Diazoniapentaphenes. Synthesis from Pyridine-2-carboxaldehyde and Structural Verifications

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Reactions of pyridine-2-carboxaldehyde (**9**) with α,α'-dibromo-*o*- and *p*-xylenes led to the corresponding bis-pyridinium aldehydes **10** and **14**. These aldehydes were quite reactive and the respective hydrates **11** and **15** were also formed. Cyclization of **10** or **11** with 48% HBr led to **12** while cyclization with PPA followed by conversion to the bis tribromide and loss of bromine led to **1**. Cyclization of **14** or **15** with 48% HBr led to **3**. Attempts to react α,α'-dibromo-*m*-xylene with pyridine-2-carboxaldehyde (**9**) were not successful for the preparation of the bis-pyridinium aldehyde **13**. The bis-pyridinium acetals **4**, **5** and **6** were prepared and cyclized to afford **1**, **2** and **3**, respectively, by the previously reported procedures. The structures of **1** and **2** were verified by ^{1}H-NMR and ^{13}C-NMR spectroscopy while that of **3** was confirmed by X-ray analysis.

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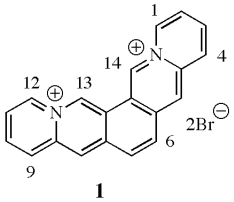
Introduction.

In 1964 Bradsher and co-workers reported the synthesis of 12a,14a- (**1**), 4a,12a- (**2**) and 4a,8a-diazoniapentaphene salts (**3**)[1]. Subsequently a German group repeated these procedures and studied their polarography [2]. Several diazonia polycyclics were also described by an Eastman Kodak (Rochester NY) group [3,4].



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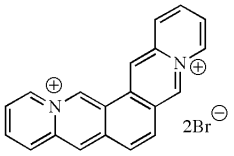

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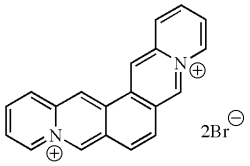

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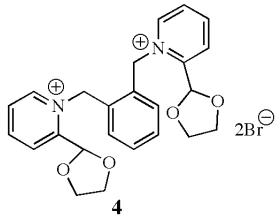
The acetal, 2-(1,3-dioxolan-2-yl) pyridine, was treated with α,α'-dibromo-*o*-, *m*-, or *p*-xylene to afford the corresponding bis-pyridinium salts **4**, **5** and **6**, respectively. These bis-quaternary salts were cyclized on heating in polyphosphoric acid (PPA) followed by precipitation with HBr/Br_2 to afford the insoluble bis-tribromide salts which on standing or heating lost Br_2 and led to the bromides **1**, **2** and **3**, respectively [1].

The initially formed acridizinium salt from the first cyclization step derived from **4** can only undergo the second cyclization step to afford a single product which was formulated as **1**. This structural formulation was verified by chemical transformations. The cyclizations of the bis-pyridinium salts **5** or **6** can either afford linear products **7** and **8** or the angular products formulated as **2** or **3**, respectively. These structural assignments were based solely on ultraviolet spectral considerations and comparisons [1].



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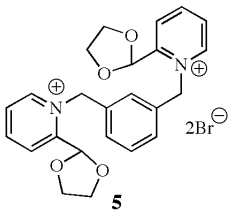

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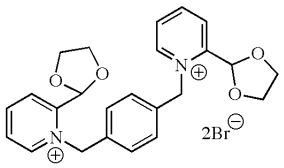

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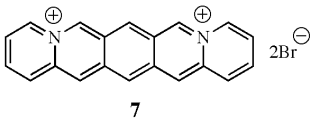

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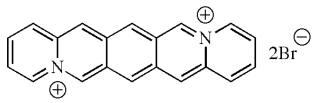

