Reactions of Halogenoquinolizinium Bromides with Aniline, Isopropylamine and Liquid Ammonia

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The reactions of quinolizinium bromide (QB) and its four monobromo derivatives with aniline, isopropylamine and liquid ammonia have been investigated. With aniline 2- and 4-bromoQB undergo substitution, whereas 1- and 3-bromoQB do not react at all. With liquid ammonia all bromo derivatives and the parent compound react with ring opening. This diversity in the reaction course is explained in terms of the HSAB principle. 2-BromoQB reacts with isopropylamine under formation of 2-isopropylaminoQB. Two molecules of isopropylamine are involved in this substitution, as we isolated an intermediate: 1-isopropylamino-4(2-pyridyl)-3-isopropyliminio-1-butene bromide (**13**). The structure of the latter compound was confirmed by X-ray analysis.

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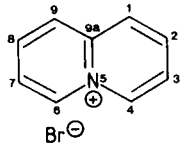
In a previous publication (1) we reported the reactions of halogenoquinolizinium bromides with diethylamine. The 2- and 4-bromo salts gave mainly substitution, the 1-and 3-bromo salts mainly ring opening. In order to find out whether this reaction pattern depends on the hardness of the nucleophile, we investigated the reactions of quinolizinium bromide and the bromo quinolizinium bromides with two other *N*-nucleophiles, *i.e.* aniline and liquid ammonia. Moreover, we investigated the reaction of 2-bromoquinolizinium bromide with isopropylamine, which took an unexpected course. The parent compound quinolizinium bromide (**1**) is from here on abbreviated as QB (Figure 1).



Quinolizinium bromide (QB)

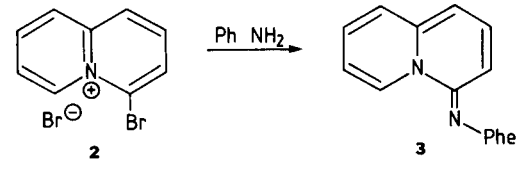
1

Results.

Reactions with Aniline.

The conversion of 2-bromoQB into 2-anilinoQB has been reported in the literature (2). 4-BromoQB (**2**) when refluxed with two equivalents of aniline in ethanol, gave 4-phenylimino-4*H*-quinolizine (**3**) in a yield of 92% (Scheme 1).

1-BromoQB (**5**) and 3-bromoQB (**10**) did not react on refluxing with two equivalents of aniline in either ethanol or *n*-propanol (4 and 16 hours, respectively). Refluxing of **5** and **10** in pure aniline resulted in the formation of a tar.

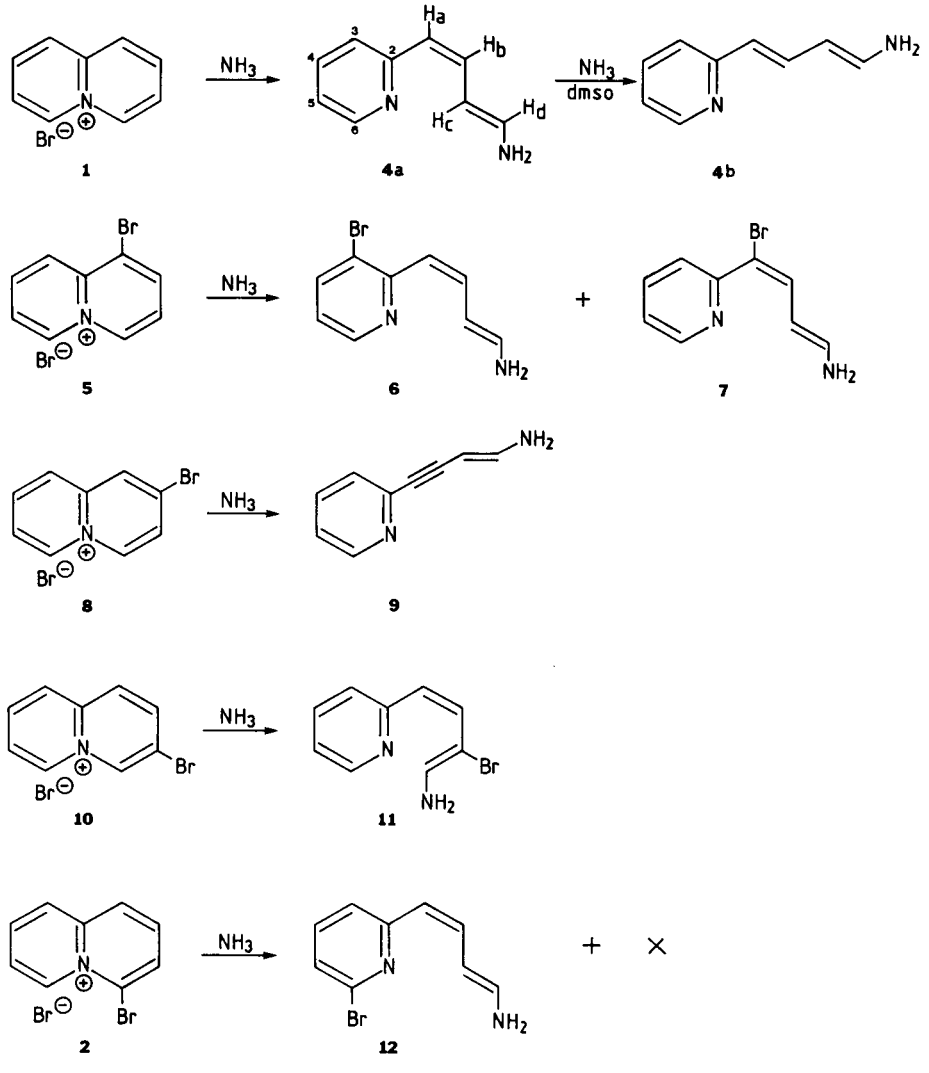


2 **3**

Reactions with Liquid Ammonia.

