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**A New Insight on the Synthesis of Cyclic Pyrazolate
Copper(I) and Copper(II) Compounds and their Application
as Catalysts for Oxidation of Cyclohexane in mild conditions.
X-Ray Crystal Structures of [trans-Cu₆(μ-OH)₆(μ-3,5-
(CF₃)₂pz)₆] and [Cu₂(μ-N,N-3,5-(NO₂)₂pz)₂(PPh₃)₂]**

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A New Insight on the Synthesis of Cyclic Pyrazolate Copper(I) and Copper(II) Compounds and their Application as Catalysts for Oxidation of Cyclohexane under mild conditions. X-Ray Crystal Structures of [*trans*-Cu₆(μ-OH)₆(μ-3,5-(CF₃)₂pz)₆] and [Cu₂(μ-N,N-3,5-(NO₂)₂pz)₂(PPh₃)₂]

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Abstract

New copper (I) and copper(II) pyrazolate compounds have been prepared by similar synthesis procedures. When the pyrazole ligand contains NO₂ in positions 3,5 the dinuclear cyclic Cu(I) compound, [Cu₂(μ-N,N-3,5-(NO₂)₂pz)₂(PPh₃)₂], **5**, was the only compound isolated in high yield

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3 while in the case of the 3,5-bis(trifluoromethyl)-pyrazole a spontaneous rearrangement to the
4 hexanuclear cyclic $[\text{trans-Cu}_6(\mu\text{-OH})_6(\mu\text{-3,5-(CF}_3)_2\text{pz})_6]$, **6**, was observed. An insight in the reaction
5 mechanism for these hexanuclear metallacycle compounds was performed and the synthesis of **6**
6 is the final proof that its formation is not templated by anions and likely it does not proceed
7 through the formation of the trinuclear derivative. The X-ray diffraction analysis of **5** revealed the
8 copper cation in a trigonal environment and involved in a six-membered Cu_2N_4 core; in **6** the metal
9 adopts a square-planar geometry, forms five-membered $\text{Cu}_2\text{N}_2\text{O}$ rings and ultimately gives rise to
10 a large $\text{Cu}_6(\text{N}_2\text{O})_6$ crown-type assembly. Compounds **5** and **6** act as very effective homogeneous
11 catalysts towards the neat microwave (MW) assisted peroxidative (with aq. *tert*-butyl
12 hydroperoxide, TBHP) oxidation of cyclohexane to cyclohexanol and cyclohexanone via formation
13 of cyclohexyl hydroperoxide (CyOOH) as primary product.
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24 Introduction

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26 Coordination chemistry of polynuclear Cu(I) and Cu(II) with N-donor ligands provides a wide
27 number of complexes which are relevant in many areas such as catalysis,¹⁻⁶ bioinorganic
28 chemistry,⁷⁻¹⁰ materials chemistry,¹¹⁻¹³ molecular magnetism.¹⁴⁻¹⁶ The above mentioned areas are
29 strictly related to each other. In fact, as in example, copper(II) ions are active catalyst in the
30 oxydation of water to molecular oxygen,¹ copper(II) 1,10-phenantroline complexes are involved in
31 aerobic oxidation of primary alcohols; moreover, dinuclear copper(II) proteins such as
32 hemocyanins, tyrosinase and catechol oxidase activate the molecular oxygen by a "side-on"
33 bridging binding mode⁸ providing different biological functions: in example, the oxygen transport,
34 the ortho-hydroxylation of phenols with further oxidation of the catechol product to o-quinone or
35 the enantioselective oxidation of Dopa (Dihydroxyphenylalanine).⁷ It is then clear that the
36 enzymatic catalysis of oxidations is largely based on cooperativity between the metal center and
37 functional organic ligands located at its surroundings. As a consequence, a strategy on the design
38 of copper based catalysts for oxidation reactions should consider a biomimetic approach.¹⁷⁻¹⁸ The
39 synthesis of bioinspired copper pyrazolate metallacycle may proceed by spontaneous self
40 assembly of deprotonated ligands and copper(II) salts or Cu(I) oxide,¹⁹⁻²⁰ by templating syntheses
41 ²¹⁻²² or by rearrangements of polynuclear copper(I) compounds to copper(II) derivatives.^{13,23} As
42 concern this last case, the reaction of a trinuclear Cu(I) metallacycle, depicted as $[\mu\text{-Cu-N,N-3,5-}$
43 $\text{pz}(\text{CF}_3)_2]_3$, where 3,5-(CF_3)₂-pz is the 3,5-bis(trifluoromethyl)pyrazolate, with a halide source such
44 as Bu_4NX or PPNNO_2 (where Bu_4N = tetrabutyl ammonium, and PPN = phosphoranylamide, X = Cl,
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3 Br, I) or Ph_3PAuCl , led to the formation of anion encapsulated adducts in 1 : 1 mole ratio^{13,16} The
4 X-ray diffraction analyses revealed for all the compounds a core containing a hexanuclear
5 copper(II) ring bridged by six hydroxyl groups and six pyrazolate ligands. The copper(II) metallacycle
6 shows selectivity for anions excluding octahedral (PF_6^-), tetrahedral (SO_4^{2-} , BF_4^- , ClO_4^-) and trigonal
7 planar anions (CO_3^{2-} , NO_3^{2-}), while act as anti-metallacrown for halides and nitrite anions. The
8 mechanism leading to these metallacycles having this metal framework is not very clear and it was
9 hypothesised that halides could template the formation of the hexanuclear cycle.

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12 A first aim of this work was to investigate the mechanism leading to the synthesis of these
13 complexes. Moreover, to center this target the synthesis has been extended to a similar
14 pyrazolate, having in 3,5 positions the nitro group. The second aim of this work was to test if they
15 possess catalytic activity towards oxidation reactions. Hence the peroxidative oxidation of
16 cyclohexane was attempted. This reaction was selected as an alkane oxidation model due to its
17 industrial and economical importance, in view of the significance of the oxidized products
18 (cyclohexanol and cyclohexanone) for the manufacturing of adipic acid and caprolactam
19 (precursors to Nylon-6,6 and polyamides). Moreover, the current industrial process for
20 cyclohexane oxidation requires 15 bar O_2 , 160 °C and leads to very low conversions (*ca.* 4%) to
21 assure a reasonable selectivity (*ca.* 85%).²⁴ Therefore, there is an urgent need to design selective
22 and effective catalytic processes for cyclohexane oxidation under mild and solvent-free conditions,
23 with environmentally benign oxidants²⁵ and, in this respect, a promising approach is presented
24 herein.

25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 **Experimental**

41 42 **Materials**

43 Elemental analyses (C,H,N,S) were performed in-house with a Fisons Instruments 1108 CHNS-O
44 Elemental Analyser. Melting points were taken on an SMP3 Stuart Scientific Instrument. MIR
45 spectra were recorded from 4000 to 600 cm^{-1} with a Perkin-Elmer SPECTRUM ONE System FT-FIR
46 instrument. NIR spectra were recorded from 4000 to 600 cm^{-1} with a Perkin-Elmer SPECTRUM ONE
47 System FT-IR instrument. IR annotations used: br = broad, m = medium, s = strong, sh = shoulder,
48 vs = very strong, w = weak and vw = very weak¹H and ³¹P NMR spectra were recorded on an
49 Oxford-400 Varian spectrometer (400.4 MHz for ¹H and 162.1 MHz for ³¹P). Chemical shifts, in
50 ppm, for ¹H NMR spectra are relative to internal Me_4Si . ³¹P NMR chemical shifts were referenced
51 to a 85% H_3PO_4 standard. The ³¹P NMR spectroscopic data were accumulated with ¹H decoupling.
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3 NMR annotations used: br = broad, d = doublet, dd = double doublet, t = triplet, m = multiplet, s =
4 singlet. Electrospray mass spectra (ESI-MS) were obtained in positive- or negative-ion mode on a
5 Series 1100 MSD detector HP spectrometer, using an acetonitrile or methanol mobile phase. The
6 compounds were added to reagent grade acetonitrile to give solutions of approximate
7 concentration 0.1 mM. These solutions were injected (1 μ l) into the spectrometer via a HPLC HP
8 1090 Series II fitted with an auto-sampler. The pump delivered the solutions to the mass
9 spectrometer source at a flow rate of 300 μ l min^{-1} , and nitrogen was employed both as a drying
10 and nebulising gas. Capillary voltages were typically 4000 V and 3500 V for the positive- and
11 negative-ion mode, respectively. Confirmation of all major species in this ESI-MS study was aided
12 by comparison of the observed and predicted isotope distribution patterns, the latter calculated
13 using the IsoPro 3.1 computer program. The used solvents were HPLC grade and they were used as
14 purchased, unless water and oxygen sensitive reactions were led. In this last case anhydrous and
15 radicals free THF was obtained by treating the solvent with Na/acetophenone under N_2
16 atmosphere.

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28 The catalytic tests under microwave irradiation (MW) were performed in a focused Anton Paar
29 Monowave 300 microwave reactor using a 5 mL capacity reaction tube with a 10 mm internal
30 diameter, fitted with a rotational system and an IR temperature detector.

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34 Gas chromatographic (GC) measurements were carried out using a FISIONS Instruments GC 8000
35 series gas chromatograph with a FID detector and a capillary column (DB-WAX, column length: 30
36 m; internal diameter: 0.32 mm) and the Jasco-Borwin v.1.50 software. The temperature of
37 injection was 240 $^{\circ}\text{C}$. The initial temperature was maintained at 100 $^{\circ}\text{C}$ for 1 min, then raised 10
38 $^{\circ}\text{C}/\text{min}$ to 180 $^{\circ}\text{C}$ and held at this temperature for 1 min. Helium was used as the carrier gas. GC-
39 MS analyses were performed using a Perkin Elmer Clarus 600 C instrument (He as the carrier gas).
40 The ionization voltage was 70 eV. Gas chromatography was conducted in the temperature-
41 programming mode, using a SGE BPX5 column (30 m \times 0.25 mm \times 0.25 μm). Reaction products
42 were identified by comparison of their retention times with known reference compounds, and by
43 comparing their mass spectra to fragmentation patterns obtained from the NIST spectral library
44 stored in the computer software of the mass spectrometer.

