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ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 8145–8150

Study on the reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with amines and thiols

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Received 2 April 2007; revised 16 May 2007; accepted 31 May 2007
Available online 6 June 2007

Abstract—Reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with amines and thiols have been investigated. Pyridine catalyzes rearrangement of the title compounds into 6-phenyl-7-oxo-7*H*-pyrrolo[3,2-*d*]pyrimidine-5-oxides. Primary and secondary amines and thiols take part in a regio- and stereoselective addition reaction to the triple bond of 5-nitro-6-phenylethynylpyrimidines to form the corresponding *syn*-addition (in the case of secondary amines) or *anti*-addition (in the case of primary amines or thiols) products.

1. Introduction

In our previous publications[1,2] it was shown that 4-amino-6-arylethynyl-5-nitropyrimidines in dry pyridine undergo smooth intramolecular cyclization to give pyrrolo[3,2-*d*]-pyrimidine-5-oxides. The latter compounds, being aza-analogues of isatogens, attract our attention as potential traps for free radicals in biological milieu.[3–5] Therefore, as continuation of our research aimed on the synthesis of pyrrolo-[3,2-*d*]pyrimidine-5-oxides via cyclization of the title compounds, in this paper we report the results of more extensive investigation, including reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with primary and secondary amines and thiols.

2. Results and discussion

Compounds **2a** and **b** were synthesized by the palladium-catalyzed Sonogashira coupling of the corresponding 4-amino-6-chloro-5-nitropyrimidines **1a** and **b** with phenylacetylene according to procedure described earlier.[1] Compounds **2a** and **b** in dry boiling pyridine underwent smooth ring closure, to give dark violet pyrrolo[3,2-*d*]pyrimidine-5-oxides **3a** and **b**. Moreover, it was established that cyclization of **2a** and **b** also proceeds using a catalytic amount of pyridine in boiling 2-propanol (Scheme 1). Encouraged by this result we decided to investigate the behaviour of the title compounds in the presence of different amines. When 4-amino-5-nitro-6-phenylethynylpyrimidines **2a** and **b** were treated with another tertiary amine—triethylamine no reaction was observed. In the presence of catalytic amount of secondary amines conversion of 5-nitro-6-phenylethynylpyrimidines **2a** and **b** was incomplete and formation of traces of intense red or orange products was observed by TLC. Performing reaction of **2a** and **b** with an equivalent amount of selected secondary amines in dichloromethane at room temperature furnished compounds **4a–f** in 90–95% yields (Scheme 1). The same products were obtained and no cyclization reaction was observed when the starting compounds were heated to reflux with secondary amines in dimethylformamide (the latter procedure was used for cyclization of 5-nitro-6-arylvinylpyrimidines into pyrrolo[3,2-*d*]pyrimidine derivatives).[6] Neither ^{13}C NMR nor IR spectra of **4a–f** showed the presence of C≡C or CO group in the molecules. In the ^{1}H NMR spectra new singlet at 6.45–6.54 ppm due to vinylic CH along with signals of the corresponding amine was observed. These data indicated that addition reaction of amines to the triple bond took place. It is noteworthy that, in the ^{1}H NMR spectra of **4a–f**, singlets of C–H and SCH_3 in position 2 of the pyrimidine ring were observed in an upfield region than usual (7.47–7.85 ppm for C2–H and 1.55–1.67 ppm for C2–SCH_3) (Table 1). Slow crystallization of **4a** from dichloromethane provided single crystals suitable for the X-ray crystallographic analysis, which enabled the outcome of the reaction to be elucidated[7] unambiguously (Fig. 1). Moreover, the crystallographic data of **4a** showed that in the solid state the molecule adopted a conformation in which the benzene ring is turned out of plane of the pyrimidine ring and C(11)H═C(12)–N(13) moiety. The torsion angle of C(11)–C(12)–C(18)–C(23) was found to be 84.85°. Thus, the hydrogen at C2 of the pyrimidine ring is constrained above the benzene ring. As a consequence an