QB itself and the four isomeric monobromoQB's underwent ring opening reactions in liquid ammonia. The results are summarized in Scheme 2. The pyridylbutadienes formed were extremely unstable and changed rapidly into a dark tar. They were identified by their nmr, uv, ir and (for some of them) mass spectra. The interpretation of the rather complicated ^{1}H-nmr spectra was possible by comparison with the spectra obtained from the 4,6-dideuterio derivatives of **1**, **5** and **10** (3) with liquid ammonia. Support for the correctness of the structure assignments was obtained by converting the pyridylbutadienes into methyl (halogeno) picolinates (oxidation and subsequent esterification) and into 1-acetylamino-4-[2-pyridyl]butane (by hydrogenation in acetic anhydride with a palladium charcoal catalyst).

QB (**1**) undergoes ring opening with formation of HaHb-*cis*, HcHd-*trans* 1-amino-4-[2-pyridyl]-1,3-butadiene (**4a**) (4). We assigned the HaHb-*cis*, HcHd-*trans* configuration to **4a** by comparing the chemical shifts and coupling constants with the values obtained for HaHb-*cis*, HcHd-*trans* 1-diethylamino-4-[2-pyridyl]-1,3-butadiene and its all-*trans* isomer (1). Isomerisation of **4a** into the all-*trans* compound is relatively slow in liquid ammonia. In a saturated solution of ammonia in hexadeuteriodimethyl sulfoxide at room temperature, however, we observed formation of **4a**



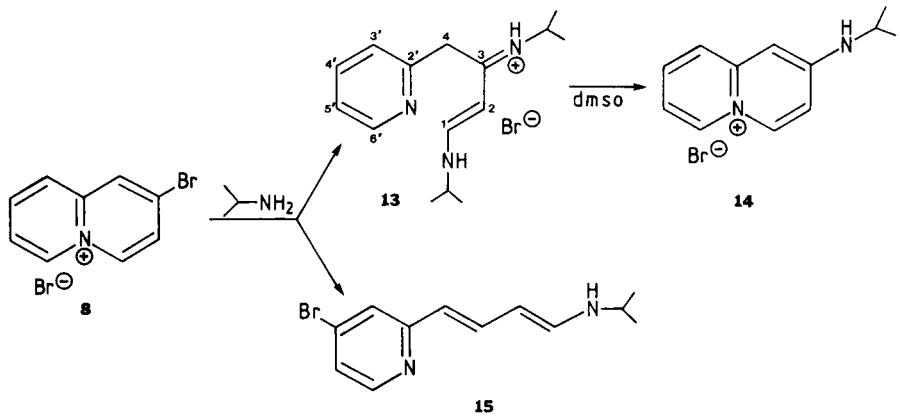
from QB, followed by isomerisation into the all-*trans* compound (**4b**).

1-BromoQB (**5**) reacts with liquid ammonia in the same way as with diethylamine (1): the nucleophile attacks mainly (about 70%) at C-6 with formation of the open-chain compound **6** and to a minor extent (about 30%) at C-4 with formation of **7**. We concluded that **7** is present from the ^{1}H-nmr spectrum of the crude reaction product and from the results of oxidation/esterification reactions, which gave a mixture of methyl 3-bromopicolinate and methyl picolinate.

2-BromoQB (**8**) undergoes ring opening upon attack of ammonia at C-4, followed by elimination of hydrobromic acid, yielding 1-amino-4-[2-pyridyl]but-1-en-3-yne (**9**). Not a trace of substitution product (2-aminoQB) could be detected.

From 3-bromoQB (**10**) the ring opening product 1-amino-2-bromo-4-[2-pyridyl]-1,3-butadiene (**11**) was obtained. Its formation results from attack of ammonia at C-4, contrary to the course of the reaction with diethylamine, where the nucleophile attacks exclusively C-6. The results of the oxidation/esterification reaction, leading to methyl picolinate and some methyl 5-bromopicolinate, indicate that to a certain extent attack at C-6 has occurred. However, this is a minor reaction, as we could not detect any signals for 1-amino-4-[5-bromo-2-pyridyl]-1,3-butadiene in the nmr spectrum. The main product **11** shows a signal for Hd in the ^{1}H-nmr spectrum at an abnormally high δ value (Table VI); therefore we assume that **11** has the preferred conformation shown in Scheme 2, in which the steric interaction of the bromine atom with the pyridine nucleus is less than in the conformer comparable to, for instance, **4a**.

Finally, 4-bromoQB (**2**) reacts with liquid ammonia with formation of the ring opening product **12**. The assignment of the structure is based on the ^{1}H-nmr spectrum and the results of oxidation and reduction reactions. Oxidation/esterification gave mainly methyl 6-bromopicolinate. However, the nmr spectrum shows that besides **12** a con-



siderable amount of a second product X is present (5).

