

Electrochemical Oxidation of *N*-*p*-Toluenesulfinamides

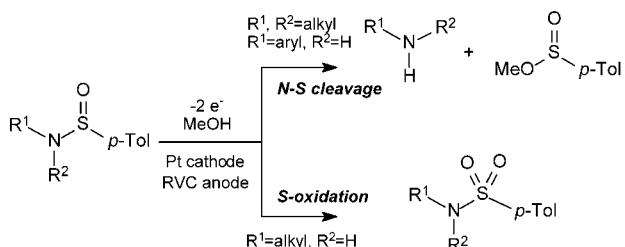
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Received March 7, 2002

ABSTRACT



Contrasting and interesting electrochemical behavior is observed in anodic oxidation of *N*-substituted *p*-toluenesulfinamides under controlled current conditions. For sulfinamides derived from secondary alkylamines and primary arylamines, the *N*-sulfinyl group is removed and the corresponding amines are formed; for sulfinamides derived from primary alkylamines, sulfur oxidation yields the corresponding sulfonamides in good yields.

In organic synthesis, electrochemical processes may offer advantages over conventional methods, such as milder reaction conditions, higher selectivity, and easier isolation of products.¹ An illustrative example is provided by the electrochemical oxidation of amides and carbamates, a highly efficient and general electrochemical reaction.² Sulfoxides and derivatives are routinely employed in organic synthesis³ and are particularly useful in asymmetric transformations. However, the electrochemical behavior of sulfur compounds has been studied to a limited extent.⁴

Electrochemical oxidation of organic sulfides in mixed media of water, methanol, acetic acid, and aprotic solvents has been reported to yield the corresponding sulfoxides, sulfones, and sulfonic acids.⁵ Anodic oxidation of 2-phenyl-1,2-benzisothiazol-3(2H)-ones in acetonitrile also yields the corresponding sulfoxide.⁶ Shono⁷ and Ross⁸ reported that anodic oxidation of *N*-sulfonamides in alcohols and acetic acid afforded α -alkoxy and α -acetoxy *N*-sulfonamides, respectively.

N-Sulfinamides are important synthons in organic synthesis,^{9,10} but so far their electrochemical oxidation behavior is unknown. Herein we report the first study of the anodic oxidation of sulfinamides and discuss the contrasting and interesting behavior observed for *N*-sulfinamides derived from primary and secondary alkylamines and aniline.

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Table 1. Anodic Oxidation of *N*-Substituted *p*-Toluenesulfinamides **1a–h**

entry	sulfinamides	<i>R</i> ¹	<i>R</i> ²	current (mA)	amines 2a–e	methyl sulfinate 3	sulfonamides 4f–h
1	1a	–(CH ₂) ₄ –		20	70%	75%	
2	1b	–(CH ₂) ₅ –		20	72%	76%	
3	1c	PhCH ₂	Me	20	78%	80%	
4	1d	<i>i</i> -Pr	Me	20	n.d.	80%	
5	1e	Ph	H	20	56%	78%	
6	1e	Ph	H	100	30%	70%	
7	1f	PhCH ₂	H	20			85%
8	1f	PhCH ₂	H	60		tr	80%
9	1g	<i>i</i> -Pr	H	20			81%
10	1g	<i>i</i> -Pr	H	60		tr	79%
11	1h	<i>t</i> -Bu	H	20			90%
12	1h	<i>t</i> -Bu	H	60			85%

The racemic *N*-*p*-toluenesulfinamides **1a–h** were prepared from their corresponding sodium *p*-toluenesulfinate. Reaction of the sodium *p*-toluenesulfinate with SOCl₂ followed by addition of anhydrous ethanol afforded the ethyl *p*-toluenesulfinate in 85% yield. The cyclic (**1a,b**) and acyclic (**1e–h**) (±)-*N*-*p*-toluenesulfinamides were prepared in good yields by the reaction of (±)-ethyl *p*-toluenesulfinate with lithium amides, which were prepared by treating the respective amines with *n*-BuLi (–78 °C, THF).¹⁰ The *N*-*p*-toluenesulfinamides **1c** and **1d** were prepared in high yield by methylation (*n*-BuLi, MeI, –78 °C, THF) of the corresponding sulfinamides **1f** and **1g**.

