An electrochemical tandem reaction: one-pot synthesis of homoallylic alcohols from alcohols in aqueous media†

Li Zhang, Zhenggen Zha,* Zhenlei Zhang, Yunfeng Li and Zhiyong Wang*

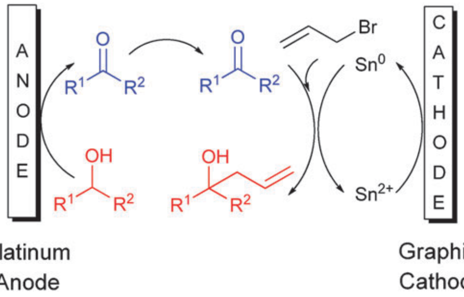
Received 19th June 2010, Accepted 5th August 2010
DOI: 10.1039/c0cc01964j

A tandem electrosynthesis of homoallylic alcohols from alcohols in one-pot was realized. In virtue of this one-pot electrosynthesis, the traditional reaction substrates of allylation were broadened from carbonyl compounds to alcohols.

The development of efficient methods for the synthesis of homoallylic alcohols is very important because of their wide applications, especially as intermediates in organic synthesis, and building blocks for natural products and bioactive compounds. A number of elegant approaches to the synthesis of homoallylic alcohols have been reported.[1] Recently, the electrochemical allylation of carbonyl compounds has also been developed.[2] For instance, electrogenerated In, Sn, Zn or cathodic reduction has mediated the allylation to give the corresponding homoallylic alcohols with good yields or good chemoselectivities. However, the previous allylations involved carbonyl compounds as the starting materials, which limited the scope of the reactions, since some carbonyl compounds are unstable and difficult to obtain. On the other hand, a variety of alcohols are readily available, and most of them are stable in storage or during reactions. Therefore, it is desirable to synthesize homoallylic alcohols by employing alcohols as substrates. Traditionally, the allylation of alcohols usually involves a multi-step procedure, including the oxidation of alcohols to carbonyl compounds[3] followed by allylation of the carbonyl compounds.[2] However, the electrosynthesis of homoallylic alcohols from alcohols directly has not yet been reported. Recently, on the basis of the paired electrosynthesis of carbonyl compounds and homoallylic alcohols in a divided cell,[4] we realized the electrosynthesis of homoallylic alcohols from alcohols directly with a tandem reaction in one pot.

As shown in Scheme 1, alcohols were oxidized to the corresponding carbonyl compounds by losing electrons without using any chemical oxidants on the surface of a platinum anode, while $SnCl_2$ was reduced to Sn on the graphite cathode. Once the produced carbonyl compound met the Sn generated *in situ* and allyl bromide in solution, the corresponding homoallylic alcohol was produced. In this electrosynthesis process, both the working electrode and the counter electrode were exploited to produce useful products. Compared with the aforementioned electrochemical method,[2,3] in which only the working electrode was exploited, we saved 50% of the energy consumption wasted on the counter electrode.[5] By this dexterously tandem design, a variety of aromatic primary alcohols could be converted into their corresponding homoallylic alcohols directly with excellent yields, avoiding the tedious separation of the intermediate aldehydes for further transformation. Moreover, the traditional reaction substrates of allylation were broadened from carbonyl compounds to alcohols.

