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Articles

Electron Transfer. 136. Decomposition of Peroxynitrite As Catalyzed by Sulfito-Bound Cobalt(III)[1]

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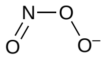
The self-decomposition of peroxynitrite in strongly basic solution, principally to O_2 and nitrite ($2O{=}N{-}O{-}O^- \rightarrow O_2 + 2NO_2^-$), is catalyzed markedly by the sulfito-substituted cobalt(III) complexes $[Co(NH_3)_5(SO_3)]^+$ and *cis*-$[Co(NH_3)_4(SO_3)_2]^-$ but not by cobalt compounds devoid of ligated sulfite. Catalysis does not entail recycling of cobalt between di- and tripositive states. As a result of *trans*-labilizing action of bound sulfite, the bis(sulfito) catalyst is taken to be converted to the corresponding *cis*-$(H_2O)_2$ complex, which, in the basic medium employed, is deprotonated to a mixture of mono- and dihydroxo complexes (both reactive), thus accounting for the two paths indicated by kinetic data taken in the presence of this catalyst. It is proposed that catalytic action is initiated when peroxynitrite replaces coordinated water at the Co(III) site, that the O−O bond undergoes homolysis by a Fenton-like act, except that the electron lost from the catalyst arises from a ligating sulfito group rather than Co(III), and that a second peroxynitrite anion rapidly undergoes two successive 1e$^-$ oxidations to yield O_2 and NO_2^-. The singular catalytic effectiveness of sulfito-bound cobalt(III) is attributed to a combination of the *trans*-effect of this ligand and its ability to undergo single-electron oxidation.

The two biologically important odd-electron diatomic species nitric oxide[2] (NO) and the superoxide anion[3] (O_2^-) react rapidly ($k = 6 \times 10^9$ M^{-1} s^{-1} at 25 °C),[4] yielding peroxynitrite ($O{=}NOO^-$), the anion of the weak acid peroxynitrous acid (pK_a 6.5).[5] This anion can be stored in solution for weeks at very high pH at −18 °C,[6] in contrast to the parent acid, which decomposes rapidly. Raman spectra[7] are consistent with a predominant *cis*-structure for the anion.



The formation of peroxynitrite in biosystems has been confirmed,[8] and its cytotoxic action has been reported.[9] It has been proposed as an active agent in the development of atherosclerotic lesions[10] and reactions associated with vascular injuries.[11]

A growing body of experimental work dealing with the reactions of peroxynitrite reflects markedly increased interest in this species. Oxidations of both inorganic[12] and organic[13] coreagents have been described, and its spontaneous "self-decomposition" has been examined.[7,14] We have focused on the effects of transition metal species on such conversions and recently described catalysis, by Cu(II), of the oxidation of sulfite

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[1] Sponsorship of this work by the National Science Foundation (Grant 9414113) is gratefully acknowledged.

[2] See, for example: Stamler, J. S.; Singel, D. J.; Loscalzo, J. *Science* **1992**, *258*, 1898.

[3] Reviews: (a) Fee, J. A.; Valentine, J. S. In *Superoxide and Superoxide Dismutase*; Michelson, A. M., McCord, J. M., Fridovich, I., Eds.; Academic Press: New York, 1979; p 19. (b) Fridovich, I. *Adv. Inorg. Biochem.* **1979**, *67*, 1.

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[7] Tsai, J.-H.; Harrison, J. G.; Martin, J. C.; Hamilton, T. P.; van der Woerd, M.; Jablonski, M. J.; Beckman, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4115.

[8] Ischiropoulos, H.; Zhu, L.; Beckman, J. S. *Arch. Biochem. Biophys.* **1992**, *298*, 446.

[9] Zhu, L.; Gunn, C.; Beckman, J. S. *Arch. Biochem. Biophys.* **1992**, *298*, 452.

[10] Steinberg, D.; Parathasarthy, S.; Carew, T. E.; Khoo, J. C.; Witstum, J. L. *N. Engl. J. Med.* **1989**, *320*, 915.

[11] Hogg, N.; Joseph, J.; Kalyanaraman, B. *Arch. Biochem. Biophys.* **1994**, *314*, 153.

