

Radico-Catalysis: Possible Involvement of a Cobalt(II) Complex in the Free Radical Reactions of Sulfur Functions

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ABSTRACT: A cobalt(II) complex is paramagnetic and can be coordinated with sulfur functions; the coordination complex delocalizes an unpaired electron from cobalt(II) to the sulfur functions such as thioester and vinyl sulfide. Thus, the generation of partial unpaired electron density on the sulfur functions induces or modifies the reactions of the organo free radical containing the sulfur function. © 2001 John Wiley & Sons, Inc. *Heteroatom Chem* 12:204–208, 2001

INTRODUCTION

We have reported on the radical reactions of sulfur-containing functions in which a cobalt complex, an organo(pyridine)dimethylglyoximatocobalt [a cobaloxime, hereafter; e.g., methylcobaloxime **1** ($R' = \text{Me}$)] (Scheme 1), coexists in the reaction system. Discussions have been focused on the effect of the interaction between the free radical intermediate and the paramagnetic cobalt(II) complex. In this account, I plan to summarize these reactions by the concept of radico-catalysis.

This article is dedicated to Professor Emeritus Naoki Inamoto of the University of Tokyo on the occasion of his 72nd birthday.

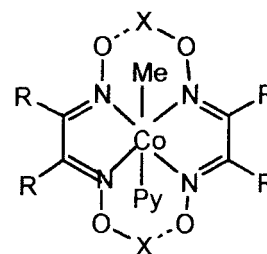
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Acid or base catalysis generates a partial electron-pair hole (Equation 1) or a partial electron-pair pool (Equation 2), respectively. In accord with this concept, radico-catalysis can be defined as the generation of a partial density of an unpaired electron in the substrate molecule (Equation 3). We have previously shown the coordination interaction between a paramagnetic cobalt(II) complex and sulfur functions such as sulfide and thioester as depicted in Scheme 2 [1].



- 1** ($R = \text{Me}$, $X = \text{H}$): Methylcobaloxime, $[\text{Co}^{\text{II}}]\text{Py}$
- 2** ($R = \text{Ph}$, $X = \text{H}$): Methyl-tetraphenylcobaloxime
- 3** ($R = \text{Me}$, $X = \text{BF}_2$): Methyl- BF_2 -cobaloxime

SCHEME 1

Methylcobaloximes **1** having *para*-substituted pyridines as axial ligands react in a similar manner, and the complex having the less basic ligand showed greater reactivity (Scheme 4) [3c]. The *trans*-effect of a pyridine derivative of weaker basicity induces more donative and hence less back-donative interaction to the cobalt-sulfur bond [7] (Figure 2). The increased coordination interaction makes the sulfur more radicophilic and induces more free radical substitution.

Next, we discuss radical rearrangements involving phenyl and thioester group migrations shown in Scheme 5 [8] and Table 1. Stannyl radicals, generated as shown in Table 1, abstract the bromine atom from bromide **6** to produce the radical **B** (entry 1 and 2). In entry 1, the radical **B** is reduced by the stannane to give product **7** or undergoes rearrangement with migration of the phenyl group to give product **8** (Y = H, CH₃) in a comparable ratio. However, the thioester migration from **B** to give **9** is only a minor process (7/8/9 = 40/53/7). The use of a distannane (entry 2) instead of the stannane gave similar results (7/8/9 = 37/53/10) although the reaction is sluggish and a considerable amount of the starting material was recovered intact.

The reaction with triphenylstannylcobaloxime (entry 3) is again sluggish, but evidently the ratio of thioester/phenyl migration increased and the direct alkyl substitution on the sulfur to give **10** became a major process (7/8(Y = CH₂)/9(Y = CH₂)/10 = 2.0/12/

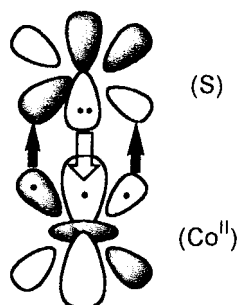


FIGURE 2 Coordinative interaction between Co(II) and sulfur.

TABLE 1 Radical Rearrangement of Phenyl vs. Thioester Group

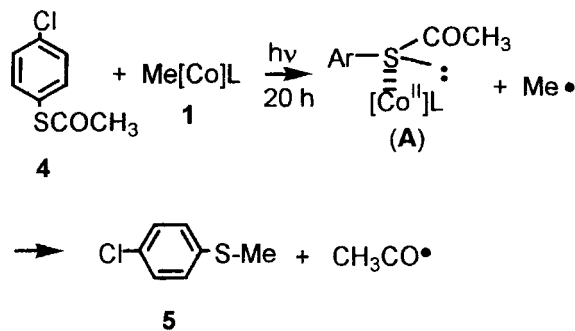
Entry	X	Conditions	Total Yield (%)	9/8	10/8
1	Br	Bu ₃ SnH-AIBN	79	0.13	0.0
2	Br	(Ph ₃ Sn) ₂ /hν	26 ^a	0.18	0.0
3	Br	Ph ₃ Sn[Co]L/hν	25 ^a	2.9	4.3
4	[Co]L	hν	45 ^a	1.7	3.6

^aThe starting materials were recovered considerably.

