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Synthesis and crystal and molecular structure of a tetranuclear cluster based on the rhenium(III)-bisorganohydrazino core:

$[\text{Re}(\text{HNNC}_4\text{H}_3\text{N}_2)(\text{NNC}_4\text{H}_3\text{N}_2)(\text{OCH}_3)_2]_4$

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Abstract

Reaction of NH_4ReO_4 with excess 2-hydrazinopyrimidine in methanol yields $[\text{Re}(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2\text{H})(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)\text{Cl}_3]$ (**1**). Attempts to recrystallize **1** by slow diffusion of methanol into DMF after 8 months produced black crystals of $[\text{Re}(\text{HNNC}_4\text{H}_3\text{N}_2)(\text{NNC}_4\text{H}_3\text{N}_2)(\text{OCH}_3)_2]_4$ (**2**). The structure of **2** consists of isolated tetranuclear clusters, constructed from $\{\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2)(\text{OCH}_3)_2\}$ units linked through the β -nitrogen of the chelating organodiazene ligand of adjacent units into a box-like aggregate.

Keywords

Crystal structures; Rhenium complexes; Organohydrazino complexes

1. Introduction

The continuing expansion of technetium- and rhenium-organohydrazine chemistry reflects not only an interest in the fundamental coordination chemistry and bonding of an unusual and robust functional group [1], but also practical applications to the development of radiopharmaceuticals [2,3]. In this latter respect, the chemistry of technetium with 2-hydrazino-nicotinamide derivatized peptides has received considerable attention [4–6]. In modeling the chemistry of the Tc-organohydrazino core of these radiopharmaceuticals, we have developed the chemistry of a class of compounds derived from the rhenium bis-pyridinodiazene core, $\{\text{Re}(\eta^2\text{-HNNC}_5\text{H}_4\text{N})(\eta^1\text{-NNC}_5\text{H}_4\text{NH})\}^{3+}$, shown schematically [7] (Scheme 1). An unusual feature of these compounds is the presence of the organohydrazine ligands as the chelating, neutral organodiazene (**A**) and the neutral pyridinium-diazenido (**B**) in the parent compound $[\text{Re}(\eta^2\text{-HNNC}_5\text{H}_4\text{N})(\eta^1\text{-NNC}_5\text{H}_4\text{-NH})\text{Cl}_3]$ and in the neutral chelating form (**A**) and as the mononegative anionic organodiazenido ligand (**C**) in the derivatives of the type $[\text{Re}(\eta^2\text{-HNNC}_5\text{H}_4\text{N})(\eta^1\text{-NNC}_5\text{H}_4\text{N})(\text{L})(\text{LL})]$ (where L is a monodentate mononegative ligand and LL is a bidentate mononegative ligand) [8] (Scheme 2).

Since hydrazinopyrimidine offers some advantages over hydrazinopyridine in terms of solubility and derivatization, we undertook an investigation of the chemistry of technetium- and rhenium 2-hydrazinopyrimidine complexes as models for potential bifunctional chelate-

metal cores. The chemistry appeared analogous to that of 2-hydrazinopyridine in the facile synthesis of $[\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2\text{H})\text{Cl}_3]$ (**1**) from NH_4ReO_4 . However, attempts to recrystallize **1** from dimethylformamide–MeOH yielded the unusual tetranuclear cluster $[\text{Re}(\text{HNNC}_4\text{H}_3\text{N}_2)(\text{NNC}_4\text{H}_3\text{N}_2)(\text{OCH}_3)_2]_4$ (**2**).

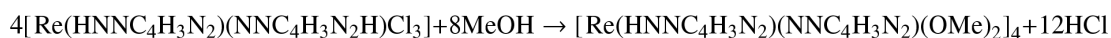
2. Results and discussion

The reaction of perrhenate with 2-hydrazinopyrimidine in MeOH–HCl involves four-electron reduction of the rhenium from the Re(VII) to the Re(III) form with concomitant two-electron oxidation and two proton elimination of each of two hydrazinopyrimidine ligands.



