ISSN 1070-4280, Russian Journal of Organic Chemistry, 2018, Vol. 54, No. 6, pp. 867–872. © Pleiades Publishing, Ltd., 2018.
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Synthesis of Amides by Nucleophilic Substitution of Hydrogen in 3-Nitropyridine

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Received September 13, 2017

Abstract—3-Nitropyridine reacted with nitrogen-centered carboxylic acid amide anions in anhydrous DMSO in the presence of $K_3Fe(CN)_6$ via oxidative nucleophilic substitution of hydrogen to give previously unknown *N*-(5-nitropyridin-2-yl) carboxamides. The reaction of nitrobenzene with urea anion in DMSO enabled one-pot synthesis of bis(4-nitrophenyl)amine.

DOI: 10.1134/S1070428018060076

The problem of direct C–H functionalization of aromatic compounds, e.g., by nucleophilic substitution without preliminary introduction of a halogen atom or other substituent into the aromatic ring, is important in modern organic chemistry. Among other methods, oxidative nucleophilic substitution of hydrogen [1–4], which is widely applicable to π-deficient arenes and hetarenes, provides a good alternative to cross-coupling reactions catalyzed by transition metals [5]. The S_N^H methodology has already found application in industry [6], and it largely conforms to the "green chemistry" principles [7, 8].

Due to cooperative effect of electron-withdrawing nitro group and endocyclic nitrogen atom, 3-nitropyridine is a highly electrophilic heteroaromatic compound which readily reacts with various nucleophiles. For example, oxidative amination of 3-nitropyridine in the system liquid ammonia–$KMnO_4$ is not selective, and it involves all *ortho* and *para* positions with respect to the nitro group, giving rise to a mixture of three isomeric 3-nitropyridinamines [9]. The oxidative amination of 3-nitropyridine was later carried out with the use of ammonia in aqueous potassium permanganate, as well as in the system DMSO–$KMnO_4$ [10, 11].

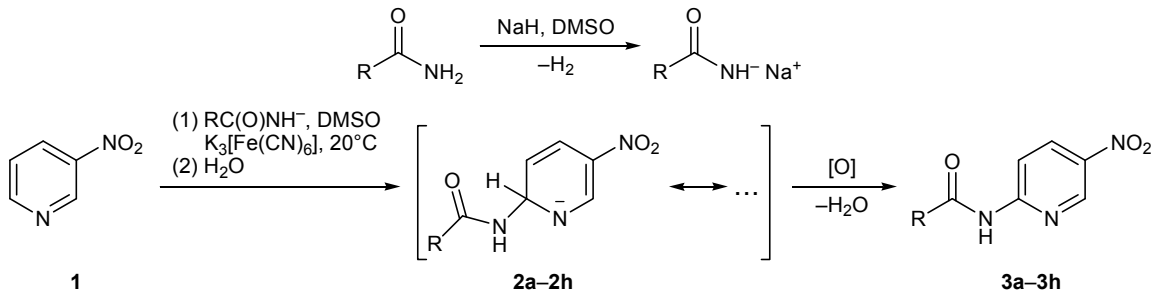
Oxidative S_N^H-alkylamination of 3-nitropyridines has been well documented [12–14]. These reactions are usually accomplished with excess alkyl- or dialkylamine used as solvent in the presence of an oxidant. Comparison of the efficiency of most common oxidants used for this purpose ($KMnO_4$, CAN, $AgPy_2MnO_4$, $AgMnO_4$) showed that the best results were obtained with a complex oxidant, dipyridinesilver permanganate ($AgPy_2MnO_4$) [13]. Verbeeck et al. [14] measured the primary kinetic isotope effect in the oxidative alkylamination of 3-nitropyridine and found that the rate-determining stage is the oxidation of intermediate σ^H-adduct. Therefore, the apparent reaction rate depends on both equilibrium concentration of the σ^H-adduct and on the oxidant nature.

The oxidative S_N^H-arylamination of 3-nitropyridines with preliminarily generated 2-, 3-, and 4-aminopyridine anions was studied in detail in [5]. The authors used nitrobenzene as a mild oxidant for the oxidation of σ^H-adducts formed in the first stage. In all cases, the *N*-nucleophile was directed to the *para* position with respect to the nitro group to afford products of oxidative nucleophilic substitution of hydrogen even in the presence of readily departing groups [5].