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3,5-Bis(trifluoromethyl)-1H-pyrazole and other chemicals were purchased by Sigma Aldrich and
used without further purification. The 3,5-dinitropyrazole was prepared as previously described.²⁶
The complex $[\text{Cu}(3,5\text{-}(\text{CF}_3)_2\text{pz})_3]$ and complexes **1**, **2**, **3**, **4** were prepared as described.^{13,27}

Synthesis of compounds 1a, 1b, 1c and 1d by the new synthesis route

3,5-trifluoromethyl-1H-pyrazole (0.050 g, 0.245 mmol) and Cu₂O were dissolved in 10 ml of MeCN. Then [Bu₄N]Cl (0.011 g; 0.040 mmol) or [Bu₄N]Br (0.013 g; 0.040 mmol) or [Bu₄N]I (0.0147 g; 0.040 mmol) or [PPNNO₂] (0.014; 0.0375 mmol) were added to the solution. Reaction mixture was left to stir for 2 h. The precipitate formed was filtered on Celite, washed with acetone and finally dried under air flow. Slowly the solution become blue or green and were dried under air flow and solids **1a** (Cl), **1b** (Br), **1c** (I), **1d** (NO₂) products were isolated by microcrystalline powders by slow evaporation.

Characterization of compound **1a**. Yields 40%; Mp 146.2-148.6 °C with decomposition; IR (cm⁻¹): 3653, 3155, 2972, 2883, 1609, 1538, 1503, 1365, 1255, 1117, 1023, 923, 816, 758, 735, 716; ESI MS (acetonitrile, HPLC grade, (-) 203.1 m/z (100%, (CF₃)₂pz), 469.1 (18%), 648.7 (20%), 1737.2 m/z (100%, (Cu₆((CF₃)₂pz)₆(OH)₆Cl)); ¹H and ¹⁹F NMR (acetone-d⁶, r. t.): 34.52 (s, pzC-H), -56.79 (s, pzCF₃); 3.48 (m, CH₂-N), 1.84 (m, -CH₂-), 1.45 (m, -CH₂-), 0.99 (t, CH₃-); Elemental analysis for C₄₆H₄₈ClCu₆F₃₆N₁₃O₆: Calc.: C 27.91, N 9.20, H 2.44; Found: C 28.24, N 9.22, H 2.03.

Characterization of compound **1b**. Yield 35%; Mp 183.4-185.6 °C with decomposition; IR (cm⁻¹): 3654, 3162, 2970, 2880, 1539, 1503, 1466, 1366, 1255, 1119, 1022, 928, 819, 760, 735, 718; ESI MS (acetonitrile, HPLC grade): (-) 157.1 m/z (80%), 426 (22%), 469.0 (12%), 603.3 (100%), 1237.4 m/z (23%), 1737.2 m/z (32%, (Cu₆((CF₃)₂pz)₆(OH)₆Cl)), 1781.3 m/z (100%, (Cu₆((CF₃)₂-pz)₆(OH)₆Br)); ¹H and ¹⁹F NMR (acetone-d⁶, r. t.): 34.45 (s, pzC-H), -56.45 (s, pzCF₃); 3.47 (m, CH₂-N); 1.84 (m, -CH₂-); 1.43 (m, -CH₂-); 0.98 (t, CH₃-); Elemental analysis for C₄₆H₄₈BrCu₆F₃₆N₁₃O₆: calc.: C, 27.30%; H, 2.39%; N, 9.00%. Found: C, 27.28%, H, 2.37%, N, 8.99%.

Characterization of compound **1c**. Yields 37%; Mp 145.2-146.4 °C; IR (cm⁻¹): 3650, 3154, 2969, 2880, 1538, 1504, 1484, 1466, 1366, 1256, 1233, 1115, 1022, 929, 819, 759, 735, 716; ESI MS (acetonitrile, HPLC grade): (-) 203.1 m/z (100%, ((CF₃)₂pz)), 648.6 (22%), 1737.2 m/z (100%, (Cu₆((CF₃)₂pz)₆(OH)₆Cl)), 1829.3 m/z (43%, (Cu₆((CF₃)₂pz)₆(OH)₆I)); ¹H and ¹⁹F NMR (acetone-d⁶, r. t.): 34.39 (s, pzC-H), -55.56 (s, pzCF₃); 3.48 (m, CH₂-N); 1.84 (m, -CH₂-); 1.46 (m, -CH₂-); 0.98 (t, CH₃-); Elemental analysis for C₄₆H₄₈Cu₆F₃₆I₁₃O₆: Calc.: C 26.68%, H, 2.34%, N, 8.79%. Found: C, 26.89%, H, 2.47%, N, 8.05%.

Characterization of compound **1d**. Yields 30%; Mp 145.2-146.4 °C; IR (cm⁻¹): 3653, 3139, 2964, 1591, 1542, 1504, 1484, 1441, 1364, 1255, 1126, 1021, 989, 814, 756, 744, 723, 691; ESI MS

(acetonitrile, HPLC grade): (-)203.1 m/z (93%, ((CF₃)₂pz)), 469.2 (100%), 735.3 (21%), 1003.3 (13%), 1535.2 (8%), 1664.3 (10%), 1737.2 m/z (100%), (Cu₆((CF₃)₂pz)₆(OH)₆Cl); ¹H and ¹⁹F-NMR (acetone-d₆, r. t.): 31.46 (s, pzCH), -57.69 (s, pzCF₃); 7.72 (m), 7.58 (m); Elemental analysis for C₆₆H₄₂Cu₆F₃₆N₁₄O₈P₂: Calc.: C 34.67%, H, 1.85%, N, 8.58%. Found: C, 35.19%, H, 1.74%, N, 8.17%.

Reaction of 3-trifluoromethyl-1H-pyrazole, Cu₂O and Bu₄NX (2), (X = Cl, Br, I)

The solid 3-trifluoromethyl-1H-pyrazole (0.50 g; 0.37 mmol) was dissolved in 5 ml of MeCN in air; to this solution solid Cu₂O (0.026 g; 0.18 mmol) and solid Bu₄NCl (0.008 g, 0.015 mmol) or Bu₄NBr (0.005 g, 0.015 mmol) were added. The reaction mixture was stirring for three days at 60 °C. The resulting green solution was filtered and concentrated by slow evaporation. Dark green insoluble solids were isolated after adding of Bu₄NCl, Bu₄NBr or Bu₄NI and they showed the same analytical characterizations. Yield 42 %.

Characterization of compound **2**: IR (cm⁻¹): 3410 (w, br), 3160 (w), 2970 (w), 2882 (w), 1660 (m), 1518 (m), 1483 (s), 1349 (s), 1244 (m), 1146 (m), 1107 (m), 1075 (m), 993 (w), 878 (w), 776 (m), 741 (s), 719 (vs). Elemental analysis for C₂₄H₂₀Cu₆F₁₈N₁₂O₇: Calc.: C 21.98%, H, 1.54%, N, 12.81%. Found: C, 22.06%, H, 1.74%, N, 12.94%.

Reaction of 3-nitro pyrazole, Cu₂O and Bu₄NX (3) (X = Cl, Br, I)

The solid 3-nitro-pyrazole (0.50 g; 0.44 mmol) was dissolved in 5 ml of MeCN on air; to this solution solid Cu₂O (0.031 g; 0.221 mmol) and solid Bu₄NCl (0.010 g, 0.018 mmol) was added. Resulting reaction mixture was let stirring for three days at room temperature. The formed green solution was filtered on a celite bed and then concentrated by slow evaporation. An insoluble green blue product was isolated and analysed. Insoluble solids were isolated after adding of Bu₄NCl, Bu₄NBr or Bu₄NI and they showed the same analytical characterizations corresponding to water encapsulated hexanuclear cycle. Yield 28%.

Characterization of compound **3**: IR (cm⁻¹): 3379 (m, br), 3150 (w), 2963 (w), 2875 (w), 1659 (w), 1531 (m), 1486 (s), 1438 (s), 1378 (m), 1349 (m), 1200 (w), 1127 (m), 1065 (w), 949 (w), 876 (m), 820 (m), 781 (s), 746 (s). Elemental analysis for C₁₈H₂₀Cu₆N₁₈O₁₉: Calc.: C 18.42 %, H, 1.72 %, N, 21.48 %. Found: C, 18.94 %, H, 1.90 %, N, 21.81 %.

Reaction of 4-nitro pyrazole, Cu₂O and Bu₄NCl (4)

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3 The solid 4-nitro-1H-pyrazole (0.020 g; 0.17 mmol) was dissolved in 10 ml of MeCN on air; to this
4 solution solid Cu₂O (0.012 g; 0.08 mmol) and solid Bu₄NCl (0.005 g, 0.036 mmol) were added. The
5 reaction mixture was let to stir for three days at room temperature. The blue solution was filtered
6 on a celite bed and a solid was recovered by slow evaporation of the solution. An insoluble blue
7 compound was isolated. Yield 32%.

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12 Characterization of Compound **4**: IR (cm⁻¹): 3135 (w), 2965 (w), 2875(w), 1648(w), 1497 (s), 1407
13 (s), 1283 (m), 1153 (w), 1037(m), 1004 (m), 870 (m), 816 (w), 754 (s). Elemental Analysis for
14 C₃₄H₅₄ClCu₆N₁₉O₁₈. Calc.: C, 28.48; H, 3.80; N, 18.56; found: C, 28.70; H, 3.70; N, 18.12.

18 19 **Synthesis of [Cu₂(μ-N,N-3,5-(NO₂)₂pz)₂(PPh₃)₂] (5)**

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21 To a mixture of Ph₃P (0.174 g; 0.66 mmol) and Cu(BF₄)₂ (0.104 g; 0.44 mmol) in dry THF, the
22 sodium pyrazole salt (0.08 g; 0.44 mmol) was added and the suspension was stirred over night at
23 room temperature. The orange suspension was evaporated under vacuum to give an orange solid.
24 The solid was dissolved in dichloromethane and extracted 3 times with 10 ml water. The organic
25 phase was dried with Na₂SO₄, filtered over a paper filter and concentrated. The solution was
26 layered with hexane and orange crystals of **5** were recovered.

