Supporting Information for

# Synthesis and evaluation of potent, highly-selective, 3-aryl-piperazinone inhibitors of protein geranylgeranyltransferase-I

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## Syntheses of compounds 30 and 31

1, 2-Dibromoethane (0.94 g, 5 mmol) and a solution of $K_2CO_3$ (0.7 g, 5 mmol) in 10 mL water were alternately added dropwise to a solution of L-phenylalanine (1.65 g, 10 mmol) and NaOH (0.4 g, 10 mmol) in water with stirring at 90 ºC. After 5 h, the reaction mixture was cooled and neutralized with concentrated HCl. The resulting precipitate was filtered off and dried under reduced pressure to give crude **18** (1 g, 4 mmol), which without further purification was refluxed with concentrated $H_2SO_4$ (0.79 g, 8 mmol) in 25 mL anhydrous methanol for 24 h to afford the piperazinone scaffold **19** as its $H_2SO_4$ salt after removal of the solvent. The solid was treated with saturated $NaHCO_3$ solution and the mixture was extracted with $CH_2Cl_2$ to afford compound **18** as a colorless oil (1.07 g, 75%): $\delta_H$ (500 MHz, d4-methanol) 1.16 (3H, t, *J* 7.0), 2.49 (1H, dd, *J* 13.5 and 9.7), 2.66 (1H, ddd, *J* 13.5, 10.0 and 3.5), 2.82 (2H, m), 3.01 (1H, dd, *J* 14.5 and 11.0), 3.23 (3H, m), 3.52 (1H, dd, *J* 10.0 and 3.5), 4.41 (2H, m), 5.00 (1H, dd, *J* 10.5 and 5.5), 7.05-7.28 (10 H, m); $\delta_C$ (125 MHz, d4-methanol) 14.6, 34.6, 38.6, 42.2, 47.0, 59.0, 60.9, 61.7, 126.9, 127.1, 128.9, 128.9, 129.0, 129.0, 129.2, 129.3, 129.6, 129.6, 137.5, 138.7, 170.1, 170.9; *m/z* (FAB) 367.2021 ($M^+$+1) 367.2022.

A mixture of compound **19** (146 mg, 0.4 mmol), N-1-trityl-deaminohistidine (150 mg, 0.4 mmol), EDCI (85 mg, 0.44 mmol), DIEA (0.09 mL, 0.44 mmol) in 3 mL anhydrous methylene chloride was stirred at rt for 5 h. The reaction mixture was diluted with 20 mL methylene chloride, and the solution was washed with 1N HCl, saturated sodium bicarbonate solution, and brine. The organic phase was dried over sodium sulfate and the solvent was removed on a rotavap to give an oil, which was purified by silica gel column chromatography with 2.5-5% MeOH/$CH_2Cl_2$ as eluant to afford **20** as a colorless oil (124 mg, 85%): $\delta_H$ (500 MHz, d4-methanol) 1.23 (3H, t, *J* 7.0), 1.42 (0.5H, m), 2.14 (0.5H, m), 2.32 (0.5H, m), 2.50-2.72 (2.5H, m), 2.75-2.86 (1.5H, m), 2.95-3.12 (2.5H, m), 3.17 (0.5H, m), 3.26 (0.5H, dd, *J* 14.0 and 6.5), 3.37 (0.5H, dd, *J* 14.0 and 6.5), 3.51 (0.5H, brd, *J* 13.5), 4.17 (2H, q, *J* 7.0), 4.40 (0.5H, m), 4.49 (0.5H, m), 5.11 (0.5H, m), 5.25 (0.5H, m), 6.28 (0.5H, m), 6.60 (0.5H, m), 6.90-7.40 (26H, m); *m/z* (FAB) 731.3600 ($M^+$+1, $C_{47}H_{47}N_4O_4$ requires 731.3597.

Deprotection of compound **20** following the general procedure described previously afforded **30** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 1.23 (3H, t, J 7.0), 1.36 (0.5 H, m), 2.33 (0.5 H, m), 2.55 (3H, m), 2.76-3.20 (8H, m), 3.56 (0.5H, brd, J 12.5), 4.17 (2H, q, J 7.0), 4.31 (0.5H, m), 4.36 (0.5H, m), 4.94 (0.5H, m), 5.02 (0.5H, m), 6.86 (0.5H, s), 6.90 (0.5H, s), 7.00-7.30 (10H, m), 8.67 (0.5H, s), 8.63 (0.5H, s); m/z (FAB) 489.2502 ($M^+$+1, $C_{28}H_{33}N_4O_4$ requires 489.2502).

Saponification of **30** following general procedure described previously afforded **31** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 1.33 (0.5H, m), 2.10 (0.5H, m), 2.26 (0.5H, m), 2.34 (0.5H, m), 2.47 (1.5 H, m), 2.60-2.84 (3.5H, m), 2.92 (1H, m), 3.07 (0.5H, dt, J 13.0 and 3.5 Hz), 3.23-3.40 (3H, m), 3.62 (0.5H, brd, J 13.2), 4.17 (0.5H, dd, J 10.0 and 3.3), 4.35 (0.5H, brd, J 13.5), 4.91 (0.5H, t, J 6.5), 5.21 (0.5H, dd, J 11.3 and 5.0), 5.26 (0.5H, dd, J 12.0 and 5.0), 6.40 (0.5H, s), 6.63 (0.5H, s), 6.72-7.25 (10H, m), 7.38 (0.5H, s), 7.45 (0.5H, s); m/z (FAB) 461.2187 ($M^+$+1, $C_{26}H_{29}N_4O_4$ requires 461.2189).

## Syntheses of compounds 35 and 37

Reaction of scaffold **12a** with 4-(4-chloromethyl-imidazol-1-ylmethyl)-benzonitrile following previously described procedure for **13a2** gave **36** as a colorless oil (193 mg, 24%): $\delta_H$ (500 MHz, d4-methanol) 2.77-2.96 (2H, m), 4.52-4.64 (2.5H, m), 4.83-5.12 (2.5H, m), 5.25 (2H, s), 5.69

(0.5H, d, *J* 5.9), 5.91 (0.5H, d, *J* 6.0), 6.20 (0.5H, dd, *J* 1.2 and 5.9), 6.34 (0.5H, dd, *J* 1.4 and 6.0), 6.99-7.34 (13H, m), 7.63 (2H, d, *J* 8.0), 7.75 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 37.3, 44.1, 51.4, 59.8, 69.4, 110.0, 110.1, 113.3, 114.0, 119.8, 120.3, 128.3, 129.5, 129.7, 129.8, 129.8, 129.9, 130.0, 131.1, 134.2, 138.9, 139.5, 144.0, 154.8, 166.3; *m/z* (FAB) 518.2192 ($M^+$+1, $C_{31}H_{27}N_5O_3$ requires 518.2192).

Reaction of scaffold **13a2** with 4-bromomethyl-benzonitrile following previously described procedure for **35** gave **37** as a colorless oil (36%): $\delta_H$ (500 MHz, d4-methanol) 2.63-2.87 (2H, m), 3.99 (0.5H, d, *J* 15.6), 4.11 (0.5Hz, d, *J* 15.6), 4.45-4.67 (1.5H, m), 4.91-5.30 (5H, m), 5.37 (0.5H, d, *J* 5.9), 5.92 (0.5H, d, *J* 5.9), 6.19 (0.5H, d, *J* 5.9), 6.85-7.60 (16H, m); $\delta_C$ (500 MHz, MeOH) 36.7, 48.2, 58.1, 58.9, 68.7, 109.6, 109.8, 110.2, 110.7, 126.7, 127.4, 128.6, 128.6, 128.8, 128.8, 128.9, 129.0, 129.8, 129.9, 132.7, 132.8, 135.7, 142.0, 152.1, 164.3; *m/z* (FAB) 518.2193 ($M^+$+1, $C_{31}H_{27}N_5O_3$ requires 518.2192).

### Syntheses of compounds 38, 39, and compounds 46-49

Deprotection of the trityl-protected **38** following the general procedure described above afforded **38** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 1.56 (1H, m), 1.79 (1H, m), 1.96 (3H, m), 2.18 (2H, t, *J* 7.2), 2.94 (1H, m), 3.02 (2H, m), 3.20 (1H, brd, *J* 12.0), 3.39 (1H, m), 3.59 (3H, s), 4.02 (1H, brd, *J* 13.0), 4.25 (1H, dd, *J* 12.5 and 7.0), 4.42 (1H, d, *J* 15.4), 4.63 (2H, m), 5.02 (1H, brs), 7.06-7.30 (6H, m), 8.58 (1H, s); $\delta_C$ (125 MHz, d4-methanol)15.6, 30.4, 31.8, 37.8, 37.4, 41.5, 47.0, 52.7, 53.3, 60.2, 118.5, 126.6, 127.7, 129.2, 129.2, 129.8, 129.9, 134.5, 137.4, 156.6, 168.8, 173.6; *m/z* (FAB) 460.2018 ($M^+$+1, $C_{22}H_{30}N_5O_4S$ requires 460.2019).

Saponification of **38** following the general procedure afforded **39** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol)1.66 (1H, m), 1.88 (1H, m), 1.92 (3H, m), 2.20 (2H, m), 2.75 (1H, ddd, *J* 14.0, 10.5 and 3.5), 2.86 (1H, brd, *J* 12.3), 3.10-3.15 (2H, m), 3.20 (1H, m), 3.75 (1H, brd, *J* 13.0), 4.04 (1H, dd, *J* 8.0 and 4.5), 4.35 (1H, d, *J* 14.8), 4.48 (1H, d, *J* 14.8), 4.65 (1H, t, *J* 5.2), 6.92 (1H, s), 7.04-7.14 (5H, m), 7.58 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 15.7, 31.8, 34.1, 38.7, 39.5, 44.5, 47.1, 56.7, 60.4, 119.2, 128.4, 130.0, 130.0, 131.3, 131.3, 134.9, 137.1, 139.1, 158.6, 170.0, 179.0; *m/z* (FAB) 446.1862 ($M^+$+1, $C_{21}H_{28}N_5O_4S$ requires 446.1862).

Reaction of trityl-protected **40**, with bromomethyl-benzene following previously described procedure for **35** gave **46** as a colorless oil (25.1 mg, 30%): $\delta_H$ (500 MHz, d4-methanol) 0.79 (6H, dd, *J* 6.1 and 22.8), 1.33-1.47 (3H, m), 2.55-2.63 (2H, m), 2.82-3.03 (2.5H, m), 3.38-3.52 (0.5H, m), 3.58 (3H, s), 4.04-4.13 (0.5H, m), 4.42-4.57 (2.5H, m), 4.79 (2.5H, brs), 5.21 (1.5H, brs), 6.89-7.29 (11H, m), 7.75 (1H, brs); $\delta_C$ (125 MHz, d4-methanol) 22.1, 23.7, 26.2, 38.5, 39.5, 40.4, 41.4, 45.8, 52.9, 54.0, 54.1, 59.9, 127.8, 128.0, 128.4, 129.1, 129.5, 129.7, 129.9, 130.4, 131.3, 138.8, 138.9, 158.8, 169.9, 176.3; *m/z* (FAB) 532.2923 ($M^+$+1, $C_{30}H_{37}N_5O_4$ requires 532.2924).

Saponification of **46** following the general procedure described previously afforded **47** (GGTI-2543) as a colorless oil in 87% yield: $\delta_H$ (500 MHz, d4-methanol) 0.77 (6H, dd, *J* 2.0 and 6.3), 1.17-1.44 (3H, m), 2.53-2.70 (2H, m), 2.76-2.84 (1H, m), 2.91-3.03 (2H, m), 3.56 (1H, brd, *J* 13.3), 3.98-4.04 (1H, m), 4.40-4.58 (3H, m), 5.23 (2H, s), 6.90-7.27 (11H, m), 7.71 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 22.70, 24.23, 26.30, 38.68, 39.18, 40.32, 44.14, 45.96, 56.39, 60.46, 127.76, 128.40, 129.49, 129.79, 130.03, 130.42, 131.27, 138.91, 139.09, 141.22, 158.42, 170.05, 181.48; *m/z* (FAB) 540.2585 ($M^+$+Na, $C_{29}H_{36}N_5O_4Na$ requires 540.2587).

Reaction of trityl-protected **40**, with 4-bromomethyl-benzonitrile following previously described procedure for **35** gave **48** as a colorless oil (26 mg, 24%): $^1$H NMR (500 MHz, d4-methanol) δ 0.79 (dd, *J* = 6.1, 23.3 Hz, 6H), 1.35-1.48 (m, 3H), 2.59-2.75 (m, 2H), 2.86-3.03 (m, 2.5H), 3.49-3.58 (br m, 0.5H), 3.58 (s, 3H), 4.06-4.16 (m, 1H), 4.35-4.57 (m, 2.5H), 4.77 (s, 2H), 5.34 (br s, 1.5H), 6.91-7.23 (m, 8H), 7.58-7.72 (m, 2H), 7.77 (br s, 1H); $^{13}$C NMR (125 MHz, d4-methanol) δ 22.2, 23.7, 23.8, 26.3, 38.5, 39.6, 40.3, 41.4, 46.0, 52.9, 54.2, 59.7, 113.3, 119.7, 128.4, 128.6, 129.8, 129.9, 130.0, 131.2, 131.3, 134.2, 138.8, 144.5, 158.8, 169.9, 176.4; *m/z* (FAB) 557.2876 ($M^+$+1, $C_{31}H_{36}N_6O_4$ requires 557.2876).

Saponification of **48** following the general procedure described previously afforded **49** as a colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 0.88 (6H, dd, *J* 4.7 and 6.3), 1.28-1.55 (3H, m), 2.70-2.95 (3H, m), 3.05-3.27 (2H, m), 3.83 (1H, d, *J* 14.7), 4.06-4.16 (1H, m), 4.45 (1H, d, *J* 15.5), 4.63-4.73 (2H, m), 5.41-5.51 (2H, m), 7.06-7.29 (8H, m), 7.73-7.91 (3H, m); $\delta_C$ (125 MHz, MeOH) δ 22.6, 24.2, 26.3, 38.6, 39.2, 40.4, 43.9, 46.2, 56.4, 60.5, 113.2, 119.7, 127.8, 128.4, 128.8, 129.8, 130.0, 131.2, 134.3, 139.0, 143.0, 144.7, 158.5, 170.1, 181.5; *m/z* (FAB) 565.2546 ($M^+$+Na, $C_{30}H_{34}N_6O_4Na$ requires 565.2539).

### Syntheses of compounds 50-51

Scaffold **14a4** was coupled to the L-methionine methyl ester isocyanate following the previously described general procedures to give trityl-protected **50** as a colorless oil in 86% yield: $\delta_H$ (500 MHz, d4-methanol) 1.42 (3H, s), 1.48 (1H, m), 1.75 (1H, m), 1.99 (1H, s), 2.14 (2H, m), 2.90 (1H, ddd, *J* 14.5, 11.0 and 3.2), 2.99 (1H, dd, *J* 13.5 and 9.0), 3.15 (1H, brd, *J* 12.0), 3.30 (1H, dd, *J* 13.5 and 3.5), 3.36 (1H, dt, *J* 12.0, 12.0 and 4.0), 3.62 (3H, s), 4.00 (1H, brd, *J* 13.0), 4.20-4.34 (2H, m), 4.38 (1H, d, *J* 14.5), 4.40-4.42 (2H, m), 4.54 (1H, d, *J* 14.5), 7.00-7.35 (21H, m); *m/z* (FAB) 716.3269 ($M^+$+1, $C_{42}H_{46}N_5O_4S$ requires 716.3270).

Deprotection of the above mentioned compound following the general procedure described previously afforded **50** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 1.62 (1H, m), 1.79 (1H, m), 2.06 (3H, s), 2.24 (2H, t, *J* 7.2), 2.40 (3H, s), 3.12 (3H, m), 3.31 (1H, brd, *J* 12.0), 3.48 (1H, m), 3.68 (3H, s), 4.11 (1H, brd, *J* 12.0), 4.33 (1H, dd, *J* 12.5 and 7.2), 4.59 (2H, brs), 4.63 (1H, m), 4.88 (1H, brs), 7.15-7.35 (5H, m), 8.46 (1H, s); $\delta_C$ (125 MHz, MeOH) 9.5, 15.7, 30.3, 31.9, 37.8, 37.9, 40.4, 47.0, 52.7, 53.2, 60.5, 124.6, 127.7, 128.7, 129.2, 129.3, 129.9, 129.9, 132.7, 137.6, 156.5, 168.4, 173.4; *m/z* (FAB) 474.2173 ($M^+$+1, $C_{23}H_{32}N_5O_4S$ requires 474.2175).

Saponification of **50** following the general procedure described previously afforded **51** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 1.62 (1H, m), 1.82 (1H, m), 1.89 (3H, s), 2.12 (3H, s), 2.15 (2H, t, *J* 7.0), 2.78 (2H, m), 3.06-3.18 (3H, m), 3.72 (1H, brd, *J* 12.0), 3.98 (1H, dd, *J* 8.0 and 4.8), 4.34 (1H, d *J* 14.8), 4.42 (1H, d *J* 14.8), 4.61 (1H, t, *J* 5.6), 7.00-7.10 (5H, m), 7.47 (1H, s); $\delta_C$ (125 MHz, MeOH) 10.3, 15.7, 31.8, 34.3, 38.8, 39.4, 42.9, 46.9, 57.0, 60.5, 128.4, 129.1, 129.6, 130.0, 130.0, 131.2, 131.2, 135.4, 138.1, 158.5, 169.9, 179.4; *m/z* (FAB) 460.2019 ($M^+$+1, $C_{22}H_{30}N_5O_4S$ requires 460.2019).

### Syntheses of compounds 52-59

Scaffold **14a4** was coupled to the D-leucine methyl ester isocyanate following the previously described general procedures to give trityl-protected **52** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.81 (3H, d, *J* 6.2), 0.85 (3H, d, *J* 6.2), 1.39 (3H, s), 1.40-1.60

(3H, m), 2.55 (1H, m), 2.86 (1H, brd, *J* 12.0), 3.17 (3H, m), 3.59 (3H, s), 3.68 (1H, brd, *J* 13.0), 4.23 (1H, m), 4.40 (2H, m), 4.67 (1H, m), 6.30 (1H, brs), 7.00-7.14 (11H, m), 7.16 (1H, s), 7.25-7.36 (9H, m); *m/z* (FAB) 498.3706 ($M^{+}$+1, $C_{43}H_{48}N_5O_4$ requires 498.3706).

Deprotection of the above mentioned compound following the general procedure described previously afforded **52** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 0.84 (3H, d, *J* 6.2), 0.88 (3H, d, *J* 6.2), 1.50 (3H, m), 2.32 (3H, s), 2.76 (1H, m), 2.86 (1H, dt, *J* 11.5 and 4.5), 3.21 (1H, m), 3.39 (2H, m), 3.63 (3H, s), 3.78 (1H, brd, *J* 14.0), 4.24 (1H, dd, *J* 10.0 and 5.0), 4.55 (2H, m), 4.77 (1H, m), 7.02-7.20 (5H, m), 8.72 (1H, s); *m/z* (FAB) 456.2612 ($M^{+}$+1, $C_{24}H_{34}N_5O_4$ requires 456.2611).

Saponification of **52** following the general procedure described previously afforded **53** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.82 (3H, d, *J* 4.5 ), 0.84 (3H, d, *J* 4.5), 1.50 (3H, m), 2.16 (3H, s), 2.61 (1H, ddd, *J* 13.5, 10.0 and 4.0), 2.73 (1H, dt, *J* 12.5 and 4.0), 3.17 (2H, m), 3.20 (1H, m), 3.56 (1H, dt, *J* 13.5 and 4.0), 4.13 (1H, dd, *J* 10.0 and 4.5), 4.34 (1H, d, *J* 14.5), 4.46 (1H, d, *J* 14.5), 4.71 (1H, t, *J* 5.5), 6.98-7.07 (5H, m), 7.44 (1H, s); *m/z* (FAB) 442.2455 ($M^{+}$+1, $C_{23}H_{32}N_5O_4$ requires 442.2454).

