Model Studies of the Stereoelectronic Effect in Rh(II) Mediated Carbenoid C-H Insertion Reactions

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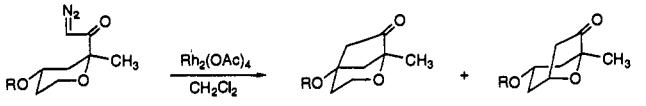
Abstract: Electronic effects of rhodium(II) catalyzed intramolecular C-H insertion reactions of 1-methyl-1-(diazoacetyl)-cyclohexane derivatives **4a**-i were studied. The C-3 H/C-5 H insertion ratio is modulated by the electron donating or withdrawing capacity of the functional groups at C-3 and C-5. The general finding was that electron donating groups α to the C-H bond in question promote the insertion reaction. As well, we found that the ligands on the catalyst also affected product ratios. The more stabilized the carbene, i.e. with electron donating ligands, proved to be the more discriminating vis-a-vis the regiochemical outcome. We were also able to demonstrate a deuterium kinetic isotope effect for the insertion reaction symmetrical substrate **4i**.

Introduction

The stereoelectronic effect in Rh(II) mediated carbenoid C-H insertion reactions has been studied in a number of laboratories.[1,2] It has been observed that, in general, an electron donating group activates the α C-H bond toward insertion and that an electron withdrawing group retards the C-H insertion process.[2c] However, many of the model compounds selected for study were acyclic and suffered from steric and conformational influences,[3,4] which are important in dictating the regiochemical outcome of C-H insertion reactions. As a consequence, product distributions for complex substrates based on stereoelectronic criteria alone are not necessarily predictive. During the course of our studies on the Rh(II) catalyzed formation of carbenes derived from diazoketones, we have concentrated on the directing effects of an ether oxygen atom.[5] Most recently, we have reported that diazoketone **1** (Scheme 1), when subjected to a catalytic amount of $Rh_2(OAc)_4$, produced **2** and **3** through transannular C-H insertion.[5a] The ratio of **2**/**3** is controlled in part by the functional group R of the equatorial oxygen substituent at C-4. In the cases studied (R = H, ^{t}BuPh$_2$Si, Ac, Me), a strong preference for **3** as the major product was observed. There is an inherent bias in the substrate **1** which makes the analysis of subtle electronic effects difficult.[6] To explore further the stereoelectronic influence on the C-H insertion reaction by substituents with electron donating capabilities, we constructed the diazoketones **4a-g** (vide infra), where steric and conformational effects are minimized. The diazoketones **4a-g** are conformationally fixed as chair-cyclohexane

Scheme 1



1 2 3

substrates for the C-H insertion reaction. The cyclohexane provides a pseudosymmetry for the two axial hydrogens coplanar with the axial carbenoid reactant. Thus, the system is poised for the idealized C-H insertion reaction to form cyclopentanones. Furthermore, the substituents at the 3 and 5 positions adopt equatorial conformations and thus sterically do not perturb the reaction in a significant way. The major effect of these substituents is to electronically influence the susceptibility of the corresponding axial hydrogens in the C-H insertion process. Finally, the potential for side reactions due to ylide formations is also minimized in our system.[7] This study demonstrates the electronic tuning of substituents to achieve regioselective transannular cyclization via carbene C-H insertion.

Preparation of Diazoketone Substrates

The preparation of the α-diazoketone precursors is described in Scheme 2 (for **4a-d**), Scheme 3 (for **4e**), Scheme 4 (for **4g**), and Scheme 5 (for **4i**). Cyclohexane derivatives **4a-d** (Scheme 2) require equatorial oxygenated functional groups at the 3 and 5 positions and an axial α-diazoketone group at the 1 position secured by an equatorial methyl group. The 1-α-diazoketone is derived from a methyl carboxylate, and the equatorial methyl at the 1 position can be installed by a simple methylation of the *cis,cis*-1-(methoxycarbonyl)-3,5-disubstituted cyclohexane. Thus, *all-cis*-cyclohexane derivative **7**[8] was monosilylated and subsequently *O*-methylated to give compound **8**,[9] which was methylated to afford a mixture (98:2) predominanting in the desired axial methyl ester **9**. The relative configuration of this compound was

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(1) For a review, see: Doyle, M. P. In *Homogeneous Transition Metal Catalyst in Organic Synthesis*; Moser, W. R., Slocum, D. W., Eds.; ACS Advanced Chemistry Series 230; American Chemical Society: Washington, DC, 1992. Chapter 30.

(2) (a) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686. (b) Padwa, A.; Austin, D. J.; Hornbuckle, S. F.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N. *J. Am. Chem. Soc.* **1992**, *114*, 1874. (c) Stork, G.; Nakatani, K. *Tetrahedron Lett.* **1988**, *29*, 2283.

(3) (a) Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958 and references cited therein. (b) Doyle, M. P.; Bagheri, V.; Pearson, M. M.; Edwards, J. D. *Tetrahedron Lett.* **1989**, *30*, 7001.

(4) Doyle, M. P.; Pieters, R. J.; Taunton, J.; Pho, H. Q.; Padwa, A.; Hertzog, D. L.; Precedo, L. *J. Org. Chem.* **1991**, *56*, 820.

(5) (a) Spero, D.; Adams, J. *Tetrahedron Lett.* **1992**, *33*, 1143. (b) Adams, J.; Poupart, M. A.; Grenier, L.; Schaller, C.; Quimet, N. *Tetrahedron Lett.* **1989**, *30*, 1753. (c) Adams, J.; Poupart, M. A.; Grenier, L. *Tetrahedron Lett.* **1989**, *30*, 1749.

(6) Factors considered are (a) the anomeric effect as seen in **1**, (b) bond lengths between C-C and C-O, (c) the dipole-dipole interaction between the ring oxygen and the carbonyl oxygen of the α-diazoketone in **1**, and (d) conformational preferences as seen in acyclic models.[3-4]

(7) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, 1765.

(8) All compounds were characterized by ^{1}NMR, IR, MS, HRMS, and C,H,N analyses.

(9) Compound **7** was prepared by (a) hydrogenation of 3,5-dihydroxybenzoic acid by following a procedure similar to that of Burgstahler and Bithos (*Org. Synth.* **1925**, *5*, 591). Also see: *J. Am. Chem. Soc.* **1960**, *82*, 5466 (by the same authors). (b) The resulting mixture of 3,5-dihydroxycyclohexanecarboxylic acid and its ethyl ester was converted to **4** by using 5% HCl in MeOH.

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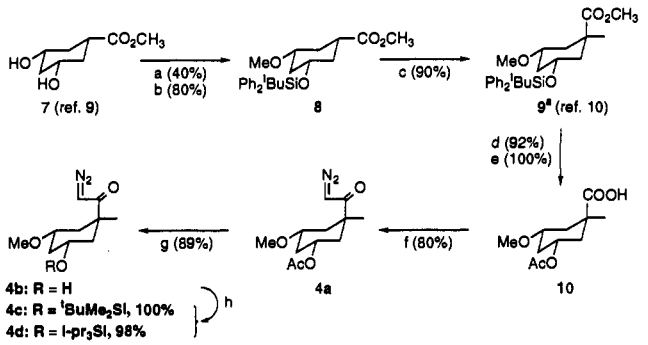
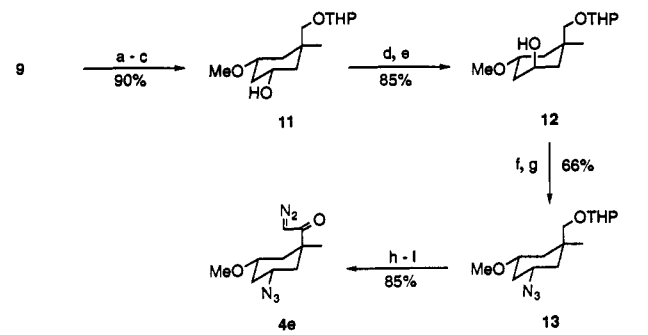
Scheme 2[a]



[a] Reagents and conditions: (a) 1 equiv of ^{t}BuPh$_2$SiCl, imidazole, DMF; (b) MeOTf, 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, reflux, overnight; (c) (1) LDA, THF/hexane, 0 °C, 1 h, (2) $(MeO)_2SO_2$; (d) *n*-Bu$_4$N$^+$F$^-$, THF; (e) (1) LiOH, MeOH/H_2O, (2) Ac_2O, pyridine; (f) (1) $SOCl_2$, neat, cat. DMF, (2) CH_2N_2, ether; (g) K_2CO_3, THF/MeOH, 2:3, 1 h; (h) ^{t}BuMe$_2$SiOTf or *i*-Pr$_3$SiOTf, 2,6-lutidine, CH_2Cl_2, 0 °C.[a] This step results in an ester group conformation, ax.:eq. = 98:2. The ratio was determined by GC–MS, and compounds were identified by 2-D NOE NMR analysis.

Scheme 3[a]



[a] Reagents and conditions: (a) $LiAlH_4$, THF; (b) dihydropyran, cat. PPTS; (c) *n*-Bu$_4$N$^+$F$^-$, THF; (d) PCC, CH_2Cl_2; (e) LS-selectride, THF; (f) MsCl, pyridine; (g) NaN_3, DMF; (h) PPTS, EtOH, 55 °C; (i) PCC; (j) NaO_2Cl; (k) $SOCl_2$, neat, cat. DMF; (l) CH_2N_2, ether.

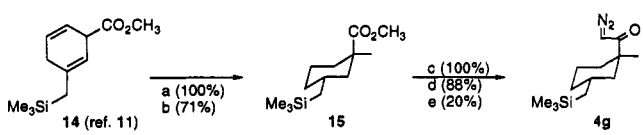
confirmed by 2-D NOE studies and by comparison with data reported in the literature for the analogous compounds.[10] Desilylation, saponification of the methyl ester, and acetylation afforded carboxylic acid **10**, which was converted to the acid chloride with neat thionyl chloride in the presence of a catalytic amount of DMF. Without purification, the acid chloride was reacted with excess diazomethane to give α-diazoketone **4a**. Hydrolysis under mild conditions afforded **4b**. This was further converted to **4c,d** by standard silylation procedures.

The key intermediate **9** also served as a precursor to **4e**, in which the methoxy and azido groups are set up as competing electron donors (Scheme 3). $LiAlH_4$ reduction of the methyl ester **9** followed by protection and desilylation provided **11** with an equatorial C-5 hydroxyl group. This was inverted by oxidation followed by a LS-selectride reduction to give the axial hydroxyl compound **12**. Mesylation and a S_N2 displacement with sodium azide put an equatorial azido group in place. Deprotection and subsequent oxidation gave in high yield the azido carboxylic acid which was then converted to **4e** by standard chemistry.

Compound **4g** was obtained from the known **14**[11] as shown in Scheme 4. Hydrogenation of **14** gave quantitative yield of *cis*-1-(methoxysilyl)methylcyclohexane, which was successfully methylated at low temperature to provide **15** as a single diastereomer in 71% yield. Methyl ester **15** was then converted to **4g** by using a reduction–oxidation pathway to generate the

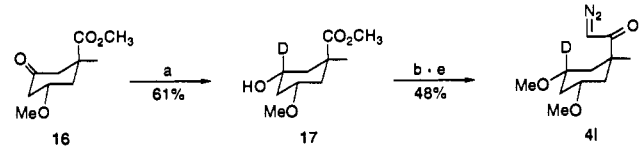
(10) The relative configuration of this compound was confirmed by 2-D NOE studies and by comparison with data reported in the literature for analogous compounds: (a) Agosta, W. C.; Wolf, S. *J. Org. Chem.* **1975**, *40*, 1027. (b) Wolf, S.; Agosta, W. C. *J. Org. Chem.* **1973**, *38*, 1694.

Scheme 4[a]



[a] Reagents and conditions: (a) H_2, Pd/C, MeOH; (b) (1) LDA, toluene/DMPU, −78 °C, 5 h, (2) $(MeO)_2SO_4$; (c) $LiAlH_4$, THF; (d) PDC, DMF; (e) $SOCl_2$, neat, cat. DMF; (f) CH_2N_2, ether.

Scheme 5[a]



[a] Reagents and conditions: (a) (1) $NaBD_4$, EtOH, −78 °C, (2) NaH, THF; (b) MeOTf, 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, reflux, overnight; (c) LiOH, MeOH/H_2O; (d) $SOCl_2$, neat, cat. DMF; (e) CH_2N_2, ether.

carboxylic acid and then by following conventional chemistry to the diazaketone.

