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A neutral halogen bonding macrocyclic anion receptor based on a pseudocyclopeptide with three 5-iodo-1,2,3-triazole subunits

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CONTENT

Synthetic Procedures

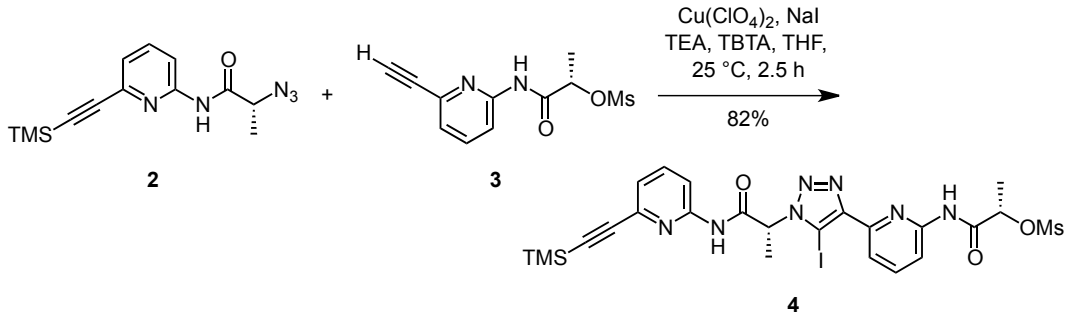
General details. Analyses were carried out as follows: melting points, Müller SPM-X 300; NMR, Bruker DPX 400 (peak assignments were confirmed by using H,H-COSY and HMQC spectra, spectra were referenced to the residual solvent signals (DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.5 ppm);[1] elemental analysis, Elementar vario Micro cube; optical rotation, Perkin Elmer 241 MC digital polarimeter (*d* = 10 cm); ITC, Microcal VP-ITC.

The following abbreviations are used: TBA, tetrabutylammonium; TMA, tetramethylammonium Epa, 2-amino-6-ethynyl-2-pyridine; Lac, CH_3CHCO; ITri, 5-iodo-1,2,3-triazole; TBTA, tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amin; TBAF, TBA fluoride; TEA, triethylamine.

The syntheses of building blocks **2** and **3** are described elsewhere.[2] TBA sulfate, TBA dihydrogenphosphate, TBA nitrate, TBA chloride, TBA bromide, TBA iodide, and TMA chloride are commercially available and were used after confirming purity by elemental analysis.

LC-ESI-MS measurements. These measurements were performed by using an Aglient 1100 HPLC coupled with an API 2000 MS. For HPLC, a gradient from 30 to 100 vol% acetonitrile in water over 30 minutes with a flow rate of 1 mL/min was used. The parameter settings for ESI were as follows: curtain gas, 35 psi; ion spray voltage, 5500 V; temperature, 450 °C; nebulizer gas, 50 psi; heater gas, 60 psi; declustering potential, 40 V; focusing potential, 200 V; entrance potential, 10 V. The measurements were performed in full scan mode with a mass range from 500 to 1300 Da.

TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs 4.

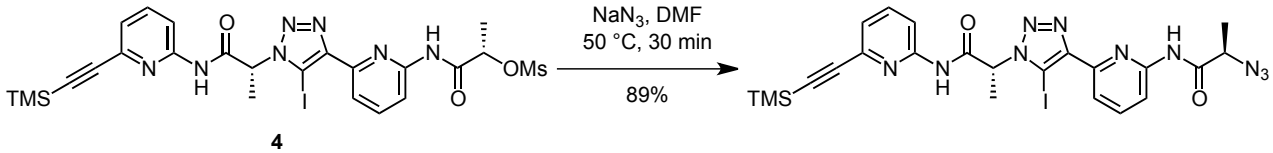


2 **3** **4**

Thoroughly dried $Cu(ClO_4)_2 \cdot 6H_2O$ (3.0 g, 8.2 mmol), TBTA (220 mg, 0.41 mmol), and NaI (2.6 g, 17.2 mmol) were suspended in dry THF (30 mL), followed by the addition of TEA (0.57 mL, 4.1 mmol). To this suspension, H-Epa-(*S*)-Lac-OMs **3** (1.1 g, 4.1 mmol) was added and the reaction

mixture was stirred for 20 min at 25 °C. A solution of TMS-Epa-(*R*)-Lac-N_3 **2** (1.4 g, 4.9 mmol) in dry THF (5 mL) was added and the resulting reaction mixture was stirred for 2 h at 25 °C. After adding water (100 mL) and a 1:1 (*v/v*) mixture of 25% aqueous NH_3 and 25% aqueous NH_4Cl (10 mL), the mixture was extracted twice with ethyl acetate (2×100 mL). The combined organic layers were washed with water three times (3×50 mL) and dried over $MgSO_4$. Pure product was obtained by column chromatography with hexane/ethyl acetate, 3:2 (*v/v*) as the eluent. Yield: 2.3 g (3.4 mmol, 82%); m.p. 105-107 °C; $[\alpha]_D^{25}$ = -41.94 (*c* = 0.1, acetone); ^{1}H NMR (400 MHz, 25 °C, DMSO-d_6) δ = 11.51 (s, 1H, NH), 10.64 (s, 1H, NH), 8.08 (d, 1H, ^3J(H, H) = 8.3 Hz, EpaH(3)), 8.02 (d, 1H, ^3J(H, H) = 8.4 Hz, EpaH(3)), 7.96 (t, 1H, ^3J(H, H) = 8.0 Hz, EpaH(4)), 7.83 (t, 1H, ^3J(H, H) = 8.0 Hz, EpaH(4)), 7.71 (d, 1H, ^3J(H, H) = 7.5 Hz, EpaH(5)); 7.31 (dd, 1H, ^3J(H, H) = 7.5 Hz, ^4J(H, H) = 0.9 Hz, EpaH(5)), 5.58 (q, 1H, ^3J(H, H) = 7.0 Hz, LacCH), 5.40 (q, 1H, ^3J(H, H) = 6.6 Hz, LacCH), 3.26 (s, 3H, $MsCH_3$), 1.97 (d, 3H, ^3J(H, H) = 7.0 Hz, $LacCH_3$), 1.55 (d, 3H, ^3J(H, H) = 6.7 Hz, $LacCH_3$), 0.25 (s, 9H, $TMSCH_3$) ppm; ^{13}C NMR (100.6 MHz, 25 °C, DMSO-d_6) δ = 168.2 (CO), 168.1 (CO), 151.7 (EpaC(2)), 150.7 (EpaC(2)), 148.4 (EpaC(6)), 147.7 (ITriC(4)), 140.1 (EpaC(6)), 139.4 (EpaC(4)), 139.3 (EpaC(4)), 123.0 (EpaC(5)), 118.3 (EpaC(5)), 113.9 (EpaC(3)), 113.3 (EpaC(3)), 103.5 (Si-C≡C), 94.1 (Si-C≡C), 84.4 (ITriC(5)); 75.2 (LacC), 60.3 (LacC), 38.2 ($MsCH_3$), 18.8 ($LacCH_3$), 17.1 ($LacCH_3$), -0.4 ($TMSCH_3$) ppm; MS (ESI) *m/z* (%): 586.0 (37) $[M–CH_3SO_3H+H]^+$, 682.0 (4) $[M+H]^+$, 704.0 (100) $[M+Na]^+$, 720.0 (8) $[M+K]^+$; elemental analysis calcd (%) for $C_{24}H_{28}IN_7O_5SSi$: C 42.29, N 14.39, H 4.14, S 4.70 found C 42.73, N 14.14, H 4.52, S 4.74.

TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*R*)-Lac-N_3.



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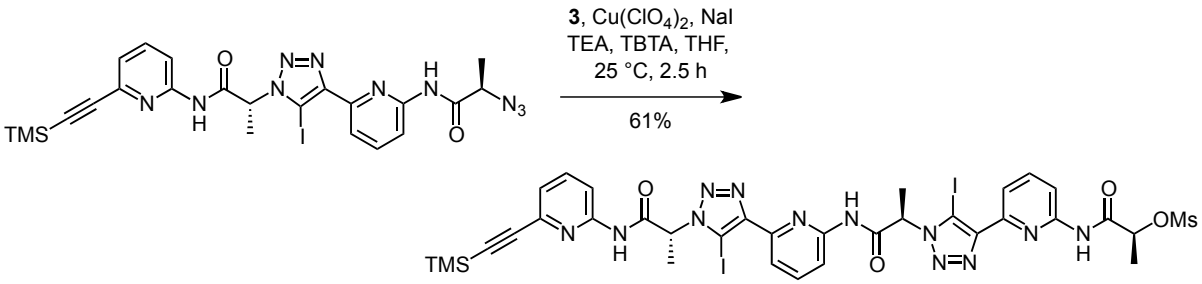
TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs **4** (2.2 g, 3.2 mmol) and sodium azide (416 mg, 6.4 mmol) were dissolved in DMF (25 mL). The mixture was stirred at 50 °C for 30 min. After adding water (100 mL), the mixture was extracted with three times with ethyl acetate (3×100 mL). The combined organic layers were dried over $MgSO_4$. Pure product was obtained by column chromatography with hexane/ethyl acetate, 2:1 (*v/v*) as the eluent. Yield: 1.8 g (2.8 mmol, 89%); MS

(ESI) *m/z* (%): 525.2 (12) $[M–I+H+Na]^+$, 629.0 (18) $[M+H]^+$, 651.0 (100) $[M+Na]^+$.

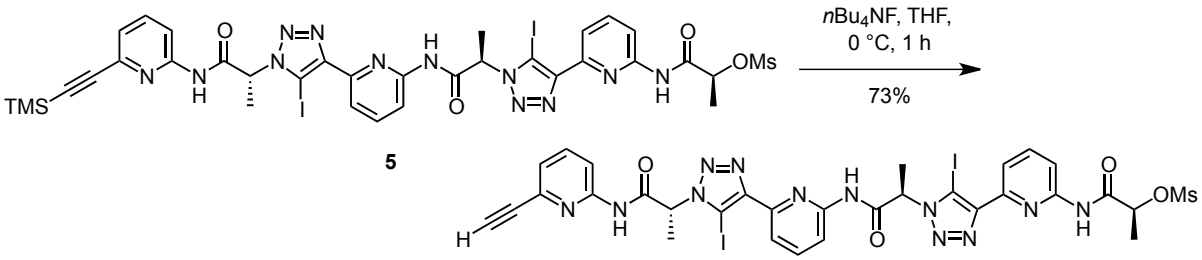
TMS-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs 5.



5

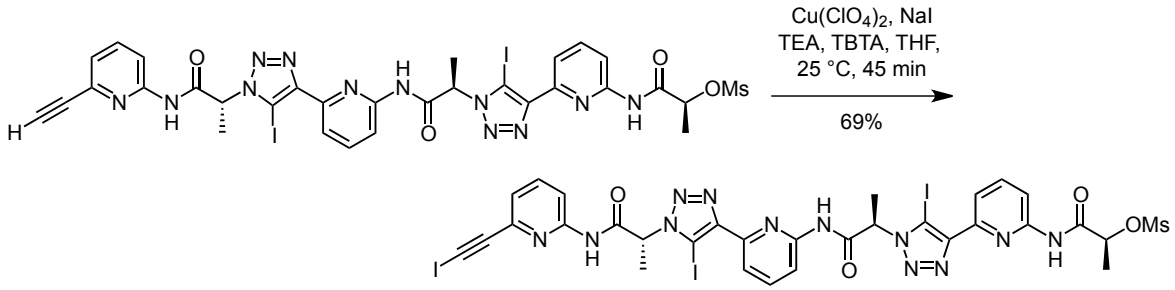
Thoroughly dried $Cu(ClO_4)_2 \cdot 6H_2O$ (889 mg, 2.4 mmol), TBTA (64 mg, 0.12 mmol), and NaI (760 mg, 5.0 mmol) were suspended in dry THF (15 mL), followed by the addition of TEA (167 µL, 1.20 mmol). To this suspension, H-Epa-(*S*)-Lac-OMs **3** (322 mg, 1.20 mmol) was added and the reaction mixture was stirred for 20 min at 25 °C. A solution of H-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs **4** (534 mg, 0.85 mmol) in dry THF (10 mL) was added and the resulting reaction mixture was stirred for 2 h at 25 °C. After adding water (100 mL) and a 1:1 (*v/v*) mixture of 25% aqueous NH_3 and 25% aqueous NH_4Cl (10 mL), the mixture was extracted twice with ethyl acetate (2×100 mL). The combined organic layers were washed with water three times (3×50 mL) and dried over $MgSO_4$. Pure product was precipitated from hexane/ethyl acetate, 1:1 (*v/v*) as a white powder. Yield: 530 mg (0.52 mmol, 61%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.51 (s, 1H, NH), 11.19 (s, 1H, NH), 10.63 (s, 1H, NH), 7.93-8.09 (m, 5H, EpaH(5) + EpaH(3)), 7.83 (t, 1H, ^3J(H, H) = 8.0 Hz, EpaH(4)), 7.70 (t, 2H, ^3J(H, H) = 7.9 Hz, EpaH(4)), 7.31 (dd, 1H, ^3J(H, H) = 7.5 Hz , ^4J(H, H) = 0.7 Hz, EpaH(5)), 5.73 (bs, 1H, LacCH), 5.59 (q, 1H, ^3J(H, H) = 6.9 Hz, LacCH), 5.38 (q, 1H, ^3J(H, H) = 6.6 Hz, LacCH), 3.25 (s, 3H, $MsCH_3$), 2.00 (d, 3H, ^3J(H, H) = 7.1 Hz, $LacCH_3$), 1.98 (d, 3H, ^3J(H, H) = 7.0 Hz, $LacCH_3$), 1.54 (d, 3H, ^3J(H, H) = 6.7 Hz, $LacCH_3$), 0.25 (s, 9H, $TMSCH_3$) ppm; MS (ESI) *m/z* (%): 1023.0 (12) $[M+H]^+$, 1045.0 (100) $[M+Na]^+$, 1060.9 (28) $[M+K]^+$.

H-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs.



TMS-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs **5** (501 mg, 0.49 mmol) was dissolved in THF (30 mL) and the solution was cooled to 0 °C. A solution of TBAF (256 mg, 0.98 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred for 1 h at 0 °C. Ethyl acetate (150 mL) and water (150 mL) were added, and the organic layer was separated. The aqueous layer was extracted four times with ethyl acetate (4×50 mL), and the combined organic layers were dried using $MgSO_4$. The solvent was evaporated, and the residue precipitated from ethyl acetate. The product was obtained as a white powder. Yield: 340 mg (0.36 mmol, 73%); MS (ESI) *m/z* (%): 855.0 (9) [M–CH_3SO_3H+H]$^+$, 950.9 (25) [M+H]$^+$, 972.9 (100) [M+Na]$^+$, 988.9 (5) [M+K]$^+$.

