Two-step α-ureidoalkylation of ureas with 4,5-dihydroxyimidazolidin-2-ones

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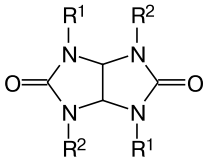
Two-step α-ureidoalkylation of ureas with various 4,5-dihydroxyimidazolidin-2-ones gave novel 1,3-dialkyl-4,5-bis(3-alkylureido)-, 1,3-dialkyl-4,5-bis[3-(2-pyrimidyl)ureido]-, or 1,3-dialkyl-4,5-bis(3,3-dialkylureido)imidazolidin-2-ones and ensembles of three imidazolidine rings. The structure of 4,5-bis(2-oxoimidazolidin-1-yl)imidazolidin-2-one was confirmed by X-ray diffraction data.

Key words: two-step α-ureidoalkylation, 4,5-dihydroxyimidazolidin-2-ones; 1,3-dialkyl-4,5-bis(3-alkylureido)-, 1,3-dialkyl-4,5-bis[3-(2-pyrimidyl)ureido]-, and 1,3-dialkyl-4,5-bis(3,3-dialkylureido)imidazolidin-2-ones; ensembles of three imidazolidine rings, X-ray diffraction analysis.

It is known[1] that ureidoalkylation reactions of ureas with glyoxal afford 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diones (glycolurils) **1**, 4,5-dihydroxyimidazolidin-2-ones (DHI) **2**, and imidazolidin-2,4-diones (hydantoins) **3**.



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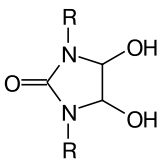

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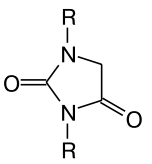

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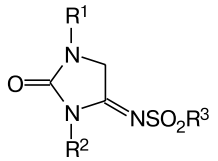
In recent years, we have extensively studied α-ureidoalkylation of ureas,[2] sulfamides,[3—5] sulfonamides,[4,5] ureido alcohols,[6] ureido acids,[6,7] thiosemicarbazide, and aminoguanidine (in the hydrochloride form)[8,9] with cyclic vicinal ureidobis(α-carbinols) **2** containing two potential α-ureidoalkylating sites. We have developed general methods for the targeted synthesis of various N-substituted glycolurils **1**, including those containing hydroxy(carboxy)alkyl substituents, and their sulfur analogs. Enantiomerically pure glycolurils have been first obtained by diastereoselective or diastereospecific α-ureidoalkylation of optically pure *N*-carbamoyl-α-amino acids.[10,11] We have found that α-ureidoalkylation of sulfamide, sulfonamides, and aminoguanidine hydrochloride gives, *via* unusual formation of the C=N bond, 4(5)-sulfonylimino- (**4**) and guanidinoiminoimidazolidin-2-ones (**5**) (see Refs 4, 5, 9). The second pathway of the reaction of DHI **2** with aminoguanidine hydrochloride leads to 4,5-bis(3-aminoguanidino)imidazolidin-2-one dihydrochlorides (**6**) (see Ref. 9). Reactions of DHI with thiosemicarbazide give both 4,5-di(thiosemicarbazido)imidazolidin-2-ones (**7**) and 5,7-dialkyl-3-thioxoperhydroimidazo[4,5-*e*][1,2,4]triazin-6-ones (**8**).[8,9]



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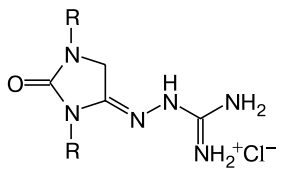

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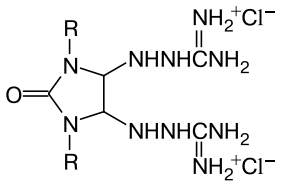

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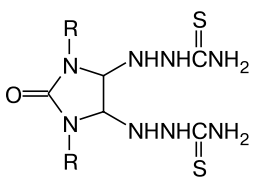

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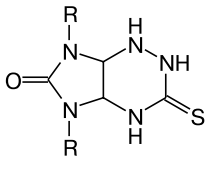

