

- 4628; H.-X. Wei, S. Willis, G. Li, *Tetrahedron Lett.* **1998**, 39, 8203–8206.
- [12] Aluminum: Y. Genisson, C. Massardier, I. Gautier-Luneau, A. E. Greene, *J. Chem. Soc. Perkin. Trans. 1* **1996**, 2869–2872; P. V. Ramachandran, M. V. R. Reddy, M. T. Rudd, J. R. de Alaniz, *Tetrahedron Lett.* **1998**, 39, 8791–8794; G. Li, H.-X. Wei, B. R. Whittlesey, N. N. Batrice, *J. Org. Chem.* **1999**, 64, 1061–1064; P. V. Ramachandran, M. V. R. Reddy, M. T. Rudd, J. R. de Alaniz, *Tetrahedron Lett.* **1999**, 40, 627–630.
- [13] V. J. Lee in *Comprehensive Organic Synthesis*, Vol. 4 (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, p. 125; A. B. Smith, S. N. Kilenyi, *Tetrahedron Lett.* **1985**, 26, 4419–4422; R. C. Larock, K. Narayanan, S. S. Hershberger, *J. Org. Chem.* **1983**, 48, 4377–4380.
- [14] G. Li, H.-X. Wei, J. J. Gao, T. D. Caputo, *Tetrahedron Lett.* **2000**, 41, 1–5.

Base-Specific Minor Groove Site Binding in Metallo-Nucleobase Polymers**

Michelle A. Shipman, Clayton Price, Mark R. J. Elsegood, William Clegg, and Andrew Houlton*

The use of metal–ligand bond formation to generate extended molecular assemblies is now a well established aspect of supramolecular chemistry.^[1] Recently this approach has been combined with the use of organic ligands which possess hydrogen-bonding functionalities in an effort to further introduce directional interactions for structure building.^[1,2] Nucleobases are a useful set of building blocks for forming such structures through a combination of these interactions, and this has been demonstrated in particular in the work of Lippert.^[3] Here we report crystal and molecular structures of two nucleobase coordination polymers containing adenine and guanine. These were formed from reactions of Cu^{II} ions with the respective purine bases derivatized with an alkyldiamine tether.^[4] Analysis of the resulting polymers reveals a base-specific metal ion binding to the minor groove site N3, with coordination observed only with adenine, and formation of a polynucleotide analogue in the case of guanine.

Aqueous solutions containing equimolar equivalents of Cu(NO₃)₂ and the appropriate nucleobase–alkyldiamine (ethylenediamine-N9-ethylguanine, G-Et-en, and ethylenediamine-N9-ethyladenine, A-Et-en) as the hydrochloride salt showed evidence for the formation of Cu:L complexes in the UV/Vis spectra (characteristic band at $\lambda = 650$ nm).^[5] This was also supported by electrospray mass spectrometry data with both solutions indicating the presence of the appropriate [CuL(NO₃)]⁺ cation (m/z : 362, L = Et-G-en; 346, L = Et-A-

en). Slow evaporation of these solutions yielded crystals suitable for single crystal X-ray analyses.^[6]

Compound **1**, [Cu(Et-N7-G-en)(H₂O)₂][NO₃Cl]·(H₂O)_x, is a coordination polymer in which the metal ion adopts a square pyramidal configuration with a {3N:2O} coordination sphere (Figure 1). The three nitrogen donor atoms are provided by

