

A Highly Regioselective Epoxide Ring Opening Reaction by Triorganylborane via Electrochemical Method

Jung Hoon Choi,* Sung Jae Lee, Choong Ryul Joo, Jung Sung Kim,[†] and Dae Jin Baek[‡]

Department of Chemistry, Hanyang University, Seoul 133-791, Korea

[†]Department of Chemical Education, Taegu University, Taegu 713-714, Korea

[‡]Department of Chemistry, Hanseo University, 360, Daegokri, Haemi, Seosan, Chung-Nam 352-820, Korea

Received July 21, 1999

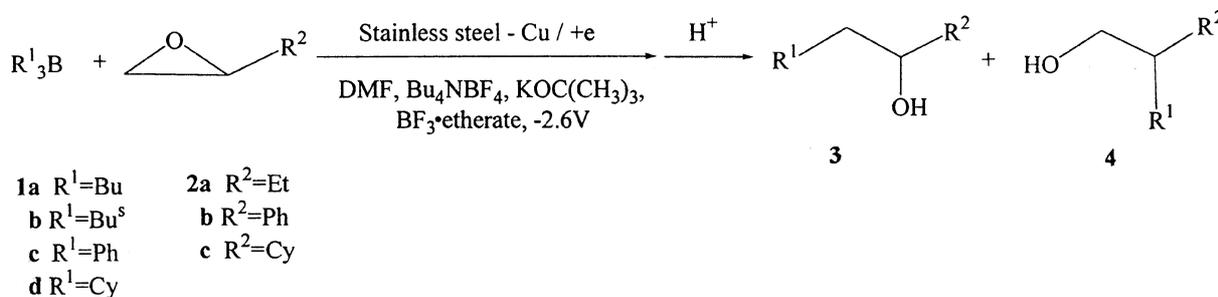
We recently described that triorganylboranes can be used as organyl group transfer agents to the carbonyl compounds by implementing an electrochemical procedure that uses copper as a sacrificial anode.¹ Secondary and tertiary alcohols are readily obtained in good yields by performing the electrochemical reaction in an undivided cell with a platinum electrode and a copper sacrificial anode. This methodology has a great attention since of its enormous potential synthetic utility.² The reaction can offer the wide scopes for the further application to various functional groups similar to Grignard reagents derived from alkyl halides.³ Therefore, we now report the epoxide ring opening reaction by the electrochemical organyl transfer of triorganylboranes at constant negative reduction potential (-2.6 V~-3.0 V) in an undivided electrolytic cell using a sacrificial metallic anode. Especially, of particular interest is the regioselectivity for the epoxide ring opening reaction by electrochemical tool. In addition, these electrochemical epoxide ring opening reactions were compared with those of corresponding Grignard reactions.

For most purposes, triorganylboranes, such as tributylborane and tri-*sec*-butylborane, adapted in this experiment would be derived from hydroboration of alkenes,⁴ however triphenylborane could not be prepared by hydroboration in this case Grignard reagent would be utilized.⁵

First of all, a variety of degassed solvents, such as DMF (entry 5), THF (entry 6), Py (entry 7), and acetonitrile (AN) (entry 8), sacrificial anodes, such as Cu (entry 5), Mg (entry 9), Al (entry 10), Zn (entry 11), and Fe (entry 12), and electrolytes, such as tetrabutylammonium tetrafluoroborate (Bu₄NBF₄) (entry 5), tetrabutylammonium perchlorate (Bu₄NClO₄) (entry 13), tetrabutylammonium hexafluorophosphate (Bu₄NPF₆) (entry 14), tetrabutylammonium chlo-

ride (Bu₄NCl) (entry 15), tetrabutylammonium bromide (Bu₄NBr) (entry 16), tetrabutylammonium iodide (Bu₄NI) (entry 17), and lithium bromide (LiBr) (entry 18) with tri-*sec*-butylborane and styrene oxide were examined to find the combination which afforded the best yield. As a result, it revealed DMF as a solvent, Cu sacrificial anode and Bu₄NBF₄ as a supporting electrolyte gave the best yield to the corresponding alcohol (entry 5).

