be the subject of future discussions.[6]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the ACS, for support of this research.

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(6) Theoretical work pertinent to the chemistry reported here has been reported by the following: (a) Kahn, S. D.; Pau, C. F.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7396. (b) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. (c) Burgess, E. M.; Liotta, C. L. *J. Org. Chem.* **1981**, *46*, 1703. (d) Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328.

Effects of Sterically Remote Substituents on π-Facial Stereoselectivity in Additions to Methylenecyclohexanes

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Received February 23, 1987
Revised Manuscript Received July 22, 1987

Changes in electronic properties of a stereogenic center without accompanying changes in steric interactions at that site offer an important method to probe stereoelectronic effects. Recently the first comprehensive study of the impact of electronic modifications of the inducing center on stereoselectivity of nucleophile capture by either a carbonyl group or a carbonium ion has been reported by le Noble and co-workers.[1] By using the sterically nonbiased system of 5-substituted 2-adamantanones, these researchers addressed the fundamental problem of the nature and importance of hyperconjugative σ assistance in such reactions. The surprisingly large effects of remote substitution observed in these studies are consistent with the model of Cieplak.[2]

We have been interested in exploitation of the same approach in an attempt to address basic questions raised by theories of π-facial stereoselection. We were particularly intrigued by the generality of stereoelectronic control in reactions of diverse mechanisms and the importance of σ assistance in sterically biased systems. For this purpose, we have carried out an investigation of various reactions of methylenecyclohexanes substituted at C(-3) by groups of varying electronegativity and large steric bulk.

A series of cyclohexanones were converted to the methylenecyclohexanes by using Corey's procedure[3] for the Wittig reaction. The reagents chosen for study with these substrates were those which gave products readily transformable to methyl carbinols allowing straightforward structure assignments[4] (Scheme I).

Reaction of the exocyclic methylenes with mercuric acetate in water effected oxymercuration of the alkene.[5] Sodium borohydride in 3 N NaOH resulted in reductive demercuration giving the methyl carbinols.[6] Oxidation of the methylenecyclohexanes with *m*-chloroperoxybenzoic acid (*m*CPBA) afforded the epoxides.

Scheme I

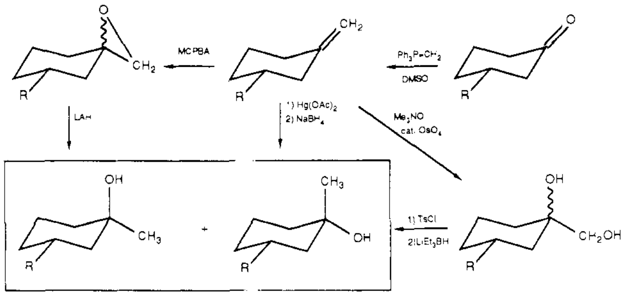
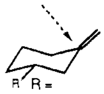


Table I. Percentage of Axial Attack in Reactions of C-3 Substituted Methylenecyclohexanes

		%		
entry	R =	$\mathbf{1}^h$ (0 °C)	$\mathbf{2}^i$ (0 °C)	$\mathbf{3}^j$ (25 °C)
a	$Si(CH_3)_3$	40	52	7
b	*t*-Bu	58,[b] 58[c]	60[d]	
c	H[a]	69,[b] 70[e]	69[f]	14[g]
d	C_6H_5	67	70	15
e	C_6H_4–CF_3-*p*	70	75	14
f	CF_3	92		

[a] The 4-*tert*-butyl derivative is used as the surrogate for the 3-*H* derivative. [b] Reference 5c. [c] Jasserand, D.; Granger, R.; Girard, J. P.; Chapat, J.-P. *C. R. Acad. Sci.* **1971**, *272C*, 1693. [d] Sevin, A.; Cense, J. M. *Bull. Soc. Chim. Fr.* **1974**, 963. [e] Jasserand, D.; Girard, J. P.; Rossi, J. C.; Granger, R. *Tetrahedron* **1976**, *32*, 1535. [f] Carlson, R. G.; Behn, N. S. *J. Org. Chem.* **1967**, *32*, 1363. [g] Patrick, D. W.; Truesdale, L. K.; Biller, S. A.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2628. [h] $Hg(OAc)_2$, H_2O. [i] *m*CPBA, CH_2Cl_2 [j] OsO_4/Me_3NO, THF/H_2O.

The mixtures of epoxides were converted into the methyl carbinols by reduction with lithium aluminum hydride.

Catalytic osmylation[7] of the methylenecyclohexanes afforded mixtures of diastereomeric vic diols. The assignments of the stereoisomers were assured by conversion of the diols to the methyl carbinols. This was accomplished by a two-step procedure. The primary alcohol was selectively tosylated, and the tosylate was removed by reduction with lithium triethylborohydride.

Oxymercuration occurs through the intervention of a mercurinium ion, apparently formed in a readily reversible process; CO bond formation (oxygen nucleophile attack) is the rate-limiting and product-determining step.[8] Peracid epoxidation[9] and cis hydroxylation with osmium tetroxide[10] are considered to occur by one step, irreversible synchronous additions to the alkene. Peracid epoxidations, in particular, are recognized to be electrophilic in nature; rates correlate with the nucleophilicity of the alkene.

