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INTERACTION OF 2-NAPHTHOL WITH γ-UREIDOACETALS. A NEW METHOD FOR THE SYNTHESIS OF 2-ARYLPYRROLIDINES

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We report a new, single-stage method for the synthesis of 2-arylpyrrolidines, based on an acid-catalyzed reaction of 2-naphthol with γ-ureidoacetals, enabling the preparation of the target compounds under mild conditions, while avoiding costly reagents and catalysts.

Keywords: acetals, 2-arylpyrrolidines, 2-naphthol, ureas, γ-ureidoacetals.

The 2-arylpyrrolidine fragment is a common feature of many natural and synthetic biologically active compounds. In particular, 2-arylpyrrolidines have been proposed as anticancer drugs [1], medications for the treatment of psychiatric and neurophysiological conditions, such as Parkinson's [2] and Alzheimer's disease [2, 3], glutamate receptor modulators [4], histamine H3 receptor antagonists [5], and PI3 kinase inhibitors [6].

2-Arylpyrrolidine derivatives have been obtained in the Negishi reaction catalyzed by palladium complexes [7], as well as by the interaction of pyrrolidines, containing hydroxy, alkoxy, or acetoxy groups at the α-position, with aromatic organomagnesium or organolithium compounds [8-11]. The arylation of pyrrolidine derivatives in the presence of ruthenium complexes is also known [12]. Another method for the synthesis of 2-arylpyrrolidines involves intra- or intermolecular cyclization of aryl-substituted 1,4-diols or their mesylates [13], 4-hydroxy-substituted amines [14], 1,4-dihalo derivatives of butane [15], and derivatives of pentenamine [16]. The syntheses of 2-arylpyrrolidines using benzaldehyde imine [17] and 4-halo-substituted butanal imine [18] should also be noted. The majority of methods for the synthesis of 2-arylpyrrolidines involve the use of palladium, copper, ruthenium, or iridium complexes as catalysts [16, 19-21].

Several publications [22-24] describe an acid-catalyzed heterocyclization of *N*-(4,4-diethoxybutyl)-amides of substituted phenylacetic acids. However, only a few condensed pyrrolidinotetrahydroisoquinolines have been obtained by this method. In addition, there is a single report of obtaining a moderate yield of 2-(phenylthio)pyrrolidine by the condensation of (4,4-diethoxybutyl)urea in the presence of thiophenol [25], but this approach was not developed further.

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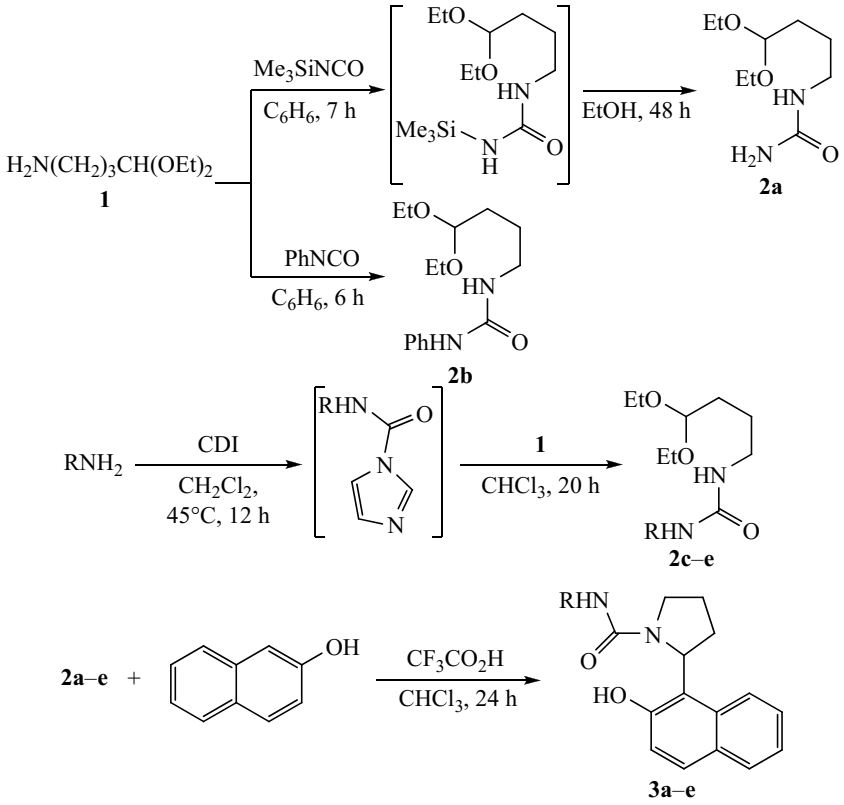
The current methods of α-arylpyrrolidine synthesis have several drawbacks – the use of costly catalysts and/or reagents, harsh reaction conditions, and the often laborious synthesis of starting materials.

