ISSN 1070-3632, Russian Journal of General Chemistry, 2019, Vol. 89, No. 2, pp. 204–211. © Pleiades Publishing, Ltd., 2019.
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Catalytic Aminomethylation of Aminobenzamides with Bis(*N*,*N*-dimethylamino)methane and Carbamides

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Received July 12, 2018; revised July 12, 2018; accepted July 16, 2018

Abstract—An effective method was developed for the synthesis of acyclic aniline derivatives bearing carbamide fragments by the reaction of carbamides with *ortho*-, *meta*-, and *para*-aminobenzamides and bis(*N*,*N*-dimethylamino)methane in the presence of $NiCl_2·6H_2O$ and $SmCl_3·6H_2O$ as catalysts.

Keywords: aminomethylation, aminobenzamides, bis(*N*,*N*-dimethylamino)methane, carbamides

DOI: 10.1134/S1070363219020063

Aminomethylation reaction of acid amides with formaldehyde and NH-acids is still the classical method for the preparation of aminomethylated acid amides [1–10]. We have shown that catalytic aminomethylation of primary alkylamines [11] or aryl carboxylic acid hydrazides [12] using bis(*N*,*N*-dimethylamino)methane and (thio)urea or *N*,*N*'-bis[(dimethylamino)methyl]-(thio)carbamides is a convenient method for the synthesis of nitrogen-containing heterocycles bearing carbamide fragments under mild conditions.

Nitrogen-containing heterocycles with carbamide fragments show antiviral and antibacterial activity [13], are promising synthons for producing alkaloids with antitumor properties [14, 15], as wells they are used as pesticides [16] and fuels bioprotectors [17]. Aminobenzamides and their derivatives are prospective enzyme glucokinase activators [18, 19], luminescent markers in biological systems [20], exhibit antitumor [21–23] and antibacterial activity [24].

Continuing the study of catalytic aminomethylation reaction at the primary amino group [11, 12], herein we reported an effective method for synthesizing *N*-substituted aniline derivatives containing urea fragments that are promising for practical use based on the aminomethylation of *ortho*-, *meta*- and *para*-aminobenzamides with use of bis(*N*,*N*-dimethylamino) methane and some carbamides (urea, biuret, semicarbazide hydrochloride), as well as *N*,*N*'-bis(dimethylaminomethyl)urea, *N*,*N*'-bis[(dimethylamino)methyl]allophanamide and *N*-({[(dimethylamino)methyl][(2-methylhydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine in the presence of transition or rare-earth metals catalysts.

Using the example of aminomethylation of *ortho*-aminobenzamide with bis(*N*,*N*-dimethylamino)methane and urea, it was found that among the tested catalysts based on *d*- and *f*-elements, $NiCl_2·6H_2O$ is better of choice (67%, see table). When using the reagents ratio *ortho*-aminobenzamide : bis(*N*,*N*-dimethylamino)methane : urea : $NiCl_2·6H_2O$ = 10 : 20 : 10 : 2, the reaction takes place in EtOH at 70°C over 12 hours to form 2-({[({[(dimethylamino)methyl]amino}carbonyl)amino]methyl}-amino)benzamide **1** (Scheme 1).

Aminomethylation of *meta*- and *para*-aminobenzamides with urea and bis(*N*,*N*-dimethylamino)methane with the reagents ratio aminobenzamide : bis(*N*,*N*-dimethylamino)methane : urea : $NiCl_2·6H_2O$ = 10 : 20 : 10 : 2 in EtOH at 70°C for 24 hours leads to the aminomethylated products **3** (64%) and **5** (70%, Scheme 2).

The minor products of the aminomethylation reaction of aminobenzamides are 2(3,4)-amino-*N*-[(dimethylamino)methyl]benzamides **2**, **4** and **6** with yields of no more than 10%. Their formation is probably due to generation of aminobenzamide complexes with $NiCl_2·6H_2O$ [25] or $SmCl_3·6H_2O$, The effect of the nature of the solvent and the catalyst on the yield of compounds **1** and **2**[a]

Catalyst	Solvent	Yield of **1** (**2**), %	Catalyst	Solvent	Yield of **1** (**2**), %
$NiCl_2 \cdot 6H_2O$	EtOH	67 (5)	$Sm(NO_3)_3 \cdot 6H_2O$	EtOH	15 (5)
″	EtOH–$CHCl_3$	59 (8)	$ZnCl_2 \cdot 2H_2O$	″	5 (5)
″	$CHCl_3$	32 (5)	Cs_2CO_3	″	5 (5)
$Ni(NO_3)_2 \cdot 6H_2O$	EtOH	54 (4)	$CuCl_2 \cdot 2H_2O$	″	5 (–)
$SmCl_3 \cdot 6H_2O$	″	24 (5)	$FeCl_3 \cdot 6H_2O$	″	– (–)