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32 Characterization of Compound **5**: Yield 78 %. M. p: 121-123°C; IR(cm⁻¹): 3154 (w), 3051.5, (w) 1586
33 (w), 1539.7 (s), 1492 (s), 1479 (s,sh), 1455 (m), 1436 (m), 1368 (s), 1329 (s), 1296 (m), 1222 (w),
34 1182 (s), 1161 (m), 1097 (s), 1076 (m), 1047 (m), 1025 (m), 1010 (w), 997 (w), 967 (m), 925 (w),
35 915 (w), 833 (s), 812 (s), 741 (s), 706 (vs), 691.05 (vs); ¹H NMR (acetone-d⁶, δ): 7.58 (s, 1H), 7.39
36 (m, 3H), 7.32 (m, 12H); ³¹P NMR (acetone-d⁶, δ): 3.76 (s); ESI (-) MS (CH₃CN; m/z) : 377 (100)
37 [(3,5(NO₂)₂pz)₂ + Cu]⁻, 157 (63) [3,5(NO₂)₂pz]⁻; ESI (+) MS (CH₃CN; m/z) : 603 (m/z), 587 (100)
38 [PPh₃)₂ + Cu]⁺; 366 (61); Elemental analysis for C₄₂H₄₂Cu₂N₈O₈P₂ calc %: C52.33; H3.34; N11.60;
39 found: C52.29, H3.38, N 11.58 (%).

46 47 **Synthesis of [trans-Cu₆(μ-OH)₆(μ-3,5-(CF₃)₂pz)₆H₂O] (6)**

48 49 **Method A:**

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53 {[3,5-(CF₃)₂Pz]Cu}₃ (0.040 g, 0.050 mmol) was dissolved in 5 ml of MeCN (HPLC GRADE). The
54 reaction mixture was stirred for 10 min and then left in air. Slowly the solution became blue and
55 after few days' blue crystals of the hexanuclear copper (II) complex **6** were formed.

56 57 58 **Method B:**

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3 The solid 3,5 trifluoromethyl pyrazole (0.100 g; 0.49 mmol) was dissolved in 5 ml of MeCN (HPLC
4 grade) on air; to this solution a solid Cu₂O (0,035 g; 0.245 mmol) was added. Resulting reaction
5 mixture was let stirring for three days at 60°C. After filtering on a celite bed, the solution was let to
6 evaporate at room temperature. A blue microcrystalline solid was collected after few days from a
7 dark green solution.
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12 Characterization of compound **6**. Yields: Method A (82%), Method B (45%); Mp 242°C with
13 decomposition; IR (cm⁻¹): 3660, 3563, 3168, 1660, 1561, 1541, 1503, 1336, 1254, 1150, 1113,
14 1023, 935, 829, 758, 734, 729; ¹H NMR (acetone-d₆, r. t.): 25.97 (s, pzC-H); ESI(-) MS (CH₃CN, m/z):
15 203.1 m/z (100) [CF₃]₂pz], 469.1 (18), 648.7 (20), 1737.2 (100) [Cu₆((CF₃)₂pz)₆(OH)₆Cl]. ESI (+) MS
16 (CH₃CN, m/z): 242.4 m/z (100) [Bu₄N]. Elemental analysis for C₃₀H₁₄Cu₆F₃₆N₁₂O₇ + 2CH₃CN: Calc. %:
17 C, 22.86, H 1.12, N 10.88 %; Found: C, 23.04%, H, 1.12%, N, 10.49 %;
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24 *X-ray crystal structure determination experimental part for compounds 5 and 6*

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27 Crystal data for **5** and **6** were collected at 203 (**5**) or 150 K (**6**) on a Bruker APEX II single-crystal
28 diffractometer, working with Mo-K α graphite monochromatic radiator (λ = 0.71073 Å) and
29 equipped with an area detector. The raw frame data [20 (**5**) or 0.5 (**6**) s per frame scan time for a
30 sphere of diffraction data were processed using SAINT software;²⁹ a correction for absorption was
31 made using SADABS³⁰. The structure was solved by direct methods with SHELXS-97 (**5**) or SIR97 (**6**)
32 ³¹ and refined against F² with SHELXL-2014/7³⁰ using anisotropic thermal parameters. The
33 hydrogen atoms attached to carbons were inserted in calculated positions, their Uiso (H) were
34 defined as 1.2Ueq of the parent carbon atoms.
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41 The pyrazolyl hydrogen atom in **6** was inserted in calculated position and refined using a riding
42 model. The hydroxyl hydrogen atom in **6** was located in the difference Fourier synthesis and
43 refined with the help of distance restraint. During the refinement of this structure (**6**), electron
44 density peaks were located and believed to be of highly disordered water molecules. All the
45 attempts made to model the solvent molecules were not successful and they were removed using
46 the SQUEEZE routine from Platon.²⁸ This procedure was applied to recover 123 electrons per unit
47 cell (total volume 602 Å³). Lattice solvent water molecules are thus present as ca. 12 water
48 molecules per unit cell. These water molecules were not included in the cif.
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56 Details for the X-ray data collection are reported in Table 1. Crystallographic data have been
57 deposited with the Cambridge Crystallographic Data Centre as supplementary publication (CCDC
58 registration numbers in Table 1). Copies of the data can be obtained free of charge on application
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3 to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, (+44) 1223 336033; e-mail,
4 deposit@ccdc.cam.ac.uk).
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Table 1. Details for the X-ray data collection for **5** and **6**

Complex	5	6
Formula	C ₄₂ H ₃₂ Cu ₂ N ₈ O ₈ P ₂	C ₃₀ H ₁₂ Cu ₆ F ₃₆ N ₁₂ O ₆
Molecular weight	965.77	1701.76
Crystal system	Triclinic	Trigonal
Space group	<i>P</i> -1	<i>R</i> -3
<i>a</i> /Å	10.093(2)	21.863(5)
<i>b</i> /Å	12.325(2)	21.863(5)
<i>c</i> /Å	19.251(3)	10.076(5)
α /°	72.496(3)	90
β /°	87.743(3)	90
γ /°	66.218(3)	120
Volume, Å ³	2080.9(6)	4171(3)
Z	2	3
D _{calc} /g cm ⁻³	1.541	2.032
F(000)	984	2466
μ (Mo-K α)/mm ⁻¹	1.163	2.425
Reflections collected	28774	20374
Unique reflections	10015	1707
Observed reflections [<i>I</i> >2 σ (<i>I</i>)]	7113 [R _{int} = 0.0486]	1282 [R _{int} = 0.0793]
<i>R</i> , <i>wR</i> [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> = 0.0400; <i>wR</i> = 0.0860	<i>R</i> = 0.0319; <i>wR</i> = 0.0635
<i>R</i> , <i>wR</i> [all data]	<i>R</i> = 0.0673; <i>wR</i> = 0.0969	<i>R</i> = 0.0601; <i>wR</i> = 0.0692
CCDC ref code	1478672	1495587

$$R = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}, \quad {}^b \text{w}R2 = \left[\frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right]^{1/2}$$

Catalytic studies experimental part

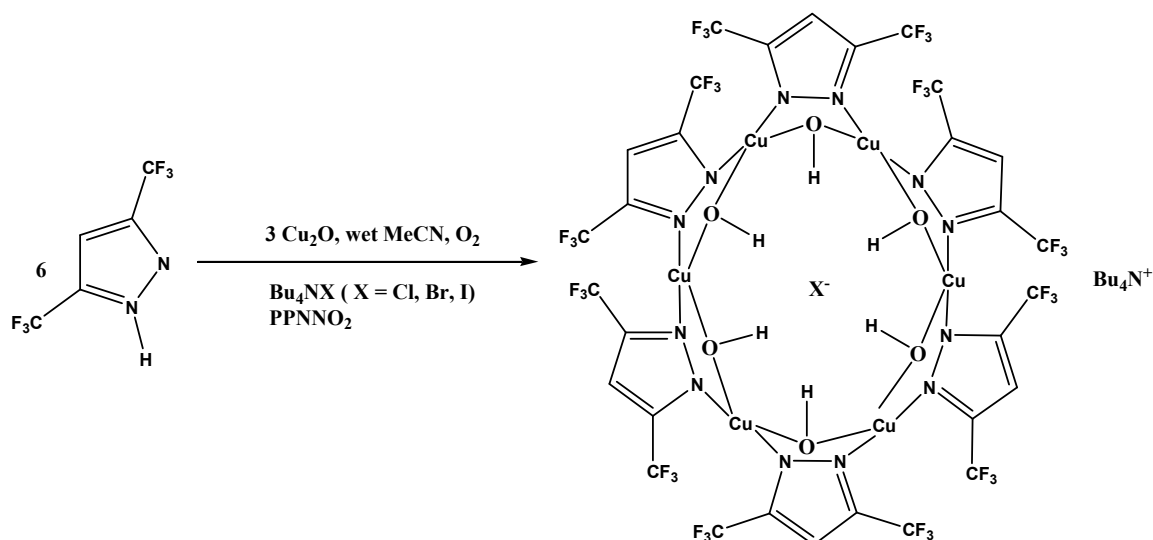
Catalytic oxidations of cyclohexane were carried out in sealed cylindrical Pyrex tubes under focused MW irradiation as follows: 1 – 10 μ mol of the catalyst was added to 5.00 mmol of

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3 cyclohexane, whereafter 10.00 mmol of 70% TBHP were introduced in the tube. This was then
4 placed in the microwave reactor and the system was stirred (650 rpm) and irradiated (5 W) for 0.5
5 - 3 h at 60 or 100 °C. After the reaction, the mixture was allowed to cool down to room
6 temperature. In the experiments with additives, the 2,2,6,6-tetramethylpiperidyl-1-oxyl radical
7 (TEMPO) or pyrazinecarboxylic acid (HPCA), 2.5- or 20 mol% vs. substrate, respectively, was added
8 to reaction medium. For the assays in the presence of the oxygen radical trap, NHPH₂, in
9 stoichiometric amount relative to the oxidant was added to the reaction mixture. Solution samples
10 were analysed by GC after addition of nitromethane (as a standard compound). Subsequently, an
11 excess of solid triphenylphosphine was added (to reduce the cyclohexyl hydroperoxide, primary
12 product, to the corresponding alcohol, and hydrogen peroxide to water) and the mixture was
13 analyzed again to estimate the amount of cyclohexyl hydroperoxide, following a method
14 developed by Shul'pin.³² For precise determination of the product concentrations only data
15 obtained after the reduction of the reaction sample with triphenylphosphine were typically used,
16 taking into account that the original reaction mixture contained cyclohexyl hydroperoxide,
17 cyclohexanol and cyclohexanone. Blank experiments, in the absence of any catalyst, were
18 performed under the studied reaction conditions and no significant conversion was observed.
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35 Results and discussion

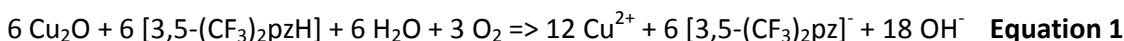
36 37 38 *Synthesis*

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40 A method for the synthesis of hexanuclear copper(II) derivatives was already reported and it
41 consists of a two steps procedure.^{13,16} The first reaction is the preparation of the Cu(I) derivative
42 by starting from neutral pyrazole, (CF₃)₂PzH, and Cu₂O in an oxygen free environment, followed by
43 the conversion of the Cu(I) trinuclear derivative to the hexanuclear complex by treating with
44 Bu₄NX in wet acetonitrile and in presence of air (X = Cl, Br, I). The water in the acetonitrile solution
45 is the source for the hydroxyl bridging groups, while the oxygen is responsible of the oxidation of
46 Cu(I) to Cu(II). With the aim to investigate thoroughly the reaction mechanism, the direct reaction
47 of the 3,5-bis(trifluoromethyl)pyrazole, Cu₂O with the anion sources in a 6 : 3 : 1 mole ratio was
48 performed according to the following reaction scheme (scheme 1).
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Scheme 1. Reaction scheme for the direct synthesis of compounds **1a (Cl)**, **1b (Br)**, **1c (I)**, **1d (NO₂)** starting from the neutral 3,5-(CF₃)₂-pyrazole.

