

Articles

An Equilibrium Halogen Transfer Reaction with Evidence for $S_{RN}1$ -like Behavior

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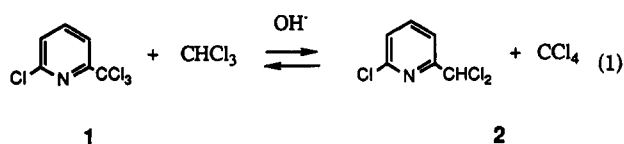
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The "reduction" of 2-chloro-6-(trichloromethyl)pyridine to the dichloromethyl derivative by chloroform under basic conditions yields carbon tetrachloride as a companion product. The reaction is demonstrated to be reversible and to have preparative value. Strong inhibition by electron capture agents and also strong acceleration by electron-donating agents is observed. The mechanistic interpretation is electron-transfer initiation followed by reversible radical chains to establish the equilibrium.

Introduction

We had need to selectively reduce the trichloromethyl side chain of 2-chloro-6-(trichloromethyl)pyridine, **1** (common name: Nitrapyrin¹), to the dichloromethyl derivative **2**. Reasonable success was experienced by the use of metals such as iron or zinc or tin dichloride under acidic conditions. On a large scale, as is met within industrial production, this can generate severe problems of waste metal ion streams and the necessity of recovery. Overreduction was also a problem. Partial solution to these problems was found in using only a small amount of the metal along with a reducing agent (in this case, cuprous chloride with hypophosphorous acid). Still it was felt that there were improvements to be made environmentally.

In an exploration of alternative practical ways of carrying out the reduction, we found that chloroform and base functioned effectively but incompletely in what proved to be an *equilibrium* halogen-transfer reaction, eq 1. This



report details a study of the reaction.

Results and Discussion

The majority of reactions were carried out in *N*-methylpyrrolidinone solvent (NMP) using 50% sodium hydroxide as base catalyst. The reaction was also found to occur in chloroform as solvent and reactant with a phase-transfer catalyst (PTC). The reversibility of eq 1 was shown by observing that the reaction of carbon tetrachloride with a previously synthesized sample of **2** gave a mixture of the same four compounds (shown in eq 1) as did chloroform and **1** under the same conditions. In addition, when carbon tetrachloride was added to a reaction mixture produced from chloroform and **1**, which

had come to apparent equilibrium, the ratio of **2** to **1** rapidly decreased to a new position. A quantitative determination by GLC established a K_{eq} :

$$[2][\text{CCl}_4]/[1][\text{CHCl}_3] = 0.05 \text{ (NMP solvent)}$$

The equilibrium constant in NMP was the same when approached from either direction.

The reaction has preparative value in spite of the low equilibrium constant. By sequentially removing a mixture of chloroform and carbon tetrachloride under vacuum and then adding fresh chloroform to an NMP solution of **1** and 50% caustic, 34.4 g of **2** was prepared from 46.2 g of **1**, a yield of 88%.

Other Solvents. Dimethyl sulfoxide (DMSO) was equally effective as NMP in establishing a rapid equilibrium; DMF was less so and other solvents tried, such as HMPA, diglyme, and tripropylene glycol monomethyl ether, resulted in a very slow reaction. With methanol as solvent, no **2** was observed after 40 min at room temperature.

Increasing the amount of sodium hydroxide increased the rate of establishment of equilibrium, and halving the amount of NMP slowed the reaction considerably. Apparently, these rate differences were not due to a changing amount of dissolved hydroxide in the organic phase, since NMP pretreated with 50% sodium hydroxide, followed by a careful phase separation was not effective in producing **2** from **1** and chloroform. With the addition of fresh caustic, the reaction behaved normally.

Phase-Transfer Catalysis. Chloroform as solvent with a phase-transfer catalyst (Bu_4NBr or Adogen 464) and 50% sodium hydroxide was also effective in establishing the equilibrium of eq 1. In this case, it was also shown that when a well-stirred mixture of chloroform, phase-transfer catalyst, and caustic was allowed to settle and then separated, the chloroform phase was not active in producing **2** from **1** until fresh caustic was added.

