4-Substituted Cyclohexanones. Predicting the Facial Selectivity of Nucleophilic Attacks from the Geometrical Changes on Cation−Carbonyl Complexation: An ab Initio Investigation

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Introduction

We have conceptualized[1] the view that in reactions of substituted cyclohexanones with nucleophiles there is first a complexation of the carbonyl oxygen with the nucleophile's cation component and that the resulting changes in the torsion angles about the carbonyl carbon must depend on the nature, location, and orientation of a ring substituent. An increase in the torsion angles of the carbonyl oxygen with the ring positions 3 and 5 on the axial face that leads to ring flattening indicates a preferred axial orientation of the electron-deficient p orbital on the carbonyl carbon and, hence, a propensity for axial attack. On the contrary, a reduction in the said torsion angles leads to ring puckering and, hence, a propensity for equatorial attack. The theory of stereoelectronic effects[2] dictates that an electron-deficient orbital, such as the above p orbital in the present case, must orient, respectively, antiperiplanar and orthogonal to an adjacent electron-donating and electron-attracting bond. Under forces of electrostatic attraction, a nucleophile is drawn to this orbital on whichever face it is to result in the predominant product.

The present approach avoids not only the often bothersome transition-state (TS) calculations but also takes care of the iminent fact that unlike the hitherto reported TS models the cationic (Lewis acid) species is retained in the carbonyl σ plane, which is of higher electron density.[3] We present herein the results of our calculations on 4-substituted cyclohexanones to show that our approach is not only stereoelectronically rational but also that it does a qualitatively decent job at facial prediction[4] and differential reaction rates.

Results and Discussion

The relevant geometrical parameters, both before and after complexation with selected cations such as H^+ and Li^+, are collected in Table 1. It is important to note that all the derivatives retained their chair structures on complexation as well. Whereas the enlargements in the torsion angles D2 and D3 on carbonyl protonation are some 17° at the 6-31G level and 13° at the 6-31G* level for the 4-ax-Cl-derivative, the related 4-eq-Cl-derivative computed, on protonation, for much smaller 5 and 6.4° changes, respectively. Likewise, whereas the 4-ax-F-cyclohexanone shows an enlargement of about 15° at the 6-31G level and 11° at the 6-31G* level in D2 and D3 on carbonyl protonation, these enlargements in the protonated 4-eq-F-cyclohexanone are about 9 and 6°, respectively. Both the 4-ax-Cl- and 4-ax-F-cyclohexanones must, therefore, exhibit larger axial selectivity than the corresponding 4-eq-derivatives. The slightly smaller D2 and D3 changes in protonated 4-ax-F-cyclohexanone in comparison to the protonated 4-ax-Cl-cyclohexanone indicate that an axial chlorine may be a slightly better axial-director than an axial fluorine. All these observations are in excellent accord with the experimental results.[5] Further, the relatively larger torsion-angle changes in the 4-eq-F-derivative in comparison to the 4-eq-Cl-species may be predictive of slightly better axial diastereoselection with the former. Unfortunately, no such experimental results have been reported to allow us to confirm this observation.

Since good experimental results are reported for the 4-OH-*trans*-1-decalones,[5] we have computed 4-OH-cyclohexanones as well. The results are revealing. Better axial diastereoselectivity must be predicted for 4-ax-OH-cyclohexanone than that for the corresponding equatorial derivative. Accordingly, *trans*-1-decalone exhibits 85% and 61% axial diastereoselection for the 4-ax- and 4-eq-OH substituents, respectively. The related mercapto derivatives were also computed. For both of the 4-SH-derivatives, axial nucleophilic attack appears to be favored for the enhancements in the said torsion angles. These selectivities appear to be slightly lower than those for the respective Cl-derivatives for the slightly lower torsion angles changes. We ourselves have determined the selectivity of 4-eq-SPh-cyclohexanone in reductions with LAH in Et_2O, $NaBH_4$ in methanol, and $Na(CN)BH_4$ in MeOH at pH 1.0. The axial attacks, computed from ^1H NMR integrals, were 55, 61, and 64%, respectively. As against the 61% axial selectivity of 4-eq-SPh-cyclohexanone in reduction with $NaBH_4$ in MeOH, the axial selectivity of 4-eq-Cl-*trans*-1-decalone is reported at 71%.[5] The slightly larger selectivity with $Na(CN)BH_4$ may be a consequence of tighter cation-carbonyl complexation, protonation in this case. Otherwise symmetric to a plane, the molecules must lose this symmetry on cation-complexation and, hence, the differences in the bond angles A1 and A2.