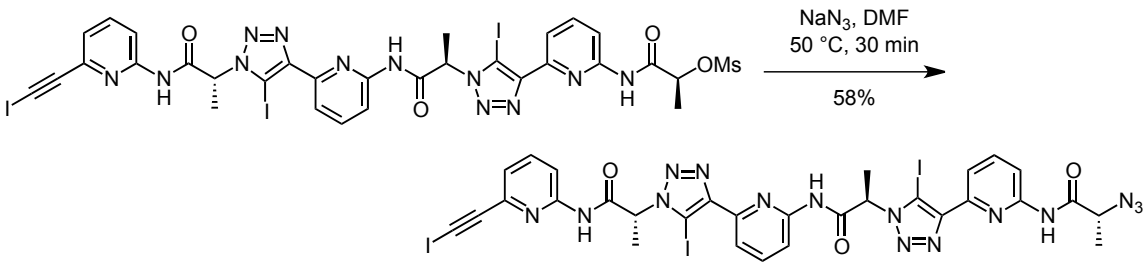
I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs.



Thoroughly dried $Cu(ClO_4)_2 \cdot 6H_2O$ (252 mg, 0.68 mmol), TBTA (18 mg, 0.03 mmol), and NaI (207 mg, 1.36 mmol) were suspended in dry THF (5 mL), followed by the addition of TEA (47.0 µL, 0.34 mmol). H-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs (320 mg, 0.34 mmol) was immediately added, and the reaction mixture was stirred for 45 min under an inert atmosphere. After adding water (100 mL) and a 1:1 (*v/v*) mixture of 25% aqueous NH_3 and 25% aqueous NH_4Cl (10 mL), the mixture was extracted twice with ethyl acetate (2×100 mL). The combined organic layers were washed with water three times (3×50) and dried over $MgSO_4$. White product was precipitated from ethyl acetate. Yield: 210 mg (0.23 mmol, 69%); MS (ESI) *m/z* (%): 972.9 (17) [M–I+H+Na]$^+$, 1076.8 (42) [M+H]$^+$, 1098.8

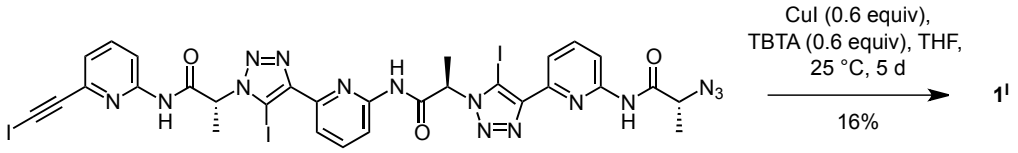
(100) $[M+Na]^+$, 1114.8 (15)) $[M+K]^+$.

I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*R*)-Lac-N$_3$.



I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs (205 mg, 0.19 mmol) and sodium azide (25 mg, 0.38 mmol) were dissolved in DMF (10 mL). The mixture was stirred at 50 °C for 30 min. After adding water (100 mL), the mixture was extracted with three times ethyl acetate (3×100 mL). The combined organic layers were dried over $MgSO_4$. Pure product was obtained by column chromatography with ethyl acetate as the eluent. Yield: 112 mg (0.11 mmol, 58%); MS (ESI) *m/z* (%): 920.0 (19) [M–I+H+Na]$^+$, 1045.9 (100) $[M+Na]^+$, 1061.8 (5) $[M+K]^+$.

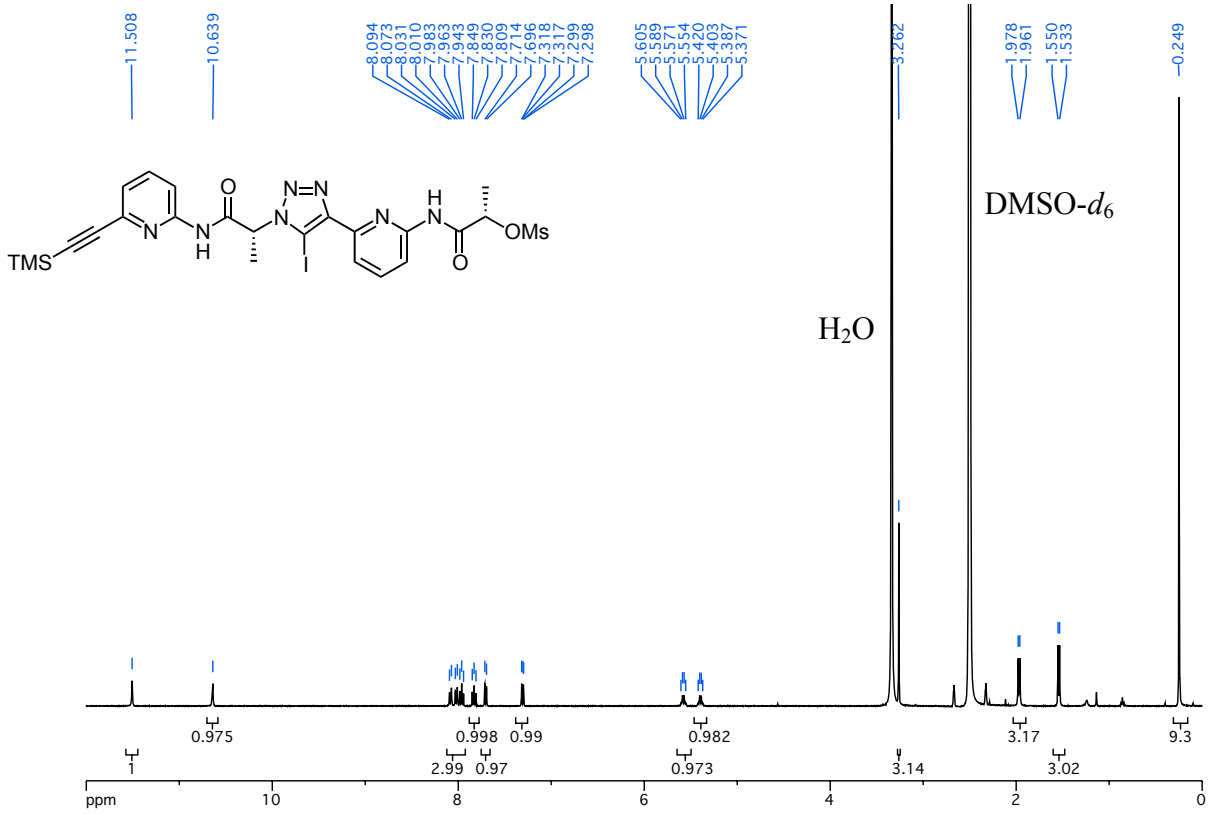
***cyclo*[(*R*)-Lac-1,4-ITri-Epa]$_3$ 1$^{\mathbf{I}}$.**



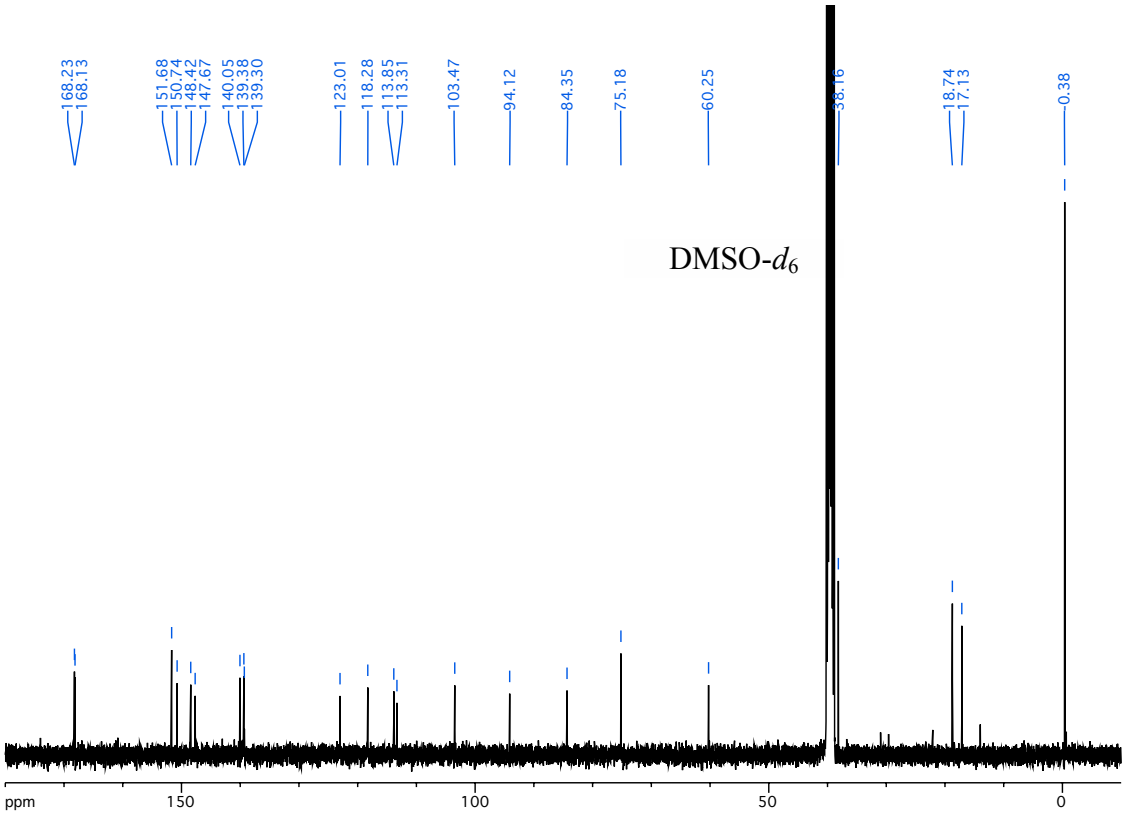
I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*R*)-Lac-N$_3$ (102 mg, 0.10 mmol), CuI (2 mg 10 µmol), and TBTA (5 mg, 10 µmol) were dissolved in dry THF (360 mL). The reaction mixture was stirred at 25 °C and its progress was followed by HPLC. Additional CuI (2 mg 10 µmol) and TBTA (5 mg 10 µmol) were added every 24 h until HPLC indicated full conversion, typically after 5 d. Isolation and purification of the cyclic product was achieved by, first, removing the solid materials from the reaction mixture by centrifugation. After adding water (50 mL) and a 1:1 (*v/v*) mixture of 25% aqueous NH_3 and 25% aqueous NH_4Cl (10 mL), the mixture was extracted three times with ethyl acetate (1×400 mL, 2×100 mL). The combined organic layers were washed with water three times (3×25 mL). The solvent was removed to afford yellowish solid. This crude product was washed with dichloromethane (3×30 mL), followed by acetone/water, 1:1 (*v/v*) (3×10 mL), and finally THF (5×45 mL) to obtain the product in analytically pure form after drying. Yield: 16 mg (16 µmol, 16%); m.p. > 200 °C (dec); $[\alpha]_D^{25}$ =

–23.7 (*c* = 0.1, DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 10.21 (s, 3H, NH), 7.90 (t, 3H, ^{3}J(H, H) = 7.8 Hz, EpaH(4)), 7.85 (d, 3H, ^{3}J(H, H) = 8.1 Hz, EpaH(5)), 7.70 (d, 3H, ^{3}J(H, H) = 7.9 Hz, EpaH(3)), 5.86 (q, 3H, ^{3}J(H, H) = 6.5 Hz, LacCH), 1.99 (d, 9H, ^{3}J(H, H) = 6.7 Hz, $LacCH_3$) ppm; ^{13}C NMR (100.6 MHz, DMSO-d_6) δ = 166.6 (CO), 149.2 (EpaC(2)), 148.3 (EpaC(6)), 145.4 (ITriC(4)) 139.3 (EpaC(4)), 117.2 (EpaC(5)), 115.1 (EpaC(3)), 83.5 (ITriC(5)), 59.4 (LacC), 16.1 ($LacCH_3$) ppm; MS (ESI) *m/z* (%): 1023.8 (16) $[M+H]^+$, 1045.8 (100) $[M+Na]^+$, 1061.8 (5) $[M+K]^+$; elemental analysis calcd (%) for $C_{30}H_{24}I_3N_{15}O_3$: C 35.21, N 20.53, H 2.36 found C 35.32, N 20.09, H 2.45.

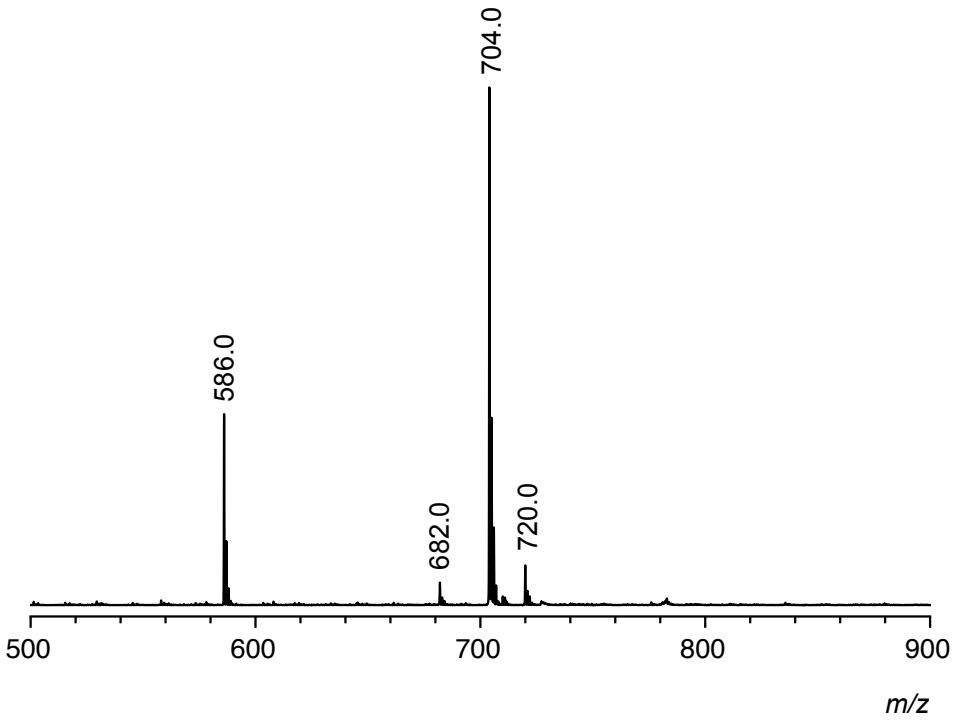
^{1}H NMR: TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs **4** (400 MHz, DMSO-d_6, 25 °C).



^{13}C NMR: TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs **4** (100.6 MHz, DMSO-d_6, 25 °C).

