Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting information

Pyrrolo[2,3-*d*]pyrimidines synthesis through activation of *N*-benzyl groups by a distal amide function

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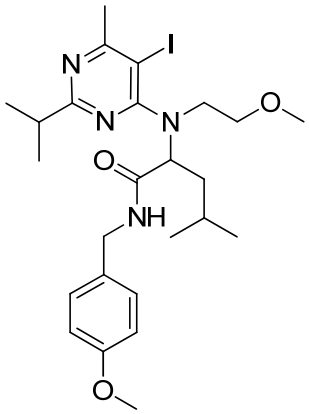
^{1}H NMR spectra were recorded on a 400 MHz spectrometer, using $CDCl_3$ solvent as reference and/or internal deuterium lock. ^{13}C NMR spectra were recorded on a 100.6 MHz spectrometer. Two-dimensional NMR spectroscopy [^{1}H -^{1}H COSY spectra, ^{1}H - ^{13}C COSY spectra (HSQC) and long-range ^{1}H -^{13}C COSY spectra (HMBC)], were carried out to determine the correlation between ^{1}H and ^{13}C. The chemical shifts for all NMR spectra are expressed in parts per million to high frequency of TMS reference. Coupling constants (J) are quoted in Hz and are recorded to the nearest 0.1 Hz.

The IR spectra were obtained using ATR accessories. High-resolution (HR) mass spectra were performed on a GC/MS system spectrometer. TLC was carried out using precoated plates of silica gel 60F254.

General procedure for the synthesis of the Smiles adducts :

To a 1 M solution of pyrimidin-4-ol in methanol were added successively 1.0 equiv. of amine, 1.0 equiv. of aldehyde and 1.0 equiv. of isocyanide. The resulting mixture was stirred at 60°C for three days. The solvent was removed afterwards under reduced pressure to afford Ugi-Smiles products after purification by flash chromatography on silica gel.

2-[(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-(2-methoxyethyl)-amino]-4-methyl-pentanoic acid 4-methoxybenzylamide



$C_{25}H_{37}IN_4O_3$
MW = 568.49 g.mol^{-1}

1a

General procedure using isovaleraldehyde (220 µL, 2 mmol), 2-methoxyethylamine (180 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methyl-pyrimidin-4-ol (560 mg, 2 mmol). Purification by flash column chromatography (silica gel; petroleum ether-diethyl ether, 70:30) gave **1a** as a colorless oil.

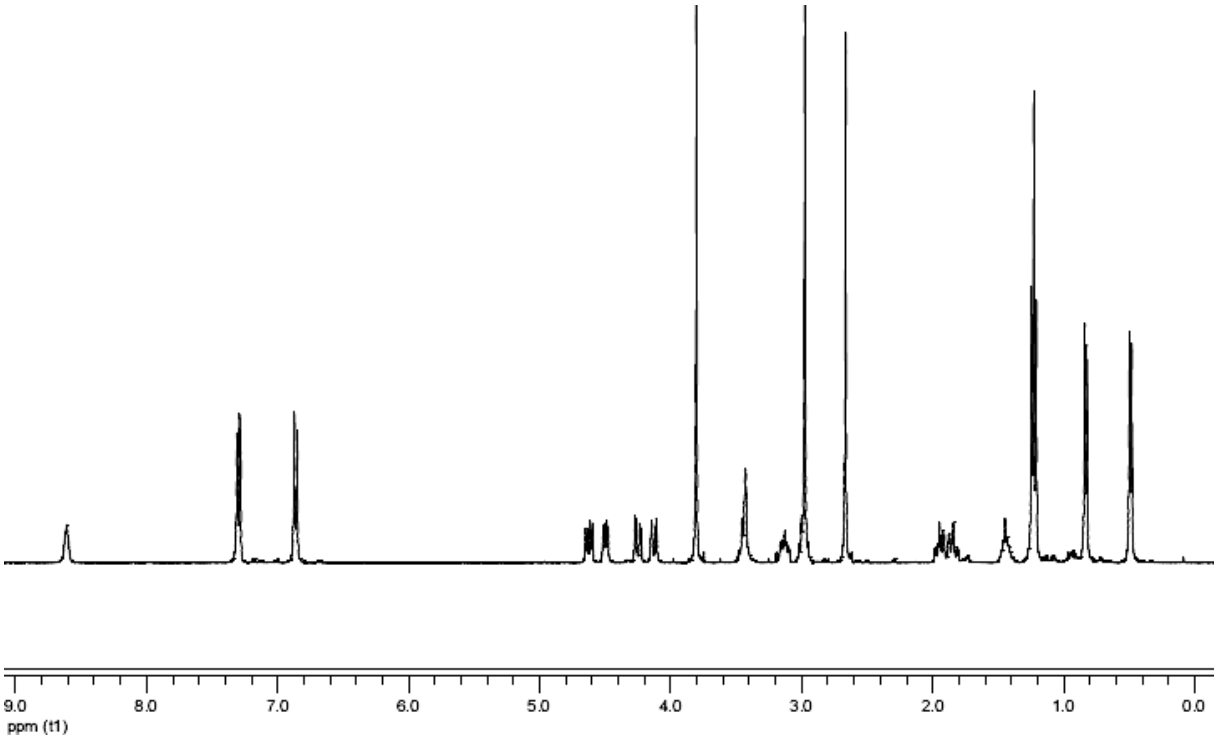
Yield 64 % (730 mg).

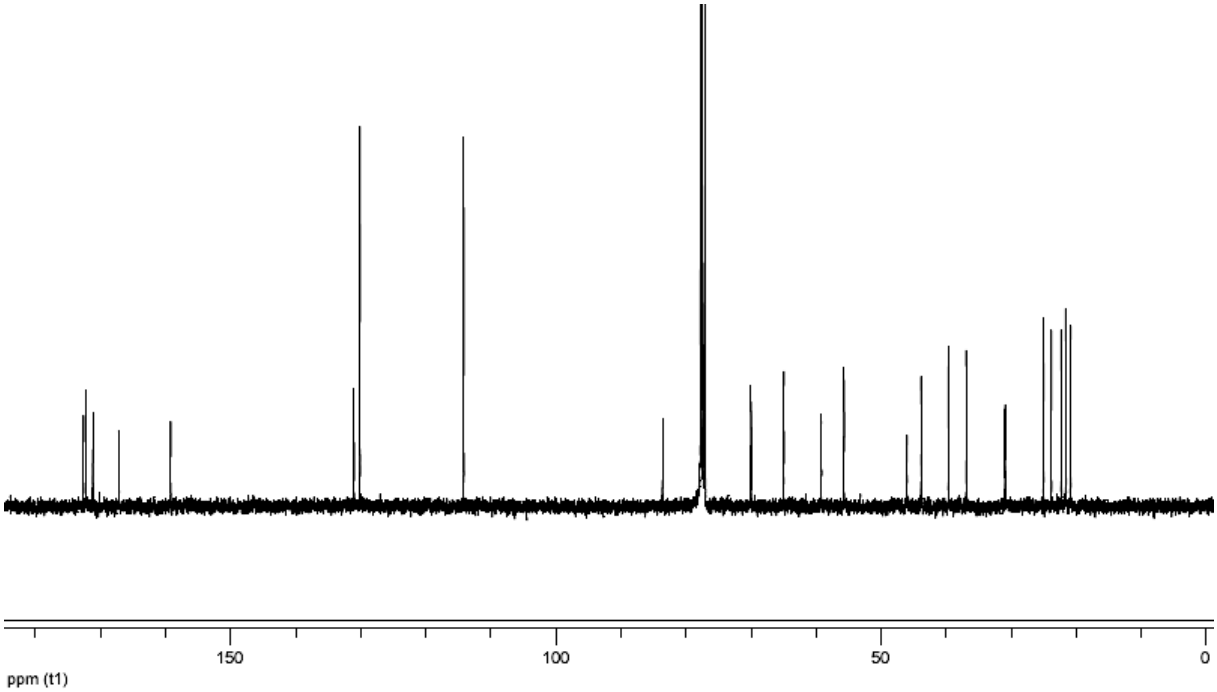
R_f 0.3 (70:30 petroleum ether / diethyl ether).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 (t, *J* = 5.6 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.62 (dd, *J* = 14.3, 6.3 Hz, 1H), 4.50 (dd, *J* = 10.7, 4.1 Hz, 1H), 4.25 (dd, *J* = 14.3, 4.3 Hz, 1H), 4.13 (d, *J* = 13.7 Hz, 1H), 3.80 (s, 3H), 3.50-3.39 (m, 2H), 3.19-3.08 (m, 1H), 3.05-2.93 (m, 1H), 2.98 (s, 3H), 2.67 (s, 3H), 2.00-1.90 (m, 1H), 1.90-1.57 (m, 1H), 1.51-1.38 (m, 1H), 1.24 (d, *J* = 7.2 Hz, 3H), 1.22 (d, *J* = 7.2 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.49 (d, *J* = 6.6 Hz, 3H).

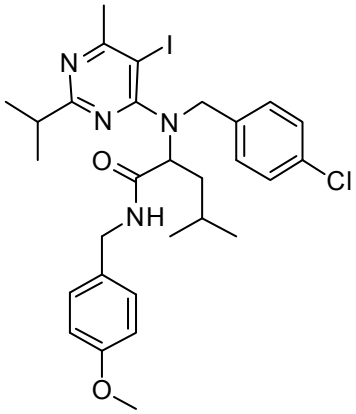
^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.6, 172.3, 171.2, 167.2, 159.2, 131.0, 130.1, 114.2, 83.6, 70.0, 65.0, 59.2, 55.7, 46.1, 43.9, 39.6, 36.9, 30.9, 25.0, 23.9, 22.3, 21.6, 20.9.

HRMS Calculated for $C_{25}H_{37}IN_4O_3$ 568.1910, found 568.1885.





2-[(4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-4-methyl-pentanoic acid 4-methoxybenzylamide



$C_{29}H_{36}ClIN_4O_2$
MW = 634.98 g.mol^{-1}

1b

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1b** as a colorless oil.

Yield 59 % (740 mg).

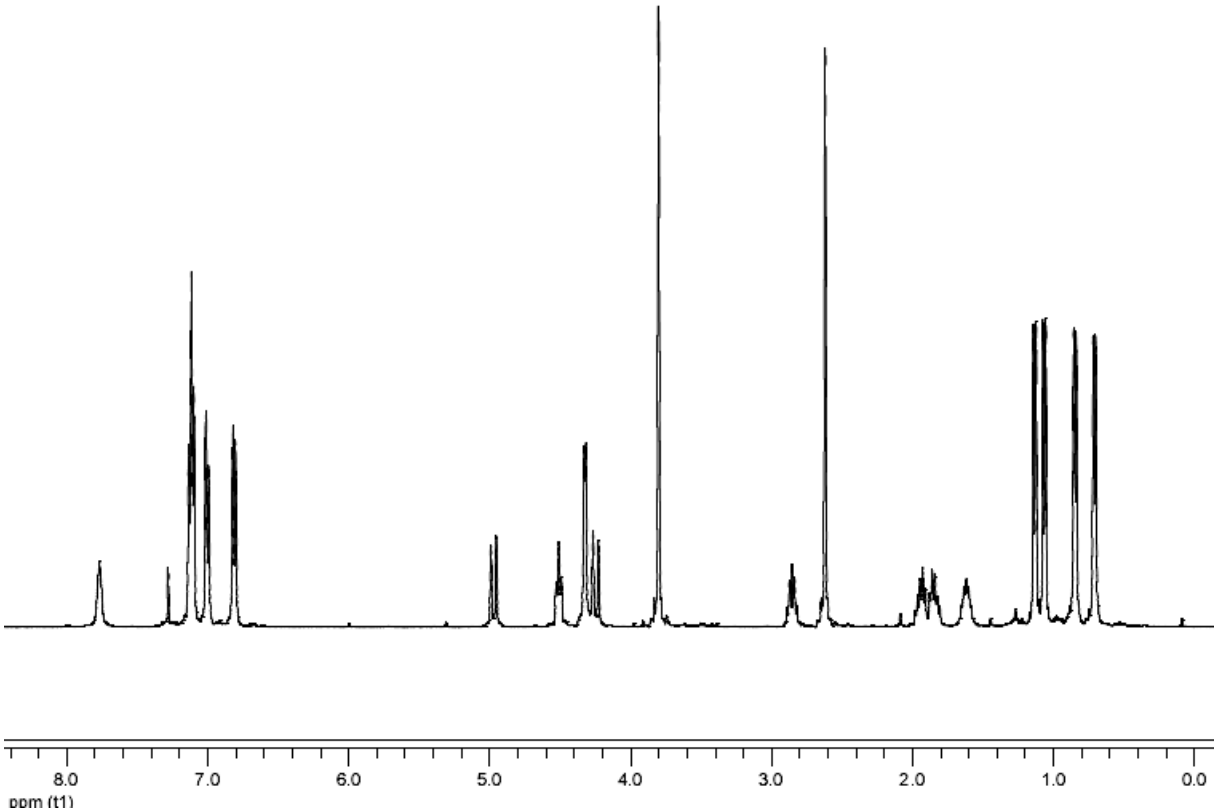
R_f 0.3 (70:30 petroleum ether / diethyl ether).

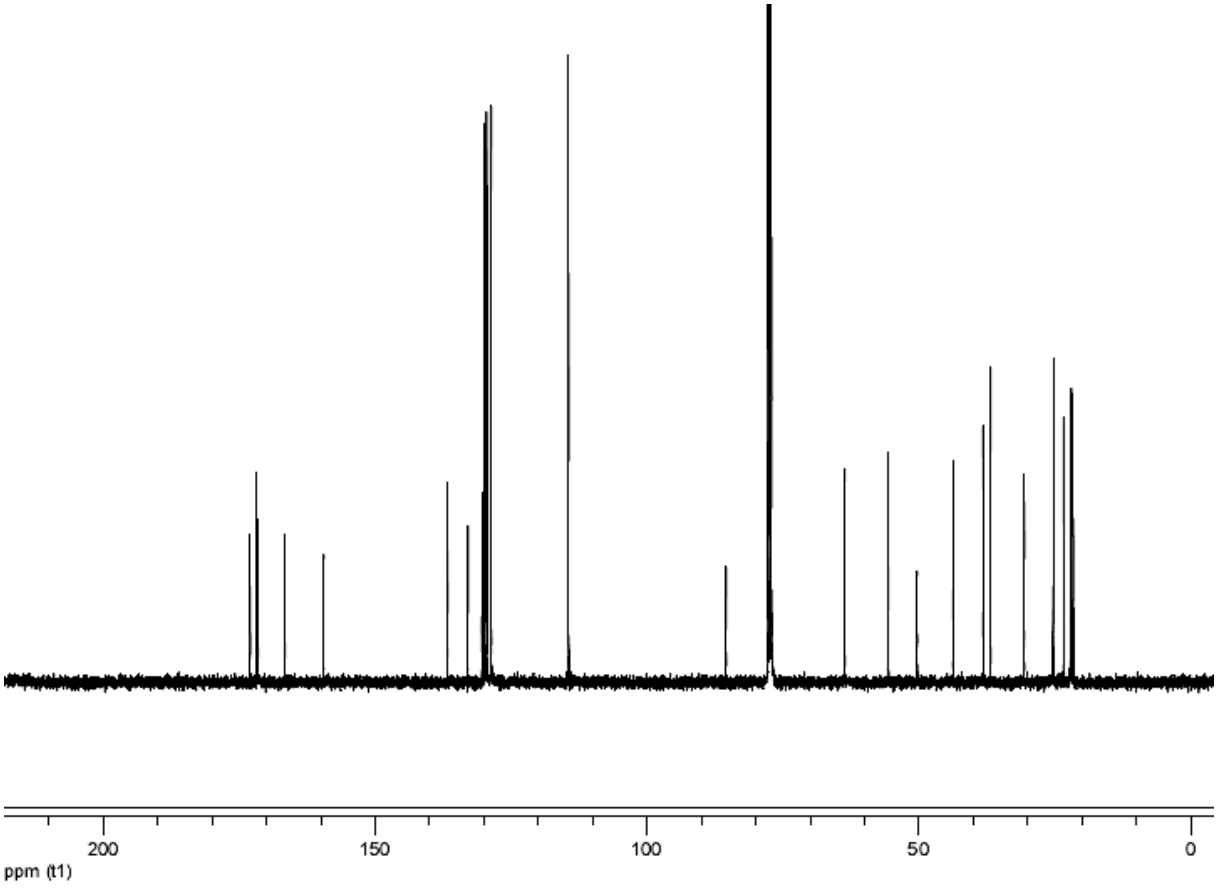
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (br s, 1H), 7.15-7.08 (m, 4H), 7.00 (d, *J* = 7.1 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 4.97 (d, *J* = 15.2 Hz, 1H), 4.51 (dd, *J* = 8.3, 6.3 Hz, 1H), 4.34 (dd, *J* = 16.2, 5.8 Hz, 1H), 4.31 (dd, *J* = 16.2, 5.3 Hz, 1H), 4.25 (d, *J* = 15.2 Hz, 1H), 3.80 (s, 3H), 2.86 (sept, *J* = 6.8 Hz, 1H), 2.62 (s, 3H), 1.99-1.89 (m, 1H), 1.89-1.79 (m, 1H), 1.68-1.56 (sept, *J* = 6.3 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.71 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 171.7, 171.5, 166.6, 159.4, 136.7, 132.9, 130.4, 129.8, 129.5, 128.7, 114.4, 85.5, 63.7, 55.7, 50.4, 43.7, 38.2, 36.9, 30.7, 25.3, 23.4, 22.1, 22.0, 21.7.

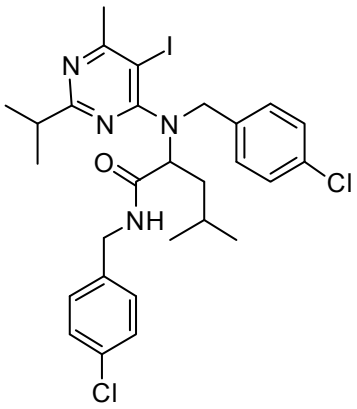
I.R. (thin film) 1654, 1612, 1560, 1513 cm^{-1}.

HRMS Calculated for $C_{29}H_{36}ClIN_4O_2$ 634.1572, found 634.1573.





2-[(4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-4-methylpentanoic acid 4-chlorobenzylamide



$C_{28}H_{33}Cl_2IN_4O$

MW = 639.40 g.mol^{-1}

1c

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1c** as a colorless oil.

Yield 69 % (885 mg).

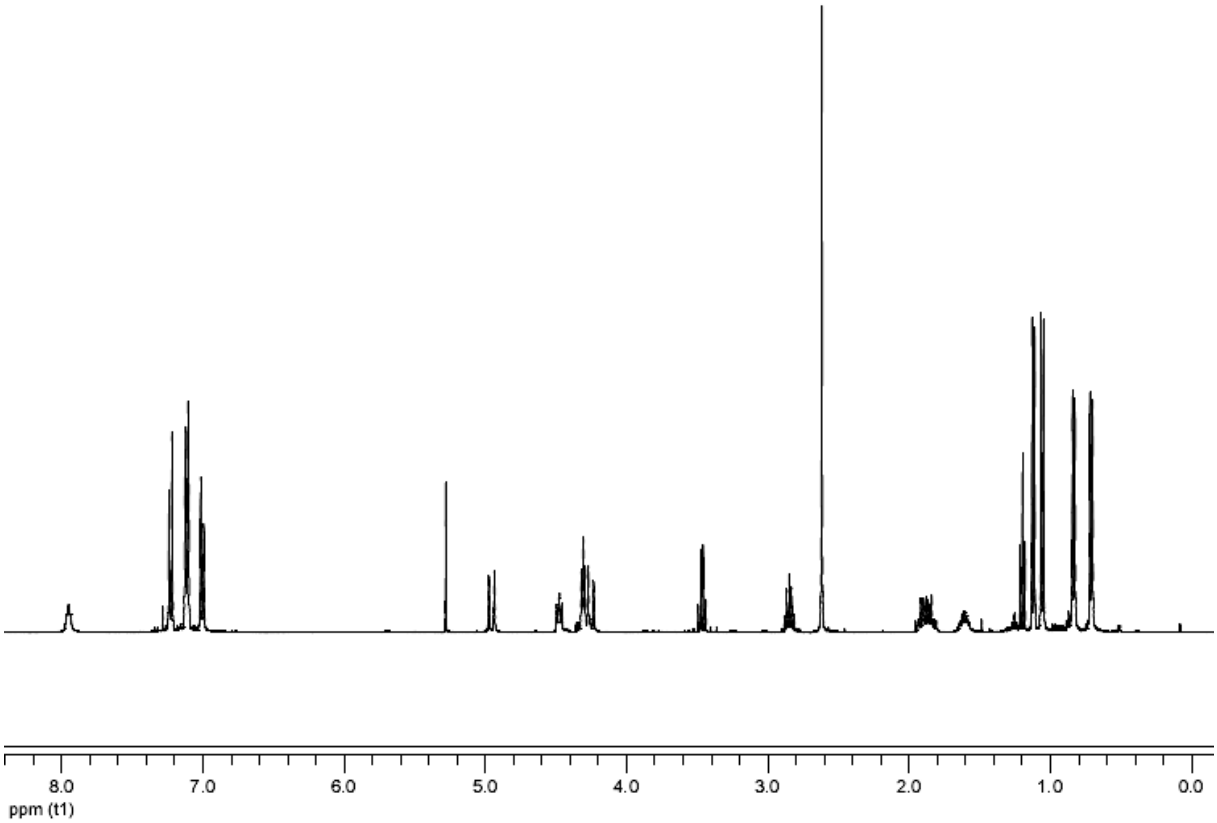
R_f 0.3 (70:30 petroleum ether / diethyl ether).

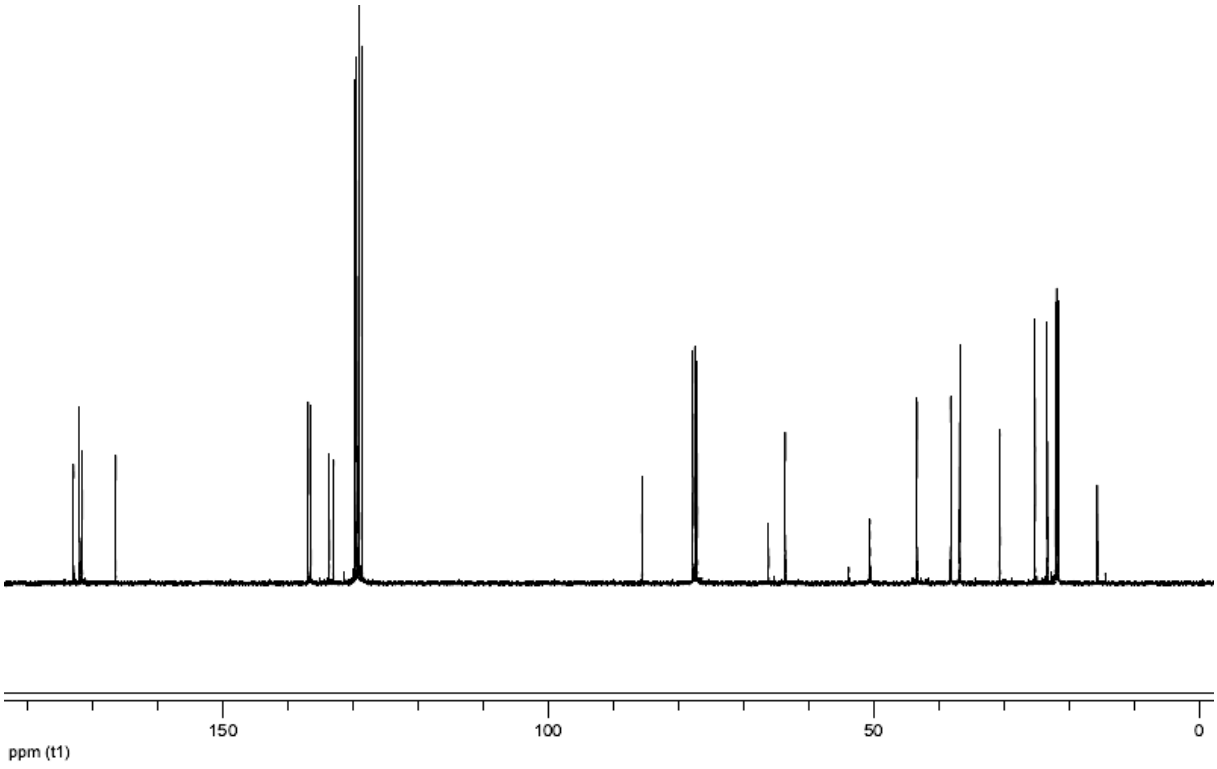
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (t, *J* = 5.3 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 4.96 (d, *J* = 15.3 Hz, 1H), 4.45 (dd, *J* = 8.4, 6.2 Hz, 1H), 4.37-4.22 (m, 3H), 2.85 (sept, *J* = 6.9 Hz, 1H), 2.62 (s, 3H), 1.98-1.79 (m, 2H), 1.67-1.55 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.71 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 172.1, 171.7, 166.6, 137.0, 136.6, 133.7, 133.1, 129.8, 129.5, 129.2, 128.7, 85.7, 63.7, 50.7, 43.4, 38.3, 36.9, 30.7, 25.3, 23.4, 22.2, 22.0, 21.7.

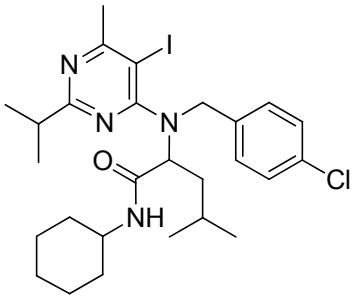
I.R. (thin film) 1667, 1533, 1512, 1492 cm^{-1}.

HRMS Calculated for $C_{28}H_{33}Cl_2IN_4O$ 638.1076, found 638.1086.





2-((4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino)-*N*-cyclohexyl-4-methylpentanamide



$C_{27}H_{38}ClIN_4O$
MW = 596.97 g.mol^{-1}

1d

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), cyclohexylbenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 80:20) gave **1d** as a colorless oil.

Yield 22 % (263 mg).

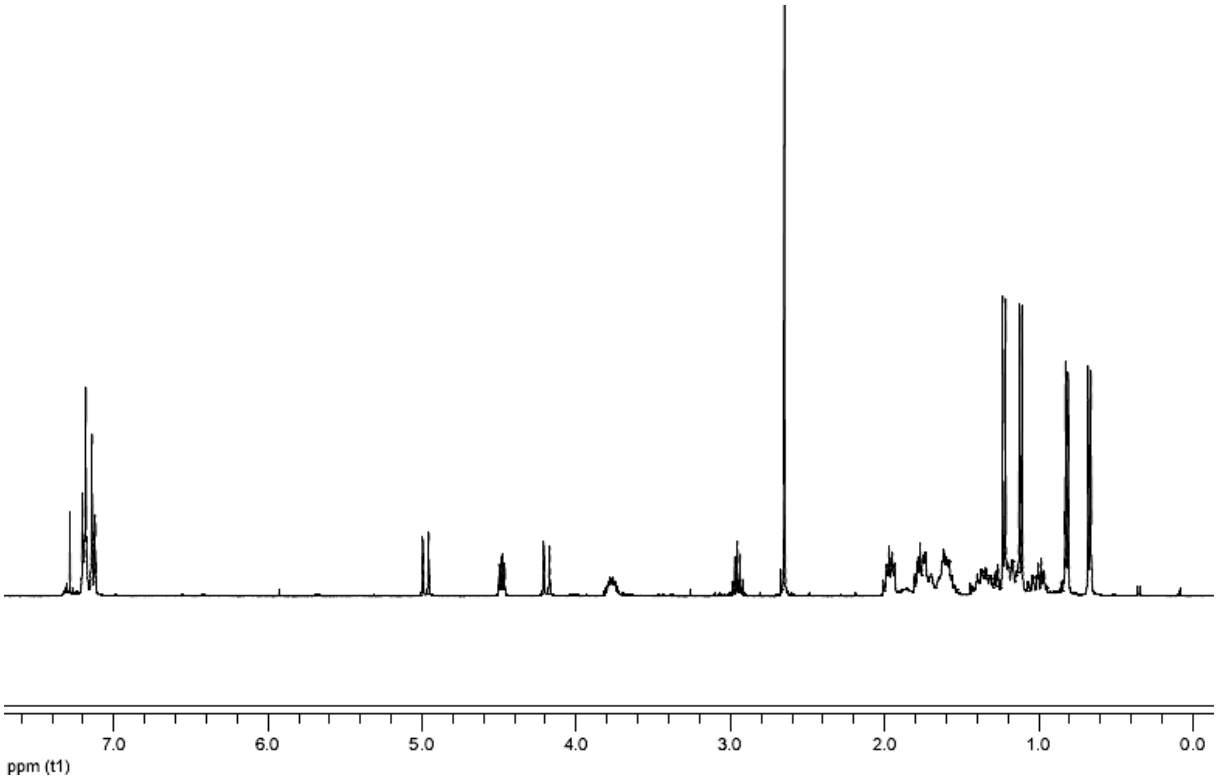
R_f 0.3 (80:20 petroleum ether / diethyl ether).

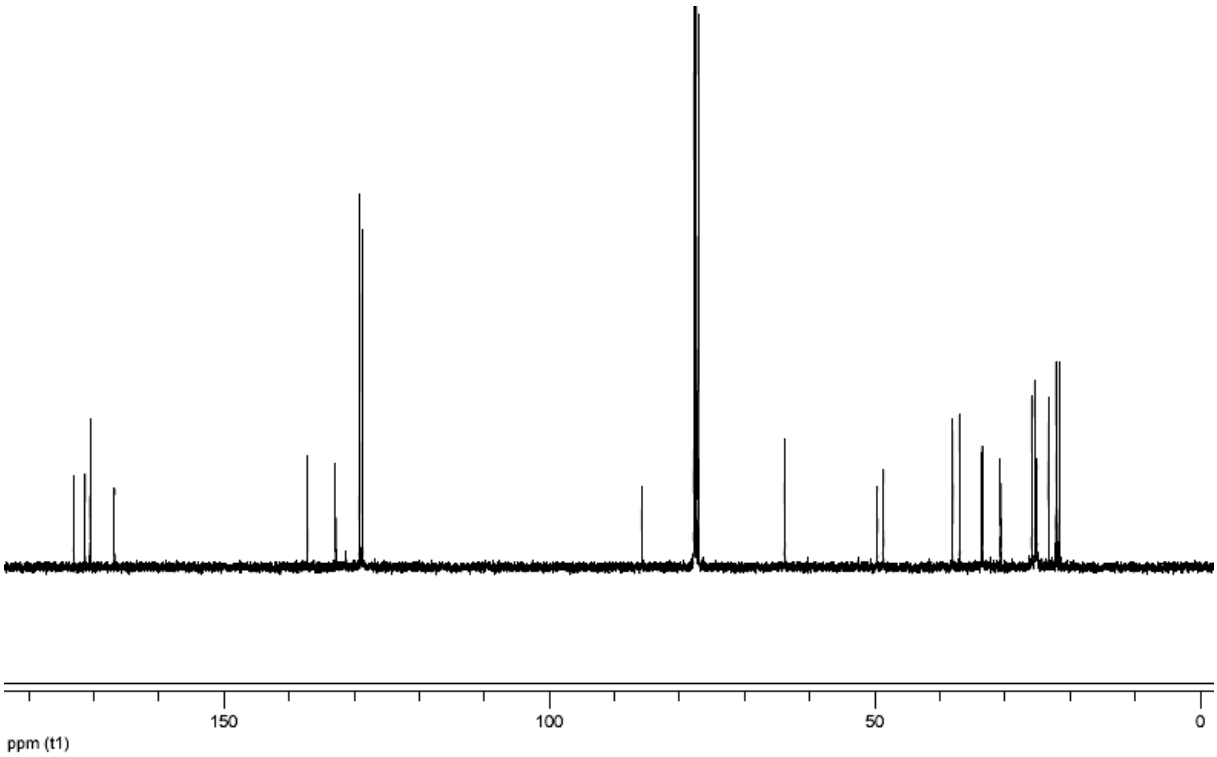
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22-7.16 (m, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 4.98 (d, *J* = 15.2 Hz, 1H), 4.48 (dd, *J* = 8.0, 6.2 Hz, 1H), 4.19 (d, *J* = 15.2 Hz, 1H), 3.83-3.71 (m, 1H), 2.96 (sept, *J* = 6.9 Hz, 1H), 2.65 (s, 3H), 2.02- 1.92 (m, 2H), 1.82-1.68 (m, 3H), 1.68-1.52 (m, 3H), 1.45-1.25 (m, 2H), 1.22 (d, *J* = 6.9 Hz, 3H), 1.21-1.14 (m, 2H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.08-0.94 (m, 1H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.67 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.1, 171.4, 170.6, 166.8, 137.2, 132.8, 129.8, 128.7, 85.8, 63.9, 49.7, 48.7, 38.1, 37.0, 33.6, 33.5, 25.9, 25.4, 25.2, 25.1, 23.3, 22.2, 22.1, 21.7.

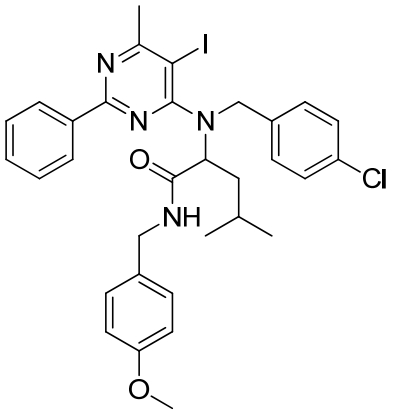
I.R. (thin film) 1661, 1533, 1507, 1449 cm^{-1}.

HRMS Calculated for $C_{27}H_{38}ClIN_4O$ 596.1779, found 596.1769.





2-((4-chlorobenzyl)-(5-iodo-6-methyl-2-phenylpyrimidin-4-yl)-amino)-*N*-(4-methoxybenzyl)-4-methylpentanamide



$C_{32}H_{34}ClIN_4O_2$
MW = 669.00 g.mol^{-1}

1e

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-phenyl-6-methylpyrimidin-4-ol (640 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1e** as a colorless oil.

Yield 68 % (910 mg).

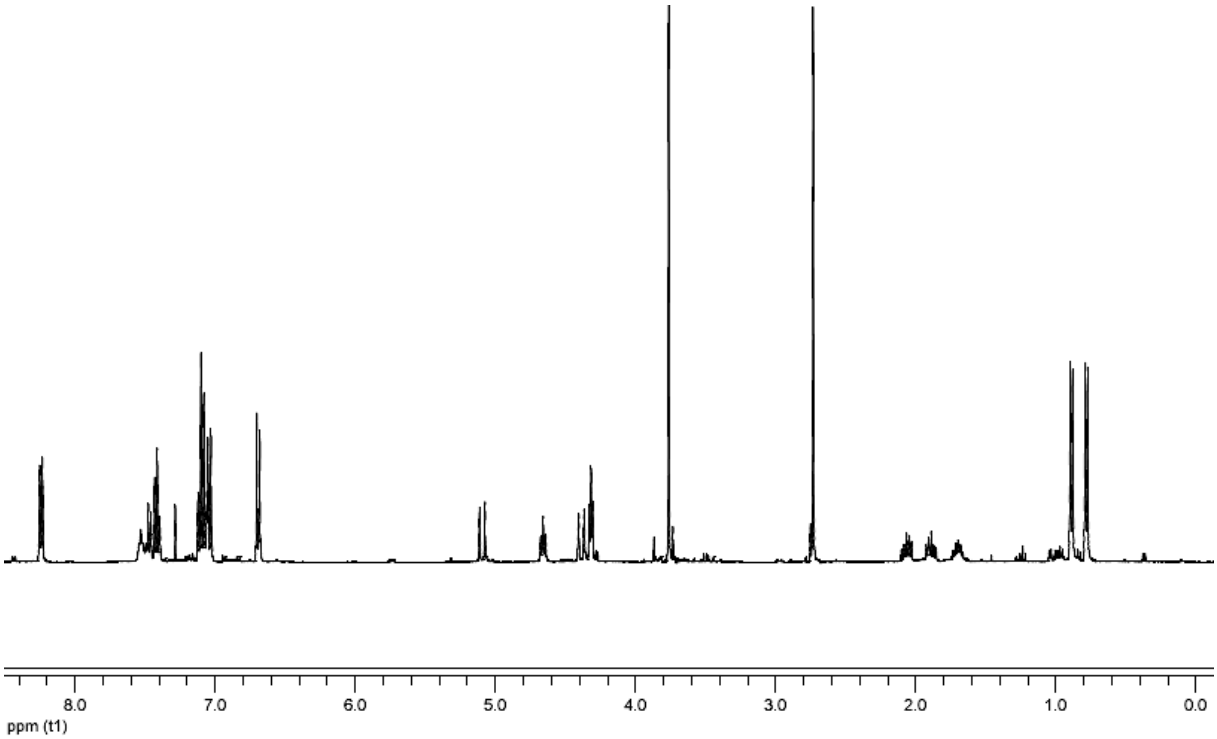
R_f 0.3 (70:30 petroleum ether / diethyl ether).

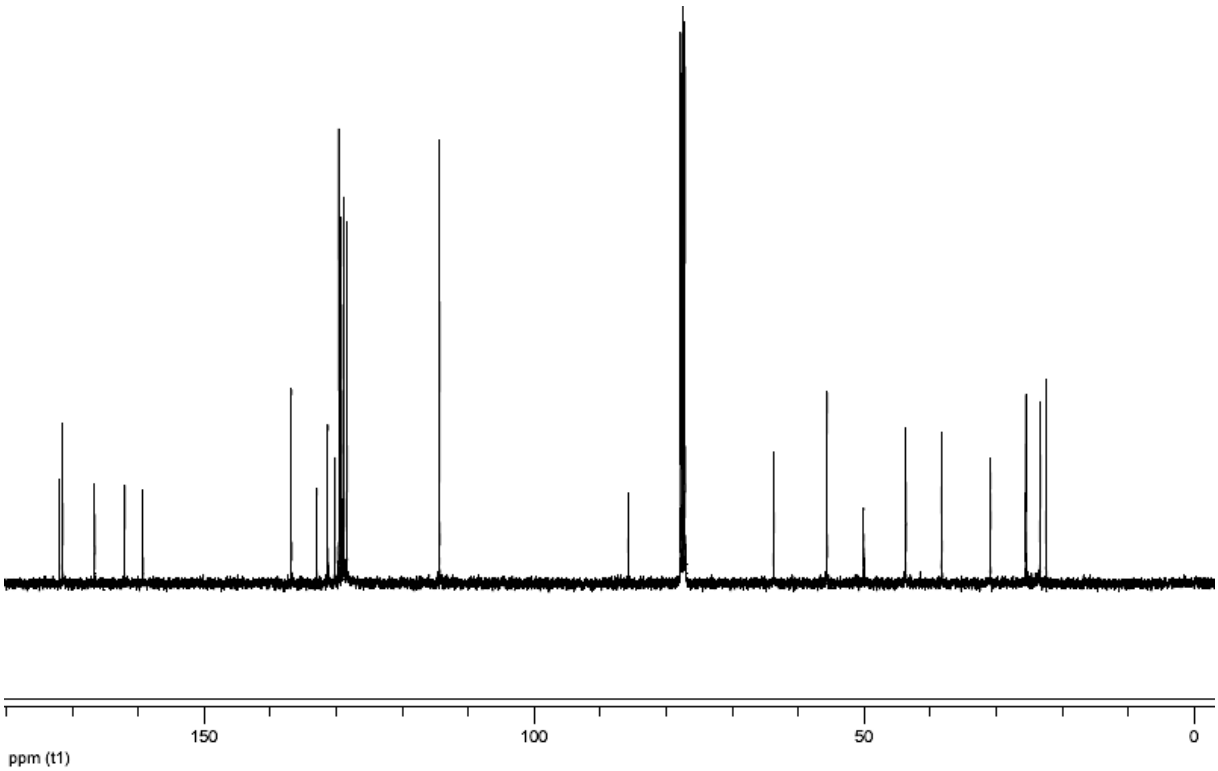
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (d, *J* = 7.2 Hz, 2H), 7.53 (t, *J* = 5.3 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.44-7.39 (m, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.69 (d, *J* = 8.6 Hz, 2H), 5.09 (d, *J* = 15.4 Hz, 1H), 4.66 (t, *J* = 7.2 Hz, 1H), 4.39 (d, *J* = 15.4 Hz, 1H), 4.36-4.26 (m, 2H), 3.77 (s, 3H), 2.74 (s, 3H), 2.11-2.02 (m, 1H), 1.94-1.84 (m, 1H), 1.76-1.64 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.5, 166.6, 162.1, 159.3, 136.8, 133.0, 131.3, 131.3, 130.2, 129.6, 129.3, 129.0, 128.8, 128.4, 114.4, 85.8, 63.7, 55.6, 50.1, 43.7, 38.3, 30.9, 25.5, 23.3, 22.4.

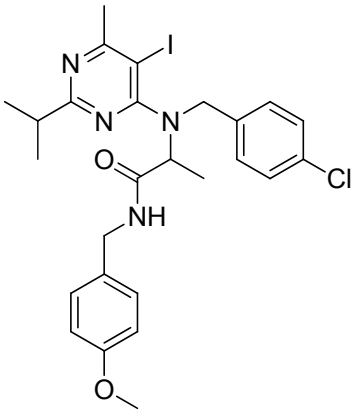
I.R. (thin film) 1656, 1510, 1428, 1371 cm^{-1}.

HRMS Calculated for $C_{32}H_{34}ClIN_4O_2$ 668.1415, found 668.1406.





2-((4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino)-*N*-(4-methoxybenzyl)-propanamide



$C_{26}H_{30}ClIN_4O_2$
MW = 592.9 g.mol^{-1}

1f

General procedure using acetaldehyde (110 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1f** as a colorless oil.

Yield 57 % (675 mg).

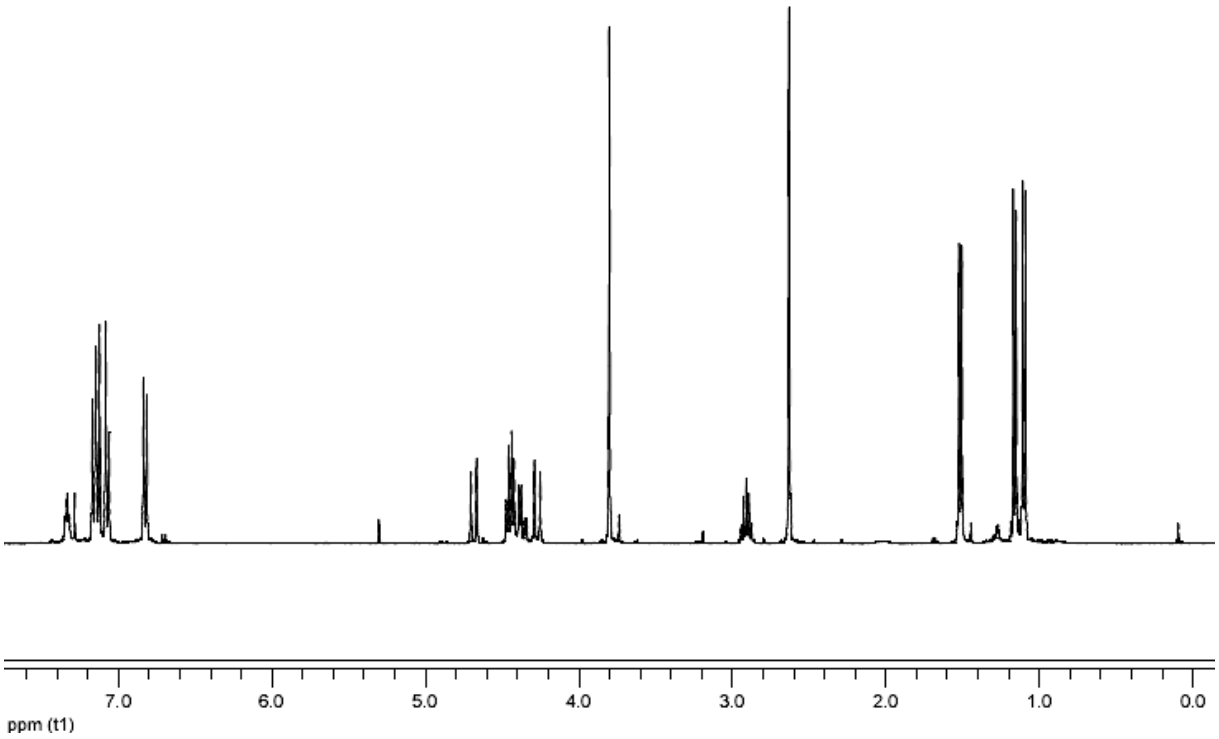
R_f 0.3 (70:30 petroleum ether / diethyl ether).

