Nucleophilic ring-opening of the azole and azine moieties in 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones*

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The effects of the nature of the nucleophile and the structure of 6-nitrotriazolo[1,5-*a*]pyrimidinones on the direction of the ring opening were investigated. The triazole ring is opened under the action of strong bases, such as alkoxides or alkalis, to form 2-cyanoaminopyrimidinones and then 2-aminopyrimidinones. The results of the reactions with N-nucleophiles depend on the accessibility of position 5 of the heterocycle. Thus, sterically hindered secondary amines react with 5-methyltriazolopyrimidinones to give 2-guanidinopyrimidinones and then 2-aminopyrimidinones. In the absence of a substituent at position 5, the azine ring is opened to form 4-alkyl-3-amino-1,2,4-triazoles and 3-amino-2-nitroacrylamides. Under the action of primary amines, only the pyrimidine fragment is cleaved.

Key words: 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones, 3-amino-1,2,4-triazoles, 3-amino-2-nitrocrotonamide, 3-amino-2-nitroacrylamides, *N*-alkyl-*N*-hetarylcyanamides, 2-alkylamino-4-methyl-5-nitropyrimidin-7-ones, ring opening, nucleophiles.

Azaindolizines are characterized by the ability to undergo ring opening of their azine or azole moieties under the action of nucleophiles. The major regularities of these processes were successfully generalized in the context of consonant and dissonant series in heterocyclic systems.[1,2] However, this concept does not reflect the effects of the nature of the nucleophile and its structure on the direction of the reaction. To reveal the characteristic features of the nucleophilic scission of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones, we studied the reactions of these heterocycles with C-, O-, and N-nucleophiles, which was of interest from the viewpoint of simulation of the reactivity and investigation of the metabolism of azaindolizines among which biologically active compounds have been found.[3]

Results and Discussion

Reactions with O-nucleophiles. The reactions of 3-alkyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (**1a—d**) with magnesium methoxide afforded *N*-alkyl-*N*-(4-methyl-5-nitro-6-oxopyrimidin-2-yl)cyanamides (**2a—d**) (Scheme 1). By analogy with the scission of 5-chloro-3-(β-D-ribofuranosyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one,[1,4] it can be assumed that the destruction of the azole fragment involves the formation of anion **A**,[1,2,5] which is isomerized to cyanamide **2**.

Heating of triazolopyrimidinones **1a—d** with ethanolic alkali afforded two types of products, *viz.*, cyanamides **2** and 2-(alkylamino)-4-methyl-5-nitro-1,6-dihydropyrimidin-6-ones (**3a—d**), the ratio between these products depending on the reaction time. Thus, the **2** : **3** ratio was 1 : 1 after 30 min, whereas aminopyrimidinones **3a—d** were obtained exclusively after 2 h. Apparently, the first stage of the reaction yielded cyanamide **2**, which was then converted into product **3**.

The IR spectra of compounds **2** have intense absorption bands corresponding to stretching vibrations of the CN group (Table 1) and stretching vibration bands of the $—NO_2$ and —CO groups. The data from mass spectrometry indicate that the molecular masses of triazolopyrimidines **1** are identical to those of cyanides **2**. Stretching vibration bands of the $—NO_2$ and —CO groups and of the secondary amine fragment can be identified in the IR spectra of compounds **3**.

In the ^{1}H NMR spectra of aminopyrimidinones **3**, the resonance signals of the NCH_2 fragment of the R^1 substituents are observed at higher field than those in the spectra of compounds **1** and **2** (δ 3.2—3.5 as opposed to δ 4.0—4.2, see Table 1). The NMR spectra also have three-proton singlet signals belonging to the *C*-methyl groups and broadened signals of the NH groups.

Reactions with CH-active compounds. The reactions of 3-alkyl-1,2,4-triazolo[1,5-*a*]pyrimidinones **1** with nitromethane, ethyl acetoacetate, or ethyl cyanoacetate in the presence of acid catalysts did not proceed even on heating. However, the reactions with the use of sodium derivatives of cyanoacetic or acetoacetic esters afforded cyanamides **2** (see Scheme 1).

Reactions with amines. We have surveyed the selected aspects of conversions of triazolopyrimidinones **1**

* Dedicated to Prof. H. Neunhoeffer on the occasion of his 65th birthday.

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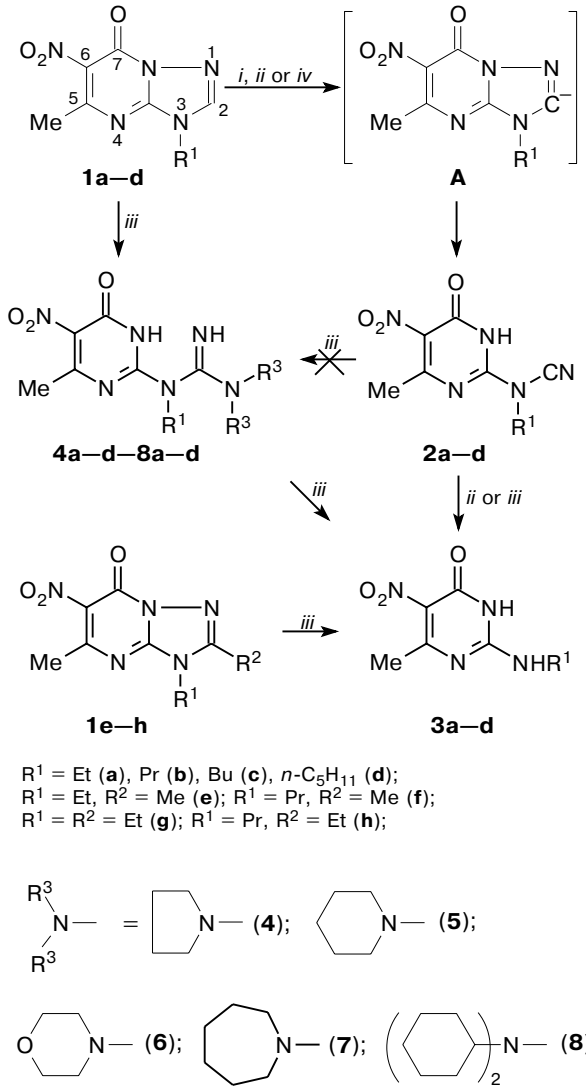
Scheme 1



