4-(3-Cyanopyridin-2-ylthio)acetoacetates in synthesis of heterocycles

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Substituted 2-amino-4-aryl-3-cyano-5-oxo-5,6-dihydro-4*H*-pyrano[2,3-*d*]pyrido[3′,2′:4,5]thieno[3,2-*b*]pyridines were synthesized by the reactions of 4-hydroxy-1*H*-thieno[2,3-*b*;4,5-*b*]dipyridin-2-ones with arylidenemalononitriles or by the three-component reactions of hydroxythienodipyridinones with aldehydes and malononitrile in DMF in the presence of triethylamine. Methods for syntheses of substituted 3-alkoxycarbonyl-6-amino-4-aryl-2-(3-cyanopyridin-2-ylthiomethyl)-4*H*-pyrans were developed on the basis of the reactions of 4-(3-cyanopyridin-2-ylthio)acetoacetates and arylidenemalononitriles or aldehydes and malononitrile. Ethyl 4-(3-cyanopyridin-2-ylthio)acetoacetate and 4-methoxybenzylidenecyanothioacetamide were used for the synthesis of 6-(pyridin-2-ylthiomethyl)-3-cyanopyridine-2(1*H*)-thione.

Key words: malononitrile, arylidenemalononitriles, 3-cyanopyridine-2(1*H*)-thiones, substituted 5,6-dihydro-5-oxo-4*H*-pyrano[2,3-*d*]pyrido[3′,2′:4,5]thieno[3,2-*b*]pyridines, 4-hydroxy-1*H*-thieno[2,3-*b*;4,5-*b*]dipyridin-2-ones, 4-(3-cyanopyridin-2-ylthio)acetoacetates, 3-alkoxycarbonyl-6-amino-4-aryl-2-(3-cyanopyridin-2-ylthiomethyl)-4*H*-pyrans, 3-cyanopyridine-6-(pyridin-2-ylthiomethyl)-2(1*H*)-thione.

We have previously[1] established that 4-(3-cyanopyridin-2-ylthio)acetoacetates are convenient starting reactants in the syntheses of inaccessible 4-hydroxy-1*H*-thieno[2,3-*b*;4,5-*b*]dipyridin-2-ones. Since esters of 4-(3-cyanopyridin-2-ylthio)acetoacetic acid contain several reaction centers, we studied these compounds in different reactions and developed methods for syntheses of various inaccessible heterocycles, including new heterocyclic systems. An interest in these compounds is evoked, first, by the high physiological activity of such their analogs as hydroxy(oxo)pyridines with different biological activities[2,3] and 2-amino-4*H*-pyrans patented as medicines, pesticides, and other practically significant compounds.[4—6] Therefore, it seems of interest to obtain substances, whose molecules simultaneously contain pyridine and pyran cycles.

Substituted 4-(3-cyanopyridin-2-ylthio)acetoacetates (**3**) can easily be synthesized from 3-cyanopyridine-2(1*H*)-thiones **1** and 4-chloroacetoacetates **2** and further transformed into 4-hydroxy-1*H*-thieno[2,3-*b*;4,5-*b*]dipyridin-2-ones **4** by two successive intramolecular Thorpe—Ziegler and Guareschi—Thorpe[1] ring closures (Scheme 1).

We used thienopyridinones **4** for the synthesis of annelated pyrans **8**, *viz.*, previously unknown heterocyclic system. As 4-hydroxyquinolin-2(1*H*)-one,[7,8] compounds **4a—c**, being CH acids, react with arylidenemalononitriles **5a—c** in the presence of triethylamine or *N*-methylmorpholine in dimethylformamide to form 2-amino-4-aryl-3-cyano-5,6-dihydro-5-oxo-4*H*-pyrano[2,3-*d*]pyrido[3′,2′:4,5]thieno[3,2-*b*]pyridines **8a—c** (method *A*). Compounds **8b—d** were also synthesized by the three-component reaction of thienodipyridinones **4b,c**, aromatic aldehydes **9a—c**, and malononitrile **10** (method *B*). This method is simpler in the preparative variant and does not need preliminary synthesis of arylidenemalononitriles **5**, which are lacrimators. It is most likely that the reaction occurs stepwise. Michael adduct **6** is primarily formed and then undergoes ring closure to iminopyrane **7**, and the latter is further transformed into annelated 2-amino-4*H*-pyran **8** (see Scheme 1).

A similar scheme of the reaction was proposed for the formation of 6-amino-4-aryl-5-cyano-2,4-dihydropyrano[2,3-c]pyrazoles from carbonyl compounds, malononitrile, and pyrazolon-5-ones,[9—11] where the corresponding Michael adducts were isolated and characterized.

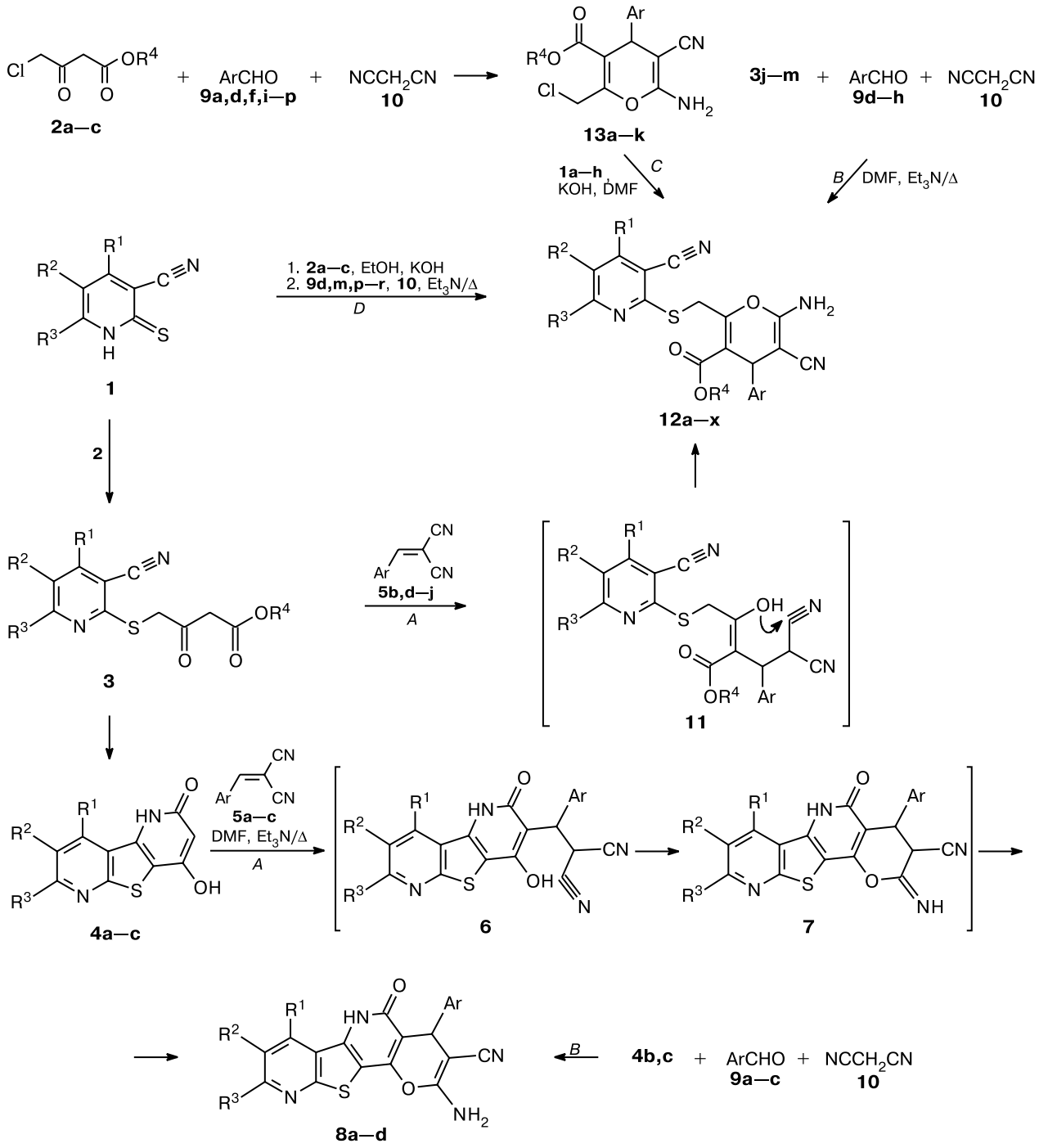
The data of instrumental methods of analysis of pyranopyridothienopyridines **8** indicate that the reactions are highly regioselective. Compounds **8** are highly melting powders, stable in air, and poorly soluble in the majority of organic solvents except DMF and DMSO.

