Effects of Ion-pairing and Adsorption on the Stereochemistry of the Cathodic Pinacolisation of Acetophenone

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The racemic : *meso* ratio for the pinacol formed from the reduction of acetophenone at a mercury cathode has been determined as a function of the water content of the dimethylformamide solvent and of electrolyte type. The results show that the stereochemistry of the coupling process is strongly influenced by ion-bridging and a ratio of 19 : 1 was found using a mixed base electrolyte to maximise ion-bridging and minimise protonation and hydrogen bonding of the intermediates. On the basis of the stereochemical data and of mechanistic measurements using linear sweep voltammetry it is suggested that adsorbed neutral ion-pairs are involved in the coupling reaction.

THE importance of stereospecific reactions in synthetic organic chemistry has stimulated considerable interest in the stereochemical implications of electro-organic mechanisms.[1] The heterogeneous nature of electrochemical processes, the ease with which surface conditions and the rates of surface processes can be controlled are unique features which could be exploited in this area. Although there is still considerable debate on the role of adsorption in a number of electro-organic reactions,[2] there are several clear examples in the literature of the influence of adsorbed additives on the stereochemistry of cathodic processes.[3] In addition, there are many examples of the effects of adsorbed species on the mechanistic outcome of cathodic processes without stereochemical interest, although often the same type of adsorbed species are involved, *e.g.* quaternary ammonium cations.[4] Adsorbed species can influence electrochemical processes in a number of ways. A reaction intermediate could be held in a particular conformation by interaction with a non-electroactive adsorbed molecule.[5] Alternatively, a

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[1] L. Eberson and L. Horner, ' Organic Electrochemistry,' ed. M. Baizer, Dekker, New York, 1973, p. 869.

[2] B. E. Conway, *Chem. Rev.*, 1967, **67**, 624; J. H. P. Utley, ' Technique of Electroorganic Synthesis,' Part I, ed. N. L. Weinberg, Wiley, New York, 1974, 793; J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 1968, **33**, 294; 2145; 1969, **34**, 2807.

[3] V. J. Puglisi, G. L. Clapper, and D. H. Evans, *Analyt. Chem.*, 1969, **41**, 279; L. Horner and D. H. Skaletz, *Tetrahedron Letters*, 1970, 3679.

[4] M. Baizer and J. P. Petrovich, *Progr. Phys. Org. Chem.*, 1970, **7**, 189.

[5] L. Horner and D. Degner, *Tetrahedron Letters*, 1968, 5889; L. Horner and D. H. Skaletz, *ibid.*, 1970, 3679.

layer of adsorbed molecules may have the more passive role of excluding another reactant, *e.g.* water, from the immediate vicinity of the electrode surface at which the intermediate is being produced; thus coupling could be favoured over a protonation step.[6] When a reaction intermediate is itself the adsorbed species there is considerable scope for influencing the course of the reaction by control of electrode material and solvent type. A further means of affecting the adsorption of an intermediate to influence the course of a coupling reaction was suggested in an earlier publication.[7] This was to form an electrically neutral ion pair from an anionic intermediate and an added cation so that adsorption would be greatly enhanced at a negatively charged electrode. It it interesting to note that Kariv *et al.* found evidence for the adsorption of a complex formed during reduction of acetophenone between the anion intermediate and the pre-reduced quinidinium cation added to induce chirality.[8] This behaviour has been confirmed by Peltier *et al.*[9]

The mechanism of reduction of acetophenone at a mercury electrode in a variety of solvent systems has been studied in some detail. There is conflicting evidence for the role of adsorption. Careful studies by Brown *et al.*[10] and Saveant *et al.*[11] in aqueous media found no detectable signs of adsorption and a homogeneous coupling process was proposed for pinacol formation. Similar conclusions are reached from measurements in dimethylformamide (DMF) solutions using cyclic voltammetry.[12] Other workers have presented electrochemical evidence favouring adsorption.[13] The major evidence pointing to adsorption has been obtained, however, from analysis of the stereochemistry of the products and the effects of additives.[3] It is possible to reconcile the two sets of data if it is assumed that there is no adsorption of the anion radical intermediate nor of its protonated conjugate, but that adsorption is possible for strongly dipolar species such as ion pairs or for couples between alkaloid cations and the anion radical. It should be borne in mind that neutral organic species which are not strongly dipolar are unlikely to be adsorbed at the high cathodic potentials required for reduction in non-aqueous media. The present work was intended to extend the earlier data[7] in the effects of ion pairing in directing the relative conformations of the partners in the coupling process and to seek further evidence for adsorption of the intermediate.

