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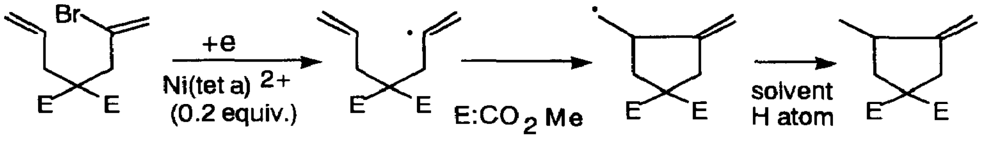
CYCLIZATION OF VINYL AND ARYL RADICALS GENERATED BY A NICKEL(II) COMPLEX CATALYSED ELECTROREDUCTION

Shigeko Ozaki, * Ikuo Horiguchi, Hidenori Matsushita, and Hidenobu Ohmori
Faculty of Pharmaceutical Sciences, Osaka University
1-6, Yamadaoka, Suita, Osaka-fu, 565 Japan

Abstract: Radical cyclization of vinyl and aryl halides was performed by indirect electroreduction using a nickel(II) complex as a catalyst.

Vinyl and aryl radicals are valuable intermediates in synthesis because they are more reacive towards cyclization than related alkyl radicals. Since Stork and Beckwith developed extensively chemistry of vinyl radicals [1] and aryl radicals, [2] there have been many useful studies on vinyl and aryl radical cyclization performed by tin hydride method from both the mechanistic [3] and synthetic [4] viewpoints. The vinyl radical induced reactions have recently been utilized for the cyclization of eneynes using phosphorus-centered radical and selenoboranes. [5] Alternative routes to vinyl radicals besides the use of tin hydrides, however, have been developed to a less extent than those to alkyl radicals [6] which have been conducted by many methods and met various synthetic applications. This must be ascribed, in part, to the fact that the generation of vinyl radicals by other methods than tin hydride method such as the atom transfer or the thiohydroxamate ester method [6b] would be more difficult than the related alkyl radicals due to the increased strength of sp^2C-X bonds (X: halogen,etc).

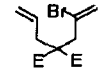
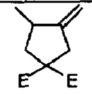
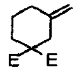
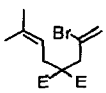
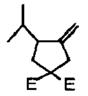
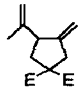
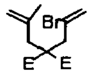
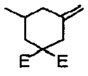
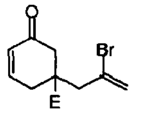
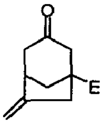
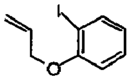
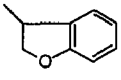
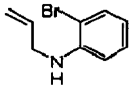
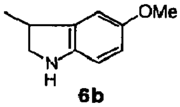
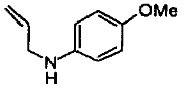
We have shown that the electroreductive generation of alkyl radicals from various halides using nickel(II) complexes as electron-transfer catalysis is a useful synthetic alternative to the tin hydride method [7a] and is particularly useful for intermolecular alkyl radical addition to olefins [7b] and intramolecular cyclization of N-allylic and N-propargyl-α-bromoamides. [7c] The advantage over tin hydride method could be attributed to the lack of the active hydrogen atom donor like tin hydride, which would elongate the lifetimes of the initially formed radicals to hydrogen atom abstraction. Herein we describe the cyclization of vinyl and aryl radicals which probably proceeds according to Scheme 1 to demonstrate the effectiveness of a Ni(II) complex for electroreductive generation of vinyl and aryl radicals.



Scheme 1

The reduction peak potentials of vinyl and aryl halides (Table 1) were shown to be more negative than those of alkyl halides (Epc for simple alkyl bromides were around -2.5 V *vs.* SCE). The cyclic voltammetric investigation [7b]indicated that nickel(I) species, electrogenerated from the nickel(II) complexes exhibiting the Ni(I)/Ni(II) redox couple at the potential less negative than that of Ni(tet a)$(ClO_4)_2$ [8] [Epc; ~ -1.35 V] are ineffective to transfer an electron to vinyl or aryl halides. Thus, we selected Ni(tet a)$(ClO_4)_2$ as the electron-transfer catalyst. The electroreductive radical cyclization was performed in DMF (20 ml) containing a supporting electrolyte ($EtNClO_4$; 0.1 M), a vinyl or aryl halide (1 mmol), Ni(tet a)$(ClO_4)_2$ (0.2 equiv. based on the halide) and a proton source to keep the catholyte buffered (NH_4ClO_4; 2 equiv. based on the halide) potentiostatically at the reductive peak potential of the nickel complex, -1.3 V using a graphite plate electrode as a cathode in an H-shaped divided cell under an inert gas. After all the halides were consumed, the catholytes were subjected to the usual extractive work-up followed by column chromatography (SiO_2) to give the cyclized products. [9] The results of the electrolysis are summarized in Table 1.

