Kinetics of Extremely Fast Ligand-exchange Reactions with Methylmercury(II)–Nitrothiophenolate Complexes: Rate–Equilibria Correlations

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Abstract

The kinetics of the $CH_3Hg(II)$ transfer from two nitrothiophenolates (4-nitro-2-sulfonato-thiophenolate and 4-nitro-3-carboxylato-thiophenolate) to a wide variety of other ligands and the reverse reaction have been investigated by means of the temperature-jump and stopped-flow methods. Over the whole wide range of equilibrium constants the exchange reactions are almost diffusion-controlled, even in the isergonic region. The protonated S-donors can also initiate directly the ligand-exchange reactions. The rate constants for the thiophenols are always smaller than those for the thiophenolates. The reactivity of the protonated S-donors is strongly dependent on the nature of the ligand to be displaced. Several features of the reaction mechanisms involved and their relevance for the transport of $CH_3Hg(II)$ in natural systems are discussed.

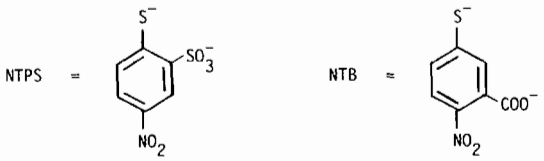
Introduction

The mechanism of ligand-substitution processes at $CH_3Hg(II)$ complexes is of chemical and toxicological interest. Aside from the well-known fact that $CH_3Hg(II)$ has a strong coordination tendency to soft ligands, it forms also quite stable complexes with N- and O-donors. This enabled us to investigate the type of rate–equilibria relationships for exchange reactions (1) over such a wide range of $\log k_{12}$, $\log k_{21}$ and $\log K_{12}$ which was not possible for any other metal ion. Eigen plots, $\log k_{12}$ *versus* $\log K_{12}$, for a given ligand Y and a variety of X show a smooth change of $\alpha = \mathrm{d} \log k_{12}/\mathrm{d} \log K_{12}$ from 1 to 0, and a $\mathrm{d} \log k_{21}/\mathrm{d} \log K_{12}$ from 0 to -1 [1]. From the shape of the curvature it follows that an Ia mechanism is operative. Various reaction series can be described by an equation which is similar to the Marcus equation for atom transfer [2]. The series are characterized by an intrinsic barrier $\Delta G_0^{\neq}$ (defined as $\Delta G^{\neq}$ at log

$$CH_3HgY^+ + X \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} CH_3HgX^+ + Y \qquad (1)$$

$K_{12} = 0$) which varies between 7 and <4 kcal/mol [1, 3, 4]. $CH_3Hg(II)$ complexes with S-donor ligands of the thione type are extremely labile. Even for isergonic reactions the diffusion-controlled limit is reached [1]. Rabenstein and Fairhurst [5] found similar extreme substitution lability for the self-exchange reaction of the $CH_3Hg(II)$–glutathione complex. However, for the $CH_3Hg(II)$–mercaptoacetate complex a much slower exchange rate was found [6]. To get a better insight into the reactivities of S-donors with different nucleophilicities we decided to include thiophenols in our study of rate–equilibria relationships. With these thiols it was also possible to study the kinetics with the protonated forms. Detailed knowledge on the reactivity of $CH_3Hg(II)$ complexes is important for a better understanding of the CH_3Hg^{II} transport and facilitates the recognition of possible pathways in biological systems.

In this paper we report results of a T-jump and stopped-flow kinetic study of CH_3Hg^{II}-transfer reactions between thiophenolates and a variety of other unidentate ligands including S-donors. The thiophenolates used were 4-nitro-2-sulfonato-thiophenolate (NTPS) and 4-nitro-3-carboxylato-thiophenolate (NTB). Both ligands are chromophores which facilitates the direct optical monitoring of the complexation reactions. NTB is a reaction product of Ellman's reagent which is used for the estimation of thiol groups in proteins [7]. NTPS is a very similar ligand which, however, has the advantage of being more stable against oxidation. This study constitutes



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the first report describing the use of these S-donors as complexing agents. The results of the ligand-exchange reactions are discussed in terms of rate–equilibria relations. It is found that CH_3Hg^{II}-transfer reactions to and from these thiophenolates are characterized by an extremely small intrinsic barrier which results in diffusion-controlled reactions. The protonated forms of the various S-donors, however, show a distinctly reduced reactivity.

Experimental

Chemicals and Solutions

Stock solutions of CH_3HgOH were prepared as described previously [8]. $K[HNTPS]\cdot H_2O$ was prepared as follows. 10 g of 2-chloro-3-nitrobenzene-sulfonic acid, prepared according to Claus and Mann [9], were dissolved in 10 ml ethanol and added to 150 ml of a 1:5 triethylamine/ethanol solution which was saturated with H_2S. After further addition of 20 g triethylamine the reaction mixture was stirred for 5 min at 50 °C. The reaction was then stopped by adding 150 ml of an ice-cooled ethanolic KHS solution. After 15 min the red–brown solid was washed with ethanol/water and diethylether and dried *in vacuo*. Yield: 6 g raw material of $K_2[NTPS]$. The solid was purified by dissolving it in O_2-free water and filtering off the unsoluble material. After addition of a $ZnSO_4$ solution the yellow Zn salt precipitated. The solid was redissolved in water and the solution was sorbed on a ion-exchange column DOWEX (H^+) 50 WX8. Elution was performed with water into a receiver which was adjusted to pH 3.5 with KOH. After immediate evaporation *in vacuo* pale-yellow needles of $K[HNTPS]\cdot H_2O$ precipitated. The compound was characterized by elemental analysis and methylmercuration. For this purpose a buffered solution (phenolsulfonic acid, pH 9.5) was titrated with CH_3HgOH. At $\lambda = 420$ nm a sharp endpoint was obtained corresponding to 98.6% purity. Normally, daily-fresh stock solutions of NTPS were prepared from the Zn salt via ion exchange. The concentration was determined spectrophotometrically, $\epsilon(420\text{ nm}) = 1.56 \times 10^4$ (M^{-1} cm^{-1}). Atomic absorption measurements showed that <0.5% Zn per thiol was present in the eluate.