35/51). The photolysis of a cobaloxime derivative **6** (X = [Co]L; L = 4-*t*-BuPy) (entry 4) gave a similar result as shown in entry 3 (7/8/9/10 = 0.0/16/26/58). In the latter two reactions, the intermediate radical **B** (Scheme 5) coexists with cobaloxime(II), and both the radical substitution to give **10** and rearrangement with migration of the thioester group to give **9** are stimulated by the cobaloxime(II), (see 10/8 and 9/8 in Scheme 5) [8], because the rate of rearrangement involving phenyl migration to give **8** is considered to be unaffected by the cobaloxime(II) and can be used as an internal clock. These behaviors are explained by the induced free radical substitution on sulfur (Scheme 3a), and the activation of the alkyl-acyl bond for the thioester rearrangement as depicted in Scheme 3b.

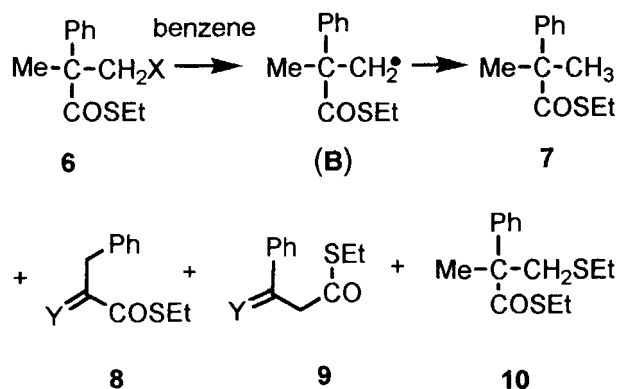
Lastly, an intramolecular *ipso/ortho* addition of a free radical to vinyl sulfides is discussed. A benzothiophene derivative **11** was treated with triphenylstannane or triphenylstannylcobaloxime to give the results depicted in Scheme 6 and Table 2.

The products from the sulfanyl radical **E**



L: 4-(CN)-Py 36 %; Py 29 %; 4-(*t*-Bu)-Py 23 %

SCHEME 4 The reaction was stopped before completion to estimate the relative reactivity of methylcobaloximes (**1**), and the starting material **4** was recovered under the reaction conditions.

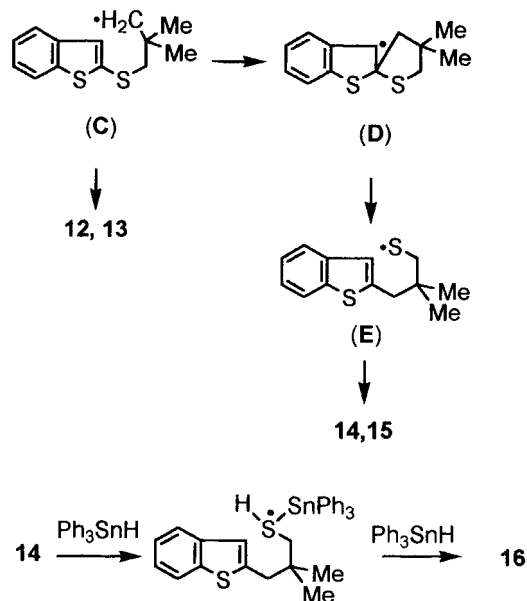


SCHEME 5

(Scheme 7) formed by the Smiles rearrangement (*ipso*-addition) [9] are major ones in both cases, but the formation of product **13** by direct *ortho*-addition becomes feasible only with the coexistence of cabaloxime(II) [10].

The reaction of the uracil derivative **17** ($n = 1$) with triphenylstannane (entry 1) gives a direct addition product **19** and products **21** and **22** after *ipso*-addition in comparable amounts, $19/(21 + 22) = 42/58$ (Scheme 8 and Table 3) [10].

