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Efficient synthesis of *S*-dipeptidothiouracil derivatives *via* a one-pot, five-component reaction under ionic liquid condition

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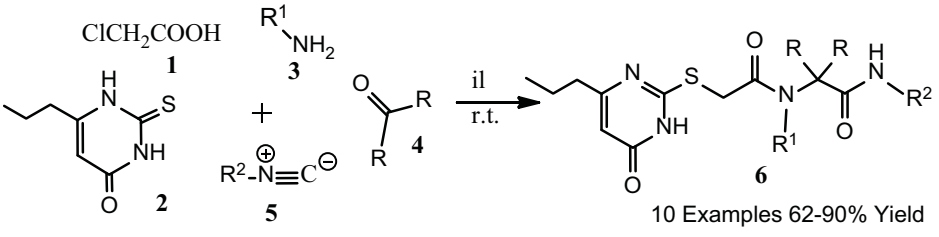
S-Dipeptidothiouracil derivatives were successfully synthesized *via* a one-pot, five-component nucleophilic addition/Ugi reaction sequence under ionic liquid conditions at room temperature. Simplicity, green condition, and high yields of products are advantages of this method.



Keywords: thiouracil; one-pot; nucleophilic addition; Ugi reaction; five-component reaction; ionic liquid

1. Introduction

Two very important classes of natural products, pyrimidine bases and pseudopeptides, play important roles in various biological systems. Thio derivatives of pyrimidine bases including 2-thiouracil, 4-propyl-2-thiouracil, and 2-thiocytosine are minor components of t-RNA and furthermore, they have contributed remarkably to biological, pharmacological and medicinal chemistry. Their *S*-, *N*-, or *S*,*N*-disubstituted analogs have shown therapeutic properties, especially antiviral, antithyroid, and antitumor activities. They have also been reported as biosensors and radio protectors. The prototropic tautomerism of thio derivatives of pyrimidine bases has attracted much attention. The tautomeric equilibrium of 2-thiouracil determines its chemoselectivity and regioselectivity, and is dependent on the temperature and on whether it is in the solution or in the solid state (*1–3*).

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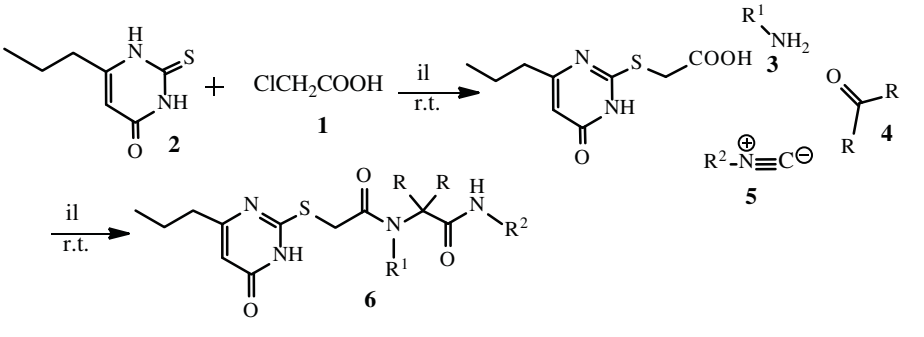
In this field, multicomponent condensation reactions based on isocyanides have been utilized efficiently in conjunction with combinatorial chemistry to prepare polyfunctional compounds in short reaction sequences (*4*, *5*). One of the best-known multicomponent reactions is the Ugi four-component reaction (4CR) which occurs in good yields (*6*). In this reaction, an isocyanide, an amine, a carboxylic acid, and an oxo compound are spontaneously condensed to yield an acylaminocarboxamide. Generally, the Ugi 4CRs were performed in organic solvents such as methanol or tetrahydrofuran at room temperature for 1–2 days (*7*). Recently, new solvents not previously utilized such as water (*8*) or ionic liquids (*9*) have been used for these reactions.

Room-temperature ionic liquids (RTILs), especially those based on 1,3-dialkylimidazolium salts, have shown great promise as attractive alternatives to the conventional solvents. They possess the unique advantages of high thermal stability, negligible vapor pressure, immiscibility with both organic compounds and water, and recyclability (*10–12*).

