Design of fused systems based on σ^H-adducts of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine with π-excessive heteroaromatic compounds

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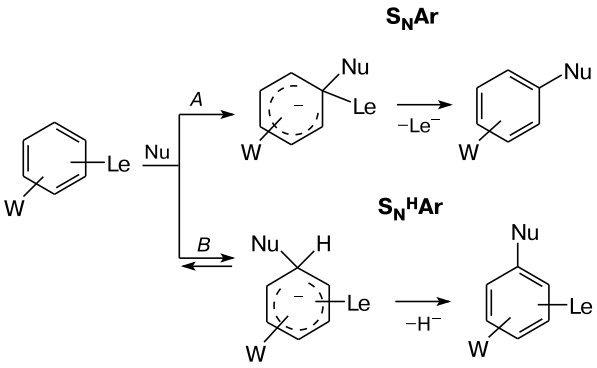
A new method was developed for the construction of tetra- and pentacyclic fused systems based on σ^H-adducts of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine with π-excessive heteroaromatic compounds. The method involves the reduction of the nitro group accompanied by the aromatization of the dihydropyrimidine ring and followed by the cyclocondensation of the amino derivative with aldehydes.

Key words: 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine, σ^H-adducts, nitro group reduction, aromatization.

Main methods of chemical modifications of π-deficient arenes and hetarenes, which are used also for the construction of fused systems, involve the nucleophilic substitution reactions of good leaving groups Le = Hal, NR_2, OR, OSO_2R, *etc*. (Scheme 1, path *A*). One of limitations of the S_NAr reactions (more precisely, $S_N^{ipso}Ar$) is that it is necessary to introduce a good leaving group Le into the substrate molecule for this reaction to occur.

In the last decades, the reactions based on the direct nucleophilic attack on the unsubstituted carbon atom C_{sp^2}—H of the (hetero)aromatic ring were actively developed as the individual synthetic methodology.[1—3] These reactions are usually completed with the substitution of hydrogen (S_N^H reactions) or are stopped at the step of formation of σ^H-adducts (A_N reactions) (Scheme 1).

Scheme 1



W is an electron-withdrawing group, Le is a good leaving group, and Nu is a nucleophilic reagent.

σ^H-Adducts essentially differ in the stability. Thus, both unstable adducts, which are spectroscopically detected only at low temperatures and which readily undergo aromatization, and very stable preparatively isolated compounds are known. Among the latter are, in particular, C-adducts of nitro derivatives of azoloazines **6—10** (Scheme 2).[3—6] Attempts to transform these dihydro compounds into aromatic systems under the action of classical hydride acceptors, such as oxygen, dichlorodicyanobenzoquinone, triphenylmethyl tetrafluoroborate, *etc*., failed. The use of stronger oxidizing agents (for example, potassium permanganate) leads to the destruction of the molecule.

Previously, we have briefly reported[4,5] on the unusual aromatization of σ^H-adducts **6** under reducing conditions (sodium dithionite, tin chloride, iron hydroxide, catalytic hydrogenation). The reduction of the nitro group is accompanied by the unexpected, on the first glance, dehydrogenation of the dihydropyrimidine ring. This provides an approach to S_N^H products **11—15** not through the conventional oxidation of the dihydropyrimidine moiety to the pyrimidine moiety followed by the transformation of the nitro group into the amino group but through the concerted process, which apparently involves the elimination of water from the intermediate **A** (Scheme 3).

This seemingly paradoxical reductive dehydrogenation has a general character and can be used for particular synthetic purposes. The vicinal arrangement of the amino group and π-excessive heterocycles opens new possibili-

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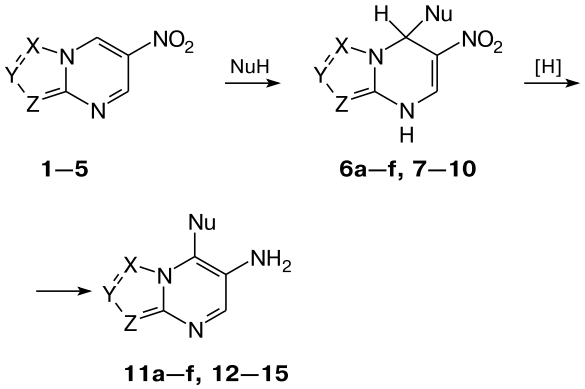
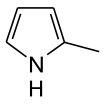
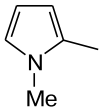
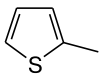
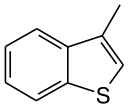
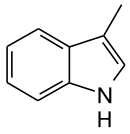
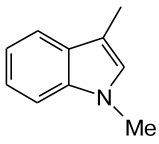
Scheme 2