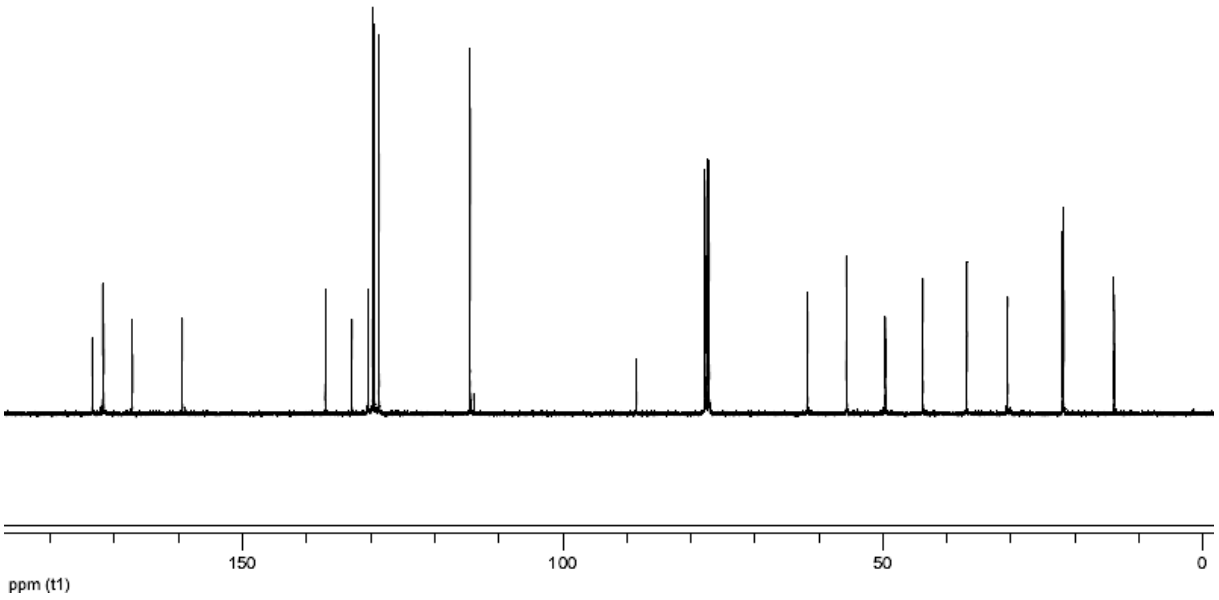
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (t, *J* = 5.3 Hz, 1H), 7.19-7.11 (m, 4H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.69 (d, *J* = 14.8 Hz, 1H), 4.49-4.42 (m, 2H), 4.36 (dd, *J* = 14.4, 5.2 Hz, 1H), 4.27 (d, *J* = 14.8 Hz, 1H), 3.80 (s, 3H), 2.91 (sept, *J* = 6.9 Hz, 1H), 2.63 (s, 3H), 1.51 (d, *J* = 7.0 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.5, 171.9, 171.7, 167.2, 159.5, 137.1, 133.0, 130.4, 129.7, 129.5, 128.7, 114.5, 88.5, 61.8, 55.7, 49.6, 43.8, 36.9, 30.5, 22.0, 21.8, 13.9.

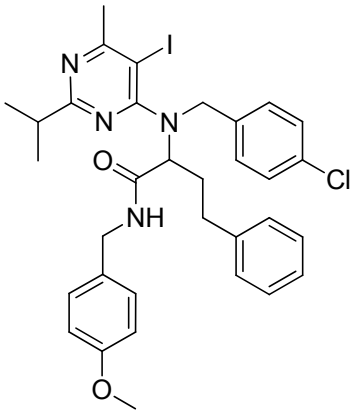
I.R. (thin film) 1667, 1538, 1512, 1444 cm^{-1}.

HRMS Calculated for $C_{26}H_{30}ClIN_4O_2$ 592.1102, found 592.1095.





2-((4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino)-*N*-(4-methoxybenzyl)-4-phenylbutanamide



$C_{33}H_{36}ClIN_4O_2$
MW = 683.02 g.mol^{-1}

1g

General procedure using 3-phenylpropionaldehyde (260 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 80:20) gave **1g** as a colorless oil.

Yield 51 % (695 mg).

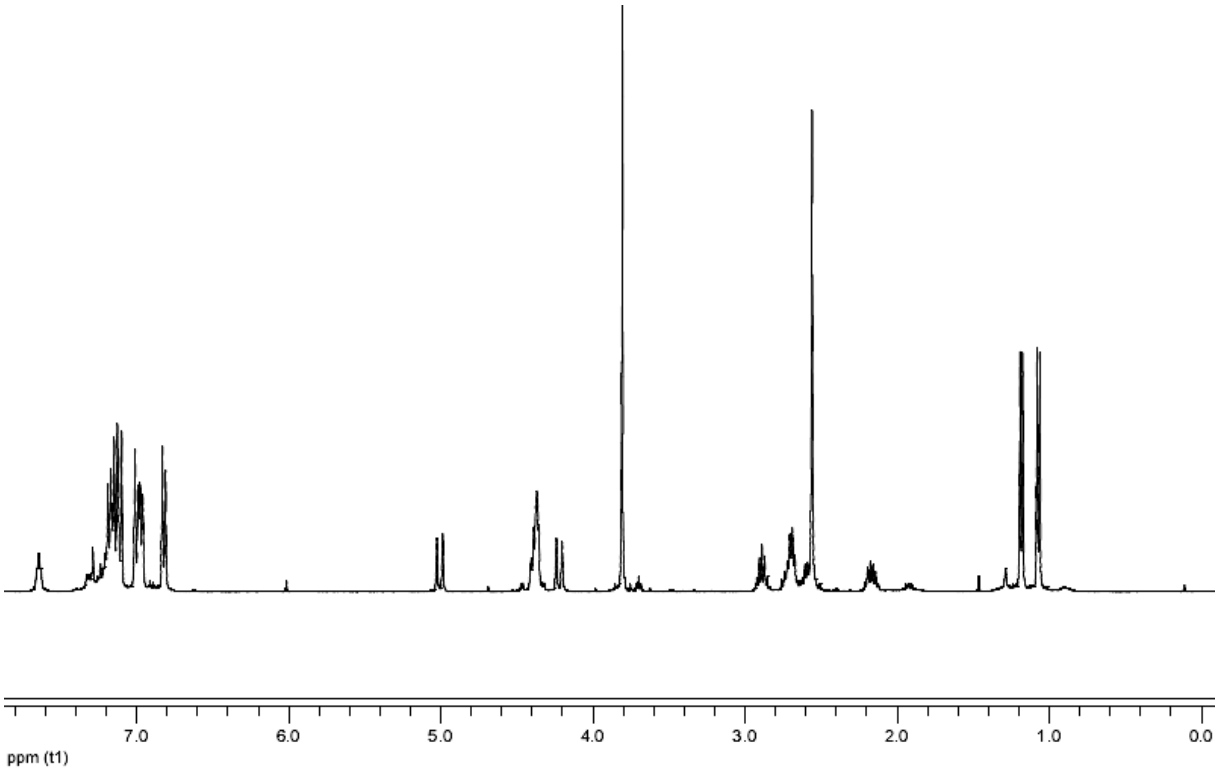
R_f 0.3 (80:20 petroleum ether / diethyl ether).

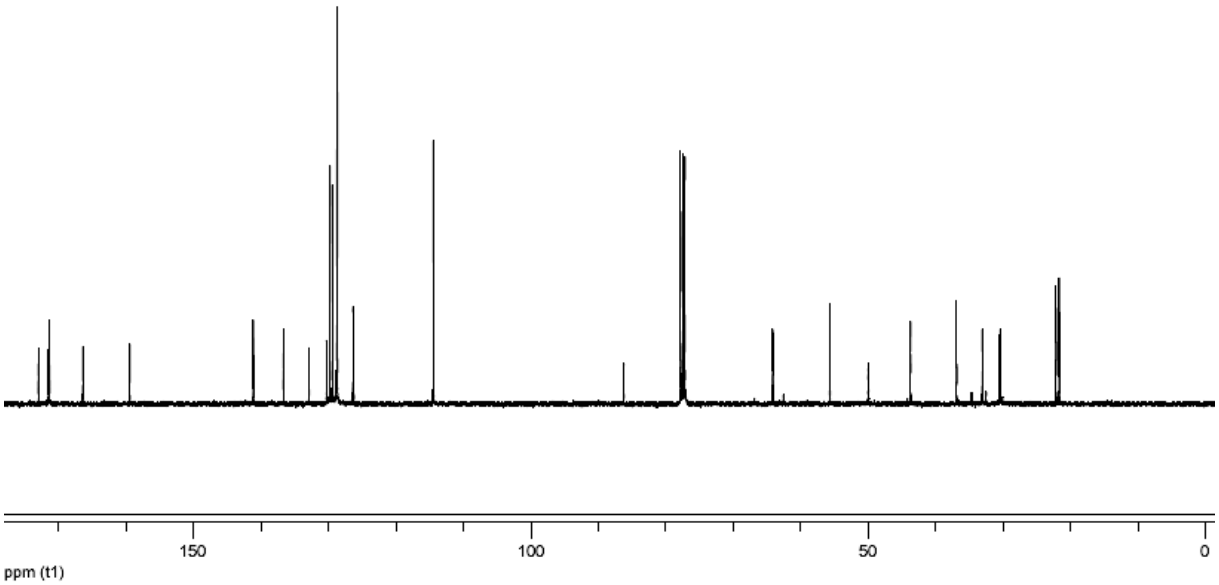
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (t, *J* = 5.2 Hz, 1H), 7.21-7.08 (m, 7H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.00 (d, *J* = 15.1 Hz, 1H), 4.42-4.34 (m, 3H), 4.22 (d, *J* = 15.1 Hz, 1H), 3.81 (s, 3H), 2.89 (sept, *J* = 6.9 Hz, 1H), 2.77-2.65 (m, 2H), 2.65-2.56 (m, 1H), 2.56 (s, 3H), 2.22-2.11 (m, 1H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 171.5, 171.4, 166.4, 159.5, 141.2, 136.7, 132.9, 130.3, 129.8, 129.4, 128.8, 128.7, 126.4, 114.5, 86.3, 64.2, 55.7, 50.0, 43.8, 36.9, 33.1, 30.6, 30.4, 22.2, 21.7.

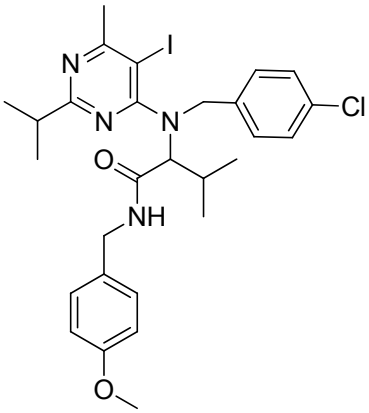
I.R. (thin film) 1673, 1533, 1512, 1454 cm^{-1}.

HRMS Calculated for $C_{33}H_{36}ClIN_4O_2$ 682.1572, found 682.1535.





2-((4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino)-*N*-(4-methoxybenzyl)-3-methylbutanamide



$C_{28}H_{34}ClIN_4O_2$
MW = 620.95 g.mol^{-1}

1h

General procedure using isobutyraldehyde (200 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1h** as a colorless oil.

Yield 42 % (522 mg).

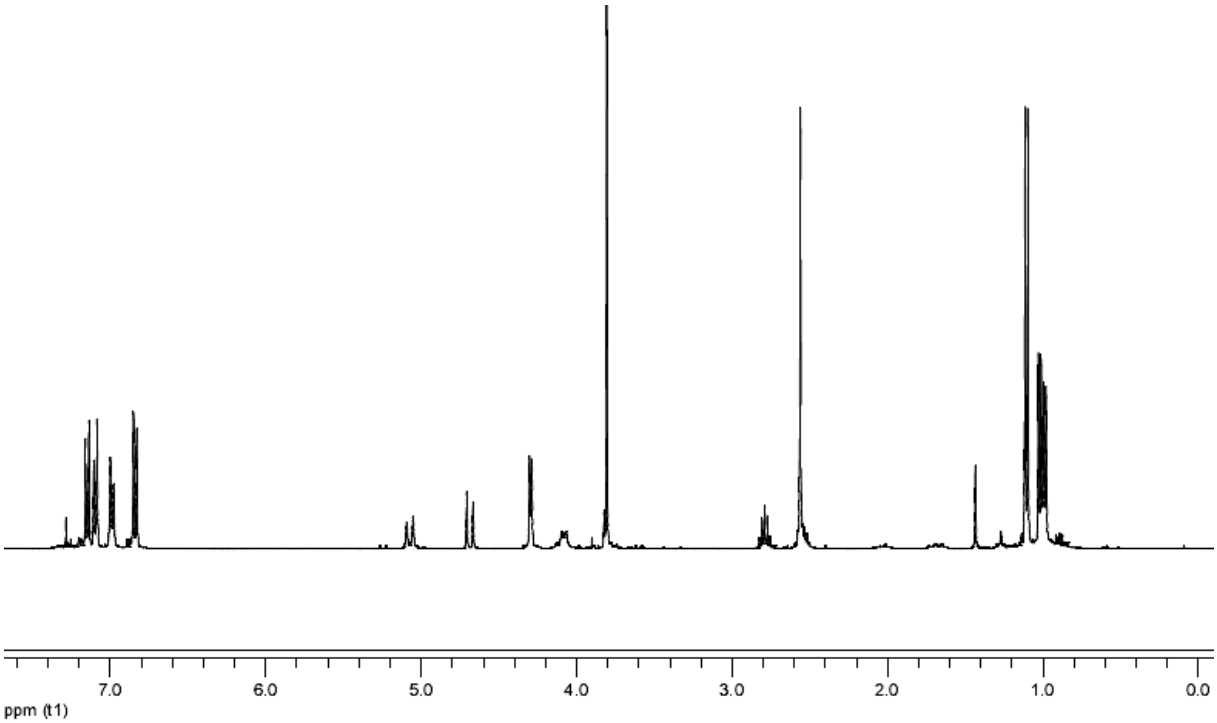
R_f 0.3 (70:30 petroleum ether / diethyl ether).

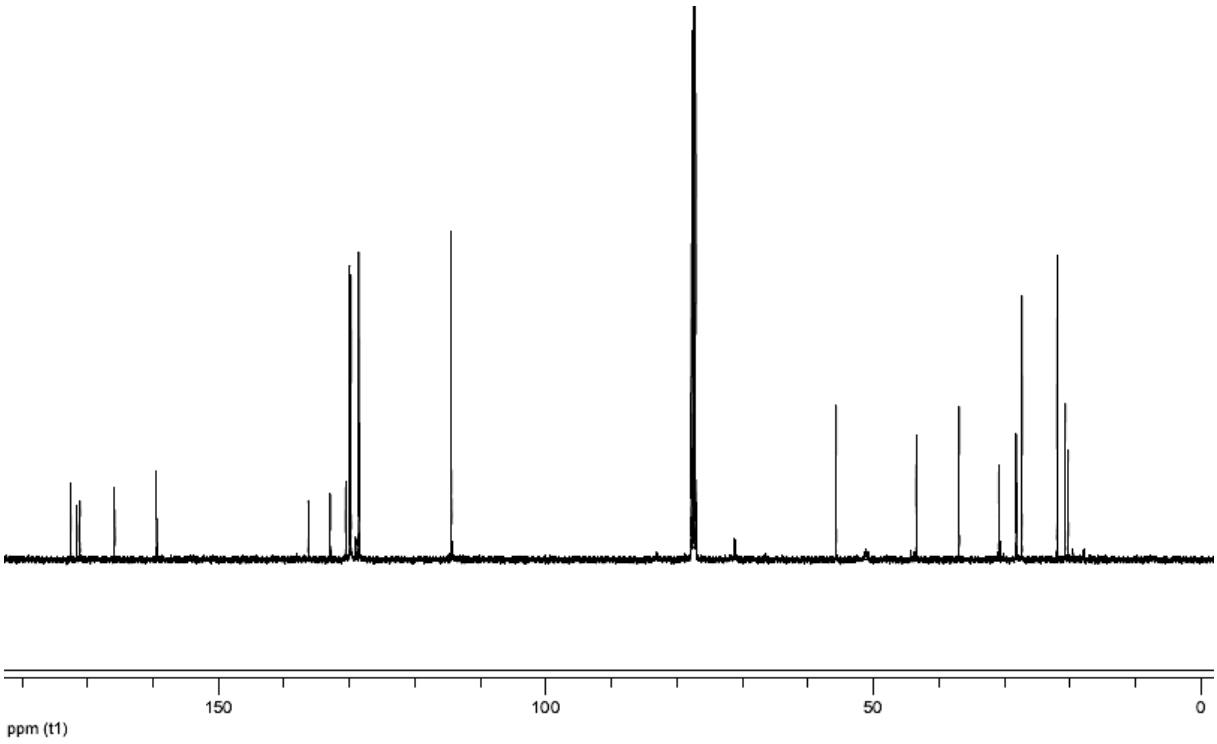
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (br s, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.08 (d, *J* = 16.2 Hz, 1H), 4.69 (d, *J* = 16.2 Hz, 1H), 4.32 (dd, *J* = 14.7, 5.8 Hz, 1H), 4.28 (dd, *J* = 14.7, 5.6 Hz, 1H), 4.09 (d, *J* = 10.9 Hz, 1H), 3.81 (s, 3H), 2.79 (sept, *J* = 6.9 Hz, 1H), 2.57 (s, 3H), 2.56-2.49 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 6H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.6, 171.6, 171.1, 165.9, 159.4, 136.3, 132.9, 130.6, 130.0, 129.8, 128.6, 114.4, 83.1, 71.2, 55.7, 51.1, 43.4, 36.9, 30.8, 28.2, 21.9, 20.7, 20.3.

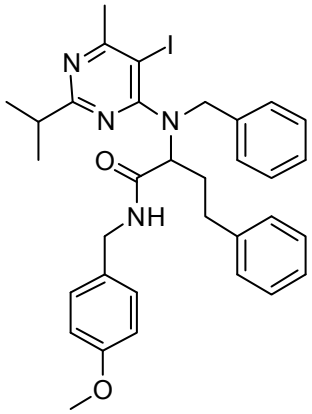
I.R. (thin film) 1672, 1534, 1512, 1468 cm^{-1}.

HRMS Calculated for $C_{28}H_{34}ClIN_4O_2$ 620.1415, found 620.1418.





2-[benzyl-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-*N*-(4-methoxybenzyl)-4-phenylbutyramide



$C_{33}H_{37}IN_4O_2$
MW = 648.58 g.mol^{-1}

1i

General procedure using 3-phenylpropionaldehyde (260 µL, 2 mmol), benzylamine (220 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 80:20) gave **1i** as a colorless oil.

Yield 51 % (660 mg).

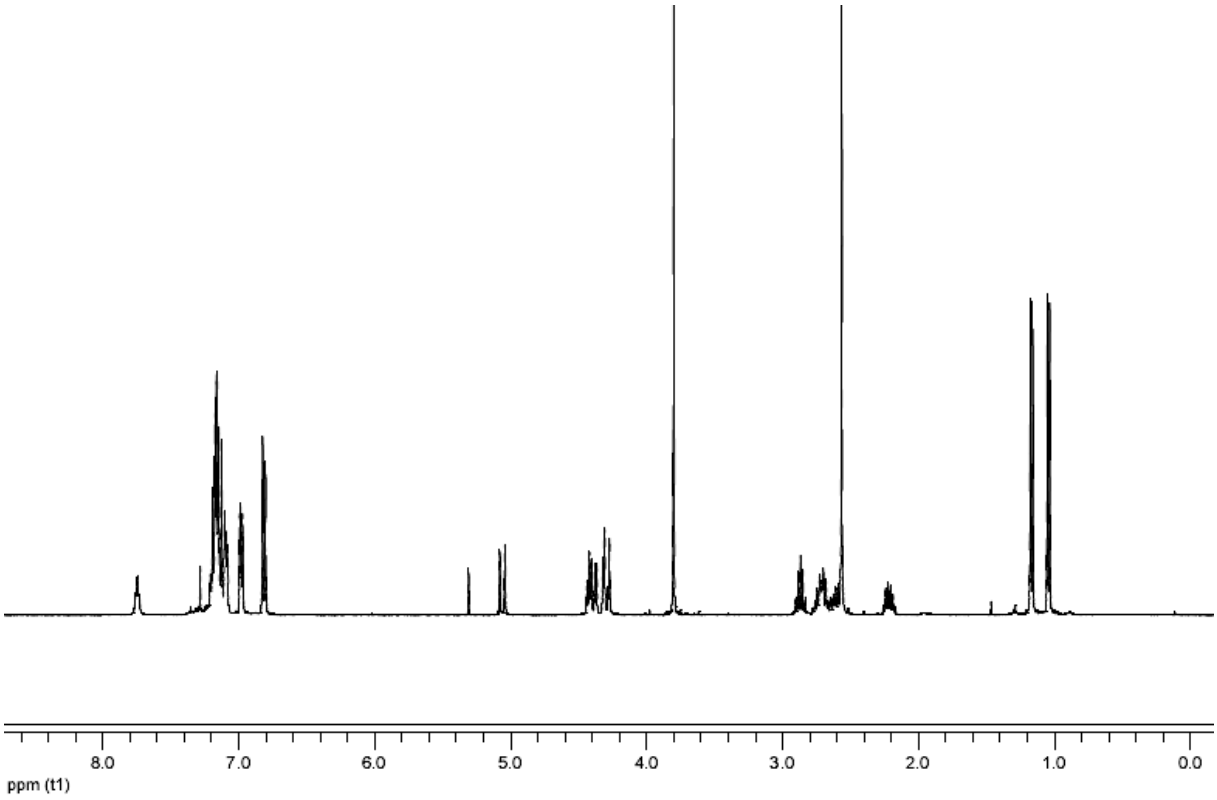
R_f 0.3 (80:20 petroleum ether / diethyl ether).

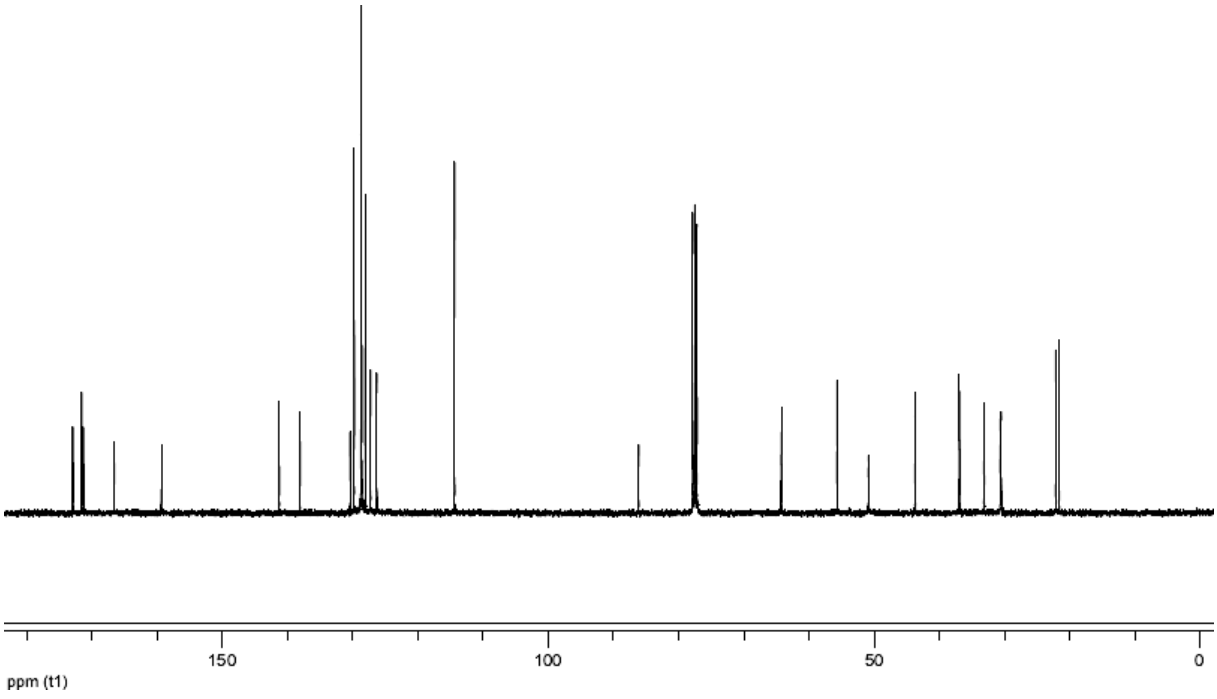
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (t, *J* = 5.2 Hz, 1H), 7.22-7.06 (m, 10H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.06 (d, *J* = 15.1 Hz, 1H), 4.45-4.36 (m, 2H), 4.33-4.26 (m, 2H), 3.80 (s, 3H), 2.87 (sept, *J* = 6.9 Hz, 1H), 2.79-2.58 (m, 3H), 2.57 (s, 3H), 2.27-2.16 (m, 1H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.9, 171.6, 171.3, 166.6, 159.4, 141.3, 138.1, 130.4, 129.8, 128.7, 128.6, 128.1, 127.3, 126.3, 114.4, 86.2, 64.2, 55.7, 50.9, 43.7, 36.9, 33.2, 30.6, 30.5, 22.2, 21.6.

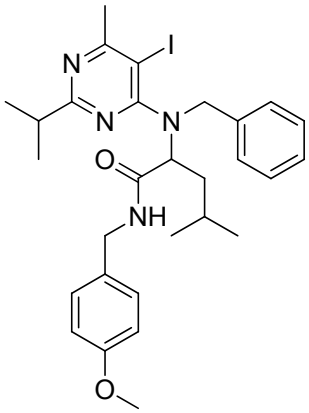
I.R. (thin film) 1672, 1534, 1510, 1454 cm^{-1}.

HRMS Calculated for $C_{33}H_{37}IN_4O_2$ 648.1961, found 648.1935.





2-(benzyl-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino)-*N*-(4-methoxybenzyl)-4-methylpentanamide



$C_{29}H_{37}IN_4O_2$
MW = 600.53 g.mol^{-1}

1j

General procedure using isovaleraldehyde (220 µL, 2 mmol), benzylamine (220 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 60:40) gave **1j** as a colorless oil.

Yield 65 % (780 mg).

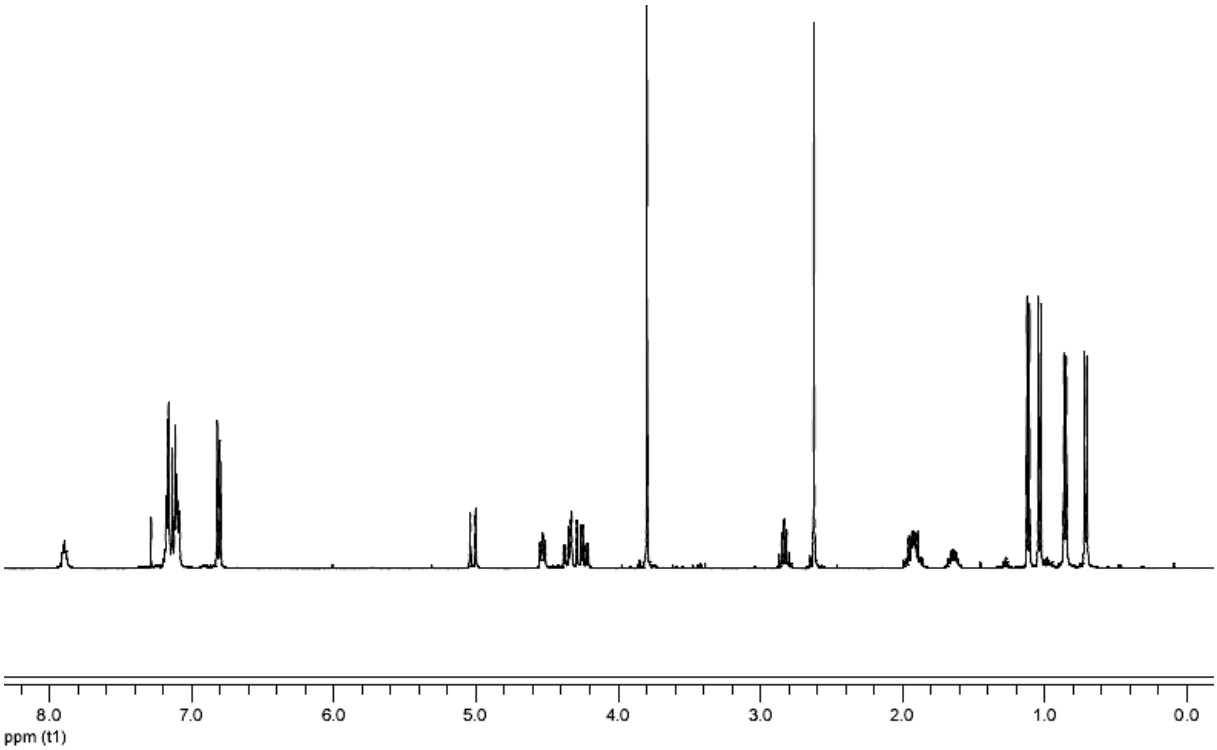
R_f 0.3 (60:40 petroleum ether / diethyl ether).

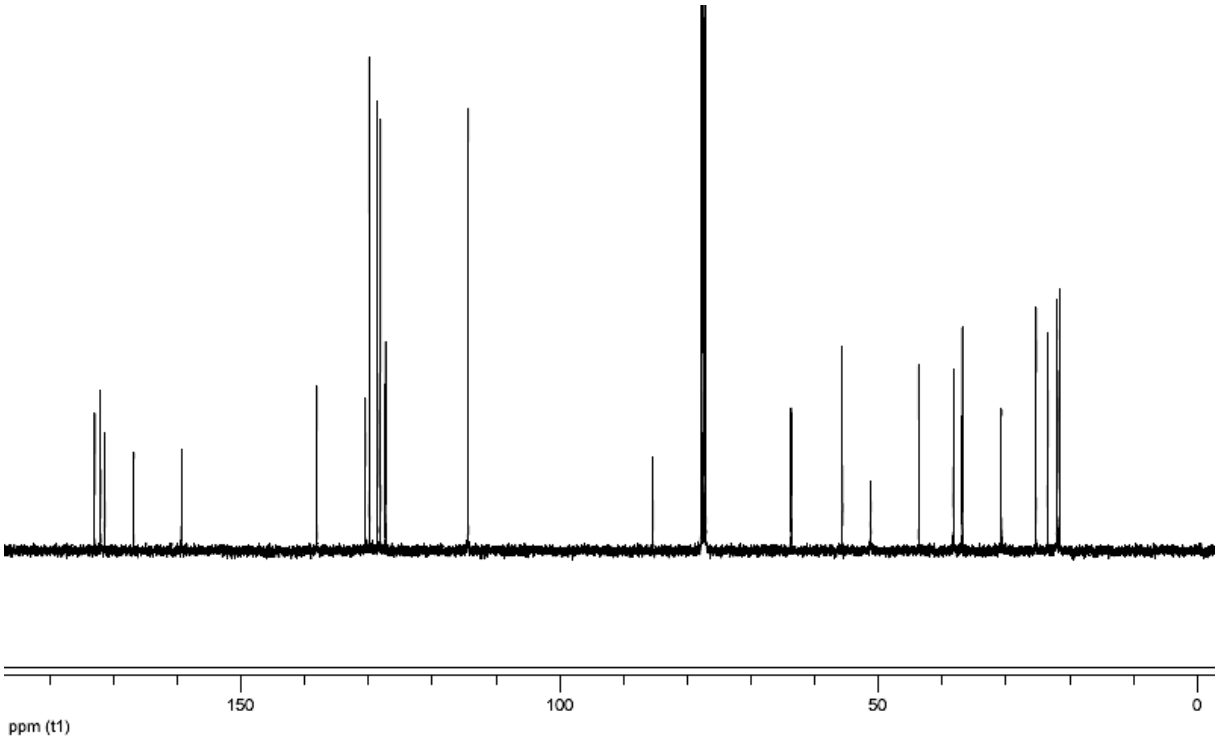
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (t, *J* = 5.3 Hz, 1H), 7.21-7.07 (m, 7H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.02 (d, *J* = 15.2 Hz, 1H), 4.53 (dd, *J* = 8.5, 6.1 Hz, 1H), 4.36 (dd, *J* = 14.3, 5.6 Hz, 1H), 4.31 (d, *J* = 15.2 Hz, 1H), 4.23 (dd, *J* = 14.3, 5.4 Hz, 1H), 3.80 (s, 3H), 2.83 (sept, *J* = 6.9 Hz, 1H), 2.62 (s, 3H), 2.00-1.84 (m, 2H), 1.72-1.59 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.71 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.9, 172.0, 171.4, 166.8, 159.3, 138.1, 130.5, 129.9, 128.6, 128.1, 127.3, 114.4, 85.4, 63.7, 55.7, 51.3, 43.7, 38.3, 36.9, 30.7, 25.3, 23.5, 22.1, 22.0, 21.6.

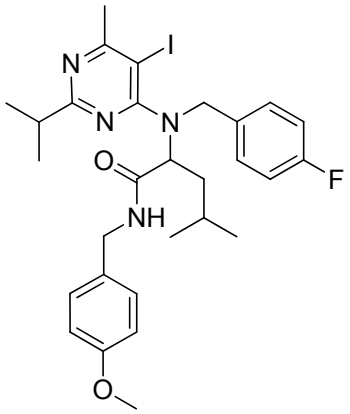
I.R. (thin film) 1661, 1534, 1511, 1454 cm^{-1}.

HRMS Calculated for $C_{29}H_{37}IN_4O_2$ 600.1961, found 600.1947.





2-[(4-fluorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{29}H_{36}FIN_4O_2$
MW = 618.52 g.mol^{-1}

1k

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-fluorobenzylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1k** as a colorless oil.

Yield 60 % (740 mg).

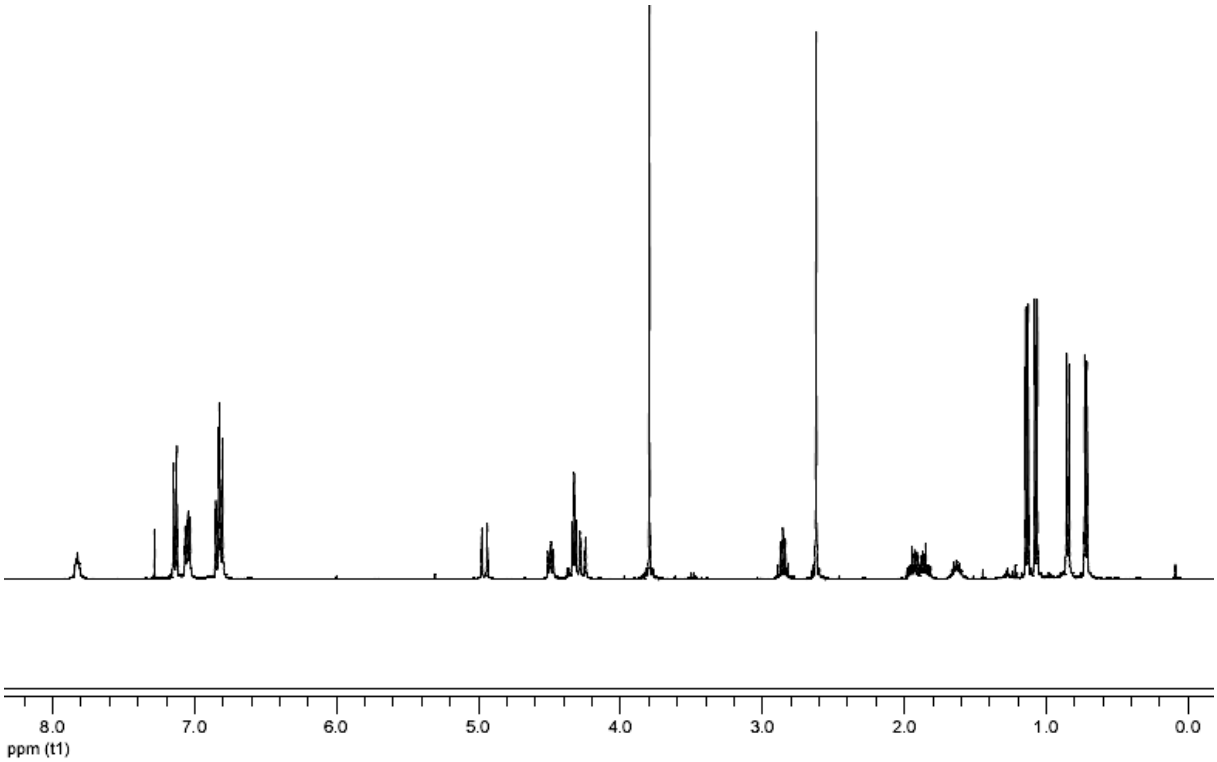
R_f 0.3 (70:30 petroleum ether / diethyl ether).

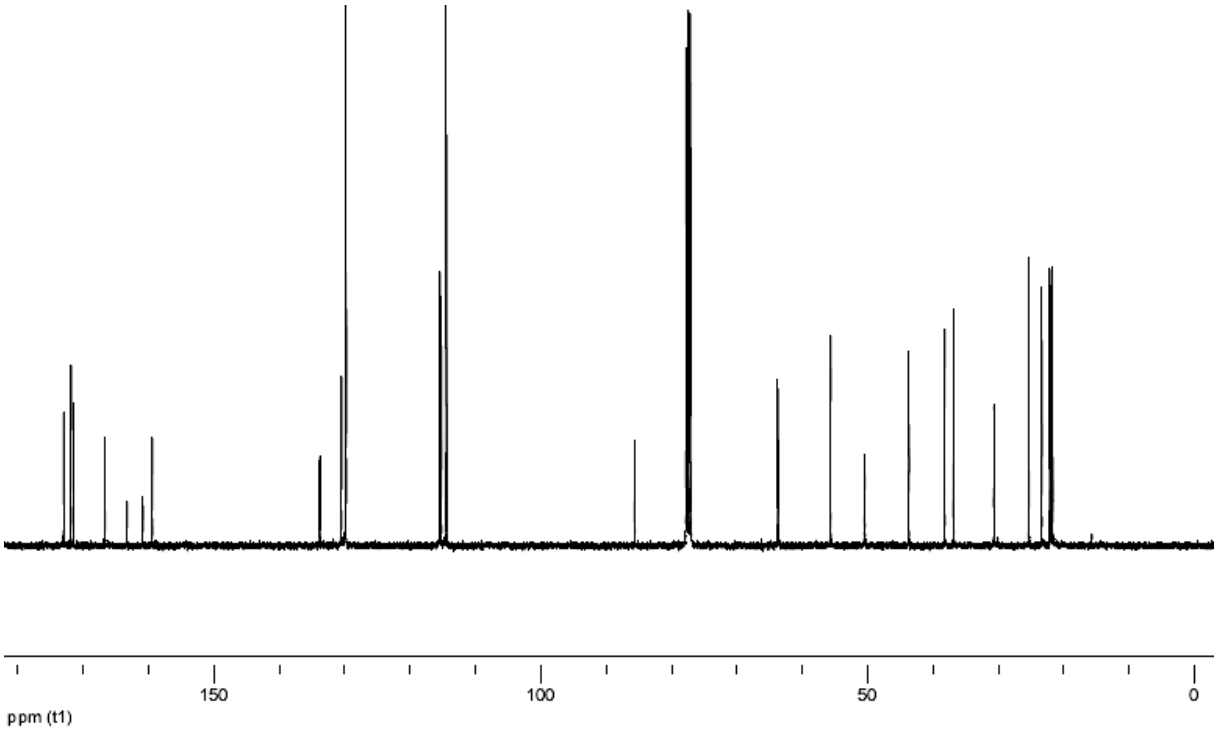
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (t, J = 5.3 Hz, 1H), 7.14 (d, J = 8.6 Hz, 2H), 7.05 (dd, $J_{H\text{-}H,\ H\text{-}F}$ = 8.6, 5.6 Hz, 2H), 6.83 (t, $J_{H\text{-}H} = J_{H\text{-}F}$ = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.96 (d, J = 15.1 Hz, 1H), 4.49 (dd, J = 8.3, 6.2 Hz, 1H), 4.35 (dd, J = 14.4, 5.3 Hz, 1H), 4.30 (dd, J = 14.4, 5.6 Hz, 1H), 4.26 (d, J = 15.1 Hz, 1H), 3.80 (s, 3H), 2.86 (sept, J = 6.9 Hz, 1H), 2.62 (s, 3H), 1.99-1.90 (m, 1H), 1.90-1.80 (m, 1H), 1.69-1.58 (m, 1H), 1.14 (d, J = 6.9 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H), 0.72 (d, J = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 171.9, 171.5, 166.7, 162.1 (d, $J_{C\text{-}F}$ = 245.2 Hz), 159.5, 133.8 (d, $J_{C\text{-}F}$ = 2.9 Hz), 130.5, 129.8, 129.8 (d, $J_{C\text{-}F}$ = 8.0 Hz), 115.3 (d, $J_{C\text{-}F}$ = 21.3 Hz), 114.4, 85.6, 63.7, 55.7, 50.5, 43.7, 38.2, 36.9, 30.7, 25.4, 23.4, 22.1, 22.0, 21.7.

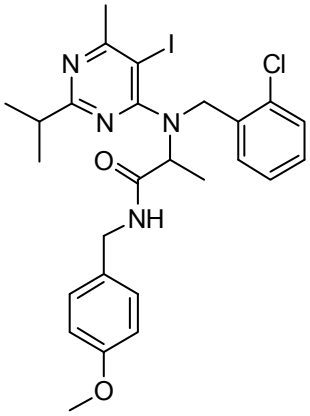
I.R. (thin film) 1664, 1537, 1511, 1466 cm^{-1}.

HRMS Calculated for $C_{29}H_{36}FIN_4O_2$ 618.1867, found 618.1840.





2-[(2-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-*N*-(4-methoxybenzyl)-propionamide



$C_{26}H_{30}ClIN_4O_2$
MW = 592.90 g.mol^{-1}

1l

General procedure using acetaldehyde (110 µL, 2 mmol), *o*-chlorobenzylamine (240 µL, 2 mmol), *p*-methoxybenzylisocyanide (300 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 80:20) gave **1l** as a colorless oil.

Yield 54 % (640 mg).

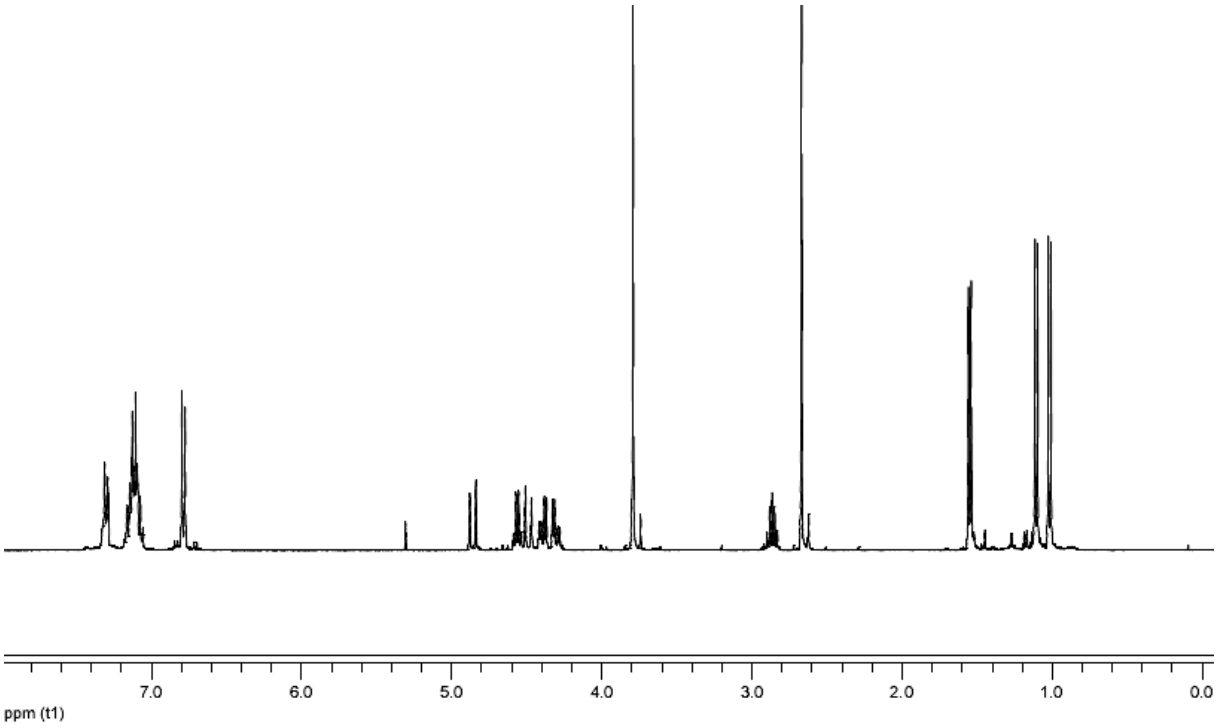
R_f 0.3 (80:20 petroleum ether / diethyl ether).