Effects of Additives. The exchange reaction in NMP was probed for possible radical or radical anion intermediates. Experiments with *p*-dinitrobenzene (*p*-DNB), an

* Abstract published in *Advance ACS Abstracts*, December 15, 1993.
 (1) *The Pesticide Manual, A World Compendium*, 6th ed.; C. R. J., Ed.; The British Crop Protection Council, 74 London Road, Croydon CRO 2TB, 1979; p 384.

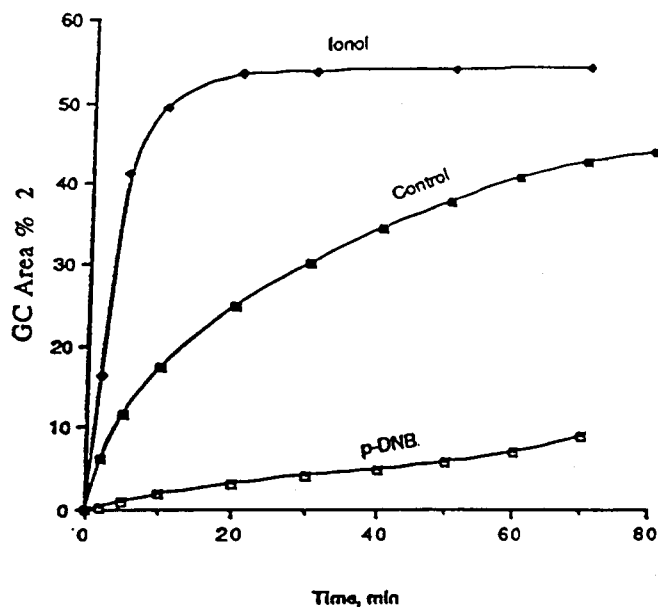


Figure 1. Effects of additives on the rate of formation of 2 from 1 by chloroform and 50% sodium hydroxide. Conditions: NMP, 15 mL; CHCl₃, 25 mL; 1, 5.8 g (25 mmol); 50% NaOH, 2.0 g; ambient temp. Ionol and p-DNB are 7 mol % based on 1.

active receptor of electrons from anions,² showed strong inhibition of the reaction rate. A common antioxidant, Ionol (2,6-di-*tert*-butyl-4-methylphenol), was then tested. It was surprising to observe a dramatic rate enhancement (Figure 1). Purging the system with nitrogen made no difference in the rate of the control reaction (ambient atmosphere) or when Ionol was present. When a control reaction mixture was purged with air, there was a small but measurable decrease in rate.

The same pattern, inhibition by p-DNB and catalysis by Ionol, was also observed when PTC conditions were used instead of NMP. Other phenols and additives were tested for their effect on the reaction rate in NMP, with variable results. Those materials which showed acceleration are shown in Figure 2; those which showed inhibition are grouped in Figure 3. Only *p*-(dimethylamino)phenol (p-DMAP) was as strong an accelerator as Ionol. Not shown are materials which at 7 mol % had little effect on rate: 2,6-dimethoxyphenol, 2,4,6-trichlorophenol, cumyl hydroperoxide, potassium superoxide, the dry potassium salt of phthalimide, and di-*tert*-butyl nitroxide (DTBN). The latter at 33 mol % showed inhibition.

Deuterium Exchange. Commercial 40% sodium deuterioxide in deuterated water (Aldrich, 99+ atom % D) was used to probe the possibility of proton abstraction from chloroform being involved in the rate-controlling step of the reduction. Figure 4 compares the rate of proton loss in chloroform (NMR) with the rate of formation of 2 (GLC). The measurements were made on the same sample of the same reaction mixture. Deuterium exchange outpaces reduction about 30-fold.

