Microwave-Assisted Facile One-Step Carbamoylation of 6-Aminouracils

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Abstract: Carbamoylation of 6-aminouracils was achieved by reacting 6-aminouracils with isocyanates under computer-controlled microwave irradiation for a short reaction time. Under known thermal conditions, most of carbamoylated uracils are obtained in poor yields with long reaction times.

Key words: microwave, 6-aminouracil, isocyanates, heterocycles, carbamoylation

6-Aminouracils and their derivatives are of great importance in medicinal chemistry and have interesting biological properties.[1,2] Among 6-aminouracil derivatives, 5-carbamoyl-6-aminouracils have attracted attention because of their effect on *c*-Jun *N*-terminal kinase inhibition and anti-inflammatory properties.[3,4] The *C*-5 position of 6-aminouracil is the preferred site for electrophilic substitution with various isocyanates, such as ethyl isocyanatoformate, phenyl isocyanate and chlorosulfonyl isocyanate.[5] 5-Carbamoyl-6-aminouracils have been used as key intermediates for the synthesis of fused pyrimidines, such as pyrimido[4,5-*d*]pyrimidines[5a,6] and isooxazolo[3,4-*d*]pyrimidines.[7] In previous studies, we reported a method for derivatizing the *C*-5 position of 6-aminouracils by coupling an aryldiazonium salt with 1-cyano-3-(2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-ylamino)-2-methylisothiourea.[8] With the continuing interest in the development of 6-aminouracil derivatives, we sought to introduce a carbamoyl group at the *C*-5 position of 6-aminouracils using various isocyanates to construct small novel drug-like organic molecules.

5-Phenylcarbamoyl-6-amino-1,3-dimethyluracil was prepared in 63% yield by reacting 6-amino-1,3-dimethyluracil (**1a**) with phenyl isocyanate in pyridine.[5c] However, for alkylisocyanates, we could not obtain the desired 5-alkylcarbamoylated-6-aminouracil under the same reaction conditions as noted in the literature.[5c] The known preparation of 5-alkylcarbamoyl-6-aminouracils involves a two-step procedure from 6-aminouracil, requiring long reaction times with fairly low yields (Figure 1). Phenylcarbamoylation at the *C*-5 position of 6-amino-1,3-dimethyluracil with substituted phenylisocyanates has also been achieved using this two-step procedure.[5c,6a] We decided to investigate the possibility of a more efficient carbamoylation with various isocyanates at the *C*-5 position of 6-aminouracils. We concentrated our efforts on applying microwave to introduce a carbamoyl group at the *C*-5 position of 6-aminouracil.

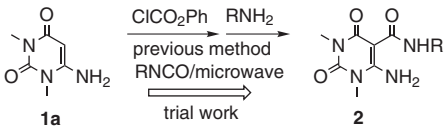
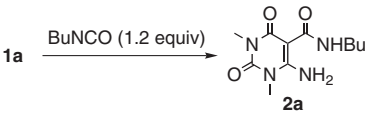


Figure 1

Following the pioneering work of Gedye et al. and Giguere et al.,[9] microwave applications in organic chemistry have become more prevalent.[10] The principal advantages of microwave mediation are reaction acceleration and an accompanying minimization of product decomposition.[10,11] The current literature includes a growing number of examples, including our report of the formation of a heterocycle, mediated by microwave irradiation.[12] Here, we report our investigation of carbamoylation at the *C*-5 position of 6-aminouracils **1** under microwave conditions.

Table 1 Studies of the Optimization of Carbamoylation with 6-Aminouracil **1a**



Entry	Reaction conditions	Time	Yield (%)
1	Thermal/pyridine/refluxing	24 h	trace [75][a]
2	Thermal/DMF/140 °C	24 h	26 [51][a]
3	Thermal/nitrobenzene/210 °C	4 h	55
4	Microwave/pyridine/120 °C	40 min	38 [51][a]
5	Microwave/DMF/150 °C	40 min	45 [38][a]
6	Microwave/nitrobenzene/210 °C	20 min	72

[a] Recovered starting materials.