Compound	X	Y	Z
1	N	CH	N
2	N	N	N
3	N	C—SMe	N
4	N	CH	C—COOEt
5	C—CN	C—CN	N
6a—f, 11a—f	N	CH	N
7, 12	N	N	N
8, 13	N	C—SMe	N
9, 14	N	CH	C—COOEt
10, 15	C—CN	C—CN	N

Nu =  (**6a**, **11a**),  (**6b**, **11b**),  (**6c**, **11c**),  (**6d**, **11d**),  (**6e**, **7—10**, **11e**, **12—15**),  (**6f**, **11f**)

ties for the cyclization, the annulation, and the design of polycyclic systems. In particular, amines **11—15** have prerequisites for the construction of tetra- and pentacyclic heterosystems because they contain several nucleophilic centers (the amino group and the carbon atoms of the π-excessive heterocycle) and can be involved in reactions with various electrophilic agents.

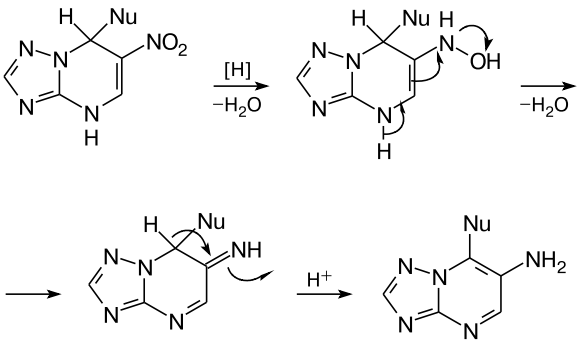
The aim of the present study was to develop the above-mentioned synthetic potential and to use it for the design of fused heterocyclic systems based on aromatic aminopyrimidines **11—15** containing fragments of π-excessive heteroaromatic compounds by the reactions with aldehydes. As a continuation of the research on the reductive dehydrogenation of compounds **6**,[4] we studied a series of σ^H-adducts **7—10**. These dihydro compounds are formed in high yields as stable bright-colored crystalline substances. It was found that, regardless of the structure of the azole moiety of the molecules, the reduction of the nitro group in adducts **6—10** is accompanied by the aromatization of the pyrimidine ring (see Scheme 2, Tables 1 and 2).

Thus, the reduction of the nitro group in adducts **6—10** with sodium dithionite in aqueous ammonia affords 6-amino-7-hetarylazolo[1,5-*a*]pyrimidines **11—15**. The acid-catalyzed condensation of amine **11a** containing the pyrrole moiety with aldehydes is not stopped at the formation of azomethine and proceeds further to give tetracyclic system **16** as the final product. In the case of amine **11b** containing the *N*-methylpyrrole moiety, compound **17** was chromatographically detected. However, in the course of isolation, the dihydropyridine fragment is oxidized by atmospheric oxygen to give aromatic products **18a—c** (Scheme 4). The structures of the latter products were confirmed by the ^{1}H NMR spectra of compounds **16** and **17** (see the Experimental section) and by the X-ray diffraction data for compound **16a** (Fig. 1).

Amine **11c** containing the thiophene moiety does not undergo heterocyclization; the reaction with benzaldehyde is stopped at the formation of the corresponding azomethine **19**.

Some of compounds synthesized according to the above-described scheme can be of interest for biological tests, because these compounds are structurally similar to alkaloids, and azepinoindole derivatives are known to serve as ligands of dopamine receptors.[7]

