(1*S*,2*S*,5*R*,6*R*)-3-Aza-3-benzyl-6-(*N*-(9-fluorenylmethoxycarbonyl)aminomethyl) bicyclo[3.1.0]hexyl-2-methanol (4). A solution of the amide **3** (6.0 g, 23 mmol) in THF (60 mL) was added dropwise to a suspension of lithium aluminum hydride (3.53 g, 93 mmol) in THF (150 mL) at rt. After the addition was complete, the reaction mixture was heated at reflux for 15 h and then cooled to 0 °C. Water (3.53 mL) was slowly added followed by 15% aqueous NaOH (3.53 mL), followed finally by water (10.6 mL). The mixture was allowed stir at rt for 30 min and the precipitate was removed by filtration. The cake was washed with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were concentrated under reduced pressure to afford the amine (5.39 g, 100%) as a pale oil which was used without further purification. A solution of the amine in 1,4-dioxane (60 mL) and saturated aqueous $NaHCO_3$ (60 mL) was cooled to 0 °C and 9-fluorenylmethyl chloroformate (6.31 g, 24.4 mmol) was added in portions. The mixture was stirred for 4 h at rt and then extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The resulting residue was purified on silica gel (1:1 EtOAc-hexanes) to give the compound **4** (8.03 g, 76% for two steps) as a thick colorless oil: $[\alpha]^{25}_D$ = -27.8° (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34-7.22 (m, 7H), 5.09 (m, 1H), 4.44 (d, *J* = 6.8 Hz, 2H), 4.23 (dd, apparent t, *J* = 6.6 Hz, 1H), 3.78 (d, *J* = 13.5 Hz, 1H), 3.68 (d, *J* = 13.5 Hz, 1H), 3.59-3.52 (m, 2H), 3.14 (dd, *J* = 4.5 , 10.0 Hz, 1H), 3.09 (t, *J* = 6.4 Hz, 2H), 3.00 (m, 1H), 2.62 (d, *J* = 10.0 Hz, 2H), 1.41-1.37 (m, 1H), 1.35-1.31 (m, 1H), 1.05-1.04 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 171.1, 156.5, 156.3, 144.0, 143.4, 141.4, 138.1, 128.7, 127.7, 127.1, 125.0, 120.0, 119.7, 80.4, 66.5, 61.6, 61.2, 48.1, 47.8, 42.6, 28.46, 24.3, 23.6, 21.1, 20.5 ppm; FTIR (film) 3337, 3250, 1700, 1540 cm^{-1}; HR-FABMS *m/z* 461.2411 (461.2416 calcd for $C_{29}H_{30}N_2O_3Li$, (M + Li)).

(1*S*,2*S*,5*R*,6*R*)-3-Aza-3-[(*tert*-butyl)oxycarbonyl]-6-(*N*-(9-fluorenylmethoxycarbonyl) aminomethyl)bicyclo[3.1.0]hexyl-2-methanol (5). Pd-C (1 g) was added to a solution of alcohol **4** (5.5 g, 12 mmol) and di-*tert*-butyl dicarbonate (2.9 g, 13 mmol) in EtOAc (40 mL). The mixture was stirred for 36 h under H_2 (200 psi), and the catalyst was removed by filtration through a Celite pad. The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel (6:4 EtOAc-hexanes) to give compound **5** as a thick colorless oil (5.4 g, 95%): $[\alpha]^{25}_D$ = -14.5 ° (*c* = 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.3, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 4.98 (m,1H), 4.41 (d, *J* = 5.8 Hz, 2H), 4.20 (dd, apparent t, *J* = 6.4 Hz, 1H), 4.12-4.07 (m, 1H), 3.71-3.56 (m, 4H), 3.40-3.37 (m, 1H), 3.21-3.15 (m,1H), 3.07-3.00 (m, 1H), 1.45-1.39 (m, 11H), 0.80-0.74 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 171.2, 156.5, 144.1, 141.4, 140.0, 128.4, 128.2, 127.8, 127.1, 127.0, 125.1, 120.1, 66.9, 66.6, 63.0, 60.4, 58.1, 55.4, 47.4, 43.5, 26.7, 25.6, 23.2, 21.1, 14.2; FTIR (film), 3510, 3332, 1701, 1521 cm^{-1}; MS (CI) *m/z* 465 (MH); Anal. Calcd for $C_{27}H_{32}N_2O_5$: C, 69.81; H, 6.94; N, 6.03. Found: C, 70.02; H, 7.08; N, 6.09.

(1*S*,2*S*,5*R*,6*R*)-3-Aza-3-[(*tert*-butyl)oxycarbonyl]-6-(*N*-(9-fluorenylmethoxycarbonyl) aminomethyl)bicyclo[3.1.0]hexane-2-carboxylic acid (6). The alcohol **5** (4.68 g, 10.1 mmol), TEMPO (0.11 g, 0.7 mmol) and $NaClO_2$ (1.8 g, 20 mmol) were added to a mixture of acetonitrile (25 mL) and aqueous NaH_2PO_4 (0.67 M, 20 mL). This mixture was warmed to 35 °C and bleach (0.28 mL) was slowly added. After 5 h at 35 °C, the reaction mixture was cooled to rt, then poured over a solution of Na_2SO_3 (2.5 g), water

(10 mL) and ice (20 g). The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were concentrated to afford a yellow residue which was dissolved in 20 mL of EtOAc. This solution was extracted with $NaHCO_3$ (10%) (2 × 20 mL). The aqueous layer was cooled to 0 °C, slowly acidified with concentrated HCl (4.5 mL) to pH 2, then extracted with EtOAc (4 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to afford the acid **6** (4.3 g, 90%) as a colorless foam: mp 94-96 °C; $[\alpha]^{25}_D$ = -41.1° (*c* = 0.96, $CHCl_3$); ^1H NMR (500MHz, $CDCl_3$) δ 10.61-10.54 (br s, 1H), 7.75 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 7.1 Hz, 2H), 4.49-4.33 (m, 2H), 4.23-4.17 (m, 1H), 3.72-3.46 (m, 4H), 3.25-3.03 (m, 1H), 2.88-2.82 (m, 1H), 1.67-1.63 (m, 1H), 1.45 (s, 5H), 1.41 (s, 4H), 0.96-0.90 (m, 1H), 0.72-0.62 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 176.1, 175.2, 156.7, 155.4, 154.4, 143.9, 143.7, 141.4, 127.8, 127.1, 125.1, 124.7, 120.0, 85.2, 80.9, 66.7, 61.2, 60.9, 60.5, 48.4, 18.2, 47.3, 42.4, 30.6, 28.4, 28.3, 27.5, 25.3, 24.3, 22.6, 22.4, 21.2, 21.01, 20.6 ppm; FTIR (KBr) 3210, 1730, 1700, 1685 cm^{-1}; HR-FABMS *m/z* 479.2172 (479.2182 calcd for $C_{27}H_{31}N_2O_6$, MH).

(4*R*)-1-[(*tert*-Butyl)oxycarbonyl]-4-(*N*-(9-fluorenylmethoxycarbonyl)aminomethyl) pyrrolidine-2-carboxylic acid (9). The acid **8** (1 g, 4.1 mmol) was dissolved in 1,4-dioxane (15 mL) and a saturated aqueous $NaHCO_3$ (15 mL). The mixture was cooled to 0 °C and 9-fluorenylmethyl chloroformate (1.1 g, 4.3 mmol) was added in portions. After 4 h at rt, the mixture was carefully acidified with concentrated HCl to pH 2 then extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The resulting white solid was purified by flash chromatography on silica gel (96:4:0.5, CH_2Cl_2-MeOH-AcOH) to give the acid **9** as a fluffy powder (1.34 g, 70%):

mp 79-81 °C; $[\alpha]^{25}_{D}$ = -42.3° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.80-10.69 (br s, 1H), 8.02-7.99 (m, 2H), 7.85-7.78 (m, 1.5 H), 7.65-7.62 (m, 2H), 7.58-7.55 (m, 2H), 7.50-7.39 (m, 0.5 H), 5.80-5.76 (m, 0.5 H),5.57-5.54 (m, 0.5H), 4.77-4.74 (m, 0.5 H), 4.67-4.57 (m, 2H), 4.46-4.43 (m, 1.5 H), 4.01-3.97 (m, 0.5 H), 3.89-3.86 (m, 0.5 H), 3.49-3.42 (m, 1.5 H), 3.33-3.27 (m, 1H), 3.20-3.16 (m, 0.5 H), 2.81-2.78 (m, 0.5 H), 2.53-2.47 (m, 0.5H), 2.41-2.36 (m, 0.5H), 2.30-2.21 (m, 0.5H), 2.15-2.09 (m, 0.5H), 2.02-1.98 (m, 0.5 H), 1.75 (s, 4.5 H), 1.70 (s, 4.5H); ^{13}C NMR (125 MHz, $CDCl_3$) 177.1, 175.4, 157.8, 156.9, 155.5, 154.2, 143.9, 141.4, 137.9, 129.1, 128.5, 127.8, 127.1, 125.4, 125.1, 124.8, 120.0, 81.1, 80.7, 67.2, 66.8, 58.8, 50.1, 49.6, 47.3, 43.6, 43.1, 38.2, 37.2, 34.0, 32.8, 28.5, 28.3, 21.5; FTIR (KBr) 3220, 1735, 1727, 1700, 1695, 1685 cm^{-1}; HR-FABMS *m/z* 473.2260 (473.2264 calcd for $C_{26}H_{30}N_2O_6Li$, (M + Li)).

General procedure for the solid phase guanylation of the proline templated amino acids : Fmoc-Gly-Wang resin (200 mg, 1.2 mmol) was swelled for 10 min in CH_2Cl_2 then washed with DMF (2 × 2 min) and then piperidine (20% in DMF, 3 mL) was added to the resin. The mixture was shaken for 30 min then washed with DMF (4 × 2 min). The PTAA (0.144 mmol, 1.2 eq), HOBt (22.1 mg, 0.144 mmol) and DIC (36.3 mg, 0.288 mmol) were added to the resin as a solution in DMF (3 mL). The mixture was shaken for 6 h then washed with DMF (3 × 2 min). The resin was submitted to another piperidine deprotection and washing cycle. The carbethoxythiourea (0.192 mmol, 1.6 eq), DIEA (24.8 mg, 0.192 mmol) and EDCI (92 mg, 0.48 mmol) were added to the mixture as a solution in DMF (3 mL). After 40 h, the resin was washed with DMF (3 × 2 min), CH_2Cl_2 (3 × 2 min) then shaken in TFA (5 mL) for 20 min. The mixture was filtered, and resin washed with TFA (3 × 5 mL). The combined organic layers were concentrated to give a thick oil that was triturated with Et_2O to yield the guanylated dipeptide as a white solid. The white solid was washed with Et_2O (3 × 20 mL) and dried under vacuum.

Dipeptide 10: ^1H NMR (CD_3OD) δ 4.27 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.93 (d, *J* = 17.7 Hz, 1H), 3.85 (d, *J* = 17.7 Hz, 1H), 3.50 (dd, *J* = 4.1, 11.3 Hz, 1H), 3.37 (d, *J* = 11. Hz, 1H), 3.25-3.20 (m, 2H), 2.02-1.98 (m, 1H), 1.82-1.80 (m, 1H), 1.57-1.54 (m, 2H), 1.28-1.23 (m, 12H), 0.86 (t, *J* = 7.1 Hz, 3H); MS/ESI *m/z* 412 (MH).

Dipeptide 11: ^1H NMR (500 MHz, CD_3OD) δ 4.25 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.88 (d, *J* = 17.7 Hz, 1H), 3.83 (d, *J* = 17.7 Hz, 1H), 3.47 (dd, *J* = 4.2, 11.4 Hz, 1H), 3.35 (d, *J* = 11.4 Hz, 1H), 3.32-3.19 (m, 5H), 1.97 (dd, *J* = 3.1, 6.7 Hz, 1H), 1.81-1.76 (m, 1H), 1.59-1.53 (m, 2H), 1.28-1.08 (m, 11H), 0.82 (t, *J* = 6.9 Hz, 3H); MS/ESI m/z 426 (MH).

Dipeptide 12: ^1H NMR (CD_3OD) δ 4.41 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.98 (d, *J* = 17.7 Hz, 1H), 3.87 (d, *J* = 17.7 Hz, 1H), 3.58 (dd, *J* = 3.1, 11.6 Hz, 1H), 3.45 (d, *J* = 11.6 Hz, 1H), 3.35-3.23 (m, 2H), 2.04-2.01 (m, 1H), 1.92-1.89 (m,1H), 1.58-1.51 (m, 3H), 1.35-1.21 (m, 23H), 0.82 (t, *J* = 6.7 Hz, 3H); MS/ESI *m/z* 496 (MH).

Dipeptide 13: ^1H NMR (500 MHz, CD_3OD) δ 4.24 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.89 (d, *J* = 17.7 Hz, 1H), 3.83 (d, *J* = 17.7 Hz, 1H), 3.47 (dd, *J* = 4.1, 11.3 Hz, 1H), 3.37 (dd, *J* = 6.5, 14.7 Hz, 1H), 3.32 (d, *J* = 11.3 Hz, 1H), 3.24-3.18 (m, 2H), 1.97 (dd, *J* = 3.5, 6.7 Hz, 1H), 1.83-175 (m, 1H), 1.38 (s, 9H),1.22 (t, J = 7.1 Hz, 3H); MS/ESI m/z 384 (MH).

Dipeptide 14: ^1H NMR (CD_3OD) δ 5.86-5.78 (m, 1H), 5.24-5.19 (m, 2H), 4.39 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.96 (d, *J* = 17.7 Hz, 1H), 3.86 (d, *J* = 17.7 Hz, 1H), 3.56 (dd, *J* = 4.4, 11.4 Hz, 1H), 3.43 (d, *J* = 11.4, 1H), 3.35 (dd, *J* = 6.7, 14.6 Hz, 1H), 3.28-3.21 (m, 3H), 2.03 (dd, *J* = 3.2, 6.7 Hz, 1H),1.90-1.86 (m, 1H), 1.34-1.29 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); MS/ESI *m/z* 368 (MH).

Dipeptide 15: [1]H NMR (CD_3OD) δ 4.33 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.93 (d, J = 17.7 Hz, 1H), 3.85 (d, J = 17.7 Hz, 1H), 3.57-3.54 (m, 1H), 3.52 (dd, J = 4.3, 11.4 Hz, 1H), 3.41 (d, J = 11.4 Hz, 1H), 3.32 (dd, J = 6.9, 14.4 Hz, 1H), 3.24-3.20 (m, 1H), 2.02-1.98 (m, 1H), 1.85-1.76 (m, 3H), 1.70-1.66 (m, 2H), 1.61-1.55 (m, 1H), 1.33-1.25 (m, 6H), 1.23 (t, J = 7.1 Hz, 3H); MS/ESI *m/z* 410 (MH).

Dipeptide 16: [1]H NMR (500 MHz, CD_3OD) δ 4.39 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.94 (d, J = 17.7 Hz, 1H), 3.85 (d, J = 17.7 Hz, 1H), 3.57 (dd, J = 4.2, 11.3 Hz, 1H), 3.43 (d, J = 11.3 Hz, 1H), 3.35 (dd. 1H, J = 6.8, 14.3 Hz, 1H), 3.29-3.21 (m, 2H), 2.05-1.99 (m, 3H), 1.89-1.86 (m, 1H), 1.73-1.68 (m, 2H), 1.60-1.52 (m, 4H), 1.33-1.28 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H); MS/ESI *m/z* 396 (MH).

Dipeptide 17: [1]H NMR (CD_3OD) δ 7.16 (d, J = 8.1 Hz, 2H), 6.94 (d, J = 8.1 Hz, 2H), 4.39 (s, 1H), 4.24-4.19 (m, 2H), 3.98 (d, J = 17.7 Hz, 1H), 3.87 (d, J = 17.7 Hz, 1H), 3.72 (s, 3H), 3.58-3.54 (m, 1H), 3.45 (d, J = 11.1 Hz, 1H), 3.37 (dd, J = 6.1, 13.9 Hz, 1H), 3.25-3.21 (m, 1H), 2.04-2.01 (m, 1H), 1.92-1.87 (m, 1H), 1.30-1.25 (m, 1H), 1.24-1.19 (m, 3H), MS/ESI *m/z* 434 (MH).

Dipeptide 18: [1]H NMR (CD_3OD) δ 7.71 (d, J = 7.2 Hz, 1H), 7.56-7.53 (m, 1H), 7.46-7.41 (m, 1H), 7.39-7.35 (m, 1H), 4.33 (s, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.95 (d, J = 17.7 Hz, 1H), 3.86 (d, J = 17.7 Hz, 1H), 3.55 (dd, J = 4.1, 11.2 Hz, 1H), 3.43-3.38 (m, 1H), 3.23-3.19 (m, 2H), 2.01-1.99 (m, 1H), 1.87-1.84 (m, 1H),1.26-1.23 (m, 1H), 1.19 (t, J = 7.1 Hz, 3H); MS/ESI *m/z* 472 (MH).

Dipeptide 19: [1]H NMR (CD_3OD) δ 7.34 (dd apparent t, J = 7.2 Hz, 1H), 7.20 (d, J = 7.2 Hz, 1H), 7.08 (d, J = 8.1 Hz, 1H), 6.97 (dd apparent t, J = 7.3 Hz, 1H), 4.39 (s, 1H), 4.24-4.20 (m, 2H), 3.98 (d, J = 17.7 Hz, 1H), 3.87 (d, J = 17.7 Hz, 1H), 3.80 (s, 3H), 3.59 (dd, *J* = 4.1, 11.2 Hz, 1H), 3.44 (dd, *J* = 6.4, 14.4 Hz, 1H), 3.24-3.20 (m, 2H), 2.06-2.02 (m,1H), 1.95-1.90 (m, 1H), 1.35-1.30 (m, 1H), 1.25-1.21 (m, 3H); MS/ESI *m/z* 434 (MH).