Scaffold **14a4** was coupled to the L-valine methyl ester isocyanate following the previously described general procedures to give trityl-protected **54** as a colorless oil in 80% yield: $\delta_H$ (500 MHz, d4-methanol) 0.76 (6H, d, *J* 7.0), 1.39 (3H, s), 1.89 (1H, m), 2.75 (1H, ddd, *J* 14.0, 10.5 and 4.0), 2.89 (1H, dt, *J* 12.5 and 3.5), 3.09-3.20 (3H, m), 3.59 (3H, s), 3.76 (1H, brd, *J* 14.0), 3.92 (1H, m), 4.41 (2H, brs), 4.68 (1H, t, *J* 5.6), 5.94 (1H, brs), 7.00-7.18 (11H, m), 7.20 (1H, s), 7.26-7.40 (9H, m); *m/z* (FAB) 484.3552 ($M^{+}$+1, $C_{42}H_{46}N_5O_4$ requires 484.3550).

Deprotection of the above mentioned compound following the general procedure described previously afforded **54** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 0.74 (6H, d, J 7.0), 1.85 (1H, m), 2.27 (3H, s), 2.85 (1H, ddd, J 14.0, 10.5 and 3.5), 2.93 (1H, dt, J 12.0 and 3.5), 3.11 (2H, m), 3.30 (1H, ddd, J 12.0, 11.0 and 4.5), 3.59 (3H, s), 3.80 (1H, brd, J 14.0), 3.86 (1H, d, J 7.2), 4.48 (1H, d, J 15.8), 4.52 (1H, d, J 15.8), 4.70 (1H, t, J 5.7), 7.00-7.05 (2H, m), 7.08-7.13 (3H, m), 8.65 (1H, s); m/z (FAB) 442.2455 ($M^{+}$+1, $C_{23}H_{32}N_5O_4$ requires 442.2454).

Saponification of **54** following the general procedure described previously afforded **55** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.67 (3H, d, J 7.0), 0.72 (3H, d, J 6.6), 1.90 (1H, m), 2.15 (3H, s), 2.80 (2H, m), 3.13 (2H, d, J 5.7), 3.17 (1H, m), 3.59 (3H, s), 3.80 (1H, brd, J 14.0), 3.86 (1H, d, J 7.2), 4.48 (1H, d, J 15.8), 4.52 (1H, d, J 15.8), 4.70 (1H, t, J 5.7), 7.00-7.05 (2H, m), 7.08-7.13 (3H, m), 7.49 (1H, s); m/z (FAB) 428.2297 ($M^{+}$+1, $C_{22}H_{29}N_5O_4$ requires 428.2298).

Scaffold **14a4** was coupled to the L-phenylalanine methyl ester isocyanate following the previously described general procedures to give trityl-protected **56** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 1.36 (3H, s), 2.42 (1H, m), 2.78 (2H, m), 2.90 (1H, dd, *J* 13.5 and 5.5), 3.07 (3H, m), 3.56 (1H, m), 3.60 (3H, s), 4.36 (2H, m), 4.40 (1H, m), 4.61 (1H, t, *J* 5.2), 6.87 (1H, brs), 7.00-7.40 (25H, m); *m/z* (FAB) 732.3547 ($M^{+}$+1, $C_{46}H_{46}N_5O_4$ requires 732.3550)

Deprotection of the above mentioned compound following the general procedure described previously afforded **56** as colorless oil in 86% yield: $\delta_H$ (500 MHz, d4-methanol) 2.26 (3H, s), 2.53 (1H, m), 2.79 (2H, m), 2.92 (1H, dd, *J* 13.5 and 5.0), 3.09 (3H, m), 3.59 (3H, s), 3.64 (1H, m), 4.37 (1H, dd, *J* 10.2 and 5.5), 4.47 (2H, brs), 4.65 (1H, t, *J* 5.2), 6.84 (1H, brs), 7.01-7.22 (10H, m), 8.69 (1H, s); *m/z* (FAB) 490.2456 ($M^{+}$+1, $C_{27}H_{32}N_5O_4$ requires 490.2454.

Saponification of **56** following the general procedure described previously afforded **57** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 2.14 (3H, s), 2.40 (1H, m), 2.67 (1H, dt, *J* 12.5 and 3.7), 2.84 (1H, dd, *J* 13.5 and 8.0), 2.89 (1H, m), 2.99 (1H, ddd, *J* 12.5, 10.0 and 4.5), 3.09 (2H, m), 3.44 (1H, brd, *J* 13.0), 4.33 (1H, m), 4.37 (2H, m), 4.64 (1H, t, *J* 5.0), 6.84 (1H, brs), 6.98-7.20 (10H, m), 7.46 (1H, s); $\delta_C$ (125 MHz, MeOH) 10.4, 38.6, 39.9, 40.1, 42.9, 46.7, 58.7, 59.5, 127.7, 128.2, 129.6, 129.6, 129.7, 129.7, 129.7, 130.9, 130.9,131.3, 131.3, 135.4, 138.8, 140.3, 145.8, 158.3, 169.9, 179.6; *m/z* (FAB) 476.2298 ($M^+$+1, $C_{26}H_{30}N_5O_4$ requires 476.2298).

Scaffold **14a4** was coupled to the β-cyclohexyl-L-alanine methyl ester isocyanate following the previously described general procedures to give trityl-protected **58** as colorless oil in 87% yield: $\delta_H$ (500 MHz, d4-methanol) 0.79 (1H, m), 0.87 (1H, m), 1.11 (2H, m), 1.19 (2H, m), 1.40 (3H, s), 1.45 (2H, m), 1.61 (4H, m), 2.63 (1H, ddd, *J* 14.0, 10.8 and 3.5), 2.85 (1H, dt, *J* 12.1 and 3.5), 3.09 (1H, dd, *J* 13.5 and 5.0), 3.16 (2H, m), 3.59 (3H, s), 3.72 (1H, brd, *J* 14.0), 4.18 (1H, m), 4.41 (2H, brs), 4.70 (1H, t, *J* 5.5), 6.31 (1H, brs), 7.00-7.19 (11H, m), 7.21 (1H, s), 7.23-7.39 (9H, m); *m/z* (FAB) 738.4021 ($M^+$+1, $C_{46}H_{52}N_5O_4$ requires 738.4019).

Deprotection of the above mentioned compound following the general procedure described previously afforded **58** as a colorless oil in 89% yield: $\delta_H$ (500 MHz, d4-methanol) 0.78 (1H, m), 0.86 (1H, m), 1.10 (2H, m), 1.17 (2H, m), 1.43 (2H, m), 1.60 (4H, m), 2.27 (3H, s), 2.72 (1H, ddd, *J* 14.0, 10.5 and 3.5), 2.88 (1H, dt, *J* 12.0 and 3.5), 3.13 (2H, m), 3.28 (1H, ddd, *J* 12.5, 10.5 and 4.0), 3.58 (3H, s), 3.76 (1H, brd, *J* 14.0), 4.14 (1H, dd, *J* 10.0 and 5.5), 4.48 (1H, d, *J* 15.5), 4.52 (1H, d, *J* 15.5), 4.71(1H, t, *J* 5.2), 6.98-7.22 (5H, m), 8.68 (1H, s); *m/z* (FAB) 496.2922 ($M^+$+1, $C_{27}H_{38}N_5O_4$ requires 496.2924).

Saponification of **58** following the general procedure described previously afforded **59** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.78 (2H, m), 1.05 (2H, m), 1.13 (2H, m), 1.27 (1H, m), 1.43 (1H, m), 1.56 (3H, m), 1.69 (1H, m), 2.14 (3H, s), 2.64 (1H, ddd, *J* 14.0, 10.5 and 3.5), 2.78 (1H, brd, *J* 12.0), 3.09-3.16 (3H, m), 3.68 (1H, brd, *J* 14.0), 4.07 (1H, dd, *J* 10.0 and 4.5), 4.35 (1H, d, *J* 15.0), 4.42 (1H, d, *J* 15.0), 4.66(1H, t, *J* 5.0), 7.00-7.06 (5H, m), 7.46 (1H, s); $\delta_C$ (125 MHz, MeOH) 10.37, 27.7, 27.8, 28.1, 33.9, 35.4, 35.9, 38.8, 39.7, 41.9, 42.9, 46.9, 55.4, 60.2, 128.4, 129.0, 129.6, 129.9, 129.9, 131.3, 131.3, 135.4, 139.1, 158.8, 169.9, 181.2; *m/z* (FAB) 482.2766 ($M^+$+1, $C_{26}H_{36}N_5O_4$ requires 482.2767).

**Syntheses of compounds 60-66**

Scaffold **14a4** was coupled to commercial available tert-butyl isocyanate following the previously described general procedures to give trityl-protected **61** as a colorless oil in 90% yield: $\delta_H$ (500 MHz, d4-methanol) 1.02 (9H, s), 1.39 (3H, s), 2.88 (1H, ddd, *J* 14.0, 11.0 and 3.5), 2.97 (1H, m), 2.99 (1H, dd, *J* 13.5 and 8.5), 3.13 (1H, dd, *J* 13.5 and 4.5), 3.18 (1H, m), 3.84 (1H, brd, *J* 14.0), 4.40 (1H, d, *J* 14.8), 4.45 (1H, d, *J* 14.8), 4.49 (1H, dd, *J* 8.5 and 4.0), 7.00-7.32 (21H, m); *m/z* (FAB) 626.3492 ($M^+$+1, $C_{40}H_{44}N_5O_2$ requires 626.3495).

Deprotection of the above mentioned compound following the general procedure described previously afforded **61** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 1.25 (9H, s), 2.54 (3H, s), 2.88 (1H, ddd, *J* 14.5, 11.0 and 4.5), 3.27 (2H, m), 3.40 (1H, dd, *J* 13.5 and 3.8), 3.58 (1H, ddd, *J* 11.6, 10.8 and 4.2), 4.13 (1H, brd, *J* 14.0), 4.78 (2H, brs), 4.79 (1H, m), 7.32-7.44 (5H, m), 8.91 (1H, s); *m/z* (FAB) 384.2401 ($M^+$+1, $C_{21}H_{30}N_5O_2$ requires 384.2400).

Scaffold **14a4** was coupled to commercial available *p*-tolyl isocyanate following the previously described general procedures to give trityl-protected **60** as colorless oil in 90% yield: $\delta_H$ (500 MHz, d4-methanol) 1.40 (3H, s), 2.17 (3H, s), 2.90 (1H, ddd, *J* = 14.5, 10.0 and 3.2), 2.98 (1H, dd, *J* 12.0 and 3.2), 3.15 (2H, d, *J* 5.5), 3.26 (2H, m), 3.90 (1H, brd, *J* 13.0), 4.40 (1H, d, *J* 14.5), 4.48 (1H, d, *J* 14.5), 6.90-7.40 (21H, m); *m/z* (FAB) 660.3342 ($M^+$+1, $C_{43}H_{42}N_5O_2$ requires 660.3339).

Deprotection of the above mentioned compound following the general procedure described previously afforded **60** as colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 2.16 (3H, s), 2.29 (3H, s), 3.01 (2H, m), 3.17 (2H, m), 3.38 (1H, ddd, *J* 12.0, 12.0 and 4.0), 3.94 (1H, brd, *J* 13.0), 4.54 (2H, m), 4.84 (2H, m), 6.92 (4H, m), 7.10 (5H, m), 8.66 (1H, s); *m/z* (FAB) 418.2242 ($M^+$+1, $C_{24}H_{28}N_5O_2$ requires 418.2243).

Scaffold **14a4** was coupled to commercial available propyl isocyanate following the previously described general procedures to give trityl-protected **62** as colorless oil in 77% yield: $\delta_H$ (500 MHz, d4-methanol) 0.86 (3H, t, *J* 7.4), 1.38-1.46 (2H, m), 1.48 (3H, s), 2.86-2.94 (1H, m), 2.99-3.10 (3H, m), 3.19 (2H, brd, *J* 5.0), 3.28-3.34 (1H, m), 3.87 (1H, brd, *J* 13.4), 4.50 (1H, d, *J* 14.8), 4.54 (1H, d, *J* 14.9), 4.76 (1H, t, *J* 5.6), 6.30 (1H, t, *J* 5.0), 6.92 (2H, t, *J* 8.7), 7.14-7.17 (8H, m), 7.28 (1H, s), 7.37-7.38 (9H, m); $\delta_C$ (125 MHz, d4-methanol) 12.1, 12.7, 24.7, 37.9, 39.6, 43.9, 44.1, 47.0, 59.7, 77.1, 116.4, 116.6, 129.7, 129.7, 130.6, 131.5, 132.9, 132.9, 135.0, 135.0, 136.2, 139.2, 143.2, 159.1, 159.1, 162.7, 164.7, 169.7; *m/z* (FAB) 630.3245 ($M^+$+1, $C_{39}H_{40}FN_5O_2$ requires 630.3244).

Deprotection of the trityl protected **62** following the general procedure described previously afforded **62** as colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 0.85 (3H, t, *J* 7.4), 1.37-1.45 (2H, m), 2.40 (3H, s), 2.99-3.05 (3H, m), 3.13 (1H, dt, *J* 3.5 and 11.9), 3.21 (2H, d, *J* 6.0), 3.41-3.48 (1H, m), 3.91 (1h, brd, *J* 13.9), 4.64 (2H, s), 4.81 (1H, t, *J* 5.8), 6.97 (2H, t, *J* 8.8), 7.12-7.16 (2H, m), 8.79 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 9.4, 11.9, 24.6, 37.8, 39.5, 41.1, 43.9, 48.1, 59.7, 116.4, 116.5, 126.0, 129.9, 132.8, 134.4, 159.1, 162.8, 164.7, 170.7; *m/z* (FAB) 388.2148 ($M^+$+1, $C_{20}H_{26}FN_5O_2$ requires 388.2149).

Scaffold **14a4** was coupled to commercial available isocyanato-cyclohexane following the previously described general procedures to give trityl-protected **63** as colorless oil in 70% yield: $\delta_H$ (500 MHz, d4-methanol) 1.00-1.85 (13H, m), 2.85-2.98 (1H, m), 3.02-3.50 (5H, m), 3.91 (1H, brd, *J* 14.2), 4.54 (2H, s), 4.75 (1H, t, *J* 6.0), 5.77 (1H, brd, *J* 5.77), 6.90-7.21 (9H, m), 7.27 (1H, s), 7.31-7.45 (10H, m); $\delta_C$ (125 MHz, d4-methanol) $\delta$ 12.6, 26.9, 27.1, 34.8, 37.8, 39.4, 44.1, 47.1, 51.7, 59.9, 77.1, 116.5, 116.7, 129.7, 130.6, 131.5, 132.9, 135.1, 136.2, 139.2, 143.2, 158.4, 162.8, 164.7, 169.7; *m/z* (FAB) 670.3556 ($M^+$+1, $C_{42}H_{44}FN_5O_2$ requires 670.3557).

Deprotection of the trityl protected **63** following the general procedure described previously afforded **63** as colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 0.86-1.12 (3H, m), 1.12-1.28 (2H, m), 1.49-1.74 (5H, m), 2.32 (3H, s), 2.92-2.99 (1H, m), 3.04-3.14 (3H, m), 3.25-3.39 (2H, m), 3.87 (1H, brd, *J* 13.9), 4.55 (2H, s), 4.71 (1H, t, *J* 6.2), 6.90 (2H, t, *J* 8.8), 7.04-7.09 (2H, m), 8.70 (1H, s); $\delta_C$ (100 MHz, d4-methanol) $\delta$ 9.4, 26.8, 27.0, 34.6, 34.8, 37.7, 39.3, 41.1, 51.6, 59.7, 116.4, 116.6, 126.0, 129.9, 132.8, 134.5, 158.3, 162.6, 165.0, 170.7; *m/z* (FAB) 428.2463 ($M^+$+1, $C_{23}H_{30}FN_5O_2$ requires 428.2462).

Scaffold **14a4** was coupled to commercial available isocyanatomethyl-benzene following the previously described general procedures to give trityl-protected **64** as colorless oil in 67% yield: $\delta_H$ (500 MHz, d4-methanol) 1.48 (3H, s), 2.92-2.99 (1H, m), 3.02-3.09 (1H, m), 3.20 (2H, d, *J* 6.0), 3.29-3.32 (1H, m), 3.90 (1H, brd, *J* 13.3), 4.27 (2H, s), 4.50 (1H, d, *J* 14.7), 4.54 (1H, d, *J* 14.8), 4.81 (1H, t, *J* 5.9), 6.91 (2H, t, *J* 8.8), 7.12-7.16 (10H, m), 7.19-7.23 (1H, m), 7.26-7.29 (3H, m), 7.37-7.39 (9H, m); $\delta_C$ (125 MHz, d4-methanol) 12.6, 37.8, 39.7, 44.1, 45.6, 47.0, 59.7, 77.1, 116.4, 116.6, 128.3, 128.6, 129.7, 129.7, 130.6, 131.5, 132.8, 132.9, 134.9, 136.2, 139.2, 141.6, 143.2, 159.0, 162.7, 164.6, 169.7; *m/z* (FAB) 678.3244 ($M^+$+1, $C_{43}H_{40}FN_5O_2$ requires 678.3244).

Deprotection of the trityl protected **64** following the general procedure described previously afforded **64** as colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 2.30 (3H, s), 2.96-3.09 (2H, m), 3.13 (2H, d, *J* 6.0), 3.33-3.41 (1H, m), 3.86 (1H, brd, *J* 13.7), 4.14 (1H, d, *J* 15.4), 4.18 (1H, d, *J* 15.4), 4.52 (1H, d, *J* 15.6), 4.57 (1H, d, *J* 15.6), 4.78 (1H, t, *J* 6.0), 6.86 (2H, t, *J* 8.8), 7.00-7.07 (4H, m), 7.10-7.23 (3H, m), 8.66 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 9.4, 37.7, 39.6, 41.1, 45.5, 48.1, 59.7, 116.4, 116.6, 125.9, 128.3, 128.5, 129.7, 132.8, 134.4, 134.8, 141.5, 159.1, 162.5, 164.9, 170.7; *m/z* (FAB) 436.2150 ($M^+$+1, $C_{24}H_{26}FN_5O_2$ requires 436.2149).

Scaffold **14a4** was coupled to commercial available 1-bromo-4-isocyanatomethyl-benzene following the previously described general procedures to give trityl-protected 65 as colorless oil in 66% yield: $\delta_H$ (500 MHz, d4-methanol) 1.45 (3H, s), 2.85-2.92 (1H, m), 3.01-3.07 (1H, m), 3.16 (1H, d, *J* 12.2), 3.27 (1H, dd, *J* 3.7 and 13.7), 3.37-3.42 (1H, m), 4.03-4.19 (3H, m), 4.41 (1H, d, *J* 14.6), 4.46 (1H, brd, *J* 5.4), 4.58 (1H, d, *J* 14.6), 6.84 (2H, t, *J* 8.5), 6.91 (2H, d, *J* 8.2), 7.08-7.13 (8H, m), 7.23 (1H, s), 7.32-7.44 (11H, m); $\delta_C$ (125 MHz, d4-methanol)12.6, 37.8, 39.6, 44.1, 44.9, 47.0, 59.7, 77.1, 116.4, 116.6, 121.9, 129.7, 129.7, 130.5, 130.6, 131.2, 131.5, 131.8, 132.8, 132.8, 132.9, 134.9, 134.9, 136.2, 139.2, 141.0, 143.2, 158.9, 162.5, 164.9, 169.6; *m/z* (FAB) 756.2351 ($M^+$+1, $C_{43}H_{39}BrFN_5O_2$ requires 756.2349).

