The Detection of Ionic Intermediates During the Bromination of 5*H*-Dibenz[*b*,*f*]azepine-5-carboxamide in 1,2-Dichloroethane

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The bromination of 5*H*-dibenz[*b*,*f*]azepine-5-carboxamide (carbamazepine) (**1**) in 1,2-dichloroethane gives only the *trans*-dibromide **2**. The reaction, followed spectrophotometrically, obeys a third-order rate law (second-order in Br_2), but the value of k_3 changes considerably depending on the monitoring wavelength. It is shown that this is due to the presence of reversibly formed Br_3^- salt intermediates, that make a more important contribution to the absorbance in the lower wavelength range of the monitored 360–540 nm region. A significant conductivity is also measured during the course of the bromination. Both spectrophotometric and conductimetric measurements are consistent with the presence of Br_3^- salt intermediates at a maximum concentration amounting to *ca.* 2% of that of the initial reagents. The structure of dibromide **2**, determined by X-ray diffraction, shows a considerable angle strain at carbons bearing bromine. This strain is responsible for an easy spontaneous debromination of **2**, as well as for a relatively high barrier for the formation of **2** from the bromonium–tribromide intermediate, that makes possible the accumulation of the intermediate itself during the bromination of **1**.

The formation of bromonium ion intermediates during the electrophilic bromination of alkenes[1] has generally been accepted since their first postulation by Roberts and Kimball.[2] It has since become clear[3] that the intermediates of this reaction can also be open β-bromocarbonium ions, depending on the alkene structure. Ions of both types can be generated and observed by NMR spectroscopy in SbF_5–SO_2 solution at low temperatures.[4] However, they cannot be directly observed under the conditions of alkene bromination, since their high reactivity towards the bromide or polybromide counteranions prevents their accumulation in the reaction medium. One exception is the adamantylideneadamantane bromonium ion, which is isolated as its tribromide salt from the reaction of the alkene with Br_2 in carbon tetrachloride,[5] because backside attack by the anion to give the dibromide is impossible for steric reasons. Ionic intermediates can also be isolated during the bromination of reactive alkenes in non-polar aprotic solvents, when the first formed bromonium ions can rearrange to more stable species by neighbouring group participation. This occurs, for instance, with cyclohex-2-enyl benzoates, that lead to isolable, resonance stabilized *trans*-4-bromo-2-phenylperhydrobenzo[*d*]-1,3-dioxol-2-ylium tribromide salts.[6]

It can be anticipated that also for reactive alkenes, unable to provide stabilization of the intermediate by rearrangement, the formation of sufficiently stabilized bromonium tribromide intermediates should be directly observable during the bromination in low polarity aprotic solvents, provided that their collapse to products can be retarded enough by structural effects.

5*H*-Dibenz[*b*,*f*]azepine derivatives appeared to be good candidates to check this expectation. An unusual angle strain at bromine-substituted carbon has been found[7] in the *trans*-dibromide obtained by bromination of the 5-carbonylchloride derivative, and this can slow down nucleophilic attack by the counteranion at the bromonium carbon. On the other hand, stabilization of the intermediate can be achieved by an appropriate choice of the nitrogen substituent. Alkyl groups or hydrogen on nitrogen are known[8,9] to favour the formation of open benzylic carbocations, that could lead to undesirable rearrangements with seven-membered ring restriction. On the other hand, a good electron acceptor like a carbonylchloride group completely prevents, by withdrawal of the nitrogen lone pair, the formation of such open ions, and favours bridged ions.[7] For this investigation we chose 5*H*-dibenz[*b*,*f*]azepine-5-carboxamide (carbamazepine) **1**, in which the low electron withdrawing ability of the carbamoyl substituent should allow the formation of partially bridged intermediates in which some stabilization of the positive charge at the benzylic carbon may be provided by the lone pair of the ring nitrogen. The presence of angle strain at bromine-substituted carbon in the corresponding *trans*-dibromide **2** has been shown in this work by X-ray diffraction, and the destabilizing effect of this strain on **2** has been proved. The course of the bromination of **1**, investigated by spectrophotometric and conductimetric techniques, has allowed us to detect the expected formation of ionic intermediates during this reaction.

