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Synthesis and structural characterization of a novel dinuclear Cu(II) complex: an efficient and recyclable bifunctional heterogeneous catalyst for the diastereoselective Henry reaction †

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Electronic Supplementary Information

Experimental section

Synthesis of *N,N'-bis*(4-pyridylmethyl)-1,4-diaminobutane-*N,N'*-diaceticacid [H_2(4-BPDC)]

It is prepared in two steps where *N,N'-bis*(pyridin-4-ylmethyl) butane-1,4-diamine (4-BPBD) is an intermediate.

Step 1, synthesis of 4-BPBD: In a 50 mL two-neck round-bottom flask (RBF), 4-pyridinecarboxaldehyde (1.9 mL, 20 mmol) was dissolved in 10 mL of methanol. To this was added 1,4-diaminobutane (1 mL, 10 mmol) in a drop wise manner at room temperature, and the mixture was stirred under inert atmosphere for 4 h. An excess of sodium borohydride (1.14 g, 1.5 equiv.) was added slowly to the above solution at 0 °C and the reaction mixture was stirred for another 6 h. Extraction of the product with chloroform followed by drying with anhydrous Na_2SO_4 and removal of the solvent under vacuum resulted in a light yellow solid. Yield: 2.45 g (91%). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.53 (4H, d), 7.25 (4H, t), 3.81 (4H, s), 2.64 (4H, m) 1.58 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 27.83, 49.30, 52.71, 122.94, 149.47, 149.83. Selected FTIR peaks (KBr cm^{-1}): 3434 (br, N-H stretch), 2937 (m, aromatic C-H stretch), 2803 (s), 1602 (s, pyridine C=C stretch), 1451 (s, pyridine C=N stretch), 1421 (s), 1351 (m, aliphatic C-H stretch), 1126 (s, aliphatic C-C stretch), 992 (s), 806 (s), 486 (s). M.P.: 60-62 ^{o}C.

Step 2, Synthesis of [H_2(4-BPDC)]: In a 50 mL RBF, a solution of 4-BPBD (1.08 g, 4 mmol) obtained from step 1 above was made in water (10 mL). An aqueous solution of potassium salt of bromoacetic acid (1.1 g, 8 mmol) was added dropwise to the above solution and stirred for 15 min. Afterwards, a solution of potassium hydroxide (450 mg, 8 mmol) in water (10 mL) was added drop wise at 0 ^{o}C to the above mixture. The resulting reaction mixture was further stirred for 90 h at room temperature (26-28 ^{o}C) and acidified with dil. HCl (pH = 5-6) at 0 ^{o}C. Upon evaporation of the solvent under vacuum, the resultant oily substance was cooled to 0 ^{o}C, treated with dry methanol (10 mL) and filtered to remove KCl and KBr (by-products). Upon removal of methanol under vacuum from the filtrate, the resultant oily substance was treated with dry acetonitrile (10 mL). A hygroscopic light brown product was isolated after decanting the solvent followed by high vacuum drying. Yield: 1.1 g (71%). ^{1}H NMR (400 MHz, CD_3OD, δ ppm): 8.48 (4H, d), 7.43 (4H, d), 4.92 (4H, s), 3.82 (4H, s), 2.61 (4H, m), 1.60 (4H, m). ^{13}C NMR (100 MHz, CD_3OD, δ ppm): 26.79, 51.65, 57.38, 71.80, 123.58, 148.63, 150.12, 176.51. ^{1}H and ^{13}C NMR are shown in Fig. S1-S4, respectively. Selected FTIR peaks (KBr cm^{-1}): 3420 (br), 1636 (m), 1594 (m), 1438 (w), 1404 (s), 1330 (w), 1003 (w), 768 (m). HRMS (ESI-TOF): m/z calcd for $[(H_2(4\text{-BPDC}))H]^+$, 387.1987; found, 387.1982 (Fig. S5).

Synthesis of $\{[Cu_2(4\text{-BPDC})_2(H_2O)_2]\cdot 9H_2O\}$ (1)

In a 10 mL RBF, $Cu(ClO_4)_2\cdot 6H_2O$ (24 mg, 0.065 mmol) was dissolved in 4 mL methanol. To this, a clear methanolic solution of disodium **4-BPDC** (25 mg, 0.065 mmol) was added with stirring. With an appearance of a bluish green precipitate, the reaction mixture was stirred for another 5 h at room temperature. A bluish green solid was obtained via filtration, washed with methanol, and air-dried. Yield: 25 mg (71%). Anal. Calcd for $C_{40}H_{70}N_8O_{19}Cu_2$ (MW 1092.334): C, 43.91; H, 6.45; N, 10.24. Found: C, 43.86; H, 6.59; N, 10.10. Selected FTIR peaks (KBr, cm^{-1}): 3428 (br), 2932 (w), 1626 (s), 1424 (m), 1375 (s), 1226 (w), 1068 (w), 812 (m). Blue crystals of **1** suitable for single crystal X-ray diffraction analysis were obtained after 9 days from the slow evaporation of an aqueous solution.

General protocol used for catalysis by 1

The catalytic reactions were carried out in screw cap glass vials with magnetic stirring. In a typical reaction, a mixture of aldehyde (0.1 mmol) and nitroethane (0.3 mmol) was added with catalyst **1** (4 mol%) in a 1 mL CH_3OH. The mixture was heated at 70 °C for 36 h, then centrifuged and filtered to remove the solid catalyst. The filtrate was evaporated under vacuum to give the crude product. The residue was dissolved in $CDCl_3$ and analysed by ^1H NMR spectroscopy. The yield and the ratio between the *syn* and *anti* isomers of the β-nitroalkanol were calculated by ^1H NMR spectroscopy according to previously reported literature.[1] In the ^1H NMR spectra, the values of vicinal coupling constants (for the β-nitroalkanol product) between the α-O-C-H and the α-N-C-H protons identify the isomers, where J = 7-9 or 3.2-4 Hz for the *syn* or *anti* isomers, respectively.[2] The ^1H-NMR spectra and the calculation of the yield and selectivity for Henry reaction are presented in Fig. S11. In order to perform the catalyst recycling experiments, the used catalyst (separated by centrifugation and filtration) was washed with MeOH and dried at room temperature. The dried catalyst was directly used for the next run as described above.

Single Crystal X-ray Data Collection and Refinements

Crystals of the **1** were transferred from mother liquor to mineral oil for manipulation, selection, and mounting. One of these crystals was transferred to a nylon loop attached to a goniometer head and placed under a cold stream of nitrogen gas for slow cooling to 100 K. Initial crystal evaluation and data collection were performed on a Kappa APEX II diffractometer equipped with a CCD detector and sealed-tube monochromated Mo Kα radiation using the program APEX2.[S1] By use of the program SAINT[S1] for the integration of the data, reflection profiles were fitted, and values of F2 and σ(F2) for each reflection were obtained. Data were also corrected for Lorentz and polarization effects. The subroutine XPREP[S1] was used for the processing of data, which included determination of space group, application of an absorption correction (SADABS)[S1], merging of data, and generation of files necessary for solution and refinement. Using Olex2[S2], the structure was solved with the ShelXT[S3] structure solution program using Intrinsic Phasing and refined with the ShelXL[S4] refinement package using least squares minimisation. The space group was chosen based on systematic absences and confirmed by the successful refinement of the structure. Positions of most of the non-hydrogen atoms were obtained from a direct methods solution. Several full-matrix least-squares/difference Fourier cycles were performed, locating the remainder of the non-hydrogen atoms. All non-hydrogen atoms, except where indicated otherwise, were refined with anisotropic displacement parameters. Hydrogen bonding parameters were generated using PLATON.[S5,S6] The solvent molecules in **1** are highly disordered. Therefore, the Olex2[S2] masking program was used to remove those peaks. The solvent molecules were calculated on the basis of combined study of TGA, elemental analysis, and removed electron counts which are included in the molecular formula. The final positional and thermal parameters of the non-hydrogen atoms for **1** are listed in the CIF files.

References

S1. *APEX2, SADABS and SAINT*, Bruker AXS Inc, Madison, WI, USA, 2008.

S2. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339–341.

S3. G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.*, 2015, **71**, 3–8.

S4. G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, 2015, **71**, 3–8.