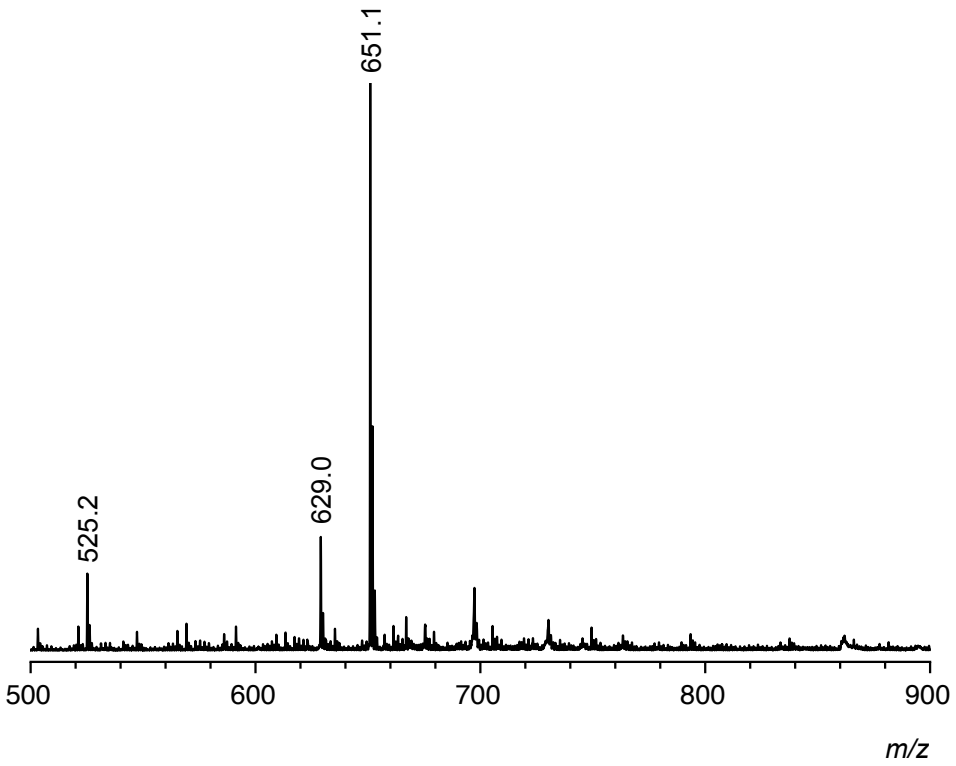


ESI-TOF MS: TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*S*)-Lac-OMs **4** (positive mode).



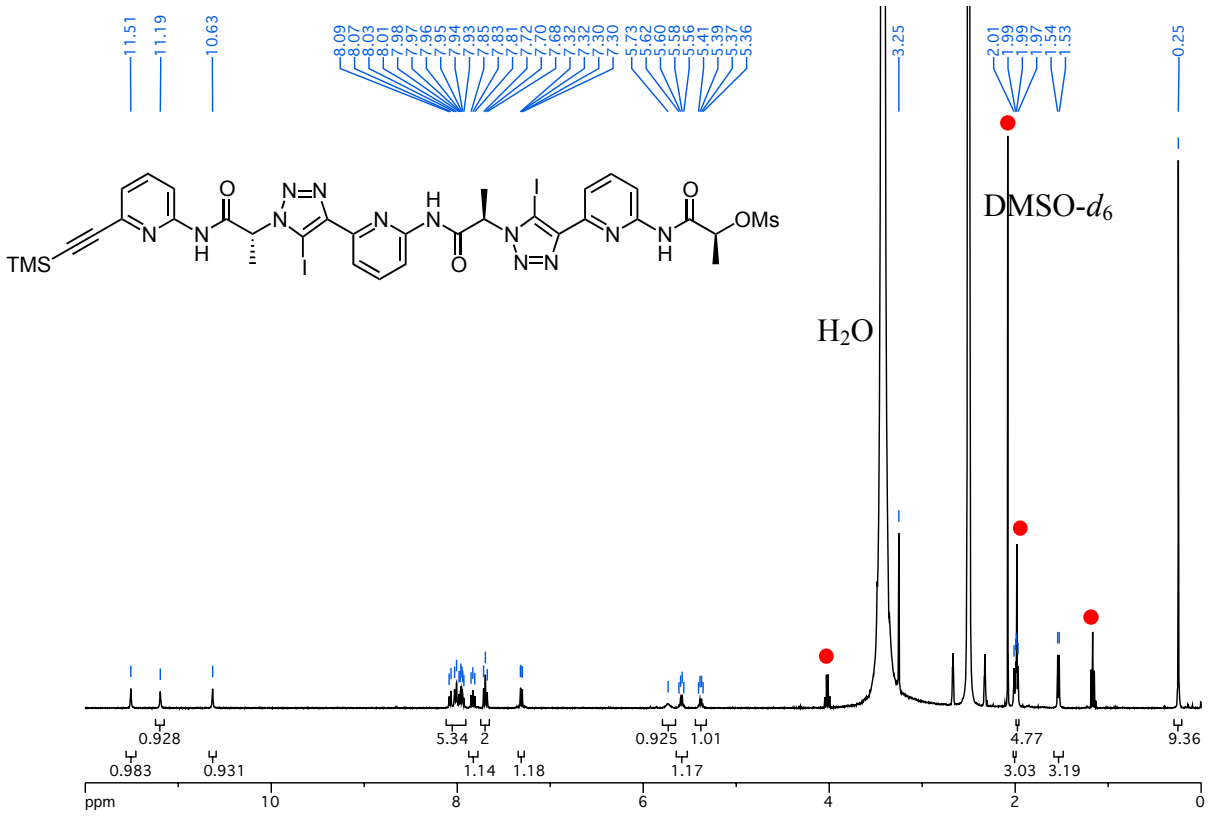
		m/z calcd.	*m/z exp.*
$[M–CH_3SO_3H+H]^+$	$C_{23}H_{24}IN_7O_2Si + H^+$	586.1	586.0
$[M+H]^+$	$C_{24}H_{28}IN_7O_5SSi + H^+$	682.1	682.0
$[M+Na]^+$	$C_{24}H_{28}IN_7O_5SSi + Na^+$	704.1	704.0
$[M+K]^+$	$C_{24}H_{28}IN_7O_5SSi + K^+$	720.0	720.0

ESI-TOF MS: TMS-Epa-(*R*)-Lac-1,4-ITri-Epa-(*R*)-Lac-N_3 (positive mode).



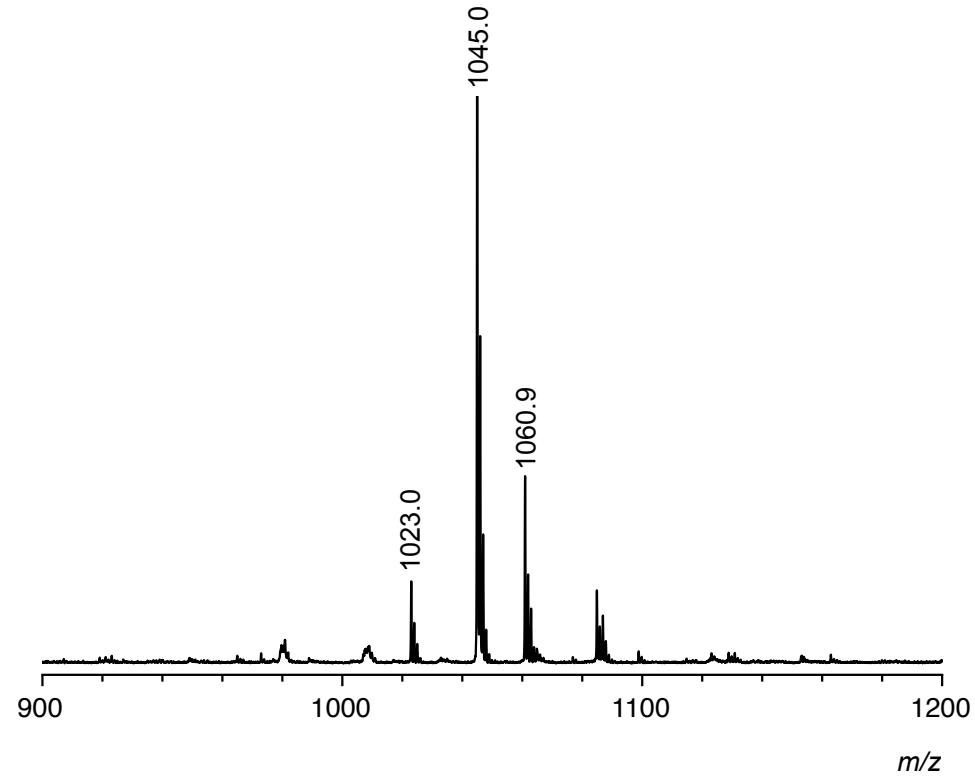
		m/z calcd.	*m/z exp.*
$[M–I+H+Na]^+$	$C_{23}H_{26}N_{10}O_2Si + Na^+$	525.2	525.2
$[M+H]^+$	$C_{23}H_{25}IN_{10}O_2Si + H^+$	629.1	629.0
$[M+Na]^+$	$C_{23}H_{25}IN_{10}O_2Si + Na^+$	651.1	651.0

^{1}H NMR: TMS-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs **5** (400 MHz, DMSO-d_6, 25 °C).



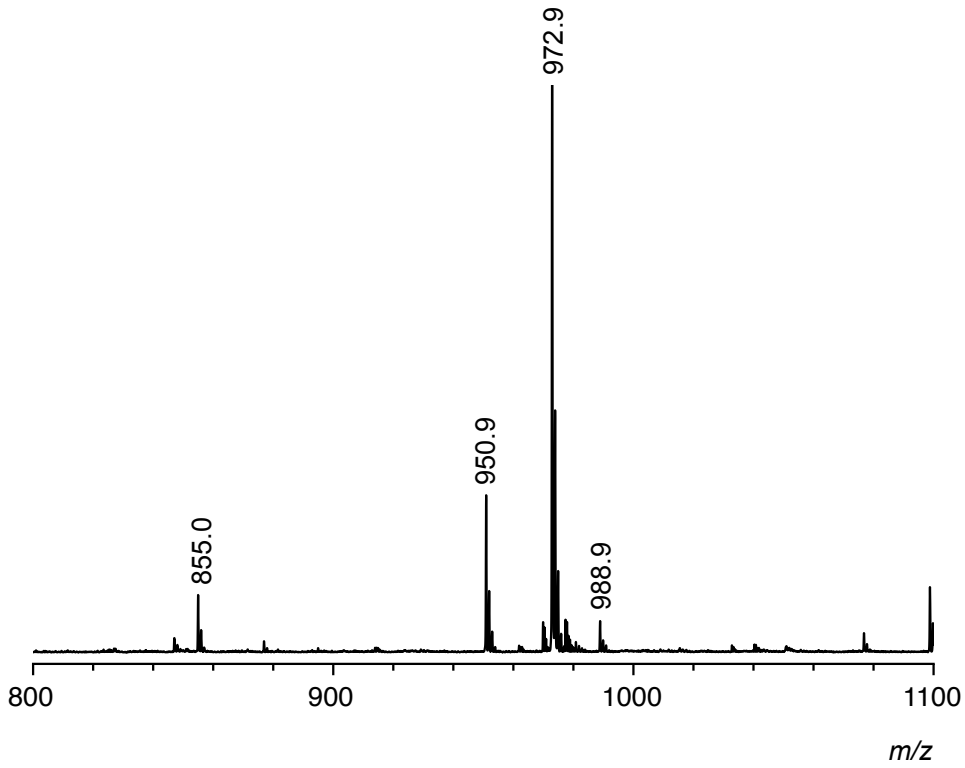
Signals of impurities (ethyl acetate, acetone) are marked with red dots.

ESI-TOF MS: TMS-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs **5** (positive mode).



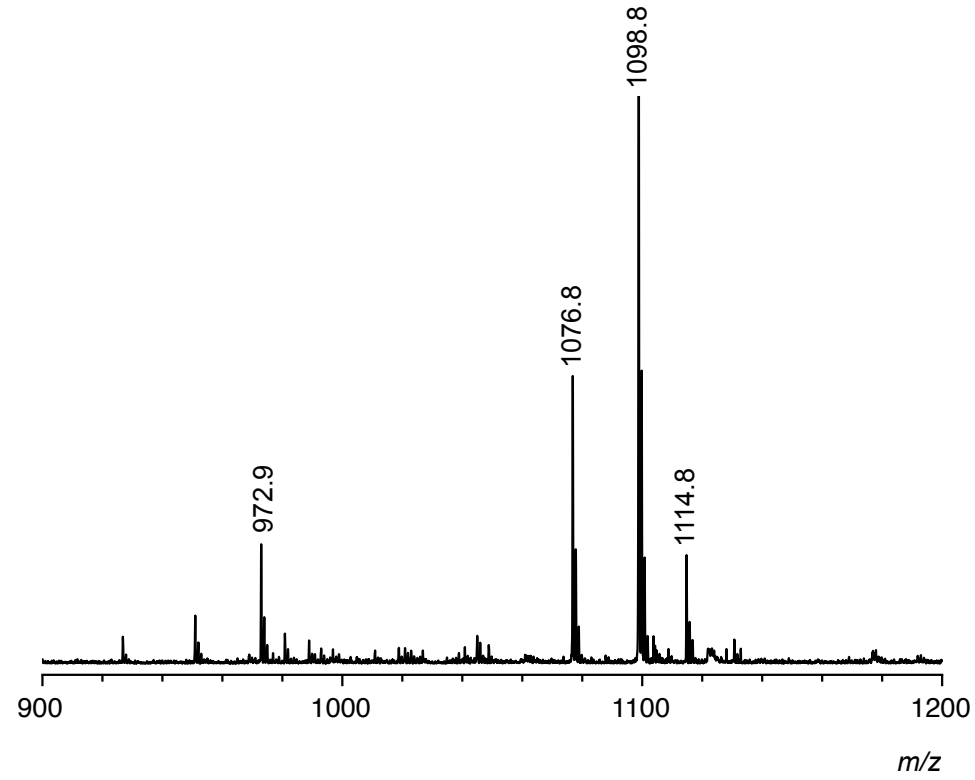
		m/z calcd.	*m/z exp.*
$[M+H]^+$	$C_{34}H_{36}I_2N_{12}O_6SSi + H^+$	1023.1	1023.0
$[M+Na]^+$	$C_{34}H_{36}I_2N_{12}O_6SSi + Na^+$	1045.0	1045.0
$[M+K]^+$	$C_{34}H_{36}I_2N_{12}O_6SSi + K^+$	1061.0	1060.9

ESI-TOF MS: H-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs (positive mode).



