4210 J. Org. Chem. 1983, 48, 4210–4214

Cathodic Birch Reduction of Methoxyaromatics and Steroids in Aqueous Solution

Essie Kariv-Miller,* Karl E. Swenson, and Dvora Zemach

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received April 20, 1983

The electroreduction of methoxybenzene, 1,2,3,4-tetrahydro-6-methoxynaphthalene, and several aromatic steroids using aqueous tetrabutylammonium hydroxide solutions is described. The reactions proceed in high yields, and the corresponding dihydro products are formed. Temperature and electrolyte concentration were found to have a strong effect on the reaction rate. A direct electron transfer to the aromatics is unlikely, and a possible reduction mechanism involving the intermediacy of tetrabutylammonium amalgam is proposed.

Solutions of alkali metals in liquid ammonia or HMPA provide electrons that can be used to carry out difficult reduction reactions,[1] and the reactions of aromatic compounds in liquid ammonia, Birch reductions, have found a wide application in synthesis.[2] In steroid chemistry the Birch reduction of methoxy-substituted aromatics has proved to be especially useful.[3] Although the yields of 1,4-dihydroaromatics with the Birch method are often high, the experimental procedure is somewhat tedious, the solutions are strongly basic, and solubility of the reactant in the medium sometimes presents a difficulty.[3] Successful attempts have been made to electrochemically duplicate the Birch reduction of simple aromatics, using liquid ammonia,[4] low molecular weight amines,[5] and HMPA.[6] In these works lithium salts were used as electrolytes and lithium metal was formed at the cathode. Electroreduction of benzene and toluene in diglyme has also been reported.[7]

Following the pioneering work of Coleman and Wagenknecht[8] we have recently briefly described[9] initial attempts to develop an electrochemical alternative to the Birch reduction using tetraalkylammonium electrolytes and aqueous solutions. The advantages of electrochemical reduction in aqueous media as compared to the Birch conditions are obvious, and in view of our results the development of such an electroreduction should be possible. In this paper we present a complete description of results obtained using aqueous solutions of tetrabutylammonium hydroxide and a mercury pool cathode.

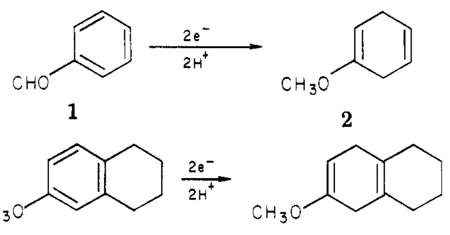
Results and Discussion

Studies have been performed with methoxybenzene and 1,2,3,4-tetrahydro-6-methoxynaphthalene as well as with several aromatic steroids. These studies involved preparative scale reductions in aqueous tetrabutylammonium hydroxide (TBA,OH). In many cases the dihydroaromatic product could be isolated in high chemical yield. The results on simple aromatics are presented first, followed by the steroid experiments. Particular attention has been paid to the temperature and electrolyte concentration and the effect of these variables on the current yield.

Table I. Effect of Temperature and TBA,OH Concentration on the Current Yields for the Reduction of 1 and 3 in Water

		current yield, %	
temp, °C	[TBA,OH], M	2	4
25	0.77	8	0
45	0.77	35	
60	0.77	50	28
90	0.77	45	29
25	1.54	25	19
60	1.54	55	40
60	0.39	36	0

Reduction of Methoxybenzene (1) and 1,2,3,4-Tetrahydro-6-methoxynaphthalene (3). Previous studies[8,9] had established that benzene could be reduced to 1,4-cyclohexadiene by using aqueous solutions of TBA,OH and a mercury cathode. We set out to demonstrate that the presumably more difficultly reduced methoxyaromatics would also produce dihydro products. In a typical experiment 5 × 10^{-3} mol of reactant was electrolyzed at 62 mA cm^{-2} for 55 min. The total amount of charge was equivalent to 3 Faradays mol^{-1}, and amounts of up to 15 g of 1 have been reduced. The initial reaction mixture consisted of two phases: the aqueous base and the organic substrate. While stirring and especially while heating, the mixture visually appeared as an emulsion, but when heating and stirring were discontinued, the two phases separated again. Samples consisting mostly of the organic phase were removed as the reaction progressed. These were extracted with ether and their composition was determined. The material recovery was 85% (±5%) based on the amount of reactant and assuming a reduction to the dihydroproduct. Upon complete conversion of the reactant, the average chemical yield of 2 was 80% and that of 4 85% of the corresponding isolated products. These chemical yields are comparable to those obtained with the classical Birch reduction conditions.[10,11]



---

[1] House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 145–227.

