4,5-Dihydroxyimidazolidin-2-ones in the reaction of α-ureidoalkylation of *N*-(carboxyalkyl)-, *N*-(hydroxyalkyl)-, and *N*-(aminoalkyl)ureas

6.* Tandem sequence of α-ureidoalkylation and esterification in the course of the reaction of *N*-(carboxyalkyl)ureas with 4,5-dihydroxy-1,3-dimethyl-4,5-diphenylimidazolidin-2-one in alcohols

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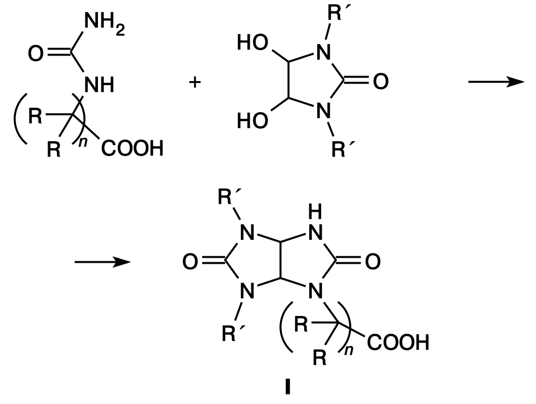
It was found for the first time that the reaction of *N*-(carboxyalkyl)ureas (ureido acids) with 4,5-dihydroxy-1,3-dimethyl-4,5-diphenylimidazolidin-2-one in methyl or isopropyl alcohol proceeds through the tandem sequence of α-ureidoalkylation and esterification to form the earlier unknown *N*-(carboxyalkyl)glycoluril methyl or isopropyl esters. *N*-(Carboxyalkyl)-glycolurils of a new-type substitution were obtained by alkaline hydrolysis of their isopropyl esters, the structure of one of them was confirmed by X-ray diffraction analysis.

Key words: α-ureidoalkylation, condensation, ureido acids, 4,5-dihydroxy-1,3-dimethyl-4,5-diphenylimidazolidin-2-one, *N*-carboxyalkyl-1,5-diphenylglycolurils, *N*-methoxy(iso-propoxy)carbonylalkyl-1,5-diphenylglycolurils, tandem reactions, alkaline hydrolysis, X-ray diffraction analysis.

In the preceding reports, we have shown that achiral *N*-(carboxyalkyl)ureas (ureido acids) can be involved into the reaction of α-ureidoalkylation with the use of 4,5-dihydroxyimidazolidin-2-one (DHI) and 1,3-dialkyl-substituted DHI as ureidoalkylating agents to yield *N*-(carboxyalkyl)glycolurils of the type **I** containing no substituents at the bridgehead carbon atoms (Scheme 1).[2—4] These reactions were studied in details and it was found that *N*-(carboxyalkyl)glycolurils **I** are formed under conditions of acidic catalysis upon heating the reagents in water for different periods of time. It was found that the reaction time (2—3 h) and structural specific features of the starting reagents affect their yields: elongation of the alkyl fragment of the ureido acid and the presence of alkyl substituents at the nitrogen atoms of DHI decrease the yields of glycolurils **I** (see Refs 2 and 3). 4,5-Dihydroxy-4,5-diphenylimidazolidin-2-ones were not involved into the analogous condensations.

Scheme 1



R, R′ = H, Alk $n = 1—3$

Since it is already known that [(1*R**,5*S**)-6,8-dimethyl-(3,7-dioxo-2,4,6,8-tetraazabicyclo[3.3.0]oct-2-yl)]-butyric acid possesses anxiolitic, sedative, and nootropic activity[5] and 1,5-diphenylglycolurils containing alkyl substituents at the nitrogen atoms have influence on the liver cytochrom-P-450-dependent monooxygenase system,[6] development of method for the preparation of glycolurils, built on the principle of combination of *N*-alkyl and *N*-carboxyalkyl fragments in one molecule together with C-phenyl substituents as qualitatively new biologically active compounds, is an actual problem.

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* For Part 5, see Ref. 1.

