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Regioselective Direct C−H Arylations of Protected Uracils. Synthesis of 5- and 6-Aryluracil Bases

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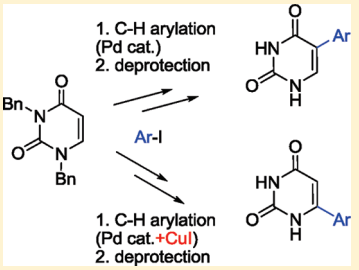
Supporting Information

ABSTRACT: A new regioselective synthesis of 5- and 6-aryluracil bases based on direct C−H arylations of diverse 1,3-protected uracils has been developed. Benzyl-protected uracils were selected as the most practical in terms of stability during the arylation and facile cleavage of the benzyl groups. Pd-catalyzed C−H arylations in the absence of CuI gave preferentially 5-aryl-, whereas the reactions in the presence of CuI gave 6-aryl-1,3-dibenzyluracils. Final deprotection either by transfer hydrogenolysis over Pd/C or by treatment with BBr_3 gave the desired free arylated uracil bases in good yields.



INTRODUCTION

Diverse uracil bases and nucleosides bearing aryl groups at positions 5 or 6 display a wide range of biological activities[1] (cytostatic, antiviral, antagonists of GnRH, etc.). Arylation at position 5 is often used for labeling of nucleotides and DNA for applications in bioanalysis or chemical biology.[2] The 5- or 6-aryluracils are most often prepared by heterocyclizations[3] or by cross-coupling reactions[4] of halouracils with arylboronic acids or -stannanes or metalated uracils with aryl halides. However, still some aryluracil derivatives are difficult to prepare, and therefore, development of alternative methodologies is of interest. In addition, cross-couplings, N-alkylation/arylation, and other reactions would be desirable to be combined in regioselective cascades in order to prepare highly substituted heterocycles. Direct C−H arylations[5] have recently emerged as an alternative to cross-couplings, and we[6] and others[7] have repeatedly shown that they are complementary and could be used for multiple substitutions of diverse heterocycles. On the other hand, there were only scarce examples of C−H arylations of electron-poor pyrimidines[8] (usually using the corresponding N-oxides[9]).

In our recent preliminary communication[10] we reported regioselective Pd-catalyzed and/or Cu-mediated direct C−H arylations of 1,3-dimethyluracil. We found that reactions in the absence of CuI provided 5-aryl-1,3-dimethyluracils as a major products, whereas the reactions in the presence of CuI gave preferentially 6-aryl-1,3-dimethyluracils. However, this chemistry did not work in unsubstituted uracil and the methyl groups at N1 and N3 are not easily cleavable. Therefore, it was needed to develop an efficient protection strategy for uracil C−H arylations. In this paper, we report on the C−H arylations of diverse protected uracils and development of a practical synthesis of free arylated uracil bases.

RESULTS AND DISCUSSION

As mentioned before, the previously reported regioselective C−H arylation was developed for 1,3-dimethyluracil (**1**). Three different sets of conditions were developed (Scheme 1, Table 1) and applied in regioselective direct arylation with 4-tolyl iodide **9a**: (A) $Pd(OAc)_2$ in combination with $P(C_6F_5)_3$ in the presence of Cs_2CO_3, (B) the same catalyst in combination with 3 equiv of CuI, and (C) CuI and Cs_2CO_3 in the absence of $Pd(OAc)_2$ and ligand. The reaction in the absence of CuI gave the 5-aryl-1,3-dimethyluracil **10a** as major product (entry 1), whereas the reactions in the presence of CuI (conditions B or C, entries 2 and 3) gave mainly or exclusively 6-aryl-1,3-dimethyluracil **11a**. The explanation of the dichotomy is probably the switch of the mechanism from concerted metalation−deprotonation (CMD)[11] to the cupration/Ullmann coupling.[12,7e] The reactions did not proceed for 1,3-unsubstituted uracil base, and therefore, for the access to free aryluracil bases, we needed a suitable protection at N1 and N3 that should be compatible with the harsh conditions of the C−H arylations but should be cleavable at the end without decomposition of the aryluracils. Thus, we have prepared (by literature procedures) a set of protected uracils **2**−**8** bearing diverse N-protecting groups: silyl (TMS,[13a] TBDMS[13b]), benzyloxymethyl (BOM),[13c] benzoyl (Bz),[13d] methoxyethoxymethyl (MEM),[13c] *p*-methoxybenzyl (PMB),[13e] and benzyl (Bn).[13e] They were all tested in C−H arylation reactions with 4-iodotoluene **9a** in order to test the stability of the protecting groups under the harsh C−H arylation conditions either in the absence (conditions A) or in the presence of CuI (conditions B) in the presence of Cs_2CO_3 at 160 °C (Scheme 1, Table 1). The Cu-catalyzed reaction in the

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Scheme 1. C−H Arylation of 1−8

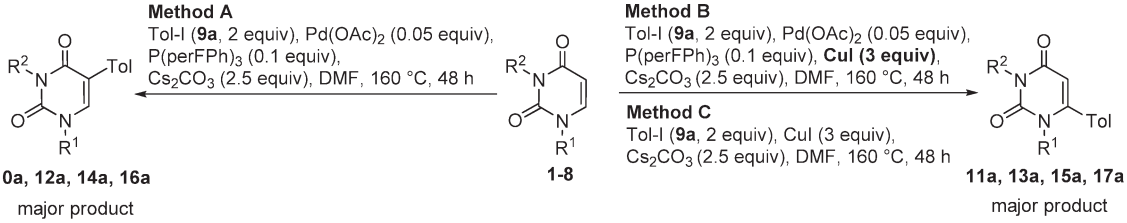

Table 1. C−H Arylation of Diverse Protected Uracils 1−8

		protecting group			products				
entry	compound	R^1	R^2	method	5-isomer	yield (%)	6-isomer	yield (%)	ratio
1[b]	**1**	$-CH_3$	$-CH_3$	A	**10a**	53	**11a**	9	86:14
2[b]	**1**	$-CH_3$	$-CH_3$	B	**10a**	5	**11a**	73	6:94
3[b]	**1**	$-CH_3$	$-CH_3$	C	**10a**	0	**11a**	35	0:100
4	**2**	TMS	TMS				unstable		
5	**3**	TBDMS	TBDMS				unstable		
6	**4**	BOM	BOM	A			complex mixture		
7	**4**	BOM	BOM	B			complex mixture		
8	**5**	H	Bz	A			complex mixture		
9	**5**	H	Bz	B			complex mixture		
10	**6**	MEM	MEM	A	**12a**	24	**13a**	0	100:0
11	**6**	MEM	MEM	B	**12a**	6	**13a**	19	25:75[a]
12	**7**	PMB	PMB	A	**14a**	47	**15a**	6	88:12
13	**7**	PMB	PMB	B	**14a**	8	**15a**	46	14:86
14	**7**	PMB	PMB	C	**14a**	4	**15a**	34	10:90
15	**8**	Bn	Bn	A	**16a**	45	**17a**	7	86:14
16	**8**	Bn	Bn	B	**16a**	10	**17a**	66	14:86
17	**8**	Bn	Bn	C	**16a**	4	**17a**	42	9:91

[a] Ratio from ^{1}H NMR spectra. [b] Taken from ref 10.

absence of Pd gave exclusively 6-substituted derivatives but in lower conversions (Method C).

Silylated uracils **2** and **3** (entries 4, 5) were unstable under the reaction conditions and quickly decomposed. The use of BOM-protected uracil **4** and 3-benzoyluracil (**5**) gave inseparable complex mixtures (entries 6−9). The MEM-protected uracil **6** was stable but gave only moderate conversions to 5-tolyl (**12a**) (the only product under conditions A, entry 10) and/or 6-tolyl (**13a**) (major product under conditions B, entry 11) derivatives. The most stable and efficient protective groups were the benzyl-type substituents: PMB or Bn. The corresponding benzylated uracils **7** and **8** reacted in almost the same manner and efficiency as the parent 1,3-dimethyluracil (**1**). The reactions in the absence of CuI (conditions A, entries 12 and 15) gave the 5-tolyluracils **14a** or **16a** as major products (ca. 7:1) in acceptable yields (47% and 45%, respectively). The Pd-catalyzed reactions in the presence of CuI (conditions B, entries 13, 16) provided the 6-tolyluracils **15a** or **17a** as major products (ca. 6:1) in reasonable yields (46% and 66%, respectively). The Cu-mediated reactions in the absence of Pd gave lower conversions (entries 14, 17).

The next task was to develop an efficient deprotection protocol for the benzylated aryluracils. The methods were tested on PMB- and Bn- protected 5-tolyluracils **14a** and **16a** (Scheme 2, Table 2).

The deprotection of bis-PMB-uracil **14a** was attempted by treatment with neat refluxing TFA,[14] $Ce(NH_4)_2(NO_3)_6$,[13e] and DDQ[15] (entries 1−3), but all of these reactions were unsuccessful (either no reaction or complex mixtures). Catalytic transfer hydrogenolysis[16] with ammonium formate over 10% Pd/C (1.1 equiv) gave only selective cleavage of one PMB group at N1 to afford monoprotected 3-PMB-derivative **18a** in 82% (entry 4). Only the treatment of **14a** with BBr_3[17] led to complete cleavage of both PMB groups to give the desired 5-tolyluracil (**20a**) in moderate yield of 62% (entry 5). Deprotection of benzyl-protected uracil **16a** was performed using catalytic transfer hydrogenation with ammonium formate over 10% Pd/C.[16] The use of 1.1 equiv of Pd/C provided a complete and efficient deprotection to give uracil **20a** in almost quantitative yield (entry 7). Decrease of the loading of Pd/C to 0.54 equiv led to incomplete deprotection giving the 3-benzyluracil **19a** as the major product in 80% yield accompanied by only minor amount of **20a** (15%). The use of BBr_3[17] in refluxing xylene converted protected uracil (**16a**) to uracil **20a** in 15% yield.

On the basis of these results, we selected benzyl protection for the preparation of arylated uracil bases. 1,3-Dibenzyluracil (**8**) was used as starting compound in a series of direct C−H arylations with diverse aryl halides **9a**−**9g** under the above-mentioned conditions (A) $Pd(OAc)_2$, $P(C_6F_5)_3$ in the presence

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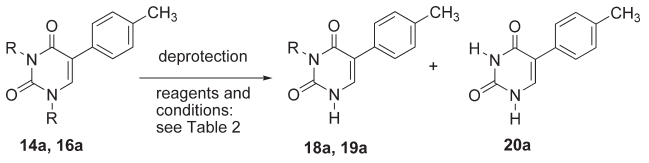
Table 2. Deprotection of 14a, 16a

entry	compounds	R	reagents	yield of **18a**/**19a** (%)	yield of **20a** (%)
1	**14a**	PMB	TFA[a]	0	0
2	**14a**	PMB	$Ce(NH_4)_2(NO_3)_6$[b]	complex mixture	complex mixture
3	**14a**	PMB	DDQ[c]	0	0
4	**14a**	PMB	NH_4HCO_2, 10% Pd/C (1.1 equiv)[d]	82 (**18a**)	0
5	**14a**	PMB	BBr_3[e]	0	62
6	**16a**	Bn	NH_4HCO_2, 10% Pd/C (0.54 equiv)[f]	80 (**19a**)	15
7	**16a**	Bn	NH_4HCO_2, 10% Pd/C (1.1 equiv)[d]	0	98
8	**16a**	Bn	BBr_3[g]	0	15

[a] TFA; reflux; 65 °C. [b] $Ce(NH_4)_2(NO_3)_6$ (4 equiv), CH_3CN/H_2O 3:1, rt; 3 h. [c] DDQ, DCM/H_2O 5:1, rt, 3.5 days. [d] 10% Pd/C (1.1 equiv), NH_4HCO_2, MeOH, 72 °C, 17 h. [e] BBr_3, *m*-xylene, pressure tube 140 °C, 5 h. [f] 10% Pd/C (0.54 equiv), NH_4HCO_2, MeOH, 72 °C, 17 h. [g] BBr_3, *m*-xylene, reflux, 140 °C, 19 h.

Scheme 2. Deprotection of 14a, 16a



of Cs_2CO_3 and (B) the same catalyst and base in the presence of 3 equiv of CuI (Scheme 3, Table 3). The reactions in the absence of CuI (conditions A) gave 5-aryl-1,3-dibenzyluracils **16a**−**g** as major products (selectivities 4:1 to 9:1) in 19−70% yields (entries 1,3,5,7,9,11,13). In all cases minor amounts of the other regioisomer (6-aryluracils **17a**−**g**) were also isolated. More bulky and less reactive aryl bromides **9f** and **9g** gave generally lower yields. The reactions in the presence of CuI gave predominantly (3:1−7:1) or even exclusively (for **9b**) 6-aryl-1,3-dibenzyluracils **17a**−**g** in 28−66% yields (entries 2, 4, 6, 8, 10, 12, 14). The regioisomers were separable by column chromatography (1% of ethyl acetate in toluene) and were assigned by HMBC NMR spectroscopy. Both electron-rich (2-bromothiofene, 2-bromofurane) and electron-poor (3-iodopyridine, 9-benzyl-6-iodopurine) hetaryl halides were also examined in these reactions under conditions A and B, but in all cases the reactions did not proceed. Apparently this methodology is only applicable to carbocyclic aryl halides.