H_2NTB was obtained according to the literature method [10] by reduction of 5,5'-dithiobis(2-nitrobenzoic acid) (Ellman's reagent). The concentration of NTB solutions was determined by methylmercuration of the thiol group or spectrophotometrically as described above.

Bis(2-cyanoethyl)sulfopropylphosphine (phos), sodium salt, was a gift from Ilford AG, Fribourg, Switzerland. All other chemicals were commercially available in puriss. quality.

The ionic strength ($I = 0.1$ M) was maintained with $NaClO_4$ which was obtained by neutralization of $HClO_4$ with aqueous NaOH. The pH (= $-\log [H^+]$) of each solution was measured with a glass electrode which was standardized as described elsewhere [11]. To avoid oxidation stock solutions of $NTPS^{2-}$ and NTB^{2-} were freshly prepared daily using doubly distilled water which had been deoxygenated by bubbling N_2 through it. At pH 11 such solutions remain stable for a few hours, whereas in acidified solutions significant amounts of the nitrothiophenols oxidized within minutes.

Evaluation of the Protonation and Methylmercuration Constants

All equilibrium measurements were carried out at 20 °C using a Beckman Acta M VII UV–Vis spectrophotometer with 1 cm quartz cells. For the pK_a determinations dilute solutions of NTPS and NTB (*ca.* 5×10^{-5} M), which contained acetic acid buffers, were used. The quotient of the two forms, (thiols and thiolates) could be evaluated directly from the spectra so that $pK_a = pH + \log[HNTPS]/[NTPS]$, *cf.* Figs. 1 and 2.

The stability constants of the $CH_3Hg(II)$ complexes with $Y = NTPS^{2-}$ and NTB^{2-}, according to eqns. (2) and (3) are too big for the direct spectro-

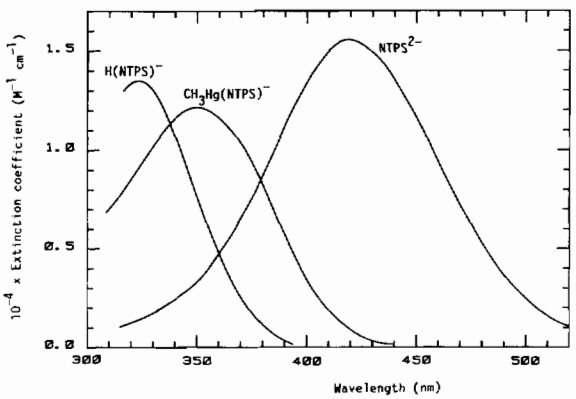


Fig. 1. Spectra of $NTPS^{2-}$, $H(NTPS)^-$ and $CH_3Hg(NTPS)^-$.

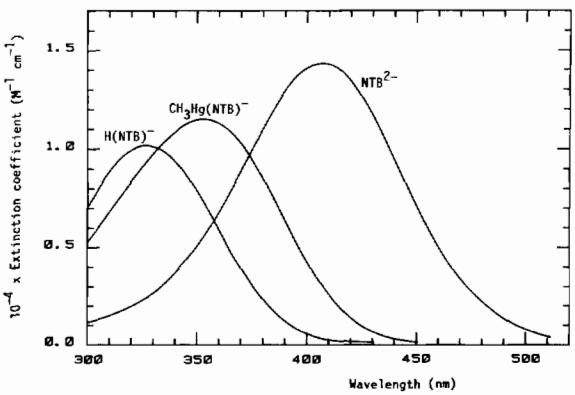


Fig. 2. Spectra of NTB^{2-}, $H(NTB)^-$ and $CH_3Hg(NTB)^-$.

photometric determination. However, with an auxiliary ligand X equilibrium (4) is established and its equilibrium constant $K(4)$ is related with $K^{Y}_{CH_3HgY}$ by eqn. (5).

$$CH_3Hg^+ + Y \rightleftharpoons CH_3HgY^+ \quad (2)$$

$$[CH_3HgY]/[CH_3Hg][Y] = K^{Y}_{CH_3HgY} \quad (3)$$

$$CH_3HgX^+ + Y \rightleftharpoons CH_3HgY^+ + X \quad (4)$$

$$K^{Y}_{CH_3HgY} = K^{X}_{CH_3HgX}K(4) \quad (5)$$

The spectra of $CH_3Hg(NTPS)^-$ and $CH_3Hg(NTB)^-$ are shown in Figs. 1 and 2. For fixed $[CH_3Hg]_t$, $[Y]_t$ and variable $[X]_t$ series of spectra were obtained with an isosbestic point. The equilibrium constant $K(4)$ was evaluated using eqn. (6).

$$K(4) = a\left(\frac{[Y]_t}{[CH_3Hg]_t - [X]_t/(1 + 1/a)} - 1\right) \quad (6)$$

$$a = \frac{A_0 - A}{A - A_\infty}$$

A = measured absorbance, A_0 = absorbance of Y, A_∞ = absorbance of CH_3HgY. The results are listed in Table 1.

