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BRIEF COMMUNICATION

# Synthesis and Crystal Structure of a Novel Glycoluril Molecular Scaffold

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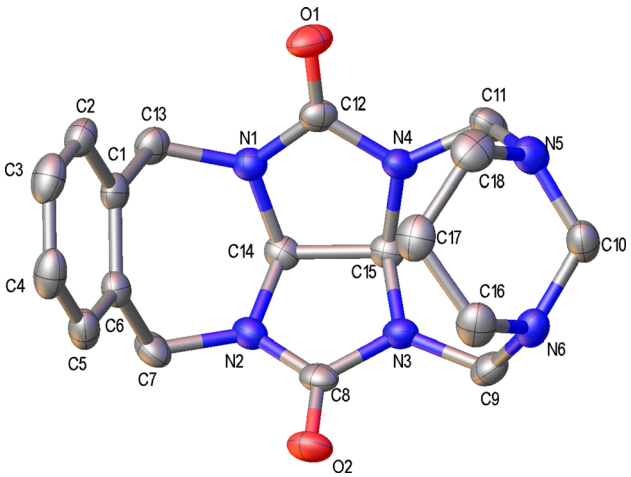
**Abstract** A novel glycoluril scaffold **1**, namely 1,6-(1,2-xylylene)-3,4-(1,3-dimetheneyl-hexahydropyrimidine)tetrahydroimidazo[4,5-d]imidazole-2,5(1*H*,3*H*)-dione, was synthesized by the Mannich reaction of 1,6-(1,2-xylylene)tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione **5** with propanediamine and paraformaldehyde. The yielded product **1** was confirmed with IR, NMR, EI-MS. X-ray crystallographic technique was also conducted and the result showed the crystal belongs to monoclinic system, space group $P2_1/c$ with unit cell parameters a = 10.6892(11) Å, b = 12.1226(9) Å, c = 13.7822(13) Å, α = 90°, β = 112.620(4)°,γ = 90°, V = 1648.5(3) $Å^3$, Z = 4, $D_c$ = 1.428, $M_r$ = 354.41, μ = 0.098 $mm^{-1}$, F(000) = 752, $R_1$ = 0.0522 and $wR_2$ = 0.1138.

**Graphical Abstract** A novel molecular scaffold, containing a heterocyclic ring instead of an aromatic ring, was synthesized by the Mannich reaction based on glycoluril.




**Keywords** Synthesis · Crystal structure · Glycoluril

## Introduction

Glycoluril and its derivatives, due to their precaved structure and special bonding vector information, are widely used as an important building blocks for supramolecular chemistry, for example, molecular scaffold [1], molecular clips [2–4] and molecular baskets [5], molecular bowls [6], molecular capsules [7–9], and the cucurbit[n]uril family of macrocycles [10–14]. Among these versatile structures, glycoluril-derived clips and scaffolds attracted much interest due to their fuctions acting as excellent receptors [15–18]. As our purpose to obtain some new artificial receptors, a novel glycouril molecular scaffold, modified from molecular clip using a heterocyclic ring instead of an aromatic ring, was synthesized and its structure were reported here.

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## Experimental

The melting point was determined with XT4A micromelting point apparatus. Infrared spectra was recorded as KBr pollets on a PE-983 spectrometer. The $^{1}H$ NMR and $^{13}C$ NMR were measured on a Bruker Avance 300 spectrometer with TMS as internal reference and DMSO-$D_6$ as solvent. MS was obtained with Finnigan Trace MS instrument using EI method.

### Synthesis of the Title Compound

The title compound was prepared according to Scheme 1. Compounds **2** [19], **3** [20], **4**, **5** [21] were synthesized according to the literature method.

*Preparation of 1*

A suspension of 0.49 g of compound **5** (2.0 mmol) in 0.5 mL of 37 % aqueous formaldehyde (6.2 mmol) and 30 mL of methanol in a 100-mL flask was brought to reflux in an oil bath with magnetic stirring. To this mixture was added slowly a solution of 0.14 g of propanediamine (2.0 mmol) in 20 mL of methanol dropwise, and refluxing was then continued overnight. The reaction mixture was cooled to room temperature, and unreacted compound **5** (0.10 g) was removed by filtration. After rotary evaporation the residue was chromatographed ($SiO_2$, methanol/ethyl acetate 1:2) to yield **1** (0.29 g, 42 %) as a white solid. M.p. 240–242 °C. IR (KBr, $cm^{-1}$): 3025w, 2912 m, 1709 s, 1650 s, 1608 s, 1456 s, 1120 s, 740 s. $^{1}H$ NMR (300 MHz, DMSO-$D_6$): δ7.30–7.20(m, 4H), 5.64(d, J = 8.0 Hz, 1H), 5.32(d, J = 7.9 Hz, 1H), 4.60–4.52(m, 6H), 4.10–4.00(m, 3H), 3.81(d, J = 11.4 Hz, 1H), 2.70–2.49(m, 4H). $^{13}C$ NMR (75 MHz, $CDCl_3$):δ156.8, 137.9, 129.2, 127.6, 76.6, 69.4, 68.0, 64.0, 46.7, 45.1. EI-MS: m/z 355 (100, $[M+1]^+$).

