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New Efficient Synthesis of 2-Thioxo-2,3-dihydropyrimidin-4(1*H*)-ones from Baylis–Hillman Adducts

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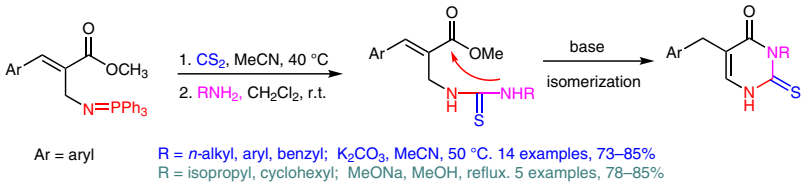

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Abstract Azides obtained from Baylis–Hillman adducts were treated with triphenylphosphine to give the corresponding iminophosphoranes, which reacted with carbon disulfide at 40 °C to produce isothiocyanates. The reaction of these isothiocyanates with primary amines provided thiourea intermediates, which in the presence of potassium carbonate or sodium methoxide were converted into 2-thioxo-2,3-dihydropyrimidin-4(1H)-ones in good yields.

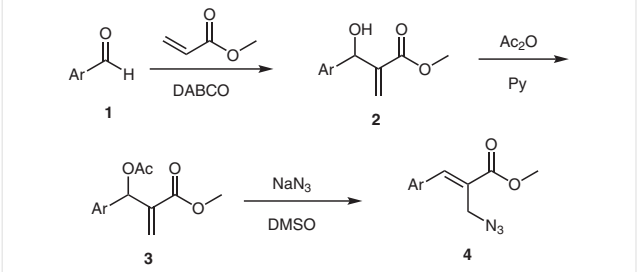
Key words Baylis–Hillman adducts, iminophosphoranes, isothiocyanates, primary amines, aza-Wittig reaction, 2-thioxo-2,3-dihydropyrimidin-4(1H)-ones

The synthesis of nitrogen containing heterocyclic compounds like 2,3-dihydropyrimidin-4(1*H*)-ones and their derivatives is an important and useful area of research in organic chemistry, because they act as building blocks for many biologically active compounds. Compounds containing a 2,3-dihydropyrimidin-4(1*H*)-one ring play a very important part in the biochemistry of living cells and have attracted attention in the past few years owing to their wide range of biological activity. A literature survey reveals that these compounds show pharmacological properties like anticancer,[1] anti-HIV,[2] anti-inflammatory,[3] antimicrobial,[4] antimycobacterial,[5] antitumor,[6] and antiviral effects.[7] Although a number of methods are available for the synthesis of 2,3-dihydropyrimidin-4(1*H*)-ones,[8] 3-alkyl- or 3-aryl-, and 5-arylmethyl-substituted 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one are not easily accessible by existing routes.

The Baylis–Hillman reaction is a carbon–carbon sigma bond formation reaction between activated alkenes and carbon electrophiles in a tandem Michael-aldol sequence,[9] and can result in densely functionalized molecules. The Baylis–Hillman adducts can undergo several synthetic organic transformations, which make them valuable building blocks for the syntheses of natural products and other organic materials.[10]

Iminophosphoranes are important reagents in synthetic organic chemistry, being key intermediates in the synthesis of natural products and compounds with biological and pharmacological activity.[11] They are also valuable for the aza-Wittig reaction,[12] and for the formation of carbodiimides,[13] sterically hindered amines,[14] and heterocycles.[15] The aza-Wittig reaction has emerged as one of the most important synthetic method for constructing novel C=N, N=N, and S=N bonds, especially for the preparation of nitrogen-containing heterocyclic compounds.[16]

Thus, it is envisioned that combining the efficiency of the Baylis–Hillman reaction with a post-condensation aza-Wittig reaction would facilitate access to a series of unreported heterocycles, which are of considerable interest as potential biologically active compounds or pharmaceuticals.[17] Recently, we have reported the synthesis of fused pyrimidin-4(3*H*)-ones based on the tandem aza-Wittig heterocumulene-mediated annulation strategy.[18] As a part of our continuing investigations on the aza-Wittig reaction and for designing new heterocyclic systems with potential biological activities,[19] an efficient synthesis of unreported

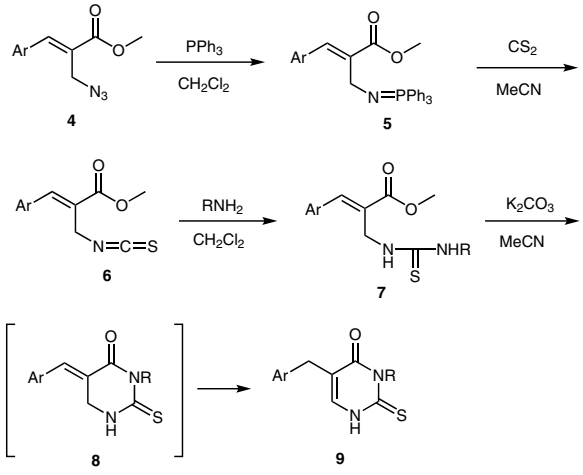


Scheme 1 Preparation of intermediate azides **4**

2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones by a new sequential aza-Wittig/intramolecular cyclization/isomerization reaction, starting from Baylis–Hillman adducts is described in this paper.

A mixture of aryl aldehyde **1** and methyl acrylate was stirred at room temperature in the presence of catalytic DABCO to form α-methylene β-hydroxy esters **2** (the Baylis–Hillman reaction). Acetylation of allylic alcohol **2** with acetic anhydride in pyridine gave the corresponding acetates **3**, which were treated with sodium azide in dimethyl sulfoxide to give the corresponding allylic azides **4** as colorless oils in good overall yields (Scheme 1).

Further, Staudinger reaction of azides **4** with triphenylphosphine at room temperature produced iminophosphoranes **5** in good yields (Scheme 2). Without isolation, intermediates **5** were reacted with excess carbon disulfide at 40 °C to give isothiocyanates **6**, which were further treated with primary amines to give 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9** in good overall yields via an intramolecular addition-elimination-cyclization reaction followed by isomerization of intermediates **8** through a 1,3-hydrogen shift under basic conditions (Scheme 2 and Table 1).



