



Pentaerythritol fragmentation during conversion to a polyamine ligand— isolation of 1,1-bis(2'-aminoethylaminomethyl)-ethene

Young Hoon Lee^a, Cindy Mora^a, Ji Young Choi^b, Jong Chul Byun^b, Jack M. Harrowfield^c, Pierre Thuéry^d, Yang Kim^{a,*}

^a Department of Chemistry & Advanced Materials, Kosin University, 149-1, Dongsam-dong, Yeongdo-gu, Busan 606-701, Republic of Korea

^b Department of Chemistry, College of Natural Science, Jeju National University, Jeju 690-756, Republic of Korea

^c Institut de Science et d'Ingénierie Supramoléculaires, Université de Strasbourg, 8, allée Gaspard Monge, 67083 Strasbourg, France

^d CEA, IRAMIS, UMR 3299 CEA/CNRS SIS2M, LCCEf, Bâtiment 125, 91191 Gif-sur-Yvette, France

ARTICLE INFO

Article history:

Received 23 June 2010

Revised 12 July 2010

Accepted 16 July 2010

Available online 21 July 2010

ABSTRACT

The reaction of pentaerythritol tribromide with ethylenediamine under strongly basic conditions leads to the quadridentate ligand 1,1-bis(2-aminoethylaminomethyl)-ethene (**2**), which is easily purified by formation and chromatographic separation of its Co(III) complex, *trans*-[Co(**2**)Cl₂]Cl·H₂O.

© 2010 Elsevier Ltd. All rights reserved.

Derivatives of pentaerythritol and tris(hydroxymethyl)ethane have been long and frequently employed for the synthesis of multidentate ligands, especially polyamines. Typically, the hydroxyl groups of these polyols are converted to good leaving entities such as aromatic sulfonate or bromide which may then be displaced by various nucleophiles.^{1–11} Polyamines can be obtained either by a direct attack of a simpler amine^{1–10} or by a reaction with azide followed by reduction.^{11,12} Such reactions have been exploited also with the derivatives of a large number of other polyols¹³ and where the attacking reagent is a tosylamide anion, this is, of course, the basis of the extremely popular Richman–Atkins method¹⁴ for the production of macrocyclic polyamines.¹⁵ Although the proximity of the functional groups on pentaerythritol and tris(hydroxymethyl)ethane frameworks can lead to cyclisation reactions,^{6–10,16} in general the C₅ entity and its connectivity remain intact in the final products. It is known,¹⁷ however, that the reactions of pentaerythritol derivatives under strongly basic conditions can lead to fragmentation and in particular to the formation of derivatives of bis(hydroxymethyl)ethane. In the present study, we have found that this pathway is particularly prominent in the reaction of pentaerythritol tribromide (2,2-bis(bromomethyl)-3-bromopropanol) with ethylenediamine (1,2-ethanediamine), a reaction that we have used otherwise^{10e,f} to prepare the hydroxyl-substituted sexadentate amine 'HOsen', tris(aminoethylaminomethyl)methanol.

Thus, heating a solution of commercially available pentaerythritol tribromide in neat ethylenediamine (en) at 120 °C for 3 days produces a mixture of polyamines (Scheme 1) which after basification and distillation to remove the bulk of the ethylenediamine, can be easily separated by formation and chromatography of their

