JOC Article

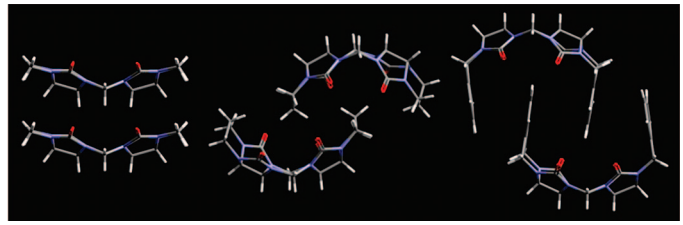
Glycoluril Dimers Bearing Hydrogen Atoms on Their Convex Face and Their Self-Assembly in the Solid State

Marek Stancl, Marek Necas, Jan Taraba, and Vladimir Sindelar*

Department of Chemistry, Masaryk University, Kotlarska 2, 611 37 Brno, Czech Republic

sindelar@chemi.muni.cz

Received March 28, 2008



A selective method for the synthesis of 1,6-substituted glycolurils has been developed. The glycolurils have been used for the synthesis of methylene-bridged glycoluril dimers bearing hydrogen atoms on their convex face. Depending on the side walls of the dimers, different modes of self-assembly in the solid state have been described using X-ray crystallography.

Introduction

Glycoluril and its derivatives are heterocyclic compounds that have been used as building blocks of various supramolecular objects. Among others, the groups of Rebek, Nolte, and Isaacs extensively studied the synthesis and the behavior of a wide variety of glycoluril derivatives. Rebek showed that molecules terminated by glycoluril units self-associate through the hydrogen bonding into dimeric pseudospherical capsules.[1] Nolte prepared a number of molecular clips based on bis(*o*-xylylenyl) diphenyl glycoluril derivatives.[2] These clip molecules have a preorganized cleft that is capable of binding aromatic guests, particularly phenols and dihydroxybenzenes. The functionalization of the molecular clips by crown and aza-crown ether moieties led to the preparation of molecular basket receptors. More recently, Isaacs reported self-association of chiral and achiral molecular clips in the crystalline state.[3] The clips are derived from glycoluril bearing two ethyl ester groups on its convex face, and their self-association is tuned by the modification of two *o*-xylylene walls. Methylene-bridged glycoluril dimers[4] were first synthesized to investigate the preparation of new cucurbituril analogs and explain the mechanism of cucurbituril formation. Depending on the reaction conditions, a diastereomeric mixture of S-shape and C-shape products was prepared. Later, it was found that suitable modification of the *o*-xylylene side walls results in C-shape dimers which self-assemble into hydrogen bonded dimeric aggregates in the solution and the solid state.[5] Enantiomeric self-recognition[6] and the self-sorting[7] of these dimers were demonstrated.

Despite of extensive work in the supramolecular chemistry of glycoluril compounds, to the best of our knowledge, there is only one examples for each of molecular dimer,[8] trimer,[9] and clip[10] containing glycoluril unit carrying two hydrogen atoms at the "bridging" positions of the two fused five-member rings. These two hydrogen atoms on the convex face are usually substituted by different groups to overcome extremely low solubility of the glycoluril-based supramolecular objects. For example, the solubility in nonpolar solvents is improved by

(1) (a) Rebek, J., Jr *Chem. Soc. Rev.* **1996**, *25*, 255–263. (b) Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647–1668. (c) Rebek, J., Jr. *Acc. Chem. Res.* **1999**, *32*, 278–286, and references therein.

(2) (a) Sijbesma, R. P.; Nolte, R. J. M. *Top. Curr. Chem.* **1995**, *175*, 25–56. (b) Rowan, A. E.; Elemans, J. A. A. W.; Nolte, R. J. M. *Acc. Chem. Res.* **1999**, 995–1006. (c) Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *Ind. Eng. Chem. Res.* **2000**, *39*, 3419–3428, and references therein.

(3) (a) Wang, Z.-G.; Zhou, B.-H.; Chen, Y.-F.; Yin, G.-D.; Li, Y.-T.; Wu, A.-X.; Isaacs, L. *J. Org. Chem.* **2006**, *71*, 4502–4508. (b) Chen, Y.; She, N.; Meng, X.; Yin, G.; Wu, A.; Isaacs, L. *Org. Lett.* **2007**, *9*, 1899–1902.

