Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

The Use of Multicomponent Reactions in the Development of Bis-boronic Acids for the Detection of β-Sialic Acid

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Table of Content

1 Synthetic section

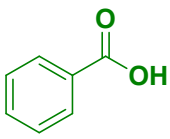
1.1 General information

Unless stated otherwise, all solvents and materials utilized were obtained from Sigma-Aldrich, TCI, Acros, Alfa Aesar, and AK Scientific and were employed without additional purification. As described in the literature, the isocyanides were synthesized following established procedures from aldehydes. The reactions were conducted in sealed vessels using the CEM Discover Benchmate™ microwave reactor. An external IR sensor was employed to monitor the temperatures during microwave-assisted reactions. Merck precoated silica gel 60 F254 plates (KGaA, Darmstadt, Germany) were used for thin-layer chromatography, while column chromatography was carried out using SiliaFlash® P60 silica gel with a particle size of 40-63µm (230-400 mesh).

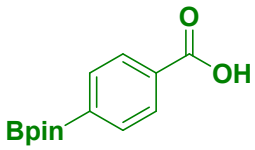
Nuclear magnetic resonance (NMR) spectra were obtained on a Bruker Avance 600 MHz spectrometer, with 600 MHz, 150 MHz, and 192.5 MHz frequencies for ^{1}H, ^{13}C, and ^{11}B, respectively. In ^{1}H NMR, chemical shifts were referenced to the internal solvent peak ($CDCl_3$ δ 7.26 ppm or CD_3OD δ 3.31 ppm), and coupling constants were reported in hertz (Hz). The spin multiplicities were denoted: s = singlet, d = doublet, t = triplet, m = multiplet, and br = broad. For ^{13}C NMR, chemical shifts were referenced to the internal solvent peak ($CDCl_3$ δ 77.16 ppm or CD_3OD δ 49.00 ppm). Chemical shifts for ^{11}B NMR were referenced to external standards ($BF_3 \cdot OEt_2$ δ 0.00 ppm). High-resolution mass spectra (HRMS) were acquired using a MICROMASS® Q-Tof PREMIER™ (Waters, ESI pos. mode) and Bruker Autoflex™ Speed Maldi-TOF/TOF instrument.

1.2 Starting Materials

Carboxylic acids

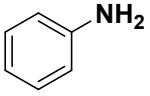


K1

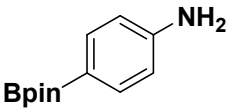


K2

Amines



L1



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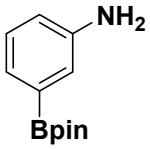
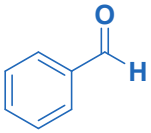
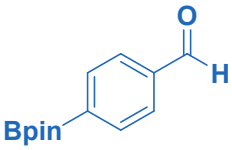


L2

Aldehydes



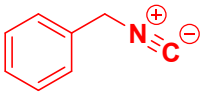
M1



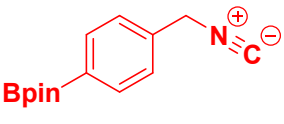
M2

M3

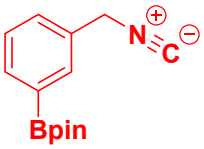
Isocyanides



N1



N2



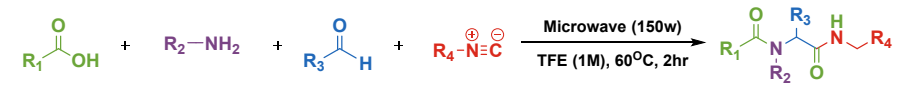
N3

Except for isocyanide **N1** and **N2** and **N3**, all starting carboxylic acids, amines, and aldehydes used in the study were commercially available. As described in the literature, isocyanide **N1**, **N2** and **N3** were synthesized following established procedures from aldehydes.

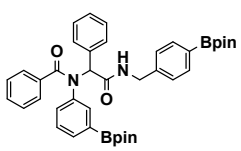
Experimental procedure of products a1-a5, b1-b3, c1, d1-d3 and e1-e2

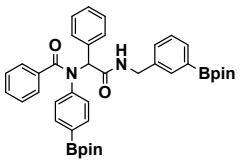
General procedure for synthesis of mono-boronate ester and bis-boronate ester analogues of five series.

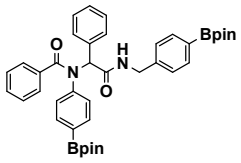
In a 10 mL glass tube equipped with a magnetic stir bar, amine **L** (1.0 mmol, 1.0 equiv), aldehyde **M** (1.0 mmol, 1.0 equiv), and 2,2,2-trifluoroethanol (1.0 mL) were initially stirred. The mixture was subjected to microwave irradiation for 15 minutes at 60 °C and 150 W, while being vigorously stirred. Following this, carboxylic acid **K** (1.2 mmol, 1.2 equiv) and isocyanide **N** (1.0 mmol, 1.0 equiv) were added. The reaction mixture was further exposed to microwave irradiation for 120 minutes at 65 °C and 150 W, under high-speed magnetic stirring. Once the reaction was complete, the crude material was concentrated and dissolved in dichloromethane. The resulting organic solution was then extracted with 1 M $HCl_{(aq)}$. Addition of a saturated aqueous solution of $NaHCO_{3(aq)}$ along with brine followed. The organic layer was subsequently dried using anhydrous $MgSO_4$ and concentrated under vacuum. The resulting residue was purified through silica gel flash column chromatography, using ethyl acetate/n-hexane (3/7) eluent initially, and acetone/methanol (13/1) eluent thereafter, to yield the desired products of a to e series in yields ranging from 31% to 75%

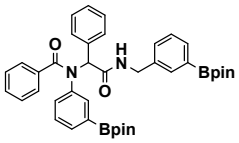


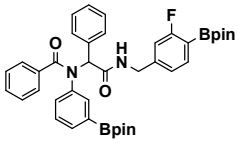
(a)


a1 75 %

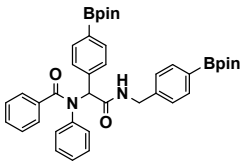

a2 59 %

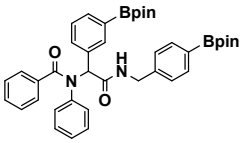

a3 45 %

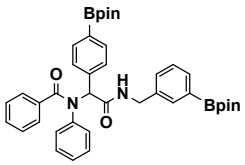

a4 42 %


a5 62 %

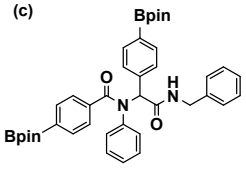
(b)


b1 60 %

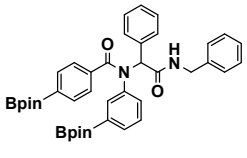

b2 60 %

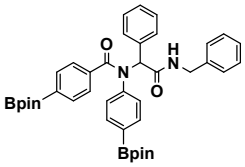

b3 31 %

(c)

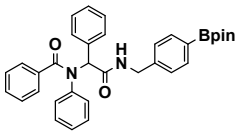

c1 41 %

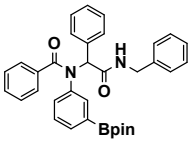
(d)

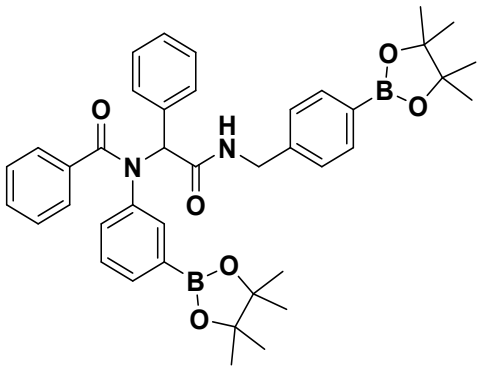

d1 56 %


d2 64 %

(e)


e1 51 %

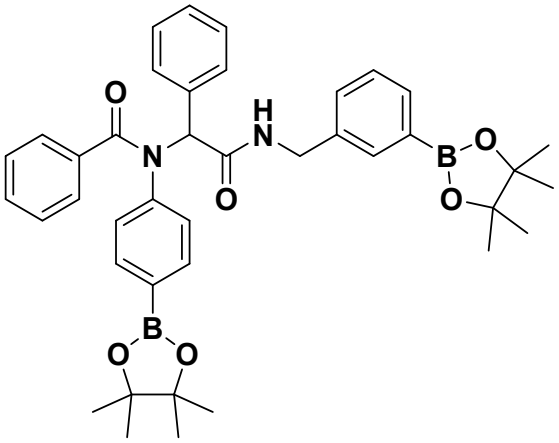

e2 54 %



a1

N-(2-oxo-1-phenyl-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)ethyl)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

