Chemistry of Heterocyclic Compounds, Vol. 42, No. 4, 2006

NUCLEOPHILIC SUBSTITUTION IN 1-ALKYL-4,5-DICHLORO-3-NITROPYRIDAZIN-6-ONES

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Treatment of 1-alkyl-4,5-dichloro-3-nitropyridazin-6-one with C-nucleophiles and with ambident nucleophiles (2-azahetarylacetonitriles) leads to a selective substitution of a chorine atom by the quaternary carbon atom of the carbanion formed from a substituted acetonitrile. The pK_a of the CH-acid 2-(1-alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)malononitrile was determined by potentiometric titration. Reaction of 2-(1-alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)-2-hetarylacetonitriles with primary amines gives 6,7-dihydro-1H-pyrrolo[2,3-d]pyridazin-7-ones.

Keywords: 2-azahetarylacetonitriles, 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones, ambident nucleophiles, 6,7-dihydro-1H-pyrrolo[2,3-*d*]pyridazin-7-ones, malonodinitrile, CH-acids, C-nucleophiles, nucleophilic substitution.

1-Alkyl-4,5-dihalopyridazin-6-ones occupy an important position amongst pyridazine compounds thanks to their broad spectrum of useful activity. Amongst these are found substances used as herbicides, bactericides, insecticides [1-4], and dyes [5]. A series of compounds have been found in recent years which have a high level of antiproliferating and/or antiviral activity [6-10] and cardiotonic properties [11]. In addition the polyfunctional nature of the 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones opens up the possibility of further structural modification.

In this work we report a study of the reaction of 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones with the malonodinitrile C-nucleophile and with 2-azahetarylacetonitrile 1,3-ambident C,N-nucleophiles. Analysis of the literature data has shown that the reaction of 4,5-dihalopyridazin-6-ones with C-nucleophiles has been little studied [12-14].

The carbanion generated from malonodinitrile in the presence of potassium carbonate base attacks the $C_{(4)}$ atom of the 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones **1a-c** to form the potassium salts of the 2-(1-alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)malononitriles **2a-c**. The three neighboring electron acceptor substituents of the sp^3-hybridized C atom cause the remaining proton to be markedly acidic. Potentiometric titration of compound **2a** gave a pK_a value of about 2.3. The salt formation is characterized by a deep coloration and by the appearance of a very strong band in the IR spectra of salts **2a-c** at 2170 cm^{-1} for the conjugated nitrile groups.

A similar pattern has been observed before in compounds with structurally similar fragments [15].

The reaction of 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones **1a-c** with the ambident C,N-nucleophiles 2-azahetarylacetonitriles **3a-f** occurs with regioselective attack by the carbanion generated from the substituted acetonitrile at the pyridazinone $C_{(4)}$ atom to give compounds **4-6**. It is known that the reaction of 1-alkyl-4,5-

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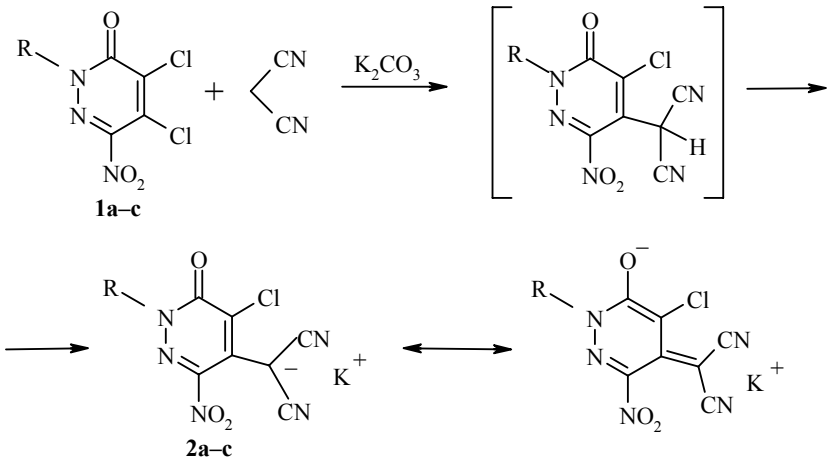
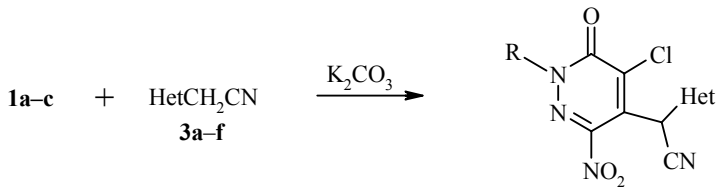