The deuterium in compound **4i** was incorporated by $NaBD_4$ reduction of the cyclohexanone **16**, which is readily available from the key intermediate **9** via desilylation and oxidation. Although this gave a 2.5:1 mixture of diastereomers, which was inseparable by flash chromatography, the desired major diastereomer **17** could be isolated in pure form after the diastereomeric mixture was subjected to sodium hydride in THF. The undesired diastereomer with an axial hydroxyl group presumably forms a lactone, which was easily separated chromatographically from the desired alcohol **17**. Methylation followed by standard chemistry provided **4i**. The deuterium incorporation was 98% as estimated by ^{1}H NMR.

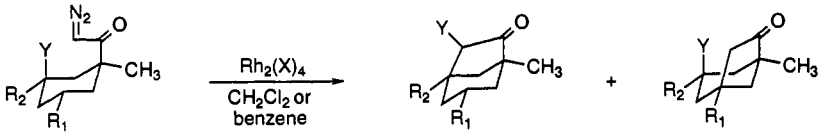
Rh(II) Mediated Cyclizations: Results and Conclusions

Initially we employed $Rh_2(OAc)_4$ under standard reaction conditions using CH_2Cl_2 as the solvent. A typical reaction was carried out under the following conditions: To $Rh_2(OAc)_4$ (1% by weight) suspended in freshly distilled CH_2Cl_2 (0.5 mL) was added diazoketones **4** (0.027 mmol, 0.025 M in CH_2Cl_2) dropwise at room temperature. Consumption of the diazoketone was monitored by TLC, and the solvent was removed in vacuo upon completion of the reaction. The crude residue was analyzed by GC–MS for product ratios. Flash chromatography provided pure products for identification and characterization. Alternatively, other Rh(II) catalysts such as $Rh_2(CaP)_4$ (where Cap is caprolactam) were employed in selected experiments, and benzene replaced CH_2Cl_2 as the solvent in some reactions.

As originally observed in the tetrahydropyranyl diazoketone **1**,[5a] where R = OAc, the electron withdrawing property of the acetyl function serves to dominate the ratio of **3**/**2** (Scheme 1) or **5**/**6** (**4a** in Table 1). Other substituents (OH, ^{t}BuMe$_2$SiO, ^{i}Pr$_3$SiO) were also examined. Here selectivities were rather modest. The hydroxyl substituent proved to be slightly more directing than methoxy; however, the resultant products included the observation of a retroaldol product. In general, O–H insertion is a facile reaction with carbenes but the equatorial geometry of the hydroxyl substituent rules out this possibility. The effects of silyl substituents were also modest although a secondary steric effect was observed such that the ratio of products increased to

(11) (a) Coughlin, D. J.; Soloman, R. G. *J. Org. Chem.* **1979**, *44*, 3784. (b) The literature procedure for the preparation of this compound (Eaborn, C.; Parker, S. H. *J. Chem. Soc.* **1954**, 939) is not clear. By private communication with Professor Soloman, we realized it is much more efficient to use sodium sand, instead of using lithium metal, to react with 3-(chlorobenzyl)-trimethylsilane to give phenylalkali, the precursor for the formation of benzoic acid. Therefore, a procedure by Gilman (Gilman, H.; Pacevitz, H. A.; Baine, O. *J. Am. Chem. Soc.* **1940**, *62*, 1514) was adopted.

Table 1



4 5 6

4	$Rh_2(X)_4$	R_1	R_2	Y	time (h)	yield[a] (%)	5[b]		6
a[c]	$Rh_2(OAc)_4$	OAc	MeO	H	3	65	>99	:	1
b	$Rh_2(OAc)_4$	OH	MeO	H	1.5	99	1	:	1.4[d]
c	$Rh_2(OAc)_4$	$^tBuMe_2SiO$	MeO	H	2	81	2.2	:	1
d	$Rh_2(OAc)_4$	i-Pr_3SiO	MeO	H	4	94	6	:	1
e	$Rh_2(OAc)_4$	N_3	MeO	H	3	56	1	:	8
f	$Rh_2(Cap)_4$	N_3	MeO	H	5	83	1	:	30
g	$Rh_2(OAc)_4$	Me_3SiCH_2	H	H	18	70	1	:	1
h	$Rh_2(Cap)_4$	Me_3SiCH_2	H	H	3	98	1	:	3.8
i	$Rh_2(OAc)_4$	MeO	MeO	D	3	80	1	:	1.2[e]
j	$Rh_2(Cap)_4$	MeO	MeO	D	5	83	1	:	2.0[e]

[a] All yields listed are isolated yields. [b] Product ratios for entries a–h were determined by GC–MS on crude reaction mixtures. [c] Reactions of **4a-e**, **4g**, and **4i** were run in CH_2Cl_2 at room temperature; reactions of **4f**, **4h**, and **4j** were run in benzene at reflux; the same product ratios were obtained when reaction of **4f** and **4h** were run in CH_2Cl_2 at reflux. [d] The ratio was based on the combined yield of compound **6** and its retroaldol condensation product. [e] See ref 15.

6:1 when the bulkier TIPS (**4d**) group was used instead of the TBS (**4c**) group. In considering a possible substituent that might be more electron donating compared with methoxy, we noted a theoretical paper by Hoz and Wolk[12] describing the electronic properties of azide. Thus, insertion α to the azide substituent in substrate **4e** dominated over insertion α to the methoxy group by a ratio of 8:1 under the standard conditions. This ratio increased to 30:1 when using the $Rh_2(Cap)_4$ catalyst either in benzene or CH_2Cl_2 (**4f**, Table 1).

Given the proven ability of electron donating substituents to favor the α C–H insertion reaction of carbenes, we postulated that a positive charge (or partial positive charge) stabilized by an electron donating substituent might be involved in the transition state of the reaction. In order to test for this possibility, we constructed the trimethylsilyl methyl diazoketone **4g**, relying on the ability of silicon to stabilize a β cation. Disappointingly, the $Rh_2(OAc)_4$ catalyzed insertion reaction showed no regioselectivity whatsoever. Nevertheless, we were aware of Doyle's and Padwa's studies in which dramatic alterations in product ratios have been observed upon varying the catalyst ligands.[2,3] Doyle has argued that the more electron rich ligand (i.e. caprolactam) provides for a later transition state whereby the reacting carbenoid is closer to the reacting C–H bond. If so, the $Rh_2(Cap)_4$ should be more discriminating vis a vis the electronic nature of the substituent (also observed in **4f**), and this was indeed observed to favor the $(TMS)CH_2$ direction with 3.8:1 preference (**4h**, Table 1). These results support our view that the C–H insertion occurs with polarization of the C–H bond placing a partial positive charge on carbon, accounting for the enhanced regioselectivity. Certainly this effect is more dramatic when the stabilizing group is a strongly electron donating heteroatom moiety.

Compound **4i** was designed to probe the primary isotope effect. Literature precedent suggests that free carbenes which react with axial hydrogens demonstrate rather small deuterium rate retardations, as compared with those reacting with equatorial hydrogens.[13] Noels and co-workers have published on the observed isotope effects for C–H insertion of ethyl diazoacetate and diazomalonate on unactivated hydrocarbon solvents and have also found small rate effects.[14] Our system involves an intramolecular axial C–H insertion, and the C–H bond is further activated by an α-ether oxygen. Using $Rh_2(OAc)_4$ as the catalyst we noted a small but measurable rate difference, as reflected by product ratios (entry **4i**, Table 1). Consistent with our results on chemoselectivity, the $Rh_2(Cap)$ catalyst was more discriminating, with an isotope effect of $K_H/K_D = 2.0$ (entry **4j**, Table 1).[15]

Doyle has proposed that the mechanism of the C–H insertion mediated by Rh(II) carbenoids involves a three-centered intermediate with a hydrogen atom transfer to the acyl cation (stabilized by the metal).[3a] Our results are consistent with this general interpretation; however, it is not mechanistically possible to distinguish between a more concerted three-centered reaction mechanism and a stepwise mechanism in which there is a discreet hydride transfer to the acyl cation, followed by reductive elimination of the metal species to form the C–C bond. Support for a three-centered reaction is offered by Taber, who demonstrated that the insertion processes occurs with retention of configuration at the carbon.[16] Nevertheless, it is still possible to conserve stereochemistry through a stepwise cationic intermediate through ion pairing. Our findings are consistent with both interpretations.

As the reacting carbene center becomes less electrophilic, due to more donating ligands on Rh, regioselectivity is enhanced (and consequently K_H/K_D is increased) due to a later transition state, in accordance with the Hammond postulate. Our experiments also indicate that, as electron density on the carbon of the axial C–H bond is increased, hydride transfer is facilitated. The bicyclic systems prepared here demonstrate stereoelectronic control, whereby the more electron rich (and sterically less congested) C–H insertion process is favored. It is anticipated that this chemistry will ultimately prove useful in elucidating the mechanism of Rh(II) mediated C–H insertion reactions and the synthesis of important target molecules.

Experimental Details

Melting points were determined on a Buchi 510 melting point apparatus and are uncorrected. High-pressure hydrogenation was conducted in a Parr 4611 General Purpose Bomb with 4317 Gage Block. Low-pressure hydrogen was conducted in a Parr 3911 medium-pressure reaction vessel. ^1H NMR spectra were recorded on a Bruker WM-250 spectrometer with tetramethylsilane as an internal standard; J values are given in Hz. IR spectra was recorded on a Perkin-Elmer 781 infrared spectrometer. Low-resolution mass spectra (MS) were recorded on a Finnegan 4023 GC/

(12) Hoz, S.; Wolk, T. L. *Tetrahedron Lett.* **1990**, *31*, 4085.
(13) Nickon, A.; Ilao, M. C.; Stern, A. G.; Summers, M. F. *J. Am. Chem. Soc.* **1992**, *114*, 9230.
(14) Demonceau, A.; Noels, A. F.; Costa, J. L.; Hubert, A. J. *J. Mol. Catal.* **1990**, *58*, 21.
(15) The product ratios **5i/6i** and **5j/6j** were determined by integration of ^2H coupled ^{13}C NMR signals for the diagnostic ^2H bearing carbons. A relaxation delay of 5 s was used to determine sufficiently accurate integrals. Estimated error in the measurement is ~5%.
(16) Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, *107*, 196.

MS/DS spectrometer. High-resolution mass spectra (HRMS) were determined by M-Scan Inc., West Chester, PA.

All reactions were monitored by thin-layer chromatography carried out on 0.25-mm E. Merck silica gel plates (60F-254) using UV light, 2.6% ethanolic *p*-anisaldehyde or 7% ethanolic phosphomolybdic acid, and heat as developing agents.

All reactions were carried out under an inert (nitrogen or argon) atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise noted. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated.

***cis,cis*-1-(Methoxycarbonyl)-3,5-dihydroxycyclohexane (7).** 3,5-Dihydroxybenzoic acid (Aldrich, 41 g, 266 mmol) was hydrogenated in 95% ethanol (225 mL) at 1700 psi and 165 °C in the presence of 5% Rh on Alumina (8 g) for 3 days (final pressure was 1480 psi at 165 °C and 1000 psi at room temperature). The remaining hydrogen in the bomb was vented out slowly in a well-circulated hood. The content of the bomb was poured into a 1000-mL beaker. The bomb was rinsed out with 95% ethanol (100–200 mL). The combined EtOH/H_2O was boiled on a hot plate and suctional filtered through a bed of Celite. The solvent was removed *in vacuo* (bath temperature 50 °C) and further removed under reduced pressure (0.1 mmHg) overnight to give 45.84 g of a colorless oil, the ^{1}H NMR spectrum of which indicated that it was mainly the 1-(ethoxycarbonyl)-3,5-dihydroxycyclohexane. No aromatic protons were observed.

