

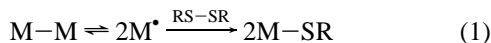
# Activation of Organic Disulfides by a Paramagnetic Heterobimetallic Tantalum/Cobalt Complex and a Comparison of Their Reactions with Cobaltocene. Evidence for a Dependence of Mechanism on the Electronic Properties of the Disulfide

Mark A. Aubart and Robert G. Bergman\*

Department of Chemistry, University of California  
Berkeley, California 94720

Received October 2, 1995

The metal-mediated cleavage of sulfur–sulfur bonds, such as those in organic disulfides, is a reaction of substantial importance in both chemistry and biology.<sup>1–9</sup> In spite of this, little mechanistic information is available on these transformations. One of the most interesting organometallic reactions in this class is the activation of organic disulfides by binuclear organometallic complexes (eq 1), a useful method for the preparation of metal thiolates. These reactions are normally



assumed to proceed via dissociation of the binuclear complex into metal radical intermediates. Because of the difficulty of isolating the reactive organometallic radicals, mechanistic studies of organic disulfide activation have so far been limited to reactions in which the metal radicals have been generated as transient species, e.g., in the photochemical dissociation of dinuclear complexes containing metal–metal bonds.<sup>4–9</sup>

A major advance in understanding the mechanism of this process would be achieved through the direct study of the reaction of disulfides with isolable monomeric organometallic radicals. We now report a system in which an organometallic radical reacts cleanly with organic disulfides, allowing us to study its mechanism carefully using kinetic, temperature dependence, solvent effect, and substituent effect techniques.

Earlier we reported the synthesis of Cp<sub>2</sub>Ta(*μ*-CH<sub>2</sub>)<sub>2</sub>CoCp, **1**, a monomeric heterobimetallic radical species in which the unpaired electron is localized at the cobalt metal center.<sup>10</sup> We have now found that treatment of **1** with aromatic disulfides at room temperature in toluene, benzene, dichloromethane, or acetonitrile solution rapidly affords the corresponding diamagnetic monothiolate complexes, Cp<sub>2</sub>Ta(*μ*-CH<sub>2</sub>)<sub>2</sub>Co(SR)Cp, **2** (see Table 1 for compound numbering), in quantitative yield (eq 2). Solution NMR and IR spectroscopic data and elemental analyses are consistent with the formulation of the products shown in eq 2.

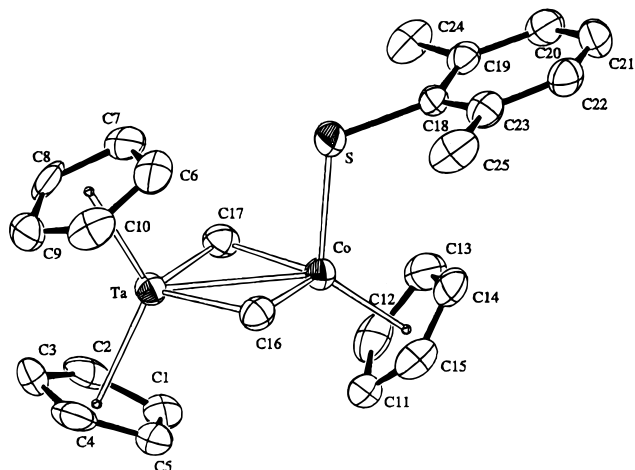


In order to confirm this structural proposal, a single-crystal X-ray diffraction study of complex **2e** was undertaken. An