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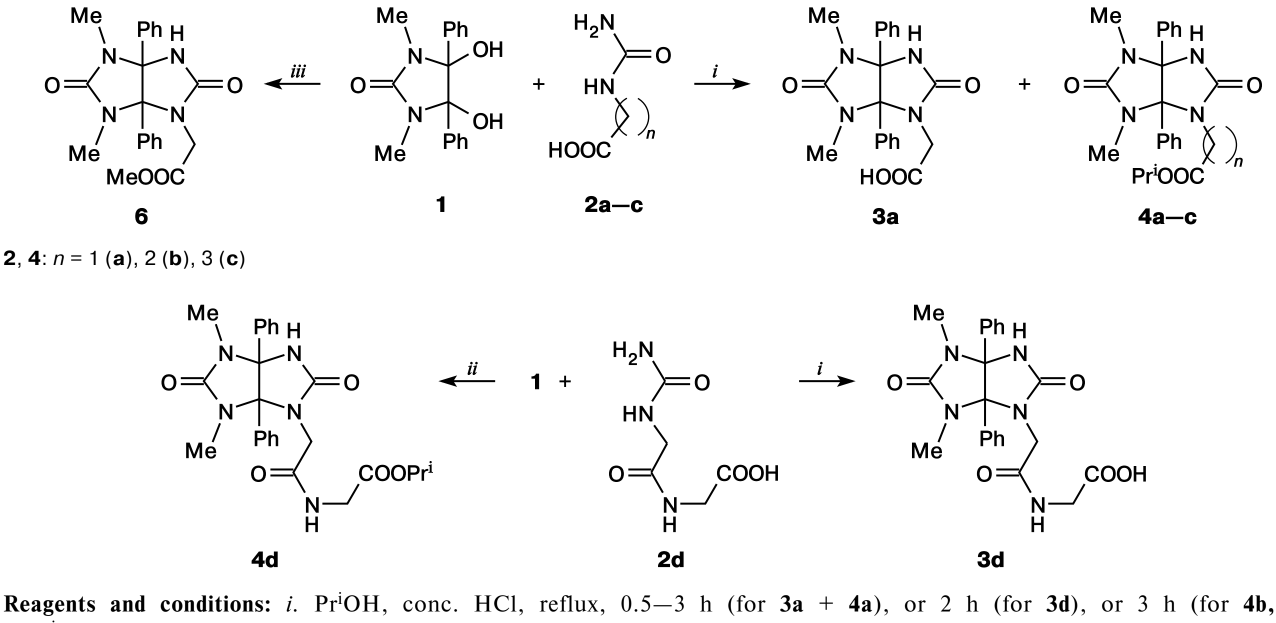
In order to synthesize *N*-(carboxyalkyl)glycolurils with the new type of substitution and search for the neurotropically active compounds among them, in the present work we have studied α-ureidoalkylation of ureido acids with 4,5-dihydroxy-1,3-dimethyl-4,5-diphenylimidazolidin-2-one (DHI **1**, Scheme 2).

