Solvent- and Reagent-induced Change of Rate-limiting Step in Acid-catalysed α-Halogenation of Amidines with Tetrahalogenomethanes

Stefan Löfås
Department of Organic Chemistry, University of Uppsala, P.O. Box 531, S-751 21 Uppsala, Sweden
Per Ahlberg *
Department of Organic Chemistry, University of Göteborg, S-412 96 Göteborg, Sweden

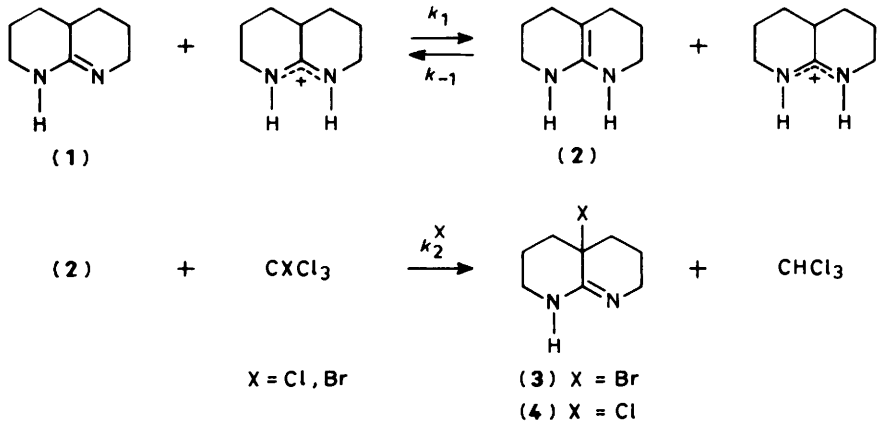
The acid-catalysed α-halogenation of amidines with tetrahalogenomethanes involves the intermediate formation of the ketene aminal tautomer, which then reacts with the tetrahalogenomethane. The kinetics of the acid-catalysed reaction of 2,10-diazabicyclo[4.4.0]dec-1-ene (**1**) with CCl_4 in benzene, methylene dichloride, and DMF, and with $CBrCl_3$ in DMF, respectively, have been investigated. The kinetics of the reaction of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (**5**) with CCl_4 in DMF and DMSO has also been studied. The reaction of amidine (**1**) with CCl_4 in DMF is first-order in [(**1**)], close to zero-order in [CCl_4], and close to pseudo-first-order in [acid], indicating rate-limiting formation of the ketene aminal (**2**). In contrast, in the non-polar solvents the rate of reaction is found to be limited by the reaction of the tautomer (**2**) with CCl_4, which is much slower than in DMF. This change of rate-limiting step is also observed for the reaction of (**1**) in benzene when $CBrCl_3$ is exchanged for CCl_4, and is most likely induced by a much faster reaction of tautomer (**2**) with $CBrCl_3$ than with CCl_4. The present results support a non-chain one-electron-transfer mechanism for the halogenation step, with formation of an intermediate radical-ion pair. A pK_a difference of 2.9 between amidine (**1**) and the α-chlorinated product (**4**) has also been determined using an appropriate ^{13}C n.m.r. method.

In a previous paper,[1] we reported on a mechanistic investigation of the novel α-halogenation of amidines with tetrahalogenomethanes.[2] Kinetics and hydrogen-isotope-effect studies of the reaction of 2,10-diazabicyclo[4.4.0]dec-1-ene (**1**) with bromotrichloromethane ($CBrCl_3$) in benzene showed that the ketene aminal tautomer (**2**) is formed in a rate-limiting acid-catalysed step, and then reacts with $CBrCl_3$, giving the α-brominated amidine (**3**) and chloroform (Scheme 1).[1] These results seem to represent the first mechanistic evidence for the intermediacy of the ketene aminal tautomer in amidine reactions.

We now present the results of kinetic investigations which reveal the influence of solvent and halogenating reagent on the acid-catalysed α-halogenation of (**1**). The reaction has been studied with the reagent carbon tetrachloride in benzene, methylene dichloride, and dimethylformamide (DMF), and with $CBrCl_3$ in DMF. The acid-catalysed α-chlorination of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (**5**) by CCl_4 in DMF and dimethyl sulphoxide (DMSO), respectively, has also been studied.

Results and Discussion

Rates of reaction of the amidines with perhalogenomethanes were determined by measuring the disappearance of the substrate amidine with high-performance liquid chromatography (h.p.l.c.). The high basicity of aliphatic amidines (pK_a up to 13.5 in 50% aqueous ethanol[3]) and their susceptibility to hydrolysis make direct quantitative analysis of these compounds difficult. However, we have developed a h.p.l.c. procedure which is highly suitable for such kinetic investigations. The system consists of an amino-column and a mobile phase composed of ethanol containing 0.8% of the amidine 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), which was used together with a high-sensitivity



Scheme 1.

