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APPLICATION OF THE RECYCLIZATION PRODUCTS OF 5-ALKYL(ARYL)AMINO-2-(3-PHTHALIMIDOPROPYL)-1,3-OXAZOLE-4-CARBONITRILES TO THE SYNTHESIS OF CONDENSED TRICYCLIC NITROGENOUS STRUCTURES

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N-Alkyl(aryl)-3-amino-5H,6H,7H-pyrrolo[1,2-a]imidazole-2-carboxamides were obtained by the interaction of 5-alkyl(aryl)amino-2-(3-phthalimidopropyl)-1,3-oxazole-4-carbonitriles with hydrazine hydrate and have been used for the synthesis of substituted 3H,4H,6H,7H,8H-pyrrolo[2,1-h]purin-4-ones, their thione analogs, and also 1,2,3,6,7,8-hexahydro-4H-pyrrolo[2',1':2,3]imidazo[4,5-d]-[1,3,2]diazaphosphinine derivatives.

Keywords: *N*-alkyl(aryl)-3-amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamides, 3-alkyl-2-mercapto-1,2,3,6,7,8-hexahydro-4*H*-pyrrolo[2',1':2,3]imidazo[4,5-*d*][1,3,2]diazaphosphinine-4-thione 2-sulfides, 3-alkyl(aryl)-3*H*,4*H*,6*H*,7H,8*H*-pyrrolo[2,1-*h*]purin-4-ones, 3-aryl-3*H*,4*H*,6*H*,7*H*,8*H*-pyrrolo-[2,1-*h*]purine-4-thiones, recyclization.

It was shown previously in [1] that 5-morpholino-2-(3-phthalimidopropyl)-1,3-oxazole-4-carbonitrile (**2**) obtained by oxazole cyclization of 2-(4-phthalimidobutanoylamino)-3,3-dichloroacrylonitrile (**1**) is subject to recyclization under the action of hydrazine hydrate with the formation of 2-(morpholin-4-ylcarbonyl)-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazol-3-amine (**3**). It was interesting to investigate whether similar behavior would be observed with carbonitriles **4a-d** containing primary amine fragments at the position 5 of the oxazole ring, the recyclization products of which in the future might be used for constructing tricyclic structures. With this aim, we synthesized oxazoles **4a-d** with residues of benzylamine, phenylethylamine, aniline, and 4-methyl phenylamine. It turned out that hydrazinolysis of them (refluxing in ethanol with hydrazine hydrate) as in the case of compound **2**, also led to recyclization products, the novel *N*-alkyl(aryl)-3-amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamides **5a-d**.

The composition and structure of compounds **5a-d** were confirmed by results of elemental analysis, chromato-mass spectrometry, as well as IR and NMR spectral data (Tables 1-3). In the ^{1}H NMR spectra of these substances, in comparison with the initial compounds **4a-d**, signals of the methylene groups in the

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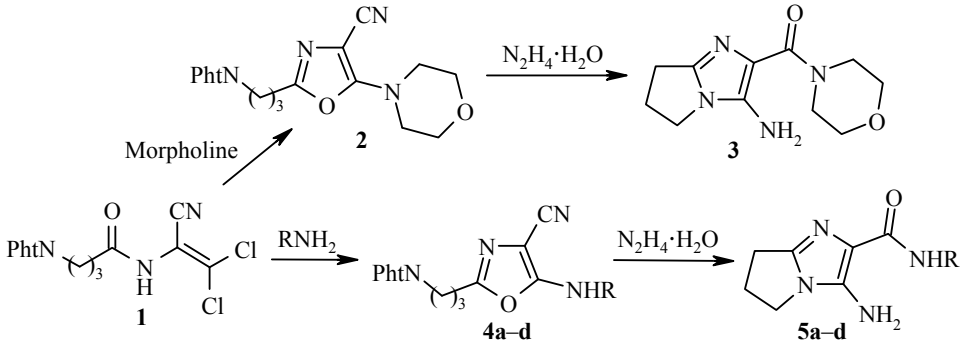
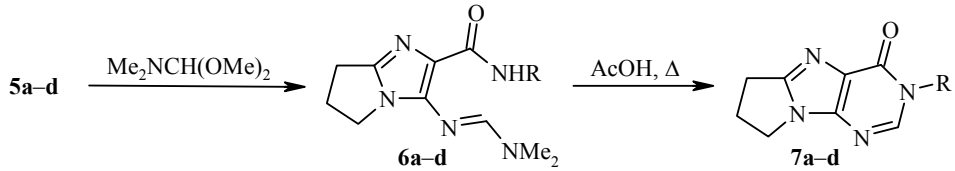


