Inorganica Chimica Acta, 67 (1982) L15–L16

EDTA-Chelation Therapy of Lead Poisoning: Lead-207 Nuclear Magnetic Resonance and X-Ray Diffraction Studies

P. G. HARRISON*, M. A. HEALY and A. T. STEEL

Department of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD, U.K.

Received March 16, 1982

Lead poisoning is commonly treated by chelation therapy using an EDTA salt (EDTA = ethylenediamine tetraacetic acid) administered either by intravenous infusion or by intramuscular injection, after which the lead–EDTA complex is excreted in the urine [1–5]. Although di- and tri-sodium salts are used (several propriety drugs are available, *e.g.* Limclair and sequestrene NA2 and NA3), disodium calcium edetate (available as the proprietary drug Ledclair) is preferred in order to avoid the possibility of hypocalcaemia and tetany. However, little is known about the precise chemistry of the interaction of these drugs with lead in aqueous media.

The effect on the ^{207}Pb n.m.r. chemical shift of a 1 *M* aqueous solution of lead(II) nitrate of the addition of aliquots of 0.1 *M* aqueous disodium edetate is shown in Fig. 1. The occurrence of an immediate interaction can readily be seen by the steady, albeit relatively small, movement of the ^{207}Pb resonance to lower field as the $[\mathrm{EDTA\text{-}Na_2}]/[\mathrm{Pb^{2+}}]$ ratio increases. At a molar ratio of *ca.* 0.15, however, serious precipitation of a lead-EDTA complex precluded further investigation by this method.

Further insight into the nature of the EDTA-Pb complex formed can be obtained by X-ray diffraction studies. Crystals of the complex were obtained by mixing 0.4 *M* aqueous solutions of lead(II) nitrate and disodium edetate and allowing to stand. After two days crystals of a 1:1 complex sesquihydrate (Found. C, 22.80; H, 3.43; N 5.34%. Calculated for $\mathrm{PbEDTA \cdot 1.5H_2O}$: C, 22.89; H, 3.27; N, 5.34%). were obtained which decomposed >212° with rapid evolution of carbon dioxide. A suitable crystal of approximate dimensions 0.4 × 0.3 × 0.5 mm^3 was loaded in a Lindemann capillary with a drop of water to prevent efflovescence. Intensities of 4470 independent non-zero reflections with $I > 3\sigma I$ were measured using Mo-K$_\alpha$ radiation (λ = 0.7107 Å). *Cell Data*: $\mathrm{C_{20}H_{34}N_4O_{19}Pb_2}$. M = 1048.66. Space group $P\bar{1}$, a = 14.5748, b = 11.5754, c = 10.2879 Å, α = 103.0261, β = 120.0751, γ = 88.8949°. U = 1454.40 Å^3. Z = 2. F(000) = 498.

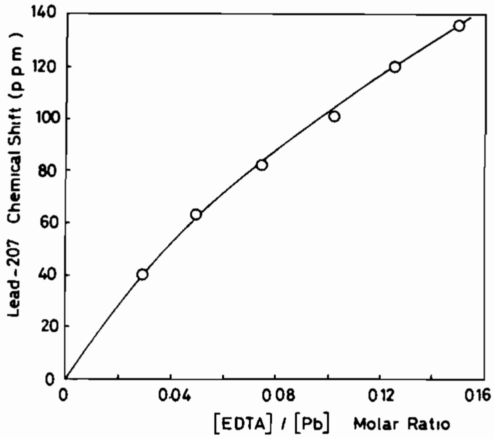

Fig. 1. Plot of lead-207 chemical shift *versus* the $[\mathrm{EDTA\text{-}Na_2}]/[\mathrm{Pb}]$ molar ratio. Chemical shifts are to low field relative to 1 Molar aqueous lead(II) nitrate (–2961.2 ppm relative to $\mathrm{Pb(CH_3)_4}$ = 0).

The structure was solved by the 'heavy atom' method using conventional Patterson and Fourier syntheses, and refined by full-matrix, least-squares anisotropic analysis to a final R-value of 6.15%.

Crystals comprise independent monomer and dimer units of composition $\mathrm{PbEDTA \cdot H_2O}$ and $[\mathrm{PbEDTA \cdot H_2O}]_2$, respectively (Fig. 2). In addition, a further molecule of water of crystallisation is hydrogen-bonded to carbonyl oxygen atoms of both monomer and dimer units (O······O = 2.68(2), 2.69(2), 2.82(2) Å). In both, the EDTA functions as an hexadentate chelating ligand towards lead. Unusually however, the coordination at each lead is quite different. The lead atom of the dimeric unit is eight-coordinated in a distorted square antiprismatic fashion by the hexadentate EDTA ligand, a water molecule, and a carboxyl oxygen atom from the EDTA ligand chelating the second lead atom of the dimer unit. Although the distances between the lead and the water and bridging carboxyl oxygen atoms are long (2.95(1) and 2.82(1) Å, respectively), the other Pb–O (2.54(1)–2.65(1) Å) and Pb–N (2.62(1) and 2.57(1) Å) have typical values [6]. The lone pair of electrons on lead appears to be stereochemically inactive, with no gross distortion of the basic square antiprismatic geometry or obvious vacancy in the first coordination sphere of the metal.