Mechanistic Interpretation. Meyers and co-workers⁴ developed a mechanism involving a caged radical anion-radical pair (RARP) to account for a similar (though not,

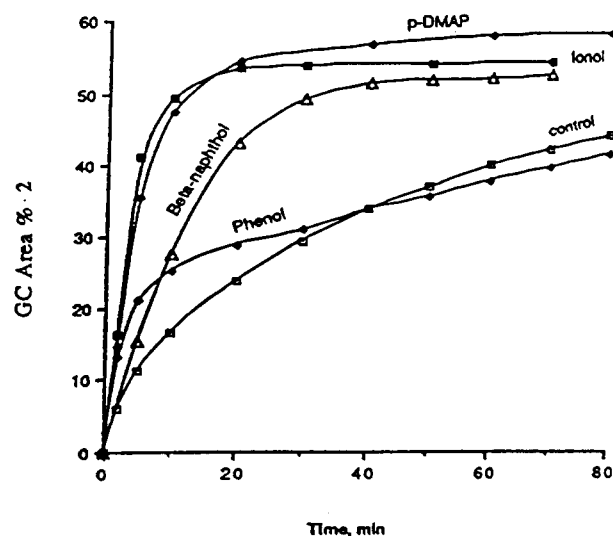


Figure 2. Rate effects of accelerating additives on formation of 2 from 1 by chloroform and 50% sodium hydroxide. Conditions: see Figure 1.

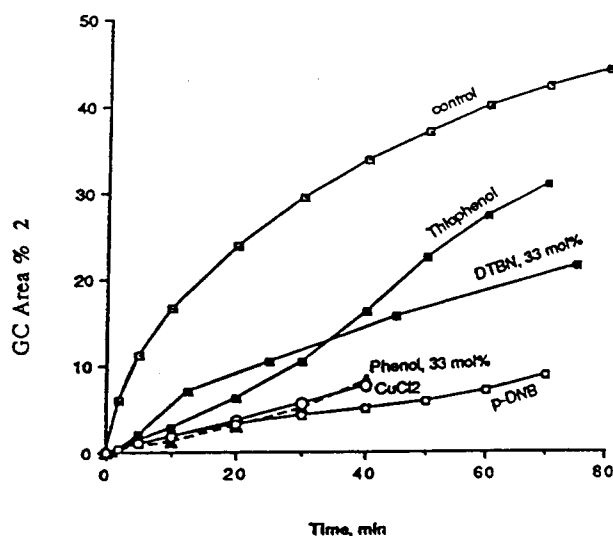


Figure 3. Rate effects of inhibiting additives on formation of 2 from 1 by chloroform and 50% sodium hydroxide. Conditions: see Figure 1. Additives are 7 mol % unless otherwise noted.

apparently, reversible⁵) reaction: carbon tetrahalide halogenation of carbanions of ketones and sulfones formed in KOH/*tert*-butyl alcohol (Scheme 1).

Since the electron transfer in the RARP mechanism takes place within a cage, there is no accounting for the effects of Ionol or p-DNB. Therefore, it does not fit well as an explanation for the reactions reported here.

A simple mechanism of trichloromethyl carbanion attack on a chlorine of 1 is difficult to rationalize with the observed pattern of additive effects. Similar strong, unmistakable retardation by nitro aromatics is discussed by Kornblum et al. in relation to electron-transfer substitution reactions in the thoroughly studied *p*-nitrocumyl system.³ Additive

(2) (a) Kerber, R. C.; Urry, G. W.; Kornblum, N. *J. Am. Chem. Soc.* 1964, 86, 3904. (b) Maki, A. J. H. J.; Geske, D. H. *J. Am. Chem. Soc.* 1961, 83, 1852.

(3) Kornblum, N.; Cheng, L.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Kerber, R. C.; Kestner, M. M.; Manthey, J. W.; Musser, M. T.; Pinnick, H. W.; Snow, D. H.; Stuchal, F. W.; Swiger, R. T. *J. Org. Chem.* 1987, 52, 196-204.

(4) (a) Meyers, C. Y.; Malte, A. M.; Matthews, W. S. *J. Am. Chem. Soc.* 1969, 91, 7510. (b) Meyers, J. C. J. Y.; Parody, T. E.; Kolb, V. M.; Hua, D. H. National Meeting of the American Chemical Society, Chicago, IL, Aug 1977; Abstracts ORG-58. (c) Meyers, C. Y.; Matthews, W. S.; Ho, L. L.; Kolb, V. M.; Parody, T. E. *Catalysis in Organic Syntheses*, 6th ed.; Smith, G. J. V. J., Ed.; Academic: New York, 1977; pp 197-278.

(5) There is a report of a similar reaction which has been demonstrated to be reversible: Sasson, Y.; Webster, O. W. *J. Chem. Soc., Chem. Commun.* 1992, 1200.