Keywords: 5-Nitro-6-phenylethynylpyrimidines; Addition; Nucleophiles; Triple bond.
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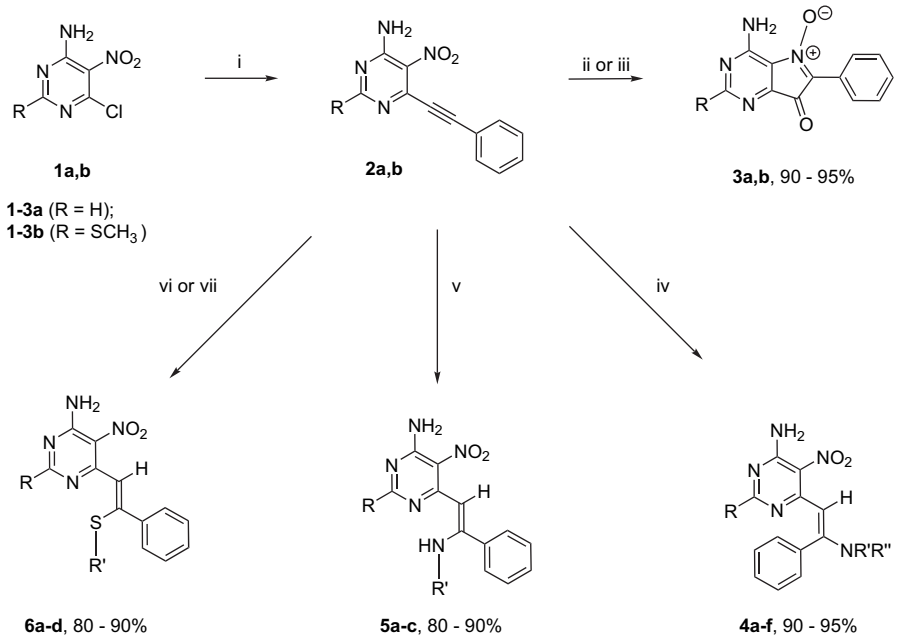
doi:10.1016/j.tet.2007.05.125



Scheme 1. Reagents and conditions: (i) 1-phenylacetylene (1.2 quiv), $PdCl_2(PPh_3)_2$ (2 mol %), CuI (1 mol %), Et_3N, Ar, 40 °C, 2 h; (ii) pyridine, reflux, 10 min; (iii) pyridine (1 drop), 2-propanol, reflux, 30 min; (iv) secondary amine (1 equiv), dichloromethane, 20 min, rt; (v) primary amine (1 equiv), dichloromethane, 48 h, rt; (vi) thiol (1 equiv), dichloromethane, 24 h, rt and (vii) sodium thiolate (1 equiv), methanol, 30 min, rt.

upfield shift of C2–H and C2–SCH_3 signals in the ^{1}H NMR spectra results from shielding effect of benzene ring on these protons. Thus, these data indicate that compounds formed in the reaction of **2a** and **b** with secondary amines were the corresponding 4-amino-5-nitro-6-[(*E*)-2-phenyl-2-(1-dialkylamino)ethenyl]pyrimidines **4a**–**f** (Scheme 1).

Compounds **2a** and **b** appeared to be less reactive towards primary amines and thiols. Full conversion of **2a** and **b** at room temperature was achieved after 48 and 72 h, respectively. When sodium thiolates in methanol were used instead of thiols, reaction was completed after 30 min. ^{1}H NMR, ^{13}C NMR and IR spectra of the obtained products showed that in the case of primary amines and thiols addition reaction to C≡C bond took place again. Singlets for C2–H and C2–SCH_3 of the pyrimidine ring in the ^{1}H NMR spectra of **6a**–**d** were observed in ordinary positions for these groups—8.20–8.71 ppm and 2.57 and 2.61 ppm, respectively. Probably, in compounds **5a**–**c** benzene ring is directed away from the pyrimidine ring and shielding effect of benzene ring in the ^{1}H NMR spectra for protons at C2 of the pyrimidine ring is absent. This can be realized if addition reaction of primary amines and thiols to the triple bond of **2a** and **b** proceeds with the formation of *anti*-addition products **5a**–**c** and **6a**–**d** (Scheme 1, Table 1).