Scheme 2 Preparation of 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9**

Table 1 Preparation of Thioureas **7a–u**and 2-Thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9a–n**[a]

Entry	Ar	R	Time (h)[b]	Product **7**	Yield (%)[c]	Time (h)[d]	Product **9**	Yield (%)[e]
1	3-ClC_6H_4	*n*-Pr	3	**7a**	83	9	**9a**	85
2	3-ClC_6H_4	Ph	5.5	**7b**	79	18	**9b**	75
3	3-ClC_6H_4	$PhCH_2$	5	**7c**	81	13	**9c**	78
4	3-BrC_6H_4	Et	3.5	**7d**	79	10	**9d**	81
5	3-BrC_6H_4	*n*-Pr	4	**7e**	83	11	**9e**	84
6	3-BrC_6H_4	Ph	6.5	**7f**	76	17	**9f**	78
7	3-BrC_6H_4	$PhCH_2$	5.5	**7g**	77	12	**9g**	82
8	3-MeC_6H_4	Et	4	**7h**	76	13	**9h**	80
9	3-MeC_6H_4	*n*-Pr	5	**7i**	83	14	**9i**	82
10	3-MeC_6H_4	*n*-Bu	6	**7j**	86	15	**9j**	83
11	3-MeC_6H_4	Ph	6.5	**7k**	75	19	**9k**	77
12	3-MeC_6H_4	4-MeC_6H_4	5.5	**7l**	75	22	**9l**	73
13	Ph	*n*-Pr	4	**7m**	85	10	**9m**	85
14	4-FC_6H_4	*n*-Pr	3	**7n**	83	8	**9n**	81
15	Ph	*i*-Pr	5	**7o**	83	24	**9o**	0
16	Ph	*c*-C_6H_{11}	6	**7p**	80	24	**9p**	0
17	3-ClC_6H_4	*i*-Pr	3.5	**7q**	86	24	**9q**	0
18	3-ClC_6H_4	*c*-C_6H_{11}	5.5	**7r**	83	24	**9r**	0
19	3-BrC_6H_4	*i*-Pr	5	**7s**	84	24	**9s**	0
20	3-BrC_6H_4	*t*-Bu	5	**7t**	78	24	**9t**	0
21	3-MeC_6H_4	*t*-Bu	6	**7u**	76	24	**9u**	0

[a] Reaction conditions: thiourea **7** (1 mmol), K_2CO_3 (1 mmol), MeCN (5 mL), 50 °C.
[b] Reaction time for the conversion of isothiocyanates **6** into thioureas **7**.
[c] Isolated yields of **7** based on azides **4**.
[d] Reaction time for the conversion of thioureas **7** into 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9**.
[e] Isolated yields based on thioureas **7**.

The structure of 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9** was confirmed from their spectral data. For example, the ^{1}H NMR spectrum of **9a** showed a singlet at δ = 10.66 assigned to the NH proton. The signals for the 6-H proton of the 2,3-dihydropyrimidin-4(1*H*)-one appeared at δ = 6.80 as doublets. The signal attributable to the benzyl group appeared at δ = 3.65 as a singlet. The ^{13}C NMR spectrum of **9a** showed a signal for the C=S carbon atom at δ = 175.8 and for the C=O carbon atom at δ = 160.7. The signal attributable to the methylene carbon atom appeared at δ = 33.1. The mass spectra showed the expected molecular ion peaks and the IR spectra displayed strong bands at 3100–3035 cm^{-1}, attributed to the NH group, and a C=O absorption band at 1691–1680 cm^{-1}. Furthermore, a single crystal of **9i** was obtained from a CH_2Cl_2/PE solution of **9i**, and the X-ray crystal structure analysis verified the proposed structure (Figure 1).[20]

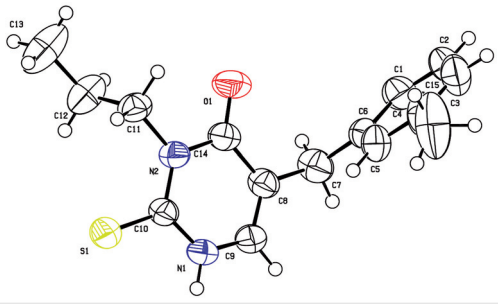
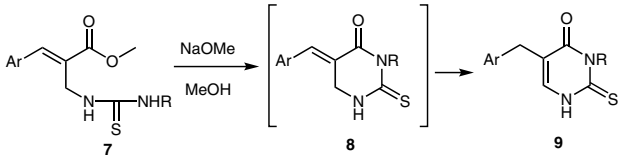


Figure 1 X-ray crystal structure of compound **9i**

According to this practical strategy, various iminophosphoranes **5** and primary amines were employed in the reaction, which proceeded smoothly to give the corresponding thioureas **7** in 68–86% yields. Generally, shorter reaction times could be employed and better yields were obtained when R was an alicyclic amine rather than an aromatic amine. The results are summarized in Table 1. Most primary amines were suitable for accessing 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9** in good yields in the presence of potassium carbonate (Table 1, entries 1–14), but no product was obtained when R was isopropyl (entries 15, 17, and 19), cyclohexyl (entries 16 and 18), or *tert*-butyl (entries 20 and 21). Coincidentally, the results of this experiment are consistent with the conclusions of Ding and co-workers.[17b] The intramolecular cyclization reaction did not take place probably due to the steric hindrance of these bulky groups and the alkalescence of potassium carbonate. Therefore, the stronger base sodium methoxide was tested, and fortunately, a noticeable improvement was observed. Thus, in those cases where no 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **9o–u** had been obtained in Table 1 (entries 15–21), good yields of cyclized products **9o–s** were obtained using sodium methoxide as shown in Table 2 (entries 1–5), when the reaction mixtures were heated for 13–17 hours. However, no product was formed after heating for 24 hours when R was a bulky *tert*-butyl group (Table 2, entries 6, 7, **9t**,**u**).

Table 2 Cyclization in the Condition of MeONa/MeOH[a]



R = *i*-Pr, *c*-C_6H_{11}, *t*-Bu

Entry	Ar	R	Time (h)	Product **9**	Yield (%)[b]
1	Ph	*i*-Pr	14	**9o**	85
2	Ph	*c*-C_6H_{11}	17	**9p**	78
3	3-ClC_6H_4	*i*-Pr	12	**9q**	88
4	3-ClC_6H_4	*c*-C_6H_{11}	15	**9r**	81
5	3-BrC_6H_4	*i*-Pr	13	**9s**	83
6	3-BrC_6H_4	*t*-Bu	24	**9t**	0
7	3-MeC_6H_4	*t*-Bu	24	**9u**	0

[a] Reaction conditions: thiourea **7** (1 mmol), MeONa (1 mmol), MeOH (5 mL), reflux.
[b] Isolated yields based on thiourea **7**.

In summary, a facile synthetic protocol for 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones was established through a sequential aza-Wittig/intramolecular cyclization/isomerization reaction, starting from Baylis–Hillman adducts in good yields under mild conditions. The method reported here utilizes easily accessible starting materials and has potential for the synthesis of various 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones, which are of considerable interest as potential biological active compounds or pharmaceuticals.

