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NEW APPROACH TO THE SYNTHESIS OF SUBSTITUTED 5-ARYLCARBAMOYL-3-CYANO-6-METHYLPYRIDINE-2(1H)-THIONES. MOLECULAR AND CRYSTAL STRUCTURE OF 2-ALLYLTHIO-3-CYANO-5-(2-METHOXYPHENYLCARBAMOYL)-6-METHYL-4-(5-METHYL-2-FURYL)-1,4-DIHYDROPYRIDINE

V. D. Dyachenko[1] **and A. N. Chernega**[2]

Morpholinium 5-arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-1,4-dihydropyridine-2-thiolates have been obtained by the interaction of enamines of acetoacetanilides with 5-methyl-2-furfurylidenecyanothioacetamide. Alkylation of the salts gives thioethers and oxidation gives the corresponding substituted pyridine-2(1H)-thiones. The structure of 2-allylthio-3-cyano-5-(2-methoxyphenylcarbamoyl)-6-methyl-4-(5-methyl-2-furyl)-1,4-dihydropyridine was studied by X-ray crystallographic analysis.

Keywords: morpholinium 5-arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-1,4-dihydropyridine-2-thiolates, enamines of acetoacetanilides, (5-methyl-2-furfurylidene)cyanothioacetamide, pyridine-2(1H)-thiones, thioethers, alkylation, X-ray structural analysis.

Previously we developed methods of synthesizing 4-aryl(heteryl)-substituted 5-arylcarbamoyl-3-cyano-6-methylpyridine-2(1H)-thiones by the interaction of aryl(heteryl)methylenecyanothioacetamides with acetocetic acid anilides [1, 2] or by a three-component condensation of aromatic aldehydes, cyanothioacetamide, and acetoacetanilides [3].

In the present investigation we have found a new approach to functionally substituted 2-mercapto-1,4-dihydropyridines, which are potential antiradical [4], cardiovascular [5], and hepatoprotective [6] agents. It comprises a regioselective reaction of enamines of acetoacetanilides **1** with 5-methyl-2-furfurylidenecyanothioacetamide **2**, leading to the corresponding Michael adduct **3**. The latter is heterocyclized *in situ* by a type of intramolecular transamination [7] with the formation of morpholinium 5-arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-1,4-dihydropyridine-2-thiolates **4**, brief boiling of which in glacial acetic acid in the air leads to protonation and dehydration to the corresponding substituted pyridine-2(1H)-thiones **5**.

The structures of compounds **4** and **5** were confirmed by data of physicochemical and spectral investigations (Tables 1, 2, Experimental), and also by alkylation of them with alkyl halides **6**. The formation of thioethers **7** and **8** in the course of this reaction is a reliable demonstration of the structure of salts **4** and thiones **5** [8].

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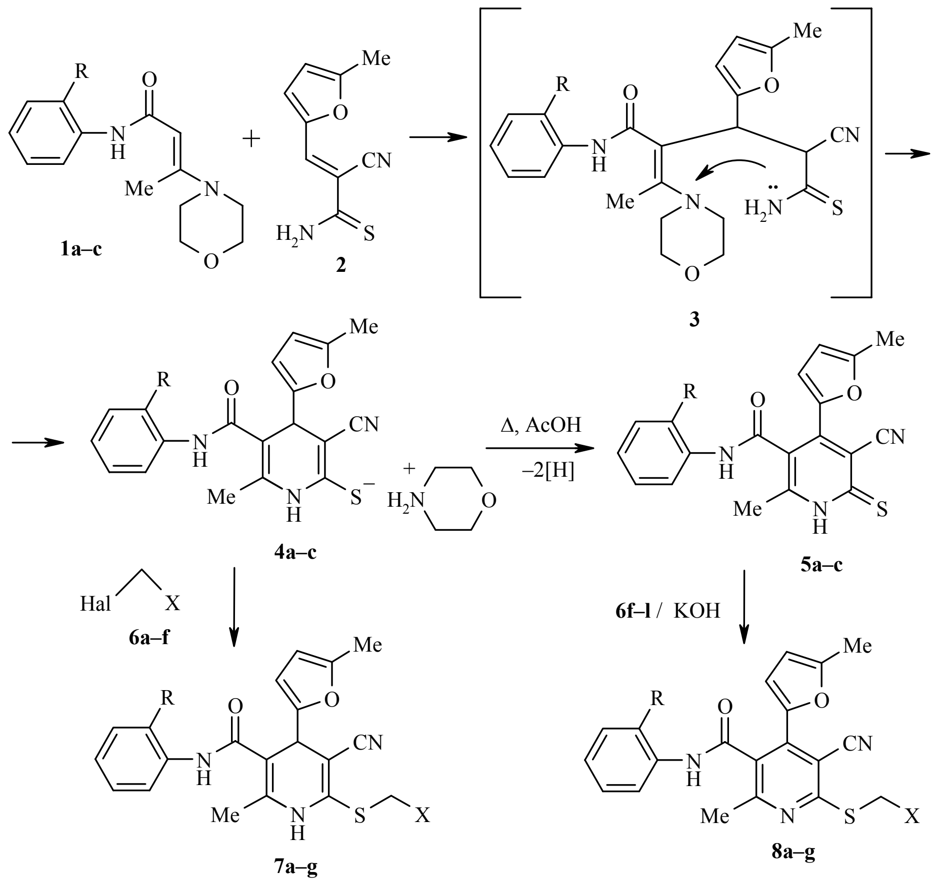
[1] Lugansk T. Shevchenko State Pedagogical University, Lugansk 91011, Ukraine; e-mail: dvd_lug@online.lg.ua. [2] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev 02094. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 51-58, January, 2006. Original article submitted July 15, 2003.



