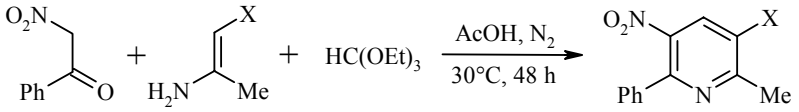
Chemistry of Heterocyclic Compounds, Vol. 45, No. 9, 2009

SYNTHESIS OF SUBSTITUTED 5-NITRO-6-PHENYLPYRIDINES BY THE CYCLO-CONDENSATION OF NITROACETOPHENONE, ETHYL ORTHOFORMATE, AND ENAMINES

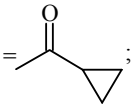
G. P. Sagitullina[1]*, A. K. Garkushenko[1], and R. S. Sagitullin[1]

Keywords: enamines, nitroacetophenone, nitropyridines.

We have previously developed a simple method for the synthesis of substituted 2,6-dimethyl-5-nitropyridines and 3,5-dinitropyridines by the cyclocondensation of nitroacetone and ethyl orthoformate with various enamines [1]. Replacing nitroacetone with nitroacetophenone permitted us to make available nitropyridines **2a-d** with a phenyl substituent in the pyridine ring. These nitropyridines may be used in the synthesis of δ-carbolines [2].



1a–d **2a–d**

1, **2 a** X = COMe; **b** X =  ; **c** X = COPh; **d** X = COOEt

The IR spectra were taken on a Specord IR-75 spectrometer in $CHCl_3$. The ^1H NMR spectra were taken on a Bruker AC-200 spectrometer at 200 MHz in $CDCl_3$ with TMS as the internal standard. The mass spectra were taken on an Agilent 5973N mass spectrometer.

2-Nitro-1-phenylethanone was obtained according to Gavrilin [3]. The synthesis of 3-amino-1-cyclopropyl-2-buten-1-one (**1b**) was described in our previous work [1].

Nitropyridines 2 (General Method). A solution of nitroacetophenone (0.99 g, 6 mmol), corresponding enamine **1a-d** (6 mmol), and ethyl orthoformate (3 ml, 18 mmol) in acetic acid (5 ml) was stirred for 48 h in an inert gas atmosphere at 30°C. The excess of the reagents was distilled off in vacuum. The residue was heated at reflux with activated charcoal in 20 ml ethanol and filtered. After cooling, the crystalline precipitate was filtered off. Nitropyridines **2a-d** were recrystallized from petroleum ether (40-70°C).

* To whom correspondence should be addressed, e-mail: Sagitullina@orgchem.univer.omsk.su.

[1] F. M. Dostoevsky Omsk State University, Omsk 644077, Russia.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1430-1431, September, 2009. Original article submitted August 13, 2009.

3-Acetyl-2-methyl-5-nitro-6-phenylpyridine (2a) was obtained in 44% yield; mp 92-93°C. IR spectrum, ν, cm^{-1}: 1680 (C=O); 1550, 1340 (NO_2). ^1H NMR spectrum, δ, ppm: 2.66 (3H, s, CH_3); 2.89 (3H, s, $COCH_3$); 7.50-7.58 (3H, m, C_6H_5); 7.93-8.01 (2H, m, C_6H_5); 8.45 (1H, s, H-4). Mass spectrum, *m/z* (I_{rel}, %): 257 $[M+1]^{+\cdot}$ (10), 256 $[M]^{+\cdot}$ (54), 228 (21), 227 (12), 184 (15), 183 (13), 167 (24), 166 (11), 81 (44), 77 (10), 43 (100). Found, %: C 65.64; H 4.57; N 11.19. $C_{14}H_{12}N_2O_3$. Calculated, %: C 65.62; H 4.72; N 10.93.

3-Cyclopropylcarbonyl-2-methyl-5-nitro-6-phenylpyridine (2b) was obtained in 40% yield; mp 105-106°C. IR spectrum, ν, cm^{-1}: 1690 (C=O); 1540, 1350 (NO_2). ^1H NMR spectrum, δ, ppm: 1.13-1.23 (2H, m, CH_2); 1.32-1.39 (2H, m, CH_2); 2.43 (1H, m, CH); 2.82 (3H, s, CH_3); 7.43-7.50 (3H, m, C_6H_5); 7.54-7.60 (2H, m, C_6H_5); 8.45 (1H, s, H-4). Mass spectrum, *m/z* (I_{rel}, %): 283 $[M+1]^{+\cdot}$ (20), 282 $[M]^{+\cdot}$ (100), 281 (10), 254 (34), 253 (20), 252 (14), 241 (16), 237 (15), 236 (12), 225 (12), 222 (11), 184 (13), 183 (20), 168 (12), 167 (72), 166 (37), 140 (17), 139 (20), 126 (27), 109 (17), 81 (78), 77 (18), 76 (12), 63 (15), 44 (14), 41 (73), 40 (13), 39 (21). Found, %: C 68.58; H 4.93; N 10.13. $C_{16}H_{14}N_2O_3$. Calculated, %: C 68.07; H 5.00; N 9.92.

3-Benzoyl-2-methyl-5-nitro-6-phenylpyridine (2c) was obtained in 25% yield; mp 79-80°C. IR spectrum, ν, cm^{-1}: 1670 (C=O); 1560, 1340 (NO_2). ^1H NMR spectrum, δ, ppm: 2.67 (3H, s, CH_3); 7.45-7.87 (10H, m, C_6H_5, COC_6H_5); 8.13 (1H, s, H-4). Mass spectrum, *m/z* (I_{rel}, %): 319 $[M+1]^{+\cdot}$ (7), 318 $[M]^{+\cdot}$ (26), 105 (100), 81 (14), 77 (74), 51 (15). Found, %: C 71.35; H 4.59; N 8.56. $C_{19}H_{14}N_2O_3$. Calculated, %: C 71.69; H 4.43; N 8.80.

Ethyl (2-methyl-5-nitro-6-phenyl)nicotinate (2d) was obtained in 40% yield; mp 65-66°C. IR spectrum, ν, cm^{-1}: 1725 (CO_2Et); 1550, 1345 (NO_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.44 (3H, $J = 7.1$, $CH_2C\underline{H}_3$); 2.97 (3H, s, CH_3); 4.44 (2H, q, $J = 7.1$, $C\underline{H}_2CH_3$); 7.43-7.50 (3H, m, C_6H_5); 7.52-7.61 (2H, m, C_6H_5); 8.59 (1H, s, H-4). Found, %: C 65.69; H 4.74; N 9.64. $C_{15}H_{14}N_2O_4$. Calculated, %: C 65.93; H 4.93; N 9.79.

This work was carried out with the financial support of the Russian Basic Research Fund (Grant 07-03-00783-a).

REFERENCES

1. G. P. Sagitullina, A. K. Garkushenko, E. G. Atavin, and R. S. Sagitullin, *Mendeleev Commun.*, **19**, 155 (2009).
2. T. Kametani, K. Ogasawara, and T. Yamanaka, *J. Chem. Soc., C*, 1006 (1968).
3. G. F. Gavrilin, L. U. Bykova, T. D. Rogachkova, E. I. Novikova, and G. S. Savel'eva, *Khim.-Farm. Zh.*, **7**, No. 3, 43 (1973).