[2] Birch, A. J.; Rao, G. S. "Advances in Organic Chemistry"; Wiley-Interscience: New York, 1972; Vol. 8, pp 1–65.

[3] Dryden, H. L., Jr. "Organic Reactions in Steroid Chemistry"; Fried, J.; Edwards, J. A., Eds; Van Nostrand Reinhold: New York, 1972; Vol. 1, pp 1–60.

[4] Birch, A. J. *Nature (London)* **1946**, *158*, 60.

[5] Benkeser, R. A.; Tincher, C. A. *J. Org. Chem.* **1968**, *33*, 2727. Benkeser, R. A.; Kaiser, E. M.; Lambert, R. F. *J. Am. Chem. Soc.* **1964**, *86*, 5272. Benkeser, R. A.; Kaiser, E. M. *J. Am. Chem. Soc.* **1963**, *85*, 2858.

[6] Sternberg, H. W.; Markby, R. E.; Wender, I.; Mohilner, D. M. *J. Am. Chem. Soc.* **1969**, *91*, 4191. *J. Electrochem. Soc.* **1966**, *113*, 1060.

[7] Misono, A.; Osa, T.; Yamagishi, T.; Kodama, T. *J. Electrochem. Soc.* **1968**, *115*, 266.

[8] Coleman, J. P.; Wagenknecht, J. H. *J. Electrochem. Soc.* **1981**, *128*, 322.

[9] Swenson, K. E.; Zemach, D.; Nanjundiah, C.; Kariv-Miller, E. *J. Org. Chem.* **1983**, *48*, 1777.

[10] Birch, A. J.; Chamberlain, K. B. "Organic Synthesis"; Johnson, C. R., Ed.; Wiley: New York, 1977; Vol. 57, p 107.

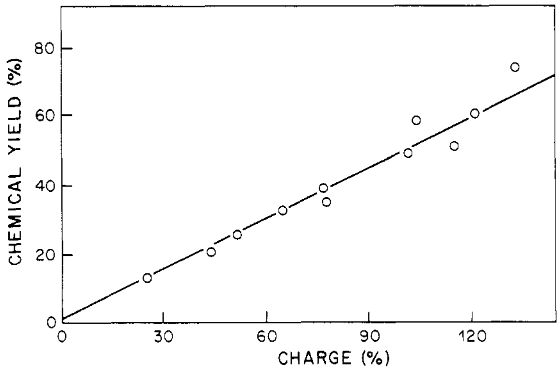


Figure 1. Yield of **2** during electrolysis of **1** at 60 °C. (0.06 mol in 50 mL of 0.77 M TBA,OH).

Table II. Current Yields for the Reduction of the Steroids **5** and **7**

reactant	[TBA,OH], M	solvent	temp, °C	current yield, % 6	current yield, % 8
5	0.77	aq	60	0	
5	1.54	aq	25	6	
5	1.54	aq	60	19	
5	0.77	aq	90	8	
5	1.54	aq	90	18	
7	0.77	aq	90		0
7	1.54	aq	60		0
7	1.54	aq	90		6
5	1.54	aq THF	25	11	
5	1.54	aq THF	60	24	
7	1.54	aq THF	60		24

