Poly(ethylenimines) as Brønsted bases and as ligands for metal ions

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ABBREVIATIONS

en	1,2-ethanediamine
dien	*N*-(2-aminoethyl)-1,2-ethanediamine
trien	*N*,*N*′-bis(2-aminoethyl)-1,2-ethanediamine
tren	*N*,*N*-bis(2-aminoethyl)-1,2-ethanediamine
penten	*N*,*N*,*N*′,*N*′-tetrakis(2-aminoethyl)-1,2-ethanediamine
PEI	poly(ethyleneimine) monomer unit, $-CH_2-CH_2-NH-$, used as abbreviation of one N-containing unit in formulas
BPEI	branched polyethyleneimine
LPEI	linear polyethyleneimine
α	degree of protonation
K_a	acid dissociation constant
g_{iso}	isotropic g tensor
A_{iso}	isotropic nuclear hyperfine splitting tensor
NH_3	ammonia
bpy	2,2-bipyridine
bpym	2,2-bipyrimidine
2,3-dpp	2,3-bis(2-pyridil)pyrazine

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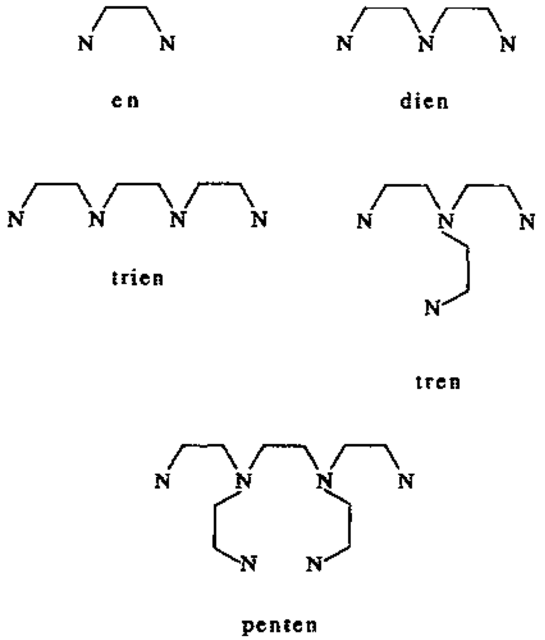
A. INTRODUCTION

Monodentate, and especially polydentate amines have played an outstanding role in the development of coordination chemistry [1,2]. Werner had made use of 1,2-diaminoethane (en) for the demonstration of chirality in complexes of the composition $M(en)_3$, thus giving further proof of the hexacoordination and of the octahedral structure of such species [3]. Open chain, multifunctional amines, such as dien [4], trien [5], tren [6] and penten [7] (see Scheme 1), were investigated thoroughly with respect to their metal-binding abilities. Macrocyclic amines as ligands have also found a wide interest [8].

The first report of the metal complex formation of a polymeric amine in the literature [9] in 1963 concerned the binding of Cu^{2+} and Ni^{2+} by branched polyethylenimine. Such complexes are highly water soluble and can, in principle, be investigated by conventional solution chemistry methods. It is therefore quite surprising that relatively few investigations of the interaction of metal ions with such polymeric ligands have been carried out, despite the fact that binding of a metal ion by a polymer has some very interesting aspects and even high potential for applications. There are many reports in which some kind of interaction between polymeric amines and metal ions was observed [10–14], yet rarely was this interaction investigated by methods generally used in coordination chemistry. Even a recent report on the chelating properties of linear and branched polyethylenimine [15] gives only cursory



Scheme 1.

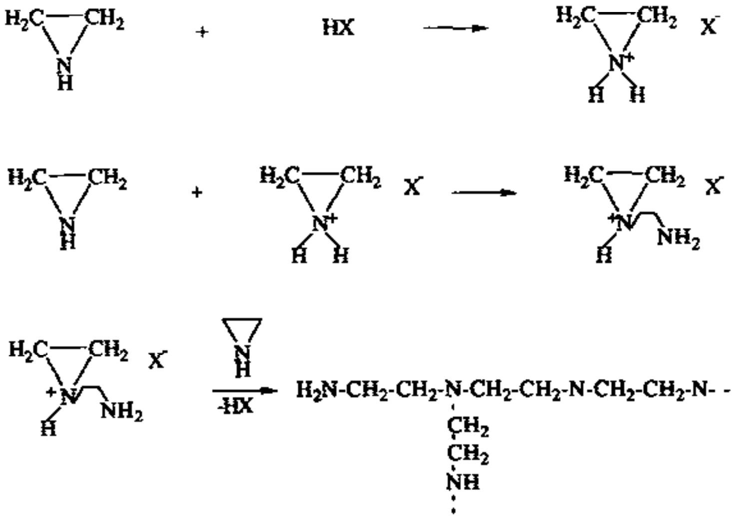
information about these interactions. It is assumed, for example, that Ni^{2+} and Cu^{2+} and several other metal ions bind to branched polyethylenimine with coordination number $n=4$, whereas it is quite obvious, using spectroscopic methods, that Ni^{2+} forms complexes with $n=6$ exclusively and Cu^{2+} has coordination numbers $n=4$ or $n=5$, depending on pH.

In this report, we want to review the properties of the polyethylenimine ligand itself and the various reports on its complex formation which have appeared in the literature. We compare these data with results obtained in our own laboratory [16,17]. Recent findings, not yet published in detail, will also be included.