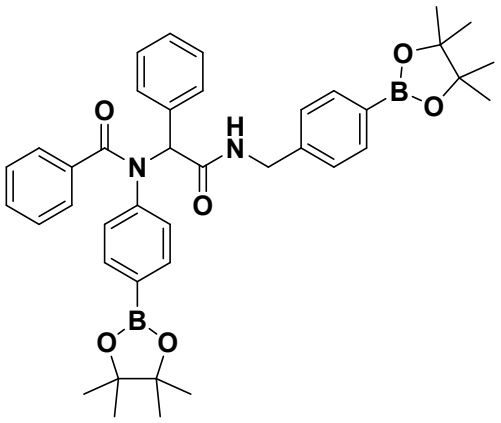
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 1H), 7.46 (br, 1H), 7.45-7.29 (m, 4H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.22 (t, *J* = 3 Hz, 3H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 3H), 7.02 (t, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 6.09 (s, 1H), 4.55 (dd, *J* = 15, 6 Hz, 2H), 1.32 (s, 12H), 1.27 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.29, 169.53, 141.27, 141.15, 135.77, 135.56, 135.04, 123.61, 133.33, 132.99, 129.90, 129.42, 128.69, 128.46, 128.39, 127.91, 127.53, 126.77, 83.76, 83.67, 67.83, 43.71, 24.78, 24.60. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.53. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34273.



a2

N-(2-oxo-1-phenyl-2-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)ethyl)-N-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

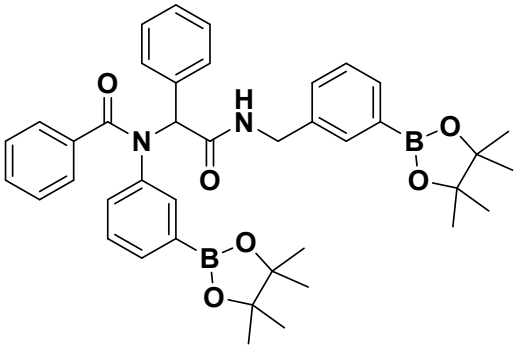
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (t, *J* = 6.9 Hz, 2H), 7.45 (d, *J* = 6.6 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 3H), 7.29 (t, *J* = 3.6 Hz, 1H), 7.28 (d, *J* = 6 Hz, 1H), 7.22 (t, *J* = 3 Hz, 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 2H), 6.99 (d, *J* = 7.8 Hz, 2H), 6.32 (t, *J* = 5.4 Hz, 1H), 6.19 (s,1H), 4.50 (d, *J* = 6 Hz, 2H), 1.32 (s, 12H), 1.29 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.18, 69.33, 144.11, 137.25, 135.75, 134.93, 134.44, 133.88, 133.77, 130.62, 129.98, 129.56, 129.15, 128.59, 128.45, 128.12, 127.63, 83.83, 83.78, 67.15, 43.74, 24.80, 24.77. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.36. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34323.



a3

N-(2-oxo-1-phenyl-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)ethyl)-N-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

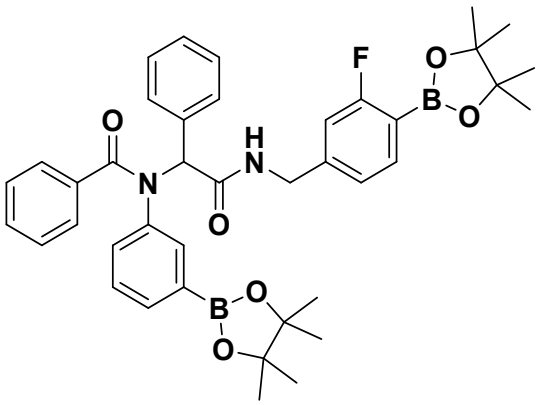
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J*= 7.8 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.32 (s, 1H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.28 (q, *J* = 3.6 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.23 (q, *J* = 3 Hz, 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.11 (q, *J* = 7.2 Hz, 2H), 6.99 (d, *J* = 7.8 Hz, 2H), 6.33 (br, 1H), 6.15 (s, 1H), 4.54 (qd, *J* = 15.6, 6 Hz, 2H), 1.33 (s, 12H), 1.28 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.16, 169.40, 144.21, 141.19, 135.74, 135.07, 134.96, 134.47, 129.95, 129.60, 129.12, 128.62, 128.53, 127.66, 126.84, 83.85, 67.35, 43.79, 24.80. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.19. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34335.



a4

N-(2-oxo-1-phenyl-2-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)ethyl)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

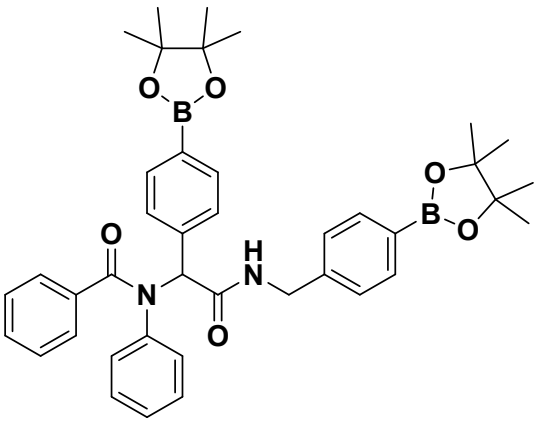
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, *J* = 10.2 Hz, 2H), 7.43 (dd, *J* = 21.9, 7.2 Hz, 2H), 7.31 (dd, *J* = 18, 7.8 Hz, 4H), 7.21 (d, *J* = 6.6 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.60 (br, 1H), 6.15 (s, 1H), 4.57-4.50 (m, 2H), 1.32 (s, 12H), 1.27 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.31, 169.58, 141.06, 137.47, 135.92, 135.81, 134.69, 133.89, 133.73, 133.32, 133.23, 130.61, 130.05, 129.42, 128.73, 128.48, 128.36, 128.13, 127.91, 127.57, 83.77, 67.56, 43.67, 43.54, 24.86, 24.65. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.34. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34356.



a5

N-(2-((3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)-2-oxo-1-phenylethyl)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

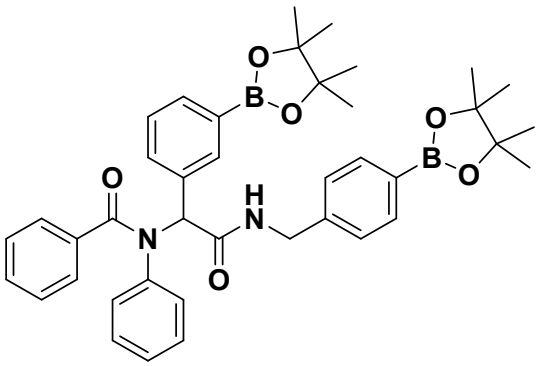
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (t, *J* = 6.9 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.39-7.30 (m, 5H), 7.24 (t, *J* = 2.7 Hz, 3H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.10 (q, *J* = 7.2 Hz, 3H), 7.03 (q, *J* = 7.2 Hz, 2H), 6.92 (d, *J* = 10.2 Hz, 1H), 6.54 (br, 1H), 6.05 (s, 1H), 4.53 (qd, *J* = 15.6, 6.6 Hz, 2H), δ 1.34 (s, 12H), δ 1.27 (d, *J* = 5.0 Hz, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.35, 169.73, 168.19, 166.52, 144.44, 144.38, 141.24, 137.14, 137.08, 135.68, 135.44, 134.53, 133.41, 132.94, 129.83, 129.54, 128.76, 128.58, 128.51, 128.01, 127.60, 122.50, 114.16, 114.00, 83.81, 68.07, 43.14, 24.85, 24.77, 24.63. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 30.67. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{45}B_2N_2O_6FNa$, 713.33400; found 713.33398.



b1

N-(2-oxo-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)-N-phenylbenzamide

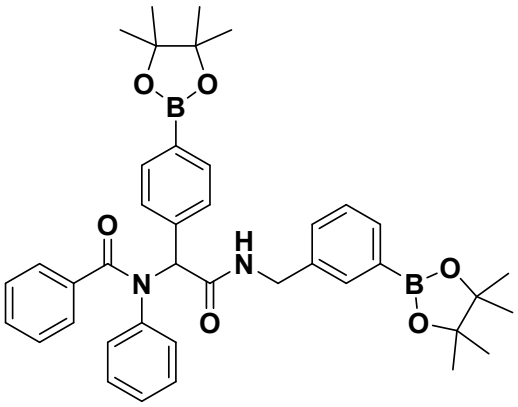
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.32 (q, *J* = 3.6 Hz, 4H), 7.28 (s, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 2H), 7.03 (s, 3H), 7.01 (br, 2H), 6.26 (br, 1H), 6.17 (s, 1H), 4.56 (qd, *J* = 15, 6 Hz, 2H), 1.35 (s, 12H), 1.34 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.24, 169.34, 141.12, 137.51, 135.12, 134.96, 129.98, 129.50, 129.28, 128.57, 128.54, 127.58, 127.19, 126.88, 83.92, 93.74, 67.34, 43.86, 24.83. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.37. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34380.



b2

N-(2-oxo-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)-N-phenylbenzamide

