4.766 (1 H, d, J = 17.3 Hz, $OCH_BC{\equiv}C$), 3.967 (2 H, s, CH_2), 0.963 (9 H, s, $(CH_3)_3C$); mass spectrum, m/e 824.3773 (calcd for $C_{48}H_{56}O_{12}$, 824.3770).

Due to the decreased solubilities of **3a** and **3b**, the crude product was isolated after acidification by filtration (a dark brown solid). Extraction of this solid with hot acetone afforded a light colored solid which could be purified by trituration and crystallization. Thus obtained in 14% yield was **3a**: mp >250 °C (CH_2Cl_2); ^1H NMR δ ($CDCl_3$) 7.49 (1 H, s, ArH), 4.88 (2 H, br s, $OCH_2C{\equiv}C$), 3.901 (3 H, s, OCH_3). Anal. ($C_{32}H_{24}O_{12}$, m/e 600.1266) C, H; m/e 600.1268.

From **1b**, dimer **3b** was obtained in 15% yield, mp >250 °C dec from 230 °C; ^1H NMR δ ($CDCl_3$) 7.490 (1 H, s, ArH), 4.89 (2 H, unresolved AB q, $OCH_2C{\equiv}C$), 4.348 (2 H, q, J = 7 Hz, OCH_2CH_3), 1.339 (3 H, tr, J = 7 Hz, CH_3); ^1H NMR δ ($CDCl_3$, -7 °C) 5.005 (1 H, d, J = 17 Hz, $OCH_AC{\equiv}C$), 4.813 (0.6 H) and 4.773 (0.4 H) (d, J = 17 Hz, $OCH_BC{\equiv}C$); mass spectrum, m/e 656.1891 (calcd for $C_{36}H_{22}O_{12}$, 656.1892).

Preparation of Mixed Dimer 5c. Slow addition of a solution containing 0.725 g (2 mM) of propyl ester **1c** and 1.87 g (10 mM) of bis(propargyloxy)benzene (**1i**) in 150 mL pyridine to a solution of 25 g (125 mM) of copper acetate in 440 mL of pyridine at 45 °C gave after workup a dark brown solid. Extraction with acetone afforded 2.6 g of acetone-soluble material. Chromatography of this crude product afforded 0.26 g of a light brown oil from which could be isolated by crystallization 55 mg (10% yield) of **5c** as colorless needles: mp 218 °C dec; ^1H NMR δ 7.498 (1 H, s, Ar'H), 6.896 (2 H, s, ArH), 4.978 (1 H, d, J = 17.6 Hz, $Ar'OCH_A$), 4.767 (1 H, d, J = 17.6 Hz, $Zr'OCH_B$), 4.729 (2 H, s, $ArOCH_2$), 4.267 (1 H, d of t, J = 11, 7 Hz, $COOCH_A$), 4.217 (1 H, d of t, J = 11, 7 Hz, $COOCH_B$), 1.7 (2 H, sextet, J = 7 Hz, $CH_2CH_2CH_3$), 0.977 (3 H, t, J = 7 Hz, CH_3); mass spectrum, m/e 540.1786 (calcd for $C_{32}H_{28}O_8$, 540.1782).

Hexadecahydro Derivatives (4a-f). Each dimer (**3** series) was catalytically hydrogenated (10% Pd/C, EtAc) to the corresponding hexadecahydro derivative (**4** series).

4a: mp 170.5-171.5 °C (EtAc-hexane); ^1H NMR δ ($CDCl_3$) 7.005 (1 H, s, ArH), 4.116 (1 H, dd, J = 7.4, 9.2 Hz, $ArOCH_A$), 3.880 (1 H, dd, J = 7.4, 4.4 Hz, $ArOCH_B$), 3.888 (3 H, s, CH_3), 1.5-2.0 (4 H, m, CH_2). Anal. ($C_{32}H_{42}O_{12}$, m/e 616.2517) C, H; m/e 616.2519.

4b: mp 140-142 °C (EtAc-hexane); ^1H NMR δ ($CDCl_3$) 7.000 (1 H, s, ArH), 4.380 and 4.333 (2 H, q of q, J = 11.1, 7.4 Hz, $COOCH_{A,B}CH_3$),[40] 4.146 (1 H, dd, J = 12.5, 8.8 Hz, $ArOCH_A$), 3.881 (1 H, dd, J = 8.8, 3.7 Hz, $ArOCH_B$), 1.5-2.0 (4 H, m, CH_2), 1.404 (3 H, t, J = 7 Hz, CH_3); mass spectrum, m/e 672.3143 (calcd for $C_{36}H_{48}O_{12}$, 672.3145).

4c: mp 102.5-104 °C (hexane); ^1H NMR δ ($CDCl_3$) 7.018 (1 H, s, ArH), 4.261 and 4.226 (2 H, q of t, J = 10.7, 7 Hz, $COOCH_{A,B}$), 4.129 (1 H, dd, J = 8, 9 Hz, $ArOCH_A$), 3.876 (1 H, m, $ArOCH_B$), 1.78 (2 H, hex, J = 7 Hz, $CH_2CH_2CH_3$), 1.5-2.0 (4 H, m, CH_2), 1.022 (3 H, t, J = 7 Hz, CH_3). Anal. ($C_{40}H_{56}O_{12}$, m/e 728.3768) C, H; m/e 728.3769.

4d, a wax: ^1H NMR δ ($CDCl_3$) 7.005 (1 H, s, ArH), 4.26 (2 H, m, $COOCH_2$), 3.87 and 4.11 (2 H, m, $ArOCH_2$), 1.3-2.0 (20 H, m, CH_2), 0.882 (3 H, t, CH_3).

4e (isomer **4e-A**): mp 83.5-84.5 °C (hexane); ^1H NMR δ ($CDCl_3$) 7.280 (1 H, s, ArH), 3.9-4.1 (4 H, m, $ArOCH_2$ and $COOCH_2$), 2.031 (1 H, nonet, J = 6.6 Hz, CH_2CHMe_2), 1.4-1.8 (4 H, m, CH_2), 0.995 (6 H, d, J = 6.6 Hz, CH_3); mass spectrum, m/e 784.4395 (calcd for $C_{44}H_{64}O_{12}$, 784.4394).

4f (from isomer **3f-A**): mp 163.5-165.5 °C (hexane); ^1H NMR δ ($CDCl_3$) 7.319 (1 H, s, ArH), 4.059 (2 H, t, J = 5.6 Hz, $ArOCH_2$), 3.990 (1 H, d, J = 11 Hz, $COOCH_A$), 3.917 (1 H, d, J = 11 Hz, $COOCH_B$), 1.75-1.2 (4 H, m, CH_2), 0.999 (9 H, s, $(CH_3)_3C$); mass spectrum, m/e 840.5021 (calcd for $C_{48}H_{72}O_{12}$, 840.5020).