S5. A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7–13.

S6. A. L. Spek, *PLATON, Version 1.62*, University of Utrecht, 1999.

Calculation for determining solvents squeezed out:

Number of electrons squeezed out = 353; therefore, no. of electrons in the formula unit = 353/z = 353/4 = 88.25

The number of electrons in 9 H_2O molecules = 9 × 10 = 90, which is in good agreement with the electrons counts calculated (88.25).

From TGA analysis:

9 H_2O (lattice) = 162.1

% weight loss = (162.1/1092.3)×100 = 14.8%, which is in good agreement with the experimental value (14.43%).

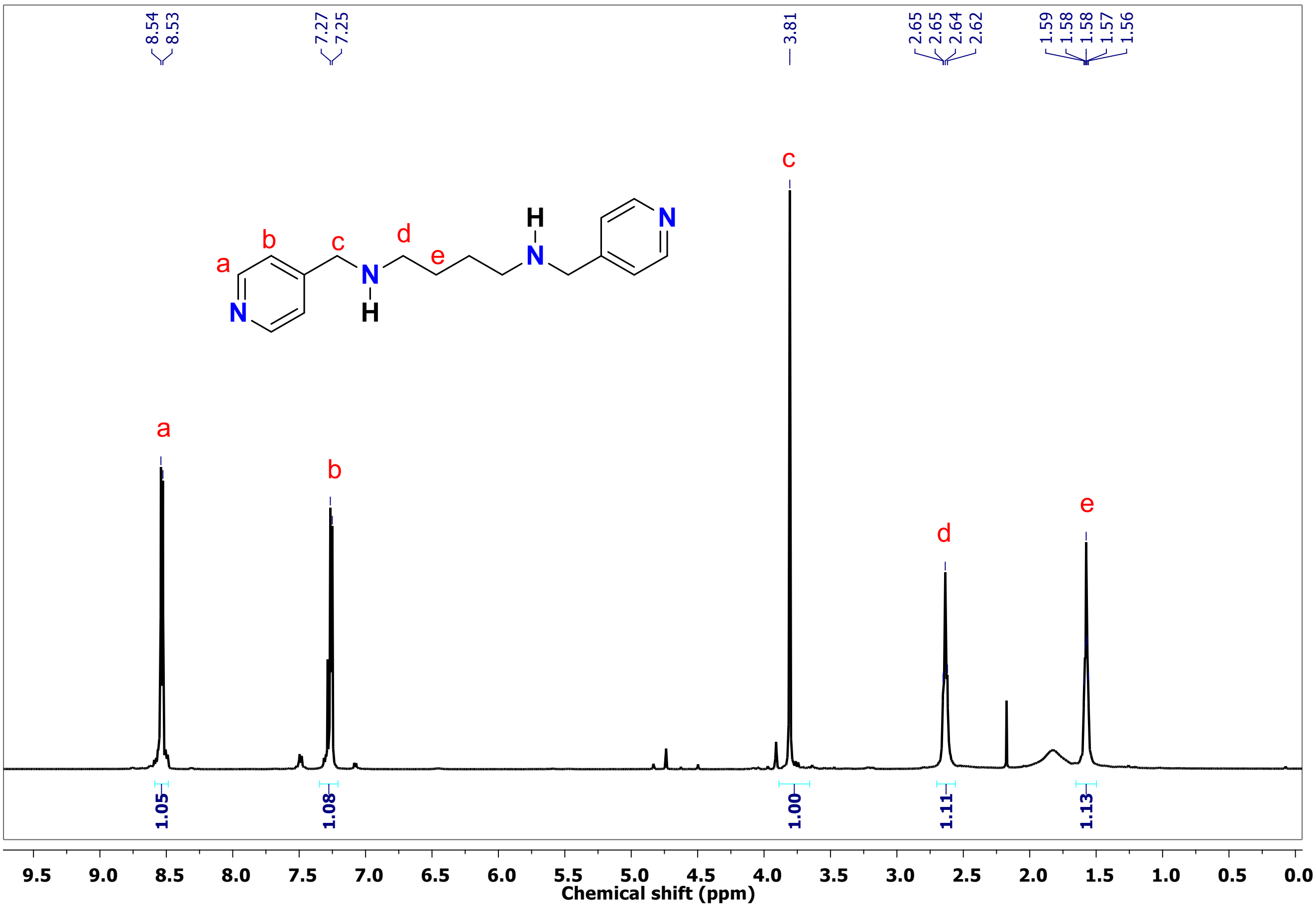


Fig. S1 ^{1}H NMR spectrum of 4-BPBD in $CDCl_3$.

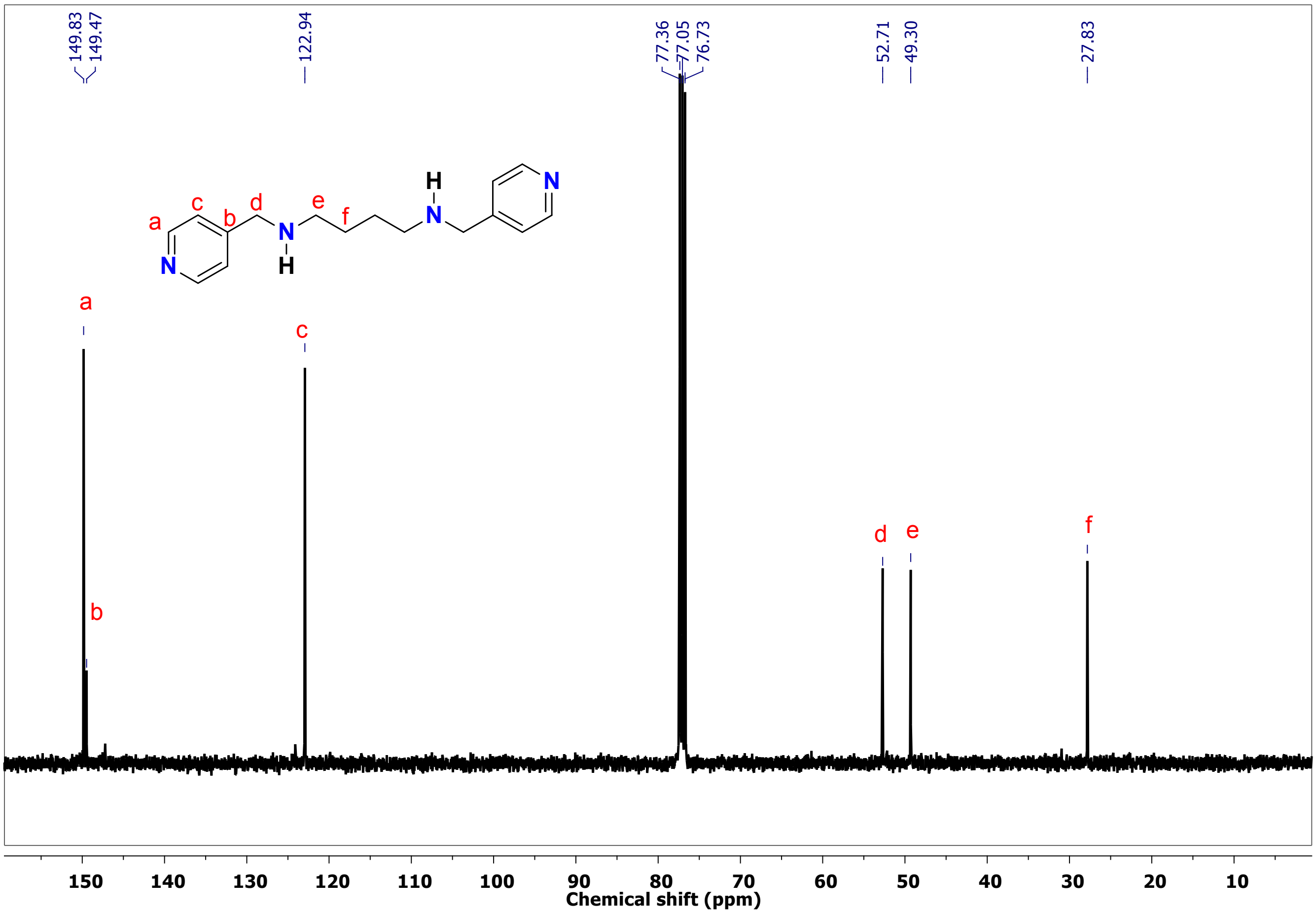


Fig. S2 ^{13}C NMR spectrum of 4-BPBD in $CDCl_3$.