Initially, different electrodes were optimized in this electrochemical allylation. To the best of our knowledge, smooth platinum and graphite are good anode materials commonly used in electrooxidation processes because they show large overpotentials for oxygen evolution in aqueous solution, while graphite is usually used as the cathode material in aqueous solution because of the large overpotential for hydrogen evolution.[6] In our system, both oxygen evolution on the anode and hydrogen evolution on the cathode were unfavorable. Therefore, we tested different combinations of these two electrodes (Table 1, entries 1–4). Among various electrodes examined, it was found that platinum was more efficient for anodic oxidation while graphite was better for cathodic reduction, as shown in entry 1 of Table 1. In order to clarify the differences between the electrodes, the morphology of the Sn generated on the surface of the two electrodes was characterized by scanning electron microscopy (SEM, Fig. S1 and S2†) and X-ray diffraction (XRD, Fig. S3†). XRD indicated that Sn generated *in situ* was of β-phase, regardless of formation from the graphite electrode or from the platinum electrode. However, different morphological structures were formed on the surface of different electrodes. The main morphology of the Sn generated on the surface of graphite was flocculent, while that on the surface of platinum was rod-shaped. It is obvious that the flocculent morphology of Sn had a larger surface area than that of rod-shaped Sn. Moreover, it was also found that *in situ*-produced Sn was easier to peel off from the surface of the graphite electrode than from the platinum, which could increase the production of metal Sn. Afterwards, different electrolytes,

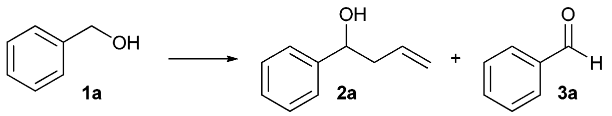


Scheme 1 Tandem electrosynthesis of homoallylic alcohols from alcohols in aqueous media with an undivided cell.

Hefei National Laboratory for Physical Science at Microscale, CAS Key Laboratory of Soft Matter Chemistry and Department of Chemistry, University of Science and Technology of China, 96 Jinzhai Road, Hefei 230026, China. E-mail: zwang3@ustc.edu.cn; Fax: +86 551-3603185; Tel: +86 551-3603185

† Electronic supplementary information (ESI) available: Experimental section, characterization data and NMR spectra of all products. See DOI: 10.1039/c0cc01964j

Table 1 Optimizing the transformation conditions of alcohol **1a** into homoallylic alcohol **2a**[a]



	Conditions					Yield (%)[b]		
Entry	Sn source	Electrolyte		Anode	Cathode	**1a**	**2a**	**3a**
1	$SnCl_2$	KNO_3	0.5 M	Pt	C	35	62.6	2.4
2	$SnCl_2$	KNO_3	0.5 M	C	Pt	94.3	5.7	0
3	$SnCl_2$	KNO_3	0.5 M	C	C	93.1	6.9	0
4	$SnCl_2$	KNO_3	0.5 M	Pt	Pt	67	33	0
5	$SnCl_2$	Bu_4NBF_4	0.5 M	Pt	C	65	35	0
6	$SnCl_2$	$LiClO_4$	0.5 M	Pt	C	58	45	0
7	$SnCl_2$	KNO_3	1 M	Pt	C	37	55	8
8	$SnCl_2$	KNO_3	2 M	Pt	C	41	51	8
9	$SnCl_2$	KNO_3	3 M	Pt	C	56	33	11
10	$SnCl_2$	KNO_3	5 M	Pt	C	42	45	13
11	$SnCl_2$	KNO_3	Saturated	Pt	C	32.5	55	12.5
12	$SnSO_4$	KNO_3	0.5 M	Pt	C	50	50	0
13	$SnSO_4$	KNO_3	Saturated	Pt	C	53.7	28.6	17.7
14[c]	$SnCl_2$	KNO_3	0.5 M	Pt	C	64.9	31.8	3.3
15[d]	$SnCl_2$	KNO_3	0.5 M	Pt	C	64.8	15.7	19.5
16[e]	$SnCl_2$	KNO_3	0.5 M	Pt	C	9	91	0

[a] Reaction conditions: the mixture of benzyl alcohol (2 mmol), allyl bromide (3 mmol) with the corresponding Sn source (1 mmol) was electrolyzed at a constant current of 20 mA for 4 h in an undivided cell, which was equipped with a three-electrode system at room temperature. The cell was sealed by film in order to minimize the volatilization of the allyl bromide. [b] GC-MS yield. [c] The amount of $SnCl_2$ was 0.5 mmol. [d] The amount of $SnCl_2$ was 0.2 mmol. [e] The reaction time was prolonged to 6 h, 2.2 F mol^{-1} of current was consumed.