Additionally, we found that the reaction time decreased with increasing their stainless steel cathode surface area from 4 h at 1 cm² (entry 19) to 1.5 h at 4 cm² (entry 5) with increasing of yield from 74% to 89%, and by addition of bases, such as potassium *tert*-butoxide (entry 5), sodium ethoxide (entry 20), sodium hydroxide (entry 21), and sodium 2,6-di-*tert*-butyl-4-methylphenoxide (entry 22), especially among them, by addition of potassium *tert*-butoxide the efficiency significantly enhanced, resulting in the reduction of reaction potential from -3.2 V to -2.6 V. Moreover, it revealed that yields of electrochemical epoxide ring opening reactions were markedly influenced by addition of Lewis acid, such as BF₃·etherate, and the electrochemical reaction of **2b** by **1b** in the presence of BF₃·etherate afforded the exclusively corresponding less substituted alcohol in 89% yield (entry 5) whereas in absence of BF₃·etherate gave in 57% yield (entry 23) under same circumstance. We also found that there was no significant difference in yield between Pt and stainless steel cathode in the electrochemical epoxide ring opening reaction with **1b**, however, it should be noticed that the regioselectivity significantly depends upon the choice of cathode; Stainless steel furnished the exclusive product **3** with extremely high regioselectivity (entry 5), whereas Pt gave two products, **3** and **4**, with somewhat low regioselectivity (entry 24) which was,



Scheme 1

however, still better than the corresponding products by the Grignard reaction. Therefore, from above results, we adapted the stainless steel ($2 \times 2 \text{ cm}^2$, cathode), Cu (anode), DMF (solvent), Bu_4NBF_4 (electrolyte), $\text{KOC}(\text{CH}_3)_3$, and $\text{BF}_3 \cdot \text{etherate}$ as our standard condition (Scheme 1).

As would be anticipated for S_N2 process, the electrochemical epoxide ring opening occurred at the less substituted position as shown in Table 1. The electrochemical epoxide ring opening reaction by a primary trialkylborane, such as **1a**, with **2a** gave a corresponding alcohol, the mixture of more highly substituted alcohol **3** and less highly substituted alcohol **4**, with the ratio of 85 : 15 in 72% chemical yield (entry 1). When **2b** was submitted to the electrochemical epoxide ring opening reaction by **1a**, the similar yield was obtained, however, it showed the surprising regioselectivity by attack exclusively at the less substituted carbon (entry 2). Its regioselectivity was so remarkable compared to that of

the Grignard reaction derived from the reaction of **2b** with alkylmagnesium bromide (74 : 26). And **2c** afforded the corresponding alcohol in moderate yield (63%) (entry 3). In the case of treatment of **2a** with secondary trialkylborane, such as **1b**, the electrochemical epoxide ring opening reaction afforded the mixture of **3** and **4** in 84% chemical yield with the 87 : 13 ratio of regioselectivity (entry 4). And **2b** by treating with **1b** electrochemically was also converted into the corresponding sole product **3** in 89% chemical yield with 100 : 0 ratio (**3** : **4**) of regioselectivity (entry 5). And when **2c** was employed in the electrochemical reaction with **1b**, it showed the moderate yield (57%) (entry 25), which was similar to that of electrochemical reaction with **1a**. In the case of triarylborane, **1c**, required more negative reduction potential (-3.0 V) than trialkylboranes (-2.6 V), **2a** furnished the corresponding alcohols in 74% yield with 91 : 9 ratio of regioselectivity (entry 26) while the Grignard reaction utiliz-

Table 1. Electrochemical epoxide ring opening reaction by triorganylboranes^{a,b,c,d,e}