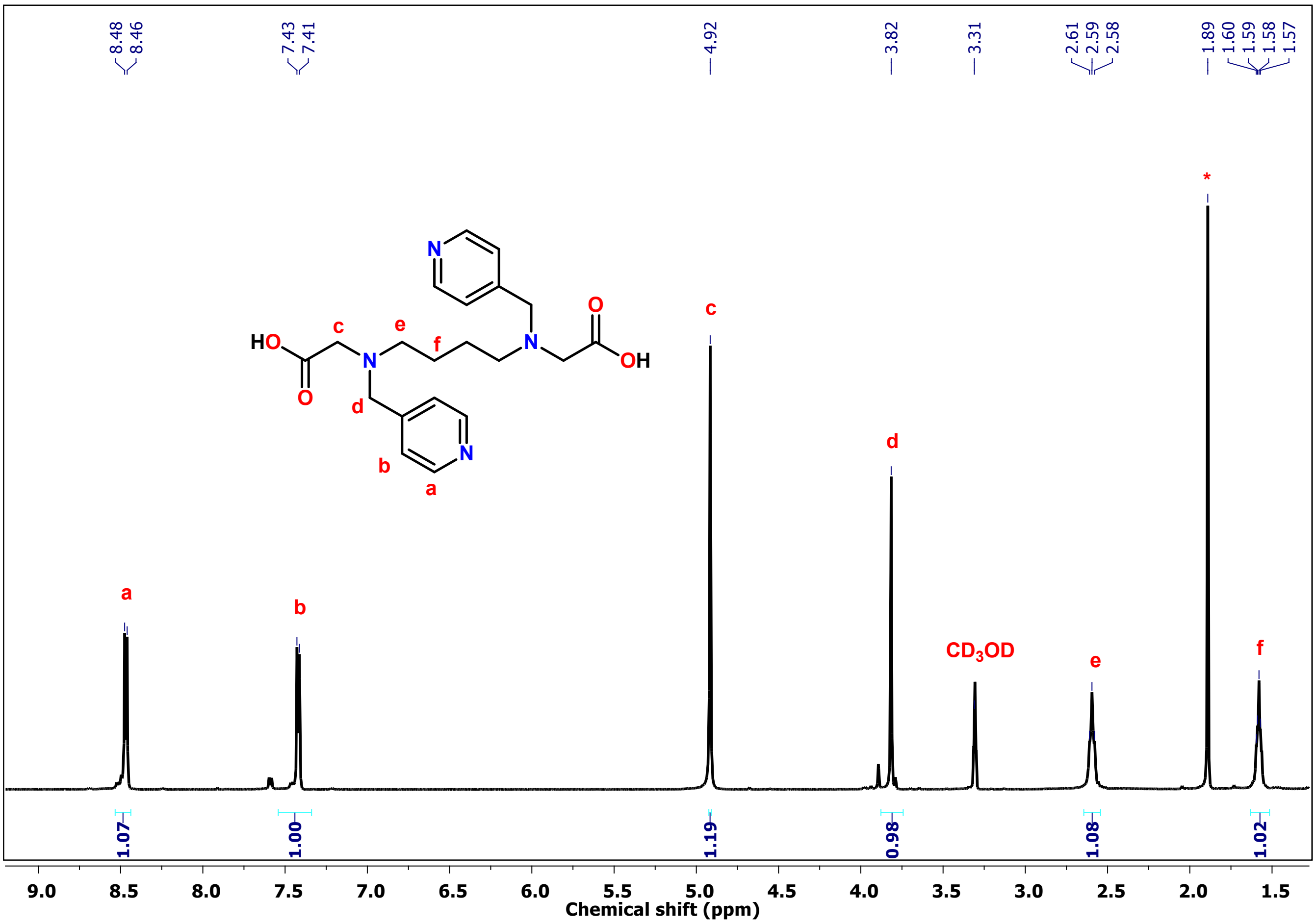


Fig. S3 ^1H NMR spectrum of H_2(4-BPDC) in CD_3OD.

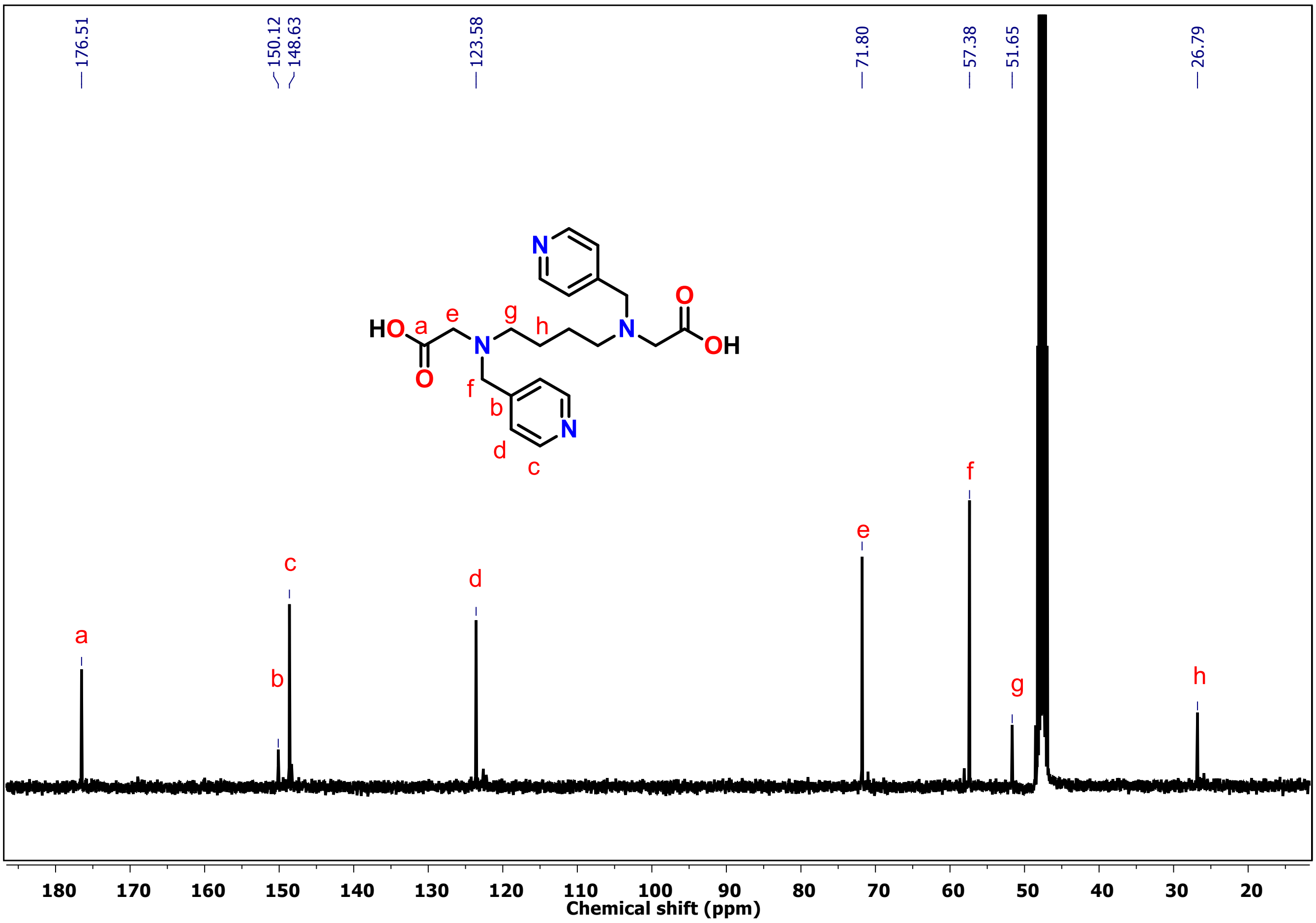


Fig. S4 ^{13}C NMR spectrum of H_2(4-BPDC) in CD_3OD.