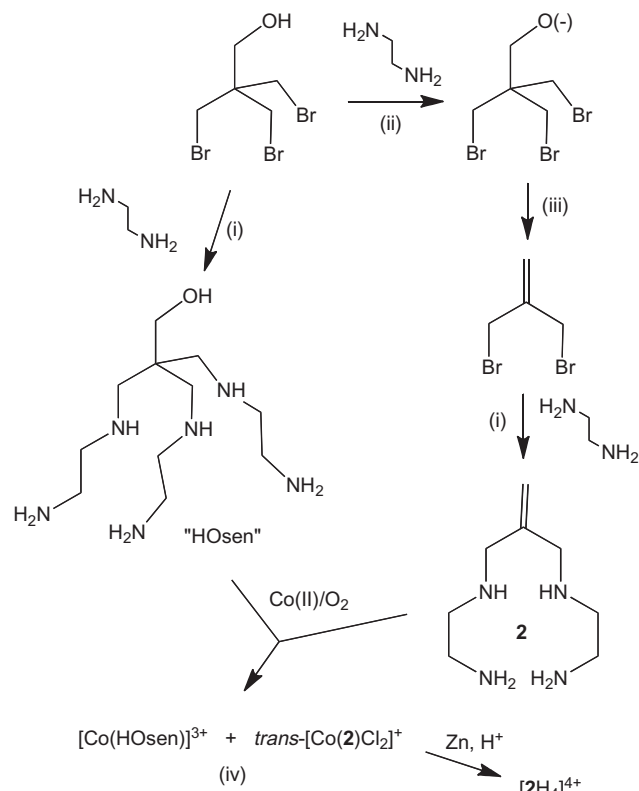
cobalt(III) complexes,¹⁸ a procedure which is effective in many similar cases.^{10a,b} Observation of a green complex **1** as a major component (56% isolated yield) was at first taken to mean that inefficiently removed residual ethylenediamine had given rise to *trans*-[Co(en)₂Cl₂]⁺ but this complex can in fact be independently detected as a minor species and is readily distinguished by its relatively rapid hydrolysis to violet (largely *cis*) aqua complexes.¹⁹

Both the ¹H and ¹³C NMR spectra²⁰ of **1** indicate the presence of unsaturated carbon in a rather symmetrical species and a crystal structure determination²¹ of **1** as the hydrated chloride salt established the presence of the quadridentate ligand 1,1-bis(2-aminoethylaminomethyl)-ethene, **2**, in the complex cation *trans*-[Co(**2**)Cl₂]⁺ (Fig. 1). The bound ligand has the R_sS_s configuration of the inner N-donor atoms, as found in saturated analogues, where again the *trans*-CoN₄Cl₂ donor atom array is usual.²² The central chelate ring has an essentially chair conformation and the only approach within the lattice of a nucleophilic species to the alkene unit involves a rather remote (~3.6 Å) contact between the terminal alkene (C8) atom and a chloride ion. Whether the reactivity of the alkene unit in solution is significantly affected by coordination to cobalt(III) remains to be established.

Reduction of the metal centre in **1** from the III to the II state under acidic conditions leads to a rapid release of **2** in its tetraprotonated form,²³ which is easily separated from free metal ions by cation exchange chromatography. A crystal structure determination²⁴ on the tetrahydrochloride confirmed that the alkene unit remained intact despite the fairly prolonged exposure to aqueous acid involved in its isolation and crystallisation. Consistent with its tetraprotonated state, the ligand adopts an extended conformation (Fig. 2) and the lattice displays an intricate hydrogen-bonding network involving the chloride anions, water molecules and protonated NH centres.

* Corresponding author.

E-mail address: ykim@kosin.ac.kr (Y. Kim).



Scheme 1. Reactions of pentaerythritol in neat ethylenediamine. (i) Nucleophilic substitution; (ii) deprotonation; (iii) retro-aldol reaction followed by Br-dissociation; (iv) separated by cation exchange chromatography.

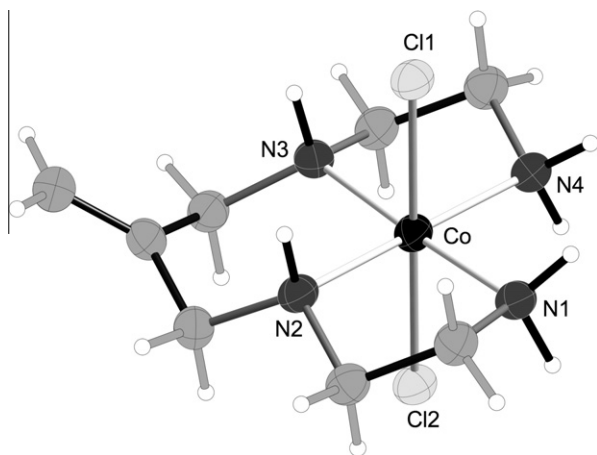


Figure 1. The cationic complex species present in the lattice of $\text{trans-}[\text{Co}(\text{2})\text{Cl}_2]\text{Cl}\cdot\text{H}_2\text{O}$. Displacement ellipsoids are shown at the 50% probability level and hydrogen atoms are shown as small spheres of an arbitrary radius of 0.1 Å.