B. POLYMERIC AMINES

Polyethylenimine (PEI) is known to exist in two forms, either as a linear structure (LPEI), or highly branched (BPEI). The structure depends on the synthetic procedure. BPEI is commercially available [18,19], whereas LPEI has to be synthesized by a quite lengthy process [20]. It has been found [15] that BPEI is, for most purposes, a more useful ligand than LPEI as the complexes of the former are usually more stable and also more soluble in aqueous solution. BPEI is therefore investigated more frequently than LPEI.

BPEI is obtained through ring-opening cationic polymerization of ethyleneimine or aziridine (see Scheme 2) and it is consequently often designated polyaziridine (e.g. in *Chemical Abstracts*) [19]. The ratio of primary, secondary and tertiary amine groups is ca. 1:2:1. The high degree of branching is due to the easy proton transfer from the tertiary aziridinium ion, which is the active species in the polymerization,



Scheme 2.

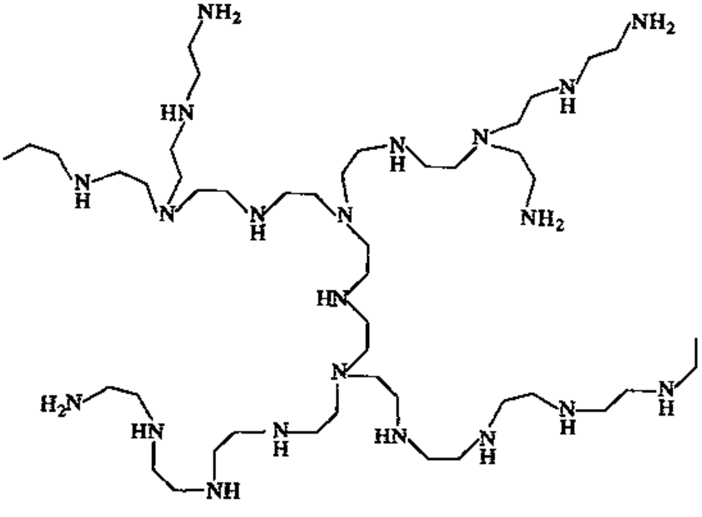
to other amine groups present in the reaction mixture [21]. In contrast to LPEI, which shows a high degree of crystallinity, BPEI is amorphous because the high number of branches prevents crystallization [22]. There is experimental evidence that branching sites are separated mainly by secondary amine groups, with about one branch for every three nitrogen atoms within a linear part of the chain [21], as depicted in Scheme 3.

BPEI is commercially available from several suppliers whose samples differ slightly in the degree of branching and molecular weight owing to different synthetic procedures. Our investigations have been carried out with BPEI obtained from Fluka (Polyimin P) as 50% aqueous solution, with a mean molecular weight in the range of ca. 6×10^5 to 1.0×10^6 g mol^{-1} [23]. At this concentration, the solution is a highly viscous syrup, and the nitrogen content, determined by the Kjedahl method, is in accordance with the composition $(CH_2{-}CH_2{-}NH{\cdot}2.6H_2O)_n$ [16].

Polyethyleneimine with a strictly linear structure (LPEI), having only secondary amine groups (see Scheme 4), can be synthesized [20] by the following methods:

(a) cationic isomerization ring-opening polymerization of 2-oxazolines, followed by hydrolysis of the resulting polyamide;

(b) polycondensation reaction of *N*-(2-aminoethyl) aziridine in aqueous solution; and



Scheme 3.

Scheme 4.

(c) cationic ring-opening polymerization of *N*-(2-tetrahydropyranyl) aziridine followed by acidic hydrolysis of the corresponding substituted polyamine.
X-ray crystallographic studies show that LPEI crystallizes in arrays of double-stranded helices [22,24].

Concentration of BPEI will be expressed in the following by the number of moles of nitrogen (monomer unit, $-CH_2-CH_2-NH-$, PEI, used as abbreviation of one N-containing unity in formulas) per litre of solution. This is the only well-defined way of expressing the concentration of a polymeric ligand in solution. Nevertheless, this overlooks the polymeric nature of the solute and thus the non-uniform distribution of the functional units throughout the solution. On a "local" scale, concentration should be expressed as moles of monomer units per effective volume of polymer. However, the effective volume of the polymer domain, which can vary in the course of an experiment due to conformational changes, is not easily accessible [25].

From now on, attention will be focused on branched polyethyleneimine (abbreviated as PEI for simplicity) since most reported investigations used this exclusively.

C. PEI AS A LIGAND

In recent years, there has been growing interest in water-soluble polymers as ligands for metal ions because polymer metal complexes are not only excellent models for metalloenzymes, but they could also lead to the development of interesting new materials. Furthermore, the study of the interaction of metal ions or metal fragments with synthetic macromolecules can give much insight into the binding of metal ions to biomacromolecules and upon the role and activity played by metal ions in the treatment of diseases [26,27].

PEI has a number of properties which makes it a noteworthy complexing agent [10,21,28], e.g.

(a) good water solubility provided by the hydrophilic amine groups, and therefore its metal complexes are also water soluble;

(b) high capacity for metal uptake due to high local concentration of functional groups;

(c) high molecular weight, which allows an easy separation, by the usual methods (e.g. membrane filtration), of polymer metal complexes from low molecular weight species present in solution;

(d) good chemical and physical stability;

(e) reversible complexation is easily achieved for labile metal ions with acids and stronger ligands; and

(f) high flexibility of the molecular conformation enable it to achieve an optimum configuration for complex formation.

The behaviour of aqueous solutions of the PEI molecule is largely determined by the combined action of the inert parts of the molecule causing hydrophobic interactions and of the polar amine groups causing hydrophilic interaction with the solvent [29].

