Rate Constants for 5-Exo Secondary Alkyl Radical Cyclizations onto Hydrazones and Oxime Ethers via Intramolecular Competition Experiments†

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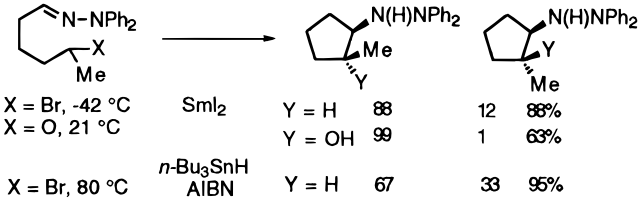
The kinetics for the 5-exo cyclizations of secondary radicals onto various imine acceptors (aryl-, alkyl-, and benzoylhydrazones, oxime ethers, etc.) have been determined. The rate constants have been established by competitive "internal radical clock" type cyclizations on the basis of the known rate constants for alkene and *N*,*N*-diphenylhydrazone systems. In refluxing benzene (80 °C) the rate constants for these 5-exo cyclizations fall within the range of 16×10^7 to 4×10^7 s^{-1} depending on the electron-withdrawing capacity of the imine acceptor (C═NR). The fastest rate constants were observed for the *N*-benzyoylhydrazone acceptor (cis, 1.2×10^8 s^{-1}), a value that is very similar to rate constant determined previously for *N*,*N*-diphenylhydrazones (cis, 1.1×10^8 s^{-1}). These rate constants are approximately 200 times faster than those for the corresponding 5-exo cyclization onto alkenes.

Introduction

The interest in free radical reactions applied to synthetic problems continues to advance, and these reactions have been used successfully for a growing number of synthetic targets.[1] Further synthetic applications and related mechanistic studies depend on a knowledge of the rate constants for the various radical reactions. This knowledge permits prediction of the radical kinetics and hence control of the product distribution.[2] In contrast to the extensive studies of cyclizations onto alkenes and carbonyl systems, it is only recently that imine acceptors have received increased scrutiny.[3] Earlier we reported our results of a radical aza-Barbier type reaction in which halohydrazones were cyclized directly, under either *n*-Bu_3SnH- or SmI_2/HMPA-mediated conditions, to afford cyclopentyl- or cyclohexylhydrazines (Scheme 1).[4] The related reaction with carbonylhydrazones provided access to β-amino alcohols after hydrazine cleavage, with a high level of diastereoselectivity. An extension of these studies involved trapping of the initial radical with carbon monoxide, prior to cyclization and reduction of the resulting cyclopentanones. This sequence afforded an alternative route to hydrazine alcohols.[5] In contrast to the extensive literature containing kinetic information on free radical additions onto carbon−carbon double bonds, there is less kinetic data for carbon−oxygen and carbon−nitrogen double bonds. Thus an additional investigation established that, for 5- and 6-*exo*-hydrazone ring closures, the rate constants for 5-exo cyclizations onto *N*,*N*-diphenylhydrazones were 1.1×10^8 and 4.6×10^7 s^{-1} at 80 °C for the cis and trans cyclopentylhydrazines, respectively.[6]

Scheme 1. Radical Cyclizations onto N,N-Diphenylhydrazones



Limited data are available concerning the best acceptors in diverse imine systems in which two different substitution patterns are present, and consequently their relative rate constants are not as well established. To help fill this void, we report the results of a comparative study of 5-exo intramolecular additions onto C═N systems in different families. The relative rate constants were established for the 5-exo cyclizations of secondary radicals based on intramolecular competitive "internal radical clock" experiments. These investigations established that for many applications, the *N*,*N*-diphenylhydrazones are the most useful acceptors due to their stability, ease of handling, homogeneous stereochemistry, and relative rates. The rate constant for the 5-exo cyclization onto *N*-benzoylhydrazones, determined below, is similar. Due to its ease of hydrolysis, in some cases it is synthetically more versatile.

A diverse family of oxime ethers and hydrazones were selected for investigation. These systems represent synthetically useful precursors. The oxime methyl ethers allow facile detection by ^1H NMR and can be converted to the parent oxime with trimethylsilyliodide. In a related fashion the benzyl oxime may be cleaved by hydrogenoly-

† This paper is dedicated to Dr. Keith U. Ingold on the occasion of his 70th birthday. Presented with respect and gratitude for his contributions to physical organic chemistry.

(1) For reviews, see: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: New York, 1986. (b) Curran, D. P. *Synthesis* **1988**, 417. (c) Curran, D. P. *Synthesis* **1988**, 489. (d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (e) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic Press: London, 1992. (f) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry;* John Wiley & Sons: New York, 1995. (g) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions;* VCH: New York, 1996.

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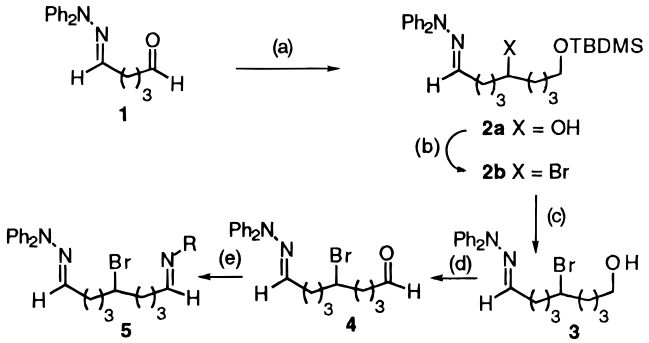
Scheme 2. Synthesis of Bromo-bis-imine Substrates[a]



[a] Key: (a) $Br(CH_2)_4OTBDMS$, Mg, THF, 0 °C, 60%; (b) $PPh_3 \cdot Br_2$, Et_3N, CH_2Cl_2, 0 °C, 75%; (c) Bu_4NF, THF, 0 °C, 80%; (d) DMSO, Et_3N, $SO_3 \cdot Py$, 21 °C, 75%; (e) H_2NR, 21−80 °C, 60−80%.

sis. The *N*,*N*-dimethylhydrazone, in which the initial nitrogen-centered radical is less stabilized, provides an example for comparison with the *N*,*N*-diphenylhydrazone and *N*-benzoylhydrazone cases. Kim and Cho[9] have demonstrated that *N*-sulfonylhydrazone systems are also good acceptors, although the initial cyclization product is prone to fragmentation.

Results and Discussion

Synthesis of Intramolecular Competition Substrates. The required substrates were prepared as outlined in Scheme 2. The *N*,*N*-hydrazone aldehyde **1**[4] was condensed with the Grignard reagent, derived from 4-bromo-1-(*tert*-butyldimethylsilyloxy)butane, to afford the secondary alcohol **2a** (X = OH). Treatment of the alcohol with triphenylphosphine dibromide gave the bromide **2b** (X = Br), and the silyl group was removed to afford the primary alcohol **3**. Of several oxidants examined the sulfur trioxide−pyridine complex was the only reagent that generated the aldehyde **4** cleanly without concomitant decomposition products. This oxidant was also required for the preparation of the aldehyde **1** from the corresponding primary alcohol. However, if the synthetic order was reversed and the *N*,*N*-diphenylhydrazone was installed later the sulfur trioxide−pyridine reagent also caused extensive decomposition. Exposure of **4** to the appropriate amino derivative afforded the desired bis-imine substrates **6**−**11** and **20** (Scheme 3).

Cyclization Studies and Reference Compounds. Treatment of compounds **6**−**11** individually, in refluxing benzene with tributyltin hydride and azobis(isobutyronitrile) (AIBN), afforded the amino-substituted cyclopentanes from 5-exo cyclization, including the cis/trans isomeric pairs illustrated in Table 1. Under these tin hydride conditions, uncyclized products from direct quenching of the initial radical **A** were not detected (Scheme 3). Thus these radicals were partitioned between the 5-*exo*-*N*,*N*-diphenylhydrazone (radical $\mathbf{B_1}$) or 5-exo imine (hydrazone or oxime, radical $\mathbf{B_2}$) cyclization pathways. Due to the potential for syn/anti isomerism, the mixtures were complex, although in most cases the anticipated signals for the cis and trans isomers could be assigned by NMR spectroscopy. These assignments

Scheme 3. Competitive *N*,*N*-Diphenylhydrazone−Imine Radical Cyclizations

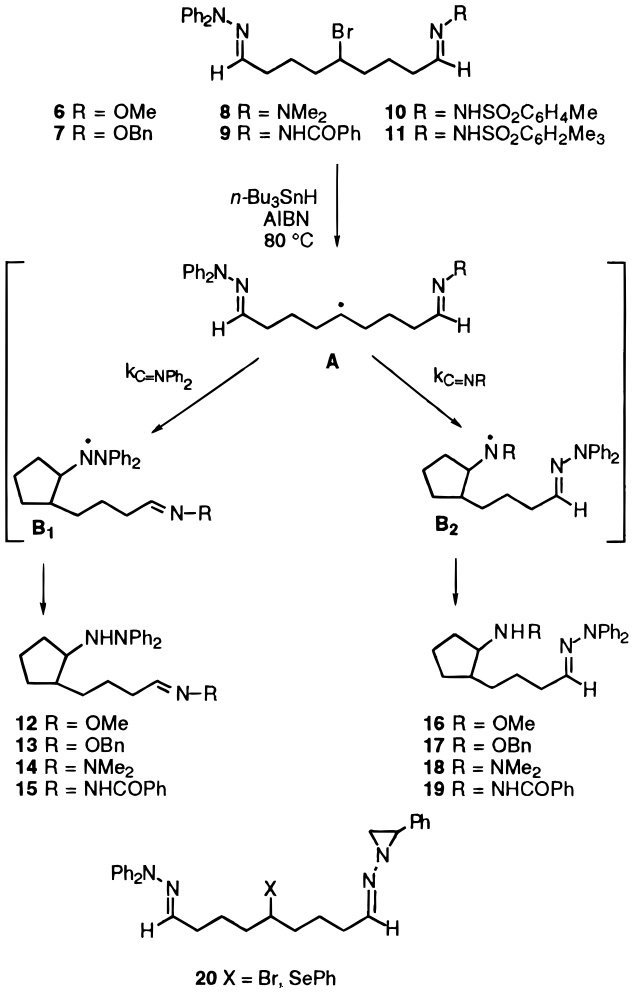
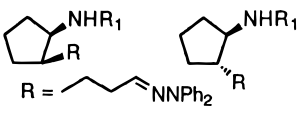


Table 1. Cis/Trans Ratios of Cyclopentanes

R_1		
OMe	1.6 ± 0.05	1
OBn	1.7 ± 0.05	1
NMe_2	2 ± 0.05	1
NCOPh	3.4 ± 0.05	1

(7) For representative examples, see: (a) Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, *24*, 2821. (b) Hart, D. J.; Seely, F. L. *J. Am. Chem. Soc.* **1988**, *110*, 1631. (c) Bartlett, P. A.; McLaren, K. L.; Ting, P. C. *J. Am. Chem. Soc.* **1988**, *110*, 1633. (d) Parker, K. A.; Spero, D. M.; Van Epp, J. *J. Org. Chem.* **1988**, *53*, 4628. (e) Marco-Contelles, J.; Pozuelo, C.; Jimeno, M. L.; Martinez, L.; Martinez-Grau, A. *J. Org. Chem.* **1992**, *57*, 2625. (f) Pattenden, G.; Schultz, D. J. *Tetrahedron Lett.* **1993**, *34*, 6787. (g) Hollingworth, G. J.; Pattenden, G.; Schultz, D. J. *Aust. J. Chem.* **1995**, *48*, 381. (h) Keck, G. E.; McHardy, S. F.; Murry, J. A. *J. Am. Chem. Soc.* **1995**, *117*, 7289.