Two different cleavage procedures D (10% Pd/C, ammonium formate, CH_3OH, refux 72 °C, 17 h) and E (BBr_3, *m*-xylene, 140 °C, pressure tube, 5 h) were further used in deprotection of 5- and 6-aryl-1,3-dibenzyluracils. The 5-aryl isomers **16a**−**d** and 6-aryl isomers **17a**−**d** bearing small electron-rich aryl groups were readily deprotected by transfer hydrogenolysis by ammonium formate over Pd/C (conditions D) to give the desired free 5-aryl- **20a**−**d** and 6-aryluracil bases **22a**−**d** in quantitative yields. The transfer hydrogenation of the 4-fluorophenyl derivatives **16e** and **17e** gave inseparable mixtures with the products of dehalogenation. Therefore, we used the treatment with BBr_3 which afforded quantitatively the fully deprotected 6-aryluracil **22e**. The corresponding 5-(fluorophenyl)uracil was unstable under these conditions and decomposed. In the case of compounds bearing bulky aromatic substituents at position 5 and 6 (**16f**, **16g**, **17f**, and **17g**), we observed only partial deprotection under conditions D giving 3-benzyluracils **19f**, **19g**, **21f**, and **21g** as major products. The catalytic hydrogenolysis over Pd/C was not improved by the use of H_2 or cyclohexadiene. Therefore, these compounds were deprotected by treatment with BBr_3 in overheated xylene (in sealed tube). Under those conditions the deprotection of **16e**−**g** and **17e**−**g** proceeded readily to afford the desired uracil bases **20f**, **20g** and **22e**−**g** in almost quantitative yields (apart from **22g**, obtained in moderate 38% yield).

In conclusion, a new method for the synthesis of 5-aryluracil and 6-aryluracil bases has been developed, based on the application of regioselective C−H arylations to 1,3-dibenzyluracil followed by deprotection. The Pd-catalyzed C−H arylations under Pd catalysis gave preferentially 5-aryluracils, whereas in the presence of CuI the regioselectivity reverted to 6-aryluracils. The debenzylation was performed either by transfer hydrogenolysis with ammonium formate over Pd/C or by treatment with BBr_3 (for more bulky aryl groups).

EXPERIMENTAL SECTION

General. All starting aryl halides **9a**−**g**, $Pd(OAc)_2$, $P(C_6F_5)_3$, copper(I) iodide (purum), Cs_2CO_3, and other reagents were purchased from commercial suppliers and used without any further treatment. Dry DMF, methanol, and *m*-xylene was used as received from supplier. Cs_2CO_3 is extremely hygroscopic and must be kept away from moisture. Cs_2CO_3 was dried at 500 °C under vacuum for 10 min prior to each use. All C−H arylations were carried out in evacuated flame-dried glassware with magnetic stirring under argon atmosphere. All compounds were fully characterized by NMR, and spectra were recorded on a 600 MHz (^1H at 600 MHz, ^{13}C at 151 MHz) or on a 500 MHz (500 MHz for ^1H and 125.7 MHz for ^{13}C) spectrometer. ^1H and ^{13}C resonances were assigned by analysis of ^1H, ^{13}C-APT, H,C-HSQC and H,C-HMBC spectra. For monoprotected derivatives, H,C-HMBC measurements showed characteristic cross-peaks between CH_2-Ph and C-2,6 (1-benzyl derivative), and CH_2-Ph and C-2,4 (3-benzyl derivative). The samples were measured in $CDCl_3$ and chemical shifts (in ppm, δ scale) were referenced to TMS as internal standard or in DMSO-d_6 referenced to the residual solvent signal (^1H NMR δ 2.50 ppm, ^{13}C NMR 39.7 ppm). Coupling constants (J) are given in Hz. IR spectra (wavenumbers in cm^{-1}) were recorded using KBr technique (Bruker IFS 88 spectrometer) or using ATR technique (Bruker Alpha FT-IR spectrometer). High resolution mass spectra were measured on a LTQ Orbitrap XL (Thermo Fisher Scientific) spectrometer using EI or ESI ionization technique. Melting points were determined on a Kofler block and are uncorrected. Elemental analyses were measured on PE 2400 Series II CHNS/O (Perkin-Elmer, USA, 1999).

Method A. General Procedure for C−H Arylation of 1,3-Dibenzyluracil 8 with Aryl Halides 9a−g at the C-5 Position. DMF (6 mL) was added through a septum to an argon-purged vial

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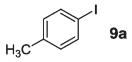
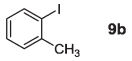
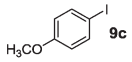
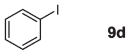
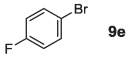
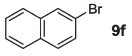
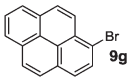
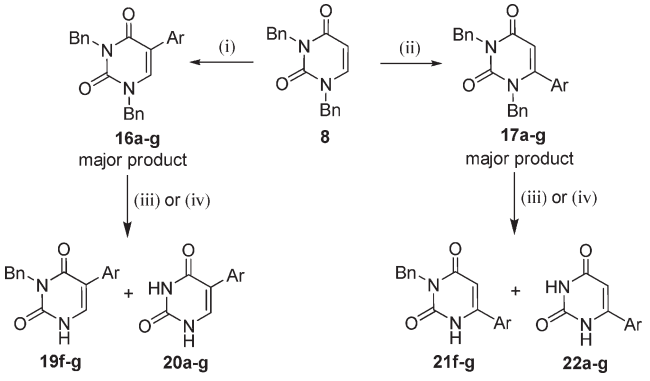
Table 3. C−H Arylations of 1,3-Dibenzyluracil 8 with Diverse Aryl Halides and Following Deprotection of 5- and 6-Regioisomers

Entry	Ar-X	Method	Yield of **16** (%)	Yield of **17** (%)	Ratio **16**:**17**	Deprot. method	Yield of **20** (%)	Yield of **22** (%)
1	 **9a**	A	45	7	87:13	D	98	-
2		B	10	66	14:86	D	-	97
3	 **9b**	A	70	18	79:21	D	97	-
4		B	0	28	0:100	D	-	94
5	 **9c**	A	45	9	86:14	D	95	-
6		B	12	38	25:75	D	-	92
7	 **9d**	A	47	8	85:15	D	97	-
8		B	7	42	15:85	D	-	94
9	 **9e**	A	49	7	90:10	D	compl. mix.	-
						E	decomp.	-
10		B	8	24	25:75	D	-	compl. mix.
						E	-	98
11	 **9f**	A	19	4	83:17	D	0 (42% **19f**)	-
						E	63	-
12		B	8	33	20:80	D	-	0 (98% **21f**)
						E	-	70
13	 **9g**	A	25	3	89:11	D	0 (67% **19g**)	-
						E	98	-
14		B	8	50	14:86	D	-	0 (83% **21g**)
						E	-	38

Scheme 3. Preparative C−H Arylations of 8 and Subsequent Deprotection[a]



[a] Reagents and conditions. (i) Method A: Ar-X (**9a**−**g**, 2 equiv), $Pd(OAc)_2$ (0.05 equiv), $P(C_6F_5)_3$ (0.1 equiv), Cs_2CO_3 (2.5 equiv), DMF, 160 °C, 48 h. (ii) Method B: Ar-X (**9a**−**g**, 2 equiv), $Pd(OAc)_2$ (0.05 equiv), $P(C_6F_5)_3$ (0.1 equiv), CuI (3 equiv), Cs_2CO_3 (2.5 equiv), DMF, 160 °C, 48 h. (iii) Method D: 10% Pd/C, NH_4HCO_2, CH_3OH, refux 72 °C, 17 h. (iv) Method E: BBr_3, *m*-xylene, 140 °C, pressure tube, 5 h.

containing a 1,3-dibenzyluracil (**8**, 292 mg, 1 mmol), aryl halide (**9a**−**g**, 2 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 5 mol %), $P(C_6F_5)_3$ (53.2 mg, 0.1 mmol, 10 mol %) and Cs_2CO_3 (814 mg, 2.5 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 120 g of silica gel in gradient toluene to 1% ethyl acetate in toluene to give regioisomer substituted in the C-5 position (**16a**−**g**) as a major product and regioisomer at the C-6 position (**17a**−**g**) as a minor product.

Method B. General Procedure for C−H Arylation of 1,3-Dibenzyluracil 8 with Aryl Halides 9a−g at the C-6 Position. DMF (6 mL) was added through a septum to an argon-purged vial containing a 1,3-dibenzyuracil (**8**, 292 mg, 1 mmol), aryl halide (**9a**−**g**, 2 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 5 mol %), $P(C_6F_5)_3$ (53.2 mg, 0.1 mmol, 10 mol %), CuI (571 mg, 3 mmol) and Cs_2CO_3 (814 mg, 2.5 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 120 g of silica gel in gradient toluene to 1% ethyl acetate in toluene to give regioisomer substituted in the C-6 position (**17a**−**g**) as a major product and regioisomer at the C-5 position (**16a**−**g**) as a minor product.

Method C. General Procedure for C−H Arylation of Protected Uracils 7, 8 with 4-Iodotoluene 9a at the C-6 Position in the Absence of Pd Catalyst and Ligand. DMF (3 mL) was added through a septum to an argon-purged vial containing protected uracils (**7**, **8**, 0.5 mmol), 4-iodotoluene (**9a**, 218 mg, 1 mmol), CuI (286 mg, 1.5 mmol) and Cs_2CO_3 (407 mg, 1.25 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 60 g of silica gel in gradient toluene to 1% ethyl acetate in toluene to give regioisomer substituted in the C-6 position (**15a**, **17a**) as a major product and regioisomer at the C-5 position (**14a**, **16a**) as a minor product.

Method D. General Procedure for the Removal of the Benzyl Protecting Groups Using Transfer Hydrogenation. A mixture of dibenzyluracil derivative **16a**−**d**, **17a**−**d** (0.3 mmol), ammonium formate (7.5 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (0.33 mmol of Pd) was refluxed at 72 °C for 17 h.

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The mixture was filtered through Celite, and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 250 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient chloroform to 2% methanol in chloroform gave the pure debenzylated products (**20a**−**d**, **22a**−**d**).

Method E. General Procedure for the Removal of the Benzyl Protecting Groups with Boron Tribromide. Boron tribromide (1.5 mmol) was added to dibenzyluracil derivate **16e**−**g**, **17e**−**g** (0.3 mmol) in *m*-xylene (6 mL). The mixture was heated ina pressure tube at 140 °C for 5 h and cooled, and MeOH (1.5 mL) was added. The mixture was stirred at room temperature for 30 min. Solvents were evaporated under reduced pressure, and products **20f**,**g** and **22e**−**g** were isolated by column chromatography on 60 g of silica gel in gradient chloroform to 5% methanol in chloroform.

3-Benzoylpyrimidine-2,4(1*H*,3*H*)-dione (5). Compound **5** was prepared from uracil according to published procedure[13d] in 61% yield, as a white crystals from $CHCl_3$/MeOH, mp 203−204 °C (lit.[18] mp 200−202 °C). ^{1}H NMR (500.0 MHz, DMSO-d_6): 5.74 (d, 1H, $J_{5,6}$ = 7.7, H-5); 7.60 (m, 2H, H-*m*-Ph); 7.66 (d, 1H, $J_{6,5}$ = 7.7, H-6); 7.77 (m, 1H, H-*p*-Ph); 7.96 (m, 2H, H-*o*-Ph); 11.61 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 100.3 (CH-5); 129.7 (CH-*m*-Ph); 130.4 (CH-*o*-Ph); 131.5 (C-*i*-Ph); 135.6 (CH-*p*-Ph); 143.5 (CH-6); 150.3 (C-2); 163.1 (C-4); 170.2 (CO). IR (KBr): 1765, 1748, 1706, 1656, 1597, 1416, 1390, 1231, 1181. MS (ESI$^+$), *m*/*z* (% relative intensity): 239 (M^+ + Na, 100). HR MS (M^+ + H): 239.0426 (calcd for $C_{11}H_8N_2NaO_3$ 239.0427).

1,3-Bis((2-methoxyethoxy)methyl)pyrimidine-2,4(1*H*,3*H*)-dione (6). To a mixture of uracil (336 mg, 3 mmol) and anhydrous K_2CO_3 (2.07 g, 15 mmol) in dry DMF (5 mL) was added dropwise $ClCH_2OC_2H_5$ (1.12 g, 9 mmol) below 0 °C. The mixture was allowed to warm to room temperature and was stirred overnight. Inorganic salts were removed by filtration, and the filtrate was concentrated under reduced pressure. The protected compound **6** were isolated by column chromatography on 60 g of silica gel in gradient chloroform to 1% methanol in chloroform in 35% yield, as a colorless oil. ^{1}H NMR (500.0 MHz, $CDCl_3$): 3.36, 3.37 (2 × s, 2 × 3H, H-6′,6″); 3.53 (m, 2H, H-4″); 3.54 (m, 2H, H-4′); 3.75 (m, 2H, H-3′); 3.80 (m, 2H, H-3″); 5.23 (s, 2H, H-1′); 5.47 (s, 2H, H-1″); 5.80 (d, 1H, $J_{5,6}$ = 8.0, H-5); 7.33 (d, 1H, $J_{6,5}$ = 8.0, H-6). ^{13}C NMR (125.7 MHz, $CDCl_3$): 59.0, 59.0 (CH_3-6′,6″); 69.0 (CH_2-3′); 69.8 (CH_2-3″); 71.0 (CH_2-1″); 71.5 (CH_2-4″); 71.6 (CH_2-4′); 77.9 (CH_2-1′); 102.6 (CH-5); 141.8 (CH-6); 151.9 (C-2); 162.8 (C-4). IR (KBr): 2821, 1719, 1671, 1638, 1452, 1103, 1089. MS (ESI$^+$), *m*/*z* (% relative intensity): 289 (M^+ + H, 6), 311 (M^+ + Na, 100), 599 ($2M^+$ + Na, 25). HR MS (M^+ + Na): 311.1213 (calcd for $C_{12}H_{20}N_2NaO_6$ 311.1214).