For example, the ^{1}H NMR spectra of compounds **8a—d**, along with signals of aliphatic and aromatic protons, contain signals of H(4) of the pyran ring at 4.50—4.92 ppm in the form of singlets and signals as singlets characteristic of the NH_2 group at 7.09—7.25 ppm

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2069—2080, October, 2003.

1066-5285/03/5210-2185 $25.00

Scheme 1



and of the NH group at 11.04—12.78 ppm. The IR spectra of compounds **8** contain bands corresponding to stretching vibrations of the nitrile group at 2200—2204 cm^{-1} and absorption bands characteristic of the amino group corresponding to stretching vibrations at 3168—3468 cm^{-1} and of the amide groups corresponding to bending vibrations at 1604—1668 cm^{-1}. A similar situation in the IR and ^1H NMR spectra has been observed previously for 2-amino-4-aryl-3-cyano-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline[8] and other annelated 2-amino-4-aryl-3-cyano-4*H*-pyrans.[9—13]

Pyridinylthioacetoacetates **3** are also involved in intermolecular reactions with electrophilic reactants. The reactions of esters **3a—i** with arylidenemalononitriles

Scheme 1 (*continued*)

1	R^1	R^2	R^3
a	Me	H	OH
b	Me	Me	Me
c	H	H	Me
d	H		$(CH_2)_5$
e	H		$(CH_2)_3$
f	H	H	4-C_5H_4N
g	H		$(CH_2)_6$
h	H		$CH_2N(Me)CH_2CH_2$

2	R^4
a	Et
b	Me
c	Pr^i

3	R^1	R^2	R^3	R^4
a	Me	H	OH	Et
b	Me	Me	Me	Et
c	Me	Me	Me	Pr^i
d	H	H	Me	Me
e	H	H	2-C_4H_3S	Et
f	4-ClC_6H_4	H	2-C_4H_3S	Et
g	H		$(CH_2)_5$	Me
h	H		$(CH_2)_5$	Et
i	H		$(CH_2)_5$	Pr^i
j	Me	H	Me	Me
k	H		$(CH_2)_3$	Et
l	H		$(CH_2)_3$	Pr^i
m	H		$(CH_2)_4$	Pr^i

4	R^1	R^2	R^3
a	2-C_4H_3S		$(CH_2)_4$
b	Me	H	Me
c	H		$(CH_2)_5$

8	R^1	R^2		R^3	Ar
a	2-C_4H_3S		$(CH_2)_4$		2-ClC_6H_4
b	Me	H		Me	Ph
c	H		$(CH_2)_5$		3-C_4H_3O
d	Me	H		Me	3-ClC_6H_4

5	Ar
a	2-ClC_6H_4
b	Ph
c	3-C_4H_3O
d	2-IC_6H_4
e	2-C_4H_3S
f	4-EtC_6H_4
g	3-$(OCH_2Ph)C_6H_4$
h	3-BrC_6H_4
i	2-(5-$NO_2C_4H_2S$)
j	3,5-$(MeO)_2C_6H_3$

9	Ar
a	Ph
b	3-C_4H_3O
c	3-ClC_6H_4
d	3-C_5H_4N
e	2-(5-$NO_2C_4H_2S$)
f	4-$NO_2C_6H_4$
g	2-Cl-5-$NO_2C_6H_3$
h	4-$(COOMe)C_6H_4$
i	2-IC_6H_4

9	Ar
j	2-C_4H_3S
k	4-EtC_6H_4
l	4-ClC_6H_4
m	3-$MeOC_6H_4$
n	3-BrC_6H_4
o	2-FC_6H_4
p	2-$CF_3C_6H_4$
q	3,5-$(MeO)_2C_6H_3$
r	2-NO_2-4,5-$(OCH_2O)C_6H_2$

13	R^4	Ar
a	Et	Ph
b	Et	2-IC_6H_4
c	Et	2-C_4H_3S
d	Me	4-EtC_6H_4
e	Et	4-ClC_6H_4
f	Me	3-$MeOC_6H_4$
g	Pr^i	4-$NO_2C_6H_4$
h	Me	3-Br-C_6H_4
i	Et	3-C_5H_4N
j	Me	2-FC_6H_4
k	Et	2-$CF_3C_6H_4$

12	R^1	R^2	R^3	R^4	Ar
a	Me	H	OH	Et	Ph
b	Me	Me	Me	Et	2-IC_6H_4
c	Me	Me	Me	Pr^i	2-C_4H_3S
d	Me	Me	Me	Pr^i	2-IC_6H_4
e	H	H	Me	Me	4-EtC_6H_4
f	H	H	2-C_4H_3S	Et	3-$(OCH_2Ph)C_6H_4$
g	4-ClC_6H_4	H	2-C_4H_3S	Et	2-C_4H_3S
h	H		$(CH_2)_5$	Me	3-BrC_6H_4
i	H		$(CH_2)_5$	Et	2-(5-$NO_2C_4H_2S$)
j	H		$(CH_2)_5$	Pr^i	3,5-$(MeO)_2C_6H_3$
k	Me	H	Me	Me	3-C_5H_4N
l	H		$(CH_2)_3$	Et	2-(5-$NO_2C_4H_2S$)

12	R^1	R^2	R^3	R^4	Ar
m	H		$(CH_2)_3$	Pr^i	4-$NO_2C_6H_4$
n	H		$(CH_2)_3$	Pr^i	2-Cl-5-$NO_2C_6H_3$
o	H		$(CH_2)_3$	Pr^i	4-$(COOMe)C_6H_4$
p	H		$(CH_2)_4$	Pr^i	2-Cl-5-NO_2-C_6H_3
q	Me	Me	Me	Et	2-C_4H_3S
r	H	H	4-C_5H_4N	Et	4-ClC_6H_4
s	H		$(CH_2)_3$	Me	3-$MeOC_6H_4$
t	H		$(CH_2)_5$	Et	3-C_5H_4N
u	H		$(CH_2)_6$	Me	3-BrC_6H_4
v	H		$CH_2N(Me)CH_2CH_2$	Me	2-FC_6H_4
w	H		$CH_2N(Me)CH_2CH_2$	Et	2-$CF_3C_6H_4$
x	H		$(CH_2)_5$	Pr^i	2-NO_2-4,5-$(OCH_2O)C_6H_2$

5b,d—j are regioselective only at one of the available active methylene groups, namely, at the CH_2COOR group and not at the SCH_2 group, resulting in the formation (likely, through intermediates **11**) of substituted 2-amino-4*H*-pyrans **12a—j** (method *A*) (see Scheme 1).

In some cases, pyranopyridines **12k—p** were synthesized by the simplified procedure without intermediate isolation of arylidenemalononitriles **5** in the three-component reaction of compound **3j—m**, the corresponding aromatic aldehyde **9d—h**, and malononitrile **10** in ethanol in the presence of a base (method *B*).

The structures of some compounds **12** were confirmed by the "encounter" synthesis. The reaction of esters **2a—c**, malononitrile (**10**), and corresponding alde-

hydes **9a,d,f,i—p** in ethanol in the presence of triethylamine afforded pyrans **13a—k**. The further reaction of pyrans **13a—k** with pyridine-2(1*H*)-thiones **1a—h** is regioselective and affords pyranopyridines **12a,b,e,h,m,q—w** (method *C*).

