Stereochemical Factors in the Cathodic Pinacolisation of Acetophenone at a Mercury Pool

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The racemic : *meso* ratio for the pinacol product from the reduction of acetophenone at a mercury cathode has been determined as a function of solvent composition and electrolyte type. It is proposed that the stereochemistry of the coupling process is strongly influenced by ion pairing when anionic intermediates are involved. and by hydrogen bonding in the case of neutral intermediates. The ratio was as high as 12·5 : 1 using dry dimethylformamide containing lithium perchlorate as electrolyte.

THE stereochemistry of the cathodic coupling reactions of organic compounds has received increasing attention during the past few years.[1,2] Particular interest has centred on achieving stereochemical specificity through the exploitation of special factors influencing electrochemical processes, *e.g.* the orientation of intermediates or reactants by direct adsorption on the surface of the cathode or by the electrical field in the double layer and orientation caused by the influence of a primary adsorbed layer of otherwise inert material. Stocker and Jenevein [3-5] have studied the factors affecting the racemic : *meso* ratio in the pinacol and glycol products from the hydrodimerisation of aldehydes and ketones. For the pinacol from acetophenone this ratio was found to change from 1·1 in acid solution to *ca.* 3·0 in alkaline solution.[3] It was proposed that the coupling species were two ketyl radicals in acid solution, and a ketyl radical with an anion radical in alkaline solution. The isomer ratio was explained in terms of the influence of hydrogen bonding between the coupling species on their relative orientations, the higher ratio observed for alkaline solutions being due to more effective hydrogen bonding involving anionic species. Support for the inter-

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[1] A. Bewick and D. Pletcher, Chem. Soc. Specialist Periodical Report, Electrochemistry, vol. 1. p. 98.

[2] A. Bewick and D. Pletcher, Chem. Soc. Specialist Periodical Report, Electrochemistry, vol. 2, p. 1.

[3] J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 1968, **33**, 294.

[4] J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 1968, **33**, 2145.

[5] J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 1969, **34**, 2807.

species hydrogen bridging mechanism was obtained from a study on the hydrodimerisation of 2-acetylpyridine.[5] In this system, the intermediate ketyl radicals form strong intramolecular hydrogen bonds which greatly reduces the interspecies bonding and leads to a preponderance of the *meso*-product. In the case of acetophenone, the stereoselectivity was essentially the same for mercury, copper, or tin cathodes and was independent of electrode potential. It was concluded that coupling took place in the solution away from the electrode surface and not between adsorbed species. Two problems concerning the conclusions of Stocker and Jenevein have already been pointed out;[1] no account was taken of the effects of the strongly hydrogen-bonding solvent on the coupling process, and the evidence against surface coupling carries little weight since strong adsorption would be expected on each of the three cathodes employed. Evidence for the importance of a surface process has been provided by Puglisi *et al.*[6] for the hydrodimerisation of benzaldehyde. The addition of adsorbable ions such as tetra-alkylammonium and iodide altered the racemic : *meso* ratio although neutral adsorbed molecules such as amyl alcohol had no effect and none of these species affected the analogous photochemical process. It should be pointed out, however, that at the rather high cathodic potentials employed in the process, the adsorption of iodide ions and amyl alcohol would be slight. Further strong evidence for the importance of adsorbed intermediates is provided by the kinetic studies of Conway *et al.*[7,8] and Brown and Lister.[9]

Experiment	Potential w.r.t. s.c.e. (V)	Solvent–electrolyte system	Racemic : *meso* ratio	Tafel slope (mV)
1	−1·80	80% Ethanol–water, *ca.* 0·4M-HCl	1·1	
2	−2·49	Absolute ethanol, 0·1M-TBAP	1·8	127
3	−1·80	Absolute ethanol, 0·1M-LiCl	2·6	48
4	−2·22	DMF, 0·1M-TBAP	4·1	120
5	−2·28	DMF + 500 p.p.m. H_2O, 0·1M-TBAP	5·4	63
6	−2·31	DMF + 1500 p.p.m. H_2O, 0·1M-TBAP	6·2	70
7	−2·28	Commercial DMF, 0·1M-TBAP	7·6	23
8	−2·25	DMF + 1500 p.p.m. H_2O + 500 p.p.m. pyridine, 0·1M-TBAP	5·0	52
9	−2·16	DMF + 1500 p.p.m. H_2O + 2500 p.p.m. pyridine, 0·1M-TBAP	6·3	52
10	−2·22	DMF, 0·1M-$LiClO_4$	12·5	
11	−2·19	DMF + 1500 p.p.m. H_2O, 0·1M-$LiClO_4$	5·7	
12	−2·22	DMF + 1500 p.p.m. H_2O, 0·1M-tetrabutylammonium iodide	4·1	124

The present study is an attempt to obtain further insight into the validity of the interspecies hydrogen-bonding mechanism and the way in which this is modified by adsorbed species. An aprotic solvent, anhydrous *NN*-dimethylformamide (DMF), was chosen as a starting point so that the effects of adding increasing amounts of water could be observed.

