A novel convenient approach to the synthesis of 2-substituted analogs of ornithine and homolysine

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A novel efficient method for the synthesis of earlier unknown 2-substituted analogs of ornithine and homolysine from substituted 5-aminopentyl- and 3-amidopropylhydantoins (prepared from cyclic imines and amino and amido ketones) was developed. Hydrolysis of hydantoins with a solution of $Ba(OH)_2$ gave the target amino acids in high yields.

Key words: 3-acyllactams, amino ketones, cyclic imines, hydantoins, amino acids, Bucherer—Bergs reaction.

In recent years, 5,5-disubstituted hydantoins attract much attention not only as convenient precursors in the synthesis of α-amino acids but also as substances with a broad spectrum of biological activity, *e.g.*, as anticonvulsants, antiparasitic and antiarrhythmic drugs,[1] and aldose reductase inhibitors.[2] Being stable crystalline substances, hydantoins can be convenient starting materials for the synthesis of other compounds. Acid or basic hydrolysis of 5,5-disubstituted hydantoins gives α-substituted analogs of natural amino acids, which are of great interest for bioorganic and medicinal chemistry and pharmacology; they are also important as the basis for many alkaloids, biologically active substances, and modern drugs.

The aim of the present work was to develop a method for the synthesis of 2-substituted derivatives of basic amino acids from amino carbonyl compounds.

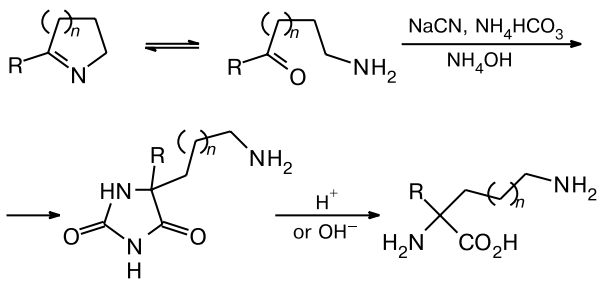
Carbonyl compounds are widely used in modern organic synthesis as starting reagents for preparation of various natural compounds, especially amino acids and their analogs. However, analysis of the literature data has revealed that amino ketones and cyclic imines are virtually not used in the synthesis of amino acids.

The syntheses of the starting compounds, namely, 6-aminohexanones,[3] five-membered cyclic imines, *N*-(4-R-4-oxobutyl)acetamides,[4] and 3-acyllactams[5] were described earlier; six- and seven-membered imines were prepared according to a known procedure.[6]

We assumed that amino ketones and cyclic imines can form hydantoins of 2-substituted analogs of basic amino acids (ornithine, lysine, and homolysine). Subsequent acid or basic hydrolysis of hydantoins can open up a convenient route to artificial analogs of these amino acids.

Hydantoins are most conveniently synthesized by the Strecker reaction modified by Bucherer and Bergs (Scheme 1).

Scheme 1



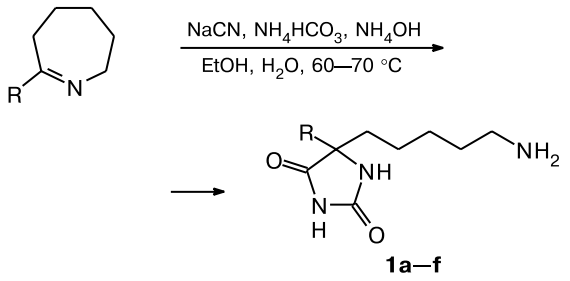
However, it turned out that the Bucherer—Bergs reaction with five- and six-membered cyclic imines (2-phenylpyrroline and 2-phenylpiperideine) yields complex mixtures mainly containing the starting imines. The course of the reaction is insensitive to variations in solvent and temperature or use of basic catalysts such as hydrazine or 1,1-dimethylhydrazine. Nevertheless, a seven-membered cyclic imine (2-phenyltetrahydroazepine) was converted into the corresponding hydantoin, namely, 5-(5-aminopentyl)-5-phenylimidazolidine-2,4-dione in 87% yield. The reaction is of general character and can be carried out with imines containing aromatic, heteroaromatic, and bulky aliphatic substituents. Under optimized reaction conditions, hydantoins **1a**—**f** were obtained in yields from high to almost quantitative. Products **1a**—**f** are derivatives of 2-substituted homolysines (Scheme 2).

Apparently, under such conditions, seven-membered cyclic imines partially hydrolyze to aminohexanones, and

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2749—2753, December, 2004.