Registry No. **1a**, 84119-03-9; **1b**, 84119-02-8; **1c**, 84119-05-1; **1d**, 84119-06-2; **1e**, 84119-07-3; **1f**, 84119-08-4; **1g**, 84119-04-0; **1h**, 84119-09-5; **1i**, 34596-36-6; **2a**, 84119-15-3; **2b**, 84119-10-8; **2c**, 84119-11-9; **2d**, 84119-12-0; **2e**, 84119-13-1; **2f**, 84119-14-2; **3a**, 84130-28-9; *syn*-**3b**, 84118-93-4; *anti*-**3b**, 84171-55-1; *syn*-**3c**, 84172-82-7; *anti*-**3c**, 84119-16-4; *syn*-**3d**, 84118-95-6; *anti*-**3d**, 84171-56-2; *syn*-**3e**, 84118-96-7; *anti*-**3e**, 84171-53-9; *syn*-**3f**, 84118-97-8; *anti*-**3f**, 84171-54-0; **3g**, 84119-00-6; **4a**, 84118-92-3; **4b**, 84130-29-0; **4c**, 84118-94-5; **4d**, 84130-30-3; **4e**, 84130-31-4; **4f**, 84118-98-9; **4g**, 84119-01-7; **5c**, 84118-99-0; diethyl 2,5-dihydroxyterephthalate, 5870-38-2; propargyl bromide, 106-96-7; hydroquinone, 123-31-9.

(40) $\Delta\nu_{AB}$ = 6.9 ± 0.4 Hz; A:B inner:outer intensity ratio = 12 ± 0.7.

Reactivity of Coordinated Disulfides. 1. Nucleophilic Cleavage of the Sulfur-Sulfur Bond

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Abstract: The rates of nucleophilic cleavage of the activated sulfur-sulfur bond in $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes have been measured in $(H/Li)ClO_4$ aqueous media (μ = 1.00 M) as a function of $[H^+]$, temperature, attacking nucleophile (OH^- and thiols), and R group (R = methyl, ethyl, isopropyl, *tert*-butyl, and valinyl). For all reactions, except base hydrolysis of the *tert*-butyl complex, heterolytic sulfur-sulfur bond cleavage leads to the thiolato complex $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$ and organic products derived from the pendant RS^+ moiety. The *tert*-butyl complex decomposes primarily by S_N1cB cobalt-sulfur bond fission. For all reactions, except the base hydrolysis of the valinyl complex, the observed rate law is rate = k_2[disulfide][nucleophile], consistent with a simple S_N2 mechanism. Decomposition of the valinyl complex is apparently complicated by the presence of diastereoisomers that react at different specific rates. In the thiol reactions, $k_2 = a + b/(H^+)$, indicating that both free thiol (RSH) and dissociated thiolate anion (RS^-) attack the coordinated disulfide linkage. For the reaction of 2-mercaptoethanol with the complex having R = methyl at 25 °C, a = 1.22 ± 0.05 M^{-1} s^{-1} (ΔH_a^* = 13.4 ± 0.1 kcal/mol, ΔS_a^* = -13.2 ± 0.4 eu) and b = 0.32 ± 0.02 s^{-1} (ΔH_b^* = 6.4 ± 0.1 kcal/mol, ΔS_b^* = -39.3 ± 0.4 eu), and for the reaction of OH^- with this complex k_2 = (1.70 ± 0.04) × 10^6 M^{-1} s^{-1} (ΔH^* = 19.0 ± 0.4 kcal/mol, ΔS^* = 37 ± 1 eu). In accordance with the S_N2 mechanism, the observed reaction rates for those complexes with simple alkyl R groups depend mainly on the steric bulk of the R group (k_2 decreasing by ca. 10^5 on going from R = CH_3 to $C(CH_3)_3$) and the nucleophilicity of the attacking moiety ($RS^- > OH^- > RSH$). Comparisons with literature data show that the specific rates of sulfur-sulfur bond cleavage in disulfides activated by coordination to cobalt(III) are 10^{10}-10^{11} times greater than those of comparable noncoordinated disulfides.

Cleavage of the sulfur-sulfur bond in disulfides by nucleophiles has been postulated to occur by a variety of mechanisms, the most important of which are as follows: (1) direct S_N2 attack on the sulfur-sulfur bond (eq 1),[2]

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$$RSSR' + Nu^- \rightarrow RSNu + R'S^- \quad (1)$$

(2) initial abstraction of a proton from an α-carbon atom followed by elimination (base hydrolysis only)[2c] (eq 2),

$$RCH_2SSR' + OH^- \rightarrow (RCH{-}SS{-}R')^- \rightarrow RCH{=}S + R'S^- \quad (2)$$

(3) β elimination (base hydrolysis only)[2c,3] (eq 3),

$$RCH_2CH_2SSR' + OH^- \rightarrow (RCH{-}CH_2S{-}SR') \rightarrow RCH{=}CH_2 + R'SS^- \quad (3)$$

(4) electrophile-assisted cleavage of disulfides by nucleophiles[4] (eq 4).

$$RSSR' + E^+ \rightarrow (RSS(E)R')^+ + Nu^- \rightarrow RSNu + R'SE \quad (4)$$

In this last mechanism the electrophile E^+ can be a metal ion, and the prevalence of metal–sulfur interactions in biological systems gives this situation special significance. However, with only one exception, there have been no systematic studies of *metal-assisted* nucleophilic cleavage of disulfides.[4c,d]

The most commonly encountered metals that are active in promoting sulfur–sulfur bond cleavage are Ag^+[5] and Hg^{2+}.[4c,d,6] Silver(I) ion is used in the synthesis of sulfenamides from disulfides (mechanism 4, Nu = amine, $E^+ = Ag^+$).[5] In the single reported systematic study of mechanism 4, methylmercury(II) catalysis of the cleavage of dimethyl disulfide by triethyl phosphite ($E^+ = CH_3Hg^+$, Nu = $P(OCH_2CH_3)_3$) has been studied.[4c,d] This reaction was found to be first order in each of disulfide, methylmercury, and triethyl phosphite, but the presumed disulfide–electrophile intermediate of mechanism 4 could not be isolated and the specific rate of nucleophilic attack on this intermediate could not be determined. Thus there is no extant measure of the extent by which coordination to a metal ion promotes nucleophilic sulfur–sulfur bond scission in organic disulfides.

In a recent paper[7] we reported the synthesis and characterization of a series of disulfide–cobalt(III) complexes suitable for investigation of mechanism 4, i.e., $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$. The metal–sulfur bond of these complexes is inert to substitution, but the sulfur–sulfur bond is activated toward nucleophilic cleavage by virtue of being bonded to the strong electrophile Co(III). Thus these complexes constitute substitution-inert analogues to the reaction intermediate depicted in mechanism 4 (E^+ = Co(III)) and allow a direct determination of the rate of metal-activated, nucleophilic sulfur–sulfur bond cleavage. In this paper we report on the kinetics and mechanism of the reaction of the disulfide–cobalt(III) complexes with the nucleophiles OH^- and RSH (thiols).

Experimental Section

Materials. Common laboratory chemicals were of reagent grade unless otherwise noted. Triply distilled, charcoal-filtered water and doubly vacuum-distilled perchloric acid (70–72%, G. F. Smith) were used in all kinetic experiments. Lithium perchlorate was prepared from Baker Ultrex lithium carbonate as previously described.[8] Succinic acid was purified by three crystallizations, the last being from triply distilled water. A stock solution of acetic acid was prepared by diluting 100 mL of Ultrex (Baker) glacial acetic acid to 1 L; the concentration of acetic acid was determined by titration with standard NaOH to a phenolphthalein end point. A stock acetate buffer solution with $[LiOOCCH_3] = [HOOCCH_3] = 0.500$ M was prepared from this acetic acid stock solution and Ultrex lithium carbonate.[9] Stock succinate buffers were prepared similarly; these stock solutions were mixed with varying amounts of 1.00 M $HClO_4$ to give buffers ranging in pH from $\simeq 4.2$ to $\simeq 6.5$.

