Supporting Information

Synthetic anion transporters that bear a terminal ethynyl group

Eun-bee Lee,[a, c] Hyunil Ryu,[b, c] Insu Lee,[c, d] Sangbaek Choi,[b, c] Jung-Ho Hong, [a, c] Sun Min Kim,[c, d] Tae-Joon Jeon,*[, b, c] and Dong-Gyu Cho*[, a, c]

[a]*Department of Chemistry, Inha University, 100 Inha-ro Namgu, Incheon 402-751, Korea. Fax:82 32 867 5664; Tel: 82 32 860 7686; E-mail: dgcho@inha.ac.kr*

[b]*Department of Biological Engineering, Inha University, 100 Inha-ro Namgu, Incheon 402-751, Korea. Fax:82 32 867 5664; Tel: 82 32 860 7686; E-mail: tjjeon@inha.ac.kr*

[c]*Biohybrid Systems Research Center, Inha University, 100 Inha-ro Namgu, Incheon 402-751, Korea.*

[d]Department of Mechanical Engineering, Inha University, 100 Inha-ro Namgu, Incheon 402-751, Korea.

Contents

General and Synthetic details

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields of synthesized compounds were measured after chromatographic purification. ^{1}H, ^{19}F, and ^{13}C-NMR spectra were measured at 25 ºC using 400-MHz spectrometers. HRMS were recorded by EI methods using a magnetic sector-electric sector double focusing analyzer. Log P values were obtianed by pH-meteric methods.

Ethyl 2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetate (**2**). Ethyl 2-azidoacetate (0.77 g, 6.0 mmol), sodium-L-ascorbate (0.24 g, 0.12 mmol), and 1,6-heptadiyne (1.36 mL, 12.0 mmol) were dissolved in a mixture of water and DMSO (17 mL, water:DMSO = 3:1). $CuSO_4 \cdot 5H_2O$ (0.15 g, 0.6 mmol) was added to the solution at room temperature and stirred at 60 °C for 4 h. The final mixture was diluted with water and ethyl acetate. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by chromatography on a short plug of silica gel (ethyl acetate:hexane 2:1). This yielded **2** as a liquid (0.57 g, 43%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (s, 1H), 5.11 (s, 2H), 4.23 (t, *J* = 7.1 Hz, 2H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.23 (td, *J* = 7.0, 2.6 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.90 (tt, *J* = 7.5, 7.1 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 147.7, 122.5, 83.9, 77.5, 77.2, 76.9, 69.1, 62.5, 50.9, 28.0, 24.5, 17.9, 14.2; HRMS–EI: m/z $[M]^+$ calcd for $C_{11}H_{15}N_3O_2$: 221.1164; found: 221.1164.

2-(4-(Pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetic acid (**3**). Compound **2** (171 mg, 0.77 mmol in 5 mL of MeOH) was dissolved in a solution (1.55 mL of 1 N NaOH). The reaction was stirred at room temperature for 6 h. After the solvent was evaporated under reduced pressure, the residue was diluted with ethyl acetate and washed with 1 N aqueous HCl. The organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The residues were purified on a short silica gel column, using MC/MeOH (10%) to afford the products (0.108 g, 72%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.79 (s, 1H), 5.24 (s, 2H), 2.84 (t, *J* = 7.6 Hz, 2H), 2.30 – 2.18 (m, 3H), 1.87 (tt, *J* = 7.6, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 170.0, 148.4, 125.0, 84.4, 70.3, 51.7, 29.5, 25.3, 18.6; HRMS–EI: m/z $[M]^+$ calcd for $C_9H_{11}N_3O_2$: 193.0851; found:193.0851.

***N*-(2-hydroxyphenyl)-2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetamide** (**4b**). DIEA (15.9 μL, 0.091 mmol) and PyBop (79.1 mg, 0.152 mmol) were added to a stirred solution of compound **3** (14.5 mg, 0.076 mmol) in anhydrous solvents (0.5 mL of DMF and 0.5 mL of CH_2Cl_2) under N_2. After 30 min, a solution of 2-aminophenol (12.4 mg, 0.114 mmol in 0.5 mL of anhydrous CH_2Cl_2) was added dropwise to the reaction mixture under N_2. The solution was stirred for 5 h. The solvent was evaporated under reduced pressure, and the residue was diluted with ethyl acetate and washed with water. The organic phases were dried with Na_2SO_4 and then concentrated under reduced pressure. The resulting residue was purified by a silica gel column, using MC:MeOH (94:6) to afford the products (12 mg, 56%)^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 9.58 (s, 1H), 7.89 (s, 1H), 7.83 (d, J = 8.1, 1H), 6.95 (dd, J = 8.0, 7.4 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.75 (dd, J = 8.1, 7.6 Hz, 1H), 5.36 (s, 2H), 2.81 (t, J = 2.6 Hz, 1H), 2.73 (t, J = 7.6 Hz, 2H), 2.22 (td, J = 7.1, 2.6 Hz, 2H), 1.78 (tt, J = 7.6, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 164.5, 147.7, 145.8, 125.6, 124.8, 123.7, 121.9, 118.9, 115.2, 84.1, 71.5, 52.1, 27.9, 24.0, 17.2; HRMS–EI: m/z $[M]^+$ calcd for $C_{15}H_{16}N_4O_2$: 284.1273; found:284.1274.

***N*-(2-hydroxyphenyl)-2-(4-pentyl-1H-1,2,3-triazol-1-yl)acetamide** (**4a**). Pd/C (10 wt% loading, 10 mg) was added to a stirred solution of **4b** (20 mg, 0.070 mmol) in MeOH (3 mL) at room temperature. The resultant mixture was degassed and saturated with H_2 before stirring under an atmosphere of H_2 (1 atm) overnight. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH) and the filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on a short plug of a silica gel (MC:MeOH = 94:6). This yielded **4a** as a white solid (19 mg, 94%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 9.57 (s, 1H), 7.82 (m, 2H), 6.94 (dd, *J* = 7.9, 7.7 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 6.75 (dd, *J* = 8.1, 7.7 Hz, 1H), 5.34 (s, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.60 (m,

2H), 1.30 (m, 4H), 0.87 (t, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 164.5, 147.7, 146.7, 125.6, 124.8, 123.4, 121.9, 118.9, 115.2, 52.0, 30.8, 28.6, 24.9, 21.8, 13.9; HRMS–EI: m/z [M]$^+$ calcd for $C_{15}H_{20}N_4O_2$:288.1586; found:288.1584.

***N*-(3-hydroxyphenyl)-2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetamide** (**4c**). By following the general procedure of **4b**, the reaction of 3-aminophenol yielded **4c** (20 mg, 60% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 9.43 (s, 1H), 7.89 (s, 1H), 7.12 (s, 1H), 7.08 (d, J = 8.1 Hz, 1H), 6.96 (d, J = 8.1 Hz, 1H), 6.48 (d, J = 7.6 Hz, 1H), 5.24 (s, 2H), 2.81 (s, 1H), 2.73 (t, J = 7.6 Hz, 2H), 2.22 (t, J = 7.1 Hz, 2H), 1.79 (tt, J = 7.6, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 164.1, 157.7, 145.7, 139.4, 129.5, 123.6, 110.9, 109.9, 106.3, 84.1, 71.5, 52.1, 27.9, 24.0, 17.2; HRMS–EI: m/z [M]$^+$ calcd for $C_{15}H_{16}N_4O_2$: 284.1273; found:284.1275.

***N*-(5-chloro-2-hydroxyphenyl)-2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (4d)**. By following the general procedure of **4b**, the reaction of 2-amino-4-chlorophenol yielded **4d** (22 mg, 62% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.32 (s, 1H), 9.75 (s, 1H), 7.99 (s, 1H), 7.88 (s, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.89 (d, J = 8.5 Hz, 1H), 5.38 (s, 2H), 2.80 (s, 1H), 2.73 (t, J = 7.6 Hz, 3H), 2.22 (t, J = 7.1 Hz, 3H), 1.77 (h, J = 7.6, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 165.0, 146.3, 145.8, 126.9, 124.0, 123.7, 122.1, 120.8, 116.1, 84.0, 71.5, 52.1, 27.9, 23.9, 17.2; HRMS–EI: m/z [M]$^+$ calcd for $C_{13}H_{15}ClN_4O_2$: 318.0884; found: 318.0883.

***N*-(3-fluoro-2-hydroxyphenyl)-2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (4e)**. By following the general procedure of **4b**, the reaction of 2-amino-6-fluorophenol yielded **4d** (19 mg, 59% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 9.85 (s, 1H), 7.89 (s, 1H), 7.64 (d, J = 8.2 Hz, 1H), 6.96 (dd, J = 8.2, 7.6 Hz, 1H), 6.78 (dd, J = 14.8, 7.6 Hz, 1H), 5.38 (s, 2H), 2.82 (s, 1H), 2.73 (d, J = 7.6 Hz, 2H), 2.22 (d, J = 7.1 Hz, 2H), 1.78 (tt, J = 7.6, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) ^{13}C NMR (101 MHz, DMSO) δ 164.9, 152.8, 150.4, 145.8, 136.0, 135.9, 128.3, 123.7, 118.8, 118.7, 117.9, 111.7, 111.5, 84.1, 71.6, 52.0, 27.9, 24.0, 17.3; HRMS–EI: m/z [M]$^+$ calcd for $C_{13}H_{15}CFN_4O_2$: 302.1179; found: 302.1180.

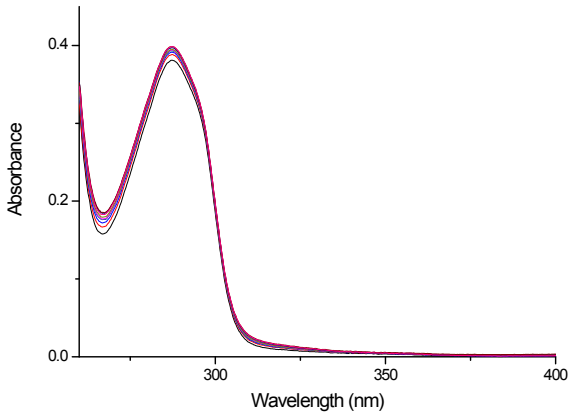
***N*-(5-fluoro-2-hydroxyphenyl)-2-(4-(pent-4-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (4f)**. By following the general procedure of **4b**, the reaction of 2-amino-4-fluorophenol yielded **4f** (23 mg, 64 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (d, J = 1.9 Hz, 1H), 9.73 (s, 1H), 7.89 (s, 1H), 7.80 (d, J = 11.9 Hz, 1H), 6.86 (dd, J = 8.9, 5.5 Hz, 1H), 6.77 (ddd, J = 8.9, 2.9, 2.9 Hz, 1H), 5.39 (s, 2H), 2.80 (t, J = 2.0 Hz, 1H), 2.73 (t, J = 7.6 Hz, 3H), 2.22 (d, J = 7.4 Hz, 2H), 1.79 (tt, J = 7.6, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, DMSO) δ 164.9, 155.9, 153.6, 145.8, 143. 5, 126.6, 126.4, 123.7, 115.2, 115.1, 110.2, 110.0, 108.1, 107.8, 84.1, 71.5, 52.1, 27.9, 24.0, 17.2; HRMS–CI: m/z [M]$^+$ calcd for $C_{15}H_{15}FN_4O_2$: 302.1179; found: 302.1178.

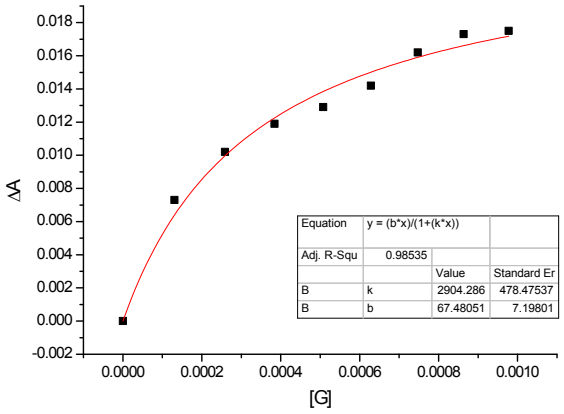
***N*-(2-hydroxyphenyl)-2-(4-(pent-4-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (4g)** Lindlar catalyst (5% palladium on calcium carbonate poisoned with lead, 2.5 mg) was added to a stirred solution of **4b** (50 mg, 0.176 mmol) in DMF (2 mL) at room temperature. The resultant mixture was degassed and saturated with H_2 before stirring under an atmosphere of H_2 (1 atm) for 4 h. The reaction mixture was then filtered through a short plug of Celite® (eluent DMF) and the filtrate was concentrated under reduced pressure. The resulting residue was purified by chromatography on a short plug of a silica gel (MC:MeOH = 94:6). This yielded **4a** as a white solid (17 mg, 34%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 9.57 (s, 1H), 7.86 (s, 1H), 7.83 (d, J = 8.6 Hz, 1H), 6.94 (dd, J = 8.1, 7.5 Hz, 1H), 6.88 (dd, J = 8.1, 1.6 Hz, 1H), 6.75 (dd, J =8.6, 7.8 Hz, 1H), 5.84 (m, 1H), 5.04 (ddt, J = 17.2, 1.6, 1.6 Hz, 1H), 4.98 (ddt, J = 10.3, 1.6, 1.1 Hz, 1H), 2.64 (t, J = 7.6 Hz, 2H), 2.08 (q, J = 7.1 Hz, 2H), 1.69 (tt, J =7.6, 7.1 Hz 2H). ^{13}C NMR (101 MHz, DMSO) δ 164.5, 147.8, 146.4, 138.3, 125.6, 124.8, 123.5, 121.9, 118.9, 115.2, 115.1, 52.1, 32.6, 28.2 24.4; HRMS–CI: m/z [M]$^+$ calcd for $C_{15}H_{18}N_4O_2$: 286.1430; found: 286.1429.

Chloride Binding Constants by UV-vis titrations

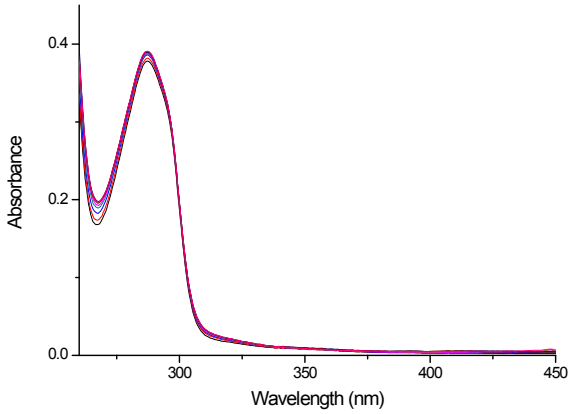
Upon addition of incremental amounts of anions to the solution of each chemosensor (from 2 equiv. to 16 equiv of each anion), absorbance change of each transportor (6.6×10^{-5} M of each transportor was used, unless otherwiswe stated) were recorded in DMSO at λ_{max}. Equilibrium constants of complexes were calculated using the equation, $y = (1 + b \times x \times K)/(1 + x \times K)$, where x = [Cl], $y = A - A_o$ (A is the absorbance of the solution of each transportor at a certain concentration of anions and A_o is the absorbance of the solution of each transportor without anions).

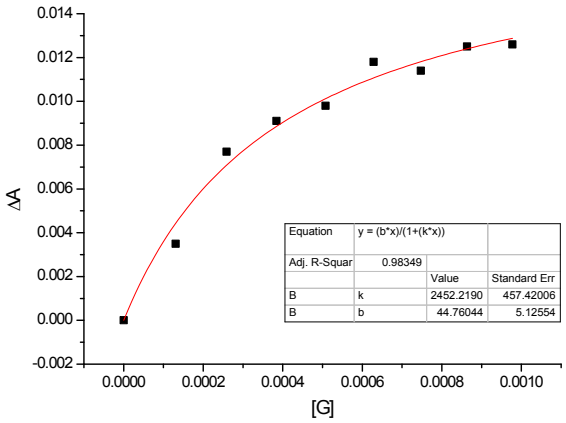
4a



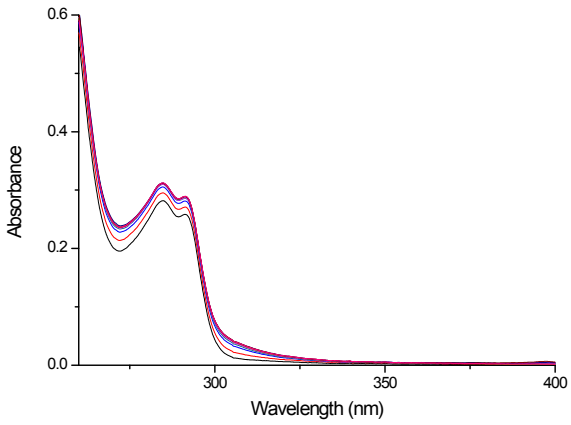


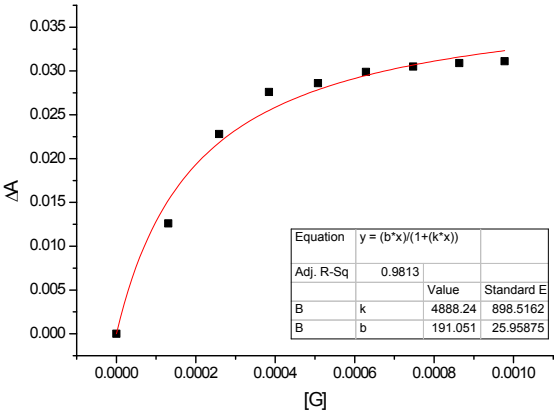
4b



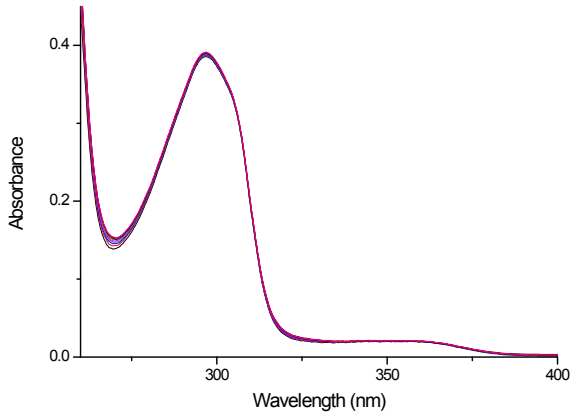


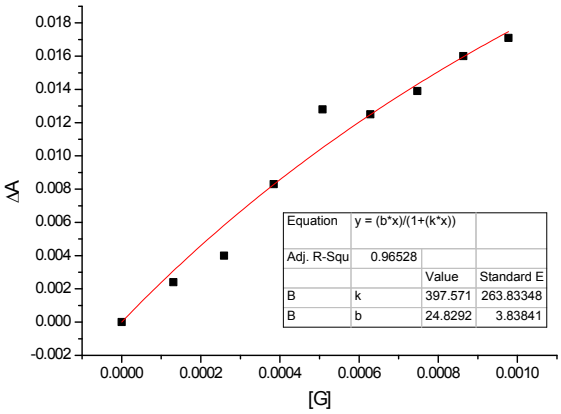
4c



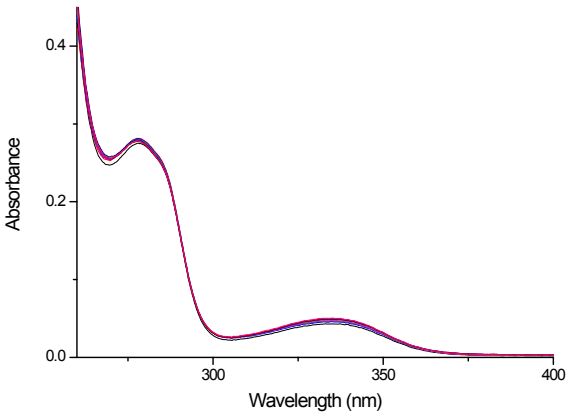


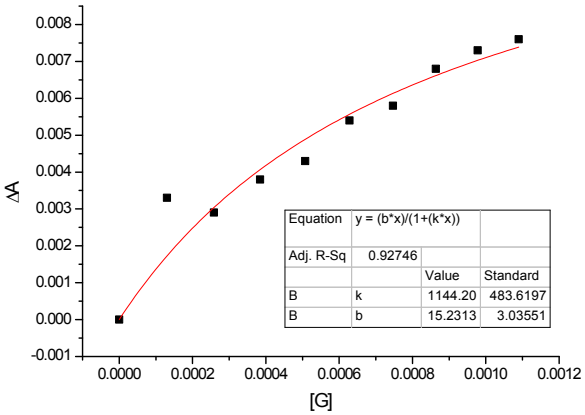
4d


Absorbance
Wavelength (nm)

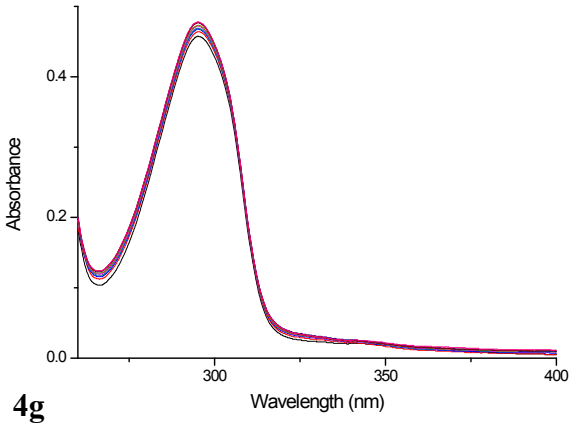

ΔA
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Squ 0.96528
Value Standard E
B k 397.571 263.83348
B b 24.8292 3.83841

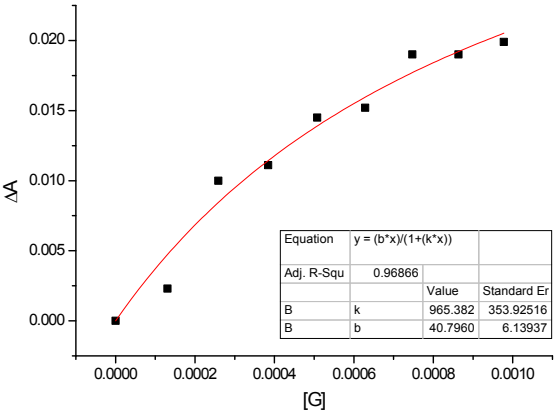
4e


Absorbance
Wavelength (nm)

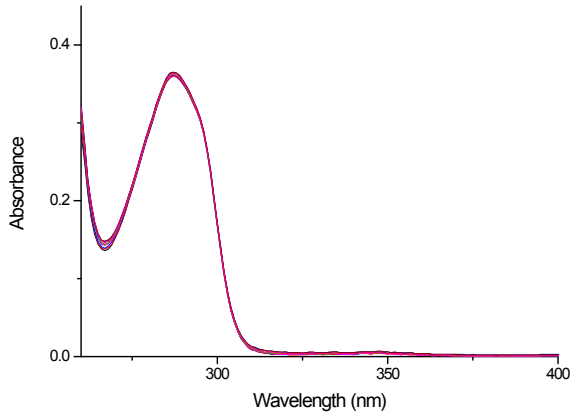

ΔA
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Sq 0.92746
Value Standard
B k 1144.20 483.6197
B b 15.2313 3.03551

