intensity) 232 (20), 201 (1), 136 (20), 121 (100); $[\alpha]_D$ -89.2° (c 1.01, $CHCl_3$). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.35; H, 6.97.

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Electrochemical Reduction of Nitroaromatics to Anilines in Basic Media: Effects of Positional Isomerism and Cathode Composition

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Introduction

This laboratory has previously reported a high yield synthesis of 3-amino-4-hydroxybenzoic acid via electrochemical reduction of the corresponding nitroaromatic in basic medium at a copper cathode.[1] The scope of reaction in basic medium, the effects of cathode material, and several electrochemical parameters have been investigated and a mechanistic hypothesis is proposed.

The electrochemical reduction of nitroaromatics with the goal of obtaining the aniline has classically been performed in acidic media. Basic conditions are sometimes desirable for solubility or because of process considerations. Synthetic endeavors in basic media have generally failed because of coupling reactions that form azoxy and other dimeric products. Reduction typically proceeds through nitroso and hydroxylamino intermediates to yield azoxy-, azo-, and hydrazobenzenes via coupling reactions and subsequent reductions.[2] Hydrazo benzenes cannot be reduced to the corresponding anilines in base under typical electrolytic conditions.

Many literature accounts indicate that azoxybenzene is obtained by electrolytic reduction of unsubstituted nitrobenzene in basic media at copper and most other cathode materials. The one exception recently reported by Belot et al.[3] is the conversion of nitrobenzene to aniline at a specially activated alloy ("Devarda copper"; 50% Cu, 45% Al, 5% Zn) at low current density (8 mA/cm^2) in 0.3 M KOH/MeOH (1.5% H_2O).

There are a few examples of the electrolytic reduction of substituted nitroaromatics to the corresponding anilines in basic media. Brown and Warner[4,5] and others[6,7] have shown that the conversion of *o*-nitrophenol to *o*-aminophenol proceeds smoothly in base. A series of cathode materials was investigated with the conclusion that copper is a suitable cathode for this chemistry only at low current density (20 mA/cm^2) while lead and zinc are the cathodes of choice at higher current densities. They also indicate the catalytic effect of Pb and Zn for reduction of nitrophenol as evidenced by the spongy surface of the electrode formed by redeposition of dissolved metal formed during the reduction.

Bradt and Hart[8] have shown that 3-nitro-4-hydroxytoluene can be converted to the aniline in sodium carbonate at a tin cathode in high yield. In contrast, Honda et al.[9] state that 2-hydroxy-4-nitrobenzoic acid cannot be converted into the aniline under basic conditions.

We report here that certain classes of ortho/para-substituted nitroaromatics give good yields of the corresponding anilines in base, *especially* when reduced at copper. High current densities (≫20 mA/cm^2) can be utilized to make this a practical synthetic procedure for consideration as more than a laboratory curiosity. Increased solubility, preclusion of Gatterman rearrangement chemistry, and ease of workup are advantages to electrochemical reduction in base for some of these compounds. A mechanistic explanation of the ortho/para effect is given and the electrocatalytic effect of copper is investigated.

Results

Cyclic Voltammetry. Voltammetry of the three isomers of nitrophenol at a glassy carbon electrode in 1 N NaOH is quite scan rate dependent. In strong base, a reversible wave at 100 mV/s is indicative of a relatively stable (on the voltammetric time scale) radical anion for the meta isomer whereas no reversibility is noted up to 1 V/s for the ortho and para isomers. Secondary reduction waves are observed for all isomers although that for the ortho isomer converges with the primary wave at low scan rates. Normal inert-electrode electron transfer is postulated at carbon.

Electrocatalytic reduction of nitrophenols at a copper electrode in the same solvent is illustrated in Figure 1. The upper portion of the figure shows a cyclic voltammetric scan at copper in 1 N NaOH with no organic substrate added which exhibits several surface waves which have been the subject of extensive investigations.[10-13] A voltammetric scan in the positive direction from a potential of -1.2 V exhibits an oxidation wave at -0.43 V that corresponds to formation of a film of Cu_2O that has barrier properties which limit its thickness. Continuing the scan to more positive potentials causes oxidation of this film and hence removal of the barrier allowing oxidation of the underlying copper surface to a much thicker film of $Cu(OH)_2$ and/or CuO (wave at -0.15 V). On the negative scan, the wave at -0.63 V corresponds to a partial reduction of the copper(II) surface species to a duplex oxide consisting of Cu_2O together with the remaining CuO. Finally, the wave at -0.99 V corresponds to reduction of the Cu_2O and CuO to copper metal.

