JOC The Journal of Organic Chemistry

Article

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Electrochemical Oxidative Amination of Sodium Sulfinates: Synthesis of Sulfonamides Mediated by NH_4I as a Redox Catalyst

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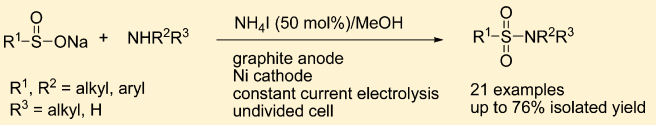
Supporting Information

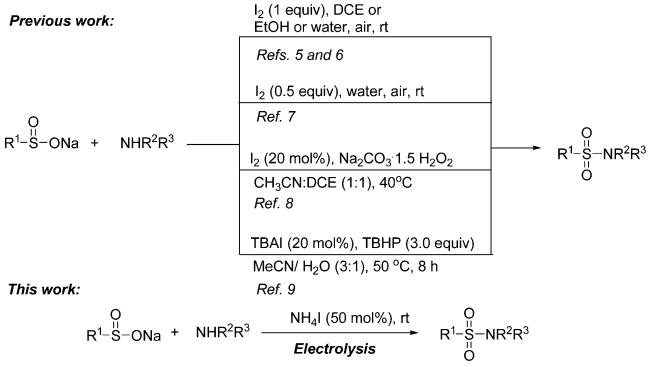
ABSTRACT: An efficient protocol for the synthesis of sulfonamides via the electrochemical oxidative amination of sodium sulfinates has been developed. The chemistry proceeds in a simple undivided cell employing a substoichiometric amount of NH_4I that serves both as a redox catalyst and a supporting electrolyte; in this manner additional conducting salt is not required. A wide range of substrates, including aliphatic or aromatic secondary and primary amines, as well as aqueous ammonia, proved to be compatible with the protocol. Scale-up was possible, thereby demonstrating the practicality of the approach. The electrolytic process avoids the utilization of external oxidants or corrosive molecular iodine and therefore represents an environmentally benign means by which to achieve the transformation.



1. INTRODUCTION

The construction of a sulfonamide bond constitutes an important transformation in organic chemistry due to the widespread presence of the sulfonamide unit in biologically active compounds and pharmaceuticals,[1] as well as its utilization as an amine protecting group.[2] Sulfonamides are classically produced from the reaction of an amine and a sulfonyl chloride in the presence of a base. Considering that direct formation of the sulfonamide bond between a sulfinate and an amine is able to avoid the prefunctionalization of the sulfonate component and therefore is a step and atom economical method, Jiang[3] and Tu[4] independently reported the Cu-catalyzed cross coupling of sodium sulfinate and amines or hydroxylamine. Later it was observed that sulfonamides could also be formed via oxidative amination of sodium sulfinate using iodine-based reagents. Along these lines, Song[5] and Wang[6] found that the sulfonamidation reaction of a variety of sodium sulfinates and amines or aqueous ammonia proceeded smoothly in the presence of a stoichiometric amount of molecular iodine (Scheme 1). Notably, the use of 0.5 equiv of molecular iodine in water also worked satisfactorily.[7] Catalyzed versions of the sulfonamidation have also been reported. For example, a combination of 20 mol % I_2 and sodium percarbonate ($Na_2CO_3{\cdot}1.5H_2O_2$) as an external oxidant was used by Yotphan and co-workers.[8] Zhao and co-workers also described a protocol for the efficient formation of sulfonamides using the versatile combination of TBAI/TBHP.[9] Although much progress has been made in the processes described above, the need to use toxic and corrosive molecular iodine or an excess of an external co-oxidant does not meet with the guiding principles of green and sustainable chemistry.[10]

Scheme 1. Oxidative Amination of Sodium Sulfinate Using Iodide-Based Reagents



Electrochemistry provides an efficient method to achieve the formation of a new chemical bond and the transformation of a functional group.[11] In this context, we are interested in electrochemically initiated oxidative functionalization of C−H bonds induced by redox catalysts.[12] Along with the development and usage of triarylimidazole-based redox catalysts,[12a,b] simple halide anions can also be employed to achieve C−H functionalization, leading to the formation of new C−C bonds

