Novel routes to *N*-amino-1*H*-pyrrolo[2,3-*b*]pyridines from α-hydroxyarylalkyl ketones and hydrazines*

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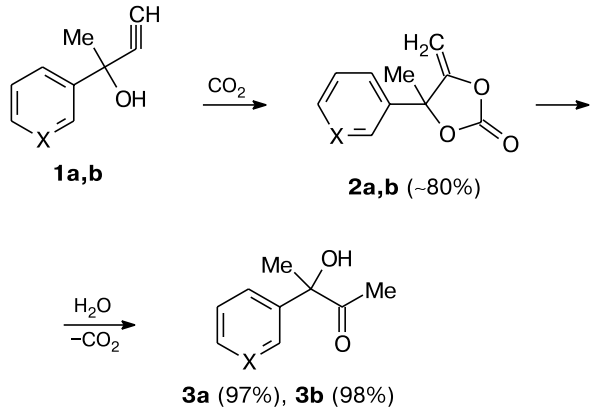
Treatment of 3-hydroxy-3-(3-pyridyl)butan-2-one hydrazone with polyphosphoric acid gave 1-amino-2,3-dimethyl-1*H*-pyrrolo[2,3-*b*]pyridine. An analogous reaction with 2,4-dinitrophenylhydrazone of the same ketone yielded 1-(2,4-dinitrophenyl)-3-methyl-4-(3-pyridyl)pyrazole.

Key words: dioxolanones, hydrazones, pyrrolo[2,3-*b*]pyridines, pyrazoles, α-hydroxy ketones, heterocyclization, polyphosphoric acid.

Earlier,[1] we have demonstrated that reactions of dioxolanones prepared from acetylenic alcohols **1** (Scheme 1) with hydrazines yield, depending on the reaction conditions, various heterocyclic systems such as *N*-aminooxazolidin-2-ones and 1,3,4-oxadiazin-2-ones. In turn, the latter can be converted into tetrahydronaphthalene or phthalazine derivatives.

Scheme 1



1a,b → **2a,b** (~80%) → **3a** (97%), **3b** (98%)

X = CH (**a**), N (**b**)

Conditions: catalyst, *p*, Δ.

We found that dioxolanones of the type **2**, which are usually very resistant to hydrolysis,[2] easily undergo ring opening on heating in moist acetonitrile in the presence of catalytic amounts of triethylamine when they contain an aryl substituent in position 4. The resulting α-hydroxy ketones **3** are obtained in virtually quantitative yields (see Scheme 1).