Sephadex SP C-25 cation-exchange resin (Pharmacia) was cleaned by methods described elsewhere[9] and then converted to the lithium form by slurrying with a 2 M solution of lithium perchlorate for 15 min; after being rinsed with water until the washings were free of perchlorate, the resin was then slurried with a minimum amount of kinetic grade 1 M $LiClO_4$ solution for 5 min. The resin was then washed exhaustively with triply distilled water and stored at 5 °C.

Commercial cysteine hydrochloride monohydrate was recrystallized 3 times from hot 20% hydrochloric acid and then dried at 50 °C (under vacuum, over P_2O_5) to yield the anhydrous compound[10] which was stored under vacuum (over P_2O_5). This material was used as a primary standard for the thiol analysis described below. Commercial 2-mercaptoethanol and 3-mercaptopropionic acid were vacuum-distilled and stored under nitrogen. Cysteamine hydrochloride (Aldrich), sodium 2-mercaptoethanesulfonate (Sigma), 4-mercaptopyridine (Aldrich), and D-penicillamine (Aldrich) were used without further purification. 2,2′-Dithiobipyridine (Aldrich) was used as received.

Stock solutions of 2,2′-dithiobipyridine (44 mg diluted to 10.0 mL with ethanol) were freshly prepared each day. Citrate buffer (0.2 M, pH 5.0) was prepared by adding 42.0 g of citric acid monohydrate to 200 mL of 2 M NaOH and diluting to 1 L. Solutions of thiols were freshly prepared each day in deaerated 0.01 M $HClO_4$ and were then standardized against cysteine hydrochloride by the procedure given below.

The disulfide complexes, $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$, were synthesized as previously described[7] and before being used in kinetic experiments were purified by either or both of two methods. (A) For R = isopropyl and *tert*-butyl, solid salts could not be isolated. Therefore, before use these disulfide complexes were charged on Sephadex C-25 resin (Li^+ form, vide supra), the column was rinsed with kinetic quality 0.15 M $LiClO_4$ ($[H^+] = 1 \times 10^{-3}$ M) to remove any $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$ (hereafter referred to as $Cocys^{2+}$), and then the disulfide complex was eluted with 1.0 M $LiClO_4$ ($[H^+] = 5 \times 10^{-3}$ M). These stock solutions of disulfide complexes were stored at 5 °C and repurified every 2 weeks to remove any $Cocys^{2+}$ formed by the decomposition reaction.[7] (B) For R = CH_3, CH_2CH_3 and $C(CH_3)_2CH(NH_2)COOH$, solid salts could be isolated and these salts were recrystallized 3 times, the last crystallization being from 0.01 M $HClO_4$. The solids were dried in air and stored in a desiccator at 5 °C. No difference in the rates of reaction were noticed with solutions derived from solids (method B) or solutions purified by ion-exchange chromatography (method A). Spectral data for the complex with R = $C(CH_3)_2CH(NH_2)COOH$ are as follows: Vis–UV 0.01 M $HClO_4$ λ_{max} (ϵ) in nm and M^{-1} cm^{-1} 494 (153), 320 (2740) sh, 282 (7380); ^1H NMR, δ 1.67 (CH_3), 2.00 (CH_3), 4.31 (CH) and 1.77 (CH_3), 1.86 (CH_3), 4.41 (CH). Spectral data for the other complexes have been previously reported.[7]

Thiol Analysis. The concentrations of free thiol (RSH) in aqueous media were spectrophotometrically determined by using excess 2,2′-dithiobipyridine which is reduced by RSH to 2-thiopyridone having a maximum absorbance at 343 nm.[11] A thiol solution of unknown concentration was quantitatively diluted with water until it was ca. 10^{-3} M in RSH; 1.00 mL of this solution and 0.1 mL of 2,2′-dithiobipyridine solution were combined and diluted to 10.0 mL with 0.2 M citrate buffer. Since some thiols react slowly with 2,2′-dithiobipyridine at pH 5.0,[12] this reaction solution was allowed to stand for 2 h before the absorbance at 343 nm was determined in a 1.00-cm cell. Known solutions of primary standard cysteine hydrochloride, prepared by weight, were used to construct a calibration plot; this plot of absorbance vs. [RSH] was linear over the concentration range from 10^{-5}–10^{-4} M, yielding a slope corresponding to $\epsilon_{343} = 8088 \pm 27$ M^{-1} cm^{-1}.

Equipment. ^1H NMR spectra were recorded on a Varian T-60 instrument in DCl/D_2O, using DSS as an internal standard. pH readings were obtained with a Beckman Research pH meter equipped with a Sensorex combination electrode. Visible–UV spectra were recorded on a Cary 210 spectrophotometer at ambient temperature. All kinetic experiments were conducted on a Cary 118B recording spectrophotometer serviced by a Haake FK-2 constant-temperature bath and equipped with a Hewlett-Packard 5105a thermal printer. Temperature was monitored

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with a USC 581 digital thermometer, which had been calibrated against an NBS-certified mercury thermometer, and was maintained to ±0.1 °C. A UNC-Chem microcomputer, interfaced with the Cary 118B, collected and stored the raw A_t–time data and also subjected this data to a preliminary linear least-squares analysis as ln $(A_t - A_\infty)$ vs. time. All other computer calculations were performed on the AMDAHL 470/V6-II system located at the University of Cincinnati.

Kinetic Measurements and Calculations. For the reactions with thiols, kinetic measurements were conducted in aqueous media at ionic strength 1.00 ± 0.01 M (H/$LiClO_4$), the thiol being present in a pseudo-first-order excess. For the reactions with base, both succinate and acetate buffer systems (μ = 1.00 ± 0.01 M maintained with $LiClO_4$) were used for each complex. No significant rate differences were observed when varying the type or concentration of buffer. The pH of the reaction solution was obtained before adding the cobalt disulfide complex (pH_i) and then after the reaction was complete (pH_f) to ensure that the capacity of the buffer was not exceeded during the reaction. For reactions conducted at temperatures other than 25 °C, the solutions were allowed to equilibrate at room temperature before the pH was measured. Any experiment wherein $|pH_i - pH_f| > 0.25$ was discarded. The average of pH_i and pH_f was taken as the observed pH of the reaction and this value was then converted to −log [H^+] by adding 0.417 pH units to account for the pH measurement being conducted at 1.00 M ionic strength.[9] Reactions were initiated by addition of a temperature equilibrated aliquot of cobalt complex in 1.00 M $LiClO_4$ to a temperature equilibrated solution of thiol or buffer.

Kinetics were monitored for more than 99% of the reaction, infinite time absorbance readings (A_∞) being obtained after this point. Absorbance changes were monitored at the characteristic 340-nm peak of the coordinated disulfides,[7] at the characteristic 282-nm ligand-to-metal charge-transfer band present in the $Cocys^{2+}$ product,[13] or at the 600-nm shoulder characteristic of this product.[13] The initial concentration of cobalt complex was in the range 5–10 mM when monitoring at 600 nm and 0.1–0.4 mM when monitoring at 340 or 280 nm. Observed rate parameters were not dependent on the monitoring wavelength.