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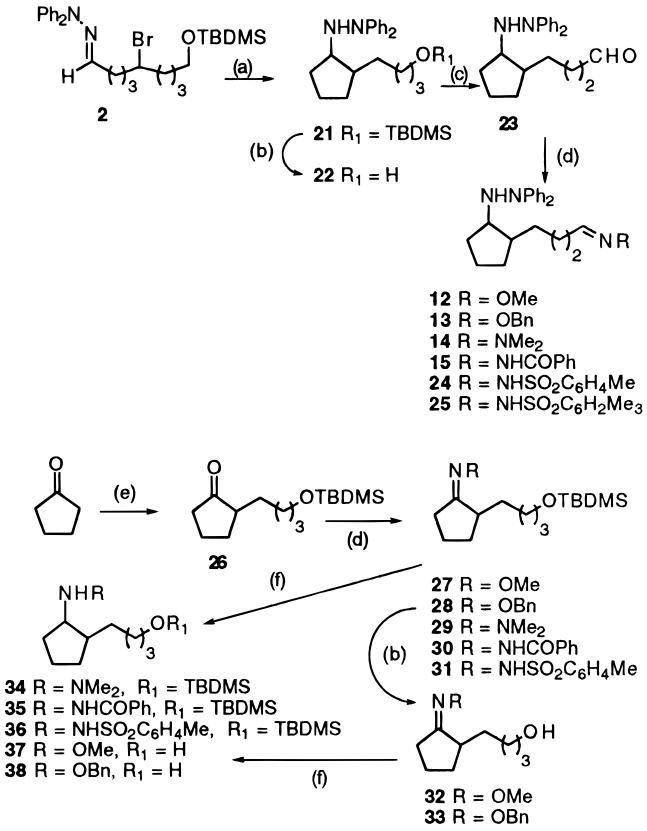
Table 2. Rate Constants for 5-*Exo*-Cyclizations of Bromoimines [80 °C, AIBN, ^{n}Bu$_3$SnH]

entry	compound	product ratio[a]	$k_{C=NR}$	cis/trans ratio	$k^{cis}_{C=NR}$	$k^{trans}_{C=NR}$
a	**6** R = OMe	**12/16** 4:1	4.0×10^7	1.6:1	2.4×10^7 s^{-1}	1.5×10^7 s^{-1}
b	**7** R = OBn	**13/17** 2.5:1	6.4×10^7	1.7:1	4.0×10^7 s^{-1}	2.4×10^7 s^{-1}
c	**8** R = NMe$_2$	**14/18** 3:1	5.3×10^7	2:1	3.5×10^7 s^{-1}	1.8×10^7 s^{-1}
d	**9** R = NHCOPh	**15/19** 1:1	1.6×10^8	3.4:1	1.2×10^8 s^{-1}	0.4×10^8 s^{-1}
e	**10** R = NHSO$_2$C$_6$H$_4$Me[b]	1:0	$<1.0 \times 10^7$			
f	**11** R = NHSO$_2$C$_6$H$_2$Me$_3$[b]	1:0	$<1.0 \times 10^7$			

[a] These ratios represent lower limits based on ^{1}H NMR (500 MHz) analysis of the total product mixture. [b] These data are estimates.

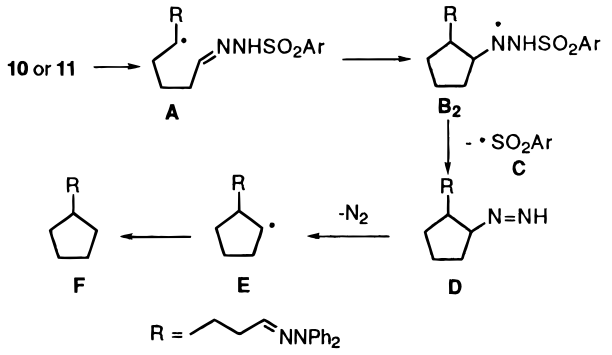
Scheme 4. Synthesis of Reference Compounds[a]



[a] Key: (a) AIBN, *n*-Bu$_3$SnH, C$_6$H$_6$, 80 °C, 98%; (b) Bu4NF, THF, 0 °C, 80%; (c) DMSO, Et$_3$N, SO$_3$·Py, 21 °C, 75%; (d) H$_2$NR, 40 °C, ~70%; (e) I(CH$_2$)$_4$OTBDMS, LDA, HMPA, Me$_2$Zn, −78 °C; (f) NaCNBH$_3$, *p*-TsOH, THF or NaBH$_4$, MeOH.

were assisted by our earlier observations[4] and current data. This indicated that for the *cis*-cyclopentane hydrazine the carbon-bearing nitrogen resonated at $\delta \approx 60$ ppm and at ~65 ppm for the trans isomer. Similarly the hydrogen attached to this carbon gave rise to a ^{1}H NMR signal in the range of $\delta \approx 3.25-3.4$ ppm for the cis product and ~3.0−3.1 ppm for the trans compound. This shift differential of approximately 0.3 ppm was a consistent pattern among the isomeric pairs. Additional confirmation was provided by the synthesis of authentic samples or closely related models. The synthetic routes to several of the aminocyclopentane products (**12**−**15**) or cyclic relatives (represented by **21**−**38**) are outlined in Scheme 4. These model systems provided accurate spectral details, in the various series, for the direct comparison of the synthetic and cyclized samples. Thus the NMR assignments established the product ratios from the expanded and integrated spectra. The synthetic sequences employed were similar to those described above with the additional step involving reduction of the imine bond with cyanoborohydride required for the aminocyclopentanes **34**−**38**. Additional simplification of the spectra was observed since the *N*,*N*-diphenylhydrazones exist exclusively in the anti orientation.

Scheme 5. Decomposition Pathways of Arylsulfonylhydrazones



Kinetic Results. The product ratios for the competitive 5-exo imine cyclizations are listed in Table 2, and as mentioned above, the cis/trans ratios of the individual products are summarized in Table 1. On the basis of the data determined previously for the *N*,*N*-diphenylhydrazone cyclizations, the rate constants were determined and tabulated.[10] Accurate numbers for comparison could not be obtained for the sulfonyl systems **10** and **11**. The values for **10** and **11** are estimates due to the instability of the sulfonylhydrazinyl radical, resulting in the loss of the sulfonyl group after cyclization as illustrated in Scheme 5. As observed earlier,[9] after cyclization, the radical $\mathbf{B_2}$ expels the arylsulfonyl radical **C** to give the azo compound **D**. Subsequent loss of nitrogen generates the cyclopentanyl radical **E**, and ultimately a monosubstituted cyclopentane **F** is usually produced. However, this compound was not detected, and the only products isolated were the hydrazines from *N*,*N*-diphenylhydrazone addition. The competition between an *N*,*N*-diphenyl and an *N*-aziridinylhydrazone as contained in **20** (Scheme 3) was also of interest, but the complex mixture derived from this experiment did not afford reliable data even when a selenide radical precursor was employed.

In addition to our own research, the synthetic potential of a variety of related acceptors has been investigated. These include oxime ethers,[7] *N*-aziridinylhydrazones,[8] mesitylsulfonylhydrazones,[9] β-allenic hydrazones,[11] *N*,*N*-

(10) The 5-exo rate constants were determined using the *N*,*N*-diphenylhydrazone rate constant (1.6×10^8 s^{-1}, 80 °C) on the basis of the following equation. $K_a = K_{cis} + K_{trans(diphenylhydrazone)}$ is the known total diphenylhydrazone cyclization rate constant, and $K_b = K_{cis} + K_{trans(oximes\ or\ other\ hydrazones)}$ is the unknown total cyclization rate constant for C=NR. Thus (P_a/P_b) is the product ratio, measured analytically and K_b is determined from the equation $-K_b = K_a(P_a/P_b)$.

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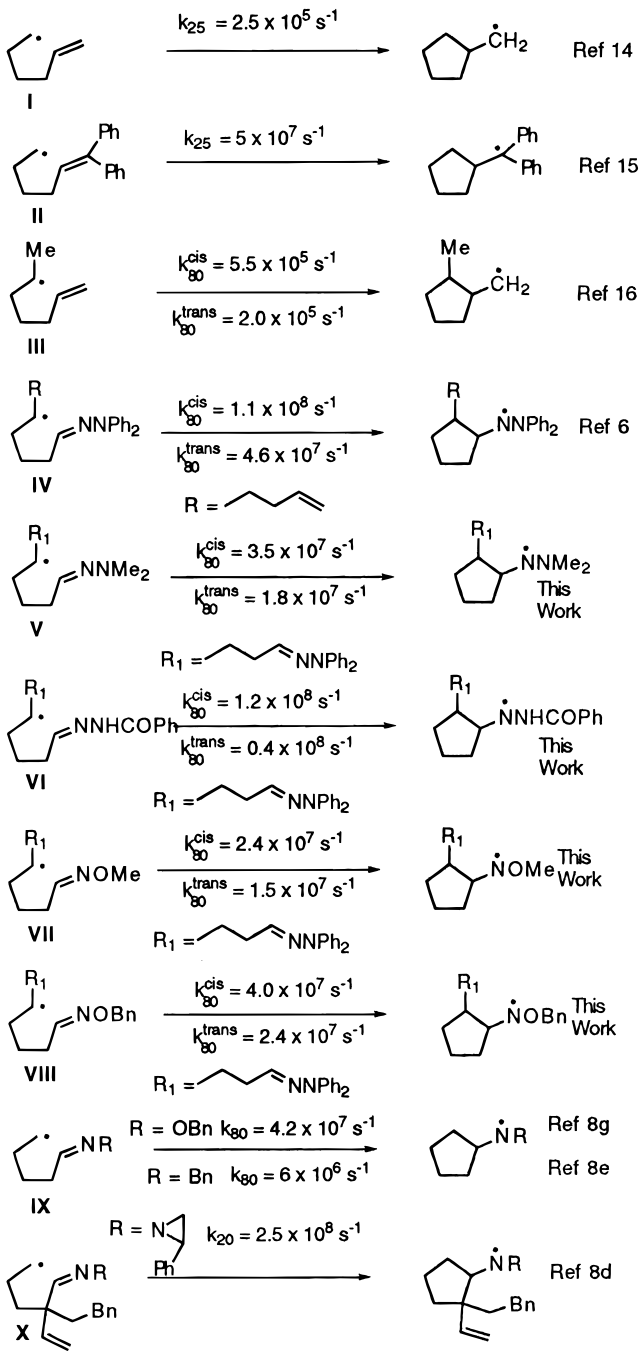
Chart 1. Rate Constants for 5-exo Cyclizations to Cyclopentanes



diphenylhydrazones,[3−5,12] and various imines.[13] Some of the rate constants from these investigations are also tabulated in Chart 1 for comparison.