Upon addition of 0.2 M nitrophenol to the electrolyte, the reductive surface wave at -0.95 V increases. (The voltammetry at glassy carbon indicates that reduction to the amine requires potentials 350-600 mV more negative than at copper for the para and meta isomers, which is

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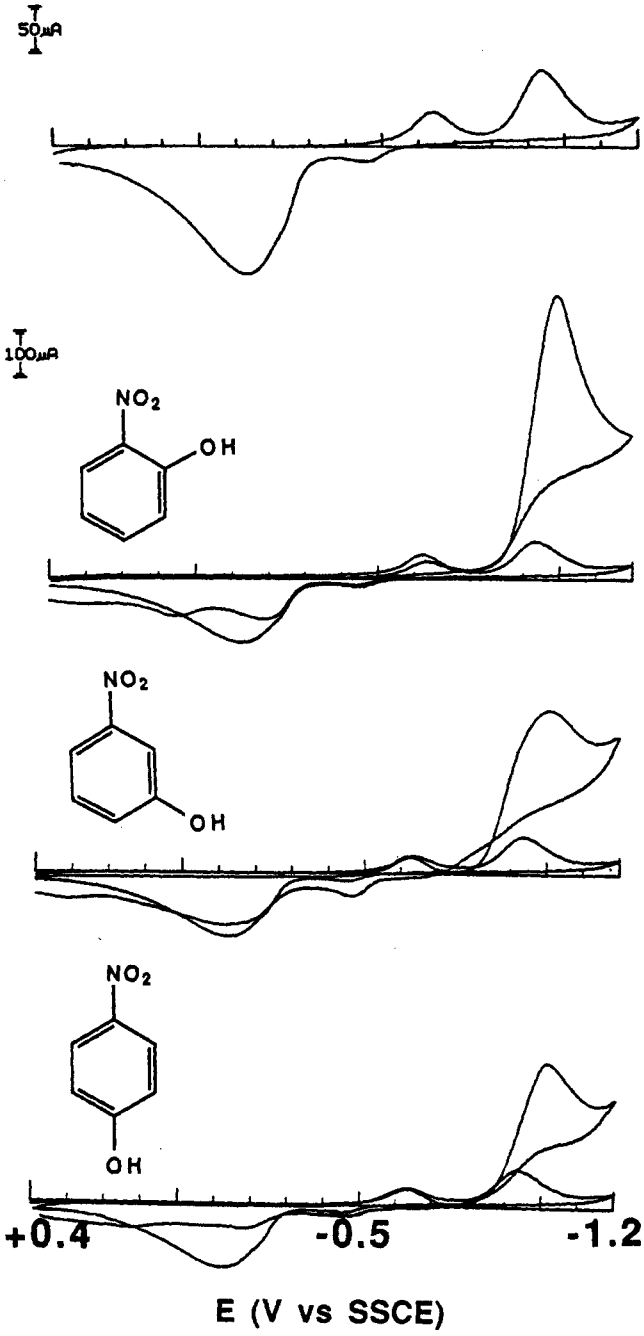


Figure 1. Cyclic voltammetry of nitrophenols at copper in 1 N NaOH at 100 mV/s: A = 1 N NaOH; B = 0.21 M *o*-nitrophenol; C = 0.18 M *m*-nitrophenol; D = 0.24 M *p*-nitrophenol.

indicative of kinetic limitations at carbon or electrocatalytic activity at copper.) On the positive scan, the surface wave at −0.15 V is attenuated. These effects are interpreted as follows: Cu metal generated at −0.95 V chemically reduces nitrophenol with formation of surface copper oxide and/or hydroxide. The surface oxidation wave at −0.15 V is attenuated on the positive scan because the copper surface is already oxidized by the organic. Hence electrolysis of nitrophenol at copper proceeds via chemical reduction with electrochemical regeneration of the copper surface—the reaction is electrocatalytic. The voltammetry of most nitroaromatics is probably similar at copper whereas significant potential shifts may be encountered at noninteractive electrodes such as carbon.