Dipeptide 21: ^{1}H NMR (500 MHz, CD_3OD) δ 7.33-7.20 (m, 5H), 4.54 (s, 2H), 4.36 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.97 (d, *J* = 17.7 Hz, 1H), 3.84 (d, *J* = 17.7 Hz, 1H), 3.51 (dd, *J* = 4.1, 11.4 Hz, 1H), 3.39-3.35 (m, 1H), 3.25-3.20 (m, 2H), 2.01-1.97 (m, 1H), 1.80-1.76 (m, 1H), 1.28-1.25 (m, 1H), 1.20 (t, *J* = 7.1 Hz, 3H), MS/ESI *m/z* 418 (MH)

Dipeptide 22: ^{1}H NMR (CD_3OD) δ 7.19 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 4.36 (s, 1H), 4.22-4.16 (m, 2H), 3.95 (d, *J* = 17.7 Hz, 1H), 3.83 (d, *J* = 17.7 Hz, 1H), 3.53 (dd, 1H, *J* = 3.8, 11.2 Hz, 1H), 3.40 (d, *J* = 11.2 Hz, 1H), 3.35 (dd, *J* = 6.9, 14.4 Hz, 1H), 3.22-3.17 (m, 1H), 2.25 (s, 3H), 2.03-1.97 (m, 1H), 1.89-1.85 (m,1H), 1.30-12.5 (m, 1H), 1.24-1.18 (m, 3H); MS/ESI *m/z* 418 (MH).

Dipeptide 23: ^{1}H NMR (CD_3OD) δ 5.84-5.79 (m, 1H), 2.23-5.18 (m, 2H), 4.43 (dd, *J* = 4.7, 9.0 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.95 (d, *J* = 17.7 Hz, 1H), 3.83 (d, *J* = 17.7 Hz, 1H), 3.55 (dd, *J* = 7.6, 11.4 Hz, 1H), 3.43 (d, *J* = 7.6 Hz, 2H), 3.24-3.21 (m, 2H), 3.06 (dd, *J* = 8.6, 11.4 Hz, 1H), 2.68-2.64 (m, 1H), 2.30-2.27 (m, 1H), 2.21-2.12 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 1H); MS/ESI *m/z* 356 (MH).

Dipeptide 24: ^{1}H NMR (CD_3OD) δ 4.43 (dd, *J* = 4.5, 8.9 Hz, 1H), 4.25-4.19 (m, 2H), 3.96 (d, *J* = 17.7 Hz, 1H), 3.85 (d, *J* = 17.7 Hz, 1H), 3.55 (dd, *J* = 7.8, 11.6 Hz, 1H), 3.40 (q, *J* = 7.0 Hz, 2H), 3.25-3.21 (m, 1H), 2.66-2.61 (m, 1H), 2.32-2.28 (m, 1H), 2.17-2.11 (m, 1H), 1.27-1.20 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.93-0.89 (m, 1H), 0.73-0.69 (m, 2H); MS/ESI *m/z* 356 (MH).

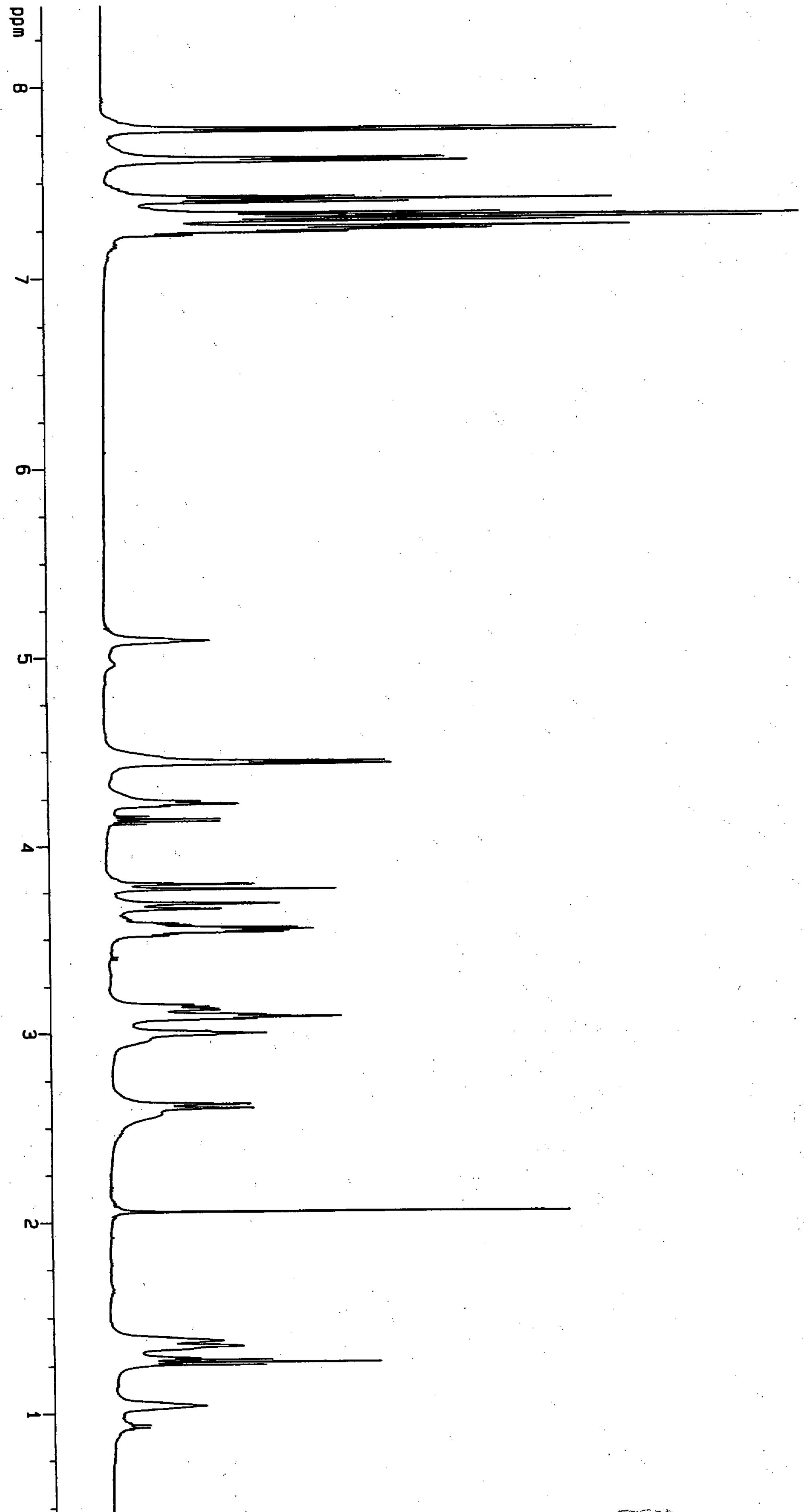
Dipeptide 25: ^{1}H NMR (CD_3OD) δ 7.36-7.23 (m, 5H), 4.52 (s, 2H), 4.41-4.38 (m, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.95 (d, J = 17.7 Hz, 1H), 3.83 (d, J = 17.7 Hz, 1H), 3.42 (d, J = 7.0 Hz, 2H), 3.25-3.20 (m, 1H), 2.99-2.93 (m, 1H), 2.73-2.68 (m, 1H), 2.27-2.21 (m, 1H), 2.20-2.15 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H); MS/ESI *m/z* 406 (MH).

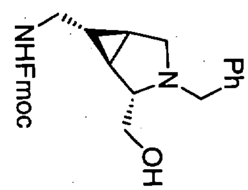
Dipeptide 26: ^{1}H NMR (CD_3OD) δ 4.40 (dd, J = 4.9, 8.8 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.91 (d, J = 17.7 Hz, 1H), 3.78 (d, J = 17.7 Hz, 1H), 3.51 (dd, J = 7.6, 11.6 Hz, 1H), 3.39 (d, J = 7.6 Hz, 2H), 3.20-3.16 (m, 1H), 3.03 (dd, J = 8.3, 11.6 Hz, 1H), 2.66-2.95 (m, 1H), 2.28-2.23 (m, 1H), 2.14-2.08 (m, 1H), 1.96-1.91 (m, 2H), 1.68-1.64 (m, 2H), 1.55-1.44 (m, 4H), 1.21 (t, J = 7.1 Hz, 3H); MS/ESI *m/z* 384 (MH).

Dipeptide 27: ^{1}H NMR (CD_3OD) δ 4.37 (dd, J = 5.1, 8.8 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.88 (d, J = 17.7Hz, 1H), 3.78 (d, J = 17.7 Hz, 1H), 3.50-3.45 (m, 1H), 3.33 (d, J = 7.4 Hz, 2H), 3.20-3.15 (m, 2H), 3.02 (dd, J = 7.9, 11.6 Hz, 1H), 2.63-2.57 (m, 1H), 2.25-2.21 (m, 1H), 2.13-2.04 (m, 1H), 1.54-1.47 (m, 2H), 1.26-1.17 (m, 11H), 0.79 (t, J = 6.9 Hz, 3H); MS/ESI *m/z* 414 (MH).

Solid phase synthesis of the pentapeptides 28 and 29: Boc-Ile PAM resin (250 mg, 0.2 mmol) was swelled for 10 min in CH_2Cl_2, shaken 5 min in TFA (50% in CH_2Cl_2), shaken 20 min in TFA (50% in CH_2Cl_2), then washed with CH_2Cl_2 (3 × 1 min) and DMF (3 × 1 min). Boc-Ala (113 mg, 0.6 mmol), DIC (190 μL, 1.2 mmol), HOBt (92 mg, 0.6 mmol) and DIEA (175 μL, 1 mmol) were successively added to the resin which was previously swelled in DMF (3 mL). The mixture was shaken for 1 h then submitted to a washing-TFA deprotection cycle. Boc-Gln (148 mg, 0.6 mmol) (for peptide **28**) or Boc-Ala (113 mg, 0.6 mmol) (for peptide **29**), DIC (190 μL, 1.2 mmol), HOBt (92 mg, 0.6 mmol) and DIEA (175 μL, 1 mmol) were successively added to the resin which was previously swelled in DMF (3 mL). The mixture was shaken for 1 h then submitted to a washing-TFA deprotection cycle. The resin was shaken for 15 min with DIEA (30% in DMF) (3 mL), washed with DMF (4 × 2 min) then swelled in DMF (3 mL). PTAA **6** (124 mg, 0.26 mmol), HOBt (40 mg, 0.26 mmol) and DIC (81 μL, 0.52 mmol) were successively added to the resin. The mixture was shaken for 6 h then washed with DMF (3 × 2min). N-Ethoxycarbonyl-N'-(cyclopentyl)-thiourea (69 mg, 0.32 mmol), DIEA (56 μL, 0.32 mmol) and EDCI (153 mg, 0.8 mmol) were successively added to the resin which was previously swelled in DMF (3 mL). The mixture was shaken for 40 h, then submitted to a washing-TFA deprotection cycle. The resin was shaken for 15 min with DIEA (30% in DMF) (3 mL), washed with DMF (4 × 2 min) then swelled in DMF (3 mL). PTAA **9** (121 mg, 0.26 mmol), HOAt (35 mg, 0.26 mmol) and DIC (81 μL, 0.52 mmol) were successively added to the resin. The mixture was shaken for 6 h then washed with DMF (3 × 2min). N-Ethoxycarbonyl-N'-(*t*-butyl)-thiourea (66 mg, 0.32 mmol) (for peptide **28**) or N-Ethoxycarbonyl-N'-(*p*-tolyl)-thiourea (76 mg, 0.32 mmol) (for peptide **29**), DIEA (56 μl, 0.32 mmol) and EDCI (153 mg, 0.8 mmol) were successively added to the resin which was previously swelled in DMF (3 mL). The mixture was shaken for 40 h, washed with DMF (3 × 2 min) and CH_2Cl_2 (4 × 2 min) then left overnight under high vaccum. The resin was suspended in TFA (6 mL) then cooled to 0 °C. Thioanisole (0.91 mL), *m*-cresol (0.2 mL) and TMSOTf (1.6 mL) were successively added to the suspension which was stirred under nitrogen for 4 h then filtered. The organic layer was quickly concentrated to afford a brown oil. Et_2O (300 mL) was added to the crude compound, after 2 h a precipitate fromed in the flask, this crude pentapeptide was washed with Et_2O

(5 × 30 mL). The yield was calculated by NMR integration: peptide **28**, 74 %, peptide **29**, 61 %).





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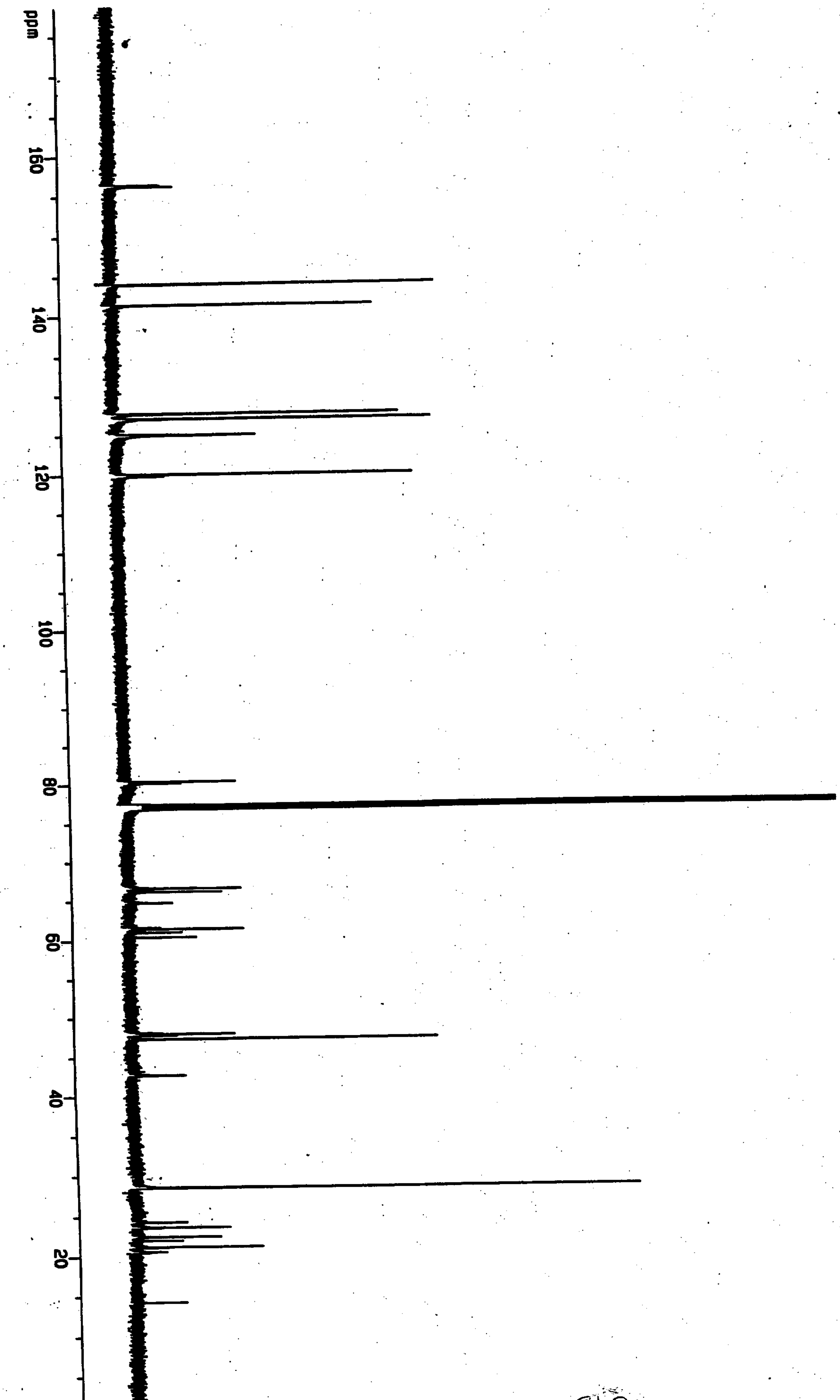