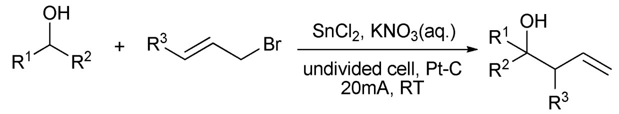
such as *n*-Bu_4NBF_4, $LiClO_4$ and KNO_3, were employed in this electrochemical reaction. It was found that KNO_3 was most efficient (Table 1, entries 1, 5 and 6). When the concentration of the KNO_3 aqueous solution was 0.5 M, the highest yield was obtained (Table 1, entries 1, 7–11). $SnSO_4$, instead of $SnCl_2$ as the Sn source, was also examined (Table 1, entries 12 and 13). The experimental results indicate that $SnCl_2$ was more adoptable. We also tried a smaller amount of $SnCl_2$. Compared with the 0.25 equiv. and 0.1 equiv. dosage, 0.5 equiv. of $SnCl_2$ gave the best yield (Table 1, entries 1, 14 and 15). It was also found that a higher reaction yield was obtained by prolonging the reaction time to 6 h. For instance, the allylation of benzyl alcohol gave the corresponding homoallylic alcohol with a yield of 91% (Table 1, entry 16).[7]

Therefore the reaction conditions were chosen as below: $SnCl_2$ as the Sn source, 0.5 M KNO_3 as the electrolyte, platinum, graphite and saturated calomel electrodes (SCE) as the working electrode, counter electrode and reference electrode, respectively. All the reactions were electrolyzed at a constant current of 20 mA for 6 h.

With the optimal reaction conditions in hand, the generality of the reaction was investigated with a variety of alcohols. The reaction results were summarized in Table 2. It was noted that solid substrates with a low solubility in water incurred lower yields compared with liquid substrates, resulting from the difficulty of electron transfer between the solid electrode and the solid substrates.[8] To solve this problem, CH_3CN was added to increase the solubility of the solid substrate. The allylation of benzyl alcohols bearing electron-donating or electron-withdrawing substituents were carried out smoothly to afford the corresponding aromatic homoallylic alcohols with high yields (Table 2, entries 1–4, 7, 8 and 10). However, *p*-NO_2 substitution on the aromatic ring of benzyl alcohols resulted in a moderate yield (Table 2, entry 11). A notable steric effect could be observed; *ortho*-substitution gave the lowest yield among *para*, *meta* and *ortho* substitution on phenyl, and 1-naphthyl substitution gave a medium yield (Table 2, entries 4–6, 8, 9 and 12). Only oxidation product and no allylation product was obtained when 1-phenylethanol was employed as a substrate (Table 2, entry 13). A heterocyclic substrate also gave a low yield (Table 2, entry 16). As for aliphatic alcohols, both primary and secondary alcohols worked well (Table 2, entries 14 and 15). Crotylation only gave a γ-product with a good yield (Table 2, entry 17).

In order to elucidate the reaction process, we measured the oxidative and reductive processes of the reaction by cyclic voltammetry (CV). As shown in Fig. 1 and Fig. 2, no oxidation or reduction waves were observed in aqueous KNO_3 solution (trace a in Fig. 1 and Fig. 2), which indicates that blank solutions could not be electroactive in the potential window of interest. When the benzyl alcohol and $SnCl_2$ were added to the blank solution, an oxidation wave (O_1), which corresponds to the electrooxidation of benzyl alcohol, was observed, as shown in trace b of Fig. 1. On the other hand, a couple of well-defined reduction waves (R_2) and oxidation waves (O_2) were exhibited, as shown in trace b of Fig. 2. The R_2 wave indicates that Sn^{2+} was reduced to Sn, while the O_2 wave on the backward potential sweep was the corresponding reverse process. In order to investigate the reactions on both electrodes in our system, CV of the two electrode reactions in one-pot were measured, respectively, as shown in trace c of Fig. 1 and Fig. 2. Compared to the CV of the single electrode reaction (trace b in Fig. 1 and Fig. 2), similar waves of CV were observed for the dual electrode reactions in the one-pot system (trace c in

