dilute phosphoric acid and extracted with ether, which was washed with aqueous carbonate buffer ($NaHCO_3$-Na_2CO_3, 1:1) and then with water. Iodometry indicates 40-80% yields of peroxide formation. The crude peroxide **1** was purified by passing through a Florisil column using *n*-hexane, *n*-hexane-CH_2Cl_2 (3:1), and then CH_2Cl_2. Elution of the peroxide was easily monitored by iodometry. Evaporation of CH_2Cl_2 under slightly reduced pressure afforded α-hydroperoxy nitrile in 20-50% yields, some of which (**1b-d**) could be crystallized by standing in a refrigerator for 2-10 days and washing with *n*-hexane. Melting points are listed in Table IV.

Attempted preparations of **1** by the reaction at −20 °C or in dimethylformamide-monoglyme at −60 °C were unsuccessful (titrated yield <2%). The washing with aqueous carbonate buffer was effective in decomposing contaminated cyanohydrin.

The purity of peroxide **1** was determined iodometrically in MeOH-AcOH-H_2O (2:1:1).[6] The structure of $R_1R_2C(OOH)CN$ was established by IR and NMR spectra (Table IV), and by the KI reduction to cyanohydrins.

Rates and Products. The rate of base-catalyzed decomposition of **1** was followed up to 80% conversion by iodometry[6] and found to be first order in **1**. The reproducibility of the k_{obsd} value was adequate (within ±5%) in the presence of EDTA, although its absence did not affect the value in most cases.

Organic products were determined by GLC analysis using propiophenone or biphenyl as an internal standard. Cyanide ion could not be detected even by benzidine-cupric acetate test.[9] Quantitative formation of cyanate ion was reported for the reaction of **1a**.[4]

Chemiluminescence. Chemiluminescence was monitored by a Hitachi MPF-2A fluorescence spectrophotometer using a 3-mL solution in a 4-mL quartz cell. The initial intensity at time zero was determined from the plot of *I* vs. time. The quantum yields were calculated according to the reported method[7,33] using the equation in footnote *d*, Table III. The incident light from a Xe arc was determined by ferrioxalate actinometry.[34]

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References and Notes

(1) (a) M. S. Kharasch and G. Sosnovsky, *Tetrahedron*, **3**, 97 (1958); (b) H. G. Aurich, *Tetrahedron Lett.*, 659 (1964).

(2) S. J. Selikson and D. S. Watt, *J. Org. Chem.*, **40**, 267 (1975).

(3) Netherlands Appl. Patent 6 406 577; *Chem. Abstr.*, **64**, 15807 (1966).

(4) L. Dulog and W. Vogt, *Tetrahedron Lett.*, 5169 (1966).

(5) (a) R. Curci and J. O. Edwards, "Organic Peroxides", Vol. 1, D. Swern, Ed., Wiley, New York, N.Y., 1970, p 256; (b) G. Sosnovsky and E. H. Zaret, *ibid.*, p 531.

(6) Y. Sawaki and Y. Ogata, *J. Am. Chem. Soc.*, **97**, 6983 (1975).

(7) Y. Sawaki and Y. Ogata, *J. Org. Chem.*, **42**, 40 (1977).

(8) W. H. Richardson and V. F. Hodge, *J. Am. Chem. Soc.*, **93**, 3997 (1971).

(9) F. Feigl, "Spot Tests in Organic Analysis", 6th ed, Elsevier, Amsterdam, 1960, p 365.

(10) E. Nachbaur, *Monatsh. Chem.*, **100**, 1998 (1969).

(11) (a) N. J. Turro, P. Lechtken, G. Shuster, J. Orell, H.-C. Steinmetzer, and W. Adam, *J. Am. Chem. Soc.*, **96**, 1627 (1974); (b) N. J. Turro, P. Lechtken, N. S. Schore, G. Shuster, H.-C. Steinmetzer and A. Yekta, *Acc. Chem. Res.*, **7**, 97 (1974).

