Stereoselective Electrochemical Reduction of Cyclic Ketones

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Summary The electrochemical reduction of 4-t-butylcyclohexanone and dihydroisophorone has been studied at controlled potential and current density and it has been found that at relatively small cathodic potentials, in the presence of acetic acid, the equatorial (stable) and axial (less stable) alcohols are formed in approximately equal amounts.

ADSORPTION at the electrode surface plays an important part in most electro-organic reactions and would be expected to result in the stereoselectivity that is associated with other heterogeneous reactions, *e.g.* catalytic hydrogenation. There are, however, few examples of such stereoselectivity in electro-organic reactions. In this context we have chosen the electro-reduction of cyclic ketones as a suitable reaction to study, as much relevant data are available for a variety of chemical methods of reduction including dissolving metal reductions, metal hydride reductions, and catalytic hydrogenation. Steroidal ketones have been reduced to the corresponding alcohols electrochemically and the more stable alcohols with equatorial hydroxy-groups were the major products.[2] This may be compared with catalytic hydrogenation at low pH which leads mainly to the corresponding axial alcohol.[3]

We have investigated the products of electrochemical reduction of the conformationally rigid ketones, 4-t-butylcyclohexanone and 3,3,5-trimethylcyclohexanone. These were reduced to the corresponding alcohols at a lead cathode under a variety of conditions. The variable parameters were current density, cathode potential (controlled), supporting electrolyte, and solvent. Our results are summarised in the Table.

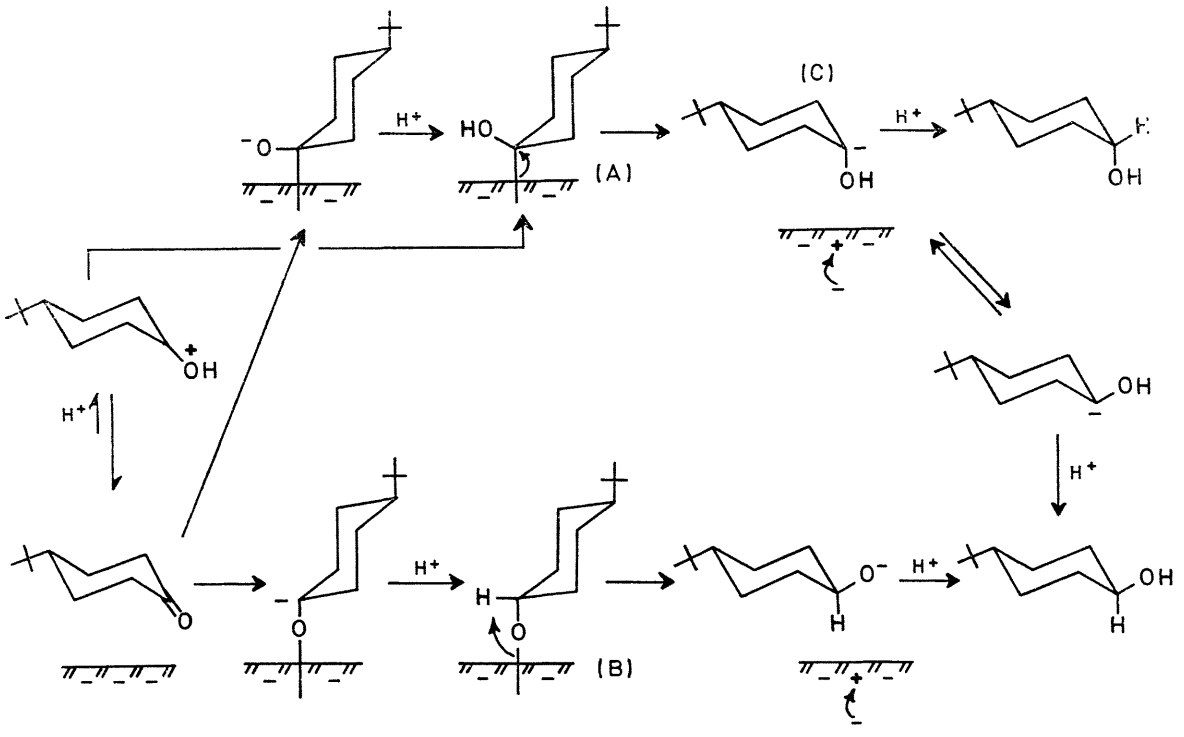
Cathodic reduction of 4-t-butylcyclohexanone and 3,3,5-trimethylcyclohexanone