Reaction of 2-BromoQB (**8**) with Isopropylamine.

2-BromoQB (**8**) when reacted with isopropylamine in dimethyl sulfoxide solution, gives 2-isopropylaminoQB (**14**) as the final product. However, when carrying out the reaction on a preparative scale in an excess of isopropylamine without using a co-solvent, we did not obtain **14** as the main product, but a compound to which we assigned the structure 1-isopropylamino-4-(2-pyridyl)-3-isopropyliminio-1-butene bromide (**13**) (Scheme 3). In addition a minor amount (20-25%) of the open-chain compound **15** was isolated.

On following the reaction of **8** with isopropylamine in hexadeuteriodimethyl sulfoxide by ^{1}H-nmr, we found that the open-chain adduct **13** is present for several hours in the reaction mixture and is then gradually converted into **14**. Compound **13** is not formed from **14**, as treatment of **14** with isopropylamine in dimethyl sulfoxide did not give **13**. On the other hand, the conversion of **13** into **14** could be realised in a separate experiment by simply heating a solution of **13** in dimethyl sulfoxide at 70° for one hour. At room temperature, the same conversion takes place, but more slowly.

It is interesting that signals, similar to those attributed to **13** are found in the ^{1}H-nmr spectra taken in the initial stage of the reactions of 2-bromoQB, 2-chloroQB, 1,2-dibromoQB and 2,7-dibromoQB with diethylamine in dimethyl sulfoxide and of 2-bromoQB with piperidine in dimethyl sulfoxide. The corresponding open-chain adducts were never isolated, however. We also tried to prepare similar compounds by reaction of 2-bromoQB with *n*-propylamine and *n*-butylamine. Although ^{1}H-nmr spectra indicate that comparable open-chain adducts were formed, we were not able to isolate them as crystalline compounds.

The structure **13** shown in Scheme 3 agrees well with the results of CH-analysis and the ^{1}H-nmr, ^{13}C-nmr, ir, mass and uv spectra (6). There were, however, some isomeric structures conceivable, which would fit the analytical data equally well. X-ray analysis gave the definite decision in favour of the structure **13**.

Crystallographic Determination of the Structure of **13**.

Crystals of the compound are orthrhombic with space group Pcab and 4 molecules in a unit cell of dimensions a = 10.344 (4), b = 16.059 (5), c = 20.990 (12) Å. A crystal of dimension 0.45 × 0.45 × 0.05 mm was used to collect 1418 intensities with $I > 2.5\,\sigma(I)$ on a NONIUS CAD4 diffractometer using graphite monochromated MoKα radiation. An absorption correction was applied (μ = 23.3 cm^{-1}).

The crystal structure was determined by means of the heavy atom technique. The H atoms were located in a ΔF-synthesis. Refinement proceeded by block-diagonal least-squares calculations, anisotropic for Br, C and N and isotropic for H. The final R value was 0.045 for the 1418 observed reflexions. A weighting scheme $w = (4.5 + F_o + 0.015F_o^2)^{-1}$ was applied and the anomalous scattering of Br was taken into account. The final coordinates are listed in Table I.

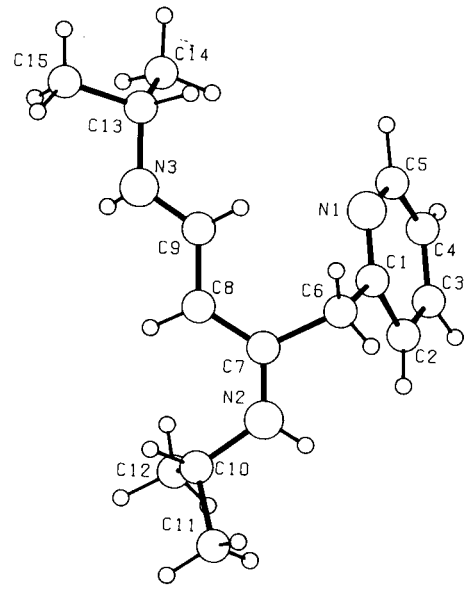
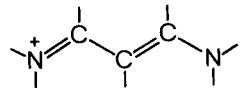


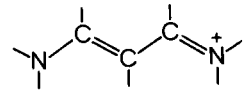
Table I

Final Coordinates and Equivalent Isotropic Thermal Parameters, with e.s.d.'s in Parentheses.
$U_{eq} = \frac{1}{3} \Sigma_i \Sigma_j U_{ij} a_i^* a_j^* a_i^- a_j^-$