4, **5 a** R = Bn, **b** R = $Ph(CH_2)_2$, **c** R = Ph, **d** R = 4-MeC_6H_4

propylene fragment were shifted downfield, while the NH group signals of the aminoalkyl and aminoaryl residues were shifted upfield (Table 2). The presence of a primary amino group in the structure of products **5a-d** was confirmed by the occurrence of a broadened singlet at 5.68-5.96 ppm in the region characteristic for such groups.

On comparing the IR spectra of compounds **5a-d** and **4a-d** the disappearance of nitrile absorption bands at 2000-2300 cm^{-1} was also observed, as was the appearance of intense absorption bands at 3000-3500 cm^{-1}, assigned to the stretching vibrations of the primary amino group. Similar spectral changes were observed on recyclization of 5-morpholino-2-(3-phthalimidopropyl)-1,3-oxazole-4-carbonitrile (**2**) into 2-(morpholin-4-yl-carbonyl)-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazol-3-amine (**3**) [1], the structure of which was reliably confirmed by correlation methods of NMR spectroscopy.

The presence of three labile hydrogen atoms of the amino groups in the structure of compounds **5a-d** raises the possibility of their subsequent use in cyclization reactions. Attempts to synthesize pyrrolo[2,1-*h*]-purin-4-ones **7a-d** on interacting products **5a-d** with an excess of triethyl orthoformate were not successful. The use of the even more reactive condensing agent (dimethylformamide dimethyl acetal) led to amidines **6a-d**, refluxing of which in anhydrous acetic acid gave pyrrolo[2,1-*h*]purin-4-ones **7a-d** in 54-65% yield. A similar approach to the synthesis of condensed purin-4-one derivatives was reported previously in [2].



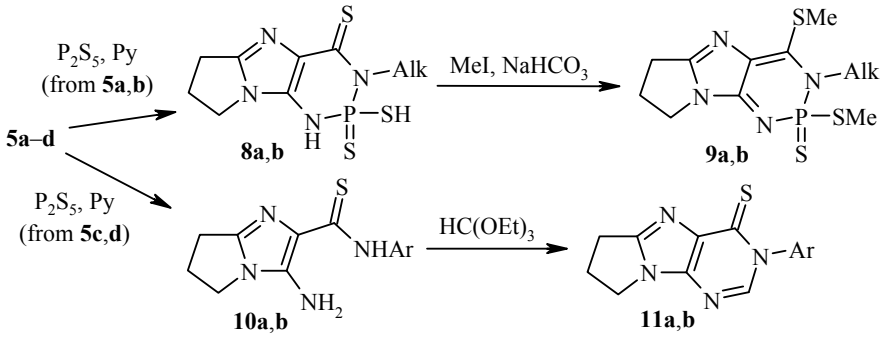
6, **7 a** R = Bn**, b** R = $Ph(CH_2)_2$, **c** R = Ph, **d** R = 4-MeC_6H_4

We have also studied the interaction of aminoimidazoles **5a-d** with phosphorus pentasulfide. It was found that on refluxing the reactants in pyridine in a molar ratio of 1:2, the diazaphosphinines **8a**,**b** were formed in the case of compounds **5a**,**b** containing an aliphatic amide residue, while in the case of compounds **5c,d** with an aromatic amide residue the reactions stopped at the stage of thioamides **10a**,**b**. The obtained 3-alkyl-2-mercapto-1,2,3,6,7,8-hexahydro-4*H*-pyrrolo[2',1':2,3]imidazo[4,5-*d*][1,3,2]diazaphosphinine-4-thione 2-sulfides **8a**,**b** were converted by the action of methyl iodide into the corresponding dimethyl derivatives **9a**,**b**. Methylation of products **8a**,**b** was effected regioselectively at the two sulfur atoms but not at the nitrogen atom of the diazaphosphinine fragment, as indicated by the absence of ^1H NMR signal splitting of one of the methyl groups. In addition, such a direction of alkylation was previously observed in similar compounds [3].