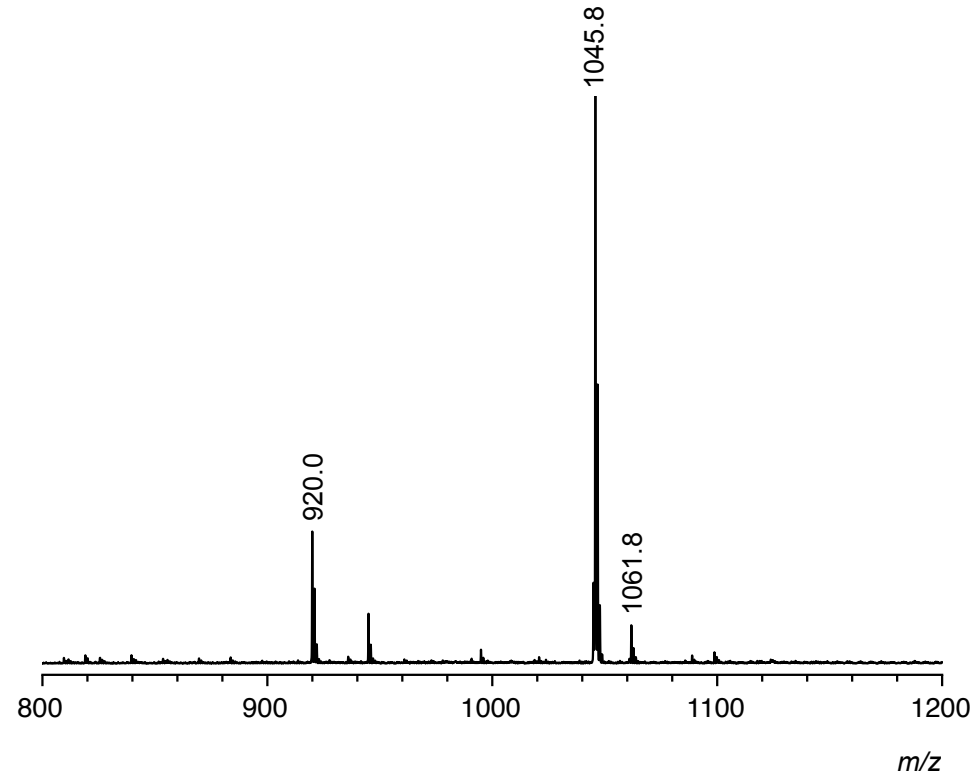
		m/z calcd.	*m/z exp.*
$[M–CH_3SO_3H+H]^+$	$C_{30}H_{24}I_2N_{12}O_3 + H^+$	855.0	855.0
$[M+H]^+$	$C_{31}H_{28}I_2N_{12}O_6S + H^+$	951.0	950.9
$[M+Na]^+$	$C_{31}H_{28}I_2N_{12}O_6S + Na^+$	973.0	972.9
$[M+K]^+$	$C_{31}H_{28}I_2N_{12}O_6S + K^+$	989.0	988.9

ESI-TOF MS: I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*S*)-Lac-OMs (positive mode).



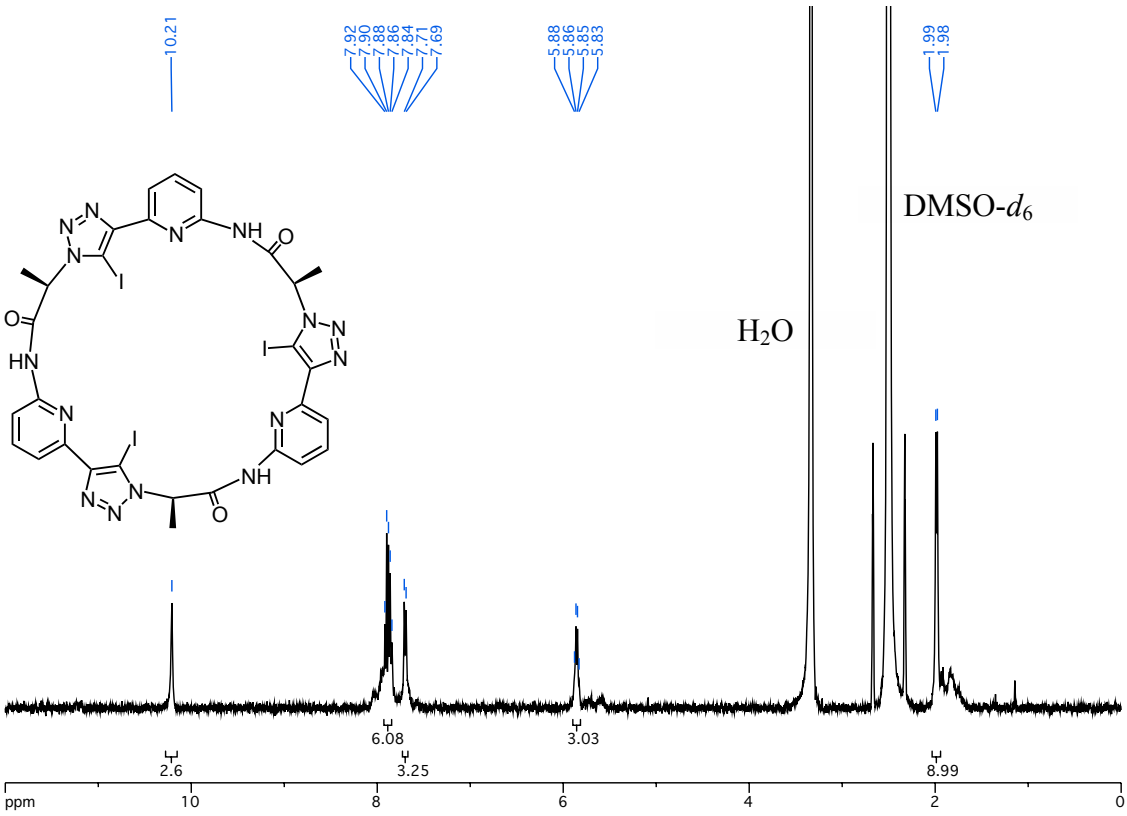
		m/z calcd.	*m/z exp.*
$[M–I+H+Na]^+$	$C_{30}H_{24}I_2N_{12}O_3 + Na^+$	973.0	972.9
$[M+H]^+$	$C_{31}H_{27}I_3N_{12}O_6S + H^+$	1076.9	1076.8
$[M+Na]^+$	$C_{31}H_{27}I_3N_{12}O_6S + Na^+$	1098.9	1098.8
$[M+K]^+$	$C_{31}H_{27}I_3N_{12}O_6S + K^+$	1114.9	1114.8

ESI-TOF MS: I-Epa-[(*R*)-Lac-1,4-ITri-Epa]$_2$-(*R*)-Lac-N_3 (positive mode).

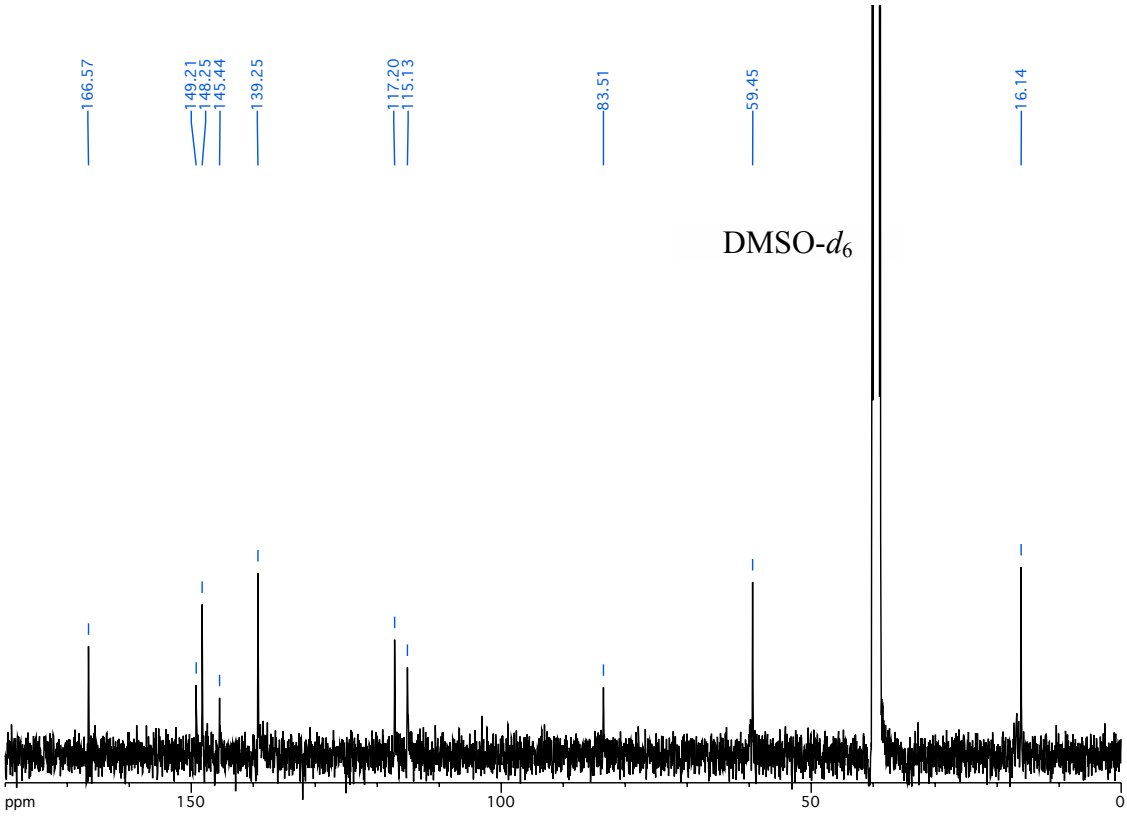


		m/z calcd.	*m/z exp.*
$[M–I+H+Na]^+$	$C_{30}H_{25}I_2N_{15}O_3 + Na^+$	920.0	920.0
$[M+Na]^+$	$C_{30}H_{24}I_3N_{15}O_3 + Na^+$	1045.9	1045.8
$[M+K]^+$	$C_{30}H_{24}I_3N_{15}O_3 + K^+$	1061.9	1061.8

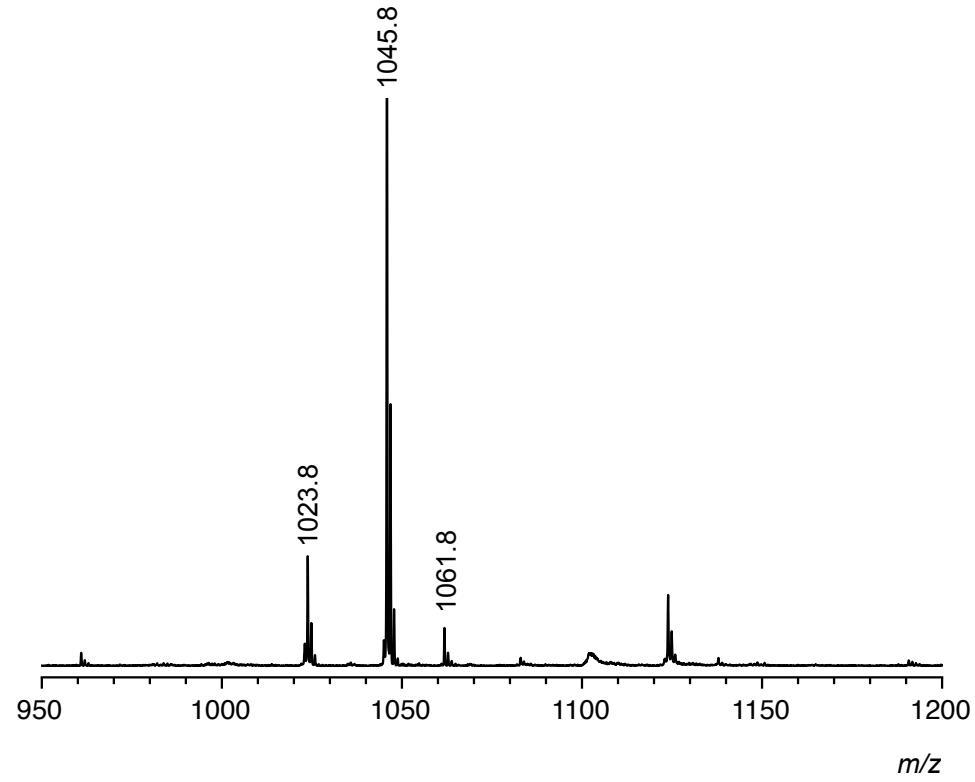
^{1}H NMR: *cyclo*[(*R*)-Lac-1,4-ITri-Epa]$_3$ **1^{I}** (400 MHz, DMSO-d_6, 25 °C).



^{13}C NMR: *cyclo*[(*R*)-Lac-1,4-ITri-Epa]$_3$ **1^{I}** (100.6 MHz, DMSO-d_6, 25 °C).

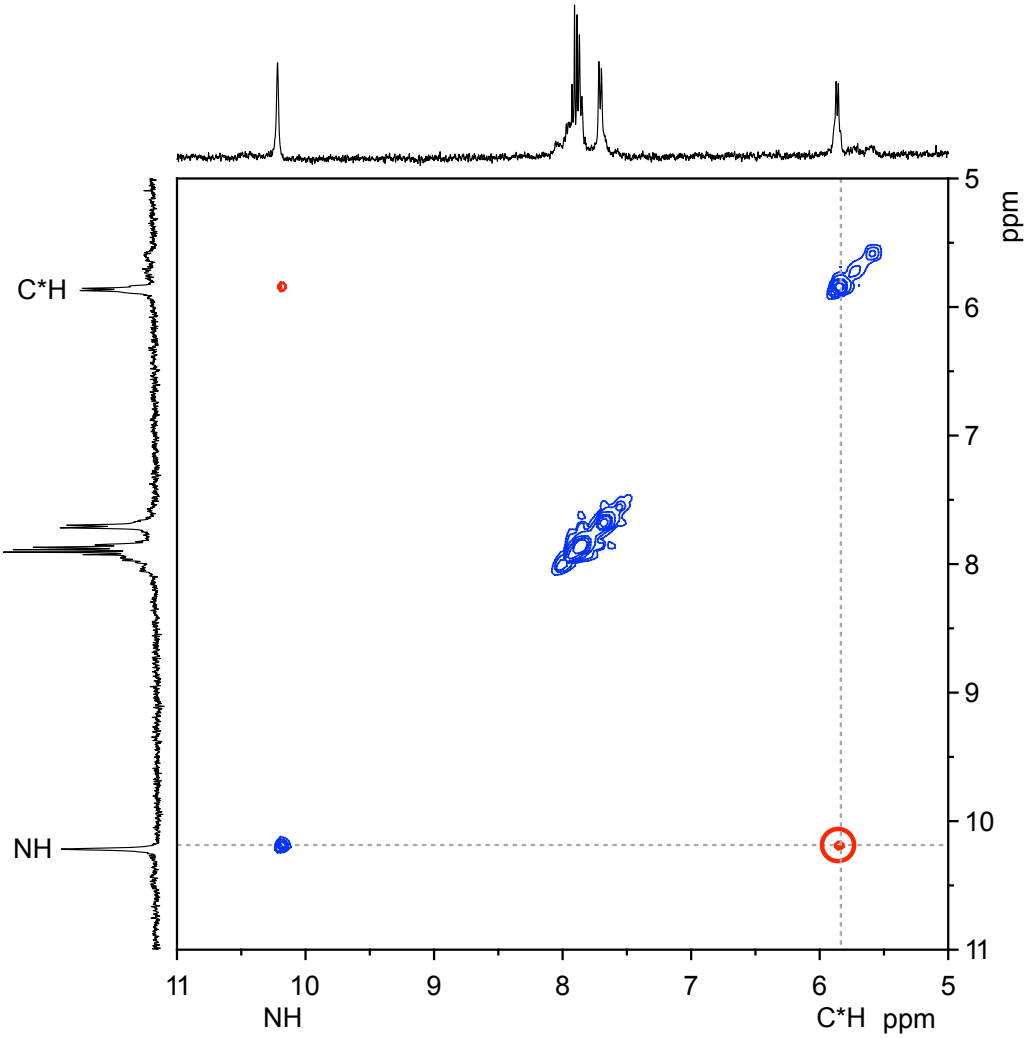


ESI-TOF MS: *cyclo*[(*R*)-Lac-1,4-ITri-Epa]$_3$ **1^{I}** (positive mode).