Received: March 22, 2016
Published: May 3, 2016

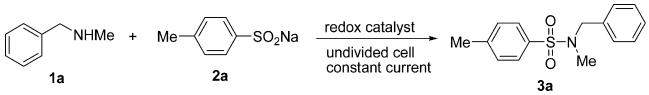
DOI: 10.1021/acs.joc.6b00615
J. Org. Chem. 2016, 81, 4713−4719

and C−N bonds.[12c−f] For example, we have achieved the electrochemical synthesis of benzoxazoles and the electrochemically initiated oxidative amination of benzoxazoles with secondary amines using NaI as a redox catalyst.[12c−f] Recently, protocols for the electrocatalytic aziridination[12d] and amino-oxygenation of alkenes[12c] mediated by *n*-Bu_4NI have also been explored. These results reveal that electrochemically generated halide species of one form or another can function as a surrogate for organic hypervalent iodine or a combination of iodine-containing catalyst and external co-oxidant. Given the fact that sulfonamides can be formed from the oxidative amination of sodium sulfinate using iodine-based reagents,[7−9] and on the basis of our observations and past experience, we propose that electrochemically generated halide species might also be applied to the reaction of oxidative amination of sodium sulfinate. If true, then the protocol may afford the following advantages: (1) stable and nontoxic halide salts, instead of the toxic, easily sublimed, and corrosive molecular iodine, can be used as the reagent. (2) The anode serves as a co-oxidant; therefore, additional terminal chemical co-oxidant is not required. Moreover, the anode is physically separated from the organic layer containing the substrate and is thus easily removed. (3) In addition, a substoichiometric amount of ammonium iodide can serve both as the redox mediator and the supporting electrolyte, thereby simplifying the workup and isolation process and leading to a reduction in waste. In addition, the electrolysis is conveniently carried out in an undivided cell. To the best of our knowledge, this work represents the first example of the electrochemically promoted oxidative amination of sulfinates.

2. RESULTS AND DISCUSSION

We started our studies by using *N*-methylbenzylamine, **1a**, and sodium *p*-methylbenzenesulfinate, **2a**, as model substrates and performed a constant current electrolysis at 5 mA/cm^2, in an undivided cell using MeOH as solvent, a graphite plate as the working electrode, and a Ni plate as the counter electrode (Scheme 2). As shown in Table 1, the desired sulfonamide **3a**

Scheme 2. Electrochemically Oxidative Amination of Sodium Benzenesulfonate 2a



was isolated in a 34% yield when 50 mol % of NH_4I was used as a redox catalyst and a conducting salt (Table 1, entry 1). Because monitoring of the reaction mixture by TLC revealed that some starting **2a** remained intact after amine **1a** was consumed completely, the ratio of **1a** to **2a** was varied in an effort to fully consume sulfinate **2a** and improve the efficiency of the transformation. We observed that the yield of **3a** improved from 44% to 57% when the ratio of **1a** to **2a** was increased from 1.5:1 to 2.5:1 (Table 1, entries 2−4). A further increase in the ratio to 3 equiv of **1a** afforded the highest yield of **3a** (Table 1, entry 5). Additional increases did not improve the efficiency (Table 1, entry 6).

Next, a screening of redox catalysts was performed. It was observed that both the anion and cation of the redox catalyst play important roles. As shown in Table 1, the ammonium cation, NH_4^+, proved to be superior to the alternatives (entries 7−12). For example, among all the iodide salts, NH_4I afforded the best results, while NaI and *n*-Bu_4NI gave lower yields (entries 7 and 8). A 63% yield of **3a** was obtained when NH_4Br was used as a redox catalyst (entry 9); other bromide salts gave less than 38% yield of **3a** (entries 10−12). With the exception of entry 9 (0.5 equiv of NH_4Br), iodides often performed better than bromides. Compare, for example, entry 5 with entries 10−12.

The effect of redox catalyst NH_4I loading was also investigated. As shown in Table 1, the yield of **3a** decreased to 37% when 0.2 equiv of NH_4I was employed (entry 13). Notably, in the absence of NH_4I, a 26% yield of **3a** was obtained (entry 14). The results reveal that a pathway involving the direct oxidative amination of sodium benzenesulfinate also occurs, though the NH_4I-mediated pathway is predominant for the formation of **3a**.

Next, we focused our attention upon the solvent. As shown in Table 1, the presence of water produced negative results undoubtedly because of the low solubility of the molecular iodine generated in situ, which remained on or near the surface of the anode (entries 15 and 16). The reaction also worked in ethanol, but a slightly inferior yield of **3a** was produced (entry 17). Comparable yields of **3a** were obtained when DMF and DMSO were used as solvents (entries 18 and 19), while the yield decreased to 45% when CH_3CN was employed (entry 20). Although comparable yields of **3a** were obtained using these solvents, additional $LiClO_4$ was used as a supporting electrolyte to improve charge transport. Upon the basis of these observations, we suggest that methanol is the best solvent for the oxidative amination of sodium benzenesulfinate.