As a starting point for developing direct alkyl carbamoylation, we studied the reaction of 6-amino-1,3-dimethyl uracil (**1a**) with butyl isocyanate for optimizing the reaction conditions, as shown in Table 1. Carbamoylation of 6-amino-1,3-dimethyl uracil (**1a**) with butyl isocyanate for 24 hours in refluxing pyridine in a pressure vessel gave a trace amount of **2a** with most of the starting material **1a**

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being recovered, as was also reported previously (entry 1).[5c] When we tried the same reaction at 140 °C in DMF instead of pyridine, the desired product **2a** was obtained in 26% yield (entry 2). The yield was not improved by adding an excess of butyl isocyanate, adding a base (Et_3N, DBU, K_2CO_3, Cs_2CO_3, or NaH), or refluxing for 48 hours. In order to increase the reaction temperature we changed the solvent to nitrobenzene. Reaction at 210 °C gave **2a** in better yield (55%) without recovering the starting material (entry 3). Based on these results, the reaction was performed under microwave conditions. With pyridine or DMF, the reaction was not completed within 40 minutes (entries 4 and 5). However, nitrobenzene at 210 °C and 20 minutes proved to be the most effective condition (entry 6).

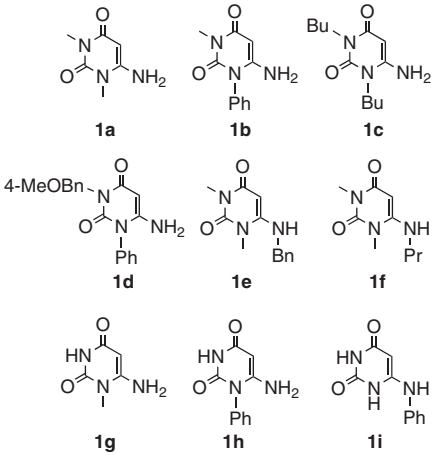
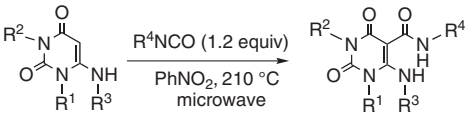


Figure 2 Various 6-aminouracils used for carbamoylation

We further investigated the carbamoylation of 6-aminouracils using various isocyanates and uracils in order to determine the scope and limitations of the reaction (Table 2). For this reaction, 6-aminouracils were prepared by the known method[13] except for the commercially available **1a** and **lg** (Figure 2). Alkyl carbamoylation of 6-amino-1,3-disubstitued uracils gave the corresponding products **2a–e** under similar reaction conditions in good yield (entries 1–5). The reactions of 6-amino-1,3-disubstitued uracils **1a–1d** with substituted aryl isocyanates were completed in ten minutes, showing no effects from electronic-donating, electron-withdrawing, or *ortho* substituents (entries 6–13). The reaction of 6-alkylaminouracils **1e** and **1f** with phenyl isocyanate gave similar yields (entries 14 and 15). Finally, we tried carbamoylation of *N*-3 unsubstituted uracil because the hydrogen at the *N*-3 position mimics that of uracil derivatives and their nucleosides. The *N*-3 hydrogen of uracil is essential for hydrogen bonding with purine bases in RNA.[14] Carbamoylation of 6-aminouracil **1g** with butyl isocyanate gave **2p** in 58% yield. When we attempted the synthesis of **2p** by reacting **1g** with butyl isocyanate under thermal conditions (nitrobenzene at 210 °C for 24 h), the starting material **1g** was recovered in 79% yield along with a trace amount of desired product **2p**. Other examples of *N*-3-unsubstituted 6-amino uracils gave yields of 70–76% (entries 17–19).