Taking into account the regioselectivity of formation of compounds **3** and **12**, it would be reasonable to assume that pyrans **12** can be obtained by a simpler method without preliminary isolation and purification of pyridinylthioacetoacetic esters **3** (method *D*). Esters **3** were generated by the reactions of pyridinethiones **1d,e,h** and esters **2a—c** in ethanol in the presence of an equimolar amount of KOH. Then equimolar amounts of aromatic aldehyde **9d,m,p—r** and malononitrile **10** and a catalytic amount of triethylamine were added to the reaction mixture. Although the yield of compounds **12j,s,t,w,x** obtained by method *D* is 48—64%, this approach is in the last analysis the most convenient and economic.

It is noteworthy that esters of acetoacetic acid have been applied previously[7,14] for the synthesis of 5-alkoxycarbonyl-2-amino-4-aryl-3-cyano-6-methyl-4*H*-pyrans. However, we studied for the first time the use of esters of 4-(3-cyanopyridin-2-ylthio)acetoacetic acid with the ambident properties for the synthesis of the corresponding pyrans **12**.

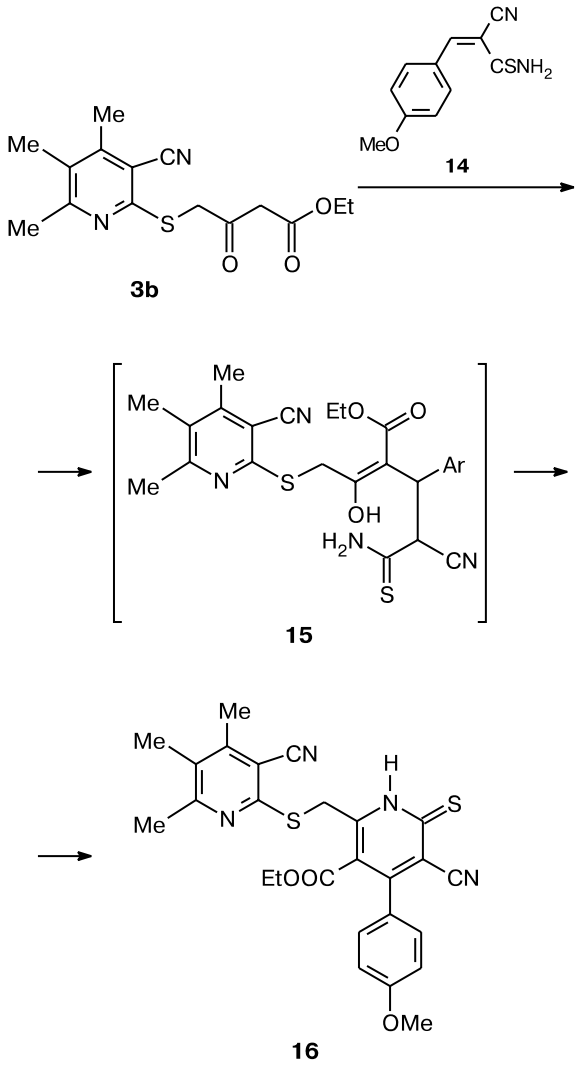
As a rule, compounds **12** are white crystalline substances highly soluble in the majority of organic solvents. The ^{1}H NMR spectra of these compounds contain the characteristic signals of H(4) of the pyran ring in the region of δ 4.25—4.99 (in the case of **12x**, 5.26 ppm) and protons of the amino group at δ 6.64—7.33. The position of the methylenic protons bonded to the sulfur atom in the region of δ 4.46—4.97 is also characteristic. The signals of the methylenic protons mainly appear as either a singlet or a doublet of doublets, and the spin-spin coupling constant for the latter is approximately unchanged and ranges within 13.0—15.1 Hz.

The IR spectra of compounds **12** are characterized by the presence of two absorption bands of the nitrile groups of the pyran and pyridine fragments at 2184—2208 and 2216—2228 cm^{-1}, respectively. The characteristic absorption bands of the carbonyl group lie at 1700—1724 cm^{-1} (in the case of compound **12j**, at 1688 cm^{-1}). The IR spectra of compounds **12** also contain the absorption bands of the amino group characteristic of bending vibrations in the region of 1668—1692 cm^{-1} and stretching vibrations in the form of two or three (due to the formation of associates) bands at 3168—3484 cm^{-1}.

Similarly, the intermolecular reaction of 4-(pyridin-2-ylthio)acetoacetate **3b** with 4-methoxybenzylidenecyanothioacetamide **14** proceeds through the Michael adduct **15** affording pyridine-2(1*H*)-thione **16** (Scheme 2).

Thus, it is established that 3-cyanopyridinylthioacetoacetates with several highly reactive centers are convenient reactants for the regioselective synthesis of functionally substituted heterocycles.

Scheme 2



Experimental

IR spectra of the compounds were obtained on Perkin—Elmer-577 and Specord M-82 instruments in KBr pellets with a concentration of 0.01 mol L^{-1}. ^{1}H NMR spectra were recorded on Bruker AM-300 (300 MHz) and Bruker WM-250 (250 MHz) instruments for 5—12% solutions in DMSO-d_6 using Me_4Si as the internal standard. Elemental analysis was carried out on a Perkin—Elmer C,H,N-analyzer instrument. The course of reactions and individual character of the synthesized compounds were monitored by thin-layer chromatography on the Silufol UV-254 plates using hexane—acetone (5 : 3) mixtures as the eluent. Iodine vapors were used for developing TLC spots.

Table 1. Physicochemical characteristics of 4-(3-cyanopyridin-2-yl-thio)acetoacatates **3**

Compound	M.p. /°C	Yield (%)	Found / Calculated (%) C	H	N	Molecular formula
3a	147—149	85	52.78 / 53.05	4.64 / 4.79	9.24 / 9.52	$C_{13}H_{14}N_2O_4S$
3b	91—93	61	57.82 / 58.08	5.75 / 5.92	8.92 / 9.14	$C_{15}H_{18}N_2O_3S$
3c	85—86	86	59.73 / 59.98	6.14 / 6.29	8.55 / 8.74	$C_{16}H_{20}N_2O_3S$
3d	76—77	66	54.35 / 54.53	4.43 / 4.58	10.32 / 10.60	$C_{12}H_{12}N_2O_3S$
3e	104—105	85	55.25 / 55.47	6.27 / 6.40	7.84 / 8.09	$C_{16}H_{14}N_2O_4S_2$
3g	93—94	73	60.14 / 60.36	5.52 / 5.70	8.63 / 8.80	$C_{16}H_{18}N_2O_3S$
3i	86—87	75	62.28 / 62.40	6.29 / 6.40	7.81 / 8.09	$C_{18}H_{22}N_2O_3S$
3j	82—83	86	55.83 / 56.10	4.86 / 5.07	9.83 / 10.06	$C_{13}H_{14}N_2O_3S$
3l	117—118	87	60.19 / 60.36	5.58 / 5.70	8.65 / 8.80	$C_{16}H_{18}N_2O_3S$
3m	94—95	81	61.67 / 61.42	6.19 / 6.06	8.72 / 8.43	$C_{17}H_{20}N_2O_3S$

Table 2. Spectroscopic characteristics of 4-(3-cyanopyridin-2-ylthio)acetoacetates **3**