TABLE 1. Physicochemical Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %					Mp*, °C	Yield, %
		C	H	N	P	S		
4c	$C_{21}H_{16}N_4O_3$	67.91 / 67.73	4.45 / 4.33	15.17 / 15.05	—	—	181-183	78
4d	$C_{22}H_{18}N_4O_3$	68.22 / 68.38	4.83 / 4.70	14.37 / 14.50	—	—	170-172	69
5a	$C_{14}H_{16}N_4O$	65.78 / 65.61	6.27 / 6.29	21.69 / 21.86	—	—	129-131	67
5b	$C_{15}H_{18}N_4O$	66.76 / 66.65	6.67 / 6.71	20.60 / 20.72	—	—	66-68	53
5c	$C_{13}H_{14}N_4O$	64.32 / 64.45	5.70 / 5.82	23.26 / 23.12	—	—	188-190 (decomp.)	75
5d	$C_{14}H_{16}N_4O$	65.70 / 65.61	6.19 / 6.29	21.95 / 21.86	—	—	242-244 (decomp)	47
6a	$C_{17}H_{21}N_5O$	65.62 / 65.57	6.63 / 6.80	22.53 / 22.49	—	—	113-115	51
6b	$C_{18}H_{23}N_5O$	66.25 / 66.44	6.92 / 7.12	21.40 / 21.52	—	—	Oil	50
6c	$C_{16}H_{19}N_5O$	64.42 / 64.63	6.53 / 6.44	23.70 / 23.55	—	—	125-127	55
6d	$C_{17}H_{21}N_5O$	65.41 / 65.57	6.70 / 6.80	22.59 / 22.49	—	—	172-174	75
7a	$C_{15}H_{14}N_4O$	67.49 / 67.65	5.18 / 5.30	21.12 / 21.04	—	—	217-219 (decomp.)	60
7b	$C_{16}H_{16}N_4O$	68.59 / 68.55	5.62 / 5.75	20.17 / 19.99	—	—	178-180	54
7c	$C_{14}H_{12}N_4O$	66.78 / 66.66	4.71 / 4.79	22.35 / 22.21	—	—	222-224 (decomp.)	62
7d	$C_{15}H_{14}N_4O$	67.60 / 67.65	5.43 / 5.30	20.93 / 21.04	—	—	202-204 (decomp.)	65
8a	$C_{14}H_{15}N_4PS_3$	45.78 / 45.89	4.22 / 4.13	15.39 / 15.29	8.61 / 8.45	26.13 / 26.25	220-222 (decomp.)	73
8b	$C_{15}H_{17}N_4PS_3$	47.19 / 47.35	4.59 / 4.50	14.65 / 14.72	8.27 / 8.14	25.40 / 25.28	214-216 (decomp.)	72
9a	$C_{16}H_{19}N_4PS_3$	48.60 / 48.71	4.69 / 4.85	14.37 / 14.20	7.97 / 7.85	24.47 / 24.38	147-149	62
9b	$C_{17}H_{21}N_4PS_3$	50.13 / 49.98	5.03 / 5.18	13.85 / 13.71	7.57 / 7.58	23.71 / 23.54	162-164	52
10a	$C_{13}H_{14}N_4S$	60.25 / 60.44	5.65 / 5.46	21.67 / 21.69	—	12.63 / 12.41	218-220 (decomp.)	55
10b	$C_{14}H_{16}N_4S$	61.81 / 61.74	5.77 / 5.92	20.68 / 20.57	—	11.63 / 11.77	159-161	52
11a	$C_{14}H_{12}N_4S$	62.80 / 62.66	4.37 / 4.51	20.70 / 20.88	—	12.17 / 11.95	250-252 (decomp.)	73
11b	$C_{15}H_{14}N_4S$	63.98 / 63.81	4.87 / 5.00	19.88 / 19.84	—	11.47 / 11.36	290-292 (decomp.)	68

*Solvents for recrystallization: EtOH (compounds **4c**,**d**, **8a**,**b**), EtOH–H_2O, 1:1 (compounds **5a-d**, **9a**,**b**, **10a**,**b**), acetone (compounds **7a-d**, **11a**,**b**).



