Zn-mediated electrochemical allylation of aldehydes in aqueous ammonia†

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An efficient electrosynthesis of homoallylic alcohols from allylic bromides and aldehydes in aqueous ammonia is achieved in an undivided cell fitted with a pair of zinc electrodes.

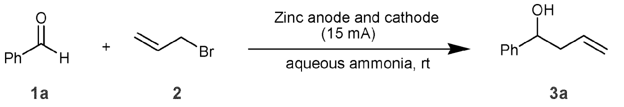
Synthesis of homoallylic alcohols by allylation of carbonyl compounds is one of the most important processes in organic synthesis due to their versatile use as important building blocks for natural product synthesis.[1] In the past two decades, extensive research has been carried out on developing organometallic type allylation reactions in aqueous media, and many metals have been found to effectively mediate such reactions.[2] Among them, zinc, a relatively cheap and low toxic material, has been demonstrated as a good reagent to mediate this Barbier-type reaction and has been applied in industry production. However, it generally requires physical or chemical activation. Among the various activation methods available, the addition of an acidic co-reagent is a commonly applied approach. Here we report a Zn-mediated electrochemical allylation reaction in aqueous ammonia.[3] This new procedure, which takes place in an aqueous alkaline solution, is efficient and a range of functional groups are stable in these mild reaction conditions.

In this one-compartment electrochemical process, Zn foils were chosen as both anode and cathode. Studies were initiated in a neutral 0.1 M $LiClO_4$ solution (entry 1, Table 1). Benzaldehyde was not consumed completely after the electrolysis has been carried out for 2 h and only 22% yield of the desired product was obtained. In an acidic 0.1 N H_2SO_4 solution, the desired homoallylic alcohol was isolated with a higher yield of 58% (entry 2, Table 1). We then tried electrolysis in 0.25 M NH_4BF_4 solution.[4] Only a trace amount of the product was detected with most of the starting material recovered (entry 3, Table 1). When we added 25% (w/w) of ammonia into the above solution (final concentration: 3 M), a 66% yield of the desired product was obtained (entry 4, Table 1). A control reaction was run in 3 M ammonia as solvent and supporting electrolyte and the yield was increased to 80% (entry 5, Table 1). This result demonstrated that NH_4BF_4 was prohibiting the reaction to a certain extent. Optimization of the amount of ammonia showed that at a concentration of 4.5 M, the yield reached 92% (entry 8, Table 1). Further increase of the concentration of ammonia resulted in a decrease of the yield (entries 9–11, Table 1). In aqueous 0.1 M NaOH, no allylation was observed (entry 12, Table 1). Finally, in the acidic aqueous 0.1 M NH_4Br, allylation occurred in a low yield of 36% (entry 13, Table 1), which shows that NH_3 and not NH_4^+ is promoting the reaction.

Hence, a standard reaction procedure is described as follows. A mixture of benzaldehyde (0.5 mmol), allyl bromide (1 mmol) in aqueous ammonia (1.5 mL of 25% (w/w) solution was diluted to 5 mL with water (4.5 M, pH = 12.6) and was electrolyzed at a constant current of 15 mA in a round-bottom flask cell equipped with a pair of zinc electrodes (1.5 cm^2) at room temperature. The electrolysis was stopped when the aldehyde was converted completely (1.5–2 h, 2F mol^{-1} of current was consumed). Usual work-up and purification afforded the desired product.

Subsequently, a variety of aldehydes were examined to generate the allylation products using the standard conditions. Table 2 summarizes the details of the results. Both the aromatic and aliphatic aldehydes can be utilized in this methodology. For the aromatic aldehydes, homoallylic alcohols can be prepared smoothly in good to excellent yield, and the functionalities including methoxyl (entry 4, Table 2),

Table 1 Optimization of the reaction conditions for the electrochemical allylation reactions in aqueous media[a]



Entry	Conditions	Yield[b]/%
1	0.1 M $LiClO_4$	22
2	0.1 N H_2SO_4	58
3	0.25 M NH_4BF_4	trace
4	0.25 M NH_4BF_4 in 3.0 M aqueous ammonia	66
5	3.0 M aqueous ammonia	80
6	3.6 M aqueous ammonia	83
7	4.2 M aqueous ammonia	86
8	4.5 M aqueous ammonia	92
9	4.8 M aqueous ammonia	91
10	5.4 M aqueous ammonia	88
11	6.0 M aqueous ammonia	84
12	0.1 M NaOH	0
13	0.1 M NH_4Br	36

[a] Benzaldehyde (0.5 mmol), allyl bromide (1 mmol) in each electrolyte was electrolyzed at a constant current of 15 mA in a round-bottom flask cell equipped with a pair of zinc electrodes (1.5 cm^2) at room temperature. [b] Isolated yield.