PEI has a compact conformation in solution, as can be deduced from the low viscosity, owing to strong interactions between neighbouring amine groups through hydrogen bonding [15]. Hence, solutions of PEI are not homogeneous in a strict sense. There are regions within the polymer coil with high concentrations of amine groups, whereas outside the coil there are no, or few coordination sites available for complexation.

PEI shows an allosteric behaviour, like biomacromolecules (e.g. the binding of O_2 to the ferrohaeme group of haemoglobin), since its chemical behaviour is reversibly altered by coordination of metal ions and by protonation [30].

As a consequence of its high flexibility, PEI displays low selectivity towards the complexation of metal ions in solution, because it can easily achieve the most favorable configuration demanded by each metal ion with minimum expense in strain energy. Thus, steric hindrance becomes critical only by coordination of bulky metal fragments.

Low molecular weight polyamines form stable complexes with many metal ions, and much knowledge has been accumulated about their structures and properties as well as about their metal complexes [1].

The complex formation of a polymer metal complex, as well as its properties and chemical behaviour, is dictated by "environmental" effects, which are characteristic of polymer complexes only and not of low molecular complexes [30]. The environmental effects are: electrostatic, conformational, statistical, steric and hydrophilic [10,30]. These effects are common to the majority of polymeric ligands.

PEI is also a suitable ligand for second-sphere coordination owing to its cationic character in acid solution. The interaction between the two coordination spheres in the case of protonated PEI and an anionic species is through hydrogen bonds and other non-covalent interactions such as electrostatic and van der Waals [31]. Indeed, the investigations carried out in our laboratories on the interactions between protonated PEI ($HPEI^+$) and several anionic metal complexes such as $[Co(CN)_6]^{3-}$, $[Cr(CN)_6]^{3-}$ and $[Cr(CN)_5NO]^{3-}$, show that PEI is an outstanding second-sphere coordination ligand [16]. Similar findings for low molecular cyclic polyamines are reported [31,32] in the literature. ^{59}Co NMR, ^{13}C NMR and the lower quantum yield of the photoaquation of $[Co(CN)_6(HPEI)_n]^{n-3}$ compared with "free" $[Co(CN)_6]^{3-}$ provided evidence of second-sphere complexation [33]. The interaction between protonated PEI and $[Cr(CN)_6]^{3-}$ and $[Cr(CN)_5NO]^{3-}$ was undoubtedly confirmed by EPR spectroscopy [34].

Since second-sphere coordination does not necessarily require the formation of hydrogen bonds, second-sphere coordination of anionic species by cationic PEI metal complexes could also be envisaged. In fact, a Cu(II)–PEI complex was incorporated in an optical sensor where it reversibly binds an anionic fluorophor [35]. Another example of binding of anionic species is that of 1-pyrenesulphonate and 1,3,6,8-pyrenetetrasulphonate by Cu(II)–, Zn(II)–, and Ag(I)–PEI complexes [36].

D. PEI AS A BASE

PEI is a strong polybase which behaves markedly different if compared with the corresponding monomers and other polybases, even at high ionic strength [21]. The potentiometric titration behaviour of PEI was hitherto investigated by several research groups [9,15,16,37]. They showed that the behaviour of PEI is accounted for by:

(a) the branched structure of the polymer containing three different types of amine group;

(b) the strong neighbouring interactions between the various amine groups both charged (electrostatic repulsion) and charged/uncharged (hydrogen bonding); and

(c) the compact structure of the polymer in aqueous solution whose conformation is pH-dependent.

The titration curve (Fig. 1) extends over a wide pH region, and shows two "buffer" regions.

Figure 2 displays the dependence of α (degree of protonation) on the pH obtained from the potentiometric titration. It turns out that protonation of PEI remains far from complete, the maximum value of $\alpha = 0.78$ is reached at pH ca. 3,

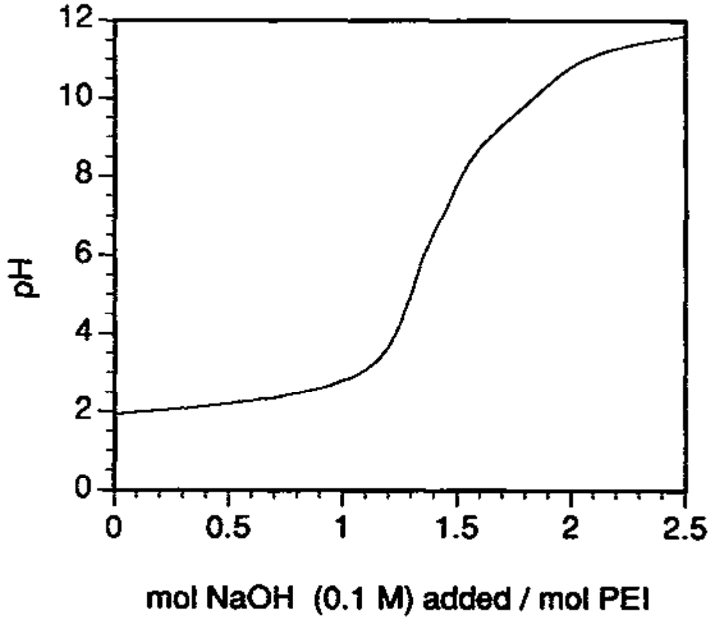


Fig. 1. Titration curve of $HPEI^+$ ($[PEI] = 8.0 \times 10^{-3}$ M, $[H^+] = 1.6 \times 10^{-2}$ M) with NaOH (0.1 M). $KNO_3 = 0.5$ M.