While the work was in progress, a note was published[10] on the pinacolisation of acetophenone in DMF and acetonitrile. However, slightly wet (unpurified commercial) solvents were employed and the effects of very aprotic conditions were not studied.

EXPERIMENTAL

Procedure.—Potentiostatic electroreduction of acetophenone was carried out at a mercury cathode (area *ca.* 7 cm^2) at 19 ± 1 °C in a cell with a separator between anolyte and catholyte. A solution containing acetophenone (1·3 ml) was made up to 100 ml with a solution that was approximately 10^{-1}M in supporting electrolyte. An electronic coulometer was attached to the potentiostat and current was passed until almost complete reduction (pinacol assumed) had occurred. Excess of solvent in the catholyte solution was then evaporated, and, in the case of DMF, the work-up involved treatment with *ca.* 10^{-1}M-hydrochloric acid (25 ml) and extracting at least three times with portions (20 ml) of diethyl ether. The ether was then dried (Na_2SO_4) and removed; the residue was analysed by n.m.r. spectroscopy following the procedure of ref. 3. This spectrum corresponded almost exactly with that given in the literature.[11] It was generally found unnecessary to neutralise any excess of acid which might have been introduced. For other solvents no hydrochloric acid was added.

Materials.—Acetophenone was distilled under reduced pressure and stored in a dry-box before use. DMF was dried by using molecular sieves followed by distillation under reduced pressure and then stored in a dry-box. Absolute alcohol was reagent grade. Tetra-n-butylammonium perchlorate was dried in a vacuum oven before use at *ca.* 60 °C and lithium perchlorate was dried by the method described by Meibuhr.[12] No special precautions were taken in drying tetra-n-butylammonium iodide or lithium chloride, although the latter is known to be deliquescent.

RESULTS AND DISCUSSION

The results are given in the Table and they include values for the Tafel slopes which may be compared with those of Conway *et al.*[7,8] for varying water content in water–methanol mixtures.

The major features of the results are the very high value for the racemic : *meso* ratio for dry DMF containing

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[6] V. J. Puglisi, G. L. Clapper, and D. H. Evans, *Analyt. Chem.*, 1969, **41**, 279.

[7] B. E. Conway, E. J. Rudd, and L. G. M. Gordon, *Discuss. Faraday Soc.*, 1968, **45**, 87.

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

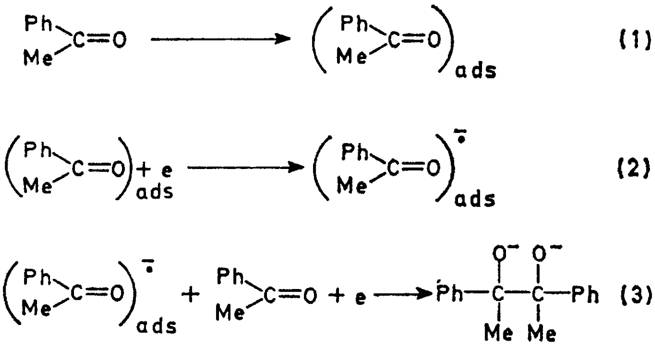
[9] O. R. Brown and K. Lister, *Discuss. Faraday Soc.*, 1968, **45**, 106.

[10] J. H. Stocker and R. M. Jenevein, *Coll. Czech. Chem. Comm.*, 1971, **36**, 925.

[11] H. Agahigian, J. F. Maraveck, and H. Gauthier, *Canad. J. Chem.*, 1963, **41**, 194.

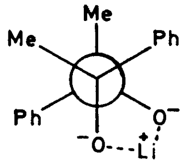
[12] S. G. Meibuhr, *J. Electrochem. Soc.*, 1970, **117**, 56.

lithium perchlorate electrolyte, expt. 10, and the dramatic fall on the addition of water, expt. 11; the increase in the ratio with increasing water concentration when the electrolyte is tetra-n-butylammonium perchlorate (TBAP), expts. 4—7; and the low value of the ratio for ethanol–lithium chloride compared with DMF containing lithium perchlorate. In order to attempt an explanation of the results, it is important as a first step to establish whether the coupling process occurs on the electrode surface and involves adsorbed species or if it occurs in the bulk solution. The former route is strongly indicated by the observed effects on the stereospecificity of the strongly adsorbed quaternary cation by iodide ion which is known to increase this adsorption [13,14] and the effect of pyridine. However, this is unlikely to be a simple coupling of two adsorbed radicals as envisaged by Conway *et al.*[7,8] A consideration of the molecular geometry shows that two species adsorbed with the aromatic ring parallel to the cathode surface (the orientation invariably observed for molecules of this type on mercury) would be unlikely to couple for steric reasons. It would be necessary for one of the species to be desorbed. In view of this, the most likely coupling mechanism is an electrochemical desorption process in which a ketone molecule is reduced while sitting on top of an adsorbed intermediate [step (3)].

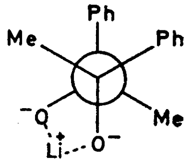


On this basis, the present results can be explained in terms of the nature of the adsorbed species, anion radicals or neutral radicals, and their ability to form hydrogen-bonded bridges or ion-paired bridges with the second species.

