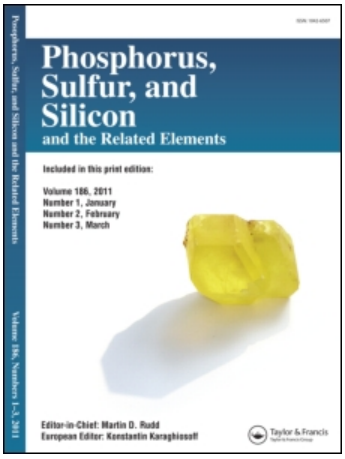


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

N-VS. O-(S-) PTC ALKYLATION OF 3-CYANO-4,6-DIMETHYL-2-OXO (THIOXO)-1,2-DIHYDROPYRIDINE

S. A. Shiba[a]; M. M. Mohamed[a]; M. A. Hassan[a]; A. M. El-sayed[a]
[a] Department of Chemistry, Faculty of Science, Ain Shams university, Cairo, Egypt

To cite this Article Shiba, S. A. , Mohamed, M. M. , Hassan, M. A. and El-sayed, A. M.(2000) 'N-VS. O-(S-) PTC ALKYLATION OF 3-CYANO-4,6-DIMETHYL-2-OXO (THIOXO)-1,2-DIHYDROPYRIDINE', Phosphorus, Sulfur, and Silicon and the Related Elements, 158: 1, 91 — 95
To link to this Article: DOI: 10.1080/10426500008042076
URL: http://dx.doi.org/10.1080/10426500008042076

Phosphorus, Sulfur and Silicon, 2000, Vol. 158, pp. 91-95
Reprints available directly from the publisher
Photocopying permitted by license only

N-vs. O-(S-) PTC ALKYLATION OF 3-CYANO-4,6-DIMETHYL-2-OXO (THIOXO)-1,2-DIHYDROPYRIDINE

S.A. SHIBA*, M.M. MOHAMED, M.A. HASSAN and A.M. EL-SAYED

Department of Chemistry, Faculty of Science, Ain Shams university, Abbassia, Cairo, Egypt

(Received March 23, 1999; Revised May 25, 1999)

N-Alkylation versus O-/or S- alkylation reactivity of 3-cyano-4,6-dimethyl-2-oxo(thioxo)-1,2-dihydropyridine have been investigated under phase transfer catalysis conditions.

In continuation of our interests [1–3] and reported PTC alkylation [4–6] in heterocyclic synthesis under phase transfer catalysis conditions, we are aiming in the present work to study N-alkylation versus O-/or S-alkylation of 3-cyano-4,6-dimethyl-2-oxo/or thioxo-1,2-dihydropyridines (**1&2**) under PTC reaction conditions, in analogy to the previously reported results. [7–9]

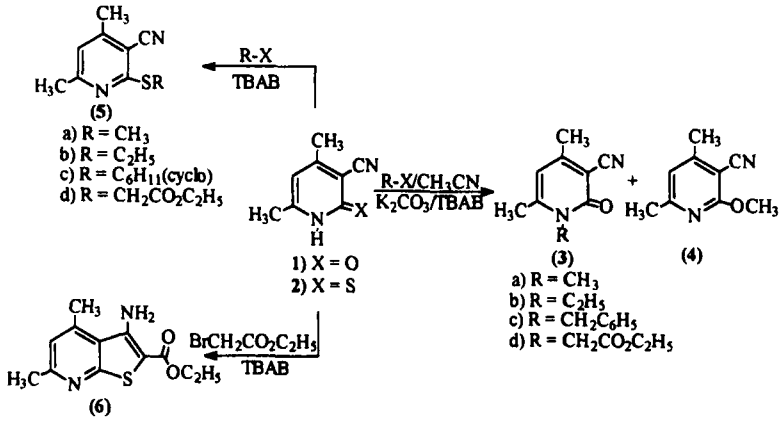
The proper PTC reaction conditions of alkylation are: acetonitrile/anhydrous potassium carbonate as solid/liquid phases [10,11] with continuous stirring of reactants for 4–8 h at 80°C, in presence of tetrabutyl ammonium bromide (TBAB) as a catalyst.

Treatment of pyridone [12] (**1**) with halo-organic compounds, e.g., ethyl bromide, benzyl chloride or ethyl bromoacetate under the optimized PTC conditions afforded, exclusively, N-alkyl derivatives (**3b-d**) in 75–87% yields. However, with methyl bromide it gave both **3a** and O-methyl derivative (**4**).

