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Synthesis and structure of 2-arylamino-substituted 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidines

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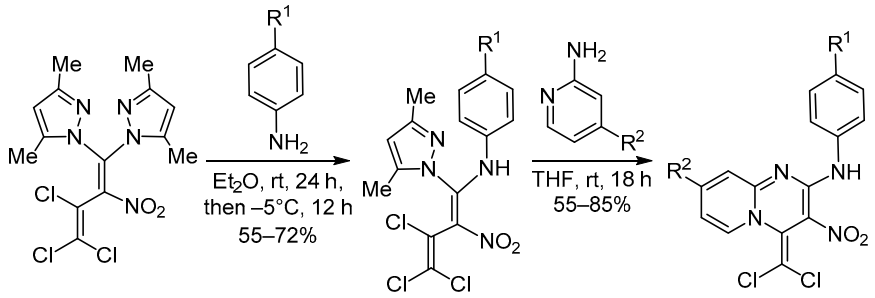


The reaction of 4-substituted anilines with 3,4,4-trichloro-1,1-bis(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dienes led to 1-arylamino-3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dienes, which under the action of 2-aminopyridines underwent heterocyclization to the corresponding 2-arylamino-substituted 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidines. The molecular structure of 4*H*-pyrido[1,2-*a*]pyrimidine containing the (4-ethoxyphenyl)amine substituent at position 2 was determined by X-ray structural analysis.

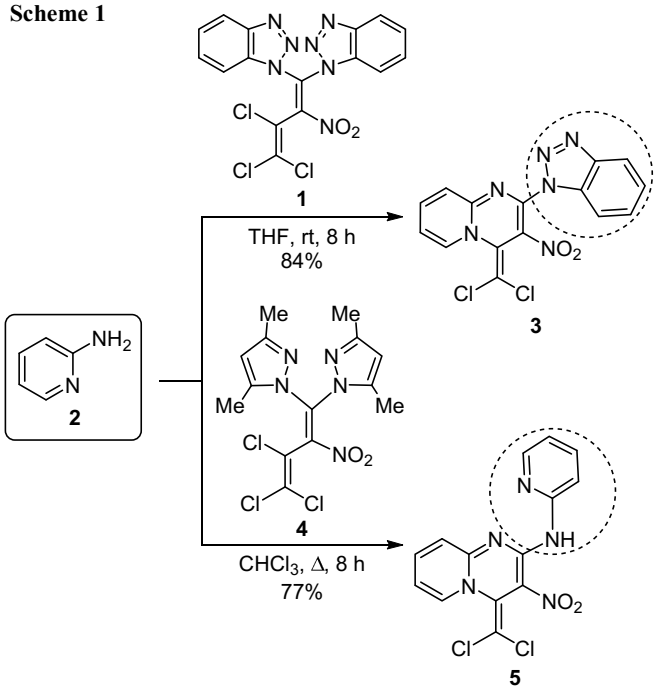
Keywords: arylamine, azole, nitrobutadiene, pyrido[1,2-*a*]pyrimidine, heterocyclization, nucleophilic substitution.

Pyrido[1,2-*a*]pyrimidines are among the privileged entities for drug discovery. They are inhibitors of enzymes elastase, reductase, urease, monoamine oxidase, and others which regulate the functioning of living systems in health and disease.[1] This causes pyrido[1,2-*a*]pyrimidines to manifest a wide spectrum of biological action, in particular antiviral, antimicrobial, antitumor, antipsychotic, and antioxidant activity.[2] Research on the chemistry of these compounds and the search for effective methods for the synthesis of their new derivatives for the creation of promising pharmaceutical substances remains of steady interest.[3]

One of the convenient approaches to the construction of the pyrido[1,2-*a*]pyrimidine system is based on the heterocyclization of the available 1,1-bis(1*H*-benzotriazol-1-yl)-3,4,4-trichloro-2-nitrobuta-1,3-diene (**1**) by the action of 2-aminopyridine (**2**). As a result of the reaction, 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidine **3** containing a benzotriazole fragment in position 2 of the pyrido[1,2-*a*]pyrimidine system is formed.[4] In the study of the generality of this synthetic approach, we found that the reaction of 2-aminopyridine (**2**) with 3,4,4-trichloro-1,1-bis-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-diene (**4**) proceeds differently and leads to the formation of 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidine **5** containing not the dimethylpyrazole fragment at position 2, as might be expected by analogy with benzotriazole derivatives, but the 2-aminopyridine fragment[5] (Scheme 1).