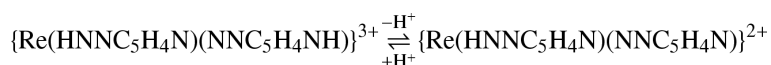
The reaction chemistry is analogous to that previously described for $[\text{Re}(\eta^2\text{-HNNC}_5\text{H}_4\text{N})(\eta^1\text{-NNC}_5\text{H}_4\text{NH})\text{Cl}_3]$ [9].

Compound **1** was insoluble in most common organic solvents, with the exception of DMF. A DMF–MeOH solution, left to stand for 8 months, yielded black crystals of the tetranuclear cluster $[\text{Re}(\eta^2\text{-HNNC}_4\text{-H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2)(\text{OCH}_3)_2]_4 \cdot 2\text{MeOH}$ (**2**·2MeOH). The synthesis of **2** from **1** requires in a formal sense the substitution of two chloride ligands on each Re site by two methoxy groups and the elimination of an HCl molecule from each Re site, which necessitates deprotonation of one of the organodiazene ligands of each $[\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2\text{H})]^{3+}$ core. In view of the facile deprotonation of the pyridinium-diazenido site (**B**) observed in previous studies, it is anticipated that the pyrimidinium diazido site of **1** provides the proton.



As shown in Fig. 1, the structure of **2**·2MeOH consists of tetranuclear clusters and isolated MeOH molecules of crystallization. The cluster exhibits a square arrangement of Re sites linked through the pyrimidinodiazene ligands which chelate to one Re center through the α -nitrogen of the hydrazine and one pyrimidine ring nitrogen and bridge to a second Re site through the β -nitrogen of the hydrazine. The coordination geometry at the Re centers is distorted octahedral, defined by the chelating nitrogen donors of the pyrimidinodiazene ligand, the α -nitrogen of a terminal pyrimidinodiazene ligand, the oxygen donors of two methoxy groups, and the β -nitrogen of an organodiazene ligand of a neighboring $\{\text{Re}(\text{HNNC}_4\text{H}_3\text{N}_2)(\text{NNC}_4\text{H}_3\text{N}_2)\}^{2+}$ subunit.

The final difference Fourier maps clearly exhibit the protonation of the α -nitrogens of the chelating pyrimidinodiazene ligands. There are no excursions of electron density associated with any of the other nitrogen sites of the cluster, confirming the deprotonation of the pyrimidine nitrogen of the parent compound. This deprotonation pattern is consistent with the decreasing basicity of the nitrogen sites: α -hydrazine nitrogen > pyrimidine nitrogen > β -hydrazine nitrogen. It is also noteworthy that substitution chemistry of **1** follows the same pattern as that of $[\text{Re}(\text{HNNC}_5\text{H}_4\text{N})(\text{NNC}_5\text{-H}_4\text{NH})\text{Cl}_3]$ wherein the overall charge of the core is adjusted by proton exchange:



The metrical parameters associated with the $\{\text{Re}(\text{HNNC}_4\text{H}_3\text{N}_2)(\text{NNC}_4\text{H}_3\text{N}_2)\}^{2+}$ cores of **2** are unexceptional. The nearly planar arrangement of this core unit and the *syn* disposition of the pyrimidine rings with respect to the N(3)–Re–N(5) vector are also common features of this core.

The isolation of **2** upon prolonged exposure of **1** in DMF/methanol confirms that cores of the type $\{\text{M}(\eta^2\text{-HNNR})(\eta^1\text{-NNRH}_x)\}^{n+}$ ($x = 0, 1$) are chemically robust, surviving both reactions at ancillary sites and treatment in organic and mixed organic–aqueous media. However, the structural characterization also reveals a complex coordination chemistry which often results in complications upon extending the chemistry to radiopharmaceutical applications.