The 4-eq-SPh-cyclohexanone was prepared from cyclohexane-1,4-dione as shown in Scheme 1. The spectral

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[1] Jeyaraj, D. A.; Yadav, A.; Yadav, V. K. *Tetrahedron Lett.* **1997**, *38*, 4483. Jeyaraj, D. A.; Yadav, V. K. *Tetrahedron Lett.* **1997**, *38*, 6095. For an excellent review giving decent description of several prominent theoretical models and the related experimental results, see: Gung, B. W. *Tetrahedron* **1996**, *52*, 5263. For a very recent work, see: Tomada, S.; Senju, T. *Tetrahedron* **1997**, *53*, 9057.

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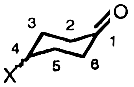
Table 1. Relevant Torsion Angles (Deg) and Angles (Deg) (D1 = C6C1OC2; D2 = OC1C2C3; D3 = OC1C6C5; A1 = OC1C2; A2 = OC1C6)

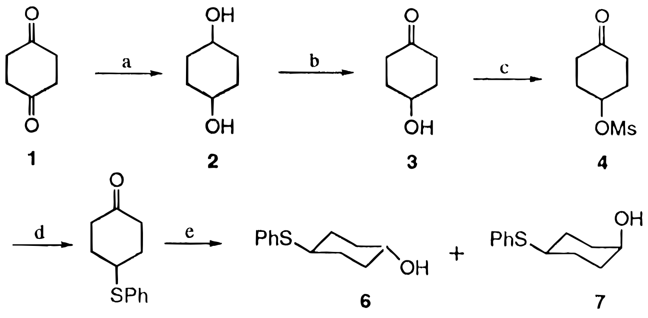


cyclohexanone
D1 = 180.75; D2 = 132.22; D3 = 132.09; A1 = 121.89; A2 = 121.90
(D1 = 179.47; D2 = 131.53 D3 = 131.53; A1 = 122.31; A2 = 122.31)[a]
4-ax-Cl-cyclohexanone
D1 = 180.72; D2 = 132.16; D3 = 131.92; A1 = 121.92; A2 = 121.94
(D1 = 179.16; D2 = 132.42; D3 = 132.42; A1 = 122.28; A2 = 122.28)[a]
4-ax-Cl-cyclohexanone; O-protonated
D1 = 183.54; D2 = 148.92; D3 = 148.40; A1 = 115.92; A2 = 121.68
(D1 = 176.73; D2 = 145.36; D3 = 145.12; A1 = 116.60; A2 = 121.98)[a]
4-ax-Cl-cyclohexanone; O-lithiated
D1 = 182.93; D2 = 141.76; D3 = 141.80; A1 = 120.55; A2 = 120.59
4-ax-F-cyclohexanone
D1 = 180.96; D2 = 132.17; D3 = 132.45; A1 = 121.96; A2 = 121.93
(D1 = 179.31; D2 = 131.52; D3 = 131.52; A1 = 122.39; A2 = 122.39)[a]
4-ax-F-cyclohexanone; O-protonated
D1 = 183.56; D2 = 147.51; D3 = 146.72; A1 = 116.03; A2 = 121.80
(D1 = 177.06; D2 = 142.92; D3 = 142.59; A1 = 116.78; A2 = 122.16)[a]
4-ax-F-cyclohexanone; O-lithiated
D1 = 183.78; D2 = 143.79; D3 = 143.93; A1 = 120.45; A2 = 120.46
4-ax-OH-cyclohexanone
D1 = 180.84; D2 = 132.60; D3 = 132.54; A1 = 121.71; A2 = 122.12
4-ax-OH-cyclohexanone; O-protonated
D1 = 183.06; D2 = 147.13; D3 = 145.71; A1 = 116.03; A2 = 121.76
4-ax-SH-cyclohexanone
D1 = 180.74; D2 = 132.53; D3 = 132.15; A1 = 121.90; A2 = 121.91
(D1 = 179.21; D2 = 132.33; D3 = 132.35; A1 = 122.35; A2 = 122.25)[a]
4-ax-SH-cyclohexanone; O-protonated
D1 = 182.85; D2 = 146.80; D3 = 146.54; A1 = 116.07; A2 = 121.69
(D1 = 177.12; D2 = 143.66; D3 = 143.86; A1 = 112.25; A2 = 121.97)[a]