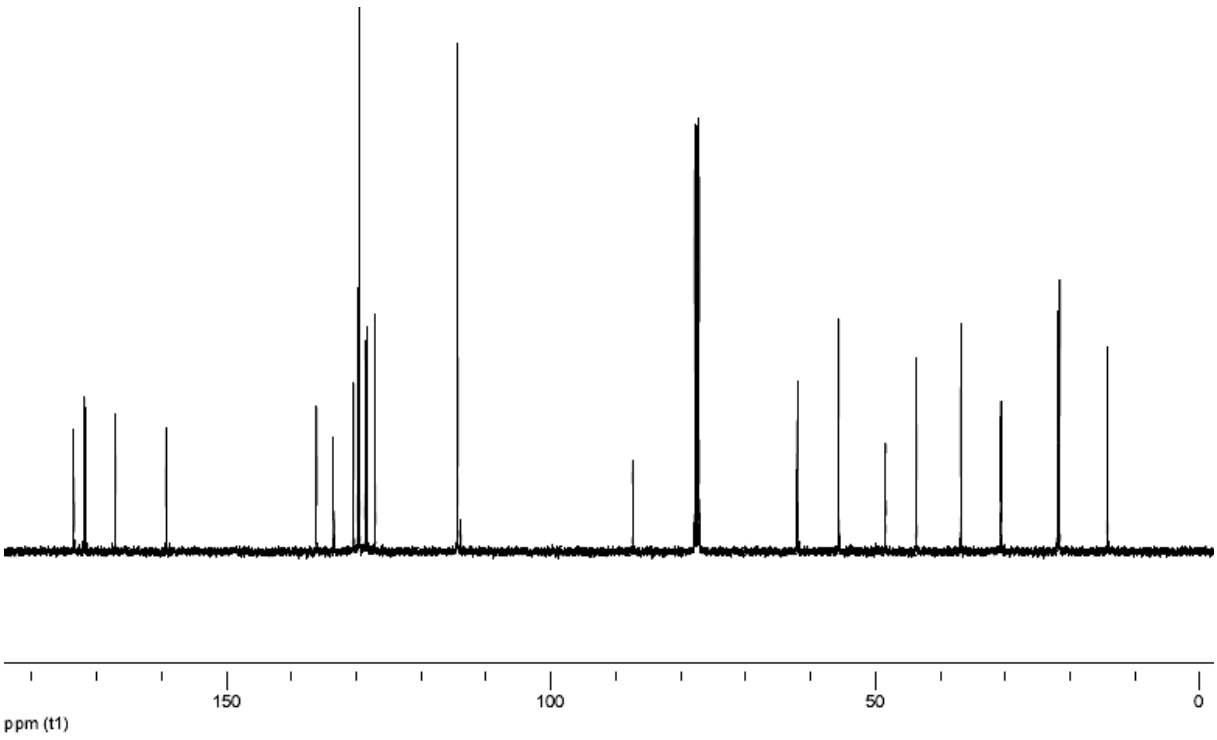
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35-7.29 (m, 2H), 7.19-7.05 (m, 5H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.86 (d, *J* = 16.2 Hz, 1H), 4.56 (q, *J* = 7.0 Hz, 1H), 4.49 (d, *J* = 16.2 Hz, 1H), 4.39 (dd, *J* = 14.4, 5.9 Hz, 1H), 4.31 (dd, *J* = 14.4, 5.3 Hz, 1H), 3.79 (s, 3H), 2.86 (sept, *J* = 6.9 Hz, 1H), 2.67 (s, 3H), 1.55 (d, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.6, 172.2, 172.0, 167.2, 159.3, 136.2, 133.5, 130.4, 129.8, 129.5, 128.6, 128.4, 127.1, 114.4, 87.4, 62.0, 55.7, 48.4, 43.7, 36.8, 30.7, 21.8, 21.6, 14.3.

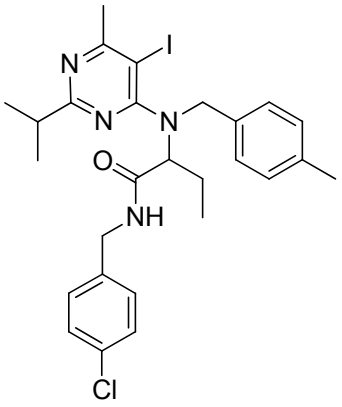
I.R. (thin film) 1667, 1534, 1511, 1443 cm^{-1}.

HRMS Calculated for [$C_{26}H_{30}ClIN_4O_2$ - $C_9H_{10}NO_2$] 428.0390, found 428.0393.





_N_-(4-chlorobenzyl)-2-[(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-(4-methylbenzyl)-amino]-butyramide



$C_{27}H_{32}ClIN_4O$
MW = 590.93 g.mol^{-1}

1m

General procedure using propionaldehyde (150 µL, 2 mmol), *p*-methylbenzylamine (260 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1m** as a colorless oil.

Yield 55 % (650 mg).

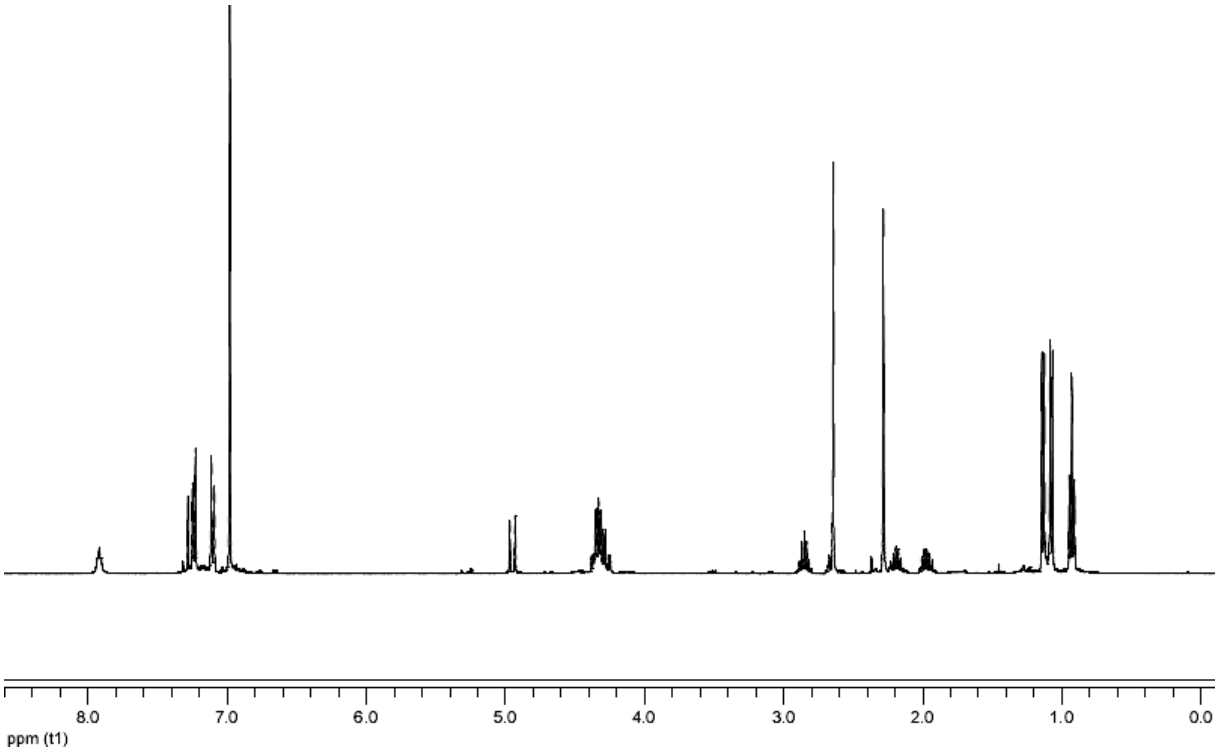
R_f 0.3 (70:30 petroleum ether / diethyl ether).

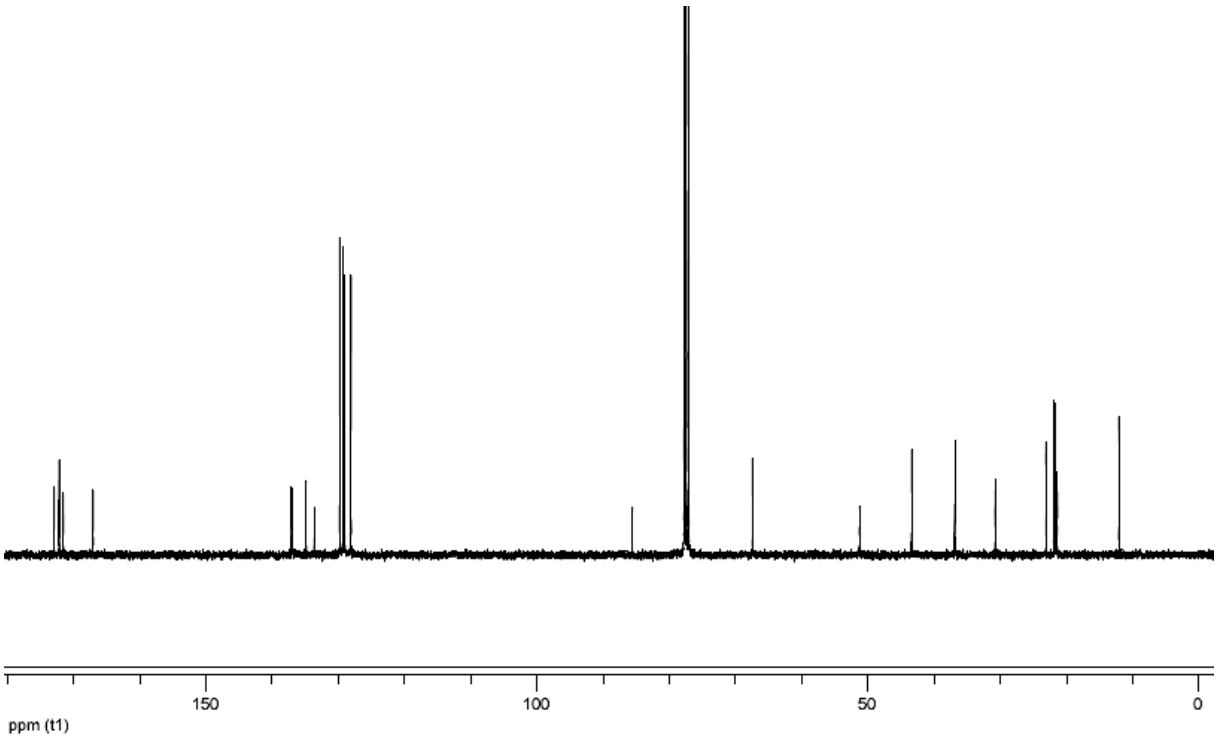
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92 (t, *J* = 5.8 Hz, 1H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 6.98 (s, 4H), 4.95 (d, *J* = 15.2 Hz, 1H), 4.39-4.24 (m, 4H), 2.85 (sept, *J* = 6.9 Hz, 1H), 2.64 (s, 3H), 2.28 (s, 3H), 2.25-2.11 (m, 1H), 2.03-1.90 (m, 1H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 172.2, 171.6, 167.1, 137.1, 137.0, 134.9, 132.6, 129.8, 129.3, 129.1, 128.1, 85.6, 67.4, 51.3, 43.4, 36.9, 30.8, 23.1, 21.9, 21.7, 21.4, 12.1.

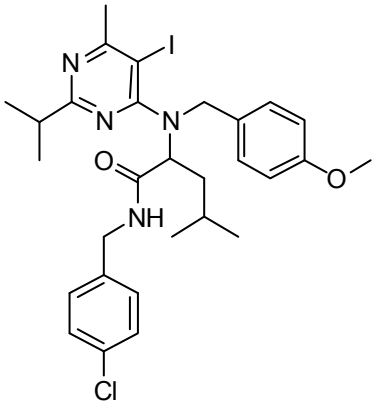
I.R. (thin film) 1661, 1531, 1515, 1344 cm^{-1}.

HRMS Calculated for $C_{27}H_{32}ClIN_4O$ 590.1309, found 509.1339.





2-[(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-(4-methoxybenzyl)-amino]-4-methyl-pentanoic acid 4-chlorobenzylamide



$C_{29}H_{36}ClIN_4O_2$

MW = 634.98 g.mol^{-1}

1n

General procedure using isovaleraldehyde (220 µL, 2 mmol), *p*-methoxybenzylamine (300 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1n** as a colorless oil.

Yield 89 % (1.15 g).

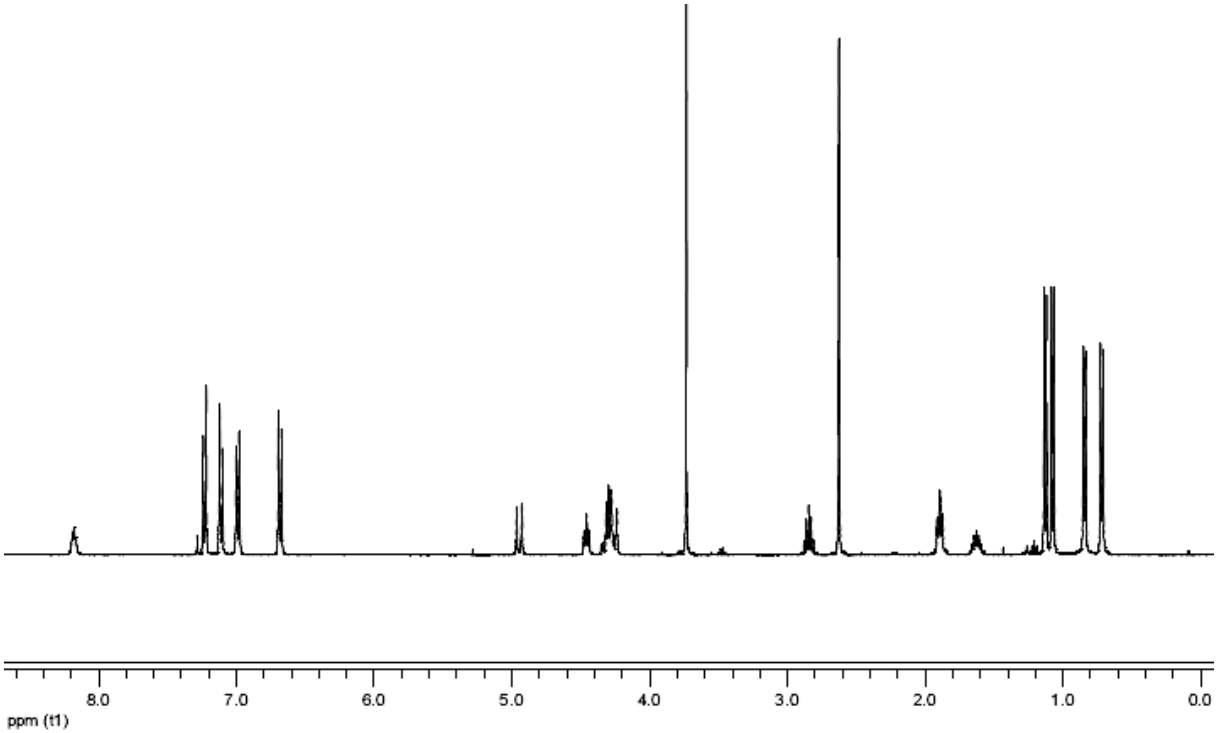
R_f 0.3 (70:30 petroleum ether / diethyl ether).

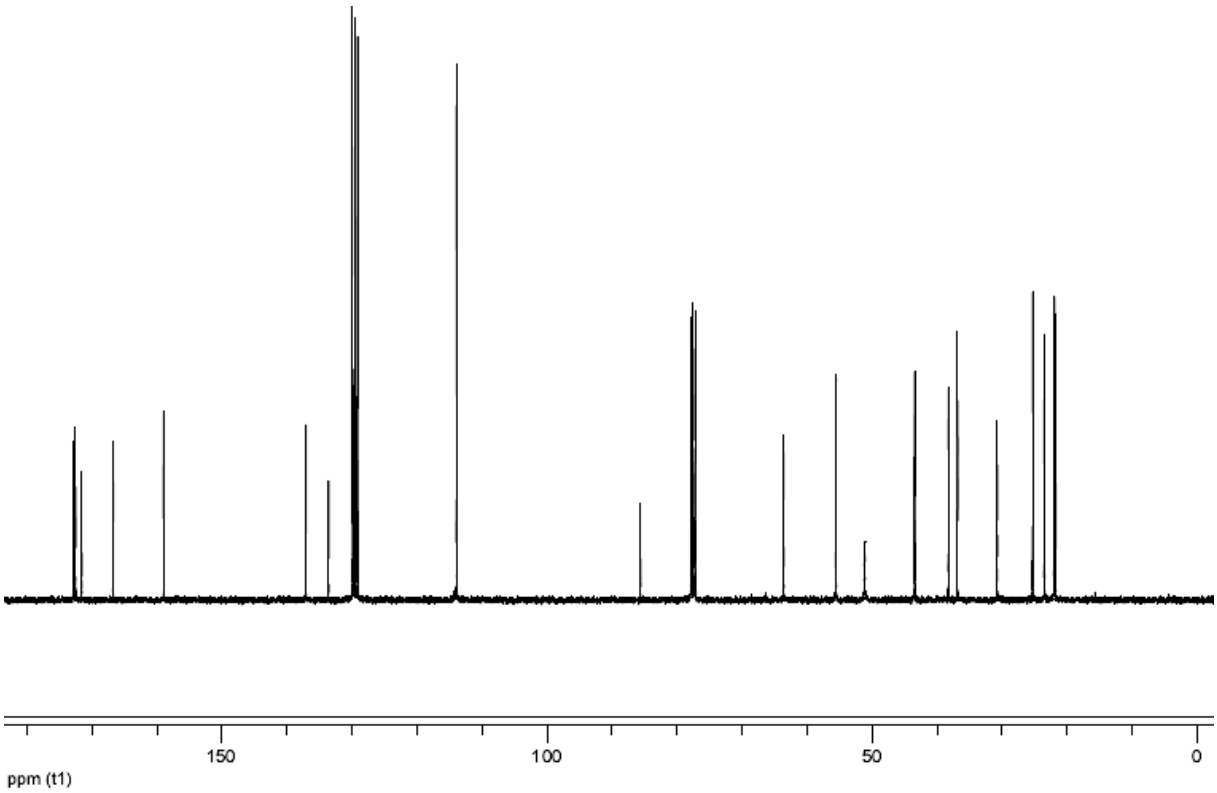
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18 (t, *J* = 5.3 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.68 (d, *J* = 8.6 Hz, 2H), 4.95 (d, *J* = 15.0 Hz, 1H), 4.46 (dd, *J* = 7.6, 7.0 Hz, 1H), 4.37-4.21 (m, 3H), 3.74 (s, 3H), 2.85 (sept, *J* = 6.9 Hz), 2.63 (s, 3H), 1.97-1.82 (m, 2H), 1.71-1.55 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.72 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.9, 172.5, 171.6, 166.7, 159.0, 137.1, 133.6, 129.9, 129.8, 129.6, 129.1, 113.9, 85.6, 63.6, 55.6, 51.2, 43.4, 38.3, 36.9, 30.8, 25.3, 23.5, 22.0, 22.0, 21.8.

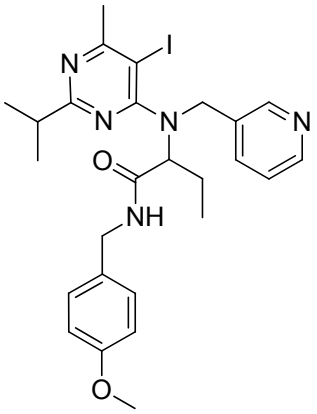
I.R. (thin film) 1667, 1534, 1510, 1459 cm^{-1}.

HRMS Calculated for [$C_{29}H_{36}ClIN_4O_2$ - C_8H_7ClNO] 466.1355, found 466.1361.


8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


150
100
50
0
ppm (t1)

2-[(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-pyridin-3-ylmethyl-amino]-*N*-(4-methoxybenzyl)-butyramide



$C_{26}H_{32}IN_5O_2$
MW = 573.47 g.mol^{-1}

General procedure using propionaldehyde (150 µL, 2 mmol), pyridin-3-ylmethylamine (250 µL, 2 mmol), *p*-methoxybenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **1o** as a colorless oil.

Yield 41 % (470 mg).

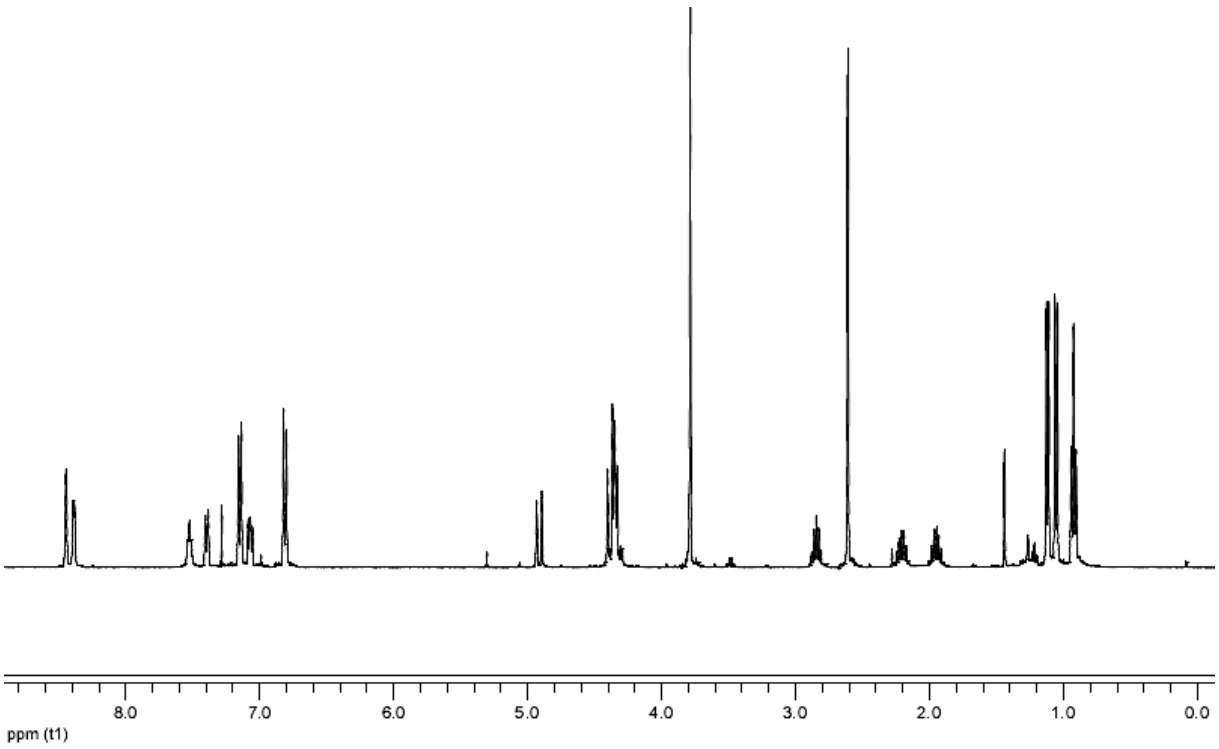
R_f 0.3 (70:30 petroleum ether / diethyl ether).

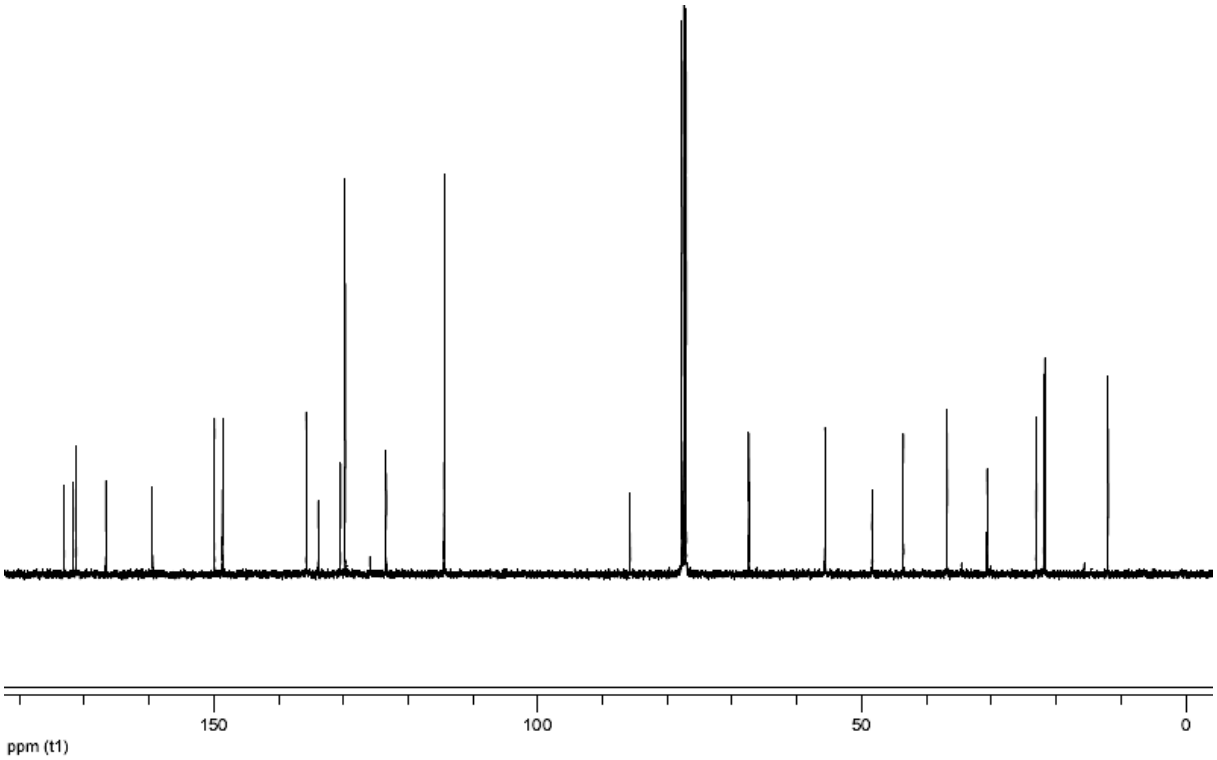
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H), 8.39 (d, *J* = 4.7 Hz, 1H), 7.52 (t, *J* = 5.3 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 7.4 Hz, 2H), 7.07 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.81 (d, *J* = 7.4 Hz, 2H), 4.91 (d, *J* = 15.2 Hz, 1H), 4.41-4.29 (m, 4H), 3.79 (s, 3H), 2.84 (sept, *J* = 6.8 Hz, 1H), 2.61 (s, 3H), 2.27-2.14 (m, 1H), 2.02-1.88 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 173.2, 171.7, 171.3, 166.7, 159.5, 149.9, 148.7, 135.7, 133.9, 130.5, 129.7, 123.4, 114.5, 85.8, 67.5, 55.7, 48.4, 43.6, 36.9, 30.7, 23.1, 21.9, 21.7, 12.0.

I.R. (thin film) 1661, 1534, 1511, 1428 cm^{-1}.

HRMS Calculated for $C_{26}H_{32}IN_5O_2$ 573.1601, found 573.1603.



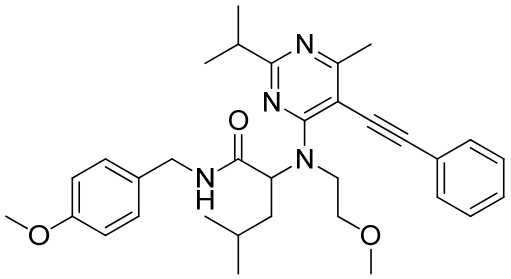


General procedure for the synthesis of the Ugi-Smiles/Sonogashira adducts :

To a 0.1 M solution of Smiles adduct in acetonitrile were successively added alkyne (1.2 equiv.), *bis*(triphenylphosphine)palladium chloride (5 mol %), CuI (5 mol%) and diisopropylethylamine (1 equiv.). The resulting mixture was stirred at 70 °C overnight.

The crude mixture was first filtered and rinsed with methanol. After removal of the volatile materials, purification by flash chromatography gave the corresponding Ugi-Smiles/Sonogashira adduct.

2-[(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-(2-methoxyethyl)-amino]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{33}H_{42}N_4O_3$
MW = 542.71 g.mol^{-1}

2a

General procedure using **1a** (280 mg, 0.52 mmol), phenylacetylene (70 µL, 0.62 mmol), *bis*(triphenylphosphine)palladium chloride (18 mg, 0.03 mmol), CuI (5 mg, 0.03 mmol) and diisopropylethylamine (90 µL, 0.52 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2a** as a colorless oil.

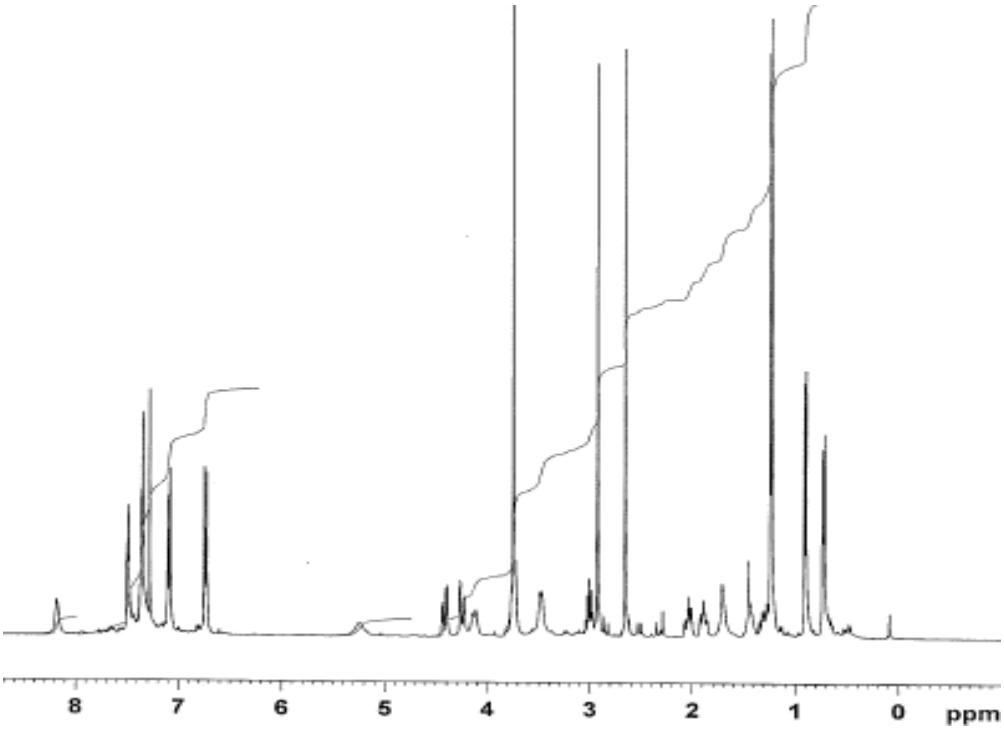
Yield 64 % (180 mg).

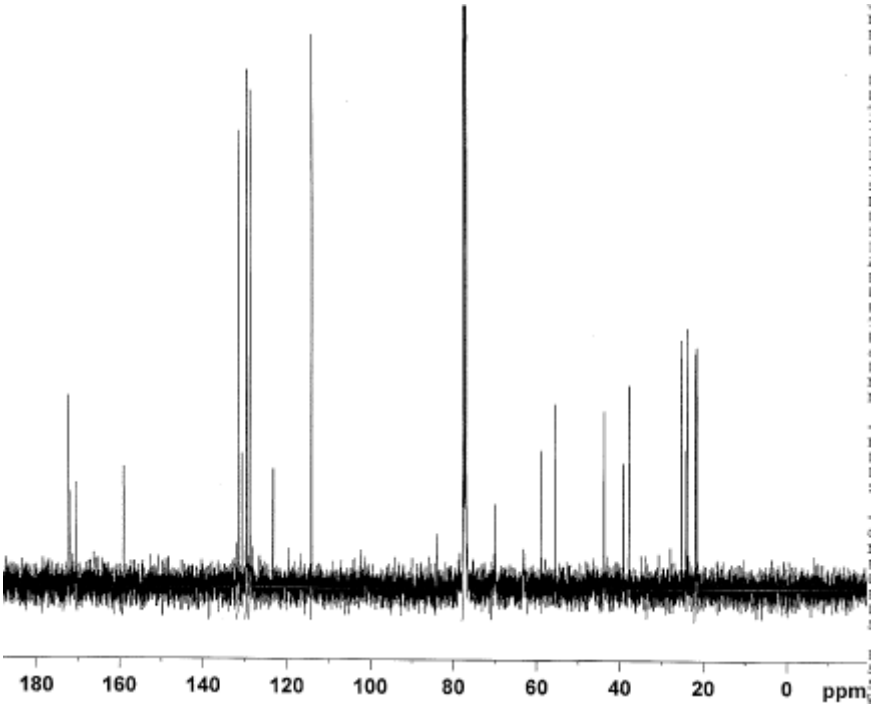
R_f 0.3 (60:40 petroleum ether / diethyl ether).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24-8.15 (br s, 1H), 7.53-7.47 (m, 2H), 7.39-7.33 (m, 3H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 5.34-5.16 (br s, 1H), 4.42 (dd, *J* = 14.4, 5.8 Hz, 1H), 4.25 (dd, *J* = 14.4, 4.5 Hz, 1H), 4.13 (d, *J* = 13.1 Hz, 1H), 3.79-3.71 (m, 1H), 3.75 (s, 3H), 3.53-3.44 (m, 2H), 3.00 (sept, *J* = 6.8 Hz, 1H), 2.93 (s, 3H), 2.66 (s, 3H), 2.09-2.00 (m, 1H), 1.95-1.84 (m, 1H), 1.50-1.38 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 6H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.73 (d, *J* = 6.6 Hz, 3H).

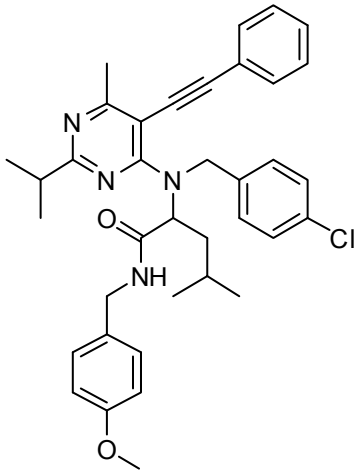
^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.4, 171.9, 170.6, 162.7, 159.1, 131.6, 130.8, 129.7, 129.0, 128.9, 123.3, 114.2, 102.3, 100.7, 84.0, 70.1, 63.4, 59.0, 55.6, 43.8, 39.2, 37.8, 25.3, 24.4, 23.9, 22.1, 21.7, 21.6.

HRMS Calculated for $C_{33}H_{42}N_4O_3$ 542.3257, found 542.3259.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynyl-pyrimidin-4-yl)-amino]-4-methylpentanoic acid 4-methylbenzylamide



$C_{37}H_{41}ClN_4O_2$
MW = 609.20 g.mol^{-1}

2b

General procedure using **1b** (740 mg, 1.17 mmol), phenylacetylene (160 µL, 1.20 mmol), *bis*(triphenylphosphine)palladium chloride (42 mg, 0.06 mmol), CuI (12 mg, 0.06 mmol) and diisopropylethylamine (200 µL, 1.17 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2b** as a colorless oil.

Yield 59 % (420 mg).

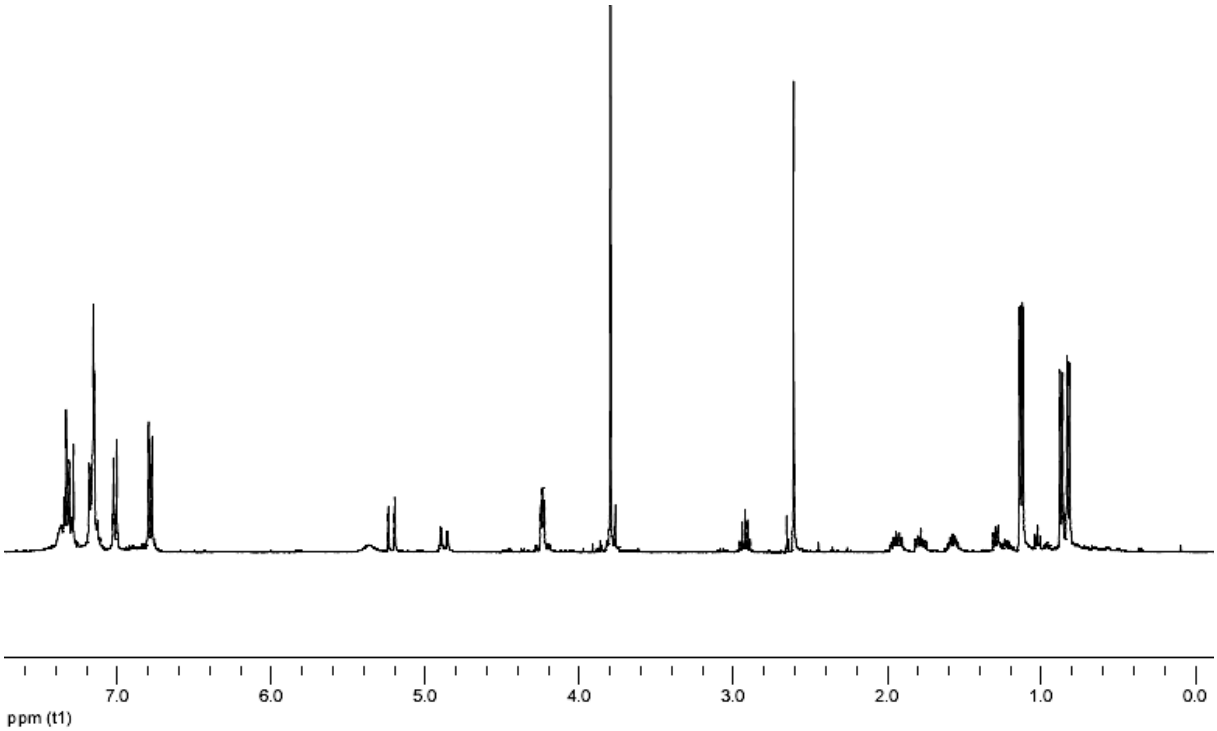
R_f 0.3 (70:30 petroleum ether / diethyl ether).

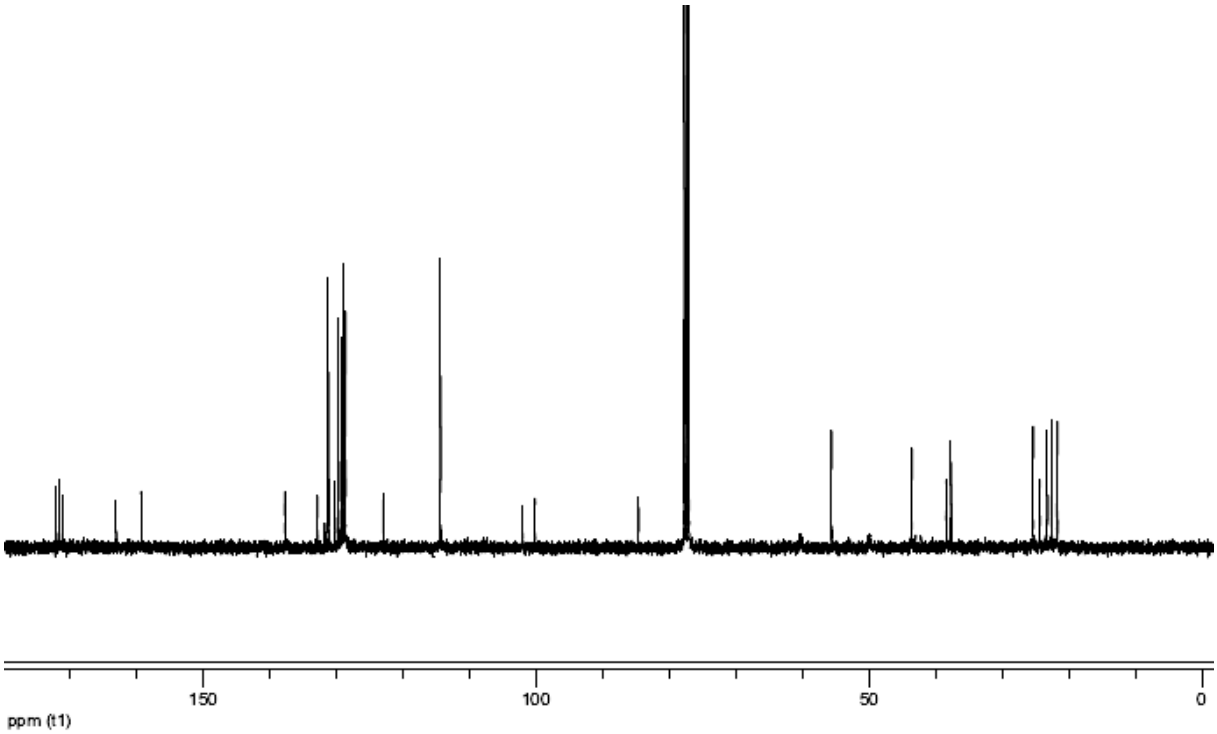
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.26 (m, 4H), 7.21-7.10 (m, 6H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 5.44-5.28 (m, 1H), 5.22 (d, *J* = 16.7 Hz, 1H), 4.87 (d, *J* = 16.7 Hz, 1H), 4.30-4.18 (m, 2H), 3.80 (s, 3H), 2.92 (sept, *J* = 6.8 Hz, 1H), 2.61 (s, 3H), 2.00-1.88 (m, 1H), 1.83-1.73 (m, 1H), 1.63-1.52 (sept, *J* = 6.6 Hz, 1H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 171.6, 171.2, 163.1, 159.4, 137.8, 132.9, 131.2, 130.3, 129.7, 129.3, 129.1, 128.9, 128.7, 123.0, 114.4, 102.1, 100.2, 84.7, 60.4, 55.7, 50.0, 43.6, 38.5, 37.8, 25.4, 24.5, 23.3, 22.7, 21.8, 21.7.

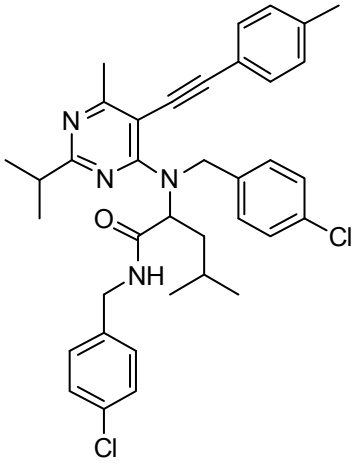
I.R. (thin film) 1676, 1514, 1491, 1465 cm^{-1}.

HRMS Calculated for $C_{37}H_{41}ClN_4O_2$ 608.2918, found 608.2923.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-p-tolylethynylpyrimidin-4-yl)-amino]-4-methyl-pentanoic acid 4-chlorobenzylamide



$C_{37}H_{40}Cl_2N_4O$

MW = 627.65 g.mol^{-1}

2c

General procedure using **1c** (800 mg, 1.25 mmol), 1-ethynyl-4-methylbenzene (190 µL, 1.50 mmol), *bis*(triphenylphosphine)palladium chloride (44 mg, 0.06 mmol), CuI (13 mg, 0.06 mmol) and diisopropylethylamine (215 µL, 1.25 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2c** as a colorless oil.

Yield 60 % (470 mg).

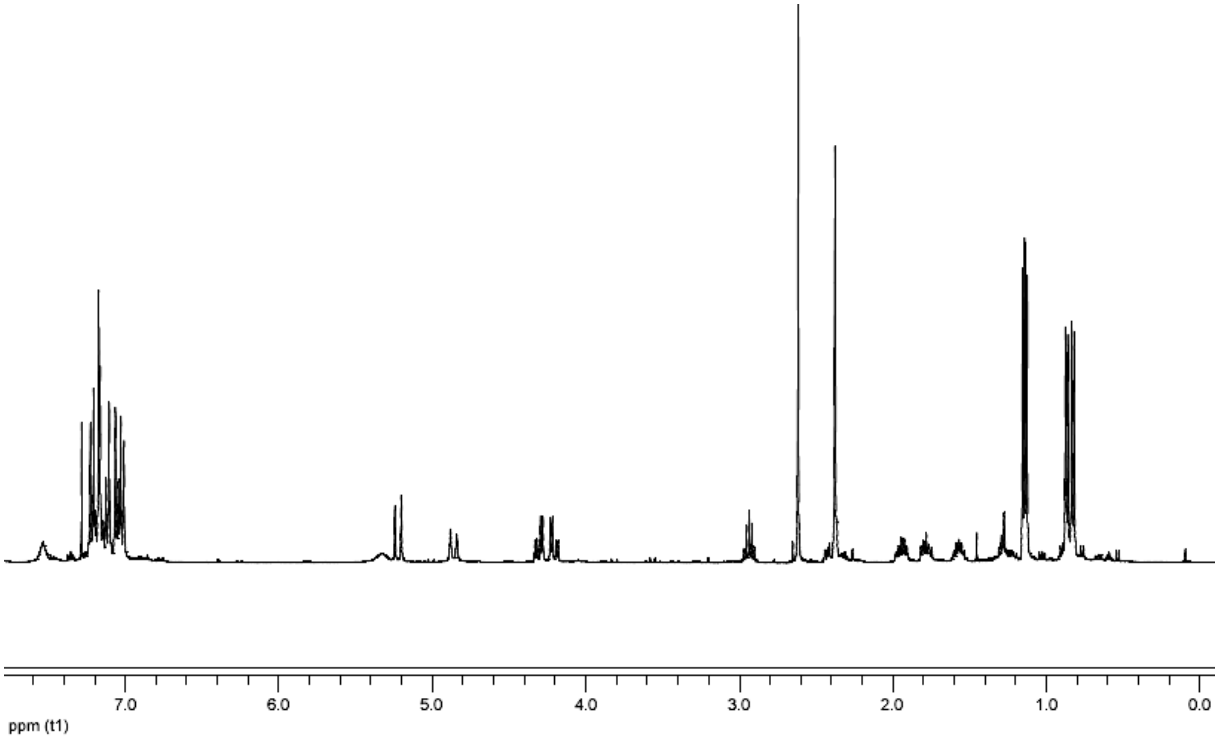
R_f 0.3 (70:30 petroleum ether / diethyl ether).