Vicarious nucleophilic amination of 3-nitropyridines with such reagents as hydroxylamine [15], 1,2,4-triazol-4-amine [15], *O*-methylhydroxylamine [16], and sulfenamides [17] was also thoroughly studied. If one more electron-withdrawing substituent was present in the pyridine ring, the nitro group itself was replaced by nucleophile. For instance, the nitro group in methyl 3-nitropyridine-4-carboxylate was replaced by the action of some anionic nucleophiles [18].

Unlike amination of azines, examples of S_N^H-amidation reactions remain very rare. The possibility of such reaction with nitrobenzene was reported for the first

Scheme 1.



R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$O_2NC_6H_4$ (**d**), 2-$O_2NC_6H_4$ (**e**), Me (**f**), Et (**g**), *i*-Pr (**h**).

time in the early 1990s [19]. Later on, benzamidation of 1,3-dinitrobenzene under anaerobic conditions afforded *N*-(2,4-dinitrophenyl)benzamide in 12% yield [20].

In continuation of our studies on direct introduction of a carboxamido group into 1,3,7-triazapyrene [21, 22] and acridine molecules [23, 24], we set ourselves the task of elucidating whether analogous S_N^H-functionalization of 3-nitropyridine is possible.

The conditions for the introduction of an amido group into 3-nitropyridine molecule were optimized using benzamide as model nucleophile. The corresponding anion was generated by the action of sodium hydride in anhydrous DMSO. If atmospheric oxygen was used as oxidant, the reaction at room temperature was too slow, and the complete conversion was not achieved after 48 h. Raising the temperature to 65–70°C accelerated the process, but elevated temperature also favored formation of a number of by-products. As in other S_N^H reactions [23–28], better results were obtained in the presence of $K_3Fe(CN)_6$ as one-electron oxidant. The reaction of 3-nitropyridine with benzamide in the presence of $K_3Fe(CN)_6$ was complete in 1 h at room temperature, and *N*-(5-nitropyridin-2-yl)benzamide (**3a**) was obtained in 79% yield (Scheme 1). Other aromatic carboxamides containing both electron-donating and electron-withdrawing substituents in the benzene ring reacted in a similar way under analogous conditions to give previously unknown amides **3b**–**3e** in 70–88% yield.

As in the reactions with 1,3,7-triazapyrenes [21], the yields of compounds **3f**–**3h** from aliphatic acid amides (acetamide, propionamide, and isobutyramide) were considerably lower (27–48%), which may be due to their low hydrolytic stability. We believe that they are hydrolyzed not only during the isolation stage but also in the reaction mixture which contains water liberated as a result of oxidative aromatization of σ^H-adducts **2** (Scheme 1).

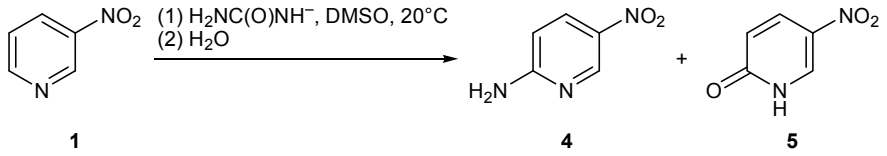
It was not surprising that an attempt to introduce a formamide group into the 3-nitropyridine molecule under analogous conditions was unsuccessful. In this case, the only isolated compound was known 5-nitropyridin-2-amine (**4**). The yield of **4** was as low as 16%, whereas the conversion of 3-nitropyridine was complete (according to the TLC data). Presumably, primary amine **4** is oxidized with $K_3Fe(CN)_6$ to give water-soluble by-products. Previously reported reaction of 3-nitropyridine derivative with formanilide anion was also accompanied by hydrolysis [29].

We then proceeded with studying the behavior of 3-nitropyridine toward urea anion in DMSO. The urea anion is a good nucleophile for the introduction of an amino group into the 1,3,7-triazapyrene and acridine molecules via S_N^H [21–24] or S_NAr reaction [30, 31]. Atmospheric oxygen acts as oxidant in the S_N^H reactions with urea anion. For example, acridin-2-amine was thus synthesized from acridine in 78% yield [24] which significantly exceeded the yield in the Chichibabin synthesis [32, 33].

