Binuclear copper(II) complexes of 5-N-(β-ketoen)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranoses: synthesis, structure, and catecholoxidase activity

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Abstract—The synthesis of 5-amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8) was carried out via 5-azido-5-deoxy-1,2:3,4-O-diisopropylidene-α-D-glucofuranose (6), its reduction with Raney-Nickel and deprotection. 5-N-(β-Ketoen)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose and β-ketoenolethers leading to ligands with symmetrically substituted double bonds (8a, 8b) and e/z isomeric mixtures with unsymmetrical substitution (8c-f). Reaction of the ligands with Cu(II) ions leads to binuclear complexes of the general formula Cu2L2. In contrast to copper(II) complexes which are not derived from amino carbohydrates the metal centers in the compounds saturate their coordination sphere by complexation of additional solvent molecules, interaction with neighboring complex molecules, or free hydroxyl groups of the own ligand. Residues of the ketoen moiety, R1 and R2, also influence the electronic properties of the metal centers. The combination of factors leads to different catalytic properties of the complexes in catecholoxidase-like reactions.

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1. Introduction

Carbohydrates combine relevant properties as ligands for the synthesis of catalysts, such as chirality and poly-functionality. They exist in a broad range of molecular sizes, obey unique conformational and configurational principles and can be selectively functionalized. Polysaccharides are able to form supramolecular structures such as fibers, gels, membranes, mono- and multilayers. In most of the known examples for structurally characterized metal sugar complexes, commercial carbohydrates act as polylolato ligands to form metal complexes under deprotonation of one or more hydroxyl groups. Another field of interest is the interaction of metal ions with N-glucosides and inositols.

Copper is one of the most important metals for transport, storage, and activation of molecular oxygen in nature. For the four-electron reduction of dioxygen binuclear (e.g., catechol oxidase) or oligonuclear (e.g., ascorbate oxidase) copper centers are favored. Studies on oligonuclear copper model compounds have been undertaken in recent years to elucidate the relationship between structure and reactivity of the active sites in enzymes and to develop new complexes with a useful catalytic performance.

By complexation of copper(II) ions using condensation products of amino sugars and substituted
2. Results and discussion

2.1. Ligand synthesis

Starting from glucuronic acid-3,6-lactone (1) we obtained 5-chloro-5-deoxy-1,2-O-isopropylidene-β-L-idofuranuronicacid-3,6-lactone (3); via acid catalyzed acetalization to 1,2-O-isopropylidene-α-D-glucurono-6,3-lactone (2), and nucleophilic substitution with sulfonyl chloride in pyridine according to literature procedures. The synthesis leads to failed. However, only mixtures and all attempts of chromatographic separation still contained 20% (1H NMR) of the starting material.

Reduction of the lactone with sodium borohydride and acetic acid in dimethoxyethane gives 5-chloro-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (4). In order to prevent the formation of 6-azido-6-deoxy-1,2-O-isopropylidene-α-D-glucurono-6,3-lactone by direct reaction of 4 with sodium azide the hydroxyl groups on C-3 and C-6 were protected, and was reacted with 2,2-dimethoxypropane and sulfuric acid (cat.) to 5-chloro-5-deoxy-1,2,3,6-O-diisopropylidene-β-L-idofuranose (5). The nucleophilic substitution with sodium azide in N,N-dimethylformamide gave 5-azido-5-deoxy-1,2,3,6-O-diisopropylidene-α-D-glucurono-6,3-lactone (6) in good yield (80%). The product still contained 20% (1H NMR) of the starting material. Both have the same R_F value on silica gel in all solvent mixtures and all attempts of chromatographic separation failed. However, only 6 could be reduced with Raney-Nickel and hydrazine hydrate to 5-amino-5-deoxy-1,2,3,6-O-diisopropylidene-α-D-glucurono-6,3-lactone (7). The product was purified by column chromatography and residual 5 regained. Deprotection of 7 with sulfuric acid in methanol/water gave 5-amino-5-deoxy-1,2-O-isopropylidene-α-D-glucurono-6,3-lactone (8) (Fig. 1).

Compound 8 reacts in methanol with the β-keto-enol ethers a-f to give the ligands 8a-f (Fig. 2). These compounds are chiral ligands differing in the residues R_1 and R_2. For the N-(β-keto)amino-saccharides 8c-f the synthesis leads to e/z isomers at the double bonds. Due to the electron delocalization between the donor nitrogen and the carbonyl groups, the C=C bonds lose their double bond character. The corresponding isomers are stabilized by NH···O hydrogen bonds of different strength causing varying ratios of the e- and the z-isomeric forms (Fig. 3). Signals could be assigned to the different isomers by two-dimensional NMR. NOE NMR experiments show beside the expected signals cross peaks for an exchange of protons of the e/z isomeric forms in case of 8c-e. Compound 8f shows no isomerization at the double bond at temperatures up to 50°C and mixture times up to 900 ms due to the electron-withdrawing influence of the nitrile group. 1H NMR data for the most abundant isomers are listed in Table 1. The 13C NMR data for the other observed isomers are also listed in Table 2.
2.2. Synthesis and structure of the copper(II) complexes

Ligands 8a–f may react under deprotonation of the amino function at C-5 and the hydroxyl group at C-6 to give cuban-like structures analogous to amino ethanol derivatives, or via an amino propanol-like reaction under complexation of the nitrogen and the hydroxyl group on C-3 of the furanose ring leading to binuclear structures. All of the synthesized ligands form stable binuclear complexes of the general formula Cu₂L₂ with...
copper(II) ions after deprotonation of the 3-OH and the NH group, due to the favored formation of six-membered chelate rings at the copper centers (Fig. 4).