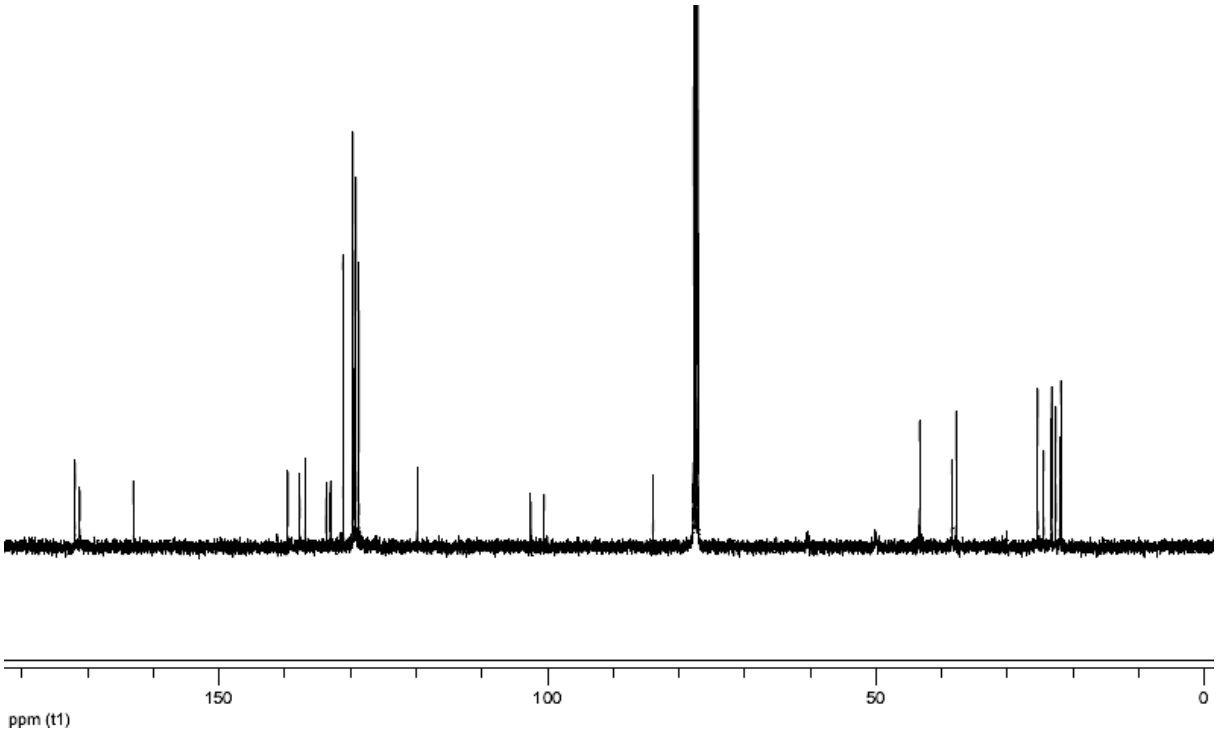
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61-7.50 (m, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.20-7.14 (m, 4H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 5.45-5.26 (m, 1H), 5.23 (d, *J* = 16.4 Hz, 1H), 4.86 (d, *J* = 16.4 Hz, 1H), 4.31 (dd, *J* = 14.7, 5.8 Hz, 1H), 4.21 (dd, *J* = 14.7, 5.6 Hz, 1H), 2.94 (sept, *J* = 6.9 Hz, 1H), 2.62 (s, 3H), 2.38 (s, 3H), 2.00-1.89 (m, 1H), 1.83-1.73 (m, 1H), 1.63-1.51 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.9, 171.2, 163.0, 139.5, 137.8, 136.9, 133.7, 133.0, 131.1, 129.7, 129.6, 129.3, 129.2, 128.7, 119.8, 102.5, 100.5, 83.9, 60.5, 50.1, 43.4, 38.5, 37.8, 25.4, 24.5, 23.3, 22.7, 22.0, 21.9, 21.8.

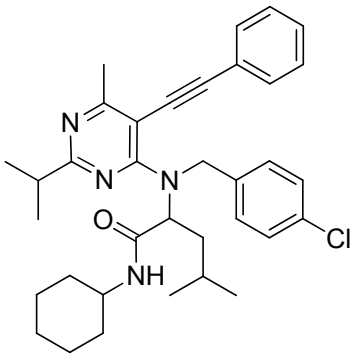
I.R. (thin film) 1679, 1530, 1511, 1496 cm^{-1}.

HRMS Calculated for $C_{37}H_{40}Cl_2N_4O$ 626.2579, found 626.2575.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-4-methylpentanoic acid cyclohexylamide



$C_{35}H_{43}ClN_4O$
MW = 571.20 g.mol^{-1}

2d

General procedure using **1d** (415 mg, 0.70 mmol), phenylacetylene (120 µL, 0.84 mmol), *bis*(triphenylphosphine)palladium chloride (25 mg, 0.04 mmol), CuI (7 mg, 0.04 mmol) and diisopropylethylamine (120 µL, 0.70 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2d** as a colorless oil.

Yield 64 % (255 mg).

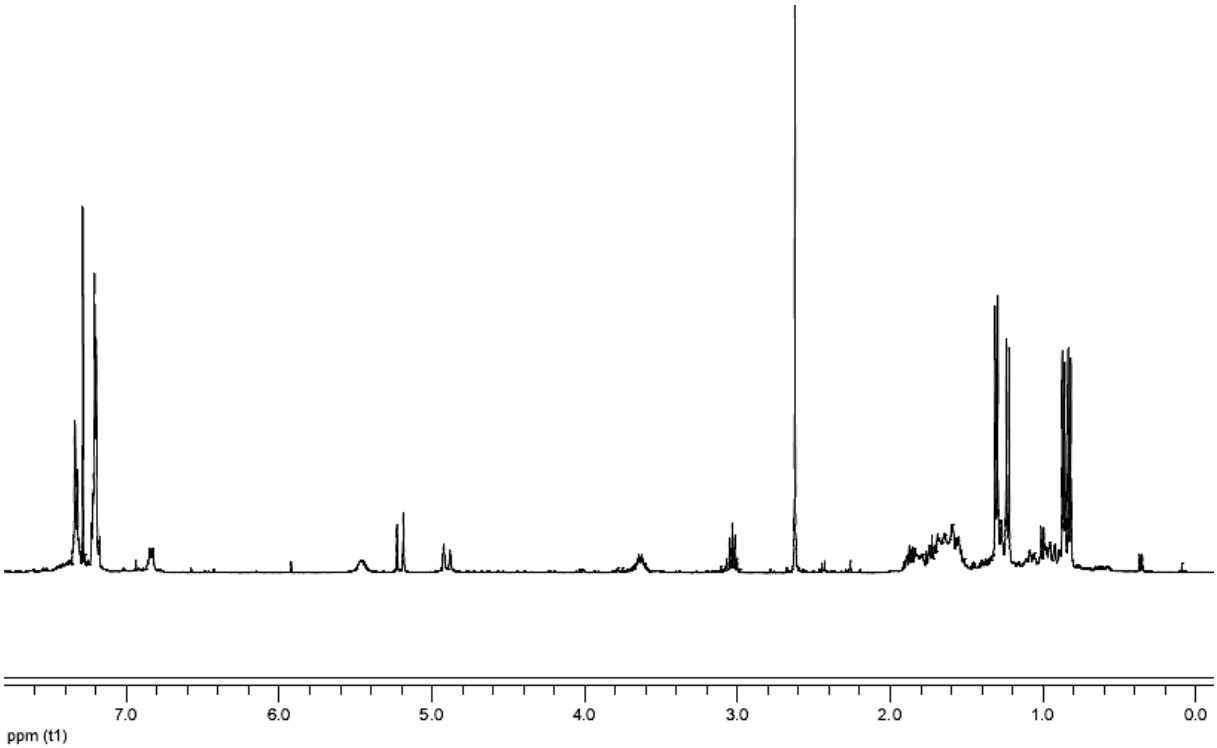
R_f 0.3 (70:30 petroleum ether / diethyl ether).

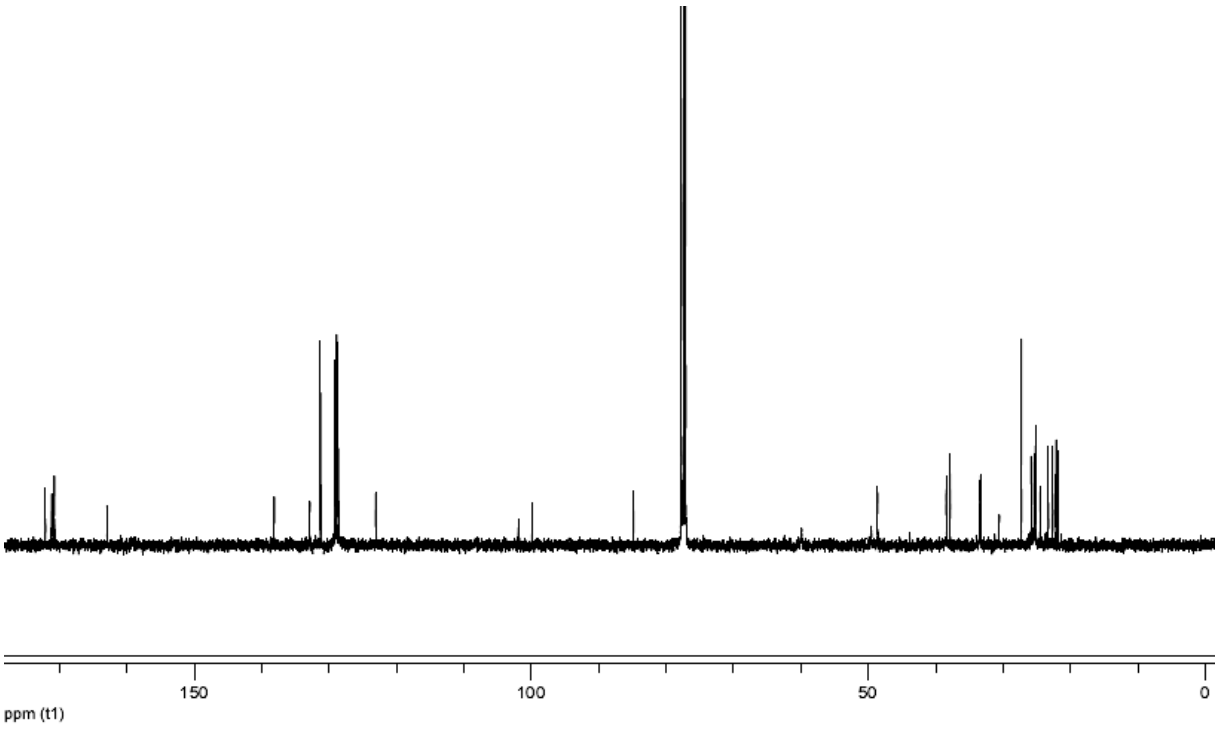
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.29 (m, 3H), 7.25-7.17 (m, 6H), 6.84 (d, *J* = 7.9 Hz, 1H), 5.54-5.40 (m, 1H), 5.21 (d, *J* = 16.6 Hz, 1H), 4.90 (d, *J* = 16.6 Hz, 1H), 3.71-3.58 (m, 1H), 3.04 (sept, *J* = 6.9 Hz, 1H), 2.62 (s, 3H), 1.93-1.77 (m, 2H), 1.77-1.48 (m, 6H), 1.30-1.24 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.15-0.88 (m, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 171.2, 170.7, 163.0, 138.1, 132.8, 131.3, 129.1, 129.1, 128.9, 128.6, 123.1, 101.9, 99.9, 84.9, 59.9, 49.6, 48.6, 37.9, 33.5, 33.3, 25.9, 25.4, 24.5, 23.3, 22.7, 22.2, 22.2, 21.9.

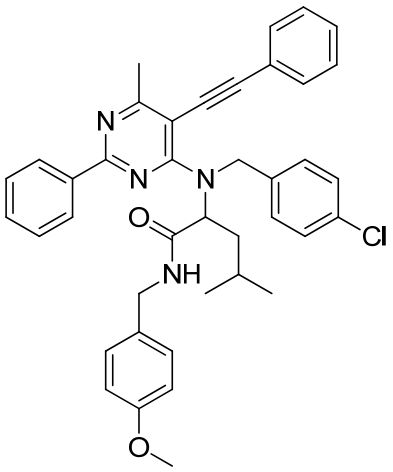
I.R. (thin film) 1678, 1528, 1491, 1407 cm^{-1}.

HRMS Calculated for $C_{35}H_{43}ClN_4O$ 570.3125, found 570.3123.





2-[(4-chlorobenzyl)-(6-methyl-2-phenyl-5-phenylethynylpyrimidin-4-yl)-amino]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{40}H_{39}ClN_4O_2$
MW = 643.22 g.mol^{-1}

2e

General procedure using **1e** (810 mg, 1.21 mmol), phenylacetylene (160 µL, 1.45 mmol), *bis*(triphenylphosphine)palladium chloride (44 mg, 0.06 mmol), CuI (12 mg, 0.06 mmol) and diisopropylethylamine (210 µL, 1.21 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2e** as a colorless oil.

Yield 66 % (515 mg).

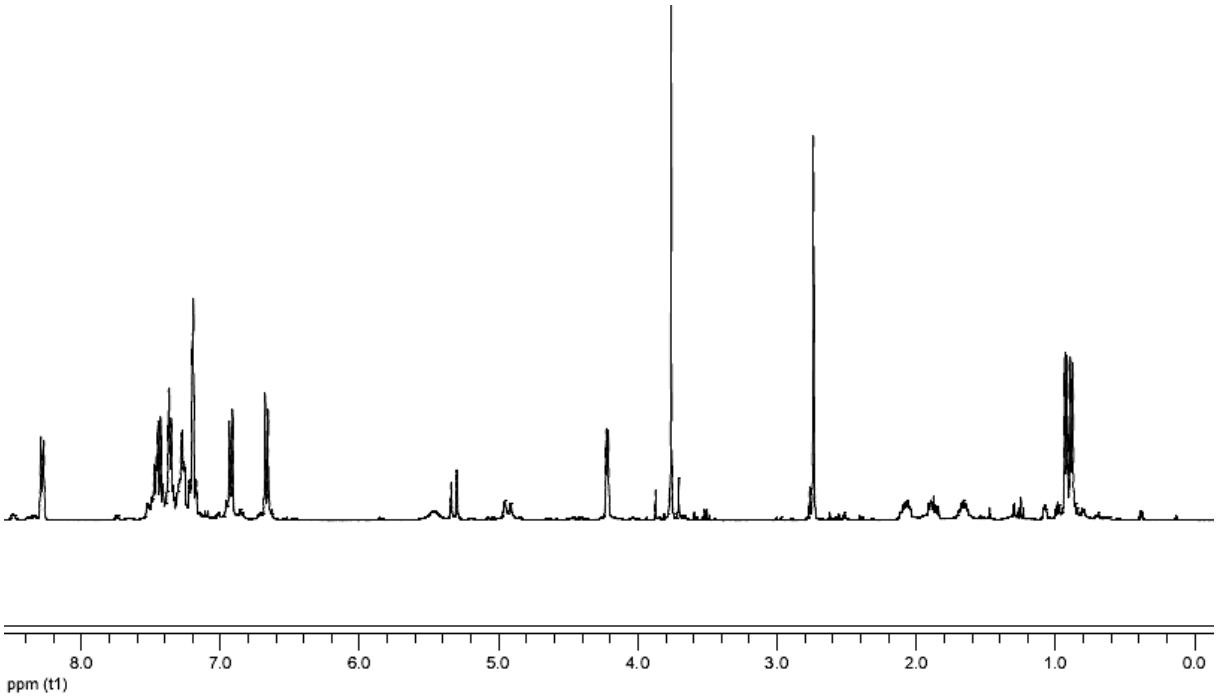
R_f 0.3 (70:30 petroleum ether / diethyl ether).

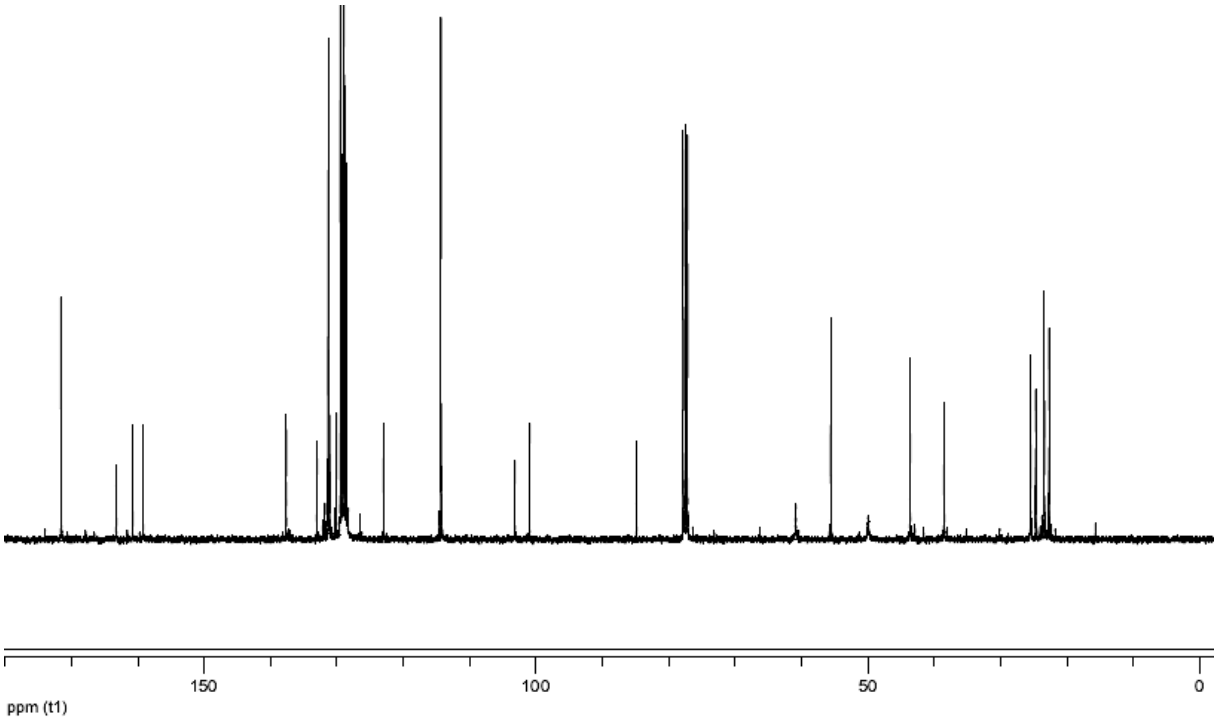
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 7.3 Hz, 2H), 7.54-7.32 (m, 7H), 7.28-7.23 (m, 2H), 7.22-7.15 (m, 4H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 8.6 Hz, 2H), 5.55-5.37 (m, 1H), 5.31 (d, *J* = 16.4 Hz, 1H), 4.91 (d, *J* = 16.4 Hz, 1H), 4.20 (d, *J* = 5.4 Hz, 2H), 3.76 (s, 3H), 2.72 (s, 3H), 2.12-2.00 (m, 1H), 1.91-1.80 (m, 1H), 1.68-1.58 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.6, 171.6, 163.3, 160.8, 159.2, 137.7, 137.6, 133.0, 131.3, 131.1, 130.1, 129.5, 129.3, 129.2, 129.0, 128.9, 128.9, 128.6, 123.0, 114.3, 103.2, 101.0, 84.9, 60.9, 55.6, 50.0, 43.7, 38.6, 25.6, 24.7, 23.4, 22.7.

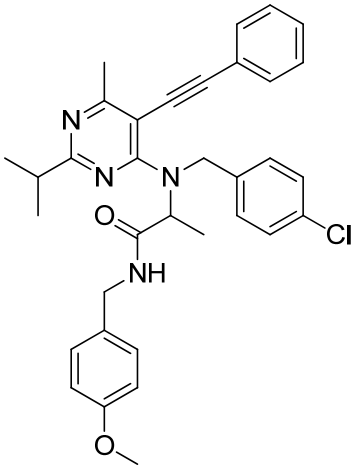
I.R. (thin film) 1673, 1513, 1493, 1403 cm^{-1}.

HRMS Calculated for $C_{40}H_{39}ClN_4O_2$ 642.2762, found 642.2737.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-*N*-(4-methoxybenzyl)-propionamide



$C_{34}H_{35}ClN_4O_2$
MW = 567.12 g.mol^{-1}

2f

General procedure using **1f** (640 mg, 1.08 mmol), phenylacetylene (140 µL, 1.30 mmol), *bis*(triphenylphosphine)palladium chloride (38 mg, 0.05 mmol), CuI (11 mg, 0.05 mmol) and diisopropylethylamine (190 µL, 1.08 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 60:40) afforded **2f** as a colorless oil.

Yield 71 % (435 mg).

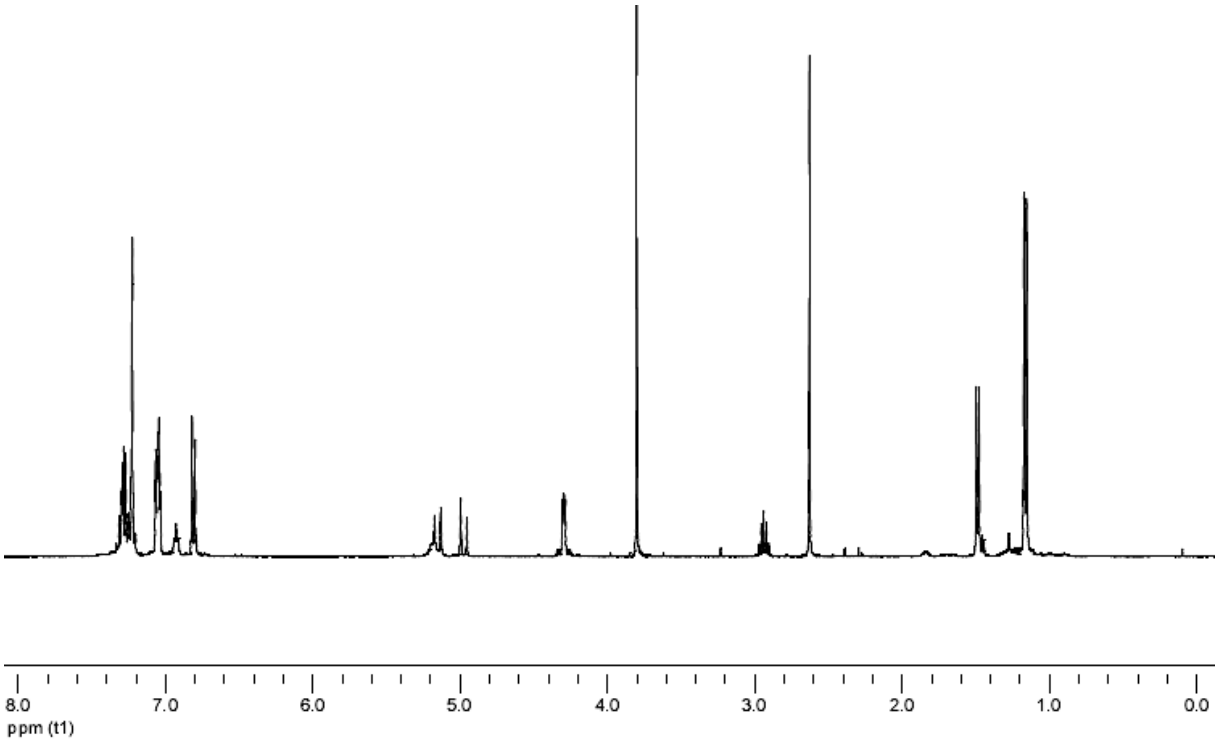
R_f 0.3 (60:40 petroleum ether / diethyl ether).

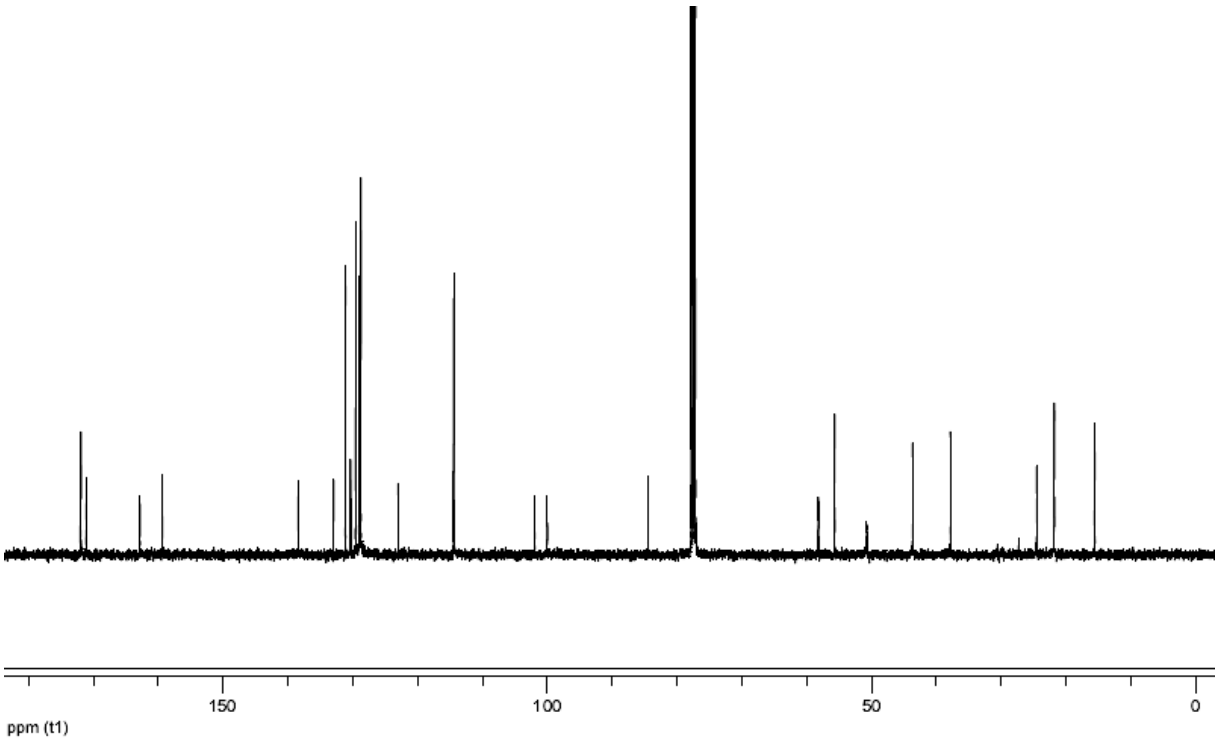
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.20 (m, 7H), 7.08-7.03 (m, 4H), 6.93 (t, *J* = 5.3 Hz, 1H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.25-5.16 (m, 1H), 5.15 (d, *J* = 16.7 Hz, 1H), 4.98 (d, *J* = 16.7 Hz, 1H), 4.32 (dd, *J* = 14.4, 5.4 Hz, 1H), 4.27 (dd, *J* = 14.4, 5.5 Hz, 1H), 3.80 (s, 3H), 2.94 (sept, *J* = 6.9 Hz, 1H), 2.63 (s, 3H), 1.49 (d, *J* = 7.0 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.9, 171.1, 162.8, 159.4, 138.4, 133.0, 131.2, 130.3, 129.6, 129.1, 129.0, 128.8, 128.8, 123.0, 114.4, 102.0, 100.0, 84.5, 58.2, 55.7, 50.7, 43.7, 37.9, 24.5, 21.9, 21.8, 15.6.

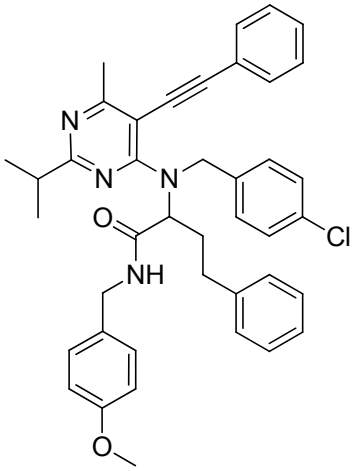
I.R. (thin film) 1661, 1527, 1512, 1493 cm^{-1}.

HRMS Calculated for $C_{34}H_{35}ClN_4O_2$ 566.2449, found 566.2453.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-*N*-(4-methoxybenzyl)-4-phenylbutyramide



$C_{41}H_{41}ClN_4O_2$
MW = 657.24 g.mol^{-1}

2g

General procedure using **1g** (680 mg, 1.00 mmol), phenylacetylene (130 µL, 1.20 mmol), *bis*(triphenylphosphine)palladium chloride (35 mg, 0.05 mmol), CuI (10 mg, 0.05 mmol) and diisopropylethylamine (170 µL, 1.00 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2g** as a colorless oil.

Yield 68 % (448 mg).

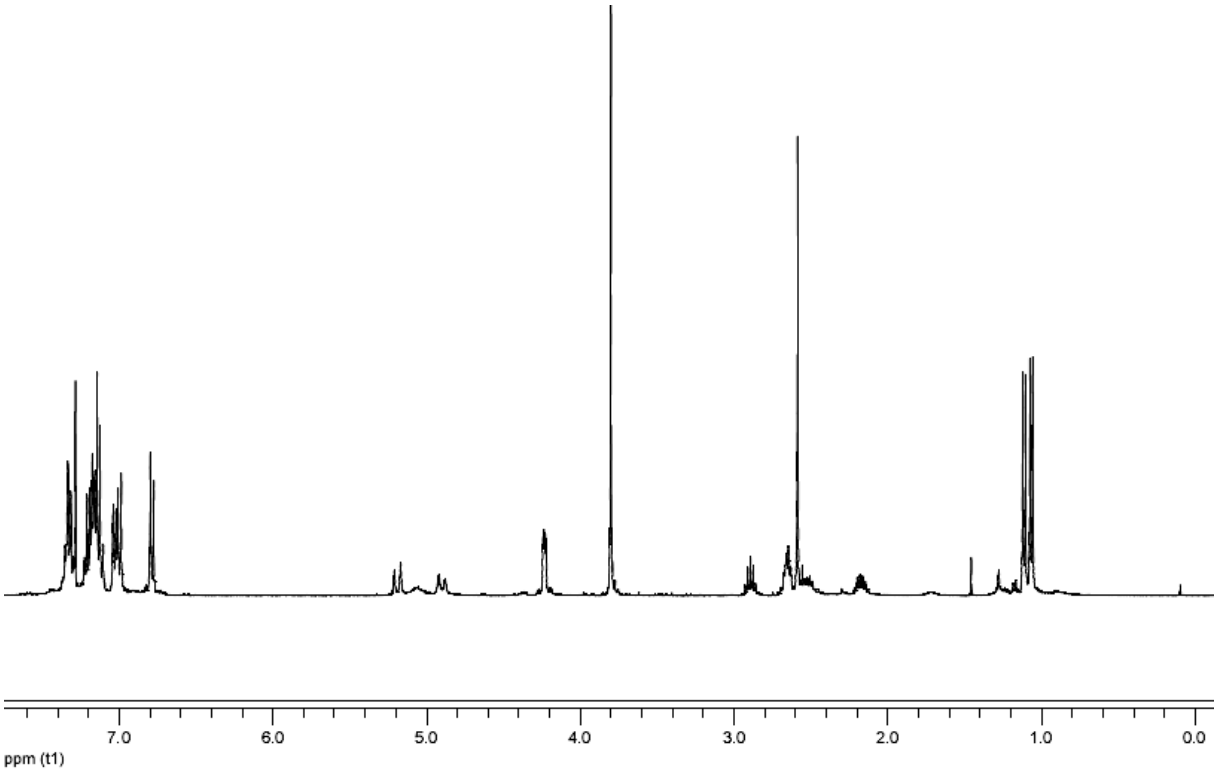
R_f 0.3 (70:30 petroleum ether / diethyl ether).

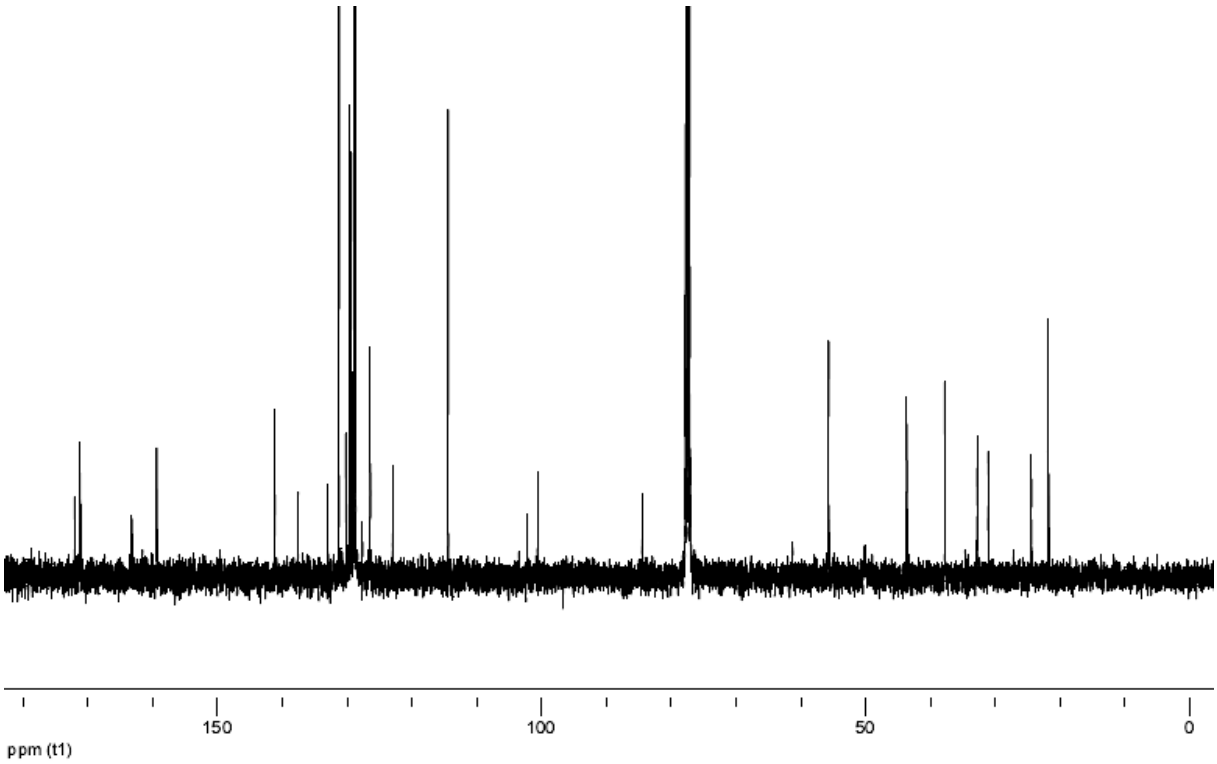
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.30 (m, 3H), 7.23-7.10 (m, 10H), 7.03 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 5.19 (d, *J* = 16.4 Hz, 1H), 5.13-5.05 (m, 1H), 4.90 (d, *J* = 16.4 Hz, 1H), 4.25 (dd, *J* = 14.4, 5.4 Hz, 1H), 4.21 (dd, *J* = 14.4, 5.5 Hz, 1H), 3.80 (s, 3H), 2.89 (sept, *J* = 6.9 Hz, 1H), 2.69-2.62 (m, 2H), 2.59 (s, 3H), 2.57-2.45 (m, 1H), 2.22-2.12 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 171.3, 171.1, 163.2, 159.4, 141.2, 137.6, 133.0, 131.2, 130.2, 129.7, 129.4, 129.1, 128.9, 128.8, 128.8, 128.7, 126.5, 123.0, 114.4, 102.2, 100.6, 84.5, 61.3, 55.7, 50.1, 43.6, 37.8, 32.8, 31.1, 24.4, 21.9, 21.7.

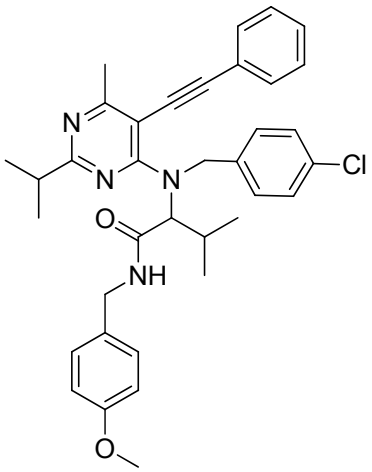
I.R. (thin film) 1676, 1534, 1513, 1491 cm^{-1}.

HRMS Calculated for $C_{41}H_{41}ClN_4O_2$ 656.2918, found 656.2922.





2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-*N*-(4-methoxybenzyl)-3-methylbutyramide



$C_{36}H_{39}ClN_4O_2$
MW = 595.17 g.mol^{-1}

2h

General procedure using **1h** (600 mg, 0.97 mmol), phenylacetylene (130 µL, 1.20 mmol), *bis*(triphenylphosphine)palladium chloride (35 mg, 0.05 mmol), CuI (10 mg, 0.05 mmol) and diisopropylethylamine (170 µL, 0.97 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2h** as a colorless oil.

Yield 74 % (430 mg).

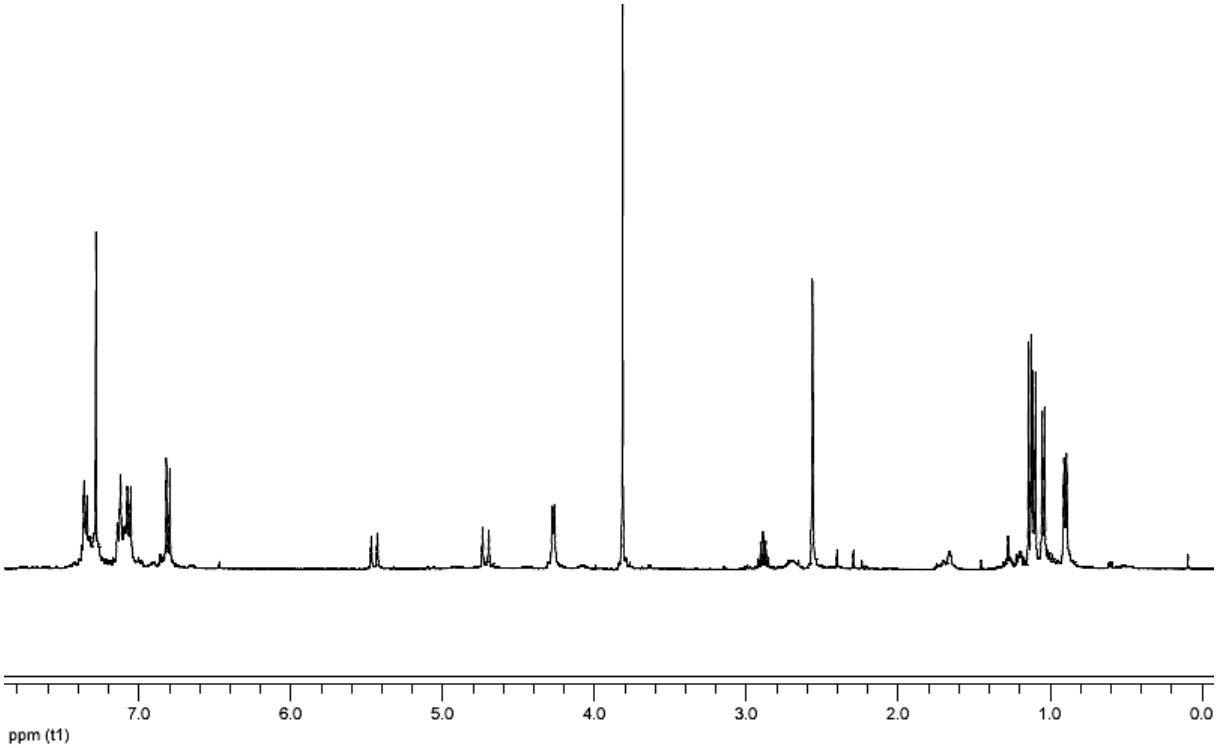
R_f 0.3 (70:30 petroleum ether / diethyl ether).

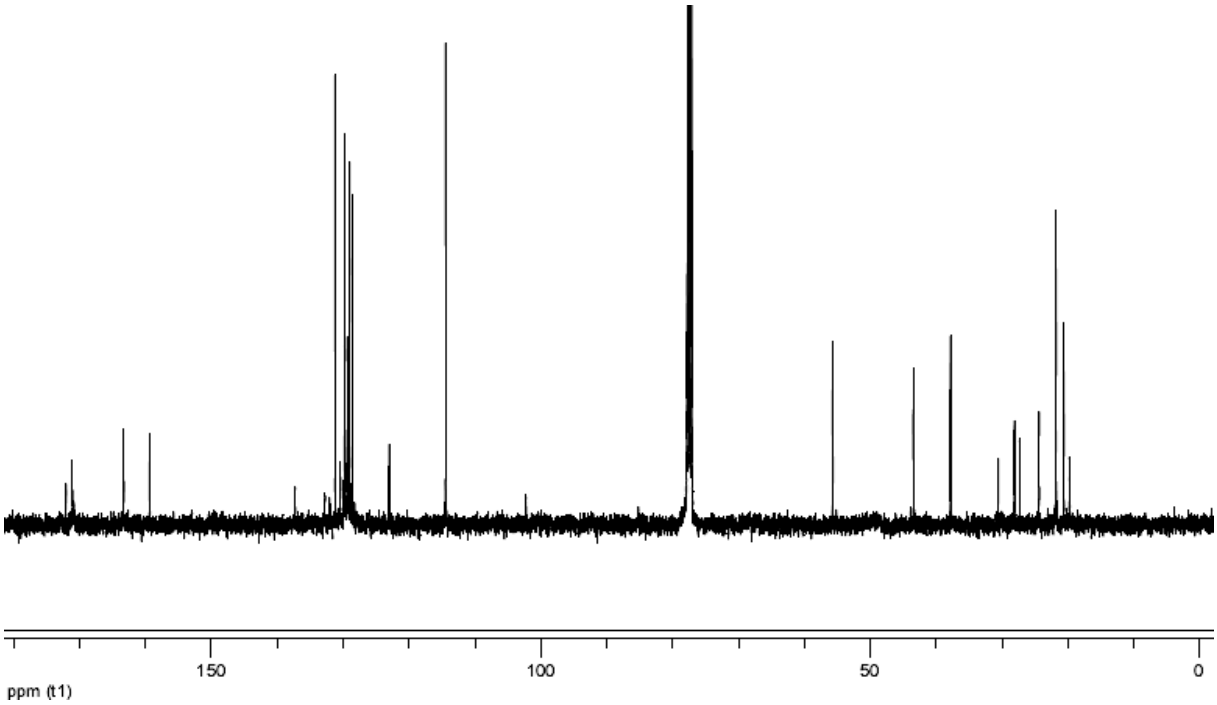
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.25 (m, 6H), 7.16-7.03 (m, 6H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.46 (d, *J* = 16.2 Hz, 1H), 4.72 (d, *J* = 16.2 Hz, 1H), 4.28 (d, *J* = 5.4 Hz, 2H), 3.81 (s, 3H), 2.90 (sept, *J* = 6.9 Hz, 1H), 2.77-2.65 (m, 1H), 2.57 (s, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 171.0, 170.9, 163.3, 159.4, 137.3, 132.7, 131.2, 130.4, 129.8, 129.4, 129.2, 129.0, 128.6, 123.0, 114.4, 102.3, 100.4, 85.2, 69.1, 55.7, 49.3, 43.4, 37.8, 28.1, 24.4, 21.8, 20.6, 19.8.

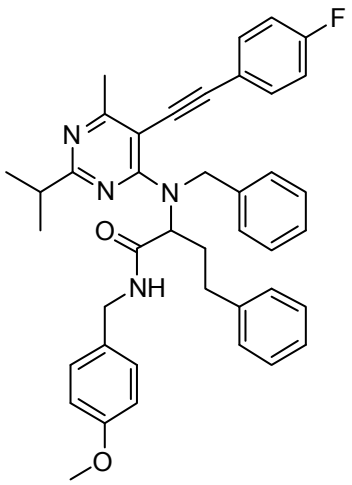
I.R. (thin film) 1679, 1530, 1515, 1493 cm^{-1}.

HRMS Calculated for [$C_{36}H_{39}ClN_4O_2$ - $C_9H_{10}NO_2$] 430.2050, found 430.2026.





2-[benzyl-[5-(4-fluorophenylethynyl)-2-isopropyl-6-methylpyrimidin-4-yl]-amino]-*N*-(4-methoxybenzyl)-4-phenylbutyramide



$C_{41}H_{41}FN_4O_2$
MW = 640.79 g.mol^{-1}

2i

General procedure using **1i** (610 mg, 0.94 mmol), *p*-fluorophenylacetylene (130 µL, 1.13 mmol), *bis*(triphenylphosphine)palladium chloride (33 mg, 0.05 mmol), CuI (10 mg, 0.05 mmol) and diisopropylethylamine (160 µL, 0.94 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 60:40) afforded **2i** as a colorless oil.

Yield 62 % (375 mg).

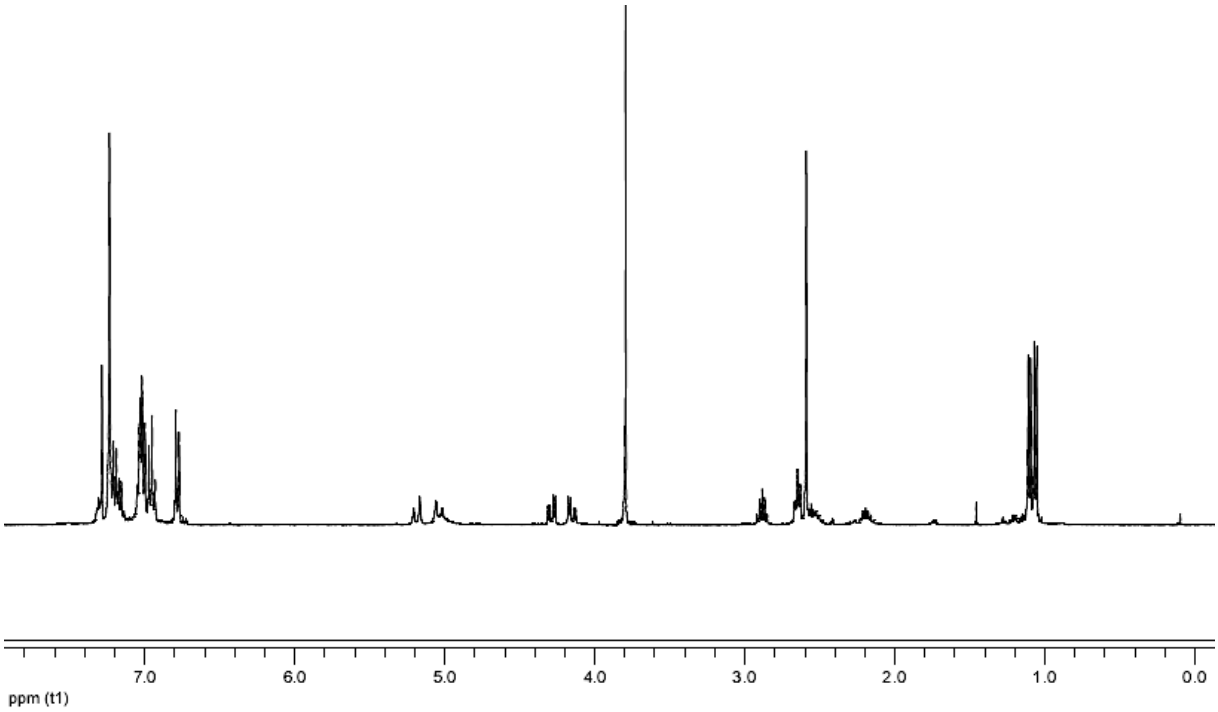
R_f 0.3 (60:40 petroleum ether / diethyl ether).