Entry	1	2	Reaction condition ^f	Reaction Time (h)	Product Yield (%) (3 + 4)	Product Ratio (3 : 4)	
						Electrochemical Reaction	Grignard Reaction (yield, %)
1	1a	2a	Cu, DMF, Bu_4NBF_4	1.5	72	85 : 15	65 : 35 (70) ⁶
2	1a	2b	Cu, DMF, Bu_4NBF_4	2	73	100 : 0	76 : 24 (65) ⁶
3	1a	2c	Cu, DMF, Bu_4NBF_4	1	73	-	-(63) ⁷
4	1b	2a	Cu, DMF, Bu_4NBF_4	1.5	84	87 : 13	69 : 31 (64) ⁶
5	1b	2b	Cu, DMF, Bu_4NBF_4	1.5	89	100 : 0	77 : 23 (76) ⁷
6	1b	2b	Cu, THF, Bu_4NBF_4	6.5	49	100 : 0	
7	1b	2b	Cu, Py, Bu_4NBF_4	12	trace	-	
8	1b	2b	Cu, AN, Bu_4NBF_4	1.5	23	100 : 0	
9	1b	2b	Mg, DMF, Bu_4NBF_4	1	87	100 : 0	
10	1b	2b	Al, DMF, Bu_4NBF_4	2.5	76	100 : 0	
11	1b	2b	Zn, DMF, Bu_4NBF_4	2.5	68	100 : 0	
12	1b	2b	Fe, DMF, Bu_4NBF_4	2.5	51	100 : 0	
13	1b	2b	Cu, DMF, Bu_4NClO_4	2	80	86 : 14	
14	1b	2b	Cu, DMF, Bu_4NPF_6	2	83	87 : 13	
15	1b	2b	Cu, DMF, Bu_4NCl	2	74	81 : 19	
16	1b	2b	Cu, DMF, Bu_4NBr	2.5	70	77 : 23	
17	1b	2b	Cu, DMF, Bu_4NI	1.5	73	85 : 15	
18	1b	2b	Cu, DMF, LiBr	1.5	71	87 : 13	
19	1b	2b	Cu, DMF, Bu_4NBF_4 ^g	4	74	100 : 0	
20	1b	2b	Cu, DMF, Bu_4NBF_4 ^h	2	81	100 : 0	
21	1b	2b	Cu, DMF, Bu_4NBF_4 ⁱ	3	88	100 : 0	
22	1b	2b	Cu, DMF, Bu_4NBF_4 ^j	1	82	100 : 0	
23	1b	2b	Cu, DMF, Bu_4NBF_4 ^k	4	57	100 : 0	
24	1b	2b	Cu, DMF, Bu_4NBF_4 ^l	5	82	91 : 9	
25	1b	2c	Cu, DMF, Bu_4NBF_4	1	57	-	-(63) ⁷
26	1c	2a	Cu, DMF, Bu_4NBF_4	2	74	91 : 9	75 : 25 (66) ⁷
27	1c	2b	Cu, DMF, Bu_4NBF_4	2	52	100 : 0	79 : 21 (59) ⁷
28	1c	2c	Cu, DMF, Bu_4NBF_4	1.5	70	-	-(72) ⁷
29	1d	2a	Cu, DMF, Bu_4NBF_4	2	87	92 : 8	66 : 34 (69) ⁷
30	1d	2b	Cu, DMF, Bu_4NBF_4	1.5	72	100 : 0	70 : 30 (71) ⁷
31	1d	2c	Cu, DMF, Bu_4NBF_4	2	71	-	-(81) ⁷

^aThe electrochemical reactions were carried out at -2.6 V vs. Ag/AgCl in an undivided cell at room temperature. ^bCombination of 1 equiv of triorganylborane and 1 equiv of epoxide. ^cSolvent (mixture of 10 mL of DMF and 1 mL of THF), triorganylborane (1 mmol), epoxide (1 mmol), electrolyte (1 mmol), $\text{KOC}(\text{CH}_3)_3$ (1 mmol), $\text{BF}_3 \cdot \text{etherate}$ (1 mmol), stainless steel cathode ($2 \times 2 \text{ cm}^2$) and sacrificial anode ($2 \times 2 \text{ cm}^2$). ^dChemical yields were estimated by GC. ^e**3** and **4** refer to product as shown Scheme 1 respectively. ^fSacrificial anode, solvent and electrolyte conditions. ^gStainless steel ($1 \times 1 \text{ cm}^2$) being used instead of stainless steel ($2 \times 2 \text{ cm}^2$). ^hSodium ethoxide being used instead of potassium *tert*-butoxide. ⁱSodium hydroxide being used instead of potassium *tert*-butoxide. ^jSodium 2,6-di-*tert*-butyl-4-methylphenoxide being used instead of potassium *tert*-butoxide. ^kThe reaction was carried out in the absence of $\text{BF}_3 \cdot \text{etherate}$. ^lPlatinum ($2 \times 2 \text{ cm}^2$) being used instead of stainless steel ($2 \times 2 \text{ cm}^2$).