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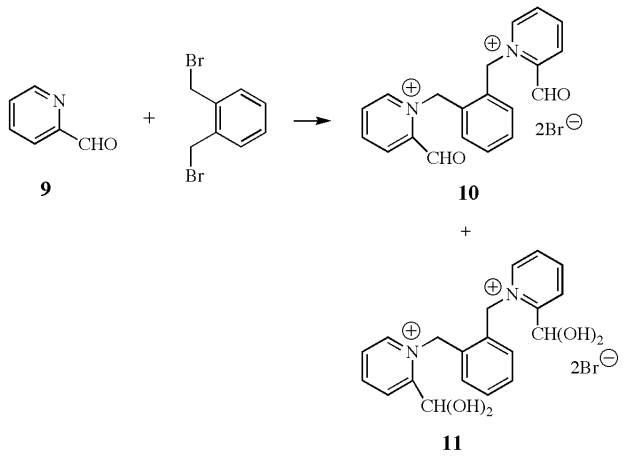
The purpose of the present research was to clearly establish the proposed structures for **1**, **2** and **3**. In addition, we wished to investigate the direct use of pyridine-2-carboxaldehyde (**9**), instead of the acetal in reactions involving α,α'-dibromo-*o*-, *m*-, and *p*-xylenes to form the corresponding bis-pyridinium salts. These latter compounds on cyclization would lead to **1**, **2** or **3**, respectively. The ultimate goal was the development of facile pathways to substituted analogues related to **1**, **2** and **3**, which were required in another investigation.

Results and Discussion.

Following the procedure described in the earlier paper [1], treatment of α,α-dibromo-*o*-xylene with 2-(1,3-dioxolan-2-

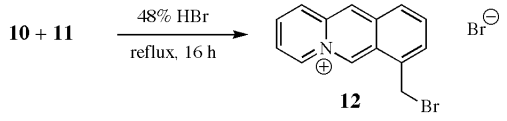
yl) pyridine led to the bis-pyridinium salt **4** which on cyclization in PPA and workup led to **1**. Both **1** and **4** were readily identifiable by their ^{1}H and ^{13}C NMR spectra.

Treatment of pyridine 2-carboxaldehyde (**9**) with α,α'-dibromo-*o*-xylene (7.2:1 molar equivalents) in DMF at 45 °C for 48 hours led to the bis-pyridinium salt **10** along with dihydrate **11** (78%).



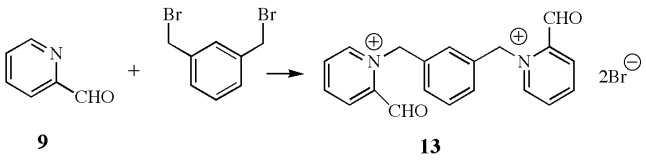
The bis-pyridinium salt **10**, as expected, was quite susceptible to hydration and, indeed if the product was isolated by filtration on a humid day, the dihydrate of the bis-pyridinium salt **11** was obtained.Addition of D_2O to the DMSO-d_6 solutions led to an nmr spectrum consistent with the dihydrate. Of obvious diagnostic values were the bridge methylene resonances at δ 6.6 and 6.2 for the bis-pyridinium aldehyde **10** and the hydrated form **11**, respectively, and the presence or absence of the CHO resonance at δ 10.3 in the proton nmr spectrum. If the crude product was dissolved in a methanol- ethyl acetate mixture, followed by evaporation of the solvent, the dihydrate **11** was the major product. On standing, the initially obtained product, which was predominantly **10**, was transformed into a mixture of bis-aldehyde **10** (60%) and the hydrated form **11** (40%, nmr analysis of the singlets at δ 6.6 and 6.2, respectively).

It is of interest to note that treatment of the dialdehyde **10** and dihydrate **11** mixture with 48% HBr led to the bromomethyl analogue of the mono cyclized product **12**, the apparent product of displacement of formally pyridine 2-carboxaldehyde by the bromide anion in the initial cyclization product.



On the other hand, the product which was obtained upon heating the mixture of **10** and **11** in PPA could be isolated as a bis-tribromide salt. This salt on standing lost Br_2, and afforded **1**. This product was identical in all aspects to the product obtained following the original procedure [1] previously described for cyclization of the bis-acetal **1**.