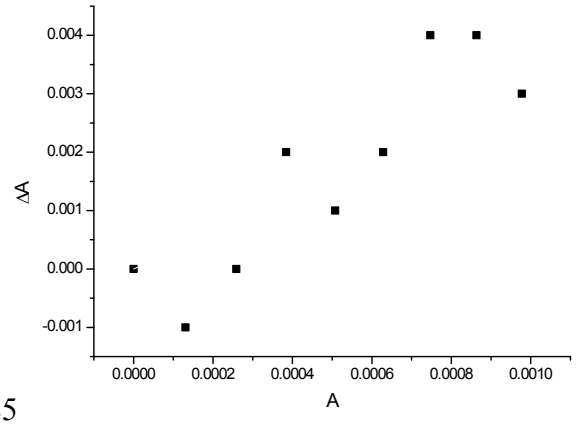
4f


Absorbance
Wavelength (nm)


ΔA
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Squ 0.96866
Value Standard Er
B k 965.382 353.92516
B b 40.7960 6.13937

4g

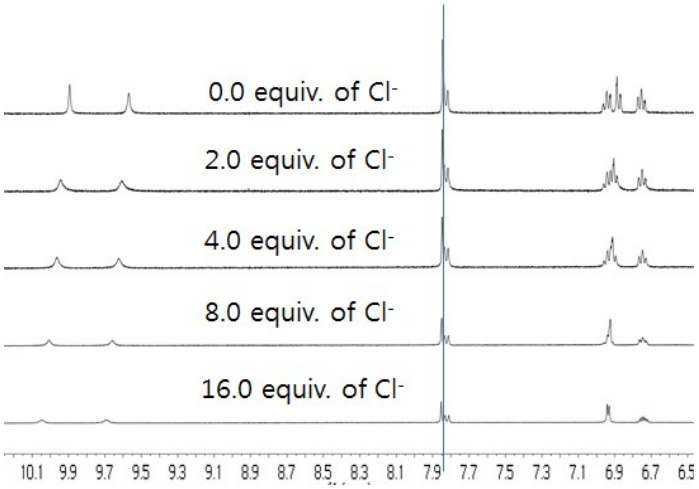

Absorbance
Wavelength (nm)

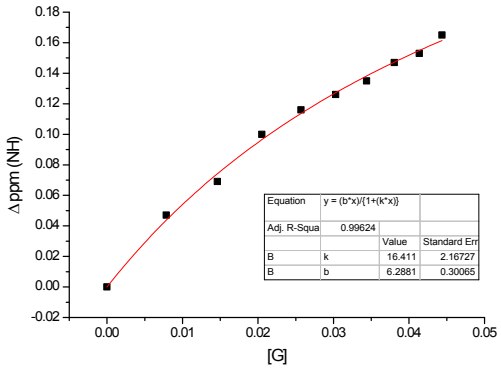

ΔA
A

Chloride Binding Constants by ^{1}H NMR titrations

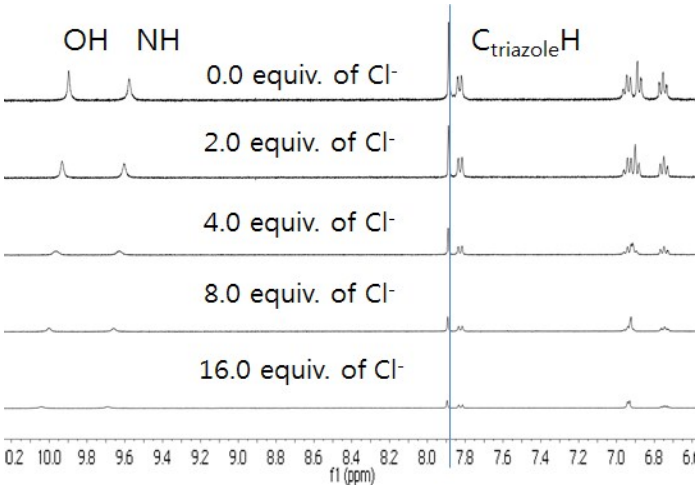
Upon addition of incremental amounts of anions to the solution of each chemosensor (from 2 equiv. to 16 equiv of each anion), ^{1}H NMR chemical shift change of each transportor (4.0×10^{-3} M of each transportor was used, unless otherwiswe stated) were recorded in DMSO-d_6. Equilibrium constants of complexes were calculated using the equation, $y = (1 + b \times x \times K)/(1 + x \times K)$, where x = [Cl], $y = \delta - \delta_o$ (δ is the NH chemical shift of each transportor at a certain concentration of anions and δ_o is the NH chemical shift of each transportor without anions).

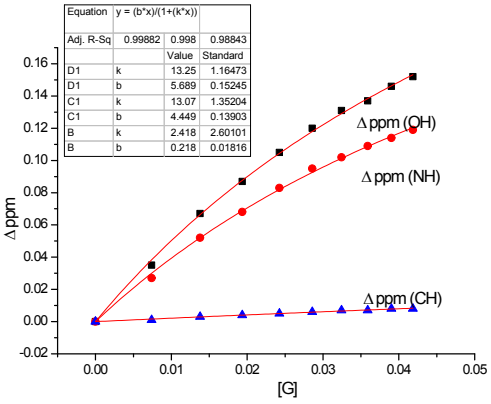
4a



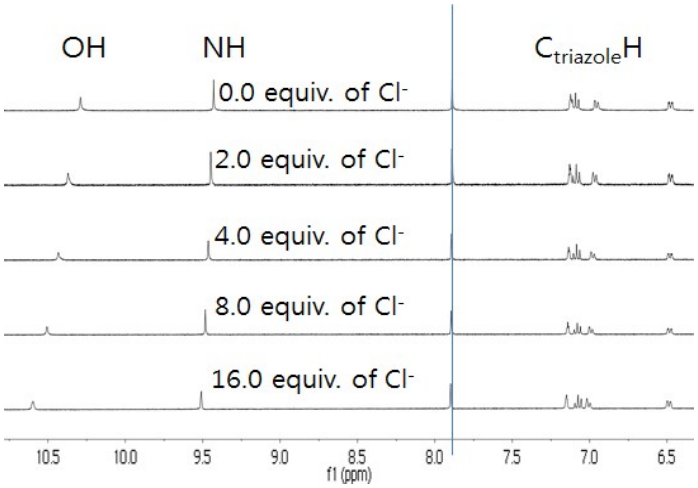


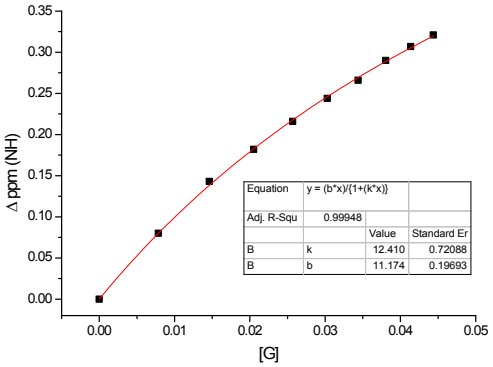
4b



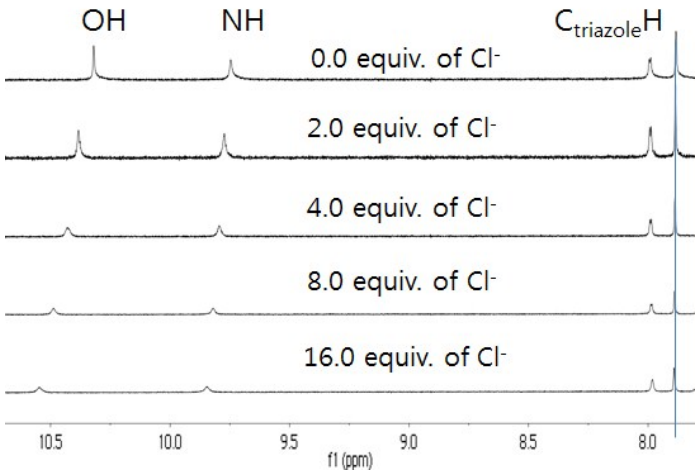


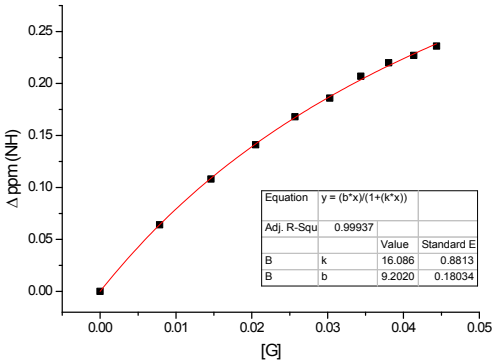
4c


OH
NH
$C_{triazole}H$
0.0 equiv. of Cl-
2.0 equiv. of Cl-
4.0 equiv. of Cl-
8.0 equiv. of Cl-
16.0 equiv. of Cl-
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5
f1 (ppm)

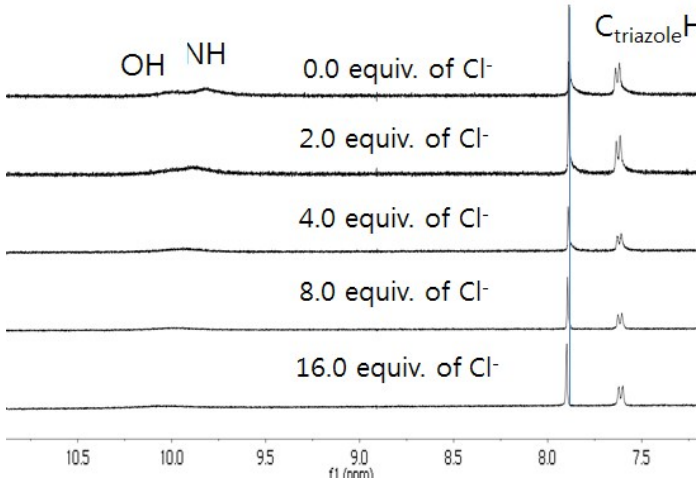

Δ ppm (NH)
0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00
0.00 0.01 0.02 0.03 0.04 0.05
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Squ 0.99948
Value Standard Er
B k 12.410 0.72088
B b 11.174 0.19693

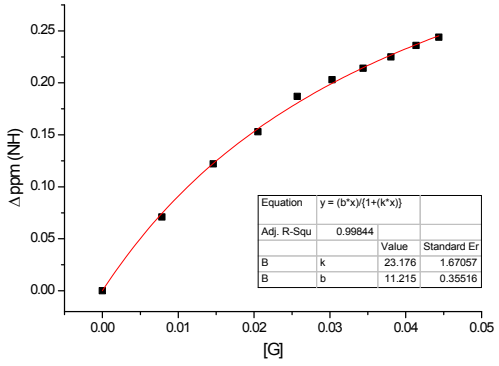
4d


OH
NH
$C_{triazole}H$
0.0 equiv. of Cl-
2.0 equiv. of Cl-
4.0 equiv. of Cl-
8.0 equiv. of Cl-
16.0 equiv. of Cl-
10.5 10.0 9.5 9.0 8.5 8.0
f1 (ppm)

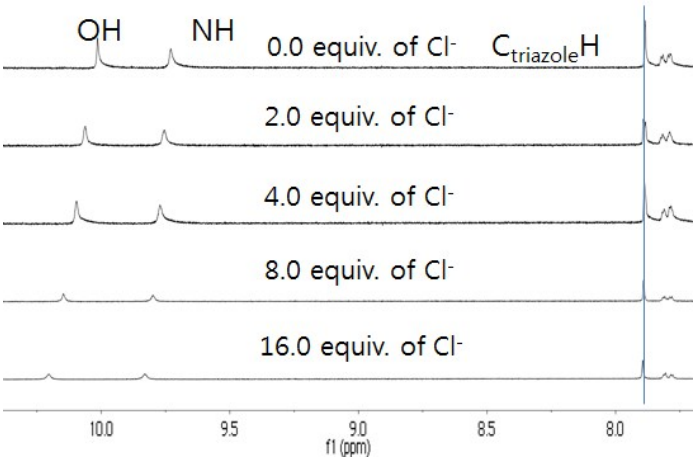

Δ ppm (NH)
0.25 0.20 0.15 0.10 0.05 0.00
0.00 0.01 0.02 0.03 0.04 0.05
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Squ 0.99937
Value Standard E
B k 16.086 0.8813
B b 9.2020 0.18034

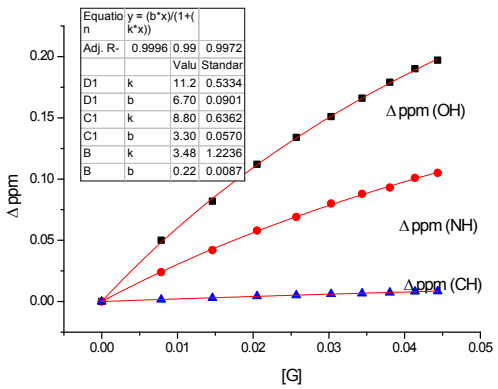
4e


OH
NH
$C_{triazole}H$
0.0 equiv. of Cl-
2.0 equiv. of Cl-
4.0 equiv. of Cl-
8.0 equiv. of Cl-
16.0 equiv. of Cl-
10.5 10.0 9.5 9.0 8.5 8.0 7.5
f1 (ppm)

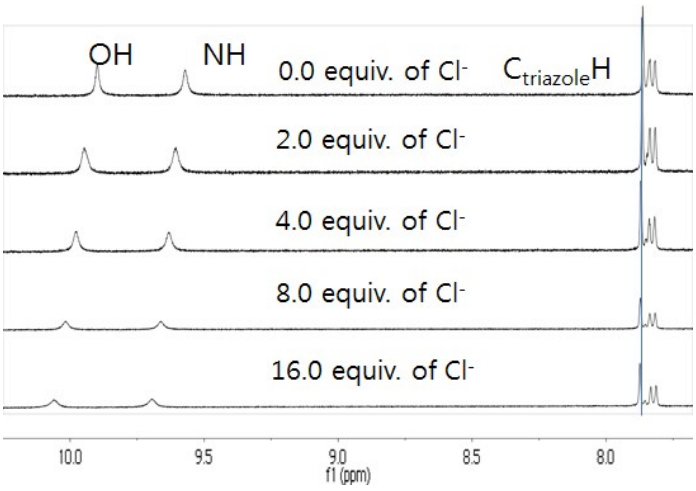

Δ ppm (NH)
0.25 0.20 0.15 0.10 0.05 0.00
0.00 0.01 0.02 0.03 0.04 0.05
[G]
Equation y = (b*x)/(1+(k*x))
Adj. R-Squ 0.99844
Value Standard Er
B k 23.176 1.67057
B b 11.215 0.35516

4f





4g



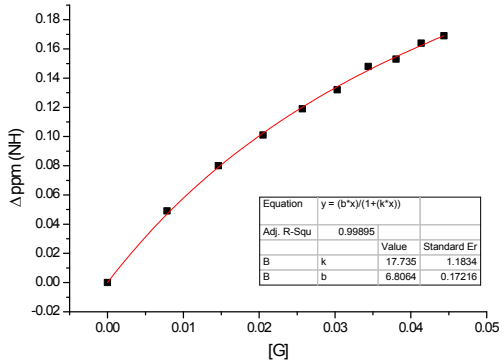


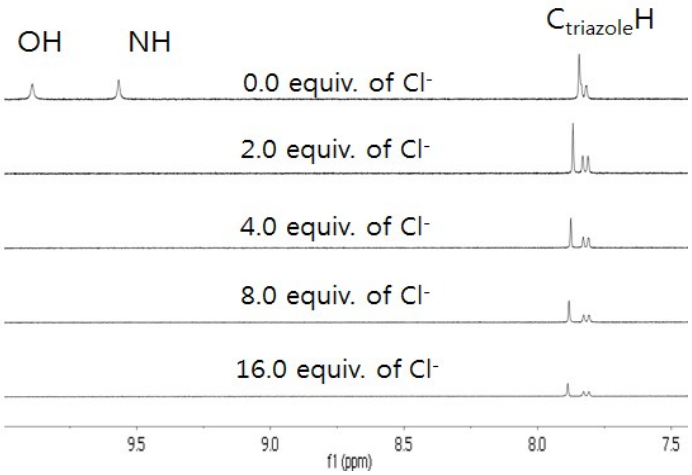
Table S1. Chloride binding constants (K_a; M^{-1})[a] of **4a**–**4g** summarized from the above titrations in DMSO at 25 °C.

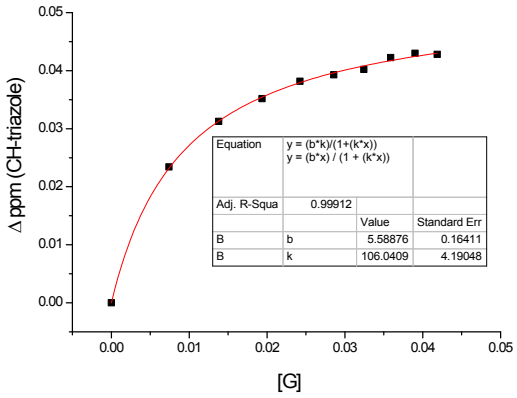
.

	4a	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**
^{1}H NMR[a]	16	13	12	16	23	11	18
UV -Vis[a]	2900	2500	4900	b	b	b	b

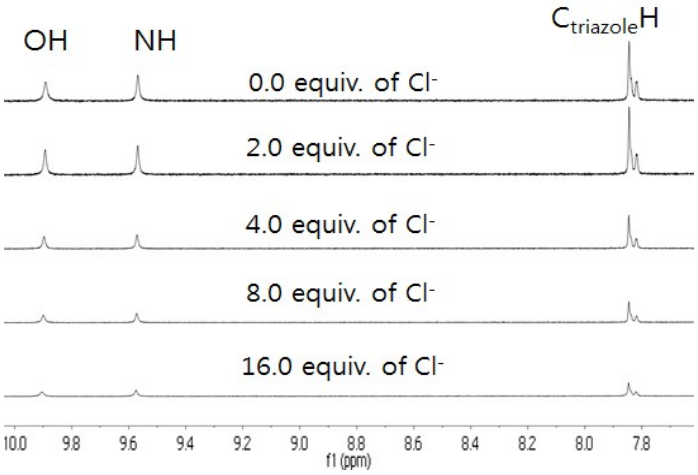
[a]The observed errors for ^{1}H NMR titrations were less than 13%, while those obtained from UV-Vis titrations were less than 20%. [b]Reliable binding constants could not be obtained due to the relatively large errors.

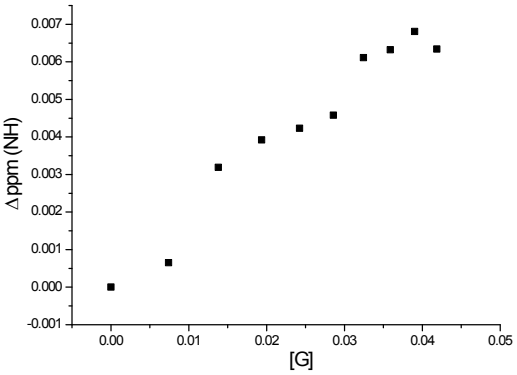
4a $H_2PO_4^-$



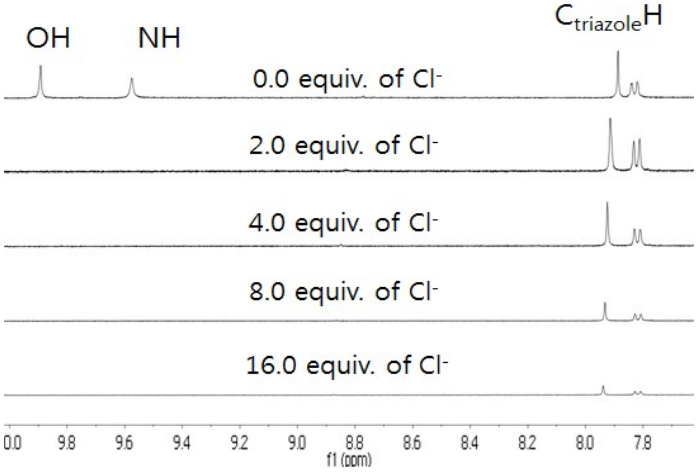


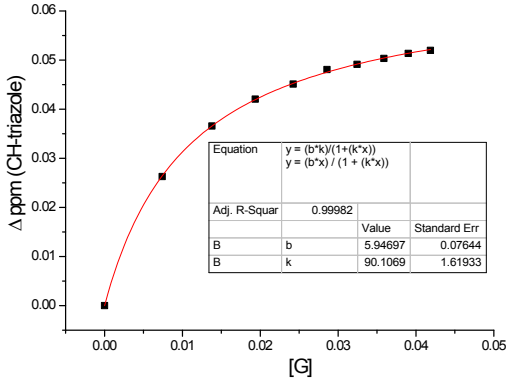
4a NO_3^-



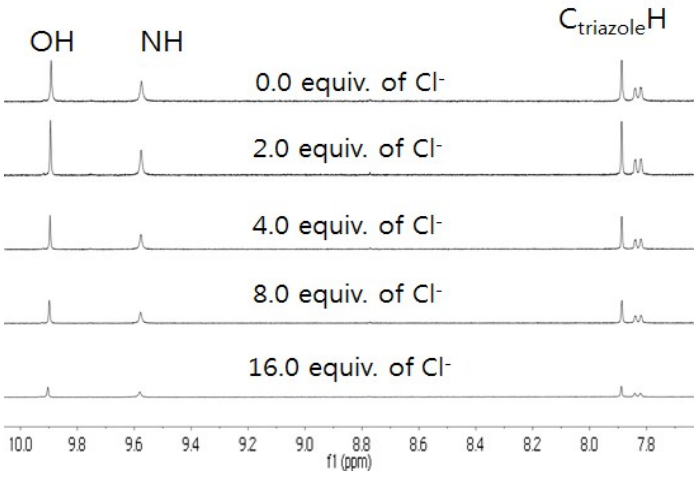


4b $H_2PO_4^-$





4b NO_3^-



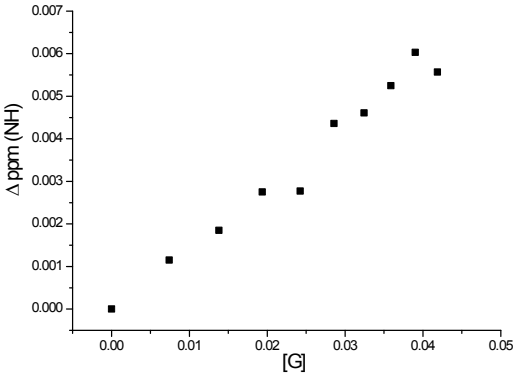


Table S2. binding constants (K_a; M^{-1})[a] of **4a** and **4b** summarized from the above titrations in DMSO at 25 °C.

