Supplementary data

Synthesis of 4,6-Unsubstituted 2-Aminodihydropyrimidine-5-Carboxylates via Sequential Staudinger/Aza-Wittig/Cyclization Reactions

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General
All melting points were determined with an AS ONE melting point apparatus ATM-02 without correction. IR spectra were measured on a JASCO FT/IR-6100. 1H NMR spectra were recorded on a Bruker AVANCE™ III 600 (600 MHz) with tetramethyldisilane (0 ppm), dimethylsulfoxide (2.49 ppm), or methanol (3.30 ppm) as an internal standard. 13C NMR spectra were recorded on a Bruker AVANCE™ III 600 (150 MHz) with chloroform (77.0 ppm), or methanol (49.0 ppm) as an internal standard. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI) method on a SHIMADZU LCMS-IT-TOF mass analyzer. Column chromatography was performed on silica gel 60 (nacalai tesque, 70–230 mesh) using the indicated solvents. TLC was performed using precoated silica gel 60 F254 plates (Merck KGaA) using the indicated solvents.

Preparation of ethyl 3-azido-2-[(tert-butoxycarbonyl)amino]methyl]acrylate 7 via 14, 15, and 16

![Chemical reaction diagram]

Ethyl 3-azido-2-hydroxypropanoate 14
To a solution of ethyl bromopyruvate 13 (4.50 g, 23.1 mmol) in MeOH (70 mL) was added NaBH₃CN (1.45 g, 23.1 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 1 h. EtOAc (200 mL), water (50 mL), and brine (50 mL) were added, and the organic layer was separated. The organic materials were extracted with EtOAc (80 mL x 3), and combined organic layers were washed with water (30 mL), brine (30 mL), and dried over anhydrous MgSO₄, and concentrated under reduced pressure to give a reduced alcohol, ethyl 3-bromo-2-hydroxypropanoate (4.26 g). To the crude product in EtOH-H₂O (1:1, total 100 mL) was added NaN₃ (3.00 g, 46.1 mmol) at room temperature (rt), and the reaction mixture was heated at 75 °C for 18 h. EtOAc (100 mL) and brine (30 mL) were added to the mixture, and
the organic layer was separated. The organic materials were extracted with EtOAc (80 mL x 2), and combined organic layers were washed with water (30 mL), brine (30 mL), and dried over anhydrous MgSO₄, and concentrated under reduced pressure to give a crude ethyl 3-azido-2-hydroxypropanoate 14 (2.27 g). ¹H NMR (CDCl₃) δ 1.33 (3H, t, J = 7.2 Hz), 3.15 (1H, d, J = 5.4 Hz), 3.51 (1H, dd, J = 13.2, 4.2 Hz), 3.65 (1H, dd, J = 13.2, 3.6 Hz), 4.30 (1H, dq, J = 10.8, 7.2 Hz), 4.32 (1H, dq, J = 10.8, 7.2 Hz), 4.36 (1H, ddd, J = 5.4, 4.2, 3.6 Hz); ¹³C NMR (CDCl₃) δ 14.8, 53.8, 62.4, 70.4, 172.2. The crude product 14 was used for the next reaction without further purification.

![Chemical structure of 14 and 15](image.png)

**Ethyl 3-[(tert-butoxycarbonyl)amino]-2-hydroxypropanoate 15**

Under a hydrogen atmosphere, a mixture of the crude azide 14 (2.27 g), di-tert-butyl dicarbonate (4.10 g, 18.8 mmol), and 10% Pd-C (0.910 g) in EtOAc (50 mL) was stirred at rt for 62 h. The reaction mixture was filtrated over celite, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography [n-hexane-EtOAc (3:1)] to give the title compound 15 (2.18 g, 9.33 mmol, 41% in three steps from 13) as a colorless oil. IR (neat) cm⁻¹: 3381, 2979, 1720, 1519, 1251, 1171; ¹H NMR (CDCl₃) δ 1.31 (3H, t, J = 7.2 Hz), 1.43 (9H, s), 3.23 (1H, q, J = 4.2 Hz), 3.42–3.57 (2H, m), 4.21–4.31 (3H, m), 4.91 (1H, s); ¹³C NMR (CDCl₃) δ 14.1, 28.2, 43.9, 62.0, 70.3, 79.7, 156.1, 173.1; HRMS-ESI (m/z): [M+Na]⁺ calcd for C₁₀H₁₉NO₃Na, 256.1155; found, 256.1155.