Table 2 Scope of the electrosynthesis of homoallylic alcohols from alcohols in aqueous media[a]



Entry	R^1	R^2	R^3	Yield (%)
1	Ph	H	H	91
2	4-Me-Ph	H	H	86
3	4-MeO-Ph	H	H	96
4	4-Cl-Ph	H	H	90[b]
5	3-Cl-Ph	H	H	82[b]
6	2-Cl-Ph	H	H	50[b]
7	4-F-Ph	H	H	85[b]
8	4-Br-Ph	H	H	87[b]
9	2-Br-Ph	H	H	70[b]
10	4-CF_3-Ph	H	H	88
11	4-NO_2-Ph	H	H	40[b]
12	1-Naphthyl	H	H	62[b]
13	Ph	CH_3	H	94[c]
14	$PhCH_2$	H	H	70
15	Cyclohexanol		H	80
16	2-Thienyl	H	H	34
17	Ph	H	CH_3	82[d]

[a] Isolated yields are given. Reaction conditions: the mixture of benzyl alcohol (2 mmol), allyl bromide (3 mmol) with $SnCl_2$ (1 mmol) was electrolyzed at a constant current of 20 mA for 6 h in an undivided cell, which was equipped with a three-electrode system at room temperature (details in the ESI). The cell was sealed by film in order to minimize the volatilization of the allyl bromide. [b] CH_3CN (1 mL) was added to increase the solubility of the solid substrate. [c] Isolated yields of oxidation. No corresponding allylation product was observed. [d] *syn* : *anti* = 1 : 1.

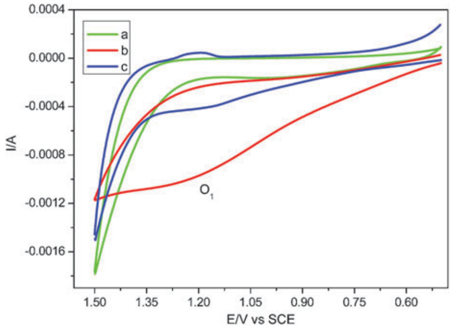


Fig. 1 Cyclic voltammogram curves of (a) 0.04 M KNO_3/H_2O; (b) 0.17 M benzyl alcohol, 0.04 M KNO_3/H_2O; (c) 0.17 M benzyl alcohol, 0.06 M $SnCl_2$ and 0.04 M KNO_3/H_2O, recorded at a Pt electrode (1.0 × 1.0 cm^2), scan rate: 100 mV s^{-1} at room temperature.

Fig. 1 and Fig. 2). This indicates that the anodic and cathodic reactions were compatible in one pot. It is noted that the oxidation peak in Fig. 1 is not well-defined, which can be ascribed to the poor solubility of benzyl alcohol in aqueous media. When CH_3CN, instead of an aqueous medium, was employed as a solvent to measure CV, a well-defined oxidation peak appeared (Fig. S4†). As a result, the CV study demonstrates that carbonyl compounds were obtained on the surface of the platinum electrode by oxidation, while Sn was generated at the graphite electrode by reduction. These two redox products then reacted with allyl bromide to afford the homoallylic alcohol in a one-pot system.

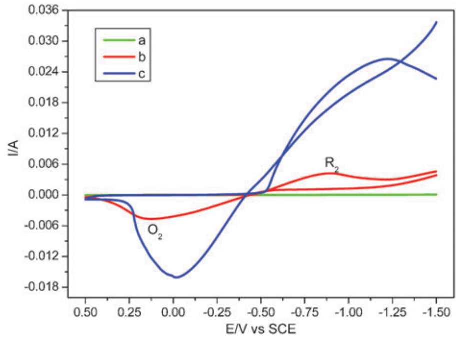


Fig. 2 Cyclic voltammogram curves of (a) 0.04 M KNO_3/H_2O; (b) 0.06 M $SnCl_2$, 0.04 M KNO_3/H_2O; (c) 0.17 M benzyl alcohol, 0.06 M $SnCl_2$ and 0.04 M KNO_3/H_2O, recorded at a glassy carbon electrode (diameter 0.4 cm), scan rate: 100 mV s^{-1} at room temperature.