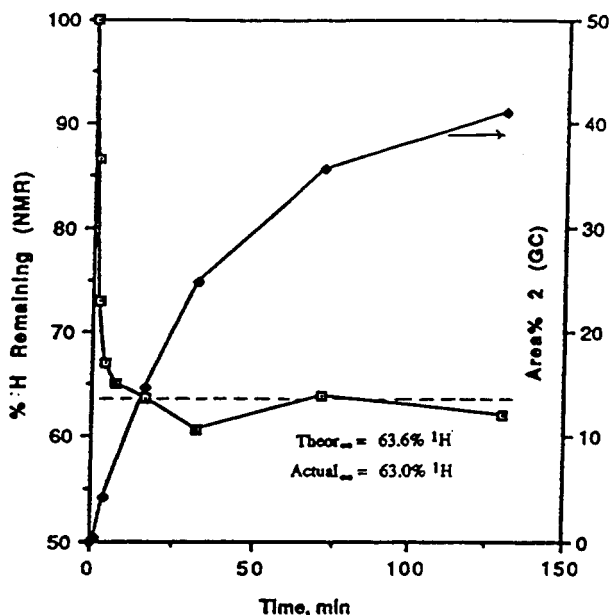
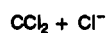
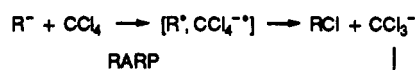
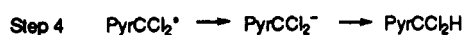
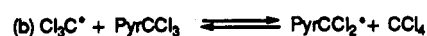
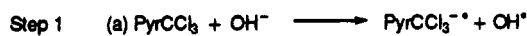


Figure 4. Relative rates of deuterium incorporation NaOD- D_2O into $CHCl_3$ (□, $t_{1/2} < 1$ min) and formation of **2** from **1** (◆, $t_{1/2}$ ca. 30 min). Conditions: NMP, 15 mL; **1**, 5.8 g (25 mmol); $CHCl_3$, 25 mL; 40% NaOD/ D_2O , 2.5 g; ambient temp.

Scheme 1. Radical Anion-Radical Pair Mechanism



Scheme 2. Mechanism for $PyrCCl_3/CHCl_3$ Exchange



effects and their importance in establishing the $S_{RN}1$ mechanism are contained in several reviews.^{10,11} The kinetic effects of the additives observed here are consistent with interpretation along similar lines.

(6) Steenken, S.; Neta, P. *J. Phys. Chem.* 1982, 86, 3661-3667.

(7) (a) Ashby, E. C.; Bae, D. H.; Park, W. S.; Depriest, R. N.; Su, W. Y. *Tetrahedron Lett.* 1984, 25, 5107-5110. (b) Ashby, E. C.; Coleman, D.; Gamasa, M. *J. Org. Chem.* 1987, 52, 4079-4085. (c) Bilkis, I. I.; Shein, S. M. *Tetrahedron* 1975, 31, 969-971.

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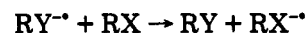
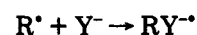
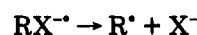
(11) (a) Bowman, W. R. Photoinduced Nucleophilic Substitution at sp^3 Carbon. In *Photoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; Elsevier: Amsterdam, 1988; Part C, Chapt. 4.8, pp 487-552. (b) Todres, Z. V. Ion-Radical Organic Reactions, *Tetrahedron Report Number* 187. *Tetrahedron* 1987, 41 (14), 2771-2823.

The observation was made by a referee that many of the inhibitors could be acting as acids to lower the concentration of sodium hydroxide. While this is true, there is good evidence to discount this as an explanation. Firstly, the acidic inhibitors do not universally decrease the rate of reaction. Ionol and *p*-(dimethylamino)phenol strongly accelerate the rate, no doubt due to the fact that the phenolic additives are put into their effective anionic form.