Both different reaction mixtures turn to green in few hours and then to an intense blue from 2 hours to 24 hours for complex **1c**. After removal of the unreacted Cu₂O by filtration, the solutions gave the blue (Cl⁻, Br⁻, NO₂⁻) and dark green (I⁻) solids by slow evaporation of the CH₃CN solutions at room temperature. The solids were washed with hexane and then crystallized by slow evaporation of acetone solutions. The solids of **1a**, **1b**, **1c** and **1d** compounds obtained by reaction of scheme 1 have been characterized by elemental analysis, ¹H NMR, ¹⁹F NMR, IR, UV-visible spectroscopy and ESI MS spectrometry and the outcomes were compared to those previously reported, resulting the same compounds.¹³ By following the scheme 1, the reaction yields are lower than those already reported. The mole ratio between Cu₂O and the neutral pyrazole in the reaction was 1 : 2, but analyzing the redox equation 1 we see that the correct mole ratio between 3,5-(CF₃)₂pzH and copper for the 4 electron redox process must be 1 : 1 affording to an excess of both Cu²⁺ and hydroxyl ions, resulting in a low yield of the hexanuclear derivative and an excess of Cu²⁺ and hydroxyl ions.

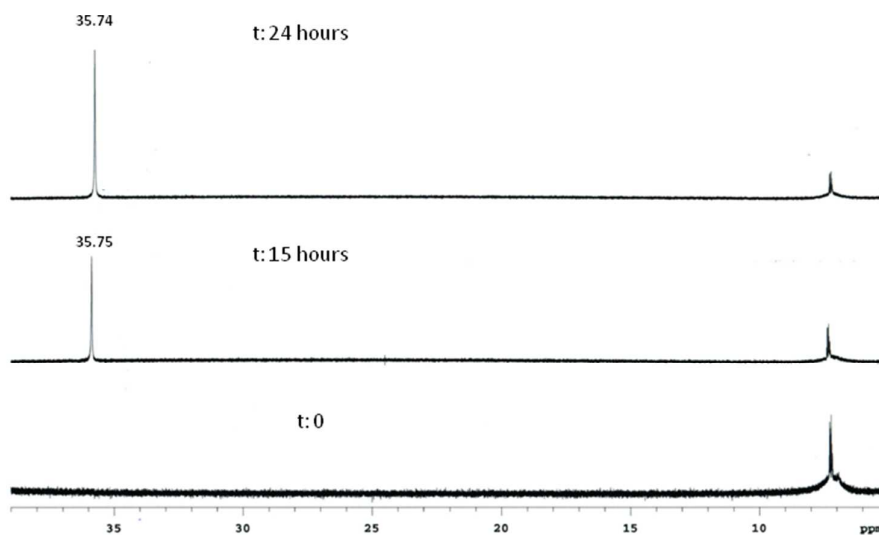


Different experimental conditions such as temperatures (r. t. or refluxing at 60°C in acetonitrile), reaction times (few hours till several days), solvents (acetone, acetonitrile, methylene chloride, THF), oxidant additives (H₂O₂) were attempted for this reaction. Moreover, many similar pyrazoles were tested such as 3,5-dinitro-pyrazole, 4-bromo-pyrazole, 3,5-dimethyl-pyrazole, 4-nitro-pyrazole, 3-CF₃ or 3-NO₂-pyrazole, some successes were obtained only for the last three cases. The

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3 result of these latter three pyrazoles can be evaluated by considering either the possibility to form
4 trinuclear cycles as reaction intermediate, or by considering the acid – base properties of the
5 pyrazoles. As concerns the formation of the $[\text{Cu}-\mu\text{-N,N}-(\text{pz})_3]$ derivative, it is reported its formation
6 for 1H-pyrazole, 1H-4-nitro-pyrazole, 1H-4-bromo-pyrazole, 1H-3-nitro-pyrazole and 1H-3,5-
7 dimethyl-4-bromo-pyrazole in addition to 1H-3,5-trifluoromethyl-pyrazole used as starting
8 material in reaction scheme 1. Hexanuclear cyclic products were obtained only in the case of 4-
9 nitropyrazole and 3- CF_3 or 3- NO_2 -pyrazoles. Moreover, if we consider the pK_a and pK_b in water
10 solution of these pyrazoles, leaving apart the 3- CF_3 -pyrazole whose data are about the gas phase,
11 (4-nitropyrazole: $\text{pK}_a = -2$; $\text{pK}_b = 9.64$; 4-nitropyrazole: $\text{pK}_a = -4.66$, $\text{pK}_b = 9.81$; 3- CF_3 -pyrazole: $\text{pK}_a =$
12 -14.5 (gas phase), $\text{pK}_b = -8.9$ (gas phase); 3,5-(CF_3)₂-pyrazole: $\text{pK}_a = -8.23$, $\text{pK}_b = 7.51$)³³ we observe
13 they have quite different acidity, but comparable basicity to that of 3,5-(CF_3)₂-pyrazole. As a
14 consequence, the results in the synthesis can be likely due to the similar basicity of the pyridine
15 type nitrogen. As above mentioned, the synthesis of the hexanuclear halide encapsulated
16 complexes were led also using 3- or 4-nitro-pyrazole, 3-trifluoromethyl-pyrazole and 3,5-dinitro-
17 pyrazole. The 3- or 4-nitro-pyrazole and 3-trifluoromethyl-pyrazole by the reaction with halide
18 sources following the scheme 1, yielded the pale soluble hexanuclear compounds whose
19 characterization by elemental analysis and IR spectroscopy showed similar trend of those recorded
20 for complexes 1 series. The 3,5-dinitro-pyrazole was attempted to synthesize the trinuclear as well
21 as the hexanuclear compounds according to all the reaction paths already reported. The syntheses
22 were all unsuccessful. This pyrazole possesses withdrawing groups which strength is comparable
23 to the CF_3 and in the same 3,5 position, but the stronger withdrawing power of the nitro groups
24 seems do not allow the cyclization arrangement. Nevertheless the reaction of the 3,5-
25 dinitropyrazole sodium salt with $\text{Cu}(\text{BF}_4)_2$ in the presence of PPh_3 affords to a new compound, **5**,
26 where the copper(I) centers are bound to two pyrazole ligands and PPh_3 is the co-ligand in a syn
27 geometry forming a dinuclear compound. The phosphane has the function to reduce the Cu(II) to
28 Cu(I) ions and to satisfy the coordination requirements of the metal center affording to a cycle
29 where two bridging pyrazoles are also required.

