Supplemental Information

Discovery of inducible Nitric Oxide Synthase (iNOS) inhibitor Development Candidate KD7332 (Part 1): Identification of a Novel, Potent and Selective series of Quinolinone iNOS Dimerization Inhibitors that are Orally Active in Rodent Pain Models

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4-((3-Chlorophenylamino)methyl)-8-fluoroquinolin-2(1H)-one (56). Compound **56** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and 3-chloroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.67 (s, 1H), 7.65 (d, 1H, *J* = 8.4 Hz), 7.42 (ddd, 1H, *J* = 10.8, 8.0, 0.8 Hz), 7.19 (m, 1H), 7.06 (t, 1H, *J* = 8.4 Hz), 6.62 (m, 2H), 6.55 (d, 2H, *J* = 7.8 Hz), 6.42 (s, 1H), 4.53 (d, 2H, *J* = 5.2 Hz). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}ClFN_2O$ 303.1, found 303.2 $[M + H]^+$.

4-((4-Chlorophenylamino)methyl)-8-fluoroquinolin-2(1H)-one (57). Compound **57** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and 4-chloroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.63 (s, 1H), 7.60 (d, 1H, *J* = 8.4 Hz), 7.38 (dd, 1H, *J* = 10.8, 7.2 Hz), 7.13 (m, 1H), 7.02 (m, 2H), 6.53 (d, 2H, *J* = 6.8 Hz), 6.48 (m, 1H), 6.36 (s, 1H), 4.46 (bs, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}ClFN_2O$ 303.1, found 303.2 $[M + H]^+$.

8-Fluoro-4-((3-fluorophenylamino)methyl)quinolin-2(1H)-one (58). Compound **58** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and 3-fluoroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 7.65 (d, 1H, *J* = 8.4 Hz), 7.42 (ddd, 1H, *J* = 11.2, 8.4, 1.2 Hz), 7.18 (m, 1H), 7.07 (m, 1H), 6.63

(t, 1H, *J* = 5.6 Hz), 6.43-6.29 (m, 4H), 4.53 (d, 2H, *J* = 6.0 Hz). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}F_2N_2O$ 287.1, found 287.2 $[M + H]^+$.

8-Fluoro-4-((3-cyanophenylamino)methyl)quinolin-2(1H)-one (59). Compound **59** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and 3-aminobenzonitrile as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.64 (s, 1H), 7.60 (d, 1H, *J* = 8.4 Hz), 7.44-7.33 (m, 1H), 7.22-7.12 (m, 2H), 6.92-6.78 (m, 3H), 6.87 (m, 1H), 6.36 (s, 1H), 4.54 (d, 2H, *J* = 2.8 Hz). LRMS (ESI+) *m*/*z*: calcd for $C_{17}H_{12}FN_3O$ 294.1, found 294.2 $[M + H]^+$.

8-Fluoro-4-((*m*-tolylamino)methyl)quinolin-2(1H)-one (60). Compound **60** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and *m*-toluidine as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (s, 1H), 7.62 (d, 1H, *J* = 8.4 Hz), 7.38 (ddd, 1H, *J* = 10.8, 7.6, 0.8 Hz), 7.13 (m, 1H), 6.89 (m, 1H), 6.39-6.31 (m, 4H), 6.17 (m, 1H), 4.48 (bs, 2H), 2.09 (s, 3H). LRMS (ESI+) *m*/*z*: calcd for $C_{17}H_{15}FN_2O$ 283.1, found 283.2 $[M + H]^+$.

8-Fluoro-4-((3-methoxyphenylamino)methyl)quinolin-2(1H)-one (61). Compound **61** was synthesized as described for compound **53** using 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**) and 3-methoxyaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 7.62 (d, 1H, *J* = 8.4 Hz), 7.38 (ddd, 1H, *J* = 10.8, 8.0, 0.8 Hz), 7.13 (m, 1H), 6.90 (t, 1H, *J* = 7.6 Hz), 6.39 (s, 1H), 6.28 (m, 1H), 6.14-6.08 (m, 3H), 4.45 (bs, 2H), 3.58 (s, 3H). LRMS (ESI+) *m*/*z*: calcd for $C_{17}H_{15}FN_2O_2$ 299.1, found 299.2 $[M + H]^+$.

2-(*tert*-Butyldimethylsilyloxy)-4-(chloromethyl)-8-fluoroquinoline (62). To a stirred solution of 4-(bromomethyl)-8-fluoroquinolin-2(1H)-one (**52**, 1.28 g, 5.0 mmol) in DMF (50 mL) at 25ºC was added *tert*-butyldimethylsilyl chloride (1.51 g, 10.0 mmol) followed by Et_3N (2.4 mL, 17.5 mmol). After 4 h, the reaction mixture was poured into ice water (500 mL), and the resulting

precipitate was collected by vacuum filtration. The filter cake was washed with water (100 mL), then dried for 18 h to afford 2-(*tert*-butyldimethylsilyloxy)-4-(chloromethyl)-8-fluoroquinoline (**62**, 1.42 g, 88%) as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (d, 1H, *J* = 8.0 Hz), 7.52-7.45 (m, 2H), 7.23 (s, 1H), 5.18 (s, 2H), 0.98 (s, 9H), 0.38 (s, 6H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{21}ClFNOSi$ 326.1, found 211.9 $[M - TBDMS + H]^+$.

2-(*tert*-Butyldimethylsilyloxy)-8-fluoro-4-(iodomethyl)quinoline (63). Sodium iodide (157 mg, 1.05 mmol) was added to a stirred solution of 2-(tert-butyldimethylsilyloxy)-4-(chloromethyl)-8-fluoroquinoline (**62**, 325 mg, 1.0 mmol) in dry acetone at 25ºC. After 2 h, the heterogeneous mixture was diluted with DCM (200 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford 2-(*tert*-butyldimethylsilyloxy)-8-fluoro-4-(iodomethyl)quinoline (**63**, 390 mg, 94%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 1H, *J* = 8.4 Hz), 7.37 (m, 1H), 7.30 (m, 1H), 7.00 (s, 1H), 4.67 (s, 2H), 1.02 (s, 9H), 0.44 (s, 6H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{21}FINOSi$ 418.0, found 303.8 $[M - TBDMS + H]^+$.

***N*-(3-Chlorophenyl)-1-methyl-1*H*-imidazole-5-carboxamide (66).** O-(7-Azabenzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate (HATU, 912 mg, 2.4 mmol) was added to a stirred mixture of 1-methyl-1*H*-imidazole-5-carboxylic acid (**65**, 252 mg, 2.0 mmol), 3-chloroaniline (**64**, 273 µL, 2.6 mmol), and Et_3N (1.1 mL, 8.0 mmol) in DMF (10 mL). After 18 h at 25ºC, the reaction mixture was diluted with 1:1 hexanes:EtOAc (200 mL), washed with 5% brine (3 x 50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude residue was purified by silica gel column chromatography (9:1 DCM/ACN) to afford N-(3-chlorophenyl)-1-methyl-1H-imidazole-5-carboxamide (**66**, 358 mg, 76%) as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 8.04 (s, 1H), 7.82 (s, 1H), 7.75 (m, 2H), 7.30 (t, 1H, *J* = 8.2 Hz), 7.07 (d, 1H, *J* = 8.0 Hz), 3.71 (s, 3H).

3-Chloro-*N*-((2-chloropyridin-4-yl)methyl)aniline (68). A mixture of 4-(bromomethyl)-2-chloropyridine (**67**,[11] 3.6 g, 15.8 mmol), 3-chloroaniline (2.0 g, 15.47 mmol), and K_2CO_3 (2.2 g, 15.78 mmol) in DMF (50 mL) was stirred for 2 h at 60°C. The resulting solution was diluted with water (150 mL) and extracted with EtOAc (2 x 100 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated to dryness under reduced pressure. The residue was purified by silica gel column chromatography (1:5 EtOAc/Hexanes) to afford 2.8 g (67%) of 3-chloro-N-((2-chloropyridin-4-yl)methyl)aniline (**68**) as a yellow solid. LRMS (ESI+) *m/z*: calcd for $C_{12}H_{10}Cl_2N_2$ 253.0, found 253.0 $[M + H]^+$.

***N*-(3-Chlorophenyl)-*N*-((2-chloropyridin-4-yl)methyl)-4-methylthiazole-5-carboxamide (69)**. 4-Methylthiazole-5-carbonyl chloride (synthesis of acid chloride described for compound **7**, 1.43 g, 7.99 mmol) was added in several batches to 3-chloro-N-((2-chloropyridin-4-yl)methyl)aniline (**68**, 1.12 g, 3.98 mmol) in DMF (20 mL) cooled to 0°C. The resulting solution was stirred at 25ºC for 2 h. The solvent was removed by evaporation under reduced pressure and the residue was purified by silica gel column chromatography (1:2 EtOAc/Hexanes) to afford 0.8 g (46%) of N-(3-chlorophenyl)-N-((2-chloropyridin-4-yl)methyl)-4-methylthiazole-5-carboxamide (**69**) as a yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.93 (s, 1H), 8.36 (d, 1H), 7.50 (m, 2H), 7.43 (d, 1H), 7.34 (m, 2H), 7.18 (d, 1H), 5.12 (s, 2H), 2.42 (s, 3H). LRMS (ESI+) *m/z*: calcd for $C_{17}H_{13}Cl_2N_3OS$ 378.0, found 378.0 $[M + H]^+$.

(2-Chloro-5,6,7,8-tetrahydroquinolin-4-yl)methanol (71). $LiAlH_4$ (190 mg, 5.00 mmol) was added to methyl 2-chloro-5,6,7,8-tetrahydroquinoline-4-carboxylate (**70**,[i] 200 mg, 0.88 mmol) in THF (10 mL) at 0°C. The resulting slurry was stirred at 0°C for 30 min. The reaction mixture was then quenched by adding water and 15% NaOH solution. The precipitate was filtered and dried to afford 250 mg (crude) of (2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methanol (**71**) as a white solid. LRMS (ESI+) *m/z*: calcd for $C_{10}H_{12}ClNO$ 198.1, found 198.0 $[M + H]^+$.

4-(Bromomethyl)-2-chloro-5,6,7,8-tetrahydroquinoline (72). PBr_3 (1.71 g, 6.31 mmol) in DCM (10 mL) was added dropwise to (2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methanol (**71**, 250 mg, 1.26 mmol) in DCM (5 mL) at 0°C. The resulting solution was stirred at 25ºC for 30 min. The reaction mixture was then quenched with water (30 mL), neutralized to pH 7 using aqueous sodium bicarbonate, and extracted with DCM (4 x 120 mL). The organics were combined, dried over Na_2SO_4, and concentrated under reduced pressure to afford 160 mg (crude) of 4-(bromomethyl)-2-chloro-5,6,7,8-tetrahydroquinoline (**72**) as a white solid.

3-Chloro-*N*-((2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methyl)aniline (73). A mixture of 4-(bromomethyl)-2-chloro-5,6,7,8-tetrahydroquinoline (**72**, 860 mg, 3.30 mmol), 3-chloroaniline (420 mg, 3.28 mmol), and Na_2CO_3 (350 mg) in DMF (20 mL) was heated to 60°C for 2 h. The resulting solution was diluted with water (60 mL) and extracted with EtOAc (5 x 300 mL). The organics were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:20 EtOAc/Hexanes) to afford 600 mg of 3-chloro-*N*-((2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methyl)aniline (**73**) as a light yellow solid. LRMS (ESI+) *m/z*: calcd for $C_{16}H_{16}Cl_2N_2$ 307.1, found 307.0 $[M + H]^+$

***N*-((2-Chloro-5,6,7,8-tetrahydroquinolin-4-yl)methyl)-*N*-(3-chlorophenyl)-4-methylthiazole-5-carboxamide (74).** 4-Methylthiazole-5-carbonyl chloride (synthesis of acid chloride described in compound **7**, 700 mg, 4.32 mmol) in DMF (15 mL) was added dropwise to 3-chloro-*N*-((2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methyl)aniline (**73**, 510 mg, 1.66 mmol) in DMF (5 mL). The resulting solution was stirred at 25ºC for 7 h. The reaction mixture was then quenched with water (60 mL) and extracted with EtOAc (4 x 240 mL). The organics were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:5 EtOAc/Hexanes) to afford 420 mg of *N*-((2-chloro-5,6,7,8-tetrahydroquinolin-4-yl)methyl)-*N*-(3-chlorophenyl)-4-methylthiazole-5-carboxamide (**74**) as a light yellow solid. LRMS (ESI+) *m/z*: calcd for $C_{21}H_{21}Cl_2N_3OS$ 432.0, found 432.0 $[M + H]^+$.

8-Fluoro-4-methyl-2*H*-chromen-2-one (77). A mixture of 1-(3-fluoro-2-hydroxyphenyl)ethanone (**75**, 13 g, 75.91 mmol) and (triphenylphosphoranylidene) acetic acid ethyl ester (**76**,[ii] 30 g, 86.2 mmol) in toluene (200 mL) was stirred at 120ºC for 18 h. The mixture was concentrated under reduced pressure and the residue was partitioned between EtOAc (100 mL) and water (200 mL). The organic layer was isolated, washed with water (200 mL), dried over Na_2SO_4, filtered, and concentrated to dryness under reduced pressure. The residue was purified by silica gel column chromatography (1:25 EtOAc/Hexanes) to afford 5 g (35%) of 8-fluoro-4-methyl-2*H*-chromen-2-one (**77**) as a yellow solid. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_7FO_2$ 179.0, found 179.2 $[M + H]^+$.

4-(Bromomethyl)-8-fluoro-2*H*-chromen-2-one (78). A mixture of 8-fluoro-4-methyl-2*H*-chromen-2-one (**77**, 5g, 25.3 mmol), NBS (6g, 33.71 mmol), AIBN (cat., 0.1 g) in CCl_4 (300 mL) was refluxed for 18 h. The reaction mixture was concentrated to dryness and the residue was purified by silica gel chromatography (1:20 EtOAc/Hexanes) to afford 1.17 g (17%) of 4-(bromomethyl)-8-fluoro-2*H*-chromen-2-one (**78**) as a yellow solid. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_6BrFO_2$ 256.9, found 257.0 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)-8-fluoro-2*H*-chromen-2-one (79). A mixture of 4-(bromomethyl)-8-fluoro-2*H*-chromen-2-one (**78**, 500 mg, 1.94 mmol) and 3-chloroaniline (0.8 mL, 7.78 mmol) in DMSO (5 mL) was heated to 70ºC for 1 h. The cooled reaction mixture was then poured into ice water, and extracted with DCM (3 x 50 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated to dryness under reduced pressure. The residue was purified by silica gel chromatography (20-50% EtOAc/Hexanes) to afford 500 mg of 4-((3-chlorophenylamino)methyl)-8-fluoro-2*H*-chromen-2-one (**79**) as a yellow solid. LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{11}ClFNO_2$ 304.0, found 303.9 $[M + H]^+$.

4-(Bromomethyl)-8-fluoroquinoline (81). A mixture of 8-fluoro-4-methylquinoline (**80**,[iii] 500 mg, 3.11 mmol), NBS (553 mg, 3.11 mmol), and AIBN (cat.) in CCl_4 (30 mL) was refluxed for 2 h. The reaction mixture was filtered to remove insoluble materials, and the filtrate was concentrated to dryness under reduced pressure. The residue was purified by silica gel chromatography (1:20 EtOAc/Hexanes) to afford 380 mg (51%) of 4-(bromomethyl)-8-fluoroquinoline (**81**) as a white solid. LRMS (ESI+) *m/z*: calcd for $C_{10}H_7BrFN$ 239.9, found 240.0 $[M + H]^+$.

3-Chloro-*N*-((8-fluoroquinolin-4-yl)methyl)aniline (82). A mixture of 4-(bromomethyl)-8-fluoroquinoline (**81**, 380 mg, 1.59 mmol), 3-chloroaniline (400 mg, 3.15 mmol), and K_2CO_3 (440 mg, 3.19 mmol) in DMF (20 mL) was heated to 60ºC for 2 h. The reaction mixture was filtered to remove insoluble materials, and then concentrated to dryness under reduced pressure. The residue was purified by silica gel chromatography (1:20 EtOAc/Hexanes) to afford 320 mg (70%) of 3-chloro-*N*-((8-fluoroquinolin-4-yl)methyl)benzenamine (**82**) as a white solid. LRMS (ESI+) *m/z*: calcd for $C_{16}H_{12}ClFN_2$ 287.1, found 287.0 $[M + H]^+$.

***N*-Allyl-*N*-benzyl-2-fluoro-6-iodobenzamide (85).** A mixture of 2-fluoro-6-iodobenzoic acid (**84**, 30 g, 113 mmol) in $SOCl_2$ (60 mL) was heated to 80°C for 1.5 h. Excess $SOCl_2$ was removed under reduced pressure and the residue was taken up with a solution of Et_3N (13.7 g, 136 mmol) in THF (50 mL). This solution was then added dropwise to a separate solution of N-benzylprop-2-en-1-amine (**83**, 16.6 g, 113 mmol) in THF (150 mL) at 5°C. The resulting reaction mixture was stirred at 25ºC for 2 h. The mixture was concentrated under reduced pressure and the residue was dissolved in EtOAc (200 mL). The organic layer was washed with aqueous $NaHSO_4$ (2 x 50 mL), aqueous sodium bicarbonate (50 mL), and brine (50 mL), dried over Na_2SO_4, and concentrated to dryness under reduced pressure to afford 30 g (67%) of N-allyl-N-benzyl-2-fluoro-6-iodobenzamide (**85**) as a white solid. LRMS (ESI+) *m/z*: calcd for $C_{17}H_{15}FINO$ 396.0, found 396.0 $[M + H]^+$.

2-Benzyl-8-fluoro-4-methylisoquinolin-1(2*H*)-one (86). A mixture of *N*-allyl-*N*-benzyl-2-fluoro-6-iodobenzamide (**85**, 198 mg, 0.50 mmol), dicyclohexylamine (362 mg, 2.00 mmol), PPh_3 (13.1 mg, 0.05 mmol), and $Pd(OAc)_2$ (12 mg, 0.03 mmol) in DMA (7 mL) was heated to 100°C for 18 h. The mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (1:30 EtOAc/Hexanes) to afford 83 mg (62%) of 2-benzyl-8-fluoro-4-methylisoquinolin-1(2*H*)-one (**86**) as a white solid. LRMS (ESI+) *m*/*z*: calcd for $C_{17}H_{14}FNO$ 268.1, found 268.0 $[M + H]^+$.

8-Fluoro-4-methylisoquinolin-1(2*H*)-one (87). A solution of 2-benzyl-8-fluoro-4-methylisoquinolin-1(2*H*)-one (**86**, 30 g, 112.36 mmol) in H_2SO_4 (450 g) was heated to 150°C for 2.5 h. Adjustment of the pH to 9 was accomplished by the addition of NaOH (4M). The resulting aqueous solution was extracted with EtOAc (3 x 100 mL). The organics were combined, washed with brine (2 x 500 mL), filtered, dried over Na_2SO_4, and concentrated under reduced pressure to afford 15.8 g (79%) of 8-fluoro-4-methylisoquinolin-1(2*H*)-one (**87**) as a white solid. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_8FNO$ 178.1, found 178.0 $[M + H]^+$.

1-Chloro-8-fluoro-4-methylisoquinoline (88). A mixture of 8-fluoro-4-methylisoquinolin-1(2*H*)-one (**87**, 3 g, 16.95 mmol) in $POCl_3$ (40 mL) was heated to 80°C for 2 h. The mixture was concentrated to dryness and the residue was partitioned between EtOAc and H_2O (1:1, 100 mL). Adjustment of the pH to 8 was accomplished by the addition of $NH_3.H_2O$ (25%). The two layers were separated and the aqueous layer was extracted with EtOAc (50 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 3.3 g (99%) of 1-chloro-8-fluoro-4-methylisoquinoline (**88**) as a white solid. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_7ClFN$ 196.0, found 196.0 $[M + H]^+$.

4-(Bromomethyl)-1-chloro-8-fluoroisoquinoline (89). Compound **89** was synthesized as described for compound **81** using 1-chloro-8-fluoro-4-methylisoquinoline (**88**) as the starting material. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_6BrClFN$ 273.9, found 274.0 $[M + H]^+$.

3-Chloro-*N*-((1-chloro-8-fluoroisoquinolin-4-yl)methyl)benzenamine (90). Compound **90** was synthesized as described for compound **82** using 1-chloro-8-fluoro-4-methylisoquinoline (**89**) and 3-chloroaniline as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{11}Cl_2FN_2$ 321.0, found 321.0 $[M + H]^+$.

3-Chloro-*N*-((8-fluoroisoquinolin-4-yl)methyl)benzenamine (91). A solution of 3-chloro-*N*-((1-chloro-8-fluoroisoquinolin-4-yl)methyl)benzenamine (**90**, 500 mg, 1.56 mmol) and Pd/C (cat.) in MeOH (20 mL) was hydrogenated (with a balloon of hydrogen) for 4 h at 25ºC. A filtration through celite was performed to remove the Pd/C and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in EtOAc (30 mL) and the organic layer was washed with aqueous sodium bicarbonate (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 380 mg (85%) of 3-chloro-*N*-((8-fluoroisoquinolin-4-yl)methyl)benzenamine (**91**) as a beige solid. ^{1}HNMR (400MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.59 (s, 1H), 7.99 (d, 1H, *J* = 8.4 Hz), 7.84 (m, 1H), 7.52 (dd, 1H, *J* = 10.8, 8.0 Hz), 7.06 (t, 1H, *J* = 8.4 Hz), 6.61 (m, 1H), 6.62-6.53 (m, 3H), 4.69 (d, 2H, *J* = 5.2 Hz). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}ClFN_2$ 287.1, found 287.0 $[M + H]^+$.

***N*-(2-Chlorophenyl)-3-oxobutanamide (98)**. Compound **98** was synthesized as described for compound **49** using 3-oxobutanoate and 2-chloroaniline (**92**) as starting materials. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.32 (dd, 1H, *J* = 8.2, 0.8 Hz), 7.37 (d, 1H, *J* = 8.0 Hz), 7.25 (t, 1H, *J* = 8.0 Hz), 7.05 (t, 1H, *J* = 8.0 Hz), 3.64 (s, 2H), 2.34 (s, 3H).

***N*-(3-Fluorophenyl)-3-oxobutanamide (99).** Compound **99** was synthesized as described for compound **49** using 3-oxobutanoate and 3-fluoroaniline (**93**) as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_{10}FNO_2$ 196.0, found 195.9 $[M + H]^+$.

***N*-(4-Fluorophenyl)-3-oxobutanamide (100).** Compound **100** was synthesized as described for compound **49** using 3-oxobutanoate and 4-fluoroaniline (**94**) as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_{10}FNO_2$ 196.0, found 196.0 $[M + H]^+$.

***N*-(2-Bromo-5-fluorophenyl)-3-oxobutanamide (101).** Compound **101** was synthesized as described for compound **49** using 3-oxobutanoate and 2-bromo-5-fluoroaniline (**95**) as starting materials. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.20 (dd, 1H, *J* = 11.0, 3.0 Hz), 7.48 (dd, 1H, *J* = 8.8, 5.6 Hz), 6.72 (m, 1H), 3.65 (s, 2H), 2.33 (s, 3H). LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_9BrFNO_2$ 273.9, found 277.9 $[M + H]^+$.

***N*-(2,3-Difluorophenyl)-3-oxobutanamide (102).** Compound **102** was synthesized as described for compound **49** using 3-oxobutanoate and 2,3-difluoroaniline (**96**) as starting materials. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.99 (m, 1H), 7.04 (m, 1H), 6.89 (s, 1H), 3.64 (s, 2H), 2.33 (s, 3H). LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_9F_2NO_2$ 214.0, found 214.1 $[M + H]^+$.

4-Bromo-*N*-(2-chlorophenyl)-3-oxobutanamide (103). Compound **103** was synthesized as described for compound **50** using *N*-(2-chlorophenyl)-3-oxobutanamide (**98**) as the starting material. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.30 (dd, 1H, J = 8.4, 1.2 Hz), 7.39 (dd, 1H, J = 8.4, 1.4 Hz), 7.27 (m, 1H), 7.07 (td, 1H, J = 8.2, 1.6 Hz), 4.07 (s, 2H), 3.87 (s, 2H).

4-Bromo-*N*-(3-fluorophenyl)-3-oxobutanamide (104). Compound **104** was synthesized as described for compound **50** using *N*-(3-fluorophenyl)-3-oxobutanamide (**99**) as the starting material. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_9BrFNO_2$ 273.9, found 273.8 $[M + H]^+$.

4-Bromo-*N*-(4-fluorophenyl)-3-oxobutanamide (105). Compound **105** was synthesized as described for compound **50** using *N*-(4-fluorophenyl)-3-oxobutanamide (**100**) as the starting material. LRMS (ESI+) *m/z*: calcd for $C_{10}H_9BrFNO_2$ 273.9, found 274.0 $[M + H]^+$.

4-Bromo-*N*-(2-bromo-5-fluorophenyl)-3-oxobutanamide (106). Compound **106** was synthesized as described for compound **50** using *N*-(2-bromo-5-fluorophenyl)-3-oxobutanamide (**101**) as the starting material. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.72 (m, 2H), 7.03 (m, 1H), 4.49 (s, 2H), 3.87 (s, 2H).

4-Bromo-*N*-(2,3-difluorophenyl)-3-oxobutanamide (107). Compound **107** was synthesized as described for compound **50** using *N*-(2,3-difluorophenyl)-3-oxobutanamide (**102**) as the starting material. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.05 (m, 1H), 7.09 (m, 1H), 6.95 (m, 1H), 4.02 (s, 2H), 3.82 (s, 2H). LRMS (ESI+) *m/z*: calcd for $C_{10}H_8BrF_2NO_2$ 291.9, found 292.0 $[M + H]^+$.

4-Bromo-2-fluoro-*N*-(2-fluorophenyl)-3-oxobutanamide (108). A mixture of 4-bromo-*N*-(2-fluorophenyl)-3-oxobutanamide (**50**, 1 g, 3.65 mmol) and Selectfluor® (0.7 g, 4.74 mmol) in ACN (30 mL) was heated to 60ºC for 2 h. The solvent was removed under reduced pressure and the residue was dissolved in DCM (30 mL). The organic layer was washed with water (2 x 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (0- 50% EtOAc/Hexanes) to afford 0.5 g of 4-bromo-2-fluoro-N-(2-fluorophenyl)-3-oxobutanamide (**108**) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.19 (m, 1H), 7.17-7.11 (m, 3H), 5.84 (d, 1H, *J* = 48.4 Hz), 4.34 (dd, 2H, *J* = 69.6, 12.8 Hz).

4-(Bromomethyl)-8-chloroquinolin-2(1H)-one (109). Compound **109** was synthesized as described for compound **52** using 4-bromo-*N*-(2-chlorophenyl)-3-oxobutanamide (**103**) as the starting material. LRMS (ESI+) *m/z*: calcd for $C_{10}H_7BrClNO$ 271.9, found 272.8 $[M + H]^+$.

4-(Bromomethyl)-7-fluoroquinolin-2(1H)-one (110). Compound **110** was synthesized as described for compound **52** using 4-bromo-*N*-(3-fluorophenyl)-3-oxobutanamide (**104**) as the starting material. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (s, 1H), 7.90 (dd, 1H, *J* = 9.0, 5.8 Hz), 7.11 (m, 2H), 6.70 (s, 1H), 4.89 (s, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_7BrFNO$ 255.9, found 255.8 $[M + H]^+$.

4-(Bromomethyl)-6-fluoroquinolin-2(1H)-one (111). Compound **111** was synthesized as described for compound **52** using 4-bromo-*N*-(4-fluorophenyl)-3-oxobutanamide (**105**) as the starting material. LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_7BrFNO$ 255.9, found 256.0 $[M + H]^+$.

8-Bromo-4-(bromomethyl)-5-fluoroquinolin-2(1H)-one (112). Compound **112** was synthesized as described for compound **52** using 4-bromo-*N*-(2-bromo-5-fluorophenyl)-3-oxobutanamide (**106**) as the starting material. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.64 (s, 1H), 7.91 (dd, 1H, *J* = 9.0, 5.0), 7.14 (m, 1H), 6.90 (s, 1H), 4.88 (s, 2H).

4-(Bromomethyl)-7,8-difluoroquinolin-2(1H)-one (113). Compound **113** was synthesized as described for compound **52** using 4-bromo-*N*-(2,3-difluorophenyl)-3-oxobutanamide (**107**) as the starting material. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (m, 1H), 7.34 (m, 1H), 6.78 (s, 1H), 4.90 (s, 2H).

4-(Bromomethyl)-3,8-difluoroquinolin-2(1H)-one (114). Compound **114** was synthesized as described for compound **52** using 4-bromo-2-fluoro-*N*-(2-fluorophenyl)-3-oxobutanamide (**108**) as the starting material. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.50 (s, 1H), 7.72 (d, 1H, *J* = 8.0 Hz), 7.47 (dd, 1H, *J* = 10.8, 7.6 Hz), 7.31 (m, 1H), 4.91 (s, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{10}H_6BrF_2NO$ 273.9, found 273.7 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)quinolin-2(1H)-one (115). Compound **115** was synthesized as described for compound **53** using 4-(bromomethyl) quinolin-2(1H)-one (**51**, commercially

available) and 3-chloroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 7.82 (dd, 1H, *J* = 8.2, 1.2 Hz), 7.51 (td, 1H, *J* = 8.4, 1.2 Hz), 7.33 (dd, 1H, *J* = 8.4, 1.2 Hz), 7.20 (td, 1H, *J* = 8.0, 1.2 Hz), 7.06 (t, 1H, *J* = 8.0 Hz), 6.61 (s, 1H), 6.54 (m, 2H), 6.37 (s, 1H), 4.54 (s, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{13}ClN_2O$ 285.1, found 285.2 $[M + H]^+$.

8-Chloro-4-((3-chlorophenylamino)methyl)quinolin-2(1H)-one (116). Compound **116** was synthesized as described for compound **53** using 4-(bromomethyl)-8-chloroquinolin-2(1H)-one (**109**) and 3-chloroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 7.84 (d, 1H, *J* = 8.4 Hz), 7.69 (d, 1H, *J* = 8.0 Hz), 7.23 (t, 1H, *J* = 7.8 Hz), 7.08 (t, 1H, *J* = 8.0 Hz), 6.64-6.56 (m, 3H), 6.46 (s, 1H), 4.58 (m, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}Cl_2N_2O$ 319.0, found 318.9 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)-7-fluoroquinolin-2(1H)-one (117). Compound **117** was synthesized as described for compound **53** using 4-(bromomethyl)-7-fluoroquinolin-2(1H)-one (**110**) and 3-chloroaniline as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{12}ClFN_2O$ 303.1, found 302.9 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)-6-fluoroquinolin-2(1H)-one (118). Compound **118** was synthesized as described for compound **53** using 4-(bromomethyl)-6-fluoroquinolin-2(1H)-one (**111**) and 3-chloroaniline as starting materials.

8-Bromo-4-((3-chlorophenylamino)methyl)-5-fluoroquinolin-2(1H)-one (119). Compound **119** was synthesized as described for compound **53** using 8-bromo-4-(bromomethyl)-5-fluoroquinolin-2(1H)-one (**112**) and 3-chloroaniline as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{11}BrClFN_2O$ 380.9, found 380.6 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)-7,8-difluoroquinolin-2(1H)-one (120). Compound **120** was synthesized as described for compound **53** using 4-(bromomethyl)-7,8-difluoroquinolin-2(1H)-

one (**113**) and 3-chloroaniline as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.70 (m, 1H), 7.30 (m, 1H), 7.08 (t, 1H, *J* = 8.0 Hz), 6.63-6.55 (m, 3H), 6.40 (s, 1H), 4.54 (m, 2H). LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{11}ClF_2N_2O$ 321.0, found 320.9 $[M + H]^+$.

4-((3-Chlorophenylamino)methyl)-3,8-difluoroquinolin-2(1H)-one (121). Compound **121** was synthesized as described for compound **53** using 4-(bromomethyl)-3,8-difluoroquinolin-2(1H)-one (**114**) and 3-chloroaniline as starting materials. LRMS (ESI+) *m*/*z*: calcd for $C_{16}H_{11}ClF_2N_2O$ 321.0, found 320.8 $[M + H]^+$.

***N*-((8-Bromo-5-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-(3-chlorophenyl)-4-methylthiazole-5-carboxamide (122).** Compound **122** was synthesized as described for compound **7** using 8-bromo-4-((3-chlorophenylamino)methyl)-5-fluoroquinolin-2(1H)-one (**119**) and 4-methylthiazole-5-carboxylic acid as starting materials. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 8.97 (s, 1H), 7.90 (dd, 1H, *J* = 8.4, 4.8 Hz), 7.56 (s, 1H), 7.34-7.31 (m, 2H), 7.27 (m, 1H), 7.10 (dd, 1H, *J* = 12.0, 8.4 Hz), 6.54 (s, 1H), 5.36 (s, 2H), 2.44 (s, 3H). LRMS (ESI+) *m*/*z*: calcd for $C_{21}H_{14}BrClFN_3O_2S$ 505.9, found 505.7 $[M + H]^+$.

Low Temperature SDS-PAGE: RAW 264.7 cells were seeded into 6-well dishes at a density of $1.5x10^6$ cells/well in 2 mL of growth media. Cells were incubated for 2-3 h at 37°C and 10% CO_2. Next, 1 mL of media was removed from each well and replaced with 1 mL of a 2X cocktail containing IFNγ (100 U/mL final), LPS (2 μg/mL final) and compound or vehicle (0.1% DMSO final) diluted in DMEM without serum. Cells were incubated overnight (~15 hr) at 37°C and 10% CO_2. Cells were washed once with ice cold PBS and then 200 μL of ice-cold lysis buffer containing protease inhibitors was added to each well. Cells were scraped from the dish and transferred to micro-centrifuge tubes on ice. Samples were sonicated for 5 seconds at setting 4 and centrifuged for 10 minutes at 4ºC. Supernatants were transferred to clean tubes and stored on ice. The concentration of protein in the cell extracts was determined using a Bradford assay with a BSA standard curve as described by the manufacturer (Advanced). Equivalent amounts of protein extracts were added to micro-centrifuge tubes and the volume was adjusted to 10 μL with lysis buffer. An equal volume of ice-cold 2X loading buffer was added to each sample and gently pipetted to mix. Samples were stored on ice until ready to load. Twenty microliters of each sample was loaded onto a 15-well 4-20% Tris-glycine polyacrylamide gel. The gel was run in pre-chilled 1X SDS running buffer in a cold room for 2.5 h at 125 V. Proteins were transferred to nitrocellulose for 2.5 h at 70 V in 1X transfer buffer. The membrane was blocked overnight in Blotto diluted in western wash buffer at 4ºC. The membrane was incubated in a 1:2500 dilution of mouse anti-iNOS antibody (BD Biosciences) in Blotto for 1 h at room temperature followed by 3 x 5 min washes in western wash buffer. The blot was then incubated in a 1:2000 dilution of goat anti-mouse HRP-conjugated secondary antibody (Santa Cruz Biotech) in Blotto for 1 hour at room temperature. Following 4 x 5 min washes, the proteins were visualized by chemiluminescence using West Dura detection reagent as described by the manufacturer (Pierce). The data were captured on a CCD-based imaging device (Alpha Inotech).