Table 1. Reaction conditions and observed rate constants for reaction of amidine (**1**) with tetrahalogenomethanes (CCl_4, $CBrCl_3$) and α-deuteriation of (**1**) in argon or nitrogen atmosphere at 25.00 ± 0.02 °C

Entry	10^3[(**1**)]/M	10^3[HBr-(**1**)]/M	10^3[$CXCl_3$[a–c]]/M	Solvent	10^4 k_{obs}/s^{-1}	k_{obs}[HBr-(**1**)]$^{-1}$/l mol^{-1} s^{-1}
1	28		650[a]	DMF	0.05	
2	28	0.52	660[a]	DMF	1.48	0.29
3	22	0.56	640[a]	DMF	1.50	0.27
4	43	0.56	650[a]	DMF	1.55	0.28
5[d]	31	0.65	600[a]	DMF	1.93	0.29
6	24	0.71	640[a]	DMF	1.87	0.26
7	32	0.94	670[a]	DMF	2.53	0.27
8[e]	29	0.94	650[a]	DMF	2.52	0.27
9	27	1.3	1 350[a]	DMF	3.34	0.26
10	30	1.4	650[a]	DMF	3.19	0.23
11	32	1.6	670[a]	DMF	3.63	0.22
12	32	0.94	650[b]	DMF	3.46	0.37
13[e]	28	0.94	660[b]	DMF	3.25	0.35
14	36	1.3	690[b]	DMF	4.10	0.32
15	30	0.94	660[a]	CH_2Cl_2	0.0056	
16[f]	27	0.95	490[a]	C_6H_6	0.015	
17[g]	30	1.1	630[b]	C_6H_6	5.3	0.48
18[h]	36	0.92	570[c]	[$^2H_6$]DMSO	1.2[i]	0.13

[a] CCl_4. [b] $CBrCl_3$. [c] $CDCl_3$ (deuterium source). [d] Di-t-butyl nitroxide (11 mM) and styrene (450 mM) added. [e] Di-t-butyl nitroxide (11 mM) added. [f] Run at 35.0 °C. [g] From ref. 1. [h] Run at 23.6 °C. [i] Rate of α-deuteriation.

Table 2. Observed rate constants for reaction of amidine (**5**) with CCl_4 in DMF and DMSO, respectively, and for α-deuteriation of (**5**) in [$^2H_6$]DMSO in nitrogen atmosphere at 25.00 ± 0.02 °C

Entry	10^3[(**5**)]/M	10^3[HCl-(**5**)]/M	10^3[$CXCl_3$[a–b]]/M	10^6 k_{obs}/s^{-1}
19[c]	32	0.57	1 250[a]	1.7
20[c]	35	1.4	530[a]	1.7
21[c]	33	1.4	1 180[a]	3.0
22[d]	35	1.4	610[a]	1.1
23[e]	34	1.5	620[b]	2.8[f]

[a] CCl_4. [b] $CDCl_3$ (deuterium source). [c] In DMF. [d] In DMSO. [e] In [$^2H_6$]DMSO. [f] Rate of α-deuteriation.

refractive index detector.[1] This type of detector was utilized because the high absorption of the mobile phase prevents the use of a u.v. detector.

The reactions were carried out in deoxygenated solutions in darkness under nitrogen or argon. A large excess (typically 22 times) of tetrahalogenomethane compared with the amount of the amidine was used. Reaction conditions and observed rate constants are summarized in Tables 1 and 2.

Reaction of Amidine (**1**).—The acid-catalysed reaction of (**1**) with carbon tetrachloride (CCl_4) to give the α-chlorinated amidine (**4**) in dimethylformamide (DMF) at 25.0 °C was first order in [(**1**)] (Figure 1). The observed rate constant (k_{obs}) was shown to be close to pseudo-first-order dependent on the concentration of added amidinium hydrobromide HBr-(**1**). In the absence of added HBr-(**1**), a slow reaction with k_{obs} *ca.* 5×10^{-6} s^{-1} took place (entry 1 in Table 1). During this reaction, the observed rate constant increased, possibly due to catalysis by acid produced in a side-reaction. An increase in [CCl_4] by a factor of 2 led to an increase in k_{obs} by 16% in the presence of 5 mol %HBr-(**1**), thus showing a close to zero-order dependence of k_{obs} on [CCl_4] (entries 9 and 10). Variation of the initial concentration of substrate (**1**) did not change k_{obs} (entries 3 and 4). Analysis by g.l.c. of these reaction mixtures showed that chloroform ($CHCl_3$) was formed at the same rate as the rate of disappearance of (**1**).