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42 These results led us to perform an investigation on the reaction's mechanism according to scheme
43 1 by monitoring the reaction in a NMR tube. Recording ^1H NMR spectra over the time we see the
44 appearance of the typical C_4H signal for the hexanuclear derivative after some hours and not
45 immediately. The spectra are reported in figure 1 and they show that after half of an hour many
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3 signals around the 7 ppm range appear. In 24 hours the high frequency signal at 35.74 ppm (C-₄H) reaches the maximum intensity and the ratio between this signal and those around 7 ppm is 10 : 1.
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30 **Figure 1.** Plot of ¹H NMR spectra after few minutes (below), after 15 hours (central) and after a
31 day (above), monitoring the formation of **1a** from 3,5(CF₃)₂pz-1H and Cu₂O and Bu₄NCl according
32 to reaction scheme 1.
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36 If the reaction occurs between the trinuclear complex [Cu-μ-3,5(CF₃)₂pz]₃ and Bu₄NCl we observe
37 a faster and cleaner conversion to the hexanuclear product **1a** (figure 2).
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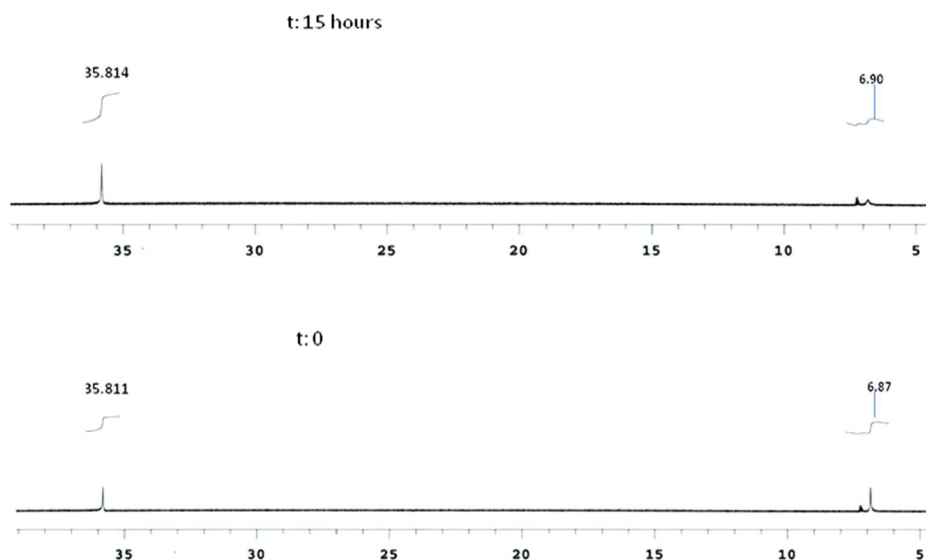
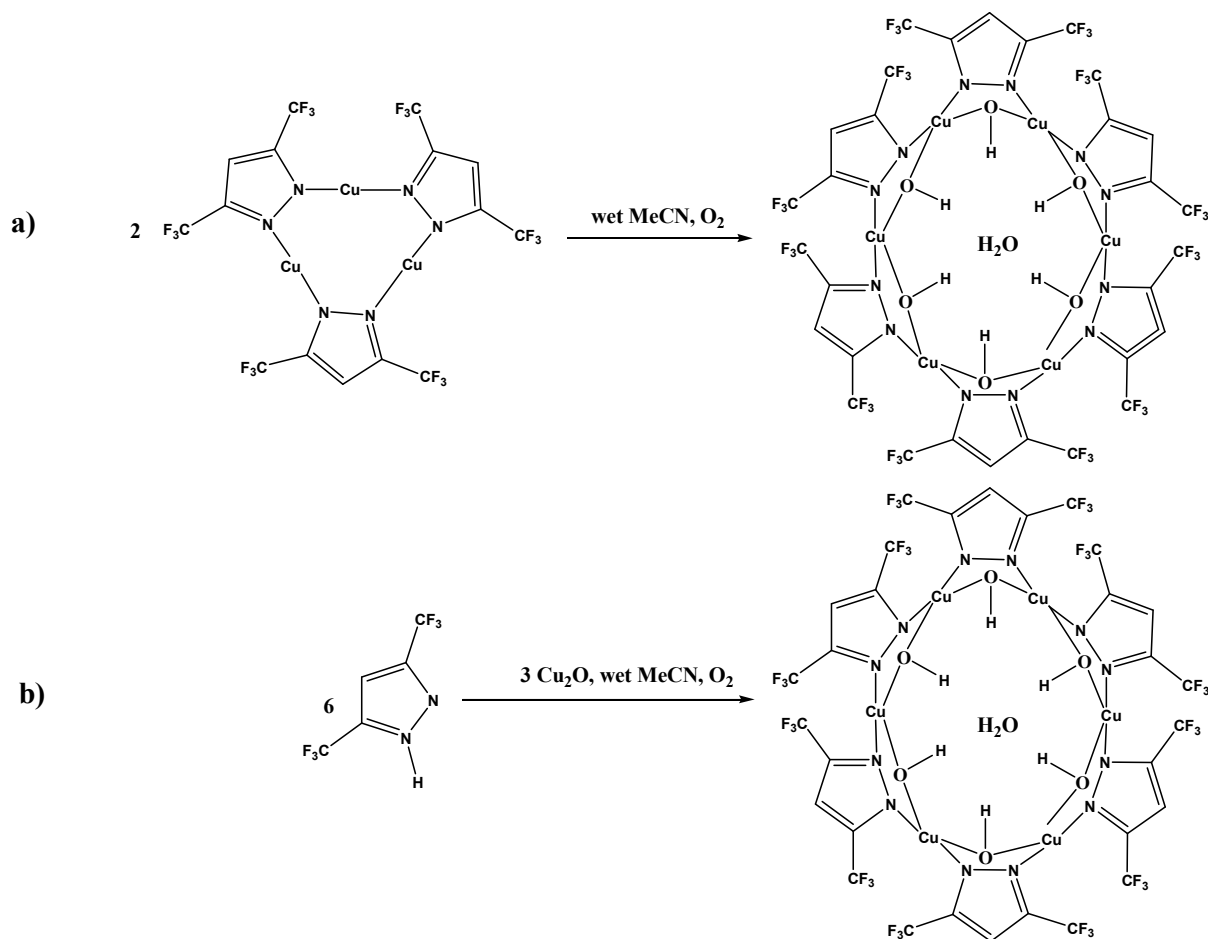


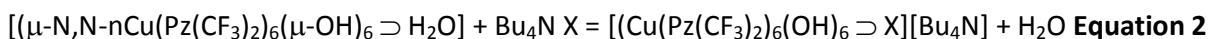
Figure 2. Plot of ^1H NMR spectra after few minutes (below) and after 15 hours (above), monitoring the formation of **1a** starting from $[\text{Cu}-\mu\text{-}3,5(\text{CF}_3)_2\text{pz}]_3$ and Bu_4NCl .

Most of the signals in the ^1H NMR monitoring are sharp, denoting fast exchange in solution and the likely absence of long life intermediate of the reaction. A possible mechanism for the synthesis of these compounds would be the template action of the anions to organize the ligand in higher nuclearity assemblies converging to the hexanuclear metallacycle. As a consequence, the reaction in the absence of any anion source was performed both starting either from $[\text{Cu}-\mu\text{-}3,5(\text{CF}_3)_2\text{pz}]_3$ and from $3,5(\text{CF}_3)_2\text{pz-}1\text{H}$ and Cu_2O . In both reactions, the hydrated hexanuclear metallacycle was obtained, compound **6**.

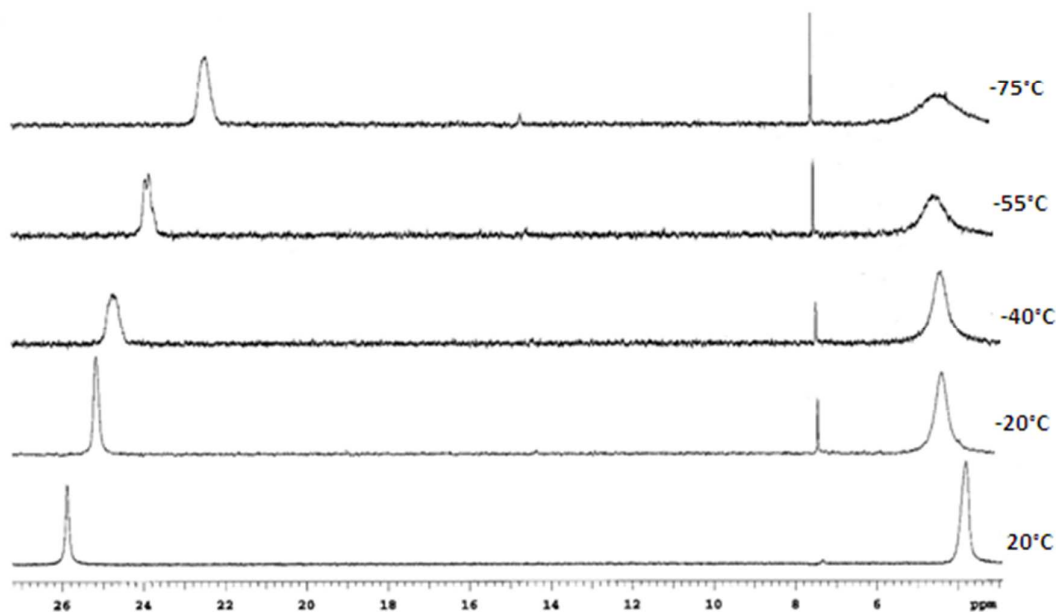


Scheme 2. Reaction schemes for the formation of compound **6** in absence of anion sources a) starting from the trimer, b) starting from the bare neutral pyrazole.

Compound **6** is a blue solid that once isolated from the acetonitrile solution shows a very poor solubility in acetonitrile and lightly better in acetone. The reaction yields are of 82 % and 45 % according to scheme 2a and scheme 2b, respectively. The elemental analysis confirms the presence of the metallacycle and the presence of two molecules of CH_3CN and one of water. To exclude the formation of the hydroxyl encapsulated metallacycle, the reaction of scheme 2a in the presence of Bu_4NOH was performed: after the adding of hydroxyl ions a ready precipitation of a green solid was observed corresponding to the $\text{Cu}(\text{OH})_2$. Compound **6** readily exchanges with halides, Cl, Br, I, and NO_2 anions in the presence of the corresponding anion source in the 1 : 1 mole ratio in acetonitrile solutions (equation 2).