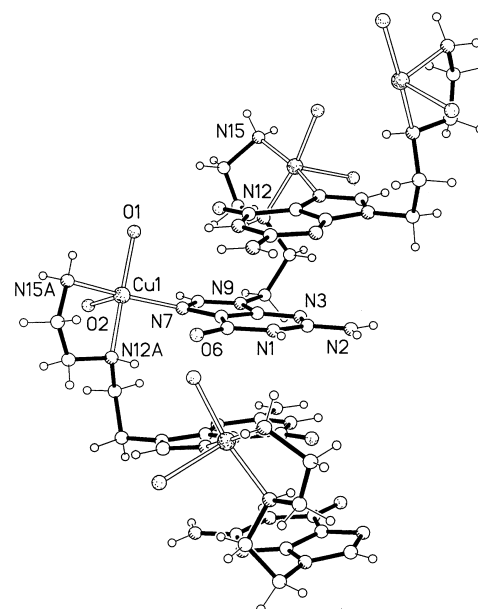


Figure 1. Polymeric chain in **1** formed by coordination through N7 and the diamine function. Metal–ligand bond lengths: Cu–O1 2.012(5), Cu–O2 2.315(7), Cu–N7 1.992(7), Cu–N12A 2.027(6), Cu–N15A 1.977(8) Å. The nucleobase lies at an angle of 70.9° to the plane formed by basal donor atoms (N7/O1/N12A/N15A), with the copper ion lying 0.208 Å above this plane. Each of the guanine residues is hydrogen bonded to uncoordinated nitrate anions (O4NO₃[−]⋯N2 2.873 and O3NO₃[−]⋯N1 2.874 Å).

the diamine function of one ligand and the N7 of the guanine from a second ligand. The extended structure contains stacked guanine bases which are rotated by 90° and inclined at 9.6° with respect to the nearest neighbor (related by a crystallographic fourfold screw axis). The 6-membered rings of the purine heterocycles in the stack lie above one another at a separation of approximately 3.157 Å. Figure 2a shows the bond density representation of the polymer chain to highlight the polymer shape. The helical arrangement has a pitch of 12.627 Å (the unit cell *c*-axis) and the copper ions spiral around the outside of the helical structure with a distance of 6.984 Å between adjacent metal ions in the backbone. Interestingly, this is close to the intrastrand P⋯P distance observed in duplex B-DNA (approximately 6.7 Å).^[7]

In fact, **1** may be considered as a cationic polyguaninyl analogue and bears relevance to several aspects of DNA chemistry. For instance, antisense technology requires a means to enhance the binding between target and probe strands.^[8] Cationic oligonucleotides based on metal ion linkages, as in **1**, may be an effective approach to this problem.

The analogous adenine complex, [CuCl(Et-A-en)][NO₃]·H₂O (**2**), is also polymeric with square pyramidal Cu^{II} ions and a {4N:Cl} donor set of ligands. However, the individual polymer chains exhibit a markedly different topology relative

[*] Dr. A. Houlton, M. A. Shipman, Dr. C. Price, Dr. M. R. J. Elsegood, Prof. W. Clegg
Department of Chemistry
University of Newcastle upon Tyne
Newcastle upon Tyne, NE1 7RU (UK)
Fax: (+44)191-222-6929
E-mail: andrew.houlton@ncl.ac.uk

[**] This work was financially supported by the EPSRC and the BBSRC. The EPSRC mass spectrometry service at the University of Wales, Swansea, is acknowledged.

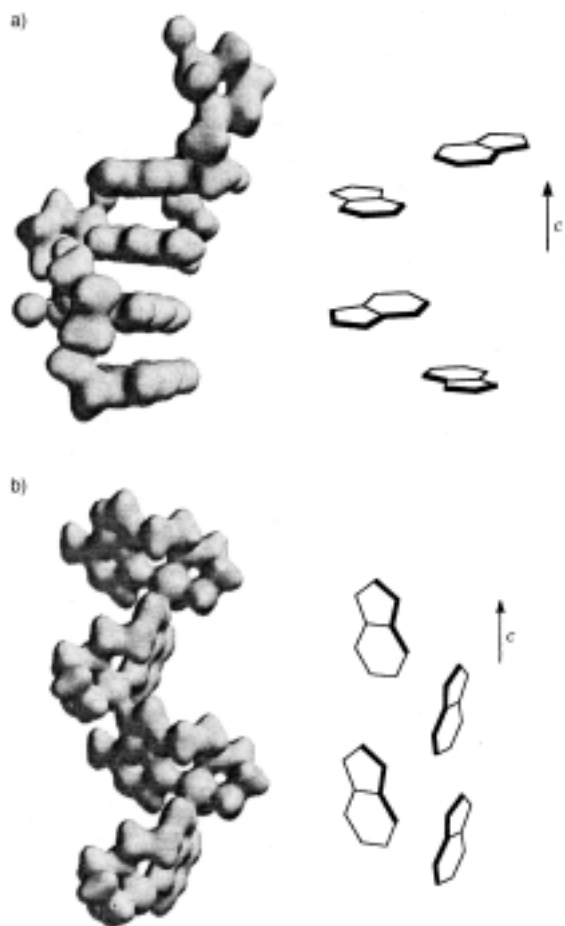


Figure 2. Bond density representation of the polymer topology in **1** and **2** (above and below, respectively).

to **1** (Figure 2b). For example, the nucleobases, no longer essentially parallel, make an angle of 74.4° with neighbors and the Cu...Cu distance is increased to $7.296 \text{ \AA}$.