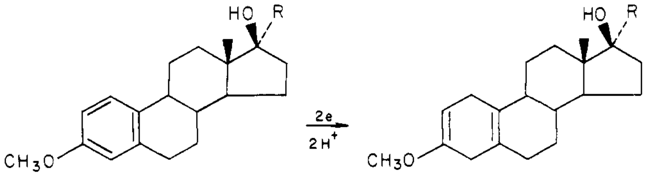
The amount of product **2** increased linearly with time as shown in Figure 1. The slope of this yield/charge plot reveals that the current yield, assuming $n = 2$, was 50% throughout the reduction of **1** under these conditions. Similar results were obtained for the buildup of **4** from **3**. In this case the current yield was 40%. The current yields of **2** and **4** were studied as a function of various reaction conditions. They were independent of the current density as shown by results obtained at 28, 42, 62, and 86 mA cm^{-2}. Current yields strongly depended on the electrolyte concentration and the temperature. As shown in Table I temperatures below 60 °C or lower TBA,OH concentrations gave less efficient reactions for both **1** and **3**.

Solubilization of **1** or **3** in the aqueous phase may be a limiting factor, and, specifically, increased solubility at higher temperatures may partially explain the significant temperature effect. Similarly, solubilization of the reactant in water by the TBA could be important. In this regard UV measurements at room temperature showed that the concentration of **1** in a saturated water solution was approximately 0.01 M. In 1 M aqueous TBA,OH the concentration of **1** was 0.2 M. In addition to solubilization of the organic by the bulky cation, the TBA,OH provides a basic solution, and this should increase the current yields by slowing hydrogen evolution. The importance of pH was demonstrated by titrating a 1.54 M solution of TBA,OH with 0.5 equiv of *p*-toluenesulfonic acid. This kept the [TBA] at 1.54 M, but made the medium less basic. The current yield of **4** at 25 °C decreased from 19% to 0%.

It is entirely possible, indeed likely, that TBA,OH plays a third role—that of a mediator. As indicated in the mechanistic scheme discussed below, reduction of TBA to a reactive amalgam is implicated in this reaction.

Steroid Reductions. As noted in the introduction, the Birch reduction has played an important role in the synthesis of steroids. In this study we have investigated several pertinent reactions. A major concern was whether the low water solubility of steroids would preclude their efficient reduction.

Positive results were obtained by using compounds **5** and **7**. The reduction of *β*-estradiol 3-methyl ether (**5**) was most satisfying. In a typical experiment 574 mg of (2.00 mmol) **5** was added to 20 mL of 1.54 M aqueous TBA,OH. When the mixture was stirred and heated to 60 °C it appeared to become an emulsion. Electrolysis was performed by using constant current of 62 mA cm^{-2} and an undivided cell (cathode area = 7 cm^2). It was continued for 45 min, at which point 6 Faradays mol^{-1} of charge had been transferred. Upon cooling to room temperature the reaction mixture separated again into two phases, but the aqueous base remained turbid. The mixture obtained was poured into water and extracted with ether. After removal of the solvent 527 mg (1.83 mmol) of **6**, which by NMR contained less than 5% **5** and no other impurities, was obtained. Recrystallizations from ethanol yielded 335 mg (1.16 mmol) of pure **6**.



5, 7 **6, 8**

5, **6**, R = H; **7**, **8**, R = C_2H_5

In Table II are the results from experiments in which the temperature and electrolyte concentration were varied by using **5** and **7** as reactants. *In all cases the chemical yields were >90%.* Similar trends were found as with the simple aromatics. That is, the current yield increased with temperature up to about 60 °C and a higher concentration of TBA,OH gave higher current yields.

Studies on the reduction of **7** were disappointing in that the current yields were extremely low. It seemed that this might result from a solubility problem and, therefore, some studies using a mixed solvent of THF and water were undertaken. Indeed, when THF (5 mL) was added to the 1.54 M aqueous TBA,OH (20 mL), the reactants dissolved and the current yields of the products increased. Moreover, the current yields of **6** and **8** which were 19% and 6% correspondingly reached the same value of 24% (Table II).