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3 The ^1H NMR characterization of compound **6**, showed the $\text{C}_4\text{-H}$ signal of the pyrazole at 25 ppm in
4 acetone- d_6 and 35 ppm in CD_3CN as already observed for the other anion centered metallacycles
5 **1a**, **1b**, **1c** and **1d**. The line width at half height of the 25 ppm signal is of 36 Hz, while the water of
6 acetone falls at 3.93 ppm instead of the 2.8 ppm; these shifts leave to suppose a likely water
7 exchange process between the “encapsulated” water molecules and the free water molecules of
8 the deuterated solvent. A VT NMR experiment was performed by changing the temperature from
9 50°C to -90°C . At low temperature, the 25 ppm signal broadens (LW at half height peak from 36
10 Hz at 20°C to 250 Hz at -90°C) and shifts toward lower frequencies, at -55°C it splits in two
11 resonances (23.93 ppm and 23.86 ppm) while the free water resonance moves to higher
12 frequencies and broaden to 280 Hz at this temperature (-55°C , 4.6 ppm) (figure 3). By adding few
13 μL of water in the NMR tube, the resonance at 23.86 ppm increases its intensity, while the one at
14 23.93 decreases: as a consequence, it is reasonable to attribute the resonance at 23.86 to the
15 “water encapsulated” metallacycle, and the other one might be due to the “empty” metallacycle.
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49 **Figure 3.** Plot of the VT ^1H NMR spectra for compound **6** since 20°C to -75°C in acetone- d_6 .
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51 Moreover, in the VT ^1H NMR spectra it is possible to calculate the rate constant at -20°C and it
52 corresponds to $7.1 \cdot 10^7 \text{ s}^{-1}$. This value is comparable with those relative to temperature dependent
53 very fast exchange regime already observed for some paramagnetic gadolinium DOTA complexes
54 reported in literature ³⁵.
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3 The MIR spectrum of compound **6** shows typical bands for the bridging hydroxyl groups, already
4 observed in the other halide adducts such as at 3650 and near 1600 cm^{-1} , while we observe the
5 presence of the band at 1660 cm^{-1} likely due to the H_2O bending vibrational mode. Actually this
6 value is pretty high as wavenumber for liquid water which is expected to be at 1610 cm^{-1} .³⁶ For
7 water belonging to the C_{2v} point group this vibration mode (ν_2 , A_1 symmetry) falls at 1595 cm^{-1} ,
8 while the symmetric (ν_1 , A_1 symmetry) and asymmetric stretchings (ν_3 , B_2 symmetry, normal
9 vibration) fall at 3657 cm^{-1} and 3756 cm^{-1} , respectively. In the MIR spectrum we can observe the
10 asymmetric stretching of water (broad, 3667 cm^{-1}) overlapping to the bridging OH stretching,
11 while the ν_2 band is visible blue-shifted at 1660 cm^{-1} . At 3167 cm^{-1} we can observe the $\text{C}_4\text{pz-H}$
12 stretching and the C=C and C=N stretchings can be attributed to 1542 and 1504 cm^{-1} , respectively.
13 The CF_3 groups are observed at 1254 cm^{-1} and 1113 cm^{-1} with intense bands due to the C-F
14 stretchings.
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25 In the FIR spectrum of **6** we can attribute the absorption of Cu-O bond at 489 cm^{-1} (slightly blue
26 shifted if compared to Cl^- or Br^- adducts, **1a** and **1b**, at 487 cm^{-1}). The Cu-N bond absorption falls at
27 295 cm^{-1} , also in this case the band is blue shifted if compared to the analogous halide structures
28 (291 cm^{-1} for Cl^- adduct, **1a** and 287 cm^{-1} for Br^- adduct. **1b**). The very weak band at 522 cm^{-1} ,
29 present only in the water encapsulated adduct **6**, might be attributed to the ν_L (hindered rotation,
30 at 600 cm^{-1} for hydrogen networked water). The NIR spectra of compound **1a**, **1b**, **1c**, **1d** and **6**
31 shows weak bands due to the O-H combination bands of the fundamental vibration modes of
32 water and hydroxyl groups. The band at 1398 (first vibrational overtone), 1614, 2187 and 2404 nm
33 are attributable to overtones of OH and water present in all adducts previously investigated. In
34 compound **6**, on the contrary of those observed for other adducts, we can observe the presence of
35 additional bands likely due to hydrogen bonding networks such as 2153 and 2353 nm, reported in
36 the NIR spectra of ice.³⁷ Around 1896 nm, a medium sharp band can be observed, due to a
37 combination of its O-H stretch and its H-O-H bending (1900 nm for liquid water). A broad large
38 band going from 1870 to 2050 nm might be due to physically adsorbed water.³⁸
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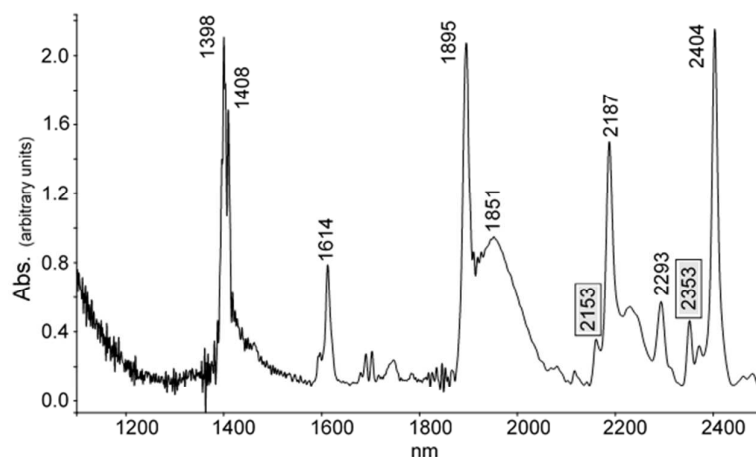


Figure 4. NIR spectrum of compound **6** in the region 1000-2500 nm. The water bands at 1398, 1614, 2187 and 2404 (liquid) and at 2153 and 2353 nm (solid), are shown.

The ESI mass spectrometry analysis of compound **6** was performed in a 1 mM solution of the compound in CH_3CN . The ESI mass spectrum in the negative mode shows many rearrangements involving chloride ions naturally present in the ionization source. In example, the following ions were detected such as $[(\text{Cu}-(3,5\text{pz}(\text{CF}_3)_2)_3 + \text{Cl})^-]$, 834.7 m/z, the $[(\text{Cu}-(3,5\text{pz}(\text{CF}_3)_2)_4 + \text{Cl})^-]$, 1100 m/z, and $[(\text{Cu}-(3,5\text{pz}(\text{CF}_3)_2)_5 + \text{Cl})^-]$, 1368.4 m/z; in addition to these ions the formation of the chloride adduct as main peak $[(\text{Cu}-(3,5\text{pz}(\text{CF}_3)_2-\text{OH})_6 + \text{Cl})^-]$, 1736 m/z, was observed; it is noteworthy that on the contrary of what found in compounds **1a**, **1b**, **1c** and **1d** ESI spectra, the bridging hydroxyl groups are present in this latter ion, and similarly also the bromide $[(\text{Cu}-(3,5\text{pz}(\text{CF}_3)_2-\text{OH})_6 + \text{Br})^-]$ was observed in trace. The peak relative to the water or hydroxyl adducts were not even detected in trace.

X-ray crystal structure analysis

The dinuclear nature of compound $[\text{Cu}-(3,5-(\text{NO}_2)_2\text{pz})(\text{PPh}_3)]_2$ (**5**) has been evidenced by single crystal X Ray diffraction analysis. The ORTEP view of the molecule is reported in Figure 5, together with the atom labeling scheme. The most important bond distances and angles are reported in the caption.

Each copper atom is trigonally coordinated considering the two nitrogen atoms of the bridging ligands and the phosphorous atom of the phosphane molecule. The coordination around the copper atoms deviates significantly from the planarity being Cu1 and Cu2 out of the pertinent

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3 coordination plane of 0.1924(4) and 0.2674(4) Å respectively. The six-member Cu-[N-N]₂-Cu ring
4 presents a boat conformation, but considering that the copper atoms lie out of the pyrazolate
5 average planes with deviations spanning from a minimum of 0.0231(4) Å for Cu1 with respect to
6 N5N6C4C5C6 ring up to 0.3376(4) for Cu2 with respect to N1N2C1C2C3 ring, the boat
7 conformation results slightly twisted. The crystal packing of the compound is built up by a strong
8 network of Van der Waals interactions between the nitro groups and between the nitro groups
9 and the nitrogen atoms of the pyrazolate ring of adjacent molecules.

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15 The asymmetric unit of compound **6** is depicted in Figure 6. It contains one sixth of the neutral
16 copper(II) hexanuclear metal core [Cu(μ-OH)(η²,μ-(CF₃)₂pz)]₆ [tFpyr = 3,5-bis(trifluoromethyl)-1H-
17 pyrazolate anion], an inversion center is sited in the middle of the core and a 3-fold axis passes
18 through that location. Two perspectives of crystal packing are shown in Figure S1 (see
19 supplementary information) and selected bond distances and angles are given in the legend of
20 Figure 6. The copper metals present distorted square-planar geometries as expressed by the
21 Houser (τ₄)³⁹ parameter of 0.29, join five-membered Cu₂N₂O rings, ultimately giving rise to a large
22 Cu₆(N₂O)₆ crown-type assembly. The structure can also be envisaged as a circular zig-zag Cu₆O₆
23 cluster where the metal cations stand in the least-square plane defined by those atoms; the
24 bridging η²-pyrazolate moieties are alternatively positioned above and below this plane, the
25 minimum intramolecular Cu...Cu distance is of 3.1425(17) Å, the Cu–O and Cu–N bond lengths are
26 of 1.917(2) and 1.970(3) (average values) Å, respectively. The structure is stabilized by
27 intermolecular hydrogen bond interactions (Figure 6) involving the pyrazolate CH groups (as
28 donors) and the F1 atoms (as acceptors) of vicinal complexes.
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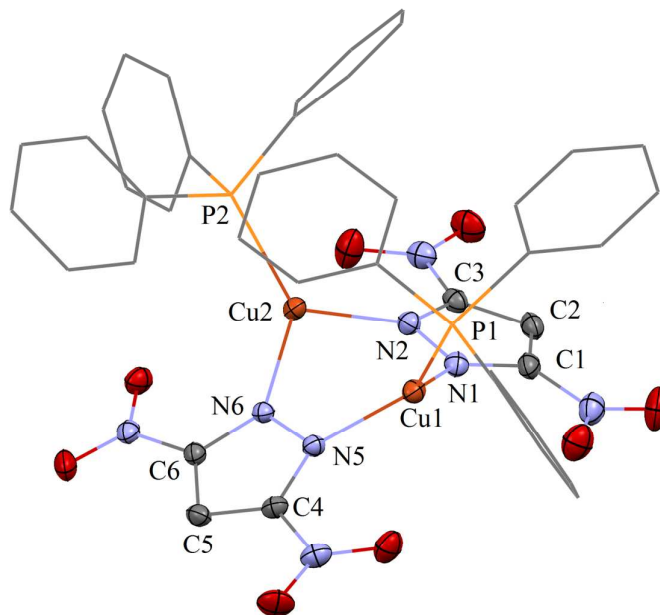


Figure 5. Ortep view of $[\text{Cu}-(3,5\text{-(NO}_2)_2\text{pz)}(\text{PPh}_3)]_2$ (**5**); phosphine ligands have been drawn in wireframe model. Ellipsoids when shown, are at their 30% level.

Selected bond distances (Å) and angles (°): N1-Cu1 2.0217(19), N5-Cu1 1.998(2), P1-Cu1 2.1981(7), N2-Cu2 1.974(2), N6-Cu2 2.004(2), P2-Cu2 2.1812(8); N5-Cu1-N1 104.09(8), N5-Cu1-P1 126.42(6), N1-Cu1-P1 126.87(6), N2-Cu2-N6 102.17(8), N2-Cu2-P2 132.41(6), N6-Cu2-P2 120.20(6).

