(Triphenyltin)cobaloxime as a Reagent for Radical Generation from Bromides

Masaru Tada* and Katsuyuki Kaneko

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku, Tokyo 169, Japan

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Intramolecular radical cyclization has increased in importance during the last decade and is widely used as a synthetic strategy.[1] Radicals are often generated from halides by the use of tributyltin hydride. This process, however, requires high dilution or slow addition of the tin hydride to avoid hydrogen transfer from the hydride to the organoradical, which results in the net reduction of the starting halide. The produced tributyltin halides are nonpolar and difficult to separate from the organic products in many cases although some efforts have been made to remove this disadvantage.[2] In this paper, we describe a new method to produce the radical pair from (triphenyltin)cobaloxime (**1**) (Figure 1) and bromides, which avoids these limitations.

(Triphenyltin)cobaloxime (**1**), a σ-bonded tin–cobalt complex, is expected to yield, upon irradiation, a triphenyltin radical and a cobaloxime radical; the former abstracts a halogen from a halide even more efficiently than the tributyltin radical does (Scheme 1).[3] The organoradical thus formed coexists with the cobaloxime-(II) complex, which has an unpaired electron but is not a reducing agent, as in the case of tributyltin hydride.

We chose 2,2-diphenyl-2-(2-propynyloxy)ethyl bromide (**2**), 2-(allyloxy)-2,2-diphenyl bromide (**5**), and 2,2-diphenyl-2-ethoxyethyl bromide (**7**) as substrates. These substrates were chosen due to their analogy with our earlier studies and the simplicity of product identification.[4,5]

We photolyzed a 1:1 mixture of (triphenyltin)cobaloxime (**1**)[6] and 2,2-diphenyl-2-(2-propynyloxy)ethyl bromide (**2**) in various solvents (Scheme 2). In these reactions, the cyclized olefin **3** was obtained as the major product in addition to a trace amount of vinylcobaloxime **4**. The varying yields of the cyclized product **3** as a function of the solvent used are attributed to the hydrogen donating ability of the solvent (Table 1). Thus the reaction in benzene produced a poor yield, and the reaction in THF resulted in a much higher yield.[7]

A 1:1 mixture of (triphenyltin)cobaloxime (**1**) and 2-(allyloxy)-2,2-diphenylethyl bromide (**5**) was photolyzed in the same manner as bromide **2**, and the same product **3** was obtained in high yield (Scheme 3). This reaction contrasts with the reaction of 2-(allyloxy)ethyl bromide and tributyltin hydride in which the reduction products before and after the cyclization were obtained (Scheme 4).[8] The present result can be accounted for by a

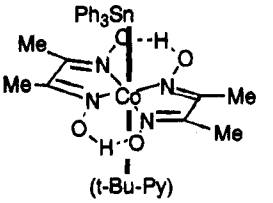
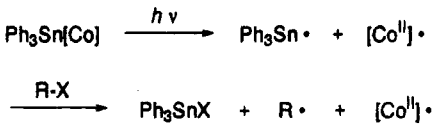


Figure 1. Triphenyltincobaloxime (**1**).

Scheme 1



Scheme 2

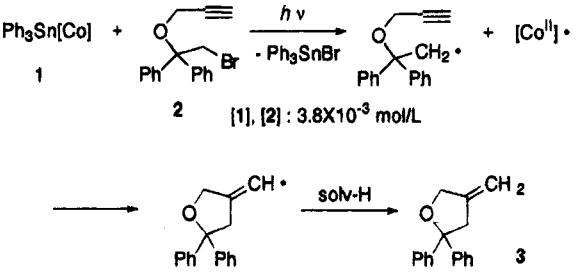
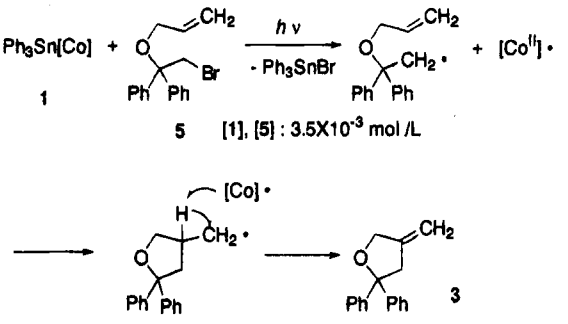