On the other hand, PTC alkylation of thiopyridone [13] (**2**) under the previous conditions afforded, exclusively, the S-alkylated products (**5a-d**).

* Correspondence Author.

However, extension of the reaction time of (**2**) with ethyl bromoacetate, under the same PTC conditions, for 48h resulted in the formation of 3-amino-2-carbethoxy-4,6-dimethylthiopheno[2,3-b]pyridine (**6**), in 77% yield. The product is formed by a normal S-alkylation to give (**5d**) that underwent a subsequent nucleophilic addition of the active methylene group on the adjacent cyano group..



Elemental analysis, I.R., ^{1}H-NMR and mass spectra have confirmed the structures of the products.

EXPERIMENTAL

Melting points reported are uncorrected. IR spectra were recorded on Pye-Unicam SP 2000 spectrophotometer, Perkin-Elmer 983 spectrophotometer and Maltson-1000 series FT-IR spectrophotometer using KBr wafer technique. The ^{1}H-NMR spectra were recorded by Varian T 60 or Gimini 200MHz, and Brucker AC 200, AMX 300, using TMS as internal standard. The chemical shifts are recorded on δ- scale in ppm. The mass spectra were recorded by AMD 604 spectrophotometer using single focusing mass spectrometer with direct inlet at beam energy 70 eV. Elemental analysis was estimated by a Perkin-Elmer 2400 or a Carlo-Erba 1106 – C, H, N analyzer.

TABLE I Spectral data of the prepared compounds:

Compd. No.	I. R., ν (cm^{-1})			^{1}H-NMR, δ (ppm)	Ms., m/z (abundance %)
	N-H	C≡N	C=O		
3a	–	2220	1665	In DMSO: 2.40 (s, 3H, $C\underline{H}_3$), 2.51 (s, 3H, $C\underline{H}_3$), 3.53 (s, 3H, N-$C\underline{H}_3$), 6.41 (s, 1H, C5-H)	–
3b	–	2218	1666	In $CDC1_3$: 1.35 (t, 3H, $C\underline{H}_3$-CH_2), 2.41 (s, 3H, $C\underline{H}_3$), 2.47 (s, 3H, $C\underline{H}_3$), 4.15 (q, 2H, CH_3-$C\underline{H}_2$-N), 6.05 (s, 1H, C5-H)	–
3c	–	2215	1660	–	$[M+1]^+$ (239, 43), M^+ (238, 92), 224 (61), 210 (10), 92 (100)
3d	–	2220	1735 1665	In DMSO: 1.32 (t, 3H, $C\underline{H}_3$-CH_2), 2.46 (s, 3H, $C\underline{H}_3$), 2.63 (s, 3H, $C\underline{H}_3$), 4.26 (q, 2H, CH_3-$C\underline{H}_2$-O), 4.93 (s, 2H, $C\underline{H}_2$-N), 6.49 (s, 1H, C5-H)	–
4	–	2210	–	In DMSO: 2.50 (s, 3H, $C\underline{H}_3$), 2.53 (s, 3H, $C\underline{H}_3$), 4.05 (s, 3H, O-$C\underline{H}_3$), 7.07 (s, 1H, C5-H)	–
5a	–	2205	–	–	–
5b	–	2210	–	In $CDCl_3$: 2.42 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 5.57 (s, 2H, S- CH_2), 6.58 (s, 1H, C5- H), 7.49–7.25 (m, 5H, Ar-H).	–
5c	–	2215	–	–	$[M+1]^+$ (247, 12), M^+ (246, 59), 232 (13), 214 (100), 192 (31), 165 (98).
5d	–	2212	1740	–	M^+ (250, 15), 219 (8), 193 (6), 191 (100), 177 (13), 164 (20), 131 (6)
6	3340 3330	–	1670	–	–

TABLE II Physical data of compounds (**3–6**):