Further screening of electrode materials demonstrated that the so-called dimension stable anode (DSA) was not suitable for the reaction and only 36% yield of **3a** was obtained (entry 21); Pt or graphite as the anode and Ni or Al as the cathode proved to be preferable (entries 22−26).

From the results described above, we conclude that the optimal reaction conditions call for using 50 mol % of NH_4I as the redox catalyst and supporting electrolyte, Pt as working electrode, and a Ni plate as the cathode. The reaction is best performed in an undivided cell using methanol as the solvent without the need for additional conducting salt.

With the optimal conditions in hand, we then studied the scope and the generality of the protocol by examining reactions of sodium *p*-methylbenzenesulfinate **2a** with a variety of amines **1**. As shown in Table 2, *aliphatic secondary amines*, such as morpholine, pyrrolidine, and diethylamine, afforded the corresponding adducts **3b**, **3c**, and **3d** in 64%, 71%, and 31% yields, respectively. Good yields of **3e** (60%) and **3f** (71%) were obtained when tetrahydroisoquinoline and 6,7-dimethoxytetrahydroisoquinoline were subjected to the standard reaction conditions with **2a**. *Aromatic secondary amines* were also suitable partners, albeit in a lower yield. For example, *N*-methylaniline gave a 14% yield of adduct **3g**.

The electrochemical reaction of **2a** with *aliphatic primary amines* also proceeded smoothly. As shown in Table 2, benzylic amines, cyclohexanamine, and ethanamine gave the desired products **3h−l** in moderate to good yields. The standard conditions could also be applied to *aromatic amines*, such as *p*-methylaniline and *p*-chloroaniline, and moderate yields of compounds **3m** and **3n** were produced. The results are quite different from previous reports wherein aromatic amines did not tolerate the chemical conditions using molecular iodine as catalyst and excess of sodium percarbonate ($Na_2CO_3·1.5H_2O_2$) as oxidant.[8] In addition, for the reaction of the nitrogen-

DOI: 10.1021/acs.joc.6b00615
J. Org. Chem. 2016, 81, 4713−4719

Table 1. Initial Optimization of Electrochemically Oxidative Amination of Sodium Sulfonate 2a[a]

entry	1a:2a (equiv/equiv)	anode/cathode	cat. (equiv)	solvent	yield (%)[b]
1	1.2:1	C/Ni	NH_4I (0.5)	CH_3OH	34
2	1.5:1	C/Ni	NH_4I (0.5)	CH_3OH	44
3	2:1	C/Ni	NH_4I (0.5)	CH_3OH	53
4	2.5:1	C/Ni	NH_4I (0.5)	CH_3OH	57
5	3:1	C/Ni	NH_4I (0.5)	CH_3OH	65
6	3.5:1	C/Ni	NH_4I (0.5)	CH_3OH	57
7	3:1	C/Ni	NaI (0.5)	CH_3OH	32
8	3:1	C/Ni	*n*-Bu_4NI (0.5)	CH_3OH	38
9	3:1	C/Ni	NH_4Br (0.5)	CH_3OH	63
10	3:1	C/Ni	NaBr (0.5)	CH_3OH	38
11	3:1	C/Ni	*n*-Bu_4NBr (0.5)	CH_3OH	28
12	3:1	C/Ni	Et_4NBr (0.5)	CH_3OH	36
13	3:1	C/Ni	NH_4I (0.2)	CH_3OH	37
14	3:1	C/Ni	NH_4I (0.0)	CH_3OH	26[c]
15	3:1	C/Ni	NH_4I (0.5)	MeOH:H_2O (9:1)	59
16	3:1	C/Ni	NH_4I (0.5)	MeOH:H_2O (1:1)	49
17	3:1	C/Ni	NH_4I (0.5)	CH_3CH_2OH	54
18	3:1	C/Ni	NH_4I (0.5)	DMSO	65[c]
19	3:1	C/Ni	NH_4I (0.5)	DMF	60[c]
20	3:1	C/Ni	NH_4I (0.5)	CH_3CN	45[c]
21	3:1	DSA/Ni	NH_4I (0.5)	CH_3OH	36
22	3:1	Pt/Ni	NH_4I (0.5)	CH_3OH	63
23	3:1	GCE/Ni	NH_4I (0.5)	CH_3OH	51
24	3:1	C/C	NH_4I (0.5)	CH_3OH	53
25	3:1	C/Fe	NH_4I (0.5)	CH_3OH	59
26	3:1	C/Al	NH_4I (0.5)	CH_3OH	64

[a]Reaction conditions: **1a** and **2a** (1.0 mmol) in 10 mL of solvent, undivided cell, room temperature, current density of 5 mA/cm^2. [b]Isolated yield from column chromatography. [c]$LiClO_4$ (0.1 M) was added as a conducting salt.

containing aromatic heterocycles, benzoimidazole, with **2a** afforded **3o** in 18% yield. However, when benzo[1,2,3]triazole was allowed to react with **2a** under the standard conditions, the expected product **3p** was not generated; instead, 1-methoxybenzo[1,2,3]triazole was isolated in an 8% yield.