Results

Bromination of Alkene **1**.—Carbamazepine (**1**) and Br_2 in 1,2-dichloroethane solution were mixed in equimolar amounts and the bromination was followed spectrophotometrically by monitoring the disappearance of the halogen at several wavelengths of its absorption band (360–540 nm). As expected for alkene bromination in this solvent,[10] the third-order rate law of eqn. (1), whose integrated form, for identical initial concentrations (C_0) of alkene and Br_2, is given by eqn. (2), was always obeyed.

$$-d[Br_2]d/t = k_3[\mathbf{1}][Br_2]^2 \quad (1)$$

$$1/C^2 - 1/C_0^2 = 2k_3t \quad (2)$$

However, the k_3 values changed considerably depending on the wavelength at which the rate constant was calculated. The highest k_3 value was found by monitoring at the Br_2 absorption tail, above 500 nm, while a value *ca.* 30% lower was obtained at the Br_2 absorption maximum (410 nm), and k_3 fell to about one sixth of its maximum value at 360 nm (Table 1). Moreover, the fitting to eqn. (2) of the data obtained at the lowest wavelength gave a poor correlation coefficient (0.995), as compared with the >0.999 values found for the fitting of the data obtained at the higher wavelengths of Table 1.

An inspection of the UV–VIS spectrum of a 1,2-dichloro-

Table 1 Apparent third-order rate constants for the bromination of carbamazepine **1** in 1,2-dichloroethane at 25 °C

[**1**]/mol dm^{-3}	[Br_2]/mol dm^{-3}	λ/nm	k_3/dm^6 mol^{-2} s^{-1} [a]
1×10^{-2}	1×10^{-2}	540	105(5)
1×10^{-2}	1×10^{-2}	480	84(4)
1×10^{-2}	1×10^{-2}	410	70(3)
1×10^{-2}	1×10^{-2}	370	43(2)
1×10^{-2}	1×10^{-2}	360	17(2)
5×10^{-3}	5×10^{-3}	540	106(5)
5×10^{-3}	5×10^{-3}	480	88(2)
5×10^{-3}	5×10^{-3}	360	17(1)

[a] All reactions were carried out at least in triplicate. The errors of the average rate constants are given as standard deviations from the average.

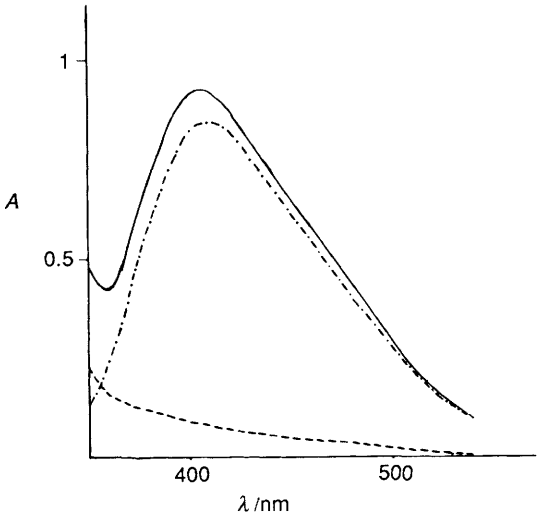
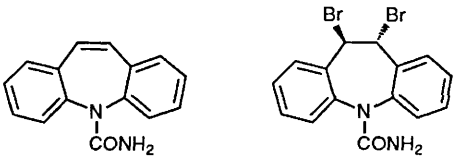


Fig. 1 UV–VIS spectra in 1,2-dichloroethane at 25 °C of 4×10^{-3} mol dm^{-3} Br_2 and 4×10^{-3} mol dm^{-3} 5*H*-dibenz[*b*,*f*]azepine-5-carboxamide **1** (——), 4×10^{-3} mol dm^{-3} Br_2 (– · – · –), and their difference (– – –)

ethane solution containing equimolar amounts of **1** and Br_2, in comparison with that of Br_2 alone, above 350 nm, where the alkene absorption did not interfere severely, showed an extra absorption that decreased with increasing wavelength and fell to zero above 500 nm. Fig. 1 shows the spectrum taken from a solution of initial 5×10^{-3} mol dm^{-3} **1** and Br_2 *ca.* 1 min after mixing, when the actual halogen concentration, as measured at 540 nm, was 4×10^{-3} mol dm^{-3}. The spectrum of Br_2 alone at the latter concentration and the difference spectrum are also shown in Fig. 1. That this difference spectrum was not due to the formation of a by-product was shown by the fact that the solution became completely transparent when the Br_2 was rapidly consumed by addition of an excess of a very reactive alkene such as cyclohexene. Moreover, the shape of the difference absorption curve was identical to that of the Br_3^- ion, as obtained from both tetrabutylammonium tribromide[11] and the adamantylideneadamantane bromonium tribromide salt.[12] Using the molar extinction coefficients of these two salts in 1,2-dichloroethane, a maximum concentration of *ca.* 1×10^{-4} mol dm^{-3} of a Br_3^- salt was calculated to be present in a solution of initial 5×10^{-3} mol dm^{-3} **1** and Br_2. The difference absorption decreased slowly during the course of the bromination, and completely disappeared only at the end. At this point an appropriate amount of a standard was added to the solution in order to quantify the product by HPLC. Only dibromide **2**, whose structure and relative configuration was established by X-ray diffraction as discussed below, was found in a 100% yield. This dibromide was also isolated in 90% yield from preparative runs by crystallization from chloroform.