(4) (a) Witt, D.; Lagona, J.; Damkaci, F.; Fettinger, J. C.; Isaacs, L. *Org. Lett.* **2000**, *2*, 755–758. (b) Isaacs, L.; Witt, D.; Lagona, J. *Org. Lett.* **2001**, *3*, 3221–3224. (c) Chakraborty, A.; Wu, A.; Witt, D.; Lagona, J.; Fettinger, J. C.; Isaacs, L. *J. Am. Chem. Soc.* **2002**, *124*, 8297–8306. (d) Wu, A.; Chakraborty, A.; Witt, D.; Lagona, J.; Damkaci, F.; Ofori, M.; Chiles, K.; Fettinger, J. C.; Isaacs, L. *J. Org. Chem.* **2002**, *67*, 5817–5830.

(5) Wu, A.; Mukhopadhyay, P.; Chakraborty, A.; Fettinger, J. C.; Isaacs, L. *J. Am. Chem. Soc.* **2004**, *126*, 10035–10043.

(6) (a) Isaacs, L.; Witt, D. *Angew. Chem., Int. Ed.* **2002**, *41*, 1905–1907.

(7) (a) Wu, A.; Chakraborty, A.; Fettinger, J. C.; Flowers, R. A., II.; Isaacs, L. *Angew. Chem., Int. Ed.* **2002**, *41*, 4028–4031.

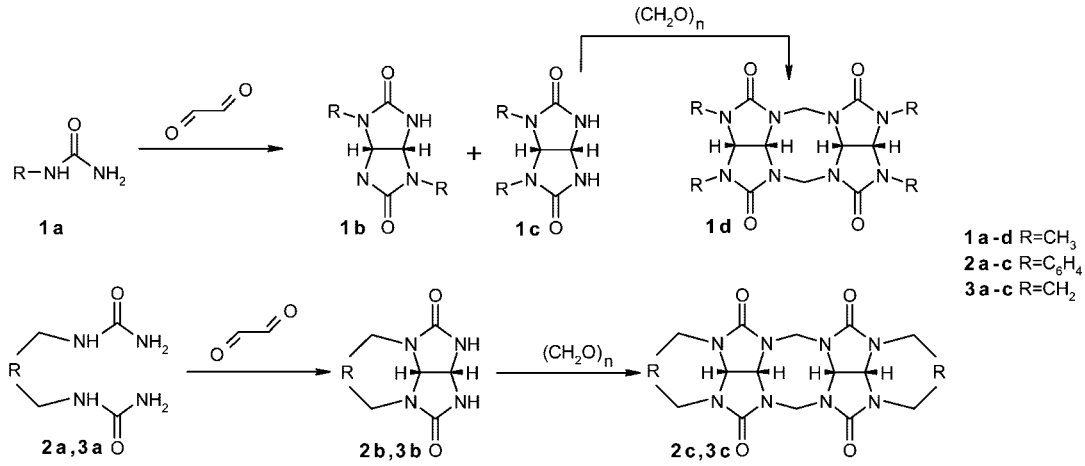
(8) Zhao, Y.; Xue, S.; Zhu, Q.; Tao, Z.; Zhang, J.; Wei, Z.; Long, L.; Hu, M.; Xiao, H.; Day, A. I. *Chin. Sci. Bull.* **2004**, *49*, 1111–1116.

(9) Huang, W. H.; Zavalij, P. Y.; Isaacs, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 7425–7427.

(10) Dave, P. R.; Forohar, F. F.; Kaselj, M.; Gilardi, R.; Trivedi, N. *Tetrahedron Lett.* **1999**, *40*, 447–450.

10.1021/jo800699s CCC: $40.75 © 2008 American Chemical Society
Published on Web 05/22/2008

SCHEME 1. Preparation of Methylene-Bridged Glycoluril Dimers



phenyl or ethyl ester groups.[11] On the other hand, molecular clips and dimers in which the glycolurils bear carboxylate or phenylenemethylene pyridinium groups show good solubility in aqueous environment.[12]

Results and Discussion

We decided to expand the chemistry of glycolurils by the preparation of the methylene-bridged glycoluril dimers **1d**, **2c**, and **3c** (Scheme 1) with hydrogens on their convex face and differing side walls. These structures were selected for at least two reasons: (1) The absence of a bulky group on the convex face of the glycoluril dimer can result in the formation of unusual self-associates in the solid state as well as in the solution. (2) The preparation of the dimers based on unsubstituted glycoluril can give more information about the mechanism of cucurbituril formation as they resemble the repeating unit of the macrocycle.