1,3-Bis((2-methoxyethoxy)methyl)-5-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (12a). DMF (2 mL) was added through a septum to an argon-purged vial containing compound **6** (86.5 mg, 0.3 mmol), 4-iodotoluene (**9a**, 131 mg, 0.6 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 5 mol %), $P(C_6F_5)_3$ (16 mg, 0.03 mmol, 10 mol %) and Cs_2CO_3 (244 mg, 0.75 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 40 g of silica gel in gradient chloroform to 1% metanol in chloroform to give regioisomer **12a** substituted in C-5 position as a major product in 24% yield, as a yellow oil. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.37 (s, 3H, CH_3); 3.36, 3.37 (2 × s, 2 × 3H, H-6′,6″); 3.54 (m, 2H, H-4″); 3.55 (m, 2H, H-4′); 3.79 (m, 2H, H-3′); 3.84 (m, 2H, H-3″); 5.30 (s, 2H, H-1′); 5.56 (s, 2H, H-1″); 7.20 (m, 2H, H-*m*-Ph); 7.40 (m, 2H, H-*o*-Ph); 7.47 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.2 (CH_3); 59.0, 59.0 (CH_3-6′,6″); 69.1 (CH_2-3′); 69.9 (CH_2-3″); 71.5 (CH_2-4″); 71.5 (CH_2-1″); 71.7 (CH_2-4′); 78.0 (CH_2-1′); 115. Five (C-5); 128.1 (CH-*o*-Ph); 129.1 (CH-*m*-Ph); 129.4 (C-*i*-Ph); 138.0 (C-*i*-Ph); 138.7 (CH-6); 151.5 (C-2); 162.1 (C-4). IR (KBr): 2820, 1715, 1666, 1516, 1453, 1353, 1279, 1103. MS (ESI$^+$), *m*/*z* (% relative intensity): 379 (M^+ + H, 26), 401 (M^+ + Na, 100). HR MS (M^+ + Na): 401.1685 (calcd for $C_{19}H_{26}N_2NaO_6$ 401.1683).

1,3-Bis(4-methoxybenzyl)pyrimidine-2,4(1*H*,3*H*)-dione (7). Compound 7 was prepared from uracil according to published procedure and experimental data are in accordance to literature.[13e] Yield 99% yield, as a white powder, mp 96−97 °C. ^{1}H NMR (600.1 MHz, $CDCl_3$): 3.78 (s, 3H, CH_3O-3); 3.80 (s, 3H, CH_3O-1); 4.83 (s, 2H, CH_2N-1); 5.07 (s, 2H, CH_2N-3); 5.71 (d, 1H, $J_{5,6}$ = 7.9, H-5); 6.83 (m, 2H, H-*m*-C_6H_4OMe-3); 6.88 (m, 2H, H-*m*-C_6H_4OMe-1); 7.07 (d, 1H, $J_{6,5}$ = 7.9, H-6); 7.21 (m, 2H, H-*o*-C_6H_4OMe-1); 7.46 (m, 2H, H-*o*-C_6H_4OMe-3). ^{13}C NMR (150.9 MHz, $CDCl_3$): 43.8 (CH_2N-3); 51.8 (CH_2N-1); 55.2 (CH_3O-3); 55.3 (CH_3O-1); 102.1 (CH-5); 113.7 (CH-*m*-C_6H_4OMe-3); 114.4 (CH-*m*-C_6H_4OMe-1); 127.1 (C-*i*-C_6H_4OMe-1); 129.1 (C-*i*-C_6H_4OMe-3); 129.7 (CH-*o*-C_6H_4OMe-1); 130.7 (CH-*o*-C_6H_4OMe-3); 141.5 (CH-6); 151.7 (C-2); 159.0 (C-*p*-C_6H_4OMe-3); 159.7 (C-*p*-C_6H_4OMe-1); 162.9 (C-4). IR (KBr): 2837, 1711, 1667, 1611, 1585, 1514, 1454, 1388, 1256, 1026. MS (ESI$^+$), *m*/*z* (% relative intensity): 353 (M^+ + H, 14), 375 (M^+ + Na, 100), 391 (M^+ + K, 30). HR MS (M^+ + H): 353.1496 (calcd for $C_{20}H_{21}N_2O_4$ 353.1496).

1,3-Bis(4-methoxybenzyl)-5-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (14a). DMF (3 mL) was added through a septum to an argon-purged vial containing a 1,3-dimethoxybenzyluracil (7, 176 mg, 0.5 mmol), 4-iodotoluene (**9a**, 218 mg, 1 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol %), $P(C_6F_5)_3$ (26.6 mg, 0.05 mmol, 10 mol %) and Cs_2CO_3 (407 mg, 1.25 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 50 g of silica gel in gradient hexane to 20% ethyl acetate in hexane to give regioisomer **14a** substituted in the C-5 position as a major product in 47% yield, as a yellow oil. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.27 (s, 3H, CH_3); 3.70 (s, 3H, CH_3O-PMB-3); 3.73 (s, 3H, CH_3O-PMB-1); 4.84 (s, 2H, CH_2-1); 5.08 (s, 2H, CH_2-3); 6.76 (m, 2H, H-*m*-PMB-3); 6.81 (m, 2H, H-*m*-PMB-1); 7.09 (m, 2H, H-*m*-C_6H_4Me); 7.18 (m, 2H, H-*o*-PMB-1); 7.19 (s, 1H, H-6); 7.24 (m, 2H, H-*o*-C_6H_4Me); 7.45 (m, 2H, H-*o*-PMB-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.2 (CH_3); 44.3 (CH_2-3); 51.9 (CH_2-1); 55.2, 55.3 (CH_3O-PMB-1,3); 113.7 (CH-*m*-PMB-3); 114.5 (CH-*m*-PMB-1); 115.0 (C-5); 127.3 (C-*i*-PMB-1); 128.2 (CH-*o*-C_6H_4Me); 129.1 (CH-*m*-C_6H_4Me); 129.2 (C-*i*-PMB-3); 129.7 (CH-*o*-PMB-1); 130.0 (C-*i*-C_6H_4Me); 131.0 (CH-*o*-PMB-3); 137.8 (C-*p*-C_6H_4Me); 138.7 (CH-6); 151.4 (C-2); 159.1 (C-*p*-PMB-3); 159.7 (C-*p*-PMB-1); 162.0 (C-4). IR (KBr): 2835, 1701, 1652, 1612, 1513, 1453, 1249, 1033. MS (ESI$^+$), *m*/*z* (% relative intensity): 443 (M^+ + H, 10), 465 (M^+ + Na, 100). HR MS (M^+ + H): 443.1964 (calcd for $C_{27}H_{27}N_2O_4$ 443.1965).

1,3-Bis(4-methoxybenzyl)-6-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (15a). DMF (3 mL) was added through a septum to an argon-purged vial containing a 1,3-dimethoxybenzyluracil (7, 176 mg, 0.5 mmol), 4-iodotoluene (**9a**, 218 mg, 1 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol %), $P(C_6F_5)_3$ (26.6 mg, 0.05 mmol, 10 mol %), CuI (286 mg, 1.5 mmol) and Cs_2CO_3 (407 mg, 1.25 mmol). Reaction mixture was stirred at 160 °C for 48 h. After cooling to rt, the mixture was diluted with chloroform (20 mL), and solvents were evaporated under reduced pressure. The crude product was chromatographed by column chromatography on 50 g of silica gel in gradient hexane to 20% ethyl acetate in hexane to give regioisomer **15a** substituted in the C-6 position as a major product in 46% yield, as a yellow oil. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.32 (s, 3H, CH_3); 3.69 (s, 3H, CH_3O-PMB-3); 3.72 (s, 3H, CH_3O-PMB-1); 4.80 (bs, 2H, CH_2-1); 5.06 (s, 2H, CH_2-3); 5.59 (s, 1H, H-5); 6.67 (m, 2H, H-*m*-PMB-1); 6.74 (m, 2H, H-*o*-PMB-1); 6.78 (m, 2H, H-*m*-PMB-3); 6.98 (m, 2H, H-*o*-C_6H_4Me); 7.11 (m, 2H, H-*m*-C_6H_4Me); 7.43 (m, 2H, H-*o*-PMB-3). ^{13}C NMR (125.7 MHz, $CDCl_3$):

21.3 (CH_3); 44.0 (CH_2-3); 48.8 (CH_2-1); 55.2 (CH_3O-PMB-1,3); 103.4 (CH-5); 113.7 (CH-*m*-PMB-3); 113.9 (CH-*m*-PMB-1); 127.9 (CH-*o*-C_6H_4Me); 128.3 (CH-*o*-PMB-1); 128.6 (C-*i*-PMB-1); 129.3 (C-*i*-PMB-3); 129.3 (CH-*m*-C_6H_4Me); 130.4 (C-*i*-C_6H_4Me); 130.8 (CH-*o*-PMB-3); 140.3 (C-*p*-C_6H_4Me); 152.5 (C-2); 154.9 (C-6); 158.9 (C-*p*-PMB-3); 159.1 (C-*p*-PMB-1); 162.1 (C-4). IR (KBr): 2836, 1703, 1660, 1613, 1513, 1441, 1248, 1034. MS (ESI^+), *m*/*z* (% relative intensity): 465 (M^+ + Na, 100). HR MS (M^+ + Na): 465.1783 (calcd for $C_{27}H_{26}N_2NaO_4$ 465.1785).

3-(4-Methoxybenzyl)-5-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (18a). A mixture of compound **14a** (50 mg, 0.113 mmol), ammonium formate (2.8 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (132 mg 10% Pd/C, 0.124 mmol of Pd, 1.1 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite, and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 120 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient chloroform to 1% methanol in chloroform gave the pure monodeprotected product **18a** in 82% yield, as a white powder, mp 175−177 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.36 (s, 3H, CH_3); 3.77 (s, 3H, CH_3O); 5.13 (s, 2H, CH_2Ph); 6.83 (m, 2H, H-*m*-C_6H_4OMe); 7.20 (m, 2H, H-*m*-C_6H_4Me); 7.26 (d, 1H, $J_{6,NH}$ = 5.9, H-6); 7.38 (m, 2H, H-*o*-C_6H_4Me); 7.49 (m, 2H, H-*o*-C_6H_4OMe); 9.62 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.18 (CH_3); 43.63 (CH_2); 55.22 CH_3O); 113.70 (CH-*m*-C_6H_4OMe); 115.09 (C-5); 128.18 (CH-*o*-C_6H_4Me); 128.90 (C-*i*-C_6H_4OMe); 129.15 (CH-*m*-C_6H_4Me); 129.75 (C-*i*-C_6H_4Me); 130.81 (CH-*o*-C_6H_4OMe); 135.25 (CH-6); 137.87 (C-*p*-C_6H_4Me); 152.53 (C-2); 159.13 (C-*p*-C_6H_4OMe); 162.31 (C-4). IR: 2920, 1713, 1628, 1611, 1512, 1440, 1292, 1245, 1150, 1038. MS (ESI^+), *m*/*z* (% relative intensity): 323 (M^+ + H, 30), 345 (M^+ + Na, 100), 667 ($2M^+$ + Na, 15). HR MS (M^+ + H): 323.1390 (calcd for $C_{19}H_{19}N_2O_3$ 323.1390).