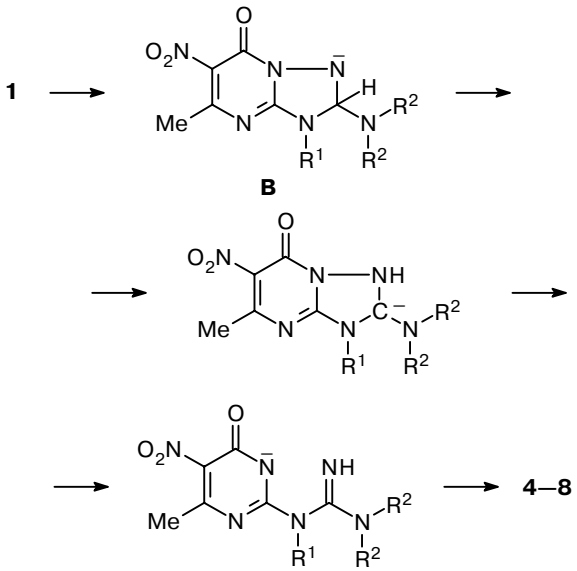
R^1 = Et (**a**), Pr (**b**), Bu (**c**), n-C_5H_{11} (**d**);
R^1 = Et, R^2 = Me (**e**); R^1 = Pr, R^2 = Me (**f**);
$R^1 = R^2$ = Et (**g**); R^1 = Pr, R^2 = Et (**h**);

Regents and conditions: *i*. $(MeO)_2Mg$, MeOH; *ii*. NaOH, EtOH, Δ; *iii*. $R^3{}_2NH$, Δ; *iv*. Na, $NCCH_2COOEt$, or $AcCH_2COOEt$.

under the action of amines in a brief communication.[6] In the present study, we examined this type of reactions in more detail. Heating of 3-alkyl-1,2,4-triazolo[1,5-*a*]pyrimidinones **1a—d** with secondary amines for 30 min afforded 1-alkyl-1-(4-methyl-5-nitro-6-oxo-1,6-dihydropyrimidin-2-yl)guanidines (**4—8**), which were converted into aminopyrimidinones **3a—d** upon further heating (see Scheme 1). The identity of products **3** obtained through different paths (*ii* and *iii*) was proved by comparing their spectral characteristics and physicochemical properties. The ^1H NMR spectra of compounds **4—8** have signals of the alkyl fragment, the methyl group of the pyrimidine ring, and the secondary amino group (see Table 1) and are in complete agreement with the proposed structures.

It can be assumed that the formation of products **4—8**, like the reactions with alkoxides and alkalis, proceeds through cyanamides **2**. However, treatment of compounds **2** with secondary amines both at room temperature and on heating gave rise to aminopyrimidinones **3** rather than to guanidines **4—8**. Therefore, the involvement of compound **2** in the formation of products **4—8** is unlikely and it is possible that conversions proceed according to another mechanism. Apparently, the low basicity of the amine prevents the formation of the anion of the type **A** and the reaction proceeds through the nucleophilic addition at C(2) to form adduct **B** followed by its transformation into pyrimidinylguanidines **4—8** (Scheme 2).

Scheme 2



With the aim of elucidating the mechanism of the azine ring-opening, we studied the reactions of 2,3-dialkyl-1,2,4-triazolopyrimidinones **1e—h** with secondary amines. We believed that the results of the reactions of this type should be unambiguous because it was stated that opening of the *C*-alkyl-substituted azole ring cannot occur in compounds of this group.[1] However, we obtained amines **3a—d** (see Scheme 1) instead of acyclic products although heating was more prolonged than that in the case of compounds **1a—d**. Such decrease in the reactivity can be explained by steric hindrances provided that an adduct of the type **B** is formed (see Scheme 2). However, the triazole ring-opening remains the only direction of the reaction.

The direction of the nucleophilic attack changes if the *C*-methyl group is removed from the pyrimidine ring. In the reaction of 3-ethyl-6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one (**9**) with pyrrolidine, only the azine ring was opened to form 2-nitro-3-pyrrolidinoacrylopyrrolidide (**10**) and 3-amino-4-ethyl-1,2,4-triazole (**11a**) (Scheme 3). The spectral characteristics and physi-

Table 1. Data from mass spectrometry and IR and ^{1}H NMR spectroscopy of the synthesized compounds