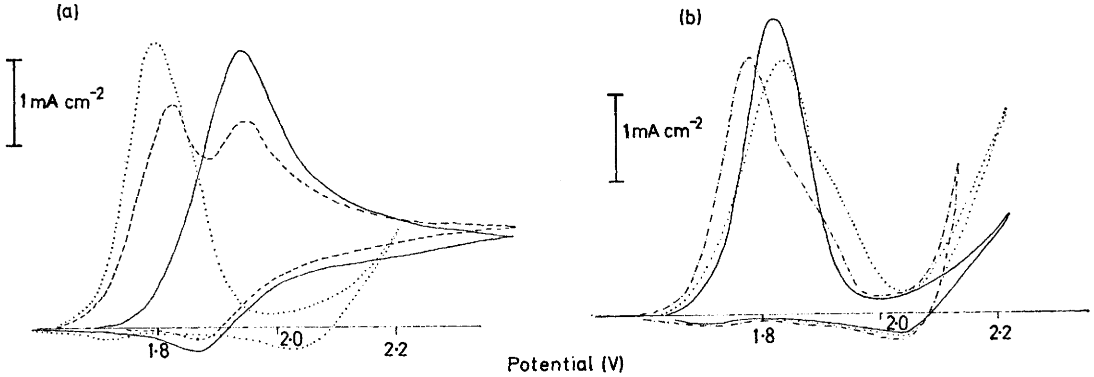

FIGURE 1 Linear sweep voltammogram at 0.2 V s^{-1} of a dry DMF solution containing 10^{-2}M-acetophenone in the presence of various base electrolytes: (a) —— 10^{-1}M-Bu$^t_4$NClO$_4$; ---- 10^{-1}M-Bu$^t_4$NClO$_4$–10^{-2}M-LiClO$_4$; ···· 10^{-1}M-Bu$^t_4$NClO$_4$–10^{-1}M-LiClO$_4$; (b) —·—·— 10^{-1}M-Bu$^t_4$NClO$_4$–2 × 10^{-1}M-LiClO$_4$; —— 10^{-2}M-Bu$^t_4$NClO$_4$–10^{-1}M-LiClO$_4$; ······ 10^{-1}M-LiClO$_4$

EXPERIMENTAL

Procedure.—The electrolysis and workup procedures were similar to those described previously.[7] All solutions were 0.1M in acetophenone and electrolysis was stopped after half the starting material had been consumed in order to keep the reaction conditions approximately constant throughout the synthesis. Racemic : *meso* ratios were determined by n.m.r. spectroscopy following the method described.[14] The residue after removal of solvent was dissolved in deuteriochloroform and the relative values of the two peaks corresponding to the racemic and *meso*-forms were determined by integration. No extraneous peaks, *e.g.* those from 1-phenylethanol, were present in the spectra. Cyclic voltammograms were recorded on a PAR 172 electrochemistry system employing a hanging mercury drop electrode thermostat at 22—24 °C.

Materials.—Acetophenone and DMF were distilled under reduced pressure and stored over activated molecular sieves in a dry box. Lithium perchlorate, rubidium perchlorate, and tetrabutylammonium perchlorate were dried in a vacuum oven at *ca.* 60 °C for five days before use.

RESULTS AND DISCUSSION

Linear sweep voltammograms for the reduction of acetophenone in DMF containing tetrabutylammonium perchlorate (TBAP), lithium perchlorate, or a mixed base

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[6] I. E. Gillet, *Chem.-Ing.-Tech.*, 1968, **40**, 573; A. P. Tomilov and V. Klimov, *Soviet Electrochem.*, 1967, **3**, 1352.

[7] A. Bewick and H. Cleghorn, *J.C.S. Perkin II*, 1973, 1410.

[8] E. Kariv, H. A. Terni, and E. Gileadi, *Electrochim. Acta*, 1973, **18**, 433; *J. Electrochem. Soc.*, 1973, **120**, 639.

[9] M. Jubautt, E. Raoult, and D. Peltier, *Electrochim. Acta*, 1974, **19**, 865.

[10] O. R. Brown, *Discuss. Faraday Soc.*, 1968, **45**, 125.

[11] L. Nadjo and J. M. Saveant, *J. Electroanalyt. Chem.*, 1971, **33**, 419.