Kinetic Measurements

The temperature-jump experiments were performed by means of a double-beam instrument by Messanlagen Studiengesellschaft, Göttingen, F.R.G. A high voltage capacitor of 0.05 μF loaded with 30 kV was discharged through a solution which had been thermostated at 17 °C, raising the temperature by 3 °C within 3 μs. The chemical relaxation process was monitored spectrophotometrically (between 420 and 475 nm in the alcaline and between 350 and 400 nm in the acidic range). The photographed oscilloscope curves were evaluated using an electronic simulator which produced exponential curves of variable time constant and amplitude. Parts of the relaxation experiments were done with a modified T-jump equipment which was interfaced to an HP-1000 computer through a transient recorder (Maurer, TM 110 and TM 1009, Luzern, Switzerland) [12]. In these experiments the relaxation times τ were resolved from the digital kinetic data using a non-linear least-squares fit of the first-order kinetic model (EVALU program [12]). The reported τ values are the average of four or five individual measurements. The reproducibility was typically 10% and often better.

The stopped-flow experiments were done with a Durrum D110 instrument. The absorbance change was monitored at a wavelength between 390 and 400 nm. The photographed oscilloscope curves were evaluated by using the above mentioned electronic simulator.

TABLE 1. Protonation and Methylmercuration Constants[a]

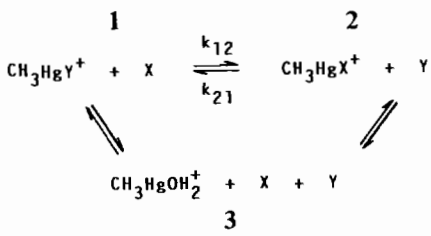
Y	pK_a	log $K(4)$ [b]	log $K^{Y}_{CH_3HgY}$ [c]
$NTPS^{2-}$	5.22(± 0.02)[d]	4.12(± 0.02)[e]	12.72(± 0.02)
NTB^{2-}	4.33(± 0.02)[f]	1.17(± 0.03)[g]	12.07(± 0.03)

[a] 20.0 °C, I = 0.1 M($NaClO_4$). [b] $K(4) = K^{Y}_{CH_3HgY}/K^{X}_{CH_3HgX}$. [c] $K^{Y}_{CH_3HgY} = [CH_3HgY]/[CH_3Hg][Y]$. [d] 6 solutions, pH 3.9–5.8. [e] 6 solutions, X = I^-, log $K^{X}_{CH_3HgX}$ = 8.60. [f] 10 solutions, pH 3.9–6.2. [g] 8 solutions, X = $S_2O_3^{2-}$, log $K^{X}_{CH_3HgX}$ = 10.90.

Results

It is well established that $CH_3Hg(II)$ transfer reactions between unidentate ligands in aqueous solution follow a mechanism according to Scheme 1 [3]. Step **1** ⇌ **2** represents the direct exchange which is governed by an associative mechanism (Ia), and **1** ⇌ **3** ⇌ **2** is the solvent pathway. As a consequence of the high stability of the thiophenolate complexes the aquaion **3** could be neglected as an intermediate by choosing appropriate concentrations (however, see ref. 8). For the direct exchange reaction the dependence of the reciprocal relaxation time on the concentrations and rate constants is given by eqn. (7) where $\delta(CH_3HgY]$ is small deviations from the equilibrium concentration. k_{12} is the rate constant for the reaction from state **1** to state **2**, and F_{12} is the concentration function for this step [13]. F_{21} is the concentration function for the same step in the reverse direction. In the general case, where also fast equilibrating side reactions are involved (e.g. protonation of X and Y), F_{12} is given by eqn. (8) [13]. For reaction systems where no side reactions are occurring the quotients $\delta[i]/\delta[CH_3HgY]$ become 1 and −1 which leads to the simple expression (9).

$$1/\tau = -(d\delta[CH_3HgY]/dt)(\delta[CH_3HgY])^{-1}$$
$$= k_{12}F_{12} = k_{21}F_{21} \quad (7)$$



Scheme 1.

$$F_{12} = [CH_3HgY]\frac{\delta[X]}{\delta[CH_3HgY]} + [X] - \frac{1}{K_{12}}\left([CH_3HgX]\frac{\delta[Y]}{\delta[CH_3HgY]} + [Y]\frac{\delta[CH_3HgX]}{\delta[CH_3HgY]}\right) \quad (8)$$

$$F_{12} = [CH_3HgY] + [X] + \frac{1}{K_{12}}([CH_3HgX] + [Y]) \quad (9)$$

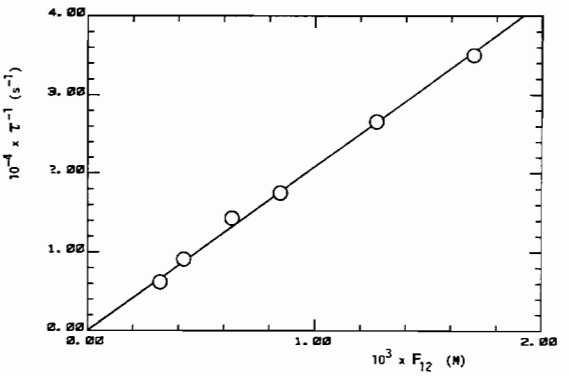


Fig. 3. Resolution of k_{12} from relaxation data for the reaction $CH_3Hg(NTPS)^- + S_2O_3^{2-} = CH_3Hg(S_2O_3)^- + NTPS^{2-}$ (plot according to eqns. (7) and (9)).

