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Electrochemical tandem synthesis of oximes from alcohols using KNO₃ as the nitrogen source, mediated by tin microspheres in aqueous medium[†]

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Electrochemical oximation of alcohols was realized with KNO₃ as the nitrogen source mediated by tin microspheres.

Oximes are valuable synthetic tools, which can either be dehydrated to nitriles or transformed to amides via an acid catalyzed Beckmann rearrangement.¹ Moreover, oximes typically function as anti-inflammatory and antibiotics drugs.² Generally, the traditional method for the synthesis of an oxime is the reaction of aldehydes or ketones with hydroxylamine. Despite its utility, the use of hydroxylamine appears to be inadvisable from a safety point of view. It seems quite dangerous, especially in large amounts in processes involving the use of hydroxylamine. The need for in situ synthesis of hydroxylamine therefore is an ever increasing challenge facing chemists. Oxidation of ammonia with dioxygen is one option.³ On the other hand, various heterogeneous catalysts for the formation of hydroxylamine from ammonia and aqueous hydrogen peroxide has also been reported.⁴ Moreover, catalytic oxidation of primary amines with hydrogen peroxide or aerobic oxidation can also give oximes.⁵ Recently, some studies have been performed to obtain oximes via cobalt or iron complex catalyzed nitrosation of olefins, applying nitric oxide or alkyl nitrites in the presence of various reductants.⁶ However, until now the nitrogen source for the synthesis of hydroxylamine has been limited.

Electrochemical denitrification has recently attracted much interest as an environmentally friendly process because electrons are inherently environmentally friendly reagents compared with conventional redox reagents.⁷ The electro-reduction of nitrate and nitrite has been conducted on different electrodes.⁸ According to the existing reports, electrochemical reduction of nitrate on various electrodes can give eight possible products as follows: NO₂, NO₂⁻, NO, N₂O, N₂, NH₂OH, NH₃ and NH₂NH₂. The major products of these eight are N₂, NH₄OH and NO. However, apart from nitrate or nitrite employed in *ipso*-nitration reactions,⁹ the use of KNO₃ to act as a nitrogen source for the synthesis of organic nitrogen-containing compounds has not yet been explored. We have been interested in developing new electrochemical synthesis methods.¹⁰ Herein, we have realized electrochemical oximation of alcohols with KNO₃ as the nitrogen source mediated by tin microspheres without introducing any template or surfactant.

Initially, in a simple electrochemical setup consisting of an undivided cell equipped with a pair of carbon-rod electrodes, a mixture of benzyl alcohol (2 mmol) and SnCl_2 (1 mmol) in a saturated KNO₃ solution (6 mL) was electrolyzed under galvanostatic conditions and stirred simultaneously for 4 h at room temperature. To our delight, the desired oxime was obtained with a yield of 47% (Table 1, entry 1). Then the electrolysis time was prolonged to six hours in order to improve the yield. However, the resulting yield remained below 60%. As far as we know, hydroxylamine is very unstable and acids are known to have a stabilizing effect.

Table 1 One-pot electrosynthesis of oxime from alcohol under
various conditions a

OH + KNO3			SnCl ₂ 25 mA, rt		
Entry	N source	Acid	Anode	Cathode	$\operatorname{Yield}^{b}(\%)$
1	KNO3		С	С	47 ^c
2	KNO ₃	HCl	С	С	73
3	KNO ₃	H_2SO_4	С	С	66
4	KNO ₃	HNO ₃	С	С	54
5	KNO ₃	HOAc	С	С	32
6	NaNO ₃	HCl	С	С	70
7	$Zn(NO_3)_2$	HCl	С	С	65
8	NaNO ₂	HCl	С	С	N. D.
9	NH ₄ Cl	HCl	С	С	N. D.
10	KNO ₃	HCl	Pt	С	43
11	KNO ₃	HCl	С	Pt	28
12	KNO ₃	HCl	Pt	Pt	59
13	KNO ₃	HCl	Pt	ITO	87
14	KNO ₃	HCl	Pt	ITO	trace ^d
15	KNO ₃	NH ₄ OH	С	Zn	53

