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ELECTROPINACOLIZATION; THE ROLE OF TETRAALKYLAMMONIUM SALTS

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Pinacolization of ketones, an underestimated method[1] to double a carbon skeleton, is usually carried out with the aid of amalgams of alkaline earth metals such as Mg and Al. The reduction can also be accomplished electrochemically but in both cases the yields are rather low; often more than 50 % of the subsequent reduction product - the alcohol - is formed. The results obtained by Stocker[2], who studied the racemic/meso ratio of the pinacoles generated in relation to the nature of the electrolytic medium, suggest that the selectivity towards pinacol might be increased by using aprotic media.

During our studies of the mechanism of the electron-induced catalytic nucleophilic aromatic substitution[3] we discovered a convenient and efficient method for electropinacolization which we further investigated. Electroreduction of acetophenone on mercury in carefully dried acetonitrile, in the presence of quaternary ammonium compounds as conducting salts afforded almost quantitative yields of acetophenone pinacol (see Table I). The reaction was found to be almost independent of the potential: even at -2.30 V no alcohol could be detected. The high yield of pinacol was ascribed to the absence of protons since a similar yield (98 %) of the pinacol was obtained when the reduction was carried out in acetonitrile containing 14 % 0.1 N KOH in water (-2.00 V, 1.35 F/mol, 0.1 M TEAP).

Table I. Electropinacolization of a number of ketones

Ketone	Conducting salt[a]	V vs.SCE	Charge passed, F/mol	Conversion,	Yield, %	
				%	Pinacol	Others
$\Phi COCH_3$	$\underset{\sim}{1}$	-1.83	1.40	100	98	b
	$\underset{\sim}{1}$	-1.90	1.25	100	98	b
	$\underset{\sim}{1}$	-2.00	1.20	78	91	b
	$\underset{\sim}{1}$	-2.30	1.45	100	98	b
$\Phi COCH(CH_3)_2$	TEAI	-2.30	2.50	100	68	$\Phi CHOHCH(CH_3)_2$, 17 %
	$\underset{\sim}{1}$	-2.30	1.88	92	62	$\Phi CHOHCH(CH_3)_2$, 30 %
$\Phi CO(CH_2)_4CO\Phi(\underset{\sim}{5})$	TEAP	-2.30	2.14	100	82($\underset{\sim}{6}$)	
$BrC_6H_4COCH_3$	TEAP	-2.00	2.00	100	10[c]	$\Phi COCH_3$, 70 %

a. Conducting salt $\underset{\sim}{1}$: $\Phi CHOHCHCH_3N^{\oplus}(CH_3)_3I^{\ominus}$; TEAI: tetraethylammonium iodide; TEAP: tetraethylammonium perchlorate. Concentration 0.05 M in dry CH_3CN.
b. No alcohol could be detected by NMR. c. Acetophenone pinacol.

The catalytic role of protons in ketone reductions is well established[4]. Our adsorption measurements[5] suggest that in aprotic media the role of the proton is taken over by the tetraalkylammonium ion (intimate ion pair formation). This is further substantiated by our observation that in dry acetonitrile/LiF the electron transfer to acetophenone is completely inhibited (see Fig.1) whereas in the presence of tetraethylammonium ions a distinct reduction peak is found. Under these aprotic conditions the coulostatic repulsion of two ketyl radical anions **2b** is sufficiently reduced to allow recombination, although the transfer of a second electron to **2b** is still prohibited. In a protic environment, the protonated ketyl radical **2a** is no longer repelled from the cathode and accepts a second electron to give anion **3**, resulting in alcohol formation, or it dimerizes to give pinacol **4**.

