One-Pot Synthesis of *N*-Alkyl Purine, Pyrimidine and Azole Derivatives from Alcohols using Ph_3P/CCl_4: A Rapid Route to Carboacyclic Nucleoside Synthesis

Mohammad Navid Soltani Rad,*[a] Ali Khalafi-Nezhad,*[b] Somayeh Behrouz,[b] Zeinab Asrari,[b] Marzieh Behrouz,[b] Zohreh Amini[a]

[a] Department of Chemistry, Faculty of Basic Sciences, Shiraz University of Technology, Shiraz 71555-313, Iran
Fax +98(711)7354523; E-mail: soltani@sutech.ac.ir, nsoltanirad@gmail.com

[b] Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

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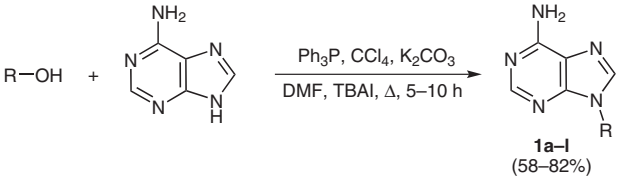
Abstract: A facile and efficient method for one-pot N-alkylation of nucleobases and azole derivatives from alcohols using triphenylphosphine in carbon tetrachloride is described. In this method, treatment of alcohols with a mixture of triphenylphosphine, carbon tetrachloride, nucleobase or azole derivatives and potassium carbonate in the presence of catalytic amounts of tetra-*n*-butylammonium iodide (TBAI) in refluxing *N*,*N*-dimethylformamide, furnishes the corresponding *N*-alkyl derivatives in good yields. This methodology is highly efficient for various structurally diverse primary alcohols and also useful for N-alkylation of other N-heterocycles containing an acidic N–H bond.

Key words: carboacyclic nucleosides, N-alkylation, nucleobase, alcohol, triphenylphosphine, carbon tetrachloride, potassium carbonate

Carboacyclic nucleosides constitute a special class of nucleoside analogues that have attracted great interest due to their broad spectrum of antiviral and anticancer activities.[1] The most common route to nucleoside synthesis involves the N-alkylation of nucleobases with alkyl halides,[2] alkyl tosylates[3] and mesylates.[4] Furthermore, the N-alkylation of purine and pyrimidine nucleobases with other carbon electrophiles such as epoxides,[5] Michael acceptors,[6] carbonates,[7] and allylic esters catalyzed by palladium(0),[8] are well known procedures. Moreover, acetoxyethyl and acetoxymethyl ethers and their analogues,[9] methylthiomethyl ethers[10] and cyclic acetals,[11] as active ethers, have also been described for the N-alkylation of nucleobases.

In view of the wide diversity and availability of alcohols, lower toxicity and ease of handling with respect to alkyl halides, the one-pot reaction of nucleobases with alcohols seems to be a suitable and attractive strategy. Unfortunately, few reports describing conditions that are suitable for accessing *N*-alkylated nucleobases from alcohols have so far been published; the methods that have are mostly based on Mitsunobu conditions.[12] However, the use of toxic, expensive and explosive reagents such as diethyl azodicarboxylate (DEAD) and diisopropyl azodicarboxylate (DIAD) restricts the applicability of this method. Since few synthetic methods efficiently provide direct access to the biologically important *N*-alkyl nucleobases from alcohols,[13] there is still an urgent need to extend and improve convenient, efficient and selective methods for one-pot N-alkylation of nucleobases using alcohols.

Use of the well-known combination of tertiary phosphanes with tetrahalomethanes have found increasing applications in preparative chemistry for halogenations, dehydrations and P–N linking reactions.[14] Among these combinations, triphenylphosphine in carbon tetrachloride is a famous reagent which can convert an alcohol into the corresponding alkyl halide[15] under mild conditions. Moreover, the triphenylphosphine in carbon tetrachloride system has found various important applications including: conversion of alcohols into nitriles[16] and esters,[17] chlorination and chlorodehydration of 1,2-diols,[18] cyclodehydration of chiral diols,[19] dehydration of aldoximes[20a] and amides,[20b] conversion of carboxylic acids into amides[21a] and acid chlorides,[21b] synthesis of benzoxazoles,[22a] [1,3,4]-oxadiazoles,[22b] β-lactams[22c] and *N*-acylindolines.[22d] However, although triphenylphosphine in carbon tetrachloride has been widely employed as an efficient and useful reagent for several organic transformations, there have been no reports on the application of this combination for the N-alkylation of nucleobases or other N-heterocycles with alcohols. In a continuation of our interest in the design and synthesis of novel carboacyclic nucleosides,[5a,6a,13,23] in this context, we report triphenylphosphine in carbon tetrachloride as a convenient and inexpensive reagent combination for the one-pot N-alkylation of nucleobases (Scheme 1 and Scheme 2), as well as azole derivatives (Scheme 3) using alcohols in the presence of potassium carbonate and a catalytic amount of tetra-*n*-butylammonium iodide (TBAI) in anhydrous *N*,*N*-dimethylformamide at reflux for 5–10 hours.



Scheme 1

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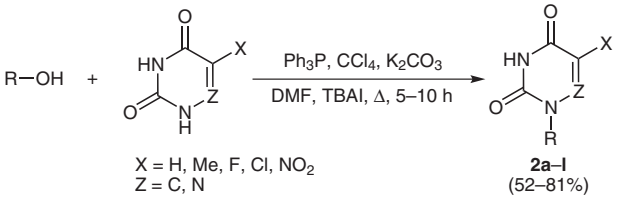
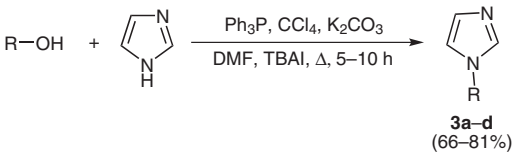


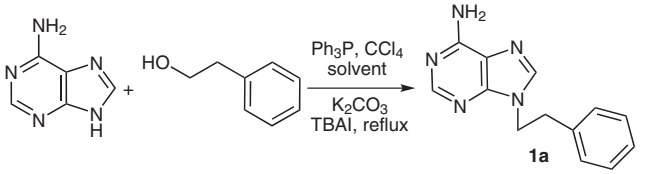
Scheme 2



Scheme 3

In order to establish optimized reaction conditions, we chose the reaction of adenine, 2-phenylethanol and potassium carbonate, in the presence of a mixture of triphenylphosphine in carbon tetrachloride and a catalytic amount of TBAI, as a reaction model. Initially, the effect of various aprotic solvents on the model reaction was studied. The results are depicted in Table 1.

