Workup and product isolation were as described above to give 90 mg (85%) of **5a** (93% ee).

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Diastereoselectivity in the Reduction of Sterically Unbiased 2,2-Diarylcyclopentanones

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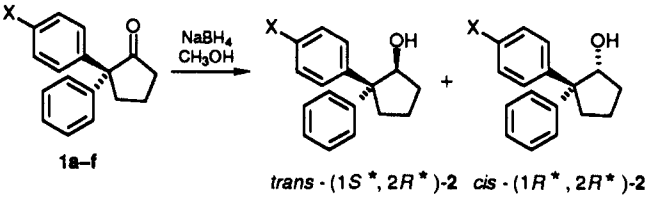
Abstract: Reduction of sterically unbiased 2-phenyl-2-(4-X-phenyl)cyclopentanones **1** (X = NO_2, Br, Cl, OCH_3, OH, NH_2) with either sodium borohydride in methanol or lithium borohydride in tetrahydrofuran at 0 °C produced diastereomeric cyclopentanols **2** in cis/trans ratios varying from 79:21 to 30:70 as determined by ^1H and ^{13}C NMR spectroscopy. These ratios correspond to an overall energy difference of 1.3 kcal/mol. In all cases the hydride was added opposite the more electron rich aromatic ring in support of Cieplak's theory for explaining stereoelectronic control in ketone reductions. A Hammet plot of log (cis/trans) versus the σ para parameter produced a linear relationship with a correlation coefficient of 0.98. An efficient synthesis of the diarylcyclopentanones is described. The diastereomeric alcohols were separable by preparatory thin layer chromatography. The stereochemistry of the products was determined by 2D NOE (NOESY) spectroscopy, ^{13}C NMR chemical shift data, and direct chemical correlation between different products.

The selective formation of one stereoisomer in organic reactions that can produce multiple isomers continues to be a general goal for synthetic chemists.[1] The selectivity in many organic transformations is thought to arise from the interplay of steric interactions, e.g. the addition of a bulky reagent to the least hindered side of a substrate. The control of stereoselective reactions by stereoelectronic effects is invoked less often and is understood much less.[2,3] Due to the paucity of suitable experimental evidence we do not know which reactions are governed by stereoelectronic effects and how strong such effects can be. Isolating stereoelectronic effects by minimizing competing steric factors should provide experimental evidence for the magnitude of stereoelectronic control in asymmetric reactions.[3] Stereoelectronic control in the reduction of ketones has been supported by results obtained with adamantanone[3] and cyclohexanone substrates.[2] As our entry into the study of stereoelectronic control of reactions, we have examined the stereoselective reduction of a functionalized 2,2-diarylcyclopentanone containing an unsubstituted phenyl group and a para-substituted phenyl group. By observing a systematic and predictable change in the selectivity for the reduction of substituted 2,2-diarylcyclopentanones in our initial study, we have found further evidence for the presence of a stereoelectronic effect in reductions of sterically nonbiased ketones and obtained an indication that our cyclopentanone system was more sensitive to stereoelectronic effects than the adamantanone[3] case.

We have chosen to study the stereoselectivity in the reduction of 2,2-diphenylcyclopentanones for several reasons. The electronically variable but sterically similar phenyl groups are located next to the carbonyl bond undergoing reaction rather than several



1a-f *trans*-(1*S**,2*R**)-**2** *cis*-(1*R**,2*R**)-**2**

X = NO_2 (**a**), Cl (**b**), Br (**c**), OCH_3 (**d**), OH (**e**), NH_2 (**f**)

bonds away as in the case of le Noble's adamantanones.[3] Since the two possible donating (or withdrawing) bonds are both carbon–carbon, we avoid the disputed question in the case of Cieplak and Johnson's cyclohexanones of whether C–C or C–H bonds are better donors/acceptors.[2b,4] The geometric equivalence of the competing transition states may be achieved due to the conformational flexibility of the cyclopentanone ring.[5] The transition state for addition of a hydride to the carbonyl in this system can readily adopt a conformation in which the adding hydride is antiperiplanar to a pseudoaxial phenyl group. This reduction of geometric concerns contrasts strongly to earlier studies with substituted cyclohexanones where approach of nucleophiles to the carbonyl is not geometrically equivalent.[2] A final reason for investigating the reduction of diarylcyclopentanones is the ease of synthesizing the needed substrates and the applicability of this synthesis to related substrates needed for the study of stereoelectronic factors in a broader range of stereoselective reactions.

Synthesis of 2,2-Diarylcyclopentanone. The syntheses of the ketone substrates **1** proceed from either a monosubstituted benzophenone or diphenylacetic acid. The synthesis of **1b** (X = Cl)

(1) For a collection of reviews on stereoselective reactions see: Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic: New York, 1984–1985; Vols. 1–5.

(2) (a) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447 and references cited therein. (b) Cieplak, A. S. *Ibid.* **1981**, *103*, 4540.

(3) (a) Cheung, C. K.; Tseng, L. T.; Lin, M.-H.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598. (b) Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *Ibid.* **1988**, *110*, 7882. (c) Srivastava, S.; le Noble, W. J. *Ibid.* **1987**, *109*, 5874.

(4) (a) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. (b) Rozeboom, M. D.; Houk, K. N. *Ibid.* **1982**, *104*, 1189. (c) Mukherjee, D.; Wu, Y.-D.; Fronczek, F. R.; Houk, K. N. *Ibid.* **1988**, *110*, 3328. (d) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Houk, K. N. *Ibid.* **1981**, *103*, 2436. (e) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277.

(5) Buchs, B. *Top. Stereochem.* **1968**, *10*, 1. Legon, A. C. *Chem. Rev.* **1980**, *80*, 231. Lambert, J. B.; Papay, J. J.; Khan, S. A.; Kappauf, K. A.; Magyar, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 6112. Adams, W. J.; Geise, H. J.; Bartell, L. S. *Ibid.* **1970**, *92*, 5013.

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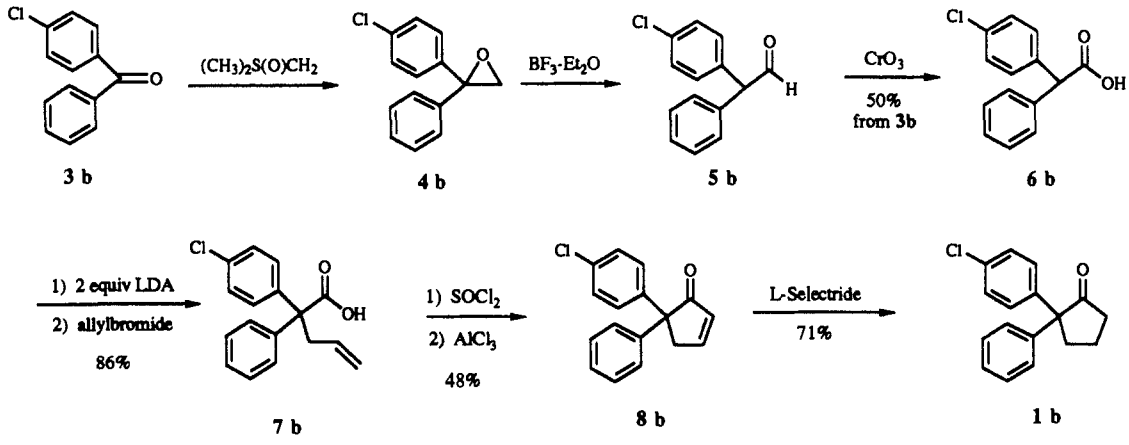
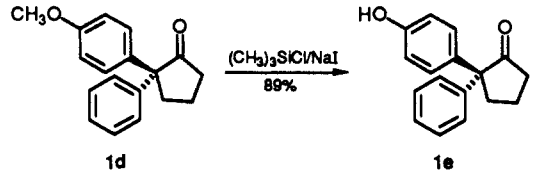
Scheme I