cyclohexanone; protonated
D1 = 179.60; D2 = 132.96; D3 = 132.94; A1 = 122.36; A2 = 121.90
(D1 = 179.94; D2 = 132.77; D3 = 132.88; A1 = 122.51; A2 = 117.18)[a]
4-eq-Cl-cyclohexanone
D1 = 180.57; D2 = 132.13; D3 = 132.03; A1 = 122.00; A2 = 122.00
(D1 = 179.03; D2 = 132.52; D3 = 132.52; A1 = 122.39; A2=122.39)[a]
4-eq-Cl-cyclohexanone; O-protonated
D1 = 181.48; D2 = 138.51; D3 = 138.42; A1 = 116.62; A2 = 122.45
(D1 = 178.38; D2 = 137.48; D3 = 137.53; A1 = 117.14; A2 = 122.59)[a]
4-eq-Cl-cyclohexanone; O-lithiated
D1 = 180.86; D2 = 133.65; D3 = 133.78; A1 = 121.20; A2 = 121.20
4-eq-F-cyclohexanone
D1 = 180.94; D2 = 133.00; D3 = 132.85; A1 = 121.97; A2 = 121.98
(D1 = 178.96; D2 = 133.04; D3 = 133.03; A1 = 122.34; A2 = 122.34)[a]
4-eq-F-cyclohexanone; O-protonated
D1 = 182.60; D2 = 142.14; D3 = 142.32; A1 = 116.47; A2 = 122.26
(D1 = 177.80; D2 = 139.17; D3 = 139.22; A1 = 117.06; A2 = 122.50)[a]
4-eq-F-cyclohexanone; O-lithiated
D1 = 181.04; D2 = 134.37; D3 = 134.07; A1 = 121.18; A2 = 121.18
4-eq-OH-cyclohexanone
D1 = 180.68; D2 = 132.16; D3 = 132.20; A1 = 122.00; A2 = 122.00
4-eq-OH-cyclohexanone; O-protonated
D1 = 182.08; D2 = 141.73; D3 = 140.95; A1 = 116.41; A2 = 122.20
4-eq-SH-cyclohexanone
D1 = 180.62; D2 = 131.95; D3 = 132.06; A1 = 122.01; A2 = 122.00
(D1 = 179.42; D2 = 131.60; D3 = 131.60; A1 = 122.43; A2 = 122.43)[a]
4-eq-SH-cyclohexanone; O-protonated
D1 = 179.53; D2 = 133.20; D3 = 133.00; A1 = 116.82; A2 = 122.56
(D1 = 179.05; D2 = 135.96; D3 = 135.89; A1 = 117.18; A2 = 122.55)[a]

[a] The numbers in parentheses are obtained from calculations at the 6-31G (d) level of theory using the Gaussian 94 program (Frisch, M. J. et al. Gaussian Inc., 1995).

Scheme 1[a]



[a] Reagents: (a) LAH, Et_2O; (b) Jones' reagent; (c) MsCl, Et_3N, CH_2Cl_2, 0 °C; (d) PhSNa, THF, 0 °C to rt, 4 h; (e) reducing reagent, solvent, 0 °C to rt.