The reaction scope with regard to the sodium sulfinates was also explored. As shown in Table 3, when benzenesulfinate and *p*-chlorobenzenesulfinate were allowed to react with *N*-methylbenzylamine, adducts **3q** and **3r** were generated in 74% and 64% yield, respectively. In the cases of sodium methanesulfinate, a good yield of desired **3s** was produced (66%).

Primary sulfonamides constitute an important starting material for the synthesis of polysubstituted sulfonamides, as well as a building block for the synthesis of pharmaceuticals.[13] Therefore, an efficient approach to their construction is desirable. We were therefore delighted to find that our electrochemical protocol could also be applied to the synthesis of primary sulfonamides. As shown in Table 4, and without further optimization of the reaction conditions, electrolysis of a mixture of aqueous ammonia and sodium sulfonate in the presence of NH_4I proceeded smoothly, and the corresponding adducts **3t**−**v** were produced in yields ranging from 50% to 61%.

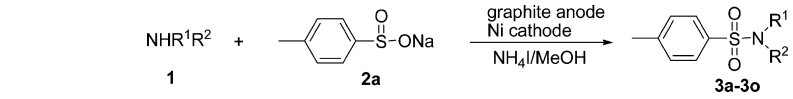
In addition, to demonstrate the practicality of the protocol, we examined the chemistry on a multigram scale. Thus, as illustrated in Scheme 3, when 18 mmol of morpholine was allowed to react with 6 mmol of **2a** under the standard conditions, adduct **3b** was isolated in a 70% yield.

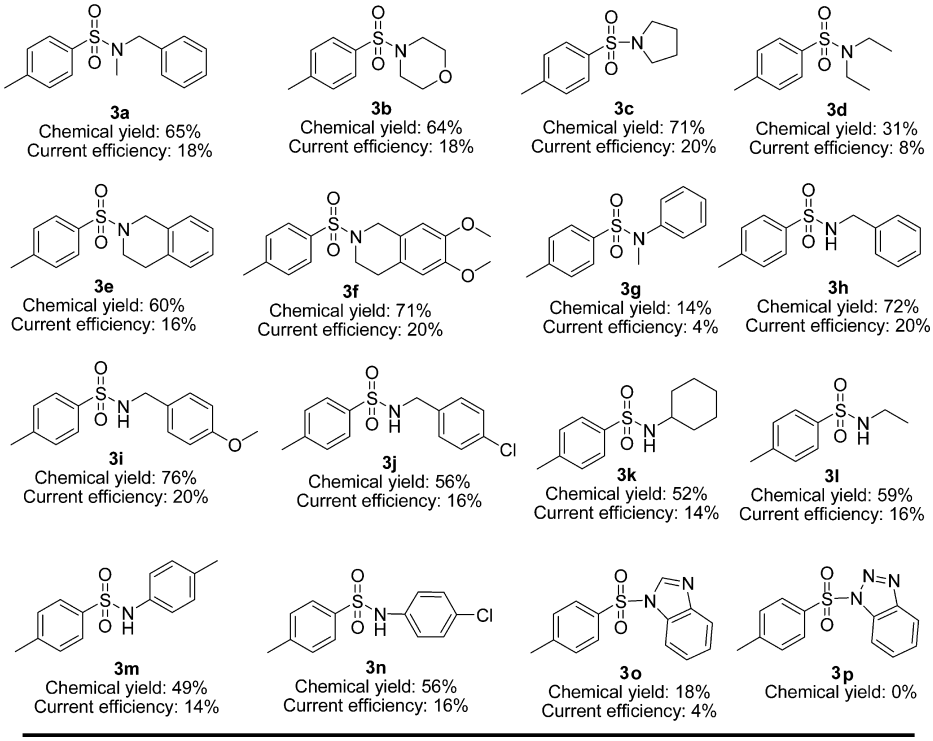
To more clearly understand the reaction mechanism, several control experiments were performed. As shown in Scheme 4, when the electrolysis of the mixture of **1a** and **2a** under the standard conditions was performed in the presence of 2.0 equiv of TEMPO (0.81 V vs $Ag/AgNO_3$),[14] a radical scavenger, a trace amount of **3a** was detected (Scheme 4a). A similar outcome was observed in the presence of 2.0 equiv of BHT, whose oxidation potential being more than 1.3 V vs $Ag/AgNO_3$ (Scheme 4b). These results imply that the reaction involves a radical process. The reaction of **1a** with **2a** in the presence of 1 equiv of molecular I_2 as an oxidant gave **3a** in good yield (Scheme 4c), thereby implicating its role as an active species in the reaction. It is well-known that the reaction of sodium sulfinate and molecular iodine forms sulfonyl iodide. Consequently, sulfonyl iodide was prepared and allowed to react with amine **1a**; **3a** was generated in a 79% yield. The result implies that sulfonyl iodide is a likely intermediate in the oxidative amination. In addition, and similar to previous reports,[6] the one pot, two-step reaction of the in situ generated *N*-iodo-*N*-methylbenzylamine and sodium sulfinate proceeded smoothly to give **3a** in excellent yield (Scheme 4e). Also, as mentioned above, 26% of **3a** was isolated when the electrolysis was conducted in the absence of NH_4I, which indicates that the direct electrochemical oxidative amination also occurs, though its efficiency is diminished.