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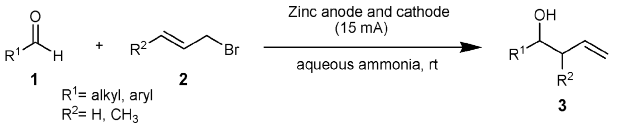
† Electronic supplementary information (ESI) available: Experimental procedure, spectroscopy, cyclic voltammetry, scanning electron microscopy, X-ray and NMR analyses data. See DOI: 10.1039/b905553c

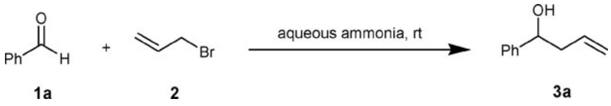
Table 2 Zn-mediated electrochemical allylation of aldehydes in an aqueous ammonia solution[a]



Entry	1	R^1	R^2	3	Yield[b]/%
1	**1a**	Ph	H	**3a**	92
2	**1b**	$PhCH_2CH_2$	H	**3b**	81
3	**1c**	PhCH=CH	H	**3c**	70
4	**1d**	$4\text{-}MeOC_6H_4$	H	**3d**	85
5	**1e**	$2\text{-}HOC_6H_4$	H	**3e**	72
6	**1f**	$2\text{-}MeC_6H_4$	H	**3f**	82
7	**1g**	$4\text{-}ClC_6H_4$	H	**3g**	70
8	**1h**	2-furyl	H	**3h**	84
9	**1i**	2-pyridyl	H	**3i**	62
10	**1j**	n-hexyl	H	**3j**	50[c]
11	**1k**	cyclohexyl	H	**3k**	53[c]
12	**1l**	HO_2C	H	**3l**	48
13[d]	**1a**	Ph	CH_3	**3m**	94[e]

[a] Aldehyde (0.5 mmol), allyl bromide (1 mmol), aqueous ammonia (5 mL, 4.5 M), I = 15 mA, zinc electrodes (1.5 cm^2), rt. [b] Isolated yield. [c] H_2O:THF (4 : 1) as solution. [d] Allyl bromide was replaced with crotyl bromide. [e] *Anti*:*syn* = 41 : 59 (determined by ^{1}H NMR analysis).

Table 3 Influence of the electrode material on the electrochemical allylation[a]



Entry	Anode–cathode	Conditions	Yield[b]/%
1[c]	—	Zn powder 4.5 M aqueous ammonia	30
2	Pt–Pt	4.5 M aqueous ammonia	0
3	Al–Al	4.5 M aqueous ammonia	20
4	Sn–Sn	4.5 M aqueous ammonia	16

[a] Benzaldehyde (0.5 mmol), allyl bromide (1 mmol) in each electrolyte was electrolyzed at a constant current of 15 mA in a round-bottom flask cell. [b] Isolated yield. [c] No power was applied, and the reaction was stirred overnight.

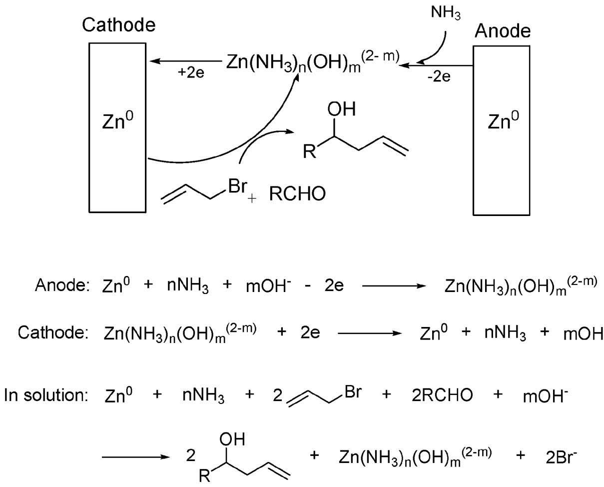


Fig. 1 Proposed reactions for the electrochemical process.

chloro (entry 7, Table 2), hydroxyl (entry 5, Table 2), pyridyl (entry 9, Table 2) and carboxylic acid (entry 12, Table 2) were not affected in this mild procedure. The allylation of α,β-unsaturated aldehyde as represented by *trans*-cinnamaldehyde (entry 3, Table 2) occurred in a regioselective manner and gave solely the 1,2-addition product. Further regioselectivity study using crotyl bromide showed that a γ-substitution product was obtained exclusively and the ratio of *anti* : *syn* was 41 : 59 (entry 13, Table 2). However, acetophenone did not perform well in this methodology, and an incomplete conversion of ketone was observed even after a prolonged reaction time (6 h).