Results obtained for the reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with amines and thiols could be

Table 1. Data of reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines **2a** and **b** with amines and thiols

Starting compound	Amine or thiol	Product	^{1}H NMR data[a](ppm)	
			C(2)–H	C(2)–SCH_3
2a	$(CH_2)_4NH$	**4a**	7.59	—
2b	$(CH_2)_4NH$	**4b**	—	1.55
2a	$(CH_2)_5NH$	**4c**	7.77	—
2b	$(CH_2)_5NH$	**4d**	—	1.67
2a	$O(CH_2)_4NH$	**4e**	7.85	—
2a	$C_6H_5CH_2NHCH_3$	**4f**	7.52	—
2a	$CH_3CH_2CH_2NH_2$	**5a**	8.21	—
2b	$CH_3CH_2CH_2NH_2$	**5b**	—	2.57
2a	$C_6H_5CH_2NH_2$	**5c**	8.20	—
2a	C_6H_5SH	**6a**	8.71	—
2b	C_6H_5SH	**6b**	—	2.61
2a	$C_6H_5CH_2SH$	**6c**	8.47	—
2a	$CH_3O_2CCH_2SH$	**6d**	8.54	—

[a] ^{1}H NMR spectra of **4a**–**e**, **5a**–**c** and **6a** were recorded in $CDCl_3$, spectra of **4f** and **6b**–**d**, in DMSO-d_6.

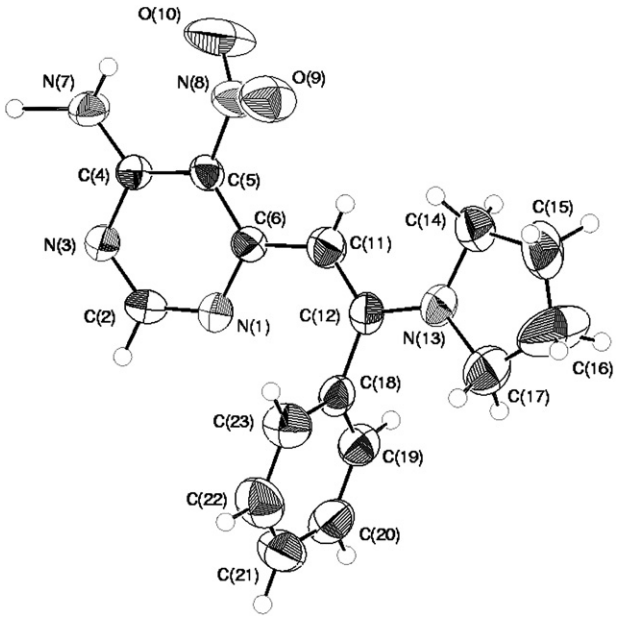
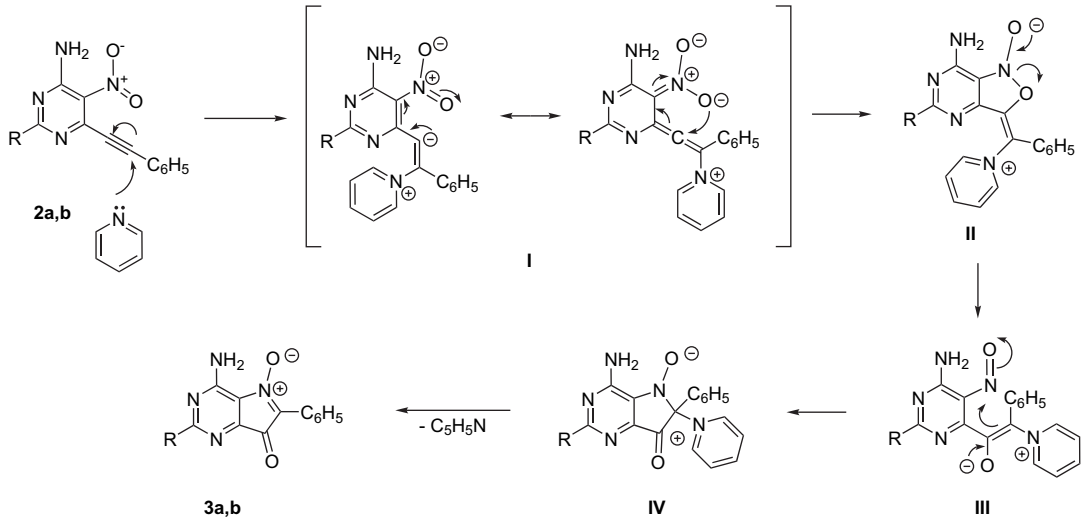
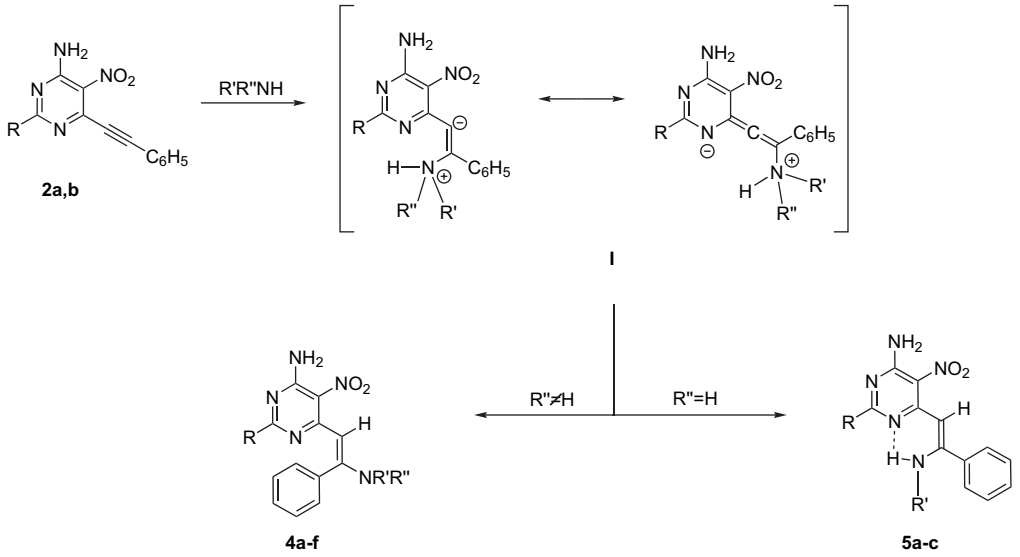


