SYNTHESIS AND DEUTERATION OF SOME HALOGENOQUINOLIZINIUM BROMIDES

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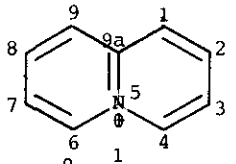
Syntheses and ^{1}H-nmr spectra are reported for the hitherto unknown 1-bromo-, 3-bromo-, 4-bromo-, 2-chloro-, 4-chloro-, 1,2-dibromo-, 3,4-dibromo- and 2,7-dibromoquinolizinium bromide. These compounds, quinolizinium bromide, 1-hydroxy-, 2-hydroxy-, 3-hydroxy-, 2-piperidino- and 2-diethylaminoquinolizinium bromide and 2- and 4-quinolizone were deuterated by heating with D_2O (Table I).

Introduction and results

Quinolizinium salts form a class of compounds whose properties have not yet been studied extensively[1].



$Br^{\ominus}$ 1

Quinolizinium bromide (QB)

The special interest in this laboratory in the behaviour of halogenohetarenes and hetarinium salts towards nucleophiles induced us to prepare several halogenoquinolizinium bromides and to study their reactivity towards nucleophiles. In this paper we report on the synthesis of 1-bromo-, 2-bromo-, 3-bromo-, 4-bromo-, 2-chloro-, 4-chloro-, 1,2-dibromo-, 3,4-dibromo- and 2,7-dibromoquinolizinium bromide (quinolizinium bromide from here on abbreviated as QB). Only 2-bromoQB[2] and 4-chloroquinolizinium perchlorate[3] have been described in the literature thus far. Since structure identification of the QB's is based mainly on their ^{1}H-nmr spectra, we prepared deuterium labelled compounds in order to support the assignments of the peaks in the spectra.

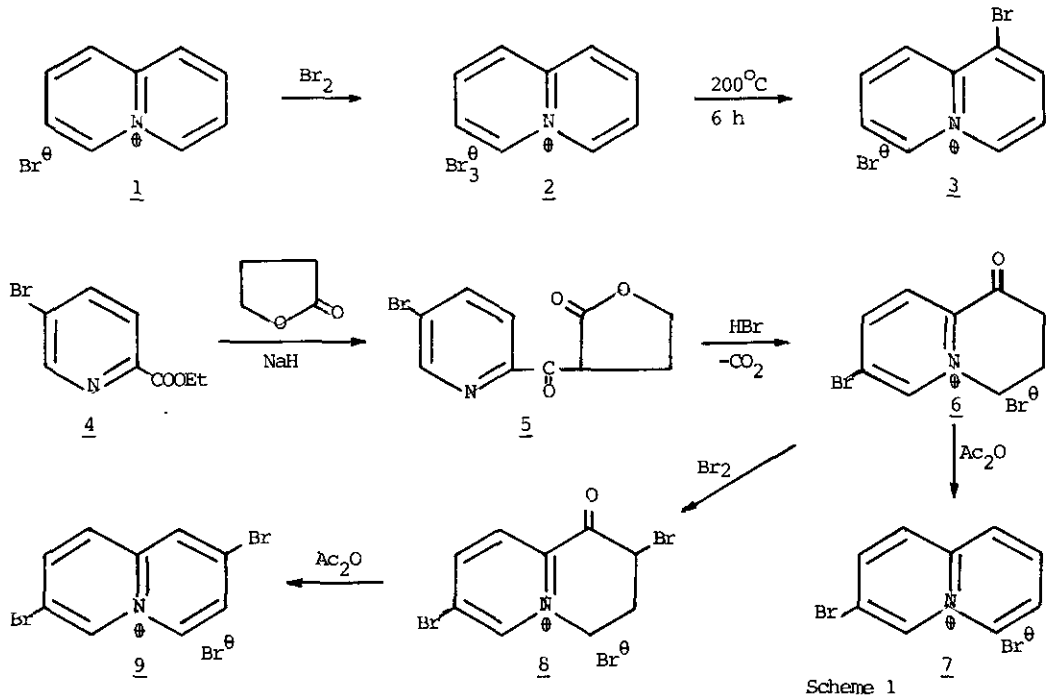
The parent compound : quinolizinium bromide (1) has been synthesized by several methods; we obtained the best overall yield (24%) by a 4-step synthesis starting from pyridine-2-carboxylic acid[4].

