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Aqueous electrosynthesis of carbonyl compounds and the corresponding homoallylic alcohols in a divided cell

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ABSTRACT

An aqueous paired electrosynthesis is studied in a divided cell. On graphite anode Br^- was oxidized to Br_2 and this generated Br_2 oxidized alcohols to the corresponding carbonyl compounds while Sn^{2+} was reduced to Sn^0 on graphite cathode. Then the produced metallic tin mediated allylation of the carbonyl compounds with allyl bromide to generate the corresponding homoallylic alcohols. In the reaction the mediators (Sn and Br_2) were generated in situ and could be reused via the electrolysis. Both working electrode and the counter electrode were utilized to generate useful products without the sacrifice of the electrode materials.

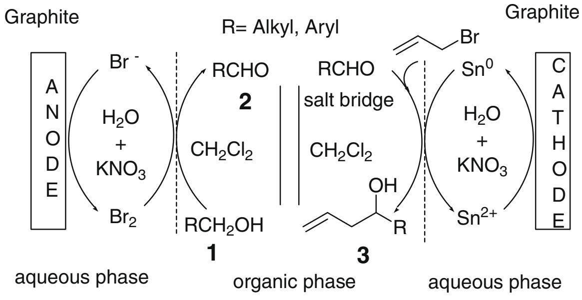
In the past two decades, electrochemical synthesis has attracted many attentions.[1] Compared to the conventional organic synthesis, electroorganic synthesis is a powerful tool for clean and safe organic synthesis. Its process is up to the standard of green chemistry.[2] Electrons are inherently environment-friendly reagents and they can substantially eliminate the waste treatment of used redox reagents.[3]

Among many electrochemical-promoted reactions, the studies of both oxidation of alcohols and the allylation of carbonyl compounds are very active due to the universal intermediates of the produced carbonyl compounds and the corresponding homoallylic alcohols for organic synthesis or pharmaceutical design. Some publications reported the electrochemical oxidation of alcohols to aldehydes, in which the electrogenerated hypobromine, chiral azabicyclo-*N*-oxyls were employed as oxidizing reagents.[4] In these reaction systems, the poor conductivity of the organic solvents led to a higher electrolysis potential and the involvement of expensive mediators or catalysts. Recently the two-phase electrolysis was developed and employed in organic synthesis. For instance, the oxidation of benzylic alcohols in sodium bromide solution was performed in an undivided cell.[5] This method can circumvent side reactions during electrolysis.

On the other hand, electrochemical allylations of carbonyl compounds have been reported by using different catalytic electrogenerated metals.[6,7] Whether electrochemical oxidation or reduction, there are still some flaws such as sacrification of the anode electrode, waste of counter electrode, use of the stoichiometric amount of mediator, byproduct incurred by over-potential and so on. To the best of our knowledge, there have been no reports on the combination of these two reactions in a divided cell simultaneously yet. Herein, we describe a new electrochemical synthesis method for the formation of the carbonyl compounds and the corresponding homoallylic alcohols without the sacrification of anode electrode and the waste of counter electrode. And only catalytic amount of mediator was used in the reaction.

Our design is shown in Scheme 1. We performed the oxidation of the alcohols and the following allylation in a divided cell simultaneously by using paired electrolysis with a salt bridge of KNO_3 under potentiostatic control. In anodic compartment, Br^- was oxidized to Br_2, which oxidized alcohols to yield corresponding carbonyl compounds[5,8] while Sn^{2+} was reduced to Sn^0 in cathodic compartment. Then the produced metallic tin mediated allylation between allyl bromide and carbonyl compounds to generate homoallylic alcohols.[7,9] With the electrolysis, Sn^{2+} and Br^- could be reused for the next cycle.

Experimentally, the salt bridge of KNO_3 was employed to connect the two separated electrolysis cells. The two cells were



Scheme 1. The design for the divided cell.

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equipped with a graphite electrode (dia. 3.0 mm) as anode, a graphite electrode (dia. 3.0 mm) as cathode, saturated calomel electrode (SCE) as reference electrode respectively. A solution of benzyl alcohol (2 mmol) in 1 mL of CH_2Cl_2 was placed in anodic compartment. To the solution, a solution of sodium bromide (2 mmol), HBr (48%, 0.4 mL) in water (5 mL) were added as aqueous phase. In cathodic compartment, $SnCl_2$ (2 mmol) in water (5 mL) was added as aqueous, a solution of benzaldehyde (2 mmol), allyl bromide (3 mmol) in CH_2Cl_2 (1 mL) as organic phase. A pair of electrode was placed in aqueous phase which was electrolyzed at a constant potential. Subsequently, the reaction conditions were optimized as follows.