The numerical calculations were done with the program KINET [13]. A graph $1/\tau$ *versus* F_{12} yields a straight line with the slope k_{12}. With the equilibrium constant K_{12}, k_{21} is obtained. As a typical example the results for the $NTPS^{2-}/S_2O_3^{2-}$ exchange reaction are shown in Fig. 3. The experimental conditions are listed in Table 2; the resulting rate constants together with the equilibrium constants in Table 3.

For the exchange reactions with phos and NTPS no measurable relaxation amplitudes were detectable in the alcaline range. However, in pH regions below the pK_a of HNTPS the amplitudes increased as a result of the coupled protolytic equilibrium NTPS/HNTPS. With decreasing pH the relaxation times got slower. This is obviously a consequence of the decreasing $NTPS^{2-}$ concentration. For a fixed pH $1/\tau$ correlates linearly with the concentration function as seen in Fig. 4. Therefore, the evaluation was performed according to reaction Scheme 2 which allowed the possibility that $Y = NTPS^{2-}$ as well as $HY^+ = H(NTPS)^-$ can initiate the ligand-exchange reaction. Since the protonation reaction $2 \rightleftharpoons 2'$ (with its protonation constant K_{HY}^{H}) is rapid under the conditions used, the reciprocal relaxation time is given by eqn. (10). A linear least-squares analysis of the data in Fig. 5 yields the kinetic constants given in Table 3. The resulting value for $k_2'_1 = (4.7 \pm 4.4) \times 10^6$ M^{-1} s^{-1} is not significantly different from a zero intercept.

TABLE 2. Experimental Conditions: Ranges of Concentrations and Relaxation Times, I = 0.1 M $NaClO_4$, 20.0 °C

X	$[CH_3Hg]_t \times 10^4$	$[Y]_t \times 10^4$	$[X]_t$	pH	τ (μs)
$Y = NTPS^{2-}$					
Br^-	0.2–1.0	0.2–1.0	0.1–0.2	9.0	36–145
Imidazole	0.1–1.0	0.1–1.0	0.05–0.2	7.0–7.1	13–75
SO_3^{2-}	0.3–5.0	0.3–5.0	$(0.2–2) \times 10^{-2}$	8.3–8.7	35–400
I^-	0.3–5.0	0.2–5.0	$(0.2–5) \times 10^{-2}$	8.0	30
OH^-	0.5–1.0	0.48–9.7	$(0.4–3) \times 10^{-3}$	10.5–11.4	25–260
$phos^-$	0.25–1.0	0.25–1.0	$(0.25–1) \times 10^{-4}$	2.7–4.0	120–2700
$S_2O_3^{2-}$	0.19–1.0	0.2–1.05	$(0.19–1) \times 10^{-4}$	8.5	28–160
CN^-	0.1–0.4	0.5–1.0	$(0.1–0.4) \times 10^{-4}$	10.0–11.4	100–320
$Y = NTB^{2-}$					
Cl^-	0.37–2.0	0.37–2.0	0.09–0.1	1.0–2.7	900–1870
NCS^-	0.5–1.0	0.5–1.0	0.1–0.2	2.0–3.1	310–480
$S_2O_3^{2-}$	0.14–0.97	0.07–0.91	$(25–1) \times 10^{-4}$	8.0	18–175
CN^-	0.1–1.0	0.1–1.0	$(0.1–10) \times 10^{-4}$	4.9–10.3	32–1740
RS^- [a]	2.0	2.0	2.0	4.0–5.4	2400–8300

Stopped flow measurements $[CH_3Hg(NTPS)]$	$[RSH]^a \times 10^3$	pH	τ (ms)
1×10^{-5}	1.06–5.27	2.70–3.20	57–460

[a] $RS^- = HOCH_2CH_2S^-$.