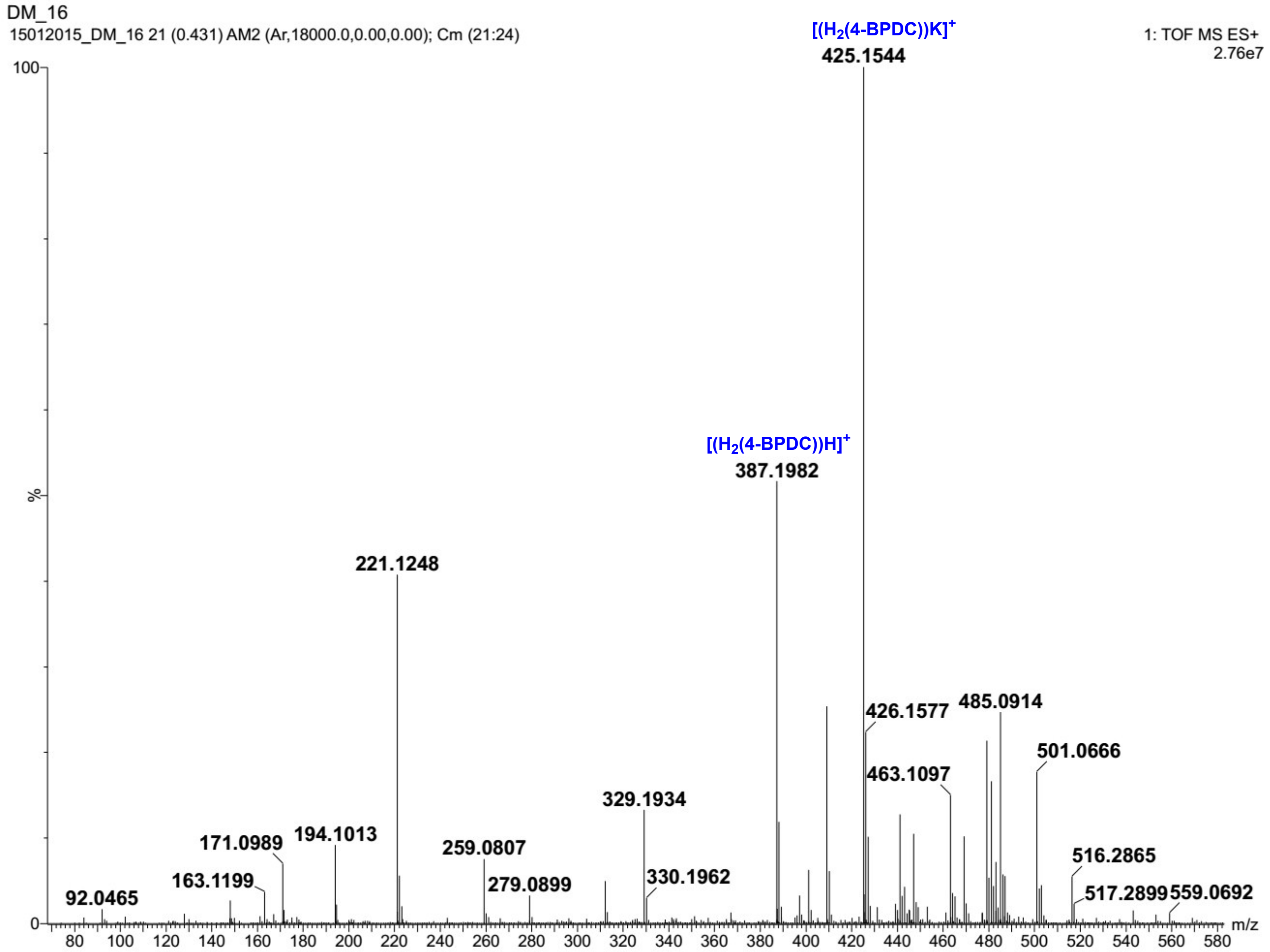


Fig. S5 HRMS (ESI-TOF) of H_2(4-BPDC).

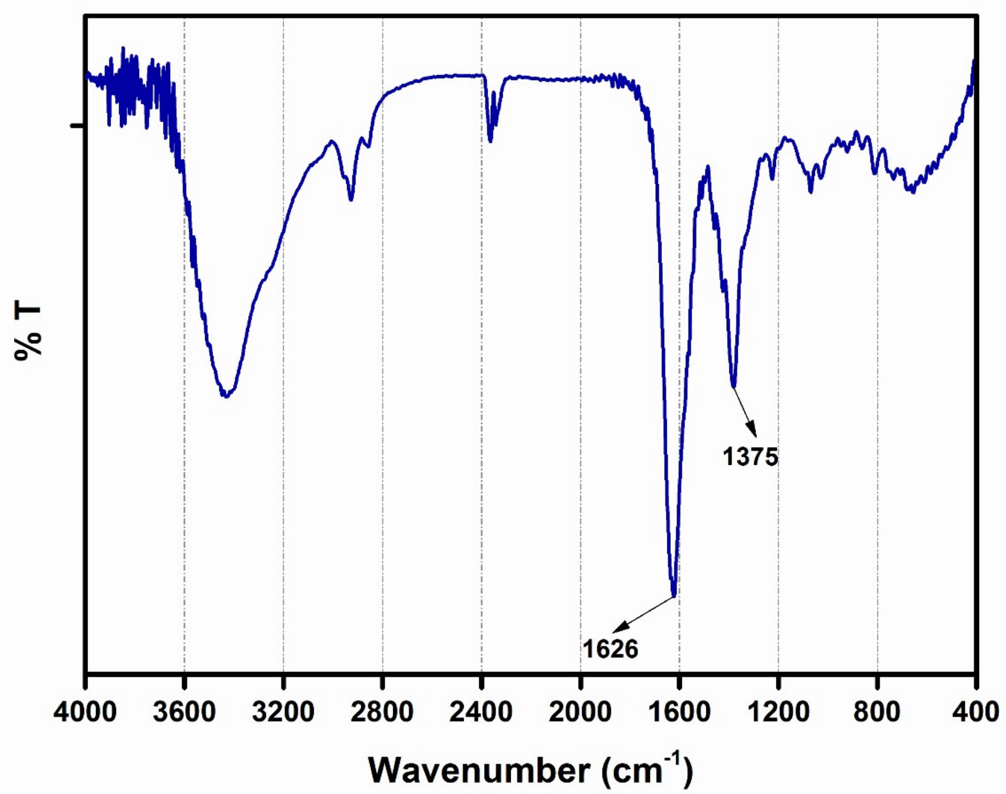


Fig. S6 FT-IR spectrum of **1**.