Since DHI **1** is not soluble in water, its reactions with ureido acids **2a—d**, synthesized by *N*-carbamoylation of glycine, β-alanine, γ-aminobutyric acid, and glycylglycine dipeptide with potassium cyanate,[7] were studied in propan-2-ol and methanol upon reflux of the reagents under conditions of acidic catalysis for different periods of time (see Scheme 2, Table 1). Reaction mixtures concentrated to dryness were analyzed by ^{1}H NMR spectroscopy and it was found that when $\mathrm{Pr^iOH}$ is used in the reactions of DHI **1** with ureido acid **2a**, a mixture of two compounds is formed, *viz.*, *N*-(carboxymethyl)glycoluril **3a** and its isopropyl ester **4a**, the esterification product of the carboxy group with propan-2-ol. The ratio of these compounds changes depending on the reaction time. Estimation of the ratio **3a** : **4a** was made using the ratio of integral intensities of the signals for the protons of the methylene groups in compound **3a** at δ 3.54 and 4.01 (both d) and in product **4a** at δ 3.65 and 4.09 (both d). When the reaction time is 15 min, 30 min, 1 h, and 2 h, the ratio of products **3a** to **4a** remains virtually unchanged and is 1 : 1, when the reaction time is 3 h, the ratio of products is 2 : 3; for 5 h it is 1 : 3, when the reaction mixture is kept for 7 h, only ester **4a** is formed without impurities of glycoluril **3a** (see Table 1, entries *1—7*). Since the reaction mixtures exhibit no signals for the protons of the starting reagents **2a** and DHI **1**, a conclusion can be drawn that the formation of bicycle reaches completion already within first 15 min of their reaction and simultaneously with this reaction, esterification of the carboxy group in glycoluril **3a** with propan-2-ol occurs. The yield of compound **4a** was 95%. Ureido acids **2b,c** under analogous conditions with the experiment duration of 1 h give no reaction with DHI **1**. If the reaction mixture was kept for 2 h, esters **4b,c** are the reaction products. In addition, the ^{1}H NMR spectra of the reaction mixtures exhibit signals for the protons of unreacted starting reagents **1** and **2b,c**, as well as benzil and 1,3-dimethylurea, the products of partial hydrolysis of DHI **1** (Scheme 3, reaction *1*). After impurities were removed, the yields of compounds **4b,c** were 51% and 64%, respectively (see Table 1, entries *9* and *12*). When the condensation time of ureido acid **2b,c** with DHI **1** was increased to 3 h, the yields of esters **4b,c** increase to 80% and 91%, respectively (see Table 1 entries *10* and *13*). When ureido acid **2b** is used, this process is also accompanied by the formation of dihydropyrimidine-2,4(1*H*,3*H*)-dione (**5**, dihydrouracyl), the cyclization product of ureido acid **2b** (see Ref. 8) (Scheme 3, reaction *2*). Attempted preparation of glycolurils **3b,c** by the reaction of ureido acids **2b,c** with DHI **1** and the reaction time in the range 1—2 h with recording the ^{1}H NMR spectra for the concentrated aliquots of the reaction mixtures taken every 15 min showed that esterification of the carboxy group in glycolurils **3b**,**c** proceeds very fast and no glycolurils with the free carboxy group was detected. Ureido acid **2d** (with the dipeptide fragment) undergoes the α-ureidoalkylation reaction with DHI **1** to form glycoluril **3d** in 74% yield for 1 h (see Table 1,

Scheme 2



2, **4**: *n* = 1 (**a**), 2 (**b**), 3 (**c**)

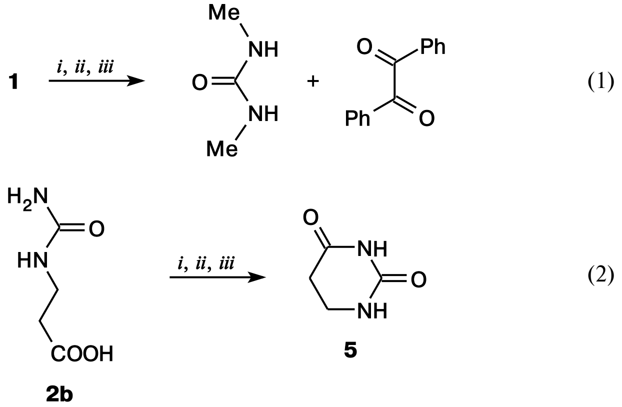
Reagents and conditions: *i*. $\mathrm{Pr^iOH}$, conc. HCl, reflux, 0.5—3 h (for **3a** + **4a**), or 2 h (for **3d**), or 3 h (for **4b,c**); *ii*. $\mathrm{Pr^iOH}$, conc. HCl, reflux, 7 h; *iii*. MeOH, conc. HCl, reflux, 2 h.

Table 1. Dependence of the yields of glycolurils **3a,d**, esters **4a—c**, and methyl ester **6** from the reaction time

Entry	τ/h	Glycolurils (ratio)	Yields (%)
1	0.25	**3a** : **4a** (1 : 1)	—
2	0.5	**3a** : **4a** (1 : 1)	—
3	1	**3a** : **4a** (1 : 1)	—
4	2	**3a** : **4a** (1 : 1)	—
5	3	**3a** : **4a** (2 : 3)	—
6	5	**3a** : **4a** (1 : 3)	—
7	7	**4a**	95
8	1	—	—
9	2	**4b**	51
10	3	**4b**	80
11	1	—	—
12	2	**4c**	64
13	3	**4c**	91
14	1	**3d**	74
15	2	**3d**	—
16	3	**3d**	—
17	7	**4d**	79
18	0.25	**6**	83
19	1	**6**	85
20	2	**6**	96
21	3	**6**	90

entry *14*), with esterification of the carboxy group in this case being absent. When the reflux time is increased from 1 h to 3 h, appearance of the signals for the protons of ester **4d** in the reaction mixture is observed, with the ratio of products being 1 : 1 and 2 : 3, respectively (see Table 1, entries *15* and *16*). To obtain ester **4d**, the reaction mixture was heated for 7 h (see Table 1, entry *17*).