According to Scheme 1, the pseudo-first-order rate constant (k_{obs}) for disappearance of amidine (**1**) is expressed by equation (1), which has been obtained assuming the steady-state

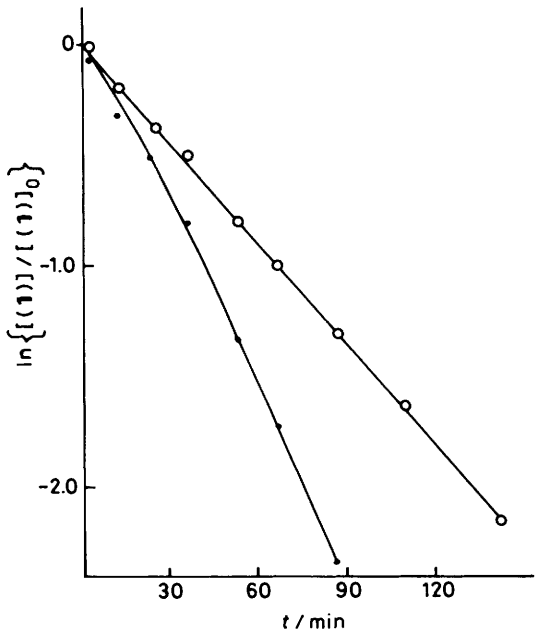


Figure 1. Dependence of ln {[(**1**)]/[(**1**)]$_0$} on time for the reaction of 32×10^{-3}M-(**1**) with 0.67M-CCl_4 (○, entry 7) and with 0.65M-$CBrCl_3$ (●, entry 12) in DMF at 25 °C with 0.94×10^{-3}M-HBr-(**1**) added

$$k_{obs} = \frac{k_1 k_2^{Cl}[\text{HBr-(1)}][CCl_4]}{k_{-1}[\text{HBr-(1)}] + k_2^{Cl}[CCl_4]} \quad (1)$$

approximation for the ketene aminal tautomer (**2**). The weak dependence of the reaction rate of (**1**) on [CCl_4] in DMF may be accounted for by Scheme 1, if the chlorination of tautomer (**2**) is assumed to be fast compared with the formation of (**2**). Taken together with the small but significant deviation from a pseudo-first-order rate dependence on [HBr-(**1**)], this indicates that k_{-1}[HBr-(**1**)] and k_2^{Cl}[CCl_4] are of the same order of magnitude in DMF.

The data in Table 1 can be used to make an accurate

determination of the ratio k_{-1}/k_2^{Cl} and the rate constant k_1, respectively. Equation (2) is obtained on inversion of equation

$$\frac{1}{k_{obs}} = \frac{k_{-1}}{k_1 k_2^{Cl}[CCl_4]} + \frac{1}{k_1[HBr\text{-}(1)]} \quad (2)$$

(1). A plot of $1/k_{obs}$ *versus* 1/[HBr-(1)] at constant $[CCl_4]$ should therefore be linear with slope $1/k_1$ and intercept $k_{-1}/k_1k_2^{Cl}[CCl_4]$. The data from the kinetics in DMF with $[CCl_4]$ 0.65 ± 0.02M (Table 1) give a second-order rate constant $k_1 = 0.31$ l mol^{-1} s^{-1} and a ratio $k_{-1}/k_2^{Cl} = 1.5 \times 10^2$ from Figure 2. Thus, the ratio $k_{-1}[HBr\text{-}(1)]/k_2^{Cl}[CCl_4]$ yields values ranging from 0.12 (entry 2) to 0.36 (entry 11). This explains the observed deviations from integer reaction orders in CCl_4 and HBr-(1).

The rates of reaction of compound (1) with bromotrichloromethane ($CBrCl_3$) in DMF under acid-catalysis conditions were measured. In contrast to the corresponding reactions of (1) with CCl_4, a small positive curvature in the $\ln\{[(1)]/[(1)]_0\}$ *versus* time plots were noticed (Figure 1). This indicates that acid is produced as the reaction proceeds, similar to the behaviour of the reaction of (1) with $CBrCl_3$ in benzene.[1] These rate constants were determined using four data points obtained from the first 60% of the reaction (entries 12—14). The results showed that the reaction of amidine (1) with $CBrCl_3$ was 30—60% faster than the reaction with CCl_4.

According to Scheme 1, the rate of reaction of the ketene aminal (2) with $CBrCl_3$ is assumed to be much higher than with CCl_4. The $k_{-1}[HBr\text{-}(1)]$ term should therefore be negligible compared with the rate of bromination of (2). The expression for k_{obs} in this case is consequently approximated with $k_{obs} = k_1[HBr\text{-}(1)]$. The increase in the acid concentration during the reaction makes an accurate determination of k_{obs} difficult. Nevertheless, the values of $k_{obs}/[HBr\text{-}(1)]$ of 0.32—0.37 (entries 12—14) correspond to the value of 0.31 for k_1 obtained from Figure 2, in line with the proposed mechanism.