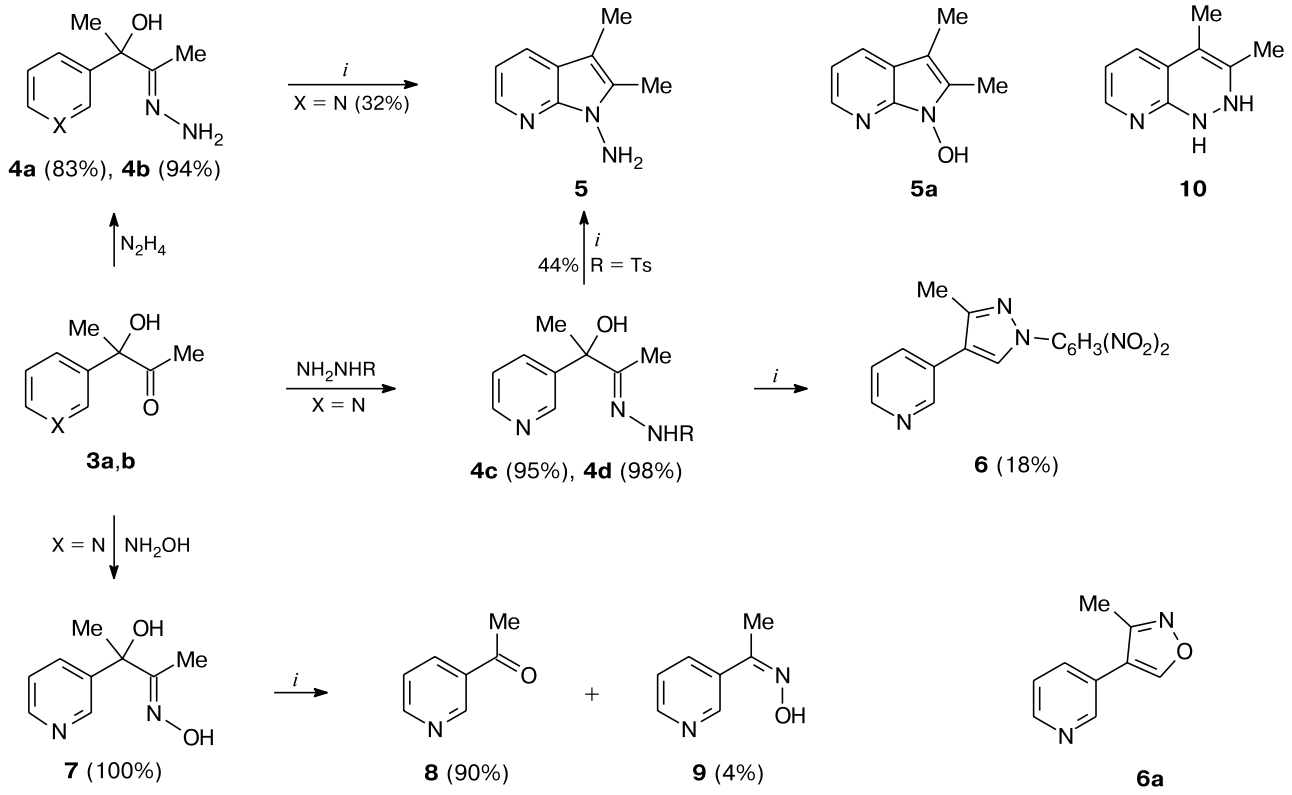
It is known that α-hydroxy ketones in an acidic medium can be dehydrated to give α,β-enones. Reactions of the latter with hydrazines or hydroxylamine produce pyrazolines[3] or isoxazolines[4] that can be easily oxidized into pyrazoles[5] or isoxazoles,[4] respectively. It was a challenge to obtain not easily accessible 4-arylpyrazoles (4-arylisoxazoles) from appropriate 4-aryldioxolanones **2** and hydrazines (or hydroxylamine). To investigate the possibility of further heterocyclization by analogy with literature examples, we synthesized a number of α-hydroxy ketone derivatives **3**: hydrazones **4a—d** and oxime **7** (Scheme 2). It turned out that the pathway of acid-catalyzed heterocyclization of the above derivatives strongly depends on the structure of the starting compound.

Heating of hydrazone **4b** in polyphosphoric acid (PPA) unexpectedly gave 1*H*-pyrrolo[2,3-*b*]pyridine derivative **5** (see Scheme 2) identified by ^{1}H and ^{15}N NMR spectroscopy (DMSO-d_6) and mass spectrometry. Its mass spectrum contains a molecular ion peak. According to ^{1}H NMR data for the reaction mixture before crystallization of the product, the conversion of compound **4b** into product **5** was above 70%, hydroxy ketone **3b** and its azine being the main by-products. After isolation and purification, the yield of product **5** was 32%. Additional evidence for the formation of the *N*-aminopyrrole ring rather than a six-membered dihydropyridazine one (see Scheme 2, compound **10**) was provided by ^{15}N NMR spectroscopy. The ^{1}H NMR spectrum shows satellite signals of that for the amino group at δ 5.55, which are due to couplings with ^{15}N nuclei ($^1J_{HN}$ = 71.4 Hz); in the ^{15}N INEPT spectrum, the two lines of the signal are spaced at 140 Hz

* Dedicated to Academician V. A. Tartakovsky on the occasion of his 75th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1552—1556, August, 2007.