X-Ray Diffraction Data: *Crystal data*: $C_{21}H_{15}ClFN_3O_2S$, f.w. = 427.87, colorless needle, triclinic, *P*-1, a = 8.8921(13), b = 17.982(3), c = 18.935(3) Å, α = 72.680(2), β = 82.543(2), γ = 77.465(2)°, V = 2814.5 Å^3, Z = 6, Z' = 3, d(calcd) = 1.515 g cm^{-3}. 16620 reflections were collected at 100 K using a Bruker D8 platform diffractometer with an APEX CCD detector and MoKα radiation. The structure was refined using 9455 independent reflections with all nonhydrogen atoms anisotropic and hydrogen atoms treated as idealized contributions. The symmetry independent structure consists of three chemically similar molecules. All software is contained in the APEX, SAINT and SHELXTL libraries of programs maintained by Bruker-AXS (Madison, WI).

Mouse Pharmacokinetics: Male (Balb/c) mice (6 to 8 weeks of age) were obtained from Charles-River Laboratories (Hollister, CA). Animals were acclimated for a minimum of 3 days prior to performing any experimental procedures. A 12-hr light: 12-hr dark cycle was maintained throughout the course of all experiments in a temperature and humidity controlled vivarium facility. Animals were fed standard laboratory rodent chow, and water *ad libitum*. For intravenous (IV) administration, 12 overnight fasted animals received a single dose of 3 or 1 mg/kg body weight (3 or 1 mL/kg) via penile vein injection under light isoflurane anesthesia in 10% DMSO; 30% PEG-400 and 60% HPβCD (30% w/v in water). For oral (PO) administration, 9 overnight fasted animals received a single dose of 10 mg/kg body weight (10 mL/kg) via oral gavage in a suspension of 0.5% Tween-80, 0.5% PVP-K30, 9% PEG-400 and 90% CMC in water (0.5% w/v). PO dose suspensions were dispersed with an electric homogenizer, followed by treatment with a sonicator probe on wet ice. Blood samples (~ 125 µL) were collected by puncture of the submandibular vein (i.e. the cheek pouch method) into lithium heparin pre-treated tubes at 0 (pre-dose), 5, 10, 20 and 40 minutes,1, 2, 4, 8, 12 and 24 hours following IV administration and at 0 (pre-dose), 0.25, 0.5, 1, 2, 4, 8, 12 and 24 hours post-dose following PO

administration, such that no animal was sampled more than 3 times. Plasma was isolated by centrifugation and stored at -80°C until analysis by LC-MS/MS.

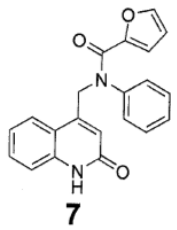
Sample analyses were performed by LC-MS using a PE Sciex API 4000 Q-Trap mass spectrometer tandem with Agilent 1100 chromatography system. Polar-RP Synergi column from Phenomenex (2.0 x 3.0 mm, 4.0 micron). Chromatography was performed using a gradient system using two mobile phases A and B. The mobile phase A consisted of 0.1% formic acid in water and mobile phase B of 0.1% formic acid in acetonitrile. Mobile phase B was ramped from 0% to 100% from 0.0 to 1.0 min and was held at 100% B from 1.0 to 1.9 min. From 2.0 to 2.7 min, column was equilibrated to the initial condition at 100% A. Flow rate for the gradient was set at 1.0 mL/min. Mass spectrometry detection was carried out on a PE Sciex API4000 Q-Trap equipped with a Turbo IonSpray source. ESI+ mass spectra were acquired with multiple reaction monitoring (MRM). The plasma samples were prepared by protein precipitation monitored with an internal standard. Standard curve was prepared by spiking control plasma with the compound and serial dilutions from this spiked solution generated different levels of the standard curve. A weighted linear least squares regression was then performed to generate a correlation between concentration and the relative amounts of analyte and internal standard for compound. Twelve standard curve were used, highest level at 10,000 ng/mL. Lowest level of detection was at 4.0 ng/mL.

Mouse Liver Microsome Assay: Test article in DMSO was added to incubation buffer such that the final DMSO concentration was 0.4% (v/v). Microsomes were stored at -70°C until use, thawed on ice and then diluted to 5 mg/mL in Phosphate buffer immediately before use. Microsome incubations were performed in 100 mM Phosphate buffer (pH 7.4), containing 0.1% BSA (fatty acid free), 1 mM EDTA, 3 mM MgCl2, alamethicin (50 µg/mg microsomal protein) and 1.25 mM D-Saccharic acid 1,4-lactone. D-saccharic acid 1,4-lactone is an inhibitor of β-glucuronidase, an enzyme which can rapidly hydrolyze glucuronide conjugates. Microsomes

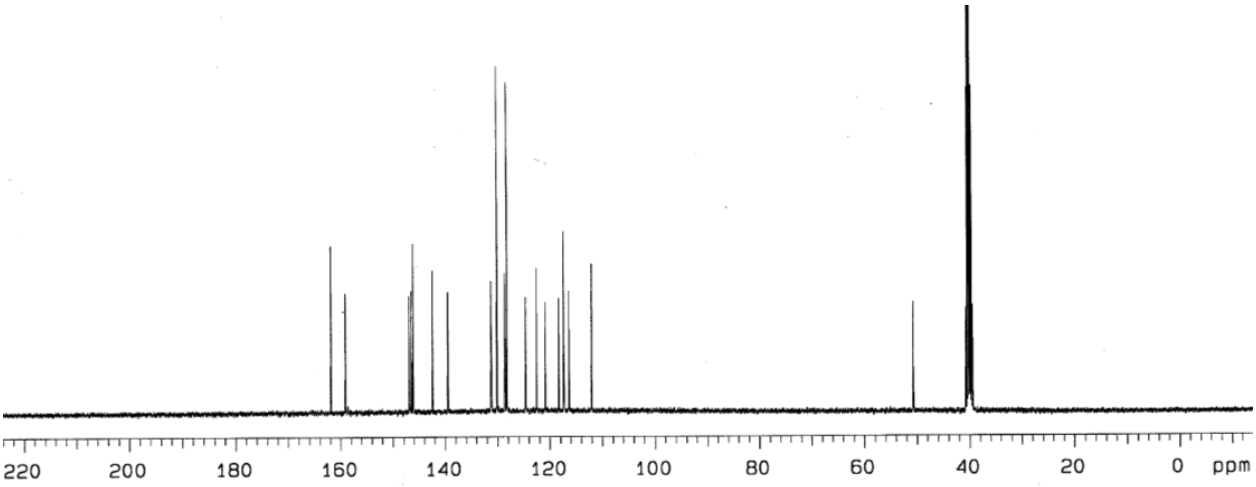
and test article in incubation buffer were pre-warmed in triplicate at 37°C for 5 minutes. Reactions were initiated by addition of 25 µL of NADPH-regenerating system (consisting of 20 mM NADP, 100 mM glucose-6-phosphate, 20 U/mL glucose-6-phosphate dehydrogenase and 100 mM UDPGA). Final incubation volume was 0.5 mL with a test article concentration of 5 µM. At specified time points, 100 µL aliquots were removed and combined with 300 µL of chilled quenching reagent (1:2 water: acetonitrile) containing internal standard (IS). Sample plates were then centrifuged at 1,500 g for 15 minutes and supernatants submitted for LC-MS/MS analysis. Relative test article concentrations were defined by the analyte/IS peak ratios in each sample.

Cytochrome P450 Inhibition Assay: Compounds were evaluated for biochemical inhibition of cytochrome P450 using the Vivid CYP450 Blue assay (Invitrogen) adapted to 1536-well plate format. Briefly, individual isozymes and their blue substrates were diluted to a 2X working concentration in 1X assay buffer. Isozyme concentrations were: 3A4, 10 nM; 2D6, 40 nM; 1A2, 12 nM; 2C9, 20 nM; and 2C19, 10 nM. 2X Regeneration System was included in the isozyme mix. Substrate concentrations were: 40 nM for 3A4 and 2D6; 20 µM for 1A2, 2C9, and 2C19. NADP+ was added to the substrate mix at a concentration of 400 µM for the assays. A volume of 2.5 µL of the isozyme mix was dispensed into black Greiner 1536-well plates. Then, 30 nL of compound was added to the wells. Subsequently, 2.5 µL of the blue substrate was added and plates were incubated for 1 hour at room temperature. Four replicate data points are obtained per compound at each concentration. Inhibition of substrate turnover was measured using a fluorescent plate reader with excitation at 405 nm and emission at 450 nm (Molecular Devices).

Compound 7: *N*-((2-Oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-phenylfuran-2-carboxamide



7



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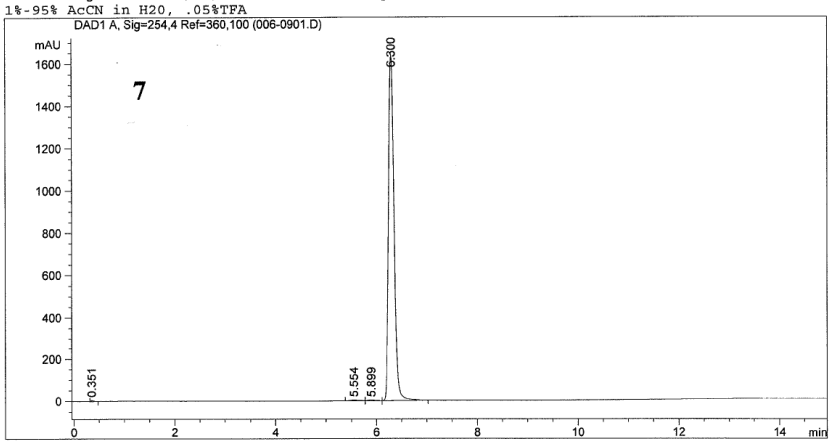


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Use Multiplier & Dilution Factor with ISTDs


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   2   5.554 VV    0.1580   40.20696    3.78339   0.3173
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Totals :                   1.26712e4  1654.09661
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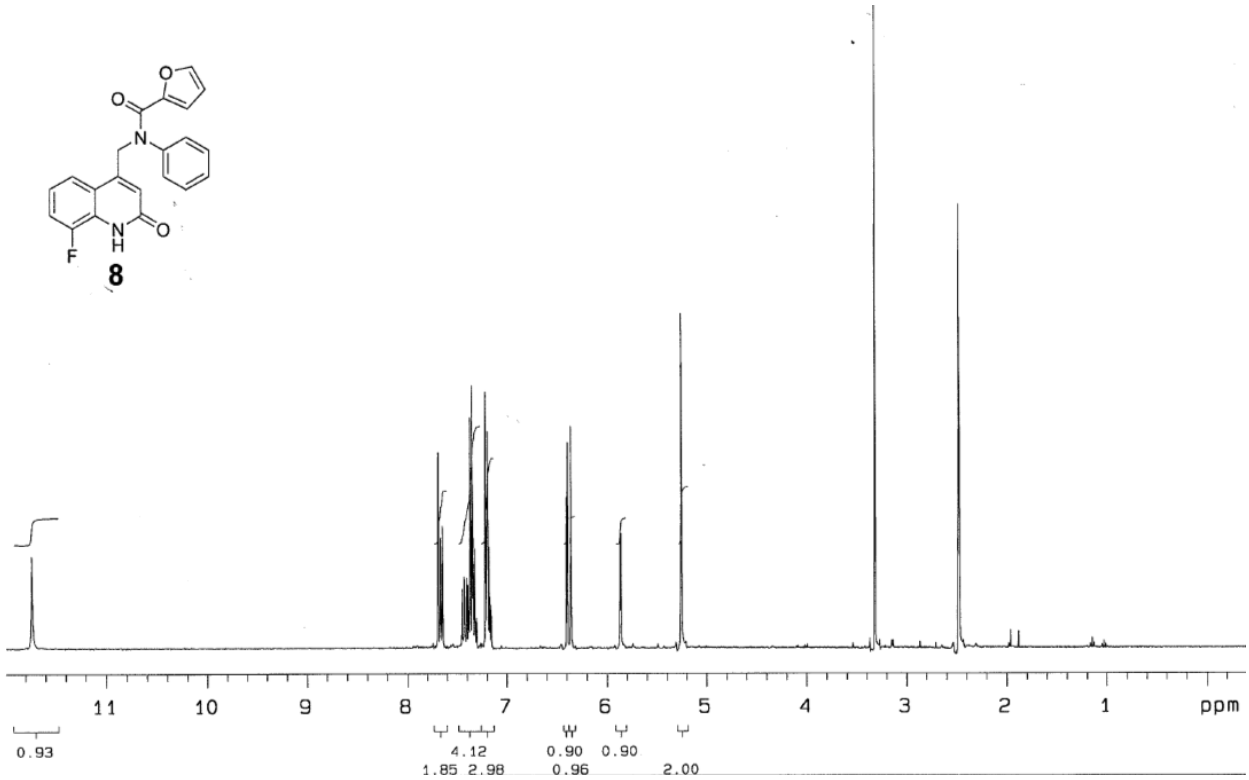
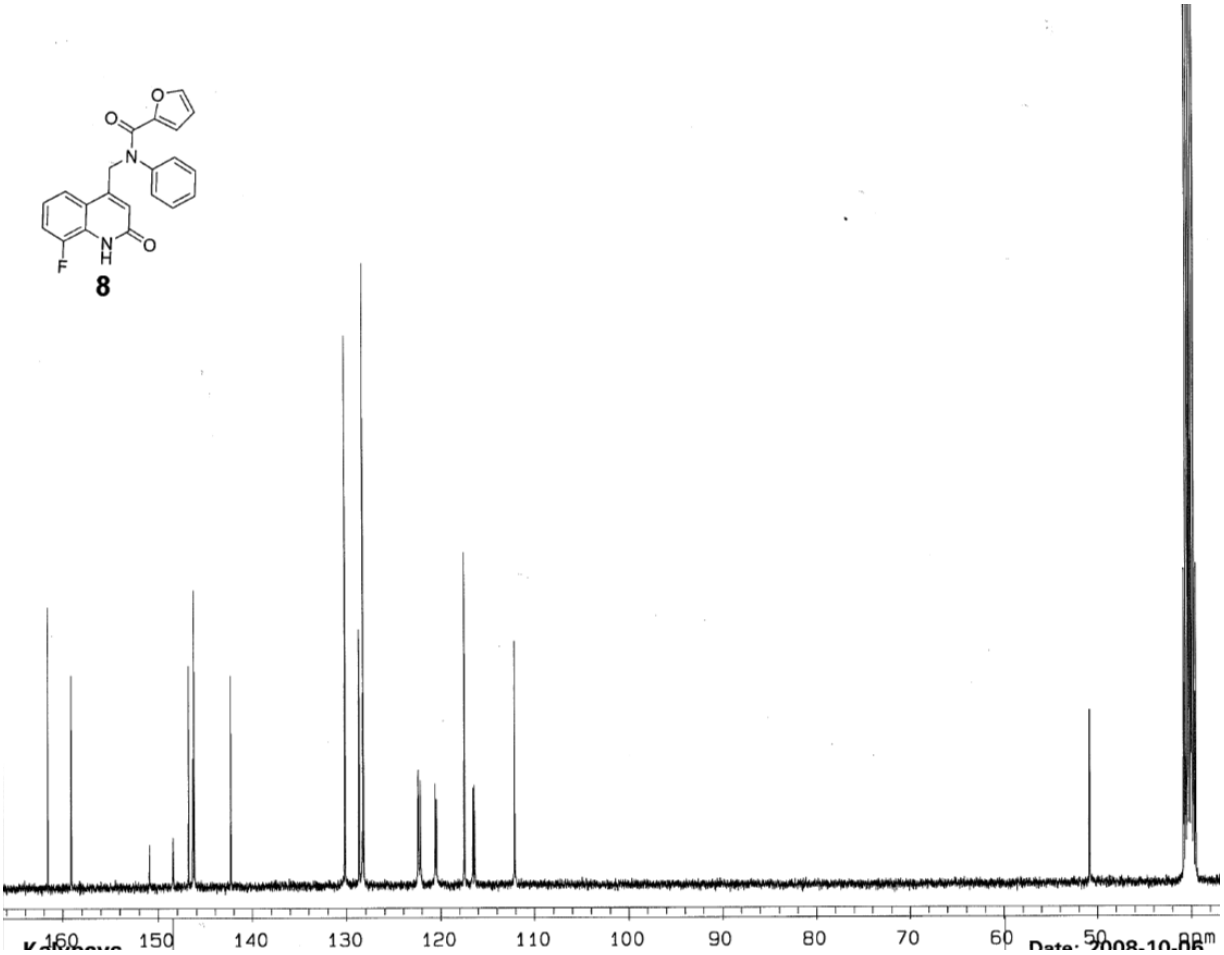
Compound 8: *N*-((8-Fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-phenylfuran-2-carboxamide



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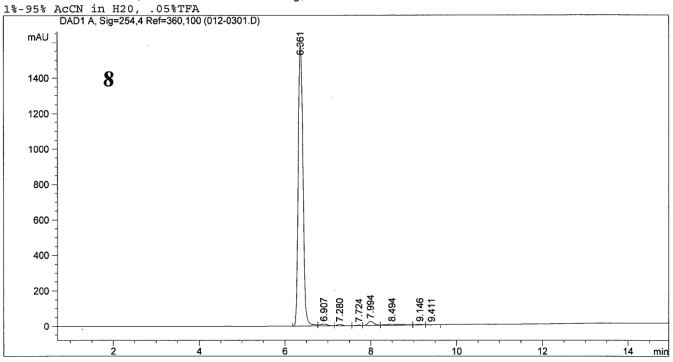


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Use Multiplier & Dilution Factor with ISTDs


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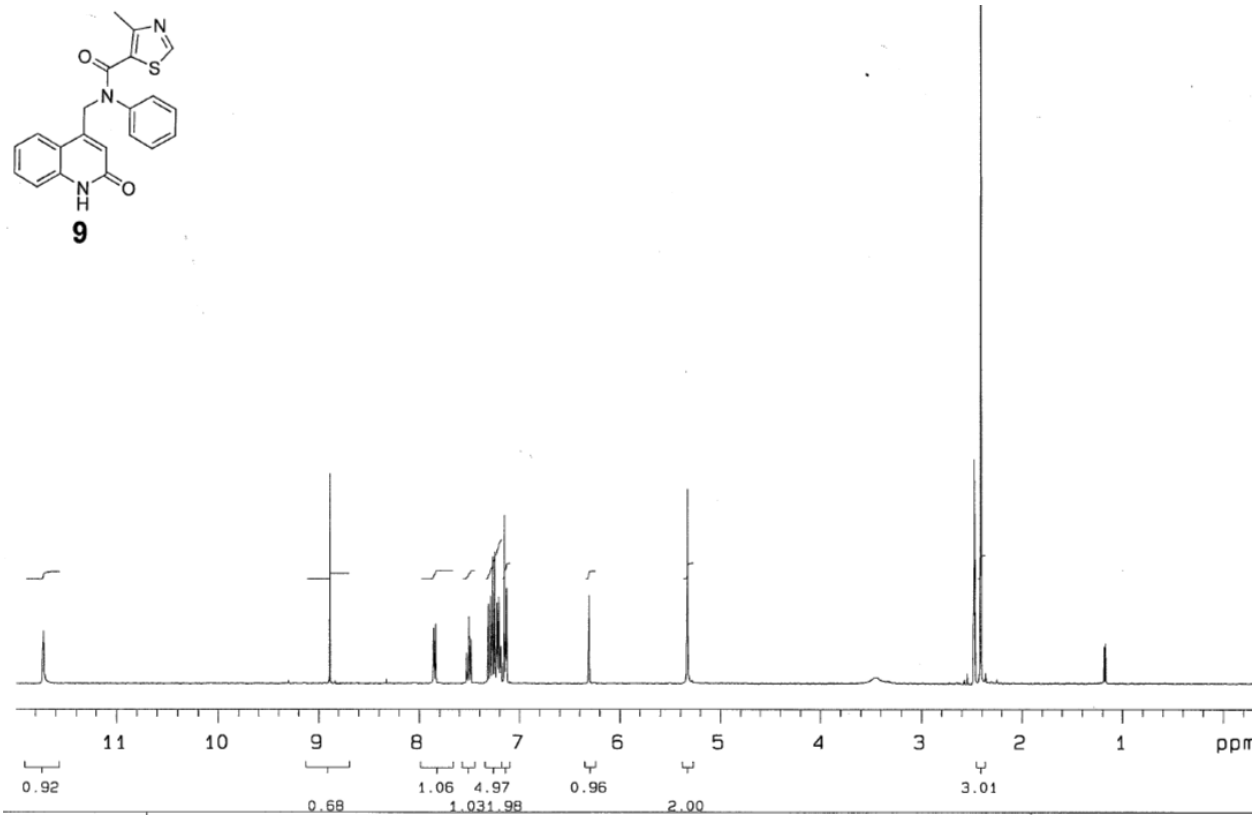
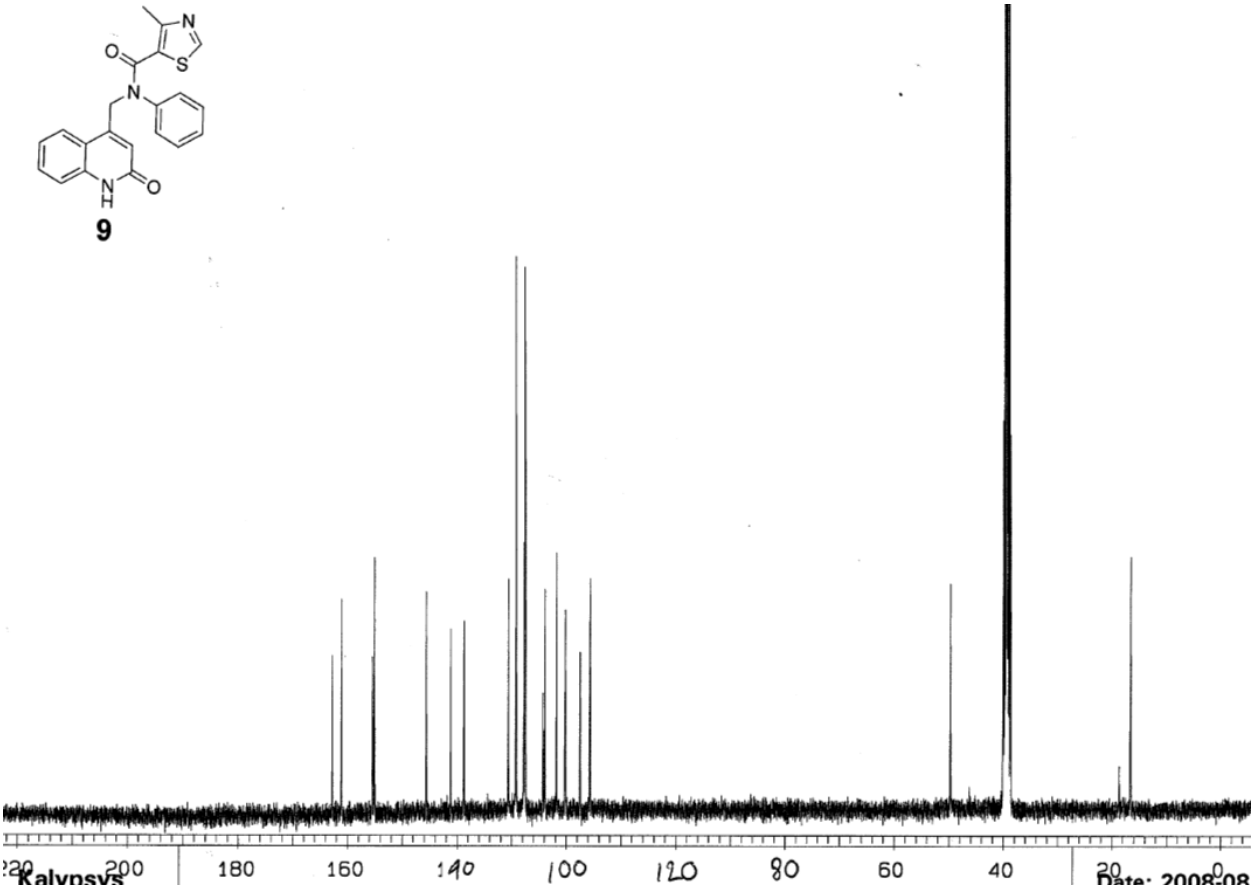
   3   7.280 VB    0.1434   60.59841    6.34656   0.4804
   4   7.724 BV    0.1402   26.92978    2.85120   0.2135
   5   7.994 VV    0.1597  228.49194   22.26974   1.8114
   6   8.494 VV    0.4207  157.33253    4.84718   1.2473
   7   9.146 VV    0.2055   47.70134    3.53321   0.3782
   8   9.411 VV    0.1967   23.38005    1.49335   0.1853

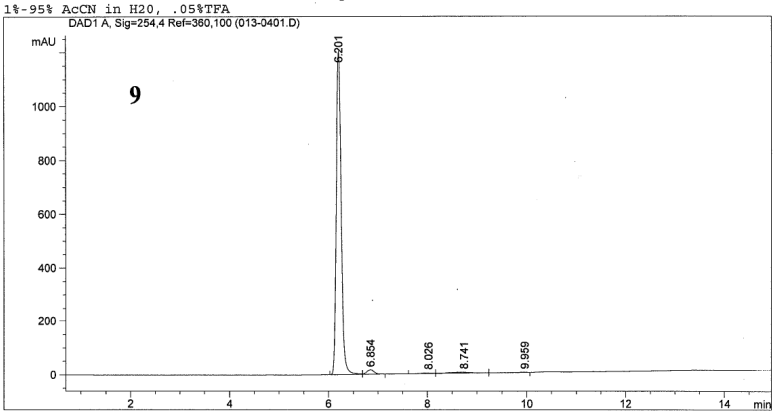
Totals :                  1.26140e4  1635.85096
```

Compound 9: 4-Methyl-*N*-((2-oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-phenylthiazole-5-carboxamide





```
==========================================================================
Injection Date  : 11/7/2007 2:26:45 PM          Seq. Line :   4
Sample Name     :                               Location : Vial 13
Acq. Operator   : 14                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/7/2007 1:38:18 PM by 14
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                          Area Percent Report
==========================================================================

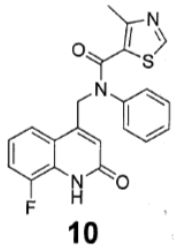
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

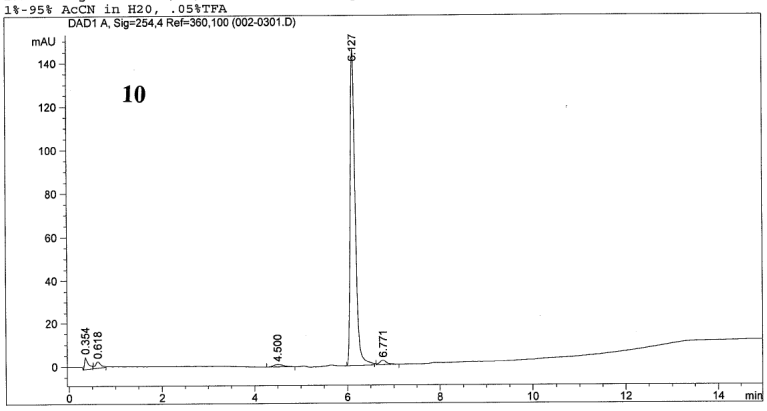
Peak RetTime Type  Width     Area      Height     Area
  #    [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.201 VV     0.1105 8315.13770 1205.21387  95.6283
   2   6.854 VB     0.1588  161.46518   15.85380   1.8569
   3   8.026 BV     0.2223   44.72888    2.68642   0.5144
   4   8.741 VV     0.5210  138.90291    3.26037   1.5975
   5   9.959 VV     0.3929   35.03724    1.07892   0.4029

Totals :                   8695.27190 1228.09338
```

Compound 10: *N*-((8-Fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methyl-*N*-phenylthiazole-5-carboxamide



```
==========================================================================
Injection Date  : 11/27/2007 3:42:02 PM          Seq. Line :   3
Sample Name     :                                Location : Vial 2
Acq. Operator   : 14                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 3 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/27/2007 11:40:02 AM by 14
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                          Area Percent Report
==========================================================================

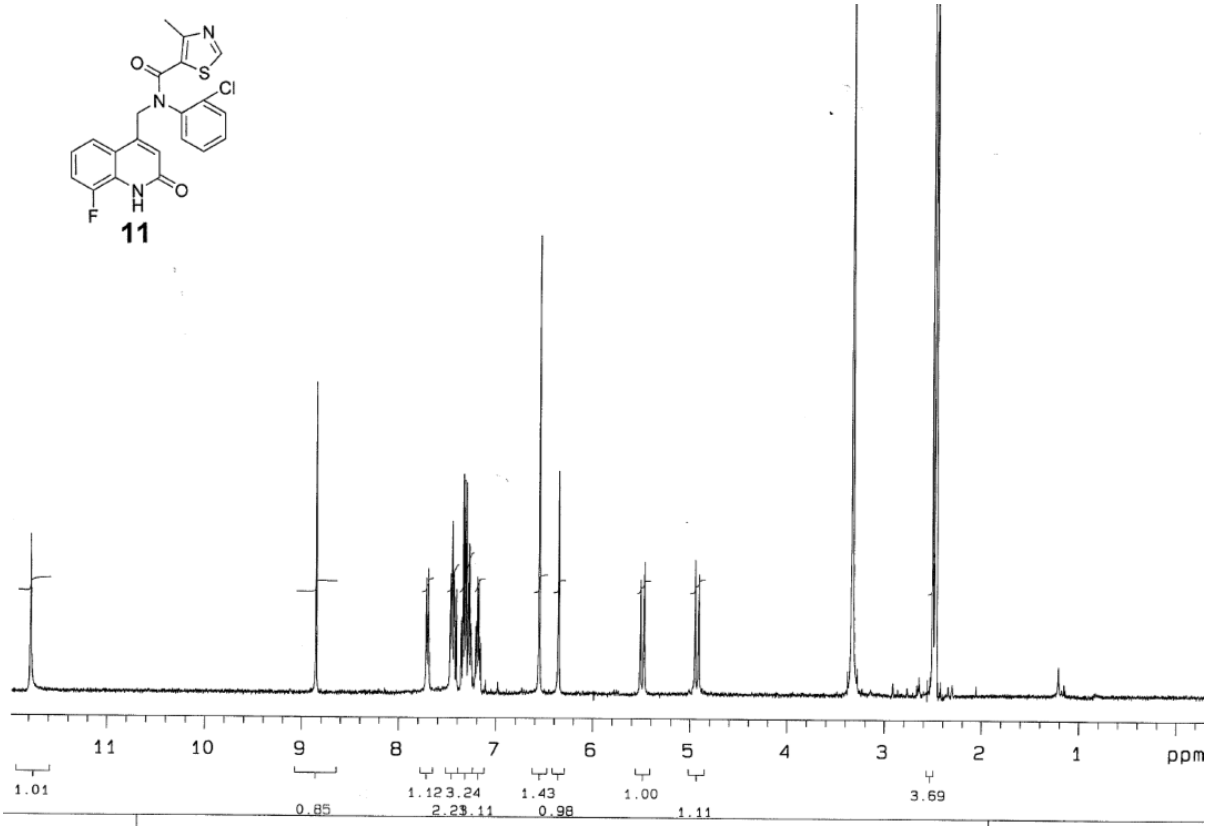
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

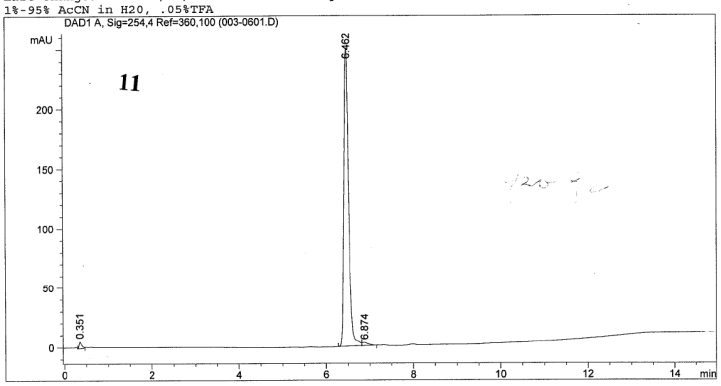
Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.354 BB    0.0708   30.18667    5.60677   2.5544
   2   0.618 BB    0.1145   23.65251    2.91858   2.0015
   3   4.500 BB    0.2099   16.30085    1.04526   1.3794
   4   6.127 BB    0.1171 1088.91956  145.80655  92.1451
   5   6.771 BB    0.1615   22.68520    2.07612   1.9196

Totals :                  1181.74478  157.45327
```

Compound 11: *N*-(2-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide



```
Injection Date  : 11/27/2007 4:35:09 PM          Seq. Line :   6
Sample Name     :                                Location : Vial 3
Acq. Operator   : 14                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 3 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/27/2007 11:40:02 AM by 14
1%-95% AcCN in H20, .05%TFA
```