The crude mixture from the above hydrogenation reaction was dissolved in 1200 mL of anhydrous methanol. Subsequently, acetyl chloride (60 mL) was added dropwise at 0 °C, and the mixture was stirred at room temperature for 2 days. Sodium bicarbonate powder (81 g, 964 mmol) was added in several portions to the reaction solution until the pH = 5 (*caution*: CO_2 *evolved vigorously*). The reaction mixture was filtered and evaporated *in vacuo*. To the semi-solid residue (containing NaCl and $NaHCO_3$) was added ethyl acetate (500 mL), and the mixture was heated to boiling and filtered. The solid was washed with 300 mL of hot ethyl acetate. The solution volume was boiled down to 500 mL, cooled to room temperature, and further cooled in a freezer to afforded pure **7** (22 g, first crop, and 2.78 g, second crop, 59% total) as a white crystal: mp 134–135 °C; IR (KBr) ν_{max} 3400, 2940, 1735, 1385, 1260, 1015 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 4.40 (b, 2 H), 3.59 (s, 3 H), 3.42 (m, 2 H), 2.32 (m, 1 H), 2.05 (m, 3 H), 1.02 (m, 3 H); MS (FAB$^+$) *m/z* (relative intensity) 175 (M^+ + H, 100), 157 (9), 154 (15), 143 (29), 139 (15), 137 (25), 125 (15); HRMS *m/z* calcd for $C_8H_{15}O_4$ $(M + H)^+$ 175.0971, found 175.0971. Anal. Calcd for $C_8H_{14}O_4$: C, 55.14; H, 8.10. Found: C, 55.04; H, 8.19.

***cis,cis*-1-Carbomethoxy-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (8).** A solution of **7** (1.69 g, 9.7 mmol), imidazole (0.726 g, 10.67 mmol), and *tert*-butylchlorodiphenylsilane (2.77 mL, 10.67 mmol) in DMF (50 mL) was stirred under N_2 at room temperature overnight. The reaction mixture was partitioned between hexane (50 mL) and water (25 mL). The aqueous layer was extracted with hexane (3 × 50 mL). The combined hexane was washed with water (50 mL) and brine (50 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (700 mL of 10% ethyl acetate in hexane and then 700 mL of 40% ethyl acetate in hexane) to afford monosilylated compound *cis,cis,cis*-1-carbomethoxy-3-((diphenyl-*tert*-butylsilyl)oxy)-5-hydroxycyclohexane (1.6 g, 40%): R_f = 0.14 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 3400, 2950, 2860, 1740, 1430, 1110, 1050, 700 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7.68–7.63 (m, 4 H), 7.46–7.33 (m, 6 H), 3.65 (s, 3 H), 3.59 (m, 1 H), 3.40 (m, 1 H), 2.09 (m, 4 H), 1.48 (m, 4 H), 1.04 (s, 9 H); CIMS *m/z* (relative intensity) 413 (M^+ + H, 23), 359 ($MH^+ - H_2O$, 50), 355 ($MH^+ - C_4H_{10}$, 21), 335 (MH^+ – Ph, 33), 317 ($MH^+ - H_2O$ – Ph, 18), 303 (MH^+ – Ph-MeOH, 40), 277 (64), 257 (MH^+ – 2PH, 60), 199 (43), 157 (48), 139 (98), 79 (100); HRMS *m/z* calcd for $C_{24}H_{33}O_4Si$ $(M + H)^+$ 413.2149, found 413.2154.

To a solution of *cis,cis,cis*-1-carbomethoxy-3-((diphenyl-*tert*-butylsilyl)oxy)-5-hydroxycyclohexane (12.12 g, 29.4 mmol) in methylene chloride (110 mL) was added 2,6-di-*tert*-butyl-4-methylpyridine (10.57 g, 51.5 mmol) followed by addition of methyl trifluoromethanesulfonate (5.0 mL, 44.1 mmol) dropwise via a syringe at room temperature. The reaction mixture was heated at reflux overnight. The solvent was removed *in vacuo* to give a mixture of solid and liquid. The solid was filtered off and washed with hexane (3 × 50 mL). The filtrate was concentrated *in vacuo*. Flash column chromatography on silica gel (hexane, 1500 mL; 20% ethyl acetate in hexane, 1500 mL) provided pure **8** (12.2 g, 97%) as a colorless oil: R_f = 0.53 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 3080, 2940, 2850, 1730, 1460, 1430, 1380, 1280, 1250, 1170, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (m, 4 H), 7.40 (m, 6 H), 3.65 (s, 3 H), 3.57 (m, 1 H), 3.23 (s, 3 H), 2.93 (m, 1 H), 2.09 (m, 4 H), 1.53 (m, 1 H), 1.23 (m, 2 H), 1.05 (s, 9 H); CIMS *m/z* (relative intensity) 427 (M^+ + H, 5), 395 (MH^+ – MeOH, 3), 369 ($MH^+ - C_4H_{10}$, 2), 349 (MH^+ – Ph, 7), 317 (MH^+ – Ph – MeOH, 5), 239 (28), 199 (51), 189 (51), 179 (100), 171 (97), 157 (52), 139 (54), 125 (13); HRMS *m/z* calcd for $C_{25}H_{35}O_4Si$ $(M + H)^+$ 427.2306, found 427.2318. Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.39; H, 8.04. Found: C, 70.33; H, 8.21.

1-Methyl-1-carbomethoxy-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (9). A 100-mL flame-dried round-bottomed flask fitted with a magnetic stirring bar was charged with freshly distilled THF (20 mL) and dry diisopropylamine (1.02 mL, 7.28 mmol). The reaction solution was cooled to 0 °C, a 2.3 M solution of *n*-BuLi in hexane (3.16 mL, 7.28 mmol) was added, and the mixture was stirred for 15 min. A solution of compound **8** (2.82 g, 6.62 mmol) in THF (24 mL) was introduced via a syringe dropwise at 0 °C, and the mixture was stirred for 1.5 h. The reaction flask was cooled to –78 °C, and dimethyl sulfate (0.94 mL, 9.93 mmol) was added followed by stirring at room temperature overnight. The reaction mixture was partitioned between ethyl ether (100 mL) and water (50 mL). The aqueous layer was extracted with ethyl ether (3 × 100 mL). The combined ethyl ether was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (15% ethyl acetate in hexane) to afford compound **9** (2.61 g, 90%) as colorless oil: R_f = 0.26 (silica, 15% ethyl acetate in hexane); GC analysis showed it is a mixture of two diastereomers in a ratio of 95:5; 2-D NMR (NOSEY) confirmed the major compound is the desired product; IR (neat) ν_{max} 2920, 2840, 1730, 1460, 1420, 1190, 1160, 1100, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (m, 4 H), 7.40 (m, 6 H), 3.60 (m, 1 H), 3.41 (s, 3 H), 3.24 (s, 3 H), 2.29 (m, 3 H), 1.29 (m, 2 H), 1.18 (s, 3 H), 1.05 (s, 9 H), 0.96 (m, 1 H); MS (FAB$^+$) *m/z* (relative intensity) 441 (M + H, 2), 410 (25), 383 (57), 363 (10), 351 (17), 323 (17), 213 (100), 199 (70), 195 (84), 167 (18); HRMS calcd for $C_{25}H_{33}O_3Si$ $(M + H)^+$ 441.2461, found 441.2438. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 70.87; H, 8.24. Found: C, 70.88; H, 8.26.

1-Carboxy-1-methyl-3-acetoxy-5-methoxycyclohexane (10). To compound **9** (3.25 g, 7.4 mmol) dissolved in THF (15 mL) was added a 1.0 M solution of *n*-$Bu_4N^+F^-$ in THF (15 mL, 15 mmol), and the mixture was stirred at room temperature overnight. The THF was removed *in vacuo* and further removed under reduced pressure (0.1 mmHg) for 2 h. Column chromatography on silica gel (700 mL of 30% ethyl acetate in hexane and then 800 mL of ethyl acetate) provided pure 1-methyl-1-(methyloxycarbonyl)-3-methoxy-5-hydroxycyclohexane (1.37 g, 92%) as a white crystal: mp 38–39 °C; R_f = 0.10 (silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 3400, 2950, 1730, 1470, 1200, 1150, 1090, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.70 (m, 1 H), 3.69 (s, 3 H), 3.37 (s, 3 H), 3.23 (m, 1 H), 2.55–2.31 (m, 3 H), 1.63 (s, 1 H), 1.26 (s, 3 H), 1.21–0.95 (m, 3 H); CIMS *m/z* (relative intensity) 203 (M^+ + H, 7), 185 ($MH^+ - H_2O$, 100), 171 (MH^+ – MeOH, 98), 153 ($MH^+ - H_2O$ h MeOH, 50), 139 (3), 125 (6), 111 (2). Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.37; H, 8.98. Found: C, 59.13; H, 9.05.

To a solution of the above 1-methyl-1-(methoxycarbonyl)-3-methoxy-5-hydroxycyclohexane (0.023 g, 0.11 mmol) in MeOH/H_2O (0.75 mL/0.25 mL, 3:1) was added LiOH monohydrate (0.019 g, 0.44 mmol), and the mixture was subsequently heated at reflux for 6 h. After the mixture was cooled, the reaction mixture was acidified with 5 N HCl solution (0.1 mL, 0.5 mmol) to pH = 2 and extracted with ether (3 × 10 mL). The combined ether was washed with water (10 mL) and brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* and further removed under reduced pressure (0.1 mmHg) for 2 h to give the crude acid (0.053 g) as a semi-solid: ^{1}H NMR (DMSO-d_6) δ 12.32 (b, 1 H), 4.77 (d, J_d = 4.7 Hz, 1 H), 3.22 (s, 3 H), 3.40 (m, 1 H), 3.16 (m, 1 H), 2.26 (m, 3 H), 1.15 (s, 3 H), 0.89 (m, 3 H).

To the crude acid was added acetic anhydride (0.5 mL) and pyridine (0.040 mL, 0.5 mmol), and the mixture was stirred at room temperature overnight. To the reaction mixture was added 1 drop of water and then it was concentrated *in vacuo*. The residue was subjected to a short plug of silica gel column (1 in., Pasteur pipet protected by a cotton ball) and eluted with 5% MeOH in ethyl acetate (10 mL). The reaction solution was evaporated *in vacuo* and coevaporated with toluene (3 × 3 mL). The remaining solvent was finally removed under reduced pressure (0.1 mmHg) overnight to give **10** (0.025 g) as a semi-solid. This compound was used in the next step without purification: ^{1}H NMR (DMSO-d_6) δ 4.71 (m,

1 H), 3.25 (m, 1 H), 3.22 (s, 3 H), 2.23 (m, 3 H), 1.98 (s, 3 H), 1.16 (s, 3 H), 0.94 (m, 3 H).

1-Methyl-1-(α-diazoacetyl)-3-acetoxy-5-methoxycyclohexane (4a). To the above crude acetoxy acid **10** (0.076 g) were added double distilled thionyl chloride (1 mL) and a catalytic amount of DMF (10 μL), and the mixture was stirred at room temperature overnight. The excess thionyl chloride was removed *in vacuo* (bath temperature 40 °C). The reaction mixture was coevaporated with toluene (2 × 3 mL) to give a white solid (very hydroscopic), which was dissolved in CH_2Cl_2 (2 mL), added into a 0.5 M CH_2N_2 solution in diethyl ether (5 mL), and stirred for 1 h at 0 °C. Solid on the wall of the reaction flask was removed with a spatula. The solvent was removed *in vacuo*, and the residue was purified by flash column chromatography on silica gel (50% ethyl acetate in hexane) to afford **4a** (0.067 g, 80%) as a yellow crystal: mp 67–68 °C; R_f = 0.25 (silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 2960, 2100, 1735, 1630, 1350, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.68 (s, 1 H), 4.73 (m, 1 H), 3.36 (s, 3 H), 3,27 (m, 1 H), 2.55 (dm, J_d = 12.8 Hz, 1 H), 2.37 (dm, J_d = 11.3 Hz, 1 H), 2.24 (dm, J_d = 13.2 Hz, 1 H), 2.05 (s, 3 H), 1.32 (m, 2 H), 1.18 (s, 3 H), 1.00 (m, 1 H); CIMS *m/z* (relative intensity) 255 (M^+ + H, 64), 223 (MH^+ – MeOH, 69), 195 (MH^+ – AcOH, 100), 167 (MH^+ –AcOH – N_2, 66), 153 (52), 135 (65); HRMS *m/z* calcd for $C_{12}H_{19}N_2O_4$ ($M + H)^+$ 255.1345, found 255.1344. Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.66; H, 7.14; N, 11.02. Found: C, 56.48; H, 7.23; N, 10.43.