All solvents and reagents were purchased from commercial sources, unless otherwise noted. Commercial reagents were used as supplied or purified by standard techniques wherever necessary. Column chromatography was performed using 200–300 mesh silica gel with the proper solvent system according to TLC analysis using I_2 stain and UV light to visualize the reaction components. Melting points were determined on a WRS-1B digital melting point instrument. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on an Agilent 400 MHz spectrometer at r.t. and resonances are relative to TMS. NMR data is reported as follows: chemical shift, multiplicity (standard abbreviations), coupling constant in hertz (Hz), and integration. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from TMS using the central peak of $CDCl_3$ (77.0 ppm) or DMSO-d_6 (39.6 ppm) as the internal standard. IR spectra were recorded on an FTIR spectrometer (KBr) and reported in cm^{-1}. HRMS data were recorded on an orbitrap MS analyzer using ESI ionization with 100 000 (FWHM) maximum resolution.

Thioureas 7a–u; General Procedure

PPh_3 (0.52 g, 2 mmol) was added to a stirred solution of azide **4**[18,21] (2 mmol) in anhyd CH_2Cl_2 (10 mL), and the mixture was stirred for 2–3 h to form the required iminophosphorane **5** (TLC monitoring). Then, the solvent was evaporated under reduced pressure and to the residue was added anhyd MeCN (5 mL) and excess CS_2 (0.25 mL, 4 mmol). After stirring the reaction mixture for 2 h at 40 °C, the solvent was removed under reduced pressure to give the corresponding isothiocyanate **6**, which was used directly without further purification. To a solution of the crude product **6** in CH_2Cl_2 (10 mL) was added the corresponding primary amine (2.4 mmol) and the resulting mixture was stirred for 3–7 h at r.t. After the reaction was completed, the solvent was evaporated, and the residue was purified by column chromatography (silica gel; PE/EtOAc 25:1 → 4:1) to give the desired thiourea **7**.

Methyl 3-(3-Chlorophenyl)-2-[(3-propylthioureido)methyl]acrylate (7a)

Colorless oil; yield: 541 mg (83%); R_f = 0.21 (PE/EtOAc 4:1).

IR (KBr): 3091, 3035, 1686, 1611, 1499, 1459, 1035 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1 H, =CH), 7.41 (s, 1 H, ArH), 7.37 (br s, 3 H, ArH), 6.37 (s, 1 H, NH), 6.27 (s, 1 H, NH), 4.52 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 3.30 (s, 2 H, CH_2), 1.61–1.53 (m, 2 H, CH_2), 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.39, 168.23, 141.71, 135.68, 134.76, 130.13, 129.49, 129.29, 128.78, 127.33, 109.98, 52.60, 29.65, 22.05, 11.36.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}ClN_2O_2S^+$ (M + H)$^+$: 327.0929; found: 327.0927.

Methyl 3-(3-Chlorophenyl)-2-[(3-phenylthioureido)methyl)]acrylate (7b)

Colorless oil; yield: 569 mg (79%); R_f = 0.10 (PE/EtOAc 4:1).

IR (KBr): 3097, 3037, 1687, 1611, 1500, 1459, 1035 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1 H, NH), 7.75 (s, 1 H, =CH), 7.45–7.29 (m, 7 H, ArH), 7.14 (d, *J* = 7.6 Hz, 2 H, ArH), 6.73 (s, 1 H, NH), 4.73 (d, *J* = 4.8 Hz, 2 H, CH_2), 3.77 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.11, 167.74, 141.73, 135.72, 134.64, 130.08, 130.01, 129.47, 129.43, 128.26, 127.55, 127.23, 124.91, 110.00, 52.40, 42.44.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{18}ClN_2O_2S^+$ (M + H)$^+$: 361.0772; found: 361.0771.

Methyl 2-[(3-Benzylthioureido)methyl]-3-(3-chlorophenyl)acrylate (7c)

Colorless oil; yield: 606 mg (81%); R_f = 0.21 (PE/EtOAc 4:1).

IR (KBr): 3097, 3041, 1685, 1608, 1499, 1462, 1033 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1 H, =CH), 7.38–7.22 (m, 9 H, ArH), 6.61 (s, 1 H, NH), 6.46 (s, 1 H, NH), 4.58 (s, 2 H, CH_2), 4.49 (s, 2 H, CH_2), 3.76 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.59, 167.90, 141.78, 135.53, 134.08, 130.06, 129.45, 129.25, 128.74, 128.50, 127.76, 127.55, 127.28, 76.68, 52.54.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{20}ClN_2O_2S^+$ (M + H)$^+$: 375.0929; found: 375.0929.

Methyl 3-(3-Bromophenyl)-2-[(3-ethylthioureido)methyl]acrylate (7d)

Colorless oil; yield: 562 mg (79%); R_f = 0.10 (PE/EtOAc 4:1).

IR (KBr): 3097, 3041, 1685, 1608, 1499, 1457, 1037 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1 H, =CH), 7.58 (s, 1 H, ArH), 7.52 (d, *J* = 8.0 Hz, 1 H, ArH), 7.41 (d, *J* = 7.6 Hz, 1 H, ArH), 7.32 (t, *J* = 7.8 Hz, 1 H, ArH), 6.36 (s, 1 H, NH), 6.19 (s, 1 H, NH), 4.52 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 3.39 (br s, 2 H, CH_2), 1.19 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.21, 168.21, 141.62, 135.96, 132.41, 132.17, 130.37, 128.78, 127.76, 122.86, 77.32, 77.00, 76.68, 52.62, 29.66, 13.94.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{18}BrN_2O_2S^+$ (M + H)$^+$: 357.0267; found: 357.0267.

Methyl 3-(3-Bromophenyl)-2-[(3-propylthioureido)methyl]acrylate (7e)

Colorless oil; yield: 621 mg (83%); R_f = 0.24 (PE/EtOAc 4:1).

IR (KBr): 3097, 3039, 1681, 1611, 1500, 1459, 1030 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1 H, =CH), 7.58 (s, 1 H, ArH), 7.52 (d, *J* = 8.0 Hz, 1 H, ArH), 7.41 (d, *J* = 6.8 Hz, 1 H, ArH), 7.32 (t, *J* = 7.8 Hz, 1 H, ArH), 6.34 (s, 1 H, NH), 6.22 (s, 1 H, NH), 4.53 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 3.30 (s, 2 H, CH_2), 1.59 (dd, *J* = 14.4, 7.2 Hz, 2 H, CH_2), 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.22, 141.60, 135.96, 132.42, 132.17, 130.37, 128.81, 127.76, 122.87, 109.99, 52.62, 29.67, 22.07, 11.38.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}BrN_2O_2S^+$ (M + H)$^+$: 371.0423; found: 371.0425.