	X	Y	Z	U_{eq} (Å^2)
Br	.30754 (9)	−.09193 (5)	.14976 (5)	.0743 (2)
C(1)	.3586 (8)	−.0123 (4)	.3540 (4)	.056 (2)
C(2)	.2385 (11)	−.0506 (7)	.3435 (5)	.096 (2)
C(3)	.1664 (13)	−.0747 (8)	.3962 (6)	.118 (3)
C(4)	.2174 (10)	−.0630 (6)	.4565 (5)	.094 (2)
C(5)	.3360 (8)	−.0276 (6)	.4624 (4)	.067 (2)
C(6)	.4364 (8)	.0199 (5)	.2980 (4)	.058 (2)
C(7)	.3831 (7)	.1019 (4)	.2737 (4)	.045 (1)
C(8)	.4034 (7)	.1767 (4)	.3064 (3)	.047 (1)
C(9)	.4848 (7)	.1820 (4)	.3586 (4)	.051 (1)
C(10)	.2492 (8)	.1675 (5)	.1893 (4)	.056 (1)
C(11)	.2272 (11)	.1423 (7)	.1201 (5)	.094 (2)
C(12)	.1294 (10)	.1932 (7)	.2212 (5)	.088 (2)
C(13)	.5919 (8)	.2553 (5)	.4458 (4)	.060 (2)
C(14)	.5186 (10)	.2340 (6)	.5057 (4)	.084 (2)
C(15)	.6522 (11)	.3409 (7)	.4467 (5)	.090 (2)
N(1)	.4061 (7)	−.0012 (4)	.4119 (3)	.060 (1)
N(2)	.3110 (6)	.0968 (4)	.2221 (3)	.054 (1)
N(3)	.5056 (7)	.2508 (4)	.3901 (3)	.059 (1)

The cation is depicted in Figure 2 which also gives the atomic numbering used in the crystallographic analysis (different from the systematic numbering). The bond distances and angles are listed in Table II. The part consisting of N(2), C(7), C(8), C(9) and N(3) is a planar conjugated system with bond lengths intermediate between the single and double bond standard values (single and double C(sp^2) — C(sp^2) 1.48 and 1.34, single and double C(sp^2) — N(sp^2) 1.45 and 1.27 Å, respectively (7)).





The two resonance structures of Figure 3 are equivalent and the positive charge will be equally shared by the two N atoms. N(2) and N(3) (at x, ½ + y, ½ − z) are at approximately equal distances from Br^- (3.38 and 3.35 Å, respectively). The planarity of the diazapentadiene system is illustrated in Table III, which lists the distances of its atoms and the adjacent atoms from the best plane through the system. The pyridine ring is planar within the limits of accuracy (see Table III).

Discussion.

The results of our experiments, including those of the reactions with diethylamine reported in a previous paper (1), can be arranged according to type of reaction occurring (ring opening, substitution) as shown in Table IV.

Table II

Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in Parentheses

C(1)—C(2)	1.404 (14)	C(2)—C(1)—C(6)	119.8 (8)
C(1)—C(6)	1.516 (12)	C(2)—C(1)—N(1)	122.1 (8)
C(1)—N(1)	1.323 (11)	C(6)—C(1)—N(1)	118.0 (7)
C(2)—C(3)	1.389 (17)	C(1)—C(2)—C(3)	118.2 (10)
C(3)—C(4)	1.384 (17)	C(2)—C(3)—C(4)	119.1 (12)
C(4)—C(5)	1.358 (14)	C(3)—C(4)—C(5)	119.0 (10)
C(5)—N(1)	1.352 (11)	C(4)—C(5)—N(1)	123.0 (8)
C(6)—C(7)	1.516 (11)	C(1)—C(6)—C(7)	111.4 (7)
C(7)—C(8)	1.399 (10)	C(6)—C(7)—C(8)	121.7 (7)
C(7)—N(2)	1.318 (11)	C(6)—C(7)—N(2)	115.4 (7)
C(8)—C(9)	1.385 (11)	C(8)—C(7)—N(2)	122.8 (7)
C(9)—N(3)	1.305 (10)	C(7)—C(8)—C(9)	122.2 (7)
C(10)—C(11)	1.525 (14)	C(8)—C(9)—N(3)	123.6 (7)
C(10)—C(12)	1.468 (14)	C(11)—C(10)—C(12)	112.5 (8)
C(10)—N(2)	1.474 (11)	C(11)—C(10)—N(2)	107.8 (7)
C(13)—C(14)	1.508 (13)	C(12)—C(10)—N(2)	111.7 (7)
C(13)—C(15)	1.510 (14)	C(14)—C(13)—C(15)	113.8 (8)
C(13)—N(3)	1.473 (11)	C(14)—C(13)—N(3)	110.2 (7)
		C(15)—C(13)—N(3)	107.8 (7)
		C(1)—N(1)—C(5)	118.6 (7)
		C(7)—N(2)—C(10)	125.6 (7)
		C(9)—N(3)—C(13)	122.9 (7)

Table III

Distances (Å) from Least Squares Planes with e.s.d.'s in Parentheses. Asterisks Indicate the Atoms Used in the Calculation of the Planes

N(2)*	−.019 (6)	N(1)*	.007 (7)
C(7)*	.015 (7)	C(1)*	.007 (8)
C(8)*	.022 (7)	C(2)*	−.015 (11)
C(9)*	−.013 (7)	C(3)*	.010 (13)
N(3)*	−.005 (7)	C(4)*	.004 (10)
C(6)	.133 (8)	C(5)*	−.013 (9)
C(10)	−.138 (8)	C(6)	.071 (8)
C(13)	−.035 (8)		

Table IV

Results of the Reactions of Quinolizinium Bromides with Various Nucleophiles

	Phe NH_2		Et_2 NH		NH_3	
	ring op	subst	ring op	subst	ring op	subst
QB	−	−	+	−	+	−
1-BrQB	−	−	+	−	+	−
2-BrQB	−	+	(+)	+	+	−
3-BrQB	−	−	+	−	+	−
4-BrQB	−	+	(+)	+	+	?

