(+)-Tetrahydrocerulenin (13). The epoxy lactone (+)-12 (49 mg, 0.2 mmol) was taken up in Et_2O (10 mL) and cooled to 0 °C. $NH_{3(g)}$ was bubbled into the mixture at 0 °C, and the reaction was stirred at that temperature (1.75 h). Concentration under reduced pressure gave 45 mg (≈99%) of (+)-tetrahydrocerulenin (13) as a white solid. Under these reaction conditions, the linear isomer of (+)-13 was predominant. Purification via flash chromatography (5/1 CH_2Cl_2/Et_2O, SiO_2) gave exclusively the linear isomer of (+)-tetrahydrocerulenin (13), mp = 84–85 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3 H, J = 6.6 Hz, CH_3), 1.24 (bs, 12 H, CH_2), 1.57 (bs, 2 H, CH_2), 2.56 (dt, 2 H, J = 7.3, 17.1 Hz, CH_2C=O), 3.71 (d, 1 H, J = 5.3 Hz, OCH), 3.85 (d, 1 H, J = 5.3 Hz, OCH), 5.44 (bs, 1 H, NH), 6.29 (bs, 1 H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.01 (CH_3), 22.55, 23.03, 28.99, 29.16, 31.71, 41.03 (CH_2), 55.27, 58.30 (OCH), 167.52 (amide C=O), 202.79 (ketone C=O); IR (film) ν 3426, 3379 (NH_2), 3165, 2919, 1717 (ketone C=O), 1647 (amide C=O) cm^{-1}; $[\alpha]_D$ = +50.0° (c = 0.45, MeOH after 24 h). Spectroscopic data were identical with reported values.[6-8]

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