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Synthesis of novel tetrahydropyrimido[4,5-*b*][1,6]naphthyridines *via* condensation of 1-benzyl-3,5-bis[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-ones with 6-aminouracils

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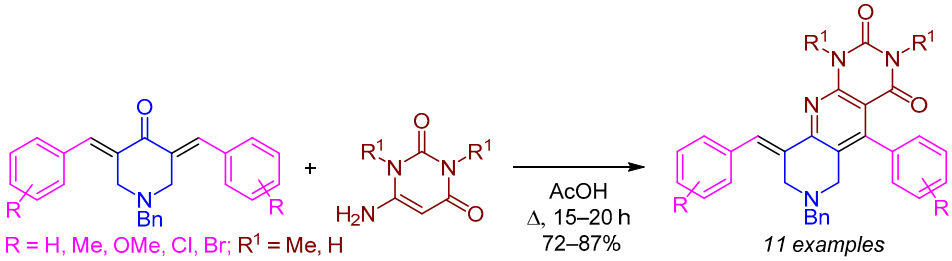


The successful synthesis of novel tetrahydropyrimido[4,5-*b*][1,6]naphthyridine derivatives is reported. 1-Benzyl-3,5-bis[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-ones prepared *via* Knoevenagel condensation of 1-benzyl-4-piperidinone with aromatic aldehydes undergo condensation with 6-aminouracils in acetic acid to afford the desired products. Structures of the products are confirmed by analytical data and X-ray crystallography analysis.

Keywords: 6-aminouracils, 1-benzyl-4-piperidinone, 1,6-naphthyridines.

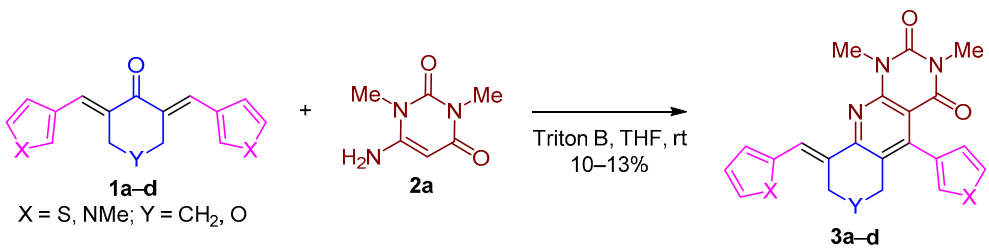
Synthesis of naphthyridine derivatives are of a particular interest due to its diverse biological activity.[1] The functionalized 1,6-naphthyridines are known to exhibit various types of biological properties including antibacterial,[2] anticonvulsant,[3] anti-human cytomegalovirus,[4] anticancer,[5] antiviral, antiretroviral,[6] and antiproliferative activities.

On the other hand, during the past decade, dihydropyrimidines have become an increasingly active area of research because of their anticarcinogenic,[7] antimicrobial,[8] and acetyl cholinesterase inhibitory[9] activities.