^{*a*} Reaction conditions: a mixture of benzyl alcohol (2 mmol), $SnCl_2$ (1 mmol), HCl (12 mol L⁻¹, 0.25 mL) and KNO₃ saturated solution (6 mL) was electrolyzed at a constant current of 25 mA for six hours in an undivided cell, which was equipped with a three-electrode system at room temperature. Further details in the ESI. ^{*b*} Isolated yields are given. ^{*c*} The period of electrolysis was four hours. ^{*d*} Without addition of SnCl₂.

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Therefore hydrochloric acid was added to the reaction mixture and the yield of oxime was enhanced to 73% (Table 1, entry 2). Encouraged by this result, various kinds of acids were examined in the reaction. It was found that hydrochloric acid was the best at stabilizing the hydroxylamine under the electrochemical conditions (Table 1, entries 2-5). Afterwards, different nitrogencontaining salts, such as NaNO₃, Zn(NO₃)₂, NaNO₂ and NH₄Cl, were examined in this reaction. The results show that only nitrate can be employed as the nitrogen source to afford the oxime (Table 1, entries 6-9). It was noted that the conventional nitrogen sources NaNO₂ and NH₄Cl can not produce oxime in this reaction (Table 1, entries 8 and 9). Finally, the reaction electrodes were optimized. After screening, we found that platinum benefited the oxidation of alcohol and tin-doped indium oxide on glass (ITO; Nanbo Co. Ltd, Shenzhen, China) was optimal for the reduction of SnCl₂ (Table 1, entries 10-13). A more detailed investigation into the effect of the electrode is clarified in the following text. It also should be noted that we only obtain oxime in a trace amount when omitting SnCl₂ (Table 1, entry 14). This result shows us that the deposited metallic Sn is the key factor for the reduction of KNO3 in this reaction. In addition, we also tested this oximation reaction mediated by metallic zinc under basic conditions. The final yield of oxime was average (Table 1, entry 15).11 According to the experimental results above, the standard reaction conditions were established as follows: KNO₃ as the nitrogen source, platinum as the anode, ITO electrode as the cathode and SnCl₂ as the mediator.

Under the optimized conditions, various substituted alcohols were investigated to expand the scope of the reaction substrates, as shown in Table 2. Aromatic benzyl alcohols with either weak electron-donating or halogenic groups on the phenyl ring worked well and the corresponding products were obtained with good yields (Table 2, entries 1, 2, 5–9). Strong electron-donating or strong electron-withdrawing groups on the phenyl ring were disfavored in this reaction and the oximes were

Table 2Scope of electrosynthesis of oxime from alcohols in aqueous $medium^a$

	OH + KNO ₃ R ₁ R ₂	SnCl ₂ /HCl	N ^{OH} II R ₁ R ₂
Entry	R_1	R_2	$\operatorname{Yield}^{b}(\%)$
1	C ₆ H ₅	Н	87
2^c	$4-CH_3C_6H_5$	Н	89
3	4-CH ₃ OC ₆ H ₅	Н	68
4	$4-CF_3C_6H_5$	Н	57
5 ^c	$4-FC_6H_5$	Н	81
6 ^{<i>c</i>}	$4-BrC_6H_5$	Н	87
7^c	$4-ClC_6H_5$	Н	90
8 ^c	$2-ClC_6H_5$	Н	83
9	$3-ClC_6H_5$	Н	92
10	C_6H_5	CH ₃	54
11	cyclohexanol	-	47
12^{d}	hydroquinone		52