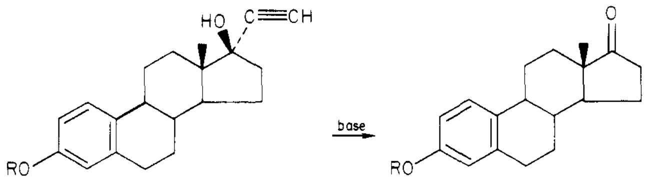
A number of other steroids were investigated less extensively than the methyl ethers **5** and **7**. Treatment of 17-ethynylestradiol 3-methyl ether (**9**) under conditions identical to electrolysis but with no charge transfer showed that it was unstable. It lost the ethynyl group and formed estrone **10**. A similar loss of ethynyl from **11** was reported[12] in the presence of NaOH. This conversion was enhanced by increasing the temperature and was negligible only at ~20 °C. At this temperature and conditions **9** could not be reduced. At 90 °C the ethynyl was completely lost and as expected the electrolysis product was **6**. The control experiment at 70 °C showed that the loss of the ethynyl was partial. The major electrolysis product at this temperature was **13** in which both the triple bond and the aromatic ring were reduced. It was identified by comparison with published IR and NMR spectra.[13] Samples taken at various reaction times hint that the reduction of the triple bond was faster than that of the aromatic ring. However, at 70 °C the reduction is complicated by the

---

(11) Wilds, A. L.; Nelson, N. A. *J. Am. Chem. Soc.* **1953**, *75*, 5360.

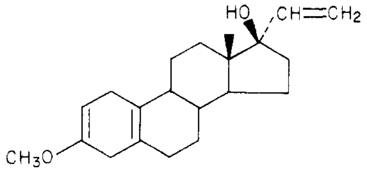
(12) Langecker, H. *Naturwissenshaften* **1959**, *46*, 601.

(13) Hiscock, A. K.; Whitehurst, J. S. *J. Chem. Soc.* **1965**, 5772.

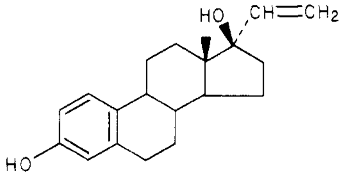


9, 11 **10, 12**

9, 10, $R = CH_3$; **11, 12**, $R = H$



13



14

reaction of **9** with the base and conclusive results could not be obtained.

The electrolysis of β-estradiol in 1.54 M TBA,OH at 70 °C led to the recovery of 38% of the starting reactant. Additionally a considerable amount of water and ether insoluble, brown, polymeric material was formed. In the corresponding control experiment, only unchanged reactant was recovered (87%). Since an undivided cell was used, it is possible that oxidation of the phenol at the anode led to the observed polymer. The triple bond of the phenol **11** could be reduced and **14** was formed and identified[14] but the chemical yield of the product was only 30%. This reaction was also complicated by the loss of the ethynyl group and the main identifiable byproduct was β-estradiol.

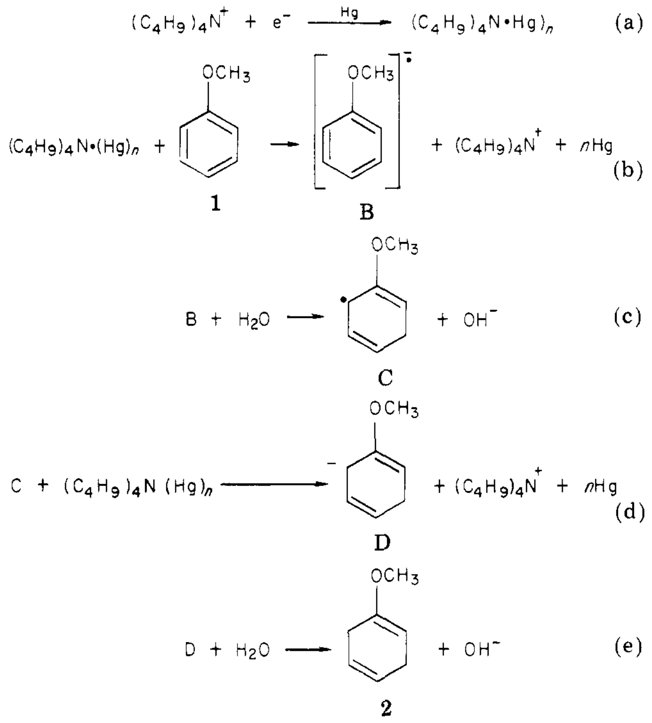
Mechanism. Although chemical Birch reductions have not been performed in aqueous solution, the structure of the dihydro products obtained chemically by using ammonia or electrochemically in water are identical. This suggests a similarity in mechanism. One mechanism for the electrochemical reaction, which exemplifies several appropriate ones, is given in Scheme I.

