Published in final edited form as:

Polyhedron. 2009 March 12; 28(4): 775–781. doi:10.1016/j.poly.2008.12.006.

Synthesis and Characterization of a Tetramethyl Furanone Functionalized Diiminedioxime, A Potential Ligand for ^{64}Cu Radiopharmaceuticals, and its Copper(II) and Nickel(II) Complexes

Salma Kiani^{a,†}, Richard J. Staples^{b,‡}, S. Ted Treves^a, and Alan B. Packard^{a,*}

^a Division of Nuclear Medicine, Children's Hospital Boston, Harvard Medical School, Boston, MA 02115

^b Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA 02138

Abstract

As part of our on-going effort to develop ^{64}Cu -based radiopharmaceuticals for PET (positron emission tomography) imaging of multidrug resistance in cancer, we prepared a tetramethylfuranone-functionalized diiminedioxime ligand, TMFPreH (TMFPreH = 4-[3-(4-Hydroxyimino-2,2,5,5-dimethyl-dihydro-furan-3-ylideneamino)-propylimino]-2,2,5,5-tetramethyl-dihydro-furan-3-one oxime) and its Cu(II) and Ni(II) complexes. When the copper(II) complex was prepared from Cu(CIO₄)₂ in ethanol, it was isolated as a Cu(II)-bridged dimer, but when it was prepared from Cu(OAc)₂ and heated in acetone, an unusual example of an acetone adduct of the ligand is formed by reduction of one of the imine double bonds by the solvent. The Ni(II) complex is square pyramidal with the perchlorate counterion at the apex.

Keywords

Acetone adduct; crystal structures; diiminedioxime; Cu(II) complexes; Ni(II) complexes

1. Introduction

Positron emission tomography (PET) is a valuable diagnostic tool, but its availability is limited because the half-lives of many PET radionuclides (e.g., ^{11}C – 20 min.) are too short to allow their delivery beyond the site where they are produced. A nationwide network has been established in the U.S. to distribute ^{18}F [FDG] (^{18}F , $t_{1/2}$ = 110 min.; FDG = 2-fluorodeoxyglucose), but there are a limited number of studies that can be performed

*Corresponding author. tel.: 617-355-7539; fax: 617-730-0619, e-mail address: alan.packard@childrens.harvard.edu (Alan B. Packard).

[†]Present Address: Antisoma, Cambridge, MA 02139

[‡]Present Address: Department of Chemistry, Michigan State University, East Lansing, MI 48824

Supplementary Material

CCDC 211872 (1), 211871 (2), and 211873 (3) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

with ^{18}F [FDG]. There is, therefore, considerable interest in the development of PET radiopharmaceuticals based on positron-emitting radionuclides with longer half-lives (e.g., ^{124}I , $t_{1/2} = 4.2$ d; $^{94\text{m}}\text{Tc}$, $t_{1/2} = 52$ min.; ^{64}Cu , $t_{1/2} = 12.7$ h) that can complement ^{18}F [FDG].

We are currently developing a ^{64}Cu radiopharmaceutical for evaluating multidrug resistance (MDR) in tumors and myocardial perfusion. Multidrug resistance is characterized by resistance of a malignant lesion to a range of structurally diverse chemotherapeutic agents, including adriamycin, vincristin, and vinblastin [1]. Pwinica-Worms, et al. observed that the SPECT (single-photon emission-computed tomography) myocardial perfusion agent $^{99\text{m}}\text{Tc}$ -MIBI (MIBI = methoxyisobutylisonitrile) is a substrate for P-glycoprotein (Pgp), a protein implicated in MDR [2], and other cationic $^{99\text{m}}\text{Tc}$ myocardial perfusion agents were also subsequently reported to be substrates for Pgp [3,4]. There are many technical advantages to performing these studies with PET rather than SPECT, but the PET radiopharmaceuticals that are currently available to evaluate myocardial perfusion suffer from significant limitations: $[^{13}\text{N}]\text{NH}_3$ (^{13}N , $t_{1/2} = 10$ min.) is only available at facilities with on-site cyclotrons, and ^{82}Rb (^{82}Rb , $t_{1/2} = 1.3$ min.), which is available from the $^{82}\text{Sr}/^{82}\text{Rb}$ generator [5], is extremely expensive, and in contrast to $^{99\text{m}}\text{Tc}$ -MIBI, have not been shown to be substrates for Pgp.