Our results are presented in Table I, where C(-3) groups are listed according to the Charton's preferred σ_I values.[11] The ratios of diastereomeric products for 4-*tert*-butylmethylenecyclohexane are used as the surrogate reference point for the hypothetical 3-H substituted compounds. In each reaction series there is an increase in the proportion of axial attack with increase in the electronegativity of the remote 3-equatorial substituent; indeed, a plot of the logarithm of the ratio of isomers versus σ_I for five oxymercurations where the σ_I values are available reveals a reasonable

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(1) Cheung, C. K.; Tseng, L. T.; Lin, M.-H.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598.

(2) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

(3) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

(4) The diastereomers which eluted slower on silica gel were assigned to have equatorial hydroxyls (Barton, D. H. R.; Cookson, R. C. *Quart. Rev.* (*London*) **1956**, *10*, 44.). The opposite diastereomers with axial hydroxyls showed increased propensities toward loss of water from the parent ion in mass spectrometry (Green, M. M. *Mass Spectrom. Stereochem.* **1975**, 35.). In ^{13}C NMR spectroscopy the compounds assigned as axial hydroxyl diastereomers exhibited the quaternary carbinol carbon signal at higher fields (Senda, Y.; Ishiyana, J.; Imaizumi, S. *Tetrahedron* **1975**, *31*, 1601. Wilson, N. K.; Stothers, J. B. *Topics Stereochem.* **1973**, *8*, 1.).

(5) (a) Brown, H. C.; Geoghegan, D. J., Jr. *J. Org. Chem.* **1970**, *35*, 1844. (b) Brown, H. C.; Kurek, J. T.; Rei, M.-H.; Thompson, K. C. *J. Org. Chem.* **1984**, *49*, 2551. (c) Senda, Y.; Kamiyama, S.; Imaizami, S. *J. Chem. Soc., Perkin Trans. 1* **1978**, 530.

(6) Bordwell, F. G.; Douglass, M. L. *J. Am. Chem. Soc.* **1966**, *88*, 993.

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(9) Lang, T. J.; Wolber, G. J.; Bach, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 3275.

(10) Schroder, M. *Chem. Rev.* **1980**, *80*, 187.

(11) Charton, M. *J. Org. Chem.* **1964**, *29*, 1222.

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linear relation (correlation coefficient of 0.94).

Thus, it is for the first time demonstrated[12] that the remote electronegative substitution of a stereogenic center can have the same significant effect on the sense of π-facial diastereoselection both in nucleophilic and electrophilic reactions.[13,14] This result constitutes a challenging test for the theories of stereoelectronic control in π-facial diastereoselection. Several propositions that explicitly deal with the nature of such a control in cyclohexane-related systems have been advanced over the last 20 years, most notably those of Felkin,[15] Klein,[16] Ashby,[17] Nguyen,[18] and Cieplak.[2] It is interesting to notice that except for the last one, these models fail to predict or explain the effects of remote [C(-3) or C(-4)] electronegative substitution of the cyclohexane ring on stereochemistry of cyclohexanone and methylenecyclohexane reactions.

Klein postulated that nucleophiles and electrophiles would display opposite preferences in a given system of 1,2-diastereoselection in apparent disagreement with the accumulated experimental data.[19] Felkin et al. and Nguyen et al. did not attribute any role in stereoselection to the interactions involving the ring CC bonds. In fact, Felkin et al.[15b] proposed that the preferred "axial" epoxidation of unhindered exocyclic olefins by peracids results from "equatorial" torsional strain, due to repulsion of the exocyclic methylene and the equatorial C(2)–H and C(6)–H bonds; obviously, no eclipsing interactions involving the incipient bond can occur in the transition state for such a reaction. The model of Nguyen et al.[18b] can be generalized to include ring CC interactions, but it predicts, then, an increase in the proportion of equatorial nucleophilic attack with an increase in the electronegativity of a remote 3-equatorial substituent in opposition to the experimental results. In contrast, the findings reported here appear to be consistent with the Cieplak postulate that the stereochemistry of reactions of cyclohexanones, methylenecyclohexanes, thianes, etc. could be controlled by the same orbital interactions regardless of the reaction mechanism.[2] The explanation of stereoselection in reactions of the cyclohexane related system based on the Cieplak proportion[2] is as follows. During axial attack of a reagent, the vacant orbital $\sigma^*_\ddagger$ that develops along with the formation of the incipient bond interacts with the filled orbitals of the C(2)–H and C(6)–H bonds. During equatorial attack, the $\sigma^*_\ddagger$ orbital interacts with the filled orbitals of the ring bonds C(2)–C(3) and C(5)–C(6). The effect of steric hindrance favors, obviously, the equatorial attack. The effect of hyperconjugative σ assistance, however, favors the axial attack, because the CH bonds are better donors than the CC bonds,[20] and consequently the σ_{CH}, $\sigma^*_\ddagger$ stabilization energy is greater than the σ_{CC}, $\sigma^*_\ddagger$ stabilization energy. If the energy level of the $\sigma^*_\ddagger$ orbital is sufficiently low, that is, if the electron affinity of the transition state is sufficiently high, the difference in σ_{CH} and σ_{CC} hyperconjugative assistance will offset the steric hindrance. It should be stressed that this must be true for any reaction—polar addition (*nucleophilic or electrophilic*!), radical addition or recombination, cycloaddition, etc.—provided the transition state is electron deficient.

