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Electrochemical reduction of 2-halo-*N*-phenylacetamides at glassy carbon cathodes in dimethylformamide

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ABSTRACT

Cyclic voltammetry and controlled-potential (bulk) electrolysis have been employed to investigate the direct electrochemical reductions of 2-bromo-*N*-phenylacetamide (**1a**) and 2-iodo-*N*-phenylacetamide (**1b**) at glassy carbon cathodes in dimethylformamide containing tetramethylammonium tetrafluoroborate ($TMABF_4$) as supporting electrolyte. Cyclic voltammograms for reduction of **1a** and **1b** each exhibit a pair of irreversible cathodic peaks; the first peak arises from a combination of one-electron and two-electron reductive cleavage of the respective carbon–halogen bond and the second peak is due to overall two-electron reductive cleavage of the carbon–halogen bond to produce a free halide ion together with 2-oxo-2-(phenylamino)ethan-1-ide. Controlled-potential (bulk) electrolysis of a 5 mM solution of **1a** or **1b** at a potential corresponding to either the first or second cathodic peak affords only phenylacetamide. However, bulk electrolysis of a 10 mM solution of **1a** or **1b** at a potential corresponding to either cathodic peak leads to a mixture of phenylacetamide and 1,4-diphenylpiperazine-2,5-dione. In the presence of a large excess of 1,1,1,3,3,3-hexafluoro-2-propanol (a proton donor), bulk electrolyses of **1a** or **1b** at a potential on the first peak give phenylacetamide exclusively. When either **1a** or **1b** is electrolyzed in the presence of 1 M D_2O, the resulting phenylacetamide is deuterated to a very significant extent (evidence for a carbanion intermediate), and a small quantity of 2-(dimethylamino)-*N*-phenylacetamide is seen as a side-product. Mechanisms to account for the behavior of **1a** and **1b** are proposed.

1. Introduction

In a previous publication [1] from our laboratory, the direct electrochemical reductions of several substituted 2-chloro-*N*-phenylacetamides at glassy carbon and silver electrodes in a dimethylformamide–tetramethylammonium tetrafluoroborate medium were described, along with a brief survey of the nickel(I) salen-catalyzed reduction of the same compounds. As indicated in our earlier paper, the electrochemical behavior of 2-haloacetamides has been a popular topic for many years [2–15], and this family of compounds has been employed for the electrosynthesis of β-lactams [4,7,13–15] and oxazolidine-2,4-diones [11]. In addition, further insight into mechanisms for the reduction of halogenated organic compounds can aid our understanding of how to develop strategies for the electrochemical remediation of environmental pollutants, an ongoing activity in our laboratory [16,17]. To the best of our knowledge, there has been no previous study of the electrochemistry of either 2-bromo- or 2-iodo-*N*-phenylacetamide, which is the subject of the present report.

Mechanistic aspects of the electrochemical reduction of 2-haloacetamides have been considered in at least four of the references cited in the preceding paragraph [1,9–11]. It has been proposed that reduction of 2-haloacetamides is a two-electron process that leads to cleavage of the carbon–halogen bond at a mercury or carbon cathode to afford a carbanion that can be protonated (possibly by the parent compound itself) to yield a dehalogenated acetamide. Formation of cyclic dimers (e.g., piperazine-2,5-diones) has also been observed [9,10].

In the present work, we have used cyclic voltammetry and controlled-potential (bulk) electrolysis to explore the electrochemical behavior of 2-bromo-*N*-phenylacetamide (**1a**) and 2-iodo-*N*-phenylacetamide (**1b**) at vitreous carbon cathodes in dimethylformamide (DMF) containing 0.050 M tetramethylammonium tetrafluoroborate ($TMABF_4$) as supporting electrolyte.

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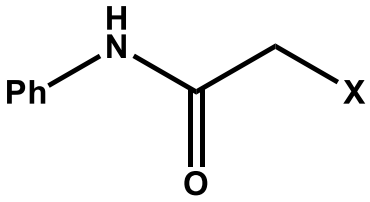


1a: X = Br

1b: X = I

Products arising from bulk electrolyses of **1a** and **1b** have been separated, identified, and quantitated with the aid of gas chromatography (GC) and gas chromatography–mass spectrometry (GC–MS). In addition, to gain insight into the reactions involved in the formation of the various products, studies in the presence of a proton donor, either 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) or deuterium oxide (D_2O), have been conducted, and mechanistic schemes are proposed for the electrochemical reductions of **1a** and **1b**.