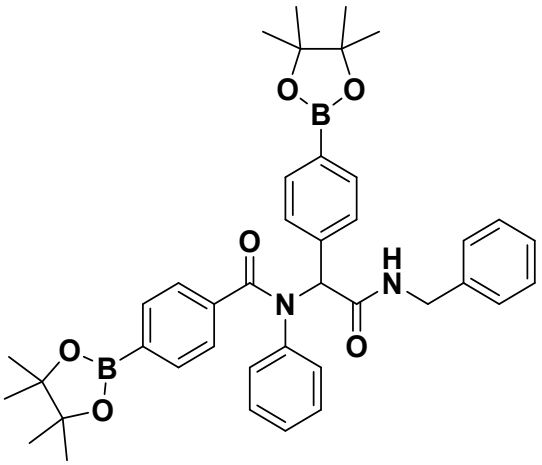
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 4.8 Hz, 2H), 7.71 (s, 1H), 7.66 (d, *J*= 7.2 Hz, 2H), 7.29 (t, *J* = 9 Hz, 3H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.17 (q, *J* = 8.4 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 2H), 6.98 (s, 5H), 6.29 (t, *J* = 5.7 Hz, 1H), 6.26 (s, 1H), 4.53 (qd, *J* = 15, 5.4 Hz, 2H), 1.32 (s, 12H), 1.3 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.22, 169.68, 141.28, 141.09, 136.86, 136.05, 135.10, 134.94, 133.81, 132.90, 130.54, 129.38, 128.54, 128.34, 127.88, 127.55, 127.14, 126.81, 83.93, 83.71, 66.65, 43.77, 24.96, 24.85, 24.76. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 30.86. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34538.



b3

N-(2-oxo-2-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)-N-phenylbenzamide

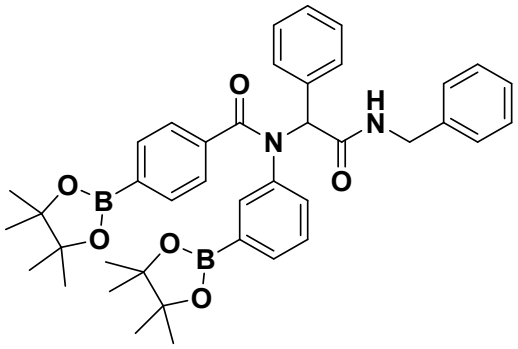
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 4H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.30 (dd, *J* = 7.2, 1.8 Hz, 5H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 2H), 7.00 (s, 5H), 6.313 (t, *J* = 5.7 Hz, 1H), 6.20 (s, 1H), 4.53 (qd, *J* = 15, 6 Hz, 2H), 1.33 (s, 12H), 1.31 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.22, 169.27, 141.38, 137.49, 137.21, 135.87, 134.90, 133.87, 133.77, 130.60, 130.01, 129.41, 129.30, 128.51, 128.44, 128.10, 127.52, 127.11, 83.83, 83.77, 67.08, 43.75, 24.80. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.19. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34407.



c1

N-(2-(benzylamino)-2-oxo-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)-N-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide

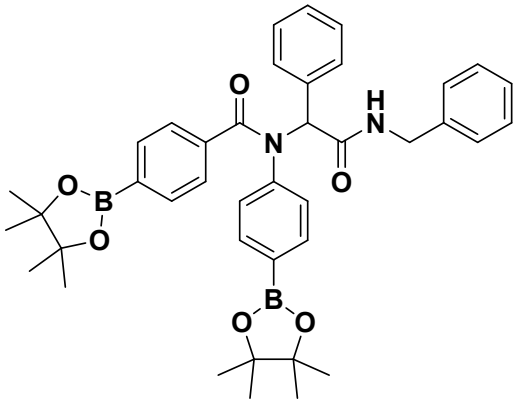
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 5H), 7.27 (s, 1H), 7.25-7.22 (m, 3H), 6.99 (s, 1H), 6.39 (br, 1H), 6.17 (s, 1H), 4.54-4.47 (m, 2H), 1.30 (d, *J* = 18.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.20, 169.33, 143.93, 138.28, 138.03, 135.00, 134.43, 134.02, 130.03, 129.17, 128.60, 128.55, 127.66, 127.60, 127.34, 83.88, 67.22, 43.81, 24.87, 24.82. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.50. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34451.



d1

N-(2-(benzylamino)-2-oxo-1-phenylethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

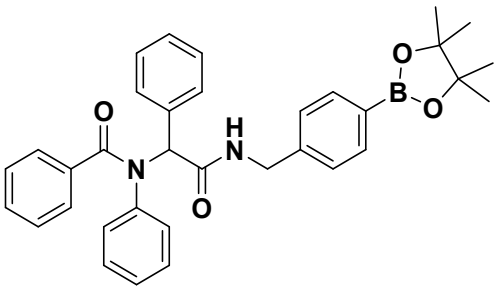
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.31 (s, 2H), 7.29 (dd, *J* = 10.5, 3.6 Hz, 6H), 7.24-7.22 (m, 5H), 7.10 (br, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.41 (br, 1H), 6.08 (s, 1H), 4.57-4.51 (m, 2H), 1.28 (d, *J* = 3 Hz, 18H), 1.27 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.34, 169.47, 140.90, 138.38, 138.12, 135.68, 134.59, 133.95, 133.47, 133.13, 130.04, 129.97, 129.47, 128.71, 128.59, 128.50, 128.45, 128.01, 127.76, 127.58, 127.29, 83.86, 83.79, 67.71, 43.76, 24.87, 24.81, 24.63. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.58. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34522.



d2

N-(2-(benzylamino)-2-oxo-1-phenylethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

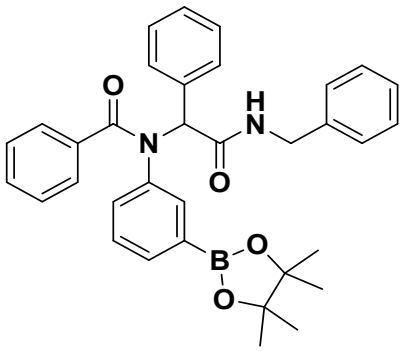
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 4.8 Hz, 2H), 7.30-7.28 (m, 6H), 7.27 (s, 2H), 7.26-7.12 (m, 4H), 6.97 (d, *J* = 7.2 Hz, 2H), 6.28 (br, 1H), 6.15 (s, 1H), 4.53 (d, *J* = 5.4 Hz, 2H), 1.30 (d, *J* = 2.4 Hz, 24H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.20, 169.33, 143.93, 138.28, 138.03, 135.00, 134.43, 134.02, 130.03, 129.17, 128.60, 128.56, 127.66, 127.60, 127.34, 83.89, 67.21, 43.81, 24.87, 24.82. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.42. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{40}H_{46}B_2N_2O_6Na$, 695.34342; found 695.34518.



e1

N-(2-oxo-1-phenyl-2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)amino)ethyl)-N-phenylbenzamide

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.25-7.18 (m, 7H), 7.15 (dd, *J* = 6.6, 1.8 Hz, 1H), 7.1 (td, *J* = 7.2, 1.2 Hz, 1H), 7.0 (s, 1H), 6.70 (br, 1H), 6.25 (s, 1H), 4.50 (qd, *J* = 15, 6 Hz, 2H), 1.33 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.11, 169.64, 141.26, 140.98, 135.78, 134.89, 134.38, 130.22, 130.04, 129.28, 128.96,128.79, 128.71, 128.38, 128.28, 128.14, 127.95, 127.40, 127.18, 126.95, 126.63, 126.22, 115.49, 83.56, 83.44, 66.54, 43.50, 43.22, 24.69.^{11}B NMR (192.5 MHz, $CDCl_3$) δ 31.41. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{34}H_{35}BN_2O_4Na$, 569.25821; found 569.25839.



e2

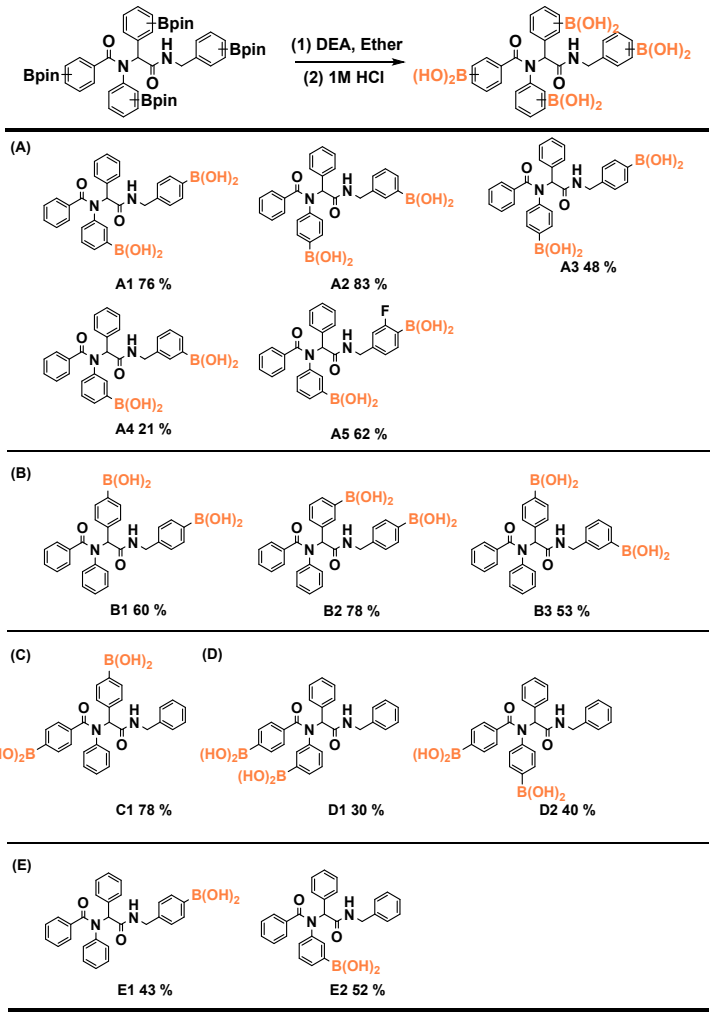
N-(2-(benzylamino)-2-oxo-1-phenylethyl)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzamide

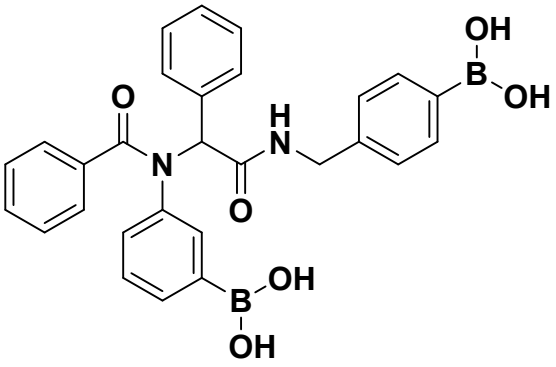
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.2 Hz, 1H), 7.34 (br, 1H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.29-7.22 (m, 6H), 7.20 (d, *J* = 3 Hz, 4H), 7.14 (dd, *J* = 6.6, 2.4 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.66 (br, 1H), 6.14 (d, *J* = 3 Hz, 1H), 4.51 (d, *J* = 3.6 Hz, 2H), 1.27 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.20, 169.52, 140.82, 138.10, 135.75, 134.54, 133.18, 133.03, 129.95, 129.25, 128.51, 128.37, 128.27, 128.23, 127.71, 127.40, 127.37, 127.14, 127.03, 83.62, 67.31, 43.50, 24.72, 24.49. ^{11}B NMR (192.5 MHz, $CDCl_3$) δ 30.67. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{34}H_{35}BN_2O_4Na$, 569.25821; found 569.25894.

1.4. Experimental procedure of products A1-A5, B1-B3, C1, D1-D2 and E1-E2

General procedure for synthesis of Ugi boronic acid analogues **A1-A5, B1-B3, C1, D1-D2** and **E1-E2.**

Boronate ester compounds **a1-a5**, **b1-b3**, **c1**, **d1-d2 and e1-e2** (0.5 mmol, 1.0 equiv), a stirring bar, diethanolamine (0.5 mmol, 1.0 equiv), and 5.00 mL of ether were added to the round-bottom flask. The reaction mixture was allowed to react at room temperature for at least 8 hours until solid precipitation occurred. The resulting solid was then filtered under vacuum, and the liquid was removed. The solid was redissolved in the original round-bottom flask, and the solvent was removed under reduced pressure. A stirring bar, 15.00 mL of 1 M HCl, and 5.00 mL of MeOH were added to the residue. The reaction mixture was allowed to react at room temperature for at least 8 hours. After completion of the reaction, the bottle opening was sealed with clean paper and secured with a rubber band. The bottle was then immersed in liquid nitrogen until the entire solution had frozen into a solid. Subsequently, the bottle was placed in a freeze dryer to remove HCl and MeOH. The resulting solid was then subjected to EA/HCl extraction, and the organic layer was treated with anhydrous magnesium sulfate to remove H_2O, followed by filtration under a vacuum. The solvent was removed under reduced pressure by rotary evaporation. Finally, the product was subjected to freeze-drying. The desired products were obtained in yields ranging from 30% to 78%, as confirmed by ^{1}H NMR, ^{11}B NMR, and ^{13}C NMR spectroscopy.

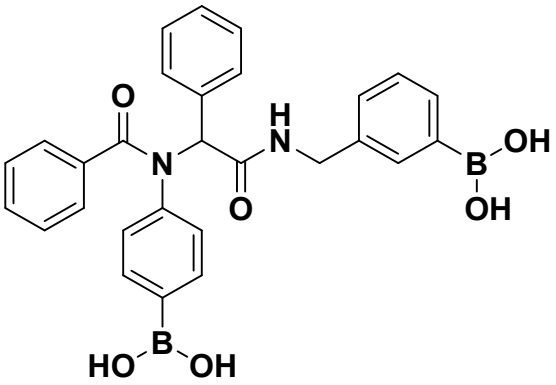




A1

(3-(N-(2-((4-boronobenzyl)amino)-2-oxo-1-phenylethyl)benzamido)phenyl)boronic acid

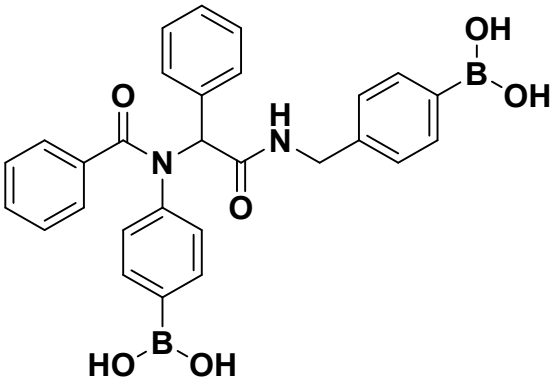
^{1}H NMR (600 MHz, CD_3OD) δ 7.52 (br, 1H), 7.32 (br, 2H), 7.25 (s, 4H), 7.20-7.16 (m, 4H), 7.12 (q, *J* = 7.2 Hz, 3H), 6.97 (br, 1H), 6.32 (s, 1H), 4.43 (q, *J* = 9.6 Hz, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.49, 172.27, 143.02, 139.71, 138.99, 135.49, 134.54, 134.05, 131.74, 131.32, 129.41, 129.36, 129.22, 128.68, 128.31, 128.20, 128.00, 67.18, 44.18. ^{11}B NMR (192.5 MHz, CD_3OD) δ 28.98. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18764.



A2

(4-(N-(2-((3-boronobenzyl)amino)-2-oxo-1-phenylethyl)benzamido)phenyl)boronic acid

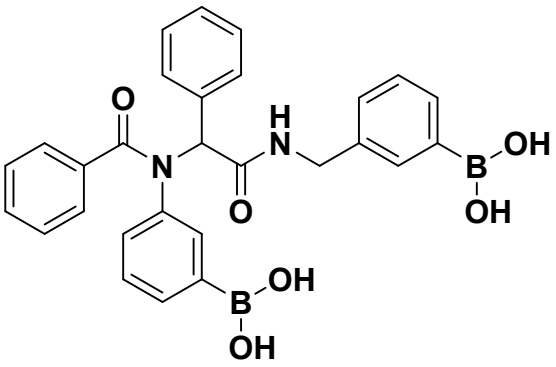
^{1}H NMR (600 MHz, CD_3OD) δ 7.76-7.44 (m, 2H), 7.30 (t, *J* = 8.1 Hz, 4H), 7.240 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 6 Hz, 3H), 7.13 (q, *J* = 7.8 Hz, 5H), 6.96 (br, 2H), 6.30 (s, 1H), 4.51-4.40 (m, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.48, 172.43, 138.69, 137.55, 135.57, 134.61, 134.18, 133.93, 133.64, 133.40, 133.18, 131.82, 131.36, 130.54, 130.28, 129.82, 129.42, 129.28, 128.72, 67.38, 67.20, 44.34. ^{11}B NMR (192.5 MHz, CD_3OD) δ 27.40. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18754.



A3

(4-((2-(N-(4-boronophenyl)benzamido)-2-phenylacetamido)methyl)phenyl)boronic acid

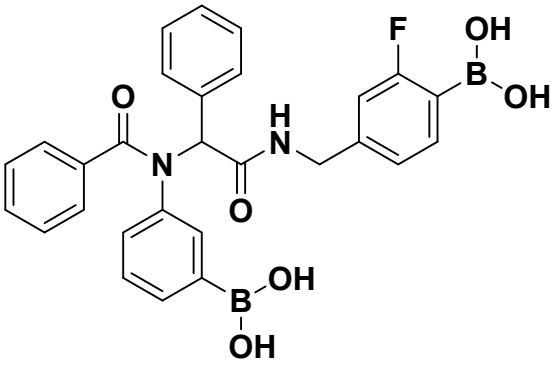
^{1}H NMR (600 MHz, CD_3OD) δ 7.66 (d, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 6.6 Hz, 1H), 2.90 (d, *J* = 7.8 Hz, 4H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.20-7.17 (m, 9H), 6.30 (s, 1H), 4.46 (s, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.50, 172.43, 137.64, 135.62, 135.06, 134.72, 134.60, 131.85, 131.62, 131.42, 130.54, 129.47, 129.28, 128.74, 127.62, 127.49, 67.27, 44.23. ^{11}B NMR (192.5 MHz, CD_3OD) δ 29.08. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18761.