1-Methyl-1-(α-diazoacetyl)-3-methoxy-5-hydroxycyclohexane (4b). To a solution of compound **4a** (0.062 g, 0.242 mmol) in THF/MeOH (2.4 mL/3.6 mL) was added anhydrous K_2CO_3 (0.067 g, 0.484 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was subjected to a short plug of silica gel column (2 × 2.5 cm, 15-mL filter funnel with centered glass) and eluted with ethyl acetate (100 mL). The solvent was removed *in vacuo* to give 0.060 g of the crude product. Flash column chromatography on silica gel (ethyl acetate) afforded pure **4b** (0.051 g, 100%) as a yellow crystal: mp 83–83 °C; R_f = 0.17 (silica, ethyl acetate); IR (neat) ν_{max} 3400, 2940, 2100, 1620, 1450, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.48 (s, 1 H), 3.72 (m, 1 H), 3.37 (s, 3 H), 3.29 (m, 1 H), 2.40–2.21 (m, 3 H), 1.64 (d, J_e = 4.6 Hz, 1 H), 1.20 (s, 3 H), 1.18 (m, 3 H); CIMS *m/z* (relative intensity) 213 (M^+ + H, 7), 195 (MH^+ – H_2O, 0.02), 185 (MH^+ – N_2, 34), 181 (MH^+ – MeOH, 5), 167 (MH^+ – H_2O – N_2, 28), 153 (MH^+ – MeOH – N_2, 100), 135 (MH^+ – MeOH – N_2 – H_2O, 8), 125 (5), 109 (2), 107 (25); HRMS *m/z* calcd for $C_{10}H_{17}N_2O_3$ ($M + H)^+$ 213.1240, found 213.1248. Anal. Calcd for $C_{10}H_{16}N_2O_3$: C, 56.57; H, 7.60; N, 13.20. Found: C, 56.47; H, 7.60; N, 13.00.

General Procedure for the Preparation of 1-Methyl-1-(α-diazoacetyl)-3-siloxy-5-methoxycyclohexane. To a solution of compound **4b** (0.0185 g, 0.087 mmol) in CH_2Cl_2 (1.0 mL) was added 2,6-lutidine (0.025 mL, 0.22 mmol) and subsequently silyl triflate (0.131 mmol) at 0 °C, and the mixture was stirred for 30 min. Without removal of the solvent, the reaction mixture was subjected to a silica gel column and eluted with 25% ethyl acetate in hexane to give the desired product.

1-Methyl-1-(α-diazoacetyl)-3-(*tert*-butyldimethylsiloxy)-5-methoxycyclohexane (4c): white crystal (0.028 g, 100%); mp 31–32 °C; R_f = 0.30 (silica, 25% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 2860, 2100, 1640, 1470, 1350, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.44 (s, 1 H), 3.68 (m, 1 H), 3.36 (s, 3 H), 3.23 (m, 1 H), 2.34–2.04 (m, 3 H), 1.25–0.96 (m, 3 H), 1.17 (s, 3 H), 0.89 (s, 9 H), 0.084 (s, 3 H), 0.079 (s, 3 H); CIMS *m/z* (relative intensity) 327 (M^+ + H, 14), 299 (MH^+ – N_2, 100), 267 (MH^+ – N_2 – MeOH, 40), 229 (34), 195 (42), 167 (39), 153 (38), 135 (19); HRMS *m/z* calcd for $C_{16}H_{31}N_2O_3Si$ ($M + H)^+$ 327.2105, found 327.2103.

1-Methyl-1-(α-diazoacetyl)-3-(triisopropylsiloxy)-5-methoxycyclohexane (4d): colorless oil (0.019 g from 0.011 g of **4b**, 98%); R_f = 0.39 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 2860, 2100, 1640, 1460, 1350, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.44 (s, 1 H), 3.79 (m, 1 H), 3.36 (s, 3 H), 3.23 (m, 1 H), 2.35–2.18 (m, 3 H), 1.17 (s, 3 H), 1.16 (m, 1 H), 1.07 (s, 18 H), 1.05 (m, 5 H); CIMS *m/z* (relative intensity) 369 (M^+ + H, 20), 341 (MH^+ – N_2, 63), 309 (MH^+ – N_2 – MeOH, 15), 195 (100); HRMS *m/z* calcd for $C_{19}H_{37}N_2O_3Si$ (M^+ + H) 369.2575, found 369.2553. Anal. Calcd for $C_{19}H_{36}N_2O_3Si$: C, 61.91; H, 9.85; N, 7.61. Found: C, 61.77; H, 9.90; N, 5.89.

1-(((Tetrahydropyranyloxy)methyl)-1-methyl-3-methoxy-5-hydroxycyclohexane (11). To a suspension of $LiAlH_4$ powder (0.55 g, 14.5 mmol) in anhydrous diethyl ether (15 mL) was added a solution of compound **9** (2.55 g, 5.80 mmol) in ether (14 mL) dropwise at 0 °C. The reaction mixture was stirred at room temperature overnight. With cooling, the reaction mixture was quenched with H_2O, 15% NaOH solution, and H_2O in a 1:1:3 fashion (0.55 mL/0.55 mL/1.65 mL), stirred for 0.5 h, and filtered. The solid was washed with ether (5 × 10 mL). The combined ether/THF was concentrated *in vacuo*. Flash column chromatography on silica gel (40% ethyl acetate in hexane) afforded pure 1-(hydroxymethyl)-1-methyl-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (2.14 g, 90%) as a colorless oil: R_f = 0.38 (silica, 40% ethyl acetate in hexane); IR (neat) ν_{max} 3520, 2940, 1470, 1430, 1380, 1110, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.94 (m, 4 H), 7.68 (m, 6 H), 3.91 (m, 1 H), 3.51 (s, 3 H), 3.35 (m, 1 H), 3.25 (db, J_d = 4.7 Hz, 1 H), 2.55 (m, 1 H), 2.10 (m, 1 H), 1.85 (m, 1 H), 1.50 (m, 1 H), 1.40 (m, 1 H), 1.33 (s, 9 H), 1.18 (m, 1 H), 1.15 (s, 3 H); CIMS *m/z* (relative intensity) 413 (M^+ + H, 10), 395 (MH^+ – H_2O, 1), 335 (MH^+ – Ph, 30), 303 (MH^+ – Ph – MeOH, 44), 257 (11), 139 (27), 125 (79), 107 (100); HRMS *m/z* calcd for $C_{25}H_{37}O_3Si$ ($M + H)^+$ 413.2513, found 413.2519.

To the above 1-(hydroxymethyl)-1-methyl-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (3.01 g, 7.31 mmol) dissolved in CH_2Cl_2 (50 mL) was added PPTS (0.184 g, 0.731 mmol) followed by addition of 3,4-dihydro-2*H*-pyran (1.33 mL, 14.61 mmol) dropwise at room temperature, and the mixture was stirred for 4 h. The solvent was removed *in vacuo*. Flash column chromatography on silica gel (20% ethyl acetate in hexane) afforded 1-(((tetrahydropyranyloxy)methyl)-1-methyl-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (3.62 g, 100%) as a diasteromeric mixture: R_f = 0.27 (silica, 15% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 1470, 1430, 1380, 1200, 1110, 1080, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (m, 4 H), 7.38 (m, 6 H), 4.96 (m, 1 H), 4.32 (m, 1 H), 3.87–3.13 (m, 5 H), 3,21 (ds, 3 H), 2.75 (m, 1 H), 2.20 (m, 1 H), 2.00–1.07 (m, 10 H), 1.05 (s, 9 H), 0.96 (ds, 3 H); CIMS *m/z* (relative intensity) 497 (M^+ + H, 4), 465 (MH^+ – MeOH, 1), 439 (MH^+ – C_4H_{10}, 14), 419 (MH^+ – Ph, 21), 413 (MH^+ – THP, 10), 341 (MH^+ – 2Ph, 3), 335 (MH^+ – Ph – THP, 13), 303 (MH^+ – Ph – THP – MeOH, 39), 241 (8.4), 125 (50), 107 (35), 85 (100); HRMS *m/z* calcd for $C_{30}H_{45}O_4Si$ ($M + H)^+$ 497.3088, found 497.3078.

To the protected 1-(((tetrahydropyranyloxy)methyl)-1-methyl-3-((diphenyl-*tert*-butylsilyl)oxy)-5-methoxycyclohexane (4.12 g, 8.31 mmol) dissolved in THF (16.6 mL) was added a 1.0 M *n*-BuN^+F^- solution in THF (16.6 mL, 16.6 mmol) dropwise at room temperature, and the mixture was stirred for 2 h. Without removal of solvent, the reaction mixture was subjected on a silica gel column (50 × 178 mm) and eluted with 80% ethyl acetate in hexane to give **11** (2.14 g, 100%) as a diasteromeric mixture: R_f = 0.22 (silica, 80% ethyl acetate in hexane); IR (neat) ν_{max} 3400, 2940, 1470, 1370, 1200, 1120, 1060, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.56 (m, 1 H), 3.81 (m, 2 H), 3.56–3.36 (m, 3 H), 3.35 (s, 3 H), 3.03 (m, 1 H), 2.36 (m, 1 H), 1.99 (m, 2 H), 1.90–1.49 (m, 7 H), 1.09 (m, 2 H), 1.04 (ds, 3 H); MS (FAB$^+$) *m/z* (relative intensity) 259 (M^+ + H, 100), 241 (32), 227 (34), 186 (29), 175 (83), 154 (45), 137 (88), 125 (94); HRMS *m/z* calcd for $C_{14}H_{27}O_4$ ($M + H)^+$ 259.1910, found 259.1891. Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.07; H, 10,15. Found: C, 64.26; H, 10.39.

1-(((Tetrahydropyranyloxy)methyl)-1-methyl-3-methoxy-5-hydroxycyclohexane (12). To compound **11** (0.26 g, 1.0 mmol) dissolved in dry CH_2Cl_2 (20 mL) was added PCC (0.43 g, 2.0 mmol) at room temperature. The reaction mixture was stirred at room temperature for 3 h. Diethyl ether (50 mL) was added, and the mixture was stirred for 0.5 h followed by filtering through Celite. The filtrate was concentrated *in vacuo*. Flash column chromatography on silica gel (50% ethyl acetate in hexane) afforded the desired ketone (0.26 g, 100%) as a colorless oil: R_f = 0.29 (silica, 50% ethyl acetate in hexane, not UV active); IR (neat) ν_{max} 2920, 1710, 1450, 1350, 1250, 1190, 1110, 1030, 960, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.55 and 4.47 (m, 1 H), 3.96–3.67 (m, 2 H), 3.56–3.42 (m, 2 H), 3.33 and 3.32 (s, and s, 3 H), 3.04–2.96 (m, 1 H), 2.78–2.70 (m, 1 H), 2.35–2.09 (m, 4 H), 1.78–1.45 (m, 7 H), 1.04 and 1.03 (s and s, 3 H); MS (FAB$^+$) *m/z* (relative intensity) 257 (MH^+, 1), 201 (1), 173 (14), 155 (5), 141 (50), 123 (25), 109 (9), 95 (15), 85 (100); HRMS *m/z* calcd for $C_{14}H_{25}O_4$ ($M + H)^+$ 257.1753, found 257.1754.

To a 1.0 M solution of LS-selectride (7.9 mL, 7.9 mmol) at −78 °C was added dropwise a solution of the above ketone (1.83 g, 7.15 mmol) in dry THF (20 mL), and the mixture was stirred at that temperature for 6 h. The reaction mixture was warmed up to room temperature gradually over 45 min, and then water/ethanol (1.4 mL/4.3 mL), 6 M NaOH solution (2.9 mL), and 30% H_2O_2 aqueous solution (4.3 mL) were sequentially added with stirring. The aqueous layer was extracted with ether (3 × 50 mL). The combined ether was washed with brine (100 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo*. Flash column chromatography on silica gel (80% ethyl acetate in hexane) provided the desired axial alcohol **12** (1.2 g, 65%) as a colorless oil: R_f = 0.14 9silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 3400, 2940,

1660, 1460, 1350, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.61 (m, 1 H), 4.15 (m, 1 H), 3.88–3.65 (m, 3 H), 3.52 (m, 2 H), 3.33 (ds, 3 H), 3.12 (m, 1 H), 1.87–1.25 (m, 12 H), 1.02 (ds, 3 H); CIMS (NH_3) m/z (relative intensity) 276 (MNH_4^+, 19), 259 (MH^+, 5), 248 (12), 230 (5), 205 (38), 192 (MNH_4^+ – THP, 100), 181 (34); HRMS m/z calcd for $C_{14}H_{27}NO_4$ $(M + H)^+$ 259.1910, found 259.1930. Anal. Calcd for $C_{14}H_{26}NO_4$: C, 65.07; H, 10.15. Found: C, 64.71; H, 10.33.