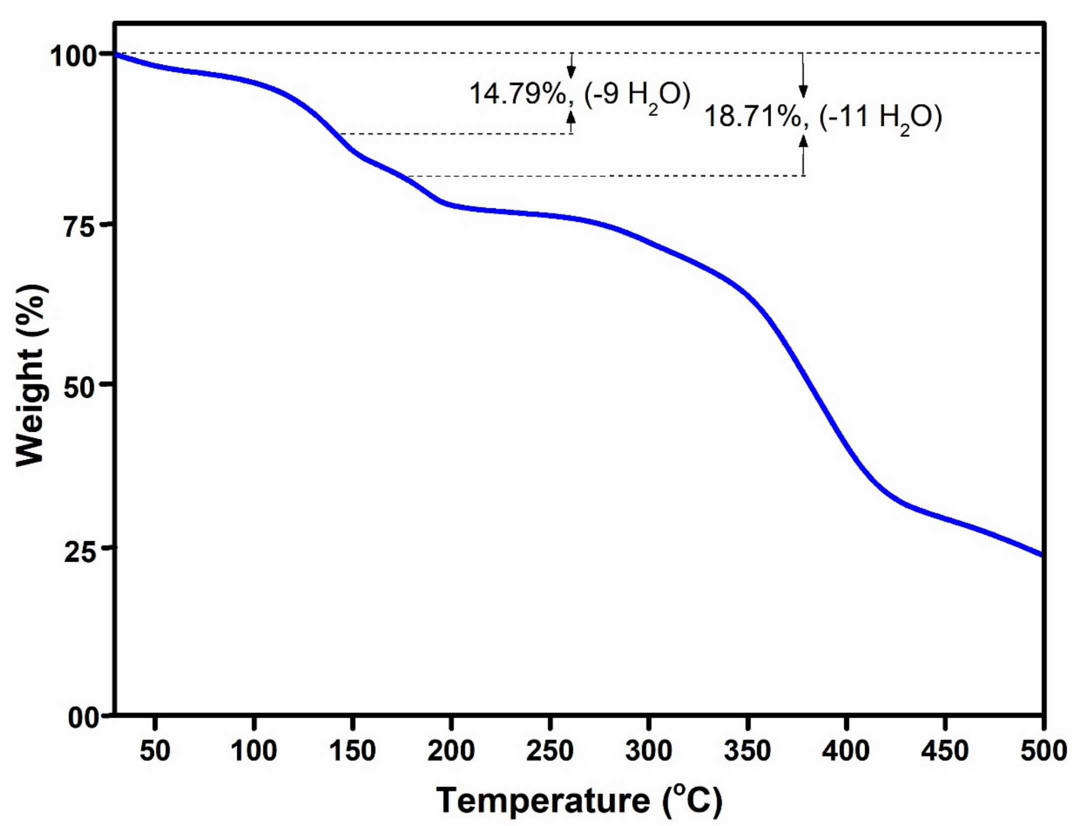
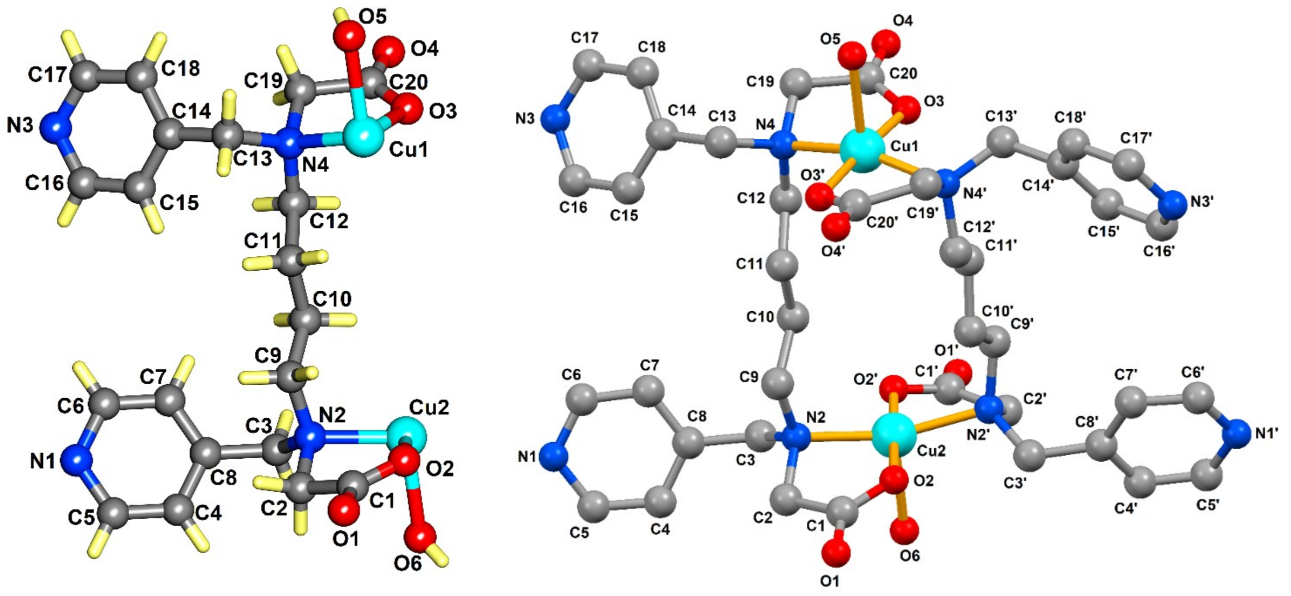


Fig. S7 TGA profile of **1**.



(a) **(b)**

Fig. S8 (a) Asymmetric unit and (b) Coordination environment around Cu(II) centers with atom labelling of **1**.

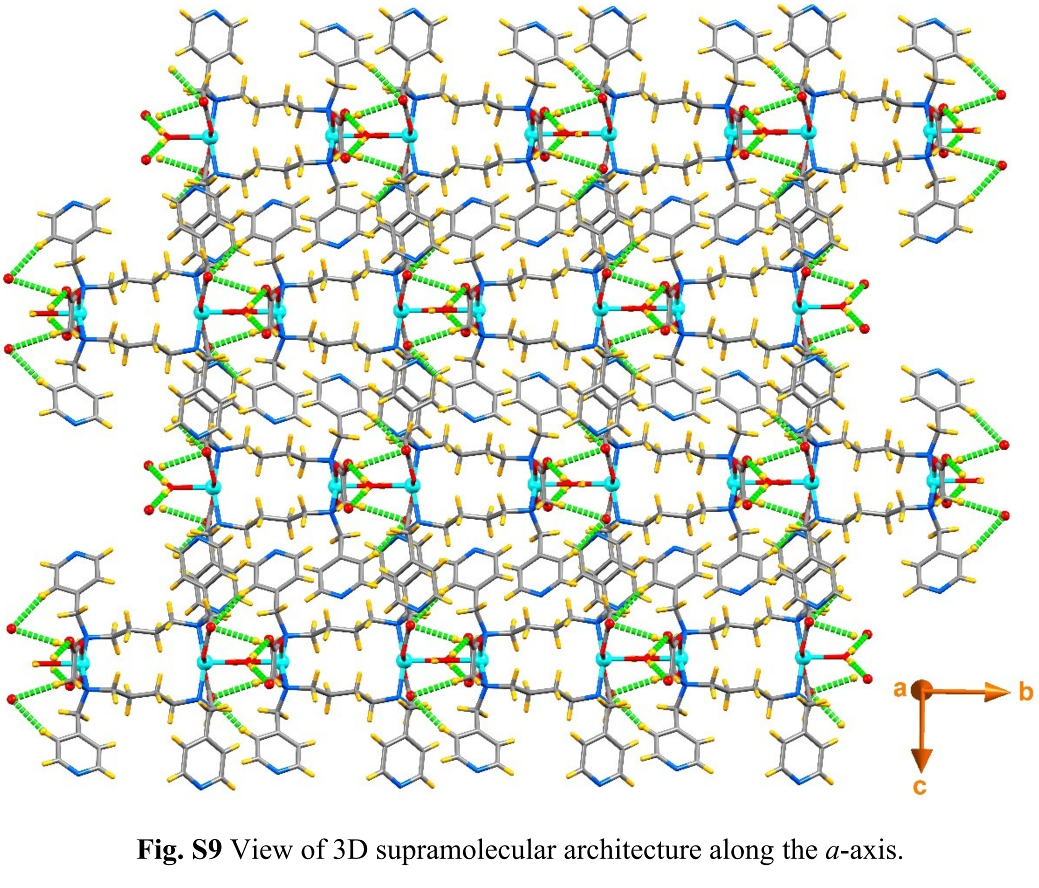


Fig. S9 View of 3D supramolecular architecture along the *a*-axis.