1066-5285/04/5312-2866

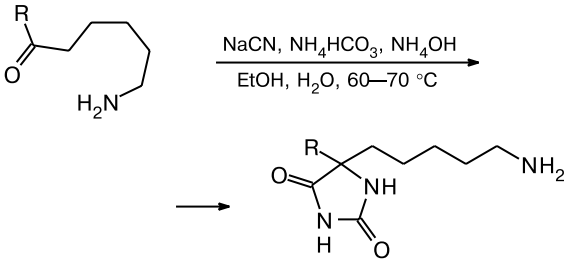
Scheme 2



Hydantoin	R	Yield (%)	Hydantoin	R	Yield (%)
1a	Ph	87	**1d**	2-Thienyl	75
1b	4-FC_6H_4	95	**1e**	2-Furyl	77
1c	4-ClC_6H_4	88	**1f**	Bu^t	75
			1g	3-Pyridyl	85

only the amino ketone form is involved in the hydantoin formation. To verify this assumption, we synthesized 6-aminohexanones by acid hydrolysis and decarboxylation of seven-membered 3-acyllactams.[5] It turned out that these amino ketones afford hydantoins in high yields (Scheme 3).

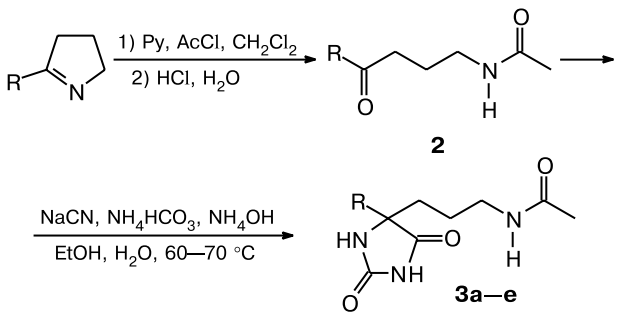
Scheme 3



Earlier,[7] it was demonstrated that 5-phthalimidopentan-2-one gives the corresponding hydantoin in 80% yield. We assumed that use of amido ketones instead of five-membered cyclic imines would facilitate the Bucherer—Bergs reaction. Starting from *N*-(4-oxoalkyl)acetamides **2**,[4] we obtained hydantoins **3a—e** (Scheme 4).

Hydrolysis of hydantoins **3** could give earlier unknown ornithine and homolysine derivatives. It was shown[8] that 5,5-disubstituted hydantoins are very resistant to both acid and basic hydrolysis. The described methods for purification of amino acids from hydantoins are based on precipitation of the latter in acidic media. However, hydantoins and amino acids containing aminoalkyl groups differ only slightly in solubility, which makes the target amino acids more difficult to isolate.

Scheme 4



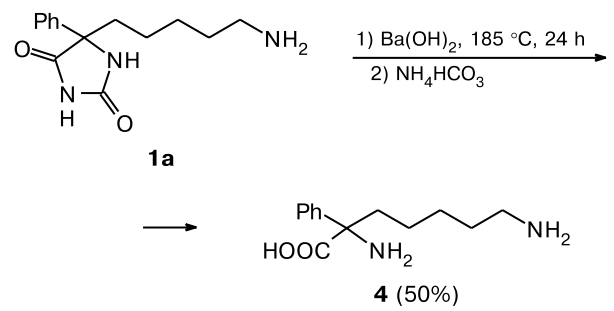
Hydantoin	R	Yield (%)	Hydantoin	R	Yield (%)
3a	Ph	93	**3d**	4-MeC_6H_4	95
3b	Bn	95	**3e**	2-Thienyl	87
3c	Me	80			

Hydantoins were hydrolyzed under a number of both acid and basic conditions, but incomplete hydrolysis prevented amino acids from being isolated in the individual state.

Our attempts to hydrolyze hydantoins modified with Ts[8] or Boc groups[9] bound to the amide and imide N atoms also failed.

Nevertheless, we found the conditions for complete hydrolysis of hydantoin **1a** with an aminoalkyl fragment: heating in a saturated $Ba(OH)_2$ solution in an autoclave at 185 °C for 24 h afforded 2-phenylhomolysine (**4**) (Scheme 5).