The result of the reaction of 2-bromoQB with isopropylamine has not been included in the Table; it is comparable to that of the reaction with diethylamine.

It is clear from the Table that substitution takes place only with 2-bromoQB and 4-bromoQB and only with aniline and diethylamine. When the bromine atom is not in an activated position, as in the case of 1-bromoQB and

3-bromoQB, we never observe substitution, but only ring opening with diethylamine and ammonia. As an explanation we propose that a soft nucleophile such as aniline attacks the soft C (Br) atom in the activated C-2 or C-4 position; substitution is then the result. With a harder nucleophile such as ammonia, attack occurs predominantly at the harder C-4 or C-6 atom, adjacent to the positive nitrogen atom, resulting in ring opening. With diethylamine, intermediate in hardness, both types of reaction occur. More or less similar explanations have been given for related reactions (8,9), thus 4-chlorothiopyrylium cation reacts with soft nucleophiles — thiophenol, aniline and methylaniline — by substitution of the chlorine atom, whereas harder nucleophiles such as dimethylamine and Grignard reagents, react with ring opening, due to attack at C-2 (8).

Concerning the ring opening reactions, the factors determining whether the nucleophile attacks the substituted ring (C-4) or the unsubstituted ring (C-6), are not quite clear. In the case of 1-bromoQB the nucleophile attacks preferably at C-6 and to some extent at C-4. Possibly a mesomeric electron-donating effect of the bromine atom deactivates C-4 for nucleophilic attack. With 3-bromoQB ammonia attacks at C-4 and diethylamine at C-6 exclusively; this difference may be attributed to a steric factor and an increased inductive electron withdrawing effect of the bromine atom. Finally, 2-bromoQB is a complicated case. Whereas ammonia attacks at C-4 exclusively, diethylamine prefers to attack C-6 in the ring opening process. We can only speculate about the resasons for these differences.

The nucleophilic substitution reaction of 4-bromoQB with diethylamine probably proceeds by the Addition-Elimination mechanism. An Elimination-Addition mechanism *via* a 3,4-didehydroquinolizinium bromide can be discarded, as we found experimentally that 1,3-dideuterio-4-bromoQB (see experimental part) gave 1,3-dideuterio-4-diethylaminoQB on reaction with diethylamine. This result also excludes the occurrence of an odd tele-substitution mechanism, starting with an initial attack of the nucleophile at C-6 (10).

The intermediate product obtained in the nucleophilic substitution reaction of 2-bromoQB with isopropylamine evidently shows that this reaction does not occur by an Addition-Elimination mechanism. Since we have good indications that analogous intermediates play a role in the reactions with other aliphatic amines, we propose for the aminodebromination of 2-bromoQB with amines a mechanism illustrated in Scheme 4 for the substitution reaction of 2-bromoQB with isopropylamine.

The initial attack of the nucleophile takes place at the relatively soft C-2 atom, carrying the bromine atom. The Meisenheimer adduct formed is neutral and does not immediately loose a bromide ion; attack by a second molecule of amine leads to expulsion of bromide ion with ring opening and aromatization of the pyridine nucleus. The resulting dienamine is converted by addition of a proton into the stable mesomeric system of **13**. Ring closure followed by elimination of isopropylamine leads to the end product **14**.

EXPERIMENTAL

1. General.

Melting points are uncorrected. The ir spectra were measured on a

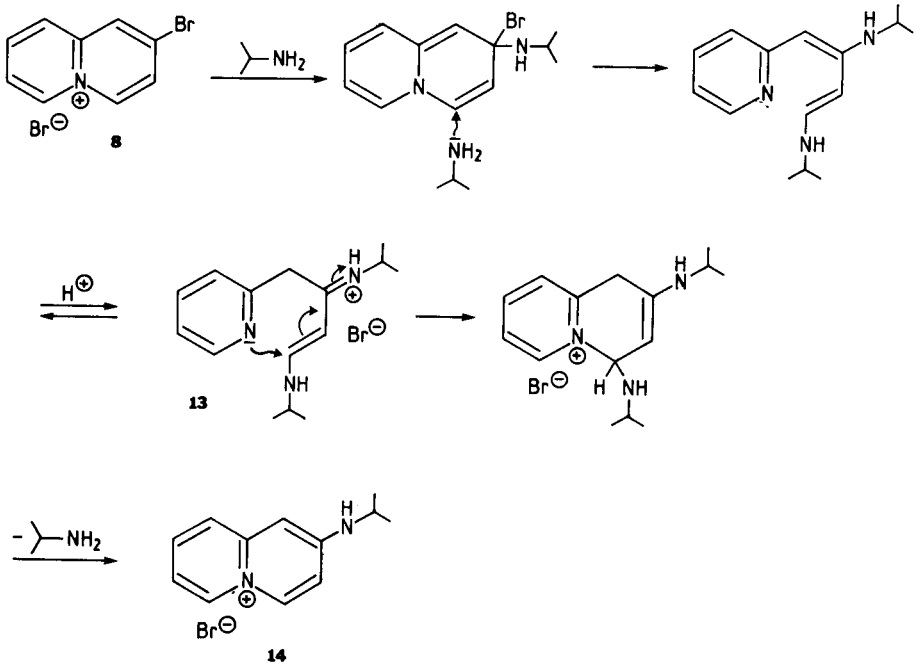


Table V

^{1}H-NMR Chemical Shifts (δ) of QB Derivatives in Hexadeuteriodimethyl Sulfoxide