The reaction of (1) with CCl_4 was also studied in benzene and methylene dichloride. The rate of reaction is much faster in DMF than in these solvents. In the presence of 3 mol % HBr-(1), k_{obs} for the disappearance of (1) in methylene dichloride at 25.0 °C is 5.6×10^{-7} s^{-1} (entry 15). The slow chlorination of (1) in benzene was carried out at 35 °C. The reaction rates showed an approximate first-order dependence on $[CCl_4]$ but were also

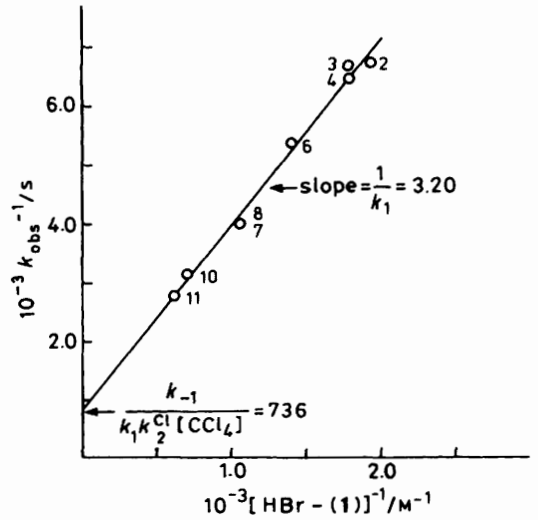


Figure 2. Dependence of $1/k_{obs}$ on 1/[HBr-(1)] for reaction of (1) with CCl_4 in DMF at 25 °C. The figures associated with the circles relate to the entries in Table 1

dependent on the acid concentration. However, reproducibility was highly sensitive to the purity of substrate (1). Thus, sublimation of (1) directly before its use gave an appreciably slower reaction than for (1) which had been stored for two months after sublimation. Both hydrocarbonate formation and oxidation of (1) might have taken place during storage. The reaction of purified (1) with CCl_4 (0.3—0.7M) under acid-catalysis conditions gave k_{obs} values in the range 1.0—2.0 $\times 10^{-6}$ s^{-1}. An example is given in entry 16.

The results of the α-bromination and the α-deuteriation of (1) in benzene revealed a value of 0.7 l mol^{-1} s^{-1} for the second-order rate constant $k_1^{C_6H_6}$ for formation of (2) in benzene.[1] Accordingly, a ratio for $k_1^{C_6H_6}/k_1^{DMF}$ of *ca.* 2 is obtained.

The α-deuteriation rate of (1) in [$^2H_6$]DMSO with deuteriochloroform as deuterium source was measured by ^{1}H n.m.r. (entry 18). The obtained rate constant of 1.2×10^{-4} s^{-1} also indicates that the formation of (2) is faster in non-polar solvents.* However, the α-chlorination of (1) with CCl_4 is much slower in benzene than in DMF. The faster formation of tautomer (2) in benzene indicates that this behaviour must be attributed to a much lower rate for the chlorination step, *i.e.* the reaction of (2) with CCl_4. In benzene, this step is rate limiting, which is shown by the large difference between observed rate of chlorination and rate of formation of (2), as well as by the estimated first-order rate dependence on $[CCl_4]$. This contrasts with the results of the reaction of (1) with CCl_4 in DMF and with the reactions of (1) with $CBrCl_3$ in benzene and in DMF, respectively, where the formation of tautomer (2) was found to be rate limiting. Consequently, the α-bromination of amidine (1) by $CBrCl_3$ is faster in benzene than in DMF, with the same amount of acid present. It may be noted that it is impossible to obtain absolute values of the rate constant k_2^x in the respective solvents, due to the unknown equilibrium constants for the tautomerization between (1) and (2).

The rate of the slow reaction of (1) with CCl_4 in benzene is highly dependent on substrate purity. This indicates that possibly some process of a radical-chain nature contributes to k_{obs} in this reaction. However, this seems not to be the case in DMF, where the effect of possible radical-chain inhibitors on the rate of reaction was investigated. Addition of the stable free radical di-t-butyl nitroxide[4] alone (entries 8 and 13) or together with styrene[5] (entry 5) did not change k_{obs} for the acid-catalysed α-halogenation reaction. This clearly shows that a radical-chain mechanism is kinetically insignificant in DMF.

