

Electron Transfer Reactions in Organic Chemistry. XIV.* The Reactivities of Some Polyhaloalkanes toward the Outer-Sphere Electron Transfer Reductants Co(II)sepulchrates²⁺ and Co(II)W₁₂O₄₀⁷⁻

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Rates were measured for the title reactions in CH₃CN/H₂O buffered at pH ~ 7 at 20 or 50 °C. The following order of reactivity toward Co(II)W₁₂O₄₀⁷⁻ was found: CBr₄ > (CBrCl₂)₂ > CBr₂Cl₂ > C₂Cl₆ > CBrCl₃ > CF₃CHClBr > CHBr₃ > CCl₄. Only CBr₄, (CBrCl₂)₂, CBr₂Cl₂ and CBrCl₃ gave measurable rates of reaction with Co(II)sepulchrates²⁺, and with the same order of reactivity as above. For these four substrates, a plot of log *k*_{ET}[Co(II)W₁₂O₄₀]⁷⁻ vs. log *k*_{ET}[Co(II)sepulchrates]²⁺ had a slope close to 1. Qualitative product studies for the reactions with Co(II)W₁₂O₄₀⁷⁻ showed that the polyhalomethanes generally reacted by losing their heaviest halogen, while the polyhaloethanes formed ethylenes by losing their heaviest halogen on each carbon atom. For some of the reactions, the intermediate radical formed in the first step could be trapped by *N*-*t*-butyl- α -phenylnitron. The resulting spin adducts were detected by ESR spectroscopy. It is argued that the rate constant difference between CBr₄ and CBrCl₃ supports the notion of a very short-lived intermediate anion radical.

Many reactions with simple alkyl halides, which in standard textbooks of organic chemistry (see, e.g., Ref. 1) are described as proceeding through polar mechanisms, have recently been claimed to proceed *via* an outer-sphere electron transfer (hereafter denoted ET) pathway.² Even though this has been questioned in some cases,³ there seems to be little doubt that alkyl halides sometimes do react by ET.⁸ Within the framework of the Marcus theory there have appeared estimates of their standard potentials and reorganization energies.⁵

Polyhalogenated alkanes have also been studied extensively in this respect, as they should be more prone to undergo ET reactions. Another important feature of these substrates is that their

radical anions might have some stability,⁶ in contrast to those of the simple alkyl halides.⁷ Thus, claims of ET reactions with polyhaloalkanes have been made⁸ and challenged,⁹ and even their toxicity[†] has been proposed to be the result of an ET reduction by cytochrome P-450. It should therefore be of interest to obtain a more quantitative picture of their ET reactivities.

In two previous articles, we have investigated the reactions of carbon tetrabromide with the heteropoly blue Co(II)W₁₂O₄₀⁷⁻ ‡ and the macrocyclic complex Co(II)sepulchrates²⁺ ^{11,Δ} (here, we introduce the abbreviations CoW⁷⁻, CoW⁶⁻ and Co(II)sep²⁺ for Co(II)W₁₂O₄₀⁷⁻, Co(II)W₁₂O₄₀⁶⁻

†For reviews, see, e.g., Ref. 6 in Ref. 10.

‡For a discussion of Co(II)W₁₂O₄₀⁷⁻, see Ref. 10 and references therein.

ΔFor a discussion of Co(II)sepulchrates²⁺, see Ref. 11 and references therein.

*Part XIII, see Ref. 10.

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§For recent reviews, see Ref. 4.

and Co(II)sepulchrate²⁺, respectively). We found them to be well-behaved ET reactions. This paper reports an extension of the investigation to other polyhaloalkanes which provides additional evidence (ESR) for the ET nature of these reactions.

Experimental

Instrumentation. A Cary 219 UV/VIS spectrophotometer was used for the kinetic measurements. A Finnigan 4021 mass spectrometer operating at 19 eV was used for recording the mass spectra. Varian 1400 and 3300 gas chromatographs together with the columns indicated in Table 1 were used for GLC analysis. ESR spectra were recorded on a Bruker ER-200D SRC instrument.