3. Experimental

3.1. Preparation of $[\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2\text{H})\text{Cl}_3]$ (**1**)

In a 25 ml Schlenk flask was placed $[\text{NH}_4][\text{ReO}_4]$ (0.015 g, 0.056 mmol), 2-hydrazinopyrimidine (0.050 g, 0.450 mmol) and 2.0 ml methanol. The reaction was stirred briefly and 0.01 ml of aqueous 36% HCl (0.30 mmol) was added dropwise. The reaction was heated to reflux for 20 min. The dark red solid was washed with 5 ml portions of MeOH and dried (0.0141 g, 49.5%). *Anal.* Calc. for $\text{C}_8\text{N}_8\text{H}_8\text{Cl}_3\text{Re}$: C, 18.9; H, 1.58; N, 22.0. Found: C, 18.9; H, 1.62; N, 21.5%

3.2. Preparation of $[\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2)(\text{OMe})_2]_4 \cdot 2\text{MeOH}$ (**2** · 2MeOH)

Compound **1** was dissolved in *N,N*-dimethylformamide. The solution was carefully layered with methanol. After 8 months, black crystals of **2** were observed on the sides of the test tube (Yield: 0.0012 g, 15%). *Anal.* Calc. for $\text{C}_{10.5}\text{H}_{15}\text{N}_8\text{O}_{2.5}\text{Re}$: C, 26.3; H, 3.13; N, 23.4. Found: C, 26.1; H, 3.06; N, 23.1%

3.3. X-ray crystallography

Data were collected on a Bruker SMART diffractometer system using graphite monochromated Mo K α radiation ($\lambda(\text{Mo K}\alpha) = 0.71073 \text{ \AA}$). Data collection was carried out at low temperature (85–94 K). The crystal parameters and other experimental details of the data collection are summarized in Tables 1–3. A complete description of the details of the crystallographic methods is given in the supporting information. The structure was solved by direct methods [10]. Neutral atom scattering factors were taken from Cromer and Waber [11] and anomalous dispersion corrections were taken from those of Creagh and McAuley [12]. All calculations were performed using SHELXTL [10]. Non-hydrogen atoms were refined anisotropically. No anomalies were encountered in the refinements of any of the structures. Atomic positional parameters for the structures have been deposited with the Cambridge Structural Database.

4. Supplementary material

All atomic and thermal parameters and all interatomic angles are available from the authors upon request. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as publication no. CCDC 139541. Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: <http://www.ccdc.cam.ac.uk>).