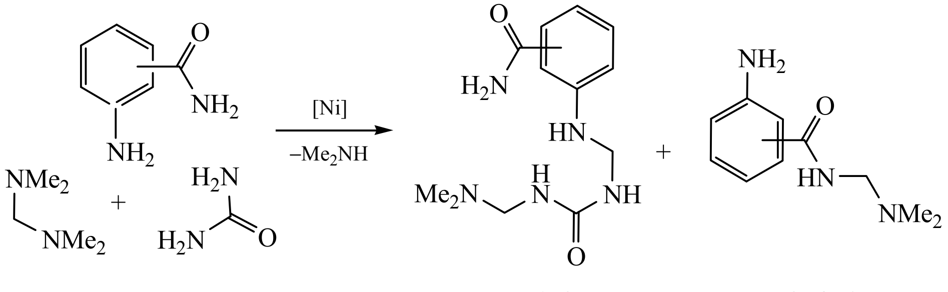
[a] Reaction conditions: aminobenzamide : bis(*N*,*N*-dimethylamino)methane : carbamide : catalyst = 10 : 20 : 10 : 2, 70°C, EtOH, 12 h.

which undergoes aminomethylation with bis(*N*,*N*-dimethylamino)methane at the amide group (Scheme 2). In the absence of a catalyst, the reaction does not proceed.

Along with urea, biuret and semicarbazide hydrochloride were involved into the reaction of catalytic aminomethylation of aminobenzamides with bis(*N*,*N*-dimethylamino)methane. Under optimal conditions [aminobenzamide : bis(*N*,*N*-dimethylamino)methane : biuret : $SmCl_3 \cdot 6H_2O$ = 10 : 20 : 10 : 2, 70°C, EtOH, 12 h] aminomethylation of *ortho*-, *meta*- and *para*-aminobenzamides results in acyclic derivatives of aminobenzamides **7** (43%), **8** (40%) and **9** (51%, Scheme 3). When $NiCl_2 \cdot 6H_2O$ is used as a catalyst, the yield of compounds **7**–**9** is 11, 10, and 15%, respectively, while the yield of 2(3,4)-amino-*N*-[(dimethylamino)methyl]benzamides **2**, **4** and **6** does not exceed 20%.

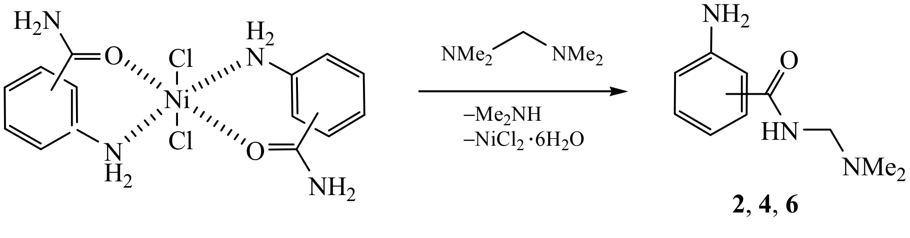
Aminomethylation with semicarbazide hydrochloride and bis(*N*,*N*-dimethylamino)methane using $SmCl_3 \cdot 6H_2O$ as a catalyst under similar conditions [aminobenzamide : bis(*N*,*N*-dimethylamino)methane : semicarbazide hydrochloride : $SmCl_3 \cdot 6H_2O$ = 10 : 30 : 10 : 2, 70°C, EtOH, 24 h] leads to the formation of 3- and 4-[({[(dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl) amino]benzamides **10** and **11** with yields of 58 and 36%, respectively. Attempts to involve *ortho*-aminobenzamide into the

Scheme 1.

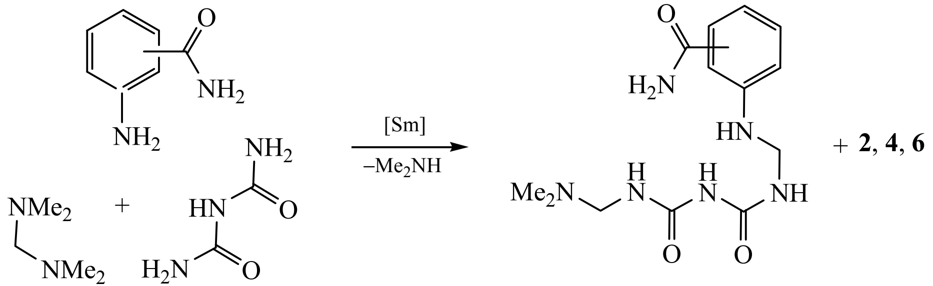


ortho (**1**, **2**), *meta* (**3**, **4**), *para* (**5**, **6**).

Scheme 2.