The $^{99\text{m}}\text{Tc}$ myocardial perfusion agents that are substrates for Pgp are all lipophilic cations, so our starting point was the synthesis of a lipophilic cationic Cu(II) complex. A suitable complex was prepared by adding alkyl substituents to a prototype diiminedioxime ligand [6]. In an animal model and in cell culture this complex showed uptake similar to that observed for $^{99\text{m}}\text{Tc}$ -MIBI [6]. But this compound also shows unacceptably high liver uptake, similar to that observed for early versions of the $^{99\text{m}}\text{Tc}$ myocardial perfusion agents [7]. For $^{99\text{m}}\text{Tc}$ -MIBI, the liver uptake was significantly decreased by inclusion of ether moieties into the ligand [8]. The myocardial perfusion agent $^{99\text{m}}\text{Tc}$ -Q12 includes alkyl ethers as well as a furanone moiety [9]. Based on these observations, we prepared a furanone derivative of the prototype diiminedioxime ligand (Chart 1) in an effort to decrease the liver uptake of the ^{64}Cu complex. In contrast to the ligand used in $^{99\text{m}}\text{Tc}$ -Q12, which are furanone analogs of salen and therefore dianionic when complexed to a metal, this new ligand is monoanionic on coordination to Cu (II) thereby producing a monocationic copper complex.

The synthesis of the ligand proceeded as expected, and when the Cu(II) and Ni(II) complex were prepared in ethanol, the crystal structures were similar to those of other diiminedioxime complexes. However, when the Cu(II) complex was prepared from $\text{Cu}(\text{OAc})_2$ in warmed mixture of acetonitrile and acetone, the crystal structure revealed an unusual example of the acetone bound to the carbon atom of what had formerly been one of the imine double bonds.

2. Experimental

All manipulations were performed in aerobic conditions using reagents as received except for ethanol, which was distilled from sodium under argon immediately before use. FTIR spectra were obtained using a Bruker Vector 22 (Billerica, MA) equipped with a Pike MIRacle single-bounce ATR accessory (Madison, WI). Elemental analyses were performed by Atlantic Microlab, Inc. (Atlanta, GA). ^1H NMR spectra were obtained using a Varian Gemini 200 or 500 MHz spectrometer (Palo Alto, CA), and chemical shifts are reported relative to the TMS. Proton shifts are annotated as follows: assignment, integral, multiplicity, coupling constant.

Caution: Although no problems were observed with these complexes, perchlorate salts are potentially explosive and should be handled with care and only in small quantities.

2.1. 2,2,5,5-Tetramethyl-furan-3,4-dione monooxime (TMF oxime)

The oxime was prepared by treating 2,2,5,5-tetramethylfuranone (TMF, Aldrich) with MeONO as described by Finke [10]. Briefly, a solution of TMF (60 mmol, 8.53 g) in ether (25 mL) and concentrated HCl (0.75 mL) was treated with methyl nitrite, which was bubbled directly into the reaction mixture over a period of approximately 2 hours. The reaction mixture was then opened to the atmosphere, the excess methyl nitrite allowed to dissipate, and the HCl was neutralized with 5 mL 5% (w/v) NaHCO₃. The solution was extracted with ether (4 × 7 mL), dried over MgSO₄, filtered (Whatman #1), and the ether removed by rotary evaporation. The resulting oil was placed in the refrigerator overnight to give the product as a white crystalline solid. The product was collected on a sintered glass filter, washed with hexane, and allowed to air dry. The yield was 50%. m.p. (uncorrected) 118–119 °C. *Anal.* Calc for C₈H₁₃NO₃: C, 56.13; H, 7.65; N, 8.18; O, 28.04. Found: C, 56.42; H, 7.67; N, 7.91; O, 28.02. Selected IR data (cm⁻¹): 1635 cm⁻¹, 1743 cm⁻¹; $\nu_{C=N}$. ¹H NMR (200 MHz, DMSO-*d*₆): δ 1.61 (-CH₃, 6H, s), 1.36 (-CH₃, 6H, s).

2.2. 4-[3-(4-Hydroxyimino-2,2,5,5-dimethyl-dihydro-furan-3-ylideneamino)-propylimino]-2,2,5,5-tetramethyl-dihydro-furan-3-one oxime) (LH₂)

The diiminedioxime ligand was prepared by Schiff base condensation of TMF oxime and 1,3-diaminopropane in ethanol [11]. Briefly, a solution of 1,3-diaminopropane (346 mg, 4.67 mmol) in ethanol (10 mL) was added dropwise (1.5 – 2 h) to a solution of the oxime (1.6 g, 9.35 mmol) in 10 mL warm ethanol (35 – 40°C) under argon, and the reaction mixture was stirred for 18 h. On cooling, a white precipitate formed which was collected on a sintered glass frit, washed with cold ethanol and acetone, and dried in a vacuum desiccator. Yield - 30%. *Anal.* Calc for C₁₉H₃₂N₄O₄: C, 59.98; H, 8.48; N, 14.73; O, 16.82. Found: C, 59.73; H, 8.54; N, 14.76; O, 17.14. Selected IR data (cm⁻¹): $\nu_{C=N}$ 1599, 1664 cm⁻¹. ¹H NMR (200 MHz, DMSO-*d*₆) 1.226 (-CH₃, 12H, s), 1.439 (CH₃, 12H, s), 1.959 (CH₂CH₂CH₂, 2H, t, 0.035), 3.825 (CH₂CH₂CH₂, 4H, t, 0.032), 12.082 (NOH, 1H, s)