Table 1 Effect of Solvents on Conversion of 2-Phenylethanol into 9-Phenethyl-9*H*-purin-6-amine (**1a**)



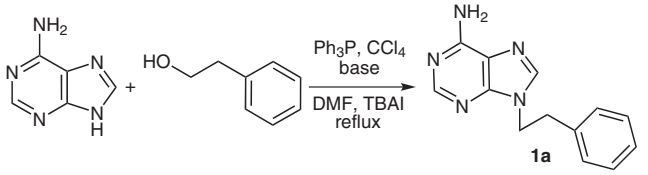
Entry	Solvent[a]	Time (h)	Yield (%)[b]
1	DMSO	7	45
2	DMF	24	NR[c]
3	DMF	5	82
4	MeCN	18	NR
5	HMPA	12	37
6	NMP	18	10
7	THF	12	NR
8	toluene	18	NR
9	acetone	12	NR

[a] All solvents except DMF (entry 2) were anhydrous.
[b] Isolated yield. NR = no reaction.
[c] No reaction after refluxing for 72 h.

As the data in Table 1 indicates, anhydrous *N*,*N*-dimethylformamide (Table 1, entry 3) was found to be the most efficient solvent and, hence, was the solvent of choice for all further reactions. In view of the fact that the generated reactive intermediates in the reaction mixture are very susceptible to moisture, the use of a well-dried solvent is essential. The explicit interference of moisture was easily observed by the comparison of results obtained using wet versus anhydrous *N*,*N*-dimethylformamide (Table 1, entries 2 and 3). Using DMSO and HMPA afforded a moderate yield of the corresponding 9-phenethyl-9*H*-purin-6-amine (**1a**).

Other solvents were inefficient even if the reaction time was extended for up to 72 hours. The choice of base for activating the N–H bonds in nucleobases and azoles for reaction with the alkoxyphosphonium salt intermediate had a great significance. We therefore evaluated the effect of various organic and inorganic bases on the reaction model (Table 2).

Table 2 Effect of Bases on Conversion of 2-Phenylethanol into 9-Phenethyl-9*H*-purin-6-amine (**1a**) in Anhydrous *N*,*N*-Dimethylformamide



Entry	Base	Time (h)	Yield (%)[a]
1	DBN	24	15
2	DBU	12	26
3	DABCO	12	35
4	DMAP	12	23
5	MgO	72	trace
6	Cs_2CO_3	7	40
7	K_2CO_3	5	82
8	Et_3N	72	trace
9	NaH	72	trace

[a] Isolated yield.

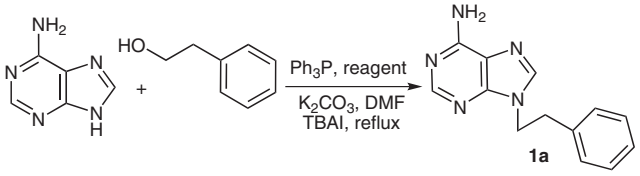
The results in Table 2 demonstrate that, of the examined bases, potassium carbonate (Table 2, entry 7) was the most appropriate base for the reaction. DBU, DABCO, and cesium carbonate (Table 2, entries 2, 3 and 6) afforded moderate yields of **1a**, while other bases were inefficient.

We also investigated the role of various phase-transfer catalysts (PTC) on the reaction model. In this case, tetra-*n*-butylammonium halides (TBAX; X = F, Cl, Br and I) were employed. In the absence of PTC, the reaction occurred in only low yields (<10%). However, the use of TBAI afforded **1a** in higher yield in a short reaction time; other PTCs were not as effective.

In a series of other experiments, we investigated the influence of several reagents as positive-halogen sources instead of carbon tetrachloride, in combination with triphenylphosphine (Table 3). According to the results in

Table 3, the triphenylphosphine in carbon tetrachloride system was found to be the most suitable and efficient reagent for the conversion of 2-phenylethanol into **1a**. The use of *N*-chlorosuccinimide, *N*-bromosuccinimide, isocyanuric chloride or molecular bromine (Table 3, entries 2–5) did not afford satisfactory results; DDQ and CHI_3 (entries 6 and 7) were also inefficient even after refluxing for 72 hours.

Table 3 Effect of Various Reagents Giving Positive-Halogens on the Conversion of 2-Phenylethanol into **1a** in Anhydrous *N*,*N*-Dimethylformamide



Entry	Reagent	Time (h)	Yield (%)[a]
1	Ph_3P, CCl_4	5	82
2	Ph_3P, NCS	12	35
3	Ph_3P, NBS	12	27
4	Ph_3P, isocyanuric chloride	18	10
5	Ph_3P, Br_2	24	12
6	Ph_3P, DDQ	72	trace
7	Ph_3P, CHI_3	72	trace

[a] Isolated yield.

The optimized stoichiometric ratio of Ph_3P–CCl_4–ROH–nucleobase–K_2CO_3 for the conversion of 2-phenylethanol into **1a** was found to be 1.5:2:1.5:1:1.

The generality and versatility of this method was demonstrated by its application to various structurally diverse alcohols and nucleobases. As the results in Table 4 indicate, a range of alcohols reacted with purine **1a–l** and pyrimidine **2a–l** nucleobases as well as azoles **3a–d** to afford the corresponding *N*-alkyl derivatives. The results demonstrate that this method is efficient and suitable for primary alcohols, including aliphatic, benzylic and allylic alcohols, while secondary and tertiary types did not give satisfactory results. For instance, N-alkylation of adenine with isopropyl alcohol afforded the corresponding product **1l** only in trace amounts (<10%). In order to demonstrate the generality of this method, the optimized conditions were also applied to other azole derivatives including: benzimidazole, 2-methyl-4-nitro-1*H*-imidazole and imidazole **3a–d**. Interestingly, ^1H NMR and ^{13}C NMR studies indicated that good regioselectivity was achieved for the N-alkylation in nucleobases.[24] The N-alkylation of purine and pyrimidine nucleobases was achieved chiefly on N9 and N1 sites, respectively, while the corresponding N7-alkyl or N1,N3-dialkyl derivatives were found in trace amounts (<5–7%).