TABLE 3. Rate Constants and Equilibrium Constants for the Exchange Reactions According to eqn. (1)[a]

X	k_{12} (M^{-1} s^{-1})	k_{21} (M^{-1} s^{-1})	$k_{1'2}$ (M^{-1} s^{-1})[b]	$\log K^{X}_{CH_3HgX}$ [c]	$\log K_{12}$
$Y = NTPS^{2-}$ ($\log K^{Y}_{CH_3HgY} = 12.72$)					
Br^-	$(2.8 \pm 1.4) \times 10^3$	$(3.6 \pm 1.8) \times 10^9$		6.62	−6.10
Imidazole[d]	$(1.8 \pm 0.5) \times 10^4$	$(7.0 \pm 2) \times 10^9$		7.14[e]	−5.58
SO_3^{2-} [f]	$(2.5 \pm 0.5) \times 10^4$	$(1.0 \pm 0.2) \times 10^9$		8.11	−4.61
I^-	$\sim 2 \times 10^5$ [g]	$\sim 3 \times 10^9$ [g]		8.60	−4.12
OH^-	$(3.3 \pm 0.2) \times 10^5$	$(7.3 \pm 0.5) \times 10^8$		9.37 [h]	−3.35
$phos^-$	$(9.1 \pm 0.6) \times 10^6$	$(3.5 \pm 0.2) \times 10^9$		10.14[i]	−2.58
$S_2O_3^{2-}$	$(2.1 \pm 0.2) \times 10^7$	$(1.3 \pm 0.1) \times 10^9$		10.90	−1.82
CN^- [k]	$(3.2 \pm 0.5) \times 10^8$	$(1.7 \pm 0.2) \times 10^7$		14.00	1.28
RS^- [l]	$(1.4 \pm 0.2) \times 10^9$	$(5.6 \pm 0.8) \times 10^5$	$(1.2 \pm 0.3) \times 10^3$	16.12	3.40
X	k_{12} (M^{-1} s^{-1})	k_{21} (M^{-1} s^{-1})	$k_{2'1}$ (M^{-1} s^{-1})[m]	$\log K^{X}_{CH_3HgX}$ [c]	$\log K_{12}$
$Y = NTB^{2-}$ ($\log K^{Y}_{CH_3HgY} = 12.07$)					
Cl^-	$(7.9 \pm 0.8) \times 10^2$	$(4.9 \pm 0.5) \times 10^9$	$(4.4 \pm 1) \times 10^6$	5.25	−6.82
NCS^-	$(1.8 \pm 0.2) \times 10^3$	$(1.8 \pm 0.2) \times 10^9$	$(1.3 \pm 0.4) \times 10^7$	6.05	−6.02
$S_2O_3^{2-}$	$(6.7 \pm 0.7) \times 10^7$	$(1.0 \pm 0.1) \times 10^9$		10.90	−1.17
CN^- [k]	$(1.2 \pm 0.2) \times 10^9$	$(1.4 \pm 0.2) \times 10^7$		14.00	1.93
RS^- [l]	$(1.7 \pm 0.4) \times 10^9$	$(1.5 \pm 0.3) \times 10^5$		16.12	4.05

[a] I = 0 1 M 20.0 °C. [b] Scheme 3. [c] Ref. 14 unless otherwise stated. [d] pK_a = 7.10. [e] Ref. 15. [f] pK_a = 6.79. [g] Approximate value (very small relaxation amplitude). [h] pK_w = 13.96. [i] Ref. 16. [k] pK_a = 9.14. [l] RS^- = $HOCH_2CH_2S^-$; pK_a = 9.52. [m] Scheme 2.

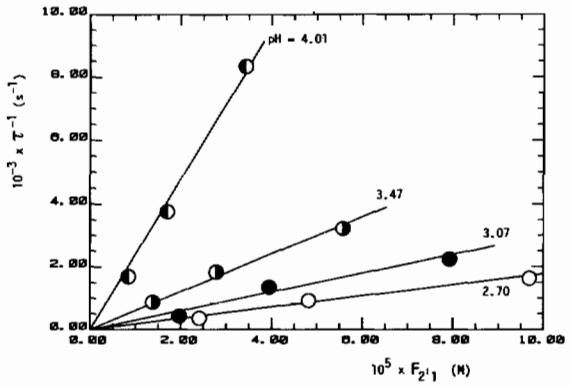


Fig. 4. Relaxation data for the reaction $CH_3Hg(phos) + H(NTPS)^- = CH_3Hg(NTPS)^- + phos^- + H^+$ at different pH values.

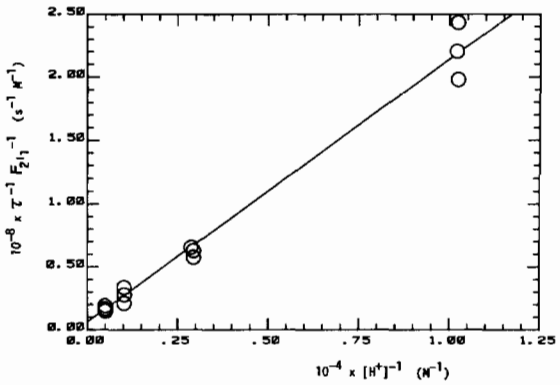
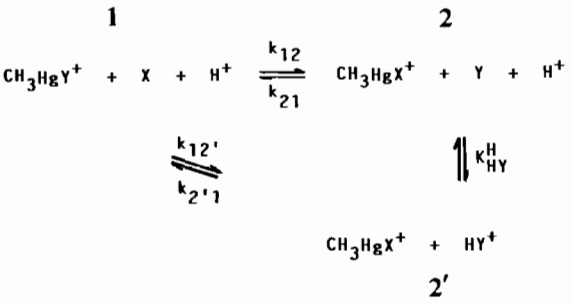


Fig. 5. Resolution of k_{21} from relaxation data for the reaction $CH_3Hg(phos) + NTPS^{2-} = CH_3Hg(NTPS)^- + phos^-$ (plot according to eqn. (10)).