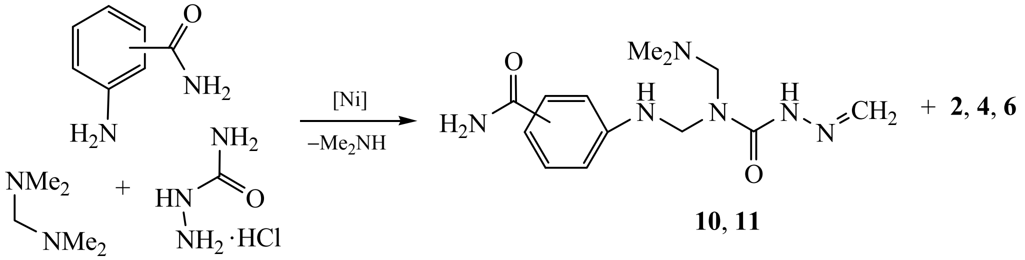
Scheme 3.



7-9

ortho (**7**), *meta* (**8**), *para* (**9**).

Scheme 4.



10, **11**

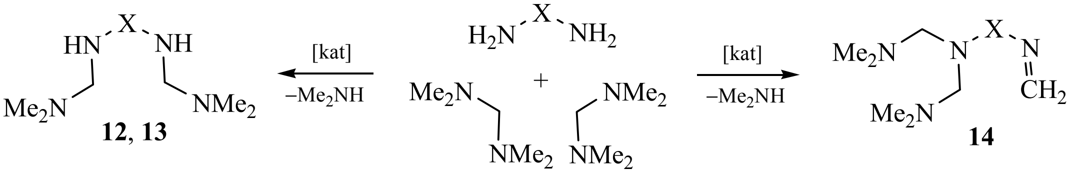
meta (**10**), *para* (**11**).

aminomethylation reaction failed (Scheme 4). Aminomethylation in the presence of $NiCl_2$ *ortho*-aminobenzamide provides the reaction products **10** and **11** in 40 and 29% yield, respectively. Under these conditions, the yield of aminomethylated products **2**, **4**, and **6** does not exceed 30%; in the absence of a catalyst, the aminomethylation reaction does not proceed.

It can be assumed [11, 12] that the aminomethylation reaction of aminobenzamides with use of bis(*N*,*N*-dimethylamino)methane and carbamides goes through a stage of intermediate formation of aminomethylated carbamide derivatives, which then react with aminobenzamides to form the target products. To verify this assumption, we synthesized *N*,*N*′-bis(dimethylaminomethyl)urea **12**, *N*,*N*′-bis [(dimethylamino)methyl]allophanamide **13** and *N*-({[(dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine **14** by aminomethylation of carbamides with bis(*N*,*N*-dimethylamino)methane [carbamide : bis(*N*,*N*-dimethylamino)methane : $SmCl_3 \cdot 6H_2O$ = 10 : 10 : 0.5, 80°C, EtOH, 8 h] (Scheme 5) [11].

N,*N*′-Bis(dimethylaminomethyl)carbamide **12** reacts with *ortho*-, *meta*- and *para*-aminobenzamides [aminobenzamide : **12** : $NiCl_2 \cdot 6H_2O$ = 10 : 10 : 2, 70°C, EtOH, 24 h] with the formation of the products **1**, **3** and **5** with yields of 30, 31 and 38%, respectively. The reaction of aminobenzamides with *N*,*N*′-bis[(dimethylamino)methyl]allophanamide (aminobenzamide : **13** : $NiCl_2 \cdot 6H_2O$ = 10 : 10 : 2, 70°C, EtOH, 24 h) takes place with the formation of compounds **7** (14%), **8** (20%) and **9** (22%, Scheme 6). In the case of *N*-({[(dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine **14**, the

Scheme 5.

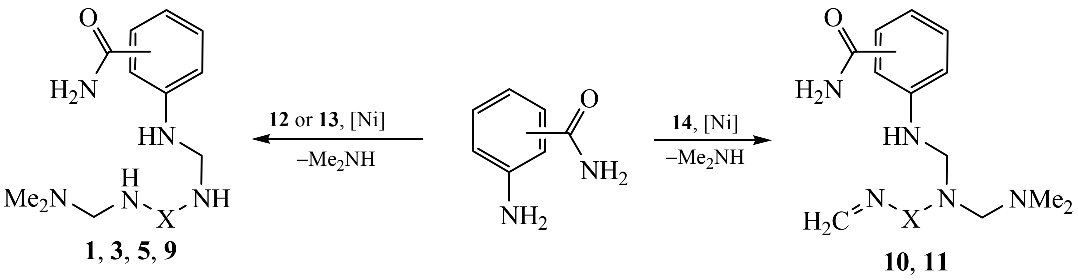


12, **13**

14

X = C=O (**12**), O=CNHC=O (**13**), C(O)NH (**14**).