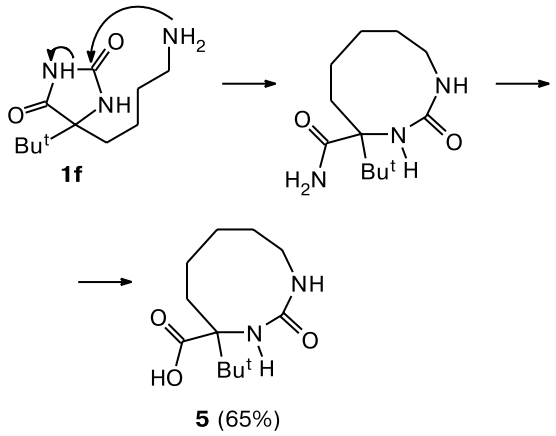
Scheme 5



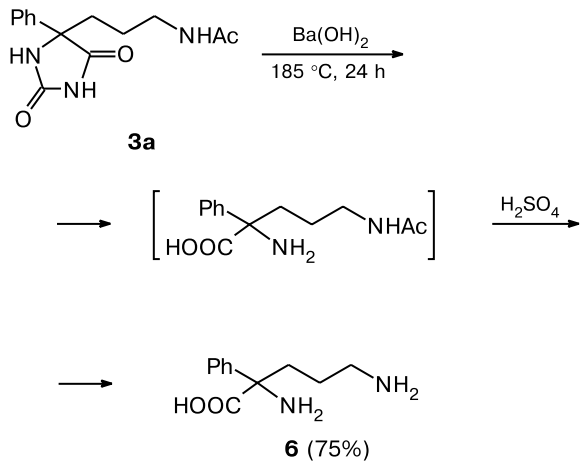
Under these conditions, the hydrolysis of 5-(5-aminopentyl)-5-*tert*-butylimidazolidine-2,4-dione (**1f**) unexpectedly gave a nine-membered cyclic urea derivative **5**, probably through intramolecular attack of the aminopentyl fragment on the carbamide CO group followed by hydrolysis of the intermediate cyclic amide (Scheme 6).

In 5-(3-acetylaminopropyl)-5-phenylimidazolidine-2,4-dione (**3a**), the acetamido group is not hydrolyzable under these conditions. Yet it is hydrolyzed with a stoichiometric amount of H_2SO_4 to give 2-phenylornithine (**6**) in high yield (Scheme 7).

Scheme 6



Scheme 7



Thus, the behavior of cyclic imines and amino and amido ketones in the synthesis of hydantoins containing an amino- or amidoalkyl fragment at the quaternary C atom was studied. The efficient method for the synthesis of earlier unknown hydantoins with 5-aminopentyl and 3-(*N*-acetylamino)propyl fragments was developed. It was found that their complete hydrolysis in a $Ba(OH)_2$ solution at a high temperature affords 2-substituted ornithine and homolysine derivatives.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$, CD_3OD, D_2O, and DMSO-d_6 with Me_4Si as the internal standard; the chemical shifts are given in ppm to within 0.01 ppm. IR spectra were recorded on a UR-20 spectrophotometer (thin film for liquids and Nujol for solids). TLC analysis was performed on Silufol UV-254 plates; spots were visualized in an acidified solution of $KMnO_4$, with a solution of ninhydrin in butanol, with the iodine vapor, or under UV light. Preparative chromatography was carried out on silica gel (63—200 mesh, Merck).

N-(4-Oxoalkyl)acetamides **2** were prepared as described earlier.[2]

Synthesis of hydantoins 1a—f (general procedure). A mixture of an amino carbonyl compound (6-aminohexanone, 7-substituted tetrahydroazepine, or amido ketone) (10 mmol), ammonium bicarbonate (3.5 g, 44 mmol), sodium cyanide (12 mmol), conc. aqueous ammonia (3 mL), ethanol (10 mL), and water (10 mL) was heated at 60—70 °C for 25 h; completion of the reaction was checked by TLC ($BuOH—H_2O—AcOH$, 4 : 1 : 1; spot visualization with a solution of ninhydrin in butanol (violet color)). The reaction mixture was evaporated to dryness and the residue was finely ground, refluxed in anhydrous EtOH (20 mL) for 5 min, and filtered hot. The filtrate was concentrated and recrystallized from EtOH (2 mL).

5-(5-Aminopentyl)-5-phenylimidazolidine-2,4-dione (1a). Yield 87%, m.p. 185 °C. Found (%): C, 63.96; H, 7.14. $C_{14}H_{19}N_2O_3$. Calculated (%): C, 64.35; H, 7.33. IR, ν/cm^{-1}: 1550 (CCONH); 1680 ($(HN)_2C=O$). ^1H NMR ($(CD_3)_2SO$), δ: 1.10—1.40 (m, 6 H, $CH_2—C\underline{H}_2—C\underline{H}_2—C\underline{H}_2—CH_2$); 1.75—2.00 (m, 2 H, $C—C\underline{H}_2—CH_2$); 2.50 (m, 2 H, $C\underline{H}_2NH_2$); 3.95 (br.s, 4 H, $N\underline{H}_2$, $N\underline{H}$); 7.25 (t, 1 H, $H_{Ar}(4)$, ^3J_H = 8 Hz); 7.33 (t, 2 H, $H_{Ar}(3)$, $H_{Ar}(5)$, ^3J_H = 8 Hz); 7.50 (d, 2 H, $H_{Ar}(2)$, $H_{Ar}(6)$, ^3J_H = 8 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 23.4, 26.3, 33.1, 38.4, 41.5 ($—CH_2—CH_2—CH_2—CH_2—CH_2—NH_2$); 67.8 ($\underline{C}—CH_2$); 125.4 ($C_{Ar}(3)$, $C_{Ar}(5)$); 127.1 ($C_{Ar}(4)$); 128.1 ($C_{Ar}(2)$, $C_{Ar}(6)$); 140.5 (C—Ph-4); 161.3 ($HN\underline{C}ONH$), 179.9 ($HN\underline{C}OC$).