Table 4 One-Pot N-Alkylation of Nucleobases and Other Azoles via Alcohols Using Ph_3P, CCl_4, K_2CO_3, TBAI in Refluxing *N*,*N*-Dimethylformamide

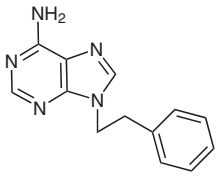
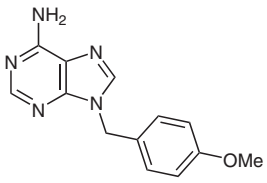
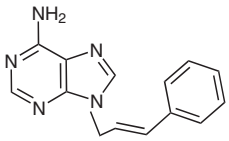
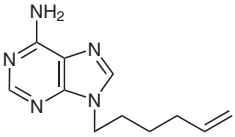
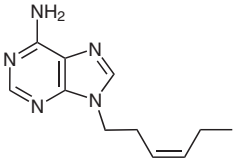
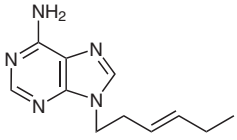
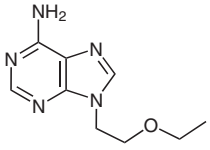
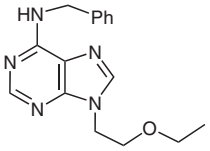
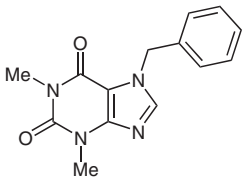
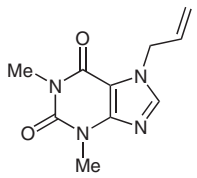
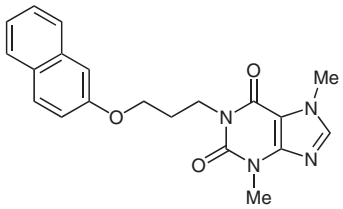
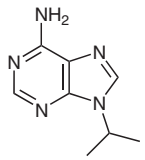
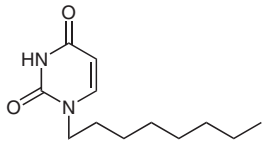
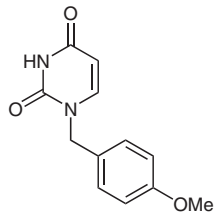
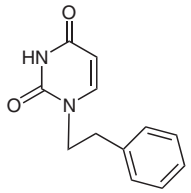
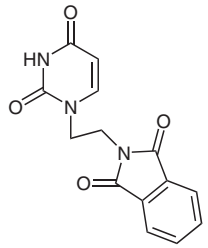
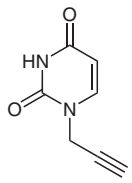
Compd	Structure[a]	Mp (°C)	Time (h)	Yield (%)[b]
1a		180.3	5	82
1b		161.4	5	75
1c		237.3	10	60
1d		141.1	6	82
1e		97.8	7	58
1f		127.0	7	77
1g		149.2	6	80
1h		124.3	5	58
1i		159.4	8	65

Table 4 One-Pot N-Alkylation of Nucleobases and Other Azoles via Alcohols Using Ph_3P, CCl_4, K_2CO_3, TBAI in Refluxing *N*,*N*-Dimethylformamide (continued)

Compd	Structure[a]	Mp (°C)	Time (h)	Yield (%)[b]
1j		103.7	8	66
1k		135.2	10	61
1l		234.8	10	trace[c]
2a		62.4	7	70
2b		118.0	6	55
2c		149.2	5	74
2d		263.6	6	78
2e		154.4	6	72

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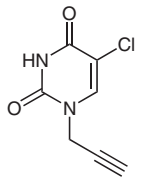
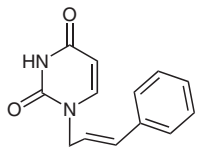
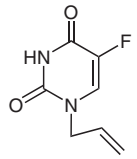
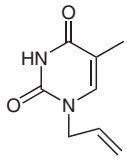
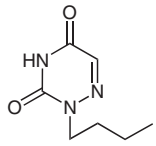
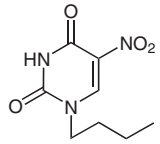
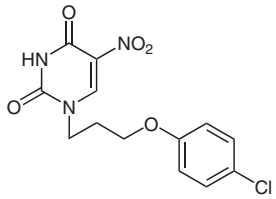
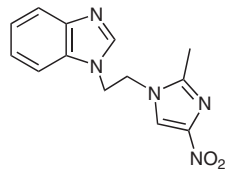
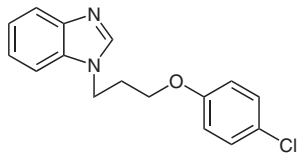
Compd	Structure[a]	Mp (°C)	Time (h)	Yield (%)[b]
2f		170.3	6	59
2g		199.2	10	71
2h		101.2	7	52
2i		123.0	7	67
2j		136.8	10	55
2k		146.3	10	81
2l		231.6	10	68
3a		223.2	9	66
3b		118.1	9	74

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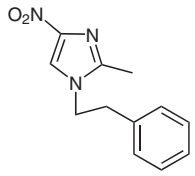
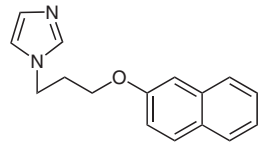
Compd	Structure[a]	Mp (°C)	Time (h)	Yield (%)[b]
3c		116.2	7	68
3d		99.4	10	81

[a] All products were characterized by ^1H and ^{13}C NMR, IR, CHN, and MS analysis.
[b] Isolated yield.
[c] This compound was produced in a trace amount (<10%).

Furthermore, O-alkylation of the pyrimidine nucleobases was not observed. When the N-alkylation of adenine and uracil was classically achieved using alkyl halide, such as (2-chloroethyl)benzene in the presence of potassium carbonate in *N*,*N*-dimethylformamide,[25] affording **1a** and **2c**, respectively, we witnessed that the ratio of N7-alkyl/N9-alkyl in adenine and/or N1, N3-dialkyl/N1-alkyl in uracil was remarkable improved with respect to the present method using 2-phenylethanol. Hence, we presume that the regioselectivity of nucleobase N-alkylation is more kinetically controlled using alkyl halides than using alcohol, and this leads to higher reactivity of alkyl halides in comparison to alcohols.

In conclusion, a novel and efficient method has been established for the one-pot N-alkylation of purines and pyrimidines as well as other azoles, using alcohols in the presence of triphenylphosphine, carbon tetrachloride, potassium carbonate and TBAI (cat.) in refluxing *N*,*N*-dimethylformamide. In this method, various primary alcohols underwent reaction with nucleobases and other *N*-heterocycles to afford *N*-alkyl derivatives in reasonable to good yields. In addition, this method can be extended to other N-heterocycles prone to N-alkylation.