Methyl 3-(3-Bromophenyl)-2-[(3-phenylthioureido)methyl]acrylate (7f)

Colorless oil; yield: 614 mg (76%); R_f = 0.25 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1678, 1608, 1499, 1459, 1033 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1 H, NH), 7.74 (s, 1 H, =CH), 7.62 (s, 1 H, ArH), 7.51 (d, *J* = 8.0 Hz, 1 H, ArH), 7.46–7.39 (m, 3 H, ArH), 7.33–7.29 (m, 3 H, ArH), 7.14 (d, *J* = 7.2 Hz, 2 H, ArH), 6.74 (s, 1 H, NH), 4.73 (s, 2 H, CH_2), 3.76 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.98, 167.70, 141.60, 135.96, 132.32, 130.23, 130.06, 128.23, 127.98, 127.19, 124.88, 122.71, 52.40, 42.38, 29.67.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{18}BrN_2O_2S^+$ (M + H)$^+$: 405.0267; found: 405.0267.

Methyl 2-[(3-Benzylthioureido)methyl]-3-(3-bromophenyl)acrylate (7g)

Colorless oil; yield: 644 mg (77%); R_f = 0.25 (PE/EtOAc 4:1).

IR (KBr): 3094, 3035, 1680, 1608, 1499, 1457, 1034 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 1 H, =CH), 7.51–7.47 (m, 2 H, ArH), 7.33–7.23 (m, 7 H, ArH), 6.64 (s, 1 H, NH), 6.49 (s, 1 H, NH), 4.58 (s, 2 H, CH_2), 4.48 (s, 2 H, CH_2), 3.75 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.59, 167.87, 141.63, 135.81, 132.33, 132.13, 130.27, 128.72, 128.54, 127.72, 127.53, 122.74, 52.52, 48.36, 41.39.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{20}BrN_2O_2S^+$ (M + H)$^+$: 419.0423; found: 419.0424.

Methyl 2-[(3-Ethylthioureido)methyl]-3-(*m*-tolyl)acrylate (7h)

Colorless oil; yield: 444 mg (76%); R_f = 0.15 (PE/EtOAc 4:1).

IR (KBr): 3100, 3041, 1685, 1608, 1499, 1457, 1041 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (s, 1 H, =CH), 7.35–7.19 (m, 4 H, ArH), 6.39 (s, 1 H, NH), 6.24 (s, 1 H, NH), 4.48 (s, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.40 (s, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 1.14 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.09, 168.48, 143.67, 138.62, 133.77, 130.38, 130.02, 128.72, 127.14, 126.36, 109.94, 52.45, 29.60, 21.30, 13.91.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{21}N_2O_2S^+$ (M + H)$^+$: 293.1318; found: 293.1318.

Methyl 2-[(3-Propylthioureido)methyl]-3-(*m*-tolyl)acrylate (7i)

Colorless oil; yield: 508 mg (83%); R_f = 0.25 (PE/EtOAc 4:1).

IR (KBr): 3100, 3041, 1693, 1608, 1504, 1457, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (s, 1 H, =CH), 7.36–7.11 (m, 4 H, ArH), 6.39 (s, 1 H, NH), 6.29 (s, 1 H, NH), 4.48 (s, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.32 (s, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 1.56–1.51 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.22, 168.51, 143.68, 138.64, 133.74, 130.40, 130.01, 128.73, 127.14, 126.36, 109.94, 52.48, 22.01, 21.32, 11.31.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{23}N_2O_2S^+$ (M + H)$^+$: 307.1475; found: 307.1475.

Methyl 2-[(3-Butylthioureido)methyl]-3-(*m*-tolyl)acrylate (7j)

Colorless oil; yield: 550 mg (86%); R_f = 0.25 (PE/EtOAc 4:1).

IR (KBr): 3095, 3034, 1688, 1608, 1499, 1457, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (s, 1 H, =CH), 7.33–7.29 (m, 1 H, ArH), 7.24–7.18 (m, 3 H, ArH), 6.49 (s, 1 H, NH), 6.36 (s, 1 H, NH), 4.49 (s, 2 H, CH_2), 3.83 (s, 3 H, CH_3), 3.35 (s, 2 H, CH_2), 2.38 (s, 3 H, CH_3), 1.49–1.46 (m, 2 H, CH_2), 1.34–1.30 (m, 2 H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.09, 169.36, 144.51, 139.46, 134.65, 131.27, 130.99, 129.59, 128.04, 127.33, 53.33, 31.69, 22.19, 20.85, 14.58.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{25}N_2O_2S^+$ (M + H)$^+$: 321.1631; found: 321.1630.

Methyl 2-[(3-Phenylthioureido)methyl]-3-(*m*-tolyl)acrylate (7k)

Colorless oil; yield: 510 mg (75%); R_f = 0.20 (PE/EtOAc 4:1).

IR (KBr): 3097, 3038, 1686, 1608, 1499, 1459, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (s, 2 H, =CH, NH), 7.46–7.41 (m, 5 H, ArH), 7.18 (d, *J* = 8.0 Hz, 2 H, ArH), 7.00 (d, *J* = 7.2 Hz, 2 H, ArH), 6.59 (s, 1 H, NH), 4.74 (s, 2 H, CH_2), 3.77 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.22, 168.73, 143.40, 138.42, 133.66, 130.28, 130.26, 128.53, 126.71, 126.62, 52.63, 52.32, 42.82, 29.22, 21.25.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{21}N_2O_2S^+$ (M + H)$^+$: 341.1318; found: 341.1318.

Methyl 3-(*m*-Tolyl)-2-{[3-(*p*-tolyl)thioureido]methyl}acrylate (7l)

Light yellow solid; yield: 531 mg (75%); mp 139–141 °C; R_f = 0.22 (PE/EtOAc 4:1).

IR (KBr): 3100, 3041, 1681, 1608, 1500, 1457, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (s, 2 H, =CH, NH), 7.34–7.29 (m, 2 H, ArH), 7.25–7.16 (m, 4 H, ArH), 7.00 (d, *J* = 7.6 Hz, 2 H, ArH), 6.59 (s, 1 H, NH), 4.74 (s, 2 H, CH_2), 3.76 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.09, 168.13, 143.75, 138.47, 133.81, 130.52, 130.34, 130.30, 128.58, 126.75, 124.95, 52.24, 42.61, 29.65, 21.33, 20.99.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{23}N_2O_2S^+$ (M + H)$^+$: 355.1475; found: 355.1476.

Methyl 3-Phenyl-2-[(3-propylthioureido)methyl]acrylate (7m)

Colorless oil; yield: 496 mg (85%); R_f = 0.18 (PE/EtOAc 4:1).