Table 2 Microwave-Assisted Synthesis of 6-Amino-5-carbamoyluracil **2**

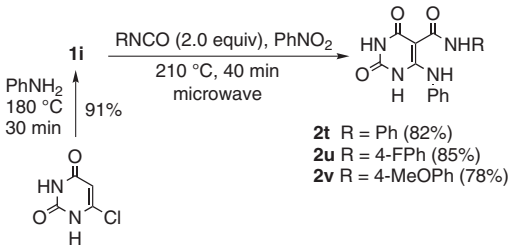


Entry	6-Aminouracil	R^4	Time (min)	Product (yield[a])
1	**1a**	Bu	20	**2a** (72)
2	**1a**	*c*-C_6H_{11}	20	**2b** (81)
3	**1a**	Et	20	**2c** (65)
4	**1b**	Bn	20	**2d** (81)
5	**1b**	*c*-C_6H_{11}	20	**2e** (83)
6	**1a**	Ph	10	**2f** (92)
7	**1a**	4-MeOPh	10	**2g** (82)
8	**1a**	4-ClPh	10	**2h** (88)
9	**1a**	2-BrPh	10	**2i** (78)
10	**1a**	2-EtPh	10	**2j** (85)
11	**1b**	Ph	10	**2k** (84)
12	**1c**	Ph	10	**2l** (62)
13	**1d**	Ph	10	**2m** (87)
14	**1e**	Ph	10	**2n** (82)
15	**1f**	Ph	10	**2o** (75)
16	**1g**	Bu	20	**2p** (58)
17	**1g**	Bn	20	**2q** (70)
18	**1g**	Ph	10	**2r** (72)
19	**1h**	Ph	10	**2s** (76)

[a] Isolated yields.

Recently, carbamoylated 6-arylaminouracils **2t–v** have shown biological activity as a *c*-Jun *N*-terminal kinase inhibitor which is a member of the mitogen-activated protein (MAP) kinase family.[3b] The synthetic method of **2t–v** was published in 5 steps from dimethyl *N*-cyanodithioiminocarbonate. However synthesis of **2t–v** was achieved in two steps with high overall yield. The desired **2t–v** were obtained by heating of commercially available 6-chlorouracil in aniline[13c] followed by carbarmoylation under microwave condition (Scheme 1).

In summary, we have established a rapid, one-pot alkyl carbamoylation of 6-aminouracils under microwave irradiation conditions. This procedure has been extended to aryl carbamoylation of 6-aminouracils. The reaction features a short reaction time and high yield. For *N*-unsubstituted 6-aminouracil, the carbamoylated uracils were



Scheme 1

obtained in good yield in contrast to conventional thermal conditions. This methodology might be applied to the parallel synthesis of 5-carbamoylated 6-aminouracils and new fused pyrimidines.

Melting points were measured on a digital Mettler Tolledo FP90 apparatus and are uncorrected. ATR–IR spectra were recorded on a SensIR Technologies TravelIR spectrometer. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker AMX 500 spectrometer in DMSO-d_6 with the solvent signals as reference. Mass spectra were obtained with a Waters ZQ mass spectrometer with an electrospray ionization source. Microwave experiments were carried out on an Emrys Creator from Personal Chemistry.

Carbamoylation of 6-Aminouracils under Microwave Irradiation; General Procedure

To a microwave reaction vessel were added 6-aminouracil **1** (1 mmol), isocyanate (1.2 mmol) and nitrobenzene (1 mL). The reaction vessel was irradiated at 210 °C for the appropriate time (Table 2). The reaction mixture was transferred to a round-bottomed flask and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc–hexane) or recrystallization (EtOH) to provide the corresponding carbamoylated 6-aminouracil **2** as a solid.

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Butylamide (2a)

Mp 125 °C (Lit.[5c] mp 130 °C).

ATR–IR: 3327, 2929, 1705, 1639, 1534, 1025 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.11 (br s, 1 H), 9.77 (br s, 1 H), 7.85 (br s, 1 H), 3.30 (s, 3 H), 3.19–3.22 (m, 2 H), 3.15 (s, 3 H), 1.43–1.47 (m, 2 H), 1.30–1.32 (m, 2 H), 0.90 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.6, 162.4, 157.8, 149.3, 81.2, 37.6, 31.3, 29.5, 27.6, 19.6, 13.6.

MS: *m*/*z* (%) = 74 (11), 173 (100), 182 (16), 255 (32) [M + 1].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Cyclohexylamide (2b)

Mp > 375 °C.

