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Synthesis, Structure and Catalysis of Tetranuclear Copper(II) Open Cubane for Henry Reaction on Water

Suribabu Jammi[a] and Tharmalingam Punniyamurthy*[a]

Keywords: C–C bond formation / Copper / Henry reaction / Heterogeneous catalysis / Water

The copper(II) open cubane **1** has been synthesized and its structure determined. It is insoluble in water and efficiently catalyzes the Henry reaction with high yield.

Introduction

Polynuclear metal clusters have attracted considerable interest because of their relevance to multielectron transfer centres in biological systems, and their interesting catalytic and magnetic properties.[1] Of these, metal cubane complexes are a well-studied class of compounds,[2] in which the four metal ions are bridged by hydroxy, alkoxo, azido, sulfide or iminato groups.[3] Many alkoxo-bridged copper(II) cubanes have been prepared and have been reported to have intracluster ferromagnetic interactions.[4] Herein, we wish to report the synthesis, structure and catalysis of an alkoxo-bridged tetranuclear copper(II) open cubane[5] **1** for Henry reaction on water. The copper(II) ions having alkoxo bridges are tetracoordinate with square-planar geometry.[6] The water-insoluble **1** has been studied for the addition of nitroalkanes to aldehydes (Henry reaction) on water.[7m–7p,8] The observed results suggest that the reactions take place on the surface of the catalyst. In comparison to the existing methods in or on water,[7m–7p] the present reaction functions with a low concentration of the cluster **1** in a shorter time to afford the nitroaldol product in high yield. To the best of our knowledge, this is the first example available employing a cubane-like cluster for aqueous organic synthesis. The reaction provides simplified product isolation, and easy recovery and recyclability of the catalyst.

Results and Discussion

The readily accessible 3,5-di-*tert*-butyl salicylaldehyde **2** was treated with $H_2NCH_2CH_2OH$ in EtOH to give Schiff base **3** as yellow solid in 90% yield. The latter underwent reaction with $Cu(OAc)_2{\cdot}H_2O$ in EtOH to afford the cluster **1** as a green powder. During purification on silica gel column chromatography with EtOAc and hexane, the cluster **1** provided single crystals in 80% yield. Their X-ray analysis revealed that the cluster **1** contains an open cubane structure (Figure 1).[9] In the crystal lattice EtOAc exhibits interaction with adjacent cluster molecules (Figure 2). The five-membered rings containing the copper(II) ion, alkoxo oxygen and imine nitrogen exist with half-chair conformation.

As the cluster **1** in its lattice contains water molecules (see Supporting Information), its catalysis was investigated for organic reactions on water.[7] First, the addition of nitroalkanes to aldehydes was performed.[7m–7p,8] Optimization of the reaction conditions was pursued with benzaldehyde as a model substrate (Table 1, entries 1–3). The best results were observed when the substrate was stirred with 5 equiv. of nitromethane and 2.5 mol-% of **1** on water. A control experiment without **1** provided the nitroaldol at 7 h in <5% conversion. However, the neat substrate without water showed no reaction. Nitromethane was more reactive compared to nitroethane and nitropropane.

The reaction of other aldehydes was further studied (entries 4–14). Benzaldehydes having 4-bromo-, 4-chloro, 4-methoxy-, 4-nitro- and 3,4-dimethoxy substituents underwent reaction in 77–92% yield. The substrate with an electron-withdrawing group showed enhanced reactivity compared to those bearing an electron-donating group. These reaction conditions were also suitable for heterocyclic and aliphatic aldehydes. Thus, 2-pyridinecarboxaldehyde, 2-thiophenecarboxaldehyde, 2-butanal, 1-heptanal, 1-nonanal and ethyl glyoxalate underwent reaction with 72–95% yield.