The facility of the formation of **2** is presumably a consequence of the presence of the residual hydroxyl group in the reactant leading to a *retro*-aldol reaction and a release of formaldehyde under strongly basic (and high-temperature) conditions, followed by bromide ion dissociation. Whether these processes occur before, after or in competition with amine substitution of the other bromo groups is presently unclear. Interestingly, the reaction of pentaerythritol dibromide with ethylenediamine under very similar conditions to those used herein^{10d} gives rise principally to products that are derived from oxetane species and formed via intramolec-

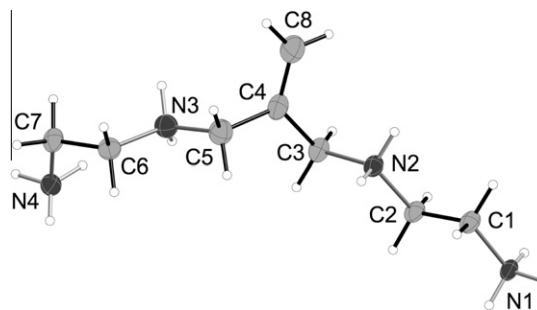


Figure 2. A perspective view of the cation present in the lattice of $[\text{2H}_4]\text{Cl}_4\cdot\text{H}_2\text{O}$. Displacement ellipsoids are shown at the 50% probability level and hydrogen atoms are shown as small spheres of an arbitrary radius of 0.1 Å.

ular nucleophilic displacement of bromide, although it is also known²⁵ that other base-catalysed reactions of pentaerythritol tribromide give rise to oxetanes and it may well be that differences in activation energies associated with different reactants give rise to marked effects on product distributions as a function of temperature.

Acknowledgement

This research was supported by the National Research Foundation of Korea (Grant 2009-0075987).