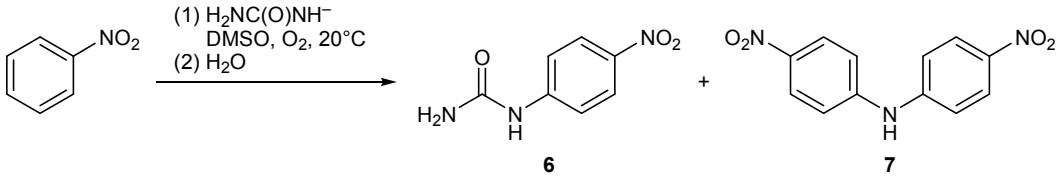
However, the use of urea anion for S_N^H-amination of 3-nitropyridine proved less successful than in the reactions with 1,3,7-triazapyrene and acridine. The reaction of **1** with 2 equiv of urea anion in anhydrous DMSO without protection from atmospheric oxygen was accompanied by considerable tar formation, and we succeeded in isolating from the reaction mixture two products with low yields, expected 5-nitropyridin-2-amine (**4**) and 5-nitropyridin-2(1*H*)-one (**5**) (Scheme 2).

Our attempts to improve the yield of **4** by varying the temperature, using $K_3Fe(CN)_6$ and other solvents (both polar and nonpolar), and varying the reactant ratio were unsuccessful. In all cases, by-product **5** was formed. Probably, urea anion acts as both N- and O-nucleophile [22] in the reaction with 3-nitropyridine.

Scheme 2.



Scheme 3.



We also tried to use nitrobenzene as a mild oxidant for the aromatization of σ^H-adduct; however, as a result, even more complex mixture of products was obtained. We presumed that under the given conditions nitrobenzene itself is also capable of reacting with urea anion. In fact, the reaction of nitrobenzene with preliminarily prepared urea anion in DMSO was complete at room temperature with the formation of a mixture of two products, 4-nitrophenylurea (**6**) and bis(4-nitrophenyl)amine (**7**) (Scheme 3).

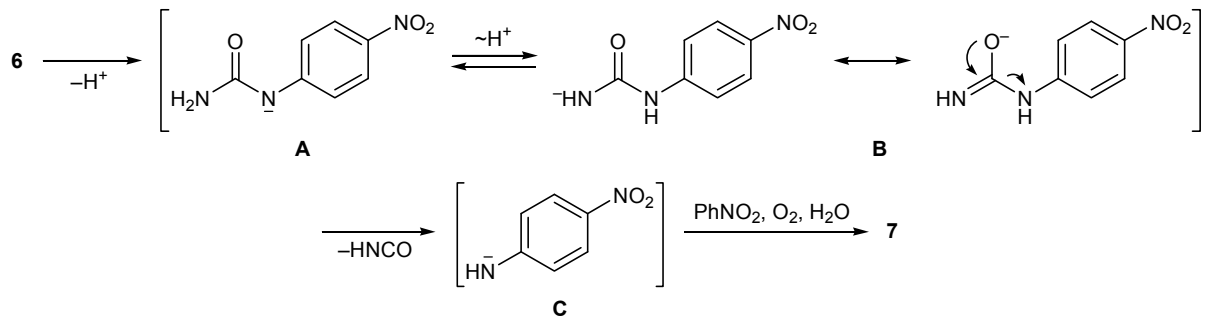
Undoubtedly, this reaction involves the addition of urea anion to give the corresponding σ^H-adduct and oxidative aromatization of the latter by the action of atmospheric oxygen. However, S_N^H-carbamoylamination products analogous to **6** were not isolated in the reactions with 1,3,7-triazapyrene [21, 22] and acridine [23, 24], since these compounds were converted to primary amines under the given conditions. More stable 4-nitrophenylurea is also partially involved in further transformations with successive generation of anions **A** and **B** and elimination of isocyanic acid (Scheme 4), but intermediate 4-nitroaniline anion **C** thus formed reacts with nitrobenzene, yielding S_N^H-arylamination product **7**. Bis(4-nitrophenyl)amine (**7**) was formed as the only product (yield 57%) when the reaction was carried out at 70°C. By special experiment we showed that, in fact, nitrobenzene reacts with 4-nitroaniline anion under the same conditions to afford 61% of bis(4-nitrophenyl)amine (**7**) (see Experimental).