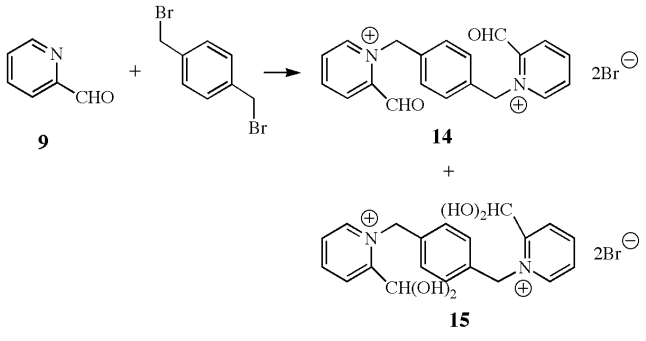
Attempts to prepare **13** (or the corresponding dihydrate) by treatment of pyridine 2-carboxaldehyde (**9**) with α,α'-dibromo-*m*-xylene (7.2:1 molar equivalents) in DMF led to a small amount of an orange solid, which readily turned



to a dark intractable gum in air. No identifiable products could be isolated from this reaction although the crude proton nmr indicated some of the desired product.

The synthesis of **5** was performed following the literature procedure [1] and **5** was cyclized in 48% HBr (PPA was used in literature) to afford **2**. The structural assignment for **2** can be established by ^{1}H nmr since fourteen proton resonances are exhibited in its spectrum. Structure **7** is excluded on this basis alone since because of symmetry only seven (two H each) proton resonances should be observed. In the ^{13}C nmr spectrum of **2** only eighteen carbons were detected (two missing). Structure **7** would exhibit ten carbon resonances.

Treatment of pyridine 2-carboxaldehyde (**9**) with α,α'-dibromo-*p*-xylene in DMF led to **14** along with dihydrate **15**. As in the case of **10**, **14** readily undergoes hydration and this product dominated when workup was performed under humid conditions. Of particular diagnostic value are the proton resonances at δ 6.3 and 6.0 for the methylene bridges in **14** and **15**, respectively. If the dialdehyde stands in air, it undergoes a facile hydration to form the stable dihydrate. The dialdehyde or mixture readily cyclized on treatment with 48% HBr to afford **3** (68%).



The bis-pyridinium salt **6** was prepared from the acetal as described previously and cyclized to afford **3**. The exclusion of structure **8** based on ^{1}H or ^{13}C nmr analysis is

quite difficult since both **3** and **8** would exhibit seven distinct protons and ten distinct carbons.

This sample readily crystallized from water.An X-ray analysis indicated the correct formulation of the double cyclodehydration of **6** as **3** [5]. The ORTEP view of **3,** which is planar, is shown in Figure 1.

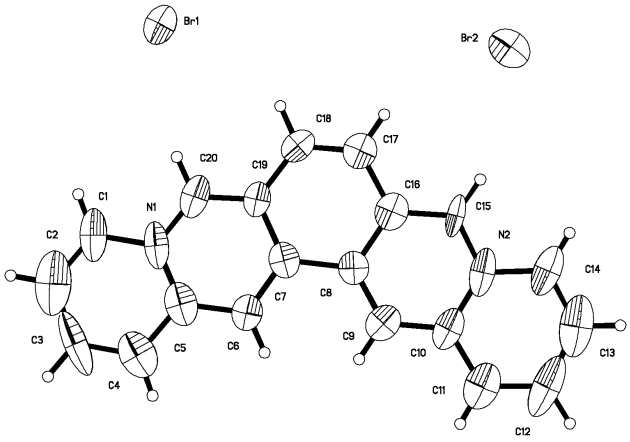


Figure 1. ORTEP view of **3**.

The structural assignments previously proposed for **1**,**2** and **3** have been verified. The pyridinium salts (and hydrates) obtained from pyridine 2-carboxaldehyde and *o*- and *p*-α,α'-dibromoxylene have been isolated and characterized. These compounds readily undergo double cyclodehydration under acidic conditions and workup to afford **1** and **3**, respectively.

