Pyridine-Derived Tetrapodal Ligands with NO_4 and NN_4 Donor Sets

Stefan Schmidt[a], Laurent Omnès[†,a], Frank W. Heinemann[‡,a], Jörg Kuhnigk[‡,b], Carl Krüger[‡,b], Andreas Grohmann[*,a]

[a] Institut für Anorganische Chemie, Universität Erlangen-Nürnberg, Egerlandstraße 1, D-91058 Erlangen, Germany

[b] Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim an der Ruhr, Germany

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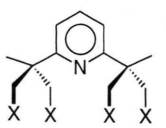
The Mg^{2+} assisted synthesis of a pyridine-derived tetraalcohol ligand with an NO_4 donor set is described. 2,6-Diethylpyridine reacts cleanly with aqueous formaldehyde solution in the presence of 1 equivalent of $MgSO_4$ hydrate in a pressurised vessel to give the quadruply hydroxymethylated product 2,6-$C_5H_3N[CMe(CH_2OH)_2]_2$ (**1**) as a crystalline solid. Two alkali/alkaline earth metal perchlorate adducts of **1** have been structurally characterised, *viz.* [(**1**)$_2$ • $LiClO_4$] (**6**) and [(**1**)$_2$ • $Ba(ClO_4)_2$] (**7**). The ligand adopts a bridging coordination mode in both **6** (distorted tetrahedral coordination of Li^+) and **7** (square prismatic coordination of Ba^{2+}). The further derivatization of **1** leads to the tetratosylate (**2**) and the tetraazide (**3**), both of which have been obtained in pure form for the first time. Reduction of **3** gives the pentaamine ligand 2,6-$C_5H_3N[CMe(CH_2NH_2)_2]_2$ (**4**), isolated as the tetrakis(hydrobromide) salt **4** • 4 HBr. The presence of four ammonio substituents and an unprotonated pyridine nitrogen atom in the solid state has been unequivocally established by an X-ray structural analysis.

Introduction

With a view to creating a concave ligand environment for octahedrally coordinating transition metal ions, we recently introduced a tetrapodal pentadentate ligand with an NN_4 donor set (**4**) and presented crystal structures of a series of cobalt(III) and nickel(II) complexes in which the ligand provides a square pyramidal coordination cap [1]. This ligand represents a novel structural motif in coordination chemistry in that one central donor atom is surrounded by *four* equivalent pendent donor groups, the former being set up to occupy the apical position of a coordination octahedron, while the latter take the equatorial positions [2]. A different type of square-pyramidally coordinating pentadentate ligand of C_2 symmetry involves a 'superstructured' porphyrin derivative of considerable architectural complexity [3, 4].



X = OH: **1**
X = OTos: **2**
X = N_3: **3**
X = NH_2: **4**

The synthesis of **4** ('$N(NH_2)_4$') requires the fourfold functionalization of 2,6-diethylpyridine and proceeds in four stages. The initial step exploits the known reactivity of *ortho* alkylpyridines towards formaldehyde to furnish a tetraalcohol precursor ('$N(OH)_4$', **1**) which is then transformed into the pentaamine ligand by fourfold tosylation ('$N(OTos)_4$', **2**), tosylate-azide exchange ('$N(N_3)_4$', **3**), and reduction [1a]. Problems inherent in a polyfunctionalization of this kind are associated chiefly with the yields of the individual steps and the purity of the intermediates. While polytosylates [5, 6] and polyazides [7, 8] may be prepared in satisfactory yields from polyalcohols by literature methods, exhaustive hydroxymethylations of *ortho* alkylpyridines using formaldehyde (*cf.* step 1 above) generally give low yields and mixtures of products [9 - 12]. Our elaboration of the above reaction sequence therefore concentrated on the first step, in addition to preparing pure samples of every intermediate. We now report an improved

* Reprint requests to Dr. A. Grohmann; E-mail: grohmann@anorganik.chemie.uni-erlangen.de;
† Visiting from Université de Rennes, Chimie, Campus de Beaulieu, 35042 Rennes Cedex, France;
‡ X-ray structure analysis.

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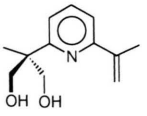
synthesis of the tetraalcohol **1**, the crystal structures of its lithium and barium perchlorate adducts, and structural details of the methanol solvate of the pentaamine tetrakis(hydrobromide), **4** • 4 HBr • CH_3OH.

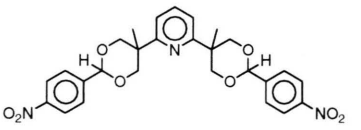
Results and Discussion

The α hydrogen atoms of 2-alkyl and/or 4-alkyl substituents on a pyridine ring are sufficiently acidic to allow replacement with hydroxymethyl groups through the action of formaldehyde under appropriate conditions [13, 14]. The tetraalcohol '$N(OH)_4$' **1** may thus be prepared from 2,6-diethylpyridine in a pressurised vessel at 135 °C. The reaction is essentially a Knoevenagel reaction where aldehydes or ketones R-C(=O)-R' (R' = H, alkyl) are treated with compounds of the form Z-CH_2-Z' to give compounds of the type R-C(OH)R'-CHZZ' (R' = H, alkyl). These may subsequently eliminate water with concomitant formation of a double bond [15]. In our case, elimination of water from partially hydroxymethylated intermediates constitutes a decomposition reaction which competes with product formation, leading to undesired side products such as **1a** [10b], which may be one of the species giving rise to olefinic resonances in the ^{1}H NMR spectra of crude **1**. The reaction is complicated further by the fact that conversion is incomplete under standard conditions, giving a mixture of products with varying degrees of hydroxymethylation in the side chains [12]. We therefore set out to optimise the synthesis of the tetraalcohol **1**.