Apparently, 3,5-dimethylpyrazole is a better leaving group than benzotriazole, and under the reaction conditions it is substituted by the 2-aminopyridine fragment.

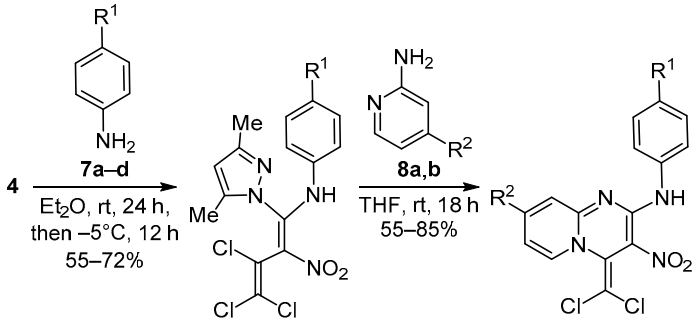
Scheme 1



To test this assumption, we decided to investigate the heterocyclization of 3,4,4-trichloro-2-nitrobuta-1,3-diene derivatives **6a**–**d**, in the molecules of which one of the dimethylpyrazole fragments is replaced by an arylamine fragment such as *p*-anisidine, phenetidine, 4-phenoxyaniline, or 4-bromoaniline. These arylamines are not good leaving groups, therefore we expected that they would not participate in the reaction and would transfer to the structures of the resulting pyrido[1,2-*a*]pyrimidines. This approach may open a convenient route to the synthesis of 2-arylamino-substituted 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidines. The preparation of 3,4,4-trichloro-1-(4-methoxyanilino)-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-diene (**6a**) and 3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1-(4-ethoxyanilino)-2-nitrobuta-1,3-diene (**6b**) was described earlier.[6] 4-Phenoxy- and 4-bromo derivatives **6c**,**d** were obtained similarly by the action of 4-phenoxyaniline (**7c**) or 4-bromoaniline (**7d**) on substituted buta-1,3-diene **4**. The synthesized 1-arylamino-1,3-butadienes **6a**–**d** (Scheme 2) were then reacted with 2-aminopyridine (**8a**) and 2-amino-4-methylpyridine (**8b**).

We have previously shown that the reaction of compound **4** and its bisbenzotriazole analog **1** with amines usually proceeds with the successive substitution of one or both azole groups by amine fragments.[6] One might expect that in the case of the reaction of buta-1,3-dienes **6a**–**d** with 2-aminopyridine (**8a**) and 2-amino-4-methylpyridine (**8b**) the process would be completed at the step of the formation of the corresponding 1-(2-aminopyridino)-1-arylamino-3,4,4-trichloro-2-nitrobuta-1,3-dienes. However, the reaction proceeded differently with the participation of the trichlorovinyl group and led to the formation of 4-(di-

Scheme 2



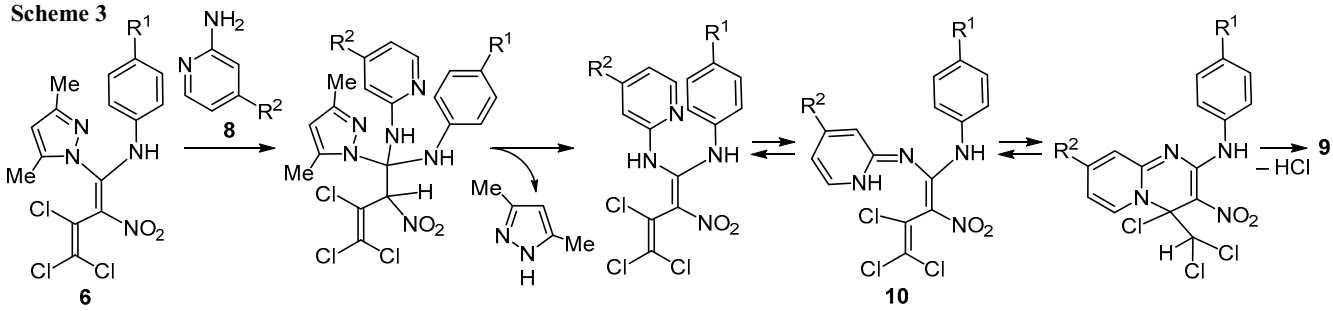
6, **7** **a** R^1 = OMe, **b** R^1 = OEt, **c** R^1 = OPh, **d** R^1 = Br;
8 **a** R^2 = H, **b** R^2 = Me; **9** **a** R^1 = OMe, R^2 = H; **b** R^1 = OMe, R^2 = Me; **c** R^1 = OEt, R^2 = H; **d** R^1 = OEt, R^2 = Me; **e** R^1 = OPh, R^2 = H; **f** R^1 = OPh, R^2 = Me; **g** R^1 = Br, R^2 = H; **h** R^1 = Br, R^2 = Me

chloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidines **9a**–**h** containing the fragment of the corresponding arylamine in position 2 in 55–85% yields (Scheme 2). 1-(2-Aminopyridino)-1-arylamino-3,4,4-trichloro-2-nitrobuta-1,3-dienes were not detected in the reaction mixtures.