Scheme 3



Reagents and conditions: *i*. Pr^{i}OH, conc. HCl, reflux, 1—5 h; *ii*. Pr^{i}OH, conc. HCl, reflux, 7 h; *iii*: MeOH, conc. HCl, reflux, 2 h.

Upon α-ureidoalkylation of ureido acids **2a—d** involving DHI **1** on reflux in methanol under conditions of acidic catalysis, only ureido acid **2a** gives cyclocondensation with DHI **1**, and for the reaction times of 0.25, 0.5, 1, 2, 3, 5, and 7 h, a tandem reaction leading to methyl ester **6** proceeds. The ^{1}H NMR spectra exhibit no signals for the protons of the carboxy group in the region δ 12 and do exhibit signals for the protons of the OMe group at δ 3.6. Depending on the reaction time, the yield of *N*-(methoxycarbonyl)methylglycoluril **6** changes from 80% to 96%. Ureido acids **2b,c** give no reaction with DHI **1** in methanol. Ureido acid **2b** cyclizes to dihydrouracyl **5**, ureido acid **2c** is isolated unchanged, whereas DHI **1** is hydrolyzed to benzil and 1,3-dimethylurea. The reaction of ureido acid **2d** with DHI **1** in methanol has not been studied because of poor solubility of the ureido acid in this solvent.

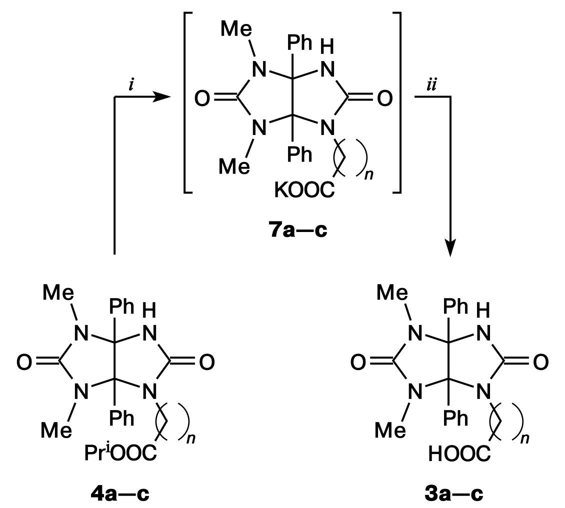
To sum up, on systematic study of α-ureidoalkylation of ureido acids **2a—d** with DHI **1** on reflux of the reagents in propan-2-ol or methanol under conditions of acidic catalysis, it was for the first time found that the formation of bicycles of *N*-(carboxyalkyl)glycolurils **3a—c** is accompanied by a tandem reaction of esterification of the carboxy group to isopropoxy- or methoxycarbonyl group, which leads to the formation of glycoluril esters **4a—c** and **6**, and only when ureido acid **2d** is used, glycoluril **3d** with the free carboxy group was obtained. A dependence of the yields of these compounds from the reaction time was established and preparative procedures for the synthesis of the earlier undescribed glycolurils **4a—c**, **3d**, and **6** were developed. The best yields (74—96%) of these glycolurils are reached when the reaction time is 7 h (for **4a**,**d**), 3 h (for **4b**,**c**), 2 h (for **6**), and 1 h (for **3d**).

To obtain glycolurils **3a—c** with the free carboxy group, we have developed a procedure of the alkaline hydrolysis of glycoluril isopropyl esters **4a—c** similar to the standard procedure of the alkaline hydrolysis of an ester group.[9] The reaction was carried out upon reflux of these compounds for 2 h in a methanol solution of KOH (3.5 moles of KOH were used per 1 mole of glycoluril) (Scheme 4). Glycolurils potassium salts **7a—c** formed (without their isolation) were neutralized by concentrated hydrochloric acid. The yields of *N*-(carboxyalkyl)glycolurils **3a—c** were 85—89%.