	H-1	H-2	H-3	H-4	H-6	H-7	H-8	H-9	Other
2-AnilinoQB	7.42	—	7.54	8.92	8.78	7.28	7.80	8.00	NH: 10.6; Phe: 7.2-7.6
2-Phenylimino-2*H*-quinolizine	6.05	—	6.44	7.72	7.69	6.25	7.14	7.28	Phe: 6.7-7.0
4-AnilinoQB (**3** + HBr)	7.46	8.23	8.10	—	9.44	8.00	8.30	8.54	NH: 10.0; Phe: 7.2-7.6
4-Phenylimino-4*H*-quinolizine (**3**)	6.40	7.28	6.33	—	9.20	6.99	7.34	7.53	Phe: 6.8-7.5
2-IsopropylaminoQB (**14**)	7.28	—	7.42	8.89	8.77	7.28	7.75	7.92	NH: 8.56; CH: 3.86; CH_3: 1.32

Perkin Elmer 237 spectrophotometer and the uv spectra on a Beckman spectrophotometer Acta C III in methanolic solution unless stated otherwise. Mass spectra were determined on an AE MS 902 mass spectrometer and gc/ms analyses were carried out on a Micromass 7070 F apparatus. The ^{1}H-nmr spectra were recorded on a 60 MHz Hitachi Perkin-Elmer R-24B spectrometer, or on a 90 MHz Varian EM 390 spectrometer, using tetramethylsilane as internal standard and hexadeuteriodimethyl sulfoxide as solvent, unless stated otherwise. The ^{1}H-nmr spectra of **3**, **9** and **12** and the ^{13}C-nmr spectra of **9** and **13** were measured on a Varian XL-100-15 spectrometer.

Chemical shifts (δ) for the protons of the QB derivatives, not being described in reference 3 and 1, are given in Table V. J values correspond with the average values given in reference 3. Integration values were in accordance with the structures assigned.

Reactions with Liquid Ammonia. General Procedure.

Finely powdered QB (1.0 g) or bromoQB was added to liquefied ammonia (100 ml); the mixture was stirred until all of the solid had dissolved (about 2 hours). Diethyl ether (100 ml) was then added and the mixture was warmed gradually to the boiling point. Insoluble salts were filtered off and the filtrate was concentrated *in vacuo* to about 5 ml and immediately used for nmr measurements.

Identification of Open-Chain Compounds.

The open-chain compounds formed by reaction with ammonia and isopropylamine (except **13**) were extremely unstable; they decompose rapidly and we could not obtain satisfactory C,H-analyses. Therefore the identification of the products was based on physical data and on the results of oxidation and reduction experiments.

Oxidation of the Open-Chain Compounds and Esterification of the Acids Formed.

The open-chain compounds were oxidized with potassium permanganate to the corresponding pyridine carboxylic acids and then esterified *via* their acid chlorides, according to the procedure already described (1). The products obtained were characterized by glc, ^{1}H-nmr, ir and ms spectroscopy and by gc/ms analysis in case of mixtures.

Reduction of Open-Chain Compounds.

The open-chain product, resulting from 1 g of the quinolizinium compound was dissolved in acetic anhydride (100 ml) (this solvent was necessary to prevent coupling reactions). The mixture was hydrogenated with 10% palladium on carbon catalyst (0.3 g) for 20 hours in a Parr apparatus under 45 psi. The mixture was filtered, evaporated and the residue was investigated by ir and ^{1}H-nmr spectroscopy and by gc/ms analysis or mass spectroscopy.

1-Amino-4-[2-pyridyl]-1,3-butadiene (**4a**).

Crude **4a** was obtained in quantitative yield; ^{1}H-nmr and uv see Table VI; ir (carbon tetrachloride): 3420, 3520 cm^{-1} (NH_2); ms: 146 (M^+).

Oxidation gave methyl picolinate; reduction gave 1-acetylamino-4-[2-pyridyl]butane.

1-Amino-4-[3-bromo-2-pyridyl]-1,3-butadiene (**6**) and 1-Amino-4-bromo-4-[2-pyridyl]-1,3-butadiene (**7**).

The mixture of **6** and **7** was obtained in quantitative yield; for ^{1}H-nmr and uv see Table VI. The nmr data for **7** are missing in the Table, as complete assignment of this minor component was not possible; ir (chloroform): 3420, 3520 cm^{-1} (NH_2). The compounds deteriorated during the mass spectrometric analysis. Oxidation gave a mixture of methyl picolinate and methyl 3-bromopicolinate; reduction gave 1-acetylamino-4-[2-pyridyl]butane.

1-Amino-4-[2-pyridyl]but-1-en-3-yne (**9**).

Crude **9** was obtained in quantitative yield; for ^{1}H-nmr and uv see Table VI; ir (chloroform): 3420, 3520 cm^{-1} (NH_2); 2190 (C≡C); ms: 144 (M^+); ^{13}C-nmr (diethyl ether): δ 75.5 (d, C-c, J = 160 Hz), 87.4 (s, C-a), 94.8 (s, C-b), 120.8 (d, C-5, J = 166 Hz), 125.8 (d, C-3, J = 165 Hz), 136.4 (d, C-4, J = 164 Hz), 139 or 146 (s, C-2), 149.5 (d, C-d, J = 165 Hz), 149.8 (d, C-6, J = 170 Hz).