5-(5-Aminopentyl)-5-(4-fluorophenyl)imidazolidine-2,4-dione (1b). Yield 87%, m.p. 99 °C. Found (%): C, 59.60; H, 6.50. $C_{14}H_{18}FN_3O_2$. Calculated (%): C, 60.20; H, 6.50. IR, ν/cm^{-1}: 1550 (CCONH); 1680 ($(HN)_2C=O$). ^1H NMR ($(CD_3)_2SO$), δ: 1.10—1.40 (m, 6 H, $CH_2—C\underline{H}_2—C\underline{H}_2—C\underline{H}_2—CH_2$); 1.75—2.00 (m, 2 H, $C—C\underline{H}_2—CH_2$); 2.50 (m, 2 H, $C\underline{H}_2NH_2$); 3.95 (br.s, 3 H, $N\underline{H}_2$, $N\underline{H}$); 7.17 (t, 1 H, $H_{Ar}(2)$, $H_{Ar}(6)$, ^3J_H = 8.9 Hz); 7.52 (dd, 2 H, $H_{Ar}(3)$, $H_{Ar}(5)$, ^3J_H = 8.9 Hz, ^3J_F = 5.24 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 23.4, 26.3, 33.1, 38.4, 41.5 ($—CH_2—CH_2—CH_2—CH_2—CH_2—NH_2$); 67.8 ($\underline{C}—CH_2$); 114.8 (d, $C_{Ar}(3)$, $C_{Ar}(5)$, ^2J_F = 22.2 Hz); 128.1 (d, $C_{Ar}(2)$, $C_{Ar}(6)$, ^3J_F = 8.9 Hz); 136.5 ($C_{Ar}(1)$); 161.5 (d, $C_{Ar}(4)$, ^1J_F = 233 Hz); 157.1 ($HN\underline{C}ONH$); 176.5 ($HN\underline{C}OC$).

5-(5-Aminopentyl)-5-(4-chlorophenyl)imidazolidine-2,4-dione (1c). Yield 87%, m.p. 175 °C. Found (%): C, 63.96; H, 7.14. $C_{14}H_{18}ClN_3O_2$. Calculated (%): C, 64.35; H, 7.33. IR, ν/cm^{-1}: 1550 (CCONH); 1680 ($(HN)_2C=O$). ^1H NMR ($(CD_3)_2SO$), δ: 1.05—1.35 (m, 6 H, $CH_2—C\underline{H}_2—C\underline{H}_2—C\underline{H}_2—CH_2$); 1.73—1.91 (m, 2 H, $C—C\underline{H}_2—CH_2$); 2.50 (s, 2 H, $C\underline{H}_2NH_2$); 3.95 (br.s, 4 H, NH_2, NH); 7.37 (d, 2 H, $H_{Ar}(3)$, $H_{Ar}(5)$, ^3J_H = 8.55 Hz); 7.51 (d, 2 H, $H_{Ar}(2)$, $H_{Ar}(6)$, ^3J_H = 8.55 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 23.3, 26.2, 29.9, 38.5, 41.4 ($CH_2—CH_2—CH_2—CH_2—CH_2—NH_2$); 67.5 ($\underline{C}—CH_2$); 127.4 ($C_{Ar}(3)$, $C_{Ar}(5)$); 128.0 ($C_{Ar}(2)$, $C_{Ar}(6)$); 121.9 ($C_{Ar}(1)$); 139.6 ($C_{Ar}(4)$); 161.1 ($HN\underline{C}ONH$); 179.5 ($HN\underline{C}OC$).

