

***pH controlled uptake/release of citrate by a tri-copper(II)
complex***

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SUPPLEMENTARY INFORMATION AVAILABLE

SYNTHESIS

1,3,5-Tris(bromomethyl)-2,4,6-triethylbenzene:

1,3,5-Tris(bromomethyl)-2,4,6-triethylbenzene was prepared according to a known procedure, with slight work-up differences (see reference 12a in main text). Zinc bromide (39.7g, 0.176 mol) was added portionwise to a mixture of paraformaldehyde (33.5g, 1.11 mol) and 1,3,5-triethylbenzene (20.0 ml, 0.106 mol) in 200 ml 33% HBr/AcOH, at room temperature. The mixture was then heated at 90°C overnight. After cooling the precipitate is filtered and washed twice with 100 ml water. Crude product was suspended in 250 ml 1.5 M HCl and kept under stirring for 30 min. Solid product was filtered, washed twice with 100 ml water, suspended in a NaHCO₃ solution (40g in 750 ml water) and kept under stirring for 2 hours. The suspension was filtered and the filtrate washed with water until neutral pH. The product was dried under vacuum at 65°C overnight, obtaining 44.8g of a white solid (Yield 95%).

hexaethyl 2,2',2''-(2,4,6-triethylbenzene-1,3,5-triyl)tris(methylene)trimalonate (L₁):

Sodium (208 mg, 9.04 mmol) was added to 10 ml anhydrous ethanol at room temperature under nitrogen atmosphere. When sodium was completely reacted, a solution obtained dissolving diethyl malonate (1.45 g, 9.06 mmol) in 10 ml anhydrous ethanol was added dropwise. After 15 min a solution of 1,3,5-Tris(bromomethyl)-2,4,6-triethylbenzene (1.00 g, 2.27 mmol) in 20 ml anhydrous toluene was added dropwise. The mixture was left at room temperature overnight. After adding 50 ml water three extractions with 25 ml diethyl ether were performed. The organic layers were collected and dried over Na₂SO₄. Solvent was removed under vacuum obtaining a pale yellow oil. Adding hexane a white precipitate formed and the pure product was isolated by filtration and needed no further purification. Yield: 65%.

ESI-MS: 701.4 [M+Na]⁺, 1379 [2M+Na]⁺

¹H-NMR (CDCl₃): δ 1.08 (t, 9 H, PhCH₂CH₃), 1.21 (t, 18 H, OCH₂CH₃), 2.62 (q, 6 H, PhCH₂CH₃), 3.28 (d, 6 H, CH₂CH(CO)₂), 3.48 (t, 3 H, malonic CH), 4.15 (q, 12 H, OCH₂CH₃)

2,2',2''-(2,4,6-triethylbenzene-1,3,5-triyl)tris(methylene)tris(N1,N3-bis(2-aminoethyl)malonamide) (L₂):

L₁ (0.5 g, 0.74 mmol) was dissolved in 70 ml freshly distilled ethylenediamine under nitrogen at room temperature. The reaction mixture was kept under stirring for 6 days. The solvent was removed under vacuum, obtaining a yellow oil. Adding methanol a

white precipitate formed. The product was isolated by suction filtration and needed no further purification. (Yield: 54%)

ESI-MS: 382.1 [M+2H]²⁺, 763.5 [M+H]⁺

¹H-NMR (CD₃OD): δ 1.02 (t, 9 H, PhCH₂CH₃), δ 2.64 (q, 6 H, PhCH₂CH₃), δ 2.71 (t, 12 H, CH₂NH₂), δ 2.78 (d, 6H, CH₂-CH(CO)₂), δ 3.26 (t, 12 H, CONHCH₂), δ 3.33 (t, 3H, CH(CO)₂)

2,2',2''-(2,4,6-triethylbenzene-1,3,5-triyl)tris(methylene)tris(N1,N3-bis(2-(quinolin-2-ylmethylamino)ethyl)malonamide) (L):