Scheme 2.

$$1/\tau = k_{21}^{obs} F_{21} = (k_{2'1} + k_{21}/K^{H}_{HY}[H])F_{2'1} \qquad (10)$$

with $F_{2'1} = F_{21} K^{H}_{HY}[H]$

Therefore, it is not possible to decide whether or not $H(NTPS)^-$ can initiate directly the ligand-exchange reaction, only an upper limit can be given ($< 4 \times 10^6$ M^{-1} s^{-1}). However, evidence for direct reaction with the protonated S-donor was found in the reaction system for $Y = NTB^{2-}$ and $X = Cl^-$ and NCS^-. In the pH range above the pK_a of HNTB the equilibrium position is strongly in favor of the $CH_3Hg(NTB)^-$ complex ($\log K_{12} = -6.82$ for Cl^- and −6.02 for

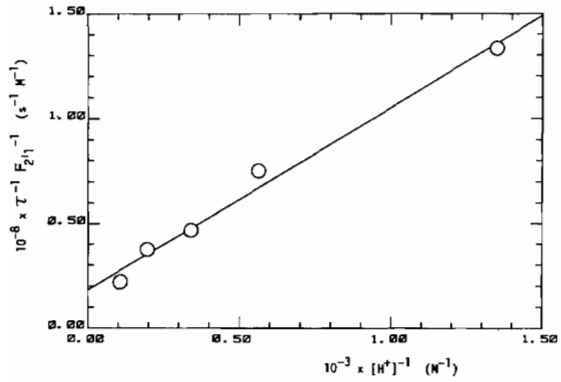


Fig. 6. Resolution of k_{21} and $k_{2'1}$ from relaxation data for the reaction $CH_3Hg(SCN) + NTB^{2-} = CH_3Hg(NTB)^- + SCN^-$ (plot according to eqn. (10)).

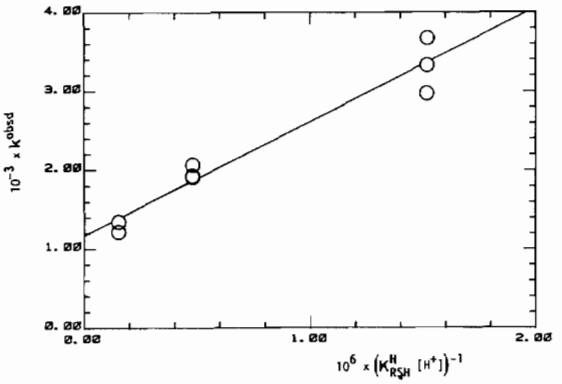
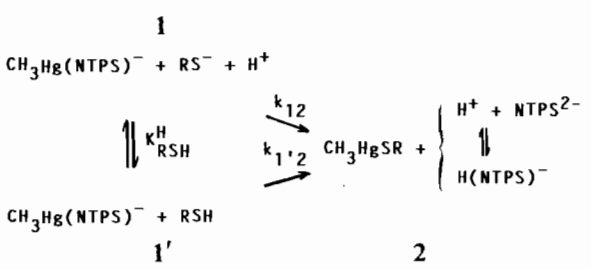


Fig. 7. Resolution of k_{12} and $k_{1'2}$ from stopped-flow data for the reaction $CH_3Hg(NTPS)^- + RSH = CH_3HgSR + H(NTPS)^-$ (plot according to eqn. (11)).

NCS^-). Therefore, no relaxation effect was detectable. In strongly acidic solutions the equilibria could be shifted in such a way that relaxation times were measurable without difficulties. The evaluation was based on Scheme 2 and eqn. (10). Figure 6 shows the results for NCS^-. From the slope one gets $k_{21} = (1.8 \pm 0.2) \times 10^9$ M^{-1} s^{-1} and from the intercept $k_{2'1} = (1.8 \pm 0.4) \times 10^7$ M^{-1} s^{-1}. The system NTB/Cl was evaluated similarly.

In the reaction system with $Y = NTPS^{2-}$ and $X = RS^-$ (RSH = mercaptoethanol) no measurable relaxation effect could be obtained in neutral and alkaline regions. In the acid range experimental conditions could be applied which moved the half-life of the reaction in the time range of the stopped-flow method. With excess of RSH at fixed pH values linear non-zero intercept correlations were obtained. With increasing pH the slope increases. From this behaviour one could postulate Scheme 3 which is analogous to Scheme 2. Accordingly, k^{obs} shows two terms as given in eqn. (11). A linear least-squares analysis of the data in Fig. 7 yields the kinetic constants, from the slope $k_{12} = 1.4(\pm 0.2) \times 10^9$ $M^{-1} s^{-1}$ and from the intercept $k_{1'2} = 1.2(\pm 0.3) \times 10^3$ $M^{-1} s^{-1}$.

$$1/\tau = k^{obs}[RSH] = (k_{1'2} + k_{12}/K^H_{RSH}[H])[RSH] \quad (11)$$



Scheme 3.

