Oxidation of *N*-Benzyl Aziridine by Molecular Iodine: Competition of Electron Transfer and Heterolytic Pathways

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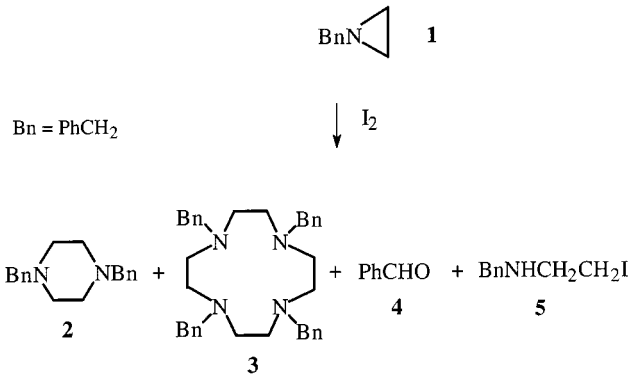
Excess *N*-benzyl aziridine (**1**) reacts with I_2 to afford dimer **2**, tetramer **3**, benzaldehyde (**4**), and iodoamine **5**. The reaction is interpreted as occurring by both electron transfer (ET) and heterolytic mechanisms. An ET mechanism is substantiated for the oxidation by I_2 of dimer **2** and tetramer **3**, both being substrates easier to oxidise by electron abstraction than **1**. Several auxiliary reactions were performed on **1** in order to firmly establish the boundaries to the competition between the ET and heterolytic mechanisms. For the reaction of **1** with **5** a reaction scheme is proposed; in a particular case, a pseudo-first order kinetic law is followed.

Introduction

We have recently briefly reported[1] on a peculiar reaction (Scheme 1) discovered while investigating the mechanism of the oxidative *N*-dealkylation of tertiary amines by metalloporphyrins. In this reaction, I_2 and *N*-benzyl aziridine (**1**) in $CDCl_3$ solution gave rise to dimer **2**, tetramer **3**, benzaldehyde (**4**), and iodoamine **5**.



Scheme 1

We have interpreted this reaction as proceeding through the formation of the radical cation of **1** by an electron transfer (ET) pathway.[1] Support for the intervention of $\mathbf{1}^{\cdot+}$ came from the literature, where tetramer **3** had been reported as the sole product of the electrochemical oxidation of **1**.[2]

Only a few oxidation reactions of aziridines by ET have been documented so far: they rely on chemical[3,4] or electrochemical[2,5] conditions, or on photosensibilization,[6] but a full characterisation of the reaction products[3] is not always reported. Mechanistic alternatives to the ET pathway do exist. For example, we have provided evidence that, under radical conditions, **1** is converted into **2** by a hydrogen atom-transfer (HAT) pathway.[1] It has also been reported that **2** and **3** can both be obtained by an acid-catalysed heterolytic mechanism (HETERO).[7,8] How do these alternative mechanisms comply with our suggestion[1] that the reaction of **1** with I_2 follows the ET mechanism?

An ET mechanism for the oxidation of tertiary aliphatic[9] or aromatic amines[10] by molecular iodine is precedented. Even molecular bromine oxidises amines, but depending on the reaction conditions adopted, either a HETERO or ET route is followed.[11–13] Aziridine derivatives were not employed as substrates until now. It appeared appropriate, therefore, to closely investigate the mechanistic details of the reaction reported in Scheme 1; the results are reported herein.

Results

The reaction of *N*-benzyl aziridine **1** with I_2 (at $\mathbf{1}/I_2$ molar ratios ranging from 2 to 5) occurs at room temperature (Scheme 1). The reaction is followed in $CDCl_3$ solution using high resolution ^{1}H-NMR; in this case, benzaldehyde is likely to be formed from adventitious water contained in the solvent. The mass balance of the identified reaction products covers 75–90% of the aziridine consumption. The initial iodine is converted into iodoamine **5**, but in part also into a triiodide anion; it could be titrated (as I^-) after aqueous workup of the reaction mixture.

A typical example of the **1** + I_2 reaction is presented in Table 1 (for $[\mathbf{1}]_0/[I_2]_0 = 3$). The reaction may be divided into four stages: (*i*) formation of the charge transfer complex (CTC) $\mathbf{1}\cdot \times \mathbf{I_2}$, where × indicates the number of iodine molecules required by one molecule of substrate; (*ii*) transformation of this complex into products **2–5**, until tetramer **3** reaches a constant concentration; (*iii*) further transformation of **1** into **2** and **5**, until all **1** is consumed; (*iv*) formation of additional **2** by consumption of **5**. During stages (*i*) and (*ii*) the production of iodide ion remains constant (at about

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Table 1. Reaction of **1** with iodine

