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Synthesis of 5-Nitro-3,4-dihydropyrimidin-2(1*H*)-ones Catalyzed by Metal Salts. Retro-Henry Reaction with Formation of *N*,*N*′-Disubstituted Ureas

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Abstract—Three-component condensation of α-nitroacetophenone with aromatic aldehydes and urea in the presence of iron(III), cobalt(II), nickel(II), and copper(II) salts as catalyst led to the formation of 4,6-diaryl-5-nitro-3,4-dihydropyrimidin-2(1*H*)-ones and *N*-benzoyl-*N*′-(1-aryl-2-nitroethyl)ureas. The latter were formed as a result of retro-nitroaldol (retro-Henry) reaction of intermediate 4,6-diaryl-6-hydroxy-5-nitro-3,4,5,6-tetrahydropyrimidin-2(1*H*)-ones.

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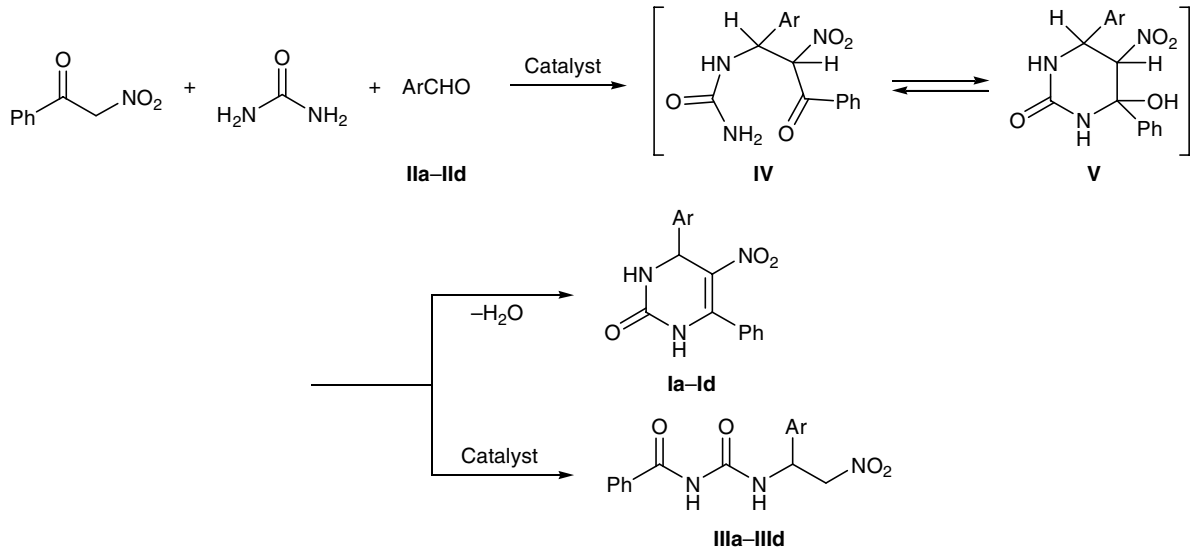
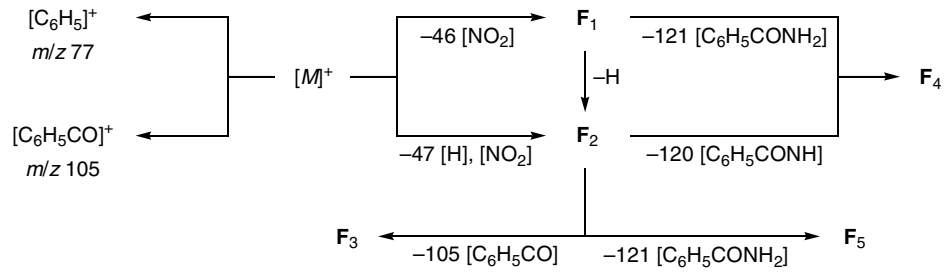
5-Alkoxycarbonyl- and amido-substituted 3,4-dihydropyrimidin-2(1*H*)-ones exhibit pronounced biological activity: nifedipine-like calcium channel blockers, antihypertensive agents, and α-adrenergic and neuropeptide antagonists were found among these compounds [1]. 3,4-Dihydropyrimidin-2(1*H*)-one derivatives are commonly synthesized by three-component condensation of aldehydes with urea and β-dicarbonyl compounds in boiling alcohol in the presence of a catalytic amount of mineral acids (Biginelli reaction) [2]. In the recent time, numerous attempts were made to modify the Biginelli reaction conditions by using various aprotic Lewis acids as catalysts, carrying out the reaction in various solvents and under solvent-free conditions, and applying microwave irradiation [3, 4]. We previously synthesized a series of 4,6-diaryl-5-nitro-3,4-dihydropyrimidin-2(1*H*)-ones **I** using α-nitroacetophenone instead of β-dicarbonyl compound in the

Scheme 1.