References and notes

- van Alphen, J. *Recl. Trav. Chim. Pays-Bas Belg.* **1938**, *57*, 265–276 (This is one of a series of publications dealing with the reactions of various di-, tri- and tetrahalo compounds with diamines.).
- Beyaert, M.; Govaert, F. *Proc. R. Dutch Acad. Sci.* **1939**, *42*, 637–640. 641–648, 776–789.
- von Doering, W.; Levy, L. K. *J. Am. Chem. Soc.* **1955**, *77*, 509–513.
- (a) Green, R. W.; Catchpole, K. W.; Phillip, A. T.; Lions, F. *Inorg. Chem.* **1963**, *2*, 597–600; (b) Phillip, A. T. *Aust. J. Chem.* **1968**, *21*, 2301–2303.
- Sarneski, J. E.; Urbach, F. L. *J. Am. Chem. Soc.* **1971**, *93*, 884–888.
- Geue, R. J.; Searle, G. H. *Aust. J. Chem.* **1983**, *36*, 927–935.
- Tomioaka, K.; Sakaguchi, U.; Yoneda, H. *Inorg. Chem.* **1984**, *23*, 2863–2867.
- Gahan, L. R.; Hart, K. E.; Kennard, C. H. L.; Kingston, M. A.; Smith, G.; Mak, T. C. W. *Inorg. Chim. Acta* **1986**, *116*, 5–10.
- (a) McAuley, A.; Subramanian, S.; Whitcombe, T. W. *Chem. Commun.* **1987**, 539–540; (b) McAuley, A.; Beveridge, K.; Subramanian, S.; Whitcombe, T. W. *Can. J. Chem.* **1989**, *67*, 1657–1665.
- (a) Harrowfield, J. M.; Kim, Y.; Mocerino, M.; Skelton, B. W.; White, A. H. *Dalton Trans.* **1995**, 2431–2444; (b) Choi, M.-H.; Harrowfield, J. M.; Kim, B. J.; Kim, L.-C.; Kim, S.-H.; Kim, Y.; Lee, M. K.; Mocerino, M.; Rukmini, E.; Skelton, B. W.; White, A. H. *Dalton Trans.* **2001**, 707–722; (c) Harrowfield, J. M.; Kim, J. Y.; Kim, Y.; Lee, J. H.; Sujandi, P. *Polyhedron* **2005**, *24*, 968–975; (d) Bernhardt, P. V.; Cho, J. H.; Harrowfield, J. M.; Kim, J. Y.; Kim, Y.; Sujandi, P. *Polyhedron* **2006**, *25*, 1811–1822; (e) Bernhardt, P. V.; Kim, Y.; Sujandi *Aust. J. Chem.* **2006**, *59*, 783–790; (f) Bernhardt, P. V.; Harrowfield, J. M.; Kim, Y.; Lee, Y. H.; Park, Y. C.; Sujandi *Bull. Korean Chem. Soc.* **2007**, *28*, 589–595.
- Gottschaldt, M.; Bohlender, C.; Müller, D.; Klette, I.; Baum, R. P.; Yano, S.; Schubert, U. S. *Dalton Trans.* **2009**, 5148–5154, and references therein.
- Fleischer, E. B.; Gebala, A. E.; Levey, A.; Tasker, P. A. *J. Org. Chem.* **1971**, *36*, 3042–3044.
- (a) See, for example, (a) Ref. 10b; (b) Gahan, L. R.; Hambley, T. W. *Inorg. Chem.* **1987**, *26*, 2532–2537; (c) Hillier, M. C.; Chen, C.-Y. *J. Org. Chem.* **2006**, *71*, 7885–7887; (d) Lee, Y. H.; Harrowfield, J. M.; Kim, Y.; Lee, M. H.; Lim, W. T.; Park, Y. C.; Thuéry, P. *Dalton Trans.* **2009**, 434–442.
- Richman, J. E.; Atkins, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 2268–2270.
- For a brief survey of the uses and developments of this method, see: Hoye, R. C.; Richman, J. E.; Dantas, G. A.; Lightbourne, M. F.; Shinneman, L. S. *J. Org. Chem.* **2001**, *66*, 2722–2725.
- Harrowfield, J. M.; Jang, G.; Kim, Y.; Thuéry, P.; Vicens, J. *Dalton Trans.* **2002**, 1241–1243, and references therein.
- (a) Riemschneider, R.; Göhring, O.; Gross, P.; Rook, A.; Brendel, K.; Faria, C. *Monatsh. Chem.* **1965**, *96*, 147–158; (b) Watanabe, K.; Sugihara, T.; Tanaka, M. *Yuki Gosei Kagaku Kyokaiishi* **1966**, *24*, 651–658.
- A mixture of pentaerythritol tribromide (6.2 g) and ethane-1,2-diamine (23 g) was heated and stirred at 120 °C for 72 h under nitrogen. NaOH (2.5 g) in methanol (20 mL) was added after cooling to room temperature and excess ethane-1,2-diamine evaporated off under reduced pressure. The residual