Entry nr.	R.time (min)	Compound[a] *Micromoles*[b] and ^{1}H NMR chemical shifts (ppm, δ scale) due to:[c] **1** Bn	R	R	**2** Bn	R	**3** Bn	R	*Ho*	**4** C*H*O	*Ho*	**5** Bn	CH_2I	NCH_2	I^- µmol [d]
							Stage (i)								
1	3	*112.5*			–		*≤ 0.1*			–		–			*11.1*
		3.45	1.91	1.39	–	–	–	2.93	–	–	–	–	–	–	
							Stage (ii)								
2	20	*97.1*			*1.2*		*1.5*			*0.8*		*2.3*			*11.5*
		3.44	1.90	1.38	3.65	2.61	3.66	2.93	7.08	10.03	7.89	3.84	3.33	2.95	
3	35	*60.2*			*7.3*		*3.9*			*2.5*		*6.5*			*11.3*
		3.42	1.87	1.34	3.64	2.62	3.66	2.93	7.08	10.03	7.89	3.84	3.33	2.95	
4	50	*41.8*			*10.3*		*5.0*			*3.3*		*9.0*			*11.7*
		3.41	1.85	1.31	3.63	2.62	3.66	2.93	7.08	10.03	7.89	3.84	3.33	2.95	
5	75	*25.0*			*13.8*		*5.8*			*3.5*		*12.2*			*11.4*
		3.39	1.83	1.29	3.62	2.62	3.66	2.93	7.08	10.03	7.89	3.83	3.32	2.95	
							Stage (iii)								
6	85	*19.1*			*15.8*		*5.7*			*3.6*		*13.8*			*11.5*
		3.38	1.81	1.26	3.59	2.61	3.66	2.93	7.08	10.03	7.89	3.83	3.32	2.95	
7	110	*12.2*			*18.1*		*5.7*			*3.8*		*14.0*			*12.1*
		3.37	1.80	1.26	3.58	2.62	3.66	2.93	7.08	10.03	7.89	3.83	3.32	2.95	
8	160	*5.6*			*20.9*		*5.8*			*3.9*		*13.8*			*14.2*
		3.37	1.79	1.25	3.59	2.66	3.66	2.93	7.08	10.03	7.89	3.83	3.33	2.96	
9	360	*0.9*			*23.4*		*5.8*			*4.0*		*13.3*			*15.7*
		3.38	1.79	1.26	3.67	2.75	3.66	2.93	7.08	10.03	7.89	3.84	3.32	2.96	
							Stage (iv)								
10	540	–			*25.1*		*5.7*			*4.1*		*9.6*			*19.9*
		–	–	–	3.81	2.92	3.67	2.93	7.08	10.03	7.89	3.85	3.33	2.96	
11	24 h	–			*28.9*		*5.8*			*4.0*		*2.0*			*28.5*
		–	–	–	3.87	3.00	3.67	2.94	7.08	10.03	7.89	3.85	3.34	2.98	

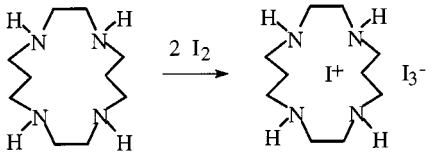
[a] Initial conditions: **1**–112.5, I_2–37.5, H_2O ~ 5.6, C_6H_{12}–9 µmol. Solvent $CDCl_3$ (0.75 mL). Temperature 22 °C. – [b] Mean value (in *italics*) calculated from the integrals (with respect to that of cyclohexane, δ = 1.425) of all peaks listed beneath it. – [c] Abbreviations: Bn = benzylic, R = aliphatic ring, H_o = aromatic *ortho* protons. – [d] Mean of two determinations (error: ± 5%).

15% of $[I_2]_0$), but it increases in the last two stages. Description of all stages is given below.

Stage (i)

The first ^{1}H-NMR spectrum (Table 1, entry 1) showed only the presence of **1**, but the signals of the benzylic and aziridine-ring protons were significantly deshielded with respect to those observed in the absence of iodine. A similar situation holds also for compounds **2** and **3** once they are formed (Table 1, entries 2–5).[14] We independently verified that addition of iodine to **2** or **3** (in excess) in $CDCl_3$ solution causes the deshielding of the corresponding aliphatic protons in their NMR spectra. Such a deshielding is precedented in the Et_3N/I_2 case.[15]

The presence of iodide anions from the very first observation (Table 1, entry 1) would require the concomitant formation of an equivalent amount of a cationic species. The NMR features of **1** do suggest the formation of a positively charged **1**. This species cannot be the conjugated acid **1**·H^+, because of its well-known[16a] high reactivity towards nucleophiles such as halide ions.[16b] Indeed, in our hands, addition of HI to a $CDCl_3$ solution of **1** (in excess) instantaneously gave a stoichiometric amount of **5**, which is the expected product of the ring-opening reaction of **1**·H^+ by I^-.[17] A more likely interpretation of the deshielding of the NMR signals of **1** is provided in the literature, where the ability of the halogens, including iodine, to form molecular complexes with tertiary amines is well documented.[15,18–21] In polar solvents, formation of ions such as $(R_3N–I)^+$ I_3^- [20] or $(R_3N–I–NR_3)^+$ I_3^- [21] is reported. For the cyclic amine **6**, which resembles our tetramer **3**, a polar structure (**6A**) for its CTC with iodine (Scheme 2) has been advanced.[22]