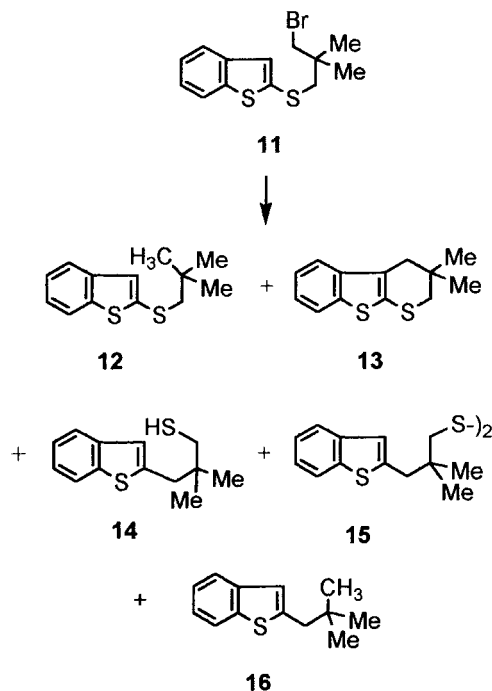
The reaction with triphenylstannylcobaloxime (entry 2) [10], in which cobaloxime(II) coexists with the intermediate radical F (Scheme 9), gave **20** as a sole product. In the case of the uracil derivative **17** ($n = 2$) (entry 3), only a direct reduction product (**18**, $n = 2$) was isolated from the reaction with the triphenylstannane, but only the *ortho*-addition to give **20**, besides hydrogen abstraction to give **18**, takes place with the triphenylstannylcobaloxime (entry 4) [10]. Thus it is evident that the coexisting cobalox-



SCHEME 7

 TABLE 2 *Ortho* vs. *Ipso* Free Radical Addition on Benzo-*thiophene*

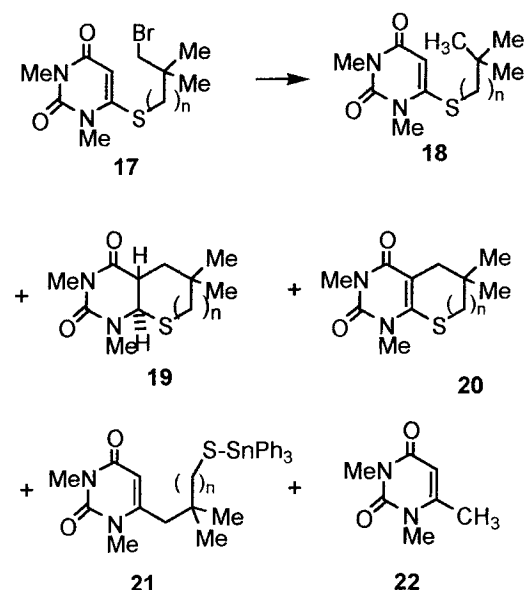
Conditions	Total Yield (%)	Product Composition (%)				
		12	13	14	15	16
Ph ₃ SnH-AIBN/80°C	96	11	—	74	—	15
Ph ₃ Sn[Co]L/130°C	87	—	20	—	80	—



SCHEME 6

 TABLE 3 *Ortho* vs. *Ipso* Free Radical Addition on Uracil

Entry	n	Conditions	Composition (%)					Total Yield (%)
			18	19	20	21	22	
1	1	Ph ₃ SnH-AIBN/ 80°C	—	42	—	49	9.0	91
2	1	Ph ₃ Sn[Co]L/h ν	—	—	100	—	—	73
3	2	Ph ₃ SnH-AIBN/ 130°C	100	—	—	—	—	82
4	2	Ph ₃ Sn[Co]L/h ν	37	—	63	—	—	75



SCHEME 8

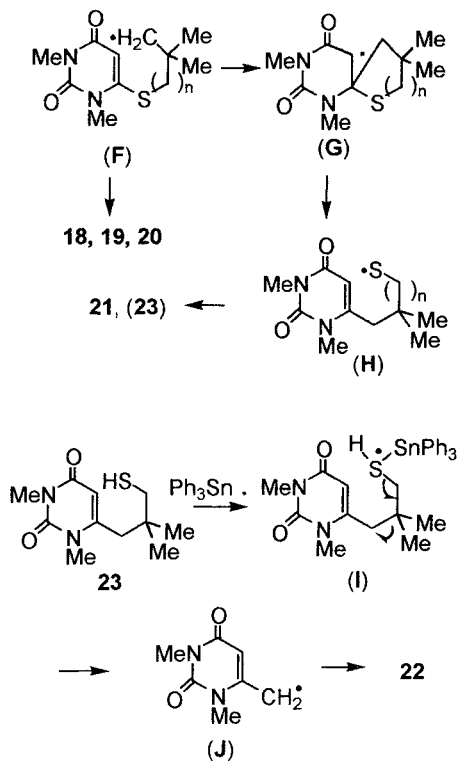
ime(II) increases the radicophilicity of the vinyl moiety of benzothioephene and uracil derivatives as depicted by Scheme 3c.

All the experimental findings described here suggest the involvement of the cobalt(II) complex in the free radical reactions of sulfur functions such as thioester and sulfide. These effects are considered to be the consequence of the coordination interaction between sulfur and cobalt(II), which induces a partial density of unpaired electron on the sulfur, and

also its hyperconjugation with an alkyl-acyl σ -bond as well as the π -conjugation with a vinyl group. This is a new concept of radico-catalysis as discussed at the beginning of this article and may be a guiding principle in designing new radical reactions.

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SCHEME 9