Here we report the preparation of three new methylene-bridged glycoluril dimers **1d**, **2c**, and **3c**. A selective method for the preparation of 1,6-protected glycolurils (dimer precursors) was developed. Glycoluril dimers **1d**, **2c**, and **3c** were studied by X-ray crystallography and different patterns of self-association depending on the side wall substituents were observed.

Glycoluril dimers are prepared in two steps. First, a precursor of glycoluril dimer is prepared. In the following step two precursor molecules are linked by condensation with formaldehyde. Usually, the precursor is a 7,8-substituted glycoluril in which two nitrogen atoms in the 1,6 positions are protected by *o*-xylylene unit. These precursors are prepared by the alkylation of the 7,8-substituted glycoluril with dihalogen-*o*-xylylene in DMSO in the presence of *t*-BuOK. Column chromatography is required to obtain the desired product from the reaction mixture. The yield of the alkylation reaction increases with increasing solubility of glycoluril derivatives, which is influenced by the type of the groups on the convex face of the molecule.[4a] Glycoluril has no substituent on the convex face. Therefore, glycoluril has extremely low solubility in organic solvents and is problematic and inconvenient to prepare precursors **1c**, **2b**, and **3b** by the alkylation method. Due to the low solubility of glycoluril we decided to follow a known procedure which allowed us to generate the precursor **1c** directly by acid catalyzed reaction of methylurea and glyoxal.[13] The reaction results in the mixture of *cis*-(1,6-dimethyl) **1c** and *trans*-(1,4-dimethyl) **1b** glycoluril derivatives. Pure products were obtained only after the extensive fractional crystallization. We optimized the separation method using the finding that pure *cis* derivatives crystallize from aqueous solution in the presence of H_3PO_4. Despite this improvement, the overall yield of the pure *cis*-dimethyl derivative is only 9%.

As both the alkylation of glycoluril and the condensation of alkylurea are not suitable methods we looked for a better way for the preparation of the dimer precursors. We envisioned that the selective preparation of the dimer precursors can be achieved by acid catalyzed intramolecular cyclocondensation of bisureas with glyoxal. In order to verify our presumption we selected bisureas **2a** and **3a** for which the intramolecular condensation of two urea groups is preferable compared to the intermolecular reaction resulting in a polymer. We found that the reaction of both aromatic **2a** and aliphatic **3a** bisureas with glyoxal in water acidified by HCl is regioselective and yields the 1,6 - protected glycoluril. The product can be easily separated from the reaction mixture by precipitation, giving rise to modest yields 75% (**2b**) and 47% (**3b**). Notice that other bisureas can be also used in the condensation reaction with glyoxal to yield 1,6-protected glycolurils. We are currently testing our method for the preparation of Rebek's tennis ball building blocks based on durene.[14]

We used the protected glycolurils **1c**, **2b**, and **3b** in acid catalyzed condensation with one equivalent of formaldehyde to obtain the dimers **1d**, **2c**, and **3c**. Reactions were performed in concd HCl. We choosed a reaction temperature of 80 °C to obtain only thermodynamically more stable C-shaped diastereomers. Indeed, under these conditions the C-shaped dimers **1d**, **2c**, and **3c** were obtained in high yields of 90, 94, and 81%,

(11) Smeets, J. W. H.; Sijbesma, R. P.; Niele, F. G. M.; Spek, A. L.; Smeets, W. J. J.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1987**, *109*, 928–929.

(12) (a) Isaacs, L.; Witt, D.; Fettinger, J. C. *Chem. Commun.* **1999**, 2549–2550. (b) Lagona, J.; Fettinger, J. C.; Isaacs, L. *Org. Lett.* **2003**, *5*, 3745–3747. (c) Lagona, J.; Fettinger, J. C.; Isaacs, L. *J. Org. Chem.* **2005**, *70*, 10381–10392. (d) Burnett, C. A.; Witt, D.; Fettinger, J. C.; Isaacs, L. *J. Org. Chem.* **2003**, *68*, 6184–6191. (e) Reek, J. N. H.; Kros, A.; Nolte, R. J. M. *Chem. Commun.* **1996**, 245–247. (f) Elemans, J. A. A. W.; Gelder, R.; Rowan, A. E.; Nolte, R. J. M. *Chem. Commun.* **1998**, 1553–1554.