^{*a*} Reaction conditions: a mixture of alcohol (2 mmol), SnCl₂ (1 mmol), HCl (0.25 mL) and KNO₃ saturated solution (6 mL) was electrolyzed at a constant current of 25 mA for six hours in an undivided cell, which was equipped with a three-electrode system at room temperature. Further details in the ESI. ^{*b*} Isolated yields are given. ^{*c*} With addition of 2 mL ethanol. ^{*d*} HCl was replaced by 0.25 mL H₂SO₄.

obtained with moderate yields (Table 2, entries 3–4). A slight steric effect can be observed when chlorine is located on different positions of the phenyl ring. The location of the chlorine at the *ortho* position gave a slightly lower yield than that of the *para* position (Table 2, entries 7–9). In addition, secondary alcohols were also employed. When 1-phenylethanol was employed as the reaction substrate, the corresponding ketoxime was obtained with a moderate yield (Table 2, entry 10). Aliphatic secondary alcohols can also be applied in this reaction to afford the oxime with a 47% yield (Table 2, entry 11). Moreover, hydroquinone was also used. An initial anodic oxidation can transform hydroquinone to benzoquinone and the final oxime product was obtained with a 52% yield (Table 2, entry 12).

We also investigated the reaction mechanism. As mentioned above, in the direct electrochemical reduction of nitrate on an electrode in the absence of SnCl₂, only a trace amount of oxime could be obtained (Table 1, entry 14). This indicated that *in situ* produced Sn was the key mediator for the reduction of KNO₃ in this reaction. On the basis of these results, we proposed a reaction pathway as shown in Fig. 1. On the surface of the platinum anode, alcohols were oxidized to the corresponding carbonyl compounds by losing an electron without using any chemical oxidants while SnCl₂ was reduced to Sn on the ITO cathode. *In situ* produced Sn then reacts with KNO₃ to produce hydroxylamine, which was separated and characterized by ¹H NMR.¹² Once the produced carbonyl compound met the hydroxylamine in solution, oxime was formed.

Moreover, we observed that the morphological structure of tin deposited on the cathode varied with the cathode material during the electrolysis process. For instance, the metal tin deposited on graphite or platinum was metallic luster while the deposition on ITO was too small to determine with eyesight alone. In order to clarify the differences between the electrodes, the morphology of the tin generated on the surface of the three electrodes was characterized by scanning electron microscopy (SEM) and X-ray diffraction (XRD). XRD indicated that the Sn deposited was all β -phase on the three electrodes.¹² SEM showed that the tin deposited on the surface of the ITO is dispersive spherical (Fig. 2) while the tin deposited on the surface of the graphite was rocklike and the tin deposited on the surface of the platinum was agglomerated spherical (Fig. 3a and Fig. 3b). After further examination, we found that the dispersive spheres deposited on the ITO are hollow as shown in Fig. 2b. So it is obvious that dispersive hollow spherical tin has a larger surface area compared with the rocklike or agglomerated tin under the condition of equal amount of deposited Sn . This was proportional to the tin mediation activity since the use of an ITO electrode gave a higher yield than that of graphite or platinum (Table 1, entries 10-13).



Fig. 1 Schematic depiction of one-pot electrosynthesis of an oxime from an alcohol.



Fig. 2 SEM image of tin deposited on the surface of ITO. a) Deposited time 5 min, scale bar: 500 nm. b) Deposited time 10 min, scale bar: 500 nm.



Fig. 3 a) SEM image of tin deposited on the surface of graphite. Scale bar: $10 \ \mu\text{m}$. b) SEM image of tin deposited on the surface of platinum. Scale bar: $10 \ \mu\text{m}$.

In conclusion, an efficient electrosynthesis of oximes from alcohols with KNO_3 as the nitrogen source has been realized for the first time. This preliminary study showed that the deposited dispersive spherical tin microstructure plays an important role in the reduction of KNO_3 . High efficiency and environmental friendliness renders this methodology an attractive alternative synthetic route to oximes. Further investigations to expand the application of KNO_3 as a nitrogen source for the synthesis of useful organic nitrogen-containing compounds is underway in our laboratory.

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- 12 Details are in the ESI[†].