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Facile Halogen Exchange Reactions: Chloroform with Bromoform and Carbon Tetrachloride with Carbon Tetrabromide

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Both of the title systems undergo rapid halogen exchange (half-life ca. 1−2 min) in *N*-methylpyrolidinone with catalytic sodium hydroxide at room temperature. Yet they differ markedly in response to added *p*-dinitrobenzene. The rate of the haloform exchange is unaffected, whereas the rate of the carbon tetrahalide exchange is severely retarded. The known base-induced halogen exchange reaction between chloroform and bromoform is shown not to proceed through a reversible carbene intermediate as claimed in the literature. It appears to be best described in terms of the so-called RARP mechanism (radical anion−radical pair). The mechanism proposed for the rapid exchange between carbon tetrachloride and carbon tetrabromide is initial electron transfer, halide ion loss, and ensuing radical chain scrambling of halogen atoms. The acronym RARC, standing for radical anion−radical chain, is proposed.

Introduction

Chloroform Exchange with Bromoform. The halogen exchange in haloforms, such as that between chloroform and bromoform, under basic conditions is well known.[1−5] This redistribution reaction has served preparative purposes.[1] The mechanism of exchange has been interpreted differently by various workers.

(a) Earlier reports attributed the exchange to reversible carbene formation[1,3] in which an opposite halide ion is encountered by a carbene, which then reverts to a haloform anion and thence to a haloform with mixed halogen atoms. This mechanism was based on products formed and the known reaction of a carbene with halide ion in solution, originally reported by Hine and coworkers.[6,7]

(b) Another explanation was advanced[4] that a carbene reacts directly with another haloform molecule to produce the mixed haloform and a different carbene. This explanation was based on the fact that phenyl trichloromethylmercury in refluxing bromoform reacted to give a mixture of chloroform, bromodichloromethane, and dibromochloromethane (3:1:8 ratio). The authors saw this process as occurring *in addition to* the carbene−halide ion reversal process. A difficulty with this explanation is that the primary process in such a system would be expected to be carbene insertion to give C_2 compounds.[8]

(c) The carbene reversal mechanism was rejected on two findings.[9] First, soluble halide added to the system under exchange conditions showed no halide incorporation ($Br^-/CHCl_3$ and $Cl^-/CHBr_3$), and second, no cyclopropane product could be detected when an alkene (1-octene) was added.

(d) A more recent report[10] emphasized the role of single electron transfer in the halogen exchange. These authors claim partial formation of disproportionation products (CH_2X_2 and CX_4) along with the exchange. They also discount the role of halide ion reversal of carbene formation. They cite ESR support for their interpretation, but with no experimental details as to how the reactions or analyses were performed.

Carbon Tetrachloride Exchange with Carbon Tetrabromide. Since we first reported this reaction,[9] Sasson et al.[11] have observed tetrabutylammonium fluoride trihydrate (TBAF)-catalyzed scrambling of halogen in $BrCCl_3$, Br_2CCl_2, and Br_3CCl, each individually. They also observed exchange between haloforms and carbon tetrahalides, but specifically reported that there was *no* exchange between bromoform and chloroform under their conditions (neat halocarbons and catalytic TBAF at room temperature). The mechanism proposed for these exchanges is polar attack of a haloform anion on a carbon tetrahalide. When only carbon tetrahalides were present initially, small amounts of haloform formed in the mixtures were presumed to be the active agent.

Much of the data on halogen exchange in haloforms have been gathered in conjunction primarily with studies of carbene reactions, where the halogen exchange was essentially a side phenomenon. The studies reported here on exchange in haloforms and tetrahalides have focused on the more rapid exchange reaction. In particular, we were interested in probing the effect on kinetics of additives, especially p-dinitrobenzene, a typical radical anion scavenger.[12] Like Sasson et al., we too observed rapid exchange between haloforms and tetrahalide under our conditions. However, we found the additive effects (mechanistic probes) difficult to interpret and therefore focused our efforts on the individual systems. We believe this approach was fruitful.

[⊗] Abstract published in *Advance ACS Abstracts*, July 1, 1996.

