

ELECTRON-INDUCED CATALYTIC NUCLEOPHILIC AROMATIC SUBSTITUTION

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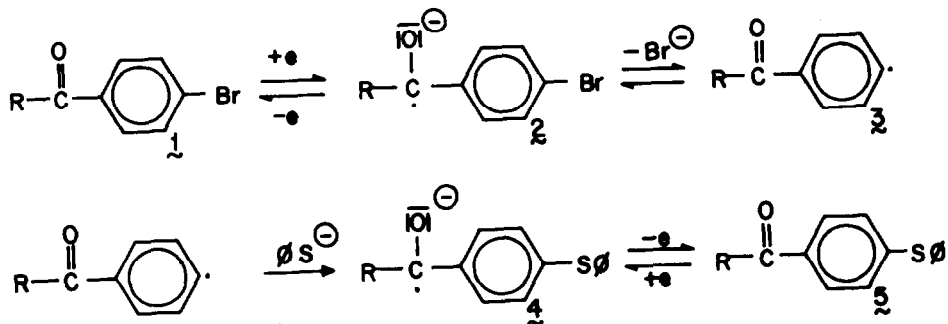
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(Received in UK 1 April 1977; accepted for publication 5 May 1977)

Anodic nucleophilic aromatic substitution suffers from the fact that usually the (mono-) substituted products exhibit lower oxidation potentials than the starting material. Polysubstitution therefore cannot be prevented unless conversion is restricted to rather low percentages. Cathodic nucleophilic substitution, first reported by Savéant and coworkers¹, is not hampered by this drawback. Being furthermore catalytic in nature with respect to the electrons used, this interesting reaction seemed worth further investigation.

The mechanism preferred by Savéant is as follows:



According to this mechanism, the substitution takes place by attack of ΦS^- generated from equimolar amounts ΦSH and Et_4NOH on the electrophilic radical $3(R = \Phi)$. Since use is made of the exchange current to re-oxidize $4(R = \Phi)$, in principle no current is used for the substitution.

New experiments yielded results inconsistent with this mechanism and suggested the occurrence of a radical chain due to electron transfer from 4 to 1 , a mechanism similar to the $S_{RN}1$ mechanism previously established by Bunnett². Which mechanism is the true one may be of importance with respect to the applicability of the reaction. In Savéant's mechanism the exchange current is a fundamental entity which can hardly be changed whereas if a radical chain mechanism is operative the reaction may be steered by means of the usual parameters such as concentration of reactants, temperature, etc.

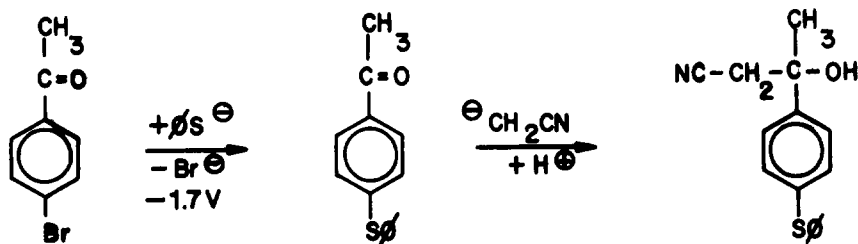
In order to discriminate between the two mechanisms we have investigated the effect of reduction potential on the yield of substituted product. As shown in Table I we did not observe a maximum yield (as required by Savéant's mechanism) when the reduction was carried out at E_2^1 (-1.70 V). Working at slightly more negative potentials even increased the yield, which might be due to the fact that relatively less current is lost as base current.

Table I
Effect of potential on the reductive substitution
of p-bromoacetophenone

Potential, V	Current, mA	Yield of $\underline{5}$ (R = CH ₃) %*
1.60	5	39
1.65	8	41
1.70	20	37
1.75	40	56
1.80	50	53

* obtained at 0.2 faraday per mole, calculated
on bromoacetophenone intake

We furthermore observed that any excess of thiophenol completely destroys the substitution process: the substrate p-bromoacetophenone loses bromide ions but the transient radical $\underline{3}$ is no longer attacked by ΦS^- and instead abstracts hydrogen atoms³ from ΦSH . This side-reaction is prevented by using an excess of tetraethylammonium hydroxide. In the presence of low concentrations of water this excess causes another side-reaction to occur. The carbonyl moiety of the substitution product is found to be attacked by $^{\ominus}CH_2CN$ ions, apparently derived from solvent acetonitrile⁴. Reduction of the basicity of the catholyte (>5 % H₂O) greatly suppresses this consecutive reaction.



We have also investigated the effect of substrate concentration on conversion and selectivity. From Table II it is apparent that the increase in substrate concentration enhances the conversion and selectivity. This observation, which contradicts Savéant's exchange current mechanism, is consistent with a bimolecular radical chain mechanism terminated by e.g. recombination of the chain-carrying radicals (see Scheme). In this mechanism tetraalkylammonium ions play a role similar to that of H^+ in carbonyl reductions. The catalytic nature of the reaction is no longer ascribed to the exchange current¹, but to disproportionation of the radical anion $\underline{4}$ with starting material (4). The length of the radical chain is limited by termination reactions such as reaction (5). Indeed the corresponding pinacol $\underline{6}$ was obtained as the main by-product. When about 1.5 faraday per mole was forced through the reactants under the same conditions, the yield of $\underline{6}$ was found to be almost quantitative. Furthermore, we found the current (Table II) to be independent of substrate concentration, which points to the occurrence of adsorbate on the electrode surface. p-Bromoacetophenone was found by tensammetry to adsorb strongly as a complex with tetraalkylammonium