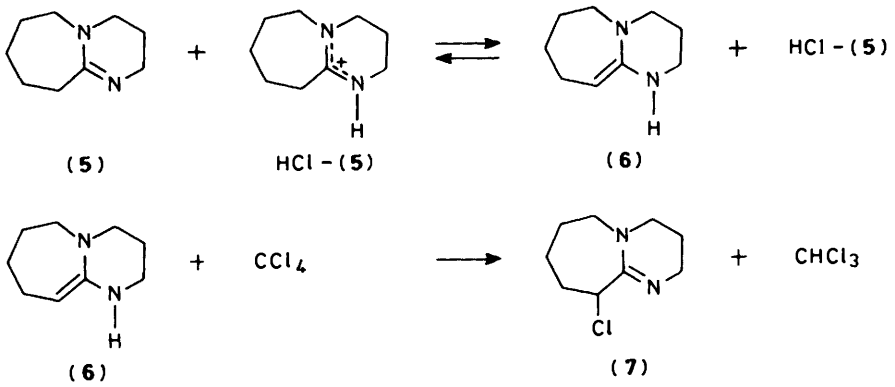
Halogen exchange reactions which produce CCl_4, $CHBrCl_2$, and CBr_2Cl_2 were observed along with the reaction of (1) with $CBrCl_3$. Such reactions were also found to be present in benzene,[1] but proceeded faster in DMF. Possible mechanisms for this type of reaction have been discussed earlier.[1]

Reaction of Amidine (5).—The rate of the acid-catalysed reaction of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (5) with CCl_4 in DMF was found to be dependent both on $[CCl_4]$ and on the concentration of acid [HCl-(5)] (entries 19—21 in Table 2). The reaction rate in dimethyl sulphoxide (DMSO) was shown to be somewhat lower than in DMF under otherwise the same conditions (entries 20 and 22).

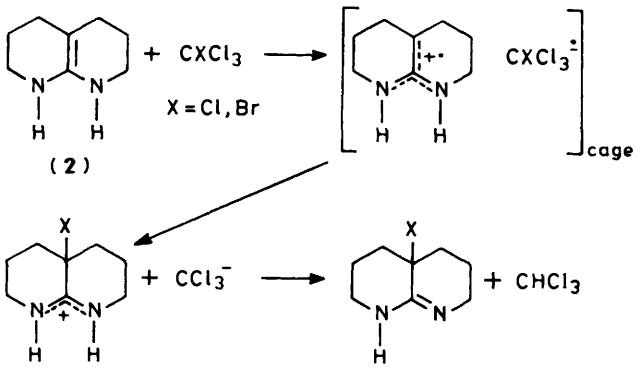
The reactivity of amidine (5) with CCl_4 in DMF is much lower than of (1) under comparable conditions (compare Tables 1 and 2). In a mechanism (Scheme 2) similar to that in Scheme 1, the smaller k_{obs} values for reaction of (5) could be the result of either slower formation of tautomer (6) or slow chlorination (or a combination of both).

The α-deuteriation of (5) in [$^2H_6$]DMSO, with $CDCl_3$ as

* This may be due to the positive charge in the ground-state amidinium ion HBr-(1) probably being more localized than in the transition state.



Scheme 2.



Scheme 3.

deuterium source, is *ca.* 40 times slower than the α-deuteriation of (**1**) under comparable conditions (entries 23 and 18).* This reflects the rate of formation of ketene aminals (**6**) and (**2**), respectively, and provides a reason for the slower α-chlorination of amidine (**5**). However, k_{obs} shows a certain dependence on both acid and CCl_4 concentration in the reaction of (**5**), entries 19—21. If the equilibrium constants for tautomerization of amidines (**5**) and (**1**) to ketene aminals (**6**) and (**2**), respectively, are of the same order of magnitude, this implies that the chlorination step is much slower for (**6**) than for (**2**). A reason for this is discussed later.

The Halogenation Step.—The large increase in the reaction rate of tautomer (**2**) with CCl_4 on changing the solvent from a nonpolar (C_6H_6, $\varepsilon_{25\,°C}$ 2.3; CH_2Cl_2, $\varepsilon_{25\,°C}$ 8.9) to a dipolar aprotic solvent (DMF, $\varepsilon_{25\,°C}$ 36.7) suggests a considerable charge separation in the transition state of this step. It is likely that a one-electron-transfer mechanism, which transforms the neutral species (**2**) and the perhalogenomethane into a radical-ion pair, is operating (Scheme 3). It is known that reaction of 1-ethyl-4-methoxycarbonylpyridyl radical with 4-nitrobenzyl halides shows a large rate increase when the solvent polarity is increased. This was taken as evidence for an electron-transfer mechanism which involves charge separation.[7]

The electron-donating properties of amino-substituted alkenes[8] like (**2**) and the electron-accepting ability of tetrahalogenomethanes[9] also make a mechanism according to Scheme 3 probable. Reduction potential measurements show that $CBrCl_3$ is 0.5 V more easily reduced than CCl_4.[10] This is in agreement with our results, showing that $CBrCl_3$ reacts much faster than CCl_4 with (**2**) in benzene.