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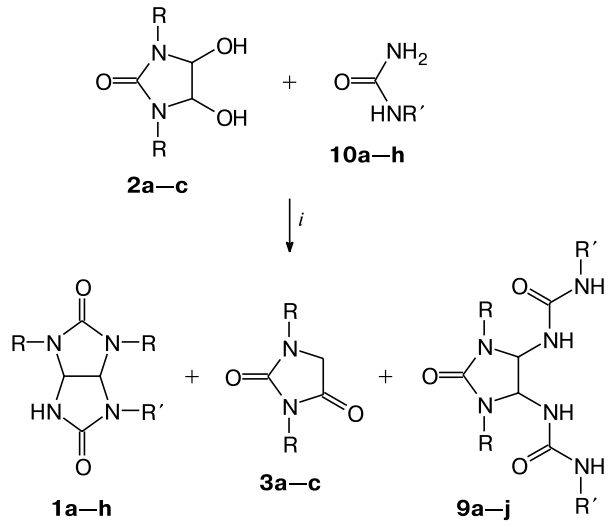
Here we systematically investigated two-step α-ureidoalkylation of various ureas (1-alkyl-, 1-aryl-, 1-(2-pyrimidyl)-, and 1,1-dialkylureas and imidazolidin-2-one (ethyleneurea)[12]) with DHI.

To obtain 4,5-disubstituted imidazolidin-2-ones **9**, first we used 1-alkyl-, 1-phenyl-, and 1-(2-pyrimidyl)ureas **10a—h** in reactions with DHI **2a—c** in the ratio 1 : 2 (DHI was added in portions) under the conditions of the formation of 4,5-di(thiosemicarbazido)imidazolidin-2-ones (pH 1, 80 °C, 1 h). These reactions yielded products of two types: earlier reported glycolurils **1a—g** (compound **1h** was characterized for the first time) and compounds producing doublets at δ 4.30—4.92 (CH—CH) and 6.40—6.87 (NH) in ^{1}H NMR spectra. The ^{1}H NMR spectra obtained match earlier unknown monocyclic compounds: 4,5-bis(3-alkylureido)-1,3-dimethyl-, 1,3-dimethyl-4,5-bis(3-phenylureido)-, and 1,3-dimethyl-4,5-bis[3-(2-pyrimidyl)ureido]imidazolidin-2-ones **9**. The yields of these compounds were 3—17% (**9a—d,f,g,i,j**), 70% (**9e**), and 92% (**9h**). In the case of cyclohexylurea (**10d**), 2-pyrimidylurea (**10f**), and phenylurea (**10h**), compounds **9e,g,h,j** were the sole reaction products. Reactions of 1,3-diethyl-DHI **2c** with ureas **10c,g** yielded only glycolurils **1f,e**, respectively. These facts suggest that the structures of both DHI and ureas affect the pathway of the ureidoalkylation of ureas **10**. At the same time, ureas **10f,h** did not react with DHI **2c**, being recovered unchanged. Hydantoins **3a—c** were obtained as by-products produced by the pinacol-type rearrangement[9] of DHI (Scheme 1).

An increase in the reaction time to 1.5 h did not affect the yields of the reaction products, only leading to increased amounts of the corresponding hydantoins **3**.

Based on the aforesaid results, one can assume that the predominant formation of 4,5-bis(alkylureido)imidazolidin-2-ones **9** occurs with ureas containing a bulky substituent at the N atom, which prevents possible closure of a second ring. A similar result can be attained by employing 1,1-dialkylureas **11a,b** in these reactions. To verify the above assumption, we studied the α-ureidoalkylation of 1,1-dimethyl- or 1,1-diethylureas (**11a,b**) with DHI **2a,b** and found that the reaction gives 4,5-bis(3,3-dialkylureido)-1,3-dimethylimidazolidin-2-ones **12a—c** in 13—52% yields and hydantoins **3a,b** (Scheme 2).

Scheme 1



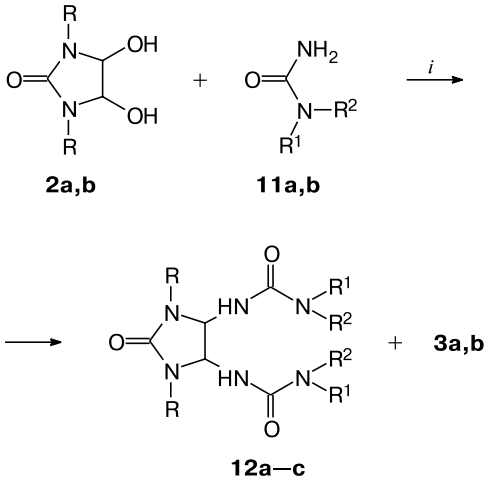
Reagents and conditions: *i*. pH 1, water or H_2O—Pr^iOH, reflux, 1 h.