		m/z calcd.	*m/z exp.*
$[M+H]^+$	$C_{30}H_{24}I_3N_{15}O_3 + H^+$	1023.9	1023.8
$[M+Na]^+$	$C_{30}H_{24}I_3N_{15}O_3 + Na^+$	1045.9	1045.8
$[M+K]^+$	$C_{30}H_{24}I_3N_{15}O_3 + K^+$	1061.9	1061.8

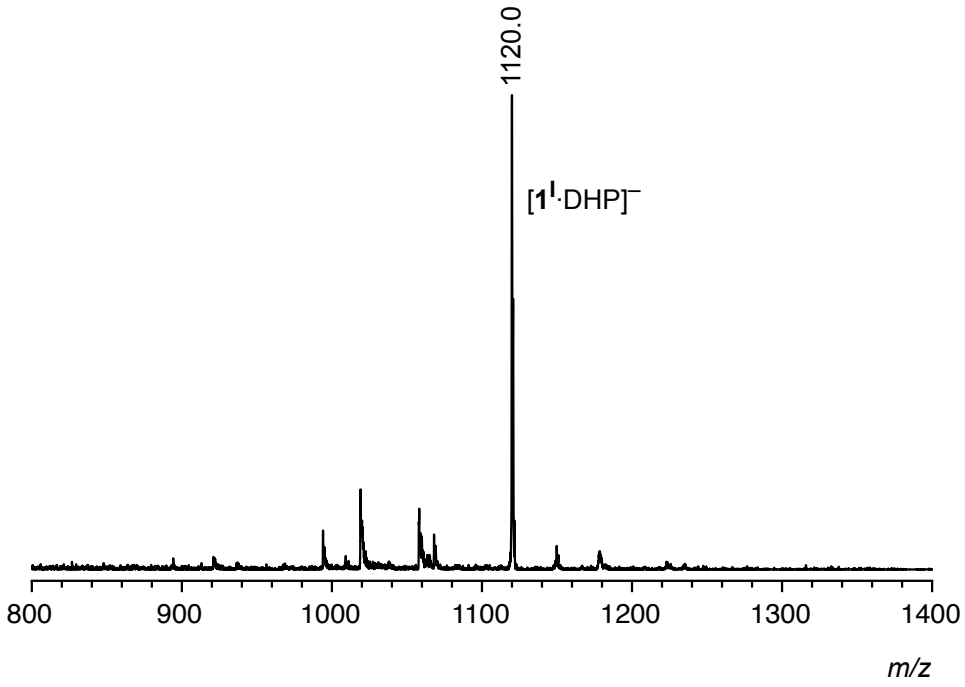
ROESY NMR Spectrum: **1**[I] (0.5 mM) in DMSO-d_6 (mixing time 300 ms) (400 MHz, 25 °C).



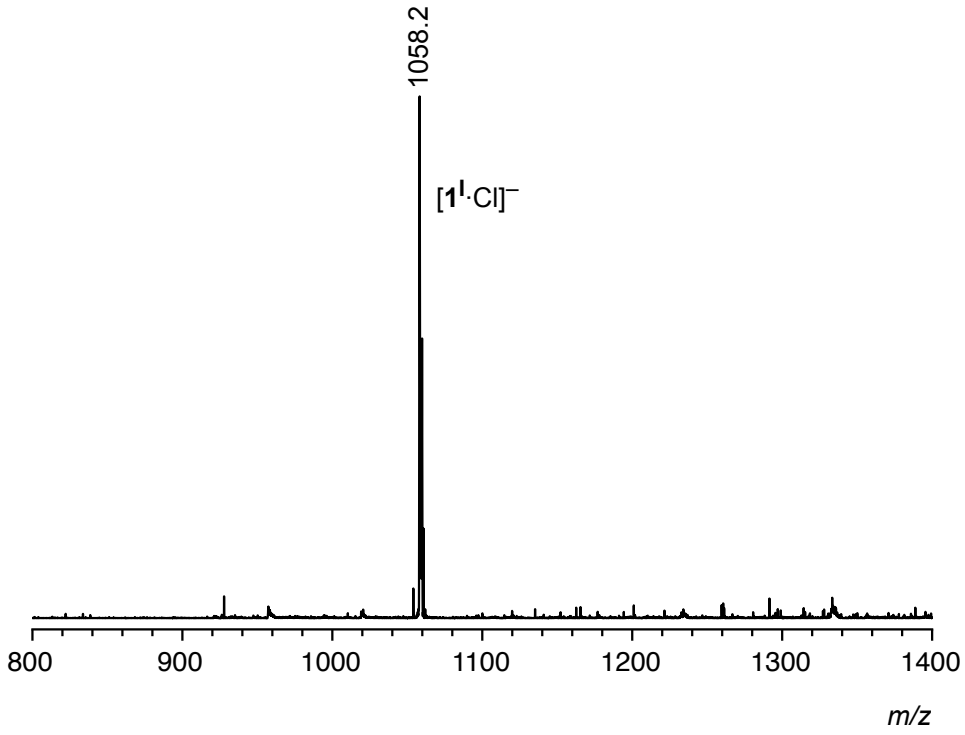
ESI-MS Measurements:

		m/z calcd.
$[\mathbf{1}^{\mathbf{I}}+Cl]^-$	$C_{30}H_{24}I_3N_{15}O_3 + Cl^-$	1057.9
$[\mathbf{1}^{\mathbf{I}}+DHP]^-$	$C_{30}H_{24}I_3N_{15}O_3 + H_2PO_4^-$	1119.9
$[\mathbf{1}^{\mathbf{I}}+TBA+SO_4]^-$	$C_{30}H_{24}I_3N_{15}O_3 + C_{16}H_{36}N^+ + SO_4^{2-}$	1361.2

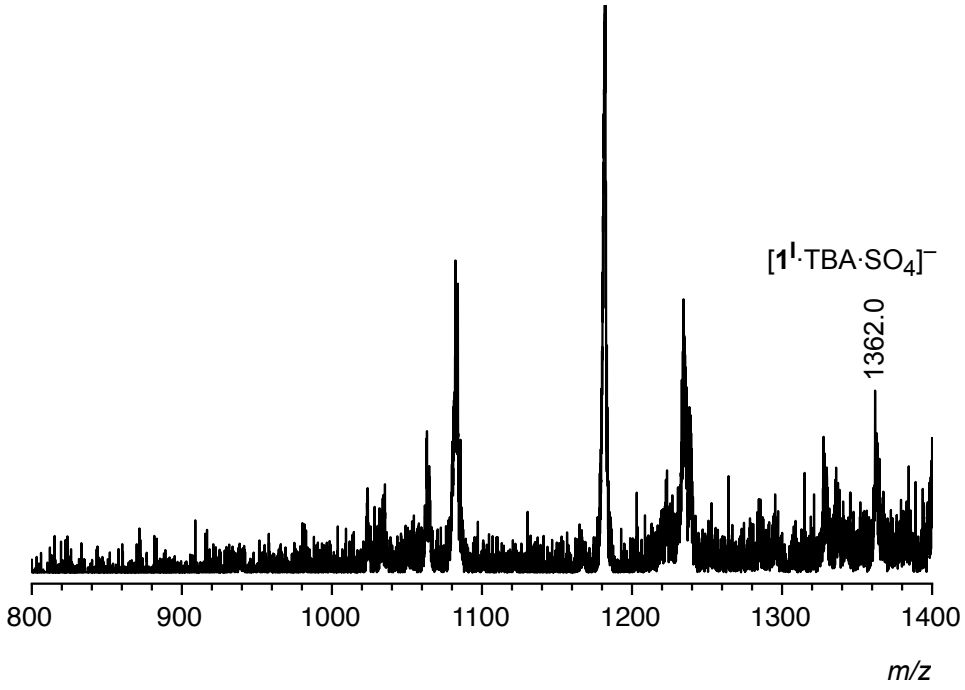
ESI MS: $\mathbf{1}^{\mathbf{I}}$ (1 mM) in DMSO/acetonitrile, 1:1 (*v/v*) in the presence of 1 equiv of TBA DHP.



ESI MS: **1**$^{\mathbf{I}}$ (1 mM) in DMSO/acetonitrile, 1:1 (*v/v*) in the presence of each 1 equiv of TBA DHP and TBA chloride.

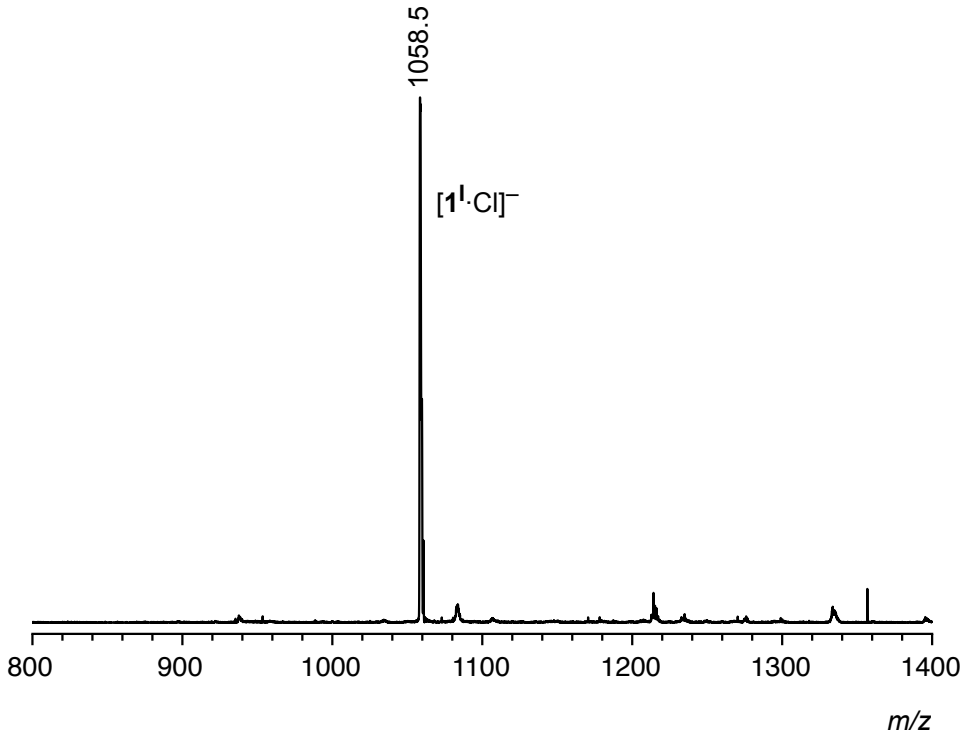


ESI MS: **1**$^{\mathbf{I}}$ (1 mM) in DMSO/acetonitrile, 1:1 (*v/v*) in the presence of 1 equiv of TBA sulfate.

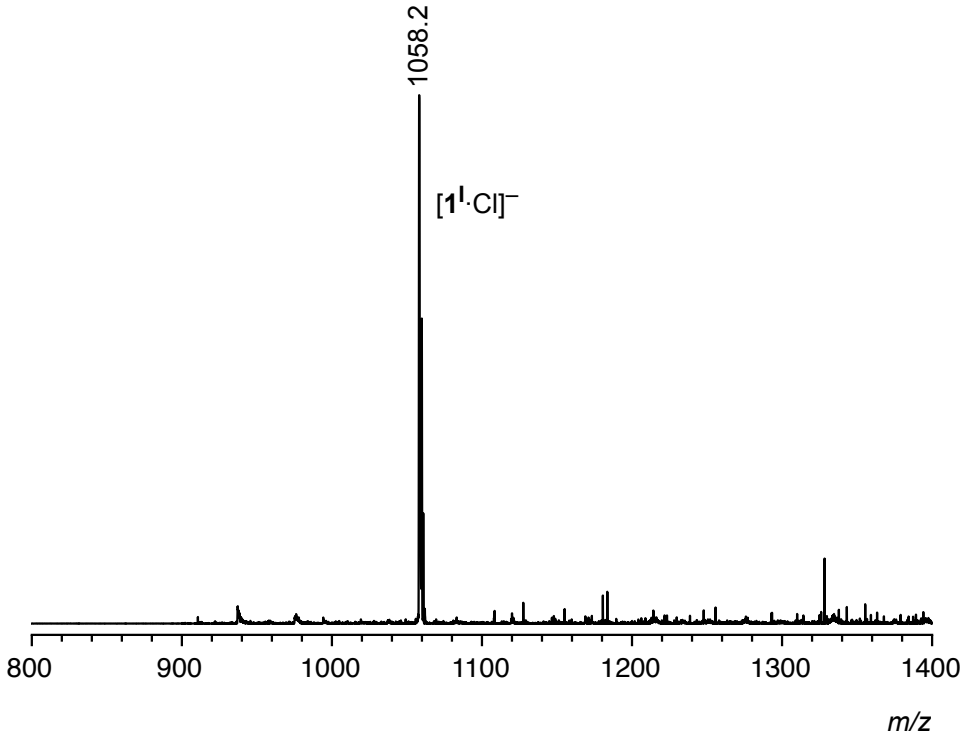


That only a very small peak is visible attributable to the sulfate complex of **1**$^{\mathbf{I}}$ indicates that the pseudopeptide is not able to stabilize the sulfate anion in the gas phase.

ESI MS: $\mathbf{1}^{\mathbf{I}}$ (1 mM) in DMSO/acetonitrile, 1:1 (*v/v*) in the presence of 1 equiv of each TBA sulfate and TBA chloride.