1a, 4a, 5a, 7e,f R = H; **1c, 4c, 5c, 7a-d, 8a,f** R = OMe; **1b, 4b, 5b, 7g, 8g** R = Me;
6a, 7a X = $CH=CH_2$; **6b, 7b** X = Et; **6c, 8a** X = PhCO; **6d, 8c** X = $(CH_2)_3Br$;
6e, 8d X = $(CH_2)_2Br$; **6f, 8e** X= CH_2Br; **6g, 8g** X = 3-coumarinylcarbonyl; **6h, 7c,f** X= H;
6i, 7d X = Me; **6j, 7e, 8f** X= Ph; **6k, 7g** X = CO_2Et; **6l, 8b** X = CO_2Bn;
6 a-g Hal = Br; **h,i** Hal = I; **j,l** Hal = Cl

To establish unequivocally the regioselectivity of the reaction of acetoacetic acid enamines with 5-methyl-2-furfurylidenecyanothioacetamide and to clarify the direction of alkylation of its products, the structure of compound **7a** was investigated by X-ray crystallographic analysis. The general shape of the **7a** molecule is given in Fig. 1. The central six-membered ring $N_{(1)}C_{(1-5)}$ is significantly nonplanar (the deviation of atoms from the mean square plane reached 0.23 Å) and has a *half-chair* conformation (modified Cremer–Pople parameters [9] $S = 0.48$, $\theta = 69.5°$, $\Psi = 1.5°$). The $N_{(1)}$ and $N_{(3)}$ atoms have a plane-trigonal configuration of bonds (the sum of the valence angles was 358.9 and 358.1°). The efficient conjugation between the unshared electron pair of the $N_{(1)}$ atom and the π-systems of the $C_{(1)}=C_{(2)}$ and $C_{(4)}=C_{(5)}$ double bonds leads to a significant shortening of the $N_{(1)}–C_{(1)}$ and $N_{(1)}–C_{(5)}$ bonds to 1.365(4) and 1.387(3) Å respectively (standard value for a pure single $N(sp^2)–C(sp^2)$ bond is 1.45 Å [10]. Similarly for $n(N_{(3)})–\pi(C_{(16)}=O_{(2)})$ the interaction causes a shortening of the $N_{(3)}–C_{(16)}$ bond to 1.354(3) Å. The $S_{(1)}–C_{(1)}$ bond length is 1.749(3) and $S_{(1)}–C_{(13)}$ is 1.816(4) Å and the $C_{(1)}S_{(1)}C_{(13)}$ bond angle is 104.4(1)°, practically coinciding with the corresponding values found in the Ph–S–Me molecule ($S–C(sp^2)$ 1.749(4), $S–C(sp^3)$ 1.803(4) Å, CSC 105.6(7)°) [11]. In the crystal, the **7a** molecules, due to intermolecular hydrogen bonds $N_{(1)}–H_{(1)}\cdots O_{(2)}$) [$N_{(1)}–H_{(1)}$ is 0.91(3), $N_{(1)}\cdots O_{(2)}$ 2.911(3), $H_{(1)}\cdots O_{(2)}$ 2.02(3) Å, $N_{(1)}–H_{(1)}\cdots O_{(2)}$ 2°] of moderate stability [12], are combined into endless spiral chains (Fig. 2).