8, **9** **a** Alk = Bn, **b** Alk = $Ph(CH_2)_2$; **10**, **11** **a** Ar = Ph, **b** Ar = 4-MeC_6H_4

TABLE 2. ^{1}H NMR Spectra of the Synthesized Compounds

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
4c	2.01-2.06 (2H, m, CH_2); 2.77 (2H, t, *J* = 6.6, CH_2); 3.70 (2H, t, *J* = 5.8, NCH_2); 7.04-7.33 (5H, m, H Ph); 7.80-7.94 (4H, m, H Ar); 10.23 (1H, s, NH)
4d	1.94-2.09 (2H, m, CH_2); 2.26 (3H, s, CH_3); 2.75 (2H, t, *J* = 6.8, CH_2); 3.70 (2H, t, *J* = 6.3, NCH_2); 7.01-7.21 (4H, m, H Ar);7.75-7.94 (4H, m, H Ar); 10.13 (1H, s, NH)
5a	2.41-2.48 (2H, m, CH_2); 2.60 (2H, t, *J* = 7.2, CH_2); 3.74 (2H, t, *J* = 6.8, NCH_2); 4.35 (2H, d, *J* = 6.0, CH_2); 5.70 (2H, s, NH_2); 7.15-7.42 (5H, m, H Ph); 7.75 (1H, t, *J* = 5.6, NH)
5b	2.42-2.49 (2H, m, CH_2); 2.51-2.60 (2H, m, CH_2); 2.77 (2H, t, *J* = 7.0, CH_2); 3.32-3.41 (2H, m, CH_2); 3.73 (2H, t, *J* = 6.4, CONHC<u>H</u>$_2$); 5.68 (2H, s, NH_2); 7.21-7.29 (6H, m, H Ph, NH)
5c	2.50-2.55 (2H, m, CH_2); 2.65 (2H, t, *J* = 7.2, CH_2); 3.77 (2H, t, *J* = 7.0, NCH_2); 5.96 (2H, br. s, NH_2); 6.92-6.98 (1H, m, H Ph); 7.19-7.27 (2H, m, H Ph); 7.68-7.79 (2H, m, H Ph); 9.12 (1H, br. s, NH)
5d	2.24 (3H, s, CH_3); 2.43-2.51 (2H, m, CH_2); 2.65 (2H, t, *J* = 7.0, CH_2); 3.76 (2H, t, *J* = 6.8, NCH_2); 5.94 (2H, br. s, NH_2); 7.05 (2H, d, *J* = 6.8, H Ar); 7.65 (2H, d, *J* = 7.0, H Ar); 9.04 (1H, br. s, NH)
6a	2.41-2.52 (2H, m, CH_2); 2.67 (2H, t, *J* = 7.5, CH_2); 2.91 (3H, s, CH_3); 3.01 (3H, s, CH_3); 3.76 (2H, t, *J* = 6.8, CH_2); 4.39 (2H, d, *J* = 6.0, NC<u>H</u>$_2$Ph); 7.21-7.32 (5H, m, H Ph); 8.06 (1H, t, *J* = 6.0, NH); 8.74 (1H, s, N=CH)
6b	2.42-2.51 (2H, m, CH_2); 2.65 (2H, t, *J* = 6.5, CH_2); 2.80 (2H, t, *J* = 7.0, CH_2); 2.90 (3H, s, CH_3); 3.00 (3H, s, CH_3); 3.37-3.44 (2H, m, CH_2); 3.78 (2H, t, *J* = 6.5, CONHC<u>H</u>$_2$); 7.22-7.34 (5H, m, H Ph); 7.59 (1H, t, *J* = 6.0, NH); 8.71 (1H, s, N=CH)
6c	2.51-2.54 (2H, m, CH_2); 2.72 (2H, t, *J* = 6.6, CH_2); 2.98 (3H, s, CH_3); 3.06 (3H, s, CH_3); 3.82 (2H, t, *J* = 6.1, NCH_2); 6.97-7.01 (1H, m, H Ph); 7.26-7.29 (2H, m, H Ph); 7.72-7.74 (2H, m, H Ph); 8.62 (1H, s, CH); 9.54 (1H, s, NH)
6d	2.24 (3H, s, ArC<u>H</u>$_3$); 2.52-2.57 (2H, m, CH_2); 2.71 (2H, t, *J* = 7.2, CH_2); 2.96 (3H, s, NCH_3); 3.05 (3H, s, NCH_3); 3.80 (2H, t, *J* = 7.2, NCH_2); 7.07 (2H, d, *J* = 8.4, H Ar); 7.61 (2H, d, *J* = 8.0, H Ar); 8.61 (1H, s, N=CH); 9.46 (1H, s, NH)