Table 2. Net Atomic Charges on Selected Atoms in 4-Substituted Cyclohexanones (a = axial, e = equatorial)

	charge (e)					
X	O	C1	C2	C3	C4	X
H	−0.545	0.496	−0.394	−0.315	−0.310	
	−0.530	0.536	−0.410	−0.332	−0.321	a
H−H$^+$	−0.630	0.653	−0.460	−0.323	−0.335	
	−0.559	0.600	−0.459	−0.349	−0.347	a
F(a)	−0.541	0.488	−0.396	−0.352	0.245	−0.479
	−0.527	0.532	−0.419	−0.373	0.264	−0.430[a]
F(a)-H$^+$	−0.634	0.653	−0.468	−0.352	0.223	−0.461
	−0.562	0.599	−0.449	−0.389	0.241	−0.412[a]
F(e)	−0.533	0.499	−0.417	−0.352	0.279	−0.475
	−0.522	0.542	−0.432	−0.379	0.302	−0.425[a]
F(e)-H$^+$	−0.628	0.662	−0.485	−0.358	0.279	−0.437
	−0.556	0.607	−0.462	−0.403	0.304	−0.388[a]
Cl(a)	−0.537	0.491	−0.398	−0.315	−0.312	−0.117
	−0.525	0.535	−0.418	−0.335	−0.248	−0.118[a]
Cl(a)-H$^+$	−0.633	0.659	−0.475	−0.308	−0.367	−0.029
	−0.561	0.604	−0.451	−0.349	−0.284	−0.048[a]
Cl(e)	−0.531	0.498	−0.407	−0.297	−0.343	−0.074
	−0.520	0.540	−0.423	−0.324	−0.262	−0.090[a]
Cl(e)-H$^+$	−0.627	0.658	−0.470	−0.297	−0.406	0.054
	−0.556	0.604	−0.451	−0.345	−0.296	0.011[a]
SH(a)	−0.542	0.496	−0.395	−0.302	−0.420	0.024
	−0.528	0.538	−0.414	−0.330	−0.317	−0.069[a]
SH(a)-H$^+$	−0.634	0.661	−0.446	−0.306	−0.465	0.054
	−0.562	0.606	−0.446	−0.345	−0.350	−0.039[a]
SH(e)	−0.537	0.496	−0.400	−0.289	−0.449	0.058
	−0.524	0.538	−0.416	−0.319	−0.339	−0.042[a]
SH(e)-H$^+$	−0.628	0.654	−0.444	−0.300	−0.496	0.162
	−0.558	0.602	−0.445	−0.339	−0.370	0.045[a]

[a] The numbers were obtained from calculations at the 6-31G (d) level of theory using the Gaussian 94 program (Frisch, M. J. et al. Gaussian Inc., 1995).

characteristics of the diol **2** and the keto alcohol **3** were in accord with the literature.[6] The oxidation of **2** to **3** was accomplished following the literature.[6] The mesylate **4** was reacted with the sodium salt of thiophenol in THF at 0 °C to rt for 4 h to furnish the desired 4-eq-SPh-cyclohexanone whose ^{1}H characteristics were as those reported in the literature.[7] The hydrogen on the carbinol carbon in the reduced products **6**/**7** resonated at δ 3.70−3.62 (well-resolved heptet) and 3.87−3.84 (ill-resolved multiplet) when it occupied axial and equatorial positions, respectively. Likewise, the C4-H resonated at δ 3.07−2.98 (m) and 3.30−3.25 (m) in the above equatorial and axial alcohols, respectively.