### X-ray Crystal Structure Determination

The colorless single crystal was cultured from a solution of methanol by slow evaporation at room temperature.

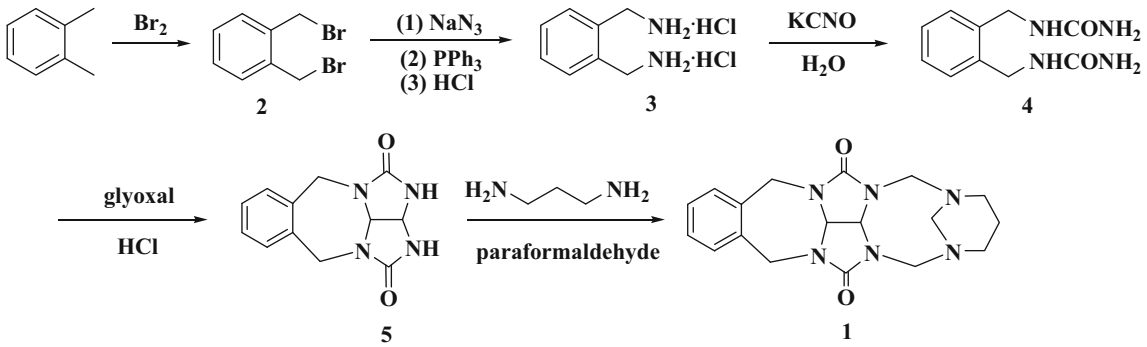
A single crystal of approximate dimensions 0.40 mm × 0.31 mm × 0.30 mm was used. X-ray diffraction data were collected at 173(2) K on a Bruker Smart-1000CCD diffractometer, using graphite monochromatized Mo Kαradiation (λ = 0.71073 Å). A total of 3739 independent reflections were collected in the range of $3.071° < \theta < 27.489°$ by ω scan mode. The crystal data, data collection, and refinement parameters for **1** were presented in Table 1.

The structure was solved by direct methods using the program SHELXS-97 [22]. Refinements were done by the full-matrix least-squares on $F^2$ using SHELXL-97. Non-hydrogen atoms were refined with anisotropic displacement parameters. Figure 1 was drawn by using the program OLEX2 [23], Figs. 2 and 3 were drawn by using the program Mercury [24].

## Results and Discussion

Selected bond distances and bond angles are listed in Table 2. Selected torsion angle are given in Table 3. An OLEX2 view of the molecule with the atomic numbering (thermal ellipsoids drawn at 50 % probability) is shown in Fig. 1.

The bond distances and bond angles of the title compound are in good agreement with the corresponding values obtained in case of related glycoluril derivatives [25–27]. Two imidazole rings which belong to the glycolurilskeleton both have certain torsion and are nonplanar. The distance between the two carbonyl oxygens C(12)=O(1)···O(2)=C(8) is 5.848(2) Å. The six-member heterocyclic ring (N5–C10–N6–C16–C17–C18) adopts a stable chair conformation. The dihedral angle between the plane A (N5–N6–C17) and plane B (C10–C16–C18) is 0.68°. The angle between the benzene ring plane and the