(13) (a) Kravchenko, A. N.; Sigachev, A. S.; Maksareva, E. Yu.; Gazieva, G. A.; Trunova, N. S.; Lozhkin, B. V.; Pivina, T. S.; Il′in, M. M.; Lyssenko, K. A.; Nelyubina, Yu V.; Davankov, V. A.; Lebedev, O. V.; Makhova, N. N.; Tartakovsky, V. A. *Russ. Chem. Bull., Int. Ed.* **2005**, *54*, 691–704. (b) Nematollahi, J.; Ketcham, R. *J. Org. Chem.* **1963**, *28*, 2378–2380.

(14) Wyler, R.; de Mendoza, J.; Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1699–1701.

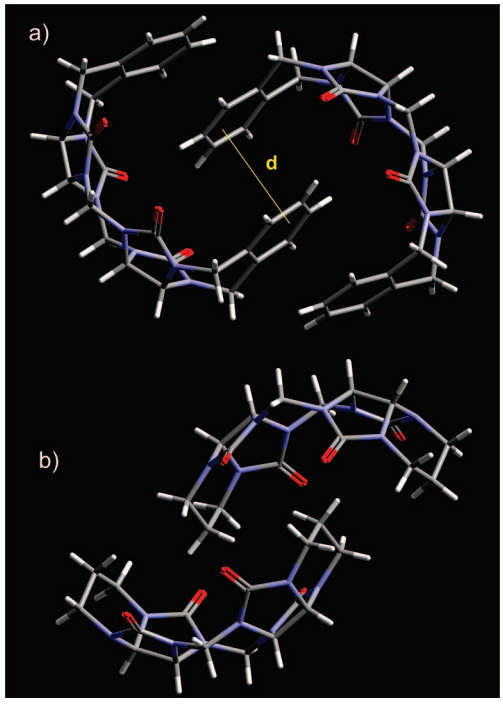


FIGURE 1. Wireframe representations of the crystal structures of methylene-bridged glycoluril dimers (a) **2c** and (b) **3c**. In **2c**, the interplanar distances *d* are, respectively, 3.940 and 4.069 Å for two crystallographically independent dimeric aggregates. Color coding: C, gray; H, white; N, blue; O, red.

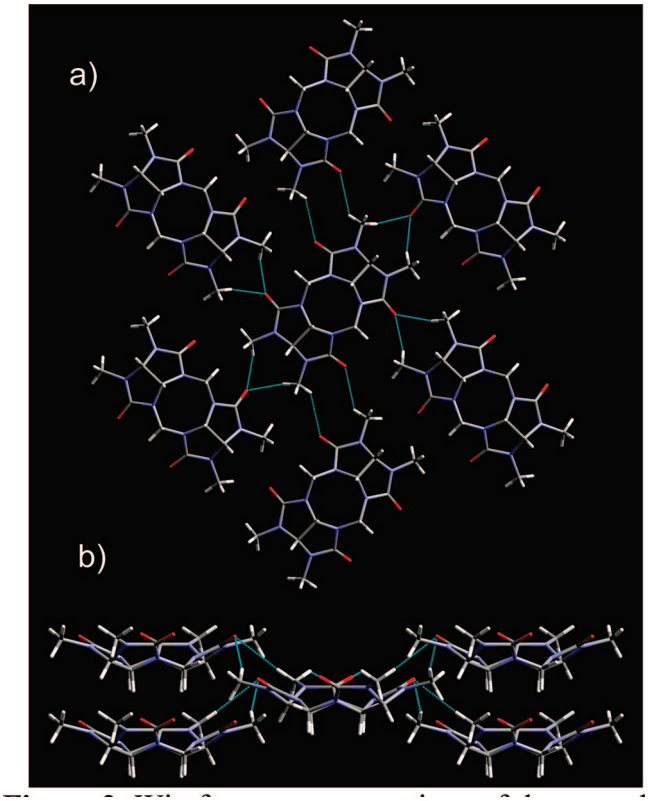


FIGURE 2. Wireframe representations of the crystal structures of methylene-bridged glycoluril dimer **1d** (a) viewed along the *c*-axis and (b) viewed along the *a*-axis. Color coding: C, gray; H, white; N, blue; O, red, C−H···O hydrogen bonding, turquoise.