Taking into account previously published data on the reactivity of 1,1,2,4,4-pentachloro-2-nitrobuta-1,3-diene derivatives and the possibility of sequential substitution of terminal and internal chlorine atoms in their molecules with the formation of heterocyclic structures,[7] we suggested the following mechanism for the formation of 2-arylamino-substituted 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]-pyrimidines **9a**–**h**. In the first steps, the dimethylpyrazole fragment in compound **6** is substituted by the aminopyridine fragment *via* addition–elimination reactions. As we have already noted, such processes are characteristic of 1,1-bisazolyl-3,4,4-trichloro-2-nitrobuta-1,3-dienes and their derivatives.[6] Next, the isomerization of the aminopyridine fragment into the iminodihydropyridine fragment takes place, followed by intramolecular heterocyclization of compound **10** *via* nucleophilic addition and elimination of HCl with the formation of a polysubstituted pyrido[1,2-*a*]-pyrimidine system (Scheme 3).

The obtained compounds were identified based on the data of IR spectroscopy, ^{1}H, ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis. In the IR spectra of the starting 1-arylamino-3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dienes **6c**,**d** and pyrido-[1,2-*a*]pyrimidines **9a**–**h** there are broadened absorption bands in the region of 3175–3255 cm^{-1} related to the stretching vibrations of the N–H bonds of the secondary amino groups, as well as absorption bands of stretching vibrations of the C=N and C=C bonds in the 1474–1649 cm^{-1} range. The bands of symmetric vibrations with frequencies of 1366–1387 cm^{-1} and antisymmetric vibrations with frequencies of 1559–1593 cm^{-1} are characteristic to nitro groups. It is interesting to note that in the ^{1}H NMR spectrum of the starting 3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitro-1-(4-phenoxyanilino)buta-1,3-diene (**6c**) one of the methyl groups appears as two singlets, whereas in the ^{13}C NMR spectrum, in addition to doubling of the signal of this methyl group, there is also a doubling

Scheme 3



of the signal of the CH group of the pyrazole ring and one of the CH groups of the aromatic fragment, which, apparently, is explained by the influence of the second phenyl ring, since no doubling of signals is observed in the ^{1}H and ^{13}C NMR spectra of compounds **6a**,**b**,**d**.

The mass spectra of compounds **6c** and **9a**–**f** contain groups of molecular ion peaks in which the ratio of the intensities of the isotopic components indicates the presence of three chlorine atoms in the molecule of buta-1,3-diene **6c** (the ratio of intensities is 100:98:32:3.5), whereas in molecules of pyrido[1,2-*a*]pyrimidines **9a**–**f** there are two chlorine atoms (intensity ratio of 100:65:1.1). In the mass spectra of compounds **6d** and **9g**,**h** the groups of molecular ion peaks have a more complex multiplicity due to the presence of bromine isotopes, but the intensity ratio of the isotopic components corresponds to three chlorine atoms and one bromine atom for the starting compound **6d** and one bromine atom and two chlorine atoms for pyrido[1,2-*a*]pyrimidines **9g**,**h**.[8]

We were able to obtain single crystals of 4-(dichloromethylidene)-*N*-(4-ethoxyphenyl)-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (**9d**), and perform X-ray structural analysis. It was found that compound **9d** crystallizes in the $P\bar{1}$ triclinic space group with two molecules in the unit cell and one molecule in the asymmetric cell (Fig. 1).

To conclude, a convenient approach for the preparation of various 2-arylamino-substituted 4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidines has been developed based on the accessible 3,4,4-trichloro-1,1-bis(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-diene.