Table 1 Electroreductive Cyclization of Vinyl and Aryl Halides using Ni(tet a)$(ClO_4)_2$ as an Electron-transfer Catalyst [a]

Substrates (E=CO_2Me)	Epc [b]	F/mol [c]	Products	Yield[d] (%)	Products	Yield (%)[d]
 **1a**	-2.83	2.6	 **1b**	47	 **1c**	4
 **2a**	-2.70	1.5 2.0	 **2b**	51 [e] 81 [f]	 **2c**	47
 **3a**	-2.79	2.3	 **3b**	32		
 **4a**	-2.02[g] -2.84	2.7	 **4b**	86		
 **5a**	-2.14	2.2	 **5b**	75		
 **6a**	-2.70	3.1	 **6b**	58	 **6c**	14

a. Electrolysed as described in the text. b. Cathodic peak potential in V vs. SCE. c. Electricity consuned for complete conversion of substrate. d. Isolated yield based on substrate. e. Determined by GC. f. Electrolysis with 2 eqv. of PH_2PH. g. Ascribed to reduction of the enone group.

The result in Table 1 show that the present method can be a reliable method for generation of vinyl and aryl radicals to give mono- and bicyclic compounds bearing double bond at a prredictable position. Cyclization of the intermediary vinyl and aryl radicals proceeded preferentially in 5-*exo* mode except for **3a** which has a methyl group on position C-5 and underwent cyclization exclusively in 6-*endo* mode. Electrolysis of **2a** afforded a mixture of **2b** and **2c** in a ratio of nearly 1:1, which could be brought about by the disproportionation between the stable tertiary radicals produced *via* 5-*exo* mode cyclization of the vinyl radicals. The lack of hydrogen atom donor seems to cause this disproportionation. Indeed, the electrolysis of **2a** in the presence of 2 equiv. of Ph_2PH used as an active hydrogen atom donor [10] gave **2b** in 81% yield as a sole product. The difference in the yields of cyclic products observed between **1b** and **2b** indicates that in the cyclization to give more stable tertiary radicals proceeds more smoothly than that giving less stable primary radical. The present nickel(II) catalysed radical generation procedure can be applied not only to alkyl radical but to vinyl or aryl radical as well under ambient temperature using catalytic amount of the nickel reagent whereas organotin hydride method usually requires reflux in benzene with use of a stoichiometric amount of the hydride. Thus, the present method should provide a convenient alternative to the organotin hydride method.

References and Notes

1. (a) G. Stork and N. H. Baine, *J. Am. Chem. Soc.*, **1982**, *104,* 2321; (b) N. M. Marinovic and H. Ramanathan, *Tetrahedron Lett.*, **1983**, *24*, 1871; (c) G. Stork and N. H. Baine, *Tetrahedron Lett.*, **1985**, *26*, 5927.
2. (a) A. L. J. Beckwith and W. G. Gara, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 593 and 795; (b) A. L. J. Beckwith and G. F. Meijis, *J. Chem. Soc., Chem. Commun.*, **1981**, 136.
3. (a) A. L. J. Beckwith and D. M. O'Shea, *Tetrahedron Lett.*, **1986** 27, 4525; (b) G. Stok and R. Moor, Jr., *Tetrahedron Lett.*, **1986**, *27*, 4529; (c) D. Crich and S. M. Fortt., *Tetrahedron Lett.*, **1987**, *28,* 2895.
4. (a) J. Knight, P. J. Parsons, and R. Southgate, *J. Chem. Soc., Chem. Commun.*, **1986**, 454; (b) H. Hanessian, P. Beaulieu, and D. Dube, *Tetrahedron Lett.*, **1986**, *27,* 5071; (c) J. Knight and P. J. Parsons *J. Chem. Soc., Perkin Trans. 1,* **1987**, 1237.
5. (a) T. Kataoka, M. Yoshimatsu, Y. Noda, H. Shimazu, and M. Hori, *J. Chem. Soc., Perkin Trans 1.* **1993**, 120; (b) J. E. Brumwell, N. S. Simpkins, and N. K. Terette, *Tetrahedron Lett.*, **1993**, *34*, 1215 and 1219.
6. The commonly used methods besides the tin hydride method for conducting alkyl radicals in application to organic synthesis are well documented: (a) *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds,* B. Gies, Pergamon Press, Oxford, Organic Chemistry series vol. 5, 1986; (b) D. P. Curran, *Synthesis*, **1988**, 417 and 489 and references therein.
7. (a) S. Ozaki, H. Matsushita, and H. Ohmori, *J. Chem. Soc., Chem. Commun.*, **1992**, 1120; (b) S. Ozaki, H. Matsushita, and H. Ohmori, *J. Chem. Soc., Perkin Trans. 1*,**1993**, 649; (c) S. Ozaki, H. Matsushita, and H. Ohmori, *J. Chem. Soc., Perkin Trans. 1,* in the press.
8. $Ni(tet\,a)(ClO_4)_2$: 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane nickel(II) perchlorate.