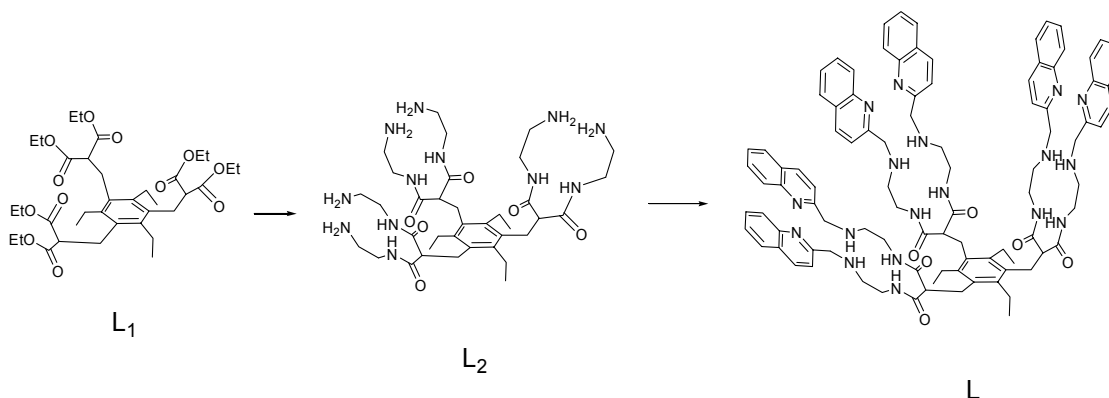
A solution of 2-quinolinecarboxaldehyde (150 mg, 0.96 mmol) in 10 ml methanol was added dropwise to 100 mg (0.13 mmol) of L₂ dissolved in 15 ml of the same solvent. The mixture was stirred at room temperature for one night, concentrated to a volume of 10 ml and left to stand for 1 hour. The precipitate was collected by suction filtration and dried under vacuum (Yield: 46%).

The Schiff base adduct was dissolved in 40 ml of refluxing methanol and excess NaBH₄ (170 mg) was added in small portions over a period of 2 hours. The mixture was cooled to room temperature and kept under stirring overnight. Solvent was removed under vacuum and the crude product was dissolved in 25 ml deionized water, extracted with 3x20 ml dichloromethane and dried over Na₂SO₄ for 45 min. Dichloromethane was removed with a rotary evaporator, obtaining a yellow solid (Yield: 74%).

Elemental analysis: calcd for $C_{96}H_{108}N_{18}O_6 \cdot CH_2Cl_2$: C 68.72, H 6.55, N14.88; found: C 68.32, H 6.24, N 14.51.

ESI-MS: 537.3 $[M+3H]^{3+}$, 805.1 $[M+2H]^{2+}$, 1609.3 $[M+H]^+$

1H -NMR (CD_3OD): δ 0.97 (t, 9 H, $PhCH_2CH_3$), δ 2.62 (q, 6 H, $PhCH_2CH_3$), δ 2.70-2.75 (m, 18 H, $CH_2NH_2 + CH_2CH(CO)_2$), δ 3.19 (t, 12 H, $CONHCH_2$), δ 3.37 (t, 3H, $CH(CO)_2$), δ 3.92 (s, 12 H, $NHCH_2$ -quinoline), δ 7.42 (d, 6H), δ 7.46 (t, 6H), δ 7.62 (t, 6H), δ 7.77 (d, 6H), δ 7.90 (d, 6H), δ 8.12 (d, 6H): H of the quinoline rings.