Steps b, c, d and e are analogues of the steps proposed[1-3] for the Birch reduction, and in effect, an electrogenerated amalgam (step a) takes the place of alkali metal.

In step c another isomeric radical might result. It is not shown, because it will carry on to the same product, **2**. In step d the radical **C**, which should be more easily reduced than **1**, could be reduced by the mercury electrode or by **B** formed near the surface instead of by amalgam. No data exists to differentiate these possibilities.

The unique aspect of this proposal is the TBA amalgam formed in step a. It was previously suggested that amalgams or solvated electrons might be involved.[8] Such amalgams have not been well-characterized[15] and in concurrent work we are attempting to elucidate this problem.

Scheme I



In the present study there are a number of observations that suggest an amalgam intermediate.

A dark grey solid was visually apparent during all these reactions. It "disappeared" after the circuit was disconnected. It was present in larger amounts at lower temperatures and in the absence of aromatic substrates. During experiments with a divided cell, the grey precipitate "settled" on the alundum cup which hung above the cathode and when taking the cell apart mercury was found in the alundum pores and sometimes in the anode compartment.

The cathode potential was measured periodically during each of the constant current reductions of **1**, **3**, **5**, and **7**. Similar results were obtained with all reactants and representative results for **3** are shown in Table III. The potential was rather constant throughout a single reaction and most values were in the range of 2.5 ± 0.4 V. There were occasional odd potential excursions (entry 1 Table III) but considering the heterogeneity of the medium and the low surface tension of mercury at this potential that is not surprising. Within the limits imposed by the crudeness of the measurement, the potential was the same at the beginning when all the reactant was present (E_{in}) and at the end when most of it was consumed (E_{end}). It was also independent of the substrate, the electrolyte concentration, and the temperature. These results could be rationalized by assuming that for the reduction of TBA step a determines the potential at constant current electrolysis. An even more interesting observation was made by discontinuing the current and measuring the potential of the working electrode at open circuit. The residual potentials thus measured were reproducible and in all cases the values were −2.1 ± 0.1 V. This is an indication that some relatively stable reductant was in contact with the working electrode both at the beginning ($E_{\mathrm{in}}^{\mathrm{res}}$) and after the reaction was completed ($E_{\mathrm{end}}^{\mathrm{res}}$). A strong support that TBA reduction produces an intermediate in the reduction of the organic substrates was found in the potential measurements taken during blank electrolysis of aqueous TBA,OH only. All potentials were similar to the corresponding values cited in Table III that were measured in

---

[14] Neudert, W.; Ropke, H. "Atlas of Steroid Spectra"; Springer-Verlag: Berlin, 1965; No. 795.

[15] Littlehailes, J. D.; Woodhall, B. J. *Discuss. Faraday Soc.* **1968**, *45*, 187. Horner, L.; Lund, H. "Organic Electrochemistry"; Baizer, M. M., Ed.; Marcel Dekker, Inc.: New York, 1973; pp 731-5. Fry, A. J. "Synthetic Organic Electrochemistry"; Harper and Row: New York, 1972; pp 189-191.

[16] Kariv-Miller, E.; Nanjundiah, C. *J. Electroanal. Chem.* **1983**, *147*, 319.

Table III. Potential Measurements during Preparative Electrolysis of 3 in Water[a]

[TBA,OH], M	current density, mA cm^{-2}	temp, °C	E_{in}[b]	E_{end}[b]	E_{in}^{res}[c]	E_{end}^{res}[c]
0.77	42	22	2.1	3.3	2.0	2.1
0.77	42	60	2.5	2.4	2.0	2.1
0.77	42	60	2.4	2.4	2.1	2.2
0.77	62	80	2.1	2.2	2.1	2.2
1.54	62	22	2.4	2.5	2.0	2.2
1.54	62	60	2.5	2.5	2.0	2.0

[a] All potentials are vs. SCE. [b] E_{in} and E_{end} are the potentials measured at the beginning and end of the electrolysis. [c] Residual potentials are the open circuit potentials measured when current was disconnected immediately after the beginning E_{in}^{res} and end E_{end}^{res} of electrolysis.