Our research group has previously studied the reaction of resorcine and its derivatives with α-ureidoacetals in the presence of trifluoroacetic acid, which resulted in the formation of 5-arylimidazolidin-2-ones [26-29]. Based on these results, and also the aforementioned examples of intramolecular heterocyclization of (4,4-diethoxybutyl)amides in the presence of acidic catalysts [22-24], we assumed that the interaction of (4,4-diethoxybutyl)ureas (γ-ureidoacetals) with phenols may also lead to the formation of aryl-substituted heterocyclic compounds.

The starting γ-ureidoacetals **2a**-**e** were obtained according to the following scheme. The acetal **2a** was synthesized by reacting the γ-aminoacetal **1** with trimethylsilyl isocyanate, followed by treatment of the intermediate with ethanol. The acetal **2b** was obtained analogously by the reaction of γ-aminoacetal **1** with phenyl isocyanate. The acetals **2c**-**e** were obtained by reacting the respective aromatic amines with 1,1'-carbonyldiimidazole (CDI), followed by the treatment of the intermediate *N*-aryl-1*H*-imidazole-1-carboxamides with the γ-aminoacetal **1**.

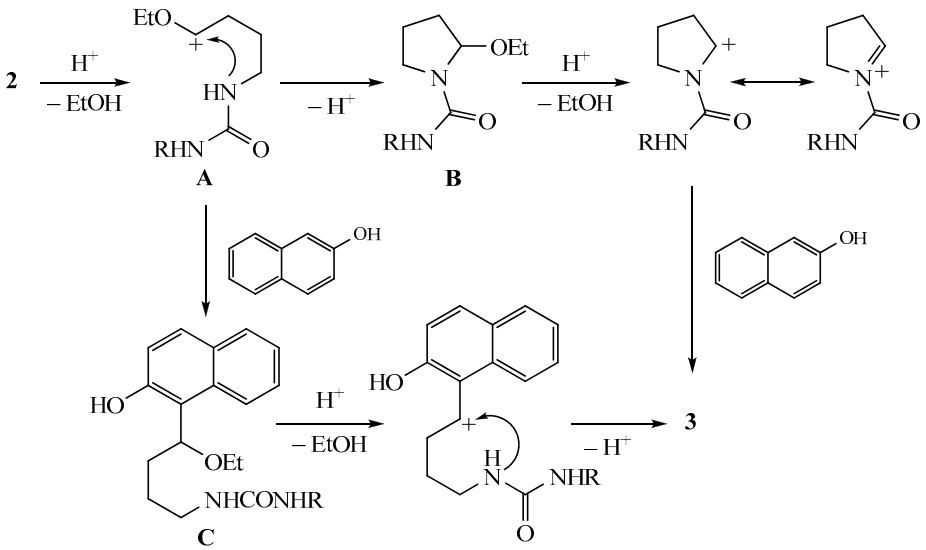
The obtained acetals **2a**-**e** reacted in a 1:1 ratio with 2-naphthol in the presence of equimolar trifluoroacetic acid in chloroform, leading to the pyrrolidines **3a**-**e** containing a naphthyl fragment at position 2 of the heterocycle. This reaction was achieved both with the unsubstituted γ-ureidoacetal **2a**, as well as the γ-ureidoacetals **2b**-**e**, containing an aryl substituent at one of the nitrogen atoms. The target compounds were obtained in 28-78% yields, and the structures were confirmed by NMR spectroscopy.



a R = H, **b** R = Ph, **c** R = *p*-$MeOC_6H_4$, **d** R = *p*-BrC_6H_4, **e** R = *p*-$O_2NC_6H_4$

Taking into account the literature data [24], we propose the following mechanism for the formation of 2-arylpyrrolidine derivatives. One of the ethoxy groups in the acetal molecule is protonated at first, followed by the elimination of an ethanol molecule and the formation of carbocation **A**. The final product may be obtained by two reaction pathways from this point. The first pathway involves an intramolecular cyclization of the