The net atomic charges on selected atoms are collected in Table 2. Four points become immediately obvious: (i) the carbonyl carbon becomes more electron-deficient on complexation, its magnitude being more or less the same irrespective of whether the substituent is axial or equato-

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[7] Cohen, T.; Yu, L.-C.; Daniewski *J. Org. Chem.* **1985**, *50*, 4596.

rial, (ii) C4 in all 4-fluoro derivatives is moderately positively charged whereas the same in the 4-Cl derivatives carries appreciable negative charge, (iii) the fluorine atom in all the fluorinated derivatives is substantially negatively charged, whereas the respective chlorine atom is either very poorly negatively charged or it is near neutral, and (iv) the charge distribution for the C−S bond is similar to that of the C−Cl bond. The magnitudes of the charges on C4 and the heteroatom on it clearly indicate that the polarity of the C−Cl and C−S bonds is opposite to that of the C−F bond. That the Cl−C bond is electron-donating finds support from a recent report of Alkorta et al.[8] Thus, the electron-donating Cl(a)−C4 bond may be expected to raise the electron density on the face axial for carbonyl. This may further stabilize, by interaction through space, the axially oriented p orbital on the carbonyl carbon. Though this interaction is likely to be weak for the long distance between the two interacting orbitals, a somewhat enhanced axial selectivity of 4-ax-Cl-cyclohexanone in comparison to that of 4-ax-F-cyclohexanone may, however, be predicted. This finds decent experimental support.[5] The electron-attracting C−F bond in the 4-eq-F-cyclohexanone renders the C2−C3 and C5−C6 ring bonds electron-deficient, which, in turn and in cooperation with the electron-donating C2−H(a) and C6−H(a) bonds, would enhance further the axial-orientating ability of the p orbital on the carbonyl carbon. On the contrary, the electron-donating character of the C−Cl bond in 4-eq-Cl-cyclohexanone would render the C2−C3 and C5−C6 bonds slightly more electron-rich than those in the parent unsubstituted cyclohexanone and reduce, thereby, the axial-orienting propensity of the carbonyl p orbital. A reduction in the level of axial attack in 4-eq-Cl-cyclohexanone in comparison to the 4-eq-F-cyclohexanone may, therefore, result. This is in line with the larger torsion angle changes in the former on protonation. The contribution of sulfur is fairly similar to that of Cl. The differential C−F/C−Cl polarity features are likely to contribute significantly to the facial discrimination in 2-ax-halocyclohexanones. A reversal in facial selectivity in such cases appears iminent.[9]

The study of C2−H and C3−H bond lengths (Table 3), both before and after protonation, is also revealing. Whereas both the C3−H(a) and C3−H(e) bonds have shortened on protonation, on one hand, both the C2−H(a) and the C2−H(e) bonds are enlarged, on the other hand. Since the C2−H bonds are on the carbon adjacent to the carbonyl function, they are likely to influence the carbonyl chemistry much more than any other C−H bond elsewhere in the molecule. From the data on the 6-31G level, the following two points emerge:

(i) The elongation in the C2−H(a) bond on protonation is more pronounced than the elongation in the C2−H(e) bond. This is to suggest further improved interaction of the former with the carbonyl function on cation complexation. The p orbital on the carbonyl carbon is enabled to develop more on the axial face for favorable stereoelectronic effects and, hence, the increased axial attack of nucleophiles.

(ii) On protonation, the elongation in C2−H(a) in 4-ax-species is 1.5−6.0 times the elongation in the same in species with 4-eq-substitution and almost 10 times the elongation in the unsubstituted cyclohexanone. These, when coupled with the observation above, may be taken to reveal that the TS for axial attack in a 4-ax-substituted cyclohexanone must be of lower barrier than the TS for axial attack on a 4-eq-substituted cyclohexanone and further that the 4-ax-substituted cyclohexanones must react faster than cyclohexanone itself. Both the revealations are in accord of experiments.[5,10]

Table 3. C2−H2(a) and C2−H2(e) Bond Lengths (Å) in 4-Substituted Cyclohexanones (a = Axial, e = Equatorial)