**Table 1.** Rate Data for Reaction of **1** and **3** with RSSR at 15 °C

compd	R	solvent ( $\epsilon^a$ )	$k_1$ (M <sup>-1</sup> s <sup>-1</sup> ) <sup>b</sup>	$k_{rel}$
<b>1</b>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ( <b>2a</b> )	C <sub>6</sub> H <sub>6</sub> (2.3)	$1.13 \times 10^{-2}$	1.0
<b>1</b>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ( <b>2a</b> )	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$4.06 \times 10^{-2}$	3.6
<b>1</b>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ( <b>2a</b> )	CH <sub>3</sub> CN (36.6)	0.377	33
<b>1</b>	<i>p</i> -OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ( <b>2b</b> )	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	0.132	12
<b>1</b>	C <sub>6</sub> H <sub>5</sub> ( <b>2c</b> )	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$3.81 \times 10^{-2}$	3.4
<b>1</b>	<i>p</i> -CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ( <b>2d</b> )	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	0.892	79
<b>1</b>	2,6-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> ( <b>2e</b> )	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$2.66 \times 10^{-3}$	0.24
<b>3</b>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$4.8 \times 10^{-4}$	0.042
<b>3</b>	<i>p</i> -OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$4.3 \times 10^{-4}$	0.038
<b>3</b>	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$1.1 \times 10^{-3}$	0.097
<b>3</b>	<i>p</i> -CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	0.32	28
<b>3</b>	2,6-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub> (8.9)	$9.7 \times 10^{-4}$	0.086

<sup>a</sup> Dielectric constant. <sup>b</sup> Reproducibility is typically  $\pm 5$ –10%.



**Figure 1.** ORTEP diagram of **2e**.

ORTEP diagram of the structure of the complex is shown in Figure 1. The most notable features of the structure are that the four-membered dimetallacyclic ring is planar and the Ta–Co distance of 2.8005(8) Å is approximately the sum of the atomic radii.<sup>11</sup> Thus the molecule's core is similar to that of the structurally characterized parent **1**.<sup>10</sup>

Preliminary insight into the reaction mechanism of disulfide activation was obtained by kinetic studies carried out on the reaction of **1** with di-*p*-tolyl disulfide in CH<sub>2</sub>Cl<sub>2</sub> solution. The quantitative reaction of **1** with di-*p*-tolyl disulfide in dichloromethane at 15 °C was studied separately under two different flooding regimes (>4.5 molar equiv of disulfide and >10 mol equiv of bimetallic complex; additional conditions for the kinetic experiments are discussed in the supporting information). This indicated that the reaction is first order in both **1** and di-*p*-tolyl disulfide and second order overall (eq 3). The

$$\frac{d[2a]}{dt} = 2k_1[1][\text{di-}p\text{-tolyl disulfide}] \quad (3)$$

second-order rate constant,  $k_1$ , for the reaction determined by flooding in disulfide is  $(4.3 \pm 0.3) \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ . The value found by flooding in **1** is  $(3.8 \pm 0.3) \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ . The agreement of these data reflects a well-behaved second-order reaction. The temperature dependence of the rate constant  $k_1$  ( $T = 14.9$ – $45.5$  °C; see supporting information) allowed calculation of the following activation parameters:  $E_a = 11.4 \pm 0.2 \text{ kcal/mol}$ ,  $\Delta H^\ddagger = 10.8 \pm 0.3 \text{ kcal/mol}$ ,  $\log_{10} A = 7.29$ , and  $\Delta S^\ddagger = -27 \pm 5 \text{ eu}$ . The  $\Delta S^\ddagger$  value is consistent with a

- (1) Dedon, P. C.; Borch, R. F. *Biochem. Pharmacol.* **1987**, *36*, 1955.  
 (2) Yotsuyanagi, T.; Ohta, N.; Futo, T.; Ito, S.; Chen, D.; Ikeda, K. *Chem. Pharm. Bull.* **1991**, *39*, 3003.  
 (3) Chen, D.; Ohta, N.; Ukai, M.; Masuda, M.; Yotsuyanagi, T. *Biol. Pharm. Bull.* **1994**, *17*, 1561.  
 (4) Schollhammer, P.; Petillon, F. Y.; Pichon, R.; Poder-Guillou, S.; Talarmin, J.; Muir, K. W.; Manojlovic-Muir, L. *Organometallics* **1995**, *14*, 2277.  
 (5) Abrahamson, H. B.; Freeman, M. L.; Hossain, M. B.; van der Helm, D. *Inorg. Chem.* **1984**, *23*, 2286.  
 (6) Abrahamson, H. B. *Organometallics* **1983**, *2*, 679.  
 (7) Brandenburg, K. L.; Heeg, M. J.; Abrahamson, H. B. *Inorg. Chem.* **1987**, *26*, 1064.