The increased cyclization rate of these imine systems compared to simple alkenes is a consequence of the polarization of the C═NR bonds and the increased stability of the substituted nitrogen radicals **B** after cyclization. Naturally, the nitrogen radical stability varies with the attached groups. The second nitrogen present in the hydrazones and the oxygen in oximes are likely involved in a two-center, three-electron bond with the developing radical on the nitrogen of the imine. This three-electron bond will help stabilize the developing nitrogen radical during cyclization. This is reflected in the positive influence of the R_2N and RO substituents on the reaction exothermicity for of these radical cyclizations compared to cyclizations onto alkenes. This may explain why the 5- and 6-exo hydrazone cyclizations were found to have lower activation barriers than the corresponding alkene cyclizations. The activation barriers for a secondary radical in 5-hexenyl-type 6-exo cyclizations are 6.5 kcal/mol for the cis product and 7.4 kcal/mol for the trans carbocycle. For comparison, the corresponding values for 6-exo cyclizations onto *N*,*N*-diphenylhydrazones are 5.6 kcal/mol (cis) and 6.2 kcal/mol for the trans product, lower than the values for the corresponding carbocycles.[6]

These features are reflected in the data in Chart 1. Thus diphenyl substituents on an alkene result in approximately a 100-fold increase in the rate constant (Chart 1, entries I and II). Similarily, the rate constants for the diphenyl hydrazinyl radical (Chart 1, entry IV) are greater than those for the dimethyl hydrazinyl case (Chart 1, entry V), although the rate constants for the *N*-benzoylhydrazone acceptor (Chart 1, entry VI) are approximately equivalent to those for the *N*,*N*-diphenylhydrazone. The oximes (Chart 1, entries VII−IX) and the *N*,*N*-dimethylhydrazones have similar rate constants, while the imine acceptor (Chart 1, entry IX, R = Bn) has the smallest rate constant and the *N*-aziridinylhydrazone (Chart 1, entry X) has the largest rate constant.

Conclusion

These investigations, employing intramolecular competition experiments, have established the rate constants for several 5-exo cyclizations onto C═N−R acceptors. These 5-*exo*-hydrazone and 5-*exo*-oxime ether secondary radical cyclizations have been shown to be relatively fast reactions in a synthetically useful range. These results establish that *N*,*N*-diphenylhydrazones and *N*-benzoylhydrazones are superior radical acceptors compared to the oxime ethers and *N*-sulfonylhydrazones. As noted above these cyclizations proceed approximately 200 times faster than the corresponding 5-exo alkene ring closures. These data should facilitate the rational design of various tandem cyclizations for the total synthesis of natural products. Synthetic application of these results are currently being explored.

Experimental Section

General. Melting points were determined in capillary tubes with a Thomas-Hoover Unit-melt apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Bomem

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Michelson 100 FTIR spectrometer. Proton magnetic resonance spectra (^{1}H NMR) were measured at 200 MHz with a Varian Gemini spectrometer and at 300 MHz with a Varian XL-300 spectrometer or at 500 MHz with a Bruker AMX500 spectrometer in deuteriochloroform unless otherwise stated. Carbon magnetic resonance spectra (^{13}C NMR) were measured at 50 MHz (Varian Gemini), at 75 MHz (Varian XL-300), or at 125 MHz (Bruker). The residual $CHCl_3$ signal was used as an internal reference: $CDCl_3$ ^{1}H, δ 7.24 ppm; ^{13}C, δ 77.0 ppm. Chemical shifts are reported in ppm downfield from trimethylsilane (δ scale). The multiplicity, coupling constants (hertz), and number of protons are indicated in parentheses. Mass spectra (MS) were determined on a V. G. micromass 7070 HS instrument using an ionization energy of 70 eV. Elemental analyses were conducted by M−H−W Laboratories, Phoenix, AZ. The purity of all title compounds was judged to be >95% as determined by a combination of GC-MS, ^{1}H NMR, and ^{13}C NMR analyses.

Unless otherwise stated, all nonaqueous reactions were performed under an atmosphere of nitrogen in flame-dried glassware equipped with stir bar and a rubber septum. Standard inert atmosphere techniques were used in handling all air- and moisture-sensitive reagents. Reactions were monitored by analytical thin-layer chromatography (TLC) using commercial aluminum sheets precoated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Product purification by conventional and flash column chromatography was performed using E. Merck silica gel 60 (70−230 or 230−400 mesh). Solutions in organic solvents were dried over anhydrous magnesium sulfate and stripped of solvents with a Büchi rotatory evaporator connected to water aspirator. Trace solvents were removed on a vacuum pump. All compounds were stored at −15 °C in vials flushed with nitrogen.

Petroleum ether refers to a mixture of hydrocarbons with a boiling range of 30−60 °C. Anhydrous diethyl ether (ether) and anhydrous tetrahydrofuran (THF) were distilled from benzophenone/sodium. Dry benzene, toluene, dichloromethane (CH_2Cl_2), and triethylamine were distilled from calcium hydride, and ethanol was distilled from magnesium ethoxide. Flash chromatography was employed for purification. Commercial starting materials were purchased from Aldrich Chemical Co. unless otherwise indicated.

General Procedure for Radical Cyclizations. The hydrazone or oxime (1 equiv) was dissolved in dry benzene (0.007 M solution), nitrogen was bubbled through the solution for 30 min, and the solution was refluxed. Tributyltin hydride (1.2 equiv) and AIBN (0.34 equiv) were dissolved in dry benzene (0.02 M solution), and the solution was purged with nitrogen for 20 min. The latter solution was then added to the refluxing hydrazone or oxime solution at a rate of 5.0 mL/h using a syringe pump. After the addition of the tin hydride was complete, the reaction mixture was refluxed for another 30 min before cooling to room temperature. The resulting solution was concentrated and chromatographed on deactivated silica gel (petroleum (pet) ether, to remove Bu_3SnH and Bu_3SnBr; followed by 50% CH_2Cl_2/pet ether). All the fractions not containing tin compounds were collected along with approximately 100 mL of additional eluent. ^{1}H NMR analysis of the "semicrude" mixture provided the ratio of the cyclized products. Authentic samples of the anticipated products or close representative products were prepared separately for comparison.

4-Bromo-1-butanol. Borane−THF complex (1.25 mL of 1 M solution, 1.25 mmol) was added dropwise to bromobutyric acid (210 mg, 1.25 mmol) in dry THF at −18 °C. The reaction was stirred overnight and warmed to 21 °C. The reaction was quenched with aqueous K_2CO_3 (1.5 mL) at 0 °C and extracted with ether (3 × 50 mL). The combined organic extracts were washed with saturated NH_4C and concentrated. Chromatography (4:1, hexane/ether) provided 161 mg (83%) of the bromo alcohol: IR (neat) 3337, 2918, 1648, 1435, 1051 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.61(t, J = 6.4 Hz, 1H), 3.40 (t, J = 6.6 Hz, 2H), 2.80 (s, 1H), 1.93−1.83 (m, 2H), 1.71−1.61 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) 61.6, 33.7, 31.0, 29.1; HRMS calcd for C_4H_7Br ($M^+ - H_2O$) 133.9731, found 133.9742.

4-Bromo-1-(*tert*-butyldimethylsilyloxy)butane. TBDMSCl (148 mg, 0.979 mmol) was added to a solution of 4-bromobutanol (100 mg, 0.653 mmol), imidazole (89 mg, 1.307 mmol), and 4-(dimethylamino)pyridine (40 mg, 0.326 mmol) in dry CH_2Cl_2 (4 mL) at 0 °C. The solution was stirred overnight, warmed to 21 °C, quenched with aqueous NH_4Cl (2.5 mL), and extracted with ether (3 × 10 mL). The combined organic extracts were washed with aqueous NaCl (3 × 3 mL), dried, filtered, concentrated, and chromatographed (pet ether) to afford 140 mg (80%) of the silyl ether as a clear colorless oil: IR (neat) 2994, 2858, 2361, 1468, 839, 776 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.61 (t, J = 6.0 Hz, 2H), 3.41 (t, J = 6.7 Hz, 2H), 1.95−1.87 (m, 2H), 1.66−1.58 (m, 2H), 0.86 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) 62.1, 33.8, 31.2, 29.4, 25.9, 25.7, −5.3; HRMS calcd for $C_6H_{14}BrOSi$ (M^+−*tert*-butyl) 208.9998, found 209.0.

