12 h. The solvent was removed in vacuo to yield a light yellow oil. To a suspension of PCC (4.38 g, 20 mmol) and Florosil (4.5 g) in 40 mL of anhydrous methylene chloride at −10 °C was added the alcohol (12.7 mmol). The suspension was allowed to slowly warm to ambient temperature over 20 h. The suspension was filtered through silica gel with 2:1 H:EA. The filtrate was concentrated to afford a residue. This residue was purified by flash chromatography on silica gel with 9:1 H:EA to afford 1.68 g (57% yield) of ketone **3**. This compound was a white solid with mp 70–71 °C. NMR ($CDCl_3$): δ 2.50 (dd, J = 9.6, 18 Hz, 1 H), 2.81 (dd, J = 6.0, 18 Hz, 1 H), 3.98 (d, J = 17.1 Hz, 1 H), 4.22 (d, J = 17.1 Hz, 1 H), 5.19 (dd, J = 6, 9.6 Hz, 1 H), 5.79 (s, 2 H), 6.79–6.90 (m, 3 H). IR (CH_2Cl_2): 1755, 1500, 1440, 1250, 1050, 1035, 940, 810, 735 cm^{-1}. MS: m/z 89, 135, 147, 148, 163, 176, 206. HRMS: calcd for $C_{11}H_{10}O_4$ 206.0579, found 206.0577. TLC (3:1 H:EA): R_f = 0.46.

5-(1,3-Benzodioxol-5-yl)-4-(hydroxymethyl)tetrahydrofuran-3-one (5). To a solution of lithium diisopropylamide (prepared from 2.1 mmol of diisopropylamine and 2.0 mmol of *n*-butyllithium) in 4 mL of THF at −78 °C was added ketone **3** (0.412 g, 2.0 mmol) in 1 mL of THF. The solution was stirred at −78 °C for 30 min, and gaseous formaldehyde (prepared by heating 20 mmol of paraformaldehyde at 150 °C with a nitrogen stream) was introduced into the solution. The reaction was quenched with acetic acid (0.25 g, 4.1 mmol). Methylene chloride and water were added. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel with 2:1 H:EA to provide 0.169 g (50%) of hydroxy ketone **5**. NMR ($CDCl_3$): δ 2.02 (bt, J = 3 Hz, 1 H), 2.44–2.53 (m, 1 H), 3.95–4.05 (m, 1 H), 3.97 (d, J = 17 Hz, 1 H), 4.36 (d, J = 17 Hz, 1 H), 5.02 (d, J = 10.2 Hz, 1 H), 5.98 (s, 2 H), 6.79–6.96 (m, 3 H). IR ($CHCl_3$): 3460, 2878, 1750, 1485, 1440, 1245, 1035, 905, 730 cm^{-1}. TLC (2:1 H:EA): R_f = 0.22.

5-(1,3-Benzodioxol-5-yl)-4-[(1,3-benzodioxol-5-ylmethoxy)methyl]-tetrahydrofuran-3-one (2). To a solution of hydroxy ketone 3 (0.130 g, 0.55 mmol) and 1,3-benzodioxol-5-ylmethyl trichloroacetimidate (0.356 g, 1.20 mmol) in 5 mL of methyene chloride at ambient temperature was added a crystal of camphorsulfonic acid. The solution was stirred for 44 h. The solution was diluted with brine and was extracted twice with ether. The organic layer was dried and concentrated. The residue was purified by chromatography on silica gel with 10:1 H:EA to provide 0.075g (42% yield) of **2**. Ketone **2** was a viscous oil. NMR ($CDCl_3$): δ 2.41–2.43 (m, 1 H), 3.50 (dd, J = 3.3, 9.6 Hz, 1 H), 3.83 (dd, J = 3.3, 9.6 Hz, 1 H), 3.97 (d, J = 17.1 Hz, 1 H), 4.31 (d, J = 17.1 Hz, 1 H), 4.32 (d, J = 11.7 Hz, 1 H), 4.43 (d, J = 11.7 Hz, 1 H), 5.11 (d, J = 9.9 Hz, 1 H), 5.95 (s, 2 H), 5.96 (s, 2 H), 6.70–6.86 (mm, 6 H). IR ($CHCl_3$): 2880, 1754, 1485, 1440, 1245, 1035, 905, 725 cm^{-1}. MS: m/z 77, 135, 149, 205, 218, 235, 260, 370. HRMS: calcd for $C_{20}H_{18}O_7$ 370.1053, found 370.1049. TLC (3:1 H:EA) R_f = 0.35.

Paulownin (1). A solution of **2** (0.030 g, 0.081 mmol) in 20 mL of benzene was degassed with argon. The solution was irradiated with a medium-pressure Hanovia lamp for 1 h. The solution was concentrated. The residue was purified by chromatography on silica gel with 5:1 H:EA to afford 0.0165 g (68% based on recovered **2**) of **1**. Alcohol **1** was a white solid with mp 82–85 °C. Both the proton NMR and the ^{13}C NMR were identical with those reported in the literature. NMR ($CDCl_3$): δ 1.62 (s, 1 H), 3.04–0.06 (m, 1 H), 3.83 (dd, J = 6.3, 9 Hz, 1 H), 3.91 (d, J = 9.3 Hz, 1 H), 4.04 (d, J = 9.3 Hz, 1 H), 4.51 (dd, J = 8.1, 9 Hz, 1 H), 4.82 (s, 1 H), 4.84 (d, J = 5.1 Hz, 1 H), 5.96 (s, 2 H), 5.98 (s, 2 H), 6.78–6.94 (m, 6 H). ^{13}C NMR ($CDCl_3$): 60.40, 71.63, 74.76, 85.77, 87.47, 91.65, 101.10, 101.23, 106.87, 107.37, 108.19, 108.57, 119.77, 120.07, 129.21, 134.56, 147.24, 147.98. IR ($CHCl_3$): 3430, 1490, 1435, 1245, 900, 730 cm^{-1}. MS: m/z 69, 77, 93, 103, 135, 149, 163, 205, 220, 235, 370. HRMS: calcd for $C_{20}H_{18}O_7$ 370.1053, found 370.1052.

Acknowledgment. We thank the Herman Frasch foundation for support of this research.

Registry No. (±)-**1**, 121123-82-8; (±)-**2**, 125783-25-7; (±)-**3**, 125783-22-4; (±)-**5**, 125783-23-5; piperonal, 120-57-0; (±)-1-(1,3-benzodioxol-5-yl)-3-buten-1-ol, 42337-03-1; 1-(1,3-benzodioxol-5-yl)-1,3,4-butanetriol, 125783-20-2; 5-(1,3-benzodioxol-5-yl)tetrahydrofuran-3-ol, 125783-21-3; 1,3-benzodioxol-5-ylmethyl trichloroacetimidate, 125783-24-6.

The Vinylogous Anomeric Effect in 3-Alkyl-2-chlorocyclohexanone Oximes and Oxime Ethers

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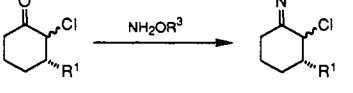
Contribution from the Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801. *Received October 10, 1989. Revised Manuscript Received December 7, 1989*

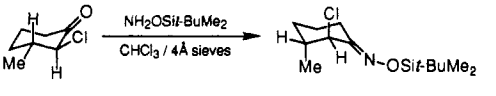
Abstract: A series of *trans*-3-alkyl-2-chlorocyclohexanones, **2** (methyl, ethyl, isopropyl, and *tert*-butyl), have been prepared and shown to exist predominantly in the diequatorial chair conformation except the *tert*-butyl derivative which prefers a twist-boat. Formation of the oximes and various oxime derivatives (methyloxime, silyloxime) results in a remarkable conformational inversion for the methyl, ethyl, and isopropyl systems. By analysis of vicinal interproton coupling constants it is believed that these compounds exist predominantly in the diaxial chair conformation. This is corroborated by an X-ray crystal structure of (*E*)-*trans*-**5a** which shows that the chair with diaxial substituents is indeed preferred in the solid state. A strong hyperconjugative stabilization of the axial conformation is proposed to be the origin of this preference which is termed the *vinylogous anomeric effect*.

The anomeric effect (and its generalized manifestations) is well recognized as an important contributor to ground-state conformational analysis of heteroatom-containing systems.[1] The value of considering these same effects in reaction mechanisms (kinetic anomeric effect[2]) has also been amply demonstrated. Although

Scheme I



Scheme II



interpretations of the *origin of the effect* differ, the experimental facts are clear that electronegative groups prefer the axial orientation at the anomeric position of tetrahydropyrans. The

(1) (a) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, 1983. (b) Riddell, F. G. *The Conformational Analysis of Heterocyclic Compounds*; Academic Press: New York, 1980; pp 66–103. (c) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983. (d) Romers, C.; Altona, C.; Buys, H. R.; Havinga, E. *Topics in Stereochemistry* **1969**, *4*, 39. (e) Szarek, W. A.; Horton, D. *Anomeric Effect, Origin and Consequences*; ACS Symposium Series 87; American Chemical Society: Washington, DC, 1979.

(2) (a) Reference 1a; pp 78–135. (b) Petrzilka, M.; Felix, D.; Eschenmoser, A. *Helv. Chim. Acta* **1973**, *56*, 2950.

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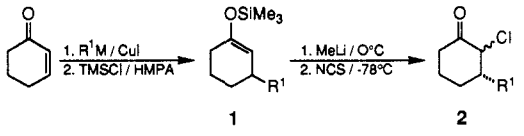
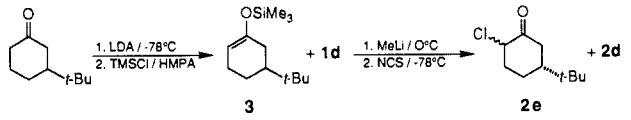
Scheme III



1 2

a: R=Me; b: R=Et; c: R=*i*-Pr; d: R=*t*-Bu

Scheme IV



3 2e

magnitude of this effect has been estimated to lie between 0.9 and 1.75 kcal/mol depending upon solvent and anomeric substituent.[3]

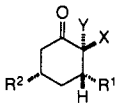
In the context of a program to develop nitrosoalkenes as heterodienes for cycloaddition,[4a] we devised a mild method of generation of these species from 2-chlorocyclohexanone oximes and silyloximes. The latter compounds were readily prepared from the corresponding 2-chlorocyclohexanones (Scheme I). During the course of this study we observed an unusual conformational change in the 3-alkyl-2-chlorocyclohexanones upon formation of oxime derivatives.[4b] Specifically, the trans isomer of 2-chloro-3-methylcyclohexanone which exists predominantly in the diequatorial chair conformation was found to exist predominantly in the diaxial chair conformation upon conversion to the (*E*)-silyloxime (Scheme II). Noting the relationship between the axial halogen atom and the oxime oxygen we suggested that a *vinylogous anomeric-type effect*[5] might be responsible for the added stability of the diaxial conformer.

We have now extended these studies with three main objectives in mind: (1) to further substantiate the existence of the effect, (2) to define the scope of the effect, and (3) to demonstrate its generality. This paper reports confirmation of our original proposal by X-ray crystallographic analysis and the conformational analysis of more highly substituted analogues.

Results

A. 2-Chlorocyclohexanones. The 3-alkyl-2-chloro ketones used in this study were prepared by sequential conjugate addition, trapping, and regioselective chlorination as outlined in Scheme III. In this manner mixtures of cis and trans isomers of **2a–c** were prepared in good yield. The isomers were easily resolved by silica gel chromatography. Unlike chlorination of the lithium enolates derived from **1a–c**, treatment of **1d** with methyllithium at 0 °C followed by *N*-chlorosuccinimide at −78 °C afforded a single α-chloro ketone in moderate yield. Initially assigned to be the cis chloro ketone, *cis*-**2d**, on the basis of a "small" value of $J_{2,3}$ the product structure was later revised to be the trans isomer, *trans*-**2d** (vide infra). The cis chloro ketone (*cis*-**2d**) was ultimately prepared by chloride ion epimerization of the trans isomer.[6a]

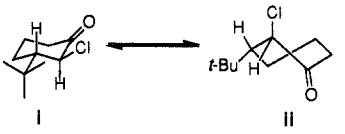
Table I. Selected Spectroscopic Data for α-Chloro and α-Methoxy Ketones **2** and **7**



compound	X	Y	R^1	R^2	ν_{CO}, cm^{-1}	δ(H–C(2)), ppm	$J_{2,3}$, Hz
cis-**2a**	H	Cl	Me	H	1715	4.13	3.0
trans-**2a**	Cl	H	Me	H	1727	4.07	9.8
cis-**2b**	H	Cl	Et	H	1725	4.22	1.2
trans-**2b**	Cl	H	Et	H	1734	4.21	9.7
cis-**2c**	H	Cl	*i*-Pr	H	1726	4.15	br s
trans-**2c**	Cl	H	*i*-Pr	H	1738	4.34	11.0
cis-**2d**	H	Cl	*t*-Bu	H	1727	4.36	br s
trans-**2d**	Cl	H	*t*-Bu	H	1727	4.14	3.3
cis-**2e**	H	Cl	H	*t*-Bu	1720[a]	4.17	0
trans-**2e**	Cl	H	H	*t*-Bu	1730[a]	4.45	13.3
trans-**7a**	OMe	H	Me	H	1720	3.32	9.4

[a] Taken from ref 6b.