ATR–IR: 3324, 2927, 1639, 1592, 1530, 1445 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.13 (br s, 1 H), 9.84–9.86 (m, 1 H), 7.86 (br s, 1 H), 3.73–3.74 (m, 1 H), 3.32 (s, 3 H), 3.16 (s, 1 H), 1.41–1.80 (m, 5 H), 1.22–1.36 (m, 5 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.8, 162.5, 157.9, 149.1, 80.2, 46.4, 32.4, 29.5, 27.6, 25.2, 24.1.

MS: *m*/*z* (%) = 69 (28), 85 (42), 281 (32) [M + H$^+$], 303 (100) [M + Na$^+$].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Ethylamide (2c)

Mp 158 °C (Lit.[5c] mp 172 °C).

ATR–IR: 3325, 1663, 1591, 1536, 1446 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.12 (s, 1 H), 9.73–9.74 (m, 1 H), 7.86 (s, 1 H), 3.31 (s, 3 H), 3.21–3.27 (m, 2 H), 3.16 (s, 3 H), 1.09 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.9, 162.9, 157.8, 149.8, 82.0, 33.7, 28.6, 28.1, 14.8.

MS: *m*/*z* (%) = 182 (42), 200 (100), 227 (23) [M + H$^+$].

6-Amino-3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Benzylamide (2d)

Mp 193 °C.

ATR–IR: 3336, 2930, 1692, 1644, 1595, 1513, 1446 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.73 (br s, 1 H), 10.18–10.20 (m, 1 H), 7.56–7.61 (m, 3 H), 7.43 (d, *J* = 7.4 Hz, 2 H), 7.31–7.36 (m, 4 H), 7.25–7.27 (m, 1 H), 6.56 (br s, 1 H), 4.47 (d, *J* = 5.9 Hz, 2 H), 3.18 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.7, 163.0, 157.6, 149.1, 139.6, 133.7, 130.0, 129.8, 129.3, 128.4, 127.2, 126.8, 80.3, 41.8, 27.4.

MS: *m*/*z* (%) = 85 (31), 126 (25) 244 (91), 262 (100), 285 (35) [M + H$^+$].

6-Amino-3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Cyclohexylamide (2e)

Mp 225 °C.

ATR–IR: 3348, 1692, 1644, 1600, 1514, 1444, 1368 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.83 (br s, 1 H), 9.85–9.87 (m, 1 H), 7.55–7.70 (m, 3 H), 7.41–7.43 (m, 2 H), 6.49 (br s, 1 H), 3.74–3.76 (m, 1 H), 3.18 (s, 3 H), 1.80–1.82 (m, 2 H), 1.64–1.67 (m, 2 H), 1.51–1.54 (m, 1 H), 1.25–1.37 (m, 5 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.7, 162.9, 157.5, 149.1, 133.7, 130.0, 129.8, 129.3, 80.3, 46.4, 32.4, 27.4, 25.2, 24.1.

MS: *m*/*z* (%) = 85 (24), 262 (26), 343 (22) [M + H$^+$], 365 (100) [M + Na$^+$].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2f)

Mp 244 °C (Lit.[5c] mp 250 °C).

ATR–IR: 3453, 1695, 1578, 1527, 1439, 1368 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.16 (s, 1 H), 10.87 (br s, 1 H), 8.64 (br s, 1 H), 7.58 (d, *J* = 8.6 Hz, 2 H), 7.27–7.34 (m, 2 H), 7.04–7.07 (m, 1 H), 3.45 (s, 3 H), 3.22 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.2, 163.0, 158.1, 149.1, 138.6, 128.9, 123.1, 119.8, 80.5, 29.7, 27.8.

MS: *m*/*z* (%) = 85 (100), 126 (58), 200 (50), 275 (35) [M + H$^+$].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (4-Methoxyphenyl)amide (2g)

Mp 185 °C.