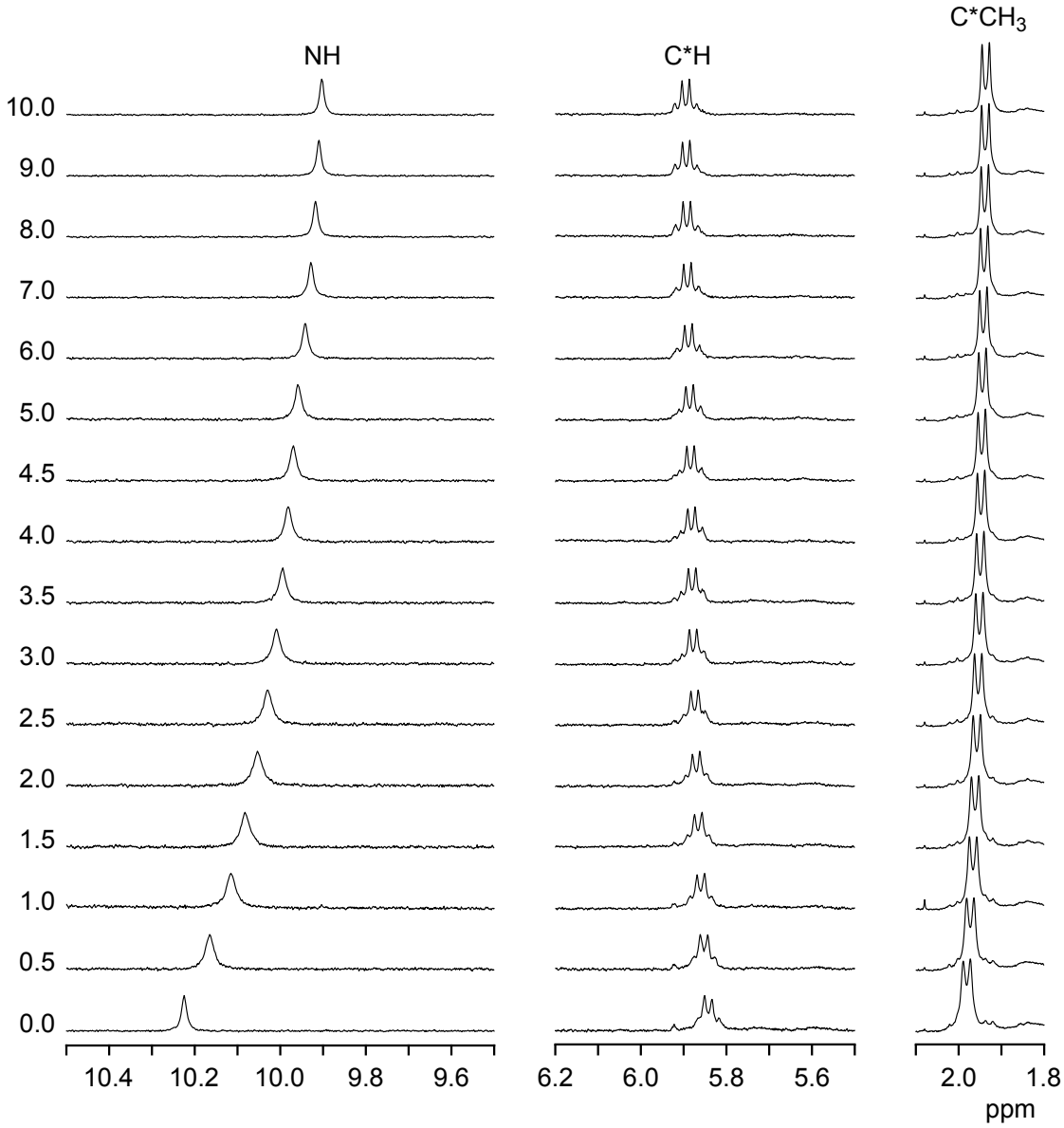
ESI MS: $\mathbf{1}^{\mathbf{I}}$ (1 mM) in DMSO/acetonitrile, 1:1 (*v/v*) in the presence of 1 equiv of each TBA DHP, TBA sulfate, and TBA chloride.



NMR Titration:

Stock solutions of **1**$^{\mathbf{I}}$ (0.5 mM), TBA chloride (5 mM), TMA chloride (5 mM), TBA bromide (5 mM), TBA iodide (5 mM), TBA sulfate (5 mM), and TBA DHP (5 mM) were prepared separately in 2.5 vol% H_2O/DMSO-d_6. Increasing amounts (0 to 300 μL) of the salt stock solution were added to 16 NMR tubes (13 NMR tubes in the case of TBA sulfate, 10 NMR tubes in the case of TMA chloride, and 11 NMR tubes in the case of TBA DHP), each containing 300 μL of the receptor stock solution. The total volume in each tube was made up to 600 μL with 2.5 vol% H_2O/DMSO-d_6. All tubes were thoroughly shaken and the ^{1}H NMR spectra were recorded (256 scans, 400 MHz). Stability constants of the anion-receptor complexes were calculated by following the shifts of the NH, C*H and C*CH_3 signals and using HypNMR2008 for global fitting.[3]

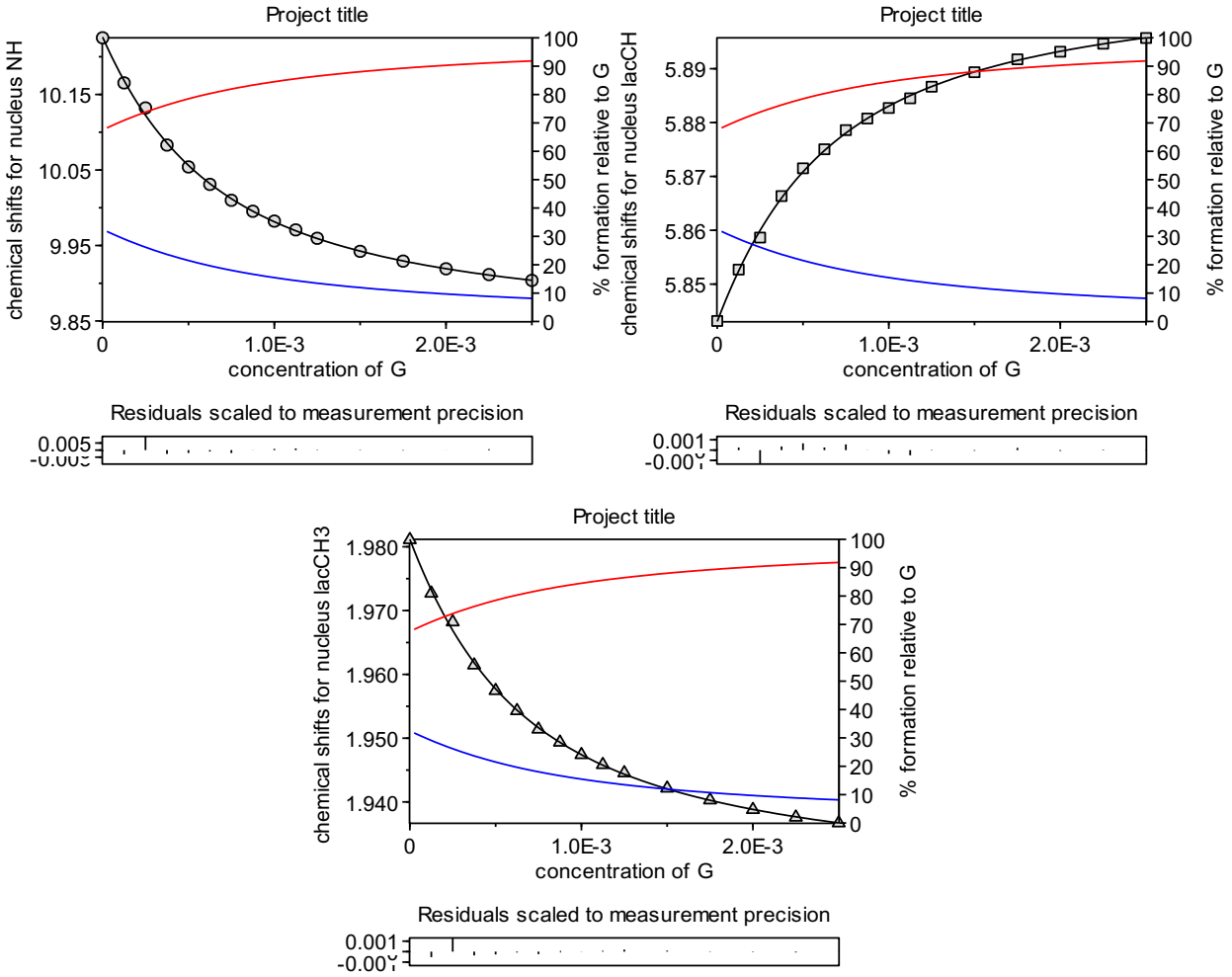
^{1}H NMR spectra of **1^{I}** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TBA chloride specified to the left of each spectrum.



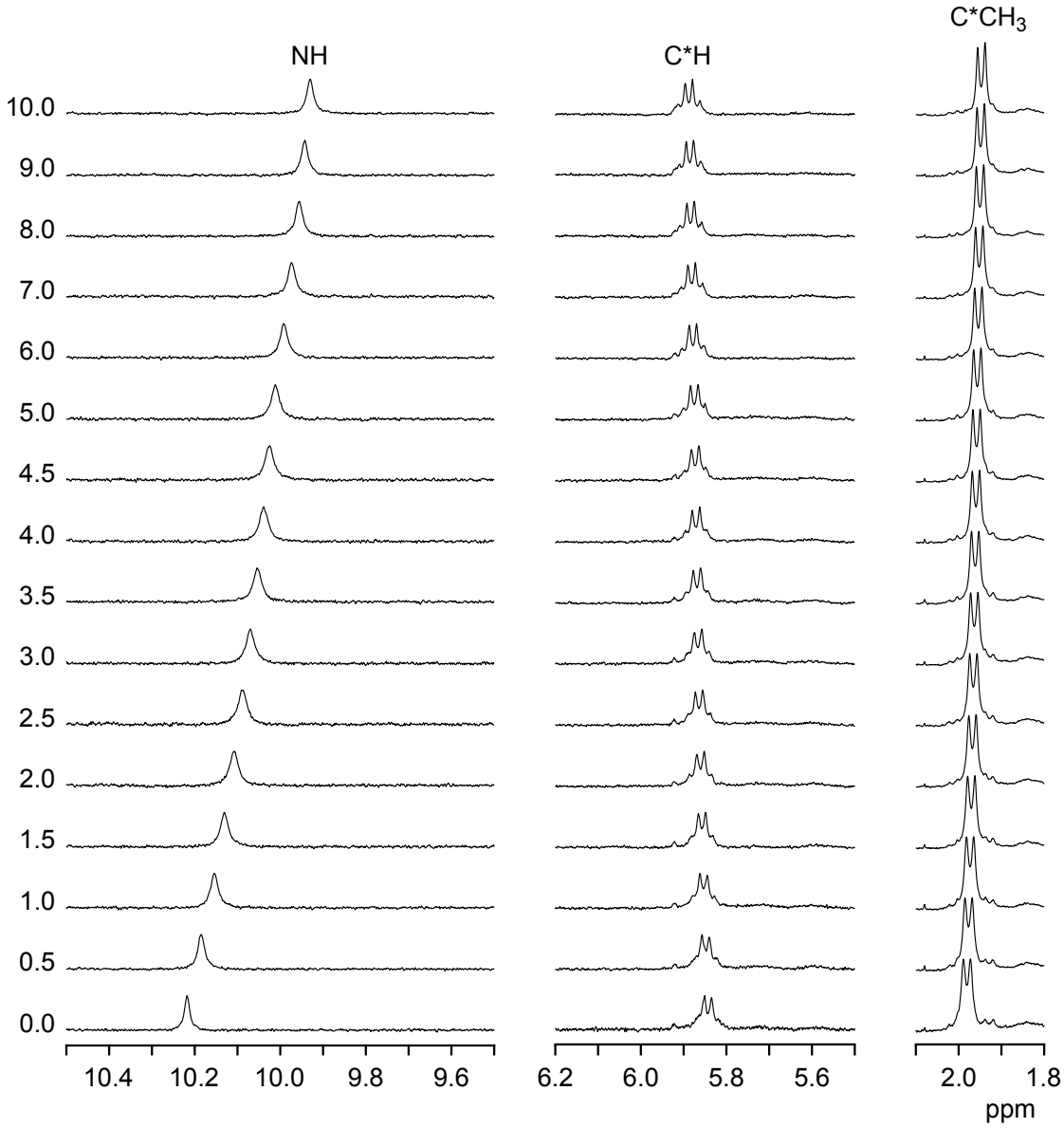
Binding isotherms and HypNMR outputs

```
Converged in 1 iterations with sigma = 0.001783

                                standard
                    value       deviation    Comments
 1 log beta(GH)     3.2838      0.0104       3.28(1)
```



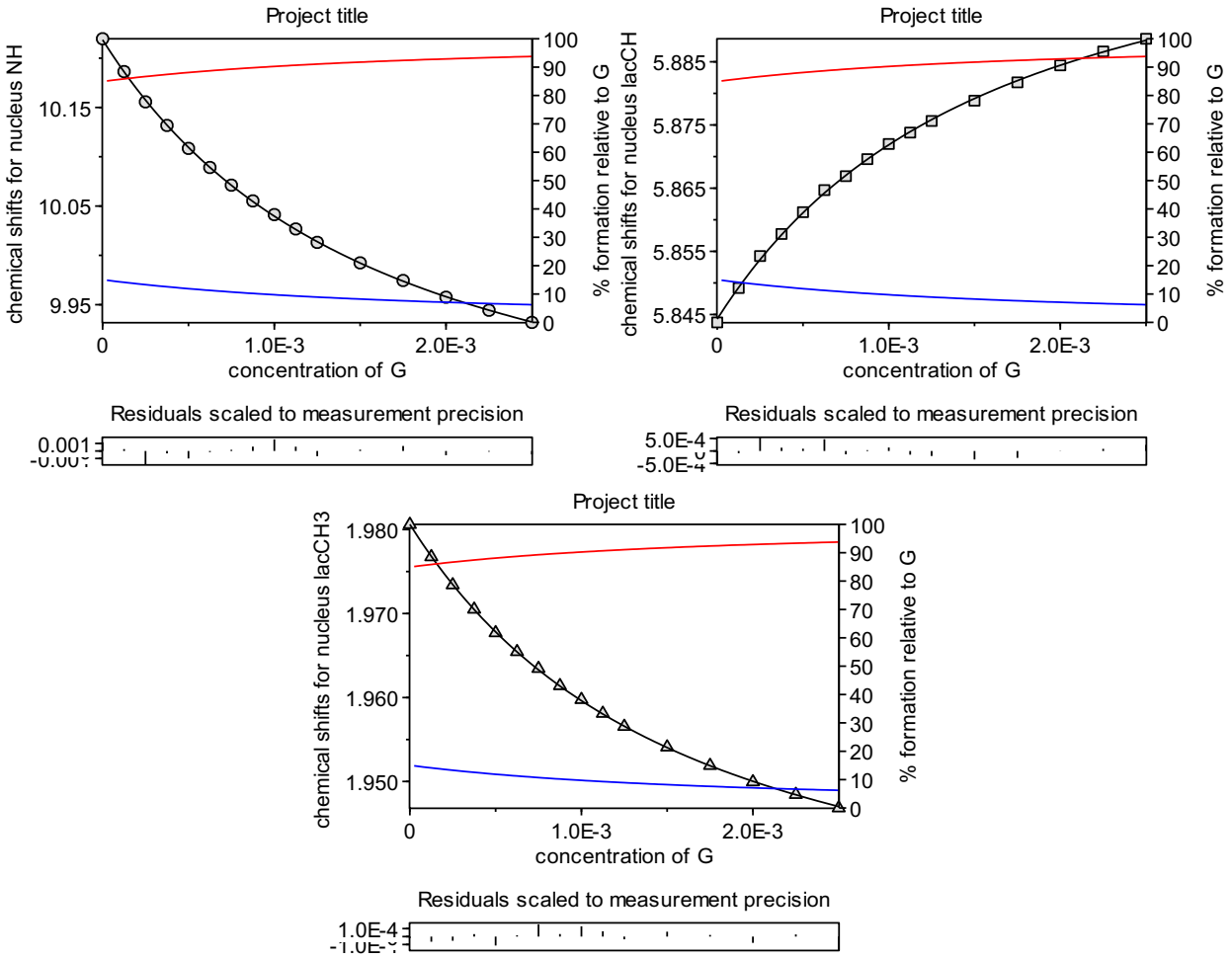
^{1}H NMR spectra of **1^I** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TBA bromide specified to the left of each spectrum.