Scheme V



I II

Treatment of *trans*-**2d** with LiCl (0.2 equiv) in DMF afforded an inseparable 85:15 mixture of *cis*/*trans*-**2d** (33%) along with 3-*tert*-butyl-2-cyclohexenone (51%). For comparison purposes we also prepared 5-*tert*-butyl-2-chlorocyclohexanone (**2e**) by chlorination of the lithium enolate derived from kinetic enolization of 3-*tert*-butylcyclohexanone (Scheme IV). The enol ethers were formed in an 89:11 ratio favoring the desired regioisomer **3**.[6c] Chlorination afforded a ternary mixture from which both *cis*- and *trans*-**2e**[6b] could be isolated in pure form after column chromatography. Table I contains the pertinent spectroscopic data.

Assignment of both configuration and predominant ring conformation for **2a–c** and **2e** follows easily from a combination of ^1H NMR and IR spectroscopic analysis. Based on well-established trends in vicinal coupling constants[7] and carbonyl stretching frequencies,[8] it is clear that the cis isomers have axially oriented chlorine atoms (lower ν_{CO} stretch, smaller $J_{2,3}$), and the trans isomers have equatorially oriented chlorine atoms (higher ν_{CO} stretch, larger $J_{2,3}$).[9]

Assignment of structure for the isomers of **2d** was less straightforward as they both displayed very small $J_{2,3}$ coupling constants and identical ν_{CO} stretches. Ultimately the assignment rests on the observation of a *W* coupling (1.16 Hz) between H–C(2) and H_β–C(6) for *trans*-**2d** and a characteristic pattern for H_2–C(6) in *cis*-**2d**. The *W* coupling in *trans*-**2d** implicates an equatorial H–C(2) which is best accommodated by a twist-boat conformation ii (see Scheme V). This would also account for the diminished $J_{2,3}$ as the dihedral angle is reduced to ca. 60°. In *cis*-**2d**, the two C(6) protons are highly anisochronous with an anomalously low-field *axial* proton 3.00 ppm). This pattern is characteristic for protons bearing a diaxial relationship to a chlorine atom in conformationally locked chairs.[4b] Moreover, the exclusive production of *trans*-**2d** from enolate chlorination is also consistent with steric approach considerations. With a secure assignment of isomers we were forced to the conclusion that

(3) (a) Reference 1a; pp 7–11. (b) Stoddart, J. F. *Stereochemistry of Carbohydrates*; Wiley-Interscience: New York, 1971. (c) Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635. (d) Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauvé, T.; Saunders, J. K. *Can. J. Chem.* **1981**, *59*, 1105. (e) Pothier, N.; Rowan, D. D.; Deslongchamps, P.; Saunders, J. K. *Ibid.* **1981**, *59*, 1132. (f) Franck, R. W. *Tetrahedron* **1983**, *39*, 3251. (g) Anderson, J. E.; Heki, K.; Hirota, M.; Jorgensen, F. S. *J. Chem. Soc., Chem. Commun.* **1987**, 554. (h) Wiberg, K. B.; Murcko, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 4821.

(4) (a) Denmark, S. E.; Dappen, M. S.; Sternberg, J. A. *J. Org. Chem.* **1984**, *49*, 4741. (b) Denmark, S. E.; Dappen, M. S. *Ibid.* **1984**, *49*, 798.

(5) Curran and Coates have independently identified the kinetic consequences of the vinylogous anomeric effect in the Claisen rearrangement. (a) Curran, D. P.; Suh, Y.-G. *J. Am. Chem. Soc.* **1984**, *106*, 5002. (b) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *Ibid.* **1987**, *109*, 1160. For a full discussion of this effect in carbohydrates, see: (c) Curran, D. P.; Suh, Y.-G. *Carbohydr. Res.* **1987**, *171*, 1612.

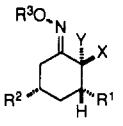
(6) (a) Moreau, P.; Casadevall, E. *C. R. Acad. Sci. Ser. C* **1971**, *272*, 801. (b) Moreau, P.; Casadevall, A.; Casadevall, E. *Bull. Soc. Chim. Fr.* **1969**, 2021. (c) Lightner, D. A.; Bouman, T. D.; Gawronski, J. K.; Gowronska, K.; Chappuis, J. L.; Crist, B. V.; Hansen, A. E. *J. Am. Chem. Soc.* **1981**, *103*, 5314.

(7) (a) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: Oxford, 1969; p 291. (b) Pan, Y.-H.; Stothers, J. B. *Can. J. Chem.* **1967**, *45*, 2943. (c) Thorpe, J. W.; Warkentin, J. *Ibid.* **1973**, *51*, 927.

(8) Corey, E. J. *J. Am. Chem. Soc.* **1953**, *75*, 2301, 3297.

(9) For a thorough discussion of these compounds, see: Eliel, E. L.; Allinger, N. L.; Angyal, S. Y.; Morrison, C. A. *Conformational Analysis*; Interscience: New York, 1965; pp 112–115, 460–469. See also: De Kimpe, N.; Verhe, R. *The Chemistry of α-Haloketones, α-Haloaldehydes and α-Haloimines*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1988; Chapter 1.

Table II. Preparation of α-Chloro *O*-Silyl and *O*-Methyl Ketoximes **5** and **6**



educt	method[a]	product	X	Y	R^1	R^2	R^3	yield, %[b]	*E*/*Z* ratio[c]
cis-**2a**	A	*cis*-**5a**	H	Cl	Me	H	TBDPS	84	60/40
trans-**2a**	A	*trans*-**5a**	Cl	H	Me	H	TBDPS	80	100/0
cis-**2b**	A	*cis*-**5b**	H	Cl	Et	H	TBDPS	84	70/30
trans-**2b**	A	*trans*-**5b**	Cl	H	Et	H	TBDPS	57	100/0
cis-**2c**	A	*cis*-**5c**	H	Cl	*i*-Pr	H	TBDPS	82	100/0
trans-**2c**	A	*trans*-**5c**	Cl	H	*i*-Pr	H	TBDPS	80	100/0
cis-**2d**	A	*cis*-**5d**	H	Cl	*t*-Bu	H	TBDPS	78	64/36
trans-**2d**	A	*trans*-**5d**	Cl	H	*t*-Bu	H	TBDPS	68	100/0
cis-**2e**	A	*cis*-**5e**	H	Cl	H	*t*-Bu	TBDPS	95	75/25
trans-**2e**	A	*trans*-**5e**	Cl	H	H	*t*-Bu	TBDPS	65	100/0
cis-**2a**	B	*cis*-**6a**	H	Cl	Me	H	Me	64	50/50
trans-**2a**	B	*trans*-**6a**	Cl	H	Me	H	Me	86	100/0
trans-**2b**	B	*trans*-**6b**	Cl	H	Et	H	Me	27	100/0

[a] See text for definition. [b] Yield after chromatography. [c] Determined by ^{1}H NMR analysis.

trans-**2d** exists in a twist-boat. An unfortunate consequence of this preference is that no useful information can be obtained from *trans*-**2d** since the chlorine atom is already pseudoaxial in the ketone. It was for this reason that **2e** was prepared.

B. α-Chloro Oxime Derivatives. In our preliminary report of the vinylogous anomeric effect we prepared both oximes and (*tert*-butyldimethylsilyl)oximes and found similar behavior.[4b] For the purposes of securing X-ray crystallographic confirmation, we used the (*tert*-butyldiphenylsilyl)oximes throughout to assure correspondence between solution and solid state data. As a further extension we have also prepared the *O*-methyloximes to illustrate generality.

Treatment of each α-chloro ketone in chloroform with *O*-(*tert*-butyldiphenylsilyl)hydroxylamine using pyridinium *p*-toluenesulfonate as a catalyst[10] in the presence of 4-Å sieves (method A) produced the α-chloro silyloximes in good yield (Table II). In every case, the trans chloro ketones produced the (*E*)-silyloximes ((*E*)-*trans*-**5**) exclusively, while the cis isomers produced a mixture of (*E*)- and (*Z*)-silyloximes (*E*/*Z*-*cis*-**5**).[11] Consequently all of the (*E*)-*trans*-silyloximes were crystalline solids, whereas the (*E*,*Z*)-cis-silyloxime mixtures were obtained as oils.

The *O*-methyloxime derivatives of selected chloro ketones were also prepared for comparison. Treatment of the chloro ketone with methyloxyamine hydrochloride and potassium acetate in glacial acetic acid (method **B**) gave the desired oxime ethers in fair to good yields (Table II). As was the case for silyloximes, trans chloro ketones **2a** and **2b** gave exclusively the (*E*)-oxime ethers (*E*)-*trans*-**6a** and (*E*)-*trans*-**6b**, while the cis isomer gave a 50/50: *E*/*Z* ratio of *cis*-**6a**.

The configurational assignment of the oxime geometry was simple due to the strong anisotropic deshielding by the oxime oxygen on the equatorial protons on C(2) or C(6).[12] These chemical shifts and the critical coupling constants for conformational analysis (vide infra) are collected in Table III. In the cis series, H–C(2) generally appeared at >1.0 ppm lower field for the (*Z*)-oximes compared to (*E*)-oximes. A complementary difference of similar magnitude was observed for H_{eq}–C(6), i.e., *E* isomers lower field than *Z* isomers. The oximes obtained in the trans series are easily identified as *E* isomers in the same fashion.

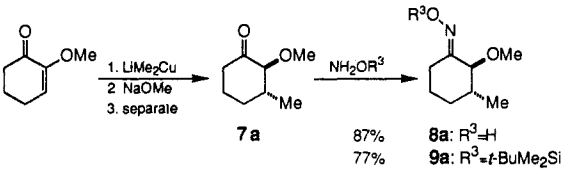
C. α-Methoxy Ketone and Oxime Derivatives. To demonstrate the generality of the observed decrease in $J_{2,3}$ upon oximation of *trans*-α-chloro ketones, we briefly examined the α-methoxy analogues. These materials were easily prepared by simple conjugate addition to 2-methoxy-2-cyclohexenone as outlined in Scheme VI. The initial cis/trans mixture was enriched by epimerization with sodium methoxide to a trans/cis: 75/25 ratio from which *trans*-**7a** could be separated in pure form. Oxime and silyloxime formation proceeded smoothly to give exclusively the (*E*)-trans isomers as in the α-chloro ketones. The relevant spectroscopic data for these compounds are also found in Tables I and III. Comparison of the coupling constants for *trans*-**7a** and the derivative **8a** and **9a** shows once again a significant decrease albeit lesser in magnitude than in the α-chloro ketones.

Table III. Selected Spectroscopic Data for α-Chloro and α-Methoxy Ketoximes

compound	^{1}H NMR, ppm H–C(2)	^{1}H NMR, ppm eq-H–C(6)	$J_{2,3}$, Hz[a]
(*E*)-*cis*-**5a**	4.62	3.54	br s
(*Z*)-*cis*-**5a**	5.77	2.35	1.2
(*E*)-*trans*-**5a**	4.34	3.33	1.8
(*E*)-*cis*-**5b**	4.66	3.50	br s
(*Z*)-*cis*-**5b**	5.87	2.25	br s
(*E*)-*trans*-**5b**	4.49	3.42	br s
(*E*)-*cis*-**5c**	4.76	3.52	br s
(*E*)-*trans*-**5c**	4.78	3.44	br s
(*E*)-*cis*-**5d**	4.84	3.53	br s
(*Z*)-*cis*-**5d**	6.14	2.27	br s
(*E*)-*trans*-**5d**	4.71	2.65	br s
(*E*)-*cis*-**5e**	4.70	3.63	2.5, 2.5[b]
(*Z*)-*cis*-**5e**	5.85	*c*	2.5, 2.5[b]
(*E*)-*trans*-**5e**	4.49	3.64	5.2, 10.0[b]
(*E*)-*cis*-**6a**	4.52	3.06	2.8
(*Z*)-*cis*-**6a**	5.33	2.22	2.8
(*E*)-*trans*-**6a**	4.29	2.88	3.2
(*E*)-*trans*-**6b**	4.42	2.97	1.9
(*E*)-*trans*-**8a**	3.34	2.66	4.9
(*E*)-*trans*-**9a**	3.43	3.00	3.2

[a] Those resonances which had no fine structure > 1.0 Hz are labeled as broad singlets. [b] $J_{2,3}$ eq, $J_{2,3}$ ax. [c] Obscured.

Scheme VI



D. Solid-State Structure of (*E*)-*trans*-5a. Confirmation of the trans-diaxial arrangement of chlorine and methyl substituents in oximes of *trans*-**2a** was ultimately achieved by X-ray crystallographic analysis of the TBDPS derivative (*E*)-*trans*-**5a**. The structure is shown in Figure 1. Several features of the structure are noteworthy;[13] foremost are (1) the establishment of the

(10) Sterzycki, R. *Synthesis* **1979**, 724.
(11) For a discussion of the origin of *E*/*Z*-oximation selectivity see ref 4b.
(12) (a) Durand, R.; Geneste, P.; Moreau, C.; Pavia, A. A. *Org. Mag. Reson.* **1974**, *6*, 73. (b) Fraser, R. R.; Capoor, R.; Bovenkamp, J. W.; Lacroix, B. V.; Pagotto, J. *Can. J. Chem.* **1984**, *61*, 2616.

