Triethylborane-Induced Radical Addition of Halogenated Compounds to Alkenes and Alkynes in Water

T. Nakamura, H. Yorimitsu, H. Shinokubo, K. Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

Fax: +81-75-761-8846; E-mail: oshima@fm1.kuic.kyoto-u.ac.jp

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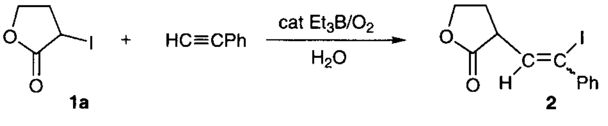
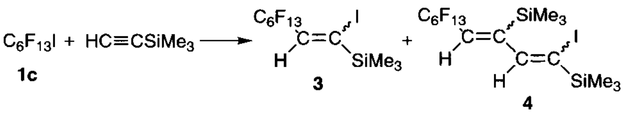
Abstract: Treatment of a mixture of α-iodo-γ-butyrolactone and phenylacetylene in water with a catalytic amount of triethylborane provided the corresponding adduct in good yield via intermolecular radical addition reaction. The triethylborane-mediated radical reaction in aqueous media could be performed under acidic or basic conditions.

Recently, much attention has been paid to free radical reactions for the synthesis of organic molecules.[1] Various organic solvents have been widely used for the radical reactions. On the other hand, there has been little investigation of the reaction in aqueous solvent.[2] We have reported that triethylborane-mediated intramolecular radical cyclization reactions of allyl iodoacetate providing γ-butyrolactone are much more efficient in water than in organic solvents such as benzene or hexane.[3] Here we report further exploitation of Et_3B-induced radical reaction in water for the intermolecular addition of halogenated compounds to carbon-carbon multiple bonds as well as the intramolecular cyclization reaction.

Triethylborane (1.0 M methanol solution (1 M = 1 mol dm^{-3}), 0.1 mL, 0.1 mmol) was added to a mixture of α-iodolactone **1a** (212 mg, 1.0 mmol) and phenylacetylene (0.31 g, 3.0 mmol) in water (9 mL) at 25°C under argon atmosphere. The resulting mixture was stirred for 20 h and the product was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residual oil by silica gel column chromatography gave an adduct **2**[4] (*E*/*Z* = 67/33, 0.29 g) in 94% yield (Scheme 1). The reaction of trimethylsilylacetylene (5.0 mmol) with perfluoroalkyl iodide, $C_6F_{13}I$ (1.0 mmol) in the presence of a catalytic amount of Et_3B (0.2 mmol) in water (9 mL) also gave the corresponding adduct **3** (*E*/*Z* = 61/39) in 58% yield along with 2:1 adduct **4** (21%, single isomer, the stereochemistry could not be determined.) (Scheme 2).

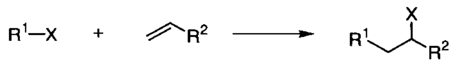


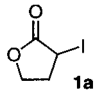
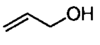
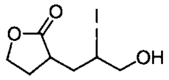
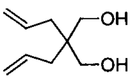
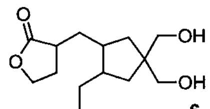
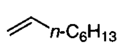
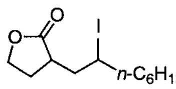
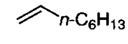
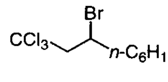
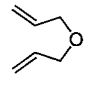
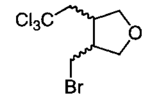
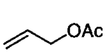
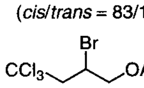
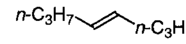
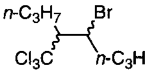
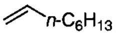
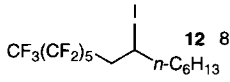
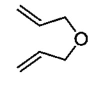
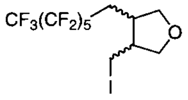
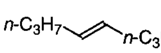
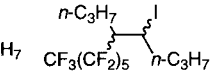
Scheme 1



Scheme 2

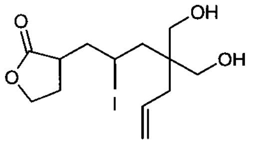
Table 1. Addition of Halogenated Compounds to Alkene[a]



Entry	Halogenated Compound	Alkene	Product	Yield (%)
1	 **1a**		 **5**[b]	92
2			 **6**	78
3			 **7**	87
4	$BrCCl_3$ **1b**		 **8**	91
5			 **9** (*cis*/*trans* = 83/17)	80
6			 **10**	70
7			 (73/27) **11**	37
8	$CF_3(CF_2)_5I$ **1c**		 **12**	87
9			 **13** (*cis*/*trans* = 89/11)	73
10			 (55/45) **14**	46

a) Halo compound (1.0 mmol), alkene (5.0 mmol), and Et_3B (1.0 M methanol solution, 0.1 mL, 0.1 mmol) were employed.
b) See ref. 7