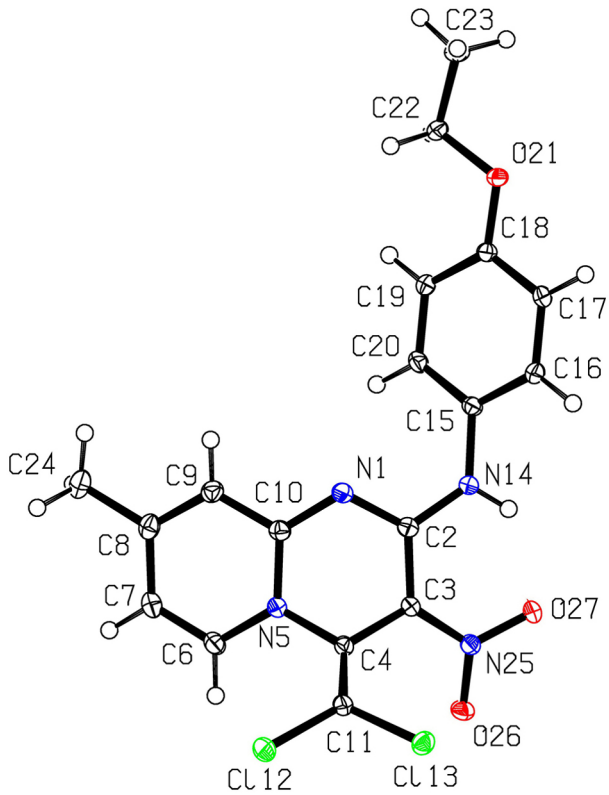


Figure 1. Molecular structure of compound **9d** with atoms represented as thermal vibration ellipsoids of 50% probability.

Experimental

IR spectra were registered on a Thermo Nicolet Protege 460 FT-IR spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance 500 spectrometer (500 and 125 MHz, respectively) in $CDCl_3$ (compounds **6c**,**d**, **9a**–**f**, and **9h**) or in DMSO-d_6 (compound **9g**). Residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H nuclei, 77.2 ppm for ^{13}C nuclei; DMSO-d_6: 2.50 ppm for ^{1}H nuclei, 40.1 ppm for ^{13}C nuclei) were used as the internal standard. The assignment of signals in the ^{13}C NMR spectra was performed using the DEPT procedure. Chromato-mass spectrometry was performed on an Agilent 1200 system with an Agilent 6410 Triple Quad with mass selective detector with electrospray ionization (ESI+, MS2 scanning mode). Agilent ZORBAX Eclipse XDB-C18 (4.6 × 50 mm, 1.8 μm) column. Mobile phase – MeCN–H_2O + 0.05% HCO_2H, gradient elution from 40 to 90% MeCN over 10 min, 0.5 ml/min flow rate. Elemental analysis was performed on a Vario MICRO cube CHNS-analyzer. Halogen content was determined by classical microanalysis according to the modified Pregl's method.[9] Melting points were determined on a Kofler bench. Monitoring of the reaction progress and assessment of the purity of synthesized compounds were done by TLC on Merck Millipore Silica gel 60 F_{254} plates, eluent Et_2O, visualization with iodine vapor.

Reagents and solvents were supplied by Sigma-Aldrich and Merck and were used without additional purification. The starting buta-1,3-dienes **6a**,**b** were synthesized by a published method.[6]

Synthesis of buta-1,3-dienes 6c,d (General method). Amine **7c**,**d** (4.5 mmol) was added to a suspension of 3,4,4-trichloro-1,1-bis(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-diene (**4**) (1.78 g, 4.5 mmol) in Et_2O (20 ml), and the mixture was stirred at room temperature for 24 h, then kept

at –5°C for 12 h. The precipitate was filtered off, washed with cold Et_2O (10 ml) followed by H_2O (20 ml), and dried under reduced pressure. The obtained compounds **6c**,**d** were used further without additional purification.

(*E*)-*N*-[3,4,4-Trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dien-1-yl]-4-phenoxyaniline (6c). Yield 1.55 g (72%), yellow crystals, mp 118–119°C. IR spectrum, ν, cm^{-1}: 3208 (NH), 3058, 1622, 1593 (NO_2), 1577, 1570, 1504, 1488, 1413, 1380 (NO_2), 1370, 1271, 1247, 1180, 1163, 1117, 1070, 1022, 967, 866, 787, 692, 571. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.94 and 1.95 (3H, s, CH_3); 2.27 (3H, s, CH_3); 5.89 (1H, s, H-4 pyrazole); 6.71 (2H, d, *J* = 8.1, H-2,6 Ph); 6.85 (2H, d, *J* = 8.6, H-2',6'); 6.97 (2H, d, *J* = 8.9, H-3',5'); 7.14 (1H, t, *J* = 7.4, H-4 Ph); 7.34 (2H, t, *J* = 8.0, H-3,5 Ph); 11.83 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 11.0, 11.6 (CH_3); 13.7 (CH_3); 106.0; 108.9, 109.9 (C-4 pyrazole); 119.3 (2CH Ar); 119.5 (2CH Ar); 123.6, 123.7 (2CH Ar); 124.3 (CH Ar); 130.1 (2CH Ar); 130.5; 141.6; 141.9; 148.7; 148.8; 152.9; 156.2; 156.6. Mass spectrum, *m*/*z* (I_{rel}, %): 979 $[2M+Na]^+$ (12), 501 $[M+Na]^+$ (18), 405 (100). Found, %: C 52.67; H 3.62; Cl 22.02; N 11.65. $C_{21}H_{17}Cl_3N_4O_3$. Calculated, %: C 52.58; H 3.57; Cl 22.17; N 11.68.