2.3. {Cu[Cu(LH)]₂}(ClO₄)₂ (1)

Solid Cu(ClO₄)₂•6 H₂O (82.5 mg, 0.221 mmol), suspended in 5 mL absolute ethanol, was added dropwise to a suspension of LH₂ (100 mg, 0.262 mmol) in warm (30–35°C) absolute ethanol (15 mL), and the reaction mixture was stirred for 2 h without further heating. The solvent was removed under vacuum, the product was suspended in water, collected on a medium frit, and washed with cold water. A crystalline red-brown product was obtained by addition of ether to a methanolic solution of the complex. Crystals suitable for x-ray diffraction were grown by slow diffusion of ether into a solution of the complex in methanol. Yield – 30–35% *Anal.* Calc for C₃₈H₆₀Cl₂Cu₃N₈O₁₆: C, 39.81; H, 5.28; Cl, 6.18; Cu, 16.63; N, 9.77; O, 22.33. Found: C, 39.96; H, 5.29; N, 9.77. Selected IR data (cm⁻¹): $\nu_{C=N}$ 1560 cm⁻¹.

2.4. [Cu(L'H)]ClO₄ (2)

Solid Cu(OAc)₂ • H₂O (23 mg, 0.12 mmol) dissolved in 1 mL acetonitrile was added to the suspension of LH₂ (70 mg, 0.18 mmol) in 3 mL acetone. The reaction mixture was refluxed for 1.5 h. and the solvent was allowed to evaporate slowly to produce a reddish-brown semi-solid to which water was added. Red crystals of **1** suitable for x-ray diffraction precipitated from this solution. Because of its instability, no elemental analysis or IR spectra were obtained for this product.

2.5. [Ni(LH)]ClO₄ (3)

The nickel(II) complex was prepared similarly to **1**. Ni(NO₃)₂•6 H₂O (38.21 mg, 0.131 mmol) was dissolved in 5 mL of absolute ethanol, and this solution was added dropwise to a suspension of LH₂ (50 mg, 0.131 mmol) in ethanol (5 mL). The color of the reaction mixture became

reddish-brown as the Ni^{II} solution was added. The deep orange product was isolated as the perchlorate salt by addition of a saturated aqueous solution of NaClO₄. The solution was cooled in the refrigerator, the product collected on a sintered-glass frit, and washed with cold H₂O. Yield – 30 mg (42%). Crystals suitable for x-ray diffraction were obtained by slow diffusion of saturated aqueous NaClO₄ into an ethanolic solution of the product. Yield - 40% *Anal.* Calc for C₁₉H₃₁ClN₄NiO₁₆: C, 42.45; H, 5.81; Cl, 6.59; N, 10.42; Ni, 10.92; O, 23.81. Found: C, 42.55; H, 5.84; N, 10.37. Selected IR data (cm⁻¹): $\nu_{C=N}$ 1561 cm⁻¹.

2.6. X-ray data collection and refinement

Data were collected using a Bruker SMART CCD (charge coupled device) diffractometer equipped with an LT-3 low-temperature apparatus operating at 213 K. Suitable crystals were chosen and mounted on glass fibers using grease. Data collection parameters are summarized in Table 1. All non-hydrogen atoms were refined anisotropically. Except as noted, hydrogens were calculated by geometrical methods and refined as a riding model. Data were measured using omega scans of 0.3° per frame for 30 seconds, such that a hemisphere of data was collected. The first 50 frames were recollected at the end of data collection to monitor for decay. None of the crystals used for the diffraction study showed any decomposition during data collection. Cell parameters were retrieved using SMART software [12] and refined using SAINT [13] on all observed reflections. Data reduction was performed using the SAINT software, which corrects for Lp and decay. The structures were solved by the direct method using the SHELXS-97 program and refined by least squares method on F² using SHELXL-97 [14], incorporated in SHELXTL-PC V 5.10 [15]. Crystal structure drawings were prepared using ORTEP-3 for Windows [16]. Least-squares planes were calculated using Platon for Windows [17].