(12) (a) G. B. Schuster, N. J. Turro, H.-C. Steinmetzer, A. P. Schaap, G. Faler, W. Adam, and J. C. Liu, *J. Am. Chem. Soc.*, **97**, 7110 (1975); (b) W. Adam, N. Duran, and G. A. Simpson, *ibid.*, **97**, 5464 (1975); (c) H. E. Zimmerman and G. E. Keck, *ibid.*, **97**, 3527 (1975); (d) E. J. H. Bechara, A. L. Baumstark, and T. Wilson, *ibid.*, **98**, 4648 (1976), and references cited therein.

(13) Y. Sawaki and Y. Ogata, *J. Am. Chem. Soc.*, **99**, 5412 (1977).

(14) Since β-scission of benzyl radical from alkoxy radical is very fast,[15] no observation of products such as bibenzyl or benzyl alcohol suggests that the decomposition of **1c** does not contain intermediary alkoxy radical $R_1R_2C(O\cdot)CN$, denying the radical pathway.

(15) Y. Sawaki and Y. Ogata, *J. Org. Chem.*, **41**, 2340 (1976), and references cited therein.

(16) W. H. Richardson, R. S. Smith, G. Snyder, B. Anderson, and G. L. Kranz, *J. Org. Chem.*, **37**, 3915 (1972).

(17) W. H. Richardson and R. S. Smith *J. Am. Chem. Soc.*, **91**, 3610 (1969).

(18) W. H. Richardson and T. C. Heesen, *J Org. Chem.*, **37**, 3416 (1972).

(19) J. E. McIsaac, Jr., L. R. Subbaraman, J. Subbaraman, H. A. Mulhausen, and E. J. Behrman, *J. Org. Chem.*, **37**, 1037 (1972).

(20) N. Peskoff and J. Meyer, *Z. Phys. Chem.* (*Leipzig*), **82**, 129 (1913).

(21) Y. Sawaki and Y. Ogata, unpublished results.

(22) Determined from the UV absorbance at 270 nm in carbonate buffer immediately after the mixing.

(23) B. Capon, *Q. Rev., Chem. Soc.*, **18**, 45 (1964).

(24) (a) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", 2nd ed, Wiley, New York, N.Y., 1961, p 288; (b) P. D. Bukley, B. D. England, and D. J. McLennan, *J. Chem. Soc. B*, 98 (1967).

(25) Another driving force may be the steric acceleration as observed in other cyclizations, e.g., epoxide[26a] and lactone[26b] formations. The relative reactivities of **1a–e** at 0 °C in MeOH are well correlated both with σ^* ($\rho = 1.93$, $r = 0.984$) and E_s ($\rho = -1.30$, $r = 0.988$); the correlation coefficients (r) are practically identical. However, the polar effect is known to be important for the addition of HOO^- to nitriles ($\rho \sim 1.7$ vs. σ).[27]

(26) (a) E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Reinhart and Winston, New York, N.Y., 1959, p 567; (b) C. Danforth, A. W. Nicholson, J. C. James, and G. H. Loudon, *J. Am. Chem. Soc.*, **98**, 4275 (1976); R. E. Winans and C. F. Wilcox, Jr., *ibid.*, **98**, 4281 (1976).

(27) K. B. Wiberg, *J. Am. Chem. Soc.*, **77**, 2519 (1955).

(28) Y. Ogata and Y. Sawaki, *Bull. Chem. Soc. Jpn.*, **38**, 194 (1965).

(29) K.-W. Lee, L. A. Singer, and K. D. Legg, *J. Org. Chem.*, **41**, 2685 (1976).

(30) M. S. Newman and R. D. Closson, *J. Am. Chem. Soc.*, **66**, 1553 (1944).

(31) E. Bowden, *J. Am. Chem. Soc.*, **60**, 131 (1938).

(32) L. Horner and H. Guesten, *Justus Liebigs Ann. Chem.*, **652**, 99 (1962).