1-BromoQB (3) was prepared in 69% yield by heating quinolizinium perbromide (2) at 200°C for 6 h

(Scheme 1) ; this procedure is analogous to that given for the preparation of 4-bromoisoquinoline[5]. The structure of the product was proved by a spin decoupling experiment : on irradiating the low field protons H(4) and H(6), the double double doublet of H(7) (J = 7Hz, 7Hz, 2Hz) and the double doublet of H(3) (J = 7Hz, 7Hz) changed into a double doublet (J = 7Hz, 2Hz) and a doublet (J = 7Hz), respectively.

It is not clear whether introduction of the bromo atom at position 1 proceeds by an electrophilic substitution mechanism or via product(s) formed by bromine addition. Attempts to detect the latter addition compounds by ^{1}H-nmr spectroscopy of the reaction mixture at several reaction temperatures, met with little success. We found further that quinolizinium perbromide is capable of brominating other compounds. Thus, anisole was converted into 4-bromoanisole at room temperature and heating of a mixture of isoquinoline and quinolizinium perbromide gave a considerable amount of 4-bromoisoquinoline. However, these facts do not permit any mechanistic conclusions.

3-BromoQB (7) was prepared from 5-bromo-2-ethoxycarbonylpyridine (4) by the same series of reactions as used for the preparation of QB (Scheme 1). By bromination of the intermediary compound 6, followed by dehydratation with acetic anhydride[6], 2,7-dibromoQB (9) was obtained.