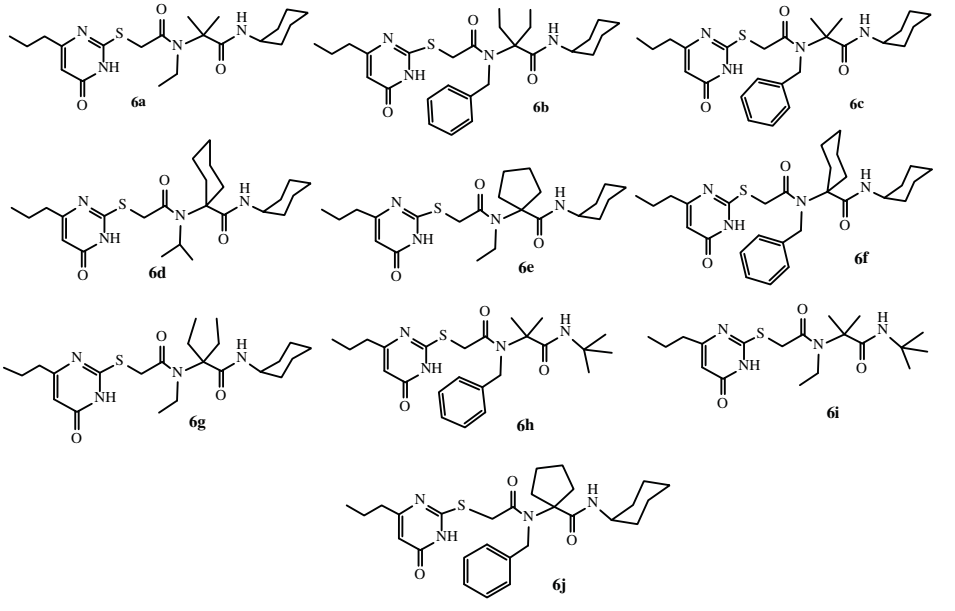
2. Results and discussion

As part of our current study on the development of new routes to the synthesis of organosulfur compounds (*13–15*), we report here an efficient and convenient procedure for the synthesis of thiouracil derivatives under ionic liquid conditions at room temperature. Thus a one-pot, five-component reaction consisting of chloroacetic acid (**1**), 4-propyl-2-thiouracil (**2**), primary amines (**3**), oxo compound (**4**), and isocyanides (**5**) leads to the pseudopeptidothiouracil derivatives as shown in Scheme 1. The connection of a dipeptide moiety to the thiouracil derivatives in **6a**–**6j** (Scheme 2) is an interesting structural feature that might increase pharmacological and biological activities of these compounds.

The structures of compounds **6a**–**6j** were verified by IR, ^{1}H NMR, and ^{13}C NMR spectral data. The mass spectra of compounds **6a**–**6j** displayed molecular ion peaks at appropriate m/z-values. The IR and ^{1}H NMR spectra of **6a**–**6j** exhibited two characteristic peaks for the NH groups. The proton-decoupled ^{13}C NMR spectra of **6a**–**6j** showed three distinct resonances for C=O groups. For example, the ^{1}H NMR spectrum of **6c** in $CDCl_3$ showed a doublet ($\delta = 5.70$ ppm) and a singlet ($\delta = 8.52$ ppm) for the NH groups. The methyl protons in **6c** appeared as a triplet ($\delta = 0.93$ ppm) and a singlet ($\delta = 1.49$ ppm). The methylene protons of *n*-propyl group in **6c** appeared as a multiplet ($\delta = 1.54$–1.63 ppm) and a triplet ($\delta = 2.39$ ppm), and the protons of SCH_2 and NCH_2 moieties exhibited two singlets at $\delta = 3.95$ and 4.82 ppm, respectively. The vinyl proton on the thiouracil ring appeared as a singlet at $\delta = 5.99$ ppm and characteristic signals for the cyclohexyl and phenyl groups were also observed. The ^{1}H-decoupled ^{13}C NMR spectrum of **6c** showed 21 signals which is in agreement with the proposed structure including three distinct