6 **6A**

Scheme 2

Therefore, ions of the type **(1·I)$^+$ I_3^-** could be formed in our case, throughout stage (*i*). Analogously, compounds **2** and **3**, which appear in stage (*ii*), might be present as **(2·I)$^+$ I_3^-** and **(3·I)$^+$ I_3^-**, respectively. For simplicity, we will refer to these ions as **1·xI_2**, **2·yI_2**, and **3·zI_2**, respectively. The formation of the triiodide ion was confirmed by UV-VIS investigation of our reaction mixture.[23]

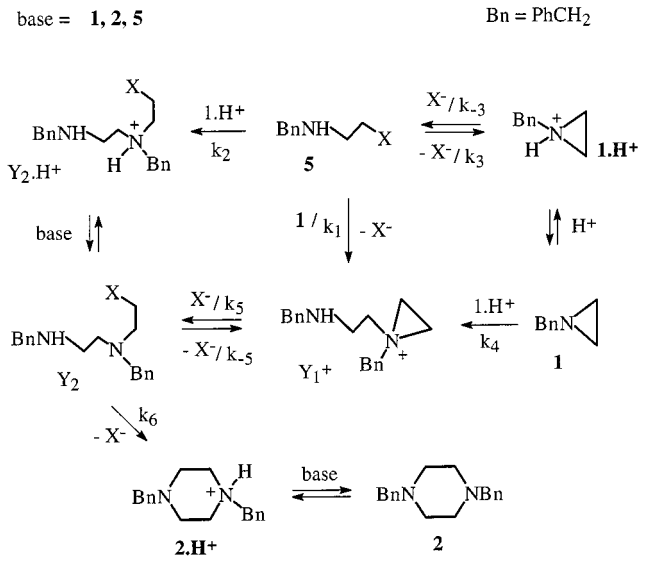
Stage (ii)

During this period, products **2–5** were gradually formed, but no additional iodide ion was produced (Table 1, entries 2–5). It can be concluded that iodine is consumed only to

yield iodoamine **5**. The negative charge due to [I_3^-] is now counterbalanced, not only by the positive charge of [**(1·I)**$^+$] (decreasing with time), but also by those of [**(2·I)**$^+$] and [**(3·I)**$^+$] (increasing with time).

Stages (iii) and (iv)

In stage (*iii*), **1** is transformed mainly into dimer **2**, whose concentration rises. The concentration of iodoamine **5** does not vary much at the beginning, but it decreases slightly towards the end of this period, and continues to do so in stage (*iv*). Meanwhile, production of iodide ion begins to increase. The main reaction occurring during the last part of stage (*iii*), and during all of stage (*iv*), is conceivably the self-condensation of **5** to yield **2·HI** (see below, Scheme 3). This transformation generates a second molecule of HI, which can be trapped by the other bases present in the reaction mixture. Evidence for the protonation of **2** and **3** comes from their broad NMR signals. In these two stages, other NMR peaks become evident, even though their importance appears to be minor according to their integrals. Attempts to ascribe some of these peaks to compounds **7–9** (see Scheme 4) were unsuccessful, due to extensive signal overlap.



Scheme 3

Discussion

There are two crucial points in the present investigation of the **1** + I_2 reaction. The first concerns the formation of tetramer **3**. Does it represent compelling evidence for the intervention of the **1**$^{\cdot+}$ species, as in the electrochemical experiments,[2] thus supporting an ET route,[1] or does it arise as a consequence of the production of various acidic species (e.g., **1·H**$^+$, HI)[7,8] during the reaction, thereby indicating a heterolytic pathway (HETERO)? The second crucial point concerns the production of **5**. How is it formed and what is the mechanistic consequence of the rise and fall of its concentration in stages (*ii*)–(*iv*)? In order to gain more information on these points, several auxiliary reactions were performed.

Changes in the Concentration of 5

Independent generation of **5** from **5·HI** reveals that it is not stable, but transforms to give dimer **2**, in accord with early work.[7b] We have verified this even in $CDCl_3$ solutions, both in the presence and in the absence of **1**. The experiments showed a complex dependence of the concentration of **5** with time,[24] but in the presence of **1**, and for the periods when I^- is not produced, the observed process is in agreement with the dimerization of **1** to **2** (Equation 1),

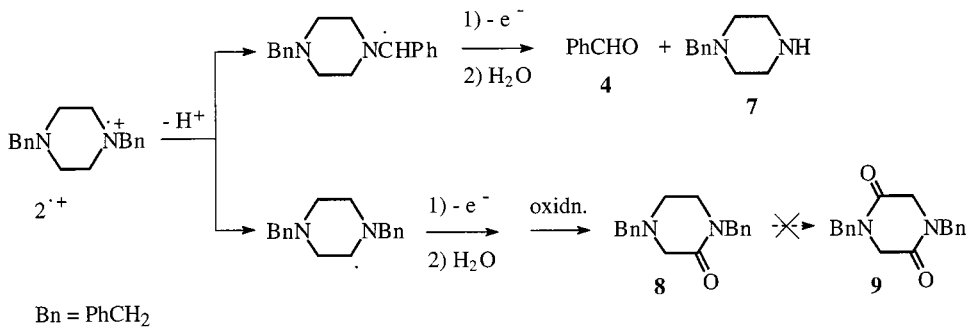
$$2 \times \mathbf{1} \Rightarrow \mathbf{2} \quad (1)$$