is described here and is quite analogous to the preparation of **1c** (X = Br) and **1e** (X = OCH_3) (Scheme I). Homologation of 4-chlorobenzophenone (**3b**) by the sodium hydride generated ylide of trimethylsulfoxonium iodide following Corey's procedure[6] afforded the mildly unstable epoxide **4b** which was not isolated but was rather immediately converted to the aldehyde **5b** by the action of BF_3 etherate (epoxide opening followed by hydride migration). The aldehyde **5b** could only be isolated with difficulty due to coelution of unreacted benzophenone and was carried forward without purification. Efforts to convert the benzophenone completely to the aldehyde by using an excess of trimethylsulfoxonium iodide were unsuccessful, producing instead dihomologated side-products. Oxidation of the unpurified aldehyde with Jones' reagent produced the acid **6b** in 52% yield from 4-chlorobenzophenone (**3b**).[7] Dianion generation by LDA and alkylation of acid **6b** with allyl bromide yielded the allyl acid **7b** now containing all of the carbons needed for the cyclopentanone product.[8] Except for some unreacted benzophenone, the preceding reactions were quite clean, and generally the synthetic material was carried through from the benzophenone without purification until the allyl acid stage where column chromatography or recrystallization gave allyl acid **7b** in 45% overall yield.

Ring formation by Friedel–Crafts acylation was accomplished by converting the allyl acid **7b** into an acid chloride by treatment with thionyl chloride and then reacting the crude acid chloride with aluminum chloride.[9] The cyclopentenone **8b** could be isolated pure in 39% yield. The desired ketone **1b** (X = Cl) was isolated in 71% yield from the reduction of enone **8b** with L-Selectride.[10] The overall yield for this seven-step sequence on preparative scale including purification of the allyl acid and cyclopentanone compounds was ca. 12% and was similar for the preparation of **1c** and **1d** (X = Br, OCH_3).

The phenol substrate **1e** (X = OH) was produced in 89% yield from the reaction of the methoxyphenyl ketone **1d** (X = OCH_3) with trimethylsilyl chloride/sodium iodide.[11]



Scheme II

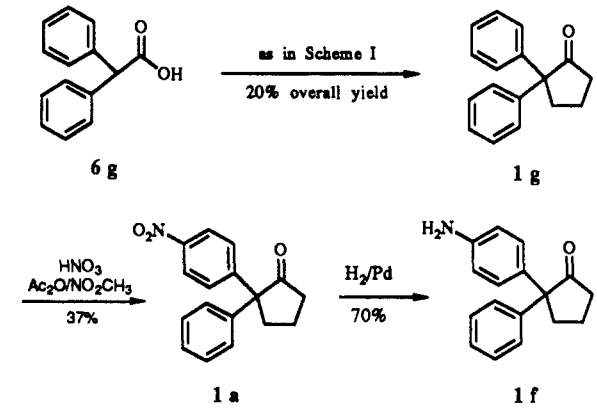


Table I. Ratios of Reduction Products

X	alcohol	σ_p	% trans	% cis	log (cis/trans)
NO_2	**2a**	0.778	21	79	0.575
Cl	**2b**	0.227	37	63	0.231
Br	**2c**	0.232	37	63	0.231
(H)	**2g**	0.0	(50	50)	0.0
OCH_3	**2d**	−0.268	57	43	−0.122
O^-	**2e**	−0.52	70	30	−0.368
NH_2	**2f**	−0.66	64	36	−0.301

Attempted synthesis of the nitro-substituted substrate **1a** according to Scheme I failed due to the inability to alkylate the highly stable dianion of **6a**. The successful alternate route starting from diphenylacetic acid (**6g**) is shown in Scheme II. Conversion of commercially available acid **6g** according to the same sequence described in Scheme I produced the "parent" ketone **1g** (X = H) in 20% overall yield.[12] Statistical nitration of cyclopentanone **1g** gave the desired nitrophenyl ketone **1a** (X = NO_2) in 37% yield (plus recovered **1g**).[13] Reduction of the nitro group by catalytic hydrogenation produced the amine substrate **1f** (X = NH_2) in 90% yield.[14]

Asymmetric Reductions. The six monosubstituted 1,1-diarylcyclopentanone substrates were subjected to reduction by sodium hydride in methanol at 0 °C.[3] The progress of the reactions was followed by thin-layer chromatography and reached completion before the reactions were quenched. The reaction mixtures were worked up by partitioning the reaction mixture between ethyl acetate and water. The aqueous portion was exhaustively extracted to prevent any diastereomeric enhancement. The combined or-

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(7) (a) Eisenbraun, E. J. *Organic Synthesis*; **1973**, *Collect. Vol. V*, 310. (b) Meinwald, J.; Crandall, J.; Hymans, W. E. *Ibid.* **1973**, *Collect. Vol. V*, 866.
(8) Ivanov, D.; Vassilev, G.; Panayotov, I. *Synthesis* **1975**, 83.
(9) Tsuji, J.; Kasuga, K.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 216.
(10) (a) Fortunato, J. M.; Ganem, B. *J. Org. Chem.* **1976**, *41*, 2194. (b) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.
(11) (a) Olah, G. A.; Narang, S. C.; Gupta, B. G.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247. (b) Friedrich, E. C.; DeLucca, G. *Ibid.* **1983**, *48*, 1678. (c) Jung, M. E.; Lyster, M. A. *Ibid.* **1977**, *42*, 3761.
(12) (a) Zimmerman, H. E.; Little, R. D. *J. Am. Chem. Soc.* **1974**, *96*, 4623. (b) Craig, P. N.; Witt, I. H. *Ibid.* **1950**, *72*, 4925. (c) Arnold, R. T.; Searles, S., Jr. *Ibid.* **1949**, *71*, 1150.
(13) (a) Dewar, J. S.; Urch, D. S. *J. Chem. Soc.* **1958**, 3079. (b) Sheehan, M.; Cram, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 3544.
(14) Secrist, J. A., III; Logue, M. W. *J. Org. Chem.* **1972**, *37*, 335.

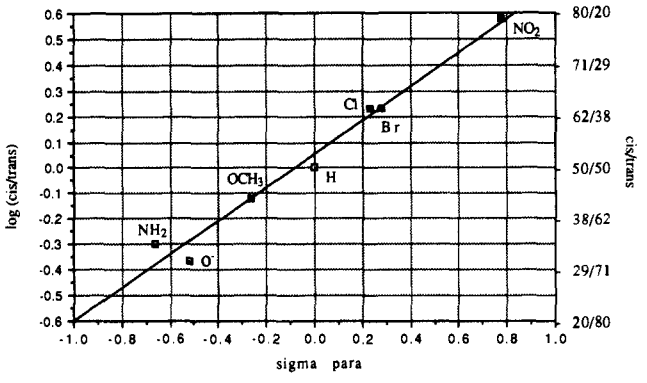


Figure 1. Graph of selectivity vs σ_p values (correlation of 0.98, slope of 0.66).

ganic portion was dried and concentrated to provide a diastereomeric mixture of alcohols. In all cases the ^1H and ^{13}C NMR spectra were recorded of the crude alcohols and the diastereomeric ratios taken from these spectra. The compounds were purified by silica gel column chromatography and fully characterized. The diastereomers could be separated by preparatory thin-layer chromatography.