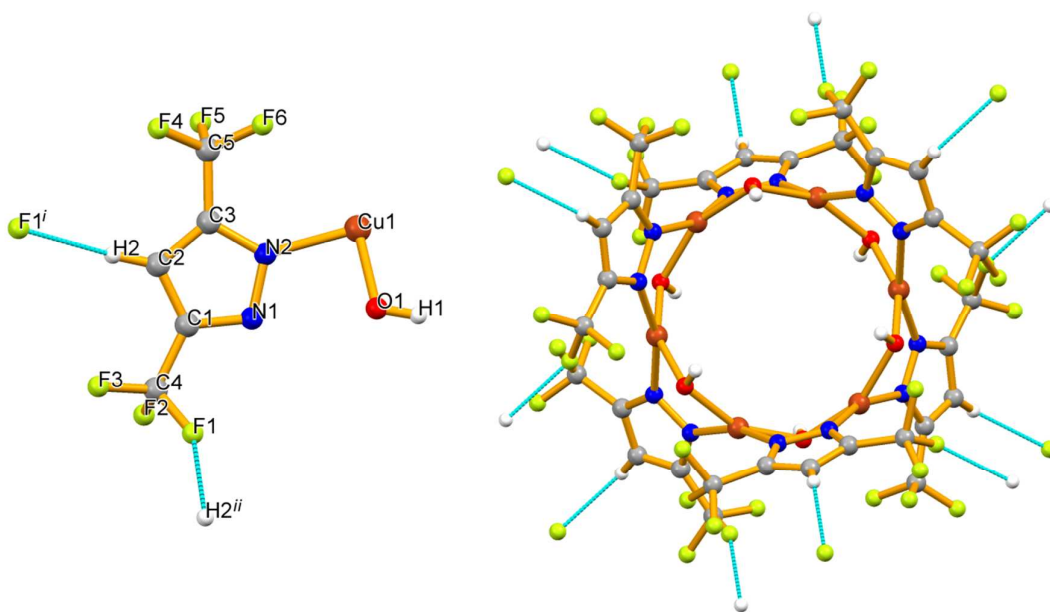
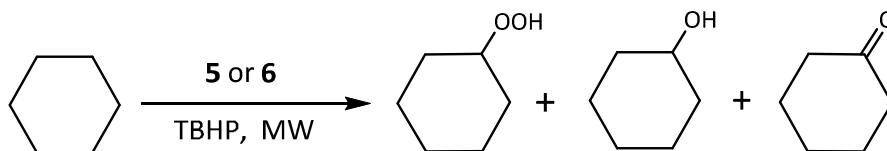


Figure 6 – The asymmetric unit with atoms labelling scheme (left) and the structure (right) of compound **1**, also showing the donor (carbon)···acceptor (fluorine) contact interactions (in dashed light blue line). Symmetry operations to generate equivalent atoms: *i*) 1.67-x+y, 1.3(3)-x, 1/3+z; *ii*) 1.3(3)-y, -1/3+x-y, -1/3+z. Selected bond distances (Å) and angles (°): N1–Cu1 1.972(3), N2–Cu1 1.965(3), O1–Cu1 1.918(2), N1–N2 1.346(4), C1–N1 1.340(4), C3–N2 1.342(4), C4–F3 1.328(4), C5–F5 1.340(4); O1–Cu1–N2 86.04(11), O1–Cu1–N1 97.84(11), N2–Cu1–N1 163.86(11), O1–Cu1–O1 155.30(14). Hydrogen bond interaction C2–H2···F1ⁱ: D···A 3.279(7) Å, ∠ D–H···A 153°.

Catalytic studies

Compounds **5** and **6** act as very effective homogeneous catalysts towards the neat microwave (MW) assisted peroxidative (with aq. *tert*-butyl hydroperoxide, TBHP) oxidation of cyclohexane to cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide (Scheme 3).



Scheme 3 – Microwave-assisted neat oxidation of cyclohexane to cyclohexyl hydroperoxide, cyclohexanol and cyclohexanone with *tert*-butyl hydroperoxide catalysed by the Cu complexes **5** or **6**.

The formation of the hydroperoxide was proved by Shul'pin's method³² and allowed us to estimate the real concentrations of alkyl hydroperoxide, alcohol and ketone: the addition of PPh₃ prior to the GC analysis of the products resulted in a marked increase of the amount of cyclohexanol (due to the reduction of CyOOH by PPh₃, with the formation of phosphane oxide) and in a corresponding decrease of cyclohexanone. The formation of cyclohexyl hydroperoxide (typical intermediate product in radical-type reactions) along with the complete suppression of the catalytic activity upon the introduction of a radical trap (Ph₂NH, Figure 10) to the reaction mixture supports the hypothesis of a free-radical mechanism for the cyclohexane oxidation carried out in this study. Radicals *tert*-BuOO• and *tert*-BuO•⁴⁰ could be produced in the catalyst promoted decomposition of TBHP with the formation of a reduced form of the catalyst and of an hydroxo-Cu species (precursor of a *tert*-butylperoxide copper species). Those radicals could then react with

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3 cyclohexane (CyH) giving rise to the cyclohexyl radical Cy• upon hydrogen abstraction. Cy• reacts
4 with oxygen, leading to CyOO•. CyOOH can be formed, e.g., upon hydrogen abstraction from tert-
5 BuOOH by CyOO•. Metal-assisted decomposition of CyOOH to CyO• would then lead to CyOH and
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cyclohexane (CyH) giving rise to the cyclohexyl radical Cy• upon hydrogen abstraction. Cy• reacts with oxygen, leading to CyOO•. CyOOH can be formed, e.g., upon hydrogen abstraction from tert-BuOOH by CyOO•. Metal-assisted decomposition of CyOOH to CyO• would then lead to CyOH and CyO products.

A very high yield, up to 58% (**6**) or 51% (**5**) of oxygenated products, is obtained at optimized conditions: 0.5 h (**6**) or 1.5 h (**5**) of MW irradiation at 100 °C (see Figure 7 and Table S1, Electronic Supporting Information), using 0.2 % molar ratio of copper catalyst relatively to the substrate, in the presence of 2,2,6,6-tetramethyl-piperidinyloxy radical (TEMPO, 2.5 % molar ratio vs. substrate).

For the Cu(II) catalytic system, the amount of catalyst plays a significant role as depicted in Figures 8 and 9. The increase from 1 to 5 μmol of **6** on the reaction medium leads to a yield increment from 22 to 37 %, whereas 10 μmol of **6** allows reaching the maximum yield faster (in 1 hour, instead of the 2 hours of MW irradiation needed for 5 μmol of **6**). The effect of the quantity of catalyst on the yield of products is not so evident for the Cu(I) system (**5**).

Moreover, addition of small amounts (2.5 mol% vs. substrate) of TEMPO to the reaction mixture allows the maximum yield of cyclohexanol and cyclohexanone to be achieved after the very short MW irradiation time of 0.5 or 1 h, for 10 or 5 μmol of **6**, respectively (Figure 7). The same behavior is observed for the Cu(I) catalytic system. The promoting effect of TEMPO may be rationalized as follows: under the used oxidizing conditions TEMPO conceivably could be oxidized to the oxoammonium species **41** and thus also operate as oxidant to transform cyclohexane into the corresponding oxygenate product, apart from acting as hydrogen-atom abstractor from TBHP, reinforcing the formation of tert-BuOO•. However, when added in higher amounts, TEMPO can exhibit its usual^{25,42} inhibiting effect: for **5**, addition of 2.5, 5, 50 and 100 mol % vs. cyclohexane led to total (cyclohexanol and cyclohexanone) yields of 21.6, 21.4, 3.8 and 0.0 %, respectively.

The alcohol to ketone ratio (A/K) is known as an indicator for catalyst selectivity, reflecting the combined conversion of cyclohexane either to directly the cyclohexanol or to cyclohexyl hydroperoxide, which subsequently is reduced to the alcohol as a result from the reduction with triphenylphosphine.³²

In the present study, cyclohexanol is obtained in a larger amount than cyclohexanone: alcohol/ketone molar ratio is of *ca.* 3 for **5** in additive-free media (Table S1). As expected, the presence of TEMPO (a well-known promotor of alcohols oxidation)⁴³ promotes the formation of

ketone (molar ratio decreases to *ca.* 1.7). For **6**, the effect is only detectable for the highest catalyst amount used (0.2 % vs. substrate).