5-(5-Aminopentyl)-5-(2-thienyl)imidazolidine-2,4-dione (1d). Yield 77%, m.p. 203 °C. Found (%): C, 53.56; H, 6.01. $C_{12}H_{17}N_3O_2S$. Calculated (%): C, 53.91; H, 6.41. IR, ν/cm^{-1}: 1550 (CCONH); 1680 ($(HN)_2C=O$). ^1H NMR ($(CD_3)_2SO$), δ: 1.10—1.40 (m, 6 H, $CH_2—C\underline{H}_2—C\underline{H}_2—C\underline{H}_2—CH_2$); 1.85—2.05 (m, 2 H, $C—C\underline{H}_2—CH_2$); 2.50 (s, 2 H, $C\underline{H}_2NH_2$); 4.10 (br.s, 2 H, NH_2); 6.99 (dd, 1 H, $H_{Ar}(4)$, ^3J_H = 4.78 Hz, ^3J_H = 3.45 Hz);

7.04 (d, 1 H, $H_{Ar}(3)$, ^3J_H = 3.45 Hz); 7.43 (d, 1 H, $H_{Ar}(5)$, ^3J_H = 4.78 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 23.2, 26.3, 32.6, 38.5, 41.2 (—CH_2—CH_2—CH_2—CH_2—CH_2—NH_2); 66.5 (C—CH_2); 124.3 ($C_{Ar}(5)$); 125.5 ($C_{Ar}(3)$); 127.3 ($C_{Ar}(4)$); 144.2 ($C_{Ar}(2)$); 158.9 (HNCONH); 177.1 (HNCOC).

5-(5-Aminopentyl)-5-(2-furyl)imidazolidine-2,4-dione (1e). Yield 75%, m.p. 103 °C. Found (%): C, 57.06; H, 6.46. $C_{12}H_{17}N_3O_3$. Calculated (%): C, 57.36; H, 6.82. IR, ν/cm^{-1}: 1540 (CCONH); 1680 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.10—1.40 (m, 6 H, CH_2—CH_2—CH_2—CH_2—CH_2); 1.81—2.05 (m, 2 H, C—CH_2—CH_2); 2.50 (m, 2 H, CH_2NH_2); 6.34 (m, 1 H, $H_{Ar}(4)$); 6.39—6.41 (m, 1 H, $H_{Ar}(5)$); 7.60 (s, 1 H, $H_{Ar}(3)$). ^{13}C NMR ($(CD_3)_2SO$), δ: 22.7, 26.2, 33.1, 34.2, 41.4 (CH_2—CH_2—CH_2—CH_2—CH_2—NH_2); 64.6 (C—CH_2); 106.7, 110.4, 142.7, 152.6 ($C_{Ar}(2)$, $C_{Ar}(3)$, $C_{Ar}(4)$, $C_{Ar}(5)$); 160.1 (HNCONH); 177.1 (HNCOC).

5-(5-Aminopentyl)-5-(*tert*-butyl)imidazolidine-2,4-dione (1f). Yield 75%, m.p. 165 °C. Found (%): C, 59.12; H, 9.33. $C_{12}H_{23}N_3O_2$. Calculated (%): C, 59.72; H, 9.61. IR, ν/cm^{-1}: 1550 (CCONH); 1680 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 0.90 (s, 9 H, Bu^t); 1.10—1.40 (m, 6 H, CH_2—CH_2—CH_2—CH_2—CH_2); 1.50 (t, 2 H, C—CH_2—CH_2, ^3J_H = 7 Hz); 1.70 (t, 2 H, CH_2NH_2, ^3J_H = 7 Hz); 4.20 (br.s, 2 H, NH_2); 7.80 (s, 1 H, CONHCO). ^{13}C NMR ($(CD_3)_2SO$), δ: 15.9 ($(H_3C)_3C$); 15.2, 18,5, 22.3, 23.8, 28.3, 32.7 (CH_2—CH_2—CH_2—CH_2—CH_2, $(H_3C)_3C$); 63.7 (HNCOC); 153.5 (HNCONH); 173.0 (HNCOC).

5-(5-Aminopentyl)-5-(3-pyridyl)imidazolidine-2,4-dione (1g). Yield 85%, m.p. 175 °C. Found (%): C, 59.12; H, 6.75. $C_{13}H_{18}N_4O_2$. Calculated (%): C, 59.53; H, 6.92. IR, ν/cm^{-1}: 1555 (CCONH); 1685 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.10—1.40 (m, 6 H, CH_2—CH_2—CH_2—CH_2—CH_2); 1.85—2.05 (m, 2 H, C—CH_2—CH_2); 2.50 (m, 2 H, CH_2NH_2); 4.10 (br.s, 2 H, NH_2); 7.40 (dd, 1 H, $H_{Ar}(5)$, ^3J_H = 7.94 Hz, ^3J_H = 4.64 Hz); 7.88 (ddd, 1 H, $H_{Ar}(6)$, ^3J_H = 7.94 Hz, ^4J_H = 1.32 Hz, ^4J_H = 1.99 Hz); 8.51 (dd, 1 H, $H_{Ar}(4)$, ^3J_H = 4.64 Hz, ^4J_H = 1.32 Hz); 8.69 (d, 1 H, $H_{Ar}(2)$, ^4J_H = 1.99 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 23.0, 25.9, 31.4, 38.1, 40.6 (CH_2—CH_2—CH_2—CH_2—CH_2—NH_2); 72.9 (C—CH_2); 123.4, 133.2, 134.9, 146.7, 148.9 ($C_{Ar}(2)$, $C_{Ar}(3)$, $C_{Ar}(4)$, $C_{Ar}(5)$, $C_{Ar}(6)$); 157.1 (HNCONH); 176.5 (HNCOC).