IR (KBr): 3100, 3041, 1688, 1611, 1499, 1453, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1 H, =CH), 7.43 (br s, 5 H, ArH), 6.41 (s, 2 H, NH), 4.49 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 3.32 (s, 2 H, CH_2), 1.59–1.50 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.24, 168.48, 143.55, 133.82, 129.57, 129.34, 128.84, 127.33, 109.94, 52.51, 22.01, 11.32.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{21}N_2O_2S^+$ (M + H)$^+$: 293.1318; found: 293.1320.

Methyl 3-(4-Fluorophenyl)-2-[(3-propylthioureido)methyl]acrylate (7n)

Colorless oil; yield: 515 mg (83%); R_f = 0.20 (PE/EtOAc 4:1).

IR (KBr): 3097, 3039, 1685, 1608, 1499, 1457, 1037 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (s, 1 H, CH_3), 7.47 (s, 2 H, ArH), 7.13 (t, *J* = 8.6 Hz, 2 H, ArH), 6.43 (s, 1 H, NH), 6.36 (s, 1 H, NH), 4.54 (s, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.31 (s, 2 H, CH_2), 1.61–1.54 (m, 2 H, CH_2), 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.36, 168.52, 164.50, 162.01, 142.32, 131.65 (d, *J* = 8.0 Hz), 129.97 (d, *J* = 3.0 Hz), 127.08, 116.10, 115.89, 109.97, 52.50, 29.63, 22.03, 11.34.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}FN_2O_2S^+$ (M + H)$^+$: 311.1224; found: 311.1220.

Methyl 2-[(3-Isopropylthioureido)methyl]-3-phenylacrylate (7o)

Colorless oil; yield: 484 mg (83%); R_f = 0.16 (PE/EtOAc 4:1).

IR (KBr): 3097, 3035, 1690, 1605, 1499, 1457, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1 H, =CH), 7.46–7.43 (m, 5 H, ArH), 6.40 (s, 1 H, NH), 6.20 (s, 1 H, NH), 4.46 (s, 2 H, CH_2), 4.18–4.11 (m, 1 H, CH), 3.85 (s, 3 H, CH_3), 1.15 (d, *J* = 6.4 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.07, 168.41, 143.42, 133.80, 129.57, 129.36, 128.86, 127.33, 109.92, 52.50, 46.29, 22.27.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{21}N_2O_2S^+$ (M + H)$^+$: 293.1318; found: 293.1318.

Methyl 2-[(3-Cyclohexylthioureido)methyl]-3-phenylacrylate (7p)

Colorless oil; yield: 530 mg (80%); R_f = 0.20 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1673, 1602, 1499, 1457, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1 H, =CH), 7.43 (br s, 5 H, ArH), 6.36 (s, 1 H, NH), 6.25 (s, 1 H, NH), 4.46 (s, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 1.96 (d, *J* = 11.6 Hz, 2 H, CH_2), 1.71–1.58 (m, 3 H, CH_2), 1.45–1.21 (m, 3 H, CH_2), 1.20–1.03 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.96, 168.42, 143.39, 133.81, 129.56, 129.36, 128.85, 127.36, 52.52, 32.53, 25.30, 24.61.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{25}N_2O_2S^+$ (M + H)$^+$: 333.1631; found: 333.1631.

Methyl 3-(3-Chlorophenyl)-2-[(3-isopropylthioureido)methyl]acrylate (7q)

Colorless oil; yield: 560 mg (86%); R_f = 0.16 (PE/EtOAc 4:1).

IR (KBr): 3097, 3055, 1691, 1611, 1499, 1454, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (s, 1 H, =CH), 7.41–7.38 (m, 4 H, ArH), 6.31 (s, 1 H, NH), 6.10 (s, 1 H, NH), 4.50 (s, 2 H, CH_2), 4.10 (s, 1 H, CH), 3.87 (s, 3 H, CH_3), 1.19 (d, *J* = 6.4 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.22, 141.69, 135.66, 130.17, 129.52, 129.29, 127.33, 109.98, 52.65, 22.37.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}ClN_2O_2S^+$ (M + H)$^+$: 327.0923; found: 327.0933.

Methyl 3-(3-Chlorophenyl)-2-[(3-cyclohexylthioureido)methyl]acrylate (7r)

Colorless oil; yield: 607 mg (83%); R_f = 0.27 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1690, 1608, 1499, 1457, 1031 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1 H, =CH), 7.40–7.37 (m, 4 H, ArH), 6.40 (s, 1 H, NH), 6.23 (d, *J* = 5.2 Hz, 1 H, NH), 4.49 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 1.97 (d, *J* = 10.4 Hz, 2 H, CH_2), 1.71 (d, *J* = 13.2 Hz, CH_2), 1.42–1.03 (m, 6 H, 3 × CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.97, 168.11, 141.54, 135.62, 134.69, 132.18, 132.08, 131.47, 130.09, 129.42, 129.26, 128.75, 128.49, 128.36, 127.31, 109.98, 52.59, 32.56, 25.29, 24.59.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{24}ClN_2O_2S^+$ (M + H)$^+$: 367.1242; found: 367.1242.

Methyl 3-(3-Bromophenyl)-2-[(3-isopropylthioureido)methyl]acrylate (7s)

Colorless oil; yield: 621 mg (84%); R_f = 0.17 (PE/EtOAc 4:1).

IR (KBr): 3097, 3039, 1681, 1611, 1500, 1459, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (s, 1 H, =CH), 7.60–7.48 (m, 2 H, ArH), 7.41 (d, *J* = 7.2 Hz, 1 H, ArH), 7.35–7.28 (m, 1 H, ArH), 6.50 (s, 1 H, NH), 6.29 (s, 1 H, NH), 4.50 (s, 2 H, CH_2), 4.14 (s, 1 H, CH), 3.85 (s, 3 H, CH_3), 1.18 (d, *J* = 6.4 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.98, 168.08, 141.50, 135.82, 132.29, 132.10, 130.28, 128.64, 127.74, 122.72, 77.32, 52.56, 22.28.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}BrN_2O_2S^+$ (M + H)$^+$: 371.0423; found: 371.0423.

Methyl 3-(3-Bromophenyl)-2-{[3-(*tert*-butyl)thioureido]methyl}acrylate (7t)

White solid; yield: 600 mg (78%); mp 137–139 °C; R_f = 0.26 (PE/EtOAc 4:1).