1a–c

2a–c

1, **2** **a** R = Me, **b** R = Et, **c** R = Pr

dichloropyridazin-6-ones with N-nucleophiles always occurs non selectively to yield the two isomeric products of nucleophilic substitution of the chlorines at position 4 and 5 in the pyridazine molecule and in a ratio of 4:5 [16]. It should be noted that treatment of 4,5-dibromopyridazin-6-ones with quinolyl-2-acetonitrile occurs non selectively to give a mixture of two isomers [13]. The introduction of a nitro group increases the mobility of the $Cl_{(4)}$ atom and yields a single isomer. The reaction occurs over several hours in aprotic solvents such as DMF or DMSO at room temperature.

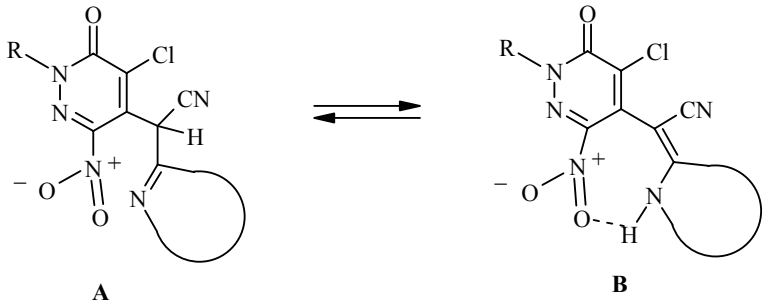


3a–f

4a,**c**,**e**,**f**, **5b–f**, **6a**,**c–f**

4 R = Me; **5** R = Et; **6** R = Pr; **a** Het = 1-Me-benzimidazol-2-yl,
b Het = 1-ethylbenzimidazol-2-yl, **c** Het = benzothiazol-2-yl,
d Het = 5-CF_3-benzothiazol-2-yl, **e** Het = benzoxazol-2-yl,
f Het = 5-NO_2-benzoxazol-2-yl

The structure of compounds **4a,c,e,f, 5b-f, 6a,c-f** can be represented by the two tautomeric forms **A** and **B**, the choice between them being made by analysis of their spectroscopic parameters.