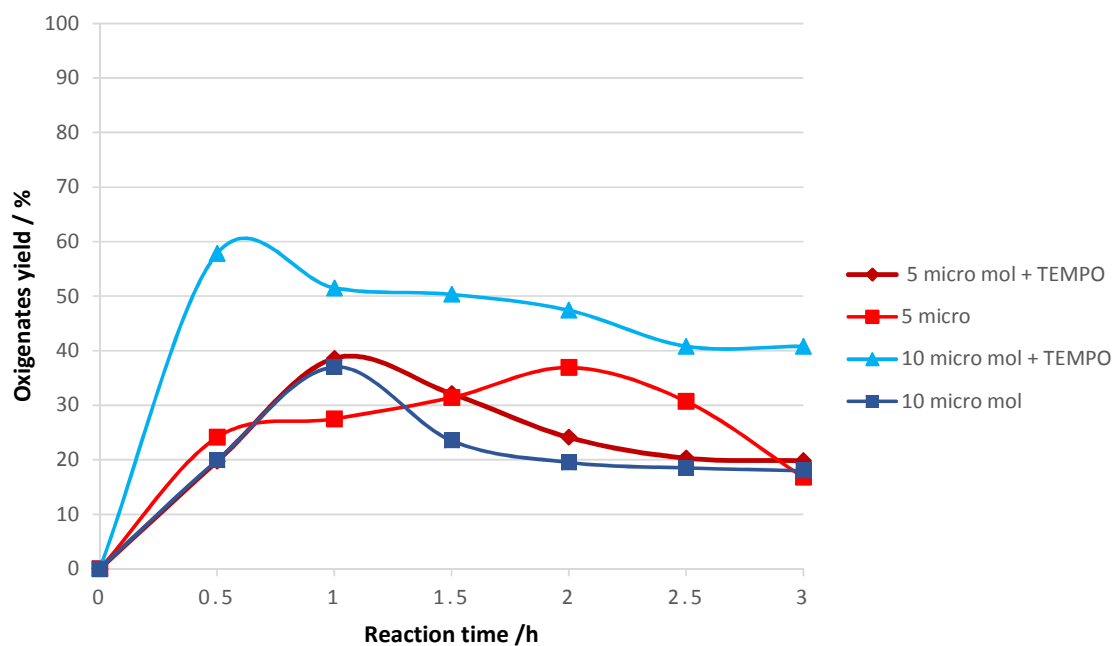
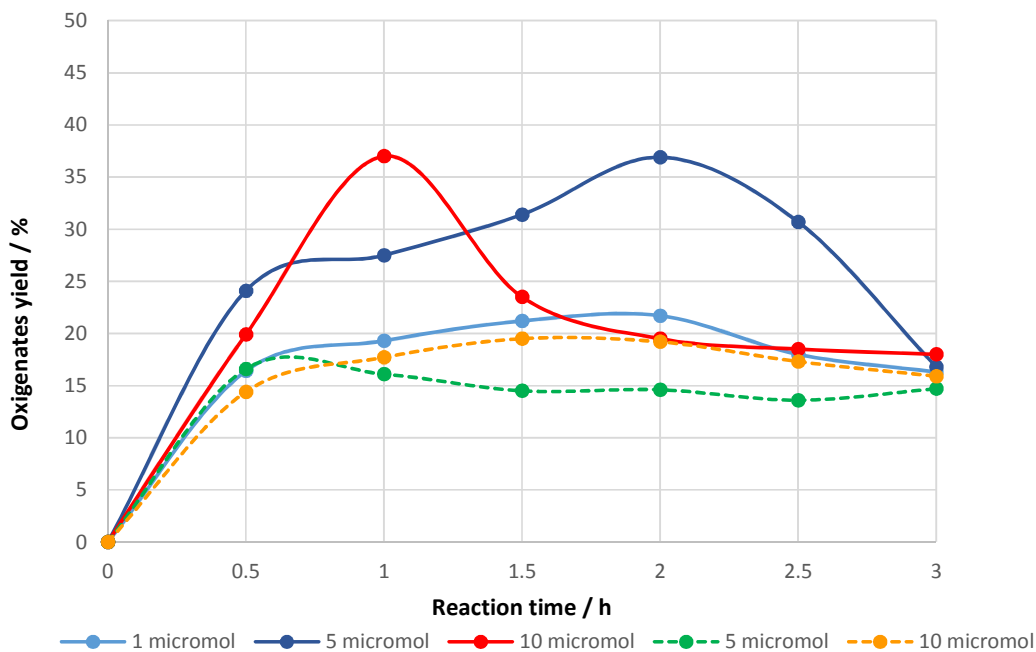
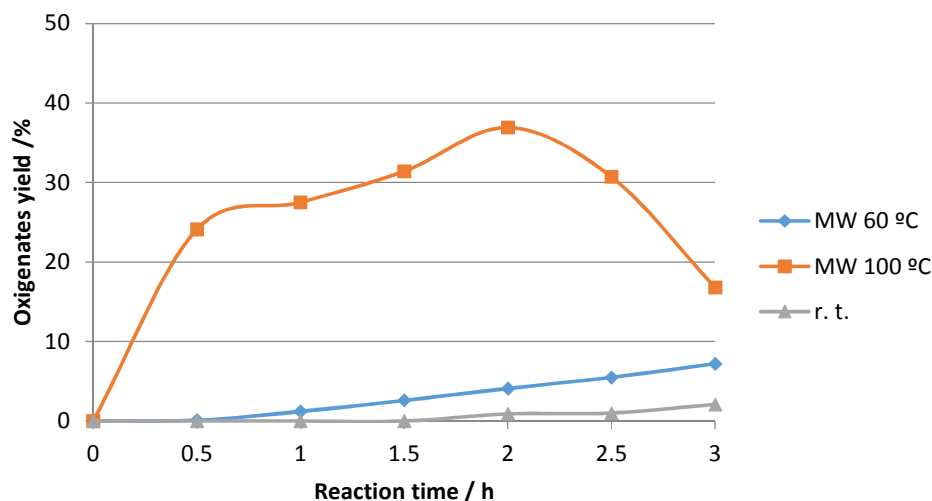


Figure 7 - Effect of the reaction time, catalyst (**6**) amount and TEMPO additive on the yield of cyclohexanol and cyclohexanone obtained by microwave-assisted neat oxidation of cyclohexane with THBP.



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3 **Figure 8** - Effect of the reaction time and catalyst (— **6** or ---- **5**) amount on the yield of
4 cyclohexanol and cyclohexanone obtained by additive-free microwave-assisted neat oxidation of
5 cyclohexane with THBP.
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9 The catalytic activity of **5** and **6** is also sensitive to the temperature as depicted in Figure 9 for **6**.



29 **Figure 9** - Effect of the reaction temperature on the yield of cyclohexanol and cyclohexanone
30 obtained by additive-free neat oxidation of cyclohexane with THBP, catalyzed by **6** (0.1% molar vs.
31 substrate).
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35 The promoting role of certain acids, in particular pyrazine carboxylic acid (Hpca), on the catalytic
36 oxidation of various cycloalkanes catalyzed by metal complexes is well known.⁴⁴ In our catalytic
37 systems, the presence of Hpca has a strong inhibiting effect on the catalytic activity of both **5** and
38 **6** (Figure 10). A similar behavior was previously found.⁴⁵
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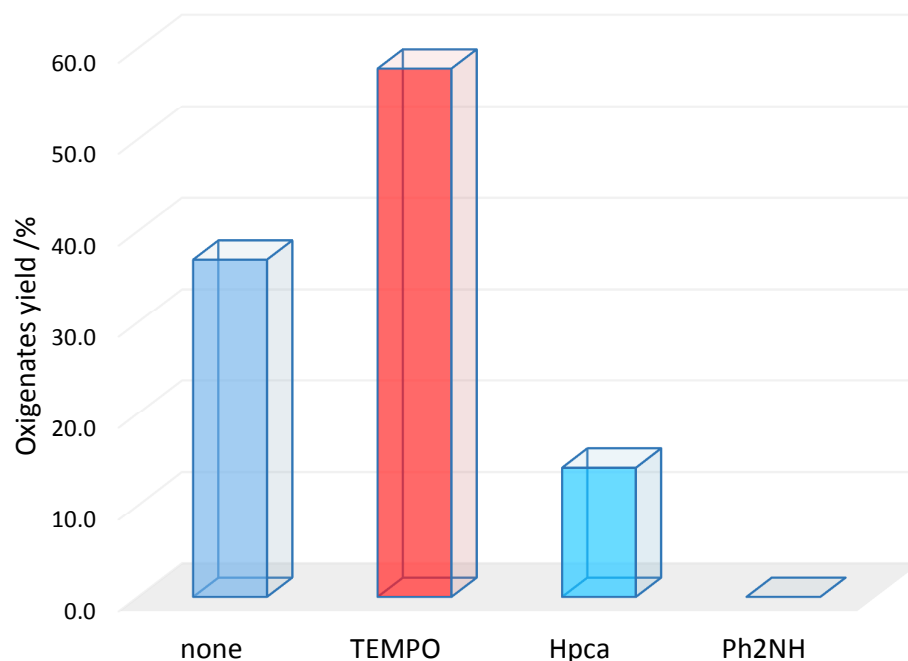


Figure 10 - Effect of different additives on the the yield of cyclohexanol and cyclohexanone obtained by microwave-assisted neat oxidation of cyclohexane with THBP, catalyzed by **6** (0.1% molar vs. substrate).

Conclusions

A new route for the synthesis of the $[\text{Bu}_4\text{N}][\text{Cu}_6(3,5\text{-pzCF}_3)_6(\text{OH})_6 \supset \text{X}]$ was found, starting from the neutral $3,5\text{-pzH}(\text{CF}_3)_2$ and Cu_2O as source both of metal and of the base (oxide) in aerated and wet acetonitrile. The reactions show lower yields if compared to that previously reported. Nevertheless, it was proved that anions do not template these reactions and a water encapsulated metallacycle, $[\text{Cu}_6(3,5\text{-pzCF}_3)_6(\text{OH})_6 \supset \text{H}_2\text{O}]$ was synthesized. In complex $[\text{Cu}_6(3,5\text{-pzCF}_3)_6(\text{OH})_6 \supset \text{H}_2\text{O}]$, the presence of the water molecules inside the cavity was analyzed by NIR spectroscopy and by determining the rate constant of the water exchange reaction in acetone solution. The value of k is $7.1 \times 10^7 \text{ sec}^{-1}$ and it is close to the value obtained for water exchange paramagnetic Gadolinium complexes studied for their employment in Magnetic Resonance Imaging. Moreover, by considering that the internal diameter of the cavity is 6.2 \AA and the height of the channel is 7.6 \AA in the average; these sizes can be compared to those of β cyclodextrins formed by seven glucose molecules connected by α -1,4 glycosidic bonds. This cyclodextrin contains many water molecules inside the cavity, but they can be displaced by hydrophobic molecules such as neutral molecules of

proper size interacting with polar C₃H or C₅H atoms of the glucopyranoside. In the hexanuclear copper(II) host upper and lower rims the CF₃ groups are merging, making the entrance very polar, while in the cavity, the OH groups are in a symmetric trans configuration forming hydrophilic environments above and below the rim with pseudo spherical hydrogen bonding symmetry; this environment makes the host able to encapsulate spherical ions but in the same meanwhile the circular disposition of electrophilic Cu(II) ions makes the host able to recognize neutral polar nucleophilic molecules with appropriate size. Many other pyrazoles have been employed in the synthesis of copper metallacycles following the reaction schemes above reported. In some cases, low soluble products were obtained. The best result was obtained with the 4-nitro pyrazole having similar pKa and pKb of 3,5-bis(trifluoromethyl)-pyrazole. In the case of 3-nitropyrazole and 3-trifluoromethyl-pyrazole only in the solid state was isolated the hexanuclear metallacycle but in low yields. When 3,5-dinitropyrazole is used neither the trinuclear Cu(I) nor the hexanuclear Cu(II) complexes were obtained and the only product was that one containing the pyrazole, Cu(I) and the additional co-ligand PPh₃. The two complexes, [Cu₂(μ-N,N-3,5-(NO₂)₂pz)₂(PPh₃)₂], **5**, and [Cu₆(3,5-pzCF₃)₆(OH)₆ · H₂O], **6**, were successfully tested as catalysts on the microwave-assisted neat oxidation of cyclohexane to the cyclohexanol and cyclohexanone mixture through a likely radical mechanism, affording considerably high yields (up to 58%) in rather short reaction times (30 min, for **6**). The presented catalytic procedure leads to significantly higher yields of cyclohexanol and cyclohexanone than those reported (although for considerably different conditions) for copper complexes with related ligands, such as the C-scorpionate Cu(II) complex [CuCl₂(Tpm^{OH})₂] (Tpm^{OH} = 2,2,2-tris(pyrazol-1-yl)ethanol), 7%;⁴⁶ copper coordination polymers with pyrazolato-based tectons, 11 %^{45a} or based on trinuclear triangular [Cu₃(μ³-OH)(μ-pz)₃]²⁺ units, 36%.⁴⁷ Moreover, our catalytic protocol (TBHP/MW) is very fast, solvent-free and using a green energy source.

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