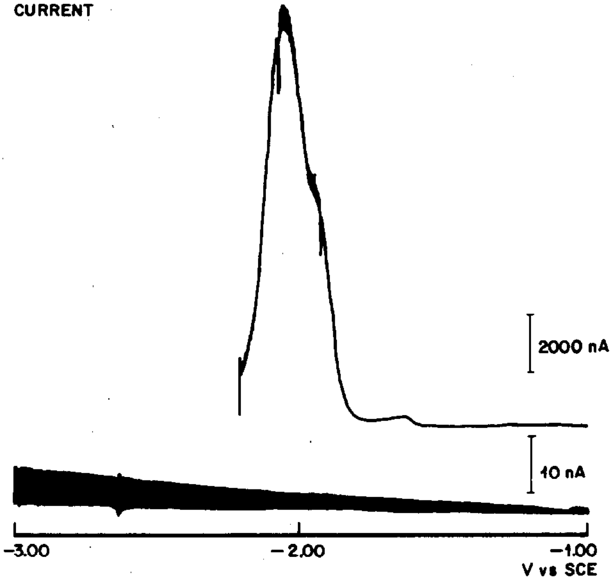
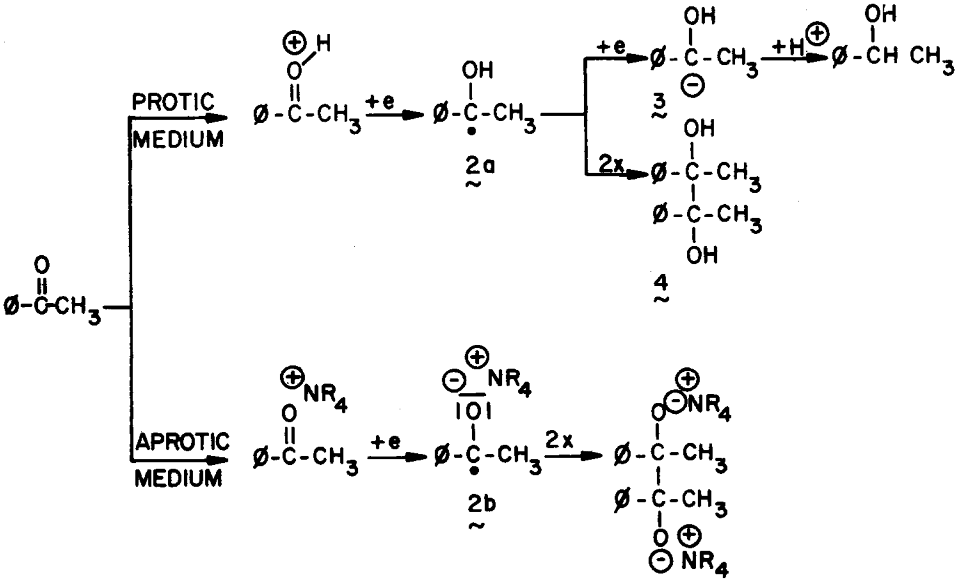


FIGURE 1

AC-polarogram (amplitude 1mV, frequency 30 Hz) of the electroreduction of acetophenone (0.08 M) in dry acetonitrile. Lower trace: 0.05 M LiF; upper trace: 0.05 M LiF + 0.05 M TEAP. Note the difference in sensitivity between both traces.

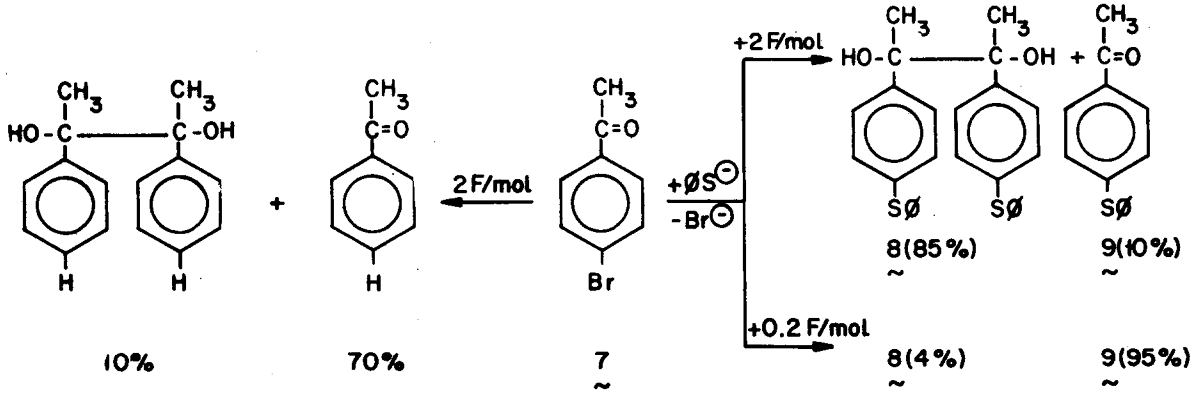


Further support for this mechanism was obtained from the following considerations and findings.