Compound	IR, ν/cm^{-1}		^{1}H NMR (300 MHz, DMSO-d_6), δ (J/Hz)					
	CN	C=O	R^1	R^2	R^3	R^4	SCH_2 (s, 2 H)	CH_2 (s, 2 H)
3a	2216	1664 br, 1720	2.20 (s, 3 H, Me)	6.03 (s, 1 H)	7.66 (s, 1 H)	1.13 (t, 3 H, Me, J = 7.1); 4.02 (q, 2 H, CH_2, J = 7.1)	3.79 (d, 1 H, J = 15.7); 3.93 (d, 1 H, J = 14.2)	3.49 (d, 1 H, J = 15.7); 3.50 (d, 1 H, J = 14.2)
3b	2220	1724, 1736	2.46 (s, 3 H, Me)	2.17 (s, 3 H, Me)	2.40 (s, 3 H, Me)	1.20 (t, 3 H, Me, J = 7.1); 4.10 (q, 2 H, CH_2, J = 7.1)	4.21	3.78
3c	2224	1728, 1748	2.48 (s, 3 H, Me)	2.17 (s, 3 H, Me)	2.41 (s, 3 H, Me)	1.19, 1.21 (both s, 3 H each, Me); 4.94 (m, 1 H, CH)	4.21	3.75
3d	2224	1720, 1748	7.99 (d, 1 H, J = 7.8)	7.14 (d, 1 H, J = 7.8)	2.53 (s, 3 H, Me)	3.68 (s, 3 H, Me)	4.20	3.77
3e	2220	1724, 1744	8.21 (d, 1 H, J = 8.8)	7.82 (d, 1 H, J = 8.2)	7.25 (m, 1 H); 7.81, 8.00 (both d, 1 H each, J = 4.2)	1.02 (t, 3 H, Me, J = 7.2); 4.01 (q, 2 H, CH_2, J = 7.2)	4.22	3.78
3g	2228	1724, 1744	7.95 (s, 1 H)	1.60 (m, 4 H, CH_2); 1.83, 2.25, 2.98 (all m, 2 H each, CH_2)		3.64 (s, 3 H, Me)	4.25	3.82
3i	2220	1724, 1744	7.83 (s, 1 H)	1.63 (m, 4 H, CH_2); 1.86, 2.78, 3.00 (all m, 2 H each, CH_2)		1.22, 1.24 (both s, 3 H each, Me); 4.96 (m, 1 H, CH)	4.17	3.67
3j	2220	1720, 1744	2.47 (s, 3 H, Me)	7.03 (s, 1 H)	2.44 (s, 3 H, Me)	3.68 (s, 3 H, Me)	4.17	3.74
3l	2224	1724, 1744	7.91 (s, 1 H)	2.13 (m, 2 H, CH_2); 2.90—3.00 (m, 4 H, CH_2)		1.23, 1.25 (both s, 3 H each, Me); 4.96 (m, 1 H, CH)	4.17	3.68
3m	2220	1724, 1744	7.81 (s, 1 H)	1.77, 1.85, 2.72, 2.85 (all m, 2 H each, CH_2)		1.22, 1.25 (both s, 3 H each, Me); 4.96 (m, 1 H, CH)	4.11	3.69

Table 3. Physicochemical characteristics of 2-amino-4-aryl-3-cyano-5-oxo-5,6-dihydro-4*H*-pyrano[2,3-*d*]pyrido-[3′,2′:4,5]thieno[3,2-*b*]pyridines **8**

Compound	Yield (%) (method)	Found / Calculated (%) C	H	N	Molecular formula
8a*	63 (*A*)	60.74 / 60.90	4.19 / 4.31	8.67 / 8.88	$C_{28}H_{19}ClN_4O_2S_2 \cdot C_4H_8O_2$
8b	75 (*A*), 71 (*B*)	65.55 / 65.98	3.88 / 4.03	13.64 / 13.99	$C_{22}H_{16}N_4O_2S$
8c	90 (*A*), 83 (*B*)	63.92 / 64.17	4.12 / 4.21	12.93 / 13.01	$C_{23}H_{18}N_4O_3S$
8d	83 (*B*)	60.57 / 60.76	3.24 / 3.48	12.56 / 12.88	$C_{22}H_{15}ClN_4O_2S$

* The complex with one dioxane molecule.

4-(3-Cyanopyridin-2-ylthio)acetoacetates 3 were synthesized by a described method.[1] The characteristics of undescribed[1] compounds **3** are presented in Tables 1 and 2.

2-Amino-4-aryl-3-cyano-5-oxo-5,6-dihydro-4*H*-pyrano[2,3-*d*]pyrido[3′,2′:4,5]thieno[3,2-*b*]pyrimidines 8. ***A.*** Arylidenemalononitrile **5** (0.01 mol) and triethylamine or *N*-methylmorpholine (0.1 mL) were added to a suspension of compound **4** (0.01 mol) in DMF (or in an ethanol—dioxane (1 : 1) mixture). The reaction mixture was refluxed for 2—3 h (chromatographic monitoring). After cessation of the reaction, concentrated HCl (1 mL) was added to the mixture. A precipitate formed was separated and washed successively with water, ethanol, and hexane. All compounds **8** had m.p. higher than 300 °C. The characteristics of compounds **8** are presented in Tables 3 and 4.

B. Aldehyde **9** (0.01 mol), malononitrile (**10**) (0.66 g, 0.01 mol), and triethylamine or *N*-methylmorpholine (0.1 mL) were added to a suspension of compound **4** (0.01 mol) in DMF. Then the reaction was carried out similarly to method *A*.

3-Alkoxycarbonyl-6-amino-4-aryl-5-cyano-2-(3-cyanopyridin-2-ylthiomethyl)-4*H*-pyrans 12. ***A.*** Arylidenemalononitrile **5** (0.01 mol) and triethylamine (0.1 mL) were added with stirring to a suspension of ester **3** (0.01 mol) in ethanol (15—20 mL), and the mixture was refluxed for 3—5 min. After cooling, water (5 mL) was added to the solution, and the resulting mixture was left for 16 h. A precipitate that formed was separated and washed with cool ethanol and hexane.

B. Aldehyde **9** (0.01 mol) malononitrile (**10**) (0.66 g, 0.01 mol), and triethylamine (0.1 mL) were added with stirring to a suspension of ester **3** (0.01 mol) in ethanol or methanol (15—20 mL), and the mixture was refluxed for 5—12 min. After cooling, water (5 mL) was added to the solution, and the mix-

Table 4. Spectroscopic characteristics of 2-amino-4-aryl-3-cyano-5-oxo-5,6-dihydro-4*H*-pyrano[2,3-*d*]pyrido[3′,2′:4,5]thieno[3,2-*b*]pyridines **8**

Compound	IR, ν/cm^{-1}		^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)						
	CN	CONH, NH_2	R^1	R^2	R^3	Ar	C(4)H (s, 1 H)	NH_2 (s, 2 H)	NH (s, 1 H)
8a[a]	2200	1648 (δ), 1668 (δ), 3176, 3352, 3448	7.09—7.95 (m, 3 H, C_4H_3S)	1.76 (d, 2 H, CH_2); 1.88, 2.63, 3.08 (all m, 2 H each, CH_2)		7.09—7.95 (m, 4 H, C_6H_4)[b]	4.92	7.09[b]	12.76
8b	2200	1632 (δ), 1668 (δ), 3180, 3288, 3364, 3420	2.58 (s, 3 H, Me)	7.28[c] (s, 1 H)	2.90 (s, 3 H, Me)	7.20—7.32[c] (m, 5 H, Ph)	4.64	7.11	11.04
8c	2200	1640 (δ), 1668 (δ), 3168, 3320, 3444	8.45 (s, 1 H)	1.66 (m, 4 H, CH_2CH_2); 1.85, 2.89, 3.11 (all m, 2 H each, CH_2)		6.39 (s, 1 H); 7.53 (d, 2 H, *J* = 8.1)	4.50	7.25	12.78
8d	2204	1636 (δ), 1668 (δ), 3184, 3324, 3468	2.59 (s, 3 H, Me)	7.26[c] (s, 1 H)	2.90 (s, 3 H, Me)	7.17—7.37[c,d] (m, 4 H, C_6H_4)	4.68	7.21[d]	11.05

[a] The complex with one dioxane molecule; for dioxane δ_H (300 MHz, DMSO-d$_6$) 3.07 (s, 8 H, 2 (—CH_2CH_2—)). Mass spectrum for compound **8a**, *m*/*z* (*I*$_{rel}$ (%)): 542 [M − dioxane]$^+$ (7), 507 (49), 442 (100), 354 (20), 252 (15), 188(19), 89 [dioxane + H] (12), 66 (89).
[b] The signals of the protons of 2-C_4H_3S, 2-ClC_6H_4, and 2-NH_2 are overlapped.
[c] The signals of the protons of C(8)H and Ar are overlapped.
[d] The signals of the protons of 2-NH_2 and Ar are overlapped.