R = H (**2a**, **3a**, **9g**), Me (**2b**, **3b**, **9a—f,h,j**), Et (**2c**, **3c**, **9i**)

Product	R	R′	Yield (%)	Product	R	R′	Yield (%)
1a	Me	Pr	45	**1e**	Et	Bu^s	35
1b	Me	Bu	40	**1f**	Et	Bu^t	65
1c	Me	Bu^s	38	**1g**	Me	Et	48
1d	Me	Bu^t	77	**1h**	Et	*cyclo*-C_6H_{11}	5

Compound	R′	Product	Compound	R′	Product
10a	Et	**9f**	**10d**	*cyclo*-C_6H_{11}	**9e**,
10b	Pr	**9a**			**9i**
10c	Bu^t	**9d**	**10f**		**9g**,
10e	Bu^n	**9b**			**9h**
10g	Bu^s	**9c**			
10h	Ph	**9j**			

Scheme 2



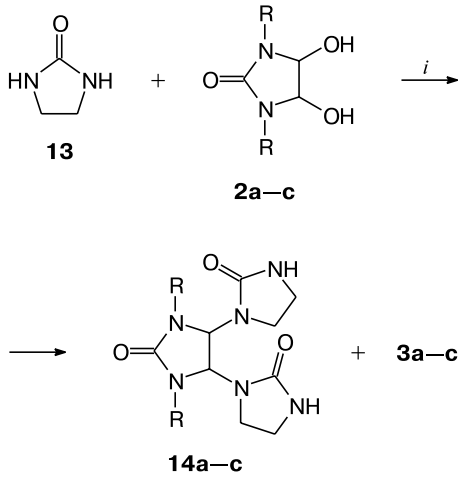
R^1 = R^2 = Me (**11a**), Et (**11b**)

Compound	R	R^1	R^2	Yield (%)
12a	H	Me	Me	20
12b	Me	Me	Me	13
12c	Me	Et	Et	52

Reagents and conditions: *i*. pH 1, water or H_2O—Pr^iOH, reflux, 1 h.

The course of α-ureidoalkylation of ethyleneurea **13** with DHI **2a—c** was monitored by ^{1}H NMR spectroscopy. In the reaction of compound **2a** with ethyleneurea, a precipitate formed after 15 min; the amount of the precipitate increased with an increase in the reaction time. No precipitation was observed in the reactions of DHI **2b,c** with ethyleneurea **13**. In the first case, the precipitate was filtered off after 1 h and recrystallized from water. In the other two cases, the reaction mixtures were concentrated to oils that solidified upon treatment with methanol—acetone (2 : 1). In the ^{1}H NMR spectra, the major signals were broadened multiplets at δ 3.35—3.40 for the CH_2—CH_2 groups of ethyleneurea, singlets at δ 5.10—5.20 for the CH—CH groups, and singlets at δ 6.50—6.75 for two NH groups of ethyleneurea. The ratio of their intensities was 4 : 1 : 1. Therefore, both hydroxy groups in the starting compounds **2a—c** are replaced during the reaction by the ethyleneurea residue to give 4,5-bis(2-oxoimidazolidin-1-yl)imidazolidin-2-ones **14a—c**, which are first representatives of ensembles of three imidazolidine rings. The yields of compounds **14a—c** were 32—44%. Hydantoins **3a—c** were also isolated from the reaction mixtures (Scheme 3).[9]

Scheme 3



R = H (**a**), Me (**b**), Et (**c**)

Reagents and conditions: *i*. pH 1—2, water, reflux, 1.5 h.

The duration of the condensation of DHI **2a** with ethyleneurea **13** was optimized with the synthesis of compound **14a** as an example. With an increase in the reaction time to 1.5 h, the yield of compound **14a** increased from 44 to 64%. After separation of compound **14a** and evaporation of the mother liquor to dryness, the ^{1}H NMR spectra contained no signals for the protons of the nonconsumed starting reagents **13** and **2a**, showing only signals for the protons of hydantoin **3a** and unidentified oligomers. The optimized conditions were applied to reactions of ethyleneurea with DHI **2b,c**. The yields of compounds **14b** and **14c** were 53 and 40%, respectively.