At first, different potentials were tested. When the potential was below 0.6 V, on the cathode Sn2+ was reduced slowly and the produced tin was coated on the electrode tightly, resulting in the difficulty for tin to peel off from the electrode into the solution and retarding the further electrolysis while on the anode Br− could not be oxidized. When the potential was over 0.6 V, many byproducts were generated. It was found that the potential of 0.6 V was the most efficient. Cyclic voltammograms showed us the oxidation and reduction reactions clearly in the divided cell. According to the curve of blank solution [Figs. 1 and 2(a)], there was no evident anodic or cathodic wave, which indicated that blank solution was not electroactive in the potential window of interest. When mediators were added and a pair of curves were recorded, as shown in Figure 1(b), Br− exhibited an oxidation wave (O1) and a reduction wave (R1). The O1 wave corresponded to the electro-oxidation of Br−, which led to the formation of Br2.[10] On the backward potential sweep, the R1 wave could be ascribed to the corresponding reverse process. In Figure 2(b), the R1 wave indicated that Sn2+ was reduced to Sn0.[11] The O1 and O2 waves were attributed to corresponding oxidation processes. After organic substrates were added, similar waves appeared [Figs. 1 and 2(c)], which indicated that mediator precursors (SnCl2 and NaBr) were reduced at the cathode and oxidized at the anode, respectively. The electrogenerated Br2 oxidized alcohols to the carbonyl compounds while Sn0 mediated allylation reaction of the corresponding carbonyl compounds to produce the corresponding homoallylic alcohols.

Afterward, the ratio of the mediator to the substrate in the reaction was optimized. When the ratio of mediator to substrate (M/S) was 1:1, the reaction was carried out smoothly. Considering that mediators (Sn and Br_2) could be regenerated by electrolysis and be used in cycle, the ratio of M/S was reduced to 1:4 (M/S). In this case, the reaction could be carried out very well to give the corresponding homoallylic alcohols with high yields. As a result, the mediators were converted to the catalysts to some extent. The total reaction in divided cell could be summarized as Scheme 2.

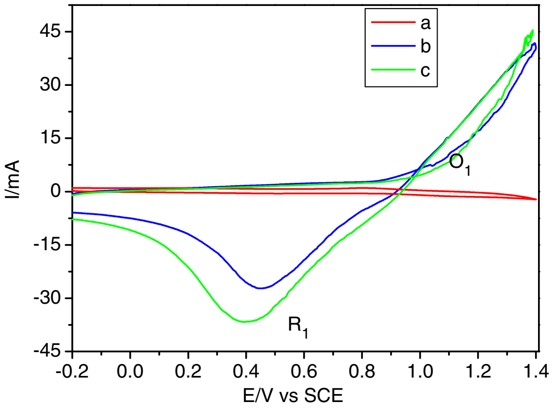


Figure 1. Cyclic voltammograms of the solutions in water with two glassy carbon electrodes (3.0 mm diameter vs SCE) using KNO_3 as supporting electrolyte at a scan rate of 10 mV/s in the presence of KNO_3 salt bridge and at room temperature. (a) 0.5 mmol KNO_3 in water (5 mL); (b) 0.05 mmol NaBr, HBr (0.01 mL) and 0.5 mmol KNO_3 in water (5 mL); (c) 0.05 mmol NaBr, HBr (0.01 mL) and 0.5 mmol KNO_3 in water (5 mL) and 1 mmol benzylic alcohol in CH_2Cl_2 (1 mL).

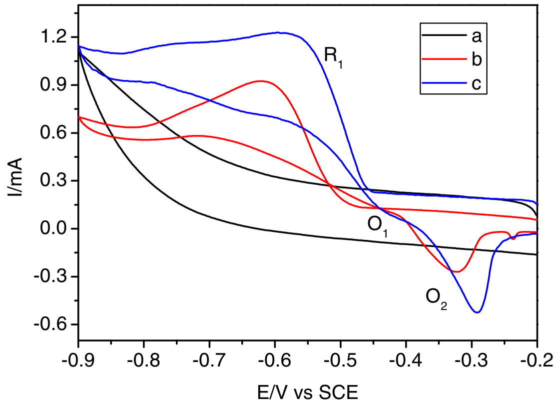
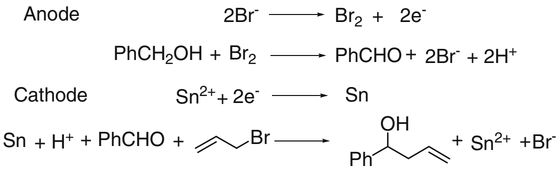