1,3-Dibenzylpyrimidine-2,4(1*H*,3*H*)-dione (8). Anhydrous DMF (35 mL) was added through a septum to an argon-purged flask containing a uracil (930 mg, 8.29 mmol) and K_2CO_3 (2.75 g, 19.89 mmol), and the mixture was stirred for 18 h, resulting in a thick gel. Benzyl bromide (2.99 mL [4.3 g], 24.87 mmol) was added, and the reaction was stirred for another 3 days. The reaction mixture was concentrated and redissolved in water and extracted with EtOAc. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography on a 150 g of silica gel (1:4 EtOAc/hexanes) afforded the product (**8**) in 89% yield, as a white crystals from hexane/ethylacetate, mp 67−69 °C (lit.[19] 67−68 °C). ^{1}H NMR (499.8 MHz, $CDCl_3$): 4.91 (s, 2H, CH_2-1); 5.15 (s, 2H, CH_2-3); 5.74 (d, 1H, $J_{5,6}$ = 7.9, H-5); 7.11 (d, 1H, $J_{6,5}$ = 7.9, H-6); 7.26 (m, 1H, H-*p*-3Bn); 7.27 (m, 2H, H-*o*-1Bn); 7.31 (m, 2H, H-*m*-3Bn); 7.36 (m, 1H, H-*p*-1Bn); 7.37 (m, 2H, H-*m*-1Bn); 7.48 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 44.41 (CH_2-3); 52.24 (CH_2-1); 102.16 (CH-5); 127.58 (CH-*p*-3Bn); 128.01 (CH-*o*-1Bn); 128.38 (CH-*m*-3Bn); 128.49 (CH-*p*-1Bn); 128.97 (CH-*o*-3Bn); 129.11 (CH-*m*-1Bn); 135.20 (C-*i*-1Bn); 136.77 (C-*i*-3Bn); 141.70 (CH-6); 151.74 (C-2); 162.81 (C-4). IR (KBr): 1700, 1663, 1605, 1585, 1495, 1452, 1393, 1218. MS (ESI^+), *m*/*z* (% relative intensity): 315 (M^+ + Na, 100). HR MS (M^+ + H): 293.1285 (calcd for $C_{18}H_{17}N_2O_2$ 293.1285).

1,3-Dibenzyl-5-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (16a). Compound **16a** was prepared from **8** according to general procedure (Method A) in 45% yield, as a yellowish oil. ^{1}H NMR (600.1 MHz, $CDCl_3$): 2.34 (s, 3H, CH_3); 4.99 (s, 2H, CH_2-1); 5.23 (s, 2H, CH_2-3); 7.17 (m, 2H, H-*m*-C_6H_4Me); 7.25 (s, 1H, H-6); 7.26 (m, 1H, H-*p*-3Bn); 7.31 (m, 4H, H-*o*-1Bn, H-*m*-3Bn); 7.33 (m, 2H, H-*o*-C_6H_4Me); 7.36 (m, 1H, H-*p*-1Bn); 7.37 (m, 2H, H-*m*-1Bn); 7.55 (m, 2H, H-*o*-3Bn). ^{13}C NMR (150.9 MHz, $CDCl_3$): 21.2 (CH_3); 44.9 (CH_2-3); 52.4 (CH_2-1); 115.1 (C-5); 127.6 (CH-*p*-3Bn); 128.0 (CH-*o*-1Bn); 128.2 (CH-*o*-C_6H_4Me); 128.4 (CH-*m*-3Bn); 128.5 (CH-*p*-1Bn); 129.1 (CH-*m*-C_6H_4Me); 129.1 (CH-*m*-1Bn); 129.4 (CH-*o*-3Bn); 129.8 (C-*i*-C_6H_4Me); 135.3 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 137.8 (C-*p*-C_6H_4Me); 138.9 (CH-6); 151.4 (C-2); 162.0 (C-4). IR (KBr): 1704, 1652, 1584, 1515, 1495, 1451, 1379, 1284, 1219, 1083. MS (ESI^+), *m*/*z* (% relative intensity): 383 (M^+ + H, 10), 405 (M^+ + Na, 100), 421 (M^+ + K, 12). HR MS (M^+ + H): 383.1754 (calcd for $C_{25}H_{23}N_2O_2$ 383.1754).

1,3-Dibenzyl-6-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (17a). Compound **17a** was prepared from **8** according to general procedure (Method B) in 66% yield, as a yellowish oil. ^{1}H NMR (499.8 MHz, $CDCl_3$): 2.38 (s, 3H, CH_3); 4.94 (bs, 2H, CH_2-1); 5.20 (s, 2H, CH_2-3); 5.70 (s, 1H, H-5); 6.90 (m, 2H, H-*o*-1Bn); 7.05 (m, 2H, H-*o*-C_6H_4Me); 7.16 (m, 2H, H-*m*-C_6H_4Me); 7.22 (m, 3H, H-*m*,*p*-1Bn); 7.29 (m, 1H, H-*p*-3Bn); 7.33 (m, 2H, H-*m*-3Bn); 7.53 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.3 (CH_3); 44.5 (CH_2-3); 49.4 (CH_2-1); 103.4 (CH-5); 126.7 (CH-*o*-1Bn); 127.5 (CH-*p*-1Bn); 127.6 (CH-*p*-3Bn); 127.8 (CH-*o*-C_6H_4Me); 128.4 (CH-*m*-3Bn); 128.5 (CH-*m*-1Bn); 129.1 (CH-*o*-3Bn); 129.3 (CH-*m*-C_6H_4Me); 130.2 (C-*i*-C_6H_4Me); 136.6 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 140.3 (C-*p*-C_6H_4Me); 152.5 (C-2); 155.0 (C-6); 162.1 (C-4). IR: 1703, 1658, 1580, 1549, 1513, 1492, 1451, 1383, 1279, 1243, 1181, 1083. MS (ESI^+), *m*/*z* (% relative intensity): 383 (M^+ + H, 4), 405 (M^+ + Na, 100), 421 (M^+ + K, 16). HR MS (M^+ + H): 383.1754 (calcd for $C_{25}H_{23}N_2O_2$ 383.1754).

3-Benzyl-5-*p*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (19a). A mixture of compound **16a** (50 mg, 0.131 mmol), ammonium formate (3.3 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (77 mg 10% Pd/C, 0.072 mmol of Pd, 0.55 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite, and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 120 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient chloroform to 1% methanol in chloroform gave the pure monodeprotected product **19a** in 80% yield, as a white powder, mp 205−208 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.28 (s, 3H, CH_3); 5.11 (s, 2H, CH_2Ph); 7.12 (m, 2H, H-*m*-C_6H_4Me); 7.19 (m, 2H, H-6, H-*p*-Bn); 7.22 (m, 2H, H-*m*-Bn); 7.30 (m, 2H, H-*o*-C_6H_4Me); 7.44 (m, 2H, H-*o*-Bn), 9.97 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.18 (CH_3); 44.19 (CH_2Ph); 115.02 (C-5); 127.68 (CH-*p*-Bn); 128.17 (CH-*o*-C_6H_4Me); 128.40 (CH-*m*-Bn); 129.11, 129.15 (CH-*m*-C_6H_4Me, CH-*o*-Bn); 129.70 (C-*i*-C_6H_4Me); 135.34 (CH-6); 136.61 (C-*i*-Bn); 137.89 (C-*p*-C_6H_4Me); 152.59 (C-2); 162.30 (C-4). IR: 3179, 1703, 1628, 1515, 1494, 1434, 1289, 1210, 1152. MS (ESI^+), *m*/*z* (% relative intensity): 315 (M^+ + Na, 100). HR MS (M^+ + H): 315.1104 (calcd for $C_{18}H_{16}N_2NaO_2$ 315.1104).

5-*p*-Tolylpyrimidine-2,4(1*H*,3*H*)-dione (20a). Compound **20a** was prepared from **16a** (100 mg, 0.261 mmol) according to general procedure (Method D), in 98% yield, as a white powder, mp 228−230 °C. ^{1}H NMR (600.1 MHz, DMSO-d_6): 2.29 (s, 3H, CH_3); 7.15 (m, 2H, H-*m*-C_6H_4Me); 7.42 (m, 2H, H-*o*-C_6H_4Me); 7.56 (s, 1H, H-6); 11.21 (bs, 2H, NH-1,3). ^{13}C NMR (150.9 MHz, DMSO-d_6): 20.95 (CH_3); 112.3 (C-5); 128.0 (CH-*o*-C_6H_4Me); 128.8 (CH-*m*-C_6H_4Me); 130.6 (C-*i*-C_6H_4Me); 136.4 (C-*p*-C_6H_4Me); 139.4 (CH-6); 151.2 (C-2); 163.4 (C-4). IR: 3079, 1747, 1718, 1665, 1618, 1515, 1444, 1423, 1230, 1109. MS (ESI^+), *m*/*z* (% relative intensity): 203 (M^+ + H, 16), 225 (M^+ + Na, 100), 427 ($2M^+$ + Na, 37). HR MS (M^+ + H): 203.0815 (calcd for $C_{11}H_{11}N_2O_2$ 203.0815). Anal. Calcd for $C_{11}H_{10}N_2O_2 \cdot 1H_2O$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.14; H, 5.12; N, 12.63.

6-*p*-Tolylpyrimidine-2,4(1*H*,3*H*)-dione (22a). Compound **22a** was prepared from **17a** (100 mg, 0.261 mmol) according to general procedure (Method D), in 97% yield, as a white powder, mp >300 °C (lit.[20] mp 315−318 °C). ^{1}H NMR (600.1 MHz, DMSO-d_6): 2.35 (s, 3H, CH_3); 5.78 (d, 1H, *J* = 1.7, H-5); 7.30 (m, 2H, H-*m*-C_6H_4Me); 7.62 (m, 2H, H-*o*-C_6H_4Me); 11.08, 11.12 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (150.9 MHz, DMSO-d_6): 21.1 (CH_3); 97.6 (CH-5); 127.0 (CH-*o*-C_6H_4Me); 128.9 (C-*i*-C_6H_4Me); 129.6 (CH-*m*-C_6H_4Me); 141.3 (C-*p*-

C_6H_4Me); 152.1 (C-2); 152.6 (C-6); 164.3 (C-4). IR (KBr): 3132, 1698, 1667, 1618, 1517, 1493, 1406, 1385, 1238, 1191. MS (ESI^+), *m/z* (% relative intensity): 203 ($M^+ + H$, 28), 225 ($M^+ + Na$, 81), 427 ($2M^+ + Na$, 100). HR MS ($M^+ + H$): 203.0815 (calcd for $C_{11}H_{11}N_2O_2$ 203.0815). Anal. Calcd for $C_{11}H_{10}N_2O_2 \cdot 1H_2O$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.65; H, 5.09; N, 12.57.

1,3-Dibenzyl-5-*o*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (16b). Compound **16b** was prepared from **8** according to general procedure (Method A) in 70% yield, as a white powder, mp 115−116 °C. ^1H NMR (499.8 MHz, $CDCl_3$): 2.17 (s, 3H, CH_3); 4.97 (s, 2H, CH_2-1); 5.22 (s, 2H, CH_2-3); 7.06 (dd, 1H, $J_{6,5}$ = 7.6, $J_{6,4}$ = 1.4, H-6-C_6H_4Me); 7.12 (s, 1H, H-6); 7.16 (m, 1H, H-5-C_6H_4Me); 7.21 (m, 1H, H-3-C_6H_4Me); 7.25 (ddd, 1H, $J_{4,3}$ = 7.6, $J_{4,5}$ = 7.0, $J_{4,6}$ = 1.4, H-4-C_6H_4Me); 7.26−7.40 (m, 8H, H-*o*,*m*,*p*-1Bn, H-*m*,*p*-3Bn); 7.54 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 20.1 (CH_3); 44.9 (CH_2-3); 52.3 (CH_2-1); 115.6 (C-5); 125.8 (CH-5-C_6H_4Me); 127.6 (CH-*p*-3Bn); 128.1 (CH-*o*-1Bn); 128.4 (CH-*m*-3Bn); 128.5, 128.5 (CH-4-C_6H_4Me, CH-*p*-1Bn); 129.2 (CH-*m*-1Bn); 129.4 (CH-*o*-3Bn); 130.1 (CH-3-C_6H_4Me); 130.5 (CH-6-C_6H_4Me); 132.3 (C-1-C_6H_4Me); 135.3 (C-*i*-1Bn); 137.0 (C-*i*-3Bn); 137.7 (C-2-C_6H_4Me); 140.2 (CH-6); 151.6 (C-2); 161.7 (C-4). IR (KBr): 1703, 1649, 1634, 1586, 1495, 1446, 1379, 1294, 1217. MS (ESI^+), *m/z* (% relative intensity): 383 ($M^+ + H$, 93), 405 ($M^+ + Na$, 100), 421 ($M^+ + K$, 30). HR MS ($M^+ + H$): 383.1753 (calcd for $C_{25}H_{23}N_2O_2$ 383.1754).