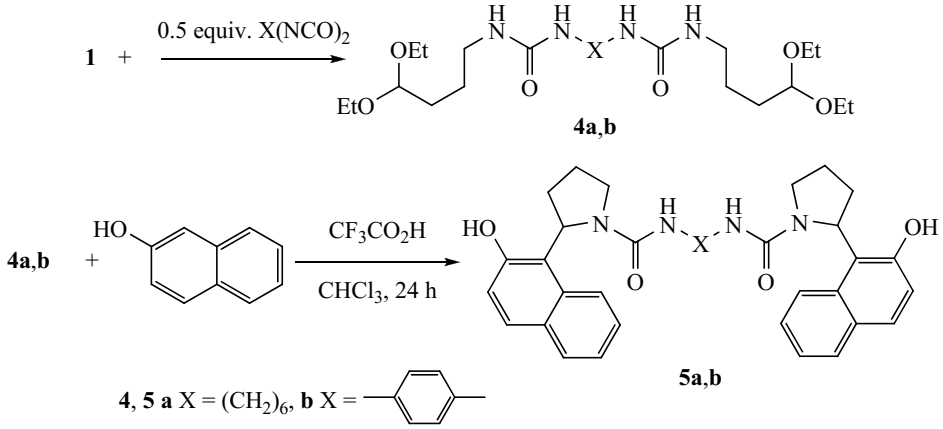
carbocation **A** with the formation of 2-ethoxypyrrolidine **B** and its subsequent interaction with naphthol. The second pathway involves an initial intramolecular reaction of the carbocation **A** with naphthol, leading to the intermediate **C**, and a subsequent intramolecular closure of the heterocycle. The available experimental data do not provide unequivocal evidence in favor of any of these two pathways.



The proposed mechanism also provides an explanation for the substantial decrease of target product yield in the case of acetal **2e**, that contains a *para*-nitro group in the phenyl ring. According to the literature data [30, 31], the phenyl ring, the π-electrons of the C=O bond, and the lone electron pairs of both nitrogen atoms form a conjugated system in phenyl-substituted ureas. The presence of an electron-withdrawing group in the phenyl substituent causes a decrease of electron density on the nitrogen atoms, and thus interferes with the intramolecular cyclization leading to the formation of arylpyrrolidine.

In the course of these investigations, we were interested in the synthesis of compounds with two pyrrolidine fragments in the molecule. For this purpose, we prepared the diacetals **4a**,**b** by interaction of hexamethylene and *para*-phenylene diisocyanate with two equivalents of the γ-aminoacetal **1**.

The reaction of the obtained diacetates **4a**,**b** with 2-naphthol in chloroform in the presence of trifluoroacetic acid led to the formation of the target compounds **5a**,**b** with two pyrrolidine nuclei. Remarkably, the yields of compounds **5a**,**b** were considerably higher than those of compounds **3a**-**e**, and were 94% (compound **5a**) and 90% (compound **5b**).



Due to the presence of two chiral centers in compounds **5a**,**b**, these molecules can exist as two diastereomers, the NMR spectra of which must be different. Nevertheless, the NMR spectra of products **5a**,**b** exhibited only a single set of signals. This may be explained both by the diastereoselectivity of the reaction, as well as by the very small difference of chemical shifts between the respective nuclei of both diastereomers.

Thus, our investigation of γ-ureidoacetal reaction with 2-naphthol has led to the discovery of a convenient single-stage synthesis of novel 2-arylpyrrolidines. The advantages of the method include high yields of the target compounds, mild reaction conditions, and the possibility of avoiding costly reagents.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer in the 400-3600 cm^{-1} interval in Nujol. ^1H NMR spectra were acquired on Bruker Avance 600 and Bruker MSL 400 spectrometers (600 and 400 MHz, respectively) relative to the residual solvent protons ($CDCl_3$ δ = 7.26, $(CD_3)_2SO$ δ 2.50 ppm). ^{13}C NMR spectra were acquired on a Bruker Avance 600 spectrometer (150 MHz) relative to the residual solvent protons ($CDCl_3$ δ = 77.0, $(CD_3)_2SO$ δ 39.5 ppm). The MALDI-TOF mass spectra were recorded on a Bruker ULTRAFLEX III TOF/TOF instrument (with 2,5-dihydroxybenzoic acid matrix). Elemental analysis was performed on Carlo Erba EA 1108 instrument. Melting points were determined in glass capillaries with a Stuart SMP 10 apparatus. Anhydrous solvents were prepared according to the standard procedures.