![Chemical structure of 15 and 16](image.png)

**Ethyl 2-[(tert-butoxycarbonyl)amino][methyl]-3-chloroacrylate 16**

To a solution of 15 (0.700 g, 3.00 mmol) in CH₂Cl₂ (25 mL) was added Dess-Martin periodinane (1.53 g, 3.61 mmol) at rt, and the reaction mixture was stirred at rt for 30 min. Et₂O (20 mL) and a solution of Na₂S₂O₅ (6.30 g) in sat. NaHCO₃ aqueous solution (25 mL) were added, and the mixture was stirred at rt for 10 min to be a clear solution. The organic layer was separated, and the organic materials were extracted with Et₂O (15 mL). The combined organic layers were washed with sat. NaHCO₃ aqueous solution (10 mL), water (10 mL), and brine (10 mL), and dried over anhydrous MgSO₄, and concentrated under reduced pressure to give the oxidized product, ethyl 3-[(tert-butoxycarbonyl)amino]-2-oxopropanoate as a colorless oil. ¹H NMR (CDCl₃) δ 1.38 (3H, t, J = 7.2 Hz), 1.46 (9H, s), 4.36 (2H, q, J = 7.2 Hz), 4.49 (2H, d, J = 4.8 Hz), 5.10 (1H, s). The crude product was used for the next reaction without further purification. Under an argon atmosphere, to a suspension of chloromethyltriphenylphosphonium
chloride (2.08 g, 5.99 mmol) in anhydrous THF (20 mL) was added n-butyllithium (1.6 M in n-hexane, 2.80 mL, 4.48 mmol) dropwise at −75 °C. Then the reaction temperature was elevated to 0 °C and stirred at the temperature for 5 min, and cooled to −75 °C again. To the mixture was added a solution of the crude ethyl 3-[(tert-butoxycarbonyl)amino]-2-oxopropanoate in anhydrous THF (10 mL) at −75 °C, and the reaction mixture was stirred at 0 °C for 2 h. Et₂O (15 mL) and cold water (10 mL) were added, and the organic layer was separated. The organic materials were extracted with Et₂O (15 mL), and combined organic layers were washed with water (5 mL), brine (5 mL), and dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography [n-hexane-EtOAc (6:1)] to give the title compound 16 (584 mg, 2.22 mmol, 74% in two steps from 15) as a 1.4:1.0 mixture of E/Z isomers. The stereochemistry of each isomer was not determined. Colorless oil. Major isomer of 16: ¹H NMR (CDCl₃) δ 1.32 (3H, t, J = 7.2 Hz), 1.44 (9H, s), 4.13–4.21 (2H, brs), 4.25 (2H, q, J = 7.2 Hz), 5.02 (1H, s), 7.38 (1H, s). Minor isomer of 16: ¹H NMR (CDCl₃) δ 1.35 (3H, t, J = 7.2 Hz), 1.44 (9H, s), 3.93–3.98 (2H, brs), 4.30 (2H, q, J = 7.2 Hz), 4.95 (1H, s), 6.78 (1H, s).

![Diagram of chemical reaction]