1 **2**

In order to check the formation of ionic intermediates at detectable concentrations, the bromination of **1** was also carried out in a conductimetric cell. Measurements were made at 25 °C, at the same 5×10^{-3} mol dm^{-3} concentration of **1** and Br_2 used for the spectrophotometric measurements. A fast initial increase in conductivity up to about 2 μS cm^{-1} was found. Using the value of molar conductance found for the adamantylideneadamantane bromonium tribromide salt, $\Lambda^m = 25$ S cm^2 mol^{-1},[12] this value of the conductivity again corresponded to a concentration of Br_3^- salt of *ca.* 1×10^{-4} mol dm^{-3}. This conductivity completely vanished on addition of an excess of cyclohexene, which immediately consumed all the remaining Br_2. This, together with the disappearance of the Br_3^- absorption, showed that a reversibly formed bromination intermediate, and not a stable by-product, was responsible for both the conductivity and the extra absorption of the **1** and Br_2 solution. In analogy with the differential absorption, the conductivity decreased slowly during the course of the reaction and only fell to zero at the end.

For comparison purposes, the bromination of (*Z*)-stilbene was examined under identical conditions both spectrophotometrically and conductimetrically. A negligible value of conductivity ($\chi = 0.1$ μS cm^{-1}) and an absorption spectrum above 350 nm identical to that of Br_2 (corrected for the very low contribute of the alkene at 350–360 nm), were found for a 1,2-dichloroethane solution of the alkene and Br_2 of initial 5×10^{-3} mol dm^{-3} concentrations.

X-Ray Structure of Dibromide **2**.—Crystals of dibromide **2** containing one molecule of chloroform were obtained by crystallization of the bromination product of carbamazepine **1** from chloroform. The molecular arrangement of **2**·$CHCl_3$ is reported in Fig. 2, which also shows the hydrogen bonding between two molecules of **2** and to the crystallization solvent. Final atomic coordinates and isotropic thermal parameters with standard deviations are listed in Table 2. Interatomic bond lengths and angles are reported in Table 3.

The tricyclic structure approximately lies on two planes at a dihedral angle of 131.5°. The first plane is defined by the atoms N(1), C(10), C(11) and the phenyl ring C(1)–C(11a) and the greatest deviation from this plane is that of the C(10) atom, 0.12 Å; the second plane contains atoms C(10), N(1) and the phenyl ring C(5a)–C(9a), and the atom deviating most from this plane is C(6) that stays 0.09 Å away. The Br(1)–C(10)—C(11)–Br(2) torsion angle is 168°, showing for the two Br atoms an approximately *anti* orientation similar to that found in *trans*-10,11-dibromo-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carbonyl chloride[7] and *trans*-10,11-dibromo-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene.[13] This conformation appears therefore to be typical of these tricyclic compounds. The molecule is planar around N(1), as shown by the values of the angles C(5a)–N(1)–C(12), C(4a)–N(1)–C(12) and C(5a)–N(1)–C(4a). The torsion angle C(5a)–N(1)–C(12)–N(2) measured 7°, whereas C(4a)–N(1)–C(12)–O measures 3°.

The lengths of the bonds C(10)–Br(1) and C(11)–Br(2) are equivalent within the estimated standard deviations and their values range around the mean value of 1.97 Å, generally observed for C–Br single bonds.[14,15] The internal angles at the bromine-substituted carbon atoms are 114(2) and 117(1)° for