A **B**

TABLE 1. Characteristics of the Synthesized Compounds **4-6, 7-15**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, %
		N	Cl	S		
4a	$C_{15}H_{11}ClN_6O_3$	23.40 / 23.42	10.01 / 9.88		235	85
4c	$C_{14}H_8ClN_5O_3S$	19.28 / 19.36	9.94 / 9.80		233	83
4e	$C_{14}H_8ClN_5O_4$	20.22 / 20.26	10.21 / 10.26		220	79
4f	$C_{14}H_7ClN_6O_6$	21.57 / 21.51	9.11 / 9.07		>300	71
5b	$C_{17}H_{15}ClN_6O_3$	21.68 / 21.72	9.22 / 9.17		202	65
5c	$C_{15}H_{10}ClN_5O_3S$	18.88 / 18.64	8.59 / 8.53		225	75
5d	$C_{16}H_9ClF_3N_5O_3S$	15.66 / 15.78		7.28 / 7.22	238	71
5e	$C_{15}H_{10}Cl\,N_5O_4$	19.45 / 19.47	10.00 / 9.86		212	70
5f	$C_{15}H_9ClN_6O_6$	20.54 / 20.76	8.89 / 8.76		> 300	68
6a	$C_{17}H_{15}ClN_6O_3$	21.68 / 21.73	9.11 / 9.17		242	80
6c	$C_{16}H_{12}ClN_5O_3S$	18.04 / 17.96		8.19 / 8.22	190	65
6d	$C_{17}H_{11}F_3ClN_5O_3S$	15.51 / 15.30		7.07 / 7.00	220	68
6e	$C_{16}H_{12}\,ClN_5O_4$	18.71 / 18.74	9.51 / 9.49		223	75
6f	$C_{16}H_{14}ClN_6O_6$	20.12 / 20.07	8.44 / 8.47		158	72
7a	$C_{22}H_{19}N_7O_3$	22.89 / 22.83			232	77
7c	$C_{21}H_{16}N_6O_3S$	19.89 / 19.43		7.29 / 7.41	252	77
7e	$C_{21}H_{16}N_6O_4$	20.09 / 20.18			258	75
8c	$C_{22}H_{18}N_6O_3S$	18.89 / 18.82		7.29 / 7.18	250	77
9a	$C_{23}H_{21}N_7O_3$	22.19 / 22.11			131	80
9e	$C_{22}H_{18}N_6O_4$	19.55 / 19.53			242	78
10c	$C_{23}H_{20}N_6O_3S$	18.30 / 18.25		7.01 / 6.96	220	82
10e	$C_{23}H_{20}N_6O_4$	18.83 / 18.91			232	70
11a	$C_{19}H_{21}N_7O_3$	24.73 / 24.80			228	75
11c	$C_{18}H_{18}N_6O_3S$	21.13 / 21.09		8.11 / 8.05	205	78
12c	$C_{19}H_{20}N_6O_3S$	20.31 / 20.38		8.01 / 7.77	210	83
13c	$C_{20}H_{22}N_6O_3S$	19.83 / 19.71		7.57 / 7.52	150	68
14a	$C_{21}H_{23}N_7O_3$	23.33 / 23.26			215	65
14c	$C_{20}H_{20}N_6O_3S$	19.87 / 19.80		7.52 / 7.55	201	72
15c	$C_{21}H_{22}N_6O_3S$	19.14 / 19.17		7.37 / 7.31	117	71

***** Compounds **5c, 6c** were purified by column chromatography on silica gel using chloroform; the remaining compounds were recrystallized form *i*-PrOH.