Compound	m/z (I_{rel} (%))	IR, ν/cm^{-1}	^{1}H NMR, δ
2a	197 (4), 97 (28), 70 (13), 55 (100)	1320, 1510 (NO_2); 1620 (CO); 2280 (CN)	1.23 (t, 3 H); 2.12 (s, 3 H); 4.10 (q, 2 H); 9.53 (br.s, 1 H)
2b	197 (16), 183 (100), 137 (28), 109 (13), 55 (31)	1320, 1520 (NO_2); 1620 (CO); 2270 (CN)	0.92 (t, 3 H); 1.41 (qt, 2 H); 2.12 (s, 3 H); 4.10 (t, 2 H); 10.30 (br.s, 1 H)
2c	209 (51), 183 (100), 137 (30), 109 (11), 55 (31)	1310, 1520 (NO_2); 1610 (CO); 2270 (CN)	0.91 (t, 3 H); 1.32 (qt, 2 H); 1.61 (tt, 2 H); 2.11 (s, 3 H); 4.08 (t, 2 H); 10.65 (br.s, 1 H)
2d	223 (54), 197 (15), 183 (100), 137 (29), 109 (13), 67 (23), 55 (25)	1320, 1520 (NO_2); 1610 (CO); 2280 (CN)	0.88 (t, 3 H); 1.00—2.00 (m, 6 H); 2.20 (s, 3 H); 4.06 (t, 2 H); 10.10 (br.s, 1 H)
3a	198 $[M]^+$ (11), 181 (93), 183 (100), 170 (27), 166 (15), 137 (78), 109 (26), 69 (56), 55 (54)	1320, 1510 (NO_2); 1680 (CO); 1250, 3280 (NH)	1.18 (t, 3 H); 2.28 (s, 3 H); 3.20—3.50 (m, 2 H); 7.33 (br.s, 1 H); 11.43 (br.s, 1 H)
3b	212 $[M]^+$ (14), 195 (85), 183 (100), 170 (18), 166 (22), 137 (58), 109 (32), 69 (39), 55 (48)	1310, 1500 (NO_2); 1680 (CO); 1260, 3300 (NH)	0.92 (t, 3 H); 1.30—1.55 (m, 2 H); 2.28 (s, 3 H); 3.20—3.40 (m, 2 H); 7.28 (br.s, 1 H); 11.40 (br.s, 1 H)
3c	226 $[M]^+$ (9), 209 (93), 183 (100), 137 (42), 109 (18), 69 (28), 55 (40)	1320, 1500 (NO_2); 1680 (CO); 1250, 3300 (NH)	0.89 (t, 3 H); 1.20—1.60 (m, 4 H); 2.28 (s, 3 H); 3.20—3.40 (m, 2 H); 7.09 (br.s, 1 H); 11.38 (br.s, 1 H)
3d	240 $[M]^+$ (12), 223 (91), 211 (15), 183 (100), 170 (33), 166 (32), 137 (69), 109 (30), 69 (41), 55 (55)	1310, 1510 (NO_2); 1680 (CO); 1280, 3320 (NH)	0.87 (t, 3 H); 1.15—1.80 (m, 6 H); 2.28 (s, 3 H); 3.10—3.50 (m, 2 H); 7.26 (br.s, 1 H); 11.45 (br.s, 1 H)
4a	294 $[M]^+$ (3), 183 (32), 181 (35), 137 (13), 123 (19), 96 (43), 70 (48), 55 (100)	1330, 1530 (NO_2); 1680 (CO)	1.17 (t, 3 H); 1.80—2.00 (m, 4 H); 2.08 (s, 3 H); 3.30—3.50 (m, 4 H); 3.78 (q, 2 H); 8.78 (br.s, 2 H)
4b	308 $[M]^+$ (3), 212 (15), 195 (47), 183 (100), 170 (15), 137 (34), 96 (46), 70 (28), 55 (43)	1310, 1510 (NO_2); 1670 (CO)	0.88 (t, 3 H); 1.62 (tq, 2 H); 1.80—2.00 (m, 4 H); 2.08 (s, 3 H); 3.30—3.50 (m, 4 H); 3.69 (t, 2 H); 8.73 (br.s, 2 H)
4c	322 $[M]^+$ (3), 226 (15), 209 (63), 183 (100), 170 (13), 166 (14), 137 (29), 96 (51), 70 (34), 55 (51)	1320, 1510 (NO_2); 1680 (CO)	0.92 (t, 3 H); 1.30 (qt, 2 H); 1.59 (tt, 2 H); 1.80—2.00 (m, 4 H); 2.08 (s, 3 H); 3.30—3.50 (m, 4 H); 3.72 (t, 2 H); 8.75 (br.s, 2 H)
4d	336 $[M]^+$ (2), 240 (5), 223 (60), 183 (100), 170 (12), 166 (12), 137 (29), 96 (43), 70 (15), 55 (40)	1320, 1510 (NO_2); 1680 (CO)	0.89 (t, 3 H); 1.20—1.40 (m, 4 H); 1.59 (tt, 2 H); 1.80—2.00 (m, 4 H); 2.07 (s, 3 H); 3.30—3.50 (m, 4 H); 3.72 (t, 2 H); 8.77 (br.s, 2 H)
5a	308 $[M]^+$ (2), 198 (30), 183 (31), 181 (36), 137 (13), 110 (47), 109 (38), 85 (41), 69 (100), 55 (57)	1320, 1530 (NO_2); 1670 (CO)	1.16 (t, 3 H); 1.50—1.70 (m, 6 H); 2.09 (s, 3 H); 3.30—3.50 (m, 4 H); 3.78 (q, 2 H); 8.71 (br.s, 2 H)
5b	322 $[M]^+$ (2), 305 (4), 212 (12), 195 (52), 183 (100), 137 (45), 110 (55), 109 (53), 84 (47), 69 (68), 67 (49), 55 (89)	1330, 1520 (NO_2); 1670 (CO)	0.89 (t, 3 H); 1.50—1.70 (m, 8 H); 2.09 (s, 3 H); 3.30—3.50 (m, 4 H); 3.68 (t, 2 H); 8.85 (br.s, 2 H)
5c	336 $[M]^+$ (2), 319 (2), 305 (3), 212 (13), 195 (45), 183 (100), 137 (37), 110 (58), 109 (42), 84 (36), 69 (72), 67 (51), 55 (92)	1330, 1520 (NO_2); 1680 (CO)	0.90 (t, 3 H); 1.28 (qt, 2 H); 1.50—1.70 (m, 8 H); 2.08 (s, 3 H); 3.30—3.50 (m, 4 H); 3.72 (t, 2 H); 8.80 (br.s, 2 H)
5d	223 (32), 183 (58), 137 (25), 84 (100), 67 (33), 55 (49)	1320, 1520 (NO_2); 1680 (CO)	0.88 (t, 3 H); 1.20—1.40 (m, 4 H); 1.50—1.70 (m, 8 H); 2.08 (s, 3 H); 3.30—3.50 (m, 4 H); 3.71 (t, 2 H); 8.77 (br.s, 2 H)
6a	310 $[M]^+$ (2), 198 (19), 181 (26), 142 (19), 123 (20), 113 (24), 86 (100), 69 (91)	1310, 1530 (NO_2); 1670 (CO)	1.09 (t, 3 H); 2.28 (s, 3 H); 3.30—3.40 (m, 4 H); 3.60—3.70 (m, 4 H); 3.80 (q, 2 H); 8.41 (br.s, 1 H); 9.81 (br.s, 1 H)
6b	324 $[M]^+$ (1), 307 (6), 212 (12), 195 (56), 183 (100), 166 (17), 137 (39), 112 (41), 67 (28)	1330, 1520 (NO_2); 1670 (CO)	0.89 (t, 3 H); 1.59 (tq, 2 H); 2.14 (s, 3 H); 3.40—3.50 (m, 4 H); 3.62—3.72 (m, 4 H); 3.72 (t, 2 H); 9.03 (br.s, 2 H)
6c	338 $[M]^+$ (2), 251 (32), 234 (17), 209 (100), 196 (30), 183 (15), 165 (14), 124 (18), 109 (25), 95 (18), 67 (27)	1320, 1510 (NO_2); 1680 (CO)	0.90 (t, 3 H); 1.28 (q, 2 H); 1.59 (tt, 2 H); 2.15 (s, 3 H); 3.40—3.50 (m, 4 H); 3.62—3.72 (m, 4 H); 3.74 (t, 2 H); 8.60 (br.s, 1 H); 9.78 (br.s, 1 H)
6d	209 (8), 196 (30), 183 (100), 165 (14), 124 (17), 109 (26), 95 (15), 67 (28)	1330, 1510 (NO_2); 1680 (CO)	0.89 (t, 3 H); 1.20—1.40 (m, 4 H); 1.60 (tt, 2 H); 2.13 (s, 3 H); 3.40—3.48 (m, 4 H); 3.60—3.70 (m, 4 H); 3.76 (t, 2 H); 9.08 (br.s, 2 H)