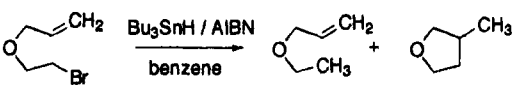
Table 1. Photoreactions of (Triphenyltin)cobaloxime (1) with Bromides

run	bromide	solvent	product (yield/%)
1	**2**	benzene	**3** (6.4)
2	**2**	benzene–THF (6:1)	**3** (52)
3	**2**	THF	**3** (64)
4	**5**	benzene	**3** (90)
5	**5**	acetonitrile	**3** (84)
6	**7**	benzene	**8** (64)

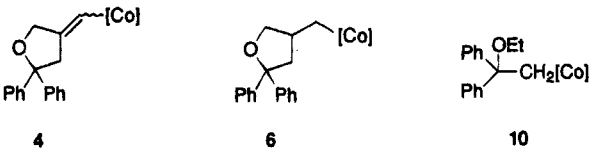
Scheme 3



Scheme 4



β-hydrogen abstraction from the cyclized radical by the cobaloxime radical (Scheme 3) or by the initial formation of organocobaloxime **6**, followed by its photolysis. This type of β-elimination is a common process in the photolysis of organocobaloximes.[9]



(1) Review: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: Oxford, 1986. (b) Curran, D. P. *Synthesis* **1988**, 417 and 489. (c) Beckwith, A. L. J. *Rev. Chem. Intermed.* **1986**, *7*, 143. (d) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.

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(6) 4-*tert*-Butylpyridine, rather than more conventional pyridine, was selected as the sixth ligand for the cobaloxime **1** due to its good solubility in organic solvents.

(7) Russell, G. A. *Free Radicals*; Kochi, J. K., Ed.; Wiley Interscience: New York, 1973; Vol. 1, Chap. 7.

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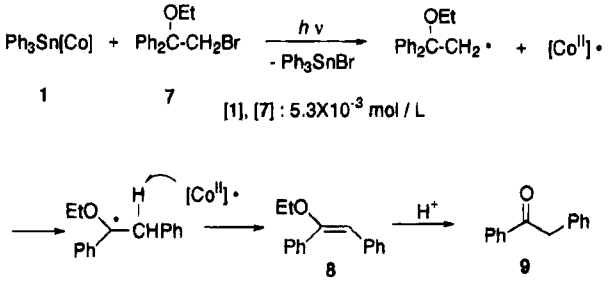
Scheme 5



Next, 2,2-diphenyl-2-ethoxyethyl bromide (**7**) in benzene was exposed to the same reaction conditions and 1,2-diphenylethoxyethene (**8**) was obtained. Though the ^{1}H NMR spectrum of the crude product clearly showed the presence of **8**, it was partly transformed into 1,2-diphenylethanone (**9**) during chromatography. Acid treatment of **8** transformed it into ketone **9** which was identical to an authentic sample (Scheme 5). The product **8** is formed by a phenyl migration of the radical followed by β-hydrogen abstraction by the cobaloxime(II) complex. The ^{1}H NMR spectrum of the crude product also showed a small amount of (2,2-diphenyl-2-ethoxyethyl)cobaloxime (**10**). This product (**10**) yielded 1,1-diphenylethene upon chromatography (SiO_2) or acid treatment. Ionic β-elimination of (2-alkoxyethyl)cobaloxime, yielding the olefin, is well documented.[10]

The reaction products described were also realized by photolysis of the corresponding organocobaloximes,[4,5] which were synthesized from bromides **2**, **5**, and **7**. The present results show that both processes, the photolysis of bromides in the presence of (triphenyltin)cobaloxime and the direct photolyses of the corresponding organocobaloximes, give the same result. Thus, (triphenyltin)-cobaloxime generates an alkyl radical under nonreductive conditions (Scheme 1) while the radical generated by tributyltin hydride is exposed to reductive conditions (Scheme 4). Furthermore, the coexistence of the cobaloxime(II) radical in the reaction mixture preserves functional groups such as the olefin and the σ-cobalt bond in the product. Although the number of tested bromides is limited, the essence of the process is bromine abstraction by the triphenyltin radical and the hydrogen abstraction by the cobaloxime(II) complex. The present methodology, therefore, is considered to be general to other halides or compounds having a radicophilic substituent. These features suggest that (triphenyltin)-cobaloxime (**1**) is a convenient reagent for use in synthetic and mechanistic studies of organoradicals.