The observed topologies of **1** and **2** (Figure 2) can be related to the details of the binding mode of the organic ligands. A significant difference is seen with regard to the minor groove based donor sites. While in **1** the metal–nucleobase interactions are restricted to N7, in **2** both the major groove site N7 and the minor groove site N3 coordinate to copper ions. Hence, Et-A-en acts as a tridentate ligand to one copper ion through the diamine function and N3 of the nucleobase (Figure 3). This binding mode generates two chelate rings (5- and 7-membered) and is analogous to that observed in $[\text{CuCl}(\text{NO}_3)(\text{Prop-A-en})]$.^[9] The Cu–N distances are 2.019 and $2.064 \text{ \AA}$ to N3A and N7, respectively, indicating that the bond to N3 is not a weak interaction. These structural data indicate that for the minor groove donor site N3, with Cu^{II} ions at least, binding at adenine is preferred over guanine.

To the best of our knowledge, there is only one structurally characterized example of a guanine N3-bound metal complex, the triplatinum derivative $[\text{N1}, \text{N7}, \text{N3}-\{\text{Pt}(\text{NH}_3)_3\}_3-9\text{-ethylguanine}]$.^[10] For adenine derivatives, however, there is an increasing number of reports of metal ions binding at this site.^[11] Examples of crystallographically characterized metal complexes featuring N3 binding can be seen in the work of

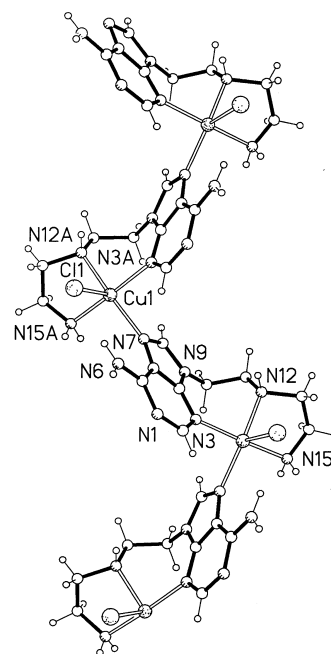


Figure 3. The polymeric chain in **2** involving coordination through N3 and N7 of adenine and through the diamine tether. Metal–ligand bond lengths: Cu–Cl $2.6737(12)$, Cu–N7 $2.064(3)$, Cu–N3A $2.019(3)$, Cu–N12A $2.040(4)$, Cu–N15A $1.980(4) \text{ \AA}$. Adenine lies at an angle of 87.9° to the plane of the basal donor atoms (N7/N3A/N12A/N15A) with the copper ion lying $0.198 \text{ \AA}$ above this plane. The polymer chains propagate along the unit cell *c*-axis.

Lippert, Sigel et al.,^[12] Loeb and co-workers,^[13] and an example reported by ourselves.^[9]

These findings, along with the data here, highlight the issue of base-specific metal ion binding in the minor groove of DNA.^[7, 14] This has been attributed in part to the markedly electronegative electrostatic potential found in the vicinity of adenine...thymine (AT) regions. This phenomenon has been proposed to account for the intrusion of monovalent cations into the minor groove spine of hydration of B-DNA.^[15] Furthermore, Mn^{II} ions have been shown to localize at AT regions in the minor groove of dodecamers.^[16] The observed preference for binding at adenine–N3 compared to guanidine–N3 seen here provides a possible contributing factor for these observations.

In conclusion, we have demonstrated that chelate-tethered nucleobases can form extended molecular assemblies by bridging metal ions. Moreover, the resulting structures, as polynucleotide analogues or in highlighting base-specific binding, are relevant to wider aspects of DNA chemistry.