(*to be continued*)

Table 1 (*continued*)

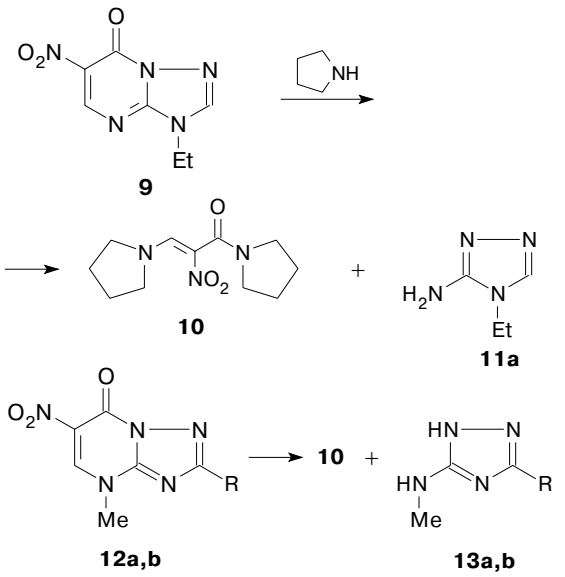
Compound	m/z (I_{rel} (%))	IR, ν/cm^{-1}	^{1}H NMR, δ
7a	322 $[M]^+$ (2), 305 (12), 261 (9), 198 (36), 183 (46), 181 (58), 125 (16), 123 (41), 98 (43), 69 (58), 55 (100)	1320, 1510 (NO_2); 1680 (CO)	1.17 (t, 3 H); 1.50—1.62 (m, 4 H); 1.62—1.80 (m, 4 H); 2.08 (s, 3 H); 3.40—3.60 (m, 4 H); 3.79 (q, 2 H); 8.89 (br.s, 2 H)
7b	336 $[M]^+$ (2), 212 (14), 198 (38), 181 (64), 167 (14), 124 (43), 98 (45), 69 (61), 55 (100)	1320, 1510 (NO_2); 1690 (CO)	0.89 (t, 3 H); 1.50—1.62 (m, 6 H); 1.62—1.80 (m, 4 H); 2.09 (s, 3 H); 3.40—3.60 (m, 4 H); 3.68 (t, 2 H); 8.85 (br.s, 2 H)
7c	350 $[M]^+$ (1), 226 (12), 198 (41), 181 (55), 124 (49), 98 (48), 69 (52), 55 (100)	1320, 1510 (NO_2); 1690 (CO)	0.90 (t, 3 H); 1.28 (qt, 2 H); 1.50—1.62 (m, 6 H); 1.62—1.80 (m, 4 H); 2.08 (s, 3 H); 3.40—3.60 (m, 4 H); 3.72 (t, 2 H); 8.80 (br.s, 2 H)
7d	240 (13), 198 (35), 181 (68), 167 (12), 124 (44), 98 (42), 69 (50), 55 (100)	1320, 1510 (NO_2); 1600, 1690 (CO)	0.88 (t, 3 H); 1.20—1.40 (m, 4 H); 1.50—1.62 (m, 6 H); 1.62—1.80 (m, 4 H); 2.08 (s, 3 H, Me); 3.40—3.60 (m, 4 H); 3.71 (t, 2 H); 8.77 (br.s, 2 H, NH)
8a	404 $[M]^+$ (3), 300 (8), 261 (5), 223 (51), 181 (71), 138 (100), 56 (98)	1340, 1530 (NO_2); 1680 (CO)	1.00—1.40 (m, 10 H); 1.18 (t, 3 H); 1.57—1.80 (m, 6 H); 1.95—2.00 (m, 4 H); 2.10 (s, 3 H, Me); 3.05—3.20 (m, 2 H); 3.68 (q, 2 H); 8.10 (br.s, 2 H, NH)
8b	418 $[M]^+$ (2), 233 (2), 195 (9), 183 (12), 181 (12), 138 (100), 56 (73)	1320, 1520 (NO_2); 1680 (CO)	0.89 (t, 3 H); 1.00—1.40 (m, 10 H); 1.57—1.80 (m, 8 H); 1.95—2.00 (m, 4 H); 2.09 (s, 3 H, Me); 3.05—3.20 (m, 2 H); 3.69 (t, 2 H); 8.12 (br.s, 2 H, NH)
8c	195 (5), 183 (16), 181 (10), 138 (100), 82 (21), 67 (23), 56 (83)	1330, 1520 (NO_2); 1680 (CO)	0.91 (t, 3 H); 1.00—1.40 (m, 12 H); 1.57—1.80 (m, 8 H); 1.95—2.00 (m, 4 H); 2.10 (s, 3 H, Me); 3.05—3.20 (m, 2 H); 3.66 (t, 2 H); 7.78 (br.s, 2 H, NH)
8d	236 (9), 181 (10), 138 (100), 82 (19), 67 (20)	1320, 1520 (NO_2); 1680 (CO)	0.89 (t, 3 H); 1.00—1.40 (m, 14 H); 1.57—1.80 (m, 8 H); 1.95—2.00 (m, 4 H); 2.10 (s, 3 H, Me); 3.05—3.20 (m, 2 H); 3.65 (t, 2 H); 8.10 (br.s, 2 H, NH)