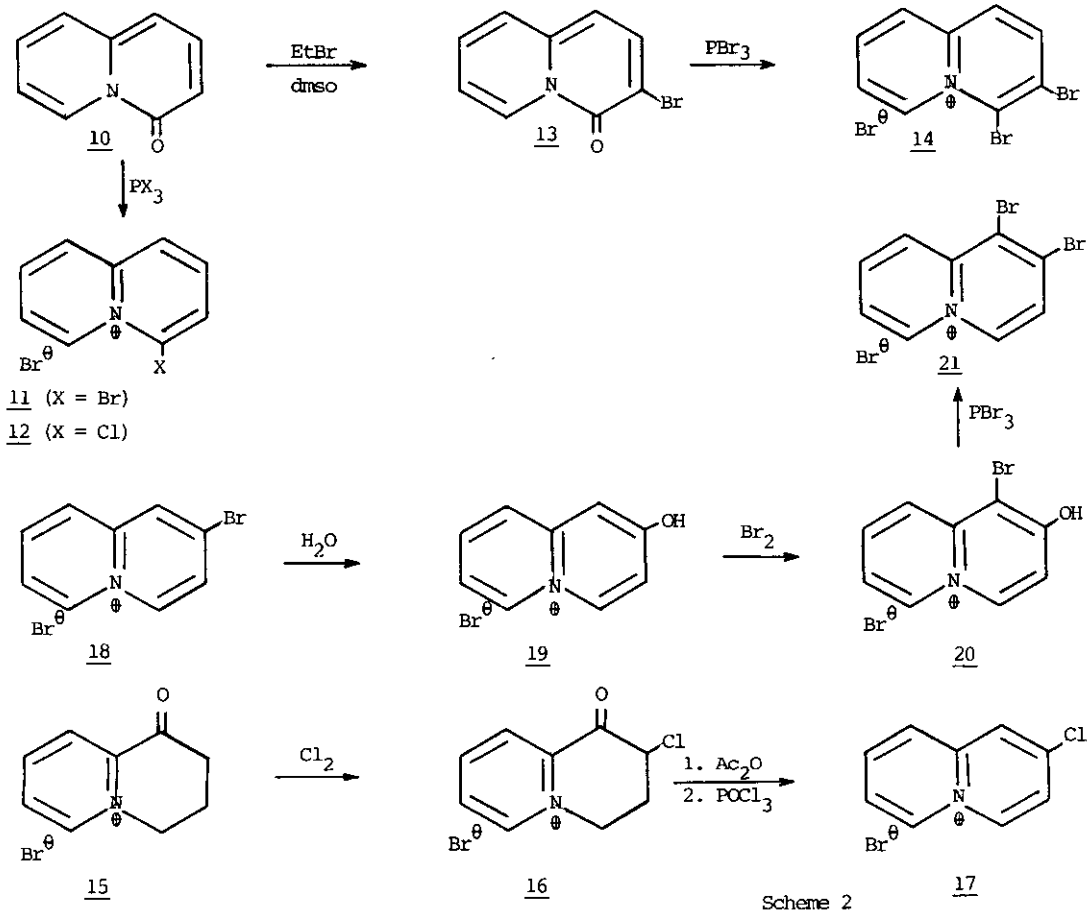


Scheme 1

4-BromoQB (11) was obtained from 4-quinolizone (10) by reaction with PBr_3. Likewise 3-bromo-4-quinolizone (13)[12,14] was converted into 3,4-dibromoQB (14). Reacting 10 with PCl_3 led to 4-chloroQB (12) (Scheme 2).

Treatment of 1-oxo-1,2,3,4-tetrahydroQB (15) with chlorine and subsequent dehydratation of the product 16 with acetic anhydride gave 2-chloroQB (17) (Scheme 2). The product obtained was inevitably contaminated with 2-hydroxyQB, therefore treatment with $POCl_3$ was necessary to obtain pure 17.

Finally, 1,2-dibromoQB (21) could be prepared by treatment of 1-bromo-2-hydroxyQB (20) with PBr_3 (Scheme 2).



Scheme 2

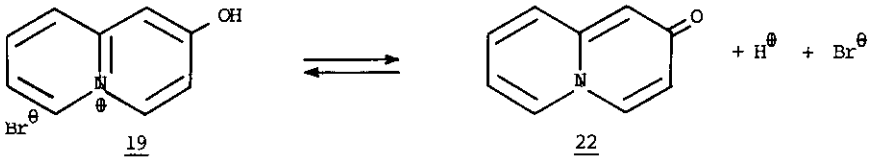
Deuteration experiments were carried out by heating the compounds with an excess of D_2O for 12 h at 220°C. It was found that under these conditions conversion of the halogen atom at C(2) into the hydroxy group took place. In the presence of halogen at C(4) unknown decomposition products were obtained. The hydroxydehalogenation at C(2) took place in about 100% yield, thus providing us with a cheaper synthesis of 2-hydroxyQB than the one with silver acetate, reported in the literature[13]. The results of the deuteration experiments are shown in Table I; for comparison the deuteration results of 2-diethylaminoQB and 2-piperidinoQB have been included.

Table I. Distribution pattern of deuterium on deuteration of QB and derivatives

exp. no	starting material	product	results: deuterium content C(1)	C(2)	C(3)	C(4)	C(6)
1	QB (1)	QB	-	-	-	100%	100%
2	1-BrQB (3)	1-BrQB	-	-	-	85%	85%
3	1-OHQB	1-OHQB	-	100%	-	100%	10%
4a	2-BrQB (18)	2-OHQB	100%	-	-	10%	10%
4b	2-BrQB (+HBr)	2-OHQB	100%	-	-	-	-
4c	2-BrQB (+$N(C_2H_5)_3$)	2-OHQB	100%	-	-	100%	30%
5	2-ClQB (17)	2-OHQB	100%	-	-	-	-
6a	2-OHQB (19)	2-OHQB	100%	-	-	50%	20%
6b	2-OHQB (+HBr)	2-OHQB	100%	-	25%	-	-
7	2-quinolizone* (22)	2-quinolizone	100%	-	-	100%	40%
8	2-NC_5H_{10}QB	2-NC_5H_{10}QB	100%	-	-	90%	90%
9	2-$N(C_2H_5)_2$QB	2-$N(C_2H_5)_2$QB	100%	-	15%	100%	100%
10	3-BrQB (7)	3-BrQB	-	-	-	100%	65%
11	3-OHQB	3-OHQB	-	-	-	100%	30%
12	4-BrQB (11)	decomp.prod.					
13	4-ClQB (12)	decomp.prod.					
14	4-quinolizone* (10)	4-quinolizone	100%	-	100%	-	-
15	1,2-diBrQB (21)	1-Br-2-OHQB	-	-	-	-	-
16	2,7-diBrQB (9)	2-OH-7-BrQB	100%	-	25%	70%	100%
17	3,4-diBrQB (14)	decomp.prod.					