Acknowledgments

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References

1. Hirsch-Kuchma M, Nicholson T, Davison A, Jones AG. *J. Chem. Soc., Dalton Trans* 1997;3189.
2. Abrams MJ, Juweid J, ten Kate CI, Schwartz DA, Hauser MM, Gaul FE, Fucello AJ, Rubin RH, Strauss HW, Zubieta J, Fischman AJ. *J. Nucl. Med* 1990;31:2022. [PubMed: 2266401]
3. Schwartz DA, Abrams MJ, Hansen MM, Gaul FE, Larsen SK, Rauh D, Zubieta J. *Bioconjugate Chem* 1991;2:33.
4. (a) Dragotakes SO, Tompkins RG, Rubin RH, Fischman AJ, Babich JW, Graham W, Barrow SA. *J. Nucl. Med* 1993;34:2176. [PubMed: 8254406] (b) Kroon D, Graham W, Abrams MJ, Tompkins RC, Rubin RH, Fischman AJ, Babich JW, Solomon H, Pike MC. *J. Nucl. Med* 1994;34:1964. [PubMed: 8229242] (c) Fischman AJ, Babich JW, Rubin RH. *Semin. Nucl. Med* 1994;24:154. [PubMed: 8023171] (d) Babich JW, Fischman AJ. *Nucl. Med. Biol* 1995;22:25. [PubMed: 7735166] (e) Babich JW, Graham W, Barrow SA, Fischman AJ. *Nucl. Med. Biol* 1995;22:643. [PubMed: 7581175]
5. Liu S, Edwards DS, Looby RJ, Harris AR, Poirier MJ, Barrett JA, Hemingway SJ, Carroll TR. *Bioconjugate Chem* 1996;7:63. (b) Edwards DS, Liu S. *Transition Met. Chem* 1998;22:425. (c) Barrett JA, Crocker AC, Damphouse DJ, Hemingway SJ, Liu S, Edwards DS, Harris AR, Looby RJ, Lazewatsky JL, Kagan M, Mazaika TJ, Carroll TR. *Bioconjugate Chem* 1997;8:155. (d) Liu S, Edwards DS, Harris AP, Hemingway SJ, Barrett JA. *Inorg. Chem* 1999;38:1326. and references therein. [PubMed: 11670921]
6. Liu S, Edwards DS. *Chem. Rev* 1999;99:2235. [PubMed: 11749481]
7. Rose DJ, Maresca KP, Nicholson T, Davison A, Jones AG, Babich J, Fischman A, Graham W, DeBord JRD, Zubieta J. *Inorg. Chem* 1998;37:2701. [PubMed: 11670406]
8. Hirsch-Kuchma M, Nicholson T, Davison A, Davis WM, Jones AG. *Inorg. Chem* 1997;36:3237. [PubMed: 11669986]
9. Nicholson T, Cook J, Davison A, Rose DJ, Maresca KP, Zubieta J, Jones AG. *Inorg. Chim. Acta* 1996;252:421.
10. Madison, WI: SHELXTL PC™ Siemens Analytical X-ray Instruments, Inc.; 1990.
11. Cromer, DT.; Waber, JT. *International Tables for X-ray Crystallography*. Vol. vol. IV. Birmingham, UK: Kynoch Press; 1974.
12. Creagh, DC.; McAuley, JWJ. *International Tables for X-ray Crystallography*. Vol. vol. C. Boston, MA: Kluwer Academic; 1992. Table 4