X	bond lengths (Å)			
	C2−H2(a)	C2−H2(e)	C3−H3(a)	C3−H3(e)
H	1.0887	1.0816	1.0868	1.0843
	1.0895	1.0826	1.0878	1.0854[a]
H−H^{+}	1.0893	1.0831	1.0843	1.0810
	1.0894	1.0844	1.0853	1.0819[a]
F(a)	1.0859	1.0810	1.0859	1.0825
	1.0869	1.0822	1.0870	1.0843[a]
F(a)-H^{+}	1.0913	1.0833	1.0832	1.0802
	1.0905	1.0813	1.0846	1.0816[a]
F(a)-Li^{+}	1.0884	1.0810	1.0845	1.0810
F(eq)	1.0888	1.0806	1.0847	1.0825
	1.0895	1.0819	1.0865	1.0843[a]
F(eq)-H^{+}	1.0922	1.0831	1.0831	1.0804
F(eq)-Li^{+}	1.0893	1.0803	1.0841	1.0810
Cl(ax)	1.0860	1.0811	1.0881	1.0813
	1.0869	1.0823	1.0882	1.0830[a]
Cl(ax)-H^{+}	1.0919	1.0838	1.0853	1.0797
	1.0911	1.0818	1.0857	1.0808[a]
Cl(ax)-Li^{+}	1.0884	1.0811	1.0867	1.0803
Cl(eq)	1.0884	1.0810	1.0841	1.0815
	1.0892	1.0821	1.0856	1.0831[a]
Cl(eq)-H^{+}	1.0909	1.0832	1.0829	1.0799
	1.0910	1.0814	1.0842	1.0811[a]
Cl(eq)-Li^{+}	1.0889	1.0808	1.0837	1.0805
SH(a)	1.0861	1.0814	1.0880	1.0836
	1.0868	1.0825	1.0885	1.0849[a]
SH(a)-H^{+}	1.0919	1.0808	1.0858	1.0809
	1.0908	1.0817	1.0862	1.0819[a]
SH(e)	1.0884	1.0814	1.0865	1.0819
	1.0893	1.0825	1.0876	1.0832[a]
SH(e)-H^{+}	1.0898	1.0797	1.0847	1.0800
	1.0905	1.0815	1.0856	1.0809[a]

[a] The numbers were obtained from calculations at the 6-31G (d) level of theory using the Gaussian 94 program (Frisch, M. J. et al. Gaussian Inc., 1995).

Shi and Boyd[4] have computed the electron-depletion on the two faces of the carbonyl function in 4-halocyclohexanones. Because the slightly enhanced depletion on the equatorial face was to support equatorial attack in contradiction to the experimental results, these authors preferred to consider the two faces "quite similar". Agreed that the (uncomplexed) molecules in question have plane of symmetry, the environment in the immediate neighborhood of the carbonyl and, hence, its two faces can never be the same for the ring arrangement of nuclei. The C2−H(a) and C6−H(a) bonds must interact with the carbonyl π-bond to perturb its charge distribution for their antiperilanar relationship and, thus, accommodate their known higher acidity and faster exchangeability than those of the equatorial hydrogens. Consequently, the depletion of electron density must be more from the axial face than that from the alternate equatorial direction. This interaction is, in fact, typical of such a spatial arrangement observed in 2-ax-X-cyclohexanones (X = Cl,

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(8) Alkorta, I.; Rozas, I.; Elguero, J. *J. Org. Chem.* **1997**, *62*, 4687.

(9) Such a facial reversal has indeed been computed by us in a separate study. The results will be reported in due course.

(10) Kwart, H.; Takeshita, T. *J. Am. Chem. Soc.* **1962**, *84*, 2833.