respectively. The presence of C-shaped dimers was confirmed by ^{1}H NMR spectra in which two doublets typical of the diastereotopic methylene protons of the central eight membered ring were observed.[4d]

Slow evaporation of aqueous solution of the dimers **1d**, **2c**, and **3c** resulted in crystals suitable for X-ray diffraction. Methylene bridged glycoluril dimer **2c** bearing two xylylene rings is organized into dimeric aggregates; the driving force of the dimerization is the van der Waals interactions together with the face-to-face $\pi-\pi$ stacking interaction of xylylene rings (Figure 1a). Previously reported analogs, which differ in the presence of two ethyl ester groups on the convex face, do not undergo dimeric aggregation.[4a] Dimer self-assembly was also observed in the crystal structure of **3c** (Figure 1b). Unlike **2c** the glycoluril skeleton of **3c** is framed with propylene chains. Thus, the dimerization can be assigned to the van der Waals interactions only. Dimeric aggregates of both **3c** and **2c** are connected by short-distance C−H···O hydrogen bonds between methylene bridges and glycoluril carbonyls and also through solvating molecules of water.

In the crystal structure of **1d** no dimerization was observed. Instead, there is a three-dimensional network of molecules which are held together by weak hydrogen bonds C−H···O. Each molecule is surrounded by two molecules with the same orientation and four molecules which are rotated by 90° relative to the central molecule (Figure 2a). The stacking of these motifs along the crystallographic *c*-axis results in columns in which the bowl-shaped molecules are packed on top of each other (Figure 2b). There is no hydrogen bonding between the molecules in the columns. The structure is held together by the hydrogen bonding between the molecules in the neighboring columns and stabilized by van der Waals interactions involving methyl groups. Among published crystal structures of glycolurils, glycoluril clips, and dimers, similar three-dimensional, well-organized arrangements have not been reported.

Compounds **1d**, **2c**, and **3c** represent first glycoluril dimers bearing hydrogen atoms on their convex face which have been characterized by X-ray crystallography. As these dimers resemble the structural motif of cucurbituril, we have closely investigated their structural features. Notice, that while **1d** dimer has a plane of symmetry, glycoluril units in **2c** and **3c** are twisted (Figure 3). This is presented by the pairs of bond angles through the methylene bridges which differ in **2c** (121.1 and 124.3°, and 119.2 and 121.8° for two crystallographically independent molecules) and **3c** (107.6 and 118.0°) and are identical in **1d** (146.4° as required by the crystallographic symmetry). As confirmed by ^{1}H NMR spectra, both glycoluril units of the dimers are identical in the solution; also there are no bulky substituents on the convex faces which could introduce strain into the structures. We therefore attribute the significant twisting of glycoluril units in **3c** to the intermolecular contacts with the solvating molecules of water.

As is obvious from the above data, **1d** adopts a more planar form than usual for this kind of molecular dimers in the solid state. This flattening is also apparent in the direction perpendicular to the long axis of the dimer; the distance between two oxygens in glycoluril units in **1d** is 6.165 Å which is remarkably higher than corresponding values in **2c** and **3c** (ranging from 5.784 to 5.987 Å) as well as in other crystallographically characterized glycoluril dimers.[17] The pronounced planarity of

(15) Becher, J.; Liebegott, H.; Berlin, P.; Klemm, D. *Cellulose* **2004**, *11*, 119–126.
(16) von Dauth, C.; Becker, H. G. O. *J. Prakt. Chem.* **1971**, *313*, 686–698.
(17) Allen, F. H. *Acta Crystallogr.* **2002**, *B58*, 380–388.