Scheme 3



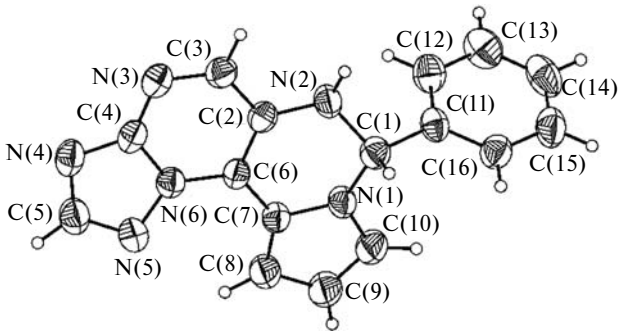
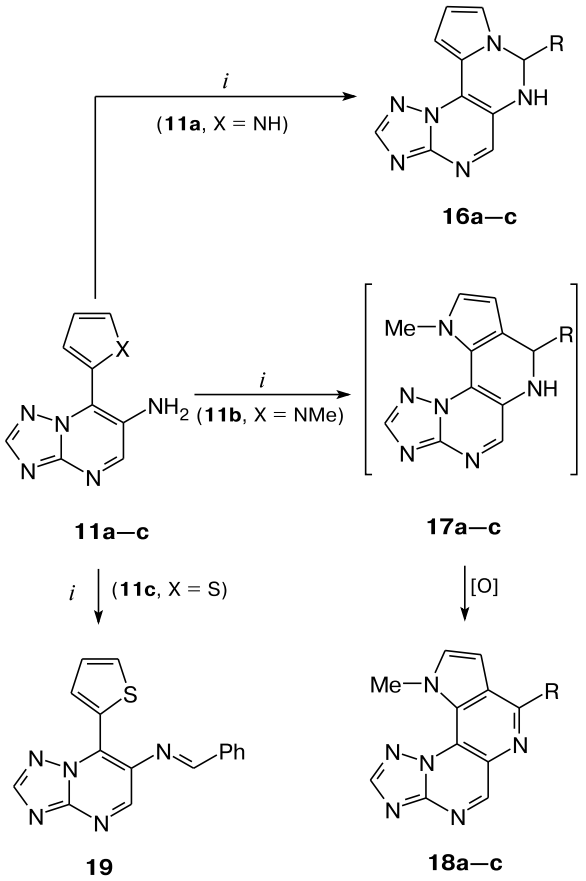


Fig. 1. Molecular structure of **16a**. Displacement ellipsoids are drawn at the probability level $p = 50\%$.

Table 1. ^{1}H NMR spectra (DMSO-d_6)