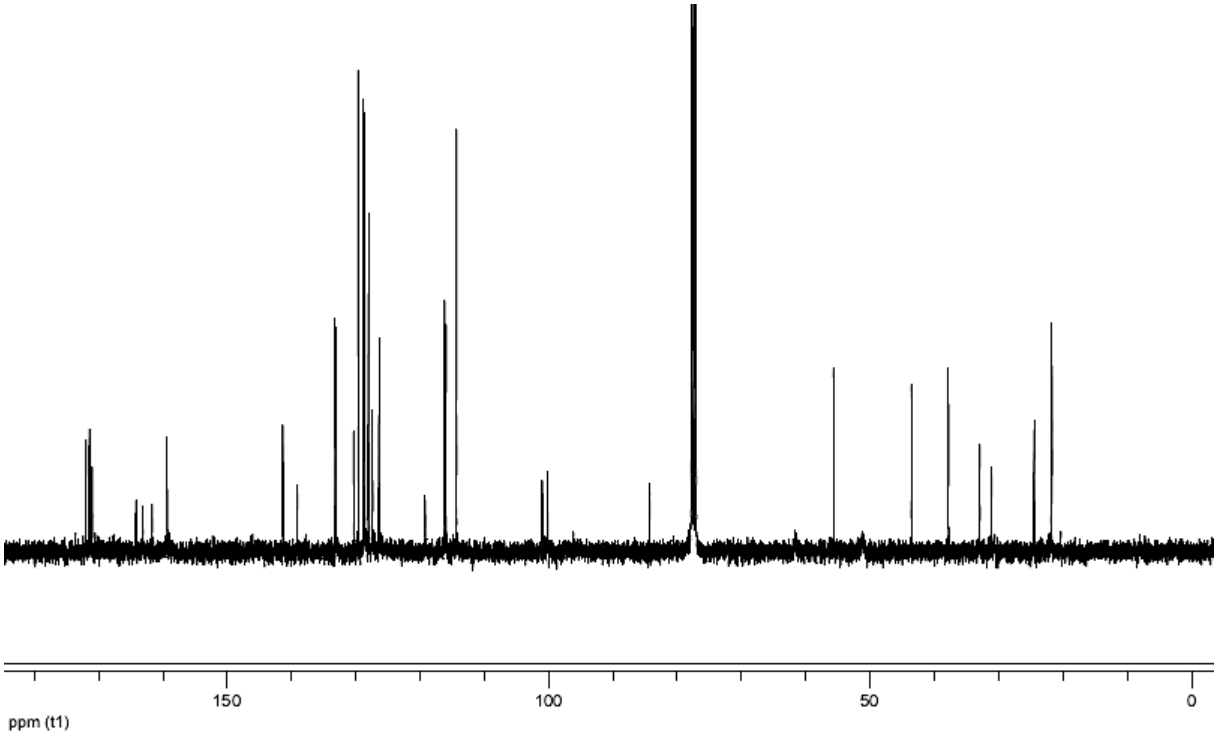
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31 (t, J = 5.3 Hz, 1H), 7.26-7.22 (m, 5H), 7.22-7.13 (m, 3H), 7.06-6.99 (m, 6H), 6.95 (t, $J_{H\text{-}H} = J_{H\text{-}F}$ = 8.8 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 5.19 (d, J = 16.3 Hz, 1H), 5.04 (d, J = 16.3 Hz, 1H), 5.00 (br s, 1H), 4.29 (dd, J = 14.4, 5.6 Hz, 1H), 4.15 (dd, J = 14.4, 5.2 Hz, 1H), 3.80 (s, 3H), 2.88 (sept, J = 6.9 Hz, 1H), 2.71-2.62 (m, 2H), 2.59 (s, 3H), 2.57-2.48 (m, 1H), 2.24-2.13 (m, 1H), 1.10 (d, J = 6.9 Hz, 3H), 1.06 (d, J = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.4, 171.0, 163.2, 163.0 (d, $J_{C\text{-}F}$ = 249.6 Hz), 159.3, 141.4, 139.1, 133.2 (d, $J_{C\text{-}F}$ = 8.2 Hz), 130.3, 129.6, 128.8, 128.8, 128.7, 128.0, 127.4, 126.4, 119.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 116.1 (d, $J_{C\text{-}F}$ = 22.0 Hz), 114.4, 101.0, 100.2, 84.3, 61.6, 55.7, 51.2, 43.6, 37.8, 33.0, 31.1, 24.5, 21.8, 21.7.

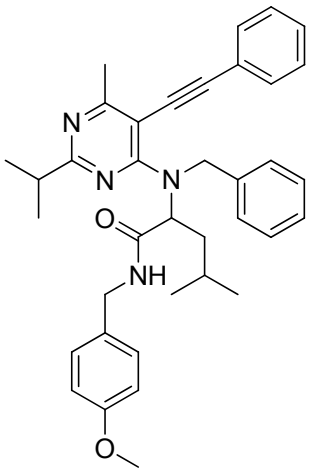
I.R. (thin film) 1674, 1529, 1505, 1453 cm^{-1}.

HRMS Calculated for $C_{41}H_{41}FN_4O_2$ 640.3214, found 640.3246.





2-[benzyl-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-4-methyl-pentanoic acid 4-methoxybenzylamide



$C_{37}H_{42}N_4O_2$
MW = 574.75 g.mol^{-1}

2j

General procedure using **1j** (760 mg, 1.26 mmol), phenylacetylene (170 µL, 1.52 mmol), *bis*(triphenylphosphine)palladium chloride (45 mg, 0.06 mmol), CuI (13 mg, 0.06 mmol) and diisopropylethylamine (220 µL, 1.26 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2j** as a colorless oil.

Yield 57 % (415 mg).

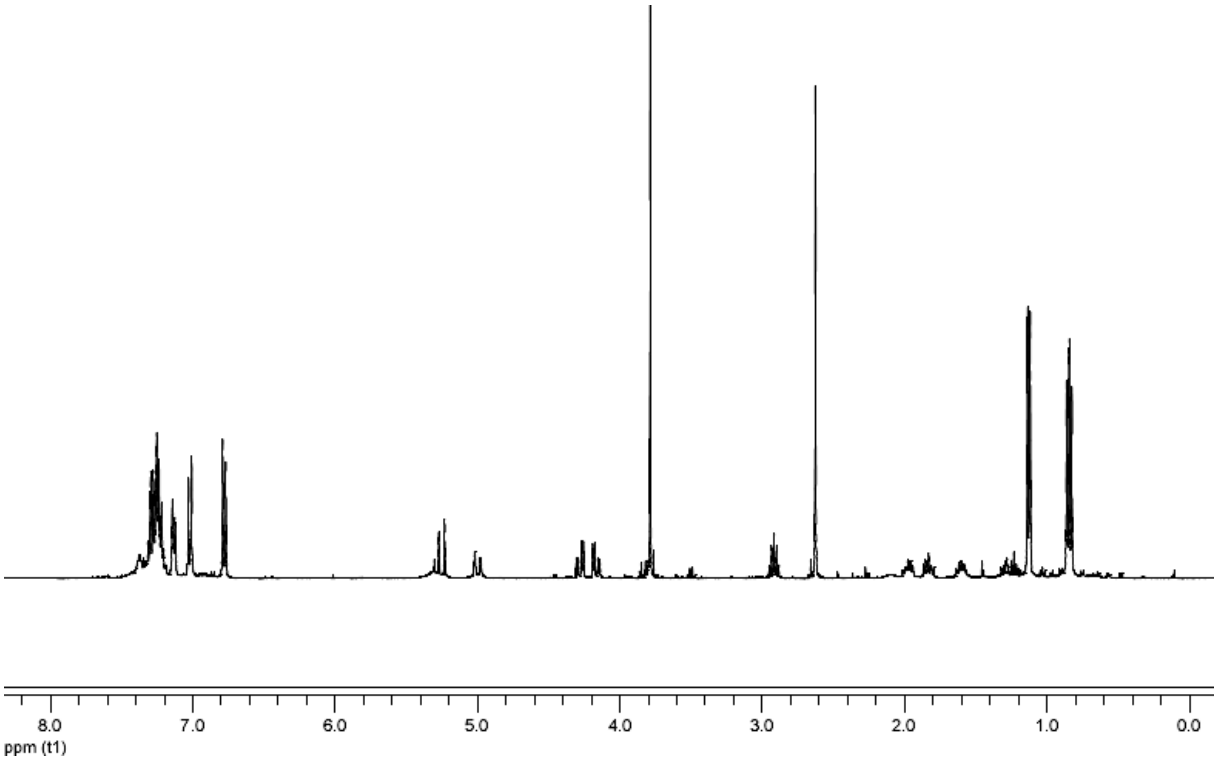
R_f 0.3 (70:30 petroleum ether / diethyl ether).

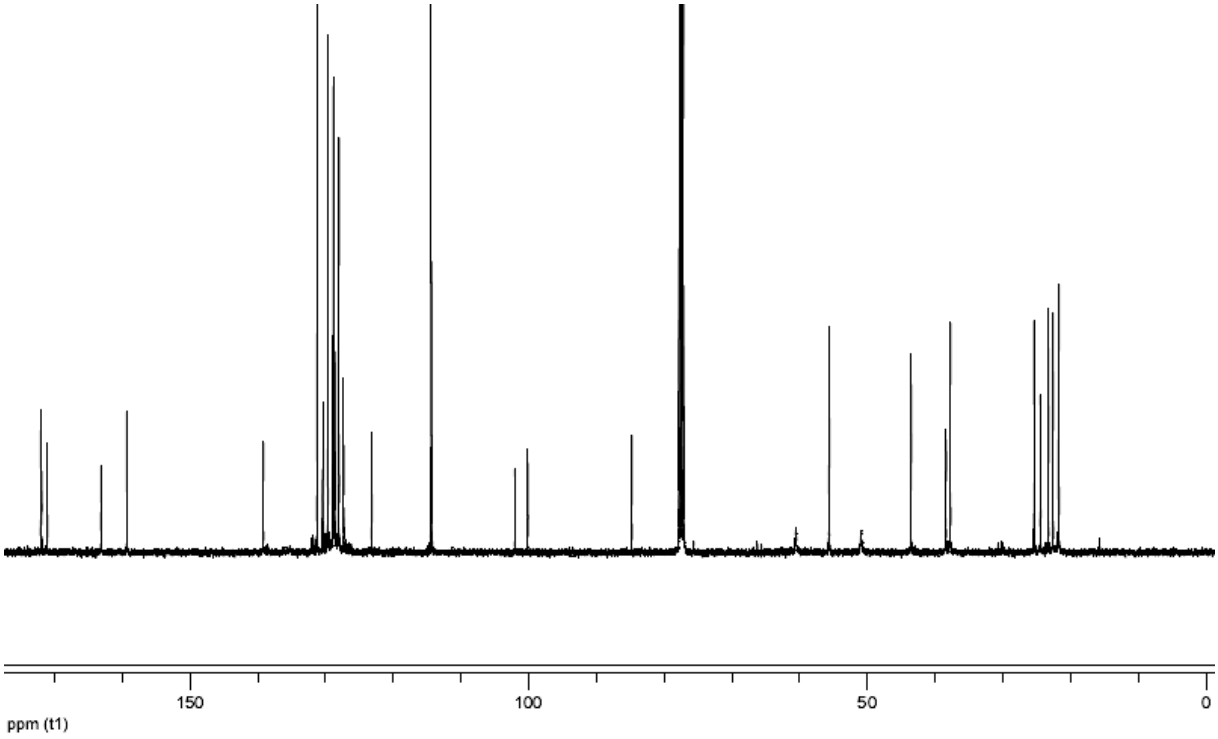
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37 (t, *J* = 5.6 Hz, 1H), 7.32-7.18 (m, 8H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 5.37-5.26 (br s, 1H), 5.25 (d, *J* = 16.4 Hz, 1H), 4.99 (d, *J* = 16.4 Hz, 1H), 4.28 (dd, *J* = 14.4, 5.5 Hz, 1H), 4.16 (dd, *J* = 14.4, 5.3 Hz, 1H), 3.79 (s, 3H), 2.91 (sept, *J* = 6.9 Hz, 1H), 2.62 (s, 3H), 2.02-1.91 (m, 1H), 1.87-1.78 (m, 1H), 1.65-1.53 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.9, 171.0, 163.1, 159.3, 139.2, 131.2, 130.4, 129.7, 128.9, 128.8, 128.6, 128.0, 127.3, 123.2, 114.4, 102.1, 100.2, 84.8, 60.6, 55.7, 51.0, 43.6, 38.5, 37.8, 25.4, 24.5, 23.3, 22.7, 21.8, 21.8.

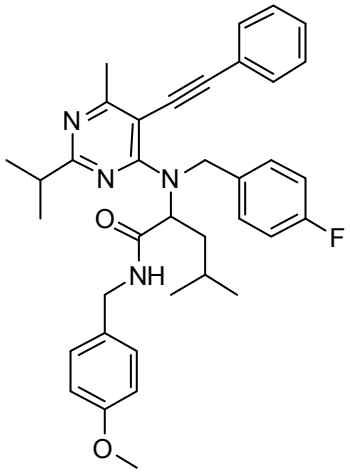
I.R. (thin film) 1675, 1530, 1513, 1497 cm^{-1}.

HRMS Calculated for $C_{37}H_{42}N_4O_2$ 574.3308, found 574.3338.





2-[(4-fluorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{37}H_{41}FN_4O_2$
MW = 592.75 g.mol^{-1}

2k

General procedure using **1k** (740 mg, 1.20 mmol), phenylacetylene (160 µL, 1.44 mmol), *bis*(triphenylphosphine)palladium chloride (45 mg, 0.06 mmol), CuI (12 mg, 0.06 mmol) and diisopropylethylamine (210 µL, 1.20 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2k** as a colorless oil.

Yield 58 % (413 mg).

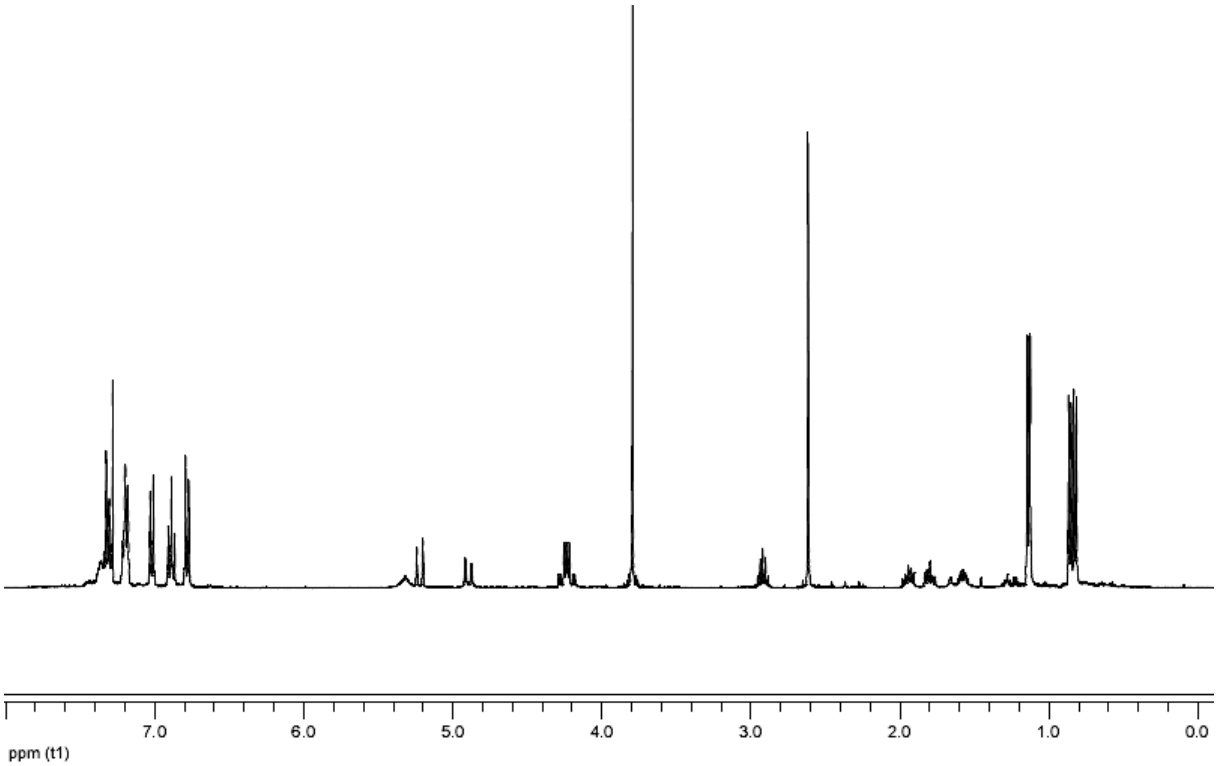
R_f 0.3 (70:30 petroleum ether / diethyl ether).

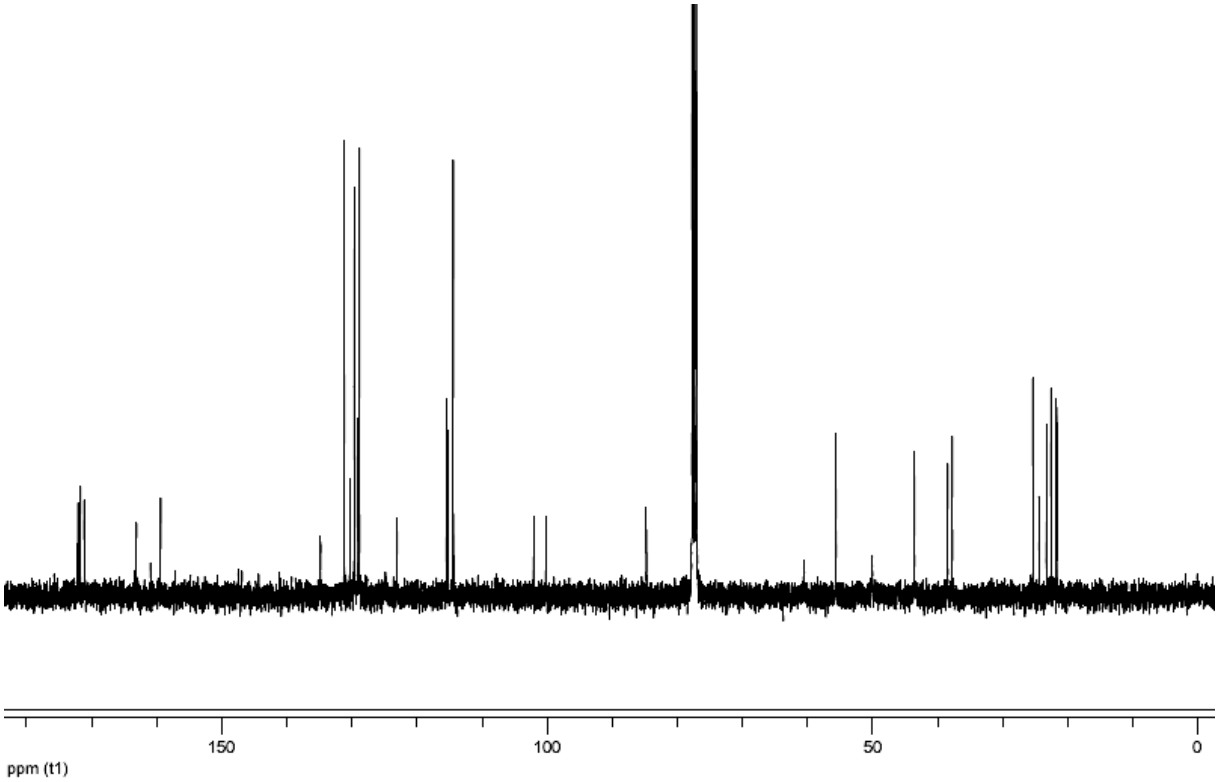
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.29 (m, 4H), 7.23-7.16 (m, 4H), 7.02 (d, J = 8.6 Hz, 2H), 6.89 (t, $J_{H\text{-}H}$ = $J_{H\text{-}F}$ = 8.7 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 5.37-5.27 (m, 1H), 5.22 (d, J = 16.2 Hz, 1H), 4.90 (d, J = 16.2 Hz, 1H), 4.27 (dd, J = 14.3, 5.4 Hz, 1H), 4.20 (dd, J = 14.3, 5.5 Hz, 1H), 3.80 (s, 3H), 2.92 (sept, J = 6.9 Hz, 1H), 2.62 (s, 3H), 1.99-1.90 (m, 1H), 1.85-1.75 (m, 1H), 1.62-1.52 (m, 1H), 1.14 (d, J = 6.9 Hz, 3H), 1.13 (d, J = 6.9 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 171.8, 171.1, 163.1, 162.2 (d, $J_{C\text{-}F}$ = 245.2 Hz), 159.4, 134.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 131.2, 130.4, 129.6 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.6, 129.1, 128.9, 115.4 (d, $J_{C\text{-}F}$ = 20.5 Hz), 114.4, 102.1, 100.2, 84.8, 60.5, 55.7, 50.1, 43.6, 38.5, 37.8, 25.4, 24.5, 23.3, 22.6, 21.8, 21.7.

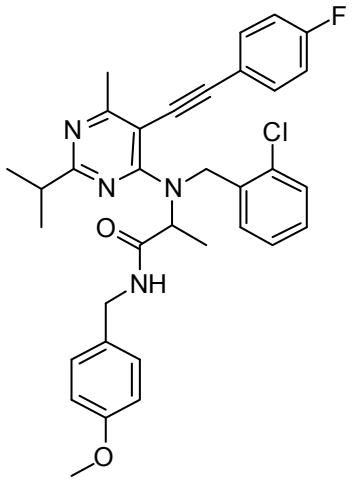
I.R. (thin film) 1669, 1530, 1511, 1495 cm^{-1}.

HRMS Calculated for $C_{37}H_{41}FN_4O_2$ 592.3214, found 592.3216.





2-[(2-chlorobenzyl)-[5-(4-fluorophenylethynyl)-2-isopropyl-6-methylpyrimidin-4-yl]-amino]-*N*-(4-methoxybenzyl)-propionamide



$C_{34}H_{34}ClFN_4O_2$
MW = 585.11 g.mol^{-1}

2l

General procedure using **1l** (590 mg, 1.00 mmol), phenylacetylene (140 µL, 1.20 mmol), *bis*(triphenylphosphine)palladium chloride (35 mg, 0.05 mmol), CuI (10 mg, 0.05 mmol) and diisopropylethylamine (170 µL, 1.00 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 60:40) afforded **2l** as a colorless oil.

Yield 60 % (385 mg).

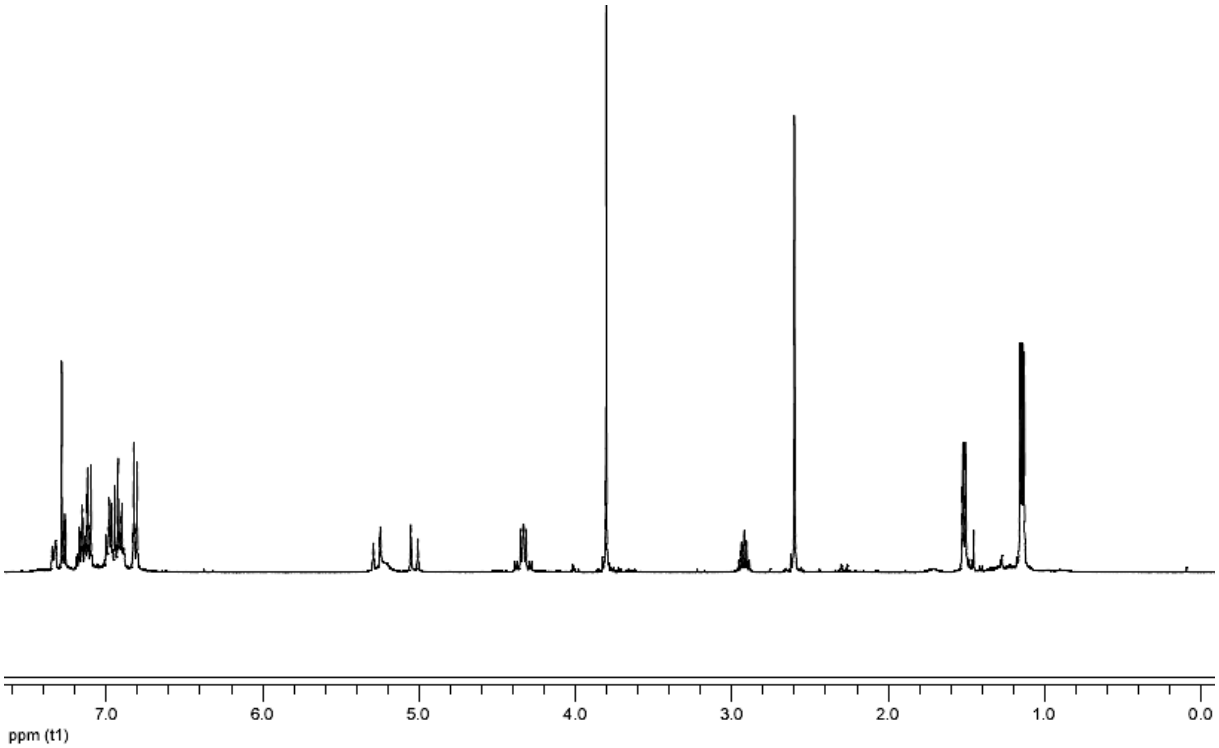
R_f 0.3 (60:40 petroleum ether / diethyl ether).

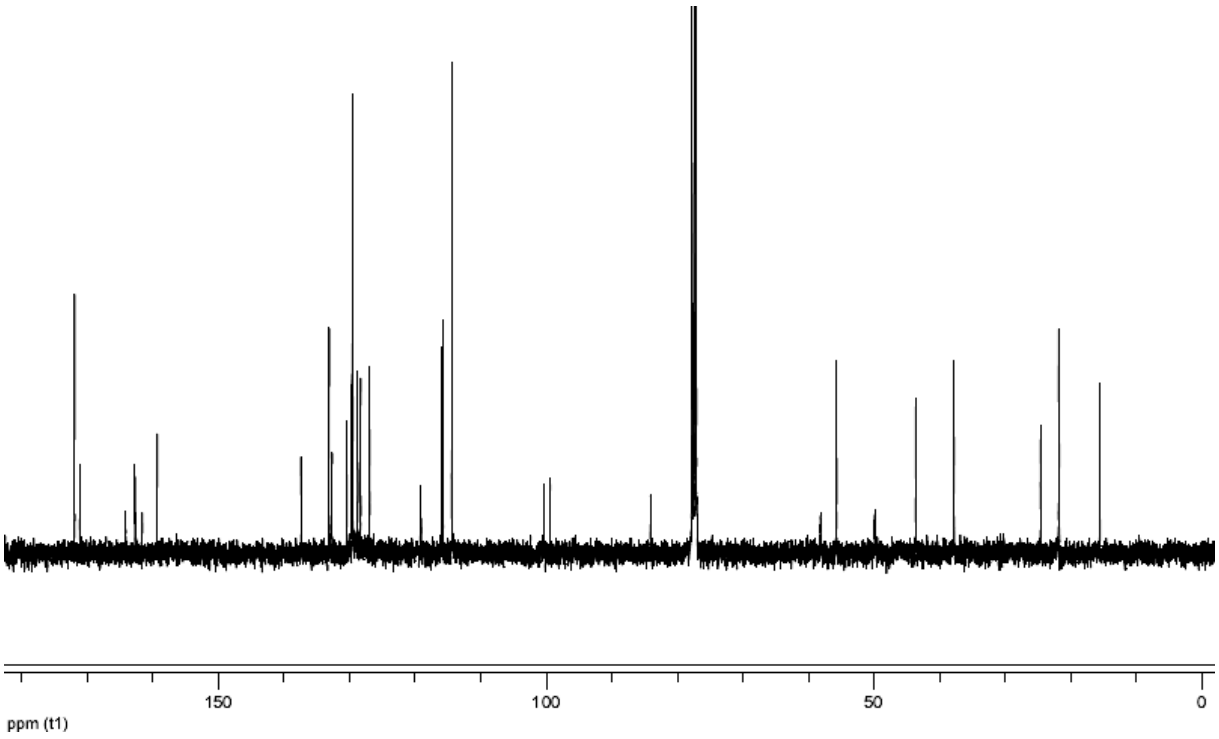
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (dd, J = 7.7, 1.8 Hz, 1H), 7.27 (dd, J = 7.7, 1.8 Hz, 1H), 7.20-7.13 (m, 2H), 7.11 (d, J = 8.6 Hz, 2H), 6.98 (dd, $J_{H\text{-}H,\ H\text{-}F}$ = 8.8, 5.5 Hz, 2H), 6.95-6.87 (m, 3H), 6.81 (d, J = 8.6 Hz, 2H), 5.27 (d, J = 17.9 Hz, 1H), 5.23 (br s, 1H), 5.03 (d, J = 17.9 Hz, 1H), 4.36 (dd, J = 14.4, 5.6 Hz, 1H), 4.31 (dd, J = 14.4, 5.4 Hz, 1H), 3.80 (s, 3H), 2.92 (sept, J = 6.9 Hz, 1H), 2.60 (s, 3H), 1.51 (d, J = 7.0 Hz, 3H), 1.15 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 172.0, 171.2, 162.9 (d, $J_{C\text{-}F}$ = 250.3 Hz), 162.7, 159.4, 137.4, 133.2 (d, $J_{C\text{-}F}$ = 8.2 Hz), 132.7, 130.5, 129.6, 129.6, 128.8, 128.3, 127.0, 119.1 (d, $J_{C\text{-}F}$ = 3.5 Hz), 115.9 (d, $J_{C\text{-}F}$ = 22.1 Hz), 114.4, 100.4, 99.4, 84.1, 58.2, 55.7, 49.9, 43.6, 37.8, 24.6, 21.8, 21.7, 15.6.

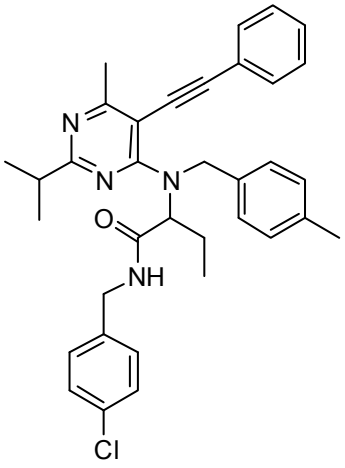
I.R. (thin film) 1660, 1530, 1506, 1467 cm^{-1}.

HRMS Calculated for $C_{34}H_{34}ClFN_4O_2$ 584.2354, found 584.2351.





_N_-(4-chlorobenzyl)-2-[(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-(4-methylbenzyl)-amino]-butyramide



$C_{35}H_{37}ClN_4O$

MW = 565.15 g.mol^{-1}

2m

General procedure using **1m** (650 mg, 1.10 mmol), phenylacetylene (150 µL, 1.32 mmol), *bis*(triphenylphosphine)palladium chloride (40 mg, 0.06 mmol), CuI (11 mg, 0.06 mmol) and diisopropylethylamine (190 µL, 1.10 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2m** as a colorless oil.

Yield 55 % (342 mg).

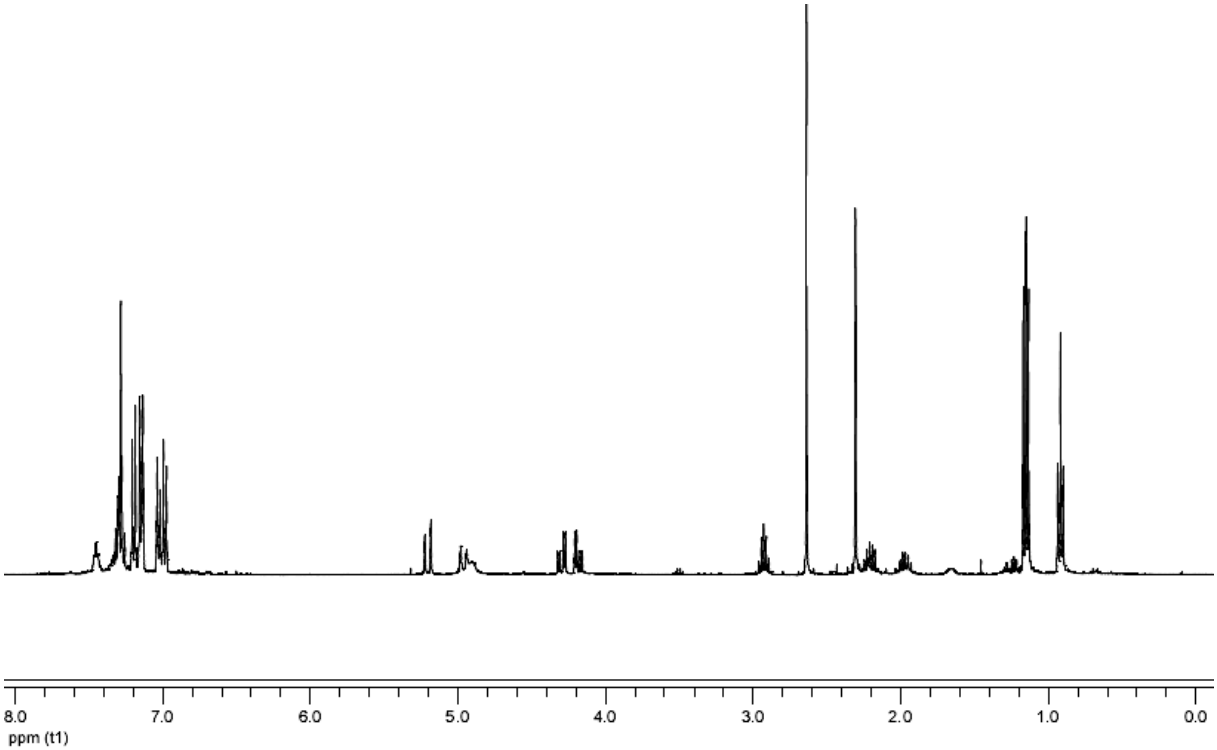
R_f 0.3 (70:30 petroleum ether / diethyl ether).

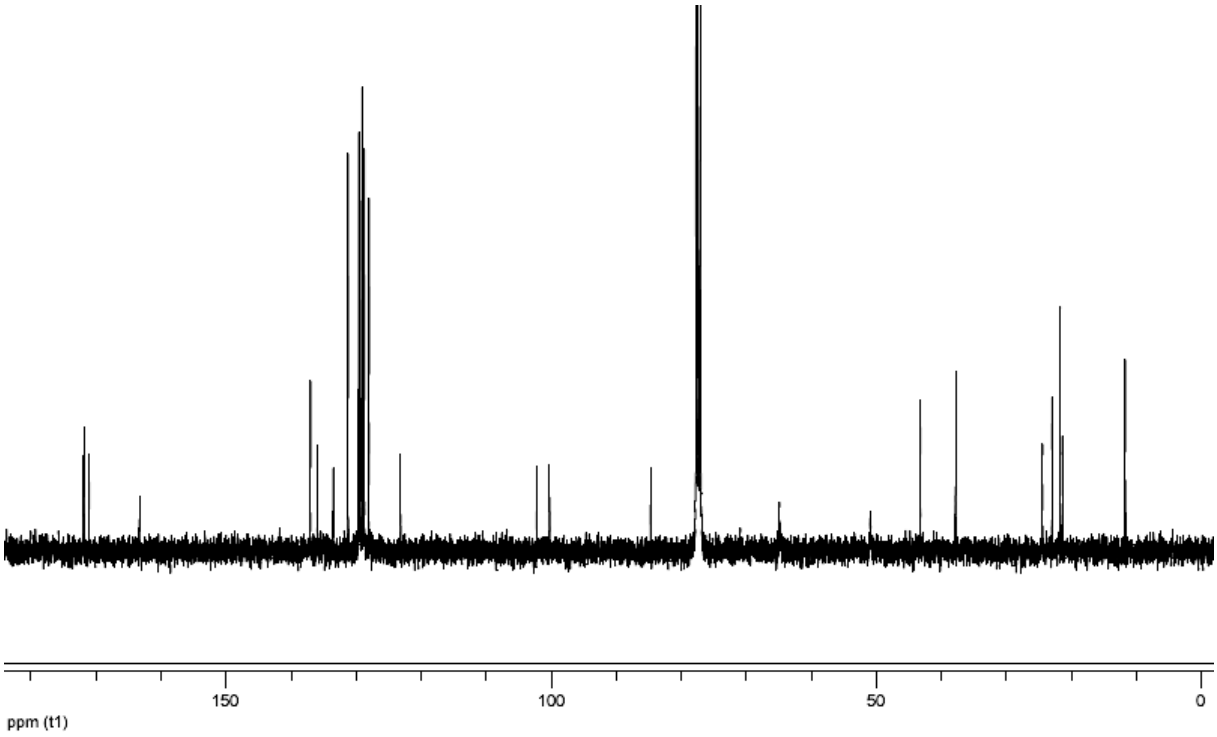
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (t, *J* = 5.6 Hz, 1H), 7.32-7.25 (m, 3H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.17-7.12 (m, 4H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 5.21 (d, *J* = 16.2 Hz, 1H), 4.96 (d, *J* = 16.2 Hz, 1H), 4.93-4.84 (m, 1H), 4.30 (dd, *J* = 14.7, 5.8 Hz, 1H), 4.18 (dd, *J* = 14.7, 5.6 Hz, 1H), 2.93 (sept, *J* = 6.9 Hz, 1H), 2.64 (s, 3H), 2.31 (s, 3H), 2.25-2.16 (m, 1H), 2.02-1.92 (m, 1H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 171.9, 171.1, 163.3, 137.0, 137.0, 136.0, 133.5, 131.3, 129.6, 129.4, 129.1, 128.9, 128.8, 128.0, 123.2, 102.2, 100.3, 84.8, 64.9, 51.0, 43.3, 37.8, 24.5, 23.0, 21.8, 21.4, 11.8.

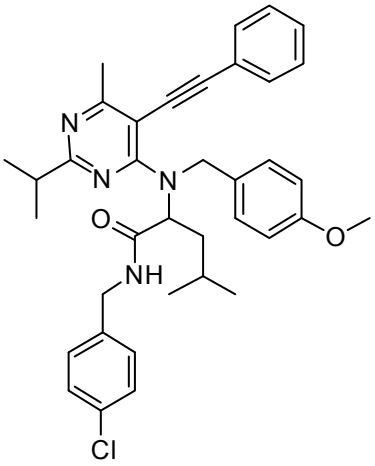
I.R. (thin film) 1672, 1526, 1491, 1409 cm^{-1}.

HRMS Calculated for $C_{35}H_{37}ClN_4O$ 564.2656, found 564.2671.





2-[(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-(4-methoxybenzyl)-amino]-4-methylpentanoic acid 4-chlorobenzylamide



$C_{37}H_{41}ClN_4O_2$
MW = 609.20 g.mol^{-1}

2n

General procedure using **1n** (670 mg, 1.06 mmol), phenylacetylene (140 µL, 1.7 mmol), *bis*(triphenylphosphine)palladium chloride (37 mg, 0.05 mmol), CuI (11 mg, 0.05 mmol) and diisopropylethylamine (180 µL, 1.06 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **2n** as a colorless oil.

Yield 61 % (394 mg).

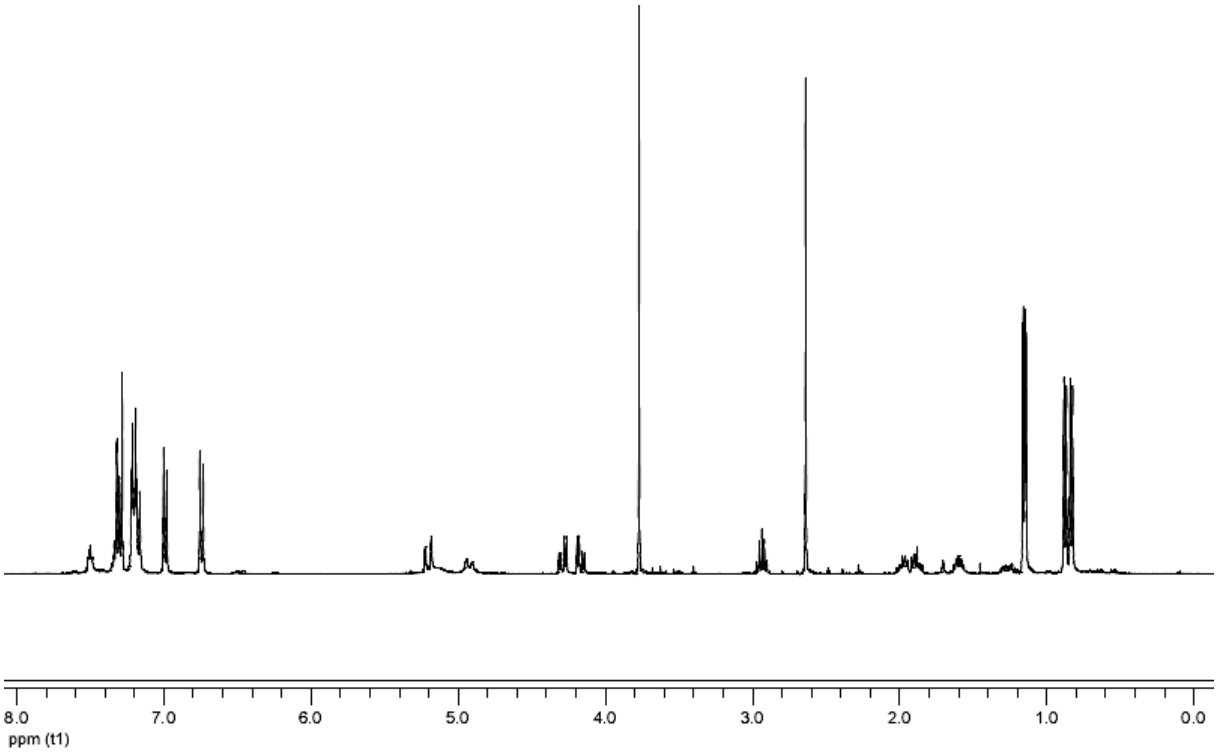
R_f 0.3 (70:30 petroleum ether / diethyl ether).

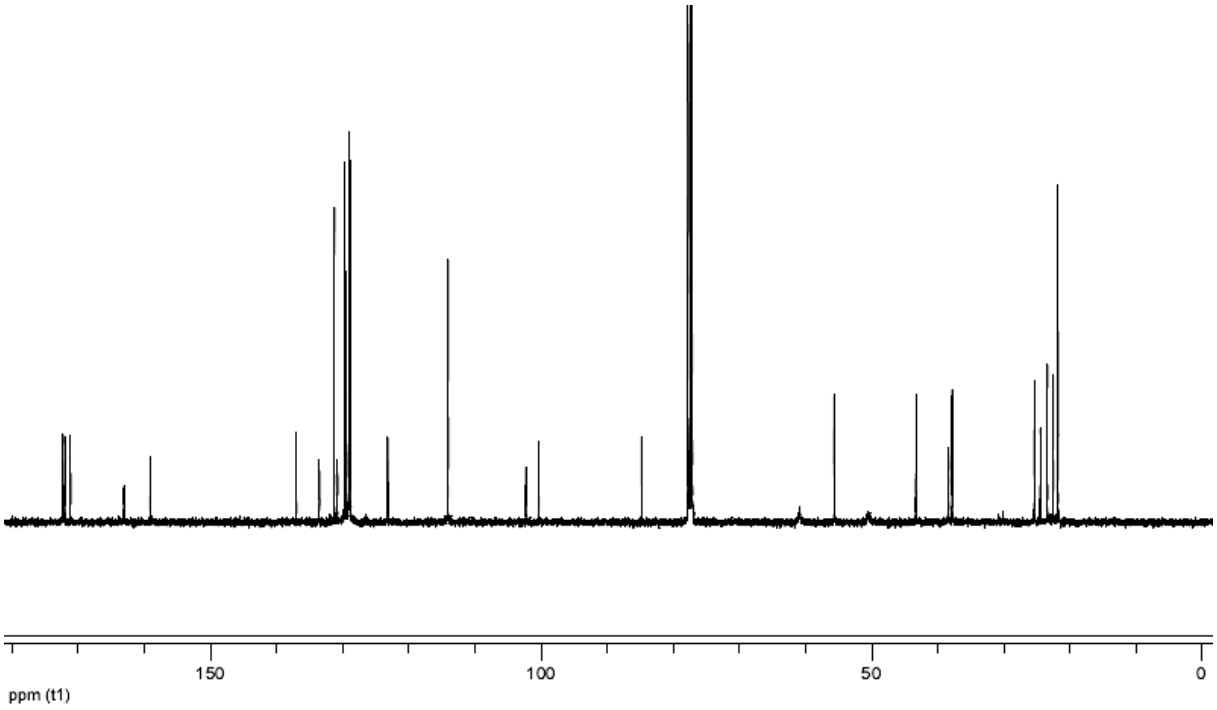
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (t, *J* = 5.3 Hz, 1H), 7.37-7.27 (m, 3H), 7.24-7.15 (m, 6H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 5.27-5.04 (m, 1H), 5.21 (d, *J* = 15.8 Hz, 1H), 4.93 (d, *J* = 15.8 Hz, 1H), 4.29 (dd, *J* = 14.7, 5.8 Hz, 1H), 4.17 (dd, *J* = 14.7, 5.5 Hz, 1H), 3.77 (s, 3H), 2.94 (sept, *J* = 6.9 Hz, 1H), 2.64 (s, 3H), 2.04-1.94 (m, 1H), 1.94-1.83 (m, 1H), 1.60 (sept, *J* = 6.6 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.3, 172.0, 171.1, 163.1, 159.1, 137.0, 133.5, 131.3, 130.8, 129.7, 129.5, 129.1, 129.0, 128.9, 123.2, 114.1, 102.3, 100.4, 84.8, 60.9, 55.7, 50.5, 43.3, 38.4, 37.8, 25.4, 24.5, 23.4, 22.6, 21.9.