Dissolving the complexes in the specified solvents and slow evaporation while standing in air gave for all complexes, except of 9d, blue to violet crystals suitable for X-ray crystal structure analysis. Selected bond lengths and angles are included in Table 3.

Crystals of 9a<sup>42,43</sup> consist of two different binuclear formula units. Figure 5 shows one of the molecules which coordinates a water molecule at one of the copper centres. In the other unit a methanol is bound to one of the copper ions.

The asymmetric unit of 9b contains two molecules (one is shown in Fig. 6). Both dimers are identical in formula and basic structure but differ in their three-dimensional shape. They are connected to each other by coordination of one of the free OH groups at C-6 of the next binuclear Cu<sub>2</sub>L<sub>2</sub> unit (O9d-Cub: 2.442(4) Å). Additional solvent molecules are not coordinated.

In contrast in 9c (Fig. 7) one copper ion binds two water molecules Cua (O91–Cua: 2.693(3) Å, O92–Cua: 2.858(3) Å). One is orientated into the direction of the furanose rings of the ligands (O92) the other one occupies the opposite coordination place (O91). The angle between the water molecules and Cua is 164.2(2)<sup>°</sup>. Cub fulfils its coordination sphere with interactions to the free hydroxyl group of its own ligand (O6b–Cub: 2.911(3) Å) and to the one of the next dimeric complex molecule (Cub–O6a: 2.744(2) Å, O6b–Cub–O6a: 147.7(2)<sup>°</sup>).

In 9e (Fig. 8) one methanol molecule is bound directly to Cua into the direction of the furanose rings of the ligands (Cua-O1: 2.465(4) Å). The bound water molecule interacts with a nitrogen atom of a nitrile group of a ligand in a second chain which runs in opposite direction (Fig. 10).

Figure 9 shows the projection of the dimeric copper(II) complex 9f. The compound crystallized from ethanol/water = 2:1 through slow evaporation of the solvents while standing in air. One water is directly bound to Cua (Cua–O1: 2.554(5) Å) and is localized in the opposite direction from the furanose rings of the ligands. The same water molecule is also weakly bound to Cub (Cub–O1: 3.265(5) Å).

The exact molecular structure of 9d could not be determined by X-ray single crystal analysis. Decomposition took place in all protic solvent mixtures from which crystallization was tried. Only in toluene under an argon atmosphere could 9d be dissolved without any disintegration. The electron spray ionization mass spectra shows a peak at m/z = 720 with an intensity of 100%. The isotope pattern indicates two copper atoms. So the peak can be assigned to [Cu<sub>2</sub>L<sub>2</sub>Na]<sup>+</sup>. The electronic spectrum showed a d–d band at 562 nm, a LMCT absorption at 353 nm, and a absorption of the ligand at 321 nm. Therefore a dimeric structure of 9d is plausible.

2.3. Supramolecular structure and puckering in the crystals

A complicated network of H-bridges involving coordinated and additional solvent molecules stabilizes the low symmetry of the complexes. In fact every furanose ring adopts a different conformation (Table 4) and the copper(II) ions exhibit diverse geometries of their coordination spheres.

In the crystals different supramolecular structures were found. In 9a a two-dimensional and in 9b, 9c, and 9e a chain-like arrangement of the binuclear copper(II) units is realized.

In 9e also a formation of chains is observed due to the hydrogen bonds between the free 6-OH groups and the oxygen atoms at C-1 (O5a–O4a: 2.904(10) Å, O5b–O4b: 2.864(10) Å). The bound water molecule interacts with a nitrogen atom of a nitrile group of a ligand in a second chain (N2b–O1: 2.830(10) Å und N2a–O1: 2.949(10) Å) which runs in opposite direction (Fig. 10).
2.4. Catecholoxidase-like activity

The synthesized copper(II) complexes were used as catalysts for the oxidation of di-tert-butylcatechol to the corresponding quinone under the already published conditions.42–44 Only 9a and 9d show a significant activity (9a: $k_{\text{cat}} = 2.8(3) \text{ h}^{-1}$, $K_M = 7.08(50) \times 10^{-3} \text{ mol/L}$, $k_{\text{obs}} = 4.0(2) \text{ h}^{-1}$ and 9d: $k_{\text{cat}} = 30.8(29) \text{ h}^{-1}$, $K_M = 3.97(7) \times 10^{-3} \text{ mol/L}$, $k_{\text{obs}} = 6.99(29) \text{ h}^{-1}$). Compounds 9b, 9c, 9e, and 9f were found to be not more active as catalysts in this reaction than the copper(II) acetate used for the synthesis of the compounds.