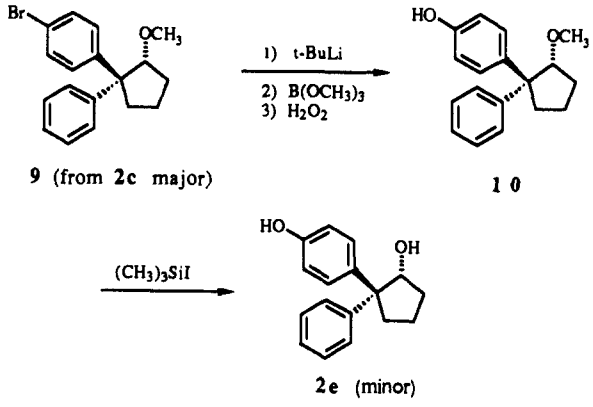
The results of the reductions are summarized in Table I. The ratios in the reduction of these "sterically achiral" carbonyls were as large as 79:21, evidence supporting the existence of a stereoelectronic effect in the reduction. The assignments of stereochemistry are crucial and are discussed below. A graph (Figure 1) of the selectivities (expressed as log(cis/trans)) versus the σ_p values for the substituents (NO_2, Cl, Br, H, OCH_3, O^-, NH_2) can be linearly correlated with a coefficient of 0.98. The value for the nondiastereomeric diphenyl product, necessarily 50/50, has been added to the experimental data set. The use of the deprotonated phenol σ_p value is justified due to the basic conditions of the reaction mixture. This assumption was checked by observing the same ratio of alcohols when the phenol substrate was deprotonated in methanol with excess sodium hydride prior to the addition of the sodium borohydride. The value for the aminophenyl compound **2f** deviates most strongly from the Hammet line, perhaps indicating the effect of metal complexation, reducing the amine's electron donating ability. In support of this notion we observed higher selectivity when the sodium borohydride reduction of ketone **1f** (X = NH_2) was run in the presence of a coordinating cosolvent such as DMPU than in methanol alone.

In all cases the isomer arising from addition of hydride opposite the more electron rich aromatic ring predominated. In order to check for solvent effects, the reductions were repeated with lithium borohydride in tetrahydrofuran.[15] The ratios of isomers produced were essentially the same (≤3% difference) as the sodium borohydride/methanol cases. The isomeric differences obtained in this current study are much larger than those found with the substituted adamantanones,[3] but as in that case, they are consistent with the notion of stereoelectronic control as postulated by Cieplak.[2b]

Structure Determination. The correct assignment of the stereochemistry of the alcohol products is crucial for providing sound evidence for stereoelectronic control and was established by three methods: ^1H NMR NOE studies, ^{13}C NMR chemical shift correlations, and correlation by chemical synthesis. The NOE studies provide the strongest evidence for assignments of the diastereomers. The chemical correlations provide unambiguous comparisons of the results from two different ketones.

For the cyclopentanols **2** where the hydrogen resonances on the substituted and unsubstituted phenyl rings were sufficiently resolved (X = NO_2, OH, OCH_3, NH_2), the 2D ^1H NOE (NOESY)[16] spectra for the major isomers with X = NO_2 and OH and

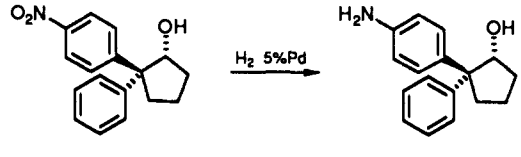
Scheme III



for the minor isomers with X = OCH_3 and NH_2 were recorded. The results of these NOE measurements support the assignments of stereochemistry given in Table I. For example, the tertiary hydrogen in the major isomer of **2a** (X = NO_2) exhibited a strong positive NOE effect with the lower field hydrogens on the substituted ring. Complementary NOE effects with the higher field of hydrogens on the unsubstituted phenyl ring were observed for the cyclopentane hydrogens cis to the hydroxyl group.

In addition to the assignment of stereochemistry by NOE methods, the ^{13}C NMR chemical shifts of all products were used to confirm isomeric assignments. Since the hydroxyl group is γ to the ipso carbons in the aromatic rings, a larger upfield shift of these carbons is expected when the ipso aromatic carbon is cis to the hydroxyl group.[17] In each case, the pattern of chemical shifts supported the assignments in Table I.

In order to correlate positively the relative assignments of various cases, several chemical correlations were performed. The alcohols **2f** (X = NH_2) produced in the sodium borohydride reduction of ketone **1f** (X = NH_2) were compared with those produced by hydrogenating the nitro group in alcohols **2a** (X = NO_2) which were derived from the reduction of ketone **1a** (X = NO_2).[14] The major isomer from hydrogenation of **2a** correlated with the minor alcohol of **2f** produced by sodium borohydride reduction of **1f**—establishing preferential approach of the hydride to opposite faces of the carbonyl in the nitro- and amino-substituted ketones.



2a(major from **1a** reduction) **2f**(minor from **1f** reduction)

The major isomer of the methyl ether **9** of the alcohol **2c** derived from reduction of ketone **1c** (X = Br) was converted by metalation/oxidation[18] to phenol **10** which upon demethylation[11] produced alcohol **2e** (X = OH) (Scheme III). The spectra of this phenol were identical with the minor isomer of the alcohol **2e** (X = OH) produced by direct reduction of ketone **1e** (X = OH). This transformation established the opposite facial preference of the phenol **1e** (X = OH) and bromo **1c** (X = Br) substrates. In order to rule out any stereochemical reversal, the major isomer of the methyl ether **9** (X = Br) was not only converted to the phenol but a portion was demethylated[11] to reform isomerically pure alcohol **2b** (X = Br) which was spectroscopically identical with the original major isomer.

(15) Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, *35*, 567.
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(17) Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic: New York, 1972; pp 404ff.
(18) Hoffmann, R. W.; Ditrich, K. *Synthesis* **1983**, 107. (b) Kidwell, R. L.; Murphy, M.; Darling, S. D. *Organic Synthesis* **1973**, *Collect. Vol. V*, 918. (c) Hawthorne, M. F. *J. Org. Chem.* **1957**, *22*, 1001. (d) Okada, K.; Tomita, S.; Oda, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 459.

Finally, the major alcohol derived from reduction of **1e** (X = OH) was monomethylated at the phenolic hydroxyl group to form a material identical with the major product of the reduction of **1d** (X = OCH_3). This correlation established the identical facial preference in the ketone reduction of the phenol **1e** and methoxyphenyl **1d** substrates. The chemical correlations described above, coupled with the results of the NOE and ^{13}C NMR chemical shift studies, provide strong evidence for the stereochemical assignments made in Table I.

Conclusion. The diastereoselective reduction of the sterically unbiased 2,2-diarylcyclopentanones described here provides strong evidence for the involvement of stereoelectronic control in carbonyl reductions as postulated by Cieplak. The levels of diastereoselectivity observed here surpass those previously observed and account for an overall energy difference of 1.3 kcal/mol. The combined use of NOE, ^{13}C NMR, and chemical correlation data enable confident assignments of stereochemistry. The diarylcyclopentane substrate has been established as a good framework for the study of stereoelectronic reactions and is currently being used in our laboratory to investigate additional stereoselective reactions of interest to synthetic chemists.

Experimental Section

General Methods. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. THF and ether were distilled from sodium benzophenone ketyl. Other reaction and chromatographic solvents were purified and/or dried by standard methods.

^1H NMR (1D and 2D) and ^{13}C NMR spectra were recorded on a Varian XL-400 instrument. Data are reported as follows: chemical shifts (δ scale) in parts per million (ppm) relative to residual solvent peaks (multiplicity, coupling constants in hertz, number of hydrogens). For ^1H NMR spectra, the peak due to residual $CHCl_3$ is listed at 7.24 ppm, and for ^{13}C NMR spectra, the central peak of the $CDCl_3$ triplet is assigned a chemical shift of 77.0 ppm. Unless otherwise noted, multiplicities and compound ratios are deduced from the electronic integration by the XL-400. Infrared spectra were obtained on the Perkin-Elmer Model 681 spectrometer and were referenced to polystyrene (1601 cm^{-1}). Only characteristic and/or strong signals are reported. Low-resolution mass spectra (reported as m/z (relative intensity at 70 eV) and high-resolution mass spectra (obtained by peak matching) were recorded on a Finnegan MAT-90 instrument. Melting points were determined in open Pyrex capillary tubes with a Thomas-Hoover Unimelt apparatus and are uncorrected.