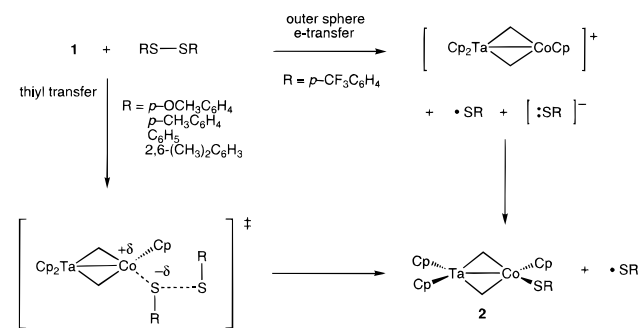
(8) Goh, L. Y.; Tay, M. S. *Organometallics* **1992**, *11*, 1711.

(9) King, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 1587.

(10) Goldberg, K. I.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 4853.

(11) Slater, J. C. *J. Chem. Phys.* **1964**, *41*, 3199.

## Scheme 1



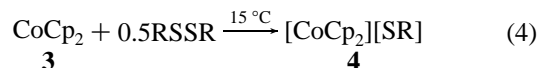
bimolecular reaction in which substantial translation entropy is lost in bringing the two reacting particles together in the transition state.

Two mechanisms consistent with the measured rate law are illustrated in Scheme 1. One involves direct attack of the cobalt center in **1** at sulfur, and the second possibility involves single (outer sphere) electron transfer from **1** to RSSR, followed by cleavage of the S—S bond in the disulfide radical anion.<sup>12</sup> We sought to distinguish these mechanisms by examining the effect of solvent and substituents on the rate of reaction. To determine the effect of changing solvent on rate, the kinetics of the reaction of **1** with a 20-fold excess of di-*p*-tolyl disulfide at 15 °C in acetonitrile, benzene, and methylene chloride solution were examined. The second-order rate constants and their relative values are listed in Table 1. The rate increases by a factor of 9 in going from methylene chloride ( $\epsilon = 8.9$ ) to acetonitrile ( $\epsilon = 36.6$ ). The modest rate difference observed suggests that there is some degree of polarization in the transition state. However, the rate acceleration is small over this substantial solvent dielectric constant change compared to what is normally observed for reactions that involve full outer sphere electron transfer.<sup>13–15</sup>

The effect of changing substituents on the aryl ring of the disulfides was also examined. Rates were measured for the reaction of **1** with bis(2,6-dimethylphenyl), bis(*p*-methoxyphenyl), bis(*p*-(trifluoromethyl)phenyl), and diphenyl disulfide by using a 20-fold N excess of disulfide in methylene chloride at 15 °C (Table 1). The most important features of these data are (1) the absence of a linear trend, which reflects the similarity in rates of the hydrogen-, methyl-, and methoxy-substituted systems, and (2) the dramatic acceleration produced by attaching the more electron withdrawing CF<sub>3</sub> group to the ring. Methyl substituents attached at the ortho positions of the aryl ring slow the reaction rate by about an order of magnitude; in view of the small rate change caused by the *p*-methyl group, this is undoubtedly due to a steric effect.

In order to better interpret the data, a model study was undertaken in which an electron-transfer pathway is expected. The 19-electron complex cobaltocene, **3**, is known to react with alkyl halides through a rate-determining outer sphere electron-transfer pathway,<sup>16,17</sup> and its reaction with disulfides should be similar. Reaction of **3** with aromatic disulfides leads to the

corresponding cobaltocenium thiolate salt (eq 4), **4**. A kinetic study under conditions identical to those used in the reaction of **1** with disulfides (flooding in disulfide) was performed while the progress of the reaction was monitored by UV–vis spectroscopy.