5-Hydroxy-9-(*tert*-butyldimethylsilyloxy)nonanal-*N*,*N*-diphenylhydrazone (2a). Aldehyde **1** (425 mg, 1.5 mmol) was disolved in dry THF (2 mL) in a two-necked flask, and the resulting solution was cooled to 0 °C. The Grignard reagent $BrMg(CH_2)_4OTBDMS$ [prepared from the bromobutane above (1.5 g, 5.6 mmol), and Mg (225 mg), in THF (2.5 mL, reflux)] was added slowly at 0 °C, and the reaction was monitored by TLC. The reaction was quenched with saturated aqueous NH_4-CI (15 mL), diluted with water and ethyl acetate (150 mL), and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with saturated aqueous NaCl (30 mL), dried, filtered, and concentrated, in vacuo. The resultant oil was chromatographed (1:4, ether/pet ether) to obtain 525 mg (60%) of **2** (X = OH): IR (neat) 3396, 3061, 2906, 1592, 1479, 1302, 1210, 910, 744, 697 cm^{-1};^{1}H NMR (200 MHz, $CDCl_3$) δ 7.39∠7.21 (m, 4H), 7.14−7.06 (m, 6H), 6.54 (t, J = 5.2 Hz, 1H), 3.64−3.56 (m, 3H), 2.31−2.28 (m, 2H), 1.80 (br s, 1H), 1.62−1.45 (m, 10H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C (50 MHz, $CDCl_3$) δ 144.3, 139.7, 129.6, 123.8, 122.3, 71.5, 63.1, 37.1, 36.9, 32.7, 32.6, 25.9, 23.0, 21.9, 18.3, 5.3; HRMS calcd for $C_{27}H_{42}N_2O_2Si$ (M^+) 454.3096, found 454.3052.

5-Bromo-9-(*tert*-butyldimethylsilyloxy)nonanal-*N*,*N*-diphenylhydrazone (2b). Triethylamine (1.2 mL, 0.79 mmol) was added to a cold solution (0 °C) of dry CH_2Cl_2 (8 mL) containing triphenylphosphine (0.207 g, 0.79 mmol). Bromine (45 mL, 0.79 mmol) was added dropwise until the reaction mixture turned a faint yellow. The mixture was stirred at 0 °C for 10 min, and then the alcohol **2** (X = H) (0.3 g, 0.66 mmol) in dichloromethane (0.7 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min and at 21 °C for 30 min and then quenched with saturated aqueous $NaHCO_3$ (3 mL). The aqueous layer was extracted with ether (3 × 10 mL), and the combined organic extracts were washed with brine, dried, concentrated, and chromatographed (4:1, hexane/ether) to afford 240 mg (75%) of **2** (X = Br) as a clear colorless oil: IR (neat) 2940, 2858, 2351, 1593, 1494, 749, 698 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) 7.41-7.32 (m, 4H), 7.16−7.06 (m, 6H), 6.52 (t, J = 5.17 Hz, 1H), 4.05 (m, 1H), 3.62 (t, J = 5.86 Hz, 2H), 2.36-2.26 (m, 2H), 1.88−1.50 (m, 10H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) 144.1, 138.7, 129.6, 123.8, 122.2, 62.8, 58.0, 38.8, 38.4, 32.1, 31.9, 25.9, 24.8, 23.9, 18.2, −5.2; HRMS calcd for $C_{27}H_{41}N_2SiBrO$ (M^+) 516.2173, found 516.2221. Anal. Calcd for $C_{27}H_{41}N_2SiBrO$: C, 62.95; H, 7.98; N, 5.41. Found: C, 62.75; H, 7.83; N, 5.49.

5-Bromo-9-hydroxynonanal-*N*,*N*-diphenylhydrazone (3). Tetrabutylammonium fluoride (0.490 mL of 1 M solution in THF, 0.49 mmol) was added to **2** (X = Br) (210 mg, 0.41 mmol) in dry THF (3.5 mL), at 0 °C, and the resulting mixture was stirred overnight. The reaction was quenched with water (2 mL) and extracted with ether, and the combined organic extracts were washed with saturated NaCl (2 × 10 mL), dried, concentrated, and chromatographed (1:1 ether/hexanes) to afford 130 mg (80%) of **3** as a faint yellow oil: IR (neat) 3360, 3060, 2916, 1592, 1210, 1091, 1062, 749, 689 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.39−7.32 (m, 4H), 7.14−7.03 (m, 6H), 6.50 (t, J = 5.2 Hz, 1H), 4.07−4.01 (t, J = 6.2 Hz, 1H), 3.65−3.59 (t, J = 6.0 Hz, 2H), 2.34−2.24 (m, 2H), 1.90−1.42 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) 144.1, 138.8, 129.6, 123.8,

122.2, 62.5, 57.9, 38.8, 38.3, 31.9, 31.8, 24.8, 23.8; HRMS calcd for $C_{21}H_{27}N_2OBr$ (M^+) 402.1297, found 402.1293.

5-Bromononanedial-9-(*N,N*-diphenylhydrazone) (4). A suspension of pyridine−sulfur trioxide complex (1.51 g, 3.23 mmol) in DMSO (3.6 mL) was added to the alcohol **3** (1.3 g, 3.23 mmol) and triethylamine (3.6 mL, 25.8 mmol) in DMSO (5.6 mL) at 21 °C. The reaction was quenched with water and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with brine (2 × 25 mL), dried, concentrated, and chromatographed (4:1 hexanes/ether) to yield 967 mg (75%) of **4** as a faint yellow oil: IR (neat) 3059, 2933, 1723, 1592, 1492, 1301, 1210, 1062 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.73 (t, J = 1.5 Hz, 1H), 7.39−7.24 (m, 4H), 7.2−7.03 (m, 6H), 6.49 (t, J = 5.2 Hz, 1H), 4.05−4.02 (m, 1H), 2.48−2.24 (m, 4H), 1.90−1.60 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.7, 144.0, 138.6, 129.6, 123.8, 122.5, 57.1, 43.0, 38.3, 38.2, 31.8, 24.7, 20.1; HRMS calcd for $C_{21}H_{25}N_2OBr$ (M^+) 400.1151, found 400.1161.

5-Bromononanedial-(1-*O*-methyloxime)-9-*N,N*-diphenylhydrazone (6). Methoxyamine hydrochloride (417 mg, 0.50 mmol) was added to a solution of the aldehyde **4** (200 mg, 0.50 mmol) at 0 °C, followed by addition of pyridine (42 μL, 0.52 mmol). The solution was stirred at this temperature until the reaction was complete. The resulting solution was concentrated and chromatographed (1:20, ether/pet ether) to yield 135 mg (63%) of **6** as a clear colorless oil: IR (neat) 3060, 2933, 2351, 1592, 1492, 1454, 1301, 1210, 1054, 883, 749, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.36−7.24 (m, 4H), 7.13−7.07 (m, 6H), 7.37, 6.61 [t, J = 5.5 Hz, 1H (syn, anti)], 6.50 (t, J = 5.1 Hz, 1H), 4.06−4.00 (m, 1H), 3.83, 3.80 [s, 3H (syn, anti)], 2.35−2.17 (m, 4H), 1.88−1.59 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.9, 150.0, 144.2, 138.7, 129.6, 123.9, 122.3, [61.6, 61.2 (syn, anti)], 57.2, [38.6, 38.5 (syn, anti)], [38.4, 38.3 (syn, anti)], 31.9, 28.8, 24.8, 24.6, 24.2; HRMS calcd for $C_{22}H_{28}N_3OBr$ (M+) 429.1417, found 429.1433.

5-Bromononanedial-(1-*O*-benzyloxime)-9-*N,N*-diphenylhydrazone (7). Benzyloxyamine hydrochloride (86 mg, 0.53 mmol) was added to a stirred solution of the aldehyde **4** (179 mg, 0.45 mmol) at 0 °C, followed by addition of pyridine (48 μL, 0.57 mmol). After completion of the reaction, the solution was concentrated and chromatographed (1:20, ether/pet ether) to afford 140 mg (62.2%) of **7** as faint yellow oil: IR (neat) 3031, 2933, 1592, 1453, 1301, 1210, 917, 748, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.44, 6.68 [t, (syn, J = 6.1 Hz, anti, J = 5.5 Hz), 1H], 7.41−7.34 (m, 9H), 7.14−7.05 (m, 6H), 6.52 (dt, J = 2.3 Hz, 5.2 Hz, 1H), 5.11, 5.05 [s, 2H, (syn, anti)], 4.04−4.01 (m, 1H), 2.41−2.24 (m, 4H), 1.86−1.59 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ [151.5, 150.6 (syn, anti)], 144.2, 138.8, [138.0, 137.7 (syn, anti)], 129.7, [128.3, 128.2 (syn, anti)], 129.7, [127.8, 127.7 (syn, anti)], 123.9, 122.3, [75.8, 75.5 (syn, anti)], 57.3, [38.6, 38.5 (syn, anti)], 38.2, 31.9, 28.8, [25.1, 24.8 (syn, anti)], [24.5, 24.2 (syn, anti)]; HRMS calcd for $C_{28}H_{32}N_3OBr$ (M^+) 505.1729, found 505.1739.

5-Bromononanedial-(1-*N,N*-dimethyl-9-*N,N*-diphenyldihydrazone) (8). *N,N*-Dimethylhydrazine (54 mg, 0.897 mmol) was added to the aldehyde **4** (120 mg, 0.299 mmol) in dry CH_2Cl_2 (2 mL). The resulting solution was stirred overnight at 40 °C. The solvent was concentrated and chromatographed (2:5 ether/pet ether) to afford 100 mg (75%) of **8** as a faint yellow oil: IR (neat) 2920, 2781, 1593, 1494, 1300, 1210, 749, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.39−7.31 (m, 4H), 7.13−7.04 (m, 6H), 6.59 (t, J = 5.42 Hz, 1H), 6.49 (t, J = 5.4 Hz, 1H), 4.05 (br q, J = 6.05 Hz, 1H), 2.70 (s, 6H), 2.33−2.19 (m, 4H), 1.90−1.59 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.1, 138.7, 138.0, 129.6, 123.8, 122.2, 57.7, 43.2, 38.3, 38.3, 32.3, 31.9, 25.6, 24.8; HRMS calcd for $C_{23}H_{31}N_4Br$ (M^+) 442.1733, found 442.1723.

5-Bromononanedial-(1-*N*-Benzoylhydrazone)-9-*N,N*-diphenylhydrazone (9). Benzoylhydrazine (106 mg, 0.78 mmol) and aldehyde **4** (250 mg, 0.625 mmol) were stirred in dry toluene (6.6 mL) at 21 °C for 24 h. The resulting mixture was concentrated and chromatographed (1:24, ether/CH_2Cl_2) to yield 230 mg (71%) of **9** as a viscous oil, which was crystallized from toluene/pet ether: mp 110−112 °C; IR (neat) 3221, 3052, 2935, 1736, 1648, 1492, 1210, 749, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.60 (br s, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.40−7.10 (m, 6H), 7.08−7.04 (m, 6H), 6.48 (t, J = 5.16 Hz, 1H), 3.99−3.94 (m, 1H), 2.30−2.23 (m, 4H), 1.84−1.57 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.4, 152.3, 144.2, 138.9, [133.1, 132.9 (syn, anti)], 131.9, 129.7, [128.5, 128.4 (syn, anti)], [127.7, 127.5 (syn, anti)], 123.9, 122.3, [57.7, 57.4 (syn, anti)], 38.5, [38.4, 38.3 (syn, anti)], 32.0, 31.9, [24.9, 24.6 (syn, anti)], 24.8; FAB accurate mass calcd for $C_{28}H_{32}N_4OBr$ (M^+ + 1) 519.17604, found 519.2069.