***N*-(4,4-Diethoxybutyl)urea (2a)**. A solution of 4,4-diethoxybutan-1-amine (**1**) (4.20 g, 26.1 mmol) in benzene (10 ml) was cooled (5-8°C) and treated by dropwise addition of trimethylsilyl isocyanate (3.00 g, 26.1 mmol). The reaction mixture was stirred for 7 h at room temperature. The solvent was removed under vacuum. The residue was dissolved in ethanol (30 ml), maintained at 20°C for 48 h. The solvent was removed, the waxy residue was dried under vacuum (3 h, 0.01 torr). Yield 3.79 g (71%). IR spectrum, ν, cm^{-1}: 1655 (C=O), 2724, 3207, 3390 (N–H). ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.21 (6H, br. t, *J* = 7.1, $2CH_3$); 1.54–1.73 (4H, m, $(CH_2)_2$); 3.15-3.22 (2H, m, CH_2N); 3.50-3.54 (2H, m) and 3.65-3.69 (2H, m, $2OCH_2$); 4.50 (1H, t, *J* = 5.1, CH). Found, %: C 53.21; H 9.93; N 13.81. $C_9H_{20}N_2O_3$. Calculated, %: C 52.92; H 9.87; N 13.71.

***N*-(4,4-Diethoxybutyl)-*N*'-phenylurea (2b)**. A solution of 4,4-diethoxybutan-1-amine (**1**) (2.03 g, 12.6 mmol) in benzene (10 ml) was cooled (5-8ºC) and treated by dropwise addition of phenyl isocyanate (1.50 g, 12.6 mmol). The reaction mixture was stirred for 6 h at room temperature. The solvent was removed under vacuum (20 torr). The light-colored low-melting solid that formed was dried under vacuum (5 h, 0.01 torr) until constant mass. Yield 3.02 g (85%). Mp 66-67°C. IR spectrum, ν, cm^{-1}: 1598 (Ar), 1637 (C=O), 2870, 2926, 2972, 3320 (N–H). ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.16 (6H, br. t, *J* = 7.1, $2CH_3$); 1.46-1.62 (4H, m, $(CH_2)_2$); 3.10-3.16 (2H, m, CH_2N); 3.37-3.50 (2H, m) and 3.51-3.66 (2H, m, $2OCH_2$); 4.39 (1H, t, *J* = 5.5, CH); 6.96 (1H, br. t, *J* = 7.3, H Ar); 7.20 (2H, br. t, *J* = 8.1, H Ar); 7.25 (2H, br. d, *J* = 7.5, H Ar). Found, %: C 64.09; H 8.71; N 9.89. $C_{15}H_{24}N_2O_3$. Calculated, %: C 64.26; H 8.63; N 9.99.

***N*-(4,4-Diethoxybutyl)-*N*'-(4-methoxyphenyl)urea (2c)**. A solution of *para*-anisidine (1.38 g, 11.2 mmol) in CH_2Cl_2 (11 ml) was treated with 1,1'-carbonyldiimidazole (2.00 g, 12.3 mmol). The reaction mixture was heated for 12 h at 45ºC, then cooled. The precipitate that formed was collected by vacuum filtration. The obtained *N*-(4-methoxyphenyl)-1*H*-imidazole-1-carboxamide solution in chloroform (10 ml) was treated with 4,4-diethoxybutan-1-amine (**1**) (1.81 g, 11.2 mmol). The mixture was stirred for 20 h at room temperature. The precipitate was collected by vacuum filtration and washed with water. The product was dried under vacuum (3 h, 0.01 torr) until constant mass. Yield 2.23 g (64%). Mp 92-93°C. IR spectrum, ν, cm^{-1}: 1584 (Ar), 1631 (C=O), 2727, 2875, 2960, 3345 (N–H). ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.17 (6H, br. t, *J* = 7.0, $2CH_3$); 1.51-1.67 (4H, m, $(CH_2)_2$); 3.17-3.25 (2H, m, CH_2N); 3.42-3.51 (2H, m) and 3.58-3.67 (2H, m, $2OCH_2$); 3.76 (3H, s, OCH_3); 4.45 (1H, t, *J* = 5.3, CH); 5.35 (1H, br. s, NH); 6.81 (2H, br. d, *J* = 8.8, H Ar); 7.03 (1H, br. s, NH); 7.18 (2H, br. d, *J* = 8.8, H Ar). Found, %: C 62.02; H 8.19; N 8.92. $C_{16}H_{26}N_2O_4$. Calculated, %: C 61.91; H 8.44; N 9.03.