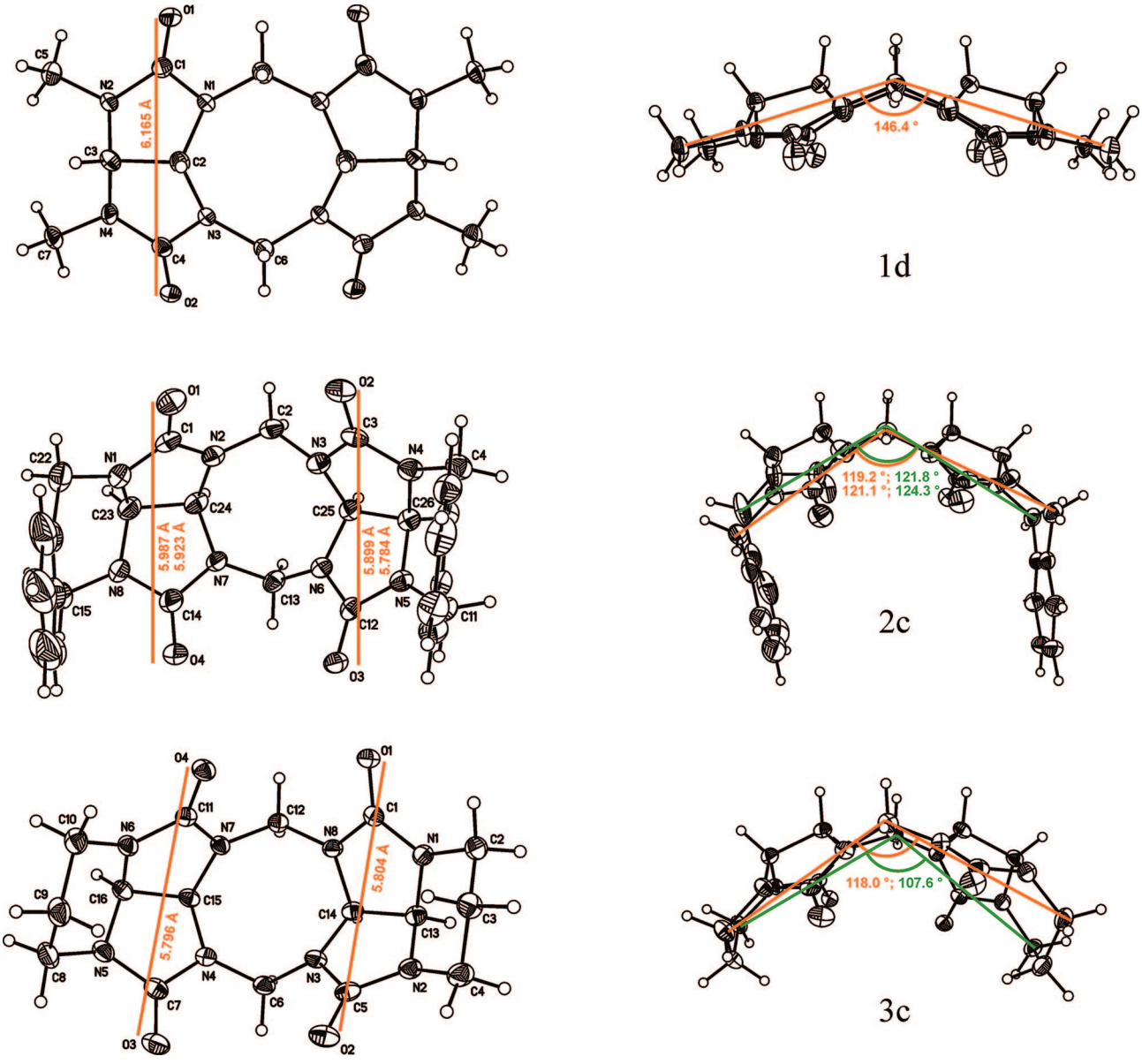


FIGURE 3. Molecular structures of glycoluril dimers **1d**, **2c**, and **3c**. Notice mutual twisting of both glycoluril units in **2c** and **3c** in their side views. In **2c**, the distances and angles for two crystallographically independent molecules are given.

1d can be explained by the presence of four methyl groups that make the dimer more flexible compared to **2c** and **3c** in which two terminal nitrogen atoms on both sides of the dimers are connected in seven- and six-member rings.

Conclusions

In conclusion, we have prepared methylene-bridged glycoluril dimers bearing two hydrogens on the convex face of the glycoluril units. A new method for the preparation of glycoluril dimer precursors, *cis*-terminated glycolurils, was developed. In the solid state **3c** and **2c** form dimeric aggregates whereas **1d** features a unique three-dimensional structure. Our findings suggest that the intermolecular contacts are important factors governing the conformation of glycoluril oligomers.