EXPERIMENTAL

The pyridine 2-carboxaldehyde and the α,α'-dibromo-*o*-, *m*- and *p*-xylenes were purchased from Acros. Melting points were taken on a Fisher-Johns apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker ARX-500 pulsed spectrometer with tetramethylsilane as an internal standard.

12a,14a-Diazoniapentaphene Bromide (**1**).

Method A.

The bis-pyridinium bromides **10** and **11** (478 mg, 0.93 mmol) were dissolved in polyphosphoric acid (3.5 mL) at 100 °C over a period of 2 hours. The solution was stirred at 150 °C for 16 hours and then was cooled to room temperature. Water (9 mL) was added and the mixture was refluxed for 2 hours. To the cooled solution HBr/Br_2 (3:1) was added to precipitate the tribromide salt, which was collected by filtration to afford a yellow powder. This product on standing at room temperature for 1 day to remove Br_2 yielded **1** (146 mg, 35%) as a yellow powder: mp > 300 °C; lit. [1] >400 °C (dec 300 °C).

^{1}H NMR (DMSO-d_6): δ 11.47 (s, 2H), 9.46 (d, J = 6.7Hz, 2H), 9.27 (s, 2H), 8.81 (d, J = 8.5 Hz, 2H), 8.50 (t, J = 7.8 Hz, 2H), 8.40 (s, 2H), 8.31 (t, J = 7.1 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 142.11, 137.40, 137.33, 137.07, 135.34, 132.96, 128.32, 126.66, 125.30, 123.08.

Method B.

The conversion of **4** to **1** (33%) was performed following the literature procedure [1]. The sample was identical in its ^{1}H nmr and ^{13}C nmr spectra to the product that was obtained in method A from **10** and **11**.

4a,12a-Diazoniapentaphene Bromide (**2**).

The 1,3-Bis(1-methylene-2-[1,3-dioxolan-2-yl]pyridinium bromide)-benzene (**5**, 250 mg, 0.39 mmol) in concd HBr (1 mL) was refluxed 16 hours and then the cooled solution was poured into THF (10 mL). The product was collected by filtration and dried under vacuum to afford **2** (98 mg, 48%) as a yellow powder; mp above 300 °C; lit. [1] >400 °C. ^{1}H-NMR (DMSO-d_6): δ 11.72 (s, 1H), 10.47 (s, 1H), 10.41 (s, 1H), 9.61-9.59 (m, 2H), 9.25 (s, 1H), 8.79 (d, J = 8.4 Hz, 1H), 8.72 (d, J = 8.3 Hz, 1H), 8.55-8.47 (m, 2H), 8.39 (d, J = 9.1 Hz, 1H), 8.29-8.26 (m, 3H). ^{13}C-NMR (DMSO-d_6): δ 142.58, 141.32, 138.24, 138.11, 137.62, 137.23, 136.89, 133.96, 131.84, 130.27, 128.79, 128.26, 127.28, 126.30, 125.75, 125.15, 123.19, 123.10.

4a,8a-Diazoniapentaphene (**3**).

Method A.

A solution of the bis quaternary salts (**14** and **15**, 200 mg, 0.42 mmol) in 48% aqueous HBr (2 mL) were refluxed for 16 hours. To the cooled solution was added THF (20 mL). The product **3** was collected by filtration as a yellow powder (184 mg, 68 %): mp: above 300 °C: lit. [1] >400°C. ^{1}H-NMR (DMSO-d_6): δ 10.28 (s, 2H), 10.27 (s, 2H), 9.56 (d, J = 6.7 Hz, 2H), 8.78 (d, J = 8.5 Hz, 2H), 8.54 (t, J = 7.7 Hz, 2H), 8.32 (dd, J = 7.0 Hz, 1.3 Hz, 2H), 8.26 (s, 2H). ^{13}C-NMR (DMSO-d_6): δ 140.16, 137.53, 136.44, 136.24, 132.27, 127.86, 127.78, 126.32, 124.94, 123.91.