IR (KBr): 3097, 3038, 1687, 1611, 1496, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (s, 1 H, =CH), 7.65 (s, 1 H, ArH), 7.51 (d, *J* = 6.0 Hz, 2 H, ArH), 7.33–7.29 (m, 1 H, ArH), 6.61 (s, 1 H, NH), 6.19 (s, 1 H, NH), 4.71 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 1.39 (s, 9 H, *t*-C_4H_9).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.27, 168.34, 141.24, 135.82, 132.29, 132.24, 130.19, 128.33, 128.02, 122.63, 62.76, 52.64, 52.48, 42.73, 29.27.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{22}BrN_2O_2S^+$ (M + H)$^+$: 385.0580; found: 385.0582.

Methyl 2-{[3-(*tert*-Butyl)thioureido]methyl}-3-(*m*-tolyl)acrylate(7u)

White solid; yield: 486 mg (76%); mp 131–133 °C; R_f = 0.25 (PE/EtOAc 4:1).

IR (KBr): 3095, 3034, 1688, 1608, 1499, 1457, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (s, 1 H, =CH), 7.38–7.26 (m, 3 H, ArH), 7.19 (d, *J* = 6.8 Hz, 1 H, ArH), 6.58 (s, 1 H, NH), 6.19 (s, 1 H, NH), 4.71 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 1.39 (s, 9 H, *t*-C_4H_9).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.76, 168.12, 143.77, 138.45, 133.73, 130.33, 130.26, 129.91, 128.56, 126.88, 126.71, 126.41, 124.67, 52.25, 42.58, 21.30.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{25}N_2O_2S^+$ (M + H)$^+$: 321.1631; found: 321.1631.

2-Thioxo-2,3-dihydropyrimidin-4(1*H*)-ones 9a–n; General Procedure

To a solution of thiourea **7** (1 mmol) in anhyd MeCN (5 mL) was added solid K_2CO_3 (0.14 g, 1 mmol), and the mixture was stirred at 50 °C for 10–18 h (TLC monitoring). The mixture was then filtered to remove K_2CO_3 and the solvent evaporated. The residue was chromatographed (silica gel; PE/EtOAc 25:1 → 4:1) to afford the desired 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one **9**.

5-(3-Chlorobenzyl)-3-propyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9a)

White solid; yield: 250 mg (85%); mp 148–150 °C; R_f = 0.34 (PE/EtOAc 4:1).

IR (KBr): 3100, 3041, 1685, 1608, 1499, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.66 (s, 1 H, NH), 7.29–7.17 (m, 3 H, ArH), 7.11 (d, *J* = 6.4 Hz, 1 H, ArH), 6.80 (d, *J* = 5.6 Hz, 1 H, = CH), 4.33–4.29 (m, 2 H, CH_2), 3.64 (s, 2 H, CH_2), 1.78–1.71 (m, 2 H, CH_2), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.82, 160.72, 139.46, 135.48, 134.52, 130.01, 128.96, 127.17, 127.14, 117.97, 109.99, 48.57, 33.11, 19.61, 11.23.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}ClN_2OS^+$ (M + H)$^+$: 295.0666; found: 295.0667.

5-(3-Chlorobenzyl)-3-phenyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9b)

White solid; yield: 246 mg (75%); mp 133–135 °C; R_f = 0.20 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1685, 1608, 1499, 1457, 1042 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.99 (s, 1 H, NH), 7.53–7.43 (m, 3 H, ArH), 7.29–7.05 (m, 6 H, ArH), 6.74 (s, 1 H, =CH), 3.63 (s, 2 H, CH_2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.00, 161.31, 139.22, 138.31, 136.34, 134.52, 130.05, 129.67, 129.12, 129.06, 127.91, 127.32, 127.21, 118.65, 33.02, 14.15.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{14}ClN_2OS^+$ (M + H)$^+$: 329.0510; found: 329.0510.

3-Benzyl-5-(3-chlorobenzyl)-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9c)

White solid; yield: 267 mg (78%); mp 140–142 °C; R_f = 0.28 (PE/EtOAc 4:1).

IR (KBr): 3094, 3041, 1685, 1608, 1501, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.43 (s, 1 H, NH), 7.46 (d, *J* = 7.2 Hz, 2 H, ArH), 7.26–7.18 (m, 6 H, ArH), 7.09 (d, *J* = 5.2 Hz, 1 H, ArH), 6.73 (d, *J* = 4.4 Hz, 1 H, =CH), 5.62 (s, 2 H, CH_2), 3.63 (s, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.31, 160.94, 139.34, 135.68, 135.50, 134.54, 130.03, 128.96, 128.45, 128.34, 127.69, 127.17, 117.92, 109.99, 49.85, 33.04.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{16}ClN_2OS^+$ (M + H)$^+$: 343.0666; found: 343.0667.

5-(3-Bromobenzyl)-3-ethyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9d)

White solid; yield: 265 mg (81%); mp 135–137 °C; R_f = 0.21 (PE/EtOAc 4:1).

IR (KBr): 3094, 3035, 1687, 1605, 1496, 1457, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.77 (s, 1 H, NH), 7.37 (d, *J* = 12.4 Hz, 2 H, ArH), 7.21–7.15 (m, 2 H, ArH), 6.80 (d, *J* = 4.4 Hz, 1 H, =CH), 4.45 (q, *J* = 6.8 Hz, 2 H, CH_2), 3.64 (s, 2 H, CH_2), 1.31 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.58, 160.57, 139.73, 135.58, 131.87, 130.29, 130.05, 127.66, 122.75, 118.00, 42.47, 33.03, 11.54.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}BrN_2OS^+$ (M + H)$^+$: 325.0005; found: 325.0007.

5-(3-Bromobenzyl)-3-propyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9e)

White solid; yield: 284 mg (84%); mp 136–137 °C; R_f = 0.30 (PE/EtOAc 4:1).

IR (KBr): 3094, 3041, 1683, 1611, 1499, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.66 (s, 1 H, NH), 7.30–7.16 (m, 3 H, ArH), 7.11 (d, *J* = 6.4 Hz, 1 H, ArH), 6.80 (d, *J* = 5.2 Hz, 1 H, =CH), 4.33–4.29 (m, 2 H, CH_2), 3.64 (s, 2 H, CH_2), 1.78–1.72 (m, 2 H, CH_2), 0.97 (t, *J* = 7.6 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.82, 160.72, 139.46, 135.47, 134.52, 130.00, 128.96, 127.17, 127.13, 117.97, 48.57, 33.11, 19.61, 11.23.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}BrN_2OS^+$ (M + H)$^+$: 339.0161; found: 339.0161.

5-(3-Bromobenzyl)-3-phenyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9f)

White solid; yield: 290 mg (78%); mp 129–131 °C; R_f = 0.28 (PE/EtOAc 4:1).