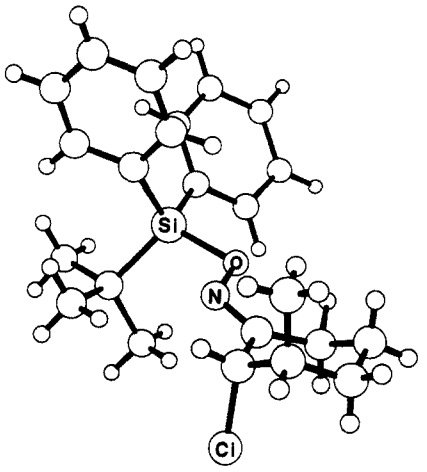


Figure 1. X-ray crystal structure of (*E*)-*trans*-**5a**.

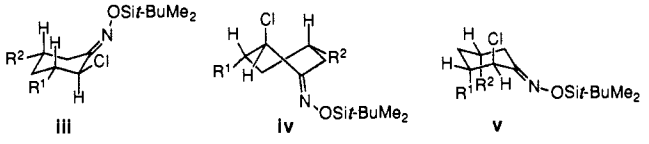


Figure 2. Possible limiting conformations for (*E*)-*trans*-**5**.

trans-diaxial orientation of the substituents (Cl–C(2)–C(3)–CH_3 dihedral angle = 168°) and (2) proof of the *E* configuration of the silyloxime moiety (C(2)–C(1)–N–O dihedral angle = 179°). The carbon–chlorine bond (1.825 Å) is significantly lengthened compared to the average for bonds of this type (1.767 Å),[14] reminiscent of the situation in the normal anomeric effect.[15] Finally, the silyl moiety is antiperiplanar to the C–N bond (C(1)–N–O–Si dihedral angle = 167°). In this orientation, the oxygen nonbonding electron pairs can maximally interact with the azomethine linkage. The significance of this orientation is discussed below.

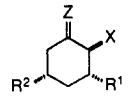
Discussion

A. Conformational Analysis of 5 and 6. Examination of the ^{1}H NMR coupling constant information in Table III clearly suggests that the dihedral angle between H–C(2) and H–C(3) in **5a–d**, and **6a** and **6b** is small. In most cases no coupling could be detected. The comparisons of the cis and trans series shown in Table III was essential to prove that no epimerization of the *trans*-chloro ketones (**2**) occurred upon oxime formation. Indeed, this process was never detected. Thus, the small $J_{2,3}$ observed in the *trans*-α-chloro ketoximes required explanation. Several reasonable proposals for the decrease in vicinal coupling constant can be formulated (Figure 2): (1) the diequatorial chair conformation iii persists, but the ^3J diaxial coupling is intrinsically reduced, (2) the ring adjusts to a twist-boat, iv, which reduces the H–C(2)/H–C(3) dihedral angle, or (3) the chair–chair equilibrium is shifted to the diaxial conformer, v, with attendant reduction in the vicinal dihedral angle.

In the following analyses, the critical comparison is the change in $J_{2,3}$ between the *trans*-α-chloro ketones and the derived oximes. The comparisons of various oxime derivatives for each substrate are collected in Table IV.

The effect of electronegative groups on vicinal H/H coupling constants was predicted theoretically[16a] and is well documented.[16b] In general, the maximum effect (minimum ^3J) is found where an antiperiplanar relationship exists between part of the coupling path and the bond to which the substituent is attached. This situation obtains in the cis series where H–C(3) is antiperiplanar to the Cl–C(2)bond. However, in iii, no such relationship exists. Furthermore, the observation of a 10-Hz $J_{2,3}$ for (*E*)-*trans*-**5e** as well as for the *cis*-4-*tert*-butyl isomer[4b] confirms that there is only a small decrease in the vicinal coupling constant upon oximation (Table IV) when the diequatorial chair conformation is forced.

Table IV. Comparison of *trans*-α-Hetero Ketones and Oximes



compound	R^1	R^2	X	Z	δ(H–C(2)), ppm	$J_{2,3}$, Hz
trans-**2a**	Me	H	Cl	O	4.07	9.8
a	Me	H	Cl	NOH	4.26	4.8
(*E*)-*trans*-**6a**	Me	H	Cl	NOMe	4.29	3.2
a	Me	H	Cl	NOSi*t*-BuMe$_2$	4.34	2.4
(*E*)-*trans*-**5a**	Me	H	Cl	NOSi*t*-BuPh$_2$	4.34	1.8
trans-**7a**	Me	H	OMe	O	3.32	9.4
(*E*)-*trans*-**8a**	Me	H	OMe	NOH	3.34	4.9
(*E*)-*trans*-**9a**	Me	H	OMe	NOSi*t*-BuMe$_2$	3.43	3.2
trans-**2b**	Et	H	Cl	O	4.21	9.7
(*E*)-*trans*-**6b**	Et	H	Cl	NOMe	4.42	1.9
(*E*)-*trans*-**5b**	Et	H	Cl	NOSi*t*-BuPh$_2$	4.49	br s
trans-**2c**	*i*-Pr	H	Cl	O	4.34	11.0
(*E*)-*trans*-**5c**	*i*-Pr	H	Cl	NOSi*t*-BuPh$_2$	4.78	br s
trans-**2d**	*t*-Bu	H	Cl	O	4.14	3.3
(*E*)-*trans*-**5d**	*t*-Bu	H	Cl	NOSi*t*-BuPh$_2$	4.71	br s
trans-**2e**	H	*t*-Bu	Cl	O	4.45	13.3
(*E*)-*trans*-**5e**	H	*t*-Bu	Cl	NOSi*t*-BuPh$_2$	4.49	10.0[b]

[a] From ref 4b. [b] $J_{2,3ax}$.

A second maximum in the effect of electronegativity on $J_{2,3}$ is expected in the synperiplanar relationship of substituent and coupling path as well. This arrangement could be accommodated by a boat conformation related to iv. This proposal, however is inconsistent with the coupling pattern for the C(6) methylene. In (*E*)-*trans*-**2a–c**, the axial proton appears as a triplet of doublets with $J_t \approx 13$ and $J_d \approx 6$. Such a pattern is best explained by a chair conformation in which the axial proton experiences two large (geminal and trans diaxial) and one small (gauche) coupling. Moreover, in (*E*)-*trans*-**6a** the equatorial H–C(6) is resolved into a doublet of triplets with $J_t = 3.8$ and $J_d = 14.7$ again best explained by a chair conformation. Finally, examination of the patterns in (*E*)-*trans*-**5d** (where a twist-boat conformation is likely) is informative. Already in the ketone, *trans*-**2d**, the twist-boat is implicated by the small $J_{2,3}$ value. The existence of such conformers in *tert*-butyl-substituted cyclohexanones is documented.[17] In this case, the preference for a twist-boat conformation presumably arises from relief of unfavorable gauche interactions between the equatorial *tert*-butyl group and the chlorine and hydrogen atoms on C(2) in the normal chair, Scheme V. The reasonable assumption that the derived oxime, (*E*)-*trans*-**5d**, also exists in a twist-boat conformation is supported by inspection of the C(O)–methylene coupling pattern. Here it is the axial proton (ddd) which is anomalously deshielded whereas in all of the other *trans*-2-chloro ketoximes, the equatorial proton (br d) is deshielded. Thus, the twist-boat iv is not an important conformation for any α-chloro ketoximes except (*E*)-*trans*-**5d**. *We therefore conclude that the chair conformation with trans-diaxial substituents, v, is most consistent with the observed solution behavior spectroscopically and is supported by the solid state structure.*

The trends evident from the data in Table IV illustrate the generality and magnitude of the effect. In the most studied case, *trans*-**2a**, it is seen that all oxime derivatives reduce $J_{2,3}$, but that silyloximes are the most effective. The variation in $J_{2,3}$ may be interpreted either as an equilibrium averaged coupling or an intrinsic difference in the coupling constants. To address this question we recorded the ^{1}H NMR spectrum of the parent oxime ($J_{2,3} = 4.8$ Hz) at low temperature. A spin equilibrium would

(13) The projection shown is enantiomeric with those drawn throughout the paper. All chiral compounds are racemic.
(14) Sutter, L. E. *Tables of Interatomic Distances and Configuration in Molecules and Ions, Spec. Publ. No. 18*; The Chemical Society: London, 1965.
(15) (a) Reference 1a; pp 52–62. (b) Jeffrey, G. A.; Yates, J. H. *Carbohydr. Res.* **1980**, *79*, 155.
(16) (a) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. (b) Reference 7a; pp 280–292.
(17) Hanack, M. *Conformation Theory*; Academic Press: New York, 1965; pp 275–299.

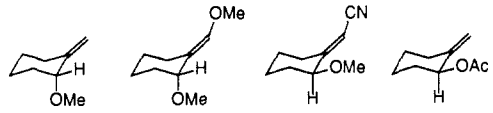


Figure 3. Conformations of selected α-hetero-substituted methylidene cyclohexanes.

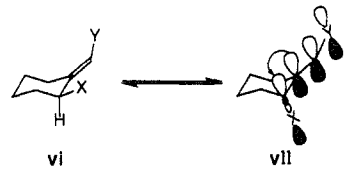


Figure 4. Preferrential stabilization of the axial conformation by $\pi-\sigma^*$ hyperconjugation.

be evidenced by a decoalescence of the H–C(2) into axial an equatorial components. As low as −100 °C (200 MHz) we observed only line broadening and a slight increase in $J_{2,3}$. Furthermore, the ^{13}C NMR spectrum displayed only seven lines. It is possible that we have not reached the decoalescence temperature even though related systems have been studied at −100 °C (vide infra). An alternative explanation invokes an anacomeric equilibrium favoring conformation v. If, however, this is the case, we cannot provide a satisfying rationalization for the dependence of $J_{2,3}$ on the derivative. Additional VT NMR studies are required to clarify this point.

Since it was impossible to experimentally determine the magnitude of the axial chlorine preference by NMR, we turned to computational methods. With the use of Allinger's MM2 force field this value was estimated by calculation of the strain energies for the two limiting conformations of (*E*)-*trans*-**2a–c**. In this series, the diequatorial conformation is slightly favored (kcal/mol): **2a**, 1.2; **2b**, 0.8; **2c**, 1.0. The modest energetic disadvantage for axial alkyl *and* chlorine groups is expected in view of the reduction in steric energy due to the 3-axial ketone effect[18] and the known axial preference for 2-chlorocyclohexanone (vide infra).[9] Unexpectedly, however, **2a** had the largest value due, presumably, to the greater ground-state strain in **2b** and **2c**. If we assume that (*E*)-*trans*-**5a–c** are predominantly diaxial (~90%), this would correspond to a $\Delta G°$ (298 °C) of ca. 1.3 kcal/mol. Thus, a *minimum* value for the magnitude of the effect is 2.0–2.5 kcal/mol. An upper limit for the value can also be estimated by the observation that in neither *cis*-4-*tert*-butyl-[4b] or *trans*-5-*tert*-butyl-2-chlorocyclohexanone is there a significant change in $J_{2,3}$ upon oximation.

B. Origin of the Effect. In order to evaluate the reasons for the strong axial preference in α-chloro ketoximes, it is necessary to describe those factors which influence the conformational equilibrium. The α-chloro ketoximes herein belong to the general class of cyclohexanes bearing an exocyclic double bond. The conformational analysis of these systems has been reviewed recently.[19] The subclass most relevant to the present discussion involves cyclohexanones and methylenecyclohexanes bearing polar, adjacent (C(2)) substituents.

The axial preference for 2-halo- and 2-methoxycyclohexanones is a well-established fact and constitutes a classic in conformational analysis.[9] Three factors have been invoked to explain this preference. The first is a minimization of dipole–dipole interactions of the polar bonds. The second is a hyperconjugative stabilization of the axial conformer of the type $\sigma_{C-X} \rightarrow \pi^*_{C=O}$ stabilization.[20] This was first proposed by Corey[20a] and has been modified by modern ideas about orbital interactions.[20] Finally, Salem has suggested the possibility of an $n_X \rightarrow \pi^*_{C=O}$ stabilization.[21] It would appear, however, that these factors, if operative, are not determinant since the parent *trans*-2-chloro (methoxy) ketones **2(7)** exist predominantly in the diequatorial conformation.