[12] J. N. Ride, unpublished data.

[13] B. E. Conway and E. J. Rudd, *Trans. Faraday Soc.*, 1971, **67**, 440.

[14] H. Agahigian, J. V. Maraveek, and H. Gauthier, *Canad. J. Chem.*, 1963, **41**, 194.

electrolyte are shown in Figures 1 and 2. The voltammogram for TBAP as base electrolyte shows a well formed cathodic peak, as expected, corresponding to the diffusion controlled reduction of acetophenone in a one electron process. The smaller anodic peak shows that, at the sweep speed employed, the anion radical has sufficient stability to give an anodic wave. The voltammogram for the lithium perchlorate base electrolyte shows, by comparison, clear evidence for ion pairing and for an adsorption effect. The anodic shift of 160 mV in the cathodic peak potential is of the order of magnitude expected for strong ion pairing between the anion radical and the lithium cation.[15] The cathodic peak is very sharp (too sharp for a normal peak) and after the peak there is a rapid cut-off to a low value of current until the onset of amalgam formation produces another rise. This type of behaviour is often observed when there is strong adsorption of a species produced after the electron transfer step and in many cases the abnormally sharp peak is produced by adsorption effects related to those involved in polarographic maxima. The sudden decrease in current, *i.e.* an inhibition, is seen very clearly at lower sweep speeds (Figure 2). These deductions are confirmed by the behaviour observed in mixed base electrolytes. When lithium perchlorate is added to the TBAP solution to give a concentration of lithium cation comparable to that of the acetophenone, then two peaks are seen on the voltammogram. The first peak is very sharp and it corresponds in shape and potential to the single peak observed at high lithium concentrations. The second peak is a smaller amplitude version of the single peak observed using TBAP. It is proposed, therefore, that the first peak is due to process (1) where A stands for acetophenone, and the

$$A + Li^+ + e \longrightarrow [A^{\cdot -}Li^+]_{ads} \qquad (1)$$

second peak corresponds to process (2). Step (1) will be

$$A + e \rightleftharpoons A^{\cdot -} \qquad (2)$$

followed either by reaction between two adsorbed species to form pinacolate or by discharge of acetophenone on top of an adsorbed ion pair to form pinacolate, the latter being an electrochemical desorption step. As would be expected on the basis of this explanation, when lithium ion is present in large excess over the substrate, only a single peak is observed even when tetrabutyl ammonium ion is also present. In addition, for low lithium ion concentration, the process of ion pair formation should remove all of the lithium from the immediate vicinity of the electrode surface and thus inhibit amalgam formation at higher potentials. This effect is shown on the voltammogram, *i.e.* no rapid rise in current beyond -2.1 V and no reverse peak corresponding to removal of lithium from the amalgam.

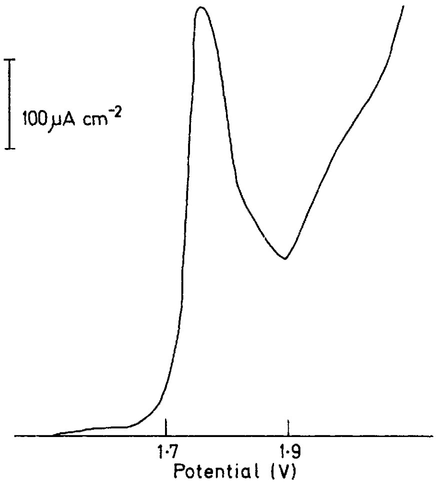

FIGURE 2 Linear sweep voltammogram at 0.01 V s^{-1} of a dry DMF solution containing 10^{-2}M-acetophenone with 10^{-1}M-$LiClO_4$ + 10^{-1}M-$Bu^t_4NClO_4$ mixed base electrolyte

Preparative Electrolysis.—The racemic : *meso* ratios for the acetophenone pinacol showing the effects of different support electrolytes and of varying amounts of water are shown in the Table together with some data from other work for comparison. The three support electrolytes lithium perchlorate, rubidium perchlorate, and TBAP together with the mixed electrolyte system were chosen to show up the effects of ion bridging and the effects of a strongly adsorbed layer of very large cations at the electrode surface. The variation of the racemic : *meso* ratio with the water content of the solvent depends markedly upon which electrolyte is present. Thus for lithium perchlorate and a very dry solvent, a value of 15 was found (slightly higher than found previously, presumably due to a lower residual water content) [7] but this fell rapidly on addition of small amounts of water. On the other hand, for TBAP, the addition of water produces a slow rise in the relatively low value of the ratio followed by a fall after *ca.* 10% water has been added. Rubidium perchlorate solutions gave quite high values of the ratio which were relatively insensitive to added water up to a concentration of *ca.* 10%, when a sharp fall was again observed. It is interesting to note that the highest selectivity towards the racemic product (19 : 1) was obtained using a mixed TBAP–lithium perchlorate electrolyte.