$K_3HCo(II)W_{12}O_{40} \cdot 15H_2O^{12}$ and $[Co(III)sepulchrate]Cl_3^{13}$ were prepared according to the literature procedures. The preparation of the heteropoly blue and Co(II)sep²⁺ solutions has been described elsewhere,^{10,11} except for the following modification: the solution of CoW⁶⁻ to be cathodically reduced was deaerated outside the cell and thereafter transferred to the deaerated electrolysis cell, whereupon the reduction was immediately started. This procedure avoided the problems associated with precipitation that might occur if the solution were deaerated in contact with the Hg cathode.

Chemicals. Carbon tetrabromide (Fluka *purum*), 1,2-dibromotetrachloroethane (Janssen) and hexachloroethane (Riedel de Haen) were all sublimed under reduced pressure. Bromotrichloromethane (Janssen Gold Label) was distilled through a Fischer Spaltrohr column (~20 theoretical plates). Dibromodichloromethane (Alfa Ventron) was shaken with 5 M NaOH and then three times with water; after each washing the two-phase system was cooled to ca. 10°C, whereupon the CBr₂Cl₂ crystallized and the water phase could be removed. Carbon tetrachloride (Riedel *p.a.*) and bromoform (Aldrich Gold Label, stabilized with 1% ethanol) were used without further purification. Halothane (ISC Chemicals Ltd., stabilized with thymol) was either passed through neutral alumina alone, or subsequently shaken with diluted NaOH, three times with water and finally distilled. *N-t*-Butyl- α -phenylnitron (Janssen) was used as received. The solvents were doubly quartz-distilled water and Riedel Pestanal acetonitrile. All other chemicals were of highest commercial purity and were used as received.

Product and kinetic studies. All solutions were deaerated with argon (<5 ppm O₂) and protected from the atmosphere. The procedures have been described elsewhere.^{10,11} The polyhaloalkane solutions were kept in the dark.

Product studies with the heteropoly blue were performed as follows. To a solution of 40 ml of

Table 1. Product studies with CoW⁷⁻ and polyhaloalkanes in CH₃CN/H₂O (40/60, v/v), 2 mM NaClO₄, 10 mM TRIS, 7 mM HClO₄ and 2 mM CoW⁷⁻.

Substrate	Conc./mM	T/°C	Products (yield/%)	Identified by m/z (% rel. int.)
CBrCl ₃	50	20	CHCl ₃ ^b (72)	83(100), 85(65), 87(10), 118(1), 120(1), 122(1)
			CHBrCl ₂ ^{a,b} (<1)	161(9), 163(15), 165(7), 167(1)
			C ₂ Cl ₆ ^b (2)	199(66), 201(100), 203(63), 205(20), 207(3)
CCl ₄	20	50	CHCl ₃ ^b	83(100), 85(60), 87(11)
CHBr ₃	20	50	CH ₂ Br ₂ ^c	172(61), 174(100), 176(56)
(CBrCl ₂) ₂	4	20	C ₂ Cl ₄ ^c	Retention time
C ₂ Cl ₆	6	20	C ₂ Cl ₄ ^c	164(82), 166(100), 168(53), 170(13), 172(1)
CF ₃ CHClBr	20	20	CF ₃ CH ₂ Cl ^d	83(72), 99(16), 101(5), 118(100), 120(32)
			CF ₂ CHCl ^d	98(100), 100(32)

^aThis is possibly only a breakdown product of CBrCl₃ in the GC/MS system. ^bAnalyzed on a Superox 30 m × 0.25 mm capillary column. ^cAnalyzed on a J and W DB-1 15 m × 0.53 mm Megabore column. ^dAnalyzed on a Poropak P 80/100 mesh 2 m stainless steel column.

Table 2. Rate constants for the reactions between polyhaloalkanes, and CoW^{7-} and Co(II)sep^{2+} in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ (64/36, v/v).