2. Experimental

2.1. Reagents

Each of the following chemicals (with sources and purities indicated in parentheses) was purchased and used as received unless otherwise noted: *n*-dodecane (Sigma Aldrich, 99 + %), 2-bromo-*N*-phenylacetamide (ChemBridge, 95%), 2-iodo-*N*-phenylacetamide (Ark Pharm, 95 + %), 2-chloro-*N*-phenylacetamide (Ark Pharm, 95 + %), sodium hydride (Sigma Aldrich, 60% dispersion in mineral oil), tetrahydrofuran (THF, Macron Chemicals, 99 + %), hexanes (VWR, 95%), diethyl ether (EMD, absolute, anhydrous), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, Matrix Scientific, 99%), deuterium oxide (D_2O, Sigma Aldrich, 99.9 atom %D), and sodium sulfate (EMD, anhydrous). We used dimethylformamide (DMF, EMD Millipore, 99.9%) as solvent for all electrochemical experiments. Tetramethylammonium tetrafluoroborate ($TMABF_4$, GFS Chemicals, 98%) was recrystallized from water and methanol, then stored in a vacuum oven at 80 °C before use as an electrolyte. Deoxygenation of all solutions for electrochemical experiments was accomplished with the aid of Air Products ultrapure (zero-grade) argon.

2.2. Cells, electrodes, and instrumentation

As described in previous publications [18,19], cyclic voltammetry was carried out in a one-compartment, three-electrode cell containing a glassy carbon working electrode, a platinum wire auxiliary electrode, and the reference electrode described at the end of this section. For construction of the working electrode, a short length of glassy carbon rod (Grade GC-20, Tokai Electrode Manufacturing Company, Tokyo, Japan) was press-fitted into a machined Teflon tube to obtain an exposed planar, circular surface with an area of 0.071 cm^2. Contact to the working electrode itself was completed by insertion of a properly sized stainless-steel rod into the opposite open end of the Teflon tube. Before use, the exposed glassy carbon disk was polished with an aqueous suspension of 0.05-μm aluminum oxide on a Master-Tex (Buehler) polishing pad, sonicated in DMF, and patted dry with a Kimwipe tissue paper. To record cyclic voltammetry data, a Princeton Applied Research Corporation (PARC) model 2273 potentiostat was used with PowerSuite® software.

Controlled-potential (bulk) electrolyses were performed in a two-compartment (divided) cell that is described and pictured elsewhere [20] with the aid of a Princeton Applied Research Corporation (PARC) model 173 potentiostat. A locally written LabView program was used to record current–time curves, and the acquired data were processed with OriginPro 2016 software. In the cathode compartment were a reticulated vitreous carbon working electrode along with the reference electrode and a magnetic stir bar, whereas the anode compartment contained a carbon rod auxiliary electrode in a solution of solvent–-supporting electrolyte that was separated from the cathode compartment by a methyl cellulose–solvent–electrolyte plug over a sintered-glass disk. Working electrodes for bulk electrolyses were reticulated vitreous carbon (RVC) disks with an approximate area of 200 cm^2 (RVC 2X1-100S, ERG Aerospace Corporation, Oakland, CA). Preparation, cleaning, and handling of these electrodes have been described earlier [21]. To begin an electrolysis after the solution in the cathode compartment had been thoroughly deoxygenated with argon, a preselected potential was applied to the cathode while the stirred catholyte (without substrate) was still under a blanket of argon. Once a background current was obtained, a desired quantity of chosen substrate was injected via syringe into the cathode compartment and the electrolysis was resumed and continued until the former background current was reobtained, at which time the electrolysis was terminated.

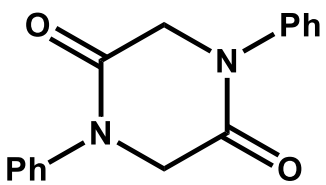
All potentials reported in this paper are given with respect to a reference electrode that consisted of a cadmium-saturated mercury amalgam (Cd/Hg) in contact with DMF that was saturated with both cadmium chloride and sodium chloride; this electrode has a potential of −0.76 V vs. the aqueous saturated calomel electrode (SCE) at 25 °C [22–24].

2.3. Separation, identification, and quantitation of electrolysis products

All product identifications were achieved by means of gas chromatography–mass spectrometry (GC–MS). An Agilent 6130 gas chromatograph, fitted with a 30 m × 0.32 mm capillary column (J & W Scientific) with a DB-5 stationary phase consisting of 5% phenylpolysiloxane and 95% methylpolysiloxane, was used in tandem with an Agilent 5973 inert mass-selective detector operating in electron ionization mode (70 eV).

Prior to each bulk electrolysis, a known volume of an internal standard (*n*-dodecane) was injected into the catholyte. At the end of each experiment, the post-electrolysis catholyte was partitioned between brine and diethyl ether, and the ether phase was dried over anhydrous sodium sulfate and concentrated by means of rotary evaporation. Products arising from each electrolysis were separated via gas chromatography with the Agilent 6130 instrument described above. Using a procedure developed in earlier research [25], we determined the product distributions tabulated in this paper from gas chromatographic response factors and peak areas measured with the aid of Agilent ChemStation software. To determine response factors, a mock cell that contained anticipated concentrations of products, along with an appropriate amount of the internal standard (*n*-dodecane), was prepared and allowed to stir (without application of a potential) for the same length of time as an actual bulk electrolysis.