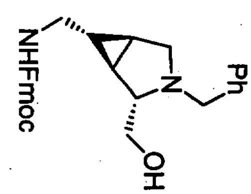

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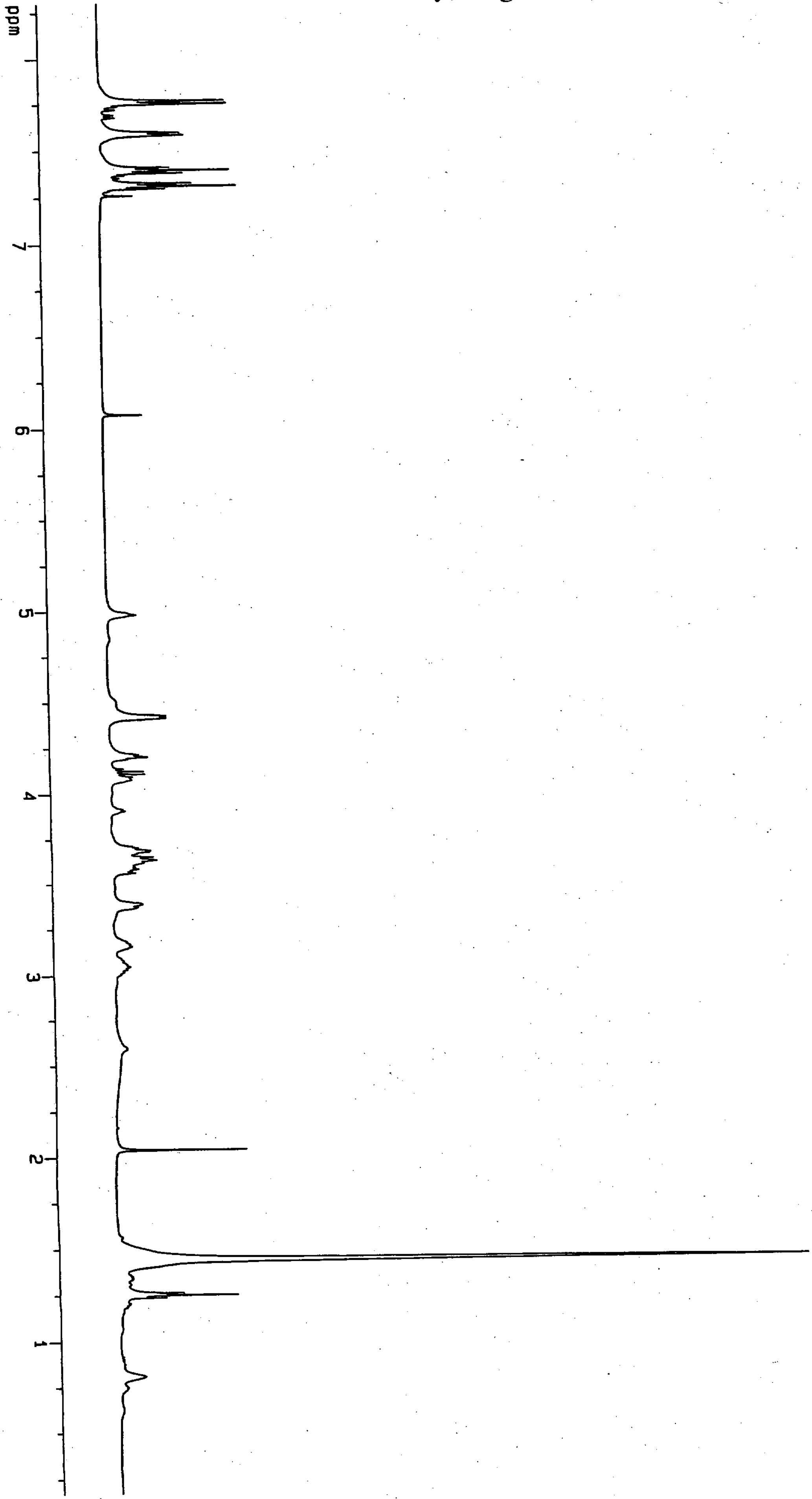
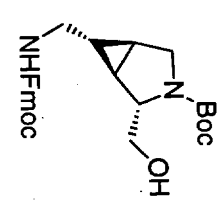
S1-2





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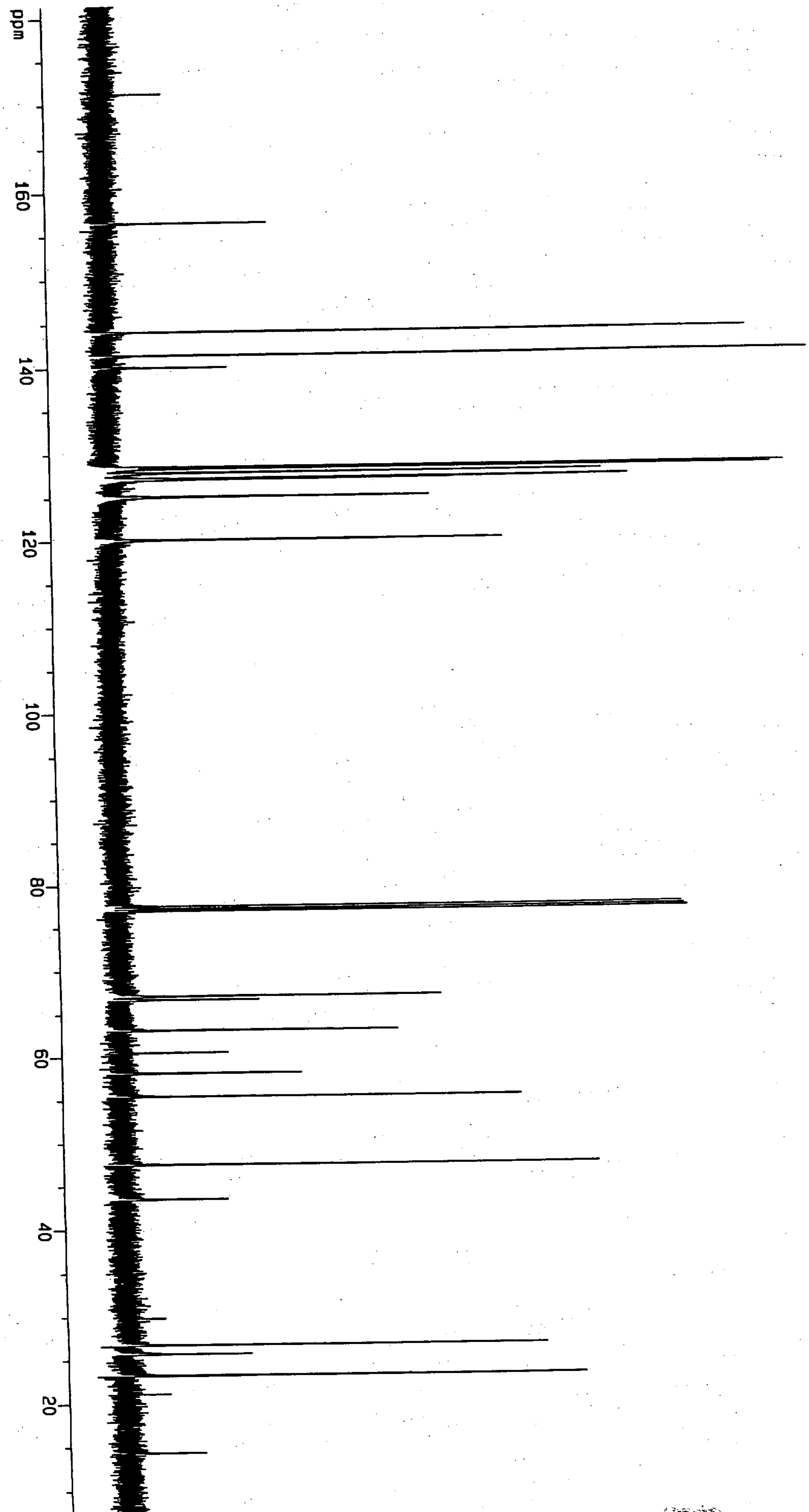

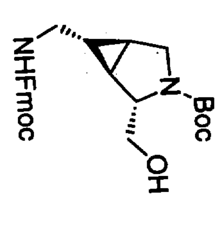

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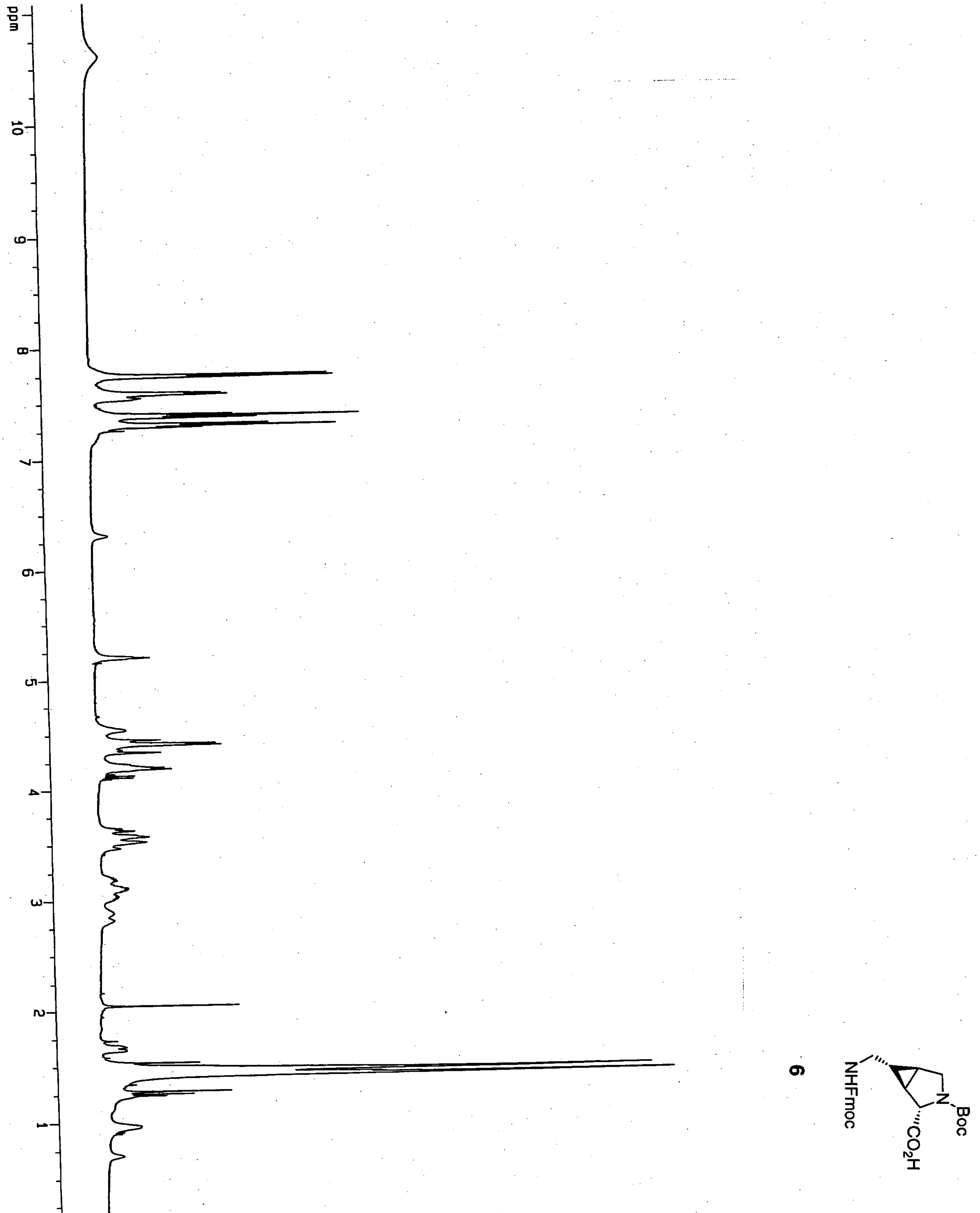
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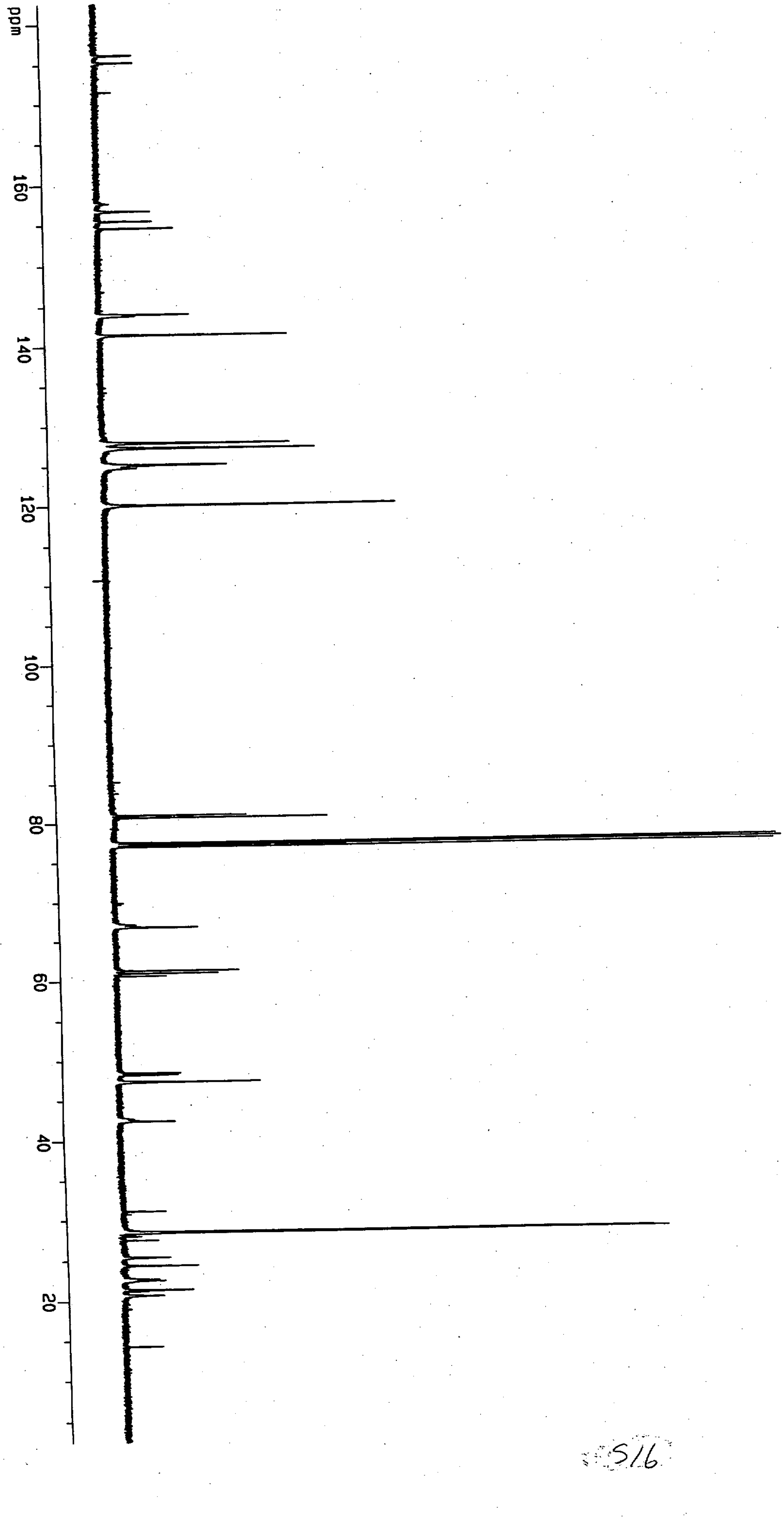

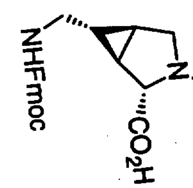

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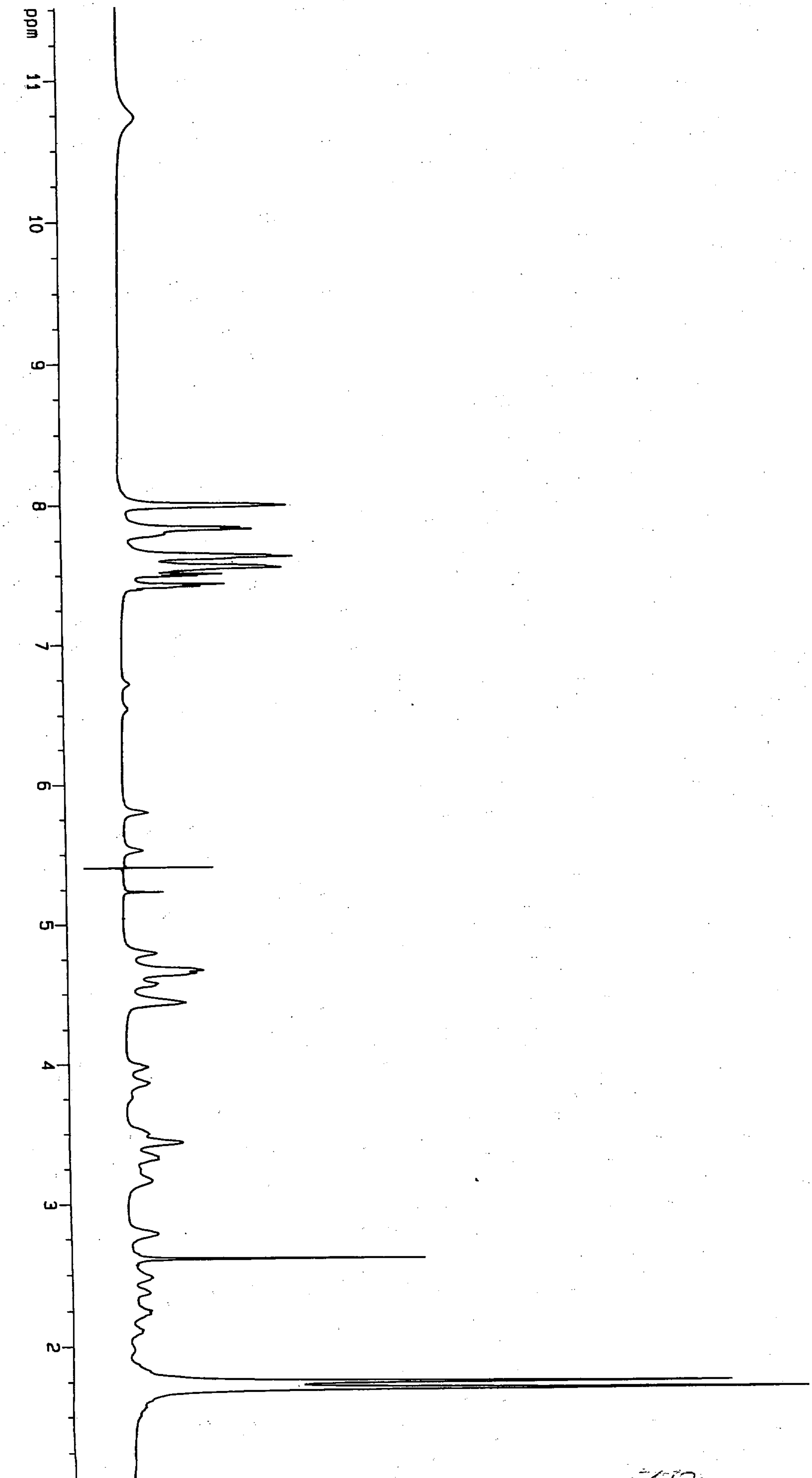