Scheme 6.



X = C=O (**1**, **3**, **5**), O=CNHC=O (**7**–**9**), C(O)NH (**11**).

reaction with *meta*- and *para*-aminobenzamides under similar conditions [aminobenzamide : **14** : $NiCl_2·6H_2O$ = 10 : 10 : 2, 70°C, EtOH, 24 h] leads to the formation of compounds **10** (15%) and **11** (11%); *ortho*-aminobenzamide did not react.

Structure of compounds **1**, **3**, **5**, **7–14** was confirmed by NMR (1D, 2D), IR spectroscopy and mass spectrometry data. According to HSQC data, in the ^{13}C and ^1H NMR spectra of **1**, **3** and **5**, the signals at δ_C ~61 ppm (δ_H ~3.9–4.3 ppm) and δ_C ~48 ppm (δ_H ~4.5 ppm) refer to the Me_2NCH_2NH and $HNCH_2NH$ fragments, respectively. A reliable confirmation of this signal assignment is the data of HMBC heteronuclear correlation experiment. A low-field signal at δ_H ~ 4.5 ppm interacts with the signal of the carbon atom of the aromatic ring $HC\underline{C}(NH_2)C$ and urea carbonyl group, while a stronger field signal at δ_H ~ 3.9–4.3 ppm correlates with the signals of urea carbonyl group and Me_2N fragment. Analysis of COSY spectral data showed that the hydrogen atoms of the methylene group (δ_H ~4.5 ppm) interact with the vicinal NH protons (δ_H ~6.3–7.6 ppm), and the methylene protons (δ_H ~3.9–4.3 ppm) correlate with the NH hydrogen atom (~7.8–8.3 ppm), which indicates its relatively greater acidity.

The obtained results were used to identify reaction products with biuret **7–9**. In the ^1H NMR spectra of aminomethylated products **10** and **11**, doublets in the region of δ_H 6.0–7.0 ppm with ^2J = 12.0 Hz indicate the presence of a terminal double bond in the molecule. We observed a similar spectral spin system in the case of *N*-({[(dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine **14**. According to HMBC data, the double bond protons are removed, and the methylene protons at δ_H ~4.2 and 4.5 ppm of the Me_2NCH_2N and $HNCH_2N$ fragments interact with the carbon atoms of the aromatic ring $HC\underline{C}(NH_2)C$ and the urea carbonyl group.

In the IR spectra of compounds **3**, **5**, **7**, **9–11**, there are broadened absorption bands in the region of 1694–1689 cm^{-1} corresponding to the stretching vibrations of the carbonyl groups (amide I band) and at 1567–1515 cm^{-1} (amide II band) due to the bending vibrations of the C–N group.

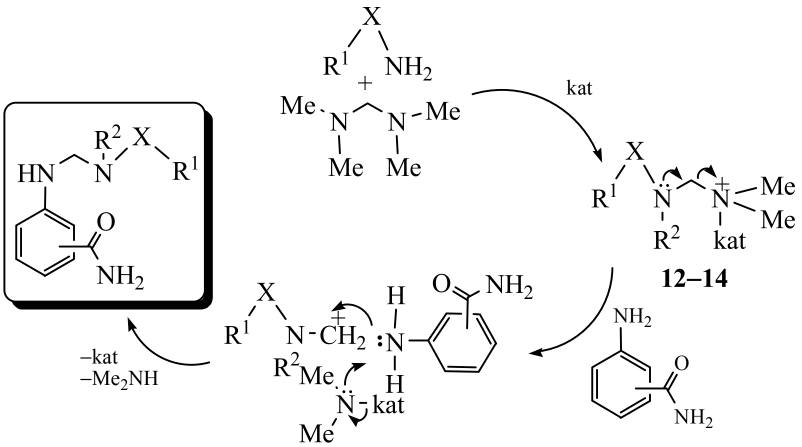
The results obtained suggest [7, 26, 27] that, under the reaction conditions, aminomethylation of carbamides with bis(*N*,*N*-dimethylamino)methane initially occurs with the formation of the corresponding aminomethylated carbamides 12–14 [11, 12], which are coordinated with the catalyst metal ion, which contributes to the shift of the electron density from the nitrogen atom to the metal ion and the formation of carbocations. Subsequent nucleophilic addition of the amino group of amino benzamides to the formed carbocation leads to the formation of the corresponding C–N bonds and acyclic molecules of **1**, **3**, **5**, **7–11** (Scheme 7).

In summary, the aminomethylation reaction of *ortho*-, *meta*- and *para*-aminobenzamides using bis(*N*,*N*-dimethylamino)methane and carbamides or *N*-aminomethylated carbamides in the presence of $NiCl_2·6H_2O$ and $SmCl_3·6H_2O$ as catalysts can be successfully used for obtain acyclic aniline derivatives bearing urea fragments.