The electrochemical oxidation of *N*-substituted *p*-toluenesulfinamides **1a–h** was carried out in an undivided cylindrical cell equipped with reticulated vitreous carbon (RVC) anode and platinum plate cathode electrodes using tetraethylammonium *p*-toluenesulfonate (Et₄NOTs) as the supporting electrolyte and methanol as the solvent.

In general, three major reaction products were formed and characterized (Table 1): the amines **2**, methyl *p*-toluenesulfinate **3** (from cleavage of the N–S bond), and *N*-*p*-toluenesulfonamides **4** (from sulfur oxidation).

We first investigated the anodic oxidation of the cyclic *N*-(alkyl)-*p*-toluenesulfinamides **1a,b** in different but constant electric currents using either RVC or Pt electrodes.¹¹

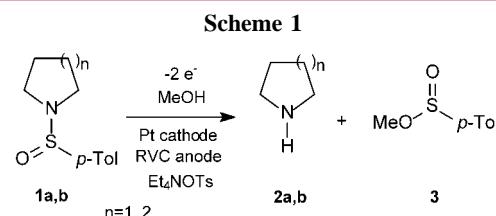
Table 1 shows that best yields were observed when using a constant current of 20 mA and RVC-anode and Pt-cathode electrodes and that the amines **2a,b** and the methyl *p*-

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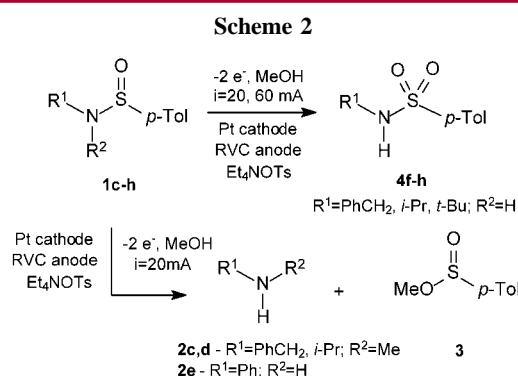
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toluenesulfinate **3** were isolated in good yields at time when 6 F mol^{–1} of electricity was passed (Table 1, entries 1 and 2). Amines **2a,b** and methyl *p*-toluenesulfinate **3** were formed by cleavage of the N–S bonds (Scheme 1).



We then investigated the electrochemical behavior of the acyclic *N*-*p*-toluenesulfinamides **1c–h** derived from secondary and primary alkylamines and aniline (Scheme 2).



In great contrast with the behavior of the cyclic amines **1a,b**, the anodic oxidation of the *N*-(alkyl)-*p*-toluenesulfin-

namides **1f–h** derived from primary amines under the same electrochemical conditions (20 mA, MeOH) promotes sulfur oxidation, thus affording the corresponding *N*-(alkyl)-*p*-toluenesulfonamides **4f–h** in good yields at time when 4 F mol⁻¹ of electricity was passed (Table 1, entries 7–12). Monitoring by GC shows that electrochemical oxidation of sulfinamides **1f–h** at 60 mA gives identical results (Table 1, entries 8, 10, and 12) plus small amounts of sulfinate **3**, whereas the *N*-(phenyl)-*p*-toluenesulfonamide **1e** afforded **2e** and **3** owing to N–S bond cleavage (Table 1, entries 5 and 6).