Scheme 2



X = CH (**3a, 4a**), N (**3b, 4b—d**); R = Ts (**4c**), 2,4-$(NO_2)_2C_6H_3$ (**4d**)

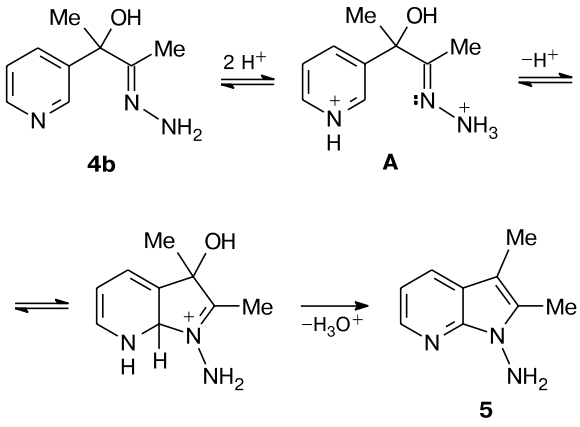
i. Polyphosphoric acid.

(*i.e.*, at an approximately doubled $^1H—^{15}N$ coupling constant. This unambiguously indicates the absence of proton exchange in the molecule (the satellite signals are observed) and allows the ^1H NMR signal at δ 5.55 (integral intensity 2 H) to be assigned to the exocyclic NH_2 group.

Usually, the synthesis of pyrrolopyridines involves multistep transformations and *N*-aminoazoles are obtained by either amination or nitrosation followed by reduction.[6,7] In our case, the heterocyclic system is constructed *via* a new C—N bond formed between the aromatic ring and the hydrazono group. According to our mechanism of the transformation **4b** → **5** (Scheme 3), the key intermediate may be species **A** resulting from protonation of the pyridine ring and the terminal NH_2 group. Apparently, the formation of a new C—N bond is possible because species **A** is relatively stable and the imine N atom bears a lone electron pair.

Our failure to synthesize an analogous *N*-aminoindole from 3-hydroxy-3-phenylbutan-2-one hydrazone (**4a**) under these conditions substantiates the necessity of a heteroatom capable of being protonated in an acidic medium (see Scheme 3). Attempted cyclization of *N*,*N*-dimethyl-, *N*-phenyl-, and *N*-(nitrophenyl)hydrazones of ketone **3b** and its semicarbazone (all prepared as described for compounds **4a,b** or according to known procedures[8]) was also unsuccessful. Heating of these hydrazones with PPA resulted in strong resinification of the reaction mixture and we always recovered only the starting hydroxy

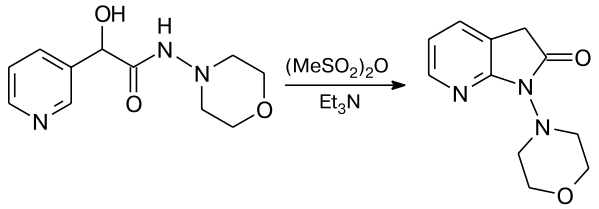
Scheme 3



ketone **3b**. Interestingly, in the case of *N*-tosylhydrazone **4c** quantitatively prepared from compound **3b** and tosylhydrazine, the yield of *N*-aminoazaindole **5** containing no tosyl group was 44% (see Scheme 2). Hydroxy ketone **3b** was a main by-product.

A similar mechanism of the formation of indolin-2-ones from 2-hydroxy-2-(3-pyridyl)acetohydrazides under the action of methanesulfonic anhydride has been described earlier[9] (Scheme 4). We found that PPA can simultaneously act as a solvent and a reagent for quaternization of the pyridine N atom, creating favorable conditions for dehydration with accompanying aromatization. In addition, we can employ unsubstituted hydrazone, which would be sulfonylated in a reaction with methanesulfonic anhydride.