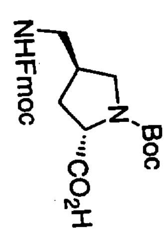

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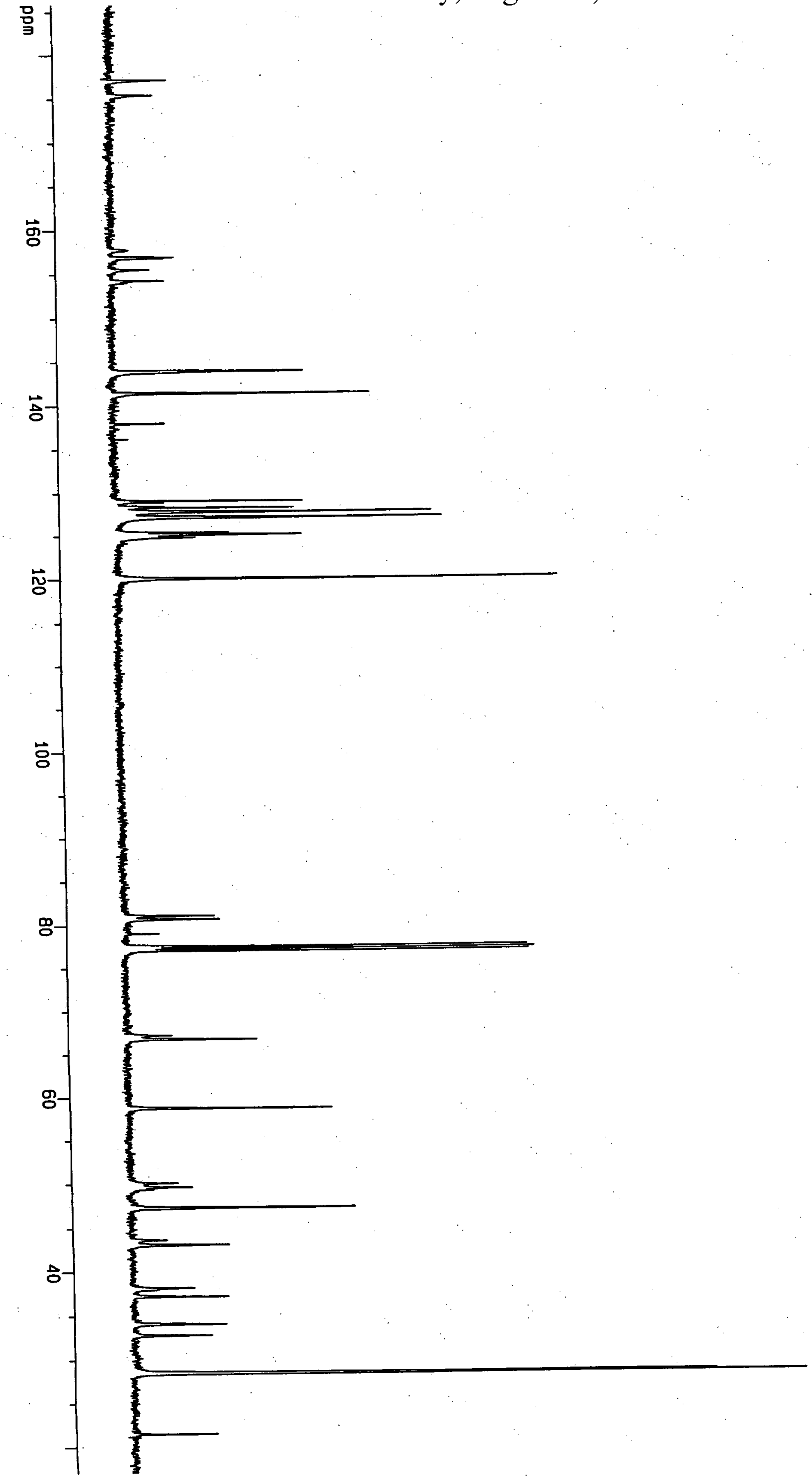
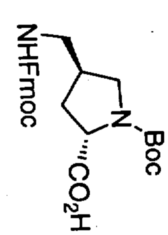
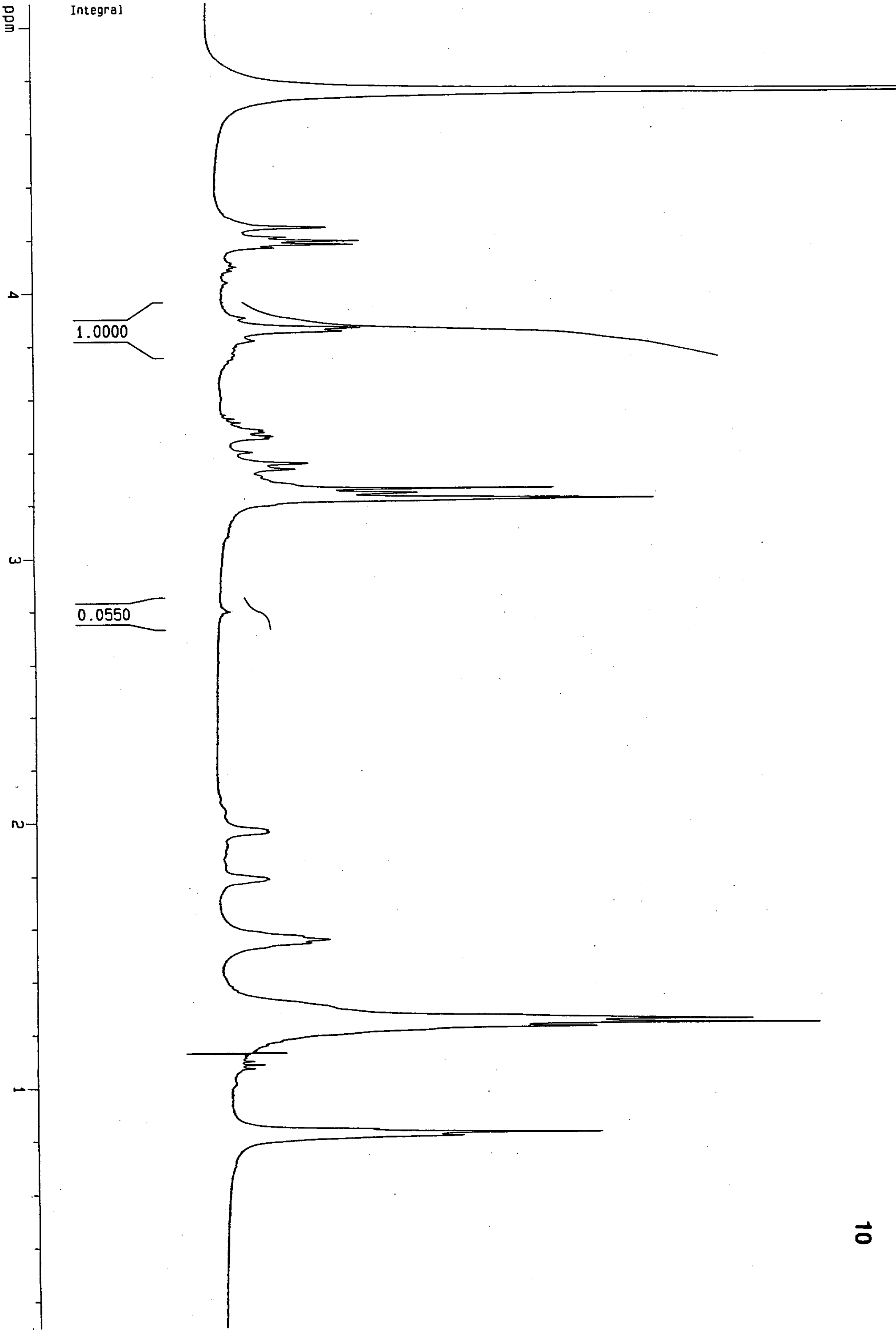
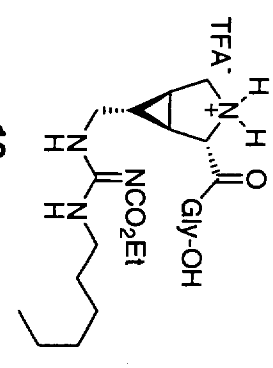




9

S18





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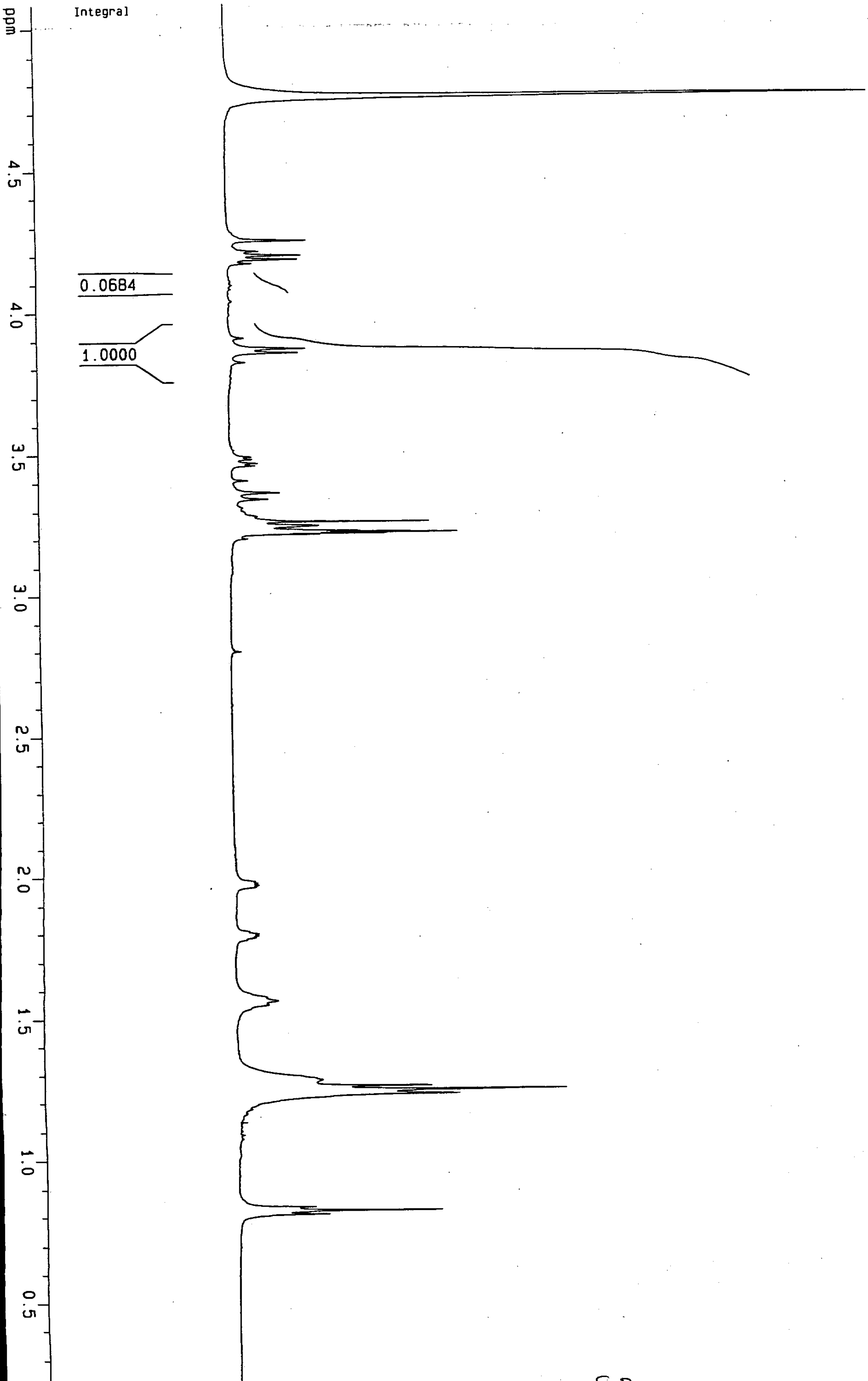
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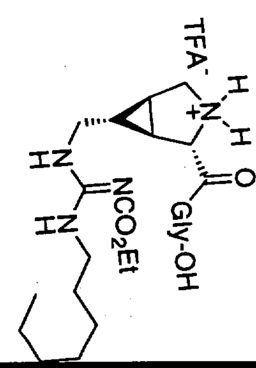
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+
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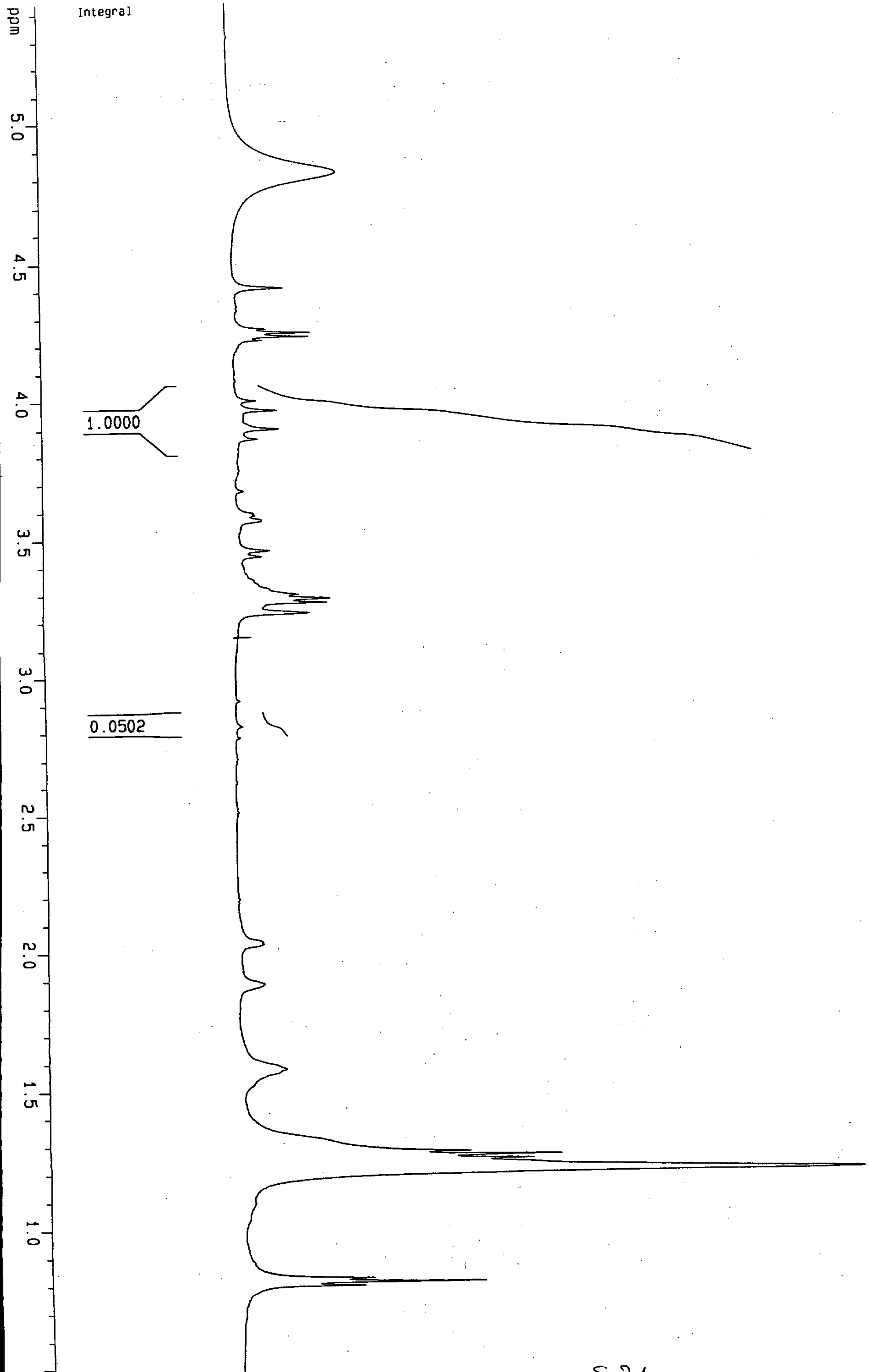
N
H
N