Secondly, assuming that all of the inhibitor reacted with the base (50% sodium hydroxide), this would still leave a concentration of 46.5% sodium hydroxide. The deuterium-exchange rate and concomitant rate of approach to equilibrium in the chlorine transfer was run in 40% sodium deuteroxide, under otherwise identical conditions. A comparison of Figure 1 with Figure 4 shows that the rate of approach to equilibrium in 40% sodium deuteroxide is about one-half of that in 50% sodium hydroxide, with a normal appearance to the curve of the rate plot. Also, DTBN and *p*-DNB are both nonacidic unless one considers the potential for the latter to form a Meisenheimer complex with the hydroxide ion, although there were no strong color formations that would suggest this. Base diminution by the acidic additives all in all is not a serious factor in their affect on rate. A mechanism which embraces the facts is outlined in Scheme 2.

This mechanism has features in common with the $S_{RN}1$ mechanism:

$S_{RN}1$ Mechanism



In Scheme 2 the first step is electron-transfer initiation. Possible donors are shown in step 1. The finding of Ionol catalysis suggests the role of hydroxide as electron donor in the normal reaction. Phenolate ions are well known to be a source of rapidly transferred single electrons.⁶ Hydroxide and alkoxide have been implicated as single electron donors in other processes.⁷ Trichloromethyl anion, on the basis of EA values (2.3 eV for trichloromethyl anion compared with 1.83 for hydroxide ion and an estimated value of 1.95 for Ionol), would be the least able of the three to transfer an electron and, considering also its low concentration, is judged to be unimportant as a source for electron transfer. Notwithstanding the fact that there have been satisfactory correlations between gas phase EA and solution phase electrochemical data,⁹ factors other than EA, such as phase distribution and solvation of the ions and steric effects, will influence catalytic effectiveness. Sodium hydroxide has virtually no solubility in the organic phase as mentioned and transfer would most likely be at the interface, whereas interfacial reaction may not be a limitation for a phenolate ion.

The second step of Scheme 2 is the dissociation of the radical anion to a radical and chloride ion. This step is

well preceded in the S_{RN}1 mechanism.¹⁰⁻¹² A strong electron acceptor such as p-DNB ought to be very effective in removing an electron from the radical anion in competition with dissociation according to step 2.

The propagation cycle (step 3) is indicated as equilibrium radical exchanges, since the overall reaction is reversible. At this point in a typical S_{RN}1 scheme, the radical reacts with an anion to produce the radical anion of the product, which is then released by transferring the odd electron to another molecule of starting material to begin the chain again. In the present case the radicals participate in a chain by reaction with a neutral molecule to achieve conversion to final product. So this mechanism has some of the characteristics of the S_{RN}1 mechanism but differs in the kind of chain which leads to product. The literature appears to support such a rapid radical chain transfer.

There are two reactions describing the proposed propagation scheme, steps 3a and 3b of Scheme 2. The first aspect of the propagation, eq 3a, is the reaction of a radical with chloroform to abstract hydrogen. Here, the literature gives an E_a (gas phase) of 6.7 kcal/mol for hydrogen abstraction by methyl radical¹³ from chloroform. No liquid phase data for this reaction was uncovered. For the second step, step 3b, literature dealing with the abstraction of chlorine from carbon tetrachloride by alkyl radicals in the gas phase¹³⁻¹⁵ and in solution^{16,17} shows that the E_a in the gas phase is ca. 10 kcal/mol and more or less independent of the nature of attacking radical. However, the E_a in solution has been measured at 4.7-5.9 kcal/mol. The remarkable increase in rate in solution over gas phase for this radical reaction has been attributed to polar effects. Rate constants for the same general reaction (liquid phase) have been reported^{16,18-20} and range from $k = 5 \times 10^8$ to $1.5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$. The average for the nine values found (rt to 50 °C) was $2.3 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. A further benefit in rate would be expected from the polar solvent effect in NMP compared to benzene and carbon tetrachloride used in the literature.

Chlorine transfer to the picoline radical could arguably be expected to be more or less competitive with hydrogen transfer according to literature values of CCl versus CH reaction kinetics of chloroform with hydrocarbon radicals.^{21a} Initially, chlorine transfer was thought unlikely,

(12) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* 1975, 14, 734. (b) Russell, G. A.; Danen, W. C. *J. Am. Chem. Soc.* 1966, 88, 5663. (c) Reference 3.

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(20) Newcomb, M.; Sanchez, R. M.; Kaplan, J. *J. Am. Chem. Soc.* 1987, 109, 1195-1199.