ATR–IR: 3438, 1702, 1664, 1584, 1534, 1447, 1238 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.00 (s, 1 H), 10.91 (br s, 1 H), 7.49 (d, *J* = 7.9 Hz, 2 H), 6.90 (d, *J* = 8.9 Hz, 2 H), 3.78 (s, 3 H), 3.36 (s, 3 H), 3.23 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 165.9, 162.9, 158.0, 149.2, 131.7, 121.3, 114.0, 80.4, 55.2, 29.7, 27.8.

MS: *m*/*z* (%) = 139 (52), 159 (100), 273 (82), 305 (12) [M + H$^+$].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (4-Chlorophenyl)amide (2h)

Mp 291 °C (Lit.[3a] mp > 270 °C).

ATR–IR: 3467, 1708, 1658, 1570, 1526, 1364 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.25 (s, 1 H), 10.77 (br s, 1 H), 8.19 (br s, 1 H), 7.62 (d, *J* = 8.9 Hz, 2 H), 7.37 (d, *J* = 8.8 Hz, 2 H), 3.36 (s, 3 H), 3.22 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.3, 163.0, 158.1, 149.1, 137.6, 128.7, 126.6, 121.3, 80.4, 29.8, 27.9.

MS: *m*/*z* (%) = 85 (100), 126 (95), 229 (38), 291 (18), 309 (8) [M + H^+].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (2-Bromophenyl)amide (2i)
Mp 285 °C.

ATR–IR: 3378, 1702, 1653, 1610, 1525, 1435, 1290 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.36 (s, 1 H), 10.77 (s, 1 H), 8.30–8.32 (m, 1 H), 8.21 (br s, 1 H), 7.65–7.38 (m, 1 H), 7.34–7.38 (m, 1 H), 7.01–7.04 (m, 1 H), 3.37 (s, 3 H), 3.23 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.5, 162.8, 158.2, 149.2, 137.0, 132.6, 127.9, 124.7, 122.9, 113.5, 80.6, 29.8, 27.9.

MS: *m*/*z* (%) = 85 (96), 126 (100), 164 (42), 229 (38), 377 (35) [M + H^+].

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (2-Ethylphenyl)amide (2j)
Mp > 375 °C.

ATR–IR: 3471, 1704, 1579, 1534, 1443 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.01 (s, 1 H), 10.94 (br s, 1 H), 8.12 (br s, 1 H), 8.04 (d, *J* = 8.1 Hz, 1 H), 7.23 (d, *J* = 7.5 Hz, 1 H), 7.18 (t, *J* = 7.8 Hz, 1 H), 7.04 (t, *J* = 7.4 Hz, 1 H), 3.36 (s, 3 H), 3.24 (s, 3 H), 2.66 (q, *J* = 7.5 Hz, 2 H), 1.19 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.3, 163.1, 158.2, 149.2, 136.2, 133.7, 128.5, 126.1, 123.7, 122.1, 80.7, 29.7, 27.9, 24.3, 14.2.

MS: *m*/*z* (%) = 182 (57), 200 (100), 223 (30), 303 (65) [M + H^+].

6-Amino-3-methyl-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2k)
Mp 227 °C.

ATR–IR: 3363, 1690, 1661, 1588, 1495, 1432, 1376 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.17 (s, 1 H), 10.58 (br s, 1 H), 7.58–7.62 (m, 5 H), 7.46–7.48 (m, 2 H), 7.32–7.33 (m, 2 H), 7.05–7.08 (m, 1 H), 6.78 (br s, 1 H), 3.25 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.2, 163.4, 157.8, 148.9, 138.6, 133.6, 130.1, 129.9, 129.3, 128.9, 123.2, 119.8, 80.6, 27.7.

MS: *m*/*z* (%) = 85 (100), 126 (48), 244 (65), 262 (53), 337 (22) [M + H^+].

6-Amino-1,3-dibutyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2l)
Mp 124 °C.

ATR–IR: 3364, 2957, 1697, 1648, 1594, 1546, 1440 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.21 (s, 1 H), 11.06 (br s, 1 H), 8.19 (br s, 1 H), 7.57–7.59 (m, 2 H), 7.29–7.34 (m, 2 H), 7.04–7.06 (m, 1 H), 3.93–4.02 (m, 2 H), 3.85–3.87 m, 2 H), 1.53–1.55 (m, 4 H), 1.30–1.34 (m, 4 H), 0.90–0.93 (m, 6 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.4, 162.7, 157.4, 148.7, 138.5, 128.8, 123.2, 119.9, 80.4, 41.8, 40.8, 29.5, 28.9, 19.6, 19.2, 13.7, 13.6.