*12 h at 170°C

Although for a detailed explanation of the results kinetic experiments are required, it seems justified to conclude that two deuteration mechanisms play a role. In the first mechanism a proton is abstracted from the most acidic position(s) [C(4) and C(6)], whereupon the resulting ylide takes up a deuteron[7a]. On the other hand, in the presence of activating hydroxy or amino groups electrophilic substitution by deuterium will occur, mainly at ortho or para positions[7b]. Thus, QB and its bromo derivatives will be deuterated *via* their ylides at positions 4 and 6 (exp. 1,2,10). In 1- and 3-hydroxyQB electrophilic substitution will be the main process (exp. 3,11). 2-HydroxyQB, when formed from 2-bromoQB, is deuterated in acidic medium, due to the formation of HBr (exp. 4a). Acid will retard ylide formation, will promote electrophilic substitution and will displace the equilibrium between 2-hydroxyQB (19) (pK_A about 4[13]) and 2-quinolizone (22) (Scheme 3) in favour of 2-hydroxyQB.



19 22

Scheme 3

Thus, the different results of exp. 4a and 6a can be explained; addition of more HBr enhances the effect (exp.4b,6b), whereas addition of base (exp.4c) leads to the deuteration pattern of 2-quinolizone (exp.7). In 1,2-dibromoQB (exp.15) slight deuteration at C(4) and C(6) was expected (cf.exp.4a); we cannot explain why this does not occur. 2-Piperidino- and 2-diethylaminoQB undergo both types of deuteration, as is evident from the results (exp.8,9).

Attempts to deuterate 4-bromoQB at lower temperatures without decomposition failed; we found either decomposition or no reaction at all. However, in the ^{1}H-nmr spectrum of 4-bromoQB in D_2O, the area for H(6) is always about 10% too low; upon measuring in H_2O this effect disappeared. Apparently the favoured position of deuteration is C(6).

Experimental part

General

Melting points are uncorrected. ^{1}H-nmr spectra were recorded on an Hitachi Perkin-Elmer R-24B spectrometer, using tetramethylsilane (TMS) as internal standard and dmso-D_6 as solvent, unless stated otherwise. The spin decoupled spectra of 3 and 1 were measured on a Varian XL-100-15 spectrometer.

For QB the assignment was supported by a spin decoupling experiment. The ^{1}H-nmr spectra of the other compounds were interpreted on basis of their coupling patterns. Chemical shifts (δ) of all quinolizinium derivatives described are given in Table II.

As to the tetrahydro-1-oxoQB's (6, 8, 16), according to their nmr spectra the bromo compounds occur for about 60% in the enol-form, the chloro compound for about 100%.

Uv spectra were measured on a Beckman Acta CIII spectrophotometer. Uv spectra of the monobromoQB's are published separately[9].

TLC analyses on QB derivatives were performed on cellulose (Avicel, Merck) plates; eluent usually n-butanol-water-formic acid 11:2:1.5.

Deuterations were carried out by heating 0.1 - 0.25 g of the compound with 5 ml of D_2O at 220°C in a sealed tube with shaking. The deuterium distribution was determined by nmr.