Ar = RC_6H_4, R = H (**a**), *m*-O_2N (**b**), *m*-F (**c**), *p*-MeO (**d**); catalyst = $FeCl_3 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, $CuSO_4 \cdot 5H_2O$, $Cu(OAc)_2 \cdot H_2O$.

Scheme 2.



Biginelli reaction with substituted benzaldehydes and urea under standard conditions (EtOH, HCl), and the products showed antiarrythmic activity [5].

With a view to elucidate whether analogous modifications could be applied to the synthesis of nitrodihydropyrimidinones **I** to raise their yields, we examined three-component condensation of α-nitroacetophenone with aromatic aldehydes **IIa**–**IId** and urea in the presence of inorganic iron(III), cobalt(II), nickel(II), and copper(II) salts as catalyst [4]. In the condensation of α-nitroacetophenone with benzaldehyde (**IIa**) and urea in the presence of $FeCl_3 \cdot 6H_2O$ in boiling ethanol, we isolated two products, the expected nitrodihydropyrimidinone **Ia** and *N*-benzoyl-*N*′-(2-nitro-1-phenylethyl)urea (**IIIa**). The reactions with other aromatic aldehydes **IIb**–**IId** also led to the formation of mixtures of two products, dihydropyrimidinones **Ib**–**Id** and *N*,*N*′-disubstituted ureas **IIIb**–**IIId** (Scheme 1). However, their overall yield did not exceed 45% (see table).

The structure of disubstituted ureas **IIIa**–**IIId** was determined on the basis of their spectral parameters and analytical data. Compounds **IIIa**–**IIIc** showed in the IR spectra (KBr) two absorption bands at 1694–1690 and 1674–1660 cm^{-1} due to stretching vibrations of the carbonyl groups, while the spectrum of **IIId** contained one absorption band at 1684 cm^{-1}; stretching vibrations of the NH groups appeared at 3335–3244 cm^{-1}. In the IR spectrum of **IIIc** recorded in mineral oil we observed two NH stretching vibration bands at 3261 and 3332 cm^{-1}, while bands assignable to OH vibrations were absent. All compounds **IIIa**–**IIId** characteristically displayed absorption bands at 1566–1546 and 1383–1378 cm^{-1} belonging, respectively, to asymmetric and symmetric stretching vibrations of the aliphatic nitro group.

The mass spectra of **IIIa**–**IIId** lack molecular ion peaks $[M]^+$; the heaviest fragment ion has an *m*/*z* value and elemental composition (determined from the high-resolution spectra) corresponding to loss of the nitro group, $[M - NO_2]^+$ (**F**$_1$), which is typical of aliphatic nitro compounds [8]. The other fragment ions (**F**$_2$–**F**$_5$) originate from subsequent decomposition of ions **F**$_1$ and **F**$_2$ ($[M - HNO_2]^+$); no ion peak with *m*/*z* 46 $[NO_2]^+$ or 30 $[NO]^+$ was found in the spectra, and the most abundant fragment ions were $[PhCO]^+$ (*m*/*z* 105, 100%) and $[C_6H_5]^+$ (*m*/*z* 77, 62–86%) (Scheme 2).

Apart from aromatic proton signals, the ^1H NMR spectra of compounds **III** contained five one-proton signals. Two downfield signals were assigned to the N^1H (s) and N^3H protons (d, J = 8.4– 8.8 Hz); the intensity of these signals decreased upon addition of CD_3OD to solutions of **IIIb** and **IIIc** in DMSO-d_6. The remaining three signals in the region δ 5.0–6.0 ppm did not change their intensity upon addition of CD_3OD over a period of 24 h and were assigned to CH protons. Two slightly distorted doublets of doublets at δ 5.00–5.50 ppm are likely to belong to protons in the CH_2NO_2 group (*AB* system, J_{AB} = 13.1–13.9 Hz). The vicinal coupling constants between 5-H_A and 5-H_B, on

Condensation of α-nitroacetophenone with aromatic aldehydes **IIa**–**IId** and urea (reactant ratio 1:1:2) in the presence of metal salts MX_n[a]

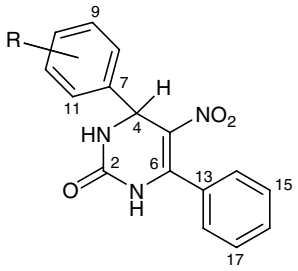
Initial aldehyde no.	Catalyst MX_n	Yield, %		Yield of **I**,[b] % [5]
		I	**III**	
IIa	$FeCl_3 \cdot 6H_2O$	27	16	63
IIb	$FeCl_3 \cdot 6H_2O$	27	9	62
IIc	$FeCl_3 \cdot 6H_2O$	16	8	57
IId	$FeCl_3 \cdot 6H_2O$	13	5	58
IIb	$CoCl_2 \cdot 6H_2O$	6	22	
IIb	$CuSO_4 \cdot 5H_2O$	–	21	
IIb	$Cu(OAc)_2 \cdot H_2O$	–	17	
IIb[c]	$CoCl_2 \cdot 6H_2O$	Traces	24	
IIb[c]	$NiCl_2 \cdot 6H_2O$	Traces	28	

[a] 25 mol % of MX_n, EtOH, 3 drops of concentrated hydrochloric acid, reflux.