Earlier, we have found that glycolurils of the type **I** are capable to crystallize as conglomerates.[2,4]

The study of the processes of crystallization of glycolurils **3a—d**, **4a—d**, and **6** obtained and search for conglomerates in their series led to the obtaining crystals suitable for X-ray diffraction study only for compound **6**. The X-ray study of the latter showed that glycoluril **6** (Fig. 1) crystallizes as a racemate (the space group *P*1). All the geometrical parameters of the molecules **6** are within the range of values characteristic of this class of compounds.[2—4] As in the glycolurils studied earlier,[2—4] substituents at the bridgehead carbon atoms C(2) and C(4) (in this case, the phenyl groups) are in *cis*-position with respect to each other. Imidazolidine rings C(2)N(1)C(1)N(2)C(4) and

Scheme 4



Reagents and conditions: *i*. MeOH, 3.5 mol equiv.$^{-1}$ KOH, reflux, 2 h.; *ii*: H_2O, HCl to pH 1, 20—23 °C.

C(2)N(3)C(3)N(4)C(4) are in the twist and envelope conformations, with the atoms C(2) and C(4) coming out of the plane of other atoms by 0.135(3) and 0.400(3) Å, respectively. Mutual arrangement of the imidazolidine rings can be described as a "half-open book" with the angle between the mean-square planes equal to 69.1(2)°.

Molecules **3a** in the crystal form centrosymmetric dimers due to the hydrogen bond N(2)—H(2N)...O(1) of medium strength (N...O 2.831(2) Å, NHO 174°). These associates are combined with each other by a multitude of weaker C—H...O- and C—H...π-contacts (the corresponding minimum distances C...O and C...C are 3.250(2) and 3.520(2) Å) to form a three-dimensional framework.

In conclusion, α-ureidoalkylation of ureido acids **2a—d** with DHI **1** as a ureidoalkylating agent has been studied for the first time to obtain glycolurils with the new type of substitution **3a,d**, **4a—d**, and **6** containing alkyl, carboxyalkyl, and methoxy- or isopropoxycarbonylalkyl substituents at the nitrogen atoms and phenyl substituents at the bridgehead carbon atoms, for whose synthesis we have developed preparative procedures. Alkaline hydrolysis of esters **4a—c** to glycolurils **3a—c** studied allowed us to broaden the circle of *N*-(carboxyalkyl)glycolurils. X-ray diffraction study showed that glycoluril **6** crystallizes in the racemic space group (*P*1).

Experimental

NMR spectra were recorded on a Bruker AM-250 (^{1}H, 250.13 MHz (^{1}H)) and Bruker AM-300 (300.13 (^{1}H) and 75.5 MHz (^{13}C)) spectrometers in DMSO-d_6, chemical shifts are given in δ-scale relatively to Me_4Si as an internal standard. Melting points were determined on a Sanyo GALLENKAMP instrument.

Compound **1** was synthesized according to the known procedure[10] by reflux of 1,3-dimethylurea with diphenylglyoxal and aqueous KOH in methanol.

[2-(4,6-Dimethyl-2,5-dioxo-3a,6a-diphenylhexahydroimidazo[4,5-*d*]imidazol-1-yl)acetylamino]acetic acid (3d). Concentrated HCl (0.6 mL, 0.008 mol) was added to a solution of DHI **1** (0.004 mol) and ureido acid **2d** (0.004 mol) in isopropyl alcohol and the mixture was refluxed for 1 h. The reaction mixture of **3d** was kept in air at room temperature for 1 day to form a precipitate, which was filtered off and washed with propan-2-ol. Physico-chemical characteristics of *N*-(carboxyalkyl)glycoluril **3d** are given in Tables 2 and 3.

Synthesis of *N*-(carboxyalkyl)-2,4-dimethyl-1,5-diphenylglycoluril isopropyl esters 4a—d (general procedure). Concentrated

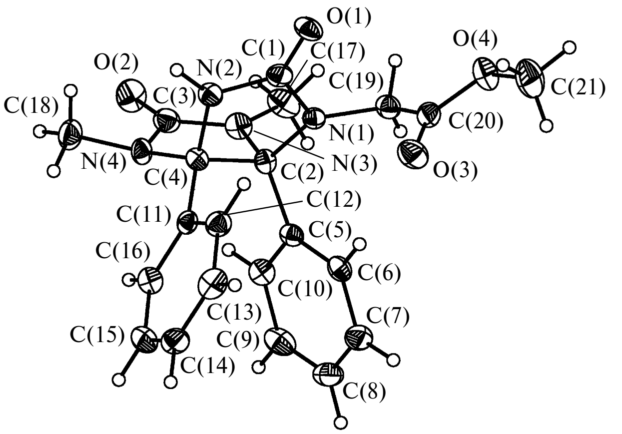


Fig. 1. General view of molecule **6** in representation of atoms by ellipsoids of thermal vibrations (*p* = 50%).