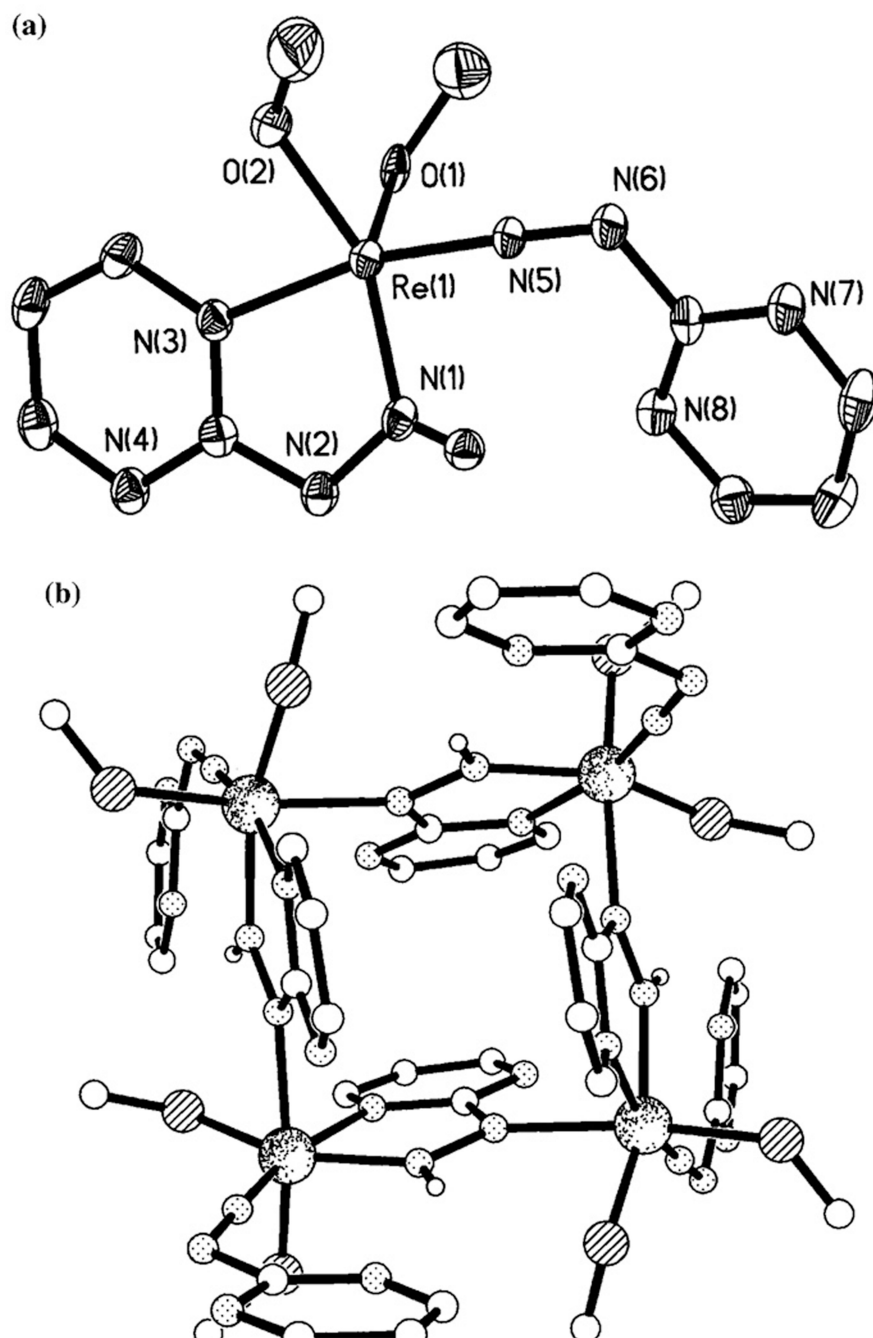
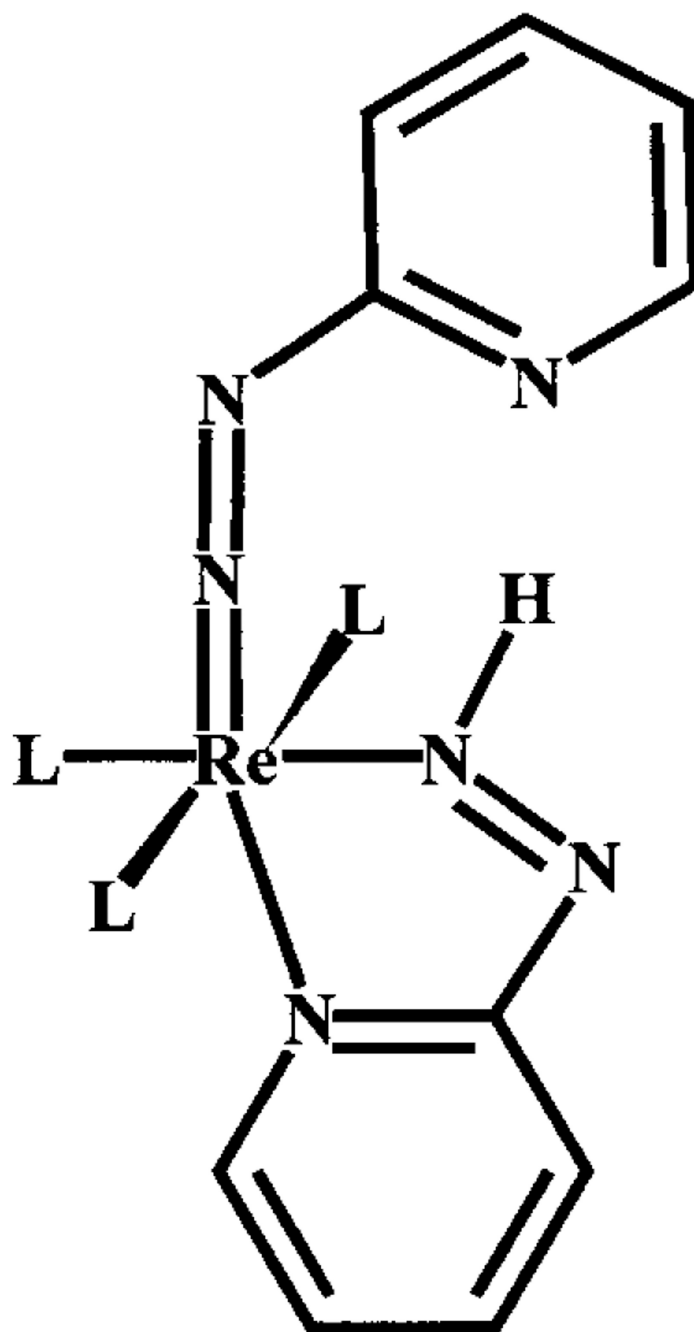