(33) M. M. Rauhut, B. G. Roberts, and A. M. Semsel, *J. Am. Chem. Soc.*, **88**, 3604 (1966).

(34) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry", Wiley, New York, N.Y., 1966, p 783.

A Model for the Transition State of the Reduction of Aliphatic Ketones by Sodium Borohydride

Jean-Claude Perlberger and Paul Müller*

Contribution from the Département de Chimie Organique, Université de Genève, 1211 Genève, Switzerland. *Received August 16, 1976*

Abstract: A simple model for the transition state of the ketone reduction with sodium borohydride is proposed. The strain energy of this model is calculated by means of a molecular mechanics program. It allows us to rationalize the distribution of epimeric alcohols formed from a given ketone with an average uncertainty of ±10% and the reduction rates over a rate range of 10^8 and an average error by a factor of 10.

The interpretation of the reduction rates of aliphatic ketones with complexed hydrides such as sodium borohydride or lithium aluminum hydride represents an old, but still unresolved, problem for mechanistically inclined chemists. The understanding of the reaction is also of interest from the synthetic viewpoint, as it should allow predictions concerning the regio- and stereospecificity of the ketone reduction.

The reaction of sodium borohydride with ketones in 2-propanol solution exhibits simple second-order kinetics; it is first order both in hydride and ketone.[1] The rate-determining step consists in the transfer of the first hydrogen from the borohydride to the carbonyl carbon. For the various ketones studied, the entropies of activation are nearly identical[2,3] so that their relative reactivities can be attributed in a first approximation to enthalpy effects alone. The electronic substituent effects are of minor importance for aliphatic ketones;[4] a value of 0.76 has been reported for Taft's reaction constant ρ^*. These effects will be neglected in our discussion.

The steric factors operating in the reaction are traditionally interpreted in terms of two fundamental concepts, "product development control" and "steric approach control".[6] "Product development control" is associated with a late (productlike) transition state;[7] it explains the predominant formation of the more stable alcohol in the reduction of unhindered cyclohexanones[8] and the rate profile for the reduction of the cyclanones.[9] "Steric approach control", on the contrary, implies an early (reactant-like) transition state;[7] the complexed hydride attacks the carbonyl group from the less hindered side. This concept is used to explain the predominant equatorial attack on sterically hindered cyclohexanones or, more generally, the preferential formation of the thermodynamically less stable alcohol in the reduction of sterically hindered ketones.[3a,6,7] In addition to this, two additional hypotheses are offered: (1) an early transition state for all ketones where the stereochemical outcome is determined by steric and torsional interactions between the partially bound hydride and the substituents of the ketone,[10,11] and (2) a late transition state where strain effects control ketone reactivity and remote steric effects direct the hydride to the less hindered side of the carbonyl group.[12] The arguments in favor of one or the other hypothesis have recently been reviewed.[11b,13,14a]

Wipke and Gund[14] applied a molecular mechanics program to the problem of stereoselectivity of carbonyl addition. In their approach an early transition state is suggested. The steric hindrance of the ketone in its ground state with respect to perpendicular approach of a nucleophile is described with an empirical function called congestion. The calculated congestions correlate well with the stereoselectivity of ketone additions by large nucleophiles, and in highly congested ketones also by small nucleophiles. For addition of small nucleophiles such as sodium borohydride to uncongested ketones another function, containing an empirical torsional correction, must be used. The torsion-corrected functions are able to reproduce the stereoselectivity of the reduction, but they do not correlate with rate constants.

Force-field calculations have been successfully used to correlate rate constants with the strain difference between reactants and hypothetical transition state models for solvolysis of bridghead halides,[15] ester hydrolysis,[16] and alcohol oxidation.[17] Application of the method to the sodium borohydride reduction of ketones requires a transition state model applicable to both hindered and unhindered ketones. We have previously described a procedure to calculate "steric approach control" and "product development control" from two independent structures. Rate constants were rationalized by a linear combination of these two factors.[18] The failure of the procedure to reproduce the stereoselectivity of the reaction suggested that both of them derive from one and the same structure.