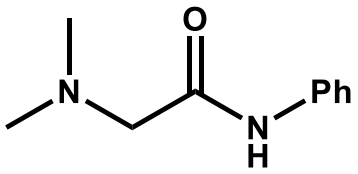
2.4. Synthesis of 1,4-diphenylpiperazine-2,5-dione (3)



We prepared 1,4-diphenylpiperazine-2,5-dione according to a procedure published by Cumine and co-workers [26]. First, sodium hydride (60% in oil) was washed with dry *n*-hexane with the aid of a cannula. Dry tetrahydrofuran (THF) was added to the sodium hydride in a flask, and the mixture was cooled to 0 °C. Then 2-chloro-*N*-

phenylacetamide in dry THF was slowly added to the flask; the mixture was stirred for 22 h as the temperature rose from 0 °C to room level. Next, the reaction was quenched by addition of 200 mL of water. After the resulting mixture was filtered, the product was isolated as a solid and subsequently washed with dichloromethane (DCM). Then the filtrate was extracted twice with DCM, and the organic phase and isolated solid were combined and concentrated to afford the desired product (1,4-diphenylpiperazine-2,5-dione) as a pale brown solid. Identity and purity of this compound were established with the aid of ^{1}H NMR and HRMS measurements: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.35 (m, 4H), 7.28 (ddt, J = 14.5, 6.7, 1.4 Hz, 6H), 4.48 (s, 4H); HRMS (EI) calculated for $C_{16}H_{14}N_2O_2$ $[M]^+$ 266.1055, found 266.1051.

2.5. Synthesis of 2-(dimethylamino)-N-phenylacetamide (4)



A pure sample of 2-(dimethylamino)-*N*-phenylacetamide was obtained by means of a procedure reported by Walker [27]. To begin the synthesis, 2-chloro-*N*-phenylacetamide and dimethylamine (40% wt.) were mixed together in a flask and refluxed for 4 h. Then the solution was cooled to room temperature and was partitioned between dichloromethane and aqueous sodium hydroxide (1 M). We extracted the aqueous phase twice more with dichloromethane, after which the combined organic layers were concentrated in vacuo to a volume of approximately 100 mL and were washed with water. Finally, the organic layer was collected and dried over anhydrous sodium sulfate, and the solvent was removed in vacuo. We confirmed the identity and purity of the product with the aid of ^{1}H NMR and HRMS data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.26 (t, J = 7.9 Hz, 2H), 7.04 (t, J = 7.4 Hz, 1H), 3.05 (s, 2H), 2.34 (s, 6H); HRMS (EI) calculated for $C_{10}H_{14}N_2O$ $[M]^+$ 178.1106, found 178.1103.

3. Results and discussion

3.1. Cyclic voltammetric behavior of 2-bromo-N-phenylacetamide (1a) and 2-iodo-N-phenylacetamide (1b) at a glassy carbon cathode

Shown in Fig. 1 are cyclic voltammograms recorded at 100 mV s^{-1} for direct reduction of 2-bromo-*N*-phenylacetamide (**1a**, dashed curve) and 2-iodo-*N*-phenylacetamide (**1b**, solid curve), respectively, at a glassy carbon electrode in oxygen-free DMF containing 0.050 M $TMABF_4$. For the reduction of either **1a** or **1b**, two irreversible cathodic peaks are seen: E_{pc1} = −0.93 V and E_{pc2} = −1.50 V for **1a**, whereas E_{pc1} = −0.63 V and E_{pc2} = −1.15 V for **1b**. As expected, reductive cleavage of the carbon–iodine bond of **1b** is more facile than reductive cleavage of the carbon–bromine bond of **1a**. As discussed later in more detail, we attribute the first cathodic peak of each cyclic voltammogram