5-Bromononanedial-[1-*N*-(*p*-toluenesulfonyl)hydrazone]-9-*N,N*-diphenylhydrazone (10). *p*-Toluenesulfonylhydrazine (134 mg, 0.625 mmol) and aldehyde **4** (200 mg, 0.50 mmol) were stirred in ethanol (1 mL) at 21 °C for 1 h. The resulting solution was concentrated and chromatographed (2:5 ether/pet ether) to afford 170 mg of **10** (60%) as a faint yellow oil: IR (neat) 3204, 2936, 1592, 1493, 1452, 1210, 1164, 1092, 902 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (br s, 1H), 7.84, 7.82 [d, (syn anti), J = 8.3 Hz, J = 8.2 Hz, 2H] 7.36−7.27 (m, 6H), 7.23−7.05 (m, 6H), 6.68 [t, J = 5.2 Hz, (anti), (syn hidden under 7.23−7.05), 1H], 6.50 (t, J = 5.0 Hz, 1H), 3.95−3.92 (m, 1H), 2.19−2.39 (s, 3H), 2.30−2.24 (m, 2H), 2.19−2.12 (m, 2H), 1.82−1.50 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ [151.9, 150.8 (syn, anti)], 144.2, 144.1, 138.8, 135.2, 129.7, 129.6, [127.9, 127.8 (syn, anti)], 123.9, 122.3, [57.3, 57.0 (syn, anti)], [38.4, 38.3 (syn anti)], [38.2, 38.1 (syn anti)], 31.8, 31.5, [26.4, 24.7 (syn, anti)], [24.0, 23.8 (syn, anti)], 21.6; FAB accurate mass calcd for $C_{28}H_{33}N_4O_2SBr$ (M^+ + 1) 569.1586, found: 569.1845.

5-Bromononanedial-[1-*N*-(2,4,6-trimethylbenzene)sulfonylhydrazone]-9-*N,N*-diphenylhydrazone (11). 2,4,6-Trimethylbenzenesulfonyl hydrazine (67 mg, 0.312 mmol) and aldehyde **4** (100 mg, 0.25 mmol) were stirred in ethanol (1 mL) at 21 °C for 1 h. The resulting solution was concentrated and chromatographed (2:5 ether/pet ether) to afford 67 mg of **11** (50%) as a faint yellow oil: IR (neat) 3267, 2937, 1597, 1494, 1453, 1371, 1210, 1153, 851, 749, 659 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.38−7.27 (m, 4H), 7.14−7.06 (m, 6H), 6.96−6.93 [overlapping s, 2H, (syn anti)], 6.63[t, J = 5.2 Hz, (anti), (syn hidden under, 7.14−7.06), 1H], 6.48 (t, J = 5.2 Hz, 1H), 3.97−3.90 (m, 1H), 2.67−2.60 [overlapping s, 6H, (syn, anti)], 2.28−2.27 [overlapping s, 3H, (syn, anti)], 2.24−2.15 (m, 2H), 1.76−1.51 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ [150.2, 149.0 (syn, anti)], 144.2, 142.8, [140.2, 140.1 (syn, anti)], [138.7, 138.6 (syn, anti)], [132.3, 132.0 (syn, anti)], [131.9, 131.8 (syn, anti)], 129.9, 123.9, 122.3, [57.2, 56.8 (syn, anti)], [38.5, 38.4 (syn, anti)], [38.2, 38.0 (syn, anti)], 31.8, 31.4, [25.9, 24.8 (syn, anti)], [23.8, 23.7 (syn, anti)], [23.1, 23.0 (syn, anti)], 20.9; FAB accurate mass calcd for $C_{30}H_{38}N_4O_2BrS$ (M^+ + 1) 597.1984, found 597.1899.

***cis*- and *trans*-4-[2-(*N,N*-Diphenylhydrazino)cyclopentyl]butanal(*O*-methyloxime) (12).** Methoxyamine hydrochloride (27 mg, 0.32 mmol) was added to the aldehyde **23** (65 mg, 0.20 mmol) in dry ethanol (1 mL) at 0 °C, followed by the addition of pyridine (33 μL, 0.40 mmol). The solution was stirred at 0 °C until the reaction was complete. The reaction was concentrated and chromatographed (1:20, ether/pet ether) to yield 52 mg (73.4%) of **12** as a clear colorless oil. Cis isomer: IR (neat) 2918, 1590, 1494, 1279, 1053, 802, 749, 696 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35−7.23 (m, 4H), 7.16−7.10 (m, 4H), 6.99−6.92 (m, 2H), 6.57 [t, J = 5.5 Hz (anti, syn hidden under 7.13−7.10), 1H], 3.92−3.87 (br s, 1H), 3.84, 3.77 [s, 3H, (syn, anti)], 3.27−3.25 (m, 1H), 2.28−2.12 (m, 2H), 1.86−1.30 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ [151.5, 150.5 (syn, anti)], 148.0, 129.0, 122.0, 120.2, 61.1, [59.1, 58.9 (syn, anti)], [44.0, 43.9 (syn, anti)], [29.9, 29.7 (syn, anti)], [29.6, 29.5 (syn, anti)], [29.5, 29.4 (syn, anti)], [29.6, 29.5 (syn, anti)], [29.5, 29.4 (syn, anti)], [28.7, 28.4 (syn, anti)], [25.7, 25.6 (syn, anti)], [22.2, 22.1 (syn, anti); HRMS calcd for $C_{22}H_{29}N_3O$ (M^+) 315.2319, found 351.2321. Trans isomer: ^1H NMR (by difference) (500 MHz, $CDCl_3$) δ 7.33−7.23 (m, 4H), 7.14−7.10 (m, 4H), 6.98−6.94 (m, 2H), 6.52 (t, J = 5.5 Hz, 1H), 3.92−3.87 (br s, 1H), 3.82, 3.79 [s, 3H, (syn, anti)], 3.05−3.04 (m, 1H), 2.27−1.50 (m, 13 H).

***cis*- and *trans*-4-[2-(*N,N*-Diphenylhydrazino)cyclopentyl]butanal(*O*-benzyloxime) (13).** Benzyloxyamine hydro-

chloride (40 mg, 0.25 mmol) was added to a stirred solution of the aldehyde **23** (50 mg, 0.15 mmol) at 0 °C, followed by the addition of pyridine (28 μL, 0.34 mmol). The reaction was concentrated and chromatographed (1:10, ether/pet ether) to afford 51 mg (79.7%) of **13** as a faint yellow oil. Cis isomer: IR (neat) 3030, 2933, 1590, 1495, 1454, 1283, 1029, 912, 814, 748, 697 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45−7.21 (m, 9H), 7.16−6.93 (m, 6H), 6.63 [t, J = 5.4 Hz (anti) (syn hidden under 7.45−7.21), 1H], 5.09, 5.02 [s, 2H, (syn, anti)], 3.91 (br s, 1H), 3.28−3.21 (m, 1H), 2.18−2.13 (m, 2H), 1.87−1.38 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ [152.1, 151.1 (syn, anti)], [148.1, 148.0 (syn, anti)], 129.0, [128.3, 128.1 (syn, anti)], [127.8, 127.7 (syn, anti)], [122.0, 121.9 (syn, anti)], [120.2, 120.0 (syn, anti)], [75.6, 75.5 (syn, anti)], [59.2, 58.9 (syn, anti)], [44.1, 43.9 (syn, anti)], [29.9, 29.7 (syn, anti)], [28.7, 28.4 (syn, anti)], 26.0, [25.5, 25.4 (syn, anti)], 22.2; HRMS calcd for $C_{28}H_{33}N_3O$ (M^+) 427.2625, found 427.2606. Trans isomer: ^{1}H NMR (by difference) (500 MHz, $CDCl_3$) δ 7.42−7.21 (m, 9H), 7.13−7.05 (m, 4H), 7.07−6.91 (m, 2H), {6.62[t, J = 5.5 Hz cis], 6.58 [t, J = 5.62 Hz trans], 1H (syn) (anti hidden under 7.42−7.21)}, 5.08−5.01 [s, 2H (syn, anti)], 3.85 (br s, 1H), 3.07−3.04 (m, 1H), 2.17−2.12 (m, 2H), 1.88−1.35 (m, 11H).

***cis*- and *trans*-4-[2-(*N*,*N*-Diphenylhydrazino)cyclopentyl]butanal(*N*,*N*-dimethylhydrazone) (14).** *N*,*N*-Dimethylhydrazine (34 mg, 0.564 mmol) was added to a solution of aldehyde **23** (50 mg, 0.153 mmol) in dry CH_2Cl_2 (1.5 mL). The resulting solution was stirred overnight at 40 °C. The reaction was concentrated and chromatographed (2:5 ether/pet ether) to afford 45 mg (80%) of **14** as a faint yellow oil. Cis isomer: IR (neat) 2909, 1591, 1482, 1029, 748, 696 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30−7.22 (m, 4H), 7.23−7.11 (m, 4H), 6.98−6.91 (m, 2H), 6.66−6.65 (m, 1H), 3.99−3.98 (br s, 1H), 3.27−3.23 (m, 1H), 2.68 (s, 6H), 2.24−2.16 (m, 2H), 1.85−1.39 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.0, 138.9, 128.9, 121.8, 120.2, 58.8, 44.2, 43.4, 33.1, [29.9, 29.6 (syn, anti)], 29.5, 28.5, 26.5, 22.2; FAB accurate mass calcd for $C_{23}H_{33}N_4$ (M^+ + 1) 365.2706, found 365.3281. Anal. Calcd for $C_{23}H_{32}N_4$: C, 75.78; H, 8.84; N, 15.36. Found: C, 75.59; H, 8.90; N, 15.23. Trans isomer: ^{1}H NMR (by difference) (500 MHz, $CDCl_3$) δ 7.35−7.23 (m, 4H), 7.19−7.11 (m, 4H), 6.97−6.93 (m, 2H), 6.55 (t, J = 5.5 Hz, 1H), 3.98−3.96 (br s, 1H), 3.05−3.03 (m, 1H), 2.67 (s, 6H), 2.20−2.17 (m, 2H), 2.16−1.34 (m, 11H);^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 139.2, 128.7, 121.9, 120.3, 63.8, 43.9, 43.4, 34.1, 31.4, 30.7, 28.5, 26.4, 23.6.