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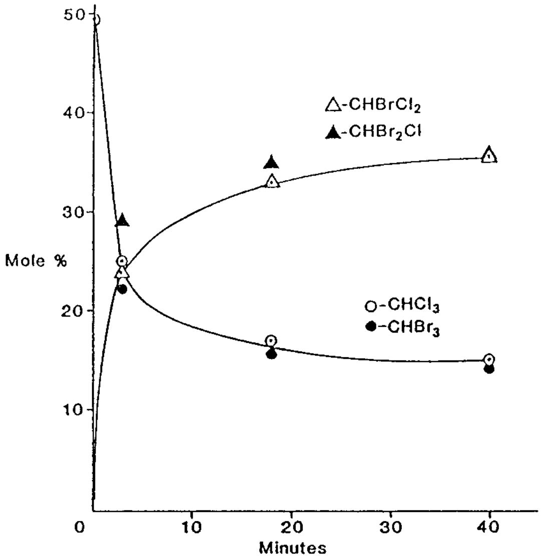


Figure 1. Halogen exchange between $CHCl_3$ (16.7 mmol) and $CHBr_3$ (16.8 mmol). Conditions: NMP solvent, 5.0 g; 50% sodium hydroxide catalyst, 0.5 g; rt. At equilibrium the mole ratios were $CHCl_3 = CHBr_3 = 1.0$; $CHBrCl_2 = CHBr_2Cl = 2.5$.

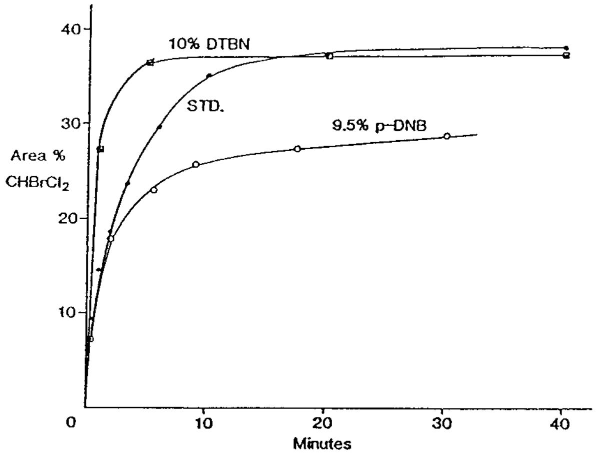


Figure 2. Effects of additives, DTBN and *p*-DNB, on the rate of halogen exchange between $CHCl_3$ and $CHBr_3$. Only $CHBrCl_2$ is shown for clarity. Conditions are the same as for Figure 1 except for the additives, expressed as mole percentage.

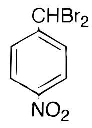
Results and Discussion

Kinetics of Exchange between $CHCl_3$ and $CHBr_3$. The exchanges were very rapid in *N*-methylpyrrolidinone (NMP) with 50% sodium hydroxide at room temperature. Kinetic measurements under the usual conditions of running the reaction (see Experimental Section) showed a half-life for exchange of about 1 min. The GC area percentages for the disappearance of starting materials and formation of products are shown as Figure 1. The product ratios are those expected for a statistical distribution from mixing of the halogen atoms.

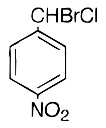
Previous workers explained halogen exchange in haloforms as occurring by a reverse reaction of dihalocarbene with a halide ion, the halide ion being bromide if the carbene is dichlorocarbene and vice versa. Reversal is a known phenomenon,[6,7] but seemed unlikely here since there is no halide ion of either kind in solution at the start, not until there is extensive haloform hydrolysis. Attempts were made to see whether inorganic halide ion would be incorporated into the haloform. Both bromide ions with chloroform and chloride ions with bromoform were tested for incorporation under the normal conditions. In these reaction mixtures the quaternary ammonium halides dissolved completely. The results were that in neither case could a trace of product be detected that would indicate incorporation of external ionic halide. After a sufficiently long period of time passed for detection of exchange in each reaction (30−60 min), the opposite haloform was added to each mixture, resulting in rapid exchange.

Lack of cyclopropane products when an alkene (1-octene) was added also indicates that carbenes are not in evidence during the rapid halogen exchange. The kinetic effects of both di-*tert*-butyl nitroxide (DTBN) and *p*-dinitrobenzene (*p*-DNB) as mechanistic probes were examined. Plots of these results are shown as Figure 2.

Effect of *p*-DNB. Even at a fairly high concentration, *p*-DNB has no effect on the rate of exchange. The maximum amount of exchange is decreased, however. Also, an unusually large amount of mixed carbon tetrahalides was present at the end of the reaction (12.6 GC area % of the total halocarbons; in a standard reaction with no additives, such as in Figure 1, this number was less than 1%). In addition, products of substitution of one of the nitro groups in *p*-DNB, apparently by a trihalomethyl anion, were detected by GC−MS. The products detected were correct in mass for I and II, with I being present in much greater abundance, especially early in the reaction (the para configuration is inferred from the original isomer configuration). Approximately 60% of the *p*-DNB was converted.