TABLE 2. Spectroscopic Parameters for Compounds **4-6, 7-15**

Compound	IR spectrum, ν, cm^{-1}		^1H NMR spectrum, δ, ppm (*J*, Hz)
	C=O	CN	
1	2	3	4
4a	1655	2180	3.57 (3H, s, NCH_3, benzimidazole); 3.60 (3H, s, NCH_3, pyridazine); 7.36 (1H, t, *J* = 8.4, H-5); 7.46 (1H, t, *J* = 9.2, H-6); 7.63 (1H, d, *J* = 8.8, H-7); 7.65 (1H, d, *J* = 8.8, H-4); 13.07 (1H, s, NH)
4c	1660	2180	3.74 (3H, s, NCH_3, pyridazine); 7.23 (1H, t, *J* = 7.6, H-5); 7.30 (1H, d, *J* = 8.0, H-4); 7.39 (1H, t, *J* = 8.0, H-6); 7.84 (1H, d, *J* = 8.0, H-7); 12.06 (1H, s, NH)
4e	1660	2185	3.72 (3H, s, NCH_3, pyridazine); 7.22 (1H, t, *J* = 7.2, H-5); 7.26 (1H, t, *J* = 7.2, H-6); 7.32 (1H, d, *J* = 6.8, H-4); 7.61 (1H, d, *J* = 8.4, H-7); NH-exchange with water
4f	1650	2175	3.60 (3H, s, NCH_3, pyridazine); 7.58 (1H, d, *J* = 8.8, H-7); 7.95 (1H, d, *J* = 9.2, H-6); 8.10 (1H, s, H-4); NH-exchange with water
5b	1660	2190	1.24 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, benzimidazole); 1.37 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 4.01 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, benzimidazole); 4.35 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.36 (1H, t, *J* = 8.0, H-5); 7.43 (1H, t, *J* = 8.8, H-6); 7.65 (1H, d, *J* = 8.8, H-4); 7.71 (1H, d, *J* = 8.8, H-7); 13.01 (1H, s, NH)
5c	1660	2190	1.32 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 4.17 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.2 (1H, t, *J* = 7.6, H-5); 7.29 (1H, d, *J* = 8.0, H-4); 7.38 (1H, t, *J* = 8.0, H-6); 7.84 (1H, d, *J* = 8.0, H-7); 12.08 (1H, s, NH)
5d	1660	2190	1.33 (3H, t, *J* = 6.8, $NCH_2\underline{CH_3}$, pyridazine); 4.17 (2H, q, *J* = 6.8, $N\underline{CH_2}CH_3$, pyridazine); 7.46 (1H, s, H-4); 7.56 (1H, d, *J* = 8.0, H-6); 8.04 (1H, d, *J* = 8.4, H-7); 12.30 (1H, s, NH)
5e	1670	2195	1.31 (3H, t, *J* = 6.8, $NCH_2\underline{CH_3}$, pyridazine); 4.15 (2H, q, *J* = 6.8, $N\underline{CH_2}CH_3$, pyridazine); 7.22 (1H, t, *J* = 7.2, H-5); 7.26 (1H, t, *J* = 7.2, H-6); 7.31 (1H, d, *J* = 6.8, H-4); 7.59 (1H, d, *J* = 7.6, H-7); NH-exchange with water
5f	1650	2175	1.25 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 4.04 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.56 (1H, d, *J* = 8.0, H-7); 7.94 (1H, d, *J* = 7.2, H-6); 8.09 (1H, s, H-4); NH-exchange with water
6a	1655	2180	0.85 (3H, t, *J* = 6.8, $NCH_2CH_2\underline{CH_3}$, pyridazine); 1.67 (2H, q, *J* = 7.2, $NCH_2\underline{CH_2}CH_3$); 3.56 (3H, s, NCH_3, benzimidazole); 3.93 (2H, t, *J* = 6.8, $N\underline{CH_2}CH_2CH_3$); 7.36 (1H, t, *J* = 8.8, H-5); 7.45 (1H, t, *J* = 8.8, H-6); 7.63 (1H, d, *J* = 8.8, H-4); 7.65 (1H, d, *J* = 8.4, H-7); 13.12 (1H, s, NH)
6c	1660	2180	0.91 (3H, t, *J* = 6.8, $NCH_2CH_2\underline{CH_3}$, pyridazine); 1.75 (2H, q, *J* = 7.2, $NCH_2\underline{CH_2}CH_3$); 4.06 (2H, t, *J* = 6.8, $N\underline{CH_2}CH_2CH_3$); 7.21 (1H, t, *J* = 7.4, H-5); 7.27 (1H, d, *J* = 8.0, H-4); 7.36 (1H, d, *J* = 7.4, H-6); 7.82 (1H, d, *J* = 8.0, H-7); 12.08 (1H, s, NH)
6d	1660	2185	0.92 (3H, t, *J* = 6.8, $NCH_2CH_2\underline{CH_3}$, pyridazine); 1.76 (2H, q, *J* = 7.2, $NCH_2\underline{CH_2}CH_3$); 4.06 (2H, t, *J* = 6.8, $N\underline{CH_2}CH_2CH_3$); 7.45 (1H, s, H-4); 7.56 (1H, d, *J* = 8.4, H-6); 8.03 (1H, d, *J* = 8.8, H-7); 12.30 (1H, s, NH)
6e	1670	2195	0.91 (3H, t, *J* = 6.8, $NCH_2CH_2\underline{CH_3}$, pyridazine); 1.77 (2H, q, *J* = 7.2, $NCH_2\underline{CH_2}CH_3$); 4.06 (2H, t, *J* = 6.8, $N\underline{CH_2}CH_2CH_3$); 7.22 (1H, t, *J* = 6.0, H-5); 7.25 (1H, t, *J* = 6.8, H-6); 7.30 (1H, d, *J* = 6.4, H-4); 7.59 (1H, d, *J* = 7.6, H-7); NH-exchange with water
6f	1655	2175	0.91 (3H, t, *J* = 6.8, $NCH_2CH_2\underline{CH_3}$, pyridazine); 1.77 (2H, q, *J* = 7.2, $NCH_2\underline{CH_2}CH_3$); 4.05 (2H, t, *J* = 6.8, $N\underline{CH_2}CH_2CH_3$); 7.77 (1H, d, *J* = 9.2, H-7); 8.02 (1H, s, H-4); 8.10 (1H, d, *J* = 8.0, H-6); NH-exchange with water
7a	1675	3400	3.65 (3H, s, NCH_3 benzimidazole); 3.67 (3H, s, NCH_3, pyridazine); 5.39 (2H, s, $\underline{CH_2}Ph$); 6.87 (2H, s, NH_2); $CH_2\underline{Ph}$: 6.95 (2H, d, *J* = 6.8, *ortho*-protons from $CH_2\underline{C_6H_5}$); 7.33 (3H, $CH_2\underline{C_6H_5}$); benzimidazole: 7.26 (2H, t, *J* = 5.6, H-5,6); 7.56 (1H, d, *J* = 7.2, H-7); 7.66 (1H, d, *J* = 7.6, H-4)