MS: *m*/*z* (%) = 213 (40), 235 (68), 276 (100), 359 (50) [M + H^+].

6-Amino-3-(4-methoxybenzyl)-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2m)
Mp 212 °C.

ATR–IR: 3454, 1699, 1653, 1611, 1511, 1423, 1247 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.10 (s, 1 H), 10.64 (br s, 1 H), 7.58–7.61 (m, 5 H), 7.49–7.51 (m, 2 H), 7.31–7.34 (m, 4 H), 6.88–6.90 (m, 3 H), 4.99 (s, 2 H), 3.73 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.2, 163.1, 158.4, 158.0, 149.0, 138.5, 133.5, 130.1, 129.9, 129.3, 129.2, 128.9, 123.3, 119.9, 113.7, 80.6, 55.0, 43.4.

MS: *m*/*z* (%) = 69 (42), 85 (100), 126 (80), 443 (33) [M + H^+].

6-Benzylamino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2n)
Mp > 375 °C.

ATR–IR: 3111, 1698, 1659, 1582, 1450, 1347 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.19 (s, 1 H), 11.44 (br s, 1 H), 7.51–7.53 (m, 2 H), 7.40–7.41 (m, 4 H), 7.29–7.36 (m, 3 H), 7.04–7.07 (m, 1 H), 4.70 (d, *J* = 5.2 Hz, 2 H), 3.49 (s, 3 H), 3.24 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.1, 163.1, 162.0, 150.4, 138.3, 137.6, 128.9, 128.8, 127.8, 127.7, 120.0, 118.2, 84.6, 50.0, 36.4, 28.0.

MS: *m*/*z* (%) = 85 (33), 126 (27), 272 (100), 365 (18) [M + H^+].

1,3-Dimethyl-2,4-dioxo-6-propylamino-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2o)
Mp 154 °C.

ATR–IR: 2959, 1703, 1642, 1585, 1537, 1441, 1231 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.22 (s, 1 H), 11.14 (br s, 1 H), 7.58 (d, *J* = 5.0 Hz, 2 H), 7.27–7.30 (m, 2 H), 6.97 (t, *J* = 7.3 Hz, 1 H), 3.42–3.45 (m, 5 H), 3.23 (s, 3 H), 1.62–1.65 (m, 2 H), 0.97 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.3, 163.0, 162.0, 150.4, 138.4, 128.3, 123.3, 120.0, 84.0, 48.5, 36.2, 27.9, 23.4, 11.1.

MS: *m*/*z* (%) = 85 (19), 224 (100), 317 (25) [M + H^+].

6-Amino-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Butylamide (2p)
Mp > 375 °C.

ATR–IR: 3269, 2957, 1693, 1605, 1531, 1414, 1377 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.09 (s, 1 H), 10.96 (s, 1 H), 9.71–9.73 (m, 1 H), 7.87 (s, 1 H), 3.19–3.24 (m, 5 H), 1.41–1.45 (m, 2 H), 1.29–1.35 (m, 2 H), 0.86–0.91 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.7, 163.3, 159.2, 148.7, 80.1, 37.5, 31.3, 28.4, 19.6, 13.7.

MS: *m*/*z* (%) = 85 (43), 165 (72), 241 (55) [M + H^+], 263 (100) [M + Na^+].

6-Amino-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Benzylamide (2q)
Mp 295 °C.

ATR–IR: 3270, 3180, 1725, 1644, 1602, 1521, 1439 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.00 (s, 2 H), 10.11–10.13 (m, 1 H), 7.94 (s, 1 H), 7.32–7.35 (m, 2 H), 7.25–7.29 (m, 3 H), 4.44 (d, *J* = 5.9 Hz, 2 H), 3.26 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.9, 163.4, 159.2, 148.7, 139.7, 128.3, 127.1, 126.8, 80.1, 41.6, 28.5.