**Ethyl 3-azido-2-{{[(tert-butoxycarbonyl)amino]methyl}acrylates (E)-7 and (Z)-7**

To a solution of 16 (1.78 g, 6.76 mmol) in DMF (34 mL) was added NaN₃ (1.32 g, 20.3 mmol), and the reaction mixture was stirred at rt for 3 h. Et₂O (40 mL) and water (20 mL) were added to the mixture, and the organic layer was separated. The organic materials were extracted with Et₂O (40 mL), and combined organic layers were washed with water (10 mL), brine (10 mL), and dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography [CH₂Cl₂-EtOAc (30:1 to 20:1)] to isolate each stereoisomer, (E)-7 (519 mg, 1.92 mmol, 28.4%) and (Z)-7 (660 mg, 2.44 mmol, 36.1%). (E)-7: pale yellow crystals; mp 62–63 °C (n-hexane); IR (KBr) cm⁻¹: 2979, 2119, 1708, 1628, 1504, 1247, 1170; ¹H NMR (CDCl₃) δ 1.31 (3H, t, J = 7.2 Hz), 1.44 (9H, s), 3.95 (2H, d, J = 5.4 Hz), 4.22 (2H, d, J = 7.2 Hz), 5.01 (1H, s), 7.52 (1H, s); ¹³C NMR (CDCl₃) δ: 14.2, 28.4, 35.1, 60.8, 79.3, 118.2, 140.0, 155.5, 166.0; HRMS-ESI (m/z): [M+Na]⁺ calcd for C₁₁H₁₈N₄O₄Na, 293.1220; found, 293.1215. (Z)-7: pale yellow crystals; mp 79–80 °C (n-hexane); IR (KBr) cm⁻¹: 3315, 2979, 2116, 1715, 1685, 1627, 1536, 1224, 1165; ¹H NMR (CDCl₃) δ 1.33 (3H, t, J = 7.2 Hz), 1.44 (9H, s), 3.83 (2H, d, J = 6.0 Hz), 4.25 (2H, d, J = 7.2 Hz), 5.00 (1H, s), 6.98 (1H, s); ¹³C NMR (CDCl₃) δ: 14.2, 28.4, 41.5, 60.8, 79.6, 116.5, 138.8, 155.6, 164.8; HRMS-ESI (m/z): [M+Na]⁺ calcd for C₁₁H₁₈N₄O₄Na, 293.1220; found, 293.1215. Exact structure assignment was made using NOE experiment: the significant NOE (1.3%) was observed between the methylene protons (δ 3.83) and 3-proton (δ 6.98) and as such, its structure was determined to (Z)-7.
General procedure for synthesis of 4,6-unsubstituted 2-aminodihydropyrimidines 11 by the sequential Staudinger/Aza-Wittig/cyclization reactions of (E)-7 with isocyanates 9 (Table 2 and Scheme 5)

![Chemical structure of 11a](image)

**1-tert-Butyl 5-ethyl 2-(phenylamino)pyrimidine-1,5(6H)-dicarboxylate 11a (entry 1)**

Under an argon atmosphere, to a solution of (E)-7 (27.0 mg, 0.100 mmol) in THF (1.5 mL) was added triphenylphosphine (31.5 mg, 0.120 mmol). After the reaction mixture was stirred at rt for 15 min, phenyl isocyanate 9a (54 μL, 0.499 mmol) was added, and the stirring was kept at the temperature for 3 h. To the reaction mixture was added EtOAc (20 mL) followed by saturated NaHCO₃ aqueous solution (5 mL), and the organic layer was separated. The aqueous layer was extracted with EtOAc (10 mL), and the combined organic layers were washed with brine (5 mL), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography [n-hexane-EtOAc-Et₃N (40:2:1)] to give 11a (26.8 mg, 0.0776 mmol, 78%) as pale yellow crystals. Mp 113–114 °C (n-hexane); IR (KBr) cm⁻¹: 2980, 1696, 1599, 1546, 1227, 1150; ¹H NMR (CDCl₃) δ 1.29 (3H, t, J = 7.2 Hz), 1.57 (9H, s), 4.21 (2H, q, J = 7.2 Hz), 4.50 (2H, d, J = 1.2 Hz), 7.11 (1H, t, J = 7.8 Hz), 7.33 (2H, t, J = 7.8 Hz), 7.50 (1H, t, J = 1.2 Hz), 7.56 (2H, d, J = 7.8 Hz), 10.30–10.60 (1H, brs); ¹³C NMR (CDCl₃) δ 14.3, 28.0, 42.8, 59.8, 84.8, 105.4, 122.1, 124.3, 128.7, 137.7, 145.2, 148.7, 154.0, 165.8; HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₅H₂₆N₅O₄, 346.1761; found, 346.1748.

![Chemical structure of 11b](image)