7a	2.52-2.61 (2H, m, CH_2); 2.88 (2H, t, *J* = 7.0, CH_2); 4.07 (2H, t, *J* = 6.3, NCH_2); 5.23 (2H, s, C<u>H</u>$_2$Ph); 7.27-7.34 (5H, m, H Ph); 8.49 (1H, s, H-2)
7b	2.59-2.62 (2H, m, CH_2); 2.90 (2H, t, *J* = 7.6, CH_2); 2.99 (2H, t, *J* = 7.0, CH_2); 4.05 (2H, t, *J* = 7.3, CH_2); 4.24 (2H, t, *J* = 7.0, CH_2); 7.19-7.31 (5H, m, H Ph); 8.05 (1H, s, H-2)
7c	2.63-2.67 (2H, m, CH_2); 2.92 (2H, t, *J* = 7.3, CH_2); 4.12 (2H, t, *J* = 7.0, NCH_2); 7.46-7.58 (5H, m, H Ph); 8.26 (1H, s, H-2)
7d	2.40 (3H, s, CH_3); 2.63-2.67 (2H, m, CH_2); 2.92 (2H, t, *J* = 7.5, CH_2); 4.11 (2H, t, *J* = 7.0, NCH_2); 7.31-7.40 (4H, m, H Ar); 8.22 (1H, s, H-2)
8a	2.55-2.63 (2H, m, CH_2); 3.01 (2H, t, *J* = 7.0, CH_2); 4.06 (2H, t, *J* = 6.6, NCH_2); 5.43 (2H, d, *J* = 10.4, C<u>H</u>$_2$Ph); 7.13-7.48 (5H, m, H Ph); 10.56 (1H, br. s, NH)*
8b	2.60-2.65 (2H, m, CH_2); 3.05 (2H, t, *J* = 7.5, CH_2); 3.09-3.13 (2H, m, CH_2); 4.06 (2H, t, *J* = 7.0, NCH_2); 4.37-4.43 (2H, m, NC<u>H</u>$_2$$CH_2$Ph); 7.22-7.45 (5H, m, H Ph); 10.52 (1H, br. s, NH)*
9a	2.10 (3H, d, *J* = 16.0, CH_3); 2.49-2.55 (2H, m, CH_2); 2.75 (2H, t, *J* = 7.0, CH_2); 2.86 (3H, s, CH_3); 3.76 (2H, t, *J* = 6.0, NCH_2); 5.10-5.42 (2H, m, C<u>H</u>$_2$Ph); 7.25-7.34 (5H, m, H Ph)
9b	2.10 (3H, d, *J* = 16.0, CH_3); 2.50-2.55 (2H, m, CH_2); 2.75 (2H, t, *J* = 7.8, CH_2); 3.03 (3H, s, CH_3); 3.10-3.31 (2H, m, CH_2); 3.74-3.79 (2H, m, CH_2); 4.05-4.21 (2H, m, CH_2); 7.24-7.37 (5H, m, H Ph)
10a	2.51-2.57 (2H, m, CH_2); 2.70 (2H, t, *J* = 7.5, CH_2); 3.82 (2H, t, *J* = 6.8, NCH_2); 7.11-7.37 (3H, m, H Ph); 7.39 (2H, br. s, NH_2); 7.77-7.85 (2H, m, H Ph); 10.28 (1H, s, NH)
10b	2.28 (3H, s, CH_3); 2.51-2.58 (2H, m, CH_2); 2.67 (2H, t, *J* = 7.6, CH_2); 3.79 (2H, t, *J* = 6.8, NCH_2); 7.12 (2H, d, *J* = 7.9, H Ar); 7.32 (2H, br. s, NH_2); 7.65 (2H, d, *J* = 7.8, H Ar); 10.20 (1H, s, NH)
11a	2.61-2.68 (2H, m, CH_2); 2.96 (2H, t, *J* = 6.8, CH_2); 4.15 (2H, t, *J* = 6.5, NCH_2); 7.43-7.57 (5H, m, H Ph); 8.55 (1H, s, H-2)
11b	2.39 (3H, s, CH_3); 2.62-2.67 (2H, m, CH_2); 2.95 (2H, t, *J* = 7.0, CH_2); 3.79 (2H, t, *J* = 6.4, NCH_2); 7.25-7.36 (4H, m, H Ar); 8.51 (1H, s, H-2)