Experimental Section

G-Et-enH·Cl and A-Et-enH·Cl: The appropriate chloroalkyl purine^[17] was stirred in excess neat anhydrous ethylenediamine at room temperature for 18 hours under an atmosphere of nitrogen. The ethylenediamine was removed in vacuo and the resulting oil dissolved in ethanol with heating. The solution was concentrated in vacuo to precipitate a white powder. This was collected by filtration, washed with ethanol, and vacuum dried. G-Et-enH·Cl: ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$): $\delta = 2.66$ (t, $\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-NH}$), 2.73 (t, $\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-NH}$), 2.85 (t, $\text{NH-CH}_2\text{-CH}_2\text{-GuaN}^9$), 3.98 (t, $\text{NH-CH}_2\text{-CH}_2\text{-GuaN}^9$), 6.62 (s, NH_2), 7.70 (s, H8); MS: m/z (%): 238 (100), $[M^+ - \text{Cl}]$; elemental analysis calcd for $\text{C}_9\text{H}_{16}\text{ClN}_7\text{O}$: C 39.49, H 5.89, N

35.82; found: C 38.84, H 5.59, N 34.46. A-Et-enH·Cl: ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$): δ = 2.85 (t, $\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-NH}$), 2.90 (t, $\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-NH}$), 3.13 (t, $\text{NH-CH}_2\text{-CH}_2\text{-AdeN}^9$), 4.30 (t, $\text{NH-CH}_2\text{-CH}_2\text{-AdeN}^9$), 7.28 (s, NH_2), 8.24 (s, H2), 8.30 (s, H8); MS: m/z (%): 222 (100), $[\text{M}^+ - \text{Cl}]$; elemental analysis calcd for $\text{C}_9\text{H}_{16}\text{ClN}_7$: C 41.94, H 6.26, N 38.04; found: C 41.24, H 6.11, N 38.20.

1 and 2: An equimolar aqueous solution of either G-Et-enH·Cl or A-Et-enH·Cl was added to a solution of copper nitrate in distilled water at room temperature. In each case blue crystals were isolated which were suitable for single crystal X-ray analysis. **1:** MS: m/z (%): 362 (100), $[\text{M}^+]$; elemental analysis calcd for $[\text{CuClCl}_9\text{N}_8\text{O}_4\text{H}_{15}]$: C 27.14, H 3.80, N 28.14; found: C 26.92, H 4.01, N 27.82. (Analyses were for pump-dried samples and correspond to an anhydrous form of **1**.) **2:** MS: m/z (%): 346 (100), $[\text{M}^+]$; elemental analysis calcd for $[(\text{CuClCl}_9\text{N}_7\text{H}_{15})(\text{NO}_3) \cdot \text{H}_2\text{O}]$: C 27.00, H 4.28, N 28.00; found: C 27.23, H 3.92, N 27.84.

Received: January 21, 2000 [Z14580]