ing phenylmagnesium bromide afforded the same products in 66% yield with 75 : 25 ratio (**3** : **4**) of regioselectivity. As the pattern of the electrochemical reaction with trialkylborane in regioselectivity, **2b** by treating with **1c** also gave exclusively the corresponding alcohol **3** in 52% yield regioselectively (100 : 0) (entry 27) while the Grignard reaction gave the two products in 59% yield with 79 : 21 ratio (**3** : **4**) of regioselectivity. The regioselectivities of the electrochemical ring opening reactions of **2b** (entry 30) and **2a** (entry 29) with **1d** were also similar to those with **1c** except a subtle enhancement of the chemical yields. And the electrochemical epoxide ring opening reaction of **2c** achieved in 74% yield to the corresponding alcohol (entry 28, 31).

Overall, the electrochemical epoxide ring opening reaction in the scope of regioselectivity was significantly affected by the structure of epoxide irrespective of the feature of triorganylborane, especially the regioselectivity of aromatic epoxide is extraordinary. Interestingly, the very similar reaction pattern was also found in our earlier report for the electrochemical epoxide ring opening reaction by alkyl halides using copper sacrificial anode, in which **2a** afforded the exclusive corresponding alcohol in good yields with 100 : 0 ratio (**3** : **4**) of regioselectivity.⁷

So far, we have not carried out the systematic study to elucidate the reaction mechanism to explain these remarkable regioselectivities by an attack at the less substituted carbon of epoxides in the presence of $\text{BF}_3 \cdot \text{etherate}$ in the electrochemical epoxide ring opening reaction, which are contrast to the common knowledge for the epoxide ring opening reactions in the presence of $\text{BF}_3 \cdot \text{etherate}$.⁸ Obviously, anyway, the electrochemical epoxide ring opening reaction would give the facile and useful methodology for the highly regioselective synthesis.

The following procedure for preparation of 3-methyl-1-phenylpentanol represents the electrochemical reactions. The electrochemical reactions were carried out with Electrolysis Model C-600 cell, EG & G PARC model 173 and BAS 100 β potentiostat. **2b** (0.120 g, 1 mmol), $\text{BF}_3 \cdot \text{etherate}$ (0.142 g, 1 mmol), 10 mL of DMF and Bu_4NBF_4 (0.329 g, 1 mmol) placed in an usual undivided cell equipped with stainless steel ($2 \times 2 \text{ cm}^2$) as a working electrode and copper plate ($2 \times 2 \text{ cm}^2$) as a sacrificial anode, and magnetic stirrer

unit. Then the mixture of **1b** (1 mL of 1 M solution in THF, 1 mmol) and potassium *tert*-butoxide (0.112 g, 1 mmol) was introduced into the reaction mixture for 0.5 h. The solution was electrolyzed at -2.6 V vs. Ag/AgCl reference electrode of a cathode potential at room temperature under nitrogen atmosphere. The reaction mixture was withdrawn by hypodermic syringe at appropriate interval, quenched with 3 mL of aqueous 2 N-HCl solution. The mixture was diluted with 3 mL of diethyl ether, and saturated with NaCl. Upon addition of n-tetradecane as an internal standard, the organic layer was analyzed with GC using a Chromosorb-WHP (10% SE-30) column, which indicated formation of 3-methyl-1-phenylpentanol in 89% yield in 1.5 h.

Acknowledgment. This work was gratefully supported by Hanyang University Research Foundation and partially supported Taegu University.

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