TABLE 2 (continued)

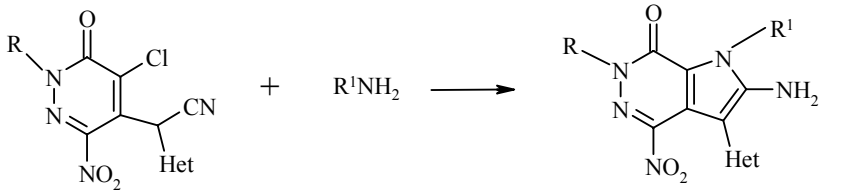
1	2	3	4
7c	1660	3447	3.70 (3H, s, NCH_3 pyridazine); 5.40 (2H, s, $\underline{CH_2}Ph$); $CH_2\underline{C_6H_5}$: 6.95 (2H, d, *J* = 7.2, *ortho*-protons $CH_2\underline{C_6H_5}$); 7.30-7.32 (3H, m, from $CH_2\underline{C_6H_5}$); benzothiazole: 7.27 (1H, t, *J* = 7.2, H-5); 7.44 (1H, t, *J* = 7.8, H-6); 7.93 (1H, d, *J* = 8.4, H-4); 8.02 (1H, d, *J* = 7.6, H-7); 8.63 (2H, br. s, NH_2)
7e	1630	3346	3.73 (3H, s, NCH_3 pyridazine); 5.40 (2H, s, $\underline{CH_2}Ph$); benzoxazole: 7.29 (2H, d, *J* = 7.6, H-4,7); 7.71 (2H, t, *J* = 5.5, H-5,6); $CH_2\underline{C_6H_5}$: 6.94 (2H, d, *J* = 6.8, *ortho*-protons from $CH_2\underline{C_6H_5}$); 7.26-7.36 (3H, m, from $CH_2\underline{C_6H_5}$); 8.06 (2H, s, NH_2)
8c	1665	3340	1.3 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$); 4.15 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$); 5.39 (2H, s, $\underline{CH_2}Ph$); CH_2–$\underline{C_6H_5}$: 6.97 (2H, d, *J* = 7.6, *ortho*-protons from $CH_2\underline{C_6H_5}$); 7.31-7.34 (3H, m, from $CH_2\underline{C_6H_5}$); benzothiazole: 7.28 (1H, t, *J* = 7.2, H-5); 7.45 (1H, t, *J* = 7.6, H-6); 7.94 (1H, d, *J* = 7.6, H-4); 8.03 (1H, d, *J* = 7.6, H-7); 8.61 (2H, s, NH_2)
9a	1650	3380	2.97 (2H, m, $CH_2\underline{CH_2}Ph$); 3.63 (3H, s, NCH_3 benzimidazole); 3.66 (3H, s, NCH_3, pyridazine); 4.27 (2H, m, $\underline{CH_2}CH_2Ph$); 6.82 (2H, s, NH_2); benzimidazole: 7.26 (2H, m, H-5,6); 7.56 (1H, d, *J* = 7.2, H-7); 7.66 (1H, d, *J* = 7.6, H-4); region 7.20-7.25 (5H, m, $CH_2\underline{C_6H_5}$)
9e	1640	3310	2.95 (2H, m, $CH_2\underline{CH_2}Ph$); 3.73 (3H, s, NCH_3 pyridazine); 4.27 (2H, m, $\underline{CH_2}CH_2Ph$); $CH_2CH_2\underline{C_6H_5}$: 7.16 (2H, d, *J* = 7.2, *ortho*-protons from $CH_2CH_2\underline{C_6H_5}$); 7.21-7.23 (3H, m, from $CH_2CH_2\underline{C_6H_5}$); benzoxazole: 7.27 (1H, t, H-5); 7.36 (1H, t, *J* = 9.8, H-6); 7.69 (1H, d, *J* = 8, H-4); 7.73 (1H, d, *J* = 8, H-7); 8.03 (2H, s, NH_2)