***N*-(4-Bromophenyl)-*N*'-(4,4-diethoxybutyl)urea (2d)** was obtained analogously to compound **2c** from *para*-bromoaniline (1.93 g, 11.3 mmol), 1,1'-carbonyldiimidazole (2.00 g, 12.3 mmol), and 4,4-diethoxybutan-1-amine (**1**) (1.63 g, 10.1 mmol). Yield 2.16 g (54%). Mp 134-135°C. IR spectrum, ν, cm^{-1}: 1591 (Ar), 1636 (C=O), 2726, 2870, 2935, 3360 (N–H). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.10 (6H, br. t, *J* = 7.0, $2CH_3$); 1.41-1.56 (4H, m, $(CH_2)_2$); 3.05-3.12 (2H, m, CH_2N); 3.39-3.47 (2H, m) and 3.52-3.61 (2H, m, $2CH_2O$); 4.46 (1H, t, *J* = 5.5, CH); 7.36-7.38 (4H, br. s, H Ar). Found, %: C 49.99; H 6.58; Br 22.19; N 7.70. $C_{15}H_{23}BrN_2O_3$. Calculated, %: C 50.15; H 6.45; Br 22.24; N 7.80.

***N*-(4,4-Diethoxybutyl)-*N*'-(4-nitrophenyl)urea (2e)** was obtained analogously to compound **2c** from *para*-nitroaniline (1.55 g, 11.2 mmol), 1,1'-carbonyldiimidazole (2.00 g, 12.3 mmol), and 4,4-diethoxybutan-1-amine (**1**) (1.11 g, 6.87 mmol). Yield 0.77 g (21%). Mp 61-62°C. IR spectrum, ν, cm^{-1}: 1333, 1558 (NO_2), 1601 (Ar), 1668 (C=O), 2725, 2890, 2920, 3365 (N–H). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.13 (6H, br. t, *J* = 7.1, CH_3); 1.52-1.64 (4H, m, $(CH_2)_2$); 3.20-3.27 (2H, m, CH_2N); 3.40-3.51 (2H, m) and 3.56-3.65 (2H, m, CH_2O); 4.41-4.45 (1H, m, CH); 6.07 (1H, br. s, NH); 7.48 (2H, br. d, *J* = 9.0, H Ar); 8.03 (2H, br. d, *J* = 8.9, H Ar); 8.62 (1H, br. s, NH). Found, %: C 55.48; H 7.20; N 12.77. $C_{15}H_{23}N_3O_5$. Calculated, %: C 55.37; H 7.13; N 12.91.

2-(2-Hydroxynaphth-1-yl)pyrrolidine-1-carboxamide (3a). A solution of compound **2a** (0.50 g, 2.45 mmol) in anhydrous chloroform (10 ml) was treated with 2-naphthol (0.35 g, 2.45 mmol) and trifluoroacetic acid (0.28 g, 2.45 mmol). The reaction mixture was stirred for 24 h at room temperature. The precipitate that formed was filtered off, washed with chloroform, and dried under vacuum (4 h, 0.01 torr). Yield 0.39 g (62%). Mp 214-215°C. IR spectrum, ν, cm^{-1}: 3459, 3335 (O–H), 3205, 3064, 2976, 2882 (N–H), 1608 (Ar), 1650 (C=O). ^{1}H NMR spectrum (600 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.80-1.93 (1H, m), 1.95-2.07 (2H, m) and 2.19-2.28 (1H, m, $(CH_2)_2$); 3.52-3.60 (1H, m) and 3.64-3.71 (1H, m, NCH_2); 5.11-5.28 (2H, br. s, NH_2); 5.51-5.56 (1H, m, CHN); 7.08 (1H, d, *J* = 8.8, H Ar); 7.21-7.26 (1H, m, H Ar); 7.35-7.40 (1H, m, H Ar); 7.62 (1H, d, *J* = 8.8, H Ar); 7.72-7.76 (1H, m, H Ar); 7.93-7.97 (1H, m, H Ar). ^{13}C NMR spectrum ($(CD_3)_2SO$), δ, ppm: 25.8; 33.9; 48.1; 54.9; 119.4; 120.0; 123.1; 123.5; 126.9; 129.4; 129.6; 129.7; 132.8; 153.4; 158.1. Mass spectrum (MALDI), *m*/*z* (I_{rel}, %): 279 $[M+Na]^+$ (100), 295 $[M+K]^+$ (10). Found, %: C 70.27; H 6.28; N 10.93. $C_{15}H_{16}N_2O_2$. Calculated, %: C 70.29; H 6.29; N 10.93.