The cluster **1** was recyclable without loss of activity. After completion of the addition of nitromethane to benzaldehyde, the cluster **1** was recovered (99%) by filtration and reused for the reaction of fresh nitromethane with benzaldehyde (Table 1, entry 1). This process was repeated for up to three runs and no loss of activity was observed. In addition, to study the leaching of the catalyst in water, the cluster **1**

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[a] Department of Chemistry, Indian Institute of Technology Guwahati,
Guwahati 781039, India
Fax: +91-361-2690762
E-mail: tpunni@iitg.ernet.in

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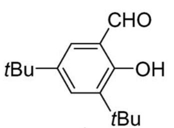

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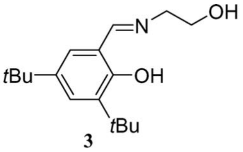

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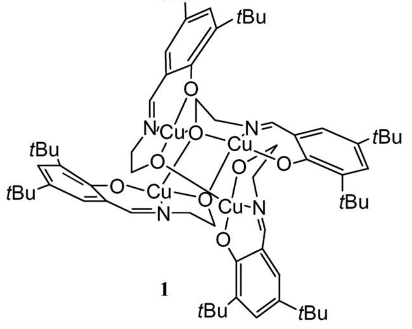


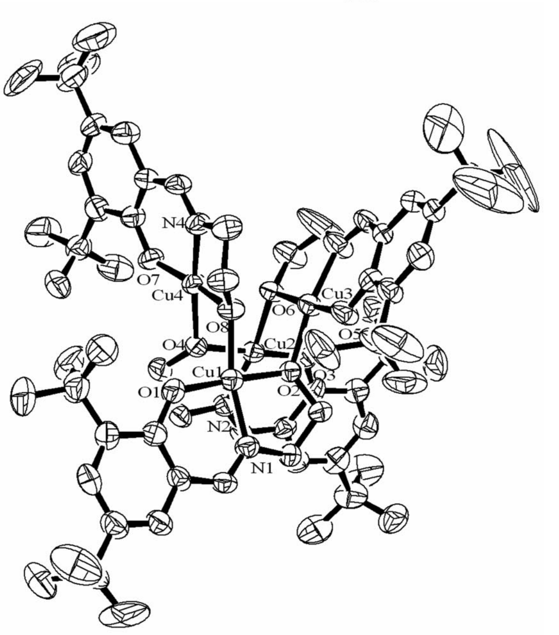


Figure 1. X-ray crystal structure of **1** with 30% ellipsoid. H atoms and solvent molecules (EtOAc and H_2O) were omitted for clarity.

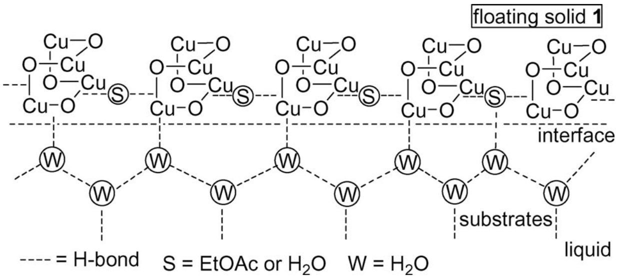
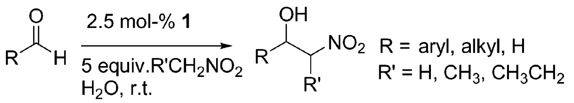
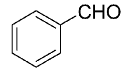
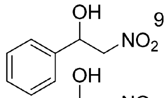
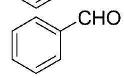
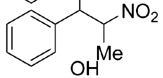
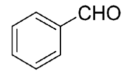
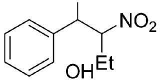
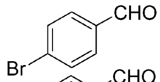
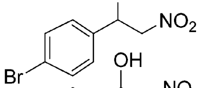
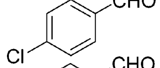
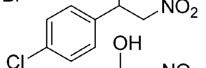
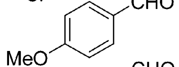
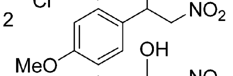
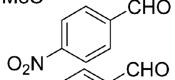
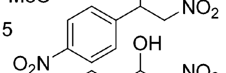
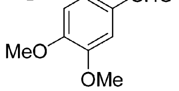
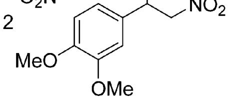
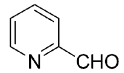
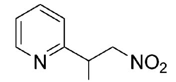
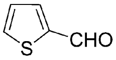
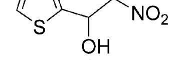
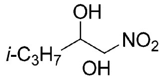
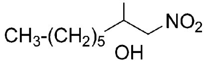
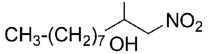
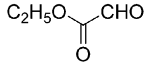
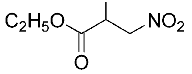