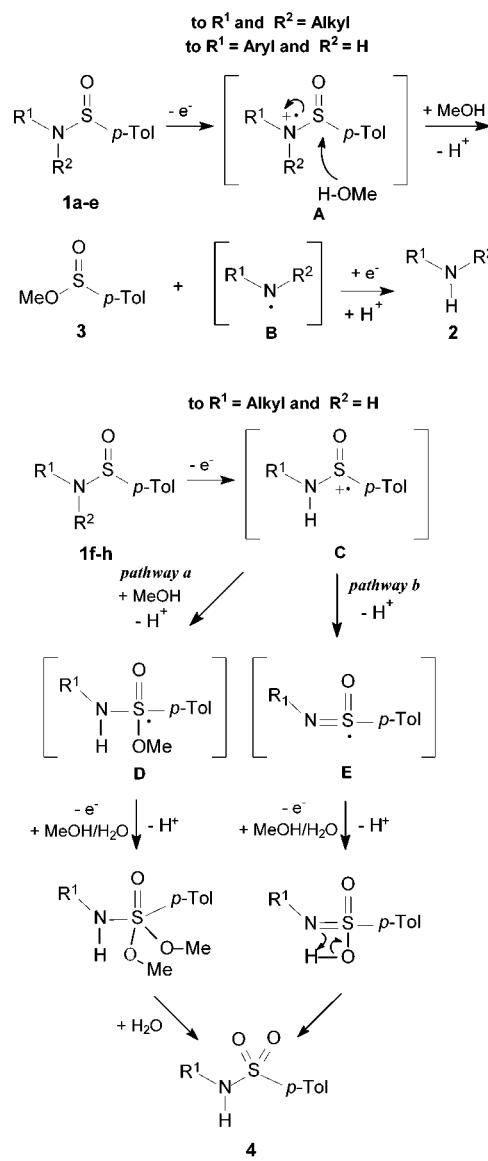
To further confirm the contrasting behavior of sulfinamides derived from secondary and primary amines, the acyclic *N*-(alkyl)-*p*-toluenesulfonamides **1c,d** (prepared by methylation of **1f,g**) were also studied. As observed for the cyclic sulfimanides **1a,b**, the anodic oxidation of **1c,d** (Scheme 2) afforded the respective amines **2c,d** and **3** (Table 1, entries 3 and 4) owing to *N*-sulfinyl group cleavage.

The contrasting electrochemical behavior of sulfinamides derived from primary and secondary amines and aniline was therefore confirmed. A mechanistic interpretation can be rationalized: the different final products observed experimentally suggest that the electron transfer takes place mainly from nitrogen in the case of sulfinamides derived from secondary alkylamines and aniline, whereas the electron transfer take mainly from sulfur in the case of sulfinamides derived from primary alkylamines.

In the case of the *N*-sulfinyl group cleavage (Scheme 3, R¹ = R² = alkyl or R¹ = aryl and R² = H), the sulfinamides **1a–e** derived from secondary alkylamines and aniline upon surrendering one electron to the anode are transformed into a N-radical cation **A** stabilized by the alkyl groups or aromatic group, respectively. Because the electron-deficient N-radical cation is a good leaving group, the attack of methanol at the sulfur cleaves the N–S bond to give N-radical **B** and methyl sulfinate **3**. The formal reduction of radical **B** by the cathodic process in galvanostatic conditions followed by protonation gives amine **2**.

In the sulfur oxidation case, for sulfinamides **1f–h** derived from primary alkylamines (Scheme 3, R¹ = alkyl and R² = H) the formation of the less stabilized N-radical cation may be less operative because of lack of stabilization of this by alkyl and hydrogen groups. In this case the sulfonamides **4** may be formed by a two-electron oxidation process, and it could be rationalized by electron transfer taking place mainly from sulfur to give the S-radical cation **C**. Two pathways can be rationalized to explain the formation of sulfonamides **4** (sulfur oxidation products): In *pathway a*, the attack by methanol at the S-radical cation **C** and elimination of a proton gives the formal S-radical **D**, which undergoes further one-electron oxidation. The attack by methanol followed by the elimination of a proton afforded the dimethoxylated compound. The dimethoxylated compound may be hydrolyzed by water in the reaction media to give the sulfonamide **4**. In *pathway b*, the electrochemical nitrogen deprotonation of the S-radical cation **C** by a cathodic process in the galvanostatic conditions¹² afforded the S-radical sulfoximine **E**. Further one-electron oxidation followed by attack of the water in

Scheme 3



the reaction media at sulfur of the **E** radical species gives the sulfonamides **4**.

To gain further insights into the mechanistic aspects and different electrochemical behavior of *N*-*p*-toluenesulfonamides, the intrinsic gas-phase reactivity¹³ of ionized sulfonamides **1a–h** with methanol is being currently investigated by sequential mass spectrometry.

In conclusion, the anodic oxidation of *N*-*p*-toluenesulfonamides could be considered a new complementary alterna-

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tive to the existing chemical strategies to remove a *N*-sulfinyl protecting group^{9,14} or oxidation of sulfinamides.¹⁵ The important features of the electrochemical methodology are the following: the reaction is operationally simple, is carried out at room temperature, and uses neutral conditions, and its products can be readily isolated. The extension of this

methodology to other *N*-sulfinamides is currently under investigation.

Acknowledgment. The authors acknowledge the Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq and the Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul-FAPERGS for the financial support.

Supporting Information Available: Experimental procedure of anodic oxidation. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL0258381

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