***cis*- and *trans*-4-[2-(*N*,*N*-Diphenylhydrazino)cyclopentyl]butanal(*N*-benzoylhydrazone) (15).** Benzoylhydrazine (33.7 mg, 0.248 mmol) and aldehyde **23** (50 mg, 0.155 mmol) were stirred in dry CH_2Cl_2 (1 mL) at 21 °C for 4 h. The reaction was concentrated and chromatographed (1:24, ether/CH_2Cl_2) to yield 55 mg (80%) of **15** as a viscous oil. Cis isomer: IR (neat) 3226, 3052, 2937, 2865, 1648, 1586, 1494, 1289, 1075, 1028, 909, 748, 696 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.1 (br s, 1H), 7.77−7.73 (m, 2H), 7.48−7.31 (m, 4H), 7.28−7.16 (m 4H), 7.12−7.02 (m, 4H), 6.99−6.90 (m, 2H), 3.80−3.79 (br s, 1H), 3.28−3.25 (m, 1H), 2.31−2.27 (m, 2H), 1.88−1.35 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.2, 152.2, 148.0, 148.0, 131.8, 129.0, 128.6, 127.3, 122.1, 120.3, 59.1, 44.1, 32.1, 29.6, 28.5, 28.5, 25.8, 22.1; HRMS calcd for $C_{28}H_{32}N_4O$ (M^+) 440.2577, found 440.2578. Trans isomer: ^{1}H NMR (500 MHz, $CDCl_3$) (by difference), δ 8.96 (br s, 1H), 7.75−7.74 (m, 2H), 7.49−7.39 (m, 4H), 7.27−7.22 (m, 4H), 7.19−7.09 (m, 4H), 6.97−6.92 (m, 2H), 3.70 (br s, 1H), 3.07−3.05 (m, 1H), 2.48−2.34 (m, 2H), 1.86−1.40 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 152.2, 147.1, 147.1, 131.8, 129.0, 128.7, 127.2, 122.2, 120.2, 59.5, 44.1, 33.9, 31.2, 30.7, 30.6, 25.2, 23.4.

***cis*- and *trans*-2-(4-*tert*-Butyldimethylsilyloxybutyl)-1-(*N*,*N*-diphenylhydrazino)cyclopentane (21).** Following the general procedure for the radical cyclization tributyltin hydride (0.390 mL, 1.45 mmol) and AIBN (53 mg, 0.33 mmol) were added to the hydrazone **2** (X = Br) (500 mg, 0.96 mmol) in dry benzene (15.6 mL). The product mixture was chromatographed (3:1 ether/pet ether) to obtain 424 mg (96%) of a 3:1 mixture of cis and trans **21** as a faint yellow oil. Cis isomer: IR (neat) 3061, 2939, 2858, 1591, 1495, 1467, 1259, 1099, 838, 748, 695 cm^{-1}; ^{1}H NMR, (200 MHz, $CDCl_3$) δ 7.32∠7.20(m, 4H), 7.16−7.10 (m, 4H), 6.97 (t, J = 6.9 Hz, 2H), 3.89 (br s, 1H), 3.58 (t, J = 6.3 Hz, 2H), 3.31−3.27 (m, 1H), 1.88−1.70 (m, 4H), 1.69−1.25 (m, 9H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.0, 129.0, 121.9, 120.2, 63.1, 59.0, 44.3, 33.0, 29.9, 29.5, 28.8, 25.9, 25.1, 22.2, 18.3, ∠5.1. Trans isomer: ^{1}H NMR (by difference) (500 MHz, $CDCl_3$) δ 7.25 (t, J = 7.8 Hz, 4H), 7.1 (d, J = 8.2 Hz, 4H), 6.97 (t, J = 7.2 Hz, 2H), 3.86 (br s, 1H), 3.55 (t, J = 6.5 Hz, 2H), 3.06−3.02, (m, 1H), 2.13−1.2 (m, 13 H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) 147.9, 128.9, 121.9, 120.1, 63.7, 63.1, 44.0, 34.4, 32.9, 31.4, 30.6, 25.9, 24.4, 23.6, 18.3, −5.1; HRMS calcd for $C_{27}H_{42}N_2OSi$ (M^+) 438.3068, found 438.3061. Anal. calcd for $C_{27}H_{42}N_2OSi$: C, 73.86; H, 9.67; N, 6.3. Found C, 73.68; H, 9.77; N, 6.48.

***cis*- and *trans*-2-(4-Hydroxybutyl)-1-(*N*,*N*-diphenylhydrazino)cyclopentane (22).** Tetrabutylammonium fluoride (1.12 mL of 1M soln. in THF, 1.12 mmol) was added to compound **21** (408 mg, 0.931 mmol) in dry THF (7.5 mL) at 0 °C, and the resulting solution was stirred overnight. The reaction was quenched with water (5 mL) and extracted with ether. The combined organic extracts were washed with brine (2 × 10 mL), concentrated, and chromatographed (1:2.5 ether/pet ether) to afford 258 mg (86%) of **22** as a faint yellow oil. Cis isomer: IR (neat) 3348, 2937, 2865, 1590, 1495, 1290, 1052, 748, 696 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.34−7.23 (m, 4H), 7.19−7.15 (m, 4H), 6.99−6.96 (m, 2H), 3.92 (br s, 1H), 3.58 (q, 1H), 3.30−3.26 (m, 1H), 1.91−1.30 (m, 13H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.0, 128.9, 121.8, 120.1, 62.5, 58.9, 44.2, 32.7, 29.8, 29.5, 28.6, 24.8, 22.2. Trans isomer: ^{1}H NMR (by difference) (500 MHz, $CDCl_3$) δ 7.30−7.20 (m, 4H), 7.16−7.13 (m, 4H), 6.99−6.95 (m, 2H), 3.80 (br s, 1H), 3.55 (t, J = 6.6 Hz, 2H), 3.08−3.07 (m, 1H), 1.89−1.76 (m, 3H), 1.65−1.28 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) 147.7, 128.8, 121.7, 120.0, 63.5, 62.4, 43.8, 34.2, 32.6, 31.3, 30.5, 24.2, 23.5; HRMS calcd for $C_{21}H_{28}N_2O$ (M^+) 324.2202, found 324.2219.

***cis*- and *trans*-4-[2-(*N*,*N*-Diphenylhydrazino)cyclopentyl]butanal (23).** A suspension of pyridine−sulfur trioxide complex (380 mg, 0.81 mmol) in DMSO (3 mL) was added to a solution of the alcohol **22** (258 mg, 0.79 mmol) and triethylamine (0.90 mL, 6.45 mmol) in DMSO (5.6 mL) at 21 °C. The reaction was quenched with water and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (2 × 10 mL), dried, and concentrated to give 250 mg (97%) of **23** as a faint yellow oil. Compound **23** could not be further purified due to its instability on silica gel. For **23**: IR (neat) 2915, 2351, 1723, 1590, 1493, 1292, 749, 696 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.48−6.92 (m, 10 H), 3.96 (br s, 1H), 3.35−3.21 (m, 1H), 2.48−2.39 (m, 2H), 1.99−1.45 (m, 11H).

***cis*- and *trans*-4-[2-(*N*,*N*-Diphenylhydrazino)cyclopentyl]butanal[*N*-(*p*-toluenesulfonyl)-hydrazone] (24).** *p*-Toluenesulfonylhydrazine (32 mg, 0.175 mmol) and aldehyde **23** (47 mg, 0.146 mmol) were stirred in ethanol (1 mL) at 21 °C for 1 h. The reaction was concentrated and chromatographed (2:5 ether/pet ether) to afford 45 mg (63.3%) of **24** as a faint yellow viscous oil: IR (neat) 3207, 3092, 2914, 1591, 1479, 1320, 1165, 1059, 909, 813, 748, 684 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84−7.75 (m, 2H), 7.29−7.22 (m, 6H), 7.15−7.08 (m, 4H), 7.07−6.94 (m, 3H), 6.63 [t, J = 5.2 Hz (anti) (syn hidden under 7.07−6.94), 1H], 3.74 (br s, 1H), [3.23−3.21 (m, cis), 2.99−2.96 (m, trans), 1H], 2.45−2.36 [overlapping s (cis, trans, syn, anti), 3H], 2.21−2.10 (m, 2H), 1.91−1.25 (m, 11H). Cis isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ [152.7, 152.2 (syn, anti)], 148.1, 143.9, 135.3, 129.5, 129.0, 127.9, 122.0, 120.3, [59.4, 59.1 (syn, anti)], 44.1, [33.7, 32.3 (syn, anti)], 29.7, 29.6, [28.5, 28.3 (syn, anti)], 25.2, [22.1, 22.0 (syn, anti)], 21.5. Trans isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ [152.7, 151.2 (syn, anti)], 147.9, 143.9, 135.3, 129.6, 129.0, 128.0, 122.0, 120.1, 63.6, 43.7, 33.7, 31.3, 30.6, 29.6, [24.8, 24.7 (syn, anti)], 23.4, 21.5; HRMS calcd for $C_{28}H_{34}N_4O_2S$ (M^+) 490.2405, found 490.2445.

***cis*- and *trans*-4-[2-(*N*,*N*-Diphenylhydrazino)cyclopentyl]butanal[*N*-(2,4,6-trimethylbenzenesulfonyl)hydrazone] (25).** 2,4,6-Trimethylbenzenesulfonylhydrazine (37 mg, 0.175 mmol) and aldehyde **23** (47 mg, 0.146 mmol) were stirred in ethanol (1 mL) at 21 °C for 1 h. The reaction was

concentrated and chromatographed (2:5 ether/pet ether) to afford 42 mg (55%) of **25** as a faint yellow oil: IR (neat) 3214, 2916, 1591, 1474, 1314, 1159, 1046, 852, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27−7.22 (m, 4H), 7.11−7.05 (m, 4H), 7.01−6.95 (m, 2H), 6.93−6.90 [overlapping s, 2H, (syn, anti)], 6.57 [t, J = 5.3 Hz (anti), (syn hidden under 7.01−6.95), 1H], 3.82−3.74 (br s, 1H), [3.22−3.20 (m, cis), 2.98−2.96 (m, trans) 1H], 2.67−2.60 [overlapping s, 6H], 2.30−2.25 (s, 3H), 2.22−2.08 (m, 2H), 1.88−1.70 (m, 4H), 1.67−1.66 (m, 3H), 1.59−1.30 (m, 4H). Cis isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 148.1, 142.7, 140.6, 132.3, 131.8, 129.0, 122.1, 120.2, 59.2, 44.0, [32.3, 32.2 (syn, anti)], 29.6, 29.5, 28.2, 25.1, 23.0, 22.0, 20.9. Trans isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 147.9, 142.7, 140.0, 132.3, 131.8, 129.0, 122.0, 120.1, 63.6, 43.8, 33.7, 31.3, 30.6, 24.5, 23.4, 23.0, 22.0, 20.9; HRMS calcd for $C_{30}H_{38}N_4O_2S$ (M^+) 518.2717, found 518.2725.