11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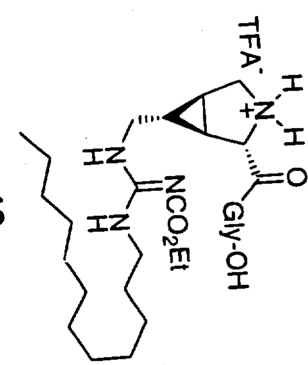
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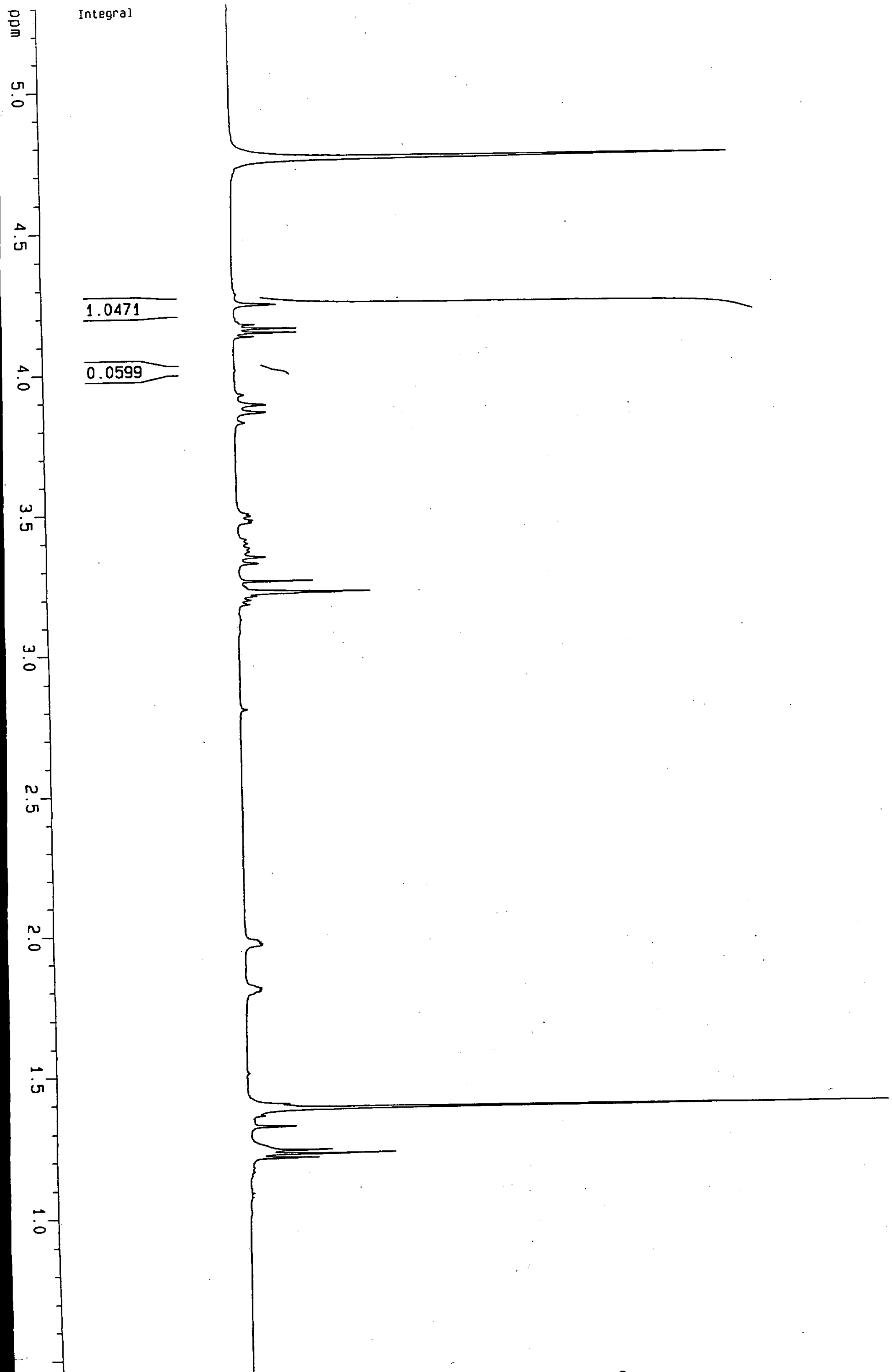
12

S21



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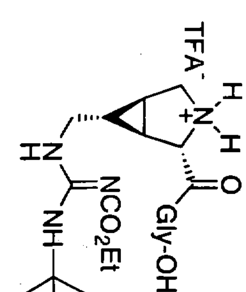

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O
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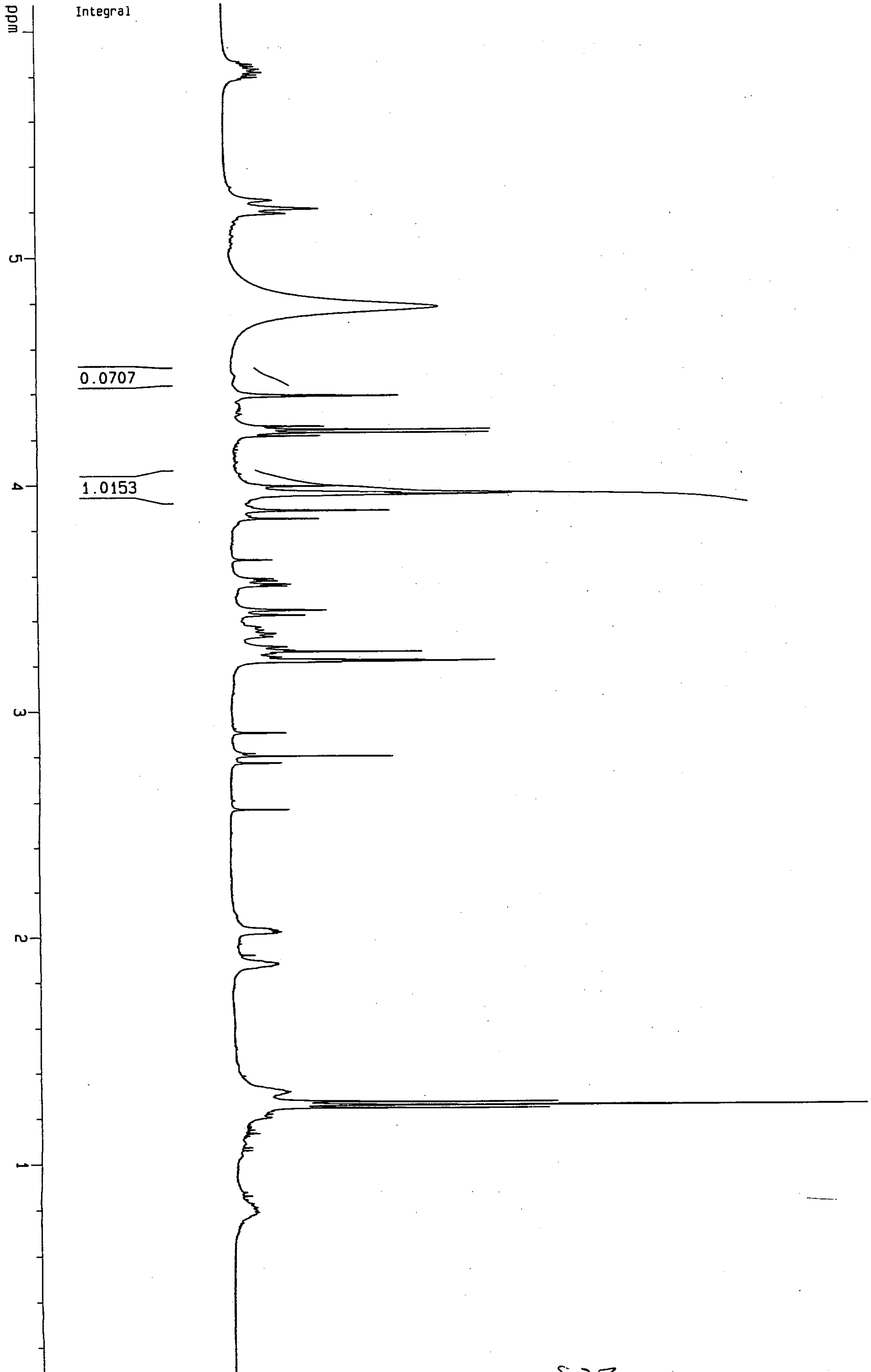
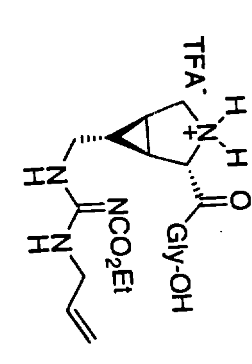
H
N

13

S22





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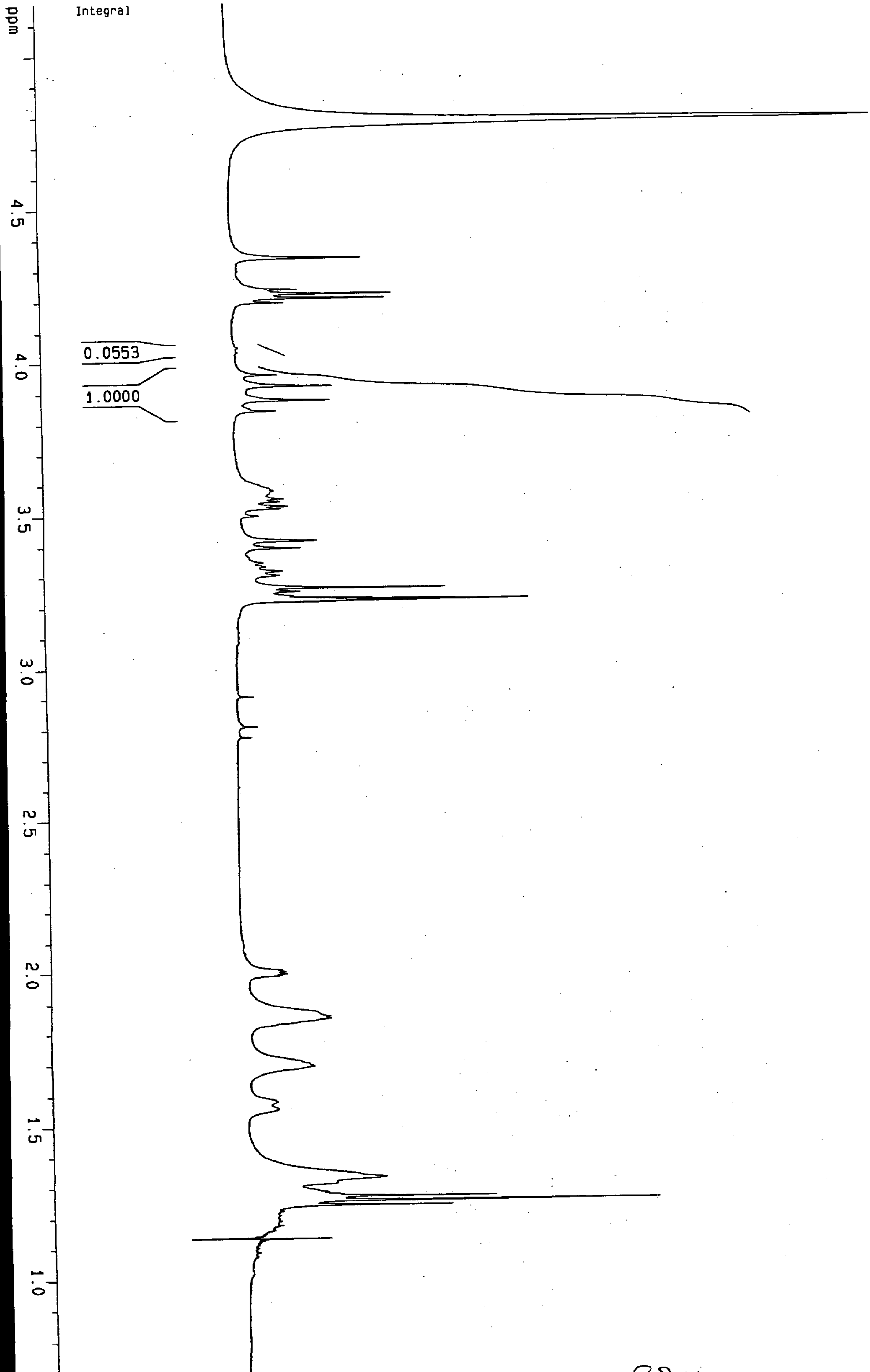
S23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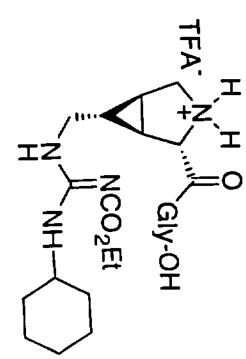
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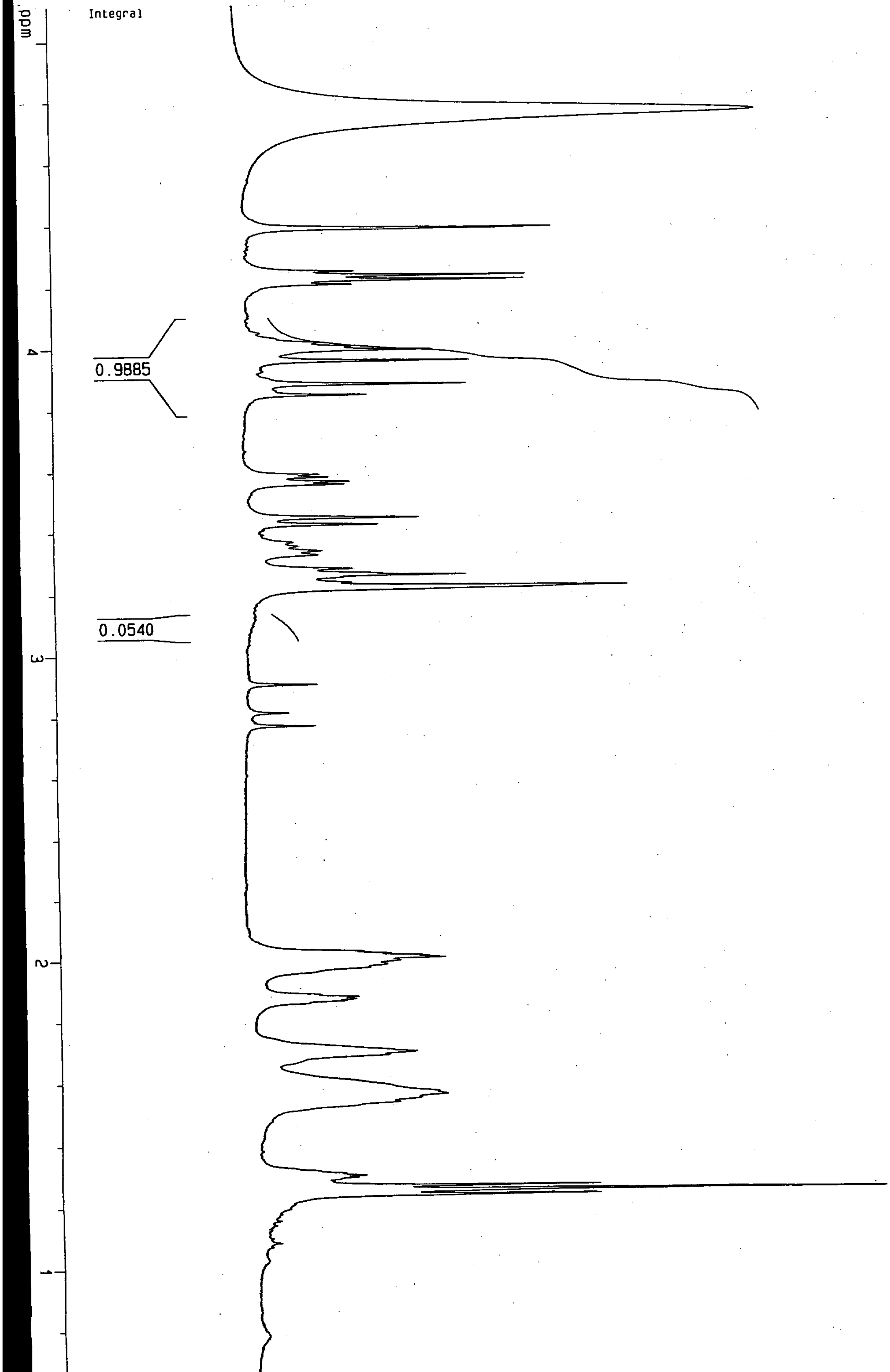
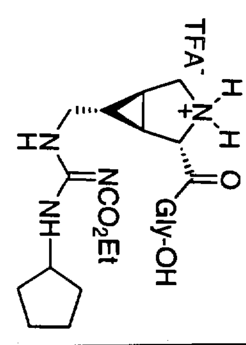
NCO_2Et
NH