Scheme I

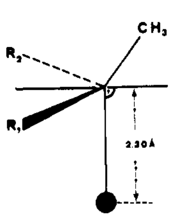

Table I. Reduction Rates of Ketones and Strain Energies

Compd	Alcohol formed	Log k_{rel}[a]	TS strain[b]	Δ strain[c]
1	2-Propanol	−1.33[e]	5.33	−5.33
2	Di-*tert*-butylmethanol	−5.05[f]	17.40	−8.29
3	Cyclobutanol	−0.09[e]	33.32	−4.81
4	Cyclopentanol[d]	−1.66[e]	11.38	−5.02
5	*cis*-4-Methylcyclohexanol	−0.52[g]	7.96	−5.34
6	*trans*-4-Methylcyclohexanol	−0.02[g]	7.28	−4.66
7	*trans*-3,3,5-Trimethylcyclohexanol	−1.92[g]	8.94	−5.89
8	*cis*-3,3,5-Trimethylcyclohexanol	−2.10[g]	9.45	−6.40
9	*cis*-2-Methycyclohexanol	−1.19[e]	8.81	−6.01
10	*trans*-2-Methylcyclohexanol	−0.84[e]	8.62	−5.82
11	2,2-Dimethylcyclohexanol	−1.56[e]	9.38	−4.64
12	7-Norbornanol	1.67[e]	28.42	−4.33
13	2-*endo*-Norbornanol	−1.55[e]	22.92	−4.56
14	2-*exo*-Norbornanol	−2.34[e]	25.12	−6.76
15	1-Methyl-*endo*-2-norbornanol	−2.52[e]	21.71	−4.51
16	1-Methyl-*exo*-2-norbornanol	−3.30[e]	24.21	−7.01
17	7,7-Dimethyl-*endo*-2-norbornanol	−4.49[e]	33.10	−11.70
18	7,7-Dimethyl-*exo*-2-norbornanol	−3.89[e]	31.84	−10.44
19	Borneol	−5.66[e]	32.53	−12.25
20	Isoborneol	−4.86[e]	31.48	−11.20
21	2-Bicyclo[2.2.2]octanol	−2.22[e]	18.72	−7.31
22	2-*endo*-Bicyclo[3.2.1]-octanol	−0.66[h]	18.17	−4.90
23	2-*exo*-Bicyclo[3.2.1]-octanol	−1.24[h]	19.37	−6.10
24	3-*endo*-Bicyclo[3.2.1]octanol	−2.89[h]	18.73	−7.13
25	3-*exo*-Bicyclo[3.2.1]octanol	−2.64[h]	17.25	−5.65
26	8-*endo*-Bicyclo[3.2.1]octanol	−2.55[i,j]	23.59	−7.81
27	8-*exo*-Bicyclo[3.2.1]octanol	0.44[j]	20.16	−4.38
28	3-*endo*-Bicyclo[3.3.1]nonanol	−5.29[j]	15.44	−8.58
29	3-*exo*-Bicyclo[3.3.1]nonanol	−6.16[j]	16.48	−9.62
30	9-Bicyclo[3.3.1]nonanol	−0.66[j]	18.35	−5.03
31	2-Adamantanol	−0.61[j]	15.42	−6.03

[a] Partial rate constants relative to cyclohexanone; the rates of the symmetric ketones are divided by 2; conditions, solvent 2-propanol at 0 °C. [b] Strain energy of transition state model, calculated from steric energy and group increments by molecular mechanics,[21,22] in kcal/mol (the stretching energy of the CH bond of 2.30 Å is not included). [c] Δ strain = strain ketone − strain transition state, in kcal/mol. [d] Half-chair form for ketone and transition state. [e] Reference 3a. [f] Reference 4. [g] Reference 23. [h] Reference 24. [i] Upper limit, estimated from ref 12b. [j] Solvent 0.025 M dioxane/water (1:1), 25 °C.[12b]