Substrate	CoW^{7-} ^a			Co(II)sep^{2+} ^b		
	Conc./mM	T/°C	k/M ⁻¹ s ⁻¹	Conc./mM	T/°C	k/M ⁻¹ s ⁻¹
CBr_4	1.6–16	20	1.1 ^c	20–120	20	0.020 ^d
CBr_4	1.6	50	12	20.6	50	0.16
$\text{C}_2\text{Br}_2\text{Cl}_4$	4.9	20	0.30	19.1	50	0.089
CBr_2Cl_2	57	20	0.053	89	50	0.014
C_2Cl_6	25	20	0.028	60	50	TS ^e
CBrCl_3	110	20	0.0145	110	50	0.0050
CF_3CHClBr	101	20	~0.005	108	50	TS ^e
CHBr_3	157	50	0.0068	156	50	TS ^e
CCl_4	180	50	0.0029	188	50	TS ^e

^a0.2 mM CoW^{7-} , 0.7 mM HClO_4 , 2 mM NaClO_4 , 1 mM TRIS. ^b1.8 mM Co(II)sep^{2+} , 9.1 mM NaClO_4 , 3.6 mM HClO_4 , 36 mM TRIS. ^cFrom Ref. 102. ^dFrom Ref. 11. ^eTS = Too slow, see text.

50/50 (v/v) $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ containing the appropriate amount of polyhaloalkane (Table 1) was added 10 ml of a solution of 10 mM CoW^{6-} in water reduced with about 0.9 F per mol, plus buffer and electrolyte. The reaction was performed either in a closed vessel (rubber septum), necessary when performing gas-phase analysis, or in a vessel protected by a slow stream of argon. After completion of the reaction it was worked up with 3×5 ml of dichloromethane, pentane or carbon disulfide. Internal standard, when used, was added in the first portion. The combined organic phases were washed twice with water, and a small portion was saved for quantitative or semi-quantitative analysis while the rest was concentrated by gentle evaporation. When analyzing the gaseous products from the halothane reaction, 1 ml of the total gas volume in the reaction vessel (ca. 10 ml) was withdrawn. The products were analyzed by GLC or GLC/MS and were identified by their mass spectra or, in some cases, by their retention times alone.

The kinetics of reactions with Co(II)sep^{2+} as reductant were performed as follows: Two ml of a solution of Co(II)sep^{2+} plus buffer and electrolyte in 60% acetonitrile (Table 2) in a cuvette were thermally equilibrated in the thermostatted cell compartment of the spectrophotometer and the reaction was started by the addition of 0.2 ml of a solution of polyhaloalkane in acetonitrile.

For the heteropoly blue runs, 2 ml of polyhaloalkane solution were thermally equilibrated

and 0.2 ml of heteropoly blue solution plus buffer and electrolyte in water was added. When the reaction was run at 50°C it was necessary to use a faster procedure. The polyhaloalkane solution was then first pre-equilibrated under a slow stream of argon in a water-bath at 50°C for ca. 10 min, and thereafter placed in the thermostatted compartment for a few min. With this procedure the time for oxygen to diffuse into the cuvette before the onset of the reaction was reduced by more than 20 min. The reactions were followed at 474 nm [Co(II)sep^{2+}] and 640 nm (CoW^{7-}), 200 data points being automatically collected at regular intervals and stored on magnetic tape. This was performed by an HP-85 computer equipped with a digital interface port connected to the spectrophotometer. The data set was then analyzed with an HP-9835 table-top computer by the non-linear regression method developed by Marquadt.¹⁴

ESR studies. The spin-trap reactions with CoW^{7-} as reductant were performed with the same solutions and concentrations as used in the product runs, but with 0.20 M *N-t*-butyl- α -phenylnitron (PBN) added as a spin trap. When Co(II)sep^{2+} was used as a reductant, 0.1 ml of an aqueous solution containing 1 mM Co(II)sep^{2+} , 200 mM TRIS, 20 mM HClO_4 and 50 mM NaClO_4 was mixed with 0.4 ml of a 0.25 M PBN solution in acetonitrile containing the appropriate amount of substrate. After completion of the reaction, the

reaction mixture was transferred to a standard quartz tube, flushed with argon and thereafter protected from air by a rubber septum. The spectra were recorded at 22°C.