Figure 1. ORTEP drawing of compound **4a**.



Scheme 2.



Scheme 3.

explained as following. Pyridine catalyzes the cyclization of starting compounds by a mechanism depicted in Scheme 2.

Another tertiary amine—triethylamine, probably, due to its hindered nitrogen could not attack the triple bond in C≡C and cyclization of 5-nitro-6-phenylethynylpyrimidines did not occur. Intramolecular cyclization failed when the title compounds were treated with primary and secondary amines, in these cases stable addition products were formed. Literature survey showed that addition reactions of nucleophiles to alkynes have been investigated by several research groups.[8,9] Nucleophilic addition with alkynes bearing electron withdrawing groups occurs rapidly and no catalyst is required.[10–13] The triple bond of the investigated compounds **2a** and **b** is electron deficient due to the electron deficient pyrimidine moiety and its nitro group, so it is easily attacked by different nucleophiles. It is likely that amines attack the triple bond of compounds **2a** and **b** in the way like pyridine to form the same zwitterionic intermediate **I**, which turns to either *syn*- or *anti*-addition products, resulting from an internal or external proton delivery.[14] Reaction of the title compounds with secondary amines led to formation of thermodynamically stable 6-[(*E*)-2-(1-dialkylamino)-2-phenylethenyl]-5-nitropyrimidines **4a**–**f**. In the case of primary amines, probably an important factor could be an extra stability of *Z*-isomer because of possible intramolecular H-bonding in compounds **5a**–**c** (Scheme 3).

When thiols or sodium thiolates were used addition reaction to the triple bond in C≡C would be expected to proceed by 'trans-addition rule',[15,16] so products of *anti*-addition **6a**–**d** were formed.

3. Conclusions

In conclusion, the study of the reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with amines and thiols showed that the triple bond of investigated compounds is easily attacked by different amines and thiols. Pyridine initiates

intramolecular cyclization of starting compounds to form pyrrolo[3,2-*d*]pyrimidine-5-oxides. Reactions of 4-amino-5-nitro-6-phenylethynylpyrimidines with secondary and primary amines as well as with thiols are regio- and stereoselective and lead to the formation of *syn*-addition (in the case of secondary amines) or *anti*-addition (in the case of primary amines or thiols) products.

4. Experimental

4.1. General

Melting points were determined in open capillaries and are uncorrected. IR spectra were run in Nujol mulls or in KBr discs on a Perkin–Elmer FT spectrophotometer Spectrum BX II. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Varian Unity INOVA spectrometer (300 MHz) using tetramethylsilane as an internal standard. Elemental analyses (C, N, H) results were found to be in good agreement (±0.4%) with the calculated values. All reactions and purity of the synthesized compounds were monitored by TLC using Silica gel 60 F_{254} aluminium plates (Merck). Visualization was accomplished by UV light.

