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′ = 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.

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].

$$\text{Acid catalysis:} RX + Acid \rightarrow R^{\delta+}\text{–}X\text{–}Acid^{\delta-} \quad (1)$$

$$\text{Base catalysis:} RX + Base \rightarrow R^{\delta-}\text{–}X\text{–}Base^{\delta+} \quad (2)$$

$$\text{Radico-catalysis:} RX + Radical \rightarrow R^{\delta\cdot}\text{–}X\text{–}Rad^{\delta\cdot} \quad (3)$$
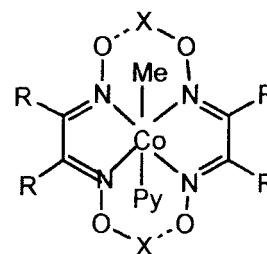
1 (R=Me, X=H): Methylcobaloxime, [Co^{II}]Py
2 (R=Ph, X=H): Methyl-tetraphenylcobaloxime
3 (R=Me, X=BF$_2$): Methyl-BF$_2$-cobaloxime

SCHEME 1

This sulfur-coordinated complex is a 19-electron complex, and the axial bond of (S–Co–N) consists of a three-centered five-electron bond, which is reinforced by the back donation from cobalt(II) to vacant d-orbitals of sulfur [1]. The unpaired electron on the SOMO orbital of the three-center bond delocalizes to the sulfur as depicted in Figure 1a.

The unpaired electron density thus formed on sulfur delocalizes further to the σ^* orbital of the alkyl-carbonyl bond of a thioester (Figure 1b) or to the π^* orbital of a vinyl sulfide (Figure 1c) by σ-hyperconjugation or π-conjugation, respectively. Thus, the interaction between sulfur and a cobalt(II) complex may alter the free radical reactivity of thioesters and vinyl sulfides. This phenomenon may be defined as *radico-catalysis*.

Herein, I will present (1) a free radical substitution on sulfur (Scheme 3a), (2) a thioester rearrangement (Scheme 3b), and (3) an *ortho*-addition of an alkyl radical to vinyl sulfides (Scheme 3c) by the concept of radico-catalysis.

RESULTS AND DISCUSSIONS

Photolysis of methylcobaloxime **1** generates a pair of methyl and cobaloxime(II) radicals [2], and the former radical gives the methyl sulfide **5** by the reaction
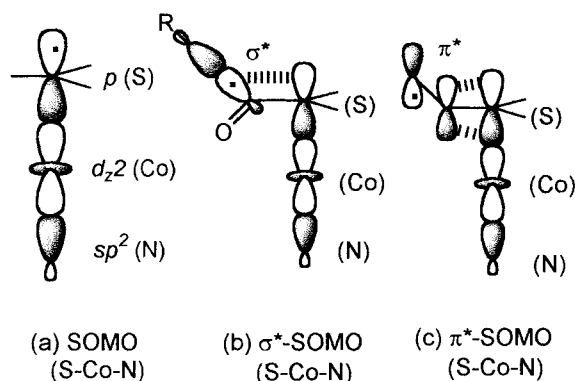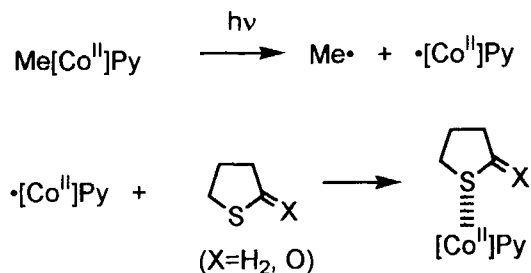
with the thioester **4** (Scheme 4) [3]. This reaction is considered to be a radical substitution by the methyl radical on the sulfur that has become more radicophilic by the cobalt coordination (see Scheme 3a and **A** in Scheme 4). The use of methyl-tetraphenylcobaloxime **2** [4] or methyl-BF$_2$-cobaloxime **3** [5] instead of methylcobaloxime **1** gave the methylsulfide **5** only in a small or trace amount, respectively, under the same conditions as those of to the reactions of cobaloxime **1**.

Photolyses of methyl-tetraphenylcobaloxime **2** and methyl-BF$_2$-cobaloxime **3**, however, generate a methyl radical more efficiently, judging from the formation of methyl-TEMPO in the presence of TEMPO [3c]. Four phenyl groups in the tetraphenylcobaloxime **2** orient perpendicularly to the planar dimethylglyoximato ligand [4] and shield the coordination site of cobalt for the sulfur. The BF$_2$ groups in BF$_2$-cobaloxime **3** are more electronegative [6] than the hydrogens in cobaloxime **1** and reduce the back donation from the central cobalt(II) to the sulfur of the thioester group. As described earlier, cobalt-sulfur bonding is mostly attributable to the back donation [1], and hence the BF$_2$ groups diminish the coordinative interaction between the sulfur and cobalt(II) complex (Figure 2).