**1-tert-Butyl 5-ethyl 2-[(4-chlorophenyl)amino]pyrimidine-1,5(6H)-dicarboxylate 11b (entry 2)**

Flash silica gel column chromatography [n-hexane-EtOAc-Et₃N (40:4:1)] to give 11b (32.3 mg, 0.0850 mmol, 85%) as pale yellow crystals. Mp 121–122 °C (n-hexane); IR (KBr) cm⁻¹: 2981, 1706, 1605, 1546, 1308, 1219; ¹H NMR (CDCl₃) δ 1.29 (3H, t, J = 7.2 Hz), 1.57 (9H, s), 4.21 (2H, q, J = 7.2 Hz), 4.49 (2H, d, J = 1.2 Hz), 7.28 (2H, d, J = 9.0 Hz), 7.47 (1H, t, J = 1.2 Hz), 7.53 (2H, d, J = 9.0 Hz), 10.35–10.65 (1H, brs); ¹³C NMR (CDCl₃) δ 14.3, 28.0, 42.9, 59.9, 85.1, 105.8, 123.3, 128.8, 129.3, 136.5, 144.8, 148.6, 154.1, 165.7; HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₅H₂₆N₅O₄Cl, 380.1372; found, 380.1368.
1-**tert**-Butyl 5-ethyl 2-[(4-(ethoxycarbonyl)phenyl)amino]pyrimidine-1,5(6**H**)dicarboxylate 11c (entry 3)

Flash silica gel column chromatography [n-hexane-**EtOAc**-**Et**₂**N** (40:3:1)] to give 11c (38.4 mg, 0.0920 mmol, 92%) as pale yellow crystals. Mp 138–139 °C (n-hexane); IR (KBr) cm⁻¹: 2984, 1703, 1646, 1599, 1542, 1304, 1276, 1224; ¹H NMR (CDCl₃) δ 1.30 (3H, t, J = 7.2 Hz), 1.39 (3H, t, J = 7.2 Hz), 1.58 (9H, s), 4.22 (2H, q, J = 7.2 Hz), 4.36 (2H, q, J = 7.2 Hz), 4.50 (2H, d, J = 1.2 Hz), 7.50 (1H, t, J = 1.2 Hz), 7.69 (2H, d, J = 8.4 Hz), 8.00 (2H, d, J = 8.4 Hz), 10.65–10.85 (1H, brs); ¹³C NMR (CDCl₃) δ 14.3 (2C), 28.0, 42.9, 60.0, 60.7, 85.2, 106.6, 120.7, 125.6, 130.5, 142.2, 144.4, 148.0, 154.1, 165.6, 166.2; HRMS-ESI (m/z): [M+H]⁺ calcd for C₂₁H₂₈N₃O₆, 418.1973; found, 419.1975.

![Diagram of molecule 11c](image)

1-**tert**-Butyl 5-ethyl 2-[(4-(trifluoromethyl)phenyl)amino]pyrimidine-1,5(6**H**)dicarboxylate 11d (entry 4)

Flash silica gel column chromatography [n-hexane-**EtOAc**-**Et**₂**N** (40:2:1)] to give 11d (39.1 mg, 0.0946 mmol, 95%) as pale yellow crystals. Mp 135 °C (n-hexane); IR (neat) cm⁻¹: 1705, 1649, 1605, 1546, 1322, 1223, 1110, 1065; ¹H NMR (CDCl₃) δ 1.30 (3H, t, J = 7.2 Hz), 1.58 (9H, s), 4.22 (2H, q, J = 7.2 Hz), 4.51 (2H, d, J = 1.2 Hz), 7.48 (1H, s), 7.56 (2H, d, J = 8.4 Hz), 7.73 (2H, d, J = 8.4 Hz), 10.65–10.80 (1H, brs); ¹³C NMR (CDCl₃) δ 14.3, 28.0, 42.9, 60.1, 85.3, 106.6, 121.4, 124.2 (J = 270 Hz), 125.7 (J = 33 Hz), 126.0 (J = 3.0 Hz), 141.2, 144.4, 148.2, 154.1, 165.6; HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₉H₂₅N₃O₂F₃, 414.1635; found, 414.1635.

![Diagram of molecule 11d](image)

1-**tert**-Butyl 5-ethyl 2-[(4-methoxyphenyl)amino]pyrimidine-1,5(6**H**)dicarboxylate 11e (entry 5)

Flash silica gel column chromatography [n-hexane-**EtOAc**-**Et**₂**N** (40:2:1)] to give 11e (24.3 mg, 0.0647 mmol, 65%) as a pale yellow oil. IR (neat) cm⁻¹: 2979, 1697, 1548, 1509, 1246, 1227, 1150; ¹H NMR (CDCl₃) δ 1.28 (3H, t, J = 7.2 Hz), 1.57 (9H, s), 3.80 (3H, s), 4.19 (2H, q, J = 7.2 Hz), 4.49 (2H, s), 6.87 (2H, d, J = 9.0 Hz), 7.43 (2H, d, J = 9.0 Hz), 7.48 (1H, s), 10.15–10.50 (1H, brs); ¹³C NMR (CDCl₃) δ 14.4, 28.0, 42.9, 55.4, 59.8, 84.7, 104.8, 114.1, 124.3, 130.6, 145.7, 149.4, 154.1, 156.7, 165.9; HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₉H₂₈N₃O₅, 376.1867; found, 376.1861.
**1-**tert-Butyl 5-ethyl 2-(2-tolylamino)pyrimidine-1,5(6H)-dicarboxylate 11f (entry 6)