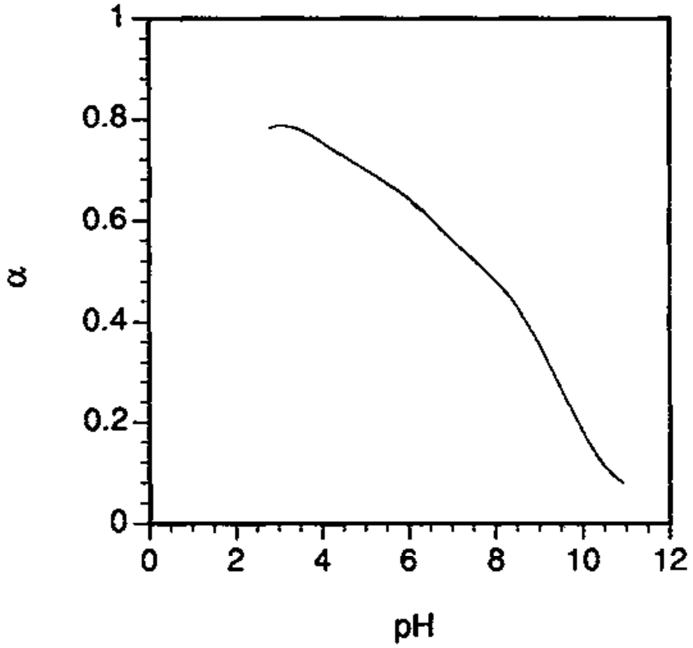
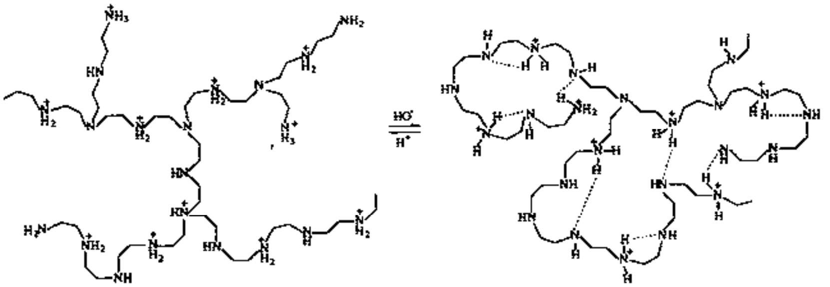


Fig. 2. Graphical representation of the dependence of α on pH.

very close to the values reported in the literature [15,21,37]. Further protonation for $pH < 3$ is precluded by strong electrostatic repulsions between charged groups, as originally proposed by Katchalsky et al. [38] to explain similar results obtained with polyvinylamine. On the other hand, there is a smooth decrease of α with increasing pH (for $pH > 3$) because hydrogen bonding between charged and uncharged amine groups becomes dominant. From Fig. 2 one can also see that PEI becomes nearly uncharged at $pH \approx 11$. It is well known that the variation of α with pH is dependent on the experimental conditions, especially on polymer and electrolyte concentrations. van Treslong et al. [37,39] observed that an increase in ionic strength results in a shift of the titration curve to higher pH values independently of α. Thus, deviations of titration data from published results are accounted for by different experimental conditions.

At low pH values, mutual charge repulsion leads to expansion of the polyion, and in the higher pH range the polymer contracts, due to hydrogen bonding [21], as illustrated by Scheme 5. According to a suggestion made by Ferruti et al. [24] based on ^{13}C and ^{15}N NMR data, PEI might exist at $pH \approx 7$ in the form of stiff structures of relatively stable six-membered rings due to hydrogen bonding between neighbouring free and charged amine groups.

The interpretation of the titration curve of $HPEI^+$ by the modified Henderson–



Scheme 5.

Hasselbalch equation

$$\mathrm{pH} = \mathrm{p}K_a - n\log[(1-\alpha)/\alpha] \tag{1}$$

gives the dissociation constant of HPEI$^+$ (pK_a) as a function of the degree of protonation (α), where n is a constant which accounts for the nearest neighbouring interactions [40]. Equation (1) is valid for the range $0.1 < \alpha < 0.8$.

It can be concluded from Fig. 3 that the HPEI$^+$ titration is split up in two almost linear parts. The first part ($\alpha < 0.3$) has an n value of 2.0 and p$K_{a1} = 8.39$.

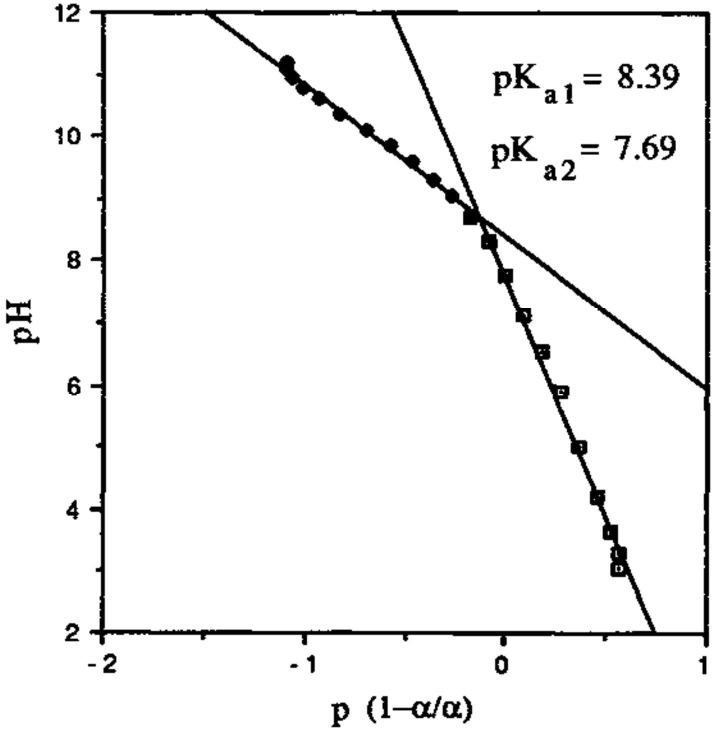


Fig. 3. Henderson–Hasselbalch diagram of HPEI$^+$ titration.