Analytical Coulometry. Controlled-potential coulometry in a divided cell is performed to determine the number of electrons (n) transferred to the various isomers

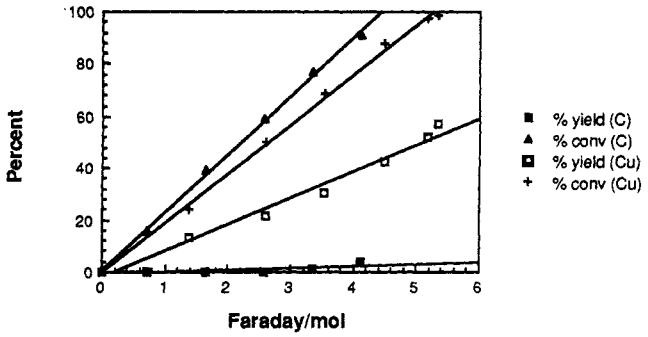


Figure 2. Percent yield and conversion of *m*-nitrophenol as a function of charge passed during controlled-potential electrolysis in 1 N NaOH. Initial *m*-nitrophenol concentration is 50 mM. Potential = −1.20 V for Cu and −1.70 V for carbon felt.

Table I. Coulometric Determination of *n* for Reduction of Nitrophenols[a] via Controlled-Potential Electrolysis in a Two-Compartment Cell in 1 N NaOH at Cu (−1.20 V) and at Carbon Felt (−1.70 V)

	ortho	meta	para
carbon	5.9 (0.3)	3.5 (0.3)	5.7 (0.2)
copper	5.85 (0.03)	5.12 (0.04)	5.8 (0.1)

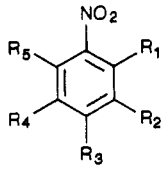
[a] Solute concentrations 4 mM. Sample standard deviation in parentheses, three determinations each. The standard deviations at carbon felt are slightly higher than those at copper because of the higher background current at more negative potentials (presumably hydrogen evolution) which is electronically compensated with a lesser precision.

of nitrophenol in basic medium at copper (electrocatalytic mechanism) and carbon (direct electron transfer mechanism). At copper the potential is controlled at −1.20 V (200 mV negative of the peak potential) whereas at carbon it is held constant at −1.70 V for all isomers (negative of the second waves observed in the voltammetric scans at 100 mV/s). The average results for three independent determinations for each isomer are tabulated in Table I.

The results at carbon (direct electron transfer) demonstrate that positional isomerism strongly affects the outcome. With the low concentrations (4 mM) used in these determinations, coupling reactions are probably minimal. Thus, at carbon, the meta isomer probably is reduced to the four-electron product (hydroxylamine) whereas the ortho and para isomers give the six-electron product (aniline). At copper there exists a statistically significant difference at the 95% confidence level between the number of electrons involved in the reduction of the meta isomer versus ortho and para. These results also indicate a significant difference in the product distribution for the meta isomer vs ortho/para, but the difference is much smaller than at carbon. In order to correlate the n values to product distributions, samples were taken during controlled potential electrolyses under conditions similar to those above and chromatographic analyses performed. The results at carbon and copper are shown in Figure 2. At carbon felt, 90% conversion of *m*-nitrophenol yields only 4% *m*-aminophenol while at copper the yield is over 50%. A higher yield of the aniline at copper is consistent with the higher n value reported above.

Significant yield of *m*-aminophenol during the reduction of *m*-nitrophenol in strong base is a surprising result, because the four-electron product (hydroxylamine) is not generally reducible unless protonated. It seems certain that these results are due to the electrocatalytic nature of the reduction at copper as distinguished from the effects of OH substitution, but more work is required to establish the detailed reaction mechanism.