Table 5. Physicochemical characteristics of 3-alkoxycarbonyl-6-amino-4-aryl-5-cyano-2-(3-cyanopyridin-2-ylthiomethyl)-4*H*-pyrans **12**

Compound	M.p. /°C	Yield (%) (method)	Found / Calculated (%) C	H	N	Molecular formula
12a	120—121	80 (*A*)	61.32	4.25	12.57	$C_{23}H_{20}N_4O_4S$
		71 (*C*)	61.59	4.49	12.49	
12b	202—203	85 (*A*),	51.46	4.11	10.07	$C_{25}H_{23}IN_4O_3S$
		94 (*C*)	51.20	3.95	9.55	
12c	183—184	87 (*A*)	60.14	5.16	11.83	$C_{24}H_{24}N_4O_3S_2$
			59.98	5.03	11.66	
12d	216—217	89 (*A*)	51.84	4.12	9.14	$C_{26}H_{25}IN_4O_3S$
			52.01	4.20	9.33	
12e	102—103	77 (*A*),	64.37	4.75	12.37	$C_{24}H_{22}N_4O_3S$
		58 (*C*)	64.56	4.97	12.55	
12f	171—172	78 (*A*)	65.44	4.18	9.07	$C_{33}H_{26}N_4O_4S_2$
			65.53	4.32	9.23	
12g	204—205	69 (*A*)	58.19	3.27	8.83	$C_{30}H_{21}ClN_4O_3S_3$
			58.38	3.43	9.08	
12h	204—205	72 (*A*),	56.41	3.94	9.81	$C_{26}H_{23}BrN_4O_3S$
		77 (*C*)	56.63	4.20	10.16	
12i	178—180	56(*A*)	55.68	4.16	12.81	$C_{25}H_{23}N_5O_5S_2$
			55.85	4.31	13.03	
12j	175—177	63 (*A*),	64.02	5.46	10.00	$C_{30}H_{32}N_4O_5S$
		48 (*D*)	64.27	5.75	9.99	
12k	216—217	83 (*B*)	60.73	4.24	15.92	$C_{22}H_{19}N_5O_3S$
			60.96	4.42	16.16	
12l	218—219	79 (*B*)	54.03	3.47	13.47	$C_{23}H_{19}N_5O_5S_2$
			54.21	3.76	13.74	
12m	211—213	58 (*B*),	60.30	4.29	13.19	$C_{26}H_{23}N_5O_5S$
		75 (*C*)	60.34	4.48	13.53	
12n	227—228	72 (*B*)	56.85	3.94	12.42	$C_{26}H_{22}ClN_5O_5S$
			56.57	4.02	12.69	
12o	172—174	38 (*B*)	63.12	4.73	10.31	$C_{28}H_{26}N_4O_5S$
			63.38	4.94	10.56	
12p	136—137	35 (*B*)	57.26	4.18	12.15	$C_{27}H_{24}ClN_5O_5S$
			57.29	4.27	12.37	
12q	195—196	71 (*C*)	59.02	4.63	12.12	$C_{23}H_{22}N_4O_3S_2$
			59.21	4.75	12.01	
12r	183—184	64 (*C*)	60.95	3.67	13.03	$C_{27}H_{20}ClN_5O_3S$
			61.19	3.80	13.21	
12s	191—192	98 (*C*)	63.12	4.42	11.52	$C_{25}H_{22}N_4O_4S$
		65 (*D*)	63.28	4.67	11.81	
12t	157—158	67 (*C*)	63.83	4.92	14.05	$C_{26}H_{25}N_5O_3S$
		55 (*D*)	64.05	5.17	14.36	
12u	167—168	65 (*C*)	57.32	4.20	9.57	$C_{27}H_{25}BrN_4O_3S$
			57.35	4.46	9.91	
12v	140—142	59 (*C*)	61.36	4.26	13.92	$C_{25}H_{22}FN_5O_3S$
			61.09	4.51	14.25	
12w	157—158	90 (*C*)	58.09	4.11	12.30	$C_{27}H_{24}F_3N_5O_3S$
		49 (*D*)	58.37	4.35	12.61	
12x	199—201	51 (*D*)	59.39	4.46	11.51	$C_{29}H_{27}N_5O_7S$
			59.07	4.62	11.88	

Table 6. Spectroscopic characteristics of 3-alkoxycarbonyl-6-amino-4-aryl-5-cyano-2-(3-cyanopyridin-2-ylthiomethyl)-4*H*-pyrans **12**

Compound	IR, ν/cm^{-1}			^1H NMR (300 MHz, DMSO-d_6), δ (*J*/Hz)							
	CN	C=O	NH_2	R^1	R^2	R^3	R^4	Ar	NH_2 (s, 2 H)	H(4)	SCH_2 (2 H)
12a	2196, 2216	1716	1676 (δ), 3200, 3328, 3392	2.33 (s, 3 H, Me)	6.45 (s, 1 H, CH)	—	1.03 (t, 3 H, Me, *J* = 7.2) 4.00 (q, 2 H, CH_2, *J* = 7.2)	7.10—7.47 (m, 5 H, Ph)	6.84	4.34	4.50, 4.62 (both d, 1 H each, *J* = 13.4)
12b	2204, 2220	1720	1684 (δ), 3180, 3312, 3448	2.42[a] (s, 3 H, Me)	2.17 (s, 3 H, Me)	2.42[a] (s, 3 H, Me)	1.00 (t, 3 H, Me, *J* = 7.3); 3.99 (q, 2 H, CH_2, *J* = 7.3)	6.96 (dd, 1 H, C_6H_4, *J* = 7.9, *J* = 7.3); 7.03 (d, 1 H, C_6H_4, *J* = 7.3); 7.37 (t, 1 H, C_6H_4, *J* = 7.3); 7.81 (d, 1 H, C_6H_4, *J* = 7.9)	6.78	4.78	4.61, 4.72 (both d, 1 H each, *J* = 14.0)
12c	2204, 2216	1712	1684 (δ), 3180, 3312, 3484	2.46 (s, 3 H, Me)	2.18 (s, 3 H, Me)	2.41 (s, 3 H, Me)	1.08 (d, 3 H, Me, *J* = 6.6); 1.19 (d, 3 H, Me, *J* = 6.6); 4.95 (m, 1 H, CH)	6.84 (d, 1 H, C(3)H, C_4H_3S, *J* = 3.6); 6.93 (dd, 1 H, C(4)H, C_4H_3S, *J* = 3.6, *J* = 4.9); 7.37 (d, 1 H, C(5)H, C_4H_3S, *J* = 4.9)	7.00	4.68	4.57, 4.71 (both d, 1 H each, *J* = 14.2)

(*to be continued*)

Table 6 (*continued*)