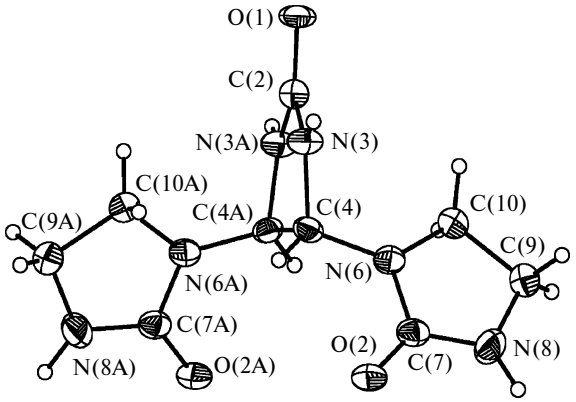


Fig. 1. General view of structure **14a**.

To confirm the structures of products **14**, we performed single-crystal X-ray diffraction analysis of compound **14a** (Fig. 1). According to X-ray diffraction data, this compound is an ensemble of three imidazolidine rings. Compound **14a** crystallizes as a racemate (space group *C*2/*c*) with two hydration water molecules and is characterized by the *C*2 symmetry with the *trans*-arranged terminal imidazolidine rings relative to the central one (torsion angle N(6)—C(4)—C(4A)—N(6A) is −142.5°). The central ring is in the twist conformation with the C(4) and C(4A) atoms deviating by 0.19 Å, while the terminal rings are in the envelope conformation with the C(9) atom deviating by 0.11 Å (Table 1).

An analysis of the crystal packing showed that molecules of **14a** in the crystal are united through N—H...O bonds (N...O 2.897(2) Å) into H-bonded homochiral layers (Fig. 2) running parallel to the crystallographic plane *bc*. The H-bonded rings form cavities each containing two water molecules (O...O 2.796(2)—2.826(2) Å). In addition, water molecules link adjacent homochiral layers by N—H...O bonds (N...O 2.861(2) Å).

Table 1. Selected bond lengths (*d*) and angles (ω) in structure **14a**

Bond	*d*/Å	Angle	ω/deg
O(1)—C(2)	1.230(3)	C(2)—N(3)—C(4)	111.6(2)
O(2)—C(7)	1.248(4)	C(4)—N(6)—C(10)	123.7(2)
C(2)—N(3)	1.349(3)	C(7)—N(6)—C(4)	123.8(2)
C(4)—N(3)	1.454(3)	C(7)—N(6)—C(10)	111.9(2)
C(4)—N(6)	1.435(3)	C(7)—N(8)—C(9)	113.0(2)
N(6)—C(7)	1.365(3)		
N(6)—C(10)	1.459(3)		
N(8)—C(7)	1.340(3)		
N(8)—C(9)	1.439(4)		

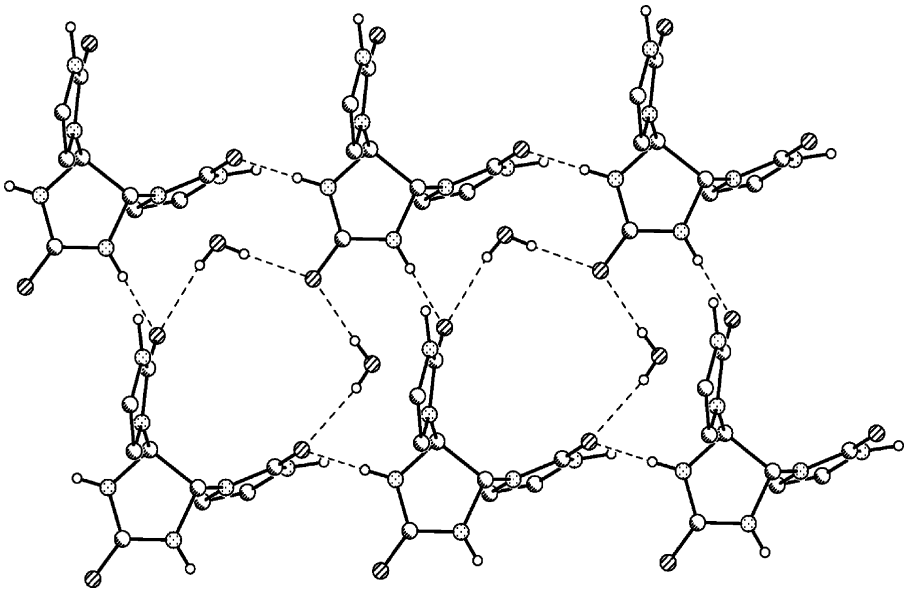


Fig. 2. Fragment of an H-bonded homochiral layer in crystalline structure **14a**.