The oxidation potentials for aminoalkenes are highly dependent on substituents.[8] The alkene becomes more easily oxidizable when the number of substituent amino groups is increased. Substituting an olefinic hydrogen for an alkyl group affects the oxidation potential in the same direction, albeit to a lesser degree.[8] For this reason, the ketene aminal (**2**) is expected to be a better electron donor than ketene aminal (**6**). As was shown above, our results of the reactions of (**1**) and (**5**) with CCl_4 in DMF indicate this behaviour.

The results thus favour a one-electron-transfer mechanism for reaction of the ketene aminal tautomer with tetrahalogenomethanes. However, the products are the very same as those expected if the mechanism is a nucleophilic substitution on halogen in the tetrahalogenomethane. This indicates that the radical-ion pair (*e.g.* in Scheme 3) is unstable and that it probably collapses within the solvent cage to yield a halogenated amidinium cation and a trichloromethyl anion. The fast reaction within a cage is supported by the absence of any effect of added radical scavengers on the rate of reaction.

This mechanism may be regarded as a neutral parallel to the radical anion/radical pair (RARP) mechanism proposed by Meyers for halogenation of charged nucleophiles with tetrahalogenomethane.[10]

Further information about the halogenation step may be obtained from reactions of tertiary enamines and ketene aminals with tetrahalogenomethanes. Preliminary results concerning the reaction of the enamine 1-pyrrolidinylcyclohexene with $CBrCl_3$ in DMSO reveal some interesting product evidence for the formation of the trichloromethyl anion in the reaction.[11] These results were found to be in accordance with the mechanism for the reaction of aminoalkenes with tetrahalogenomethanes proposed herein.

pK_a *Difference between* (**1**) *and* (**4**).—In the derivation of equation (1), α-proton abstraction from HBr-(**1**), giving (**2**), by the α-chlorinated product (**4**) is neglected. In order to justify this neglect, the pK_a difference between (**1**) and (**4**) was measured. This was done by a ^{13}C n.m.r. method, which uses the fact that carbons in the same position in the amidine base and in its amidinium ion may have appreciably different chemical shifts. Determination of the ΔpK_a of [(**1**)] and [(**4**)] in [$^2H_6$]DMSO was made. Thus, equal amounts of the amidinium salt HCl-(**1**) and the α-chlorinated (**4**) were mixed in [$^2H_6$]DMSO. Equilibrium (3) was then reached. Owing to fast proton exchange, the observed shifts in ^{13}C n.m.r. are weighted

* The lower deuteriation rate of (**5**) is probably due to a reduced rate of ketene aminal formation, caused by a combination of steric and conformational effects in the different ring systems. An investigation of the deuteriation of 1-methyl-2-aroyliminolactams in CD_3OD at 70 °C showed that the rate of deuterium incorporation was dependent on the ring size. The six-membered ring was deuteriated four and eight times faster than the five- and seven-membered ring systems, respectively.[6]

averages for shifts of exchanging carbons in the free base and its protonated form. Knowing the individual shifts for these two species, calculation of the composition of the reaction mixture is easy. Thus, the observed average shifts of (**1**) and HCl-(**1**) in the obtained mixture [equation (3)] were found to differ by only

$$\text{HCl-(1)} + \text{(4)} \overset{K}{\rightleftharpoons} \text{(1)} + \text{HCl-(4)} \qquad (3)$$

$3.5 \pm 0.3\%$ from the ^{13}C shifts of HCl-(**1**). The value of the equilibrium constant K for equation (3) is therefore $K = (0.035)^2/(0.965)^2 = (1.3 \pm 0.2) \times 10^{-3}$ which gives $\Delta pK_a = 2.9 \pm 0.1$.

Thus, the measured pK_a difference of (**1**) and (**4**), substrate (**1**) being the stronger base, suggests that the rate of proton abstraction by (**4**) is much lower than that by (**1**). It also implies that [HBr-(**1**)] is approximately constant and much larger than [HBr-(**4**)] for a major part of the α-halogenation reaction.

The observation that amidine (**1**) is 2.9 pK_a units more basic than the α-chlorinated (**4**) is readily explained by hyperconjugation.[12,13] In the bicyclic ring system in (**1**) and (**4**) the σ-orbitals for the α-C–H bond in (**1**) and the α-C–Cl bond in (**4**), respectively, are in an eclipsed position with respect to the carbon *p*-orbital lobe of the amidinium cation. An optimal hyperconjugative interaction is therefore obtained, which is much less for the α-chlorinated amidinium cation HCl-(**4**) than for HCl-(**1**).[12] The stabilization on going from free base to amidinium ion is consequently larger for (**1**) than for (**4**), and the α-chlorinated (**4**) becomes accordingly much less basic than amidine (**1**).