Of greater relevance are the studies on the conformational behavior of 2-substituted methylenecyclohexanes. The effects of polar 2-substituents on conformation have been studied extensively by the groups of Lessard[22] and Zefirov.[23] A general preference for the axial orientation of polar groups has been observed and several examples are shown in Figure 3. To explain these facts three effects, different from those described above, have been identified and roughly quantified. The first is the allylic $A^{1,3}$ strain[24] which represents a nondipolar steric effect. In the compounds **10–13**, this is a small contribution. Zefirov[23a] estimated the decrease in equatorial preference for the 2-substituent versus the related cyclohexyl derivative is 0.6 kcal/mol for methyl and 0.3 kcal/mol for methoxy or acetoxy.[25] By this factor alone, **10** and **11** would still be expected to exist in primarily equatorial conformations. To explain the axial preference, a hyperconjugative interaction related to the generalized anomeric effect has been proposed.[22b] The interaction is viewed as a $\pi \rightarrow \sigma^*_{C-X}$ donation which is only capable of stabilizing the axial conformation (Figure 4). The intervention of such an interaction was first suggested by Tronchet[26] to explain the conformational behavior of allylic ethers with different olefinic substituents. Tronchet's analysis provides a clear explanation for the increased and decreased axial preferences in **11** and **12**, respectively. It is intuitively expected and supported by calculation[26] that the $\pi \rightarrow \sigma^*_{C-X}$ interaction will be stronger (weaker) as the π-orbital is raised (lowered) in energy by substitution. Further, experimental support for the angular dependence of this interaction (i.e., minimal in vi, maximal in vii) is provided by studies on ionization potentials by Brown.[27] Using both flexible and rigid allylic ethers and alcohols he found uniformly higher π-ionization energies for those molecules with dihedral angles (RO—C—C=C) closer to 90°. From conformational equilibria Lessard has estimated the magnitude of this interaction be ca. 0.7 kcal/mol in **10** and 1.1 kcal/mol in **11**.[22b]

Another intuitive expectation, that the $\pi \rightarrow \sigma^*_{C-X}$ interaction should increase as the σ^*_{C-X} orbital is lowered in energy, has also been demonstrated by Zefirov.[23c] However, this feature is obscured for 2-(acyloxy)methylenecyclohexanes by an unknown, third effect ("unsaturation effect")[22a] which strongly favors the equatorial conformation, viz **13**.

In the α-chloro and α-methoxy ketoximes, only the first two effects are relevant. Since all of the oximes are of *E* geometry, the contribution from $A^{1,3}$ strain is minimal due to the small *A* value for chlorine (0.43 kcal/mol)[28] and the lack of a substituent on the oxime nitrogen. We estimate this contribution to be less than 0.2 kcal/mol. Thus, nearly the full extent of the 2.0–2.5 kcal/mol increase in axial preference for the 2-substituent in the oxime over the ketone derives from the hyperconjugative interaction identified by Lessard and Tronchet.

While more accurate quantitation of the magnitude of the effect must await additional VT NMR studies, it is nonetheless intriguing to speculate on the amplification of this effect in oximes compared

(18) (a) Reference 9; pp 112–115. (b) Reference 17; pp 149–152.
(19) Lambert, J. B. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P., Ed.; VCH: Weinheim, 1989; Chapter 2.
(20) (a) Corey, E. J.; Burke, H. J. *J. Am. Chem. Soc.* **1955**, *77*, 5418. (b) Kosower, E. M.; Wu, G.-S.; Sorensen, T. S. *Ibid.* **1961**, *83*, 3147. (c) Allinger, N. L.; Tai, J. C.; Miller, M. A. *Ibid.* **1966**, *88*, 4495. (d) Cantacuzene, J.; Jantzen, R.; Ricard, D. *Tetrahedron* **1972**, *28*, 717. (e) Robinson, M. J. T. *Ibid.* **1974**, *30*, 1971. (f) Dosen-Micovic, L.; Allinger, N. L. *Ibid.* **1978**, *34*, 3385. (g) Cantacuzene, J.; Tordeux, M. *Can. J. Chem.* **1976**, *54*, 2759.
(21) Eisenstein, O.; Anh, N. T.; Jean, Y.; Devaquet, A.; Cantacuzene, J.; Salem, L. *Tetrahedron* **1974**, *30*, 1717.
(22) (a) Ouedraogo, A.; Viet, M. T. P.; Saunders, J. K.; Lessard, J. *Can. J. Chem.* **1987**, *65*, 1761. (b) Lessard, J.; Tan, P. V. M.; Martino, R.; Saunders, J. K. *Ibid.* **1977**, *55*, 1015. (c) Lessard, J.; Saunders, J. K.; Viet, M. T. P. *Tetrahedron Lett.* **1982**, *23*, 2059. (d) Viet, M. T. P.; Lessard, J.; Saunders, J. K. *Ibid.* **1979**, 317.
(23) (a) Zefirov, N. S.; Baranenkov, I. V. *Tetrahedron* **1983**, *39*, 1769. (b) Zefirov, N. S. *Ibid.* **1977**, *33*, 3193. (c) Zefirov, N. S.; Baranenkov, I. V. *J. Org. Chem. USSR (Eng. Transl.)* **1979**, 4875.
(24) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.
(25) Clearly $A^{1,3}$-strain will be more important with syn substituents on the double bond (0.3-2.1 kcal/mol).
(26) Tronchet, J. M. J.; Xuan, T. N. *Carbohydrate Res.* **1978**, *67*, 469.
(27) (a) Brown, R. S.; Marcinko, R. W.; Tse, A. *Can. J. Chem.* **1979**, *57*, 1890. (b) Brown, R. S.; Marcinko, R. W. *J. Am. Chem. Soc.* **1978**, *100*, 5721.
(28) Hirsch, J. A. *Topics Stereochem.* **1967**, *1*, 199.

to methylidenes. A priori, it is expected that the azomethine linkage would function as a *poorer* π-donor than an olefinic linkage (e.g. in **10**) due to the electronegativity of the nitrogen and correspondingly lower energy π-orbital. However, φ_2 of the molecular orbitals generated by mixing $\pi_{C=N}$ and $\pi^*_{C=N}$ with n_O is effectively higher in energy than $\pi_{C=N}$ and may be higher than $\pi_{C=C}$. Of course, the net result of this mixing is stabilizing (oxime resonance) which has been cited[29] as the origin of the large formation constants for oximes even in water. Recently, Wiberg has questioned the validity of stabilization through resonance effects in oximes.[30] Whether this resonance delocalization is the actual reason for the stability of oximes is questionable, however its existence is not. Therefore, we suggest that a combination of two factors both deriving from the π- and π^*-orbital energies of an oxime linkage compared to an olefinic bond is responsible for the enhanced axial preference in **5–9** compared to **10**. The first effect is based on the $\sigma_{C-X} \rightarrow \pi^*$ hyperconjugation proposed for the axial preference in α-chloro ketones. This effect should increase in the series C=C < C=N < C=O. The second and presumably more important effect is the ability of the group, C=Y, in X—C—C=Y—Y systems to donate π electron density to σ^*_{C-X}. This effect should increase in the series C=O < C=N < C=C. However, because of the mixing of $\pi_{C=N}$ and n_O orbitals, the oximes are believed to be more effective than the C=C bond in olefins. This is the same reasoning which explains the higher axial preference in the vinyl ether **11** compared to the olefin **10**.

Conclusions

This study has demonstrated that the axial preference for α-chloro- and α-methoxy oximes and oxime derivatives is a general phenomenon. The preference is of sufficient magnitude to force a β-alkyl substituent into an axial position. X-ray crystallographic data has provided a strong foundation for the proposals of solution structure based on vicinal ^{1}H NMR coupling constants. The magnitude of the decrease in $J_{2,3}$ was shown to depend on the nature of the oxime derivative (H, C, Si) but VT NMR analysis down to −100 °C failed to produce decoalescence of any of the signals. The increase in axial preference upon oximation of 2-chlorocyclohexanones has been estimated to be roughly 2.0–2.5 kcal/mol. The origin of this preference is suggested to derive primarily from enhanced $\pi_{C=N} \rightarrow \sigma^*_{C-X}$ hyperconjugation of the azomethine linkage.

Further studies are planned to more accurately quantify the magnitude of the effect and to demonstrate applications in conformationally directed stereoselective reactions.

Experimental Section

1. General Methods. (See Supplementary Material). Alkyllithium reagents were standardized by titration using diphenylacetic acid as indicator. *N*-Chlorosuccinimide (NCS) was recrystallized from benzene; cuprous iodide was purified by the method of Kauffmann.[31] All other chemicals were used as obtained or purified by distillation or recrystallization as needed. All reactions were performed in oven (140 °C) or flame-dried glassware under an atmosphere of dry nitrogen or argon.

2. Starting Materials. Compounds **1a**, **1d**, and *cis*- and *trans*-**2a** have been described previously from these laboratories.[4b,32] *O*-(*tert*-Butyldimethylsilyl)hydroxylamine and *O*-(*tert*-butyldiphenylsilyl)hydroxylamine were prepared by the method of Bottaro.[33] 2-Methoxy-2-cyclohexenone was prepared as described by Wenkert.[34]

3. Preparation of Silyl Enol Ethers. 3-Ethyl-1-(trimethylsiloxy)cyclohexene (1b). A 500-mL, three-necked flask equipped with mechanical stirrer, thermometer, and addition funnel was charged with magnesium turnings (1.82 g, 75 mmol) and treated dropwise with a solution of ethyl bromide (9.15 g, 84 mmol) in ether (100 mL). A crystal of iodine was added after 10 mL of the ethyl bromide/ether solution had been added. The mixture was heated at reflux for 30 min, stirred at room temperature for 1 h, and then cooled to −30 °C, and copper(I) iodide (0.95 g, 0.005 mol) was added. A solution of cyclohexenone (4.8 g, 50 mmol) in ether (50 mL) was added dropwise keeping the temperature below −30 °C. The mixture was stirred at −40 °C for 1 h, and HMPA (9.86 g, 55 mmol), triethylamine (10.12 g, 100 mmol), and chlorotrimethylsilane (10.86 g, 100 mmol) were added sequentially via the addition funnel. After stirring at −60 °C for 2 h, the solution was warmed to room temperature and quenched with saturated aqueous sodium bicarbonate solution (30 mL). The reaction mixture was poured onto a biphase of saturated aqueous sodium bicarbonate solution (250 mL) with use of pentane (200 mL) and stirred for 2.5 h when the mixture turned colorless. The organic layer was separated, and the aqueous layer was extracted with pentane (2 × 250 mL). The combined organic layers were washed with water (250 mL), saturated aqueous sodium bicarbonate (100 mL), and brine (100 mL). The dried ($MgSO_4$) solution was filtered and concentrated, and the residue was distilled to afford 6.7 g (65% yield) of **1b** as a clear colorless liquid: bp 95–100 °C (27 Torr), ^{1}H NMR (300 MHz) δ 4.80 (s, 1 H, H-C(2)), 1.97 (m, 3 H), 1.72 (m, 2 H), 1.55 (m, 1 H), 1.29 (m, 2 H), 1.09 (m, 1 H), 0.88 (t, J = 7.4 Hz, 3 H, CH_3CH_2-C(3)), 0.18 (s, 9 H, $(CH_3)_3Si$); ^{13}C NMR 150.16 (C(1)), 109.11 (C(2)), 36.16, 29.94, 29.55, 28.37, 21.73, 11.19, 0.10 ppm; IR (thin film) 2973 s, 2923 s, 2853 m, 1663 s, 1450 m, 1368 m, 1252 s, 1188 s cm^{-1}; MS (70 eV) *m/e* 199 (6), 197 (5), 140 (10), 130 (24), 126 (12), 125 (17), 124 (28), 115 (19), 112 (28), 111 (24), 101 (22), 99 (20), 98 (18), 97 (46), 96 (68), 95 (31), 87 (64), 85 (16), 83 (32), 83 (65), 81 (29), 74 (12), 73 (100), 72 (24), 71 (13), 70 (17), 69 (45), 68 (24), 67 (33), 60 (21), 57 (72), 56 (15), 55 (54), 45 (15), 43 (40). Anal. Calcd for $C_{11}H_{22}OSi$: C, 66.60; H, 11.18. Found: C, 66.66; H, 11.22.

3-(1-Methylethyl)-1-(trimethylsiloxy)cyclohexene (1c). A 250-mL, three-necked flask equipped with a thermometer and nitrogen inlet was charged with magnesium turnings (2.43 g, 100 mmol) and ether (50 mL). A solution of 2-bromopropane (13.53 g, 110 mmol) in ether (100 mL) was added dropwise through the addition funnel. A crystal of iodine was added after 10 mL of the 2-bromopropane solution had been added. The mixture was stirred at room temperature for 2 h then cooled to −30 °C and copper(I) iodide (1.90 g, 10 mmol) was added. A solution of cyclohexenone (4.80 g, 50 mmol) was added dropwise keeping the temperature below −20 °C. After stirring at −30 °C for 2 h HMPA (17.9 g, 100 mmol), chlorotrimethylsilane (10.8 g, 100 mmol), and triethylamine (10 g, 100 mmol) were added sequentially, and the mixture was stirred at −30 °C for 3 h and then allowed to warm to room temperature. The reaction mixture was then poured into saturated aqueous sodium bicarbonate solution (200 mL) and pentane (250 mL) and stirred vigorously for 3 h. The organic layer was separated, and the aqueous layer was extracted with pentane (2 × 100 mL). The combined organic layers were washed with 15% aqueous sodium hydroxide solution 3 × 50 mL), brine (50 mL), dried ($MgSO_4$), filtered, and concentrated, and the residue was distilled to give 4.21 g (40% yield) of **1c** as a clear colorless liquid: bp 71–73 °C (0.8 Torr); ^{1}H NMR (200 MHz) δ 4.76 (s, 1 H, H-C(2)), 1.92 (m, 2 H), 1.70 (m, 1 H), 1.50 (m, 4 H), 1.10 (m, 1 H), 0.85, 0.80 (2d, J = 2.8, 2.8 Hz, 6 H, $(CH_3)_2CHC(3)$), 0.14 (s, 9 H); ^{13}C NMR (75.5 MHz) 150.71 (C(1)), 108.12 (C(2)), 41.19 (C(3)), 32.55 (C(6)), 30.04, 25.38, 22.37, 19.55, 19.50, 0.33 ppm; IR (thin film) 2950 s, 2920 s, 2863 s, 2830 s, 1658 s, 1450 m, 1362 s, 1255 s, 1245 s, 1175 s, 1128 m, 985 m, 900 s cm^{-1}; MS (70 eV) *m/e* 212 (M^+, 2.2), 170 (16), 169 (100), 75 (14), 73 (45). Anal. Calcd for $C_{12}H_{24}OSi$: C, 67.86; H, 11.39. Found: C, 67.93; H, 11.62.