Table IV. Results of Preparative Electrolyses and NMR Peaks Used for Determining the Composition of the Reaction Mixtures at Various Reaction Times

reactant	NMR, ppm	product	NMR, ppm	chemical yield, %
1	3.70 (s, 3 H, OCH_3)	2	3.45 (s, 3 H, OCH_3)	80
3	3.77 (s, 3 H, OCH_3)	4	3.56 (s, 3 H, OCH_3)	85
5	6.85–6.65 (m, 2 H, H-2 and H-4)	6	4.65 (t, 1 H, J = 2 Hz, H-2)	90
7	6.86–6.55 (m, 2 H, H-2 and H-4)	8	4.60 (t, 1 H, J = 2 Hz, H-2)	90
9	6.80–6.45 (m, 2 H, H-2 and H-4), 2.60 (s, 1 H, H-21)	13	5.20–4.90 (m, 2 H, H-21), 4.50 (t, 1 H, J = 2 Hz, H-2)	40
11	6.70–6.45 (m, 2 H, H-2 and H-4)	14	5.12 (dd J = 18, 2 Hz), 5.10 (dd J = 10, 2 Hz)	30

the presence of the substrates.

We have previously reported[9] evidence from cyclic voltammetry for the intermediacy of an unstable oxidizable species formed by TBA,OH in the reduction of benzene in aqueous solution. Similar but more definitively interpretable results have been obtained on the formation of tetraalkylammonium amalgams in nonaqueous solution. The electrochemical behavior of dimethylpyrollidinium cation in DMF was investigated.[16] In that case, it was established that the reduction involved one electron per ammonium ion to produce an insoluble amalgam. This dimethylpyrollidinium amalgam in DMF is relatively stable, but will act to reduce organic substrates. Thus, there is considerable indirect evidence to support the mechanism exemplified by steps a–e.

Experimental Section

Materials and Purification Methods. Mercury (General Refineries, Inc.) was purified before use. The tetrabutylammonium hydroxide (TBA,OH) used for preparative electrolysis was a 1.54 M solution in water (Aldrich or Sigma). Aqueous TBA,OH (1.0 m), electrometric grade (Southwest Analytical), was used as a solvent for UV spectroscopy and electrochemical measurements. Methoxybenzene (**1**) (Baker), Baker grade, 1,2,3,4-tetrahydro-6-methoxynaphthalene (**3**) (Aldrich), technical grade, and the steroids **5**, **9**, **11**, (Sigma) and **7** (Steraloids) were used as substrates for reduction.

Cells and Electrodes. Two undivided cylindrical cells were used depending on the size of the sample. Both were 12 cm high, and mercury pools at the bottom served as the cathodes. The cathode areas were 28 cm^2 and 7 cm^2. Stainless steel wire coils (3 mm diameter) were used as anodes. The reference electrode was a SCE Fisher Scientific (catalog number 13-639-51) and was brought within 1 mm of the mercury surface. All potentials reported are vs. SCE. The cells were fitted with a reflux condenser and two inlets of gas allowed passage of nitrogen during electrolysis. When THF was used as a co-solvent a divided cell was necessary and Pt foil was the counter electrode. An alundum cup (Fisher AN 889) dipping into the cell served as the anode compartment and the anode was placed in it.

Instrumentation. Preparative electrolyses were performed at constant current with a Hewlett Packard 6266B or a Princeton Applied Research PAR-373 galvanostat and an Acromag Model 212-LX-1 coulometer. For electrochemical measurements a Princeton Applied Research PAR-173 potentiostat, PAR-175 universal programmer, and a Houston Omnigraphic 200 X-Y recorder were used. CV's at fast potential scan rates were recorded with a Physical Data, Inc. transient store recorder Model 512A.