Preparative column chromatography was performed on flash silica gel (E. Merck Reagents silica gel 60, 230–400 mesh ASTM). Preparative thin-layer chromatography was accomplished with 500 μm E. Merck silica gel 60 F-254.

2-(4-Nitrophenyl)-2-phenylcyclopentanone (1a). To a solution of ketone **1g** (1.51 g, 6.40 mmol) in acetic anhydride (15 mL) and nitromethane (15 mL) was added a solution of fuming nitric acid (0.34 mL, 7.97 mmol) in acetic anhydride (5 mL) and nitromethane (5 mL). After being stirred at 50 °C for 48 h and at 23 °C for an additional 48 h, the mixture was poured into an ice and water bath and then partioned between CH_2Cl_2 and water. The organic portion was dried over Na_2SO_4 and concentrated. Purification via column chromatography (SiO_2, 4:1 petroleum ether–ethyl acetate) gave **1a** as a yellow oil in 37% yield. ^1H NMR (400 MHz, $CDCl_3$) 8.04 (d, J = 8.98 Hz, 2 H), 7.39–7.17 (m, 7 H), 2.80 (m, 1 H), 2.58 (m, 1 H), 2.46–2.34 (m, 2 H), 1.98–1.85 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 216.25, 150.33, 140.13, 129.10, 128.98, 128.87, 127.69, 127.46, 123.29, 62.40, 38.05, 37.75, 18.76; IR (film) 2960, 1740, 1595, 1515, 1345 cm^{-1}; MS (EI 70 eV) m/z 281 (M^+, 98), 237 (41), 225 (100), 178 (99.7), 165 (64); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{15}NO_3$ 281.1052, obsd 281.1046.

2-(4-Chlorophenyl)-2-phenylcyclopentanone (1b). General Enone Reduction. To a −78 °C solution of enone **8b** (1.00 g, 3.72 mmol) in THF (12.4 mL) was added 1.0 M L-Selectride (3.80 mL, 3.80 mmol). After the solution was stirred under nitrogen at −78 °C for 0.5 h, 10% NaOH (7 mL) was added to the reaction mixture and it was allowed to warm to 0 °C. H_2O_2 (30%, 5 mL) was added and the mixture was stirred for 16 h. The solution was extracted with ether. The organic portion was washed and saturated $NaHSO_3$ and brine, dried over sodium sulfate, and concentrated. Purification via column chromatography (SiO_2, 8:2 petroleum ether–ether) gave a 71% yield of **1b** as an orange oil. ^1H NMR (400 MHz, $CDCl_3$) 7.41–7.14 (m, 9 H), 2.77–2.61 (m, 2 H), 2.55–2.43 (m, 2 H), 1.98–1.90 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 217.03, 141.39, 140.76, 132.45, 129.33, 128.38, 128.24, 127.67, 126.81, 61.74, 37.93, 37.82, 18.63; IR (film) 2960, 1735, 1595, 1490, 825, 755, 698 cm^{-1}; MS (EI 70 eV) m/z 272 (M^+ + 2, 19), 270 (M^+, 64), 216 (32), 214 (100), 207 (27), 179 (66); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{15}ClO$ 270.0812, obsd 270.0813.

2-(4-Bromophenyl)-2-phenylcyclopentanone (1c). Following the general enone reduction with **8c** (1.40 mmol, 0.440 g) followed by chromatography (SiO_2, 8:2 petroleum ether–ether) gave a 96% yield of **1c** as a pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.38–7.03 (m, 9 H), 2.71–2.56 (m, 2 H), 2.43–2.38 (m, 2 H), 1.93–1.86 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 217.21, 141.39, 141.36, 131.36, 129.79, 128.53, 127.80, 126.98, 120.86, 61.98, 38.09, 37.92, 18.75; IR (film) 2960, 1735, 1595, 1485, 820, 750, 700 cm^{-1}; MS (EI 70 eV) m/z 316 (M^+ + 2, 57), 314 (M^+, 58), 261 (27), 259 (27), 236 (20), 207 (86), 179 (100), 165 (42); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{15}BrO$ 314.0364, obsd 314.0300.

2-(4-Methoxyphenyl)-2-phenylcyclopentanone (1d). Following the general enone reduction with **8d** (2.73 mmol, 0.721 g) followed by chromatography (SiO_2, 8:2 petroleum ether–ether) gave a 73% yield of **1d** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.30–7.13 (m, 7 H), 6.83 (d, J = 8.79 Hz, 2 H), 3.77 (s, 3 H), 2.71–2.65 (m, 2 H), 2.44 (t, J = 7.56 Hz, 2 H), 1.94–1.90 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 218.06, 158.29, 142.66, 133.58, 129.12, 128.30, 127.92, 126.62, 113.74, 61.84, 55.16, 38.22, 38.07, 18.78; IR (film) 2960, 1735, 1605, 1510, 1250 cm^{-1}; MS (EI 70 eV) m/z 266 (M^+, 28), 238 (11), 210 (100), 195 (18), 165 (12); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{18}H_{18}O_2$ 266.1307, obsd 266.1312.

2-(4-Hydroxyphenyl)-2-phenylcyclopentanone (1e). To a solution of sodium iodide (0.412 g, 2.75 mmol) and ketone **1d** (0.334 g, 1.25 mmol) in CH_3CN (2.5 mL) was added chlorotrimethylsilane (0.35 mL, 2.75 mmol) at 23 °C. After heating under reflux for 16 h the reaction was quenched with water and extracted with ether. The organic layer was washed with saturated NaS_2O_3 and brine, dried over Na_2SO_4, and evaporated. Column chromatography (SiO_2, 1:1 petroleum ether–ether) gave an 89% yield of **1e** as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) 7.31–7.19 (m, 5 H), 7.08 (d, J = 8.74 Hz, 2 H), 6.77 (d, J = 8.60 Hz, 2 H), 2.73–2.63 (m, 2 H), 2.48–2.44 (m, 2 H), 1.96–1.89 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 218.96, 154.50, 142.48, 133.40, 129.29, 128.32, 127.90, 126.66, 115.28, 61.96, 38.24, 38.13, 18.74; IR (film) 3400, 2980, 1730, 1617, 1520 cm^{-1}; MS (EI 70 eV) m/z 252 (M^+, 26), 196 (100), 181 (32); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{16}O_2$ 252.1150, obsd 252.1142.

2-(4-Aminophenyl)-2-phenylcyclopentanone (1f). A solution of ketone **1a** (0.243 g, 0.864 mmol), 5% palladium on carbon (0.10 g), absolute ethanol (40 mL), and chloroform (2 mL) was agitated under 40 psi of hydrogen for 16 h. The Pd/C was removed by filtration and 10% NaOH (10 mL) was added to the filtrate. After extracting with CH_2Cl_2, the organic portion was dried over Na_2SO_4 and concentrated to give ketone **1f** in 90% crude yield as a brown oil. ^1H NMR (400 MHz, $CDCl_3$) 7.33–7.20 (m, 5 H), 7.06 (d, J = 8.55 Hz, 2 H), 6.66 (d, J = 8.55 Hz, 2 H), 3.67 (br s, 2 H), 2.78–2.59 (m, 2 H), 2.48–2.44 (m, 2 H), 1.99–1.91 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 218.33, 145.15, 143.15, 130.86, 128.99, 128.20, 127.99, 126.47, 115.04, 61.86, 38.23, 38.06, 18.77; IR (film) 3460, 3370, 2970, 1740, 1625, 1520 cm^{-1}; MS (EI 70 eV) m/z 251 (M^+, 44), 223 (20), 195 (100), 180 (27); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{17}NO$ 251.1310, obsd 251.1306.