Figure 2. Proposed Henry reaction on water.

was stirred on water in the presence, as well as in the absence, of nitromethane for 7 h and filtered. The filtrates were independently investigated for the addition of nitromethane to benzaldehyde. Both experiments provided the corresponding nitroaldol in <5% conversion, which is similar to that of the blank reaction. Furthermore, the filtrates were analyzed using a UV/Vis spectrophotometer and no absorption peak was observed for the presence of the cluster **1**. These results clearly suggest that no leaching of the metal complex is involved and the reaction is a heterogeneous process. Thus, the reaction may take place on the surface of the catalyst (Scheme 1). The coordination of the nitroalkane on the surface of the catalyst **1** can generate intermediate ***a***, which can undergo reaction with water to generate intermediate ***b***. Intramolecular 1,2-addition of the nitronate to the coordinated aldehyde can generate the intermediate ***c***, which can complete the catalytic cycle by reaction with fresh nitroalkane, giving the nitroaldol product.[8n] In these reactions, the cluster **1** floats on the surface

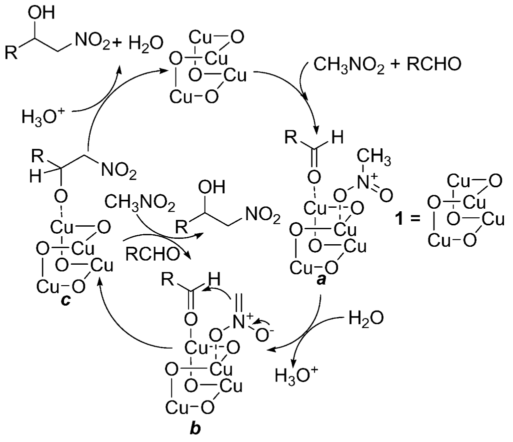
Table 1. Cluster **1** catalyzed Henry reaction on water.



Entry	Substrate	Nitroalkane	Time [h]	Product	Yield [%][a,b,c]
1		CH_3NO_2	7		92,90[d] 89[e]
2		$EtNO_2$	24		10
3		nPrNO$_2$	24		n.r.
4		CH_3NO_2	4		89
5		CH_3NO_2	6		85
6		CH_3NO_2	12		77
7		CH_3NO_2	1.5		92
8		CH_3NO_2	12		81
9		CH_3NO_2	1		95
10		CH_3NO_2	10		90
11	i-C_3H_7–CHO	CH_3NO_2	8		82
12	CH_3-$(CH_2)_5$-CHO	CH_3NO_2	12		78
13	CH_3-$(CH_2)_7$-CHO	CH_3NO_2	12		72
14		CH_3NO_2	12		85

[a] Substrate (5 mmol), cluster **1** (2.5 mol-%) and nitroalkane (25 mmol) stirred on water (15 mL) at ambient temperature. [b] Isolated yield. [c] Heterogeneous process. Recovered **1** used. [d] Second run. [e] Third run.

of water and the organic compounds are in water, which is to be stirred. Thus, the observed reactivity could be attributed to the occurrence of the reaction at the solid–liquid interface of water droplets (Figure 2).[7h]



Scheme 1. Proposed catalytic cycle for Henry reaction.