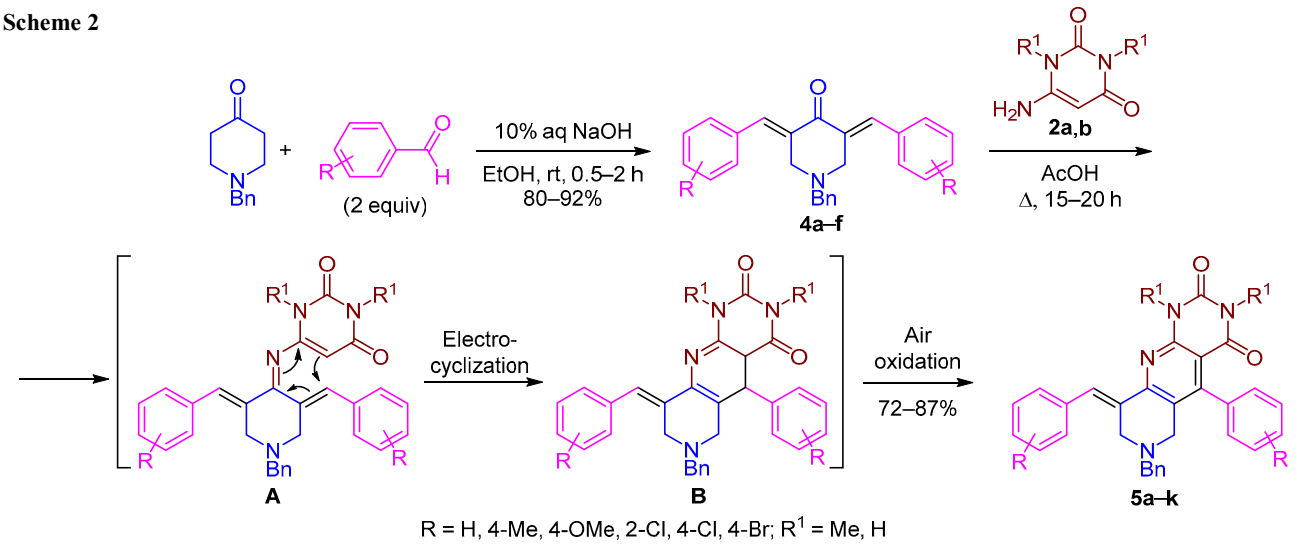
Known methods used for the synthesis of 1,6-naphthyridines include cyclization of tosylhydrazine, carbonyl compounds, and 2-alkynyl-3-formylquinolines,[10] Mitsunobu reaction with glycine derivatives followed by a Dieckmann cyclization in the presence of sodium methoxide,[11] inverse electron demand Diels–Alder reaction between 3,5-dinitro-*N*-methylpyridone and piperidone,[12] and tandem reaction of isoquinoline, dialkyl acetylenedicarboxylates, and 3-chloropentane-2,4-dione or alkyl 3-chloroacetoacetates.[13]

In 2013, a two-component reaction of bischalcones **1a–d** with 6-amino-1,3-dimethyluracil (**2a**) for the synthesis of pyrimidine monoadducts **3a–d** was described.[14] Compounds **3a–d** displayed cytotoxic activity with a massive vacuolation in different human cell lines *in vitro* (Scheme 1).[14] These results prompted us to investigate the two-component reaction of 1-benzyl-3,5-bis[(*E*)-arylmethylidene]-tetrahydropyridin-4(1*H*)-ones **4a–f** with 6-aminouracils **2a**,**b** since these reactions could afford the formation of fused heterocyclic compounds **5a–k** encompassing both 1,6-naphthyridine and tetrahydropyrimidine motifs with

Scheme 1



Scheme 2



individual biological activities (Scheme 2). It should be noted that the synthesis of uracil derivatives is of great importance due to their potential activity as antiviral and anticancer agents.[15]

Initially, 1-benzyl-3,5-bis[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-one derivatives **4a**–**f** were prepared *via* Knoevenagel condensation of 1-benzyl-4-piperidinone with aromatic aldehydes using the previously reported synthetic procedure (Scheme 2).[16]

Adducts **4a**–**f** were subsequently treated with 6-aminouracil **2a**,**b** in AcOH and heated at reflux to afford the desired products **5a**–**k** (Scheme 2, Table 1). We assume that the formation of tetrahydropyrimido[4,5-*b*][1,6]-naphthyridine derivatives **5a**–**k** can be explained by the attack of the NH_2 group to the most reactive carbonyl functionality in compounds **4a**–**f**, which in the acidic conditions resulted in the formation of intermediate **A** (Scheme 2).[16] Subsequent 6π-electron cyclization reaction allows to obtain dihydropyrimidinedione intermediates **B** that under air oxidation process afford products **5a**–**k**.

The structures of products **5a**–**k** were established by elemental analysis, MS, IR, and ^{1}H and ^{13}C NMR spectroscopy. Unambiguous evidence for the structure of compound **5g** was obtained by single crystal X-ray diffraction analysis (Fig. 1).