1a

Polyalcohols such as **1** cannot be distilled without decomposition owing to their high boiling points but may be purified by chromatographic methods [16, 17] usually giving highly viscous liquids or syrups [18]. In order to obtain a derivative of **1** which would enable purification by recrystallization, we prepared the bis(acetal) **5** from crude **1** and two equivalents of 4-nitrobenzaldehyde with azeotropic removal of water [19, 20]. Contrary to our expectations, the material thus obtained was itself an oil (due to the presence of impurities) and could not be induced to crystallise. Purification and isolation of a crystalline solid were achieved by HPLC (*cf.* Experimental) but did not appear to be practical for larger quantities of material.



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In view of the extensive coordination chemistry of carbohydrates [21 - 23] and other polyalcohols with alkali and alkaline earth cations [24], complex formation of **1** with suitable metal salts suggested itself as an alternative means of purification. A series of experiments employing salts such as $LiClO_4$, Na_2SO_4, $NaNO_3$, CH_3COOK, $MgSO_4$, $Mg(ClO_4)_2$, $Ca(NO_3)_2$, $Ba(ClO_4)_2$ or $Ba(SCN)_2$ were unsuccessful, giving resinous materials throughout [25 - 27]. However, solutions of crude **1** in $CHCl_3$ which had been treated with Na_2SO_4 showed better resolved signals in their ^{1}H NMR spectra. This observation suggested a certain degree of complex formation and led us to explore the possibility of using metal ions to preorganise the reactants in the preparation of the tetraalcohol **1**. In addition to a possible template effect, we expected the presence of a metal cation of suitable charge/radius ratio to increase the electrophilic character of the aldehyde component through complexation. At the same time, the anion was to be unreactive under the given conditions. For these reasons, we chose $MgSO_4$ as the metal salt and ran a series of hydroxymethylation reactions in the presence of varying amounts of this material. Optimal results were obtained with a 1 : 1 ratio of 2,6-diethylpyridine and $MgSO_4$: The reaction gave virtually pure tetraalcohol **1**, and yields were comparable to those of previous reactions without added metal salt where the reaction time had been more than twice as long, at the expense of introducing considerable amounts of impurities. Whether or not the reaction between 2,6-diethylpyridine and 4 equivalents of formaldehyde in the presence of 1 equivalent of $MgSO_4$ in fact proceeds through an intermediate where the magnesium cation coordinates to the pyridine nitrogen atom and helps to direct the incoming aldehyde moieties must remain an open question at this stage. It should be noted, however, that such action of an alkaline earth cation in the formation of polyalcohols would not be

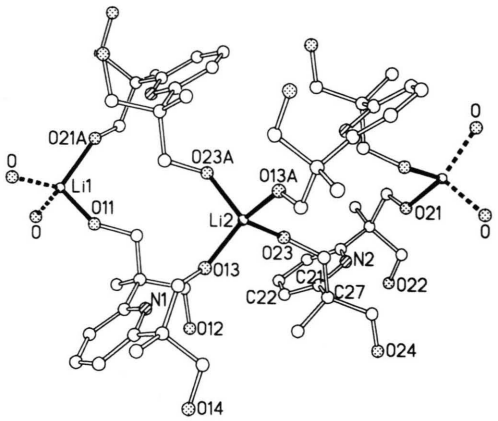

Fig. 1. Partial view of the solid state structure of the pyridine tetraalcohol/lithium perchlorate adduct **6**. For clarity, a ball-and-stick representation is shown where hydrogen atoms are omitted.

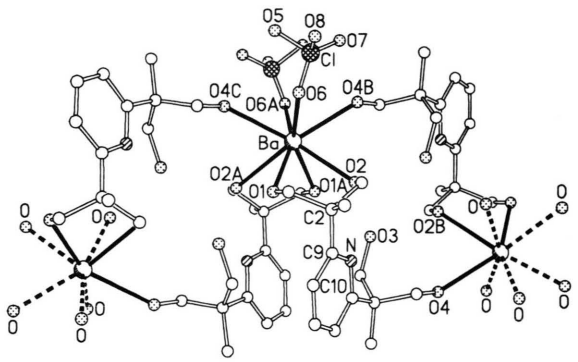

Fig. 2. Partial view of the solid state structure of the pyridine tetraalcohol/barium perchlorate adduct **7**. For clarity, a ball-and-stick representation is shown where hydrogen atoms are omitted.

entirely unprecedented, an example being the base-catalysed condensation of formaldehyde in the presence of $Ca(OH)_2$ (the "formose reaction") where the coordination of intermediates to the calcium ion appears to be essential [28].

The specificity with which the tetraalcohol **1** is produced in the presence of $MgSO_4$ allows its subsequent isolation in a pure form. After aqueous work-up, a methylene chloride solution of **1** was treated with 4 Å molecular sieves to remove water, leading to the formation of a white crystalline precipitate which was identified as the hemihydrate **1** • 0.5 H_2O by elemental analysis. The ^1H NMR spectrum shows excellent resolution of signals including a three-line pattern for the hydroxyl protons.