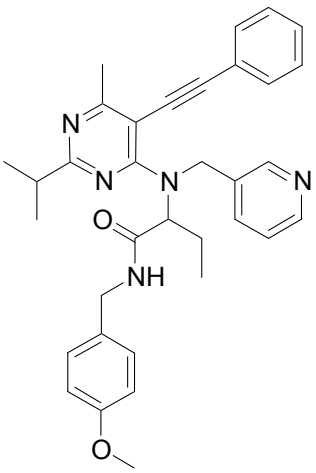
I.R. (thin film) 1676, 1530, 1512, 1492 cm^{-1}.

HRMS Calculated for $C_{37}H_{41}ClN_4O_2$ 608.2918, found 608.2940.





2-[(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-pyridin-3-ylmethylamino]-*N*-(4-methoxybenzyl)-butyramide



$C_{34}H_{37}N_5O_2$
MW = 547.69 g.mol^{-1}

General procedure using **1o** (390 mg, 0.68 mmol), phenylacetylene (90 µL, 0.82 mmol), *bis*(triphenylphosphine)palladium chloride (25 mg, 0.03 mmol), CuI (3 mg, 0.03 mmol) and diisopropylethylamine (120 µL, 0.68 mmol). Purification by flash chromatography (diethyl ether) afforded **2o** as a colorless oil.

Yield 58 % (216 mg).

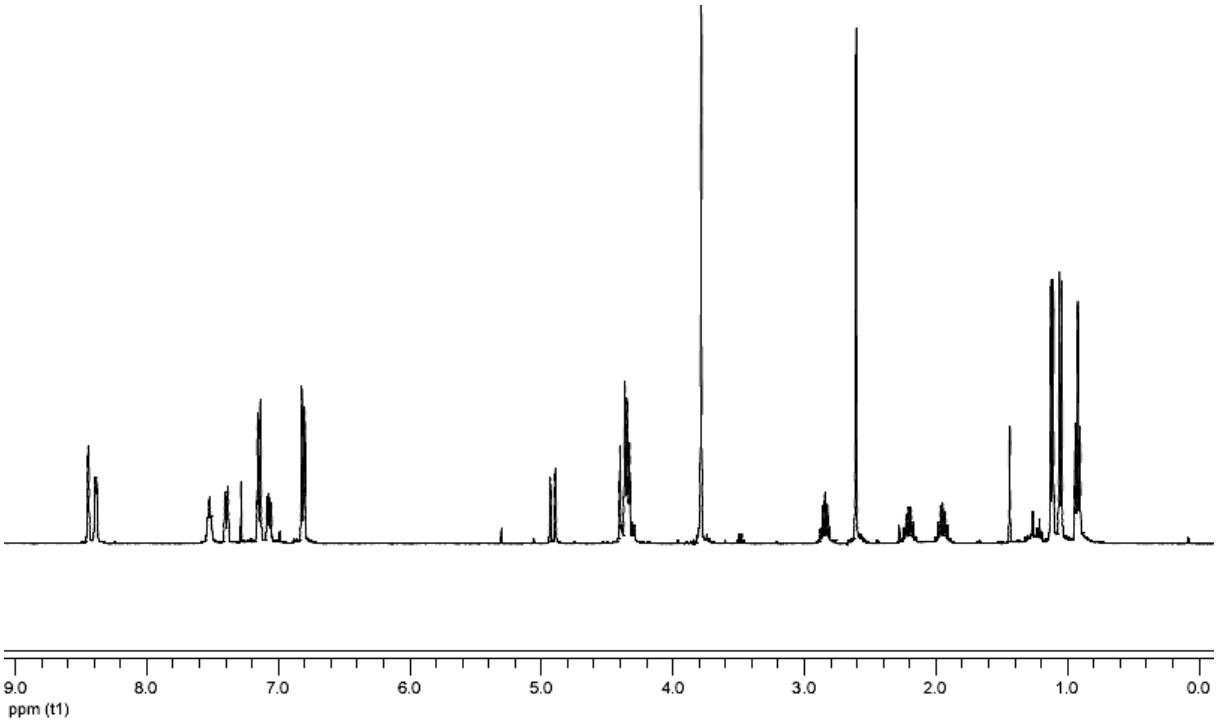
R_f 0.3 (diethyl ether).

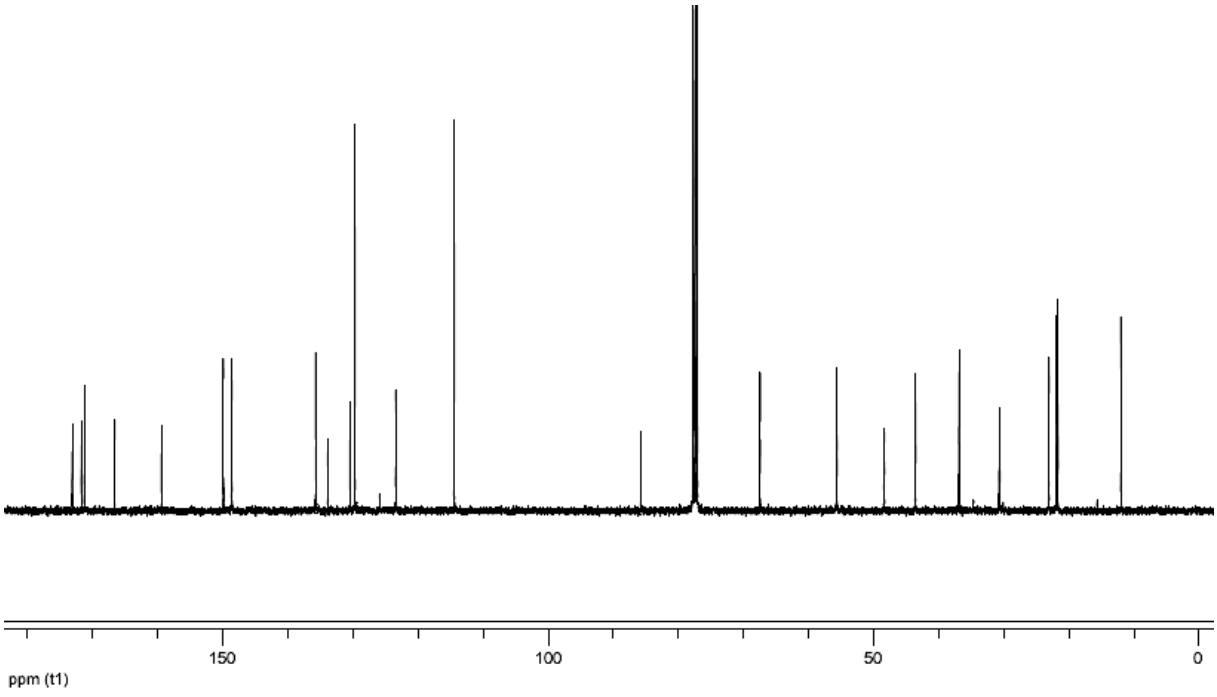
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 8.43 (d, *J* = 4.7 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.38-7.29 (m, 4H), 7.22 (d, *J* = 7.3 Hz, 2H), 7.10 (dd, *J* = 7.9, 4.7 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 5.25 (d, *J* = 16.3 Hz, 1H), 5.19 (t, *J* = 7.6 Hz, 1H), 4.85 (d, *J* = 16.3 Hz, 1H), 4.29 (dd, *J* = 14.4, 5.6 Hz, 1H), 4.24 (dd, *J* = 14.4, 5.8 Hz, 1H), 3.78 (s, 3H), 2.90 (sept, *J* = 6.9 Hz, 1H), 2.60 (s, 3H), 2.21-2.09 (m, 1H), 1.96-1.84 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.2, 171.2, 171.2, 163.4, 159.4, 149.6, 148.5, 135.4, 134.9, 131.2, 130.3, 129.7, 129.2, 128.9, 123.4, 122.9, 114.5, 102.4, 100.4, 84.6, 64.2, 55.7, 48.2, 43.6, 37.8, 24.4, 23.2, 21.8, 21.7, 11.5.

I.R. (thin film) 1675, 1527, 1514, 1492 cm^{-1}.

HRMS Calculated for $C_{34}H_{37}N_5O_2$ 547.2947, found 547.2960.

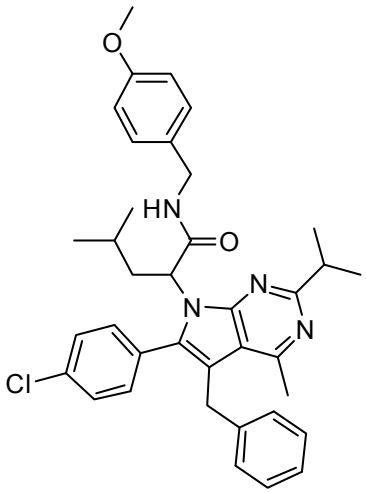




General procedure for pyrrolo[2,3-*d*]pyrimidines:

To a 0.2 M solution of Sonogashira adduct in DMF was added 1.2 equiv. of NaH (95 %). The resulting mixture was stirred overnight at room temperature.
Solvent was then removed by extraction and the organic phases were collected and concentrated *in vacuo* to afford pyrrolo[2,3-*d*]pyrimidines after purification by flash chromatography on silica gel.

2-[5-benzyl-6-(4-chlorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{37}H_{41}ClN_4O_2$
MW = 609.20 g.mol^{-1}

3b

General procedure using **2b** (100 mg, 0.16 mmol) and NaH (5 mg, 0.20 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3b** as a yellow oil.

Yield 76 % (76 mg).

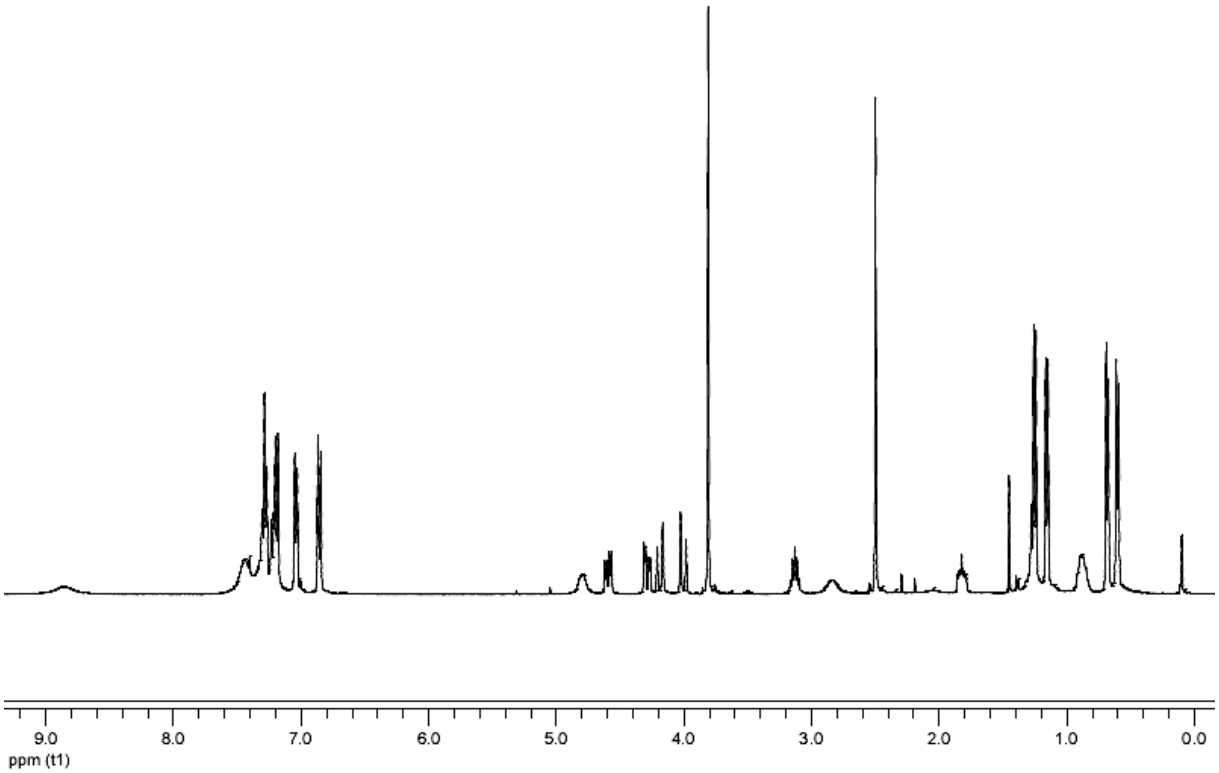
R_f 0.3 (70:30 petroleum ether / diethyl ether).

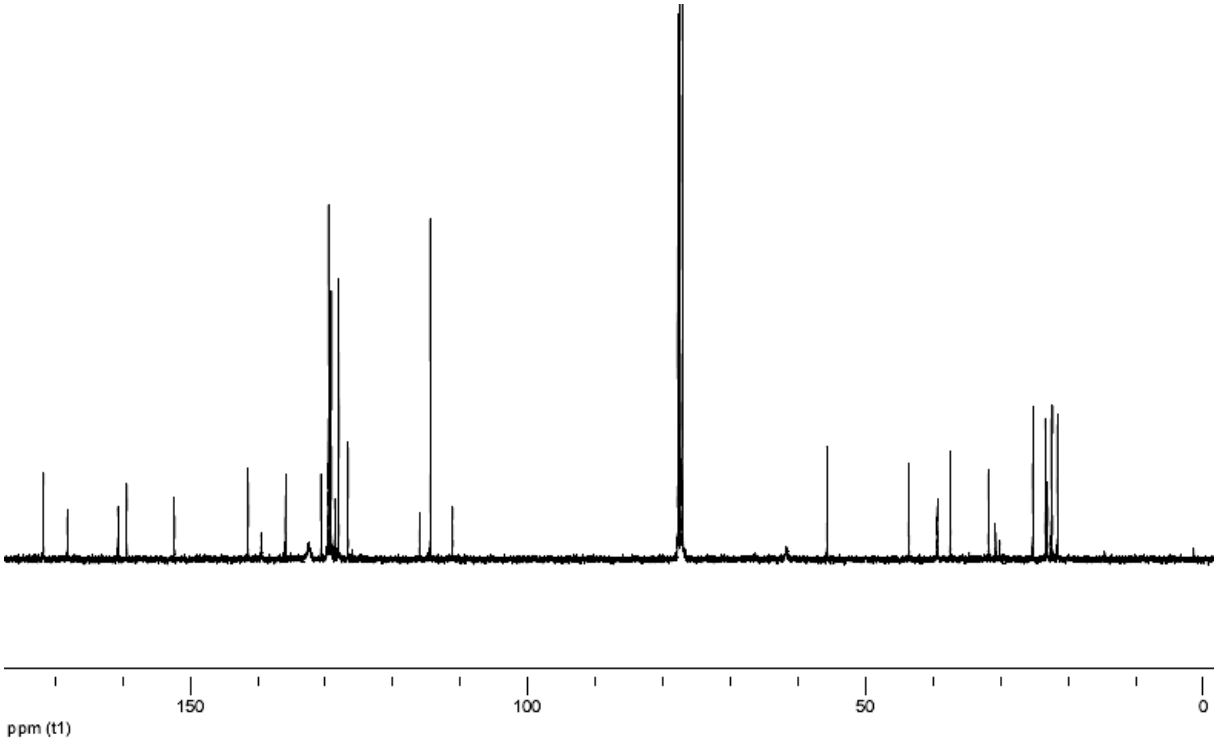
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (br s, 1H), 7.59-7.37 (m, 2H), 7.36-7.25 (m, 3H), 7.24-7.15 (m, 4H), 7.04 (d, *J* = 7.4 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.90-4.70 (br s, 1H), 4.60 (dd, *J* = 14.7, 6.1 Hz, 1H), 4.29 (dd, *J* = 14.7, 4.8 Hz, 1H), 4.19 (d, *J* = 17.1 Hz, 1H), 4.00 (d, *J* = 17.1 Hz, 1H), 3.81 (s, 3H), 3.13 (sept, *J* = 6.8 Hz, 1H), 2.98-2.75 (br s, 1H), 2.50 (s, 3H), 1.88-1.78 (m, 1H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.96-0.82 (m, 1H), 0.68 (d, *J* = 6.6 Hz, 3H), 0.60 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.7, 168.2, 160.7, 159.4, 152.3, 141.4, 139.5, 135.9, 132.4, 130.6, 129.5, 129.1, 128.6, 128.0, 126.6, 116.0, 114.5, 111.2, 61.7, 55.7, 43.6, 39.4, 37.5, 31.8, 25.2, 23.4, 23.1, 22.5, 22.3, 21.6.

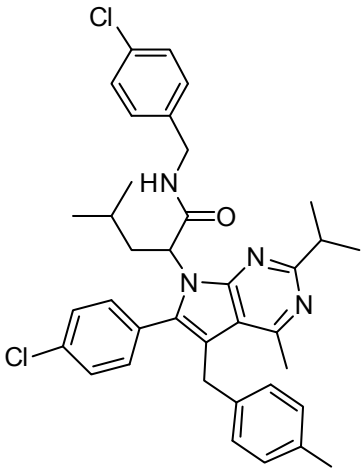
I.R. (thin film) 1671, 1566, 1513, 1421 cm^{-1}.

HRMS Calculated for $C_{37}H_{41}ClN_4O_2$ 608.2918, found 608.2931.





2-[6-(4-chlorophenyl)-2-isopropyl-4-methyl-5-(4-methylbenzyl)-pyrrolo[2,3-*d*]pyrimidin-7-yl]-4-methylpentanoic acid 4-chlorobenzylamide



$C_{37}H_{40}Cl_2N_4O$
MW = 627.65 g.mol^{-1}

3c

General procedure using **2c** (300 mg, 0.48 mmol) and NaH (14 mg, 0.58 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3c** as a yellow oil.

Yield 68 % (205 mg).

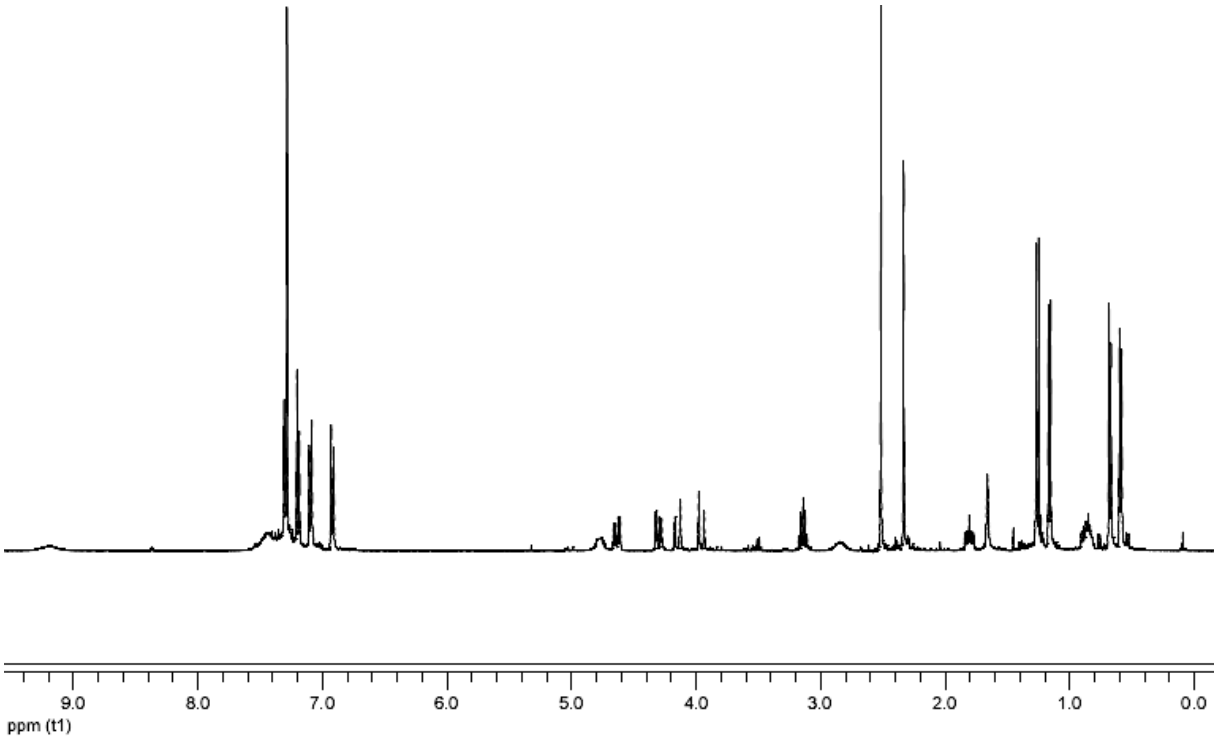
R_f 0.3 (70:30 petroleum ether / diethyl ether).

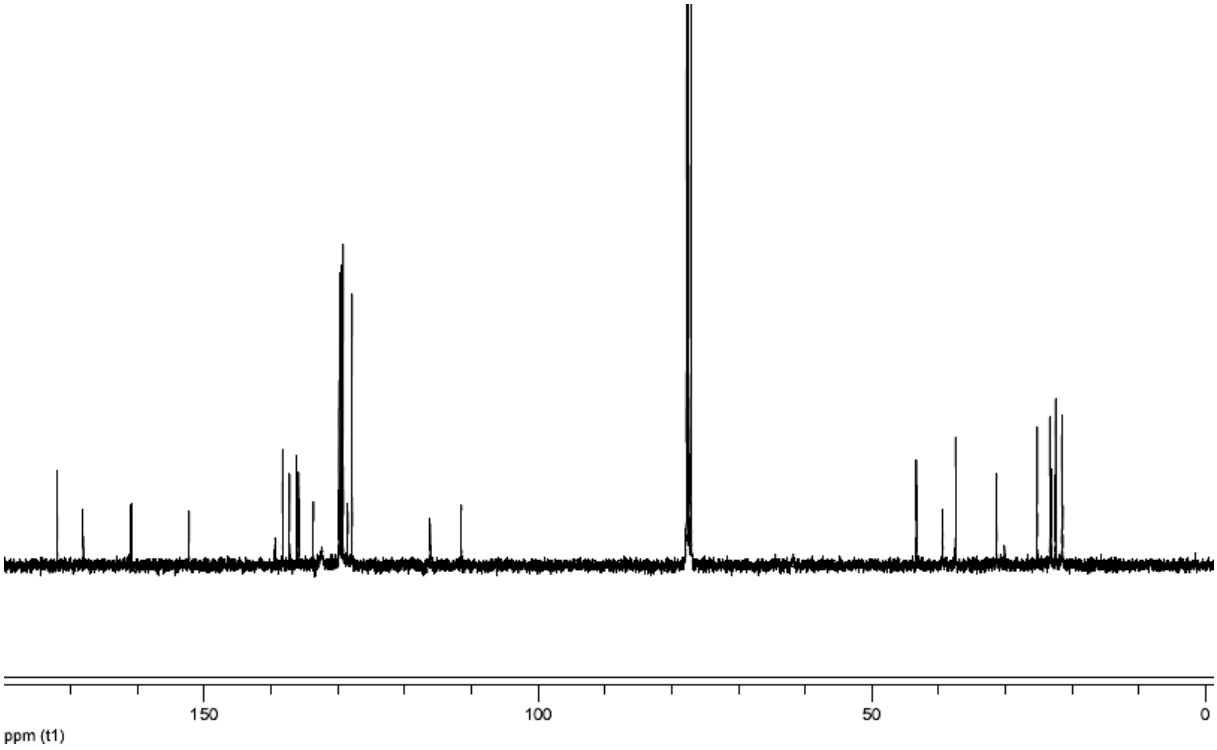
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.20 (br s, 1H), 7.59-7.23 (m, 6H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.92 (d, *J* = 7.9 Hz, 2H), 4.78 (br s, 1H), 4.64 (dd, *J* = 15.0, 6.4 Hz, 1H), 4.30 (dd, *J* = 15.0, 5.1 Hz, 1H), 4.15 (d, *J* = 17.0 Hz, 1H), 3.96 (d, *J* = 17.0 Hz, 1H), 3.14 (sept, *J* = 6.9 Hz, 1H), 2.83 (br s, 1H), 2.52 (s, 3H), 2.34 (s, 3H), 1.85-1.76 (m, 1H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.92-0.80 (m, 1H), 0.68 (d, *J* = 6.6 Hz, 3H), 0.59 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 168.1, 161.0, 152.3, 139.4, 138.3, 137.2, 136.2, 135.9, 133.6, 129.8, 129.5, 129.2, 127.9, 128.5, 116.2, 111.5, 61.8, 43.3, 39.4, 37.4, 31.3, 25.2, 23.3, 23.2, 22.5, 22.4, 21.6, 21.4.

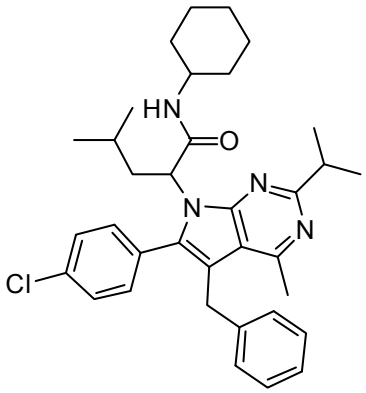
I.R. (thin film) 1671, 1564, 1490, 1422 cm^{-1}.

HRMS Calculated for $C_{37}H_{40}Cl_2N_4O$ 626.2579, found 626.2591.





2-[5-benzyl-6-(4-chlorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-4-methylpentanoic acid cyclohexylamide



$C_{35}H_{43}ClN_4O$
MW = 571.19 g.mol^{-1}

3d

General procedure using **2d** (140 mg, 0.25 mmol) and NaH (7 mg, 0.29 mmol). Purification by flash chromatography (cyclohexane-diethyl ether, 90:10) gave **3d** as a yellow oil.

Yield 57 % (80 mg).

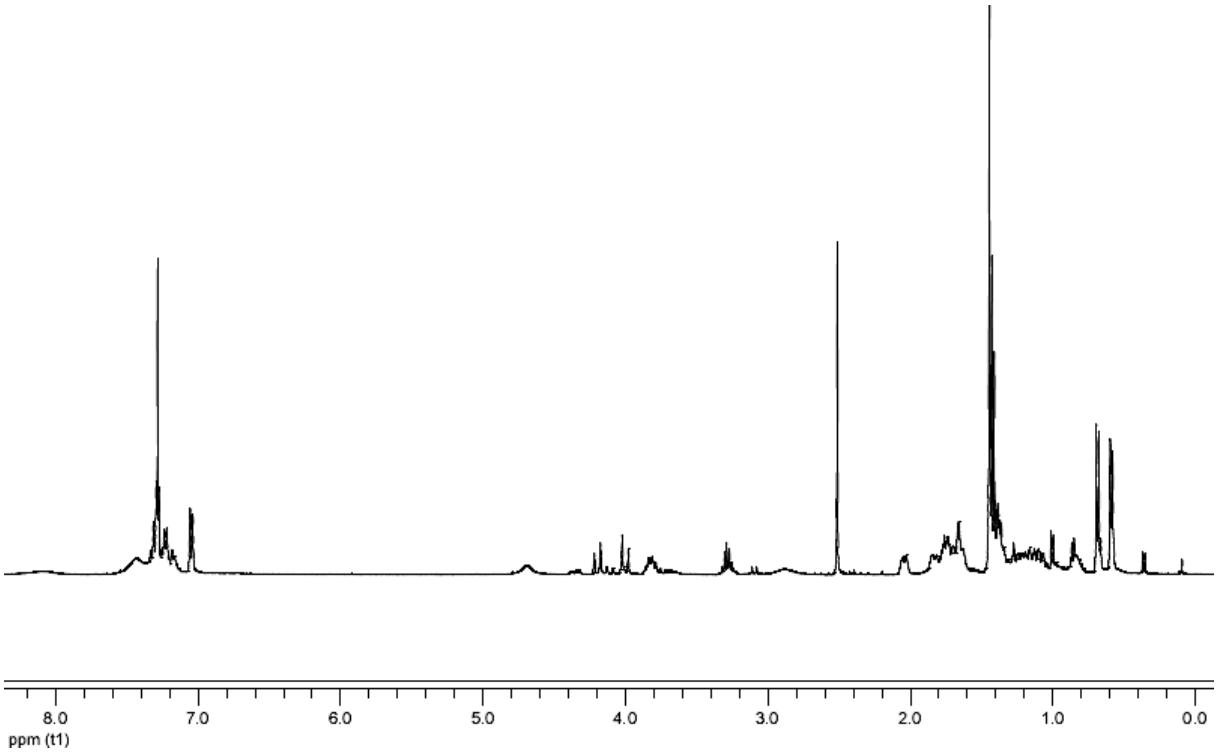
R_f 0.3 (90:10 cyclohexane / diethyl ether).

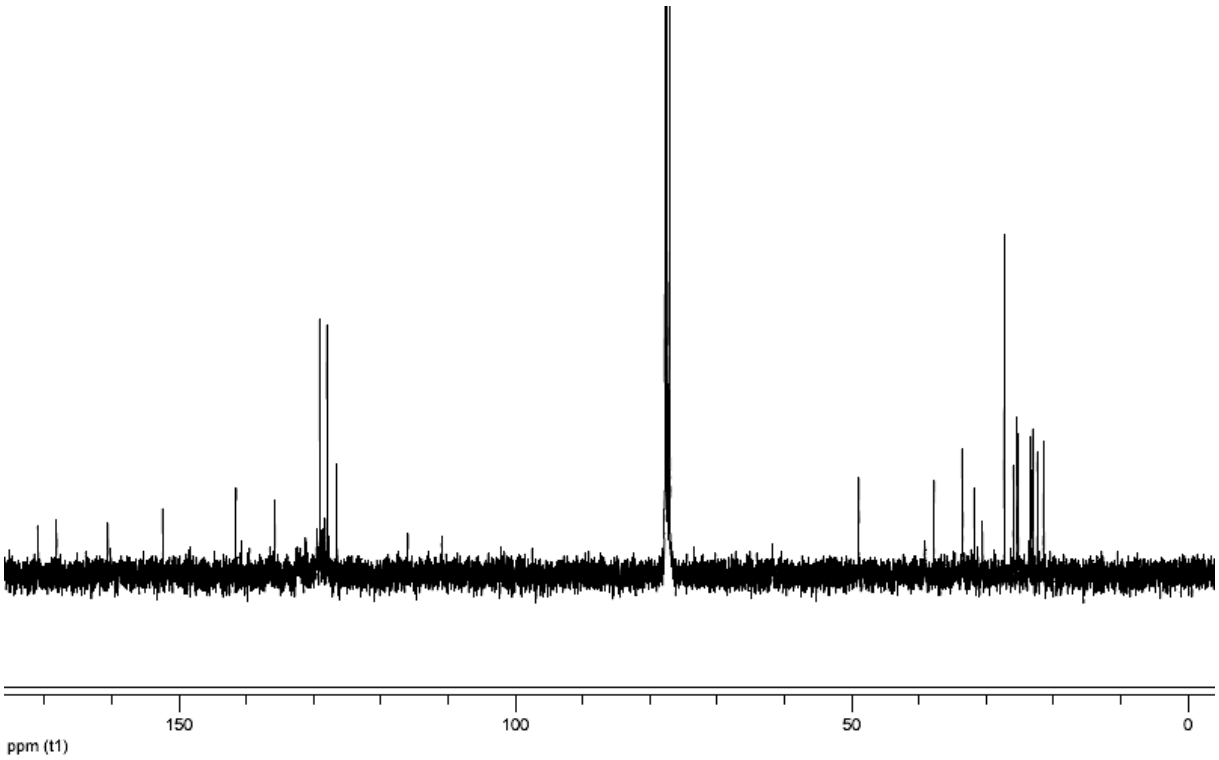
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28-7.94 (br s, 1H), 7.53-7.10 (m, 7H), 7.02 (d, *J* = 7.2 Hz, 2H), 4.67 (br s, 1H), 4.17 (d, *J* = 17.2 Hz, 1H), 3.97 (d, *J* = 17.2 Hz, 1H), 3.86-3.74 (m, 1H), 3.26 (sept, *J* = 6.9 Hz, 1H), 2.86 (br s, 1H), 2.49 (s, 3H), 2.06-1.97 (m, 1H), 1.86-1.57 (m, 4H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.37-0.74 (m, 7H), 0.66 (d, *J* = 6.5 Hz, 3H), 0.57 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.6, 167.8, 160.2, 152.0, 141.1, 140.3, 135.4, 130.8, 128.9, 128.5, 127.9, 127.6, 126.2, 115.6, 110.6, 61.4, 48.5, 38.7, 37.3, 33.1, 33.0, 31.4, 25.5, 25.5, 25.0, 24.8, 23.0, 22.7, 22.6, 22.0, 21.0.

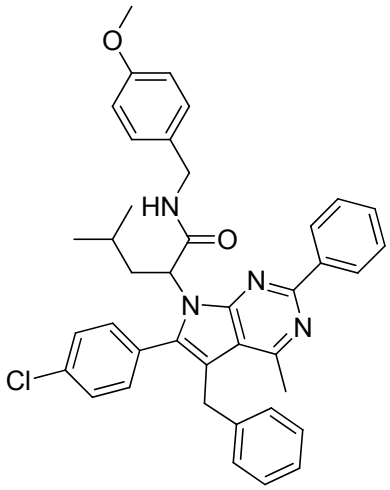
I.R. (thin film) 1668, 1563, 1452, 1420 cm^{-1}.

HRMS Calculated for $C_{35}H_{43}ClN_4O$ 570.3125, found 570.3125.





2-[5-benzyl-6-(4-chlorophenyl)-4-methyl-2-phenylpyrrolo[2,3-*d*]pyrimidin-7-yl]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{40}H_{39}ClN_4O_2$
MW = 643.22 g.mol^{-1}

3e

General procedure using **2e** (160 mg, 0.26 mmol) and NaH (8 mg, 0.31 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3e** as a yellow oil.

Yield 63 % (100 mg).

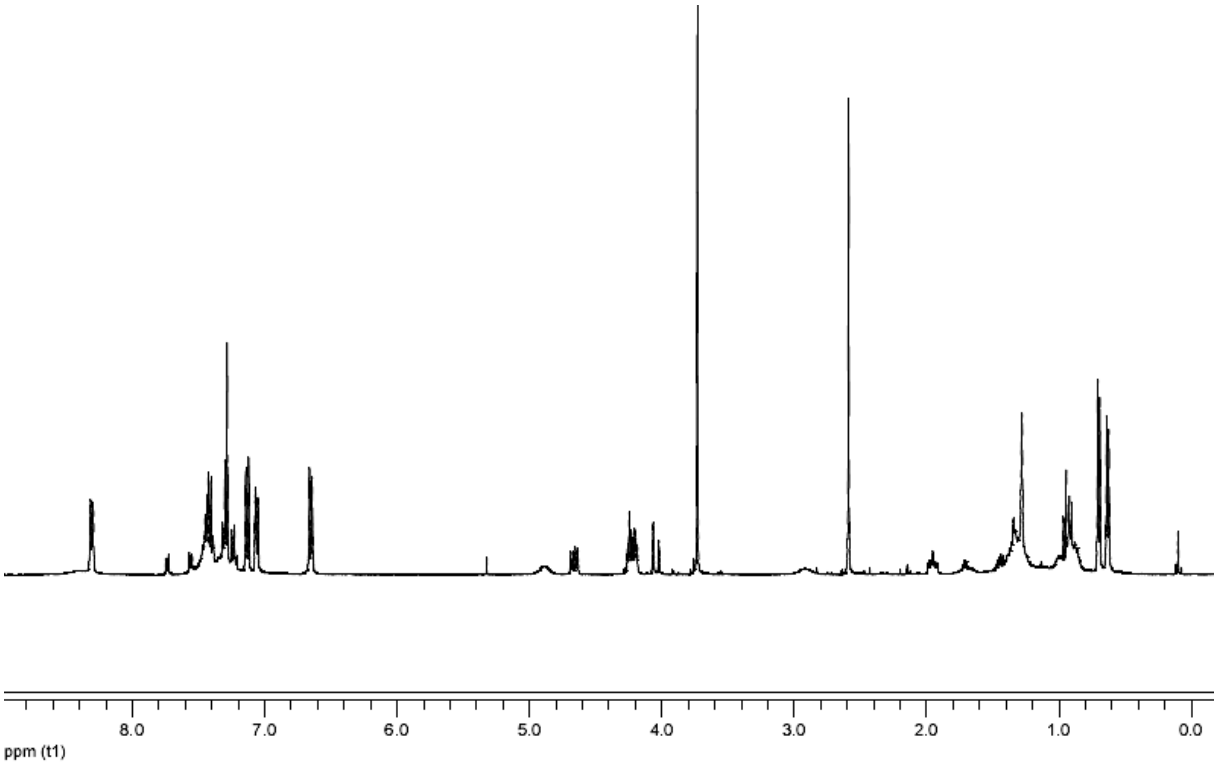
R_f 0.3 (70:30 petroleum ether / diethyl ether).

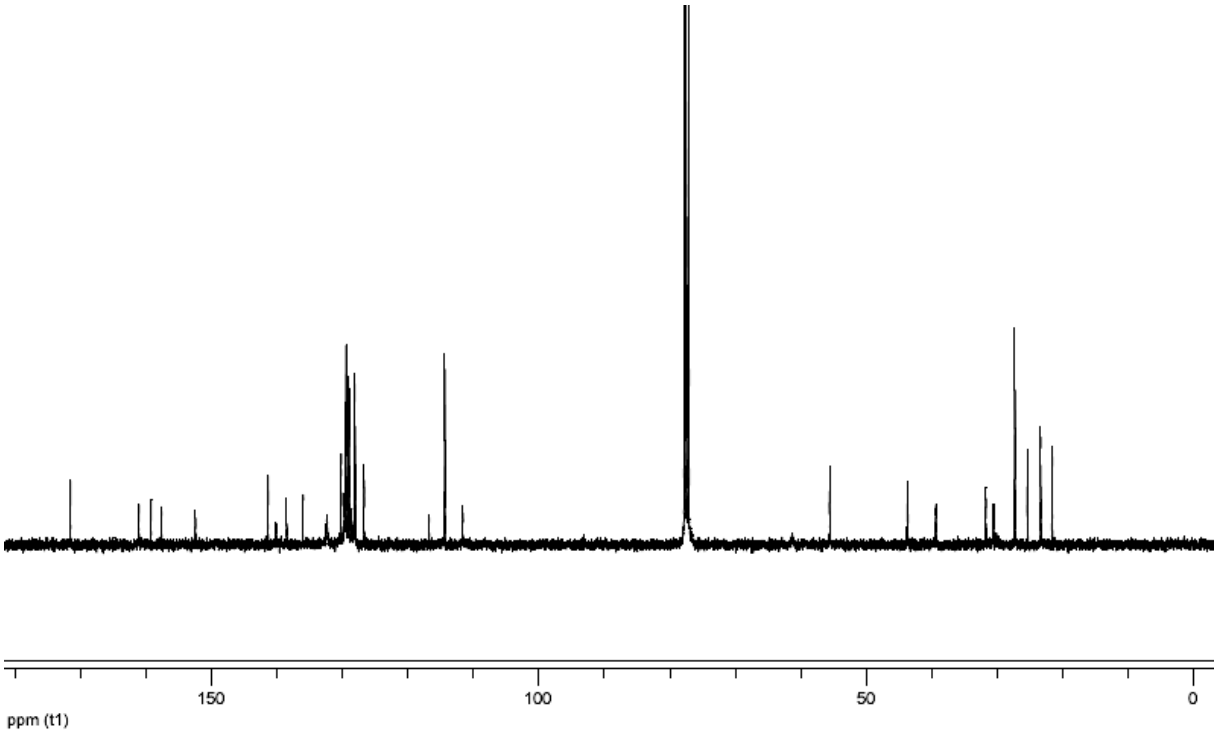
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (d, *J* = 7.1 Hz, 2H), 7.56-7.20 (m, 11H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 7.1 Hz, 2H), 6.66 (d, *J* = 8.6 Hz, 2H), 4.98-4.79 (br s, 1H), 4.67 (dd, *J* = 14.5, 6.5 Hz, 1H), 4.27-4.17 (m, 2H), 4.05 (d, *J* = 17.2 Hz, 1H), 3.73 (s, 3H), 3.06-2.85 (br s, 1H), 2.59 (s, 3H), 2.00-1.89 (m, 1H), 1.06-0.94 (m, 1H), 0.70 (d, *J* = 6.6 Hz, 3H), 0.63 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.5, 161.0, 159.2, 157.6, 152.4, 141.4, 140.1, 138.5, 136.0, 132.4, 130.2, 129.6, 129.4, 129.2, 128.9, 128.5, 128.1, 128.0, 126.7, 116.8, 114.4, 111.6, 61.3, 55.6, 43.7, 39.4, 31.8, 25.4, 23.4, 21.7.

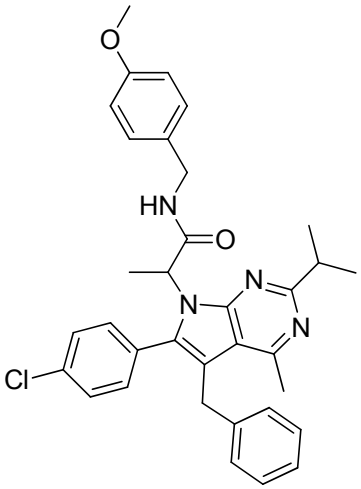
I.R. (thin film) 1668, 1564, 1513, 1416 cm^{-1}.

HRMS Calculated for $C_{40}H_{39}ClN_4O_2$ 642.2762, found 642.2781.





2-[5-benzyl-6-(4-chlorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-*N*-(4-methoxybenzyl)-propionamide



$C_{34}H_{35}ClN_4O_2$
MW = 567.12 g.mol^{-1}

3f

General procedure using **2f** (200 mg, 0.35 mmol) and NaH (10 mg, 0.42 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3f** as a yellow oil.

Yield 65 % (130 mg).

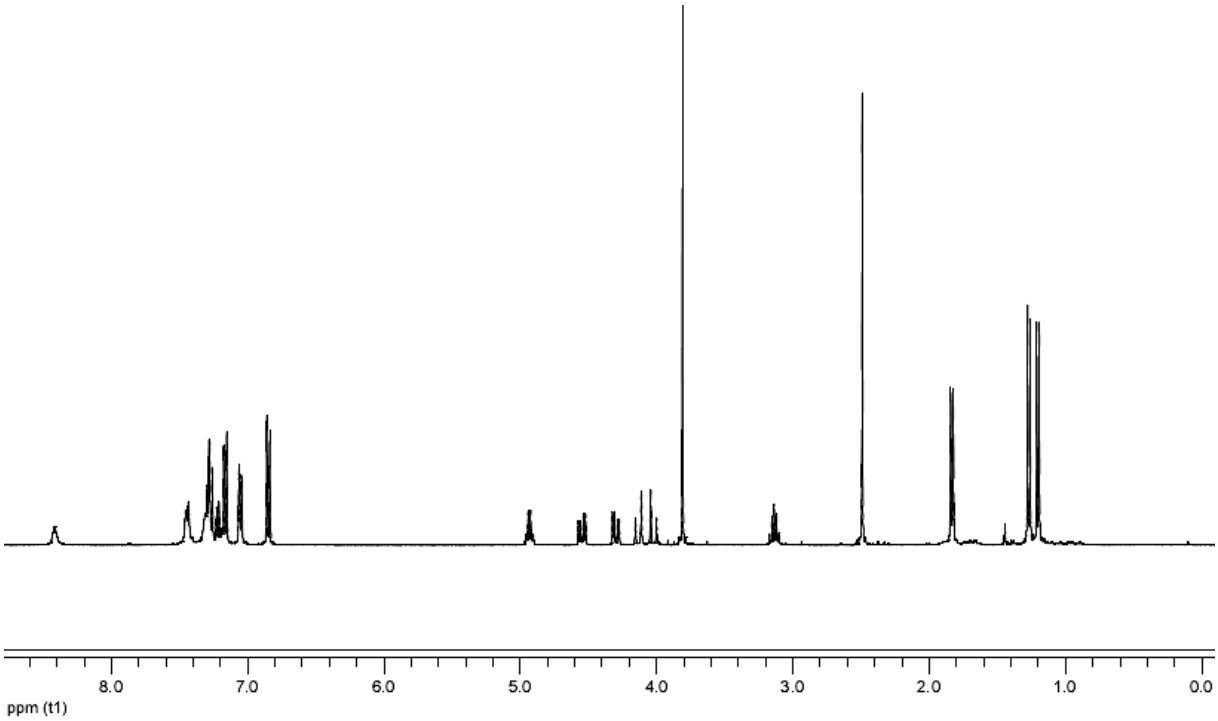
R_f 0.3 (70:30 petroleum ether / diethyl ether).