*The signal of the SH proton was not observed as a result of deuterium exchange.

TABLE 3. IR and Mass Spectra of the Synthesized Compounds

Compound	IR spectrum, ν, cm^{-1}*	Mass spectrum, *m/z* $[M+H]^+$
4c	1672*[2], 1713 sh (C=O), 2220 (CN), 3146–3323 (NH)	373
4d	1670*[2], 1719 sh (C=O), 2223 (CN), 3129–3367 (NH)	387
5a	1621 (C=O), 3027–3408 (NH, NH_2)	257
5b	1614 (C=O), 3134–3492 (NH, NH_2)	271
5c	1634 (C=O), 3171–3433 (NH, NH_2)	243
5d	1637 (C=O), 3162–3412 (NH, NH_2)	257
6a	1648 (C=O), 3367–3435 (NH)	312
6b	1653 (C=O), 3355–3410 (NH)	326
6c	1655 (C=O), 3365–3420 (NH)	298
6d	1659 (C=O), 3147–3368 (NH)	312
7a	1677 sh (C=O)	267
7b	1681 sh (C=O)	281
7c	1697 sh (C=O)	253
7d	1703 sh (C=O)	267
8a	1598, 3026–3221 (NH, SH)	367
8b	1602, 3060–3265 (NH, SH)	381
9a	1578, 1617	395
9b	1575, 1613	409
10a	1594, 3132–3360 (NH, NH_2)	259
10b	1597, 3162–3350 (NH, NH_2)	273
11a	1587	269
11b	1584	283

* High intensity bands in the ranges 1500-1700, 2100-2300, and 3000-3600 cm^{-1} are indicated.

*[2] Band caused by 5-amino-1,3-oxazole fragment [4].

Pyrrolo[2,1-*h*]purine-4-thiones **11a**,**b**, thioxo analogs of compounds **7c,d**, were synthesized from thioamides **10a**,**b**. It should be mentioned that in condensation with triethyl orthoformate, thioamides **10a,b** proved to be more reactive than amides **5c**,**d**, and after refluxing for 3 h gave the corresponding thioxopurines **11a**,**b** in yields of 73 and 68%, respectively.

A method has therefore been developed for the synthesis of new representatives of pyrrolo[2,1-*h*]purin-4-ones, pyrrolo[2,1-*h*]purine-4-thiones, and pyrrolo[2',1':2,3]imidazo[4,5-*d*][1,3,2]diazaphosphinine-4-thiones, using *N*-alkyl(aryl)-3-amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamides that were obtained by recyclization of 5-alkyl(aryl)amino-2-(3-aminopropyl)-1,3-oxazole-4-carbonitriles.

EXPERIMENTAL

The IR spectra were recorded on a Vertex 70 spectrometer in KBr pellets. The ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance DRX-500 instrument (at working frequencies of 500, 125, and 202 MHz respectively) in DMSO-d_6 solution. Chemical shifts are given relative to TMS (internal standard for ^1H and ^{13}C nuclei) or 85% H_3PO_4 (external standard for ^{31}P nuclei). The mass spectra were recorded on a chromato-mass spectrometer of the Agilent 1100 Series, fitted with a diode matrix and an Agilent LC\MSD SL mass selective detector; column was Zorbax SB-C18, 4.6×15 mm, 1.8 μm (PN 821975-932); solvents A – MeCN–H_2O (95:5), 0.1% trifluoroacetic acid, and B – 0.1% aqueous trifluoroacetic acid; eluent flow rate 3 ml/min; injection volume 1 μl; UV detectors, 215, 254, 285 nm; ionization method CI at atmospheric pressure, scanning range *m/z* 80-1000. Elemental analysis was carried out in the analytical laboratory of the Institute of Bioorganic Chemistry and

Petrochemistry, National Academy of Sciences of Ukraine. Melting points were determined on a Fisher-Johns instrument.

2-(4-Phthalimidobutyrylamino)-3,3-dichloroacrylonitrile (**1**) and **5-alkylamino-2-(3-phthalimidopropyl)-1,3-oxazole-4-carbonitriles 4a**,**b** were obtained by the procedure of [1].