	[c]$H_2PO_4^-$	NO_3^-
4a	110 ± 4	[b]
4b	90 ± 2	[b]

[a]The above binding constants were obtained ^1H NMR titrations. [b]Reliable binding constants could not be obtained due to the relatively large errors. [C]The chemical shifts of NH and OH were disappeared upon the addition of $H_2PO_4^-$. These titrations don't provide enough information to support that there is less significant interactions are found for **4b** and the possible anions ($H_2PO_4^-$ and NO_3^-) during the Cl^- efflux assay than the interactions for **4a** and the anions in the organic solvent.

a) b)

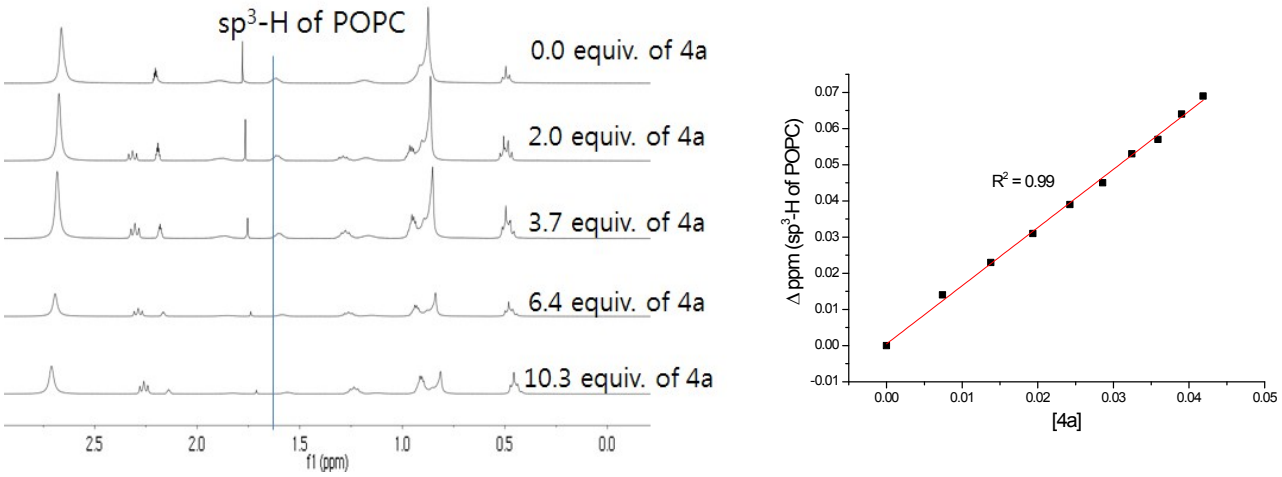


Figure S1. (a) Partial ^{1}H-NMR spectra recorded during the titration of POPC **(**[H] = 4.0 × 10^{-3} M in $CDCl_3$/DMSO (4/1, v/v) with **4a**. (b) The linear-trace data were obtained by following the chemical shift changes of sp^3-H of POPC.

a) b)

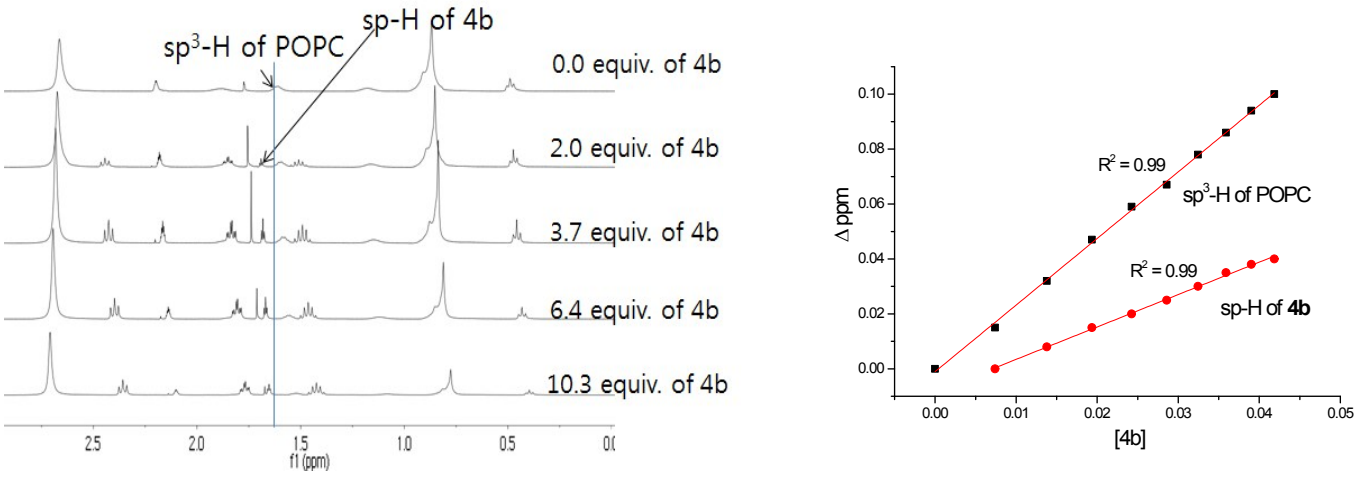


Figure S2. (a) Partial ^{1}H-NMR spectra recorded during the titration of POPC **(**[H] = 4.0 × 10^{-3} M in $CDCl_3$/DMSO (4/1, v/v) with **4b**. (b) The linear-trace data were obtained by following the chemical shift changes of sp^3-H of POPC and sp-H of **4b**.

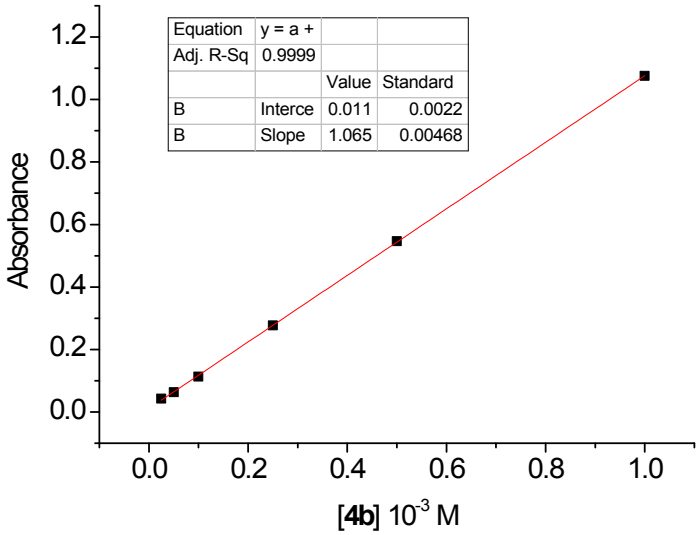


Figure S3. The absorbance changes at a various concentrations of **4b (**from 1 mM to 25 μM) in DMSO at 303.5 nm.

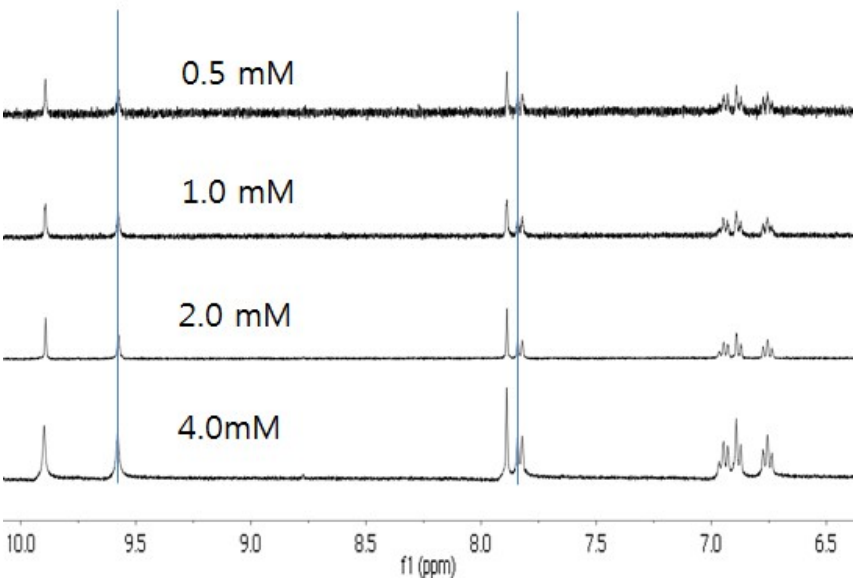


Figure S4. Partial ^{1}H-NMR spectra recorded at a various concentrations of **4b.**

Preparation of liposomes containing fluorophore

1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine(POPC, Avanti Polar Lipids, Alabaster, AL) was obtained as in 20 mg/mL solution in $CHCl_3$ from). The lipid solution was dried under argon and further dried in a dessicator under vacuum overnight to fully remove chloroform. The dried lipid film was rehydrated in solution containing 475 mM NaCl and 25 mM fluorophore 8-aminonaphthalene-1,3,6-trisulfonic acid(ANTS) buffered at pH 7.2 at room temperature overnight. The suspension was sequentially sonicated for 1–2 min in a bath sonicator (G112SPIT, Laboratory Supplies Co., Hicksville, NY), frozen-thawed for 4-5 times, and extruded 21 times at room temperature using an Avanti mini-extruder with a 0.2 µm polycarbonate membrane filter(Alabaster, AL), resulting in large unilamelar vesicles(LUVs) containing ANTS. The extuded suspenstion was dispersed in 500 mM $NaNO_3$ buffered at pH 7.2 (Na buffer) to 1:20 ratio and stored at 12°C in the dark. All the LUV-ANTS stocks were not stored over 24 hours.

Fluorescence spectroscopy

The ANTS fluorescence emission was measured at 25°C using a fluorometer. The emmision was scaned from 350 nm to 700 nm (excitation: 352 nm). LUV-ANTS stock was diluted to measure fluorescence. Each LUV-ANTS stock was mixed with Na buffer, Tl buffer (475 mM $NaNO_3$, 25mM $TlNO_3$, pH 7.2), Tl buffer with 2 mol% of triton X, respectivly to the ratio of 5:5, and a DMSO solution of **4d**–**4f** (4 mol% relative to POPC) was added. Emmision scan was conducted for each mixture after 3 min reaction.

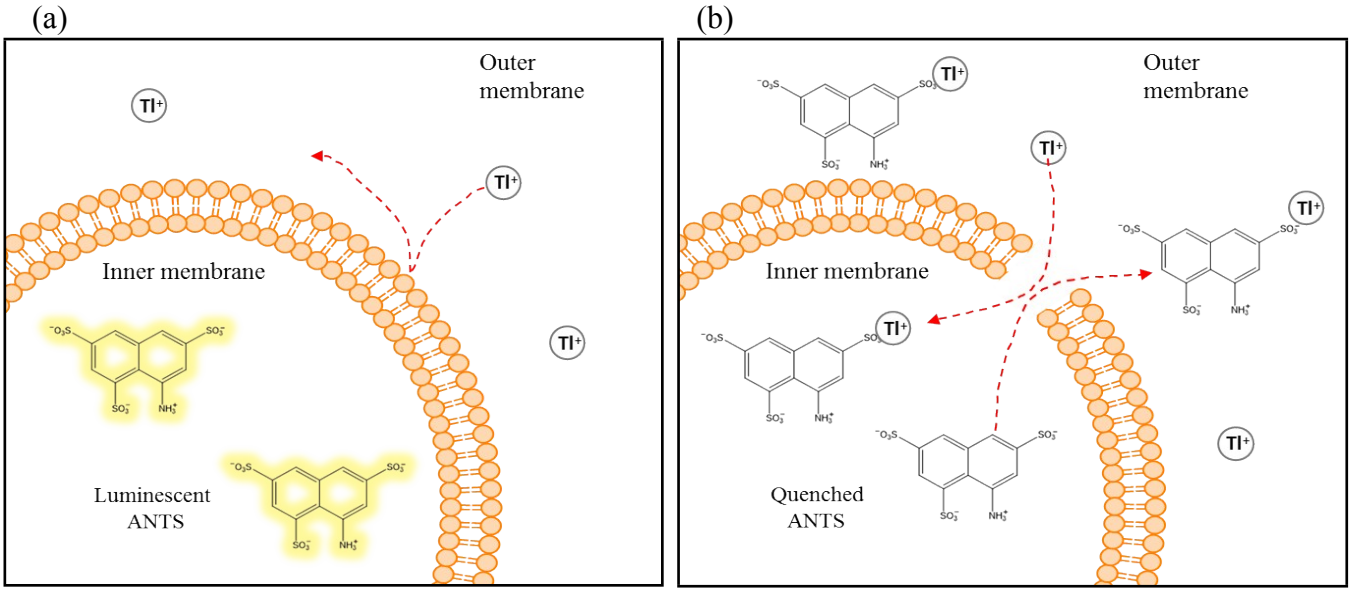


Figure S5. Schematic image of LUV-ANTS experiment. (a) If the compounds (**4d-4f**) don't rupture (or damage) the LUV, (2) If the compounds (**4d-4f**) are involved in the rupture (or damage)of the LUV.

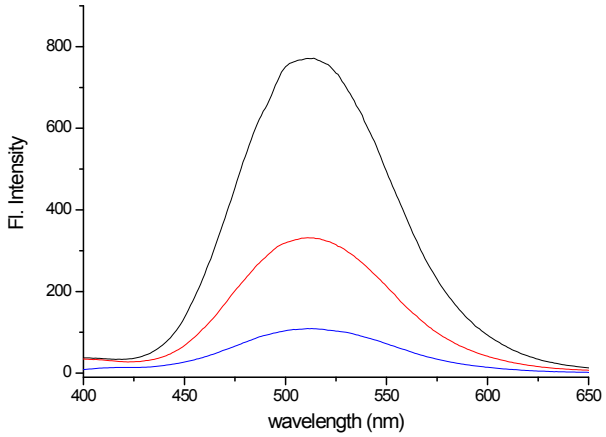


Figure S6. Fluorescence changes of ANTS-LUV solutions which are mixed with Na buffer (Black line), Tl buffer (Red line), Tl buffer and 2 mol% of triton X (Blue line) in the presense of 4 mol% **4d**.

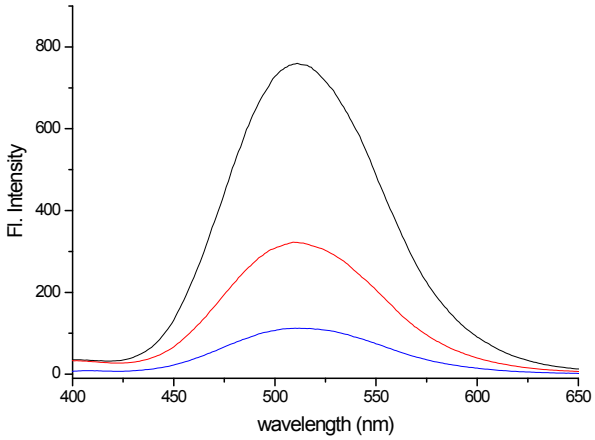


Figure S7. Fluorescence changes of ANTS-LUV solutions which are mixed with Na buffer (Black line), Tl buffer (Red line), Tl buffer and 2 mol% of triton X (Blue line) in the presense of 4 mol% **4e**.

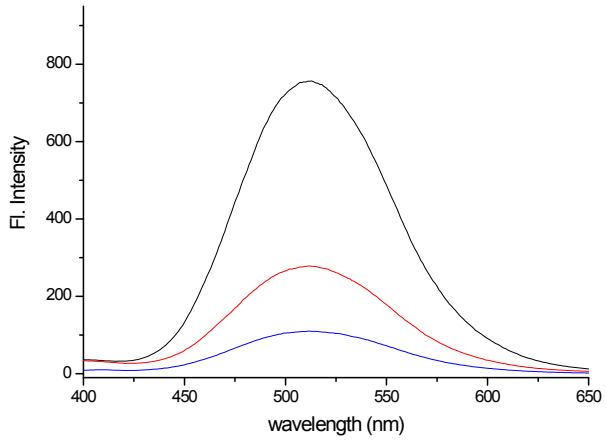


Figure S8. Fluorescence changes of ANTS-LUV solutions which are mixed with Na buffer (Black line), Tl buffer (Red line), Tl buffer and 2 mol% of triton X (Blue line) in the presense of 4 mol% **4f**.

Preparation of POPC Vesicles

A lipid film of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) was formed from chloroform solution (20mg/ml) under the gentle stream of nitrogen gas and dried under vacuum for at least 2 hours. The lipid film was then rehydrated in buffer solution (488 mM NaCl and 5 mM phosphate buffer, pH 7.2) and the solution was vortexed. The lipid suspension was then subjected to seven freeze–thaw cycles and left at room temperature for 30 minuntes, followed by extrusion through a 200 nm polycarbonate membrane 31 times. The resulting unilamellar vesicles were dialyzed to remove unencapsulated NaCl salts.

Chloride Transport Assays

Unilamellar POPC vesicles, prepared as described above, were suspended in 488 mM $NaNO_3$ solution buffered at pH 7.2 with 5 mM sodium phosphate salts. The lipid concentration of each sample was 1 mM. The carrier molecules dissolved in DMSO (4 mol%) were added to monitor chloride efflux using a chloride selective electrode. At 10 min.

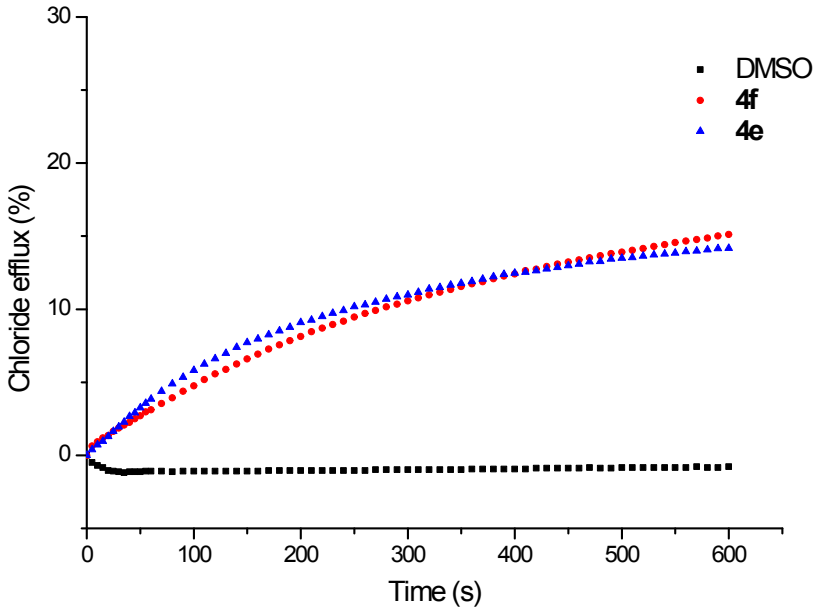


Figure S9. Chloride efflux upon addition of **4f** and **4e** (4 mol% relative to POPC) to vesicles composed of POPC. The vesicles contained NaCl (488 mM) and were immersed in $NaSO_4$ (488 mM), pH 7.0 solution; at 600 s, they were lysed to obtain 100% chloride efflux.□

Chloride Transport Assays at variable pH

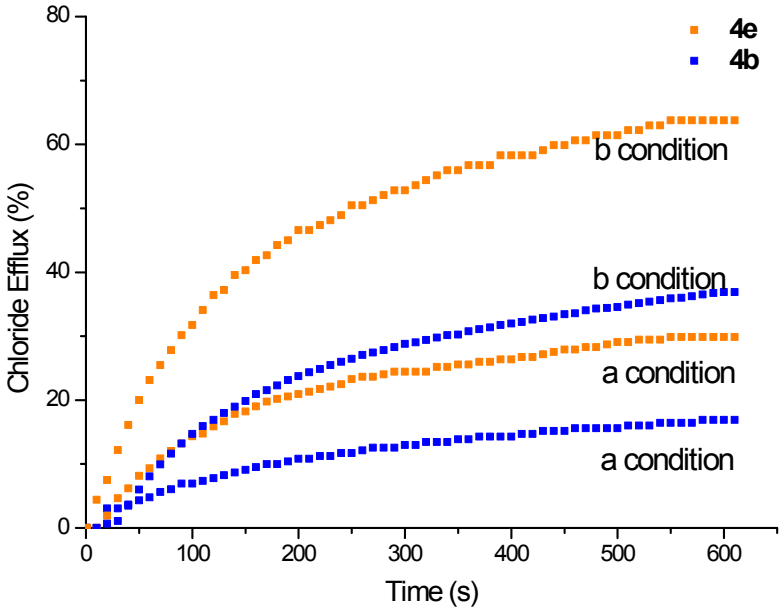


Figure S10. Chloride efflux induced upon addition of **4b** and **4e** (4 mol% relative to POPC) to vesicles containing 488 mM NaCl (X1 solution) immersed in 488 mM $NaNO_3$ (X2 solution) at two differnt pH conditions, (a) inside vesicle, pH 4.0: outside vesicle, pH 6.7, X1 = citric acid (pH 4.0) and X2 = sodium phosphate (pH 6.7) (b) inside and outside vesicle, pH 7.0, X1 and X2 = sodium phosphate (pH 7.0). X1 and X2 are mixed to obtain 1 mM solution of POPC. At 600 s, vesicles were ruptured using detergent (Triton X-100) to obtain 100% chloride efflux.

Cell culture

HT-29 and DLD-1, both human colon epithelial cancer cell lines, were cultured in DMEM(Dulbecco's Modified Eagle Medium, Gibco®) with 10%(v/v) FBS(Fetal Bovine Serum, Gibco®) and 1% Penicillin-Streptomycin(Gibco®) at 37 °C incubator under 5% CO_2 and 95% air.

Cell viability assay

Both cancinoma cell lines were seeded on the 96 well plates (Corning®), approximately 2,500 cells per each well, and subsequently incubated for 48 hours at 37 °C incubator under 5% CO_2 and 95% air. DMSO (Dimethyl sulfoxide, biotech. grade, 99.8%, Sigma-Aldrich Co.) was used as solvent for compounds, **4d** and **4e**. The compounds were diluted to 100, 250, and 500 μM concentratios in DMEM (1% DMSO), respectively. 48 hours after addition of each compound to each well, cell viability assay was conducted. LIVE/DEAD Viability/Cytotoxicity Kit (Molecular Probes®) was used with 2 μM calcein AM and 4 μM EthD-1 solution. Using inverted fluorescence microscope (Ti-U, Nikon), we confirmed green and red fluorescence shown in live and dead cells, respectively.