Deprotection of the trityl protected **65** following the general procedure described previously afforded **65** as colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 2.40 (3H, s), 3.08-3.24 (4H, m), 3.37-3.49 (1H, m), 3.96 (1H, brd, *J* 14.8), 4.19 (2H, s), 4.64 (2H, s), 4.85 (1H, t, *J* 6.2), 6.96 (2H, t, *J* 8.6), 7.03 (2H, d, *J* 7.8), 7.07-7.16 (2H, m), 7.42 (2H, d, *J* 7.5), 8.79 (1H, s); $\delta_C$ (125 MHz, d4-methanol) $\delta$ 9.4, 37.7, 39.5, 41.1, 44.9, 48.1, 59.6, 116.4, 116.6, 121.9, 125.9, 129.9, 130.5, 132.7, 134.5, 134.8, 140.9, 158.9, 162.5, 165.0, 170.6; *m/z* (FAB) 514.1254 ($M^+$+1, $C_{24}H_{25}BrFN_5O_2$ requires 514.1254).

Scaffold **14a4** was coupled to commercial available 1-isocyanatomethyl-naphthalene following the previously described general procedures to give trityl-protected **66** as colorless oil in 68% yield: $\delta_H$ (500 MHz, d4-methanol) 1.39 (3H, s), 2.97-3.11 (2H, m), 3.17 (1H, dt, *J* 2.6 and 11.9), 3.34 (1H, dd, *J* 3.6 and 13.8), 3.41-3.49 (1H, m), 4.16 (1H, brd, *J* 13.6), 4.39 (1H, d, *J* 14.6), 4.57 (1H, d, *J* 14.6), 4.61-4.68 (1H, m), 6.06 (1H, s), 6.94 (2H, t, *J* 8.6), 7.00-7.05 (7H, m), 7.18-7.37 (16H, m), 7.51 (1H, dd, *J* 1.8 and 7.3), 7.70 (1H, d, *J* 8.5); $\delta_C$ (125 MHz, d4-methanol) 12.1, 37.3, 38.0, 43.6, 45.7, 61.4, 75.5, 116.3, 116.5, 121.3, 121.4, 125.6, 125.9, 126.2, 126.3, 128.2, 128.4, 128.4, 128.7, 128.8, 130.3, 131.6, 131.7, 133.7, 135.4, 138.3, 142.0, 155.6, 161.3, 163.8, 166.7; *m/z* (FAB) 714.3244 ($M^+$+1, $C_{46}H_{40}FN_5O_2$ requires 714.3244).

Deprotection of the trityl protected **66** following the general procedure described previously afforded **66** as colorless oil in 100% yield: $\delta_H$ (500 MHz, d4-methanol) 2.33 (3H, s), 3.17-3.31 (4H, m), 3.51-3.58 (1H, m), 4.14 (1H, brd, *J* 14.0), 4.60 (2H, s), 4.96-4.99 (1H, m), 6.98 (2H, t, *J* 8.8), 7.11 (1H, dd, *J* 0.9 and 7.4), 7.19-7.23 (2H, m), 7.31-7.43 (4H, m), 7.66 (1H, d, *J* 8.3), 7.77 (1H, d, *J* 8.6), 8.66 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 9.5, 37.8, 39.7, 41.1, 48.3, 59.8, 116.6, 116.8, 124.4, 125.6, 126.0, 126.8, 127.4, 128.0, 129.5, 130.0, 130.8, 132.0, 133.1, 134.5, 135.7, 136.1, 158.2, 162.7, 165.1, 170.6; *m/z* (FAB) 472.2149 ($M^+$+1 requires 472.2149).

## Syntheses of compounds 67, 68, 71 and 72

Compounds **11b** and **11d** were synthesized using conditions similar to that described for the synthesis of compound **11a**, and were purified using the same chromatographic condition. Using Cbz-β-(1-naphthyl)-L-alanine, compound **11b** was obtained as a white solid in 80% yield: m.p. 131-132 °C; $\delta_H$ (500 MHz, $CDCl_3$) 3.10 (3H, s), 3.15 (3H, s), 3.39 (1H, m), 3.61 (1H, m), 3.82 (1H, t, *J* 5.5), 4.50 (1H, m), 5.10 (2H, brs), 5.28 (1H, m), 5.59 (1H, m), 7.28-7.38 (7H, m), 7.48 (1H, t, *J* 7.5), 7.54 (1H, t, *J* 7.5), 7.75 (1H, d, *J* 8.0), 7.84 (1H, d, *J* 8.0), 8.21 (1H, d, *J* 8.5); *m/z* (FAB) 437.2075 ($M^+$+1, $C_{25}H_{29}N_2O_5$ requires 437.2076).

Using Cbz-D-phenylalanine, compound **11d** was obtained as a white solid in 99% yield: m.p. 123-124 °C; $\delta_H$ (500 MHz, $CDCl_3$) 2.99 (1H, m), 3.09 (1H, m), 3.26 (3H, s), 3.27 (3H, s), 4.16 (1H, t, *J* 5.5), 4.35 (1H, m), 5.07 (2H, brs), 5.31 (1H, m), 5.74 (1H, m), 7.15-7.36 (10H, m); *m/z* (FAB) 387.1921 ($M^+$+1, $C_{21}H_{27}N_2O_5$ requires 387.1920).

The naphthyl-derived scaffold **12b** was synthesized using conditions slightly different from that described for the synthesis of compound **12a**. Compound **11b** (3.1 g, 7.1 mmol) was dissolved in 100 mL 70% TFA/$H_2O$ and the solution was stirred at rt overnight. The solvent was removed under reduced pressure to give a yellow oil, which was dissolved in 150 mL ethyl acetate and washed with saturated $NaHCO_3$ and brine. The organic phase was dried over anhydrous $Na_2SO_4$, and the solvent was removed to give a mixture of the uncyclized aldehyde and the desired product. The mixture was subjected to silica gel column chromatography using hexanes/EtOAc (2:1 – 1:1) as eluant to afford compound **12b** as a yellowish oil (700 mg, 25%): $\delta_H$ (500 MHz, $CDCl_3$) 3.23 (0.6H, dd, *J* 14.0 and 10.2), 3.23 (0.4H, dd, *J* 14.0 and 7.3), 3.56 (1H, m), 3.82 (0.6H, d, *J* 12.0), 4.72 (0.6H, d, *J* 12.0), 4.97 (0.4H, d, *J* 12.0), 5.03 (0.4H, d, *J* 12.0), 5.08 (0.6H, dd, *J* 9.5 and 3.5), 5.25 (0.4H, t, *J* 6.5), 5.35 (0.2H, d, *J* 5.5), 5.36 (0.2H, d, *J* 5.5), 5.75 (0.3H, d, *J* 5.5), 5.76 (0.3H, d, *J* 5.5), 6.05 (0.4H, d, *J* 6.0), 6.43 (0.6H, d, *J* 6.0), 6.61 (1H, d, *J* 7.5), 7.10-8.15 (11H, m); *m/z* (FAB) 373.1551 ($M^+$+1, $C_{23}H_{21}N_2O_3$ requires 373.1552).

Compound **12d** was synthesized using conditions similar to that described for the synthesis of compound **12a**. Compound **12d** was obtained in 88% yield as a colorless solid: m.p. 141-142 °C; $\delta_H$ (500 MHz, $CDCl_3$) 2.91-3.07 (2H, m), 4.48 (0.5H, d, *J* 12.0), 4.66 (0.5H, t, *J* 6.8), 4.95 (0.5H, d, *J* 12.0), 5.03 (0.5H, d, *J* 12.0), 5.05 (0.5H, t, *J* 6.8), 5.11 (0.5H, d, *J* 12.0), 5.40 (0.25H, d, *J* 5.0), 5.41 (0.25H, d, *J* 5.0), 5.65 (0.25H, d, *J* 5.0), 5.66 (0.25H, d, *J* 5.0), 6.16 (0.5H, d, *J* 5.5), 6.38 (0.5H, d, *J* 5.5), 7.07-7.36 (10H, m), 7.56 (1H, s); *m/z* (FAB) 323.1396 ($M^+$+1, $C_{19}H_{19}N_2O_3$ requires 323.1396).

Alkylation of compounds **12b** or **12d** with 4-chloromethyl-5-methyl-1-tritylimidazole[26] (**9**) using conditions similar to that described for the synthesis of compound **13a2**, afforded compounds **13b** and **13d** as colorless oils with 65-70% yields.

Compound **13b** $\delta_H$ (500 MHz, $CDCl_3$) 1.45 (1.2H, s), 1.46 (1.8H, s), 3.08-3.48 (2H, m), 3.72 (0.5H, d, *J* 12.0), 4.51 (0.5H, d, *J* 14.5), 4.53 (1H, m), 4.67 (0.5H, d, *J* 12.0), 4.76 (0.5H, d, *J* 14.5), 4.91 (0.5H, d, *J* 12.5), 4.95 (0.5H, d, *J* 12.5), 5.08 (0.5H, m), 5.22 (0.5H, m), 5.73 (0.4H, d, *J* 6.0), 6.03 (0.6, d, *J* 6.0), 6.07 (0.4H, d, *J* 6.0), 6.42 (0.6H, d, *J* 6.0), 6.56 (1H, d, *J* 7.0), 7.07-8.14 (28H, m); *m/z* (FAB) 709.3181 ($M^+$+1, $C_{47}H_{41}N_4O_3$ requires 709.3179).

Compound **13d** $\delta_H$ (500 MHz, $CDCl_3$) δ 1.44 (1.5 H, s), 1.48 (1.5H, s), 2.77-2.95 (2H, m), 4.39 (0.5 H, d, *J* 12.0), 4.47 (0.5H, d, *J* 15.0), 4.49 (0.5 H, d, *J* 15.0), 4.62 (0.5H, d, *J* 14.5), 4.73 (0.5H, d, *J* 4.5), 4.88 (0.5H, t, *J* 7.0), 5.06 (0.5H, d, *J* 2.0), 4.90 (0.5H, d, *J* 12.0), 4.98 (0.5H, d, *J* 12.0), 5.03 (0.5H, t, *J* 7.0), 5.75 (0.5H, d, *J* 6.0), 5.92 (0.5H, d, *J* 6.0), 6.14 (0.5H, d, *J* 6.0), 6.36 (0.5H, d, *J* 6.0), 7.04-7.35 (26H, m); *m/z* (FAB) 659.3025 ($M^+$+1, $C_{43}H_{39}N_4O_3$ requires 659.3022).

Compounds **14b** and **14d** were obtained as colorless oils in 95-99% yields by hydrogenation of compounds **13b** or **13d**, using similar conditions described previously. Compound **14b**: $\delta_H$ (500 MHz, $CDCl_3$) 1.45 (3H, s), 2.71 (1H, m), 2.90-3.01 (2H, m), 3.27 (1H, dt, *J* 12.0 and 3.5), 3.39 (1H, m), 3.67 (1H, dd, *J* 11.0 and 3.0), 3.52 (1H, dd, *J* 14.0 and 2.5), 4.42 (1H, d, *J* 14.5), 4.63 (1H, d, *J* 14.5), 7.04-7.35 (17H, m), 7.39-7.48 (3H, m), 7.68 (1H, dd, *J* 7.5 and 1.5), 7.78 (1H, d, *J* 7.5), 8.17 (1H, d, *J* 7.5); *m/z* (FAB) 577.2968 ($M^+$+1, $C_{39}H_{37}N_4O$ requires 577.2967).

Compound **14d**: $\delta_H$ (500 MHz, $CDCl_3$) 1.41 (3H, s), 2.42 (1H, br), 2.76 (2H, m), 2.98 (1H, dt, *J* 12.5 and 4.0), 3.29 (2H, m), 3.38 (1H, dd, *J* 13.7 and 3.5), 3.52 (1H, dd, *J* 10.0 and 3.5), 4.33 (1H, d, *J* 14.5), 4.61 (1H, d, *J* 14.5), 7.04-7.26 (21H, m); *m/z* (FAB) 527.2812 ($M^+$+1, $C_{35}H_{35}N_4O$ requires 527.2811).

Scaffold **14b** was coupled to L-leucine methyl ester isocyanate following the previously described general procedures to give trityl-protected **67** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, $CDCl_3$) 0.58 (3H, d, *J* 6.0), 0.60 (3H, d, *J* 6.0), 1.43 (3H, s), 3.07-3.26 (4H, m), 3.36 (1H, m), 3.43 (3H, s), 3.81 (1H, dd, *J* 14.0 and 7.0), 4.00 (1H, dd, *J* 14.0 and 3.0), 4.16 (1H, brd, *J* 13.5), 4.37 (1H, d, *J* 14.7), 4.55 (1H, brd, *J* 9.3), 4.60 (1H, d, *J* 14.7), 7.03-7.32 (19H, m); 7.45 (1H, t, *J* 7.5), 7.55 (1H, t, *J* 7.5), 7.69 (1H, d, *J* 8.0), 7.79 (1H, d, *J* 8.0); *m/z* (FAB) 748.3861 ($M^+$+1, $C_{47}H_{50}N_5O_4$ requires 748.3863).

Deprotection of the above mentioned compound following the general procedure described previously afforded **67** as a colorless oil in 88% yield: $\delta_H$ (500 MHz, d4-methanol) 0.43 (1H, m), 0.61 (3H, d, *J* 6.5), 0.63 (3H, d, *J* 6.5), 0.81 (1H, m), 0.89 (1H, m), 2.28 (3H, s), 3.11 (1H, m), 3.18-3.33 (2H, m), 3.43 (1H, m), 3.47 (3H, s), 3.87 (2H, m), 4.02 (1H, m), 4.16 (1H, brd, *J* 11.0), 4.40 (1H, d, *J* 15.0), 4.53 (1H, d, *J* 15.0), 4.82 (1H, m), 7.18 (1H, d, *J* 7.0), 7.29 (1H, t, *J* 7.5), 7.45 (1H, t, *J* 7.5), 7.51 (1H, t, *J* 7.5 ), 7.70 (1H, d, *J* 8.5), 7.79 (1H, d, *J* 8.5), 8.13 (1H, d, *J* 8.5), 8.31 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 9.23, 22.07, 22.61, 24.48, 35.12, 37.10, 40.48, 41.10, 47.06, 52.38, 54.70, 69.68, 123.34, 124.32, 126.05, 126.55, 127.38, 128.61, 128.73, 128.92, 129.53, 131.76, 132.94, 132.94, 134.27, 156.86, 168.97, 174.06; *m/z* (FAB) 506.2767 ($M^+$+1, $C_{28}H_{36}N_5O_4$ requires 506.2767).

Saponification of **67** following the general procedure described previously afforded **68** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.61 (3H, d, *J* 6.5), 0.63 (3H, d, *J* 6.5), 0.80 (1H, m), 0.89 (1H, m), 1.12 (1H, m), 2.15 (3H, s), 2.89 (2H, m), 3.16 (1H, m), 3.40 (1H, dd, *J* 14.0 and 8.5), 3.78 (3H, m), 4.40 (2H, s), 7.16 (1H, d, *J* 7.0 Hz), 7.20 (1H, t, *J* 7.8), 7.36 (1H, t, *J* 7.8), 7.43 (1H, t, *J* 7.5), 7.60 (1H, s), 7.63 (1H, d, *J* 8.0), 7.73 (1H, d, *J* 8.0), 8.12 (1H, d, *J* 8.0); $\delta_C$ (125 MHz, d4-methanol) 10.2, 22.4, 23.9, 25.9, 35.6, 38.8, 42.7, 43.0, 46.9, 55.6, 60.4, 125.1, 126.9, 127.2, 128.0, 129.1, 129.2, 129.2, 129.9, 130.3, 133.9, 135.2, 135.3, 135.7, 158.7, 170.1, 180.5; *m/z* (FAB) 492.2613 ($M^+$+1, $C_{27}H_{34}N_5O_4$ requires 492.2611).

Scaffold **14d** was coupled to D-leucine methyl ester isocyanate following the previously described general procedures to give trityl-protected **71** as colorless oil in 87% yield: $\delta_H$ (500 MHz, d4-methanol) 0.82 (3H, d, *J* 6.5), 0.85 (3H, d, *J* 6.5), 1.11 (1H, m), 1.33 (1H, m), 1.44 (3H, s), 1.47 (1H, m), 2.84 (1H, ddd, *J* 13.5, 10.0 and 3.0), 3.05 (1H, dd, *J* 14.0 and 8.5), 3.10 (1H, dt, *J* 12.0 and 3.0), 3.38 (2H, m), 3.64 (3H, s), 3.82 (1H, brd, *J* 8.5), 3.98 (1H, brd, *J* 14.0), 4.06

(1H, m), 4.38 (1H, m), 4.41 (1H, d, *J* 14.5), 4.60 (1H, d, *J* 14.5), 7.07-7.37 (21H, m); *m/z* (FAB) 698.3706 ($M^+$+1, $C_{43}H_{48}N_5O_4$ requires 698.3706).

Deprotection of the above mentioned compound following the general procedure described previously afforded **71** as a colorless oil in 86% yield: $\delta_H$ (500 MHz, d4-methanol) 0.80 (3H, d, *J* 6.7), 0.83 (3H, d, *J* 6.7), 1.20 (1H, m), 1.34 (1H, m), 1.47 (1H, m), 2.34 (3H, s), 2.94 (1H, ddd, *J* 14.0, 10.5 and 3.5), 3.05 (1H, m), 3.30 (1H, dd, *J* 13.5 and 3.5), 3.44 (1H, ddd, *J* 2.0, 12.0 and 4.0), 3.59 (3H, s), 3.93 (1H, brd, *J* 13.0), 4.05 (1H, m), 4.41 (1H, m), 4.51 (1H, m), 4.53 (2H, s), 7.12-7.24 (5H, m), 8.39 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 9.5, 22.0, 23.1, 25.1, 38.1, 38.2, 40.4, 41.1, 46.8, 52.4, 52.8, 60.7, 124.7, 127.6, 128.7, 129.3, 129.3, 129.8, 129.8, 132.7, 137.6, 157.3, 168.4, 174.6; *m/z* (FAB) 456.2612 ($M^+$+1, $C_{24}H_{34}N_5O_4$ requires 456.2611).

Saponification of **71** following the general procedure described previously afforded **72** as a colorless oil in 85% yield: $\delta_H$ (500 MHz, d4-methanol) 0.82 (3H, d, *J* 6.5), 0.83 (3H, d, *J* 6.0), 1.42-1.60 (3H, m), 2.17 (3H, s), 2.61 (1H, ddd, *J* 13.5, 10.0, and 3.5), 2.75 (1H, dd, *J* 12.5 and 3.5), 3.15-3.26 (2H, m), 3.57 (1H, dt, *J* 13.5 and 4.0), 4.12 (1H, dd, *J* 10.0 and 4.8), 4.35 (1H, d, *J* 14.8), 4.47 (1H, d, *J* 14.8), 4.71 (1H, t, *J* 5.5), 6.97-7.10 (5H, m), 7.53 (1H, s); $\delta_C$ (125 MHz, d4-methanol) 10.3, 22.6, 24.1, 26.5, 38.9, 40.3, 42.8, 43.4, 46.8, 55.8, 59.5, 128.2, 129.1, 129.5, 129.7, 129.7, 131.2, 131.2, 135.3, 139.0, 158.7, 170.3, 180.5; *m/z* (FAB) 442.2455 ($M^+$+1, $C_{23}H_{32}N_5O_4$ requires 442.2454).

X-ray Structure Report
Reference Number: Compound **3**

## Data Collection

A colorless column crystal of $C_{23}H_{25}N_2O_3F$ having approximate dimensions of 0.15 x 0.24 x 0.24 mm was mounted on a glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-K$\alpha$ radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using ten ($1^o$ in $\omega$, 10s exposure, de-zingered) data frames, corresponded to a primitive orthorhombic cell with dimensions: a = 12.174(1) Å, b = 21.549(1) Å, c = 7.6755(3) Å, and V = 2013.6(4) Å$^3$. For Z = 4 and F.W. = 396.46, the calculated density is 1.31 g/cm$^3$. The systematic absences of: h00: h = 2n+1, 0k0: k = 2n+1, 00l: l = 2n+1; uniquely determine the space group to be: $P2_12_12_1$ (#19).