Experimental Section

1,6-Dimethylglycoluril (1c). This was prepared according to published procedure.[13b] Separation from 1,4-derivative **1b** was carried out as follows:

Reaction mixture (after reaction between methylurea and glyoxal) was evaporated to dryness, and the resulting solid was dissolved in boiling 8% H_3PO_4. The solution was left to cool to room temperature. Needles, which separated in a few minutes, were filtered off. This crystallization procedure was repeated once or twice to produce pure crystalline 1,6-dimethylglycoluril **1c**. Yield is around 9%. mp 252−254 °C (dec.) (lit.[13b] 298−300 °C). ^{1}H NMR (300 MHz, DMSO-d_6): 7.39 (s, 2 H), 5.17 (d, J = 8.3, 1 H), 5.10 (d, J = 8.3, 1 H), 2.78 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): 159.7, 75.2, 60.2, 29.2. HRMS (ESI+) *m/z* calcd for $[C_6H_{10}N_4O_2 + H]^+$: 171.0882; found: 171.0880.

Tetramethylglycoluril Dimer (1d). 1,6-Dimethylglycoluril **1c** (340 mg; 2 mmol) was mixed with paraformaldehyde (60 mg; 2 mmol) and 3.2 mL of concd HCl. Resulting mixture was heated to 80 °C (bath temperature) for 4 h and then evaporated to dryness. Product could be crystallized from water, if necessary. White solid (327 mg, 90%). mp > 300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 5.63 (d, J = 14.6, 2 H), 5.32 (d, J = 8.6, 2 H), 5.10 (d, J = 8.6, 2 H), 4.11 (d, J = 14.6, 2H), 2.84 (s, 12 H). ^{13}C NMR (75 MHz, DMSO-d_6): 106.1, 71.4, 70.4, 52.3, 29.8. HRMS (ESI+) *m/z* calcd for $[C_{14}H_{20}N_8O_4 + H]^+$ 365.1686; found: 365.1667.

***o*-Xylylenebisurea (2a).** *o*-Xylylenediamine dihydrochloride hemihydrate[15] (6.96 g; 31.9 mmol) was dissolved in 200 mL of water. Potassium cyanate (5.17 g; 63.8 mmol) was added in one portion. Resulting mixture was stirred at room temperature overnight. Separated solid was filtered off, washed with water and acetone, and dried *in vacuo*. White solid (5.44 g, 76%). mp 224−225 °C (lit.[16] 219−220 °C) ^{1}H NMR (300 MHz, DMSO-d_6): 7.25−7.18 (m, 4 H), 6.41 (br s, 2 H), 5.55 (br s, 4 H), 4.20 (d, J = 5.7, 4 H). ^{13}C NMR (75 MHz, DMSO-d_6): 158.6, 137.8, 127.4, 126.5. Note: Signal of methylene carbons is overlapped by solvent signal. HRMS (ESI+) m/z calcd for $[C_{10}H_{14}N_4O_2 + H]^+$: 223.1195; found: 223.1189.

***o*-Xylyleneglycoluril (2b).** *o*-Xylylenebisurea **2a** (5.44 g, 24.4 mmol) was mixed with 540 mL of water and stirred under reflux. After all material was dissolved, 40% water solution of glyoxal (2.8 mL, 24.4 mmol) was added. Reaction mixture was acidified with 0.4 mL of concd HCl. After 1.5 h of reflux, the reaction mixture was cooled and left in the refrigerator overnight. Crystalline material was filtered off and washed with ice−water. White crystalline solid (4.49 g, 75%). mp > 300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 7.31 (s, 2 H), 7.27−7.19 (m, 4 H), 5.61 (d, J = 7.6, 1 H), 5.20 (d, J = 7.6, 1 H), 4.58−4.46 (m, 4 H). ^{13}C NMR (75 MHz, DMSO-d_6): 158.0, 138.1, 129.1, 127.2, 72.7, 59.4, 44.6. HRMS (ESI+) m/z calcd for $[C_{12}H_{12}N_4O_2 + H]^+$: 245.1039; found: 245.1033.