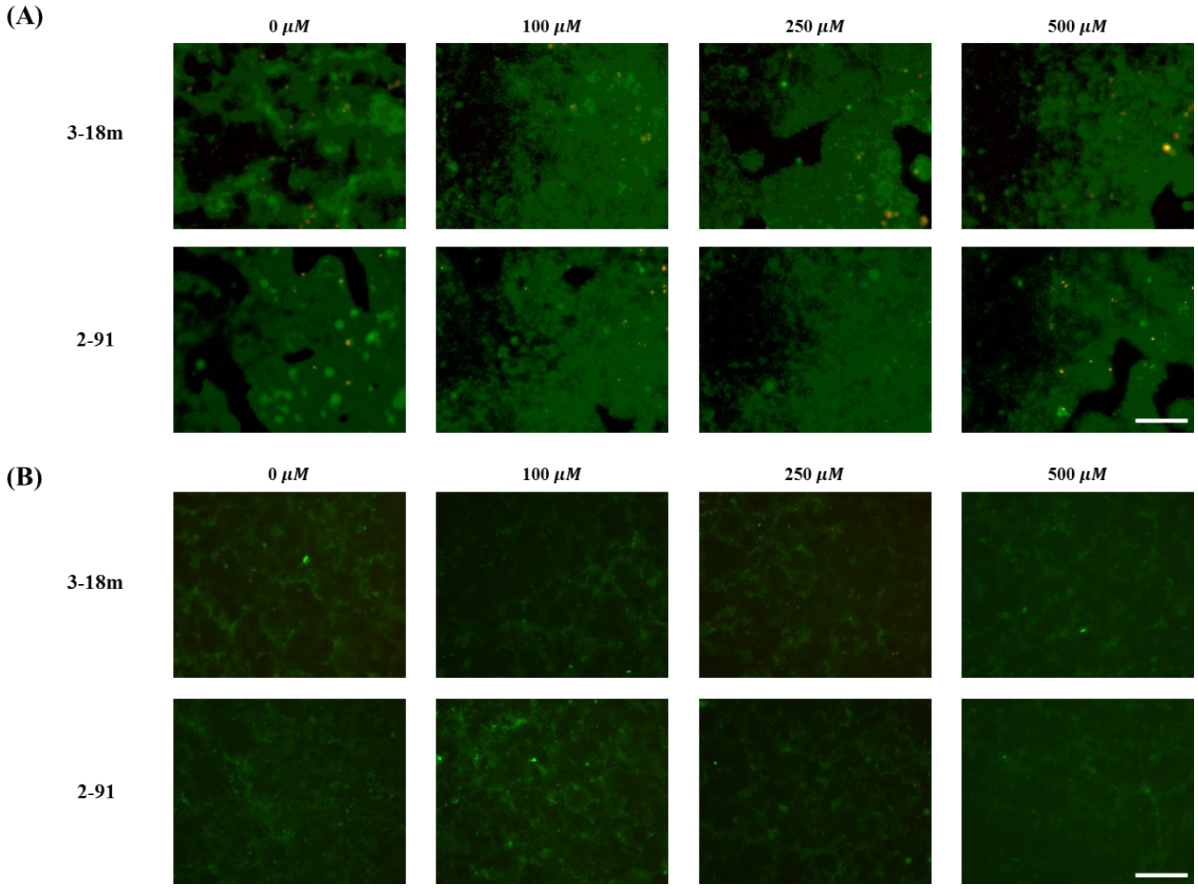


Figure S11. Live/dead assay for **(A)** HT-29 and **(B)** DLD-1 human colon carcinoma cell line to validate cell toxicity of compounds **4d** and **4e**. Contentrations of compounds are 0, 100, 250, and 500 μM, respectively. (scale bar is 100 μM)

Electrical measurement across lipid bilayer membranes

A lipid bilayer membrane was reconstructed using a convetional method in ~100 um aperture that was made using a spark generator (DAEDALON) on a 10 μm thick PTFE film (Good Fellow). DPhPC (1,2,-diphytanoyl-sn-glycero-3-phosphocholine, Avanti Polar Lipid, Inc.) dissolved in n-decane (MP biomedicals) at concentration of 30 mg/ml was used as lipid solution. The lipid solution was pre-painted around the aperture in the PTFE film and was dried for 30 minutes. The film was placed horizontally in the chamber filled with buffer solution (1 M NaCl, 10 mM HEPES, and 1 mM EDTA pH 7.2). The **4d-4f** was add to both chambers (cis and trans) from 20 μM to dk2 mM. Electrical measurement across lipid bilayer membrane was done using Axopatch 200b patch clamp(Molecular device). The data was acquired via 250 kHz sampling rate with lowpass Bessel filter 1kHz using Clampfit 10.3 (Molecular Devices) and was analyzed using Clampex 10.3 program.

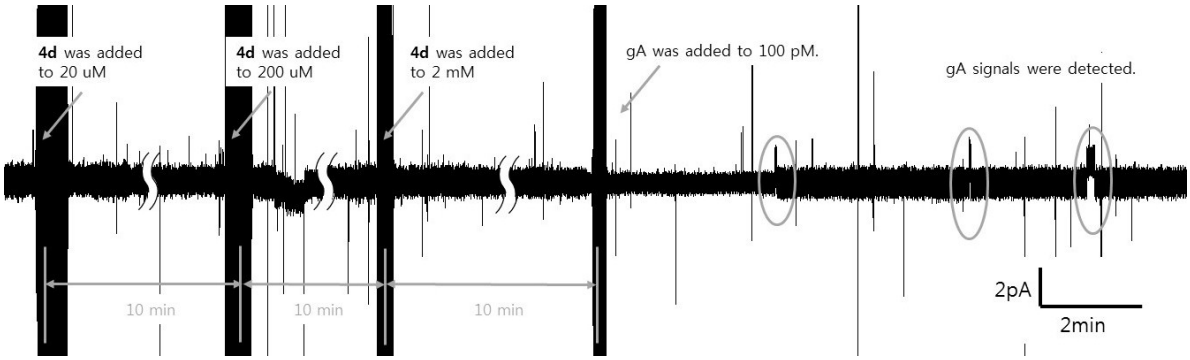
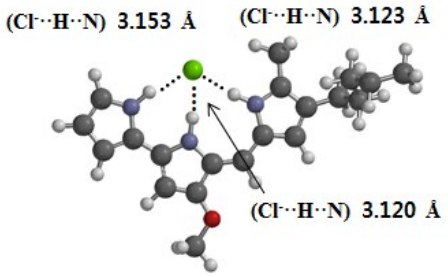


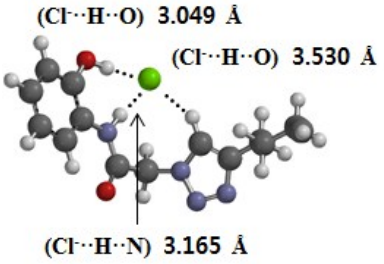
Figure S12. Electrical measurments across lipid bilayer membrane in the presence of **4d** (20 μM -2 mM). **4d** did not show any effect to the conductance of the lipid bilayers. 200 pM of gA that creates ion channels was added to verify exsistense of bilayer for control experiment. The data was digitally filtered by 300 Hz Bessel filter. The result of **4e** and **4f** is omitted as as no noticeable change was observed, also.

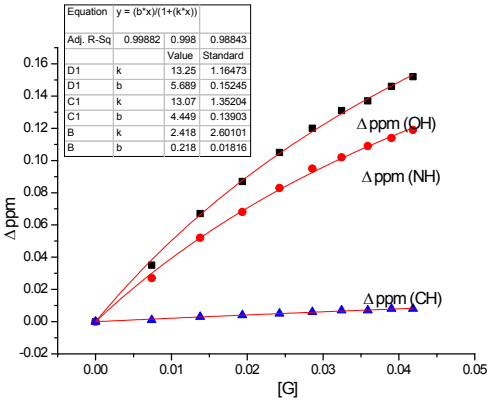
Computational calculations and detailed ^{1}H NMR titrations

a)

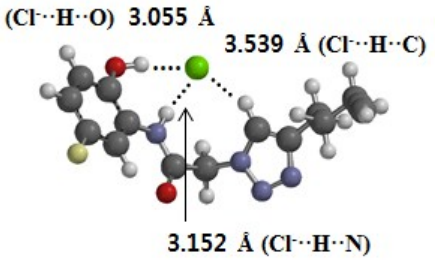


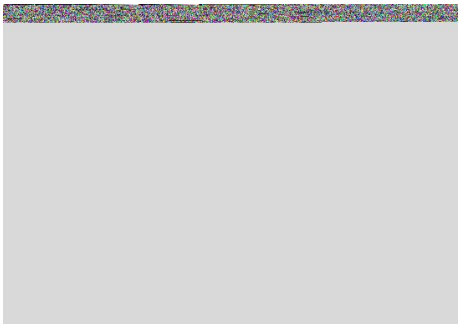
b)





c)





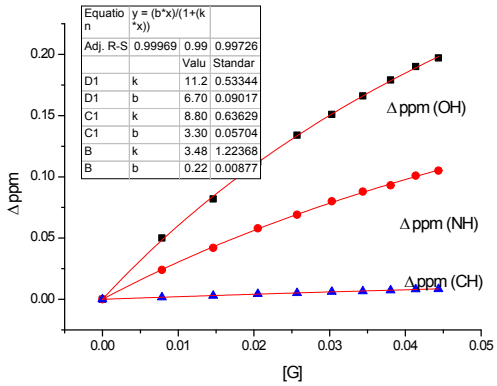


Figure S13. DFT optimized structures of a) prodigiosin·Cl$^-$, b) **4b** · Cl$^-$ and ^{1}H NMR titrations of **4b**, and c) **4f** · Cl$^-$ and ^{1}H NMR titrations of **4f**. The structures were optimized based on the density functional theory (DFT) using the EDF2/6–31G* theoretical level. The alkyl substitutes of prodigiosin are omitted for clarity.

Table S4. EDF2/6–31G* optimized structure of **4b** · Cl^-.
Energy = -1410.276309 hartrees
This structure has no imaginary frequency.

Cartesian Coordinates (Angstroms)			
Atom	X	Y	Z
1	C C1	4.4953107	-2.1727891	-0.3447064
2	C C4	3.4048644	-0.5068629	1.5729735
3	C C2	3.6010352	-1.1777011	-0.7525102
4	C C6	4.8463737	-2.3405292	0.9862416
5	C C5	4.2965560	-1.5028495	1.9501534
6	C C3	3.0455893	-0.3216191	0.2320125
7	H H6	5.5450724	-3.1245794	1.2653754
8	H H5	4.5553152	-1.6175754	2.9984880
9	H H4	2.9722239	0.1607943	2.3038188
10	N N1	2.1520027	0.6900118	-0.1667468
11	H H3	1.8586666	0.6979296	-1.1547386
12	C C7	1.5980040	1.6638431	0.6018285
13	N N3	-1.5572840	2.7055734	0.8652949
14	N N2	-0.7428202	2.1519782	-0.0525866
15	C C9	-1.3856145	1.1971638	-0.7623075
16	C C10	-2.6570254	1.1874861	-0.2360774
17	N N4	-2.7174642	2.1225725	0.7530721
18	H H11	-0.8939955	0.6688931	-1.5701762
19	C C8	0.6385775	2.5779711	-0.1780807
20	H H7	0.7004277	3.5714867	0.2647619
21	H H12	0.8828623	2.6071012	-1.2428648
22	O O2	1.7928134	1.8536002	1.7962139
23	C C11	-3.8341864	0.3459014	-0.5982912
24	H H8	-3.6522065	-0.1307611	-1.5685273
25	H H9	-4.7125008	0.9927509	-0.7233153
26	C C12	-4.1532249	-0.7238739	0.4500973
27	H H1	-4.3020383	-0.2442203	1.4223724
28	H H10	-3.2999589	-1.4011348	0.5611439
29	C C13	-5.4033769	-1.5327100	0.0740460
30	H H14	-5.2517949	-1.9993077	-0.9088304
31	H H15	-6.2538959	-0.8480247	-0.0474004
32	C C14	-5.7477986	-2.5604731	1.0468148
33	H H13	-6.2543273	-4.1550222	2.5826278
34	C C15	-6.0241858	-3.4078906	1.8597738
35	Cl Cl1	1.1423891	0.6592329	-3.1661473
36	H H16	4.9033887	-2.8093677	-1.1230060
37	O O1	3.3715105	-1.1133340	-2.0764241
38	H H2	2.6329185	-0.5162806	-2.3754284

Table S4. EDF2/6–31G* optimized structure of **4f** · Cl^-.
Energy = -1509.485821 hartrees
This structure has no imaginary frequency.

Cartesian Coordinates (Angstroms)				
Atom	X	Y	Z	
1	C	C1	-4.2657272	-1.3864007	1.5296133
2	C	C4	-3.1543462	-1.1410043	-0.9938871
3	C	C2	-3.3434653	-0.3615362	1.3017260
4	C	C6	-4.6435777	-2.2795496	0.5367836
5	C	C5	-4.0713505	-2.1345642	-0.7130232
6	C	C3	-2.7773233	-0.2360050	0.0064906
7	H	H6	-5.3607686	-3.0709943	0.7229639
8	H	H4	-2.7281245	-1.0450099	-1.9813895
9	N	N1	-1.8569238	0.7940466	-0.2412572
10	H	H3	-1.5815724	1.3835183	0.5594530
11	C	C7	-1.2540907	1.1076312	-1.4200144
12	N	N3	1.9262885	1.7244740	-2.1738175
13	N	N2	1.0923125	1.8391631	-1.1237346
14	C	C9	1.6999732	1.4648567	0.0257365
15	C	C10	2.9697842	1.1098045	-0.3678352
16	N	N4	3.0639985	1.2843934	-1.7159856
17	H	H11	1.1874452	1.5269169	0.9779185
18	C	C8	-0.2756983	2.2868177	-1.3050614
19	H	H7	-0.3046122	2.8299523	-2.2489251
20	H	H12	-0.5270822	2.9413602	-0.4663055
21	O	O2	-1.4237699	0.5483906	-2.4956523
22	C	C11	4.1139257	0.5911137	0.4371244
23	H	H8	3.9128036	0.7545101	1.5022114
24	H	H9	5.0162353	1.1668635	0.1932820
25	C	C12	4.3909186	-0.8935518	0.1839228
26	H	H1	4.5538295	-1.0507813	-0.8865418
27	H	H10	3.5127795	-1.4870263	0.4584483
28	C	C13	5.6119066	-1.3891879	0.9730247
29	H	H14	5.4473064	-1.2145340	2.0451291
30	H	H15	6.4874096	-0.7836785	0.7016685
31	C	C14	5.9125424	-2.7975064	0.7552179
32	H	H13	6.3477967	-4.9968860	0.3930503
33	C	C15	6.1500847	-3.9649940	0.5658644
34	Cl	Cl1	-0.8801772	2.5363112	2.1974195
35	H	H16	-4.6812330	-1.4550925	2.5290771
36	O	O1	-3.0948112	0.4383171	2.3563344
37	H	H2	-2.3559713	1.0965021	2.2542588
38	F	F1	-4.4195165	-2.9951840	-1.7007133

pH-metric method

Log P values were obtianed by pH-meteric methods shown below.

pH-metric

Sample name:	4a	Experiment start time:	03/04/2015 08:07:09
Assay name:	pH-metric medium logP	Analyst:	KRICT
Assay ID:	15D-03015	Instrument ID:	T313101
Filename:	D:\Data\Customer\15D-03015_4a_pH-metric medium logP.t3r		

Overall results

RMSD	0.331
Average Ionic strength	0.160 M
Average temperature	25.0°C
Partition ratio	0.2697 : 1
Analyte concentration range	2199.6 µM to 2350.5 µM
Total points considered	42 of 52

Warnings and errors

Errors	None
Warnings	Sample concentration factor out of range

Four-Plus parameters

Alpha	0.194	03/04/2015 08:07:09	D:\Data\Customer\15D-02024_Blank standardisation.t3r
S	0.9897	03/04/2015 08:07:09	D:\Data\Customer\15D-02024_Blank standardisation.t3r
]H	1.4	03/04/2015 08:07:09	D:\Data\Customer\15D-02024_Blank standardisation.t3r
]OH	-0.5	03/04/2015 08:07:09	D:\Data\Customer\15D-02024_Blank standardisation.t3r

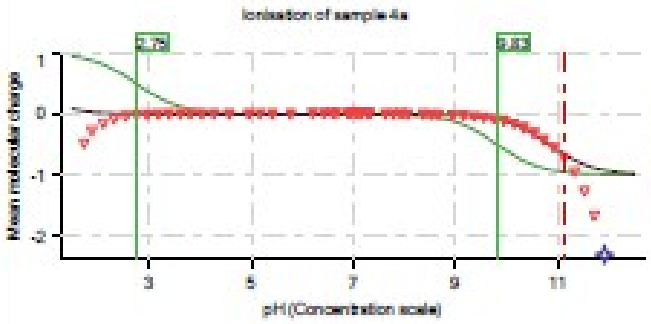
Titrants

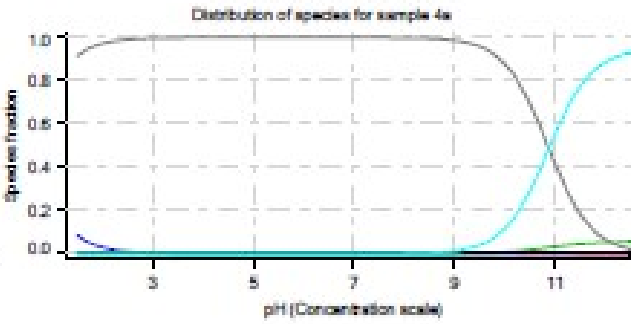
0.50 M HCl	0.997167	03/04/2015 08:07:09	D:\Data\Customer\15D-02024_Blank standardisation.t3r
0.50 M KOH	1.003080	03/04/2015 08:07:09	D:\Data\Customer\15A-27013_KHP_Base standardisation using KHP.t3r

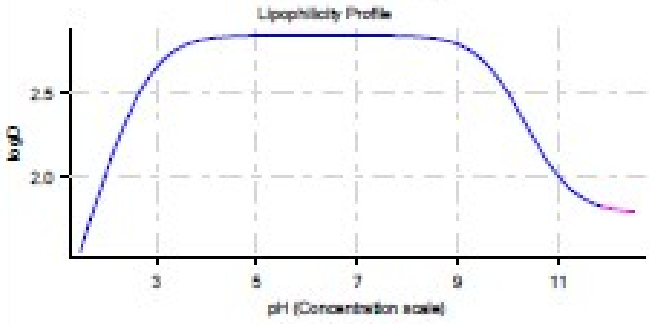
Sample

4a concentration factor	1.525
Base pKa 1	2.75
Acid pKa 2	9.83
logP (XH2 +)	-6.36
logP (neutral XH)	2.64
logP (X -)	1.79

Sample graphs







pH-metric

Sample name: 4a
Assay name: pH-metric medium logP
Assay ID: 15D-03015
Filename: D:\Data\Customer\15D-03015_4a_pH-metric medium logP.t3r

Experiment start time: 03/04/2015 08:07:09
Analyst: KRICT
Instrument ID: T313101

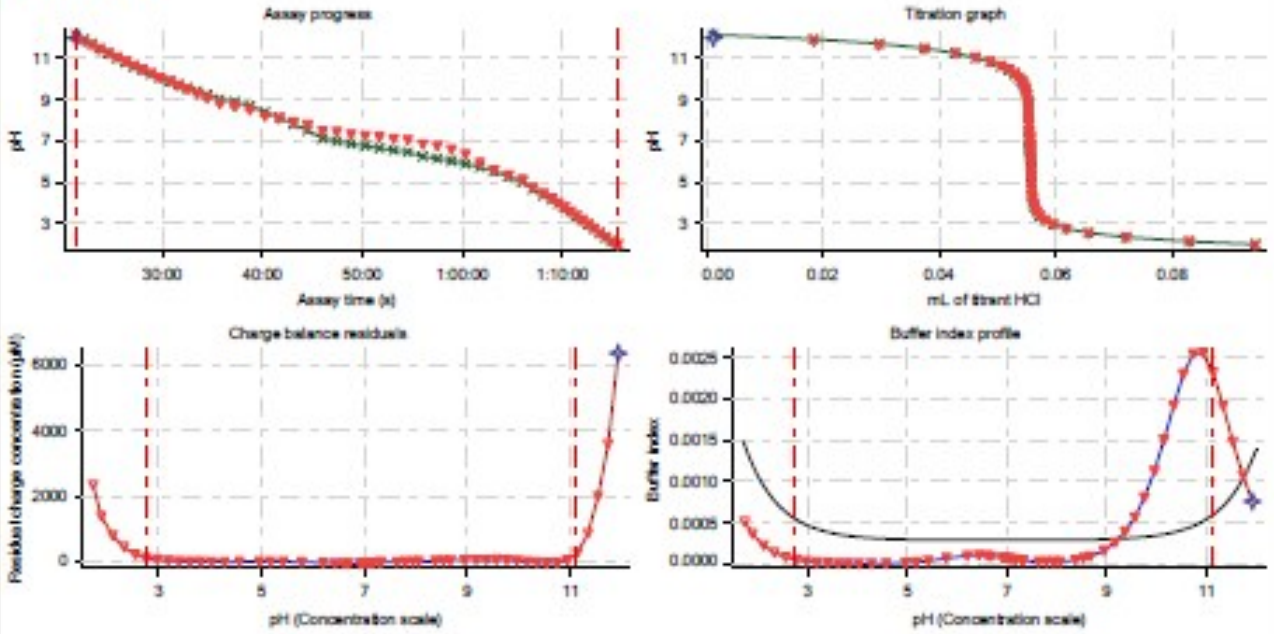
Sample logD and percent species

pH	4a logD	4a 4aH2	4a 4aH	4a 4a	4a 4aH2*	4a 4aH*	4a 4a*	Comment
1.000	1.08	23.07 %	0.41 %	0.00 %	0.00 %	76.52 %	0.00 %	
1.200	1.28	15.91 %	0.45 %	0.00 %	0.00 %	83.64 %	0.00 %	Stomach pH
2.000	2.02	2.91 %	0.52 %	0.00 %	0.00 %	96.57 %	0.00 %	
3.000	2.65	0.30 %	0.53 %	0.00 %	0.00 %	99.17 %	0.00 %	
4.000	2.82	0.03 %	0.53 %	0.00 %	0.00 %	99.44 %	0.00 %	
5.000	2.84	0.00 %	0.53 %	0.00 %	0.00 %	99.46 %	0.00 %	
6.000	2.84	0.00 %	0.53 %	0.00 %	0.00 %	99.47 %	0.00 %	
6.500	2.84	0.00 %	0.53 %	0.00 %	0.00 %	99.46 %	0.00 %	
7.000	2.84	0.00 %	0.53 %	0.00 %	0.00 %	99.45 %	0.01 %	
7.400	2.84	0.00 %	0.53 %	0.00 %	0.00 %	99.43 %	0.03 %	Blood pH
8.000	2.83	0.00 %	0.53 %	0.01 %	0.00 %	99.33 %	0.13 %	
9.000	2.79	0.00 %	0.53 %	0.08 %	0.00 %	98.09 %	1.31 %	
10.000	2.50	0.00 %	0.47 %	0.69 %	0.00 %	87.22 %	11.62 %	
11.000	2.01	0.00 %	0.22 %	3.28 %	0.00 %	41.37 %	55.13 %	
12.000	1.82	0.00 %	0.04 %	5.24 %	0.00 %	6.61 %	88.11 %	