Compounds **2a** and **b** were prepared according to method published earlier.[1]

4.1.1. 4-Amino-2-methylthio-5-nitro-6-phenylethynylpyrimidine (2b). Yield 70%; yellow needles; mp 169–170 °C; IR (KBr) cm^{-1}: 3445, 3264, 2205. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 2.56 (3H, s, SCH_3), 7.55–7.78 (5H, m, ArH), 7.81 (2H, br s, NH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 15.4; 87.8; 99.5; 119.8; 123.0; 130.6; 132.3; 134.4; 147.7; 158.5; 176.3. Anal. Calcd for $C_{13}H_{10}N_4O_2S$ (286.31) C, 54.54; H, 3.52; N, 19.57; found C, 54.62; H, 3.62; N, 19.36.

4.1.2. Synthesis of 4-amino-7-oxo-6-phenyl-7*H*-pyrrolo[3,2-*d*]pyrimidine-5-oxides (3a and b). To a solution of the corresponding alkynes **2a** or **b** (1 mmol) in 2-propanol (3 mL) one drop of pyridine was added and the reaction mixture was heated to reflux for 30 min. After cooling to room temperature, the precipitate was filtered off and recrystallized to give compounds **3a** and **b** as dark violet solids. Data for compound **3a** have been published in the previous paper.[1]

4.1.2.1. 4-Amino-2-methylthio-7-oxo-6-phenyl-7*H*-pyrrolo[3,2-*d*]pyrimidine-5-oxide (3b). Yield 85%; dark violet crystals; mp 210–212 °C; IR (KBr) cm^{-1}: 3429, 3226, 1725. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.60 (3H, s, SCH_3), 7.20 (1H, s, NH), 7.47–7.50 (3H, m, ArH), 8.19 (1H, s, NH), 8.39–8.43 (2H, m, ArH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.9; 119.1; 125.3; 126.5; 127.9; 129.4; 148.9; 150.6; 151.1; 174.2; 185.7. Anal. Calcd for $C_{13}H_{10}N_4O_2S$ (286.31) C, 54.54; H, 3.52; N, 19.57; found C, 54.42; H, 3.36; N, 19.79.

4.1.3. Reaction of 4-amino-2-methylthio-5-nitro-6-phenylethynylpyrimidines (2a and b) with amines. General procedure. To a solution of the corresponding alkynes **2a** or **b** (1 mmol) in dichloromethane (5 mL), the corresponding amine (1 mmol) was added. The reaction mixture was kept at room temperature for 20 min (in the case of secondary amine) or for 48 h (in the case of primary amine). The solvent was evaporated under reduced pressure, the residue was recrystallized to give compounds **4a–f** or **5a–c**.

4.1.3.1. 4-Amino-5-nitro-6-[(*E*)-2-phenyl-2-(1-pyrrolidinyl)ethenyl]pyrimidine (4a). Yield 95%; orange needles; mp 189–190 °C; IR (KBr) cm^{-1}: 3369, 3246. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99–2.02 (4H, m, $(CH_2)_2$), 3.29–3.33 (4H, m, $N(CH_2)_2$), 6.46 (1H, s, CH), 7.26 (2H, br s, NH_2), 7.27–7.40 (5H, m, ArH), 7.59 (1H, s, C(2)H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.6; 50.6; 95.6; 122.6; 128.1; 128.5; 128.6; 138.5; 156.6; 158.4; 160.7; 162.5. Anal. Calcd for $C_{16}H_{17}N_5O_2$ (311.34) C, 61.72; H, 5.50; N, 22.49; found C, 61.72; H, 5.72; N, 22.45.

4.1.3.2. 4-Amino-2-methylthio-5-nitro-6-[(*E*)-2-phenyl-2-(1-pyrrolidinyl)ethenyl]pyrimidine (4b). Yield 92%; orange needles; mp 226–228 °C; IR (KBr) cm^{-1}: 3436, 3258. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (3H, s, SCH_3), 1.87 (2H, br s, CH_2), 1.92 (2H, br s, CH_2), 3.10–3.15 (2H, m, NCH_2), 3.51–3.55 (2H, m, NCH_2), 6.56 (1H, s, CH), 7.26—7.39 (5H, m, ArH), 7.52 (2H, br s, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.9; 24.7; 49.0; 93.4; 119.2; 127.9; 128.2; 128.5; 138.1; 156.8; 158.5; 161.1; 169.4. Anal. Calcd for $C_{17}H_{19}N_5O_2S$ (357.44) C, 57.13; H, 5.36; N, 19.59; found C, 57.18; H, 5.30; N, 19.76.