***o*-Xylyleneglycoluril Dimer (2c).** *o*-Xylyleneglycoluril **2b** (1.00 g, 4.1 mmol) was mixed with paraformaldehyde (0.123 g, 4.1 mmol) and 20 mL concd HCl. Resulting mixture was heated to 80 °C (bath temperature) for 3 h, then cooled. Resulting solid was filtered off, washed with water and dried *in vacuo*. 0.99 g (94%) white solid. mp > 300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 7.22−7.14 (m, 8 H), 5.60 (d, J = 8.1, 2 H), 5.47 (d, J = 14.6, 2 H), 5.42 (d, J = 8.1, 2 H), 4.60−4.49 (m, 8 H), 4.19 (d, J = 14.6, 2 H).^{13}C NMR (75 MHz, DMSO-d_6): 154.7, 137.5, 129.1, 127.5, 69.4, 68.8, 52.1, 45.0. HRMS (ESI+) m/z calcd for $[C_{26}H_{24}N_8O_4 + H]^+$: 513.1999; found: 513.2005.

Propylenebisurea (3a). 1,3-Diaminopropane (5.00 g; 67 mmol) was dissolved in 20 mL of water. The resulting mixture was cooled with ice−water, and concd HCl (11.8 mL) was added. Still under cooling, potassium cyanate (10.87 g; 134 mmol) was added. The reaction mixture was then refluxed for 1 h, cooled, and left in refrigerator overnight. The crystalline material was filtered off and washed with cold water. White crystalline solid (8.47 g, 78%). mp 183−185 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 6.00 (br s, 2 H), 5.40 (br s, 4 H), 2.98−2.92 (m, 4 H), 1.47−1.38 (m, 2 H).^{13}C NMR (75 MHz, DMSO-d_6): 158.8, 36.8, 31.0. HRMS (ESI+) m/z calcd for $[C_5H_{12}N_4O_2 + H]^+$: 161.1039; found: 161.1030.

Propyleneglycoluril (3b). Propylenebisurea **3a** (1.00 g, 6.24 mmol) was dissolved in 100 mL of water. Glyoxal (crystalline trimer dihydrate, 0.44 g, 1 equiv) was added; the resulting mixture was acidified with 0.2 mL of concd HCl and heated to reflux for 2 h. The resulting solution was partially evaporated to the formation of crystalline phase and then left in refrigerator overnight. Separated crystals were filtered off and washed with a small volume of ice−water. White crystals (0.53 g, 47%). mp > 300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 7.55 (s, 2H), 5.21 (d, J = 7.5, 1 H), 5.18 (d, J = 7.5, 1 H), 3.77−3.71 (m, 2H), 3.02−2.94 (m, 2 H), 1.39 (d, J = 13.1, 1 H), 1.15−1.00 (m, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): 158.7, 67.5, 59.9, 38.5, 23.0. HRMS (ESI+) m/z calcd for $[C_7H_{10}N_4O_2 + H]^+$: 183.0882; found: 183.0872.

Propyleneglycoluril dimer (3c). Propyleneglycoluril **3b** (500 mg; 2.74 mmol) was dissolved in 4 mL of concd HCl. Paraformaldehyde (82 mg; 2.74 mmol) was added, and the resulting mixture was heated to 80 °C (bath temperature). After 3 h, the reaction mixture was cooled in the refrigerator for one hour. Separated crystalline material was filtered off and washed with acetone. White crystals (0.43 g, 81%). mp > 300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 5.49 (d, J = 7.7, 2 H), 5.46 (d, J = 14.5, 2 H), 5.24 (d, J = 7.7, 2 H), 4.28 (d, J = 14.5, 2 H), 3.82−3.76 (m, 4H), 3.13−3.05 (m, 4H), 1.48 (d, J = 12.9, 2H), 1.25−1.12 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): 155.1, 69.7, 63.1, 52.2, 38.8, 23.2. HRMS (ESI+) m/z calcd for $[C_{16}H_{20}N_8O_4 + H]^+$: 389.1686; found: 389.1671.

Acknowledgment. This work was supported by the Grant Agency of the Czech Republic (203/07/P382). We thank J. František for the HRMS analyses.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all new compounds, X-ray crystallographic files (CIF) for **1d**, **2c**, and **3c**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800699S