In contrast, the valence shell of the lead atom of the monomer unit exhibits a large space on the opposite side of the metal to the EDTA chelate,

---

*Author to whom correspondence should be addressed.

0020-1693/82/0000-0000/$02.75

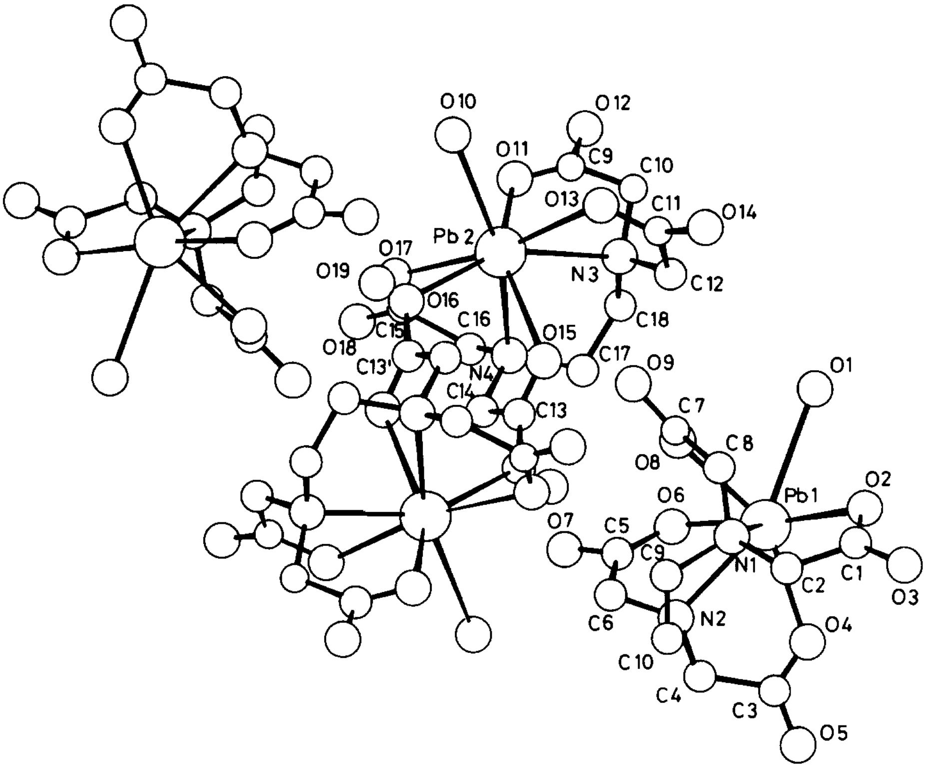

Fig. 2. View of the structure of the lead(II)–EDTA complex showing the eight-coordinated dimeric and seven-coordinated monomeric units.

strongly suggestive of lone pair stereochemical activity. Assuming the lone pair to occupy a coordination site in this case, the coordination of lead in the monomer unit is similar to that found in the dimer, in which the bridging carboxyl oxygen atom is replaced by the lone pair. The metal–ligand bond distances in the monomer ($Pb-OH_2$ = 2.97(1); Pb–O = 2.49(1)–2.74(1) Å; Pb–N = 2.52(1), 2.60(1) Å) are, not unexpectedly, similar to the corresponding distances in the dimer unit.

This precise knowledge of the solid-state structure of the Pb–EDTA complex enables further speculation concerning the nature of the species present in solution. It is possible that similar monomer and dimer units also exist in solution in mutual equilibrium, although it would be expected that mononuclear units would predominate at low concentrations. However, irrespective of whether monomer or dimer species, or both, are present in solution, it is clear from these data that the lead is tightly held by the hexadentate EDTA ligand in a neutral but, because of the presence of the four carboxyl groups, hydrophilic molecule which is, therefore, readily excreted in the urine.

Acknowledgements

We thank the S.R.C for a Research Studentship (to A.T.S.), the Esso Petroleum Co. Ltd. for financial assistance, and Professor T. J. King for assistance with the X-ray studies.

References

1 E. L. Belknap, *Industrial Medicine, 21,* 805 (1952).
2 S. P. Bessman, H. Reid and M. Rubin, *Medica. Annals of the District of Columbia, 21,* 372 (1952)
3 F. E. Karpinski, F. Rieders and L. S Girsh, *J Paediatrics, 42,* 687 (1953).
4 H. Foreman, C. Finnegan and C. C. Lushbaugh, *J Am. Medical Assoc , 160,* 1042 (1956).
5 J. J. Chisholm, *Paediatric Clinics of North America, 17,* 591 (1970).
6 P. G. Harrison, *Coord Chem Revs , 20,* 1 (1976).