Discussion

The high stability of the $CH_3Hg(II)$ complexes with the nitrothiophenolate ligands $NTPS^{2-}$ and NTB^{2-} is in excellent agreement with the earlier established LFER between $\log K^X_{CH_3HgX}$ and pK_a of HX [3] which spans now 20 logarithmic units in $\log K^X_{CH_3HgX}$ between thiodiethylsulfonate ($\log K = 1.91$ [17]) and S^{2-} ($\log K = 21.0$ [14]). The transfer of $CH_3Hg(II)$ between the S-donating ligands $NTPS^{2-}$ and NTB^{2-} and a series of representative unidentate ligands X belong to the fastest ligand-exchange reactions at metal centers. This can be clearly seen from the Eigen-type plot of $\log k_{12}$ and $\log k_{21}$ *versus* $\log K_{12}$ in Fig. 8. The full line shows the rate– equilibria correlation which is expected for diffusion-controlled reactions taking into account the charge asymmetry for the forward and reverse reaction (12) [18].

$$CH_3Hg(NTPS)^- + X^- \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} CH_3HgX + NTPS^{2-} \quad (12)$$

For neutral X the maximum values for $\log k_{12}$ and $\log k_{21}$ are bigger whereas for X^{2-} these values are smaller as indicated in Fig. 8. To our knowledge, this is the first time that for any metal ion a rate–equilibria correlation for exchange reactions with unidentate ligands could be established over such a wide range: 11 orders of magnitude for equilibrium constants and 7 orders of magnitude for rate constants. The correlation of these various different ligands with the maximum values for $\log k$ over the whole $\log K_{12}$ range is remarkable. It is surprising that even in the isergonic region the exchange reactions are almost diffusion controlled. This extreme lability is all the more interesting because these thiophenolate complexes are 2–4 orders of magnitude more stable than the thione complexes for which similar rate–equilibria correlations were found [1]. Obviously

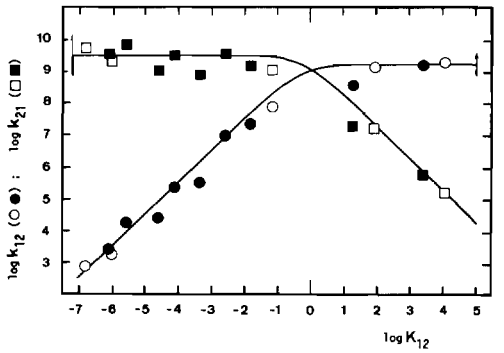
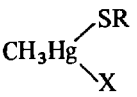


Fig. 8. log k *vs.* log K-dependence for $CH_3Hg(II)$ transfer reactions. Y = $NTPS^{2-}$, log k_{12} (●), log k_{21} (■). Experimental points refer to the following X, from left to right: Br^-, imidazole, SO_3^{2-}, I^-, OH^-, $phos^-$, $S_2O_3^{2-}$, CN^-, RS^-. Y = NTB^{2-}, log k_{12} (○), log k_{21} (□). Experimental points refer to the following X, from left to right: Cl^-, SCN^-, $S_2O_3^{2-}$, CN^-, RS^-. The full lines correspond to diffusion-controlled reactions for the (0/−2) and −1/−1) charged reactants. The arrows indicate the displacement of the maximum rates for different charge types.

$CH_3Hg(II)$ is very mobile within the transition state complex.



As for ligands X besides S-donors halides, amines, and phosphines are also capable of following such an ideal associative reaction path. Less favourable are C-donors [4] and OH^- [3]. For ligand-substitution reactions of CH_3HgOH with a whole series of ligands the correlation between rate and equilibria could be described with a Marcus-type equation for atom-group transfer with an intrinsic barrier $\Delta G_0^{\neq} = 7$ kcal/mol [1]. It is interesting to note that the rate for the reaction of CH_3HgOH with $NTPS^{2-}$ ($\log k_{21} = 8.87$) is clearly below the maximum rate although the reaction is rather exergonic ($\log K_{21} = 3.35$). This kinetic behaviour is consistent with the above mentioned intrinsic barrier for substitution reactions with OH^- and fits very well in the reaction series as described elsewhere [1].

It is not quite clear if the deviation of the CN^-/$NTPS^{2-}$ system ($\log k_{12} = 8.51$, $\log K_{12} = 1.28$) reflects a certain intrinsic barrier which is involved with CN^-. On the other hand, the corresponding $CH_3Hg(II)$-transfer reaction from NTB^{2-} to CN^- ($\log k_{12} = 9.08$, $\log K_{12} = 1.93$) is not significantly retarded. To clarify this result, we have reinvestigated the stability of CH_3HgCN by means of the spectrophotometric method analogous to that as described in 'Experimental'. Using NTPS as an auxiliary ligand we got $\log K^{CN}_{CH_3HgCN} = 13.92$ which is within the error limit as given by Schwarzenbach and Schellenberg [14] who used the pHg method.

The rate equilibria relationships for $CH_3Hg(II)$-transfer reactions from and to nitrothiophenolates together with those found for the thiones 1-methylpyridine-2-thione and 1-methylquinaldine-4-thione [1] demonstrate clearly that the vast majority of $CH_3Hg(II)$ complexes are extremely labile. It is possible now to reliably predict rate constants from equilibrium constants (and vice versa). The identification of the elementary steps as well as their course in time is an important prerequisite for the understanding of the detailed mechanisms of $CH_3Hg(II)$-transport processes in biological systems. These elementary steps are also relevant for the characterization of $CH_3Hg(II)$-catalyzed reactions.