The availability of pure **1** led us to reinvestigate its complex formation with a variety of alkali and alkaline earth metal salts, such as $LiClO_4$ • 3 H_2O, Na_2SO_4, $Mg(ClO_4)_2$ • 6 H_2O, $Ca(NO_3)_2$ • 4 H_2O, $Ba(SCN)_2$ • 3 H_2O, and $Ba(ClO_4)_2$; $ZnBr_2$ and $NiCl_2$ • 6 H_2O were also tested. Solid state structures have so far been determined for [(**1**)$_2$ • $LiClO_4$] (**6**) and [(**1**)$_2$ • $Ba(ClO_4)_2$] (**7**). In the case of **6** (Fig. 1), the lithium ions are coordinated in a distorted tetrahedral fashion by four hydroxyl groups, each belonging to a different tetraalcohol molecule (Li-O: 1.88(1) - 2.02(2) Å). In each tetraalcohol molecule, one hydroxyl group of each 1,3-diol functionality is coordinated to a lithium ion while the other hydroxyl group remains uncoordinated, as does the pyridine nitrogen atom; hydrogen bonds are not formed. Consequently, **1** does not act as a podand in this structure [29]; rather, the lithium ion asserts its strong preference for tetrahedral coordination, and the overall bonding situation is reminiscent of the lithium iodide methanol solvate $[Li(CH_3OH)_4]^+I^-$ (Li-O: 1.919(5) Å) [30].

Complexes of barium (M) with aminoalcohols (L) have been isolated both as 1 : 1 and as 1 : 2 (M : L) species [18, 26]. In the X-ray structure of the 1 : 2 complex **7**, the tetraalcohol **1** again acts as a bridging ligand (albeit with partial chelation) rather than a podand (Fig. 2). The coordination geometry of the barium cation is square prismatic (coordination number 8). One of the faces of the prism is formed by the hydroxyl oxygen atoms of two chelating 1,3-diol units of two different tetraalcohol molecules (O1, O2, O1A, O2A). The opposite face is made up of two diagonally disposed hydroxyl oxygen atoms of two further tetraalcohol molecules (O4B, O4C) and two oxygen atoms of two terminally coordinated perchlorate anions (O6, O6A). Each tetraalcohol molecule chelates one barium ion through one of its 1,3-diol units (O1, O2) and coordinates to a second barium ion through one hydroxyl group of its other 1,3-diol unit (O4), which also forms a hydrogen bond to one of the non-coordinated perchlorate oxygen atoms (O7B; O4···O7B = 2.83(1) Å; O4···O7B corresponds to O4B···O7). The second hydroxyl group (O3) remains uncoordinated but forms a bifurcated hydrogen bond, recipients being a barium-coordinated hydroxyl oxygen atom within the same tetraalcohol molecule (O2) and one of the hydroxyl oxygen atoms of the chelating 1,3-diol functionality

of another tetraalcohol molecule (O2B; O2···O3 = 2.929(4) Å; O2B···O3 = 2.896(4) Å). The pyridine nitrogen atom is uncoordinated. The barium ions and tetraalcohol molecules form rings of the type M_2L_2, which are linked into infinite arrays at the barium centers. The Ba-OH distances (2.654(3) - 2.823(3) Å) fall within the range observed for other alcohol complexes of barium perchlorate [26, 31], while the comparatively short distance Ba-$OClO_3$ (2.790(5) Å) indicates stronger binding of the perchlorate anions in **7** than, e.g., in the barium perchlorate complex of triethanolamine (2.941(3) Å and 2.989(3) Å) [26]. The ^{1}H NMR spectra of **7** show no complexation-induced shifts suggesting weak coordination (if any) of the tetraalcohol ligand to the barium ion in solution. Pending an X-ray structural study, however, podand-like coordination of **1** cannot be ruled out for smaller alkaline earth cations such as magnesium.

The further derivatization of **1** requires the introduction of tosyl groups to allow nucleophilic displacement in a subsequent step. The preparation of the tetratosylate 'N(OTos)$_4$' **2** from **1** and 4 equivalents of toluene-4-sulfonyl chloride in pyridine gives good yields provided that the reaction is carried out at sufficiently low temperatures (- 5 to 0 °C). Higher temperatures have been found to lead to reduced yields in related reactions, and it has been suggested that this is due to the formation of quaternary pyridinium tosylates [5]. If pure tetraalcohol **1** is used in the synthesis, the resulting tetratosylate **2** is of high purity, whereas employment of crude **1** introduces considerable impurities into the product which persist during work-up. Recrystallization from ethanol is feasible but works well only with small quantities of impure **2**, as larger amounts tend to lead to the separation of syrupy phases. Since we were interested in the spatial orientation of the 1,3-difunctionalised sidearms of the molecule, we undertook an X-ray structural study of the tetratosylate. Single crystals were obtained from a mixture of ethanol, diethyl ether, methylene chloride, and water (40 : 40 : 15 : 5), but were found to be of moderate quality and to diffract poorly. While the obtained data set did allow the solution of the structure, refinement could not be achieved beyond values of $R1 \approx 0.10$ and $wR2 \approx 0.30$ which are unacceptably high. The preliminary data show the molecule to have C_2 symmetry in the solid state, with the pyridine nitrogen atom and the carbon atom in the 4-position of the pyridine ring lying on the two-fold rotation axis. In each 1,3-ditosylate sidearm the tosyl groups point away from each other in order to minimise steric congestion. Two tosylate phenyl rings on diagonally opposite oxygen atoms (with respect to the NO_4 set of heteroatoms) approach the pyridine ring in face-to-face fashion from either side, which suggests the presence of weak intramolecular π-π stacking interactions.