2,2-Diphenylcyclopentanone (1g). Following the general enone reduction with **8g** (6.83 mmol, 1.60 g) followed by chromatography (SiO_2, 7:3 petroleum ether–ether) gave a 71% yield of **1g** as white crystals, mp 87–88 °C. ^1H NMR (400 MHz, $CDCl_3$) 7.41–7.31 (m, 10 H), 2.82 (t, J = 6.60 Hz, 2 H), 2.57–2.53 (m, 2 H), 2.04 (quintuplet, J = 7.08 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 217.79, 142.17, 128.42, 128.07, 126.79, 62.52, 38.26, 38.18, 18.89; IR (KBr pellet) 2970, 1740, 1600, 1495, 1445 cm^{-1}; MS (EI 70 eV) m/z 236 (M^+, 60), 180 (100), 165 (41); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{16}O$ 236.1201, obsd 236.1201.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Chlorophenyl)-2-phenylcyclopentanol (2b). General Ketone Reduction.** To a solution of sodium borohydride (0.279 g, 7.39 mmol) in CH_3OH (17 mL) at 0 °C was added ketone **1b** (0.500 g, 1.85 mmol) dissolved in CH_3OH (20 mL). The reaction mixture was stirred at 0 °C for 45 min under a nitrogen atmosphere and then quenched at 0 °C with water. The solution was partitioned between saturated aqueous ammonium chloride solution and ethyl acetate and repeatedly extracted with additional ethyl acetate. The combined organic portion was dried over magnesium sulfate and concentrated to give a quantitative crude alcohol **2b** as a pale yellow oil, which appeared clean by ^1H NMR. The diastereomers were separated via preparative TLC (SiO_2, 5 developments with 8:2 petroleum ether–ether). The major–minor ratio equals 37:63 by ^1H NMR in C_6D_6. ^1H NMR (400 MHz, $CDCl_3$) minor (higher rf) 7.31–7.20 (m, 9 H), 4.87 (m, 1 H), 2.64 (m, 1 H), 2.32 (m, 1 H), 2.13 (m, 1 H), 1.93 (m, 1 H), 1.73–1.60 (m, 2 H), 1.24 (br s, 1 H); ^1H NMR (400 MHz, $CDCl_3$)

major (lower rf) 7.36–7.21 (m, 9 H), 4.83 (m, 1 H), 2.68 (m, 1 H), 2.27 (m, 1 H), 2.11 (m, 1 H), 1.95 (m, 1 H), 1.75–1.60 (m, 2 H), 1.30 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 146.47, 142.92, 132.20, 129.94, 128.53, 128.33, 126.87, 126.12, 77.56, 59.20, 34.73, 31.89, 19.22; ^{13}C NMR (100 MHz, $CDCl_3$) major 145.61, 143.64, 131.67, 128.63, 128.41, 128.31, 126.58, 77.50, 59.18, 34.67, 31.64, 19.78; IR (film) 3430, 3050, 2960, 1493, 1093, 1012 cm^{-1}; MS (EI 70 eV) m/z 274 (M^+ + 2, 12), 272 (M^+, 37), 203 (33), 201 (100), 165 (17); HRMS (EI, 70 eV) m/z (M^+) calcd for $C_{17}H_{17}ClO$ 272.0968, obsd 272.0968.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Nitrophenyl)-2-phenylcyclopentanol (2a).** Following the general reduction with **1a** (1.26 mmol, 0.355 g) for 30 min gave an 80% crude yield of **2a** as a yellow/orange oil. Diastereomers separated via preparative TLC (SiO_2, 5 developments with 8:2 petroleum ether–ethyl acetate). The major–minor ratio equals 79:21 by cut and weigh integration of the ^{1}H NMR spectrum obtained in $CDCl_3$. ^{1}H NMR (400 MHz, $CDCl_3$) minor (lower rf) 8.15 (d, J = 8.74 Hz, 2 H), 7.49 (d, J = 8.93 Hz, 2 H), 7.32–7.20 (m, 5 H), 4.94 (m, 1 H), 2.66 (m, 1 H), 2.42 (m, 1 H), 2.16 (m, 1 H), 1.97 (m, 1 H), 1.74–1.64 (m, 2 H), 1.26 (m, 1 H); ^{1}H NMR (400 MHz, $CDCl_3$) major (higher rf) 8.14 (d, J = 8.79 Hz, 2 H), 7.51 (d, J = 8.98 Hz, 2 H), 7.47–7.23 (m, 5 H), 4.85 (m, 1 H), 2.75 (m, 1 H), 2.25 (m, 1 H), 2.12 (m, 1 H), 1.98 (m, 1 H), 1.73–1.62 (m, 2 H), 1.33 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 152.58, 145.37, 135.16, 129.47, 128.61, 126.82, 126.58, 123.40, 77.82, 59.91, 34.54, 32.29, 19.76; ^{13}C NMR (100 MHz, $CDCl_3$) major 155.05, 142.37, 133.51, 128.80, 128.52, 128.06, 127.03, 123.46, 77.23, 59.43, 34.87, 31.64, 19.49; IR (film) 3460, 3000, 1608, 1530, 1360 cm^{-1}; MS (EI 70 eV) m/z 283 (M^+, 95), 266 (75), 222 (82), 192 (100), 165 (85); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{17}NO_3$ 283.1208, obsd 283.1195.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Bromophenyl)-2-phenylcyclopentanol (2c).** Following the general reduction with **1c** (2.00 mmol, 0.63 g) for 30 min gave a 92% crude yield of **2c** as a yellow oil. Diastereomers separated via preparative TLC (SiO_2, 5 developments with 8:2 petroleum ether–ether). The major–minor ratio equals 63:37 by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) minor (higher rf) 7.46–7.15 (m, 9 H), 4.85 (m, 1 H), 2.62 (m, 1 H), 2.30 (m, 1 H), 2.13 (m, 1 H), 1.91 (m, 1 H), 1.73–1.60 (m, 2 H), 1.22 (br s, 1 H); ^{1}H NMR (400 MHz, $CDCl_3$) major (lower rf) 7.41–7.19 (m, 9 H), 4.81 (m, 1 H), 2.67 (m, 1 H), 2.25 (m, 1 H), 2.08 (m, 1 H), 1.94 (m, 1 H), 1.74–1.57 (m, 2 H), 1.27 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 146.39, 143.46, 131.49, 130.34, 128.34, 126.87, 126.14, 120.37, 77.54, 57.06, 34.68, 31.90, 19.81; ^{13}C NMR (100 MHz, $CDCl_3$) major 146.17, 143.56, 131.28, 128.86, 128.67, 128.42, 126.63, 119.83, 77.47, 59.27, 34.65, 31.67, 19.80; IR (film) 3485, 2970, 1640, 1495, 1015, 823, 764, 705 cm^{-1}; MS (EI 70 eV) m/z 318 (M^+ + 2, 45), 316 (M^+, 47), 247 (100), 245 (99), 192 (20), 165 (29); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{17}BrO$ 316.0463, obsd 316.0463.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Methoxyphenyl)-2-phenylcyclopentanol (2d).** Following the general reduction with **1d** (0.378 mmol, 0.100 g) for 1 h gave a quantitative crude yield of **2d** as a yellow oil. Diastereomers separated via preparative TLC (SiO_2, 4 developments with 9:1 petroleum ether–ethyl acetate). The major–minor ratio equals 57:43 by ^{1}H NMR and ^{13}C NMR gated decoupling experiment. ^{1}H NMR (400 MHz, $CDCl_3$) major (lower rf) 7.31–7.13 (m, 7 H), 6.84 (d, J = 8.17 Hz, 2 H), 4.82 (m, 1 H), 3.77 (s, 3 H), 2.62 (m, 1 H), 2.26 (m, 1 H), 2.09 (m, 1 H), 1.90 (m, 1 H), 1.72–1.57 (m, 2 H), 1.27 (br s, 1 H); ^{1}H NMR (400 MHz, $CDCl_3$) minor (higher rf) 7.33–7.17 (m, 7 H), 6.80 (d, J = 8.11 Hz, 2 H), 4.84 (m, 1 H), 3.77 (s, 3 H), 2.63 (m, 1 H), 2.29 (m, 1 H), 2.08 (m, 1 H), 1.85 (m, 1 H), 1.75–1.56 (m, 2 H), 1.29 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) major 157.95, 147.33, 136.21, 129.57, 128.19, 126.94, 125.83, 113.88, 77.54, 58.97, 55.19, 34.99, 31.80, 19.97; ^{13}C NMR (100 MHz, $CDCl_3$) minor: 157.53, 144.62, 138.98, 128.57, 128.36, 127.92, 126.29, 113.52, 77.83, 59.21, 55.15, 34.59, 31.69, 20.06; IR (film) 3440, 2960, 1613, 1515, 1460, 1254 cm^{-1}; MS (EI 70 eV) m/z 269 (M^+, 23), 268 (23), 223 (44), 198 (100); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{18}H_{20}O_2$ 268.1463, obsd 268.1462.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Hydroxyphenyl)-2-phenylcyclopentanol (2e).** Following the general reduction with **1e** (0.464 mmol, 0.117 g) for 30 min gave a quantitative crude yield of **2e** as a colorless oil. Diastereomers separated via preparative TLC (SiO_2, 3 developments with 1:1 petroleum ether–ether). The major–minor ratio equals 70:30 by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) minor (lower rf) 7.38–7.31 (m, 4 H), 7.26–7.18 (m, 3 H), 6.81 (d, J = 8.55 Hz, 2 H), 5.62 (s, 1 H), 4.91 (m, 1 H), 2.68 (m, 1 H), 2.34 (m, 1 H), 2.17 (m, 1 H), 1.97 (m, 1 H), 1.79 (m, 1 H), 1.65 (m, 1 H); ^{1}H NMR (400 MHz, $CDCl_3$) major (higher rf) 7.40–7.34 (m, 4 H), 7.28–7.21 (m, 3 H), 6.78 (d, J = 8.11 Hz, 2 H), 5.78 (s, 1 H), 4.91 (m, 1 H), 2.68 (m, 1 H), 2.36 (m, 1 H), 2.15 (m, 1 H), 1.97 (m, 1 H), 1.79 (m, 1 H), 1.67 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 153.72, 144.44, 138.69, 128.60, 128.32, 128.03, 126.35, 115.03, 77.96, 59.17, 34.56, 31.53, 20.00; ^{13}C NMR (100 MHz, $CDCl_3$) major 154.16, 147.09, 136.00, 129.71, 128.17, 126.86, 125.85, 115.41, 77.64, 59.01, 34.94, 31.67, 19.56; IR (KBr pellet) 3600, 2970, 1600, 1515, 1450, 1250 cm^{-1}; MS (EI 70 eV) m/z 254 (M^+, 25), 209 (7.3), 183 (100), 165 (6.2); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{18}O_2$ 254.1307, obsd 254.1305.