10c	1650	3440	1.30 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 2.96 and 4.25 (4H, m, $CH_2\underline{CH_2}Ph$); 4.16 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$ pyridazine); $CH_2CH_2\underline{C_6H_5}$: 7.17 (2H, d, *J* = 6.4, *ortho*-protons from $CH_2CH_2\underline{C_6H_5}$); 7.30-7.34 (3H, m, from $CH_2CH_2\underline{C_6H_5}$); benzothiazole: 7.27 (1H, t, *J* = 6.8, H-5); 7.45 (1H, t, *J* = 7.4, H-6); 7.96 (1H, d, *J* = 7.6, H-4); 8.01 (1H, d, *J* = 8.0, H-7); 8.58 (2H, s, NH_2)
10e	1660	3440	1.30 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 2.95 and 4.26 (4H, m, $CH_2\underline{CH_2}Ph$); 4.17 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$ pyridazine); benzoxazole + $CH_2CH_2\underline{C_6H_5}$: 7.14-7.71 (9H, m); 8.03 (2H, s, NH_2)
11a	1660	3400	0.87 (3H, m, $\underline{CH_3}C_3H_6$); 1.26 (2H, m, $CH_3\underline{CH_2}C_2H_4$); 1.58 (2H, m, $CH_3CH_2\underline{CH_2}CH_2$); 3.62 (3H, s, NCH_3, benzimidazole); 3.68 (3H, s, NCH_3, pyridazine); 3.99 (2H, m, $C_3H_7\underline{CH_2}$); 6.74 (2H, s, NH_2); benzimidazole: 7.24 (2H, t, *J* = 6.8, H-5,6); 7.55 (1H, d, *J* = 7.2, H-7); 7.65 (1H, d, *J* = 7.6, H-4)
11c	1655	3430	0.86 (3H, m, $\underline{CH_3}C_3H_6$); 1.24 (2H, m, $CH_3\underline{CH_2}C_2H_4$); 1.58 (2H, m, $CH_3CH_2\underline{CH_2}CH_2$); 3.70 (3H, s, NCH_3, pyridazine); 3.97 (2H, m, $C_3H_7\underline{CH_2}$); 7.30 (1H, t, *J* = 7.8, H-5); 7.44 (1H, t, *J* = 7.6, H-6); 7.92 (1H, d, *J* = 8.4, H-4); 7.99 (1H, d, *J* = 8.0, H-7); 8.47 (2H, s, NH_2)
12c	1660	3440	0.87 (3H, m, $\underline{CH_3}C_3H_6$); 1.24 (2H, m, $CH_3\underline{CH_2}C_2H_4$); 1.31 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 1.59 (2H, m, $CH_3CH_2\underline{CH_2}CH_2$); 3.97 (2H, m, $C_3H_7\underline{CH_2}$); 4.18 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.30 (1H, t, *J* = 8.0, H-5); 7.43 (1H, t, *J* = 7.2, H-6); 7.92 (1H, d, *J* = 7.6, H-4); 8.00 (1H, d, *J* = 8.0, H-7); 8.48 (2H, s, NH_2)
13c	1655	3440	0.85 (3H, m, $\underline{CH_3}C_4H_8$); 1.24 (4H, m, $CH_3\underline{CH_2}\underline{CH_2}C_2H_4$); 1.31 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 1.61 (2H, m, $C_3H_7\underline{CH_2}CH_2$); 3.96 (2H, m, $C_4H_9\underline{CH_2}$); 4.18 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.30 (1H, t, *J* = 8.0, H-5); 7.43 (1H, t, *J* = 7.2, H-6); 7.92 (1H, d, *J* = 7.6, H-4); 8.00 (1H, d, *J* = 8.0, H-7); 8.47 (2H, s, NH_2)