Table 2. Yields, melting points, and elemental analysis data of compounds **3a—d**, **4a—d**, and **6**

Compound	Yield (%)	T_m/°C	Found / Calculated (%) C	H	N	Molecular formula
3a	87	305—307	63.23 63.15	5.26 5.30	14.90 14.73	$C_{20}H_{20}N_4O_4$
3b	89	238—240	64.17 63.95	5.66 5.62	14.08 14.20	$C_{21}H_{22}N_4O_4$
3c	85	286—288	64.77 64.69	5.86 5.92	13.90 13.72	$C_{22}H_{24}N_4O_4$
3d	74	194—196	60.44 60.40	5.26 5.30	16.13 16.01	$C_{22}H_{23}N_5O_5$
4a	95	207—209	65.23 65.39	6.26 6.20	13.20 13.26	$C_{23}H_{26}N_4O_4$
4b	80	155—157	66.17 66.04	6.46 6.47	12.78 12.84	$C_{24}H_{28}N_4O_4$
4c	91	186—188	66.77 66.66	6.86 6.71	12.31 12.44	$C_{25}H_{30}N_4O_4$
4d	79	246—248	62.70 62.62	6.16 6.10	14.63 14.60	$C_{25}H_{29}N_5O_5$
6	96	260—262	65.83 63.95	5.60 5.62	14.27 14.20	$C_{21}H_{22}N_4O_4$

Table 3. ^{1}H and ^{13}C NMR spectra of compounds **3a—d**, **4a—d**, and **6** (in DMSO-d$_6$)