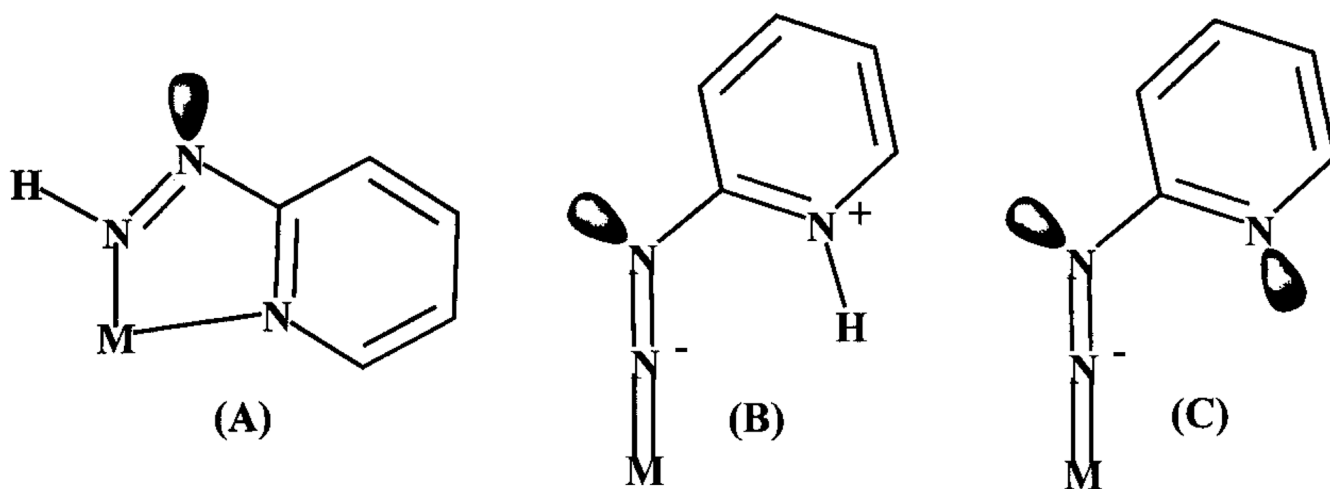