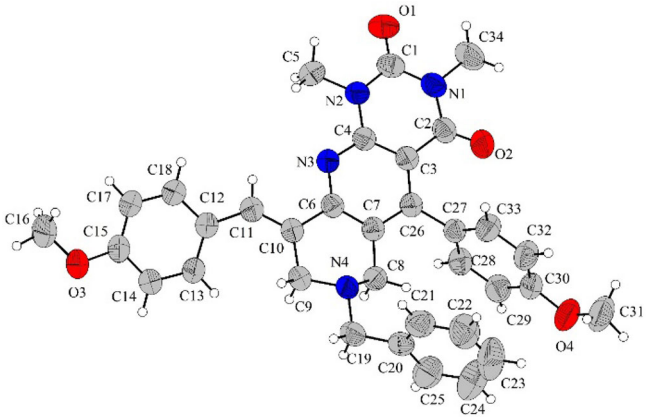


Figure 1. Molecular structure of compound **5g** with atoms represented as thermal vibration ellipsoids of 50% probability.

Table 1. Yields of tetrahydropyrimido[4,5-*b*][1,6]-naphthyridines **5a**–**k**

Adduct	R	6-Aminouracil	R^1	Time, h	Product	Yield, %
4a	H	**2a**	Me	15	**5a**	79
4a	H	**2b**	H	16	**5b**	86
4b	4-Cl	**2a**	Me	18	**5c**	84
4b	4-Cl	**2b**	H	15	**5d**	75
4c	4-Me	**2a**	Me	20	**5e**	87
4c	4-Me	**2b**	H	15	**5f**	81
4d	4-OMe	**2a**	Me	16	**5g**	85
4d	4-OMe	**2b**	H	18	**5h**	92
4e	2-Cl	**2a**	Me	18	**5i**	81
4e	2-Cl	**2b**	H	17	**5j**	78
4f	4-Br	**2a**	Me	15	**5k**	72

In conclusion, the initially prepared 1-benzyl-3,5-bis-[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-one derivative underwent reaction with 6-aminouracils in acetic acid to afford the tetrahydropyrimido[4,5-*b*][1,6]naphthyridines in high yields. These novel structures broaden the scope of hybrid scaffolds obtained from the two-component reaction and many of them may be valuable for medicinal chemistry studies in the future.

Experimental

IR spectra were recorded on a Bomem B100 series spectrophotometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer (500 and 125 MHz, respectively) in DMSO-d_6. Solvent signals were used as internal standard (2.50 ppm for ^{1}H nuclei and 39.5 ppm for ^{13}C nuclei). Mass spectra were recorded on an Agilent Technologies 5937 Series Mass Selective Detector. Elemental analyses were carried out by a Heraeus CHN-O-Rapid automatic elemental analyzer with TCD detection. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected.

All commercially available chemicals and reagents were purchased from Merck Chemical Company and used without further purification.

1-Benzyl-3,5-bis[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-one derivatives **4a**–**f** were obtained by adapting previously reported procedure.[16]

Synthesis of compounds 5a–k (General method). 6-Aminouracil **2a**,**b** (1.0 mmol) was added to a stirring solution of 1-benzyl-3,5-bis[(*E*)-arylmethylidene]tetrahydropyridin-4(1*H*)-one derivative **4a**–**f** (1.0 mmol) in AcOH (3 ml). The mixture was heated at reflux for the appropriate time (see Table 1). After completion of the reaction indicated by TLC, saturated 10% aq solution of $NaHCO_3$ (10 ml) was added and the mixture was extracted with EtOAc (15 ml). The organic phase was dried over Na_2SO_4, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, eluent *n*-hexane–EtOAc, 3:1).