Results

The kinetics of the reactions with Co(II)sep^{2+} were first-order in Co(II)sep^{2+} and the experimental curves were fitted well by eqn. (1), where A_∞ (A = absorbance) and k_{obs} were the adjustable parameters. A_0 was taken directly from the experiments. The symbols have their usual meanings. The first 20 points in each run were dis-

$$A = A_0 + (A_\infty - A_0) \exp(-k_{\text{obs}} t) \quad (1)$$

carded in order to ensure that thermal equilibrium had been reached.

For Co(II)sep^{2+} , unpurified substrates in fact gave the same results as the purified ones. The uncertainty in the rate constants was estimated to be about $\pm 10\%$. The reactions were too slow to permit calculation of rate constants for CCl_4 , CHBr_3 , CF_3CHClBr and C_2Cl_6 , since it was difficult to assess how much of the reaction that did occur was due to slow oxygen diffusion into the cell.

The kinetics were much more sensitive to impurities when the more reactive CoW^{7-} was used as reductant, and even after purification of the substrates the results were not as reproducible as

with Co(II)sep^{2+} . The polyhalomethanes showed more reproducible kinetics the more reactive they were, with an uncertainty in k_{obs} of 10–20% for the respective reactions. However, when we used a standard linear evaluation method for one of the runs which gave the worst fit to the non-linear regression [eqn. (1)], we obtained a line with hardly discernible curvature and a correlation coefficient of 0.998. The rate constant thus calculated was the same as that obtained using the non-linear method. This comparison with the standard first-order kinetic analysis lends credence to an interpretation of these reactions as first-order in CoW^{7-} .

The polyhalogenated ethanes were less well-behaved than the methanes, and thus the reactions with $\text{C}_2\text{Br}_2\text{Cl}_4$ and C_2Cl_6 were fitted well by eqn. (1) only after excluding data for the first half-life of the reactions. Attempts to fit the whole data set to a three-parameter equation¹⁵ allowing for back electron transfer were only slightly more successful than allowing A_0 to be a third adjustable parameter in eqn. (1). Thus, a reversible ET step was not considered probable, at least not to the extent of affecting the kinetics. The reproducibility of the rate constant was poor but acceptable, about $\pm 30\%$. For halothane the situation was reversed. The experimental curves were fitted well by the two-parameter version of eqn. (1), but the calculated rate constants varied by a factor of four. It was checked that this was not due to evaporation of the highly volatile ha-

Table 3. ESR parameters for the spin adducts with PBN. For experimental parameters, see text.

Reductant	Substrate	Solvent	Type of signal	a^{H}/G^a	a^{N}/G^b
CoW^{7-}	CBr_4	40% AN	Triplet (+ quartet)	—	14.97
	CCl_4	40% AN	Triplet of doublets	2.25	14.75
	CF_3CHClBr	40% AN	Triplet of doublets	2.67	
15.37					
Co(II)sep^{2+}	CBr_4	80% AN	Triplet (+ quartet)	—	14.97
	CBrCl_3	80% AN		2.01	14.51
Cathode ^c	CBr_4	100% AN	Triplet ^d	—	14.32
	CBrCl_3	100% AN	Triplet of doublets	1.84	14.23
	CCl_4	100% AN	Triplet of doublets	1.87	14.19
	CF_3CHClBr	100% AN	Triplet of doublets	2.16	14.68
None (light) ^e	CBr_4	40% AN	Quartet	—	14.16

^aCoupling with β -hydrogen, see text. ^bCoupling with aminoxyl nitrogen, see text. ^cFrom Ref. 17. ^dPossibly also a quartet, see text. ^eWith CoW^{6-} , see text.

lothane during the deaerating procedure. The geometrical mean of the two extreme values of the rate constants is given in Table 1, but should be regarded as very preliminary. To make the results for the different reactions more comparable, all rate constants for reactions with CoW^{7-} in Table 2 were calculated after discarding data for the first half-life of the reaction.