Compound	δ (*J*/Hz)
7	12.40 (s, 1 H, NH); 11.23 (s, 1 H, NH); 8.50 (s, 1 H, C(5)H); 7.50 (d, 1 H, *J* = 2.8); 7.37—7.29 (m, 3 H, C(7)H, Ar); 7.09—7.06 (m, 1 H); 7.00—6.97 (m, 1 H)
8	12.42 (s, 1 H, NH); 11.20 (s, 1 H, NH); 8.51 (s, 1 H, C(5)H); 7.54 (d, 1 H, *J* = 2.8); 7.36—7.29 (m, 3 H, C(7)H, Ar); 7.04—7.02 (m, 1 H); 7.00—6.96 (m, 1 H); 2.36 (s, 3 H, CH_3)
9	11.21 (s, NH); 10.89 (s, NH); 8.26 (s, 1 H, C(5)H); 7.12 (s, 1 H, C(2)H); 7.49 (d, 1 H, CH, *J* = 2.8); 7.36—7.30 (m, 2 H, Ar); 7.09—7.05 (m, 1 H, Ar); 6.99—6.95 (m, 1 H, Ar); 6.91 (s, 1 H, C(7)H); 4.30—4.25 (q, 2 H, CH_2, *J* = 7.0); 1.28 (t, 3 H, CH_3, *J* = 7.1)
10	12.43 (s, 1 H, NH); 11.35 (s, 1 H, NH); 8.44 (s, 1 H, C(5)H); 7.59 (d, 1 H, *J* = 2.8); 7.39 (d, 1 H, *J* = 8); 7.14—7.06 (m, 3 H, C(7)H, Ar); 6.98—6.94 (m, 1 H)
12	12.10 (s, 1 H, NH); 8.67 (s, 1 H, C(5)H); 8.60—8.58 (m, 1 H); 8.56 (d, 1 H, *J* = 2.8); 7.57 (m, 1 H); 7.31—7.25 (m, 2 H); 5.66 (s, 2 H, NH_2)
13	11.93 (s, 1 H, NH); 8.54 (s, 1 H, C(5)H); 8.05 (d, 1 H, *J* = 2.8); 7.53 (d, 1 H, *J* = 8); 7.21—7.17 (m, 1 H); 7.10—7.06 (m, 1 H, Ar); 5.04 (s, 2 H, NH_2); 2.55 (s, 3 H, CH_3)
14	11.89 (s, 1 H, NH); 8.60 (s, 1 H, C(5)H); 8.29 (s, 1 H, C(2)H); 7.97 (d, 1 H, *J* = 2.8); 7.53 (d, 1 H, Ar, *J* = 8); 7.25—7.18 (m, 2 H, Ar); 7.08—7.04 (m, 1 H, Ar); 5.12 (s, 2 H, NH_2); 4.30—4.25 (q, 2 H, CH_2, *J* = 7.1); 1.31 (t, 3 H, CH_3, *J* = 7.1)
15	11.94 (s, 1 H, NH); 8.72 (s, 1 H, C(5)H); 7.84 (d, 1 H, *J* = 2.8); 7.55 (d, 1 H, Ar, *J* = 8); 7.26—7.21 (m, 2 H, Ar); 7.08—7.05 (m, 1 H, Ar); 5.48 (s, 2 H, NH_2)
16a	8.58 (s, 1 H, C(5)H); 8.53 (s, 1 H, C(2)H); 7.51—7.46 (m, 2 H, Ph); 7.42—7.40 (m, 3 H, Ph); 7.33—7.30 (two dd, 2 H, pyrrol, J_1 = 3.8, J_2 = 1.5); 6.96—6.73 (dd, 1 H, pyrrol, J_1 = 3, J_2 = 1.5); 6.72 (d, 1 H, NH, *J* = 2); 6.49—6.48 (dd, 1 H, C(7)H, J_1 = 3.8, J_2 = 2.5)
16b	8.55 (s, 1 H, C(5)H); 8.52 (s, 1 H, C(2)H); 7.37—7.32 (two dd, 2 H, pyrrol, J_1 = 3.8, J_2 = 1.5); 6.86 (d, 1 H, NH, *J* = 2); 6.46—6.44 (dd, 1 H, pyrrol, J_1 = 3.8, J_2 = 2); 5.62—5.60 (dt, 1 H, C(7)H, J_1 = 5.8, J_2 =3.2); 1.86—1.83 (m, 2 H, CH_2); 1.23—0.88 (m, 10H); 0.78 (t, 3 H, CH_3, *J* = 6.7)
16c	8.69 (s, 1 H, C(5)H); 8.55 (s, 1 H, C(2)H); 7.38—7.36 (two dd, 2 H, pyrrol, J_1 = 3.8, J_2 = 1.5); 6.48—6.46 (dd, 1 H, pyrrol, J_1 = 3.8, J_2 = 1.4); 5.64 (t, 1 H, C(7)H, *J* = 5.8); 1.86—1.83 (m, 2 H, CH_2); 1.26—1.17 (m, 16 H); 0.84 (t, 3 H, CH_3, *J* = 6.7)