10	193 (13), 124 (23), 97 (65), 72 (100)	1310, 1530 (NO_2); 1670 (CO)	1.80—2.20 (m, 8 H); 3.20—3.80 (m, 8 H); 8.35 (s, 1 H)
11b	126 $[M]^+$ (100), 84 (77), 57 (16)	1330, 1650, 3210, 3450 (NH_2); 2870 (Alk)	0.87 (t, 3 H); 1.71 (tq, 2 H); 3.67 (t, 2 H); 4.58 (br.s, 2 H); 7.73 (s, 1 H)
11c	140 $[M]^+$ (100), 84 (69), 57 (12)	1340, 1645, 3210, 3430 (NH_2); 2890 (Alk)	0.92 (t, 3 H); 1.33 (tq, 2 H); 1.68 (tt, 2 H); 3.73 (t, 2 H); 4.77 (br.s, 2 H); 7.56 (s, 1 H)
11d	154 $[M]^+$ (100), 130 (6), 98 (9), 84 (67), 57 (14)	1330, 1650, 3212, 3445 (NH_2); 2890 (Alk)	0.88 (t, 3 H); 1.00—2.00 (m, 6 H); 3.68 (t, 2 H); 4.42 (br.s, 2 H); 7.55 (s, 1 H)
11e	126 $[M]^+$ (100), 98 (81), 71 (14)	1330, 1650, 3445 (NH_2); 2920, 2890 (Alk)	1.14 (t, 3 H); 2.17 (s, 3 H); 3.71 (q, 2 H); 5.53 (br.s, 2 H)
13a	98 $[M]^+$ (100), 97 (100), 70 (69), 57 (54)	1040, 1180, 1330, 1650, 2870, 3210, 3450	2.75 (d, 3 H); 5.90 (br.s, 1 H); 7.35 (br.s, 1 H); 12.10 (br.s, 1 H)
14	145 $[M]^+$ (48), 129 (9), 128 (100), 127 (38), 85 (76), 83 (18), 69 (17)	1270, 1370, 1510 (NO_2); 1650 (CO); 3150, 3300 (NH)	2.14 (s, 3 H); 7.35 (br.s, 1 H); 7.75 (br.s, 1 H); 8.90 (br.s, 1 H); 9.80 (br.s, 1 H)
15	225 $[M]^+$ (46), 179 (66), 165 (100), 124 (62), 109 (25), 96 (30), 82 (83), 67 (37), 56 (67)	1350, 1550 (NO_2); 1600, 1650 (CO); 3450 (NH)	2.07 (s, 3 H); 3.72—3.82 (m, 2 H); 4.10—4.18 (m, 2 H); 5.00—5.30 (m, 4 H); 5.75—6.05 (m, 2 H); 8.56 (t, 1 H); 10.79 (t, 1 H)
16	309 $[M]^+$ (39), 263 (12), 211 (34), 185 (75), 139 (42), 99 (100)	1360, 1540 (NO_2); 1610, 1650 (CO); 3230, 3350 (NH)	1.10—1.40 (m, 12 H); 1.60—1.80 (m, 8 H); 2.09 (s, 3 H); 3.00—3.20 (m, 2 H); 8.70 (br.s, 1 H); 9.40 (br.s, 1 H)
17	211 $[M]^+$ (43), 165 (72), 151 (100), 96 (32), 56 (54)	1320, 1530 (NO_2); 1650 (CO); 3380 (NH)	3.72—3.85 (m, 4 H); 4.10—4.20 (m, 2 H); 5.03—5.30 (m, 4 H); 8.31 (s, 1 H); 8.60 (br.s, 1 H); 10.50 (br.s, 1 H)
18	143 $[M]^+$ (100), 125 (36), 96 (11), 83 (30), 67 (86)	1080, 1470 (NO_2); 1680 (CO); 3200, 3380 (NH)	2.23 (s, 3 H); 7.23 (br.s, 2 H)

cochemical properties of aminotriazole **11a** are identical with those reported previously.[7]