2-(1-Hydroxynaphth-1-yl)-*N*-phenylpyrrolidine-1-carboxamide (3b) was obtained analogously to compound **3a** from compound **2b** (0.50 g, 1.79 mmol), 2-naphthol (0.26 g, 1.70 mmol), and trifluoroacetic acid (0.20 g, 1.79 mmol) in anhydrous chloroform (10 ml). Yield 0.46 g (78%). Mp 219-220°C. IR spectrum, ν, cm^{-1}: 3388 (O–H), 3053, 2978, 2874 (N–H), 1618 (C=O), 1594 (Ar). ^{1}H NMR spectrum (600 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.96-2.24 (3H, m) and 2.30-2.39 (1H, m, $(CH_2)_2$); 3.79-3.89 (2H, m, NCH_2); 5.78-5.84 (1H, m, CHN); 6.83-6.88 (1H, m, H Ar); 7.12-7.17 (2H, m, H Ar); 7.20 (1H, d, *J* = 8.8, H Ar); 7.25-7.29 (2H, m, H Ar); 7.29-7.34 (1H, m, H Ar); 7.45-7.50 (1H, m, H Ar); 7.71 (1H, d, *J* = 8.8, H Ar); 7.68-7.78 (1H, br. s, NH); 7.80-7.84 (1H, m, H Ar); 8.08-8.13 (1H, m, H Ar). ^{13}C NMR spectrum ($(CD_3)_2SO$), δ, ppm: 26.0; 33.2; 48.3; 55.1; 119.4; 119.9; 122.2; 123.1; 123.4; 126.9; 129.2 (2C); 129.5 (2C); 129.7; 132.9; 141.3; 153.4; 154.4. Mass spectrum, *m*/*z* (I_{rel}, %): 355 $[M+Na]^+$ (100), 370 $[M+K]^+$ (24). Found, %: C 75.87; H 6.08; N 8.42. $C_{21}H_{20}N_2O_2$. Calculated, %: C 75.88; H 6.06; N 8.43.

2-(2-Hydroxynaphth-1-yl)-*N*-(4-methoxyphenyl)pyrrolidine-1-carboxamide (3c) was obtained analogously to compound **3a** from compound **2c** (0.30 g, 0.97 mmol), 2-naphthol (0.12 g, 0.97 mmol), and trifluoroacetic acid (0.11 g, 0.97 mmol) in anhydrous chloroform (5 ml). Yield 0.17 g (47%). Mp 201-202°C. IR spectrum, ν, cm^{-1}: 3396 (O–H), 3051, 2976, 2870 (N–H), 1614 (C=O), 1587 (Ar). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.92-2.06 (1H, m), 2.08-2.20 (2H, m) and 2.27-2.37 (1H, m, $(CH_2)_2$); 3.64 (3H, s, OCH_3); 3.75-3.86 (2H, m, NCH_2); 5.72-5.79 (1H, m, CHN); 6.68-6.73 (2H, m, H Ar); 7.10-7.14 (2H, m, H Ar); 7.16 (1H, d, *J* = 8.4, H Ar); 7.25-7.30 (1H, m, H Ar); 7.41-7.46 (1H, m, H Ar); 7.50-7.55 (1H, br. s, NH); 7.67 (1H, d, *J* = 8.4, H Ar); 7.76-7.80 (1H, m, H Ar); 8.04-8.09 (1H, m, H Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 362 $[M]^+$ (10), 385 $[M+Na]^+$ (100), 401 $[M+K]^+$ (5). Found, %: C 72.90; H 6.10; N 7.72. $C_{22}H_{22}N_2O_3$. Calculated, %: C 72.91; H 6.12; N 7.73.

***N*-(4-Bromophenyl)-2-(2-hydroxynaphth-1-yl)pyrrolidine-1-carboxamide (3d)** was obtained analogously to compound **3a** from compound **2d** (0.10 g, 0.28 mmol), 2-naphthol (0.04 g, 0.28 mmol), and trifluoroacetic acid (0.03 g, 0.28 mmol) in anhydrous chloroform (5 ml). Yield 0.07 g (62%). Mp 183-184°C. IR spectrum, ν, cm^{-1}: 3378 (O–H), 3052, 2980, 2873 (N–H), 1629 (C=O), 1587 (Ar). ^{1}H NMR spectrum (600 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.95-2.05 (1H, m), 2.06-2.17 (2H, m) and 2.26-2.35 (1H, m, $(CH_2)_2$); 3.74-3.85 (2H, m, NCH_2); 5.74-5.80 (1H, m, CH); 7.14 (1H, d, *J* = 8.8, H Ar); 7.25-7.30 (5H, m, H Ar); 7.41-7.46 (1H, m, H Ar); 7.65 (1H, d, *J* = 8.8, H Ar); 7.76-7.80 (1H, m, H Ar); 7.93-8.00 (1H, br. s, NH); 8.04-8.09 (1H, m, H Ar). ^{13}C NMR spectrum ($(CD_3)_2SO$), δ, ppm: 26.1; 33.0; 48.4; 55.3; 113.5; 119.5; 120.1; 121.3; 123.1; 123.4; 126.8; 129.2; 129.4; 129.6; 131.9; 133.0; 140.9; 153.2; 154.2. Mass spectrum, *m*/*z* (I_{rel}, %): 434 $[M+Na]^+$ (100), 449 $[M+K]^+$ (21). Found, %: C 61.32; H 4.67; Br 19.41; N 6.80. $C_{21}H_{19}BrN_2O_2$. Calculated, %: C 61.33; H 4.66; Br 19.43; N 6.81.