We chose three halogenated compounds (**1a**, **1b**, and **1c**) and examined the addition reactions of these compounds to a variety of alkenes.[5] The representative results are shown in Table 1. Several comments are worth noting. (1) These halogenated compounds easily reacted with terminal alkenes as well as terminal alkynes to give the corresponding atom transfer[6] products in good yields. (2) Internal alkenes were less reactive compared to terminal alkenes in the addition reaction of the halogenated compounds and provided the adducts in only moderate yields. For instance, treatment of (*E*)-4-octene with **1b** or **1c** in the presence of triethylborane gave the corresponding adduct **11** or **14** in 37% or 46% yield, respectively (Entry 7 and 10). (3) The use of dienes such as diallyl ether and 2,2-diallyl-1,3-propanediol provided cyclized products **6**, **9**, and **13** upon treatment with the halogenated compounds in water in the presence of a catalytic amount of triethylborane (Entry 2, 5, and 9). (4) The reactions in water were much more effective compared to the reactions without solvent. For instance, treatment of a mixture of **1a** (1.0 mmol) and allyl alcohol (5.0 mmol) with Et_3B (1.0 M methanol solution, 0.1 mL, 0.1 mmol) without any solvent provided **5** in only 32% yield along with recovered **1a** (61%) after 3 days at 25°C.[8] The reaction of **1a** with 2,2-diallyl-1,3-propanediol without solvent was also less effective than the reaction in water and gave the desired product **6** in only 5% along with a complex mixture containing **15** (46%). (5) The reaction proceeded equally well in aqueous methanol. Thus, treatment of a mixture of **1a** (1.0 mmol) and phenylacetylene (3.0 mmol) in aqueous MeOH (MeOH (9 mL) and H_2O (3 mL)) with Et_3B (0.1 mmol) afforded **2** in 95% yield.



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It is interesting that this Et_3B-induced radical reaction proceeded in various acidic and basic aqueous solution. The reaction between bromotrichloromethane **1b** and diallyl ether in 1 M HCl or 1 M NaOH afforded the adduct **9** in 71% or 59% yield, respectively.[9] Moreover, the reaction took place even in concentrated HCl to give **9** in 38% yield. The results indicated that triethylborane was fairly stable in these aqueous solution and acted as a radical initiator in the presence of a trace amount of oxygen.

Acknowledgment

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References and Notes

(1) (a) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH Verlagsgesellschaft mbH.; Weinheim, 1996; (b) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Org. React.* **1996**, *48*, 301-856; (c) Curran, D. P. in *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Heathcock, C. H. Eds; Pergamon Press: Oxford, 1991. Vol. 4, Chap. 4.1 p 715; (d) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177-194.

(2) Minisci, F. *Synthesis* **1973**, 1-24; Yamazaki, O.; Togo, H.; Nogami, G.; Yokoyama, M. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2519–2523.

(3) Yorimitsu, H.; Nakamura, T.; Shinokubo, H. Oshima, K. *J. Org. Chem.* in press.

(4) **2** (*E*/*Z* = 67/33): IR (nujol) 1762, 1449, 1154, 1018, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30–7.50 (m, 5H), 6.38 (d, 0.67H), 6.02 (d, 0.33H), 4.45 (ddd, 0.33H), 4.33 (ddd, 1H), 4.09 (ddd, 0.67H), 3.70 (ddd, 0.33H), 3.26 (ddd, 0.67H), 2.77 (m, 0.33H), 2.28 (m, 0.67H), 2.17 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 29.0, 29.5, 42.5, 48.1, 66.3, 66.8, 101.1, 110.8, 128.4, 128.5, 128.6 (2C), 128.9, 129.0, 133.1, 136.4, 140.9, 142.2, 176.1, 176.5. Found: C, 45.59; H, 3.62%. Calcd for $C_{12}H_{11}IO_2$: C, 45.88; H, 3.53%.

(5) The reaction of 2-iodopropane with trimethylsilylacetylene gave an adduct in only 14% yield (*E*/*Z* = 94/6) upon treatment with Et_3B in water.

(6) Curran, D. P.; Chang, C. -T. *Tetrahedron. Lett.* **1987**, *28*, 2477-2480.

(7) **5** (44:56 diastereomer mixture): IR (neat) 3324, 2912, 1753 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.74–4.65 (m, 0.44H), 4.46–4.34 (m, 1H), 4.31–4.19 (m, 1.56H), 3.92–3.75 (m, 2H), 2.94–2.71 (m, 1.44H), 2.60–2.42 (m, 1.56H), 2.31–2.21 (m, 0.56H), 2.17–1.81 (m, 2.44H); ^{13}C NMR ($CDCl_3$) δ 179.4, 178.2, 68.5, 67.8, 66.7, 66.5, 39.6, 39.1, 37.5, 36.8, 36.0 (2C), 29.4, 28.7. Found: C, 30.83; H, 4.08%. Calcd for $C_7H_{11}IO_3$: C, 31.13; H, 4.11%.

(8) The reaction proceeded in benzene and gave **5** in 74% yield after stirring for 30 h. In aqueous methanol (MeOH (5 mL) and H_2O (5 mL)), **5** was obtained in 85% yield after stirring for 7 h.

(9) Representative experimental procedure: Triethylborane (1.0 M methanol solution, 0.1 mL, 0.1 mmol) was added to a heterogeneous solution of **1b** (198 mg, 1.0 mmol) and diallyl ether (0.49 g, 5.0 mmol) in 1 M HCl (10 mL) at 25°C with vigorous stirring. Extractive work up (ethyl acetate and brine) followed by purification by silica gel column chromatography gave **9** (0.22 g) in 71% yield.