(21) (a) Dutsch, H.-R.; Fischer, H. *Int. J. Chem. Kinet.* 1981, 13, 527-541; this reference shows that selectivity toward H or Cl in chloroform, and therefore presumably H or Br in bromoform, changes considerably with the attacking radical. (b) Reference 3 shows a factor of 20 for k_H in CHCl_3 vs k_{Br} in CBrCl_3 in competition for methyl radical. However this comparison is with the same leaving group, CCl_3 . In the current case the leaving group for Br is CHBr_2 , worse than the leaving group for H which is CBr_3 . (c) Karasch, M. S.; Kuderna, B. M.; Urry, W. *J. Org. Chem.* 1948, 895-902; the general relative reactivity is stated as $\text{CBr} > \text{CH} > \text{CCl}$. (d) Kryger, R. G.; Lorand, J. P.; Stevens, N. R.; Herron, N. R. *J. Am. Chem. Soc.* 1977, 99, 7589-7600. (e) Tilset, M.; Parker, V. *Acta*

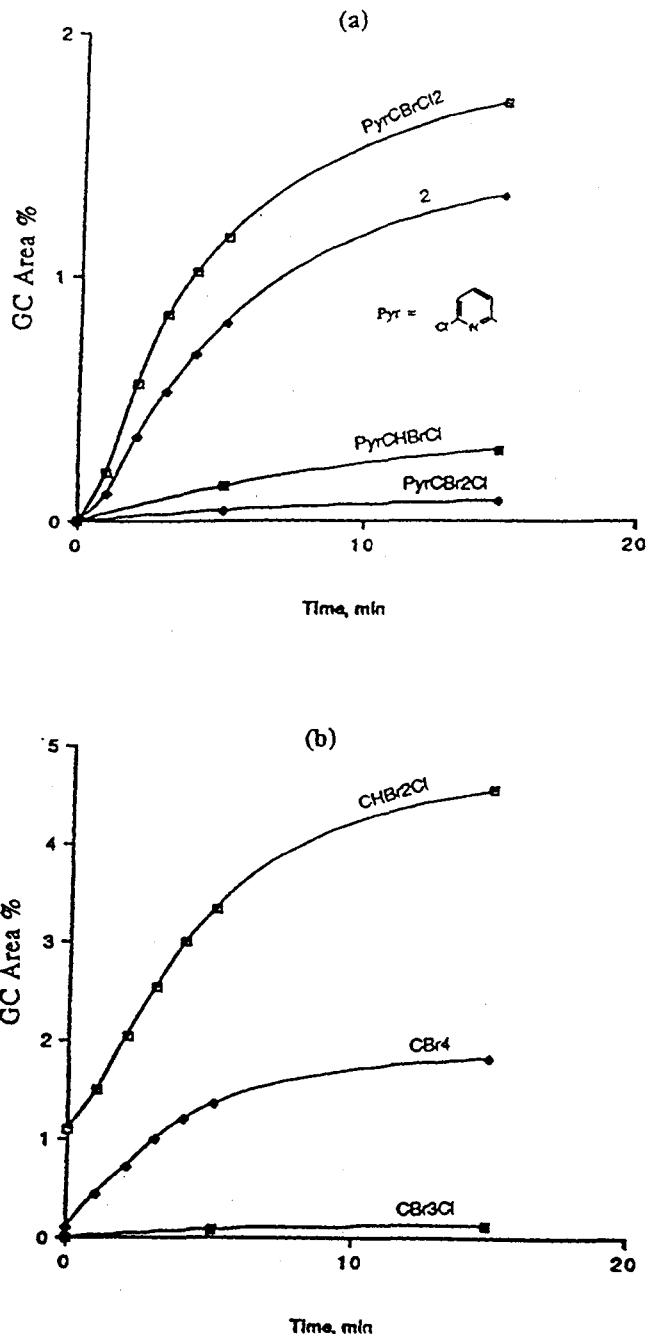


Figure 5. Initial products generated from the halogen-exchange reaction between 1 and bromoform: (a) products relating to 1; (b) products relating to bromoform.