TABLE 1. Characteristics of the Synthesized Compounds **4a-c**, **5a-c**, **7a-g**, and **8a-g**

Compound	Empirical formula	Found, % Calculated, %			mp, °C	Yield, %
		C	H	N		
4a	$C_{23}H_{26}N_4O_3S$	62.80 62.99	5.79 5.98	12.81 12.76	139-141	83
4b	$C_{24}H_{28}N_4O_3S$	63.50 63.69	6.31 6.24	12.25 12.38	291-293	88
4c	$C_{24}H_{28}N_4O_4S$	61.40 61.52	5.87 6.02	12.14 11.96	140-143	72
5a	$C_{19}H_{15}N_3O_2S$	65.20 65.31	4.41 4.33	11.85 12.03	298-300*	70
5b	$C_{20}H_{17}N_3O_2S$	65.92 66.10	4.80 4.71	11.43 11.56	288-290	65
5c	$C_{20}H_{17}N_3O_3S$	63.14 63.31	4.63 4.52	10.88 11.07	262-264	68
7a	$C_{23}H_{23}N_3O_3S$	65.50 65.54	5.33 5.50	10.12 9.97	118-120	85
7b	$C_{23}H_{25}N_3O_3S$	65.10 65.23	6.12 5.95	9.74 9.92	136-138	72
7c	$C_{21}H_{21}N_3O_3S$	63.81 63.78	5.39 5.35	10.50 10.62	142-143	67
7d	$C_{22}H_{23}N_3O_3S$	64.30 64.54	5.71 5.66	10.02 10.26	147-148	79
7e	$C_{26}H_{23}N_3O_2S$	70.58 70.72	5.18 5.25	9.64 9.52	164-166	78
7f	$C_{20}H_{19}N_3O_2S$	65.69 65.73	5.33 5.24	11.38 11.50	156-158	80
7g	$C_{24}H_{25}N_3O_4S$	63.95 63.84	5.44 5.58	9.19 9.31	161-163	71
8a	$C_{28}H_{23}N_3O_4S$	67.40 67.59	4.37 4.66	8.52 8.44	160-161	85
8b	$C_{29}H_{25}N_3O_5S$	65.89 66.02	4.60 4.78	8.12 7.96	116-117	67
8c	$C_{24}H_{24}BrN_3O_3S$	55.81 56.03	4.64 4.70	8.25 8.17	222-224	79
8d	$C_{23}H_{22}BrN_3O_3S$	55.32 55.21	4.30 4.43	8.25 8.40	206-208	62
8e	$C_{22}H_{20}BrN_3O_3S$	54.42 54.33	3.89 4.14	8.50 8.64	273-275	64
8f	$C_{27}H_{23}N_3O_3S$	68.87 69.06	5.11 4.94	9.04 8.95	174-175	75
8g	$C_{31}H_{23}N_3O_5S$	67.49 67.75	4.12 4.22	7.73 7.65	247-248	72

* Sublimation occurs at 200°C.

EXPERIMENTAL

The IR spectra of the synthesized compounds were recorded on a IKS 29 instrument in nujol. The ^{1}H NMR spectra were recorded on Gemini 200 (200 MHz) (for compounds **7a-d**, **8a-f**), Bruker AC 200 (200 MHz) (for compounds **7f,g**, **8g**), and Bruker WP 100 SY (100 MHz) (for compounds **4a-c**, **5a-c**, **7e**) instruments in DMSO-d_6, internal standard was Me_4Si. The mass spectra were taken on a Kratos MS 890 (70 eV) spectrophotometer. Melting points were determined on a Kofler block. A check on the progress of reactions and the purity of the compounds obtained was effected by TLC (Silufol UV 254, acetone–hexane, 3:5, visualization with iodine vapor).