[12] See, for example: (a) Halfpenny, E.; Robinson, P. L. *J. Chem. Soc. A* **1952**, 928 (Br^-). (b) Hughes, M. N.; Nicklin, H. G.; Sackrule, W. A. C. *J. Chem. Soc. A* **1971**, 3722 (I^-, SCN^-). (c) Hughes, M. N.; Nicklin, H. G. J. *Chem. Soc. A* **1970**, 925 (CN^-, NH_2OH). (d) Goldstein, S.; Czapski, G. *Inorg. Chem.* **1995**, *34*, 4041 ($Fe(CN)_6^{4-}$, Ni^{II}(cyclam)). (e) Al-Ajlouni, A. M.; Gould, E. S. *Inorg. Chem.* **1996**, *35*, 7892 (As^{III}, Sb^{III}, Sn^{II}).

[13] See, for example: (a) Beckman, T. W.; Chen, J.; Marshall, P. A.; Freeman, B. A. *Proc. Natl. Acad. Sci. U.S.A.* **1990**, *87*, 1620 (1,2-glycols). (b) Radi, R.; Beckman, J. S.; Bush, K. M.; Freeman, B. A. *J. Biol. Chem.* **1991**, *266*, 4244 (thiols). (c) Pryor, W. A.; Jin, X.; Squadrito, G. L. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 11173 (thioethers). (d) Ischiropoulos, H.; Zhu, L.; Chen, M.; Tsai, M.; Martin, J. C.; Smith, C. D.; Beckman, J. S. *Arch. Biochem. Biophys.* **1992**, 298, *431* (amino acids). (e) Bartlett, D.; Church, D. F.; Bounds, P. L.; Koppenol, W. H. *Free Radicals Biol. Med.* **1995**, *18*, 85 (ascorbate).

[14] (a) Benton, D. J.; Moore, P. *J. Chem. Soc. A* **1970**, 3179. (b) Anbar, M.; Taube, H. *J. Am. Chem. Soc.* **1954**, *76*, 331.

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Table 1. Catalyzed Decomposition of Peroxynitrite: Evolution of O_2[a]

amt of catalyst, moles × 10^6	amt of peroxynitrite, moles × 10^5	amt of O_2 formed, moles × 10^5	Δ(mol of peroxynitrite)/ Δ(mol of O_2)
6.0	5.0	1.85	2.8
8.5	8.5	3.25	2.6
6.0	10.0	3.80	2.7

[a] Reactions were carried out at 20 °C and were catalyzed by *cis*-$[Co(NH_3)_4(SO_3)_2]$. $[OH^-] = 0.40$ M; $\mu = 1.0$ M ($NaClO_4$). Reaction time: 15 min.

by peroxynitrite at high pH.[15] The present work deals with the effects of sulfite-bound cobalt(III) species on the decomposition of peroxynitrite. Again, reactions were examined in strongly basic media to minimize complications resulting from H^+ catalysis of this reaction.

Experimental Section

Materials. Solutions were prepared from Millipore water which had been boiled for 2 h, and then purged with N_2 for 2 h more to remove dissolved O_2. The pH was maintained by dilution of standard solutions of sodium hydroxide. Ionic strength was regulated by addition of $NaClO_4$.

The bis(sulfito) catalyst *cis*-$[Co(NH_3)_4(SO_3)_2]^-$ was prepared as its ammonium salt using the procedure of Bailar[16] and was characterized spectrophotometrically ($\epsilon_{\max}^{295} = 2.1 \times 10^4$ M^{-1} cm^{-1}).[17] The mono(sulfito) complex $[Co(NH_3)_5(SO_3)]^+$ was prepared as its perchlorate as described by Siebert[18] and was crystallized from 7% NH_3 solution ($\epsilon_{\max}^{278} = 1.95 \times 10^4$ M^{-1} cm^{-1}).[17] Peroxynitrite solutions were prepared using slight modifications of literature methods,[12a,d,e] were kept at −18 °C, and were standardized spectrophotometrically each day ($\epsilon_{\max}^{302} = 1670$ M^{-1} cm^{-1}).[12d]

Stoichiometric Studies. The stoichiometry of the decomposition of peroxynitrite as catalyzed by *cis*-$[Co(NH_3)_4(SO_3)_2]^-$ was examined under N_2 in 0.40 M NaOH at 20 °C. The volume of the reacting solution was 1.0−2.0 mL. The gaseous product was shown to be pure O_2 (mass spectrometry). The decomposition was carried out in a 5.0 mL tube which was connected to a graduated 2.0 mL syringe to determine the volume of the gas produced. Results are summarized in Table 1.