2-(2-Hydroxynaphth-1-yl)-*N*-(4-nitrophenyl)pyrrolidine-1-carboxamide (3e) was obtained analogously to compound **3a** from compound **2e** (0.10 g, 0.31 mmol), 2-naphthol (0.04 g, 0.31 mmol), and trifluoroacetic acid (0.04 g, 0.31 mmol) in anhydrous chloroform (5 ml). Yield 0.03 g (28%). Mp 185-186°C. IR spectrum, ν, cm^{-1}: 3360 (O–H), 3211, 3050, 2973, 2880 (N–H), 1644 (C=O), 1541, 1340 (NO_2). ^{1}H NMR spectrum (600 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.96-2.07 (1H, m), 2.07-2.19 (2H, m) and 2.28-2.37 (1H, m, CH_2); 3.77-3.91 (2H, m, NCH_2); 5.78-5.83 (1H, m, CHN); 7.12 (1H, d, *J* = 8.8, H Ar); 7.25-7.30 (1H, m, H Ar); 7.41-7.46 (1H, m, H Ar); 7.58-7.63 (2H, m, H Ar); 7.64 (1H, d, *J* = 8.8, H Ar); 7.75-7.79 (1H, m, H Ar); 8.02-8.09 (3H, m, H Ar); 8.64-8.80 (1H, br. s, NH). ^{13}C NMR spectrum ($(CD_3)_2SO$), δ, ppm: 25.7; 32.4; 48.1; 55.3; 118.1; 119.1; 119.7; 122.6; 122.9; 125.1; 126.4; 128.7; 128.9; 129.1; 132.6; 140.9; 147.9; 152.8; 153.0. Mass spectrum (MALDI), *m*/*z* (I_{rel}, %): 400 $[M+Na]^+$ (100). Found, %: C 66.80; H 5.10; N 11.09. $C_{21}H_{19}N_3O_4$. Calculated, %: C 66.83; H 5.07; N 11.13.

1,1'-Hexane-1,6-diylbis[3-(4,4-diethoxybutyl)urea] (4a). Compound **1** (3.60 g, 22.4 mmol) was added dropwise with cooling (5-8°C) to a solution of 1,6-diisocyanatohexane (1.88 g, 11.2 mmol) in benzene (20 ml). The reaction mixture was stirred for 72 h at room temperature. The precipitate was filtered off. The white precipitate was dried under vacuum (3 h, 0.01 torr). Yield 4.79 g (88%). Mp 138-139°C. IR spectrum, ν, cm^{-1}: 3325, 2983, 2874 (N–H), 1619 (C=O). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.12 (12H, br. t, *J* = 6.8, $4CH_3$); 1.20-1.29 (4H, m, $2CH_2$); 1.34-1.42 (4H, m, $2CH_2$); 1.44-1.52 (4H, m, $2CH_2$); 1.53-1.62 (4H, m, $2CH_2$); 3.01-3.16 (8H, m, $4CH_2N$); 3.37-3.48 (4H, m, $2CH_2O$); 3.52-3.63 (4H, m, $2CH_2O$); 4.37-4.44 (2H, m, 2CH). Found, %: C 59.00; H 10.02; N 11.11. $C_{24}H_{50}N_4O_6$. Calculated, %: C 58.75; H 10.27; N 11.42.