The model adopted is shown in Scheme I. It has a CH_3 group bound to an sp^3-hybridized carbon atom and an only partially bound carbinolic hydrogen at 2.30 Å perpendicular to the carbonyl carbon. The CH_3 group simulates the steric requirements of the alcohol product, for which our program is not parametrized.[19] This part of the model reflects "product development control". The carbinolic hydrogen at 2.30 Å serves as a measure for the strain hindering perpendicular attack of the complexed hydride. Although theoretical considerations suggest a wider angle,[20] perpendicular approach was retained for the model for reasons of simplicity. The steric energy of the model was calculated with the Engler force field[21a] incorporated in the BIGSTRN program of Schleyer[21] and

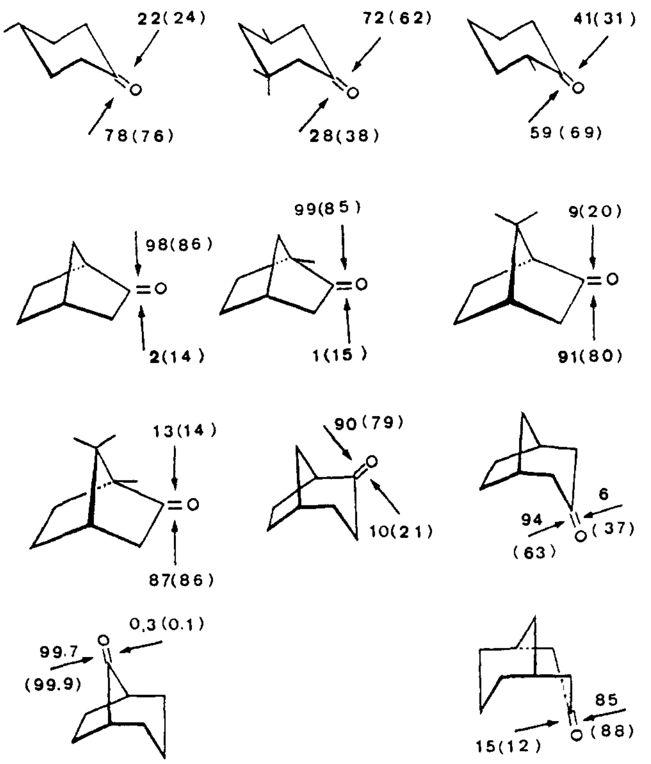

Figure 1. Exo/endo preference for carbonyl attack, in percent, calculated using ln k(endo/exo) = [strain TS exo − strain TS endo]/RT. Experimental values in parentheses. References as in Table I.

Table II. Calculated Thermodynamic Properties of Ketones

Ketone	$\Delta H_f{}^{\circ\,a}$	Strain^b
Cyclopentanone^c	−46.56	6.36
2-Methylcyclohexanone	−62.26	2.80
2,2-Dimethylcyclohexanone	−68.43	4.74
7-Norbornanone	−33.14	24.09^d
1-Methyl-2-norbornanone	−48.14	17.20
7,7-Dimethyl-2-norbornanone	−50.89	21.40
Bicyclo[2.2.2]octanone	−51.01	11.41
3-Bicyclo[3.2.1]nonanone	−60.75	6.86

[a] Gas phase standard enthalpies of formation in kcal/mol of ketones calculated from steric energies and general increments according to Allinger.[25] [b] Strain energy from $\Delta H_f{}^\circ$ and strainless increments of Allinger,[25] kcal/mol. [c] Half-chair form (most stable conformation). [d] The value of 29.09 quoted in ref 17a is in error. [e] Chair-chair form.