(*E*)-7-Benzyl-9-benzylidene-1,3-dimethyl-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5a). Yield 0.395 g (79%), yellow solid, mp 212–213°C. IR spectrum, ν, cm^{-1}: 2798, 1701, 1654. ^1H NMR spectrum, δ, ppm: 3.10 (3H, s, CH_3); 3.16 (2H, s, $PhCH_2$); 3.47 (2H, s, NCH_2); 3.67 (3H, s, CH_3); 3.72 (2H, s, NCH_2); 7.01–7.14 (7H, m, H Ar); 7.30 (4H, s, H Ar); 7.36 (4H, s, H Ar); 8.10 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 28.3; 30.0; 52.5; 53.1; 60.6; 107.0; 125.0; 127.3; 127.4; 127.6; 128.3; 128.4; 128.9; 129.2; 130.1; 130.5 (2C); 132.5; 136.2; 137.4; 137.9; 149.6; 151.3; 151.7; 153.7; 160.1. Mass spectrum, *m*/*z* (I_{rel}, %): 501 $[M]^+$ (82), 409 (100), 91 (98). Found, %: C 76.80; H 5.67; N 11.28. $C_{32}H_{28}N_4O_2$. Calculated, %: C 76.78; H 5.64; N 11.19.

(*E*)-7-Benzyl-9-benzylidene-5-phenyl-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5b). Yield 0.406 g (86%), yellow solid, mp 227–230°C. IR spectrum, ν, cm^{-1}: 3193, 3053, 2812, 1695, 1551. ^1H NMR spectrum, δ, ppm: 3.18 (2H, s, $PhCH_2$); 3.49 (2H, s, NCH_2); 3.72 (2H, s, NCH_2); 7.04–7.17 (9H, m, H Ar); 7.31–7.41 (6H, m, H Ar); 8.01 (1H, s, =CH); 11.04 (1H, s, NH); 11.50 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 52.6; 53.1; 60.7; 106.7; 124.9; 127.4; 127.5; 127.7; 128.2; 128.4; 129.1; 129.2; 129.9, 130.1; 132.6; 136.2; 137.1; 137.9; 150.7; 151.3; 151.5; 154.4; 161.7. Mass spectrum, *m*/*z* (I_{rel}, %): 472 $[M]^+$ (15), 381 (40), 304 (20), 227 (17), 169 (10), 91 (100). Found, %: C 76.18; H 5.17; N 11.88. $C_{30}H_{24}N_4O_2$. Calculated, %: C 76.25; H 5.12; N 11.86.

(*E*)-7-Benzyl-9-(4-chlorobenzylidene)-5-(4-chlorophenyl)-1,3-dimethyl-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]-naphthyridine-2,4(1*H*,3*H*)-dione (5c). Yield 0.394 g (84%), yellow solid, mp 213–216°C. IR spectrum, ν, cm^{-1}: 2801, 1703, 1651, 1554. ^1H NMR spectrum, δ, ppm: 3.13 (3H, s, CH_3); 3.19 (2H, s, $PhCH_2$); 3.52 (2H, s, NCH_2); 3.68 (3H, s, CH_3); 3.72 (2H, s, NCH_2); 7.04–7.12 (4H, m, H Ar); 7.15–7.22 (3H, m, H Ar); 7.38–7.44 (6H, m, H Ar); 8.07 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 28.4; 30.0; 52.3; 52.8; 60.4; 107.2; 125.0; 127.5; 128.4; 128.5 (2C); 128.9; 129.2, 129.3; 131.9; 132.5; 133.0; 133.1; 135.1; 136.3; 137.9; 149.6; 150.4; 151.3; 153.6; 160.2. Mass spectrum, *m*/*z* (I_{rel}, %): 569 $[M]^+$ (4), 568 (9), 477 (25), 443 (17), 91 (100). Found, %: C 67.42; H 4.71; N 9.80. $C_{32}H_{26}Cl_2N_4O_2$. Calculated, %: C 67.49; H 4.60; N 9.84.