Conclusions

In summary, the synthesis, structure and application of an alkoxo-bridged tetranuclear copper(II) open cubane **1** have been presented for Henry reaction on water. It is a clean technological process and the cluster **1** is recyclable without loss of activity.

Experimental Section

General Methods: NMR spectra were recorded with a Varian-400 spectrometer. FTIR spectra were obtained with a Nicolet-400 spectrometer. UV/Vis spectra were obtained with a Perkin–Elmer Lambda-25 spectrophotometer. EPR spectrum was recorded with a JES-FA-200 spectrometer. X-ray data were collected with a Bruker SMART APEX equipped with CCD area detector using Mo-K_α radiation. The structure was solved using SHELXL-97 (Göttingen, Germany). Column chromatography was performed on 60–120 mesh silica gel. Elemental analysis was carried out using a Perkin–Elmer-2400 CHNS analyzer. Melting points were determined using a Buchi B-540 apparatus and were uncorrected.

CCDC-718865 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2,4-Bis(1,1-dimethylethyl)-6-{[(2-hydroxyethyl)imino]methyl}phenol (3): 3,5-Di-*tert*-butylsalicylaldehyde (234 mg, 1 mmol) and $NH_2CH_2CH_2OH$ (61 mg, 1 mmol) were stirred for 5 h in EtOH (5 mL). Evaporation of the solvent gave a residue that was purified by silica gel column chromatography using 9:1 hexane/EtOAc to afford **3** as a yellow solid in 90% (249.3 mg) yield. $R_f = 0.33$; m.p. 63–65 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.40 (s, 1 H), 7.38 (s, 1 H), 7.10 (s, 1 H), 3.91 (t, J = 5.2 Hz, 2 H), 3.73 (t, J = 5.6 Hz, 2 H), 2.0 (s, 1 H), 1.32 (s, 9 H), 1.29 (s, 9 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.1, 158.3, 140.2, 136.8, 127.2, 126.2, 117.9, 62.2, 61.7, 31.6, 29.6 ppm. FTIR (KBr): $\tilde{\nu}_{max}$ = 3365, 2958, 2871, 1734, 1633, 1469, 1441, 1390, 1361, 1274, 1252, 1201, 1173, 1063, 1047, 878 cm^{-1}. UV/Vis (CH$_2$Cl$_2$): λ_{max} = 342 (ε = 6022), 263 nm (ε = 20639 mol^{-1}dm^{3}cm^{-1}). $C_{17}H_{27}NO_2$ (277.40): calcd. C 73.61, H 9.81, N 5.05; found C 73.70, H 9.85, N 5.08.

Preparation of the Copper(II) Cluster 1: Schiff base **3** (277 mg, 1 mmol) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1 mmol) were stirred in EtOH (5 mL) for 12 h at ambient temperature. The solvent was evaporated and the residue was purified by silica gel column chromatography using 9:1 hexane/EtOAc to give **1** as green crystals in 80% (257.6 mg) yield. FTIR (KBr): $\tilde{\nu}_{max}$ = 2957, 2905, 2866, 1740, 1633, 1528, 1459, 1434, 1323, 1256, 1165, 1057, 911, 872, 638, 616, 513 cm^{-1}. UV/Vis (CH$_2$Cl$_2$): λ_{max} = 384 (ε = 25303), 278 nm (ε = 79848 mol^{-1}dm^{3}cm^{-1}). EPR (solid): g = 2.04, A = 330 mT. $C_{72}H_{110}Cu_4N_4O_{11}$ (1461.85): calcd. C 59.16, H 7.58, N 3.83; found C 59.25, H 7.62, N 3.88.

General Procedure for Henry Reaction: A mixture of aldehyde (5 mmol), nitroalkane (25 mmol) and cluster **1** (2.5 mol-%) was stirred on water (15 mL). Progress of the reaction was monitored by TLC. After completion, the cluster **1** was filtered and the filtrate extracted with EtOAc (2 × 25 mL). Drying (Na$_2$SO$_4$) and evaporation of the solvent gave a residue that was passed through a short pad of silica gel using EtOAc/hexane as eluent to provide analytically pure nitroaldols in high yield.