NMR spectra were recorded on a Varian FT-80 or a Hitachi-Perkin Elmer R-24B by $CDCl_3$ and tetramethylsilane as an internal standard. IR spectra were determined with a Perkin Elmer 297 infrared spectrophotometer. UV spectra were measured at constant temperature with a Cary 17D spectrophotometer and a Lauda Brinkman RC-3 recirculating thermostated bath.

Preparative Electrolysis. Experiments were performed under nitrogen at constant current (28–86 mA cm^{-2}) and the cell was immersed in a constant temperature bath. TBA,OH (20–50 mL) of the appropriate concentration and substrate (2–139 mmol) were introduced into the cell. When a divided cell was used (THF co-solvent) the substrate was added only to the catholyte. The mixture was magnetically stirred and it was allowed to reach (~10 min) constant temperature prior to electrolysis. The potential of the working electrode was measured at the beginning, the end, and several times during electrolysis. The reference was an SCE dipping in the reaction solution. The potential was relatively constant during each electrolysis at ±0.4 V but varied from one electrolysis to another in the range of −2.0 to −3.3 V (SCE). The substrates did not dissolve but formed emulsions under the rapid stirring. Residual potentials were also measured and are shown in Table III. Those were obtained by measuring the open circuit potentials when the current was disconnected shortly after electrolysis began E_{in}^{res} and after electrolysis was complete E_{end}^{res}. They were different than the open circuit potentials measured before electrolysis (−0.3 V SCE). When the electrolysis solution was allowed to stand without current decay of the residual potential the original open circuit value was observed. At room temperature, a heavy grey solid (possibly TBA amalgam) formed immediately and could be seen "streaming off" the surface of the mercury. The precipitate was distinctly less obvious at higher temperatures. Samples of the organic phase were taken at various reaction times. The samples and the reaction mixtures obtained after completion were worked up in the same manner. They were poured into water and repeatedly extracted with ether. The combined ether extracts were washed with water and dried over $MgSO_4$. After removal of the ether, the residue was weighted and the mixture was analyzed to determine the products and their yields.

Identification of Products. For each reactant electrochemical reactions were run to completion and the pure products were isolated. **2**[10], **4**[11], **6**[17] and **8**[18] were compared to samples obtained

---

(17) Pelc, B. *Collect. Czech. Chem. Commun.* **1962**, *27*, 2706. Neudert, W.; Ropke, H. "Atlas of Steroid Spectra"; Springer-Verlag: Berlin, 1965; No. 677.

(18) Colton, F. B.; Nysted, L. N.; Riegel, B.; Raymond, A. L. *J. Am. Chem. Soc.* **1957**, *79*, 1123.

by Birch reduction of the corresponding reactants. **13**[13] and **14**[14] were identified by comparing their NMR and IR to published spectra. The products **2** and **4** were sensitive and rearomatized with time or when submitted to TLC or GC analysis. In these cases the yields (Table IV) were determined by NMR. Other yields quoted are for isolated products. The composition of reaction mixtures of less than 100% conversion was determined by NMR. Cyclohexane, δ 1.40 (s, 12 H), was used as an internal standard for the reaction mixtures of 1. For all others 1,1,2,2-tetrachloroethane, δ 5.90 (s, 2 H), was used. Integration was repeated several times and results were averaged.

Control Experiments. Each set of electrolysis conditions was accompanied by a blank experiment in which the substrate was exposed to all electrolysis conditions but no charge was transferred. The resulting mixture was worked up by the same procedure as described for preparative electrolysis. The isolated product was weighed compared to the original reactant and identified when different. Starting compounds were quantitatively recovered from control experiments with **1**, **3**, **5**, and **7**.

Solubility of Methoxybenzene (1) in Water and 1.0 M TBA,OH. A 25 mL volumetric flask was charged with 4.1433 g (0.03831 mol) of 1 in 25 mL of distilled water. This was thoroughly mixed and the layers allowed to separate. Then 1 mL of the aqueous layer was diluted to 10 mL. Examination of this solution by UV at 269 nm (by using UV spectrum [λ_{max} 269 (ϵ 1480)][19]) showed the concentration of 1 to be 0.013 M. In a similar manner the concentration of 1 in 1.0 M aqueous TBA,OH was measured to be 0.196 M.