15





16

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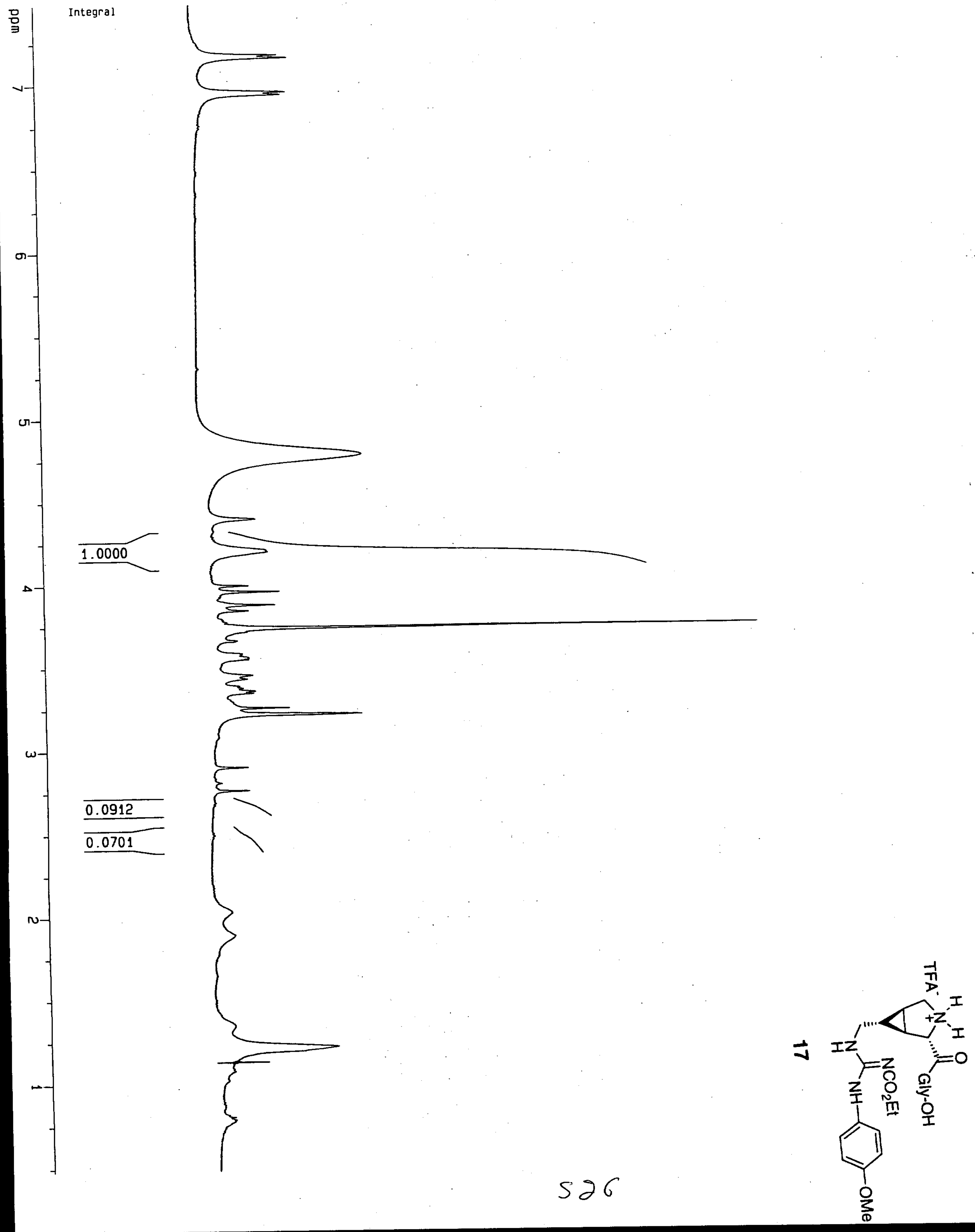
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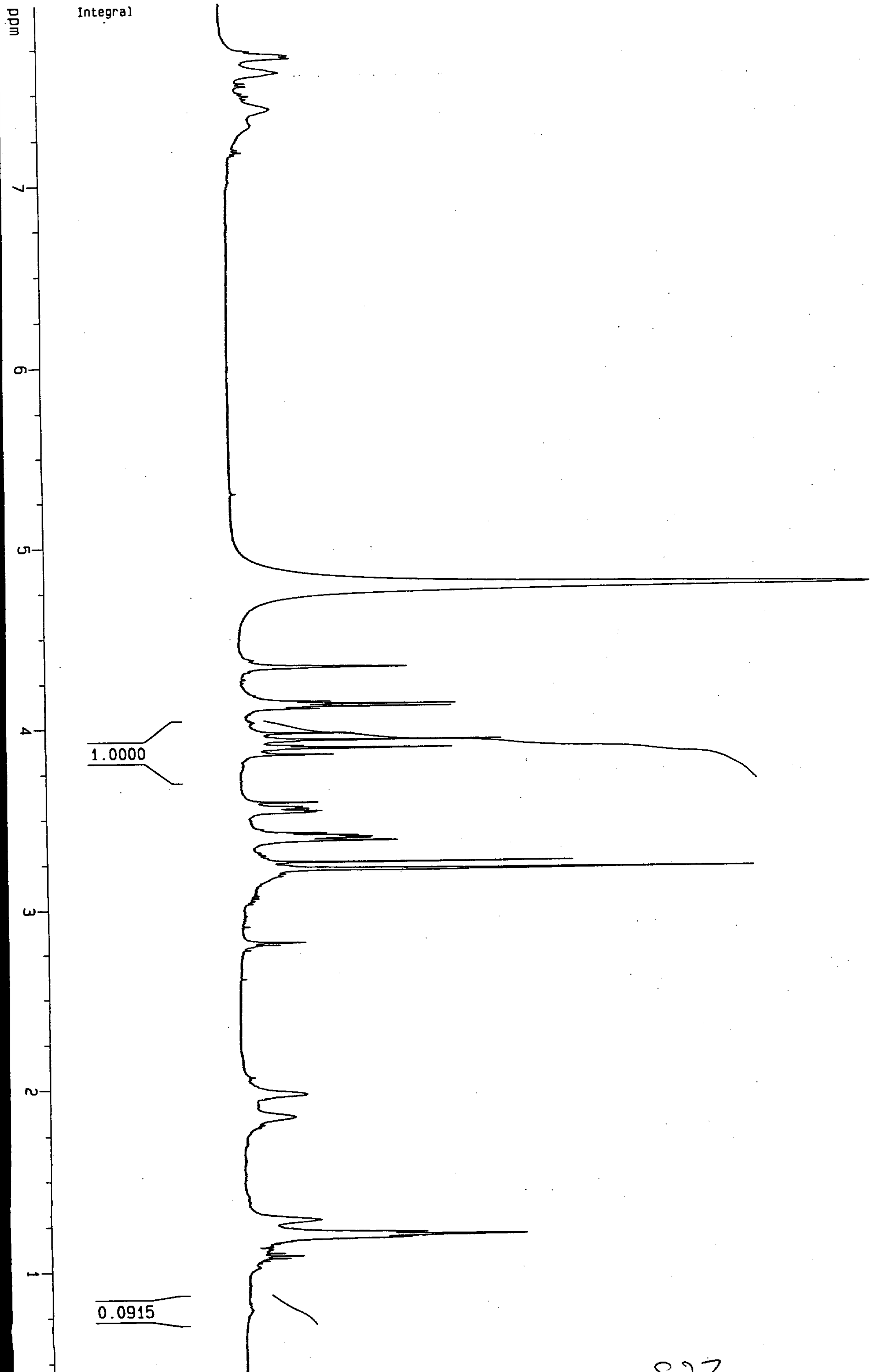
17

S26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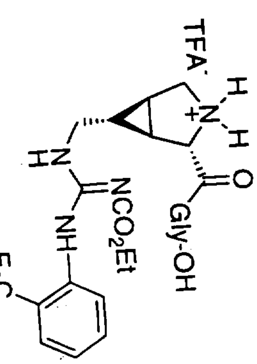
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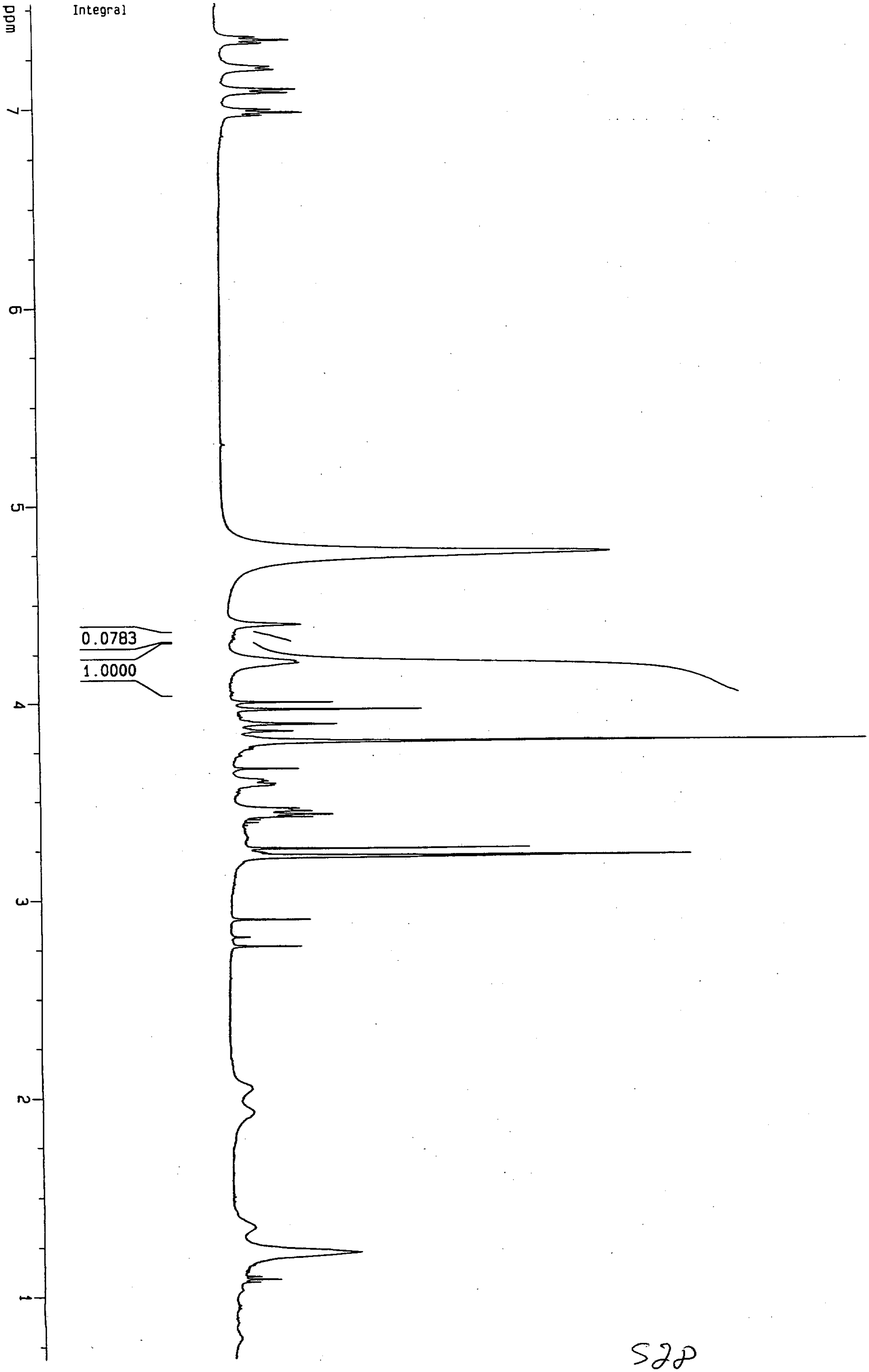
S27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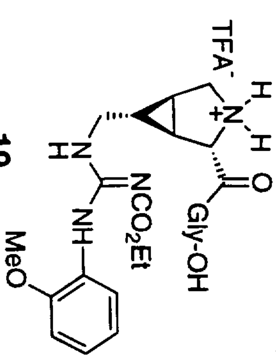
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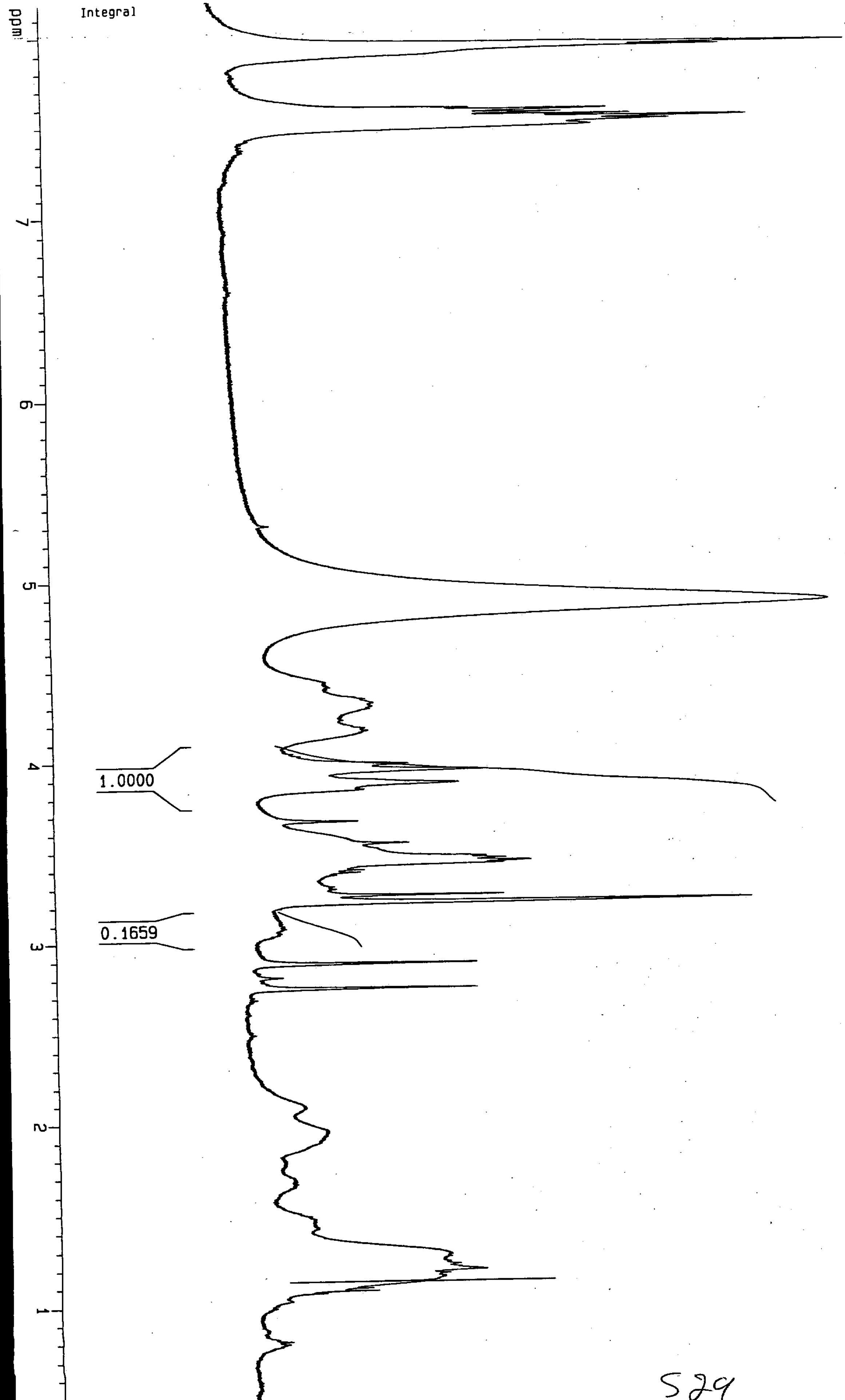
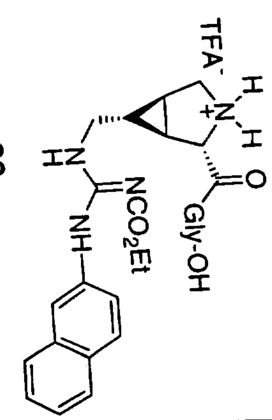
19