(1*R,2*R**)- and (1*S**,2*R**)-2-(4-Aminophenyl)-2-phenylcyclopentanol (2f).** Following the general reduction with **1f** (0.80 mmol, 0.200 g) in 2:1 methanol–DMPU solution for 1 h gave a 64% crude yield of **2f** as a brown oil. Diastereomers separated via preparative TLC (SiO_2, 2 developments with 1:1 petroleum ether–ethyl acetate). The major–minor ratio equals 64:36 by ^{1}H NMR and ^{13}C NMR gated decoupling. ^{1}H NMR (400 MHz, $CDCl_3$) minor (higher rf) 7.25–7.00 (m, 7 H), 6.53 (d, J = 8.30 Hz, 2 H), 4.76 (m, 1 H), 2.55 (m, 1 H), 2.24 (m, 1 H), 2.04 (m, 1 H), 1.85 (m, 1 H), 1.69–1.53 (m, 2 H); ^{1}H NMR (400 MHz, $CDCl_3$) major (lower rf) 7.30–7.01 (m, 7 H), 6.60 (d, J = 8.57 Hz, 2 H), 4.75 (t, J = 5.13 Hz, 1 H), 2.57 (m, 1 H), 2.19 (m, 1 H), 2.05 (m, 1 H), 1.85 (m, 1 H), 1.66 (m, 1 H), 1.53 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 144.91, 143.86, 137.62, 128.46, 128.31, 127.72, 126.12, 115.07, 77.83, 59.18, 34.42, 31.66, 20.08; ^{13}C NMR (100 MHz, $CDCl_3$) major 147.52, 144.29, 134.13, 129.41, 128.05, 126.90, 125.65, 115.34, 77.40, 58.88, 34.90, 31.68, 19.93; IR (KBr pellet) 3290, 2965, 1615, 1520, 1265 cm^{-1}; MS (EI 70 eV) m/z 253 (M^+, 48), 209 (7.1), 208 (19), 182 (100); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{17}H_{19}NO$ 253.1467, obsd 253.1466.

2-(4-Chlorophenyl)-2-phenylethanal (5b). General Homologation Procedure. A slurry of sodium hydride (5.00 g, 125 mmol) and trimethylsulfoxonium iodide (27.5 g, 125 mmol) in THF (50 mL) was stirred at 55 °C for 6 h. To this 55 °C solution was added 4-chlorobenzophenone (**3b**) (21.7 g, 100 mmol) in THF (50 mL). After being stirred at 55 °C for 16 h, the reaction mixture was quenched with water and extracted with ether and water. The organic layer was dried over sodium sulfate and concentrated to yield crude epoxide **4b**. A solution of this crude epoxide in benzene (160 mL) was shaken with boron trifluoride etherate (15.3 mL, 121 mmol) in a separatory funnel for 2 min and allowed to stand for 3 min. The mixture was extracted twice with 125 mL of saturated aqueous sodium bicarbonate. The organic layer was dried over Na_2SO_4 and concentrated to yield crude aldehyde **5b** as an orange oil in 93%. ^{1}H NMR (400 MHz, $CDCl_3$) 9.93 (s, 1 H), 7.50–7.10 (m, 9 H), 4.89 (s, 1 H).

2-(4-Bromophenyl)-2-phenylethanal (5c). Following the general homologation procedure with 4-bromobenzophenone (**3c**) (100 mmol, 26.11 g) yielded crude aldehyde **5c** as an orange oil in quantitative crude yield. ^{1}H NMR (400 MHz, $CDCl_3$) 9.99 (s, 1 H), 7.58–7.14 (m, 9 H), 4.93 (s, 1 H).

2-(4-Methoxyphenyl)-2-phenylethanal (5d). Following the general homologation procedure with 4-methoxybenzophenone (**3d**) (100 mmol, 21.33 g) yielded crude aldehyde **5d** as a yellow oil in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) 10.43 (s, 1 H), 7.91–7.42 (m, 9 H), 5.36 (s, 1 H), 4.31 (s, 3 H).