Experimental

The chromatographic system used in the determination of the reaction rates for the α-halogenation of amidines with tetrahalogenomethanes was an Optilab HSRI 931 high-performance liquid chromatograph, equipped with an interference refractive index detector. A Hewlett–Packard 20 cm 5 μm NH_2-column or a Brownlee 10 cm 5 μm amino-column and a mobile phase containing absolute ethanol–benzene–DBN (85:14:0.8 v/v) was used in the analysis. The flow rate was 1.2 ml min^{-1}, which eluted amidine (**5**) after 5 min and (**1**) after 7 min. A Hewlett–Packard 3990 A integrator, connected to the detector, was used for integration of the chromatograms.

G.l.c. analyses were made with a Hewlett–Packard 5880 A instrument on a glass column filled with 10% Carbowax 20M on Chromosorb W-AW DMCS. The oven temperature was 60 °C and the carrier gas flow rate was 10 ml min^{-1} in the analysis of the polyhalogenomethanes. N.m.r. spectra were recorded on a JEOL JNM-FX 100 Fourier transform spectrometer, equipped with a 5 mm ^1H–^{13}C dual probe or a 5 mm ^1H probe.

Reaction and volumetric flasks, n.m.r. tubes, *etc.*, were treated with concentrated alkali solution for at least 24 h. They were then rinsed with distilled water, 1M-hydrochloric acid, distilled water and 1M-ammonia, respectively, and finally ten times with distilled water. Syringes, needles, and valves were rinsed with ethanol and then treated in a similar way as described above, excluding the alkali treatment. The glassware (except volumetric flasks and syringes) were dried at 150 °C for at least 8 h. All equipment was dried in a Leybold Heraeus vacuum oven operated at 50 °C at 0.01 mmHg. The vacuum oven was connected to a Mecaplex glove box, thus allowing transfer of the dried equipment to the glove box without exposure to air. The nitrogen atmosphere in the glove box was dried by recirculation through molecular sieves (5 Å).

Materials.—2,10-*Diazabicyclo*[4.4.0]*dec*-1-*ene* (**1**). The synthesis of (**1**) has been described earlier.[14] Amidine (**1**) was sublimed directly before its use and handled in nitrogen atmosphere in the glove box. 2,10-Diazabicyclo[4.4.0]dec-1-ene hydrobromide HBr-(**1**) was prepared according to the literature.[1] A solution of HBr-(**1**) in methylene dichloride was stored at −20 °C between the kinetic runs. 1,8-Diazabicyclo-[5.4.0]undec-7-ene (DBU) (**5**) (Fluka; purum) was distilled at reduced pressure under N_2, b.p. 81—82 °C at 0.01 mmHg. *NN*-Dimethylformamide (Fluka; p.a.) was dried with 4 Å molecular sieves for 24 h and then over potassium hydroxide for 5 h. The decanted solution was distilled at reduced pressure in darkness under N_2 through a 40 cm column filled with glass helices. The middle fraction, b.p. 56.4—56.5 °C at 25 mmHg, was collected and placed in the glove box. Dimethyl sulphoxide (Merck; Uvasol) was distilled from sodium amide[15] at reduced pressure (b.p. 28—29 °C at 0.01 mmHg). Benzene (Merck; spectroscopic grade) was dried with 4 Å molecular sieves, then refluxed over calcium hydride, followed by distillation under N_2. A fraction with b.p. 79.5—79.6 °C was collected and kept in the glove box. Methylene dichloride (Fison; h.p.l.c. grade) was dried with 4 Å molecular sieves. Carbon tetrachloride (Merck; Uvasol) was dried with 4 Å molecular sieves, then shaken with anhydrous potassium carbonate, distilled under N_2, and stored in darkness in the glove box. Bromotrichloromethane (Fluka; purum) was shaken with a 5M-sodium hydroxide solution and four portions of distilled water. It was dried with 4 Å molecular sieves and distilled in darkness under N_2, b.p. 104.9—105.0 °C. The distilled bromotrichloromethane was stored under dry N_2 at −20 °C between kinetic runs. Hexadeuteriodimethyl sulphoxide (Ciba Geigy; >99.5% D) was dried with 4 Å molecular sieves. Deuteriochloroform (Ciba Geigy; >99.5%) was used without further purification. Styrene was distilled. Di-t-butyl nitroxide (Polyscience) was used as obtained.