In summary, we have developed a procedure for the synthesis of *N*-(5-nitropyridin-2-yl) carboxamides by direct nucleophilic substitution of hydrogen in 3-nitropyridine using N-centered carboxamide anions as nucleophiles. Nitrobenzene reacts with urea in DMSO in the presence of sodium hydride at room temperature to give bis(4-nitrophenyl)amine as a result of tandem S_N^H–S_N^H reaction.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance HD 400 spectrometer at 400 and 100 MHz, respectively; the chemical shifts were measured relative to the residual proton and carbon signals of deuterated dimethyl sulfoxide [34] (DMSO-d_5, δ 2.50 ppm; DMSO-d_6, δ_C 40.45 ppm) or tetramethylsilane (in $CDCl_3$). The mass spectra were obtained with a Bruker UHR-TOF Maxis™ Impact mass spectrometer (electrospray ionization). The IR spectra were measured on a Shimadzu IRTracer-100 instrument. The melting points were determined with REACH Devices RD-MP and Electrothermal IA 9200

Scheme 4.



melting point apparatuses. Compounds obtained by different methods were identified by comparing their IR spectra. The progress of reactions and the purity of the isolated compounds were monitored by TLC on Silufol UV-254 plates. Sodium hydride was used as a 60% suspension in mineral oil (Merck). Commercial reagents were used without additional purification.

Compounds 3a–3h (*general procedure*). Sodium hydride, 40 mg (1 mmol), was added with stirring to a solution of 1 mmol of the corresponding amide in 4 mL of anhydrous DMSO. When the evolution of hydrogen ceased (~0.5 h), 62 mg (0.5 mmol) of 3-nitropyridine and 329 mg (1 mmol) of $K_3Fe(CN)_6$ were added, and the mixture was vigorously stirred for 1–3 h at room temperature. The mixture was then poured into 50 mL of cold water and neutralized with dilute aqueous HCl to pH ~7. The precipitate was filtered off, washed with water, and dried. The products were additionally purified by recrystallization from appropriate solvents.

***N*-(5-Nitropyridin-2-yl)benzamide (3a).** Reaction time 1 h. Yield 96 mg (79%), gold yellow crystals, mp 168–169°C (from EtOH). IR spectrum (film), ν, cm^{-1}: 3265, 1686, 1582, 1535, 1505, 1342. ^{1}H NMR spectrum, δ, ppm: in DMSO-d_6: 7.55 m (2H, 3-H, 5-H), 7.64 t (1H, 4-H, J = 7.4 Hz), 8.03 d (2H, 2-H, 6-H, J = 7.1 Hz), 8.44 d (1H, 3′-H, J = 9.3 Hz), 8.66 d.d (1H, 4′-H, J = 9.3, 2.8 Hz), 9.23 d (1H, 6′-H, J = 2.8 Hz), 11.54 br.s (1H, NH); in $CDCl_3$: 7.48 d.d (2H, 3-H, 5-H, J = 7.3, 7.4 Hz), 7.57 d.t (1H, 4-H, J = 7.4, 1.1 Hz), 7.87 d.d (2H, 2-H, 6-H, J = 7.1, 1.1 Hz), 8.47 d.d (1H, 4′-H, J = 9.2, 2.5 Hz), 8.53 d (1H, 3′-H, J = 9.2 Hz), 8.87 br.s (1H, NH), 9.09 d (1H, 6′-H, J = 2.5 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 113.6, 128.4, 128.5, 132.6, 133.4, 134.2, 140.1, 144.6, 156.5, 166.7. Found: m/z 244.0697 $[M + H]^+$. $C_{12}H_{10}N_3O_3$. Calculated: M + H 244.0717. Found: m/z 266.0546 $[M + Na]^+$. $C_{12}H_9N_3NaO_3$. Calculated: M + Na 266.0536.