1,1'-Phenylene-1,4-diylbis[3-(4,4-diethoxybutyl)urea] (4b). 1,4-Diisocyanatophenylene (0.89 g, 5.59 mmol) was added to a solution of compound **1** (1.80 g, 11.2 mmol) in toluene (30 ml). The mixture was stirred for 96 h. The precipitate was filtered off. The white precipitate was dried under vacuum (3 h, 0.01 torr). Yield 2.44 g (91%). Mp 189-190°C. IR spectrum, ν, cm^{-1}: 3331, 2969, 2870 (N–H), 1629 (C=O), 1565 (Ar). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.11 (12H, br. t, *J* = 7.0, $4CH_3$); 1.39-1.48 (4H, m, $2CH_2$); 1.49-1.56 (4H, m, $2CH_2$); 3.02-3.10 (4H, m, $2CH_2N$); 3.39-3.48 (4H, m, $2CH_2O$); 3.52-3.61 (4H, m, $2CH_2O$); 4.47 (2H, t, *J* = 5.47, 2CH); 7.21 (4H, br. s, H Ar). Found, %: C 60.01; H 8.96; N 11.84. $C_{24}H_{42}N_4O_6$. Calculated, %: C 59.73; H 8.77; N 11.61.

***N*,*N*'-Hexane-1,6-diylbis[2-(2-hydroxynaphth-1-yl)pyrrolidine-1-carboxamide] (5a)**. A solution of compound **4a** (0.50 g, 1.02 mmol) in anhydrous chloroform (10 ml) was treated with 2-naphthol (0.29 g, 2.04 mmol) and trifluoroacetic acid (0.24 g, 1.02 mmol). The reaction mixture was stirred for 24 h at room temperature. The precipitate that formed was filtered off and dried under vacuum (4 h, 0.01 torr). Yield 0.57 g (94%). Mp 189-190°C. IR spectrum, ν, cm^{-1}: 3417 (O–H), 3056, 2934, 2872 (N–H), 1609 (C=O), 1590, 1563 (Ar). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 0.60-0.65 (4H, br. m, $2CH_2$); 0.88-0.95 (4H, br. m, $2CH_2$); 1.85-1.95 (2H, m), 2.01-2.12 (4H, m) and 2.21-2.30 (2H, m, $4CH_2$); 2.64-2.72 (2H, m) and 2.74-2.82 (2H, m, $2CH_2$); 3.56-3.64 (2H, m) and 3.68-3.75 (2H, m, $2CH_2$); 5.08-5.15 (2H, br. s, 2NH); 5.54-5.60 (2H, m, 2CHN); 7.09 (2H, d, *J* = 8.8, H Ar); 7.21-7.26 (2H, m, H Ar); 7.37-7.41 (2H, m, H Ar); 7.61 (2H, d, *J* = 8.8,

H Ar); 7.71-7.75 (2H, m, H Ar); 7.96-8.00 (2H, m, H Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 617 $[M+Na]^+$ (100). Found, %: C 72.21; H 7.12; N 9.40. $C_{36}H_{42}N_4O_4$. Calculated, %: C 72.20; H 7.12; N 9.42.

***N*,*N*'-Phenylene-1,4-diylbis[2-(2-hydroxynaphth-1-yl)pyrrolidine-1-carboxamide] (5b)** was obtained analogously to compound **5a** from compound **4b** (0.50 g, 1.04 mmol), 2-naphthol (0.30 g, 2.07 mmol), and trifluoroacetic acid (0.24 g, 2.07 mmol). Yield 0.55 g (90%). Mp 218-219°C. IR spectrum, ν, cm^{-1}: 3390 (O–H), 3058, 2973, 2875 (N–H), 1620 (C=O), 1598 (Ar). ^{1}H NMR spectrum (400 MHz, $(CD_3)_2SO$), δ, ppm (*J*, Hz): 1.84-1.96 (2H, m), 2.00-2.11 (4H, m), and 2.18-2.27 (2H, m, $4CH_2$); 3.66-3.73 (4H, m, $2CH_2$); 5.63-5.69 (2H, m, 2CHN); 6.92-6.96 (4H, br. s, H Ar); 7.07 (2H, d, *J* = 8.8, H Ar); 7.19-7.24 (2H, m, H Ar); 7.34-7.39 (2H, m, H Ar); 7.44-7.54 (2H, br. s, 2NH); 7.60 (2H, d, *J* = 8.8, H Ar); 7.70-7.74 (2H, m, H Ar); 7.95-8.00 (2H, m, H Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 587 $[M+H]^+$ (11), 609 $[M+Na]^+$ (100), 625 $[M+K]^+$ (6). Found, %: C 73.68; H 5.83; N 9.53. $C_{36}H_{34}N_4O_4$. Calculated, %: C 73.70; H 5.84; N 9.55.

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