TABLE 2. Spectral Characteristics of Compounds **4a-c**, **5a-c**, **7a-g**, **8a-g**

Compounds	IR spectrum ν, cm^{-1} CN, CONH	^{1}H NMR spectrum, δ, ppm (*J*, Hz)		
		$C_{(6)}CH_3$, $C_{(5')}CH_3$, both s	CONH, br. s	other signals
1	2	3	4	5
4a*	2188, 1674	2.04, 2.16	9.72	2.98 (4H, t, $J = 4.4$, CH_2NCH_2); 3.97 (4H, t, $J = 4.6$, CH_2OCH_2); 4.61 (1H, s, $H_{(4)}$); 5.81 (2H, m, $H_{(3)}$ and $H_{(4)}$ furyl); 6.98-7.70 (5H, m, C_6H_5); 9.15 (1H, br. s, NH)
4b*	2195, 1670	2.03, 2.20	9.32	1.62 (3H, s, CH_3); 3.05 (4H, t, $J = 4.4$, CH_2NCH_2); 3.92 (4H, t, $J = 4.7$, CH_2OCH_2); 4.57 (1H, s, $H_{(4)}$); 5.92 (2H, m, $H_{(3)}$ and $H_{(4)}$ furyl); 6.98-7.39 (4H, m, C_6H_4); 8.51 (1H, br. s, NH)
4c*	2190, 1678	2.16, 2.23	9.67	3.06 (4H, t, $J = 4.4$, CH_2NCH_2); 3.76 (4H, t, $J = 4.6$, CH_2OCH_2); 3.81 (3H, s, CH_3O); 4.25 (1H, s, $H_{(4)}$); 5.93 (2H, m, $H_{(3)}$ and $H_{(4)}$ furyl); 6.72-7.25 (4H, m, C_6H_4); 8.01 (1H, br. s, NH)
5a	2224, 1669	2.10, 2.41	10.40	6.40 (1H, d, $J = 3.4$, $H_{(4)}$ furyl); 7.15-7.57 (6H, m, C_6H_5 and $H_{(3)}$ furyl); 14.11 (1H, br. s, NH)
5b	2220, 1660	2.12, 2.23	9.71	2.47 (3H, s, CH_3); 6.44 (1H, d, $J = 3.4$, $H_{(3)}$ furyl); 7.15-7.58 (5H, m, C_6H_4 and $H_{(4)}$ furyl); 13.95 (1H, br. s, NH)
5c	2225, 1667	2.16, 2.47	9.46	3.78 (3H, s, CH_3O); 6.27 (1H, d, $J = 3.4$, $H_{(3)}$ furyl); 6.95 (3H, m, C_6H_4); 7.34 (1H, d, $J = 3.42$, $H_{(4)}$ furyl); 8.03 (1H, d, $J = 7.5$, C_6H_4); 13.85 (1H, br. s, NH)
7a	2194, 1682	2.22, 2.29	9.23	3.39 and 3.46 (by 1H, two d, $J = 5.94$, SCH_2); 3.77 (3H, s, CH_3O); 4.50 (1H, s, $C_{(4)}H$); 5.04 and 5.10 (by 1H, two d, $J_{cis} = 5.24$ and $J_{trans} = 12.30$, respectively, $=CH_2$); 5.78 (1H, m, CH=); 5.92 (1H, d, $J = 2.94$, $H_{(3)}$ furyl); 6.07 (1H, d, $J = 2.94$, $H_{(4)}$ furyl); 6.89 (3H, m, C_6H_4); 8.12 (1H, s, NH); 8.16 (1H, d, $J = 7.98$, C_6H_4)
7b	2204, 1670	2.22, 2.28	9.29	1.04 (3H, t, $J = 7.14$, CH_3); 1.65 (2H, m, CH_2); 2.79 (2H, m, SCH_2); 3.80 (3H, s, CH_3O); 4.54 (1H, s, $C_{(4)}H$); 5.97 (1H, d, $J = 3.40$, $H_{(3)}$ furyl); 6.10 (1H, d, $J = 3.40$, $H_{(4)}$ furyl); 6.90 (3H, m, C_6H_4); 8.09 (1H, d, $J = 7.78$, C_6H_4); 8.27 (1H, s, NH)
7c	2202, 1666	2.22, 2.29	9.20	2.50 (3H, s, SCH_3); 3.79 (3H, s, CH_3O); 4.45 (1H, s, $C_{(4)}H$); 5.93 (1H, d, $J = 3.04$, $H_{(3)}$ furyl); 6.07 (1H, d, $J = 3.04$, $H_{(4)}$ furyl); 6.86 (3H, m, C_6H_4); 8.12 (1H, d, $J = 9.20$, C_6H_4); 8.16 (1H, s, NH)
7d	2193, 1662	2.22, 2.29	9.25	1.28 (3H, t, $J = 7.02$, CH_3); 2.80 and 3.10 (by 1H, two m, SCH_2); 3.79 (3H, s, CH_3O); 4.58 (1H, s, $C_{(4)}H$); 5.95 (1H, d, $J = 2.54$, $H_{(3)}$ furyl); 6.09 (1H, d, $J = 2.54$, $H_{(4)}$ furyl); 6.87 (3H, m, C_6H_4); 8.11 (1H, d, $J = 9.72$, C_6H_4); 8.16 (1H, s, NH)