Carbonate and acidity

Carbonate 0.185 mM
Acidity error 0.305 mM

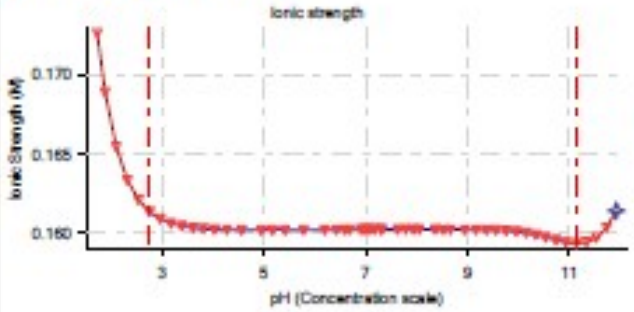
Other graphs

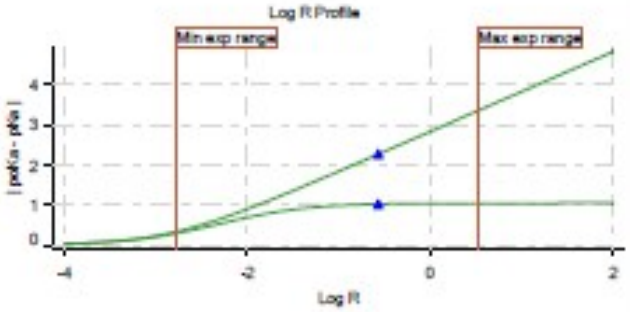


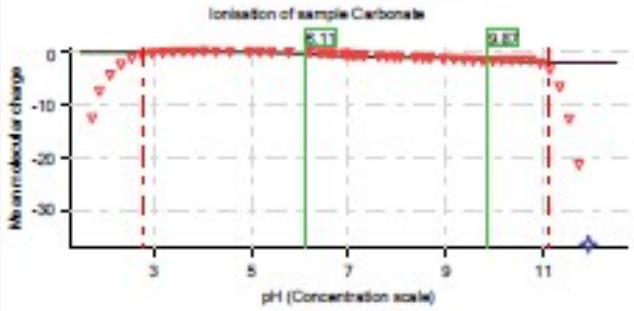
pH-metric

Sample name:	4a	Experiment start time:	03/04/2015 08:07:09
Assay name:	pH-metric medium logP	Analyst:	KRICT
Assay ID:	15D-03015	Instrument ID:	T313101
Filename:	D:\Data\Customer\15D-03015_4a_pH-metric medium logP.t3r		

Other graphs (continued)







pH-metric

Sample name:	**4b**	Experiment start time:	**03/04/2015 11:12:00**
Assay name:	**pH-metric medium logP**	Analyst:	**KRICT**
Assay ID:	**15D-03018**	Instrument ID:	**T313101**
Filename:	**D:\Data\Customer\15D-03018_4b_pH-metric medium logP.t3r**		

Overall results

RMSD	0.229
Average Ionic strength	0.158 M
Average temperature	25.0°C
Partition ratio	0.2774 : 1
Analyte concentration range	1784.4 µM to 1888.8 µM
Total points considered	33 of 43

Warnings and errors

Errors	None
Warnings	None

Four-Plus parameters

Alpha	0.194	03/04/2015 11:12:00	D:\Data\Customer\15D-02024_Blank standardisation.t3r
S	0.9697	03/04/2015 11:12:00	D:\Data\Customer\15D-02024_Blank standardisation.t3r
]H	1.4	03/04/2015 11:12:00	D:\Data\Customer\15D-02024_Blank standardisation.t3r
]OH	-0.5	03/04/2015 11:12:00	D:\Data\Customer\15D-02024_Blank standardisation.t3r

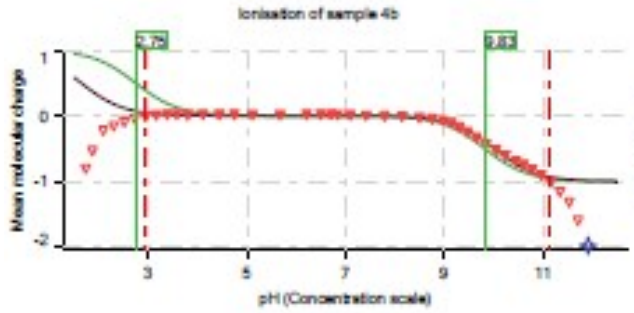
Titrants

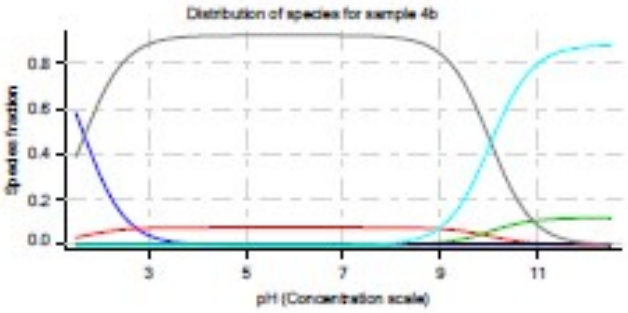
0.50 M HCl	0.997167	03/04/2015 11:12:00	D:\Data\Customer\15D-02024_Blank standardisation.t3r
0.50 M KOH	1.003080	03/04/2015 11:12:00	D:\Data\Customer\15A-27013_KHP_Base standardisation using KHP.t3r

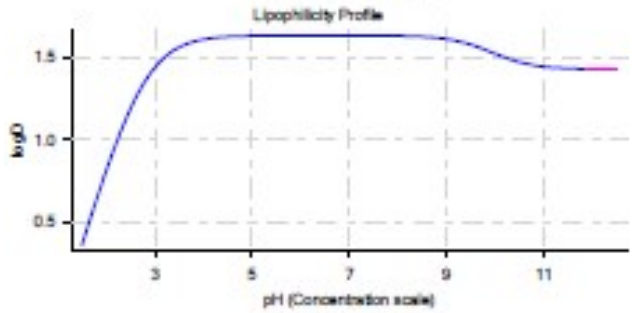
Sample

4b concentration factor	0.917
Base pKa 1	2.75
Acid pKa 2	9.83
logP (XH2 +)	-9.28
logP (neutral XH)	1.63
logP (X -)	1.42

Sample graphs







Sample name: 4b
Assay name: pH-metric medium logP
Assay ID: 15D-03018
Filename: D:\Data\Customer\15D-03018_4b_pH-metric medium logP.t3r

Experiment start time: 03/04/2015 11:12:00
Analyst: KRICT
Instrument ID: T313101

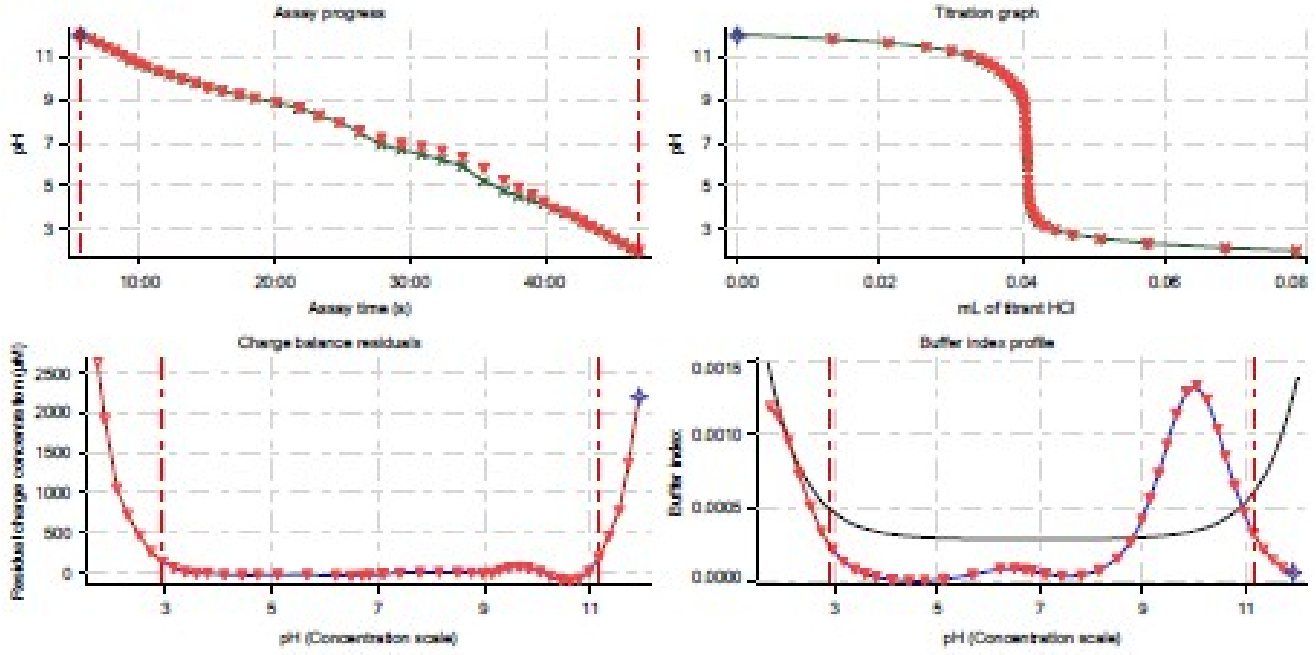
Sample logD and percent species

pH	4b logD	4b 4bH2	4b 4bH	4b 4b	4b 4bH2+	4b 4bH+	4b 4b+	Comment
1.000	-0.13	81.42 %	1.45 %	0.00 %	0.00 %	17.13 %	0.00 %	
1.200	0.07	73.44 %	2.07 %	0.00 %	0.00 %	24.49 %	0.00 %	Stomach pH
2.000	0.81	30.47 %	5.42 %	0.00 %	0.00 %	64.12 %	0.00 %	
3.000	1.44	4.20 %	7.46 %	0.00 %	0.00 %	88.34 %	0.00 %	
4.000	1.61	0.44 %	7.76 %	0.00 %	0.00 %	91.81 %	0.00 %	
5.000	1.63	0.04 %	7.79 %	0.00 %	0.00 %	92.17 %	0.00 %	
6.000	1.63	0.00 %	7.79 %	0.00 %	0.00 %	92.20 %	0.01 %	
6.500	1.63	0.00 %	7.79 %	0.00 %	0.00 %	92.18 %	0.03 %	
7.000	1.63	0.00 %	7.78 %	0.01 %	0.00 %	92.12 %	0.08 %	
7.400	1.63	0.00 %	7.77 %	0.03 %	0.00 %	91.99 %	0.21 %	Blood pH
8.000	1.63	0.00 %	7.72 %	0.11 %	0.00 %	91.33 %	0.84 %	
9.000	1.61	0.00 %	7.11 %	1.05 %	0.00 %	84.10 %	7.74 %	
10.000	1.52	0.00 %	3.97 %	5.87 %	0.00 %	46.95 %	43.22 %	
11.000	1.44	0.00 %	0.73 %	10.83 %	0.00 %	8.67 %	79.77 %	
12.000	1.43	0.00 %	0.08 %	11.83 %	0.00 %	0.95 %	87.14 %	

Carbonate and acidity

Carbonate 0.160 mM
Acidity error 0.060 mM

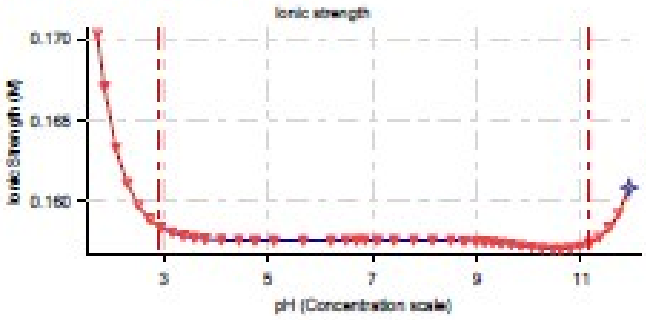
Other graphs

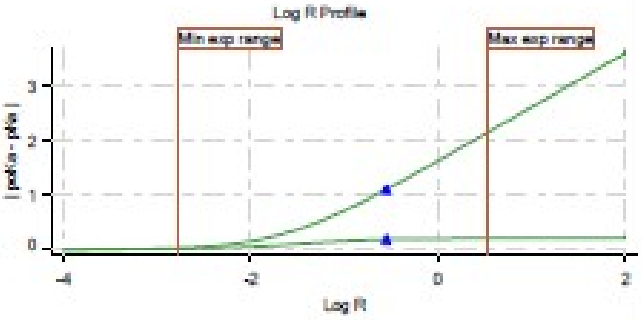


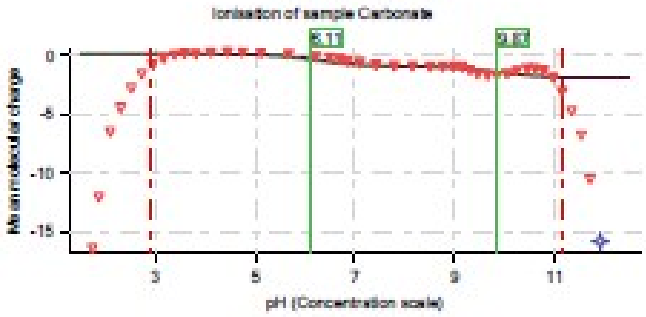
pH-metric

Sample name:	4b	Experiment start time:	03/04/2015 11:12:00
Assay name:	pH-metric medium logP	Analyst:	KRICT
Assay ID:	15D-03018	Instrument ID:	T313101
Filename:	D:\Data\Customer\15D-03018_4b_pH-metric medium logP.t3r		

Other graphs (continued)







sirius

pH-metric

ample name:	4e	Experiment start time:	03/04/2015 13:48:06
ssay name:	pH-metric medium logP	Analyst:	KR/CT
ssay ID:	15D-03021	Instrument ID:	T313101
ilename:	D:\Data\Customer\15D-03021_4c_pH-metric medium logP.t3r		

)verall results

tMSD	0.103
verage Ionic strength	0.158 M
verage temperature	25.0°C
artition ratio	0.2765 : 1
nalyte concentration range	1698.1 µM to 1798.6 µM
otal points considered	36 of 49

Varnings and errors

rrors	None
Varnings	None

our-Plus parameters

Alpha	0.194	03/04/2015 13:48:06	D:\Data\Customer\15D-02024_Blank standardisation.t3r
S	0.9897	03/04/2015 13:48:06	D:\Data\Customer\15D-02024_Blank standardisation.t3r
H	1.4	03/04/2015 13:48:06	D:\Data\Customer\15D-02024_Blank standardisation.t3r
OH	-0.5	03/04/2015 13:48:06	D:\Data\Customer\15D-02024_Blank standardisation.t3r

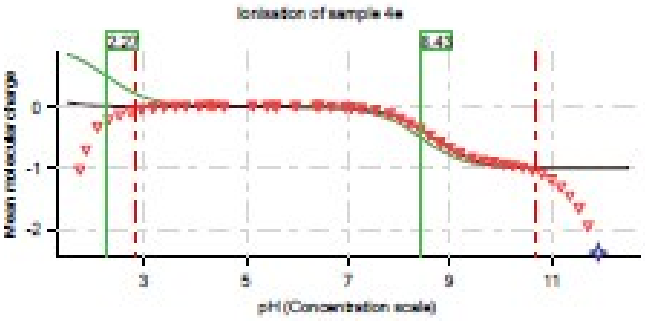
itrants

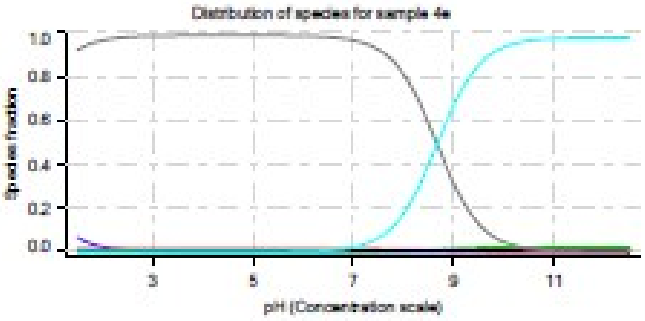
0.50 M HCl	0.997167	03/04/2015 13:48:06	D:\Data\Customer\15D-02024_Blank standardisation.t3r
0.50 M KOH	1.003080	03/04/2015 13:48:06	D:\Data\Customer\15A-27013_KHP_Base standardisation using KHP.t3r

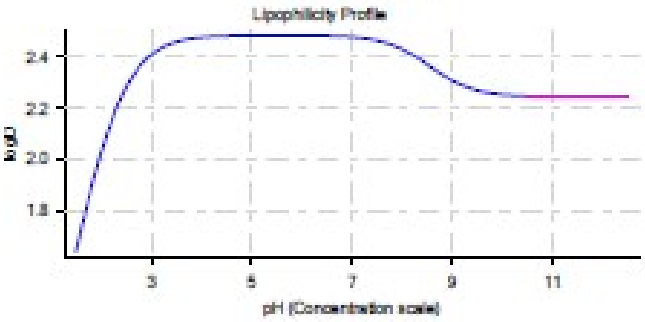
ample

4e concentration factor	0.971
Base pKa 1	2.27
Acid pKa 2	8.43
logP (XH2 +)	-3.24
logP (neutral XH)	2.48
logP (X -)	2.24

ample graphs







pH-metric

Sample name: 4e
Assay name: pH-metric medium logP
Assay ID: 15D-03021
Filename: D:\Data\Customer\15D-03021_4c_pH-metric medium logP.t3r

Experiment start time: 03/04/2015 13:48:06
Analyst: KRICT
Instrument ID: T313101

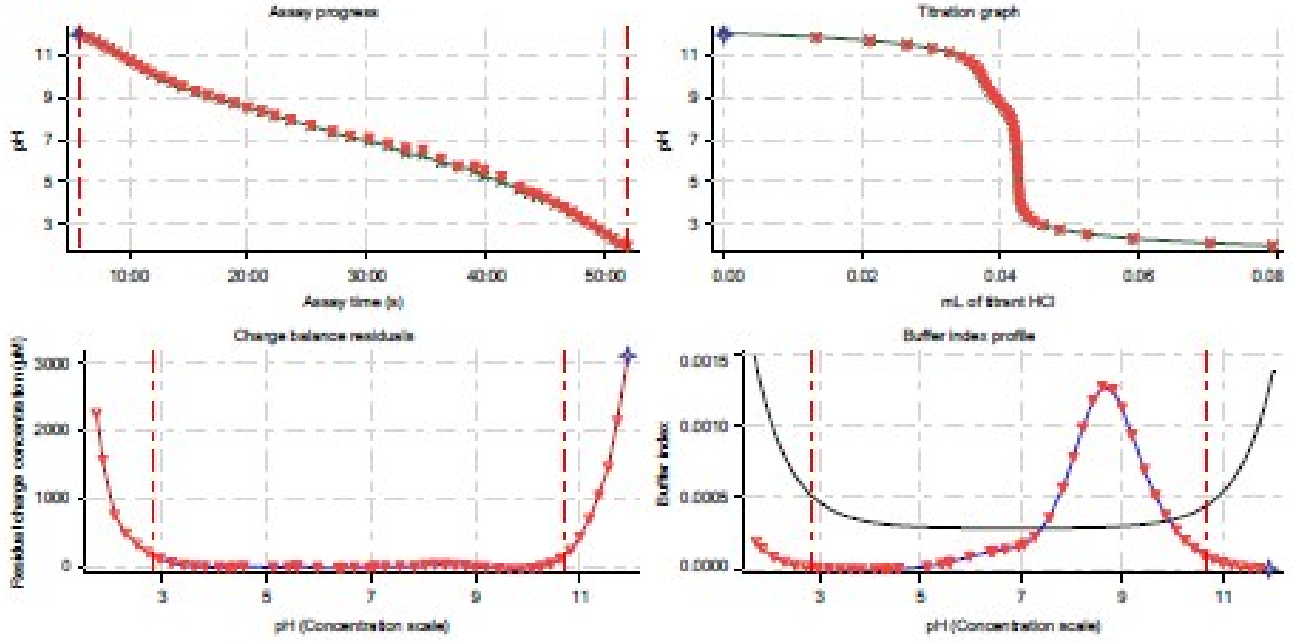
Sample logD and percent species

pH	4e logD	4e 4eH2	4e 4eH	4e 4e	4e 4eH2+	4e 4eH+	4e 4e+	Comment
1.000	1.19	18.06 %	0.97 %	0.00 %	0.00 %	80.97 %	0.00 %	
1.200	1.37	12.21 %	1.04 %	0.00 %	0.00 %	86.75 %	0.00 %	Stomach pH
2.000	2.02	2.16 %	1.16 %	0.00 %	0.00 %	96.69 %	0.00 %	
3.000	2.41	0.22 %	1.18 %	0.00 %	0.00 %	98.60 %	0.00 %	
4.000	2.47	0.02 %	1.18 %	0.00 %	0.00 %	98.79 %	0.00 %	
5.000	2.48	0.00 %	1.18 %	0.00 %	0.00 %	98.79 %	0.02 %	
6.000	2.48	0.00 %	1.18 %	0.00 %	0.00 %	98.60 %	0.21 %	
6.500	2.48	0.00 %	1.18 %	0.01 %	0.00 %	98.14 %	0.67 %	
7.000	2.47	0.00 %	1.16 %	0.04 %	0.00 %	96.71 %	2.06 %	
7.400	2.46	0.00 %	1.12 %	0.10 %	0.00 %	93.70 %	5.07 %	Blood pH
8.000	2.43	0.00 %	0.97 %	0.36 %	0.00 %	81.17 %	17.49 %	
9.000	2.31	0.00 %	0.37 %	1.39 %	0.00 %	31.14 %	67.10 %	
10.000	2.25	0.00 %	0.05 %	1.93 %	0.00 %	4.35 %	93.67 %	
11.000	2.24	0.00 %	0.01 %	2.01 %	0.00 %	0.45 %	97.53 %	
12.000	2.24	0.00 %	0.00 %	2.02 %	0.00 %	0.05 %	97.93 %	

Carbonate and acidity

Carbonate 0.173 mM
Acidity error 0.156 mM

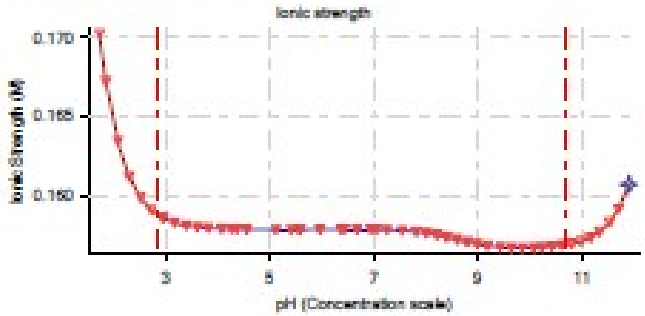
Other graphs

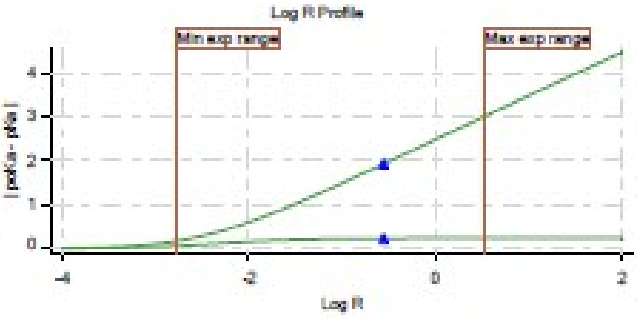


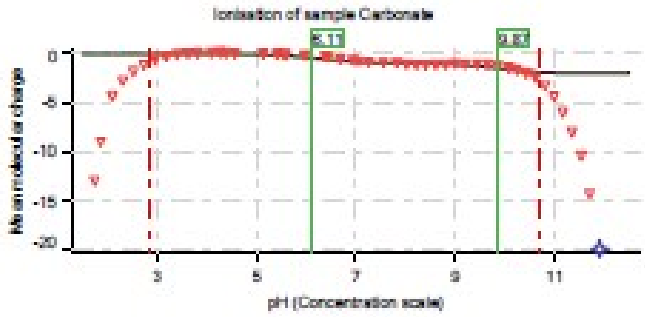
pH-metric

Sample name:	4e	Experiment start time:	03/04/2015 13:48:06
Assay name:	pH-metric medium logP	Analyst:	KRICT
Assay ID:	15D-03021	Instrument ID:	T313101
Filename:	D:\Data\Customer\15D-03021_4c_pH-metric medium logP.t3r		