All chemicals were purchased from either Fluka or Merck. Solvents were purified and dried by standard procedures, and stored over 3 Å molecular sieves. Reactions were followed by TLC using SILG/UV 254 silica-gel plates. Column chromatography was performed on silica gel 60 (0.063–0.200 mm, 70–230 mesh; ASTM). Melting points were obtained using a Büchi-510 apparatus in open capillaries and are uncorrected. IR Spectra were obtained using a Shimadzu FT-IR-8300 spectrophotometer. ^1H- and ^{13}C NMR Spectra were obtained using a Bruker Avance-DPX-250 spectrometer operating at 250/62.5 MHz, respectively (δ in ppm, *J* in Hz). GC/MS were performed on a Shimadzu GC/MS-QP 1000-EX apparatus (*m*/*z*; rel. %). Elemental analyses (CHNS) were performed on a Perkin–Elmer 240-B micro-analyzer.

One-Pot N-Alkylation of Nucleobases Using Alcohols: General Procedure

To a double-necked round-bottom flask (100 mL) equipped with a condenser was added a mixture of PPh_3 (0.015 mol), CCl_4 (0.02 mol), alcohol (0.015 mol), nucleobase or other N-heterocycle (0.01 mol), K_2CO_3 (0.01 mol) and a catalytic amount of TBAI (0.1 g) in anhydrous DMF (30 mL). The mixture was refluxed for the appropriate time until TLC monitoring indicated no further improvement in the conversion (Table 4). The solvent was evaporated under vacuum and the remaining foam was dissolved in $CHCl_3$ or EtOAc (100 mL) and subsequently washed with H_2O (2 × 100 mL). The organic layer was dried on Na_2SO_4, filtered and evaporated. The crude product was purified by short column chromatography on silica gel eluting with suitable solvents.

9-Phenethyl-9*H*-purin-6-amine (1a)[13]

Column chromatography (SiO_2, EtOAc) afforded the product as white needle crystals.

Yield: 1.96 g (82%); mp 180.3 °C; R_f = 0.23 (EtOAc).

IR (KBr): 3335 (NH_2), 3142, 2928 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 3.12 (t, *J* = 7.2 Hz, 2 H, PhCH_2), 4.37 (t, *J* = 7.2 Hz, 2 H, NCH_2), 7.08–7.28 (m, 7 H, Ph and NH_2), 7.79 [s, 1 H, C(2)-H, adenine], 8.16 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 35.2, 44.2, 118.5, 126.2, 127.9, 128.1, 138.1, 140.4, 149.4, 152.0, 155.7.

MS (EI): *m*/*z* (%) = 239 (35).

Anal. Calcd for $C_{13}H_{13}N_5$: C, 62.25; H, 5.48; N, 29.27. Found: C, 62.29; H, 5.49; N, 29.26.

9-(4-Methoxybenzyl)-9*H*-purin-6-amine (1b)[13]

Column chromatography (SiO_2, EtOAc) afforded the product as white needle crystals.

Yield: 1.91 g (75%); mp 161.4 °C; R_f = 0.22 (EtOAc).

IR (KBr): 3315 (NH_2), 3155, 2930 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 3.67 (s, 3 H, OMe), 5.37 (s, 2 H, NCH_2), 6.86 [d, *J* = 8.6 Hz, 2 H, C(2,6)-H, aryl], 7.01 [s, 1 H, C(2)-H, adenine], 7.23 [d, *J* = 8.6 Hz, 2 H, C(3,5)-H_{Ar}], 7.31 (s, 2 H, NH_2, adenine), 8.48 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 45.8, 54.9, 113.9, 118.6, 121.4, 135.1, 140.5, 149.2, 152.4, 155.8, 158.9.

MS (EI): *m*/*z* (%) = 255 (40).

Anal. Calcd for $C_{13}H_{13}N_5O$: C, 61.17; H, 5.13; N, 27.43. Found: C, 61.20; H, 5.12; N, 27.46.

(*E*)-9-Cinnamyl-9*H*-purin-6-amine (1c)[13]

Column chromatography (SiO_2, EtOAc) afforded the product as pale-yellow needle crystals.

Yield: 1.51 g (60%); mp 237.3 °C; R_f = 0.32 (EtOAc).

IR (KBr): 3355 (NH_2), 3130, 2950.

^1H NMR (250 MHz, DMSO-d_6): δ = 4.92 (d, *J* = 5.1 Hz, 2 H, NCH_2), 6.43 (d, *J* = 16.4 Hz, 1 H, =C*H*-Ph), 7.20–7.31 (m, 6 H, CH_2-C*H*, aryl), 7.35 [s, 1 H, C(2)-H, adenine], 7.40 (s, 2 H, NH_2, exch D_2O), 8.15 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 44.4, 118.6, 124.4, 126.6, 127.4, 128.7, 132.3, 135.8, 140.5, 149.1, 152.3, 155.9.

MS (EI): *m*/*z* (%) = 251 (29.8).

Anal. Calcd for $C_{14}H_{13}N_5$: C, 66.92; H, 5.21; N, 27.87. Found: C, 66.89; H, 5.25; N, 27.90.

9-(Hex-5-enyl)-9*H*-purin-6-amine (1d)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as white prism crystals.

Yield: 1.78 g (82%); mp 141.1 °C; R_f = 0.36 (EtOAc).

IR (KBr): 3330 (NH_2), 3115, 2948 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 1.33 (m, 2 H, CH_2), 1.84 (m, 2 H, CH_2), 2.06 (m, 2 H, CH_2), 4.19 (t, J = 6.9 Hz, 2 H, NCH_2), 4.93 (dd, J = 1.3, 9.2 Hz, 2 H, =CH_2), 5.76 (m, 1 H, =C*H*), 7.34 (br s, 2 H, NH_2, exch D_2O), 8.22 [s, 1 H, C(2)-H, adenine], 8.25 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 25.2, 29.0, 32.4, 42.4, 114.8, 118.6, 138.1, 140.7, 149.4, 152.5, 155.8.

MS (EI): *m*/*z* (%) = 217 (21.0).

Anal. Calcd for $C_{11}H_{15}N_5$: C, 60.81; H, 6.96; N, 32.23. Found: C, 60.84; H, 7.01; N, 32.22.

(*Z*)-9-(Hex-3-enyl)-9*H*-purin-6-amine (1e)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as pale-yellow prism crystals.

