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ELECTROORGANIC CHEMISTRY—XI

THE STEREOCHEMISTRY OF ELECTROREDUCTION OF CYCLIC KETONES

T. SHONO AND M. MITANI
Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto, Japan

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Abstract—Cyclic ketones were electrolytically reduced in isopropanol and in H_2SO_4-H_2O-MeOH. It was found that, in isopropanol the stereoisomer ratios of the products were approximately equal to the thermodynamic relative stabilities, whereas in H_2SO_4-H_2O-MeOH the thermodynamically unstable epimeric alcohols formed were more than that anticipated from the relative stabilities. The mechanism of this electroreduction involving the stereoselective adsorption and electron transfer is discussed.

INTRODUCTION

THE STEREOCHEMISTRY of the reduction of cyclic ketones by various chemical reducing agents is controlled mainly by two factors,[1] i.e., product stability (or eclipsed effect in transition state[2]) and steric approach strain. When the size of the reducing agent is sufficiently small, product stability control is predominant, whereas steric approach strain plays an important role in the reduction with a bulkier reducing agent.[3] The stereochemistry in the reduction by solvated electron is reported to be controlled by thermodynamic stability of products.[4] On the other hand, it was found previously that a thermodynamically unstable stereoisomer was the only product in the intramolecular cycloaddition of nonconjugate olefinic ketones by electroreduction where the initiation step seemed to be similar to that in the reduction with a solvated electron.[5] This remarkable stereoselectivity in the electroreductive cycloaddition may be largely due to the huge bulkiness of electrode. Thus, it could be expected that, when a cyclic ketone is electrolytically reduced in a good proton donating solvent, the intermediate anion species abstracts a proton at the vicinity of the surface of electrode and the stereochemistry is controlled by steric factors, whereas in a poor proton donating solvent, the proton is abstracted after the active species has diffused into solution and thus the stereochemistry is controlled by the thermodynamic stability of the product. We report the stereochemistry and mechanism of the electrochemical reduction of some cyclic ketones in H_2SO_4-H_2O-MeOH and in isopropanol.

RESULTS AND DISCUSSION

The electrochemical reduction of cyclic ketones (I ~ VIII) was carried out at a cathode potential of $-2{\cdot}5 \sim -2{\cdot}7$ Volt *vs* SCE (0·15 A) using a carbon rod electrode in isopropanol containing tetraethyl ammonium *p*-toluenesulfonate as the supporting electrolyte and in H_2SO_4-H_2O-MeOH at the cathode potential of $-1{\cdot}7 \sim -1{\cdot}9$ Volt *vs* SCE (0·15 A). These results are summarized in Table 1. The stereochemistry of reduction of I ~ VIII by other methods and the relative thermo-

TABLE 1. ELECTROREDUCTION OF CYCLIC KETONES IN ISOPROPANOL AND IN H_2SO_4–H_2O–MeOH

Ketone	Epimer ratio (*trans/cis*)		Alcohol total yield[a], %	
	Isopropanol	H_2SO_4-H_2O -MeOH	Isopropanol	H_2SO_4-H_2O -MeOH
3-Methylcyclohexanone(I)	22/78	52/48	58	48
4-Methylcyclohexanone(II)	78/22	38/62	60	45
4-t-Butylcyclohexanone(III)	85/15	48/52	56	55
3,3,5-Trimethylcyclohexanone(IV)	26/74	40/60	55	50
2-Methylcyclopentanone(V)	59/41	50/50	58	42
2-i-Propylcyclopentanone(VI)	58/42	42/58	54	40
Norcamphor(VII)	16/84[b]	98/2[b]	60	30
Camphor(VIII)	76/24[b]		55	

[a] Analysed by VPC.

[b] Epimer ratio(*endo/exo*).