For complex **3**, the disorder in C10 was refined to ratio of C10/C10B = 0.77. The hydrogen between O1 and O2 was modeled 50% on O1 and 50% on O2.

3. Results and discussion

A new furanone-containing diiminedioxime ligand and its Cu(II) and Ni(II) complexes were prepared and characterized. The ligand itself is unusual in that there are very few examples of ligands in which furanone is incorporated into the ligand backbone. One example of this is the Tc-Q12 complexes referred to previously [9]. In the Q12 case, the furanone replaces the benzene ring in the Schiff's base salen, and the ligand has a -2 charge when complexed to a metal. Another example is found in the work of Gottschaldt, et al in which furanone replaces the ethylenediamine backbone of a salen-type ligand and the ligand again has a -2 charge when complexed to the metal [18]. For Cu(II), these ligands would produce neutral complexes that would not be expected either to accumulate in the myocardium or be substrates for Pgp. The diiminedioxime derivative is, we believe, the first example of a monoanionic furanone-functionalized ligand.

3.1 Synthesis

The tetramethyl furanone ligand, **LH₂**, was prepared using a method analogous to that used previously to prepare linear alkyl derivatives of the diiminedioxime ligand system [6]. In contrast to previous derivatives of the diiminedioxime system, the TMF derivative contains a cyclic ether moiety, which is expected to improve the rate at which the ⁶⁴Cu complex is cleared from the blood and liver. It may also be the case that the increased ligand rigidity imposed by the TMF system increases the in vivo stability of the ⁶⁴Cu complex. This possibility will be evaluated when the ⁶⁴Cu complex is prepared.

The syntheses of the Cu(II) and Ni(II) complexes were readily accomplished when the reactions were carried out in ethanol. However, an unexpected result was encountered when the copper complex was prepared from Cu(OAc)₂ with acetone in the solvent mixture. In this case, there was significant decomposition of the reaction mixture and a product was isolated that contained an acetone adduct of the ligand. This is an unusual, but not unprecedented, result. There are several examples of acetone adducts of imine ligands in the literature [19–21] including one Cu(II) complex [19]. This is, however, apparently the first example of this being observed in a ligand of this type.

3.2. Descriptions of the Structures

3.2.1 {Cu[Cu(LH)]₂}(ClO₄)₂ (1)—An ORTEP drawing of **1** is shown in Figure 1. Selected bond lengths and angles are summarized in Table 2. The complex crystallizes as a Cu(II)-bridged dimer with the central Cu(II) atom bonded to four oxime oxygens. The two halves of the dimer are related by a center of symmetry at Cu1, and the molecules are linked in infinite chains along the *c* axis by weak interactions between Cu2 and the perchlorate counter-ions (Cu2-O5, 2.532(3) Å, Cu2-O8 2.577(3) Å) (Fig. 1).

The bridging Cu(II) atom is coplanar with the four oxime oxygen atoms, while the second Cu(II) atom sits slightly (0.0400(4) Å) above the plane defined by the four nitrogen atoms. The four Cu-N bonds are very similar in length (range – 1.990(2) Å to 1.994(2) Å) and are somewhat longer than the Cu-N values observed in the prototypical complex of this series, [Cu(PreH)]⁺ (PreH₂ = 3,3'-(trimethylenedinitrilo)bis(2-butanone oxime)), where they range between 1.945(7) Å and 1.972(7) Å [22]. The difference in bond lengths is apparently due to spreading of the ligand by the bridging copper atom. This spreading can be seen in the greater distance between the oxime oxygen atoms in **1** versus [Cu(PreH)]⁺, 3.021 Å for **1** compared to 2.492 Å for [Cu(PreH)]⁺, and in the smaller displacement of the Cu(II) atom from the basal plane (0.0400 Å vs. 0.097 Å).

There are relatively few examples of oxime-bridged Cu(II)-dimers. One example is [Cu(Cu(PreH))₂][ClO₄]₂ [23], the Cu(II)-bridged dimer of [Cu(PreH)H₂O]⁺. The structures of the two dimers are, however, strikingly different. Complex **1** is almost planar with O2-Cu1-O2 and O1-Cu1-O1 angles of 180° and the Cu atom located in the plane defined by the four oxime oxygen atoms. The coordination environment about the central Cu atom in [Cu(Cu(PreH))₂][ClO₄]₂ is, in contrast, distorted tetrahedral with O-Cu-O angles of 152.26(7)° and 158.47(7)°. And while **1** is essentially planar, in [Cu(Cu(PreH))₂][ClO₄]₂ the two sides of the dimer are bent upwards at almost 60° relative to the CuO₄ core, and the two CuN₄ centers are loosely connected through the ClO₄[–] counter-ion (Cu-O 2.838(2) Å). In contrast to this intramolecular ClO₄[–] bridge, in complex **1** the dimers are linked in infinite chains along *b* by the perchlorate counter-ion (Fig. 2). One possible reason for the difference in conformations between the two complexes is the steric effect of the methyl groups on the furanone rings. Examination of space-filling models suggests that these groups will interact with those on the opposite side of the dimer if the two sides are folded towards each other, as they are in [Cu(Cu(PreH))₂][ClO₄]₂.