and the simple, pseudo-first order kinetic law (2) is obeyed,

$$\ln \{[\mathbf{1}]_0/[\mathbf{1}]\} = k \times t \times [\mathbf{5}]_0 \quad (2)$$

where $k = 5 \times 10^{-5}$ (± 10%) M^{-1} s^{-1} (at 22 °C). This means that iodoamine **5** is consumed during the rate determining step (or prior to it), but it is rebuilt in a faster subsequent step, thus explaining its constant concentration.

These data for the reaction **5** (+ **1**) → **2** are in accord with a scheme formerly proposed.[7b] We adapted this proposal to our case, as delineated in Scheme 3, where $\mathbf{Y_1}$ and $\mathbf{Y_2}$ indicate transient species. The tendency of the reaction to proceed as indicated is assured by the ease with which the aziridinium ring is opened by nucleophiles[16] (see **1·H**$^+$ → **5**; $\mathbf{Y_1^+}$ → $\mathbf{Y_2}$). In our case, there is a powerful nucleophile, namely the iodide ion, generated from the unimolecular step **5** → **1·H**$^+$ + I^-. The dimerization reaction ends when all remaining **5** is entirely converted into **5·HI**. Once again, whenever the iodide concentration is kept very small and



Scheme 4

constant the reaction scheme is considerably simplified and the above Equations (1) and (2) hold, where:

$$k \approx 2 \times k_1 \text{ (if } k_{-3} >> k_2, k_4) \quad (3)$$

This means that the rate determining step is the nucleophilic attack of the nitrogen lone pair of tertiary amine **1** on the saturated carbon atom of primary iododerivative **5**. From Equations (2) and (3) follows Equation (4):

$$k_1 \approx 2.5 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1} \text{ (at 22 °C, in } CDCl_3) \quad (4)$$

The value obtained for k_1 agrees well with that given, i.e., 3.0×10^{-5} M^{-1}s^{-1} (at 25 °C, in $CHCl_3$), for the comparable reaction between Et_3N and EtI, yielding $Et_4N^+ I^-$.[25]

Addition of iodine to a solution of **5** in chloroform ($[\mathbf{5}]_0/[I_2]_0 = 2.5$) does not change the heterolytic course of the reaction depicted in Scheme 3. More precisely, no tetramer **3** is formed.

From Scheme 3 it is evident that a HETERO mechanism does not explain the rise of [**5**] during stage (*ii*). Let us see if the ET pathway can explain it. If **1**$^{\cdot+}$ is produced in stages (*i*) and (*ii*), it could easily eliminate a proton.[26] The same would be true for **2**$^{\cdot+}$ and **3**$^{\cdot+}$, when they begin to form in stage (*ii*). Any amine present in the reaction mixture could act as a base and scavenge the proton from **1**$^{\cdot+}$, **2**$^{\cdot+}$, and **3**$^{\cdot+}$. Clearly the most likely base is **1**, in view of the higher relative concentration it keeps throughout the reaction.[27] The transient aziridinium cation **1**·**H**$^+$ would accordingly be formed and suffer nucleophilic ring-opening from the iodide ion previously generated in stage (*i*), to afford iodoamine **5**. Each deprotonation step will thus produce a molecule of **5**.

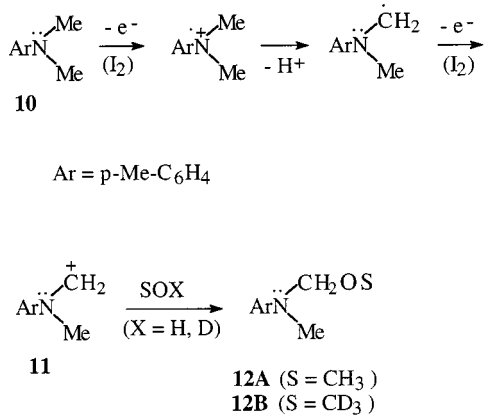
The Formation of 3

It is known that a tertiary aziridine undergoes heterolytic tetramerization in the presence of catalytic *p*-toluenesulfonic acid,[8] but *not* dimerization. Previous experiments[7b] also suggested that high yields of dimer (like **2**) are obtained only if iodide ions are present; otherwise, substantial amounts of 'polymers' are formed.[7b] This is in agreement with our experimental findings: *only* dimer **2** is produced from protonated **1** in a medium containing iodide anions (even when 'masked' as iodoamine **5**; see Scheme 3), while tetramer **3** (and *not* dimer **2**) is formed in the presence of phosphate buffers at pH = 5–8.[24] This dichotomy might be ascribed to the different nature of the two nucleophiles involved. In fact, I^- is both a good nucleophile and leaving group, while phosphate anion is a good leaving group but a poorer nucleophile. Therefore, the aziridinium ring of $\mathbf{Y}_1^+$ (formed from **1** and **1**·**H**$^+$ in k_4 of Scheme 3) is not opened when X^- = phosphate, but can be opened with a nucleophile such as **1**. This is due in particular to its high availability throughout the reaction. Repetition of this step leads to tetramer **3**. Incidentally, no cyclic trimer is formed, probably because it would be a strained 9-membered ring as opposed to the large and strain-free 12-membered cyclic tetramer **3**.