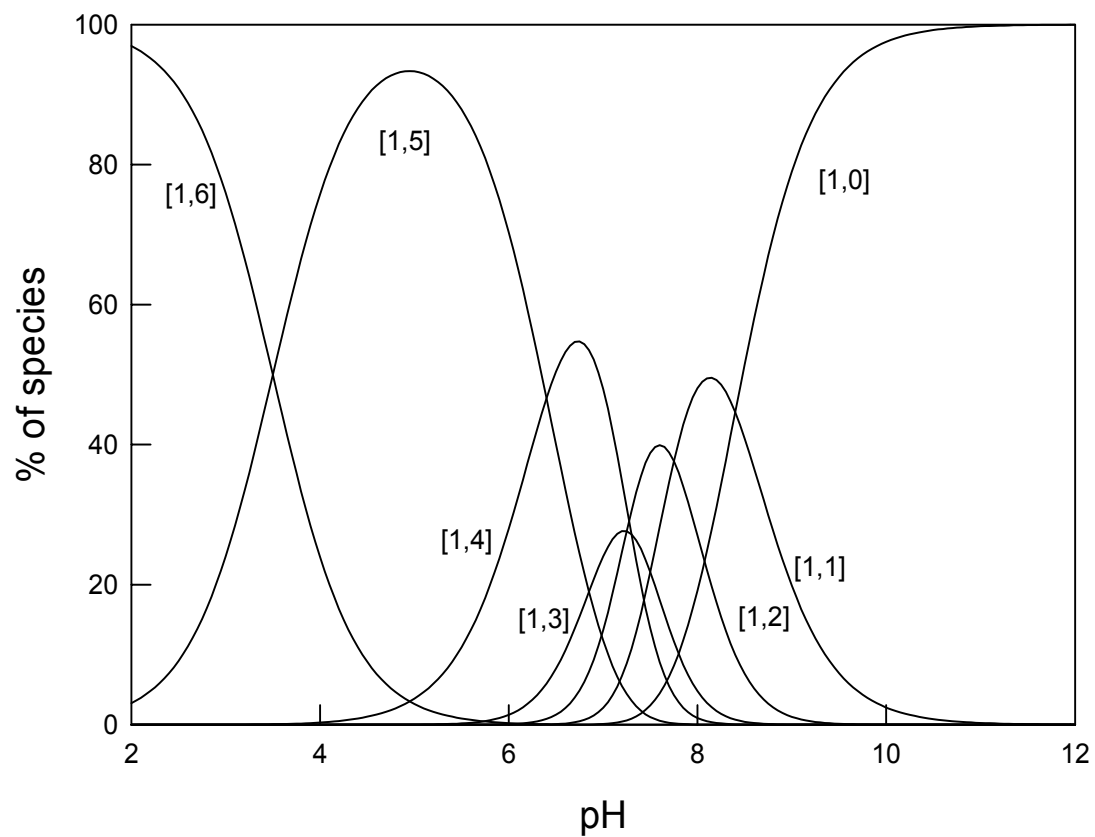


Figure S1 Distribution diagram for the system $[L,H^+]$ obtained from a potentiometric titration, as described in the experimental part. For relative stability constants see table 1 in main text.

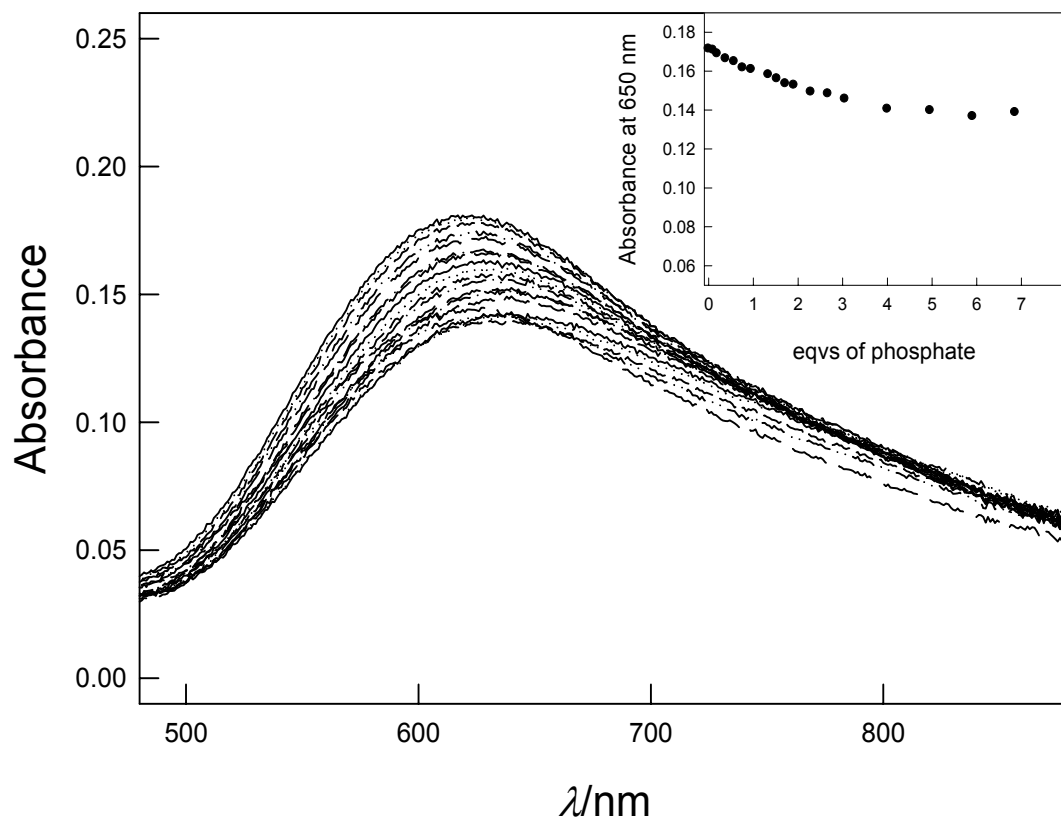


Figure S2 Spectrophotometric titration of $[\text{Cu}_3\text{L}]^{6+}$ with phosphate at pH 5.8. Inset: titration profile obtained at 650 nm