TABLE 2 (continued)

1	2	3	4	5
7e	2198, 1670	2.09, 2.16	9.60	4.15 and 4.39 (by 1H, two d, $^2J = 14.1$, SCH_2); 4.76 (1H, s, $C_{(4)}H$); 5.88 (2H, m, $H_{(3)}$ and $H_{(4)}$ furyl); 7.00-7.57 (10H, m, $2C_6H_5$); 9.21 (1H, br. s, NH)
7f	2194, 1665	2.08, 2.18	9.63	2.50 (3H, s, SCH_3); 4.80 (1H, s, $C_{(4)}H$); 5.96 (2H, m, $H_{(3)}$ and $H_{(4)}$ furyl); 7.07 (1H, m, C_6H_5); 7.26 (2H, m, C_6H_5); 7.58 (2H, d, $J = 7.03$, C_6H_5); 9.07 (1H, br. s, NH)
7g	2198, 1674	2.09, 2.15	9.11	1.23 (3H, t, $J = 6.18$, $CH_2\underline{CH_3}$); 2.25 (3H, s, CH_3); 3.79 and 3.95 (by 1H, two d, $^2J = 16.12$, SCH_2); 4.14 (2H, q, $J = 6.18$, OCH_2); 4.85 (1H, s, $C_{(4)}H$); 5.92 (1H, d, $J = 2.50$, $H_{(3)}$ furyl); 6.01 (1H, d, $J = 2.50$, $H_{(4)}$ furyl); 7.00-7.29 (4H, m, C_6H_4); 8.92 (1H, s, NH)
8a	2202, 1661	2.23, 2.27	9.64	3.75 (3H, s, CH_3O); 4.79 (2H, s, CH_2); 6.25 (1H, d, $J = 3.42$, $H_{(3)}$ furyl); 6.93 (2H, m, C_6H_5); 7.05 (1H, d, $J = 3.42$, $H_{(4)}$ furyl); 7.13 (1H, d, $J = 3.30$, H_{arom}); 7.57 (3H, m, H_{arom}); 7.97 (1H, d, $J = 6.38$, H_{arom}); 8.07 (2H, d, $J = 6.94$, H_{arom})
8b	2190, 1648	2.24, 2.42	9.48	3.79 (3H, s, CH_3O); 4.12 (2H, s, SCH_2); 5.17 (2H, s, OCH_2); 6.27 (1H, d, $J = 3.08$, $H_{(3)}$ furyl); 6.84-7.05 (3H, m, C_6H_4); 7.12 (1H, d, $J = 3.08$, $H_{(4)}$ furyl); 7.35 (5H, br. s, C_6H_5); 8.04 (1H, d, $J = 7.76$, C_6H_4)
8c	2198, 1657	2.21, 2.59	9.50	1.93 (2H, m, CH_2); 2.44 (2H, m, CH_2); 3.05 (2H, m, SCH_2); 3.35 (2H, m, CH_2Br); 3.77 (3H, s, CH_3O); 6.21 (1H, d, $J = 3.40$, $H_{(3)}$ furyl); 6.88-7.13 (4H, m, $H_{(4)}$ furyl and C_6H_4); 8.02 (1H, d, $J = 7.76$, C_6H_4)
8d	2190, 1664	2.23, 2.60	9.57	2.44 (2H, m, CH_2); 3.07 (2H, m, SCH_2); 3.41 (2H, m, CH_2Br); 3.78 (3H, s, CH_3O); 6.24 (1H, d, $J = 2.72$, $H_{(3)}$ furyl); 6.89-7.15 (4H, m, $H_{(4)}$ furyl and C_6H_4); 8.03 (1H, d, $J = 7.20$, C_6H_4)
8e	2202, 1675	2.23, 2.61	9.46	2.47 (2H, m, SCH_2); 3.68 (2H, m, CH_2Br); 3.79 (3H, s, CH_3O); 6.23 (1H, d, $J = 3.52$, $H_{(3)}$ furyl); 6.82-7.21 (4H, m, $H_{(4)}$ furyl and C_6H_4); 8.07 (1H, d, $J = 6.30$, C_6H_4)
8f	2204, 1673	2.22, 2.63	9.43	3.79 (3H, s, CH_3O); 4.52 (2H, s, CH_2); 6.21 (1H, d, $J = 3.42$, $H_{(3)}$ furyl); 6.88-7.47 (9H, m, H_{arom}); 8.06 (1H, d, $J = 7.82$, C_6H_4)
8g	2188, 1680	2.14, 2.31	9.71	2.99 (3H, s, CH_3); 4.81 (2H, s, CH_2); 6.33 (1H, d, $J = 3.48$, $H_{(3)}$ furyl); 7.02-7.99 (9H, m, H_{arom}); 8.74 (1H, s, $H_{(4)}$ coumarinyl)