A4

(3-((2-(N-(3-boronophenyl)benzamido)-2-phenylacetamido)methyl)phenyl)boronic acid

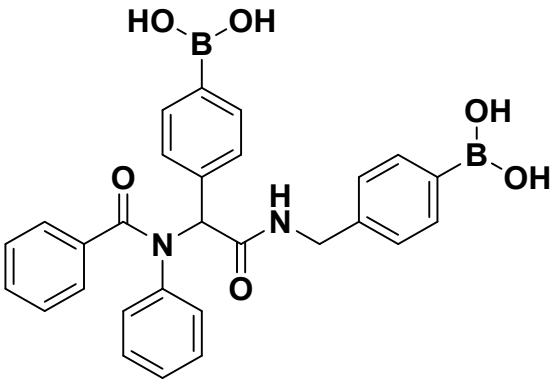
^{1}H NMR (600 MHz, CD_3OD) δ 7.87-7.20 (m,1H), 6.10 (d, *J* = 6.6 Hz, 1H), 7.55-7.49 (m, 1H), 7.30 (t, *J* = 9 Hz, 4H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 3H), 7.13 (q, *J* = 7.8 Hz, 6H), 6.93 (br, 1H), 6.31 (br, 1H), 4.53-4.41 (m, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.61, 172.51, 137.67, 135.66, 133.94, 133.64, 133.39, 133.19, 131.88, 130.45, 130.28, 129.80, 129.39, 129.30, 128.73 67.27, 44.34. ^{11}B NMR (192.5 MHz, CD_3OD) δ 28.77. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18765.



A5

(3-(N-(2-((4-borono-3-fluorobenzyl)amino)-2-oxo-1-phenylethyl)benzamido)phenyl)boronic acid

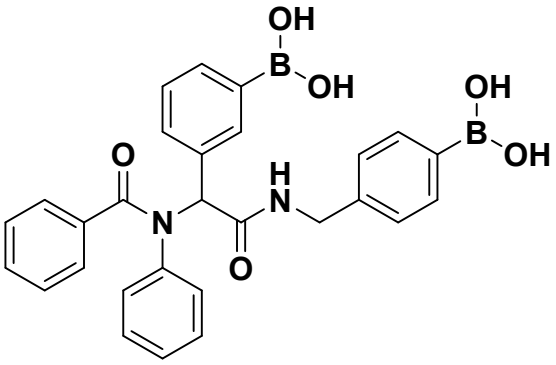
^{1}H NMR (600 MHz, CD_3OD) δ 7.33-7.30 (m, 2H), 7.29 (s, 1H), 7.28 (d, *J* = 1.8 Hz, 1H), 7.15 (tt, *J* = 7.8, 16.8 Hz, 11H), 6.96 (br, 2H), 6.28 (d, *J* = 23.4 Hz, 1H), 4.46 (s, 2H).^{13}C NMR (150 MHz, CD_3OD) δ 172.17, 171.24, 136.22, 134.16, 131.99, 130.45, 129.03, 128.07, 127.30, 122.52, 113.16, 112.99, 65.97, 65.74, 42.18. ^{11}B NMR (192.5 MHz, CD_3OD) δ 29.21. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6FNa$, 549.17750; found 549.17750.



B1

(4-(2-((4-boronobenzyl)amino)-2-oxo-1-(N-phenylbenzamido)ethyl)phenyl)boronic acid

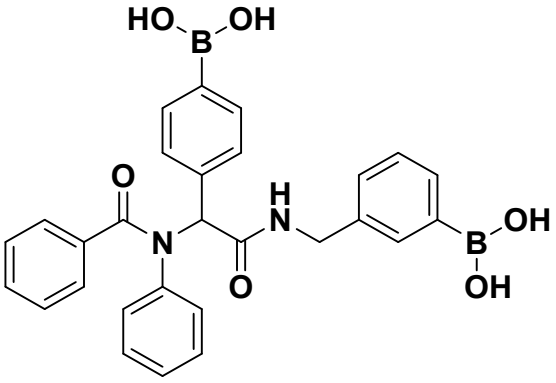
^{1}H NMR (600 MHz, CD_3OD) δ 7.66 (br, 1H), 7.53 (br, 2H), 7.38 (br, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.24 (br, 2H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 4H), 7.00 (br, 2H), 6.90 (d, 3.6 Hz, 3H), 6.30 (s, 1H), 4.60 (s, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.59, 172.37, 141.45, 137.66, 135.05, 134.75, 134.36, 132.44, 130.99, 130.47, 129.23, 129.04, 128.73, 128.29, 127.51, 67.24, 44.21. ^{11}B NMR (192.5 MHz, CD_3OD) δ 29.31. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18694.



B2

(4-((2-(3-boronophenyl)-2-(N-phenylbenzamido)acetamido)methyl)phenyl)boronic acid

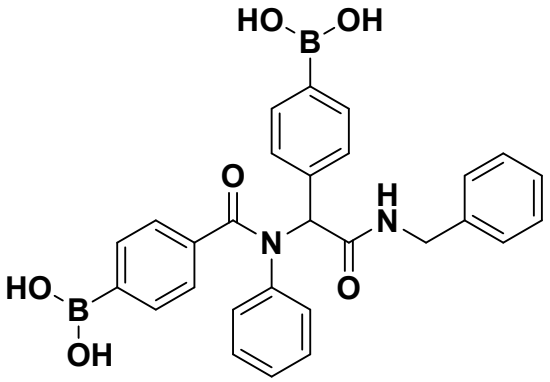
^{1}H NMR (600 MHz, CD_3OD) δ 7.65 (br, 2H), 7.59 (br, 2H), 7.28 (d, *J* = 7.8 Hz), 7.24 (t, *J* = 6.3 Hz, 2H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 3H), 7.09 (br, 1H), 6.98 (br, 2H), 6.91 (s, 3H), 6.32 (t, *J* = 17.4 Hz, 1H), 4.55-4.39 (m, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.65, 172.53, 141.34, 137.63, 135.03, 134.66, 133.48, 132.43, 130.46, 129.17, 129.03, 128.92, 128.73, 128.46, 128.25, 127.49, 67.35, 44.22. ^{11}B NMR (192.5 MHz, CD_3OD) δ 28.38 HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18746.



B3

(3-((2-(4-boronophenyl)-2-(N-phenylbenzamido)acetamido)methyl)phenyl)boronic acid

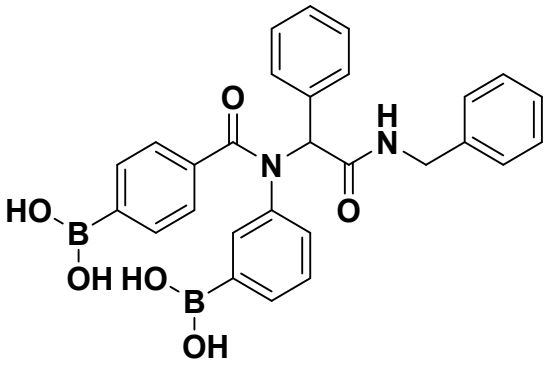
^{1}H NMR (600 MHz, CD_3OD) δ 7.76 (s, 1H), 7.61 (d, *J* = 6.6 Hz, 1H), 7.26 (s, 1H), 7.58 (d, *J* = 12.6 Hz, 1H), 7.30 (t, *J* = 9 Hz, 3H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 1.8 Hz, 4H), 7.00 (br, 1H), 6.91 (s, 3H), 6.30 (s, 1H), 4.53-4.04 (m, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.59, 172.37, 141.47, 138.69, 137.59, 134.78, 134.34, 133.94, 133.64, 133.15, 132.39, 130.95, 130.48, 130.30, 129.26, 129.04, 128.72, 128.28, 67.36, 44.35. ^{11}B NMR (192.5 MHz, CD_3OD) δ 29.68. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18653.



C1

(4-(2-(benzylamino)-1-(4-borono-N-phenylbenzamido)-2-oxoethyl)phenyl)boronic acid

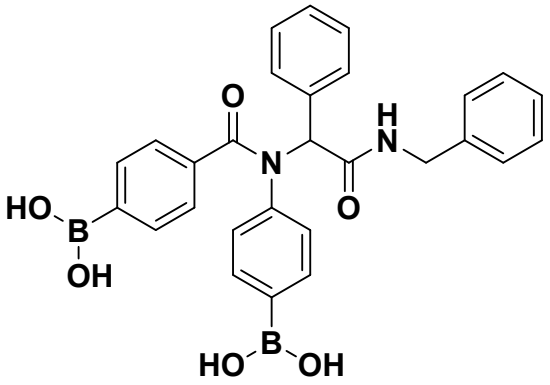
^{1}H NMR (600 MHz, CD_3OD) δ 7.56 (br, 2H), 7.28 (d, *J* = 4.2 Hz, 6H), 7.22 (d, *J* = 4.2 Hz, 1H), 7.20 (d, *J* = 4.2 Hz, 2H), 7.18 (s, 1H), 7.03 (br, 2H), 6.93 (s, 3H), 6.33 (s, 1H), 4.47 (t, *J* = 16.8 Hz, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.71, 172.33, 141.40, 139.85, 134.80, 134.12, 132.43, 131.01, 129.46, 129.08, 128.43, 128.36, 128.25, 128.10, 67.26, 44.28. ^{11}B NMR (192.5 MHz, CD_3OD) δ 27.22 HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18637.