All these data are in contrast with the fact that tetramer **3** is formed in stage (*ii*) despite the presence of I^- (and I_3^-) anions in the medium. This means that generation of **3** from **1** and I_2 must occur by *a different mechanism*, probably a non-heterolytic one.

Independent investigation of the reaction of **2** with I_2 shows that after 24 hours about 7% of **2** has reacted to give **4**, *N*-benzylpiperazine (**7**), and 2-keto-derivative **8** in a 1:1:6 molar ratio, accompanied by the iodohydrate **2**·**HI** (and/or triiodohydrate) and minor amounts of other unidentified compounds (Scheme 4). Formation of dioxoderivative **9**, i.e., an oxidation product of **8**, was not supported (NMR) by the addition of pure **9** to the reaction mixture. Based on reacted **2**, the NMR calculated yields of **4** (or **7**) and **8** are 10 and 57%, respectively.

The structurally comparable *N*,*N*-dimethyl-*p*-toluidine (**10**) is known to undergo iodine-induced oxidation by an ET mechanism (Scheme 5).[10] We have trapped the transient carbonium ion **11** as **12A**, from the reaction of **10** with I_2 performed in a dimethylformamide/methanol mixture,[10] or as **12B** from the same reaction in $CDCl_3/CD_3OD$; this occurred even in the presence of **2**, which once again gave the above reported products (**4** + **7** + **8**).



Scheme 5

We conclude that an ET oxidative *N*-dealkylation mechanism operates both in the **10** + I_2 (Scheme 5) and in the **2** + I_2 (Scheme 4) reactions. In the latter case, the observed products **4**, **7**, and **8** derive from the two corresponding carbon-centred radicals, formed by proton abstraction from the two kinds of (N$^{\cdot+}$)*C*–*H* bonds available in the radical cation **2**$^{\cdot+}$: the benzylic (for **4** and **7**) and piperazinic (for **8**) bonds. Formation of **8** actually requires a further oxidation step with respect to the formation of **4**. The proton-abstraction steps from **2**$^{\cdot+}$ would be assisted by substrate **2** itself, i.e., the only base present in this case.

Under the same conditions adopted for the **2** + I_2 reaction in $CDCl_3$, tetramer **3** reacted somewhat faster to yield a complex mixture, from which only **4** and iodohydrate **3**·**HI** (and/or triiodohydrate) were identified. After 8 hours, about 20% of **3** had reacted to give **4** in ca. 43% yield (we assume that one molecule of **3** gives rise to four molecules of **4**).

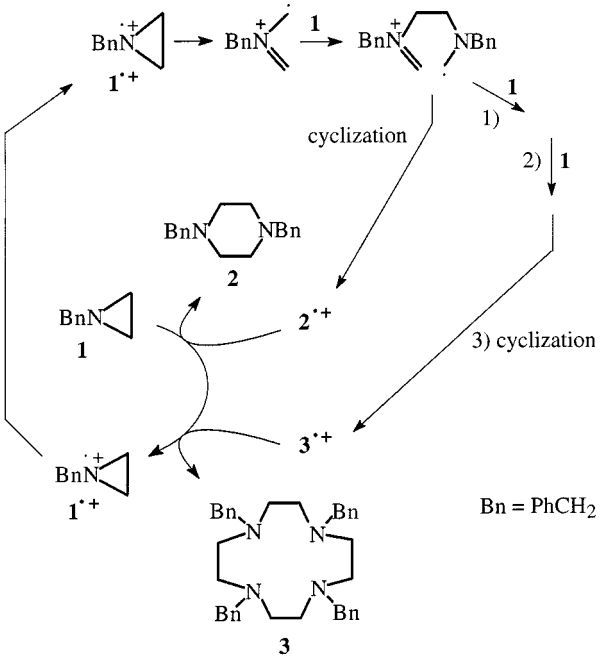
Mechanism of the 1+ I_2 Reaction

According to all these facts, the reaction of aziridine **1** with I_2 in $CDCl_3$ may be interpreted as a combination of

ET and HETERO routes, as outlined in Schemes 6 and 3, respectively. While this specifically holds for the present case, due to the particular nature of substrate **1**,[1] the ET pathway is indeed widely accepted for reaction of tertiary amines with molecular halogens.[9,10,12,13]

In more detail, the reaction starts with the formation of the polar complex **1**·x$\mathbf{I_2}$ and the subsequent generation[28] of **1**$^{\cdot+}$ (plus iodide/triiodide anions), which suffers nucleophilic attack by a second molecule of **1** to give a linear dimeric radical cation. This may undergo cyclization to **2**$^{\cdot+}$, or consecutively add two molecules of **1** to finally yield, after cyclization, **3**$^{\cdot+}$. In this way, both **2**$^{\cdot+}$ and **3**$^{\cdot+}$ are generated. As already proved by us,[1] **2**$^{\cdot+}$ and **3**$^{\cdot+}$ can react separately with **1** (in excess) to give the corresponding neutral molecules **2** and **3,** while re-generating **1**$^{\cdot+}$. These two cycles would transform all of **1** into a mixture of **2** and **3**, without the intervention of any other iodine molecule.