TABLE 2 (continued)

1	2	3	4
14a	1670	3320	region 1.27-2.27 (10H, m, cyclohexyl); 3.68 (3H, s, NCH_3, benzimidazole); 3.84 (3H, s, NCH_3, pyridazine); 7.05 (2H, s, NH_2); benzimidazole: 7.65 (2H, t, *J* = 6.8, H-5,6); 7.85 (1H, d, *J* = 6.8, H-7); 8.02 (1H, d, *J* = 7.6, H-4)
14c	1650	3490	region 1.27-2.32 (10H, m, cyclohexyl); 3.72 (3H, s, NCH_3, pyridazine); 7.32 (1H, m, H-5); 7.45 (1H, m, H-6); 7.90 (1H, d, *J* = 6.8, H-4); 8.01 (1H, d, *J* = 6.0, H-7); 8.40 (2H, s, NH_2)
15c	1660	3480	region 1.30-2.32 (10H, m, cyclohexyl); 1.31 (3H, t, *J* = 7.2, $NCH_2\underline{CH_3}$, pyridazine); 4.19 (2H, q, *J* = 7.2, $N\underline{CH_2}CH_3$, pyridazine); 7.33 (1H, t, *J* = 7.6, H-5); 7.46 (1H, t, *J* = 7.2, H-6); 7.90 (1H, d, *J* = 7.6, H-4); 8.00 (1H, d, *J* = 7.2, H-7); 8.40 (2H, s, NH_2)

The IR spectra of the given compounds show strong absorption bands in the region 2195-2175 cm^{-1} which are typical of a conjugated nitrile group [13] as well as stretching bands for the carbonyl group at 1670-1650 and N–H bond at 3363-3122 cm^{-1}. The broad spread for the N–H stretching vibrations is due to the formation of an intramolecular hydrogen bond. The ^1H NMR spectra in DMSO-d_6 solvent show a one proton, broad singlet in the region 12.06-13.20 ppm which disappears upon addition of D_2O. The data supports the existence of the compounds **4a,c,e,f, 5b-f** and **6a,c-f** as the N–H tautomer **B**.