D1

(4-((2-(benzylamino)-2-oxo-1-phenylethyl)(3-boronophenyl)carbamoyl)phenyl)boronic acid

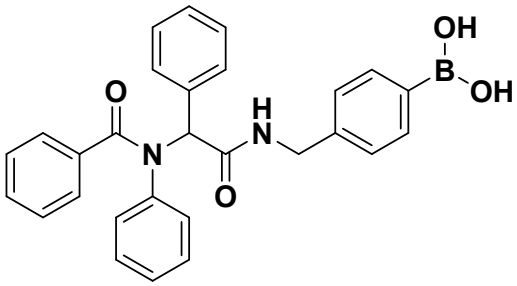
^{1}H NMR (600 MHz, CD_3OD) δ 7.59-7.46 (br, 1H), 7.41-7.36 (br, 2H), 7.32 (br, 1H), 7.29 (d, *J* = 4.2 Hz, 5H), 7.23 (q, *J* = 4.2 Hz, 1H), 7.19 (t, *J* = 6.9 Hz, 3H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.06-7.03 (br, 1H), 6.96-6.88 (br, 1H), 6.36 (s, 1H), 4.49 (s, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.64, 172.48, 139.86, 135.69, 131.90, 129.44, 129.31, 128.42, 128.31, 128.08, 67.20, 44.27. ^{11}B NMR (192.5 MHz, CD_3OD) δ 27.54 HRMS (ESI, negative ion)(*m/z*): $[M - H]^-$, calcd for $C_{28}H_{25}B_2N_2O_6$, 507.19042; found 507.19079.



D2

(4-((2-(benzylamino)-2-oxo-1-phenylethyl)(4-boronophenyl)carbamoyl)phenyl)boronic acid

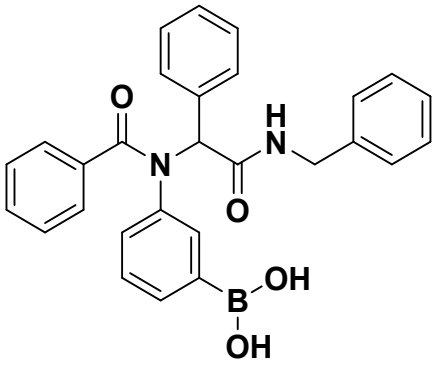
^{1}H NMR (600 MHz, CD_3OD) δ 7.54-7.52 (br, 1H), 7.34 (br, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.28 (s, 2H), 7.27 (d, *J* = 1.8 Hz, 2H), 7.26-7.20 (m, 4H), 7.15 (q, *J* = 7.2Hz, 3H), 7.00 (br, 1H), 6.34 (s, 1H), 4.47 (q, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.58, 173.50, 172.38, 139.86, 135.64, 134.63, 134.13, 131.87, 131.46, 130.60, 139.51, 129.48, 129.33, 128.80, 128.45, 128.33, 128.11, 67.30, 44.30. ^{11}B NMR (192.5 MHz, CD_3OD) δ 27.46. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{26}B_2N_2O_6Na$, 531.18692; found 531.18725.



E1

(4-((2-phenyl-2-(N-phenylbenzamido)acetamido)methyl)phenyl)boronic acid

^{1}H NMR (600 MHz, CD_3OD) δ 7.69 (s, 1H), 7.55 (s, 1H), 7.29 (d, *J* =7.2 Hz, 2H), 7.25 (br, 2H), 7.18 (q, *J* = 7.2 Hz, 4H), 7.15-7.11 (m, 5H), 7.00 (br, 1H), 6.91 (s, 3H), 6.33 (s, 1H), 4.46 (q, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.58, 172.48, 141.45, 137.69, 135.66, 135.11, 132.49, 131.90, 130.50, 129.48, 129.31, 129.25, 129.07, 128.77 128.30, 127.54, 67.25, 44.23. ^{11}B NMR (192.5 MHz, CD_3OD) δ 29.07. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{25}BN_2O_4Na$, 487.17996; found 487.18049.



E2

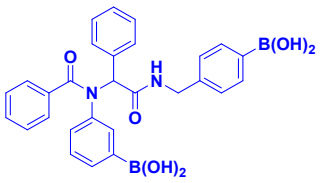
(3-(N-(2-(benzylamino)-2-oxo-1-phenylethyl)benzamido)phenyl)boronic acid

^{1}H NMR (600 MHz, CD_3OD) δ 7.29 (d, *J* = 7.2 Hz, 3H), 7.26 (s, 2H), 7.25 (d, *J* = 1.2 Hz, 2H), 7.24-7.18 (m, 2H), 7.17 (d, *J* = 3 Hz, 1H), 7.16 (d, *J* = 1.8 Hz, 2H), 7.15 (s, 1H), 7.13 (s, 2H), 7.12 (d, *J* = 3 Hz, 2H), 7.10 (d, *J* = 1.2 Hz, 1H), 6.93 (br, 1H), 6.29 (br, 1H), 4.45 (s, 2H). ^{13}C NMR (150 MHz, CD_3OD) δ 173.56, 172.44, 139.81, 137.68, 135.67, 131.85, 130.41, 129.39, 129.25, 128.71, 128.36, 128.02, 67.16, 44.20. ^{11}B NMR (192.5 MHz, CD_3OD) δ 28.01. HRMS (ESI, positive ion)(*m/z*): $[M + Na]^+$, calcd for $C_{28}H_{25}BN_2O_4Na$, 487.17996; found 487.17999.

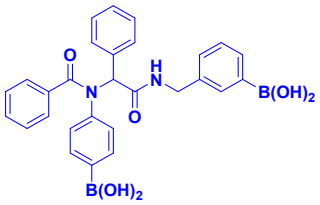
2 Analysis section

Materials of various boronic acid analogs investigated

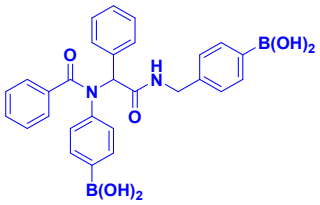
A series



A1



A2



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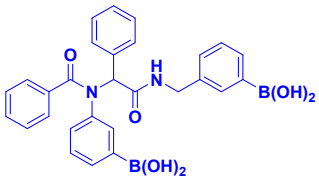
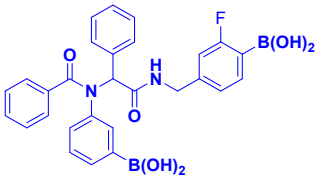
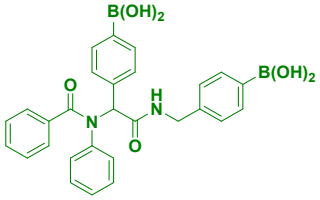


A4

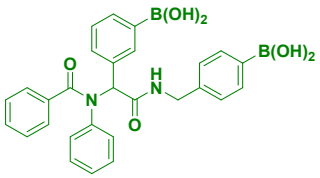


A5

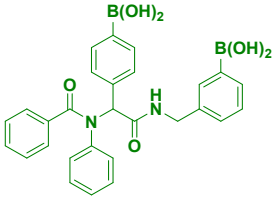
B series



B1

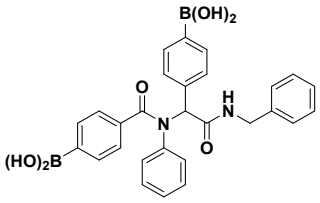


B2



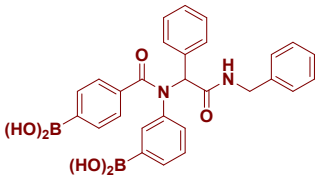
B3

C series

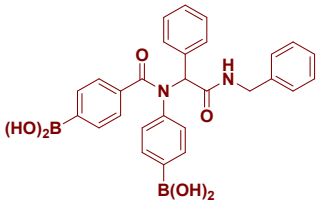


C1

D series

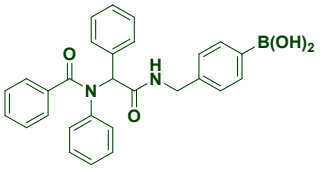


D1

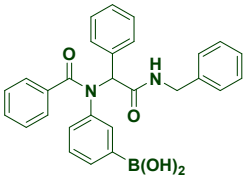


D2

E series



E1



E2

All materials utilized were synthesized and purified by the abovementioned procedure.

Measurements and Calculations of Binding Constant

The binding constants of ARS and boronic acid were determined through spectroscopic methods. ARS stock solution ($4.5x10^{-5}$ M) was prepared in deionized water and 0.5M stock sodium phosphate buffer at different pH levels (6.0, 6.5, 7.0, and 7.5). Mono- and bis-boronic acid stock solutions were prepared in both deionized water and DMSO/H_2O (8:2) for each boronic acid, while sialic acid or saccharide stock solutions were prepared in DMSO/H_2O (8:2).

Two 200 µl solutions were created from these stocks. The first solution contained boronic acid, phosphate buffer, water, and DMSO/H_2O (8:2). The second solution contained the same boronic acid solution, ARS, phosphate buffer, water, and sialic acid or saccharide dissolved in DMSO/H_2O (8:2). A non-fluorescent ARS standard was prepared as a solution of ARS and phosphate buffer in the absence of boronic acid and used as a fluorescent blank.