Product studies were carried out with CoW^{7-} as reductant. The experimental parameters and results are given in Table 1. Except in the case of CBrCl_3 , the product studies are qualitative in nature, and only rough estimates of the amounts of products were made to see whether they were in agreement with the reaction schemes outlined in the Discussion section. Furthermore, the high substrate-to-reagent ratio in the kinetic runs, sometimes amounting to 10^3 , made it necessary to establish that the observed kinetics were not attributable to reaction with impurities present in the substrate. It should be emphasized that possible dimerization products would probably be found only in yields near the detection limit, and that any polyhalobutane formed would probably not pass unchanged through any GLC column available. The close relationship between the reactions of CoW^{7-} and Co(II)sep^{2+} , respectively, with carbon tetrabromide, seen on comparing the two previous papers,^{10,11} and the uncomplicated kinetics for the reactions between Co(II)sep^{2+} and the other polyhaloalkanes in this study made complementary product studies with Co(II)sep^{2+} unnecessary.

The results of the spin-trap experiments are



Fig. 1. ESR spectrum obtained in the reduction of CCl_4 with CoW^{7-} in the presence of PBN.

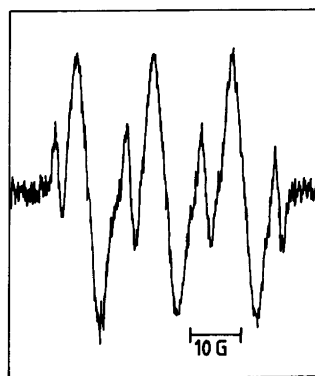
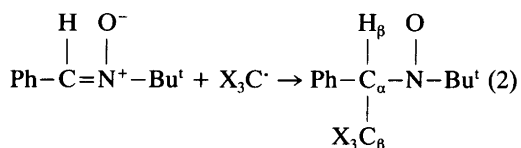
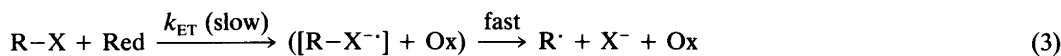


Fig. 2. ESR spectrum obtained in the reduction of CBr_4 with CoW^{7-} in the presence of PBN.

listed in Table 3. It can be seen (Fig. 1) that a triplet of doublets was obtained for all substrates except CBr_4 . This could be explained on the basis of radical addition to the α -carbon [eqn. (2)], which is the normal way for nitrones to react with radicals.¹⁶ The aminoxyl nitrogen splits the signal into three lines which are further split into two lines each by the β -hydrogen [eqn. (2)]. The signals are further broadened by coupling with the halogens on the β -carbon. In the case of CBr_4 , this broadening engulfed the doublets so that only the nitrogen splitting could be seen. The results are consistent with those obtained for cathodic reduction of the polyhalo compounds in the presence of PBN,¹⁷ which are also listed in Table 3. However, our CBr_4 experiments also gave rise to a quartet (Fig. 2) which slowly diminished with time. This quartet was also found as a weak but clear signal in a control experiment in which all the chemicals used in the CoW^{7-} reaction with CBr_4 were mixed, except that CoW^{7-} was exchanged for the non-reducing CoW^{6-} and exposed to laboratory light for 30 min. No signal due to the normal spin adduct was found. The spectrum obtained by Stronks¹⁷ for the cathodic reduction of CBr_4 was badly resolved, but was very similar to our spectra before they were resolved by spectral accumulation.





Scheme 1.

Discussion

We have previously studied the reactions between CBr_4 , and Co(II)sep^{2+} and CoW^{7-} , respectively.^{10,11} Both reactions were found to follow Scheme 1, with the first step rate-determining. Here, RX is CBr_4 and Red is Co(II)sep^{2+} or CoW^{7-} . Almost all of the tribromomethyl radical produced in the first step was further reduced to the corresponding anion. On applying the steady-state assumption to $[R^{\cdot}]$ we obtain the rate law given by eqn. (7).

$$v = 2k_{\text{ET}} [\text{RX}][\text{Red}] \quad (7)$$

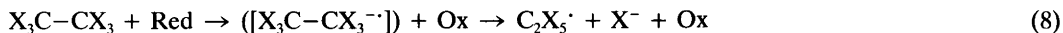
found only for halothane (CF_3CHClBr). This can

There is no reason to assume that the other polyhalomethanes employed in this study would react differently. Their structures are very similar and they are known to be electrochemically reduced via the same mechanism;¹⁸ furthermore, in all cases the radicals should be easier to reduce than their parent compounds. Thus, as seen in Table 1, only products consistent with Scheme 1 were found.