Values of k_{obsd} (as well as its associated standard deviation, $\sigma_{k_{obsd}}$), A_0 and A_∞ which best fit the observed A_t–t data within the first-order rate expression

$$A_t = A_\infty - (A_\infty - A_0)e^{-k_{obsd}t} \quad (5)$$

were calculated with standard nonlinear least-squares techniques.[14] The A_t–t data for the reaction of OH^- with the complex where R = $C(CH_3)_2CH(NH_2)COOH$ were treated similarly, using the expression

$$A_t = A_\infty - (A_\infty - A_0)e^{-k_{obsd}t} - (A_\infty - A_0')e^{-k_{obsd}'t} \quad (6)$$

Values of the second-order rate parameter k_2 (and its associated standard deviation, σ_{k_2}) were calculated by linear least-squares analysis of the k_{obsd}–reagent data, each value of k_{obsd} being weighted by $1/\sigma_{k_{obsd}}^2$. In the weighted nonlinear least-squares calculation of activation parameters,[14] each individual k_2 value was weighted by $1/\sigma_{k_2}^2$. The errors associated with ΔH^* and ΔS^* values are the standard deviations derived from these calculations.

Product Analysis. (1) Base Hydrolysis: After 4 half-lives the hydrolysis reactions were quenched by adding $HClO_4$ to bring the pH to ca. 1.0. The inorganic reaction products were separated by column chromatography on Sephadex SP C-25 resin (Na^+ form) and the yield of each product was determined by analysis of each collected band for total cobalt content. Total cobalt analyses were conducted with a modified Kitson procedure.[15] The identity of the species comprising each band was determined by visible–UV spectrophotometry (including determination of extinction coefficients) and, in some cases, by analysis of the band for both total sulfur and total cobalt content. The organic reaction products were not identified, although in the case where R = phenyl, diphenyl disulfide precipitated from the reaction solution (mp = 60–61 °C; lit.[16] mp 61 °C).

(2) Thiol attack: With 4-mercaptopyridine as the attacking nucleophile, after 4 half-lives the reaction was quenched by a 50-fold dilution with cold water. This diluted solution was then subject to ion-exchange chromatography and the inorganic products separated as above. The organic products were separated by thin-layer chromatography on reversed-phase plates containing a fluorescent indicator (Whatman $MKC_{18}F$), using a 90% methanol/water mobile phase. Product species were visualized with UV irradiation.

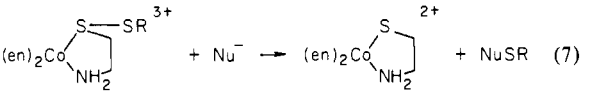
Table II. Derived Second-Order Rate Constants and Activation Parameters Governing the Base Hydrolysis of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ Complexes

R	k_2,[a] s^{-1} M^{-1}	ΔH^*, kcal/mol	ΔS^*, eu
CH_3	(1.70 ± 0.04) × 10^6	19.9 ± 0.4	37 ± 1
CH_2CH_3	(5.55 ± 0.13) × 10^5	19.2 ± 1.0	32 ± 3
$CH(CH_3)_2$	(1.98 ± 0.12) × 10^4	24.1 ± 0.7	42 ± 2

[a] Conditions: 25 °C, μ = 1.00 M $LiClO_4$.

Results

Stoichiometry. For all reactions save one, the sulfur–sulfur bond of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes is cleaved by the nucleophiles OH^- and RSH to yield >95% $Cocys^{2+}$ and organic products according to eq 7. The single exception is the base



(7)

hydrolysis of the complex with R = *tert*-butyl which is complicated by Co–S bond cleavage. Time-dependent visible–UV spectra from 650–260 nm show that for OH^- and RSH attack on the complexes with R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$ (vide infra for base hydrolysis), and $C(CH_3)_2CH(NH_2)COOH$ (only base hydrolysis was investigated) at least two isosbestic points are maintained throughout the reaction. The $Cocys^{2+}$ product is readily identified by its characteristic visible–UV spectrum[13] and ion-exchange behavior. The identities of the noncoordinated, sulfur-containing products resulting from the base hydrolysis reactions were not determined due to the inherent instability of noncoordinated sulfenic acids (RSOH).[5] When 4-mercaptopyridine is the attacking nucleophile, TLC analysis of the product mixture shows three distinct spots which are identified as $Cocys^{2+}$, 4-pyridylalkyl disulfide, and unreacted excess 4-mercaptopyridine. The observed R_f values are as follows: $Cocys^{2+}$, 0; 4-pyridylalkyl disulfide, 0.58 (methyl), 0.53 (ethyl), 0.48 (isopropyl), 0.43 (*tert*-butyl); 4-mercaptopyridine, 0.93.

Kinetics of Base Hydrolysis. For all $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes except that with R = $C(CH_3)_2CH(NH_2)COOH$, plots of ln $(A_t - A_\infty)$ vs. time are linear and the A_t–time data are adequately described by eq 5. All applicable plots of k_{obsd} vs. [OH^-] are linear with no significant intercept, and thus the rate law governing base hydrolysis is

$$-d[\text{disulfide complex}]/dt = k_2[OH^-][\text{disulfide complex}] \quad (8)$$

Table I[17] lists the observed pseudo-first-order rate constants, k_{obsd}, and the derived second-order rate constants, k_2, as a function of temperature, ionic strength, buffer concentration, and buffer type; each value of k_2 is derived from at least three independently measured values of k_{obsd}. These data, and the derived activation parameters, are summarized in Table II. For the two complexes investigated (R = CH_3 and CH_2CH_3), k_2 increases when the ionic strength is lowered from 1.0 to 0.10 M.

For R = $C(CH_3)_2CH(NH_2)COOH$ plots of ln $(A_t - A_\infty)$ vs. time are not linear. However, the A_t–time data are adequately described by eq 6 and the resulting values of k_{obsd}, k_{obsd}', k_2, and k_2' are listed in Table III. The rate of decomposition of the complex with R = C_6H_5 is so rapid that only a lower limit of k_2 > 10^9 M^{-1} s^{-1} (25 °C, 0.1 M $HClO_4$) can be obtained.

Kinetics of Thiol Attack. For all complexes plots of ln $(A_t - A_\infty)$ vs. time are linear and the A_t–time data are adequately described by eq 5. All plots of k_{obsd} vs. [RSH] are linear with no significant intercept, and thus the rate law governing thiol attack is

$$-d[\text{disulfide complex}]/dt = k_2[RSH][\text{disulfide complex}] \quad (9)$$