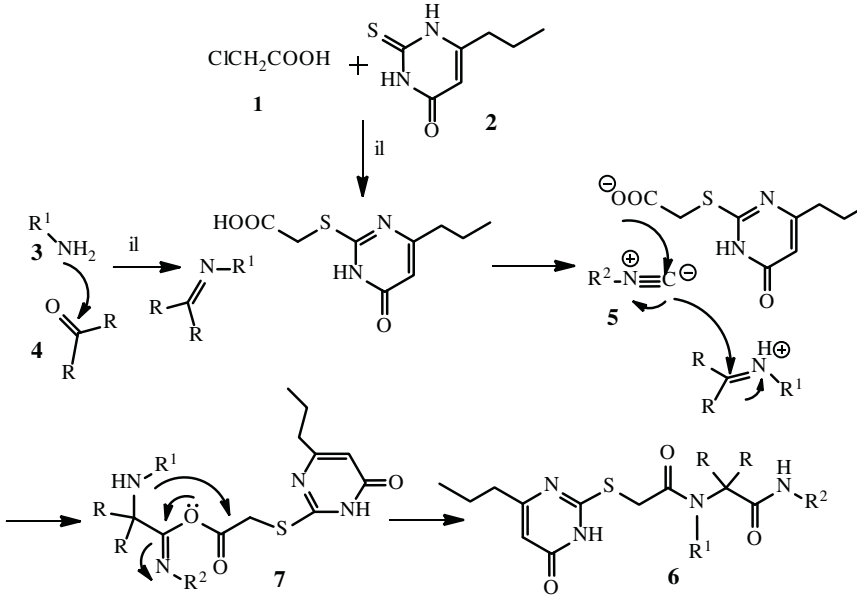
Scheme 1. Synthesis of *S*-thiouracil derivatives *via* a five-component reaction.



Scheme 2. Chemical structures of *S*-thiouracil derivatives **6a–6j**.

resonances for the C=O groups. Partial assignments of aromatic and cyclohexyl resonances are given in Section 4. The mass spectrum of **6c** displayed the molecular ion peak at $m/z = 484$.

The advantage of the present procedure is that all five starting materials were mixed in a one-pot reaction without any catalyst and without the need for separation of intermediates. A tentative mechanism for this transformation is proposed in Scheme 3. Presumably, the reaction proceeds step by step to generate the intermediate **7**, which would then undergo acyl transfer reaction (the Mumm rearrangment) to produce final products.



Scheme 3. Proposed mechanism for the formation of compounds **6**.

3. Conclusions

In conclusion, we have described an efficient method for the synthesis of *S*-dipeptidothiouracil derivatives in high yields, *via* a one-pot, five-component reaction using an ionic liquid as a new solvent. Reaction times were dramatically reduced, and yields were generally improved by this new method. The reaction scope is broad, which permits the use of three points of diversity in the starting materials. Due to the well-recognized utility of thiouracil derivatives, many libraries of compounds can be prepared using this method as structural scaffolds for further diversification.

4. Experimental

4.1. *General*

Chloroacetic acid, 4-propylthiouracil, amines, alkylisocyanides, and ketones were obtained from Merck and were used without further purification. [bmim]Br was synthesized from the reaction of *N*-methylimidazole and *n*-butyl bromide (*16*). Melting points were obtained uncorrected using an Electrothermal-9100 apparatus. IR spectra were recorded with a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX-300 Avance instrument using $CDCl_3$ as the deuterated solvent containing tetramethylsilane as internal standard, at 300 and 75 MHz, respectively, in parts per million, and J in hertz. Electron impact ionization-mass spectroscopy (EI-MS) (70 eV): mass spectra were obtained with a Finnigan-MAT-8430 mass spectrometer (in m/z). Elemental analyses (C, H, N) were obtained with a Heraeus CHN-O-Rapid analyzer.