18a	9.54 (s, 1 H, C(5)H); 8.78 (s, 1 H, C(2)H); 8.04—8.01 (m, 3 H, pyrrol, Ph); 7.65—7.59 (m, 3 H, Ph); 7.10 (d, 1 H, pyrrol, *J* = 2.8); 4.72 (s, 3 H, CH_3)
18b	9.45 (s, 1 H, C(5)H); 8.75 (s, 1 H, C(2)H); 7.96 (d, 1 H, pyrrol, *J* = 2.8); 7.13 (d, 1 H, pyrrol, *J* = 2.8); 4.69 (s, 3 H, CH_3), 3.19 (t, 2 H, CH_2, *J* = 7.6); 1.88—1.84 (m, 2 H, CH_2); 1.41—1.15 (m, 10 H); 0.85 (t, 3 H, CH_3, *J* = 6.9)
18c	9.44 (s, 1 H, C(5)H); 8.75 (s, 1 H, C(2)H); 7.93 (d, 1 H, pyrrol, *J* = 2.8); 7.14 (d, 1 H, pyrrol, *J* = 2.8); 4.66 (s, 3 H, CH_3), 3.20 (t, 2 H, CH_2, *J* = 7.0); 1.87—1.84 (m, 2 H, CH_2); 1.43—1.15 (m, 10 H); 0.83 (t, 3 H, CH_3, *J* = 6.8)
19	9.07—9.06 (m, 1 H, thiophene); 9.05 (s, 1 H, CH); 9.03 (s, 1 H, C(5)H); 8.82 (s, 1 H, C(2)H); 8.25—8.23 (dd, 1 H, thiophene, J_1 = 5.1, J_2 = 1.2); 8.14—8.12 (m, 2 H, Ph); 7.66—7.63 (m, 3 H, Ph); 7.46—7.44 (m, 1 H, thiophene)
21a	12.39 (s, NH); 9.16 (d, 1 H, C(1)H, *J* = 2.8); 8.57 (s, 1 H, C(8)H); 8.53 (s, C(11)H); 7.54 (d, 1 H, Ar, *J* = 8); 7.23—7.20 (m, 1 H, Ar); 7.14—7.10 (m, 2 H, Ar); 7.06—6.97 (m, 1 H, Ar); 6.92 (d, 2 H, Ar, *J* = 7.4); 5.76 (s, 1 H, C(6)H)
21b	9.15 (s, 1 H, C(1)H); 8.57 (s, 1 H, C(8)H); 8.54 (s, 1 H, C(11)H); 7.63 (d, 1 H, Ar, *J* = 8); 7.35—7.31 (m, 1 H, Ar); 7.15— 7.11 (m, 2 H, Ar); 7.09—7.03 (m, 1 H, Ar); 6.93 (d, 2 H, Ar, *J* = 7.4); 5.84 (s, 1 H, C(6)H), 4.08 (s, 3 H, CH_3)
21c	12.42 (s, 1 H, NH); 9.18 (d, 1 H, C(1)H, *J* = 3.0); 8.74 (s, 1 H, C(8)H); 8.73 (s, 1 H, C(11)H); 7.47—7.45 (m, 1 H, Ar); 7.20—7.16 (m, 1 H, Ar); 6.99—6.97 (m, 1 H, Ar); 4.53 (t, 1 H, C(6)H, *J* = 6.4); 1.39—1.17 (m, 12 H); 0.81 (t, 3 H, CH_3, *J* = 6.8)
21d	12.43 (s, 1 H, NH); 9.16 (d, 1 H, C(1)H, *J* = 3.0); 8.77 (s, 1 H, C(8)H); 8.71 (s, 1 H, C(11)H); 7.48—7.47 (m, 1 H, Ar); 7.23—7.19 (m, 1 H, Ar); 7.04—7.02 (m, 1 H, Ar); 4.54 (t, 1 H, C(6)H, *J* = 6.4); 1.57—1.13 (m, 14 H); 0.80 (t, 3 H, CH_3, *J* = 6.8)
21e	12.50 (s, 1 H, NH); 9.19 (d, 1 H, C(1)H, *J* = 3.0); 8.79 (s, 1 H, C(8)H); 8.78 (s, 1 H, C(11)H); 7.49—7.47 (m, 1 H, Ar); 7.21—7.17 (m, 1 H, Ar); 7.00— 6.99 (m, 1 H, Ar); 4.57 (t, 1 H, C(6)H, *J* = 6.5); 1.39—1.31 (m, 2 H, CH_2); 1.24—1.06 (m, 16 H); 0.84 (t, 3 H, CH_3, *J* = 6.8)
21f	12.38 (s, 1 H, NH); 9.16 (d, 1 H, C(1)H, *J* = 3.0); 8.72 (s, 1 H, C(8)H); 8.68 (s, 1 H, C(11)H); 7.48—7.46 (m, 1 H, Ar); 7.22—7.18 (m, 1 H, Ar); 7.03—7.01 (m, 1 H, Ar); 4.52 (t, 1 H, C(6)H, *J* = 6.4); 1.27—1.13 (m, 14 H); 0.83 (t, 3 H, CH_3, *J* = 6.8)