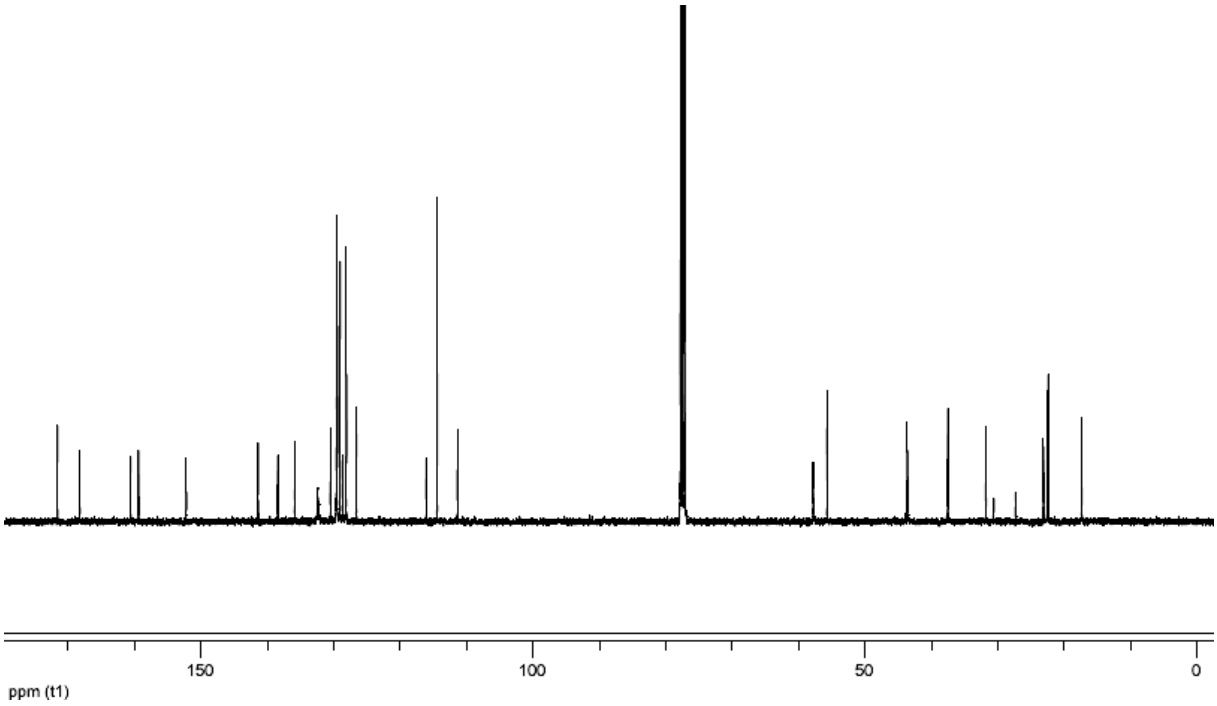
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.42 (t, *J* = 5.3 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 2H), 7.36-7.19 (m, 5H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 7.2 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.93 (q, *J* = 7.4 Hz, 1H), 4.55 (dd, *J* = 14.6, 6.0 Hz, 1H), 4.30 (dd, *J* = 14.6, 5.0 Hz, 1H), 4.13 (d, *J* = 17.1 Hz, 1H), 4.02 (d, *J* = 17.1 Hz, 1H), 3.81 (s, 3H), 3.13 (sept, *J* = 6.9 Hz, 1H), 2.49 (s, 3H), 1.83 (d, *J* = 7.4 Hz, 3H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.6, 168.3, 160.6, 159.4, 152.2, 141.4, 138.4, 135.9, 132.4, 130.5, 129.6, 129.5, 129.1, 128.7, 128.1, 126.6, 116.1, 114.4, 111.4, 57.8, 55.7, 43.6, 37.5, 31.8, 23.1, 22.5, 22.4, 17.4.

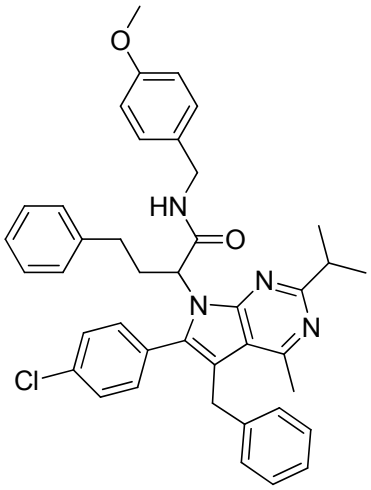
I.R. (thin film) 1667, 1564, 1513, 1421 cm^{-1}.

HRMS Calculated for $C_{34}H_{35}ClN_4O_2$ 566.2449, found 566.2459.





2-[5-benzyl-6-(4-chlorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-*N*-(4-methoxybenzyl)-4-phenylbutyramide



$C_{41}H_{41}ClN_4O_2$
MW = 657.24 g.mol^{-1}

3g

General procedure using **2g** (330 mg, 0.50 mmol) and NaH (14 mg, 0.60 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3g** as a yellow oil.

Yield 62 % (205 mg).

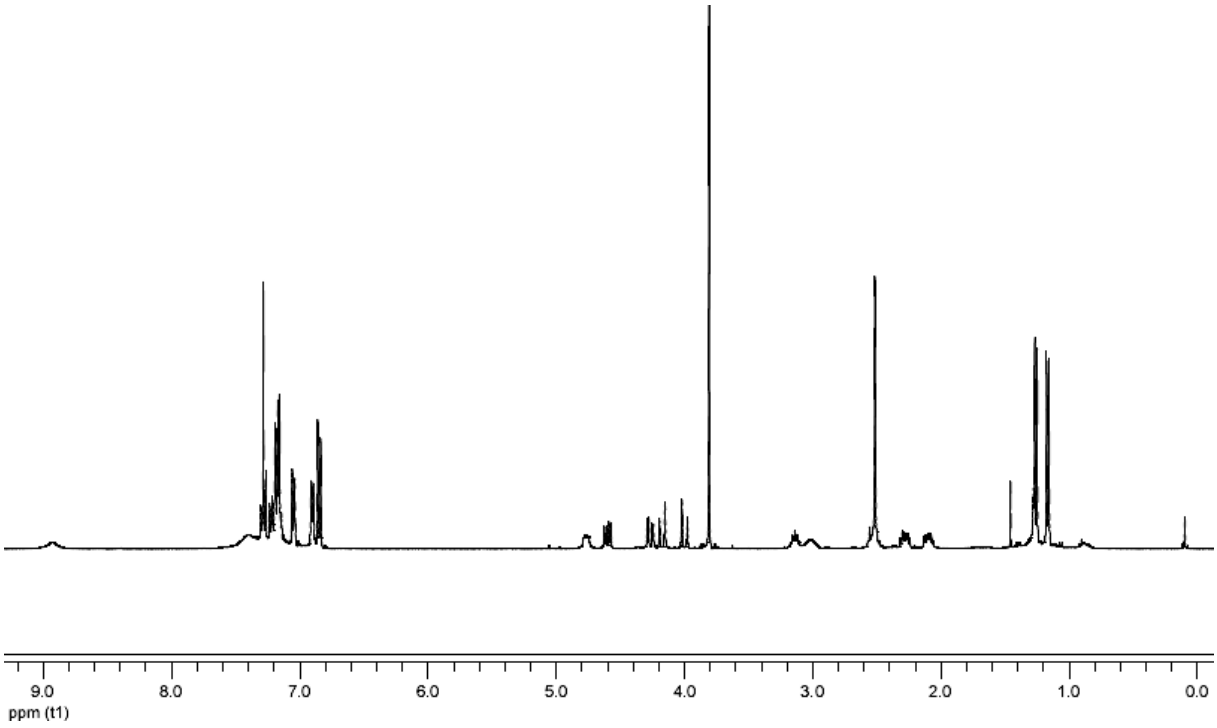
R_f 0.3 (70:30 petroleum ether / diethyl ether).

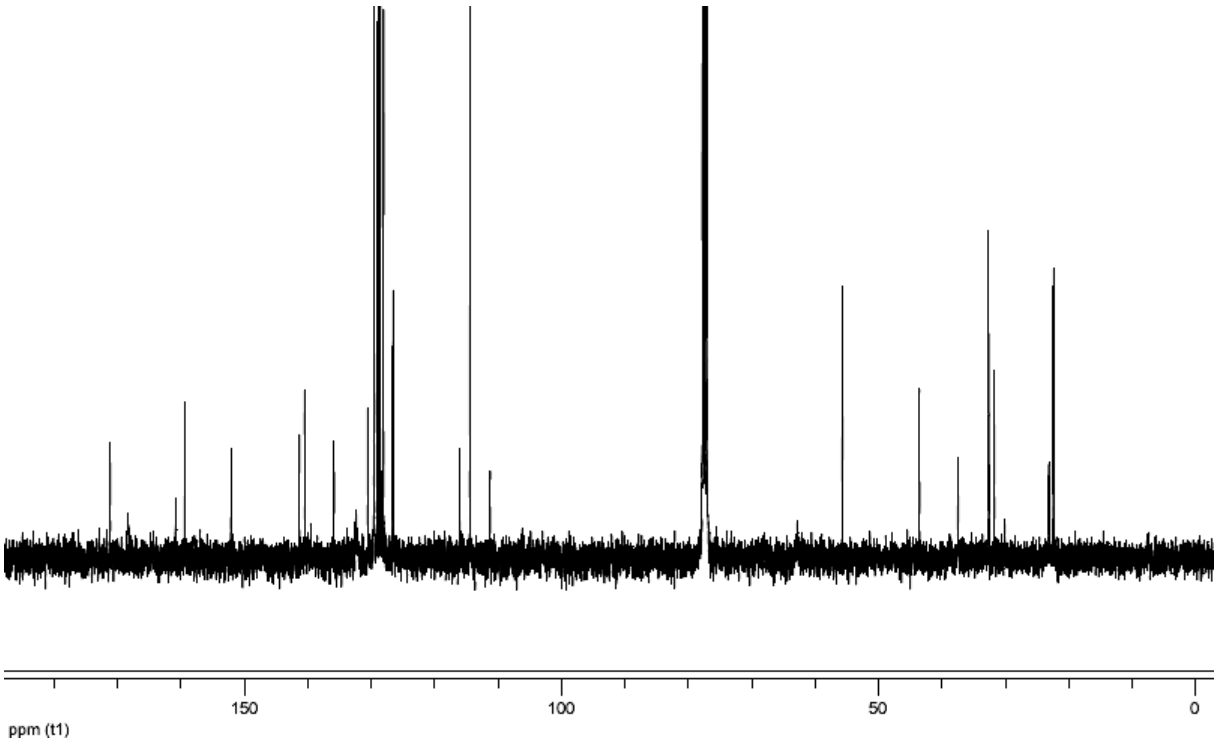
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.94 (br s, 1H), 7.57-7.32 (m, 2H), 7.25-7.11 (m, 6H), 7.05 (d, *J* = 7.2 Hz, 2H), 6.90 (d, *J* = 7.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.82-4.71 (m, 1H), 4.60 (dd, *J* = 14.6, 6.2 Hz, 1H), 4.27 (dd, *J* = 14.6, 4.8 Hz, 1H), 4.18 (d, *J* = 17.1 Hz, 1H), 4.00 (d, *J* = 17.1 Hz, 1H), 3.81 (s, 3H), 3.14 (sept, *J* = 6.9 Hz, 1H), 3.08-2.95 (m, 1H), 2.58-2.52 (m, 1H), 2.51 (s, 3H), 2.33-2.23 (m, 1H), 2.14-2.05 (m, 1H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.2, 168.3, 160.9, 159.4, 152.2, 141.4, 140.5, 139.5, 135.8, 132.4, 130.6, 129.5, 129.1, 128.8, 128.6, 128.1, 126.7, 126.5, 116.1, 114.5, 111.2, 62.8, 55.7, 43.6, 37.5, 32.6, 32.6, 31.8, 23.2, 22.5, 22.4.

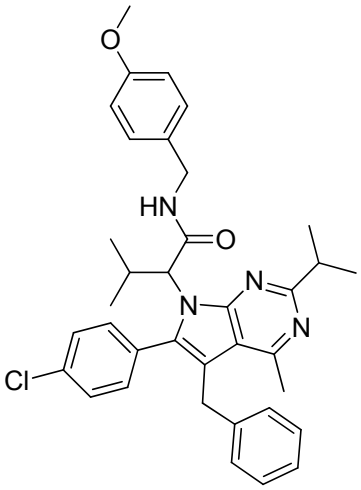
I.R. (thin film) 1669, 1567, 1513, 1425 cm^{-1}.

HRMS Calculated for $C_{41}H_{41}ClN_4O_2$ 656.2918, found 656.2910.





2-[5-benzyl-6-(4-chlorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-d]pyrimidin-7-yl]-*N*-(4-methoxybenzyl)-3-methylbutyramide



$C_{36}H_{39}ClN_4O_2$
MW = 595.17 g.mol^{-1}

3h

General procedure using **2h** (300 mg, 0.50 mmol) and NaH (14 mg, 0.60 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3h** as a yellow oil.

Yield 55 % (165 mg).

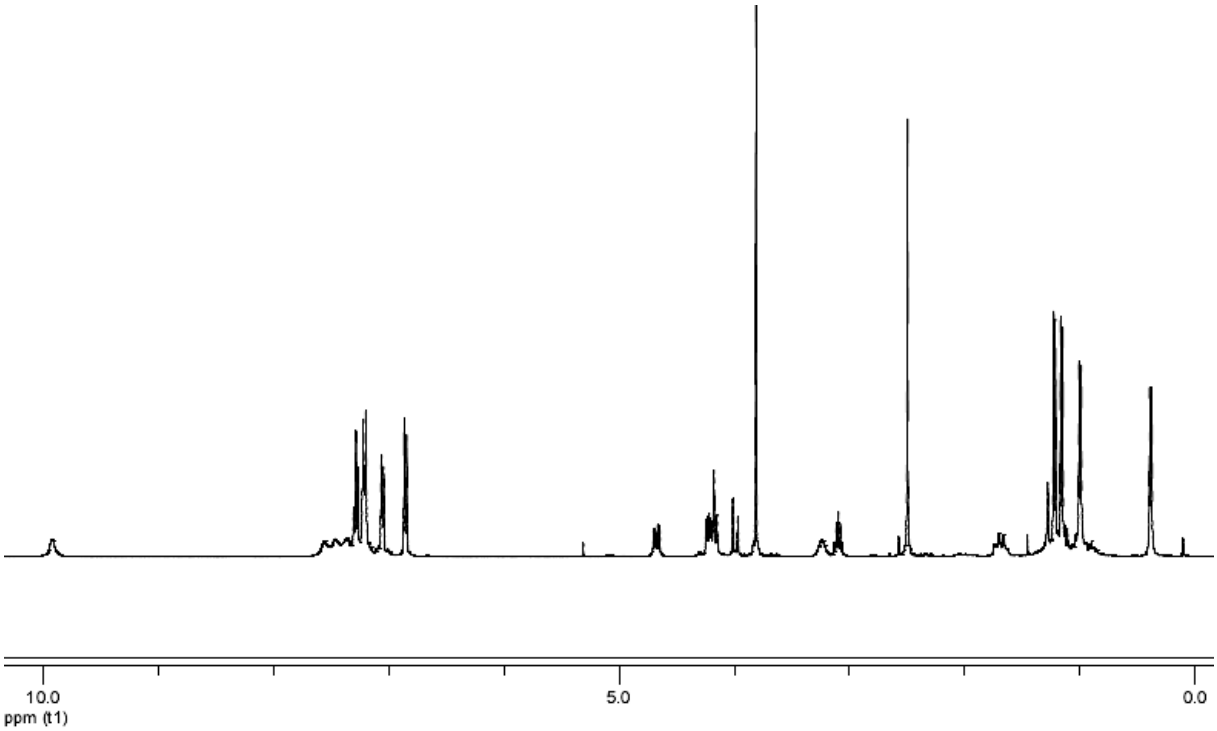
R_f 0.3 (70:30 petroleum ether / diethyl ether).

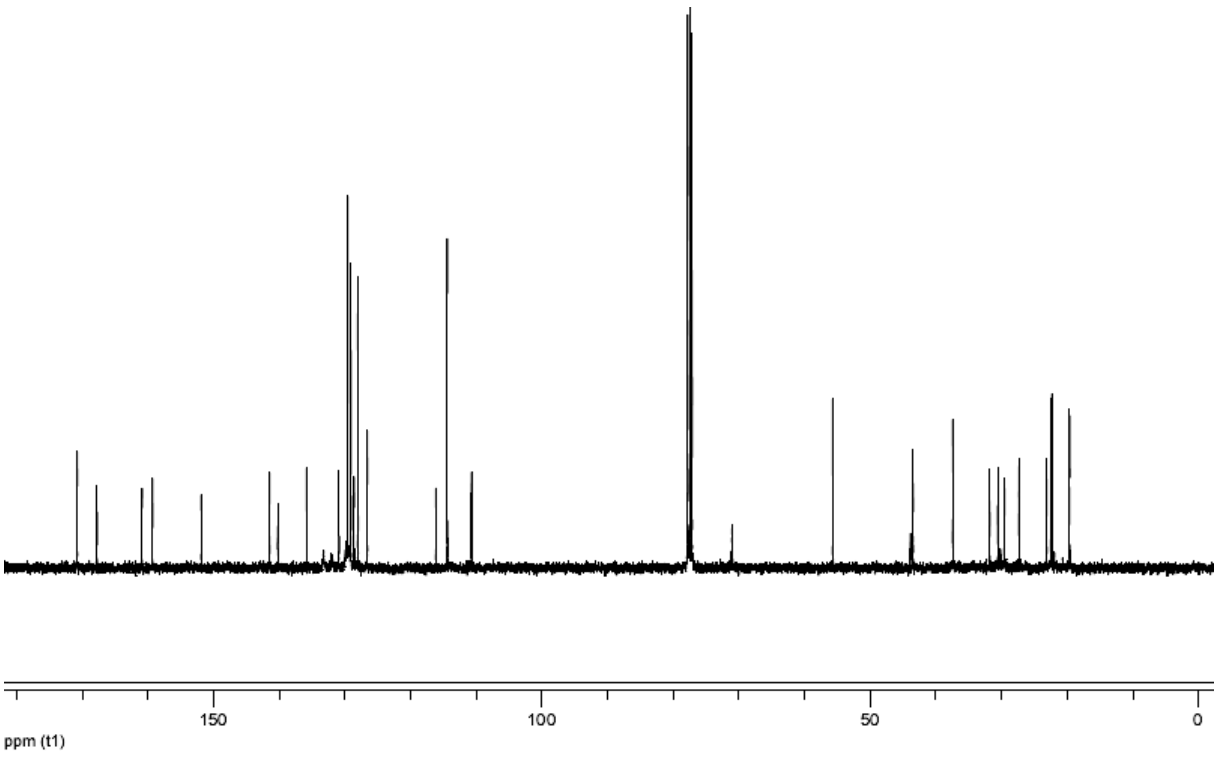
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.93 (br s, 1H), 7.64-7.32 (m, 3H), 7.32-7.25 (m, 2H), 7.25-7.18 (m, 4H), 7.06 (d, *J* = 7.3 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.68 (dd, *J* = 14.5, 6.4 Hz, 1H), 4.25-4.13 (m, 3H), 3.99 (d, *J* = 17.2 Hz, 1H), 3.81 (s, 3H), 3.30-3.17 (m, 1H), 3.10 (sept, *J* = 6.9 Hz, 1H), 2.50 (s, 3H), 1.22 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.38 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.8, 167.7, 160.9, 159.3, 151.9, 141.5, 140.2, 135.8, 130.9, 129.6, 129.1, 128.6, 128.0, 126.6, 116.1, 114.4, 110.7, 71.1, 55.7, 43.5, 37.4, 31.8, 29.6, 23.2, 22.5, 22.3, 19.7, 19.6.

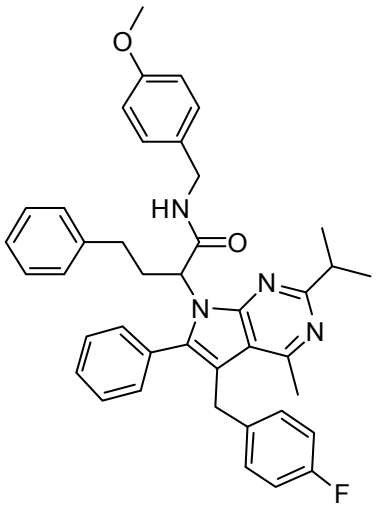
I.R. (thin film) 1672, 1565, 1513, 1421 cm^{-1}.

HRMS Calculated for $C_{36}H_{39}ClN_4O_2$ 594.2761, found 594.2730.





2-[5-(4-fluorobenzyl)-2-isopropyl-4-methyl-6-phenylpyrrolo[2,3-*d*]pyrimidin-7-yl]-*N*-(4-methoxybenzyl)-4-phenylbutyramide



$C_{41}H_{41}FN_4O_2$
MW = 640.79 g.mol^{-1}

3i

General procedure using **2i** (260 mg, 0.41 mmol) and NaH (12 mg, 0.49 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 60:40) gave **3i** as a yellow oil.

Yield 51 % (132 mg).

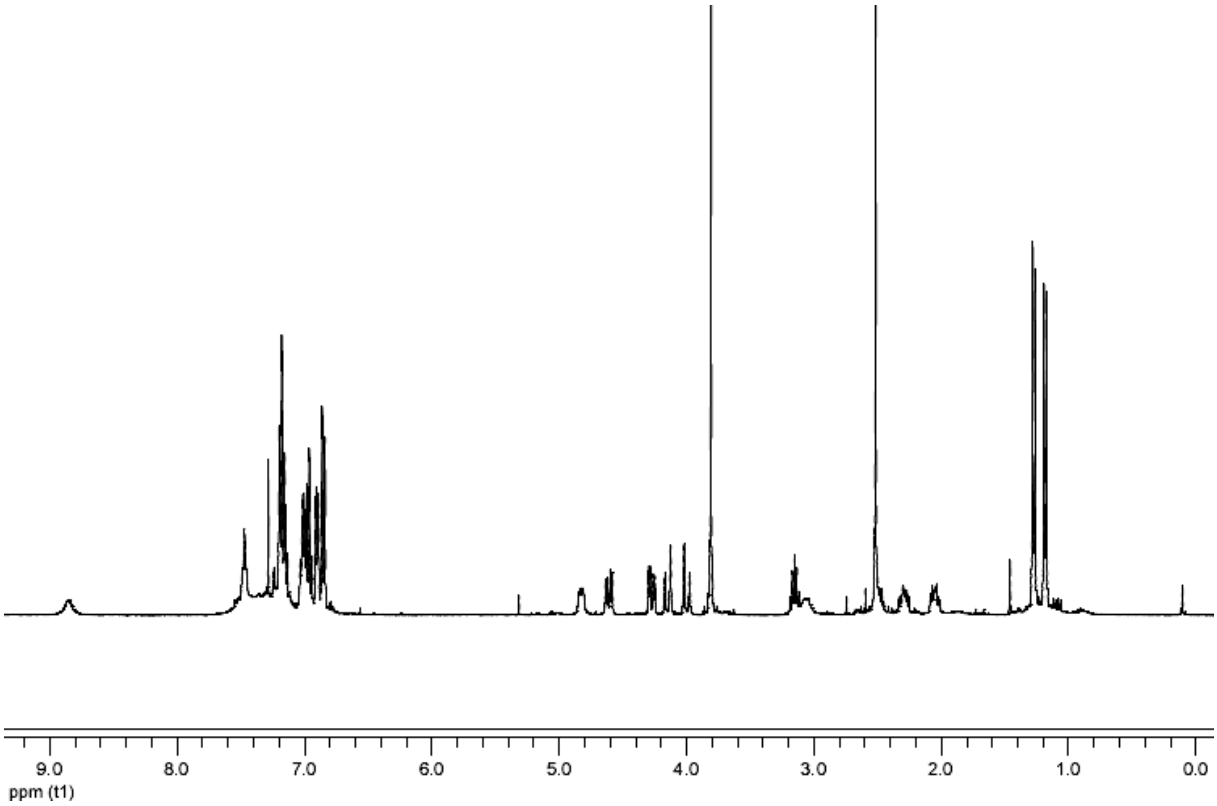
R_f 0.3 (60:40 petroleum ether / diethyl ether).

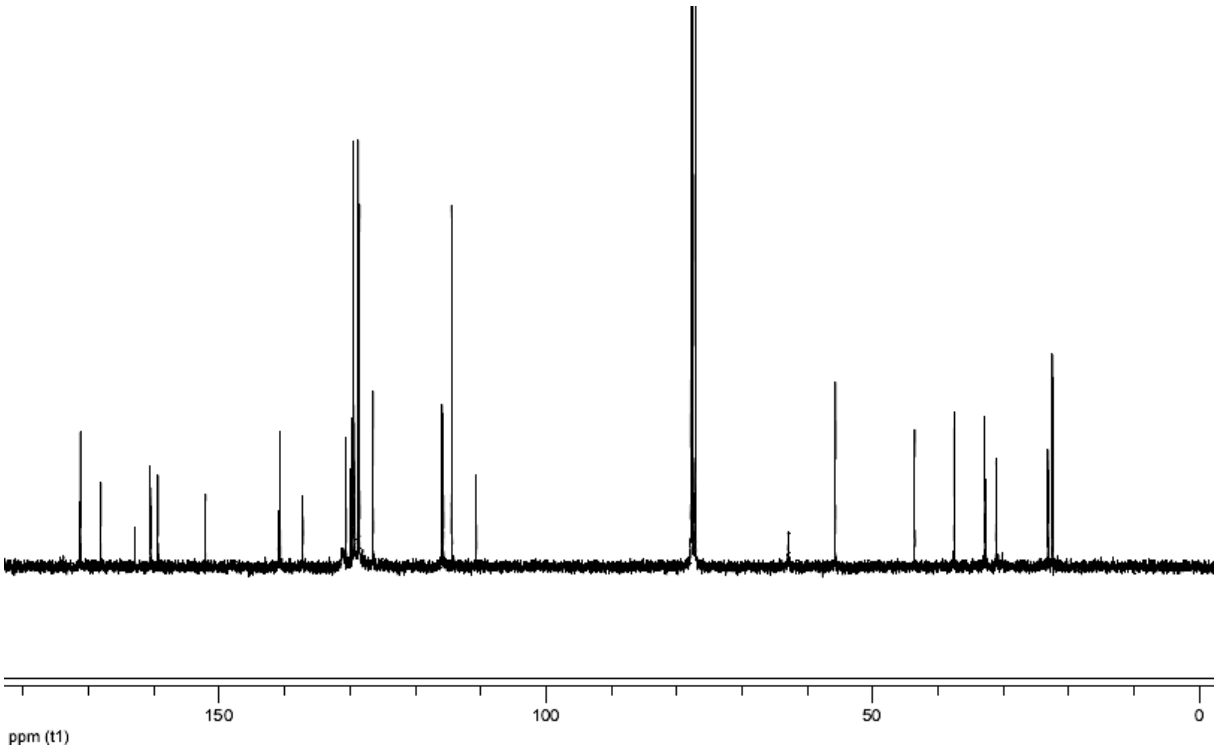
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (br s, 1H), 7.67-7.28 (m, 4H), 7.26-7.07 (m, 6H), 7.02 (dd, $J_{H\text{-}H,\ H\text{-}F}$ = 8.8, 5.5 Hz, 2H), 6.96 (t, $J_{H\text{-}H}$ = $J_{H\text{-}F}$ = 8.8 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 4.83 (dd, J = 10.4, 5.0 Hz, 1H), 4.61 (dd, J = 14.6, 6.3 Hz, 1H), 4.27 (dd, J = 14.6, 4.8 Hz, 1H), 4.15 (d, J = 17.0 Hz, 1H), 4.00 (d, J = 17.0 Hz, 1H), 3.81 (s, 3H), 3.15 (sept, J = 6.9 Hz, 1H), 3.11-2.99 (m, 1H), 2.52 (s, 3H), 2.51-2.45 (m, 1H), 2.34-2.24 (m, 1H), 2.10-2.00 (m, 1H), 1.27 (d, J = 6.9 Hz, 3H), 1.19 (d, J = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.3, 168.2, 161.7 (d, $J_{C\text{-}F}$ = 243.0 Hz), 160.5, 159.4, 152.1, 141.0, 140.7, 137.3 (d, $J_{C\text{-}F}$ = 3.0 Hz), 130.6, 129.9, 129.7, 129.5, 129.4 (d, $J_{C\text{-}F}$ = 8.0 Hz), 128.8, 128.6, 126.5, 116.0, 115.8 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.5, 110.7, 63.0, 55.7, 43.6, 37.5, 32.8, 32.7, 31.1, 23.2, 22.5, 22.4.

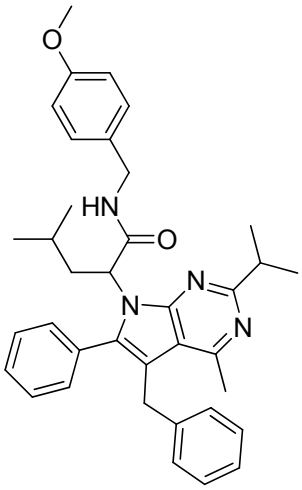
I.R. (thin film) 1668, 1571, 1508, 1422 cm^{-1}.

HRMS Calculated for $C_{41}H_{41}FN_4O_2$ 640.3214, found 640.3216.





2-(5-benzyl-2-isopropyl-4-methyl-6-phenylpyrrolo[2,3-*d*]pyrimidin-7-yl)-4-methylpentanoic acid 4-methoxybenzylamide



$C_{37}H_{42}N_4O_2$
MW = 574.75 g.mol^{-1}

3j

General procedure using **2j** (290 mg, 0.50 mmol) and NaH (14 mg, 0.60 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3j** as a yellow oil.

Yield 66 % (192 mg).

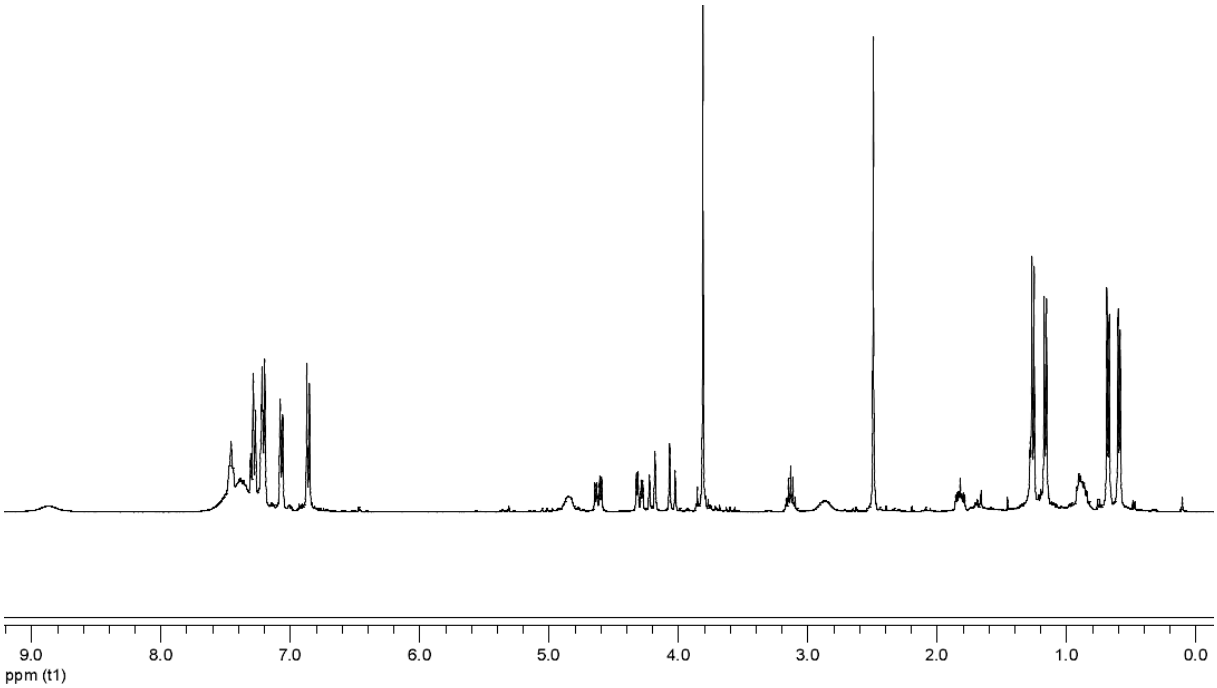
R_f 0.3 (70:30 petroleum ether / diethyl ether).

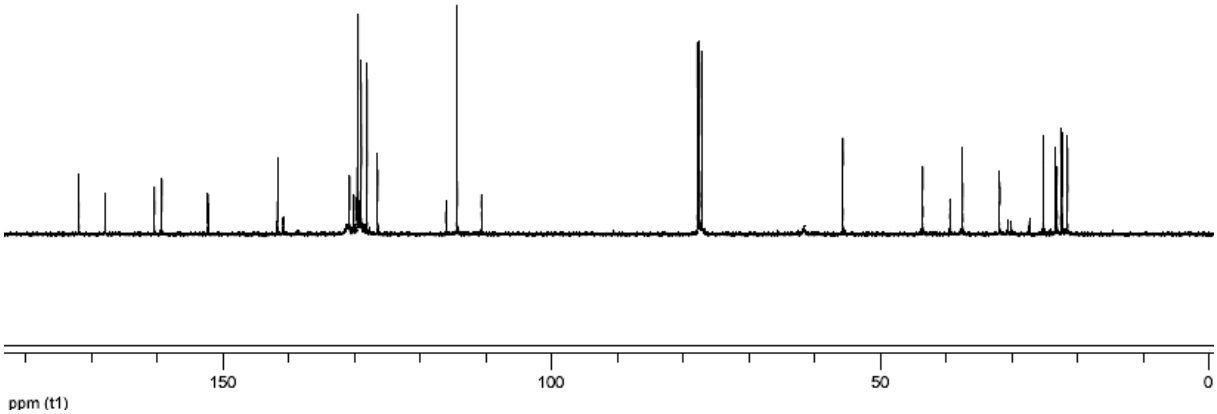
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64-7.32 (m, 5H), 7.32-7.25 (m, 3H), 7.24-7.18 (m, 3H), 7.06 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.92-4.78 (br s, 1H), 4.62 (dd, *J* = 14.6, 6.2 Hz, 1H), 4.30 (dd, *J* = 14.6, 4.9 Hz, 1H), 4.20 (d, *J* = 17.2 Hz, 1H), 4.04 (d, *J* = 17.2 Hz, 1H), 3.81 (s, 3H), 3.13 (sept, *J* = 6.9 Hz, 1H), 2.96-2.76 (br s, 1H), 2.49 (s, 3H), 1.86-1.77 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.93-0.80 (m, 1H), 0.67 (d, *J* = 6.6 Hz, 3H), 0.59 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.0, 168.0, 160.5, 159.4, 152.3, 141.8, 140.9, 130.8, 130.1, 129.6, 129.5, 129.2, 129.0, 128.1, 126.5, 116.1, 114.4, 110.7, 61.7, 55.7, 43.6, 39.4, 37.5, 31.9, 25.2, 23.4, 23.2, 22.5, 22.4, 21.5.

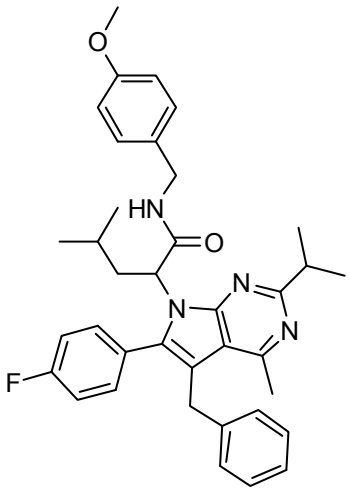
I.R. (thin film) 1668, 1567, 1512, 1420 cm^{-1}.

HRMS Calculated for $C_{37}H_{42}N_4O_2$ 574.3308, found 574.3303.





2-[5-benzyl-6-(4-fluorophenyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-4-methylpentanoic acid 4-methoxybenzylamide



$C_{37}H_{41}FN_4O_2$
MW = 592.75 g.mol^{-1}

3k

General procedure using **2k** (110 mg, 0.19 mmol) and NaH (6 mg, 0.25 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) gave **3k** as a yellow oil.

Yield 73 % (80 mg).

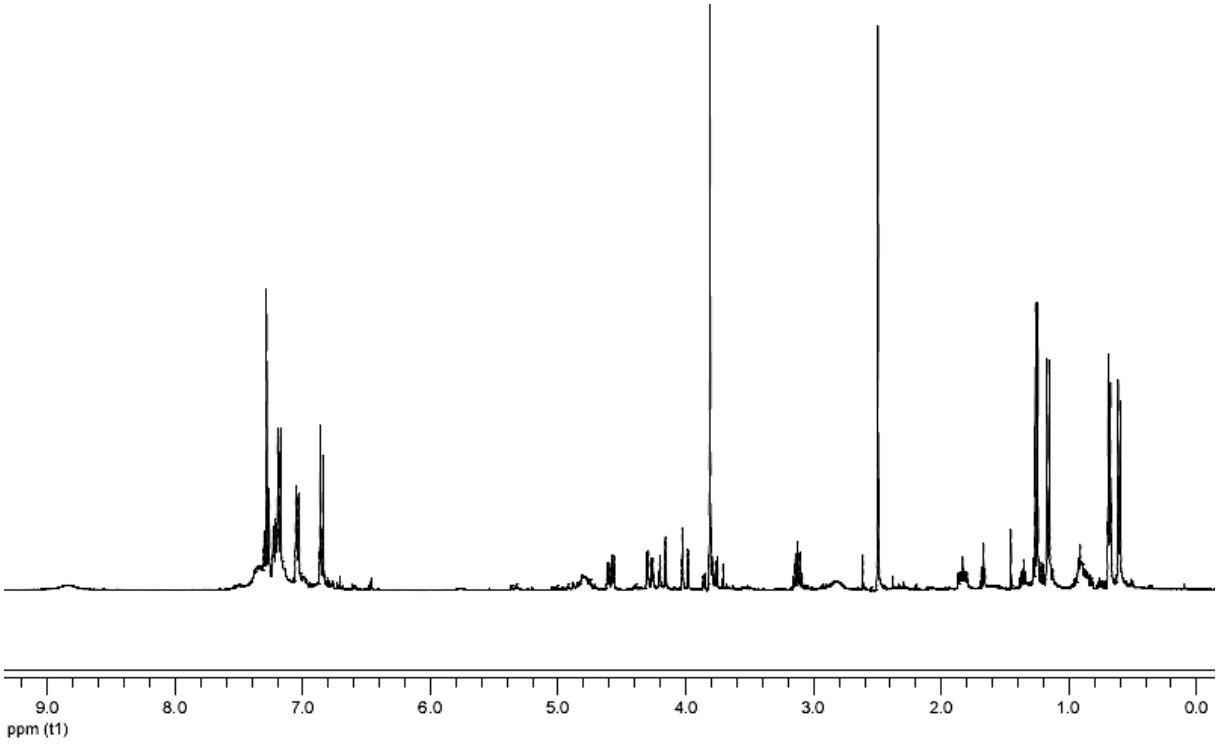
R_f 0.3 (70:30 petroleum ether / diethyl ether).

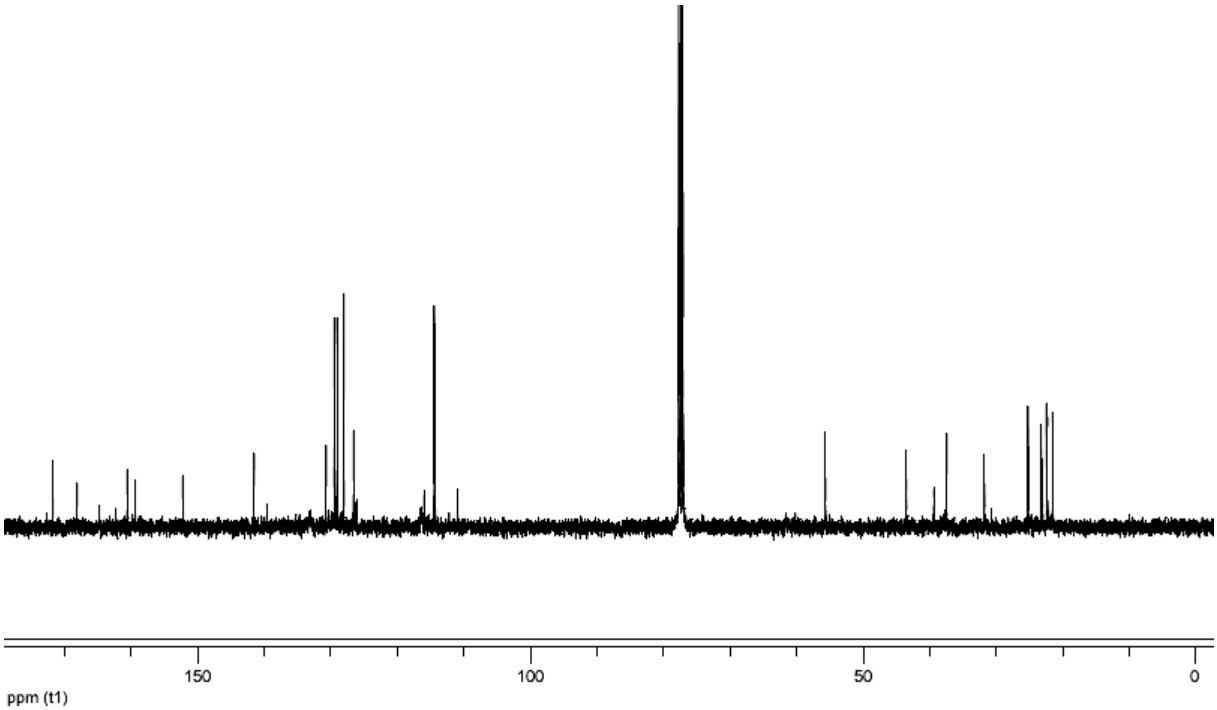
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (br s, 1H), 7.43-7.25 (m, 4H), 7.24-7.14 (m, 5H), 7.04 (d, *J* = 7.2 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.87-4.74 (br s, 1H), 4.59 (dd, *J* = 14.6, 6.2 Hz, 1H), 4.28 (dd, *J* = 14.6, 5.0 Hz, 1H), 4.18 (d, *J* = 17.2 Hz, 1H), 4.00 (d, *J* = 17.2 Hz, 1H), 3.81 (s, 3H), 3.14 (sept, *J* = 6.9 Hz, 1H), 2.90-2.74 (br s, 1H), 2.50 (s, 3H), 1.88-1.78 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.96-0.84 (m, 1H), 0.68 (d, *J* = 6.6 Hz, 3H), 0.61 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.8, 168.1, 163.6 (d, $J_{C\text{-}F}$ = 251.0 Hz), 160.6, 159.4, 152.3, 141.5, 139.6, 130.7, 129.5, 129.3 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.1, 128.1, 126.6, 126.2 (d, $J_{C\text{-}F}$ = 2.9 Hz), 116.4 (d, $J_{C\text{-}F}$ = 20.5 Hz), 116.0, 114.4, 111.0, 61.6, 55.7, 43.6, 39.4, 37.5, 31.8, 25.2, 23.3, 22.5, 22.3, 21.6.

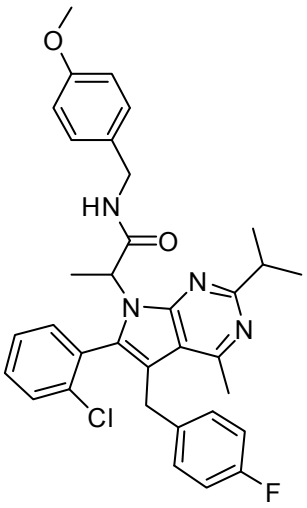
I.R. (thin film) 1668, 1560, 1511, 1421 cm^{-1}.

HRMS Calculated for $C_{37}H_{41}FN_4O_2$ 592.3214, found 592.3210.





2-[6-(2-chlorophenyl)-5-(4-fluorobenzyl)-2-isopropyl-4-methylpyrrolo[2,3-*d*]pyrimidin-7-yl]-*N*-(4-methoxybenzyl)-propionamide



$C_{34}H_{34}ClFN_4O_2$
MW = 585.11 g.mol^{-1}

3l

General procedure using **2l** (260 mg, 0.44 mmol) and NaH (13 mg, 0.53 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 50:50) gave **3l** as a yellow oil. Two atropoisomers were obtained in a 1:1 ratio.

Yield 54 % (140 mg).