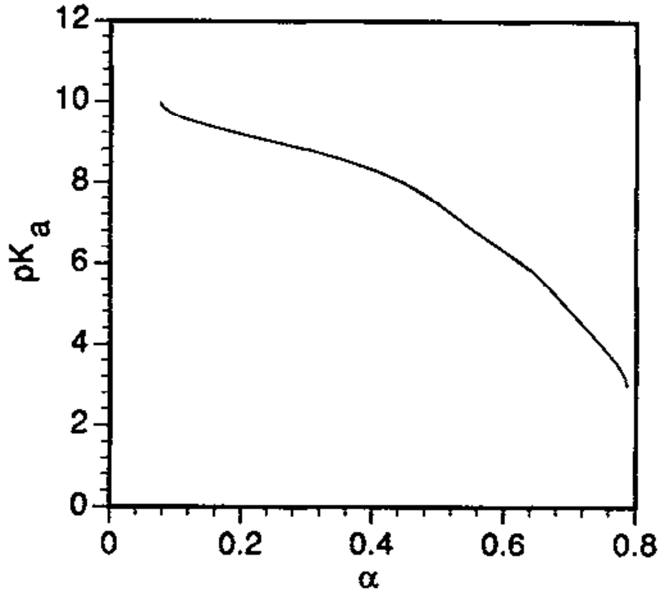


Fig. 4. Graphical representation of the dependence of pK_a on α.

While the second part ($\alpha > 0.3$) has an anomalous high n value of 7.0 and $pK_{a2} = 7.69$. The Henderson–Hasselbalch equation is valid for the range $0.1 < \alpha < 0.8$, and the pK_a values were obtained from the intercept of the straight lines. These observations show that nearest neighbouring interactions become dominant for $\alpha > 0.3$. They are responsible for the division of the titration curve into two parts.

PEI exhibits a strong affinity for the first 30–40% of the protons. The basic character decreases with further protonation, as can be concluded from Fig. 4, which shows a steep decrease in pK_a values for $\alpha > 40\%$. This phenomenon had already been observed for other polyelectrolytes and cyclic polyamines [37,39,41].

Protonated PEI has a great tendency to form polyelectrolyte complexes with polyanions. Indeed, it has been shown by colloid titrations that the reaction between protonated PEI and polyvinylsulphate occurs stoichiometrically with complete pairing of the ionic groups [42].

E. COMPLEX FORMATION

The complexation of metal ions by PEI occurs generally through intramolecular formation of chelates, giving rise to homogeneous solutions. Intermolecular polymer metal complexes would, in general, be insoluble in water [30]. This is observed, however, only upon complete evaporation of the solvent (vide infra). Structurally well-defined PEI metal complexes can only be obtained upon interaction of metal ions with PEI by using an excess of nitrogen binding sites. The interaction of metal ions with PEI, for low PEI : M ratios (less than the coordination number of the metal) undoubtedly leads to the formation of complexes with PEI and other ligands in the coordination sphere of the metal. It is very likely that complete loading of PEI by metal ions is not achieved, due to statistical factors and neighbouring charge repulsion between metal centres. The evaporation of PEI metal complex solutions yields amorphous solids that are generally no longer soluble in water, probably due to crosslinking [43,44].

Complex formation is obviously pH-dependent. In strongly acidic solutions no complexation takes place, protonated PEI and aqua–metal complexes co-exist in solution. In alkaline solutions, hydroxo complexes are formed, or at least there is competition between HO^- and amine groups for metal coordination and the formation of mixed complexes cannot be ruled out. Therefore, the intermediate pH range ($4 < pH < 9$) is the most appropriate for the formation of "single" PEI metal complexes for the majority of metal ions. In the course of complex formation, a decrease in pH is observed due to the binding of metal ions or metal complexes to PEI with simultaneous release of H^+ according to the equation

$$n(HPEI)^+ + M^{x+} \rightarrow [M(PEI)_n]^{x+} + nH^+ \qquad (2)$$

The establishment of M–N bonds induces local bending of the polymer and therefore makes its conformation more favourable for further complexation. This conformational change of the PEI molecule is a cooperative effect, which is analogous to the chelate effect observed in low molecular weight polyamine–metal complexes. However, the cooperative effect is much stronger than the chelate effect and it is markedly reflected in the kinetics and thermodynamic stability of PEI metal complexes [30]. Hence, complexation of metal ions or metal complexes by PEI induces a contraction of the polymer. Nevertheless, the conformation adopted by PEI metal complexes is determined by the electrostatic repulsion between the cationic chromophoric units.

Since, in a PEI metal complex, the chromophoric units are integrated in a macromolecule, their characteristics are not only determined by the coordination sphere but also by the microenvironment provided by the polymer. Therefore, PEI metal complexes often show a distinct chemical behaviour compared with analogous low molecular weight amine complexes.

Furthermore, a wide variety of PEI metal complexes can be obtained by varying the stoichiometry between the polymer and the metal ion, loading the polymer with two or more different metals or even by choosing different counter ions. In this way an enormous variety of new materials can be obtained.