4.1.3.3. 4-Amino-5-nitro-6-[(*E*)-2-phenyl-2-(1-piperidinyl)ethenyl]pyrimidine (4c). Yield 95%; red needles; mp 139–140 °C; IR (KBr) cm^{-1}: 3361, 3305. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.67–1.73 (6H, m, $(CH_2)_3$), 3.28–3.32 (4H, m, $N(CH_2)_2$), 6.34 (1H, s, CH), 7.15 (2H, br s, NH_2), 7.29–7.38 (5H, m, ArH), 7.77 (1H, s, C(2)H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.2; 26.0; 50.6; 98.3; 123.5; 128.4; 129.1; 129.3; 137.1; 156.6; 157.7; 161.5; 164.4. Anal. Calcd for $C_{17}H_{19}N_5O_2$ (325.36) C, 62.65; H, 5.89; N, 21.52; found C, 62.82; H, 6.02; N, 21.66.

4.1.3.4. 4-Amino-2-methylthio-5-nitro-6-[(*E*)-2-phenyl-2-(1-piperidinyl)ethenyl]pyrimidine (4d). Yield 92%; orange needles; mp 203–205 °C; IR (KBr) cm^{-1}: 3439, 3247. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65–1.70 (6H, m, $(CH_2)_3$), 1.67 (3H, s, SCH_3), 3.27–3.31 (4H, m, $N(CH_2)_2$), 6.52 (1H, s, CH), 7.20 (2H, br s, NH_2), 7.29–7.40 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.0; 24.3; 26.0; 50.6; 98.8; 120.8; 128.6; 129.1; 129.6; 137.3; 143.2; 157.4; 161.1; 164.8; 171.1. Anal. Calcd for $C_{18}H_{21}N_5O_2S$ (371.46) C, 58.20; H, 5.70; N, 18.85; found C, 58.18; H, 5.55; N, 18.95.

4.1.3.5. 4-Amino-5-nitro-6-[(*E*)-2-(4-morpholinyl)-2-phenylethenyl]pyrimidine (4e). Yield 90%; red needles; mp 168–170 °C; IR (KBr) cm^{-1}: 3416, 3358. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.25 (4H, t, J=4.5 Hz, $N(CH_2)_2$), 3.79 (4H, t, J=4.5 Hz, $O(CH_2)_2$), 6.24 (1H, s, CH), 6.86 (2H, br s, NH_2), 7.30–7.38 (5H, m, ArH), 7.85 (1H, s, C(2)H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.1; 66.6; 99.5; 124.9; 128.5; 129.3; 129.5; 135.9; 156.9; 157.9; 161.4; 162.7. Anal. Calcd for $C_{16}H_{17}N_5O_3$ (327.34) C, 58.71; H, 5.23; N, 21.39; found C, 59.01; H, 5.31; N, 21.22.

4.1.3.6. 4-Amino-5-nitro-6-{(*E*)-2-[benzyl(methyl)-amino]-2-phenylethenyl}pyrimidine (4f). Yield 90%; red needles; mp 144–146 °C; IR (KBr) cm^{-1}: 3423, 3276. ^1H NMR (300 MHz, DMSO-d_6): δ 2.93 (3H, s, NCH_3), 4.32 (2H, s, NCH_2), 6.07 (1H, s, CH), 7.23–7.32 (10H, m, 2ArH), 7.52 (1H, s, C(2)H), 7.54 (2H, br s, NH_2). ^{13}C NMR (75 MHz, DMSO-d_6): δ 26.1; 56.5; 96.9; 125.8; 127.6; 127.7; 128.5; 128.9; 129.0; 129.6; 137.6; 137.7; 156.6; 157.6; 160.1; 162.5. Anal. Calcd for $C_{20}H_{19}N_5O_2$ (361.40) C, 66.47; H, 5.30; N, 19.38; found C, 66.53; H, 5.38; N, 19.26.