Flash silica gel column chromatography [n-hexane-EtOAc-Et₂N (40:2:1)] to give 11f (17.0 mg, 0.0473 mmol, 47%) as pale yellow crystals. Mp 120–122 °C (n-hexane); IR (KBr) cm⁻¹: 2978, 1719, 1698, 1645, 1556, 1305, 1227, 1152, 1108. ¹H NMR (CDCl₃) δ 1.28 (3H, t, J = 7.2 Hz), 1.58 (9H, s), 2.31 (3H, s), 4.19 (2H, q, J = 7.2 Hz), 4.51 (2H, d, J = 1.2 Hz), 7.08 (1H, t, J = 7.8 Hz), 7.18–7.23 (2H, m), 7.46 (1H, t, J = 1.2 Hz), 7.76 (1H, d, J = 7.8 Hz), 10.10–10.40 (1H, brs); ¹³C NMR (CDCl₃) δ 14.4, 18.2, 28.0, 43.0, 59.8, 84.8, 104.9, 124.9, 125.4, 126.4, 130.5, 131.2, 136.1, 145.7, 149.6, 154.2, 165.9; HRMS-ESI (m/z): [M+H]⁺ calc'd for C₁₉H₂₆N₄O₄, 360.1918; found, 360.1910.

**1-**tert-Butyl 5-ethyl 2-(naphthalen-1-ylamino)pyrimidine-1,5(6H)-dicarboxylate 11g (entry 7)

Flash silica gel column chromatography [n-hexane-EtOAc-Et₂N (40:2:1)] to give 11g (21.5 mg, 0.0544 mmol, 54%) as a pale yellow oil. IR (KBr) cm⁻¹: 3435, 2979, 1695, 1637, 1540, 1151; ¹H NMR (CDCl₃) δ 1.28 (3H, t, J = 7.2 Hz), 1.61 (9H, s), 4.20 (2H, q, J = 7.2 Hz), 4.57 (2H, s), 7.45 (1H, s), 7.46–7.52 (2H, m), 7.55 (1H, t, J = 7.2 Hz), 7.70 (1H, d, J = 7.2 Hz), 7.86 (1H, d, J = 8.4 Hz), 7.96 (1H, d, J = 7.2 Hz), 8.04 (1H, d, J = 8.4 Hz), 10.50–11.10 (1H, brs); ¹³C NMR (CDCl₃) δ 14.4, 28.1, 43.1, 59.9, 85.0, 105.2, 121.7, 122.1, 125.6, 125.7, 125.9, 126.4, 128.1, 128.5, 133.3, 134.2, 145.4, 149.9, 154.3, 165.8; HRMS-ESI (m/z): [M+H]⁺ calc'd for C₂₂H₂₆N₄O₄, 396.1918; found, 396.1919.

**1-**tert-Butyl 5-ethyl 2-(benzylamino)pyrimidine-1,5(6H)-dicarboxylate 11h and ethyl 1,3-dibenzyl-2,4-dioxo-2,3,4,6-tetrahydro-1H-pyrimido[1,2-a][1,3,5]triazine-7-carboxylate 18 (Scheme 5)