Fig. 1.

(a) A view of the asymmetric unit of **2**, showing the atom-labeling scheme and 50% thermal ellipsoids. (b) A view of the tetranuclear cluster. Re sites are large speckled spheres; nitrogen atoms are dotted spheres; carbon atoms are intermediate, lined spheres.



Scheme 1.



Scheme 2.

Table 1

Summary of crystal data for the structural study of $[\text{Re}(\eta^2\text{-HNNC}_4\text{H}_3\text{N}_2)(\eta^1\text{-NNC}_4\text{H}_3\text{N}_2)(\text{OMe})_2]_4 \cdot 2\text{MeOH}$ ($2 \cdot 2\text{MeOH}$)

Empirical formula	$\text{C}_{10.5}\text{H}_{15}\text{N}_8\text{O}_{2.5}\text{Re}$
Formula weight	479.51
Crystal system	tetragonal
Space group	$I4_1/a$
a (Å)	12.0690(4)
b (Å)	12.0690(4)
c (Å)	39.342(2)
Volume (Å ³)	5730.5(3)
Z	16
Density (g cm ⁻³)	2.223
R_1^a	0.0450
wR_2^b	0.0727

$$^a R_1 = \Sigma(F_o - F_c) / \Sigma(F_o).$$

$$^b wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma w(F_o^2)^2]^{1/2}.$$

Table 2Atomic positional parameters ($\times 10^4$) and isotropic thermal parameters ($\text{\AA}^2 \times 10^3$) for **2**

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq}
Re(1)	2962(1)	9592(1)	1184(1)	21(1)
O(1)	2724(3)	11 058(3)	931(1)	20(1)
O(2)	1716(3)	9016(3)	920(1)	29(1)
O(3)	5662(8)	8154(8)	−494(2)	48(2)
C(1)	5076(4)	9179(4)	818(1)	21(1)
C(2)	5468(5)	8785(4)	265(1)	26(1)
C(3)	4347(5)	8852(4)	177(1)	27(1)
C(4)	3614(5)	9036(4)	434(1)	24(1)
C(5)	2878(4)	10 719(4)	2101(1)	22(1)
C(6)	3210(5)	11 137(5)	2651(1)	34(1)
C(7)	4323(5)	11 223(5)	2587(2)	33(1)
C(8)	4654(5)	11 089(4)	2252(1)	27(1)
C(9)	1818(6)	1166(6)	996(2)	43(2)
C(10)	731(6)	8722(8)	1039(2)	65(2)
C(11)	5000	7500	−643(3)	82(4)
N(1)	4492(4)	9764(4)	1327(1)	21(1)
N(2)	5391(4)	9470(3)	1139(1)	21(1)
N(3)	3955(4)	9178(3)	759(1)	21(1)
N(4)	5840(4)	8940(4)	581(1)	24(1)
N(5)	2433(3)	10 072(4)	1578(1)	22(1)
N(6)	2098(4)	10 402(4)	1859(1)	25(1)
N(7)	2459(4)	10 890(4)	2412(1)	26(1)
N(8)	3957(4)	10 824(4)	2005(1)	24(1)

Table 3Selected bond lengths (Å) and angles (°) for **2**^a

Re(1)–N(5)	1.775(4)
Re(1)–N(1)	1.941(4)
Re(1)–O(2)	1.957(4)
Re(1)–O(1)	2.051(3)
Re(1)–N(3)	2.115(4)
Re(1)–N(2)#1	2.170(4)
N(1)–N(2)	1.361(6)
N(5)–N(6)	1.241(6)
N(5)–Re(1)–N(1)	93.11(19)
N(5)–Re(1)–O(2)	107.67(18)
N(1)–Re(1)–O(2)	157.43(17)
N(5)–Re(1)–O(1)	95.27(17)
N(1)–Re(1)–O(1)	100.49(16)
O(2)–Re(1)–O(1)	86.59(15)
N(5)–Re(1)–N(3)	166.18(18)
N(1)–Re(1)–N(3)	73.45(17)
O(2)–Re(1)–N(3)	86.11(16)
O(1)–Re(1)–N(3)	84.29(15)
N(5)–Re(1)–N(2)#1	92.36(18)
N(1)–Re(1)–N(2)#1	88.39(17)
O(2)–Re(1)–N(2)#1	82.18(16)
O(1)–Re(1)–N(2)#1	167.93(14)
N(3)–Re(1)–N(2)#1	90.51(15)
N(2)–N(1)–Re(1)	124.9(3)
N(1)–N(2)–Re(1)#3	124.7(3)
N(6)–N(5)–Re(1)	177.8(4)

^aSymmetry transformations used to generate equivalent atoms: #1 $-y+5/4, x+1/4, -z+1/4$; #2 $-x+1, -y+3/2, z+0$; #3 $y-1/4, -x+5/4, -z+1/4$.