During stage (*ii*), all the newly reacted iodine is found in iodoamine **5**, i.e., the product of all the deprotonation steps (not shown in Scheme 6). Consequently, the temporary yields of **2** and **3** must be higher than 100%, when calculated with respect to the reacted oxidant (I_2). Indeed, using the data from Table 1, the yields of **2** and **3** were found to be 225 and 120%, respectively, after 35 min reaction time.



Scheme 6

Whenever **1** and **5** begin to co-exist, the heterolytic mechanism leading to dimer **2** might take place, as discussed previously (Scheme 3). Could this be the major pathway to **2**? For stage (*ii*), the HETERO contribution might be approximated from Equation (2), by considering small intervals of time for which [**5**] may be taken as constant. Calculations reveal that the heterolytic mechanism accounts for less than 1% of the experimentally found yield of **2**. Unfortunately, similar calculations cannot be done for stage (*iii*), because Equation (2) no longer applies. Moreover, as demonstrated above, the HETERO mechanism is not able to explain an additional production of **5**, at least at the beginning of this stage.[29] Therefore, as long as the concentration of **5** continues to rise, an ET mechanism must operate through stages (*i*) and (*ii*); a contribution of the HETERO route cannot be excluded, however, for the production of **2** during stage (*iii*).

Conclusion

The reaction of **1** with iodine appears to start, and continue, by an ET mechanism (Scheme 6) until iodoamine **5** no longer forms. Within this reaction period [stages (*ii*) and in part (*iii*)], dimer **2** and tetramer **3** are formed, together with oxidation products deriving from them, including **4**; iodoamine **5** results from all deprotonation steps. By the end of stage (*iii*), when the concentration of **1** becomes increasingly lower, a parallel HETERO mechanism (Scheme 3) begins to contribute to the formation of additional I^- and **2**. After full consumption of **1**, only the heterolytic mechanism operates [stage (*iv*)]. Our initial hypothesis,[1] that the formation of tetramer **3** from **1** and I_2 could be interpreted as an ET process, finds experimental support in the present investigation.

Experimental Section

General Remarks: Melting points were taken with a Kofler hot plate and are uncorrected. NMR spectra were registered with a Gemini A 300A Varian apparatus, using Me_4Si as the internal standard. GC-MS and LC-MS instruments and conditions were described previously.[1] UV-VIS determinations were performed using a Carl Zeiss Specord spectrophotometer.

1-Benzylaziridine (1): Instead of the methods indicated in literature,[30] we preferred that used for the synthesis of the 1-phenyl derivative,[31] i.e., starting from *N*-(2-bromo-ethyl)benzylammonium bromide.[32] Yield 84%. Bp 56–58 °C at 1–2 Torr (ref.[30b] bp 86–88 °C at 12 Torr, ref.[30e] bp 84–87 °C at 8 Torr). ^{1}H NMR (δ, ppm, $CDCl_3$): 1.21+1.76 (2 H+2 H, m+m, CH_2–CH_2), 3.31 (2 H, s, Ph–CH_2), 7.18–7.30 (5 H, m, Ph). ^{13}C NMR (δ, ppm, $CDCl_3$): 27.59 (CH_2–CH_2), 65.29 (Ph–CH_2), 127.09 (C_{para}), 128.03 (C_{ortho}), 128.41 (C_{meta}), 139.28 (C_{ipso}).

1,4-Dibenzylpiperazine (2): was synthesized as in ref.[33]. M.p. 91–92 °C (ref.[33] m.p. 91–92 °C). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.48 (8 H, s, CH_2–CH_2), 3.51 (4 H, s, Ph–CH_2), 7.21–7.3 (10 H, m, Ph).

1,4,7,10-Tetrabenzyl-1,4,7,10-tetraazacyclododecane (3): was prepared according to ref.[8]. M.p. 141–142 °C (ref.[8] m.p. 142–143 °C). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.68 (16 H, s, CH_2–CH_2), 3.43 (8 H, s, Ph–CH_2), 7.21 (4 H, t, H_{para}), 7.24 (8 H, t, H_{meta}), 7.35 (8 H, dd, H_{ortho}).