Yield: 1.26 g (58%); mp 97.8 °C; R_f = 0.19 (EtOAc).

IR (KBr): 3300 (NH_2), 3110, 2950 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 0.66 (t, J = 7.6 Hz, 3 H, Me), 1.70 (m, 2 H, MeCH_2), 2.59 (m, 2 H, NCH_2CH_2), 4.13 (t, J = 6.7 Hz, 2 H, NCH_2), 5.39 [m, 2 H, 2(=C*H*)], 7.31 (br s, 2 H, NH_2, exch D_2O), 8.12 [s, 1 H, C(2)-H, adenine], 8.19 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 13.5, 19.8, 27.1, 42.4, 118.7, 124.2, 134.0, 140.9, 149.7, 152.2, 155.7.

MS (EI): *m*/*z* (%) = 217 (22.3).

Anal. Calcd for $C_{11}H_{15}N_5$: C, 60.81; H, 6.96; N, 32.23. Found: C, 60.79; H, 7.02; N, 32.25.

(*E*)-9-(Hex-3-enyl)-9*H*-purin-6-amine (1f)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as white prism crystals.

Yield: 1.67 g (77%); mp 127.0 °C; R_f = 0.27 (EtOAc).

IR (KBr): 3310 (NH_2), 3110, 2950 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 0.51 (t, J = 7.2 Hz, 3 H, Me), 1.03 (m, 2 H, MeCH_2), 1.65 (m, 2 H, NCH_2CH_2), 4.46 (t, J = 4.0 Hz, 2 H, NCH_2), 5.39 [m, 2 H, 2(=C*H*)], 7.07 (s, 2 H, NH_2, exch D_2O), 7.83 [s, 1 H, C(2)-H, adenine], 7.91 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 13.5, 21.4, 33.4, 44.3, 118.6, 124.7, 134.1, 140.3, 149.2, 152.4, 155.8.

MS (EI): *m*/*z* (%) = 217 (21.7).

Anal. Calcd for $C_{11}H_{15}N_5$: C, 60.81; H, 6.96; N, 32.23. Found: C, 60.84; H, 6.98; N, 32.19.

9-(2-Ethoxyethyl)-9*H*-purin-6-amine (1g)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as white needle crystals.

Yield: 1.65 g (80%); mp 149.2 °C; R_f = 0.12 (EtOAc).

IR (KBr): 3310 (NH_2), 3160, 2985 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 1.00 (t, J = 6.8 Hz, 3 H, Me), 3.36 (q, J = 6.8 Hz, 2 H, MeCH_2), 3.69 (t, J = 5.2 Hz, 2 H, NCH_2), 4.27 (t, J = 5.2 Hz, 2 H, OCH_2), 7.24 (s, 2 H, NH_2, exch D_2O), 8.06 [s, 1 H, C(2)-H, adenine], 8.48 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 14.9, 65.1, 67.5, 67.6, 118.5, 141.0, 149.6, 152.0, 156.0.

MS (EI): *m*/*z* (%) = 207 (23).

Anal. Calcd for $C_9H_{13}N_5O$: C, 52.16; H, 6.32; N, 33.79. Found: C, 52.19; H, 6.29; N, 33.84.

Benzyl-[9-(2-ethoxyethyl)-9*H*-purin-6-yl]amine (1h)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as white needle crystals.

Yield: 1.72 g (58%); mp 124.3 °C; R_f = 0.41 (EtOAc).

IR (KBr): 3300 (NH_2), 3130, 2900 cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 1.00 (t, J = 6.9 Hz, 3 H, Me), 3.36 (q, J = 6.9 Hz, 2 H, MeCH_2), 3.70 (t, J = 5.2 Hz, 2 H, NCH_2), 4.27 (t, J = 5.2 Hz, 2 H, OCH_2), 4.72 (br s, 2 H, PhCH_2), 7.13–7.66 (m, 5 H, H_{Ar}), 8.09 [s, 1 H, C(2)-H, adenine], 8.22 [s, 1 H, C(8)-H, adenine], 8.51 (br s, 1 H, NH, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 15.3, 40.9, 43.2, 65.8, 68.0, 119.3, 126.9, 127.5, 128.5, 140.5, 141.5, 149.2, 152.7, 154.9.

MS (EI): *m*/*z* (%) = 297 (20.1).

Anal. Calcd for $C_{16}H_{19}N_5O$: C, 64.63; H, 6.44; N, 23.55. Found: C, 64.62; H, 6.48; N, 23.57.

7-Benzyl-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (1i)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as white needle crystals.

Yield: 1.75 g (65%); mp 159.4 °C; R_f = 0.48 (EtOAc).

IR (KBr): 3100, 2980, 2895, 1720 (C=O), 1705 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 3.32 [s, 3 H, N(3)-Me], 3.51 [s, 3 H, N(1)-Me], 5.52 [s, 2 H, N(7)-CH_2], 7.12–7.31 (m, 5 H, H_{Ar}), 7.62 [s, 1 H, C(8)-H].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 28.1, 29.5, 50.0, 106.5, 127.5, 127.7, 128.6, 135.3, 140.8, 148.7, 151.5, 155.1.

MS (EI): *m*/*z* (%) = 270 (31.4).

Anal. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.22; H, 5.24; N, 20.71.

7-Allyl-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (1j)
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as white needle crystals.

Yield: 1.45 g (66%); mp 103.7 °C; R_f = 0.38 (EtOAc).

IR (KBr): 3050, 2987, 2890, 1725 (C=O), 1708 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 3.17 [s, 3 H, N(3)-Me], 3.36 [s, 3 H, N(1)-Me], 4.73 (d, J = 5.2 Hz, 2 H, NCH_2), 5.00–5.13 (dd, J = 11.5, 16.4 Hz, 2 H, =CH_2), 5.77–5.93 (m, 1 H, =C*H*), 7.40 [s, 1 H, C(8)-H].

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 27.80, 29.61, 48.83, 106.71, 119.18, 132.06, 140.71, 148.64, 151.50, 154.95.

MS (EI): *m*/*z* (%) = 220.09 (25.4).

Anal. Calcd for $C_{10}H_{12}N_4O_2$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.61; H, 5.53; N, 25.40.

3,7-Dimethyl-1-[3-(naphthalen-2-yloxy)propyl]-1*H*-purine-2,6(3*H*,7*H*)-dione (1k)
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as pale-yellow prism crystals.

Yield: 2.22 g (61%); mp 135.2 °C; R_f = 0.33 (EtOAc).