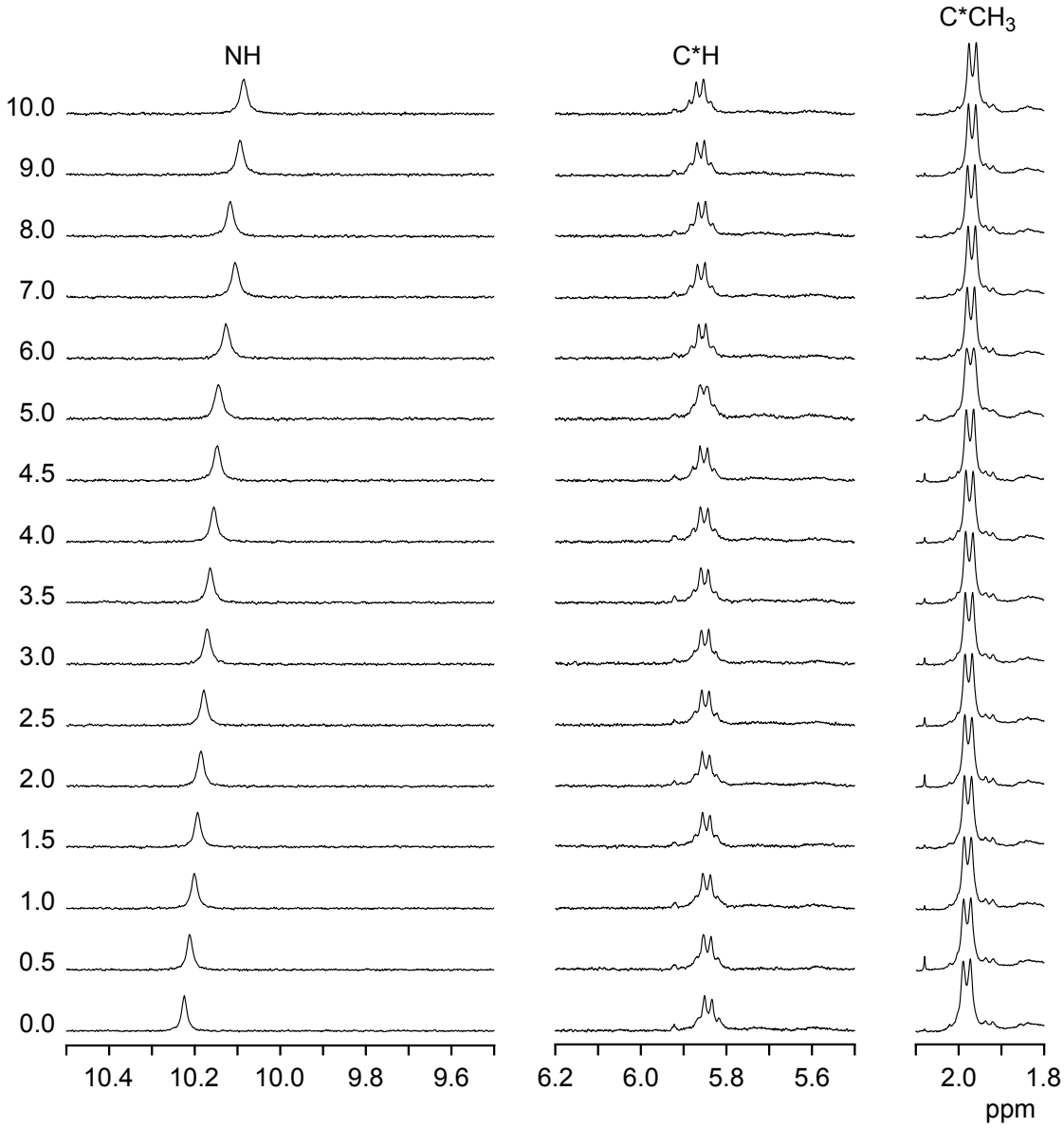
Binding isotherms and HypNMR outputs

```
Converged in 4 iterations with sigma = 0.000534

                                standard
                    value       deviation   Comments
1 log beta(GH)      2.8506      0.0043      2.851(4)
```



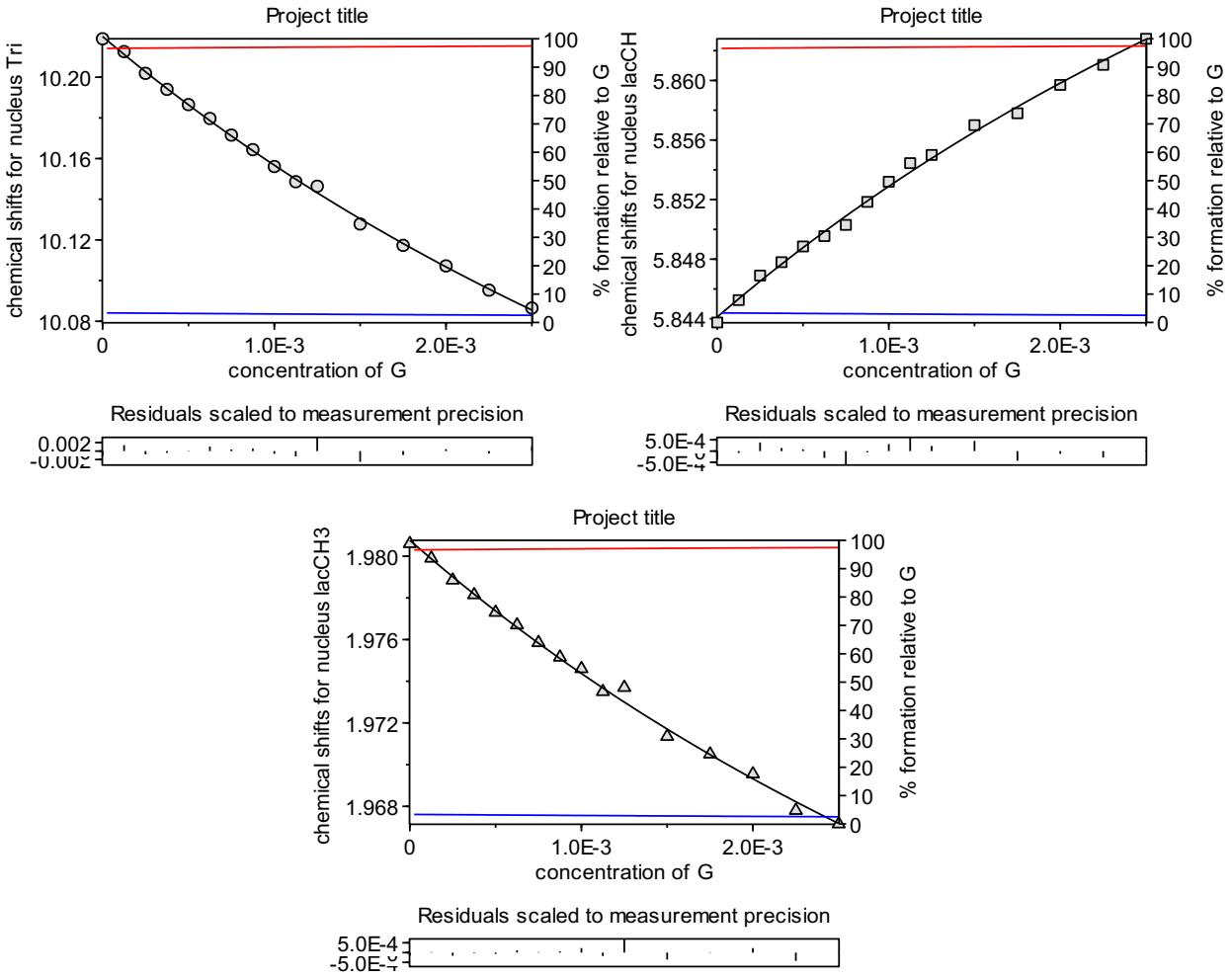
^{1}H NMR spectra of **1^I** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TBA iodide specified to the left of each spectrum.



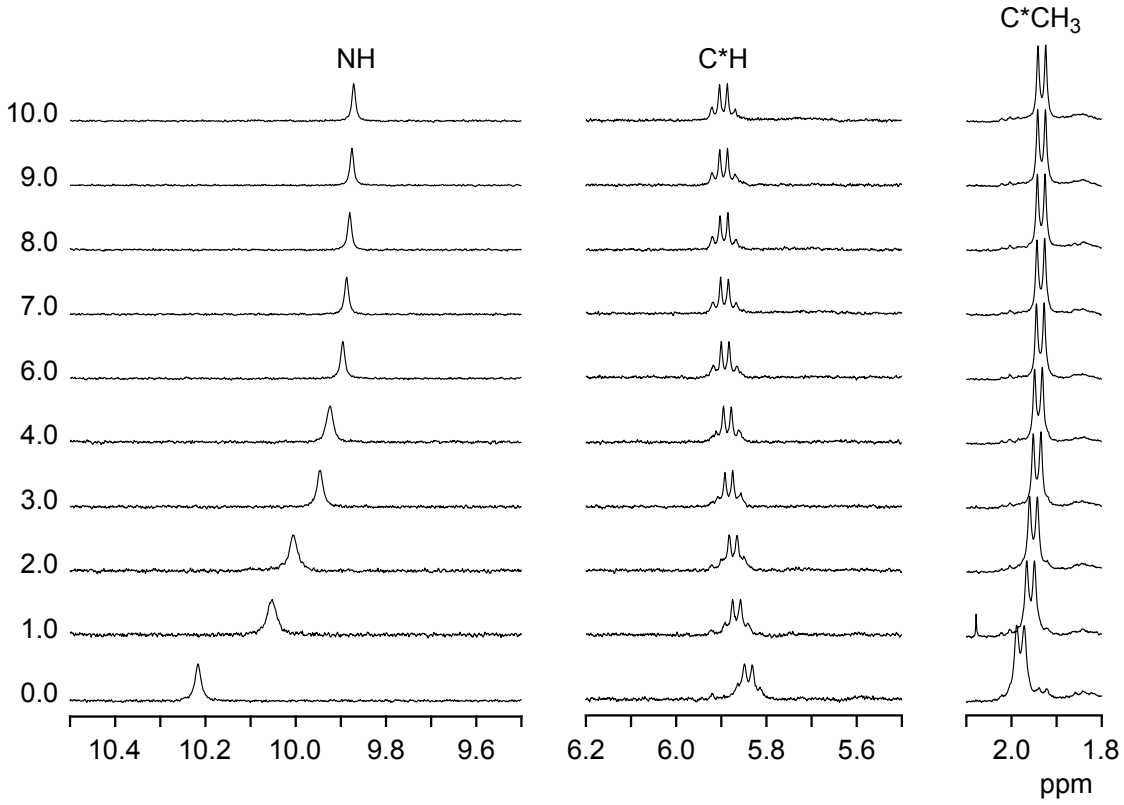
Binding isotherms and HypNMR outputs

```
Converged in 4 iterations with sigma = 0.000849
```

	value	standard deviation	Comments
1 log beta(GH)	2.1477	0.0335	2.15(3)



^{1}H NMR spectra of **1^{I}** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TMA chloride specified to the left of each spectrum.