```
                          Area Percent Report

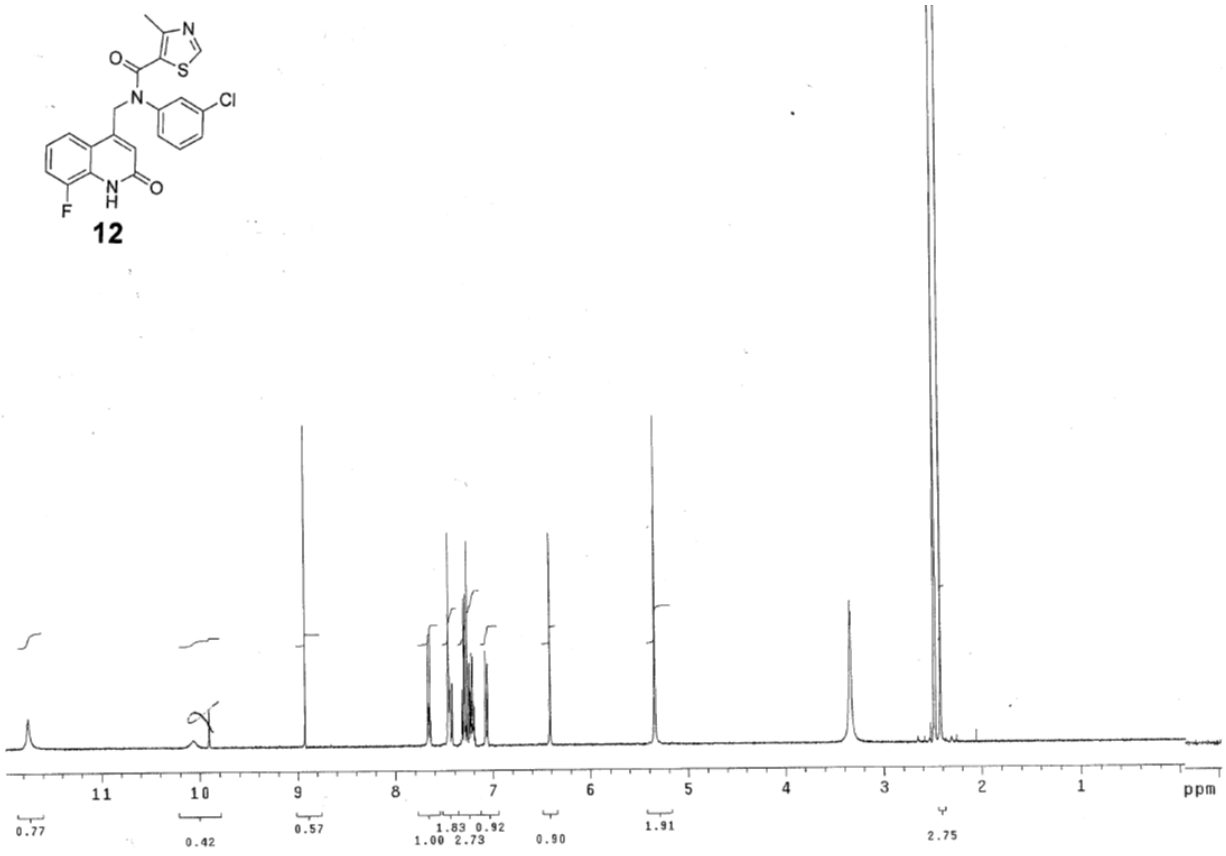
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

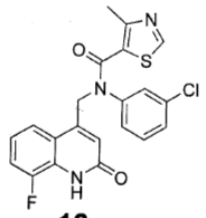

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
   #   [min]       [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   0.351 BB    0.0580   23.17265    5.63480   1.2100
   2   6.462 BV    0.1169 1866.23193  250.50536  97.4513
   3   6.874 VB    0.1403   25.63676    2.57253   1.3387

Totals :                  1915.04134  258.71268
```

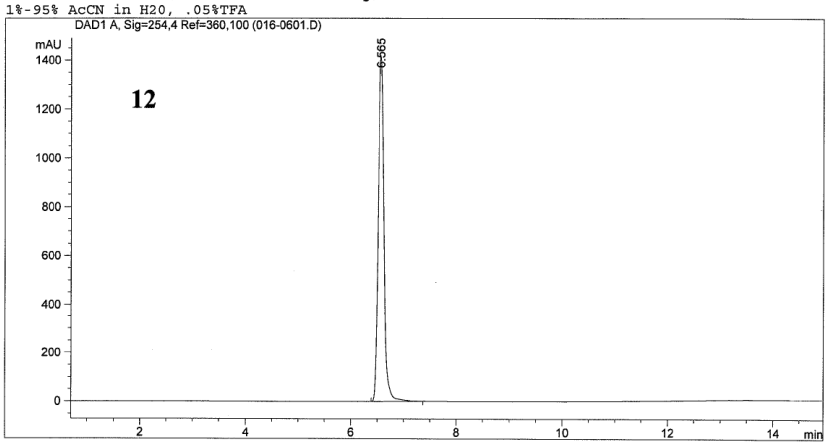
Compound 12: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





12


```
======================================================================
Injection Date  : 10/31/2007 4:55:38 PM          Seq. Line :   6
Sample Name     :                                Location : Vial 16
Acq. Operator   : 14                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/31/2007 4:08:49 PM by 14
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

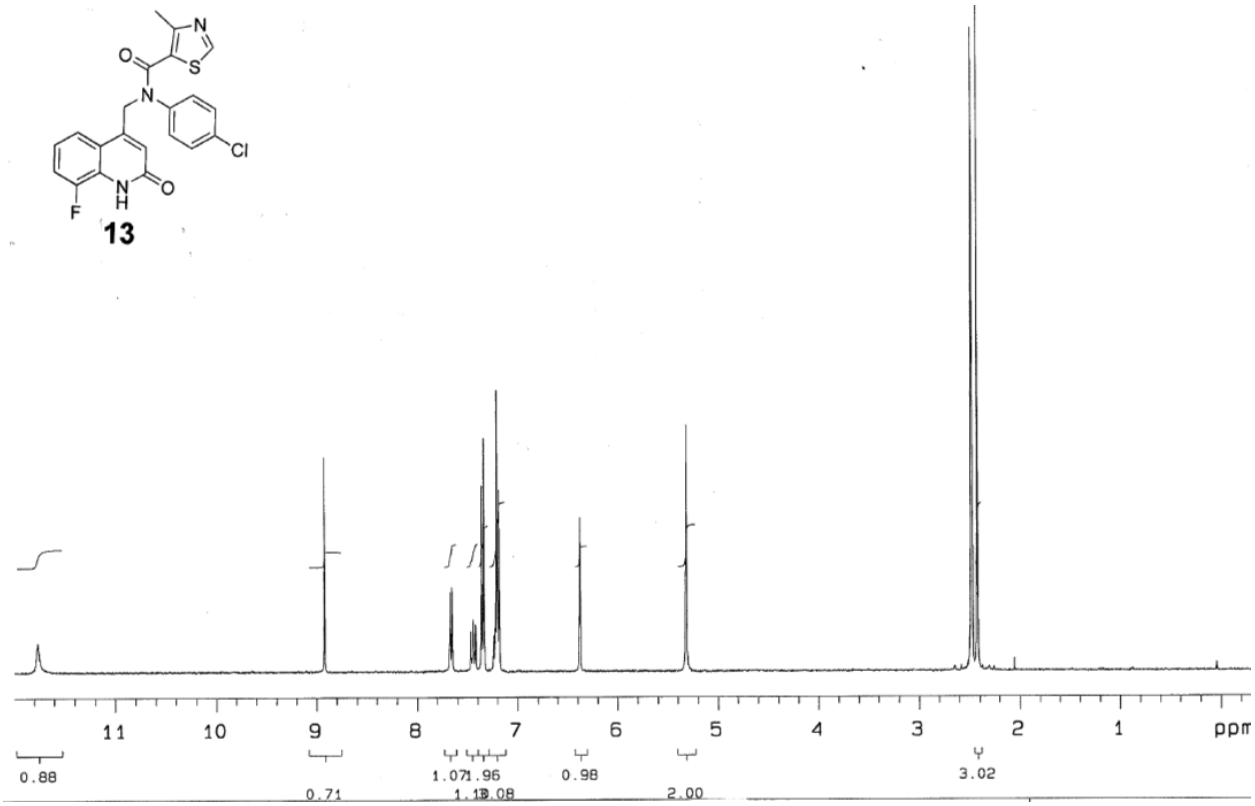
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

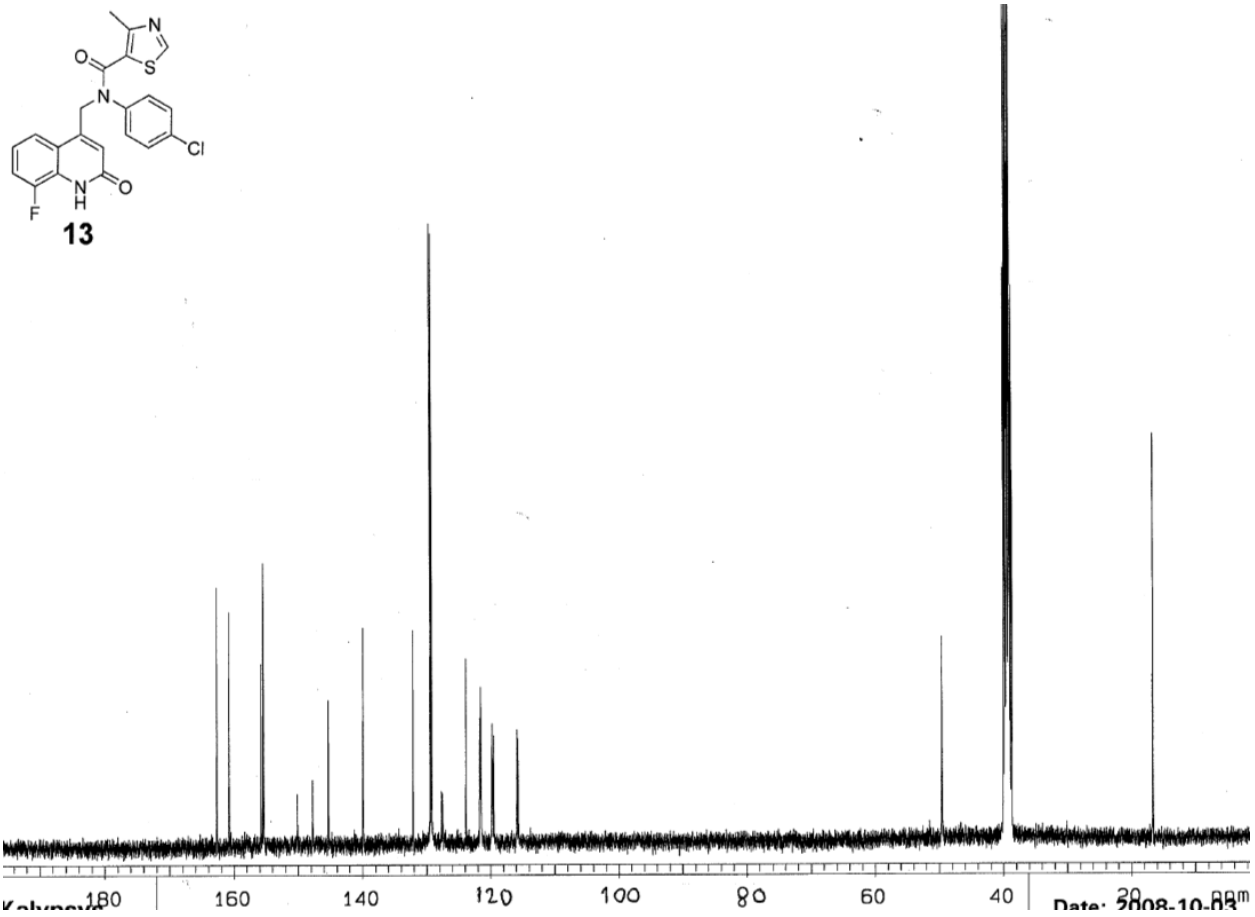

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.565 BB    0.1230 1.10909e4  1421.47742 100.0000

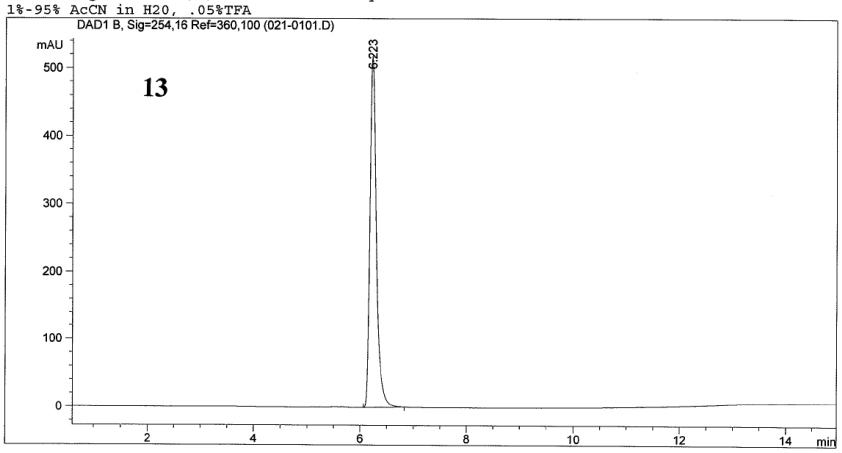
Totals :                  1.10909e4  1421.47742
```

Compound 13: *N*-(4-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
==========================================================================
Injection Date  : 10/1/2008 4:10:25 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 21
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/1/2008 4:09:37 PM by 1
1%-95% AcCN in H20, .05%TFA
```



13

```
==========================================================================
                          Area Percent Report
==========================================================================

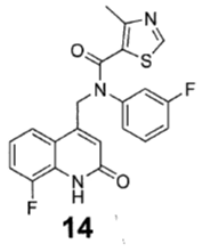
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

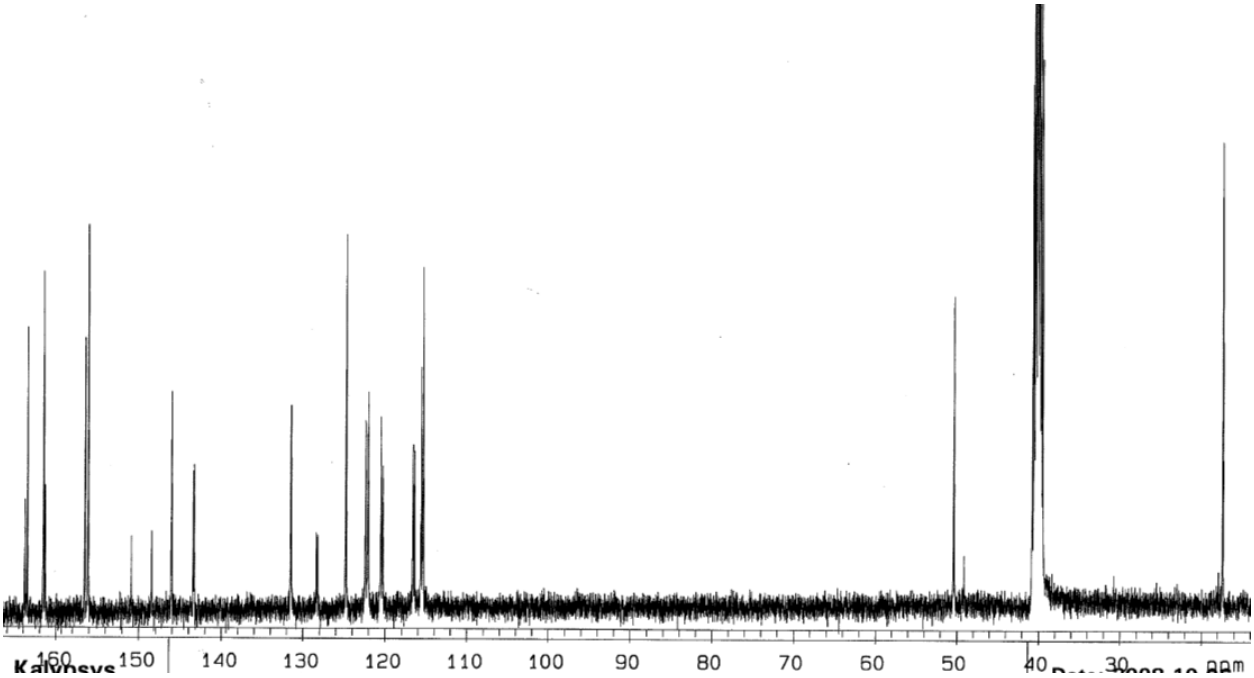
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.223 BB    0.1289 4391.39551  518.17761 100.0000

Totals :                  4391.39551  518.17761
```

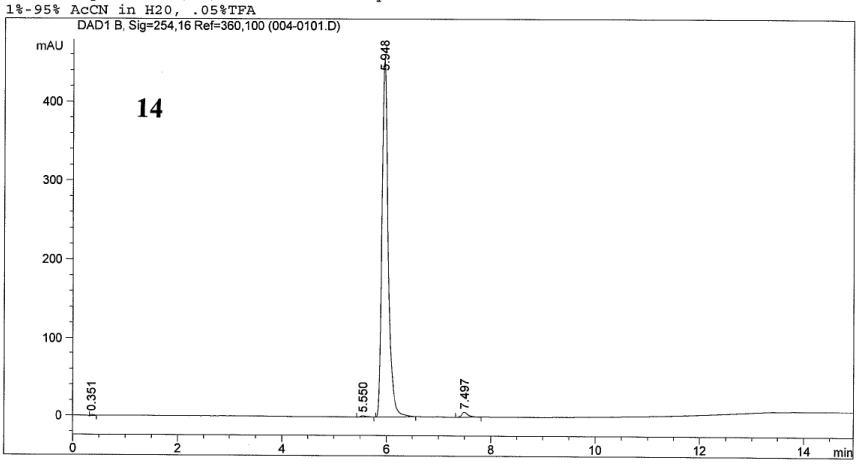
Compound 14: *N*-((8-Fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-(3-fluorophenyl)-4-methylthiazole-5-carboxamide



14




```
======================================================================
Injection Date  : 9/12/2008 1:49:15 PM          Seq. Line :   1
Sample Name     :                                Location : Vial 4
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/12/2008 1:48:22 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

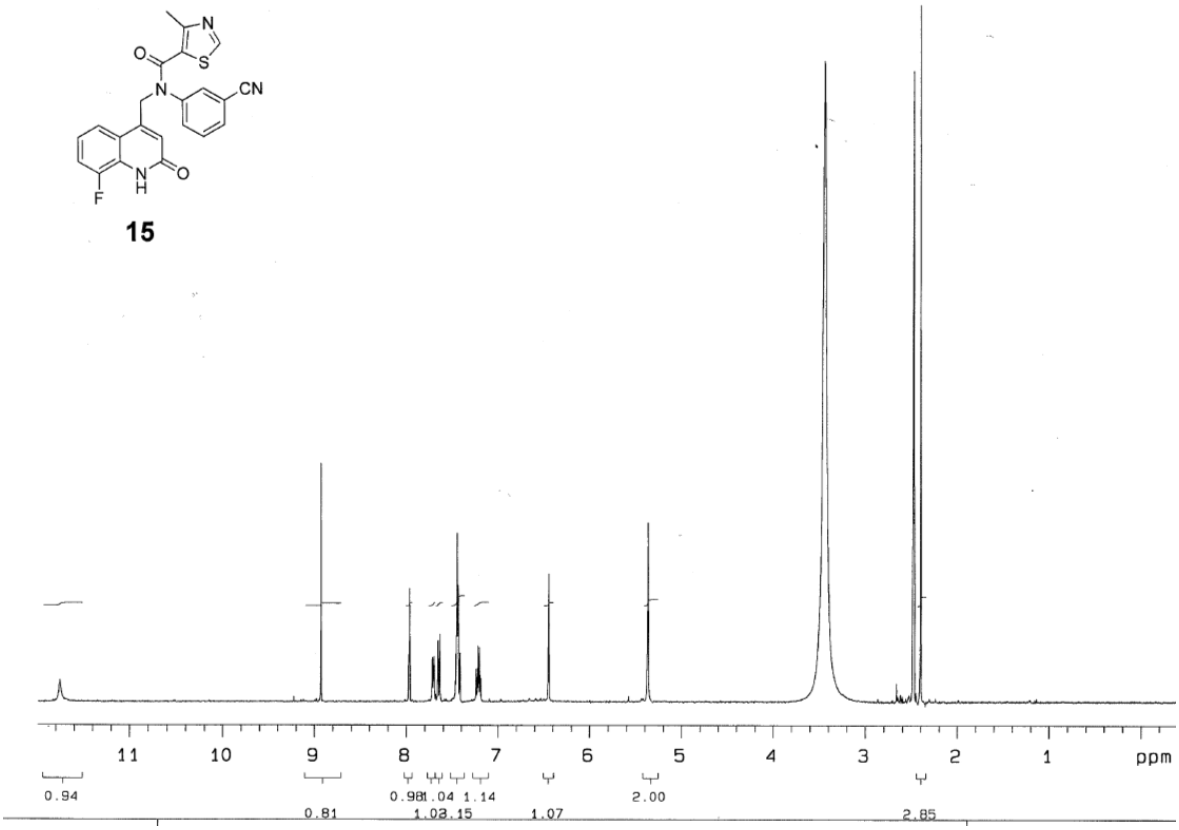
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

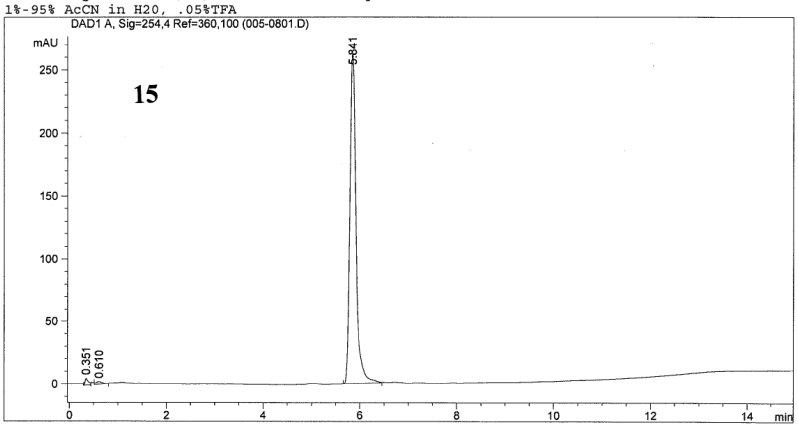
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.351 BB    0.0617    8.05800    1.81914   0.2081
   2   5.550 BB    0.1198   13.38379    1.66535   0.3456
   3   5.948 BB    0.1249 3795.24316  457.13010  97.9946
   4   7.497 BB    0.1411   56.22499    6.12265   1.4518

Totals :                  3872.90994  466.73725
```

Compound 15: *N*-(3-Cyanophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide




```
========================================================================
Injection Date  : 11/27/2007 5:10:29 PM          Seq. Line :   8
Sample Name     :                                Location : Vial 5
Acq. Operator   : 14                                Inj :   1
Acq. Instrument : Kalypsys                      Inj Volume : 3 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/27/2007 11:40:02 AM by 14
1%-95% AcCN in H20, .05%TFA
```




```
========================================================================
                        Area Percent Report
========================================================================

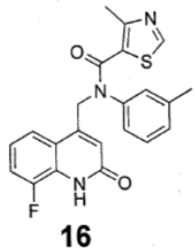
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

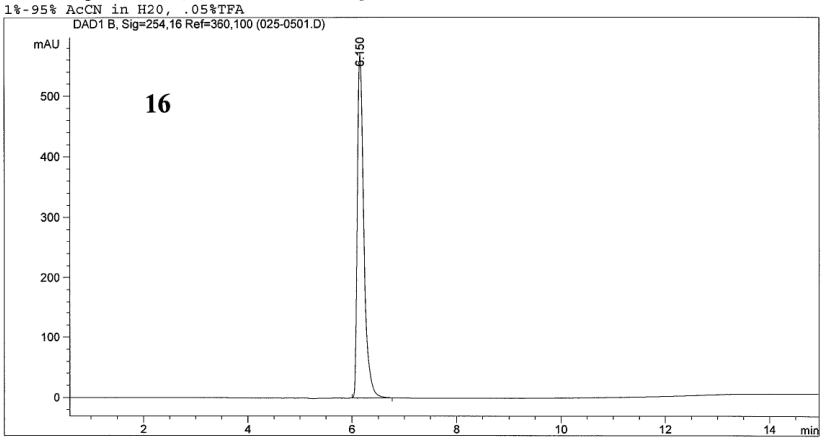
Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.351 BB    0.0616   25.06884    5.67219   1.0586
   2   0.610 BB    0.1147   18.22931    2.19980   0.7698
   3   5.841 BB    0.1372 2324.79004  262.91180  98.1716

Totals :                  2368.08819  270.78378
```

Compound 16: *N*-(3-Methylphenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide




```
========================================================================
Injection Date  : 10/1/2008 5:18:45 PM           Seq. Line :   5
Sample Name     :                                Location : Vial 25
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                      Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/1/2008 4:09:37 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
========================================================================
                        Area Percent Report
========================================================================

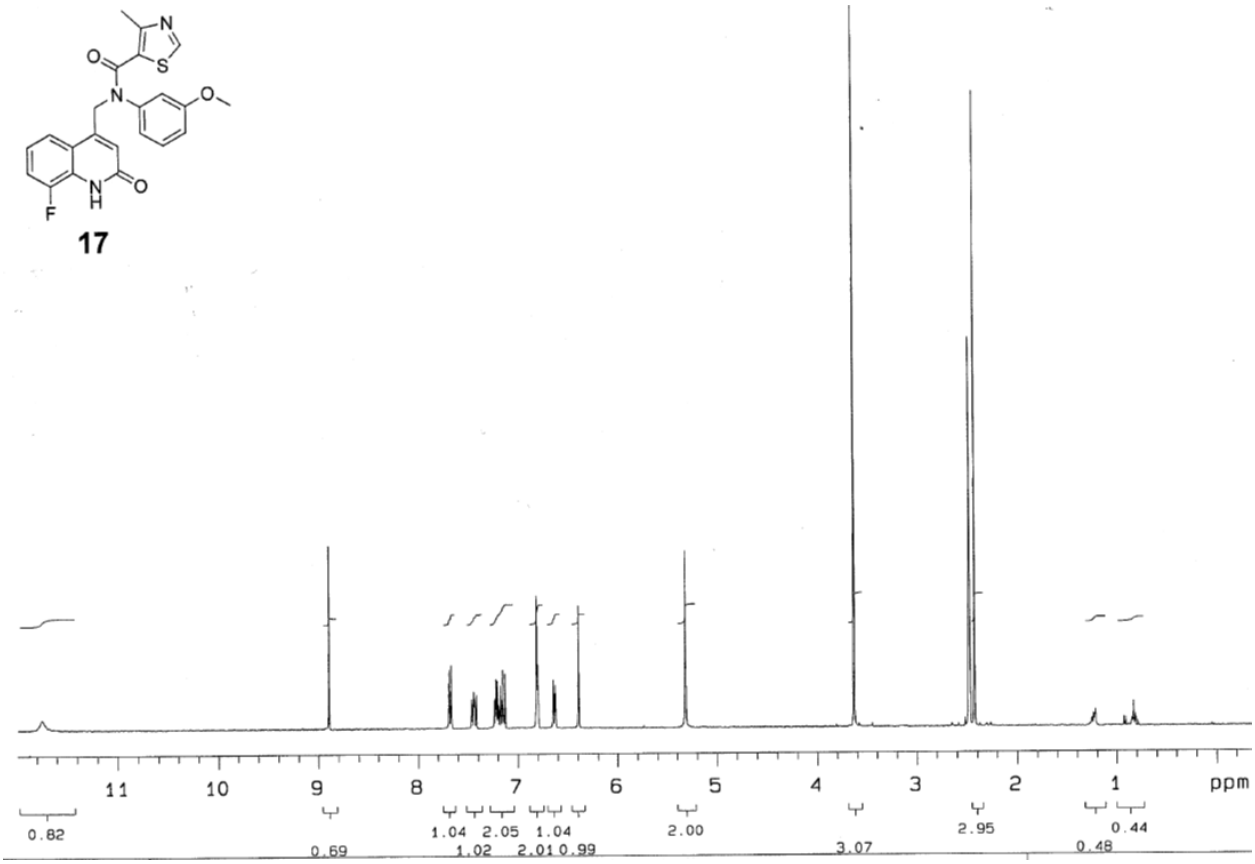
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

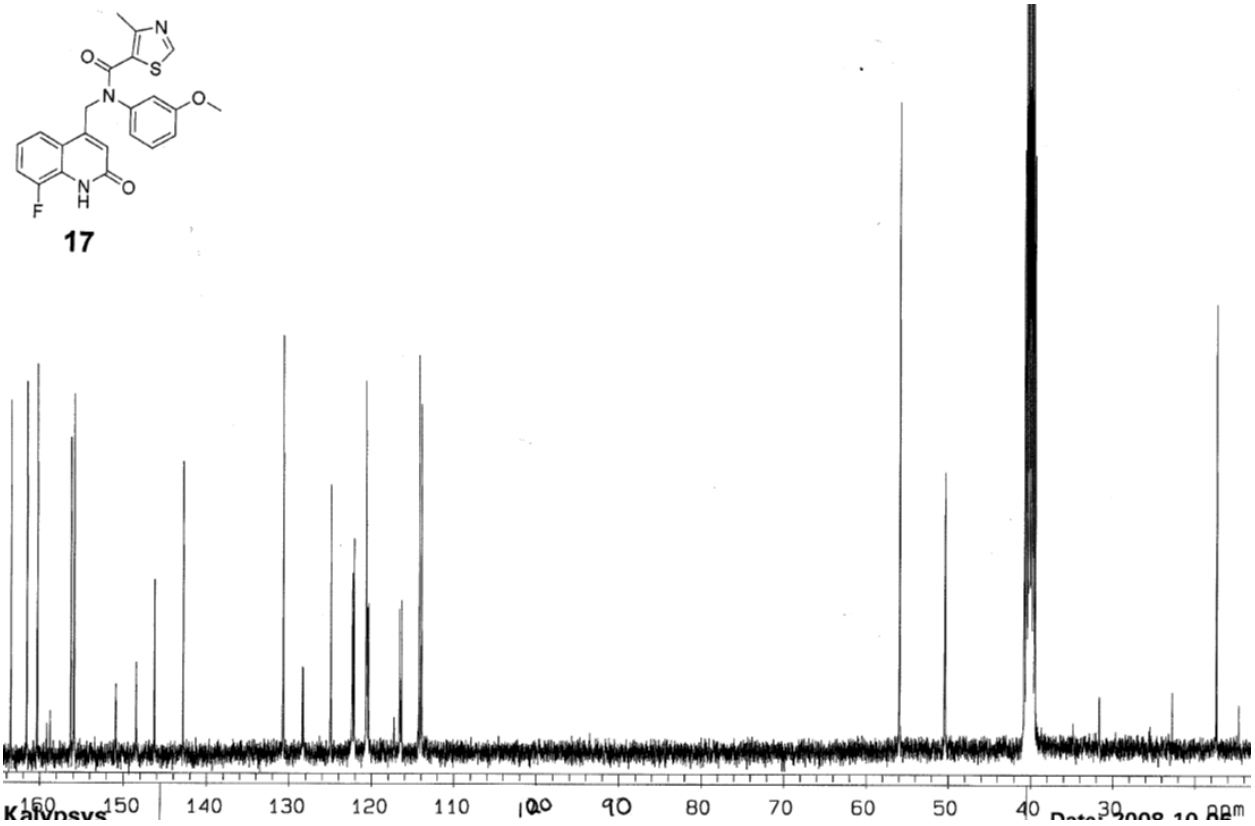

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.150 BB    0.1320 4889.76270  570.37274 100.0000

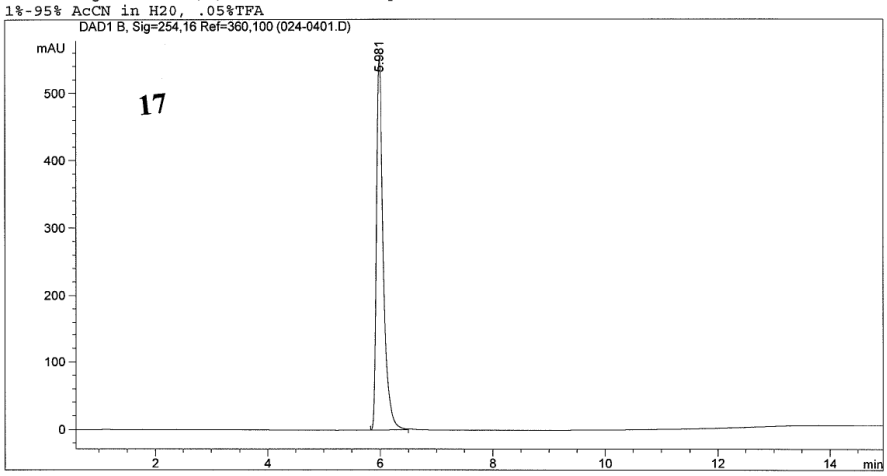
Totals :                  4889.76270  570.37274
```

Compound 17: *N*-(3-Methoxyphenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
=====================================================================
Injection Date  : 10/1/2008 5:01:39 PM          Seq. Line :   4
Sample Name     : [redacted]                    Location : Vial 24
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/1/2008 4:09:37 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
=====================================================================
                        Area Percent Report
=====================================================================

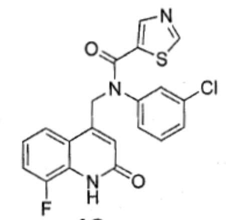
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

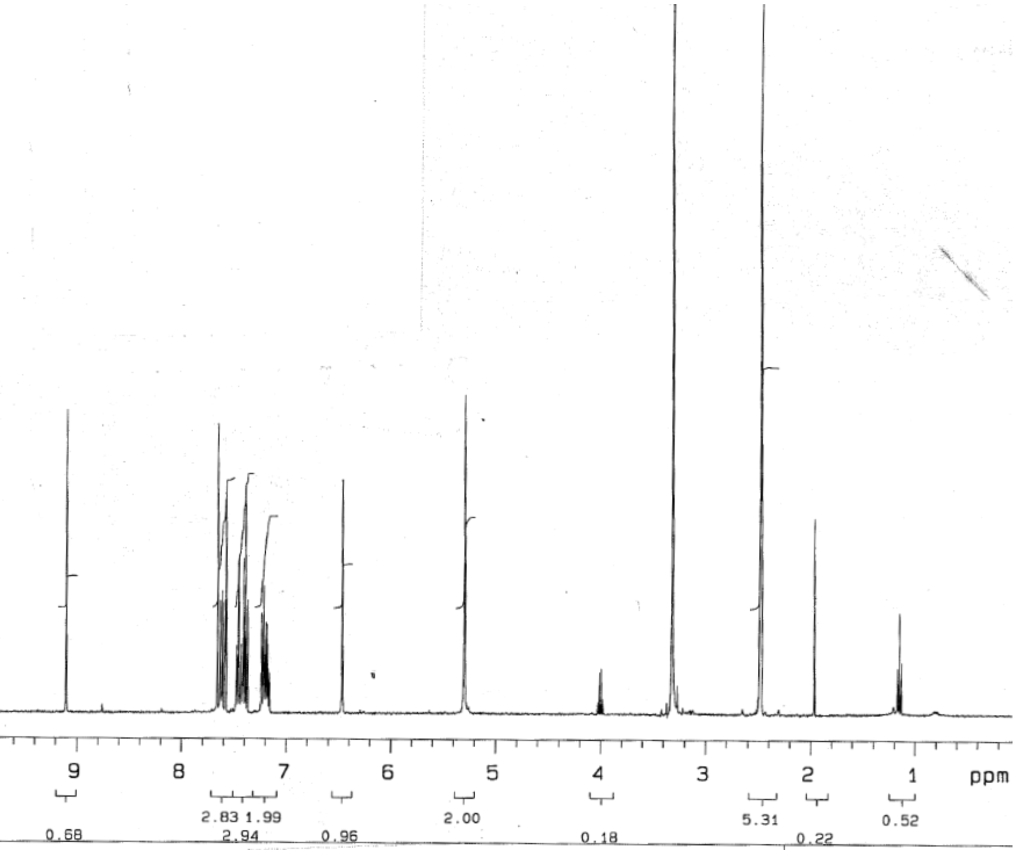
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.981 BB    0.1301 4735.00977  552.03058 100.0000