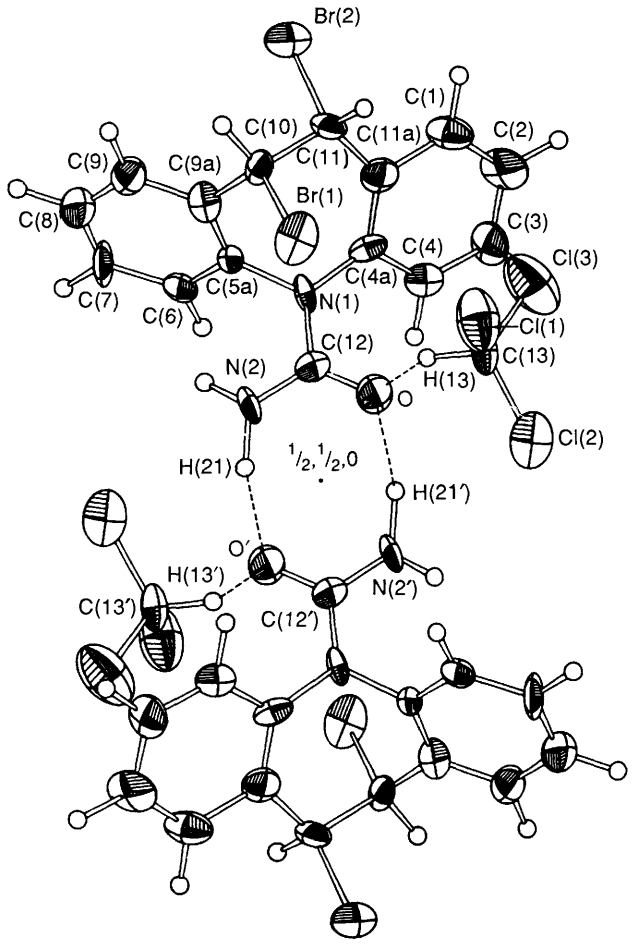


Fig. 2 View of the molecular structure of dibromide **2** projected on a direction of low superimposition showing the numbering scheme and the hydrogen bonding around the inversion centre at $\frac{1}{2}, \frac{1}{2}, 0$

C(9a)–C(10)–C(11) and C(10)–C(11)–C(11a), respectively. The latter value, remarkably larger than the ideal tetrahedral value, suggests a considerable sp^2 character at C(11) and is indicative of angle strain.

The atoms labelled with the prime in Fig. 2 belong to a molecule related to the asymmetric unit by the inversion around the centre at $\frac{1}{2}, \frac{1}{2}, 0$. The atoms C(12), N(2), O, C(12′), N(2′) and O′ are nearly coplanar and the N(2) atom interacts strongly with the O′ atom being 2.81(2) Å apart. This interaction is achieved through the atom H(21), that has been found in the difference Fourier map but has been refined imposing geometrical constraint. The distance H(21)···O′ at the end of the refinement was 1.81 Å.

The chloroform molecule that crystallizes together with **2** is also connected by a hydrogen bond to the oxygen atom. The C(13)···O distance is 3.22 Å and the H(13)···O distance is 2.37 Å.

Debromination of Dibromide **2**.—When stored at room temperature, colourless crystals of dibromide **2** slowly turned to yellow and HPLC analysis showed the presence of alkene **1**, besides the starting dibromide. Typically, the amount of **1** was *ca.* 10% after two months. This debromination was much faster in solution, especially in aprotic dipolar solvents. Table 4 shows the % yields of **1** and the recovered dibromide **2** found by HPLC when **2** was left in dimethylformamide, dimethyl sulfoxide and acetonitrile solutions at 25 °C. As time passed these solutions become intensely yellow-orange coloured, and the chromatograms showed additional peaks due to other unidentified products, probably consisting of acridine derivatives. In

Table 2 Atomic coordinates of non-hydrogen atoms in $C_{15}H_{12}N_2OBr_2{\cdot}CHCl_3$[a]

Atom	*x/a*	*y/b*	*z/c*
Br(1)	0.204 7(2)	0.143 8(3)	0.086 27(9)
Br(2)	0.094 9(2)	0.335 6(3)	0.253 02(9)
C(1)	0.455(2)	0.279(2)	0.250 8(8)
C(2)	0.597(2)	0.341(3)	0.262 0(8)
C(3)	0.647(2)	0.457(3)	0.226 9(8)
C(4)	0.559(2)	0.501(2)	0.181 8(7)
C(4a)	0.417(2)	0.441(2)	0.167 5(7)
N(1)	0.337(1)	0.491(1)	0.117 6(5)
C(5a)	0.185(2)	0.535(2)	0.117 5(6)
C(6)	0.149(2)	0.694(2)	0.106 7(6)
C(7)	0.001(2)	0.739(2)	0.098 2(7)
C(8)	−0.110(2)	0.628(3)	0.104 0(8)
C(9)	−0.072(2)	0.471(2)	0.118 3(8)
C(9a)	0.075(2)	0.429(2)	0.125 3(7)
C(10)	0.113(2)	0.265(2)	0.140 7(6)
C(11)	0.213(2)	0.249(2)	0.196 3(7)
C(11a)	0.364(2)	0.331(2)	0.201 2(7)
C(12)	0.401(2)	0.478(2)	0.068 9(7)
O	0.528(1)	0.430(2)	0.068 7(5)
N(2)	0.319(1)	0.526(2)	0.023 7(6)
Cl(1)	0.546 1(6)	−0.118 3(7)	0.061 4(3)
Cl(2)	0.780 6(5)	0.097 5(7)	0.043 2(3)
Cl(3)	0.668 6(8)	0.084 5(9)	0.147 1(3)
C(13)	0.622(2)	0.066(2)	0.077 6(8)

[a] Estimated standard deviations given in parentheses refer to the last significant digits.