5-(1,1-Dimethylethyl)-1-(trimethylsiloxy)cyclohexene (3). In a flame-dried, 50-mL, 3-necked, round-bottom flask fitted with thermometer, nitrogen inlet tube, and rubber septa was placed a solution of diisopropylamine (144 mg, 1.42 mmol) in THF (5 mL) and cooled to −78 °C. To this solution was added *n*-butyllithium (1.03 mL of a 1.38 M solution, 1.42 mmol). The resulting solution was warmed to 0 °C and stirred for 15 min. After recooling to −78 °C a solution of 3-(1,1-dimethylethyl)cyclohexanone (200 mg, 1.30 mmol) in THF (5 mL) was added dropwise. The resulting colorless solution was stirred at −78 °C for 1 h, warmed to 0 °C for 5 min, recooled to −78 °C, and then treated with HMPA (280 mg, 1.56 mmol), triethylamine (158 mg, 1.56 mmol), and chlorotrimethylsilane (170 mg, 1.56 mmol). The mixture was stirred at −78 °C for 1 h, warmed to room temperature, and then poured onto water (25 mL). The mixture was extracted with ether (3 × 25 mL), and the ether extracts were washed with water (25 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford a pale yellow oil. Distillation afforded 255 mg (87% yield) of **3** as a colorless oil: bp 90 °C (0.4 Torr); ^{1}H NMR (300 MHZ) δ 4.84

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(m, 1 H, H-C(2)), 1.70–2.05 (m, 5 H), 1.34 (m, 1 H), 1.04 (m, 1 H), 0.96 (s, 9 H, $(CH_3)_3Si$); ^{13}C NMR (75.5 MHz) 150.65 (C(1)), 103.47 (C(2)), 44.90 (C(5)), 32.14 ($(CH_3)_3C$–), 31.72 (C(6)), 27.16 ($(CH_3)_3C$), 24.45 (C(3)), 23.76 (C(4)), 0.32 ($(CH_3)_3Si$) ppm; GC t_R 12.90 min (50 m OV-101, 80 °C (1 min), 10 °C/min, 250 °C (2 min)) contains 11% of **1d** (12.60 min).

4. General Procedure for Synthesis of 2-Chlorocyclohexanones. To a 0 °C solution of the silyl enol ether (1.0 equiv) in THF (0.7 M) was added methyllithium (1.2 equiv of a 1.25 M solution in ether). After stirring at room temperature for 1 h the enolate solution was added via cannula to a −60 °C solution of *N*-chlorosuccinimide (1.2 equiv) mechanically stirred in THF (0.2 M) at such a rate that the temperature never rose above −60 °C. After stirring at −70 °C for 1 h the reaction was quenched by the slow addition of saturated aqueous sodium bicarbonate solution. The reaction mixture was warmed to room temperature and was extracted with pentane. The pentane extracts were washed with water and brine, dried over magnesium sulfate, and concentrated. The crude products were purified by column chromatography.

***trans*-2-Chloro-3-ethylcyclohexanone (*trans*-2b).** Yield 45% (after column chromatography (benzene/hexane 4/1): bp 88–89 °C (0.9 Torr); ^1H NMR (300 MHz) δ 4.21 (d, J = 10.2 Hz, 1 H, H-C(2)), 2.73 (m, 1H, eq-H-C(6)), 2.34 (ddd, J = 6.1, 12.8, 12.8 Hz, 1 H, ax-H-C(6)), 2.14–1.40 (m, 7 H) 0.95 (t, J = 7.5 Hz, 3 H, CH_3CH_2-C(3)); ^{13}C NMR (75.5 MHz) 202.92 (C(1)), 68.51 (C(2)), 48.34 (C(6)), 40.10 (C(3)), 28.42, 25.85, 24.57, 10.12 (CH_3CH_2-C(3)) ppm; IR (thin film) 2960 s, 2924 s, 2865 s, 1723 s, 1445 s, 1425 m, 1378 m, 1318, 1250 m, 1170 m, 1105 m cm^{-1}; MS (70 eV) m/e 162 (M^+, ^{37}Cl, 2.6), 160 (M^+, ^{35}Cl, 7.4), 125 (14), 124 (71), 122 (38), 116 (21), 111 (38), 107 (32), 97 (36), 96 (100), 95 (26), 94 (17), 83 (31), 82 (42), 81 (37), 79 (13), 71 (23), 70 (11), 69 (17), 68 (63), 67 (51), 66 (13), 55 (51); TLC R_f 0.17 (EtOAc/hexane 1/20). Anal. Calcd for $C_8H_{13}ClO$: C, 59.81; H, 8.16. Found: C, 59.70; H, 8.23.

***cis*-2-Chloro-3-ethylcyclohexanone (*cis*-2b).** Yield 36% (after column chromatography (benzene/hexane 4/1)): bp 82–85 °C (0.9 Torr); ^1H NMR (300 MHz) δ 4.22 (d, J = 1.2 Hz, 1 H, H-C(2)), 2.95 (ddd, J = 6.8, 13.2, 13.2 Hz, 1 H, ax-H-C(6)), 2.25 (m, 1 H, eq-H-C(6)), 2.03 (m, 1 H, H-C(3)), 1.86 (m, 1 H), 1.78–1.43 (m, 5 H), 0.91 (t, J = 7.4 Hz, 3 H, CH_3CH_2-C(3)); ^{13}C NMR (75.5 MHz) 205.28 (C(1)), 65.42 (C(2)), 45.41 (C(6)), 36.09 (C(3)), 25.22, 25.15, 24.50, 10.92 (CH_3CH_2-C(3)) ppm; IR (CCl_4) 2967 s, 2867 s, 1725 s, 1460 m, 1246 m cm^{-1}; TLC R_f 0.28 (EtOAc/hexane 1/20). Anal. Calcd for $C_8H_{13}ClO$: C, 59.81; H, 8.16. Found: C, 59.90; H, 8.23.

***trans*-2-Chloro-3-(1-methylethyl)cyclohexanone (*trans*-2c).** Yield 40% (after column chromatography (EtOAc/hexane 1/6)): bp 132–135 °C (0.8 Torr); ^1H NMR (300 MHz) δ 4.34 (d, J = 11.0 Hz, 1 H, H-C(2)), 2.48 (m, 1 H, eq-H-C(6)), 2.21 (ddd, J = 5.3, 12.5, 12.5, 1 H, ax-H-C(6)), 2.68 (m, 1 H, H-C(3)), 2.40–1.40 (m, 5 H), 0.98, 0.88 (2 d, J = 7.2, 6.8 Hz, 6 H, $(CH_3)_2CH$-C(3)); ^{13}C NMR (75.5 MHz) 202.77 (C(1)), 67.97 (C(2)), 52.36 (C(6)), 40.48 (C(3)), 27.68, 24.73, 23.54, 20.76, 15.09 ($(CH_3)_2CH$-C(3)) ppm; IR (CCl_4) 2965 s, 2872 s, 1738 s, 1466 m, 1175 m; MS (70 eV) m/e 176 (M^+, ^{37}Cl, 5), 174 (M^+, ^{35}Cl, 14), 156 (12), 138 (15), 132 (32), 131 (13), 130 (100), 121 (24), 120 (12), 110 (20), 97 (24), 96 (33), 95 (74), 83 (21), 82 (26), 81 (19), 79 (10), 70 (14), 69 (61), 67 (32), 56 (16), 55 (36); TLC R_f 0.13 (EtOAc/hexane 1/20). Anal. Calcd for $C_9H_{15}ClO$: C, 61.89; H, 8.66. Found: C, 61.88; H, 8.74.

***cis*-2-Chloro-3-(1-methylethyl)cyclohexanone (*cis*-2c).** Yield 50% (after column chromatography (EtOAc/hexane 1/6)): bp 105–107 °C (0.9 Torr); ^1H NMR (300 MHz) δ 4.15 (s, 1 H, H-C(2)), 2.98 (ddd, J = 6.6, 13.8, 13.8 Hz, 1 H, ax-H-C(6)), 2.23 (dd, J = 1.6, 13.8 Hz, 1 H, eq-H-C(6)), 2.07 (m, 1 H, $(CH_3)_2CH$-C(3)), 1.87–1.44 (m, 5 H), 0.82, 0.87 (2d, J = 6.6, 6.6 Hz, 6 H, $(CH)_3)_2CH$-C(3)); ^{13}C NMR (75.5 MHz) 204.83 (C(1)), 64.22 (C(2)), 50.19 (C(6)), 35.12 (C(3)), 28.87, 25.15, 22.63, 20.56, 19.40 ppm; IR (CCl_4) 2967 s, 2870 s, 1726 s, 1475 m, 1315 m, 1250 m cm^{-1}; MS (70 eV) m/e 176 (M^+, ^{37}Cl, 7.6), 174 (M^+, ^{35}Cl, 23), 156 (14), 138 (17), 132 (36), 131 (23), 130 (100), 123 (10), 121 (23), 110 (18), 97 (23), 96 (31), 95 (72), 83 (22), 82 (22), 81 (15), 70 (12), 69 (54), 67 (25), 56 (16), 55 (28); TLC R_f 0.3 (EtOAc/hexane 1/20). Anal. Calcd for $C_9H_{15}ClO$: C, 61.89; H, 8.66. Found: C, 62.06; H, 8.60.

***trans*-2-Chloro-3-(1,1-dimethylethyl)cyclohexanone (*trans*-2d).** Yield 47%: ^1H NMR (300 MHz) δ 4.14 (dd, J = 1.16, 3.27 Hz, 1 H, H-C(2)), 2.90 (m, 1 H), 2.24 (m, 1 H), 2.10–1.93 (m, 4 H), 1.45 (m, 1 H), 0.94 (s, 9 H, $(CH_3)_3C$-C(3)); ^{13}C NMR (75.5 MHz) 205.71 (C(1)), 61.11 (C(2)), 55.10 (C(3)), 36.04, 34.14 ($(CH_3)_3C$-C(3)), 27.98 ($(CH_3)_3$-C-C(3)), 22.86, 21.56 ppm; IR (CCl_4) 2965 s, 2871 m, 1727 m, 1476 m, 1457 w, 1425 w, 1401 w, 1370 m, 1346 w, 1316 w, 1256 w, 1225 m, 1157 w, 1113 w, 1102 w, 930 w, 890 w, 862 w, 833 w cm^{-1}; MS (10 eV) m/e 190 (M^+, ^{37}Cl, <0.5), 188 (M^+, ^{35}Cl, 3.3), 97 (100), 57 (56); TLC R_f 0.13 (EtOAc/hexane 1/30); GC t_R 12.47 (50m OV-101, 80 °C (1 min), 10 °C min (250 °C/2 min)); high-resolution MS calcd for $C_{10}H_{17}{}^{35}ClO$ 188.09680, found 188.09688.

Preparation of *cis*-2-Chloro-3-(1,1-dimethylethyl)cyclohexanone (*cis*-2d).[6a] A solution of *trans*-2-chloro-3-(1,1-dimethylethyl)cyclohexanone (99 mg, 0.52 mmol) in dry *N,N*-dimethylformamide (2.5 mL) was treated with lithium chloride (4.4 mg, 0.10 mmol). The mixture was heated to 50 °C for 23 h, cooled, poured into water (5 mL), and extracted with pentane (3 × 15 mL). The pentane extracts were washed with water (5 mL) and saturated brine (5 mL), combined, dried over Na_2SO_4, filtered, and concentrated to leave a pale yellow oil (84 mg). Purification by column chromatography (10 mm × 15 cm SiO_2, EtOAc/hexane 1/16) gave the chloro ketones (32 mg, 0.17 mmol, 33%) as an 85:15 cis/trans mixture (GC) and 3-(1,1-dimethylethyl)-2-cyclohexenone (40 mg, 0.26 mmol, 51%): ^1H NMR (300 MHz) δ 4.36 (br s, 1 H, H-C(2)), 3.00 (ddd, J = 6.9, 14.0, 14.0 Hz, 1 H, ax-H-C(6)), 2.23 (br d, J = 14.0 Hz, 1 H, eq-H-C(6)), 2.11 (m, 1 H), 1.89 (ddd, J = 3.7, 13.4, 13.4 Hz, 1 H), 1.72 (br d, J = 14.0 Hz, 1 H), 1.59 (ddd, J = 2.5, 2.5, 12.0 Hz, 1 H), 1.50 (ddd, J = 4.4, 4.4, 13.4 Hz, 1 H); ^{13}C NMR (75.5 MHz) 205.40 (C(1)), 64.53 (C(2)), 52.50 (C(3)), 35.46, 33.54 ($(CH_3)_3C$-C(3)), 28.30 ($(CH_3)_3$C-C(3)), 25.54 20.61 ppm; IR (CCl_4) 2965 s, 2870 m, 1727 s, 1480 w, 1470 w, 1460 w, 1429 w, 1400 w, 1369 m, 1317 w, 1294 w, 1261 w, 1238 m, 1214 w, 1183 w, 1111 w, 1043 w, 935 w, 910 w cm^{-1}; MS (10 eV) m/e 190 (M^+, ^{37}Cl, 1.3), 188 (M^+, ^{35}Cl, 5.1), 131 (7), 97 (100), 57 (62); TLC R_f 0.13 (EtOAc/hexane 1/30); GC t_R 12.54 (50 m OV-101, 80 °C (1 min), 10 °C/min, 250 °C (2 min); high-resolution MS calcd for $C_{10}H_{17}{}^{35}ClO$ 188.09680, found 188.09681.