Oxidation gave methyl picolinate; reduction gave 1-acetylamino-4-[2-pyridyl]butane.

1-Amino-2-bromo-4-[2-pyridyl]-1,3-butadiene (**11**).

Crude **11** was obtained in quantitative yield; for ^{1}H-nmr and uv see Table VI; ir (chloroform): 3420, 3520 cm^{-1} (NH_2). The compound deteriorated during the mass spectrometric analysis. Oxidation gave mainly methyl picolinate with some methyl 5-bromopicolinate; reduction gave 1-acetylamino-4-[2-pyridyl]butane.

1-Amino-4-[6-bromo-2-pyridyl]-1,3-butadiene (**12**).

A mixture of **12** and X (probably 1-amino-4-[6-amino-2-pyridyl]-1,3-butadiene) was obtained in quantitative yield; for ^{1}H-nmr and uv see Table VI; ir (chloroform): 3400, 3500 cm^{-1} (NH_2). The compounds deteriorated during the mass spectrometric analysis. Oxidation gave mainly methyl 6-bromopicolinate; methyl 6-aminopicolinate, which would have resulted from the oxidation of an aminopyridyl compound is probably not stable under the conditions of the oxidation. Reduction gave a mixture of 1-acetylamino-4-[2-pyridyl]butane and some 1-acetylamino-4-[6-bromo-2-pyridyl]butane. We did not detect any 6-acetylaminopyridine derivative.

1-Isopropylamino-4-[4-bromo-2-pyridyl]-1,3-butadiene (**15**).

Compound **15** was obtained in 20-25% yield according to the procedure described before for the reactions with diethylamine (1); for ^{1}H-nmr and uv see Table VI; ir (chloroform): 3460 cm^{-1} (NH). Exact mass determination: Calcd. for $C_{12}H_{15}BrN_2$: 268.0399 and 266.0419. Found: 268.0400 and 266.0420. Oxidation gave mainly methyl 4-chloropicolinate, which is probably formed from the corresponding bromo compound with thionyl chloride, used in the esterification procedure.

4-Phenylimino-4*H*-quinolizine (**3**).

A solution of 4-bromoQB (0.50 g) in absolute ethanol (6 ml) was refluxed with aniline (0.32 g) for 4 hours with stirring. The mixture was then poured into dry diethyl ether (25 ml) and cooled in ice. The precipitate was collected, washed with ether and purified by column chromatography (alumina, act. V, eluent: water saturated ethyl acetate/methanol). The yield of **3** was 0.35 g (92%), mp 110-113°, after crystallisation from ethyl acetate/petroleum ether (60-80°), mp 113-114°; uv (ethanol): λ max (ε) 254 nm (10700), 395 nm (10400); uv (ethanol/sodium hydroxide): λ max (ε) 253 nm (11200), 285 nm (8400), 417 nm (11900); uv (ethanol/hydro-

Table VI

^{1}H-NMR and UV Spectral Data of Ring Opening Products Obtained from (Halogeno)Quinolizinium Bromides and Ammonia or Isopropylamine (a)

	δ								UV
	H-3	H-4	H-5	H-6	H-a	H-b	H-c	H-d	λ (max) nm
H_a, H_b-*cis*									
4a (b)	6.91	7.35	6.74	8.38	5.61	6.11	7.09	6.37	352 (b)
6 (b)	—	7.64	6.65	8.31	6.04	6.27	6.75	6.49	370 (b)
11 (b)	7.33	7.53	6.96	8.46	6.00	6.28	—	7.74	347 (b)
12 (b)	6.86	7.34	6.97	—	5.74	6.22	7.07	6.50	372 (d)
H_a, H_b-*trans*									
4b (c)	7.13	7.53	6.93	8.31	5.96	7.20	5.36	6.66	
15 (c)	7.31	—	7.08	8.14	5.89	7.28	5.18	6.65	381, 327 (d)
enyne									
9 (b)	7.11	7.44	6.93	8.32	—	—	4.64	6.84	329 (b)

(a) Average J-values for the open-chain compounds: $J_{3,4}$ = 8 Hz; $J_{4,5}$ = 7.5 Hz; $J_{3,5}$ = 1-2 Hz; $J_{5,6}$ = 5 Hz; $J_{4,6}$ = 2 Hz; $J_{ab(cis)}$ = 11 Hz; $J_{ab(trans)}$ = 15 Hz; J_{bc} = 11 Hz; $J_{cd(trans)}$ = 13 Hz; $J_{d(NH)}$ = 10 Hz. For compound **9** J_{cd} = 14 Hz. (b) In diethylether. (c) In hexadeuteriodimethyl sulfoxide. (d) In methanol.

bromic acid): λ max (ε) 262 nm (9700), 384 nm (13600); ir (potassium bromide): NH absorption absent.

Anal. Calcd. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49. Found: C, 81.8; H, 5.5.

2-AnilinoQB.

2-AnilinoQB was prepared as described in reference 2, mp 182-184°. By reaction with sodium hydroxide we prepared 2-phenylimino-2*H*-quinolizine analogous to the directions in the literature (11), in order to compare the ^{1}H-nmr spectrum with that of **3** (Table V).