EXPERIMENTAL

One-dimensional (^1H, ^{13}C), homo- (COZY) and heteronuclear (HSQC, HMBC) NMR experiments were performed on a Bruker Avance 400 [100.62 (^{13}C) and 400.13 MHz (^1H)] spectrometer using DMSO-d_6 as the solvent. Mass spectra were recorded on a MALDI TOF/TOF AUTOFLEX III Bruker

Scheme 7.



$R^1 = N(H)CH_2NMe_2$, R^2 = H (**a**); $R^1 = N(H)C(O)N(H)CH_2NMe_2$, R^2 = H (**b**); $R^1 = N(H)N{=}CH_2$, $R^2 = CH_2NMe_2$ (**c**).

instrument. IR spectra were taken on a Bruker Vertex 70 V spectrometer from a suspension in liquid paraffin. Melting points were determined on a PHMK 80/2617 instrument. The reaction progress was monitored by TLC using Sorbfil plates (PTSH-AF-B) and detecting with iodine vapors. KSK silica gel (100–200 μm) was used for column chromatography.

Synthesis of compounds 1–11 *(general procedure). a.* A mixture of 1 mmol of carbamide in 5 mL of ethanol, 2.5 mmol of bis(*N*,*N*-dimethylamino)methane and 0.2 mmol of catalyst $NiCl_2·6H_2O$ or $SmCl_3·6H_2O$ was stirred for 5 min, then solution of 1 mmol of aminobenzamide in 5 mL of ethanol was added. The temperature was raised to 80°C, and the reaction mixture was stirred for 12 h. The target products were isolated by column chromatography on SiO_2.

b. A mixture of 1 mmol of *N*,*N*'-bis(dimethylaminomethyl)urea, *N*,*N*'-bis[(dimethylamino)methyl])-allophanamide or *N*-({[(dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine in 5 mL of ethanol and 0.2 mmol of catalyst $NiCl_2·6H_2O$ or $SmCl_3·6H_2O$ was stirred for 5 min, then 1 mmol of aminobenzamide in 5 mL of ethanol was added, and the mixture was stirred for 24 h at 80°C. The target products were isolated by column chromatography on SiO_2.

2-({[({[(Dimethylamino)methyl]amino}carbonyl)-amino]methyl}amino)benzamide (1). Yield 0.18 g (67%, method *a*), 0.08 g (30%, method *b*), cream gummy substance. IR spectrum, ν, cm^{-1}: 3401–3334, 2965, 2781, 1667, 1615, 1556, 1468, 1395, 1263, 1159, 1022, 756, 630. ^{1}H NMR spectrum, δ, ppm: 2.54 br. s (6H, NCH_3), 4.25 br. s (2H, $MeNC\underline{H}_2NH$), 4.52 t (2H, $HNC\underline{H}_2NH$, ^3J = 5.5 Hz), 6.45 t (1H, $\underline{H}C_{Ar}$, ^3J = 7.6 Hz), 6.65 d (1H, $\underline{H}C_{Ar}$, ^3J = 8.0 Hz), 7.07 t (1H, $\underline{H}C_{Ar}$, ^3J = 7.5 Hz), 7.49 d (1H, $\underline{H}C_{Ar}$, ^3J = 8.0 Hz); 6.71 br. s, 7.40 br. s and 8.34 br. s (3H, $N\underline{H}$). ^{13}C NMR spectrum, δ_C, ppm: 40.50 (NCH_3), 48.33 ($HNCH_2NH$), 61.71 ($HN\underline{C}H_2NMe$), 114.10 (Ph), 114.99 (Ph), 116.89 (Ph), 129.12 (Ph), 132.25 (Ph), 148.64 (Ph), 159.28 (C=O), 172.08 [$\underline{C}(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 266.176 $[M + H]^+$, 288.154 $[M + Na]^+$, 304.130 $[M + K]^+$.

2-Amino-*N*-[(dimethylamino)methyl]benzamide (2). Yield 0.06 g (30%, method *a*), cream amorphous powder, mp 40–46°C. IR spectrum, ν, cm^{-1}: 3438, 2923–2854, 1654, 1607, 1585, 1461, 1305, 1281, 1152, 1035, 722. ^{1}H NMR spectrum, δ, ppm: 2.25 br. s (6H, NCH_3), 4.06 br. s (2H, $MeNC\underline{H}_2NH$), 6.40 br. s (2H, NH_2), 6.54 t (1H, $\underline{H}C_{Ar}$, ^3J = 7.4 Hz), 6.86 d (1H, $\underline{H}C_{Ar}$, ^3J = 8.3 Hz), 7.21 t (1H, $\underline{H}C_{Ar}$, ^3J = 8.3 Hz), 7.56 d (1H, $\underline{H}C_{Ar}$, ^3J = 7.4 Hz), 8.23 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.77 (NCH_3), 61.07 ($HN\underline{C}H_2NMe$), 112.25 (Ph), 115.10 (Ph), 115.31 (Ph), 129.49 (Ph), 132.76 (Ph), 150.36 (Ph), 170.18 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 232.110 $[M + K]^+$.