Table II

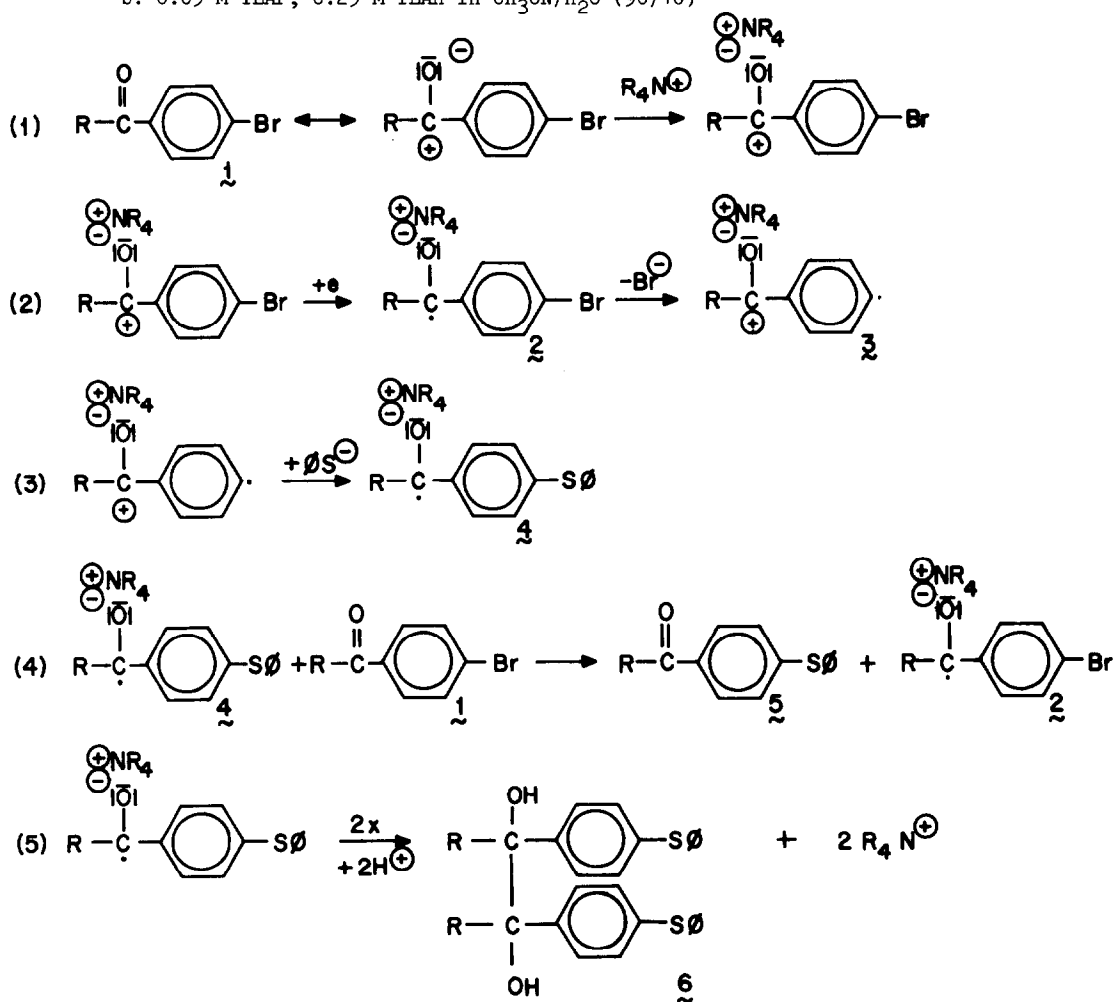
Effect of substrate concentration on the conversion and selectivity of the thiophenolation of p-bromoacetophenone (-1.70 V vs SCE)

[Substrate], mmol/l	Current, mA	Charge passed, F/mol	Conversion of 1(R = CH ₃), %	Selectivity to 5(R = CH ₃) %
4.5 ^a	28	0.21	50	50
9.0 ^a	32	0.20	60	60
13.5 ^a	27	0.20	90	68
18.0 ^b	42 ^b	0.20	100	95

a. 0.05 M tetraethylammoniumperchlorate (TEAP)

0.13 M tetraethylammonium hydroxide (TEAH) in CH₃CN/H₂O (93/7)

b. 0.05 M TEAP, 0.25 M TEAH in CH₃CN/H₂O (90/10)



Scheme

ions onto a mercury electrode⁵. Direct evidence against Savéant's "exchange current" mechanism was obtained by measuring the exchange current. The usual procedure to determine exchange currents (by extrapolation of the Tafel plot) could not be adopted, since the electron transfer is insufficiently reversible. AC polarography⁶, however (300 Hz, 0.005 V amplitude, with phase-sensitive detection (0° to exclude capacitive double layer effects)), indicated the exchange current to be $<10^{-3}$ A.cm⁻², a current density which can only explain $\approx 2\%$ of the total product formation.

The mechanism proposed is essentially the same as the S_{RN}1 mechanism, of e.g. iodide replacement (by NH₂) in iodopseudocumenes, suggested by Bunnett². Important differences, however, are that in our case the electron is transferred to a side-chain substituent group and not to the aromatic nucleus, and that the initiation and termination reactions are well defined. Our results show that in addition to alkali metal⁷ and photochemical⁸ initiation, the S_{RN}1 radical-chain mechanism can successfully be initiated electrochemically.

From the proposed mechanism it appears essential that the reduction potential of 2 be equal to, or lower than, that of the starting material 1. This condition might limit the applicability of this interesting aromatic substitution. Work is in progress to extend the scope of this electrochemically initiated reaction with respect to the nucleophile and to aromatic substrates containing substituents other than carbonyl.

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