IR (KBr): 3115, 2973, 2885, 1720 (C=O), 1710 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 2.17–2.22 (m, 2 H, CH_2), 3.50 [s, 3 H, N(3)-Me], 3.79 [s, 3 H, N(7)-Me], 4.12 (*t*, J = 5.8 Hz, 2 H, NCH_2), 4.20 (*t*, J = 5.8 Hz, 2 H, OCH_2), 6.96–7.04 (m, 2 H, H_{Ar}), 7.23–7.39 (m, 3 H, H_{Ar}), 7.61 [s, 1 H, C(8)-H], 7.64–7.69 (m, 2 H, H_{Ar}).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 27.37, 29.12, 32.89, 38.48, 65.65, 106.03, 107.07, 118.25, 122.93, 125.69, 126.16, 127.00, 128.31, 128.61, 133.97, 140.86, 148.18, 150.95, 154.69, 156.26.

MS (EI): *m*/*z* (%) = 364.15 (22.3).

Anal. Calcd for $C_{20}H_{20}N_4O_3$: C, 65.92; H, 5.53; N, 15.38. Found: C, 65.86; H, 5.49; N, 15.45.

9-Isopropyl-9*H*-purin-6-amine (1l)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as white cube crystals.

Yield: 0.14 g (8%); mp 234.8 °C; R_f = 0.26 (EtOAc).

IR (KBr): 3310 (NH_2), 3160, 2985, 2850 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 1.45 (d, *J* = 6.5 Hz, 6 H, 2 × Me), 4.66 (m, 1 H, C*H*), 7.16 (br s, 2 H, NH_2, exch D_2O), 8.09 [s, 1 H, C(2)-H, adenine], 8.17 [s, 1 H, C(8)-H, adenine].

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 22.0, 46.4, 119.0, 138.7, 148.9, 152.0, 155.6.

MS (EI): *m*/*z* (%) = 177 (31.9).

Anal. Calcd for $C_8H_{11}N_5$: C, 54.22; H, 6.26; N, 39.52. Found: C, 54.19; H, 6.31; N, 39.50.

1-Octylpyrimidine-2,4(1*H*,3*H*)-dione (2a)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as pale-yellow needle crystals.

Yield: 1.57 g (70%); mp 61.4 °C; R_f = 0.55 (EtOAc).

IR (KBr): 3200 (NH), 3100, 2895, 1735 (C=O), 1710 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.2 Hz, 3 H, Me), 1.26–1.31 (m, 10 H, 5 × CH_2), 1.48–1.53 (m, 2 H, CH_2), 3.73 (t, *J* = 7.2 Hz, 2 H, NCH_2), 5.74 [d, *J* = 7.8 Hz, 1 H, C(5)-H uracil], 7.20 [d, *J* = 7.8 Hz, 1 H, C(6)-H uracil], 10.48 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.0, 22.4, 26.9, 29.0, 29.1, 31.7, 40.5, 48.7, 102.0, 144.5, 151.0, 164.5.

MS (EI): *m*/*z* (%) = 224 (34.9).

Anal. Calcd for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; N, 12.49. Found: C, 64.28; H, 9.00; N, 12.43.

1-(4-Methoxybenzyl)pyrimidine-2,4(1*H*,3*H*)-dione (2b)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as white cube crystals.

Yield: 1.28 g (55%); mp 118.0 °C; R_f = 0.38 (EtOAc).

IR (KBr): 3250 (NH), 3100, 2895, 1728 (C=O), 1715 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.70 (s, 3 H, OMe), 3.75 (s, 2 H, NCH_2), 5.58 [d, *J* = 7.8 Hz, 1 H, C(5)-H uracil], 6.84 [d, *J* = 8.5 Hz, 2 H, C(2,6)-H_{Ar}], 6.90 [d, *J* = 8.5 Hz, 2 H, C(3,5)-H_{Ar}], 7.72 [d, *J* = 7.8 Hz, 1 H, C(6)-H uracil], 11.17 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 49.6, 55.1, 101.2, 113.5, 128.6, 129.1, 145.3, 150.7, 158.7, 163.4.

MS (EI): *m*/*z* (%) = 232 (55.4).

Anal. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.00; H, 5.19; N, 12.00.

1-Phenethylpyrimidine-2,4(1*H*,3*H*)-dione (2c)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as white cube crystals.

Yield: 1.60 g (74%); mp 149.2 °C; R_f = 0.29 (EtOAc).

IR (KBr): 3250 (NH), 3110, 2895, 1730 (C=O), 1720 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 2.83 (t, *J* = 7.2 Hz, 2 H, PhCH_2), 3.91 (t, *J* = 7.2 Hz, 2 H, NCH_2), 5.45 [d, *J* = 7.8 Hz, 1 H, C(5)-H uracil], 7.15–7.29 (m, 5 H, H_{Ar}), 7.50 [d, *J* = 7.8 Hz, 1 H, C(6)-H uracil], 11.24 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 34.2, 48.7, 100.4, 126.2, 128.3, 128.6, 137.7, 145.6, 150.7, 163.7.

MS (EI): *m*/*z* (%) = 216 (27).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.66; H, 5.64; N, 12.91.

2-{2-[2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]ethyl}isoindoline-1,3-dione (2d)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 60:40) afforded the product as white cube crystals.

Yield: 2.22 g (80%); mp 263.6 °C; R_f = 0.29 (EtOAc).

IR (KBr): 3200 (NH), 3210, 2895, 1730–1710 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.83–3.87 (m, 4 H, 2NCH_2), 5.46 [d, *J* = 7.8 Hz, 1 H, C(5)-H uracil], 7.52 [d, *J* = 7.8 Hz, 1 H, C(6)-H uracil], 7.79–7.87 (m, 4 H, aryl), 11.15 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 36.2, 46.3, 101.2, 123.0, 131.4, 134.3, 145.4, 151.1, 163.7, 167.6.

MS (EI): *m*/*z* (%) = 285 (40).

Anal. Calcd for $C_{14}H_{11}N_3O_4$: C, 58.96; H, 3.89; N, 14.73. Found: C, 59.98; H, 3.91; N, 14.75.

1-(Prop-2-ynyl)pyrimidine-2,4(1*H*,3*H*)-dione (2e)[13,25]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 70:30) afforded the product as white cube crystals.

Yield: 1.08 g (72%); mp 154.4 °C; R_f = 0.28 (EtOAc).