I



II

The following evidence supports this assignment:

(a) The nitro group on an appropriately deactivated aromatic ring can often be a better leaving group than fluoride;[13] (b) trihalomethyl anions can substitute on deactivated aromatic rings;[14,15] and (c) an example of a reversible reduction of a trichloromethyl side chain to a dichloromethyl with chloroform and base has been reported.[16] Scheme 1 is proposed as the origin of **I** and **II**.

Mechanism of $CHCl_3$/$CHBr_3$ Halogen Atom Exchange. The evidence above shows a rapid, base-catalyzed halogen atom exchange, with lack of kinetic inhibition by *p*-DNB. In addition, there were observed neither two-carbon species nor methylene dihalide species. These observations are consistent with a direct nucleophilic attack of a trihalomethyl anion on a halogen atom of a haloform. However, the radical anion-radical pair (RARP) mechanism developed by Meyers and coworkers[17] offers an alternative mechanistic view that is

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(13) Beck, J. R. Nucleophilic Displacement of Aromatic Nitro Groups, Tetrahedron Report No. 54. *Tetrahedron* **1978**, *34*, 2057−2068.

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(15) Atkinson, P. J.; Gold, V. *J. Chem. Soc., Chem. Commun.* **1983**, 140.

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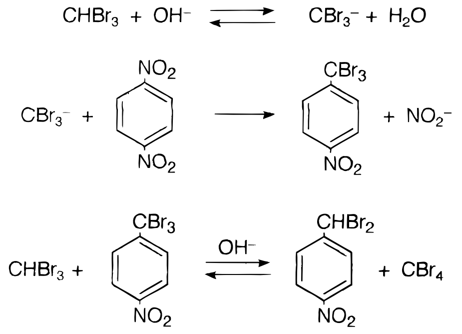
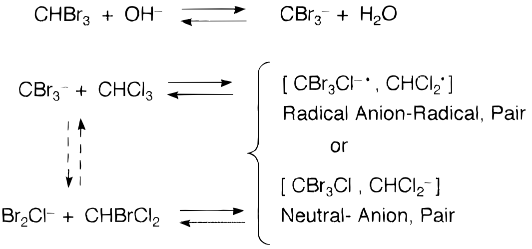
(17) Meyers, C. Y.; Matthews, W. S.; Ho, L. L.; Kolb, V. M.; Parody, T. E. *Catalysis in Organic Synthesis*, 6th ed.; Smith, G. J. V. J., Ed.; Academic: New York, 1977; pp 197−278.

Scheme 1



Scheme 2



also consistent with the observed facts. Scheme 2 outlines the two mechanisms as applied to the halogen exchange in haloforms. The essential difference in these two proposals is the electron transfer characteristics of the bracketed pair that exchanges halogens. The first reactive species is presumed to be the tribromomethyl anion (bromoform deprotonates much more rapidly than chloroform),[18] which is assumed to be at a steady state concentration. This attacks a chloroform molecule with a net transfer of a chlorine radical to the bromoform anion within a cage. This combination rapidly exchanges halogens to a more or less statistical distribution before diffusing apart as a new haloform−haloform anion pair. Direct anion attack (the bottom bracketed pair) would be favored by the principle of Ockham's razor but appears to be more highly energetic than electron transfer. Calculations from thermodynamic data estimate an uphill energy of about 20 kcal/mol for the ionic transfer versus about 11−12 kcal/mol uphill for the electron transfer.[19] While such calculations are approximate, they are supportive of the RARP mechanism. The key exchange reaction occurring within a solvent cage accounts for the lack of inhibition by *p*-DNB. Our best explanation of the rate-enhancing effect of DTBN is that it is able, by electron acceptance from a tribromomethyl anion, to initiate a few radical chains via the tribromomethyl radical.[20]

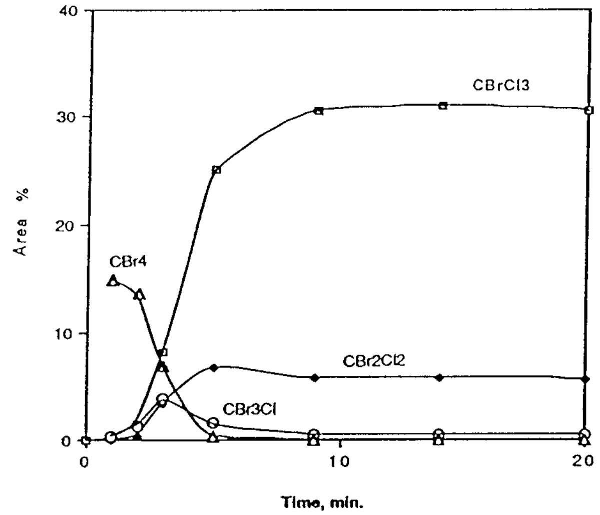


Figure 3. Halogen exchange between CCl_4 (26 mmol) and CBr_4 (3.0 mmol). Conditions: NMP solvent, 5.0 g; 50% sodium hydroxide catalyst, 0.5 g; rt. CCl_4 not shown for reasons of scale. Smaller mole ratio of CBr_4 used due to limited solubility in the system.