No.	*Time (temp. °C)*	*M.Formula (M.Wt.)*	*Solvent of Crystallization (Color)*	*m.p. °C (Yield %)*	*Elemental Analysis Calc./Found*		
					C%	*H%*	*N%*
3a	5days	$C_9H_{10}N_2O$	Benzene	195–6	66.66	6.22	17.27
	(25)	(162.17)	(Colorless)	(62)	66.77	6.49	17.12
3b	4 h	$C_{10}H_{12}N_2O$	P.E. 80–100	172–4	68.16	6.86	15.90
	(81)	(176.22)	(Colorless)	(17)	68.30	6.64	16.24
3c	6 h	$C_{15}H_{14}N_2O$	P.E. 80–100	120–2	75.61	5.92	11.76
	(81)	(238.29)	(Colorless)	(74)	75.77	6.08	11.64
3d	4 h	$C_{12}H_{14}N_2O_3$	P.E. 80–100	159–160	61.53	6.02	11.96
	(81)	(234.25)	(Colorless)	(60)	61.38	6.10	11.84
4	5days	$C_9H_{10}N_2O$	P.E. 60–80	94–6	66.66	6.22	17.27
	(25)	(162.17)	(Colorless)	(30)	66.63	6.20	17.35
5a	12 h	$C_9H_{10}N_2S$	P.E. 80–100	98–100	60.64	5.65	15.72
	(81)	(178.26)	(Colorless)	(75)	60.73	5.83	15.84
5b	8 h	$C_{15}H_{14}N_2S$	P.E. 80–100	97–99	70.83	5.55	11.01
	(81)	(254.36)	(Colorless)	(72)	71.18	5.75	11.20
5c	6 h	$C_{14}H_{18}N_2S$	P.E. 40–60	94–5	68.25	7.36	11.37
	(81)	(246.38)	(Colorless)	(81)	68.09	7.45	11.51
5d	6 h	$C_{12}H_{14}N_2O_2S$	Benzene	80–2	57.85	5.64	11.19
	(81)	(250.32)	(Colorless)	(85)	57.77	5.61	11.23
6	48 h	$C_{10}H_{13}NO$	P.E. 80–100	99–100	67.02	7.31	7.82
	(81)	(179.22)	(Colorless)	(39)	67.02	7.34	8.04

PTC-Alkylation of 1,2-dihydro pyridone derivatives (1&2)

General procedure

To a solution of 1,2-dihydropyridones (**1&2**) (0.01 mole) in acetonitrile (50 mL), anhydrous K_2CO_3 (0.02 mole) and tetrabutyl ammonium bromide (TBAB) (0.003 mole) were added. After stirring for 30 min at 80–82 °C the halogen compound, such as, methyl bromide, ethyl bromide, benzyl chloride, cyclohexyl bromide and ethyl bromoacetate (0.012 mole) was added. The reaction mixture was stirred and controlled by TLC over the reaction period at different temperatures; Table II. At the end of reaction time, the organic layer was separated and the solvent was evaporated. The residue was triturated with proper solvent and finally crystallized from suitable solvents; Table II.

References

1. M. A. Hassan, D. Döpp; *Heterocycles, 45*, 451 (1997).
2. M. A. Hassan, M. M. Mohamed, S. A. Shiba, A. Khalil; *Phosphorus, Sulfur and Silicon*, in press.
3. S. A. Shiba, N. M. S. Harb, M. A. El-Kassaby, M. A. Hassan, M. K. Abou El-Regal; *Phosphorus, Sulfur and Silicon, 104*, 15 (1995).
4. P. Singh, K. Deep, H. Singh; *J. Chem. Res., Synop., 71*, 3 (1984).
5. P. Singh, S. K. Aggarwal, R. Sarin, N. Malhotra, H. Singh; *Indian J. Chem., 24B*, 263 (1985).
6. M. Lissel, S. Schmidt, B. Neumann; *Synthesis*, 1986, 382.
7. H. J. -M. Dou, P. Hassanaly, J. Metzger; *Heterocycl. Chem. 14*, 321 (1977).
8. H. J. -M. Dou, P. Hassanaly, J. Kister, G. Vernin, J. Metzger; *Helv. Chim. Acta, 61*, 3143 (1978).
9. P. Hassanaly, H. J. -M. Dou, M. Ludwikow; *Bull. Soc. Chim. Belg., 91*, 661 (1982).
10. D. Landini, F. Montanari, A. Maia; *J. Amer. Chem. Soc., 100*, 2796 (1978).
11. J. E. Gorden, R. Z. Kutina; *ibid., 99*, 3903 (1977).
12. T. Kato, M. Sato, A. Wagai; *J. Heterocycl. Chem., 18*, 603 (1981).
13. E. S. Ratemi, N. Namdev, M. S. Gibson; *ibid., 30*, 1513 (1993).