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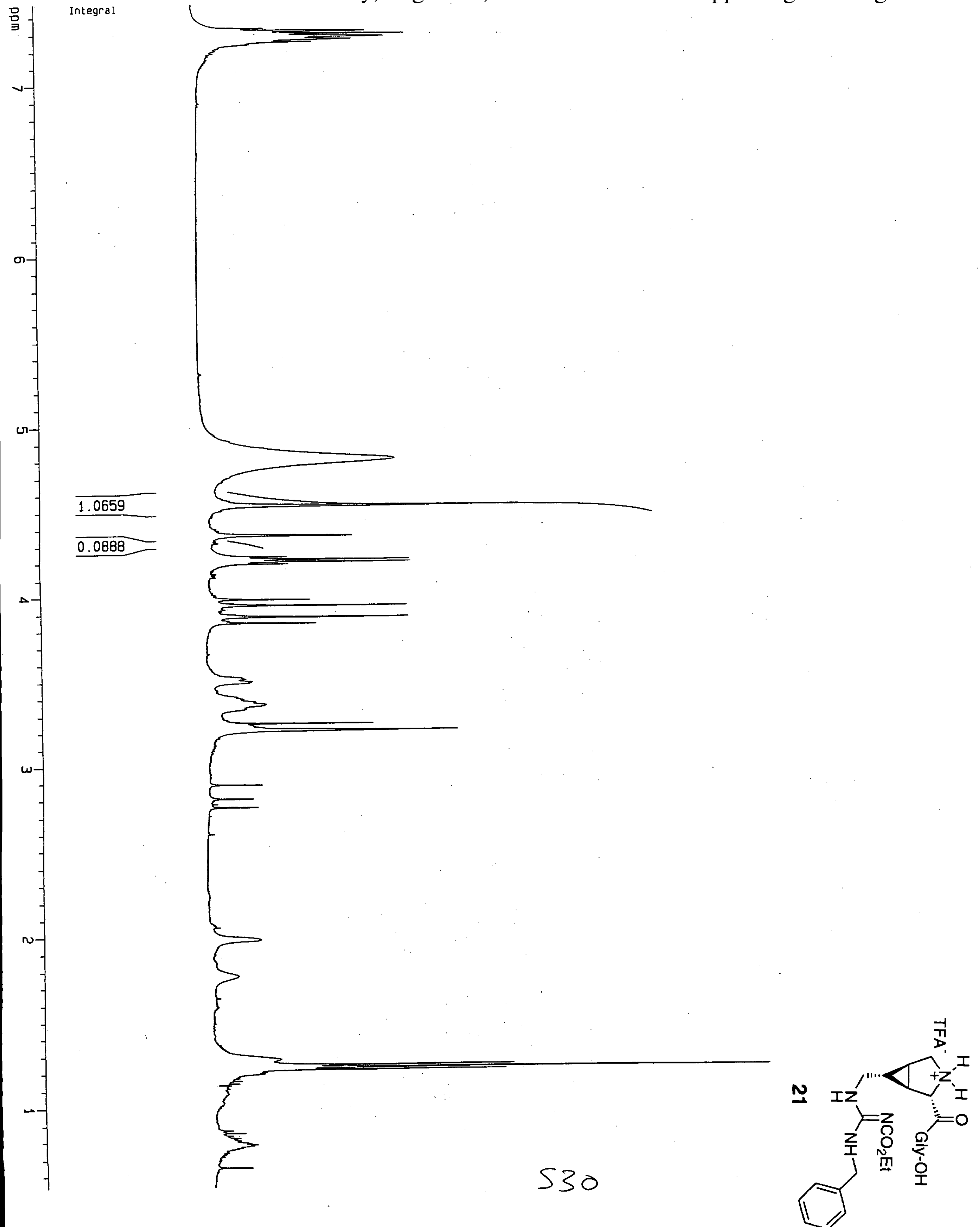
S29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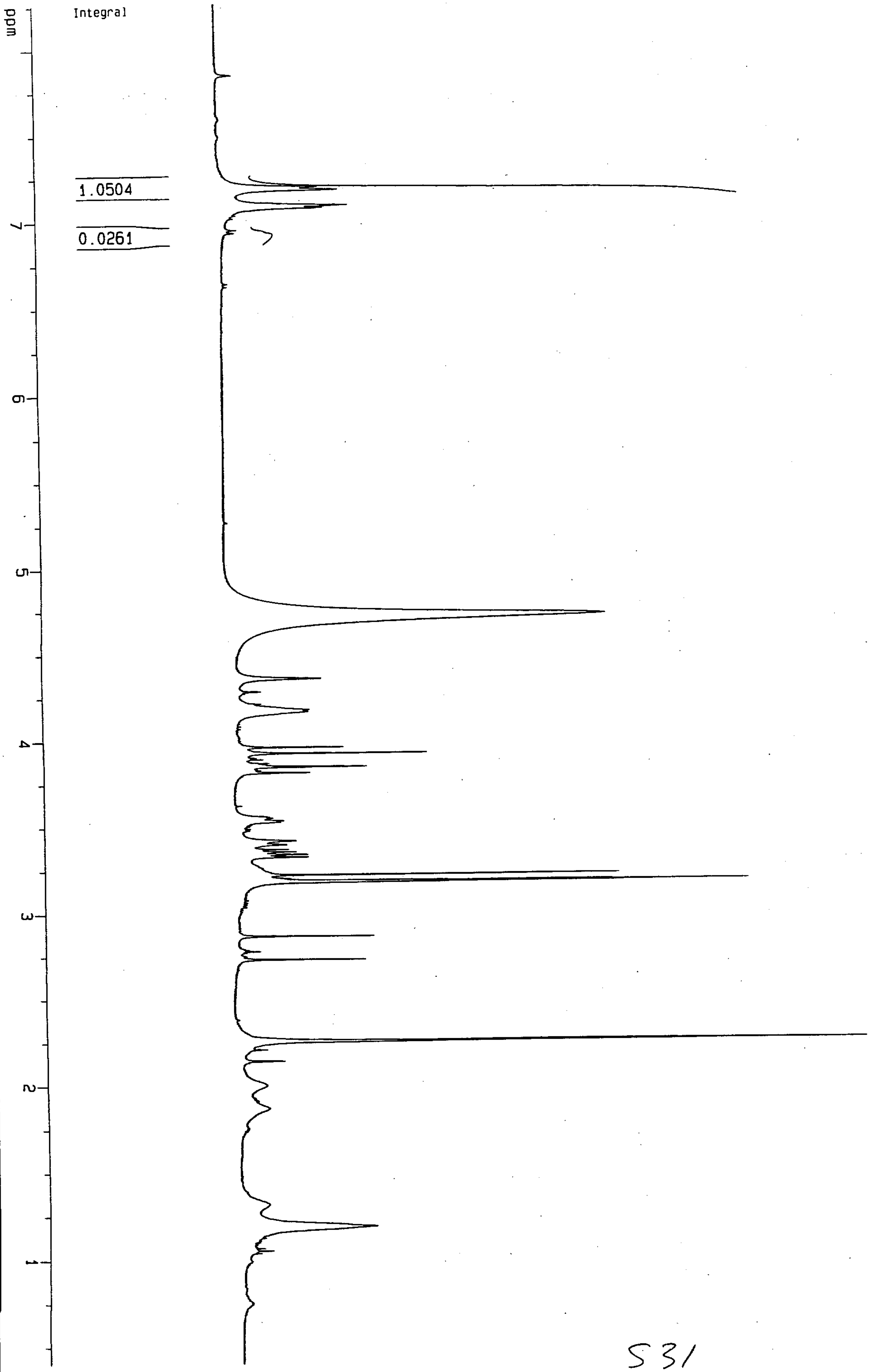
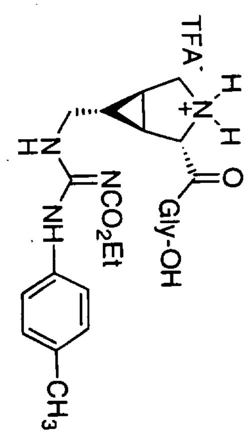
21
S30





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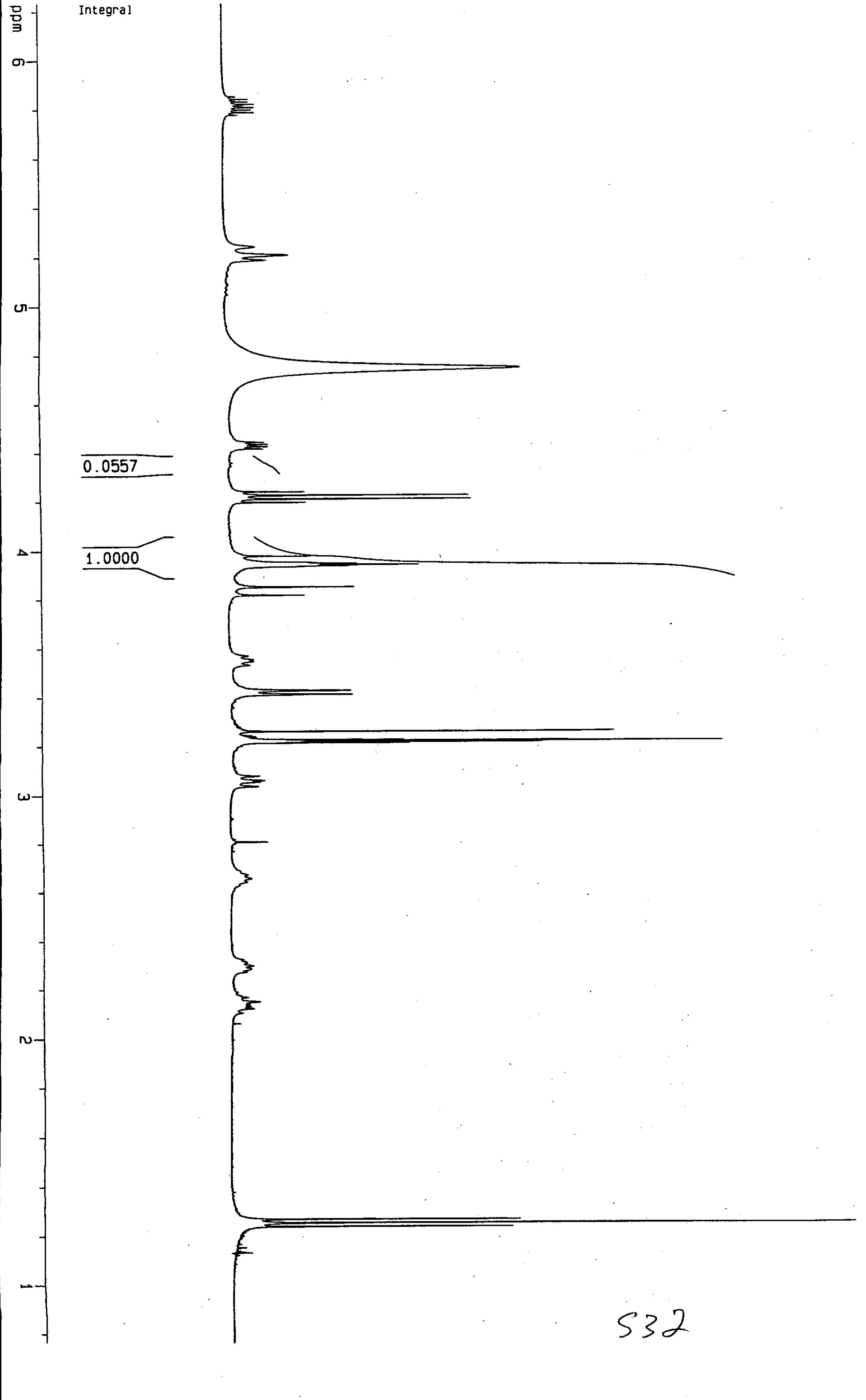

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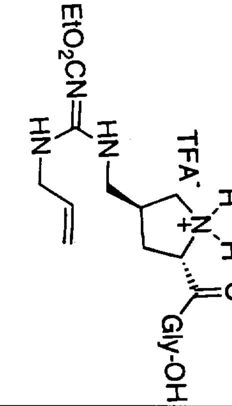

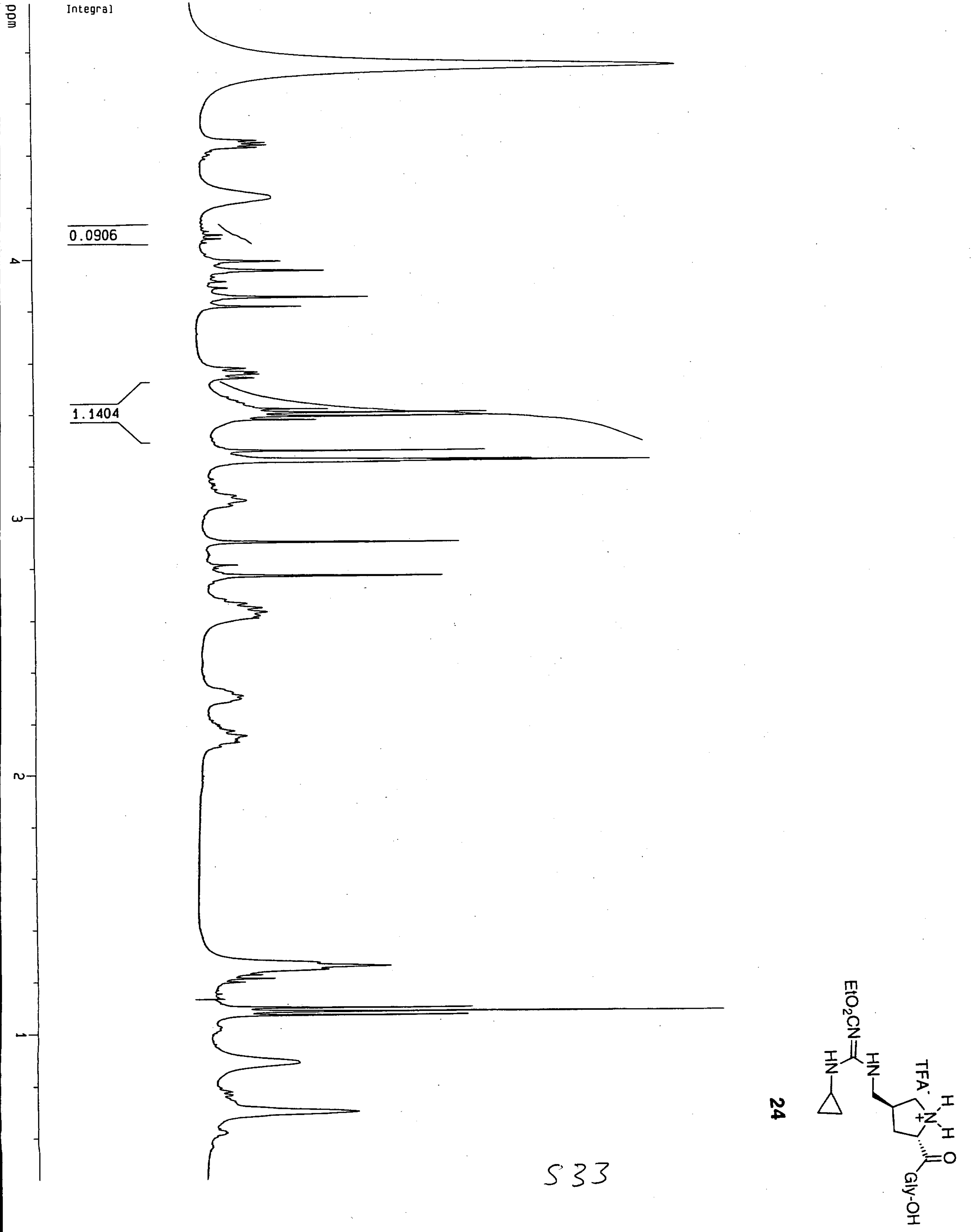

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O
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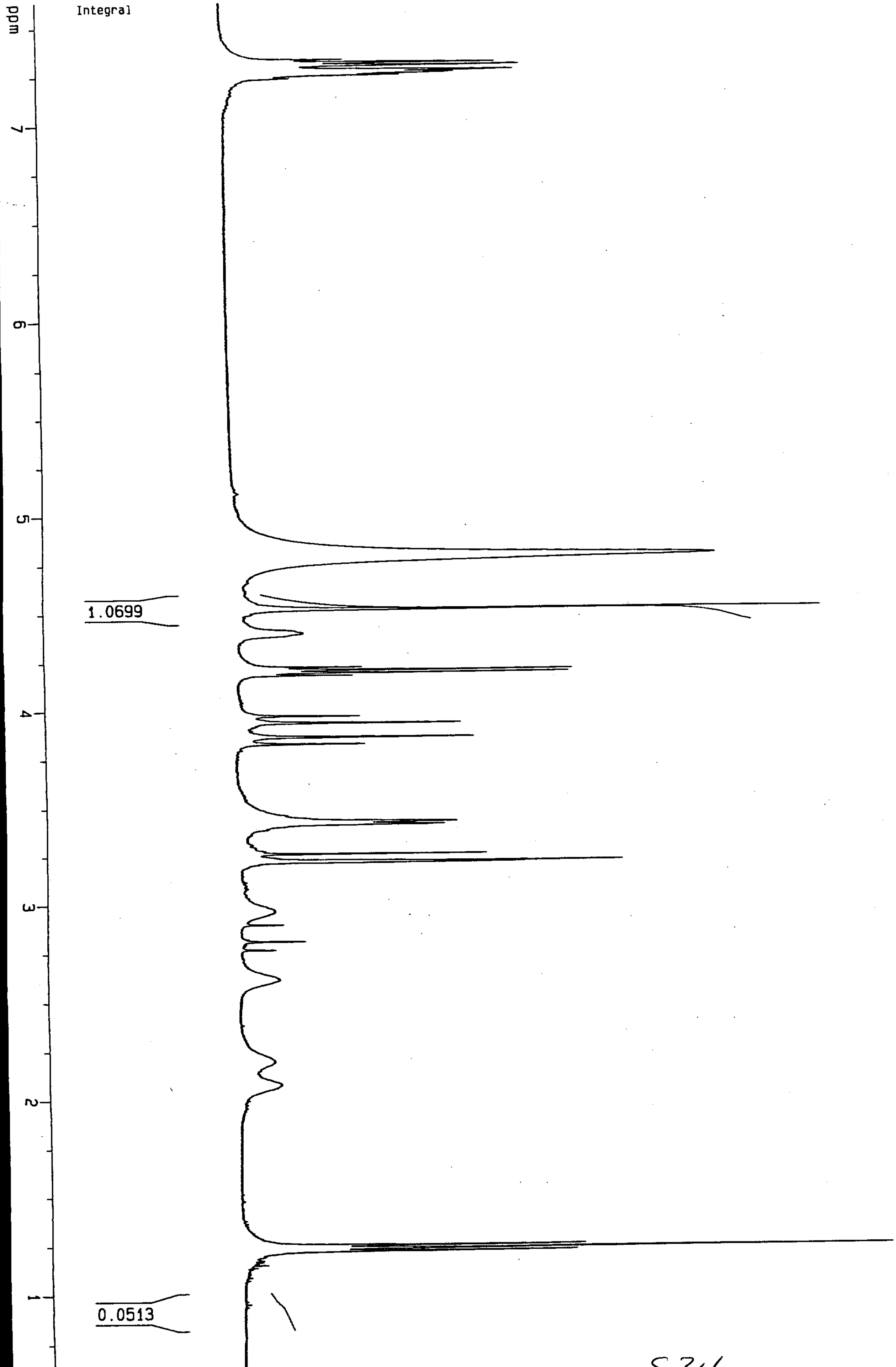
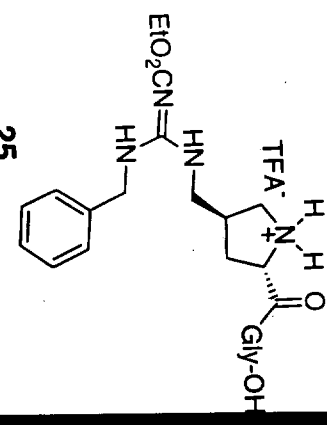
24
S33