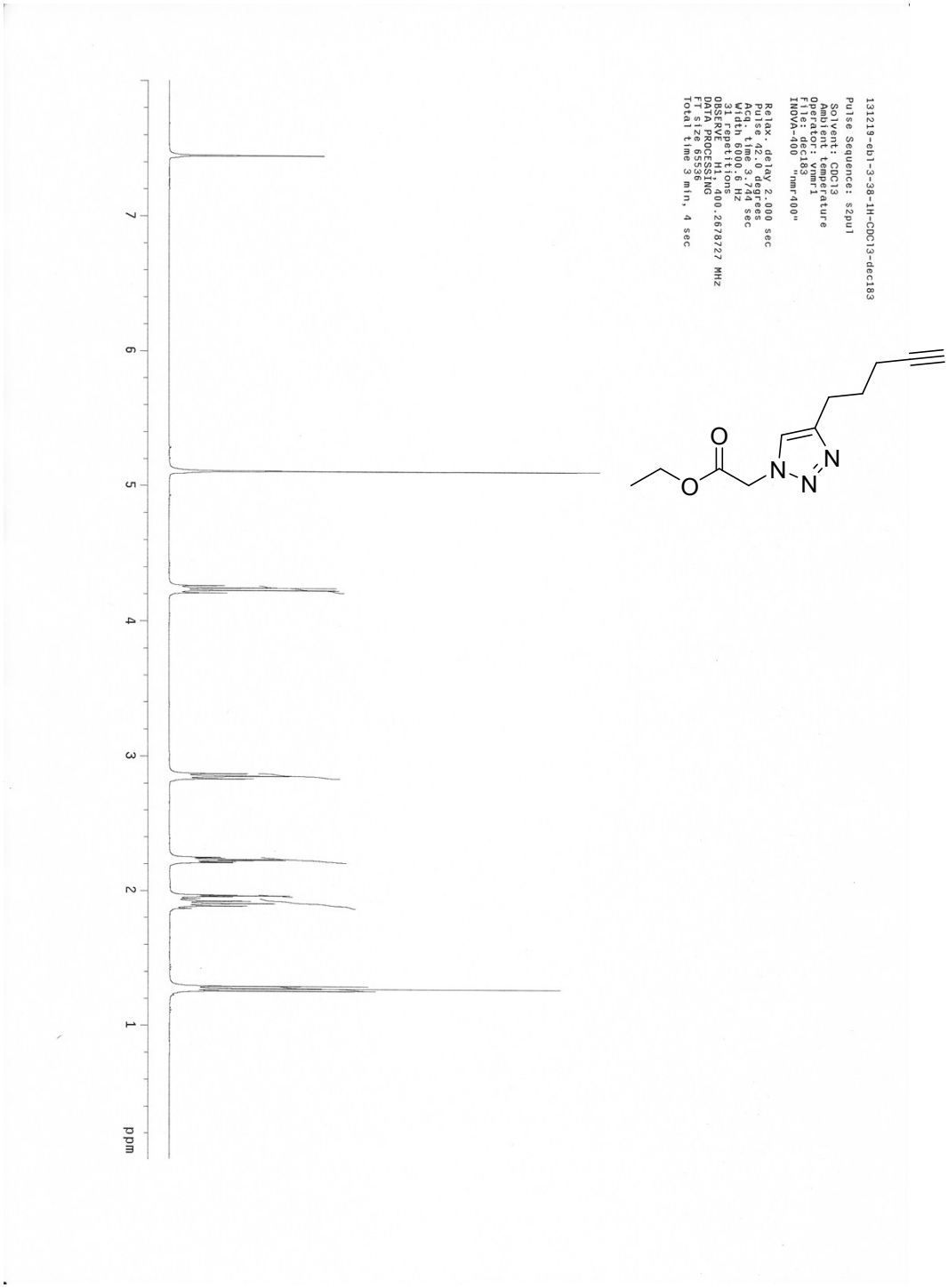
Other graphs (continued)



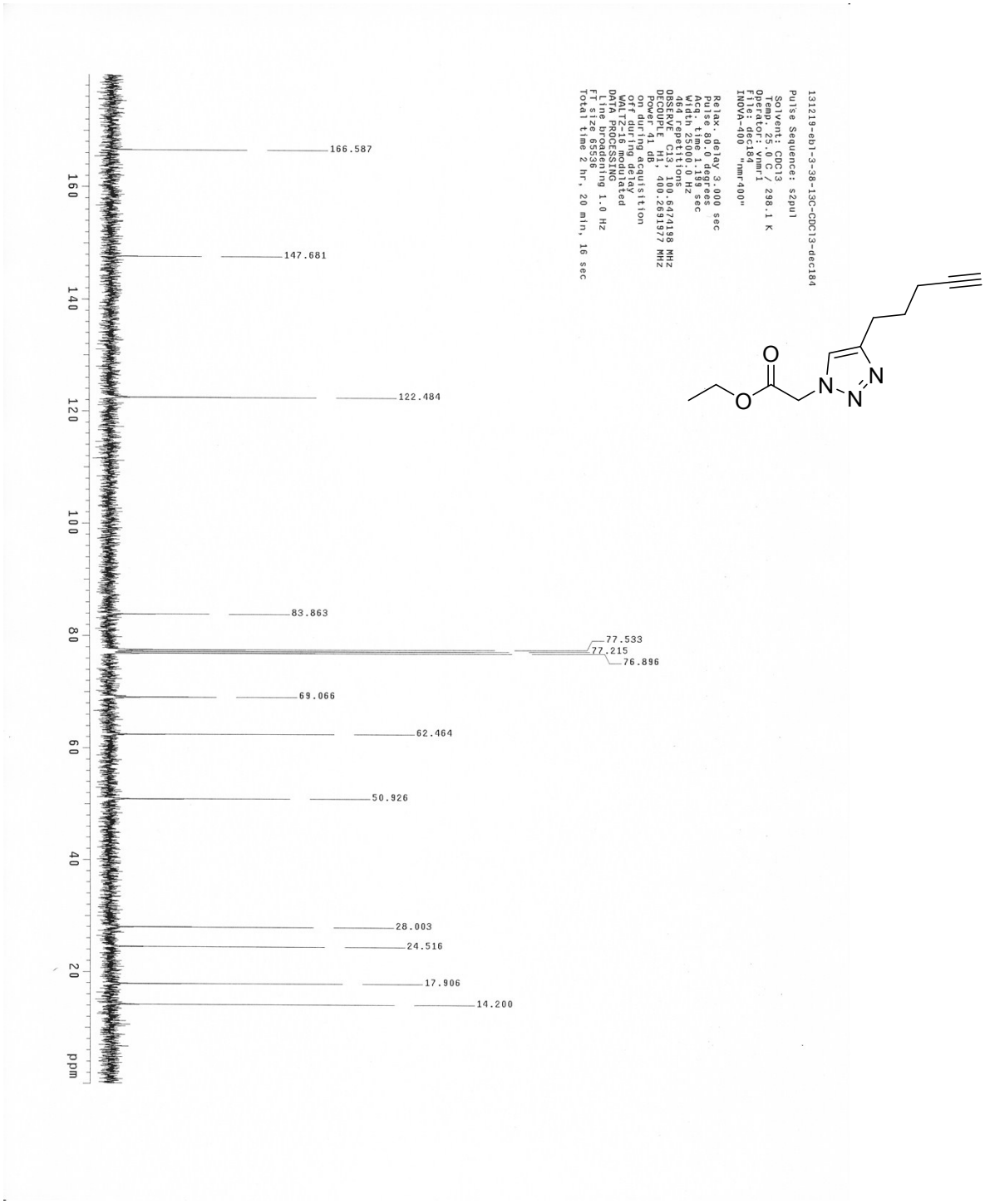




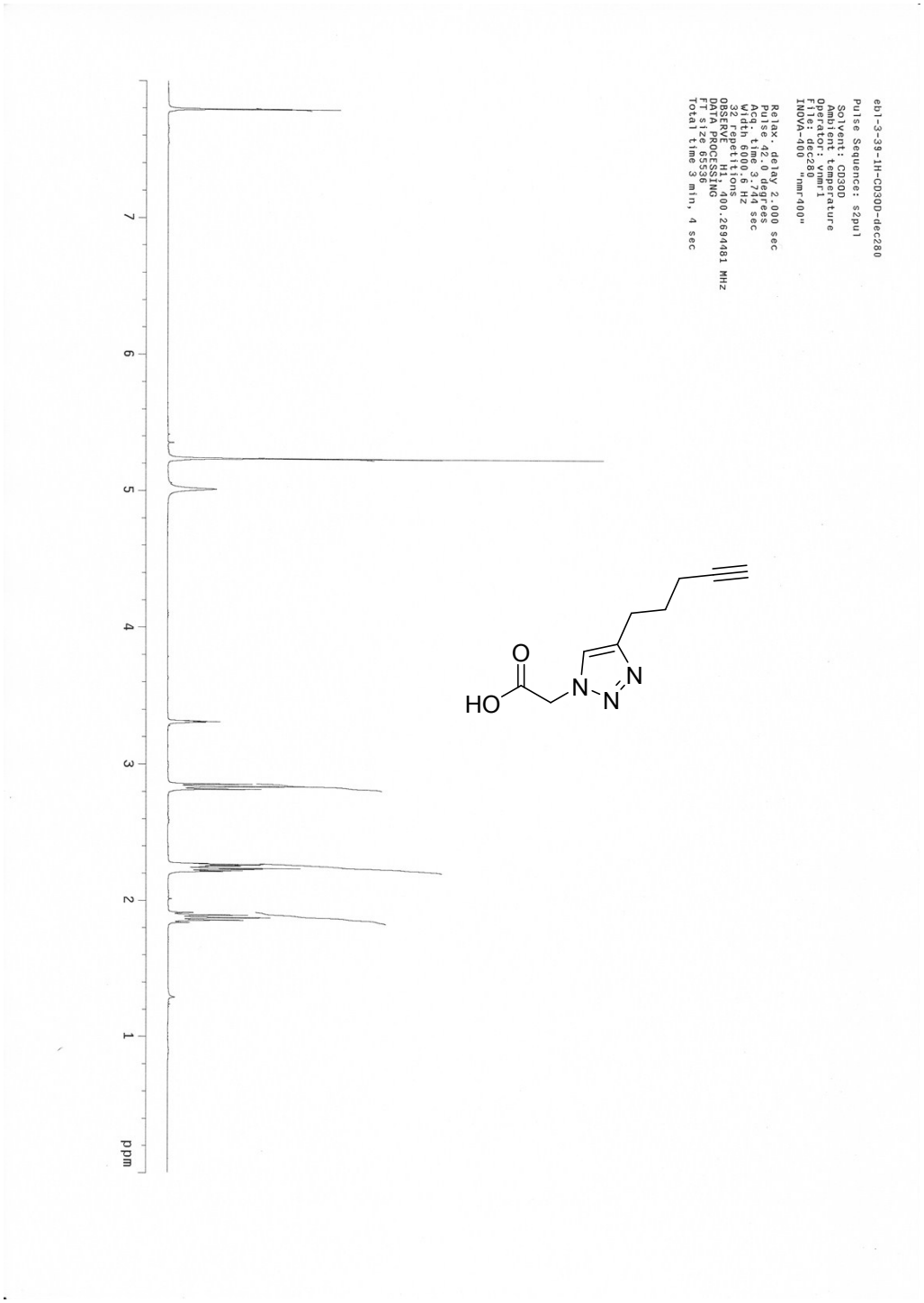
NMR Spectra



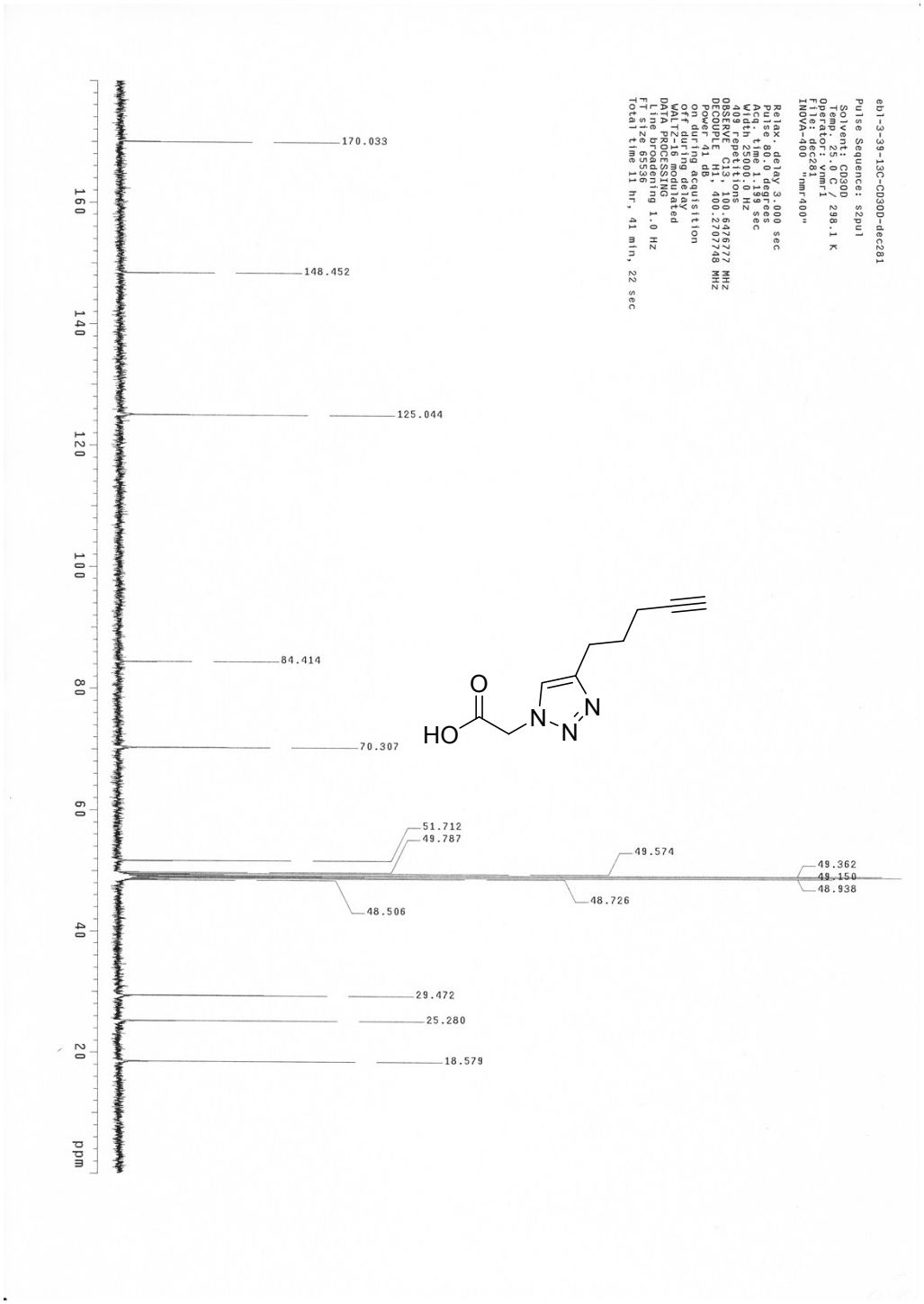
^{1}H NMR spectrum of **2** recorded in $CDCl_3$



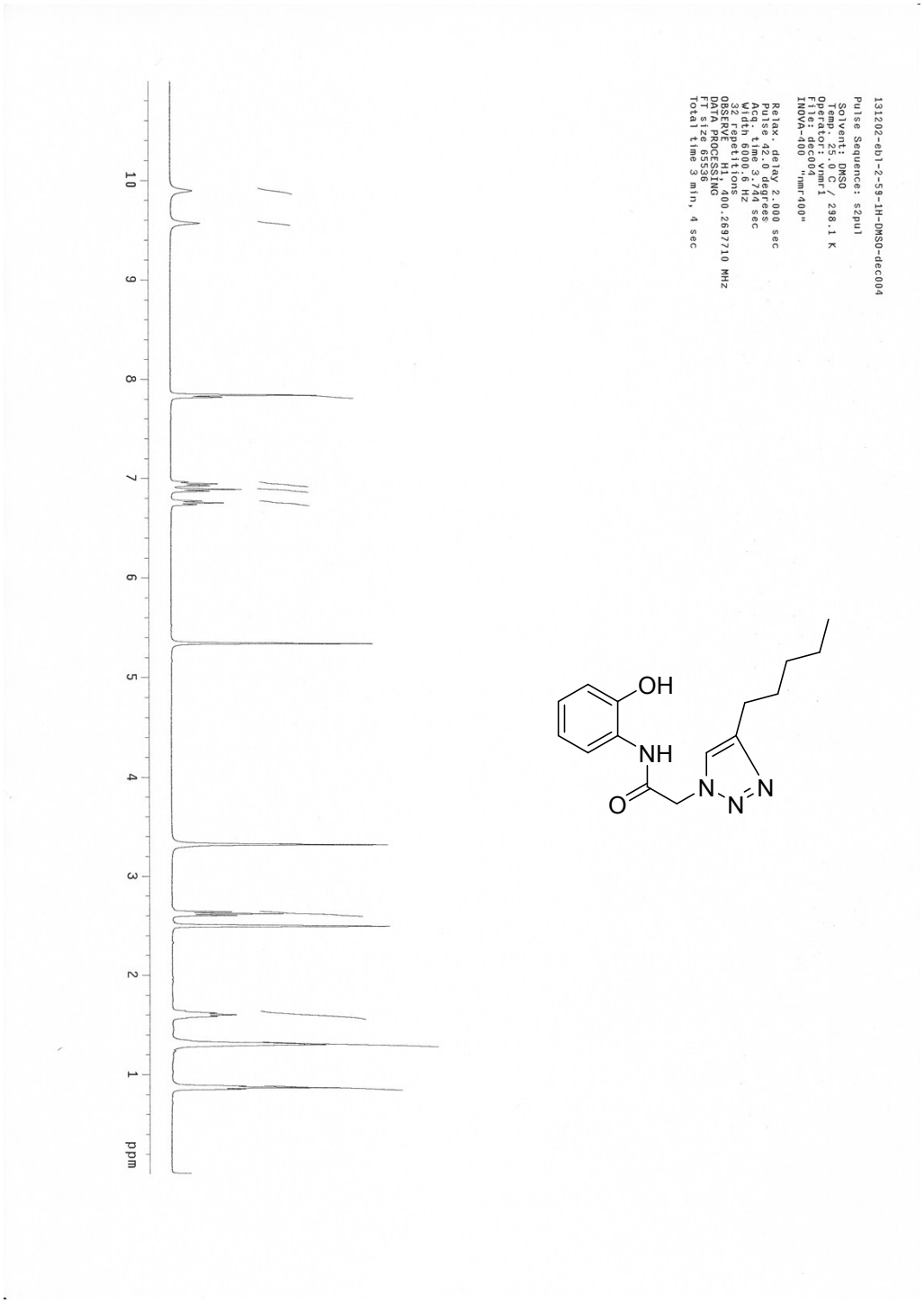
^{13}C NMR spectrum of **2** recorded in $CDCl_3$



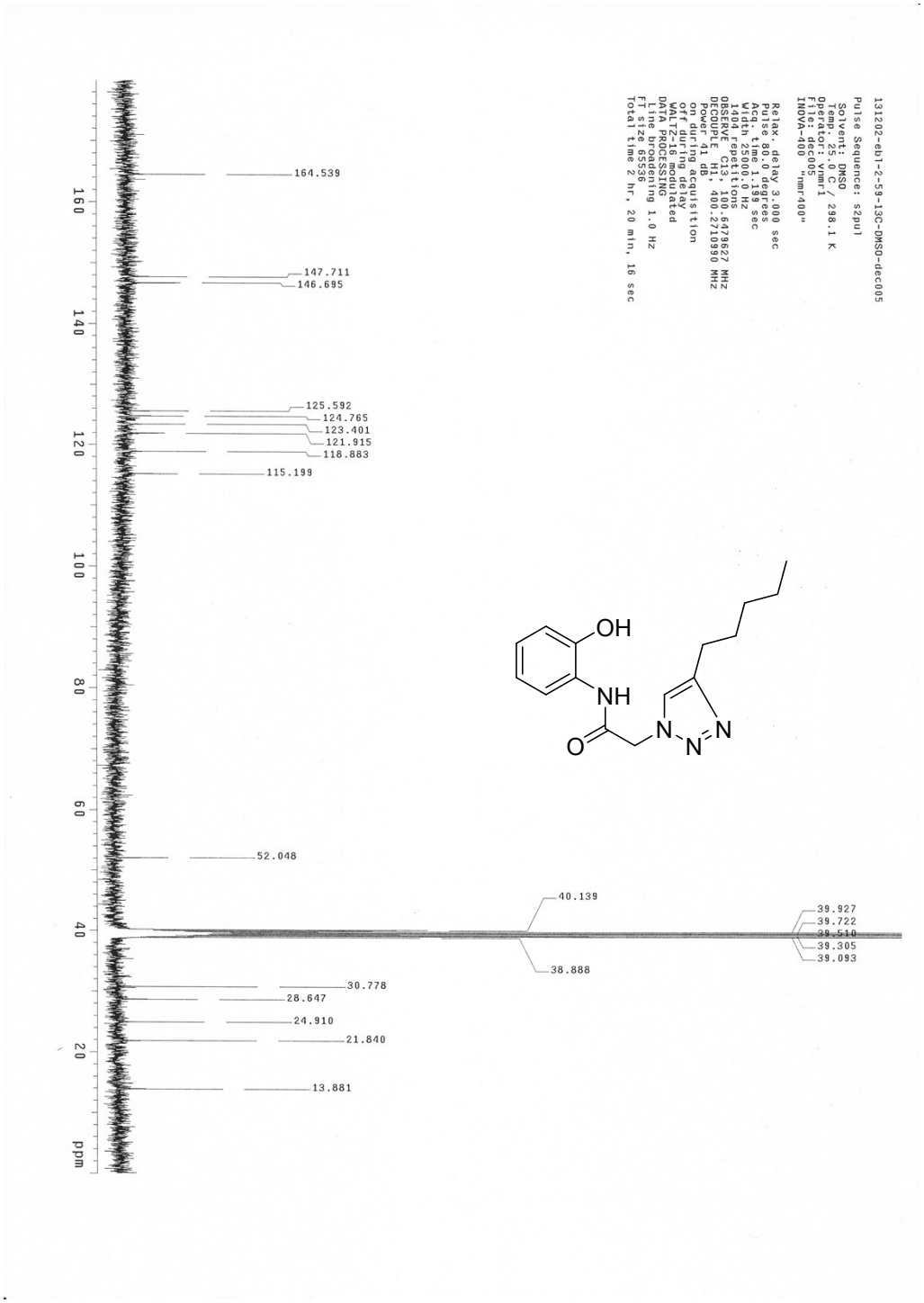
^{1}H NMR spectrum of **3** recorded in CH_3OH-d_4