This model predicts that the electron-withdrawing substitution at the C-(3), which decreases donor power of the ring bonds, will decrease σ_{CC} assistance of the equatorial transition state and, thereby, increase the percentage of the axial approach. The findings reported here appear consistent with the Cieplak model but are in opposition to those predicted by application of the Felkin,[15] Klein,[16] Ashley,[17] and Nguyen[18] models.

Acknowledgment is made to the donors of the Petroleum Research Fund administrated by the American Chemical Society and to the National Science Foundation (CHE86-07956) for support of the work at Wayne State University.

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[12] Srivastava and le Noble have recently reached the same conclusions; see the preceding communication.

[13] For the reports on the examination of such effects in reactions of nucleophilic additions to ketones, see: ref 1 and Danishefsky et al. (Danishefsky, S. J.; Langer, M. *J. Org. Chem.* **1985**, *50*, 3672.).

[14] Several earlier studied that pioneered this approach were flawed for various reasons: (a) Agami, C.; Kazakos, A.; Levisalles, J. *Tetrahedron Lett.* **1975**, *16*, 2035. (The C-3 substituents are axial.) (b) Moreau, G. *Bull. Soc. Chim. Fr.* **1972**, 2814. (The use of 2-*t*-Bu group to lock cyclohexanone conformation has been questioned, see: references in Cotterill, W. D.; Robinson, M. J. T. *Tetrahedron* **1964**, *20*, 765, 777.) (c) Giddings, M. R.; Hudec, J. *Can. J. Chem.* **1981**, *59*, 459. (Wrong assignment of the diasteromer structures, see ref 1.)

[15] (a) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, *9*, 2199. (b) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, *9*, 2203.

[16] (a) Klein, J. *Tetrahedron Lett.* **1973**, *14*, 4307. (b) Klein, J. *Tetrahedron* **1974**, *30*, 3349.

[17] Ashby, E. C.; Boone, J. R. *J. Org. Chem.* **1976**, *41*, 2890. (Predictions of Klein's and Ashby's models are identical.)

[18] Nguyen, T. A.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61. (b) Huet, J.; Maroni-Barnaud, Y.; Nguyen, T. A.; Seyden-Penne, J. *Tetrahedron Lett.* **1976**, *17*, 159.

[19] Agami, Kazakos, and Levisalles (ref 14a) were first to suggest that the effect of ring substitution on the stereochemistry of hydride reduction of cyclohexanones refutes the Klein model.

[20] This assumption is consistent with a wealth of data on the properties of the axial and equatorial bonds and on conformational equilibria of cyclohexane derivatives, see ref 2. See, also: Brown, H. C.; Periasamy, M.; Perumal, P. T. *J. Org. Chem.* **1984**, *49*, 2754 (for a recent appraisal of the Baker–Nathan order problem). Edlund, U. *Org. Magn. Reson.* **1978**, *11*, 516 (for a demonstration of the Baker–Nathan order in the ground state).

Crystal Structure of the Complex 5-Phenyladamantan-2-one–Pentachloroantimony. Hyperconjugative Effects in an Activated Ketone

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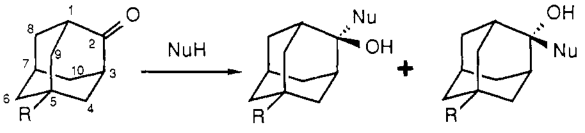
Received May 8, 1987

The addition of a nucleophile to a carbonyl group is one of the most important C–C bond-forming processes. Many efforts have been made to explain and predict the diastereoselectivity of nucleophilic attack.[1] The importance of steric factors is generally accepted, but the nature of electronic interaction between the carbonyl group and adjacent groups is controversial.[2-4] LeNoble et al.[5] have recently shown that nucleophilic addition to adamantan-2-ones with substituents at C5 of **1** must be controlled by electronic factors (steric factors being practically equal for both faces of the carbonyl group). Electron-withdrawing substituents favor syn approach (product *trans*-**2**) and electron-donating groups lead to anti approach (product *cis*-**2**). Hyperconjugative interactions in **1** are described by resonance formulas of type **1′** and **1*** in the "first sphere" and of type **1″** and **1**** in the "second sphere". If the C5–R bond is a better donor than the C7–H bond, then the primed resonance formulas are more important than the starred ones. If C7–H is a better donor than C5–R, then the starred resonance formulas have higher weights. Finally, σ participation[5] can be described by resonance formulas of type $\mathbf{1}^\dagger$ (cf. the Wagner–Meerwein rearrangement[6]). The contribution



(1)

1 *cis*-**2** *trans*-**2**

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