On the basis of the results described above and literature reports, the electrochemical oxidative amination of sulfinate may proceed via three pathways and is illustrated in Scheme 5. The reaction sequence begins with the anodic oxidation of iodide ion to form molecular iodine and its subsequent reaction with sodium sulfinate **2** to afford sulfonyl iodide **4**, which readily reacts with the amine to form the product (pathway 1). Simultaneously, the in situ-generated molecular iodine is able to

DOI: 10.1021/acs.joc.6b00615
J. Org. Chem. 2016, 81, 4713−4719

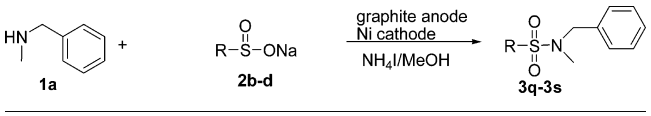
Table 2. Substrate Scope of Amines[a]

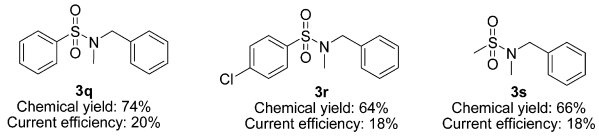




[a]Reaction conditions: amine **1** (3 mmol), **2a** (1 mmol) and NH_4I (0.5 equiv) in 10 mL of methanol, undivided cell, room temperature, current density of 5 mA/cm^2.

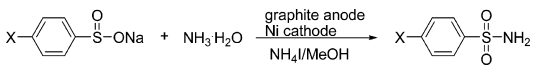
Table 3. Substrate Scope of Sodium Sulfinates[a]

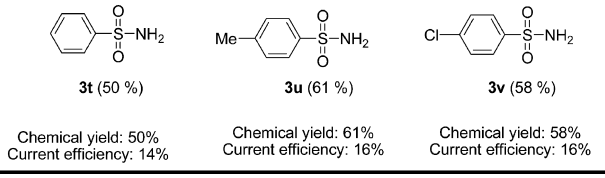




[a]Reaction conditions: amine **1a** (3 mmol), **2** (1 mmol), and NH_4I (0.5 equiv) in 10 mL of methanol, undivided cell, room temperature, current density of 5 mA/cm^2.

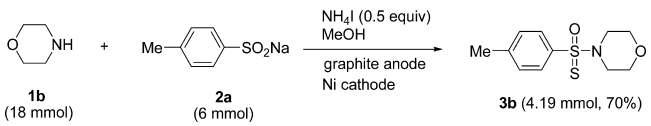
Table 4. Electrochemical Synthesis of Primary Sulfonamide[a]



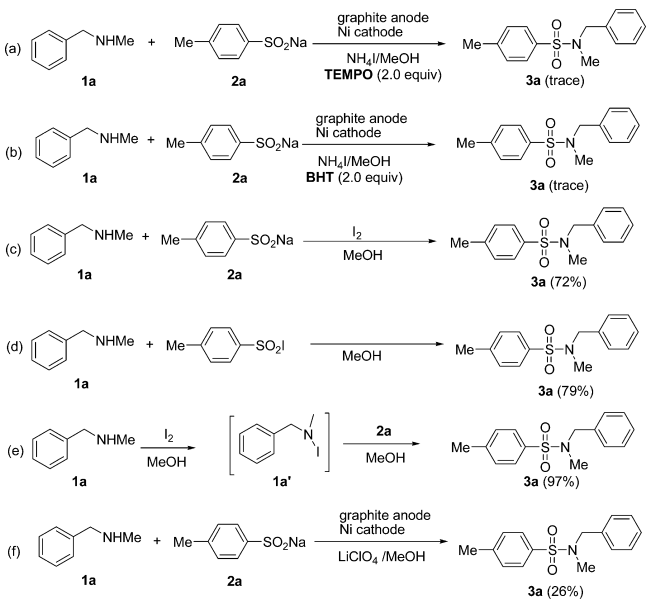


[a]Reaction conditions: aqueous ammonia (5 mL), sodium sulfinate (1 mmol), and NH_4I in 10 mL of MeOH, undivided cell, room temperature, current density of 5 mA/cm^2.