Br, OH, OAc) where the UV λ_{max} shift to higher values by 10−30 nm.[11]

Shi and Boyd[4] have implicated, at least in part, the electrostatic repulsion between the attacking nucleophile and the C2−H(a) bond in the equatorial TS to explain its larger energy barrier compared to that of the axial TS where such a repulsion does not exist. They have computed the C2−H(a) bond to be more electron rich than the C2−C3 bond. As stated above, the C2−H(a) bond is geometrically parallel to the carbonyl π-plane, and hence, its electron density must be hyperconjugatively delocalized into the latter to render it actually electron defficient, more so on cation complexation, as we have observed in the present study. We, therefore, disfavor Boyd's above contention of electrostatic repulsion. The electron-deprived orbital on the carbonyl carbon that has oriented axial and the resultant flattening, both on cation complexation, may be reasons enough to accommodate the difference in barriers.[12]

We conclude that the torsion angle changes[13] around the carbonyl carbon of 4-substituted cyclohexanones after cation complexation predict well the facial discrimination in reactions with nucleophiles. The hyperconjugative electron donations from C2−H(a) and C6−H(a) to the electron-depleted p orbital on the carbonyl carbon make them electron-defficient, and hence, any electrostatic repulsion for a nucleophile in an equatorial attack, as proposed by Shi and Boyd,[4] can be ruled out safely. The axial substituents exert their influence on diastereoselectivity primarily through the field effects. The present approach of facial prediction is rapid, reliable, and practical. It avoids the often painful TS calculations.[14]

Experimental Section

^1H NMR spectra were measured on a Bruker DRX-300 spectrometer. All chromatographic separations and filtrations were performed over silica gel (100−200 mesh) using petroleum ether (bp 60−80 °C) and EtOAc mixtures as the eluants. The other general experimental remarks are as reported elsewhere.[15]

4-(Mesyloxy)cyclohexanone (4). To a solution of 4-hydroxycyclohexanone (0.104 g, 1.0 mmol) in dry CH_2Cl_2 (4 mL) at 0 °C were added Et_3N (1.3 mmol, 0.18 mL) and MsCl (1.2 mmol, 0.1 mL). The reaction mixture was stirred for 30 min for the reaction to complete (TLC). This was diluted with CH_2Cl_2 (10 mL) and washed with water (2 × 5 mL) and brine (1 × 5 mL). Drying and solvent removal furnished the crude mesylate in quantitative yield.

4-eq-SPh-cyclohexanone (5). To a solution of the above crude mesylate in THF (5 mL) was added PhSNa (0.198 g, 1.5 mmol) and the resultant mixture stirred at room temperature for 4 h. The solvent was evaporated under reduced pressure and the residue extracted with EtOAc (2 × 5 mL). The EtOAC was removed and the residue chromatographed to isolate pure **5** in >75% yield.

Reduction of 5 with LAH. LAH (8 mg, 0.2 mmol) was added to a solution of **5** (21 mg, 0.1 mmol) in Et_2O (3 mL) at 0 °C, and the contents were stirred until the reaction was complete (2 h). Water (2−3 drops) was added and the contents stirred for 5 min. This was dried with Na_2SO_4 and filtered. Evaporation of the solvent and filtration of the residue through a short silica gel column furnished a mixture of the equatorial and axial alcohols in 55:45 proportion in quantitative yield.

Reduction of 5 with $NaBH_4$. To a solution of **5** (21 mg, 0.1 mmol) in MeOH (3 mL) was added $NaBH_4$ (8 mg, 0.2 mmol). The contents were stirred for 30 min when the solvent was removed under reduced pressure on a rotovap. Saturated aqueous NH_4Cl (2 mL) was added, and the contents were stirred and extracted with EtOAc (3 × 3 mL). The combined EtOAc extract was dried and the solvent removed. The residue was filtered through a short bed of silica gel to isolate a 61:39 mixture of the equatorial and axial alcohols, respectively.

Reduction of 5 with $Na(CN)BH_3$. To a solution of **5** (21 mg, 0.1 mmol) in MeOH (3 mL) were added few drops of 2 N aqueous HCl to achieve a pH of 1.0. $Na(CN)BH_3$ (13 mg, 0.2 mmol) was added, and the contents were stirred at room temperature for 30 min. The methanol was removed and the residue extracted with Et_2O (3 × 5 mL). The combined Et_2O extract was washed with saturated aqueous $NaHCO_3$ and dried. The Et_2O was removed and the residue filtered through a short bed of silica gel to obtain a 64:36 mixture of the equatorial and axial alcohols, respectively.

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