STUDIES ON HETEROCYCLIC COMPOUNDS XXXV.[1] FACILE SYNTHESIS OF 3-METHYLAMINO-1,2,4-TRIAZOLO[4,3-*a*]PYRIDINE WITH NICKEL PEROXIDE

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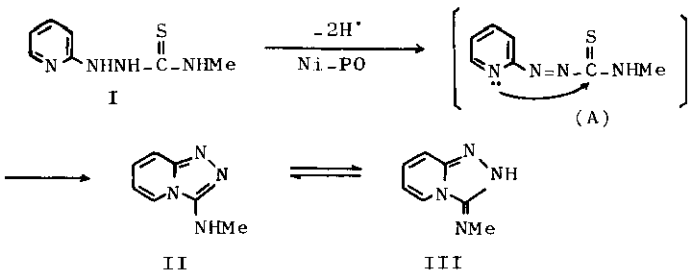
3-Methylamino-1,2,4-triazolo[4,3-a]pyridine (II) was obtained from the reaction of 1-(2-pyridyl)-4-methylthiosemicarbazide (I) and Nickel Peroxide (Ni-PO) in a good yield.

Nickel Peroxide (Ni-PO) is readily obtained by the treatment of nickel salts with sodium hypochloride in alkaline solution.[2] Previously, we reported the synthesis of 1,2,3-triazolo[1,5-*a*]pyridines by oxidative cyclization with Ni-PO.[3] The reaction was initiated by hydrogen radical abstraction from the substrate.[4]

This paper reports the facile synthesis of 3-methylamino-1,2,4-triazolo-[4,3-*a*]pyridine (II) by the oxidation of 1-(2-pyridyl)-4-methylthiosemicarbazide (I) with Ni-PO. I was readily obtained in a good yield (94%) by refluxing 2-hydrazinopyridine with methyl isothiocyanate in benzene for 3 hr.



I (A) II III

Chart 1

A mixture of I (5 mmol) and Ni-PO (4.0 g) in CH_3CN was stirred at room temperature for 1 hr. After the reaction mixture was filtrered through a glass filter (G-4), the oxidant was washed with CH_3CN. The combined filtrate was evaporated under a reduced pressure and the residue was crystallized from benzene (Yield: 89%). Physical data of the product (II) were as follows: Mp 114-116° (dec.): *Anal.* Calcd for $C_7H_8N_4$: C, 56.74; H, 5.44; N, 37.82. Found; C, 56.93; H, 5.51; N, 38.10: ^{1}NMR (DMSO-d_6) δ (ppm): 3.20 (3H, s, CH_3), 7.40-8.30 (3H, m, 6,7,8-H), 8.72 (1H, dd, J=6 and 2 Hz, 5-H), 10.47 (1H, bs, NH): Mass (m/z): 148 (M^+), 79 ($M^+-C_2H_3N_3$), 78 ($M^+-C_2H_4N_3$): ^{13}C NMR (DMSO-d_6, TMS as an internal standard) δ (ppm): 195.1 (3-C), 161.6 (8a-C), 149.4 (5-C), 138.9 (7-C), 126.5 (8-C), 114.8 (6-C), 31.6 (CH_3): IR ν_{max}^{KBr} cm^{-1}: 3150, 3050, 2960, 1585, 1550, 1375, 1070, 785: UV λ_{max}^{MeOH} nm (log ε): 245 (4.12), 288 (3.84)

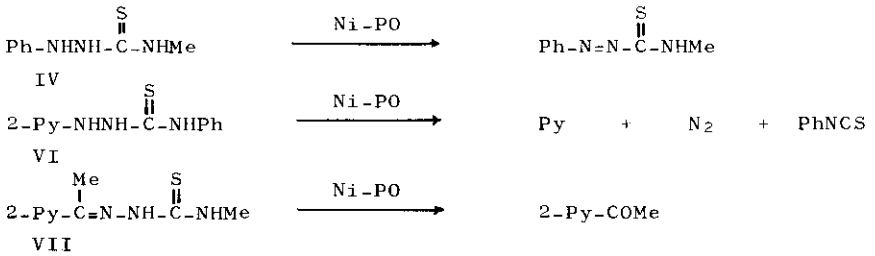


Chart 2

The cyclization mechanism presumably proceeds through an initial formation of azo-compound (A) and the lone pair electrons of pyridine nitrogen attack to thiocarbonyl carbon. The structure of II appears to exist predominantly in the imino form (III) from the spectral data.

The synthesis of II from the reaction of 1-(2-pyridyl)-4-methylsemicarbazide and Ni-PO failed under the same conditions. Treatment of IV with Ni-PO afforded azo-compound (V), a similar compound of the intermediate (A), but the cyclization reaction could not occur. Similarly, the cyclization of V and VII could not occur either.

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