It is a very interesting result that excellent electrochemical allylation yield can only be achieved in basic aqueous ammonia solution, and not in traditional acidic or neutral solution (see Table 1). We then studied the allylation of benzaldehyde using commercial Zn powder in 4.5 M ammonia (entry 1, Table 3). After stirring the solution overnight, the allylated product was obtained in 30% yield only. No allylation occurred when the electrolysis was carried out with inert Pt electrodes in 4.5 M ammonia (entry 2, Table 3). Next, we investigated the electrochemical generation of Al(0) and Sn(0) to mediate the allylation of benzaldehyde in 4.5 M ammonia using Al and Sn electrodes, but the yields of allylated product were much lower (20 and 16%, respectively, as seen in entries 3 and 4, Table 3). Thus, Zn(0) electrodeposited from aqueous ammonia is a much better allylation mediator.

Hence, based on the above observation, we hypothesized that the electrochemical allylation carried out in this alkaline solution is promoted by ammonia. In the process of electrolysis (Fig. 1), the sacrificial zinc anode is continuously oxidized to form complexes of zinc(II) with ammonia tentatively represented as $Zn(NH_3)_n(OH)_m^{(2-m)}$. These complexes are electro-reduced on the Zn cathode to give active Zn particles, which mediate the allylation of aldehydes *via* the formation of allyl Zn(II) species as nucleophiles.

The deposition of Zn(0) from different solutions of Zn(II) in the absence of aldehyde and allyl bromide was studied too.[5] It was found that from the 0.1 M $LiClO_4$ and 0.1 M NaOH solutions, only a trace amount of powder was deposited on the cathode. From the 0.1 N H_2SO_4 solution, 11 mg of deposit were collected. From the 4.5 M ammonia solution, a 34 mg deposit was obtained.[6] XRD analysis showed that the deposits from both 4.5 M aqueous ammonia and 0.1 N H_2SO_4 solutions consisted of pure Zn(0) with a good crystalline structure. However, the SEM image (Fig. 2) showed that the deposits from 4.5 M ammonia were loosely packed and formed a porous network with pore sizes of several hundred nanometers and a thickness of approximately 1 μm. In contrast, the deposit from the 0.1 N H_2SO_4 solution was composed of densely packed flakes.[7] The porous structure of the ammonia solution deposit of Zn(0) as well as its high activity in the *in situ*[8] allylation reaction are most probably due to the complexation of the Zn(II) cation with ammonia.[9] The activity in the alkaline medium is noteworthy.[10]

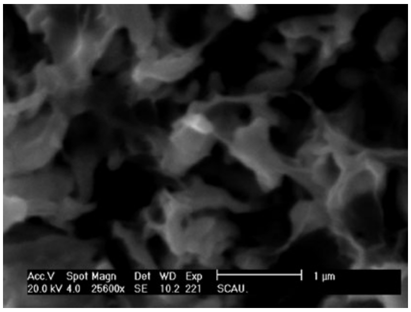


Fig. 2 SEM image of deposits from aqueous ammonia.

In conclusion, an efficient electrosynthesis of homoallylic alcohols from allylic bromides and aldehydes in aqueous ammonia has been developed. This preliminary study shows that soluble Zn^{2+}–ammonia complexes formed by electrodissolution of a Zn(0) anode (sacrificial anode) give a deposit of Zn(0) with a porous network structure when reduced at the cathode. This deposit is fairly active for the allylation of aldehydes in ammonia. The obvious advantages of this electrochemical procedure are simplicity, efficiency and environmental friendliness. Further investigation to settle a precise mechanism and expand the scope of this reaction is underway in our laboratory.

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5 For the procedure of electrodeposition, see ESI†.

6 The electrochemistry of Zn deposition from 0.1 N H_2SO_4, 0.1 M $LiClO_4$, 0.1 M NaOH and 4.5 M aqueous ammonia solutions was investigated by cyclic voltammetry (CV) with the same concentration of zinc(II) salt, see ESI†.

7 See ESI† for a SEM image of deposits from 0.1 N H_2SO_4.

8 It was reported that the pre-prepared nano zinc was too active to exist in water and could not mediate the Barbier-type allylation in water: Z. Wang, Z. Zha and C. Zhou, *Org. Lett.*, 2002, **4**, 1683.

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10 The pH changed slightly to 12.3 from 12.6 after the electrosynthesis finished. Control reactions have been run by performing the In and Sn powder mediated Barbier-type reaction in 4.5 M aqueous ammonia solutions, and no allylated product was obtained for both metals.