It is known from the literature that steric crowding in the ketone strongly influences the pinacol/alcohol ratio in the products in that it promotes the formation of the alcohol. Isobutyrophenone *e.g.* was reported by Horner[6] to yield only 13 % of pinacol (the amount of pinacol could be increased by using N-methylephedrine-hydrochloride). Under aprotic conditions, however, we obtained a 68 % yield of pinacol and only 17 % of the corresponding alcohol (Table I). The essential role of protons in the reduction of ketones to alcohols becomes evident from our observation that under comparable conditions, in the presence of a conducting salt that possesses an alcoholic moiety (1), the yield of alcohol increased from 17 to 30 % at the cost of the pinacol yield.

The potential applicability of our method is evident from the intramolecular pinacolization observed in the reduction of 1,6-diphenylhexa-1,6-dione 5 in aprotic media, which gave 82 % yield of 1,2-diphenyl-1,2-dihydroxycyclohexane 6.

In the literature there is much confusion[7] concerning the question whether the pinacolization occurs in the bulk of the solution or at the surface of the cathode. We here report clearcut evidence in support of the former type of process. When *p*-bromo-acetophenone 7 was reduced in acetonitrile using 2F/mol we observed a 100 % conversion of the starting material. No p-bromoacetophenone pinacol was formed, however, and a 70 % yield of acetophenone together with 10 % of acetophenone pinacol was obtained instead. Apparently, the bromide atom of 7 was first reductively splitt off and part of the acetophenone formed was, subsequently reduced to pinacol. When this reduction was carried out in the presence of thiophenolate anions (2F/mol) we obtained a 85 % yield of substituted pinacol 8 together with only 10 % of substituted acetophenone 9 (Table II).



As reported previously[3] an almost quantitative yield of the substitution product 9 is obtained if a current of 0.2 F/mol is applied. Under these catalytic conditions the yield of 9 proved to depend on the substrate (7) concentration. We have now found (Table II) that this yield (9) is also inversely related to the amount of pinacol (8) formed, (*i.e.* an increased substrate concentration increases the chain length of the reaction and thus reduces the yield of the

TABLE II. Relation between propagation and termination (substitution and pinacolization) in the nucleophilic substitution by $\Phi S^{\ominus}$ of p-bromoacetophenone **7**

[**3**] mmol/l	Charge, passed, F/mol	Yield, %	
		$\Phi S\text{-}C_6H_4COCH_3$ (9)	$(\Phi SC_6H_4C(OH)CH_3)_2$ (8)
4.5[a]	0.21	50	25
9.0[a]	0.20	60	19
13.5[a]	0.20	68	9
18.0[b]	0.20	95	4
9.0[a]	2.00	10	85

a. 0.05 M TEAP, 0.13 M TEAH (tetraethylammonium hydroxide) in CH_3CN/H_2O 93/7.
b. 0.05 M TEAP, 0.25 M TEAH in CH_3CN/H_2O 90/10.

termination product (**8**). Therefore, the pinacol **8** must originate from termination, which certainly does not take place at the electrode surface, particularly, because we never observed the formation of any bromo-substituted pinacol, even in the initial stages of the (catalytic) reaction.

In our opinion our conclusions have important implications for the electro-reduction of ketones, e.g. (1) they show that optimal yields of pinacols are obtained under strictly anhydrous conditions in the presence of tetraalkylammonium ions, and (2) they explain why the reduction of ketones in the presence of asymmetric conducting salts never[8,9] showed asymmetric induction in the pinacols (in protic media: dimerization of **2a**) although asymmetric induction was observed in the alcohols obtained (process occurring at the electrode surface).

In a subsequent letter we will show that under carefully chosen conditions considerable asymmetric induction in electro-generated pinacols is observed.

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