Totals :                  4735.00977  552.03058
```

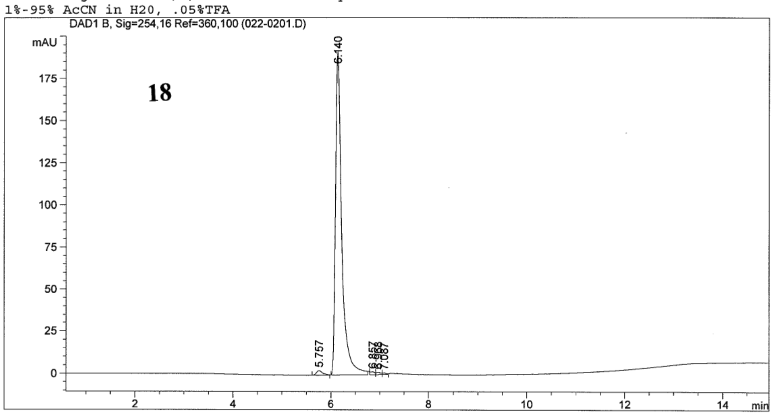
Compound 18: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)thiazole-5-carboxamide



18




```
=================================================================
Injection Date  : 10/1/2008 4:27:30 PM          Seq. Line :   2
Sample Name     : [illegible]                    Location : Vial 22
Acq. Operator   : 1                                   Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/1/2008 4:09:37 PM by 1
1%-95% AcCN in H2O, .05%TFA
```



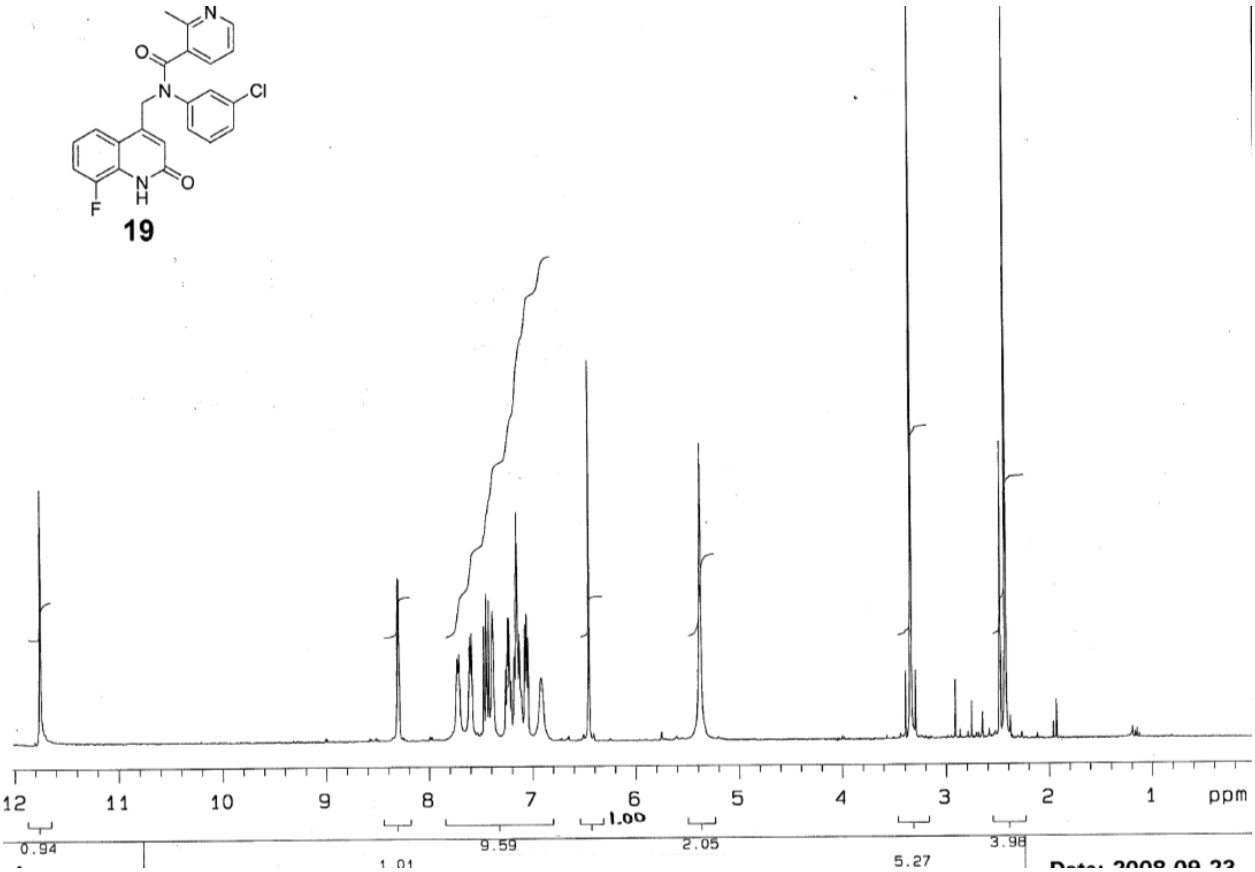

```
=================================================================
                     Area Percent Report
=================================================================

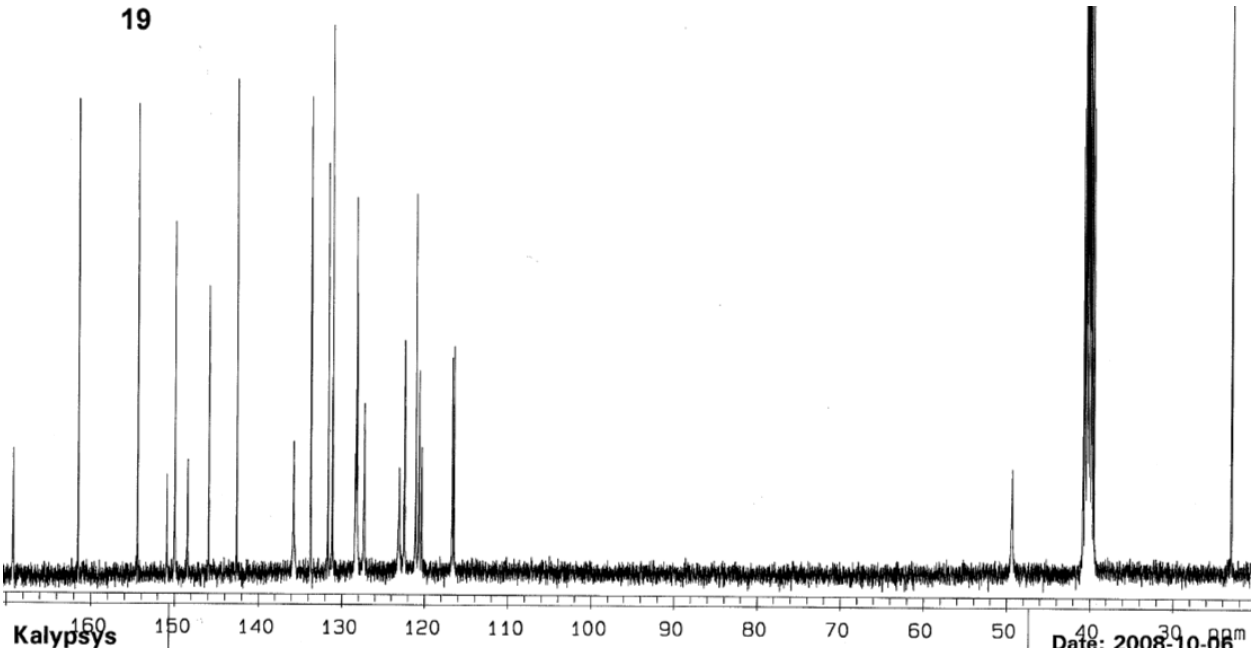
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100
```

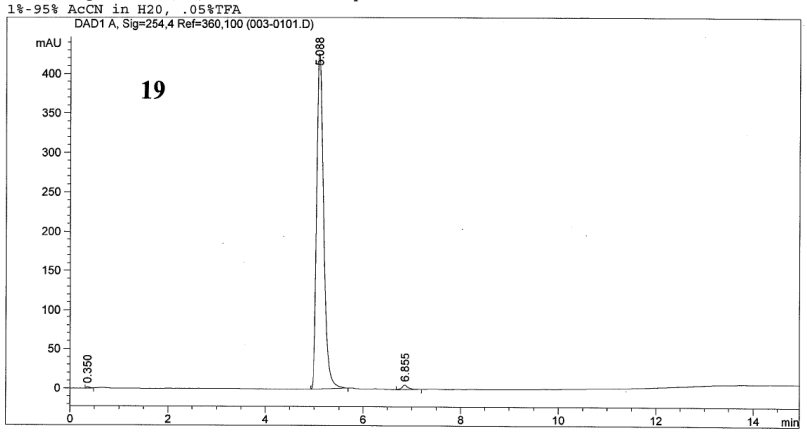
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.757	BB	0.1324	23.04755	2.67786	1.3293
2	6.140	BB	0.1267	1685.81738	191.56599	97.2305
3	6.857	BV	0.0829	10.52154	1.73202	0.6068
4	6.968	VV	0.0937	9.06845	1.39767	0.5230
5	7.087	VB	0.0734	5.38075	1.02166	0.3103
Totals :				1733.83567	198.39520	

Compound 19: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-2-methylnicotinamide


19
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.94
1.01
9.59
1.00
2.05
5.27
3.98


19
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm
Kalypsys

```
======================================================================
Injection Date  : 8/21/2008 9:06:13 AM          Seq. Line :   1
Sample Name     : [redacted]                    Location : Vial 3
Acq. Operator   : 1                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/21/2008 9:05:30 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

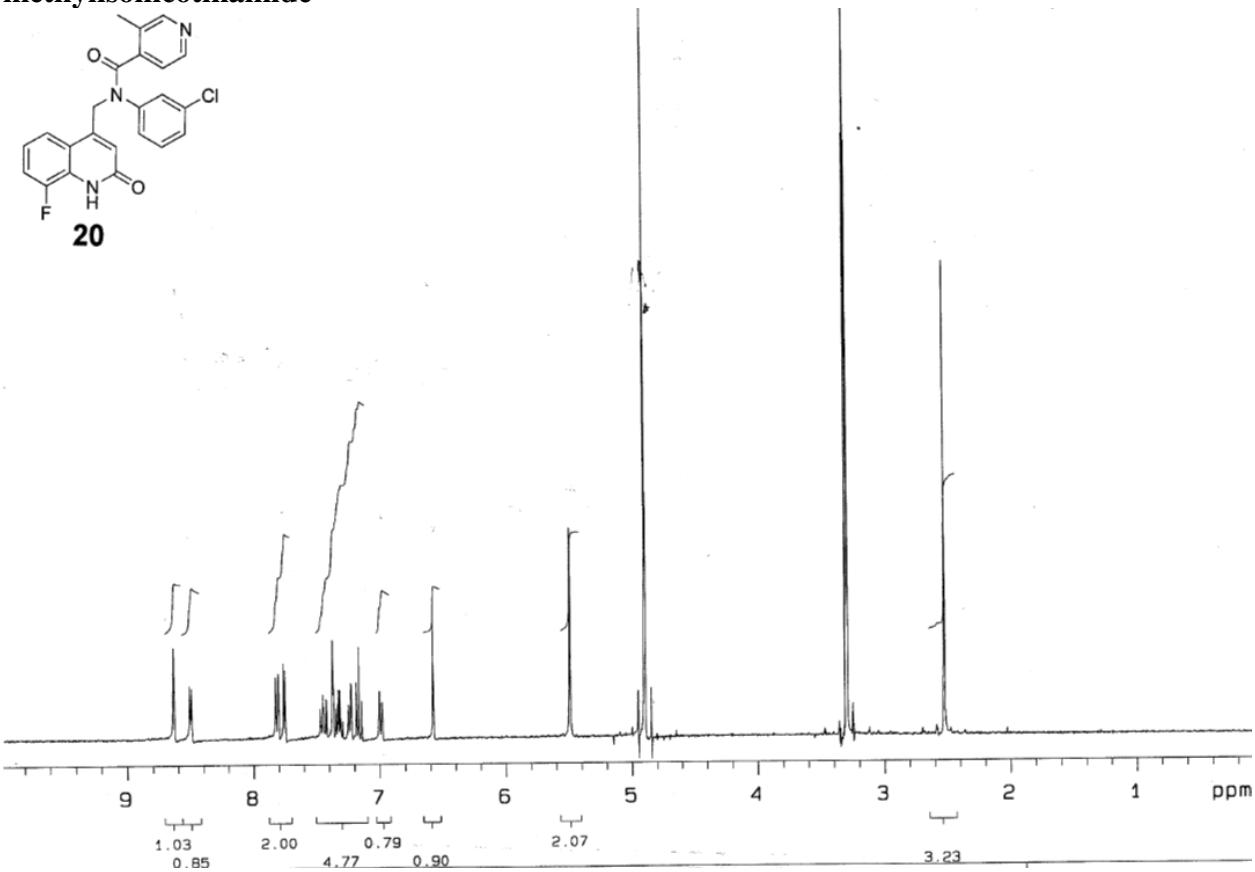

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.350 BB    0.0633    9.55625    2.01589   0.2243
   2   5.088 BB    0.1527 4193.13330  426.41476  98.3991
   3   6.855 VB    0.1300   58.66541    6.22083   1.3767

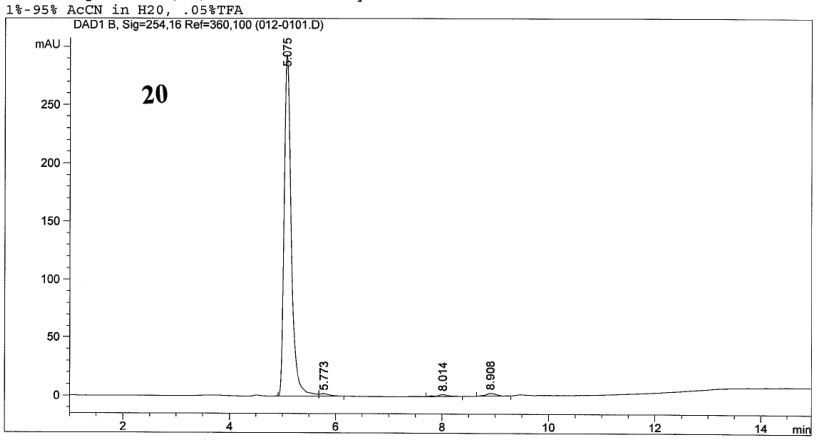
Totals :                  4261.35497  434.65149
```

Compound 20: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-3-

methylisonicotinamide




```
======================================================================
Injection Date  : 9/17/2008 3:48:29 PM          Seq. Line :   1
Sample Name     : [redacted]                    Location : Vial 12
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 3:45:51 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

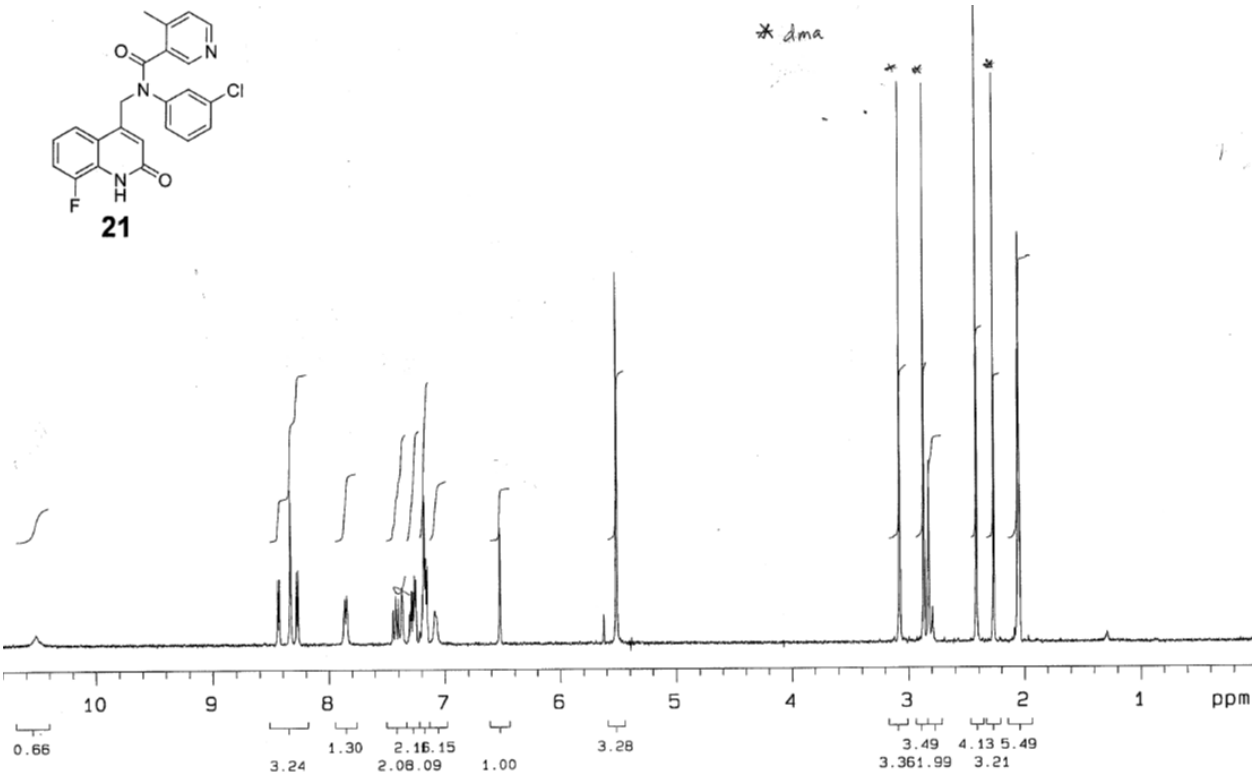
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

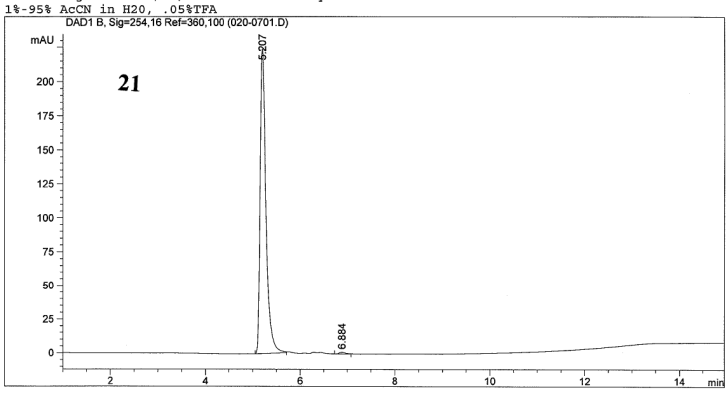
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   5.075 BV    0.1425 2732.61450  293.73938  97.0194
   2   5.773 VB    0.1941   27.88361    2.05772   0.9900
   3   8.014 BB    0.2333   25.16622    1.55136   0.8935
   4   8.908 BB    0.1801   30.89947    2.33886   1.0971

Totals :                  2816.56381  299.68731
```

Compound 21: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylnicotinamide




```
======================================================================
Injection Date  : 9/17/2008 11:27:04 AM          Seq. Line :   7
Sample Name     : K070921C                       Location : Vial 20
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20,  05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

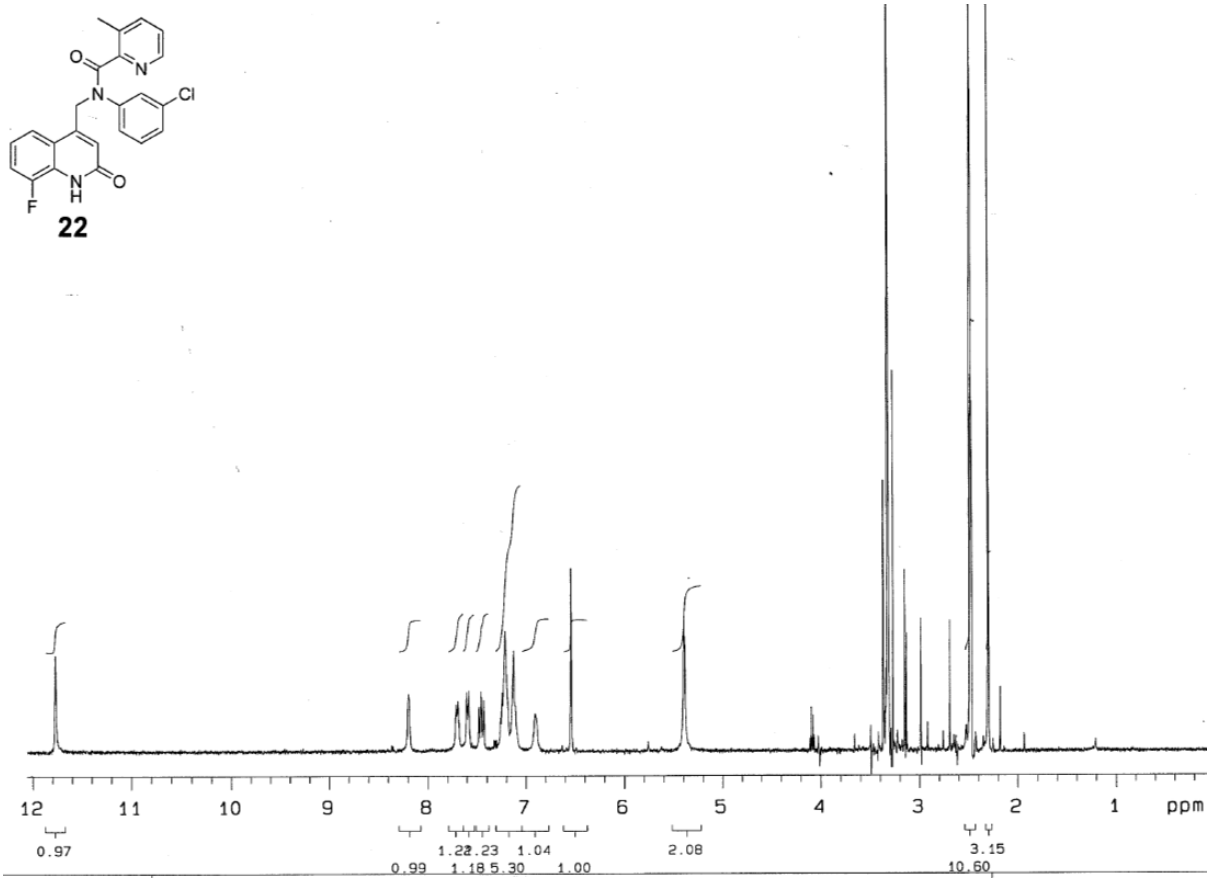
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

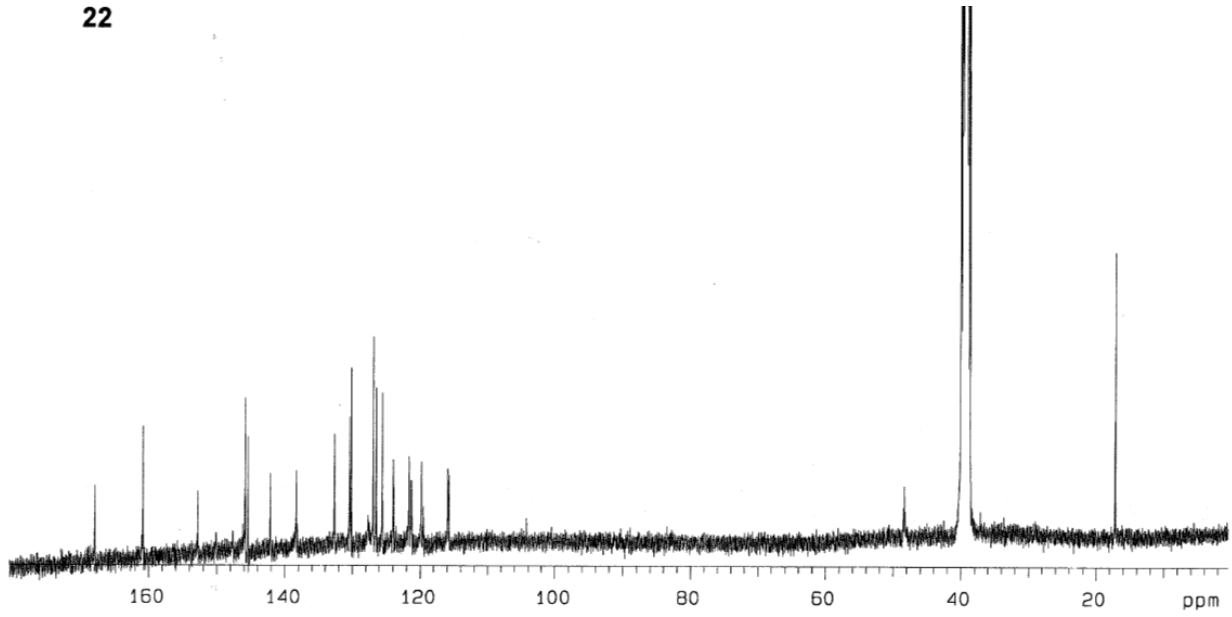

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.207 BB    0.1263 1890.65259  224.32071  99.3888
   2   6.884 BB    0.1347   11.62758    1.27117   0.6112

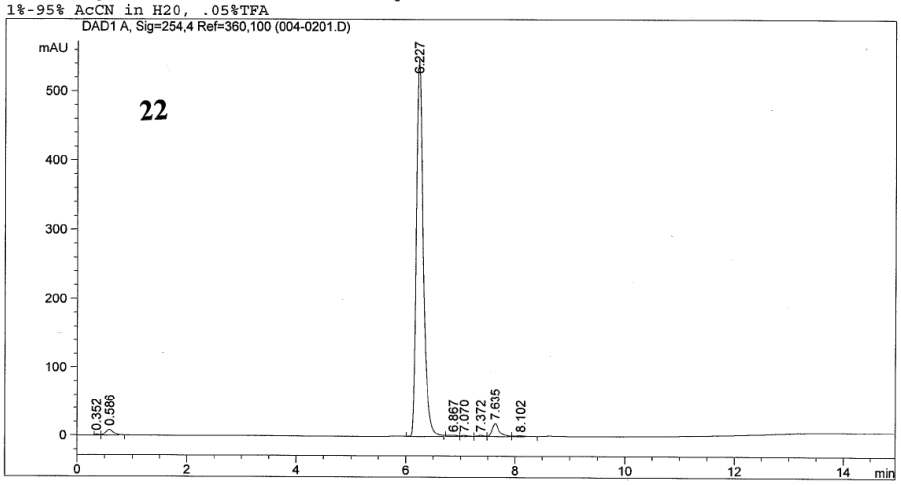
Totals :                  1902.28016  225.59188
```

Compound 22: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-3-methylpicolinamide


O
N
N
Cl
F
N
H
O
22
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.97
0.99
1.22
2.23
1.18
5.30
1.04
1.00
2.08
3.15
10.60


22
160
140
120
100
80
60
40
20
ppm

```
==================================================================
Injection Date  : 8/21/2008 9:23:22 AM          Seq. Line :   2
Sample Name     : KM-080811838                  Location : Vial 4
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/21/2008 9:05:30 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
==================================================================
                        Area Percent Report
==================================================================

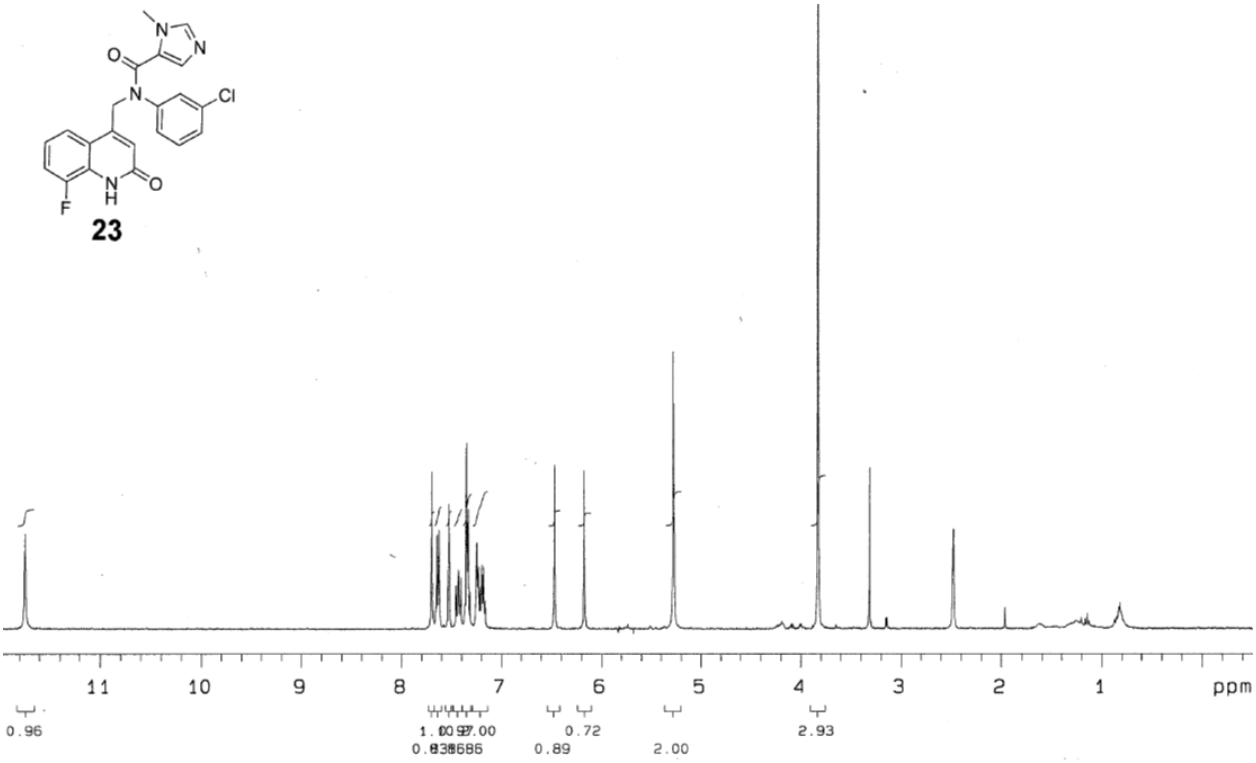
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

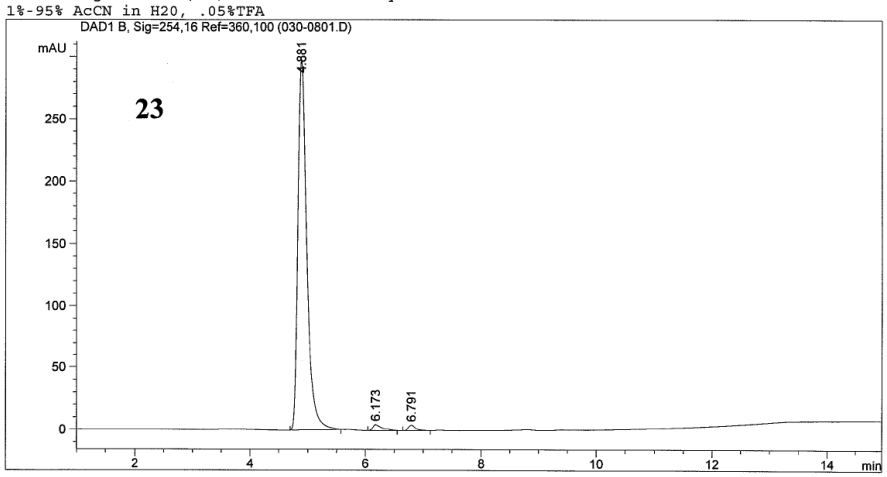
Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.352 BV   0.0612    8.59179    1.95778   0.1670
   2   0.586 VB   0.1521   86.37466    8.53455   1.6788
   3   6.227 BB   0.1323 4790.86719  546.42548  93.1151
   4   6.867 BV   0.1732   25.04912    2.01291   0.4869
   5   7.070 VV   0.1394   16.96075    1.68596   0.3296
   6   7.372 VV   0.1357   15.52606    1.71333   0.3018
   7   7.635 VB   0.1399  180.23767   19.12549   3.5031
   8   8.102 BB   0.2099   21.49721    1.30676   0.4178

Totals :                 5145.10444  582.76227
```

Compound 23: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-1-methyl-1*H*-imidazole-5-carboxamide




```
======================================================================
Injection Date  : 9/17/2008 11:44:12 AM          Seq. Line :   8
Sample Name     :                                Location : Vial 30
Acq. Operator   : 1                                  Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

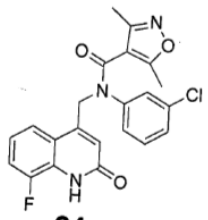
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.881 BB    0.1637 3212.71289  298.23834  97.2035
   2   6.173 BB    0.1564   54.31204    4.78523   1.6433
   3   6.791 BB    0.1327   38.11776    4.33170   1.1533