DMSO after 24 h dibromide **2** had completely disappeared and alkene **1** was formed in 50% yield. The debromination was slower in DMF, where smaller amounts of by-products were also formed, and was slowest in acetonitrile, where 20% of **1** was found after 8 days. Similar behaviour has been observed for *trans*-10,11-dibromo-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carbonyl chloride,[7] but not for *meso*- and (±)-1,2-dibromo-1,2-diphenylethane, acyclic analogues of **2**. The latter dibromides have been reported[16] to be debrominated in DMF to a negligible extent at 60 °C and only in refluxing DMF 80% debromination of the *meso* isomer was found after 10 h. The present data, together with those previously reported,[7] show a peculiar tendency of 10,11-dibromides of the 5*H*-dibenz[*b*,*f*]azepine tricyclic system to undergo a spontaneous loss of bromine, that can be related to the angle strain at the bromine-bearing carbons shown by X-ray diffraction.

Discussion

The bromination of alkenes in low polarity aprotic solvents, where the reaction exhibits overall third-order kinetics, first-order in alkene and second-order in Br_2, can be briefly represented as shown in Scheme 1. Bromonium- (or β-bromocarbonium, depending on the alkene structure) tribromide intermediates are formed by a slow ionization of alkene–bromine charge transfer complexes,[17] and are assumed to collapse rapidly to products. The reversibility of this ionization step has been conclusively established.[7,13,18] Furthermore, the possibility of rate determination during the product forming step has been recently shown.[19,20]

The present results provide direct evidence for the formation of ionic intermediates during the bromination of carbamazepine in 1,2-dichloroethane. The conductivity of **1** and Br_2 solutions shows the presence of salt species. Although no information as to the structure of these intermediates can be inferred from conductimetric measurements, a Br_3^- structure is shown for the anionic moiety by the UV–VIS spectrum. The structure of the countercation cannot be directly established by these spectrophotometric measurements, since this species does not absorb in

Table 3 Relevant structural parameters for $C_{15}H_{12}N_2OBr_2 \cdot CHCl_3$[a]

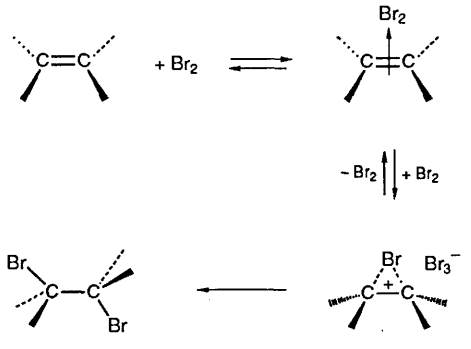
Bond lengths			
Br(1)–C(10)	1.95(2)	Br(2)–C(11)	1.99(2)
C(1)–C(2)	1.39(3)	C(8)–C(9)	1.41(3)
C(1)–C(11a)	1.46(2)	C(9)–C(9a)	1.37(2)
C(2)–C(3)	1.42(3)	C(7)–C(8)	1.40(3)
C(3)–C(4)	1.35(2)	C(6)–C(7)	1.39(2)
C(4)–C(4a)	1.39(2)	C(5a)–C(6)	1.41(2)
C(4a)–C(11a)	1.37(3)	C(5a)–C(9a)	1.37(2)
C(4a)–N(1)	1.42(2)	N(1)–C(5a)	1.43(2)
C(9a)–C(10)	1.48(3)	C(11)–C(11a)	1.53(2)
C(10)–C(11)	1.56(2)	N(1)–C(12)	1.39(2)
C(12)–O	1.22(2)	C(12)–N(2)	1.33(2)
Cl(1)–C(13)	1.74(2)	Cl(2)–C(13)	1.76(2)
Cl(3)–C(13)	1.72(2)	N(2)–H(21)	1.08
C(13)–H(13)	1.08	O···H(13)	2.37
O···H(21′)[b]	1.81		
Bond angles			
Br(1)–C(10)–C(11)	107(1)	Br(2)–C(11)–C(10)	106(1)
Br(1)–C(10)–C(9a)	115(1)	Br(2)–C(11)–C(11a)	108(1)
C(9a)–C(10)–C(11)	114(2)	C(10)–C(11)–C(11a)	117(1)
C(9)–C(9a)–C(10)	119(2)	C(1)–C(11a)–C(11)	110(1)
C(5a)–C(9a)–C(10)	120(1)	C(4a)–C(11a)–C(11)	129(1)
C(5a)–C(9a)–C(9)	121(1)	C(1)–C(11a)–C(4a)	121(1)
C(2)–C(1)–C(11a)	119(2)	C(8)–C(9)–C(9a)	119(2)
C(1)–C(2)–C(3)	119(2)	C(7)–C(8)–C(9)	121(2)
C(2)–C(3)–C(4)	120(2)	C(6)–C(7)–C(8)	119(2)
C(3)–C(4)–C(4a)	123(2)	C(5a)–C(6)–C(7)	120(2)
C(4)–C(4a)–C(11a)	118(2)	C(6)–C(5a)–C(9a)	120(1)
C(4)–C(4a)–N(1)	118(1)	N(1)–C(5a)–C(6)	117(1)
N(1)–C(4a)–C(11a)	123(1)	N(1)–C(5a)–C(9a)	123(1)
C(4a)–N(1)–C(5a)	119(1)	C(4a)–N(1)–C(12)	120(1)
C(5a)–N(1)–C(12)	121(1)	N(1)–C(12)–O	120(2)
N(1)–C(12)–N(2)	117(1)	O–C(12)–N(2)	123(2)
Cl(1)–C(13)–Cl(2)	111(1)	Cl(2)–C(13)–Cl(3)	110(1)
Cl(1)–C(13)–Cl(3)	111(1)		