Nucleophilic displacement of the tosyl groups in **2** by azide ion leads to the tetraazide 'N(N$_3$)$_4$' **3** which may be obtained as a pure material (by ^{1}H NMR) when starting from pure tetratosylate **2**. Subsequent reduction of **3** with triphenylphosphine and aqueous workup gives the pentaamine ligand **4** which is conveniently isolated as the hydrochloride salt [1]. The use of pure tetraazide **3** gives virtually pure reduction product **4**. The tetrakis(hydrochloride) adduct **4** • 4 HCl is obtained by treatment of an ethanolic solution of **4** with concentrated aqueous HCl, while prolonged reaction with HCl leads to the formation of the pentakis(hydrochloride) salt **4** • 5 HCl. In both cases, the chloride equivalents were determined by rhodanometric titration. This fractional precipitation is reminiscent of tris(2-aminoethyl)amine (tren) where the hydrochloride salts tren • 3 HCl and tren • 4 HCl are also separately accessible [32, 33]. In both tren and the pentaamine ligand **4**, the central nitrogen atom is expected to be less basic in aqueous solution than the primary amino functionalities, due to the inability of a tertiary amine to disperse charge to the solvent by hydrogen bonding [34]. In the case of **4** • 4 HCl, the pyridine nitrogen atom should therefore remain unprotonated. While no suitable single crystals could be obtained of this adduct, an X-ray structural analysis of the tetrakis(hydrobromide) salt methanol solvate **4** • 4 HBr • CH_3OH supports this conclusion.

The structure contains $[2,6\text{-}C_5H_3N\{CMe(CH_2NH_3)_2\}_2]^{4+}$ cations, four Br^- counterions, and one molecule of methanol per formula unit as lattice solvent. The cation (Fig. 3) has no crystallographically imposed symmetry. Its conformation with respect to the orientation of the ammonio substituents, while irregular, minimises the electrostatic repulsion between these groups [35]. While the pyridine ring is largely undistorted, the angles subtended by the *ortho* substituents at C11 and C15 deviate more markedly from the ideal

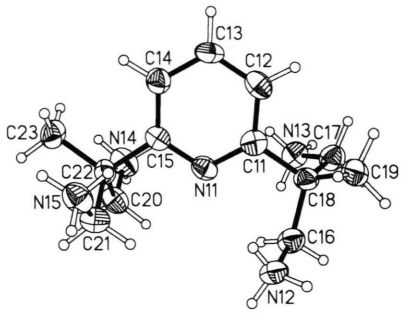

Fig. 3. Molecular structure of the cation $[2,6\text{-}C_5H_3N\{CMe(CH_2NH_3)_2\}_2]^{4+}$ in the tetrakis(hydrobromide) salt **4** • 4 HBr • CH_3OH (thermal ellipsoids at the 50 % probability level). See text for the treatment of the hydrogen atoms.

value of 120°, resulting in a slight displacement of the 1,3-diammonio-2-methyl-prop-2-yl groups towards the pyridine nitrogen atom. The sidearms show the usual conformation of a paraffinic chain with unexceptional bond distances (d(C-N) =1.49 - 1.51 Å; d(C-C) = 1.52 - 1.56 Å) and angles (105.4 - 114.3°) [36 - 38]. All hydrogen atoms were identified as residual electron density in the correct tetrahedral disposition around the carbon and, in particular, the primary amino nitrogen atoms. In order to prevent unreasonably short C-H and N-H distances, however, the H atoms were allowed for as riding atoms in geometrically optimised positions. No electron density maximum in a reasonable position could be located at the pyridine nitrogen atom (*cf.* Experimental). These findings, together with the number of counterions, provide clear evidence for the aromatic nitrogen atom to be unprotonated. Further, the structure is characterised by a complex network of hydrogen-bonded N···Br contacts (3.30 - 3.37 Å; sum of the van der Waals radii for N and Br: 3.40 Å [39]) emanating from the ammonio but not from the pyridine nitrogen atoms. The methanol molecule also participates in hydrogen bonding to the ammonio groups and the bromide counterions. From the present structure determination of **4** • 4 HBr it is obvious that the amino-substituted sidearms of the pentaamine **4** are reoriented considerably upon coordination to a single metal ion [1].

The synthetic procedure described above thus allows the preparation of uncontaminated pentaamine ligand **4**, and the synthesis of multifunctional ligands on the basis of **4** is currently in progress.

Experimental Section

CAUTION! Although no problems were encountered in this work, organic polyazides are potentially explosive and should be handled with due precautions.

Materials and instrumentation.

All manipulations were performed under dry dinitrogen using standard Schlenk techniques unless indicated otherwise. Solvents were dried and distilled before use. Reagents were AR grade or better and were purchased from Merck, Fluka, and Aldrich. HPLC was carried out using a Knauer instrument (HPLC pump 64; UV/VIS filter photometer, λ = 254 nm; column: Nucleosil 120 C18, 250 × 32 mm, 5 μm). NMR and IR spectra were recorded on JEOL JNM-EX 270, JEOL JNM-LA 400, and Perkin Elmer 16PC FT-IR instruments, respectively. Mass spectra were obtained on a JEOL MSTATION 700 spectrometer. Elemental analysis was carried out using a Carlo Erba Elemental Analyzer 1106.