***N*-[3-(2,5-Dioxo-4-phenylimidazolidin-4-yl)propyl]acetamide (3a).** Yield 93%, m.p. 120 °C. Found (%): C, 56.71; H, 6.01. $C_{14}H_{17}N_3O_3$. Calculated (%): C, 56.85; H, 6.13. IR, ν/cm^{-1}: 1650 (H_3CCONH); 1720 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.20—1.35 (m, 2 H, CH_2—CH_2—CH_2); 1.75 (s, 3 H, CH_3CO); 1.70—2.00 (m, 2 H, C—CH_2—CH_2—CH_2—NH); 2.90—3.05 (m, 2 H, CH_2—NH); 7.20 (t, 1 H, $H_{Ar}(4)$, ^3J_H = 7.95 Hz); 7.30 (t, 2 H, $H_{Ar}(3)$, $H_{Ar}(5)$, ^3J_H = 7.95 Hz); 7.50 (t, 1 H, $H_{Ar}(2)$, $H_{Ar}(6)$, ^3J_H = 7.95 Hz); 7.65 (s, 1 H, CONHCO); 7.92 (t, 1 H, CH_3CONH, ^3J_H = 7.01 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 22.5 (CH_3CO); 24.3 (CH_2—CH_2—CH_2); 36.2 (C—CH_2—CH_2); 38.5 (CH_2—NH); 67.7 (C—CH_2); 125.5 ($C_{Ar}(2)$, $C_{Ar}(6)$); 126.5 ($C_{Ar}(4)$); 128 ($C_{Ar}(3)$, $C_{Ar}(5)$); 141.5 ($C_{Ar}(1)$); 156.7 (NHCONH); 169.0 (CH_3CONH); 175.4 (CCONH).

***N*-[3-(4-Benzyl-2,5-dioxoimidazolidin-4-yl)propyl]acetamide (3b).** Yield 95%, m.p. 120 °C. Found (%): C, 62.11; H, 6.52. $C_{15}H_{19}N_3O_3$. Calculated (%): C, 62.27; H, 6.62. IR, ν/cm^{-1}: 1650 (H_3CCONH); 1720 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.16—1.48 (m, 2 H, CH_2—CH_2—CH_2); 1.51—1.73 (m, 2 H, C—CH_2); 1.77 (s, 3 H, CH_3CO); 1.70—2.00 (m, 2 H, C—CH_2—CH_2—CH_2—NH); 2.76 (Ph—CH_2); 2.96—3.06 (m, 2 H, CH_2—NH); 7.11—7.15 (m, 2 H, H_{Ar}); 7.17—7.25 (m, 3 H, H_{Ar}); 7.69 (s, 1 H, CONHCO); 7.90 (m, 1 H, CH_3CONH). ^{13}C NMR ($(CD_3)_2SO$), δ: 22.6 (CH_3CO); 23.7 (CH_2—CH_2—CH_2); 34.4 (C—CH_2—CH_2); 38.5 (CH_2—NH); 42.2 (Ar—CH_2); 66.6 (C—CH_2); 126.6 ($C_{Ar}(4)$); 127.8 ($C_{Ar}(2)$, $C_{Ar}(6)$); 130.2 ($C_{Ar}(3)$, $C_{Ar}(5)$); 135.6 ($C_{Ar}(1)$); 158.8 (NHCONH); 169.1 (CH_3CONH); 179.0 (CCONH).

***N*-[3-(4-Methyl-2,5-dioxoimidazolidin-4-yl)propyl]acetamide (3c).** Yield 80%, m.p. 120 °C. Found (%): C, 50.81; H, 6.97. $C_9H_{15}N_3O_3$. Calculated (%): C, 50.69; H, 7.09. IR, ν/cm^{-1}: 1650 (H_3CCONH); 1720 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.11—1.61 (m, 7 H, C—CH_2—CH_2, CH_3CO); 1.76 (s, 3 H, CH_3C); 2.96 (m, 2 H, CH_2—NH); 7.84 (m, 1 H, CONHCO); 7.89 (s, 1 H, CONHCO). ^{13}C NMR ($(CD_3)_2SO$), δ: 22.6 (CH_3CO); 23.55 (CH_2—CH_2—CH_2); 23.6 (H_3C—C); 34.7 (C—CH_2—CH_2); 38.3 (CH_2—NH); 61.8 (C—CH_2); 156.3 (NHCONH); 169.0 (CH_3CONH); 178.5 (CCONH).