IR (KBr): 3290 (≡CH), 3200 (NH), 3100, 2895, 2145 (C≡C), 1740 (C=O), 1715 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.13 (s, 1 H, ≡C*H*), 4.26 (s, 2 H, NCH_2), 5.44 [d, *J* = 7.8 Hz, 1 H, C(5)-H uracil], 7.65 [d, *J* = 7.8 Hz, 1 H, C(6)-H uracil], 11.11 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 36.6, 75.6, 78.3, 101.4, 144.6, 150.2, 163.5.

MS (EI): *m*/*z* (%) = 150 (55.7).

Anal. Calcd for $C_7H_6N_2O_2$: C, 56.00; H, 4.03; N, 18.66. Found: C, 55.98; H, 4.08; N, 18.60.

5-Chloro-1-(prop-2-ynyl)pyrimidine-2,4(1*H*,3*H*)-dione (2f)[13,25]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 70:30) afforded the product as white cube crystals.

Yield: 1.09 g (59%); mp 170.3 °C; R_f = 0.29 (EtOAc).

IR (KBr): 3310 (≡CH), 3250 (NH), 3100, 2890, 2150 (C≡C), 1735 (C=O), 1715 (C=O) cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.18 (s, 1 H, ≡C*H*), 4.26 (s, 2 H, NCH_2), 8.23 [s, 1 H, C(6)-H uracil], 11.56 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 36.3, 75.4, 78.6, 102.7, 145.4, 150.8, 163.2.

MS (EI): *m*/*z* (%) = 184 (51.8).

Anal. Calcd for $C_7H_5ClN_2O_2$: C, 45.55; H, 2.73; Cl, 19.21; N, 15.18. Found: C, 45.62; H, 2.78; Cl, 19.17; N, 15.17.

(*E*)-1-Cinnamylpyrimidine-2,4(1*H*,3*H*)-dione (2g)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 50:50) afforded the product as white cube crystals.

Yield: 1.62 g (71%); mp 199.2 °C; R_f = 0.65 (EtOAc).

IR (KBr): 3250 (NH), 3050, 2895, 1730 (C=O), 1710 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 4.51 (d, J = 5.6 Hz, 2 H, NCH_2), 5.67 [d, J = 7.8 Hz, 1 H, C(5)-H uracil], 6.36 (m, 1 H, CH_2-CH), 6.64 (d, J = 16.0 Hz, 1 H, =CH-Ph), 7.26–7.68 (m, 5 H, H_{Ar}), 7.71 [d, J = 7.8 Hz, 1 H, C(6)-H uracil], 11.36 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 48.4, 101.2, 124.2, 126.3, 127.8, 128.5, 132.5, 135.8, 145.2, 150.7, 163.7.

MS (EI): m/z (%) = 228 (31.4).

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.42; H, 5.29; N, 12.31.

1-Allyl-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (2h)[8a,b,13,26]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 70:30) afforded the product as white needle crystals.

Yield: 0.88 g (52%); mp 101.2 °C; R_f = 0.27 (EtOAc).

IR (KBr): 3220 (NH), 3050, 2895, 1725 (C=O), 1715 (C=O) cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 4.34 (d, J = 5.8 Hz, 2 H, NCH_2), 5.35 (dd, J = 11.0, 16.3 Hz, 2 H, =CH_2), 5.82 (m, 1 H, CH), 7.29 [d, $^3J_{HF}$ = 5.4 Hz, 1 H, C(6)-H uracil], 9.66 (s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 51.4, 121.5, 128.2, 131.1, 141.0, 150.8, 158.8.

MS (EI): m/z (%) = 170 (38.0).

Anal. Calcd for $C_7H_7FN_2O_2$: C, 49.41; H, 4.15; F, 11.17; N, 16.46. Found: C, 49.43; H, 4.10; F, 11.19; N, 16.51.

1-Allyl-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (2i)[8a,b,13,27]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 60:40) afforded the product as white cube crystals.

Yield: 1.11 g (67%); mp 123.2 °C; R_f = 0.25 (EtOAc).

IR (KBr): 3200 (NH), 3100, 2980, 1734 (C=O), 1720 (C=O) cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.89 (s, 3 H, Me), 4.33 (d, J = 5.5 Hz, 2 H, NCH_2), 5.21 (dd, J = 10.8, 16.1 Hz, 2 H, =CH_2), 5.82 (m, 1 H, =CH), 6.96 [s, 1 H, C(6)-H uracil], 10.25 (br s, 1 H, N3-H, exch D_2O).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 13.5, 51.8, 112.3, 121.4, 133.2, 141.4, 152.2, 167.1.

MS (EI): m/z (%) = 166 (43.2).

Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.86; H, 6.00; N, 16.91.

2-Butyl-1,2,4-triazine-3,5(2*H*,4*H*)-dione (2j)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 40:60) afforded the product as white needle crystals.

Yield: 0.93 g (55%); mp 136.8 °C; R_f = 0.77 (EtOAc–*n*-hexane, 4:1).

IR (KBr): 3200 (NH), 3210, 2985 2895, 1725–1715 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 0.63 (t, J = 6.2 Hz, 3 H, CH_3), 1.01 (m, 2 H, CH_2CH$_3$), 1.25 (m, 2 H, NCH$_2$CH_2), 3.46 (t, J = 6.5 Hz, 2 H, NCH_2), 7.20 [s, 1 H, C(5)-H azauracil], 12.32 (s, 1 H, N3-H exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 13.4, 19.4, 28.6, 38.3, 134.5, 148.9, 156.1.

MS: m/z (%) = 169 (35).

Anal. Calcd for $C_7H_{11}N_3O_2$: C, 49.70; H, 6.55; N, 24.84. Found: C, 49.65; H, 6.51; N, 24.80.

1-Butyl-5-nitropyrimidine-2,4(1*H*,3*H*)-dione (2k)[13]
Column chromatography (SiO_2, EtOAc–*n*-hexane, 60:40) afforded the product as pale-yellow needle crystals.

Yield: 1.73 g (81%); mp 146.3 °C; R_f = 0.68 (EtOAc–*n*-hexane, 4:1).

IR (KBr): 3250 (NH), 3210, 2985 2890, 1730–1715 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 0.83 (t, J = 6.7 Hz, 3 H, CH_3), 1.26 (m, 2 H, CH_2CH$_3$), 1.59 (m, 2 H, NCH$_2$CH_2), 3.81 (t, J = 6.5 Hz, 2 H, NCH_2), 9.23 [s, 1 H, C(6)-H uracil], 11.96 (s, 1 H, N3-H uracil exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 18.6, 24.1, 35.6, 54.1, 129.7, 154.4, 155.8, 160.1.