Compound	^{1}H NMR, δ, J/Hz	^{13}C NMR {[H$_6$]DMSO}, δ
3a	2.58 (s, 3 H, NMe); 2.68 (s, 3 H, NMe); 3.54 and 4.01 (both d, 1 H each, CH$_2$, J = 18); 6.78—7.19 (m, 10 H, Ph); 8.61 (s, 1 H, NH); 12.4 (br.s, 1 H, COOH)	26.46, 27.67 (NMe); 43.81 (CH$_2$); 82.85, 87.05 (CPh); 127.42, 127.88, 127.99, 128.29, 128.56, 133.03, 134.99 (Ph); 158.69, 159.00 (CO); 170.36 (COOH)
3b	2.59, 2.80 (both s, 3 H each, NMe); 2.49—2.59 (m, 1 H, CH$_2$); 2.70—2.80 (m, 1 H, CH$_2$); 2.95—3.05 (m, 1 H, CH$_2$); 3.46—3.56 (m, 1 H, CH$_2$); 6.78—7.16 (m, 10 H, Ph); 8.57 (s, 1 H, NH); 12.30 (br.s, 1 H, COOH)	26.32, 28.09 (NMe); 33.77 (CH$_2$); 38.77 (CH$_2$); 82.61; 87.68 (CPh); 127.34, 127.90, 128.31, 128.55, 132.93, 134.77 (Ph); 158.58, 159.46 (CO); 170.33 (COOH)
3c	1.62—1.77 (m, 1 H, CH$_2$); 1.85—2.01 (m, 1 H, CH$_2$); 2.13—2.31 (m, 2 H, CH$_2$); 2.61 and 2.81 (both s, 3 H each, NMe); 2.69—2.79 (m, 1 H, CH$_2$); 3.31—3.41 (m, 1 H, CH$_2$); 6.73—7.13 (m, 10 H, Ph); 8.45 (s, 1 H, NH); 12.05 (br.s, 1 H, COOH)	24.74 (CH$_2$); 26.14, 28.02 (NMe); 31.05 (CH$_2$); 42.07 (CH$_2$); 82.53, 87.75 (CPh); 127.30, 127.90, 128.24, 128.29, 128.47, 133.12, 134.70 (Ph); 135.48 (C, Ph); 158.50, 159.42 (CO); 173.96 (COOH)
3d	2.58 (s, 3 H, NMe); 2.64 (s, 3 H, NMe); 3.45 and 4.05 (both d, 1 H each, CH$_2$, J = 17); 3.75 (m, 2 H, CH$_2$); 6.74—7.17 (m, 10 H, Ph); 8.09 (t, 1 H, NH, J = 5.5); 8.57 (s, 1 H, NH); 11.86 (br.s. 1 H, COOH)	26.42, 27.71 (NMe); 40.73 (CH$_2$); 44.57 (CH$_2$); 82.69; 87.36 (Ph); 127.45, 127.92, 128.11, 128.34, 128.58, 133.04, 135.06 (Ph); 158.65, 159.20, 168.34 (CO); 171.16 (COOH)
4a	1.18 and 1.20 (both d, 3 H each, Me, J = 6.4); 2.61 and 2.69 (both s, 3 H each, NMe); 3.65 and 4.09 (both d, 1 H each, CH$_2$, J = 18); 4.87—4.97 (m, 1 H, CH); 6.80—7.15 (m, 10 H, Ph); 8.63 (s, 1 H, NH)	21.46, 21.49 (Me); 26.47, 27.68 (NMe); 43.97 (CH$_2$); 68.37 (CH); 83.04, 86.95 (CPh); 127.42, 127.91, 127.98, 128.30, 128.37, 128.61, 132.94, 135.02 (Ph); 158.65, 158.90 (CO); 168.46 (COO)
4b	1.14 and 1.15 (both d, 3 H each, Me, J = 6.2); 2.60 and 2.80 (both s, 3 H each, NMe); 2.50—2.58 (m, 1 H, CH$_2$); 2.66—2.76 (m, 1 H, CH$_2$); 2.99—3.08 (m, 1 H, CH$_2$); 3.49—3.59 (m, 1 H, CH$_2$); 4.77—4.89 (m, 1 H, CH); 6.77—7.13 (m, 10 H,Ph); 8.57 (s, 1 H, NH)	21.56 (Me); 26.35, 28.20 (NMe); 34.10 (CH$_2$); 38.81 (CH$_2$); 67.50 (CH); 82.75; 87.72 (Ph); 127.38, 127.96, 128.37, 128.62, 132.93, 134.73 (Ph); 158.65, 159.50 (CO); 170.40 (COO)
4c	1.09 and 1.11 (both d, 3 H each, Me, J = 2); 1.66—1.80 (m, 1 H, CH$_2$); 1.88—2.02 (m, 1 H, CH$_2$); 2.17–2.32 (m, 2 H, CH$_2$); 2.61 and 2.81 (both s, 3 H each, NMe); 2.70—2.80 (m,1 H, CH$_2$); 3.30—3.40 (m, 1 H, CH$_2$); 4.76—4.89 (m, 1 H,CH); 6.73—7.30 (m, 10 H, Ph); 8.47 (s, 1 H, NH)	21.47 (Me); 24.64 (CH$_2$); 26.11, 28.03 (NMe); 31.20 (CH$_2$); 41.98 (CH$_2$); 67.01 (CH); 82.48, 87.73 (CPh); 126.98, 127.49, 128.18, 128.24, 128.34, 128.41, 134.67, 135.48 (Ph); 158.50, 159.41 (CO); 171.85 (COO)
4d	1.18 (d, 6 H each, 2 Me, J = 6); 2.60 and 2.67 (both s, 3 H each, NMe); 3.47 and 4.07 (both d, 1 H each, CH$_2$, J = 17); 3.73—3.88 (m, 2 H, CH$_2$); 4.84—4.96 (m, 1 H, CH); 6.74—7.17 (m, 10 H, Ph); 8.21 (t, 1 H, NH, J = 5.7); 8.67 (s, 1 H, NH)	21.49 (Me); 26.31, 27.63 (NMe); 40.89 (CH$_2$); 44.55 (CH$_2$); 67.93 (CH); 82.55; 87.25 (Ph); 127.36, 127.80, 128.11, 128.24, 128.46, 133.03, 135.03 (Ph); 158.50, 159.06, 168.32 (CO); 169.13 (COO)
6	2.58 and 2.67 (both s, 3 H each, NMe); 3.62 (s, 3 H, OMe); 3.71 and 4.13 (both d, 1 H each, CH$_2$, J = 18); 6.82—7.24 (m, 10 H, Ph); 8.66 (s, 1 H, NH)	26.49, 27.69 (NMe); 43.64 (CH$_2$); 51.95 (OMe); 83.00, 87.98 (CPh); 127.42, 127.90, 127.96, 128.31, 128.60, 132.90, 134.90 (Ph); 158.64, 158.94 (CO); 169.59 (COO)