IR (KBr): 3097, 3038, 1683, 1608, 1501, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.67 (d, *J* = 5.2 Hz, 1 H, NH), 7.56–7.50 (m, 2 H, ArH), 7.47–7.34 (m, 4 H, ArH), 7.32–7.22 (m, 2 H, ArH), 7.15 (d, *J* = 7.2 Hz, 2 H, ArH), 3.61 (s, 2 H, CH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.69, 161.25, 142.05, 139.26, 138.66, 131.44, 130.50, 129.20, 129.08, 128.62, 128.16, 127.89, 121.66, 116.29, 32.19.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{14}BrN_2OS^+$ (M + H)$^+$: 373.0005; found: 373.0005.

3-Benzyl-5-(3-bromobenzyl)-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9g)

White solid; yield: 317 mg (82%); mp 143–145 °C; R_f = 0.27 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1687, 1611, 1499, 1459, 1030 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.69 (d, *J* = 4.8 Hz, 1 H, NH), 7.53–7.45 (m, 2 H, ArH), 7.38 (d, *J* = 7.6 Hz, 1 H, ArH), 7.31–7.18 (m, 7 H, ArH), 5.50 (s, 2 H, CH_2), 3.60 (s, 2 H, CH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.05, 160.85, 142.07, 138.42, 136.33, 131.27, 130.50, 129.20, 128.27, 127.78, 127.27, 127.07, 121.68, 115.72, 109.66, 48.77, 40.23, 40.02, 32.19.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{16}BrN_2OS^+$ (M + H)$^+$: 387.0161; found: 387.0163.

3-Ethyl-5-(3-methylbenzyl)-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9h)

White solid; yield: 208 mg (80%); mp 143–144 °C; R_f = 0.30 (PE/EtOAc 4:1).

IR (KBr): 3094, 3041, 1689, 1608, 1501, 1457, 1033 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.48 (d, *J* = 3.6 Hz, 1 H, NH), 7.26 (d, *J* = 5.6 Hz, 1 H, ArH), 7.16 (t, *J* = 7.6 Hz, 1 H, ArH), 7.05–6.99 (m, 3 H, ArH), 4.31 (q, *J* = 6.8 Hz, 2 H, CH_2), 3.37 (s, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 1.15 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 175.01, 160.52, 138.87, 137.50, 137.45, 129.34, 128.30, 126.97, 125.80, 116.68, 41.11, 32.46, 21.09, 11.58.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{17}N_2OS^+$ (M + H)$^+$: 261.1056; found: 261.1056.

5-(3-Methylbenzyl)-3-propyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9i)

White solid; yield: 225 mg (82%); mp 136–138 °C; R_f = 0.40 (PE/EtOAc 4:1).

IR (KBr): 3100, 3038, 1683, 1608, 1499, 1459, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.95 (s, 1 H, NH), 7.19 (t, *J* = 7.4 Hz, 1 H, ArH), 7.06–7.02 (m, 3 H, ArH), 6.72 (d, *J* = 5.2 Hz, 1 H, =CH), 4.34–4.30 (m, 2 H, CH_2), 3.62 (s, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 1.76–1.72 (m, 2 H, CH_2), 0.96 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.53, 160.94, 138.40, 137.14, 135.49, 129.70, 128.61, 127.61, 125.96, 118.95, 48.46, 33.22, 21.33, 19.61, 11.20.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{19}N_2OS^+$ (M + H)$^+$: 275.1213; found: 275.1213.

3-Butyl-5-(3-methylbenzyl)-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9j)

White solid; yield: 239 mg (83%); mp 152–154 °C; R_f = 0.35 (PE/EtOAc 4:1).

IR (KBr): 3094, 3041, 1691, 1608, 1499, 1458, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.96 (s, 1 H, NH), 7.20 (t, *J* = 7.6 Hz, 1 H, ArH), 7.06–6.98 (m, 3 H, ArH), 6.73 (d, *J* = 5.2 Hz, 1 H, =CH), 4.40–4.32 (m, 2 H, CH_2), 3.62 (s, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 1.73–1.67 (m, 2 H, CH_2), 1.43–1.37 (m, 2 H, CH_2), 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.48, 160.91, 138.42, 137.13, 135.47, 129.71, 128.62, 127.62, 125.97, 118.96, 46.93, 33.22, 28.22, 21.34, 20.15, 13.69.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{21}N_2OS^+$ (M + H)$^+$: 289.1369; found: 289.1369.

5-(3-Methylbenzyl)-3-phenyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9k)

White solid; yield: 237 mg (77%); mp 153–155 °C; R_f = 0.21 (PE/EtOAc 4:1).

IR (KBr): 3097, 3041, 1685, 1611, 1500, 1457, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.07 (s, 1 H, NH), 7.53–7.43 (m, 3 H, ArH), 7.20 (t, *J* = 6.8 Hz, 3 H, ArH), 7.06 (d, *J* = 7.6 Hz, 1 H, ArH), 6.99 (d, *J* = 8.4 Hz, 2 H, ArH), 6.66 (d, *J* = 4.0 Hz, 1 H, =CH), 3.61 (s, 2 H, CH_2), 2.32 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.79, 161.41, 138.50, 138.41, 136.86, 136.17, 129.88, 129.62, 129.06, 128.71, 127.91, 127.76, 126.13, 119.83, 33.14, 21.36.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}N_2OS^+$ (M + H)$^+$: 309.1056; found: 309.1057.

5-(3-Methylbenzyl)-2-thioxo-3-(*p*-tolyl)-2,3-dihydropyrimidin-4(1*H*)-one (9l)

White solid; yield: 234 mg (73%); mp 166–168 °C; R_f = 0.23 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1687, 1608, 1499, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.88 (s, 1 H, NH), 7.63 (d, *J* = 8.4 Hz, 1 H, ArH), 7.31 (d, *J* = 8.0 Hz, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.07 (d, *J* = 8.0 Hz, 3 H, ArH), 7.00 (d, *J* = 8.4 Hz, 2 H, ArH), 6.70 (s, 1 H, =CH), 3.62 (s, 2 H, CH_2), 2.41 (s, 2 H, CH_3), 2.33 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.97, 161.43, 139.11, 136.91, 135.93, 132.94, 130.39, 129.94, 129.78, 128.73, 127.77, 127.53, 126.18, 119.92, 33.20, 29.68, 21.38.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{19}N_2OS^+$ (M + H)$^+$: 323.1213; found: 323.1213.

5-Benzyl-3-propyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9m)

White solid; yield: 221 mg (85%); mp 128–130 °C; R_f = 0.40 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1680, 1611, 1499, 1457, 1036 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.76 (s, 1 H, NH), 7.32 (t, *J* = 7.2 Hz, 2 H, ArH), 7.20 (d, *J* = 7.2 Hz, 2 H, ArH), 6.72 (d, *J* = 5.2 Hz, 1 H, =CH), 4.36–4.28 (m, 2 H, CH_2), 3.66 (s, 2 H, CH_2), 1.78–1.72 (m, 2 H, CH_2), 0.97(t, *J* = 7.4Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.61, 160.89, 137.24, 135.39, 129.01, 128.77, 126.89, 118.89, 48.51, 33.36, 29.66, 19.62, 11.23.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{17}N_2OS^+$ (M + H)$^+$: 261.1056; found: 261.1054.