4-Methyl-*N*-(5-nitropyridin-2-yl)benzamide (3b). Reaction time 1.5 h. Yield 90 mg (70%), yellow crystals, mp 196–197°C (from EtOH). IR spectrum (film), ν, cm^{-1}: 3269, 1687, 1583, 1532, 1501, 1339. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 s (3H, CH_3), 7.26 d (2H, 3-H, 5-H, J = 8.1 Hz), 7.76 d (2H, 2-H, 6-H, J = 8.1 Hz), 8.46 d.d (1H, 4′-H, J = 9.2, 2.7 Hz), 8.51 d (1H, 3′-H, J = 9.2 Hz), 8.90 br.s (1H, NH), 9.03 d (1H, 6′-H, J = 2.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.6, 112.0, 126.4, 128.8, 129.3, 133.1, 139.5, 143.0, 143.8, 154.6, 164.7. Found: m/z 258.0875 $[M + H]^+$. $C_{13}H_{12}N_3O_3$. Calculated: M + H 258.0873. Found: m/z 280.0700 $[M + Na]^+$. $C_{13}H_{11}N_3NaO_3$. Calculated: M + Na 280.0693.

4-Methoxy-*N*-(5-nitropyridin-2-yl)benzamide (3c). Reaction time 1.5 h. Yield 102 mg (75%), yellow crystals, mp 195–196°C (from EtOH). IR spectrum (film), ν, cm^{-1}: 3100, 1679, 1601, 1578, 1496, 1342. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.83 s (3H, OCH_3), 6.95 d (2H, 3-H, 5-H, J = 8.8 Hz), 7.85 d (2H, 2-H, 6-H, J = 8.8 Hz), 8.47 d.d (1H, 4′-H, J = 9.2, 2.5 Hz), 8.51 d (1H, 3′-H, J = 9.2 Hz), 8.77 br.s (1H, NH), 9.09 d (1H, 6′-H, J = 2.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 54.6, 111.9, 113.3, 124.2, 128.4, 133.1, 139.5, 143.8, 154.7, 162.5, 164.1. Found: m/z 296.0648 $[M + Na]^+$. $C_{13}H_{11}N_3NaO_4$. Calculated: M + Na 296.0642.

4-Nitro-*N*-(5-nitropyridin-2-yl)benzamide (3d). Reaction time 1 h. Yield 127 mg (88%), yellow–orange crystals, mp 219–220°C (from EtOH). IR spectrum (film), ν, cm^{-1}: 3465, 3181, 1676, 1582, 1562, 1345. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 8.24 d (2H, 2-H, 6-H, J = 8.8 Hz), 8.35 d (2H, 3-H, 5-H, J = 8.8 Hz), 8.44 d (1H, 3′-H, J = 9.2 Hz), 8.69 d.d (1H, 4′-H, J = 9.2, 2.8 Hz), 9.25 d (1H, 6′-H, J = 2.8 Hz), 11.90 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 113.8, 123.5, 129.9, 134.3, 139.1, 140.4, 144.6, 149.6, 156.1, 165.4. Found: m/z 289.0580 $[M + H]^+$. $C_{12}H_9N_4O_5$. Calculated: M + H 289.0567.

2-Nitro-*N*-(5-nitropyridin-2-yl)benzamide (3e). Reaction time 3 h. Yield 104 mg (72%), yellow crystals, mp 216–217°C (from EtOH). IR spectrum (film), ν, cm^{-1}: 3276, 1673, 1581, 1505, 1345. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.79–7.91 m (3H, 4-H, 5-H, 6-H), 8.20 d (1H, 3-H, J = 8.2 Hz), 8.39 d (1H, 3′-H, J = 9.2 Hz), 8.69 d.d (1H, 4′-H, J = 9.2, 2.8 Hz), 9.20 d (1H, 6′-H, J = 2.8 Hz), 11.95 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 113.2, 124.3, 129.4, 131.4, 131.8, 134.47, 134.52, 140.3, 144.8, 145.9, 155.8, 166.0. Found: m/z 289.0567 $[M + H]^+$. $C_{12}H_9N_4O_5$. Calculated: M + H 289.0567. Found: m/z 311.0396 $[M + Na]^+$. $C_{12}H_8N_4NaO_5$. Calculated: M + Na 311.0387.