- [1] *Comprehensive Supramolecular Chemistry* (Eds.: J. L. Atwood, J.-M. Lehn), Pergamon, New York, **1996**.
- [2] See, for example: a) A. D. Burrows, C.-W. Chan, M. M. Chowdhry, J. E. McGrady, D. M. P. Mingos, *Chem. Soc. Rev.* **1995**, 24, 329–339; b) D. Braga, F. Grepioni, G. R. Desiraju, *J. Organomet. Chem.* **1997**, 548, 33–43; c) M. D. Ward, *Chem. Soc. Revs.* **1997**, 26, 365–375; d) M. Munakata, L. P. Wu, M. Yamamoto, T. KurodaSowa, M. Maekawa, *J. Am. Chem. Soc.* **1996**, 118, 3117–3124.
- [3] See, for example: a) J. A. R. Navarro, B. Lippert, *Coord. Chem. Rev.* **1999**, 186, 653–667; b) H. Rauter, I. Mutikainen, M. Blomberg, C. J. L. Lock, P. Amoochoa, E. Freisinger, L. Randaccio, E. Zangrando, E. Chiarparin, B. Lippert, *Angew. Chem.* **1997**, 109, 1353–1357; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 1296–1301; c) R. K. O. Sigel, S. M. Thompson, E. Freisinger, B. Lippert, *Chem. Commun.* **1999**, 19–20; d) J. A. R. Navarro, M. B. L. Janik, E. Freisinger, B. Lippert, *Inorg. Chem.* **1999**, 38, 426–432.
- [4] a) C. Price, M. R. J. Elsegood, W. Clegg, N. H. Rees, A. Houlton, *Angew. Chem.* **1997**, 109, 1823–1825; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 1762–1764; b) C. Price, N. H. Rees, M. R. J. Elsegood, W. Clegg, A. Houlton, *J. Chem. Soc. Dalton Trans.* **1998**, 2001–2006.
- [5] J. Bjerrum, E. J. Nielsen, *Acta Chem. Scand.* **1948**, 297–318; b) H. B. Jonassen, T. H. Dexter, *J. Am. Chem. Soc.* **1949**, 71, 1553–1556.
- [6] a) Crystal data for **1**: $[\text{C}_9\text{H}_{19}\text{CuN}_7\text{O}_3][\text{NO}_3]\text{Cl}$, $M_r = 434.3$, tetragonal, space group $I4_1/a$, $a = 25.184(3)$, $c = 12.6272(15)$ Å, $V = 8008.8(16)$ Å³, $Z = 16$, $\rho_{\text{calcd}} 1.441$ g cm^{−3}; $\text{MoK}\alpha$ radiation, $\lambda = 0.71073$ Å, $\mu = 1.16$ mm^{−1}, $T = 160$ K. 17849 measured reflections were corrected for absorption, 3516 were unique ($R_{\text{int}} = 0.152$, $\theta = 25.0^\circ$); $R = 0.0946$ (F values, $F^2 > 2\sigma$), $R_w = 0.2497$ (F^2 values, all data), GOF = 1.075 for 217 parameters, residual electron density between 0.64/−0.53 e Å^{−3}. The structure contains substantial regions of diffuse electron density modelled by the SQUEEZE procedure (A. L. Spek, PLATON, University of Utrecht, The Netherlands, **1999**) and corresponding to disordered chloride anion and approximately 6 water molecules per asymmetric unit according to total electron density and volumes. The chloride anion, required for overall charge balance and by chemical analysis results, is included in the chemical formula and derived crystal data above; addition of 6 H₂O gives $M_r = 542.3$, $\rho_{\text{calcd}} = 1.799$ g cm^{−3}. This substantial disorder is responsible for the generally weak diffraction data. Other program used: SHELXTL (G. Sheldrick, Bruker AXS Inc., Madison, WI, USA, 1998, Version 5.1). b) Crystal data for **2**: $[\text{C}_9\text{H}_{15}\text{ClCuN}_7][\text{NO}_3] \cdot \text{H}_2\text{O}$, $M_r = 400.3$, monoclinic, space group $P2_1/c$, $a = 10.767(2)$, $b = 11.754(2)$, $c = 11.875(2)$ Å, $\beta = 100.287(4)^\circ$, $V = 1478.7(5)$ Å³, $Z = 4$, $\rho_{\text{calcd}} 1.798$ g cm^{−3}; $T = 160$ K. The very small crystal size ($0.11 \times 0.03 \times 0.02$ mm) and the relatively poor quality necessitated data collection with synchrotron radiation (SRS at Daresbury Laboratory, station 9.8, $\lambda = 0.6920$, $\mu = 1.69$ mm^{−1}). 8557 reflections were measured, 3135 were unique ($R_{\text{int}} = 0.053$, $\theta = 26.0^\circ$); $R = 0.0529$, $R_w = 0.1425$, GOF = 0.976 for 229 parameters, residual electron density between 2.03/−0.99 e Å^{−3} with the largest features close to Cu. c) 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-139134 (**1**) and -139135 (**2**). Copies of the data