*2,6-$C_5H_3N\{CMe(CH_2OH)_2\}_2$ (**1**)*

The preparation was carried out largely in air. An autoclave was charged with 2,6-diethylpyridine (34 g, 0.25 mol), $MgSO_4$ hydrate (42.3 g, 0.25 mol), and aqueous formaldehyde solution (37 %, 203 ml, 2.7 mol), and the mixture heated to 135 °C for 20 h. After cooling to room temperature, the yellow solution was decanted from solid $MgSO_4$ and filtered. Volatiles were removed in an oil pump vacuum (12 h, 100 °C) and the remaining yellow syrup taken up in chloroform (300 ml). Residual $MgSO_4$ was removed by filtration, and the filtrate extracted with water (4 × 200 ml). The aqueous extract was taken to dryness on a rotary evaporator, the residue dissolved in methylene chloride (150 ml), the solution dried briefly over Na_2SO_4, filtered, and stirred with molecular sieves (4 Å, residue/mol. sieves ≈ 1 : 1 v/v) under nitrogen. After *ca.* 30 min, the solution began to precipitate copious amounts of a white solid. Stirring was continued for 12 h, after which time the suspension was decanted onto a glass frit (porosity G4). The solid was collected, washed with a small amount of cold methylene chloride, and dried *in vacuo* to give **1** as a white, crystalline, very hygroscopic material (5.5 g). Evaporation of the filtrate gave more **1** as a yellow syrup containing minor impurities (by ^{1}H NMR; 22.8 g; combined yield: 28.3 g, 44 %).

$C_{13}H_{22}NO_{4.5}$ (**1** • 0.5 H_2O)
Calcd C 59.07 H 8.39 N 5.30 %,
Found C 58.67 H 8.34 N 5.22 %.

ν_{max}/cm^{-1} 3348 s, 2944s, 2875s, 1588s, 1577s, 1456s, 1018s, 814m, 752m (KBr). δ_H (DMSO-d_6) 7.63 (AB_2 spin system, 3 lines, 1 H, H^4), 7.21 (AB_2, 2 lines, 2 H, $H^{3,5}$),

4.66 (3 lines, 4 H, CH_2OH), 3.63 (4 lines, CH_2OH, 8 H), 1.18 (s, CH_3, 6 H). δ_C (DMSO-d_6; all singlets) 163.12 (py-C2/6), 136.47 (py-C4), 119.10 (py-C3/5), 66.53 (-CH_2-), 47.07 (>C<), 19.74 (-CH_3).

*2,6-$C_5H_3N\{CMe(CH_2OTs)_2\}_2$ (**2**)*

This compound was prepared as described previously [1]. Careful adjustment of the temperature during the addition of toluene-4-sulfonyl chloride gave improved yields of up to 68 % [5]. A pure sample of **2** was obtained by recrystallization from ethanol.

$C_{41}H_{45}NO_{12}S_4$
Calcd C 56.47 H 5.20 N 1.61 S 14.71 %,
Found C 56.50 H 5.24 N 1.63 S 14.56 %.

ν_{max}/cm^{-1} 1597m, 1456m, 1359s, 1175s, 818s, 553m (KBr). δ_H (DMSO-d_6) 7.61 (AA'XX', 8 H, $C_6H_2H_2SO_3$), 7.54 (AB_2, 3 lines, 1 H, H^4), 7.40 (AA'XX', 8 H, $C_6H_2H_2CH_3$), 7.10 (AB_2, 2 lines, 2 H, $H^{3,5}$), 4.13 (3 lines, -CH_2-, 8 H), 2.39 (s, $C_6H_4CH_3$, 12 H), 1.07 (s, CH_3, 6 H). δ_C (DMSO-d_6; all singlets) 157.94 (py-C2/6), 145.05 (C1 = *C*-SO_3-CH_2-), 137.76 (py-C4), 131.69 (C4), 130.13 (C3/5), 127.49 (C2/6), 119.50 (py-C3/5), 72.47 (-CH_2-), 44.52 (>C<), 21.09 ($C_6H_4CH_3$), 18.91 (-CH_3).

*2,6-$C_5H_3N\{CMe(CH_2N_3)_2\}_2$ (**3**)*

This compound was prepared as described previously [1]. Starting from pure tetratosylate **2**, the tetraazide could be obtained nearly quantitatively as a light yellow oil which was pure by ^{1}H NMR. ν_{max} /cm^{-1} 2965m, 2102s, 1576m, 1463m, 1263m, 1045m, 813m (KBr). δ_H (DMSO-d_6) 7.77 (AB_2 spin system, 3 lines, 1 H, H^4), 7.35 (AB_2, 2 lines, 2 H, $H^{3,5}$), 3.82 (d, ^2J(HH) = 12.10 Hz, -C*H*H-N_3, 4 H), 3.68 (d, ^2J(HH) = 12.10 Hz, -CH*H*-N_3, 4 H), 1.32 (s, CH_3, 6 H). δ_C (DMSO-d_6; all singlets): δ 160.44 (py-C2/6), 137.60 (py-C4), 119.56 (py-C3/5), 57.37 (-CH_2-), 46.16 (>C<), 20.67 (-CH_3).