3.2.2. [Cu(L'H)]ClO₄ (2)—Selected interatomic distances and angles for **2** are summarized in Tables 3 and 4, and an ORTEP drawing of the complex is shown in Figure 2. The coordination geometry around the Cu(II) atom approximately square planar with the Cu(II) atom 0.0268(6) Å above the plane defined by the four nitrogen atoms.

The most distinctive feature of this complex is the reduction of the N2-C3 double bond by addition of acetone across the imine bond with concomitant acetone adduct formation at C3 and addition of a hydrogen atom to N2. The C3 atom is clearly *sp*³, in contrast to C14, the corresponding atom in the second furanone ring in the complex, which is *sp*². The difference between the two carbon atoms can be clearly seen in the differences in the bond lengths and

angles as well as the differences between the amine and imine nitrogen atoms, N2 and N3 (Tables 3 and 4). The parameters for the imine nitrogen are similar to those observed in the diiminedioxime complex $[\text{Cu}(\text{PreH})\text{H}_2\text{O}]^+$ [22], while the parameters for the amine nitrogen are similar to those observed in the diaminedioxime complexes $[\text{Cu}(\text{ReO}_4)(\text{PnAO})]$ (HPnAO = 2,2'-(1,3-diaminopropane)bis(2-methyl-3-butanone oxime)) [24] and $[\text{Cu}(\text{CN})(\text{PnAO})]$ [25]. This pattern is also observed when N2- and N3-Cu bonds are compared. The remainder of the ligand is structurally similar to **1** and $[\text{Cu}(\text{PreH})\text{H}_2\text{O}]^+$ [22].

In contrast to the other examples of acetone adducts [19–21] in which the oxygen atom is oriented away from the metal, in this case the oxygen atom occupies an axial position in the complex; Cu-O = 2.399(4) Å. This compares to the 2.294(6) Å Cu-O distance for an acetone oxygen in a Cu-dien complex [26]. The somewhat greater distance in this case is perhaps a consequence of geometric constraints imposed by the ligand which displace the oxygen away from an ideal apical location (N2-Cu-O5 = 82.3(1)°).

Other than O8 of the perchlorate counter-ion (Cu-O8, 2.649(5) Å), there are no significant intermolecular interactions.

3.2.3. Structure $[\text{Ni}(\text{LH})]\text{ClO}_4$ (3**)**—An ORTEP drawing of this complex is shown in Figure 3, and selected bond lengths and angles are summarized in Table 5. The complex crystallizes with two independent molecules in the asymmetric unit. In molecule A, the Ni(II) atom is 0.1435(6) Å above the plane defined by the four N atoms, and in molecule B, the Ni(II) atom is 0.1108(6) Å above the plane. When viewed edge on, molecule A is slightly more distorted from planarity than molecule B as evidenced by the larger displacements of the ether oxygen atoms in the furanone ring from the N₄ plane. In molecule A, the O3 and O4 atoms are −0.385(4) Å and −0.623(4) Å below the plane versus −0.271(4) Å and −0.202(4) Å for molecule B.

The coordination environment around the two independent Ni(II) atoms is unremarkable. The Ni-N bond lengths range from 1.884(4) to 1.921(4) Å, slightly longer than those observed for $[\text{Ni}(\text{PreH})]\text{ClO}_4$, which range from 1.869(5) to 1.892(5) Å [27] and Ni-Me₂PreH, which range from 1.866(5) to 1.887(3) Å [28]. The lengthening of the Ni-N bonds is presumably due to the greater displacement of the Ni atom from the plane in this complex than in the two previous examples (0.018 Å for Ni-PreH [27] and 0.056 Å for Ni-Me₂PreH [28]) and shorter Ni-O (perchlorate) distance (2.504(5) Å and 2.512(4) Å) in this complex compared to the two Ni-PreH complexes (2.84 Å and 2.902(5) Å). The structure of the ligand itself is similar to that seen in **1** and **2** except that in this case the central carbon atom of the trimethylene bridge is disordered in molecule A. There are no significant intermolecular interactions.