[a] Distances are in Å, angles in degrees. Estimated standard deviations given in parentheses refer to the last significant digits. The deviations for the distances C–H have not been reported owing to the ideal geometry imposed during the refinement. [b] $' = 1 - x, 1 - y, -z$.

Table 4 Debromination of *trans*-10,11-dibromo-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide **2** in solution at 25 °C

			% Yields[a]	
[**2**]/mol dm^{-3}	Solvent	time/h	**1**	**2**
6×10^{-2}	DMSO	24	50	—
6×10^{-2}	DMF	24	15	70
		78	50	25
3×10^{-2}	CH_3CN	24	<1	98
		192	20	54

[a] The reported percentages are averages of three experiments, which were reproducible within ±2%.



Scheme 1

the useful wavelength region. However, there is little doubt that this cation should be a reversible formed bromonium ion (see below), because it is able to transfer bromine to another more reactive alkene, as shown by the immediate loss of conductivity and of Br_3^- absorption of the solution of **1** and Br_2 on addition of cyclohexene. Furthermore, no product other than the *trans* dibromide **2** was found at the end of the reaction, thus excluding the possibility that the conducting and absorbing species could result from a rearrangement of the first formed bromonium ion to a more stable species leading finally to a by-product, as found in the bromination of 5*H*-dibenzo[*a*,*d*]cycloheptene.[13]

Spectrophotometric and conductimetric measurements agree in indicating, on the basis of the known molar extinction coefficient and molar conductance of a stable bromonium tribromide salt,[12] that the maximum concentration attained by the intermediate during the bromination under the employed conditions amounted to *ca.* 2% of the initial reagent concentrations. This amount is low enough not to affect severely the determinations of the rate constant k_3 based on the disappearance of free Br_2 at wavelengths where the molar absorptivity of the Br_3^- species is not higher than that of Br_2 (>440 nm). However, the contribution to the absorbance by the Br_3^- intermediate becomes more and more important when the monitoring wavelength is shifted below the absorption maximum of Br_2 (410 nm) and the resulting k_3 values are therefore greatly affected. This explains the large change in the apparent values of k_3 (Table 1) found monitoring the disappearance of Br_2 in the 540–360 nm wavelength range.

It is noteworthy that neither absorption by a Br_3^- intermediate salt nor appreciable conductivity have been observed in 1,2-dichloroethane solutions of Br_2 and (*Z*)-stilbene, an acyclic analogue of **1** lacking the nitrogen bridge between the *ortho* positions of the two phenyl rings. The lack of accumulation of a bromonium tribromide intermediate in the bromination of this, and most other alkenes, is consistent with a rate of collapse of this intermediate to product and/or of its reversal to reagents much higher than the rate of formation of the intermediate itself. On the other hand, the fact that the intermediate is accumulated at a detectable concentration during the bromination of carbamazepine indicates a reduction in the rate of disappearance of the intermediate by collapse to product and by reversal to reagents. This can result from at least two effects.

Firstly, the rate of attack of the counteranion at the carbon atoms of the cationic intermediate may be slowed down by the angle strain introduced in the dibromide product. This strain is shown directly by the large (117°) value of the C(10)–C(11)–C(11a) angle observed in the X-ray structure of **2**. It is also shown indirectly by the unusual ease of spontaneous debromination of **2** in solutions of dipolar aprotic solvents. In analogy with the corresponding *N*-carbonyl chloride derivative,[7] such debromination probably occurs by ionization of a benzylic C–Br bond at a carbon having a strained valence angle near to 120°, followed by a loss of a Br^+ ion from the other carbon to give back the starting alkene. Such angle strain should increase the energy of dibromide **2** and therefore the barrier for its formation from the ionic intermediate of the bromination of **1**.