Figure 2. Cyclic voltammograms of the solutions in water with two glassy carbon electrodes (3.0 mm diameter vs SCE) using KNO_3 as supporting electrolyte at a scan rate of 10 mV/s and in the presence of KNO_3 salt bridge at room temperature. (a) 0.5 mmol KNO_3 in water (5 mL); (b) 0.05 mmol $SnCl_2$ and 0.5 mmol KNO_3 in water (5 mL); (c) 0.05 mmol $SnCl_2$ and 0.5 mmol KNO_3 in water (5 mL) and 1 mmol benzaldehyde and 1.5 mmol allyl bromide in CH_2Cl_2 (1 mL).

The reaction indicated that carbonyl compounds and homoallylic alcohols were synthesized in anodic and cathodic compartment respectively. Both working electrode and the counter electrode were utilized to generate synthetically useful products in the reaction. In this case current efficiency was improved one fold in comparison with that only using working electrode alone.

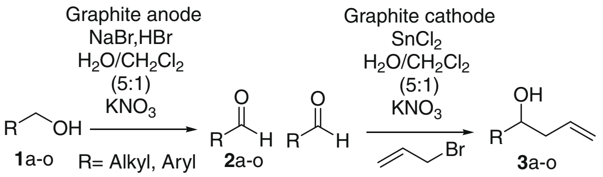
Finally, different supporting electrolytes were optimized. The different electrolytes such as CTAB (cetyltrimethyl–ammoniumbromide), Et_4NBr, Bu_4NI, KNO_3 and $LiClO_4$ were examined under the conditions. It was found that the supporting quaternary ammonium salt electrolyte disfavored this reaction and resulted in many side reactions in organic phase. Eventually, KNO_3 was selected as supporting electrolyte.

Subsequently the reactions were carried out under the optimized conditions.[12] The experimental results were listed in Table 1. From Table 1, it can be seen that halogen substituents at the *para* position gave the corresponding products with higher yields (entries 3 and 4) compared to aromatic alcohols without substitution (entries 1 and 2). *Para*-NO_2 and *para*-CH_3 substituents on the benzylic alcohol gave medium yields (entries 5 and 6). *Ortho*-Br substituent on the benzylic alcohol also favored the allylation (entry 7). However, *ortho*-NO_2 substitution had a negative effect on this allylation (entry 8). When aliphatic alcohols or secondary alcohols were employed as the reaction substrates, the reaction could be carried out smoothly to afford the corresponding products with moderate yields (entries 9–13). Heteroaromatic substrates also worked well (entries 14 and 15). It should be noted that rich-electron heteroaromatic substrate gave a higher yield than poor-electron heteroaromatic substrate. In anodic compartment, there was no significant effect of the substituents on the electrochemical oxidation. Compared to the previously reported

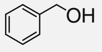
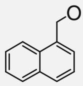
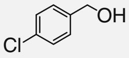
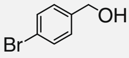
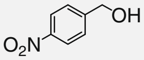
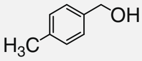
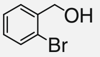
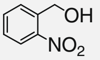
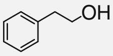
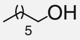
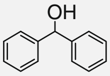
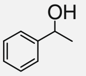
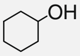
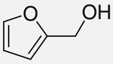
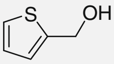


Scheme 2. The total reaction in this electrochemical process.