| Table 3. Selected interatomic distances, bond lengths [Å], and angels [°] at the copper centres of 9b, 9c, 9e, 9f (for 9a see lit. 43) |
|-------|-------|-------|-------|
| 9b    |       |       |       |
| Cua–Cub   | 3.003(4) | Cuc–Cud   | 3.003(5) |
| Cua–N1a    | 1.903(2) | Cuc–N1c    | 1.907(2) |
| Cub–N1b    | 1.901(2) | Cub–N1d    | 1.921(2) |
| Cua–O1a    | 1.921(2) | Cuc–O1c    | 1.9184(19) |
| Cub–O1b    | 1.9297(19) | Cub–O1d   | 1.9335(19) |
| Cua–O2a    | 1.9238(19) | Cuc–O2c   | 1.9081(19) |
| Cub–O2b    | 1.9188(19) | Cub–O2d   | 1.9245(18) |
| Cub–O2b    | 1.926(2) | Cub–O2d    | 1.9316(19) |
| Cub–O2a    | 1.960(2) | Cub–O2c    | 1.9470(19) |
| CubO9d    | 2.442(2) | O6b–O9c   | 2.730(5) |
| N1a–Cua–O1a | 92.69(9) | N1e–Cuc–O1e | 92.83(9) |
| N1a–Cua–O2a | 96.68(9) | N1e–Cuc–O2c | 96.66(9) |
| O2a–Cua–O2b | 78.31(8) | O2c–Cuc–O2d | 77.91(8) |
| N1b–Cub–O1b | 92.14(9) | N1d–Cud–O1d | 92.26(9) |
| N1b–Cub–O2b | 96.76(9) | N1d–Cud–O2d | 96.47(9) |
| O2b–Cub–O2a | 77.60(8) | O2d–Cud–O2c | 77.16(8) |
| 9c    |       |       |       |
| Cua–Cub   | 3.013(4) | Cub–O6b   | 2.911(3) |
| Cua–N5a    | 1.912(3) | Cub–N5b    | 1.902(3) |
| Cua–O3a    | 1.927(3) | Cub–O3b    | 1.932(3) |
| Cua–O7a    | 1.906(3) | Cub–O7b    | 1.924(3) |
| Cua–O3b    | 1.938(3) | Cub–O3a    | 1.937(3) |
| Cua–O9l    | 2.693(3) | Cua–O92    | 2.858(3) |
| O7a–Cua–N5a | 93.02(14) | O7b–Cub–N5b | 91.52(13) |
| N5a–Cua–O3a | 96.38(13) | N5b–Cub–O3b | 96.08(13) |
| O3a–Cua–O3b | 77.43(12) | O3b–Cub–O3a | 77.33(12) |
| 9e    |       |       |       |
| Cua–Cub   | 2.980(2) | Cua–O1    | 2.465(4) |
| Cua–N1a    | 1.925(4) | Cub–N1b    | 1.923(4) |
| Cua–O2a    | 1.922(3) | Cub–O2b    | 1.928(3) |
| Cua–O1a    | 1.903(3) | Cub–O1b    | 1.934(3) |
| Cua–O2b    | 1.949(3) | Cub–O2a    | 1.920(3) |
| O1a–Cua–N1a | 92.36(15) | O1b–Cub–N1b | 92.89(16) |
| N1a–Cua–O2a | 96.42(14) | N1b–Cub–O2b | 96.06(15) |
| O2a–Cua–O2b | 77.35(12) | O2b–Cub–O2a | 77.92(12) |
| 9f    |       |       |       |
| Cua–Cub   | 2.933(9) | Cua–O1    | 2.554(5) |
| Cua–N1a    | 1.925(4) | Cub–N1b    | 1.928(5) |
| Cua–O7a    | 1.902(4) | Cub–O7b    | 1.895(4) |
| Cua–O1a    | 1.912(4) | Cub–O1b    | 1.919(4) |
| Cua–O7b    | 1.924(4) | Cub–O7a    | 1.932(4) |
| O1a–Cua–N1a | 93.61(19) | O1b–Cub–N1b | 94.7(2) |
| N1a–Cua–O7a | 98.13(19) | N1b–Cub–O7b | 97.31(18) |
| O7a–Cua–O7b | 77.09(16) | O7b–Cub–O7a | 77.07(17) |
2.5. Conclusions

In contrast to complexes derived from 3-aminopropanol, which form stable and highly symmetric binuclear copper(II) complexes, carbohydrate derived compounds lead to structures of low symmetry and supramolecular architecture. The furanose rings induce a ‘strain’ on the metal centres. The copper ions are forced to saturate their coordination sphere by complexation of additional donor atoms originating in solvent molecules, free hydroxyl groups of the same ligand, or interactions to oxygen atoms of the next complex molecule. For 9a and 9d, this results in a catalytic activity in the catecholoxidase-like reaction.

3. Experimental section

3.1. General methods

Electronic spectra were recorded with a Varian Cary 1 or Cary 5E spectrophotometer at room temperature. IR spectra were measured on a Perkin–Elmer 2000 spectrometer; NMR spectra on a Bruker AC-200, mass spectra on a Finnigan MAT SSQ 710 or a Finnigan MAT 95XL TRAP and elemental analyses on a Leco CHNS 932.

3.2. Procedure A (synthesis of 8a–f)

To a solution of 3.2 mmol (700 mg) 5-amino-5-deoxy-1,2-0-isopropylidene-α-D-glucofuranose (8) in 50 mL dry MeOH 3.5 mmol (355 mg) Et3N and 3.5 mmol of the corresponding compound a–f were added. The solution was stirred 1–24 h until the starting material was not longer detected by TLC. The solution was stirred 1–24 h until the starting material was not longer detected by TLC. The solvent was evaporated and the samples were dried. Cleaning was carried out by column chromatography over silica gel 60 (0.063–0.2 mm) in the specified solvents.

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<th>Compound</th>
<th>Ring</th>
<th>Sequence</th>
<th>Conformation</th>
<th>Ratio twist:envelope [%]</th>
<th>Puckering parameter</th>
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3.3. Procedure B

To a solution of 0.3 mmol of the ligand and 0.6 mmol (61 mg) Et₃N in 30 mL MeOH 0.3 mmol (54.3 mg) copper(II) acetate were added and the solution was stirred for at least 24 h. The solvent was evaporated and the sample was dried. The product was extracted with and crystallized from different solvents (see below).