The data were collected at a temperature of -90 $\pm$ $1^oC$ to a maximum 2$\theta$ value of $55.0^o$. Two omega scans consisting of 65 and 18 data frames, respectively, were collected with a scan width of $1.6^o$ and a detector-to-crystal distance, Dx, of 35mm. Each frame was exposed twice (for the purpose of de-zingering) for 32s. The data frames were processed and scaled using the DENZO software package. (Z. Otwinowski and W. Minor, “Processing of X-Ray Diffraction Data Collected in Oscillation Mode,” Methods in Enzymology, vol. 276: Macromolecular Crystallography, part A, 307-326, 1997, C.W. Carter, Jr. & R.M. Sweet, Eds., Academic Press).

## Data Reduction

Of the 4459 reflections which were collected, 2639 were unique ($R_{int}$ = 0.043). No decay correction was applied. The linear absorption coefficient, $\mu$, for Mo-K$\alpha$ radiation is 0.9 cm$^{-1}$ and no absorption correction was applied. The data were corrected for Lorentz and polarization effects.

## Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. In the case of the methyl group hydrogen atoms, one hydrogen was located in the difference map and included at an idealized distance to set the orientation of the other two hydrogen atoms. The final cycle of full-matrix least-squares refinement[3] was based on 1645 observed reflections ($I > 3.00\sigma(I)$) and 262 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma \,||Fo| - |Fc|| \,/\, \Sigma\, |Fo| = 0.041$$

$$R_W = [( \Sigma\, w\, (|Fo| - |Fc|)^2 / \Sigma\, w\, Fo^2)]^{1/2} = 0.040$$

The standard deviation of an observation of unit weight[4] was 1.48. The weighting scheme was based on counting statistics and included a factor (p = 0.020) to downweight the intense reflections. Plots of $\Sigma\, w\, (|Fo| - |Fc|)^2$ versus |Fo|, reflection order in data collection, sin $\theta/\lambda$, and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.20 and -0.18 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5]. Anomalous dispersion effects were included in Fcalc[6]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[8]. All calculations were performed using the teXsan[9] crystallographic software package of Molecular Structure Corporation.

*References*

(1) SIR92: Altomare, A., Burla, M.C., Camalli, M., Cascarano, M., Giacovazzo, C., Guagliardi, A., & Polidori, G.; *J. Appl. Cryst.*, 27, 435-436 (1994).

(2) DIRDIF94: Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., de Gelder, R., Israel, R. and Smits, J.M.M.(1994). The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.

(3) Least-Squares:

Function minimized $Sw(|F_o|-|F_c|)^2$

where $w = 4F_o^2/{}^2(F_o^2)$

and $s^2(F_o^2) = [S^2(C+R^2B) + (pF_o^2)^2]/Lp^2$

S = Scan rate
C = Total integrated peak count
R = Ratio of scan time to background counting time
B = Total background count
Lp = Lorentz-polarization factor
*p* = p-factor

(4) Standard deviation of an observation of unit weight:

$[Sw(|F_o|-|F_c|)^2/(N_o-N_v)]^{1/2}$

where $N_o$ = number of observations and $N_v$ = number of variables

(5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(6) Ibers, J. A. & Hamilton, W. C.; *Acta Crystallogr*., 17, 781 (1964).

(7) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(8) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(9) teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

# *EXPERIMENTAL DETAILS*

## A. Crystal Data

| | |
|---|---|
| Empirical Formula | $C_{23}H_{25}N_2O_3F$ |
| Formula Weight | 396.46 |
| Crystal Color, Habit | colorless, column |
| Crystal Dimensions | 0.15 X 0.24 X 0.24 mm |
| Crystal System | orthorhombic |
| Lattice Type | Primitive |
| Lattice Parameters | a = 12.174(1)Å<br>b = 21.549(1) Å<br>c = 7.6755(3) Å |
| | V = 2013.6(4) $Å^3$ |
| Space Group | $P2_12_12_1$ (#19) |
| Z value | 4 |
| $D_{calc}$ | 1.308 $g/cm^3$ |
| $F_{000}$ | 840.00 |
| $\mu(MoK\alpha)$ | 0.93 $cm^{-1}$ |

## B. Intensity Measurements

| | |
|---|---|
| Diffractometer | Nonius KappaCCD |
| Radiation | $MoK\alpha$ ($\lambda$ = 0.71069 Å)<br>graphite monochromated |
| Take-off Angle | $2.8^o$ |
| Crystal to Detector Distance | 35 mm |
| Temperature | $-90.0^oC$ |
| Scan Rate | 32s/frame |
| Scan Width | $1.6^o$/frame |
| $2\theta_{max}$ | $55.0^o$ |

| | |
|---|---|
| No. of Reflections Measured | Total: 4459<br>Unique: 2639 ($R_{int}$ = 0.043) |
| Corrections | Lorentz-polarization |

## C. Structure Solution and Refinement

| | |
|---|---|
| Structure Solution | Direct Methods (SIR92) |
| Refinement | Full-matrix least-squares |
| Function Minimized | $\Sigma$ w (\|Fo\| - \|Fc\|)$^2$ |
| Least Squares Weights | 1/$\sigma^2$ (Fo) |
| p-factor | 0.0200 |
| Anomalous Dispersion | All non-hydrogen atoms |
| No. Observations (I>3.00$\sigma$(I)) | 1645 |
| No. Variables | 262 |
| Reflection/Parameter Ratio | 6.28 |
| Residuals: R; Rw | 0.041 ; 0.040 |
| Goodness of Fit Indicator | 1.48 |
| Max Shift/Error in Final Cycle | 0.00 |
| Maximum peak in Final Diff. Map | 0.20 $e^-/Å^3$ |
| Minimum peak in Final Diff. Map | -0.18 $e^-/Å^3$ |

Table 1. Atomic coordinates and $B_{iso}$/$B_{eq}$

| atom | x | y | z | $B_{eq}$ |
|---|---|---|---|---|
| F(1) | 0.6883(2) | 0.43533(10) | 1.2060(2) | 4.42(5) |
| O(1) | 0.2904(2) | 0.3702(1) | 0.5359(3) | 3.26(5) |
| O(2) | 0.3227(2) | 0.15429(9) | 0.4989(3) | 3.01(5) |
| O(3) | 0.5075(2) | 0.14654(9) | 0.5265(3) | 2.84(5) |
| N(1) | 0.4364(2) | 0.2342(1) | 0.4271(3) | 1.93(5) |
| N(2) | 0.4731(2) | 0.3588(1) | 0.4797(3) | 2.18(5) |
| C(1) | 0.3661(2) | 0.3394(1) | 0.4781(4) | 2.28(7) |
| C(2) | 0.3472(2) | 0.2781(1) | 0.3855(4) | 2.16(6) |
| C(3) | 0.5433(2) | 0.2583(1) | 0.4125(4) | 2.15(7) |
| C(4) | 0.5590(2) | 0.3184(2) | 0.4323(4) | 2.28(7) |
| C(5) | 0.3395(2) | 0.2898(1) | 0.1879(3) | 2.26(6) |
| C(6) | 0.2873(2) | 0.2384(1) | 0.0803(4) | 2.45(7) |
| C(7) | 0.1635(3) | 0.2359(2) | 0.1082(4) | 3.75(8) |
| C(8) | 0.3129(3) | 0.2480(2) | -0.1112(4) | 3.68(9) |
| C(9) | 0.4138(2) | 0.1765(1) | 0.4866(3) | 2.18(7) |
| C(10) | 0.4998(3) | 0.0834(2) | 0.5927(4) | 3.32(8) |
| C(11) | 0.5490(3) | 0.0808(1) | 0.7708(4) | 2.50(7) |
| C(12) | 0.4902(3) | 0.0999(2) | 0.9147(5) | 3.77(9) |
| C(13) | 0.5368(4) | 0.0987(2) | 1.0776(5) | 5.2(1) |
| C(14) | 0.6417(5) | 0.0771(2) | 1.0990(5) | 5.3(1) |
| C(15) | 0.7008(3) | 0.0574(2) | 0.9583(5) | 4.22(10) |
| C(16) | 0.6550(3) | 0.0593(2) | 0.7945(4) | 3.15(8) |
| C(17) | 0.4999(2) | 0.4221(2) | 0.5391(4) | 2.74(7) |
| C(18) | 0.5511(3) | 0.4242(1) | 0.7187(4) | 2.23(6) |
| C(19) | 0.6613(2) | 0.4380(1) | 0.7385(4) | 2.67(7) |
| C(20) | 0.7075(2) | 0.4423(2) | 0.9022(4) | 2.94(8) |
| C(21) | 0.6425(3) | 0.4321(2) | 1.0430(4) | 2.84(7) |
| C(22) | 0.5328(2) | 0.4174(2) | 1.0307(4) | 2.68(7) |
| C(23) | 0.4889(2) | 0.4136(2) | 0.8651(4) | 2.66(7) |
| H(1) | 0.2796 | 0.2610 | 0.4244 | 2.5868 |
| H(2) | 0.6035 | 0.2316 | 0.3886 | 2.5782 |
| H(3) | 0.6304 | 0.3350 | 0.4140 | 2.7311 |
| H(4) | 0.2975 | 0.3265 | 0.1707 | 2.7173 |
| H(5) | 0.4119 | 0.2961 | 0.1453 | 2.7173 |
| H(6) | 0.3180 | 0.1999 | 0.1159 | 2.9359 |
| H(7) | 0.1330 | 0.2759 | 0.0899 | 4.4981 |
| H(8) | 0.1320 | 0.2074 | 0.0281 | 4.4981 |
| H(9) | 0.1484 | 0.2227 | 0.2238 | 4.4981 |
| H(10) | 0.3901 | 0.2519 | -0.1262 | 4.4117 |
| H(11) | 0.2871 | 0.2134 | -0.1761 | 4.4117 |
| H(12) | 0.2777 | 0.2847 | -0.1512 | 4.4117 |

Table 1. Atomic coordinates and $B_{iso}/B_{eq}$ (continued)

| atom | x | y | z | $B_{eq}$ |
|---|---|---|---|---|
| H(13) | 0.4248 | 0.0713 | 0.5981 | 3.9785 |
| H(14) | 0.5385 | 0.0561 | 0.5173 | 3.9785 |
| H(15) | 0.4168 | 0.1140 | 0.9010 | 4.5238 |
| H(16) | 0.4962 | 0.1129 | 1.1755 | 6.2106 |
| H(17) | 0.6734 | 0.0758 | 1.2121 | 6.3043 |
| H(18) | 0.7736 | 0.0423 | 0.9734 | 5.0647 |
| H(19) | 0.6965 | 0.0457 | 0.6969 | 3.7763 |
| H(20) | 0.5500 | 0.4399 | 0.4586 | 3.2855 |
| H(21) | 0.4341 | 0.4458 | 0.5411 | 3.2855 |
| H(22) | 0.7057 | 0.4445 | 0.6383 | 3.2056 |
| H(23) | 0.7831 | 0.4521 | 0.9160 | 3.5242 |
| H(24) | 0.4893 | 0.4102 | 1.1314 | 3.2129 |
| H(25) | 0.4135 | 0.4033 | 0.8520 | 3.1870 |

$B_{eq} = 8/3\ \pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos\gamma + 2U_{13}(aa^*cc^*)\cos\beta + 2U_{23}(bb^*cc^*)\cos\alpha)$

Table 2. Anisotropic Displacement Parameters

| atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|---|---|---|---|---|---|---|
| F(1) | 0.067(1) | 0.067(2) | 0.033(1) | -0.021(1) | -0.015(1) | 0.003(1) |
| O(1) | 0.037(1) | 0.045(1) | 0.043(1) | 0.013(1) | 0.002(1) | -0.010(1) |
| O(2) | 0.034(1) | 0.036(1) | 0.044(1) | -0.009(1) | 0.001(1) | 0.001(1) |
| O(3) | 0.037(1) | 0.028(1) | 0.043(1) | 0.0011(10) | -0.009(1) | 0.008(1) |
| N(1) | 0.021(1) | 0.025(1) | 0.027(1) | 0.002(1) | 0.000(1) | 0.005(1) |
| N(2) | 0.030(1) | 0.027(1) | 0.026(1) | 0.002(1) | 0.000(1) | -0.002(1) |
| C(1) | 0.031(2) | 0.032(2) | 0.023(2) | 0.006(1) | -0.002(2) | 0.004(2) |
| C(2) | 0.023(2) | 0.032(2) | 0.027(1) | 0.001(1) | 0.000(1) | 0.003(2) |
| C(3) | 0.022(2) | 0.032(2) | 0.028(2) | -0.002(1) | 0.001(1) | 0.004(2) |
| C(4) | 0.027(2) | 0.033(2) | 0.027(2) | -0.003(1) | 0.002(1) | 0.002(2) |
| C(5) | 0.030(2) | 0.030(2) | 0.026(1) | 0.000(1) | -0.003(1) | 0.002(2) |
| C(6) | 0.035(2) | 0.029(2) | 0.029(2) | 0.004(1) | -0.005(2) | 0.000(2) |
| C(7) | 0.045(2) | 0.059(2) | 0.039(2) | -0.015(2) | -0.007(2) | -0.008(2) |
| C(8) | 0.046(2) | 0.061(3) | 0.032(2) | 0.002(2) | -0.006(2) | -0.010(2) |
| C(9) | 0.033(2) | 0.030(2) | 0.020(1) | 0.001(2) | -0.003(2) | -0.003(2) |
| C(10) | 0.055(2) | 0.026(2) | 0.045(2) | -0.003(2) | -0.011(2) | 0.003(2) |
| C(11) | 0.040(2) | 0.022(2) | 0.033(2) | -0.004(2) | -0.004(2) | 0.003(2) |
| C(12) | 0.052(2) | 0.044(2) | 0.048(2) | 0.007(2) | 0.008(2) | 0.003(2) |
| C(13) | 0.109(4) | 0.048(3) | 0.039(2) | -0.003(3) | 0.013(3) | -0.005(2) |
| C(14) | 0.103(3) | 0.056(3) | 0.041(2) | -0.031(3) | -0.032(3) | 0.012(2) |
| C(15) | 0.044(2) | 0.049(2) | 0.067(3) | -0.014(2) | -0.022(2) | 0.024(2) |
| C(16) | 0.035(2) | 0.034(2) | 0.051(2) | -0.005(2) | -0.001(2) | 0.009(2) |
| C(17) | 0.044(2) | 0.027(2) | 0.033(2) | 0.001(2) | -0.003(2) | -0.003(2) |
| C(18) | 0.039(2) | 0.021(2) | 0.025(1) | 0.001(1) | 0.002(2) | -0.004(1) |
| C(19) | 0.036(2) | 0.032(2) | 0.034(2) | -0.005(2) | 0.004(2) | 0.000(2) |
| C(20) | 0.035(2) | 0.037(2) | 0.039(2) | -0.007(2) | -0.004(2) | 0.004(2) |
| C(21) | 0.046(2) | 0.032(2) | 0.029(2) | -0.007(2) | -0.012(2) | -0.001(2) |
| C(22) | 0.042(2) | 0.034(2) | 0.025(2) | -0.003(2) | 0.003(2) | -0.002(2) |
| C(23) | 0.032(2) | 0.034(2) | 0.034(2) | -0.001(2) | -0.001(2) | -0.005(2) |

The general temperature factor expression:
$\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$

Table 3. Bond Lengths(Å)

| atom | atom | distance | atom | atom | distance |
|---|---|---|---|---|---|
| F(1) | C(21) | 1.371(3) | O(1) | C(1) | 1.219(3) |
| O(2) | C(9) | 1.211(3) | O(3) | C(9) | 1.346(3) |
| O(3) | C(10) | 1.454(4) | N(1) | C(2) | 1.475(4) |
| N(1) | C(3) | 1.406(3) | N(1) | C(9) | 1.354(4) |
| N(2) | C(1) | 1.368(4) | N(2) | C(4) | 1.409(4) |
| N(2) | C(17) | 1.473(4) | C(1) | C(2) | 1.518(4) |
| C(2) | C(5) | 1.540(4) | C(3) | C(4) | 1.318(4) |
| C(5) | C(6) | 1.520(4) | C(6) | C(7) | 1.523(4) |
| C(6) | C(8) | 1.517(4) | C(10) | C(11) | 1.494(4) |
| C(11) | C(12) | 1.378(4) | C(11) | C(16) | 1.383(4) |
| C(12) | C(13) | 1.373(6) | C(13) | C(14) | 1.369(6) |
| C(14) | C(15) | 1.366(6) | C(15) | C(16) | 1.376(4) |
| C(17) | C(18) | 1.513(4) | C(18) | C(19) | 1.383(4) |
| C(18) | C(23) | 1.374(4) | C(19) | C(20) | 1.380(4) |
| C(20) | C(21) | 1.357(4) | C(21) | C(22) | 1.376(4) |
| C(22) | C(23) | 1.381(4) | | | |

Table 4. Bond Lengths(Å) for the Hydrogen Atoms

| atom | atom | distance | atom | atom | distance |
|---|---|---|---|---|---|
| C(2) | H(1) | 0.95 | C(3) | H(2) | 0.95 |
| C(4) | H(3) | 0.95 | C(5) | H(4) | 0.95 |
| C(5) | H(5) | 0.95 | C(6) | H(6) | 0.95 |
| C(7) | H(7) | 0.95 | C(7) | H(8) | 0.95 |
| C(7) | H(9) | 0.95 | C(8) | H(10) | 0.95 |
| C(8) | H(11) | 0.95 | C(8) | H(12) | 0.95 |
| C(10) | H(13) | 0.95 | C(10) | H(14) | 0.95 |
| C(12) | H(15) | 0.95 | C(13) | H(16) | 0.95 |
| C(14) | H(17) | 0.95 | C(15) | H(18) | 0.95 |
| C(16) | H(19) | 0.95 | C(17) | H(20) | 0.95 |
| C(17) | H(21) | 0.95 | C(19) | H(22) | 0.95 |
| C(20) | H(23) | 0.95 | C(22) | H(24) | 0.95 |
| C(23) | H(25) | 0.95 | | | |

Table 5. Bond Angles($^{o}$)

| atom | atom | atom | angle | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|
| C(9) | O(3) | C(10) | 118.2(2) | C(2) | N(1) | C(3) | 115.3(2) |
| C(2) | N(1) | C(9) | 120.9(2) | C(3) | N(1) | C(9) | 123.7(2) |
| C(1) | N(2) | C(4) | 121.0(2) | C(1) | N(2) | C(17) | 119.8(2) |
| C(4) | N(2) | C(17) | 119.1(2) | O(1) | C(1) | N(2) | 123.3(3) |
| O(1) | C(1) | C(2) | 122.0(3) | N(2) | C(1) | C(2) | 114.5(2) |
| N(1) | C(2) | C(1) | 110.2(2) | N(1) | C(2) | C(5) | 111.3(2) |
| C(1) | C(2) | C(5) | 109.1(3) | N(1) | C(3) | C(4) | 119.2(3) |
| N(2) | C(4) | C(3) | 122.0(3) | C(2) | C(5) | C(6) | 116.1(3) |
| C(5) | C(6) | C(7) | 111.3(3) | C(5) | C(6) | C(8) | 109.9(3) |
| C(7) | C(6) | C(8) | 110.1(3) | O(2) | C(9) | O(3) | 124.7(3) |
| O(2) | C(9) | N(1) | 125.1(3) | O(3) | C(9) | N(1) | 110.2(2) |
| O(3) | C(10) | C(11) | 109.2(3) | C(10) | C(11) | C(12) | 120.9(3) |
| C(10) | C(11) | C(16) | 120.5(3) | C(12) | C(11) | C(16) | 118.6(3) |
| C(11) | C(12) | C(13) | 120.6(3) | C(12) | C(13) | C(14) | 120.1(4) |
| C(13) | C(14) | C(15) | 120.1(3) | C(14) | C(15) | C(16) | 120.0(3) |
| C(11) | C(16) | C(15) | 120.6(3) | N(2) | C(17) | C(18) | 113.7(3) |
| C(17) | C(18) | C(19) | 120.4(3) | C(17) | C(18) | C(23) | 120.9(2) |
| C(19) | C(18) | C(23) | 118.7(3) | C(18) | C(19) | C(20) | 120.7(3) |
| C(19) | C(20) | C(21) | 118.5(3) | F(1) | C(21) | C(20) | 118.8(3) |
| F(1) | C(21) | C(22) | 118.0(3) | C(20) | C(21) | C(22) | 123.2(3) |
| C(21) | C(22) | C(23) | 116.9(3) | C(18) | C(23) | C(22) | 122.0(3) |