In conclusion, we have reported a tandem electrosynthesis of homoallylic alcohols directly from alcohols in one pot. In virtue of this one-pot electrosynthesis, the traditional substrates of allylation were broadened from carbonyl compounds to alcohols. The results exhibit a new avenue of green synthesis, in which conventional oxidants could be avoided and the tedious separation of the reaction intermediates could be circumvented. Other efficient energy-saving and environmental-friendly reactions are under way in our laboratory.

We are grateful for financial support from the National Science Foundation of China (no. 20772118, 20932002, 20972144 and 90813008).

Notes and references

1 (*a*) S. E. Denmark and S. T. Nguyen, *Org. Lett.*, 2009, **11**, 781; C.-J. Li, *Chem. Rev.*, 1993, **93**, 2023; (*b*) C.-J. Li, *Chem. Rev.*, 2005, **105**, 3095; (*c*) A. Chanda and V. V. Fokin, *Chem. Rev.*, 2009, **109**, 725.
2 (*a*) G. Hilt, *Angew. Chem., Int. Ed.*, 2003, **42**, 1720; (*b*) Z. G. Zha, A. L. Hui, Y. Q. Zhou, Q. Miao, Z. Y. Wang and H. C. Zhang, *Org. Lett.*, 2005, **7**, 1903; (*c*) J.-M. Huang and Y. Dong, *Chem. Commun.*, 2009, **26**, 3943; (*d*) F. Amemiya, K. Fuse, T. Fuchigami and M. Atobe, *Chem. Commun.*, 2010, **46**, 2730.
3 (*a*) T. Raju, S. Manivasagan, B. Revathy, K. Kulangiappear and A. Muthukumaran, *Tetrahedron Lett.*, 2007, **48**, 3681; (*b*) T. Yoshida, M. Kuroboshi, J. Oshitani, K. Gotoh and H. Tanaka, *Synlett*, 2007, **17**, 2691; (*c*) K. Mitsudo, H. Kumagai, F. Takabatake, J. Kubota and H. Tanaka, *Tetrahedron Lett.*, 2007, **48**, 8994.
4 L. Zhang, Z. G. Zha, Z. Y. Wang and S. Q. Fu, *Tetrahedron Lett.*, 2010, **51**, 1426.
5 M. M. Baizer, in *Organic Electrochemistry*, ed. M. M. Baizer and H. Lund, Marcel Dekker, New York, 1991, ch. 35, pp. 1421–1430 and selected examples: (*a*) M. Ishifune, H. Yamashita, M. Matsuda, H. Ishida, N. Yamashita, Y. Kera, S. Kashimura, H. Masuda and H. Murase, *Electrochim. Acta*, 2001, **46**, 3259; (*b*) S. Kim, R. Uchiyama, Y. Kitano, M. Tada and K. Chiba, *J. Electroanal. Chem.*, 2001, **507**, 152.
6 J. Grimshaw, *Electrochemical Reactions and Mechanisms in Organic Chemistry*, Elsevier, Amsterdam, 2000.
7 Without electrolysis, the homoallylic alcohol was not obtained and benzyl alcohol was recovered.
8 (*a*) S. Nad and R. Breinbauer, *Angew. Chem., Int. Ed.*, 2004, **43**, 2297; (*b*) T. Tajima and T. Fuchigami, *Angew. Chem., Int. Ed.*, 2005, **44**, 4760; (*c*) T. Tajima and T. Fuchigami, *J. Am. Chem. Soc.*, 2005, **127**, 2848.