Secondly, the cationic intermediate can be stabilized mesomerically by the ring nitrogen. When formed in the debromination of **2** in dipolar aprotic solvents this cation is probably a solvent-stabilized open β-bromocarbonium ion, as suggested by the significant formation of side-products. Although the structures of these side-products have not been investigated, their UV–VIS absorption features point to acridine derivatives arising by an initial rearrangement of a carbocationic species involving ring contraction. On the other hand, the formation of the *trans* dibromide **2** in 100% yield in the bromination in the low polarity 1,2-dichloroethane solvent, incapable of nucleophilic solvation, rather suggests a partially bridged cationic

intermediate in which the partial positive charge at C(10) and C(11) is further delocalized by mesomeric interaction with the ring nitrogen lone pair. This mesomeric stabilization can lower the energy of the ionic intermediate in the bromination of **1** relative to that of (*Z*)-stilbene, thus increasing the barrier for its reversion to reagents.

Thus, the results of the present investigation show that the mechanism of this common reaction cannot be simplified as a multistep process in which the product-forming step is always very much faster than the formation of the ionic intermediate. As recently stressed,[20] a spectrum of situations ranging from essentially irreversible ion formation, with rate determination in the ionization step, to prevalent ion reversal, corresponding to rate determination in the product forming step, does exist. The present seems to be an intermediate case, in which relatively high barriers (*i.e.* relatively slow rates) for both product formation and reversal to reagents make it possible to observe by direct experimental measurements the formation of an ionic intermediate during alkene bromination in a low polarity aprotic solvent.

Experimental

Melting points were determined on a Kofler block and are uncorrected. The ^{1}H NMR spectrum of **2** was taken on a Bruker AC200 instrument in $CDCl_3$ with tetramethylsilane (TMS) as internal reference. UV–VIS spectra and kinetic measurements were obtained with a Varian Cary 2200 instrument. Conductivities were measured at 25 ± 0.5 °C with a Philips PW9509 digital conductivity meter. HPLC analyses were carried out with a Waters Model 600E apparatus equipped with a Model 990 photodiode-array detector and a Spherisorb S5 ODS2 column using acetonitrile–methanol–water (20:30:50) as eluent at a flow rate of 1 cm^3 min^{-1}.

5*H*-Dibenz[*b*,*f*]azepine-5-carboxamide **1** (Sigma) was pure to HPLC. All solvents were reagent grade. Commercial 1,2-dichloroethane was treated as reported previously.[21] Bromine was withdrawn from 1 cm^3 sealed vials (C. Erba, RPE grade, >99.5%) opened immediately before use.

trans-10,11-*Dibromo*-10,11-*dihydro*-5H-*dibenz*[b,f]*azepine*-5-*carboxamide* **2**.—A 1,2-dichloroethane solution of Br_2 (0.1 mol dm^{-3}, 25 cm^3) was added to a solution (25 cm^3) of **1** (2 mmol) in the same solvent and the mixture was left for 2 h at room temperature in the dark. The reaction mixture was then washed with saturated aqueous $NaHSO_3$ and water, dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The residue was crystallized from $CHCl_3$ to give 0.7 g of the pure (HPLC) dibromide **2**, m.p. 157–159 °C (decomp.) (Found: C, 37.6; H, 2.35; N, 5.3; Br, 30.85; Cl, 20.85. $C_{15}H_{12}N_2OBr_2{\cdot}CHCl_3$ requires C, 37.28; H, 2.54; N, 5.43, Br, 31.00; Cl, 20.63%); δ_H 4.75 (s, 2 H, CHBr), 5.54 (s, 2 H, NH_2), 7.26–7.56 (m, 8 aromatic protons).

Spectrophotometric and Conductimetric Measurements.—Bromine solutions in 1,2-dichloroethane were prepared shortly before use and the concentrations adjusted to twice the desired initial ones (Table 1). These solutions were thermostatted at 25 °C, rapidly mixed with equal volumes of pre-thermostatted solutions of **1** of identical concentration in the same solvent, and then divided into two parts.

One part was used to follow the reaction spectrophotometrically by recording periodically the UV–VIS spectrum in the 350–550 nm range. The bromine spectrum at the appropriate concentration was also registered in this wavelength range. The UV–VIS spectrum of the reaction mixture and the difference spectrum are reported in Fig. 1. The decay of the Br_2 absorption was followed at 540, 480, 410, 370 and 360 nm down to *ca.* 80% conversion. The absorbance–time data were fitted to the third-order integrated rate equation [eqn. (2)] and the rate constants obtained with the usual linear least-squares procedure. The k_3 values reported in Table 1 are averages of three independent measurements.

