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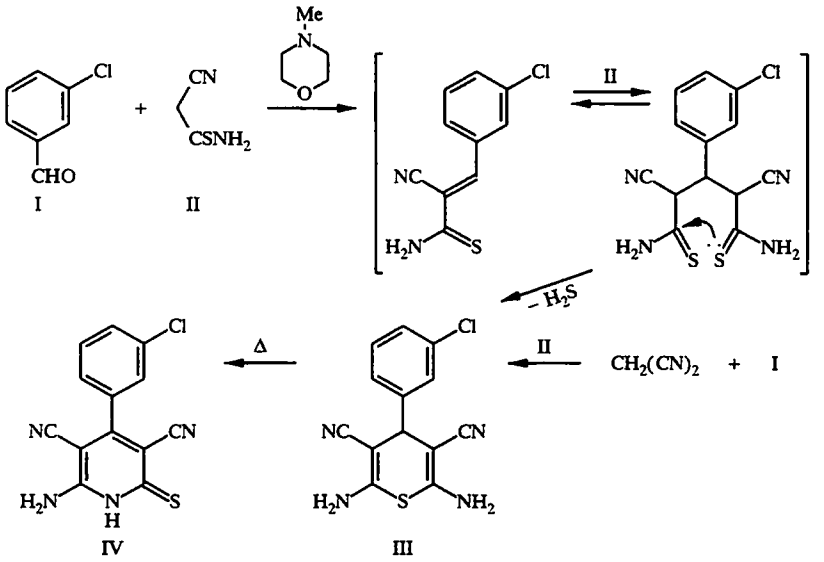
LETTERS TO THE EDITOR

SYNTHESIS OF 2,6-DIAMINO-3,5-DICYANO-4-(3'-CHLOROPHENYL)-4H-THIOPYRAN

V. D. Dyachenko and V. P. Litvinov

Arylmethylenecyanothioacetamides (low-molecular protein tyrosine kinase inhibitors) are obtained by condensation of aromatic aldehydes with cyanothioacetamide in the presence of amines in ethanol [1-3] or in the presence of Al_2O_3 in methanol [4]. When a two-fold excess of cyanothioacetamide and N-methylmorpholine is used, N-methylmorpholinium 6-amino-4-aryl-3,5-dicyano-1,4-dihydropyridine-2-thiolates are formed [5].

We have established that when 3-chlorobenzaldehyde (I) is reacted with cyanothioacetamide (II) in ethanol at 20°C in the presence of a catalytic amount of N-methylmorpholine, regardless of the ratio of reagents, 2,6-diamino-3,5-dicyano-4-(3'-chlorophenyl)-4H-thiopyran (III) is formed, identical to the compound obtained by an independent method from aldehyde (I) and malononitrile [6]. On boiling in ethanol, thiopyran III undergoes recyclization to thione IV.



2,6-Diamino-3,5-dicyano-4-(3'-chlorophenyl)-4H-thiopyran (III). Yield, 2.0 g (70%). mp 200-202°C (ethanol). IR spectrum (in Vaseline oil): 2188 ($\nu C\equiv N$), 3310, 3445 (ν_{NH_2}), 1640 cm^{-1} (δ_{NH_2}). PMR spectrum (in DMSO-D_6): 4.37 (1H, s, 4-H); 7.01 (4H, broad s, $2NH_2$); 7.20-7.48 ppm (4H, m, C_6H_4). Found, %: C 53.85; H 3.02; N 19.54; S 11.19. $C_{13}H_9ClN_4S$. Calculated, %: C 54.07; H 3.14; N 19.40; S 11.10.

6-Amino-3,5-dicyano-4-(3'-chlorophenyl)pyridine-2(1H)-thione (IV). Yield, 2.2 g (78%). mp 253-255°C (AcOH). IR spectrum (in Vaseline oil): 3388, 3483 (ν_{NH_2}), 2220 ($\nu C\equiv N$). PMR spectrum (in DMSO-D_6): 8.08 (2H, broad s, NH_2): 7.30-7.63 ppm (4H, m, C_6H_4). Found, %: C 54.29; H 2.28; N 19.70; S 11.32. $C_{13}H_7ClN_4S$. Calculated, %: C 54.45; H 2.46; N 19.54; S 11.18.

T. G. Shevchenko Lugansk State Pedagogical Institute, Lugansk 348011. N. D. Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 995-996, July, 1997. Original article submitted February 24, 1997.

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