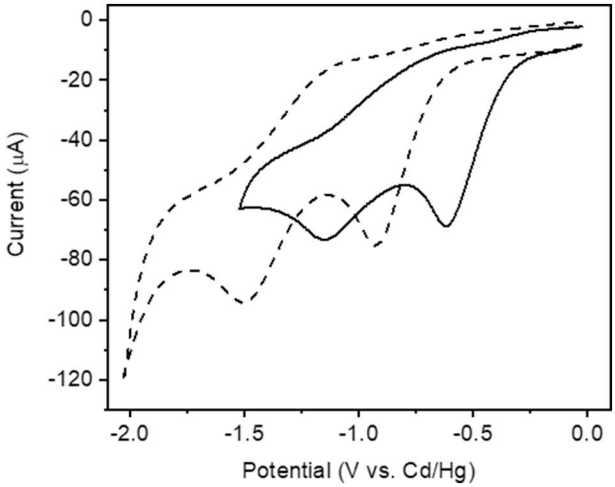
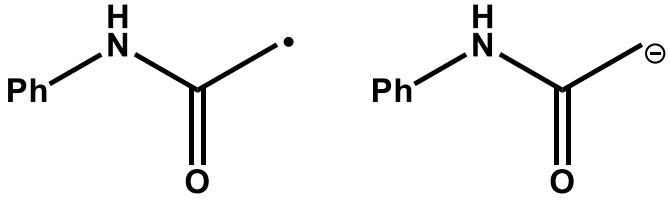


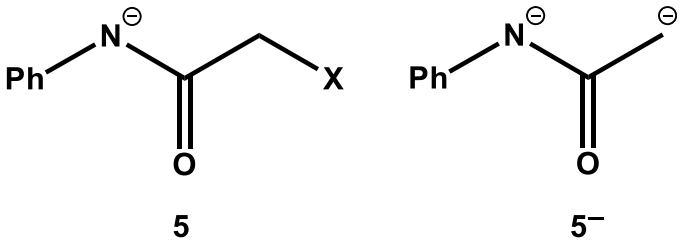
Fig. 1. Cyclic voltammograms recorded with a glassy carbon electrode (area = 0.071 cm^2) at 100 mV s^{-1} in oxygen-free DMF containing 0.050 M $TMABF_4$ and 5.0 mM 2-bromo-*N*-phenylacetamide (**1a**, dashed curve) or 5.0 mM 2-iodo-*N*-phenylacetamide (**1b**, solid curve). Potentials are given with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam (Cd/Hg), in contact with DMF saturated with both cadmium chloride and sodium chloride; this electrode has a potential of −0.76 V versus an aqueous saturated calomel electrode (SCE) at 25 °C. For **1a**, the scan goes from 0 to −2.0 to 0 V; for **1b**, the scan goes from 0 to −1.5 to 0 V.

shown in Fig. 1 to a **combination** of (a) one-electron reductive cleavage of the respective carbon–halogen bond to afford a halide ion along with a radical intermediate (**1**·) and (b) two-electron reduction of the carbon–halogen bond to form anion **1**$^-$ and a halide ion:



1• **1**$^-$

Owing to the difference in carbon–halogen bond energies, E_{pc1} for **1a** is more negative than E_{pc1} for **1b**. On the other hand, the second cathodic peak of each cyclic voltammogram in Fig. 1 can be ascribed to overall two-electron reductive cleavage of the carbon–halogen bond of the conjugate base **5** of **1a** or **1b** to produce a free halide ion (Br^- or I^-), along with anion **5**$^-$:



5 **5**$^-$

In addition to the preceding observations, we examined the cyclic voltammetric behavior of **1a** and **1b** in the presence of an excess of a deliberately added proton donor (1,1,1,3,3,3-hexafluoro-2-propanol, HFIP). Fig. 2 compares cyclic voltammograms recorded at 100 mV s^{-1} with a freshly polished glassy carbon electrode for the reduction of separate 5.0 mM solutions of **1a** and **1b** in oxygen-free DMF containing