4.2. *General procedure for the synthesis of thiouracil derivatives 6a–6j*

4-Propyl thiouracil (**2**) (1 mmol) was added to chloroacetic acid (**1**) (1 mmol) in 1 ml of [bmim]Br and the mixture was stirred at room temperature for 0.5 h. Then, primary amine **3** (1 mmol) and oxo compound **4** (1.2 mmol) were added and stirred for 15 min, and is followed by addition of isocyanide **5** (1 mmol). The reaction was detected by TLC (*n*-hexane–EtOAc, 3/1) and was completed after 5 h. The residue was dissolved in diluted $NaHCO_3$ (30 ml) and the mixture was extracted with AcOEt (2 × 15 ml) and was dried on Na_2SO_4. The solvent was evaporated under reduced pressure to leave a residue that was dried by column chromatography [silica gel (230–400 mesh; Merck), hexane/AcOEt, 3:1] to afford desired pure products **6a**–**6j**.

4.2.1. *N-Cyclohexyl-2-(N-ethyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-2-methyl propanamide (**6a**)*

White powder, m.p. 89–90 °C; yield: 0.35 g (83%). IR (KBr): 3342, 3321, 1646, 1576, 1570 cm^{-1}. ^{1}H NMR: $\delta = 0.95$ (3H, t, $^3J = 7.3$ Hz, Me), 1.01–1.90 (10H, m, 5CH_2), 1.34 (3H, t, $^3J = 7.0$ Hz, Me), 1.50 (6H, s, 2Me), 1.62–1.70 (2H, m, CH_2), 2.49 (2H, t, $^3J = 7.3$ Hz, CH_2), 3.61–3.76 (1H, m, CH), 3.65 (2H, q, $^3J = 7.0$ Hz, CH_2), 4.10 (2H, s, SCH_2), 5.58 (1H, d, $^3J = 8.0$ Hz, NH), 6.02 (1H, s, CH), 7.10 (1H, br s, NH). ^{13}C NMR: $\delta = 13.8$ (Me), 16.7 (Me), 21.4 (CH_2), 24.6 (CH_2), 24.9 (2 Me), 25.4 (2CH_2), 32.6 (2CH_2), 33.6 (CH_2), 39.3 (CH_2), 39.6 (CH), 48.3 (CH_2), 62.6 (C), 107.1 (C), 155.0 (CH), 160.0 (C), 162.6 (C=O), 169.6 (C=O), 173.9 (C=O). EI-MS: m/z (%) = 422 (M^+, 2.5), 211 (28), 169 (15), 125 (21), 97 (45), 57 (33), 43 (27), 29 (18). Anal. Calcd for $C_{21}H_{34}N_4O_3S$ (422.58): C, 59.69; H, 8.11; N, 13.26; Found: C, 59.95; H, 8.58; N, 13.11%.

4.2.2. *N-Benzyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido-N-cyclohexyl-2-ethylbutanamide (**6b**)*

White powder, m.p. 77–80 °C; yield: 0.40 g (78%). IR (KBr): 3286, 3064, 1677, 1665, 1570 cm^{-1}. ^1H NMR: $\delta = 0.90$ (6H, t, $^3J = 7.1$ Hz, 2Me), 0.98 (3H, t, $^3J = 7.3$ Hz, Me), 1.10–2.02 (16H, m, $8CH_2$), 2.64 (2H, t, $^3J = 7.3$ Hz, CH_2), 3.72–3.92 (1H, m, CH), 4.75 (2H, s, SCH_2), 4.86 (2H, s, NCH_2), 5.79 (1H, d, $^3J = 7.7$ Hz, NH), 6.18 (1H, s, CH), 7.28 (1H, t, $^3J = 7.1$ Hz, CH), 7.41 (2H, t, $^3J = 7.1$ Hz, 2CH), 7.76 (2H, d, $^3J = 7.1$ Hz, 2CH), 8.31 (1H, br s, NH). ^{13}C NMR: $\delta = 13.6$ (Me), 13.7 (2Me), 21.1 (CH_2), 24.7 (CH_2), 24.9 ($2CH_2$), 25.4 ($2CH_2$), 33.1 ($2CH_2$), 33.9 (CH_2), 39.1 (CH), 48.6 (CH_2), 49.8 (CH_2), 65.0 (C), 107.8 (C), 127.5 (C), 127.6 (2CH), 128.7 (CH), 129.2 (2CH), 137.7 (CH), 160.9 (C), 168.8 (C=O), 168.9 (C=O), 170.4 (C=O). EI-MS: m/z (%) = 512 (M^+, 1.5), 483 (21), 211 (29), 125 (18), 97 (38), 91 (100), 57 (40), 29 (33). Anal. Calcd for $C_{28}H_{40}N_4O_3S$ (512.71): C, 65.59; H, 7.86; N, 10.93; Found: C, 65.89; H, 8.08; N, 11.17%.