1-(((Tetrahydropyranyloxy)methyl)-1-methyl-3-azido-5-methoxycyclohexane (13). To compound **12** (0.35 g, 1.36 mmol) dissolved in CH_2Cl_2 (10 mL) was added dry pyridine (0.72 mL, 8.95 mmol) followed by addition of methanesulfonyl chloride (0.35 mL, 4.48 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for 1 h. Without removal of the solvents, the reaction mixture was subjected to a silica gel column and eluted with 50% ethyl acetate in hexane to afford the desired mesylate (0.45 g, 99%) as a diasteromeric mixture: R_f = 0.28 (silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 1460, 1350, 1170, 1030, 930 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.07 (m, 1 H), 4.56 (m, 1 H), 3.82 (m, 1 H), 3.71 (m, 1 H), 3.55–3.43 (m, 2 H), 3.31 (ds, 3 H), 3.01 (m, 4 H), 2.19 (m, 1 H), 1.90–1.42 (m, 12 H), 1.11 (ds, 3 H); MS (FAB^+) m/z (relative intensity) 337 (M^+ + H, 97), 253 (100), 22 (13), 155 (31); HRMS calcd for $C_{15}H_{29}O_6S$ $(M+H)^+$ 337.1686, found 337.1693.

To the mesylate (0.44 g, 1.31 mmol) prepared from the above procedure was added NaN_3 (1.14 g, 17.5 mmol) in dry DMF (8.7 mL), and the mixture was heated at 90 °C overnight. The reaction mixture was quenched with H_2O (10 mL). The aqueous phase was extracted with ether (3 × 50 mL). The combined ether layer was washed with brine (50 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo*, and the residue was purified by flash column chromatography on silica gel (20% ethyl acetate in hexane) to afforded **13** (0.25 g, 67%) as a colorless oil: R_f = 0.27 (silica, 20% ethyl acetate in hexane); IR (neat) ν_{max} 2930, 2080, 1460, 1360, 1250, 1120, 1090, 1060, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.56 (m, 1 H), 3.80 (m, 1 H), 3.60–3.36 (m, 4 H), 3.35 (s, 3 H), 3.05 (m, 1 H), 2.38 (m, 1 H), 2.01 (m, 2 H), 1.78–1.52 (m, 6 H), 1.20–0.96 (m, 6 H); CIMS (NH_3) m/z (relative intensity) 301 (MNH_4^+, 3), 284 (MH^+, 1), 256 ($MH^+ - N_2$, 31), 224 ($MH^+ - N_2$ – MeOH, 40), 198 (MH^+ – THP, 27), 172 ($MH^+ - N_2$ – THP, 100), 166 (MH^+ – THP – MeOH, 10), 140 ($MH^+ - N_2$ – THP – MeOH, 83), 125 (18); HRMS m/z calcd for $C_{14}H_{26}N_3O_3$ $(M + H)^+$ 284.1976, found 284.1959. Anal. Calcd for $C_{14}H_{25}N_3O_3$: C, 59.32; H, 8.90; N, 14.83. Found: C, 64.01; H, 10.33; N, 5.25.

1-(α-Diazoacetyl)-1-methyl-3-azido-5-methoxycyclohexane (4e). Compound **13** (0.2 g, 0.707 mmol) and PPTS (0.018 g, 0.0707 mmol) in absolute EtOH (6 mL) were heated at 55 °C for 10 h. The reaction solution was concentrated *in vacuo*. Flash column chromatography on silica gel (50% ethyl acetate in hexane) afforded the pure 1-(hydroxymethyl)-1-methyl-3-azido-5-methoxycyclohexane (0.14 g, 100%) as a colorless oil: R_f = 0.09 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 3400 (b), 2920, 2080, 1465, 1370, 1250, 1080, 1060, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.44 (m, 2 H), 3.53–3.29 (m, 2 H), 3.36 (s, 3 H), 2.40 (m, 1 H), 1.99 (m, 2 H), 1.43 (b, 1 H), 1.13 (m, 3 H), 1.02 (s, 3 H); CIMS m/z (relative intensity) 200 (M^+ + H, 16), 172 ($MH^+ - N_2$, 72), 157 ($MH^+ - HN_3$, 44), 140 ($MH^+ - N_2$ – MeOH, 100), 125 ($MH^+ - HN_3$ – MeOH, 96), 122 (64), 107 (79), 95 (67); HRMS m/z calcd for $C_9H_{18}N_3O_2$ $(M + H)^+$ 200.1400, found 200.1396.

To the above 1-(hydroxymethyl)-1-methyl-3-azido-5-methoxycyclohexane (0.026 g, 0.13 mmol) dissolved in CH_2Cl_2 (2.2 mL) was added PCC (0.11 g, 0.52 mmol), and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with ether (5 mL) and stirred for 0.5 h followed by filtration through Celite. The solvent was removed *in vacuo*. Flash column chromatography on silica gel (25% ethyl acetate in hexane) afforded the pure azido aldehyde (0.022 g, 85%) as a colorless oil: R_f = 0.35 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 2820, 2700, 2080, 1720, 1460, 1370, 1250, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.39 (s, 1 H), 3.37 (s, 3 H), 3.36 (m, 1 H), 3.13 (m, 1 H), 2.31 (m, 3 H), 1.15 (m, 3 H), 1.13 (s, 3 H); CIMS m/z (relative intensity) 198 (MH^+, 8), 180 (6), 170 ($MH^+ - N_2$, 15), 155 ($MH^+ - HN_3$, 100), 138 ($MH^+ - N_2$ – MeOH, 50), 123 (27), 108 (50); HRMS m/z calcd for $C_9H_{16}NO_2$ $(MH - N_2)^+$ 170.1182, found 170.1179.

To the above azido aldehyde (0.022 g, 0.11 mmol) in ^{t}BuOH (0.19 mL) was added 2-methyl-2-butene (0.54 mL, 5.14 mmol), NaH_2PO_4 monohydrate (buffer, 0.185 g, 1.34 mmol), H_2O (0.5 mL), and finally NaO_2Cl (0.12 g, 1.34 mmol) at room temperature, and the mixture was stirred overnight. The reaction mixture was diluted with H_2O (10 mL) and extracted with ethyl acetate (5 × 10 mL). The combined ethyl acetate was washed with brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* to give the crude acid (0.022 g, 94%) as a light yellow oil: IR (neat) ν_{max} 3600–2300 (b), 2920, 2080, 1720, 1465, 1380, 1250, 1190, 1150, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.46 (m, 3 H), 3.38 (s, 3 H), 3.28 (m, 1 H), 2.75–2.34 (m, 3 H), 1.25 (s, 3 H), 1.10 (m, 3 H); CIMS m/z (relative intensity) 214 (M^+ + H, 0.6), 186 ($MH^+ - N_2$, 25), 182 (MH^+ – MeOH, 25), 171 ($MH^+ - HN_3$, 100), 154 (69), 139 (24), 126 (10), 108 (23).

The above azido acid (0.0095 g, 0.045 mmol) was coevaporated with toluene (3 × 3 mL) and dried under reduced pressure (0.1 mmHg) for 2 h. Double distilled $SOCl_2$ (0.3 mL) and a catalytic amount of DMF (0.008 mL) were subsequently added, and the mixture was stirred at room temperature overnight. The reaction mixture was coevaporated with toluene (2 × 3 mL). The residue dissolved in CH_2Cl_2 (1 mL) was added into a 0.5 M CH_2N_2 solution in ether (5 mL) and kept at 0 °C for 1 h. The solvent was removed *in vacuo*. Flash column chromatography on silica gel (30% ethyl acetate in hexane) afforded pure azido α-diazoketone **4e** (0.011 g, 100%) as a yellow oil: R_f = 0.35 (silica, 30% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 2090 (b), 2700, 2080, 1630, 1460, 1350, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.47 (s, 1 H), 3.47 (m, 1 H), 3.37 (s, 3 H), 3.27 (m, 1 H), 2.43–2.25 (m, 3 H), 1.21 (s, 3 H), 1.19–1.05 (m, 3 H); MS (FAB^+) m/z (relative intensity) 238 (M + H, 100), 210 (39), 206 (52), 195 (56), 182 (24), 176 (27), 166 (29), 154 (23), 123 (36); HRMS m/z calcd for $C_{10}H_{16}N_5O_2$ $(M + H)^+$ 238.1306, found 238.1304. Anal. Calcd for $C_{10}H_{15}N_5O_2$: C, 50.61; H, 6.38; N, 29.53. Found: C, 51.38; H, 6.49; N, 26.76.

Literature Procedure for Preparation of [(3-Carbomethoxy-1,4-cyclohexadien-1-yl)methyl]trimethylsilane (14).[11a,b] (3-Chlorobenzyl)-trimethylsilane. A three-neck flame-dried round-bottomed flask fitted with a 150-mL additional funnel and reflux condenser was charged with Mg turnings (3.6 g, 150 mmol) and 30 mL of dry ether. Ten drops of a solution of 3-chlorobenzyl bromide (30.9 g, 19.7 mL, 150 mmol) in 50 mL of dry ether were added to the reaction flask via the additional funnel. The reaction was initiated with a heating gun. Once the reaction started, the rest of the 3-chlorobenzyl bromide solution was added in a way that keep the ether at a gentle reflux. After the addition was completed, the reaction mixture was heated at reflux for 1 h. Upon cooling, chlorotrimethylsilane (20.9 mL, 165 mmol) was added dropwise. The greendish clear solution turned cloudy after 15 min. The reaction mixture was heated at reflux overnight. Upon cooling to 0 °C, 1 N H_2SO_4 (50 mL) was added dropwise to the reaction solution until the solution pH = 1. The reaction mixture became separated. The aqueous layer was extracted with either (3 × 50 mL). The combined ether was washed with H_2O (100 mL) and brine (100 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* to give a crude product as a light yellow oil. This was purified by fractional distillation (a 7-in. vigreux column was used) under reduced pressure (4 mmHg) [*Caution: the boiling point for the starting material (109-110 °C 12 mmHg) is very close to that of the product. Fractional distillation has to be carried out with care: heat gently and keep the distillation rate at 1 drop every 2 s.*] to afforded (3-chlorobenzyl)trimethylsilane (25.4 g, 85%) as a colorless oil: bp 68 °C, 4 mmHg (lit. 228–229 °C, 760 mmHg); IR (neat) ν_{max} 2940, 2880, 1595, 1470, 1420, 1240, 1150, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.26–7.00 (m, 3 H), 6.90 (m, 1 H), 2.08 (s, 2 H), 0.03 (s, 9 H); CIMS m/z (relative intensity) 201 (M^+ + H + 2, 38), 199 (M^+ + H, 100), 185 (M^+ + H + 2 – CH_3, 28), 183 (M^+ + H – CH_3, 79), 163 (M^+ – Cl, 59), 119 (28).

3-((Trimethylsilyl)methyl)benzoic acid.[11b] Sodium (4.73 g, 205.9 mmol) was washed with hexane, weighed, and cut into sizes of peas. The pieces were placed in a 500-mL flamed-dried round-bottom flask capped with a rubber septa with a argon outlet. Anhydrous toluene (150 mL) was added, and the reaction flask was heated by a heating gun until the toluene boiled and sodium melted. The argon outlet was discharged, and the reaction flask was shaked vigirously by hand, protected by a pair of heat-proof gloves. This process was repeated five times until the sodium became a very fine sand. Upon cooling, (3-chlorobenzyl)trimethylsilane (16.3 g, 82.3 mmol) was added dropwise to the reaction mixture at room temperature. After the mixture was stirred for 10 min, the temperature of the reaction flask began to rise. A water bath was used to keep the temperature of the reaction at below 40 °C. A dark color developed slowly. The reaction mixture became thick after stirring for 2 h. Once the temperature stopped rising without a cooling bath, the dark reaction mixture was poured onto dry ice in a 1000-mL Erlenmeyer flask. After the temperature of this mixture rose close to 0 °C, EtOH (100 mL) was added and stirred for 2 h the mixture was to destroy the remaining sodium. The reaction mixture was partitioned between H_2O (200 mL) and toluene/ether (100 mL). The organic phase was extracted with a 2 N NaOH solution (2 × 100 mL). The combined aqueous layer was washed with

ether (200 mL) and acidified with a 5 N HCl solution to pH = 2. This was extracted with ethyl acetate (5 × 100 mL). The combined ethyl acetate extracts were washed with brine (100 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* to give the desired product (14.77 g, 86%). An analytical sample was recrystallized from light petroleum ether: mp 94–95 °C (lit.[11b] 96.5 °C).