Scheme 4

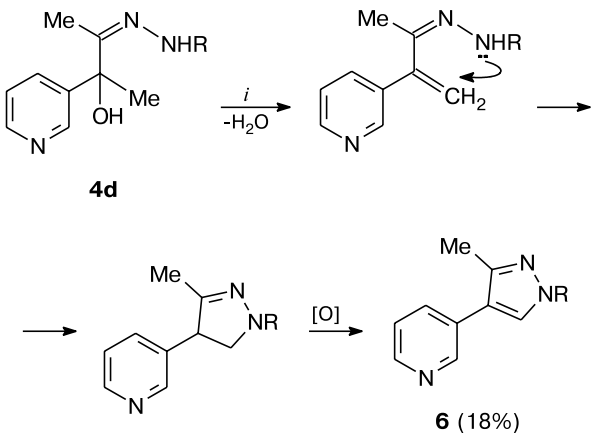


We carried out the transformation **4b** → **5** under the conditions cited in Ref. 9: treatment with methanesulfonic anhydride in anhydrous chloroform in the presence of triethylamine. However, we recovered the starting compound **4b** partially mesylated at the amino group; the reaction was accompanied by appreciable resinification. The reaction in boiling 1,4-dioxane gave an azine of ketone **3b** in ~70% yield and compound **3b** itself.

Treatment of 2,4-dinitrophenylhydrazone **4d** with PPA afforded pyrazole derivative **6** in 18% yield (see Scheme 2) instead of the expected *N*-dinitroanilinoazaindole. Apparently, the dinitrophenyl group as a strong electron acceptor lowers the basicity of the neighboring N atom so that it remains unprotonated under these conditions (Scheme 5). As the result, its lone electron pair can intramolecularly attack the terminal atom of the C=C bond of the Michael acceptor, thus closing a pyrazoline ring further oxidized into pyrazole by atmospheric oxygen. The absence of pyrazole derivatives like compound **6** in the reaction of tosylhydrazone **4c** can be associated with easy elimination of the tosyl group on heating in PPA.

Treatment of oxime **7** (prepared from compound **3b** and hydroxylamine, see Scheme 2) with PPA could be expected to give either *N*-hydroxyazaindole **5a** (see Scheme 3) or 4-(3-pyridyl)isoxazole **6a** (see Scheme 5). However, we isolated 3-acetylpyridine **8** (90%), which probably results from dehydration of the hydroxyimino group and cleavage of the C—C bond with liberation of an acetonitrile molecule, along with oxime **9** (4%).

Scheme 5



R = 2,4-$(NO_2)_2C_6H_3$

i. Polyphosphoric acid.

Experimental

NMR spectra were recorded on a Bruker DRX-500 instrument (500.13 MHz) in DMSO-d_6 (unless otherwise specified). Mass spectra were recorded on a Kratos MS-30 instrument (direct inlet probe, EI, 70 eV, ionization chamber temperature 250 °C). The course of the reactions was monitored by TLC on Baker-flex plates (IB-F silica gel). The following commercial solvents (≥99.9% purity) were used: light petroleum (LP), ethyl acetate (EA), benzene, *tert*-butyl methyl ether (TBME), toluene, and chloroform. The content of P_2O_5 in polyphosphoric acid (PPA) was not lower than 84 wt.%.

The starting alkynol **1b** and dioxolanones **2a,b** were prepared as described earlier.[1]

α-Hydroxy ketones 3 (general procedure). An appropriate dioxolanone (0.2 mol) was dissolved in acetonitrile (25 mL). Water (3.78 mL, 0.21 mol) and triethylamine (5 mL) were added. The mixture was refluxed for 30 min and evaporated to dryness. 3-Hydroxy-3-phenylbutan-2-one (**3a**) was crystallized from LP. The yield was 31.8 g (97%); its physicochemical constants and spectra agree with the literature data.[10]