Totals :                  3305.14268  307.35527
```

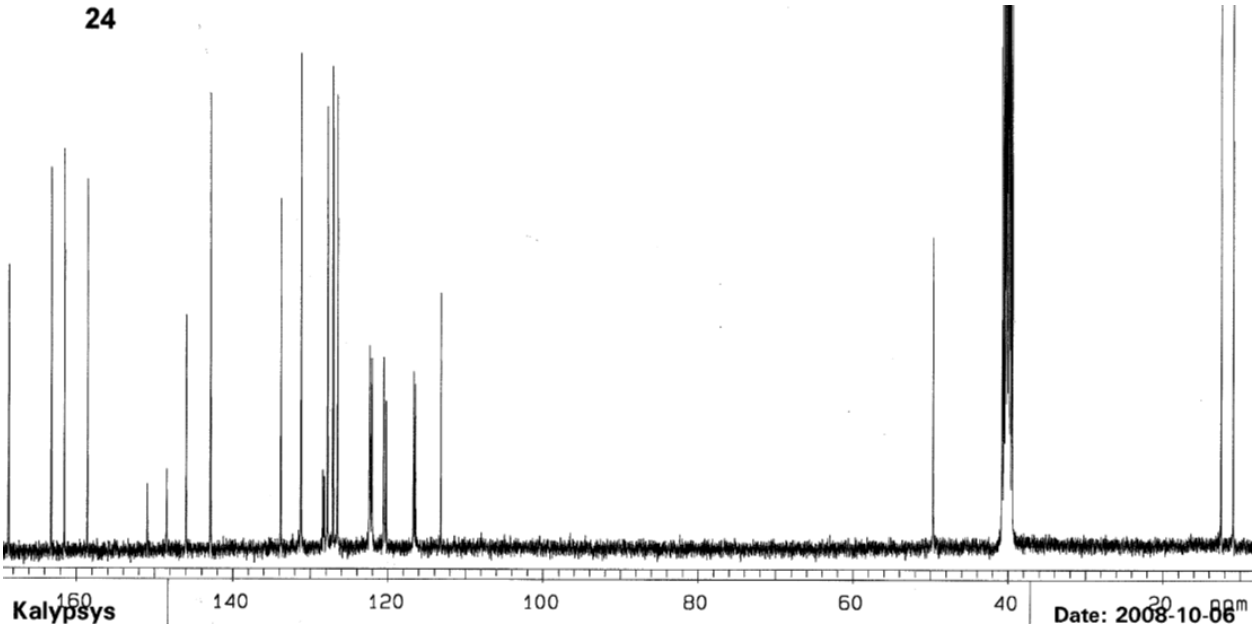
Compound 24: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-3,5-dimethylisoxazole-4-carboxamide


N
O
O
N
Cl
F
N
H
O

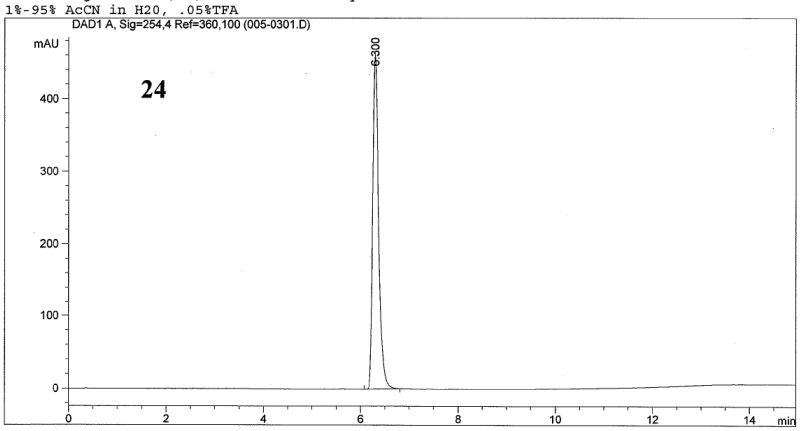
24

11
10
9
8
7
6
5
4
3
2
1
ppm
0.92
2.04 1.04
1.09 3.03
1.00
2.09
6.81
1.45
6.41

24


160
140
120
100
80
60
40
20
ppm
Kalypsys
Date: 2008-10-06

```
==========================================================================
Injection Date  : 8/21/2008 9:40:27 AM          Seq. Line :   3
Sample Name     : KLYP[illegible]103                Location : Vial 5
Acq. Operator   : 1                                    Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/21/2008 9:05:30 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                        Area Percent Report
==========================================================================

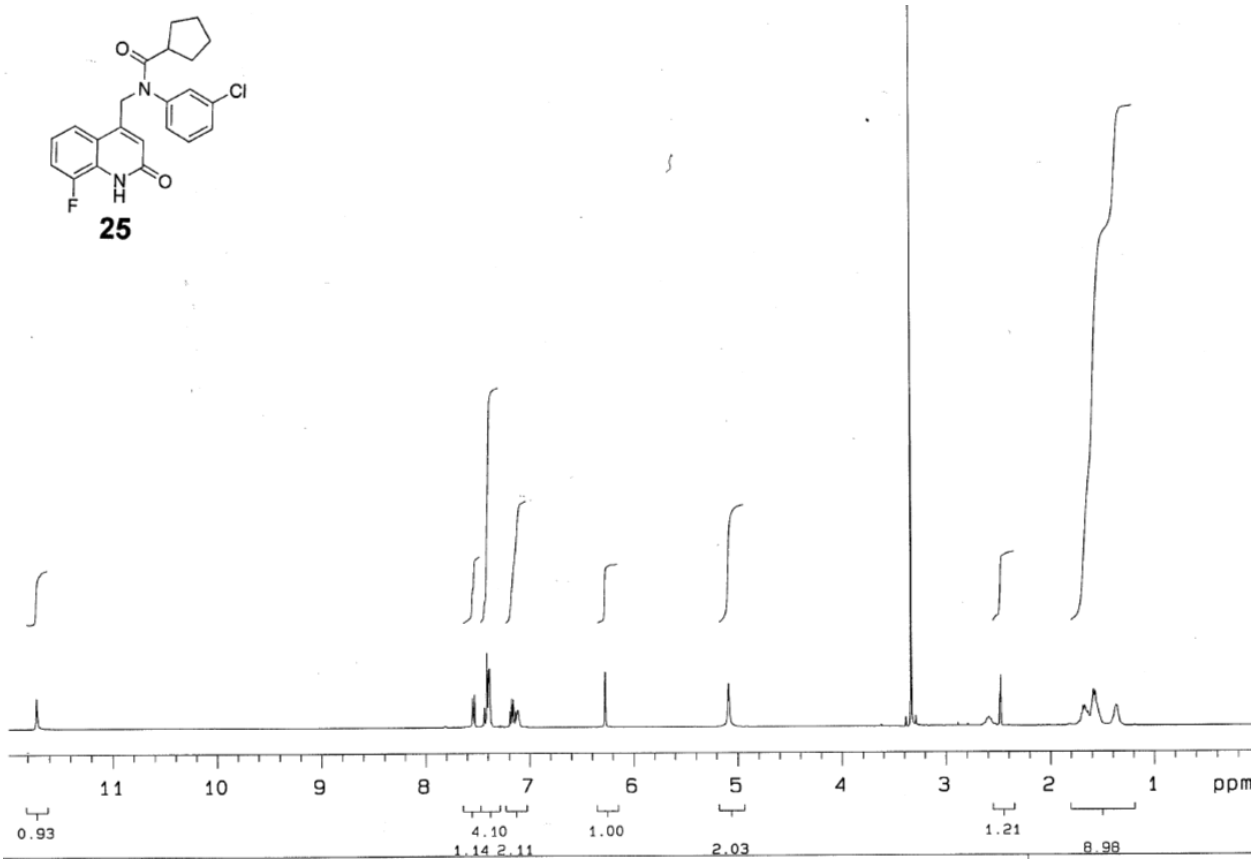
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

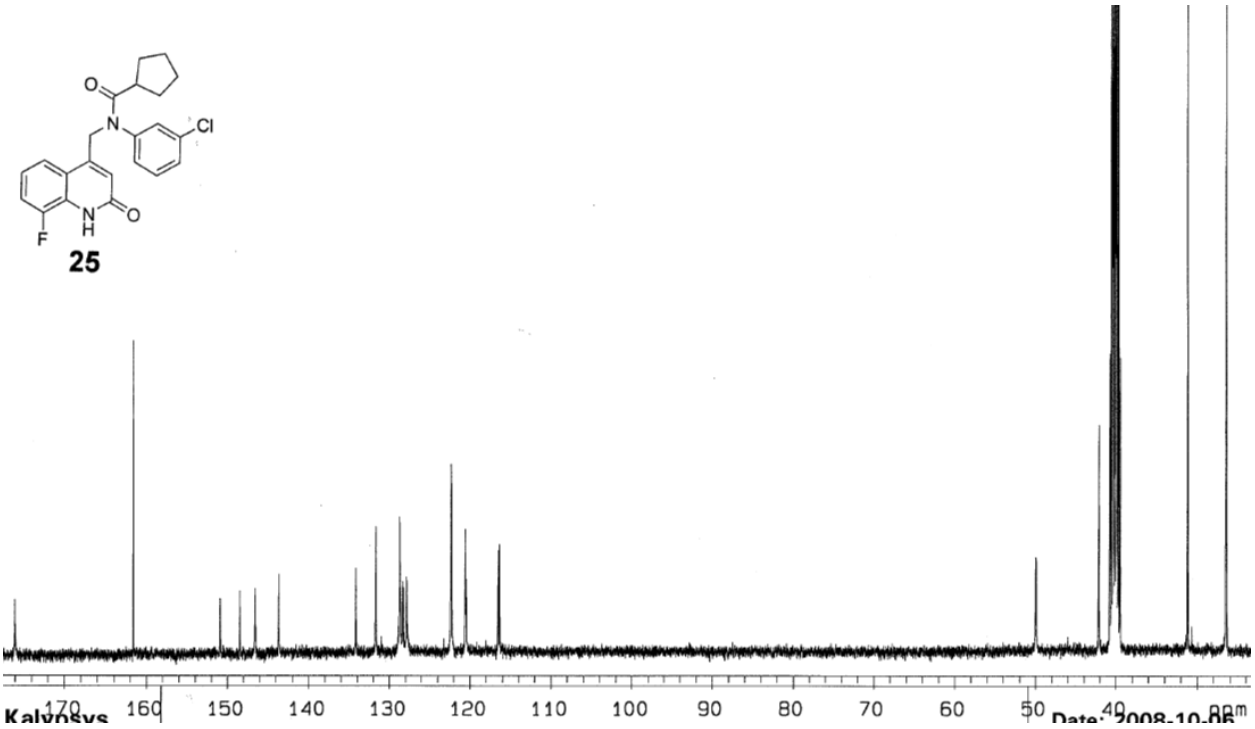

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.300 BB     0.1308 3914.82495  462.19650 100.0000

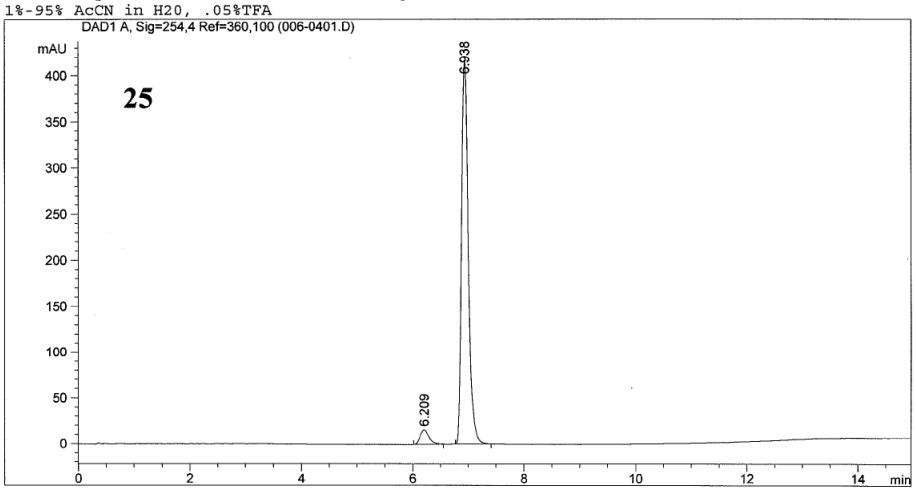
Totals :                   3914.82495  462.19650
```

Compound 25: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)cyclopentanecarboxamide






```
======================================================================
Injection Date  : 8/21/2008 9:57:31 AM          Seq. Line :   4
Sample Name     :                                Location : Vial 6
Acq. Operator   : 1                                  Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/21/2008 9:05:30 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

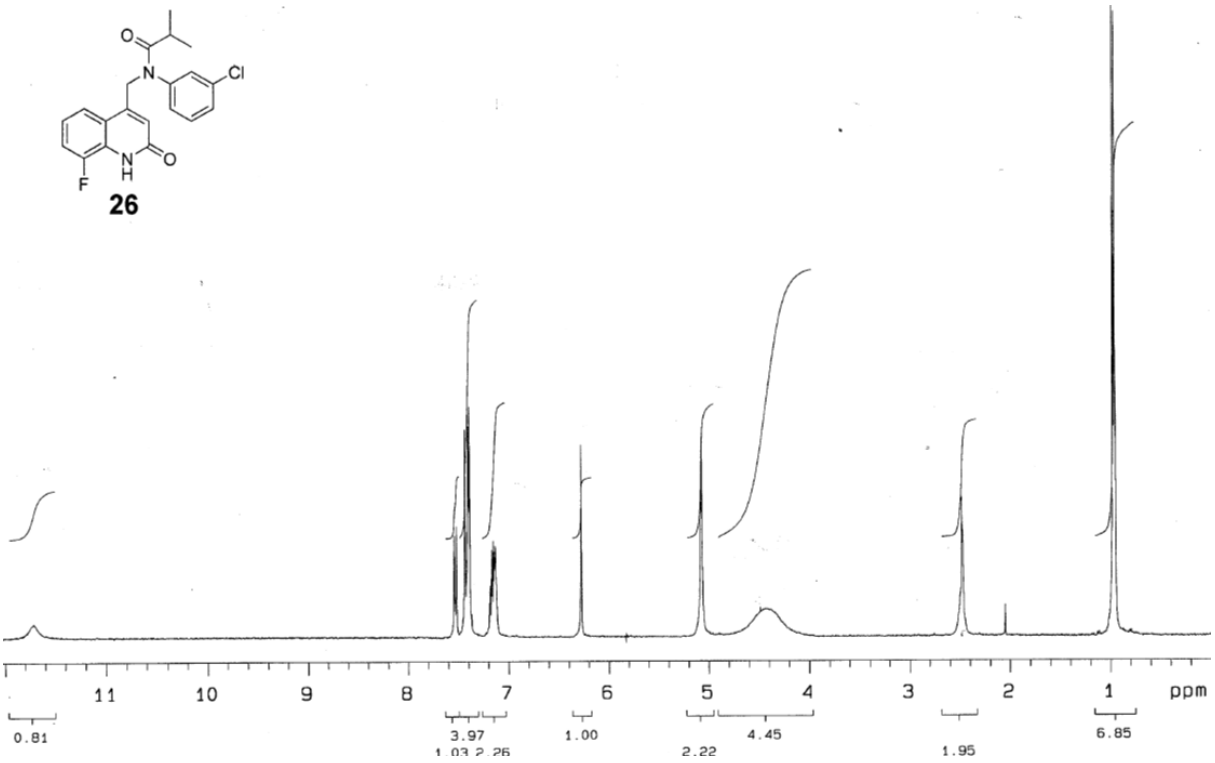
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

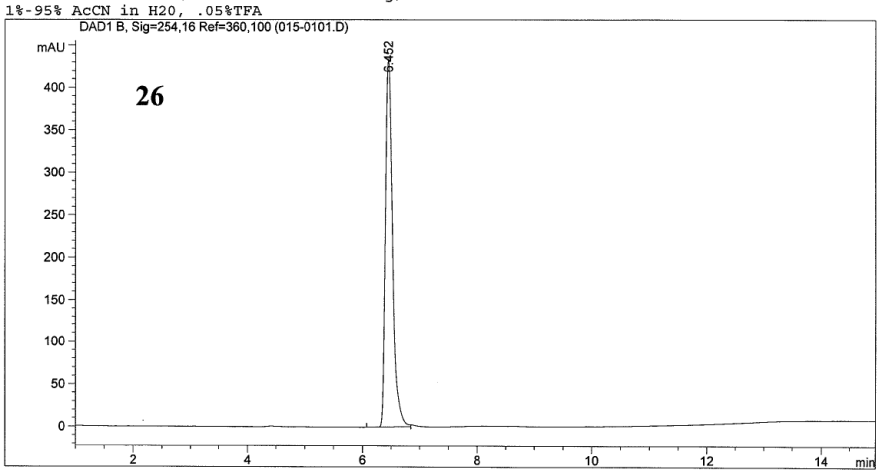
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.209 BB    0.1766  175.76521   15.46430   4.7737
   2   6.938 BB    0.1320 3506.20996  417.41055  95.2263

Totals :                   3681.97517  432.87486
```

Compound 26: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)isobutyramide




```
======================================================================
Injection Date  : 9/16/2008 4:41:40 PM          Seq. Line :   1
Sample Name     : Klyp930041                    Location : Vial 15
Acq. Operator   : 1                               Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/16/2008 4:40:41 PM by 1
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

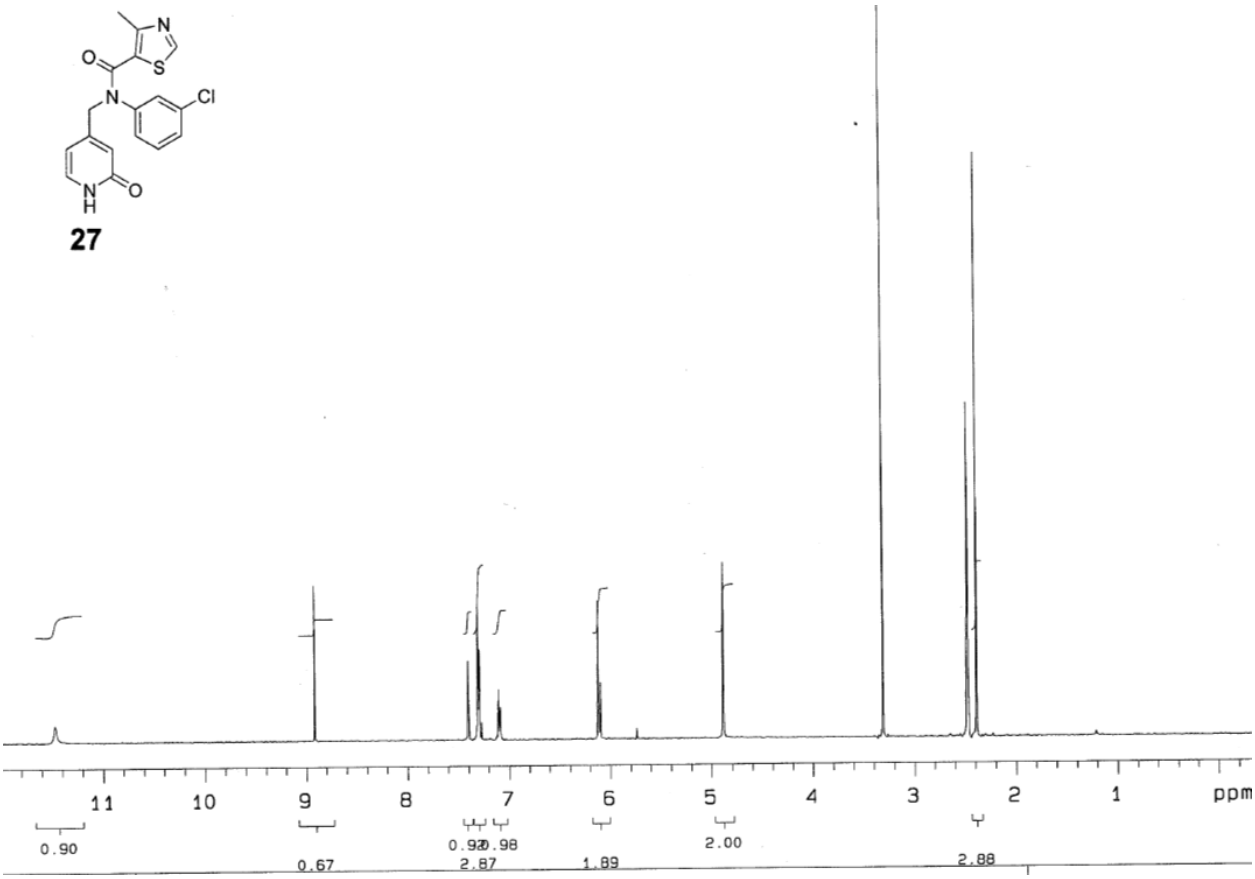
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

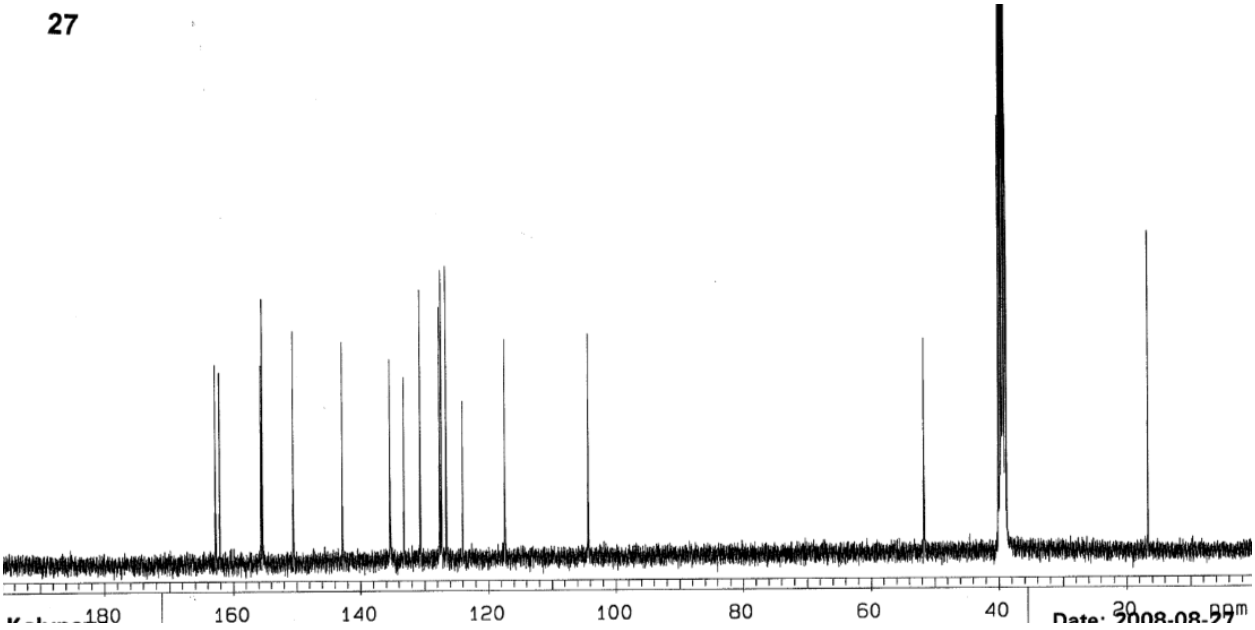

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.452 BB    0.1345 3737.32983  433.85001 100.0000

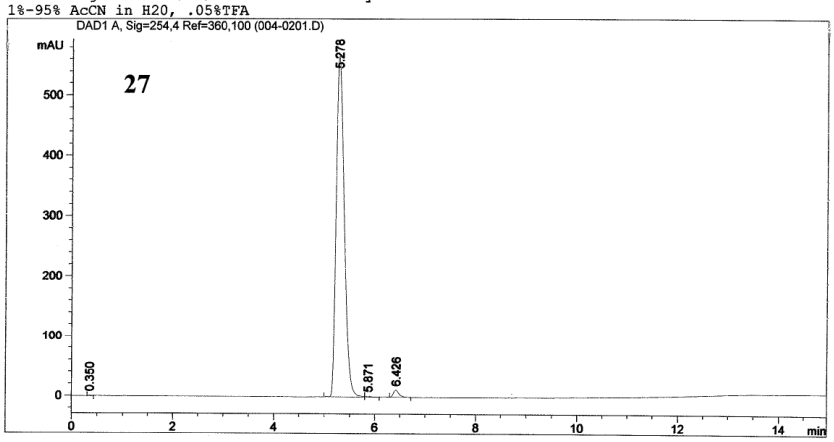
Totals :                  3737.32983  433.85001
```

Compound 27: *N*-(3-Chlorophenyl)-4-methyl-*N*-((2-oxo-1,2-dihydropyridin-4-yl)methyl)thiazole-5-carboxamide





```
Injection Date  : 8/14/2008 3:51:00 PM          Seq. Line :   2
Sample Name     : [illegible]                   Location : Vial 4
Acq. Operator   : /                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 3:32:58 PM by 7
1%-95% AcCN in H20, .05%TFA
```




```
                          Area Percent Report

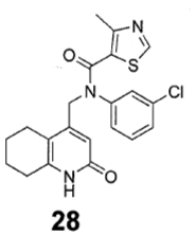
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

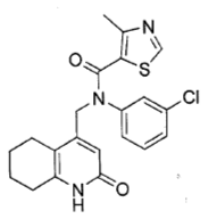
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
-----|--------|----|-------|----------|----------|--------|
   1   0.350 BB    0.0535    5.19504    1.39454   0.0821
   2   5.278 BV    0.1701 6213.00684  565.70599  98.1694
   3   5.871 VV    0.1339   15.86114    1.65419   0.2506
   4   6.426 VB    0.1200   94.80267   12.02695   1.4979

Totals :                  6328.86569  580.78168
```

Compound 28: *N*-(3-Chlorophenyl)-4-methyl-*N*-((2-oxo-1,2,5,6,7,8-hexahydroquinolin-4-yl)methyl)thiazole-5-carboxamide

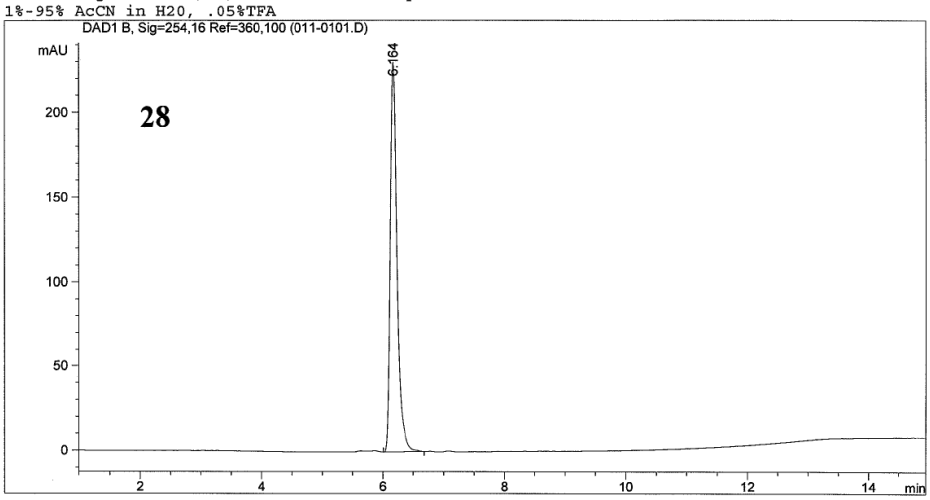


28



28


```
======================================================================
Injection Date  : 9/17/2008 9:44:34 AM          Seq. Line :   1
Sample Name     : klyp930748                     Location : Vial 11
Acq. Operator   : 1                                  Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

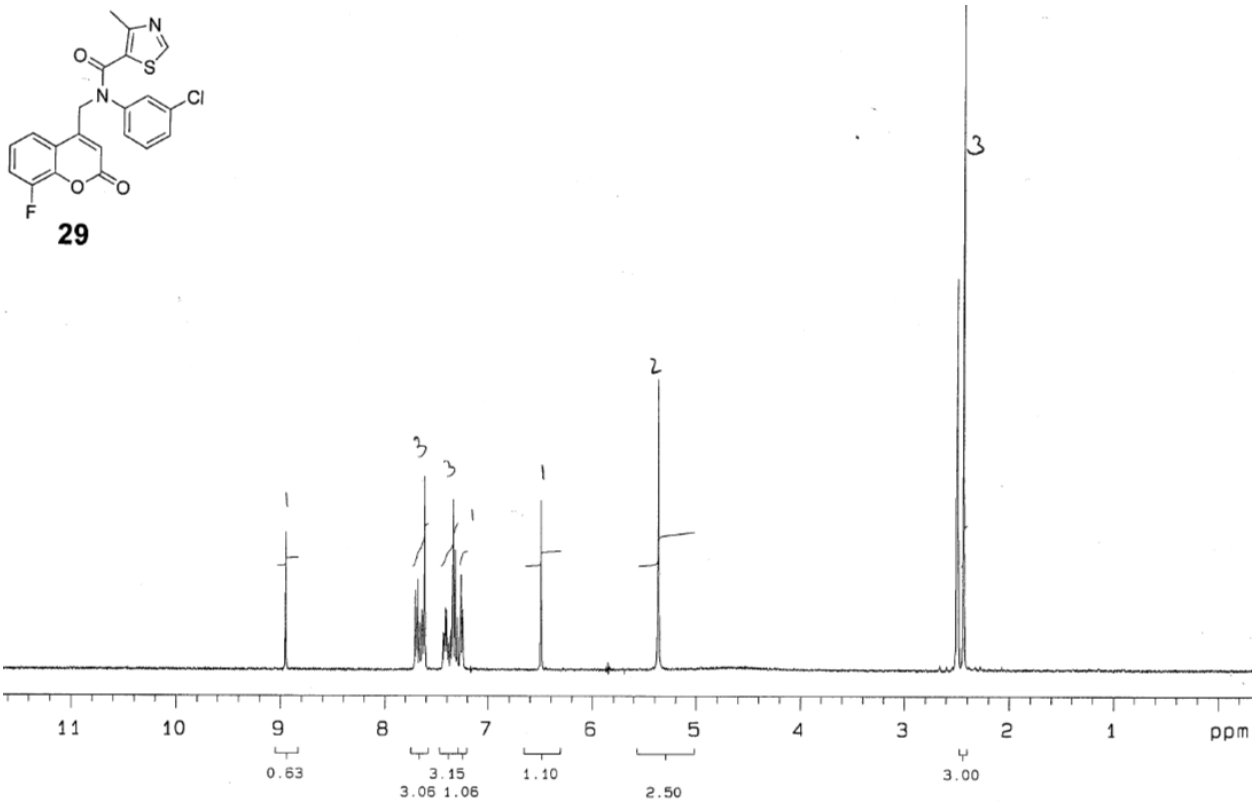
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

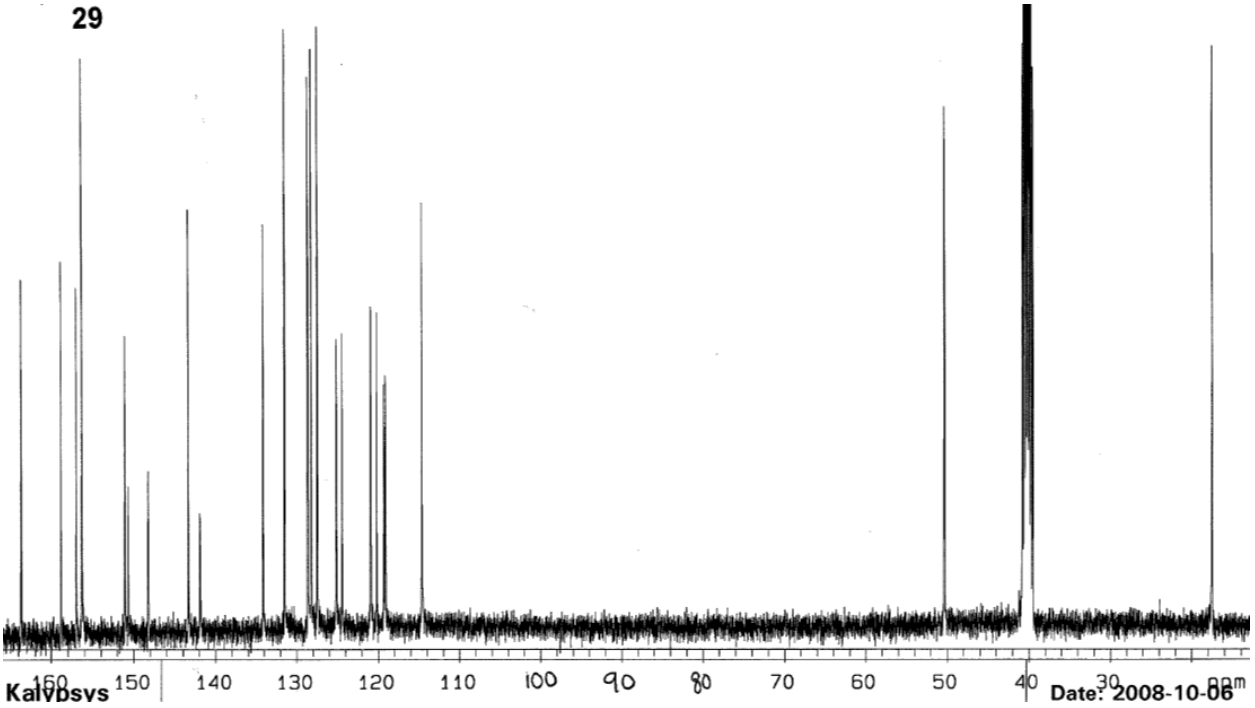

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.164 VB    0.1144 1747.68481  230.53638 100.0000

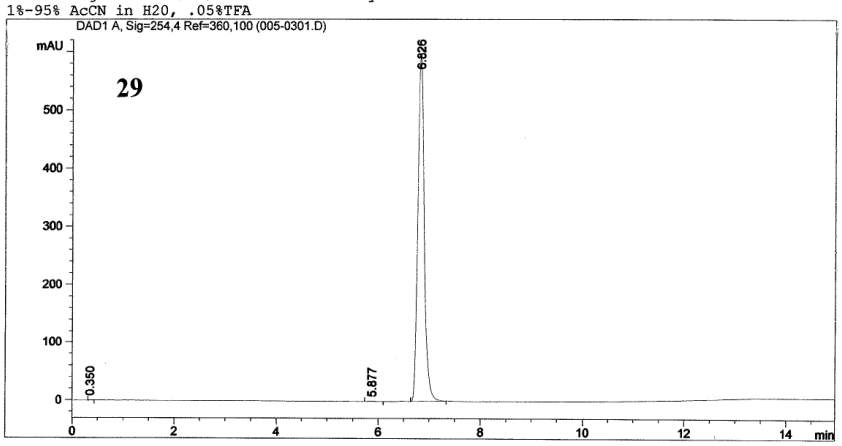
Totals :                  1747.68481  230.53638
```

Compound 29: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-oxo-2*H*-chromen-4-yl)methyl)-5-methylthiazole-4-carboxamide





```
==========================================================================
Injection Date  : 8/14/2008 4:08:06 PM          Seq. Line :   3
Sample Name     : KLYE009086r                   Location : Vial 5
Acq. Operator   : 7                                Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 3:32:58 PM by 7
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                          Area Percent Report
==========================================================================

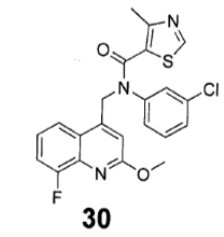
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.350 BB    0.0534    5.40977    1.38898   0.0985
   2   5.877 BB    0.1149    9.61642    1.15747   0.1751
   3   6.826 VB    0.1438 5477.54199  592.62488  99.7264