Fluorescence values were measured using a microplate analyzer, with samples excited at 468 nm and emission measured at 572 nm. In the first solution, fluorescence increased with boronic acid concentration, while in the second solution, fluorescence decreased with sugar concentration. The competition among boronic acid, ARS, and diol was leveraged to determine binding constants using a formula from the literature.

Stock solution concentration (M)

ARS	sodium phosphate buffer		Boronic acid	
$4.5x10^{-5}$	0.5		$2.25x10^{-3}$ ~ $1.25x10^{-4}$	
Sialic acid	pH 6.0	$6x10^{-2}$ ~ $2.8x10^{-2}$	Boronic acid	$4.5x10^{-4}$
	pH 6.5	$6x10^{-2}$ ~ $5x10^{-2}$		$5x10^{-4}$
	pH 7.0	$1x10^{-1}$ ~ $7x10^{-2}$		$1.25x10^{-4}$
	pH 7.5	$1x10^{-1}$ ~ $3x10^{-2}$		$4.5x10^{-4}$
Fructose	pH 6.0 and 6.5	$9x10^{-2}$ ~ $5x10^{-2}$		$5x10^{-4}$
	pH 7.0 and 7.5	$1x10^{-2}$ ~ $3.5x10^{-3}$		$2x10^{-3}$
Galactose	pH 7.0 and 7.5	$3x10^{-1}$ ~ $2.5x10^{-2}$		$2.5x10^{-4}$
Glucose	pH 7.0 and 7.5	$5x10^{-1}$ ~ $2.5x10^{-2}$		

- Plot of (1/ fluorescence intensity) against (1/ [BA])
- **K_{ARS} = intercept / slope**
- Plot of [Diol] / P against Q.

$$\text{Q value} = \frac{((F\,BA - ARS - blank) - (F\,BA - SA - blank))}{F\,BA - SA - blank}$$

$$\text{P value} = [BA] - \frac{1}{(Q\,x\,KARS)} - \frac{[ARS]}{(1+Q)}$$

- **K_{eq} = K_{ARS} / slope**

DFT calculations

All density functional calculations in this work were performed using the CAM-B3LYP functional as implemented in Gaussian 09. All atoms were described using the 6-31+G(d,p) basis set. Solvation energies were calculated using a polarized continuum model for the solvate containing dimethyl sulfoxide and water (9:16 ratio) with dielectric constant ε = 67.2 for all calculations. All optimized structures were characterized by vibrational frequency calculations. All optimized structures were characterized by vibrational frequency calculations, which are with zero imaginary frequency and obtained thermodynamically corrected at 298 K.

The reaction energy used to calculate the binding constant for bis-boronic acid binding to one sialic acid is defined as Equation A, where we consider the boronic acid compound as a whole:

$$\Delta G = G_{Ugi+SA} + G_{H2O} - (G_{Ugi} + G_{SA}) \quad \textbf{(Equation A)}$$

where G_{Ugi+SA} is the free energy of Ugi-SA complex. G_{Ugi}, G_{SA} and G_{H2O} are the energy of isolated Ugi structure, sialic acid and water molecule, respectively.

The reaction energy used to calculate the binding constant for bis-boronic acid binding to two sialic acids is defined as Equation B, where we consider the boronic acid compound as a whole:

$$\boxed{\Delta G = G_{Ugi+2SA} + 2G_{H2O} - (G_{Ugi} + 2G_{SA})} \quad \textbf{(Equation B)}$$

where $G_{Ugi+2SA}$ is the free energy of bis-boronic acids with two sialic acids complex (Ugi-2SA). G_{Ugi}, G_{SA} and G_{H2O} are the energy of isolated Ugi structure, sialic acid and water molecule, respectively.

$$\Delta G = \Delta E + \Delta E_{ZPE} - T\Delta S$$

This equation considers the factors such as zero-point energy (ΔE_{ZPE}) and entropy change (ΔS) to better represent the real-world scenarios accurately.

3 Supplementary Tables and Figures

1 Copies of ^{1}H NMR, ^{13}C NMR, ^{11}B NMR and Mass spectra

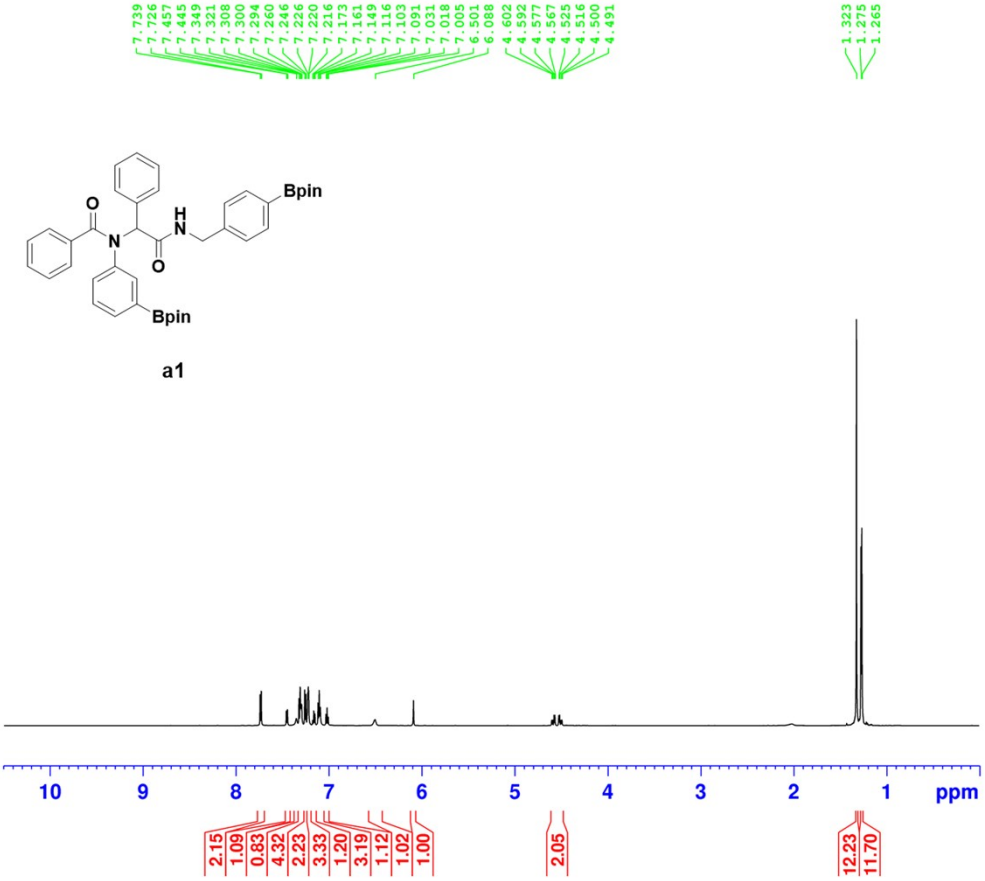
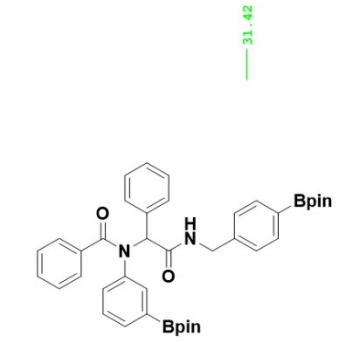


Figure S1. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **a1**
Figure S2. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **a1**



a1

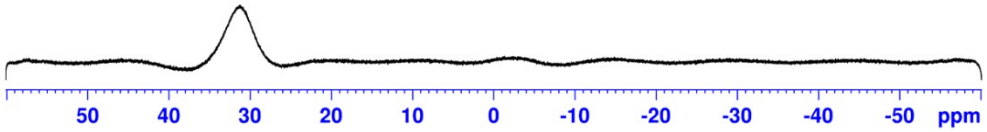
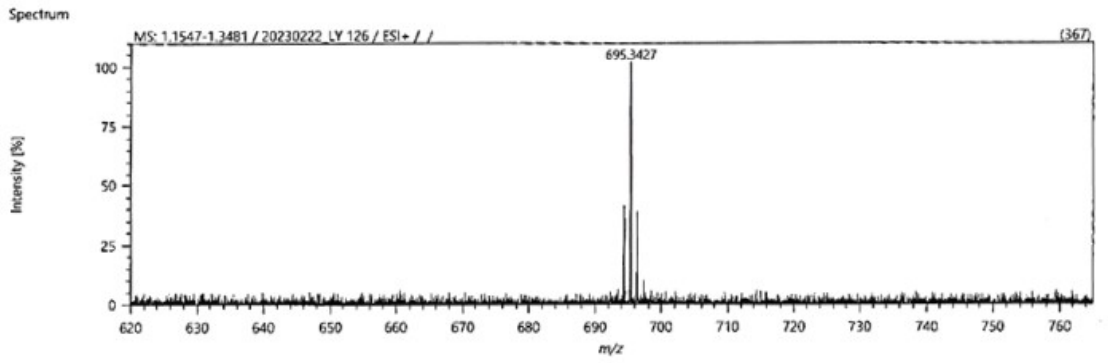