TABLE 2. REDUCTION OF CYCLIC KETONES BY VARIOUS REDUCING AGENTS AND THE RELATIVE STABILITIES OF CORRESPONDING ALCOHOLS

Ketone	Epimer ratio(*trans/cis*)					Thermodynamic relative stability (*trans/cis*)[c]
	Li/NH_3	LAH	LiAlH(OMe)$_3$	IPC_2BH[a]	LPBH[b]	
I	6/94[d]	16/84[f]		35/65[k]	59/41[f]	22/78[m]
II	99/1[d]	83/17[f]		67/33[k]	48/52[f]	70/30[m]
III	99/1[d]	92/8[g]		63/37[k]	46/54[f]	79/21[m]
IV	1/99[d]	82/18[g]			99/1[f]	6/94[n]
V		82/18[h]	56/44[j]	6/94[l]		
VI		43/57[i]				
VII	85/15[d,e]	89/11[j,e]	98/2[j,e]	94/6[k,e]	99/1[f,e]	20/80[o,e]
VIII	89/11[d,e]	8/92[j,e]	1/99[j,e]	0/100[k,e]	1/99[f,e]	71/29[o,e]

[a] IPC_2BH represents di-i-pinocamphenylborane.

[b] LPBH represents lithium perhydro-9b-boraphenalyhydride.

[c] Obtained after long reaction time with Al(O-iPr)$_3$.

[d] J. W. Huffman and J. T. Charles, *J. Am. Chem. Soc.* **90**, 6486 (1968)

[e] Epimer ratio (*endo/exo*).

[f] H. C. Brown and W. C. Dickason, *J. Am. Chem. Soc.* **92**, 709 (1970).

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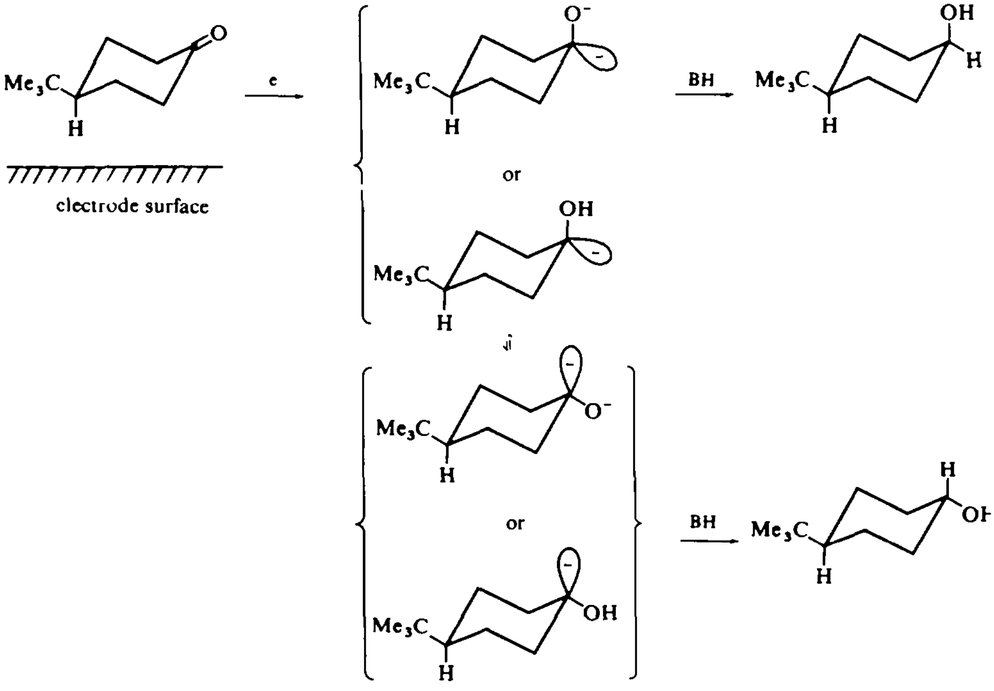
dynamic stability of the stereoisomers of the corresponding alcohols are shown in Table 2.

