Synthesis of Nitrogen Heterocycles by Electrochemical Radical Cyclization Using an Arene Mediator

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Radical cyclization is a useful method for synthesis of cyclic compounds. Carbon radicals are usually generated from the corresponding organic halides by their reaction with AIBN-Bu_3SnH. However, there are several drawbacks in this method: the toxicity of tin compounds and the difficulty in isolation of products due to contamination of R_3SnX. On the other hand, electrochemical reduction of alkenyl or aryl halides using a Ni(II) catalyst, oxygen mediator, and arene mediator has been reported to generate the corresponding radicals, which afford the cyclization products (1).

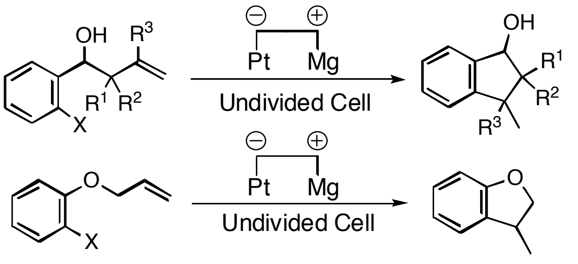
In order to develop an environmentally benign method for radical cyclization, we have studied on the electrochemical reductive cyclization of aryl halides carrying *ortho*-3-butenyl group by using an arene mediator. We have already reported that electrolysis of various aryl halides carrying an *ortho*-1-hydroxy-3-butenyl group with a platinum cathode and magnesium anode in the presence of phenanthrene as a mediator gave radical cyclization product in good yields. Benzofuran derivatives were also obtained from allyl 2-iodophenyl ether in the same method (Scheme 1) (2). In this paper, we report on a synthesis of nitrogen heterocycles by this method. Since the reaction conditions are moderate and the mediator could mostly be recovered and used repeatedly after the electrolysis, the method for generation of aryl radicals is useful for environmentally benign organic synthesis of cyclic compounds.

Electrolysis of *N*-allyl-*N*-methyl-(2-iodoaniline) (**1a**) in acetonitrile solution containing 0.1M TEAP and phenanthrene (2 equiv.) with a platinum cathode and a magnesium anode gave 2,3-dihydro-1,3-dimethylindole (**2a**) in 60% isolated yield (Table 1, entry 1). When DMF was used as a solvent, a cyclization occurred efficiently but a formylated dihydroindole, 2,3-dihydro-1-methyl-3-formylmethylindole, was obtained as a by-product. Similar electrochemical cyclization of **1b** and **1c** also gave dihydroindole **2b** and **2c** in good yields. It is noteworthy that 5-exo cyclization occurred to give five-membered ring **2b** even in the case of *N*-methallylaniline **1b** although usual cyclization of **1b** using AIBN-Bu_3SnH gave 5-exo and 6-endo cyclization products. We found that vinyl bromide also works as a radical precursor. Electrolysis of vinyl bromides **1d** and **1e** gave the desired 5-exo cyclization products **2d** and **2e** in 58-61% yields (entries 4 and 5). We also found an interesting result, in which aromatic double bond can work as an acceptor of vinyl radical. Electrolysis of **1f** gave spiro-typed product **3f** as well as usual cyclization product **2f** (Scheme 2).

REFERENCES

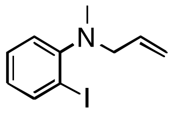
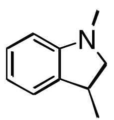
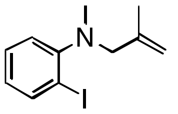
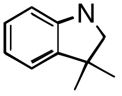
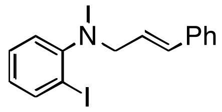
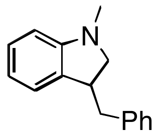
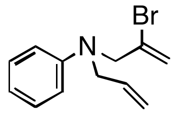
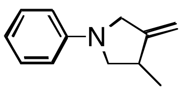
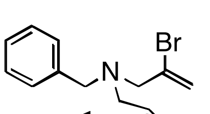
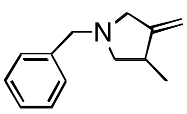
1. S. Ozaki, H. Matsushita, and H. Ohmori, *J. Chem. Soc., Chem. Commun.,* 1120 (1992). S. Ozaki, H. Matsushita, and H. Ohmori, *J. Chem. Soc., Perkin Trans. 1,* 2339 (1993). O. Sandra and E. Duñach, *Synlett,* 531 (1994). R. Munusamy, K. S. Dhathathreyan, K. K. Balasubramanian, and C. H. Venkatachalam, *J. Chem. Soc., Perkin Trans. II,* 1154 (2001). M. Dias, M. Gibson, J. Grimshaw, I. Hill, J. Trocha-Grimshaw, and O. Hammerich, *Acta Chem. Scand.,* **52**, 549 (1998).

2. M. Tokuda, N. Kurono, and E. Honda, in Reactive Intermediates in Organic and Biological Electrochemistry /2001, D. G. Peters, H. J. Schäfer, M. S. Workentin, and J. Yoshida, Editors, PV2001-14, p.9, The Electrochemical Society Proceedings Series, Pennington, NJ (2001).

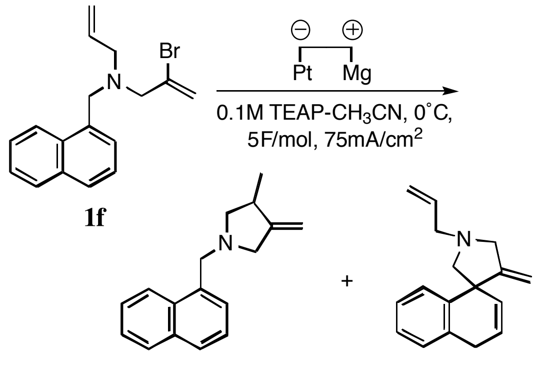


Scheme 1

Table 1. Electrochemical Radical Cyclization using Phenanthrene Mediator[a)]

Entry	Substrate	Product	Yield (%) [b)]
1	 **1a**	 **2a**	60
2	 **1b**	 **2b**	51
3	 **1c**	 **2c**	73
4	 **1d**	 **2d**	61
5	 **1e**	 **2e**	58

a) Electrolysis was carried out in acetonitrile containing 0.1M TEAP and phenanthrene with current density of 75 mA/cm^2. Electricity passed was 5 F/mol.
b) Isolated yields.



Scheme 2