***trans*-2-Chloro-5-(1,1-dimethylethyl)cyclohexanone (*trans*-2e).**[6b] Yield 14%: mp 47–48 °C (lit. mp 49–50 °C); ^1H NMR (300 MHz) δ 4.45 (ddd, J = 1.0, 5.6, 13.3 Hz, 1 H, H-C(2)), 2.66 (ddd, J = 2.8, 2.8, 13.2, 1 H, eq-H-C(6)), 2.53 (m, 1 H), 2.14 (ddd, J = 1.0, 13.2, 13.2 Hz, 1 H, ax-H-C(6)), 2.01–1.77 (m, 2 H), 1.56–1.47 (m, 2 H, 0.93 (s, 9 H, $(CH_3)_3$-C(5)); ^{13}C NMR (75.5 MHz) 202.83 (C(1)), 64.13 (C(2)), 49.75 (C(5)), 42.98, 37.36, 32.72 ($(CH_3)_3C$-C(5)), 27.15 ($(CH_3)_3C$-C(5)), 26.67 ppm; TLC R_f 0.24 (benzene/hexane 1/1); GC t_R 14.46 min (50 m OV-101, 80 °C (1 min), 10 °C/min, 250 °C (2 min)).

***cis*-2-Chloro-5-(1,1-dimethylethyl)cyclohexanone (*cis*-2e).**[6b] Yield 32%: ^1H NMR (300 MHz) δ 4.17 (s, 1 H, H-C(2)), 2.74 (dd, J = 13.5, 13.5 Hz, 1 H, ax-H-C(6)), 2.26–2.35 (m, 2 H), 1.74–2.01 (m, 3 H), 1.46 (m, 1 H), 0.91 (s, 9 H, $(CH_3)_3$-C(5)); ^{13}C NMR (75.5 MHz) 206.26 (C(1)), 59.84 (C(2)), 49.58 (C(5)), 37.94, 33.80, 32.88 ($(CH_3)_3C$-C(5)), 27.10 ($(CH_3)_3$C-C(5)), 20.06 ppm; TLC R_f 0.28 (benzene/hexane 1/1); GC t_R 12.64 min (50 m OV-101, 80 °C (1 min), 10 °C/min, 250 °C (2 min)).

***O*-(*tert*-Butyldiphenylsilyl)hydroxylamine.** Hydroxylamine hydrochloride (243 mg, 3.5 mmol) was added to a solution of ethylenediamine (0.234 mL, 210 mg, 3.5 mmol) in dichloromethane (1.5 mL) and stirred for 24 h. To the resulting biphasic mixture was added a solution of *tert*-butyldiphenylchlorosilane (962 mg, 3.5 mmol) in dichloromethane (2.5 mL) in five portions via syringe. The mixture was stirred for 36 h and filtered, and the precipitate was washed with dichloromethane (15 mL). The solvent was evaporated in vacuo, and the residue was distilled bulb-to-bulb (175 °C/0.6 Torr) to give a clear colorless liquid which crystallized on standing. Recrystallization from ether/pentane gave the hydroxylamine. Yield 75%: mp 74–75 °C (ether/pentane); ^1H NMR (300 MHz) δ 7.79 (d, J = 7.21 Hz, 2 H, ArH), 7.46–7.44 (m, 3 H, ArH), 5.29 (s, 2 H, NH_2), 1.15 (s, 9 H, $(CH_3)_3$C-Si); ^{13}C NMR (75.5 MHz) 135.41, 133.31, 129.62, 127.62, 27.16, 19.03 ppm; IR (CCl_4) 3074 m, 2934 s, 2858 s, 2578 s, 1471 m, 1429 s, 1182 m, 1115 s, 907 s, 817 s; MS (70 eV) m/e 215 (19), 214 (100), 199 (39), 197 (34), 138 (15). Anal. Calcd for $C_{16}H_{21}NOSi$: C, 70.80; H, 7.80; N, 5.16. Found: C, 71.09; H, 7.70; N, 5.20.

5. General Procedure for Formation of (*tert*-Butyldiphenylsilyl)-oximes. The α-chloro ketone (1 equiv) dissolved in chloroform or dichloromethane (0.7 M) was treated with *O*-(*tert*-butyldiphenylsilyl)-hydroxylamine (1 equiv), 4A molecular sieves (crushed), and a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS). The mixture was stirred at room temperature for 12 h and then was filtered through Celite; the precipitate was rinsed with chloroform, and the solvent was evaporated in vacuo. The crude silyloximes were purified by radial chromatography.

(*E*)-*trans*-2-Chloro-3-methylcyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*trans*-5a). Yield 66% (after radial chromatography (pentane). An analytical sample was recrystallized from methanol/H_2O: mp 78–79 °C (MeOH/H_2O); ^1H NMR (300 MHz) δ 7.70 (m, 4 H, ArH), 7.38 (m, 6 H, ArH), 4.34 (d, J = 1.8, 1 H, H-C(2)), 3.33 (d, J = 14.9, 1 H, eq-H-C(6)), 2.32 (m, 2 H), 1.78–1.2 (m, 4 H), 1.12 (s, 9 H, $(CH_3)_3$C-Si), 0.91 (d, J = 7.4, 3 H, CH_3-C(3)); ^{13}C NMR (75.5 MHz) 161.69 (C(1)), 135.49, 135.45, 133.68, 129.67, 127.59, 63.31 (C(2)), 38.16 (C(6)), 27.12 (C(3)), 26.06 (C(5)), 20.69, 19.89, 19.51, 17.00 ppm; IR (CCl_4) 3074 w, 3053 w, 2934 s, 2893 m, 2858 m, 1472

m, 1462 w, 1429 m, 1367 w, 1223 w, 1115 s, 1192 w, 1016 w, 968 m, 951 s, 929 w; MS (70 eV) *m/e* 254 (43), 185 (35), 173 (12), 159 (11), 158 (78), 157 (100), 128 (20), 127 (20), 113 (20), 100 (87), 99 (28), 81 (25), 71 (14), 58 (15), 57 (27), 55 (28), 43 (55), 42 (22), 41 (33), 39 (14), 31 (42), 30 (58). Anal. Calcd for $C_{23}H_{30}ClNOSi$: C, 69.06; H, 7.56; N, 3.50; Cl, 8.86. Found: C, 68.93; H, 7.69; N, 3.41; Cl, 8.95.

(*E*,*Z*)-*cis*-2-Chloro-3-methylcyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*,*Z*)-*cis*-5a). Yield 84% (after radial chromatography (EtOAc/hexane 1/15)): ^{1}H NMR (300 MHz) δ 7.78–7.73 ((m, 4 H, ArH), 7.48–7.39 (m, 6 H, ArH), 5.77 (d, J = 1.2 Hz, 0.4 H, *Z*-H-C(2)), 4.62 (s, 0.6 H, *E*-H-C(2)), 3.54 (d, J = 12.7 Hz, 0.6 H, *E*-eq-H-C(6)), 2.57 (ddd, J = 5.5, 13.9, 13.9 Hz, 0.4 H, *Z*-ax-H-C(6)), 2.35 (br d, J = 12.9 Hz, 0.4 H, *Z*-eq-H-C(6)), 2.25 (ddd, J = 5.8, 14.0, 14.0 Hz, 6 H, *E*-ax-H-C(6)), 1.94 (m, 4 H), 1.82–1.62 (m, 3 H), 1.58–1.38 (m, 6 H), 1.17, 1.16 (2s, 9 H, $(CH_3)_3$-CSi, 1.10 (d, J = 6.5 Hz, 3 H, CH_3-C-(3)); ^{13}C NMR (75.5 MHz) 163.78 (*E*-C(1)), 161.98 (*Z*-C(1)), 135.44, 133.58, 133.50, 133.41, 129.63, 127.84, 127.56, 126.91, 65.87 (*Z*-C(2)), 54.48 (*E*-C(2)), 38.64 (*E*-C(6)), 37.09 (*Z*-C(6)), 27.57, 27.10, 26.52, 25.66, 24.56, 19.72, 19.46, 18.80 ppm; IR (CCl_4) 3074 w, 3051 w, 2963 m, 2933 m, 2861 m, 1473 m, 1458 w, 1429 m, 1116 s, 967 m, 950 m, 909 s cm^{-1}; MS (70 eV) *m/e* 344 ($M^+ - C_4H_9$, ^{37}Cl, 13), 342 ($M^+ - C_4H_9$, ^{35}Cl, 33), 199 (15), 108 (100), 81 (34); TLC R_f 0.52 (hexanes). Anal. Calcd for $C_{23}H_{30}ClNOSi$: C, 69.06; H, 7.56; N, 3.50; Cl, 8.86. Found: C, 68.96; H, 7.39; N, 3.38; Cl, 8.98.

(*E*)-*trans*-2-Chloro-3-ethylcyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*trans*-5b). Yield 75% (after radial chromatography (EtOAc/hexane 1/15)): ^{1}H NMR (360 MHz) δ 7.74–7.70 (m, 4 H, ArH), 7.43–7.35 (m, 6 H, ArH), 4.49 (s, 1 H, H-C(2)), 3.42 (d, J = 15.6 Hz, 1 H, eq-H-C(6)), 2.31 (ddd, J = 6.2, 13.3, 13.3 Hz, 1 H, ax-H-C-(6)), 2.20 (m, 1 H, H-C(3)), 2.04 (m, 1 H, H-C(5)), 1.73 (m, 1 H, H-C(5)), 1.55 (m, 2 H, H-C(4)), 1.28 (m, 2 H, CH_3CH_2-C(3)), 1.12 (s, 9 H, $(CH_3)_3$C-Si), 0.86 (t, J = 7.4 Hz, 3 H, CH_3CH_2-C(3)); ^{13}C NMR (75.5 MHz) 161.80 (C(1)), 135.40, 133.44, 129.59, 127.52, 62.05 (C(2)), 44.98 (C(6)), 27.08 (C(3)), 23.50 (C(5)), 23.43, 20.44, 19.84, 19.42, 11.63 ppm; IR (CCl_4) 3978 w, 3087 m, 3064 m, 2989 s, 2938 s, 2907 m, 2875 m, 2369 s, 2938 s, 2907 m, 2975 m, 2369 w, 1498 w, 1482 m, 1467 m, 1440 m, 1139 s, 954 s, 929 m, 870 m cm^{-1}; MS (70 eV) *m/e* 358 ($M^+ - C_4H_9$, ^{37}Cl, 39), 357 ($M^+ - C_4H_8$, ^{35}Cl, 27), 356 ($M^+ - C_4H_9$, ^{35}Cl, 100), 320 (11), 278 (24), 217 (15), 199 (273), 160 (12), 157 (27), 122 (43), 116 (26), 111 (20), 107 (11), 96 (10), 95 (23), 82 (31), 81 (33), 71 (11), 67 (14), 55 (26). Anal. Calcd for $C_{24}H_{32}ClNOSi$: C, 69.96; H, 7.83; N, 3.40; Cl, 8.60. Found: C, 69.62; H, 8.01; N, 3.47; Cl, 8.97.

(*E*,*Z*)-*cis*-2-Chloro-3-ethylcyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*,*Z*)-*cis*-5b). Yield 84% (after radial chromatography (EtOAc/hexane 1/25)): ^{1}H NMR (300 MHz) δ 7.72–7.69 (m, 8 H, ArH), 7.41–7.37 (m, 6 H, ArH), 5.87 (br s, 0.3 H, *Z*-H-C(2)), 4.66 (br s, 0.7 H, *E*-H-C(2)), 3.50 (br d, J = 13.3 Hz, 0.7 H, *E*-eq-H-C(6)), 2.54 (ddd, J = 5.8, 14.0, 14.0 Hz, 0.3 H, *Z*-ax-H-C(6)), 2.25 (br d, J = 13.3 Hz, 0.3 H, *Z*-eq-H-C(6)), 2.20 (ddd, J = 5.8, 14.0, 14.0 Hz, 0.7 H, *E*-ax-H-C(6)), 2.04–1.14 (m, 15 H), 1.10, 1.09 (2s, 9 H, $(CH_3)_3$-C-Si), 0.98 (t, J = 7.0 Hz, 0.9 H, *Z*-CH_3CH_2), 0.89 (t, J = 7.0 Hz, 2.1 H, *E*-CH_3CH_2-C(3)); ^{13}C NMR (75.5 MHz) 163.47 (*E*-C(1)), 162.00 (*Z*-C(1)), 135.51, 135.46, 135.40, 129.60, 129.40, 127.57, 127.54, 127.46, 127.46, 65.10 (*Z*-C(2)), 63.61 (*E*-C(2)), 53.49 (*Z*-C(3)), 45.29 (*E*-C(3)), 29.70, 27.05, 25.91, 24.52, 20.28, 19.44, 10.94; IR (CCl_4) 3075 m, 3054 m, 2963 s, 2934 s, 2861 s, 1591 w, 1487 w, 1472 m, 1462 m, 1429 s, 1391 w, 1381 w, 1362 w, 1266 w, 1192 w, 1115 s, 1009 w, 947 s, 875 m, 847 m cm^{-1}; MS (70 eV) *m/e* 358 ($M^+ - C_4H_9$, ^{37}Cl, 24), 357 ($M^+ - C_4H_8$, ^{35}Cl, 17), 356 ($M^+ - C_4H_9$, ^{35}Cl 65), 278 (13), 254 (12)e, 217 (18), 199 (32), 157 (18), 122 (100), 95 (44), 81 (20); TLC R_f 0.78 (EtOAc/hexane 1/7). Anal. Calcd for $C_{24}H_{32}ClNOSi$ C, 69.96; H, 7.83; N, 3.40; Cl, 8.60. Found: C, 70.12, H, 7.96; N, 3.49; Cl, 8.30.