Medium	Cathode (potential V *vs.* S.C.E.)	Current (mA)[b]	Chem. yield[d] (%)	Current[e] efficiency (%)	*eq*-OH (%)	*ax*-OH (%)
4-*t*-*Butylcyclohexanone*[a]						
LiCl–HMPA–EtOH[c]	Pt	200	87	87	95	5
TBA[f]–MeOH	Pb (−2·4)	110—190	82	66	88	12
NaOAc–MeOH[g]	Pb (−2·07 to −2·27)	200	81	14	85	15
NaOAc–MeOH[g]	Pb (−2·05 to −2·25)	50	92	12	71	29
NaOAc–MeOH–HOAc[h]	Pb (−1·80 to −1·87)	200	87	11	44	56
NaOAc–MeOH–HOAc[h]	Pb (−1·30 to −1·60)	100	61	6	44	56
H_2SO_4–H_2O–MeOH[i]	Pb (−1·60 to −1·65)	300	0	0	—	—
3,3,5-*Trimethylcyclohexanone*[a]						
LiCl–HMPA–EtOH[j]	Pt	200	65	50	91	9
TBA–MeOH[f]	Pb (−2·3)	220—300	72	60	83	17
NaOAc–MeOH–HOAc[h]	Pb (−1·61 to −1·70)	200	20	2	54	46

[a] All solutions *ca.* 0·2 M in ketone.
[b] Lead cathode, nominal surface area 2·45 cm.^{2} Platinum cathode, nominal surface area 3·40 cm.^{2}
[c] Hexamethylphosphoramide, HMPA, containing 4 mol % ethanol.
[d] Based on starting material consumed.
[e] Calc. for 2F/mol.
[f] Tetra-n-butylammonium acetate (TBA), (0·63 molal) in methanol.
[g] Sodium acetate (2·5 molal) in methanol.
[h] Sodium acetate (0·5 molal), acetic acid (2·0 molal) in methanol.
[i] Sulphuric acid (*ca.* 2·0 M) in methanol containing 10 vol. % water.
[j] Hexamethylphosphoramide, HMPA, containing 10 mol % ethanol.

We confirm earlier observations that the equatorial isomer is the predominant product of reduction in neutral or basic solution but have found that the proportion of axial isomer is increased in the presence of acetic acid. The reaction conditions which give the highest amount of axial alcohol produce it at lowest efficiency and we think it significant that under these conditions some reduction to the hydrocarbon is observed. In strongly acidic solutions steroidal ketones have been reduced almost exclusively to the corresponding hydrocarbons[4] in an "electrochemical Clemmensen reduction" and organo-lead and organo-mercury compounds have been reported as products of the electro-reduction of ketones.[5] These observations strongly suggest that bond formation between the carbonyl carbon and the electrode is likely under the conditions we used to produce the alcohols rich in the axial epimer. The low current efficiency is probably a result of the competing discharge of protons. In aqueous methanolic sulphuric acid this process excludes ketone reduction at the currents used.

We rationalise our results according to the Scheme. It is highly unlikely that intermediates with carbon–electrode bonds axial will be on a preferred pathway. This argument applies, albeit less firmly, to intermediates with oxygen–electrode bonds axial. We therefore envisage reduction mainly *via* the intermediates with equatorial bonds to the electrode [(A) and (B)], that with the bond to carbon, (A), leading to both axial and equatorial alcohols and that with the electrode bonded to oxygen, (B), leading exclusively to the equatorial alcohol. Increased proportions of the axial alcohol would result from factors favouring cathodic discharge at the carbonyl carbon and efficient protonation of the carbanion, (C), near to the electrode surface. The relatively low cathodic potentials (*ca.* −1·7 V) associated with reduction leading to increased amounts of axial alcohol suggest that discharge of protonated ketone, leading to intermediate (A), may be significant. The results of a polarographic study of the reduction of arylalkyl ketones as a function of pH support this view.[6] A possibly important role of the acetic acid is the protonation at the electrode surface of the intermediate carbanion (C) prior to establishment of the conformational equilibrium. Efficient electroreduction of ketones to predominantly equatorial alcohols may be achieved indirectly *via* solvated electrons produced by electrolysis of a LiCl–EtOH–HMPA mixture.[7]



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