Reactivity of Protonated Ligands

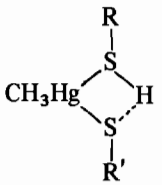
Protonated imidazole cannot directly initiate the ligand exchange; this is obviously a consequence of the distribution of the electron density in the aromatic ring. In the case of HCN one cannot exclude that it may react in a first step with the N atom. However, in the present study we did not find any indication that HCN can initiate the ligand-substitution reaction. Obviously protonated S-donor ligands show some nucleophilic reactivity towards Hg^{II} corresponding to the available electron density. In a stopped-flow study Hasinoff *et al.* [19] found that *p*-chloromercuribenzoate reacts with the deprotonated (RS^-) as well as with the protonated form (RSH) of mercaptoethanol. Rabenstein and Reid [6] in a ^1H NMR study investigated the pH dependence of thiol-exchange reactions with CH_3-Hg(II) complexes. Their main conclusion is that under physiological pH conditions ligand-exchange reactions take place predominantly with the thiol-deprotonated forms, although in the acidic range the protonated forms show a certain reactivity. At pH < 1 an additional pathway was found, namely a proton-assisted dissociation of the complex which is followed by the reaction of the free thiol with CH_3Hg^{II}. Under our experimental conditions (at pH > 1) no indication for such proton-assisted dissociation was found. As for the different reactivities of thiols in the protonated and deprotonated forms our study revealed some interesting new information. The efficiency of the protonated S-donors $H(NTPS)^-$, $H(NTB)^-$ and RSH in initiating ligand-substitution reactions is strongly dependent on the nature of the ligand to be displaced.

In Scheme 2 one may interpret step $2' \rightleftharpoons 1$ in terms of a two-step mechanism (13), in which $2' \rightarrow 1'$ represents the rate-determining step, and the protolytic equilibrium $1' \rightleftharpoons 1$ is fast established. With the experimental value of $k_{2'1}(= k_{2'1'})$ and $k_{1'2'} = 2 \times 10^9$ M^{-1} s^{-1} (taken from the diagram in Fig. 8) one obtains the complex stability of CH_3-

$$CH_3HgX + HY \underset{k_{1'2'}}{\overset{k_{2'1'}}{\rightleftharpoons}} \underset{2'}{CH_3Hg(HY)^+} + X^- \underset{k_{11'}}{\overset{k_{1'1}}{\rightleftharpoons}} \underset{1'}{} \quad CH_3HgY + X^- + H^+ \quad (13)$$

$$\underset{1}{}$$

Hg(HY). For $X = Cl^-$ and $Y = NTB^{2-}$ one gets $\log K^{HY}_{CH_3HgHY} = 2.6$. This is plausible if one assumes that a complex with a protonated S-donor has a stability which is similar to that with a thioether ligand. With thiodiglycol the stability for the CH_3-Hg(II) complex is $\log K = 3.38$ [20], and with thiodiethylsulfonate, $\log K = 1.91$ [17]. It is interesting to note that Hasinoff *et al.* [19] found that for the exchange reaction of *p*-chloromercuribenzoate with RS^- and RSH the rate constants are $k_{21} = 7.5 \times 10^9$ M^{-1} s^{-1} and $k_{2'1} = 6.5 \times 10^6$ M^{-1} s^{-1}, respectively. If one interprets the latter rate constant in terms of eqn. (13) the stability of the corresponding mercuribenzoate complex with RSH is very similar ($\log K \approx 2.6$) to that of $CH_3Hg(HSR)$. This shows that the suggested two-step mechanism is reasonable. However, for the analogous reaction system CH_3HgSCN/RSH a slightly too high $\log K$ value (= 3.8) is calculated. This indicates that for this system eqn. (13) is not quite appropriate. An even more pronounced discrepancy arises from the system $X = NTPS^{2-}/Y = RS^-$. With $k_{2'1} = k_{2'1'} = 1.2 \times 10^3$ M^{-1} s^{-1} one gets $\log K^{HY}_{CH_3HgHY} = 6.4$ which is certainly too big a value compared to that of 2.6 which is calculated for the *p*-mercuribenzoate complex with the same HY. A reasonable (smaller) stability constant would result only if one would insert a $k_{1'2'}$ value which is several orders of magnitude above the diffusion-controlled limit. This shows clearly that for such reaction systems where an S-donor ligand $R'S^-$ is displaced by another protonated S-donor RSH, eqn. (13) is no longer valid. Obviously, another type of intermediate occurs. An attractive possibility for such an intermediate or transition state in the course of an energetically more favourable reaction path would be a bridged complex.



Here the ligand-substitution is concerted with an intramolecular-proton transfer. A protonated leaving group is more weakly bound and would explain the higher rate for ligand exchange. An intramolecular H^+ transfer of this type is plausible if one considers the fact that H^+-transfer reactions from and to NTPS are kinetically not favourable [21]. A four-center bridge complex was postulated by Bach and Weibel [22] for reactions of $CH_3Hg(II)$ complexes in non-aqueous solutions. Thus it appears that two pathways are possible if ligand-exchange is initiated by a protonated S-donor ligand. In cases where aprotic ligands like Cl^- have to be displaced, eqn. (13) is an appropriate description. When S-donor ligands have to be displaced, the reactivity of an incoming protonated S-donor will be enhanced if a concerted mechanism via the bridged complex is followed. It is to be expected that under physiological conditions such concerted thiol-displacement reactions are important for $CH_3Hg(II)$-transfer reactions.

Acknowledgement

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