*2,6-$C_5H_3N\{CMe(CH_2NH_2)_2\}_2$ (**4**)*

This compound was prepared in pure form from pure tetraazide **3** by reduction with triphenylphosphine in 85 - 90 % yield [1]. **4** was obtained as a light yellow viscous oil which was taken up in ethanol and treated with concentrated HCl to precipitate the tetrakis(hydrochloride) salt **4** • 4 HCl as a light yellow solid in 70 % yield.

$C_{13}H_{29}N_5Cl_4$ • 0.75 H_2O (**4** • 4 HCl • 0.75 H_2O)
Calcd C 38.02 H 7.49 N 17.05 %,
Found C 38.43 H 7.66 N 17.06 %.

Rhodanometric titration gave 4 eq. of chloride. ν_{max}/cm^{-1} 2916s, 1590m, 1510m, 1456m (KBr). The material was pure by ^{1}H NMR. δ_H (DMSO-d_6) 8.19 (s(br), 12 H, NH_3^+), 7.87 (AB_2 spin system, 3 lines, 1 H, H^4), 7.50 (AB_2, 2 lines, 2 H, $H^{3,5}$), 3.59 (d(br), ^2J(HH) = 8.1 Hz, -C*H*H-NH_2, 4 H), 3.09 (d(br), ^2J(HH) = 8.1 Hz, -CH*H*-NH_2, 4 H), 1.56 (s, CH_3, 6 H). An attempt to grow single crystals from methanol led to the formation of a 1 : 1 methanol solvate. δ_C (DMSO-d_6; all singlets) 158.04 (py-C2/6), 139.38 (py-C4), 121.84 (py-C3/5), 48.66 (CH_3OH), 45.72 (>C<), 42.89 (-CH_2-), 20.39 (-CH_3). Prolonged action of HCl resulted in the formation of the pentakis(hydrochloride) salt **4** • 5 HCl.

$C_{13}H_{30}N_5Cl_5$ • H_2O (**4** • 5 HCl • H_2O)
Calcd C 34.57 H 7.14 N 15.50 %,
Found C 34.67 H 6.98 N 15.42 %.

Rhodanometric titration gave 5 eq. of chloride. The tetrakis(hydrobromide) salt methanol solvate **4** • 4 HBr • CH_3OH was prepared from **4** by reaction with concentrated aqueous hydrogen bromide and recrystallisation from methanol.

$C_{13}H_{29}N_5Br_4$ • CH_3OH (**4** • 4 HBr • CH_3OH)
Calcd C 27.70 H 5.48 N 11.54 %,
Found C 28.17 H 5.79 N 11.53 %.

Rhodanometric titration gave 4 eq. of bromide. ν_{max}/cm^{-1} 3403m (NH str); 3024s (br); 1631m, 1612s (NH_3^+ asym def); 1585s, 1554m, 1515s, 1489s (C=C or C=N str/NH_3^+ sym def); 1451m (CH_2 scissor); 1102m, 1074m (NH_3^+ rock); 790s, 733m (CH oop def for 2,6-disubstituted pyridine) (KBr disc). NMR data are for material from which methanol was removed by drying *in vacuo*. δ_H (DMSO-d_6) 7.79 (s(br), 12 H, NH_3^+), 7.96 (AB_2 spin system, 3 lines, 1 H, H^4), 7.55 (AB_2, 2 lines, 2 H, $H^{3,5}$), 3.53 (m, -C*H*H-NH_2, 4 H), 3.20 (m, -CH*H*-NH_2, 4 H), 1.56 (s, CH_3, 6 H). δ_C (DMSO-d_6; all singlets) 158.05 (py-C2/6), 139.50 (py-C4), 121.71 (py-C3/5), 45.51 (>C<), 42.61 (-CH_2-), 19.63 (-CH_3).

*2,6-$C_5H_3N\{\overline{CMeCH_2OCH(C_6H_4\text{-}4\text{-}NO_2)OCH_2}\}_2$ (**5**).*

Crude tetraol **1** (5.9 g, $\leq$ 23 mmol), 4-nitrobenzaldehyde (6.9 g, 46 mmol), and 4-toluenesulfonic acid hydrate (10.5 g, 55 mmol) were mixed with benzene (160 ml), and the mixture refluxed for 4 h while water was azeotropically removed with a Dean-Stark trap. While still warm, the resulting two-phase mixture was poured into a solution of K_2CO_3 (15 g, 109 mmol) in water (200 ml) with vigorous stirring. The phases were separated, the organic phase washed with water (2 × 50 ml), and the aqueous phase extracted with chloroform (2 × 40 ml). The combined organic phases were dried over $MgSO_4$, filtered, and taken to dryness to leave a dark brown oil (3 g). Approx. 0.5 g of this material was purified by HPLC (CH_3CN/H_2O = 5 : 1). Five fractions were collected, of

Table I. Crystallographic data for $[2,6\text{-}C_5H_3N\{CMe(CH_2NH_3)_2\}_2](Br)_4 \bullet CH_3OH$ (**4** • 4 HBr • CH_3OH), $[2,6\text{-}C_5H_3N\{CMe(CH_2OH)_2\}_2]_2 \bullet LiClO_4$ (**6**), and $[2,6\text{-}C_5H_3N\{CMe(CH_2OH)_2\}_2]_2 \bullet Ba(ClO_4)_2$ (**7**).