3.4. Procedure C

To a solution of 0.3 mmol of the ligand and 0.6 mmol (61 mg) Et₃N in 30 mL THF 0.3 mmol (40.3 mg) copper(II) chloride were added and the solution was stirred for 24 h at room temperature. The formed precipitate (triethylammonium chloride) was filtered off and the solvent was evaporated.

3.5. 5-Chloro-5-deoxy-1,2-O-isopropylidene-β-L-idofuranose (4)⁶⁰ ⁶²

Eleven grams (47 mmol) of 3 were diluted in 350 mL dimethoxyethane. The solution was cooled to −10 °C and 5.6 g acetic acid were added drop wise. Then, 7.3 g NaBH₄ were added slowly to the cooled solution. The reaction mixture was stirred for at least 8 h (TLC in ethyl acetate/petrol ether 5:1), with the temperature was kept below 0 °C. Excessive acetic acid was neutralized by adding solid NaHCO₃ and stirring for 24 h at room temperature. The solution was filtered, evaporated, and poured into ice/sodium chloride. The mixture was extracted with chloroform, dried with Na₂SO₄, and evaporated. Traces of starting material were removed by dissolving the crude product in petrol ether and elution over silica gel until 3 is not longer detected by TLC. Compound 4 was eluted from the silica gel with ethyl acetate. Evaporation yielded 7.5 g (67%) colorless oil: [α]_D −9.0° (c1, CHCl₃); IR (ATR); cm⁻¹ 3410s, 2988w, 2937w, 2893w, 1633vw, 1376s, 1233w, 1295w, 1255w, 1215s, 1163s, 1068vs, 1007vs, 951s, 882s, 855s, 792w, 705w; DEIMS: m/z (relative intensity, %) 239 [(M+1)+, 60]; Anal. Calcd for C₉H₁₅ClO₅ (M = 238.67 g/mol): C, 45.29; H, 6.33; Cl, 14.85. Found: C, 44.68; H, 6.47; Cl, 14.32.

3.6. 5-Chloro-5-deoxy-1,2,3,6-O-diisopropylidene-β-L-idofuranose (5)⁶³

7.3 g (30.6 mmol) of 4, 20 mL 2,2-dimethoxypropane, and 20 g molecular sieves (A4) were dissolved in 150 mL acetone. Under stirring 0.4 mL conc. H₂SO₄ was added drop wise. The solution was stirred at room temperature until the starting material is no longer detected by TLC (2 h, TLC: solvent ethyl acetate/petrol ether 1:1, RF-value of 5: 0.91). CaO was added for neutralization and the suspension is stirred overnight. The solution was filtered and evaporated. The crude product filtered over silica gel, yielded 6.6 g (75%) colorless oil: bp 102–105 °C/0.15mmHg; [α]_D +46.0° (c1, CHCl₃); lit.⁶² oil; [α]_D +48.8° (c1, CHCl₃); DEIMS: m/z (relative intensity, %) 279 [(M+1)+, 30]; Anal. Calcd for C₁₂H₁₉ClO₅ (M = 278.73 g/mol): C, 51.88; H, 6.91; Cl, 12.76. Found: C, 51.99; H, 6.79; Cl, 12.28.
3.7. 5-Amino-5-deoxy-1,2:3,6-O-diisopropylidene-α-D-glucofuranose (7)

10.2 g (36.5 mmol) of 5 was dissolved in 200 mL N,N-dimethylformamide and stirred together with 14.2 g NaNO3 for 72 h at 120 °C. TLC control of the reaction is difficult as 5 and the formed 5-azido-5-deoxy-1,2:3,6-O-diisopropylidene-α-D-glucofuranose (6) have the same RF value (e.g., 0.6 for ethyl acetate/petrol ether 1:5). The reaction mixture was evaporated to dryness, dissolved in water, and extracted with ethyl acetate. The organic phase was dried over Na2SO4 and evaporated. The ratio of 5 to 6 is about 1:4 (NMR). 10.1 g (ca. 35.4 mmol) of 6 was dissolved in 200 mL MeOH and heated to 40 °C. Freshly prepared Raney-Nickel suspension was added portion wise under stirring until there was no longer development of gas. The suspension is heated under reflux for 1 h, filtered and evaporated. To regain the unreacted chloride 5 the mixture is eluted over silica gel with ethyl acetate/petrol ether 3:1 until negative detection of 5 by TLC. The product than is eluted with MeOH. The solution is evaporated, the product is tried, and recrystallized from ethyl acetate/heptane yielded 6.1 g (65%) of colorless needles: mp 68–69 °C. DEIMS: m/z (relative intensity, %) 260 [M+1]+, 80; Anal. Calcd for C15H23NO5 (M = 259.30 g/mol): C, 55.60; H, 8.11; N, 3.74; Found: C, 55.14; H, 7.77; N, 4.50.