The formation of PEI metal complexes has been mainly investigated by potentiometric and spectroscopic methods. Complexation can be detected simply by potentiometric titrations since the binding of metal ions to the amine groups is accompanied by H^+ release. Further information concerning the composition of the complexes can be furnished by UV/VIS and NMR spectroscopy, whenever the nuclear spin of the metal is non-zero. EPR spectroscopy provides valuable information about the local environment of metal ions, their distribution and metal–metal interactions. In the magnetic resonance methods, the shape of the signals depends mainly on the rotational correlation times, which are slower for macromolecular complexes than for low molecular weight analogous metal complexes [16,45]. Moreover, the use of analogous ethylenediamine metal complexes for comparison purposes turned out to be helpful in the characterization of PEI metal complexes.

(i) Labile metal ions

It is known that PEI forms complexes with a great number of metal ions such as Cu^{2+}, Zn^{2+}, Ni^{2+}, Mn^{2+}, Co^{2+}, Cd^{2+} and Pb^{2+} [10–16,21,46–49], but the complexation has so far been investigated thoroughly only for Cu^{2+} and Ni^{2+}. The experiments reported in the literature with other metal ions did not yet yield detailed characterization of the nature of PEI metal complexes.

Recently, Suh et al. [50] have reported the preparation of PEI-based macrocyclic complexes obtained by condensation of PEI with diketones in the presence of Fe^{3+}, Co^{2+}, Zn^{2+} and Ni^{2+}. However, the exact structure of the chromophoric units anchored to PEI is unknown.

Weiss [48] has investigated in detail the interaction of Cu^{2+} with PEI by pH titration and by UV/VIS and EPR spectroscopy. The UV/VIS spectra of solutions having $PEI:Cu^{2+} = 20$, at different pH values show that, at low pH ($pH < 2$), no complexation takes place. The only absorbing species present in solution is $Cu^{2+}(aq)$ ($\lambda_{max} = 813$ nm, $\varepsilon = 120\ M^{-1}\ cm^{-1}$). Below pH ca. 5, an absorption band occurs at $\lambda_{max} = 615$ nm with $\varepsilon = 100\ M^{-1}\ cm^{-1}$, indicating the formation of $Cu(PEI)_4^{2+}$ complex. For $pH > 5$, there is a bathochromic shift of the d–d transition band ($\lambda_{max} = 650$ nm, $\varepsilon = 750\ M^{-1}\ cm^{-1}$), which is ascribed to the formation of a new species $Cu(PEI)_5^{2+}$. The bathochromic shift of the absorption band is the well-known pentamine effect, already observed for low molecular weight amine Cu(II) complexes [51].

Additional information furnished by EPR spectra of PEI solutions loaded with Cu^{2+} is in agreement with the conclusions obtained by UV/VIS spectroscopy. The EPR spectra of Cu(II)–PEI complexes at different pH values for a ratio of $PEI:Cu^{2+} = 20$ show, at low pH ($pH < 2$), an isotropic signal ($g = 2.280$) attributed to $Cu^{2+}(aq)$, confirming once again that in very acidic solutions there is no binding of Cu^{2+} to the polymer. An increase of pH leads to the appearance of hyperfine structure in the EPR spectra, indicating clearly the formation of Cu(II)–PEI complexes. The detailed investigation by evolving factor analysis [49,52] again yields two species, one below pH ca. 5 with $g_{iso} = 2.103$ and $A_{iso} = 91 \times 10^{-4}\ cm^{-1}$ and one above pH ca. 6 with $g_{iso} = 2.04$ and $A_{iso} = 79 \times 10^{-4}\ cm^{-1}$, corresponding to CuN_4 and CuN_5 chromophores, respectively. The EPR spectra taken at $pH = 7$ and for $5 \leqslant PEI:Cu^{2+} \leqslant 23$ point to the occurrence of metal–metal interactions for $PEI:Cu^{2+} < 6$, even if the total Cu^{2+} concentration is low, and therefore the spectra show no hyperfine structure. This phenomenon is designated the "clothes-line" effect [16]. For PEI : $Cu^{2+} > 6$, the spectra are anisotropic with hyperfine structure.

The complexation of Ni^{2+} by PEI was studied in our laboratories by pH titration, UV/VIS spectroscopy and using $Ni(en)_3^{2+}$ as a model compound for comparison [49]. Once again, in very acidic solutions the only species detected was Ni^{2+}(aq). In solutions having PEI : $Ni^{2+} < 10$, precipitation of $Ni(OH)_2$ occurs in the pH range 7–9, depending on the PEI : Ni^{2+} ratio, whereas solutions with PEI : $Ni^{2+} > 10$ are violet and stay clear, even at high pH values. The formation of only one species, NiN_6 chromophore, was confirmed by the UV/VIS spectrum, which displays two absorption bands ($\lambda_{max} = 350$ and 540 nm) very close to the d–d transitions of $Ni(en)_3^{2+}$ observed at 333 and 541 nm [53].

(ii) Inert metal ions

The investigations concerning the interaction of inert metal ions and PEI found in the literature are rather superficial, and were only performed with Pt^{2+}, Rh^{3+} and Co^{3+} [54–56].

$Pt(PEI)_2Cl_2$ was obtained by reaction of $PtCl_4^{2-}$ with PEI for PEI : $Pt^{2+} \leqslant 4$. The complex is obviously insoluble in water and it was characterized by UV/VIS, IR and mass spectroscopy. Furthermore, in vitro tests revealed that it has anticancer activity [54,57].