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Table III. Observed First-Order and Derived Second-Order Rate Constants for the Base Hydrolysis of $[(en)_2Co(S(SC(CH_3)_2CH(NH_3)CO_2H)CH_2CH_2NH_2)]^{4+}$ [a]

buffer	conc, M	t, °C	$[OH^-]_{av}$, [b] M	$k_{obsd} \times 10^3$, s^{-1}	k_2 [e] $\times 10^{-6}$, M^{-1} s^{-1}	$k_{obsd}' \times 10^3$, s^{-1}	k_2' [e] $\times 10^{-6}$, M^{-1} s^{-1}
S	5.0×10^{-2}	25	3.98×10^{-10}	15.6 ± 0.9*	40.1 ± 2.1	1.95 ± 0.09*	6.32 ± 0.75
			1.90×10^{-9}	77.7 ± 0.4*		10.0 ± 0.8*	
			6.44×10^{-10}	35.9 ± 1.9*		46.2 ± 0.27*	
			2.84×10^{-9}	108 ± 50*		17.0 ± 0.08*	
			2.02×10^{-9}	102 ± 4[c]	50.5[c]	14.0 ± 0.9[c]	6.93[c]
A	5.0×10^{-2}		2.37×10^{-10}	12.5 ± 0.7	52.7	1.33 ± 0.05	5.61
S	5.0×10^{-2}		6.47×10^{-10}	75.7 ± 7.2[d]	117[d]	10.8 ± 1.5[d]	16.7[d]
			3.84×10^{-10}	51.4 ± 4.2[d]	134[d]	7.78 ± 0.53[d]	20.3[d]
S	5.0×10^{-2}	35	1.99×10^{-9}	121 ± 8	60.8	24.1 ± 1.5	12.1
			7.15×10^{-10}	83.3 ± 4.4	116	15.4 ± 0.7	21.5
			2.44×10^{-10}	23.9 ± 0.9	97.9	4.20 ± 0.12	17.2
S	5.0×10^{-2}	45	6.37×10^{-10}	261 ± 49	409	44.5 ± 3.0	70.0
			2.01×10^{-10}	110 ± 9	547	18.7 ± 1.0	93.0

[a] Conditions: $[Co] = 3 \times 10^{-4}$ M; $\mu = 1.00 \pm 0.02$ M $LiClO_4$ unless otherwise noted; $\lambda = 330$ nm unless otherwise noted. [b] $-\log [H^+] = pH_{av} + 0.417$, where $pH_{av} = (pH_i + pH_f)/2$. [c] $\mu = 0.10$ M. [d] $\lambda = 283$ nm. [e] Values calculated at a particular temperature with only the experiments signified by asterisks.

Table VI. Derived Rate Parameters Governing the Reaction of $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$ with Thiols: Rate = k_2[Complex][Thiol], $k_2 = a + b/[H^+]$ [a]

no.	thiol	pK_a	$a = k^{RSH}$, M^{-1} s^{-1}	$b = K_a k^{RS^-}$, s^{-1}	k^{RS^-} [f], M^{-1} s^{-1}
1	2-mercaptoethanol	9.72[b]	1.22 ± 0.05	0.320 ± 0.018	1.68×10^9
2	3-mercaptopropionic acid	10.84[b]	1.40 ± 0.07	0.453 ± 0.020	3.13×10^{10}
3	2-mercaptoethanesulfonic acid	9.37[c]	1.27 ± 0.02	1.04 ± 0.01	2.44×10^9
4	cysteamine	8.23[b]	0.74 ± 0.05	1.18 ± 0.03	2.00×10^8
5	L-cysteine	8.48[d]	3.24 ± 0.49	5.19 ± 0.19	1.57×10^9
6	D-penicillamine	7.97[e]	1.09 ± 0.12	2.52 ± 0.07	2.35×10^8

[a] Conditions: $\mu = 1.00 \pm 0.01$ M $LiClO_4$, $t = 25$ °C. [b] Reference 18. [c] Reference 19. [d] Reference 20. [e] Reference 21. [f] $k^{RS^-} = b/K_a$. Standard deviations are not calculated because of the uncertainty in pK_a values.

Table VII. Derived Rate Constants and Activation Parameters Governing the Reaction of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ Complexes with 2-Mercaptoethanol: Rate = k_2[Complex][Thiol], $k_2 = a + b/[H^+]$ [a]

R	t, °C	$a = k^{RSH}$, M^{-1} s^{-1}	$b = K_a k^{RS^-}$, s^{-1}	k^{RS^-} [b], M^{-1} s^{-1}
CH_3	15.0 ± 0.1	0.543 ± 0.021	0.202 ± 0.006	
	25.0 ± 0.1	1.22 ± 0.05	0.320 ± 0.020	1.68×10^9
	35.0 ± 0.1	2.60 ± 0.13	0.444 ± 0.032	
	45.0 ± 0.2	5.55 ± 0.38	0.640 ± 0.113	
CH_2CH_3	25.0 ± 0.1	0.610 ± 0.039	0.165 ± 0.007	8.66×10^8
$CH(CH_3)_2$	25.0 ± 0.1	$(4.44 \pm 0.15) \times 10^{-2}$	$(1.76 \pm 0.06) \times 10^{-2}$	9.23×10^7
$C(CH_3)_3$	25.0 ± 0.1	$(2.70 \pm 0.06) \times 10^{-5}$	$(7.76 \pm 0.17) \times 10^{-6}$	4.07×10^4
	33.6 ± 0.2	$(7.78 \pm 0.42) \times 10^{-5}$	$(1.72 \pm 0.15) \times 10^{-5}$	
	45.3 ± 0.2	$(2.05 \pm 0.27) \times 10^{-4}$	$(4.13 \pm 0.70) \times 10^{-5}$	
	54.9 ± 0.3	$(4.28 \pm 0.50) \times 10^{-4}$	$(8.97 \pm 1.80) \times 10^{-5}$	

R	ΔH_a^* [c]	ΔS_a^* [c]	ΔH_b^*	ΔS_b^*	$\Delta H_{RS^-}^*$ [b]	$\Delta S_{RS^-}^*$ [b]
CH_3	13.4 ± 0.1	−13.2 ± 0.4	6.44 ± 0.12	−39.3 ± 0.4	0.2	−16
$C(CH_3)_3$	18.4 ± 1.3	−17.8 ± 4.3	15.4 ± 0.4	−30.3 ± 1.2	9.2	−7

[a] Conditons: $\mu = 1.00 \pm 0.01$ M $LiClO_4$. [b] $k^{RS^-} = b/K_a$. Standard deviations are not calculated because of the uncertainty in pK_a values. [c] ΔH^* in kcal/mol, ΔS^* in eu.

Table IV[17] lists the observed pseudo-first-order rate constants, k_{obsd}, and the derived second-order rate constants, k_2, for attack on the complex with R = CH_3 by several thiols (2-mercaptoethanol, 3-mercaptopropionic acid, 2-mercaptoethanesulfonic acid, cysteamine, L-cysteine, and D-penicillamine) as a function of acid and thiol concentration. Table V[17] lists the observed pseudo-first-order rate constants governing attack by 2-mercaptoethanol on several complexes (R = CH_3, CH_2CH_3, $CH(CH_3)_2$, and $C(CH_3)_3$) as a function of acid concentration and temperature. For all systems studied, plots of k_2 vs. $[H^+]^{-1}$ are linear over the range $[H^+] = 0.10$–1.0 M, and thus

$$k_2 = a + b/[H^+] \quad (10)$$

Values of a and b, derived from linear least-squares analyses, for the attack of several thiols on $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$, along with literature values of the acid dissociation constants (K_a) of these thiols, are given in Table VI. Equivalent data for the attack of 2-mercaptoethanol on several complexes are given in Table VII. Activation parameters for attack of 2-mercaptoethanol on the complexes with R = CH_3 and $C(CH_3)_3$ are also shown in Table VII.