Refluxing compounds **4a,c,e, 5a,c,e** with primary amines causes substitution of the remaining Cl atom by the alkylamino group. However, the IR spectra of the compounds obtained show the absence of the absorption for the nitrile group. This infers an addition of the secondary amino group to the nitrile accompanied by closure of the pyrrole ring to form the pyrrolo[2,3-*d*]pyridazin-7-ones **7a,c,e, 8c, 9a,e, 10c,e, 11a,c, 12c, 13c, 14a,c** and **15c**.



4a,c,e, 5a,c **7a,c,e, 8c, 9a,e, 10c,e, 11a,c, 12c, 13c, 14a,c, 15c**

7, **9**, **11**, **14** R = Me, **8**, **10**, **12**, **13**, **15** R = Et; **7**, **8** R^1 = $PhCH_2$; **9**, **10** R^1 = $Ph(CH_2)_2$; **11**, **12** R^1 = *n*-Bu; **13** R^1 = *n*-C_5H_{11}; **14**, **15** R^1 = *cyclo*-C_6H_{11}

This is confirmed by the two absorption bands for a primary amino group at 3450-3300 cm^{-1}. The amino group protons appear in the ^1H NMR spectra as two signals. Their non equivalence is due to the participation of one of them in the formation of the intramolecular hydrogen bond to the ring nitrogen atom (8.6 ppm), the "free" proton absorbing at 6.8 ppm.

EXPERIMENTAL

^1H NMR spectra were recorded on a Varian Mercury-400 spectrometer (400 MHz) using DMSO-d_6 solvent and TMS internal standard. IR spectra were taken on a Pye-Unicam SP3-300 instrument for KBr tablets. Melting points were measured on a Boetius microscope heating stage using a VEB Analytik PHMK 05 viewing

attachment. Monitoring of the reaction course and the purity of the compounds obtained was carried out by TLC on Silufol UV-254 plates in the system chloroform–methanol (9:1).

Physicochemical parameters and spectroscopic parameters for compounds **4-15** are given in Tables 1 and 2.

Preparation of the Potassium Salts of 2-(1-Alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)malononitriles 2a-c (General Method). Malonodinitrile (5 mmol) and potassium carbonate (10 mmol) were added to a solution of the 1-alkyl-4,5-dichloro-3-nitropyridazine **1a-c** (5 mmol) in DMF (10 ml). The mixture was held at room temperature for 10-12 h. The completion of the reaction was determined by TLC. The solvent was evaporated and water (5 ml) was added. The product was filtered off and recrystallized from *i*-PrOH.

Synthesis of 2-(1-Alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)-2-hetarylacetonitriles 4a,c,e,f, 5b-f, 6a,c-f (General Method). The hetarylacetonitrile (5 mmol) and potassium carbonate (10 mmol) were added to a solution of the corresponding 1-alkyl-4,5-dichloro-3-nitropyridazin-6-one [14] (5 mmol) in DMF (10 ml). The mixture was left at 25°C for 10-15 h. The completion of the reaction was determined by TLC. Water (100 ml) was added, the product was neutralized with acetic acid to pH 7, and the precipitate was filtered off and recrystallized from the appropriate solvent.

Synthesis of 6,7-dihydro-1H-pyrrolo[2,3-d]pyridazin-7-ones 7a,c,e, 8c, 9a,e, 10c,e, 11a,c, 12c, 13c, 14a,c and 15c (General Method). The primary amine (10 mmol) was added to a solution of the corresponding 2-(1-alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyridazinyl)-2-hetarylacetonitrile (5 mmol) in *i*-PrOH (30 ml) and refluxed for 2-5 h. The reaction course was monitored by TLC. Solvent was evaporated, water (50 ml) was added, and the precipitate was filtered off and recrystallized from *i*-PrOH.

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