[(3-Carbomethoxy-1,4-cyclohexadien-1-yl)methyl]trimethylsilane (14).[11a] Two 1000-mL three-neck flame-dried round-bottom flasks were each fitted with a cold finger and magnetic stirring bar. Sodium metal was introduced into the reaction flask on the left. Ammonia gas was then condensed with the aid of the cold finger cooled at –78 °C to the desired (375 mL). Meanwhile, the reaction flask on the right was charged with 3-(trimethylmethyl)benzoic acid (3.75 g, 18 mmol), dry ether (75 mL), and dry ^{t}BuOH (distilled from 4-Å molecular sieves, 8.5 mL, 90 mmol) and subsequently cooled at –78 °C. The liquid ammonia condensed in the reaction flask on the left was slowly distilled into the reaction flask on the right via a cold-proof hard plastic tube. Lithium wire (5.02 g, 717 mmol) prewashed with hexane and ethanol and cut into about 12 pieces was added over 1 h. A deep blue color developed immediately. The reaction mixture was stirred at –78 °C overnight. The magnetic stirring bar was replaced with mechanical stirring equipment. NH_4Cl (42.7 g, 798 mmol) was added in small portions, care being taken to avoid foaming of the liquid NH_3. The dry ice condenser was removed and the liquid NH_3 allowed to evaporate from the flask. Ether (500 mL) was added to the flask followed by water (100 mL). The organic layer was extracted with 2 N NaOH (2 × 250 mL). The aqueous phase was combined and washed with ether (500 mL), acidified with concentrated HCl (36.5%, 325 mL) to pH = 2 at 0 °C, and subsequently extracted with ethyl acetate (3 × 250 mL). The ethyl acetate extracts were washed with water (500 mL) and brine 9500 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* to give the [(3–Carboxyl-1,4-cyclohexadien-1-yl)methyl]trimethylsilane (3.47 g, 96%) contaminated with 4.5% of the starting material by ^{1}H NMR: ^{1}H NMR ($CDCl_3$) δ 10.80 (b, 1 H), 5.93–5.78 (m, 2 H), 5.34 (bs, 1 H), 3.79 (m, 1 H), 2.57 (m, 2 H), 1.52 (s, 2 H), 0.03 (s, 9 H). The resulting acid was dissolved in CH_2Cl_2 (10 mL) and added into a 0.5 M CH_2N_2 solution in ether (100 mL) at 0 °C. The mixture was stirred for 0.5 h. The solvent was removed *in vacuo* to afford **14** (3.74 g, 96%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.84 (m, 2 H), 5.33 (m, 1 H), 3.75 (m, 1 H), 3.70 (s, 3 H), 2.58 (m, 2 H), 1.51 (s, 2 H), 0.02 (s, 9 H).

1-Carbomethoxy-1-methyl-3-((trimethylsilyl)methyl)cyclohexane (15). Compound **14** (3.74 g, 16.7 mmol) in absolute MeOH (100 mL) was hydrogenated at 50 psi in the presence of 10% Pd on charcoal (0.18 g, 5% by weight) at room temperature overnight. The reaction mixture was filtered through Celite and concentrated *in vacuo* to give 3.81 g of the desired product contaminated with 17% methyl 3-((trimethylsilyl)methyl)-benzoate. Fractional distillation gave the 1-carbomethoxy-3-((trimethylsilyl)methyl)cyclohexane with 13% impurity: bp 94 °C, 1 mmHg. This mixture was subjected to the next step of the reaction without further purification: IR (neat) ν_{max} 2920, 2840, 1740, 1430, 1240, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.65 (s, 3 H), 2.30 (m, 1 H), 1.94–1.60 (m, 4 H), 1.45–1.23 (m, 2 H), 1.09 (m, 1 H), 0.97–0.82 (m, 2 H), 0.50 (d, J_d = 6.8 Hz, 2 H), –0.006 (s, 9 H); CIMS *m/z* (relative intensity) 228 (M^+, 1), 213 ($M^+ - CH_3$, 14), 185 ($M^+ - COCH_3$, 4), 159 (5), 146 (5), 124 (16), 89 (63), 73 (100); HRMS *m/z* calcd for $C_{12}H_{25}O_2Si$ $(M + H)^+$ 229.1625, found 229.1610.

To diisopropylamine (1.34 mL, 9.60 mmol) in dry toluene (5 mL) was added a 1.44 M *n*-BuLi solution in hexane (6.7 mL, 9.65 mmol) dropwise at 0 °C, and the mixture was stirred for 30 min. The reaction mixture was cooled to –78 °C, and the above mixture containing 13% impurity (1.68 g, 7.38 mmol) in dry toluene (2 mL) was added dropwise followed by DMPU (5 mL, 33% by volume). The reaction mixture was stirred at –78 °C for 4 h. Dimethyl sulfate (1.40 mL, 14.76 mmol) was added dropwise, and the mixture was stirred overnight at room temperature. The reaction mixture was partitioned between ether (25 mL) and water (25 mL). The aqueous phase was extracted with ether (3 × 25 mL). The combined ether layer was washed with brine (50 mL), dried over Na_2SO_4, and filtered. Flash column chromatography on silica gel (30% CH_2Cl_2 in hexane) afforded the pure **15** (one peak by GC, 1.1 g, 71%) as a colorless oil: R_f = 0.27 (silica, 30% CH_2Cl_2 in hexane); IR (neat) ν_{max} 2940, 1730, 1460, 1250, 1210, 1150, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.67 (s, 3 H), 2.22–2.12 (m, 2 H), 1.66–1.54 (m, 2 H), 1.45–1.21 (m, 2 H), 1.12 (s, 3 H), 1.05–0.7 (m, 3 H), 0.45 (m, 2 H), 0.01 (s, 9 H); CIMS *m/z* (relative intensity) 243 (M + H, 100), 227 ($MH^+ - CH_4$, 62), 195 ($MH^+ - 2CH_4$, 12), 183 (9), 133 (22), 121 (10), 109 (6); HRMS *m/z* calcd for $C_{13}H_{27}O_2Si$ $(M + H)^+$ 243.1781, found 243.1788. Anal. Calcd dor $C_{13}H_{26}O_2Si$: C, 64.42; H, 10.82. Found: C, 64.78; H, 10.91.

1-(α-Diazoacetyl)-1-methyl-3-((trimethylsilyl)methyl)cyclohexane (4g). To a suspension of $LiAlH_4$ powder (0.095 g, 2.5 mmol) in THF (8 mL) was added a solution of compound **15** (0.242 g, 1 mmol) in THF (2 mL) dropwise at 0 °C. The reaction mixture was stirred at room temperature overnight. With cooling, the reaction mixture was quenched with H_2O, 15% NaOH solution, and H_2O in a 1:1:3 (0.1 mL/0.1 mL/0.3 mL) fashion, stirred for 0.5 h, and filtered. The solid was washed with ether (10 × 5 mL). The combined ether/THF was concentrated *in vacuo*. Flash column chromatography on silica gel (20% ethyl acetate in hexane) afforded pure 1-(hydroxymethyl)-1-methyl-3-((trimethylsilyl)methyl)-cyclohexane (0.214 g, 100%) as a white crystal: mp 48–50 °C, R_f = 0.35 (silica, 20% ethyl acetate in hexane); IR (KBr) ν_{max} 3360, 2940, 2900, 2880, 2840, 1450, 1380, 1245, 1030, 860, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.94 (m, 4 H), 7.68 (m, 6 H), 3.91 (m, 1 H), 3.51 (s, 3 H), 3.50 (dd, J_d = 15.4 Hz, J_d = 4.6 Hz, 2 H), 1.73–0.93 (m, 8 H), 0.89 (S, 3 H), 0.44 (d, J_d = 6.7 Hz, 2 H), 0.80 (m, 2 H), –0.005 (s, 9 H); CIMS *m/z* (relative intensity) 213 (8), 197 ($MH^+ - H_2O$, 100), 181 (27), 123 (58), 109 (15), 95 (21); HRMS *m/z* calcd for $C_{12}H_{24}Si$ $(MH - H_2O)^+$ 197.1726, found 197.1724.

To the above 1-(hydroxymethyl)-1-methyl-3-(trimethylsilyl)methyl)-cyclohexane (0.214 g, 1 mmol) dissolved in dry DMF (5 mL) was added PDC (1.32 g, 3.5 mmol) at room temperature, and the mixture was stirred overnight. Water (10 mL) was added, and the reaction mixture was extracted with ethyl acetate (5 × 10 mL). The combined ethyl acetate layer was washed with water (2 × 25 mL) and brine (50 mL), dried over Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was coevaporate with toluene (3 × 3 mL) to afforded the desired 1-carboxyl-1-methyl-3-((trimethylsilyl)methyl)cyclohexane (0.20 g, 88%) as a light yellow oil: IR (KBr) ν_{max} 3450 (b), 2940, 1700, 1460, 1380, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.16 (m, 2 H), 1.69–1.23 (m, 4 H), 1.19 (S, 3 H), 1.06–0.72 (m, 3 H), 0.47 (d, J_d = 6.8 Hz, 2 H), 0.01 (s, 9 H); CIMS *m/z* (relative intensity) 229 (M^+ + H, 57), 213 ($MH^+ - CH_4$, 100), 183 (M^+ –COOH, 33), 167 ($M^+ - COOH - CH_4$, 7), 119 (51); HRMS calcd for $C_{12}H_{24}O_2Si$ $(M)^+$ 228.1546, found 228.1560.

The above acid (0.19 g, 0.83 mmol) was coevaporated with toluene (3 × 3 mL) and dried under reduced pressure (0.1 mmHg) for 2 h. Subsequently double distilled $SOCl_2$ (1.0 mL) and a catalytic amount of DMF (0.020 mL) were added, and the mixture was stirred at room temperature overnight. The reaction mixture was coevaporated with toluene (2 × 3 mL). The residue dissolved in CH_2Cl_2 (1 mL) was added into a 0.5 M CH_2N_2 solution in ether (10 mL) and kept at 0 °C for 1 h. The solvent was removed *in vacuo*. Flash column chromatography on silica gel (10% ethyl acetate in hexane) afforded pure α-diazoketone **4g** (0.040 g, 19%) as a yellow oil: R_f = 0.30 (silica, 10% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 2090, 1630, 1450, 1340, 1240, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.41 (s, 1 H), 2.07–1.99 (m, 2 H), 1.70–1.23 (m, 4 H), 1.07 (m, 1 H), 1.05 (s, 3 H), 0.89–0.77 (m, 2 H), 0.46 (d, J_d = 6.8 Hz, 2 H), 0.02 (s, 9 H); CIMS *m/z* (relative intensity) 253 (M + $^+NH_4$, 6), 225 ($MH^+ - N_2$, 80), 184 (12), 152 (21), 138 (19), 128 (11), 121 (15); HRMS *m/z* calcd for $C_{13}H_{25}N_2OSi$ $(M + H)^+$ 253.1738, found 253.1755.

1-Methyl-1-(methoxycarbonyl)-3-methoxy-5-hydroxy-5-deuteriocyclohexane (17). To 1-methyl-1-(methoxycarbonyl)-3-methoxy-5-hydroxycyclohexane (0.202 g, 1 mmol) dissolved in freshly distilled CH_2Cl_2 (15 mL) was added PCC (0.431 g, 2 mmol) at room temperature, and the mixture was stirred overnight. The reaction mixture was diluted with diethyl ether (10 mL), further diluted with hexane (30 mL), and finally filtered through Celite. The filtrate was concentrated *in vacuo*. Flash column chromatography on silica gel (50% ethyl acetate in hexane) furnished the desired ketone **16** (0.192 g, 96%) as a colorless oil: R_f = 0.33 (silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 2960, 1730, 1460, 1320, 1200, 1130, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 3 H), 3.49 (m, 1 H), 3.35 (s, 3 H), 2.85 (dm, J_d = 14.8 Hz, 1 H), 2.77 (dm, J_d = 14.8 Hz, 1 H), 2.55 (dm, J_d = 13.3 Hz, 1 H), 2.22 (ddd, J_d = 14.8 Hz, J_d = 12.2 Hz, J_d = 1.0 Hz, 1 H), 2.13 (dd, J_d = 14.8 Hz, J_d = 1.0 Hz, 1 H), 1.60 (dd, J_d = 13.4 Hz, J_d = 10.4 Hz, 1 H), 1.37 (s, 3 H); EIMS *m/z* (relative intensity) 201 (MH^+, 5), 186 ($MH^+ - CH_3$, 12), 169, 141. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.97; H, 8.06. Found: C, 59.68; H, 8.04.