***N*-{3-[4-(4-Methylphenyl)-2,5-dioxoimidazolidin-4-yl]propyl}acetamide (3d).** Yield 95%, m.p. 120 °C. Found (%): C, 62.13; H, 6.62. $C_{15}H_{19}N_3O_3$. Calculated (%): C, 62.27; H, 6.62. IR, ν/cm^{-1}: 1650 (H_3CCONH); 1720 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.16—1.48 (m, 2 H, CH_2—CH_2—CH_2); 1.51—1.73 (m, 2 H, C—CH_2); 1.77 (s, 3 H, CH_3CO); 1.70—2.00 (m, 2 H, C—CH_2—CH_2—CH_2—NH); 2.25 (s, 3 H, CH_3—Ar); 2.96—3.06 (m, 2 H, CH_2—NH); 7.11—7.15 (m, 2 H, H_{Ar}); 7.17—7.25 (m, 3 H, H_{Ar}); 7.69 (s, 1 H, CONHCO); 7.90 (m, 1 H, CH_3CONH). ^{13}C NMR ($(CD_3)_2SO$), δ: 21.2 (CH_3—Ar); 22.6 (CH_3CO); 23.7 (CH_2—CH_2—CH_2); 35.2 (C—CH_2—CH_2); 38.0 (CH_2—NH); 66.6 (C—CH_2); 126.6 ($C_{Ar}(4)$); 127.8 ($C_{Ar}(2)$, $C_{Ar}(6)$); 130.2 ($C_{Ar}(3)$, $C_{Ar}(5)$); 135.6 ($C_{Ar}(1)$); 158.8 (NHCONH); 169.1 (CH_3CONH); 179.0 (CCONH).

***N*-{3-[2,5-Dioxo-4-(2-thienyl)imidazolidin-4-yl]propyl}acetamide (3e).** Yield 87%, m.p. 120 °C. Found (%): C, 51.29; H, 5.27. $C_{12}H_{15}N_3O_3S$. Calculated (%): C, 51.23; H, 5.37. IR, ν/cm^{-1}: 1650 (H_3CCONH); 1720 ($(HN)_2C$=O). ^{1}H NMR ($(CD_3)_2SO$), δ: 1.20—1.35 (m, 2 H, CH_2—CH_2—CH_2); 1.75 (s, 3 H, CH_3CO); 1.70—2.00 (m, 2 H, C—CH_2—CH_2—CH_2—NH); 2.90—3.05 (m, 2 H, CH_2—NH); 7.01 (dd, 1 H, $H_{Ar}(4)$, ^3J_H = 5.13 Hz, ^3J_H = 3.76 Hz); 7.06 (dd, 1 H, $H_{Ar}(3)$, ^3J_H = 3.76 Hz, ^3J_H = 1.37 Hz); 7.47 (dd, 1 H, $H_{Ar}(5)$, ^3J_H = 5.13 Hz, ^3J_H = 1.37 Hz); 7.65 (s, 1 H, CONHCO); 7.92 (t, 1 H, CH_3CONH, ^3J_H = 7 Hz). ^{13}C NMR ($(CD_3)_2SO$), δ: 22.5 (CH_3CO); 23.8 (CH_2—CH_2—CH_2); 35.9 (C—CH_2—CH_2); 38.1 (CH_2—NH); 66.0 (C—CH_2); 124.5, 125.8, 128.3, 143.2 (C_{Ar}); 156.7 (NHCONH); 169.0 (CH_3CONH); 175.4 (CCONH).

Hydrolysis of hydantoins 1a,f and 3a to amino acids (general procedure). A mixture of hydantoin (5 mmol) and barium hydroxide octahydrate (3.17 g, 10 mmol) in 20 mL of water was heated in a steel autoclave (oil bath, 165—185 °C) for 24 h, cooled to room temperature, and transferred to a flask. Ammonium bicarbonate (1.2 g) was added and the reaction mixture was slightly refluxed for 3 to 4 h. The precipitate of barium carbonate that formed was filtered off and the filtrate was evaporated to dryness in a rotary evaporator. The residue was triturated in a porcelain mortar with hot anhydrous ethanol, the precipitate was filtered off, and the filtrate was evaporated to dryness. The resulting residue was recrystallized from anhydrous

ethanol and dried with continuous stirring at 80 to 90 °C *in vacuo* (oil pump, 1—1.5 h).