Table II. Results from Galvanostatic Electrolysis of Various Substituted Nitrobenzenes in 1 N NaOH at a Copper Cathode at 80 mA/cm²



						6.0 F/mol		7.5 F/mol	
compd	R_1	R_2	R_3	R_4	R_5	% yield	% conv	% yield	% conv
1a	OH			CO_2H		85	83	89	93
2a	OH		CO_2H			88	92	96	100
3a		CO_2H	OH			83	89	89	96
4a	OH					81	86	97	97
5a[c]			OH			93	95		
6a		OH				44	81		
7a	CO_2H					24[a]	72		
8a			CO_2H			23	100		
9a		CO_2H				0[a]	100		
10a[b]	OMe					41	85	52	94
11a[b]			OMe			63	88	70	93
12a[b]		OMe				18	100	22	100
13a	OH			CH_3		73	88	92	95
14a	CH_3	OH				36	98	42	100
15a[c]	CH_3		OH			93	94	100	100
16a[c]	OH		CH_3			103	95	111	100
17a	OH				CH_3	85	89	101	100
18a[b]			OEt			60	90	68	100
19a[b]						25	90	28	92
20a[b]	Cl					49	95	48	100
21a[b]			Cl			30	91	33	100
22a[b]			CH_3					55	100
23a			SO_3H			14	99	13	100

[a] Terminated electrolysis at 4.5 F/mol. [b] Methanol added for solubility. [c] 60 °C. [d] Corresponding products listed as **b**, e.g. **23b**.

Preparative Results; Scope of Reaction. Several classes of nitroaromatics are subjected to galvanostatic reduction in basic media at a copper electrode. Table II summarizes the results. The presence of an *o*- or *p*-hydroxy substituent minimizes coupling products often encountered in electrolytic reductions of nitro compounds in base. Other substituents (OMe, OEt, Cl, and Me) in the ortho or para position also increase the yield of the aniline over that obtained from nitrobenzene, although to a lesser extent. Carboxylate and sulfonate substituents do not increase the yield of the corresponding aniline over that obtained from nitrobenzene itself, although it is interesting to note that there does exist a difference between meta and ortho/para substitution for the carboxylate case.

The effect of electrode material is not examined for all compounds but the results above indicate that copper yields significant quantities of anilines in the marginal cases (i.e., meta substitution) whereas electrodes showing only direct electron transfer do not. As previously reported, Pt, Ni, Pb, Sn, stainless steel, Co, Ag, carbon, and Cu are all efficient electrodes for the conversion of 3-nitro-4-hydroxybenzoic acid (an *o*-nitrophenol) to the aniline in a base (80–100 mA/cm²) with chemical yields of 80–95% and current efficiencies in the same range at 6 F/mol. However, Pb and Sn corrode to a significant extent due to an electrocatalytic mechanism in which the chemical reduction step appears to be somewhat faster than observed at Cu. (Cobalt is discolored, which indicates a similar phenomenon at a somewhat lower rate.) The other aforementioned electrodes appear to exhibit normal electron-transfer behavior.

Several parameters have also been examined for electrolysis of 3-nitro-4-hydroxybenzoic acid at a copper cathode as reported previously. Temperatures from 5 °C to 60 °C have minimal effect on the chemistry although the cell voltage is lower with increasing temperature. Electrolyte cationic and anionic speciation are not critical. For example, KOH, K_2CO_3, Na_2CO_3, and $NaHCO_3$ are all suitable electrolytes. Even with the mass-transfer limitations of the laboratory flange cell[14] only a relatively small effect on current efficiency is noted at current density from 20 to 150 mA/cm². In large-scale preparative flow cells with good mass transfer, we find high yields and current efficiencies at 135 mA/cm² (average current density) for 98% conversion of 10% solutions.

Discussion

Previous studies using mercury electrodes indicate that the mechanism and product distribution for the reduction of nitroaromatics in aqueous media is quite pH dependent.[15–25] In acid (pH <2), a six-electron reduction occurs

(14) The nitrogen purge mass transfer in the laboratory cell is not as efficient as parallel plate flow cells. For a discussion, see: Weinberg, N. L.; Tilak, B. V. *Technique of Electroorganic Synthesis, Part III*; Wiley & Sons: New York, 1982.