(*E*)-4-Bromo-*N*-[3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dien-1-yl]aniline (6d). Yield 1.20 g (57%), yellow crystals, mp 119–120°C. IR spectrum, ν, cm^{-1}: 3255 (NH), 2926, 1621, 1594, 1567 (NO_2), 1487, 1473, 1437, 1400, 1371 (NO_2), 1283, 1270, 1173, 1114, 1069, 1010, 975, 935, 872, 829, 809, 703, 637, 598, 548, 497. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.92 (3H, s, CH_3); 2.29 (3H, s, CH_3); 5.90 (1H, s, H-4 pyrazole); 6.60 (2H, d, *J* = 8.6, H-2',6'); 7.37 (2H, d, *J* = 8.6, H-3',5'); 11.65 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 11.6 (CH_3); 13.7 (CH_3); 100.0; 109.2; 110.2 (C-4 pyrazole); 120.7; 123.6 (2CH Ar); 126.0; 133.0 (2CH Ar); 135.0; 141.8; 148.4; 153.3. Mass spectrum, *m*/*z* (I_{rel}, %): 487 $[M+Na]^+$ (22), 465 $[M+H]^+$ (43), 301 (100). Found, %: C 38.77; H 2.74; Hal 39.65; N 12.12. $C_{15}H_{12}BrCl_3N_4O_2$. Calculated, %: C 38.62; H 2.59; Hal 39.93; N 12.01.

Synthesis of pyrido[1,2-*a*]pyrimidines 9a–h (General method). Aminopyridine **8a**,**b** (9 mmol) was added to a solution of substituted (*E*)-*N*-[3,4,4-trichloro-1-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-nitrobuta-1,3-dien-1-yl]aniline **6a**–**d** (3 mmol) in THF (30 ml). The reaction mixture was stirred at 20°C for 18 h, then poured into H_2O (200 ml). The precipitate was filtered off, washed with H_2O (2×10 ml) and MeOH (1×10 ml), and dried under reduced pressure. The crude product was heated under reflux in $CHCl_3$ (20 ml) until complete dissolution. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, eluent Et_2O).

4-(Dichloromethylidene)-*N*-(4-methoxyphenyl)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9a). Yield 0.70 g (61%), orange crystals, mp 141–143°C (decomp.). IR spectrum, ν, cm^{-1}: 3227 (NH), 3115, 3092, 3047, 3006, 2962, 2915, 2838, 1635, 1607, 1595, 1562 (NO_2), 1545, 1510, 1479, 1465, 1438, 1390, 1372 (NO_2), 1274, 1244, 1201, 1169, 1149, 1120, 1089, 1023, 877, 828, 755, 700, 614, 550. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.82 (3H, s, OCH_3); 6.84 (1H, t, *J* = 6.7, H Ar); 6.90 (2H, d, *J* = 8.8, H-2',6'); 7.17 (1H, d, *J* = 8.8, H Ar); 7.56 (2H, d, *J* = 8.8, H-3',5'); 7.64 (1H, t, *J* = 7.6, H Ar); 8.02 (1H, d, *J* = 6.6, H Ar); 11.47 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 55.6 (OCH_3); 103.4; 114.8 (CH Ar); 114.2 (2CH Ar); 118.3; 123.2 (CH Ar); 124.7 (2CH Ar); 126.6; 130.2; 136.2 (CH Ar); 140.0 (CH Ar); 152.4; 153.6; 157.4. Mass spectrum, *m*/*z* (I_{rel}, %): 779 $[2M+Na]^+$ (25), 401 $[M+Na]^+$ (12), 379 $[M+H]^+$ (100). Found, %: C 50.69; H 3.27; Cl 18.57; N 14.62. $C_{16}H_{12}Cl_2N_4O_3$. Calculated, %: C 50.68; H 3.19; Cl 18.70; N 14.78.