For the polyhaloethanes, the same rate law applies but a somewhat different mechanism (Scheme 2) is used to explain the products obtained. Here, no evidence was found for dimer-

ization or H atom abstraction but this does not rule out the possibility that they might play a minor role. Products from reaction (11) were be rationalized by the higher bond strength of the C-F bond than those of the C-Cl and C-Br bonds, making reaction (10) slow enough for the protonation to compete successfully in the haloethane case.

The spin-trap studies provide evidence for the formation of intermediate radicals in the case of the most and least reactive substrates, respectively, for both Co(II)sep^{2+} and CoW^{7-} . We also trapped a radical in the kinetically troublesome reaction between CoW^{7-} and halothane. Comparison with the products formed in each reaction shows that the radical trapped must be the parent compound minus its heaviest halogen atom. This is further confirmed by comparison with the spectra obtained by Stronks¹⁷ following *in situ* electrolysis of the polyhaloalkanes in the presence of the spin trap (Table 3). Unfortunately, we are not able to assign the extra quartet in the spectra obtained with CBr_4 as substrate. We note, however, that it seems to be present also in the unresolved spectrum obtained by Stronks, and that we find it as a weak signal in the control experiment in the absence of reductant (see Results). This presumably means that it is the result of a direct reaction between CBr_4 and the spin trap



Scheme 2.

(possibly catalyzed by light and/or by a strong reductant present).

It is seen in Table 1 that for the compounds containing both bromine and chlorine, bromine was almost exclusively the leaving group. Only for CBrCl_3 could traces of a product (CHBrCl_2) possibly derived by C–Cl scission be found. The same results have been obtained in pulse radiolysis experiments with halothane in water and alcohols,¹⁹ and in studies of the reduction of halothane and CBrCl_3 with cytochrome P-450.²⁰ This is consistent with the higher bond energy of the C–Cl bond (e.g., 70 kcal mol⁻¹ for CCl_4) than that of the C–Br bond (e.g., 56 kcal mol⁻¹ for CBrCl_3). The results are, however, in sharp contrast to those obtained in pulse radiolysis studies of CBrCl_3 , CBrCl_2H and CBrClH_2 in frozen matrices at 77 K.²¹ Here, it was found that while Br^- was the only leaving group when radiolysis was performed with the pure compounds, Cl^- was preferred if the substrates were solvated by CD_3OD . This was explained on the basis of better solvation of Cl^- than of the larger Br^- in the good anion-solvating medium, CD_3OD . Evidently both bond strength and solvation determine the outcome of the reaction, but in most cases the former seems to be the governing factor.

In the discussion of the product studies above, we have assumed, on the basis of our studies of the model compound CBr_4 ,^{10,11} that our reactions are of the outer-sphere type and that the kinetics follow the rate law in eqn. (7). Thus, we can now turn our attention to the difference in reactivities, first between the reagents and thereafter between the polyhaloalkanes.

The difference in reactivity between CoW^{7-} and Co(II)sep^{2+} can, at least qualitatively, be checked by the Marcus theory¹⁰ [eqns. (12)–(14)]. From eqns. (13) and (14) we can calculate the difference in driving force for the reactions of Co(II)sep^{2+} and CoW^{7-} with CBr_4 , i.e., $\Delta G^{\circ'} = \Delta G^{\circ'}_{\text{Co(II)sep}^{2+}} - \Delta G^{\circ'}_{\text{CoW}^{7-}} = -0.8$ kcal mol⁻¹.