Mislow,[22] and its enthalpy of formation and strain by using the general and strainless increments of Schleyer.[21a] All internal coordinates were relaxed except the 90° angle of the carbinolic hydrogen and its bond length. The latter was varied systematically until (at 2.30 Å) the model reproduced the isomer distribution in the reduction of camphor correctly. Application to other ketones required a reduction of the H-H nonbonded distance from 3.20 to 2.50 Å for the hydrogen probe. Further modification of the parameters produced no improvement. The results of the calculations are summarized in Table I, which also contains the partial rate constants for reduction. For clarity the names of the alcohols are given so that the partial rate constants refer to formation rates. Inspection of Figure 1 shows good agreement between experimental and calculated stereoselectivity (±10%), except in one case (3-bicyclo[3.2.1]-octanone). For all ketones studied the model predicts the predominant isomer correctly. It is applicable to hindered and unhindered cyclohexanones as well as to other hindered ketones, and there appears no need to invoke different transition states as the ketone structure varies.

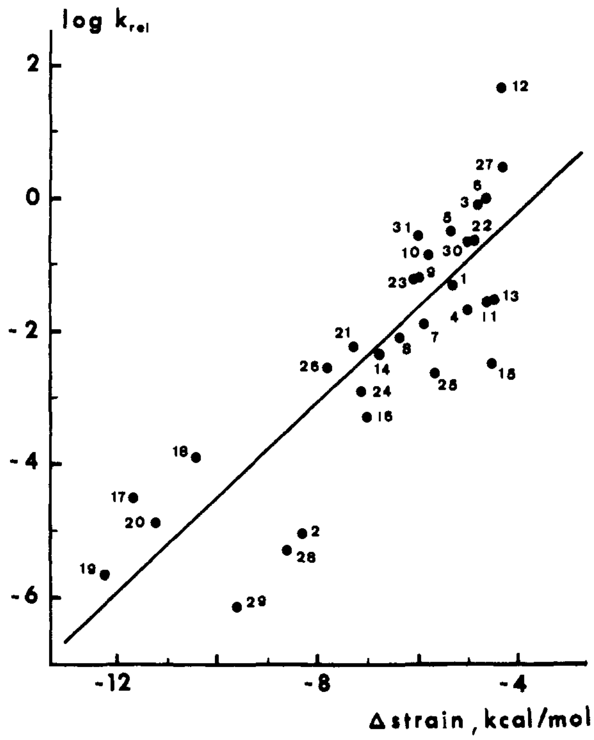

Figure 2. Plot of log k_{rel} vs. Δ strain. Data from Table I.

In order to rationalize rate constants for reduction the strain of the starting carbonyl compounds must also be known. Since very few reliable experimental data are available, we use the strain energies calculated by the force-field method of Allinger;[17,25] calculations for new compounds are summarized in Table II. The strain difference between ketone and TS model (Δ strain) is found in the last column of Table I.

In Figure 2 the partial rate constants for ketone reduction relative to cyclohexanone (log k_{rel}) are plotted against Δ strain. The plot covers a rate range of 10^8. The slope of the regression line is 0.71, the intercept 2.58, the correlation coefficient 0.85, and the standard deviation on log k = 1.0. Thus the correlation allows us to rationalize rate constants with an average error of a factor of 10. If log k is transformed in energetic units by multiplying with 2.303 RT the slope of the correlation becomes 0.97, in good agreement with the theoretical value of 1.0. From this viewpoint the model reflects the properties of the transition state reasonably well. Although agreement between calculations and experiment is much less than for the isomer distribution, the trend is still significant. The most important deviations are due to the very reactive as well as to the very unreactive ketones. Their rate constants are known to be somewhat less reliable.[3a] An additional uncertainty may come from the use of a different solvent system for compounds **27–31**.