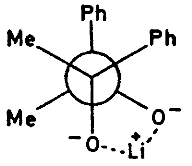
In the aprotic system, dry DMF with lithium perchlorate electrolyte, the adsorbed intermediate will be the anion radical which should readily form a contact ion pair with a lithium cation,[15,16] and this neutral species will be more strongly adsorbed. When a ketone molecule is reduced on top of this ion pair, the resulting anion radical will be most likely to be orientated to maximise the electrostatic interaction with the lithium cation of the ion pair thus favouring coupling to the racemic product. The transition state for the electron transfer step might well involve the lithium cation. There are three possibilities for the coupling step involving bridging by the lithium ion. Of these, (1) will be more favoured since it minimises interaction between the aromatic rings. This is similar to the interspecies hydrogen bonding of Stocker and Jenevein [3] but the effect will be much stronger (energies >10 kcal mol^{-1} are to be expected for ion pairing to the lithium cation [16] compared with 5 kcal mol^{-1} for hydrogen bonding) and will lead to a very high racemic : *meso* ratio as is observed. The same scheme with much weaker ion-pairing effects can be applied when the lithium cation is replaced by the tetrabutylammonium ion. The *meso*-configuration will now be much more important, particularly since configurations related to (4) will be favoured in the absence of cation bridging or hydrogen bonding effects. As water is added to the DMF–lithium perchlorate system, the adsorbed species will become increasingly protonated to the neutral radical, with a consequent reduction in the ion-pairing effects. As a result, interspecies hydrogen bonding will become increasingly important in directing the coupling reaction. The results show that the race-



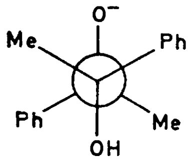
(1)
yields racemate



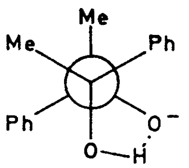
(2)
yields racemate.



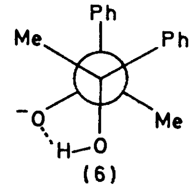
(3)
yields *meso*-compound



(4)
yields *meso*-compound



(5)
yields racemate



(6)
yields racemate

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[13] M. A. Devanathan and M. J. Fernando, *Trans. Faraday Soc.*, 1962, **58**, 368.

[14] Tsa-Chuan-Lin and Z. Jofo, *Doklady Akad. Nauk S.S.S.R.*, 1959, **125**, 125.

[15] L. A. Avaca and A. Bewick, *J. Electroanalyt. Chem.*, 1973, **41**, 405.

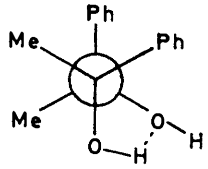
[16] N. Hirota and S. I. Weissman, *J. Amer. Chem. Soc.*, 1964, **86**, 2538; K. S. Chen, S. W. Mao, K. Nakamura, and N. Hirota, *ibid.*, 1971, **93**, 6004; M. Szwarc, *Accounts Chem. Res.*, 1969, **2**, 87.

mic : *meso* ratio falls sharply but remains higher than in hydrogen-bonded solvents, expts. 1 and 2. In these two cases, hydrogen bonding to the solvent will weaken the effects of the bonding between the coupling species.

A different effect is observed as water is added to the DMF–TBAP system since the strongly adsorbed quaternary cations maintain relatively anhydrous and aprotic surface conditions. At lower water concentrations, the adsorbed species will be the non-protonated anion radical whereas the anion radical resulting from electron transfer to the oncoming ketone molecule will be in a protic environment and conversion into the radical will occur. Thus there is a slow increase in the racemic : *meso* ratio with increasing water content as the stronger hydrogen bonding in structures (5) and (6) replaces the very weak ion-pairing interactions. The result for commercial DMF and 0·1M-TBAP agrees closely with that obtained by Stocker[10] for 0·25M-tetraethylammonium bromide in the same solvent. Replacement of perchlorate by iodide, expts. 6 and 12, causes more efficient exclusion of water from the surface layer due to enhanced adsorption of tetrabutylammonium cations and the ratio decreases accordingly.

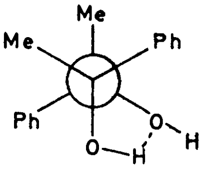
At higher water concentrations, it would be expected that structures (7)—(9), in which the hydrogen bonding is weaker, would become important thus causing a drop in the racemic : *meso* ratio. The interspecies bonding will be weakened still further due to competition with hydrogen bonding to the solvent system.

Although the results for DMF–water mixtures do not extend to a sufficiently high water concentration to show the position of the maximum in the racemic: *meso* ratio expected from these effects, the results for expt. (2) can be taken as a very strong indication that there must be a fall at high water content.



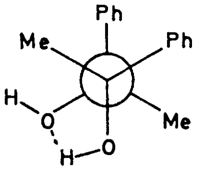
(7)

yields *meso*-compound



(8)

yields racemate



(9)

yields racemate

The Tafel slopes do not provide any further hard evidence for or against the proposed mechanism. This mechanism would lead to values between 40 and 120 mV depending upon the surface coverage of the adsorbed intermediate and the nature of its adsorption isotherm. The measured values lie within this range.

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