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A Facile Hydroxymethylation of Acetylene Derivatives with Paraformaldehyde by Use of an Electrogenerated Base (EG Base)

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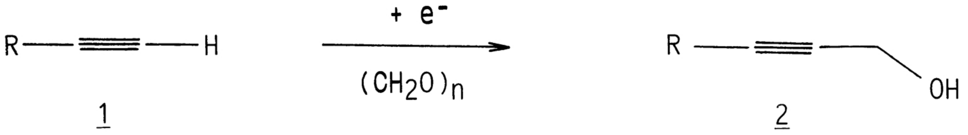
Electrolysis of a mixture of paraformaldehyde and terminal acetylene derivatives smoothly provided the corresponding hydroxymethylated compounds in high yields by passing less than 1 F/mol of electricity. Electroreduction of paraformaldehyde generated in situ an efficient base (EG base), which catalyzed hydroxymethylation of the acetylenes.

Recently, electrogenerated base (EG Base) has been extensively exploited and proved to have an intriguing potential for organic synthesis.$^{1)}$ As a probase for the electroreduction, several substrates have been innovated, e.g. alkyl halides,$^{2)}$ azobenzene,$^{3)}$ carbonyl compounds,$^{4)}$ amides,$^{5)}$ and so on.$^{1)}$ In our laboratory, it has been already reported that the electrolysis of a mixture of o-nitrotoluene and paraformaldehyde gives a useful intermediate for the synthesis of indole derivatives, where paraformaldehyde plays an important role as both probase and reacting substrate.$^{6)}$

Now we wish to report here on a facile hydroxymethylation of the terminal acetylene compounds **1** by electroreduction of paraformaldehyde to afford the propargylic alcohols **2**. Our results are summarized in Table 1.



General experimental procedure is as follows. A mixture of the substrate **1** (1 mmol), commercial paraformaldehyde (30 mg), and tetraethylammonium tosylate (800 mg) in DMF (12 ml) was electrolyzed by using platinum electrode in cathode compartment under constant current density (3.3 $mAcm^{-2}$). Usual workup and purification gave the product **2** in the yields indicated in Table 1.

Some important points are worth noting. Reactions employing acetylene derivatives having base susceptible functionalities such as protected or nonprotected hydroxy groups adjascent to the sp carbon (entry 2-6) and epoxide (entry 7) proceed readily at ambient temperature. Less than 1 $Fmol^{-1}$ of electricity is sufficient for the completion of the reaction. The efficiency of the EG Base obviously appears on its catalytic feature. Indeed, the conventional bases such as metal hydroxides, alkoxides in the presence or absence of ammonium salts, and tetrabutylammonium hydroxide were submitted to the same reaction mixture, but very low yield (<20%) was obtained. Thus, the electroreduction of paraformaldehyde generates in situ an efficient base which catalyzes hydroxymethylation of the acetylene compounds **1**. In particular, 1,4-diol derivatives (entry 2-8), which are versatile intermediates to synthesize a class of important natural products such as cyclopentenoids,7) terpenoids,8) and vitamin D,9) could be easily obtained by employing our method. Further works to extend the EG Base are on going.10)

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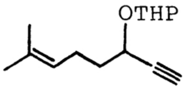
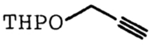
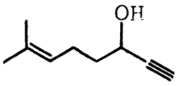
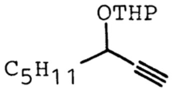
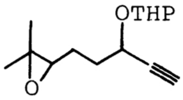
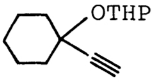
Table 1.

Entry	Substrate **1**	Electricity F mol^{-1}	Product, **2** Yield/%	Entry	Substrate **1**	Electricity F mol^{-1}	Product, **2** Yield/%
1	Ph—≡	0.46	81	5		0.75	91
2		0.75	92	6		0.75	66
3		0.75	96	7		0.75	79
4		0.75	73	8		0.75	95

All products gave satisfactory 200 MHz ^{1}H NMR and 50 MHz ^{13}C NMR spectra.

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10) A detail of mechanism and property of EG Base from paraformaldehyde will be discussed in due course by combination with other investigations.

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