5-Arylamino-2-(3-phthalimidopropyl)-1,3-oxazole-4-carbonitriles 4c,d (General Method). The corresponding aromatic amine (80 mmol) was added to compound **1** (7.04 g, 20 mmol) in DMF (20 ml). The mixture was maintained at 20-25°C for a week, water (80 ml) was added, the solid was filtered off, washed with water, and purified by recrystallization. ^{13}C NMR spectrum of compound **4c**, δ, ppm: 24.8 ($NCH_2\underline{C}H_2CH_2$); 25.2 ($NCH_2CH_2\underline{C}H_2$); 37.2 ($N\underline{C}H_2CH_2CH_2$); 88.4 (C-4 oxazole); 114.8 (CN); 118.8; 123.3; 123.4; 129.7; 132.1; 134.8; 139.1; 155.3; 157.0; 168.5 (C=O). ^{13}C NMR spectrum of compound **4d**, δ, ppm: 20.8 (CH_3); 24.8 ($NCH_2\underline{C}H_2CH_2$); 25.2 ($NCH_2CH_2\underline{C}H_2$); 37.2 ($N\underline{C}H_2CH_2CH_2$); 87.4 (C-4 oxazole); 114.9 (CN); 119.3; 123.4; 130.1; 132.1; 132.6; 134.8; 136.4; 154.8; 157.4; 168.5 (C=O).

***N*-Alkyl(aryl)-3-amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamides 5a-d (General Method)**. Hydrazine hydrate (0.25 ml, 5.2 mmol) was added to a suspension of oxazole **4a-d** (5 mmol) in EtOH (20 ml). The mixture was refluxed for 6 h, cooled, and EtOH evaporated in vacuum. The residue was suspended in 4% aqueous HCl solution (14 ml), the solid was filtered off, and 25% aqueous NaOH solution was added to the filtrate to pH ~10. The solution was extracted with CH_2Cl_2 (5×5 ml), dried over Na_2SO_4, the solvent was removed in vacuum, the residue was dissolved in CH_2Cl_2 and washed with 5% aqueous NaOH solution. The solvent was removed in vacuum, the residue was washed with hexane, and purified by recrystallization. ^{13}C NMR spectrum of compound **5a**, δ, ppm: 22.5 ($NCH_2\underline{C}H_2CH_2$); 26.5 $NCH_2CH_2\underline{C}H_2$; 41.8 ($CONH\underline{C}H_2$); 42.2 ($N\underline{C}H_2CH_2CH_2$); 115.9 (C-$NH_2$); 126.6; 127.8; 128.8; 141.3; 141.4; 145.6; 165.1 (CO). ^{13}C NMR spectrum of compound **5d**, δ, ppm: 20.9 (CH_3); 22.5 ($NCH_2\underline{C}H_2CH_2$); 26.5 ($NCH_2CH_2\underline{C}H_2$); 42.3 ($N\underline{C}H_2CH_2CH_2$); 115.7 (C-$NH_2$); 119.4; 129.3; 131.2; 137.7; 142.5; 145.9; 163.3 (CO).

***N*-Alkyl(aryl)-3-[(dimethylamino)methylidene]amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamides 6a-d (General Method)**. A solution of compound **5a-d** (2 mmol) in dimethylformamide dimethyl acetal (15 ml) was refluxed for 4 h, and the solvent removed in vacuum. The solid was filtered off, washed with hexane, and compounds **6a-d** were used for subsequent syntheses without additional purification. ^{13}C NMR spectrum of compound **6d**, δ, ppm: 20.9 (CH_3); 23.2 ($NCH_2\underline{C}H_2CH_2$); 26.2 ($NCH_2CH_2\underline{C}H_2$); 34.0 (2×$NCH_3$); 42.8 ($N\underline{C}H_2CH_2CH_2$); 119.5; 122.0; 129.4; 131.6; 137.5; 143.7; 147.7; 158.1; 162.3 (CO).

3-Alkyl(aryl)-3*H*,4*H*,6*H*,7*H*,8*H*-pyrrolo[2,1-*h*]purin-4-ones 7a-d (General Method). A solution of amidine **6a-d** (2 mmol) in anhydrous AcOH (15 ml) was refluxed for 24 h. The solvent was removed in vacuum, the residue was washed with water, and purified by recrystallization. ^{13}C NMR spectrum of compound **7a**, δ, ppm: 23.4 ($NCH_2\underline{C}H_2CH_2$); 26.4 ($NCH_2CH_2\underline{C}H_2$); 42.8 ($N\underline{C}H_2CH_2CH_2$); 48.9 ($\underline{C}H_2Ph$); 127.9; 128.0; 128.2; 129.0; 137.9; 146.5; 147.8; 156.2; 158.3 (CO).