2-IsopropylaminoQB (**14**).

2-BromoQB (2.0 g), absolute ethanol (20 ml) and isopropylamine (20 ml) were refluxed for 30 minutes and then poured into ice water. The aqueous layer was washed with dichloromethane and evaporated. Crude **14** (2.16 g) was thus obtained and purified by chromatography over a column of alumina (act. V, eluent: water saturated ethyl acetate/methanol 9:1). The pure fractions were crystallized from absolute ethanol/ethyl acetate with a drop of concentrated hydrobromic acid. Yield of pure **14** was 0.34 g (18%), mp 216-219°; uv (methanol): λ max (ε) 238 nm (25400), 311 nm (15700), 354 nm (6700); ir (potassium bromide): 3160 cm^{-1} (NH); ^{1}H-nmr: see Table V.

Anal. Calcd. for $C_{12}H_{15}BrN_2$: C, 53.94; H, 5.66. Found: C, 53.8; H, 5.8.

1-Isopropylamino-4-[2-pyridyl]-3-isopropyliminio-1-butene Bromide (**13**).

2-BromoQB (5.0 g) was added to isopropylamine (250 ml) in small portions with stirring at room temperature. Stirring was continued until all starting material had dissolved (usually 2.5 hours). Then dry diethyl ether (200 ml) was added and the mixture was concentrated to 100 ml. Again dry ether (200 ml) was added and the mixture was concentrated to 100 ml. Finally, dry diethyl ether (250 ml) was added, the precipitate formed was collected and washed with ether (the filtrate contained a small amount, about 25%, of the open-chain compound **15**). The crude product was refluxed for 1 hour with active coal in acetone and crystallised twice from acetone/ethyl acetate. Yield of pure **13** was 2.4 g (45%), mp 171-172°; uv (methanol): λ max (ε) 262 nm (4200), 268 nm (3800), 317 nm (37600); ir (potassium bromide): 3200 cm^{-1} (NH), 3160 cm^{-1} (NH). In the ^{1}H-nmr spectrum two signals are found for H-1 and H-2, corresponding with different conformations of the molecule; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.10-1.25 (several d, CH_3, 12H), 3.73 (m, CH (isopropyl), 2H), 4.16 (s, H-4, 2H), 5.44 and 5.40 (ratio 60/40) (d, H-2, 1H, J = 12 Hz and 12.5 Hz), 7.26 (ddd, H-5', 1H, J = 7.5 Hz, J = 5 Hz, J = 1 Hz), 7.50 (ddd, H-3', 1H, J = 7.5 Hz, J = 1 Hz, J = 0.5 Hz), 7.73 (ddd, H-4', 1H, J = 7.5 Hz, J = 7.5 Hz, J = 2 Hz), 8.29 and 8.00 (ratio 60/40) (broad d, H-1, 1H, J = 12 Hz and 12.5 Hz), 8.51 (ddd, H-6', 1H, J = 5 Hz, J = 2 Hz, J = 0.5 Hz), 9.59, 9.30 and 9.23 (bs, NH). Upon addition of deuterium oxide the NH signals disappeared and the broadened signals for H-1 sharpened.

In the ^{13}C-nmr spectrum we also found two signals for C-1, C-2 and C-3; ^{13}C-nmr (deuterated water): δ 21.3 and 22.6 (q, CH_3, J = 130 Hz), 40.5 (t, C-4, J = 135 Hz), 46.4, 46.6, 46.8 and 52.1 (d, CH (isopropyl), J = 140 Hz), 87.7 and 89.7 (d, C-2, J = 155 Hz), 123.8 (d, C-5' and C-3', J = 165 Hz), 139.3 (d, C-4', J = 165 Hz), 149.7 (d, C-6', J = 180 Hz), 156.4 (s, C-2'), 157.1 and 159.9 (d, C-1, J = 170 Hz), 167.2 and 168.7 (s, C-3). The assignments are in full agreement with selective decoupling experiments.

Anal. Calcd. for $C_{15}H_{24}BrN_3$: C, 55.21; H, 7.41. Found: C, 55.1; H, 7.4.

4-Bromo-1,3-dideuterioQB.

This compound was prepared from 1,3-dideuterio-4-quinolizone as described in a previous publication (3).

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(4) The reaction of QB with ammonia has been mentioned by Mörler and Kröhnke (D. Mörler and F. Kröhnke, *Ann. Chem.*, **744**, 65 (1970)).

(5) Product X is probably 1-amino-4-[6-amino-2-pyridyl]-1,3-butadiene, on account of the ^{1}H-nmr spectrum. Oxidation and reduction experiments did not give indications for the formation of aminopyridyl compounds. However, when the mixture of open-chain compounds was acetylated with acetic anhydride before oxidation/esterification, we found a small amount of methyl 6-acetylaminopicolinate, by gc/ms analysis. Since 2-bromopyridine is not converted into 2-aminopyridine by liquid ammonia under our conditions, we assume that compound X, when formed at all, arises from substitution followed by ring opening.

(6) The relatively high value for λ max (317 nm) is in accordance with the data given in the literature for the cyanine analogs; $Me_2N^+ = CH - (CH=CH)_n - NMe_2$; for n = 1, λ max = 309 nm (H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Specroscopy", John

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