It also appeared that the presence of the *N*-alkyl group has no effect on the scission of the pyrimidine ring because the reactions of 4-methyltriazolopyrimidinones **12a,b** with pyrrolidine also afforded acrylamide **10** and 3-methylamino-5-R-1,2,4-triazoles (**13a,b**). The spectral characteristics and the melting point of triazole **13b** are in complete agreement with those reported previously[8] (Table 2).

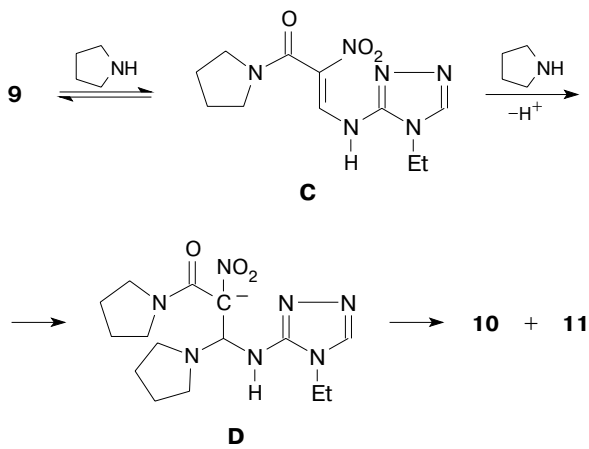
Apparently, the pyrimidine ring-opening involves two processes, *viz.*, the reaction of amine with the carbonyl

Scheme 3



group and the attack at the C(5) atom (Scheme 4). According to earlier studies,[9] the first stage of conversions involves the reversible reaction of the nucleophile with the carbonyl C(7) atom followed by the reaction of amide **C** [10] with the second amine molecule to form intermediate **D** and its decomposition into acrylamide **10** and triazole **11**.

Scheme 4

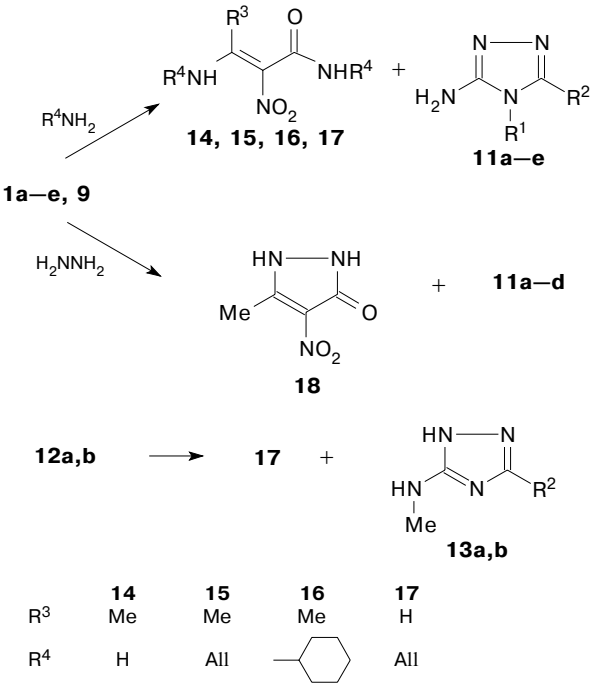


Evidently, the pyrimidine ring-opening in triazolopyrimidinones **9**, **12**, and **13** is controlled by the accessibility of the C(5) atom for the nucleophilic attack in the stage of formation of the anion of the type **D**. The absence of the *C*-methyl group in the pyrimidine ring in compounds **9**, **12**, and **13** favors their scission.

This assumption was confirmed by the reactions of *N*-alkyltriazolo[1,5-*a*]pyrimidinones with primary amines whose nucleophilic centers are more accessible compared to those in secondary amines.

Ammonia, cyclohexylamine, and allylamine reacted with 5-methyl-6-nitrotriazolopyrimidinones **1a—e** to form 4-alkyl- and 4,5-dialkyl-3-amino-1,2,4-triazoles (**11a—d** and **11e**) and 3-amino-2-nitrocrotonamides (**14—16**) (Scheme 5). The reaction of allylamine with triazolopyrimidinone **9** gave rise to nitroacrylamide **17** and aminotriazole **11a**, which is in complete agreement with the proposed mechanism.

Scheme 5



	14	15	16	17
R^3	Me	Me	Me	H
R^4	H	All		All

As expected, a change of the position of the *N*-methyl group in the heterocycle did not change the direction of its decomposition. The reactions of 4-methyl-6-nitrotriazolo[1,5-*a*]pyrimidinones (**12a,b**) with allylamine gave rise to acrylamide **17** and 3-methylamino-1,2,4-triazoles (**13a,b**) as well (see Scheme 5).

The ^{1}H NMR spectra of compounds **11b—e** and **13a,b** have resonance signals for the alkyl substituents R^1, the H(2) proton, and the amino group. The characteristics of aminotriazole **11a** are consistent with the published data. The mass spectra of compounds **11b—e**, **13a**,**b**, and **14—17** exhibit peaks of molecular ions. The IR spectra of compounds **14—17** reveal the presence of the carbonyl, nitro, and amino groups (see Table 1).