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* The protons of the N^+H_2 fragment of the morpholinium cation were not observed, probably as a result of deuterium exchange.

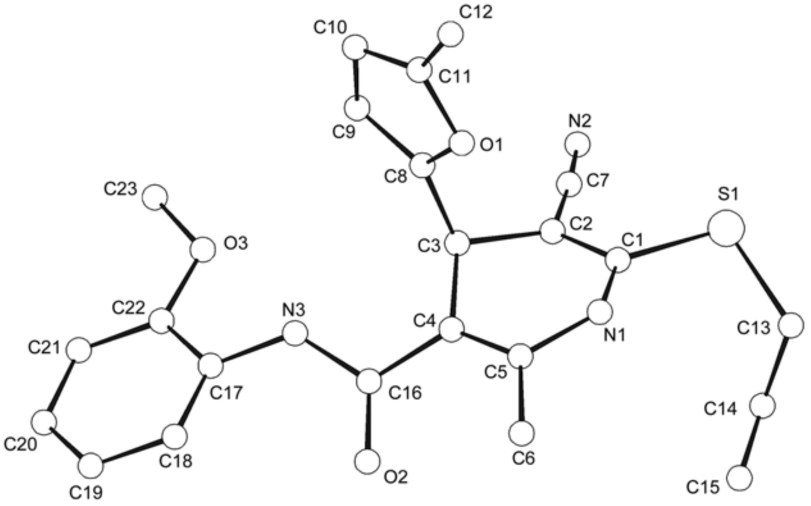

Fig. 1. General shape of the **7a** molecule. Main bond lengths (*l*, Å) and valence angles (ω, deg): $S_{(1)}$–$C_{(1)}$ 1.749(3), $S_{(1)}$–$C_{(13)}$ 1.816(4), $N_{(1)}$–$C_{(1)}$ 1.365(4), $N_{(1)}$–$C_{(5)}$ 1.387(3), $N_{(2)}$–$C_{(7)}$ 1.137(4), $N_{(3)}$–$C_{(16)}$ 1.354(3), $N_{(3)}$–$C_{(17)}$ 1.411(4), $C_{(1)}$–$C_{(2)}$ 1.347(4), $C_{(2)}$–$C_{(3)}$ 1.520(3), $C_{(3)}$–$C_{(4)}$ 1.525(3), $C_{(4)}$–$C_{(5)}$ 1.353(4), $C_{(4)}$–$C_{(16)}$ 1.489(3); $C_{(1)}S_{(1)}C_{(13)}$ 104.4(1), $C_{(1)}N_{(1)}C_{(5)}$ 120.5(2), $C_{(16)}N_{(3)}C_{(17)}$ 126.3(3), $N_{(1)}C_{(1)}C_{(2)}$ 120.0(2), $C_{(1)}C_{(2)}C_{(3)}$ 120.4(2), $C_{(2)}C_{(3)}C_{(4)}$ 107.26(19), $C_{(3)}C_{(4)}C_{(5)}$ 120.2(2), $N_{(1)}C_{(5)}C_{(4)}$ 119.5(2).