Kinetic Studies. Reactions were carried out at 24.0 °C in basic solutions (0.002−0.500 M in NaOH) with ionic strength maintained at 1.0 M ($NaClO_4$). Kinetic data for the decomposition of peroxynitrite as catalyzed by the bis(sulfito)cobaltIII) complex were collected by recording absorbance decreases at 333 nm[19] using a Shimadzu 1601 spectrophotometer (optical path length 1.00 cm). Reaction mixtures were prepared in the cell, with peroxynitrite added last. Decay profiles were nearly exponential but exhibited some deceleration late in the reaction due to the slow decomposition of the catalyst in the basic solution. To minimize complications resulting from loss of catalyst, kinetic dependencies were based upon initial rates, as calculated using the method of Chandler,[20] in which absorbances (*A* values) during the first few percent of reaction were related to reaction times (*t*) by the polynomial expression (1). Least-squares treatment of absorbance data

$$A = A_0 + a_1t + a_2t^2 + at^3 + ... \tag{1}$$

(20 points per experiment) gave estimates of a_1, which were divided by ϵ for peroxynitrite to obtain the initial rates. Replicate runs generally yielded rates agreeing to better than 5%. Reactions were first order in peroxynitrite throughout. Rates were nearly proportional to [catalyst] at low concentrations of the latter, but at higher concentrations, this dependency became less marked. Acceleration by increase in $[H^+]$ was observed but was less steep than that corresponding to unit order. Marginal inhibition by added ammonia and acceleration by added sulfite were noted, but these effects were too slight to generate meaningful quantitative relationships.

Table 2. Kinetic Data for Self-Decomposition of Peroxynitrite As Catalyzed by *cis*-$[Co(NH_3)_4(SO_3)_2]^-$ (24 °C, $\mu = 1.0$ M)

$[O{=}NOO^-]$, mM	[catalyst], M × 10^5	$[H^+]$, M × 10^{13}	rate × 10^6 [a]
0.228	5.0	2.0	2.19 ± 0.07 (2.54)
0.470	5.0	2.0	4.5 ± 0.2 (5.2)
0.690	5.0	2.0	8.1 ± 0.3 (7.7)
0.861	5.0	2.0	9.5 ± 0.3 (9.6)
1.03	5.0	2.0	11.8 ± 0.4 (11.5)
0.568	0.50	2.0	1.59 ± 0.05 (1.52)
0.567	1.00	2.0	2.36 ± 0.06 (2.41)
0.503	2.0	2.0	3.5 ± 0.1 (3.3)
0.484	5.0	2.0	5.6 ± 0.2 (5.4)
0.506	7.5	2.0	6.7 ± 0.2 (7.1)
0.496	10.0	2.0	7.5 ± 0.2 (8.1)
0.500	2.0	0.20	1.16 ± 0.03 (1.09)
0.554	2.0	0.50	2.00 ± 0.06 (1.64)
0.520	2.0	5.00	7.7 ± 0.2 (6.4)
0.410	2.0	20.0	10.0 ± 0.3 (10.3)

[a] Initial rates of disappearance of peroxynitrite; measurements were at 333 nm. Parenthetical values were calculated using eq 7, taking pK_A as 12.6, k_A as 4.1×10^2 M^{-1} s^{-1}, k_{HA} as 1.6×10^3 M^{-1} s^{-1}, and $K_D = 4.9 \times 10^5$ M^{-1}.

The mono(sulfito) complex, $[Co(NH_3)_5(SO_3)]^+$, showed catalytic activity comparable to that of the bis(sulfito) derivative, but the quantitative study of its effectiveness was severely complicated by its rapid decomposition (and the resultant precipitation of Co_2O_3) in the medium employed. This decomposition could be inhibited by addition of NH_3, but under such conditions the catalytic action was lost.