Table II. Chemical shifts in the ^{1}H-nmr spectra of QB and derivatives in dmso-D_6[a]

	δ							
	H(1)	H(2)	H(3)	H(4)	H(6)	H(7)	H(8)	H(9)
QB 1	8.69	8.43	8.14	9.58	9.58	8.14	8.43	8.69
1-BrQB 3	-	8.79	8.02	9.50	9.56	8.22	8.55	8.75
2-BrQB 18	9.07	-	8.36	9.42	9.51	8.13	8.41	8.54
3-BrQB 7	8.62	8.62	-	10.00	9.48	8.19	8.47	8.73
4-BrQB 11	8.74	8.59	8.34	-	9.69	8.25	8.52	8.74
2-ClQB 17	8.90	-	8.26	9.50	9.47	8.09	8.40	8.57
4-ClQB 12	8.75	8.48	8.44	-	9.67	8.22	8.51	8.84
1,2-diBrQB 21	-	-	8.48	9.46	9.49	8.20	8.54	8.80
3,4-diBrQB[b] 14	8.27	8.52	-	-	9.82	8.28	8.58	9.06
2,7-diBrQB[b] 9	8.58	-	8.13	8.93	9.25	-	8.41	8.16
2-OHQB 19	7.68	-	7.62	9.23	9.06	7.63	7.99	8.23
2-NC_5H_{10}QB	7.57	-	7.62	8.83	8.63	7.20	7.64	7.82
2-$N(C_2H_5)_2$QB	7.44	-	7.51	8.89	8.72	7.24	7.68	7.94
1-OHQB	-	7.64	7.92	8.90	9.32	8.05	8.30	8.55
3-OHQB	8.59	8.12	-	9.01	9.44	8.00	8.18	8.55
2-quinolizone 22	6.36	-	6.57	8.30	8.13	6.67	7.17	7.30
4-quinolizone 10	6.79	7.72	6.47	-	8.98	7.14	7.45	7.71
1-Br-2-OHQB 20	-	-	7.54	9.02	8.95	7.59	8.02	8.25
3-Br-4-quinolizone 13	6.78	8.08	-	-	8.98	7.26	7.59	7.82
7-Br-1-oxo-1,2,3,4-tetrahydroQB 6 keto	-	2.5-3.0	2.5-3.0	4.5-5.0	9.60	-	8.95	8.33
7-Br-1-oxo-1,2,3,4-tetrahydroQB 6 enol	-	5.78	2.5-3.0	4.5-5.0	9.39	-	8.71	7.87
2,7-diBr-1-oxo-1,2,3,4-tetrahydroQB 8 keto	-	5.53	3-3.5	5.00	9.66	-	8.99	8.45
2,7-diBr-1-oxo-1,2,3,4-tetrahydroQB 8 enol	-	-	3.14	4.78	9.42	-	8.77	7.96
2-Cl-1-oxo-1,2,3,4-tetrahydroQB 16 enol	-	-	3.07	4.86	9.03	7.95	8.58	8.09

[a] Average values for the coupling constants in QB derivatives are: $J_{1,2}$= 8-9Hz, $J_{2,3}$= 6.5-8Hz, $J_{3,4}$= 6.5-8Hz, $J_{1,3}$ = 2-3Hz, $J_{2,4}$= 1-2Hz, $J_{1,4} \leq$ 1Hz. Only 2- and 4-quinolizone deviate slightly ($J_{7,8} \sim$ 5.5Hz)[8].

[b] in CF_3COOH solution.

Syntheses

a. Quinolizinium bromide (1)[4], m.p. 263-265°C, overall yield 24%; 2-bromoquinolizinium bromide (18)[4b,2], m.p. 261-263°C; 1-hydroxyquinolizinium bromide[2], m.p. 184-185°C (monohydrate); 2-quinolizone (22)[13], m.p. 127-128°C; 3-hydroxyquinolizinium bromide[16], m.p. 256-258°C; these compounds were prepared according to the procedures given in the literature.

b. 1-Bromoquinolizinium bromide (3). While mixing thoroughly, 8.46 g of bromine were added slowly to 10 g of finely powdered 1. An orange-red substance was obtained which is probably quinolizinium perbromide (2) ($C_9H_8N^{\oplus}Br_3^{\ominus}$, m.p. 184-196°C; ^{1}H-nmr spectrum nearly identical to that of 1; anal.calcd.: C, 29.22; H, 2.18; found: C, 29.0; H, 2.2).