MS (EI): m/z (%) = 213 (25).

Anal. Calcd for $C_8H_{11}N_3O_4$: C, 45.07; H, 5.20; N, 19.71. Found: C, 45.03; H, 5.21; N, 19.73.

1-[3-(4-Chlorophenoxy)propyl]-5-nitropyrimidine-2,4(1*H*,3*H*)-dione (2l)
Column chromatography (SiO_2, EtOAc–*n*-hexane, 60:40) afforded the product as yellow cube crystals.

Yield: 2.21 g (68%); mp 231.6 °C; R_f = 0.68 (EtOAc).

IR (KBr): 3200 (NH), 3100, 2980, 2895, 1730 (C=O), 1715 (C=O) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 2.07–2.09 (m, 2 H, CH_2), 4.02–4.04 (m, 4 H, NCH_2, OCH_2), 6.85 (d, J = 8.1 Hz, 2 H, H_{Ar}), 7.25 (d, J = 8.1 Hz, 2 H, H_{Ar}), 9.25 [s, 1 H, C(6)-H, uracil], 11.99 (s, 1 H, N3-H uracil, exch D_2O).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 27.58, 47.11, 65.47, 116.01, 124.27, 124.79, 129.11, 149.34, 150.83, 154.96, 157.03.

MS (EI): m/z (%) = 325.04 (35).

Anal. Calcd for $C_{13}H_{12}ClN_3O_5$: C, 47.94; H, 3.71; Cl, 10.89; N, 12.90. Found: C, 47.89; H, 3.77; Cl, 10.83; N, 12.97.

1-[2-(2-Methyl-4-nitro-1*H*-imidazol-1-yl)ethyl]-1*H*-benzo[*d*]imidazole (3a)[13]
Column chromatography (SiO_2, EtOAc) afforded the product as pale-yellow cube crystals.

Yield: 1.79 g (66%); mp 223.2 °C; R_f = 0.30 (MeOH–EtOAc, 1:10).

IR (KBr): 3210, 3100, 2980, 2895 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.84 (s, 3 H, Me), 4.45 (t, J = 6.2 Hz, 2 H, NCH_2), 4.70 (t, J = 6.2 Hz, 2 H, NCH_2), 7.17 (m, 2 H, H_{Ar}), 7.21 (d, J = 7.5 Hz, 1 H, H_{Ar}), 7.65 (d, J = 7.5 Hz, 1 H, H_{Ar}), 8.01 [s, 1 H, C(5)-H, imidazole], 8.16 [s, 1 H, C(2)-H, benzimidazole].

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 12.0, 44.3, 46.1, 109.7, 119.4, 121.7, 122.1, 122.5, 133.3, 143.1, 143.8, 145.0, 145.4.

MS (EI): m/z (%) = 271 (33.2).

Anal. Calcd for $C_{13}H_{13}N_5O_2$: C, 57.56; H, 4.83; N, 25.82. Found: C, 57.50; H, 4.90; N, 25.84.

1-[3-(4-Chlorophenoxy)propyl]-1*H*-benzo[*d*]imidazole (3b)
Column chromatography (SiO_2, EtOAc) afforded the product as pale-yellow cube crystals.

Yield: 2.12 g (74%); mp 118.1 °C; R_f = 0.4 (EtOAc).

IR (KBr): 3160, 3100, 2985, 2890 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 2.25–2.28 (m, 2 H, CH_2), 3.79 (t, J = 6.1 Hz, 2 H, NCH_2), 4.35 (t, J = 6.1 Hz, 2 H, OCH_2), 6.73 (d, J = 7.7 Hz, 2 H, H_{Ar}), 7.20 (d, J = 7.7 Hz, 2 H, H_{Ar}), 7.25–7.35 (m, 4 H, aryl), 7.81 [s, 1 H, C(2)-H, benzimidazole].

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 29.33, 41.35, 64.10, 109.53, 115.68, 120.43, 122.16, 122.99, 125.97, 129.42, 133.70, 143.16, 143.88, 156.97.

MS (EI): *m*/*z* (%) = 286.09 (28.1).

Anal. Calcd for $C_{16}H_{15}ClN_2O$: C, 67.02; H, 5.27; Cl, 12.36; N, 9.77. Found: C, 67.05; H, 5.26; Cl, 12.35; N, 9.72.

2-Methyl-4-nitro-1-phenethyl-1*H*-imidazole (3c)
Column chromatography (SiO_2, EtOAc) afforded the product as white cube crystals.

Yield: 1.57 g (68%); mp 116.2 °C; R_f = 0.62 (EtOAc).

IR (KBr): 3135, 2950, 2878 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.05 (s, 3 H, CH_3), 2.99 (t, *J* = 6.0 Hz, 2 H, PhCH_2), 4.10 (t, *J* = 6.0 Hz, 2 H, NCH_2), 6.96–6.98 (m, 2 H, H_{Ar}), 7.20–7.25 (m, 3 H, H_{Ar}), 7.52 [s, 1 H, C(5)-H, imidazole].

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 12.64, 36.88, 48.66, 119.71, 127.39, 128.62, 128.98, 136.29, 145.01, 146.23.

MS (EI): *m*/*z* (%) = 231.1 (12.4).

Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.37; H, 5.71; N, 18.15.

1-[3-(Naphthalen-2-yloxy)propyl]-1*H*-imidazole (3d)
Column chromatography (SiO_2, EtOAc) afforded the product as white cube crystals.

Yield: 1.57 g (68%); mp 99.4 °C; R_f = 0.19 (EtOAc).

IR (KBr): 3150, 2948, 2887 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.15–2.25 (m, 2 H, CH_2), 3.93 (t, *J* = 5.6 Hz, 2 H, NCH_2), 4.11 (t, *J* = 5.6 Hz, 2 H, OCH_2), 6.89 [s, 1 H, C(5)-H, imidazole], 7.06 [s, 1 H, C(4)-H, imidazole], 7.12–7.15 (m, 2 H, H_{Ar}), 7.30–7.40 (m, 2 H, H_{Ar}), 7.46 [s, 1 H, C(2)-H, imidazole], 7.68 (s, 1 H, H_{Ar}), 7.72–7.76 (m, 2 H, H_{Ar}).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 30.71, 43.45, 63.74, 106.74, 118.59, 119.02, 123.84, 126.51, 126.77, 127.66, 129.10, 129.57, 129.63, 134.46, 137.31, 156.37.

MS (EI): *m*/*z* (%) = 252.12 (38.0).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.11; H, 6.45; N, 11.13.

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