The reaction scale was 0.2 mmol of (E)-7. Flash silica gel column chromatography [n-hexane-EtOAc-Et₂N (40:3:1) and CH₂Cl₂-EtOAc (50:1 to 10:1)] to give 11h (11.5 mg, 0.0320 mmol, 16%) and 18 (43.3 mg, 0.103 mmol, 52%). 11h: pale yellow oil; IR (neat) cm⁻¹: 2979, 1708, 1691, 1562, 1271, 1150; ¹H NMR (CDCl₃) δ 1.28 (3H, t, J = 7.2
Hz), 1.51 (9H, s), 4.19 (2H, q, J = 7.2 Hz), 4.42 (2H, d, J = 1.2 Hz), 4.60 (2H, d, J = 4.8 Hz), 7.27–7.36 (5H, m), 7.50 (1H, t, J = 1.2 Hz), 8.78 (1H, s); $^{13}$C NMR (CDCl$_3$) δ 14.4, 28.0, 43.1, 45.7, 59.7, 84.4, 103.5, 127.5, 127.8, 128.7, 137.9, 146.3, 151.7, 154.0, 166.2; HRMS-ESI (m/z): [M+H]$^+$ calc for C$_{19}$H$_{26}$N$_3$O$_4$, 360.1918; found, 360.1910. 18: colorless oil; IR (KBr) cm$^{-1}$: 1743, 1698, 1687, 1546, 1449, 1288; $^1$H NMR (CDCl$_3$) δ 1.28 (3H, t, J = 7.2 Hz), 4.21 (2H, q, J = 7.2 Hz), 4.62 (2H, d, J = 1.8 Hz), 5.03 (2H, s), 5.20 (2H, s), 7.26–7.34 (6H, m), 7.39 (1H, t, J = 1.8 Hz), 7.44–7.49 (4H, m); $^{13}$C NMR (CDCl$_3$) δ 14.3, 43.0, 46.1, 46.3, 60.5, 107.6, 128.0, 128.2, 128.4, 128.6, 129.1, 129.2, 135.7, 135.9, 142.8, 145.1, 147.8, 148.7, 164.9; HRMS-ESI (m/z): [M+H]$^+$ calc for C$_{23}$H$_{22}$N$_3$O$_4$, 419.1714; found, 419.1714.

**General procedure for deprotection of N-protecting group (Boc) of 11 to synthesize N-unsubstituted dihydropyrimidines 12 (Scheme 6)**

![Diagram](image)

**Ethyl 2-(phenylamino)-1,6-dihydropyrimidine-5-carboxylate 12a**

To a solution of 11a (57.0 mg, 0.165 mmol) in CH$_2$Cl$_2$ (2 mL) was added trifluoroacetic acid (0.490 mL, 6.60 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, and 2 M NaOH aqueous solution (5 mL) and EtOAc (20 mL) were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were washed with water (5 mL), brine (5 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by recrystallization (n-hexane-EtOAc) to give 12a (35.9 mg, 0.146 mmol, 89%) as colorless crystals. Mp 192 °C; IR (KBr) cm$^{-1}$: 2865, 1652, 1592, 1232, 1203; $^1$H NMR (CD$_3$OD) δ 1.26 (3H, t, J = 7.2 Hz), 3.99 (2H, s), 4.15 (2H, q, J = 7.2 Hz), 7.04 (2H, dd, J = 7.8, 0.6 Hz), 7.06 (1H, dt, J = 7.8, 0.6 Hz), 7.30 (2H, t, J = 7.8 Hz), 7.33 (1H, s); $^{13}$C NMR (CD$_3$OD) δ 14.7, 40.4, 61.0, 100.5, 124.5, 124.8, 130.4, 142.4, 144.9, 151.4, 167.9; HRMS-ESI (m/z): [M+H]$^+$ calc for C$_{13}$H$_{16}$N$_3$O$_2$, 246.1237; found, 246.1238.

![Diagram](image)

**Ethyl 2-[(4-chlorophenyl)amino]-1,6-dihydropyrimidine-5-carboxylate 12b**

The crude product (0.132 mmol reaction scale) was purified by recrystallization (n-hexane-EtOAc) to give 12b (32.5 mg, 0.116 mmol, 88%) as colorless crystals. Mp 207–210 °C; IR (KBr) cm$^{-1}$: 2839, 1656, 1588, 1489, 1240, 1200; $^1$H NMR (CD$_3$OD) δ 1.26 (3H, t, J = 7.2 Hz), 3.97 (2H, s), 4.15 (2H, q, J = 7.2 Hz), 6.98 (2H, d, J = 8.7 Hz), 7.28 (2H, t, J = 7.8 Hz), 7.30 (1H, s); $^{13}$C NMR (CD$_3$OD) δ 14.7, 40.4, 61.1, 100.8, 125.9, 129.5, 130.3, 140.8, 145.1, 150.5, 167.7; HRMS-ESI (m/z): [M+H]$^+$ calc for C$_{13}$H$_{15}$N$_3$O$_2$Cl, 280.0847; found, 280.0842.