Table 6. Bond Angles($^{o}$) for the Hydrogen Atoms

| atom | atom | atom | angle | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|
| N(1) | C(2) | H(1) | 108.7 | C(1) | C(2) | H(1) | 108.7 |
| C(5) | C(2) | H(1) | 108.7 | N(1) | C(3) | H(2) | 120.4 |
| C(4) | C(3) | H(2) | 120.4 | N(2) | C(4) | H(3) | 119.0 |
| C(3) | C(4) | H(3) | 119.0 | C(2) | C(5) | H(4) | 107.8 |
| C(2) | C(5) | H(5) | 107.8 | C(6) | C(5) | H(4) | 107.8 |
| C(6) | C(5) | H(5) | 107.8 | H(4) | C(5) | H(5) | 109.5 |
| C(5) | C(6) | H(6) | 108.4 | C(7) | C(6) | H(6) | 108.4 |
| C(8) | C(6) | H(6) | 108.4 | C(6) | C(7) | H(7) | 109.5 |
| C(6) | C(7) | H(8) | 109.5 | C(6) | C(7) | H(9) | 109.5 |
| H(7) | C(7) | H(8) | 109.5 | H(7) | C(7) | H(9) | 109.5 |
| H(8) | C(7) | H(9) | 109.5 | C(6) | C(8) | H(10) | 109.5 |
| C(6) | C(8) | H(11) | 109.5 | C(6) | C(8) | H(12) | 109.5 |
| H(10) | C(8) | H(11) | 109.5 | H(10) | C(8) | H(12) | 109.5 |
| H(11) | C(8) | H(12) | 109.5 | O(3) | C(10) | H(13) | 109.5 |
| O(3) | C(10) | H(14) | 109.5 | C(11) | C(10) | H(13) | 109.5 |
| C(11) | C(10) | H(14) | 109.5 | H(13) | C(10) | H(14) | 109.5 |
| C(11) | C(12) | H(15) | 119.7 | C(13) | C(12) | H(15) | 119.7 |
| C(12) | C(13) | H(16) | 120.0 | C(14) | C(13) | H(16) | 120.0 |
| C(13) | C(14) | H(17) | 119.9 | C(15) | C(14) | H(17) | 119.9 |
| C(14) | C(15) | H(18) | 120.0 | C(16) | C(15) | H(18) | 120.0 |
| C(11) | C(16) | H(19) | 119.7 | C(15) | C(16) | H(19) | 119.7 |
| N(2) | C(17) | H(20) | 108.4 | N(2) | C(17) | H(21) | 108.4 |
| C(18) | C(17) | H(20) | 108.4 | C(18) | C(17) | H(21) | 108.4 |
| H(20) | C(17) | H(21) | 109.5 | C(18) | C(19) | H(22) | 119.7 |
| C(20) | C(19) | H(22) | 119.7 | C(19) | C(20) | H(23) | 120.8 |
| C(21) | C(20) | H(23) | 120.8 | C(21) | C(22) | H(24) | 121.5 |
| C(23) | C(22) | H(24) | 121.5 | C(18) | C(23) | H(25) | 119.0 |
| C(22) | C(23) | H(25) | 119.0 |  |  |  |  |

Table 7. Torsion Angles($^{o}$)

| atom | atom | atom | atom | angle | atom | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|---|---|
| F(1) | C(21) | C(20) | C(19) | 178.9(3) | F(1) | C(21) | C(22) | C(23) | -179.1(3) |
| O(1) | C(1) | N(2) | C(4) | 171.7(3) | O(1) | C(1) | N(2) | C(17) | -5.6(4) |
| O(1) | C(1) | C(2) | N(1) | -144.0(3) | O(1) | C(1) | C(2) | C(5) | 93.5(3) |
| O(2) | C(9) | O(3) | C(10) | -1.3(4) | O(2) | C(9) | N(1) | C(2) | 5.6(4) |
| O(2) | C(9) | N(1) | C(3) | -179.2(3) | O(3) | C(9) | N(1) | C(2) | -175.9(2) |
| O(3) | C(9) | N(1) | C(3) | -0.7(4) | O(3) | C(10) | C(11) | C(12) | 80.4(4) |
| O(3) | C(10) | C(11) | C(16) | -99.3(3) | N(1) | C(2) | C(1) | N(2) | 40.5(3) |
| N(1) | C(2) | C(5) | C(6) | 76.0(3) | N(1) | C(3) | C(4) | N(2) | 4.5(4) |
| N(1) | C(9) | O(3) | C(10) | -179.9(2) | N(2) | C(1) | C(2) | C(5) | -82.0(3) |
| N(2) | C(17) | C(18) | C(19) | 108.0(3) | N(2) | C(17) | C(18) | C(23) | -73.0(4) |
| C(1) | N(2) | C(4) | C(3) | -11.3(4) | C(1) | N(2) | C(17) | C(18) | 105.3(3) |
| C(1) | C(2) | N(1) | C(3) | -47.6(3) | C(1) | C(2) | N(1) | C(9) | 128.0(3) |
| C(1) | C(2) | C(5) | C(6) | -162.2(2) | C(2) | N(1) | C(3) | C(4) | 26.4(3) |
| C(2) | C(1) | N(2) | C(4) | -12.9(4) | C(2) | C(1) | N(2) | C(17) | 169.9(2) |
| C(2) | C(5) | C(6) | C(7) | 73.0(3) | C(2) | C(5) | C(6) | C(8) | -164.6(3) |
| C(3) | N(1) | C(2) | C(5) | 73.6(3) | C(3) | C(4) | N(2) | C(17) | 165.9(3) |
| C(4) | N(2) | C(17) | C(18) | -72.0(3) | C(4) | C(3) | N(1) | C(9) | -149.1(3) |
| C(5) | C(2) | N(1) | C(9) | -110.8(3) | C(9) | O(3) | C(10) | C(11) | -119.6(3) |
| C(10) | C(11) | C(12) | C(13) | -178.4(4) | C(10) | C(11) | C(16) | C(15) | 179.3(3) |
| C(11) | C(12) | C(13) | C(14) | -1.5(6) | C(11) | C(16) | C(15) | C(14) | -0.3(5) |
| C(12) | C(11) | C(16) | C(15) | -0.4(5) | C(12) | C(13) | C(14) | C(15) | 0.9(6) |
| C(13) | C(12) | C(11) | C(16) | 1.3(5) | C(13) | C(14) | C(15) | C(16) | 0.0(6) |
| C(17) | C(18) | C(19) | C(20) | 177.6(3) | C(17) | C(18) | C(23) | C(22) | -177.7(3) |
| C(18) | C(19) | C(20) | C(21) | 0.6(5) | C(18) | C(23) | C(22) | C(21) | -0.3(5) |
| C(19) | C(18) | C(23) | C(22) | 1.3(5) | C(19) | C(20) | C(21) | C(22) | 0.4(5) |
| C(20) | C(19) | C(18) | C(23) | -1.4(5) | C(20) | C(21) | C(22) | C(23) | -0.5(5) |

Table 8. Non-bonded Contacts out to 3.60 Å

| atom | atom | distance | ADC | atom | atom | distance | ADC |
|---|---|---|---|---|---|---|---|
| F(1) | C(20) | 3.291(4) | 66502 | F(1) | C(19) | 3.296(4) | 66502 |
| F(1) | O(2) | 3.396(3) | 55703 | F(1) | C(4) | 3.441(4) | 55601 |
| F(1) | C(17) | 3.447(4) | 55601 | O(1) | C(16) | 3.386(4) | 45603 |
| O(1) | O(3) | 3.496(3) | 45603 | O(1) | C(14) | 3.525(4) | 45703 |
| O(2) | C(4) | 3.306(3) | 45603 | O(2) | C(19) | 3.337(4) | 45603 |
| C(11) | C(18) | 3.587(4) | 64604 | | | | |

The ADC (atom designator code) specifies the position of an atom in a crystal. The 5-digit number shown in the table is a composite of three one-digit numbers and one two-digit number: TA (first digit) + TB (second digit) + TC (third digit) + SN (last two digits). TA, TB and TC are the crystal lattice translation digits along cell edges a, b and c. A translation digit of 5 indicates the origin unit cell. If TA = 4, this indicates a translation of one unit cell length along the a-axis in the negative direction. Each translation digit can range in value from 1 to 9 and thus ±4 lattice translations from the origin (TA=5, TB=5, TC=5) can be represented.

The SN, or symmetry operator number, refers to the number of the symmetry operator used to generate the coordinates of the target atom. A list of symmetry operators relevant to this structure are given below.

For a given intermolecular contact, the first atom (origin atom) is located in the origin unit cell and its position can be generated using the identity operator (SN=1). Thus, the ADC for an origin atom is always 55501. The position of the second atom (target atom) can be generated using the ADC and the coordinates of the atom in the parameter table. For example, an ADC of 47502 refers to the target atom moved through symmetry operator two, then translated -1 cell translations along the a axis, +2 cell translations along the b axis, and 0 cell translations along the c axis.

An ADC of 1 indicates an intermolecular contact between two fragments (eg. cation and anion) that reside in the same asymmetric unit.

Symmetry Operators:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (1) | X, | Y, | Z | (2) | 1/2-X, | -Y, | 1/2+Z |
| (3) | 1/2+X, | 1/2-Y, | -Z | (4) | -X, | 1/2+Y, | 1/2-Z |

X-ray Structure Report
Reference Number: Compound **12a**

## Data Collection

A colorless plate crystal of $C_{19}H_{18}N_2O_3$ having approximate dimensions of 0.10 x 0.17 x 0.24 mm was mounted on a glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-K$\alpha$ radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using ten ($1^o$ in $\omega$, 10s exposure, de-zingered) data frames, corresponded to a primitive monoclinic cell with dimensions: a = 7.884(1) Å, b = 5.6159(4) Å, $\beta$ = 90.753(4)$^o$, c = 17.964(1), and V = 795.3(1) Å$^3$. For Z = 2 and F.W. = 322.36, the calculated density is 1.35 g/cm$^3$. Based on the systematic absences of: 0k0: k = 2n+1; packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be: $P2_1$ (#4).

The data were collected at a temperature of -90 $\pm$ $1^o$C to a maximum $2\theta$ value of $50.0^o$. Three omega scans consisting of 54, 55, and 54 data frames, respectively, were collected with a scan width of $2.0^o$ and a detector-to-crystal distance, Dx, of 35 mm. Each frame was exposed twice (for the purpose of de-zingering) for 180s. The data frames were processed and scaled using the DENZO software package. (Z. Otwinowski and W. Minor, “Processing of X-Ray Diffraction Data Collected in Oscillation Mode,” Methods in Enzymology, vol. 276: Macromolecular Crystallography, part A, 307-326, 1997, C.W. Carter, Jr. & R.M. Sweet, Eds., Academic Press).

## Data Reduction

Of the 2796 reflections which were collected, 1563 were unique ($R_{int}$ = 0.033). No decay correction was applied. The linear absorption coefficient, $\mu$, for Mo-K$\alpha$ radiation is 0.9 cm$^{-1}$ and no absorption correction was applied. The data were corrected for Lorentz and polarization effects.

## Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically. Some hydrogen atoms were refined isotropically (the N-H hydrogen atom), the rest were included in fixed positions. The final cycle of full-matrix least-squares refinement[3] was based on 1148 observed reflections ($I > 3.00\sigma(I)$) and 220 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma \,||Fo| - |Fc|| \,/\, \Sigma\, |Fo| = 0.040$$
$$R_w = [(\,\Sigma\, w\, (|Fo| - |Fc|)^2 \,/\, \Sigma\, w\, Fo^2)]^{1/2} = 0.042$$

The standard deviation of an observation of unit weight[4] was 1.51. The weighting scheme was based on counting statistics and included a factor (p = 0.010) to downweight the intense reflections. Plots of $\Sigma\, w\, (|Fo| - |Fc|)^2$ versus |Fo|, reflection order in data collection, sin $\theta/\lambda$, and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.17 and -0.18 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5]. Anomalous dispersion effects were included in Fcalc[6]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[8]. All calculations were performed using the teXsan[9] crystallographic software package of Molecular Structure Corporation.

## *References*

(1) SIR92: Altomare, A., Burla, M.C., Camalli, M., Cascarano, M., Giacovazzo, C., Guagliardi, A., & Polidori, G.; *J. Appl. Cryst.,* 27, 435-436 (1994).

(2) DIRDIF94: Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., de Gelder, R., Israel, R. and Smits, J.M.M.(1994). The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.

(3) Least-Squares:

Function minimized $Sw(|F_o|-|F_c|)^2$

where $w = 4F_o^2/^2(F_o^2)$
and $s^2(F_o^2) = [S^2(C+R^2B) + (pF_o^2)^2]/Lp^2$
S = Scan rate
C = Total integrated peak count
R = Ratio of scan time to background counting time
B = Total background count
Lp = Lorentz-polarization factor
*p* = p-factor

(4) Standard deviation of an observation of unit weight:

$[Sw(|F_o|-|F_c|)^2/(N_o-N_v)]^{1/2}$
where $N_o$ = number of observations and $N_v$ = number of variables

(5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(6) Ibers, J. A. & Hamilton, W. C.; *Acta Crystallogr*., 17, 781 (1964).

(7) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(8) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(9) teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

## *EXPERIMENTAL DETAILS*

### A. Crystal Data

| | |
|---|---|
| Empirical Formula | $C_{19}H_{18}N_2O_3$ |
| Formula Weight | 322.36 |
| Crystal Color, Habit | colorless, plate |
| Crystal Dimensions | 0.10 X 0.17 X 0.24 mm |
| Crystal System | monoclinic |
| Lattice Type | Primitive |
| Lattice Parameters | a = 7.884(1)Å<br>b = 5.6159(4) Å<br>c = 17.964(1) Å<br>$\beta$ = 90.753(4)$^o$<br>V = 795.3(1) Å$^3$ |
| Space Group | $P2_1$ (#4) |
| Z value | 2 |
| $D_{calc}$ | 1.346 g/cm$^3$ |
| $F_{000}$ | 340.00 |
| $\mu$(MoK$\alpha$) | 0.92 cm$^{-1}$ |

### B. Intensity Measurements

| | |
|---|---|
| Diffractometer | Nonius KappaCCD |
| Radiation | MoK$\alpha$ ($\lambda$ = 0.71069 Å)<br>graphite monochromated |
| Take-off Angle | 2.8$^o$ |
| Crystal to Detector Distance | 35 mm |
| Temperature | -90.0$^o$C |
| Scan Rate | 180s/frame |
| Scan Width | 2.0$^o$/frame |

| | |
|---|---|
| $2\theta_{max}$ | 50.0$^{o}$ |
| No. of Reflections Measured | Total: 2796 Unique: 1563 ($R_{int}$ = 0.033) |
| Corrections | Lorentz-polarization |

## C. Structure Solution and Refinement

| | |
|---|---|
| Structure Solution | Direct Methods (SIR92) |
| Refinement | Full-matrix least-squares |
| Function Minimized | $\Sigma$ w (\|Fo\| - \|Fc\|)$^{2}$ |
| Least Squares Weights | $1/\sigma^{2}(Fo)$ |
| p-factor | 0.0100 |
| Anomalous Dispersion | All non-hydrogen atoms |
| No. Observations ($I>3.00\sigma(I)$) | 1148 |
| No. Variables | 220 |
| Reflection/Parameter Ratio | 5.22 |
| Residuals: R; Rw | 0.040 ; 0.042 |
| Goodness of Fit Indicator | 1.51 |
| Max Shift/Error in Final Cycle | 0.00 |
| Maximum peak in Final Diff. Map | 0.17 $e^{-}/Å^{3}$ |
| Minimum peak in Final Diff. Map | -0.18 $e^{-}/Å^{3}$ |

Table 1. Atomic coordinates and $B_{iso}$/$B_{eq}$

| atom | x | y | z | $B_{eq}$ |
|---|---|---|---|---|
| O(1) | 0.9225(3) | 0.0038 | 0.4274(1) | 3.42(6) |
| O(2) | 0.2570(3) | 0.3374(8) | 0.3704(1) | 3.19(6) |
| O(3) | 0.3960(2) | 0.0261(8) | 0.3174(1) | 2.72(6) |
| N(1) | 0.5452(3) | 0.3096(8) | 0.3771(1) | 2.27(7) |
| N(2) | 0.8172(3) | 0.3547(9) | 0.4716(1) | 3.22(8) |
| C(1) | 0.8229(4) | 0.173(1) | 0.4229(2) | 2.69(9) |
| C(2) | 0.7046(4) | 0.196(1) | 0.3555(1) | 2.29(7) |
| C(3) | 0.5595(4) | 0.513(1) | 0.4223(2) | 2.92(8) |
| C(4) | 0.6951(4) | 0.534(1) | 0.4667(2) | 3.27(9) |
| C(5) | 0.8004(4) | 0.3475(10) | 0.2978(1) | 2.72(8) |
| C(6) | 0.7158(4) | 0.3657(10) | 0.2225(2) | 2.21(8) |
| C(7) | 0.7453(4) | 0.1946(10) | 0.1690(2) | 2.66(8) |
| C(8) | 0.6763(4) | 0.212(1) | 0.0978(2) | 3.12(9) |
| C(9) | 0.5754(4) | 0.407(1) | 0.0800(2) | 3.12(9) |
| C(10) | 0.5414(4) | 0.578(1) | 0.1330(2) | 3.13(9) |
| C(11) | 0.6126(4) | 0.558(1) | 0.2041(2) | 2.80(9) |
| C(12) | 0.3874(4) | 0.232(1) | 0.3557(2) | 2.24(9) |
| C(13) | 0.2361(4) | -0.0940(10) | 0.3025(2) | 2.74(8) |
| C(14) | 0.1922(4) | -0.0971(10) | 0.2207(2) | 2.14(8) |
| C(15) | 0.2359(4) | 0.083(1) | 0.1730(2) | 3.01(9) |
| C(16) | 0.1869(4) | 0.074(1) | 0.0982(2) | 3.03(9) |
| C(17) | 0.0916(4) | -0.116(1) | 0.0719(2) | 3.06(9) |
| C(18) | 0.0464(4) | -0.297(1) | 0.1194(2) | 3.08(9) |
| C(19) | 0.0978(4) | -0.288(1) | 0.1936(2) | 2.63(8) |
| H(1) | 0.6819 | 0.0423 | 0.3355 | 2.7469 |
| H(2) | 0.4745 | 0.6333 | 0.4212 | 3.5058 |
| H(3) | 0.7091 | 0.6742 | 0.4957 | 3.9275 |
| H(4) | 0.907(4) | 0.364(9) | 0.506(2) | 4.5(8) |
| H(5) | 0.8124 | 0.5039 | 0.3173 | 3.2580 |
| H(6) | 0.9095 | 0.2791 | 0.2913 | 3.2580 |
| H(7) | 0.8146 | 0.0615 | 0.1812 | 3.1956 |
| H(8) | 0.6980 | 0.0930 | 0.0617 | 3.7418 |
| H(9) | 0.5293 | 0.4222 | 0.0311 | 3.7388 |
| H(10) | 0.4698 | 0.7089 | 0.1210 | 3.7534 |
| H(11) | 0.5903 | 0.6766 | 0.2403 | 3.3620 |
| H(12) | 0.2441 | -0.2535 | 0.3199 | 3.2878 |
| H(13) | 0.1487 | -0.0137 | 0.3283 | 3.2878 |
| H(14) | 0.2999 | 0.2148 | 0.1911 | 3.6151 |
| H(15) | 0.2191 | 0.1978 | 0.0653 | 3.6328 |
| H(16) | 0.0572 | -0.1211 | 0.0210 | 3.6770 |
| H(17) | -0.0196 | -0.4266 | 0.1015 | 3.6937 |
| H(18) | 0.0682 | -0.4142 | 0.2262 | 3.1568 |