Method B.

Cyclization of **6** following the literature procedure led to **3** (84%) [1] which was identical in its nmr spectra to the sample obtained by method A.

1,2-Bis(1-methylene-2-[1,3-dioxolan-2-yl]pyridinium bromide) benzene (**4**).

This compound was prepared *via* the literature procedure in 78% yield [1]. ^{1}H NMR (DMSO-d_6): δ 8.94 (d, J = 6.2 Hz, 2H), 8.02 (t, J = 7.8 Hz, 2H), 8.39 (d, J = 7.0 Hz, 2H), 8.26 (t, J = 6.8 Hz, 2H), 7.43 (m, 2H), 6.82 (m, 2H), 6.48 (s, 2H), 6.15 (s, 4H), 4.38 (s, 8H). ^{13}C NMR (DMSO-d_6): δ 153.26, 148.72, 147.85, 131.89, 131.26, 129.75, 129.21, 127.55, 98.20, 66.73, 58.77.

1,3-Bis(1-methylene-2-[1,3-dioxolan-2-yl]pyridinium Bromide (**5**).

The 2-(1,3-dioxolan-2-yl)pyridine (0.62 g, 0.0041 mmol) and α,α'-dibromo-*m*-xylene (0.41 g, 0.0015 mmol) [2.7 molar equivalents] were placed in DMF (0.5 mL). The solution was stirred at 30 °C for 20 h and then kept without stirring for 96 h at rt. After this period a rock-like colorless solid coated the bottom of the flask. The solid was collected by filtration and washed with ether. This material was recrystallized from MeOH-EtOAc (soluble in MeOH, insoluble in EtOAc) to afford gorgeous white

rhombic crystals (0.55 g, 89%); mp 160-165 °C: lit. [1] 95.5-97 °C.^{1}H-NMR (DMSO-d_6): δ 9.08 (d, J=5.8, 2H), 8.74 (t, J= 7.7, 2H), 8.32 (d, J = 8.0 Hz, 2H), 8.26-8.19 (m, 2H), 7.51 (t, J = 7.4 Hz,1H), 7.38 (dd, J = 7.6, 1.3 Hz, 2H), 7.27 (s, 1H), 6.45 (s, 2H), 6.01 (s, 4H), 4.09 (s, 8H). ^{13}C-NMR (DMSO-d_6): δ 152.00, 147.30, 147.23, 134.50, 129.78, 128.61, 128.54, 127.86, 126.06, 96.98, 65.57, 59.51.

1,4-Bis(1-methylene-2-[1,3-dioxolan-2-yl]pyridinium Bromide (**6**).

This compound was prepared using the literature procedure in a 74% yield [1]. ^{1}H NMR (DMSO-d_6): δ 9.06 (d, J = 6.2 Hz, 2H), 8.73 (t, J = 7.9 Hz, 2H), 8.32 (d, J = 7.9 Hz, 2H), 8.22 (t, J = 7.5 Hz, 2H), 7.39 (s, 4H), 6.46 (s, 2H), 6.02 (s, 8H). ^{13}C NMR (DMSO-d_6 + D_2O): δ 153.14, 148.44, 148.00, 135.20, 129.89, 129.66, 127.49, 98.14, 66.85, 61.03.

1,2-Bis(1-methylene-2-[carboxaldehyde]pyridinium bromide)-benzene **10** and Dihydrate **11**.