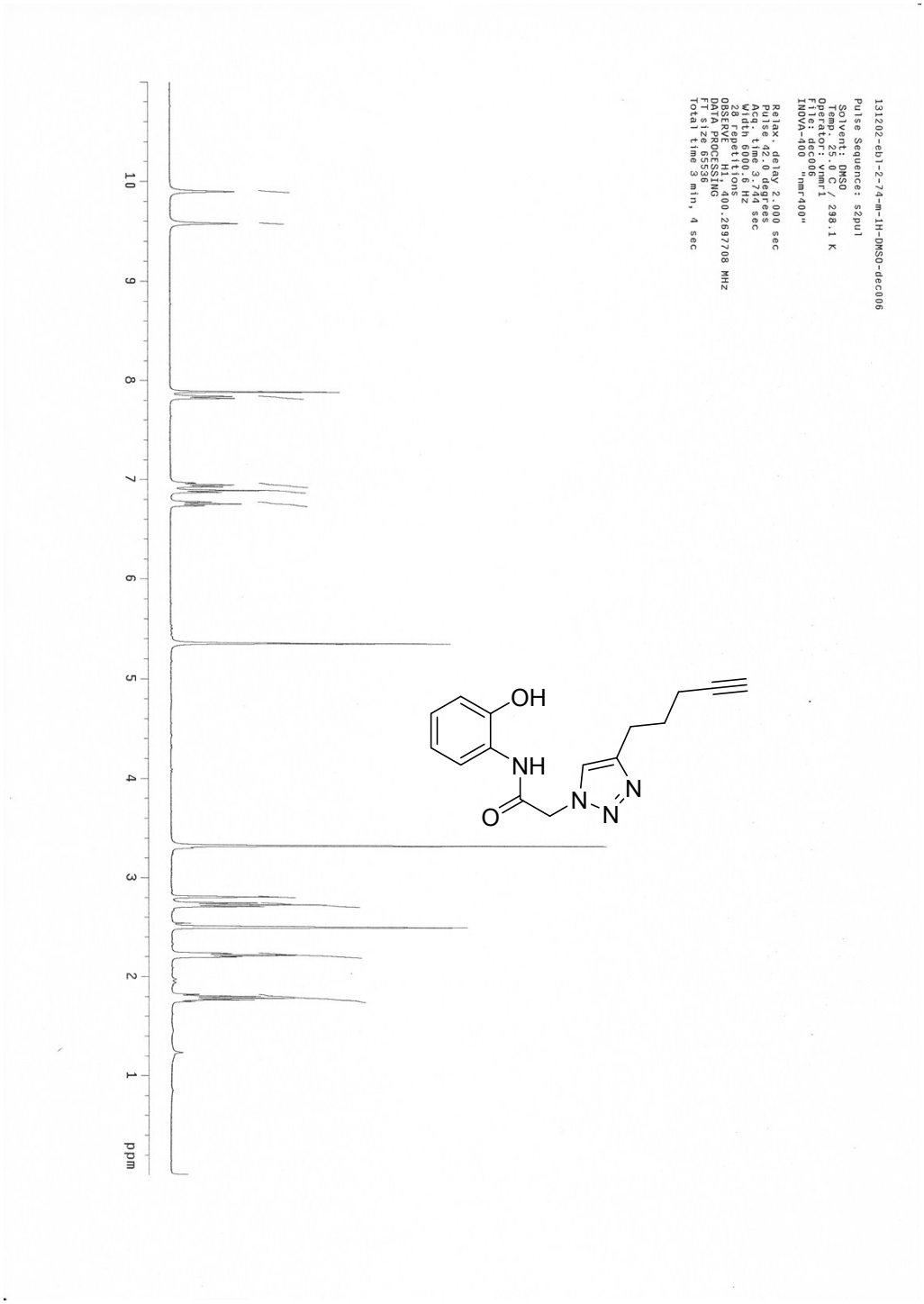
^{13}C NMR spectrum of **3** recorded in CH_3OH-d_4



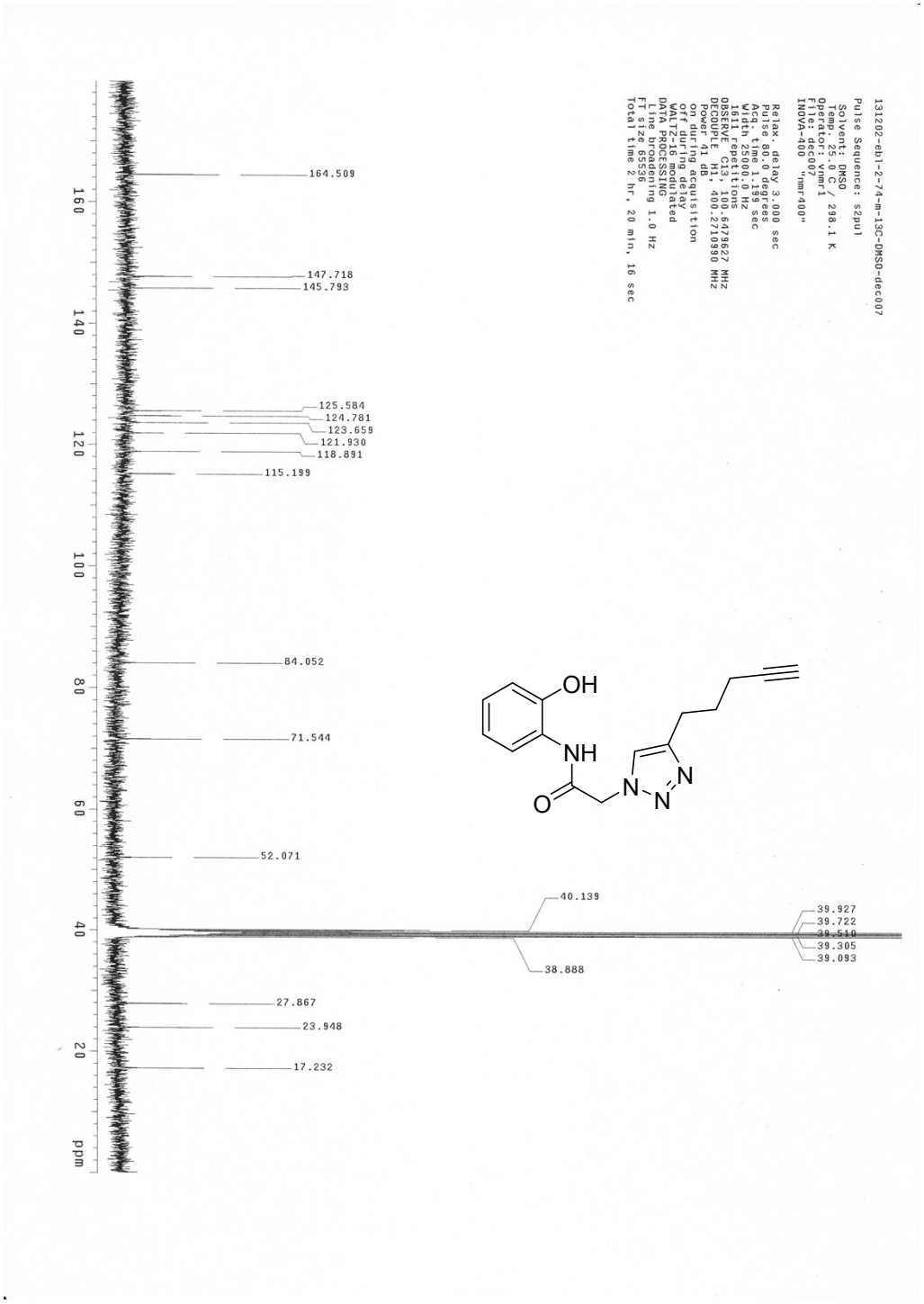
^{1}H NMR spectrum of **4a** recorded in DMSO-*d6*



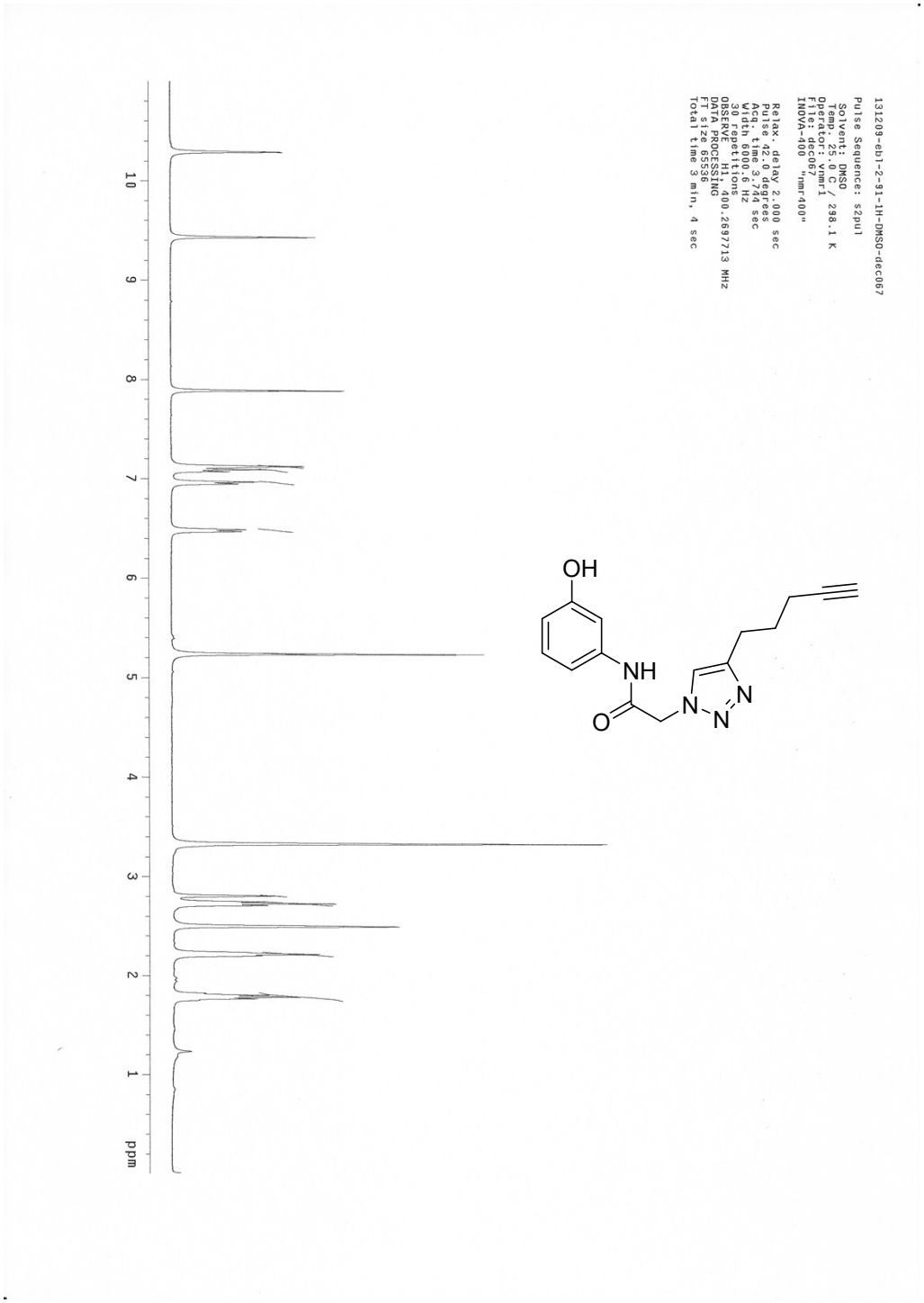
^{13}C NMR spectrum of **4a** recorded in DMSO-*d6*



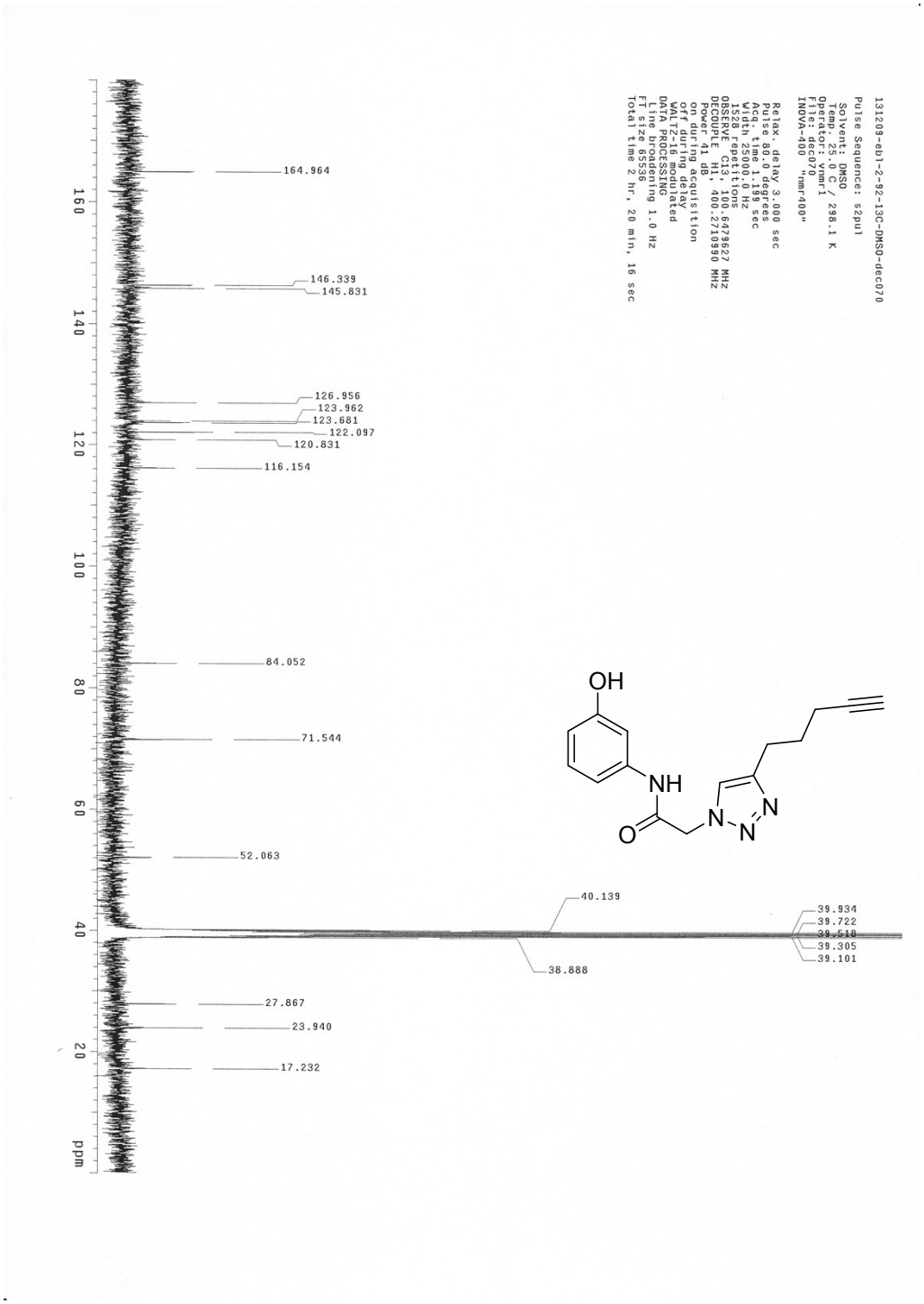
^{1}H NMR spectrum of **4b** recorded in DMSO-*d6*



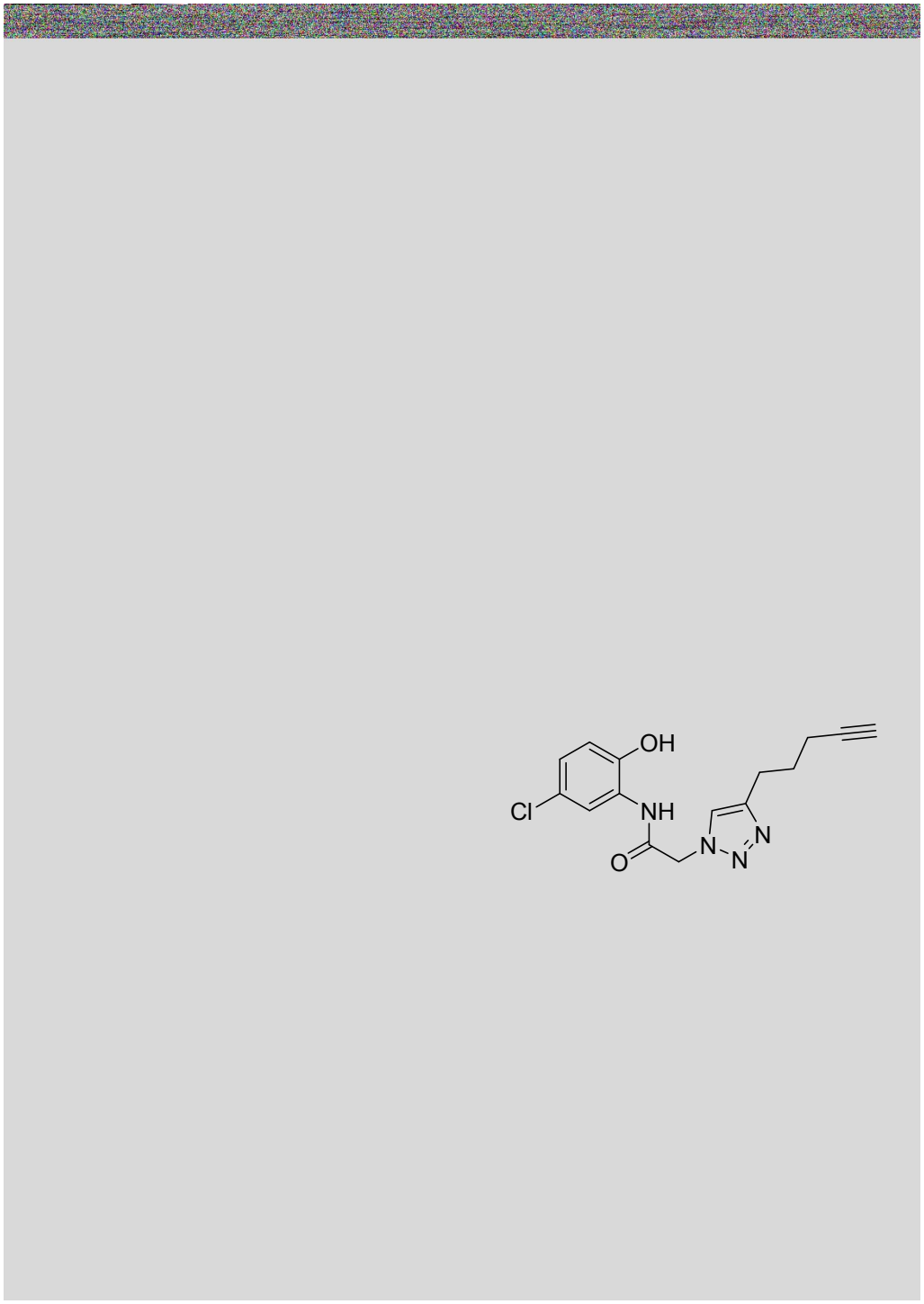
^{13}C NMR spectrum of **4b** recorded in DMSO-*d6*



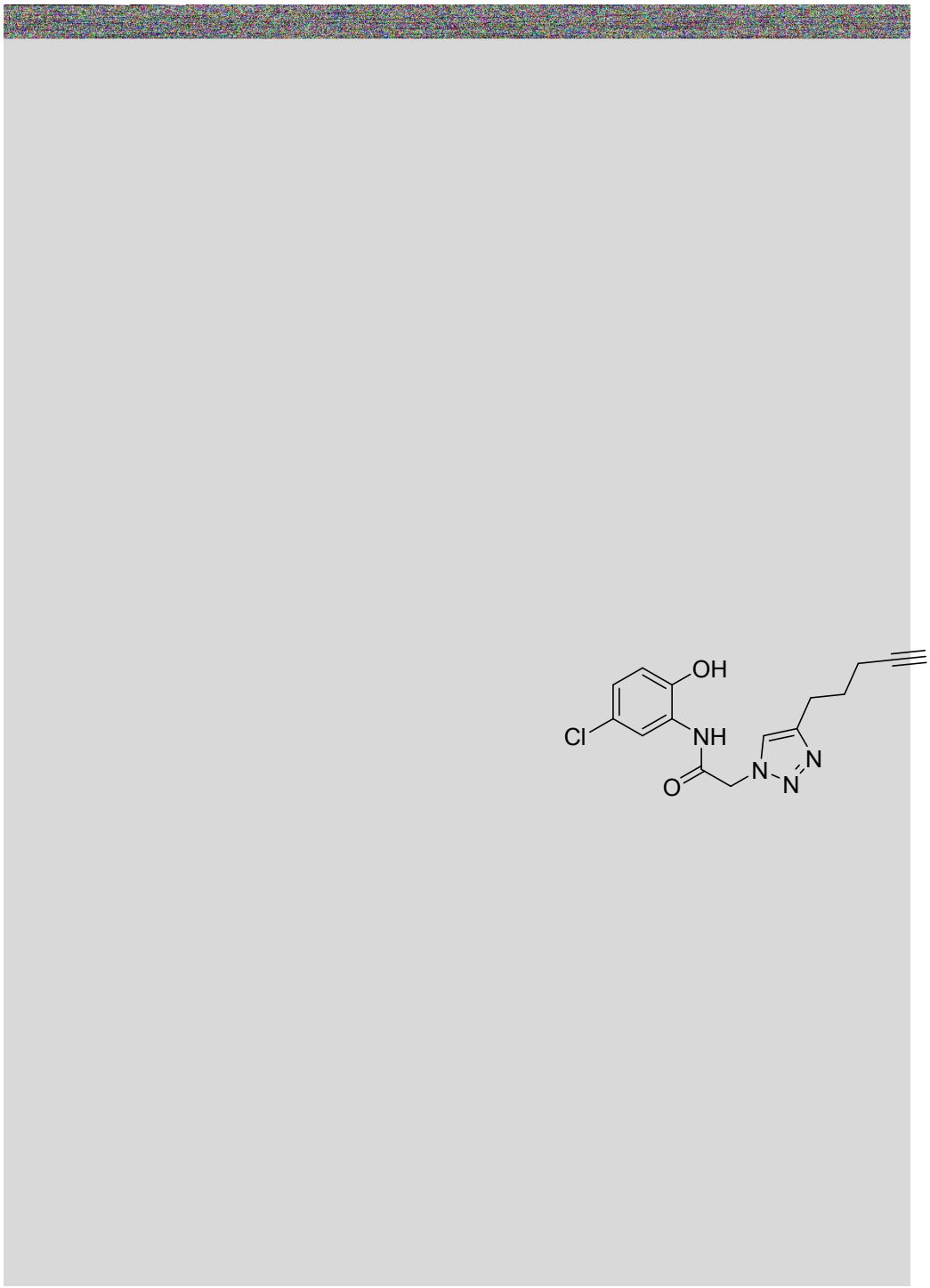
^{1}H NMR spectrum of **4c** recorded in DMSO-*d6*