Table 5 Experimental data for the crystallographic analysis of $C_{15}H_{12}N_2OBr_2{\cdot}CHCl_3$

Formula	$C_{16}H_{13}Br_2Cl_3N_2O$
M	515.46
Space group	$P2_1/n$
a/Å	9.045(3)
b/Å	8.512(4)
c/Å	24.609(8)
β/°	96.19(3)
U/Å^3	1884(1)
Z	4
D_c/Mg m^{-3}	1.818
Reflections for lattice parameters: number	25
Reflections for lattice parameters: *θ* range/°	9–13
Radiation	Mo-Kα_1
λ/Å	0.709 30
F(000)	1008
T/K	294
Crystal size/mm	0.23 × 0.17 × 0.38
Diffractometer	Philips PW1100
μ/cm^{-1}	46.98
Absorption corrections (min., max.)	0.63–1.38
Slowest scan speed/° s^{-1}	0.08
Scan width/°	1.60
θ-range/°	2.5–20
h-range	−8–8
k-range	0–8
l-range	0–23
Standard reflections	0 0 6, 0 2 3, 0 2 −3
Intensity variation	$< \pm 3\sigma(I_{sr})$[a]
Scan mode	$\theta/2\theta$
Condition for observed reflections	$I > 2\sigma(I)$
No. of collected reflections	1442
No. of reflections used in the refinement	1210
Anisotropic least-squares on *F*	full-matrix
Max. least-squares shift-to-error ratio	0.4
Min./max. height in final Fourier map, *ρ*/e Å^{-3}	−0.66, 0.75
No. of refined parameters	220
$R = \Sigma\Delta F/\Sigma\lvert F_o\rvert$	0.0696
$R' = [\Sigma w(\Delta F)^2/\Sigma w F_o^2]^{\frac{1}{2}}$	0.0707
Weighting scheme	$1/\sigma^2(F_o)$

[a] I_{sr} is the mean of the intensities measured on the standard reflection.

The second portion of the 1,2-dichloroethane solution of **1** and Br_2 was transferred into a conductimetric cell and the conductivity measured during the course of the reaction. The reagents were also directly mixed in the conductimetric cell in order to observe the fast initial increase in conductivity.

When both the absorbance in the 350–550 nm range and the conductivity were reduced to zero, samples of the solution were withdrawn and analysed by HPLC after addition of *trans*-10,-11-dihydroxy-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide[22] as a standard for the quantification of the produced dibromide **2**. A 100±2% yield was found in four independent measurements.

Debromination of **2**.—Solutions of **2** in dimethyl sulfoxide, *N*,*N*-dimethylformamide or acetonitrile at the concentrations reported in Table 4 were thermostatted at 25 °C in the dark. After the times reported in Table 4, samples were withdrawn, an appropriate amount of *trans*-10,11-dihydroxy-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide[22] was added as a standard, and subjected to HPLC analysis for the quantification of both dibromide **2** and alkene **1**. The product yields are reported in Table 4.

Crystal Structure Analysis of Dibromide **2**.—Prismatic colour-

less crystals of dibromide **2** were mounted within Lindemann capillaries, and studied by the Weissenberg technique. The photographs showed monoclinic symmetry and systematic absences suggested $P2_1/c$ (n. 14) as the unique possible space group. We have preferred the non-standard setting $P2_1/n$ to have β value nearest to 90°. This preliminary study was useful for the choice of the most suitable crystal for intensity data collection, which was carried out following the experimental conditions summarized in Table 5.

The intensities were corrected for Lorentz and polarization effects and for absorption by using the Ψ scan method.[23] Automatic direct methods[24] revealed the position of the bromine atoms. A Fourier synthesis (phases of the structure factors obtained from the positions of the bromine atoms) showed the chlorine and a number of carbon atoms. The molecule was completed by alternating cycles of structure refinement with Fourier syntheses. After a further absorption correction by the method of Walker and Stuart[25] and introduction of anisotropic thermal factors for the halogen atoms, a maximum observed near to the N(2) atom in difference Fourier synthesis was attributed to the hydrogen atom H(21). The position of H(22) was calculated and the $-NH_2$ was refined as a rigid group. The other hydrogen atoms were introduced in calculated positions with a thermal factor fixed as $U = 0.05$ and were considered as riding on the connected carbon atoms. Table 2 contains a list of the coordinates of non-hydrogen atoms. Table 5 presents some statistical parameters obtained in the last refinement cycle.

The atomic scattering factors were taken from ref. 26. The calculations were performed on an IBM 3081 computer of the *Centro Nazionale Universitario di Calcolo Elettronico*, CNUCE (Pisa). The programmes SHELX 76,[27] PARST[28] and ORTEPII[29] were also used. Tables of anisotropic thermal parameters, hydrogen atom coordinates and a view of the crystal packing have been deposited at the Cambridge Crystallographic Data Centre.*

Acknowledgements

This work was supported by grants from the CNR and MURST. The authors wish to thank Professor P. F. Zanazzi (University of Perugia) for collection of intensity data.

* See 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1992, Issue 1, pp. xx–xxv.

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Paper 1/06018J
Received 27*th November* 1991
Accepted 6*th January* 1992