A characteristic feature of the reactions of triazolopyrimidinones **1a—e** with hydrazine is the formation of 5-methyl-4-nitro-1,2-dihydropyrazol-3-one (**18**) along with triazoles **11a—e** (see Scheme 5).

The ^{1}H NMR and IR spectra of pyrazolone **18** do not contradict the proposed structure. The mass spec-

Table 2. Yields, melting points, and data from elemental analysis of the synthesized compounds

Compound	Yield (%)	M.p.[a] /°C	Found / Calculated (%) C	H	N	Molecular formula
2a	78	250	43.20 43.05	3.98 4.06	31.51 31.38	$C_8H_9N_5O_3$
2b	72	210	45.44 45.57	4.82 4.67	29.37 29.52	$C_9H_{11}N_5O_3$
2c	67	180	47.76 47.81	5.16 5.22	28.01 27.87	$C_{10}H_{13}N_5O_3$
2d	54	155	49.93 49.81	5.74 5.66	26.46 26.40	$C_{11}H_{15}N_5O_3$
3a	87	285	42.36 42.42	5.00 5.09	28.21 28.27	$C_7H_{10}N_4O_3$
3b	83	270	45.11 45.28	5.79 5.70	26.28 26.40	$C_8H_{12}N_4O_3$
3c	77	240	47.92 47.79	5.98 6.19	24.69 24.78	$C_9H_{14}N_4O_3$
3d	79	174	50.04 50.00	6.65 6.67	23.37 23.33	$C_{10}H_{16}N_4O_3$
4a	55	270	48.90 48.97	6.36 6.16	28.62 28.55	$C_{12}H_{18}N_6O_3$
4b	63	270	50.46 50.64	6.72 6.54	27.18 27.26	$C_{13}H_{20}N_6O_3$
4c	58	260	52.00 52.16	6.93 6.88	25.98 26.07	$C_{14}H_{22}N_6O_3$
4d	43	255	53.58 53.56	7.00 7.19	24.98 24.98	$C_{15}H_{24}N_6O_3$
5a	68	250	50.58 50.64	6.73 6.54	27.22 27.26	$C_{13}H_{20}N_6O_3$
5b	71	255	52.07 52.16	6.90 6.88	26.04 26.07	$C_{14}H_{22}N_6O_3$
5c	63	260	53.53 53.56	7.22 7.19	24.90 24.98	$C_{15}H_{24}N_6O_3$
5d	54	260	54.78 54.84	7.55 7.48	23.92 23.98	$C_{16}H_{26}N_6O_3$
6a	73	180[b]	46.52 46.45	5.93 5.85	26.94 27.08	$C_{12}H_{18}N_6O_4$
6b	70	235[b]	48.10 48.14	6.31 6.22	26.02 25.91	$C_{13}H_{20}N_6O_4$
6c	64	162[b]	49.58 49.70	6.54 6.55	24.82 24.84	$C_{14}H_{22}N_6O_4$
6d	48	218[b]	51.11 51.13	6.93 6.86	23.91 23.85	$C_{15}H_{24}N_6O_4$
7a	83	270	52.07 52.16	6.75 6.88	26.01 26.07	$C_{14}H_{22}N_6O_3$
7b	76	275	53.52 53.56	7.21 7.19	25.02 24.98	$C_{15}H_{24}N_6O_3$
7c	80	270	54.79 54.84	7.60 7.48	23.87 23.98	$C_{16}H_{26}N_6O_3$
7d	52	260	55.99 56.03	7.80 7.74	23.12 23.06	$C_{17}H_{28}N_6O_3$
8a	59	230	59.37 59.39	7.94 7.97	20.84 20.78	$C_{20}H_{32}N_6O_3$
8b	64	210	60.15 60.26	8.28 8.19	20.14 20.08	$C_{21}H_{34}N_6O_3$
8c	55	190	60.99 61.09	8.23 8.39	19.46 19.43	$C_{22}H_{36}N_6O_3$
8d	43	170	61.96 61.86	8.62 8.58	18.98 18.82	$C_{23}H_{38}N_6O_3$
10	53	—	55.16 55.22	6.98 7.16	17.66 17.56	$C_{11}H_{17}N_3O_3$
11a	82	195[c]	—	—	—	—
11b	77	180[d]	47.54 47.60	8.06 7.99	44.37 44.41	$C_5H_{10}N_4$
11c	74	132[e]	51.25 51.41	8.78 8.63	39.78 39.97	$C_6H_{12}N_4$
11d	64	108	54.69 54.52	9.24 9.15	36.21 36.33	$C_7H_{14}N_4$
11e	91	144[d]	47.49 47.60	7.92 7.99	44.52 44.41	$C_5H_{10}N_4$
13a	87	112[d]	36.80 36.73	6.14 6.16	57.02 57.11	$C_3H_6N_4$
13b	92	138	—	—	—	—
14	77	202	33.13 33.11	4.82 4.86	28.84 28.96	$C_4H_7N_3O_3$
15	62	65	53.47 53.32	6.83 6.71	18.46 18.65	$C_{10}H_{15}N_3O_3$
16	43	22	62.19 62.11	8.66 8.80	13.45 13.58	$C_{16}H_{27}N_3O_3$
17	59	47	51.22 51.18	6.34 6.20	19.77 19.89	$C_9H_{13}N_3O_3$
18	78—86	273[c]	—	—	—	—

[a] From a 1 : 1 water—propan-2-ol mixture.
[b] From a 1 : 2 ether—dichloromethane mixture.
[c] Lit. data: m.p. of compounds **11a** [6,7] and **18** [11] are 200—201 °C and 276 °C, respectively.
[d] From ethanol.
[e] From chloroform.

trum has a molecular ion peak $[M]^+$ (m/z 143). The spectral characteristics of compound **18** correspond to those of the specimens obtained by nitration of 5-methyl-1,2-dihydropyrazol-3-one. The melting point of **18** (273—275 °C) is consistent with the published data[11] (276 °C).