(*E*)-7-Benzyl-9-(4-chlorobenzylidene)-5-(4-chlorophenyl)-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5d). Yield 0.405 g (75%), yellow solid, mp 230–233°C. IR spectrum, ν, cm^{-1}: 3140, 3034, 2825, 1698, 1559. ^1H NMR spectrum, δ, ppm: 3.17 (2H, s, $PhCH_2$); 3.30 (2H, s, NCH_2); 3.68 (2H, s, NCH_2); 7.07–7.17 (7H, m, H Ar); 7.30–7.42 (6H, m, H Ar); 7.98 (1H, s, =CH); 11.09 (1H, s, NH); 11.52 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 52.4; 52.8; 60.4; 106.9; 124.9; 127.5; 128.3; 128.5; 128.8; 129.1; 129.3; 129.6; 131.6; 132.5; 133.0; 133.2; 136.0; 136.9; 138.0; 150.0; 150.6; 151.5; 154.2; 161.8. Mass spectrum, *m*/*z* (I_{rel}, %): 541 $[M]^+$ (28), 540 (52), 449 (34), 415 (18), 91 (100). Found, %: C 66.45; H 4.13; N 10.42. $C_{30}H_{22}Cl_2N_4O_2$. Calculated, %: C 66.55; H 4.10; N 10.35.

(*E*)-7-Benzyl-1,3-dimethyl-9-(4-methylbenzylidene)-5-(*p*-tolyl)-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]-naphthyridine-2,4(1*H*,3*H*)-dione (5e). Yield 0.485 g (92%), yellow solid, mp 205–208°C. IR spectrum, ν, cm^{-1}: 2942, 1702, 1654. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.28 (3H, s, 4-CH_3 Ar); 2.32 (3H, s, 4-CH_3 Ar); 3.09 (3H, s, CH_3); 3.16 (2H, s, $PhCH_2$); 3.60 (2H, s, NCH_2); 3.64 (3H, s, CH_3); 3.68 (2H, s, NCH_2); 6.87 (2H, d, ^3J = 7.7, H Ar); 7.06–7.16 (9H, m, H Ar); 7.22 (2H, d, ^3J = 7.9, H Ar); 8.03 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 21.3 (2C); 28.3; 29.9; 52.6; 53.2; 60.7; 106.9; 125.1; 127.3; 127.4; 128.4; 128.9; 129.1; 129.5; 130.2; 130.5; 131.7; 133.4; 134.5; 136.7; 138.0; 138.1; 149.6; 151.3; 151.8; 153.8; 160.1. Mass spectrum, *m*/*z* (I_{rel}, %): 529 $[M]^+$ (78), 438 (100), 424 (31), 91 (67). Found, %: C 77.35; H 6.05; N 10.68. $C_{34}H_{32}N_4O_2$. Calculated, %: C 77.25; H 6.10; N 10.60.

(*E*)-7-Benzyl-9-(4-methylbenzylidene)-5-(*p*-tolyl)-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5f). Yield 0.436 g (87%), yellow solid, mp 220–222°C. IR spectrum, ν, cm^{-1}: 3162, 3025, 2804, 1703, 1551. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.31 (3H, s, 4-CH_3 Ar); 2.33 (3H, s, 4-CH_3 Ar); 3.19 (2H, s, $PhCH_2$); 3.51 (2H, s, NCH_2); 3.71 (2H, s, NCH_2); 6.93 (2H, d, ^3J = 8.5, H Ar); 7.09–7.21 (11H, m, H Ar); 8.02 (1H, s, =CH); 11.01 (1H, s, NH); 11.45 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 21.3 (2C); 52.7; 53.2; 60.7; 106.6; 125.0; 127.4; 127.5; 128.4; 128.8; 129.2; 129.7; 129.9; 130.0; 130.1; 131.7; 133.4; 134.1; 136.7; 138.0; 150.7; 151.4; 151.5; 154.5; 161.7. Mass spectrum, *m*/*z* (I_{rel}, %): 501 $[M]^+$ (20), 500 (60), 409 (35), 317 (10), 91 (100). Found, %: C 76.74; H 5.70; N 10.99. $C_{32}H_{28}N_4O_2$. Calculated, %: C 76.78; H 5.64; N 11.19.