Table 2. Anisotropic Displacement Parameters

| atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|---|---|---|---|---|---|---|
| O(1) | 0.032(1) | 0.055(2) | 0.043(1) | 0.001(2) | -0.008(1) | 0.015(2) |
| O(2) | 0.033(1) | 0.037(2) | 0.051(1) | 0.006(2) | 0.002(1) | 0.002(2) |
| O(3) | 0.025(1) | 0.038(2) | 0.041(1) | -0.003(1) | -0.0058(9) | -0.011(2) |
| N(1) | 0.026(1) | 0.031(2) | 0.030(1) | 0.001(2) | -0.002(1) | -0.001(2) |
| N(2) | 0.036(2) | 0.055(3) | 0.031(1) | -0.006(2) | -0.010(1) | -0.002(2) |
| C(1) | 0.027(2) | 0.045(3) | 0.030(2) | -0.008(2) | -0.003(1) | 0.011(2) |
| C(2) | 0.027(2) | 0.032(3) | 0.028(2) | 0.000(2) | -0.004(1) | 0.002(2) |
| C(3) | 0.042(2) | 0.034(3) | 0.035(2) | -0.003(2) | 0.002(2) | -0.003(2) |
| C(4) | 0.052(2) | 0.040(3) | 0.032(2) | -0.006(3) | 0.000(2) | -0.003(2) |
| C(5) | 0.035(2) | 0.038(3) | 0.030(2) | -0.001(2) | -0.002(1) | 0.000(2) |
| C(6) | 0.029(2) | 0.028(3) | 0.027(2) | -0.001(2) | 0.001(1) | 0.003(2) |
| C(7) | 0.032(2) | 0.034(3) | 0.035(2) | 0.005(2) | -0.001(1) | 0.007(2) |
| C(8) | 0.041(2) | 0.042(3) | 0.036(2) | -0.006(2) | 0.003(2) | -0.007(3) |
| C(9) | 0.035(2) | 0.050(3) | 0.034(2) | -0.004(2) | -0.007(2) | 0.011(3) |
| C(10) | 0.032(2) | 0.039(3) | 0.048(2) | 0.004(2) | -0.001(2) | 0.010(3) |
| C(11) | 0.038(2) | 0.033(3) | 0.036(2) | -0.003(2) | 0.002(2) | 0.002(2) |
| C(12) | 0.033(2) | 0.027(3) | 0.024(2) | 0.001(2) | -0.002(1) | 0.004(2) |
| C(13) | 0.027(2) | 0.035(3) | 0.042(2) | -0.004(2) | -0.006(1) | 0.002(2) |
| C(14) | 0.020(2) | 0.026(3) | 0.036(2) | -0.001(2) | -0.003(1) | 0.003(2) |
| C(15) | 0.035(2) | 0.035(3) | 0.044(2) | -0.004(2) | -0.005(2) | 0.002(3) |
| C(16) | 0.041(2) | 0.033(3) | 0.041(2) | 0.003(2) | 0.000(2) | 0.012(2) |
| C(17) | 0.035(2) | 0.048(3) | 0.033(2) | 0.003(2) | -0.002(1) | -0.001(2) |
| C(18) | 0.037(2) | 0.038(3) | 0.042(2) | -0.003(2) | -0.002(2) | -0.009(3) |
| C(19) | 0.032(2) | 0.028(3) | 0.040(2) | -0.004(2) | 0.003(1) | 0.000(2) |

The general temperature factor expression:
$\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$

Table 3. Bond Lengths(Å)

| atom | atom | distance | atom | atom | distance |
|---|---|---|---|---|---|
| O(1) | C(1) | 1.236(5) | O(2) | C(12) | 1.218(4) |
| O(3) | C(12) | 1.349(4) | O(3) | C(13) | 1.452(4) |
| N(1) | C(2) | 1.467(4) | N(1) | C(3) | 1.407(5) |
| N(1) | C(12) | 1.367(4) | N(2) | C(1) | 1.344(6) |
| N(2) | C(4) | 1.395(6) | C(1) | C(2) | 1.523(4) |
| C(2) | C(5) | 1.547(5) | C(3) | C(4) | 1.330(4) |
| C(5) | C(6) | 1.503(4) | C(6) | C(7) | 1.382(5) |
| C(6) | C(11) | 1.389(5) | C(7) | C(8) | 1.386(4) |
| C(8) | C(9) | 1.385(6) | C(9) | C(10) | 1.382(6) |
| C(10) | C(11) | 1.393(4) | C(13) | C(14) | 1.506(4) |
| C(14) | C(15) | 1.372(5) | C(14) | C(19) | 1.390(5) |
| C(15) | C(16) | 1.394(4) | C(16) | C(17) | 1.383(6) |
| C(17) | C(18) | 1.377(6) | C(18) | C(19) | 1.388(4) |

Table 4. Bond Lengths(Å) for the Hydrogen Atoms

| atom | atom | distance | atom | atom | distance |
|---|---|---|---|---|---|
| N(2) | H(4) | 0.94(3) | C(2) | H(1) | 0.95 |
| C(3) | H(2) | 0.95 | C(4) | H(3) | 0.95 |
| C(5) | H(5) | 0.95 | C(5) | H(6) | 0.95 |
| C(7) | H(7) | 0.95 | C(8) | H(8) | 0.95 |
| C(9) | H(9) | 0.95 | C(10) | H(10) | 0.95 |
| C(11) | H(11) | 0.95 | C(13) | H(12) | 0.95 |
| C(13) | H(13) | 0.95 | C(15) | H(14) | 0.95 |
| C(16) | H(15) | 0.95 | C(17) | H(16) | 0.95 |
| C(18) | H(17) | 0.95 | C(19) | H(18) | 0.95 |

Table 5. Bond Angles($^{o}$)

| atom | atom | atom | angle | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|
| C(12) | O(3) | C(13) | 116.3(3) | C(2) | N(1) | C(3) | 116.4(3) |
| C(2) | N(1) | C(12) | 124.5(3) | C(3) | N(1) | C(12) | 119.1(3) |
| C(1) | N(2) | C(4) | 122.3(3) | O(1) | C(1) | N(2) | 124.6(3) |
| O(1) | C(1) | C(2) | 119.8(4) | N(2) | C(1) | C(2) | 115.4(4) |
| N(1) | C(2) | C(1) | 110.1(3) | N(1) | C(2) | C(5) | 111.4(3) |
| C(1) | C(2) | C(5) | 106.2(2) | N(1) | C(3) | C(4) | 118.3(4) |
| N(2) | C(4) | C(3) | 121.6(4) | C(2) | C(5) | C(6) | 115.2(3) |
| C(5) | C(6) | C(7) | 120.1(3) | C(5) | C(6) | C(11) | 121.3(4) |
| C(7) | C(6) | C(11) | 118.5(3) | C(6) | C(7) | C(8) | 121.6(4) |
| C(7) | C(8) | C(9) | 119.2(4) | C(8) | C(9) | C(10) | 120.3(3) |
| C(9) | C(10) | C(11) | 119.7(4) | C(6) | C(11) | C(10) | 120.7(4) |
| O(2) | C(12) | O(3) | 125.1(3) | O(2) | C(12) | N(1) | 123.6(4) |
| O(3) | C(12) | N(1) | 111.3(3) | O(3) | C(13) | C(14) | 111.9(3) |
| C(13) | C(14) | C(15) | 123.0(3) | C(13) | C(14) | C(19) | 117.8(3) |
| C(15) | C(14) | C(19) | 119.2(3) | C(14) | C(15) | C(16) | 120.3(3) |
| C(15) | C(16) | C(17) | 120.0(4) | C(16) | C(17) | C(18) | 120.0(3) |
| C(17) | C(18) | C(19) | 119.7(4) | C(14) | C(19) | C(18) | 120.7(4) |

Table 6. Bond Angles($^{o}$) for the Hydrogen Atoms

| atom | atom | atom | angle | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|
| C(1) | N(2) | H(4) | 116(2) | C(4) | N(2) | H(4) | 121(2) |
| N(1) | C(2) | H(1) | 109.7 | C(1) | C(2) | H(1) | 109.7 |
| C(5) | C(2) | H(1) | 109.7 | N(1) | C(3) | H(2) | 120.8 |
| C(4) | C(3) | H(2) | 120.8 | N(2) | C(4) | H(3) | 119.2 |
| C(3) | C(4) | H(3) | 119.2 | C(2) | C(5) | H(5) | 108.0 |
| C(2) | C(5) | H(6) | 108.0 | C(6) | C(5) | H(5) | 108.0 |
| C(6) | C(5) | H(6) | 108.0 | H(5) | C(5) | H(6) | 109.5 |
| C(6) | C(7) | H(7) | 119.2 | C(8) | C(7) | H(7) | 119.2 |
| C(7) | C(8) | H(8) | 120.4 | C(9) | C(8) | H(8) | 120.4 |
| C(8) | C(9) | H(9) | 119.8 | C(10) | C(9) | H(9) | 119.8 |
| C(9) | C(10) | H(10) | 120.2 | C(11) | C(10) | H(10) | 120.2 |
| C(6) | C(11) | H(11) | 119.7 | C(10) | C(11) | H(11) | 119.7 |
| O(3) | C(13) | H(12) | 108.9 | O(3) | C(13) | H(13) | 108.9 |
| C(14) | C(13) | H(12) | 108.9 | C(14) | C(13) | H(13) | 108.9 |
| H(12) | C(13) | H(13) | 109.5 | C(14) | C(15) | H(14) | 119.8 |
| C(16) | C(15) | H(14) | 119.8 | C(15) | C(16) | H(15) | 120.0 |
| C(17) | C(16) | H(15) | 120.0 | C(16) | C(17) | H(16) | 120.0 |
| C(18) | C(17) | H(16) | 120.0 | C(17) | C(18) | H(17) | 120.2 |
| C(19) | C(18) | H(17) | 120.2 | C(14) | C(19) | H(18) | 119.6 |
| C(18) | C(19) | H(18) | 119.6 | | | | |

Table 7. Torsion Angles($^{o}$)

| atom | atom | atom | atom | angle | atom | atom | atom | atom | angle |
|---|---|---|---|---|---|---|---|---|---|
| O(1) | C(1) | N(2) | C(4) | -175.8(3) | O(1) | C(1) | C(2) | N(1) | 148.3(3) |
| O(1) | C(1) | C(2) | C(5) | -91.0(4) | O(2) | C(12) | O(3) | C(13) | -9.4(4) |
| O(2) | C(12) | N(1) | C(2) | -175.3(3) | O(2) | C(12) | N(1) | C(3) | 4.1(5) |
| O(3) | C(12) | N(1) | C(2) | 5.2(4) | O(3) | C(12) | N(1) | C(3) | -175.5(3) |
| O(3) | C(13) | C(14) | C(15) | -32.6(5) | O(3) | C(13) | C(14) | C(19) | 149.7(3) |
| N(1) | C(2) | C(1) | N(2) | -36.0(4) | N(1) | C(2) | C(5) | C(6) | -67.8(4) |
| N(1) | C(3) | C(4) | N(2) | -3.0(5) | N(1) | C(12) | O(3) | C(13) | 170.1(3) |
| N(2) | C(1) | C(2) | C(5) | 84.7(4) | C(1) | N(2) | C(4) | C(3) | 12.6(6) |
| C(1) | C(2) | N(1) | C(3) | 45.7(4) | C(1) | C(2) | N(1) | C(12) | -135.0(3) |
| C(1) | C(2) | C(5) | C(6) | 172.4(4) | C(2) | N(1) | C(3) | C(4) | -27.5(4) |
| C(2) | C(1) | N(2) | C(4) | 8.7(5) | C(2) | C(5) | C(6) | C(7) | -86.9(4) |
| C(2) | C(5) | C(6) | C(11) | 95.7(5) | C(3) | N(1) | C(2) | C(5) | -71.9(3) |
| C(4) | C(3) | N(1) | C(12) | 153.1(3) | C(5) | C(2) | N(1) | C(12) | 107.5(3) |
| C(5) | C(6) | C(7) | C(8) | -176.6(3) | C(5) | C(6) | C(11) | C(10) | 177.0(3) |
| C(6) | C(7) | C(8) | C(9) | 0.0(5) | C(6) | C(11) | C(10) | C(9) | -0.8(5) |
| C(7) | C(6) | C(11) | C(10) | -0.4(5) | C(7) | C(8) | C(9) | C(10) | -1.2(6) |
| C(8) | C(7) | C(6) | C(11) | 0.8(5) | C(8) | C(9) | C(10) | C(11) | 1.6(6) |
| C(12) | O(3) | C(13) | C(14) | 113.4(3) | C(13) | C(14) | C(15) | C(16) | -177.9(3) |
| C(13) | C(14) | C(19) | C(18) | 177.1(3) | C(14) | C(15) | C(16) | C(17) | 1.0(5) |
| C(14) | C(19) | C(18) | C(17) | 1.0(5) | C(15) | C(14) | C(19) | C(18) | -0.7(5) |
| C(15) | C(16) | C(17) | C(18) | -0.7(5) | C(16) | C(15) | C(14) | C(19) | -0.3(5) |
| C(16) | C(17) | C(18) | C(19) | -0.3(5) | | | | | |

Table 8. Non-bonded Contacts out to 3.60 Å

| atom | atom | distance | ADC | atom | atom | distance | ADC |
|---|---|---|---|---|---|---|---|
| O(1) | N(2) | 2.848(3) | 74602 | O(1) | C(4) | 3.273(6) | 54501 |
| O(1) | O(2) | 3.403(3) | 65501 | O(1) | C(13) | 3.404(4) | 65501 |
| O(1) | C(4) | 3.548(4) | 74602 | O(2) | C(4) | 3.404(4) | 64602 |
| O(2) | C(13) | 3.421(5) | 56501 | C(4) | C(12) | 3.449(5) | 65602 |

The ADC (atom designator code) specifies the position of an atom in a crystal. The 5-digit number shown in the table is a composite of three one-digit numbers and one two-digit number: TA (first digit) + TB (second digit) + TC (third digit) + SN (last two digits). TA, TB and TC are the crystal lattice translation digits along cell edges a, b and c. A translation digit of 5 indicates the origin unit cell. If TA = 4, this indicates a translation of one unit cell length along the a-axis in the negative direction. Each translation digit can range in value from 1 to 9 and thus ±4 lattice translations from the origin (TA=5, TB=5, TC=5) can be represented.

The SN, or symmetry operator number, refers to the number of the symmetry operator used to generate the coordinates of the target atom. A list of symmetry operators relevant to this structure are given below.

For a given intermolecular contact, the first atom (origin atom) is located in the origin unit cell and its position can be generated using the identity operator (SN=1). Thus, the ADC for an origin atom is always 55501. The position of the second atom (target atom) can be generated using the ADC and the coordinates of the atom in the parameter table. For example, an ADC of 47502 refers to the target atom moved through symmetry operator two, then translated -1 cell translations along the a axis, +2 cell translations along the b axis, and 0 cell translations along the c axis.

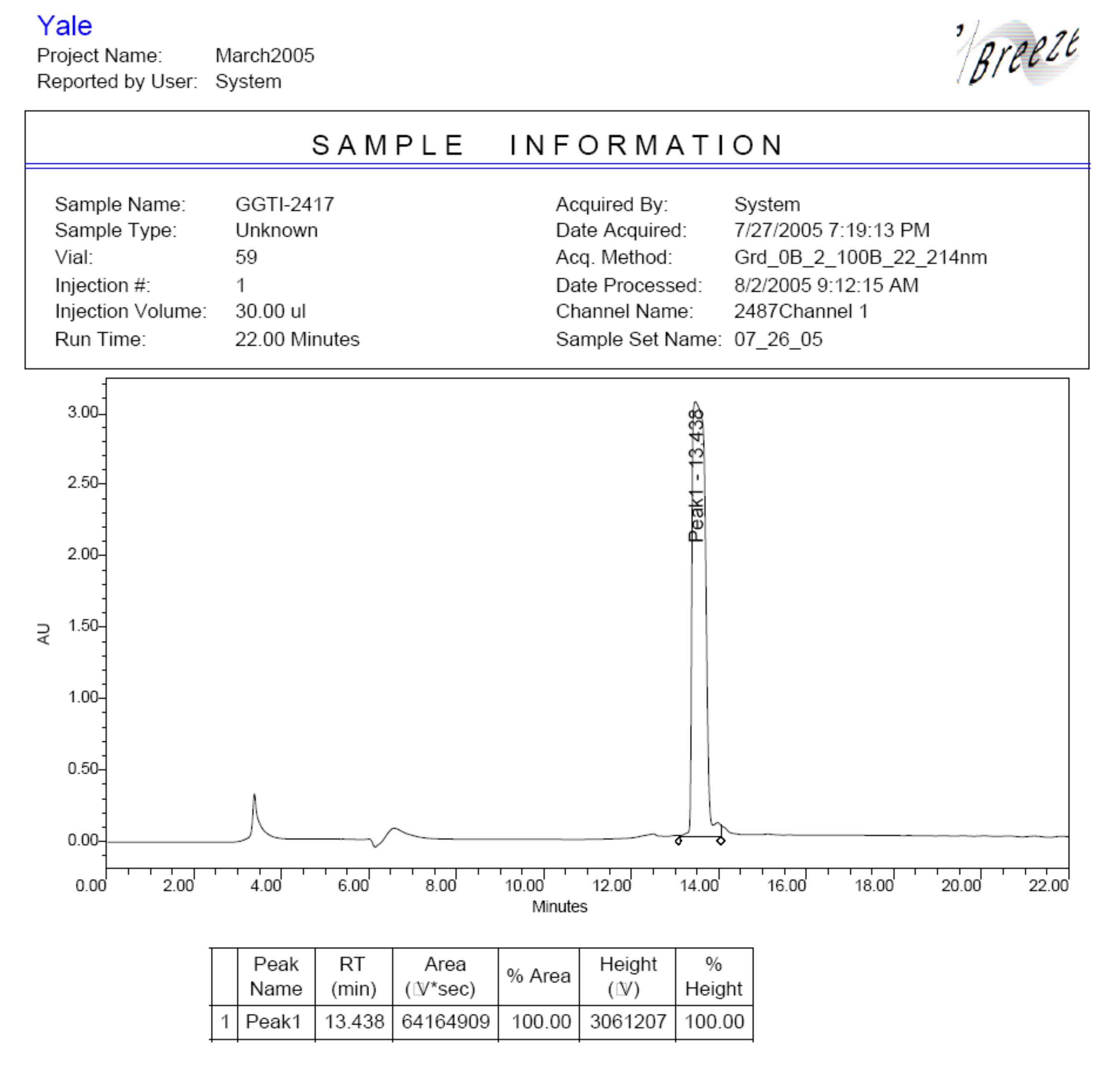
An ADC of 1 indicates an intermolecular contact between two fragments (eg. cation and anion) that reside in the same asymmetric unit.