- brown oil was dissolved in methanol (100 mL) and mixed with a methanolic solution (150 mL) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (5.4 g). A stream of air was bubbled through the reaction mixture for 1 h before acetic acid (2.0 mL) was added. Aeration was continued for a further 5 h. The resulting solution was evaporated to dryness under reduced pressure after adding 2 mol L^{-1} HCl (10 mL). The residue was dissolved in water (200 mL) and filtered through Celite before chromatography on Dowex 50W-x2 with 2 mol L^{-1} HCl as eluant. A pink band of Co^{2+} (aq) was eluted first, followed by two minor bands of green $\text{trans-}[\text{Co}(\text{en})_2\text{Cl}_2]^+$ and purple $\text{cis-}[\text{Co}(\text{en})_2\text{Cl}_2]^+$ (en = ethane-1,2-diamine). The next, major green band was collected and evaporated to dryness under vacuum. Yield, 3.8 g (56%). Crystals suitable for the structure determination were grown by vapour diffusion of ethanol into an aqueous solution of the residue. Anal. Calcd for $[\text{Co}(\mathbf{2})\text{Cl}_2]\text{Cl} \cdot \text{H}_2\text{O} = \text{C}_8\text{H}_{22}\text{Cl}_3\text{CoN}_4\text{O}$: C, 27.02; H, 6.24; N, 15.76. Found: C, 26.9; H, 6.4; N, 15.8. Visible spectrum (in water): $\lambda_{\text{max}} = 412 \text{ nm}$ (sh), $\log \epsilon_{\text{max}} = 1.52$; $\lambda_{\text{max}} = 455 \text{ nm}$ (sh), $\log \epsilon_{\text{max}} = 1.41$; $\lambda_{\text{max}} = 625 \text{ nm}$, $\log \epsilon_{\text{max}} = 1.53$. The final band of yellow material, obtained by this chromatography contained the Co(III) complex of 'Hosen', was characterised previously.^{10e,f}
19. Baldwin, M. E.; Chan, S. C.; Tobe, M. L. *J. Chem. Soc.* **1961**, 4637–4645.
 20. ^1H NMR (400 MHz, D_2O): The spectrum of the N–H form of the complex shows a complicated manifold of resonances for the methylene protons plus a sharp signal for the alkene protons overlapped by broad NH resonances (δ 6.20, 5.40, 5.25, each 2H); after N-deuteration, δ 5.32 (2H, s, $=\text{CH}_2$), 3.29, 3.03 (dd, 4H, $=\text{CCH}_2\text{N}$), 2.90 (m, 8H, CH_2CH_2); ^{13}C NMR (100 MHz, D_2O): δ 43.14, 54.37, 54.93, 122.33, 139.84.
 21. $[\text{Co}(\mathbf{2})\text{Cl}_2]\text{Cl} \cdot \text{H}_2\text{O} = \text{C}_8\text{H}_{22}\text{Cl}_3\text{CoN}_4\text{O}$, M_r 355.58; monoclinic, space group $P2_1/n$; $a = 6.3112(5)$, $b = 25.488(3)$, $c = 9.2059(9) \text{ \AA}$; $\beta = 106.589(6)^\circ$; 100(2) K. For 2695 independent reflections, $R_1 = 0.038$, $wR_2 = 0.099$, $S = 1.061$. CCDC 778875.
 22. Bosnich, B.; Gillard, R. D.; McKenzie, E. D.; Webb, G. A. *J. Chem. Soc., A* **1967**, 1331–1337. See also Ref. 10b.
 23. Zn powder (2.0 g) was added to a solution of $[\text{Co}(\mathbf{2})\text{Cl}_2]\text{Cl} \cdot \text{H}_2\text{O}$ (2.0 g) in water (100 mL) and 2 mol L^{-1} HCl (100 mL) was then added dropwise with stirring. Stirring was continued for a further 2 h before the mixture was filtered. The filtrate was diluted to 500 mL and absorbed on Dowex 50W-x2 (H^+ form). After using 1 mol L^{-1} HCl (200 mL) to remove Zn(II) and Co(II), the protonated amine was eluted with 4 mol L^{-1} HCl, the eluate was dried under vacuum and the white residue crystallised from water by addition of ethanol. Yield, 1.6 g. Anal. Calcd for $2 \cdot 4\text{HCl} \cdot \text{H}_2\text{O} = \text{C}_8\text{H}_{26}\text{Cl}_4\text{N}_4\text{O}$: C, 28.59; H, 7.80; N, 16.67. Found: C, 28.4; H, 7.9; N, 16.7. ^1H NMR (400 MHz, D_2O): δ 3.35–3.45 (8H, m, $\text{NHCH}_2\text{CH}_2\text{NH}_2$), 3.82 (4H, s, CH_2NH), 5.65 (2H, s, $\text{CH}_2=\text{C}$). ^{13}C NMR (100 MHz, D_2O): δ 43.12, 54.48, 54.91, 122.31, 139.82.
 24. $[\mathbf{2H}_4]\text{Cl}_4 \cdot \text{H}_2\text{O} = \text{C}_8\text{H}_{26}\text{Cl}_4\text{N}_4\text{O}$, M_r 336.13; crystals were grown by vapour diffusion of ethanol into an aqueous solution; monoclinic, space group $P2_1/c$; $a = 6.1584(3)$, $b = 10.8024(8)$, $c = 24.0597(18) \text{ \AA}$; $\beta = 90.633(5)^\circ$; 100(2) K. For 3025 independent reflections, $R_1 = 0.078$, $wR_2 = 0.204$, $S = 1.137$. CCDC 778876.
 25. Salvador, R. L.; Saucier, M. *Can. J. Chem.* **1968**, 46, 751–755.