Scheme 3. Scaling Up

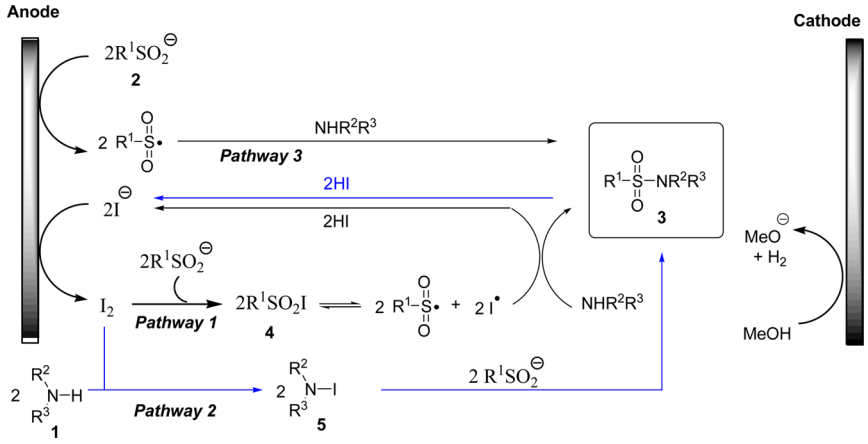


Scheme 4. Control Experiments



DOI: 10.1021/acs.joc.6b00615
J. Org. Chem. 2016, 81, 4713−4719

Scheme 5. Proposed Mechanism for the Electrochemical Synthesis of Sulfonamide



react with amine **1** to form *N*-iodoamine **5**. After further reaction with sulfinate **2**, sulfonamide **3** is produced (pathway 2). As the oxidation potential of sulfinate **2** is close to that of iodide ion (0.60 V for benzenesulfinate **1a** and 0.48 V for iodide ion vs $Ag/AgNO_3$ in 0.1 M CH_3CN),[14] the direct anodic oxidation of sulfinate is also possible, which generates sulfonyl radical. Then further reaction with the amine leads to the final products. This hypothesis is demonstrated by the fact that 26% yield of **3a** was isolated in the absence of NH_4I (see Table 1, entry 14). Meanwhile, the cathodic reduction of methanol leads to the formation of methoxide anion and hydrogen evolution. The former neutralizes the in situ-generated HI and maintains the electrical neutrality of the entire solution (Scheme 5).

3. CONCLUSION

In summary, we have developed an efficient electrochemical protocol for the synthesis of sulfonamides via the oxidative amination of sodium sulfinates. The chemistry proceeds in a simple undivided cell, employing a substoichiometric amount of NH_4I that serves both as a redox catalyst and supporting electrolyte; in this manner, additional conducting salt is not required. A wide range of substrates proved to be compatible with the protocol, including secondary and primary amines, as well as aqueous ammonia. Scale up experiments demonstrated the practicality of the protocol. Mechanistic studies, including a series of control experiments, revealed that the electrochemical oxidative amination of sodium sulfinates likely involves three pathways. These results further reveal that electrochemically generated halide species can function as a surrogate for organic hypervalent iodine reagents or a combination of iodine-containing catalyst and external co-oxidant. Application of these ideas and results to other types of reactions is underway in our laboratory.

4. EXPERIMENTAL SECTION

4.1. Instruments and Reagents. All melting points were measured with an electrothermal melting point apparatus and are uncorrected. NMR spectra were recorded using a 400 MHz spectrometer (400 MHz ^1H frequency, 100 MHz ^{13}C frequency). Chemical shifts are given as δ values (internal standard: TMS). Coupling constants are reported in hertz. Starting materials and solvents were obtained from commercial sources and used without further purification. Products were purified by chromatography on silica gel (petroleum ether/EtOAc).