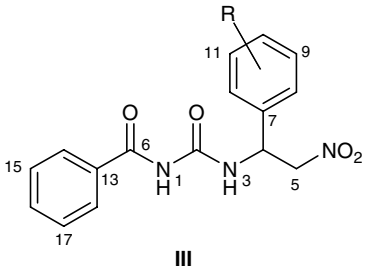
[b] Concentrated hydrochloric acid, 2-propanol, reflux.

[c] In acetonitrile; compound **Ib** was detected in the reaction mixture by TLC (Silufol, $CHCl_3$–EtOH, 15:1).

the one hand, and 4-H, on the other, depend on mutual arrangement of these protons (^3J = 8.0–8.5 and 4.4–5.4 Hz, respectively). The 4-H signal appears as a double doublet of doublets or a multiplet at δ 5.50–6.00 ppm. It should be noted that H–D exchange at the nitrogen atoms in molecule **IIIb** (DMSO-d_6–CD_3OD) leads to the transformation of the 4-H signal into a doublet of doublets (J = 4.4, 8.4 Hz). When an NMR ampule containing a solution of compound **IIIb** in DMSO-d_6–CD_3OD was kept for a month at room temperature, the appearance of the three CH signals and the intensity of the 5-H_A and 5-H_B signals changed as a result of deuterium exchange in the CH_2NO_2 fragment (1-H: 3-H:4-H:5-H_A:5-H_B = 0.17:0.19:1:0.4:0.4). In this case, hydrogen–deuterium exchange is facilitated due to electron-acceptor effect of the nitro group.



I



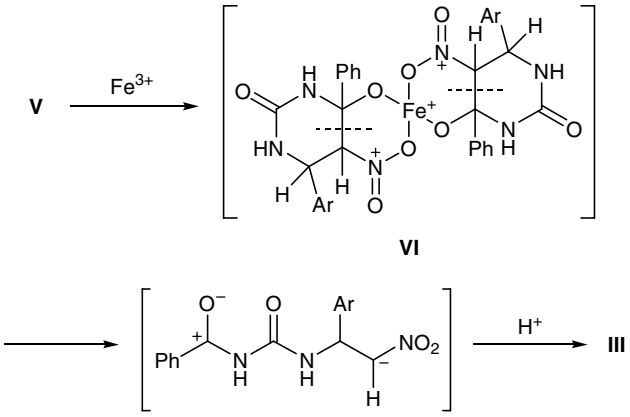
III

The ^{13}C NMR spectra of compounds **III** were fully consistent with the assumed structure. The spectra contained signals from aromatic carbon atoms, downfield signals from the carbonyl carbon atoms (C^6, δ_C 168.27–168.43 ppm; C^2, δ_C 152.82–153.13 ppm), and upfield signals from the C^4 (δ_C 50.67–51.20 ppm) and C^5 carbon atoms (δ_C 77.66–78.49 ppm).

The formation of disubstituted ureas **III** in the reaction under study may be rationalized according to Scheme 1. The primary condensation product is N-substituted urea **IV** which undergoes heterocyclization to hexahydropyrimidin-2-one **V**. The latter may be regarded as a cyclic β-nitro alcohol. It is known that dehydration of β-nitro alcohols usually gives nitrovinyl derivatives [6, 7, 9] and that some compounds can decompose into nitro and carbonyl compounds via dissociation of the C–C bond (retro-Henry reaction) in acetone or tetrahydrofuran [10] in the presence of quaternary ammonium bases [9, 11], Al_2O_3 [9], or SiO_2 [6], and by the action of $NaBH_4$ [12], Al/Hg [6], or $CuSO_4/SiO_2$ [13]. The yield of the retro-nitroaldol reaction products in the presence of $CuSO_4/SiO_2$ attains 75%. Analogous transformations were observed previously for aliphatic [9, 11, 14], cyclic [10, 12, 13], and heterocyclic compounds [10, 15].

In our experiments, an iron salt present in the reaction mixture could exert the same catalytic effect on the decomposition of cyclic β-nitro alcohols **V** as that of copper and other metal salts [10, 13]. Therefore, by analogy with published data [13], we presume intermediate formation of complex **VI** in which the metal ion favors dissociation of the endocyclic C^5–C^6 bond with formation of acyclic nitro derivatives, *N*-benzoyl-*N*′-(1-aryl-2-nitroethyl)ureas **III** (Scheme 3). When the reaction with *m*-nitrobenzaldehyde (**IIIb**) was performed in the presence of 2 equiv of $FeCl_3 \cdot 6H_2O$, the yield of the retro-Henry reaction product did not increase (**IIIb**, 8.4%).