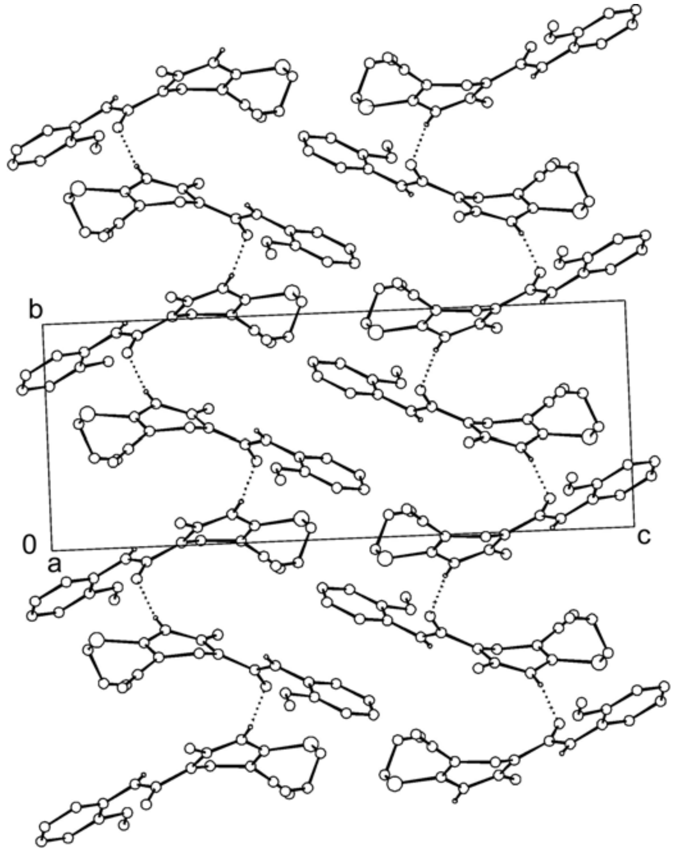

Fig. 2. Crystal packing of compound **7a** (dotted lines indicate intermolecular hydrogen bonds). For simplicity the $C_4H_2O–CH_3$ substituent at the $C_{(3)}$ atom is not shown.

X-Ray Structural Investigation of a Monocrystal of Compound 7a of linear dimensions 0.37 × 0.43 × 0.47 mm was carried out at room temperature on an automatic Enraf-Nonius CAD-4 four-circle diffractometer (MoKα radiation, ratio of scanning rates $2\theta/\omega = 1.2$, $\theta_{max} = 27°$, segment of sphere $0 \leq h \leq 17$, $0 \leq k \leq 10$, $-27 \leq l \leq 27$. In all 5935 reflections were collected, of which 5322 were symmetrically independent ($R_{int} = 0.012$). The crystals of **7a** were monoclinic, $a = 13.535(4)$, $b = 8.367(2)$, $c = 21.847(8)$ Å; $\beta = 99.08(2)°$; $V = 2443(1)$; M = 421.51; $Z = 4$; $d_{calc} = 1.15$ g/cm^3; $\mu = 1.50$ cm^{-1}; $F(000) = 888.62$; space group $P2_1/n$. The structure was solved by the direct method and refined by least squares in a full-matrix anisotropic approach using the CRYSTALS [13] set of programs. In the refinement 2565 reflections with $I > 4(I)$ (279 refined parameters, number of reflections per parameter 9.2). All the hydrogen atoms (apart from the H atoms at $C_{(14)}$ and $C_{(15)}$) were made apparent from an electron density difference synthesis. The $H_{(1)}$ and $H_{(3)}$ atoms were refined isotropically, the remaining hydrogen atoms were included in the refinement with fixed positions and thermal parameters. An estimate of absorption in the crystal was carried out with the aid of the azimuthal scanning method [14]. The Chebyshev weighting factor method [15] was used in the refinement with the three parameters: 2.21, 2.19, and 1.59. The final values of the divergence factors $R = 0.069$ and $R_W = 0.068$, $GOF = 1.125$. The residual electron density from the Fourier difference series was 1.15 and -0.36 e/Å^3. The coordinates of the nonhydrogen atoms may be obtained from the authors.