Savinova et al. [55] carried out reactions between $RhCl_3$ and PEI for low PEI : Rh^{3+} ratios. UV/VIS spectroscopy together with the use of model complexes of ethylenediamine pointed to the formation of $Rh(PEI)_2(Cl_4)^-$ and $Rh(PEI)_4(Cl_2)^+$, depending on the PEI : Rh^{3+} ratios. These complexes proved to be very good catalysts for hydrogen evolution from water.

The interaction between Co^{3+} and PEI for PEI : $Co^{3+} > 10$ led to the formation of a species which was claimed to be $Co(PEI)_6^{3+}$ [56]. The experiments carried out in our laboratories [44] between Co^{3+} and PEI also led to the formation of $Co(PEI)_6^{3+}$, for $8 \leqslant$ PEI : $Co^{3+} \leqslant 24$, either by direct reaction of PEI with $CoCl_2$ or by substitution of ammonia in $(Co(NH_3)_5Cl)^{2+}$. The UV/VIS spectrum of $Co(PEI)_6^{3+}$ resembles that of $Co(en)_3^{3+}$, but for the former complex, the band at 465 nm is red-shifted.

We have studied in detail the interaction of a series of Pt(II) complexes with PEI in aqueous solution [17,43]. The investigations were performed for $PtCl_4^{2-}$ and a series of complexes with the general formula $Pt(LL)Cl_2$, where LL = *cis*-$(NH_3)_2$, en, bpy, 2,2-bpym and 2,3-dpp. The products obtained upon interaction of Pt(II) complexes with PEI were characterized by UV/VIS, ^{195}Pt NMR spectroscopy*, pH titration and by comparison with analogous ethylenediamine Pt(II) complexes.

$Pt(PEI)_4^{2+}$ was obtained after reaction between $PtCl_4^{2-}$ and partially protonated

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* The ^{195}Pt chemical shift data are reported relative to $K_2[PtCl_6]$.

PEI in solutions containing $6 \leqslant \mathrm{PEI}:\mathrm{Pt}^{2+} \leqslant 16$. The complex formation occurs at room temperature, and the best pH range proved to be 6–8, where the reaction is completed within one hour. In more acidic solutions, the reaction is rather slow, while in basic solutions hydroxo complexes of platinum are formed. The reaction was followed by UV/VIS spectroscopy, which gave clear evidence of the formation of $\mathrm{Pt(PEI)}_4^{2+}$ by the disappearance of the absorption bands of PtCl_4^{2-} [53]. ^{195}Pt NMR spectra of solutions, which contain, according to UV/VIS spectra, the $\mathrm{Pt(PEI)}_4^{2+}$ complex, consist of only one line at −2958 ppm, very close to the chemical shift observed for $\mathrm{Pt(en)}_2^{2+}$. This strongly indicates the formation of a "single species", $\mathrm{Pt(PEI)}_4^{2+}$.

The interaction of *cis*-$\mathrm{Pt(NH_3)_2Cl_2}$ and $\mathrm{Pt(en)Cl_2}$ with PEI, for solutions having $\mathrm{PEI}:\mathrm{Pt}^{2+} = 8$ and 16 at pH = 6, led to the formation of a variety of species due to release of ammonia and ethylenediamine induced by PEI. The identification of the various chromophores cannot be done on the basis of the UV/VIS spectroscopy alone, because it does not provide sufficiently distinctive spectral features. ^{195}Pt NMR spectra of solutions of *cis*-$\mathrm{Pt(NH_3)_2Cl_2}$ and $\mathrm{Pt(en)Cl_2}$ after reaction with PEI, exhibit four resonance lines. In each case, two resonance lines were observed within the range of $\mathrm{PtN_4}$ chromophores corresponding to the formation of $\mathrm{Pt(NH_3)_2(PEI)}_2^{2+}$, $\mathrm{Pt(en)(PEI)}_2^{2+}$ and $\mathrm{Pt(PEI)}_4^{2+}$. The two peaks observed in the downfield region (−2111 and −1781 ppm) are due to the displacement of ammonia and ethylenediamine, which are substituted by water or OH^- in a first step. Release of ammonia and ethylenediamine is a slow process since, after two weeks, the spectra of those solutions do not show any peaks between −2111 ppm and −1781 ppm.

Further proof of the loss of ammonia and ethylenediamine was furnished by ^{14}N NMR spectroscopy. The linewidths of ^{14}N signals are very different if the nuclei are located either in a polymer species or in small molecules due to quadrupolar relaxation. The signal of ^{14}N in PEI and in its metal complexes is broadened beyond detection. The formation of NH_4^+ (360 ppm, relative to nitromethane) and enH_2^{2+} (351 ppm) in the solutions of *cis*-$\mathrm{Pt(NH_3)_2Cl_2}$ and $\mathrm{Pt(en)Cl_2}$ upon reaction with PEI at pH = 6 can therefore be detected conveniently by the appearance of the corresponding relatively narrow ^{14}N signals.

The reaction of $\mathrm{Pt(bpy)Cl_2}$ with PEI, for a ratio of $\mathrm{PEI}:\mathrm{Pt}^{2+} = 8$, 16 yields stable light yellow solutions whose spectra are very similar to those of $\mathrm{Pt(bpy)(NH_3)}_2^{2+}$ and $\mathrm{Pt(bpy)(en)}^{2+}$ [58,59]. These observations strongly indicate the formation of $\mathrm{Pt(bpy)(PEI)}_2^{2+}$. Furthermore, the ^{195}Pt NMR spectrum presents only one line at ca. −2780 ppm, very close to the chemical shift observed for $\mathrm{Pt(bpy)(en)}^{2+}$.