Compound	IR, ν/cm^{-1}			^{1}H NMR (300 MHz, DMSO-d$_6$), δ (*J*/Hz)							
	CN	C=O	NH_2	R^1	R^2	R^3	R^4	Ar	NH_2 (s, 2 H)	H(4)	SCH_2 (2 H)
12d	2208, 2220	1716	1680 (δ), 3180, 3324, 3476	2.46 (s, 3 H, Me)	2.20 (s, 3 H, Me)	2.42 (s, 3 H, Me)	0.78, 1.20 (both d, 3 H each, Me, *J* = 6.6); 4.85 (m, 1 H, CH)	6.97 (t, 1 H, C_6H_4, *J* = 8.0); 7.06 (d, 1 H, C_6H_4, *J* = 8.0); 7.30 (t, 1 H, C_6H_4, *J* = 8.0); 7.82 (d, 1 H, C_6H_4, *J* = 8.0)	6.76	4.77	4.60, 4.78 (both d, 1 H each, *J* = 13.2)
12e	2196, 2220	1720	1680 (δ), 3188, 3328, 3444	8.10 (d, 1 H, CH, *J* = 8.0)	7.10 (d, 1 H, CH, *J* = 8.0)	2.55 (s, 3 H, Me)	3.59 (s, 3 H, Me)	1.16 (t, 3 H, Me, *J* = 7.5); 2.56 (q, 2 H, CH_2, *J* = 7.5); 6.99 (d, 1 H, C_6H_4, *J* = 7.5); 7.20 (d, 1 H, C_6H_4, *J* = 7.5)	6.83	4.27	4.69 (s)
12f	2196, 2220	1716	1680 (δ), 3196, 3328 3448	8.21 (d, 1 H, CH, *J* = 8.9)	7.82 (d, 1 H, CH, *J* = 8.9)	7.23[b] (m, 1 H, C_4H_3S); 7.81 (d, 1 H, C_4H_3S, *J* = 4.0); 8.00 (d, 1 H, C_4H_3S, *J* = 4.4)	1.02 (t, 3 H, Me, *J* = 7.2); 4.01 (q, 2 H, CH_2, *J* = 7.2)	5.06 (s, 2 H, OCH_2); (m, 2 H, C_6H_4); 6.90 (d, 1 H, C_6H_4, *J* = 8.4); 7.23[b] (m, 1 H, C_6H_4); 7.32—7.48 (m, 5 H, Ph)	6.78[c]	4.36	4.72, 4.83 (both d, 1 H each, *J* = 14.3)
12g	2184, 2220	1716	1668 (δ), 1632 sh (δ), 3176, 3332, 3452	7.68 (d, 2 H, C_6H_4, *J* = 7.9); 7.77 (d, 2 H, C_6H_4, *J* = 8.5)	7.92 (s, 1 H, CH)	6.95 (dd, 1 H, C_4H_3S, *J* = 2.4, *J* = 4.9); 7.38 (d, 1 H, C_4H_3S, *J* = 4.9); 8.12 (d, 1 H, C_4H_3S, *J* = 2.4)	1.15 (t, 3 H, Me, *J* = 6.7); 4.12 (q, 2 H, CH_2, *J* = 6.7)	6.89 (d, 1 H, C_4H_3S, *J* = 1.8); 7.25 (dd, 1 H, C_4H_3S, *J* = 4.9, *J* = 1.8); 7.92 (d, 1 H, C_4H_3S, *J* = 4.9)	6.99	4.75	4.72, 4.84 (both d, 1 H each, *J* = 14.0)
12h	2208, 2216	1720	1688 (δ), 3184, 3312, 3460	7.81 (s, 1 H, CH)	1.62 (m, 4 H, CH_2, CH_2); 1.83, 2.77, 2.92 (all m, 2 H each, CH_2)		3.62 (s, 3 H, Me)	7.11 (d, 1 H, C_6H_4, *J* = 7.5); 7.20 (m, 2 H, C_6H_4); 7.34 (d, 1 H, C_6H_4, *J* = 8.1)	6.71	4.31	4.64, 4.76 (both d, 1 H each, *J* = 14.3)
12i	2188, 2220	1700	1668 (δ), 3184, 3300, 3348	7.96[d] (s, 1 H, CH)	1.42—1.53 (m, 4 H, CH_2); 1.76, 2.72, 2.89 (all m, 2 H each, CH_2)		1.18 (t, 3 H, Me, *J* = 7.9); 4.14 (q, 2 H, CH_2, *J* = 7.9)	6.97, 7.96[d] (both d, 1 H each, C_4H_2S, *J* = 4.1)	7.33	4.73	4.51, 4.92 (both d, 1 H each, *J* = 13.6)

(*to be continued*)

Table 6 (*continued*)

Compound	IR, ν/cm^{-1}			^{1}H NMR (300 MHz, DMSO-d$_6$), δ (*J*/Hz)								
	CN	C=O	NH_2	R^1	R^2	R^3	R^4	Ar	NH_2 (s, 2 H)	H(4)	SCH_2 (2 H)	
12j	2192, 2216	1688	1668 (δ), 3216, 3332, 3408	7.93 (s, 1 H, CH)	1.58 (m, 4 H, CH_2); 1.80, 2.77, 2.97 (all m, 2 H each, CH_2)		1.00, 1.16 (both d, 3 H each, Me, *J* = 5.9); 4.87 (m, 1 H, CH)	3.69 (s, 6 H, 2 MeO); 6.26 (s, 2 H, C_6H_3); 6.36 (s, 1 H, C_6H_3)	6.73	4.25	4.63, 4.71 (both d, 1 H each, *J* = 13.8)	
12k	2192, 2220	1724	1680 (δ), 3308, 3372	2.33 (s, 3 H, Me)	7.12 (s, 1 H, CH)	2.42 (s, 3 H, Me)	3.54 (s, 3 H, Me)	7.30 (dd, 1 H, C_5H_4N, *J* = 4.3, *J* = 8.0); 7.45 (d, 1 H, C_5H_4N, *J* = 8.0); 8.34 (s, 1 H, C_5H_4N); 8.43 (d, 1 H, C_5H_4N, *J* = 4.3)	7.05	4.38	4.63, 4.74 (both d, 1 H each, *J* = 14.5)	
12l	2204, 2224	1720	1676 (δ), 3188, 3352, 3452	7.89 (s, 1 H, CH)	2.09 (m, 2 H, CH_2); 2.84—2.93 (m, 4 H, CH_2)		1.21 (t, 3 H, Me, *J* = 7.1); 4.22 (q, 2 H, CH_2, *J* = 7.1)	6.95, 7.86 (both d, 1 H each, C_4H_2S, *J* = 4.8)	7.12	4.68	4.56, 4.76 (both d, 1 H each, *J* = 14.3)	
12m	2196, 2224	1704	1692 (δ), 3320, 3336, 3412	7.93 (s, 1 H, CH)	2.08 (m, 2 H, CH_2); 2.76—2.98 (m, 4 H, CH_2)		1.00, 1.18 (both d, 3 H each, Me, *J* = 6.6); 4.90 (m, 1 H, CH)	7.37, 8.12 (both d, 2 H each, C_6H_4, *J* = 7.9)	6.88	4.46	4.65, 4.73 (both d, 1 H each, *J* = 14.4)	
12n	2204, 2228	1720	1680 (δ), 3184, 3360, 3460	7.82 (s, 1 H, CH)	2.02 (m, 2 H, CH_2); 2.54—2.91 (m, 4 H, CH_2)		0.93 (d, 3 H, Me, *J* = 6.6); 1.19 (d, 3 H, Me, *J* = 5.1); 4.87 (m, 1 H, CH)	7.67, 8.04 (both d, 2 H each, C_6H_3, *J* = 8.5); 7.90 (s, 1 H, C_6H_3)	6.96	4.98	4.52, 4.92 (both d, 1 H each, *J* = 13.8)	
12o	2200, 2228	1708	1680 (δ), 3220, 3184, 3332, 3428	7.91 (s, 1 H, CH)	2.07 (m, 2 H, CH_2); 2.71—2.98 (m, 4 H, CH_2)		0.97 (d, 3 H, Me, *J* = 5.9); 1.16 (d, 3 H, Me, *J* = 6.6); 4.88 (m, 1 H, CH)	3.87 (s, 3 H, Me); 7.22, 7.86 (both d, 2 H each, C_6H_4, *J* = 7.9)	6.77	4.37	4.67 (s)	
12p	2200, 2220	1716	1676 (δ), 3316, 3480	7.80[d] (s, 1 H, CH)	1.70 (m, 2 H, CH_2); 2.45, 2.69 (m, 4 H, CH_2)		0.90 (d, 3 H, Me, *J* = 6.6); 1.21 (d, 3 H, Me, *J* = 5.9); 4.89 (m, 1 H, CH)	7.68, 8.05 (both d, 1 H each, C_6H_3, *J* = 8.5); 7.80[d] (s, 1 H, C_6H_3)	6.93	4.99	4.46, 4.97 (both d, 1 H each, *J* = 14.4)	
12q	2200, 2220	1720	1676 (δ), 3184, 3328, 3476	2.44 (s, 3 H, Me)	2.18 (s, 3 H, Me)	2.40 (s, 3 H, Me)	1.16 (t, 3 H, Me, *J* = 7.5); 4.15 (q, 2 H, CH_2, *J* = 7.5)	6.83 (d, 1 H, C_4H_3S, *J* = 2.4); 6.93 (m, 1 H, C_4H_3S); 7.35 (d, 1 H, C_4H_3S, *J* = 4.9)	6.91	4.57	4.59, 4.70 (both d, 1 H each, *J* = 13.2)	