	4 • 4 HBr • CH_3OH	**6**	**7**
Formula	$C_{14}H_{33}Br_4N_5O$	$C_{26}H_{42}ClLiN_2O_{12}$	$C_{26}H_{42}BaCl_2N_2O_{16}$
Formula mass [g mol^{-1}]	607.09	617.01	846.79
Space group	$P2_1/c$ (no. 14)	$P2_12_12$ (no. 18)	$C2/c$ (no. 15)
Crystal system	monoclinic	orthorhombic	monoclinic
a [Å]	10.306(1)	12.715(3)	18.612(2)
b [Å]	14.845(2)	22.168(7)	13.2073(7)
c [Å]	14.389(2)	10.304(4)	14.864(1)
α [°]	90	90	90
β [°]	94.502(9)	90	107.083(7)
γ [°]	90	90	90
V [Å^3]	2194.6(5)	2904(2)	3492.5(5)
Z	4	4	4
T [K]	200(2)	293(2)	293(2)
λ^a [Å]	0.710 73	0.710 73	0.710 69
D_c [g cm^{-3}]	1.837	1.411	1.611
μ [mm^{-1}]	7.348	0.198	1.362
$R1^b$	0.0625	0.0836	0.0447
$wR2^c$	0.1867	0.2507	0.1336
m/n^c	0.0739/14.792	0.1018/0	0.1000/0

[a]MoKα, graphite monochromator; [b]$R1 = \sum||F_o| - |F_c||/\sum|F_o|$ for $F > 4\sigma(F)$; [c]$wR2 = (\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2])^{0.5}$, where $w = 1/[\sigma^2(F_o^2) + (mP)^2 + nP]$ and $P = (F_o^2 + 2F_c^2)/3$ for all data.

which one yielded pure **5** as a faintly yellow crystalline solid (145 mg) upon evaporation of the solvent.

$C_{27}H_{27}N_3O_8$
Calcd C 62.18 H 5.22 N 8.06 %,
Found C 62.43 H 5.37 N 7.83 %.

ν_{max}/cm^{-1} 1612m, 1534s, 1349s, 1115s, 1090s, 1012s, 853m, 751m, 552w. δ_H ($CDCl_3$) 8.12 (AA'XX', 4 H, -C.(CH)$_2$.(C*H*)$_2$.C-NO_2), 7.65 (AB_2, 4 lines, 1 H, H^4), 7.53, (AA'XX', 4 H, -C.(C*H*)$_2$.(CH)$_2$.C-NO_2), 7.50 (AB_2, 2 lines, 2 H, $H^{3,5}$), 5.63 (s, -O-C*H*Ar-O-), 4.73 (d, ^2J(HH) = 11.7 Hz, -C*H*H-), 3.94 (d, ^2J(HH) = 11.7 Hz, -CH*H*-), 1.16 (s, -CH_3). δ_C (CD_2Cl_2; all singlets): δ 162.71 (py-C2/6), 148.47 (C1 = -C-NO_2), 145.35 (C4), 136.75 (py-C4), 127.66 (C3/5), 123.63 (C2/6), 119.67 (py-C3/5), 100.48 (-O-*C*HAr-O-), 75.96 (-CH_2-), 40.55 (>C<), 21.85 (-CH_3). MS (FD): *m/z* (relative intensity) 521 (100), M^+; 1042 (12) $[M_2]^+$.

*$[2,6\text{-}C_5H_3N\{CMe(CH_2OH)_2\}_2]_2 \bullet LiClO_4$ (**6**).*

A solution of pure tetraol **1** (1.25 g, 4.90 mmol) in a mixture of CH_2Cl_2 (30 ml) and THF (4 ml) was added dropwise to a stirred solution of $LiClO_4 \bullet 3\ H_2O$ (0.87 g, 5.42 mmol) in a mixture of CH_2Cl_2 (60 ml) and THF (30 ml). The mixture was stirred at room temperature for 48 h. Ether (50 ml) was added and the mixture kept at - 18 °C for several days. The fine colourless precipitate which had formed was removed by filtration and dried *in vacuo*.

$C_{26}H_{42}LiClN_2O_{12} \bullet H_2O$
Calcd C 49.18 H 6.98 N 4.41 %,
Found C 49.30 H 7.06 N 4.16 %.

More ether (60 ml) was added to the filtrate and the solution set aside at room temperature to give single crystals suitable for an X-ray structural analysis after several days.

*$[2,6\text{-}C_5H_3N\{CMe(CH_2OH)_2\}_2]_2 \bullet Ba(ClO_4)_2$ (**7**).*

A solution of pure tetraol **2** (1.25 g, 4.90 mmol) in acetonitrile (25 ml) was added dropwise to a stirred solution of $Ba(ClO_4)_2$ (0.84 g, 2.50 mmol) in acetonitrile (20 ml). The mixture was filtered to remove a slight cloudiness and stirred at room temperature for 18 h. Ether (50 ml) was added and the mixture kept at - 18 °C for 48 h after which time a fine colourless precipitate had formed which was removed by filtration and dried *in vacuo*.

$C_{26}H_{42}BaCl_2N_2O_{16}$
Calcd C 36.88 H 5.00 N 3.31 %,
Found C 36.70 H 5.42 N 2.87 %.

More ether (25 ml) was added to the filtrate and the solution set aside at room temperature to give single crystals suitable for an X-ray structural analysis after several days.