1,3-Dibenzyl-6-*o*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (17b). Compound **17b** was prepared from **8** according to general procedure (Method B) in 28% yield, as a white crystals from hexane/ethylacetate, mp 131−132 °C. ^1H NMR (499.8 MHz, $CDCl_3$): 1.97 (s, 3H, CH_3); 4.69 and 4.91 (2 × bd, 2 × 1H, J_{gem} = 14.9, CH_2-1); 5.22 and 5.26 (2 × d, 2 × 1H, J_{gem} = 13.7, CH_2-3); 5.65 (s, 1H, H-5); 6.78 (m, 2H, H-*o*-1Bn); 6.98 (dd, 1H, $J_{6,5}$ = 7.6, $J_{6,4}$ = 1.4, H-6-C_6H_4Me); 7.16 (m, 1H, H-5-C_6H_4Me); 7.18 (m, 2H, H-*m*-1Bn); 7.19 (m, 2H, H-*p*-1Bn); 7.20 (m, 1H, H-3-C_6H_4Me); 7.29 (m, 1H, H-*p*-3Bn); 7.35 (m, 3H, H-4-C_6H_4Me and H-*m*-3Bn); 7.55 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 19.2 (CH_3); 44.7 (CH_2-3); 49.0 (CH_2-1); 103.2 (CH-5); 125.9 (CH-5-C_6H_4Me); 127.4 (CH-*o*-1Bn); 127.6 (CH-*p*-3Bn); 127.7 (CH-*p*-1Bn); 128.4, 128.4 (CH-*m*-1Bn and CH-*m*-3Bn); 128.5 (CH-6-C_6H_4Me); 129.1 (CH-*o*-3Bn); 130.1 (CH-4-C_6H_4Me); 130.5 (CH-3-C_6H_4Me); 132.4 (C-1-C_6H_4Me); 135.8 (C-2-C_6H_4Me); 136.2 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 152.7 (C-2); 154.0 (C-6); 162.2 (C-4). IR (KBr): 1698, 1660, 1621, 1585, 1495, 1438, 1395, 1344, 1216. MS (EI^+), *m/z* (% relative intensity): 65 (19), 77 (13), 91 (100), 103 (7), 115 (15), 132 (21), 149 (5), 186 (32), 220 (3), 248 (7), 289 (10), 367 (46), 382 (M^+, 33). HR MS (M^+): 382.1674 (calcd for $C_{25}H_{22}N_2O_2$ 382.1681).

5-*o*-Tolylpyrimidine-2,4(1*H*,3*H*)-dione (20b). Compound **20b** was prepared from **16b** (100 mg, 0.261 mmol) according to general procedure (Method D), in 97% yield, as a white powder, mp 265−268 °C. The experimental data are in accordance with literature.[21] ^1H NMR (499.8 MHz, DMSO-d_6): 2.15 (s, 3H, CH_3); 7.10 (dd, 1H, $J_{6,5}$ = 7.4, $J_{6,4}$ = 1.6, H-6-C_6H_4Me); 7.17 (m, 1H, H-5-C_6H_4Me); 7.21 (m, 2H, H-3-C_6H_4Me); 7.24 (ddd, 1H, $J_{4,3}$ = 7.5, $J_{4,5}$ = 6.7, $J_{4,6}$ = 1.6, H-4-C_6H_4Me); 7.36 (s, 1H, H-6); 11.00, 11.19 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 19.9 (CH_3); 113.5 (C-5); 125.7 (CH-5-C_6H_4Me); 127.9 (CH-4-C_6H_4Me); 129.8 (CH-3-C_6H_4Me); 130.8 (CH-6-C_6H_4Me); 133.5 (C-1-C_6H_4Me); 137.6 (C-2-C_6H_4Me); 140.4 (CH-6); 151.5 (C-2); 163.1 (C-4). IR (KBr): 3100, 1748, 1699, 1662, 1603, 1574, 1490, 1385, 1233. MS (ESI^+), *m/z* (% relative intensity): 203 ($M^+ + H$, 6), 225 ($M^+ + Na$, 100), 427 ($2M^+ + Na$, 77). HR MS ($M^+ + H$): 203.0814 (calcd for $C_{11}H_{11}N_2O_2$ 203.0815).

6-*o*-Tolylpyrimidine-2,4(1*H*,3*H*)-dione (22b). Compound **22b** was prepared from **17b** (80 mg, 0.209 mmol) according to general procedure (Method D), in 94% yield, as a white powder, mp 185−187 °C. ^1H NMR (600.1 MHz, DMSO-d_6): 2.30 (s, 3H, CH_3); 5.40 (s, 1H, H-5); 7.28 (m, 1H, H-5-C_6H_4Me); 7.31 (m, 2H, H-3,6-C_6H_4Me); 7.39 (td, 1H, $J_{4,3} = J_{4,5}$ = 7.4, $J_{4,6}$ = 1.8, H-4-C_6H_4Me), 11.03, 11.14 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (150.9 MHz, DMSO-d_6): 19.6 (CH_3); 100.6 (CH-5); 126.2 (CH-5-C_6H_4Me); 128.7 (CH-6-C_6H_4Me); 130.1 (CH-4-C_6H_4Me); 130.7 (CH-3-C_6H_4Me); 133.2 (C-1-C_6H_4Me); 135.7 (C-2-C_6H_4Me); 151.7 (C-2); 153.9 (C-6); 164.3 (C-4). IR: 3158, 1731, 1656, 1600, 1577, 1485, 1385, 1292. MS (ESI^+), *m/z* (% relative intensity): 203 ($M^+ + H$, 23), 225 ($M^+ + Na$, 100), 427 ($2M^+ + Na$, 65). HR MS ($M^+ + H$): 203.0815 (calcd for $C_{11}H_{11}N_2O_2$ 203.0815).

1,3-Dibenzyl-5-(4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (16c). Compound **16c** was prepared from **8** according to general procedure (Method A) in 45% yield, as a yellowish oil. ^1H NMR (499.8 MHz, $CDCl_3$): 3.80 (s, 3H, OCH_3); 4.99 (s, 2H, CH_2-1); 5.23 (s, 2H, CH_2-3); 6.89 (m, 2H, H-*m*-C_6H_4OMe); 7.22 (s, 1H, H-6); 7.26 (m, 1H, H-*p*-3Bn); 7.31 (m, 4H, H-*o*-1Bn, H-*m*-3Bn); 7.36 (m, 1H, H-*p*-1Bn); 7.37 (m, 4H, H-*m*-1Bn, H-*o*-C_6H_4OMe); 7.55 (m, 2H, H-*o*-3Bn). ^{13}C NMR (150.9 MHz, $CDCl_3$): 45.0 (CH_2-3); 52.4 (CH_2-1); 55.3 (CH_3); 113.9 (CH-*m*-C_6H_4OMe); 114.8 (C-5); 125.1 (C-*i*-C_6H_4OMe); 127.6 (CH-*p*-3Bn); 128.0 (CH-*o*-1Bn); 128.4 (CH-*m*-3Bn); 128.5 (CH-*p*-1Bn); 129.1 (CH-*m*-1Bn); 129.3 (CH-*o*-3Bn); 129.5 (CH-*o*-C_6H_4OMe); 135.4 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 138.5 (CH-6); 151.4 (C-2); 159.4 (C-*p*-C_6H_4OMe); 162.1 (C-4). IR (KBr): 1702, 1651, 1609, 1515, 1495, 1451, 1380, 1249, 1179, 1049. MS (ESI^+), *m/z* (% relative intensity): 399 ($M^+ + H$, 100), 421 ($M^+ + Na$, 88), 819 ($2M^+ + Na$, 37). HR MS ($M^+ + H$): 399.1704 (calcd for $C_{25}H_{23}N_2O_3$ 399.1703).

1,3-Dibenzyl-6-(4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (17c). Compound **17c** was prepared from **8** according to general procedure (Method B) in 38% yield, as a yellowish oil. ^1H NMR (600.1 MHz, $CDCl_3$): 3.82 (s, 3H, OCH_3); 4.95 (bs, 2H, CH_2-1); 5.20 (s, 2H, CH_2-3); 5.70 (s, 1H, H-5); 6.86 (m, 2H, H-*m*-C_6H_4OMe); 6.91 (m, 2H, H-*o*-1Bn); 7.09 (m, 2H, H-*o*-C_6H_4OMe); 7.22 (m, 3H, H-*m*,*p*-1Bn); 7.28 (m, 1H, H-*p*-3Bn); 7.33 (m, 2H, H-*m*-3Bn); 7.53 (m, 2H, H-*o*-3Bn). ^{13}C NMR (150.9 MHz, $CDCl_3$): 44.6 (CH_2-3); 49.4 (CH_2-1); 55.4 (CH_3O); 103.5 (CH-5); 114.0 (CH-*m*-C_6H_4OMe); 125.3 (C-*i*-C_6H_4OMe); 126.6 (CH-*o*-1Bn); 127.5 (CH-*p*-1Bn); 127.6 (CH-*p*-3Bn); 128.4 (CH-*m*-3Bn); 128.6 (CH-*m*-1Bn); 129.1 (CH-*o*-3Bn); 129.4 (CH-*o*-C_6H_4OMe); 136.6 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 152.6 (C-2); 154.8 (C-6); 160.8 (C-*p*-C_6H_4OMe); 162.1 (C-4). IR (KBr): 1702, 1651, 1514, 1495, 1449, 1378, 1248, 1178, 1070. MS (ESI^+), *m/z* (% relative intensity): 399 ($M^+ + H$, 35), 421 ($M^+ + Na$, 100), 437 ($M^+ + K$, 30), 819 ($2M^+ + Na$, 10). HR MS ($M^+ + H$): 399.1703 (calcd for $C_{25}H_{23}N_2O_3$ 399.1703).

5-(4-Methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (20c). Compound **20c** was prepared from **16c** (128 mg, 0.321 mmol) according to general procedure (Method D), in 95% yield, as a white powder, mp > 300 °C. The experimental data are in accordance to literature.[22] ^1H NMR (499.8 MHz, DMSO-d_6): 3.75 (s, 3H, OCH_3); 6.91 (m, 2H, H-*m*-C_6H_4OMe); 7.46 (m, 2H, H-*o*-C_6H_4OMe); 7.52 (s, 1H, H-6); 11.14 (bs, 2H, NH-1,3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 55.3 (OCH_3); 112.2 (C-5); 113.7 (CH-*m*-C_6H_4OMe); 125.8 (C-*i*-C_6H_4OMe); 129.4 (CH-*o*-C_6H_4OMe); 138.9 (CH-6); 151.2 (C-2); 158.6 (C-*p*-C_6H_4Me); 163.6 (C-4). IR (KBr): 3080, 1762, 1711, 1672, 1616, 1579, 1518, 1492, 1450, 1301, 1255, 1183, 1078. MS (ESI^+), *m/z* (% relative intensity): 219 ($M^+ + H$, 98), 241 ($M^+ + Na$, 100), 257 ($M^+ + K$, 32), 459 ($2M^+ + Na$, 35). HR MS ($M^+ + H$): 219.0764 (calcd for $C_{11}H_{11}N_2O_3$ 219.0764).

6-(4-Methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (22c). Compound **22c** was prepared from **17c** (100 mg, 0.251 mmol) according to general procedure (Method D), in 92% yield, as a yellowish powder, mp 286−288 °C (lit.[23] mp 288 °C). ^1H NMR (500.0 MHz, DMSO-d_6): 3.81 (s, 3H, OCH_3); 5.76 (s, 1H, H-5); 7.03 (m, 2H, H-*m*-C_6H_4OMe); 7.71 (m, 2H, H-*o*-C_6H_4OMe); 11.01, 11.06 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 55.7 (OCH_3); 996.8

(CH-5); 114.4 (CH-*o*-C_6H_4OMe); 123.7 (C-*i*-C_6H_4OMe); 128.8 (CH-*m*-C_6H_4OMe); 152.1, 152.2 (C-2,6); 161.7 (C-*p*-C_6H_4OMe); 164.3 (C-4). IR (KBr): 3140, 1714, 1677, 1653, 1609, 1572, 1521, 1491, 1446, 1297, 1263, 1183, 1082. MS (ESI^+), *m*/*z* (% relative intensity): 219 ($M^+ + H$, 100), 241 ($M^+ + Na$, 75), 257 ($M^+ + K$, 27), 459 ($2M^+ + Na$, 80). HR MS ($M^+ + H$): 219.0764 (calcd for $C_{11}H_{11}N_2O_3$ 219.0764).

1,3-Dibenzyl-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (16d). Compound **16a** was prepared from **8** according to general procedure (Method A) in 47% yield, as a white powder, mp 125−126 °C. ^1H NMR (500.0 MHz, $CDCl_3$): 5.00 (s, 2H, CH_2-1); 5.24 (s, 2H, CH_2-3); 7.28 (s, 1H, H-6); 7.28−7.40 (m, 11H, H-*o*,*m*,*p*-1Bn, H-*m*,*p*-3Bn, H-*m*,*p*-Ph); 7.44 (m, 2H, H-*o*-Ph); 7.56 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 45.0 (CH_2-3); 52.4 (CH_2-1); 115.1 (C-5); 127.7 (CH-*p*-3Bn); 127.9 (CH-*p*-Ph); 128.0 (CH-*o*-1Bn); 128.3 (CH-*o*-Ph); 128.4 (CH-*m*-3Bn); 128.4 (CH-*m*-Ph); 128.5 (CH-*p*-1Bn); 129.2 (CH-*m*-1Bn); 129.4 (CH-*o*-3Bn); 132.8 (C-*i*-Ph); 135.3 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 139.3 (CH-6); 151.4 (C-2); 161.9 (C-4). IR (KBr): 1698, 1648, 1602, 1581, 1495, 1455, 1439, 1378, 1337, 1280, 1206, 1181, 1078. MS (ESI^+), *m*/*z* (% relative intensity): 369 ($M^+ + H$, 11), 391 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 369.1597 (calcd for $C_{24}H_{21}N_2O_2$ 369.1598).