To a suspension of $NaBD_4$ powder (0.193 g, 4.6 mmol) in absolute EtOH (10 mL) was added a solution of the above ketone (0.84 g, 4.2 mmol) in absolute EtOH (10 mL) at –78 °C dropwise, and the mixture was stirred for 30 min. The reaction mixture was quenched with saturated $NaHCO_3$ solution at –78 °C, warmed to room temperature, filtered

through a bed of Celite, and partitioned between ethyl acetate and water. The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined ethyl acetate was washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and filtered. Flash chromatography on silica gel (75% ethyl acetate in hexane) gave a 2.7:1 ratio (estimated by ^1H NMR for the crude mixture) of the deuterated alcohol (0.79 g, 93%) as a colorless oil.

To sodium hydride (0.153 g, 60% suspension in mineral oil) prewashed with hexane (three times) suspended in dry THF (18 mL) was added a solution of the above mixture (0.78 g, 3.84 mmol) in dry THF (20 mL), and the mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with water (10 mL) and partitioned between ethyl acetate (30 mL) and water (30 mL). The aqueous layer was extracted with ethyl acetate (4 × 30 mL). The combined ethyl acetate was washed with brine (100 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo*. Flash chromatography on silica gel (75% ethyl acetate in hexane) provided the desired **17** (0.51 g, 66%) as a colorless oil: R_f = 0.24 (silica, 75% ethyl acetate in hexane); IR (neat) ν_{max} 3400, 2940, 1720, 1460, 1190, 1150, 1090; ^1H NMR ($CDCl_3$) δ 3.69 (s, 3 H), 3.36 (s, 3 H), 3.22 (m, 1 H), 2.55–2.30 (m, 3 H), 1.56 (bs, 1 H), 1.26 (s, 3 H), 1.23–0.95 (m, 3 H); MS (FAB$^+$) m/z (relative intensity) 204 (MH^+, 7), 186 (100), 172 (83), 154 (60), 140 (26), 131 (18), 126 (41), 112 (30), 94 (13); HRMS m/z calcd for $C_{10}H_{18}DO_4$ $(M + H)^+$ 204.1346, found 204.1344. Anal. Calcd for $C_{10}H_{17}DO_4$: C, 59.08; H, 8.43. Found: C, 57.47; H, 9.02.

1-(α-Diazoacetyl)-1-methyl-3-methoxy-3-deuterio-5-methoxycyclohexane (4i). To a solution of the above deuterated alcohol **17** (0.47 g, 2.29 mmol) in methylene chloride (8 mL) was added 2,6-di-*tert*-butyl-4-methylpyridine (0.83 g, 4.05 mmol) followed by addition of methyl trifluoromethanesulfonate (0.39 mL, 3.44 mmol) dropwise via a syringe at room temperature. The reaction mixture was heated at reflux overnight. The solvent was removed *in vacuo* to give a mixture of solid and liquid. The solid was filtered and washed with hexane (3 × 5 mL). The filtrate was concentrated *in vacuo*. Flash column chromatography on silica gel (40% ethyl acetate in hexane) provided the desired methyl ether (0.39 g, 77%) as a colorless oil: R_f = 0.25 (silica, 40% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 1730, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.70 (s, 3 H), 3.36 (s, 6 H), 3.18 (m, 1 H), 2.54–2.39 (m, 3 H), 1.26 (s, 3 H), 1.02 (m, 3 H); CIMS m/z (relative intensity) 218 (MH^+, 1), 215 (1), 210 (2), 200 (1), 186 (100), 154 (36), 126 (27), 94 (32); HRMS m/z calcd for $C_{11}H_{20}DO_4$ $(M + H)^+$ 218.1503, found 218.1496.

To a solution of the above 1-methyl-1-(methoxycarbonyl)-3-methoxy-5-methoxy-5-deuteriocyclohexane (0.33 g, 1.51 mmol) in MeOH/H_2O (9 mL/3 mL, 3:1) was added LiOH monohydrate (0.254 g, 6.05 mmol), and the mixture was subsequently heated at reflux for 3 h. After cooling, the reaction mixture was acidified with a 5 N HCl solution (0.1 mL, 0.5 mmol) to pH = 2 and extracted with ether (3 × 10 mL). The combined ether was washed with water (10 mL) and brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo* and further removed under reduced pressure (0.1 mmHg) for 2 days to give the acid (0.22 g, 71%) as a white crystal: mp 154–156 °C; IR (neat) ν_{max} 3500–2500 (b), 1730, 1475, 1310, 1200, 1170, 1130, 1090 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.21 (s, 6 H), 3.10 (m, 1 H), 2.31 (m, 3 H), 1.15 (s, 3 H), 0.88 (m, 3 H); CIMS m/z (relative intensity) 204 (MH^+, 1), 186 (8), 172 (100), 154 (21), 140 (67), 126 (37), 112 (26), 96 (66), 94 (49); HRMS m/z calcd for $C_{10}H_{17}DO_4$ $(M + H)^+$ 204.1346, found 204.1342.

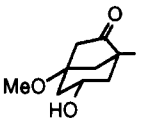
To the above acid (0.22 g, 1.08 mmol) were added double distilled thionyl chloride (2 mL) and catalytic amount of DMF (10 μL), and the mixture was stirred at room temperature overnight. The excess thionyl chloride was removed (bath temperature 40 °C). The reaction mixture was coevaporated with toluene (2 × 3 mL) to give a white solid (very hydroscopic) which was dissolved in CH_2Cl_2 (2 mL) and added into a 0.5 M CH_2N_2 solution in diethyl ether (5 mL). The mixture was stirred for 1 h at 0 °C. Solid on the walls of the reaction flask was removed with a spatula. The solvent was removed *in vacuo*, and the residue was purified by flash column chromatography on silica gel (75% ethyl acetate in hexane) to afford **4i** (0.21 g, 85%) as a yellow oil: R_f = 0.29 (silica, 75% ethyl acetate in hexane); IR (neat) ν_{max} 2960, 2100, 1735, 1630, 1350, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.48 (s, 1 H), 3.37 (s, 6 H), 3.25 (m, 1 H), 2.48–2.42 (md, J_d = 9.3 Hz, 1 H), 2.37–2.30 (dm, J_d = 13.1 Hz, 2 H), 1.19 (s, 3 H), 1.13–0.95 (m, 3 H); CIMS m/z (relative intensity): 228 (MH^+, 11), 200 (28), 196 (38), 168 (100), 156 (28), 136 (60), 128 (62), 116 (37), 110 (66); HRMS m/z calcd for $C_{11}H_{18}DN_2O_3$ $(M + H)^+$ 228.1459, found 228.1454. Anal. Calcd for $C_{11}H_{17}DN_2O_3$: C, 58.11; H, 7.54; N, 12.33. Found: C, 57.69; H, 7.96; N, 11.92.

General Procedure for the Rh Mediated C–H Insertion Reactions. To Rh catalyst (1% by weight) suspended in freshly distilled CH_2Cl_2 (or benzene) (total concentration of **4** is 0.025 M) was added compound **4** dissolved in CH_2Cl_2 (or benzene) dropwise at room temperature, and the mixture was stirred for a designated time either at room temperature or at reflux. The solvent was removed *in vacuo*. The residue was analyzed by ^1H NMR (or ^{13}C NMR) and GC–MS. Flash column chromatography on silica gel provided the pure compound for identification.

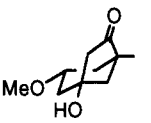
Compound 5a: 65%, from 0.027 mmol of **4a** (silica gel, 50% ethyl acetate in hexane); R_f = 0.38 (silica, 50% ethyl acetate in hexane); IR (neat) ν_{max} 2960, 1740, 1230, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.85 (m, 1 H), 3.31 (s, 3H), 2.54–2.31 (m, 3 H), 2.03 (s, 3 H), 1.98–1.90 (m, 1 H), 1.87 (d, J_d = 1.2 Hz, 2 H), 1.73 (m, 1 H), 1.43 (t, J_t = 11.9 Hz, 1 H), 1.12 (s, 3 H); CIMS (NH_3) m/z (relative intensity) 244 ($M + {}^+NH_4$), 167 (MNH_4^+ – AcOH); CIMS m/z (relative intensity) 227 (MH^+, 7), 195 (MH^+ – MeOH, 3), 167 (MH^+ – CH_3COOH, 100), 135 (2); HRMS m/z calcd for $C_{12}H_{19}O_4$ (M^+ + H) 227.1283, found 227.1283.

Compounds 5b, 6b, and 6b'. The ratio of **5b**, **6b**, and **6b'** determined by both GC analysis and chromatography isolation is 2.7:1:2.6.

Compounds 5b and 6b. Compounds **5b** and **6b** were not separable by flash column chromatography (silica gel, 80% ethyl acetate in hexane) but can be separated by GC. ^1H NMR and IR spectra were obtained



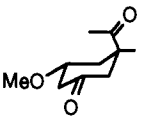
5b



6b

from a mixture of these two compounds. Low-resolution and high-resolution mass spectrum were obtained from the pure compound separated by GC [0.0072 g in a ratio of 2.25:1, 60% total from 0.0136 g of diazoketone **4b**, 42% for **5b** and 18% for **6b**]: R_f = 0.26 (silica, 80% ethyl acetate in hexane); IR (neat) ν_{max} 3423, 2935, 1743, 1315, 1077 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (m, 1 H), 3.35 (m, 1 H), 3.33 and 3.31 (s, 3H), 2.37 (m, 3 H), 2.02–1.69 (m, 5 H), 1.40–1.23 (m, 1 H), 1.12 (s, 3 H); MS for **5b** CIMS m/z (relative intensity) 185 (M + H, 17), 167 (MH^+ – H_2O, 100), 153 (MH^+ – MeOH, 13), 127 (75); HRMS m/z calcd for $C_{10}H_{16}O_3$ $(M)^+$ 184.1110, found 184.1098; MS for **6b** CIMS m/z (relative intensity) 185 (M + H, 28), 167 (MH^+ – H_2O, 28), 153 (MH^+ – MeOH, 100); HRMS m/z calcd for $C_{10}H_{136}O_3$ (M^+) 184.1110, found 184.1093.

Compound 6b': 0.0047 g, 39% from 0.0136 g of diazoketone **4b** (silica gel, 80% ethyl acetate in hexane); R_f = 0.38 (silica, 80% ethyl acetate in hexane); IR (neat) ν_{max} 2968, 2934, 2828, 1714, 1461, 1359, 1100

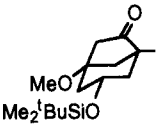


6b'

cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.43 (m, 1 H), 3.33 (s, 3H), 2.81–2.66 (m, 2 H), 2.44 (m, 1 H), 2.26 (m, 1 H), 2.17 (s, 3 H), 2.08 (m, 1 H), 1.67 (m, 1 H), 1.34 (s, 3 H); CIMS m/z (relative intensity) 185 (M + H, 38), 153 (MH^+ – MeOH, 100), 135 (MH^+ – MeOH – H_2O, 14); HRMS m/z calcd for $C_{10}H_{16}O_3$ $(M)^+$ 184.1110, found 184.1110.

Compounds 5c and 6c. The ratio of **5c** and **6c** determined by both GC analysis and chromatography isolation is 2.2:1.

Compound 5c: 0.0033 g, 56% from 0.0065 g of diazoketone **4c** (silica gel, 10% ethyl acetate in hexane); R_f = 0.27 (silica, 10% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 2860, 1745, 1460, 1359, 1310, 1250,

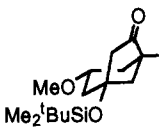


5c

1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (m, 1 H), 3.32 (s, 3 H), 2.35 (s, 2 H), 2.20 (m, 1 H), 1.90–1.74 (m, 4 H), 1.37 (t, J_t = 11.8 Hz, 1 H), 1.10 (s, 3 H), 0.86 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); CIMS m/z (relative intensity) 299 (M + H, 98), 283 (MH^+ – CH_4, 24), 267 (MH^+

– MeOH, 61), 255 ($MH^+ - C_3H_8$, 10), 241 ($MH^+ - C_4H_{10}$, 11), 213 ($MH^+ - Si^tBuMe_2$, 9), 195 ($MH^+ - Si^tBuMe_2 - H_2O$, 3), 167 ($MH^+ - HOSi^tBuMe_2$, 100); HRMS *m/z* calcd for $C_{16}H_{31}O_3Si$ $(M + H)^+$ 299.2043, found 299.2044.