The perbromide was heated for 6 h at 200°C; while still fluid, the product was poured into a mortar. After solidification the material was powdered and stirred with 125 ml of isopropanol at 60°C for 2 h in order to dissolve any unreacted starting material. The warm mixture was filtered; the residue (5 g of crude 3) was crystallized from abs.ethanol/ethyl acetate, giving 3.8 g of 3, m.p. 301-303°C. Anal.calcd. for $C_9H_7Br_2N$ (288.99): C, 37.40; H, 2.44; found: C, 37.4; H, 2.7. From the filtrate 6 g of pure starting material were obtained by evaporation and crystallization from abs. ethanol/ethyl acetate. Yield of 3, corrected for recovered starting material, 69%.

c. 3-Bromoquinolizinium bromide (7)

c.1. 5-bromo-2-ethoxycarbonylpyridine (4).

5-Bromo-2-pyridinecarboxylic acid. 35 g of 5-bromo-2-methylpyridine[10] and 70 g of $KMnO_4$ were stirred for 6 h in 1.5 l of water at 100°C[11]. 200 ml of water were then removed by distillation (from the distillate 10 g of starting material were recovered by ether extraction). The cold reaction mixture was filtered, the filtrate concentrated to 100 ml and acidified with conc. HCl to pH = 3. The remaining water was distilled off and the residue of crude 5-bromo-2-pyridine-carboxylic acid was dried azeotropically with toluene. Recrystallization from water gave a product with m.p. 175-176°C.

5-Bromo-2-ethoxycarbonylpyridine (4). 200 ml of thionylchloride were added with stirring to the crude 5-bromo-2-pyridinecarboxylic acid, obtained from 65 g of 5-bromo-2-methylpyridine, and the mixture was refluxed for 2 h. The excess of thionylchloride was removed by distillation in vacuo; 100 ml of dry toluene and then 200 ml of abs.ethanol were added slowly and the mixture was refluxed for 2 h. The cold reaction mixture was brought to pH = 8 by careful addition of a saturated $NaHCO_3$ solution. Extraction with ether, washing with water, drying and evaporation gave 62 g of 5-bromo-2-ethoxycarbonylpyridine. Overall yield from 2-methylpyridine 57%; m.p. 59-60°C. Anal.calcd. for $C_8H_8BrNO_2$ (230.07): C, 41.76; H, 3.50; found: C, 41.7; H, 3.3.

c.2. α-[5-bromopicoloyl] -γ-butyrolactone (5) was prepared from 4 in accordance with directions given in the literature for the preparation of α-picoloyl-γ-butyrolactone[4b], except that 4 and γ-butyrolactone were added as a solution in dry toluene. Yield after recrystallization from ethanol: 47%, m.p. 107-109°C. Anal.calcd. for $C_{10}H_8BrNO_3$ (270.09): C, 44,47; H, 2.99; found: C, 44,5; H, 3.1.

c.3. 7-Bromo-1-oxo-1,2,3,4-tetrahydroquinolizinium bromide (6). 10.0 g of 5 and 100 ml of 47% HBr were refluxed for 20 min. The reaction mixture was concentrated in vacuo to a volume of 20 ml and then poured into 250 ml of water. The mixture was extracted with chloroform, the chloroform layer

was dried shortly (5 min) on $MgSO_4$ and the chloroform was evaporated. The residue was dissolved in 100 ml of 1,2-dichloroethane and refluxed for 2 h. A precipitate was formed, which was filtered off after cooling the reaction mixture to room temperature. Yield: 6.1 g (54%) of crude 6, m.p. 257-262°C. Crystallization from ethanol raised the m.p. to 261-264°C. Anal.calcd. for $C_9H_9Br_2NO$ (307.00): C, 35.21; H, 2.96; found: C, 35.4; H, 2.7.

c.4. 3-Bromoquinolizinium bromide (7) was prepared from crude 6 by treatment with acetic anhydride according to the procedure given for the preparation of quinolizinium bromide[4c]. Yield after crystallization from abs.ethanol/ethyl acetate: 67%, m.p. 259-261°C. Anal.calcd. for $C_9H_7Br_2N$ (288.99): C, 37.40; H, 2.44; found: C, 37.4; H, 2.3.