4.2.3. *2-(N-Benzyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-N-cyclohexyl-2-methyl propanamide (**6c**)*

White powder, m.p. 98–100 °C; yield: 0.43 g (89%). IR (KBr): 3546, 3339, 1697, 1658, 1589 cm^{-1}. ^1H NMR: $\delta = 0.93$ (3H, t, $^3J = 7.2$ Hz, Me), 1.00–1.95 (10H, m, $5CH_2$), 1.49 (6H, s, 2Me), 1.54–1.63 (2H, m, CH_2), 2.39 (2H, t, $^3J = 7.2$ Hz, CH_2), 3.68–3.85 (1H, m, CH), 3.95 (2H, s, SCH_2), 4.82 (2H, s, NCH_2), 5.70 (1H, d, $^3J = 7.7$ Hz, NH), 5.99 (1H, s, CH), 7.31 (1H, t, $^3J = 7.2$ Hz, CH), 7.41 (2H, t, $^3J = 7.2$ Hz, 2CH), 7.53 (2H, d, $^3J = 7.2$ Hz, 2CH), 8.52 (1H, br s, NH). ^{13}C NMR: $\delta = 14.1$ (Me), 21.4 (CH_2), 24.8 (CH_2), 25.4 (2Me), 25.9 ($2CH_2$), 33.3 ($2CH_2$), 34.6 (CH_2), 39.9 (CH), 48.5 (CH_2), 49.0 (NCH_2), 63.6 (C), 108.5 (C), 126.4 (2CH), 127.5 (C), 127.9 (CH), 129.5 (2CH), 138.3 (CH), 160.3 (CH), 168.9 (C=O), 169.6 (C=O), 173.9 (C=O). EI-MS: m/z (%) = 484 (M^+, 1.5), 211 (30), 169 (21), 125 (24), 97 (39), 91 (100), 57 (45), 43 (18). Anal. Calcd for $C_{26}H_{36}N_4O_3S$ (484.65): C, 64.43; H, 7.49; N, 11.56; Found: C, 64.86; H, 7.58; N, 11.07%.

4.2.4. *N-Cyclohexyl-1-(N-isopropyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)cyclohexanecarboxamide (**6d**)*

White powder, m.p. 93–96 °C; yield: 0.29 g (62%). IR (KBr): 3416, 3150, 1712, 1702, 1659 cm^{-1}. ^1H NMR: $\delta = 0.99$ (3H, t, $^3J = 7.3$ Hz, Me), 0.87–1.80 (20H, m, $10CH_2$), 1.15 (6H, d, $^3J = 6.5$ Hz, 2Me), 1.67–1.75 (2H, m, CH_2), 2.51 (2H, t, $^3J = 7.3$ Hz, CH_2), 3.75 (2H, s, SCH_2), 3.95–4.11 (2H, m, 2CH), 5.87 (1H, d, $^3J = 8.0$ Hz, NH), 6.11 (1H, s, CH), 7.45 (1H, br s, NH). ^{13}C NMR: $\delta = 13.8$ (Me), 19.8 (CH_2), 20.0 ($2CH_2$), 21.0 (2Me), 24.7 (CH_2), 24.9 ($2CH_2$), 26.5 (CH_2), 27.6 ($2CH_2$), 30.9 (CH_2), 31.5 ($2CH_2$), 33.8 (CH), 42.2 (CH), 47.7 (CH_2), 54.5 (C), 108.8 (C), 155.0 (CH), 160.7 (C), 167.7 (C=O), 169.3 (C=O), 172.7 (C=O). EI-MS: m/z (%) = 476 (M^+, 4), 433 (15), 211 (100), 209 (21), 125 (28), 97 (36), 57 (41), 43 (52). Anal. Calcd for $C_{25}H_{40}N_4O_3S$ (476.68): C, 62.99; H, 8.46; N, 11.75; Found: C, 63.12; H, 8.78; N, 11.23%.