3-({[({[(Dimethylamino)methyl]amino}carbonyl)-amino]methyl}amino)benzamide (3). Yield 0.17 g (64%, method *a*), 0.09 g (31%, method *b*), cream amorphous powder, mp 65–70°C. IR spectrum, ν, cm^{-1}: 3402, 2923–2854, 2724, 1654 br, 1607, 1581, 1460, 1377, 1168, 1152, 1030, 973, 722. ^{1}H NMR spectrum, δ, ppm: 2.19 br. s (6H, NCH_3), 4.04 br. s (2H, $MeNC\underline{H}_2NH$), 4.46 br. s (2H, $HNC\underline{H}_2NH$), 5.64 br. s

(2H, NH_2), 6.82, 7.07–7.16 m (4H, HC_{Ar}); 6.28 br. s, 6.70 br. s and 8.50 br. s (3H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.46 (NCH_3), 48.78 ($HN\underline{C}H_2NH$), 62.27 ($HN\underline{C}H_2NMe$), 111.82 (Ph), 115.97 (Ph), 116.99 (Ph), 129.15 (Ph), 135.54 (Ph), 147.69 (Ph), 159.02 (C=O), 169.13 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 266.074 $[M + H]^+$, 288.061 $[M + Na]^+$, 304.007 $[M + K]^+$.

3-Amino-*N*-[(dimethylamino)methyl]benzamide (4). Yield 0.03 g (16%, method *a*), cream amorphous powder, mp 86–89°C. IR spectrum, ν, cm^{-1}: 3332, 2925–2854, 1651, 1606, 1584, 1455, 1304, 1280, 1154, 1030, 722. ^1H NMR spectrum, δ, ppm: 2.20 br. s (6H, NCH_3), 3.86 br. s (2H, $MeNC\underline{H_2}NH$), 6.98–7.15 m (4H, HC_{Ar}), 6.60 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 42.47 (NCH_3), 61.58 ($HN\underline{C}H_2NMe$), 113.36 (Ph), 113.55 (Ph), 115.16 (Ph), 129.02 (Ph), 136.84 (Ph), 149.11 (Ph), 168.24 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 232.097 $[M + K]^+$.

4-({[({[(Dimethylamino)methyl]amino}carbonyl)-amino]methyl}amino)benzamide (5). Yield 0.19 g (70%, method *a*), 0.10 g (38%, method *b*), cream amorphous powder, mp 124–126°C. IR spectrum, ν, cm^{-1}: 3438–3353, 2921, 2870–2730, 1666 br, 1614 br, 1555, 1454, 1351, 1215, 1142, 1039, 757, 668. ^1H NMR spectrum, δ, ppm: 2.27 br. s (6H, NCH_3), 3.94 br. s (2H, $MeNC\underline{H_2}NH$), 4.45 t (2H, $HNC\underline{H_2}NH$, ^3J = 6.0 Hz), 5.67 br. s (2H, NH_2), 6.68 d (2H, HC_{Ar}, ^3J = 8.6 Hz), 7.66 d (2H, HC_{Ar}, ^3J = 8.6 Hz), 6.86 br. s and 6.94 br. s (3H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.90 (NCH_3), 48.48 ($HN\underline{C}H_2NH$), 62.11 ($HN\underline{C}H_2NMe$), 113.00 (Ph), 121.80 (Ph), 129.35 (Ph), 150.50 (Ph), 159.13 (C=O), 168.80 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 266.063 $[M + H]^+$, 287.250 $[M + Na - H]^+$.

4-Amino-*N*-[(dimethylamino)methyl]benzamide (6). Yield 0.03 g (18%, method *a*), cream amorphous powder, mp 85–90°C. IR spectrum, ν, cm^{-1}: 3400, 2923–2854, 1657, 1606, 1584, 1462, 1304, 1283, 1153, 1031, 722. ^1H NMR spectrum, δ, ppm: 2.21 br. s (6H, NCH_3), 4.05 br. s (2H, $MeNC\underline{H_2}NH$), 6.54 d (2H, HC_{Ar}, ^3J = 8.6 Hz), 7.59 d (2H, HC_{Ar}, ^3J = 8.6 Hz), 8.57 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 42.93 (NCH_3), 61.50 ($HN\underline{C}H_2NMe$), 112.15 (Ph), 121.02 (Ph), 129.38 (Ph), 152.28 (Ph), 167.69 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 194.281 $[M + H]^+$.