Symmetry Operators:

(1) X, Y, Z

(2) -X, 1/2+Y, -Z

HPLC tract Compound **44**



Yale

Project Name: March2005

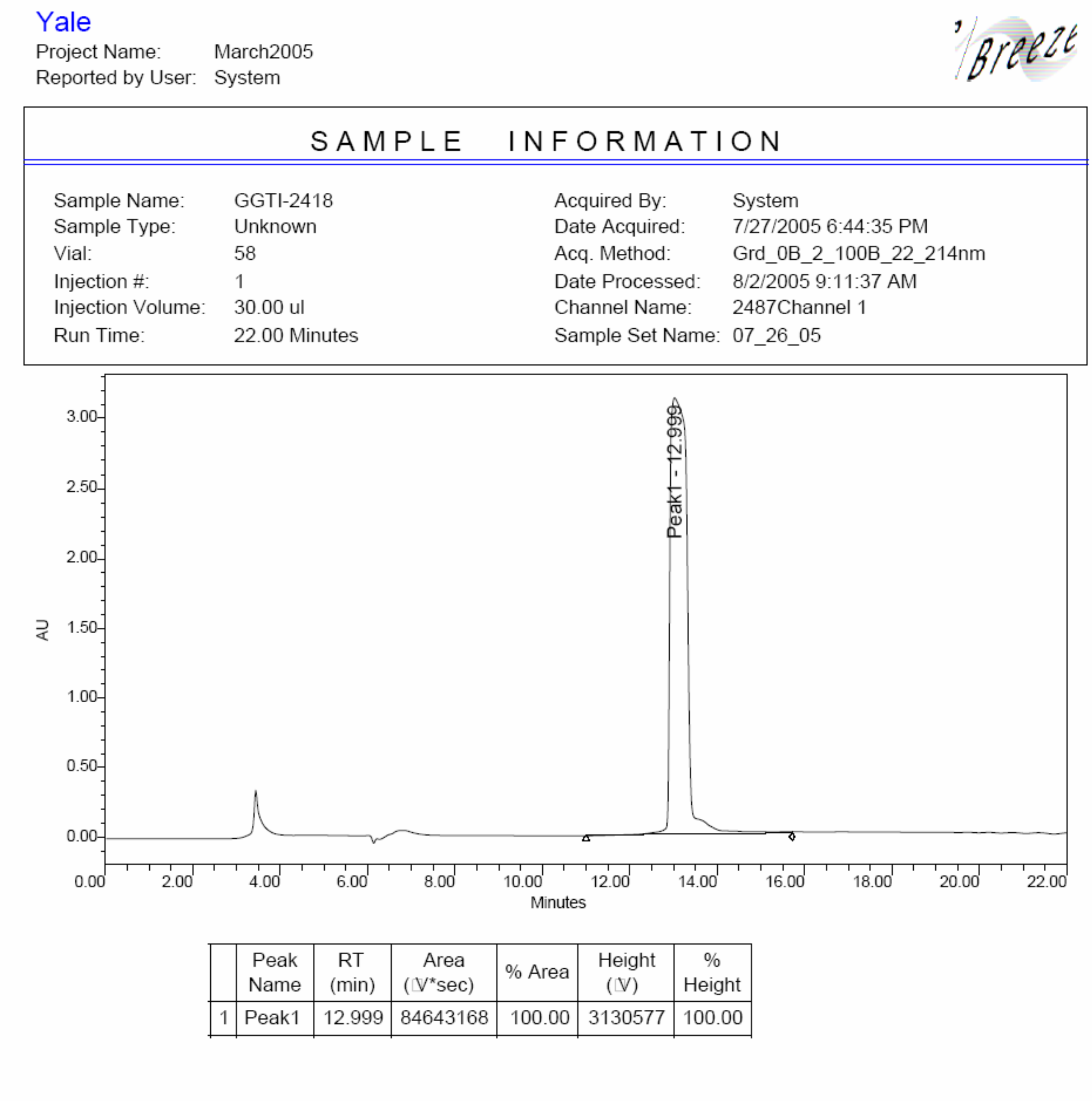
Reported by User: System

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2417 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 7:19:13 PM |
| Vial: | 59 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:12:15 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 13.438 | 64164909 | 100.00 | 3061207 | 100.00 |

HPLC tract Compound **45**



Yale

Project Name: March2005

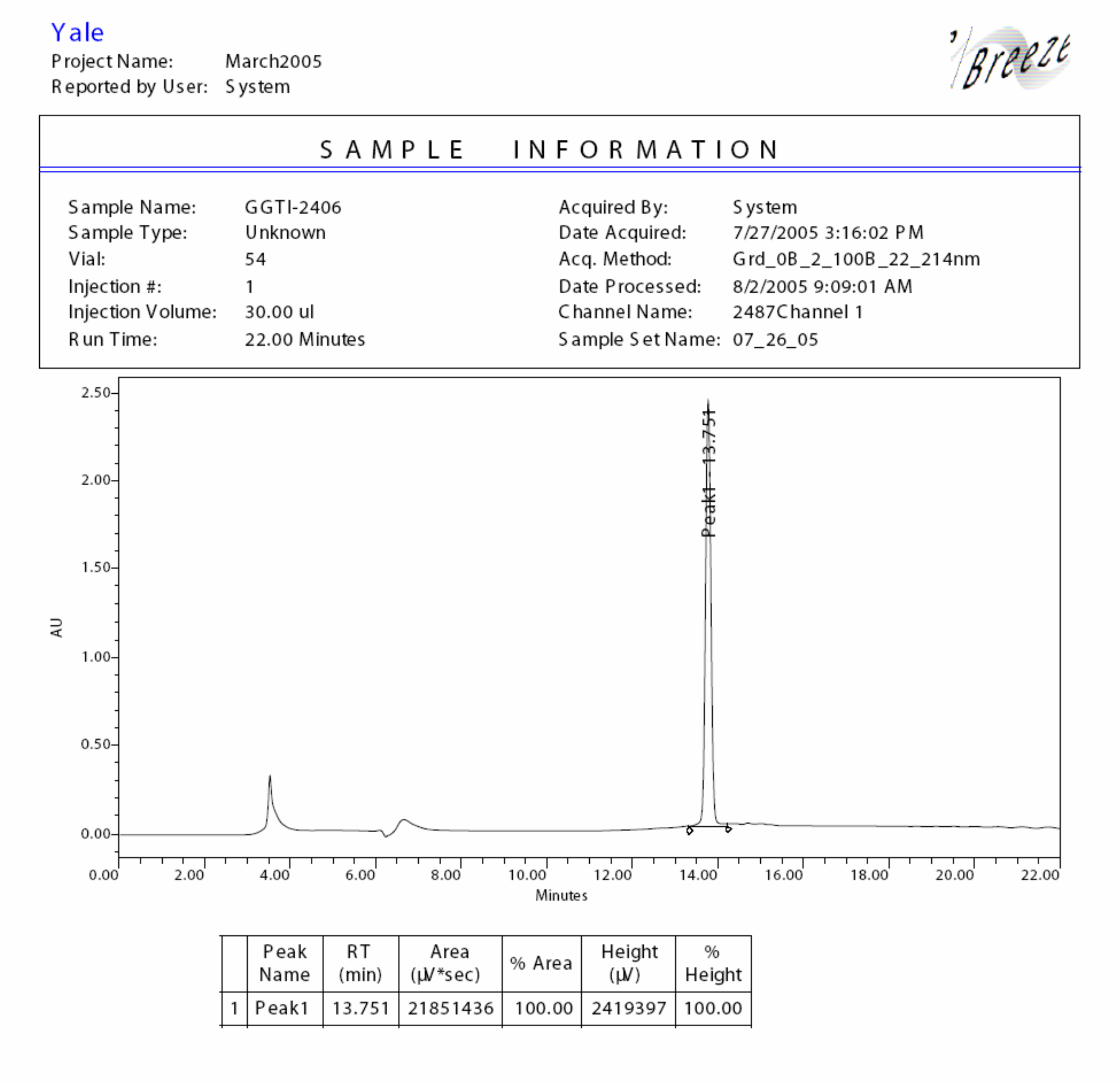
Reported by User: System

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2418 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 6:44:35 PM |
| Vial: | 58 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:11:37 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 12.999 | 84643168 | 100.00 | 3130577 | 100.00 |

HPLC tract Compound **59**



Yale
Project Name: March2005
Reported by User: System

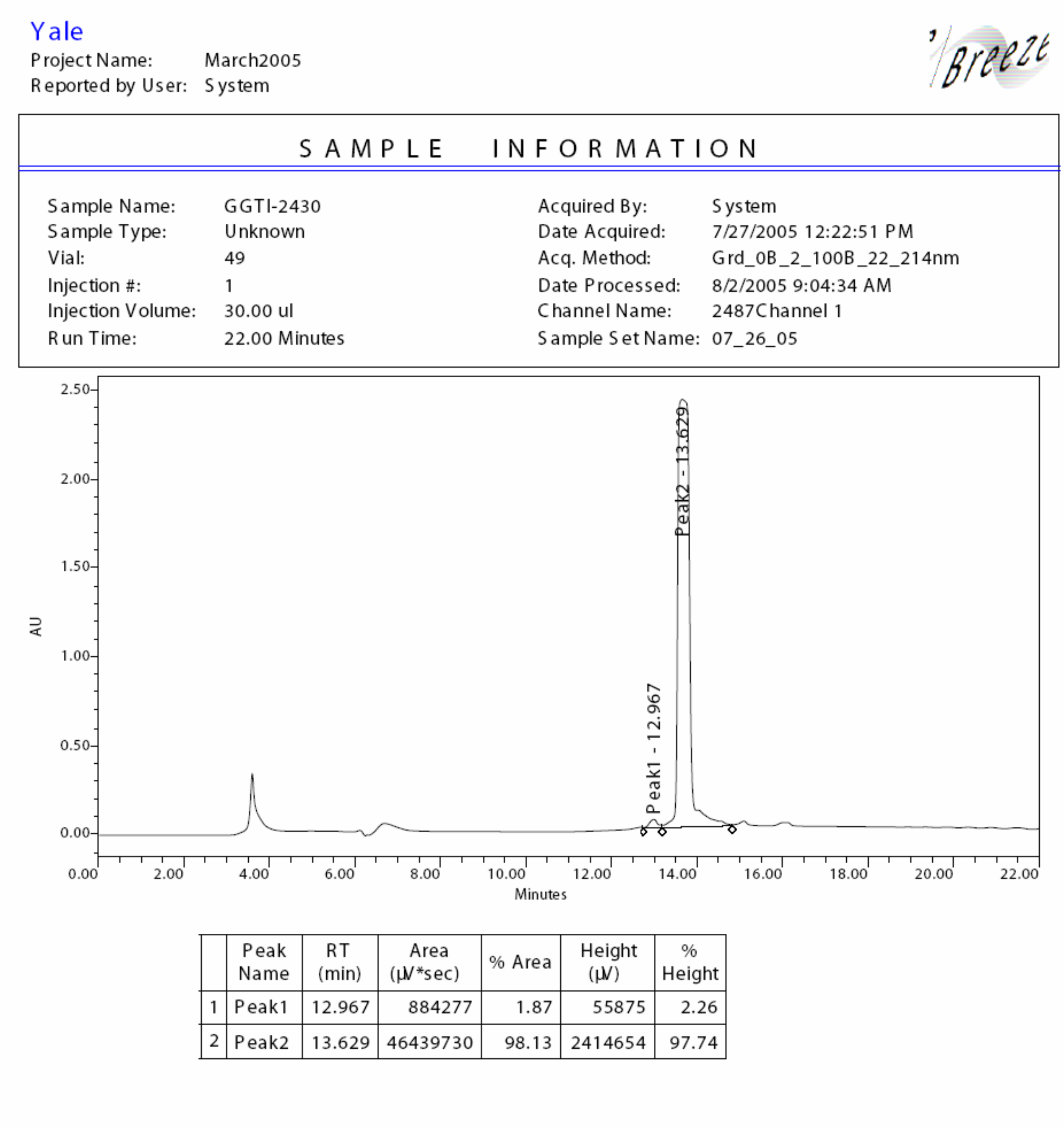
Breeze

S A M P L E   I N F O R M A T I O N

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2406 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 3:16:02 PM |
| Vial: | 54 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:09:01 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 13.751 | 21851436 | 100.00 | 2419397 | 100.00 |

HPLC tract Compound **68**



Yale

Project Name: March2005

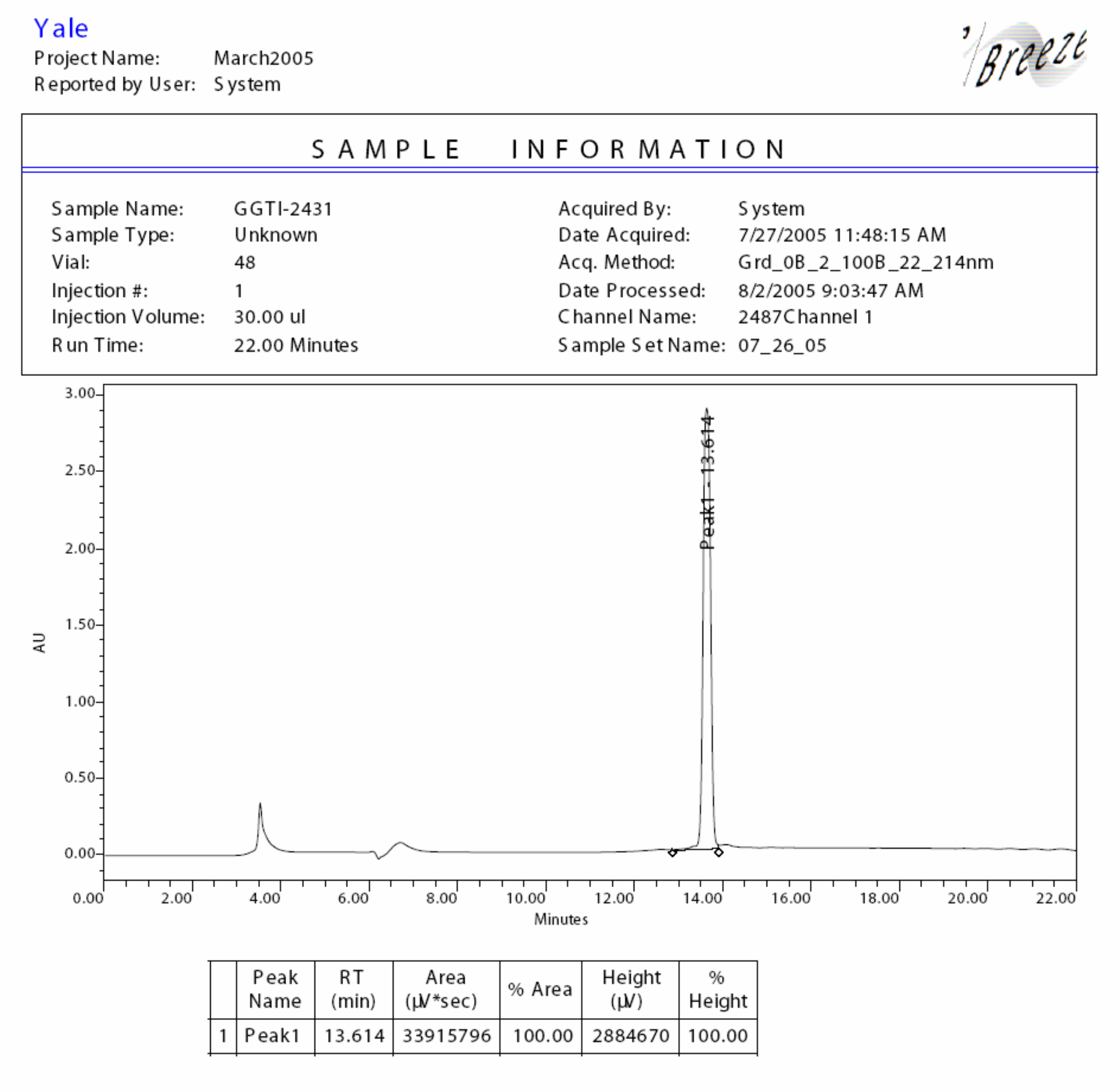
Reported by User: System

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2430 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 12:22:51 PM |
| Vial: | 49 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:04:34 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 12.967 | 884277 | 1.87 | 55875 | 2.26 |
| 2 | Peak2 | 13.629 | 46439730 | 98.13 | 2414654 | 97.74 |

HPLC tract Compound **69**



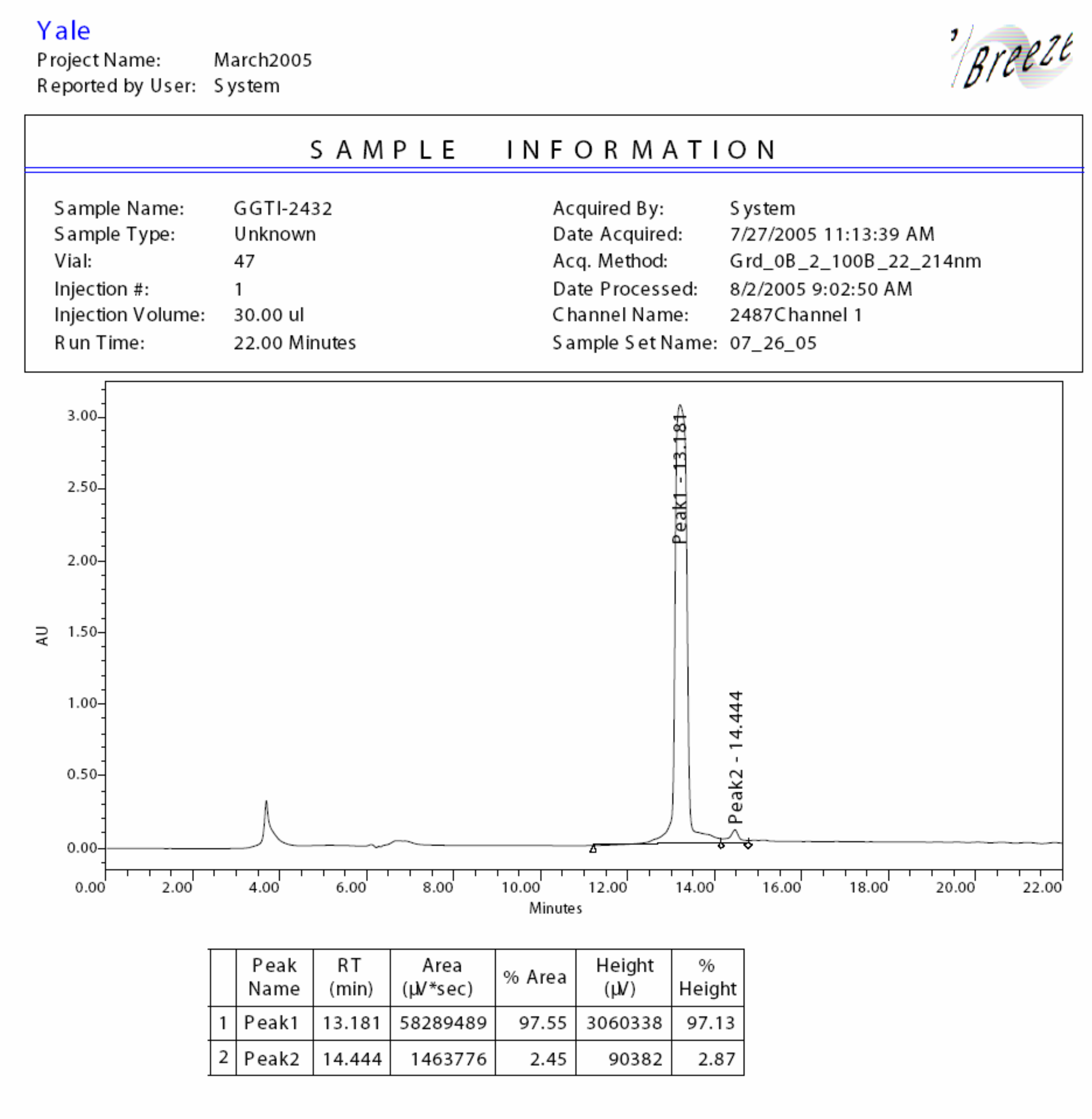
Yale
Project Name: March2005
Reported by User: System