1,3-Dibenzyl-6-phenylpyrimidine-2,4(1*H*,3*H*)-dione (17d). Compound **17d** was prepared from **8** according to general procedure (Method B) in 42% yield, as a white powder, mp 76−78 °C. The experimental data are in accordance with literature.[24] ^1H NMR (600.1 MHz, $CDCl_3$): 4.93 (bs, 2H, CH_2-1); 5.21 (s, 2H, CH_2-3); 5.71 (s, 1H, H-5); 6.86 (m, 2H, H-*o*-1Bn); 7.14 (m, 2H, H-*o*-Ph); 7.21 (m, 3H, H-*m*,*p*-1Bn); 7.29 (m, 1H, H-*p*-3Bn); 7.33 (m, 2H, H-*m*-3Bn); 7.35 (m, 2H, H-*m*-Ph); 7.44 (m, 1H, H-*p*-Ph); 7.54 (m, 2H, H-*o*-3Bn). ^{13}C NMR (150.9 MHz, $CDCl_3$): 44.6 (CH_2-3); 49.4 (CH_2-1); 103.5 (CH-5); 126.7 (CH-*o*-1Bn); 127.5 (CH-*p*-1Bn); 127.6 (CH-*p*-3Bn); 127.9 (CH-*o*-Ph); 128.4 (CH-*m*-3Bn); 128.5 (CH-*m*-1Bn); 128.6 (CH-*m*-Ph); 129.2 (CH-*o*-3Bn); 130.1 (CH-*p*-Ph); 133.0 (C-*i*-Ph); 136.55 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 152.5 (C-2); 154.8 (C-6); 162.0 (C-4). IR (KBr): 1705, 1659, 1604, 1574, 1496, 1450, 1437, 1389, 1349, 1242, 1205, 1192, 1075. MS (ESI^+), *m*/*z* (% relative intensity): 369 ($M^+ + H$, 7), 391 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 369.1597 (calcd for $C_{24}H_{21}N_2O_2$ 369.1598).

5-Phenylpyrimidine-2,4(1*H*,3*H*)-dione (20d). Compound **20d** was prepared from **16d** (100 mg, 0.271 mmol) according to general procedure (Method D), in 97% yield, as a white powder, mp > 300 °C (lit.[25] mp >350 °C). ^1H NMR (600.1 MHz, DMSO-d_6): 7.26 (m, 1H, H-*p*-Ph); 7.35 (m, 2H, H-*m*-Ph); 7.53 (m, 2H, H-*o*-Ph); 7.61 (s, 1H, H-6); 11.15, 11.25 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (150.9 MHz, DMSO-d_6): 112.3 (C-5); 127.2 (CH-*p*-Ph); 128.2 (CH-*o*-Ph); 128.2 (CH-*m*-Ph); 133.5 (C-*i*-Ph); 139.9 (CH-6); 151.2 (C-2); 163.4 (C-4). IR (KBr): 3062, 1749, 1688, 1676, 1631, 1605, 1498, 1448, 1353, 1236, 1078. MS (ESI^+), *m*/*z* (% relative intensity): 189 ($M^+ + H$, 35), 211 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 189.0657 (calcd for $C_{10}H_9N_2O_2$ 189.0659).

6-Phenylpyrimidine-2,4(1*H*,3*H*)-dione (22d). Compound **22d** was prepared from **17d** (100 mg, 0.271 mmol) according to general procedure (Method D), in 94% yield, as a white powder, mp 268−271 °C (lit.[26] mp 270 °C). ^1H NMR (600.1 MHz, DMSO-d_6): 5.81 (s, 1H, H-5); 7.49 (m, 2H, H-*m*-Ph); 7.54 (m, 1H, H-*p*-Ph); 7.72 (m, 2H, H-*o*-Ph); 11.14, 11.16 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (150.9 MHz, DMSO-d_6): 98.3 (CH-5); 127.2 (CH-*o*-Ph); 129.0 (CH-*m*-Ph); 131.3 (CH-*p*-Ph); 131.8 (C-*i*-Ph); 152.1 (C-2); 152.1 (C-6); 164.3 (C-4). IR (KBr): 3098, 1721, 1652, 1600, 1578, 1489, 1446, 1354, 1239, 1079. MS (ESI^+), *m*/*z* (% relative intensity): 189 ($M^+ + H$, 34), 211 ($M^+ + Na$, 100), 399 ($2M^+ + Na$, 100). HR MS ($M^+ + H$): 189.0658 (calcd for $C_{10}H_9N_2O_2$ 189.0659).

1,3-Dibenzyl-5-(4-fluorophenyl)pyrimidine-2,4(1*H*,3*H*)-dione (16e). Compound **16e** was prepared from **8** according to general procedure (Method A) in 49% yield, as a yellow powder, mp 45−47 °C. ^1H NMR (499.8 MHz, $CDCl_3$): 5.00 (s, 2H, CH_2-1); 5.23 (s, 2H, CH_2-3); 7.04 (m, 2H, H-*m*-C_6H_4F); 7.25 (s, 1H, H-6); 7.26−7.34 (m, 5H, H-*o*-1Bn, H-*m*,*p*-3Bn); 7.34−7.43 (m, 5H, H-*m*,*p*-1Bn, H-*o*-C_6H_4F); 7.54 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 45.0 (CH_2-3); 52.5 (CH_2-1); 114.2 (C-5); 115.4 (d, $J_{C,F}$ = 21.6, CH-*m*-C_6H_4F); 127.7 (CH-*p*-3Bn); 128.0 (CH-*o*-1Bn); 128.4 (CH-*m*-3Bn); 128.6 (CH-*p*-1Bn); 128.7 (d, $J_{C,F}$ = 3.3, C-*i*-C_6H_4F); 129.2 (CH-*m*-1Bn); 129.3 (CH-*o*-3Bn); 130.1 (d, $J_{C,F}$ = 8.1, CH-*o*-C_6H_4F); 135.2 (C-*i*-1Bn); 136.8 (C-*i*-3Bn); 139.1 (CH-6); 151.3 (C-2); 161.9 (C-4); 162.5 (d, $J_{C,F}$ = 247.7, C-*p*-C_6H_4F). $^{19}F\{^1H\}$ NMR (470.3 MHz, $CDCl_3$): −109.95. IR: 1701, 1646, 1602, 1510, 1495, 1448, 1408, 1378, 1222, 1159, 1080. MS (ESI^+), *m*/*z* (% relative intensity): 387 ($M^+ + H$, 54), 409 ($M^+ + Na$, 100), 425 ($M^+ + K$, 35), 795 ($2M^+ + Na$, 8). HR MS ($M^+ + H$): 387.1503 (calcd for $C_{24}H_{20}FN_2O_2$ 387.1503).

1,3-Dibenzyl-6-(4-fluorophenyl)pyrimidine-2,4(1*H*,3*H*)-dione (17e). Compound **17e** was prepared from **8** according to general procedure (Method B) in 24% yield, as a yellowish oil. ^1H NMR (499.8 MHz, $CDCl_3$): 4.92 (bs, 2H, CH_2-1); 5.22 (s, 2H, CH_2-3); 5.69 (s, 1H, H-5); 6.86 (m, 2H, H-*o*-1Bn); 7.04 (m, 2H, H-*m*-C_6H_4F); 7.11 (m, 2H, H-*o*-C_6H_4F); 7.22 (m, 3H, H-*m*,*p*-1Bn); 7.30 (m, 1H, H-*p*-3Bn); 7.33 (m, 2H, H-*m*-3Bn); 7.54 (m, 2H, H-*o*-3Bn). ^{13}C NMR (125.7 MHz, $CDCl_3$): 44.7 (CH_2-3); 49.4 (CH_2-1); 103.9 (CH-5); 115.9 (d, $J_{C,F}$ = 22.0, CH-*m*-C_6H_4F); 126.5 (CH-*o*-1Bn); 127.7 (CH-*p*-1Bn); 127.7 (CH-*p*-3Bn); 128.4 (CH-*m*-3Bn); 128.7 (CH-*m*-1Bn); 129.1 (d, $J_{C,F}$ = 3.6, C-*i*-C_6H_4F); 129.2 (CH-*o*-3Bn); 130.0 (d, $J_{C,F}$ = 8.5, CH-*o*-C_6H_4F); 136.3 (C-*i*-1Bn); 136.8 (C-*i*-3Bn); 152.5 (C-2); 153.8 (C-6); 161.9 (C-4); 163.5 (d, $J_{C,F}$ = 251.5, C-*p*-C_6H_4F). ^{19}F NMR (470.3 MHz, $CDCl_3$): −105.64. IR (KBr): 1705, 1665, 1621, 1600, 1511, 1496, 1441, 1392, 1345, 1226, 1160, 1071. MS (ESI^+), *m*/*z* (% relative intensity): 387 ($M^+ + H$, 42), 409 ($M^+ + Na$, 100), 425 ($M^+ + K$, 25), 795 ($2M^+ + Na$, 8). HR MS ($M^+ + H$): 387.1504 (calcd for $C_{24}H_{20}FN_2O_2$ 387.1503).

6-(4-Fluorophenyl)pyrimidine-2,4(1*H*,3*H*)-dione (22e). Compound **22e** was prepared from **17e** (120 mg, 0.311 mmol) according to general procedure (Method E), in 98% yield, as a white powder, mp > 300 °C (lit.[20] mp 311−313 °C). ^1H NMR (600.1 MHz, DMSO-d_6): 5.81 (s, 1H, H-5); 7.34 (m, 2H, H-*m*-C_6H_4F); 7.79 (m, 2H, H-*o*-C_6H_4F); 11.15, 11.16 (2 × bs, 2 × 1H, NH). ^{13}C NMR (150.9 MHz, DMSO-d_6): 98.3 (CH-5); 116.0 (d, $J_{C,F}$ = 21.9, CH-*m*-C_6H_4F); 128.3 (d, $J_{C,F}$ = 3.1, C-*i*-C_6H_4F); 129.8 (d, $J_{C,F}$ = 8.9, CH-*o*-C_6H_4F); 151.7 (C-6); 152.0 (C-2); 163.8 (d, $J_{C,F}$ = 249.0, C-*p*-C_6H_4F); 164.2 (C-4). $^{19}F\{^1H\}$ NMR (376.5 MHz, DMSO-d_6): −109.94. IR: 3115, 1699, 1652, 1647, 1601, 1488, 1452, 1422, 1356, 1231, 1166, 1081. MS (ESI^+), *m*/*z* (% relative intensity): 229 ($M^+ + Na$, 100), 435 ($2M^+ + Na$, 20). HR MS ($M^+ + H$): 229.0383 (calcd for $C_{10}H_7FN_2NaO_2$ 229.0384).

1,3-Dibenzyl-5-(naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (16f). Compound **16f** was prepared from **8** according to general procedure (Method A) in 19% yield, as yellowish powder, mp 62−64 °C. ^1H NMR (499.8 MHz, $CDCl_3$): 5.04 (bs, 2H, CH_2-1); 5.27 (s, 2H, CH_2-3); 7.28 (m, 1H, H-*p*-3Bn); 7.33 (m, 2H, H-*m* −3Bn); 7.35 (m, 2H, H-*o*-1Bn); 7.37 (m, 1H, H-*p*-1Bn); 7.40 (m, 2H, H-*m*-1Bn); 7.41 (s, 1H, H-6); 7.46 (m, 1H, H-6-naphth); 7.48 (m, 1H, H-7-naphth); 7.56 (dd, 1H, $J_{3,4}$ = 8.5, $J_{3,1}$ = 1.9, H-3-naphth); 7.58 (m, 2H, H-*o*-3Bn); 7.81 (m, 1H, H-8-naphth); 7.82 (m, 2H, H-4,5-naphth); 7.94 (m, 1H, H-1-naphth). ^{13}C NMR (150.9 MHz, $CDCl_3$): 45.0 (CH_2-3); 52.5 (CH_2-1); 115.1 (C-5); 126.1 (CH-3-naphth); 126.2 (CH-6,7-naphth); 127.2 (CH-1-naphth); 127.6 (CH-8-naphth); 127.7 (CH-*p*-3Bn); 128.0 (CH-4 or 5-naphth); 128.0 (CH-*o*-1Bn); 128.1 (CH-4 or 5-naphth); 128.4 (CH-*m*-3Bn); 128.6 (CH-*p*-1Bn); 129.2 (CH-*m*-1Bn); 129.3 (CH-*o*-3Bn); 130.3 (C-2-naphth); 132.8 (C-4a-naphth); 133.2 (C-8a-naphth); 135.3 (C-*i*-1Bn); 136.8 (C-*i*-3Bn); 139.6 (CH-6); 151.4 (C-2); 162.0 (C-4). IR (KBr): 1703, 1652, 1600, 1586, 1495,

1449, 1380, 1280, 1219, 1081, 1050. MS (ESI^+), *m/z* (% relative intensity): 419 ($M^+ + H$, 84), 441 ($M^+ + Na$, 100), 457 ($M^+ + K$, 9), 859 ($2M^+ + Na$, 28). HR MS ($M^+ + H$): 419.1758 (calcd for $C_{28}H_{23}N_2O_2$ 419.1754).