Thus, PEI has the ability to induce release of ligands such as $\mathrm{NH_3}$ and ethylenediamine, while the strong chelating ligand bipyridine remains coordinated to platinum upon interaction of $\mathrm{Pt(bpy)Cl_2}$ with the polymer. Similar findings are reported in the literature for the interaction of *cis*-$\mathrm{Pt(NH_3)_2Cl_2}$, $\mathrm{Pt(en)Cl_2}$ and $\mathrm{Pt(bpy)Cl_2}$ with biomolecules such as aminoacids [60], peptides and proteins containing a thiol group [61] at pH = 6.

The interaction of $Pt(BL)Cl_2$ (where BL is the bridging ligand = bpym, 2,3-dpp) with PEI, for a ratio of PEI : Pt^{2+} = 8, 16, yielded homogeneous orange solutions, whose UV/VIS spectra resemble those of $Pt(bpym)(en)^{2+}$ and $Pt(2,3\text{-dpp})(en)^{2+}$. Thus, UV/VIS spectroscopy points to the formation of $Pt(BL)(PEI)_2^{2+}$. However, in both cases the ^{195}Pt NMR spectra present two lines at −2953 ppm and at ca. −2881 ppm. The latter resonance line is assigned to the $Pt(BL)(PEI)_2^{2+}$ chromophore, whereas that at −2953 ppm is due to the presence of $Pt(PEI)_4^{2+}$ in solution. Therefore, it turns out that bpym and 2,3-dpp is displaced by PEI, very likely due to steric hindrance or to intrinsic instability of the $Pt(BL)(PEI)_2^{2+}$ complexes.

Additional evidence of the formation of Pt(II)–PEI complexes was furnished by pH titrations. In every case, the Pt(II)–PEI complex solutions are more acidic compared with the solution of PEI itself. Moreover, the acidity increases with decreasing PEI : Pt^{2+} ratio. These observations show that Pt(II) is coordinated to PEI-occupying nitrogen sites that are no longer available for protonation. The solution of $Pt(bpy)(PEI)_2^{2+}$ complex is more basic compared with that of $Pt(PEI)_4^{2+}$ (with the same PEI : Pt^{2+} ratio), indicating that, in the first case, platinum is bound to a lower number of polymer nitrogen atoms. The $Pt(PEI)_4^{2+}$ and $Pt(bpy)(PEI)_2^{2+}$ complexes seem to be very stable, since no decomposition occurs, even in strongly acidic medium (pH = 2).

F. FINAL REMARKS

PEI has already found a wide variety of technical applications which are based on its physico-chemical properties, surface activity, and its ability to form complexes with anionic species, metal ions or metal complexes. The commercial use of PEI started out as a flocculating agent in paper manufacture [21]. It has been widely used in the treatment of waste water for removing heavy metal ions and in hydrometallurgy for the recovery of noble metals [10,13,14,21,28]. In addition, PEI is employed in coating and in the textile industry [21]. Several metal complexes of PEI (Pd, Rh) were used in catalysis, either homogeneous, or bound on a surface, heterogeneous catalysis, and proved to be efficient in hydrogen evolution from water, and in organic synthesis for hydrogenation of aromatics and double bonds [55,62].

Applications of PEI in the field of high technology are reported in the literature. PEI complexes of alkali metals were incorporated in high-energy density batteries, and a Cu(II)–PEI complex was used in an optical sensor [35,63].

Other fields of PEI applications that deserve attention are biochemistry and medicine. In fact, PEI was used as a precipitating agent for protein purification [64], and it was incorporated in a membrane for trapping carcinogens [65]. It is further known that PEI strongly binds lipids and accelerates the hydrolysis of long-chain fatty acid esters at physiological pH [21]. Moreover, it was found that PEI has anticancer activity by inhibition of the growing of cancer cells, probably due to the interaction of the polycation with the negatively charged phosphate groups of the

DNA. PEI seems to be a very suitable polymeric matrix for use as a carrier in drug delivery systems [66]. Indeed, Carraher et al. [54] have synthesized $Pt(PEI)_2Cl_2$ whose in vitro tests showed anticancer activity.

Despite the fact that some PEI metal complexes were already applied in several fields, the reactions between PEI and metal ions or metal complexes and their mechanisms have been only scarcely and incompletely investigated from the coordination chemistry point of view. Research in this field is far from being exhausted and involves several disciplines, including chemistry, medicine, biology and engineering.

Indeed, further interesting applications for PEI metal complexes could be envisaged in semiconductor devices, ceramics, catalysts, photochemical devices, fertilizers, pesticides, pigments and dyes.

Concerning biochemistry and medicine, further research involving PEI or PEI–metal complexes could throw light upon certain biological processes and bring interesting results for the treatment of diseases. In fact, natural polyamines such as spermidine ($C_7H_{19}N_3$), spermine ($C_{10}H_{26}N_4$), putrescine ($C_4H_{12}N_2$), and cadaverine ($C_{10}H_{14}N_2$) bind nucleotides strongly, and play an important role in nucleic acid and protein synthesis, and cell growth [1,32,67,68]. The synthesis of some biomacromolecules (e.g. DNA) is believed to occur by anion–anion reactions [68]. Therefore we could expect from PEI some enzyme-like action in this type of reaction. Moreover, modifying PEI by attaching bioactive moieties (e.g. nucleobases) could be a fruitful way to mimic important biological processes. PEI is probably biocompatible, and thus a promising candidate for being used as a drug carrier in human patients.

It is clear that, in view of its excellent complexing properties, future practical applications of PEI are dependent upon the collaboration of coordination chemists.

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