Scheme 3.



VI

The reaction of ArCHO with urea and α-(*p*-nitrophenoxy)acetophenone (**VII**) instead of α-nitroacetophenone in the presence of $FeCl_3 \cdot 6H_2O$ gave neither appreciable amount of 5-(4-nitrophenoxy)-4,6-diphenyl-3,4-dihydropyrimidin-2(1*H*)-ones nor other compounds whose formation could indicate the occurrence of three-component condensation. From the reaction mixture we isolated initial acetophenone **VII** (90%). Presumably, the reason is reduced reactivity of the α-methylene group in **VII** as compared to nitroacetophenone.

In the condensation with aldehyde **IIb** as an example we examined the effect of other metal salts,

$CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, $CuSO_4 \cdot 5H_2O$, and $Cu(OAc)_2 \cdot H_2O$. The results are collected in table. It is seen that all these metal ions are more efficient in the retro-Henry reaction than Fe^{3+}. The Cu(II)-catalyzed reaction gave no pyrimidinone **Ib** (according to the TLC data). In other experiments, the amount of the corresponding product was also insignificant. In the reaction catalyzed by $CoCl_2 \cdot 6H_2O$, the yield of **Ib** was 5.9%, i.e., it was lower by a factor of almost 4 than the yield of urea **IIIb**. The use of acetonitrile as solvent in the Co^{2+} and Ni^{2+}-catalyzed reactions led to a relatively high yield of urea **IIIb**, while the concentration of pyrimidine **Ib** in the reaction mixture was very small (compound **Ib** was detected only by chromatography).

Thus we were the first to demonstrate that the three-component condensation of α-nitroacetophenone with aromatic aldehydes and urea in the presence of Fe^{3+}, Co^{2+}, Ni^{2+}, and Cu^{2+} salts leads to the formation of 4,6-diaryl-5-nitro-3,4-dihydropyrimidin-2(1*H*)-ones and *N*-benzoyl-*N*′-(1-aryl-2-nitroethyl)ureas. The latter are products of the retro-nitroaldol reaction of intermediate cyclic β-nitro alcohols, 4,6-diaryl-6-hydroxy-5-nitro-3,4,5,6-tetrahydropyrimidin-2(1*H*)-ones. Cobalt(II), nickel(II), and copper(II) salts turned out to be more effective catalysts in the retro-Henry reaction than iron(III) salts. Therefore, the examined modifications of the cyclocondensation conditions could not compete with the procedure proposed previously [5] for the synthesis of nitrodihydropyrimidinones **I** (see table). On the other hand, the reaction in the presence of mineral salts may be used to obtain difficultly accessible nitroethyl-substituted ureas.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Bruker Vector-22 spectrophotometer. The UV spectra of solutions in ethanol were recorded on a Specord M-40 spectrophotometer. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT 8200 instrument with direct sample admission into the ion source. The ^1H and ^{13}C NMR spectra were measured on Bruker AC-200 and AM-400 spectrometers from solutions in DMSO-d_6 using the solvent signals as reference (δ 2.50, δ_C 39.50 ppm). The purity of the products was checked by TLC on Silufol UV-254 plates using $CHCl_3$–EtOH (15:1) as eluent.

General procedure for three-component condensation of α-nitroacetophenone with aromatic aldehydes and urea. Three drops of concentrated hydrochloric acid were added to a solution of 15 mmol of α-nitroacetophenone, 15 mmol of aromatic aldehyde **IIa**–**IId**, 30 mmol of urea, and 3.7 mmol of the corresponding metal salt MX_n in 30 ml of ethanol or acetonitrile. The mixture was heated for 6 h under reflux and cooled to room temperature, and the precipitate was filtered off, washed with ethanol, water (2×10 ml), and aqueous ethanol (1:1, 2×5 ml), dried, and recrystallized. Compounds **IIIa**–**IIId** were thus isolated. The filtrate was poured into 3 volumes of water, and oily material separated and was ground with alcohol, and the precipitate was filtered off, washed with aqueous alcohol (1:1, 3×5 ml), and recryctallized. Compounds **Ia**–**Id** were characterized by melting points, IR spectra, and TLC data (cf. [5]).

5-Nitro-4,6-diphenyl-3,4-dihydropyrimidin-2(1*H*)-one (Ia). mp 206–208°C (from EtOH) [5].