No changes were observed upon heating of 1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones **1a—h** with tertiary amines, such as triethylamine or *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

Thus, the predominant direction of decomposition of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones under the action of amines involves the pyrimidine ring-opening to form hetarylaminoacrylamides of the type **C**, the secondary nucleophilic attack at the enamine C atom, and the scission of the anion of the type **D** to form amides **10** and **14—17** and aminotriazoles **11** and **13**. Since the presence of the bulky methyl group in the azine fragment hinders the second stage of conversion to form intermediate **D**, the azine ring-opening occurs only in

the reactions with primary amines. Due to steric hindrances, secondary amines cannot react with triazolopyrimidinones **1** giving rise to anions of the type **D** and the reactions follow a different pathway resulting in decomposition of the azole fragment to form hetarylguanidines **4—8** and then amines **3**. Alkalis, alkoxides, and C-nucleophiles act as bases and decompose exclusively the azole ring in triazolopyrimidinones, decomposition proceeding only in the absence of substituents in this ring.

Experimental

The ^{1}H NMR spectra were recorded on a Bruker WH-250 spectrometer (250 MHz) in DMSO-d_6 with Me_4Si as the internal standard. The mass spectra were obtained on a Varian MAT-311A instrument (70 eV, EI). The IR spectra were measured on a Specord IR-75 instrument in KBr pellets. The course of the reaction and the purities of the products were monitored by TLC on Silufol UV-254 plates using $CHCl_3$—EtOH (2 : 1) as the eluent; visualization was carried out with UV light.

N*-Alkyl-*N*-(4-methyl-5-nitro-6-oxopyrimidin-2-yl)cyanamides (2).** ***A. A solution of NaOH (0.08 g, 2 mmol) in EtOH (2 mL) was added to a solution of compound **1** (1.35 mmol) in EtOH (3 mL). The reaction mixture was refluxed for 20 min, neutralized, and concentrated *in vacuo*. The residue was dissolved in a minimum volume of hot water. The precipitate that formed upon cooling was filtered off.

B. Triazolopyrimidinone **1** (1.35 mmol) was added to a solution of $Mg(OMe)_2$ (5 mol L^{-1}) in MeOH (5 mL). The reaction mixture was refluxed for 1 h and then neutralized. The solvent was evaporated *in vacuo*. The product was isolated as described above.

2-(Alkylamino)-4-methyl-5-nitropyrimidin-7-ones (3). ***A.*** A solution of NaOH (0.08 g, 2.03 mmol) in EtOH (2 mL) was added to a solution of compound **1** (1.35 mmol) in hot EtOH (3 mL). The reaction mixture was refluxed for 2 h and then concentrated *in vacuo*. The residue was dissolved in a minimum volume of hot water and cooled. The precipitate that formed was filtered off.

B. A mixture of compound **1** (2 mmol) and secondary amine (10 mmol) was refluxed for 2 h. Then EtOH (15 mL) was added. The reaction mixture was neutralized and the precipitate that formed was crystallized from water.

1-Alkyl-1-(4-methyl-5-nitro-6-oxopyrimidin-2-yl)guanidines (4—8) (general procedure). A mixture of 3-alkyl-5-methyl-6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one (**1**) (1.35 mmol) and secondary amine (10 mmol) was heated to obtain a solution (10—30 min) and then concentrated *in vacuo*. The residue was crystallized (see Table 2).

4-Alkyl- and 4,5-dialkyl-3-amino-1,2,4-triazoles (11) and 3-amino-2-nitrobut-2-enamide (14). A mixture of compound **1** (1.88 mmol) and saturated methanolic ammonia (5 mL) was kept for 7 days. The solvent was evaporated and the residue was dissolved in hot water. Amide **14** that precipitated upon cooling was filtered off, the filtrate was concentrated, and the residue was crystallized from EtOH.

4-Alkyl- and 4,5-dialkyl-3-amino-1,2,4-triazoles (11), *N*-allyl- and *N*-cyclohexyl-3-(allyl- and cyclohexylamino)-2-nitrobut-2-enamides (15 and 16), and *N*-allyl-3-allylamino-2-nitroacrylamide (17). A mixture of compound **1** or **9** (1.8 mmol) and the amine (3 mL) was refluxed for 10—15 min. Product **11** was precipitated from the solution by the addition of EtOH (15 mL), filtered off, and crystallized from EtOH. The filtrate was concentrated and the residue was triturated with hexane. Amides **15**, **16**, or **17** were crystallized from *n*-octane.

3-Methylamino- and 5-methyl-3-methylamino-1,2,4-triazoles (13a,b) and 3-pyrrolidino- or 3-allylamino-2-nitroacrylamides (10 and 17). A mixture of compounds **12a,b** (1.8 mmol) in pyrrolidine or allylamine (3 mL) was refluxed for 10—15 min. Products **13a,b** were precipitated from the solution by the addition of EtOH (15 mL), filtered off, and crystallized from EtOH. Amides **10** and **17** were isolated as described above.

5-Methyl-4-nitro-1,2-dihydropyrazol-3-one (18). Hydrazine hydrate (4 mmol) was added to a solution of compound **1** (2 mmol) in EtOH (15 mL). The reaction mixture was kept at ~20 °C for 2 days and concentrated to dryness. Pyrazolone **18** was crystallized from a 1 : 2 ethanol—water mixture.

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