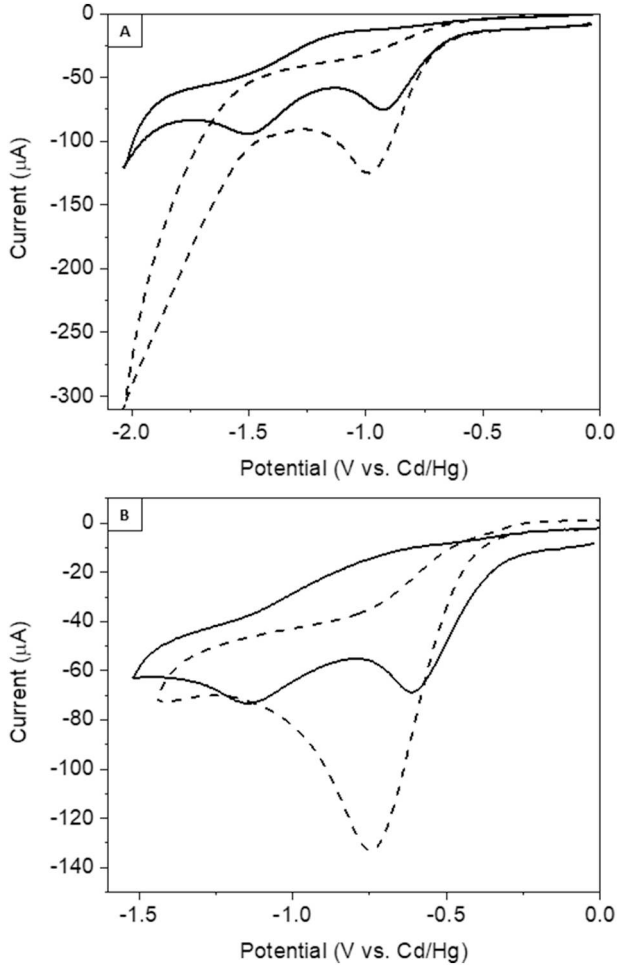


Fig. 2. Cyclic voltammograms recorded with a glassy carbon electrode (area = 0.071 cm^2) at 100 mV s^{-1} in oxygen-free DMF containing (panel A) 0.050 M $TMABF_4$ and 5.0 mM **1a** (solid curve), or 5.0 mM **1a** in the presence of 100 mM HFIP (dashed curve) and (panel B) 0.050 M $TMABF_4$ and 5.0 mM **1b** (solid curve), or 5.0 mM **1b** in the presence of 100 mM HFIP (dashed curve). Potentials are given with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam (Cd/Hg), in contact with DMF saturated with both cadmium chloride and sodium chloride; this electrode has a potential of −0.76 V versus an aqueous saturated calomel electrode (SCE) at 25 °C. For panel A, the scan goes from 0 to −2.0 to 0 V; for panel B, the scan goes from 0 to −1.5 to 0 V.

0.050 M $TMABF_4$ with no added proton donor (solid curves) and in the presence of 100 mM HFIP (dashed curves). When HFIP is present, only a single, but enhanced first cathodic peak is observed for reduction of either **1a** or **1b**, which is in sharp contrast to the two-step reduction of each starting material seen when HFIP is absent (Fig. 1). In the presence of HFIP, the production of **5** is blocked, so that the second cathodic peak is not observed. As a measure of the day-to-day reproducibility of our experiments, it can be seen from a side-by-side comparison of each cyclic voltammogram in Fig. 1 with the corresponding solid curve shown in each panel of Fig. 2 that the respective cathodic peak potentials for the two-step reductions of **1a** and **1b** are virtually identical in the absence of HFIP.

3.2. Controlled-potential (bulk) electrolyses of 2-bromo-N-phenylacetamide (1a) and 2-iodo-N-phenylacetamide (1b) at reticulated vitreous carbon cathodes

A series of controlled-potential electrolyses of separate 5.0 and 10.0 mM solutions of **1a** and **1b** at reticulated vitreous carbon cathodes in DMF containing 0.050 M $TMABF_4$ was conducted. Coulometric data and product distributions for these experiments are shown in Table 1. Each entry corresponds to the average of at least triplicate experiments. Product yields, which were reproducible to ± 10% absolute, represent the amount of starting material incorporated into each species.

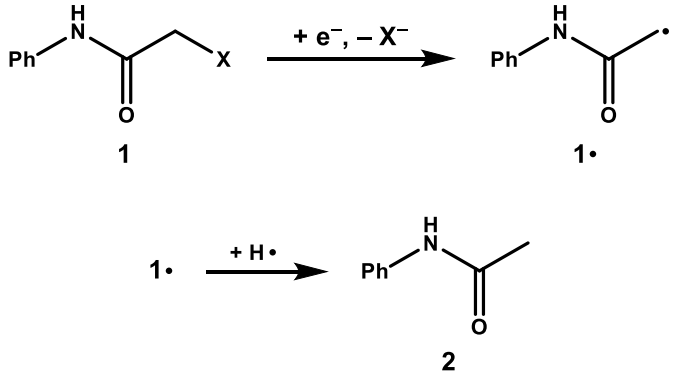
Table 1
Coulometric *n* values and product distributions for reduction of 2-bromo-*N*-phenylacetamide (**1a**) and 2-iodo-*N*-phenylacetamide (**1b**) at reticulated vitreous carbon cathodes in oxygen-free DMF containing 0.050 M $TMABF_4$.