**Scheme 1** Preparation of the title compound

**Table 1** Crystal data, summary of data collection and structure refinement

| | |
|---|---|
| CCDC No. | 1426236 |
| Empirical formula | $C_{18}H_{22}N_6O_2$ |
| Formula weight | 354.41 |
| Crystal system | Monoclinic |
| Space group | $P2_1/c$ |
| Cell dimensions | a = 10.6892(1) Å |
| | b = 12.1226(9) Å |
| | c = 13.7822(1) Å |
| | β = 112.620(4)° |
| Volume (Å$^3$) | 1648.5(3) |
| Z | 4 |
| Density (calculated) (Mg/m$^3$) | 1.428 |
| Absorption coefficient (mm$^{-1}$) | 0.098 |
| $F_{000}$ | 752 |
| Index ranges | $-13 \leq h \leq 13$ |
| | $-15 \leq k \leq 15$ |
| | $-17 \leq l \leq 17$ |
| Reflections collected | 11,421 |
| Independent reflections | 3739 ($R_{int}$ = 0.0264) |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission coefficients | 1.0000 and 0.8889 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 3739/0/235 |
| Goodness-of-fit on $F^2$ | 1.163 |
| Final R indices [$I > 2\sigma(I)$] | $R_1$ = 0.0484, $wR_2$ = 0.1117 |
| R indices (all data) | $R_1$ = 0.0522, $wR_2$ = 0.1138 |
| Extinction coefficient | n/a |
| Largest diff. peak and hole, e (A$^{-3}$) | 0.249 and −0.219 |

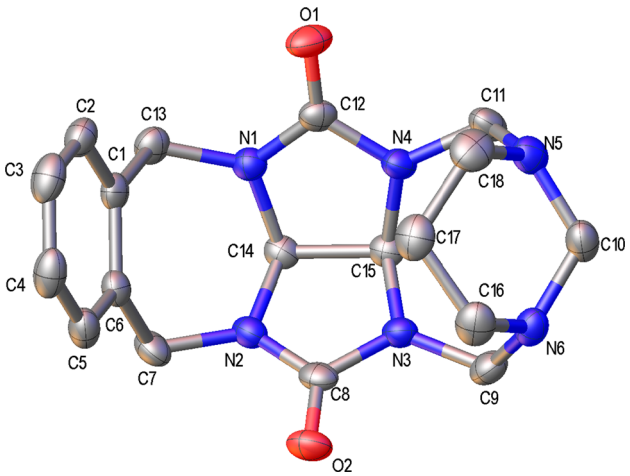



**Fig. 1** Molecular structure of the title compound

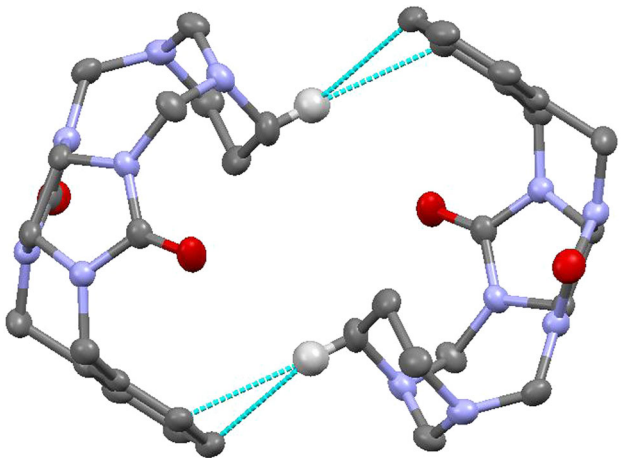


**Fig. 2** The dimeric aggregates via C—H…π hydrogen bond. Symmetry code: 1 − x, 1 − y, 1 − z

plane A (C16–C17–C18), plane B (C16–C18–N5–N6) is 54.70° and 10.83° respectively. The distance between the benzene ring centroid and six-member heterocyclic ring centroid is 6.078 Å. The glycoluril scaffold has a rigid cavity, which may be suitable for binding some small guest by hydrogen bond.

Viewed from Fig. 2, dimeric aggregates are formed through C18—H18B···π hydrogen bond. The distance