can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

- [7] *Nucleic Acids in Chemistry and Biology* (Eds. G. M. Blackburn, M. J. Gait), IRL Press, Oxford, **1990**; b) *Bioinorganic Chemistry* (Eds. I. Bertini, H. B. Gray, S. J. Lippard, J. S. Valentine), University Science Books, California, **1994**; c) G. Pratviel, J. Bernadou, B. Meunier, *Adv. Inorg. Chem.* **1998**, 45, 251–312, and references therein.
- [8] E. Uhlmann, A. Peymann, *Chem. Rev.* **1990**, 90, 543–584.
- [9] C. Price, M. R. J. Elsegood, W. Clegg, A. Houlton, *J. Chem. Soc. Chem. Commun.* **1995**, 2285–2286.
- [10] G. Rauduschlsieber, H. Schollhorn, U. Thewalt, B. Lippert, *J. Am. Chem. Soc.* **1985**, 107, 3591–3595.
- [11] a) C. A. Blindauer, A. Holy, H. Dvorakova, H. Sigel, *J. Biol. Inorg. Chem.* **1998**, 3, 423–433; b) B. Song, S. A. Sajadi, F. Gregan, N. Pronayova, H. Sigel, *Inorg. Chim. Acta* **1998**, 273, 101–105; c) C. A. Blindauer, A. H. Emwas, A. Holy, H. Dvorakova, E. Sletten, H. Sigel, *Chem. Eur. J.* **1997**, 3, 1526–1536; d) S. S. Massoud, H. Sigel, *Eur. J. Biochem.* **1989**, 179, 451–458; e) H. Sigel, *Coord. Chem. Rev.* **1995**, 144, 287–319, and references therein.
- [12] C. Meiser, B. Song, E. Freisinger, M. Peilert, H. Sigel, B. Lippert, *Chem. Eur. J.* **1997**, 3, 388–398.
- [13] J. E. Kickham, S. J. Loeb, S. L. Murphy, *Chem. Eur. J.* **1997**, 3, 1203–1213.
- [14] a) R. Lavery, B. Pullman, *J. Biomol. Struct. Dyn.* **1985**, 5, 1021–1032; b) L. D. Higgins, M. S. Searle, *Chem. Commun.* **1999**, 1861–1862, and references therein.
- [15] M. A. Young, B. Jayaram, D. L. Beveridge, *J. Am. Chem. Soc.* **1997**, 119, 59–69.
- [16] N. V. Hud, J. Feigon, *J. Am. Chem. Soc.* **1997**, 119, 5756–5757.
- [17] a) D. T. Browne, J. Eisinger, N. J. Leonard, *J. Am. Chem. Soc.* **1968**, 90, 7302–7323; b) O. F. Schall, G. W. Gokel, *J. Am. Chem. Soc.* **1994**, 116, 6089–6100; c) M. R. Harnden, R. L. Jarvest, T. H. Bacon, M. R. Boyd, *J. Med. Chem.* **1987**, 30, 1636–1642; d) M. Ashwell, C. Bleasdale, B. T. Golding, I. K. O'Neill, *J. Chem. Soc. Chem. Commun.* **1990**, 955–956.

Coordinated and Clathrated Molecular Diiodine in $[\text{Rh}_2(\text{O}_2\text{CCF}_3)_4\text{I}_2] \cdot \text{I}_2^{**}$

F. Albert Cotton,* Evgeny V. Dikarev, and Marina A. Petrukhina

The tetrakis(trifluoroacetate) dirhodium(II) molecule, $[\text{Rh}_2(\text{O}_2\text{CCF}_3)_4]$, has been shown to be a versatile, bifunctional Lewis acid, able to coordinate in solution an extraordinary variety of donor molecules to the axial positions.^[1] Recent work in our laboratory employing a “solventless” synthetic technique has further extended the chemical and structural range of products to include those with aromatic and alkyne ligands, polymeric and oligomeric structures, and reaction products with dirhodium(II) units.^[2] As a result of finding $[\text{Rh}_2(\text{O}_2\text{CCF}_3)_4]$ to be such an exceptionally avid

[*] Prof. F. A. Cotton, Dr. E. V. Dikarev, Dr. M. A. Petrukhina
Laboratory for Molecular Structure and Bonding
Department of Chemistry
Texas A&M University
P.O. Box 30012, College Station, TX 77842-3012 (USA)
Fax: (+1) 979-845-9351
E-mail: cotton@tamu.edu

[**] Studies of Dirhodium(II) Tetrakis(trifluoroacetate), part 7. This work was supported by the Robert A. Welch Foundation. Part 6: ref. [2c].