Experimental Section

Starting Materials and Authentic Syntheses of the Products. All the starting bromides **2**,[11] **5**,[4] and **7**[5] and the product **3**[11] were synthesized by the reported methods and identified by spectroscopic data.

Triphenyltin(4-^{t}Bu-pyridine)cobaloxime (1). Chloro(4-^{t}Bu-pyridine)cobaloxime[12] (4.66 g, 10 mmol) in 45 mL of deaerated methanol (argon bubbling under ultrasonic irradiation) was treated with 3 mL of aqueous NaOH (410 mg, 10.2 mmol) and $NaBH_4$ (386 mg, 10.2 mmol) under argon. After stirring at rt for 30 min, the mixture was treated with triphenyltin chloride (3.85 g, 10 mmol) and further stirred at rt for 8 h in the dark. The reaction mixture was concentrated and extracted three times with 30 mL of CH_2Cl_2 after addition of 50 mL of water, and the extract was subjected to chromatography on Florisil eluted by the mixed solvent of CH_2Cl_2–ethyl acetate (4:1). The product thus obtained was dissolved in CH_2Cl_2 and crystallized out of the solution by slow additon of ethyl ether (diffusion in a sealed system) to give cobaloxime **1** in 53% yield. Mp 180–182 °C dec; ^{1}H NMR(90 MHz, $CDCl_3$) δ 1.24(9H, s), 1.71 (12H, s), 7.03–7.83 (17H, m), 8.40 (2H, d, J = 5.1 Hz), 18.43–18.52 (2H, bs); IR ($CHCl_3$) 3060, 1616, 1550 cm^{-1}. Anal. Calcd for $C_{35}H_{42}CoN_5O_4Sn$: C, 54.28; H, 5.47; N, 9.05. Found: C, 54.35; H, 5.43; N, 9.04.

General Procedure for the Photoreactions. Irradiation was carried out with a Ushio 450 w high pressure mercury lamp mounted on a merry-go-round type rotary irradiation apparatus (Riko-400) or Rayonett Photochemical Reactor (RPR-100) equipped with 350 nm lamps. Both gave the same result except for the reaction time, and the irradiation times by the former apparatus were recorded. The solutions in Pyrex cylindrical vessels were deaerated by bubbling argon under an ultrasonic wave. The solutions were irradiated for 25 h in the case of bromide **2** and 26 h in the cases of bromide **5** and **6**. The solutions were concentrated and the residues from bromides **2** and **5** were subjected to chromatography (SiO_2/benzene) to give the product **3** which was identified by comparison with an authentic sample.[11] The yield of the product **3** was determined by gas chromatography (a SE-30 CBWP-W12–300 column, N_2) by using benzophenone as an internal standard. Product **3**, mp 58 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.10–3.31 (2H, m), 4.30–4.50 (2H, m), 4.70–5.03 (2H, m), 7.00–7.45 (10H, m). Anal. Calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.31; H, 6.71.

The concentrate containing the *cis*- and *trans*-1,2-diphenylethoxyethylene (**8**)[13] from the photolysis of bromide **7** was treated with a 5:3:1 mixture of ethyl ether, methanol, and aqueous HCl (6 mol/L) at rt for 12 h. The organic layer was washed with saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated. The residue thus obtained was separated by preparative TLC (Merck Kieselgel 60, 0.2 × 20 × 20 cm; benzene–hexane, 1:4) into 1,2-diphenylethanone (**9**) and 1,1-diphenylethene (**10**). The yield of the photoproduct **8** was estimated from the isolated yield of **9**.

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