4-(Dichloromethylidene)-*N*-(4-methoxyphenyl)-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9b). Yield 0.80 g (68%), orange crystals, mp 148–150°C (decomp.). IR spectrum, ν, cm^{-1}: 3175 (NH), 3114, 3062, 2979, 2929, 2886, 1637, 1595, 1563 (NO_2), 1543, 1486, 1425, 1376 (NO_2), 1347, 1299, 1270, 1244, 1197, 1162, 1144, 1120, 1088, 1049, 1027, 974, 929, 834, 771, 757, 708, 680, 632, 562. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.38 (3H, s, CH_3); 3.82 (3H, s, OCH_3); 6.68 (1H, dd, *J* = 7.0, *J* = 1.9, H Ar); 6.90 (2H, d, *J* = 9.0, H-2',6'); 6.98 (1H, s, H Ar); 7.57 (2H, d, *J* = 9.0, H-3',5'); 7.92 (1H, d, *J* = 7.0, H Ar); 11.48 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 21.9 (CH_3); 55.6 (OCH_3); 103.6; 114.2 (2CH Ar); 115.2 (CH Ar); 117.9; 121.8 (CH Ar); 124.6 (2CH Ar); 126.6; 130.4; 135.3 (CH Ar); 152.1; 153.1; 153.9; 157.3. Mass spectrum, *m*/*z* (I_{rel}, %): 807 $[2M+Na]^+$ (14), 393 $[M+H]^+$ (100). Found, %: C 52.03; H 3.79; Cl 17.87; N 14.14. $C_{17}H_{14}Cl_2N_4O_3$. Calculated, %: C 51.93; H 3.59; Cl 18.03; N 14.25.

4-(Dichloromethylidene)-*N*-(4-ethoxyphenyl)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9c). Yield 0.87 g (74%), yellow crystals, mp 136–138°C (decomp.). IR spectrum, ν, cm^{-1}: 3195 (NH), 3145, 3083, 3057, 3000, 2964, 2854, 1649, 1580 (NO_2), 1552, 1503, 1492, 1434, 1414, 1370 (NO_2), 1342, 1303, 1284, 1245, 1191, 1164, 1108, 1066, 1039, 1003, 936, 858, 828, 796, 745. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 4.04 (2H, q, *J* = 7.0, $C\underline{H}_2CH_3$); 6.83 (1H, td, *J* = 6.8, *J* = 1.2, H Ar); 6.89 (2H, d, *J* = 9.0, H-2',6'); 7.17 (1H, d, *J* = 8.8, H Ar); 7.55 (2H, d, *J* = 9.0, H-3',5'); 7.60–7.66 (1H, m, H Ar); 8.02 (1H, dd, *J* = 6.8, *J* = 0.8, H Ar); 11.47 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 15.0 ($CH_2\underline{C}H_3$); 63.8 ($\underline{C}H_2CH_3$); 103.4; 112.8 (CH Ar); 114.8 (2CH Ar); 118.2; 123.2 (CH Ar); 124.7 (2CH Ar); 126.7; 130.1; 136.2 (CH Ar); 140.0 (CH Ar); 152.4; 153.6; 156.8. Mass spectrum, *m*/*z* (I_{rel}, %): 807 $[2M+Na]^+$ (55), 415 $[M+Na]^+$ (28), 393 $[M+H]^+$ (100). Found, %: C 52.12; H 3.65; Cl 18.00; N 14.20. $C_{17}H_{14}Cl_2N_4O_3$. Calculated, %: C 51.93; H 3.59; Cl 18.03; N 14.25.

4-(Dichloromethylidene)-*N*-(4-ethoxyphenyl)-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9d). Yield 0.93 g (76%), yellow crystals, mp 157–159°C (decomp.). IR spectrum, ν, cm^{-1}: 3221 (NH), 3126, 2977, 2926, 1642, 1566 (NO_2), 1541, 1493, 1475, 1458, 1426, 1383 (NO_2), 1353, 1272, 1248, 1198, 1162, 1090, 1050, 1011, 980, 882, 869, 818, 797, 755, 616, 529. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.40 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 2.37 (3H, s, OCH_3); 4.02 (2H, q, *J* = 7.0, $C\underline{H}_2CH_3$); 6.68 (1H, dd, *J* = 7.0,