3-Hydroxy-3-(3-pyridyl)butan-2-one (3b) was crystallized from benzene—LP. The yield was 32.3 g (98%), m.p. 64—65 °C, R_f = 0.51 (EA). Found (%): C, 65.51; H, 6.79; N, 8.39. $C_9H_{11}NO_2$. Calculated (%): C, 65.44; H, 6.71; N, 8.48. ^{1}H NMR, δ: 1.56, 2.11 (both s, 3 H each, Me); 6.28 (s, 1 H, OH); 7.37 (dd, 1 H, Py, J = 6.4 Hz, J = 4.2 Hz); 7.81 (d, 1 H, Py, J = 6.4 Hz); 8.49 (d, 1 H, Py, J = 4.2 Hz); 8.55 (s, 1 H, Py). MS (M = 165), m/z (I_{rel} (%)): 165 (1); 148 (5); 122 (100); 80 (17); 78 (12); 51 (14); 43 (93).

Hydrazones 4a,b (general procedure). An appropriate α-hydroxy ketone (10 mmol) was dissolved in methanol (20 mL), and hydrazine hydrate (50 mmol) was added. The mixture was refluxed for 20 min. Volatile substances were removed *in vacuo*, toluene (5 mL) was added to the residue, and the mixture was evaporated to dryness.

3-Hydroxy-3-phenylbutan-2-one hydrazone (4a) was crystallized from TBME. The yield was 1.477 g (83%), m.p.

105—106 °C, R_f = 0.24 (EA). Found (%): C, 67.52; H, 7.97; N, 15.59. $C_{10}H_{14}N_2O$. Calculated (%): C, 67.39; H, 7.92; N, 15.72. ^{1}H NMR, δ: 1.45, 1.52 (both s, 3 H each, Me); 5.36 (s, 1 H, OH); 5.91 (s, 2 H, NH_2); 7.18 (t, 1 H, Ph, *J* = 7.5 Hz); 7.28 (t, 2 H, Ph, *J* = 7.5 Hz); 7.34 (d, 2 H, Ph, *J* = 7.5 Hz). MS (M = 178), *m*/*z* (I_{rel} (%)): 178 (7); 162 (6); 135 (22); 121 (78); 94 (50); 77 (45); 57 (100); 43 (78).

3-Hydroxy-3-(3-pyridyl)butan-2-one hydrazone (4b) was crystallized from toluene. The yield was 1.629 g (91%), m.p. 97 °C, R_f = 0.17 (EA). Found (%): C, 60.47; H, 7.37; N, 23.33. $C_9H_{13}N_3O$. Calculated (%): C, 60.32; H, 7.31; N, 23.45. ^{1}H NMR, δ: 1.48, 1.55 (both s, 3 H each, Me); 5.60 (s, 1 H, OH); 5.86 (s, 2 H, NH_2); 7.31 (dd, 1 H, Py, *J* = 8.4 Hz, *J* = 5.2 Hz); 7.68 (d, 1 H, Py, *J* = 8.4 Hz); 8.41 (d, 1 H, Py, *J* = 5.2 Hz); 8.53 (s, 1 H, Py). MS (M = 179), *m*/*z* (I_{rel} (%)): 179 (5); 163 (3); 136 (10); 122 (68); 106 (19); 78 (27); 57 (100); 43 (96).

***N′*-[3-Hydroxy-3-(3-pyridyl)but-2-ylidene]-4-methylbenzenesulfonohydrazide (4c).** Compound **3b** (0.825 g, 5 mmol) and tosylhydrazine (0.930 g, 5 mmol) were dissolved in toluene (25 mL). The mixture was refluxed with a Dean—Stark trap until water evolution ceased. On cooling, the resulting crystals of compound **4c** were filtered off, washed with toluene, and dried. The yield was 1.582 g (95%), m.p. 207—209 °C, R_f = 0.64 (EA). Found (%): C, 57.74; H, 5.69; N, 12.55. $C_{16}H_{19}N_3O_3S$. Calculated (%): C, 57.64; H, 5.74; N, 12.60. ^{1}H NMR, δ: 1.46, 1.61, 2.42 (all s, 3 H each, Me); 5.88 (s, 1 H, OH); 7.23 (dd, 1 H, Py, *J* = 8.2 Hz, *J* = 4.6 Hz); 7.38 (d, 1 H, Py, *J* = 8.2 Hz); 7.42, 7.74 (both d, 2 H each, Ts, *J* = 8.0 Hz); 8.30 (s, 1 H, Py) 8.40 (d, 1 H, Py, *J* = 4.6 Hz); 10.10 (s, 1 H, NH). MS (M = 332), *m*/*z* (I_{rel} (%)): 333 (1); 212 (12); 178 (20); 139 (28); 122 (100); 106 (38); 91 (72); 78 (23); 65 (40); 57 (95); 43 (91).