(*to be continued*)

Table 6 (*continued*)

Compound	IR, ν/cm^{-1}			^{1}H NMR (300 MHz, DMSO-d$_6$), δ (*J*/Hz)							
	CN	C=O	NH_2	R^1	R^2	R^3	R^4	Ar	NH_2 (s, 2 H)	H(4)	SCH_2 (2 H)
12r	2200, 2224	1704	1668 (δ), 3300, 3348	8.30 (d, 1 H, CH, *J* = 8.4)	7.99 (d, 1 H, CH, *J* = 8.4)	8.06, 8.71 (both d, 2 H each, C_5H_4N, *J* = 5.3)	1.09 (t, 3 H, Me, *J* = 7.4); 4.02 (q, 2 H, CH_2, *J* = 7.4)	7.16, 7.37 (both d, 2 H each, C_6H_4, *J* = 7.9)	6.64	4.39	4.82, 4.92 (both d, 1 H each, *J* = 14.4)
12s	2208, 2220	1728	1676 (δ), 3184, 3296, 3452	8.01 (s, 1 H, CH)	2.03 (m, 2 H, CH_2); 2.74—2.90 (m, 4 H, CH_2)		3.61 (s, 3 H, Me)	3.69 (s, 3 H, MeO); 6.59 (s, 1 H, C_6H_4); 6.67, 6.79 (both d, 1 H each, C_6H_4, *J* = 7.9); 7.17 (t, 1 H, C_6H_4, *J* = 7.9)	6.82	4.26	4.61, 4.71 (both d, 1 H each, *J* = 14.4)
12t	2192, 2228	1700	1676 (δ), 3244, 3372, 3444	7.83 (s, 1 H, CH)	1.62 (m, 4 H, CH_2); 1.84, 2.77, 2.92 (all m, 2 H, CH_2)		1.10 (t, 3 H, Me, *J* = 7.5); 4.06 (q, 2 H, CH_2 each, *J* = 7.5)	7.26 (dd, 1 H, C_5H_4N, *J* = 4.4, *J* = 8.1); 7.44 (d, 1 H, C_5H_4N, *J* = 8.1); 8.33 (s, 1 H, C_5H_4N); 8.40 (m, 1 H, C_5H_4N)	6.80	4.36	4.70 (s)
12u	2204, 2220	1720	1684 (δ), 3180, 3316, 3460	7.48 (s, 1 H, CH)	1.35, 1.67, 2.75, 2.82 (all m, 2 H each, CH_2)		3.62 (s, 3 H, Me)	7.12 (d, 1 H, C_6H_4, *J* = 7.5); 7.21 (m, 2 H, C_6H_4); 7.35 (d, 1 H, C_6H_4, *J* = 7.9)	6.75	4.32	4.66, 4.74 (both d, 1 H each, *J* = 14.3)
12v	2204, 2224	1720	1668 (δ), 3184, 3320, 3448	7.97 (s, 1 H, CH)	2.36 (s, 3 H, Me); 2.62—2.84 (m, 4 H, CH_2); 3.50 (s, 2 H, CH_2)		3.57 (s, 3 H, Me)	7.07—7.25 (m, 4 H, C_6H_4)	6.91	4.61	4.62, 4.72 (both d, 1 H each, *J* = 14.3)
12w	2200, 2228	1712	1668 (δ), 3184, 3324, 3376	7.88 (s, 1 H, CH)	2.42 (s, 3 H, Me); 2.71 (m, 2 H, CH_2); 2.88 (m, 2 H, CH_2); 3.53 (s, 2 H, CH_2)		0.94 (t, 3 H, Me, *J* = 7.2); 3.98 (q, 2 H, CH_2, *J* = 7.2)	7.29 (d, 1 H, C_6H_4, *J* = 7.5); 7.38—7.52 (m, 1 H each, C_6H_4); 7.63 (d, 1 H, C_6H_4, *J* = 8.0)	6.69	4.77	4.63, 4.73 (both d, 1 H each, *J* = 14.5)
12x	2204, 2228	1708	1680 (δ), 3184, 3324, 3476	7.84 (s, 1 H, CH)	1.62 (m, 4 H, CH_2); 1.85, 2.77, 2.94 (all m, 2 H each, CH_2)		0.95, 1.12 (both d, 3 H each, Me, *J* = 5.9); 4.86 (m, 1 H, CH)	6.15 (s, 2 H, OCH_2O); 6.63, 7.40 (both s, 1 H each, C_6H_2)	6.79	5.26	4.67, 4.74 (both d, 1 H each, *J* = 14.4)

[a] The signals of the protons of the methyl groups are overlapped.
[b] The signals of the protons of the aryl substituents are overlapped.
[c] The signals of the proton of the amino group are overlapped with the signals of the protons of the aryl substituent.
[d] The signal of the proton of the pyridine ring is overlapped with the signals of the protons of the aryl substituent.

Table 7. Physicochemical characteristics of 5-alkoxycarbonyl-2-amino-4-aryl-6-chloromethylene-5-cyano-1*H*-pyrans **13**

Compound	M.p. /°C	Yield (%)	Found / Calculated (%) C	H	N	Molecular formula
13a	161—162	86	60.56 / 60.29	4.83 / 4.74	8.94 / 8.79	$C_{16}H_{15}ClN_2O_3$
13b	184—186	91	43.04 / 43.22	3.05 / 3.17	6.07 / 6.30	$C_{16}H_{14}ClIN_2O_3$
13c	175—177	84	52.04 / 51.77	4.36 / 4.03	8.95 / 8.63	$C_{14}H_{13}ClN_2O_3S$
13d	147—148	39	61.64 / 61.36	5.04 / 5.15	8.12 / 8.42	$C_{17}H_{17}ClN_2O_3$
13e	152—154	90	54.36 / 54.41	3.84 / 4.00	7.70 / 7.93	$C_{16}H_{14}Cl_2N_2O_3$
13f	173—174	49	57.18 / 57.41	4.36 / 4.52	8.12 / 8.37	$C_{16}H_{15}ClN_2O_4$
13g	106—107	65	53.82 / 54.05	4.14 / 4.27	10.85 / 11.12	$C_{17}H_{16}ClN_3O_5$
13h	170—171	58	46.72 / 46.96	3.01 / 3.15	7.05 / 7.30	$C_{15}H_{12}BrClN_2O_3$
13i	184—186	94	56.17 / 56.35	4.20 / 4.41	12.82 / 13.14	$C_{15}H_{14}ClN_3O_3$
13j	179—180	53	55.97 / 55.83	3.72 / 3.75	8.75 / 8.68	$C_{15}H_{12}ClFN_2O_3$
13k	161—162	65	52.53 / 52.79	3.44 / 3.65	7.02 / 7.24	$C_{17}H_{14}ClF_3N_2O_3$

Table 8. Spectroscopic characteristics of 5-alkoxycarbonyl-2-amino-4-aryl-6-chloromethylene-5-cyano-1*H*-pyrans **13**