Morpholinium 5-Arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-1,4-dihydropyridine-2-thiolates 4a-c. A mixture of acetoacetanilide enamine **1** (10 mmol) and (5-methyl-2-furfurylidene)cyanothioacetamide **2** (1.92 g, 10 mmol) in ethanol (15 ml) was stirred for 20 min and left. After 1 day the solid which had formed was filtered off, washed with ethanol, and with hexane. Salts **4a-c** were obtained (Tables 1, 2).

5-Aroylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)pyridine-2(1H)-thiones 5a-c were obtained on recrystallizing the appropriate salt **4a-c** from glacial acetic acid (Tables 1, 2). Mass spectrum of compound **5c**, *m/z* (I_{rel}, %): 379 (48) $[M]^+$, 271 (10), 257 (100), 229 (11), 123 (44), 92 (10), 77 (9), 65 (11), 43 (14).

5-Arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-2-X-methylthio-1,4-dihydropyridines 7a-g. A mixture of the appropriate salt **4** (10 mmol) and alkyl halide **6** (10 mmol) in DMF (8 ml) was stirred for 4 h, diluted with water (10 ml), and left for 1 day. The resulting solid was filtered off, washed with water, then with ethanol and with hexane. Compounds **7a-g** were obtained, which were recrystallized from ethanol (Tables 1, 2).

Mass spectra of compounds **7a-d**, *m/z* (I_{rel}, %). **7a**: 421 (10) $[M]^+$, 380 (42), 299 (38), 271 (35), 257 (100), 135 (14), 123 (58), 108 (19), 77 (13), 41 (27). **7b**: 423 (22) $[M]^+$, 380 (46), 338 (82), 299 (38), 273 (66), 259 (84), 123 (100), 108 (30), 77 (14), 65 (19), 43 (58). **7c**: 395 (22) $[M]^+$, 393 (13) $[M-2]^+$, 380 (16), 338 (28), 273 (44), 271 (100), 245 (22), 123 (43), 77 (11), 65 (17). **7d**: 409 (27) $[M]^+$, 380 (35), 366 (20), 338 (65), 287 (39), 259 (100), 257 (48), 123 (86), 108 (24), 92 (21), 77 (12), 65 (18), 43 (17).

5-Arylcarbamoyl-3-cyano-6-methyl-4-(5-methyl-2-furyl)-2-Z-methylpyridines 8a-g. An aqueous 10% solution (5.6 ml, 10 mmol) of KOH and alkyl halide **6** (10 mmol) were added with stirring to a suspension of the appropriate pyridinethione **5** (10 mmol) in DMF (8 ml), after which the mixture was stirred for 4 h. The reaction mixture was then diluted with water (10 ml), and left for a day. The resulting solid was filtered off, washed with water, with ethanol, and with hexane. Compound **8** was obtained and was recrystallized from glacial acetic acid (Tables 1, 2).

Mass spectra of compounds **8a-f**, *m/z* (I_{rel}, %). **8a**: 497 (9) $[M]^+$, 392 (11), 376 (13), 375 (57), 105 (100), 77 (37). **8b**: 527 (18) $[M]^+$, 405 (88), 269 (13), 241 (14), 155 (12), 91 (100), 65 (12). **8c**: $[M]^+$ absent, 434 (100) $[M-Br]^+$, 348 (12), 311 (69), 284 (72), 257 (41), 225 (18), 123 (38), 108 (14), 87 (16), 55 (17), 43 (39). **8d**: $[M]^+$ absent, 420 (80) $[M-Br]^+$, 297 (100), 277 (76), 257 (40), 241 (10), 127 (69), 108 (20), 92 (19), 77 (11), 43 (35). **8e**: $[M]^+$ absent, 406 (95) $[M-Br]^+$, 313 (27), 283 (64), 257 (32), 123 (100), 77 (14), 40 (38). **8f**: 469 (42) $[M]^+$, 468 (27) $[M-1]^+$, 347 (74), 91 (100), 65 (20).

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