The following reagents, when added at the 10^{-4} M level, exhibited no catalytic action toward the decomposition of peroxynitrite: NH_4VO_3, $MnSO_4$, NH_4ReO_4, $(NH_4)_2MoO_4$, $ZnSO_4$, and $Co(en)_3(ClO_4)_3$. The cobalt(III) complexes $Co(NH_3)_6^{3+}$, $Co(NH_3)_5H_2O^{3+}$, $Co(NH_3)_5NO_3^{2+}$, $Co(NH_3)_5SO_4^+$, and $Co(NH_3)_5CO_3^+$ were found to accelerate the loss of peroxynitrite marginally, but each of these complexes suffered early decomposition with precipitation of Co_2O_3 in our medium.

Spent reaction mixtures in which the decomposition of peroxynitrite was promoted by our most effective catalyst, *cis*-$[Co(NH_3)_4(SO_3)_2]^-$, gave positive tests for unbound sulfate.

Results and Discussion

Although the decomposition of peroxynitrite into O_2 and nitrite (eq 2) requires 2 mol of $OON{=}O^-$/mol of O_2 released,

$$2[OON{=}O]^- \rightarrow O_2 + 2NO_2^- \tag{2}$$

the measured stoichiometry, 2.6−2.8 (Table 1), lies somewhat above this value. Since one or both of the ligating sulfito groups of the catalyst are converted partially to unbound sulfate, a portion of the additional peroxynitrite which is lost (although not all of it) may be utilized in oxidation of the catalyst. The remaining minor portion (10−20%) is almost certainly consumed in the recognized[14] conversion of peroxynitrite to nitrate

$$[O{=}N{-}O{-}O]^- \rightarrow NO_3^- \tag{3}$$

a reaction for which a cyclic (three-membered ring) transition state has been proposed.[14b]

Kinetic data pertaining to initial rates for the decomposition of peroxynitrite as catalyzed by the bis(sulfito) complex appear in Table 2. Rates are seen to be proportional to

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(15) Al-Ajlouni, A. M.; Gould, E. S. *Inorg. Chem.* **1997**, *36*, 362.

(16) Bailar, J. C., Jr.; Peppard, D. F. *J. Am. Chem. Soc.* **1940**, *62*, 105.

(17) Spitzer, U.; van Eldik, R. *Inorg. Chem.* **1982**, *21*, 4008.

(18) Siebert, H.; Wittke, G. *Z. Anorg. Allg. Chem.* **1973**, *399*, 43.

(19) This wavelength, at which ϵ for peroxynitrite is 1050 M^{-1} cm^{-1}, was chosen because absorbance changes due to interconversion of catalytic species were negligible.

(20) (a) Chandler, W. D.; Lee, E. J.; Lee, D. G. *J. Chem. Educ.* **1987**, *64*, 878. (b) Chandra, S. K.; Gelerinter, E.; Gould, E. S. *Inorg. Chem.* **1995**, *34*, 4057.

$[O{=}N{-}O{-}O^-]$, and reactions are accelerated by increases in [catalyst] and $[H^+]$, with the latter two responses less steep than that corresponding to unit order. The "leveling" off in the case of catalyst may be attributed to partial conversion of the cobalt(III) center to a dimeric species,[21] whereas the $[H^+]$ dependency is that reflecting variable protonation of a reactant within the pH range examined. Since peroxynitrite features no acidic center with pK_A 12−13, the latter equilibrium must also involve the catalyst, which then exists in three rapidly interconverted forms, $(\mathrm{cat})_{\mathrm{HA}}$, $(\mathrm{cat})_{\mathrm{A}}$, and $(\mathrm{cat}_{\mathrm{A}})_2$, of which the first two are active:

$$(\mathrm{cat})_{\mathrm{HA}} \overset{K_{\mathrm{A}}}{\rightleftharpoons} (\mathrm{cat})_{\mathrm{A}} + \mathrm{H}^+ \qquad (4)$$

$$2(\mathrm{cat})_{\mathrm{A}} \overset{K_{\mathrm{D}}}{\rightleftharpoons} (\mathrm{cat}_{\mathrm{A}})_2 \qquad (5)$$

$$\mathrm{rate} = [\mathrm{ONO_2}^-][k_{\mathrm{A}}(\mathrm{cat})_{\mathrm{A}} + k_{\mathrm{HA}}(\mathrm{cat})_{\mathrm{HA}}] \qquad (6)$$