Substrate	Concentration (mM)	*E* (V vs. Cd/Hg)	*n*[b]	Product distribution (%)[a]			
				2	**3**	**4**	Total
1a	5.0	−1.1	1.0	99	–	–	99
	5.0	−1.7	1.2	82	–	–	82
	10.0	−1.1	1.0	52	43	–	95
	10.0	−1.7	1.0	68	27	–	95
	10.0[c]	−1.1	1.5	96	–	–	96
	10.0[d]	−1.1	1.0	48	39	–	87
	10.0[d]	−1.7	1.0	66	11	7	84
1b	5.0	−0.8	1.0	91	–	–	91
	5.0	−1.4	1.2	86	–	–	86
	10.0	−0.8	1.0	53	38	–	91
	10.0	−1.4	1.1	64	36	–	100
	10.0[c]	−0.8	1.7	100	–	–	100
	10.0[d]	−0.8	1.0	60	40	–	100
	10.0[d]	−1.4	1.0	59	34	TR[e]	93

2 = phenylacetamide; **3** = 1,4-diphenylpiperazine-2,5-dione; **4** = 2-(dimethylamino)-*N*-phenylacetamide.
[a] Yield expressed as percentage of substrate converted to product.
[b] Average number of electrons per molecule of substrate.
[c] 100 mM HFIP was present.
[d] 1 M D_2O was present.
[e] TR = trace.

As revealed in Table 1, when a 5.0 mM solution of **1a** or **1b** is electrolyzed at a potential corresponding to the first cyclic voltammetric peak (−1.1 V or −0.8 V, respectively), the coulometric *n* value is essentially 1.0 and the only product is phenylacetamide (**2**). However, if a 5.0 mM solution of **1a** or **1b** is reduced at a potential corresponding to the second cyclic voltammetric peak (−1.7 V or −1.4 V, respectively), the coulometric *n* value is slightly elevated (1.2), but phenylacetamide (**2**) is again the sole product. Although electrolyses of 10.0 mM solutions of **1a** or **1b** at potentials corresponding to either the first or second cyclic voltammetric peak result in coulometric *n* values of 1.0–1.1, significant amounts of 1,4-diphenylpiperazine-2,5-dione (**3**) are formed in addition to **2**.

To seek evidence that carbanions are involved as intermediates in the reduction of **1a** or **1b** at a glassy carbon cathode, we conducted bulk electrolyses of each substrate in the presence of an excess of either HFIP or D_2O. For the first set of experiments, electrolyses of 10 mM solutions of **1a** or **1b** in DMF containing 0.050 M $TMABF_4$ and 100 mM HFIP were carried out at a potential corresponding to the first cathodic peak for each substrate ($E_{\mathbf{1a}}$ = −1.1 V and $E_{\mathbf{1b}}$ = −0.8 V). For these experiments, reduction of **1a** and **1b** afforded phenylacetamide (**2**) as the only product; the yield of **2** obtained from **1a** was 96%, whereas the yield of **2** arising from **1b** was 100%, and the coulometric *n* values were 1.5 for **1a** and 1.7 for **1b**. These findings suggest that reduction of both **1a** and **1b** at a potential corresponding to the first cathodic peak occurs through a combination of one- and two-electron pathways. In the second set of experiments, electrolyses of **1a** and **1b** in DMF containing 0.050 M $TMABF_4$ and 1 M D_2O were conducted at a potential corresponding to each cathodic peak ($E_{\mathbf{1a}}$ = −1.1 V, −1.7 V; and $E_{\mathbf{1b}}$ = −0.8 V, −1.4 V). For these experiments, the average *n* value for reduction of both **1a** and **1b** was 1.0. For electrolyses of **1a** at −1.1 V, the product distribution consisted of phenylacetamide (**2**) in 48% yield (with 70–74% monodeuteration) and 1,4-diphenylpiperazine-2,5-dione (**3**) in 39% yield. For electrolyses of **1a** at −1.7 V, the product



Scheme 1. Proposed mechanistic scheme for controlled-potential electrochemical reduction of 2-bromo-*N*-phenylacetamide (**1a**, X = Br) or 2-iodo-*N*-phenylacetamide (**1b**, X = I) at a reticulated vitreous carbon cathode in DMF–0.050 M $TMABF_4$.