5-Nitro-4-(3-nitrophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (Ib). mp 220–222°C (from EtOH); published data [5]: mp 221–223°C. ^1H NMR spectrum (400 MHz), δ, ppm: 5.82 s (1H, 4-H), 7.38–7.55 m (5H, H_{arom}), 7.72 d.d (1H, 11-H, $^3J_{10,11}$ = 7.2, $^3J_{11,12}$ = 7.6 Hz), 7.89 d (1H, 10-H, $^3J_{10,11}$ = 7.2 Hz), 8.19 d (1H, 12-H, $^3J_{11,12}$ = 7.6 Hz), 8.27 s (1H, 8-H), 8.47 s (1H, 3-H), 10.19 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 53.61 (C^4), 121.34 (C^8), 121.57 (C^5), 122.96 (C^{10}), 127.68 (C^{14}, C^{18}), 128.34 (C^{15}, C^{17}), 129.94 (C^{11}), 130.57 (C^{16}), 132.12 (C^{13}), 132.93 (C^{12}), 144.25 (C^7), 148.02 (C^9), 149.98 (C^6), 150.29 (C^2).

4-(3-Fluorophenyl)-5-nitro-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (Ic). mp 202–204°C (from EtOH); published data [5]: mp 203–205°C. ^1H NMR spectrum (400 MHz), δ, ppm: 5.69 d (1H, 4-H, $^3J_{3,4}$ = 3.4 Hz), 7.20 d.t (1H, 10-H, $^3J_{HF}$ = 8.0, $^3J_{10,11}$ = 8.0, $^4J_{8,10}$ = 2.1 Hz), 7.23 t.d (1H, 8-H, $^3J_{HF}$ = 10, $^4J_{8,10}$ = 2.1, $^4J_{8,12}$ = 1.0 Hz), 7.31 d (1H, 12-H, $^3J_{11,12}$ = 7.2 Hz), 7.42–7.54 m (6H, C_6H_5, 11-H), 8.39 d (1H, 3-H, $^3J_{3,4}$ = 3.4 Hz), 10.10 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 53.76 (C^4), 113.35 d (C^8, $^2J_{CF}$ = 22.0 Hz), 114.86 d (C^{10}, $^2J_{CF}$ = 21.0 Hz), 121.99 (C^5), 122.22 d (C^{12}, $^4J_{CF}$ = 2.0 Hz), 127.69 (C^{14}, C^{18}), 128.33 (C^{15}, C^{17}), 129.86 (C^{16}), 130.93 d (C^{11}, $^3J_{CF}$ = 8.0 Hz), 132.28 (C^{13}), 144.91 d (C^7, $^3J_{CF}$ = 7.0 Hz), 149.81 (C^6), 150.16 (C^2), 162.25 d (C^9, $^1J_{CF}$ = 223 Hz).

4-(4-Methoxyphenyl)-5-nitro-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (Id). mp 246–248°C (from EtOH); published data [5]: mp 247–249°C. ^1H NMR spectrum (200 MHz), δ, ppm: 3.77 s (3H, MeO), 5.60 d (1H, 4-H, $^3J_{3,4}$ = 3.2 Hz), 6.98 d (2H, 9-H, 11-H, $^3J_{8,9}$ = 8.6 Hz), 7.37 d (2H, 8-H, 12-H, $^3J_{8,9}$ =

8.6 Hz), 7.41–7.53 m (5H, C_6H_5), 8.31 d (1H, 3-H, $^3J_{3,4}$ = 3.2 Hz), 10.00 s (1H, 1-H).

***N*-Benzoyl-*N′*-(2-nitro-1-phenylethyl)urea (IIIa).** mp 183–186°C (from EtOH). UV spectrum, λ_{max}, nm (log ε): 203 (4.51), 235 (4.26), 270 sh (3.15). IR spectrum, ν, cm^{-1}: 3287, 3244, 3131 (NH); 1690, 1660 (C=O); 1554, 1529, 1504, 1383. ^{1}H NMR spectrum (400 MHz), δ, ppm: 5.11 d.d (1H, 5-H_A, $^2J_{AB}$ = 13.6, $^3J_{4,5}$ = 4.8 Hz), 5.25 d.d (1H, 5-H_B, $^2J_{AB}$ = 13.6, $^3J_{4,5}$ = 8.1 Hz), 5.69 d.d.d (1H, 4-H, $^3J_{4,5A}$ = 4.8, $^3J_{4,5B}$ = 8.1, $^3J_{4,3}$ = 8.4 Hz), 7.34 t (1H, 10-H, $^3J_{10,9}$ = $^3J_{10,11}$ = 7.4 Hz), 7.41 t (2H, 9-H, 11-H, $^3J_{9,8}$ = $^3J_{9,10}$ = 7.4 Hz), 7.49 d (2H, 8-H, 12-H, $^3J_{8,9}$ = 7.4 Hz), 7.52 t (2H, 15-H, 17-H, $^3J_{15,14}$ = $^3J_{15,16}$ = 7.7 Hz), 7.63 t (1H, 16-H, $^3J_{16,15}$, $^3J_{16,17}$ = 7.7 Hz), 7.99 d (2H, 14-H, 18-H, $^3J_{14,15}$ = 7.7 Hz), 9.49 d (1H, 3-H, $^3J_{3,4}$ = 8.4 Hz), 10.84 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 51.20 (C^4), 78.45 (C^5), 126.64 (C^8, C^{12}), 127.94 (C^{10}), 128.08 (C^{14}, C^{18}), 128.39 and 128.62 (C^9, C^{11}, C^{15}, C^{17}), 132.23 (C^{13}), 132.78 (C^{16}), 137.61 (C^7), 152.89 (C^2), 168.30 (C^6). Mass spectrum, *m*/*z* (I_{rel}, %): 267 (17.3) $[M - NO_2]^+$, 266 (27.7) $[M - HNO_2]^+$, 161 (12.6), 146 (28.2), 145 (18.4), 105 (100), 77 (61.8). Found, %: C 61.10; H 4.83; N 13.30. *m*/*z* 267.1133. $C_{16}H_{15}N_3O_4$. Calculated, %: C 61.33; H 4.83; N 13.41. ($M - NO_2$) 267.1133 ($C_{16}H_{15}N_2O_2$).