3.8. 5-Amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8a)

4.4 g (17 mmol) of 7 are dissolved in 30 mL MeOH. Then, a solution of 1.2 g conc. H2SO4 in 20 mL water is added dropwise and the solution stirred for 72 h at room temperature. A large excess of BaCO3 is added and the suspension is stirred overnight and heated under reflux for again 3 h. The barium salts are filtered off and the product is cleaned by elution over silica gel (solvent MeOH), yielded 3.1 g (80%) colorless needles: mp 175 °C; lit.64 178 °C; [α]D 13.3° (c1, MeOH); IR (ATR); cm⁻¹ 3316, 3216, 2923w, 2861w, 1649w, 1564w, 1415s, 1374s, 1303s, 1237s, 1214s, 1164w, 1066w, 956w, 882w, 854s, 790s, 644w, 617w; DCIMS: m/z (relative intensity, %) 360 [(M+1)+, 70]; UV/vis (dioxane); λmax 293 nm (Ige = 4.1740); Anal. Calcd for C15H23NO5 (M = 259.30 g/mol): C, 55.14; H, 7.77; N, 3.74. Found: C, 54.98; H, 8.34; N, 6.34.

3.9. 5-N-(2′,2′-Diacetylvinyl)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8b)

Procedure A. Chromatography (ethyl acetate and recrystallization from ethanol/petrol ether yielded 770 mg (62%) colorless needles suitable for X-ray structure analysis: mp 157 °C, [α]D −34.1° (c1, MeOH); Rf 0.38 (ethyl acetate); IR (ATR); cm⁻¹ 3338s, 3171w, 2979s, 2935s, 2878s, 1689vs, 1657vs, 1614s, 1466w, 1425s, 1376s, 1322s, 1269s, 1211vs, 1164s, 1147w, 1122w, 1071vs, 1008s, 886s, 858w, 798s, 747w, 625w; DCIMS: m/z (relative intensity, %) 390 [(M+1)+, 70]; UV/vis (MeOH); λmax 278 nm (Ige = 4.3454), 222 nm (Ige = 4.0746); Anal. Calcd for C17H23NO8 (M = 389.40 g/mol): C, 52.44; H, 6.99; N, 3.60; Found C, 52.44; H, 7.11; N, 3.60.

3.10. 5-N-(2′,2′-Dietoxy carbonylvinyl)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8b)

Procedure A. Chromatography (ethyl acetate) and recrystallization from ethanol/petrol ether yielded 817 mg (71%) colorless oil: mp 30–31 °C; [α]D −34.6° (c1, MeOH); Rf 0.18 (ethyl acetate/hexane 2:1); IR (ATR); cm⁻¹ 3372s, 2984s, 2935w, 1737w, 1671s, 1631vs, 1562s, 1415s, 1374s, 1303s, 1237s, 1214s, 1164w, 1066w, 1009s, 956w, 882w, 854s, 790s, 644w, 617w; DCIMS: m/z (relative intensity, %) 359 [(M+1)+, 70]; UV/vis (dioxane); λmax 293 nm (Ige = 4.1715), 233 nm (Ige = 4.1740); Anal. Calcd for C16H25NO8 (M = 359.38 g/mol): C, 53.51; H, 7.02; N, 3.90. Found C, 51.62; H, 7.34; N, 3.65.

3.11. 5-N-(2′-Acetyl-2′-ethoxy carbonylvinyl)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8c)

Procedure A. Chromatography (ethyl acetate/MeOH 3:1) yielded 817 mg (71%) colorless oil: [α]D −34.6° (c1, MeOH); Rf 0.18 (ethyl acetate/hexane 2:1); IR (ATR); cm⁻¹ 3372s, 2984s, 2935w, 1737w, 1671s, 1631vs, 1562s, 1415s, 1374s, 1303s, 1237s, 1214s, 1164w, 1066w, 1009s, 956w, 882w, 854s, 790s, 644w, 617w; DCIMS: m/z (relative intensity, %) 360 [(M+1)+, 70]; UV/vis (dioxane); λmax 293 nm (Ige = 4.1715), 233 nm (Ige = 4.1740); Anal. Calcd for C16H25NO8 (M = 359.38 g/mol): C, 53.51; H, 7.02; N, 3.90. Found C, 51.62; H, 7.34; N, 3.65.

3.12. 5-N-(2′-acetylvinyl)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (8d)

Procedure A. Chromatography (ethyl acetate/MeOH 3:1) yielded 505 mg (55%) yellow oil: [α]D −83.2° (c1, MeOH); Rf 0.18 (ethyl acetate); IR (ATR); cm⁻¹ 3309s, 2986w, 2937w, 2885vw, 1735w, 1635s, 1515s, 1493s, 1375s, 1257s, 1213s, 1164s, 1067vs, 1009s, 958s, 882w, 858w, 790s, 746w, 669w, 618w; DCIMS: m/z (relative intensity, %) 288 [(M+1)+, 80]; UV/vis (dioxane); λmax 296 nm (Ige = 4.2085); Anal. Calcd for C13H22NO7 (M = 287.31 g/mol): C, 54.38; H, 7.37; N, 4.88. Found: C, 52.73; H, 7.49; N, 4.44.
3.13. 5-N-(2'-Ethoxycarbonyl-2'-phenylcarbonylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranose (8e)

Procedure A. Chromatography (ethyl acetate) yielded 1050 mg (78%) colorless oil; [α] -23.9° (c 1, MeOH); Rf 0.45 (ethyl acetate); IR (ATR); cm⁻¹ 3373s, 3286s, 3060w, 2984s, 2936s, 2910v, 1666vs, 1619vs, 1560s, 1446w, 1376s, 1307s, 1214vs, 1163s, 1067s, 1009vs, 853w, 785s, 724v, 698s, 669s, 616w; DCIMS: m/z (relative intensity, %) 422 [(M+1)⁺, 50]; UV/vis (MeOH); λ_max 246 nm (lgε = 4.2735), 302 nm (lgε = 4.3076); Anal. Caled for C₁₅H₂₂N₂O₇ (M = 421.45 g/mol): C, 59.89; H, 6.46; N, 3.33. Found: C, 59.40; H, 6.33; N, 3.20.