Table 1
Paired electrochemical synthesis homoallylic alcohols from alcohols in a divided cell



1k-m was secondary alcohol,
2k-m and **3**k-m were the corresponding products

Entry	Substrate **1**	Product **2**	Yield[a] (%)	Product **3**	Yield[a] (%)
1		**2a**	95	**3a**	91
2		**2b**	85	**3b**	93
3		**2c**	97	**3c**	93
4		**2d**	97	**3d**	92
5		**2e**	84	**3e**	92
6		**2f**	85	**3f**	88
7		**2g**	97	**3g**	90
8		**2h**	45	**3h**	33
9		**2i**	46	**3i**	76
10		**2j**	82	**3j**	80
11		**2k**	99	**3k**	0
12		**2l**	98	**3l**	20
13		**2m**	88	**3m**	87
14		**2n**	85	**3n**	96
15		**2o**	82	**3o**	71

[a] Isolated yield.

oxidation in one cell,[5] the yields were enhanced largely, especially for the substrates of 4-nitrobenzyl alcohol, heptanal and diphenyl methanol (entries 4, 10 and 11). It should be noted that the method of paired electrosynthesis facilitated the reaction of two electrodes. Also, we found that the amount of $SnCl_2$ and NaBr could be reduced to the catalytic amount and could be reused for five times without obvious loss in catalytic activity. For example, the carbonyl compound and corresponding homoallylic alcohol were obtained with a high yield of more than 80% after the fifth round. The slight decrease of the reaction yield was possibly due to the loss of $SnCl_2$ and NaBr in the extraction (Fig. 3).

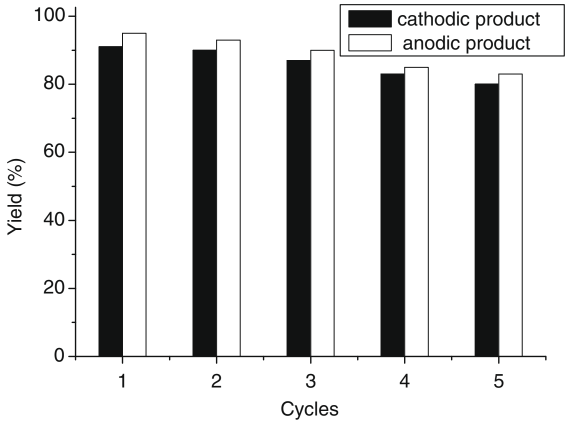


Figure 3. The reaction yields of each round for the paired electrosynthesis of benzaldehyde and the corresponding homoallylic alcohols.

In summary, the carbonyl compounds and the corresponding homoallylic alcohols can be prepared by using a simple paired electrosynthesis in a divided cell. The employment of these paired electrodes makes mediators approach to catalysts without the sacrification of electrodes. Moreover, this electrochemical method should be potential in organic synthesis. The application of this paired electroysnthesis to other reactions is in progress in our laboratory.

Acknowledgments

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12. Typical procedures: A divided cell with salt bridge of KNO_3 was equipped with a graphite electrode (dia.3.0 mm) as anode, a graphite electrode (dia.3.0 mm) as cathode and the saturated calomel electrode at room temperature. A solution of benzyl alcohol (2 mmol) in 1 mL of CH_2Cl_2 was added in anodic compartment. To the solution, a solution of 0.1 M sodium bromide solution (5 mL), 48% HBr (0.1 mL) and KNO_3 (0.05 M) were added as aqueous phase. In cathodic compartment, 0.1 M $SnCl_2$ (5 mL) and KNO_3 (0.05 M) were added as aqueous, a solution of benzaldehyde (2 mmol), allyl bromide (3 mmol) in 1 mL

of CH_2Cl_2 as organic phase. The pair of electrodes were placed in the upper layer of the aqueous phase and the upper layer was electrolyzed under controlled potential at 0.6 V versus SCE, then stopped electrolyzing and started stirring alternately until substrates completely transformed for about 6-7 h. The reaction product was separated by extraction and purified with a column chromatography. *Benzaldehyde* (**2a**) ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ = 10.02 (s, 1H), 7.88 (d, J = 6.9 Hz, 2 H), 7.72–7.61 (m, 1 H), 7.61-7.45 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 192.3, 136.5, 134.4, 129.7, 128.9; IR (liquid film, cm^{-1}): ν = 3387, 3064, 2819, 2737, 1702, 1655, 1584, 1203, 827, 745, 688, 649. *Phenylbut-3-en-1-ol* (**3a**) ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ = 7.39–7.21 (m, 5H), 5.90–5.69 (m, 1H), 5.21–5.10 (q, 2H), 4.78–4.60 (q, 1H), 2.42–2.62 (m, 2H), 2.00 (s,1H); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 144.0, 134.6, 128.5, 127.6, 125.9, 118.4, 73.4, 43.9; IR (liquid film, cm^{-1}): ν = 3401, 3077, 3030, 2979, 2908, 1641, 1493, 1453, 1307, 1048, 1001, 916, 758, 700, 644, 609.