Discussion

Base Hydrolysis. Except for the case when R = *tert*-butyl, the base hydrolysis of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes is adequately described by S_N2 attack of OH^- at the exo sulfur atom of the coordinated disulfide. This attack quantitatively yields coordinated thiol, i.e., $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$, and pre-

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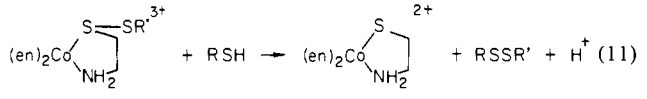
sumably also yields the noncoordinated RS^+ derivative RSOH. Free sulfenic acids, RSOH, are notoriously unstable species,[5] decomposing to give a variety of products including RSSR. Decomposition of the phenyl complex $[(en)_2Co(S(SC_6H_5)CH_2CH_2NH_2)]^{3+}$ does indeed yield $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$ and diphenyl disulfide. Attack by carboxylate does not appear to be competitive since in the pH range 4.2–6.5 the rate of base hydrolysis is independent of buffer type (acetate or succinate) and buffer concentration.

As expected for S_N2 attack of OH^- on the exo sulfur atom of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$, the rate of reaction decreases markedly with increasing steric bulk of the R group. Thus, varying R from CH_3 to $CH(CH_3)_2$ decreases the rate by a factor of 85, this steric effect being manifested predominantly in a larger ΔH^* for the $CH(CH_3)_2$ derivative (Table II). When R is *tert*-butyl, steric hindrance reduces the rate of sulfur–sulfur bond cleavage to the point that S_N1cB Co–S bond cleavage becomes competitive. Indeed, for most of the conditions investigated in this work $[(en)_2Co(S(SC(CH_3)_3)CH_2CH_2NH_2)]^{3+}$ decomposes predominantly by Co–S bond fission rather than by S–S bond fission; the details of this disparate process will be the subject of a future publication. Also as expected for S_N2 attack, resonance stabilization of the transition state causes the phenyl complex to react much more rapidly than any of the alkyl complexes; $k_2^{Ph} > 10^9$ M^{-1} s^{-1}, relative to $k_2^{Me} = 2.2 \times 10^6$ M^{-1} s^{-1} (25 °C, μ = 0.1 M). Formation of the transition state from oppositely charged reactants is reflected in higher reaction rates at lower ionic strengths (Table I) and positive activation entropies (Table II).

When $R = C(CH_3)_2CH(NH_2)COOH$, base hydrolysis proceeds normally in that $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$ is quantitatively produced and the time-dependent visible–UV spectra exhibit three isosbestic points. However, the reaction does not follow first-order kinetics. Rather, the kinetics are adequately described by concurrent first-order reactions (eq 6). This observation can be understood in light of the ^1H NMR spectrum of this penicillamine complex: the methyl region (δ 2.0–1.4) exhibits four methyl signals, two large and two small; the methine region (ca. δ 4.3) exhibits two peaks, one large and one small. These data indicate the presence of two chemically different methine protons, and two chemically different CH_3 pairs. Thus, the synthesis of $[(en)_2Co(S(SC(CH_3)_2CH(NH_2)COOH)CH_2CH_2NH_2)]^{3+}$ from *dl*-penicillamine and racemic $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$ leads to at least one, and probably two, diastereoisomeric pairs. The observed kinetic behavior can be accounted for by these diastereomers having different rates of reaction with OH^-. Consistent with this interpretation, the ratio of peak heights of the two types of methyl and methine proton signals (ca. 10/1) corresponds approximately to the ratio of A_0 and A_0' values resulting from kinetic analysis within eq 6. Within this interpretation, both forms of the penicillamine complex react faster than does the methyl complex, implying effective anchimeric assistance by the pendant COOH and/or NH_2 groups.

Thiol Attack. Cleavage of the sulfur–sulfur bond in $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes by water-soluble thiols is adequately described by S_N2 attack of the thiol at the exo sulfur atom of the coordinated disulfide.



This attack quantitatively yields coordinated thiol, i.e., $[(en)_2Co(SCH_2CH_2NH_2)]^{2+}$, and also yields the noncoordinated $R'S^+$ derivative RSSR'. This initial mixed disulfide product could in principle react further by thiol–disulfide interchange:

$$RSSR' + RSH \rightarrow RSSR + R'SH \quad (12)$$

a reaction which is thermodynamically favored in the presence of excess RSH. However, when the attacking thiol is 4-mercaptopyridine (RSH), only the mixed disulfide (RSSR') and excess RSH are detected, indicating that under the experimental conditions employed the rate of reaction 12 is considerably slower than that of reaction 11. This conclusion is exactly as expected,

Table VIII. Relative Rates of Cleavage of the Sulfur–Sulfur Bond in $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ Complexes by OH^-, $HOCH_2CH_2SH$, and $HOCH_2CH_2S^-$ plus Comparable Rates for the Reaction of SO_3^{2-} with $RSSO_3^-$[a]

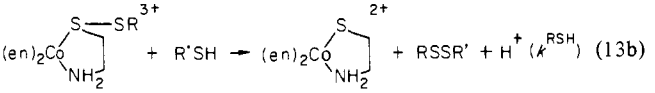
R	OH^-[b]	$HOCH_2CH_2SH$[b]	$HOCH_2CH_2S^-$[b]	SO_3^{2-}[c]
C_6H_5	500			
$C(CH_3)_2CH(NH_2)CO_2H$	24.5			
CH_3	1.00	1.00	1.00	1.00
CH_2CH_3	0.326	0.500	0.520	0.5
$CH(CH_3)_2$	1.16×10^{-2}	3.64×10^{-2}	5.50×10^{-2}	7×10^{-3}
$C(CH_3)_3$		2.21×10^{-5}	2.43×10^{-5}	6×10^{-6}

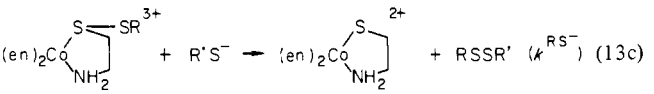
[a] t = 25 °C. Data relative to $R = CH_3$. [b] This work. [c] Reference 25.

reaction 11 involving nucleophilic cleavage of a sulfur–sulfur bond that is activated by coordination to the electrophilic cobalt(III) center, while reaction 12 involves the analogous cleavage of an unactivated sulfur–sulfur linkage.

Consistent with S_N2 attack, the rate of sulfur–sulfur bond cleavage is first order in attacking thiol and first order in the disulfide–cobalt(III) complex. The acid dependence of the second-order rate constant, $k_2 = a + b/[H^+]$, suggests that both thiol (R'SH) and thiolate anion ($R'S^-$) can attack the sulfur–sulfur bond.

$$R'SH \rightleftharpoons R'S^- + H^+ \quad (13a)$$





$$k_2 = k^{RSH} + k^{RS^-}K_a/[H^+] \quad (14a)$$

$$a = k^{RSH} \quad (14b)$$

$$b = K_a k^{RS^-} \quad (14c)$$

Within this scheme the observed rate parameter a represents k^{RSH}, the second-order rate constant governing attack by RSH, and the observed rate parameter b is interpreted as $K_a k^{RS^-}$, where k^{RS^-} is the second-order rate constant governing attack by RS^-. Table VI lists values of k^{RSH} and k^{RS^-} (calculated by using literature values of K_a) for attack on the methyl complex $(en)_2Co(S(SCH_3)CH_2CH_2NH_2)^{3+}$ by a variety of thiols.