2-(4-Chlorophenyl)-2-phenylethanoic Acid (6b). General Oxidation Procedure. To a −10 °C solution of aldehyde **5b** (17.1 g, 74.2 mmol) in acetone (300 mL) was added dropwise Jones' reagent (2.98 M, 12.5 mL, 37.1 mmol). Isopropyl alcohol was then added dropwise until the solution turned bright green. The chromium salts were removed by filtration through Cellite. The filtrate was concentrated and dissolved in 1:1 petroleum ether–ether solvent and made basic and extracted with more petroleum ether–ether. The aqueous layer was acidified and extracted with ethyl acetate. The combined organic layer was dried over sodium sulfate and evaporated to give pure acid **6b** as white crystals in 52% overall yield from starting 4-chlorobenzophenone, mp 115–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) 7.37–7.27 (m, 9 H), 5.03 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) 178.81, 137.31, 136.25, 133.47, 130.02, 128.77, 128.48, 127.70, 56.29; IR (KBr pellet) 2960, 1700, 1610, 1495, 1420, 1310 cm^{-1}; MS (EI 70 eV) m/z 248 (M^+ + 2, 1.7), 246 (M^+, 17), 203 (37), 201 (100), 166 (42), 165 (84).

2-(4-Bromophenyl)-2-phenylethanoic Acid (6c). Following the general oxidation procedure with aldehyde **5c** (89.0 mmol, 24.50 g) gave acid **6c** as white crystals in 53% overall yield from 4-bromobenzophenone, mp 110–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) 7.47 (d, J = 8.53 Hz, 2 H), 7.46–7.27 (m, 5 H), 7.22 (d, J = 8.39 Hz, 2 H), 5.02 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) 178.45, 137.24, 136.80, 131.73, 130.37, 128.78, 128.48, 127.72, 56.33; IR (KBr pellet) 3000, 1720, 1500, 1235 cm^{-1}; MS (EI 70 eV) m/z 292 (M^+ + 2, 20), 290 (M^+, 21), 247 (93), 245 (96), 165 (100).

2-(4-Methoxyphenyl)-2-phenylethanoic Acid (6d). Following the general oxidation procedure with aldehyde **5d** (100 mmol, 22.63 g) gave acid **6d** as pale brown crystals in 46% overall yield from 4-methoxybenzophenone, mp 98–99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) 7.33–7.24 (m, 7 H), 6.87 (d, J = 8.60 Hz, 2 H), 5.01 (s, 1 H), 3.79 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 179.11, 158.87, 138.21, 129.99, 129.77,

128.63, 128.53, 127.40, 114.03, 56.18, 55.23; IR (KBr pellet) 2900, 1690, 1603, 1500, 1245 cm^{-1}; MS (EI 70 eV) m/z 242 (M^+, 20), 197 (100), 153 (22).

2-(4-Chlorophenyl)-2-phenyl-4-pentenoic Acid (7b). General Alkylation Procedure. To a solution of diisopropylamine (17.0 mL, 121.6 mmol) in THF (50 mL) under nitrogen at −10 °C was added *n*-butyllithium (2.45 M in hexane, 22.0 mL, 111.5 mmol). After being stirred at −10 °C for 10 min, a solution of acid **6b** (12.5 g, 50.7 mmol) in THF (50 mL) was then added. The mixture was warmed to 23 °C and stirred for 1 h and then cooled to 0 °C. Allyl bromide (8.77 mL, 101.3 mmol) was added and the mixture was warmed to 23 °C and stirred for 16 h. The reaction was quenched with saturated ammonium chloride, acidified with 2 N HCl, and extracted with ether. The organic portion was washed with saturated ammonium chloride, dried over Na_2SO_4, and concentrated. Recrystallization from boiling hexane, with a small quantity of ether gave an 86% yield of pure allyl acid **7b** as white crystals, mp 110–111 °C. ^1H NMR (400 MHz, $CDCl_3$) 7.28–7.17 (m, 9 H), 5.55 (m, 1 H), 4.94–4.87 (m, 2 H), 3.15–3.04 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 180.39, 141.48, 140.47, 133.39, 132.92, 130.56, 128.82, 128.05, 127.94, 127.26, 118.88, 59.83, 42.35; IR (KBr pellet) 3000, 1695, 1495, 1263 cm^{-1}; MS (EI 70 eV) m/z 287 (M^+, 8.3), 247 (32), 245 (100), 203 (15), 201 (40), 165 (38).

2-(4-Bromophenyl)-2-phenyl-4-pentenoic Acid (7c). Following the general alkylation procedure with acid **6c** (48.63 mmol, 13.38 g) gave **7c** as pale yellow crystals in quantitative crude yield, mp 114–115 °C. ^1H NMR (400 MHz, $CDCl_3$) 7.45–7.16 (m, 9 H), 5.57 (m, 1 H), 4.97–4.93 (m, 2 H), 3.21–3.08 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 179.34, 141.56, 141.20, 133.49, 130.99, 130.88, 128.86, 128.04, 127.24, 121.11, 118.86, 59.92, 42.34; IR (film) 2910, 1700, 1490, 1250 cm^{-1}; MS (EI 70 eV) m/z 332 (M^+ + 2, 1.3), 330 (M^+, 1.3), 291 (99), 289 (100), 210 (21).

2-(4-Methoxyphenyl)-2-phenyl-4-pentenoic Acid (7d). Following the general alkylation procedure with acid **6d** (35.72 mmol, 8.65 g) gave **7d** as pale yellow crystals in quantitative yield, mp 91.5 °C. ^1H NMR (400 MHz, $CDCl_3$) 7.32–7.23 (m, 7 H), 6.43 (d, J = 8.86 Hz, 2 H), 5.59 (m, 1 H), 4.96–4.92 (m, 2 H), 3.81 (s, 3 H), 3.17–3.09 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 180.48, 158.41, 142.20, 133.95, 133.82, 130.21, 128.96, 127.81, 126.92, 118.39, 113.20, 59.48, 55.16, 42.51; IR (KBr pellet) 2960, 1695, 1610, 1515, 1250 cm^{-1}; MS (EI 70 eV) m/z 282 (M^+, 4.3), 241 (100), 195 (54).

2,2-Diphenyl-4-pentenoic Acid (7g). Following the general alkylation procedure with acid **6g** (100 mmol, 21.22 g) and recrystallization from boiling hexane gave **7g** in 100% yield as white crystals, mp 139 °C (lit.[12c] mp 141.5–141.9 °C). ^1H NMR (400 MHz, $CDCl_3$) 7.29–7.20 (m, 10 H), 5.34 (m, 1 H), 4.91–4.83 (m, 2 H), 3.12 (d, J = 6.80 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 180.33, 141.94, 133.88, 129.09, 127.88, 127.04, 118.48, 60.20, 42.45; IR (KBr pellet) 3000, 1700, 1626, 1500, 1360 cm^{-1}; MS (EI 70 eV) m/z 252 (M^+, 2.3), 211 (35), 165 (27), 102 (82), 86 (100), 44 (91).

2-(4-Chlorophenyl)-2-phenylcyclopent-4-enone (8b). General Enone Synthesis. To allyl acid **7b** (4.00 g, 14.0 mmol) in CH_2Cl_2 (28 mL) was added thionyl chloride (5.10 mL, 69.8 mmol) at 23 °C. After the mixture was stirred at this temperature for 16 h, the excess solvent was evaporated to yield a crude acid chloride. To a 0 °C solution of aluminum chloride (2.94 g, 22.0 mmol) in CH_2Cl_2 (25 mL) was added the crude acid chloride (4.48 g, 14.7 mmol) in CH_2Cl_2 (25 mL). After being stirred at 0 °C for 0.5 h, the reaction mixture was poured into 100 mL of ice and water. The solution was extracted with ether, and the organic layer was backwashed with cold saturated sodium bicarbonate and brine. The organic portion was dried over Na_2SO_4 and concentrated. Purification by column chromatography (SiO_2, CH_2Cl_2) gave a 39% yield of enone **8b** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.85 (m, 1 H), 7.36–7.14 (m, 9 H), 6.27 (m, 1 H), 3.49–3.41 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 208.30, 162.29, 142.73, 141.61, 132.70, 129.38, 128.53, 127.78, 126.93, 57.04, 47.52; IR (film) 3060, 2920, 1705, 1590, 1490 cm^{-1}; MS (EI 70 eV) m/z 270 (M^+ + 2, 31), 268 (M^+, 100), 239 (19), 205 (39).