since carbon tetrachloride was the only other observed product of the reaction and chlorine transfer was expected to lead to a byproduct of dichloromethane. None of the latter was detected. In hopes of learning more about the reactions subsequent to step 2 in Scheme 2 and the possibility of competing halogen abstraction, a reaction was performed by substituting bromoform for chloroform. The reaction was slowed by using a lower percentage of NMP so early samples could be taken at low conversion in order to detect any initial preference of Br versus H. The initial ratio favored the PyrCBrCl₂ compound over 2 by a value of 1.7 (Figure 5a; area percentages were relied on since the individual response factors are unknown). The question arises as to whether this initial value reflects

a kinetic or an equilibrium ratio. Attempts to use literature data^{21a-e} to arrive at a prediction of a kinetic ratio yielded nothing in which to place confidence for this particular case outside of a general statement that $k_{Br} > k_H > k_{Cl}$. The kinetic data of Figure 5a shows a stable early ratio followed by a smooth decrease to a final value of 1. Since the reaction has been shown to be an equilibrium, this suggests a thermodynamic control of the initial H/X transfer ratio, the decrease in ratio reflecting the change in composition of the mixture. With bromoform, as with chloroform, there was no evidence for radical dimer products. Neither were there detected any dihalomethanes, although the appearance of $\text{PyrCBr}_2\text{Cl}_2$ would presume the cogeneration of the dibromomethyl radical, step 5a.

The fate of a *free* dibromomethyl radical ought to be described by three reactions, eqs 2-4. Since there was no



dibromomethane observed in the product mixture, eq 2 (eq 4 being an identity reaction) must determine overwhelmingly the fate of the dibromomethyl radical, with eq 3 being of little importance. Perhaps a better explanation is that there is no free dihalomethyl radical, i.e., the right hand side of step 5a is so unstable with respect to reversal that it leads only to a halogen scrambling reaction essentially in a solvent cage.

The experiment with bromoform did show that absence of dichloromethane mentioned earlier did not prove the absence of chlorine transfer. Inhibition by p-DNB of both H and Br transfer also shows that both products are generated from the same reactive intermediate and that bromoform behaves similarly to chloroform.

Turning attention to the companion products in the reaction of 1 with bromoform, Figure 5b shows that the largest product is dibromochloromethane, followed by carbon tetrabromide, with a small amount of tribromochloromethane. It might have been expected that tribromochloromethane would be the second most abundant companion product instead of carbon tetrabromide, reflecting the relative concentrations of the two major products in Figure 5a (assuming that the radicals on the right hand side of step 5 abstract a chlorine atom from 1). The explanation for the appearance of carbon tetrabromide is simply a rapid exchange between the initially formed tribromochloromethane and bromoform to give carbon tetrabromide and dibromochloromethane, an equilibrium product distribution. This is shown by the following:

(a) In separate experiments it has been observed that when two different polyhalomethanes are mixed with 1 under exchanging conditions, the two methane partners exchange with each other at a much greater rate than they exchange with 1.

(b) The same mixture of products obtained in Figure 5b was produced also in an attempt to prepare tribromochloromethane from bromoform and aqueous sodium hypochlorite with PTC.

(c) Adding p-DNB to the system makes reaction immeasurably slow, so in this respect bromoform behaves the same as chloroform.

Regarding termination reactions, step 4 is consistent with overall reversibility and lack of observable amounts of radical dimerization products: electron transfer (source unspecified) to a propagating radical, followed by reaction with a proton source.

Other Additive Effects. The moderate inhibition of the reaction by 33 mol % DTBN (Figure 3) may be an indication of free radical chains. The usual reactivity expected of DTBN is as a radical trap, but has other modes of reactivity. Especially pertinent is its ability to accept electrons^{22,23} and so could intercept a radical anion prior to dissociation, as in step 2.

Copper ion catalysis in the Sandmeyer and related reactions has been described in terms of a cycle of one electron transfers with copper shuttling between the cuprous and cupric state.²⁴ One of the important properties of copper in these reactions is its ability to capture electrons from radical anions.²⁵ In our system cupric chloride appears to have an initial inhibiting effect as strong as p-DNB.