4 Conclusions

The tetramethylfuranone diiminedioxime ligand 4-[3-(4-Hydroxyimino-2,2,5,5-dimethyl-dihydro-furan-3-ylideneamino)-propylimino]-2,2,5,5-tetramethyl-dihydro-furan-3-one oxime) (**LH₂**) was successfully synthesized as were its Cu(II) and Ni(II) complexes. However, when the synthesis of the Cu(II) complex was attempted in a mixture of acetonitrile and acetone, an unusual example of an acetone adduct of the ligand was observed. This observation suggests that caution should be observed when using acetone as a solvent to prepare copper-imine complexes.

Efforts are currently underway to prepare the corresponding ⁶⁴Cu complex so that the effect of the tetramethylfuranone moiety on the biodistribution of the complex can be determined.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by NIH grant CA-81084 (ABP) and U.S. Army BCRP grant DAMD17-99-1-9125 (ABP). The CCD-based x-ray diffractometer at Harvard University was purchased through NIH grant 1S10RR11937-01.

References

1. Gottesman MM, Pastan I. Annu Rev Biochem 1993;62:385. [PubMed: 8102521]
2. Piwnica-Worms D, Chiu ML, Budding M, Kronauge JF, Kramer RA, Croop JM. Cancer Res 1993;53:977. [PubMed: 8094997]
3. Crankshaw CL, Marmion M, Luker GD, Rao V, Dahlheimer J, Burleigh BD, Webb E, Deutsch KF, Piwnica-Worms D. J Nucl Med 1998;39:77. [PubMed: 9443741]
4. Ballinger JR, Bannerman J, Boxen I, Firby P, Hartman NG, Moore MJ. J Nucl Med 1996;37:1578. [PubMed: 8790223]
5. Neirinckx RD, Kronauge JF, Loberg MD. Int J Appl Radiat Isot 1983;34:721.
6. Packard AB, Kronauge JF, Barbarics E, Kiani S, Treves ST. Nuc Med Biol 2002;29:289.
7. Holman BL, Jones AG, Lister-James J, Davison A, Abrams MJ, Kirshenbaum JM, Tumeh SS, English RJ. J Nucl Med 1984;25:1350. [PubMed: 6334145]
8. Wackers FJ, Berman DS, Maddahi J, Watson DD, Beller GA, Strauss HW, Boucher CA, Picard M, Holman BL, Fridrich R. J Nucl Med 1989;30:301. [PubMed: 2525610]
9. Rossetti C, Vanoli G, Paganelli G, Kwiatkowski M, Zito F, Colombo F, Bonino C, Carpinelli A, Casati R, Deutsch K, Marmion M, Woulfe SR, Lunghi F, Deutsch E, Fazio F. J Nucl Med 1994;35:1571. [PubMed: 7931652]
10. Finke RG, Smith BL, McKenna WA, Christian PA. Inorg Chem 1981;20:687.
11. Gagne' RR, Allison JL, Gall RS, Koval CA. J Am Chem Soc 1977;99:7170. [PubMed: 915148]
12. SMART V 5.054 (NT). Software for the CCD Detector System. Bruker Analytical X-ray Systems; Madison, WI: 1998.
13. SAINT V 6.01 (NT). Software for the CCD Detector System. Bruker Analytical X-ray Systems; Madison, WI: 1999.
14. Sheldrick G. Acta Crystallographica Section A 2008;64:112.
15. SHELXTL 5.10 (PC/NT-Version). Program library for Structure Solution and Molecular Graphics. Bruker Analytical X-ray Systems; Madison, WI: 1998.
16. Farrugia L. J Appl Crystallogr 1997;30:565.
17. Farrugia, LJ. PLATON for Windows, 1.14. University Of Glasgow; Glasgow: 2008.
18. Gottschaldt M, Koth D, Gorls H. Org Biomol Chem 2005;3:1170. [PubMed: 15785801]
19. MacLachlan MJ, Park MK, Thompson LK. Inorg Chem 1996;35:5492. [PubMed: 11666735]
20. Kamenar B, Kaitner B, Katovic V, Busch DH. Inorg Chem 1979;18:815.
21. Seok WK, Karaghiosoff K, Klapotke TM, Mayer P. Z Naturforsch 2003;58b:1087.
22. Anderson OP, Packard AB. Inorg Chem 1979;18:1940.
23. Luneau D, Oshio H, Okawa H, Kida S. J Chem Soc, Dalton Trans 1990:2283.
24. Liss IB, Schlemper EO. Inorg Chem 1975;14:3035.
25. Schlemper EO, Hussain MS, Murmann RK. Acta Crystallogr, Sect B 1981;B37:234.
26. Scott MJ, Holm RH. J Am Chem Soc 1994;116:11357.
27. Wang YM, Chung CS, Cheng CY, Wang SL. Acta Crystallogr Sec C: Cryst Struct Commun 1990;C46:1429.
28. Lu TH, Tseng F, Luh H, Chung CS. Acta Crystallogr, Sec C: Cryst Struct Commun 1993;C49:666.