3-Alkyl-2-mercapto-1,2,3,6,7,8-hexahydro-4*H*-pyrrolo[2',1':2,3]imidazo[4,5-*d*][1,3,2]diazaphosphinine-4-thione 2-Sulfides 8a,b (General Method). P_2S_5 (0.88 g, 4 mmol) was added to a suspension of compound **5a**,**b** (2 mmol) in pyridine (5 ml). The reaction mixture was refluxed for 2 h, cooled, 10% HCl solution (30 ml) was added, the precipitated solid was filtered off, washed with water, and purified by recrystallization. ^{31}P NMR spectrum of compound **8a**, δ, ppm: 88.2. ^{31}P NMR spectrum of compound **8b**, δ, ppm: 85.8. ^{13}C NMR spectrum of compound **8b**, δ, ppm: 23.7 ($NCH_2\underline{C}H_2CH_2$); 25.9 ($NCH_2CH_2\underline{C}H_2$); 34.7; 46.5; 48.7; 126.7; 128.8; 129.0; 132.3; 140.0; 149.5; 152.3; 178.3 (CS).

3-Alkyl-2,4-bis(methylthio)-3,6,7,8-tetrahydro-2*H*-pyrrolo[2',1':2,3]-imidazo[4,5-*d*][1,3,2]diazaphosphinine 2-Sulfides 9a,b (General Method). $NaHCO_3$ (0.84, 10 mmol) was added to a suspension of compound **8a**,**b** (2 mmol) in a 1:3 mixture of H_2O–EtOH (15 ml), and then MeI (0.85 g, 6 mmol) was added dropwise with stirring. The reaction mixture was stirred at 20-25°C for 48 h, the resulting solid was filtered off, washed with water, and purified by recrystallization. ^{31}P NMR spectrum of compound **9a**, δ, ppm: 81.0. ^{31}P NMR spectrum of compound **9b**, δ, ppm: 78.64. ^{13}C NMR spectrum of compound **9b**, δ, ppm: 15.9; 19.7; 23.5 ($NCH_2\underline{C}H_2CH_2$); 25.9 ($NCH_2CH_2\underline{C}H_2$); 37.0; 41.3; 49.2; 127.3; 129.0; 129.3; 138.4; 153.8; 154.1; 156.6; 160.2.

***N*-Alkyl(aryl)-3-amino-5*H*,6*H*,7*H*-pyrrolo[1,2-*a*]imidazole-2-thiocarboxamides 10a,b (General Method)**. P_2S_5 (0.88 g, 4 mmol) was added to a suspension of compound **5c**,**d** (2 mmol) in pyridine (5 ml). The reaction mixture was refluxed for 2 h, cooled, and water (30 ml) added. The precipitated solid was filtered off, washed with water, and purified by recrystallization.

3-Aryl-3*H*,4*H*,6*H*,7*H*,8*H*-pyrrolo[2,1-*h*]purine-4-thiones 11a,b (General Method). A suspension of imidazole **10a**,**b** (2 mmol) in triethyl orthoformate (15 ml) was refluxed for 4 h, the precipitated solid was filtered off, washed with hexane, and purified by recrystallization. ^{13}C NMR spectrum of compound **11a**, δ, ppm: 23.7 ($NCH_2\underline{C}H_2CH_2$); 26.3 ($NCH_2CH_2\underline{C}H_2$); 43.0 ($N\underline{C}H_2CH_2CH_2$); 128.8; 129.5; 129.7; 140.6; 141.0; 141.7; 147.5; 161.4; 177.5 (CS).

REFERENCES

1. S. A. Chumachenko, O. V. Shablykin, A. N. Vasilenko, and V. S. Brovarets, *Khim. Geterotsikl. Soedin.*, 1238 (2011). [*Chem. Heterocycl. Compd*., **47**, 1020 (2011).]
2. J. M. Fevig, J. Cacciola, J. Buriak, K. A. Rossi, R. M. Knabb, J. M. Luettgen, P. C. Wong, S. A. Bai, R. R. Wexler, and P. Y. S. Lam, *Bioorg. Med. Chem. Lett.*, **16**, 3755 (2006).
3. D. B. Nilov, A. V. Kadushkin, N. P. Solov'eva, Yu. N. Sheinker, and V. G. Granik, *Khim. Geterotsikl. Soedin.*, 113 (2004). [*Chem. Heterocycl. Compd.*, **40**, 106 (2004).]
4. B. S. Drach, E. P. Sviridov, A. A. Kisilenko, and A. V. Kirsanov, *Zh. Org. Khim.*, **9**, 1818 (1973).