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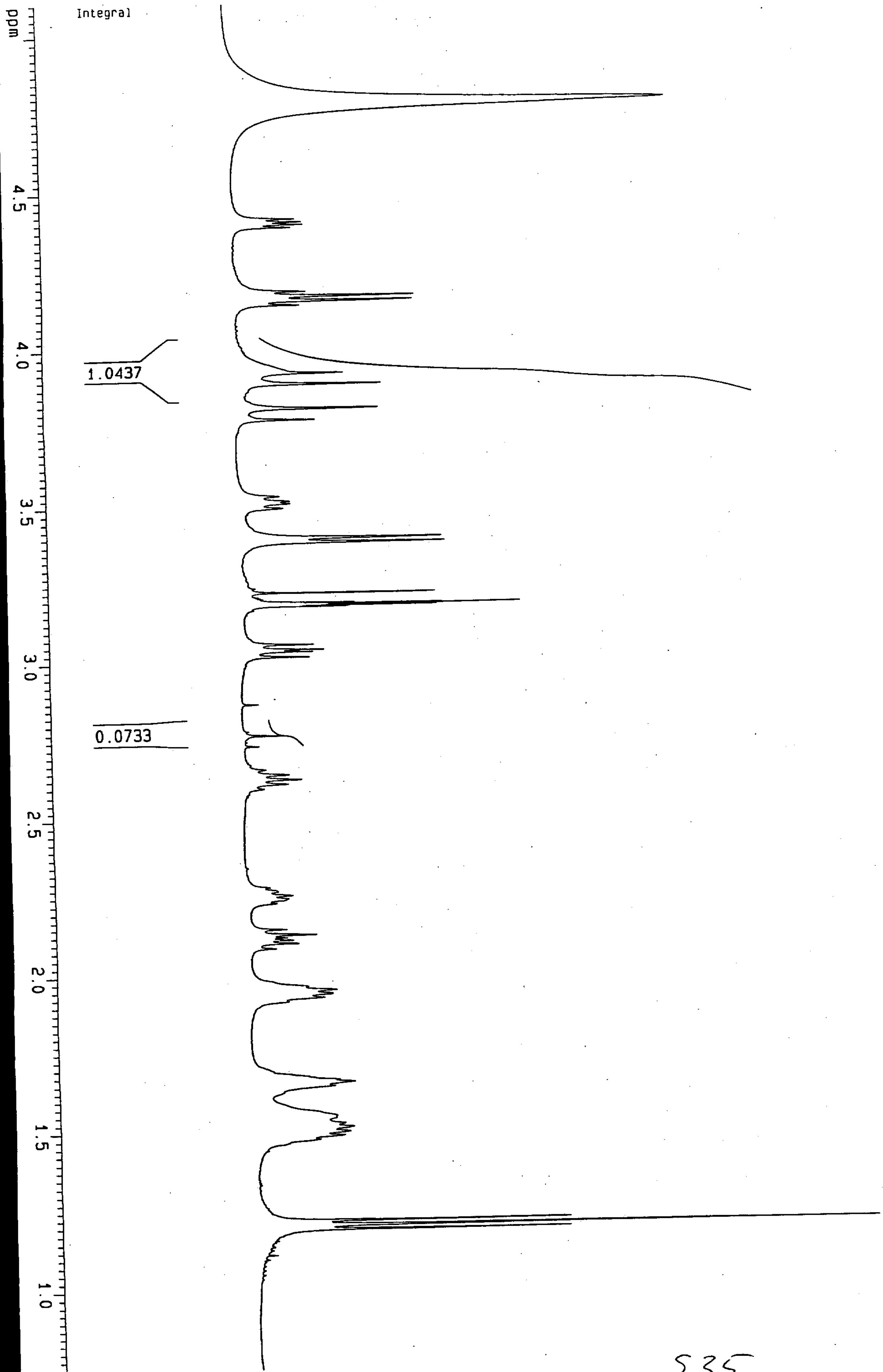
S34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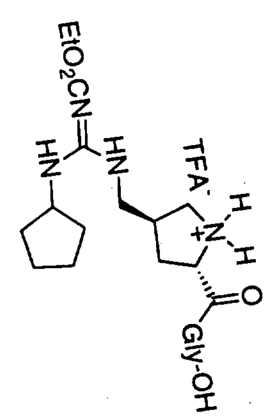
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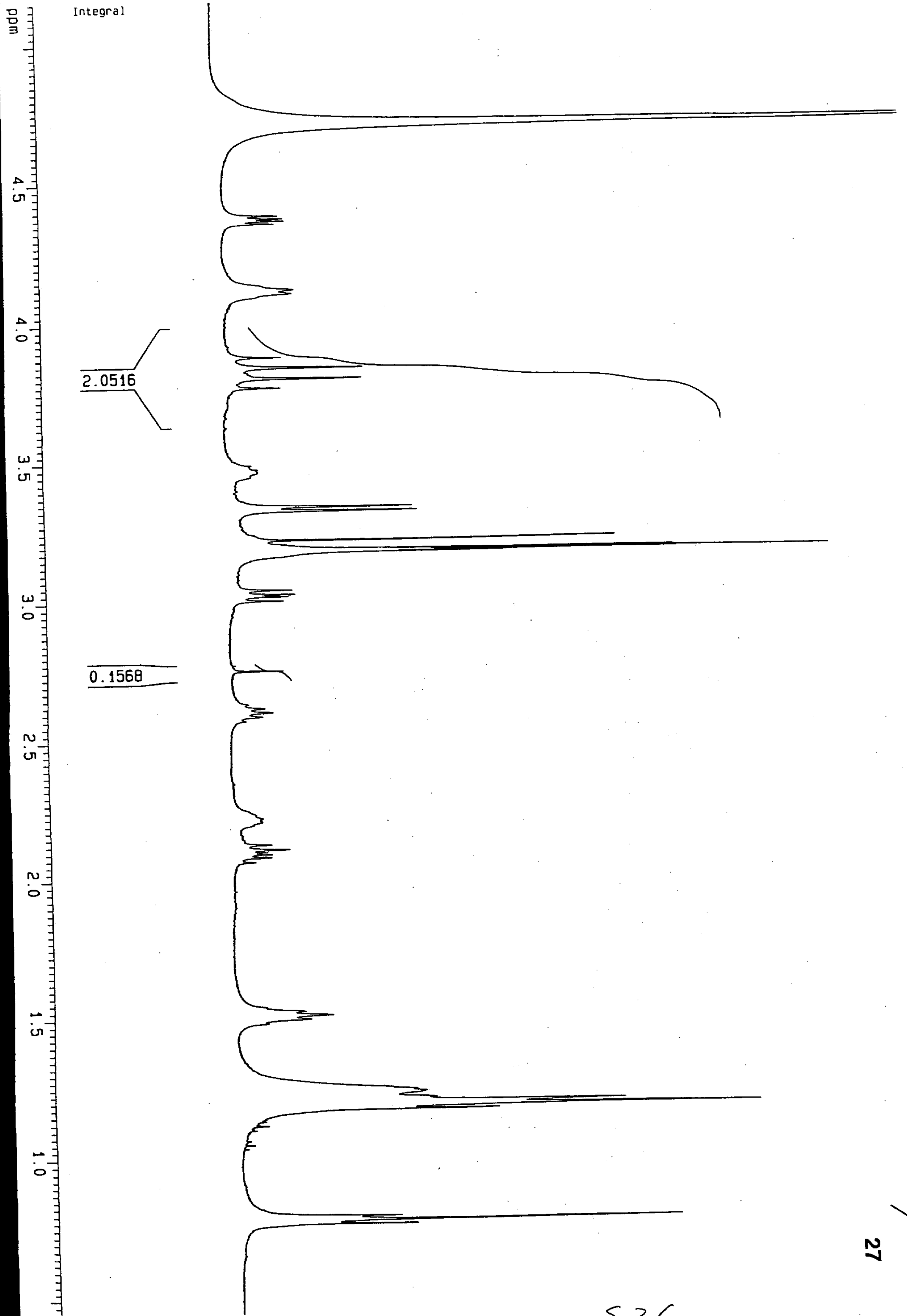
26

S35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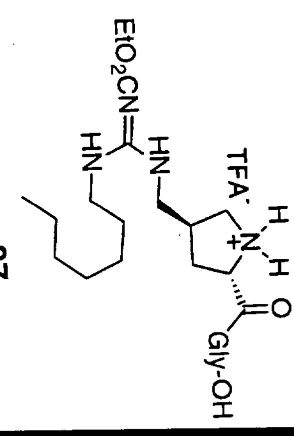
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H
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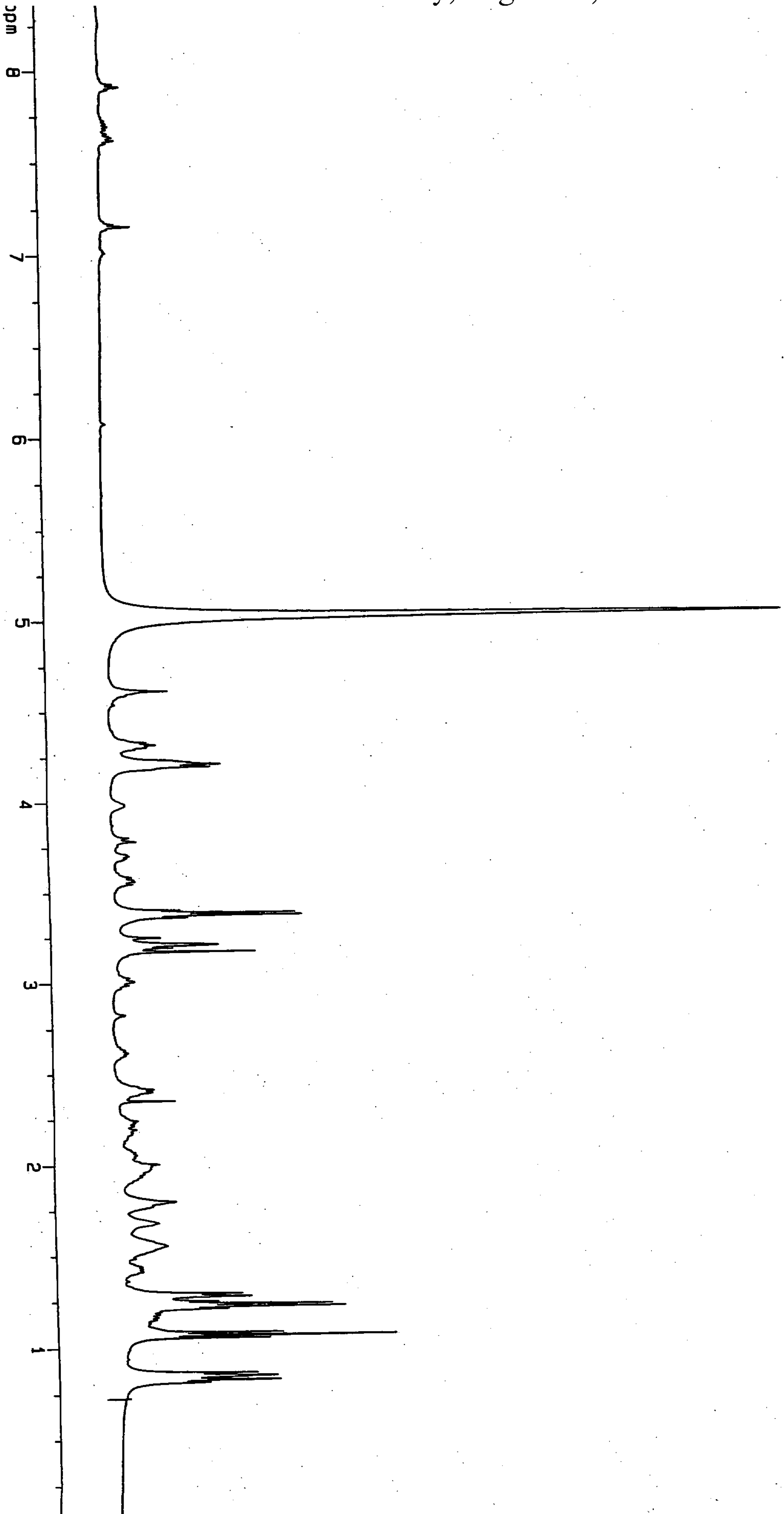
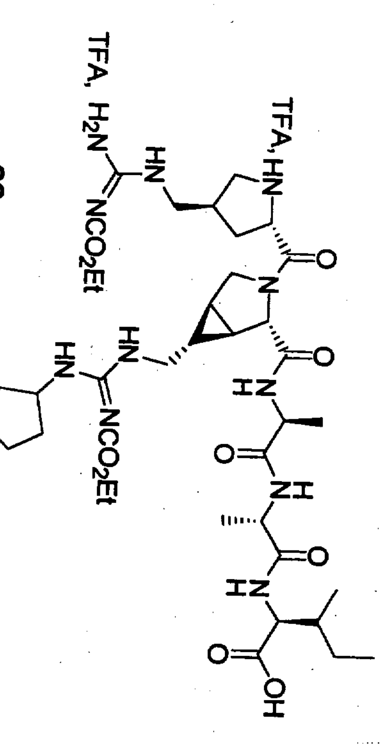
+
O
Gly-OH

27

S36





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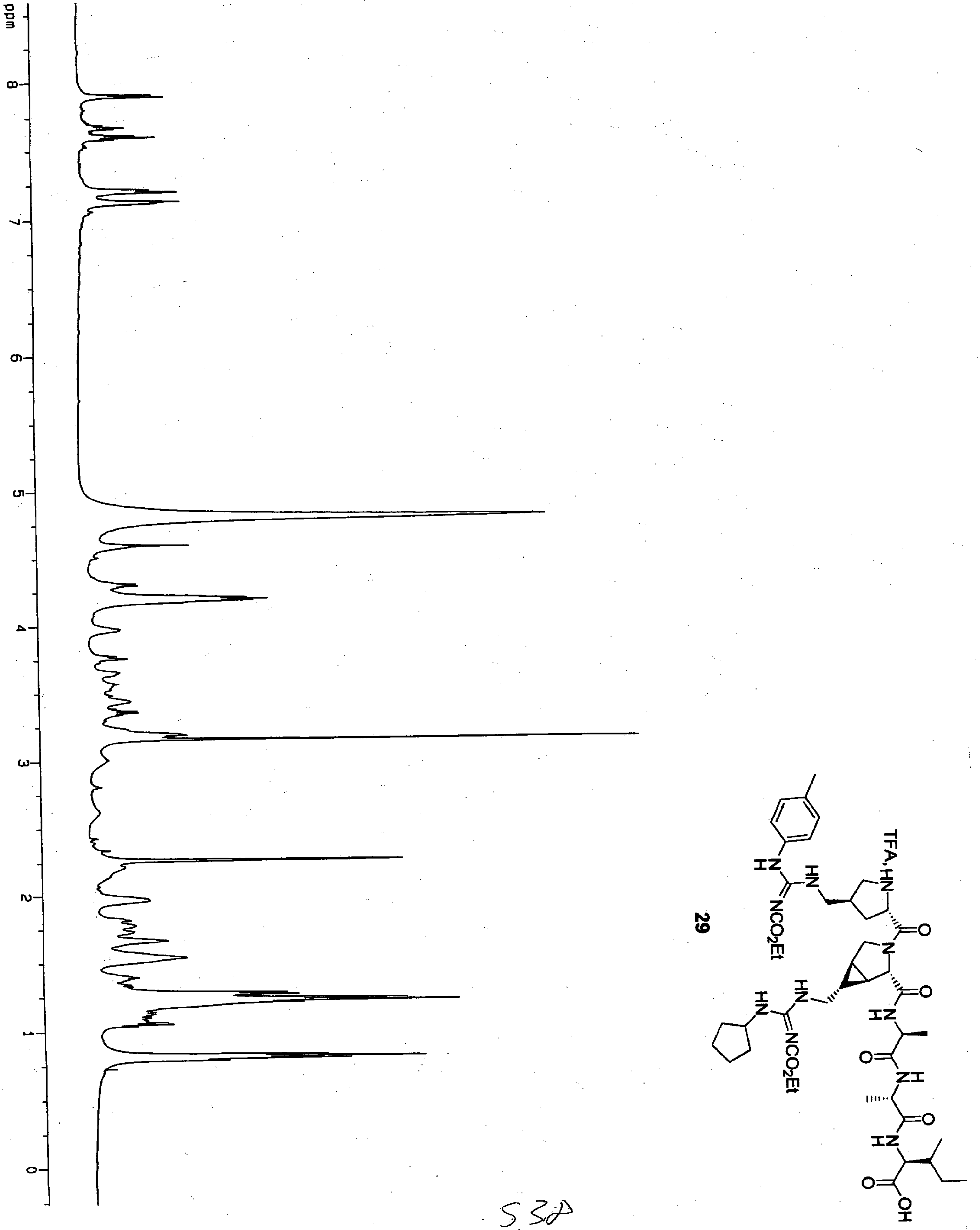

S 38