2-[(8-Methyl-3,5-dioxo-2,4,6,8-tetraazanon-1-yl)-amino]benzamide (7). Yield 0.13 g (43%, method *a*), 0.04 g (14%, method *b*), colorless gummy substance. IR spectrum, ν, cm^{-1}: 3327, 2946, 2867–2782, 1694 br, 1640 br, 1567–1519, 1455, 1384, 1260, 1162, 1032, 752, 632. ^1H NMR spectrum, δ, ppm: 2.18 br. s (6H, NCH_3), 3.98 d (2H, $MeNC\underline{H_2}NH$, ^3J = 6.1 Hz), 4.66 br. s (2H, $HNC\underline{H_2}NH$); 6.52 m, 6.69 m, 7.14 m and 7.53 m (4H, HC_{Ar}); 7.95 br. s, 8.02 br. s, 8.13 br. s and 8.56 br. s (4H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.77 (NCH_3), 48.00 ($HN\underline{C}H_2NH$), 61.73 ($HN\underline{C}H_2NMe$), 114.10 (Ph), 115.05 (Ph), 116.84 (Ph), 128.70 (Ph), 132.40 (Ph), 148.40 (Ph), 155.47 (C=O), 155.94 (C=O), 171.79 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 307.328 $[M + H]^+$.

3-[(8-Methyl-3,5-dioxo-2,4,6,8-tetraazanon-1-yl)-amino]benzamide (8). Yield 0.12 g (40%, method *a*), 0.06 g (20%, method *b*), creamy gummy substance. IR spectrum, ν, cm^{-1}: 3337, 2948, 2854–2782, 1689 br, 1652 br, 1539, 1464, 1383, 1255, 1139, 1032, 753, 692. ^1H NMR spectrum, δ, ppm: 2.14 br. s (6H, NCH_3), 3.95 br. s (2H, $MeNC\underline{H_2}NH$), 4.55 br. s (2H, $NC\underline{H_2}NH$); 6.84–6.85 m, 7.06–7.10 m and 7.11–7.17 m (4H, HC_{Ar}); 6.57 br. s, 6.64 br. s, 7.95 and 8.85 br. s (4H, NH), 8.73 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 41.86 (NCH_3), 52.40 ($HNC\underline{H_2}NH$), 61.84 ($HN\underline{C}H_2NMe$), 111.62 (Ph), 115.73 (Ph), 116.07 (Ph), 129.15 (Ph), 135.82 (Ph), 147.91 (Ph), 155.48 (C=O), 155.93 (C=O), 169.00 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 307.353 $[M + H]^+$.

4-[(8-Methyl-3,5-dioxo-2,4,6,8-tetraazanon-1-yl)-amino]benzamide (9). Yield 0.16 g (51%, method *a*), 0.07 g (22%, method *b*), cream amorphous powder, mp >350°C. IR spectrum, ν, cm^{-1}: 3306, 2923, 2854, 1694 br, 1605 br, 1515, 1462, 1377, 1261, 1189, 1030, 841, 768. ^1H NMR spectrum, δ, ppm: 2.13 br. s (6H, NCH_3), 4.01 (2H, $MeNC\underline{H_2}NH$), 4.61 br. s (2H, $HNC\underline{H_2}NH$), 6.79 br. s (2H, NH_2), 6.67–6.73 m (2H, HC_{Ar}), 7.65–7.70 m (2H, HC_{Ar}); 6.82 br. s, 6.78 br. s, 6.94 br. s and 8.43 br. s (4H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.93 (NCH_3), 48.03 ($HN\underline{C}H_2NH$), 61.79 ($HN\underline{C}H_2NMe$), 111.86 (Ph), 121.98 (Ph), 129.37 (Ph), 150.15 (Ph), 154.89 (C=O), 155.43 (C=O), 168.38 [$C(O)NH_2$]. Mass spectrum, *m/z* (I_{rel}, %): 307.378 $[M + H]^+$.

3-[({[(Dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl]amino]benzamide (10). Yield 0.12 g (40%, method *a*), 0.04 g (15%, method *b*), creamy gummy substance. IR spectrum, ν, cm^{-1}: 3401, 2860–2786, 1666, 1606, 1538, 1468, 1385, 1285, 1121, 1022, 759, 622. ^1H NMR spectrum, δ, ppm: 2.40 br. s (6H, $NC\underline{H_3}$), 4.18 br. s (2H, MeNC$\underline{H}_2$NH), 4.54 t (2H, NC$\underline{H}_2$NH, ^3J = 5.9 Hz), 6.18 d and 6.82 d (2H, N=CH$_2$, ^2J = 12.0 Hz); 6.69 m and 7.03–7.20 m (4H, HC$_{Ar}$),7.38 br. s and 8.80 br. s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 40.89 (NCH$_3$), 52.26 (NC$\underline{H}_2$NH), 61.43 (HN$\underline{C}$H$_2$NMe), 113.35 (Ph), 115.07 (Ph), 117.11 (Ph), 129.25 (Ph), 131.26 (N=CH$_2$), 135.11 (Ph), 147.83 (Ph), 156.10 (C=O), 168.65 [C(O)NH$_2$]. Mass spectrum, *m/z* (I_{rel}, %): 293.135 [M + H]$^+$, 331.081 [M + K].