Compound 6c: 0.0015 g, 25% from 0.0065 g of diazoketone **4c** (silica gel, 10% ethyl acetate in hexane); R_f = 0.35 (silica, 10% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 2860, 1745, 1460, 1310, 1250, 1080, 835

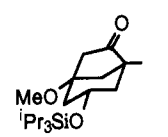


6c

cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.31 (s, 3 H), 3.28 (m, 1 H), 2.34 (m, 3 H), 1.97 (m, 1 H), 1.83 (m, 1 H), 1.68 (t, J_t = 10.6 Hz, 1 H), 1.28 (m, 2 H), 1.10 (s, 3 H), 0.87 (s, 9 H), 0.12 (s, 3 H), 0.11 (s, 3 H); CIMS *m/z* (relative intensity) 299 (M + H, 40), 283 ($MH^+ - CH_4$, 47), 267 (MH^+ – MeOH, 93), 255 ($MH^+ - C_3H_8$, 28), 241 ($MH^+ - C_4H_{10}$, 46), 227 (100), 167 ($MH^+ - HOSi^tBuMe_2$, 47); HRMS *m/z* calcd for $C_{16}H_{31}O_3Si$ $(M + H)^+$ 299.2043, found 299.2034.

Compounds 5d and 6d. The ratio of **5d** and **6d** determined by both GC analysis and chromatography isolation is 6:1.

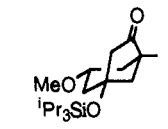
Compound 5d: 0.006 g, 80% from 0.0081 g of diazoketone **4d** (silica gel, 15% ethyl acetate in hexane); R_f = 0.28 (silica, 15% ethyl acetate in hexane); IR (neat) ν_{max} 2943, 2867, 1747, 1463, 1313, 1099, 1004, 883



5d

cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (m, 1 H), 3.32 (s, 3 H), 2.34 (s, 2 H), 2.24 (m, 1 H), 1.86 (m, 4 H), 1.39 (m, 1 H), 1.10 (s, 3 H), 1.03 (s, 18 H), 0.96 (m, 3 H); CIMS *m/z* (relative intensity) 341 (M + H, 72), 309 (MH^+ – MeOH, 69), 297 ($MH^+ - C_3H_8$, 100), 269 ($MH^+ - C_3H_8 - CO$, 41), 167 (60); HRMS *m/z* for $C_{19}H_{37}O_3Si$ $(M + H)^+$ calcd 341.2513, found 341.2496.

Compound 6d: 0.001 g, 14% from 0.0081 g of diazoketone **4d** (silica gel, 15% ethyl acetate in hexane); R_f = 0.37 (silica, 15% ethyl acetate in hexane); IR (neat) ν_{max} 2943, 2867, 1747, 1463, 1312, 1143, 1102, 882

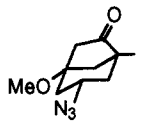


6d

cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.31 (s, 3 H), 3.29 (m, 1 H), 2.39 (s + m, 3 H), 2.00–1.68 (m, 4 H), 1.24 (m, 1 H), 1.11 (s, 3 H), 1.05 (s, 18 H), 1.03 (m, 3 H); CIMS *m/z* (relative intensity) 341 (M + H, 100), 309 (MH^+ – MeOH, 48), 297 ($MH^+ - C_3H_8$, 41), 269 ($MH^+ - C_3H_8 - CO$, 15), 167 (90); HRMS *m/z* calcd for $C_{19}H_{37}O_3Si$ $(M + H)^+$ 341.2513, found 341.2511.

Compounds 5e and 6e from 4e. To $Rh_2(OAc)_4$ (1%) suspended in anhydrous CH_2Cl_2 (0.4 mL) was added compound **4e** (0.0055 g, 0.023 mmol) dissolved in CH_2Cl_2 (0.5 mL) dropwise at room temperature followed by stirring at room temperature overnight. The solvent was removed *in vacuo*. Flash column chromatography (25% ethyl acetate in hexane) provided compounds **5e** and **6e** as light yellow oils. The ratio of **5e**/**6e** determined by GC analysis is 1:8. Yields indicated below are not accurate due to the analytical scale of the reaction. **6e** was assigned to the following structure according to 2-D NOE studies, which showed interaction of methoxy protons with its α proton on the cyclohexane ring. This interaction was not observed for the compound **5e**.

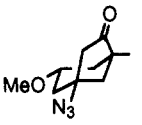
Compound 5e/f: 0.001 g, 21% from 0.0055 g of diazoketone **4a** (silica gel, 25% ethyl acetate in hexane); R_f = 0.34 (silica, 25% ethyl acetate in hexane); IR (neat) ν_{max} 2920, 2080, 1745, 1310, 1250, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.36 (m, 1 H), 3.33 (s, 3 H), 2.39 (m, 3 H), 1.97–1.92 (m, 1 H), 1.92 (m, 2 H), 1.73 (m, 1 H), 1.33 (t, J_t = 11.7 Hz, 1 H), 1.14 (s, 3 H); MS (FAB$^+$) *m/z* (relative intensity) 210 (MH^+, 8), 182 (MH^+



5e/f

– N_2, 13), 167 (100), 150 (70), 139 (14), 125 (38), 110 (34), 95 (15); HRMS *m/z* calcd for $C_{10}H_{17}N_3O_2$ $(MH - N_2)^+$ 182.1182, found 182.1178.

Compound 6e/f: 0.0017 g, 35% from 0.0055 g of **4e** (silica gel, 25% ethyl acetate in hexane); R_f = 0.26 (silica, 25% ethyl acetate in hexane);

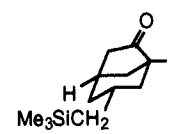


6e/f

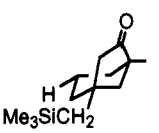
IR (neat) ν_{max} 2940, 2080, 1740, 1450, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.46 (m, 1 H), 3.33 (s, 3 H), 2.39 (d, J_d = 1.5 Hz, 2 H), 2.36–2.28 (m, 1 H), 1.96–1.72 (m, 4 H), 1.38 (t, J_t = 12.4 Hz, 1 H), 1.14 (s, 3 H); MS (FAB$^+$) *m/z* (relative intensity) 210 (MH^+, 9), 182 ($MH^+ - N_2$, 58), 167 (100), 150 (48), 139 (15), 125 (45), 122 (28), 110 (44); HRMS *m/z* calcd for $C_{10}H_{16}NO_2$ $(MH - N_2)^+$ 182.1182, found 182.1180.

Compounds 5f and 6f from 4f. To $Rh_2(Cap)_4$ (0.0002 g, 0.00203 mmol) suspended in anhydrous benzene (0.4 mL) was added compound **4f** (0.0054 g, 0.023 mmol) dissolved benzene (0.5 mL) dropwise at room temperature followed by heating at reflux for 5 h. The solvent was removed *in vacuo*. Flash column chromatography (25% ethyl acetate in hexane) provided compounds **5f** (<0.0001 g) and **6f** (0.004 g, 83%) as light yellow oils. The ratio of **5f**/**6f** determined by GC analysis is 1:30.

Compounds 5g and 6g from 4g. To $Rh_2(OAc)_4$ (0.0002 g, 0.0005 mmol) suspended in freshly distilled CH_2Cl_2 (1.0 mL) was added compound **4g** (0.0126 g, 0.05 mmol) dissolved in CH_2Cl_2 (2 mL) dropwise at room temperature, and the mixture was stirred at room temperature overnight. The solvent was removed *in vacuo*. The residue was analyzed by GC–MS. Flash column chromatography (5% ethyl acetate in hexane) provided compound **6g** (0.003 g, 17%) and a mixture of **5g** and **6g** (0.0094



5g/h



6g/h

g, 53%) which cannot be separated completely by flash column chromatography (silica gel, 5% ethyl acetate in hexane) but can be separated by GC. Spectral data for **5g** were obtained from the above mixture. Low-resolution and high-resolution mass spectrum were obtained from the pure compound separated by GC.

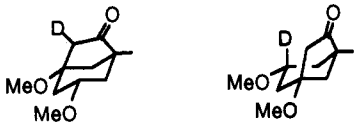
Compound 6g: R_f = 0.24 (silica, 5% ethyl acetate in hexane); IR (neat) ν_{max} 2940, 2840, 1740, 1240, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.19 (md, J_d = 18.2 Hz, 1 H), 1.97 (d, J_d = 18.2 Hz, 1 H), 1.74–1.23 (m, 8 H), 0.99 (s, 3 H), 0.85 (d, J_d = 0.7 Hz, 2 H), 0.05 (s, 9 H); EIMS *m/z* (relative intensity) 224 (M^+, 3), 209 ($M^+ - CH_3$, 4), 196 ($M^+ - CO$, 6), 181 ($M^+ - COCH_3$, 14), 131 (3), 119 (4), 73 (100); HRMS *m/z* calcd for $C_{13}H_{25}OSi$ $(M + H)^+$ 225.1676, found 225.1677.

Compound 5g: MS for **5g** EIMS *m/z* (relative intensity) 224 (M^+, 3), 209 ($M^+ - CH_3$, 2), 181 ($M^+ - COCH_3$, 12), 168 (9), 134 (8), 119 (4), 93 (11), 73 (100); HRMS *m/z* calcd for $C_{13}H_{25}OSi$ (M^+ + H) 225.1676, found 225.1668.

Compounds 5h and 6h from 4h. To **4h** (0.0126 g, 0.05 mmol) dissolved in benzene (2 mL) was added $Rh_2(Cap)_4$ (0.0003 g, 0.0005 mmol), and the mixture was heated at reflux for 3 h. The solvent was removed *in vacuo*. Flash column chromatography (5% ethyl acetate in hexane) provided compound **6h** (0.003 g, 27%) and a mixture of **5h** and **6h** (0.008 g, 71%). The ratio of **5h**/**6h** determined by GC analysis is 3.8:1.

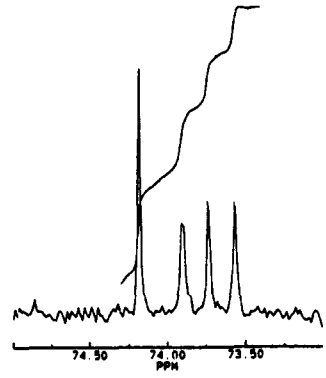
Compounds 5i and 6i from 4i. To $Rh_2(Cap)_4$ (0.0002 g, 0.00203 mmol) (or $Rh_2(OAc)_4$, 1%) suspended in anhydrous benzene (or CH_2Cl_2) (4 mL) was added compound **4i** (0.046 g, 0.203 mmol) dissolved in benzene (or CH_2Cl_2) (4.1 mL) dropwise at room temperature followed by heating

at reflux for 5 h (or stirring at room temperature overnight for reaction with $Rh_2(OAc)_4$ in CH_2Cl_2). The solvent was removed *in vacuo*. Flash column chromatography (30% ethyl acetate in hexane) provided compounds **5i** and **6i** (0.033 g, 83%) as an unseparable mixture. The product



5i/j 6i/j

ratios **5i**/**6i** and **5j**/**6j** from both reactions were determined by integration of ^2H coupled ^{13}C NMR signals for the diagnostic ^2H bearing carbons (δ 74.17, s to 73,73, t, J = 21.1 Hz). A relaxation delay of 5 s was used to determined sufficiently accurate integrals. Estimated error in measurement is ~5%. This ratio was determined to be 1:1.2 for the reaction of **4i** and 1:2 for the reaction of **4j**: R_f = 0.18 (silica, 30% ethyl acetate in hexane); ^1H NMR ($CDCl_3$) δ 3.35–3.31 (m) and 3.33 (s) and 3.32 (s) (total 6.6 H), 2.40–2.35 (m) and 2.37 (s) (total 2.8 H), 2.01–1.97 (m, 1 H), 1.88–1.82 (m) and 1.86 (s) (total 2.2 H), 1.71–16.7 (m, 1 H), 1.30–1.25 (m, 1 H), 1.12 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 216.71, 216.67, 74.17, 73.73 (t, J_t = 21.1 Hz), 56.30, 56.27, 50.75, 50.29, 48.72, 48.40 (t, J_t = 21.1 Hz), 46.99, 42.96, 42.83, 38.97, 38.94, 38.86, 19.57.



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