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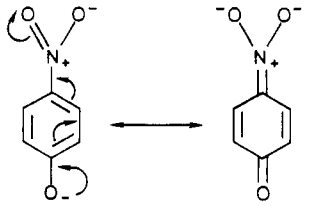
to form the aniline for nearly all nitroaromatics (exclusive of the Gatterman rearrangement, which occurs at a significant rate only at high temperatures) including the well studied, isomeric nitrophenols. This has been documented coulometrically, polarographically, and synthetically.

The pK_a's for the nitrophenols are 7.17, 8.28, and 7.15 (o, m, p, respectively). In alkaline solution, the phenate probably exists predominantly in the quinoid form for the ortho and para isomers. The radical anions of nitro-



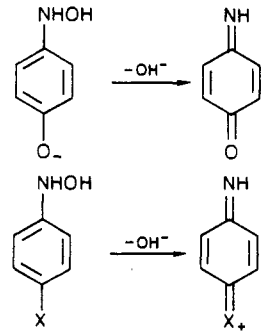
benzene and radical dianions of related compounds are relatively stable and have been detected by UV–vis absorption,[26,27] ESR,[28,29] and cyclic voltammetry.[25,30] Adams et al.[31] have electrochemically generated the radical dianions of all three nitrophenols in 0.1 M LiOH and detected them via ESR. Further reduction of the radical dianions, protonation, and loss of OH^- gives aryl nitroso compounds, which are reported to be the final reduction product under some conditions.[32] Subsequent two-electron reduction gives arylhydroxylamines.

Reductions of nitrophenols exemplify various mechanistic pathways depending upon pH and positional isomerism. The reduction of *o*- and *p*-nitrophenol is assumed to occur via the phenylhydroxylamine intermediate followed by a protonation/dehydration in acid (or isomerization with loss of hydroxide from the phenate in base) to yield an easily reducible quinone imine (+0.20 V vs SCE at pH 4.9).[15] This potential is even more positive than for the reduction of the nitroso intermediate (−0.08 V); thus formation of the three-electron azoxy product is precluded and the aniline is obtained in basic as well as acidic solutions.

Mechanistic hypotheses have often been put forth from analytical determinations of *n* via polarographic or voltammetric experiments. Our voltammetry at carbon electrodes indicates that the experimental time scale is important in assessing *n* from transient methods. Adsorption has also been implicated as a factor which complicates the interpretation of polarographic data for nitroaromatics.[24,25] Thus, the various interpretations of polarographic or voltammetric data are best resolved by complementary data from coulometric and synthetic experiments. These results indicate that in basic media the ortho and para isomers behave similarly at carbon and copper ($n = 6$) with high yields of aminophenol. However, the results for the meta isomer are electrode dependent as noted in Table I.

The mechanism for the reduction of nitroaromatics at copper is clearly indicated by the cyclic voltammetry for the isomeric nitrophenols in Figure 1. This is an example of classical electrocatalysis at a metal electrode. (Several examples exist in the literature, the most well known being the oxidation of alcohols at an oxide-covered nickel electrode.[2,35]) The interaction of the copper electrode and substrate is to be contrasted with the simple electron transfer which probably occurs at the inert, glassy carbon electrode and is believed to give rise to the difference in the observed *n* for the *m*-nitrophenol.

Since most of the substituents studied in this work are electron donating, the hydroxylamines are not made more easily reducible by simple inductive effects. The high yield of anilines for *o*- and *p*-aminophenols results from the formation of neutral quinone imine structures in base as discussed above. A similar pathway has been noted for *o*- and *p*-amino substitution[33] and is probable for *o*- and



p-sulfhydryl substitution as well. Acid-catalyzed dehydration is apparently general for arylhydroxylamines containing ortho and para substituents (X) in which a lone pair of electrons is present on the atom bonded to the ring (Cl, OMe, and OEt in the present discussion). In these cases, the formation of an easily reducible arenium ion is postulated in acid. (For alkyl substituents, hyperconjugation effects could lead to similar pathways.) Reduction of such dehydrated intermediates gives the anilines.