4.2. Typical Procedure for the Synthesis of Sulfonamides. An undivided cell was equipped with a carbon anode (2.5 × 1 cm^2) and a Ni plate cathode (2.5 × 1 cm^2) and connected to a DC regulated power supply. To the cell were added the desired sodium sulfonate (1 mmol), amine (3 mmol), NH_4I (0.5 mmol), and 10 mL of methanol. The mixture was electrolyzed using constant current conditions (~5 mA/cm^2) at room temperature under magnetic stirring. When TLC analysis indicated that the electrolysis was complete (witnessed by the disappearance of the sulfinate), the solvent was removed under reduced pressure. The residue was poured into a saturated aqueous solution of $Na_2S_2O_3$, and the product was then extracted with DCM (3 × 20 mL), dried over Na_2SO_4, and concentrated in vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/EtOAc (v:v = 5:1) as eluent to afford the desired pure product.

N-Benzyl-N,4-dimethylbenzenesulfonamide (***3a***):[15] mp = 91−93 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.48 (s, 3H), 2.60 (s, 3H), 4.14 (s, 2H), 7.31−7.35 (m, 5H), 7.38 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 135.7, 134.4, 129.8, 128.6, 128.4, 127.9, 127.5, 55.2, 34.3, 21.5.

N-(4-Methylphenylsulfonyl)morpholine (***3b***):[3] mp = 144−146 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 2.99−3.01 (m, 4H), 3.74−3.76 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 132.1, 129.7, 127.9, 66.1, 46.0, 21.5.

1-[(4-Methylphenyl)sulfonyl]pyrrolidine (***3c***):[3] mp = 121−123 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.75−1.78 (m, 4H), 2.45 (s, 3H), 3.23−3.27 (m, 4H), 7.34 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 134.0, 129.6, 127.6, 47.9, 25.2, 21.5.

N,N-Diethyl-4-methylbenzenesulfonamide (***3d***):[6] mp = 39−42 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.13 (t, J = 7.2 Hz, 6H), 2.42 (s, 3H), 3.24 (q, J = 7.2 Hz, 4H), 7.29 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 137.4, 129.6, 127.0, 42.0, 21.5, 14.2.

2-(p-Tolylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (***3e***):[16] mp = 143−145 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 2.95 (t, J = 5.6 Hz, 2H), 3.78 (t, J = 5.6 Hz, 2H), 4.27 (s, 2H), 7.03−7.17 (m, 4H), 7.34 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 133.3, 133.1, 131.6, 129.7, 128.8, 127.8, 126.7, 126.4, 126.3, 47.6, 43.8, 28.9, 21.5.

1,2,3,4-Tetrahydro-6,7-dimethoxy-2-(p-tolylsulfonyl)isoquinoline (***3f***):[17] mp = 133−135 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 2.86 (t, J = 6.0 Hz, 2H), 3.35 (t, J = 6.0 Hz, 2H), 3.83 (s, 3H), 3.84 (s, 3H), 4.19 (s, 2H), 6.52 (s, 1H), 6.57 (s, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 147.7, 143.6, 133.3, 129.7, 127.7, 125.0, 123.4, 111.3, 109.0, 55.9, 55.8, 47.3, 43.8, 28.4, 21.5.

N-Methyl-N-phenyl-4-methylbenzenesulfonamide (***3g***):[3] mp = 86−88 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.18 (s, 3H), 7.11 (d, J = 8.4 Hz, 2H), 7.25−7.33 (m, 5H), 7.45 (d, J = 8.4 Hz, 2H);

DOI: 10.1021/acs.joc.6b00615
J. Org. Chem. 2016, 81, 4713−4719

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 141.6, 133.6, 129.3, 128.8, 127.9, 127.2, 126.6, 38.1, 21.6.

N-Benzyl-4-methylbenzenesulfonamide (**3h**):[6] mp = 109−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 4.15 (d, *J* = 5.6 Hz, 2H), 4.68 (br, 1H), 7.21−7.30 (m, 5H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 136.9, 136.4, 129.7, 128.7, 127.9, 127.9, 127.2, 47.2, 21.6.

N-(4-Methoxybenzyl)-4-methylbenzenesulfonamide (**3i**):[7] mp = 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 3.80 (s, 3H), 4.08 (d, *J* = 5.6 Hz, 2H), 4.53 (br, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 143.4, 137.0, 129.7, 129.3, 128.4, 127.2, 114.0, 55.3, 46.8, 21.5.

N-[(4-Chlorophenyl)methyl]-4-methylbenzenesulfonamide (**3j**):[7] mp = 80−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 4.12 (br, 2H), 4.73 (br, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 136.8, 135.0, 133.6, 130.0, 129.2, 128.7, 127.1, 46.5, 21.5.