Pyridine-2-carboxaldehyde (1.41 g, 0.013 mole) and α,α'-dibromo-*o*-xylene (0.49 g, 0.0018 mole) were dissolved in DMF (3 mL). The solution was placed in an oil bath pre-heated to 48 °C. After 18 h a yellow solid appeared and the mixture was heated for a period of 48 h. The mixture was removed from the bath and the solid (0.54 g, 78%), was collected by filtration and washed with ether. A trace of DMF and about 10% hydrate was detectable in the nmr spectrum. ^{1}H NMR (DMSO-d_6): δ 10.29 (s, 2H), 9.12 (d, J = 6.0 Hz, 2H), 9.01-8.95 (m, 2H), 8.77-8.72 (m, 2H), 8.50-8.44 (m, 2H), 7.46-7.40 (m, 2H), 6.95-6.91 (m, 2H), 6.54 (s, 4H). ^{1}H NMR (DMSO-d_6 + D_2O): δ 8.95 (d, J = 5.7 Hz, 2H), 8.78 (t, J = 7.6 Hz, 2H), 8.45 (d, J = 7.5 Hz, 2H), 8.13 (t, J = 6.9 Hz, 2H), 7.41-7.36 (m, 4H), 6.69-6.66 (m, 4H), 6.25 (s, 4H), 6.20 (s, 2H) (trace C**H**O resonance at _ 10.33). ^{13}C NMR (DMSO-d_6 + D_2O): δ 157.14, 147.47, 146.36, 132.33, 129.43, 127.73, 127.20, 126.16, 85.40, 56.88.

7-Bromomethylacridizinium Bromide (**12**).

A solution of bis-quaternary salts **10** and **11** (460 mg, 0.75 mmol) in 48% aqueous HBr (1.1 mL) was refluxed for 16 hours. The cooled solution was poured into THF (20 mL) on which a brown oily material formed. On trituration, a yellow powder formed along with a brown paste. The yellow powder was collected by filtration (71 mg, 48%); mp 230 °C (darkens) still solid > 300 °C. ^{1}H-NMR (DMSO-d_6): δ 10.68 (s, 1H), 9.48 (d, J = 6.9 Hz, 1H), 9.32 (s, 1H), 8.6 (d, J = 8.9 Hz, 1H), 8.38 (d, J = 8.6 Hz, 1H), 8.19-8.12 (m, 2H), 8.10-8.02 (m, 2H), 5.41 (s, 2H). ^{13}C-NMR (DMSO-d_6): δ 137.75, 137.19, 135.93, 135.61, 132.47, 131.81, 128.18, 125.71, 123.81, 122.95, 29.75.

Anal. Calcd. for $C_{14}H_{11}Br_2N$: C, 47.63; H, 3.14; N, 3.97. Found: C, 47.40; H, 2.98; N, 3.80.

1,4-Bis(1-methylene-2-[carboxaldehyde]pyridinium bromide)-benzene **14** and Dihydrate **15**.

Pyridine-2-carboxaldehyde (1.37 g, 0.012 mol) and α,α'-dibromo-*p*-xylene (0.53 g, 0.002 mol) were dissolved in DMF (3 mL). The solution was placed in an oil bath at 42 °C and a yellow solid was visible after 17 hours at this temperature. The mixture was heated for a total of 64 hours. The solid was collected by filtration and washed with ether to afford a pale yellow solid (0.37 g, 50%) which in the nmr showed trace amounts of the solvent DMF and an absorption peak at δ 5.4 indicative of protons of a–CH_2Br moiety (half-reacted analogue): ^{1}H-NMR (DMSO-d_6): δ 10.30 (s, 2H), 9.28 (t, J=6.0, 2H), 8.90 (t, J=7.9, 2H), 8.65-8.60 (m, 2H), 8.46-8.39 (m, 2H), 7.42 (s, 4H), 6.30 (s, 4H). ^{1}H-NMR (DMSO-d_6 + D_2O): δ 8.89 (d, J = 6.1 Hz, 2H), 8.65 (t, J = 7.8 Hz, 2H), 8.34 (d, J = 7.6 Hz, 2H), 8.06 (t, J = 6.7 Hz, 2H), 7.32 (s, 4H), 6.17 (s, 2H), 6.00 (s, 4H). ^{13}C NMR (DMSO-d_6 + D_2O): δ 156.84, 147.46, 146.86, 135.08, 128.93, 128.02, 126.37, 85.57, 59.40.

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[5] Crystallographic data will be presented in an appropriate Journal.