In basic media, formation of arenium ions is apparently not a significant factor in bulk solution as evidenced by the abundant literature for synthesis of N–N coupled products at most electrodes. Furthermore, there is no evidence for nucleophilic substitution which should predominate if arenium ions were formed in bulk solution (e.g., the reduction of *o*-nitroanisole at copper in NaOMe/MeOH yields methoxyaniline and no dimethoxyaniline). Either the copper electrode is capable of reducing the unprotonated hydroxylamine or it promotes formation of the arenium ion at the surface and subsequent reaction occurs via this easily reducible, surface-bound intermediate.

Conclusions

The electrochemical synthesis of substituted anilines in basic media depends upon several factors—the most important being the functionality and the positional isomerism of these substituents and the cathode composition. For ten classes of compounds studied, significant yields (>50%) of anilines in base are obtained when substitution by OH, OEt, OMe, or CH_3 is ortho or para to the nitro group. Chloride substitution also favors reduction to aniline to some degree over unsubstituted nitrobenzene. The propensity of (*o*- and *p*-hydroxyphenyl)hydroxylamines to form easily reducible, neutral, conjugated imines is responsible for the high yield of aminophenols. Substitution by NH_2 or SH should yield similar results.

For compounds not exhibiting the favorable substitution pattern described above, the choice of electrode material

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is also important. The electrocatalytic reduction at copper gives higher yields of substituted anilines for these compounds than at electrodes which exhibit conventional electron transfer. Copper-promoted formation of surface-bound arenium ions or electrocatalytic reduction of the hydroxylamine is postulated.

Experimental Section

Coulometry and Preparative Electrolyses. A flange-type cell is designed similarly to that described by Goodridge and King.[34] Each of the two compartments has a nominal volume of 25 mL when separated by a membrane with a gasket on each side. The design includes a Luggin capillary for potentiostatic electrolyses. Three 14/20 joints on each compartment allow for electrode connection, condensor placement, and sample withdrawal. The membrane (Nafion 324) is supported between Viton gaskets to expose an area of 6 cm^2. The electrode to electrode separation is 2.5 cm. Mass transport is accomplished by nitrogen sparge through a glass frit in the bottom of the cell.

Voltammetry. A single-compartment beaker-type cell is used. All operations are performed under nitrogen. Potentials are reported vs a sodium chloride saturated calomel electrode (SSCE).

Analytical. Liquid chromatography with a Hewlett-Packard 1090 allows simultaneous determination of the UV–vis spectrum of the electrolytic products for comparison with authentic spectra. Retention time and spectral matches yield high confidence levels in structural assignment. Quantitation is via response factor obtained from authentic anilines.

Typical Electrolysis Procedure. The cathode is a 6.3 cm^2 flag of 99.9% Cu and the anode is a Ni-200 alloy expanded-metal flag of equal area. The anolyte and catholyte are separated by the cation-exchange membrane of equal exposed area. The catholyte is composed of 1 g of 3-nitro-4-hydroxybenzoic acid dissolved in 20 mL of 1 N NaOH. The anolyte consists of 25 mL of 5 N NaOH. The temperature is controlled at 25 (±1) °C.

A constant current of 0.500 A (79.4 mA/cm^2) is applied after deoxygenation. Nitrogen sparge is continuous throughout the electrolysis for mass transport. The reaction is followed via liquid chromatography. The chemical yield, current efficiency, and conversion are calculated with a correction for the small (but linear) increase in catholyte volume with charge passed.

Acknowledgment. We express our appreciation to Z. Lysenko for helpful discussions.

Registry No. **1a**, 616-82-0; **1b**, 1571-72-8; **2a**, 619-14-7; **2b**, 2374-03-0; **3a**, 96-97-9; **3b**, 89-57-6; **4a**, 88-75-5; **4b**, 95-55-6; **5a**, 100-02-7; **5b**, 123-30-8; **6a**, 554-84-7; **6b**, 591-27-5; **7a**, 552-16-9; **7b**, 118-92-3; **8a**, 62-23-7; **8b**, 150-13-0; **9a**, 121-92-6; **9b**, 99-05-8; **10a**, 91-23-6; **10b**, 90-04-0; **11a**, 100-17-4; **11b**, 104-94-9; **12a**, 555-03-3; **12b**, 536-90-3; **13a**, 119-33-5; **13b**, 95-84-1; **14a**, 5460-31-1; **14b**, 53222-92-7; **15a**, 2581-34-2; **15b**, 2835-99-6; **16a**, 700-38-9; **16b**, 2835-98-5; **17a**, 4920-77-8; **17b**, 2835-97-4; **18a**, 100-29-8; **18b**, 156-43-4; **19a**, 98-95-3; **19b**, 62-53-3; **20a**, 88-73-3; **20b**, 95-51-2; **21a**, 100-00-5; **21b**, 106-47-8; **22a**, 99-99-0; **22b**, 106-49-0; **23a**, 138-42-1; **23b**, 121-57-3; Cu, 7440-50-8; C, 7440-44-0; NaOH, 1310-73-2; Cu_2O, 1317-39-1; CuO, 1317-38-0; $Cu(OH)_2$, 20427-59-2.