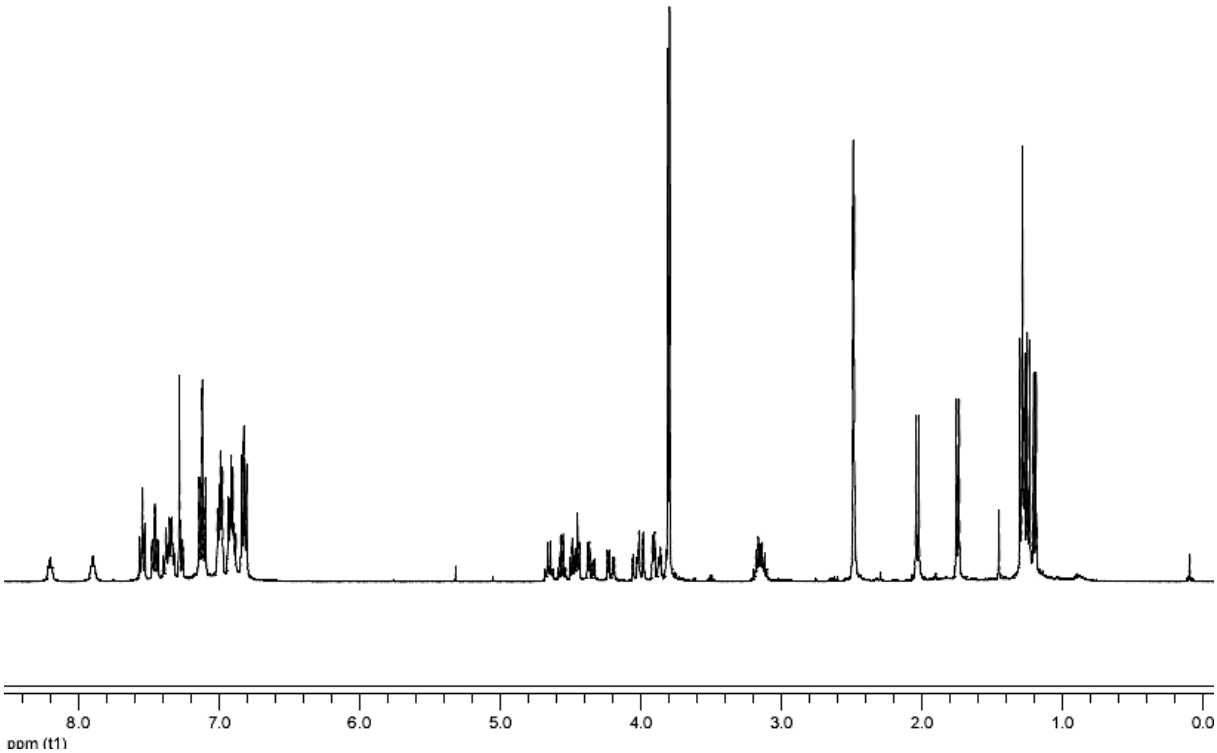
R_f 0.3 (70:30 petroleum ether / diethyl ether).

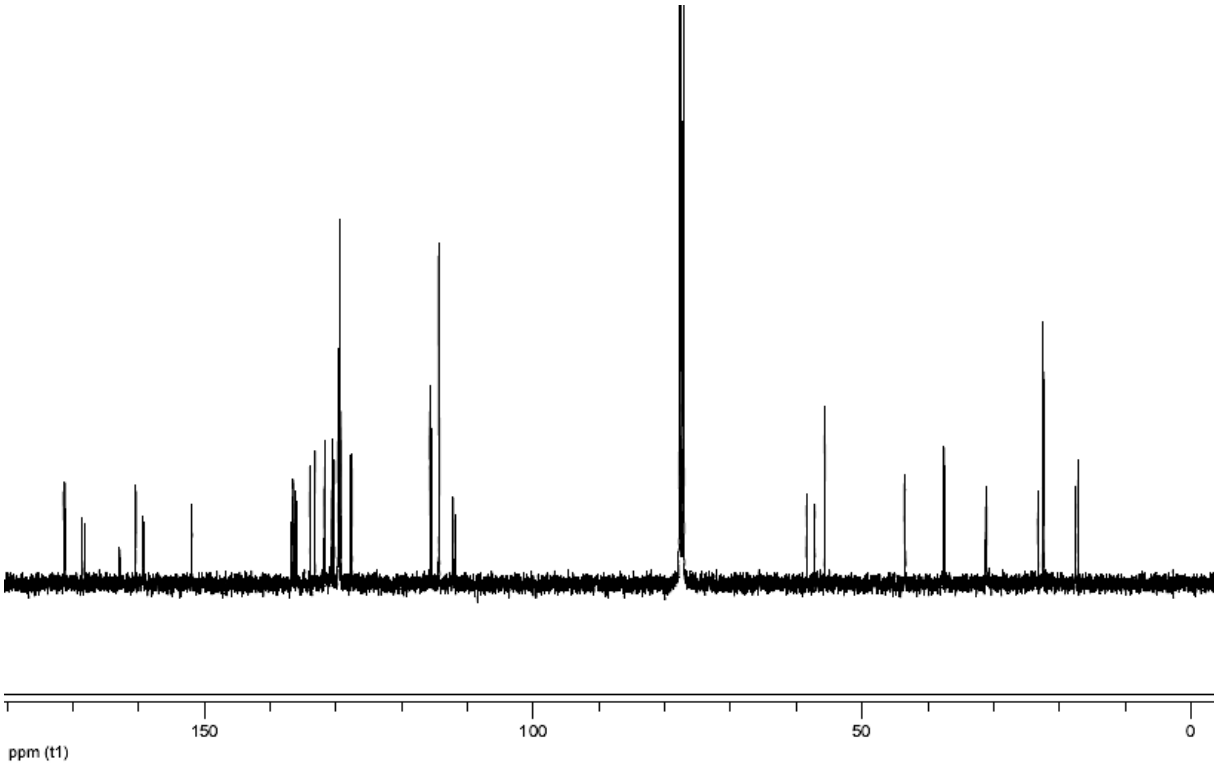
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (t, J = 5.3 Hz, 1H), 7.90 (t, J = 5.3 Hz, 1H), 7.58-7.52 (m, 2H), 7.49-7.43 (m, 2H), 7.41-7.31 (m, 3H), 7.27 (dd, J = 7.6, 1.5 Hz, 1H), 7.12 (d, J = 8.6 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 7.00 (dd, $J_{H\text{-}H,\ H\text{-}F}$ = 8.7, 5.6 Hz, 4H), 6.92 (t, $J_{H\text{-}H}$ = $J_{H\text{-}F}$ = 8.7 Hz, 2H), 6.91 (t, $J_{H\text{-}H}$ = $J_{H\text{-}F}$ = 8.7 Hz, 2H), 6.85-6.79 (m, 4H), 4.65 (q, J = 7.3 Hz, 1H), 4.56 (q, J = 7.3 Hz, 1H), 4.51-4.43 (m, 2H), 4.35 (dd, J = 14.7, 5.4 Hz, 1H), 4.21 (dd, J = 14.7, 5.0 Hz, 1H), 4.07-3.97 (m, 2H), 3.93-3.85 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.16 (sept, J = 6.9 Hz, 1H), 3.14 (sept, J = 6.9 Hz, 1H), 2.49 (s, 3H), 2.48 (s, 3H), 2.03 (d, J = 7.3 Hz, 3H), 1.75 (d, J = 7.3 Hz, 3H), 1.30 (d, J = 6.9 Hz, 3H), 1.28 (d, J = 6.9 Hz, 3H), 1.24 (d, J = 6.9 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.5, 171.2, 168.6, 168.3, 161.7 (d, $J_{C\text{-}F}$ = 245.2 Hz), 160.5, 160.4, 159.4, 159.3, 152.0, 151.9, 136.8, 136.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 136.5, 136.2, 136.0, 134.0, 133.2, 131.8, 131.7, 130.7, 130.6, 130.5, 130.3, 129.7 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.6 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.6, 129.5, 129.4, 129.3, 127.8, 127.6, 115.7, 115.6 (d, $J_{C\text{-}F}$ = 21.2 Hz), 115.6 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.4, 114.3, 112.2, 111.9, 58.4, 57.2, 55.7, 55.7, 43.6, 43.4, 37.6, 37.5, 31.2, 31.1, 23.3, 23.2, 22.6, 22.4, 22.4.

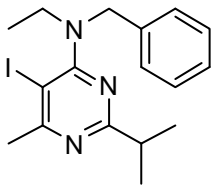
I.R. (thin film) 1669, 1562, 1500, 1422 cm^{-1}.

HRMS Calculated for $C_{34}H_{34}ClFN_4O_2$ 584.2354, found 584.2329.





benzylethyl-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amine



$C_{17}H_{22}IN_3$
MW = 395.28 g.mol^{-1}

To a 0.5 M solution of 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (600 mg, 1.4 mmol) in THF was added benzylethylamine (520 µL, 2.5 equiv.) and the resulting mixture was stirred at 45°C for two days. Purification by flash chromatography (petroleum ether-diethyl ether, 95:05) gave benzylethyl-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amine as a colorless oil.

Yield 36 % (200 mg).

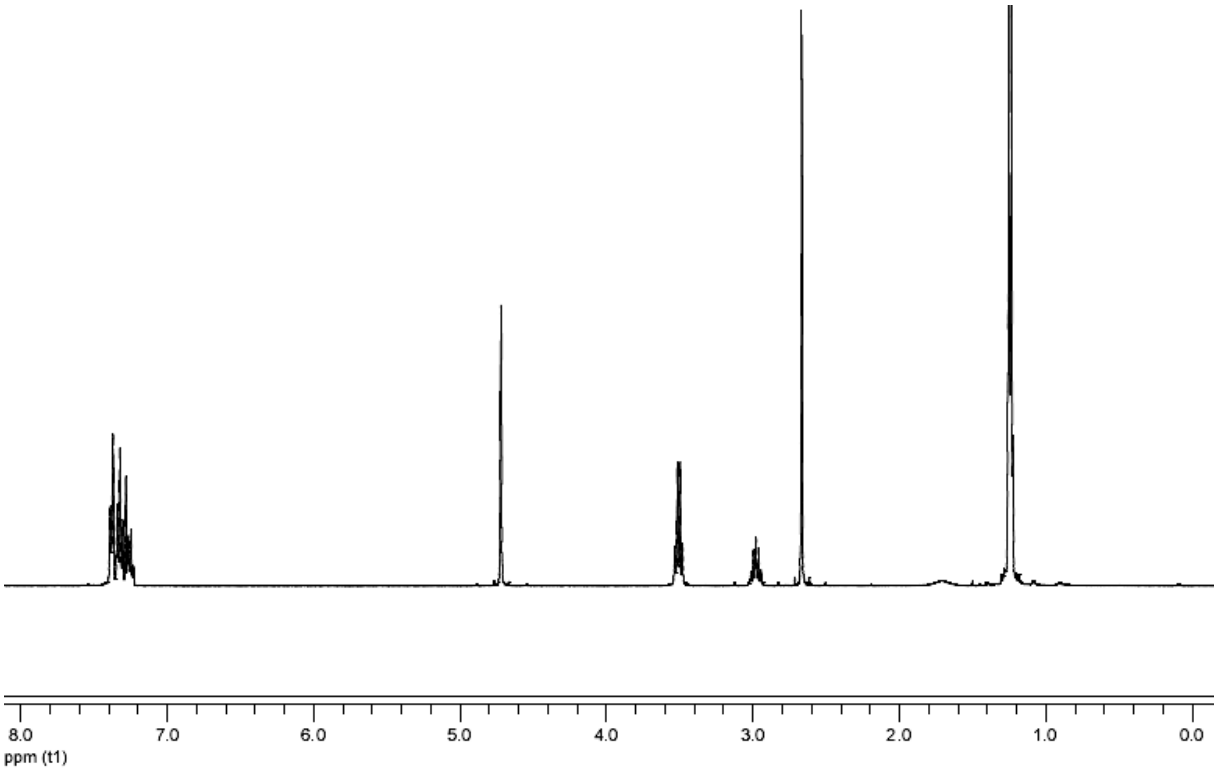
R_f 0.3 (95:05 petroleum ether / diethyl ether).

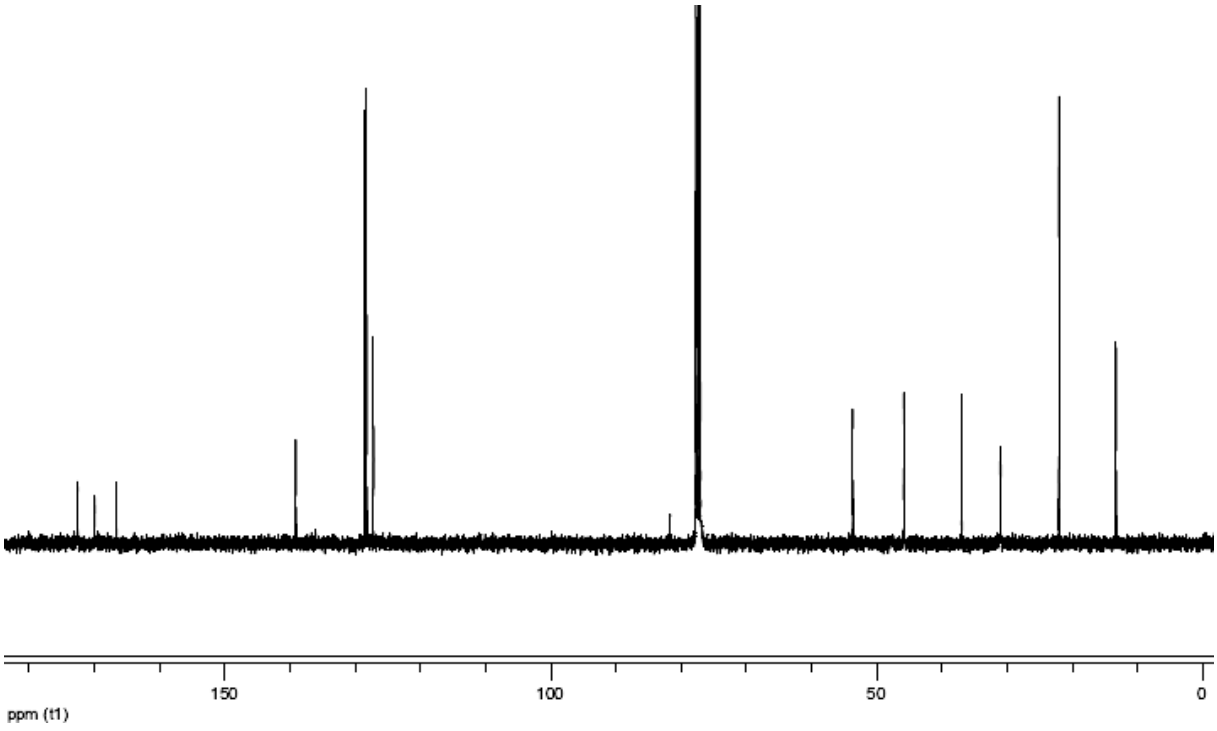
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.36 (m, 2H), 7.36-7.30 (m, 2H), 7.28-7.22 (m, 1H), 4.72 (s, 2H), 3.51 (q, *J* = 7.0 Hz, 2H), 2.98 (sept, *J* = 6.8 Hz, 1H), 2.67 (s, 3H), 1.27-1.22 (m, 9H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.6, 170.0, 166.7, 139.1, 128.6, 128.2, 127.2, 81.7, 53.7, 45.9, 37.0, 31.0, 22.1, 13.3.

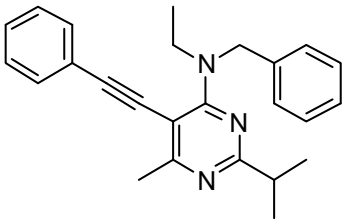
I.R. (thin film) 1536, 1511, 1426, 1347 cm^{-1}.

HRMS Calculated for $C_{17}H_{22}IN_3$ 395.0858, found 395.0858.





benzylethyl-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amine



$C_{25}H_{27}N_3$
MW = 369.50 $g.mol^{-1}$

4

General procedure using benzylethyl-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amine (200 mg, 0.51 mmol), phenylacetylene (80 µL, 0.61 mmol), *bis*(triphenylphosphine)palladium chloride (18 mg, 0.03 mmol), CuI (5 mg, 0.03 mmol) and diisopropylethylamine (90 µL, 0.51 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **4** as a colorless oil.

Yield 32 % (60 mg).

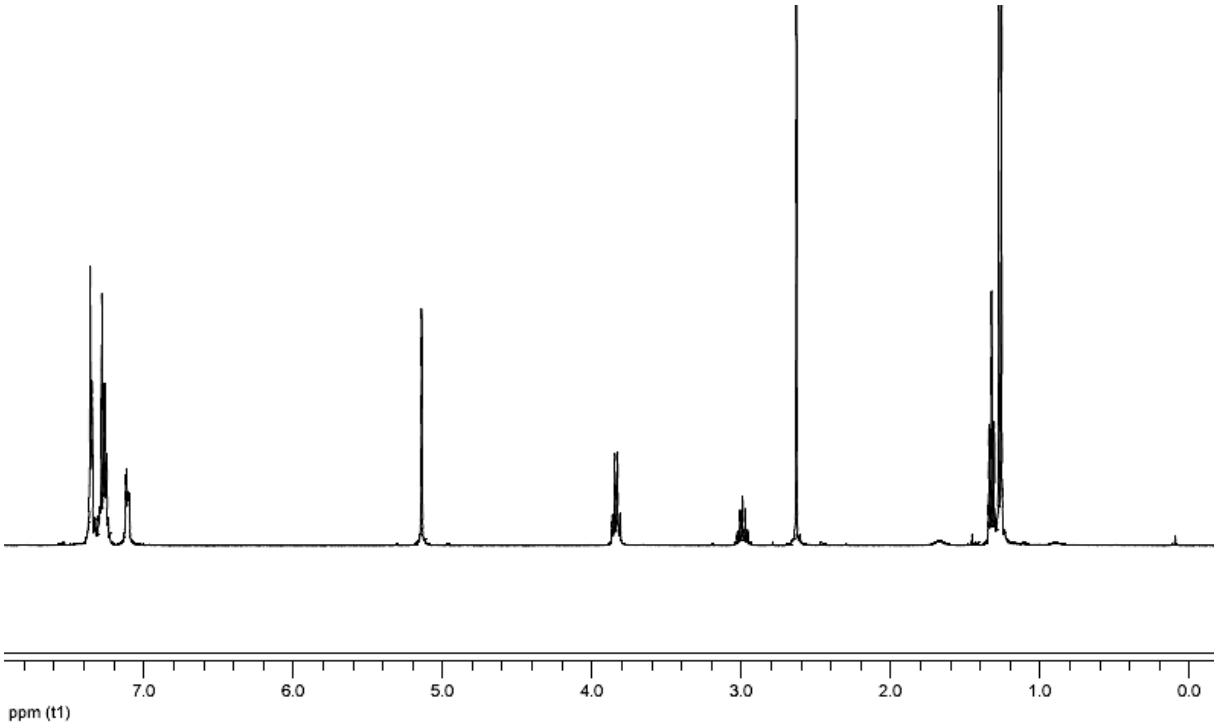
R_f 0.3 (90:10 petroleum ether / diethyl ether).

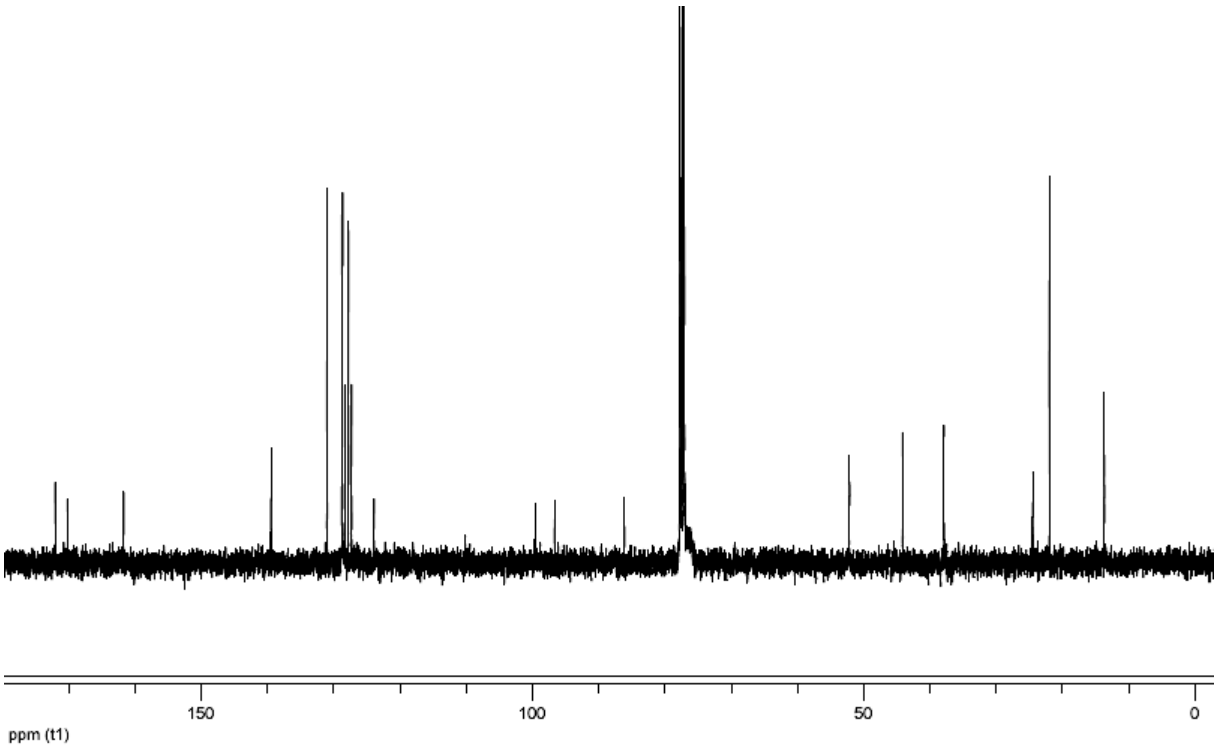
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.34 (m, 4H), 7.28-7.23 (m, 4H), 7.14-7.09 (m, 2H), 5.14 (s, 2H), 3.84 (q, J = 7.0 Hz, 2H), 2.99 (sept, J = 6.8 Hz, 1H), 2.63 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H), 1.27 (d, J = 6.8 Hz, 6H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.1, 170.2, 161.7, 139.5, 131.0, 128.8, 128.7, 128.3, 127.8, 127.3, 123.9, 99.6, 96.7, 86.1, 52.2, 44.1, 37.9, 24.5, 22.0, 13.7.

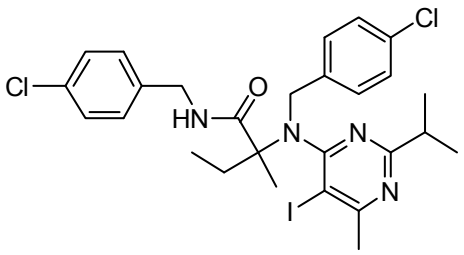
I.R. (thin film) 1529, 1490, 1430, 1360 cm^{-1}.

HRMS Calculated for $C_{25}H_{27}N_3$ 369.2205, found 369.2213.





_N_-(4-chlorobenzyl)-2-[(4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-2-methylbutyramide



$C_{27}H_{31}Cl_2IN_4O$
MW = 625.37 g.mol^{-1}

General procedure using butan-2-one (180 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and 5-iodo-2-isopropyl-6-methylpyrimidin-4-ol (560 mg, 2 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 50:50) gave the Ugi-Smiles adduct as a colorless oil.

Yield 9 % (110 mg).

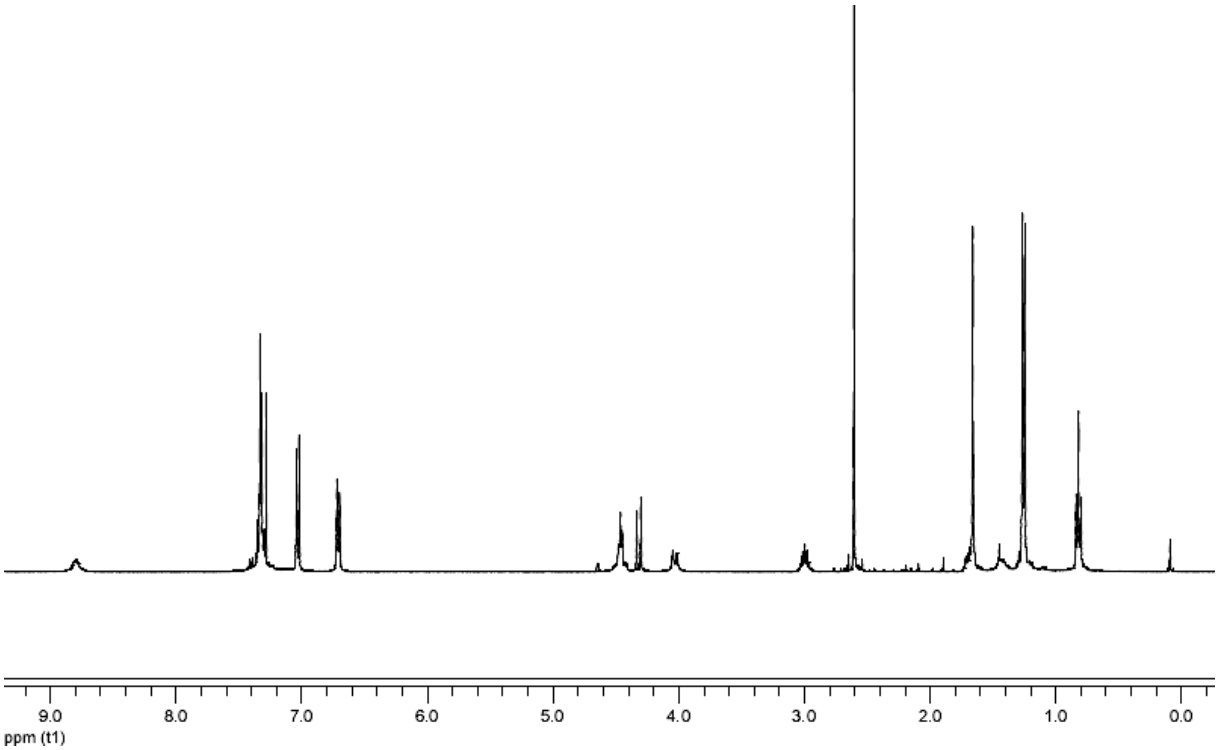
R_f 0.3 (60:40 petroleum ether / diethyl ether).

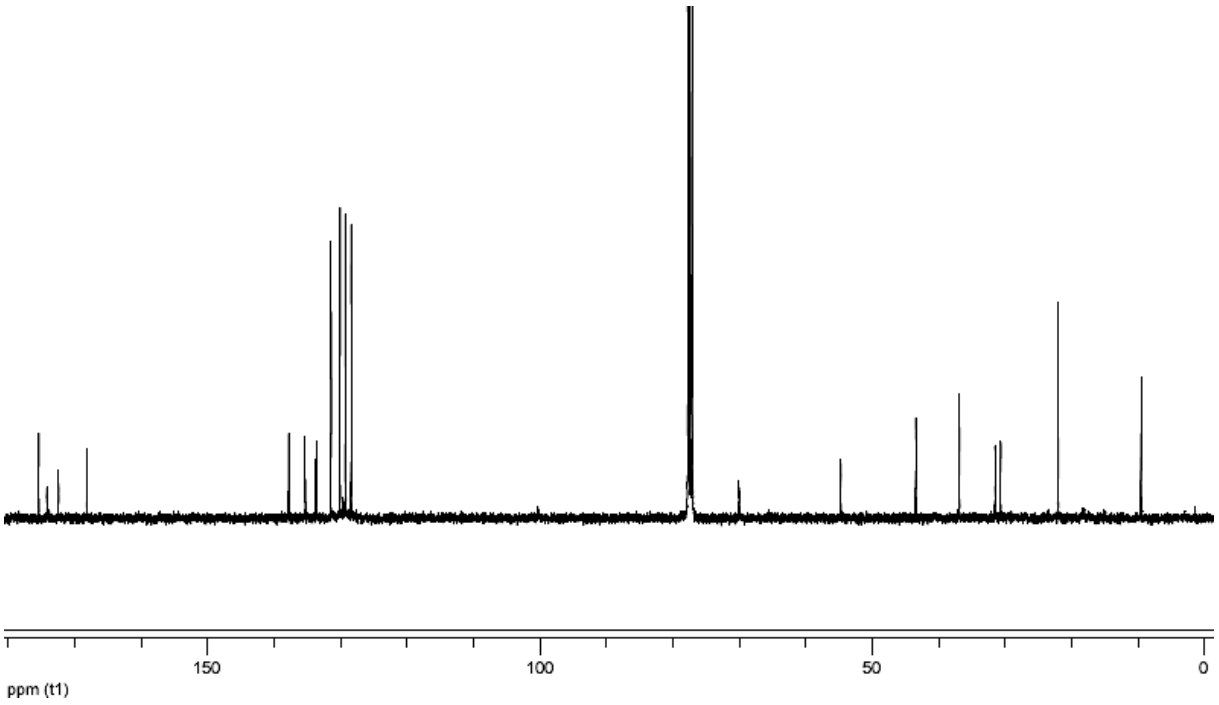
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.80 (s, 1H), 7.36-7.29 (m, 4H), 7.03 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 8.3 Hz, 2H), 4.53-4.40 (m, 2H), 4.33 (d, *J* = 13.0 Hz, 1H), 4.03 (d, *J* = 13.0 Hz, 1H), 3.00 (sept, *J* = 6.8 Hz, 1H), 2.61 (s, 3H), 1.75-1.66 (m, 1H), 1.66 (s, 3H), 1.51-1.37 (m, 1H), 1.26 (d, *J* = 6.8 Hz, 6H), 0.82 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.4, 174.2, 172.5, 168.2, 137.8, 135.3, 133.8, 133.6, 131.4, 130.1, 129.3, 128.4, 100.3, 70.0, 54.8, 43.5, 36.9, 31.6, 30.7, 22.1, 18.3, 9.6.

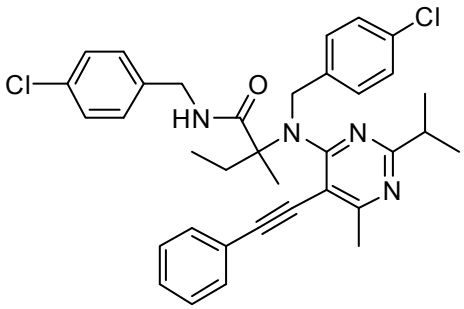
I.R. (thin film) 1672, 1531, 1507, 1492 cm^{-1}.

HRMS Calculated for $C_{27}H_{31}Cl_2IN_4O$ 624.0920, found 624.0916.





_N_-(4-chlorobenzyl)-2-[(4-chlorobenzyl)-(2-isopropyl-6-methyl-5-phenylethynylpyrimidin-4-yl)-amino]-2-methylbutyramide



$C_{35}H_{36}Cl_2N_4O$
MW=599.59 g.mol^{-1}

5

General procedure using *N*-(4-chlorobenzyl)-2-[(4-chlorobenzyl)-(5-iodo-2-isopropyl-6-methylpyrimidin-4-yl)-amino]-2-methylbutyramide (150 mg, 0.24 mmol), phenylacetylene (40 µL, 0.29 mmol), *bis*(triphenylphosphine)palladium chloride (8 mg, 0.01 mmol), CuI (2 mg, 0.01 mmol) and diisopropylethylamine (40 µL, 0.24 mmol). Purification by flash chromatography (petroleum ether-diethyl ether, 70:30) afforded **5** as a colorless oil.

Yield 57 % (82 mg).

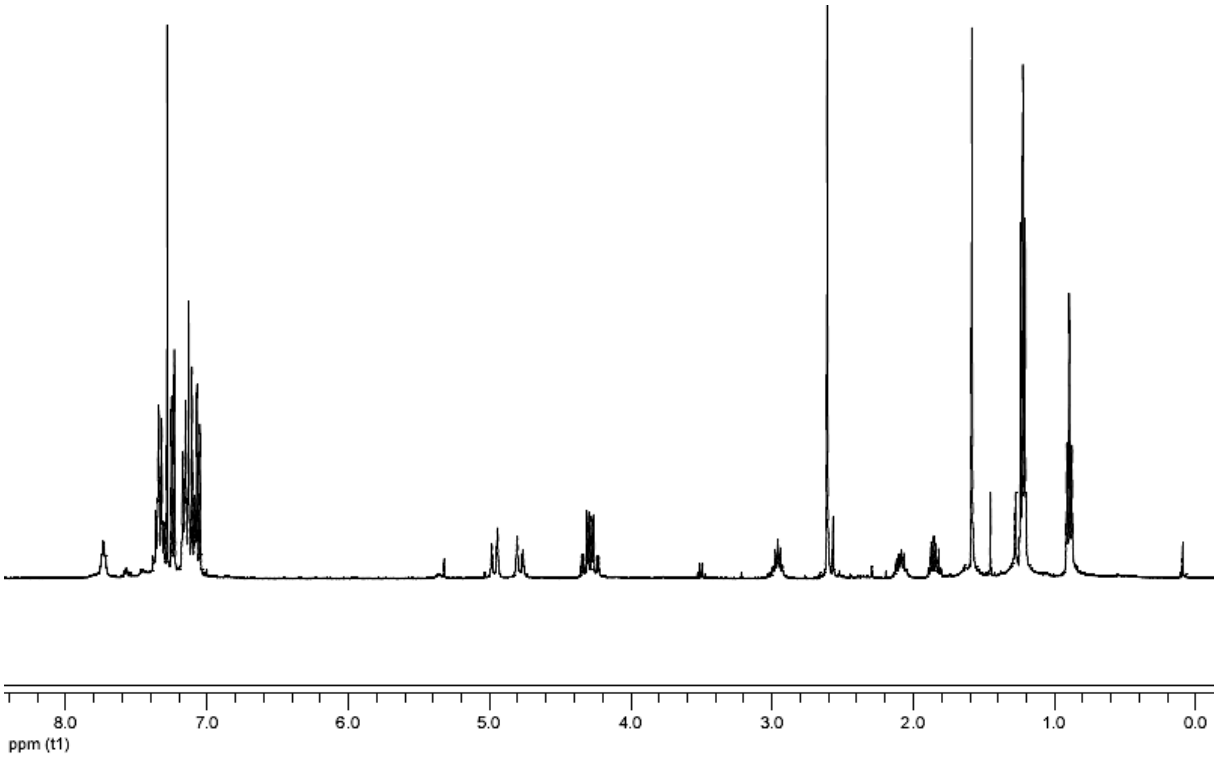
R_f 0.3 (70:30 petroleum ether / diethyl ether).

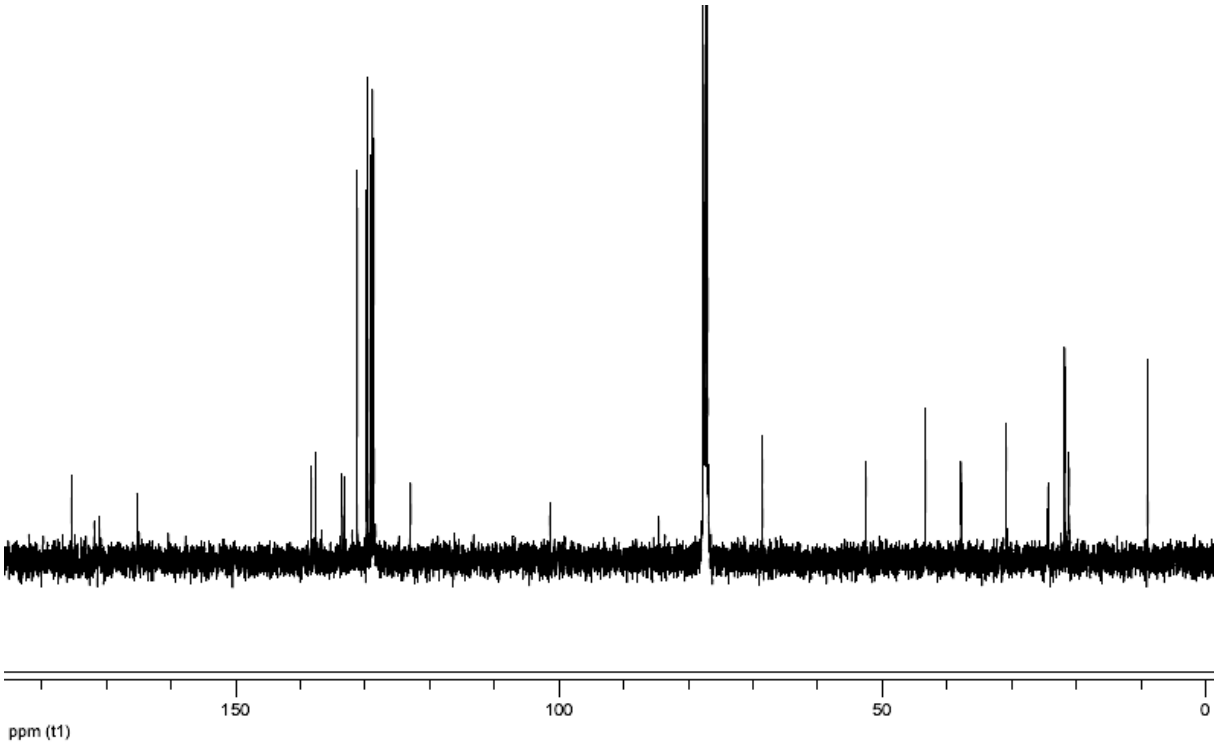
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (t, *J* = 6.1 Hz, 1H), 7.37-7.31 (m, 3H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.18-7.04 (m, 8H), 4.97 (d, *J* = 16.0 Hz, 1H), 4.79 (d, *J* = 16.0 Hz, 1H), 4.32 (dd, *J* = 14.7, 6.0 Hz, 1H), 4.25 (dd, *J* = 14.7, 5.5 Hz, 1H), 2.96 (sept, *J* = 6.8 Hz, 1H), 2.61 (s, 3H), 2.15-2.03 (m, 1H), 1.90-1.80 (m, 1H), 1.59 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.4, 171.9, 171.1, 165.3, 138.3, 137.7, 133.6, 133.2, 131.3, 129.8, 129.6, 129.2, 129.1, 128.9, 128.7, 123.0, 107.2, 101.4, 84.6, 68.6, 52.6, 43.4, 37.9, 30.9, 24.4, 21.9, 21.8, 21.2, 9.0.

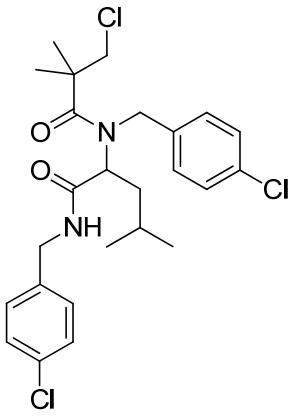
I.R. (thin film) 1667, 1523, 1490, 1404 cm^{-1}.

HRMS Calculated for $C_{35}H_{36}Cl_2N_4O$ 598.2266, found 598.2256.





2-(3-chloro-*N*-(4-chlorobenzyl)-2,2-dimethylpropanamido)-*N*-(4-chlorobenzyl)-4-methylpentanamide



$C_{25}H_{31}Cl_3N_2O_2$
MW = 497.88 g.mol^{-1}

6

General procedure for this Ugi adduct using isobutyraldehyde (200 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and 3-chloro-2,2-dimethylpropionic acid (273 mg, 2 mmol). Purification by flash column chromatography (petroleum ether-diethyl ether, 50:50) gave **6** as a colorless oil.

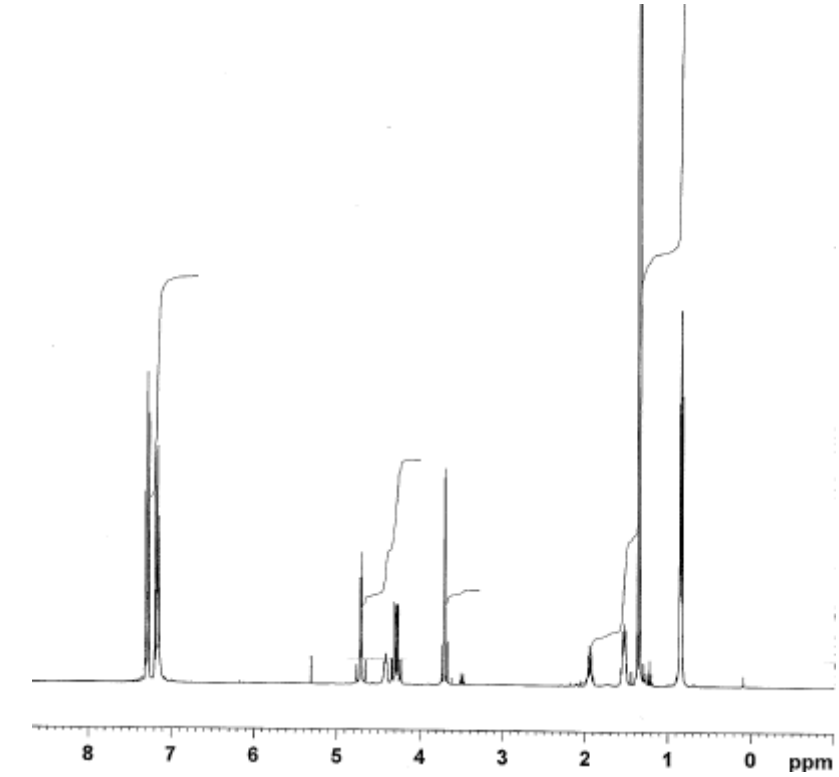
Yield 81 % (810 mg).

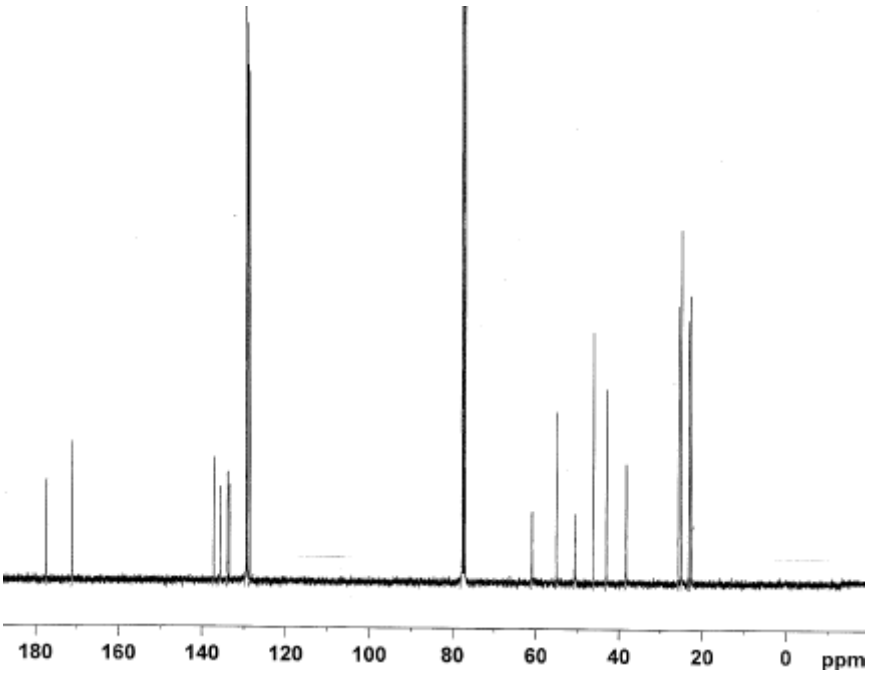
R_f 0.3 (70:30 petroleum ether / diethyl ether).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 4.75 (d, *J* = 17.2 Hz, 1H), 4.69 (d, *J* = 17.2 Hz, 1H), 4.46-4.38 (m, 1H), 4.33 (dd, *J* = 14.9, 6.0 Hz, 1H), 4.26 (dd, *J* = 14.9, 6.0 Hz, 1H), 3.73 (d, *J* = 10.8 Hz, 1H), 3.69 (d, *J* = 10.8 Hz, 1H), 2.01-1.89 (m, 1H), 1.59-1.47 (m, 2H), 1.37 (s, 3H), 1.34 (s, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H).

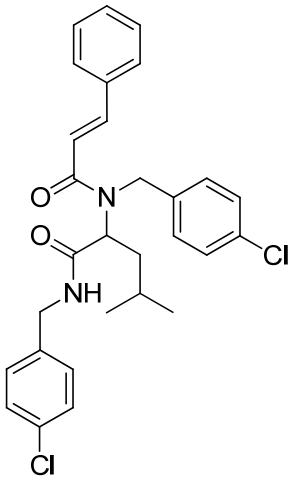
^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 177.4, 171.2, 137.2, 135.7, 133.9, 133.5, 61.0, 55.1, 50.7, 46.2, 43.1, 38.3, 25.8, 25.0, 23.2, 22.8.

HRMS Calculated for $C_{25}H_{31}Cl_3N_2O_2$ 496.1451, found 496.1452.





_N_-(4-chlorobenzyl)-2-(_N_-(4-chlorobenzyl)cinnamamido)-4-methylpentanamide



$C_{29}H_{30}Cl_2N_2O_2$
MW = 509.47 g.mol^{-1}

7

General procedure for this Ugi adduct using isobutyraldehyde (200 µL, 2 mmol), *p*-chlorobenzylamine (250 µL, 2 mmol), *p*-chlorobenzylisocyanide (260 µL, 2 mmol) and *trans*-cinnamic acid (296 mg, 2 mmol). Purification by flash column chromatography (petroleum ether-diethyl ether, 60:40) gave **7** as a colorless oil.

Yield 86 % (880 mg).

R_f 0.3 (60:40 petroleum ether / diethyl ether).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 15.3 Hz, 1H), 7.44-7.34 (m, 5H), 7.34-7.25 (m, 4H), 7.21-7.15 (m, 4H), 7.12 (t, *J* = 5.3 Hz, 1H), 6.65 (d, *J* = 15.3 Hz, 1H), 5.20 (t, *J* = 7.6 Hz, 1H), 4.75 (d, *J* = 18.0 Hz, 1H), 4.69 (d, *J* = 18.0 Hz, 1H), 4.39 (dd, *J* = 15.0, 5.9 Hz, 1H), 4.32 (dd, *J* = 15.0, 6.0 Hz, 1H), 1.96-1.86 (m, 1H), 1.53 (sept, *J* = 6.5 Hz, 1H), 1.48-1.37 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 171.1, 169.1, 145.2, 137.2, 136.7, 135.0, 133.7, 133.6, 130.6, 129.4, 129.4, 129.3, 129.2, 128.4, 127.9, 117.6, 56.6, 48.1, 43.1, 37.5, 25.6, 23.3, 22.8.

HRMS Calculated for $C_{29}H_{30}Cl_2N_2O_2$ 508.1684, found 508.1677.