3.14. 5-N-(2'-Ethoxycarbonyl-2'-nitrilyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranose (8f)

Procedure A. Chromatography (ethyl acetate) yielded 710 mg (65%) colorless oil; [α] -33.0° (c 1, MeOH); Rf 0.55 (ethyl acetate); IR (ATR); cm⁻¹ 3373s, 3294s, 2984w, 2936v, 2210vs, 1677vs, 1615vs, 1436w, 1378s, 1332w, 1240v, 1163s, 1067s 1009w, 955s, 860w, 782s, 676w, 617w; DCIMS: m/z (relative intensity, %) 343 [(M+1)⁺, 70]; UV/vis (MeOH); λ_max 281 nm (lgε = 4.3603), 205 nm (lgε = 4.0816); Anal. Caled for C₁₅H₂₀N₂O₇ (M = 342.35 g/mol): C, 52.66; H, 6.48; N, 8.19. Found: C, 51.76; H, 6.82; N, 7.76.

3.15. Bis-(5-N(2'-2'-diacyethylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-aquodicopper(II)-bis-(5-N(2'-2'-diacyethylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-methanolodicopper(II) (9a)

Procedure B. The residue was dissolved in toluene. During the slow evaporation of the solvent a violet toluene containing compound crystallizes. Recrystallization from water/MeOH = 1:1 leads to the precipitation of 28 mg (24.00%) deep blue crystals of 9a in a quality suitable for X-ray crystal structure determination: IR (KBr); cm⁻¹ 3331w, 2984s, 2928s, 1719w, 1649w, 1584v, 1457s, 1395s, 1357s, 1283s, 1257s, 1213s, 1165s, 1125s, 1059s, 1008v, 946s, 882s, 844s, 732s, 696w, 638s; UV/vis (MeOH); λ_max 651 nm (lgε = 2.2201), 373 nm (lgε = 3.1284); ESIMS: m/z 1585 (Cu₂L₂Na⁺); 1173 (Cu₅L₄Na⁺); 804 (Cu₅L₄Na⁺); 783 (Cu₅L₃H⁺); 423 (Cu₅L(MeOH)); 391 (Cu⁺); Anal. Caled for Cu₂H₂₄N₄O₁₅Cu₂[Cu₂L₂H₂OCH₂OH] (M = 1667.62 g/mol); C, 43.94; H, 5.80; N, 3.36. Found: C, 44.05; H, 5.87; N, 3.31.

3.16. Bis-(5-N(2'-2'-Diethoxycarbonylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-dicopper(II) (9b)

Procedure C. The residue was extracted with toluene to give a blue solid, which can be recrystallized from MeOH/water to give 66 mg (49%) of deep-blue crystals suitable for X-ray crystal structure analysis: IR (KBr); cm⁻¹ 3426w, 2955s, 2984s, 2854s, 1733wv, 1675w, 1604s, 1461s, 1412w, 1377s, 1347w, 1259s, 1215w, 1160w, 1068v, 1013vs, 868w, 796s, 727w, 642w; UV/vis (MeOH); λ_max 583 nm (lgε = 2.6685), 352 nm (lgε = 3.4462), 292 nm (lgε = 3.9691), 225 nm (lgε = 4.5733); ESIMS: m/z 2728 (Cu₅L₄Na⁺); 1827 (Cu₄L₄Na⁺); 1353 (Cu₃L₃Na⁺), 925 (Cu₂L₄Na⁺); Anal. Caled for C₃₆H₃₆N₁₂O₁₆Cu₂ [Cu₂L₂] (M = 901.86 g/mol): C, 45.28; H, 5.59; N, 3.11. Found: C, 45.47; H, 5.48; N, 3.21.

3.17. Bis-(5-N(2'-acetyl-2'-ethoxycarbonylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-diquodicopper(II) (9c)

Procedure B with 150 mg (0.42 mmol) 8c. The residue was extracted with toluene to give a blue solid, which can be recrystallized from MeOH/water to give 77 mg (42%) of deep-blue crystals suitable for X-ray crystal structure analysis: IR (ATR); cm⁻¹ 3519w, 2981w, 2936w, 2897v, 1662s, 1640s, 1442s, 1410s, 1373s, 1279s, 1207w, 1167w, 1133w, 1062s, 998s, 956w, 885w, 843w, 822w, 778w, 729w; UV/vis (ethanol); λ_max 350.4 nm (lgε = 4.0003), 302 nm (lgε = 4.3407), 244 nm (lgε = 4.6613); ESIMS: m/z 863 (Cu₅L₄Na⁺); Anal. Caled for C₃₆H₃₆N₁₂O₁₆Cu₂[Cu₂L₂2H₂OCH₂OH] (M = 908.22 g/mol); C, 43.64; H, 5.99; N, 3.08. Found: C, 45.75; H, 5.99; N, 2.99.