S A M P L E I N F O R M A T I O N

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2431 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 11:48:15 AM |
| Vial: | 48 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:03:47 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 13.614 | 33915796 | 100.00 | 2884670 | 100.00 |

HPLC tract Compound **70**



Yale

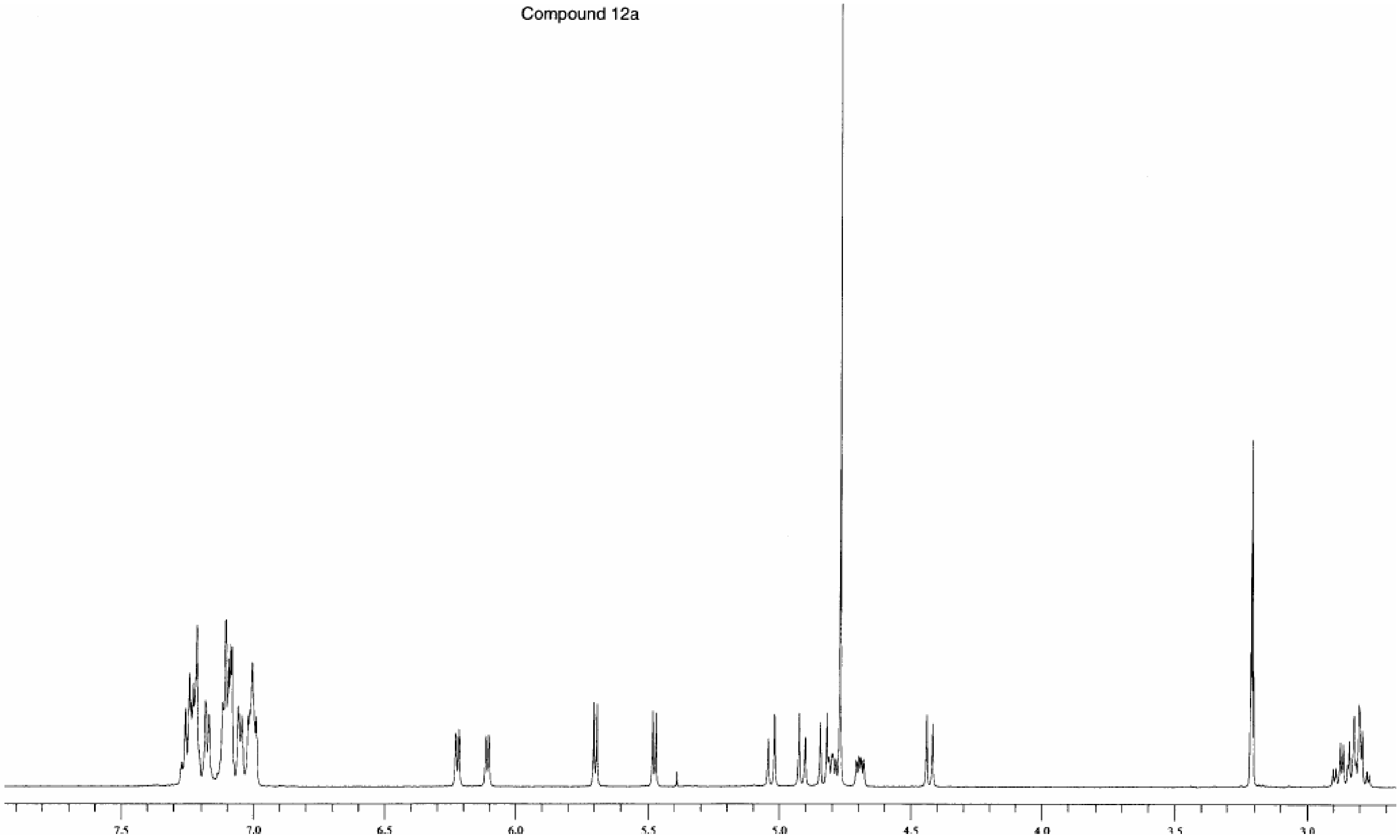
Project Name: March2005

Reported by User: System

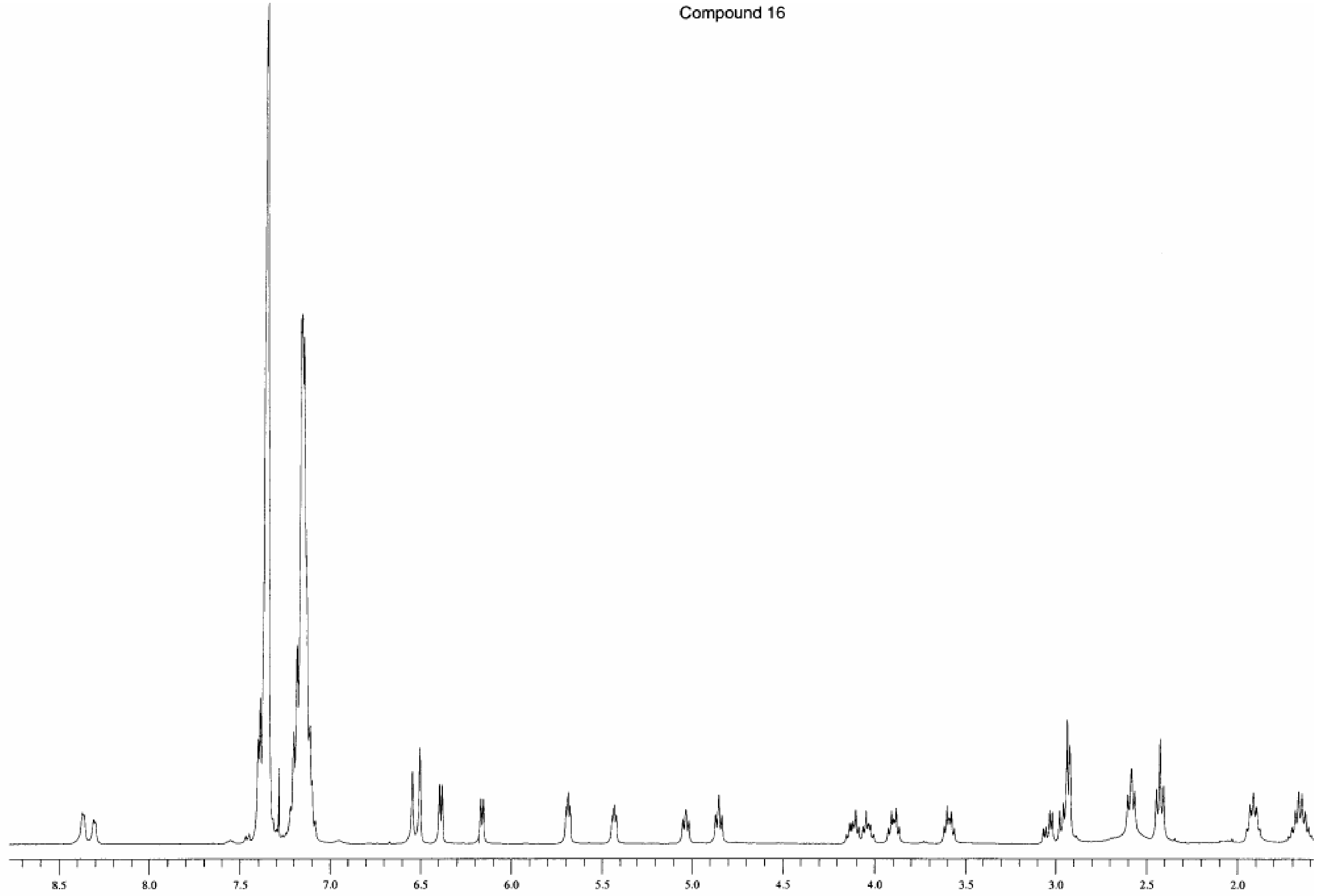
SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | GGTI-2432 | Acquired By: | System |
| Sample Type: | Unknown | Date Acquired: | 7/27/2005 11:13:39 AM |
| Vial: | 47 | Acq. Method: | Grd_0B_2_100B_22_214nm |
| Injection #: | 1 | Date Processed: | 8/2/2005 9:02:50 AM |
| Injection Volume: | 30.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 22.00 Minutes | Sample Set Name: | 07_26_05 |

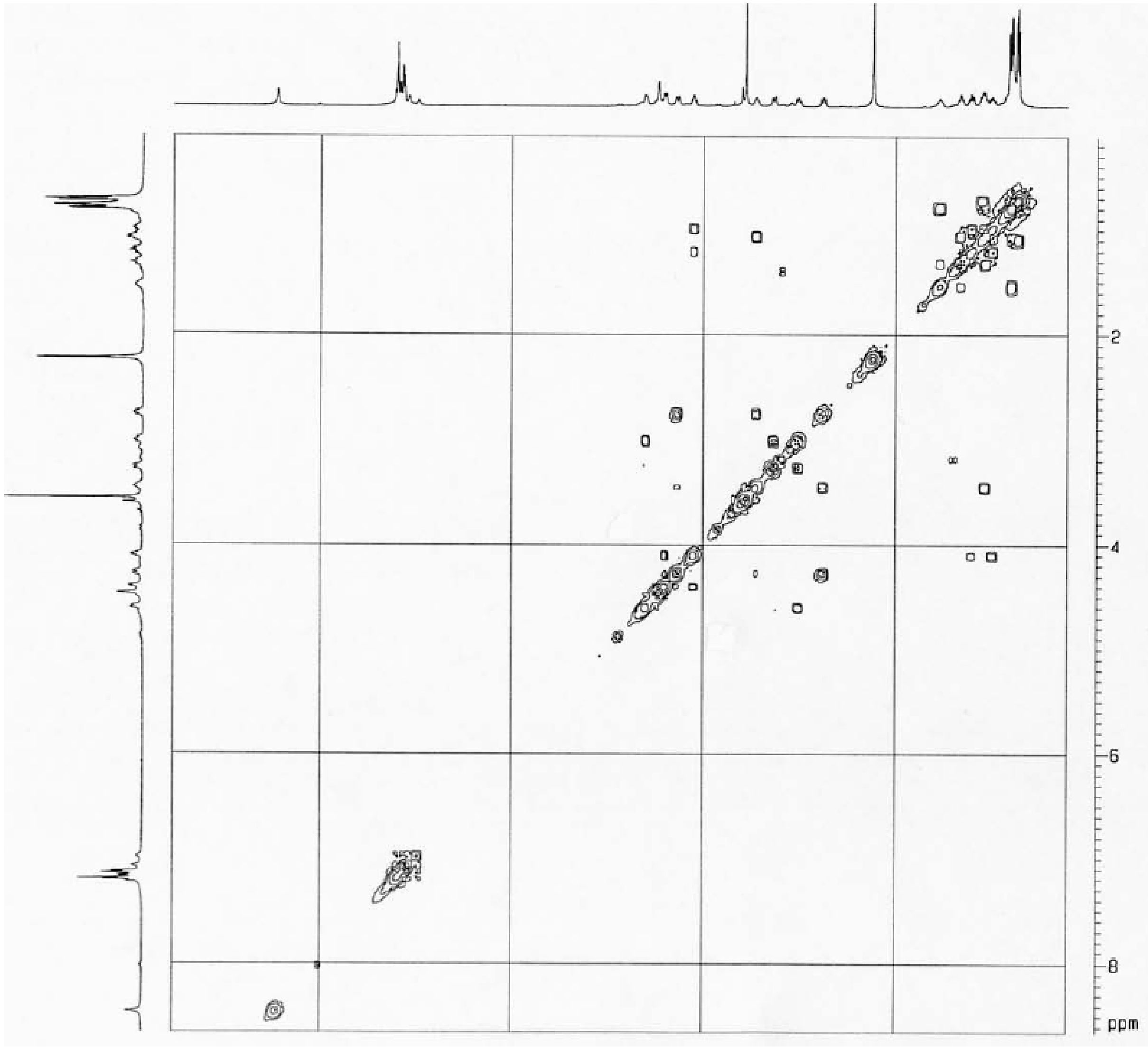
| | Peak Name | RT (min) | Area (µV*sec) | % Area | Height (µV) | % Height |
|---|---|---|---|---|---|---|
| 1 | Peak1 | 13.181 | 58289489 | 97.55 | 3060338 | 97.13 |
| 2 | Peak2 | 14.444 | 1463776 | 2.45 | 90382 | 2.87 |



Compound 12a

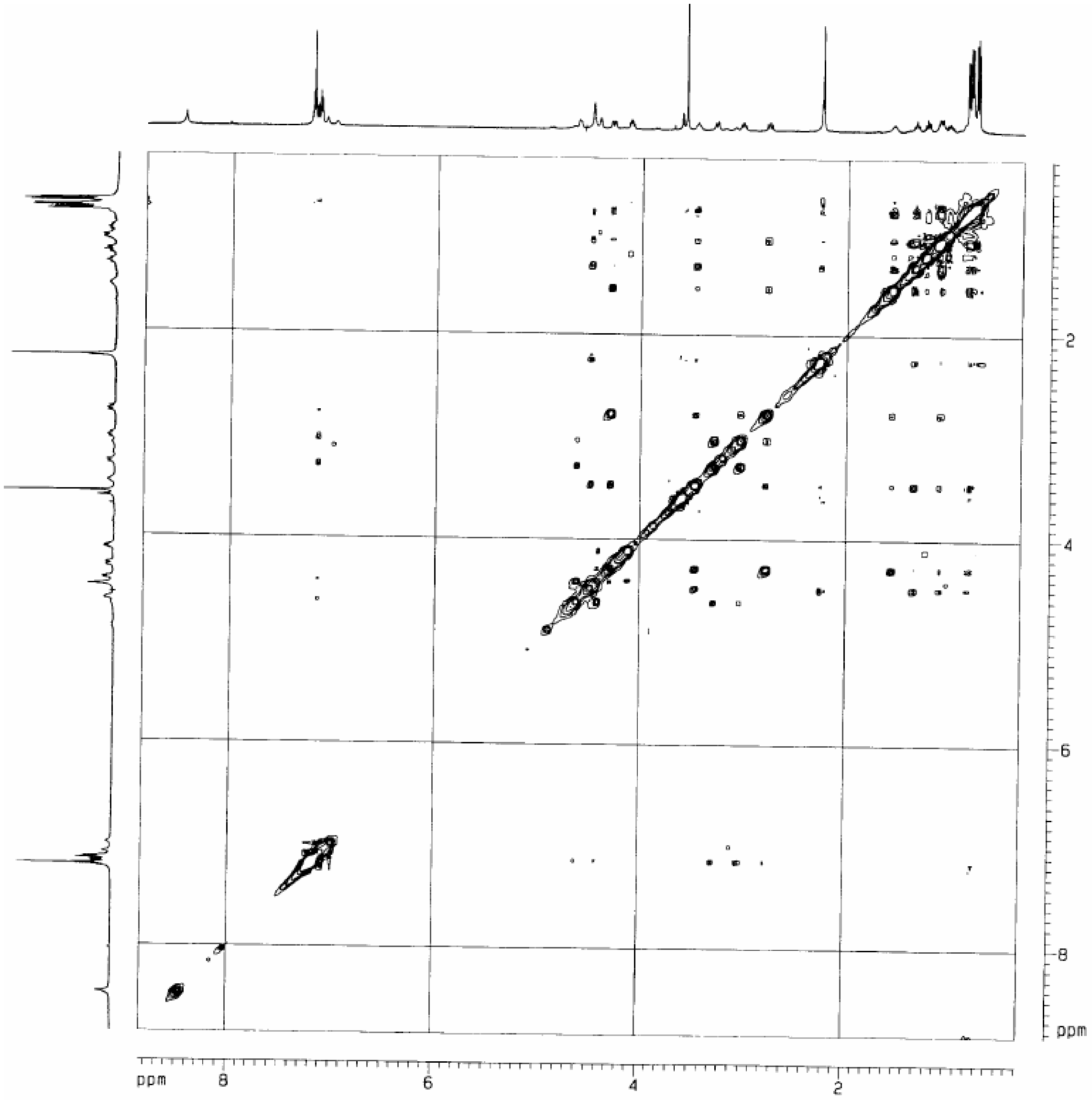


Compound **25** COSY



```
VIP number 1230428
CHP279
COSYGSSW CDCl3 usr2 peng 1

        Current Data Parameters
NAME        Aug03-2001-pon
EXPNO                   31
PROCNO                   1

      F2 - Acquisition Parameters
Date_             20010803
Time                 11.17
INSTRUM              spect
PROBHD       5 mm BBO BB-
PULPROG             cosygs
TD                    2048
SOLVENT              CDCl3
NS                       1
DS                       8
SWH               7936.508 Hz
FIDRES            3.875248 Hz
AQ               0.1290740 sec
RG                      64
DW                  63.000 usec
DE                    6.50 usec
TE                   300.0 K
d0              0.00000300 sec
D1              1.51146005 sec
d13             0.00000300 sec
D16             0.00020000 sec
IN0             0.00012600 sec

============ CHANNEL f1 ============
NUC1                    1H
P0                    7.70 usec
P1                    7.70 usec
PL1                  -4.00 dB
SFO1           500.1335278 MHz

============ GRADIENT CHANNEL ======
P16                1000.00 usec

      F1 - Acquisition parameters
ND0                      1
TD                     128
SFO1              500.1335 MHz
FIDRES           62.003967 Hz
SW                  15.869 ppm

      F2 - Processing parameters
SI                    1024
SF             500.1300460 MHz
WDW                   SINE
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.40

      F1 - Processing parameters
SI                    1024
MC2                     QF
SF             500.1300460 MHz
WDW                   SINE
SSB                      0
LB                    0.00 Hz
GB                       0

        2D NMR plot parameters
CX2                  15.00 cm
CX1                  15.00 cm
F2PLO                9.534 ppm
F2LO               4768.32 Hz
F2PHI                0.205 ppm
F2HI                102.52 Hz
F1PLO                8.651 ppm
F1LO               4326.54 Hz
```

Compound **25** NOESY



```
            Current Data Parameters
NAME                    chp279
EXPNO                       13
PROCNO                       1

         F2 - Acquisition Parameters
Date_                 20010803
Time                     18.09
INSTRUM                  spect
PROBHD        5 mm BBO BB-
PULPROG                noesytp
TD                        2048
SOLVENT                  CDCl3
NS                           8
DS                          16
SWH                   4280.822 Hz
FIDRES                2.090245 Hz
AQ                   0.2392064 sec
RG                         181
DW                     116.800 usec
DE                        6.50 usec
TE                       300.0 K
d0                  0.00000300 sec
D1                  1.00000000 sec
D8                  0.60000002 sec
IN0                 0.00011680 sec

============ CHANNEL f1 ============
NUC1                        1H
P1                        8.50 usec
PL1                      -4.00 dB
SFO1               500.1297215 MHz

         F1 - Acquisition parameters
ND0                          2
TD                         256
SFO1                  500.1297 MHz
FIDRES               16.721960 Hz
SW                       8.559 ppm

         F2 - Processing parameters
SI                        1024
SF                 500.1274378 MHz
WDW                      QSINE
SSB                          2
LB                        0.00 Hz
GB                           0
PC                        1.00

         F1 - Processing parameters
SI                        1024
MC2                       TPPI
SF                 500.1274378 MHz
WDW                      QSINE
SSB                          2
LB                        0.00 Hz
GB                           0

          2D NMR plot parameters
CX2                      15.00 cm
CX1                      15.00 cm
F2PLO                    8.846 ppm
F2LO                   4424.11 Hz
F2PHI                    0.286 ppm
F2HI                    143.28 Hz
F1PLO                    8.846 ppm
F1LO                   4424.10 Hz
F1PHI                    0.286 ppm
F1HI                    143.28 Hz
F2PPMCM                0.57063 ppm/cm
F2HZCM               285.38815 Hz/cm
```