d. 4-Bromoquinolizinium bromide (11). 9.0 g of 4-quinolizone (10)[12] were stirred with 45 ml of PBr_3 for 7 h in an oilbath of 180°C. The excess PBr_3 was removed by distillation in vacuo. The residue was dissolved in 200 ml of distilled water and left for 2 h on a 1-litre column filled with Dowex 21 K (Br^{θ}). The substance was eluted with distilled water. After evaporation the residue was treated for 2 h with active coal in boiling ethanol. Crystallization from ethanol/ethyl acetate afforded 8.3 g (45%) of 11, m.p. 277°C (dec.). Anal.calcd.for $C_9H_7Br_2N$(288.99): C, 37.40; H, 2.44; found: C, 37.2; H, 2.6; Br^{θ} (determined by titration with $Hg(ClO_4)_2$): calcd. 27.65; found 27.4.

e. 2-Chloroquinolizinium bromide (17)

e.1. 2-Chloro-1-oxo-1,2,3,4-tetrahydroQB (16). A solution of 2.65 g of Cl_2 in 40 ml of acetic acid was added at room temperature to a stirred solution of 8.0 g of 1-oxo-1,2,3,4-tetrahedroQB (15)[4b] in 50 ml of acetic acid and 10 ml of conc. HCl, over a period of 30 min. After another 1½ h of stirring at room temperature, the resulting solution was evaporated and the residue crystallized from abs. ethanol/ethyl acetate. Yield: 5.15 g (56%), m.p. 156-158°C. Anal.calcd. for $C_9H_9BrClNO$ (262.54): C, 41.17; H, 3.46; found: C, 40.9; H, 3,2.

e.2. 2-ChloroQB (17). A mixture of 5.0 g of 16 and 150 ml of acetic anhydride was refluxed for 3 h; after evaporation in vacuo the residue was stirred with 30 ml of $POCl_3$ at 90-100°C for 2 h. The excess of $POCl_3$ was removed in vacuo, the residue treated as aqueous solution on a column of Dowex 21 K (Br^-) (see under d). Recrystallizing twice from abs. ethanol/ethyl acetate gave 2.8 g (60%) of 17, m.p. 245-246°C. Anal.calcd. for C_9H_7BrClN (244.53): C, 44,20; H, 2.88; found: C, 44.0; H, 3.0. Uv (methanol) λ_{max} 229 (22 900), 288 (2900), 317 (12 600), 324 (10 600), 331 (20 100) nm.

f. 4-Chloroquinolizinium bromide (12). 12 was synthesized in accordance with directions given in the literature[3] for the perchlorate. 5.0 g of 10[12] and 10 ml of $POCl_3$ were stirred for 10 min at 90°C. The solid material was filtered off and treated as aqueous solution on a Dowex 21 K (Br^-) column (see under d). The resulting product was crystallized from abs. ethanol/ethyl acetate; yield 3.90 g (46%) of 12, m.p. 313-316°C. Anal.calcd. for C_9H_7BrClN (244.53): C, 44.20; H, 2.88; found: C, 44.4; H, 3.0. Uv(water) λ_{max} 237 (20 700), 292 (3900), 320 (10 000), 334 (15 800) nm.

g. 1,2-Dibromoquinolizinium bromide (21)

g.1. 2-Hydroxyquinolizinium bromide (19). 3.0 g of 2-bromoQB (18) and 30 ml of dist.H_2O were heated with shaking for 12 h at 220°C. The reaction mixture was evaporated, giving almost pure 2-hydroxyQB in quantitative yield; m.p. 259-265°C (lit. 258-263°C[13] for the hemihydrate).

g.2. 1-Bromo-2-hydroxyquinolizinium bromide (20)[13], m.p. unsharp (272-306°C).

g.3. 1,2-Dibromoquinolizinium bromide (21). 0.50 g of 20 was heated with 5 ml of PBr_3 for 6 h at 200°C. After evaporation in vacuo the residue was treated as aqueous solution on a Dowex 21 K (Br^-) column (see under d). Crystallization from abs. ethanol/ethyl acetate gave 0.39 g (65%) of 21, m.p. 281-284°C. Anal. calcd. for $C_9H_6Br_3N$ (367.89): C, 29.38; H, 1.64; found: C, 29.4; H, 1.4. Uv (methanol) λ_{max} 222 (26 200), 238 (23 100), 298 (4400), 328 (11 500), 342 (17 700) nm.