Fig. 1.
Molecular structure of $\{\text{Cu}[\text{Cu}(\text{LH})]_2\}^{2+}$ dimer (**1**) showing atom labeling scheme.

Fig. 2.
Molecular structure of [Cu(L'H)]⁺ cation (acetone adduct) (2) showing atom labeling scheme.

Fig. 3.
Molecular structure of $[\text{Ni}(\text{LH})]^+$ cations (**3**) showing atom labeling scheme.

Chart 1.
TMFPreH Ligand

Table 1

Crystallographic data

Compound	1	2	3
Formula	C ₃₈ H ₆₀ Cl ₂ Cu ₃ N ₈ O ₁₆	C ₂₂ H ₃₇ ClCuN ₄ O ₉	C ₃₈ H ₆₂ Cl ₂ N ₈ Ni ₂ O ₁₆
Formula weight, (g mol ⁻¹)	1146.46	600.55	537.64
Color of crystal, habit	red, needle	red, needle	red, needle
Space group	P2 ₁ /c	P2 ₁ /c	P2 ₁ /c
<i>a</i> (Å)	12.765(2)	13.6145(17)	27.472(3)
<i>b</i> (Å)	14.147(2)	8.0878(9)	7.9667(9)
<i>c</i> (Å)	13.954(2)	24.249(3)	25.588(3)
β (°)	102.485(3)	97.105(2)	114.988(2)
<i>V</i> (Å ³)	2460.3(7)	2649.5(6)	4877.6(9)
<i>Z</i>	2	4	8
<i>T</i> (K)	213(2)	213(2)	213(2)
Radiation	Mo K α	Mo K α	Mo K α
ρ_{calc} (g cm ⁻³)	1.548	1.506	1.464
μ (mm ⁻¹)	1.467	0.982	0.955
θ Range	2.08 to 28.28°	1.51 to 28.03°	1.66 to 25.00°
Reflections Collected	15735	16676	25019
Independent Reflections	5868	5782	8597
Data/restraints/parameters	5868/0/312	5782/0/334	8597/0/619
GOF on <i>F</i> ²	1.154	0.921	1.122
<i>R</i> _{<i>I</i>} ^{<i>a</i>} [<i>I</i> > 2 σ (<i>I</i>)]	0.0460	0.0536	0.0651
<i>wR</i> ₂ ^{<i>b</i>} [<i>I</i> > 2 σ (<i>I</i>)]	0.1271	0.1133	0.1297
<i>R</i> _{<i>I</i>} (all data)	0.0600	0.1446	0.0955
<i>wR</i> ₂ (all data)	0.1359	0.1345	0.1409

$$^a R_I = \Sigma ||F_O| - |F_C|| / \Sigma |F_O|$$

$$^b wR_2 = [\Sigma w(|F_O|^2 - |F_C|^2) / \Sigma w(F_O)^2]^{1/2}, w = 1 / [(F_O)^2 + (0.01103P)^2], \text{ where } P = (F_O^2 + 2 F_C^2) / 3$$

Table 2Selected bond lengths (Å) and angles (°) for {Cu[Cu(LH)]₂}(ClO₄)₂ (**1**).

<i>Bond Lengths</i>		
Cu(1) - O(2)		1.936(2)
Cu(1) - O(1)		1.955(2)
Cu(2) - N(1)		1.990(2)
Cu(2) - N(2)		1.992(3)
Cu(2) - N(3)		1.991(3)
Cu(2) - N(4)		1.994(2)
Cu(2) - O(5)		2.532(3)
<i>Bond Angles</i>		
O(1) - Cu(1) - O(1) ^a		180.0
O(1) - Cu(1) - O(2)		101.86(9)
O(1) - Cu(1) - O(2) ^a		78.14(9)
O(1) ^a - Cu(1) - O(2)		78.14(9)
O(1) ^a - Cu(1) - O(2) ^a		101.86(9)
O(2) - Cu(1) - O(2) ^a		180.0(1)
N(1) - Cu(2) - N(2)		83.9(1)
N(1) - Cu(2) - N(3)		97.9(1)
N(1) - Cu(2) - N(4)		177.6(1)
N(1) - Cu(2) - O(5)		93.7(1)
N(2) - Cu(2) - N(3)		176.4(1)
N(2) - Cu(2) - N(4)		94.1(1)
N(2) - Cu(2) - O(5)		85.6(1)
N(3) - Cu(2) - N(4)		84.0(1)
N(3) - Cu(2) - O(5)		97.4(1)
N(4) - Cu(2) - O(5)		87.5(1)

^a Symmetry transformations used to generate equivalent atoms: #1 -x+1, -y, -z+1

Table 3Selected bond lengths (Å) [Cu(L'H)]ClO₄ (**2**).