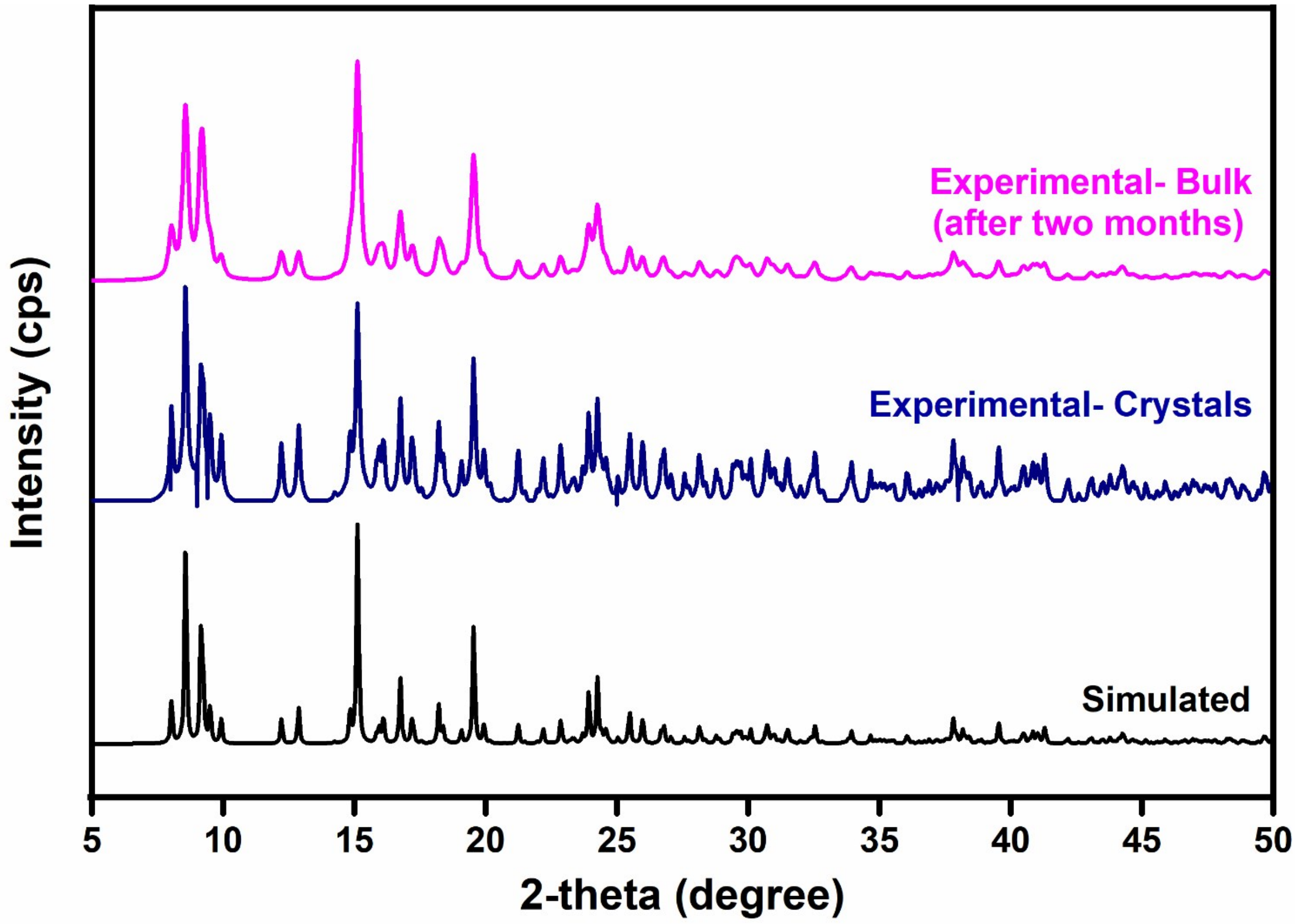


Fig. S10 Simulated and experimental PXRD patterns of **1**.

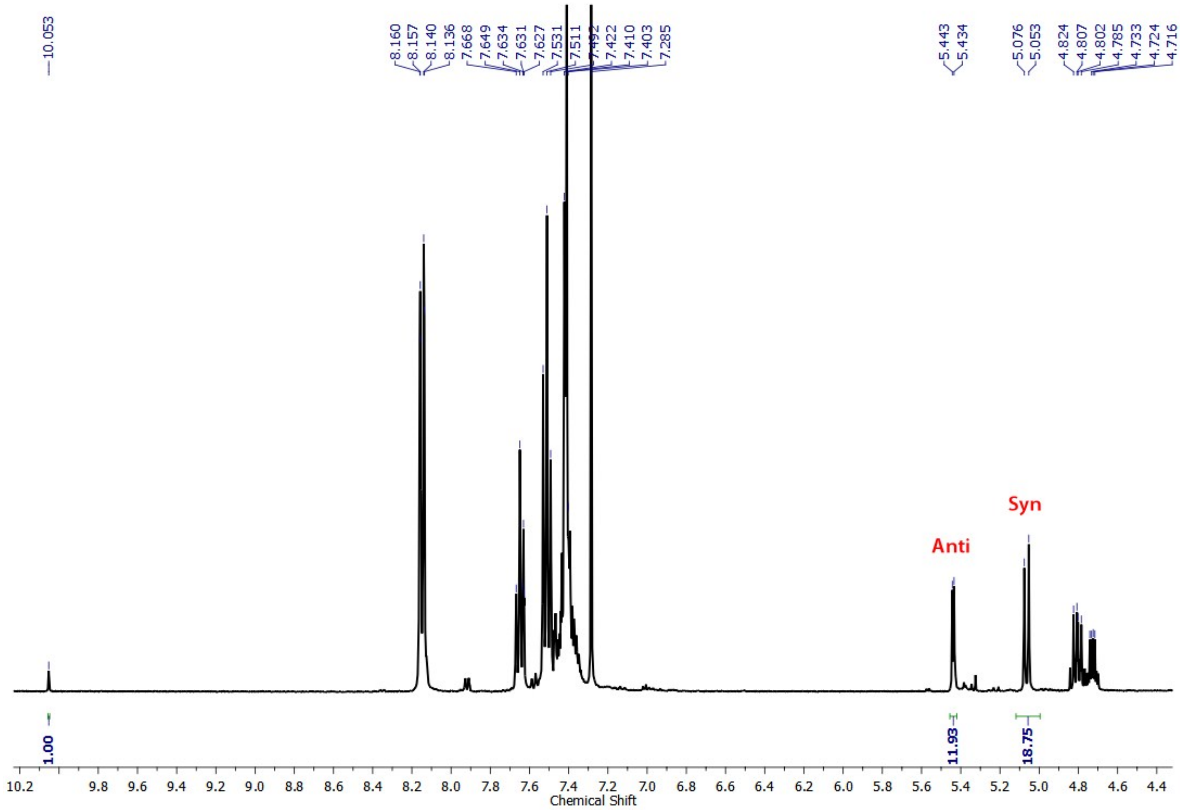


Fig. S11 Example of integration in the ^{1}H NMR spectrum for the determination of the product yield and selectivity (entry 4, Table 1).

Calculation of Product Yield:
Total amount of compounds:
benzaldehyde + *anti* + *syn* = 1 + 11.93 + 18.75 = 31.68
Percentage of the unreacted aldehyde: (1/31.68) × 100 = 3.15%
Yield of *product*= 100 – 3.15 = 96.8%
Yield of *anti* = (11.93/31.68)x100 = 37.4%
Yield of *syn* = (18.75/31.68)x100 = 59.1%

Product Diastereoselectivity:
(*syn* +*anti*) = 37 + 60 = 97 (100%).
Selectivity of *anti* = (37/97)x100 = 38%
Selectivity of *syn* = (60/97)x100 = 62%