The accuracy of the calculations is of course far from perfect and needs refinement. Such refinements may be possible by slightly changing the position and the van der Waals radius of the carbinolic hydrogen or even the function for the nonbonded interactions. Further improvement could be possible with a force field for alcohols. However, it appears that the main problem comes from the strain energies of the ketones, which need not to be considered in the calculation of the isomer distribution. In fact, preliminary experiments[26] show considerable disagreement between experimental and calculated enthalpies of formation of bicyclic ketones. From the limited amount of data available at the present time it is impossible to predict if a modified ketone force field will lead to better results. This point is currently under investigation.

From the results of the calculations it appears possible to rationalize, within the limitations indicated, rates and isomer distributions of the borohydride reduction of ketones with only one transition state.

The approach used here is not limited to the treatment of the ketone reduction. It is possible to adapt the parameters to other nucleophiles and other functional groups, such as double bonds. It should therefore be of general interest in mechanistic and synthetic chemistry.

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References and Notes

(1) H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, **1**, 214 (1957).

(2) H. C. Brown and K. Ichikawa, *Tetrahedron*, 1, 221 (1957).

(3) (a) H. C. Brown and J. Muzzio, *J. Am. Chem. Soc.*, **88**, 2811 (1966); (b) D. C. Wigfield and D. J. Phelps, *J. Org. Chem.*, **41**, 2396 (1976).

(4) H. C. Brown and K. Ichikawa, *J. Am. Chem. Soc.*, **84**, 373 (1962).

(5) K. Bowden and M. Hardy, *Tetrahedron*, **22**, 1169 (1966).

(6) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).

(7) D. C. Wigfield and D. J. Phelps, *Can. J. Chem.*, **50**, 388 (1972).

(8) G. Just and R. Nagarajan, *Experientia*, **18**, 402 (1962); H. C. Brown and H. R. Deck, *J. Am. Chem. Soc.*, **87**, 5620 (1965).

(9) H. C. Brown, R. S. Fletcher, and R. B. Johannesen, *J. Am. Chem. Soc.*, **73**, 212 (1951); H. C. Brown, *J. Chem. Soc.*, 1248 (1956).

(10) M. Chérest and H. Felkin, *Tetrahedron Lett.*, 2205 (1968); M. Cherest, H. Felkin, and N. Prudent, *ibid.*, 2199 (1968).

(11) (a) E. C. Ashby and S. A. Noding, *J. Am. Chem. Soc.*, **98**, 2010 (1976); (b) E. C. Ashby and J. T. Laemmle, *Chem. Rev.*, **75**, 521 (1975).

(12) (a) P. Geneste, G. Lamaty, and J. P. Roque, *Tetrahedron Lett.*, 5007 (1970); P. Geneste, G. Lamaty, C. Moreau, and J. P. Roque, *ibid.*, 5011 (1970); (b) C. Moreau, Ph.D. Thesis, Université des Sciences et Techniques du Languedoc, Montpellier, 1972.

(13) (a) H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 54–70; (b) E. Goller, *J. Chem. Educ.*, **51**, 183 (1974).

(14) (a) W. T. Wipke and P. Gund, *J. Am. Chem. Soc.*, **98**, 8107 (1976); (b) *ibid.*, **96**, 299 (1974).

(15) R. C. Bingham and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **93**, 3189 (1971); J. L. Fry, E. M. Engler, and P. v. R. Schleyer, *ibid.*, **94**, 4628 (1972); W. Parker, R. L. Tranter, C. I. F. Watt, L. W. K. Chang, and P. v. R. Schleyer, *ibid.*, **96**, 7121 (1974).

(16) D. F. de Tar, *J. Am. Chem. Soc.*, **96**, 1254, 1255 (1974); D. F. de Tar and C. J. Tanpas, *ibid.*, **98**, 4567 (1976).

(17) (a) P. Müller and J. C. Perlberger, *J. Am. Chem. Soc.*, **97**, 6862 (1975); (b) *ibid.* **98**, 8407 (1976).

(18) P. Müller and J. C. Perlberger, *Helv. Chim. Acta*, **59**, 1880 (1976).