5-(4-Fluorobenzyl)-3-propyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9n)

Colorless oil; yield: 225 mg (81%); R_f = 0.36 (PE/EtOAc 4:1).

IR (KBr): 3094, 3039, 1685, 1611, 1500, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.52 (s, 1 H, NH), 7.18 (dd, *J* = 8.4, 5.6 Hz, 2 H, ArH), 7.00 (t, *J* = 8.6 Hz, 2 H, ArH), 6.76 (s, 1 H, =CH), 4.30 (br s, 2 H, CH_2), 3.64 (s, 2 H, CH_2), 1.81–1.74 (m, 2 H, CH_2), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.68, 162.95, 160.83, 160.51, 135.38, 132.96 (d, *J* = 4.0 Hz), 130.43 (d, *J* = 8.0 Hz), 118.64, 115.69, 115.47, 48.48, 32.66, 19.60, 11.19.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}FN_2OS^+$ (M + H)$^+$: 279.0962; found: 279.0966.

2-Thioxo-2,3-dihydropyrimidin-4(1*H*)-ones 9o–s; General Procedure

Anhyd MeOH (5 mL) and solid NaOMe (54 mg, 1 mmol) were added to thiourea **7** (1 mmol), and the mixture was heated to reflux for 13–17 h to form 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one **9**. After the reaction was completed (TLC monitoring), the solvent was evaporated, and the residue was purified by column chromatography (silica gel; PE/EtOAc 25:1 → 4:1) to give the desired 2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one **9**.

5-Benzyl-3-isopropyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9o)

White solid; yield: 221 mg (85%); mp 170–172 °C; R_f = 0.37 (PE/EtOAc 4:1).

IR (KBr): 3097, 3038, 1689, 1608, 1499, 1457, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.39 (s, 1 H, NH), 7.35–7.18 (m, 5 H, ArH), 6.60 (d, *J* = 4.4 Hz, 1 H, =CH), 5.93–5.83 (m, 1 H, CH), 3.64 (s, 2 H, CH_2), 1.54 (d, *J* = 6.8 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.20, 137.18, 134.79, 129.09, 128.81, 126.89, 33.02, 29.67, 18.50.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{17}N_2OS^+$ (M + H)$^+$: 261.1056; found: 261.1057.

5-Benzyl-3-cyclohexyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9p)

White solid; yield: 234 mg (78%); mp 160–162 °C; R_f = 0.35 (PE/EtOAc 4:1).

IR (KBr): 3094, 3038, 1688, 1611, 1500, 1459, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.69 (s, 1 H, NH), 7.32 (t, *J* = 7.2 Hz, 2 H, ArH), 7.28–7.23 (m, 1 H, ArH), 7.19 (d, *J* = 7.2 Hz, 2 H, ArH), 6.62 (d, *J* = 5.2 Hz, 1 H, =CH), 5.51–5.48 (m, 1 H, CH), 3.63 (s, 2 H, CH_2), 2.46 (d, *J* = 11.6 Hz, 2 H, CH_2), 1.84 (d, *J* = 12.8 Hz, 2 H, CH_2), 1.74–1.62 (m, 3 H, CH_2), 1.39–1.24 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.69, 161.31, 137.28, 134.74, 129.03, 128.78, 126.85, 120.28, 100.28, 63.14, 33.11, 29.66, 27.60, 26.26, 25.17.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{21}N_2OS^+$ (M + H)$^+$: 301.1369; found: 301.1368.

5-(3-Chlorobenzyl)-3-isopropyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9q)

White solid; yield: 259 mg (88%); mp 174–176 °C; R_f = 0.38 (PE/EtOAc 4:1).

IR (KBr): 3097, 3041, 1683, 1608, 1501, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.75 (s, 1 H, NH), 7.29–7.16 (m, 3 H, ArH), 7.10 (d, *J* = 6.4 Hz, 1 H, NH), 6.70 (d, *J* = 5.2 Hz, 1 H, =CH), 5.89–5.85 (m, 1 H, CH), 3.62 (s, 2 H, CH_2), 1.53 (d, *J* = 7.2 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.59, 161.05, 139.41, 135.00, 134.50, 130.00, 128.98, 127.16, 127.09, 119.22, 109.97, 32.75, 29.65, 18.47.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}ClN_2OS^+$ (M + H)$^+$: 295.0666; found: 295.0666.

5-(3-Chlorobenzyl)-3-cyclohexyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9r)

White solid; yield: 271 mg (81%); mp 156–158 °C; R_f = 0.30 (PE/EtOAc 4:1).

IR (KBr): 3097, 3041, 1687, 1605, 1499, 1459, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.79 (s, 1 H, NH), 7.28–7.16 (m, 3 H, ArH), 7.10 (d, *J* = 6.4 Hz, 1 H, ArH), 6.71 (d, *J* = 5.2 Hz, 1 H, =CH), 5.54–5.47 (m, 1 H, CH), 3.61 (s, 2 H, CH_2), 2.42 (d, *J* = 10.0 Hz, 2 H, CH_2), 1.86–1.65 (m, 5 H, CH_2), 1.41–1.28 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.89, 161.15, 139.49, 134.91, 134.50, 129.99, 128.96, 127.14, 127.08, 119.31, 109.98, 63.19, 32.85, 29.66, 27.59, 26.25, 25.15.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{20}ClN_2OS^+$ (M + H)$^+$: 335.0979; found: 335.0979.

5-(3-Bromobenzyl)-3-isopropyl-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one (9s)

White solid; yield: 281 mg (83%); mp 171–172 °C; R_f = 0.40 (PE/EtOAc 4:1).

IR (KBr): 3097, 3038, 1689, 1608, 1459, 1608, 1499, 1459, 1033 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.78 (s, 1 H, NH), 7.42–7.30 (m, 2 H, ArH), 7.23–7.11 (m, 2 H, ArH), 6.70 (s, 1 H, =CH), 5.89–5.85 (m, 1 H, CH), 3.61 (s, 2 H, CH_2), 1.53 (d, *J* = 6.8 Hz, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.58, 161.05, 139.72, 135.04, 131.86, 130.28, 130.00, 127.63, 122.73, 119.19, 54.79, 32.72, 18.48.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}BrN_2OS^+$ (M + H)$^+$: 339.0161; found: 339.0162.

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Supporting Information

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