Scheme 4



i. RCHO/HCl. **16—18**: Ph (**a**), C_7H_{15} (**b**), $C_{11}H_{23}$ (**c**)

The condensation of aminotriazolopyrimidines **11e,f** with aldehydes (Scheme 5) in aprotic solvents affords the corresponding azomethines capable of forming fused structures **21** and **22.**

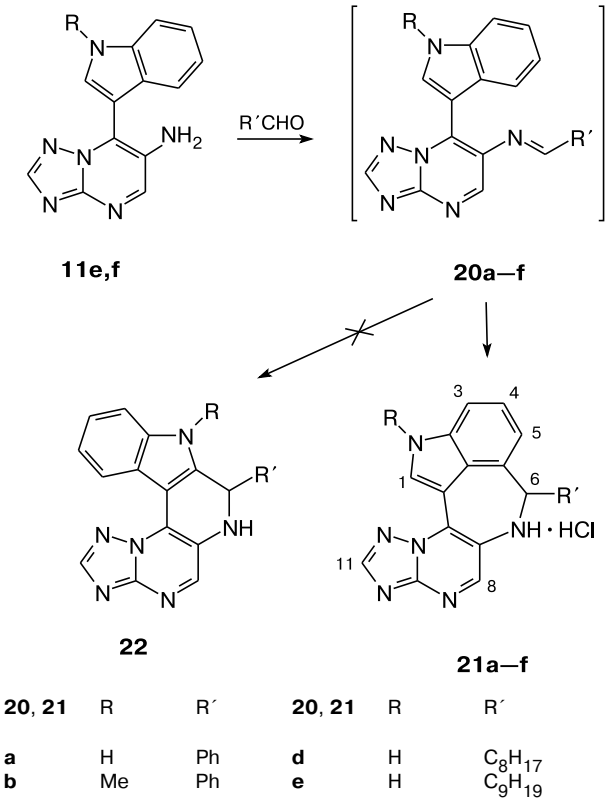
It was found that the heterocyclization of **11e,f** with aldehydes in an acidic medium occurs with the involvement of the benzene ring of indole rather than at position 2 of the pyrrole ring and affords the only product, *viz.*, 6-R-1,2,4-triazolo[1″,2″: 1,2]pyrimido[6′,5′:6,7]-azepino[5,4,3-*cd*]indole **(21)**. This is confirmed by the fact that the ^{1}H NMR spectra show a one-proton signal for the atom H(1) (δ = 9.15—9.16), which appears as a singlet or a doublet depending on the nature of the substituent (R = CH_3 or H, respectively). In addition, the ^{1}H NMR spectra show a singlet for H(6), signals of the three-spin system of the indole moiety, and signals for aromatic protons. An alternative structure **22** can be rejected because it is inconsistent with the ^{1}H NMR spectra. In addition, compound **21d** was studied by X-ray diffraction (Fig. 2).

To sum up, let us note that the nitro group plays a key role in the above-considered method for the design of fused systems. The nitro group activates the heterocycle for the nucleophilic attack and stabilizes σ^H-adducts, and the reduction of the nitro group results in the initiation of the aromatization of the ring apparently through the intermediate formation of hydroxylamine **A**.[4] Finally, the transformation of the nitro group into the amino group provides structural prerequisites for cyclocondensation reactions.