4.1.3.7. 4-Amino-5-nitro-6-[(*Z*)-2-phenyl-2-(propyl-amino)ethenyl]pyrimidine (5a). Yield 92%; red needles; mp 174–176 °C; IR (KBr) cm^{-1}: 3380, 3359, 3298. ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (3H, t, J=7.2 Hz, CH_3), 1.60–1.65 (2H, m, CH_2), 3.22 (2H, q, J=7.2 Hz, NH*CH*$_2$), 6.40 (1H, s, CH), 7.29 (2H, br s, NH_2), 7.43–7.49 (5H, m, ArH), 8.21 (1H, s, C(2)H), 11.67 (1H, t, J=7.2 Hz, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.4; 24.0; 47.2; 92.3; 119.4; 127.7; 128.5; 129.4; 136.7; 156.8; 158.4; 159.1; 166.7. Anal. Calcd for $C_{15}H_{17}N_5O_2$ (299.33) C, 60.19; H, 5.72; N, 23.40; found C, 60.36; H, 5.86; N, 23.61.

4.1.3.8. 4-Amino-2-methylthio-5-nitro-6-[(*Z*)-2-phenyl-2-(propylamino)ethenyl]pyrimidine (5b). Yield 80%; red needles; mp 168–170 °C; IR (KBr) cm^{-1}: 3414, 3258, 3220. ^1H NMR (300 MHz, $CDCl_3$): δ 1.00 (3H, t, J=7.2 Hz, CH_3), 1.60–1.64 (2H, m, CH_2), 2.57 (3H, s, SCH_3), 3.23 (2H, q, J=7.2 Hz, NH*CH*$_2$), 6.46 (1H, s, CH), 7.20 (2H, br s, NH_2), 7.44–7.48 (5H, m, ArH), 11.39 (1H, t, J=7.2 Hz, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5; 14.3; 24.0; 47.3; 92.3; 117.4; 127.7; 128.5; 129.4; 136.8; 157.7; 158.9; 166.4; 171.7. Anal. Calcd for $C_{16}H_{19}N_5O_2S$ (345.43) C, 55.64; H, 5.54; N, 20.27; found C, 55.54; H, 5.57; N, 20.14.

4.1.3.9. 4-Amino-5-nitro-6-[(*Z*)-2-phenyl-2-(benzyl-amino)ethenyl]pyrimidine (5c). Yield 83 %; red needles; mp 133–135 °C; IR (KBr) cm^{-1}: 3424, 3262, 3220. ^1H NMR (300 MHz, $CDCl_3$): δ 4.50 (2H, d, J=6.6 Hz, NH*CH*$_2$), 6.46 (1H, s, CH), 7.15 (2H, br s, NH_2), 7.24–7.45 (10H, m, 2ArH), 8.20 (1H, s, C(2)H), 11.93 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.1; 92.8; 126.6; 127.4; 127.8; 128.5; 128.8; 129.5; 136.4; 138.5; 156.9; 158.2; 159.4; 166.3. Anal. Calcd for $C_{19}H_{17}N_5O_2$ (347.37) C, 65.69; H, 4.93; N, 20.16; found C, 65.88; H, 5.14; N, 19.90.

4.1.4. Reaction of 4-amino-2-methylthio-5-nitro-6-phenylethynylpyrimidines 2a and b with thiols. General procedures.

4.1.4.1. Method A. To a solution of the corresponding alkynes **2a** or **b** (1 mmol) in dichloromethane (5 mL), the corresponding thiol (1 mmol) was added. The reaction mixture was kept at room temperature for 72 h. The solvent was evaporated under reduced pressure, the residue was recrystallized to give compounds **6a–d**.

4.1.4.2. Method B. To a solution of the corresponding alkynes **2a** or **b** (1 mmol) in methanol (5 mL), the corresponding sodium thiolate, prepared from sodium (0.023 g, 1 mmol), anhydrous methanol (3 mL) and corresponding thiol (1 mmol) were added. The reaction mixture was stirred for 30 min at room temperature. The precipitate was filtered off and recrystallized to give compounds **6a–d**.

*4.1.4.2.1. 4-Amino-5-nitro-6-[(Z)-2-phenyl-2-(phenylthio)ethenyl]pyrimidine (**6a**).* Yield 69% (method A), 82% (method B); yellow needles; mp 167–169 °C; IR (KBr) cm^{-1}: 3435, 3268. ^1H NMR (300 MHz, $CDCl_3$): δ 7.02 (2H, br s, NH_2), 7.07–7.09 (3H, m, ArH), 7.19–7.23 (5H, m, ArH), 7.36 (1H, s, CH), 7.45–7.49 (2H, m, ArH), 8.71 (1H, s, C(2)H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 124.0; 127.6; 128.2; 128.7; 128.8; 129.2; 133.1; 134.1; 138.8; 152.8; 157.5; 158.6; 159.2. Anal. Calcd for $C_{18}H_{14}N_4O_2S$ (350.40) C, 61.70; H, 4.03; N, 15.99; found C, 61.78; H, 3.99; N, 16.23.