1,3-Dibenzyl-6-(naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (17f). Compound **17f** was prepared from **8** according to general procedure (Method B) in 33% yield, as yellowish powder, mp 55−58 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): 4.97 (bs, 2H, CH_2-1); 5.24 (s, 2H, CH_2-3); 5.81 (s, 1H, H-5); 6.86 (m, 2H, H-*o*-1Bn); 7.19 (m, 3H, H-*m*,*p*-1Bn); 7.23 (dd, 1H, $J_{3,4}$ = 8.5, $J_{3,1}$ = 1.9, H-3-naphth); 7.30 (m, 1H, H-*p*-3Bn); 7.35 (m, 2H, H-*m*-3Bn); 7.54 (ddd, 1H, $J_{7,8}$ = 8.2, $J_{7,6}$ = 6.9, $J_{7,5}$ = 1.4, H-7-naphth); 7.55 (m, 2H, H-*o*-3Bn); 7.58 (ddd, 1H, $J_{6,5}$ = 8.2, $J_{6,7}$ = 6.9, $J_{6,8}$ = 1.4, H-6-naphth); 7.63 (d, 1H, $J_{1,3}$ = 1.9, H-1-naphth); 7.74 (m, 1H, H-8-naphth); 7.83 (d, 1H, $J_{4,3}$ = 8.5, H-4-naphth); 7.87(m, 1H, H-5-naphth). ^{13}C NMR (125.7 MHz, $CDCl_3$): 44.63 (CH_2-3); 49.70 (CH_2-1); 103.76 (CH-5); 124.58 (CH-3-naphth); 126.72 (CH-*o*-1Bn); 127.18 (CH-7-naphth); 127.56 (CH-*p*-1Bn); 127.63 (CH-6-naphth); 127.65 (CH-*p*-3Bn); 127.80 (CH-5-naphth); 128.10 (CH-1-naphth); 128.35 (CH-8-naphth); 128.42 (CH-*m*-3Bn); 128.53 (CH-4-naphth); 128.55 (CH-*m*-1Bn); 129.16 (CH-*o*-3Bn); 130.31 (C-2-naphth); 132.46 (C-8a-naphth); 133.47 (C-4a-naphth); 136.54 (C-*i*-1Bn); 136.90 (C-*i*-3Bn); 152.56 (C-2); 154.93 (C-6); 162.05 (C-4). IR (KBr): 1705, 1662, 1617, 1495, 1472, 1440, 1392, 1340, 1273, 1187, 1070. MS (ESI^+), *m/z* (% relative intensity): 419 ($M^+ + H$, 59), 441 ($M^+ + Na$, 100), 457 ($M^+ + K$, 10), 859 ($2M^+ + Na$, 22). HR MS ($M^+ + H$): 419.1756 (calcd for $C_{28}H_{23}N_2O_2$ 419.1754).

3-Benzyl-5-(naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (19f). A mixture of compound **16f** (60 mg, 0.143 mmol), ammonium formate (4 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (168 mg 10% Pd/C, 0.158 mmol of Pd, 1.1 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 120 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient hexane to 20% ethylacetate in hexane gave the pure monodebenzylated product **19f** in 42% yield, as a white powder, mp 200−202 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): 5.08 (bs, 2H, CH_2Ph); 7.26 (m, 1H, H-*p*-Bn); 7.32 (m, 2H, H-*m*-Bn); 7.33 (m, 2H, H-*o*-Bn); 7.49 (m, 1H, H-6-naphth); 7.51 (m, 1H, H-7-naphth); 7.70 (dd, 1H, $J_{3,4}$ = 8.6, $J_{3,1}$ = 1.9, H-3-naphth); 7.86 (s, 1H, H-6); 7.90 (m, 3H, H-4,5,8-naphth); 8.14 (d, 1H, $J_{1,3}$ = 1.9, H-1-naphth). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.4 (CH_2Ph); 111.8 (C-5); 126.2 (CH-6-naphth); 126.3 (CH-7-naphth); 126.7 (CH-3-naphth); 126.8 (CH-1-naphth); 127.3 (CH-*p*-Bn); 127.4 (CH-8-naphth); 127.6 (CH-4 or 5-naphth); 127.9 (CH-*o*-Bn); 128.1 (CH-4 or 5-naphth); 128.6 (CH-*m*-Bn); 131.3 (C-2-naphth); 132.2 (C-4a-naphth); 133.0 (C-8a-naphth); 137.5 (C-*i*-Bn); 139.2 (CH-6); 151.1 (C-2); 162.4 (C-4). IR (KBr): 3173, 1724, 1711, 1688, 1627, 1597, 1496, 1439, 1364, 1213, 1189, 1081. MS (ESI^+), *m/z* (% relative intensity): 329 ($M^+ + H$, 48), 351 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 329.1285 (calcd for $C_{21}H_{17}N_2O_2$ 329.1285).

3-Benzyl-6-(naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (21f). A mixture of compound **17f** (110 mg, 0.263 mmol), ammonium formate (6.6 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (308 mg 10% Pd/C, 0.289 mmol of Pd, 1.1 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 200 mL). Removal of solvents under reduced pressure and following column chromatography on 70 g of silica gel in gradient hexane to 20% ethylacetate in hexane gave the pure monodebenzylated product **21f** in 98% yield, as a white powder, mp 183−185°. ^{1}H NMR (500.0 MHz, DMSO-d_6): 5.03 (bs, 2H, CH_2Ph); 6.18 (s, 1H, H-5); 7.26 (m, 1H, H-*p*-Bn); 7.33 (m, 4H, H-*o*,*m*-Bn); 7.61 (m, 1H, H-7-naphth); 7.64 (m, 1H, H-6-naphth); 7.84 (dd, 1H, $J_{3,4}$ = 8.6, $J_{3,1}$ = 2.0, H-3-naphth); 7.99 (m, 1H, H-5-naphth); 8.01 (m, 1H, H-8-naphth); 8.04 (m, 1H, H-4-naphth); 8.43 (d, 1H, $J_{1,3}$ = 2.0, H-1-naphth). ^{13}C NMR (125.7 MHz, DMSO-d_6): 42.9 (CH_2Ph); 98.1 (CH-5); 124.0 (CH-3-naphth); 127.2 (CH-7-naphth); 127.3 (CH-*p*-Bn); 127.5 (CH-1-naphth); 127.7 (CH-*o*-Bn); 127.8 (CH-5-naphth); 128.1 (CH-6-naphth); 128.5 (CH-*m*-Bn); 128.7 (CH-4-naphth); 128.7 (C-2-naphth); 129.0 (CH-8-naphth); 132.5 (C-8a-naphth); 134.1 (C-4a-naphth); 137.5 (C-*i*-Bn); 151.2 (C-6); 152.0 (C-2); 163.0 (C-4). IR: 3165, 1722, 1711, 1698, 1625, 1483, 1466, 1439, 1377, 1244, 1213, 1150, 1128, 1081. MS (ESI^+), *m/z* (% relative intensity): 329 ($M^+ + H$, 70), 351 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 329.1283 (calcd for $C_{21}H_{17}N_2O_2$ 329.1285).

5-(Naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (20f). Compound **20f** was prepared from **16f** (100 mg, 0.239 mmol) according to general procedure (Method E), in 63% yield, as a yellowish powder, mp > 300 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 7.49 (ddd, 1H, $J_{6,5}$ = 8.8, $J_{6,7}$ = 6.8, $J_{6,8}$ = 1.7, H-6-naphth); 7.70 (ddd, 1H, $J_{7,8}$ = 8.8, $J_{7,6}$ = 6.8, $J_{7,5}$ = 1.7, H-7-naphth); 7.70 (dd, 1H, $J_{3,4}$ = 8.5, $J_{3,1}$ = 1.8, H-3-naphth); 7.77 (bd, 1H, $J_{6,NH}$ = 5.6, H-6); 7.87−7.91 (m, 3H, H-4,5,8-naphth); 8.12 (m, 1H, H-1-naphth); 11.23 (bd, 1H, $J_{NH,6}$ = 5.6, NH-1); 11.31 (bs, 1H, NH-3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 112.2 (C-5); 126.1 (CH-6-naphth); 126.3 (CH-7-naphth); 126.5 (CH-1-naphth); 126.6 (CH-3-naphth); 127.4 (CH-4-naphth); 127.6 (CH-5-naphth); 128.1 (CH-8-naphth); 131.2 (C-2-naphth); 132.1 (C-4a-naphth); 133.0 (C-8a-naphth); 140.4 (C-6); 151.2 (C-2); 163.5 (C-4). IR: 3135, 1748, 1664, 1597, 1509, 1445, 1330, 1228, 1127, 1075. MS (ESI^+), *m/z* (% relative intensity): 239 ($M^+ + H$, 30), 261 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 239.0814 (calcd for $C_{14}H_{11}N_2O_2$ 239.0815).

6-(Naphthalen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (22f). Compound **22f** was prepared from **17f** (100 mg, 0.261 mmol) according to general procedure (Method E), in 70% yield, as a yellowish powder, mp > 300 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): 5.98 (d, 1H, J = 1.9, H-5); 7.61 (ddd, 1H, $J_{6,5}$ = 8.7, $J_{6,7}$ = 6.9, $J_{6,8}$ = 1.9, H-6-naphth); 7.63 (ddd, 1H, $J_{7,8}$ = 8.7, $J_{7,6}$ = 6.9, $J_{7,5}$ = 1.9, H-7-naphth); 7.81 (dd, 1H, $J_{3,4}$ = 8.7, $J_{3,1}$ = 2.0, H-3-naphth); 7.99 (m, 1H, H-5-naphth); 8.01 (m, 1H, H-8-naphth); 8.02 (m, 1H, H-4-naphth); 8.39 (m, 1H, H-1-naphth); 11.19, 11.23 (2 × bs, 2 × 1H, NH-1,3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 98.63 (CH-5); 124.00 (CH-3-naphth); 127.16 (CH-6-naphth); 127.28 (CH-1-naphth); 127.80 (CH-5-naphth); 127.96 (CH-7-naphth); 128.62 (CH-4-naphth); 128.96 (CH-8-naphth); 129.00 (C-2-naphth); 132.47 (C-8a-naphth); 134.02 (C-4a-naphth); 152.06 (C-2); 152.47 (C-6); 164.27 (C-4). IR (KBr): 3132, 1722, 1650, 1613, 1594, 1517, 1494, 1447, 1424, 1337, 1217, 1082. MS (ESI^+), *m/z* (% relative intensity): 239 ($M^+ + H$, 10), 261 ($M^+ + Na$, 28), 399 ($2M^+ + Na$, 100). HR MS ($M^+ + H$): 239.0814 (calcd for $C_{14}H_{11}N_2O_2$ 239.0815).

1,3-Dibenzyl-5-(pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (16g). Compound **16g** was prepared from **8** according to general procedure (Method A) in 25% yield, as a yellow powder, mp 82−84 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): 5.05 (bs, 2H, CH_2-1); 5.31 (s, 2H, CH_2-3); 7.30 (m, 1H, H-*p*-3Bn); 7.35 (m, 2H, H-*m*-3Bn); 7.37 (m, 3H, H-*o*,*p*-1Bn); 7.40 (m, 2H, H-*m*-1Bn); 7.41 (s, 1H, H-6); 7.62 (m, 2H, H-*o*-3Bn); 7.86 (d, 1H, $J_{2,3}$ = 7.8, H-2-pyrenyl); 7.87 (d, 1H, $J_{10,9}$ = 9.2, H-10-pyrenyl); 8.00 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrenyl); 8.01 (d, 1H, $J_{9,10}$ = 9.2, H-9-pyrenyl); 8.04 (d, 1H, $J_{4,5}$ = 8.9, H-4-pyrenyl); 8.08 (d, 1H, $J_{5,4}$ = 8.9, H-5-pyrenyl); 8.15 (d, 1H, $J_{3,2}$ = 7.8, H-3-pyrenyl); 8.16 (dd, 1H, $J_{8,7}$ = 7.6, $J_{8,6}$ = 1.1, H-8-pyrenyl); 8.19 (dd, 1H, $J_{6,7}$ = 7.6, $J_{6,8}$ = 1.1, H-6-pyrenyl). ^{13}C NMR (125.7 MHz, $CDCl_3$): 45.1 (CH_2-3); 52.5 (CH_2-1); 114.4 (C-5); 124.4 (CH-10-pyrenyl); 124.6 (CH-3-pyrenyl); 124.6 (C-10c-pyrenyl); 124.9 (CH-10b-pyrenyl); 125.2 (CH-8-pyrenyl); 125.4 (CH-6-pyrenyl); 126.1 (CH-7-pyrenyl); 127.2 (CH-4-pyrenyl); 127.4 (C-1-pyrenyl); 127.7 (CH-*p*-3Bn); 127.8 (CH-9-pyrenyl); 127.9 (CH-5-pyrenyl); 128.2 (CH-*o*-1Bn); 128.3 (CH-2-pyrenyl); 128.5 (CH-*m*-3Bn); 128.6 (CH-*p*-1Bn); 129.2 (CH-*m*-1Bn); 129.6 (CH-*o*-3Bn); 129.8 (C-10a-pyrenyl); 130.8 (C-8a-

pyrenyl); 131.2 (C-5a-pyrenyl); 131.4 (C-3a-pyrenyl); 135.3 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 141.7 (CH-6); 151.6 (C-2); 162.4 (C-4). IR: 1700, 1649, 1602, 1584, 1495, 1432, 1389, 1341, 1179, 1070. MS (ESI$^+$), *m*/*z* (% relative intensity): 493 ($M^+ + H$, 15), 515 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 493.1909 (calcd for $C_{34}H_{25}N_2O_2$ 493.1911).