***N*-(2-Iodoethyl)benzylammonium Iodide (5·HI):** A 57% aqueous solution (52 g; 0.23 mol) of hydrogen iodide (Merck) was dropped at 5 °C, with stirring, into 10 g (0.066 mol) of 2-benzylaminoethanol (Merck). The mixture was heated under reflux for 2 hours and the excess HI distilled off. The brown solid residue was washed with 4 × 15 mL of cold ethanol and then recrystallized from ethanol, to afford 13 g (yield 50%) of **5·HI** as colourless crystals, m.p. 169–170

°C. Calculated for $C_9H_{15}I_2N$,%: C (27.64), H (3.87), I (64.91), N (3.58). Found,%: C (27.35), H (3.60), I (64.98), N (3.76). ^{1}H NMR (δ, ppm, [D$_6$]DMSO): 3.27–3.42 (4 H, m, CH_2–CH_2), 4.24 (2 H, s, Ph–CH_2), 7.3–7.52 (5 H, m, Ph), 8.92 (2 H, br. s, NH_2^+; disappears on shaking with D_2O). ^{13}C NMR (δ, ppm, [D$_6$]DMSO): –4.08 (*C*H$_2$-I), 48.62 (N–CH$_2$–CH$_2$), 49.67 (Ph–CH$_2$), 128.77+129.66 ($C_{ortho}+C_{meta}$), 129.13 (C_{para}), 131.63 (C_{ipso}).

***N*-(2-Iodoethyl)benzylamine (5):** About 1 mmol of **5·HI** was dissolved in the minimum amount of water (ca. 30 mL), and 2.5 mL of organic solvent (CH_2Cl_2, $CHCl_3$) was added. After cooling at 0°C, 1.1 molar equivalents of NaOH, dissolved in the minimum amount of water, were added dropwise, with stirring. The organic layer was separated, while the aqueous phase was extracted with 2 × 2 mL of cold organic solvent. The combined organic layers were dried (Na_2SO_4) and then diluted to 4 mL with fresh solvent. After the addition of a convenient amount of toluene (internal standard), an aliquot was diluted to 0.7 mL with $CDCl_3$ directly in the NMR tube and the spectrum recorded. The yields were 80–90% (from NMR). For the reactions with **5** (vide infra), the solvent used was $CDCl_3$ and the scale reduced to one-half. All operations required after the addition of NaOH had to be executed within 10 minutes, in order to minimise any transformation to dimer **2**. ^{1}H NMR (δ, ppm, $CDCl_3$): 2.01 (1 H, s, N*H*, disappears on shaking with D_2O), 2.94 (2 H, t, J = 6.3 Hz, N–CH_2–CH$_2$I), 3.31 (2 H, t, J = 6.3 Hz, CH_2-I), 3.81 (2 H, s, Ph–CH_2), 7.35–7.50 (5 H, m, Ph).

1-Benzylpiperazine (7): was prepared by following a published procedure.[34a] Bp 120–123 °C at 2 Torr (ref.[34b] bp 122–124 °C at 2.5 Torr). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.46 (4 H, br. s, 2–CH_2 and 6–CH_2), 2.93 (4 H, bt, J = 4.6 Hz, 3–CH_2 and 5–CH_2), 3.14 (1 H, br. s, N*H*), 3.50 (2 H, s, Ph–CH_2), 7.20–7.37 (5 H, m, Ph).

1,4-Dibenzyl-2-piperazinone (8): was obtained[35] from 2-piperazinone[36] *via* 4-benzyl-2-piperazinone.[35] Bp 201–205 °C at 1 Torr (ref.[35] bp 205–207 °C at 1 Torr). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.62 (2 H, t, J = 5.5 Hz, 5–CH_2), 3.21 (2 H, t, J = 5.5 Hz, 6–CH_2), 3.25 (2 H, s, 3–CH_2), 3.55 (2 H, s, 4-Ph–CH_2), 4.60 (2 H, s, 1-Ph–CH_2), 7.23–7.37 (10 H, m, 2 × Ph).

1,4-Dibenzyl-2,5-piperazindione (9): was prepared from *N*-benzyl-2-chloro-acetamide[37] according to a published procedure.[38] M.p. 178–179 °C (ref.[39] m.p. 178–180 °C). ^{1}H NMR (δ, ppm, $CDCl_3$): 3.93 (4 H, s, 3–CH_2 + 6–CH_2), 4.58 (4 H, s, 2 × Ph–CH_2), 7.24–7.30 + 7.30–7.39 (4H + 6 H, m, 2 × Ph). The NMR data quoted in ref.[39] appear to be not correct.