J = 1.8, H Ar); 6.88 (2H, d, *J* = 9.0, H-2',6'); 6.97 (1H, s, H Ar); 7.55 (2H, d, *J* = 9.0, H-3',5'); 7.91 (1H, d, *J* = 7.0, H Ar); 11.47 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 15.0 ($CH_2\underline{C}H_3$); 21.8 (OCH_3); 63.8 ($\underline{C}H_2CH_3$); 103.6; 114.7 (2CH Ar); 115.2 (CH Ar); 117.8; 121.7 (CH Ar); 124.5 (2CH Ar); 126.6; 130.2; 135.2 (CH Ar); 152.0; 153.1; 153.7; 156.6. Mass spectrum, *m*/*z* (I_{rel}, %): 407 $[M+H]^+$ (100). Found, %: C 53.32; H 4.05; Cl 17.15; N 13.79. $C_{18}H_{16}Cl_2N_4O_3$. Calculated, %: C 53.09; H 3.96; Cl 17.41; N 13.76.

4-(Dichloromethylidene)-3-nitro-*N*-(4-phenoxyphenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9e). Yield 0.73 g (55%), yellow crystals, mp 143–145°C (decomp.). IR spectrum, ν, cm^{-1}: 3189 (NH), 3118, 3100, 3054, 2921, 2854, 1636, 1594, 1559 (NO_2), 1542, 1487, 1419, 1393, 1374 (NO_2), 1347, 1272, 1248, 1196, 1166, 1145, 1122, 1088, 876, 773, 750, 710, 688, 498. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.87 (1H, td, *J* = 6.9, *J* = 1.4, H Ar); 7.00–7.06 (4H, m, H Ar); 7.12 (1H, tt, *J* = 7.4, *J* = 1.1, H Ar); 7.20 (1H, dq, *J* = 9.0, *J* = 0.7, H Ar); 7.35 (1H, d, *J* = 7.4, H Ar); 7.36 (1H, d, *J* = 7.4, H Ar); 7.62–7.69 (3H, m, H Ar); 8.05 (1H, dq, *J* = 6.8, *J* = 0.7, H Ar); 11.54 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 103.5; 113.0 (CH Ar); 118.4; 119.1 (2CH Ar); 119.2 (2CH Ar); 123.2 (CH Ar); 123.6 (CH Ar); 124.6 (2CH Ar); 126.6; 130.0 (2CH Ar); 132.6; 136.3 (CH Ar); 140.1 (CH Ar); 152.4; 153.7; 154.8; 157.3. Mass spectrum, *m*/*z* (I_{rel}, %): 905 (100), 903 $[2M+Na]^+$ (70), 463 $[M+Na]^+$ (51), 441 $[M+H]^+$ (79). Found, %: C 57.35; H 3.27; Cl 15.91; N 12.64. $C_{21}H_{14}Cl_2N_4O_3$. Calculated, %: C 57.16; H 3.20; Cl 16.07; N 12.70.

4-(Dichloromethylidene)-8-methyl-3-nitro-*N*-(4-phenoxyphenyl)-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9f). Yield 0.85 g (62%), yellow crystals, mp 187–189°C (decomp.). IR spectrum, ν, cm^{-1}: 3182 (NH), 3068, 3055, 3036, 2953, 2922, 2853, 1645, 1613, 1602, 1575 (NO_2), 1541, 1505, 1486, 1470, 1425, 1381, 1366 (NO_2), 1359, 1343, 1319, 1289, 1271, 1250, 1232, 1199, 1184, 1169, 1155, 1125, 1088, 1071, 1037, 1020, 1013, 982, 967, 912, 886, 864, 832, 799, 756, 739, 699, 692, 648, 547, 515, 474. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.41 (3H, s, CH_3); 6.70 (1H, dd, *J* = 7.0, *J* = 1.9, H Ar); 6.97–7.07 (5H, m, H Ar); 7.12 (1H, tt, *J* = 7.4, *J* = 1.0, H Ar); 7.35 (1H, d, *J* = 7.4, H Ar); 7.36 (1H, d, *J* = 7.4, H Ar); 7.65 (2H, d, *J* = 9.0, H Ar); 7.95 (1H, d, *J* = 7.0, H Ar); 11.55 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 21.9 (CH_3); 104.9; 115.4 (CH Ar); 117.8; 119.1 (2CH Ar); 119.3 (2CH Ar); 121.8 (CH Ar); 123.6 (CH Ar); 124.6 (2CH Ar); 127.0; 130.0 (2CH Ar); 132.6; 134.4 (CH Ar); 142.1; 153.2; 153.9; 155.5; 160.7. Mass spectrum, *m*/*z* (I_{rel}, %): 931 $[2M+Na]^+$ (16), 477 $[M+Na]^+$ (47), 455 $[M+H]^+$ (100). Found, %: C 58.23; H 3.54; Cl 15.31; N 12.11. $C_{22}H_{16}Cl_2N_4O_3$. Calculated, %: C 58.04; H 3.54; Cl 15.57; N 12.31.