FIGURE 1   SOMO(S–Co–N) and its conjugation with σ^*/π^* orbitals of thioester and vinyl sulfide.
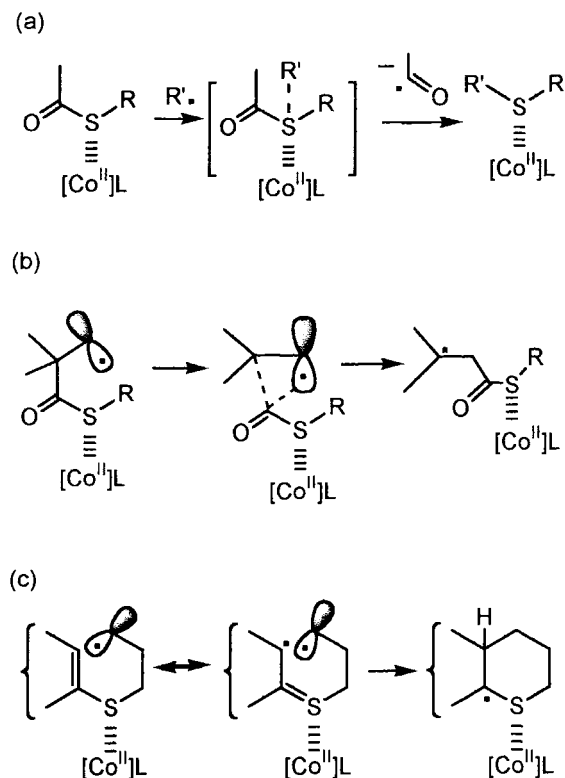
SCHEME 2

SCHEME 3

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, CH$_3$) 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 = CH$_2$)/9(Y = CH$_2$)/10** = 2.0/12/

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.

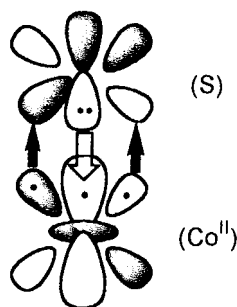The products from the sulfanyl radical **E**

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

TABLE 1 Radical Rearrangement of Phenyl vs. Thioester Group

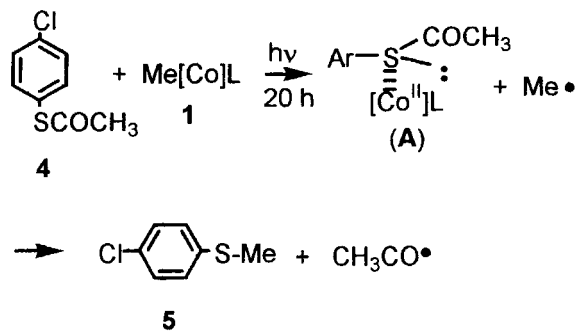| Entry	X	Conditions	Total Yield (%)	9/8	10/8
1	Br	Bu$_3$SnH-AIBN	79	0.13	0.0
2	Br	(Ph$_3$Sn)$_2$/hν	26^a	0.18	0.0
3	Br	Ph$_3$Sn[Co]L/hν	25^a	2.9	4.3
4	[Co]L	hν	45^a	1.7	3.6

^{a}The starting materials were recovered considerably.

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.
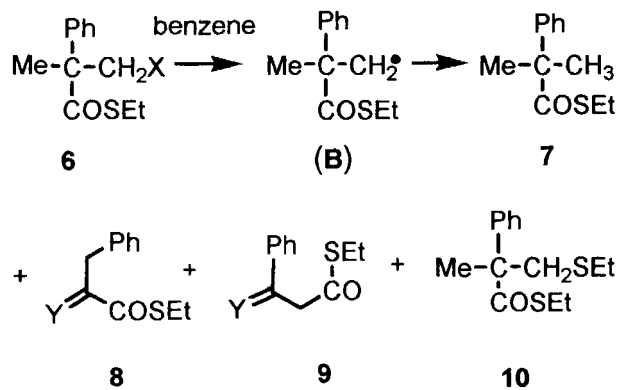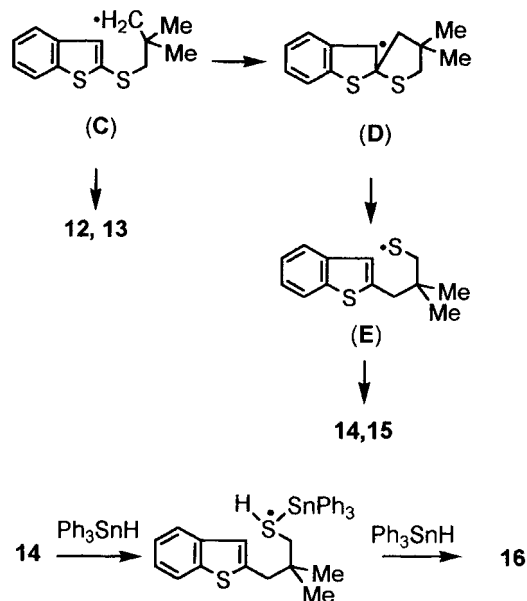
SCHEME 5