***N*-Benzoyl-*N′*-[2-nitro-1-(3-nitrophenyl)ethyl]-urea (IIIb).** mp 199–200°C (from EtOH–dioxane). UV spectrum, λ_{max}, nm (log ε): 208 (4.43), 237 (4.37), 263 sh (4.06). IR spectrum, ν, cm^{-1}: 3253, 3168 (NH); 1695, 1674 (C=O); 1566, 1529, 1504, 1377, 1358. ^{1}H NMR spectrum (200 MHz), δ, ppm: 5.21 d.d (1H, 5-H_A, $^2J_{AB}$ = 13.9, $^3J_{4,5}$ = 4.4 Hz), 5.40 d.d (1H, 5-H_B, $^2J_{AB}$ = 13.9, $^3J_{4,5}$ = 8.4 Hz), 5.86 d.d.d (1H, 4-H, $^3J_{4,5A}$ = 4.4, $^3J_{4,5B}$ = 8.4, $^3J_{3,4}$ = 8.6 Hz), 7.51 t (2H, 15-H, 17-H, $^3J_{15,14}$ = $^3J_{15,16}$ = 7.3 Hz), 7.64 t (1H, 16-H, $^3J_{16,15}$ = $^3J_{16,17}$ = 7.3 Hz), 7.71 t (1H, 11-H, $^3J_{11,10}$ = $^3J_{11,12}$ = 8.0 Hz), 7.92–8.04 m (3H, 10-H, 14-H, 18-H), 8.19 d.d (1H, 12-H, $^3J_{11,12}$ = 8.0, $^4J_{8,12}$ = 1.5 Hz), 8.43 t (1H, 8-H, $^4J_{8,10}$ = $^4J_{8,12}$ = 1.5 Hz), 9.61 d (1H, 3-H, $^3J_{3,4}$ = 8.6 Hz), 10.89 s (1H, 1-H). ^{13}C NMR spectrum (50 MHz), δ_C, ppm: 50.67 (C^4), 77.66 (C^5), 121.80 (C^8), 122.94 (C^{10}), 128.18 (C^{14}, C^{18}), 128.48 (C^{15}, C^{17}), 130.20 (C^{11}), 132.30 (C^{13}), 132.90 (C^{16}), 133.70 (C^{12}), 140.20 (C^7), 147.90 (C^9), 153.08 (C^2), 168.27 (C^6). Mass spectrum, *m*/*z* (I_{rel}, %): 312 (42.2) $[M - NO_2]^+$, 311 (60.8) $[M - HNO_2]^+$, 206 (12.2), 191 (14.7), 190 (30.8), 105 (100), 77 (85.8). Found, %: C 53.38; H 3.90; N 15.44. *m*/*z* 312.0984. $C_{16}H_{14}N_4O_6$. Calculated, %: C 53.63; H 3.94; N 15.64. ($M - NO_2$) 312.0984 ($C_{16}N_{14}N_3O_4$).