(*E*)-*trans*-2-Chloro-3-(1-methylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*trans*-5c). Yield 80% (after radial chromatography (EtOAc/hexane 1/15)): mp 77–78 °C; ^{1}H NMR (360 MHz) δ 7.77 (t, J = 7.8 Hz, 4 H, ArH), 7.46 (m, 6 H, ArH), 4.78 (s, 1 H, H-C(2)), 3.44 (d, J = 14.5 Hz, 1 H, eq-H-C(6)), 2.40 (ddd, J = 14.5, 14.5, 6.1 Hz, 1 H, ax-H-C(6)), 2.20 (m, 1 H, H-C(3)), 1.81–1.26 (m, 4 H, H-C(4), H-C(5)), 1.18 (s, 9 H, $(CH_3)_3$C-Si), 0.94, 0.89 (2d, J = 6.7, 6.7 Hz, 6 H, $(CH_3)_2$CH-C(3)); ^{13}C NMR (75.5 MHz) 161.98 (C-(1)), 135.40, 133.64, 133.44, 129.56, 127.48, 61.28 (C(2)), 27.12, 27.07, 26.77, 21.69, 20.50, 20.01, 19.39 ppm; IR (CCl_4) 3073 m, 2963 s, 2858 s, 1471 m, 1462 m, 1429 s, 1115 s, 952 s, 935 s cm^{-1}; MS (70 eV) *m/e* 372 ($M^+ - C_4H_9$, ^{37}Cl, 39), 371 ($M^+ - C_4H_8$, ^{35}Cl, 28), 370 ($M^+ - C_4H_9$, ^{37}Cl, 100), 292 (26), 263 (12), 217 (10), 199 (32), 157 (21), 136 (23), 95 (18); TLC R_f 0.45 (EtOAc/hexane 1/20). Anal. Calcd for $C_{25}H_{34}ClNOSi$: C, 70.14; H, 8.00; N, 3.27; Cl, 8.28. Found: C, 70.09; H, 8.02; N, 3.20; Cl, 8.22.

(*E*)-*cis*-2-Chloro-3-(1-methylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*cis*-5c). Yield 82% (after radial chromatography (hexane)): ^{1}H NMR (MHz) δ 7.73–7.69 (m, 4 H, ArH), 7.45–7.35 (m, 6 H, ArH), 4.76 (br s, 1 H, H-C(2)), 3.52 (br d, J = 14.1 Hz, 1 H, eq-H-C(6)), 2.27 (ddd, J = 5.6, 14.1, 14.1 Hz, 1 H, ax-H-C(6)), 2.01–1.18 (m, 6 H), 1.10 (s, 9 H, $(CH_3)_3$C-Si), 0.94, 0.93 (2d, J = 5.4, 6.3 Hz, 6 H, $(CH_3)_2$-C(3)); ^{13}C NMR (75.5 MHz) 164.07 (C(1)), 135.41, 133.38, 129.63, 127.57, 62.90 (C(2)), 50.54 (C(3)), 29.64, 27.03, 24.54, 23.79, 20.72, 20.20, 19.88, 19.43 ppm; IR 3074 m, 2963 s, 2860 m, 1473 m, 1429 m, 1388 w, 1369 w, 1271 w, 1115 s, 1047 w, 951 s, 877 s, 817 s cm^{-1}; MS (70 eV) *m/e* 372 ($M^+ - C_4H_9$, ^{37}Cl, 40), 371 ($M^+ - C_4H_8$, ^{35}Cl, 28), 370 ($M^+ - C_4H_9$, ^{35}Cl, 100), 199 (14), 136 (33), 95 (12); TLC R_f *Z* 0.39, *E* 0.45 (EtOAc/hexane 1/35). Anal. Calcd for $C_{25}H_{34}ClNOSi$: C, 70.14; H, 8.00; N, 3.27; Cl, 8.28. Found: C, 70.03; H, 7.73; N, 3.44; Cl, 8.24.

(*E*)-*trans*-2-Chloro-3-(1,1-dimethylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*trans*-5d). Yield 68%: mp 93.5–94.5 °C (pentane); ^{1}H NMR (300 MHz) δ 7.72 (m, 4 H, ArH), 7.41 (m, 6 H, ArH), 4.71 (br s, 1 H, H-C(2)), 3.05 (ddd, J = 7.3, 10.4, 17.8 Hz, 1 H, ax-H-C(6)), 2.65 (br d, J = 17.8 Hz, 1 H, eq-H-C(6)), 2.11 (ddd, J = 1.0, 6.8, 10.1 Hz, 1 H), 2.06–1.80 (m, 3 H), 1.19 (m, 1 H), 1.12 (s, 9 H, $(CH_3)_3$C-C(3)), 0.88 (s, 9 H, $(CH_3)_3$C-Si); ^{13}C NMR (75.5 MHz) 163.43 (C(1)), 135.34, 133.57, 129.58, 127.52, 58.61 (C(2)), 54.73 (C-(3)), 34.18 (($CH_3)_3C$-C(3)), 27.17 (($CH_3)_3$C-C(3)), 27.00 (($CH_3)_3$C-Si), 23.16 (C(6)), 22.42 (C(4)), 19.35 (($CH_3)_3$C-Si), 18.85 (C(5)) ppm; IR (CCl_4) 3075 w, 2963 s, 2861 m, 1472 w, 1429 m, 1117 s, 953 s, 928 m, 841 7 cm^{-1}; MS (70 eV) 387 ($M^+ - C_4H_8$, ^{37}Cl, 10), 386 ($M^+ - C_4H_9$, ^{37}Cl, 39), 385 ($M^+ - C_4H_8$, ^{35}Cl, 28), 384 ($M^+ - C_4H_9$, ^{35}Cl, 100), 348 (17), 306 (11), 292 (15), 252 (23), 251 (12), 250 (66), 199 (38), 157 (23), 109 (15), 94 (25), 67 (13), 57 (54). Anal. Calcd for $C_{26}H_{336}ClNOSi$: C, 70.63; H, 8.21, N, 3.17, Cl, 8.02. Found: C, 70.58; H, 8.29; N, 3.27; Cl, 8.05.

(*E*)-*cis*-2-Chloro-3-(1,1-dimethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*cis*-5d). Yield 50%: ^{1}H NMR (300 MHz) δ 7.71 (m, 4 H, ArH), 7.41 (m, 6 H, ArH), 4.84 (br s, 1 H, H-C(2)), 3.53 (ddd, J = 3.5, 3.5, 14.2 Hz, 1 H, eq-H-C(6)), 2.25 (ddd, J = 6.0, 14.2, 14.2 Hz, 1 H, ax-H-C(6)), 2.02 (br d, J = 12.6 Hz, 1 H), 1.81 (ddd, J = 3.5, 12.6, 12.6 Hz, 1 H), 1.69 (br d, J = 11.9, 1 H), 1.43 (ddd, J = 2.8, 2.8, 11.9 Hz, 1 H), 1.34 (ddd, J = 4.3, 4.3, 13.6 Hz, 1 H), 1.12 (s, 9 H, $(CH_3)_3$C-C(3)), 1.01 (s, 9 H, $(CH_3)_3$C-Si); ^{13}C NMR 164.30 (C(1)), 135.48, 133.00, 129.62, 127.55, 62.54 (C(2)), 52.96 (C(3)), 33.28 (($C-H_3)_3C$-C(3)), 28.22 (($CH_3)_3$C-C(3)), 27.09 (($CH_3)_3$CSi), 24.91, 21.56, 20.33, 19.44 (($CH_3)_3$CSi) ppm; IR (CCl_4) 3075 m, 3054 w, 2961 s, 2861 m, 1472 m, 1429 m, 1397 w, 1368 m, 1233 w, 1115 s, 957 s, 880 s, 849 s cm^{-1}; MS (70 eV) *m/e* 387 ($M^+ - C_4H_8$, ^{37}Cl, 11), 386 ($M^+ - C_4H_9$, ^{37}Cl, 40), 385 ($M^+ - C_4H_8$, ^{35}Cl, 29), 384 ($M^+ - C_4H_9$, ^{35}Cl, 100), 252 (12), 250 (32), 199 (21), 94 (13), 57 (25); CI-MS 444 ($M^+ + H$, ^{37}Cl, 1.9), 442 ($M^+ + H$, ^{35}Cl, 5.3), 407 (17), 386 (25), 385 (19), 384 (64), 367 (10), 366 (40), 365 (28), 364 (100), 350 (19), 330 (17), 328 (27), 199 (15); TLC R_f 0.33 (EtOAc/hexane 1/30); high-resolution MS calcd for $C_{26}H_{37}ClNOSi$ ($M^+ + H$) 442.23330, found 442.23243.

(*Z*)-*cis*-2-Chloro-3-(1,1-dimethylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*Z*)-*cis*-5d). Yield 28%: ^{1}H NMR (300 MHz) δ 7.71 (m, 4 H, ArH), 7.39 (m, 6 H, ArH), 6.14 (br s, 1 H, H-C(2)), 2.58 (ddd, J = 5.4, 13.9, 13.9 Hz, ax-H-C(6)), 2.27 (br d, J = 13.9 Hz, 1 H, eq-H-C(6)), 1.96 (m, 1 H), 1.78 (m, 2 H), 1.32 (m, 2 H) 1.10 (s, 9 H, $(CH_3)_3$C-C(3)), 1.06 (s, 9 H, $(CH_3)_3$C-Si); ^{13}C NMR (75.5 MHz) 156.55 (C(1)), 135.51, 129.63, 127.56, 51.67 (C(2)), 51.32 (C(3)), 28.32 (($CH_3)_3$C-C(3)), 27.07, 27.06 (($CH_3)_3$C-Si), 26.41, 21.52, 19.39 (($C-H_3)_3C$-Si) ppm; IR (CCl_4) 3075 w, 3052 w, 2962 s, 2861 m, 1472 m, 1429 m, 1368 m, 1115 s, 936 s, 884 w, 833 m cm^{-1}; MS (70 eV) *m/e* 387 ($M^+ - C_4H_8$, ^{37}Cl, 2), 385 ($M^+ - C_4H_8$, ^{35}Cl, 6), 199 (7), 119 (31), 118 (98), 117 (100), 83 (17), 82 (24), 47 (25), 35 (15); CI-MS (CH_4) *m/e* 444 ($M^+ + H$, ^{37}Cl), 442 ($M^+ + H$, ^{35}Cl, 4.5), 407 (16), 406 (45), 386 (26), 385 (20), 384 (64), 367 (10), 366 (40), 365 (27), 364 (100), 350 (20), 330 (19), 328 (26), 199 (17); TLC R_f 0.24 (EtOAc/hexane 1/30); high-resolution MS calcd for $C_{26}H_{37}ClNOSi$ ($M^+ + H$) 442.23330, found 442.23286.

(*E*)-*trans*-2-Chloro-5-(1,1-dimethylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*)-*trans*-5e). Yield 65%: bp 240 °C (0.08 Torr); ^{1}H NMR (300 MHz) δ 7.78 (m, 4 H), 7.39 (m, 6 H), 4.49 (dd, J = 5.2, 10.0 Hz, 1 H, H-C(2)), 3.64 (ddd, J = 2.4, 3.6, 14.2 Hz, eq-H-C(6)), 2.43 (m, 1 H, ax-H-C(6)), 1.97–1.76 (m, 3 H), 1.52–1.29 (m, 2 H), 1.17 (s, 9 H, $(CH_3)_3$C-C(5)), 0.97 (s, 9 H, $(CH_3)_3$C-Si); ^{13}C NMR (75.5 MHz) 161.97 (C(1)), 135.55, 135.45, 133.80, 133.73, 129.50, 127.44, 57.82 (C(2)), 46.05 (C(5)), 36.90 (C(6)), 32.82 (($C-H_3)_3C$-*C*(5)), 27.39, 27.37 (($CH_3)_3$C-C(5)), 27.16 (($CH_3)_3$C-Si), 26.13, 25.67, 19.58 (($CH_3)_3C$-Si) ppm; IR CCl_4) 3075 w, 3056 w, 2963 s, 2894 m, 2861 m, 1472 m, 1429 m, 1368 w, 1115 s, 972 m, 938 s cm^{-1}; MS (70 eV) *m/e* 387 ($M^+ - C_4H_8$, ^{37}Cl, 11), 386 ($M^+ - C_4H_9$, ^{37}Cl, 37), 385 ($M^+ - C_4H_8$, ^{35}Cl, 30), 384 ($M^+ - C_4H_9$, ^{35}Cl, 100), 254 (21), 199 (15), 150 (10), 109 (20), 108 (21), 94 (19), 57 (12). Anal. Calcd for

$C_{26}H_{36}ClNOSi$: C, 70.63; H, 8.21; N, 3.17; Cl, 8.02. Found: C, 70.75; H, 8.17; N, 3.18; Cl, 7.93.