2-(4-*tert*-Butyldimethylsilyloxybutyl)cyclopentanone (26). *n*-Butyllithium (14.35 mL of 2.5 M solution, 35.8 mmol) was added dropwise to a cold solution (−78 °C) of diisopropylamine (4.16 g, 41.11 mmol) in dry THF (42.6 mL). This solution was stirred for 15 min, and then cyclopentanone (2.7 g, 33.12 mmol) in THF (21.2 mL) was added and stirred for a further 20 min. HMPA (27.73 mL, 163.8 mmol) was added, followed by dimethyl zinc (16.3 mL of 1 M solution, 16.3 mmol) and $ICH_2CH_2CH_2CH_2OTBDMS$ (2.6 g, 8.28 mmol) as a solution in THF (32.2 mL). The reaction was stirred at −78 °C for 4 h and then warmed to 21 °C. The reaction was quenched with aqueous NH_4Cl (50 mL) and extracted with ether (3 × 150 mL). The combined organic extracts were washed with brine (3 × 50 mL), dried, concentrated, and chromatographed (6% ether/pet ether) to afford 1.34 g (60%) of **26** as a clear colorless oil: IR (neat) 2942, 2859, 1740, 1465, 1360, 1253, 1152, 1100, 1006, 840, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.57 (t, J = 6.45 Hz, 2H), 2.29−2.16 (m, 2H), 2.10−1.94 (m, 3H), 1.78−1.72 (m, 2H), 1.54−1.50 (m, 3H), 1.45−1.31 (m, 2H), 1.26−1.20 (m, 1H), 0.85 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 221.3, 62.9, 49.1, 38.1, 32.7, 29.5, 29.4, 25.9, 23.8, 20.7, 18.3, −5.3; HRMS calcd for $C_{11}H_{21}O_2Si$ (M^+−*t*-Bu) 213.1312, found 213.1315. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.68; H, 11.17. Found: C, 66.65; H, 10.94.

2-[(4-*tert*-Butyldimethylsilyloxy)butyl]cyclopentanone-*O*-methyloxime (27). Methoxyamine hydrochloride (102 mg, 1.22 mmol) was added to a solution of ketone **26** (300 mg, 1.11 mmol) in dry ethanol (5 mL) at 0 °C, followed by the addition of pyridine (107 μL, 1.33 mmol), and the reaction was stirred at 0 °C. The reaction was concentrated and chromatographed (1:20, ether/pet ether) to yield 290 mg (87%) of **27** as a clear colorless oil: IR (neat) 2942, 2859, 1486, 1387, 1361, 1253, 1100, 1052, 1006, 841, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.54 (t, J = 6.4 Hz, 2H), 2.46−2.35 (m, 2H), 2.28−2.21 (m, 1H), 1.92−1.86 (m, 1H), 1.77−1.64 (m, 2H), 1.57−1.41 (m, 3H), 1.39−1.24 (m, 4H), 0.83 (s, 9H), −0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, [62.9, 62.8, (syn, anti)], 61.1, [43.1, 39.7 (syn, anti)], 32.8, 32.3, 31.4, 27.5, 25.8, 23.9, 22.5, 18.2, −5.3; HRMS calcd for $C_{16}H_{33}NO_2Si$ (M^+) 299.2282, found 299.2286.

2-[4-(*tert*-Butyldimethylsilyloxy)butyl]cyclopentanone-*O*-benzyloxime (28). Benzyloxyamine hydrochloride (150 mg, 0.937 mmol) was added to a stirred solution of ketone **26** (230 mg, 0.852 mmol) at 0 °C, followed by the addition of pyridine (83 μL, 1.02 mmol). The reaction was worked up immediately and chromatographed (1:10, ether/pet ether) to afford 275 mg (86%) of **28** as a faint yellow oil: IR (neat) 2941, 2858, 2362, 1462, 1253, 1049, 1036, 839, 776, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36−7.23 (m, 5H), 5.07 (s, 2H), 3.5 (t, J = 6.4 Hz, 2H), 2.57−2.34 (m, 3H), 1.97−1.70 (m, 3H), 1.62−1.45 (m, 3H), 1.39−1.29 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 130.4, 128.1, 127.9, 127.4, 75.4, [63.1, 62.9 (syn, anti)], [43.2, 40.1 (syn, anti)], [32.8, 32.7 (syn, anti)], [32.7, 31.0 (syn, anti)], [31.5, 30.6 (syn, anti)], 28.0, 25.9, [23.8, 23.6 (syn, anti)], [23.0, 22.5 (syn, anti)], 18.3, −5.3; HRMS calcd for $C_{22}H_{37}NO_2Si$ (M^+) 375.2595, found 375.2586.

2-[4-(*tert*-Butyldimethylsilyloxy)butyl]cyclopentanone-*N*,*N*-dimethylhydrazone (29). *N*,*N*-Dimethylhydrazine (77 μL, 1.02 mmol) was added to a solution of the ketone **26** (250 mg, 926 mmol) in dry CH_2Cl_2 (1.5 mL). The resulting solution was stirred overnight at 40 °C. The reaction was concentrated and chromatographed (1:1 ether/pet ether) to afford 121 mg (42%) of **29** as a faint yellow oil: IR (neat) 2943, 2858, 1654, 1468, 1387, 1253, 1100, 975, 840, 776; ^1H NMR (500 MHz, $CDCl_3$) δ 3.51 (t, J = 6.5 Hz, 2H), 2.47−2.41 (m, 1H), 2.38 (s, 6H), 2.35−2.20 (m, 2H), 1.88−1.61 (m, 3H), 1.55−1.17 (m, 7H), 0.80 (s, 9H), −0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 63.0, 46.9, 44.4, 33.0, 32.9, 30.2, 29.3, 25.8, 23.8, 22.7, 18.1, −5.4; HRMS calcd for $C_{17}H_{36}N_2OSi$ (M^+) 312.2598, found 312.2600.

2-[4-(*tert*-Butyldimethylsilyloxy)butyl]cyclopentanone-*N*-benzoylhydrazone (30). Benzoylhydrazine (122 mg, 0.88 mmol) and ketone **26** (200 mg, 0.74 mmol) were stirred in dry toluene (8 mL) at 21 °C for 4 h. The reaction was concentrated and chromatographed (1:24, ether/CH_2Cl_2) to yield 178 mg (62%) of **30** as a viscous oil: IR (CCl_4) 3180, 3069, 2913, 1657, 1577, 1463, 1383, 1254, 1102 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.58 (br s, 1H), 7.85−7.65 (m, 2H), 7.43−7.34 (m, 3H), 3.54 (m, 2H), 2.52−2.17 (m, 3H), 2.02−1.67 (m, 4H), 1.59−1.19 (m, 6H), 0.83 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.9, 163.3, 133.5, [131.4, 131.2 (syn, anti)], [128.1, 128.0 (syn, anti)], [127.3, 127.0 (syn, anti)], 62.9, 44.7, 32.7, 32.1, 30.6, 27.6, 25.8, 23.8, 22.4, 18.1, −0.05; HRMS calcd for $C_{22}H_{36}N_2O_2Si$ (M^+) 388.2547, found 388.2517.

2-[4-(*tert*-Butyldimethylsilyloxy)butyl]cyclopentanone-*N*-(*p*-toluenesulfonyl)hydrazone (31). *p*-Toluenesulfonylhydrazine (163 mg, 0.88 mmol) and ketone **26** (200 mg, 0.74 mmol) were stirred in ethanol (3 mL) at 21 °C for 1 h. The resulting solution was concentrated and chromatographed (2:5 ether/pet ether) to afford 213 mg (66%) of **31** as a faint yellow viscous oil: IR (neat) 3212, 2911, 1660, 1597, 1461, 1398, 1369, 1254, 1166, 1096, 924, 829, 776, 679 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 6.9 Hz, 2H), 7.39 (br s, 1H), 7.26 (d, J = 10.9 Hz, 2H), 3.55−3.51 (m, 2H), 2.39 (s, 3H), 2.36−2.20 (m, 2H), 2.09−2.03 (m, 2H), 1.93−1.79 (m, 2H), 1.66−1.39 (m, 2H), 1.27−1.11 (m, 4H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 143.7, 135.9, 129.3, 128.0, 63.0, 44.7, 32.8, 31.6, 31.1, 28.0, 25.9, 23.5, 22.5, 21.5, 18.3, −5.2; HRMS calcd for $C_{18}H_{29}N_2O_3SSi$ (M^+−*t*-Bu) 381.1669, found 381.1655.

2-(4-Hydroxybutyl)cyclopentanone-*O*-methyloxime (32). Tetrabutylammonium fluoride (0.609 mL of 1 M solution in THF, 0.609 mmol) was added to the oxime ether **27** (190 mg, 0.609 mmol) in dry THF (4.2 mL) at 0 °C, and the resulting mixture was stirred overnight. The reaction was quenched with water (2 mL) and extracted with ether. The combined organic extracts were washed with brine (2 × 10 mL), dried, concentrated, and chromatographed (2:3, ether/hexanes) to afford 150 mg (80%) of **32** as a faint yellow oil: IR (neat) 3369, 2914, 2363, 1652, 1450, 1176, 1053, 873, 847 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.79−3.60 [overlapping s, 3H (syn, anti)], 3.56−3.44 (m, 2H), 3.06 (br s, 1H), 2.44−2.10 (m, 2H), 1.89−1.10 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.2, [62.0, 61.9 (syn, anti)], [42.9, 39.6 (syn, anti)], [32.3, 31.8 (syn, anti)], [31.2, 30.4 (syn, anti)], [30.7, 30.6 (syn, anti)], 27.4, 23.5, 22.7, 22.3; HRMS calcd for $C_{10}H_{19}NO_2$ (M^+) 185.1416, found 185.1397.