MS: *m*/*z* (%) = 85 (36), 165 (100), 186 (20), 275 (8) [M + H^+].

6-Amino-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2r)
Mp 320 °C.

ATR–IR: 3270, 3180, 1711, 1670, 1585, 1530, 1443 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.14 (s, 1 H), 11.24 (s, 1 H), 10.84 (s, 1 H), 8.16 (s, 1 H), 7.56 (d, *J* = 8.1 Hz, 2 H), 7.27–7.33 (m, 2 H), 7.05 (t, *J* = 7.2 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.3, 164.7, 160.4, 149.4, 139.5, 129.6, 123.8, 120.4, 80.9, 28.8.

MS: *m*/*z* (%) = 64 (100), 101 (37), 157 (22), 261 (8) [M + H^+].

6-Amino-2,4-dioxo-1-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2s)
Mp 311 °C.

ATR–IR: 3342, 3095, 1725, 1586, 1512, 1416 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.14 (s, 1 H), 11.39 (s, 1 H), 10.58 (s, 1 H), 7.57–7.61 (m, 5 H), 7.47–7.51 (m, 2 H), 7.31–7.34 (m, 2 H), 7.05–7.07 (m, 1 H), 6.81 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.2, 164.2, 159.2, 148.3, 138.6, 133.1, 130.1, 129.8, 123.1, 119.7, 80.4.

MS: *m*/*z* (%) = 85 (21), 126 (25), 248 (100), 323 (35) [M + H^+].

2,4-Dioxo-6-phenylamino-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid Phenylamide (2t)
Mp 144 °C.

ATR–IR: 3309, 3234, 3137, 1703, 1619, 1586, 1520 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.59 (s, 1 H), 12.12 (s, 1 H), 11.18 (br s, 1 H), 11.02 (s, 1 H), 7.56–7.60 (m, 2 H), 7.45–7.48 (m, 2 H), 7.32–7.37 (m, 3 H), 7.06–7.15 (m, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.5, 165.1, 156.8, 148.4, 138.3, 135.5, 129.6, 128.9, 126.8, 125.2, 123.3, 119.9, 81.0.

MS: *m*/*z* (%) = 69 (25), 230 (30), 263 (28), 323 (23) [M + H^+], 345 (100) [M + Na^+].

2,4-Dioxo-6-phenylamino-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (4-Fluorophenyl)amide (2u)
Mp > 375 °C.

ATR–IR: 3384, 3113, 1727, 1663, 1612, 1497, 1372 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.55 (s, 1 H), 12.08 (s, 1 H), 11.18 (s, 1 H), 10.99 (br s, 1 H), 7.59–7.62 (m, 2 H), 7.45–7.48 (m, 2 H), 7.33–7.36 (m, 3 H), 7.15–7.19 (m, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.4, 165.0, 156.7, 148.3, 135.4, 134.6, 135.4, 129.6, 126.9, 125.2, 121.8, 115.5, 115.4, 80.8.

MS: *m*/*z* (%) = 85 (100), 165 (67), 229 (34), 341 (18) [M + H^+].

2,4-Dioxo-6-phenylamino-1,2,3,4-tetrahydropyrimidine-5-carboxylic Acid (4-Methoxyphenyl)amide (2v)
Mp 268 °C.

ATR–IR: 3408, 3404, 3042, 1712, 1665, 1588, 1555, 1441, 1415 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 12.67 (s, 1 H), 11.91 (s, 1 H), 11.14 (s, 1 H), 10.99 (br s, 1 H), 7.44–7.50 (m, 4 H), 7.33–7.36 (m, 3 H), 6.90–6.92 (m, 2 H), 3.74 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.1, 165.0, 156.6, 148.3, 135.5, 132.9, 131.3, 129.6, 126.8, 125.2, 121.5, 119.9, 114.0, 80.9, 55.2.

MS: *m*/*z* (%) = 85 (75), 165 (100), 230 (40), 271 (50), 353 (43) [M + H^+].

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