For the six thiols investigated, observed values of k^{RSH} vary only by a factor of 4.4, indicating that k^{RSH} is relatively insensitive to the pK_a, charge, and chemical nature of the attacking thiol. The small variations in k^{RSH} values can be interpreted as arising from electrostatic effects (the positively charged cysteamine exhibits the smallest k^{RSH}), steric effects (k^{RSH} for penicillamine is only one-third that of the less hindered cysteine), and the effects of anchimeric assistance. Thus, even though L-cysteic acid (which contains NH_2 and COOH groups but no thiol functionality) does not attack $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$ at a measurable rate, cysteine (which contains NH_2, COOH, and SH groups) exhibits the largest observed k^{RSH}. These observations strongly imply that the NH_2 and COOH groups of cysteine do not directly attack the sulfur–sulfur bond but rather stabilize in some manner the transition state wherein the thiol group cleaves the sulfur–sulfur linkage. This may occur through a "tautomeric" activated complex in which a proton is partially transferred from SH to NH_2 or COOH, thus increasing the nucleophilicity of the sulfur atom.

In contrast to the relative insensitivity of k^{RSH}, k^{RS^-} is very sensitive to the nature of the attacking thiol. Values of k^{RS^-} vary by a factor of 150 for the six thiols investigated, this range resulting largely from variations in the pK_a of the thiol. The Brønsted plot relating k^{RS^-} to the pK_a of the attacking thiol is shown in Figure 1; if a linear relationship is assumed, the correlation coefficient

Table IX. Selected Rates for Nucleophilic Cleavage of Disulfides, both with and without Assistance by Electrophiles[a]

R[a]	R'[a]	Nu[a]	E[a]	conditions	t, °C	k, M^{-1} s^{-1}	ref
CH_3	CH_3	OH^-		1.0 M KCl	25	8.3×10^{-6}	4b
CH_3	CH_3	OH^-	$CH_3Co(dmg)_2$	1.0 M KCl	35	5.5×10^{-4}	4b
CH_2CH_2OH	CH_2CH_2OH	OH^-		1.0 M KCl	25	2.8×10^{-5}	4b
CH_2CH_2OH	CH_2CH_2OH	OH^-	$CH_3Co(dmg)_2$	1.0 M KCl	35	2.5×10^{-3}	4b
$4\text{-}NO_2C_6H_4$	$4'\text{-}NO_2C_6H_4$	OH^-		60% aqueous butanol	30	3.67	2a
C_6H_5	$4\text{-}CH_3COC_6H_4$	OH^-		60% aqueous butanol	30	2.19	2a
Ell[d]	Ell	OH^-			26.4	0.54	26
Ell	Ell	OH^-		CATB micelles	26.4	8.4	26
Ell	Ell	OH^-		DPDAC vesicles	26.4	840	26
CH_3	$CH_2CH_2NH_2$[b]	OH^-	$(en)_2Co^{III}$ [b]	1.0 M $LiClO_4$	25	1.70×10^6	c
CH_2CH_3	$CH_2CH_2NH_2$[b]	OH^-	$(en)_2Co^{III}$ [b]	1.0 M $LiClO_4$	25	5.55×10^5	c
$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	$n\text{-}C_4H_9SH$		CH_3OH	25	3.85×10^{-5}	2b
CH_3	$CH_2CH_2NH_2$[b]	$HOCH_2CH_2SH$	$(en)_2Co^{III}$ [b]	aqueous $HClO_4$	25	1.22	c
CH_3	CH_3	CH_3S^-		0.1 M NaOH-CH_3OH	25	8.8×10^{-2}	2b
$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	$n\text{-}C_4H_9S^-$		0.1 M NaOH-CH_3OH	25	0.26	2b
$C(CH_3)_3$	$C(CH_3)_3$	$C(CH_3)_3S^-$		0.1 M NaOH-CH_3OH	25	1×10^{-7}	2b
	$(CH_2)_3$	$n\text{-}C_4H_9S^-$		0.1 M NaOH-CH_3OH	25	1.4×10^3	2b
Ell	Ell	$HOCH_2CH_2S^-$		0.05 M phosphate	30	2.0×10^5	27
Ell	$CH_2CH_2CH_2OH$	$HOCH_2CH_2S^-$		1.0 M KCl	25	2.55×10^4	23
4-pyridyl	4'-pyridyl	$HOCH_2CH_2S^-$		0.05 M phosphate	25	1.3×10^5	22
4-pyridyl	4'-pyridyl	$HOOCCH_2CH_2S^-$		0.05 M phosphate	25	2.9×10^5	22
4-pyridyl	4'-pyridyl	$H_2NCH_2CH_2S^-$		0.05 M phosphate	25	6.0×10^4	22
2-pyridyl	2'-pyridyl	$HOCH_2CH_2S^-$		aqueous, μ = 0.1 M	25	7.2×10^4	12
CH_3	$CH_2CH_2NH_2$[b]	$HOCH_2CH_2S^-$	$(en)_2Co^{III}$ [b]	aqueous $HClO_4$	25	1.68×10^9	c
C_6H_5	C_6H_5	CN^-		60% aqueous butanol	30	0.159	2a
$4\text{-}CH_3COC_6H_4$	$4'\text{-}CH_3COC_6H_4$	CN^-		60% aqueous butanol	30	12.3	2a
CH_3	CH_3	$(CH_3)_2S$	CH_3^+	CH_3NO_2	0	10^5	28
CH_3	CH_3	$P(OCH_2CH_3)_3$	CH_3Hg^+	CH_2Cl_2	41	1.24×10^{-2}	4c,d

[a] Disulfides are of the form RSSR'. The cleavage reaction proceeds by one of the following two paths: (1) RSSR' + Nu^- → RSNu + R'S^-, or (2) RSSR' + E^+ → $(RSS(E)R')^+$ + Nu^- → RSNu + R'SE. [b] The nitrogen atom is also coordinated to Co(III). [c] This work. [d] Ell = 3-carboxy-4-nitrophenyl.

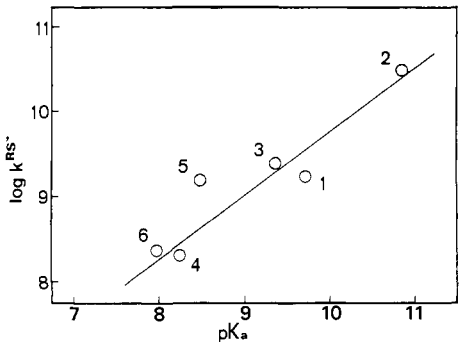


Figure 1. Brønsted plot for the reaction of $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$ with thiols. The numbers refer to the thiols listed in Table VI. Conditions: 25 °C, μ = 1.00 M $LiClO_4$.

is 0.93 and the slope yields a β_{nuc} value of 0.68 ± 0.14. Thus, to a first approximation the reactivity of thiolate anions with respect to cleavage of the sulfur–sulfur bond in $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$ is proportional to the basicity of the anion. The β_{nuc} value observed in this system is larger than β_{nuc} values observed for attack of alkyl thiols on noncoordinated disulfides: for 4,4'-bipyridyl disulfide, β_{nuc} = 0.34;[22] for 5,5'-dithiobis(2-nitrobenzoic acid), β_{nuc} = 0.53;[23] for 3-carboxy-(4-nitrophenyl)-3'-hydroxypropyl disulfide, β_{nuc} = 0.57.[23] These comparisons suggest that the exo sulfur atom of the coordinated disulfide is harder than is the sulfur atom of a noncoordinated disulfide, an effect presumably resulting from association with the very hard cobalt(III) center.