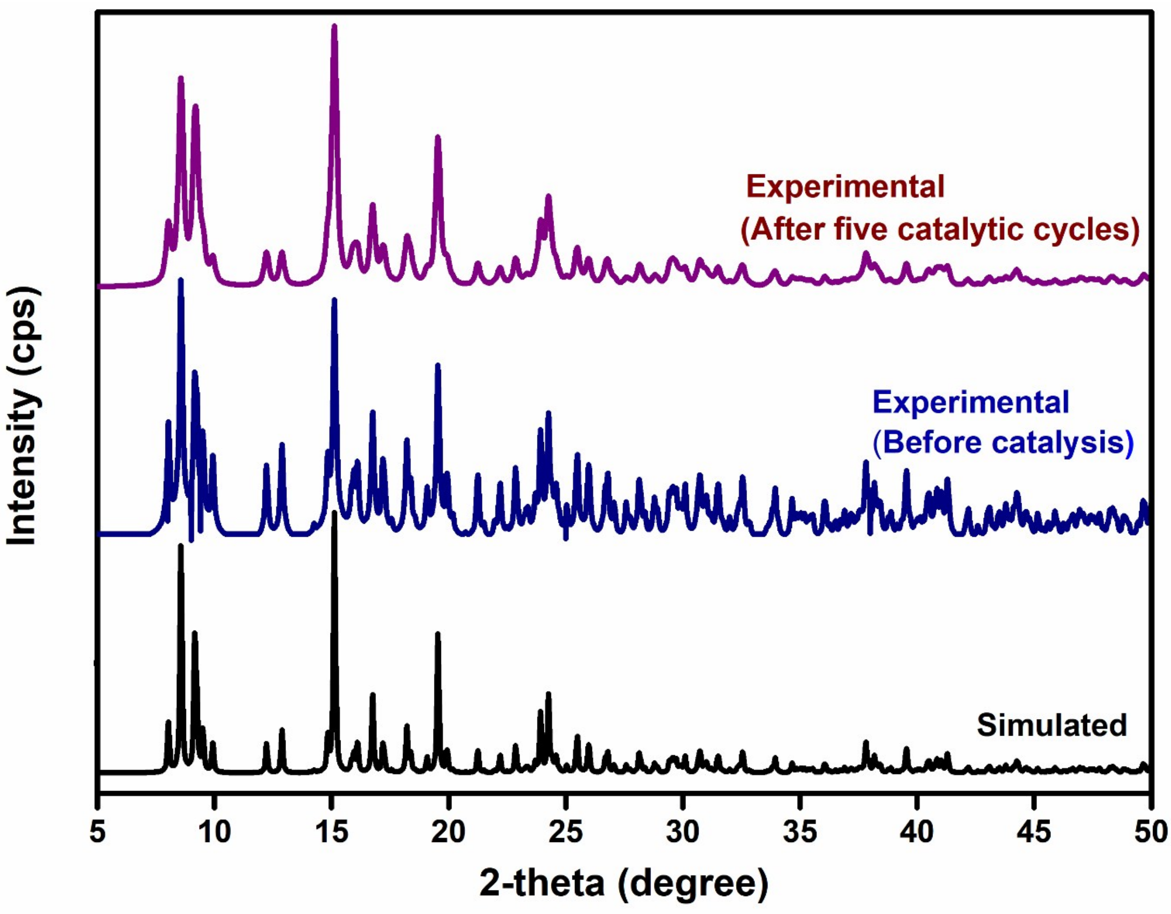


Fig. S12 Simulated, experimental (before catalysis) and after catalysis PXRD patterns of **1.**

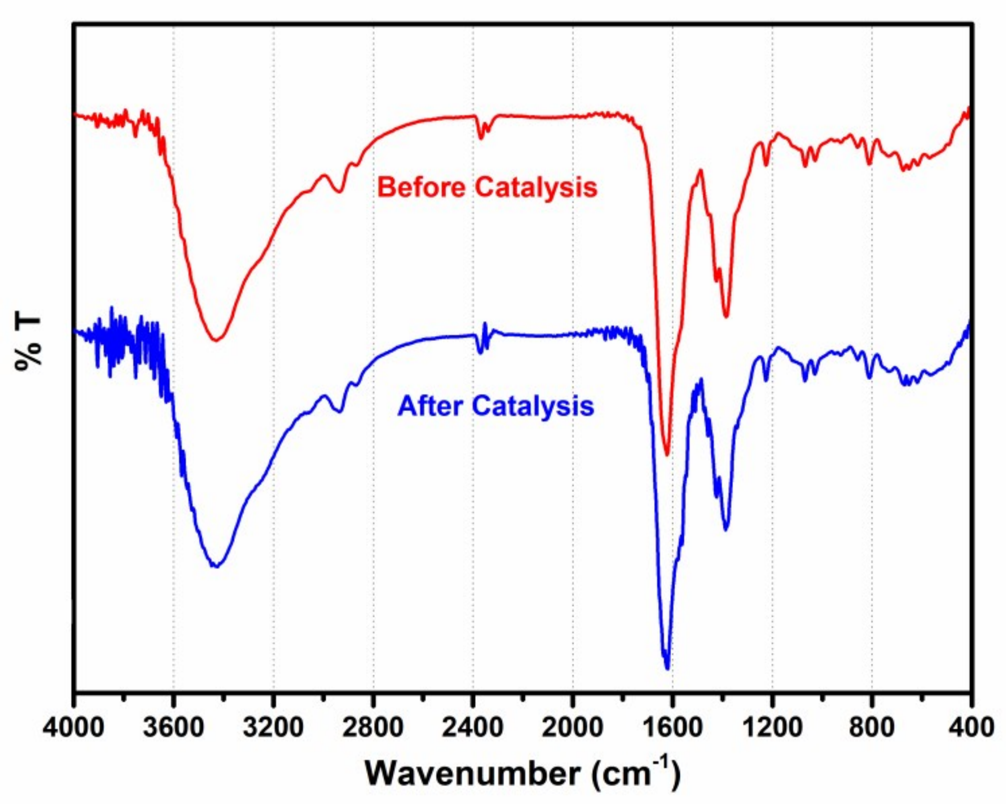


Fig. S13 FTIR spectra of **1** (before and after five catalytic cycles).

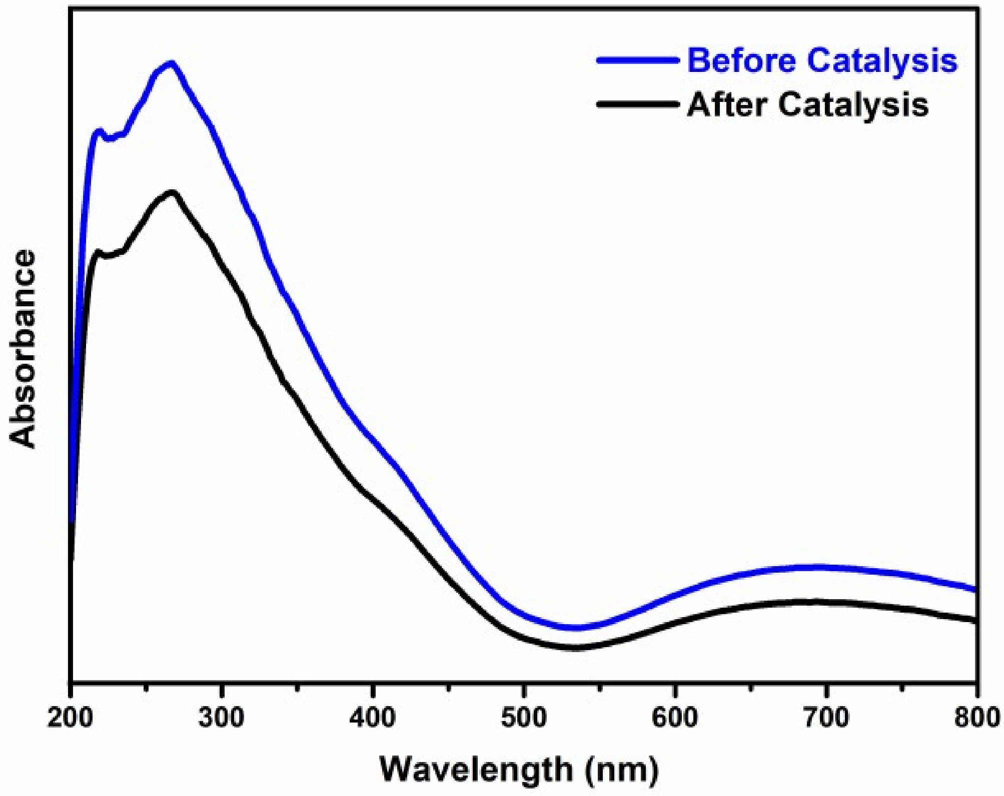
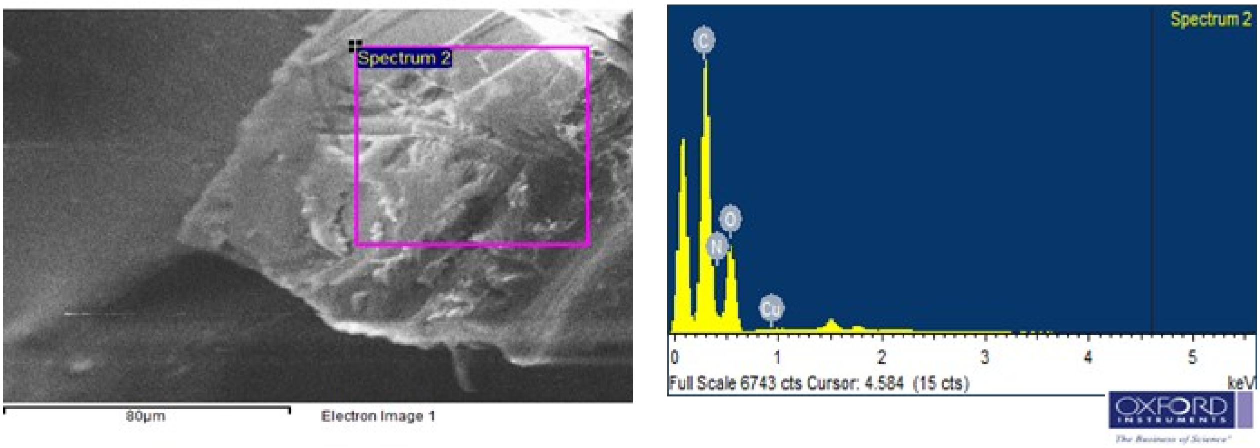
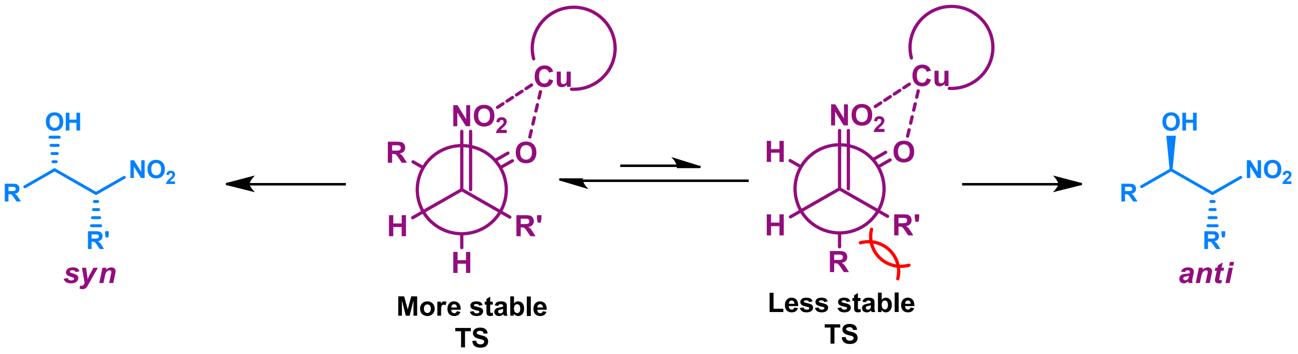