***N*-(5-Nitropyridin-2-yl)acetamide (3f).** Reaction time 2 h. Yield 31 mg (34%), light yellow crystals, mp 198–199°C (from PhH). IR spectrum (film), ν, cm^{-1}: 3205, 1687, 1544, 1496, 1344. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.16 s (3H, CH_3), 8.28 d (1H, 3′-H, J = 9.3 Hz), 8.58 d.d (1H, 4′-H, J = 9.3, 2.8 Hz), 9.16 d (1H, 6′-H, J = 2.8 Hz), 11.22 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 24.1, 112.4, 134.2, 139.7, 144.7, 156.2, 170.2. Found:

m/*z* 204.0380 $[M + Na]^+$. $C_7H_7N_3NaO_3$. Calculated: *M* + Na 204.0380.

***N*-(5-Nitropyridin-2-yl)propanamide (3g).** Reaction time 2 h. Yield 26 mg (27%), brown crystals, mp 152–153°C (from PhH). IR spectrum (film), ν, cm^{-1}: 3203, 1682, 1533, 1501, 1341. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.07 t (3H, CH_3, *J* = 7.5 Hz), 2.46 q (2H, CH_2, *J* = 7.5 Hz), 8.30 d (1H, 3′-H, *J* = 9.3 Hz), 8.59 d.d (1H, 4′-H, *J* = 9.3, 2.8 Hz), 9.15 d (1H, 6′-H, *J* = 2.8 Hz), 11.18 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 9.1, 29.5, 112.3, 134.2, 139.6, 144.8, 156.2, 173.8. Found: *m*/*z* 218.0380 $[M + Na]^+$. $C_8H_9N_3NaO_3$. Calculated: *M* + Na 218.0380.

2-Methyl-*N*-(5-nitropyridin-2-yl)propanamide (3h). Reaction time 3 h. Yield 50 mg (48%), light yellow crystals, mp 175–176°C (from PhH). IR spectrum (film), ν, cm^{-1}: 3490, 3357, 1691, 1590, 1501, 1332. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.10 d [6H, $CH(CH_3)_2$, *J* = 6.8 Hz], 2.81 m (1H, CH), 8.30 d (1H, 3′-H, *J* = 9.3 Hz), 8.58 d.d (1H, 4′-H, *J* = 9.3, 2.7 Hz), 9.15 d (1H, 6′-H, *J* = 2.7 Hz), 11.18 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 19.2, 34.7, 112.5, 134.2, 139.7, 144.7, 156.4, 177.1. Found: *m*/*z* 210.0872 $[M + H]^+$. $C_9H_{12}N_3O_3$. Calculated: *M* + H 210.0873.

5-Nitropyridin-2-amine (4). Reaction time 1.5 h. Yield 15 mg (16%), yellow crystals, mp 185–186°C (from PhH); published data [9]: mp 188–189°C. IR spectrum (film), ν, cm^{-1}: 3394, 3319, 1652, 1601, 1572, 1332, 1318. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 6.49 d (1H, 3-H, *J* = 9.3 Hz), 7.54 br.s (2H, NH_2), 8.12 d.d (1H, 4-H, *J* = 9.3, 2.8 Hz), 8.84 d (1H, 6-H, *J* = 2.8 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 107.2, 132.6, 134.4, 147.0, 163.3. Found: *m*/*z* 140.0460 $[M + H]^+$. $C_5H_6N_3O_2$. Calculated: *M* + H 140.0455.

Reaction of 3-nitropyridine with urea anion. Sodium hydride, 40 mg (1 mmol), was added at room temperature to a solution of 60 mg (1 mmol) of urea in 1.25 mL of anhydrous DMSO. When the evolution of hydrogen ceased (~0.5 h), 62 mg (0.5 mmol) of 3-nitropyridine was added, and the mixture was vigorously stirred for 2 h at room temperature. The mixture was then poured into 50 mL of cold water, neutralized with dilute aqueous HCl to pH ~7, and filtered. The aqueous filtrate was extracted with ethyl acetate (5×10 mL), the combined extracts were evaporated to dryness under reduced pressure, and the residue was purified by dry-column flash chromatography on silica gel. The column was eluted first with benzene–ethyl acetate (7:3) and then with ethyl acetate (both fractions were yellow). Removal of the solvent from the first fraction left 7.6 mg (11%) of 5-nitropyridin-2-amine (**4**), and 6.3 mg (9%) of 5-nitropyridin-2(1*H*)-one (**5**) was isolated from the second fraction.