All kinetic experiments demonstrated typical pseudo-first-order behavior and confirmed the operation of an electron-transfer mechanism. Rates were measured for the reaction of **3** with bis(2,6-dimethylphenyl), bis(*p*-methoxyphenyl), bis(*p*-(trifluoromethyl)phenyl), di-*p*-tolyl, and diphenyl disulfide by using a 20-fold N excess of disulfide in methylene chloride at 15 °C (Table 1). Electron-donating groups decrease the reaction rate relative to electron-neutral groups, while the strongly electron withdrawing *p*-trifluoromethyl group induces rate acceleration. If a purely outer sphere pathway was operative in both cases, then by examination of the reduction potential values for oxidation (**1**,  $E^\circ = -0.38$  V (NHE));<sup>10</sup> **3**,  $E^\circ = -0.95$  V (SCE)<sup>18</sup>) one would predict larger  $k_1$  values for the cobaltocenium reactions. The absolute rate constant values obtained for the reaction of **3** with disulfides are significantly less than those obtained for the reaction of **1** with disulfides. Also in contrast to the reaction of bis(2,6-dimethylphenyl) disulfide with **1**, methyl substituents attached at the ortho positions of the aryl ring do not slow the analogous reaction with **3**. The rate of the reaction of **3** with di-*p*-tolyl disulfide is significantly increased when the reaction is carried out in acetonitrile solvent. This rate enhancement, which is 110 times faster than in methylene chloride, contrasts with the 9-fold rate increase that is observed in the analogous reaction of **1** with di-*p*-tolyl disulfide.<sup>13–15,19</sup> These data clearly show that the reaction of **3** with disulfides occurs by outer sphere electron transfer, while the reaction of **1** with disulfides that have electron-neutral and electron-donating groups involves a transition state structure with a much smaller degree of charge separation.

For the reaction of **1** with electron-neutral and -donating substituents, the strong steric effect suggests a tight transition state, such as the one illustrated in Scheme 1 in which the cobalt center directly attacks one sulfur atom of the disulfide reactant. In the case of bis(*p*-(trifluoromethyl)phenyl) disulfide, the substituent effect data suggest that there may be a change to the outer sphere path.

In summary, careful studies of the kinetics of tantalum/cobalt radical **1** with organic disulfides have established that S—S bond activation can occur by either initial radical attack or outer sphere electron transfer. The mechanistic choice appears to be dependent on the electronic character of the disulfide, with electron-withdrawing groups inducing a change to the outer sphere mechanism.

**Acknowledgment.** We thank Dr. Frederick J. Hollander, Director of the UC Berkeley X-ray Diffraction Facility (CHEXRAY), for determination of the crystal structure of **2e**. We are grateful for support of this work from the National Science Foundation (Grant No. CHE-9113261).

**Supporting Information Available:** Spectroscopic and analytical data for complexes **2a–4**, tables containing complete crystal and data collection parameters, positional parameters with estimated standard deviations, and intramolecular distances and angles for compound **2e**, and representative kinetic data for the reactions of **1** and **3** with disulfides (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

(12) Andrieux, C. P.; Robert, M.; Saeva, F. D.; Saveant, J.-M. *J. Am. Chem. Soc.* **1994**, *116*, 7864.

(13) Typical rate enhancements for outer sphere electron-transfer reactions in going from CH<sub>2</sub>Cl<sub>2</sub> to CH<sub>3</sub>CN range from 35× to 1000× (see refs 14 and 15).

(14) Kosower, E. M.; Mohammad, M. *J. Am. Chem. Soc.* **1968**, *90*, 3271.

(15) Marzilli, L. G.; Marzilli, P. A.; Halpern, J. *J. Am. Chem. Soc.* **1970**, *92*, 5752.

(16) Herberich, G. E.; Schwarzer, J. *J. Organomet. Chem.* **1972**, *34*, C43.

(17) Herberich, G. E.; Carstensen, T.; Klein, W.; Schmidt, M. U. *Organometallics* **1993**, *12*, 1439.

(18) Koelle, U. *J. Organomet. Chem.* **1978**, *152*, 225.

(19) The reaction of **1** with bis(*p*-(trifluoromethyl)phenyl) disulfide in acetonitrile was too fast to measure accurately using standard methods. Stop-flow experiments were thwarted by the air sensitivity of the starting materials and products.