Compound	IR, ν/cm^{-1}			^{1}H NMR (300 MHz, DMSO-d$_6$), δ (*J*/Hz)				
	CN	C=O	NH_2	CH_2Cl (s, 2 H)	NH_2 (br.s)	R^4	C(4)H (s)	Ar
13a	2188	1696	1676 (δ), 3412, 3332	4.71	6.95	1.08 (t, 3 H, Me, *J* = 7.1); 4.03 (q, 2 H, CH_2, *J* = 7.1)	4.48	7.12—7.38 (m, 5 H)
13b	2196	1704	1680 (δ), 3416, 3328	4.73	6.99*	1.03 (t, 3 H, Me, *J* = 7.1); 4.00 (q, 2 H, CH_2, *J* = 7.1)	4.83	6.99* (m, 1 H); 7.12 (d, 1 H, *J* = 8.1); 7.39 (m, 1 H); 7.33 (d, 1 H, *J* = 7.4)
13c	2192	1696	1676 (δ), 3408, 3328	4.68	7.01	1.18 (t, 3 H, Me, *J* = 7.1); 4.14 (q, 2 H, CH_2, *J* = 7.1)	4.73	6.87 (d, 1 H, C(3)H, *J* = 2.9); 6.96 (m, 1 H, C(4)H); 7.49 (d, 1 H, C(5)H, *J* = 7.1)
13d	2192	1704	1680 (δ), 3416, 3336	4.70	6.92	3.60 (s, 3 H, Me)	4.34	1.18 (t, 3 H, Me, *J* = 7.2); 2.58 (q, 2 H, CH_2, *J* = 7.2); 7.06, 7.17 (both d, 2 H each, *J* = 7.9)
13e	2196	1700	1680 (δ), 3408, 3332	4.67, 4.75 (both d, 1 H each, *J* = 12.9)	7.04	1.07 (t, 3 H, Me, *J* = 7.1); 4.04 (q, 2 H, CH_2, *J* = 7.1)	4.40	7.19, 7.40 (both d, 2 H each, *J* = 7.1)
13f	2196	1704	1680 (δ), 3408, 3328	4.69, 4.75 (both d, 1 H each, *J* = 12.9)	7.01	3.60 (s, 3 H, Me)	4.47	3.74 (s, 3 H, Me); 6.69 (s, 1 H); 6.74, 6.84 (both d, 1 H each, *J* = 8.5); 7.35 (t, 1 H, *J* = 8.5)
13g	2196	1724	1688 (δ), 3330, 3376	4.70, 4.79 (both d, 1 H each, *J* = 11.8)	7.05	0.95 (d, 3 H, Me, *J* = 5.9); 1.16 (d, 3 H, Me, *J* = 6.6); 4.85 (m, 1 H, CH)	4.57	7.46, 8.21 (both d, 2 H each, *J* = 8.5)
13h	2192	1704	1672 (δ), 3412, 3328	4.68, 4.75 (both d, 1 H each, *J* = 12.9)	7.08	3.61 (s, 3 H, Me)	4.41	7.18 (d, 1 H, *J* = 8.5); 7.32 (m, 1 H); 7.46 (d, 1 H, *J* = 8.5)
13i	2200	1724	1684 (δ), 3352, 3304	4.67, 4.78 (both d, 1 H each, *J* = 11.4)	7.00	1.08 (t, 3 H, Me, *J* = 7.3); 4.06 (q, 2 H, CH_2, *J* = 7.3)	4.47	7.48 (m, 1 H, C(5)H); 7.57 (d, 1 H, C(4)H, *J* = 7.8); 8.41 (s, 1 H, C(2)H); 8.46 (d, 1 H, C(6)H, *J* = 4.3)

(*to be continued*)

Table 8 (*continued*)

Compound	IR, ν/cm^{-1}			^{1}H NMR (300 MHz, DMSO-d$_6$), δ (*J*/Hz)				
	CN	C=O	NH_2	CH_2Cl (s, 2 H)	NH_2 (br.s)	R^4	C(4)H (s)	Ar
13j	2200	1704	1680 (δ), 3416, 3332	4.72	6.93	3.58 (s, 3 H, Me)	4.69	7.10—7.34 (m, 4 H)
13k	2212	1724	1684 (δ), 3480, 3320	4.71	6.95	0.92 (t, 3 H, Me, *J* = 7.2); 3.97 (q, 2 H, CH_2, *J* = 7.2)	4.79	7.37 (d, 1 H, *J* = 7.9); 7.46 (t, 1 H, *J* = 7.9); 7.67 (m, 2 H)

* The signals of the protons are overlapped.

ture was left for 16 h. A precipitate that formed was separated and washed with cool ethanol and hexane.

C. Pyran **13** (0.01 mol) was added with stirring to a suspension of pyridinethione **1** (0.01 mol) in ethanol or methanol (15—20 mL), and the mixture was stirred for 0.5—1 h at 40—45 °C. After cooling, water (5 mL) was added to the solution, and the mixture was left for 16 h. A precipitate formed was separated and washed with cool ethanol and hexane.

D. 4-Chloroacetoacetate **2** (0.042 mol) was added with stirring to a suspension of pyridinethione **1** (0.004 mol) in ethanol or methanol (15—20 mL), and stirring was continued at 40—45 °C for 12—15 min. Then aldehyde **9** (0.0043 mol), malononitrile (**10**) (0.28 g, 0.0043 mol), and triethylamine (0.1 mL) were added to the solution, and the mixture was refluxed for 3—5 min. After cooling, water (5 mL) was added to the solution, and the mixture was stored for 16 h. A precipitate of compound **12** was separated and washed with cool ethanol and hexane.

Compounds **12** were recrystallized from ethanol or methanol.

The characteristics of compounds **12** are presented in Tables 5 and 6.

5-Alkoxycarbonyl-2-amino-4-aryl-6-chloromethylene-5-cyano-1*H*-pyrans 13. Triethylamine (0.1 mL) was added to a suspension of ester **2a—c** (0.01 mol), aldehyde **9** (0.01 mol), and malononitrile (**10**) (0.66 g, 0.01 mol) in ethanol or methanol. The mixture was refluxed for 5—7 min and stored at ~20 °C for 10—12 h. A precipitate formed was separated and washed with ethanol or hexane.

The data on compounds **13** are presented in Tables 7 and 8.

5-Cyano-3-ethoxycarbonyl-2-(3-cyanopyridin-2-ylthiomethyl-4-(4-methoxyphenyl)-4,5,6-trimethyl)pyridine-6(1*H*)-thione 16. Morpholine (0.17 mL, 0.002 mol) was added to a suspension of ester **3b** (0.61 g, 0.002 mol) and 4-methoxybenzylidenecyanothioacetamide **14** (0.44 g, 0.002 mol) in ethanol (20 mL), and the mixture was refluxed for 2 h. The reaction mixture was stored for 16 h in a refrigerator. A precipitate formed was filtered off and crystallized from ethanol. Compound **16** (0.54 g, 54%) was obtained as a yellow powder with m.p. 206—208 °C. Found (%): C, 62.02; H, 4.84; N, 12.89; S, 12.55. $C_{26}H_{24}N_4O_3S_2$. Calculated (%): C, 61.89; H, 4.79; N 11.12; S, 12.71. IR, ν/cm^{-1}: 2220, 2225 (CN); 1716 (CO). ^{1}H NMR (250 MHz, DMSO-d$_6$), δ: 0.84 (t, 3 H, Me, *J* = 7.2 Hz); 2.20, 2.40, 2.59 (all s, 3 H each, Me); 3.72 (s, 3 H, MeO); 3.88 (q, 2 H, CH_2O, *J* = 7.2 Hz); 4.64 (s, 2 H, CH_2S); 7.04, 7.37 (both d, 2 H each, Ar, *J* = 7.9 Hz). MS, *m/z* (I_{rel} (%)): 504 $[M]^+$ (7), 458 $[M - EtOH]^+$ (18), 328 (85), 178 (120), 134 (87%).

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Received March 6, 2003;
in revised form July 11, 2003