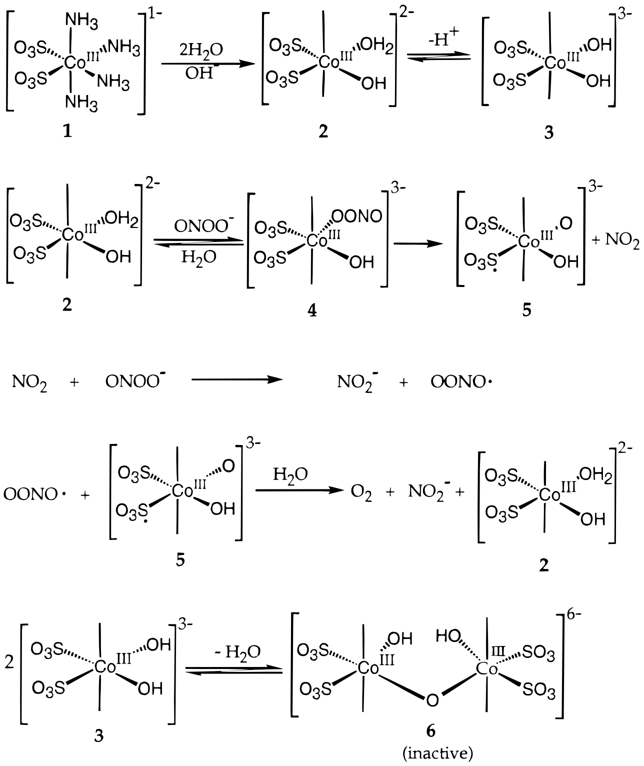
This partition then generates rate law 7 (see Appendix) where

$$\mathrm{rate} = [\mathrm{ONO_2}^-]\left(\frac{k_{\mathrm{A}} + k_{\mathrm{HA}}\dfrac{[\mathrm{H}^+]}{K_{\mathrm{A}}}}{4K_{\mathrm{D}}}\right)\left\{\sqrt{1 + \frac{[\mathrm{H}^+]^2}{K_{\mathrm{A}}} + 8K_{\mathrm{D}}[\mathrm{cat}]_{\mathrm{T}}} - \frac{[\mathrm{H}^+]}{K_{\mathrm{A}}} - 1\right\} \qquad (7)$$

$[\mathrm{cat}]_{\mathrm{T}}$ designates the total concentration of added catalyst and k_{A} and k_{HA} are rate constants associated with the two protonation levels. Refinement of kinetic data in terms of (7) yields $pK_{\mathrm{A}} = 12.6 \pm 0.2$, $k_{\mathrm{HA}} = (1.6 \pm 0.4) \times 10^3$ $\mathrm{M^{-1}\ s^{-1}}$, $k_{\mathrm{A}} = (4.1 \times 1.7) \times 10^2$ $\mathrm{M^{-1}\ s^{-1}}$, and $K_{\mathrm{D}} = (4.9 \pm 1.1) \times 10^5$ $\mathrm{M^{-1}}$. Rates calculated by (7) are compared to observed values at the right of Table 2.[22]

Undoubtedly, the most striking aspect of the present work is the unique ability of sulfito-substituted cobalt(III) to assume an effective catalytic role; all other cobalt complexes examined are devoid of significant activity. Moreover, oxidation of ligated sulfite to sulfate cannot be a step in the catalytic sequence, since this irreversible conversion would soon exhaust the catalyst, which is added at a level much lower than that of peroxynitrite. Furthermore, the sequence cannot involve recycling of cobalt between 2+ and 3+ states (in analogy to other peroxide reactions proceeding via Fenton-related mechanisms),[23] for the ligating groups about Co(III), needed for retention of activity, would be lost rapidly at the substitution-labile Co(II) stage. Instead, it may be assumed that cobalt remains in the tripositive state during the progress of the reaction. Note also that the conversion of peroxynitrite to O_2 and NO_2^- (the principal transformation) requires two acts of electron transfer involving O−O-bonded species.