4-[({[(Dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)amino]benzamide (11). Yield 0.08 g (29%, method *a*), 0.03 g (11%, method *b*), creamy gummy substance. IR spectrum, ν, cm^{-1}: 3443, 2852–2796, 1659 br, 1608, 1529, 1469, 1395, 1273, 1193, 1108, 1021, 843, 593. ^{1}H NMR spectrum, δ, ppm: 2.45 br. s (6H, NCH$_3$), 4.24 br. s (2H, MeNC$\underline{H}_2$NH), 4.55 br. s (2H, NC$\underline{H}_2$NH), 6.31 d and 6.89 d (2H, N=CH$_2$, ^2J = 12.1 Hz), 6.52 d (2H, HC$_{Ar}$, ^3J = 8.5 Hz), 6.89 d (2H, HC$_{Ar}$, ^3J = 8.5 Hz), 6.96 br. s and 8.96 br. s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 41.13 (NCH$_3$), 51.80 (NCH$_2$NH), 65.35 (HN$\underline{C}$H$_2$NMe), 111.76 and 129.47 (Ph), 131.13 (N=CH$_2$), 132.87 (Ph), 150.58 (Ph), 156.03 (C=O), 168.72 [C(O)NH$_2$]. Mass spectrum, *m/z* (I_{rel}, %): 293.142 [M + H]$^+$.

Synthesis of bis-*gem*-diamines 12–14 *(general procedure).* A mixture of 5 mmol of bis(*N*,*N*-dimethylamino)methane, 0.1 mmol of $SmCl_3 \cdot 6H_2O$ and 2 mmol of carbamide dissolved in 10 mL of ethanol was stirred for 8 h at room temperature. The target products were isolated by column chromatography on SiO$_2$.

***N*,*N'*-Bis(dimethylaminomethyl)carbamide (12).** Yield 0.34 g (99%), gummy substance. Mass spectrum, *m/z* (I_{rel}, %): 213.551 [M + K]$^+$. Spectral data are given in [11].

***N*,*N'*-Bis[(dimethylamino)methyl]allophanamide (13).** Yield 0.42 g (96%), colorless gummy substance. IR spectrum, ν, cm^{-1}: 3322, 2952–2786, 1674, 1538, 1470, 1385, 1230, 1167, 1032, 769, 600. ^{1}H NMR spectrum, δ, ppm: 2.11 br. s (12H, NCH$_3$), 3.92 br. s (4H, HNC$\underline{H}_2$NH), 7.84 br. s [2H, NHC(O)], 8.77 br. s [1H, C(O)NHC(O)]. ^{13}C NMR spectrum, δ_C, ppm: 41.92 (NCH$_3$), 61.84 (NCH$_2$N), 155.56 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 218.174 [M + H]$^+$, 236.138 [M + H$_2$O + H]$^+$.

***N*-({[(Dimethylamino)methyl][(2-methylenehydrazino)carbonyl]amino}methyl)-*N*,*N*-dimethylamine (14).** Yield 0.32 g (80%), colorless gummy substance. IR spectrum, ν, cm^{-1}: 3439, 2785, 1668, 1581–1536, 1469, 1384, 1335, 1143, 1022, 923, 612. ^{1}H NMR spectrum, δ, ppm: 2.54 br. s (6H, NCH$_3$), 4.32 d (2H, HNC$\underline{H}_2$NH, ^3J = 6.9 Hz), 6.32 d and 6.93 d (2H, CH$_2$=N, ^2J = 12.0 Hz), 7.82 t [1H, CH$_2$N$\underline{H}$C(O), ^3J = 6.9 Hz], 10.81 br. s [1H, NNHC(O)]. ^{13}C NMR spectrum, δ_C, ppm: 41.00 (NCH$_3$), 61.12 (HN$\underline{C}$H$_2$NH), 133.70 (CH$_2$=N), 155.87 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 143.037 [M – H]$^+$, 145.049 [M + H]$^+$, 167.079 [M + Na]$^+$.

FUNDING

This work was performed in accordance with the research plan of the Institute of Petrochemistry and Catalysis of the Russian Academy of Sciences on the topic “Metal complex catalysis in the synthesis of hetero- and metal heterocycles” (state registration number AAAA-A17-117012610060-7, 2017–2019) using equipment of the Center for collective use “Agidel.”

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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