2-(4-Bromophenyl)-2-phenylcyclopent-4-enone (8c). Following the general enone synthesis with allyl acid **7c** (10.60 mmol, 3.51 g) followed by column chromatography (SiO_2, 8:2 petroleum ether–ether) gave a 44% yield of enone **8c** as a pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.85 (m, 1 H), 7.45–7.09 (m, 9 H), 6.28 (m, 1 H), 3.55–3.40 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 208.21, 162.28, 142.64, 142.16, 132.69, 131.48, 129.75, 128.55, 127.77, 126.94, 120.87, 57.02, 47.45; IR (film) 3055, 2920, 1705, 1591, 1486 cm^{-1}; MS (EI 70 eV) m/z 314 (M^+ + 2, 100), 312 (M^+, 95), 286 (16), 284 (21), 204 (56), 178 (27).

2-(4-Methoxyphenyl)-2-phenylcyclopent-4-enone (8d). Following the general enone synthesis with allyl acid **7d** (7.55 mmol, 2.13 g) followed by column chromatography (SiO_2, 8:2 petroleum ether–ethyl acetate) gave a 47% yield of enone **8d** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.82 (m, 1 H), 7.31–7.12 (m, 7 H), 6.83 (d, J = 8.74 Hz, 2 H), 6.26 (m, 1 H), 3.78 (s, 3 H), 3.49–3.47 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 209.04, 162.24, 158.20, 143.53, 134.91, 132.60, 128.97, 128.32, 127.78, 126.58, 113.68, 59.10, 55.14, 47.80; IR (film) 2930, 1705, 1600, 1510 cm^{-1}; MS (EI 70 eV) m/z 264 (M^+, 100), 235 (48).

2,2-Diphenylcyclopent-4-enone (8g). Following the general enone synthesis with allyl acid[12c] **7g** (8.55 mmol, 2.16 g) followed by column chromatography (SiO_2, 8:2 petroleum ether–ethyl acetate) gave a 44% yield of enone **8d** as white crystals, mp 97 °C (lit.[12b] mp 97–98.5 °C). ^1H NMR (400 MHz, $CDCl_3$) 7.81 (m, 1 H), 7.33–7.23 (m, 10 H), 6.26 (m, 1 H), 3.49 (d, J = 2.25 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 208.40, 162.38, 142.91, 132.19, 128.10, 127.63, 126.41, 59.51, 47.40; IR (KBr pellet) 3060, 1700, 1592, 1495 cm^{-1}; MS (EI 70 eV) m/z 234 (M^+, 100), 205 (77), 178 (28), 165 (35).

2-(4-Bromophenyl)-1-methoxy-2-phenylcyclopentane (9). A solution of alcohol **2c** (0.330 g, 1.04 mmol) in dimethylformamide (5 mL) was added to a mixture of sodium hydride (0.116 g, 4.16 mmol) in dimethylformamide (5 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 30 min. Methyl iodide (0.32 mL, 5.20 mmol) was added and the reaction mixture was heated at 65 °C for 12 h. After quenching with water and extracting with CH_2Cl_2 the organic layer was dried over $MgSO_4$ and concentrated. Purification via column chromatography (SiO_2, 8:2 petroleum ether–ether) gave a 39% yield of **10** as a pale yellow oil. The diastereomers were separated via preparative TLC (SiO_2, 3 elutions with 7:3 petroleum ether–methylene chloride). ^1H NMR (400 MHz, $CDCl_3$) minor (higher rf) 7.31 (d, J = 8.55 Hz, 2 H), 7.23–7.20 (m, 4 H), 7.14–7.08 (m, 3 H), 4.24 (m, 1 H), 3.27 (s, 3 H), 2.47 (m, 1 H), 2.31 (m, 1 H), 1.94–1.81 (m, 2 H), 1.73–1.60 (m, 2 H); ^1H NMR (400 MHz, $CDCl_3$) major (lower rf) 7.33 (d, J = 8.68 Hz, 2 H), 7.23–7.18 (m, 4 H), 7.15–7.08 (m, 3 H), 4.19 (m, 1 H), 3.26 (s, 3 H), 2.50 (m, 1 H), 2.27 (m, 1 H), 1.93–1.82 (m, 2 H), 1.70 (m, 1 H), 160 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) minor 146.79, 144.47, 130.63, 130.43, 128.25, 126.76, 125.98, 119.56, 86.82, 58.45, 56.89, 35.07, 27.53, 19.74; ^{13}C NMR (100 MHz, $CDCl_3$) major 146.60, 144.67, 131.17, 128.73, 128.51, 127.68, 125.77, 119.62, 86.85, 58.43, 56.94, 35.00, 27.47, 19.66; IR (film) 2960, 1480, 1095, 817, 695 cm^{-1}; MS (EI 70 eV) m/z 332 (M^+ + 2, 32), 330 (M^+, 33), 300 (36), 298 (37), 219 (100), 197 (61), 178 (59); HRMS (EI 70 eV) m/z (M^+) calcd for $C_{18}H_{19}BrO$ 330.0619, obsd 330.0617.

(1*S,2*R**)-2-(4-Hydroxyphenyl)-1-methoxy-2-phenylcyclopentane (10).** To a solution of (1*S**,2*R**)-2-(4-bromophenyl)-1-methoxy-2-phenylcyclopentane (**9**) (0.086 g, 0.260 mmol) in THF (1.5 mL) containing powdered 4A molecular sieves (0.10 g) was added *tert*-butyllithium (1.7 M, 0.460 mL, 0.780 mmol) at −78 °C. After being stirred at −78 °C for 10 min, trimethyl borate (0.065 mL, 0.519 mmol) in THF (1.5 mL, dried over 0.050 g of powdered 4A molecular sieves) was added. The mixture was stirred for 5 min at −78 °C and then warmed to 23 °C. The reaction was quenched with three drops of 1 N hydrochloric acid. The layers were separated and 2.5 M NaOH (0.10 mL, 0.26 mmol) and 30% H_2O_2 (0.05 mL, 0.52 mmol) were added to the organic portion. After being stirred at 23 °C for 3.5 h, the solution was acidified with 1 N HCl and extracted with ether. The organic portion was dried over $MgSO_4$ and concentrated. Purification via preparative TLC (SiO_2, 8:2 petroleum ether–ethyl acetate) gave a 34% yield of **10** as a pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.31–7.21 (m, 4 H), 7.16–7.09 (m, 3 H), 6.67 (d, J = 8.30 Hz, 2 H), 4.67 (br s, 1 H), 4.25 (m, 1 H), 3.32 (s, 3 H), 2.50 (m, 1 H), 2.31 (m, 1 H), 1.97–1.85 (m, 2 H), 1.74–1.59 (m, 2 H), 1.26 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) 153.35, 147.80, 137.50, 129.73, 128.11, 126.81, 125.68, 114.53, 87.16, 65.26, 57.00, 35.38, 27.68, 19.75; IR (KBr pellet) 3300, 2920, 1510, 1085 cm^{-1}; MS (EI 70 eV) m/z 268 (M^+, 100), 236 (30), 209 (19), 183 (30).

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