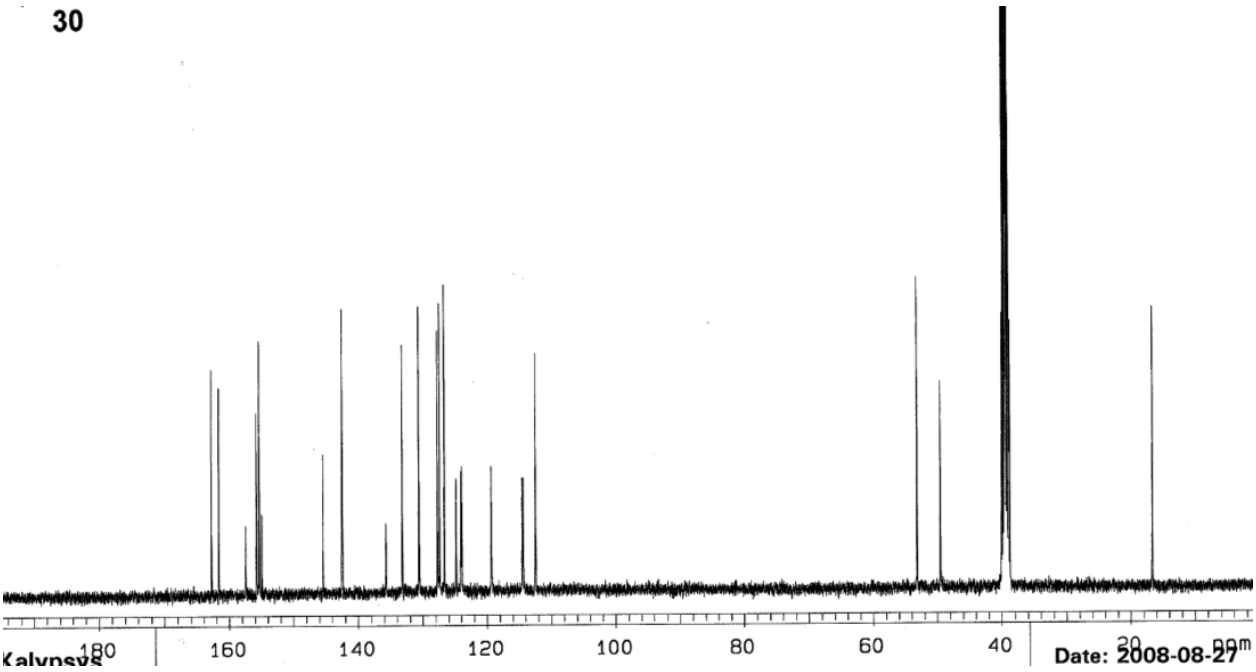
Totals :                   5492.56818  595.17133
```

Compound 30: *N*-(3-Chlorophenyl)-*N*-((8-fluoro-2-methoxyquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide

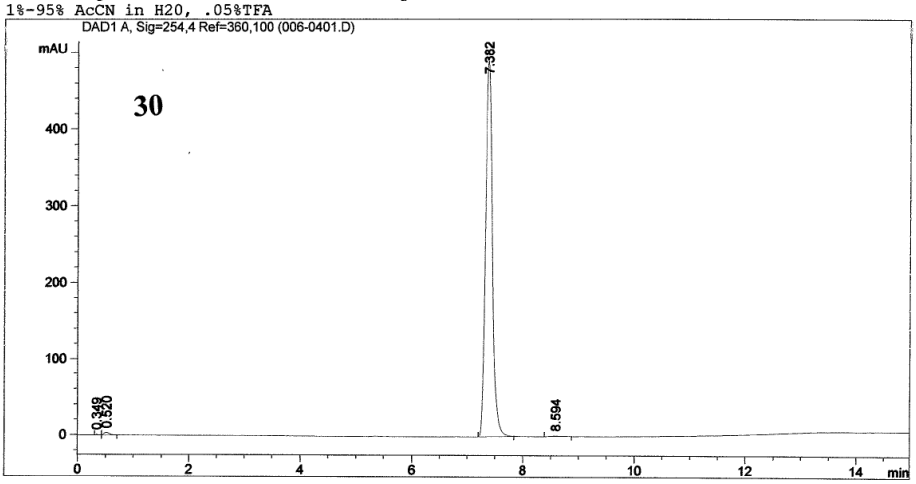


30

30




```
========================================================================
Injection Date  : 8/14/2008 4:25:10 PM          Seq. Line :   4
Sample Name     : [illegible]                    Location : Vial 6
Acq. Operator   : 7                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 3:32:58 PM by 7
1%-95% AcCN in H20, .05%TFA
```




```
========================================================================
                        Area Percent Report
========================================================================

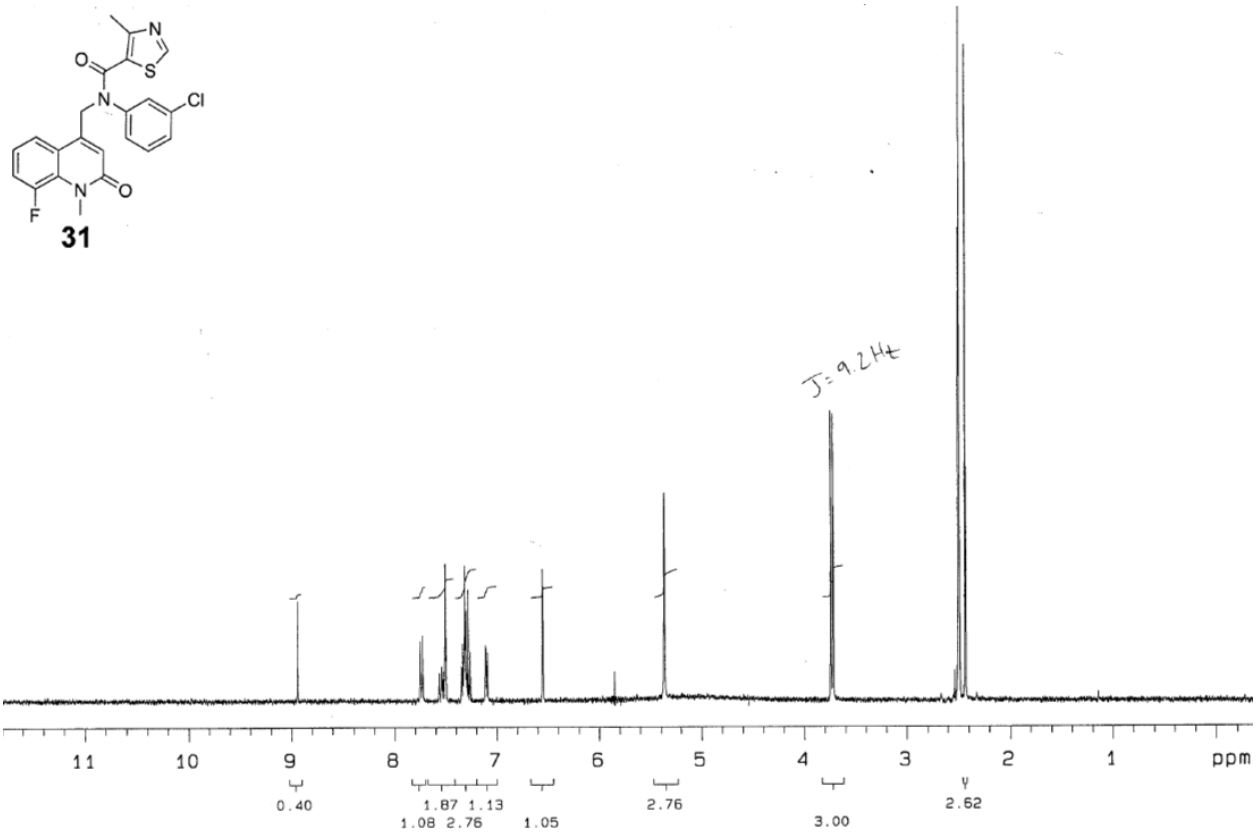
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

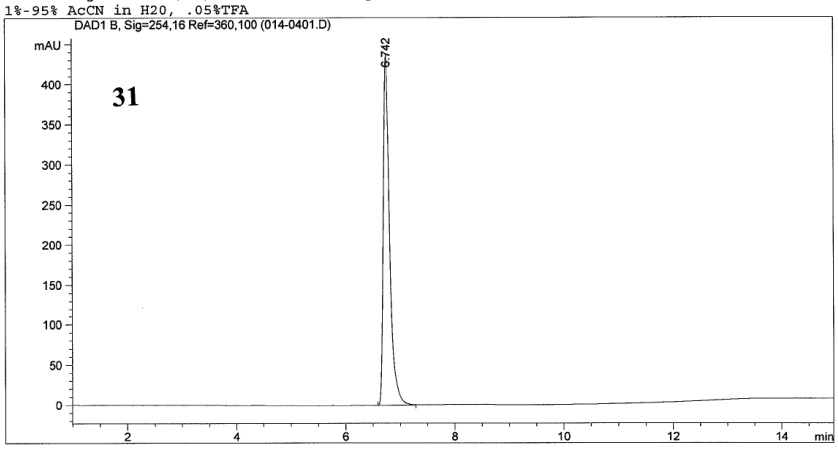
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.349 BV    0.0527    5.65914    1.47844   0.1282
   2   0.520 VB    0.1057   25.36127    3.53634   0.5743
   3   7.382 BB    0.1398 4368.42920  490.92468  98.9293
   4   8.594 BB    0.1743   16.26006    1.21402   0.3682

Totals :                  4415.70966  497.15347
```

Compound 31: *N*-(3-chlorophenyl)-*N*-((8-fluoro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide




```
======================================================================
Injection Date  : 9/17/2008 10:35:48 AM          Seq. Line :   4
Sample Name     : [illegible]                    Location : Vial 14
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                      Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

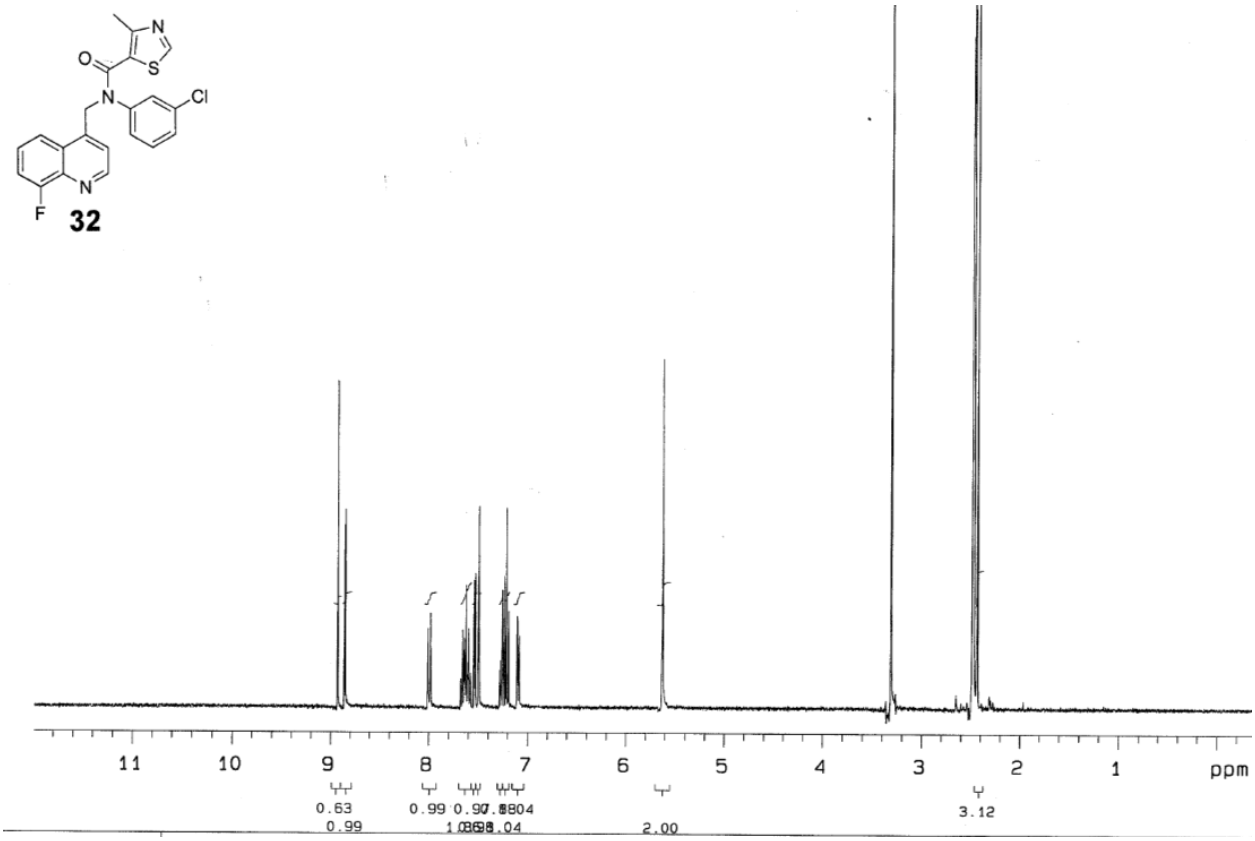
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

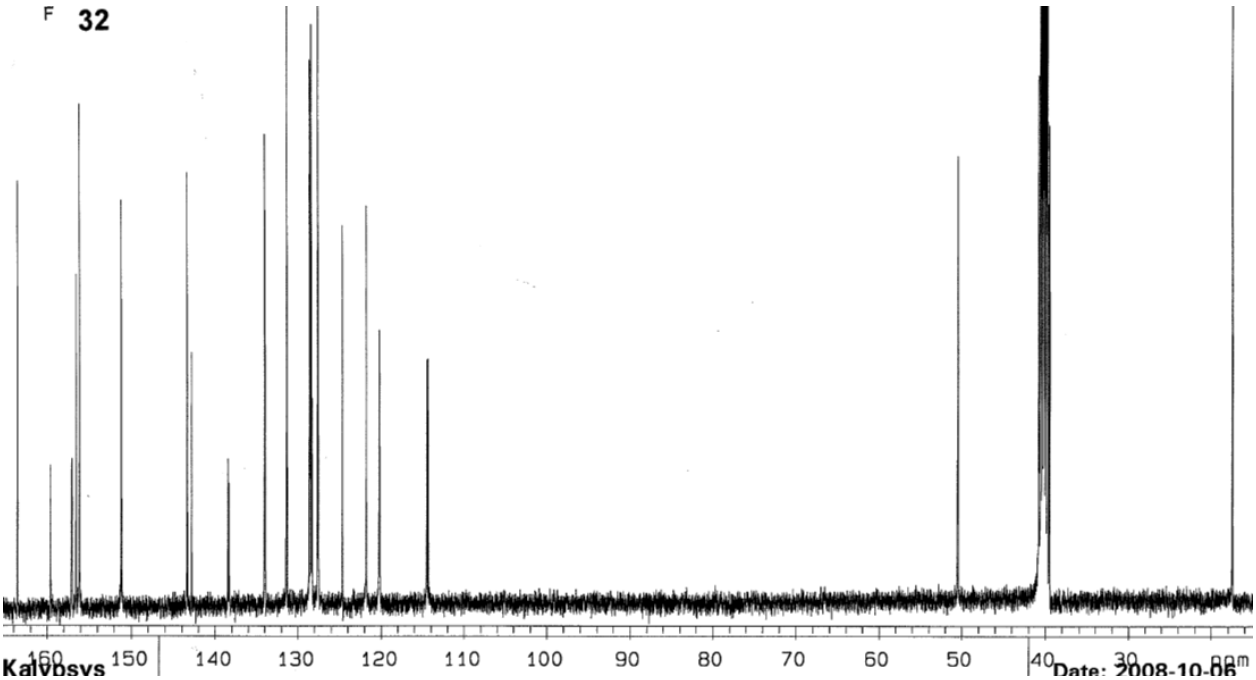

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.742 BB    0.1259 3586.06836  436.33945 100.0000

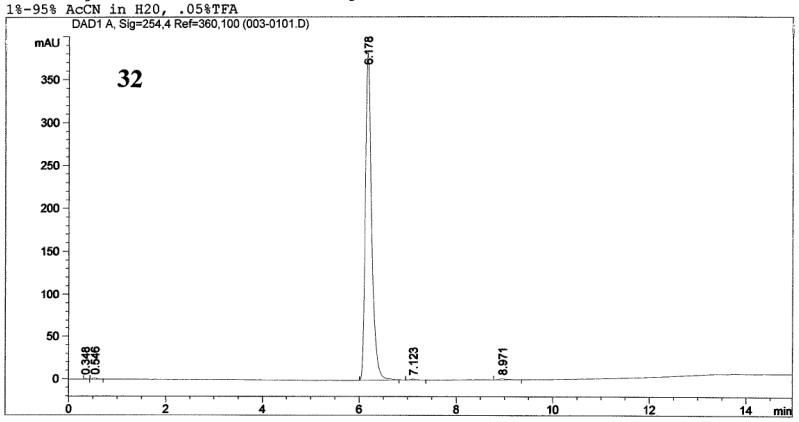
Totals :                  3586.06836  436.33945
```

Compound 32: *N*-(3-Chlorophenyl)-*N*-((8-fluoroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
Injection Date  : 8/14/2008 3:33:52 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 3
Acq. Operator   : 7                                Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 3:32:58 PM by 7
1%-95% AcCN in H20, .05%TFA
```




```
                          Area Percent Report

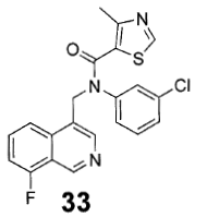
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

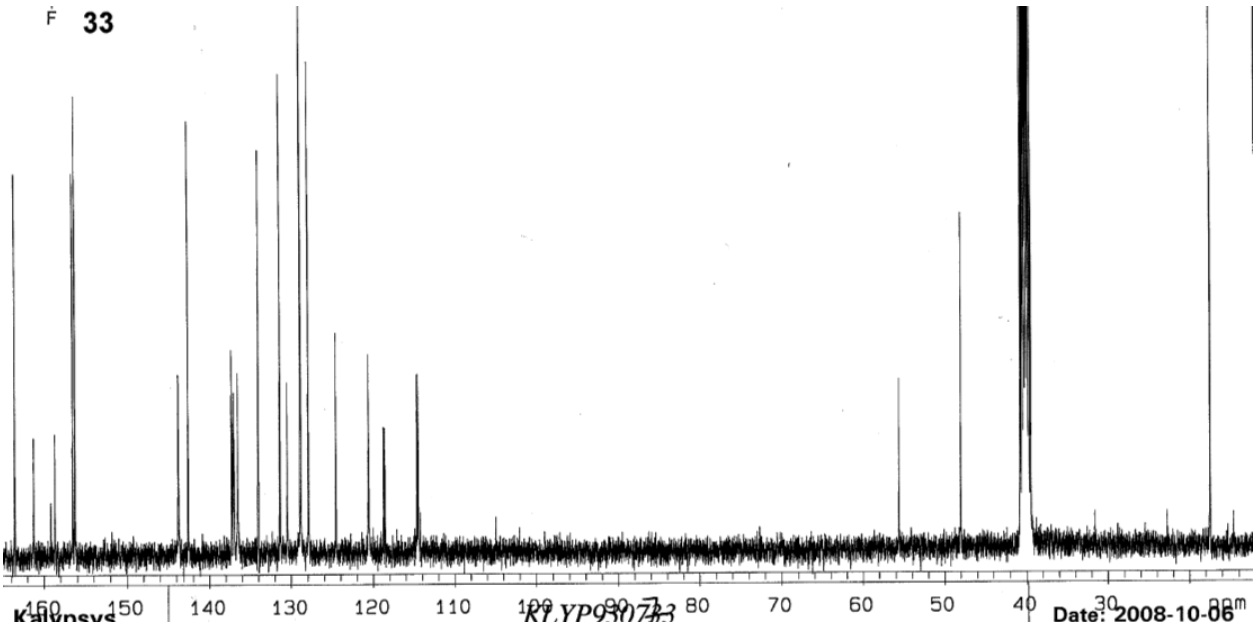
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.348 BB    0.0559    5.04605    1.23030   0.1418
   2   0.546 BB    0.1076   10.31966    1.34320   0.2899
   3   6.178 BB    0.1393 3518.86621  382.50143  98.8519
   4   7.123 BB    0.1209    9.53856    1.22391   0.2680
   5   8.971 BB    0.1785   15.96533    1.14651   0.4485

Totals :                   3559.73581  387.44535
```

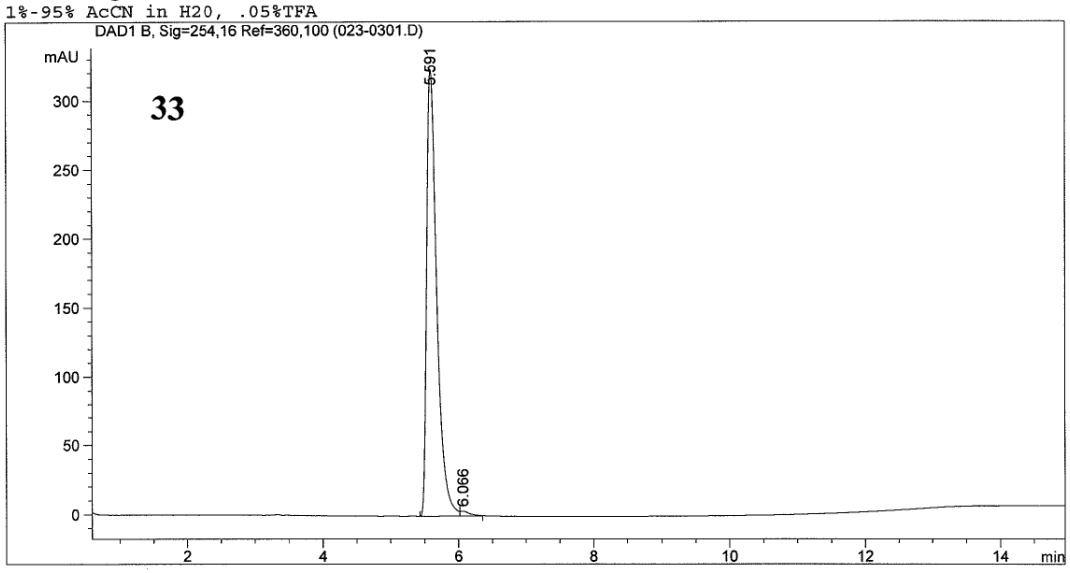
Compound 33: *N*-(3-Chlorophenyl)-*N*-((8-fluoroisoquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide



33




```
==========================================================================
Injection Date  : 10/1/2008 4:44:33 PM          Seq. Line :   3
Sample Name     : [redacted]                    Location : Vial 23
Acq. Operator   : 1                                Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/1/2008 4:09:37 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                        Area Percent Report
==========================================================================

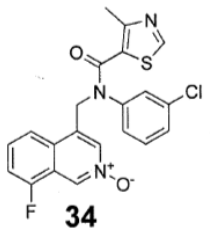
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

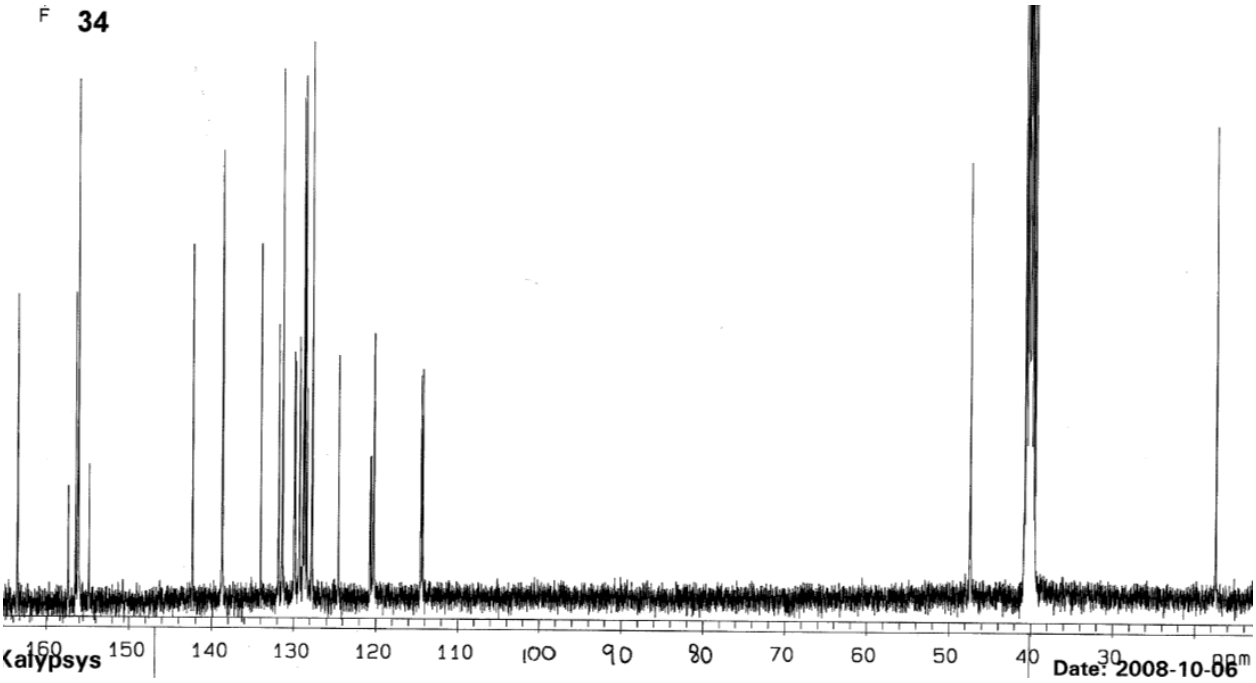
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.591 BV    0.1579 3324.59595  323.44287  98.9476
   2   6.066 VB    0.1395   35.35905    3.57165   1.0524

Totals :                  3359.95499  327.01452
```

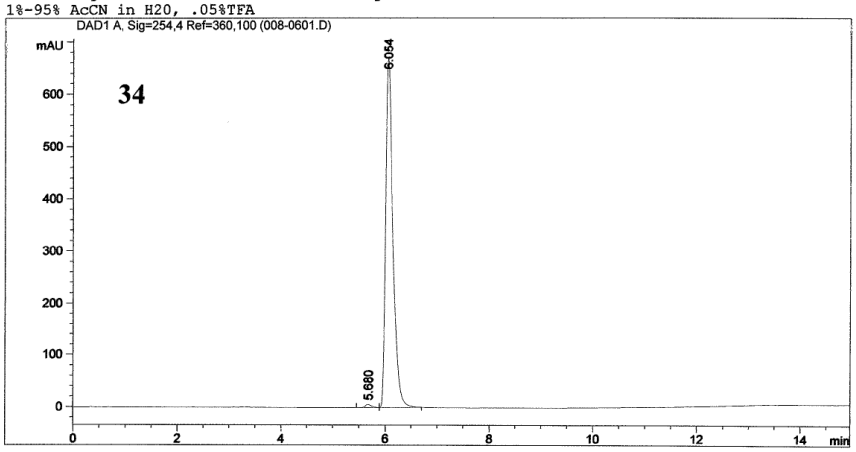
Compound 34: 4-((*N*-(3-Chlorophenyl)-4-methylthiazole-5-carboxamido)methyl)-8-fluoroisoquinoline 2-oxide



34



```
================================================================================
Injection Date  : 8/14/2008 4:59:20 PM          Seq. Line :   6
Sample Name     :                               Location : Vial 8
Acq. Operator   : 7                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 3:32:58 PM by 7
1%-95% AcCN in H20, .05%TFA
```




```
================================================================================
                              Area Percent Report
================================================================================

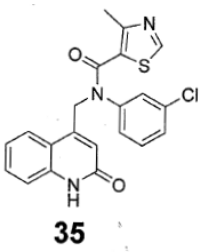
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.680 BV    0.1255   53.81546    6.30801   0.7916
   2   6.054 VB    0.1509 6744.15088  672.89453  99.2084

Totals :                   6797.96634  679.20254
```

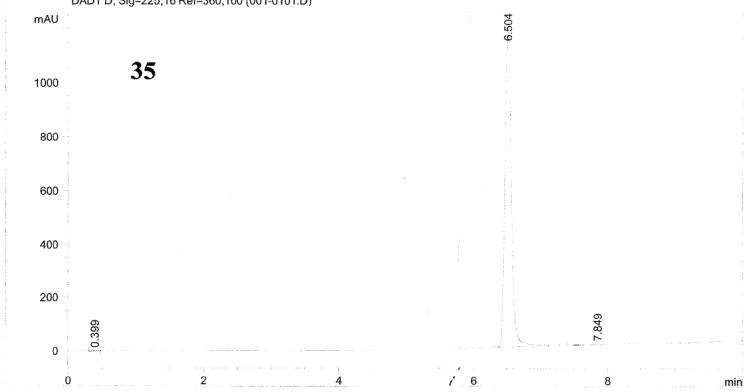
Compound 35: *N*-(3-chlorophenyl)-4-methyl-*N*-((2-oxo-1,2-dihydroquinolin-4-yl)methyl)thiazole-5-carboxamide



35

```
Injection Date  : 12/20/2007 10:05:19 AM          Seq. Line :   1
Sample Name     : [illegible]                     Location : Vial 1
Acq. Operator   : 14                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 2 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF LC2.S
Method          : C:\CHEM32\1\METHODS\1-95 LC.M
Last changed    : 12/20/2007 10:02:24 AM by 14
1%-95% AcCN in H20, .05%TFA
```

DAD1 D, Sig=225,16 Ref=360,100 (001-0101.D)



Area Percent Report

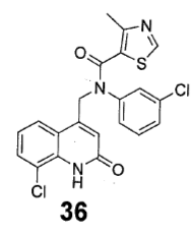
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=225,16 Ref=360,100

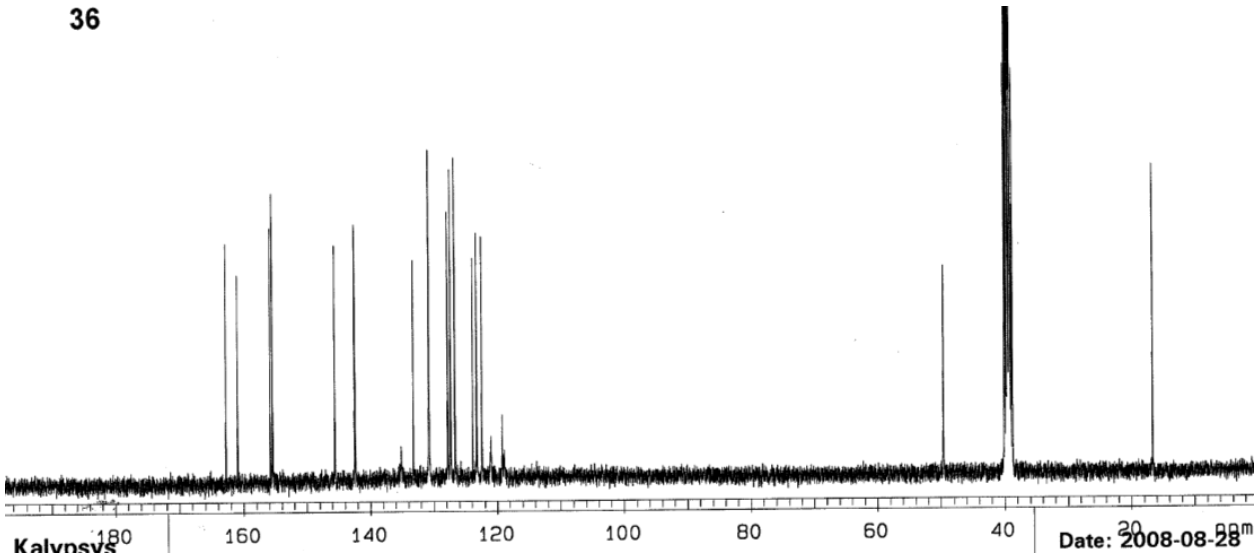
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.399 BB    0.0631    7.58044    1.66403   0.0924
   2   6.504 VB    0.1080 8110.57080 1182.15222  98.8637
   3   7.849 BV    0.2657   85.64225    4.54814   1.0439

Totals :                  8203.79349 1188.36439
```

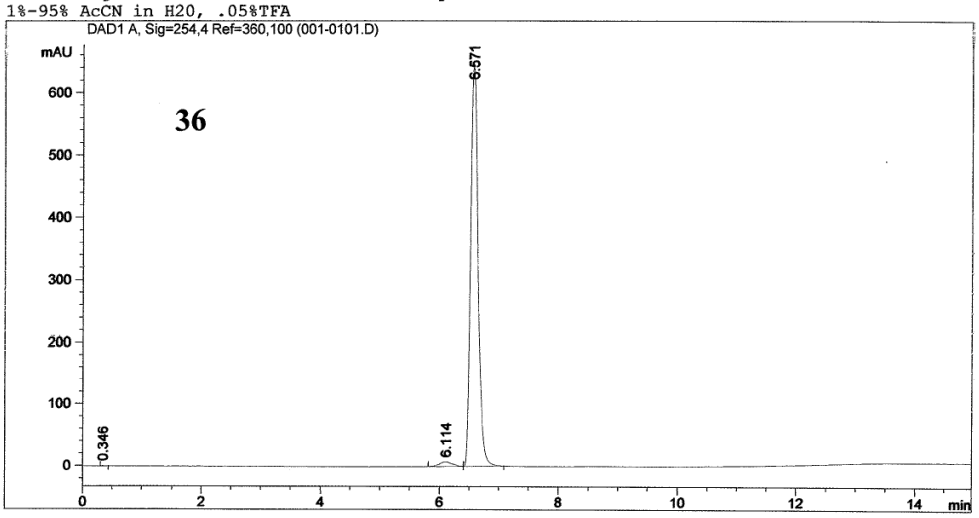
Compound 36: *N*-((8-Chloro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-*N*-(3-chlorophenyl)-4-methylthiazole-5-carboxamide



36




```
================================================================================
Injection Date  : 8/14/2008 11:29:31 AM          Seq. Line :   1
Sample Name     : [redacted]                      Location : Vial 1
Acq. Operator   : 7                                    Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/14/2008 11:28:36 AM by 7
1%-95% AcCN in H20, .05%TFA
```




```
================================================================================
                          Area Percent Report
================================================================================

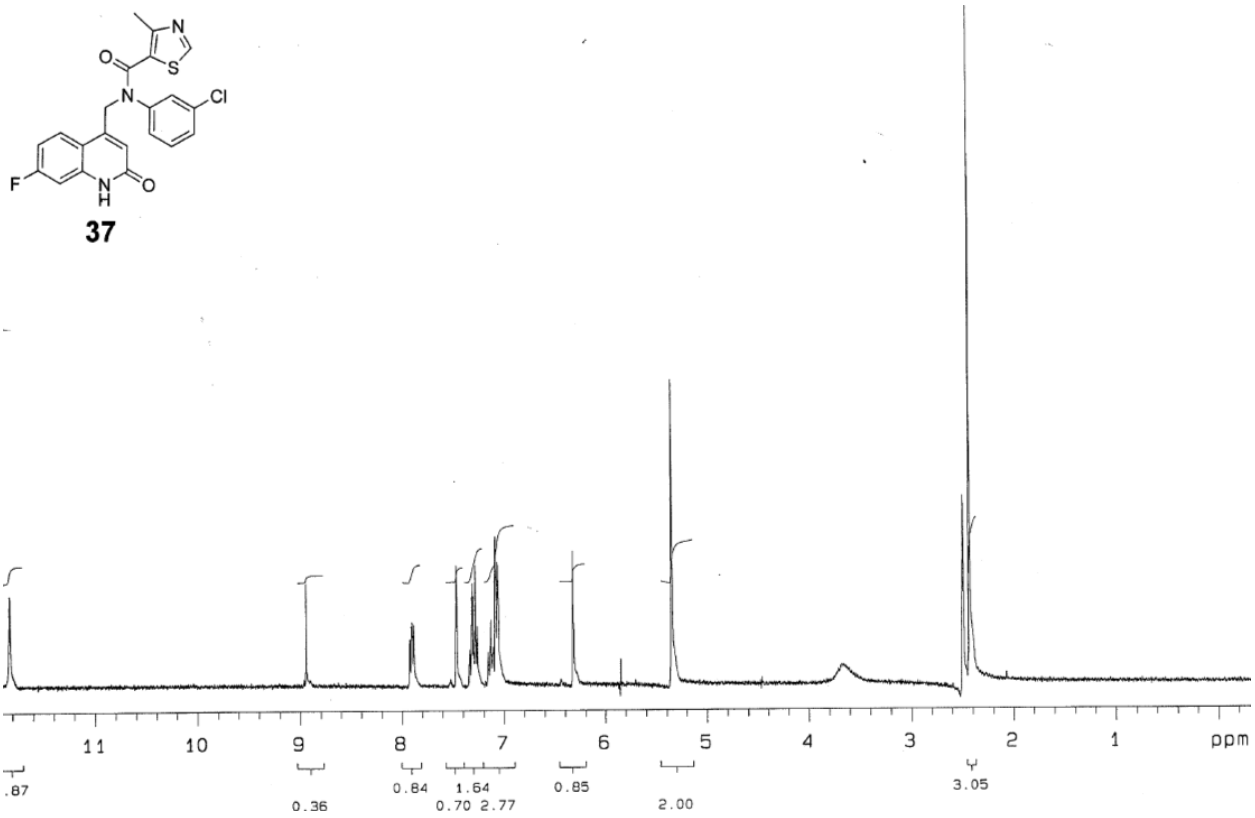
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