2-(4-Hydroxybutyl)cyclopentanone-*O*-benzyloxime (33). Tetrabutylammonium fluoride (0.806 mL of 1 M solution in THF, 0.806 mmol) was added to a solution of the oxime ether **28** (275 mg, 0.733 mmol) in dry THF (5 mL) at 0 °C, and the resulting solution was stirred overnight. The reaction was quenched with water (2 mL) and extracted with ether. The combined organic extracts were washed with brine (2 × 10 mL), dried, concentrated, and chromatographed (1:1, ether/pet ether) to afford 133 mg (87%) of **33** as a faint yellow oil. IR (neat) 3365, 2936, 2863, 1496, 1454, 1365, 1037, 906, 737, 698 cm^{-1};^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.23 (m, 5H), 5.03 (s, 2H), [3.56 (t, J = 6.4 Hz), 3.52 (t, J = 6.5 Hz), 2H (syn, anti)], 2.56−2.31 (m, 4H), 1.84−1.66 (m, 3H), 1.61−1.51 (m, 3H), 1.49−1.30 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ [169.0, 168.8 (syn, anti)], [138.3, 138.2 (syn, anti)], [128.2, 128.1 (syn anti)], [127.9, 127.8 (syn, anti)], [127.5, 127.4 (syn, anti)], 75.4, [65.7, 62.4 (syn, anti)], [41.1, 39.9 (syn, anti)], [32.5, 30.1 (syn, anti)], [31.9, 30.6 (syn, anti)], [31.5, 30.6 (syn, anti)], 28.0, [23.5,

22.9 (syn, anti)], 22.5; HRMS calcd for $C_{16}H_{23}NO_2(M^+)$ 261.1729, found 261.1751.

***cis*- and *trans*-2-[4-(*t*-Butyldimethylsilyloxy)butyl]-1-(*N*,*N*-dimethylhydrazino)cyclopentane (34).** A suspension of sodium cyanoborohydride (12.6 mg, 0.199 mmol), the dimethylhydrazone **29** (50 mg, 0.166 mmol) and a few milligrams of Bromocresol Green in dry MeOH (1 mL) was stirred under nitrogen. A solution of *p*-toluenesulfonic acid (190 mg, 1 mmol) in MeOH (1 mL) was slowly added at 0 °C to maintain the pH at 3.5. The reaction mixture was stirred at 0 °C for 1 h, quenched with water, and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (2 × 3 mL), dried, filtered, concentrated, and chromatographed (1:1, ether/pet ether) to afford 25 mg (50%, 1:1.4 mixture of cis and trans) of **34** as a faint yellow viscous oil: IR (neat) 3395, 2909, 2361, 1464, 1253, 1100, 839 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.59−3.55 [overlapping t, 2H (*cis*, *trans*)], [3.22−3.20 (m, cis), 2.93−2.89 (m, trans), 1H], 1.87−1.20 (m, 13 H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ [64.0, 59.6 (cis, trans)], [63.2, 63.0 (cis, trans)], [47.6, 46.9 (cis, trans)], [44.2, 43.4 (cis, trans)], [34.5, 33.5 (cis, trans)], [33.0, 31.3 (cis, trans)], [32.1, 31.1 (cis, trans)], [29.5, 28.5 (cis, trans)], 25.9, [24.8, 24.5 (cis, trans)], [22.5, 21.8 (cis, trans)], 18.2, −5.3; FAB accurate mass calcd for $C_{17}H_{39}N_2OSi$ ($M^+ + 1$) 315.2833, found 315.3075.

***cis*- and *trans*-2-[4-(*tert*-Butyldimethylsilyloxy)butyl]-1-(*N*-benzoylhydrazino)cyclopentane (35).** Sodium borohydride (40 mg, 1.12 mmol) was added to a solution of the benzoylhydrazone **30** (220 mg, 0.563 mmol) in dry methanol (4 mL), and the resulting mixture was stirred overnight at 21 °C. The reaction was quenched with acetone (3 mL) and extracted with ether (3 × 25 mL). The combined organic extracts were washed with brine, dried, concentrated, and chromatographed (2% $MeOH/CH_2Cl_2$) to afford 124 mg (56%, 1:1.2 mixture of cis and trans) of **35** as a faint yellow oil: IR (neat) 3277, 2911, 2352, 1638, 1577, 1457, 1253, 1097, 817 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75−7.71 (m, 2H), 7.49−7.23 (m, 3H), [3.59, t, J = 6.4 Hz (cis), 3.54, t, J = 6.5 Hz (trans), 2H], [3.51−3.43, m (cis), 3.17−3.10, m, (trans), 1H], 1.89−1.15 (m, 13H), [0.86, 0.85 overlapping s (cis, trans) 9H], [0.25, 0.00 overlapping s (cis, trans), 6H]. Cis isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 133.0, 131.6, 128.5, 126.7, 63.3, 63.1, 43.9, 33.0, 30.3, 29.3, 29.1, 25.9, 24.9, 21.8, 15.1, −5.3. Trans isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 132.9, 131.6, 128.5, 128.5, 67.3, 63.0, 44.2, 34.5, 32.9, 31.2, 31.0, 25.9, 24.4, 23.1, 15.1, −5.3; HRMS calcd for $C_{22}H_{38}N_2O_2Si$ (M^+) 390.2704, found 390.2685.

***cis*- and *trans*-2-[4-(*tert*-Butyldimethylsilyloxy)butyl]-1-[*N*-(*p*-toluenesulfonylhydrazino)]cyclopentane (36).** A suspension of sodium cyanoborohydride (34 mg, 0.545 mmol), *p*-toluenesulfonylhydrazone **31** (200 mg, 0.448 mmol), and a few milligrams of bromocresol green in dry THF (10 mL) was stirred under nitrogen. A solution of *p*-toluenesulfonic acid (190 mg, 1.0 mmol) in THF (1 mL) was then slowly added at 0 °C to maintain the pH at 3.5, indicated by the tan color of the indicator. The reaction mixture was stirred at 21 °C for 18 h, quenched with water, and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (2 × 10 mL), dried, filtered, concentrated, and chromatographed (1:1, ether/pet ether) to afford 100 mg (50%, 1.3:1.0 mixture of cis and trans) of **36** as a faint yellow viscous oil: IR (neat) 3245, 2940, 2859, 1598, 1466, 1321, 1251, 1160, 1097, 838, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.27−7.26 (m, 2H), 3.58−3.52 (overlapping t, 2H), [3.12−3.11, m (cis), 2.78−2.76, m (trans), 1H], [2.39, 2.36, overlapping s (cis, trans), 3H], 1.73−1.01 (m, 13H), 0.85 (s, 9H), 0.01 (s, 6H). Cis isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 135.6, 129.4, 128.1, 63.1, 62.6, 43.3, 33.0, 30.7, 29.5, 28.6, 25.9, 24.9, 21.5, 21.3, 18.3, −5.3. Trans isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 135.6, 129.2, 128.1, 63.3, 62.2, 43.8, 34.1, 33.0, 30.5, 29.2, 25.9, 24.3, 22.7, 21.3, 18.3, −5.3.

***cis*- and *trans*-4-[2-(*N*-Methoxylamino)cyclopentyl]-1-butanol (37).** A suspension of sodium cyanoborohydride (76 mg, 1.216 mmol), the *O*-methyloxime **32** (150 mg, 0.811 mmol), and a few milligrams of bromocresol green in methanol (5 mL) was stirred under nitrogen. A solution of *p*-toluenesulfonic acid (190 mg, 1 mmol) in methanol (1 mL) was slowly added at 21 °C to maintain the pH at 3.5. The reaction was stirred at 21 °C for 3 h, quenched with water, and extracted with ether (3 × 5 mL). The combined organic extracts were washed with brine (2 × 5 mL), dried, filtered, concentrated, and chromatographed (1:20, ether/pet ether) to afford 90 mg (60%, 1:2 mixture of cis and trans) of **37** as a clear colorless oil: IR (neat) 3342, 2909, 1453, 1360, 1034, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.58−3.55 [overlapping t (cis, trans), 2H], [3.47, 3.45 overlapping s (cis, trans), 3H] [3.36−3.35, 3.04−3.01 m (cis, trans), 1H] 1.82−1.64 (m, 3H), 1.58−1.29 (m, 8H), 1.22−1.10 (m, 2H). Cis isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ 67.3, 62.6, 61.9, 43.0, 34.5, 32.8, 31.4, 30.4, 24.7, 23.3. Trans isomer ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.9, 62.5, 61.6, 43.0, 32.7, 29.8, 29.4, 28.4, 24.7, 21.8; HRMS calcd for $C_{10}H_{21}NO_2$ (M^+) 187.1533, found 187.1557.

***cis*- and *trans*-4-[2-(*N*-Benzyloxyamino)cyclopentyl]-1-butanol (38).** A suspension of sodium cyanoborohydride (32 mg, 0.509 mmol), the *O*-benzyloxime **33** (133 mg, 0.509 mmol), and a few milligrams of bromocresol green in methanol (5 mL) was stirred under nitrogen. A solution of *p*-toluenesulfonic acid (190 mg, 1 mmol) in methanol (1 mL) was then slowly added at 21 °C to maintain the pH at 3.5. The reaction was stirred at 21 °C for 3 h, quenched with water, and extracted with ether (3 × 5 mL). The combined organic extracts were washed with brine (2 × 5 mL), dried, filtered, concentrated, and chromatographed (1:20, ether/pet ether) to afford 90 mg (67%, 1:2 mixture of cis and trans) of **38** as a clear colorless oil: IR (neat) 3353, 2910, 2361, 1453, 1361, 1035, 742, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.23 (m, 5H), [4.69, 4.67, s (cis, trans), 2H], [3.60−3.56 overlapping s (cis, trans, syn, anti), 2H], [3.43−3.42 (m, cis), 3.12−3.09 (m, trans) 1H], 1.85−1.13 (m, 14H). Cis isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 128.3, 128.1, 127.6, 76.3, 67.5, 62.7, 43.0, 34.5, 32.8, 31.4, 30.6, 24.3, 23.4. Trans isomer 13C NMR (125 MHz, $CDCl_3$) δ 137.9, 128.3, 128.2, 127.6, 75.4, 63.0, 62.6, 43.1, 34.5, 29.8, 29.5, 28.5, 24.7, 21.8; HRMS calcd for $C_{16}H_{25}NO_2$ (M^+) 263.1886, found 263.1861.

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