The behaviors of phenol and thiophenol illustrate the complex nature of additive effects in this system. Intuitively, it was anticipated that thiophenol would behave somewhat like Ionol. Its inhibiting action was therefore unexpected. One suggestion for what is happening is that thiophenolate ion is substantially less effective than Ionol as an electron-donating initiator,²⁶ but is still able to participate in other reactions of a chain-terminating nature.²⁷ Both thiophenol and phenol anions are significantly more difficult to oxidize to the radical than would be the Ionol anion on the basis of electrochemical data.^{28,29}

The action of phenol as a slight accelerator at 7 mol % but an inhibitor at 33 mol % suggests that both initiation and termination (or chain interruption) can be differentially influenced by the same class of additives. This phenomenon has been observed also in the case of nitroarenes.³

Experimental Section

Rate Measurements. In a typical kinetic experiment, the substrate was weighed into a 25-mL Erlenmeyer flask and the requisite amounts of solvents and additives if any were then added. The magnetically stirred solution was allowed to come to ambient temperature (ca. 22-24 °C) and a weighed amount of 50% sodium hydroxide was added. This was time zero. Reaction exotherms were rarely more than 2-3 °C for the fastest reactions. Samples of 10 drops were removed at appropriate intervals and quenched in a mixture of dilute aqueous hydrochloric acid and 0.5 mL of either carbon tetrachloride or dichloromethane, depending on separations and identifications required. After vigorous mixing, the organic phase was separated

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(23) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* 1973, 38, 1407.

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(25) Russell, G. A. *Reactions between Radicals and Anions*. In *Essays on Free-Radical Chemistry*; Special Publication No. 24, The Chemical Society, Burlington House Publ.: London, 1970; Chapt. 10, p 279.

(26) Bordwell, F. G.; Wilson, C. A. *J. Am. Chem. Soc.* 1987, 109, 5470-5474. These authors point out energy level "matching" of the electron donating with the electron receiving parties must be balanced as one criterion for effective single electron transfer ($E_{ox} \sim E_{red}$) in turn determining reaction mechanism (polar vs SET).

(27) Rico, I.; Cantacuzene, D.; Wakselman, C. *J. Org. Chem.* 1983, 48, 1979-1982, for examples of thiophenoxide reactions with polyhalomethanes under chain reaction conditions.

(28) Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* 1991, 113, 1736-1743.

(29) Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satish, A. V.; Zhang, X. *J. Am. Chem. Soc.* 1991, 113, 9790-9795.

and analyzed by GC (6-ft glass column, 10% SP 2100/chromosorb W/100-120 mesh). Programmed elution was used of 70–250 °C at either 8 °C or 16 °C/min with a 2-min initial delay.

Product Identification. All product identifications were made by GC-mass spectrum combination and confirmed by spiking with known materials where available from a commercial source (see Materials). Samples of 2 were available from both Fe⁰/HCl (methanol or acetic acid solvent) reduction of 1 and the chloroform reduction of 1 as described in Results and Discussion. Compound 2: ¹H NMR (300 MHz, CDCl₃) δ 7.82–7.71 (m, 2H, ring), 7.36–7.34 (d, 1H, ring), 6.66 (s, 1H, CHCl₂); ¹³C NMR δ 158.57, 150.34, 140.25, 125.24, 119.70, 70.39; mp 52.5–54 °C.

Usually pure 1 was used as starting material, but occasionally technical grade nitrapyrin was used. This contains up to 6% of 2,4-dichloro-6-(trichloromethyl)pyridine along with other minor impurities. This made no apparent differences in the kinetic results observed, but did result in the presence of the additional

dichloromethyl exchange product of the major impurity in a chlorine transfer equilibrium similar to that of 1 ↔ 2.

Materials. Technical grade and recrystallized (from 95% ethanol, >99% purity) Nitrapyrin from Dow Chemical was the source of 1. The Ionol was a sample from Shell Chemical. The other materials: additives, *N*-methylpyrrolidinone (NMP), chloroform, bromoform, carbon tetrachloride, carbon tetrabromide, bromotrichloromethane, dibromodichloromethane, bromodichloromethane, dibromochloromethane, chlorodibromomethane, dibromomethane, dichloromethane, deuteriochloroform, and 40% deuterium oxide in deuterated water were from Aldrich. The chlorotribromomethane was from Columbia Organic Chemicals. General lab chemicals were from J. T. Baker. All were used without further purification.

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