Binding isotherms and HypNMR outputs

```
Converged in 1 iterations with sigma = 0.004043

                                standard
                    value       deviation    Comments
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```
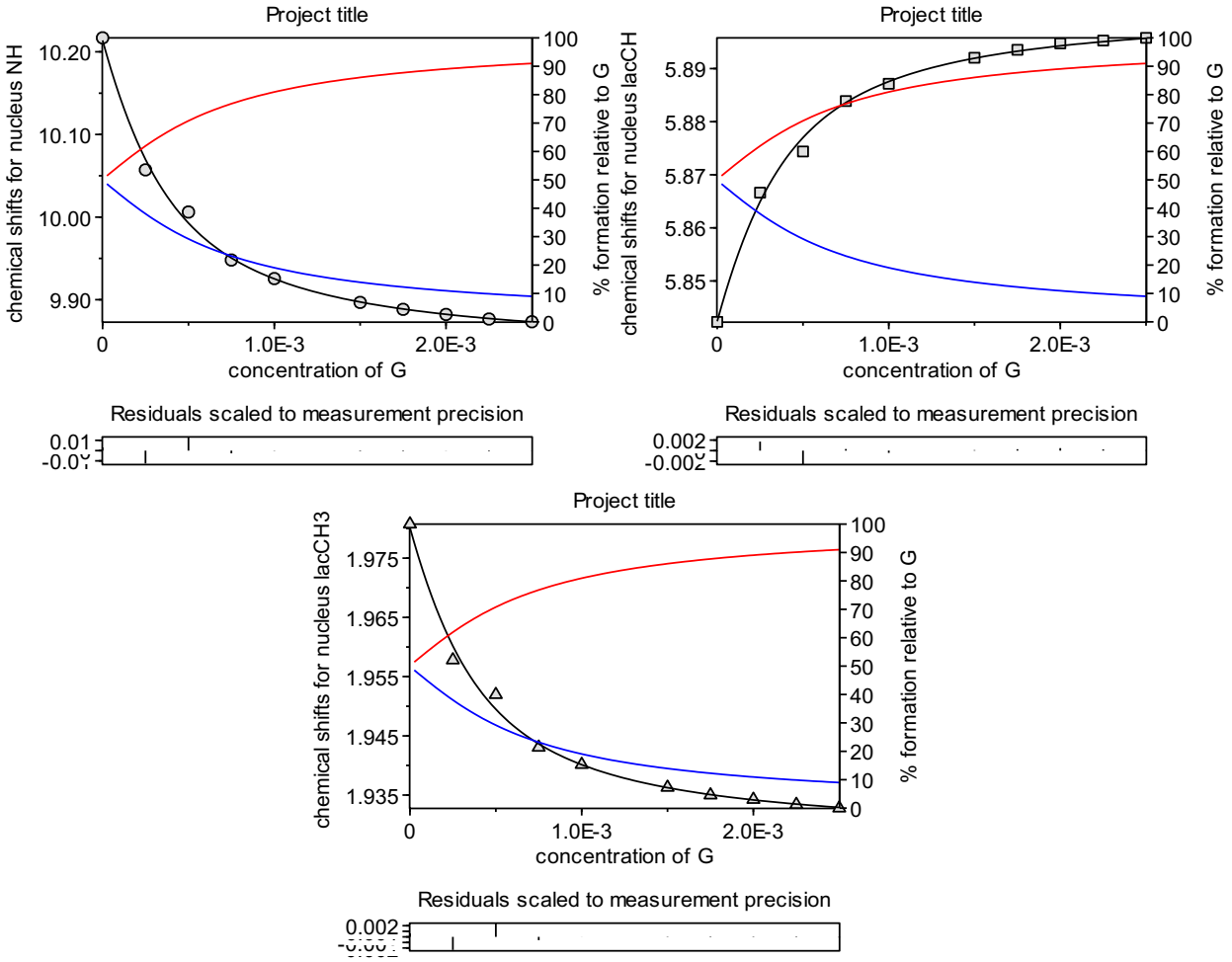
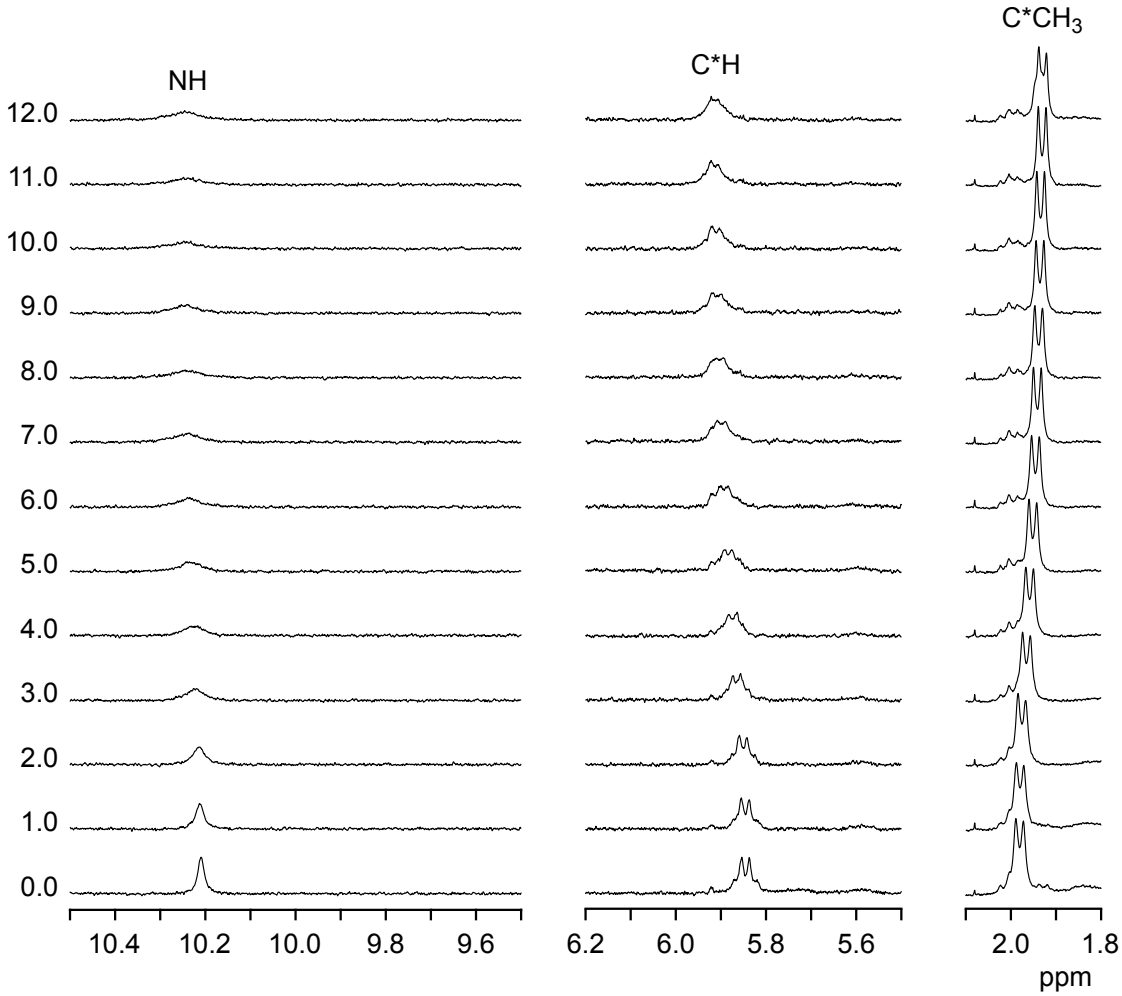
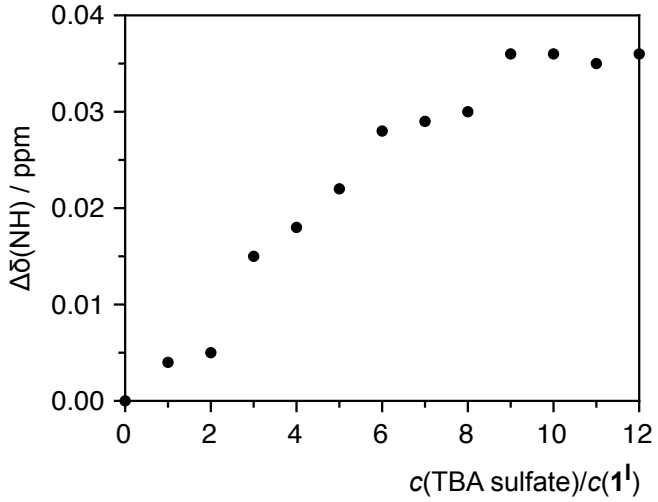
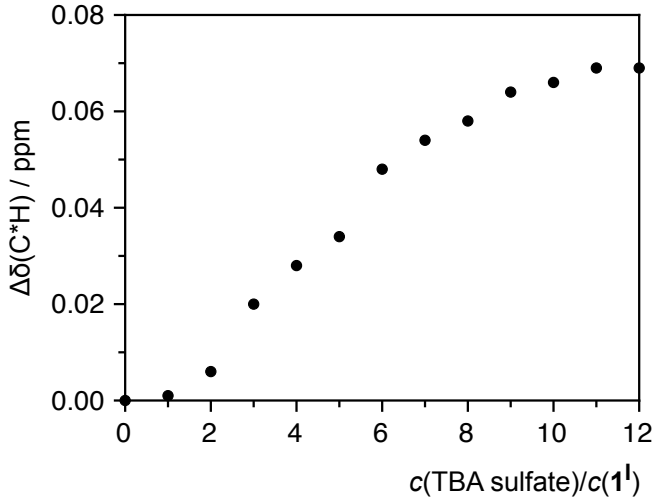



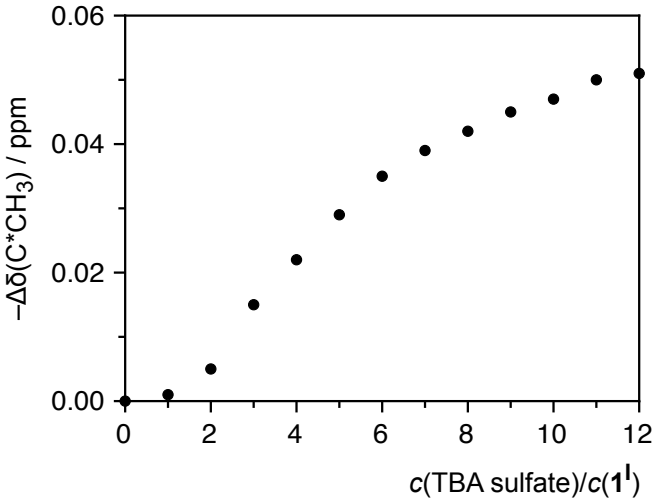
^{1}H NMR spectra of **1$^{\mathbf{I}}$** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TBA sulfate specified to the left of each spectrum.



Binding isotherms

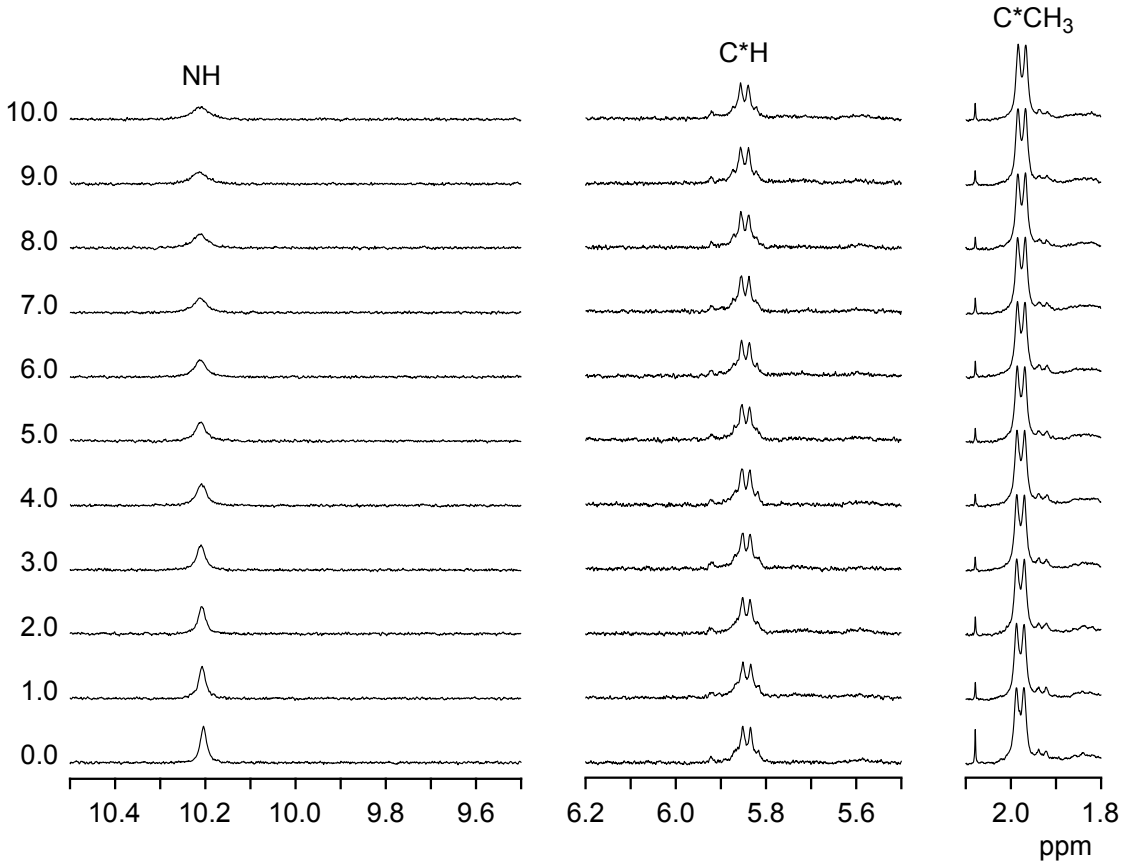






The binding isotherms observed in the titration with TBA sulfate exhibited a sigmoidal shape, indicating that complex formation is not consistent with a simple 1:1 equilibrium. We did not succeed, however, to fit these isotherms to a reasonable other binding model.

^{1}H NMR spectra of **1^{I}** (0.25 mM) in 2.5 vol% H_2O/DMSO-d_6 (400 MHz) containing the increasing equivalents of TBA DHP specified to the left of each spectrum.



No signal shifts are visible, indicating that DHP is not bound by **1^{I}** under these conditions.

ITC Titrations:

The ITC experiments were carried out in 2.5 vol% water/DMSO. The anionic substrates were used as their TBA salts. The salts and receptor **1**$^{\mathbf{I}}$ were weighed using an analytical precision balance, dissolved in known volumes of the respective solvent mixture, and loaded into the system for immediate analysis.

The measurements were carried out at 25 °C using a reference power of 25 μJ/s, a filter period of 2 s, a stirrer speed of 307 rpm. Other experimental parameters of the individual titrations are specified in the Table S1. Automated baseline assignment and peak integration of raw thermograms were accomplished by singular value decomposition and peak-shape analysis using NITPIC.[4a] Estimation of best-fit parameter values by weighted nonlinear least-squares fitting and calculation of 68.3% confidence intervals were performed with the public-domain software SEDPHAT,[4b] as explained in detail elsewhere.[4c,d]

Table S1. Concentrations and experimental parameters of the individual titrations.

guest anion as TBA salt	c(**1**$^{\mathbf{I}}$) / mM	c(salt) / mM	injection volume / μL	no. of injections	spacing time / s
chloride	0.7	26.5	8	29	180
bromide	0.9	32.5	8	29	180

The heat changes observed during the titration with TBA bromide turned out to be too small to allow reliable quantification of binding strength.

Titration of **1^{I}** with TBA chloride: The blue spheres show the experimental results and the red line the fitted curve calculated by using the one site binding model. The inset shows the heat pulses of the measurement from which the isotherm was generated.

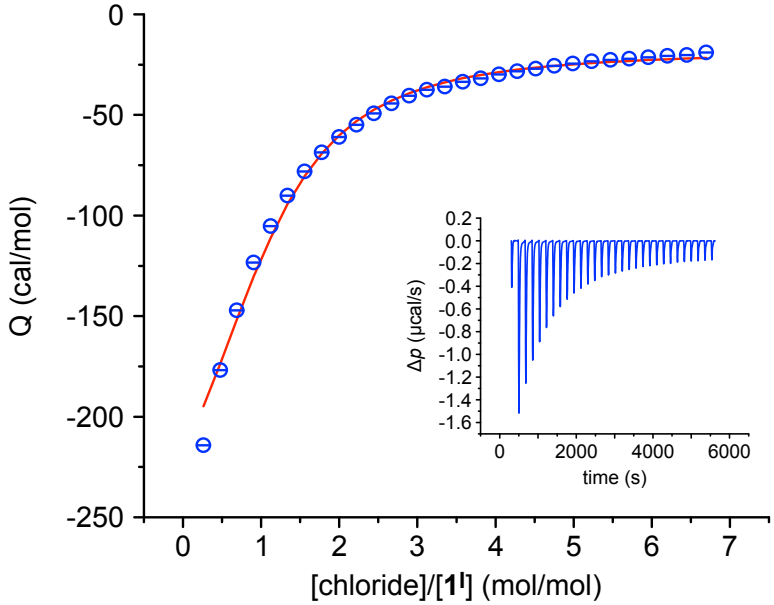


Table S2. Comparison of the anion affinity of **1^{I}** in 2.5 vol% H_2O/DMSO-d_6 with that of the corresponding prototriazole derivative **1^{H}** in 2.5 vol% D_2O/DMSO-d_6.[2]

anion	**1^{I}**	**1^{H}**
chloride	log $K_{1:1}$ = 3.28	no binding detectable in solution
bromide	log $K_{1:1}$ = 2.85	no binding detectable in solution
iodide	log $K_{1:1}$ = 2.15	no binding detectable in solution
DHP	no binding detectable in solution	log $K_{1:1}$ = 3.21; log $K_{1:2}$ = 3.10[a]
sulfate	complex binding equilibrium saturation is reached only in the presence of 12 equiv of TBA sulfate	log $K_{1:1}$ = 4.22; log $K_{2:1}$ < 2.1[b]

[a] binding constant referring to the formation of a 1:2 complex with two DHP anions binding to one pseudopeptide; [b] binding constant referring to the formation of a 2:1 complex with two pseudopeptides binding to one sulfate anion.

References

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2 D. Mungalpara, H. Kelm, A. Valkonen, K. Rissanen, S. Keller and S. Kubik, *Org. Biomol. Chem.*, 2017, **15**, 102-113.

3 C. Frassineti, S. Ghelli, P. Gans, A. Sabatini, M. S. Moruzzi and A. Vacca, *Anal. Biochem.*, 1995, **231**, 374-382.

4 (a) S. Keller, C. Vargas, H. Zhao, G. Piszczek, C. A. Brautigam and P. Schuck, *Anal. Chem.*, 2012, **84**, 5066-5073; (b) J. C. D. Houtman, P. H. Brown, B. Bowden, H. Yamaguchi, E. Appella, L. E. Samelson and P. Schuck, *Protein Sci.*, 2007, **16**, 30-42; (c) G. Krainer, J. Broecker, C. Vargas, J. Fanghänel and S. Keller, *Anal. Chem.*, 2012, **84**, 10715-10722; (d) G. Krainer, S. Keller, *Methods*, 2015, **76**, 116-123.