***N*-Benzoyl-*N′*-[1-(3-fluorophenyl)-2-nitroethyl]-urea (IIIc).** mp 186–187°C (from EtOH). UV spectrum, λ_{max}, nm (log ε): 206 (4.44), 236 (4.30), 269 sh (3.51). IR spectrum, ν, cm^{-1}: 3334, 3264 (NH); 1690, 1672 (C=O); 1545, 1536, 1379, 1353. ^{1}H NMR spectrum (400 MHz), δ, ppm: 5.15 d.d (1H, 5-H_A, $^2J_{AB}$ = 13.6, $^3J_{4,5}$ = 4.4 Hz), 5.31 d.d (1H, 5-H_B, $^2J_{AB}$ = 13.6, $^3J_{4,5}$ = 8.5 Hz), 5.69–5 80 m (1H, 4-H), 7.17 t (1H, 10-H, $^3J_{10,11}$ = $^3J_{HF}$ = 8.4 Hz), 7.34 d (1H, 12-H, $^3J_{11,12}$ = 7.7 Hz), 7.39 d (1H, 8-H, $^3J_{HF}$ = 10.3 Hz), 7.45 m (1H, 11-H), 7.51 t (2H, 15-H, 17-H, $^3J_{15,14}$ = $^3J_{15,16}$ = 7.7 Hz), 7.62 t (1H, 16-H, $^3J_{16,15}$ = $^3J_{16,17}$ = 7.7 Hz), 7.99 d (2H, 14-H, 18-H, $^3J_{14,15}$ = 7.7 Hz), 9.51 d (1H, 3-H, $^3J_{3,4}$ = 8.8 Hz), 10.92 s (1H, 1-H). ^{13}C NMR spectrum (100 MHz), δ_C, ppm: 50.83 (C^4), 78.13 (C^5), 113.86 d (C^8, $^2J_{CF}$ = 22 Hz), 114.94 d (C^{10}, $^2J_{CF}$ = 21 Hz), 123.03 (C^{12}), 128.27 (C^{14}, C^{18}), 128.56 (C^{15}, C^{17}), 130.79 d (C^{11}, $^3J_{CF}$ = 8 Hz), 132.32 (C^{13}), 132.98 (C^{16}), 140.69 d (C^7, $^3J_{CF}$ = 7 Hz), 153.13 (C^2), 162.28 d (C^9, $^1J_{CF}$ = 242 Hz), 168.43 (C^6). Mass spectrum, *m*/*z* (I_{rel}, %): 285 (28.0) $[M - NO_2]^+$, 284 (41.2) $[M - HNO_2]^+$, 179 (13.3), 164 (26.6), 163 (17.7), 105 (100), 77 (76.3). Found, %: C 57.84; H 4.16; F 5.93; N 12.58. *m*/*z* 285.1008. $C_{16}H_{14}FN_3O_4$. Calculated, %: C 58.00; H 4.26; F 5.74; N 12.68. ($M - NO_2$) 285.1039 ($C_{16}H_{14}FN_2O_2$).

***N*-Benzoyl-*N′*-[1-(4-methoxyphenyl)-2-nitro-ethyl]urea (IIId).** mp 181–182°C (from EtOH). IR spectrum, ν, cm^{-1}: 3432, 3261 (NH); 1684 (C=O); 1556, 1533, 1515, 1379, 1354. ^{1}H NMR spectrum (200 MHz), δ, ppm: 3.74 s (3H, MeO), 5.04 d.d (1H, 5-H_A, $^2J_{AB}$ = 13.1, $^3J_{4,5}$ = 5.4 Hz), 5.19 d.d (1H, 5-H_B, $^2J_{AB}$ = 13.1, $^3J_{4,5}$ = 8.0 Hz), 5.60 d.d.d (1H, 4-H, $^3J_{4,5A}$ = 5.4, $^3J_{4,5B}$ = 8.0, $^3J_{3,4}$ = 8.7 Hz), 6.95 d (2H, 9-H, 11-H, $^3J_{8,9}$ = 8.8 Hz), 7.40 d (2H, 8-H, 12-H, $^3J_{8,9}$ = 8.8 Hz), 7.50 d.d (2H, 15-H, 17-H, $^3J_{14,15}$ = 7.0 Hz, $^3J_{15,16}$ = 7.3 Hz), 7.61 t.t (1H, 16-H, $^3J_{16,15}$ = $^3J_{16,17}$ = 7.3 Hz, $^4J_{16,14}$ = $^4J_{16,18}$ = 1.4 Hz), 7.97 d.d (2H, 14-H, 18-H, $^3J_{14,15}$ = 7.0 Hz, $^4J_{14,16}$ = 1.4 Hz), 9.39 d (1H, 3-H, $^3J_{3,4}$ = 8.7 Hz), 10.82 s (1H, 1-H). ^{13}C NMR spectrum (50 MHz), δ_C, ppm: 50.76 (C^4), 55.07 (MeO), 78.49 (C^5), 114.06 (C^9, C^{11}), 127.97 (C^8, C^{12}), 128.08 (C^{14}, C^{18}), 128.42 (C^{15}, C^{17}), 129.51 (C^7), 132.25 (C^{13}), 132.80 (C^{16}), 152.82 (C^2), 158.96 (C^{10}), 168.29 (C^6). Mass spectrum, *m*/*z* (I_{rel}, %): 297 (13.8) $[M - NO_2]^+$, 296 (51.0) $[M - HNO_2]^+$, 191 (6.0), 176 (97.3), 175 (61.6), 105 (100), 77 (78.7). Found, %: C 59.31; H 4.95; N 12.10. *m*/*z* 296.1156. $C_{17}H_{17}N_3O_5$. Calculated, %: C 59.47; H 4.99; N 12.24. ($M - HNO_2$) 296.1161 ($C_{17}N_{16}N_2O_3$).