HCl (0.6 mL, 0.008 mol) was added to a solution of DHI **1** (0.004 mol) and the corresponding ureido acid **2a—d** (0.004 mol) in isopropyl alcohol and the mixture was refluxed for 7 h (for the synthesis of **4a** and **4d**) or 3 h (for the synthesis of **4b**,**c**). Compounds **4a—c** were isolated by concentration of the reaction mixtures to dryness and washing the precipitates on the filter from impurities of benzil with diethyl ether, from impurities of 1,3-dimethylurea with water. The reaction mixture of glycoluril **4d** was kept in air at room temperature for 1 day to form a precipitate, which was filtered off and washed with propan-2-ol. Precipitates of **4a—c** were dissolved in chloroform, filtered off from the undissolved DHI **1**, the filtrate was concentrated to dryness to obtain esters **4a—c**. Physico-chemical characteristics of *N*-(isopropoxycarbonylalkyl)glycolurils **4a—d** are given in Tables 2 and 3.

***N*-(Carboxymethyl)-2,4-dimethyl-1,5-diphenylglycoluril methyl ester (6).** Concentrated HCl (0.6 mL, 0.008 mol) was added to a solution of DHI **1** (0.004 mol) and ureido acid **2a** (0.004 mol) in methyl alcohol and the mixture was refluxed for 2 h. A precipitate of **6** was filtered off, washed with diethyl ether from impurities of benzil. Physico-chemical characteristics of *N*-(carboxymethyl)glycoluril **6** are given in Tables 2 and 3.

Synthesis of glycolurils 3a—c (general procedure for the alkaline hydrolysis of esters 4a—c). Potassium hydroxide (0.014 mol) was added to a solution of ester **4a—c** (0.004 mol) in methyl alcohol (15 mL) and the mixture was refluxed for 2 h. The reaction mixture was concentrated to dryness, followed by addition of water (15 mL), neutralized to pH 1 with conc. hydrochloric acid. The neutralization process was accompanied by the forma-

Table 4. Principal crystallografic data and parameters of refinement of compound **6**

Parameter	**6**
Molecular formula	$C_{21}H_{22}N_4O_4$
Molecular weight	394.43
T/K	120
Crystal system	Triclinic
Space group	$P1$
Z	2
a/Å	8.1577(9)
b/Å	9.1979(10)
c/Å	13.5166(16)
α/deg	99.368(3)
β/deg	91.102(3)
γ/deg	106.718(4)
V/Å^3	956.03(19)
d_{calc}/g cm^{-3}	1.370
μ/cm^{-1}	0.97
F(000)	416
$2\theta_{\max}$/deg	52
Number of reflections	
measured	8625
independent	3754
with $I > 2\sigma(I)$	1916
Number of refining parameters	265
R_1	0.0394
wR_2	0.0682
GOOF	0.852
Residual electron density, e Å^{-3}($d_{\max}$/$d_{\min}$)	0.228/–0.212

tion of a white precipitate. The precipitates of glycolurils **3a—c** were filtered off. Physico-chemical characteristics of *N*-(carboxyalkyl)glycolurils **3a—c** are given in Tables 2 and 3.

X-ray diffraction study of compound **6** was performed on a SMART 1000 CCD diffractometer (MoKα-irradiation, graphite monochromator, ω-scanning). The structure was solved by the direct method and refined by the least squares method in anisotropic full-matrix approximation on F^2_{hkl}. The hydrogen atom of the NH group is localized from the differential Fourier-syntheses of electron density. Positions of the rest of hydrogen atoms were calculated geometrically. All the hydrogen atoms were refined in isotropic approximation using the riding model. The principal crystallografic data and parameters of refinement of **6** are given in Table 4. All the calculations were performed using the SHELXTL PLUS program package.[11]

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