4.2.5. *N-Cyclohexyl-1-(N-ethyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)cyclopentane carboxamide (**6e**)*

White powder, m.p. 96–98 °C; yield: 0.32 g (71%). IR (KBr): 3454, 3340, 1677, 1666, 1656 cm^{-1}. ^1H NMR: $\delta = 0.98$ (3H, t, $^3J = 7.7$ Hz, Me), 1.10–1.94 (20H, m, $10CH_2$), 1.32 (3H, t, $^3J = 7.0$ Hz, Me), 2.73 (2H, t, $^3J = 7.7$ Hz, CH_2), 3.61 (2H, q, $^3J = 7.0$ Hz, CH_2), 3.86–3.90 (1H, m,

CH), 4.09 (2H, s, SCH_2), 5.87 (1H, d, $^3J = 7.5$ Hz, NH), 6.16 (1H, s, CH), 7.76 (1H, br s, NH). ^{13}C NMR: $\delta = 13.7$ (Me), 16.3 (Me), 21.1 (CH_2), 23.0 ($2CH_2$), 24.7 (CH_2), 25.4 ($2CH_2$), 25.5 ($2CH_2$), 32.6 ($2CH_2$), 33.0 (CH_2), 39.1 (CH_2), 39.9 (C), 48.3 (CH_2), 65.9 (C), 108.1 (C), 159.9 (CH), 160.5 (C), 170.4 (C=O), 170.5 (C=O), 172.5 (C=O). EI-MS: m/z (%) = 448 (M^+, 2), 419 (19), 211 (100), 195 (16), 125 (28), 97 (41), 57 (37), 29 (24). Anal. Calcd for $C_{23}H_{36}N_4O_3S$ (448.62): C, 61.58; H, 8.09; N, 12.49; Found: C, 61.75; H, 8.78; N, 12.27%.

4.2.6. *1-(N-Benzyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-N-cyclohexylcyclohexanecarboxamide (**6f**)*

White powder, m.p. 73–74 °C; yield: 0.44 g (85%). IR (KBr): 3285, 3064, 1686, 1667, 1590 cm^{-1}. ^{1}H NMR: $\delta = 0.934$ (3H, t, $^3J = 7.0$ Hz, Me), 1.38–1.88 (22H, m, $11CH_2$), 2.42 (2H, t, $^3J = 7.0$ Hz, CH_2), 3.68–3.87 (1H, m, CH), 3.99 (2H, s, SCH_2), 4.84 (2H, s, NCH_2), 6.02 (1H, s, CH), 6.42 (1 H, d, $^3J = 7.7$ Hz, NH), 7.28 (1H, t, $^3J = 7.5$ Hz, CH), 7.30 (2H, t, $^3J = 7.5$ Hz, 2CH), 7.39 (2H, d, $^3J = 7.5$ Hz, 2CH), 8.31 (1H, br s, NH). ^{13}C NMR: $\delta = 14.0$ (Me), 21.5 (CH_2), 23.4 (CH_2), 25.2 (CH_2), 25.7 ($2CH_2$), 25.9 ($2CH_2$), 30.1 ($2CH_2$), 33.2 ($2CH_2$), 33.3 (CH_2), 39.1 (CH), 48.9 (CH_2), 49.1 (CH_2), 67.5 (C), 107.8 (C), 126.4 (2CH), 127.9 (C), 129.4 (2CH), 129.9 (CH), 148.4 (CH), 168.5 (C=O), 169.0 (C), 170.5 (C=O), 172.0 (C=O). EI-MS: m/z (%) = 524 (M^+, 1), 211 (20), 209 (12), 125 (18), 97 (43), 91 (100), 57 (42), 43 (24). Anal. Calcd for $C_{29}H_{40}N_4O_3S$ (524.72): C, 66.38; H, 7.68; N, 10.68; Found: C, 66.48; H, 7.88; N, 10.17%.