Table II. Selected bond lengths (Å) and angles (°) for [2,6-$C_5H_3N\{CMe(CH_2NH_3)_2\}_2$]$(Br)_4$ • CH_3OH(**4** • 4 HBr • CH_3OH), [2,6-$C_5H_3N\{CMe(CH_2OH)_2\}_2]_2$ • $LiClO_4$ (**6**), and [2,6-$C_5H_3N\{CMe(CH_2OH)_2\}_2]_2$ • $Ba(ClO_4)_2$ (**7**).

Compound **4** • 4 HBr • CH_3OH:			
N(11)-C(11)	1.35(1)	C(14)-C(15)	1.39(1)
N(11)-C(15)	1.33(1)	C(11)-C(18)	1.54(1)
C(11)-C(12)	1.39(1)	C(18)-C(19)	1.55(1)
C(12)-C(13)	1.38(1)	C(16)-C(18)	1.54(1)
C(13)-C(14)	1.38(1)	C(16)-N(12)	1.49(1)
N(11)-C(11)-C(12)	122.0(9)	N(11)-C(15)-C(22)	115.1(7)
C(11)-C(12)-C(13)	119.1(9)	C(14)-C(15)-C(22)	123.8(8)
C(12)-C(13)-C(14)	118.2(8)	C(11)-C(18)-C(16)	111.1(8)
C(13)-C(14)-C(15)	120.2(9)	C(11)-C(18)-C(19)	111.2(7)
C(14)-C(15)-N(11)	121.0(8)	C(16)-C(18)-C(17)	109.2(7)
C(15)-N(11)-C(11)	119.5(8)	C(16)-C(18)-C(19)	110.0(8)
N(11)-C(11)-C(18)	117.3(8)	C(17)-C(18)-C(19)	105.4(8)
C(12)-C(11)-C(18)	120.6(8)	C(18)-C(16)-N(12)	112.3(8)
Compound **6**:			
Li(1)-O(11)	1.90(2)	Li(2)-O(13)	1.88(1)
Li(1)-O(21A)	2.01(1)	Li(2)-O(23)	2.02(1)
O(13)-Li(2)-O(23)	105.1(4)	N(2)-C(21)-C(27)	115.5(9)
O(13A)-Li(2)-O(23)	103.0(4)	C(22)-C(21)-C(27)	123.7(10)
O(13)-Li(2)-O(13A)	132.1(13)	N(2)-C(21)-C(22)	120.6(10)
O(23A)-Li(2)-O(23)	106.6(11)		
Compound **7**:			
Ba-O(1)	2.655(3)	Cl-O(7)	1.412(9)
Ba-O(2)	2.823(3)	Cl-O(8)	1.32(1)
Ba-O(4B)	2.705(4)	O(2)···O(3)	2.929(4)
Ba-O(6)	2.789(5)	O(2B)···O(3)	2.896(4)
Cl-O(5)	1.45(1)	O(4B)···O(7)	2.83(1)
Cl-O(6)	1.362(5)		
O(2)-Ba-O(1)	65.0(1)	O(6A)-Ba-O(6)	115.5(2)
O(2A)-Ba-O(1)	73.2(1)	C(2)-C(9)-N	117.8(4)
O(1A)-Ba-O(1)	97.7(1)	C(10)-C(9)-C(2)	121.6(4)
O(2A)-Ba-O(2)	114.4(1)	C(10)-C(9)-N	120.6(4)
O(4B)-Ba-O(4C)	123.2(1)		

Crystallography.

Data for **4** • 4 HBr • CH_3OH were collected on a Siemens P4 four-circle diffractometer (MoKα radiation, graphite monochromator). The structure was solved by direct methods and refined on F^2 using the program package SHELXTL 5.03. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located in the difference Fourier map, and no reasonable maximum of electron density could be found at the pyridine nitrogen atom (the highest 100 peaks of residual electron density were considered). In view of the relatively high absorption coefficient and in order to avoid unreasonably short C-H and N-H distances, the hydrogen atoms were incorporated in the final calculation as riding atoms in geometrically optimised positions. The residual electron density was + 0.92/- 0.88 $e\text{Å}^{-3}$. Crystal data and data collection parameters are listed in Table I, and selected distances and angles are given in Table II. Data for **6** were measured on a Nonius MACH 3 diffractometer (MoKα radiation, graphite monochromator, rotating anode). The structure was solved by direct methods and refined on F^2 using the program package SHELXTL 5.03. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were positioned geometrically except for the hydroxyl H atoms which were not included in the calculation. The residual electron density was + 0.37/- 0.33 $e\text{Å}^{-3}$. Crystal data, data collection parameters, and selected distances and angles are listed in Tables I and II, respectively. Data for **7** were measured on an Enraf Nonius CAD4 diffractometer (MoKα radiation, graphite monochromator). The structure was solved by direct methods (SHELXS 86) and refined on F^2 using SHELXL 93. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located in a difference Fourier map, and the residual electron density was + 1.13/- 1.14 $e\text{Å}^{-3}$. Crystal data and data collection parameters as well as selected distances and angles for **4** • 4 HBr • CH_3OH, **6** and **7** are given in Tables I and II, respectively. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-101 563 (**4** • 4 HBr • CH_3OH), CCDC-101 564 (**6**), and CCDC-101 565 (**7**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code +44 (1223) 336-033; E-mail: deposit@ccdc.cam.ac.uk].

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