Reaction of 1 with I_2. – (a) Kinetic Measurements: A typical procedure is described. Two $CDCl_3$ solutions were prepared: one containing **1** (freshly distilled; 0.525 M) and the standard (toluene or cyclohexane; 0.042 M; for integral measurement), the other with iodine (0.07 M; titrated against sodium thiosulfate). Appropriate volumes of these solutions were mixed together to yield 3.5 mL of a reaction mixture containing **1** (0.15 M) and iodine (0.05 M). About 0.75 mL (solution A) was used for the NMR measurements (after sealing the tube) and the rest (solution B) for the iodide determination. The reaction temperature was measured and maintained constant by the temperature control unit of the NMR instrument; solution B was kept at the same temperature by using a thermostat. At the same reaction time, an NMR spectrum was registered (solution A) and a sample withdrawn from solution B for iodide titration. In the latter case, two 100 μL-aliquots were taken with a microsyringe from solution B, in order to make two iodide determinations at each point. Each aliquot was diluted with 2 mL of chloroform, shaken with 3 × 2 mL of water, and the combined aqueous layers titrated with $AgNO_3$ solution (0.001 M) against starch-iodine complex. The two determinations agreed within 5%. The values of I^- given in Table 1 were corrected for blank titrations (no **1** present). **(b) Product analysis:** A reaction mixture like solution A was prepared and analysed by NMR as above. After some time [usually during stage (*ii*); see text], samples of **2–5** were added and spectra recorded for the identification of the products. Alternatively, the original solution A was monitored by NMR until completion of the reaction. The mixture was then diluted with 1 mL of chloroform, poured into excess NaOH (10% aqueous solution), shaken until colourless, and the organic phase separated. Two more extractions with fresh chloroform were done and the combined organic layers dried (Na_2SO_4) and then concentrated. Analysis by GC-MS and LC-MS confirmed the presence of **2** and **3**. **(c) UV-VIS Analyses:** An aliquot of solution B, prepared as before, was diluted 1000 times with chloroform, and the electronic spectrum recorded using chloroform as reference.

Reaction of 1 with HI or 5: (a) To a solution of **1** (0.1 mmol) and a standard (0.03 mmol) in $CDCl_3$ (0.7 mL), 0.05 mmol of HI (as a 57% aqueous solution) was added all at once with a microsyringe. The ^{1}H NMR spectrum was recorded as soon as possible (ca. 2 min). It consisted of the spectra of **1** and **5**, in the appropriate molar ratio.[40] The mixture can be used to follow the reaction between **1** and **5**. (b) Alternatively, amine **5** was generated from **5·HI** and NaOH in a $CDCl_3/H_2O$ mixture. After determination of its concentration, the desired amount of **1** was added and the reaction followed by NMR (in a sealed tube) and by iodide titration. Kinetic measurements were performed at $[\mathbf{1}]_0$ = 0.05–0.1 M and $[\mathbf{5}]_0$ = 0.02–0.1 M. The kinetic law expressed by Equation (2) was followed until no iodide ion was detected (50–80% consumption of **1**). Similar results were obtained using procedure (a).

Self-Condensation of 5 to Yield Dimer 2: was performed as indicated before (procedure b), but without additional **1**. In order to avoid a premature precipitation of solid material, it is more convenient to use dilute solutions ($[\mathbf{5}]_0 < 0.1$ M). The solid precipitated at the end of reaction was a **2·HI** + **5·HI** mixture (NMR evidence). If the same reaction is performed in CCl_4, **5·HI** precipitates since the beginning; the identification was made by NMR and by a mixed melting point with an authentic sample.

Reaction of 2 (or 3) with Iodine: The reaction was followed in a sealed NMR tube containing a $CDCl_3$ solution of **2** or **3** (0.04–0.07 M), iodine (1/3 or 1/4 with respect to [**2**] or [**3**]), and a standard (for integral measurement). After a suitable reaction time, addition of authentic samples of **4**, **7**, **8**, and **9** confirmed the formation of the first three compounds, but not of the latter. The analogous solution of **3** (5.5μmol) and iodine (11μmol) gradually separated to give a solid after some hours. The supernatant coloured solution showed the presence of unchanged **3** (3 μmol), **4** (ca. 0.3 μmol), and several unidentified reaction products in smaller amounts. Addition of aziridine **1** (105 μmol) at this stage gave a yellow homogeneous solution containing **1** (98 μmol), **3** (5.5 μmol), **2** (ca. 0.6 μmol), **4** (ca. 0.4 μmol), and iodoamine **5** (2.6 μmol) (first NMR spectrum). A simple calculation revealed that most of **5** (ca. 2 μmol) came from the reaction **1** + **3·HI** → **5** + **3**.

Oxidation of 10 (with or without 2) to 12B: A solution of iodine (26 μmol) and cyclohexane (as standard; 0.5 μL) was prepared in 0.8 mL of a $CDCl_3/CD_3OD$ (3/1, v/v) mixed solvent. To this solution, toluidine **10** (104 μmol, Merck) was added at once, and ^{1}H-NMR spectra were recorded after shaking. Although the ether **12B** was observed since the first spectrum, integrals measurements were done after some hours because of transient peak broadening. The final spectrum contained the signals of **10** (+ **10·HI**), in addition

to the following ones, that we ascribe to **12B**: 2.26 (3 H, s, *p*-Me), 3.06 (3 H, s, N–Me), 4.73 (2 H, s, N–CH_2–O), 6.79 (2 H, d, J = 8.3 Hz, H_{ortho}), 7.07 (2 H, d, J = 8.3 Hz, H_{meta}). The NMR features of **12B** compare well with those quoted for the analogous *N*-(ethoxymethyl)-*N*-methylaniline.[41] The amount of **12B** corresponded to the consumption of about 1/3 of the initially added iodine. When starting from a **2** + **10** mixture, all products **4**, **7**, **8**, and **12B** were analogously obtained.

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