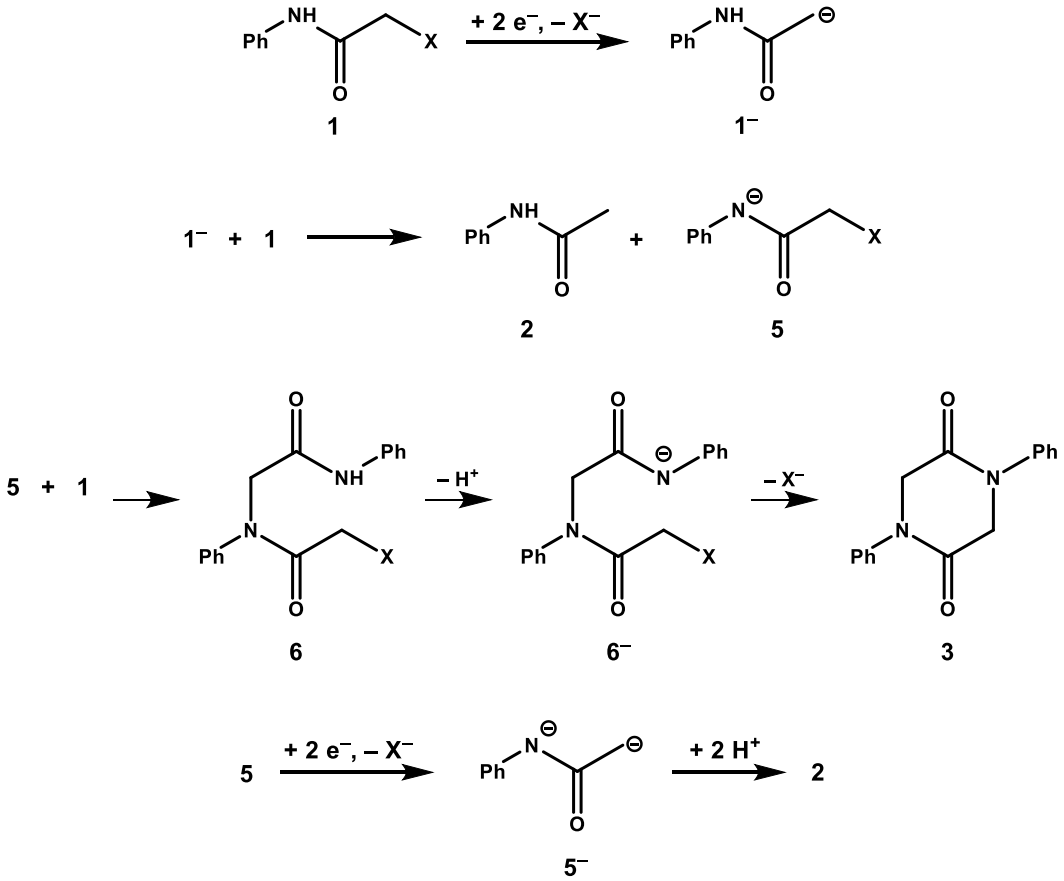
distribution consisted of **2** in 66% yield (with 79% monodeuteration), **3** in 11% yield, and 2-(dimethylamino)-*N*-phenylacetamide (**4**) in 7% yield. For electrolyses of **1b** at −0.8 V, the product distribution consisted of **2** in 60% yield (with 63% monodeuteration) and **3** in 40% yield. For electrolyses of **1b** at −1.4 V, the product distribution consisted of **2** in 59% yield (with 78% monodeuteration), **3** in 34% yield, and a trace of **4**.

In Table 1 it is interesting to note that formation of 1,4-diphenylpiperazine-2,5-dione (**3**) is suppressed when HFIP is the proton donor, but not when D_2O is employed. These observations are consistent with the fact that HFIP has a higher acidity in comparison with D_2O. Using information available in the literature [28–30], we have calculated that the pK_a values for HFIP and D_2O in DMF are 18.7 and 34.2, respectively.

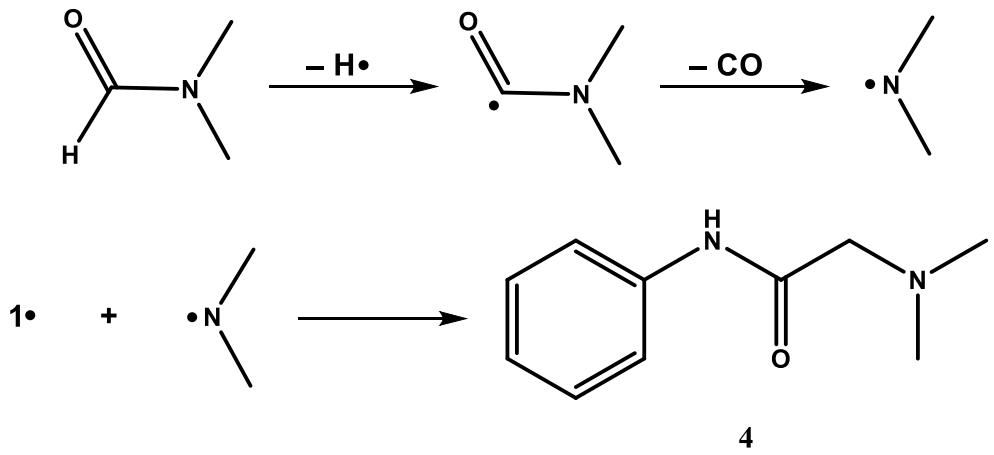
3.3. Mechanistic features of the electroreduction of 2-bromo-*N*-phenylacetamide (*1a*) and 2-iodo-*N*-phenylacetamide (*1b*)

As described earlier, in the absence of either a proton or deuteron donor, bulk electrolyses of 5.0 mM solutions of **1a** or **1b** at a potential (−1.1 V and − 0.8 V, respectively, Table 1) corresponding to the first cyclic voltammetric peak for each starting material afford phenylacetamide (**2**) as the only product via a one-electron process. Therefore, as illustrated in Scheme 1, we propose that under these conditions **1a** and **1b** undergo reductive cleavage of the respective carbon–halogen bond to give a radical intermediate (**1**·) which abstracts a hydrogen atom from the solvent to give **2**. This mechanistic picture is analogous to that proposed earlier [1] for the electroreduction of both 2-chloro-*N*-methyl- and 2-chloro-*N*-ethyl-*N*-phenylacetamide at glassy carbon and silver cathodes.