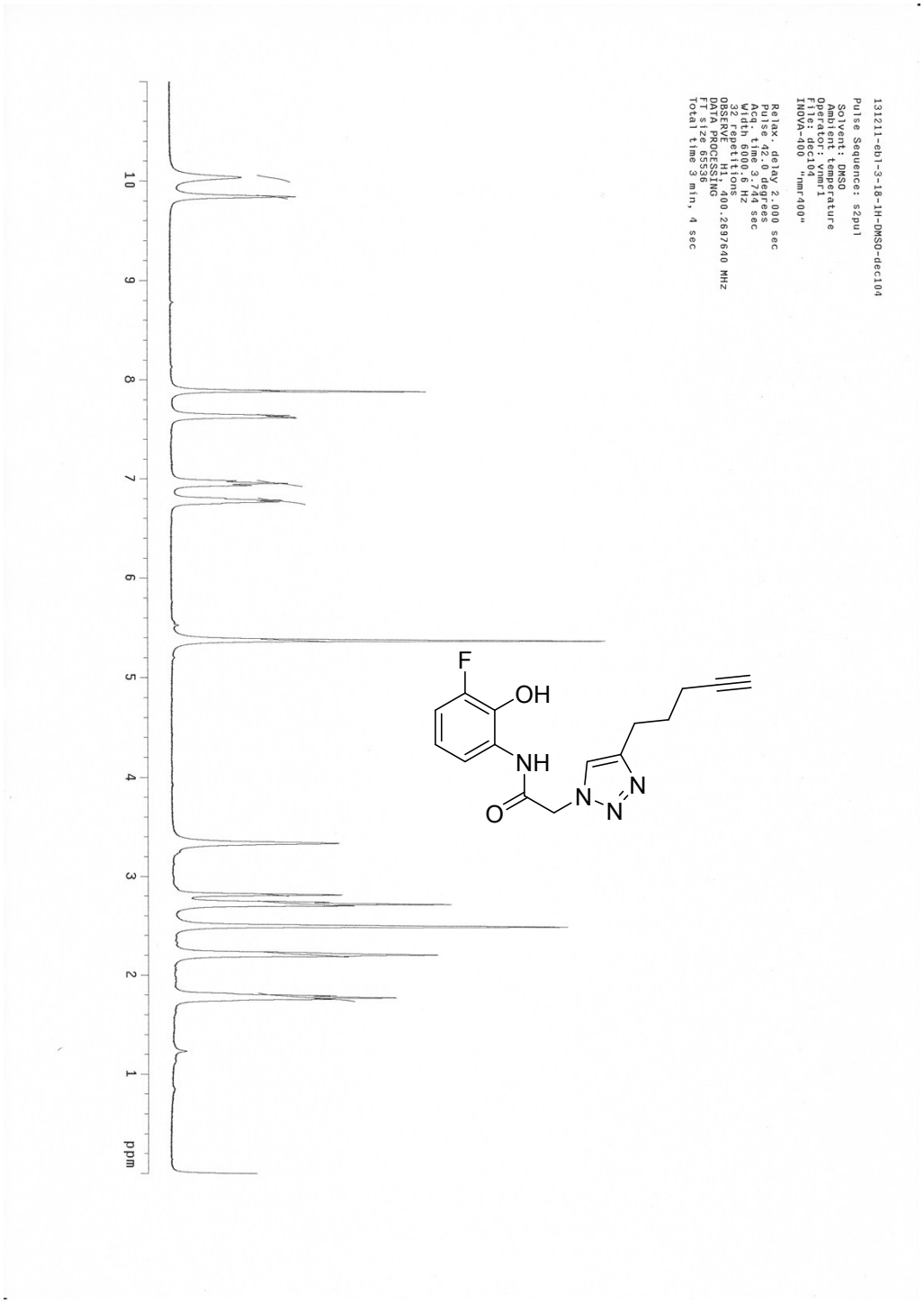
^{13}C NMR spectrum of **4c** recorded in DMSO-*d6*



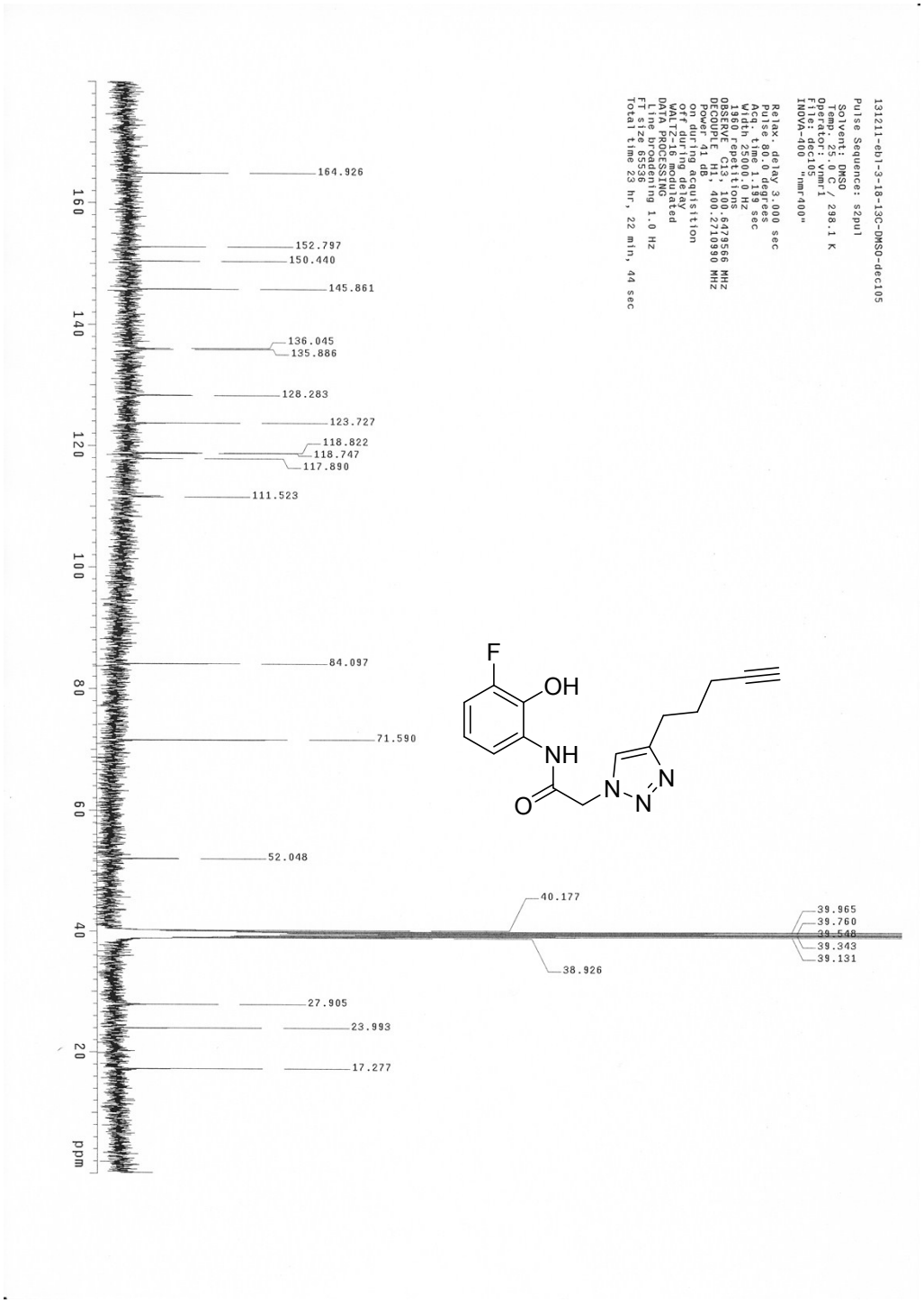
^{1}H NMR spectrum of **4d** recorded in DMSO-*d6*



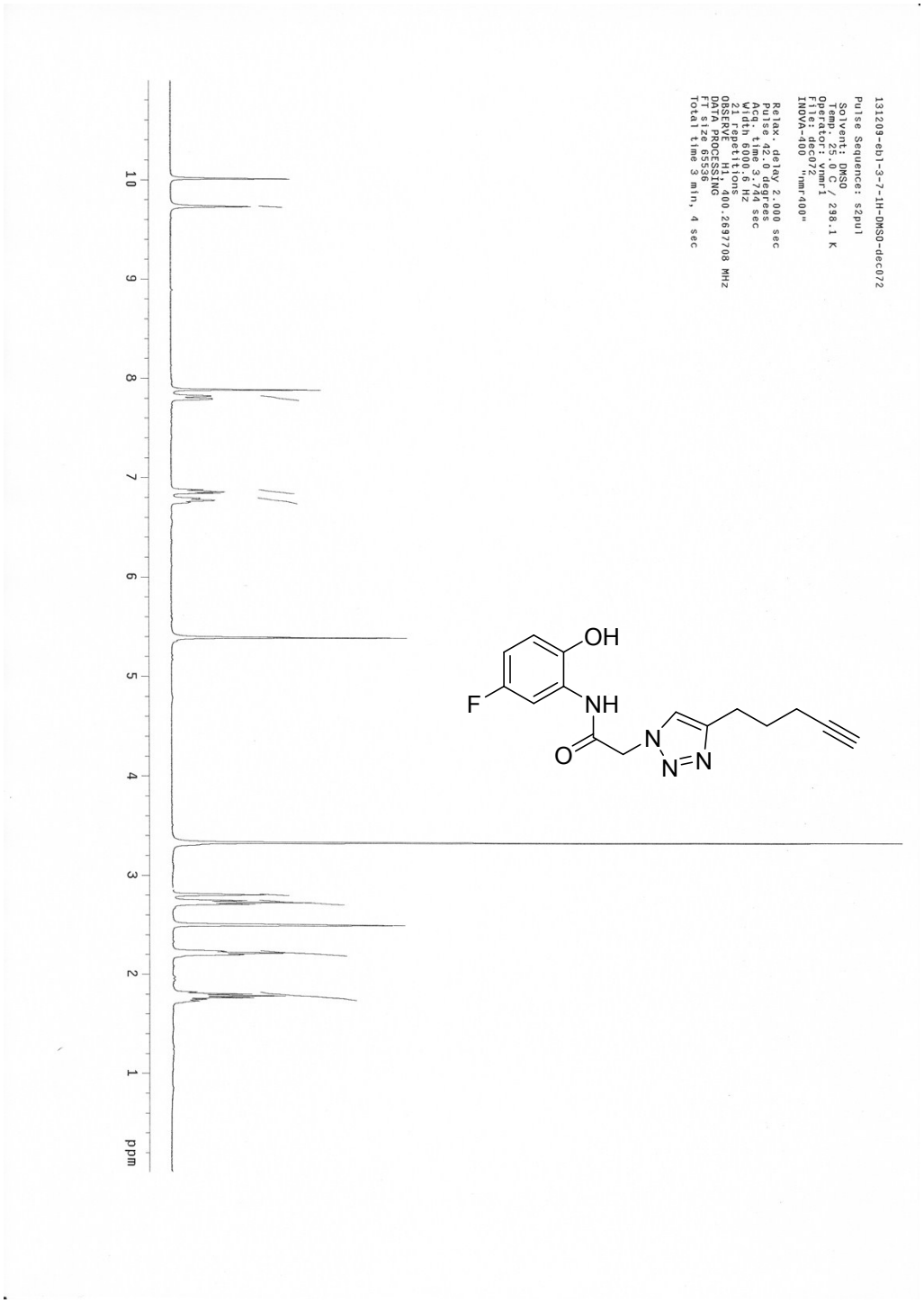
^{13}C NMR spectrum of **4d** recorded in DMSO-*d6*



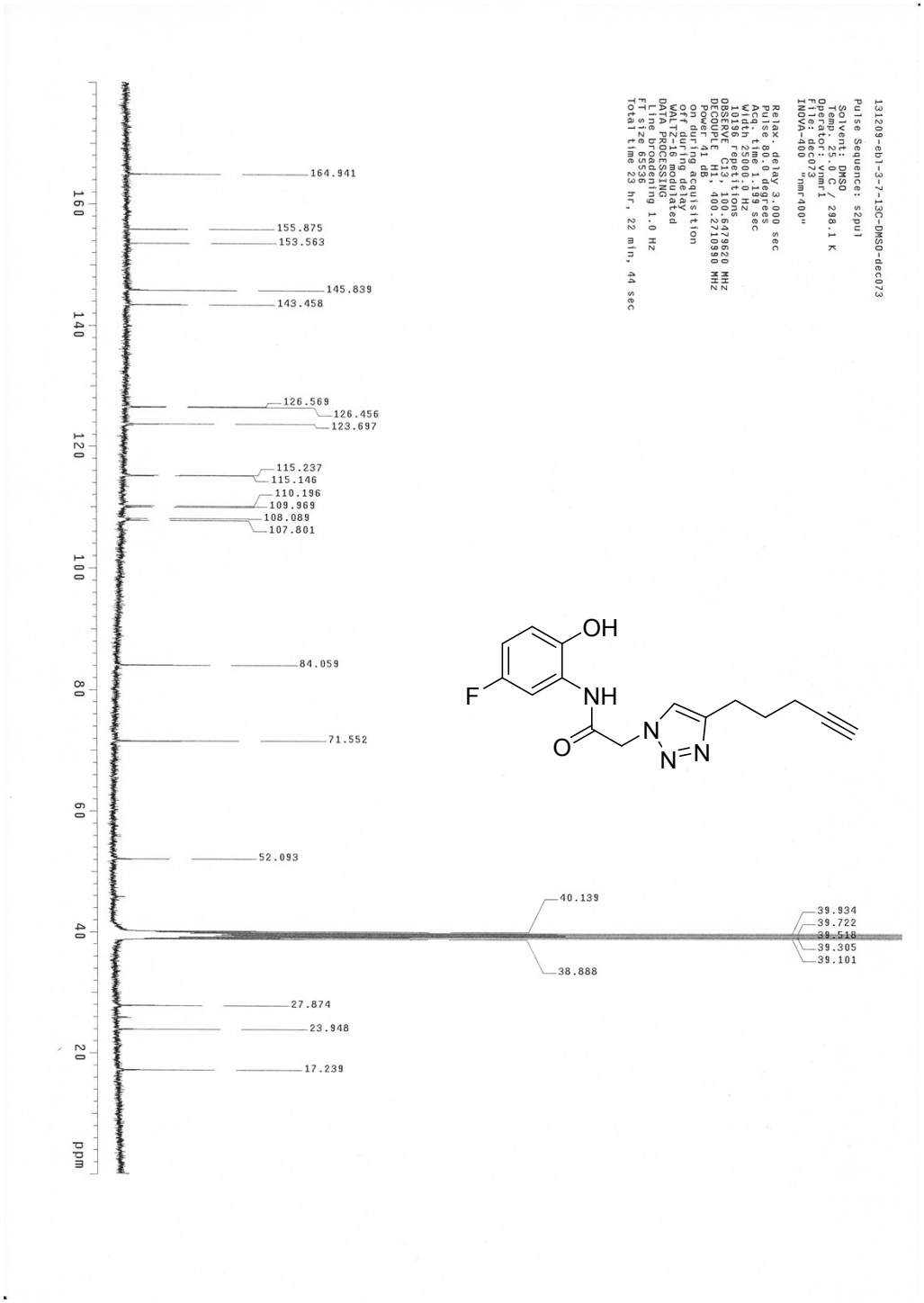
^{1}H NMR spectrum of **4e** recorded in DMSO-*d6*



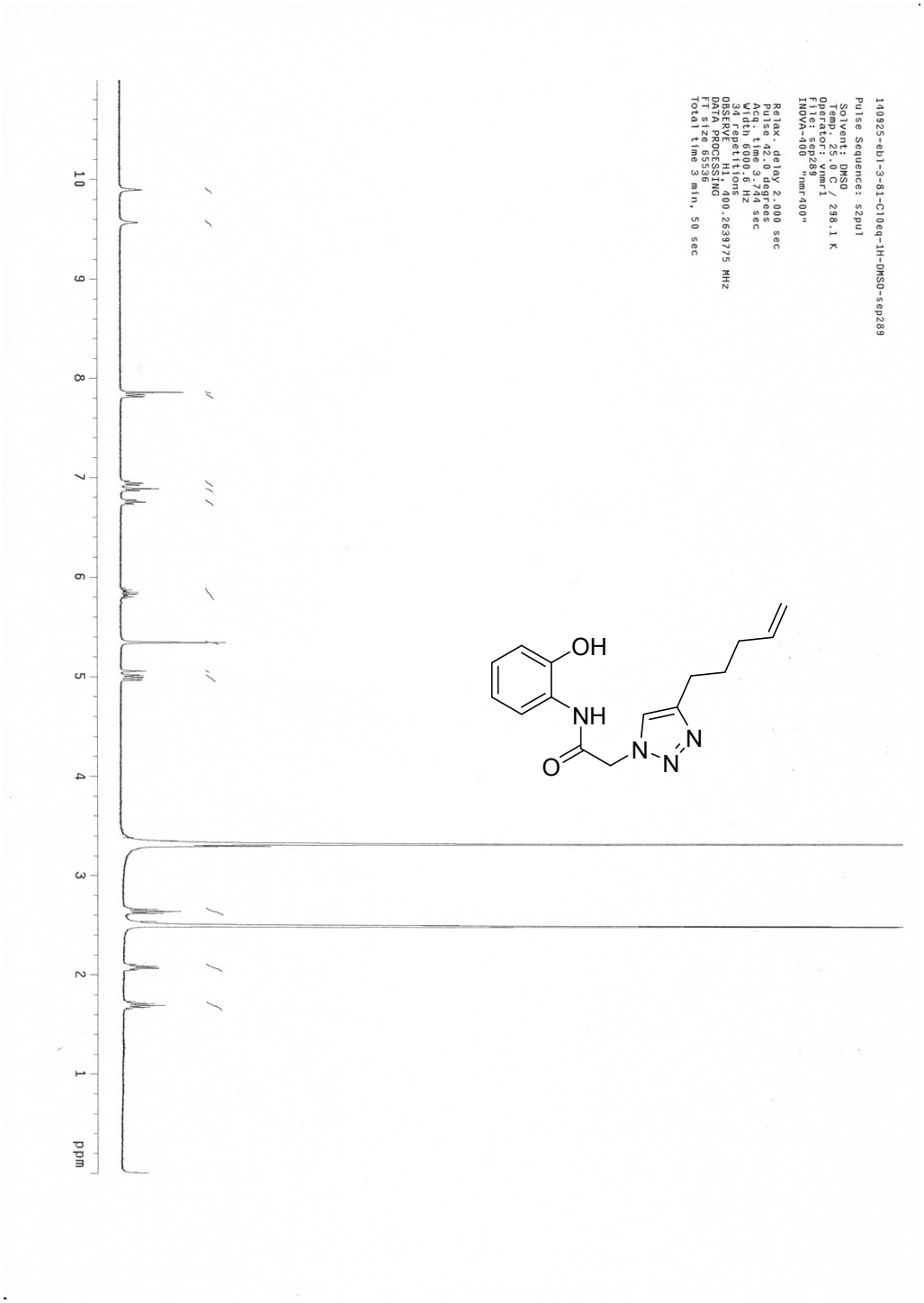
^{13}C NMR spectrum of **4e** recorded in DMSO-*d6*



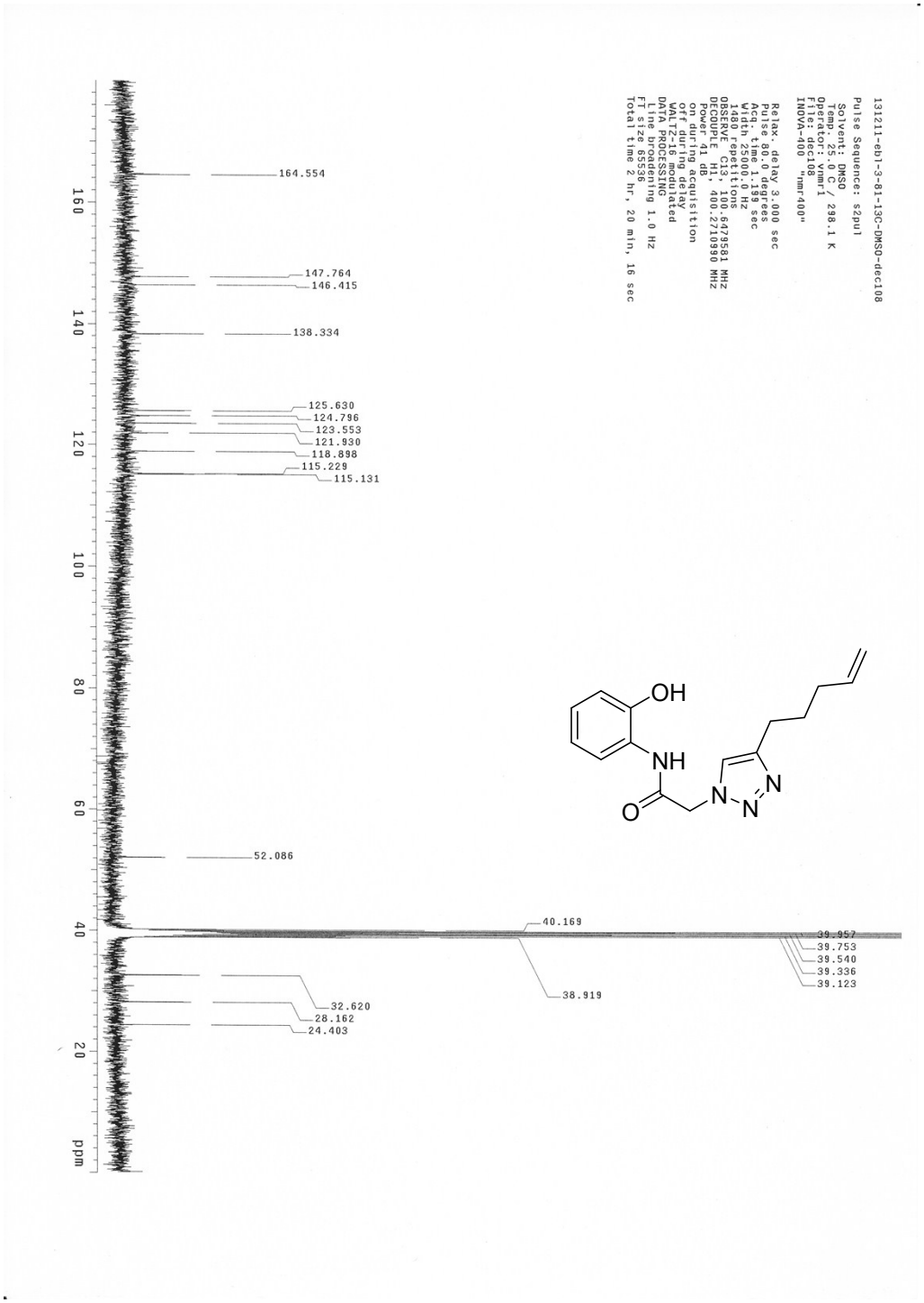
^{1}H NMR spectrum of **4f** recorded in DMSO-*d6*



^{13}C NMR spectrum of **4f** recorded in DMSO-*d6*



^{1}H NMR spectrum of **4g** recorded in DMSO-*d6*



^{13}C NMR spectrum of **4g** recorded in DMSO-*d6*