3-Hydroxy-3-(3-pyridyl)butan-2-one (2,4-dinitrophenyl)hydrazone (4d). 2,4-Dinitrophenylhydrazine (0.594 g, 3 mmol) was dissolved under heating in ethanol (6 mL) and added to a solution of compound **3b** (0.495 g, 3 mmol) in ethanol (4 mL). The mixture was refluxed for 10 min and cooled to 0 °C. The resulting crystals were filtered off, washed with cold ethanol, and dried in air. The yield of hydrazone **4d** was 1.014 g (98%), m.p. 253—254 °C, R_f = 0.60 (EA). Found (%): C, 52.30; H, 4.37; N, 20.17. $C_{15}H_{15}N_5O_5$. Calculated (%): C, 52.17; H, 4.38; N, 20.28. ^{1}H NMR, δ: 1.80, 1.96 (both s, 3 H each, Me); 6.32 (s, 1 H, OH); 7.63 (dd, 1 H, Py, *J* = 8.4 Hz, *J* = 4.7 Hz); 7.92 (d, 1 H, $Ph(NO_2)_2$, *J* = 9.3 Hz); 8.11 (d, 1 H, Py, *J* = 8.4 Hz); 8.42 (dd, 1 H, $Ph(NO_2)_2$, *J* = 9.3 Hz, *J* = 2.4 Hz); 8.63 (d, 1 H, Py, *J* = 4.7 Hz); 8.77 (s, 1 H, Py); 8.88 (d, 1 H, $Ph(NO_2)_2$, *J* = 2.4 Hz); 10.78 (s, 1 H, NH). MS (M = 344), *m*/*z* (I_{rel} (%)): 327 (2); 310 (9); 280 (19); 239 (22); 192 (10); 166 (10); 130 (32); 117 (50); 104 (69); 90 (21); 77 (89); 63 (60); 51 (100).

1-Amino-2,3-dimethyl-1*H*-pyrrolo[2,3-*b*]pyridine (5). ***A.*** Hydrazone **4b** (20 mmol, 3.58 g) was dissolved under heating in chloroform (3 mL). Polyphosphoric acid (15 g) was added and the mixture was gradually (in order to avoid strong foaming) concentrated in a rotary evaporator at 60 °C. Then the mixture was heated with stirring to 110 °C and kept for 10 min. On cooling, the mixture was poured onto ice and alkalified to pH ~9 by adding 12 *M* NaOH. Organic material was extracted with ethyl acetate (3×10 mL). The combined extracts were dried over Na_2SO_4 and concentrated to an oily brown residue (4.8 g; the content of compound **5** was ~70% (^{1}H NMR)). The residue was dissolved in 5% HCl (30 mL). Neutral impurities were extracted with ethyl acetate (2×10 mL). The aqueous phase was separated and alkalified with 12 *M* NaOH to pH 9. Organic material was extracted with ethyl acetate (2×10 mL) and the organic extracts were dried over Na_2SO_4 and concentrated. Crystallization of the residue from EA—TBME gave colorless needle-like crystals. The yield of compound **5** was 1.03 g (32%), m.p. 138—139 °C, R_f = 0.55 (EA). Found (%): C, 66.94; H, 6.84; N, 26.22. $C_9H_{11}N_3$. Calculated (%): C, 67.05; H, 6.88; N, 26.07. ^{1}H NMR, δ: 2.18, 2.35 (both s, 3 H each, Me); 5.55 (s, 2 H, NH_2); 6.99 (dd, 1 H, Ar, *J* = 7.9 Hz, *J* = 4.3 Hz); 7.77 (d, 1 H, Ar, *J* = 7.9 Hz); 8.13 (d, 1 H, Ar, *J* = 4.3 Hz). MS (M = 161), *m*/*z* (I_{rel} (%)): 161 (99%), 146 (35%), 129 (12%), 120 (41%), 105 (100%), 92 (13%), 77 (38%).