To account for the appearance of 1,4-diphenylpiperazine-2,5-dione (**3**) when 10.0 mM solutions of **1a** or **1b** are electrolyzed at a potential (−1.1 V and − 0.8 V, respectively, Table 1) that corresponds to the first stage of reduction, we postulate that **3** arises via a carbanion intermediate (**1**$^-$) that is part of the two-electron process depicted in Scheme 2. This carbanion intermediate (**1**$^-$) can accept a proton either from (a) residual water or (b) itself (self-protonation). A self-protonation mechanism for amides has been proposed before [1,3,5,6,8,10] and is supported by our observations from the proton-donor studies. In the presence of an excess of an acid (e.g., HFIP) that is stronger than the amide, the electrogenerated carbanion is protonated quantitatively to afford **2** and the second cathodic peak (corresponding to reduction of intermediate **5**) disappears. However, coulometric *n* values for



Scheme 2. Proposed mechanistic scheme for controlled-potential electrochemical reduction of 2-bromo-*N*-phenylacetamide (**1a**, X = Br) or 2-iodo-*N*-phenylacetamide (**1b**, X = I) at a reticulated vitreous carbon cathode in DMF–0.050 M $TMABF_4$.



4

Scheme 3. Proposed mechanistic scheme for production of 2-(dimethylamino)-*N*-phenylacetamide (**4**) via controlled-potential reduction of **1a** at a reticulated vitreous carbon cathode in DMF–0.050 M $TMABF_4$.

reduction of **1a** and **1b** in the presence of HFIP were between 1 and 2, which suggests that the overall mechanism for reduction of **1a** and **1b** is a combination of both radical and carbanion pathways.

To emphasize the compatibility of coulometric data and product distributions listed in Table 1 with the mechanistic pictures described above, the third entry for reduction of **1a** is instructive. In that triplicate set of electrolyses of **1a** at −1.1 V, the average coulometric *n* value was 1.0 and the average yields of **2** and **3** were 52% and 43%, respectively. If the *n* value for formation of **2** is 1.0 and if the *n* value for formation of **3** is also 1.0 (because two molecules of **1a** are incorporated into each molecule of **3** that arises from a net two-electron process), the *n* value of 0.95 that is based on the product distribution agrees well with the coulometric *n* value.

For electrolyses done in the presence of D_2O, a third product [2-(dimethylamino)-*N*-phenylacetamide, **4**] is observed. Although the mechanism for its formation is still unclear and requires further investigation, we show in Scheme 3 a plausible pathway. In this suggested mechanism, dimethylformamide loses a hydrogen atom, followed by decarbonylation to give the dimethylamino radical, and the latter species can couple with **1**· to afford 2-(dimethylamino)-*N*-phenylacetamide.

3.4. Conclusions

Electrochemical reductions of 2-bromo-*N*-phenylacetamide (**1a**) and 2-iodo-*N*-phenylacetamide (**1b**) at glassy carbon cathodes in DMF containing 0.050 M $TMABF_4$ proceed via two different mechanisms. Reduction of **1a** and **1b** at a concentration of 5 mM leads exclusively to the formation of *N*-phenylacetamide. On the other hand, reduction of **1a** and **1b** at the 10 mM level affords a mixture of products: *N*-phenylacetamide (**2**) and 1,4-diphenylpiperazine-2,5-dione (**3**); **2** is proposed to arise via a combination of radical and carbanion intermediates, whereas **3** forms exclusively from anion intermediates. In the presence of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), reduction of 10 mM solutions of **1a** and **1b** leads to a significant increase in the *n* value as well as formation of *N*-phenylacetamide only. For electrolyses of both **1a** and **1b** in the presence of 1 M D_2O, there is significant incorporation of deuterium into *N*-phenylacetamide. Moreover, reduction of **1a** at a potential corresponding to its second cathodic peak, and in the presence of D_2O, leads to production of 2-(dimethylamino)-*N*-phenylacetamide; the latter compound is believed to arise via reaction of the radical (**1**·) arising from one-electron reductive cleavage of the carbon–halogen bond of either **1a** or **1b** with a solvent-derived dimethylamino radical, namely $\cdot N(CH_3)_2$.

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