Scheme 1



The reaction sequence indicated in Scheme 1 appears to be consistent with our observations. (Axial NH_3 ligands are omitted from all formulas except **1** to improve clarity.) Because of the recognized strongly *trans*-labilizing action of the bound sulfito ligands,[17,24] the added bis(sulfito) catalyst (**1**) is taken to be rapidly and completely converted (before addition of peroxynitrite), to the corresponding *cis*-$(H_2O)_2$ complex

$$cis\text{-}[\mathrm{Co(NH_3)_4(SO_3)_2}]^- \xrightarrow{2\mathrm{H_2O}} [\mathrm{Co(NH_3)_2(H_2O)_2(SO_3)_2}]^- + 2\mathrm{NH_3} \qquad (8)$$

The latter, in the basic medium employed, is deprotonated to a mixture of mono- and dihydroxo complexes (**2** and **3**). Catalytic action is initiated when peroxynitrite replaces coordinated water (**2** → **4**). We propose that homolysis of the O−O bond in **4** proceeds by a Fenton-like process but that the electron lost from the catalyst arises from the ligating sulfito group, rather than from the cobalt center, leaving behind the odd-electron intermediate **5**. It is further suggested that a second unit of peroxnitrite undergoes two successive rapid acts of electron removal, the first by NO_2 and the second by the oxidizing species **5**, to give, upon action of water, the principal products O_2 and NO_2^- and to regenerate intermediate **2**. In addition, a second component (not shown) involves the deprotonated species **3** instead of **2**, accounting for the slower k_{A}-dependent path. Reversible dimerization of **2** is reflected in the less-than-first-order dependence on catalyst at high concentrations of the latter.

If the suggested sequence, or one similar to it, is applicable, the singular catalytic effectiveness of sulfito-bound cobalt(III) may be attributed to a combination of the *trans*-effect of this ligand and its ability to undergo single-electron oxidation. Whether other cobalt complexes featuring S-donor ligands will show comparable catalytic activity remains to be seen.

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(21) Kinetic complications arising from partial conversion of a metal center catalyst to an inactive dimeric species have also been described for Fe(III) catalysis of metal-bound peroxo reactions. See, for example: Ghosh, S. K.; Gould, E. S. *Inorg. Chem.* **1988**, *27*, 4228; **1989**, *28*, 3651.

(22) Our data do not allow a more elaborate analysis that might evaluate the (minor) concentrations of additional species such as $(\mathrm{cat_{HA}}{\cdot}\mathrm{cat_A})$.

(23) See, for example: (a) Sosnovsky, G.; Rawlinson, D. J. In *Organic Peroxides*; Swern, D., Ed.; Wiley: New York, 1971; Vol. II, pp 153−268. (b) Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidation of Organic Compounds*; Academic Press: New York, 1981; pp 34−49.

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Appendix. Derivation of Eq 7

The rate-determining steps of the two Co(III)-catalyzed paths for decomposition are assumed to be the homolysis of peroxynitrito complex **4** and its deprotonated analogue, both of which are taken to be in rapid equilibrium with $O{=}NOO^-$ and the respective catalytic anion

$$\text{rate} = [O{=}NO_2^-]([\text{cat}]_{HA}Q_{HA}k'_{HA} + [\text{cat}]_A Q_A k'_A) \qquad (a)$$

where the Q's are association quotients and the k' values are rate constants for the two homolyses. Under the conditions used, dissolved cobalt, $[\text{Co}]_T$, is taken to be partitioned principally into complexes **2**, **3**, and **6**, of which only the first two are catalytically active.

$$[\text{Co}]_T = [\text{cat}]_{HA} + [\text{cat}]_A + 2[(\text{cat}_A)_2] \qquad (b)$$

Expression of $[\text{cat}]_{HA}$ (**2**), $[\text{cat}]_A$ (**3**), and $(\text{cat}_A)_2$ (**6**) in terms of the dimerization constant K_D (eq 5) and the acidity constant K_A for **2**, followed by substitution into (b) yields

$$[\text{Co}]_T = [\text{cat}]_A + \frac{[\text{cat}]_A[H^+]}{K_A} + 2K_D[\text{cat}]_A^{\,2} \qquad (c)$$

Solving for $[\text{cat}]_A$ and substituting into (a) yield (7), in which the individual rate constants correspond to the Qk' products in (a).

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