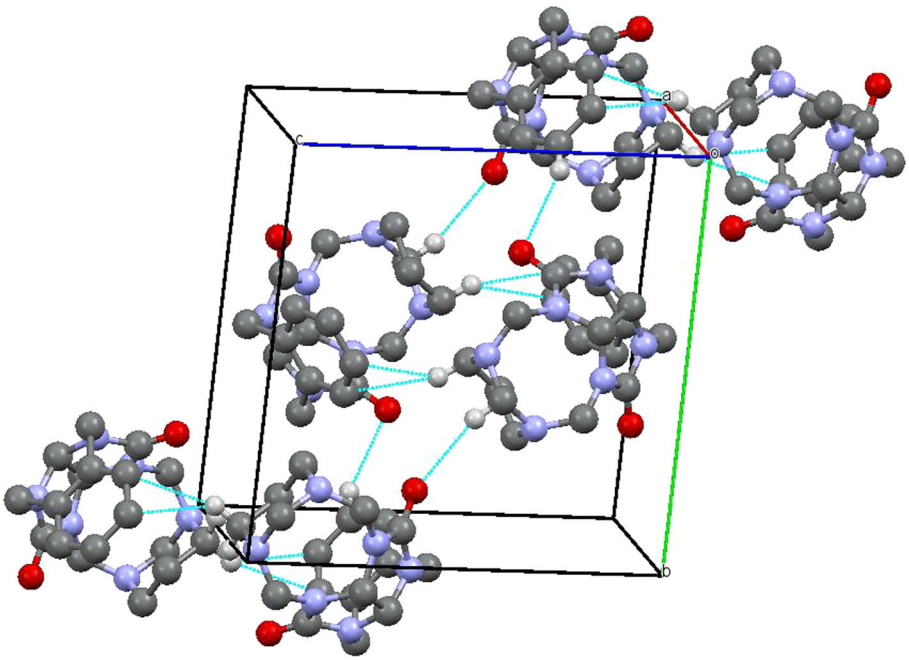



**Fig. 3** The packing arrangement viewed down the b-axis. Hydrogen bonds are shown by dashed lines

**Table 2** Selected bond lengths (Å) and angles (°) for non-hydrogen atoms

| | | | |
|---|---|---|---|
| O1–C12 | 1.2207(18) | C10–N5–C18 | 111.16(13) |
| O2–C8 | 1.2248(18) | C11–N5–C10 | 117.50(13) |
| N1–C12 | 1.3714(18) | C11–N5–C18 | 116.13(13) |
| N1–C13 | 1.4589(18) | C9–N6–C10 | 118.51(12) |
| N1–C14 | 1.4469(18) | C9–N6–C16 | 116.21(12) |
| N2–C8 | 1.3634(19) | C10–N6–C16 | 100.49(13) |
| C1–C2 | 1.387(2) | C2–C1–C6 | 119.61(13) |
| C14–C15 | 1.5501(19) | C2–C1–C13 | 119.55(13) |
| C14–N1–C13 | 122.08(11) | O1–C12–N1 | 125.79(14) |
| C8–N2–C7 | 122.56(12) | O1–C12–N4 | 126.03(14) |
| C8–N2–C7 | 112.82(11) | N1–C12–N4 | 108.14(12) |
| C14–N2–C7 | 122.56(12) | N1–C13–C1 | 113.31(11) |

between the hydrogen atom 18B and the centroid of the aromatic ring is 3.506 Å, and the bond angle of the C18—H18B···π hydrogen bond is 140.72°. π–π stacking interactions is not found in the crystal structure.

The packing arrangement viewed down the b-axis is show in Fig. 3. The title compound assembles to a two-dimensional chain structure by intermolecular hydrogen bond C14—H14···O2 [2.594(3) Å, 143.4°] with symmetry code −x, 1 − y, −z.

In conclusion, a novel glycoluril molecular scaffold was synthesized by the Mannich reaction of **5** with propanediamine and paraformaldehyde. The glycoluril scaffold has a rigid cavity, may be suitable for binding some small guest by hydrogen bond. Futher studies on its molecular recognition are in progress.

**Table 3** Selected torsion angles (°) for non-hydrogen atoms

| | | | |
|---|---|---|---|
| N1–C14–C15–N3 | 122.17(11) | C11–N4–C12–N1 | 170.17(12) |
| N2–C14–C15–N3 | 2.30(13) | C11–N4–C15–C14 | −172.60(13) |
| N2–C14–C15–N4 | −117.61(11) | C11–N5–C10–N6 | −85.15(17) |
| N6–C16–C17–C18 | −49.98(18) | C11–N5–C18–C17 | 88.89(17) |
| C1–C6–C7–N2 | 62.88(18) | C12–N1–C13–C1 | −81.65(17) |
| C4–C5–C6–C7 | −179.81(13) | C12–N4–C15–N3 | −111.45(13) |
| C5–C6–C7–N2 | −116.77(15) | C12–N4–C15–C14 | 0.38(15) |
| C7–N2–C8–N3 | −167.10(12) | C13–N1–C12–O1 | −17.8(2) |
| C7–N2–C14–N1 | 52.33(17) | C15–N3–C8–N2 | 4.76(15) |
| C7–N2–C14–C15 | 164.38(12) | C15–N3–C9–N6 | 81.13(18) |
| C8–N2–C7–C6 | 86.31(17) | C15–N4–C11–N5 | −83.91(18) |
| C8–N3–C15–C14 | −4.36(14) | C16–C17–C18–N5 | 48.70(18) |

## Electronic Supplementary Material

Supplementary material CCDC-1426236 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk.

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