It is particularly noteworthy that the k^{RS^-} values of Table VI are very large, i.e., at or near the diffusion-controlled limit. However, the observed rate of thiolate anion attack is moderated by $K_a/[H^+]$; i.e., $k_{obsd}^{RS^-} = b = K_a k^{RS^-}/[H^+]$. Thus, for the relatively basic alkyl thiols (pK_a = 8–11), $k_{obsd}^{RS^-}$ can be determined by conventional kinetic techniques when $[H^+]$ is in the range 0.10–1.0 M. However, aryl thiols are much more acidic (e.g., the pK_a of 4-mercaptopyridine is 1.43[24]) and thus even at $[H^+]$ = 1.0 M they react too rapidly to allow the determination of $k_{obsd}^{RS^-}$ by conventional means.

The data of Table VII show that the rate of cleavage of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes by 2-mercaptoethanol decreases dramatically with increasing steric bulk of the R group. This is exactly as expected for S_N2 attack on the sulfur–sulfur linkage. The magnitudes of both k^{RSH} and k^{RS^-} are similarly affected, the relative rates for the methyl, ethyl, isopropyl, and *tert*-butyl derivatives being listed in Table VIII. These relative rates are essentially the same for (a) k^{RSH}, (b) k^{RS^-}, (c) base hydrolysis of $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes (vide supra), and (d) the reaction of sulfite ion with organic thiosulfates[25] (Table VIII). Thus, the magnitude of the steric retardation of sulfur–sulfur bond scission in $[(en)_2Co(S(SR)CH_2CH_2NH_2)]^{3+}$ complexes appears to be quite normal and does not reflect any special coordination effects. As expected, steric retardation is manifested largely in the activation enthalpy; ΔH^* for k^{RSH} increases ca. 5.0 kcal/mol and ΔH^* for k^{RS^-} increases ca. 9.0 kcal/mol on going from R = CH_3 to R = $C(CH_3)_3$ (Table VII). By use of available thermodynamic data for the acid dissociation of 2-mercaptoethanol,[18] activation parameters associated with k^{RS^-} can be calculated from the activation parameters associated with the observed rate parameter b (eq 14c). These calculated values are also listed in Table VII, the near-zero value of $\Delta H^*_{RS^-}$ for R = CH_3 being consistent with the nearly diffusion-controlled rate of this reaction.

Reactivity Trends. The relative rates of cleavage of sulfur–sulfur bonds are affected by the steric requirements of the sulfur–sulfur linkage (vide supra). This steric effect can account for ca. 5 orders of magnitude in specific rate on going from CH_3 to $C(CH_3)_3$ (Table VIII). More dramatically, the rates of sulfur–sulfur bond cleavage depend on the nucleophilicity of the attacking group; for attack on $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$ specific rates (25

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°C, M^{-1} s^{-1}) decrease in the order RS^- (1.7×10^9) > OH^- (1.7×10^6) > RSH (1.2). Within a series of RS^- nucleophiles, basicity appears to be the prime determining factor, the stronger bases being more effective nucleophiles (see Figure 1). However, the most dramatic reactivity effect encountered in this work involves the relative rates of cleavage of coordinated and noncoorddinated disulfides. Table IX summarizes rate data for the reaction of organic disulfides with various nucleophiles, both with and without electrophilic assistance. For all relevant comparisons, the rate of reaction is much greater in the presence of an electrophile, but the effect induced by coordination of the disulfide to an inert cobalt(III) center is truly striking. From Table IX it is seen that coordination of a dialkyl disulfide to cobalt(III) enhances the rate of OH^- cleavage of the sulfur–sulfur bond by about 11 orders of magnitude and enhances the rate of RS^- cleavage by about 10 orders of magnitude. These very large effects reflect the inherent ability of the electrophilic cobalt(III) center to activate the disulfide linkage toward nucleophilic attack. It is just this sort of specific and effective activation of disulfide linkages that may be important in biological processes.

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Registry No. $[(en)_2Co(S(SCH_3)CH_2CH_2NH_2)]^{3+}$, 74037-02-8; $[(en)_2Co(S(SCH_2CH_3)CH_2CH_2NH_2)]^{3+}$, 74037-05-1; $[(en)_2Co(S(SCH(CH_3)_2)CH_2CH_2NH_2)]^{3+}$, 74037-00-6; $[(en)_2Co(S(SC(CH_3)_3)CH_2CH_2NH_2)]^{3+}$, 74036-99-0; $[(en)_2Co(S(SC(CH_3)_2CH(NH_2)COOH)CH_2CH_2NH_2)]^{3+}$, 84194-99-0; OH^-, 14280-30-9; 2-mercaptoethanol, 60-24-2; 3-mercaptopropionic acid, 107-96-0; 2-mercaptoethanesulfonic acid, 3375-50-6; cysteamine, 60-23-1; L-cysteine, 52-90-4; D-penicillamine, 52-67-5.

Supplementary Material Available: Table I, k_{obsd} and k_2 values for base hydrolysis reactions, Tables IV and V, k_{obsd} and k_2 values for thiol cleavage reactions (7 pages). Ordering information is given on any current masthead page.

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Kinetic Study for Reactions of Phenylseleno Radical with Vinyl Monomers

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Abstract: The reactivities of the phenylseleno radical (PhSe·) generated by flash photolysis of diphenyl diselenide have been determined. Low reactivities of PhSe· toward oxygen, hydrogen-atom donors, and halogen-atom donors have been confirmed. With vinyl monomers (CH_2=CHY) PhSe· reacts in a reversible fashion; by the addition of oxygen as a selective radical trap to the adduct radicals ($PhSeCH_2C{\cdot}HY$), the absolute addition rate constants have been determined. The reverse rate constants and the equilibrium constants have been estimated as relative ones from which the thermodynamic stabilities of the adduct radicals have been elucidated. The addition rates increase mainly with the stabilities of the adduct radicals and subsequently with the polar nature of the transition state. The lower reactivity of PhSe· compared with the phenylthio radical (PhS·) is attributed to the greater stabilization of an unpaired electron in PhSe· than that in PhS·.

Organoselenium compounds are useful for synthetic chemistry[1] and photochemistry.[2,3] Important reaction intermediates generated by photolysis of organoselenium compounds are the organoseleno radicals (RSe·);[4] the reaction products of the radical reactions with phosphines[5] and alkenes[6,7] have been identified. The reactivities of RSe·, however, have not been clarified compared with those of the organothio radicals.[8,9] We have shown that the flash photolysis technique is very valid in the kinetic study for the addition reactions of the phenylthio radical (PhS·) with vinyl monomers.[10,11] By the application of this technique to the free-radical addition reactions which are usually reversible, the relative equilibrium constants can be estimated by the addition of an appropriate selective radical trap; therefore, the reactivities of the free radicals can be discussed on the basis of the thermodynamic parameters. In this paper we applied the flash photolysis technique to the phenylseleno radical (PhSe·) in order to clarify the reactivities toward various substrates such as vinyl monomers. The results for PhSe· have been compared with those for PhS· observed previously by the same method.[10,11]

Results and Discussion

The transient absorption band (spectrum a in Figure 1) was observed at 490 nm by the flash photodecomposition of diphenyl diselenide (spectrum c in Figure 1) in carbon tetrachloride. The species of the 490-nm band was ascribed to PhSe· since a similar sharp absorption band was reported for *p*-methoxybenzeneseleno radical at 535 nm by means of pulse radiolysis;[12] such a shift of the absorption peaks between both the radicals is reasonable since

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