(*E*)-7-Benzyl-9-(4-methoxybenzylidene)-5-(4-methoxyphenyl)-1,3-dimethyl-6,7,8,9-tetrahydropyrimido[4,5-*b*]-[1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5g). Yield 0.476 g (85%), yellow solid, mp 215–217°C. IR spectrum, ν, cm^{-1}: 2953, 1708, 1660, 1605. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.09 (3H, s, CH_3); 3.17 (2H, s, $PhCH_2$); 3.47 (2H, s, NCH_2); 3.63 (3H, s, CH_3); 3.68 (2H, s, NCH_2); 3.75 (3H, s, OCH_3); 3.76 (3H, s, OCH_3); 6.82–6.92 (6H, m, H Ar); 7.04–7.20 (5H, m, H Ar); 7.27 (2H, d, ^3J = 8.8, H Ar); 8.01 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 52.6; 53.8; 55.4 (2C); 55.6 (2C); 60.8; 106.8; 113.7; 114.4; 125.0; 127.4; 128.4; 128.7 (2C); 129.2; 129.4; 130.3; 130.5; 132.9; 138.0; 149.6; 151.3; 151.4; 154.0; 158.9; 159.5; 160.1. Mass spectrum, *m*/*z* (I_{rel}, %): 561 $[M]^+$ (81), 470 (85), 454 (26), 440 (37), 91 (100). Found, %: C 72.60; H 5.90; N 10.10. $C_{34}H_{32}N_4O_4$. Calculated, %: C 72.84; H 5.75; N 9.99.

(*E*)-7-Benzyl-9-(4-methoxybenzylidene)-5-(4-methoxyphenyl)-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5h). Yield 0.430 g (81%),

yellow solid, mp 238–240°C. IR spectrum, ν, cm^{-1}: 3161, 3031, 2831, 1689, 1553. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.19 (2H, s, $PhCH_2$); 3.30 (2H, s, NCH_2); 3.49 (2H, s, NCH_2); 3.75 (3H, s, OCH_3); 3.76 (3H, s, OCH_3); 6.84–6.97 (6H, m, H Ar); 7.10–7.19 (5H, m, H Ar); 7.27 (2H, d, ^3J = 8.8, H Ar); 7.98 (1H, s, =CH); 10.97 (1H, s, NH); 11.40 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 52.7; 53.4; 55.4; 55.6; 60.8; 106.5; 113.6; 114.6; 125.0; 127.4; 128.5; 128.7; 129.0; 129.2; 129.9; 130.6; 131.6; 131.7; 138.0; 150.6; 151.0; 151.5; 154.7; 158.9; 159.5; 161.7. Mass spectrum, *m*/*z* (I_{rel}, %): 532 $[M]^+$ (17), 441 (38), 334 (25), 227 (22), 169 (8), 91 (100). Found, %: C 72.08; H 5.37; N 10.55. $C_{32}H_{28}N_4O_4$. Calculated, %: C 72.17; H 5.30; N 10.52.

(*E*)-7-Benzyl-9-(2-chlorobenzylidene)-5-(2-chlorophenyl)-1,3-dimethyl-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]-naphthyridine-2,4(1*H*,3*H*)-dione (5i). Yield 0.467 g (81%), yellow solid, mp 208–210°C. IR spectrum, ν, cm^{-1}: 3065, 1705, 1663, 1555. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.13–3.21 (5H, m, CH_3, $PhCH_2$); 3.44–3.63 (7H, m, CH_3, $2NCH_2$); 6.97–7.18 (6H, m, H Ar); 7.23–7.37 (5H, m, H Ar); 7.44 (1H, d, ^3J = 8.1, H Ar); 7.52 (1H, d, ^3J = 7.7, H Ar); 8.21 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 28.4; 29.9; 52.0; 52.2; 60.0; 107.6; 116.0 (2C); 124.9; 127.4 (2C); 127.5; 127.6; 128.4; 129.0; 129.1; 129.3; 129.8; 129.9; 130.2; 130.8; 131.1; 133.7; 133.9; 134.2; 136.2; 137.8; 148.8; 149.7; 151.2; 153.7; 160.0. Mass spectrum, *m*/*z* (I_{rel}, %): 570 $[M]^+$ (30), 568 (40), 534 (15), 477 (13), 441 (45), 91 (100). Found, %: C 67.49; H 4.65; N 9.79. $C_{32}H_{26}Cl_2N_4O$. Calculated, %: C 67.49; H 4.60; N 9.84.