Thus, we studied the two-step α-ureidoalkylation of various ureas (**10**, **11**, and **13**) with DHI **2** and demonstrated that these reactions give earlier unknown 4,5-disubstituted imidazolidin-2-ones: 4,5-bis(3-alkylureido)-, 4,5-bis(3-phenylureido)-, 4,5-bis[3-(2-pyrimidyl)ureido]-, or 4,5-bis(3,3-dialkylureido)imidazolidin-2-ones and ensembles of three imidazolidine rings. Their structures were confirmed by spectroscopic and X-ray diffraction data.

Experimental

NMR spectra were recorded on Bruker AM-250 (^{1}H, 250 MHz) and Bruker AM-300 spectrometers (^{13}C, 75.5 MHz). Chemical shifts are given on the δ scale with reference to Me_4Si as the internal standard. Melting points were determined on a GALLENKAMP instrument (Sanyo). Mass spectra were recorded on a Kratos MS-30 mass spectrometer (70 eV). 4,5-Dihydroxyimidazolidin-2-ones were prepared by reactions of appropriate ureas with glyoxal according to published proce-

Table 2. Yields, melting points, and elemental analysis data for 4,5-disubstituted imidazolidin-2-ones **1h**, **9a**—**j**, **12a**—**c**, and **14a**—**c**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%)*			Molecular formula
			C	H	N	
1h	4—6	222—224	60.01 59.98	8.61 8.63	19.95 19.98	$C_{14}H_{24}N_4O_2$
9a	4—6	198—200	49.69 49.67	8.31 8.34	26.71 26.73	$C_{13}H_{26}N_6O_3$
9b	6—8	203—204	52.58 52.61	8.82 8.83	24.55 24.54	$C_{15}H_{30}N_6O_3$
9c	3—5	208—210	52.63 52.61	8.81 8.83	24.53 24.54	$C_{15}H_{30}N_6O_3$
9d	8—10	210—212	52.60 52.61	8.84 8.83	24.51 24.54	$C_{15}H_{30}N_6O_3$
9e	90—92	230—232	57.87 57.85	8.70 8.69	21.27 21.30	$C_{19}H_{34}N_6O_3$
9f	6—8	215—217	46.16 46.14	7.71 7.74	29.34 29.35	$C_{11}H_{22}N_6O_3$
9g	15—17	206—208	43.60 43.58	3.93 3.94	39.06 39.09	$C_{13}H_{14}N_{10}O_3$
9h	68—70	234—235	46.61 46.63	4.72 4.70	36.24 36.25	$C_{15}H_{18}N_{10}O_3$
9i	4—6	228—230	59.69 59.64	9.06 9.08	19.89 19.91	$C_{21}H_{38}N_6O_3$
9j	8—10	283—285	61.45 61.47	6.38 6.40	20.47 20.41	$C_{21}H_{26}N_6O_3$
12a	18—21	176—178	41.85 41.83	7.02 6.99	32.54 32.56	$C_9H_{18}N_6O_3$
12b	12—14	220—221	46.14 46.17	7.74 7.79	29.35 29.36	$C_{11}H_{22}N_6O_3$
12c	51—53	198—199	52.61 52.57	8.83 8.86	24.54 24.56	$C_{15}H_{30}N_6O_3$
14a	62—64	250—252	42.52 42.55	5.55 5.51	33.05 33.08	$C_9H_{14}N_6O_3$
14b	51—53	263—264	46.80 46.79	6.43 6.45	29.77 29.74	$C_{11}H_{18}N_6O_3$
14c	38—40	270—273	50.31 50.34	7.15 7.17	27.08 27.05	$C_{13}H_{22}N_6O_3$

* All the compounds obtained were pulverized and dried to remove the hydration water.

dures.[5,13,14] Ureas were synthesized from KOCN and appropriate amine hydrochlorides according to known procedures.[15] Aqueous 40% glyoxal, amines, KOCN, and ethyleneurea (Acros) were used.