5-Nitropyridin-2(1*H*)-one (5). Yellow crystals, mp 187–188°C; published data [35]: mp 182–183°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 6.42 d (1H, 3-H, *J* = 10.1 Hz), 8.11 d.d (1H, 4-H, *J* = 10.1, 3.2 Hz), 8.65 d (1H, 6-H, *J* = 3.2 Hz), 12.65 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 98.8, 119.01, 134.3, 138.7, 162.07. Found: *m*/*z* 141.0294 $[M + H]^+$. $C_5H_5N_2O_3$. Calculated: *M* + H 141.0292.

Reaction of nitrobenzene with urea anion. *a*. A 60% suspension of sodium hydride, 80 mg (2 mmol), was added with stirring to a solution of 60 mg (1 mmol) of urea in 4 mL of anhydrous DMSO. When the evolution of hydrogen ceased (~0.5 h), 61.5 mg (0.5 mmol) of nitrobenzene was added, and the mixture was vigorously stirred for 25 h at room temperature. The mixture was then poured into 50 mL of cold water, and the precipitate of compound **7** was filtered off, washed with water, and dried. The filtrate was extracted with ethyl acetate (3×10 mL), and the combined extracts were evaporated to obtain compound **6**. The products were purified by recrystallization from appropriate solvents.

***N*-(4-Nitrophenyl)urea (6).** Yield 23 mg (25%), light brown crystals, mp 269–270°C (from EtOAc–PhH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 6.21 br.s (2H, NH_2), 7.63 d (2H, 2-H, 6-H, *J* = 9.2 Hz), 8.13 d (2H, 3-H, 5-H, *J* = 9.2 Hz), 9.31 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 116.9, 125.1, 140.4, 147.3, 155.3. Found: *m*/*z* 182.0566 $[M + H]^+$. $C_7H_8N_3O_3$. Calculated: *M* + H 182.0560.

4-Nitro-*N*-(4-nitrophenyl)aniline (7). Yield 49 mg (38%), orange crystals, mp 219–220°C (from PhH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.36 d (4H, *o*-H, *J* = 9.2 Hz), 8.20 d (4H, *m*-H, *J* = 9.2 Hz), 9.98 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 117.1, 125.8, 140.5, 147.6. Found: *m*/*z* 282.0490 $[M + Na]^+$. $C_{12}H_9N_3NaO_4$. Calculated: *M* + Na 282.0485.

b. A 60% suspension of sodium hydride, 80 mg (2 mmol), was added with stirring to a solution of 60 mg (1 mmol) of urea in 4 mL of anhydrous DMSO. When the evolution of hydrogen ceased (~0.5 h), 61.5 mg (0.5 mmol) of nitrobenzene was added, and the mixture was vigorously stirred for 3 h at 70°C. The mixture was then poured into 50 mL of cold water, and

the precipitate of compound **7** was filtered off, washed with water, dried, and recrystallized from an appropriate solvent. Yield 74 mg (57%).

c. A 60% suspension of sodium hydride, 20 mg (0.5 mmol), was added with stirring to a solution of 0.5 mmol of 4-nitroaniline in 4 mL of anhydrous DMSO. When the evolution of hydrogen ceased (~0.5 h), 61.5 mg (0.5 mmol) of nitrobenzene was added, and the mixture was vigorously stirred for 25 h at room temperature. The mixture was then poured into 50 mL of cold water, and the precipitate of compound **7** was filtered off, washed with water, dried, and recrystallized from benzene. Yield 79 mg (61%).

This study was performed under financial support by the Ministry of Education and Science of the Russian Federation in the framework of state assignment (project nos. 4.141.2014/K, 4.6306.2017/BCh).

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