(*E*)-7-Benzyl-9-(2-chlorobenzylidene)-5-(2-chlorophenyl)-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]naphthyridine-2,4(1*H*,3*H*)-dione (5j). Yield 0.422 g (78%), yellow solid, mp 233–235°C. IR spectrum, ν, cm^{-1}: 3175, 3051, 2834, 1688, 1566. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.10 (1H, d, ^3J = 15.6, PhCH); 3.21 (1H, d, ^3J = 15.6, PhCH); 3.43–3.58 (4H, m, $2NCH_2$); 7.05–7.53 (13H, m, H Ar); 8.13 (1H, s, =CH); 11.15 (1H, s, NH); 11.63 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 52.2; 52.4; 60.0; 107.3; 124.7; 127.4; 128.4; 129.0; 129.1; 129.2; 129.8; 129.9; 130.2; 130.9; 131.2; 133.7; 134.4; 135.9; 136.3; 137.8; 148.3; 150.6; 151.5; 154.3; 161.5. Mass spectrum, *m*/*z* (I_{rel}, %): 541 $[M]^+$ (20), 540 (53), 506 (22), 449 (21), 415 (27), 91 (100). Found, %: C 66.47; H 4.22; N 10.56. $C_{30}H_{22}Cl_2N_4O_2$. Calculated, %: C 66.55; H 4.10; N 10.35.

(*E*)-7-Benzyl-9-(4-bromobenzylidene)-5-(4-bromophenyl)-1,3-dimethyl-6,7,8,9-tetrahydropyrimido[4,5-*b*][1,6]-naphthyridine-2,4(1*H*,3*H*)-dione (5k). Yield 0.472 g (72%), yellow solid, mp 238–239°C. IR spectrum, ν, cm^{-1}: 2932, 2084, 1700, 1650. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.09 (3H, s, CH_3); 3.16 (2H, s, $PhCH_2$); 3.44 (2H, s, NCH_2); 3.63 (3H, s, CH_3); 3.68 (2H, s, NCH_2); 6.87 (2H, d, ^3J = 7.7, H Ar); 7.05–7.16 (9H, m, H Ar); 7.22 (2H, d, ^3J = 7.9, H Ar); 8.03 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 28.3; 29.0; 52.3; 52.8; 60.0; 106.0; 115.5; 124.5; 126.0; 128.4; 128.5; 128.9; 129.0; 129.3; 132.1; 132.5; 133.0; 134.0; 135.7; 136.3; 137.8; 150.0; 150.6; 152.7; 153.4; 161.0. Mass spectrum, *m*/*z* (I_{rel}, %): 658 $[M]^+$ (26), 656 (23), 567 (31), 487 (14), 91 (100). Found, %: C 58.36; H 3.96; N 8.57. $C_{32}H_{26}Br_2N_4O_2$. Calculated, %: C 58.38; H 3.98; N 8.51.

X-ray structural study of compound 5g was performed on a MARresearch diffractometer equipped with mar345 Image Plate Detector System (MoKα radiation, λ 0.71073 Å, 295 K). The structure was solved by direct methods using SHELXS-97 and the obtained model refined with SHELXL-2014.[17] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed at calculated positions and refined using the "rider" model. Full crystallographic data is deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1941896).

Supplementary information file containing ^1H and ^{13}C NMR spectra of compounds **5a**–**k** is available at the journal website at http://link.springer.com/journal/10593.

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