1-Nitro-2-octanol: Colourless liquid, yield 78%, R_f = 0.36 (1:9 EtOAc/hexane). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.42–4.31 (m, 2 H), 4.29–4.26 (m, 1 H), 2.30 (s, 1 H), 1.52–1.43 (m, 4 H), 1.36–1.21 (m, 6 H), 0.85 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 80.8, 68.9, 33.8, 31.7, 29.0, 25.2, 22.5, 14.0 ppm. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400, 2931, 2857, 1556, 1517, 1458, 1383, 1252, 1091, 835, 743 cm^{-1}. $C_8H_{17}NO_3$ (175.23): calcd. C 54.84, H 9.78, N 7.99; found C 54.88, H 9.80, N 8.04.

1-Nitro-2-decanol: Colourless liquid, yield 72%, R_f = 0.38 (1:9 EtOAc/hexane). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.41–4.30 (m, 2 H), 4.27 (s, 1 H), 2.83 (s, 1 H), 1.51–1.38 (m, 4 H), 1.31–1.23 (m, 10 H), 0.84 (t, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 80.9, 68.9, 33.9, 31.9, 29.5, 29.5, 29.3, 25.3, 22.7, 14.2 ppm. FTIR (KBr): $\tilde{\nu}_{max}$ = 3416, 2926, 2856, 1557, 1518, 1464, 1383, 1252, 1093, 835, 742 cm^{-1}. $C_{10}H_{21}NO_3$ (203.28): calcd. C 59.08, H 10.41, N 6.89; found C 59.15, H 10.40, N 6.93.

The products are known compounds, α-(nitromethyl)benzenemethanol,[7o] α-(1-nitroethyl)benzenemethanol,[8s] 4-bromo-α-(nitromethyl)benzenemethanol,[7o] 4-chloro-α-(nitromethyl)benzenemethanol,[7o] 4-methoxy-α-(nitromethyl)benzenemethanol,[7o] 4-nitro-α-(nitromethyl)benzenemethanol,[7o] 3,4-dimethoxy-α-(nitromethyl)benzenemethanol,[8p] α-(nitromethyl)2-pyridine methanol,[7m] α-(nitromethyl)thiophene methanol,[8l] 3-methyl-1-nitro-2-butanol[8s] and ethyl 2-hydroxy-3-nitropropanoate,[7m] and their analytical data were identical with those reported in the literature.

Supporting Information (see also the footnote on the first page of this article): Crystal data and EPR spectra of **1**, and NMR (^{1}H and ^{13}C) spectra of **3** and nitroaldol products of Table 1, entries 12 and 13.

Acknowledgments

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[9] X-ray data were collected with a Bruker SMART APEX equipped with a CCD area detector using Mo-K_{α} radiation in the scan range $1.30° < \theta < 27.96°$. The structure was solved using SHELXL-97 (Göttingen, Germany). $C_{144}H_{216}Cu_8N_8O_{21}$, $M = 2903.57$, monoclinic, space group $P2_1/c$, $a = 14.868(3)$ Å, $b = 29.556(5)$ Å, $c = 18.797(3)$ Å, $\alpha = 90.00°$, $\beta = 101.441(9)°$, $\gamma = 90.00°$, $V = 8096(2)$ Å^3, $Z = 2$, $T = 296(2)$ K, μ ($\lambda = 0.71073$ Å) = 1.089 mm^{-1}, $d_{calcd} = 1.191$ Mg/m^3, 99235 reflections measured, 18024 unique ($R_{int} = 0.1383$), $R_1 = 0.0743$, $wR_2 = 0.1896$ [$1 > 2\sigma(1)$], $R_1 = 0.2304$, $wR_2 = 0.2388$ (all data), GOF = 0.996.

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