N-Cyclohexyl-4-methylphenylsulfonamide (**3k**):[6] mp = 83−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14−1.29 (m, 5H), 1.49 (s, 1H), 1.49−1.54 (m, 2H), 1.62−1.66 (m, 2H), 1.74−1.77 (m, 2H), 2.44 (s, 3H), 3.11−3.16 (m, 1H), 4.64 (d, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 138.5, 129.6, 126.9, 52.6, 33.9, 25.1, 24.6, 21.5.

N-Ethyl-4-methylphenylsulfonamide (**3l**):[3] mp = 57−59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (t, *J* = 7.2 Hz, 3H), 2.44 (s, 3H), 2.97−3.05 (m, 2H), 4.58 (br, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 137.0, 129.7, 127.1, 38.2, 21.5, 15.0.

N-(4-Methylphenyl)-4-methylbenzenesulfonamide (**3m**):[6] mp = 105−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H), 2.40 (s, 3H), 6.54 (br, 1H), 6.69 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 136.0, 135.1, 133.9, 129.8, 127.3, 122.1, 21.6, 20.9.

N-(4-Chlorophenyl)-4-methylbenzenesulfonamide (**3n**):[6] mp = 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H), 7.04 (d, *J* = 8.8 Hz, 2H), 7.20 (br, 1H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 135.6, 135.3, 131.0, 129.8, 129.4, 127.3, 122.7, 21.6.

1-[(4-Methylphenyl)sulfonyl]benzimidazole (**3o**):[5] mp = 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H), 7.31−7.42 (m, 4H), 7.77−7.79 (m, 4H), 8.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2, 144.0, 141.2, 134.6, 130.8, 130.3, 127.3, 125.6, 124.8, 121.1, 21.7.

N-Benzyl-N-methylbenzenesulfonamide (**3q**):[5] mp = 81−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.63 (s, 3H), 4.18 (s, 2H), 7.29−7.37 (m, 5H), 7.57−7.65 (m, 3H), 7.65−7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.4, 135.6, 132.7, 129.2, 128.7, 128.4, 128.0, 127.5, 54.1, 34.5.

N-Benzyl-N-methyl-p-chlorobenzenesulfonamide (**3r**):[15] mp = 82−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.63 (s, 3H), 4.17 (s, 2H), 7.31−7.38 (m, 5H), 7.56 (d, 2H), 7.80 (d, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 136.0, 135.3, 129.5, 128.9, 128.7, 128.4, 128.1, 54.1, 34.3.

N-Methyl-N-benzyl methylesulfonamide (**3s**):[15] Liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.78 (s, 3H), 2.84 (s, 3H), 4.33 (s, 2H), 7.31−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 128.8, 128.4, 128.1, 53.9, 34.3.

Benzenesulfonamide (**3t**):[5] mp = 139−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (br, 2H), 7.53−7.64 (m, 3H), 7.96 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.8, 129.2, 127.2, 126.4.

4-Methylbenzenesulfonamide (**3u**):[5] mp = 129−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 4.92 (br, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 139.1, 129.7, 126.5, 21.5.

4-Chlorobenzenesulfonamide (**3v**):[18] mp = 131−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 (br, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 129.4, 128.7, 128.0.

1-Methoxybenzotriazole:[19] mp = 89−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (s, 3H), 7.36−7.40 (m, 1H), 7.49−7.54 (m, 2H), 8.06−8.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 133.2, 127.0, 123.6, 119.7, 108.8, 33.9.

4-Methylbenzenesulfonyl Iodide:[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H).

4.3. Scale-up Electrolysis for the Synthesis of Sulfonamide 3b. An undivided cell was equipped with a carbon anode (2.5 × 2 cm^2) and a Ni plate cathode (2.5 × 2 cm^2) and connected to a DC regulated power supply. To the cell was added the corresponding morpholine (16 mmol) and sodium sulfinate **2a** (6 mmol), the mixture was electrolyzed using constant current conditions (∼5 mA/cm^2) at room temperature under magnetic stirring. When TLC analysis indicated that the electrolysis was complete (witnessed by the disappearance of the sodium sulfinate), the solvent was removed under reduced pressure. The residue was poured into a saturated aqueous solution of $Na_2S_2O_3$, and the product was then extracted with DCM (3 × 20 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/EtOAc (v:v = 5:1) as eluent to afford the desired pure product as a white solid in a 70% yield.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00615.

Copies of ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by grants from the National Natural Science Foundation of China (nos. 21272021, 21472011) and the National Key Technology R&D Program (2011BAD23B01). Z.C.C. and R.D.L. are grateful to the US National Science Foundation supported PIRE-ECCI (OISE-0968399) and the Center for the Sustainable Use of Renewable Feedstocks (CenSURF), an NSF Center for Chemical Innovation (CHE-1240194) for fostering our international collaboration.

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