Synthesis of 6-cyclohexyl-2,4-diethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (1h); 1,3-dimethyl-4,5-bis(3-propylureido)- (9a), 4,5-bis(3-butylureido)-1,3-dimethyl- (9b), 4,5-bis(3-*sec*-butylureido)-1,3-dimethyl- (9c), 4,5-bis(3-*tert*-butylureido)-1,3-dimethyl- (9d), 4,5-bis(3-cyclohexylureido)-1,3-dimethyl- (9e), 4,5-bis(3-ethylureido)-1,3-dimethyl- (9f), 1,3-dimethyl-4,5-bis[3-(2-pyrimidyl)ureido]- (9h), and 1,3-dimethyl-4,5-bis(3-phenylureido)imidazolidin-2-ones (9j); 4,5-bis[3-(2-pyrimidyl)ureido]imidazolidin-2-one (9g); and 4,5-bis(3-cyclohexylureido)-1,3-diethylimidazolidin-2-one (9i) (general procedure). Concentrated HCl (0.2 mL; in aqueous medium, to pH 1) was added to a solution of appropriate urea **10a—h** (0.02 mol) and appropriate DHI **2a—c** (0.01 mol) in a minimum amount of water or propan-2-ol (depending on the solubilities of the starting reagents). The reaction mixture was refluxed for 1 h. In the case of urea **10c**, the reaction mixture was concentrated by half and left in a refrigerator for 12 h. The precipitate of compound **1d** or **1f** that formed was filtered off and recrystallized from MeOH. Compounds **1a—c,e,g,h** were extracted with $CHCl_3$ (10×10 mL) and the extracts were concentrated *in vacuo* to an oily residue, which were triturated with acetone—ether (1 : 3, 10 mL). The resulting precipitates of compounds **1a—c,e,g,h** were filtered off and crystallized from MeOH. The yields and physicochemical characteristics of compounds **1a—g** have been reported earlier;[2] those of product **1h** is given in Table 2.

After the isolation of compounds **1a—h**, the reaction mixtures were concentrated to an oily residue, which was triturated in acetone (10 mL). The resulting precipitates of compounds **9a—d,f,i** were filtered off and crystallized from MeOH. Hydantoin **3a** was isolated by trituration of the concentrated filtrate with MeOH and filtration of the resulting precipitate; hydantoins **3b,c** were isolated by extraction with Et_2O followed by concentration *in vacuo*. The physicochemical characteristics of compounds **3a—c** were in agreement with the literature data.[4]

In the reactions of ureas **10d,f,h** with DHI **2a,b**, the reaction mixtures were cooled to 20 °C and the resulting precipitates of compounds **9e,g,h,j** were filtered off and washed with MeOH.

The yields and physicochemical characteristics of compounds **9a—j** are given in Tables 2—4.

Table 3. ^{1}H NMR spectra (DMSO-d_6) of compounds **1h**, **9a—j**, **12a—c**, and **14a—c**