4.2.7. *N-Cyclohexyl-2-ethyl-2-(N-ethyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)butanamide (**6g**)*

White powder, m.p. 81–84 °C; yield: 0.35 g (77%). IR (KBr): 3316, 3210, 1686, 1643, 1590 cm^{-1}. ^{1}H NMR: $\delta = 0.84$ (6H, t, $^3J = 7.2$ Hz, 2Me), 0.96 (3H, t, $^3J = 7.6$ Hz, Me), 1.05–2.10 (16H, m, $8CH_2$), 1.42 (3H, t, $^3J = 7.1$ Hz, Me), 2.44 (2H, t, $^3J = 7.6$ Hz, CH_2), 3.55 (2H, q, $^3J = 7.1$ Hz, NCH_2), 3.74–3.81 (1H, m, CH), 4.09 (2H, s, SCH_2), 5.68 (1H, d, $^3J = 8.0$ Hz, NH), 6.02 (1H, s, CH), 7.79 (1H, br s, NH). ^{13}C NMR: $\delta = 8.4$ (2Me), 13.7 (Me), 17.2 (Me), 21.1 (CH_2), 23.4 (CH_2), 24.9 (2 CH_2), 25.6 ($2CH_2$), 32.9 ($2CH_2$), 34.4 (CH_2), 39.1 (CH_2), 39.9 (C), 48.6 (CH_2), 65.9 (C), 108.1 (C), 160.1 (CH), 164.2 (C), 170.4 (C=O), 170.5 (C=O), 172.3 (C=O). EI-MS: m/z (%) = 450 (M^+, 3.5), 421 (32), 211 (100), 197 (18), 125 (21), 97 (28), 57 (40), 29 (26). Anal. Calcd for $C_{23}H_{38}N_4O_3S$ (450.6): C, 61.30; H, 8.50; N, 12.43; Found: C, 61.89; H, 8.78; N, 12.23%.

4.2.8. *2-(N-Benzyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-N-(tert-butyl)-2-methylpropanamide (**6h**)*

White powder, m.p. 75–76 °C; yield: 0.41 g (90%). IR (KBr): 3417, 3031, 1689, 1660, 1610 cm^{-1}. ^{1}H NMR: $\delta = 0.91$ (3H, t, $^3J = 7.3$ Hz, Me), 1.32 (9H, s, CMe_3), 1.46 (6H, s, 2Me), 1.53–1.61 (2H, m, CH_2), 2.39 (2H, t, $^3J = 7.3$ Hz, CH_2), 4.02 (2H, s, SCH_2), 4.81 (2H, s, NCH_2), 5.65 (1H, s, NH), 5.99 (1H, s, CH), 7.29 (1H, t, $^3J = 7.1$ Hz, CH), 7.39 (2H, t, $^3J = 7.1$ Hz, 2CH), 7.46 (2H, d, $^3J = 7.1$ Hz, 2CH), 8.01 (1H, br s, NH). ^{13}C NMR: $\delta = 14.0$ (Me), 21.4 (CH_2), 24.9 (2Me), 28.9 (CMe_3), 31.3 (CH_2), 39.4 (C), 48.7 (CH_2), 51.6 (NCH_2), 64.1 (C), 108.1 (C), 126.4 (2CH), 127.6 (C), 127.9 (CH), 129.5 (2CH), 138.4 (CH), 165.3 (C), 168.4 (C=O), 169.3 (C=O), 173.9 (C=O). EI-MS: m/z (%) = 458 (M^+, 1.6), 401 (18), 211 (27), 143 (23), 99 (22), 91 (100), 57 (61). Anal. Calcd for $C_{24}H_{34}N_4O_3S$ (458.62): C, 62.85; H, 7.47; N, 12.22; Found: C, 63.15; H, 7.78; N, 12.36%.