3.18. Bis-(5-N(2'-acetylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-diquodicopper(II) (9d)

Procedure B. The residue was extracted with toluene and the solvent was evaporated to give 86 mg (82%) violet solid. The substance could not be crystallized from any solvent we tried: IR (ATR); cm⁻¹ 3358s, 2985s, 2917s, 1667w, 1600vs, 1515vs, 1455w, 1398vs, 1381vs, 1258w, 1213s, 1164w, 1125w, 1062s, 1006s, 955s, 883s, 843s, 822s, 750w, 647w, 619w; ESIMS: m/z 719 (Cu₅L₄Na⁺); 372 (CuLNa⁺); UV/vis (MeOH); λ_max 321 nm (lgε = 4.3217), 353 nm (lgε = 4.0174), 562 nm (lgε = 3.3393); Anal. Caled for C₂₀H₂₀N₁₂O₁₆Cu₂ [Cu₂L₂] (M = 697.69 g/mol); C, 44.86; H, 5.50; N, 4.02. Found: C, 43.30; H, 6.17; N, 3.59.

3.19. Bis-(5-N(2'-ethoxycarbonyl-2'-phenylcarbonylvinyl)amino-5-desoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-methanolodicopper(II) (9e)

Procedure B. The crude product was extracted with toluene, evaporated, and recrystallized from MeOH/water to give 75 mg (52%) of violet crystals suitable for
X-ray crystal structure analysis: IR (ATR); cm⁻¹ 3460w, 3060vw, 2984w, 2937w, 2897w, 1611s, 1600vs, 1497w, 1453vs, 1409vs, 1369vs, 1281vs, 1217s, 1166s, 1126s, 1050s, 1007s, 872w, 778s, 738s, 701vs, 646s, 619s; ESIMS: m/z 989 (Cu₂L₂+Na⁺); UV/vis (MeOH); λ_max 205 nm (Iₑ₉ = 4.6255), 252 nm (Iₑ₉ = 4.6857), 327 nm (Iₑ₉ = 4.3677); Anal. Calcd for C₄₂H₅₀Cu₂N₂O₁₉·1/₂H₂O: [Cu₂L₂] (M = 965.95 g/mol): C, 52.32; H, 5.23; N, 2.91. Found: C, 52.34; H, 4.99; N, 2.92.

3.20. Bis-(5-N-(2’-ethoxycarbonyl-2’-nitrivinyl)amino-5-deoxy-1,2-O-isopropylidene-α-D-glucofuranoso)-aquodicopper(II) (9f)

Procedure C with 450 mg (1.3 mmol) of 8f. The residual was recrystallized from toluene/MeOH to give 223 mg (42%) of violet crystals suitable for X-ray crystal structure analysis: IR (ATR); cm⁻¹ 3496s, 2986w, 2935w, 2900w, 2206vs, 1682w, 1630vs, 1515s, 1471w, 1438s, 1414s, 1378s, 1315s, 1299w, 1257s, 1207s, 1165w, 1120w, 1060s, 995s, 885w, 870w, 843w, 831w, 758w, 645w, 611wv; ESIMS: m/z 830 (Cu₂L₂+Na⁺); UV/vis (MeOH); λ_max 342 nm (Iₑ₉ = 3.8503), 294 nm (Iₑ₉ = 4.4347), 259 nm (Iₑ₉ = 4.1853), 225 nm (Iₑ₉ = 4.5733). Anal. Calcd for C₃₀H₄₀Cu₂N₂O₁₄·[Cu₂L₂] (M = 807.76 g/mol): C, 44.61; H, 4.99; N, 6.94. Found: C, 44.66; H, 5.10; N, 6.89.

4. Crystal structure determination

The intensity data for the compounds were collected on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo-Kα radiation. Data were corrected for Lorentz and polarization effects, but not for absorption.65,66

The structures were solved by direct methods (SHELXS86) and refined by full-matrix least squares techniques against Fo² (SHELXL-97). For compound 8b (FO977) the hydrogen atoms of the amin-, the hydroxyl group and the ring-atoms were located by difference Fourier synthesis and refined isotropically. The hydrogen atoms of the other structures were included at calculated positions with fixed thermal parameters. All nonhydrogen atoms were refined anisotropically. ORTEP32 was used for structure representations.

Further details of the crystal structure investigations are available on request from the director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB2 1 EZ, on quoting the depository number CCSD-185925 (8b, fo977), CCDC-129253 (9a, fo1063), CCSD-185924 (9b, fo1556), CCSD-192874 (9c, fo1714), CCSD-185923 (9e, fo1495), and CCSD-185922 (9f, fo1468) and the names of the authors, and the journal citation.

4.1. Crystal data for 8b (FO977)

C₁₇H₂₇NO₈, Mᵣ = 389.40 g mol⁻¹, colorless prism, size 0.30×0.20×0.20 mm³, monoclinic, space group P2₁, a = 11.6522(6), b = 7.3797(4), c = 12.5751(7) Å, β = 107.677(3)°, V = 1030.31(1) Å³, T = 20 °C, Z = 2, ρ_calcd = 1.255 g cm⁻³, μ (Mo-Kα) = 1.02 cm⁻¹, F(000) = 416, 4089 reflections in h=−14/14, k=−9/9, l=−15/15, measured in the range 3.24° ≤ Θ ≤ 26.84°, completeness Θ_max = 99%, 4078 independent reflections, R(int) = 0.042, 3140 reflections with Fₒ > 4σ(Fₒ), 281 parameters, 1 restraints, R₁(obs) = 0.056, wR²(obs) = 0.119, R₁(all) = 0.079, wR²(all) = 0.131, GOOF = 1.074, Flack-parameter 0.7(3), largest difference peak and hole: 0.351/−0.192 e Å⁻³.