1,3-Dibenzyl-6-(pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (17g). Compound **17g** was prepared from **8** according to general procedure (Method B) in 50% yield, as a yellow powder, mp 78−80 °C. ^{1}H NMR (600.1 MHz, $CDCl_3$): 4.49, 5.12 (2 × d, 2 × 1H, J_{gem} = 15.5, CH_2-1); 5.30, 5.37 (2 × d, 2 × 1H, J_{gem} = 13.3, CH_2-3); 5.94 (s, 1H, H-5); 6.58 (m, 2H, H-*o*-1Bn); 6.99 (m, 2H, H-*m*-1Bn); 7.08 (m, 2H, H-*m*-1Bn); 7.34 (m, 1H, H-*p*-3Bn); 7.40 (m, 2H, H-*m*-3Bn); 7.63 (d, 1H, $J_{2,3}$ = 7.9, H-2-pyrenyl); 7.64 (m, 2H, H-*o*-3Bn); 7.82 (d, 1H, $J_{10,9}$ = 9.1, H-10-pyrenyl); 8.08 (m, 3H, H-3,4,5-pyrenyl); 8.09 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.7, H-7-pyrenyl); 8.18 (d, 1H, $J_{9,10}$ = 9.1, H-9-pyrenyl); 8.25 (dd, 1H, $J_{8,7}$ = 7.7, $J_{8,6}$ = 1.2, H-8-pyrenyl); 8.29 (dd, 1H, $J_{6,7}$ = 7.7, $J_{6,8}$ = 1.2, H-6-pyrenyl). ^{13}C NMR (150.9 MHz, $CDCl_3$): 44.8 (CH_2-3); 49.5 (CH_2-1); 105.0 (C-5); 123.1 (CH-10-pyrenyl); 124.2 (C-10c-pyrenyl); 124.3 (CH-10b-pyrenyl, CH-3-pyrenyl); 126.2 (CH-8-pyrenyl); 126.3 (CH-7-pyrenyl); 126.3 (CH-6-pyrenyl); 126.6 (CH-1-pyrenyl); 126.7 (CH-4-pyrenyl); 127.0 (CH-*o*-1Bn); 127.1 (CH-5-pyrenyl); 127.5 (CH-*p*-1Bn); 127.7 (CH-*p*-3Bn); 128.3 (CH-*m*-1Bn); 128.4 (C-10a-pyrenyl); 128.5 (CH-*m*-3Bn); 129.0 (CH-9-pyrenyl); 129.3 (CH-*o*-3Bn); 129.4 (CH-2-pyrenyl); 130.6 (C-8a-pyrenyl); 131.1 (C-5a-pyrenyl); 132.4 (C-3a-pyrenyl); 136.3 (C-*i*-1Bn); 136.9 (C-*i*-3Bn); 152.7 (C-2); 153.8 (C-6); 162.1 (C-4). IR: 1700, 1652, 1601, 1584, 1494, 1430, 1389, 1340, 1179, 1070. MS (ESI$^+$), *m*/*z* (% relative intensity): 493 ($M^+ + H$, 16), 515 ($M^+ + Na$, 100), 531 ($M^+ + K$, 30), 1007 ($2M^+ + Na$, 13). HR MS ($M^+ + H$): 493.1910 (calcd for $C_{34}H_{25}N_2O_2$ 493.1911).

3-Benzyl-5-(pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (19g). A mixture of compound **16g** (50 mg, 0.102 mmol), ammonium formate (2.6 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (120 mg 10% Pd/C, 0.113 mmol of Pd, 1.1 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite, and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 120 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient 10% ethylacetate in hexane to 50% ethylacetate in hexane gave the pure monodebenzylated product **19g** in 67% yield, as a yellow powder, mp > 300 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 5.11 (bs, 2H, CH_2-3); 7.28 (m, 1H, H-*p*-Bn); 7.36 (m, 2H, H-*m*-Bn); 7.38 (m, 2H, H-*o*-Bn); 7.78 (d, 1H, $J_{6,NH}$ = 5.5, H-6); 7.96 (d, 1H, $J_{2,3}$ = 7.8, H-2-pyrenyl); 8.01 (d, 1H, $J_{10,9}$ = 9.2, H-10-pyrenyl); 8.08 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrenyl); 8.15 (d, 1H, $J_{9,10}$ = 9.2, H-9-pyrenyl); 8.21 (s, 2H, H-4,5-pyrenyl); 8.30 (d, 1H, $J_{3,2}$ = 7.8, H-3-pyrenyl); 8.31 (m, 2H, H-6,8-pyrenyl); 11.65 (bd, 1H, $J_{NH,6}$ = 5.5, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.5 (CH_2Ph); 112.0 (C-5); 124.0 (C-10c-pyrenyl); 124.1 (CH-10b-pyrenyl); 124.8 (CH-3-pyrenyl); 125.4 (CH-10-pyrenyl); 125.5, 125.6 (CH-6,8-pyrenyl); 126.5 (CH-7-pyrenyl); 127.4 (CH-*p*-Bn); 127.4 (CH-9-pyrenyl); 127.5 (CH-4-pyrenyl); 127.7 (CH-5-pyrenyl); 127.9 (CH-*o*-Bn); 128.6 (CH-*m*-Bn); 129.2 (CH-2-pyrenyl); 129.3 (C-1-pyrenyl); 129.7 (C-10a-pyrenyl); 130.6 (C-8a-pyrenyl); 130.7 (C-3a-pyrenyl); 131.0 (C-5a-pyrenyl); 137.6 (C-*i*-Bn); 140.7 (CH-6); 151.6 (C-2); 162.9 (C-4). IR (KBr): 3169, 1711, 1635, 1583, 1495, 1440, 1417, 1329, 1281, 1212, 1150, 1068. MS (ESI$^-$), *m*/*z* (% relative intensity): 401 ($M^- - H$, 100), 825 ($2[M^- - H] + Na$, 19). HR MS ($M^- - H$): 401.1296 (calcd for $C_{27}H_{17}N_2O_2$ 401.1296).

3-Benzyl-6-(pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (21g). A mixture of compound **17g** (50 mg, 0.102 mmol), ammonium formate (2.6 mL of a 0.4 N solution in dry MeOH) and 10% palladium−charcoal (120 mg 10% Pd/C, 0.113 mmol of Pd, 1.1 equiv of Pd) was refluxed at 72 °C for 17 h. The mixture was filtered through Celite, and the solid residue was extensively washed with MeOH and $CHCl_3$ (ca. 120 mL). Removal of solvents under reduced pressure and following column chromatography on 40 g of silica gel in gradient 10% ethylacetate in hexane to 50% ethylacetate in hexane gave the pure monodebenzylated product **21g** in 83% yield, as a yellow powder, mp 291−293 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): 5.10 (s, 2H, CH_2Ph); 5.92 (s, 1H, H-5); 7.30 (m, 1H, H-*p*-Bn); 7.38 (m, 2H, H-*m*-Bn); 7.43 (m, 2H, H-*o*-Bn); 8.15 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.7, H-7-pyrenyl); 8.16 (d, 1H, $J_{2,3}$ = 7.9, H-2-pyrenyl); 8.26 (d, 1H, $J_{9,10}$ = 9.1, H-9-pyrenyl); 8.31 (m, 3H, H-4,5,10-pyrenyl); 8.39 (m, 3H, H-3,6,8-pyrenyl); 11.81 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.0 (CH_2Ph); 101.9 (C-5); 123.7 (C-10c-pyrenyl); 123.9 (CH-10b-pyrenyl); 124.2 (CH-10-pyrenyl); 124.8 (CH-3-pyrenyl); 126.1, 126.3 (CH-6,8-pyrenyl); 126.8 (CH-9-pyrenyl); 127.0 (CH-7-pyrenyl); 127.35, 127.38 (CH-2-pyrenyl, CH-*p*-Bn); 127.6 (C-1-pyrenyl); 128.0 (CH-*o*-Bn); 128.1 (C-10a-pyrenyl); 128.6 (CH-*m*-Bn); 128.9 (CH-4,5-pyrenyl); 130.4, 130.9 (C-5a,8a-pyrenyl); 132.2 (C-3a-pyrenyl); 137.6 (C-*i*-Bn); 151.7 (C-2); 151.8 (C-6); 162.9 (C-4). IR (KBr): 3154, 1711, 1636, 1584, 1488, 1437, 1422, 1357, 1236, 1179, 1089, 1050. MS (ESI$^-$), *m*/*z* (% relative intensity): 401 ($M^- - H$, 100), 825 ($2[M^- - H] + Na$, 66). HR MS ($M^- - H$): 401.1293 (calcd for $C_{27}H_{17}N_2O_2$ 401.1296). Anal. Calcd for $C_{27}H_{18}N_2O_2 \cdot 0.75H_2O$: C, 77.96; H, 4.73; N, 6.73. Found: C, 78.21; H, 4.72; N, 6.35.

5-(Pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (20g). Compound **20g** was prepared from **16g** (95 mg, 0.193 mmol) according to general procedure (Method E), in 98% yield, as a white powder, mp > 300 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 7.67 (d, 1H, $J_{6,NH}$ = 5.8, H-6); 7.93 (d, 1H, $J_{2,3}$ = 7.8, H-2-pyrenyl); 8.02 (d, 1H, $J_{10,9}$ = 9.2, H-10-pyrenyl); 8.08 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrenyl); 8.16 (d, 1H, $J_{9,10}$ = 9.2, H-9-pyrenyl); 8.20 (s, 2H, H-4,5-pyrenyl); 8.28−8.32 (m, 3H, H-3,6,8-pyrenyl); 11.23 (bdd, 1H, $J_{NH,6}$ = 5.5, $J_{NH,NH}$ = 2.0, NH-1); 11.39 (bd, 1H, $J_{NH,NH}$ = 2.0, NH-3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 112.5 (C-5); 124.0 (C-10c-pyrenyl); 124.1 (CH-10b-pyrenyl); 124.7 (CH-3-pyrenyl); 125.3, 125.5 (CH-6,8-pyrenyl); 125.6 (CH-10-pyrenyl); 126.5 (CH-7-pyrenyl); 127.3 (CH-9-pyrenyl); 127.5, 127.6 (CH-4,5-pyrenyl); 129.1 (CH-2-pyrenyl); 129.2 (C-1-pyrenyl); 129.7 (C-10a-pyrenyl); 130.6, 130.7 (C-3a,8a-pyrenyl); 131.0 (C-5a-pyrenyl); 141.9 (CH-6); 151.7 (C-2); 163.9 (C-4). IR: 3140, 1721, 1698, 1636, 1555, 1480, 1437, 1363, 1344, 1236, 1179, 1089. MS (ESI$^+$), *m*/*z* (% relative intensity): 313 ($M^+ + H$, 30), 335 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 313.0972 (calcd for $C_{20}H_{13}N_2O_2$ 313.0972).

6-(Pyren-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (22g). Compound **22g** was prepared from **17g** (100 mg, 0.203 mmol) according to general procedure (Method E), in 38% yield, as a yellow powder, mp > 300 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 71 (d, 1H, $J_{5,NH}$ = 1.8, H-5); 8.12 (d, 1H, $J_{2,3}$ = 7.9, H-2-pyrenyl); 8.15 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrenyl); 8.26 (d, 1H, $J_{4,5}$ = 9.1, H-4-pyrenyl); 8.27 (d, 1H, $J_{9,10}$ = 9.3, H-9-pyrenyl); 8.308 (d, 1H, $J_{5,4}$ = 9.1, H-5-pyrenyl); 8.314 (d, 1H, $J_{10,9}$ = 9.3, H-10-pyrenyl); 8.38 (d, 1H, $J_{3,2}$ = 7.9, H-3-pyrenyl); 8.39 (d, 2H, $J_{6\text{ and }8,7}$ = 7.6, H-6,8-pyrenyl); 11.29, 11.41 (2 × bs, 2 × 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 102.40 (C-5); 123.75 (C-10c-pyrenyl); 123.84 (CH-10b-pyrenyl); 124.17 (CH-10-pyrenyl); 124.82 (CH-3-pyrenyl); 126.06, 126.28 (CH-6,8-pyrenyl); 126.60 (CH-2-pyrenyl); 126.96 (CH-7-pyrenyl); 127.37 (CH-4-pyrenyl); 127.97 (C-1-pyrenyl); 128.09 (C-10a-pyrenyl); 128.82, 128.84 (CH-5,9-pyrenyl); 130.41 (C-8a-pyrenyl); 130.89 (C-5a-pyrenyl); 132.07 (C-3a-pyrenyl); 151.81 (C-2); 153.06 (C-6); 164.16 (C-4). IR: 3138, 1721, 1699, 1636, 1580, 1488, 1436, 1422, 1357, 1344, 1236, 1170, 1081. MS (ESI$^+$), *m*/*z* (% relative intensity): 313 ($M^+ + H$, 33), 335 ($M^+ + Na$, 100). HR MS ($M^+ + H$): 313.09714 (calcd for $C_{20}H_{13}N_2O_2$ 313.09715).

■ ASSOCIATED CONTENT

Supporting Information. Copies of all NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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