*4.1.4.2.2. 4-Amino-2-methylthio-5-nitro-6-[(Z)-2-phenyl-2-(phenylthio)ethenyl]pyrimidine (**6b**).* Yield 57% (method A), 85% (method B); yellow needles; mp 173–175 °C; IR (KBr) cm^{-1}: 3461, 3263. ^1H NMR (300 MHz, DMSO-d_6): δ 2.61 (3H, s, SCH_3), 7.10–7.48 (10H, m, 2ArH), 7.31 (1H, s, CH), 8.50 (2H, br s, NH_2). Anal. Calcd for $C_{19}H_{16}N_4O_2S_2$ (396.49) C, 57.56; H, 4.07; N, 14.13; found C, 57.73; H, 4.38; N, 14.02.

*4.1.4.2.3. 4-Amino-5-nitro-6-[(Z)-2-(benzylthio)ethenyl-2-phenyl]pyrimidine (**6c**).* Yield 57% (method A), 80% (method B); yellow needles; mp 185–187 °C; IR (KBr) cm^{-1}: 3438, 3279. ^1H NMR (300 MHz, DMSO-d_6): δ 3.54 (2H, s, SCH_2), 6.91 (1H, s, CH), 7.01–7.04 (2H, m, ArH), 7.17–7.20 (3H, m, ArH), 7.43–7.48 (5H, m, ArH), 7.96 (2H, br s, NH_2), 8.47 (1H, s, C(2)H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 37.5; 122.1; 126.4; 127.7; 127.8; 127.9; 128.1; 128.3; 128.4; 136.6; 139.3; 151.6; 156.4; 157.1; 163.3. Anal. Calcd for $C_{19}H_{16}N_4O_2S$ (364.42) C, 62.62; H, 4.43; N, 15.37; found C, 62.82; H, 4.56; N, 15.56.

*4.1.4.2.4. Methyl {[(Z)-2-(6-amino-5-nitro-4-pyrimidinyl)-1-phenylethenyl]thio}acetate (**6d**).* Yield 60% (method A), 90% (method B); yellow needles; mp 153–155 °C; IR (KBr) cm^{-1}: 3432, 3260, 1738. ^1H NMR (300 MHz, DMSO-d_6): δ 3.16 (2H, s, SCH_2), 3.51 (3H, s, OCH_3), 6.98 (1H, s, CH), 7.40–7.45 (5H, m, ArH), 8.03 (2H, br s, NH_2), 8.54 (1H, s, C(2)H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 34.4; 51.4; 122.9; 125.7; 127.7; 128.1; 128.3; 138.6; 150.4; 156.3; 156.4; 157.1; 168.4. Anal. Calcd for $C_{15}H_{14}N_4O_4S$ (346.36) C, 52.02; H, 4.07; N, 16.18; found C, 52.02; H, 3.99; N, 16.08.

Acknowledgements

We express our gratitude to *M. Kreneviciene* and *A. Karosiene* for recording the NMR and IR spectra, to *E. Kersuliene* and *M. Gavrilova* for performing the elemental analyses and to *Dr. S. Belyakov* (Institute of Organic Synthesis, Ryga, Latvia) for the X-ray measurements.

References and notes

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7. Crystal structure analysis for **4a**: $C_{16}H_{17}N_5O_2$, M_r=311.34 g mol^{-1}, orthorhombic, space group *Pbca*, a=7.2102(2), b=15.5331(5), c=27.4642(12) Å, $\alpha=\beta=\gamma=90$ °, V=3075.9 Å^3, Z=8, ρ=1.345 g cm^3, μ=0.09 mm^{-1}, $F(000)$=1312. X-ray diffraction data were collected on a Nonius Kappa CCD diffractometer at the temperature 293 K using graphite-monochromated Mo Kα radiation (λ=0.71073 Å). Structure **4a** was solved by direct methods with SIR97 program[17] and refined by full-matrix least squares techniques with anisotropic non-hydrogen atoms. Hydrogen atoms were refined in the riding model. The refinement calculations were carried out with the help of SHELX97 program.[18] ORTEP[19] view of the molecule is shown in Figure 1. Crystallographic data for structure **4a** have been deposited at the Cambridge Crystallographic Data Centre (CCDC number 634831).
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