Table 2. Melting points, yields, and elemental analysis data

Compound	Yield (%)	M.p. /°C	Found / Calculated			Molecular formula
			C	H	N	
7	70	208—210	50.87 / 50.89	3.18 / 3.20	34.65 / 34.61	$C_{12}H_9N_7O_2$
8	85	146—148	51.20 / 51.21	3.66 / 3.68	25.62 / 25.59	$C_{14}H_{12}N_6O_2S$
9	87	238—240	57.79 / 57.79	4.30 / 4.28	19.83 / 19.82	$C_{17}H_{15}N_5O_4$
10	84	232—234	58.03 / 58.01	2.74 / 2.74	29.57 / 29.59	$C_{16}H_9N_7O_2$
12	49	216—218	57.35 / 57.37	3.60 / 3.61	39.00 / 39.02	$C_{12}H_9N_7$
13	44	188—190	56.77 / 56.74	4.10 / 4.08	28.32 / 28.36	$C_{14}H_{12}N_6S$
14	66	>300	63.50 / 63.54	4.70 / 4.71	21.82 / 21.79	$Cl_7H_{15}N_5O_2$
15	68	230—232	64.24 / 64.21	3.00 / 3.03	32.77 / 32.76	$C_{16}H_9N_7$
16a	69	221—223	66.60 / 66.66	4.17 / 4.20	29.17 / 29.15	$C_{16}H_{12}N_6$
16b	40	Oil	65.72 / 65.78	7.15 / 7.14	27.10 / 27.07	$C_{17}H_{22}N_6$
16c	55	112—114	68.85 / 68.82	8.27 / 8.25	22.96 / 22.93	$C_{21}H_{30}N_6$
18a	50	256—258	67.97 / 67.99	4.00 / 4.03	27.97 / 27.98	$C_{17}H_{12}N_6$
18b	49	161—162	67.07 / 67.06	6.90 / 6.88	26.06 / 26.07	$C_{18}H_{22}N_6$
18c	51	122—124	69.79 / 69.81	7.98 / 7.99	22.21 / 22.20	$C_{22}H_{30}N_6$
19	61	198—200	62.92 / 62.93	3.64 / 3.63	22.93 / 22.93	$C_{16}H_{11}N_5S$
21a	60	262—264	64.07 / 64.09	4.04 / 4.03	22.40 / 22.42	$C_{20}H_{14}N_6$ · HCl
21b	78	232—234	64.88 / 64.86	4.41 / 4.41	21.62 / 21.61	$C_{21}H_{16}N_6$ · HCl
21c	62	162—164	63.54 / 63.55	6.33 / 6.35	21.18 / 21.17	$C_{21}H_{24}N_6$ · HCl
21d	65	168—170	64.33 / 64.30	6.60 / 6.62	20.46 / 20.45	$C_{22}H_{26}N_6$ · HCl
21e	70	195—197	64.99 / 65.00	6.87 / 6.88	19.77 / 19.78	$C_{23}H_{28}N_6$ · HCl
21f	58	123—125	65.66 / 65.66	7.10 / 7.12	19.13 / 19.14	$C_{24}H_{30}N_6$ · HCl

Scheme 5



20, 21	R	R′	20, 21	R	R′
a	H	Ph	**d**	H	C_8H_{17}
b	Me	Ph	**e**	H	C_9H_{19}

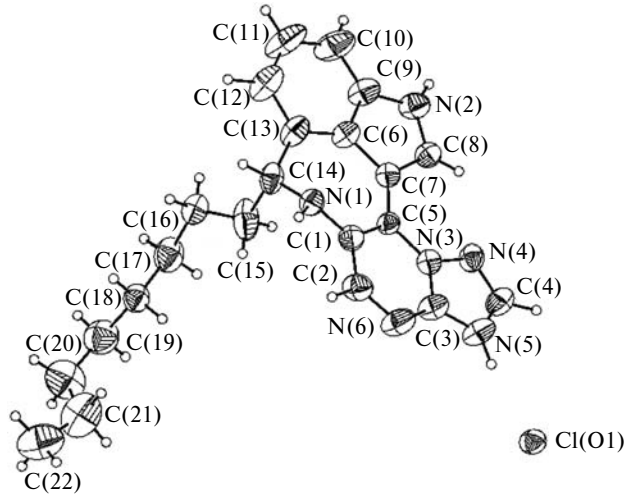


Fig. 2. Molecular structure of **21d**. Displacement ellipsoids are shown at the probability level $p = 50\%$. The disorder of the alkyl fragment (see the Experimental section) is not shown.

Experimental

The course of the reactions was monitored and the purity of the reaction products was checked by TLC on plates with a fixed Sorbfil layer using a 9 : 1 chloroform—methanol mixture as the eluent; spots were visualized by UV irradiation. The ^{1}H NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 MHz) in [$^2H_6$]DMSO with Me_4Si as the internal standard. The elemental analysis was carried out on an automated Carlo Erba 1108 CHNO analyzer. The melting points were determined on combined Boetius hot stages and are uncorrected.

The results of the X-ray diffraction studies of compounds **16a** and **21d** were deposited with the Cambridge Crystallographic Data Centre* (CCDC 731801 for **21d** and 731802 for **16a**).

Synthesis of 7-(indol-2-yl)-6-nitro-4,7-dihydroazolo-[1,5-*a*]pyrimidines 7—10 (general method). The corresponding 6-nitroazolo[1,5-*a*]pyrimidine (1 mmol) and indole (1 mmol) were refluxed in acetonitrile (3 mL). The solution was cooled, and the product that precipitated was separated by filtration and twice washed with diethyl ether.

Synthesis of 6-amino-7-(indol-2-yl)azolo[1,5-*a*]pyrimidines 12—15 (general method). Sodium dithionite (6 mmol) was added with stirring to a solution of the corresponding adduct **7—10** (1 mmol) in aqueous ammonia (3—5 mL). The reaction mixture was kept at 60—70°C for 30 min and then at room temperature for 3—5 h. The product that precipitated was separated by filtration, washed with water, and crystallized from ethanol.