4.2. Crystal data for 9a (FO1063)

C₃₀H₄₂Cu₂N₂O₁₄·1/₂CH₂OH·H₂O, Mᵣ = 837.79 g mol⁻¹, blue prism, size 0.28×0.24×0.20 mm³, monoclinic, space group P2₁, a = 10.3923(3), b = 13.8859(5), c = 25.9903(8) Å, β = 101.517(2)°, V = 3675.71(2) Å³, T = −90 °C, Z = 4, ρ_calcd = 1.514 g cm⁻³, μ (Mo-Kα) = 12.33 cm⁻¹, F(000) = 1748, 15126 reflections in h=0/14, k=−19/19, l=−25/27, measured in the range 2.30° ≤ Θ ≤ 30.52°, completeness Θ_max = 78.2%, 14812 independent reflections, R(int) = 0.041, 11657 reflections with Fₒ > 4σ(Fₒ), 933 parameters, 1 restraints, R₁(obs) = 0.080, wR²(obs) = 0.141, R₁(all) = 0.110, wR²(all) = 0.153, GOOF = 1.095, Flack-parameter 0.35(1), largest difference peak and hole: 0.646/−0.695 e Å⁻³.

4.3. Crystal data for 9b (FO1556)

C₃₄H₅₂Cu₂N₂O₁₉·1/₂H₂O, Mᵣ = 928.86 g mol⁻¹, blue prism, size 0.12×0.10×0.08 mm³, monoclinic, space group P2₁, a = 10.4383(1), b = 25.9592(3), c = 15.8939(2) Å, β = 102.435(1)°, V = 4205.74(8) Å³, T = −90 °C, Z = 4, ρ_calcd = 1.467 g cm⁻³, μ (Mo-Kα) = 10.9 cm⁻¹, F(000) = 1940, 18571 reflections in h=−13/13, k=−33/33, l=−20/20, measured in the range 2.05° ≤ Θ ≤ 27.4°, completeness Θ_max = 99.7%, 18542 independent reflections, R(int) = 0.028, 16847 reflections with Fₒ > 4σ(Fₒ), 1056 parameters, 1 restraints, R₁(obs) = 0.035, wR²(obs) = 0.082, R₁(all) = 0.043, wR²(all) = 0.087, GOOF = 1.010, Flack-parameter 0.004(6), largest difference peak and hole: 0.874/−0.455 e Å⁻³.

4.4. Crystal data for 9c (FO1714)

C₃₂H₄₀Cu₂N₂O₁₆·2 H₂O, Mᵣ = 877.82 g mol⁻¹, blue prism, size 0.10×0.08×0.06 mm³, triclinic, space group P1, a = 7.8448(2), b = 9.0849(3), c = 14.2672(4) Å, α = 97.892(1), β = 100.267(1), γ = 97.698(1)°, V = 977.87(5) Å³, T = −90 °C, Z = 1, ρ_calcd = 1.491 g cm⁻³, μ
(Mo-Kα) = 11.64 cm⁻¹, F(000) = 458, 7081 reflections in h(−9/10), k(−11/9), l(−17/18), measured in the range 2.51° ≤ Θ ≤ 27.46°, completeness Θ_max = 99.2%, 7074 independent reflections, R_int = 0.050, 5945 reflections with F_o > 4σ(F_o), 503 parameters, 3 restraints, R1_obs = 0.038, wR2_obs = 0.079, R1_all = 0.054, wR2_all = 0.085, GOOF = 0.994, Flack-parameter −0.008(9), largest difference peak and hole: 0.318/−0.363 eÅ⁻³.

4.5. Crystal data for 9e (FO1495)

C_{42}H_{60}Cu_{2}N_{4}O_{15}·3/2CH_{2}OH·1/2 H_{2}O, M_r = 1020.98 g mol⁻¹, colorless prism, size 0.12 × 0.12 × 0.08 mm³, orthorhombic, space group P2₁2₁2₁, a = 11.0545(4), b = 16.1507(3), c = 27.4101(9) Å, V = 4893.7(3) Å³, T = –90 °C, Z = 4, ρ_calcd = 1.386 g cm⁻³, μ (Mo-Kα) = 9.42 cm⁻¹, F(000) = 2128, 10612 independent reflections, R_int = 0.071, 6259 reflections with F_o > 4σ(F_o), 589 parameters, 0 restraints, R1_obs = 0.051, wR2_obs = 0.118, R1_all = 0.086, wR2_all = 0.123, GOOF = 0.964, Flack-parameter 0.024(13), largest difference peak and hole: 1.364/−0.386 eÅ⁻³.

4.6. Crystal data for 9f (FO1468)

C_{36}H_{56}Cu_{3}N_{4}O_{15}·1/2C_{2}H_{2}O, M_r = 859.79 g mol⁻¹, purpur prism, size 0.12 × 0.12 × 0.10 mm³, orthorhombic, space group P2₁2₁2₁, a = 17.8764(4), b = 26.6582(6), c = 7.9868(2) Å, V = 3806.13(15) Å³, T = –90 °C, Z = 4, ρ_calcd = 3.500 g cm⁻³, μ (Mo-Kα) = 11.92 cm⁻¹, F(000) = 1784, 8201 reflections in h(−22/22), k(−34/34), l(−10/10), measured in the range 2.28° ≤ Θ ≤ 27.49°, completeness Θ_max = 98.1%, 8167 independent reflections, R_int = 0.065, 6091 reflections with F_o > 4σ(F_o), 465 parameters, 1 restraint, R1_obs = 0.069, wR2_obs = 0.190, R1_all = 0.086, wR2_all = 0.198, GOOF = 1.066, Flack-parameter 0.052(2), largest difference peak and hole: 1.721/−0.779 eÅ⁻³.

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