$$\Delta G^* = W + \frac{\lambda}{4} \left(1 + \frac{\Delta G^{\circ'}}{\lambda} \right)^2 \quad (12)$$

$$\Delta G^{\circ'} = \frac{331.3 (Z_1 - Z_2 - 1) B}{D r_{12}} + \Delta G^{\circ} \quad (13)$$

$$B = 10^{-21.9} r_{12} (\mu DT)^{1/2} \quad (14)$$

Here, we have used the following parameter values: $D = 51.8$,^{*} $r_{\text{CBr}_4} = 3.9$ Å, $r_{\text{Co(II)sep}^{2+}} = 4.5$ Å, $r_{\text{CoW}^{7-}} = 5.6$ Å, $T = 293$ K, $\mu_{\text{Co(II)sep}^{2+}} = 0.02$ M, $\mu_{\text{CoW}^{7-}} = 0.0083$ M, $E^{\circ}_{\text{Co(II)sep}^{2+}/\text{Co(III)sep}^{2+}} = -0.30$ V¹¹ and $E^{\circ}_{\text{CoW}^{7-}/\text{CoW}^{6-}} = -0.44$ V.¹⁰ Thus the driving force is slightly larger for Co(II)sep^{2+} , despite its lower standard potential. The intrinsic reorganization energy for the self-exchange reaction of Co(II)sep^{2+} is ~ 50 kcal mol⁻¹,^{*} while that for CoW^{7-} is only ~ 10 kcal mol⁻¹.¹⁰ This will give a smaller reorganization energy, λ , for the CoW^{7-} reactions, and thereby a smaller ΔG^* [eqn. (12)], which explains the higher rate constants found for CoW^{7-} (Table 2).

The reactivities of the polyhaloalkanes are a more complicated matter. The two, general structure-activity relationships for polyhaloalkanes which hold for most reactions are: the heavier the halogen substituents and the more halogen substituents on the carbon, the more reactive. These effects are thought to be dependent on the LUMO energies,²³ and on the carbon-halogen bond strengths in the compounds. The trends have been seen in cathodic reductions,¹⁸ oxidative addition,²⁴ halogen atom abstractions²⁵ and in reactions which proceed either by an ET mechanism or by attack on a positive halogen.²⁶ Thus, the trends *per se* cannot be used as evidence for one type of mechanism or the other. The reactivity trends above can be seen in this study in the following comparisons: $\text{CBr}_4 > \text{CBr}_2\text{Cl}_2 > \text{CBrCl}_3 > \text{CCl}_4$, $\text{CBr}_4 > \text{CHBr}_3$ and $\text{C}_2\text{Cl}_6 > \text{CCl}_4$. The rules are, however, not easily used in more subtle reasoning, e.g., why we find halothane (CF_3CHClBr) to be almost ten times more reactive than CCl_4 towards CoW^{7-} (after correcting for the differences in reaction temperature by using the rate constants for CBr_4 at 20 and 50 °C). Nevertheless, from a biological viewpoint this is an interesting finding because CCl_4 is a well-known hepatotoxin (see Introduction) and halothane is a widely used anaesthetic. We can only note that halothane is considered to be less hepatotoxic than CCl_4 ²⁰ and that this can be explained by the complexity of the *in vivo* biochemical systems involved, in which clearly many more factors must be accounted for in order to determine the toxicity of a compound.

We see in Table 2 that only four of the sub-

*Calculated as in Ref. 11.

*Calculated from rate data in Ref. 12.

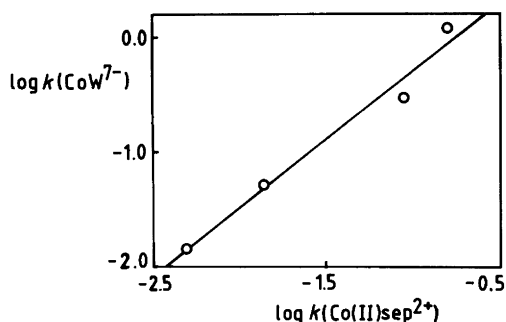


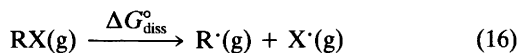
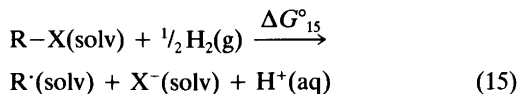
Fig. 3. Plot of $\log k_{\text{ET}}(\text{CoW}^{7-})$ vs. $\log k_{\text{ET}}[\text{Co(II)sep}^{2+}]$.