Compound	δ, *J*/Hz
1h	1.16 (m, 10 H, 2 Me, 2 CH_2); 1.65 (m, 6 H, 3 CH_2); 3.03, 3.20 (both m, 2 H each, NCH_2); 3.38 (m, 1 H, NCH); 5.19, 5.31 (both d, 1 H each, 2 CH, *J* = 8.1); 7.56 (s, 1 H, NH)
9a	0.82 (t, 6 H, 2 Me, *J* = 7.7); 1.36 (m, 4 H, 2 CH_2); 2.55 (s, 6 H, 2 NMe); 2.95 (m, 4 H, 2 NCH_2); 4.91 (d, 2 H, 2 CH, *J* = 8.3); 6.00 (t, 2 H, 2 NH, *J* = 5.5); 6.62 (d, 2 H, 2 NH, *J* = 8.3)
9b	0.87 (t, 6 H, 2 Me, *J* = 7.4); 1.32 (m, 8 H, 4 CH_2); 2.56 (s, 6 H, 2 NMe); 3.01 (m, 4 H, 2 NCH_2); 4.91 (d, 2 H, 2 CH, *J* = 8.8); 5.97 (t, 2 H, 2 NH, *J* = 5.9); 6.62 (d, 2 H, 2 NH, *J* = 8.8)
9c	0.80 (m, 6 H, 2 Me); 1.13 (m, 6 H, 2 Me); 1.45 (m, 4 H, 2 CH_2); 2.57 (s, 6 H, 2 NMe); 3.59 (m, 2 H, 2 NCH); 4.87 (d, 2 H, 2 CH, *J* = 8.6); 5.97 (m, 2 H, 2 NH); 6.64 (d, 2 H, 2 NH, *J* = 8.6)
9d	1.21 (s, 18 H, 2 Bu^t); 2.48 (s, 6 H, 2 NMe); 4.30 (d, 2 H, 2 CH, *J* = 8.5); 5.75 (s, 2 H, 2 NH); 6.87 (d, 2 H, 2 NH, *J* = 8.5)
9e	1.12 (m, 6 H, 3 CH_2); 1.30 (m, 4 H, 2 CH_2); 1.61 (m, 6 H, 3 CH_2); 1.79 (m, 4 H, 2 CH_2); 2.59 (s, 6 H, 2 NMe); 3.39 (m, 2 H, 2 NCH); 4.85 (d, 2 H, 2 CH, *J* = 8.5); 5.73 (d, 2 H, 2 NH, *J* = 7.9); 6.40 (d, 2 H, 2 NH, *J* = 8.5)
9f	0.99 (t, 6 H, 2 Me, *J* = 7.2); 2.56 (s, 6 H, 2 NMe); 3.03 (m, 4 H, 2 NCH_2); 4.92 (d, 2 H, 2 CH, *J* = 8.3); 5.97 (t, 2 H, 2 NH, *J* = 5.0); 6.66 (d, 2 H, 2 NH, *J* = 8.3)
9g	5.58 (d, 2 H, 2 CH, *J* = 7.7); 6.63 (t, 2 H, 2 CH, *J* = 4.8); 6.96 (br.s, 2 H, 2 NH); 7.88 (d, 2 H, 2 NH, *J* = 7.7); 8.27 (d, 4 H, 4 CH, *J* = 4.8)
9h*	2.63 (s, 6 H, 2 Me); 5.59 (d, 2 H, 2 CH, *J* = 8.6); 6.65 (t, 2 H, 2 CH, *J* = 4.9); 7.84 (d, 2 H, 2 NH, *J* = 8.6); 8.28 (d, 4 H, 4 CH, *J* = 4.9)
9i	1.09 (m, 12 H, 2 Me + 3 CH_2); 1.25 (m, 4 H, 2 CH_2); 1.55 (m, 6 H, 3 CH_2); 1.69 (m, 4 H, 2 CH_2); 3.03, 3.19 (both m, 2 H each, NCH_2); 3.39 (m, 2 H, 2 NCH); 4.89 (d, 2 H, 2 CH, *J* = 8.5); 5.92 (d, 2 H, 2 NH, *J* = 6.6); 6.50 (d, 2 H, 2 NH, *J* = 8.5)
9j	2.62 (s, 6 H, 2 Me); 5.35 (d, 2 H, 2 CH, *J* = 7.5); 6.63 (d, 2 H, 2 NH, *J* = 7.5); 6.92 (t, 2 H, 2 CH, *J* = 6.7); 7.22 (t, 4 H, 4 CH, *J* = 6.7); 7.38 (d, 4 H, 4 CH, *J* = 6.7); 8.69 (s, 2 H, 2 NH)
12a	2.79 (s, 12 H, 2 NMe_2); 5.20 (d, 2 H, 2 CH, *J* = 7.7); 6.70 (br.s, 2 H, 2 NH); 6.93 (d, 2 H, 2 NH, *J* = 7.7)
12b	2.57 (s, 6 H, 2 NMe); 2.80 (s, 12 H, 2 NMe_2); 5.12 (d, 2 H, 2 CH, *J* = 7.3); 6.95 (d, 2 H, 2 NH, *J* = 7.3)
12c	1.00 (t, 12 H, 4 Me, *J* = 7.1); 2.84 (s, 6 H, 2 NMe); 3.05 (m, 8 H, 4 CH_2); 5.06 (d, 2 H, 2 CH, *J* = 7.6); 6.88 (d, 2 H, 2 NH, *J* = 7.6)
14a	3.35 (m, 8 H, 4 CH_2); 5.17 (s, 2 H, 2 CH); 6.50 (br.s, 2 H, 2 NH); 6.90 (s, 2 H, 2 NH)
14b	2.61 (s, 6 H, NMe); 3.40 (m, 8 H, 4 CH_2); 5.10 (s, 2 H, 2 CH); 6.75 (br.s, 2 H, 2 NH)
14c	1.10 (m, 6 H, 2 Me); 2.75 (m, 2 H, NCH_2); 3.11 (m, 2 H, NCH_2); 3.37 (m, 8 H, 4 CH_2); 5.20 (s, 2 H, 2 CH); 6.70 (s, 2 H, 2 NH)

* ^{13}C NMR (DMSO-d_6), δ: 27.9 (NMe); 68.7 (CH—CH); 111.6 (CH); 161.9 (CO).