In the hydrolysis of 5-phenyl-5-(3-acetylaminopropyl)hydantoin **3a**, the reaction mixture from the autoclave was treated with conc. H_2SO_4 (0.52 mL). The precipitate of barium sulfate that formed was filtered off, the aqueous phase was concentrated, and the product was extracted from the dry residue with hot methanol (30 mL). The solvent was removed and the product was dried *in vacuo* (oil pump).

2,7-Diamino-2-phenylheptanoic acid (4) was obtained in 50% yield, m.p. 175 °C (decomp.). Found (%): C, 58.17; H, 8.75. $C_{13}H_{24}N_2O_4$. Calculated (%): C, 58.33; H, 8.88. IR, ν/cm^{-1}: 1610 (COOH). ^{1}H NMR (CD_3OD), δ: 1.37—1.55 (m, 4 H, $CH_2—C\underline{H}_2—C\underline{H}_2—CH_2—CH_2—NH_2$); 1.65—1.76 (m, 2 H, $C\underline{H}_2—CH_2—NH_2$); 2.31 (m, 2 H, $C—C\underline{H}_2—CH_2$); 2.92 (m, 2 H, $C\underline{H}_2NH_2$); 7.34 (t, 1 H, $H_{Ar}(4)$, ^3J_H = 7.03 Hz); 7.41 (dd, 2 H, $H_{Ar}(3)$, $H_{Ar}(5)$, ^3J_H = 7.83 Hz, ^3J_H = 7.03 Hz); 7.58 (d, 2 H, $H_{Ar}(2)$, $H_{Ar}(6)$, ^3J_H = 7.83 Hz). ^{13}C NMR (CD_3OD), δ: 24.5, 27.4, 28.0, 37.0, 40.5 ($—CH_2—CH_2—CH_2—CH_2—CH_2—NH_2$); 68.0 ($\underline{C}—CH_2$); 127.3 ($C_{Ar}(3)$, $C_{Ar}(5)$); 129.4 ($C_{Ar}(4)$); 129.8 ($C_{Ar}(2)$, $C_{Ar}(6)$); 139.8 ($C_{Ar}(1)$); 175.0 (COOH).

4-(*tert*-Butyl)-2-oxo-1,3-diazacyclononane-4-carboxylic acid (5) was obtained as dihydrate in 65% yield, m.p. 185—187 °C. Found (%): C, 59.48; H, 9.83. $C_{12}H_{22}N_2O_3$. Calculated (%): C, 59.48; H, 9.15. IR, ν/cm^{-1}: 1612 (COOH). ^{1}H NMR (CD_3OD), δ: 1.00 (s, 9 H, Bu^t); 1.25—1.55 (m, 6 H, $CH_2—C\underline{H}_2—C\underline{H}_2—C\underline{H}_2—CH_2$); 1.78 (m, 2 H, $C—C\underline{H}_2$); 2.63 (m, 2 H, $C\underline{H}_2NH_2$); 4.88 (br.s, 2 H, $N\underline{H}CON\underline{H}$). ^{13}C NMR ($CD_3OD$), δ: 24.7 ($CH_2$); 25.3 ($(H_3\underline{C})_3C$); 27.9, 31.7, 33.1, 38.0, 42.2 ($CH_2—CH_2—CH_2—CH_2$, $(H_3C)_3\underline{C}$); 73.1 ($HN\underline{C}COOH$); 161.0 (HNCONH); 180.6 (COOH).

2-Phenylornithine (6) was obtained in 75% yield, m.p. 233—235 °C (decomp.). Found (%): C, 63.07; H, 7.75. $C_{11}H_{16}N_2O_2$. Calculated (%): C, 63.44; H, 7.74. IR, ν/cm^{-1}: 1610 (COOH). ^{1}H NMR (D_2O), δ: 1.63—1.95 (m, 2 H, $CH_2—C\underline{H}_2—CH_2$); 2.29—2.50 (m, 2 H, $CC\underline{H}_2CH_2$); 3.10 (m, 2 H, $C\underline{H}_2NH_2$); 7.45—7.50 (m, 5 H, H_{Ar}). ^{13}C NMR (CD_3OD), δ: 23.3 ($CH_2—\underline{C}H_2—CH_2$); 36.0 ($\underline{C}H_2CCOOH$); 39.25 ($\underline{C}H_2NH_2$); 66.3 ($CH_2\underline{C}COOH$); 127.0 ($C_{Ar}(2)$, $C_{Ar}(6)$); 130.4 ($C_{Ar}(3)$, $C_{Ar}(5)$); 130.7 ($C_{Ar}(4)$); 136.5 ($C_{Ar}(1)$); 171.8 (COOH).

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Received July 2, 2004