B. Tosylhydrazone **4c** (0.833 g, 2.5 mmol) was added to PPA (25 g) preheated to 40 °C. The mixture was thoroughly stirred at 120 °C for 10 min to complete homogenization; the reaction mixture darkened. On cooling, the product was isolated and purified as described in procedure *A*. The conversion of the starting tosylhydrazone into compound **5** was ~60% (^{1}H NMR). The yield of purified compound **5** was 0.177 g (44%).

1-(2,4-Dinitrophenyl)-3-methyl-4-(3-pyridyl)pyrazole (6). Dinitrophenylhydrazone **4d** (2.07 g, 6 mmol) was added to PPA (30 g) preheated to 40 °C. The mixture was thoroughly stirred at 90 °C for 10 min and then at 110 °C for an additional 10 min. The substrate dissolved incompletely. Complete homogenization was attained at 125 °C; at this temperature, the reaction mixture was stirred for 10 min. On cooling, the mixture was poured onto ice and neutralized to pH ~7 by adding 12 *M* NaOH. The product was extracted with ethyl acetate (3×10 mL). The combined extracts were dried over Na_2SO_4 and concentrated to a brown oil. The oil was dissolved in hot ethanol. On cooling, the solution produced yellow crystals. The yield of compound **6** was 0.352 g (18%), m.p. 185—186 °C, R_f = 0.48 (EA). Found (%): C, 55.16; H, 3.42; N, 21.74. $C_{15}H_{11}N_5O_4$. Calculated (%): C, 55.38; H, 3.41; N, 21.53. ^{1}H NMR, δ: 2.38 (s, 3 H, Me); 7.50 (dd, 1 H, Py, *J* = 5.2 Hz, *J* = 2.9 Hz); 8.00 (d, 1 H, Py, *J* = 5.2 Hz); 8.17 (d, 1 H, $Ph(NO_2)_2$, *J* = 9.4 Hz); 8.55 (d, 1 H, Py, *J* = 2.9 Hz); 8.65 (dd, 1 H, $Ph(NO_2)_2$, *J* = 9.4 Hz, *J* = 2.4 Hz); 8.83 (s, 1 H, Ar); 8.86 (d, 1 H, $Ph(NO_2)_2$, *J* = 2.4 Hz); 9.00 (s, 1 H, Ar). MS (M = 325), *m*/*z* (I_{rel} (%)): 325 (100); 295 (40); 249 (46); 208 (21); 159 (15); 131 (19); 117 (24); 91 (21); 64 (23); 43 (28).

3-Hydroxy-3-(3-pyridyl)butan-2-one oxime (7). Hydroxy ketone **3b** (1.16 g, 7 mmol) and hydroxylamine hydrochloride (0.49 g, 7 mmol) were dissolved in water (5 mL). A solution of Na_2CO_3 (0.42 g, 4 mmol) in water (4 mL) was added with stirring for 15 min. The reaction mixture was stirred for 30 min and the precipitate that formed was filtered off, washed with water, and dried *in vacuo* at 60 °C. The yield of oxime **7** was 1.26 g (100%), m.p. 155 °C, R_f = 0.45 (EA). Found (%): C, 60.07; H, 6.77; N, 15.36. $C_9H_{12}N_2O_2$. Calculated (%): C, 59.98; H, 6.71; N, 15.55. ^{1}H NMR, δ: 1.59, 1.61 (both s, 3 H each, Me); 5.81 (s, 1 H, C—OH); 7.34 (dd, 1 H, Py, *J* = 8.1 Hz, *J* = 4.6 Hz); 7.71 (d, 1 H, Py, *J* = 8.1 Hz); 8.42 (d, 1 H, Py, *J* = 4.6 Hz); 8.58 (s, 1 H, Py); 10.75 (s, 1H, N—OH). MS (M = 180), *m*/*z* (I_{rel} (%)): 180 (1); 163 (2); 123 (68); 106 (10); 78 (19); 51 (23); 43 (100).