Table 4. Mass spectra of compounds **9e** and **14a—c**

Compound	m/z (I_{rel} (%))
9e	252 (39) [M − $NH_2C(O)NHC_6H_{11}$]$^+$, 154 (90), 153 (23), 142 (19), 127 (100), 113 (40), 99 (22), 70 (22), 61 (43)
14a	168 (5) [M − $C_3H_6N_2O$*]$^+$, 86 (100), 69 (8), 56 (11)
14b	196 (100) [M − $C_3H_6N_2O$*]$^+$, 141 (10), 128 (11), 112 (12), 97 (9), 86 (8), 70 (10)
14c	224 (63) [M − $C_3H_6N_2O$*]$^+$, 196 (15), 168 (14), 140 (33), 127 (25), 113 (27), 97 (31), 86 (100), 83 (32), 70 (62), 69 (37), 60 (18)

* $C_3H_6N_2O$ is ethyleneurea.

Synthesis of 4,5-bis(3,3-dimethylureido)- (12a), 4,5-bis(3,3-dimethylureido)-1,3-dimethyl- (12b), and 4,5-bis(3,3-diethylureido)-1,3-dimethylimidazolidin-2-ones (12c) (general procedure). Concentrated HCl was added dropwise down to pH 1 to a solution of an appropriate urea **11a,b** (0.04 mol) and DHI **2a,b** (0.02 mol) in water (50 mL). The reaction mixture was stirred at 60—70 °C for 1 h. The resulting precipitates of compounds **12a—c** were filtered off and washed with MeOH. The yields and physicochemical characteristics of compounds **12a—c** are given in Tables 2 and 3. Hydantoins **3a,b** were isolated as described above.

Synthesis of 1,3-unsubstituted (14a), 1,3-dimethyl- (14b), and 1,3-diethyl-4,5-bis(2-oxoimidazolidin-1-yl)imidazolidin-2-ones (14c) (ensemble of three imidazolidine rings) (general procedure). A catalytic amount of HCl (pH 1) was added to an aqueous solution of ethyleneurea (imidazolidin-2-one) **13** (0.02 mol) and an appropriate DHI **2a—c** (0.01 mol). The reaction mixture was refluxed for 1.5 h. In the case of product **14a**, the precipitate that formed was filtered off and recrystallized from water. In the case of products **14b,c**, the reaction mixture was thickened to an oil and triturated with methanol—acetone (1 : 1). The resulting precipitates of compounds **14b,c** were filtered off and crystallized from MeOH. The yields and physicochemical characteristics of compounds **14a—c** are given in Tables 2—4. Hydantoins **3a—c** were isolated as described above.

X-ray diffraction analysis of compound 14a. The crystals of compound **14a** ($C_9H_{18}N_6O_5$) are monoclinic, space group $C2/c$, at $T = 120$ K $a = 11.759(2)$ Å, $b = 9.335(2)$ Å, $c = 11.386(3)$ Å, $\beta = 92.977(6)°$, $V = 1248.2(5)$ Å^3, $Z = 4$ ($Z' = 0.5$), $M = 290.29$, $d_{calc} = 1.545$ g cm^{-3}, μ(Mo-Kα) = 1.27 cm^{-1}, $F(000) = 616$. The intensities of 2478 reflections were measured on a Smart 1000 CCD automatic diffractometer at 120 K ($2\theta < 54°$) and 1285 independent reflections ($R_{int} = 0.04711$) were used in calculations. The structure was solved by the direct method and refined by the full-matrix least-squares method in the anisotropic-isotropic approximation on F^2. Hydrogen atoms were located from the electron density difference maps. Final residuals were $R_1 = 0.0504$ (on F for 684 observed reflections with $I > 2\sigma(I)$), $wR_2 = 0.1020$, and GOOF = 0.917 (for all reflections). All calculations were performed with the SHELXTL PLUS 5.0 program package.

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