(*E*,*Z*)-*cis*-2-Chloro-5-(1,1-dimethylethyl)cyclohexanone *O*-(*tert*-Butyldiphenylsilyl)oxime ((*E*,*Z*)-*cis*-5e). Yield 95%: bp 240 °C (0.08 Torr); ^{1}H NMR (300 MHz) δ 7.70 (m, 4 H), 7.40 (m, 6 H), 5.85 (dd, *J* = 2.5, 2.5 Hz, 0.25 H, *Z*-H-C(2)), 4.70 (dd, *J* = 2.5, 2.5 Hz, 0.75 H, *E*-H-C(2)), 3.63 (ddd, *J* = 1.6, 3.3, 13.4 Hz, 0.75 H, *E*-eq-H-C(6)), 2.43–2.21 (m, 2 H), 1.97, (dd, *J* = 13.4, 13.4 Hz, 0.75 H, *E*-ax-H-C-(6)), 1.87–1.67 (m, 4.5 H), 1.11, 1.10 (2s, 9 H, $(CH_3)_3$C-C(5)), 0.98, 0.90 (2s, 9 H, $(CH_3)_3$C-Si; ^{13}C NMR (75.5 MHz) 164.37 (C(1)), 135.52, 133.58, 129.73, 127.63, 58.96, 48.35, 47.99, 35.41, 32.69, 28.68, 27.33, 27.15, 27.10, 21.98, 21.09, 20.92, 19.47 ppm; IR (CCl_4) 3074 w, 2963 s, 2896 m, 2859 m, 1472 m, 1429 s, 1395 w, 1368 m, 1240 w, 1117 s, 938 s, 880 w, 830 m cm^{-1}; MS (70 eV) *m/e* 387 ($M^+ - C_4H_8$, ^{37}Cl, 11), 386 ($M^+ - C_4H_9$, ^{37}Cl, 41), 385 ($M^+ - C_4H_8$, ^{35}Cl, 31), 384 ($M^+ - C_4H_9$, ^{35}Cl, 100), 250 (11), 199 (7), 150 (7), 57 (7). Anal. Calcd for $C_{26}H_{36}ClNOSi$: C, 70.63; H, 8.21; N, 3.17; Cl, 8.02. Found: C, 70.99; H, 8.09; N, 3.15; Cl, 8.10.

6. Preparation of *O*-Methyloximes. A solution of the chloro ketone (1.0 equiv) in glacial acetic acid (0.33 M) was treated with potassium acetate (2.0 equiv) and methoxyamine hydrochloride (2.0 equiv). The mixture was stirred at room temperature for 0.5 h, poured into water, and neutralized with solid sodium bicarbonate. The aqueous mixture was extracted with ether (3×). The ether extracts were washed with water and saturated brine, combined, dried over Na_2SO_4, filtered, and concentrated to afford the crude oximes. Bulb-to-bulb distillation gave the pure *O*-methyloximes.

(*E*)-*trans*-2-Chloro-3-methylcyclohexanone *O*-Methyloxime ((*E*)-*trans*-6a). Yield 86%: bp 100 °C (6 Torr); ^{1}H NMR (300 MHz) δ 4.29 (d, *J* = 3.2 Hz, 1 H, H-C(2)), 3.85 (s, 3 H, CH_3O), 2.88 (ddd, *J* = 3.8, 3.8, 14.7 Hz, 1 H, eq-H-C(6)), 2.32–2.11 (m, 3 H), 1.59 (m, 2 H), 1.38 (m, 1 H), 1.01 (d, *J* = 7.25 Hz, 3 H, CH_3-C(3); ^{13}C NMR (75.5 MHz) 156.01 (C(1)), 63.28 (C(2)), 61.58 (OCH_3), 38.13 (C(3)), 26.17 (C(6)), 20.68 (C(4)), 19.66 (C(5)), 17.23 (CH_3-C(3)) ppm; IR (CCl_4) 2970 m, 2941 s, 2900 m, 2874 w, 2820 w, 1458 w, 1435 w, 1380 w, 1222 w, 1050 s, 947 m, 911 w, 873 w, 856 w cm^{-1}; MS (70 eV) *m/e* 177 (M^+, ^{37}Cl, 8), 175 (M^+, ^{35}Cl, 23), 140 (100), 110 (22), 108 (26), 102 (16), 82 (17), 81 (34), 80 (12), 73 (25), 67 (16), 55 (12), 44 (11); GC t_R 10.76 min (50 m OV-1, 80 °C (1 min), 10 °C/min, 250 °C). Anal. Calcd for $C_8H_{14}ClNO$: C, 54.70; H, 8.03; N, 7.97; Cl, 20.19. Found: C, 54.57, H, 8.22; N, 7.97; Cl, 20.16.

(*E*,*Z*)-*cis*-2-Chloro-3-methylcyclohexanone *O*-Methyloxime ((*E*,*Z*)-*cis*-6a). Yield 64%: bp 100 °C (6 Torr); ^{1}H NMR (300 MHz) δ 5.33 (d, *J* = 2.8 Hz, 0.5 H, *Z*-H-C(2)), 4.52 (d, *J* = 2.8 Hz, 0.5 H, *E*-H-C(2)), 3.84, 3.86 (2s, 3 H, OCH_3), 3.06 (br d, *J* = 14.0 Hz, 0.5 H, *E*-eq-H-C(6)), 2.46 (ddd, *J* = 5.1, 14.0, 14.0 Hz, 0.5 H, *E*-ax-H-C(6)), 2.22 (br d, *J* = 14.3 Hz, 0.5 H, *Z*-eq-H-C(6)), 2.09 (ddd, *J* = 5.7, 14.3, 14.3 Hz, 0.5 H, *Z*-ax-H-C(6)), 1.96–1.22 (m, 5 H, HC(3), 2H-C(4), 2H-C(5)), 1.07 (d, *J* = 6.6 Hz, 1.5 H, *Z*-CH_3-C(3)), 1.05 (d, *J* = 6.5 Hz, 1.5 H, *E*-CH_3-C(3); ^{13}C NMR (300 MHz) 158.23 (C(1)), 157.06 (C(1)), 61.59 (OCH_3), 65.97 (C(2)), 54.66 (C(2)), 38.62 (C(3)), 37.02 (C(3)), 27.27, 27.40, 26.46, 25.66, 24.39, 19.63, 18.90 (CH_3-C(3)), 18.63 (CH_3-C(3)) ppm; IR (CCl_4) 2967 m, 2938 s, 2901 m, 2863 m, 2820 w, 1460 m, 1437 m, 1379 w, 1051 s, 947 m, 912 m, 857 w, 843 w cm^{-1}; MS (70 eV) *m/e* 177 (M^+, ^{37}Cl, 11), 175 (M^+, ^{35}Cl, 33), 140 (100), 139 (10), 110 (33), 108 (41), 102 (21), 93 (13), 87 (13), 82 (17), 81 (46), 80 (18), 73 (17), 69 (12), 67 (18), 56 (10), 55 (15), 54 (11); GC t_R 10.52, 10.79 min (50 m OV-1, 80 °C (1 min), 10 °C/min, 250 °C (2 min); high-resolution MS calcd for $C_8H_{14}ClNO$ 175.07640, found 175.07716.

(*E*)-*trans*-2-Chloro-3-ethylcyclohexanone *O*-Methyloxime ((*E*)-*trans*-6b). Yield 27%: ^{1}H NMR (360 MHz) δ 4.42 (d, *J* = 1.9 Hz, 1 H, H-C(2)), 2.85 (s, 3 H, CH_3O), 2.97 (br d, J_d = 13.8 Hz, 1 H, eq-H-C(6)), 2.22–2.02 (m, 3 H), 1.63 (m, 1 H), 1.56, 1.32 (m, 4 H), 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2-C(3)); IR (CCl_4) 2951 s, 2874 s, 2870 s, 1633 m, 1460 s, 1381 m, 1284 w, 1255 w, 1217 s, 1180 m, 1118 m, 1097 m, 1051 s, 958 s, 935 s, 908 s cm^{-1}. Anal. Calcd. for $C_9H_{16}ClNO$: C, 56.99; H, 8.52; N, 7.38. Found: C, 57.04; H, 8.34; N, 6.99.

7. Preparation of 2-Methoxy-3-methylcyclohexanone and Derivatives. *trans*-2-Methoxy-3-methylcyclohexanone (7a). To a cold (−40 °C) suspension of 1.59 g (8.32 mmol) of copper(I) iodide in 40 mL of dry ether was added dropwise 11.24 mL (16.64 mmol) of methyllithium (1.48 M in Et_2O). The resulting clear, colorless solution was stirred at 0 °C for 10 min and then was treated with a solution of 700 mg (5.54 mmol) of 2-methoxy-2-cyclohexenone in 10 mL of Et_2O over 5 min. After stirring for 1.5 h at 0 °C, the reaction mixture was quenched by addition of 20 mL of a saturated aqueous NH_4Cl solution. The mixture was poured into 60 mL of water and extracted with Et_2O (3 × 100 mL). The individual organic extracts were washed in series with water (100 mL) and brine (100 mL), then combined and dried ($MgSO_4$). Rotary evaporation of solvent and distillation in vacuo of the remaining residue yielded 581 mg (74%) of **7a** (bp 100–110 °C (2 Torr)) as a 55/45 mixture of cis/trans isomers, as judged by GC analysis (column C).

A solution of 570 mg (4.01 mmol) of **7a** in 20 mL of methanol was treated with 12 mg (0.23 mmol) of sodium methoxide. After 24 h GC analysis indicated a 28:71 mixture cis/trans isomers, and this mixture was neutralized with 2 drops of 2 N aqueous HCl solution, and the solvent was removed by rotary evaporation. The residue was poured into 20 mL of water and extracted with ether (3 × 60 mL). The individual organic extracts were washed in series with water (20 mL) and brine (20 mL), then combined and dried ($MgSO_4$). Rotary evaporation of the solvent and purification by silica gel chromatography (EtOAc/hexane 1/3) gave 257 mg of pure trans **7a**: ^{1}H NMR (360 MHz) δ 3.43 (s, 3 H, OCH_3), 3.32 (d, *J* = 9.44 Hz, H-C(2)), 2.47–1.43 (7 H), 1.10 (d, *J* = 6.32 Hz, C(3)-CH_3); IR 2900 s, 1720 s, 1445 m, 1327 w, 1300 w, 1240 w, 1185 m, 1147 s, 1112 s, 1055 m, 1005 m, 904 m, 883 m cm^{-1}.

(*E*)-*trans*-2-Methoxy-3-methylcyclohexanone Oxime ((*E*)-*trans*-8a). To a magnetically stirred solution of **7a** (109 mg, 0.77 mmol) in 1.5 mL of glacial acetic acid was added hydroxylamine hydrochloride (80 mg, 1.15 mmol) and potassium acetate (113 mg, 1.15 mmol). After stirring at room temperature for 1.5 h, the reaction mixture was poured into water (20 mL) and extracted with ether (3 × 20 mL). The combined ether extracts were washed with water (2 × 20 mL) and brine (20 mL). The dried (Na_2SO_4) solution was concentrated and purified by silica gel chromatography (EtOAc/hexane 1/2) to afford 105 mg (87%) of **8a** as a white solid: ^{1}H NMR (360 MHz) δ 3.34 (d, *J* = 4.85 Hz, 1 H, H-C(2)), 3.30 (s, 3 H, OCH_3), 2.66 (dt, *J* = 14.0, 5.2 Hz, 1 H, eq-H-C(6)), 2.34 (m, 1 H, ax-H-C(6)), 2.07 (m, 1 H), 1.95 (m, 1 H), 1.6 (m, 2 H), 1.30 (m, 1 H), 0.95 (d, *J* = 7.06 Hz, 3 H, C(2)-CH_3).

(*E*)-*trans*-2-Methoxy-3-methylcyclohexanone *O*-(*tert*-Butyldimethylsilyl)oxime ((*E*)-*trans*-9a). Prepared as described in Section 5 with the use of *O*-(*tert*-butyldimethylsilyl)hydroxylamine.[4a] Yield 77%: ^{1}H NMR (90 MHz) δ 3.43 (d, *J* = 3.2 Hz, 1 H, H-C(2)), 3.34 (s, 3 H, OCH_3), 3.00 (ddd, *J* = 13.5, 4.5, 4.5 Hz, 1 H, eq-H-C(6)), 2.25–1.25 (6 H), 1.12 (d, *J* = 7 Hz, 3 H, C(2)-CH_3), 1.09 (s, 9 H, $(CH_3)_3$CSi), 0.32 (s, 6 H, $(CH_3)_2$Si); IR 2880 s, 1455 m, 1345 m, 1146 w, 1082 s, 917 s, 887 s cm^{-1}.

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Supplementary Material Available: A description of the general experimental procedures, along with tables of bond lengths, bond angles, and torsional angles for (*E*)-*trans*-5a, are provided (30 pages). Ordering information is given on any current masthead page.