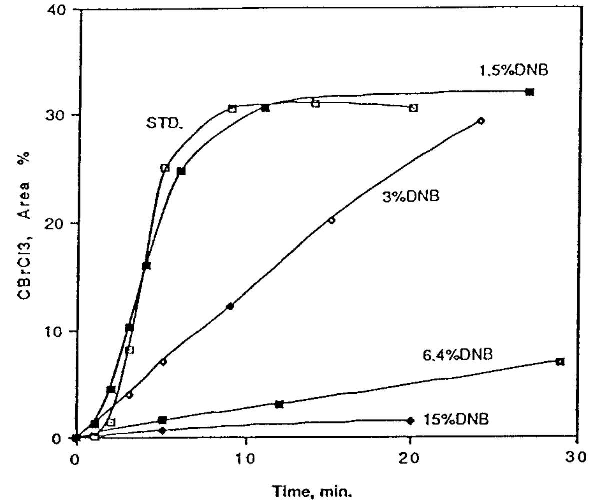
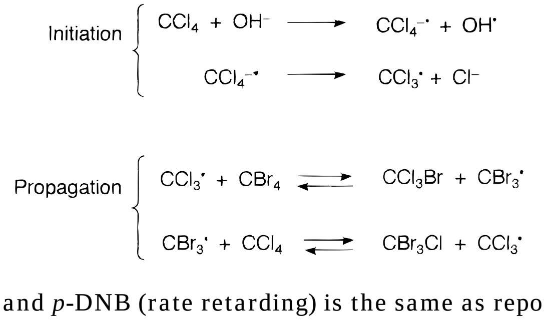


Figure 4. Effect of *p*-DNB on the rate of halogen exchange betweeen CCl_4 and CBr_4. Conditions are the same as for Figure 3, except for the indicated mol % of p-DNB.

Scheme 3



Kinetics of Exchange between CBr_4 and CCl_4. This reaction shows a decidedly different pattern of additive effects on the kinetics of exchange. As Figure 4 shows, *p*-DNB is a strong inhibitor. Both Ionol and DTBN (not shown) were found to accelerate the reaction. Reliance on the effect of DTBN as a mechanistic probe seems doubtful due to its different possible modes of reaction.[20] However, the pattern of Ionol (rate enhancing) and *p*-DNB (rate retarding) is the same as reported for the effect on the halogen exchange between chloroform and 2-chloro-6-trichloromethylpyridine.[16] Thus the probability is strong for a similar mechanism (Scheme 3). Electron transfer from hydroxide (or Ionol anion) to a carbon tetrahalide followed by halide ion loss to generate a trihalomethyl radical constitutes initiation. Propagation is through a series of reversible reactions with a carbon tetrahalide. Termination reactions are speculative, the only evidence for which may be the

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(18) Hine, J. *Divalent Carbon*; Ronald Press: New York, 1964; p 39.

(19) Lias, S. J.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17* (Suppl. 1).

(20) Known ability of DTBN to accept electrons: (a) Forrester, A. R.; Hay, J. M.; Thomson, R. H. *Organic Chemistry of Stable Free Radicals*; Academic Press: New York, 1968; Chapter 7. (b) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 1407.

appearance of a small amount of chloroform indicating reduction. However, this is extremely small. In the standard reaction (Figure 3), only 0.05% was detected by 9 min, with nothing before that.

A convenient shorthand notation to the pathway described in Scheme 3 would be RARC, for radical anion−radical chain.

Can the mechanism described by Sasson[11] account for our results? A simple anionic attack of a trace of bromoform anion on a chlorine of carbon tetrachloride, for example, cannot account for the strong inhibition by *p*-DNB or the rapid rate of reaction. An exchange between bromoform and carbon tetrachloride where both were substantially equimolar had a half-life of about 1 min. This would mean that vanishingly small amounts of adventitious haloform should lead to extremely slow reaction. As mentioned above, no traces of haloforms were detected in the carbon tetrachloride−carbon tetrabromide exchange (half-life of 2−3 min) until equilibrium was nearly complete. This is difficult to account for by a direct polar reaction.

Experimental Section

The general experimental procedure is the same as that given previously.[16] Solvent NMP was "Gold Label" from Aldrich. Commercial chemicals were used without further purification. All identifications were made by GC−MS.

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