3-Acetylpyridine (8) and its oxime (9). Oxime **7** (0.72 g, 4 mmol) was added to PPA (20 g) preheated to 40 °C. The reaction mixture was thoroughly stirred at 100 °C for 10 min to

complete homogenization. On cooling, the mixture was poured onto ice and alkalified to pH ~10 by adding 12 *M* NaOH. The product was extracted with ethyl acetate (2×10 mL). The combined extracts were dried over Na_2SO_4 and concentrated to a transparent, light brown oil (0.457 g). According to ^{1}H NMR data, the contents of compounds **8** and **9** were 95.7 and 4.3 mol.%, respectively (the corresponding yields were 94 and 4 wt.%). Compounds **8** and **9** were not separated. In the ^{1}H NMR spectrum of their mixture, the signals for compound **8** coincided with those for authentic 3-acetylpyridine. ^{1}H NMR, δ: 2.63 (s, 3 H, Me); 7.57 (dd, 1 H, Py, J = 8.4 Hz, J = 4.8 Hz); 8.29 (d, 1 H, Py, J = 8.4 Hz); 8.80 (d, 1 H, Py, J = 4.8 Hz); 9.13 (s, 1 H, Py). Compound **9**. ^{1}H NMR, δ: 2.20 (s, 3 H, Me); 7.42 (dd, 1 H, Py, J = 7.9 Hz, J = 5.3 Hz); 8.02 (d, 1 H, Py, J = 7.9 Hz); 8.57 (d, 1 H, Py, J = 5.3 Hz); 8.85 (s, 1 H, Py); 11.49 (s, 1 H, N—OH). The mass spectrum of the mixture contained the molecular ion peaks for compounds **9** (M = 136) and **8** (M = 121).

References

1. Yu. B. Chudinov, S. B. Gashev, and V. V. Semenov, *Izv. Akad. Nauk, Ser. Khim.*, 2006, 2156 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, 2238].
2. G. Cardillo, M. Orena, G. Porzi, S. Sandri, and C. Tomasini, *J. Org. Chem.*, 1984, **49**, 701.
3. R. F. Smith, B. H. Augustine, L. A. Dennis, W. J. Ryan, S. C. Liptak, and B. R. Capparelli, *J. Heterocycl. Chem.*, 1989, **26**, 141.
4. J. F. Hansen, Y. In Kim, S. E. McCrotty, S. A. Strong, and D. E. Zimmer, *J. Heterocycl. Chem.*, 1980, **17**, 475.
5. E. E. Schweizer and S. N. Hirwe, *J. Org. Chem.*, 1982, **47**, 1652.
6. J. M. Ruxer, C. Lachoux, J. B. Ousset, J. L. Torregrosa, and G. Mattioda, *J. Heterocycl. Chem.*, 1994, **31**, 1561.
7. J. Hynes, W. W. Doubleday, A. J. Dyckman, J. D. Godfrey, J. A. Grosso, S. Kiau, and K. Leftheris, *J. Org. Chem.*, 2004, **69**, 1368.
8. W. C. Johnson, R. J. Shennan, and R. A. Reed, *Organic Reagents for Organic Analysis*, Hopkin and Williams Research Laboratory, USA, 1946.
9. C. A. Teleha, R. A. Greenberg, and R. J. Chorvat, *J. Heterocycl. Chem.*, 1998, **35**, 145.
10. I. Jirkovski and M. N. Cayen, *J. Med. Chem.*, 1982, **25**, 1154.

Received June 6, 2007;
in revised form August 23, 2007