Acknowledgment. Support of this work by the National Science Foundation and the Graduate School, University of Minnesota, is gratefully acknowledged.

Registry No. 1, 100-66-3; **2**, 2886-59-1; **3**, 1730-48-9; 4, 3469-31-6; **5**, 1035-77-4; **6**, 1091-93-6; **7**, 17550-03-7; **8**, 1042-57-5; **9**, 72-33-3; **10**, 1624-62-0; **11**, 57-63-6; **12**, 53-16-7; **13**, 4350-64-5; **14**, 7678-95-7; β-estradiol, 50-28-2.

---

[19] Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectrometric Identification of Organic Compounds", 3rd ed.; Wiley: New York, 1965; p 89.

Relative Reactivities of Hetaryl Radicals in Hydrogen Atom Abstraction and Nucleophilic Addition Reactions

John A. Zoltewicz* and George A. Locko

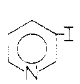
Department of Chemistry, University of Florida, Gainesville, Florida 32611

Received May 23, 1983

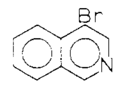
The 3-pyridyl, 4-isoquinolyl and 3-quinolyl σ radicals were generated photochemically from their corresponding halides in the presence of sodium methoxide and thiophenoxide in methanol. Each radical in competition abstracts a hydrogen atom from either methoxide ion or methanol or adds thiophenoxide ion. The corresponding reduction to substitution product ratios give rate constant ratios which are similar for the three hetaryl radicals, showing only a small influence of radical structure on relative reactivity. The thiolate ion is 2–5 times more reactive than methoxide ion; methoxide on the average is 39 times more reactive than methanol.

Little is known about the factors which influence the rates of addition of nucleophiles to aryl or hetaryl σ radicals. Some nucleophiles add with rates at or near the diffusion-controlled limit while many others simply do not react at all.[1-8]

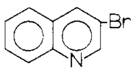
We report the results of quantitative experiments in which a thiolate ion adds to three related hetaryl radicals, two being benzologues of the first (see below). This addition competes with hydrogen atom abstraction by the radicals from the solvent. The much better understood hydrogen atom transfer reaction serves as a convenient reference for the addition reaction.



1



2



3

Results

Although our main focus is the competition between reduction and substitution, the reduction process also was studied exclusively with one substrate in order to learn how dehalogenation changes in the presence of a thiolate ion nucleophile and how photochemically initiated reduction compares with our earlier observations dealing with thermally induced reduction.[9]

Reductive Dehalogenation. 3-Iodopyridine (1) is rapidly reduced to pyridine when irradiated with Pyrex-filtered light in methanolic sodium methoxide. Observations indicate that (a) methoxide ion is required but that further addition in excess of about 1 equiv has little influence on the rate, (b) removal of dissolved oxygen produces a rate acceleration, and (c) reduction can be inhibited by 2-methyl-2-nitrosopropane.

When solutions of 1 without added methoxide ion are irradiated, the rate is very slow (Table I, run 1; hereafter references to table entries are designated as, for example, I-1). But in the presence of 2.2 M $NaOCH_3$ conversion to pyridine is rapid and complete (run I-2).

---

[1] Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

[2] Saveant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323.

[3] Rossi, R. A. *Acc. Chem. Res.* **1982**, *15*, 164.

[4] Wolfe, J. F.; Carver, D. R. *Org. Prep. Proced. Int.* **1978**, *10*, 225.

[5] Amatore, C.; Chaussard, J.; Pinson, J.; Saveant, J. M.; Thiebault, A. *J. Am. Chem. Soc.* **1979**, *101*, 6012.

[6] Galli, C.: Bunnett, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 7140.

[7] Tremelling, M. J.; Bunnett, J. F. *J. Am. Chem. Soc.* **1980**, *102*, 7375.

[8] Komin, A. P.; Wolfe, J. F *J. Org. Chem.* **1977**, *42*, 2481.

[9] Zoltewicz, J. A.; Oestreich, T. M.; Sale, A. A. *J. Am. Chem. Soc.* **1975**, *97*, 5889.

0022-3263/83/1948-4214$01.50/0