h. 3,4-Dibromoquinolizinium bromide (14). 4.0 g of 3-bromo-4-quinolizone (13)[14,12] and 25 ml of PBr_3 were heated for 6 h at 180°C. After evaporation in vacuo the residue was treated as aqueous solution on a Dowex 21 K (Br^-) column (see under d). By repeated crystallization from methanol/ethyl acetate 0.75 g (11%) of pure 14 was obtained: m.p. 321-326°C. Anal.calcd. for $C_9H_6Br_3N$ (367.89): C, 29.38; H, 1.64; found: C, 29.5; H, 1.6.Uv (ethanol) λ_{max} 249 (18 400), 305 (6800), 337 (9400), 350 (12 200) nm.

i. 2,7-Dibromoquinolizinium bromide (9)

i.1. 2,7-Dibromo-1-oxo-1,2,3,4-tetrahydroquinolizinium bromide (8)[15]. A solution of 1.64 g of bromine in 20 ml of 47% aq.HBr was added in 30 min to a stirred solution of 3.07 g of 6 in 40 ml of 47% aq.HBr. After 5 min of stirring the mixture was heated until complete solution. Evaporation in vacuo and crystallization from abs. ethanol/ethyl acetate gave 2.80 g (72%) of product; m.p. 194-196°C. Anal. calcd. for $C_9H_8Br_3NO$ (385.91): C, 28.01; H, 2.09; found: C, 27.8; H, 2.0.

i.2. 2,7-Dibromoquinolizinium bromide (9). 2,5 g of 8 and 150 ml of acetic anhydride were refluxed for 3 h with stirring. The excess of acetic anhydride was decomposed with 200 ml of water. Evaporation, followed by two crystallizations from methanol, gave 1.24 g (52%) of pure 9; m.p. > 355°C. Anal. calcd. for $C_9H_6Br_3N$ (367.89): C, 29.38; H, 1.64; found: C, 29.1; H, 1.5. Uv (water) λ_{max} 231 (37 400), 245 (31 500), 289 (5200), 296 (5500), 325 (14 000), 340 (18 500).

j. 2-Piperidinoquinolizinium bromide. 2.00 g of 2-bromoQB (18), 1.20 g of piperidine and 25 ml of abs. ethanol were refluxed for 2 h with stirring. To the ice-cooled reaction mixture 50 ml of dry diethyl ether were added; 2.67 g of a mixture of 2-piperidinoQB and piperidinium bromide precipitated. Three recrystallizations from abs. ethanol/acetone gave 0.46 g (23%) of 2-piperidinoQB, m.p. 231-233°C. Anal.calcd. for $C_{14}H_{17}BrN_2$ (293.21): C, 57.34; H, 5.84; found: C, 57.6; H, 6.1. Uv (methanol) λ_{max} 242 (22 700), 324 (21 100) nm.

k. 2-Diethylaminoquinolizinium bromide. 2.00 g of 2-bromoQB (18), 10 ml of abs.ethanol and 10 ml of dry diethylamine were refluxed for 10 min and then poured into 200 ml of ice-water. The mixture

was washed with 5 portions of CH_2Cl_2, the aqueous layer was filtered and evaporated. The residue was solved in as little abs. ethanol/ethyl acetate as possible, and then cooled in dry ice/acetone; 0.65 g of diethylammonium bromide precipitated. Evaporation of the filtrate and crystallization from acetone gave 1.10 g (56%) of 2-diethylaminoQB, m.p. 122-124°C. The compound is very hygroscopic and attracted water during analysis. Anal. calcd. for $C_{13}H_{17}BrN_2$(281.20): C, 55.52; H, 6.09; found for the vacuum-dried product: C, 50.8; H, 6.8, corresponding with 1½ mole of H_2O per mole of aminoQB (calcd. C, 50.66; H, 6.54). Uv (methanol) λ_{max} 241 (24 300), 323 (21 800) nm.

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References

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