(19) A force-field program parametrized for alcohols and other oxygen-containing functions has recently been described; cf. N. L. Allinger and D. Y. Chung, *J. Am. Chem. Soc.*, **98**, 6798 (1976).

(20) H. B. Bürgi, J. D. Dunitz, J. M. Lehn, and G. Wipf, *Tetrahedron*, **30**, 1563 (1974); H. B. Bürgi, *Angew. Chem., Int. Ed. Engl.*, **14**, 460 (1975).

(21) (a) E. M. Engler, J. D. Andose, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **95**, 8005 (1973); (b) J. E. Williams, P. J. Stang, and P. v. R. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968).

(22) J. D. Andose and K. Mislow, *J. Am. Chem. Soc.*, **96**, 2168 (1974).

(23) B. Rickborn and M. T. Wuesthoff, *J. Am. Chem. Soc.*, **92**, 6894 (1970).

(24) E. Volpi, G. Biggi, and F. Pietra, *J. Chem. Soc., Perkin Trans. 2*, 571 (1973).

(25) N. L. Allinger, M. T. Tribble, and M. A. Miller, *Tetrahedron*, **28**, 1173 (1972).

(26) P. Müller and W. V. Steele, unpublished.

H/D Exchange in Electrolytic Reduction Reactions of Phenyl Ketones[1]

A. F. Diaz,* Y. Y. Cheng, and M. Ochoa

Contribution from the IBM Research Laboratory, San Jose, California 95193.
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Abstract: Reduction of phenacyl chloride in DMF containing 1% D_2O is electrochemically irreversible. The observed products at the reduction potential are acetophenone plus dimeric product. Recovery of the ketone after short reaction times reveals the presence of considerable H/D exchange of the methylene hydrogens in competition with the reduction reaction. Similarly, in the reduction of 1,2-diphenylpropanone, which proceeds with asymmetric induction, H/D exchange of the α hydrogen is very important. The exchange process appears to be part of the electrochemical reaction and is associated with the first electron transfer step.

A survey of the electrochemical literature reveals that studies on "electrochemical irreversible" systems do not provide evidence for the presence of reactions which regenerate the starting material from the reaction intermediate. This situation is not expected with those electrochemically irreversible cases where one and only one reaction pathway is available for the oxidation–reduction process as is usually the case with metal cations. However, in the case with larger organic molecules more than one reaction pathway may be available for the oxidation–reduction process. Even with these cases no evidence of the regeneration reaction is available. For example, the electrolytic reductions of alkyl halides is presumed to proceed with no regeneration of RX from $RX^{-}\cdot$. And while the more facile reduction of halides which are allylic, benzylic, or α to a carbonyl is associated with the formation of an initially formed radical ion, no evidence of regeneration is available (eq 1).[2,3] We now present the results of a study aimed at establishing the relative importance of reactions which regenerate the alkyl halide from the radical ion. For technical convenience the easily reducible phenacyl chloride was studied using a platinum electrode in order to avoid the usual adsorption and mercuration problems of the mercury electrode[3] and in moist dimethylformamide in order to avoid solvent problems.[4]

$$RX \overset{+e}{\rightleftharpoons} [RX^{-}\cdot] \rightarrow R\cdot + X^{-} \rightarrow \rightarrow RH \qquad (1)$$

Results and Discussion

Phenacyl Derivatives. All electrochemical reductions were performed using a PAR Model 170. The electrolysis experiments were performed in DMF containing the appropriate amount of D_2O or CH_3OD plus 0.1 M tetraethylammonium fluoroborate. As seen in Figure 1, cyclic voltammetry of phenacyl chloride (10^{-3} M) using a platinum button as the working electrode shows electrochemical irreversibility at scan rates between 0.1 and 10 V/s. E_{pc} appears at -2.0 V with $I_p/V^{1/2}C$ equal to 0.19 A s$^{1/2}$/V$^{1/2}$M at a scan rate of 200 mV/s. With these DMF–D_2O solutions used, the background currents become significant at -2.5 V and finally break down at -2.8