Fig. S14 UV-Vis spectra of **1** (before and after five catalytic cycles).



Element	Weight %	Atomic %
C K	56.00	62.60
N K	4.33	4.15
O K	39.61	33.24
Cu K	0.06	0.01
Total	100	

Fig. S15 EDX analysis of catalyst-free product isolated via centrifugation and filtration.



Scheme S1 Proposed mechanism for the formation of syn/anti products, where the relative stability of respective transition states through the Lewis acidic site in **1** (an open metal center upon loss of the coordinated water molecule) dictates the outcome.

Table S1 Crystal structure data and refinement parameters for **1**

Compound	**1**
Chemical formula	$C_{40}H_{52}Cu_2N_8O_{10}$
Formula weight (g mol^{-1})	1035.57
Temperature (K)	100 (2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	*C*2/c
a (Å)	11.6917(8)
b (Å)	21.9618(18)
c (Å)	19.2926(15)
α (°)	90
β (°)	93.630(5)
γ (°)	90
Z	4
V (Å^3)	4943.8(7)
Density (g/cm^3)	1.252
μ(mm^{-1})	0.917
F(000)	1944.00
Theta range (°)	1.85 to 25.00
Reflections collected	16147
Independent reflections	4323
Reflections with I >2σ(I))	3368
R_{int}	0.0312
Number of parameters	268
GOF on F^2	1.049
Final $R_1{}^a$ / w$R_2{}^b$ ($I > 2\sigma(I)$)	0.0457/0.1384
$R_1{}^a$ / w$R_2{}^b$ (all data)	0.0595/0.1486
Largest diff. peak and hole (eÅ^{-3})	0.60 and -0.52

$^a R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. $^b wR_2 = [\Sigma w(F_o{}^2 - F_c{}^2)^2/\Sigma w(F_o{}^2)^2]^{1/2}$, where $w = 1/[\sigma^2(F_o{}^2) + (aP)^2 + bP]$, $P = (F_o{}^2 + 2F_c{}^2)/3$.

Table S2 Selected bond distances and bond angles for **1**

Bond distances (Å)

Cu1–O3	1.938(2)	Cu2–O2	1.939(3)
Cu1–O3^1	1.938(2)	Cu2–O2^1	1.939(3)
Cu1–O5	2.248(3)	Cu2–O6	2.261(5)
Cu1–N4	2.052(2)	Cu2–N2	2.043(3)
Cu1–N4^1	2.052(2)	Cu2–N2^1	2.043(3)

Bond angles (^{0})

O3–Cu1–O3^1	175.59(12)	O2^1–Cu2–O2	178.91(14)
O3–Cu1–O5	92.21(6)	O2^1–Cu2–O6	90.54(7)
O3^1–Cu1–O5	92.21(6)	O2–Cu2–O6	90.54(7)
O3–Cu1–N4^1	95.47(10)	O2^1–Cu2–N2^1	82.73(10)
O3–Cu1–N4	83.82(10)	O2^1–Cu2–N2	97.12(10)
O3^1–Cu1–N4	95.47(10)	O2–Cu2–N2	82.73(10)
O3^1–Cu1–N4^1	83.82(10)	O2–Cu2–N2^1	97.12(10)
N4^1–Cu1–O5	99.27(6)	N2–Cu2–O6	98.22(7)
N4–Cu1–O5	99.27(6)	N2^1–Cu2–O6	98.22(7)
N4^1–Cu1–N4	161.46(13)	N2–Cu2–N2^1	163.57(13)

Symmetry codes for equivalent position:

^{1} = 1-X,+Y,1/2-Z

Table S3 Hydrogen bonding parameters with symmetry codes[a]

D–H...A	**r (D-H) (Å)**	**r (H…A) (Å)**	**r (D…A) (Å)**	**∠D-H…A (^{0})**	**Symmetry**
O5–H5…O1	0.79(4)	2.04(4)	2.832(3)	172(4)	1/2+x,-1/2+y,z
C2–H2A…O4	0.99	2.55	3.540(4)	175.0	-1/2+x,1/2+y,z
C3–H3A…O2	0.99	2.55	2.992(4)	107.0	Intramolecular
C4–H4…O4	0.95	2.47	3.397(5)	165.0	-1/2+x,1/2+y,z
C13–H13B…O3	0.99	2.57	3.021(4)	108.0	Intramolecular

[a]Numbers in parenthesis are estimated standard deviations in the last significant digits. D = donor, A = acceptor.

Table S4 Comparison of Cu(II) based catalysts in the diastereoselective Henry reaction of 4-nitrobenzaldehyde and nitroethane.

Entry	**Catalyst**	**Amount (mol %)**	**Time (h)**	**Solvent**	**Temp (ºC)**	**Yield (*syn*:*anti*)**	**Ref.**
1	$[Cu_2(4\text{-BPDC})_2(H_2O)_2]\cdot 9H_2O$	4	36	MeOH	70	97 (62:38)	**This work**
2	$[Cu_2(L1)_2]$	8	8	H_2O/MeOH	45	93 (73:27)	24
3	$[CuCl(Tpms^{Ph})(H_2O)]$	0.5	24	MeOH	RT	93 (51:49)	26
4	$[Cu(L2)(H_2O)_4]$	3	30	H_2O	70	94 (80:20)	25
5	$[(S)\text{-}H_2mpz][Cu(H_2O)_4](SO_4)_2\cdot 2H_2O$	2	24	MeOH	20	35 (0:100)	23
6	$[CuL3(\mu_{1,5}\text{-NCNCN})]_n\cdot nH_2O$	1	48	H_2O	70	94 (78:22)	27

L1 = *bis*(2-pyridyl)oxalohydrazide; $Tpms^{Ph}$ = tris(3-phenylpyrazol-1-yl)methane; L2 = 2-propionamidoterephthalate; (*S*)-mpz= (*S*)-2-methylpiperazine; L3 = 2-(2-pyridylmethyleneamino)benzenesulfonate.