Comparing the results in Table 1 with the relative stabilities in Table 2, it is apparent that stereoisomer ratios of electroreduction of cyclic ketones in isopropanol are approximately equal to the relative stabilities. On the other hand, in H_2SO_4-H_2O-MeOH, the formation of thermodynamically unstable stereoisomers are higher than that anticipated from the relative stabilities. This stereoselectivity requires the consideration of two factors, i.e., the stereospecific adsorption of the CO group and stereospecific proton abstraction of the intermediate active species. Accordingly, the stereochemistry of electroreduction of cyclic ketones in a good proton donating solvent (i.e., H_2SO_4-H_2O-MeOH) seemed to reflect intimately the conformation of the adsorption of the CO group on the surface of the electrode. As shown in Table 2, the stereochemistry of electroreduction in H_2SO_4-H_2O-MeOH is similar to that observed in the reduction by IPC_2BH and LPBH, which is controlled mainly by steric factors owing to their bulkiness. Consequently, the following mechanism may be suggested for the electroreduction of cyclic ketones. The CO group is adsorbed stereoselectively on the surface of electrode from its less hindered site, and is electrochemically reduced into an anionic species. In a good proton donating solvent, such as H_2SO_4-H_2O-MeOH, the anionic species abstracts a proton at the vicinity of the surface of a bulky electrode prior to its diffusion into solution. Thus steric factors preferentially control the stereochemistry of the reducing products. On the other hand, in a poor proton donating solvent, such as isopropanol, the proton abstraction takes place after the active species has diffused into solution, and the thermodynamic stability of the products predominantly controls the stereochemistry of reduction.



Thus, it could be expected from this mechanism that the stereochemistry of the reduction product may be controlled over a wide range by varying the proton donating ability of the solvent. From this point of view, the electroreduction of cyclic ketones would have a considerable potential in synthetic chemistry.

EXPERIMENTAL

Electroreduction in isopropanol. In a 100 ml cylindrical cell, equipped with a reflux condenser, two carbon rod electrodes and reference electrode was placed a soln of a cyclic ketone (I ~ VIII; 0·014 mole) and tetraethylammonium *p*-toluenesulfonate(6g) in isopropanol (30 ml). The soln was electrolysed at a cathode potential of −2·5 to −2·7 Volt (SCE) and a current of 0·15 amp (total 1·8 amp-hr) with a magnetic stirring. The mixture was poured into excess water and extracted with ether. The ethereal soln was dried over $MgSO_4$ and distilled to remove ether. The residue was evaporated under reduced pressure. The product was isolated by preparative VPC and identified by comparison with the authentic material (IR, VPC). The yield and the stereoisomer ratio were determined by VPC analysis of the original reaction mixture. VPC analysis was performed on Shimadzu GC-4B IT using a 10-ft. column of PEG 20M on a support of 60–80 mesh Celite and, in the case of norborneols, a 16-ft column of Ucon Oil-LB-550 X on a support of 80 mesh Neopak 1A was employed.

Electroreduction in H_2SO_4–H_2O–MeOH. A cyclic ketone (I ~ VIII; 0·014 mole) was reduced in the mixed solvent of H_2SO_4 (0·2 g), MeOH (30 ml) and H_2O (10 ml) using the same apparatus described above. Electrolysis was carried out at a cathode potential of −1·7 to −1·9 Volt (SCE) and a current of 0·15 amp (total 3·0 amp-hr). The mixture was neutralized with anhyd K_2CO_3 and the resulting soln was extracted with ether. The product was isolated from the ethereal soln by the method mentioned above.

Authentic synthesis of cyclic alcohols. trans-3-Methylcyclohexanol, *cis*-3-methylcyclohexanol, *trans*-4-methylcyclohexanol and *cis*-4-methylcyclohexanol were prepared according to the method of Eliel and Lukach.[6] *cis*-4-t-Butylcyclohexanol and *trans*-4-t-butylcyclohexanol were synthesized according to the method of Eliel and Ro.[7]

Cis-2-Methylcyclopentanol and *trans*-2-methylcyclopentanol were prepared by Umland's method.[8]

cis-3,3,5-Trimethylcyclohexanol and *trans*-3,3,5-trimethylcyclohexanol were obtained following to the procedure of Eliel and Haubenstock.[9]

cis-2-i-Propylcyclopentanol and *trans*-2-i-propylcyclopentanol were synthesized following to the Hückels' procedure.[10]

exo-Norborneol was obtained as described by Schmering.[11]

endo-Norborneol and isoborneol were prepared according to the procedure of Wilcox.[12]

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