1,8-*Diazabicyclo*[5.4.0]*undec-7-ene hydrochloride* HCl-(**5**). A solution of DBU (**5**) (2.0 g, 13 mmol) in methylene dichloride (70 ml) was shaken with concentrated hydrochloric acid (2 ml). The organic phase was dried with magnesium sulphate. Evaporation of the solvent gave an oil which was dried under reduced pressure (0.01 mmHg) at room temperature for several hours, leaving a solid, HCl-(**5**) (0.6 g, 25% yield). The hygroscopic HCl-(**5**) was kept in the glove box, m.p. 148—150 °C (uncorrected); δ_H([$^2H_6$]DMSO) 1.6, 1.9 (8 H), 2.76 (2 H), 3.19 (2 H), 3.52 (4 H), and 10.7 (1 H, br s). A 0.51M solution of HCl-(**5**) in DMF was prepared for use in the kinetics.

Kinetic Studies.—A solution of the substrate amidine was prepared and 2.5 ml of the solution was transferred in the glove box to the reaction flask, which was either a vial with Mininert® valve or a flask developed locally with a Rotaflo® PTFE valve.[1] This flask enables flushing with an inert atmosphere while sampling with a syringe. The acid catalyst was added with a syringe to the amidine solution which was then deoxygenated by freeze–pump–thaw cycles or by nitrogen bubbling. After thermostatting in darkness in a HETO 02 PT 623 thermostat, the reaction was started by addition of the tetrahalogenomethane with a syringe which had been filled in the glove box. Aliquot portions (100 μl each: 6—9) of the reaction mixture were taken with a 100 μl syringe with flushing with argon. Each aliquot portion was added to 600 μl of a mixture of ethanol and DBN (0.8 vol %). This solution was immediately analysed by h.p.l.c. The volume which was injected into the column by means of a Valco loop valve injector was the same within 0.5% in each analysis. The reactions were followed up to 75% consumption of the substrate amidine.

A linear least-squares analysis of the ln[substrate amidine] *versus* time plots gave rate constants with correlation coefficients typically better than 0.998.

α-*Deuterium Incorporation in Amidines.*—A solution of the amidine and the amidinium salt in [$^2H_6$]DMSO was prepared

and transferred in the glove box to a 5 mm n.m.r. tube with septum and screwcap. The incorporation of α-deuterium was started by the addition of $CDCl_3$, and the rate was measured by integration of the increasing signal from $CHCl_3$. The integrations were made on one-pulse spectra in order to avoid relaxation effects (T_1 for $CHCl_3$ *ca.* 50 s). In the case of amidine (**5**), the n.m.r. tube was placed in the thermostat at 25.0 °C between the integrations. For amidine (**1**), the n.m.r. tube with the reaction mixture was kept in the probe at 23.6 °C during the α-deuterium incorporation.

Acknowledgements

We are grateful to the Swedish Natural Science Research Council for their financial support.

References

1 S. Löfås and P. Ahlberg, *J. Am. Chem. Soc.*, 1985, **107**, 7534.
2 S. Löfås and P. Ahlberg, *J. Chem. Soc., Chem. Commun.*, 1981, 998.
3 D. H. R. Barton, J. D. Elliott, and S. D. Gèro, *J. Chem. Soc., Perkin Trans. 1*, 1982, 2085.
4 S. F. Nelsen and P. D. Bartlett, *J. Am. Chem. Soc.*, 1966, **88**, 143; N. Kornblum, S. D. Boyd, and N. Ono, *ibid.*, 1974, **96**, 2580.
5 W. J. Lautenberger, E. N. Jones, and J. G. Miller, *J. Am. Chem. Soc.*, 1968, **90**, 1110, present an example on styrene inhibition of radical-chain reactions.
6 V. G. Granik, A. M. Zhidkova, T. F. Vlasova, R. G. Glushkov, and Yu. N. Sheinker, *Khim. Geterotsikl. Soedin.*, 1974, 533.
7 M. Muhammed and E. M. Kosower, *J. Am. Chem. Soc.*, 1971, **93**, 2713.
8 J. M. Fritsch, H. Weingarten, and J. D. Wilson, *J. Am. Chem. Soc.*, 1970, **92**, 4038.
9 L. Eberson, *Acta Chem. Scand., Ser. B*, 1983, **36**, 533 and references therein.
10 C. Y. Meyers, W. S. Matthews, L. L. Ho, V. M. Kolb, and T. E. Parady in 'Catalysis in Organic Syntheses,' ed. G. V. Smith, Academic Press, New York, 1977, p. 197.
11 S. Löfås and P. Ahlberg, manuscript in preparation.
12 I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions,' Wiley, London, 1976, p. 80 and references therein.
13 P. Ahlberg, *Chem. Scr.*, 1973, **3**, 183; A. Thibblin and P. Ahlberg, *J. Am. Chem. Soc.*, 1977, **99**, 7926.
14 S. Löfås and P. Ahlberg, *J. Heterocycl. Chem.*, 1984, **21**, 583.
15 W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum, and N. R. Vanier, *J. Am. Chem. Soc.*, 1975, **97**, 7006.

Received 16*th September* 1985; *Paper* 5/1591