***N*-(4-Bromophenyl)-4-(dichloromethylidene)-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9g)**. Yield 1.09 g (85%), yellow crystals, mp 145–147°C (decomp.). IR spectrum, ν, cm^{-1}: 3244 (NH), 3122, 1636, 1603, 1561 (NO_2), 1547, 1474, 1412, 1377 (NO_2), 1342, 1272, 1247, 1208, 1158, 1122, 1090, 1072, 1035, 1005, 976, 935, 878, 829, 760, 747, 699, 543. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.15 (1H, td, *J* = 6.9, *J* = 1.4, H Ar); 7.31 (1H, d, *J* = 8.6, H Ar); 7.54 (2H, d, *J* = 8.6, H-2',6'); 7.73 (2H, d, *J* = 8.6, H-3',5'); 7.92–8.00 (1H, m, H Ar); 8.59 (1H, dd, *J* = 6.8, *J* = 0.7, H Ar); 11.21 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 103.0; 115.2 (CH Ar); 117.3; 117.5; 122.7 (CH Ar); 125.4 (2CH Ar); 127.4; 132.0 (2CH Ar); 137.5; 138.0 (CH Ar); 142.7 (CH Ar); 152.0; 153.5. Mass spectrum, *m*/*z* (I_{rel}, %): 879 (100), 875 $[2M+Na]^+$ (77), 449 $[M+Na]^+$ (51), 427 $[M+H]^+$ (45). Found, %: C 42.22; H 2.30; Hal 35.01; N 13.02. $C_{15}H_9BrCl_2N_4O_2$. Calculated, %: C 42.09; H 2.12; Hal 35.23; N 13.09.

***N*-(4-Bromophenyl)-4-(dichloromethylidene)-8-methyl-3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-2-amine (9h)**. Yield 0.72 g (55%), yellow crystals, mp 146–148°C (decomp.). IR spectrum, ν, cm^{-1}: 3241 (NH), 3118, 3083, 3055, 2923, 1643, 1607, 1560 (NO_2), 1478, 1467, 1387 (NO_2), 1358, 1338, 1269, 1242, 1205, 1178, 1092, 885, 828, 747, 505. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.42 (3H, s, CH_3); 6.74 (1H, dd, *J* = 7.0, *J* = 1.7, H Ar); 7.03 (1H, s, H Ar); 7.47 (2H, d, *J* = 8.8, H-2',6'); 7.60 (2H, d, *J* = 8.8, H-3',5'); 7.97 (1H, d, *J* = 7.0, H Ar); 11.55 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 22.0 (CH_3); 103.6; 109.1; 115.7 (CH Ar); 118.2; 121.8 (CH Ar); 124.4 (2CH Ar); 126.4; 132.0 (2CH Ar); 135.4 (CH Ar); 136.7; 151.9; 153.6; 153.9. Mass spectrum, *m*/*z* (I_{rel}, %): 907 (100), 903 $[2M+Na]^+$ (78), 463 $[M+Na]^+$ (41), 441 $[M+H]^+$ (59). Found, %: C 43.56; H 2.60; Hal 34.05; N 12.51. $C_{16}H_{11}BrCl_2N_4O_2$. Calculated, %: C 43.47; H 2.51; Hal 34.11; N 12.67.

X-ray structural analysis of compound 9d was performed on a Bruker Smart APEX II diffractometer at 100 K using MoKα radiation (λ 0.71073 Å). The structure was solved by direct methods using the SIR2014 program[10] and refined against F^2 by the least-squares technique in the full-matrix anisotropic approximation using the SHELXL-2014 program.[11] The positions of hydrogen atoms were calculated geometrically and refined according to the "rider" model with $U_{iso}(H) = 1.5U_{eq}(C)$ for the methyl group and $U_{iso}(H) = 1.2U_{eq}(C)$ for other groups. Molecular rendering was done using the PLATON software.[12] The full set of X-ray structural data was deposited at the Cambridge Crystallographic Data Center (deposit CCDC 2001089).

Supplementary information file containing ^{1}H and ^{13}C NMR spectra for compounds **6c**,**d** and **9a**–**h** as well as X-ray structural analysis data for compound **9d** is available at the journal website at http://link.springer.com/journal/10593.

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