4.2.9. *N-(tert-Butyl)-2-(N-ethyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-2-methylpropanamide (**6i**)*

White powder, m.p. 79–81 °C; yield: 0.31 g (79%). IR (KBr): 3459, 3346, 1739, 1690, 1653 cm^{-1}. ^1H NMR: $\delta = 0.94$ (3H, t, $^3J = 7.3$ Hz, Me), 1.20 (9H, s, CMe_3), 1.27 (3H, t, $^3J = 7.2$ Hz, Me), 1.49 (6H, s, 2Me), 1.63–1.65 (2H, m, CH_2), 2.41 (2H, t, $^3J = 7.3$ Hz, CH_2), 3.58 (2H, q, $^3J = 7.2$ Hz, NCH_2), 3.99 (2H, s, SCH_2), 5.58 (1H, s, NH), 5.98 (1H, s, CH), 8.10 (1H, br s, NH). ^{13}C NMR: $\delta = 14.2$ (Me), 16.8 (Me), 21.1 (CH_2), 24.6 (2Me), 28.6 (CMe_3), 29.7 (CH_2), 33.5 (CH_2), 39.9 (C), 50.9 (CH_2), 63.0 (C), 107.4 (C), 154.0 (CH), 169.2 (C), 170.4 (C=O), 170.5 (C=O), 173.8 (C=O). EI-MS: m/z (%) = 396 (M^+, 4), 367 (21), 211 (100), 143 (17), 99 (28), 57 (75), 29 (10). Anal. Calcd for $C_{19}H_{32}N_4O_3S$ (396.55): C, 57.55; H, 8.13; N, 14.13; Found: C, 57.50; H, 8.48; N, 13.96%.

4.2.10. *1-(N-Benzyl-2-((6-oxo-4-propyl-1,6-dihydropyrimidin-2-yl)thio)acetamido)-N-cyclohexylcyclopentanecarboxamide (**6j**)*

White powder, m.p. 87–88 °C; yield: 0.34 g (67%). IR (KBr): 3325, 3098, 1685, 1660, 1640 cm^{-1} ^1H NMR: $\delta = 0.91$ (3H, t, $^3J = 7.5$ Hz, Me), 0.89–1.92 (20H, m, $10CH_2$), 2.39 (2H, t, $^3J = 7.5$ Hz, CH_2), 3.65–3.70 (1H, m, CH), 3.96 (2H, s, SCH_2), 4.83 (2H, s, NCH_2), 5.68 (1H, d, $^3J = 8.0$ Hz, NH), 6.01 (1H, s, CH), 7.32 (1H, t, $^3J = 7.2$ Hz, CH), 7.41 (2H, t, $^3J = 7.2$ Hz, 2CH), 7.49 (2H, d, $^3J = 7.2$ Hz, 2CH), 7.82 (1H, br s, NH). ^{13}C NMR: $\delta = 14.1$ (Me), 21.1 (CH_2), 22.7 ($2CH_2$), 24.3 (CH_2), 24.9 ($2CH_2$), 25.5 ($2CH_2$), 31.8 ($2CH_2$), 32.8 (CH_2), 39.4 (CH), 48.2 (CH_2), 48.9 (CH_2), 63.2 (C), 108.0 (C), 126.1 (2CH), 127.5 (C), 127.6 (CH), 129.1 (2CH), 135.3 (CH), 166.0 (C), 168.3 (C=O), 169.3 (C=O), 173.7 (C=O). EI-MS: m/z (%) = 510 (M^+, 1.7), 211 (29), 195 (18), 97 (21), 91 (100), 57 (33), 43 (13). Anal. Calcd for $C_{28}H_{38}N_4O_3S$ (510.69): C, 65.85; H, 7.50; N, 10.97; Found: C, 66.18; H, 7.68; N, 11.17%.

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