Dependence of the racemic : *meso* ratio of the pinacol on the catholyte composition

Electrolyte system	Racemic : *meso* ratio
80% EtOH–H_2O; 0.4M-HCl [a]	1.1
EtOH, 0.1M-TABP [a]	1.8
EtOH, 0.1M-LiCl [a]	2.6
DMF, 0.1M-TBAP [a]	4.1
DMF + 1 500 p.p.m. H_2O, TBAP	5.3
DMF + 3 000 p.p.m. H_2O, TBAP	5.6
DMF + 6 000 p.p.m. H_2O, TBAP	5.7
DMF + 15 000 p.p.m. H_2O, TBAP	6.6
DMF + 60 000 p.p.m. H_2O, TBAP	8.5
DMF + 150 000 p.p.m. H_2O, TBAP	7.9
DMF + 500 000 p.p.m. H_2O, TBAP	3.3
DMF, 0.1M-$LiClO_4$	15
DMF + 1 500 p.p.m. H_2O, $LiClO_4$	5.7
DMF + 6 000 p.p.m. H_2O, $LiClO_4$	5.5
DMF, $RbClO_4$	11.5
DMF + 1 500 p.p.m. H_2O, $RbClO_4$	9.5
DMF + 3 000 p.p.m. H_2O, $RbClO_4$	8.3
DMF + 15 000 p.p.m. H_2O, $RbClO_4$	8.3
DMF + 75 000 p.p.m. H_2O, $RbClO_4$	9.3
DMF + 300 000 p.p.m. H_2O, $RbClO_4$	3.6
DMF, 0.1M-TBAP, 10^{-3}M-$LiClO_4$	13.5
DMF, 0.1M-TBAP, 10^{-2}M-$LiClO_4$	19
DMF, 0.1M-TBAP 10^{-1}M-$LiClO_4$	14.5
DMF, 0.1M-$LiClO_4$, 10^{-3}M-TBAP	14
DMF, 0.1M-$LiClO_4$, 10^{-2}M-TBAP	12

[a] Ref 7

The linear sweep results and the results of preparative

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[15] M. K. Kalinowski, *Chem. Phys. Letters*, 1970, **7**, 55.

electrolyses confirm the explanation presented earlier [7] of the effects of ion bridging and hydrogen bonding on the stereochemistry of the coupling process and they also confirm that adsorption plays an important part in the mechanism. The effect of hydrogen bonding appears to be at its largest for TBAP solutions containing 60 000 p.p.m water. For a maximum effect one of each pair of coupling species needs to be protonated but in addition competitive hydrogen bonding to the solvent needs to be minimised. Thus larger amounts of water lead to a decrease in stereospecificity towards the values obtained in aqueous or ethanolic solutions. As would be expected, the ion-bridging effect of the rubidium cation is appreciably lower than that of the lithium cation in dry solutions, and, as a result, the addition of small amounts of water produces only a relatively minor drop in the stereospecificity in rubidium perchlorate solutions. The values of the ratio obtained for these solutions are comparable to the maximum value for wet TBAP solutions as might be expected from the competing effects of ion-bridging and hydrogen bonding. The effect of the addition of increasing amounts of lithium perchlorate to TBAP solutions is particularly interesting. The addition of only 10^{-3}M-$LiClO_4$ has a dramatic effect on the racemic:*meso* ratio, increasing the value from 4.1 to 13.5. Further increasing the concentration of lithium cation produces an enhancement of the ratio at 10^{-2}M and then a decrease at 10^{-1}M. This might be expected since the sterically directing effects of cationic bridging between two coupling anions will be greater than the effects between two ion pairs.

We are grateful for the assistance of Mr. P. F. G. Banfill and Mr. W. G. Blakey in carrying out preparative experiments. The provision of equipment by Professor L. Horner for carrying out the linear sweep experiments is also gratefully acknowledged.

[6/436 *Received, 3rd March,* 1976]