strates reacted fast enough with Co(II)sep^{2+} to give a measurable rate constant. For these substrates a plot of $\log k_{\text{ET}}(\text{CoW}^{7-}$ at 20°C) vs. $\log k_{\text{ET}}[\text{Co(II)sep}^{2+}$ at 50°C] gives a straight line with a slope close to 1 (Fig. 3). This is to be expected in view of the close similarity between the substrates, the reagents and the mechanisms of the reactions.

There is a large discrepancy between the results for CoW^{7-} and Co(II)sep^{2+} as regards the rate constant for hexachloroethane relative to the rate constants of the other substrates. Thus, while C_2Cl_6 was twice as reactive as CBrCl_3 towards CoW^{7-} , its reaction with Co(II)sep^{2+} was too slow to be measurable (in this case, at least five times less reactive than CBrCl_3). Even though one would not expect the chloroalkanes to exactly follow the relative reactivities of the bromo compounds toward the two reagents, this large effect is difficult to explain. Clearly, rate constants for reactions of C_2Cl_6 with other ET reagents are needed to establish its relative reactivity. The small rate constants found for CCl_4 and CHBr_3 with CoW^{7-} make it probable that their reactions with Co(II)sep^{2+} are too slow to be measurable, while halothane in this context is a borderline case.

Finally, it is interesting to note that if we consider the reaction of eqn. (3) to be a dissociative ET reaction, one predicts that CBrCl_3 and CBr_4 should react equally fast. Thus, it has been shown that if the ET reduction of alkyl halides is dissociative [eqn. (15)], it is possible to calculate the standard potential for the reaction^{5a,27} [eqn. (15)]:

We use the same equations here, but to simplify the arguments we now consider the gas



$$\Delta G_{15}^\circ = \Delta G_{\text{diss}}^\circ - \Delta G_{\text{fl}}^\circ[\text{X}\cdot(\text{g})] + \Delta G_{\text{fl}}^\circ[\text{X}^-(\text{soln})] + \Delta G_{\text{soln}}^\circ \quad (17)$$

phase dissociation reaction of eqn. (16) and thereby obtain eqn. (17). $\Delta G_{\text{soln}}^\circ$ is the difference between the solvation energies of the parent organic halide and its radical, and is not likely to differ between CBr_4 and CBrCl_3 . The only term that can differ is therefore $\Delta G_{\text{diss}}^\circ$, as $\text{X}\cdot$ and X^- are the same for the two compounds. However, $\Delta H_{\text{diss}}^\circ$ is known for CBrCl_3 ²⁸ (55.7 kcal mol⁻¹) and for CBr_4 ²⁹ (56.2 kcal mol⁻¹), and $\Delta S_{\text{diss}}^\circ$ can be calculated to be almost identical for the two substrates; we then find $E_{\text{CBr}_4}^\circ - E_{\text{CBrCl}_3}^\circ = +0.01$ V.

Furthermore, a good linear relationship between reorganization and dissociation energies has been shown to exist for the dissociative ET reduction of simple aliphatic halides.^{4a} This suggests that the λ values for CBrCl_3 and CBr_4 are also the same if the reaction is truly dissociative. If we now look at the Marcus equation for determining ΔG^\ddagger [eqn. (12)], it is evident that CBrCl_3 and CBr_4 will have the same activation energy and therefore also the same rate constant. The $k_{\text{CBr}_4}/k_{\text{CBrCl}_3}$ ratios for CoW^{7-} (80) and for Co(II)sep^{2+} (30) may therefore be considered as evidence against a dissociative process. This is consistent with the previously mentioned findings that CCl_4 ^{6c} and CBr_4 ^{6a} do exist, and also with theoretical considerations.³⁰

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