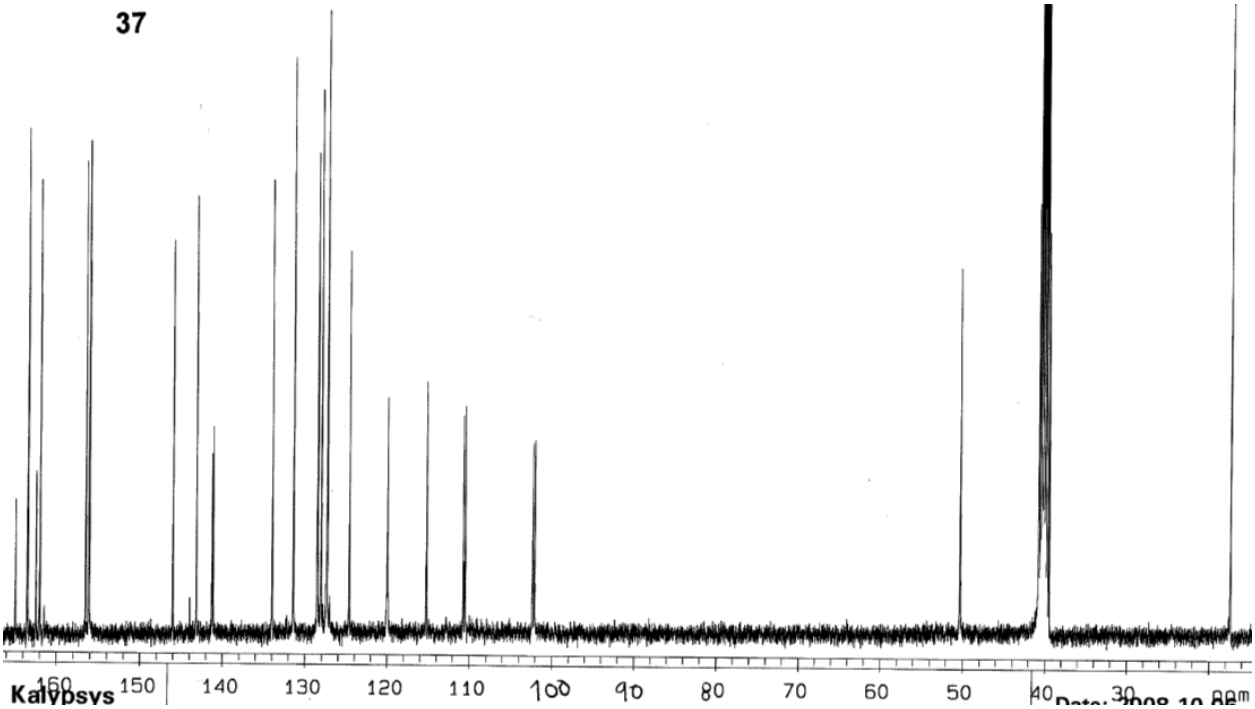

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.346 BB    0.0540    5.09558    1.29184   0.0870
   2   6.114 BV    0.2265  118.75190    7.50753   2.0272
   3   6.571 VB    0.1377 5734.09131  644.85773  97.8858

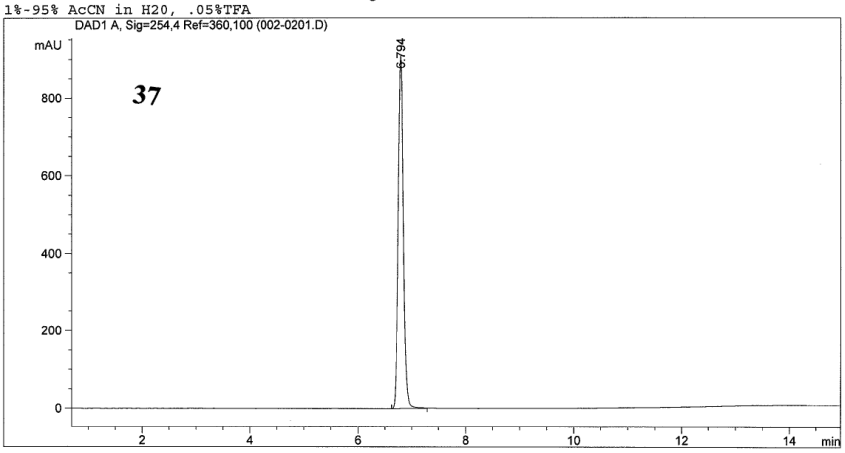
Totals :                   5857.93879  653.65710
```

Compound 37: *N*-(3-Chlorophenyl)-*N*-((7-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
==========================================================================
Injection Date  : 11/1/2007 9:00:56 AM          Seq. Line :   2
Sample Name     : KL2-0011138                   Location : Vial 2
Acq. Operator   : 14                               Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/1/2007 8:47:36 AM by 14
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```



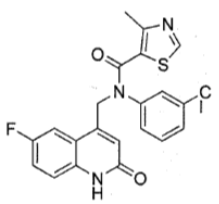

```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

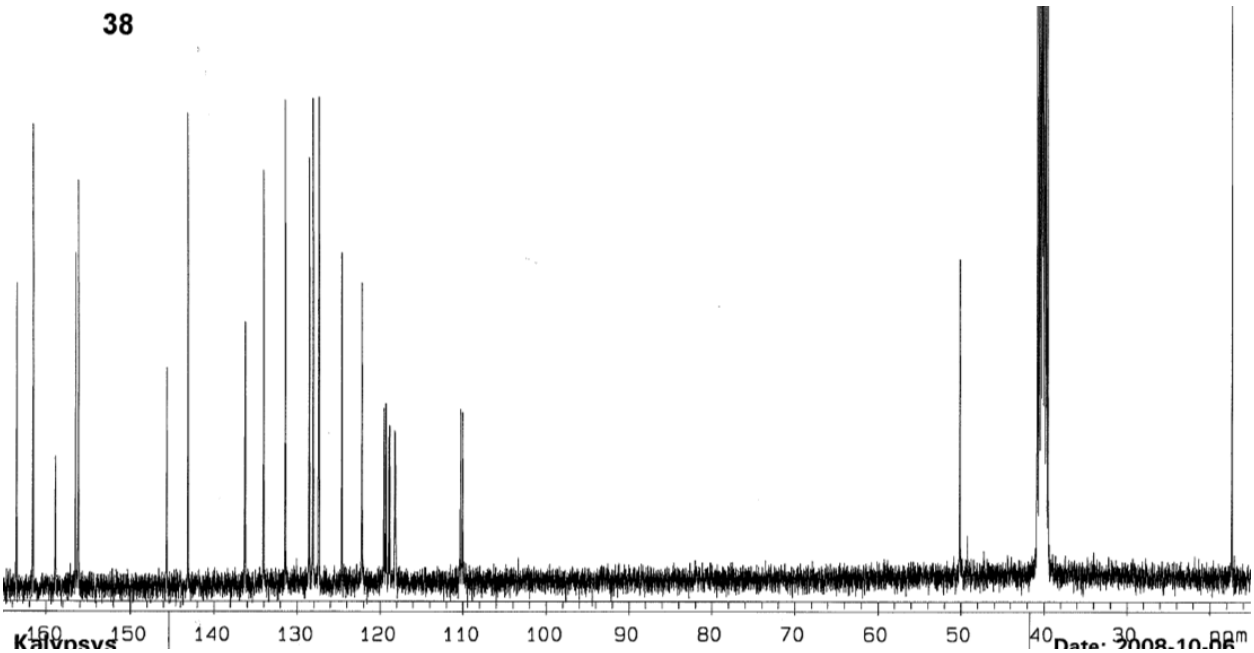

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.794 BB    0.1070 6161.84814  909.76367 100.0000
```

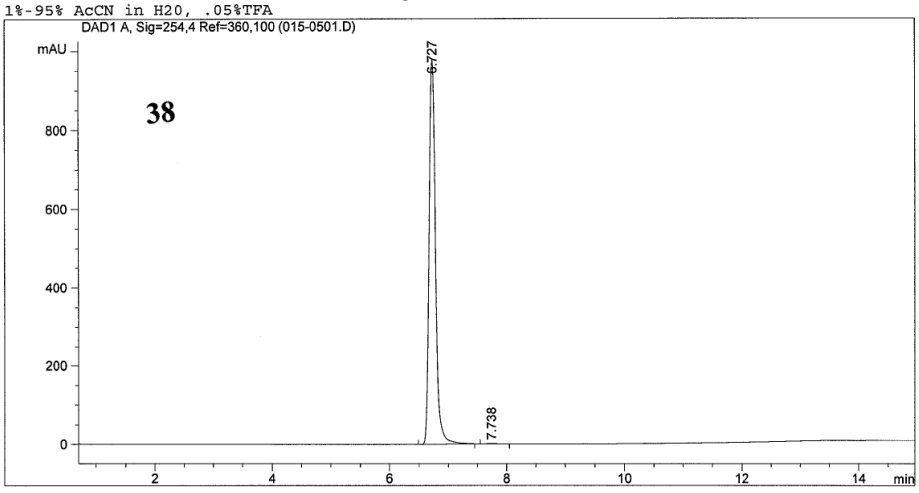
Compound 38: *N*-(3-chlorophenyl)-*N*-((6-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide



38




```
======================================================================
Injection Date  : 10/31/2007 4:37:56 PM          Seq. Line :   5
Sample Name     : [illegible]                    Location : Vial 15
Acq. Operator   : 14                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/31/2007 4:08:49 PM by 14
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

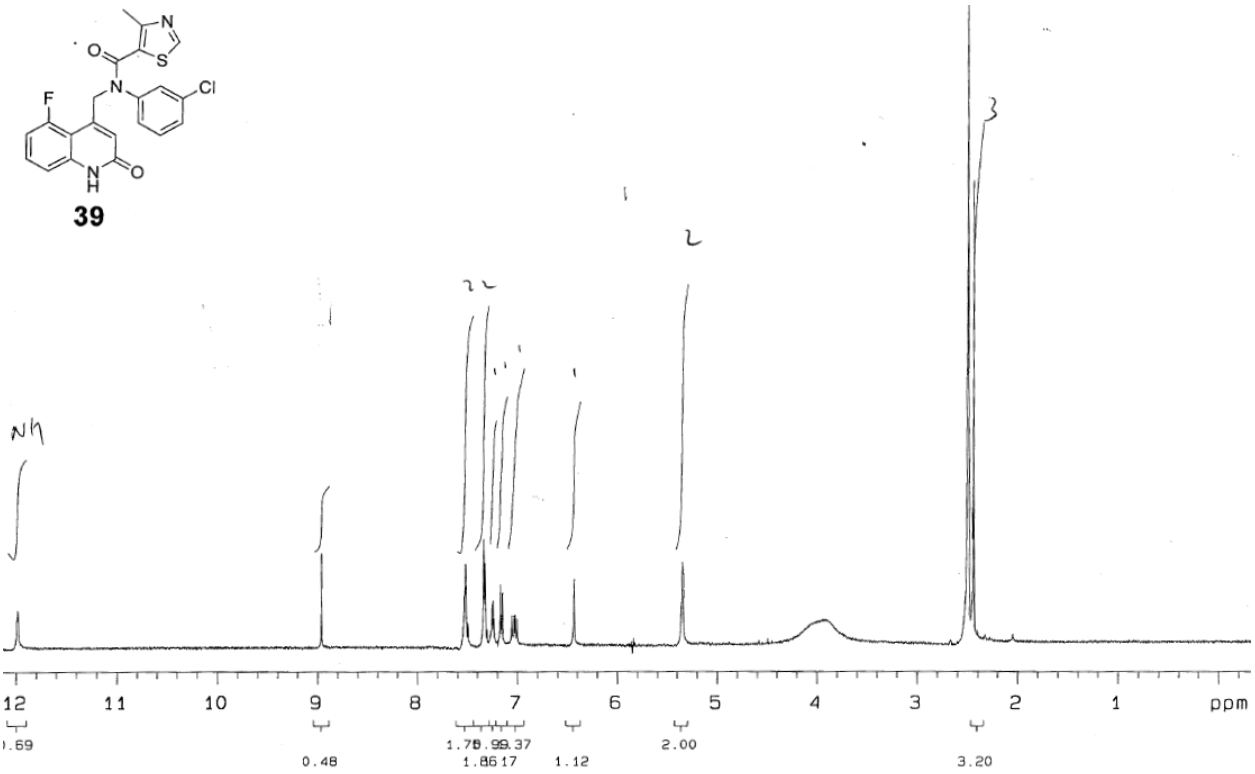
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

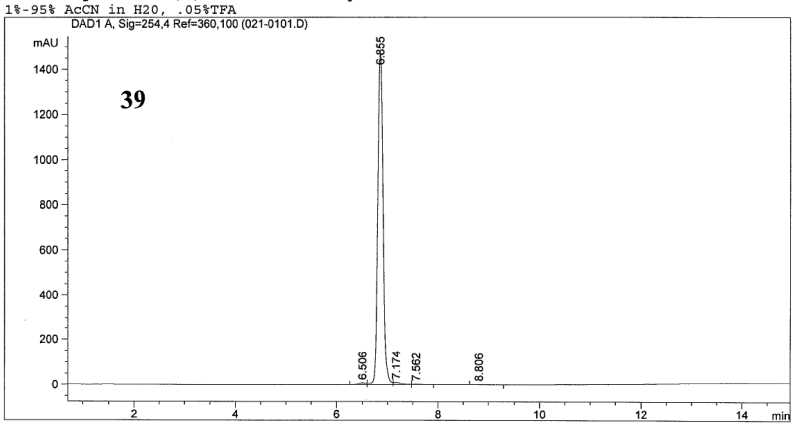
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.727 VB    0.1187 7429.33447  977.27155  99.8732
   2   7.738 BB    0.1415    9.43596    1.15217   0.1268

Totals :                  7438.77044  978.42371
```

Compound 39: *N*-(3-Chlorophenyl)-*N*-((5-fluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide




```
=====================================================================
Injection Date  : 11/2/2007 3:20:00 PM          Seq. Line :   1
Sample Name     : KLYP00930562                  Location : Vial 21
Acq. Operator   : 14                              Inj :   1
Acq. Instrument : Kalypsys                    Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 11/2/2007 3:18:26 PM by 14
1%-95% AcCN in H20, .05%TFA
```




```
=====================================================================
                        Area Percent Report
=====================================================================

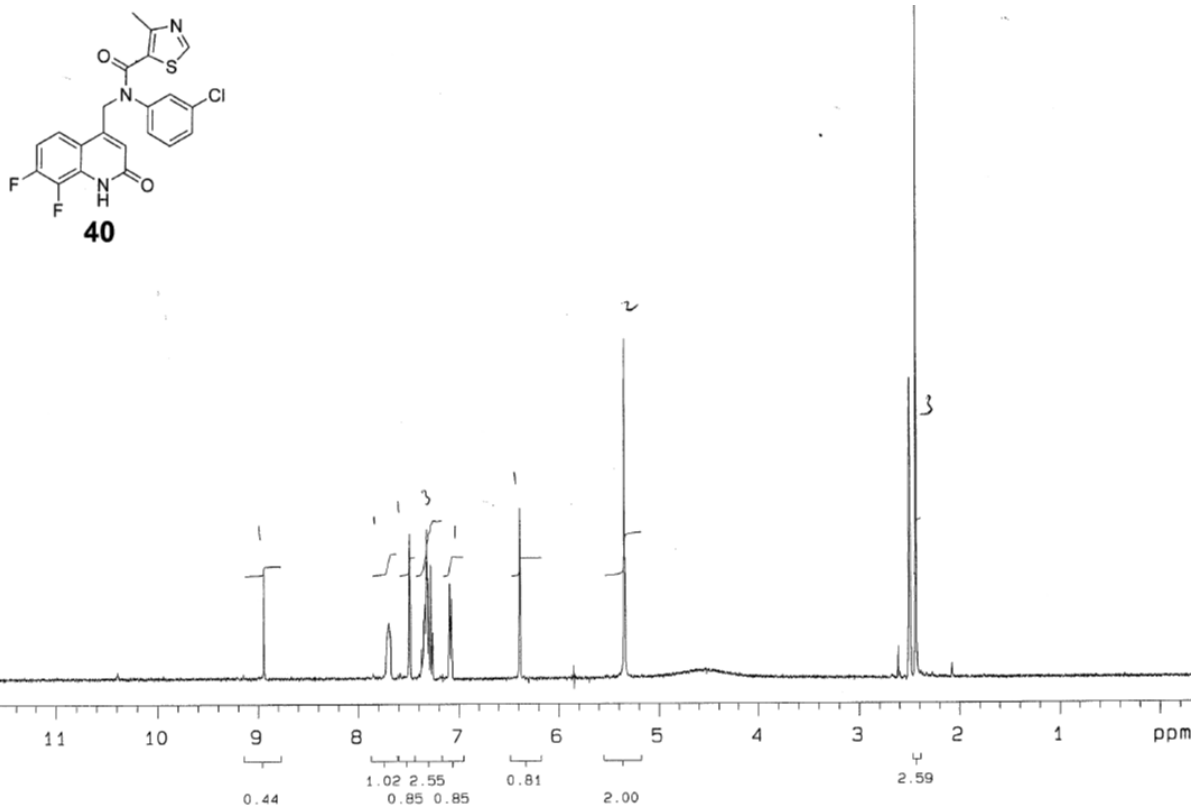
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

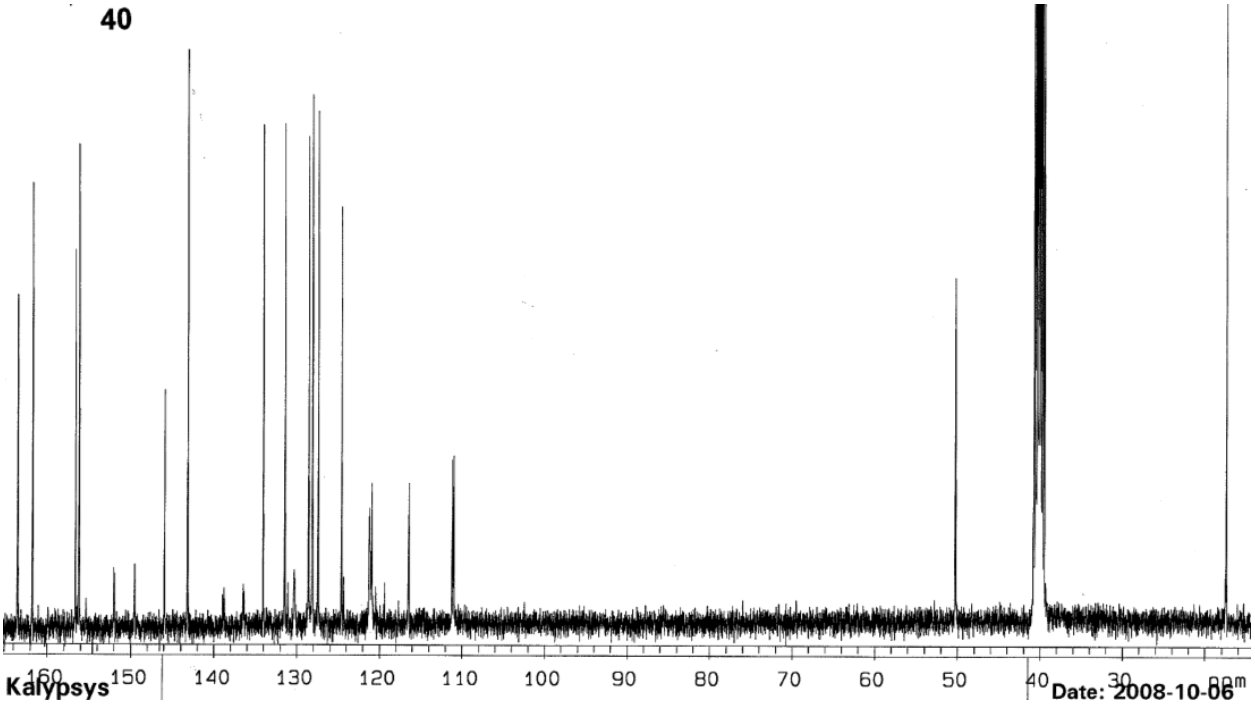

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.506 VV    0.1451   88.75094    8.99890   0.8156
   2   6.855 VV    0.1160 1.06199e4  1474.15771  97.5994
   3   7.174 VV    0.1705  118.12183   10.24750   1.0856
   4   7.562 VB    0.1791   29.25771    2.17250   0.2689
   5   8.806 BB    0.2285   25.08071    1.62121   0.2305

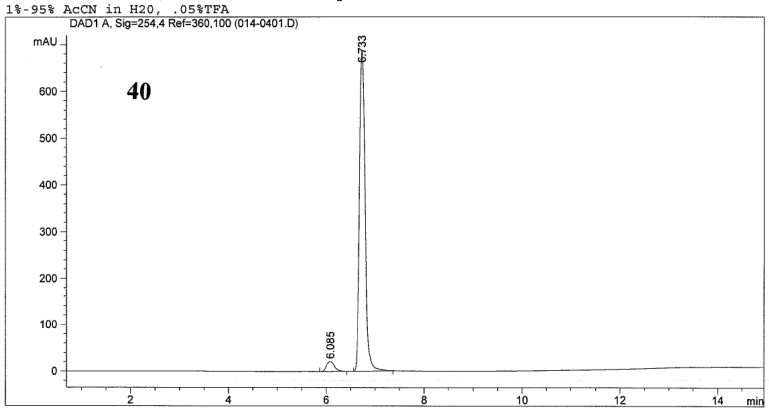
Totals :                  1.08811e4  1497.19783
```

Compound 40: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
================================================================
Injection Date  : 10/31/2007 4:20:14 PM          Seq. Line :    4
Sample Name     : KNP0092994                     Location : Vial 14
Acq. Operator   : 14                                Inj :    1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/31/2007 4:08:49 PM by 14
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
================================================================
                      Area Percent Report
================================================================

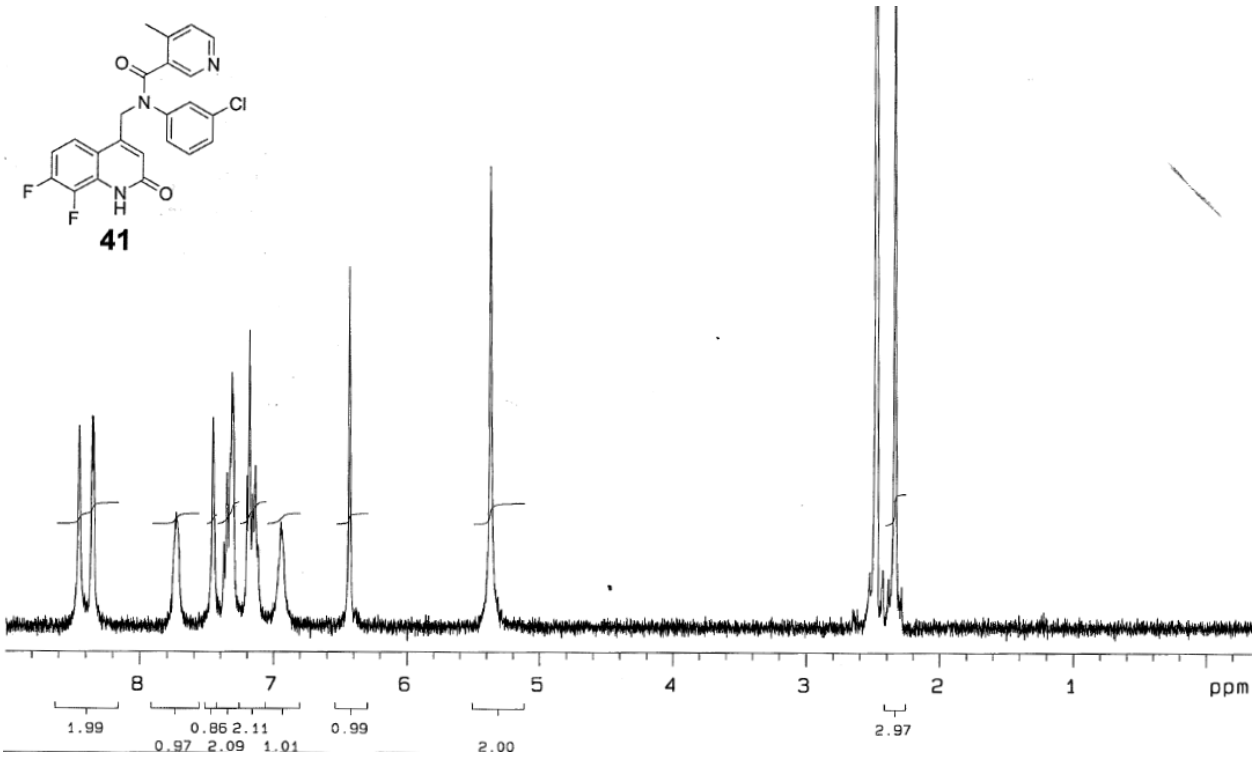
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

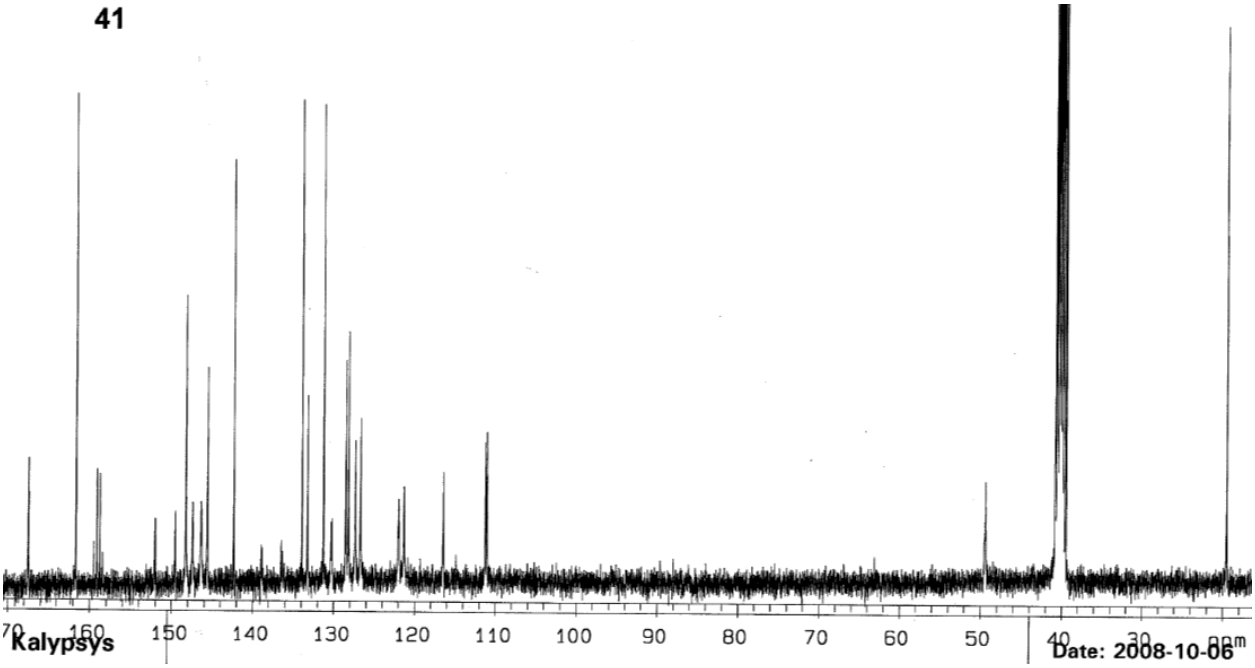
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.085 BB    0.1860  237.99170   20.41873   4.0796
   2   6.733 BB    0.1291 5595.63916  686.26837  95.9204

Totals :                   5833.63086  706.68711
```

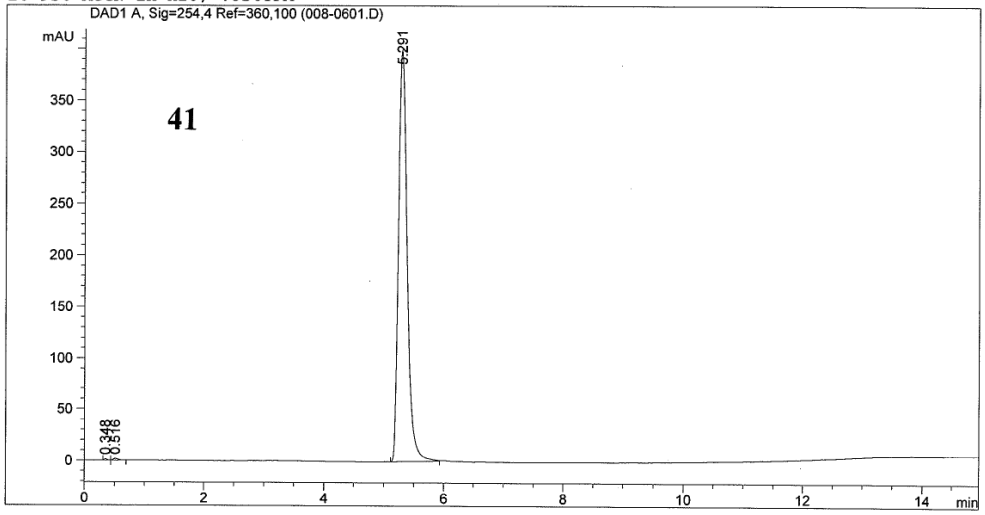
Compound 41: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylnicotinamide



41




```
======================================================================
Injection Date  : 8/21/2008 10:31:41 AM          Seq. Line :   6
Sample Name     : KMYP00930165                    Location : Vial 8
Acq. Operator   : 1                                  Inj :   1
Acq. Instrument : Kalypsys                      Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/21/2008 9:05:30 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

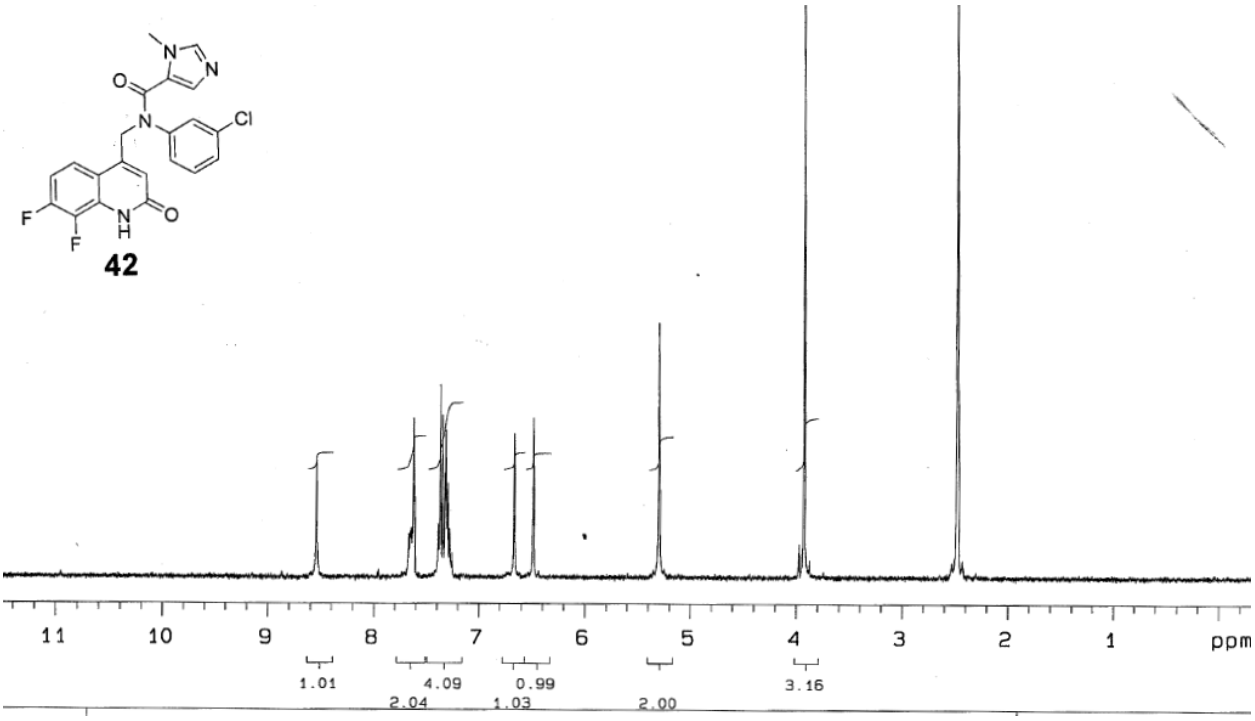
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

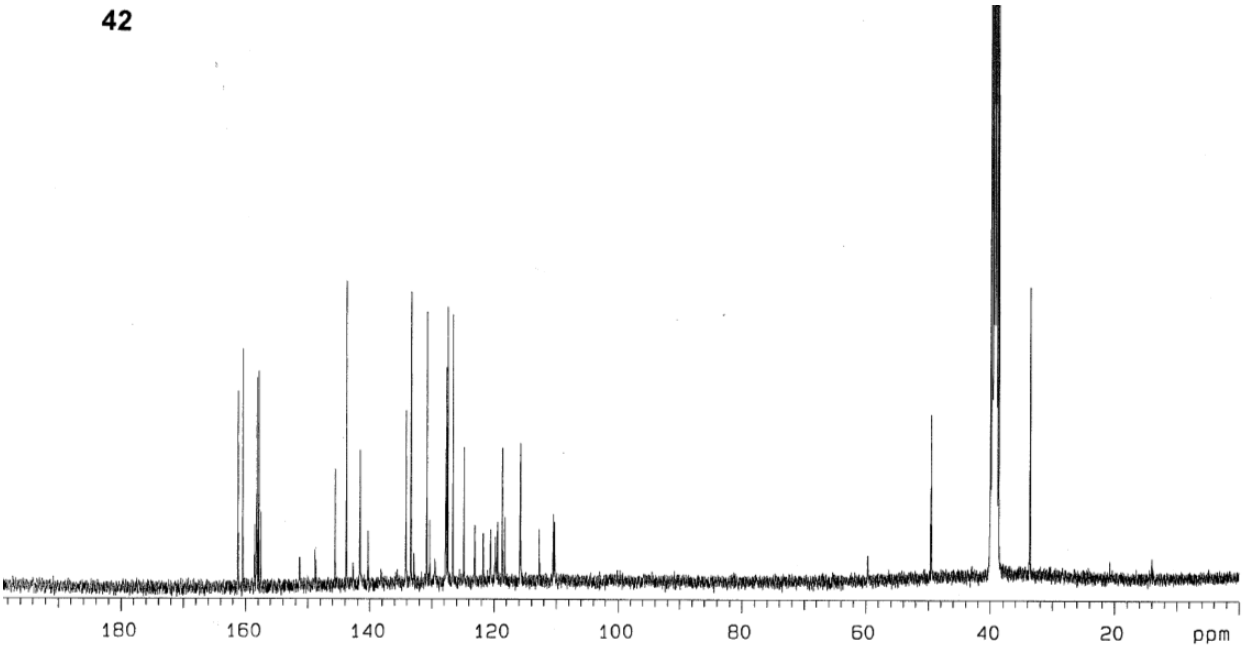

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   0.348 BV    0.0493    5.58121    1.65513   0.1385
   2   0.516 VB    0.1011   12.56408    1.80846   0.3119
   3   5.291 BB    0.1550 4010.66528  399.90155  99.5496

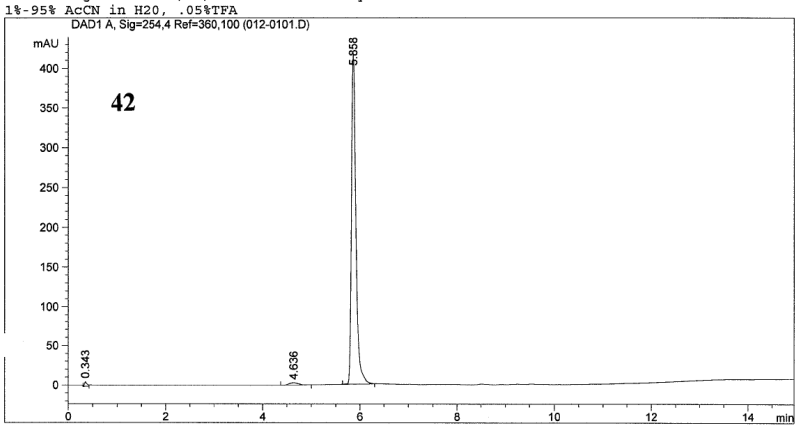
Totals :                   4028.81058  403.36513
```