Reactions of Amides with Potassium Permanganate in Neutral Aqueous Solution

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Oxidation reactions of organic compounds by $KMnO_4$ are widely used in organic synthesis. Indeed, numerous examples and reviews of the reaction have been reported in the literature.[1,2] In the course of preparation of several aminobenzoic acid derivatives, we attempted to oxidize N-acetylated or N-benzoylated toluidines and xylidines with $KMnO_4$ to the corresponding carboxylic acid derivatives. The stoichiometry of the reaction shows a 1:2 molar reaction of the substrate and $KMnO_4$ (eq 1).[3] However,

$$RCH_3 + 2KMnO_4 \rightarrow RCOOK + 2MnO_2 + KOH + H_2O \quad (1)$$

to our surprise, the reaction did not go to completion when the ratio of 1:2 was employed. Instead, significant recovery of the toluidides was observed in all cases. On the other hand, the oxidizing agent seemed to be consumed completely. This puzzling observation led us to investigate systematically the oxidation reaction of toluidines and xylidines by $KMnO_4$.

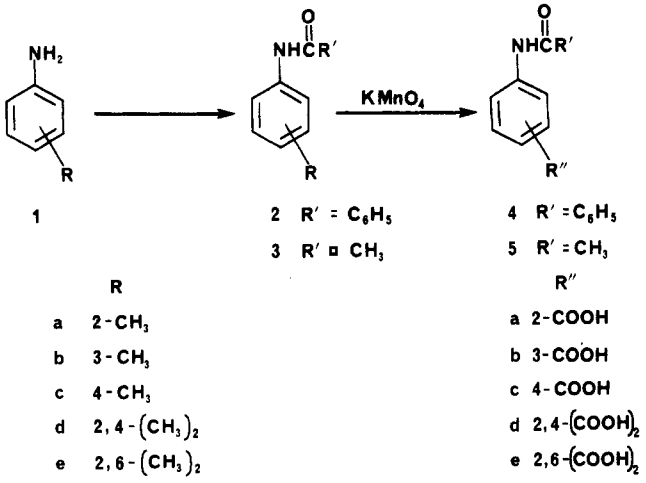
Table I. Results of Oxidation Reaction of Toluidides 2 and 3 by $KMnO_4$[a]

substrate	product	yield of product,[b] %	mp, °C	lit. mp, °C	recovery of substrate,[b] %
2a	**4a**	35	177–179	181[13,17]	50
2b	**4b**	30	255–256	252–253[13,17]	60
2c	**4c**	40	286–287	278[13,17]	50
2d	**4d**	30	283–283	–	55
2e	**4e**	35	193–196	221–222 dec[8]	55
3a	**5a**	60	186–187	185[13,17]	30
3b	**5b**	35	241–243	248,[13] 248–250[17]	40
3c	**5c**	70	257–259	250,[13] 256.5[17]	20
3d	**5d**	25	269–271	270[14]	60
3e	**5e**	20	210 dec	216–217 dec,[8] 208[14]	60

[a] Substrate: $KMnO_4$ = 1:4 by mole; reflux for 1.5 h. [b] The yields are average values of at least three runs.

Results and Discussion

Although there are countless reports on the subject of oxidation of $KMnO_4$, only a few examples of reaction with N-acylated toluidines (**2** and **3**) can be found in the literature. *p*-Acetotoluidide (**3c**) was oxidized by 3 equiv of



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