Cu(2) - N(1)	1.965(4)
Cu(2) - N(2)	1.995(3)
Cu(2) - N(3)	1.965(3)
Cu(2) - N(4)	1.964(4)
Cu(2) - O(5)	2.399(4)
N(2) - C(3)	1.486(5)
N(2) - C(11)	1.484(5)
N(3) - C(13)	1.460(5)
N(3) - C(14)	1.273(5)
C(3) - C(4)	1.567(6)
C(3) - C(5)	1.573(6)
C(5) - C(5c)	1.526(7)
C(5c) - C(6)	1.491(7)
C(5c) - O(5)	1.226(6)

Table 4Selected bond angles (°) for [Cu(L'H)]ClO₄ (**2**).

N(1) - Cu(1) - N(2)	83.5(2)
N(1) - Cu(1) - N(3)	178.7(2)
N(1) - Cu(1) - N(4)	95.01(2)
N(2) - Cu(1) - N(3)	97.7(1)
N(2) - Cu(1) - N(4)	175.6(2)
N(3) - Cu(1) - N(4)	83.9(2)
N(1) - Cu(1) - O(5)	84.9(1)
N(2) - Cu(1) - O(5)	82.3(1)
N(3) - Cu(1) - O(5)	94.5(1)
N(4) - Cu(1) - O(5)	101.7(2)
Cu(1) - N(2) - C(3)	106.8(3)
Cu(1) - N(2) - C(11)	117.0(3)
C(3) - N(2) - C(11)	118.4(3)
Cu(1) - N(3) - C(13)	126.4(3)
Cu(1) - N(3) - C(14)	109.5(3)
C(13) - N(3) - C(14)	124.0(4)
N(2) - C(3) - C(1)	108.0(3)
N(2) - C(3) - C(4)	118.6(4)
N(2) - C(3) - C(5)	111.0(4)
C(1) - C(3) - C(4)	100.7(4)
C(1) - C(3) - C(5)	109.0(4)
C(4) - C(3) - C(5)	108.8(4)
N(3) - C(14) - C(15)	120.1(4)
N(3) - C(14) - C(17)	133.0(4)
C(15) - C(14) - C(17)	106.9(4)
Cu(1) - O(5) - C(5c)	123.3(3)

Table 5Selected bond lengths (Å) and angles (°) [Ni(LH)]ClO₄ (**3**).

<i>Bond Lengths</i>		
Ni(1) - N(1)		1.891(4)
Ni(1) - N(2)		1.911(4)
Ni(1) - N(3)		1.890(4)
Ni(1) - N(4)		1.905(4)
Ni(1) - O(5)		2.504(5)
Ni(1A) - N(1A)		1.885(4)
Ni(1A) - N(2A)		1.910(4)
Ni(1A) - N(3A)		1.884(4)
Ni(1A) - N(4A)		1.921(4)
Ni(1A) - O(5A)		2.512(4)
<i>Bond Angles</i>		
N(1) - Ni(1) - N(2)		83.8(2)
N(1) - Ni(1) - N(3)		94.2(2)
N(1) - Ni(1) - N(4)		171.1(2)
N(1) - Ni(1) - O(5)		99.0(2)
N(2) - Ni(1) - N(3)		171.4(2)
N(2) - Ni(1) - N(4)		96.3(2)
N(2) - Ni(1) - O(5)		97.3(2)
N(3) - Ni(1) - N(4)		84.4(2)
N(3) - Ni(1) - O(5)		91.2(2)
N(4) - Ni(1) - O(5)		89.8(2)
N(1A) - Ni(1A) - N(2A)		84.6(2)
N(1A) - Ni(1A) - N(3A)		93.6(2)
N(1A) - Ni(1A) - N(4A)		173.2(2)
N(1A) - Ni(1A) - O(5A)		97.7(2)
N(2A) - Ni(1A) - N(3A)		173.1(2)
N(2A) - Ni(1A) - N(4A)		96.5(2)
N(2A) - Ni(1A) - O(5A)		84.0(2)
N(3A) - Ni(1A) - N(4A)		84.4(2)
N(3A) - Ni(1A) - O(5A)		102.9(2)
N(4A) - Ni(1A) - O(5A)		89.1(2)