Compound 42: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-1-methyl-1H-imidazole-5-carboxamide





```
================================================================
Injection Date  : 10/19/2006 4:44:45 PM          Seq. Line :   1
Sample Name     : jap396-087                     Location : Vial 12
Acq. Operator   : 12                                 Inj :   1
Acq. Instrument : Kalypsys                   Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 10/19/2006 4:43:23 PM by 12
1%-95% AcCN in H20, .05%TFA
```




```
================================================================
                    Area Percent Report
================================================================

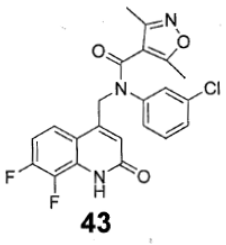
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

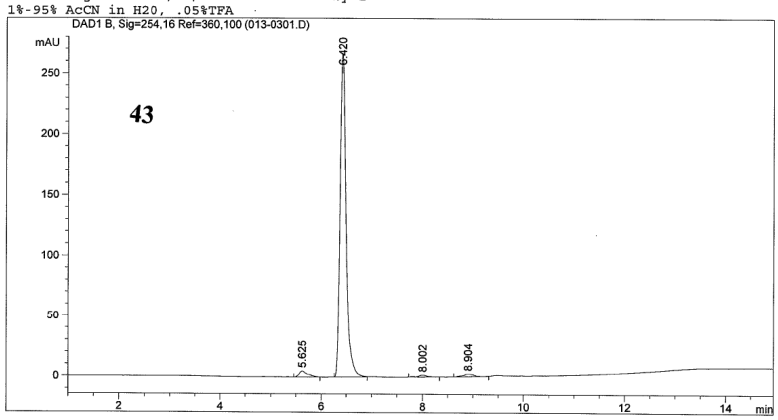
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.343 BV    0.0492   23.21497    6.26424   0.8574
   2   4.636 BB    0.2101   41.80192    3.04532   1.5438
   3   5.858 BB    0.0959 2642.70508  417.25275  97.5988

Totals :                   2707.72197  426.56230
```

Compound 43: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-3,5-dimethylisoxazole-4-carboxamide



```
==========================================================================
Injection Date  : 9/17/2008 10:18:43 AM          Seq. Line :   3
Sample Name     : [illegible]                    Location : Vial 13
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                        Area Percent Report
==========================================================================

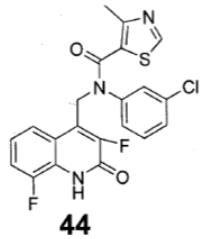
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   5.625 BB    0.1758   61.87328    5.08936   2.6711
   2   6.420 BB    0.1279 2200.80347  267.82324  95.0108
   3   8.002 BB    0.2029   22.16524    1.56772   0.9569
   4   8.904 BB    0.1949   31.52971    2.20464   1.3612

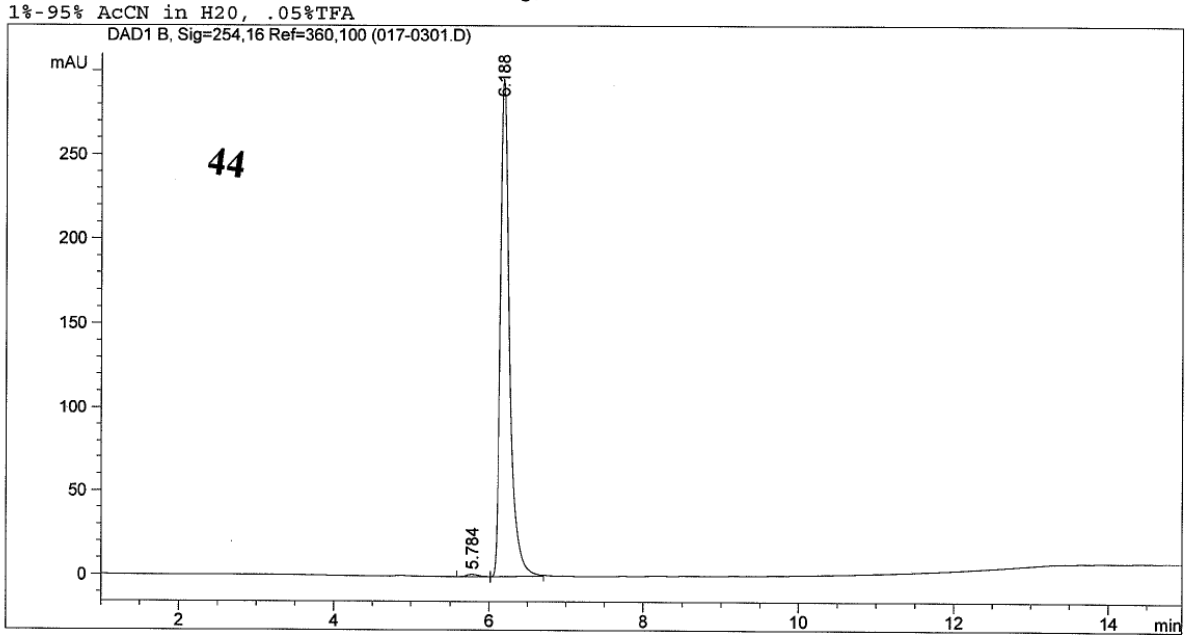
Totals :                  2316.37169  276.68496
```

Compound 44: *N*-(3-Chlorophenyl)-*N*-((3,8-difluoro-2-oxo-1,2-dihydroquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide



44

```
==========================================================================
Injection Date  : 9/16/2008 5:15:52 PM          Seq. Line :   3
Sample Name     : Kalyp91021                    Location : Vial 17
Acq. Operator   : 1                                 Inj :   1
Acq. Instrument : Kalypsys                   Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/16/2008 4:40:41 PM by 1
                  (modified after loading)
1%-95% AcCN in H20, .05%TFA
```




```
==========================================================================
                        Area Percent Report
==========================================================================

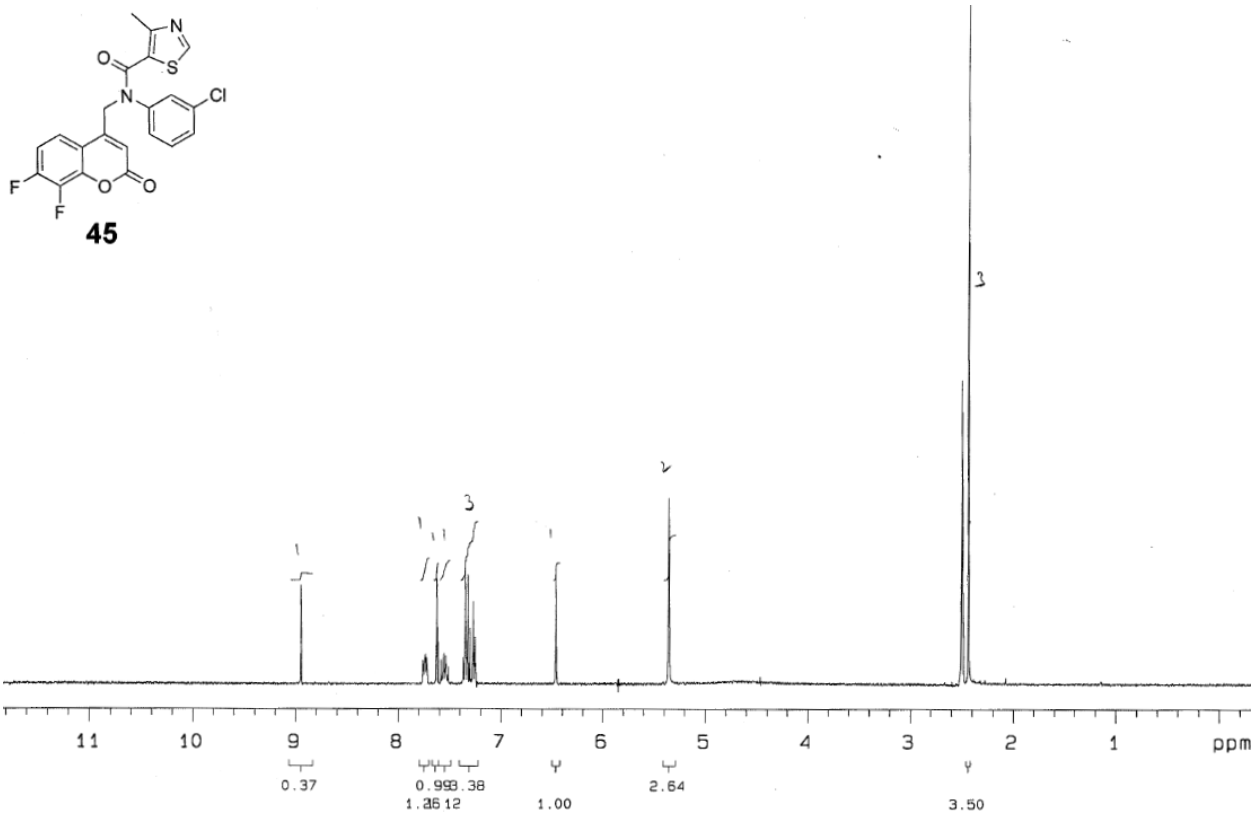
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

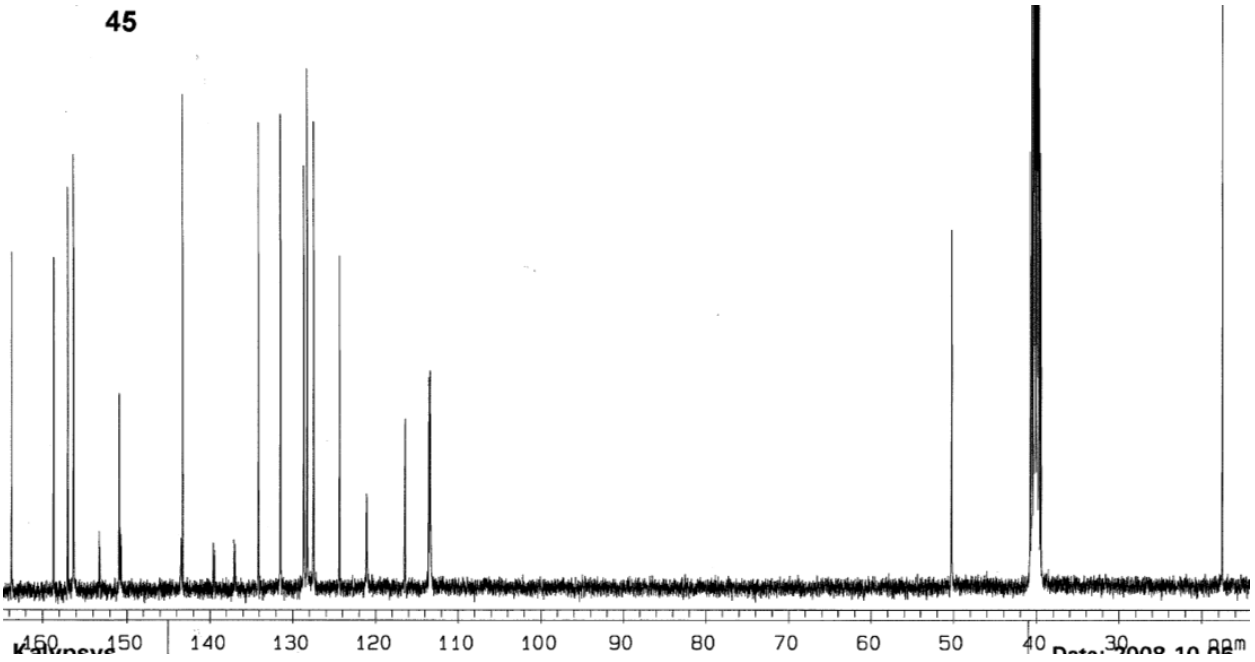

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   5.784 BV    0.1519   13.32413    1.34143   0.5392
   2   6.188 VB    0.1228 2457.83154  296.34518  99.4608

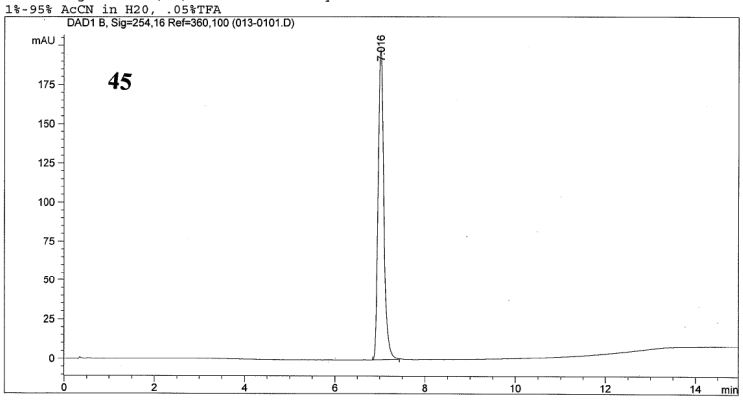
Totals :                   2471.15567  297.68662
```

Compound 45: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoro-2-oxo-2H-chromen-4-yl)methyl)-4-methylthiazole-5-carboxamide





```
======================================================================
Injection Date  : 8/25/2008 2:51:48 PM          Seq. Line :   1
Sample Name     : KJ1F00331222                  Location : Vial 13
Acq. Operator   : 1                                Inj :   1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 8/25/2008 2:50:32 PM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

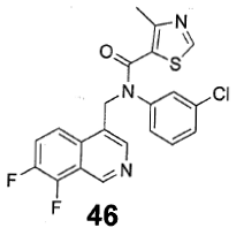
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

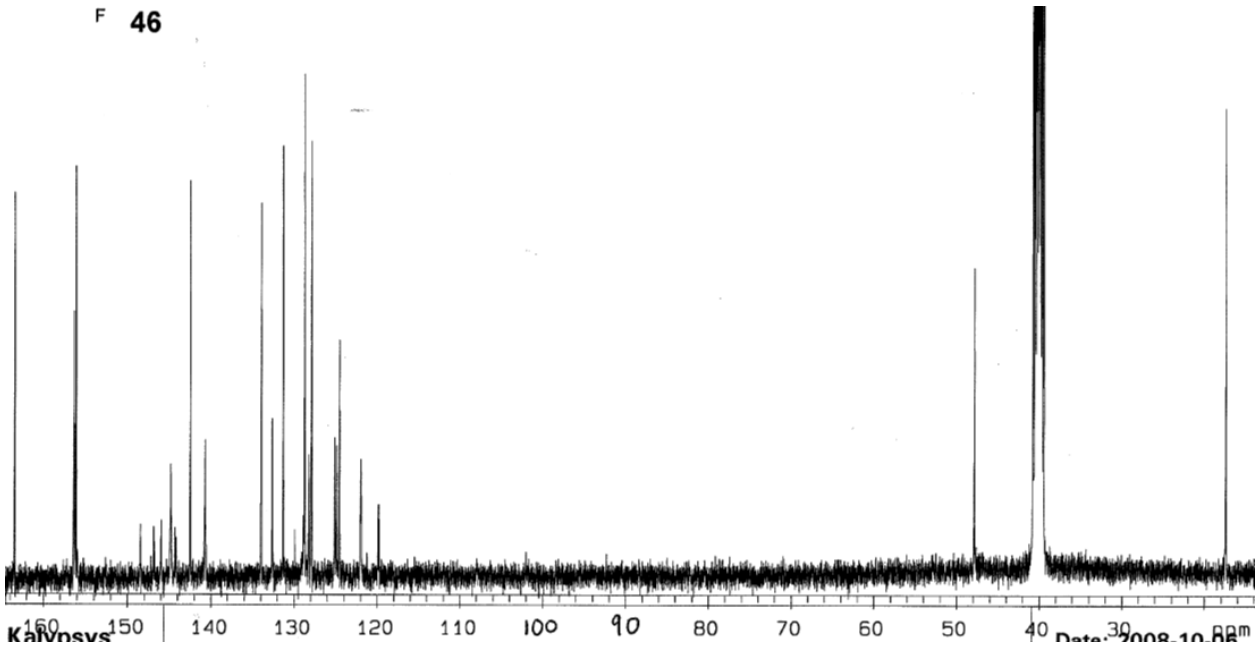

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.016 BB    0.1384 1735.29309  197.66359 100.0000

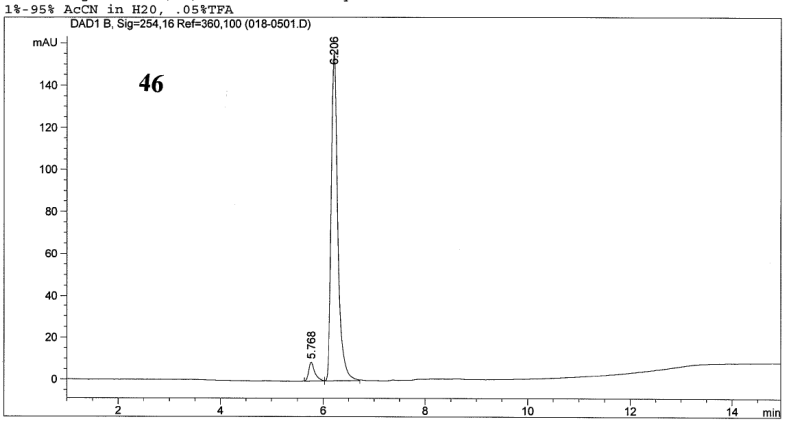
Totals :                  1735.29309  197.66359
```

Compound 46: *N*-(3-Chlorophenyl)-*N*-((7,8-difluoroisoquinolin-4-yl)methyl)-4-methylthiazole-5-carboxamide






```
======================================================================
Injection Date  : 9/17/2008 10:52:53 AM          Seq. Line :   5
Sample Name     : Kalypsys153                     Location : Vial 18
Acq. Operator   : 1                                  Inj :  1
Acq. Instrument : Kalypsys                     Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

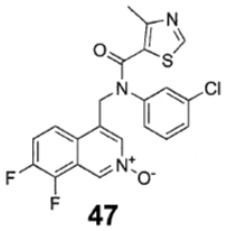
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.768 BV    0.1225   75.00073    9.07174   5.0770
   2   6.206 VB    0.1347 1402.25647  156.24416  94.9230

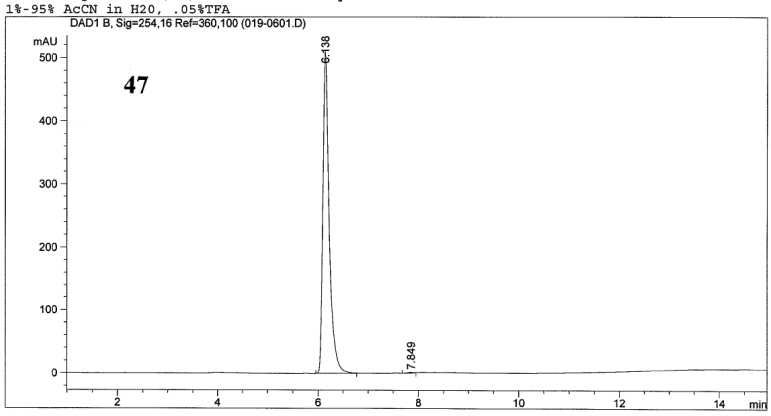
Totals :                   1477.25720  165.31590
```

Compound 47: 4-((*N*-(3-Chlorophenyl)-4-methylthiazole-5-carboxamido)methyl)-7,8-difluoroisoquinoline 2-oxide



47


```
======================================================================
Injection Date  : 9/17/2008 11:09:58 AM          Seq. Line :   6
Sample Name     : klyp531232                     Location : Vial 19
Acq. Operator   : 1                                 Inj :  1
Acq. Instrument : Kalypsys                      Inj Volume : 5 µl
Sequence File   : C:\CHEM32\1\SEQUENCE\DEF_LC2.S
Method          : C:\CHEM32\1\METHODS\1-95_LC.M
Last changed    : 9/17/2008 9:43:27 AM by 1
1%-95% AcCN in H20, .05%TFA
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.138 BB    0.1322 4564.39355  510.85843  99.7648
   2   7.849 BV    0.1494   10.76014    1.12715   0.2352

Totals :                  4575.15370  511.98558
```

Compound #	MF	MW	ESI+ Exact m/z	ESI+ Measured m/z	ESI+ Mass Defect (ppm)	ESI- Exact m/z	ESI- Measured m/z	ESI- Mass Defect (ppm)
7	C21H16N2O3	344.1161	345.1239	345.1239	0.00	343.1083	343.1085	0.58
8	C21H15N2O3F	362.1067	363.1145	363.1141	-1.10	361.0989	361.0985	-1.11
9	C21H17N3O2S	375.1041	376.1119	376.1121	0.53	374.0963	374.0959	-1.07
10	C21H16N3O2FS	393.0947	394.1025	394.1026	0.25	392.0869	392.0870	0.26
11	C21H15N3O2FSCl	427.0558	428.0636	428.0641	1.17	426.0480		
12	C21H15N3O2FSCl	427.0558	428.0636	428.0641	1.17	426.0480	426.0486	1.41
13	C21H15N3O2FSCl	427.0558	428.0636			426.0480	426.0478	-0.47
14	C21H15N3O2F2S	411.0853	412.0931	412.0923	-1.94	410.0775	410.0771	-0.98
15	C22H15N4O2FS	418.09	419.0978	419.0971	-1.67	417.0822	417.0821	-0.24
16	C22H18N3O2FS	407.1104	408.1182	408.1176	-1.47	406.1026	406.1027	0.25
17	C22H18N3O3FS	423.1053	424.1131	424.1125	-1.41	422.0975	422.0974	-0.24
18	C20H13N3O2FSCl	413.0401	414.0479	414.0472	-1.69	412.0323	412.0323	0.00
19	C23H17N3O2FCl	421.0993	422.1071			420.0915	420.0919	0.95
20	C23H17N3O2FCl	421.0993	422.1071			420.0915	420.0915	0.00
21	C23H17N3O2FCl	421.0993	422.1071			420.0915	420.0919	0.95
22	C23H17N3O2FCl	421.0993	422.1071			420.0915	420.0919	0.95
23	C21H16N4O2FCl	410.0946	411.1024	411.1019	-1.22	409.0868	409.0863	-1.22
24	C22H17N3O3FCl	425.0942	426.1020	426.1028	1.88	424.0864	424.0865	0.24
25	C22H20N2O2FCl	398.1197	399.1275	399.1274	-0.25	397.1119	397.1122	0.76
26	C20H18N2O2FCl	372.1041	373.1119	373.1118	-0.27	371.0963	371.0957	-1.62

27	C17H14N3O2SCl	359.0495	360.0573	360.0576	0.83	358.0417	358.0417	0.00
28	C21H20N3O2SCl	413.0965	414.1043	414.1046	0.72	412.0887	412.0889	0.49
29	C21H14N2O3FSCl	428.0398	429.0476	429.0470	-1.40	427.0320	427.0321	0.23
30	C22H17N3O2FSCl	441.0714	442.0792	442.0785	-1.58	440.0636	440.0640	0.91
31	C22H17N3O2FSCl	441.0714	442.0792	442.0789	-0.68	440.0636		
32	C21H15N3OFSCl	411.0608	412.0686	412.0681	-1.21	410.0530	410.0533	0.73
33	C21H15N3OFSCl	411.0608	412.0686	412.0682	-0.97	410.0530		
34	C21H15N3O2FSCl	427.0558	428.0636	428.0644	1.87	426.0480	426.0486	1.41
35	C21H16N3O2SCl	409.0652	410.0730	410.0733	0.73	408.0574	408.0568	-1.47
36	C21H15N3O2SCl2	443.0262	444.0340			442.0184	442.0186	0.45
37	C21H15N3O2FSCl	427.0558	428.0636	428.0641	1.17	426.0480	426.0482	0.47
38	C21H15N3O2FSCl	427.0558	428.0636	428.0628	-1.87	426.0480	426.0472	-1.88
39	C21H15N3O2FSCl	427.0558	428.0636			426.0480	426.0487	1.64
40	C21H14N3O2F2SCl	445.0463	446.0541	446.0537	-0.90	444.0385	444.0381	-0.90
41	C23H16N3O2F2Cl	439.0899	440.0977	440.0974	-0.68	438.0821	438.0820	-0.23
42	C21H15N4O2F2Cl	428.0852	429.0930	429.0922	-1.86	427.0774	427.0773	-0.23
43	C22H16N3O3F2Cl	443.0848	444.0926			442.0770	442.0767	-0.68
44	C21H14N3O2F2SCl	445.0463	446.0541			444.0385	444.0380	-1.13
45	C21H13N2O3F2SCl	446.0303	447.0381	447.0375	-1.34	445.0225	445.0220	-1.12
46	C21H14N3OF2SCl	429.0514	430.0592	430.0585	-1.63	428.0436		
47	C21H14N3O2F2SCl	445.0463	446.0541	446.0542	0.22	444.0385	444.0382	-0.68

Table 1. Crystal data and structure refinement for Cpd 12.

Identification code	Cpd 12	
Empirical formula	C21 H15 Cl F N3 O2 S	
Formula weight	427.87	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.8921(13) Å	α= 72.680(2)°
	b = 17.982(3) Å	β= 82.543(2)°
	c = 18.935(3) Å	γ = 77.465(2)°
Volume	2814.5(7) $Å^3$	
Z	6	
Density (calculated)	1.515 g/cm^3	
Absorption coefficient	0.349 mm^{-1}	
F(000)	1320	
Crystal size	0.22 x 0.08 x 0.04 mm^3	
Theta range for data collection	1.87 to 25.00°	
Index ranges	-10<=h<=9, -21<=k<=21, -22<=l<=22	
Reflections collected	16620	
Independent reflections	9455 [R(int) = 0.0512]	
Completeness to theta = 25.00°	98.2 %	
Absorption correction	None	
Max. and min. transmission	0.9862 and 0.9272	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9455 / 0 / 794	
Goodness-of-fit on F^2	1.011	
Final R indices [I>2sigma(I)]	R1 = 0.0584, wR2 = 0.1363	
R indices (all data)	R1 = 0.1099, wR2 = 0.1593	
Largest diff. peak and hole	0.837 and -0.406 e $Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)for Cpd 12. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1")	15733(1)	1875(1)	-4548(1)	40(1)
Cl(1')	7275(2)	129(1)	4646(1)	34(1)
Cl(2')	7634(6)	2718(3)	2227(3)	38(2)
Cl(1)	-591(1)	6491(1)	2212(1)	40(1)
F(1")	9436(3)	-1324(1)	724(1)	32(1)
F(1')	3760(3)	2140(1)	-858(1)	34(1)
F(1)	7590(3)	4120(1)	-774(1)	34(1)
S(1')	3114(1)	2472(1)	4075(1)	30(1)
S(1")	9455(2)	1661(1)	-5145(1)	39(1)
S(1)	3886(1)	5846(1)	4048(1)	33(1)
O(1')	6577(3)	-148(2)	825(2)	31(1)
O(1")	6706(3)	967(2)	-1006(1)	29(1)
O(1)	9523(3)	5310(2)	791(2)	29(1)
O(2')	424(4)	2050(2)	2883(2)	36(1)
O(2")	9226(4)	459(2)	-3675(2)	45(1)
O(2)	6936(4)	4254(2)	3388(2)	35(1)
N(1")	8461(4)	-126(2)	-492(2)	24(1)
N(1')	4837(4)	966(2)	345(2)	26(1)
N(1)	8103(4)	4660(2)	349(2)	25(1)
N(2')	1854(4)	3907(2)	3441(2)	30(1)
N(2")	9220(4)	3036(2)	-4959(2)	39(1)
N(2)	6244(5)	5937(2)	4643(2)	34(1)
N(3')	2974(4)	1470(2)	2834(2)	26(1)
N(3")	10935(4)	833(2)	-3131(2)	24(1)
N(3)	4964(4)	5036(2)	2717(2)	25(1)
C(1")	10276(5)	-1303(2)	66(2)	25(1)
C(1')	2995(5)	2140(3)	-188(2)	29(1)
C(1)	6562(5)	4034(2)	-174(2)	26(1)
C(2")	11541(5)	-1881(2)	35(2)	28(1)
C(2')	1719(5)	2719(3)	-144(2)	29(1)
C(2)	5325(5)	3698(2)	-159(2)	26(1)
C(3")	12379(5)	-1847(3)	-650(2)	29(1)
C(3')	961(5)	2698(3)	559(2)	33(1)

C(3)	4282(5)	3622(2)	474(2)	30(1)
C(4')	1498(5)	2123(3)	1178(2)	30(1)
C(4")	11930(5)	-1245(2)	-1266(2)	26(1)
C(4)	4521(5)	3888(2)	1049(2)	28(1)
C(5")	10625(5)	-650(2)	-1226(2)	22(1)
C(5')	2810(5)	1534(2)	1129(2)	27(1)
C(5)	5795(5)	4238(2)	1031(2)	22(1)
C(6")	10120(5)	16(2)	-1855(2)	23(1)
C(6')	3437(5)	904(2)	1762(2)	25(1)
C(6)	6080(5)	4559(2)	1608(2)	21(1)
C(7")	8844(5)	548(2)	-1781(2)	25(1)
C(7')	4654(5)	350(2)	1648(2)	27(1)
C(7)	7293(5)	4926(2)	1517(2)	26(1)
C(8")	7916(5)	491(2)	-1087(2)	24(1)
C(8')	5446(5)	358(3)	924(2)	26(1)
C(8)	8385(5)	4987(2)	873(2)	25(1)
C(9')	3564(5)	1548(2)	425(2)	26(1)
C(9")	9776(5)	-686(2)	-549(2)	22(1)
C(9)	6840(5)	4314(2)	401(2)	22(1)
C(10')	2676(5)	846(3)	2537(2)	30(1)
C(10")	11106(5)	52(2)	-2575(2)	28(1)
C(10)	5035(5)	4446(2)	2316(2)	26(1)
C(11')	4521(5)	1425(3)	3012(2)	26(1)
C(11")	12176(5)	1247(2)	-3168(2)	27(1)
C(11)	3925(5)	5780(2)	2462(2)	25(1)
C(12")	13188(5)	1383(2)	-3789(2)	27(1)
C(12')	5101(5)	839(3)	3637(2)	30(1)
C(12)	2356(5)	5774(3)	2486(2)	25(1)
C(13")	14414(5)	1737(3)	-3775(2)	28(1)
C(13')	6532(5)	845(2)	3848(2)	29(1)
C(13)	1365(5)	6485(3)	2209(2)	28(1)
C(14')	7372(5)	1418(3)	3448(2)	34(1)
C(14")	14675(5)	1947(3)	-3162(2)	34(1)
C(14)	1908(6)	7192(3)	1938(2)	33(1)
C(15")	13661(6)	1790(3)	-2539(2)	36(1)
C(15')	6806(5)	1988(3)	2819(2)	32(1)
C(15)	3452(5)	7193(3)	1922(2)	32(1)
C(16")	12420(5)	1442(3)	-2535(2)	31(1)

C(16')	5371(5)	1990(3)	2599(2)	30(1)
C(16)	4486(5)	6476(3)	2175(2)	29(1)
C(17")	9987(5)	962(3)	-3686(2)	31(1)
C(17')	1766(5)	2028(3)	3004(2)	29(1)
C(17)	5924(5)	4855(3)	3277(2)	27(1)
C(18")	9828(5)	1717(3)	-4287(2)	30(1)
C(18')	2118(5)	2643(2)	3306(2)	24(1)
C(18)	5692(5)	5387(2)	3770(2)	27(1)
C(19')	2660(5)	3473(3)	3998(2)	30(1)
C(19")	9106(5)	2669(3)	-5440(2)	39(1)
C(19)	4747(6)	6133(3)	4647(2)	37(1)
C(20')	1530(5)	3436(3)	3043(2)	27(1)
C(20")	9648(5)	2491(3)	-4288(2)	35(1)
C(20)	6805(5)	5482(2)	4153(2)	31(1)
C(21')	557(5)	3831(3)	2401(2)	36(1)
C(21")	9882(6)	2804(3)	-3679(2)	42(1)
C(21)	8487(5)	5150(3)	4110(3)	40(1)

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