REFERENCES

1. Kappe, C.O., *Eur. J. Med. Chem*., 2000, vol. 35, p. 1043; Kappe, C.O., *Acc. Chem. Res*., 2000, vol. 33, p. 879.
2. Kappe, C.O., *Tetrahedron*, 1993, vol. 49, p. 6937.
3. Narsaiah, A.V., Basak, A.K., and Nagaiah, K., *Synthesis*, 2004, p. 1253; Khodaei, M.M., Salehi, P., Zolfigol, M.A., and Sirouszadeh, S., *Pol. J. Chem*., 2004, vol. 78, p. 385; Srinivas, K.V.N.S. and Das, B., *Synthesis*, 2004, p. 2091; see also references therein.
4. Lu, J. and Ma, H.R., *Synlett*, 2000, p. 63; Tu, S.-J., Zhou, J.-F., Cai, P.-J., Wang, H., and Feng, J.-C., *Synth. Commun*., 2002, vol. 32, p. 147; Lu, Y. and Bai, Y., *Synthesis*, 2002, p. 466; Xue, S., Shen, Y.-C., Li, Y.-L., Shen, X.-M., and Guo, Q.-X., *Chin. J. Chem*., 2002, vol. 20, p. 385; Shanmugam, P., Annie, G., and Perimal, P.T., *J. Heterocycl. Chem*., 2003, vol. 40, p. 879; Choudhary, V.R., Tillu, V.H., Narkhede, V.S., Borate, H.B., and Wakharkar, R.D., *Catal. Commun*., 2003, vol. 4, p. 449; Lu, J., Bai, Y.-J., Guo, Y.-H., Wang, Z.-J., and Ma, H.-R., *Chin. J. Chem*., 2002, vol. 20, p. 681; Lu, J., Wang, F.L., Yin, Y.-J., and Lac, W., *Chin. J. Org. Chem*., 2002, vol. 22, p. 788; Gohain, M., Prajapati, D., and Sandhu, J.S., *Synlett*, 2004, p. 235.
5. Sedova, V.F., Voevoda, T.V., Tolstikova, T.G., and Shkurko, O.P., *Khim.-Farm. Zh*., 2002, vol. 36, no. 6, p. 4.
6. Luzzio, F.A., *Tetrahedron*, 2001, vol. 57, p. 915.
7. Christensen, Ch., Juhl, K., Hazell, R.G., and Jorgensen, K.A., *J. Org. Chem*., 2002, vol. 67, p. 4875; Kogami, Y., Nakajima, T., Ikeno, T., and Yamada, T., *Synthesis*, 2004, p. 1947; see also references therein.
8. Zaikin, V.G., Varlamov, A.V., Mikaya, A.I., and Prostakov, N.S., *Osnovy mass-spektrometrii organicheskikh soedinenii* (Principles of Mass Spectrometry of Organic Compounds), Moscow: Nauka/Interperiodika, 2001, p. 133.
9. Shvekhgeimer, M.-G., *Usp. Khim*., 1998, vol. 67, p. 39.
10. Remennikov, G.Ya., Boldyrev, I.V., Kravchenko, S.A., and Pirozhenko, V.V., *Khim. Geterotsikl. Soedin*., 1993, p. 1290; Ballini, R., Bartoli, G., Giovannini, R., Marcantoni, E., and Petrini, M., *Tetrahedron Lett*., 1993, vol. 34, p. 3301.
11. Menzel, A., Ohrlein, R., Griesser, H., Wehner, V., and Jaeger, V., *Synthesis*, 1999, p. 1691.
12. Bez, G., Saikia, A.K., Kalita, D., Bezbarua, M.S., and Barua, N.C., *Indian J. Chem., Sect. B*., 1998, vol. 34, p. 325; *Chem. Abstr*., 1998, vol. 129, no. 148593.
13. Saikia, A.K., Hazarika, M.J., Barua, N.C., Bezbarua, M.S., Sharma, R.P., and Ghosh, A.C., *Synthesis*, 1996, p. 981; Bezbarua, M.S., Saikia, A.K., Barua, N.C., Kalita, D., and Ghosh, A.C., *Synthesis*, 1996, p. 1289; Bez, G., Bezbarua, M.S., Saikia, A.K., and Barua, N.C., *Synthesis*, 2000, p. 537.
14. Ballini, R. and Bosica, G., *J. Org. Chem*., 1997, vol. 62, p. 425.
15. Rodinovskaya, L.A., Shestopalov, A.M., and Chunikhin, K.S., *Tetrahedron*, 2002, vol. 58, p. 4273.