Synthesis of 7-R-6,7-dihydropyrrolo[1,2-*c*]-1,2,4-triazolo-[5′,1′:2,3]pyrimido[4,5-*e*]pyrimidines (16a—c) (general method). Equivalent amounts of amine **11a** and the corresponding aldehyde were refluxed for 30 min in a 2 *M* HCl—EtOH mixture (1 : 4). The reaction mixture was applied on silica gel, and the product was isolated by column chromatography in a chloroform : methanol system (30 : 1) (R_f = 0.8—0.9).

Synthesis of 7-substituted 10-methylpyrrolo[2′,3′:4,5]-pyrido[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidines (18a—c) (general method). Equivalent amounts of amine **11b** and the corresponding aldehyde were refluxed for 30 min in a 2 *M* HCl—EtOH mixture (1 : 4). The reaction mixture was applied on silica gel, and the product was isolated by column chromatography in a chloroform : methanol system (30 : 1) (R_f = 0.8—0.9).

6-Benzylideneamino-7-(thiopen-2-yl)-1,2,4-triazolo[1,5-a]pyrimidine (19). Amine **11c** (0.5 mmol) and benzaldehyde (0.5 mmol) were refluxed in a 2 *M* HCl—EtOH mixture (1 : 4, 5 mL) for 30 min. Then the solution was cooled. The product that precipitated was separated by filtration, washed with ethanol, and dried in a vacuum desiccator.

Synthesis of 2-R-6-R′-1,2,4-triazolo[1″,2″:1,2]pyrimido-[6′,5′:6,7]azepino[5,4,3-*cd*]indoles (21a—f) (general method). Equivalent amounts of amine **11e** or **11f** and the corresponding aldehyde were refluxed for 30 min in a 2 *M* HCl—EtOH mixture (2 : 1). The precipitate that formed after cooling was washed with water, crystallized from aqueous ethanol, and dried *in vacuo*.

Crystallographic data for compounds 16a and 21d. Single crystals of compounds **16a** and **21d** were grown by crystallization from EtOH. The X-ray diffraction data were collected on a Xcalibur 3 diffractometer equipped with a CCD detector (λ(MoKα) = 0.71073, graphite monochromator, ω- and φ-scanning technique, T = 295 K). The structure was solved by direct methods with the use of the SHELXS-97 program package and refined by the full-matrix least-squares method first isotropically and then anisotropically using the SHELXL-97 program package. The hydrogen atoms were located in difference electron density maps and refined using a riding model.

* These data can be obtained, free of charge, on application to www.ccdc.cam.ac.uk/data_request/cif.

Table 3. X-ray data collection and structure refinement statistics

Parameter	**21d**	**16a**
Molecular formula	$C_{22}H_{27}ClN_6$	$C_{16}H_{12}N_6$
Molecular weight	410.95	288.32
Crystal system	Rhombohedral	Orthorhombic
Space group	*R*-3	*Pbca*
a/Å	31.253(4)	7.5474(15)
b/Å	31.253(4)	14.308(3)
c/Å	11.2903(14)	24.448(4)
α/deg	90.00	90.00
β/deg	90.00	90.00
γ/deg	120.00	90.00
V/Å^3	9550(2)	2640.1(8)
Z	18	8
d_{calc}/g cm^{-3}	1.286	1.451
μ/ mm^{-1}	0.201	0.094
Scanning range	$26.39 \geq \theta \geq 2.69$	$26.37 \geq \theta \geq 2.97$
Number of measured reflections (R_{int})	4178 0	2652 0.0511
Number of reflections with $I > 2\sigma(I)$	2178	1409
Number of refined parameters	384	203
R_1 (based on reflections with $I > 2\sigma(I)$)	0.0581	0.0508
wR_2 (based on reflections) with $I > 2\sigma(I)$	0.1571	0.1035
R_1 (based on all reflections)	0.1236	0.1009
wR_2 (based on all reflections)	0.1739	0.1168

In molecule **21d**, the alkyl fragment is disordered over three sites with occupancies of 0.4, 0.3, and 0.3.

The X-ray data collection and structure refinement statistics are given in Table 3.

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