9. *Spectral data for selected products*:
1b: ^{1}H NMR (200 MHz, CDCl$_3$) 1.10(3H, d, *Me*CH), 1.76(1H, d, C*H*HCHMe), 2.55-2.61(2H m, CH*H*CHMe), 2.89(1H, d, C*H*H=CH2), 3.05(1H, d, CH*H*C=CH2), 3.73(3H, s, MeCO$_2$), 3.74(3H, s, MeCO2), 4.81(1H, s, CHH=), 4.91(1H, s, CH*H*=), **1c**: ^{1}H NMR(200 MHz, CDCl$_3$) 1.67-1.70(2H, m, CH$_2$C*H*$_2$CH$_2$), 2.04-2.15(4H, m, CH2CH2CH2), 2.68(2H, s, C*H*$_2$C=CH$_2$), 3.72(6H, s, 2 X MeCO$_2$), 4.74(2H, s, C*H*$_2$=C), ^{13}C(67.8 MHz, CDCl3) 24.17, 31.16, 33.86, and 39.66(CH$_2$), 52.51(*C*H$_3$CO$_2$), 56.73[*C*(CO$_2$Me)$_2$], 110.64(*C*H$_2$=C), 171.63 (*C*O$_2$Me). **2b**: ^{1}H NMR(200 MHz, CDCl$_3$) 0.81(3H, d, CH*Me*Me), 0.85(3H, d, CHMe*Me*), 1.89 (2H, m, C*H*HCHCH), 2.40-2.65(2H, m, CH*H*CHCH), 2.89(2H, m, C*H*$_2$C=CH$_2$), 3.73(6H, s, 2 x MeCO$_2$), 4.81(1H, s, C*H*H=C), 4.99(1H, s, CH*H*=C); **2c**: ^{1}H NMR(270 MHz, CDCl$_3$), 1.65 (3H, s, C*Me*=CH$_2$), 2.13(1H, dd, C*H*HCHCMe), 2.48-2.57(1H, m, CH*H*CHMe), 2.88-3.14(2H, m, C*H*$_2$C=CH$_2$), 3.29[1H, m, C*H*C(Me)=CH$_2$], 3.73(3H, s, MeCO$_2$), 3.75(3H, s, MeCO$_2$), 4..80(1H, s, C*H*H=C), 4.84[2H, s, C(Me)=C*H*$_2$], 5.02(1H, s, CH*H*=C); **3b**: 1H NMR(270 MHz, CDCl$_3$), 0.96(3H, d, MeCH), 1.34-1.43(1H, m, CHMe), 1.58-1.79(2H, m, CH$_2$=CC*H*$_2$CHMe), 2.25(1H, d, CH*HC*HMe), 2.35(1H, s, C*H*HC=CH2), 2.40(1H, s, CH*H*C=CH$_2$), 2.91(1H, d, CH*H*CHMe), 3.71(3H, s, MeCO$_2$), 3.72(3H, s, MeCO$_2$), 4.72(2H, s, =CH$_2$),; **4b**: ^{1}H NMR(270 MHz, CDCl$_3$) 2.04(1H, dd, CHC*H*axHeqC), 2.62-2.89(6H,, m, CHCHax*H*eqC, COC*H*axHeqC, COC*H*$_2$CH,and C*H*$_2$C=CH2), 3.07(1H, d, COHax*H*eqC), 3.73(3H, s, MeCO$_2$), 4.94(1H, s, C*H*H=C), 5.03(1H, s, CH*H*=C), ^{13}C NMR(67.8 MHz, CDCl3) 40.83, 41,35, and 50.64(-CH$_2$-), 41.89(CH), 49.79(*C*CO2Me), 52.72(*C*H$_3$CO$_2$), 108.93(*C*H$_2$=C), 150.49(*C*=CH$_2$), 174.89 (*C*O$_2$Me), 208.32(CH$_2$*C*OCH$_2$); **5b**: ^{1}H NMR(200 MHz, CDCl$_3$) 1.33(3H, d, Me), 3.55(1H, m, CHMe), 4.07(1H, dd, C*H*HO), 4.86(1H, t, CH*H*O), 6.75-6.92(2H, m, ArH),7.05-7.20(2H, m, ArH); **6b**: 1H NMR(270 MHz, CDCl$_3$) 1.03(3H, d, MeCH), 3.08(1H, t, NC*H*H), 3.16(1H, br, s, NH), 3.33(1H, m, CHMe), 3.67(1H, t, NCH*H*), 3.75(3H, s, MeO), 6.59(2H, s, ArH), 6.71(1H, s, ArH).

10. M. C. Helvenston and C. E. Castro, *J. Am. Chem. Soc.*, **1992**, *114*, 8490.

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