(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 Benzothiophene

	Total	Product Composition (%)				
Conditions	Yield (%)	**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	—
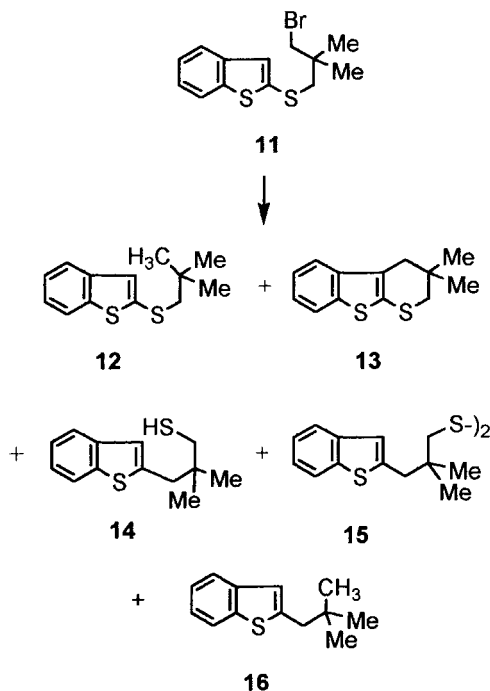
TABLE 3 *Ortho* vs. *Ipso* Free Radical Addition on Uracil

				Composition (%)					Total Yield
Entry	n	Conditions		**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/hν		—	—	100	—	—	73
3	2	Ph$_3$SnH-AIBN/	130°C	100	—	—	—	—	82
4	2	Ph$_3$Sn[Co]L/hν		37	—	63	—	—	75
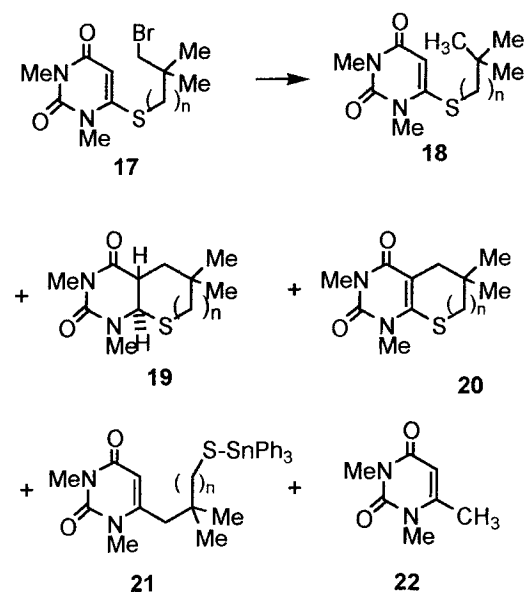
SCHEME 6

SCHEME 8

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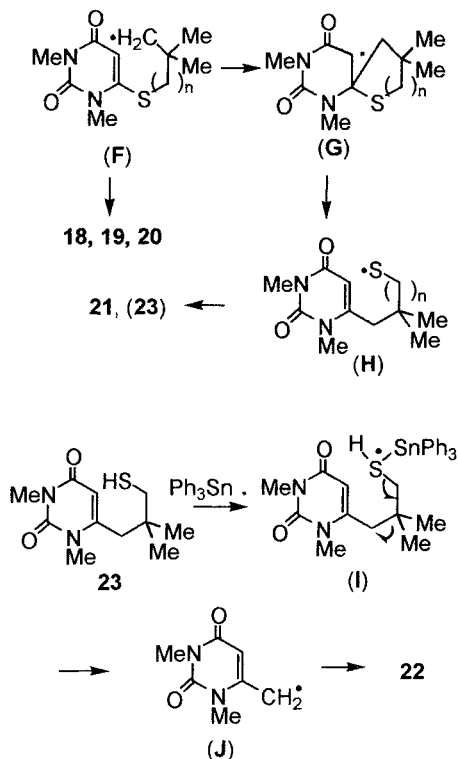
also its hyperconjugation with an alkyl-acyl σ-bond as well as the π-conjugation with a vinyl group. This is a new concept of radico-catalysis as discussed at the beginning of this article and may be a guiding principle in designing new radical reactions.

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SCHEME 9