Figure S3. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound a1



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	Na	B
Electron:	Odd/Even	Min	0	0	6	2	1	2
Charge:	+1	Max	100	400	6	2	1	2
DBE:	-99.0 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
695.34273	C40 H46 B2 N2 O6 Na	695.34342	-0.69	-0.99	19.5

Figure S4. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **a1**

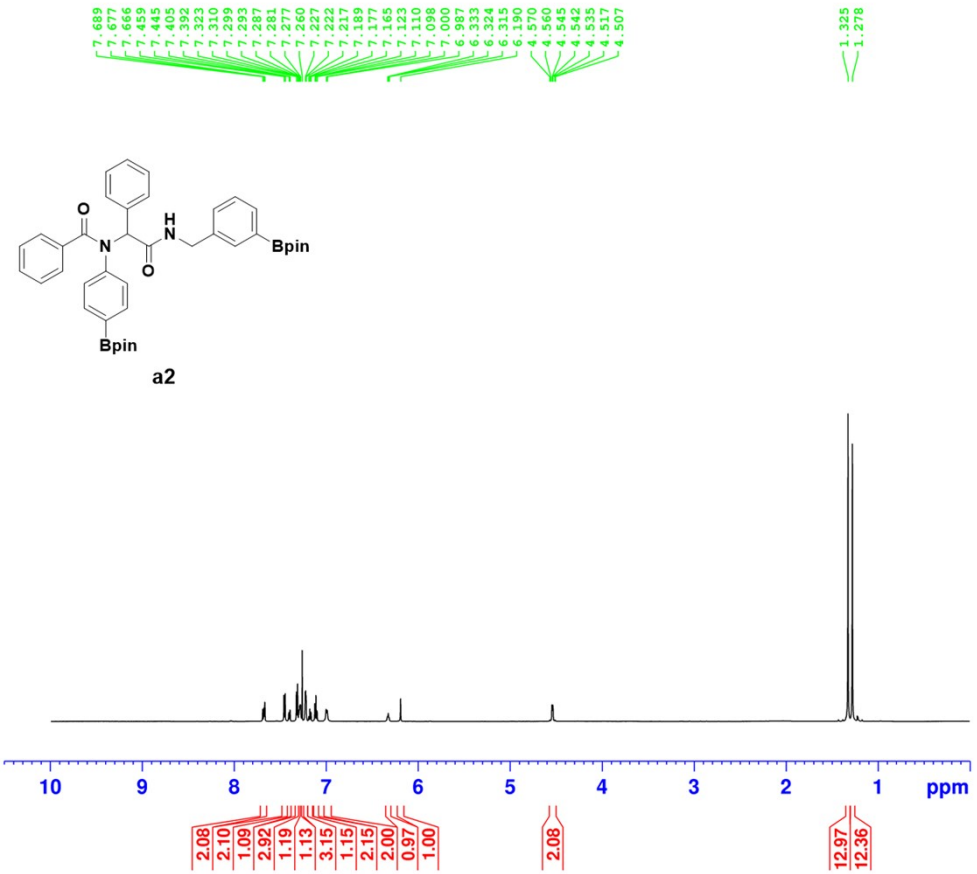


Figure S5. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **a2**

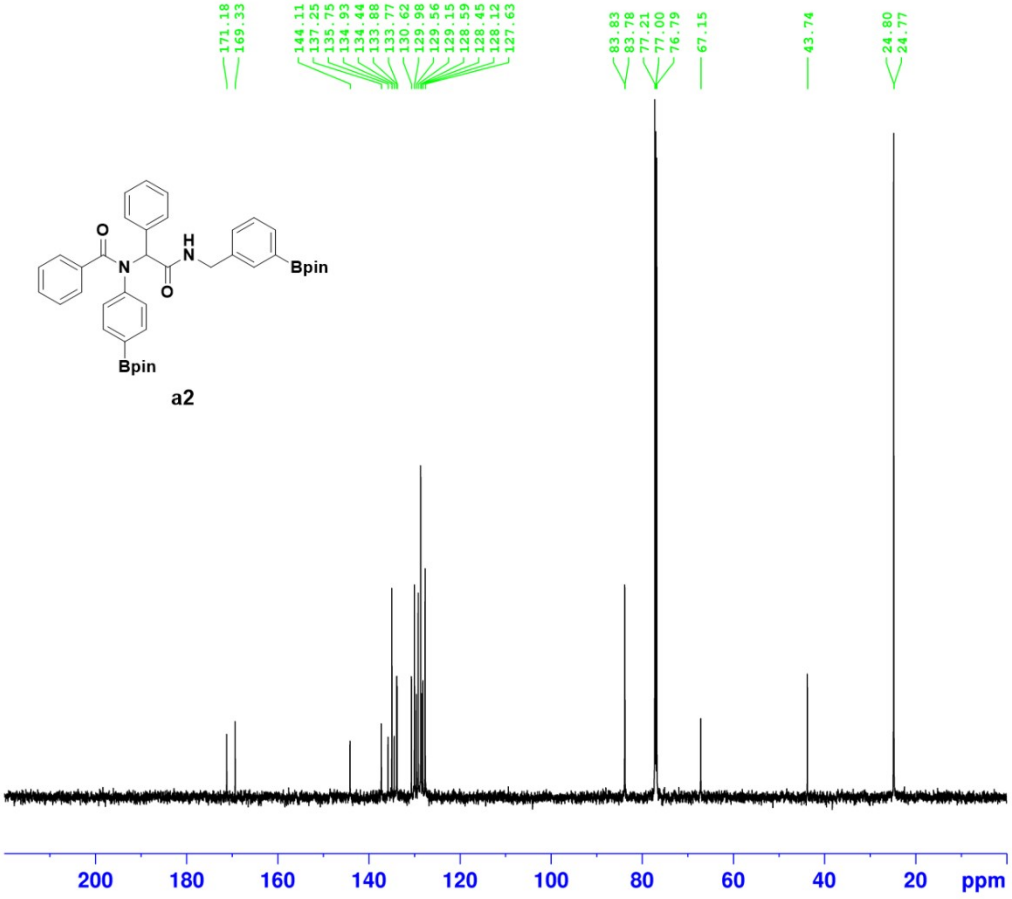


Figure S6. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **a2**

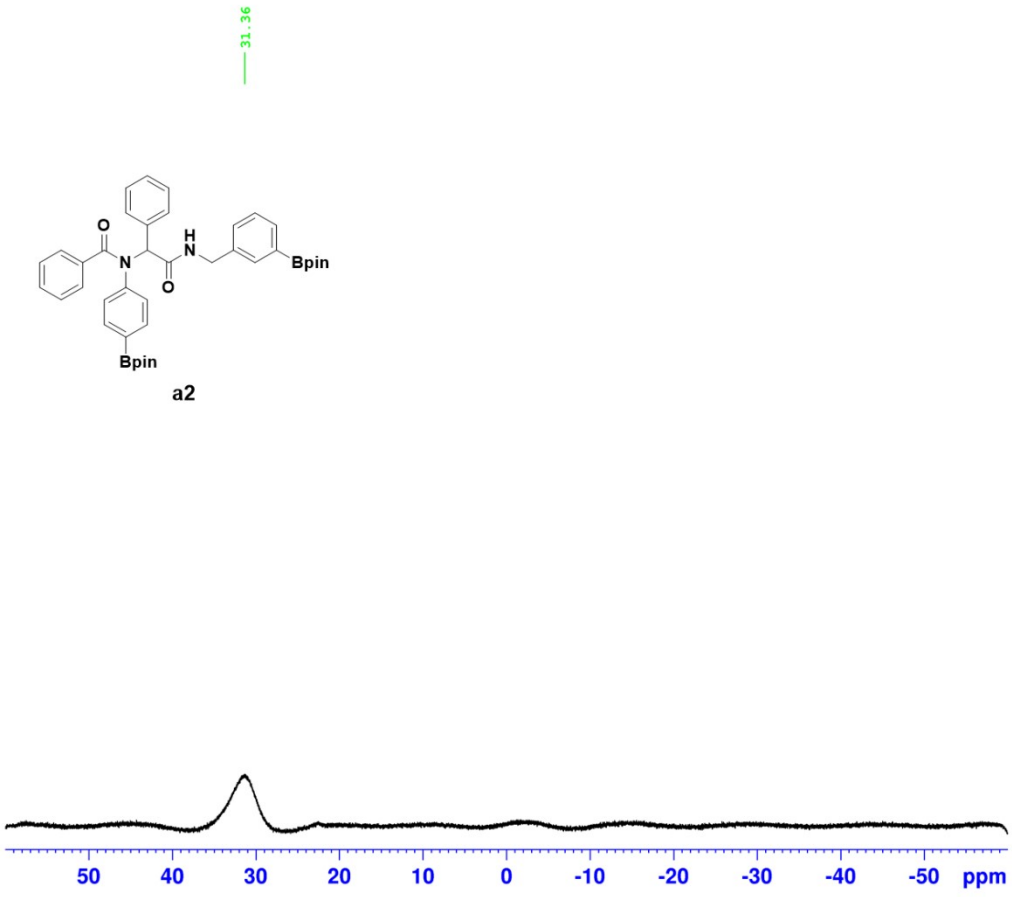


Figure S7. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound a2

Figure S8. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **a2**

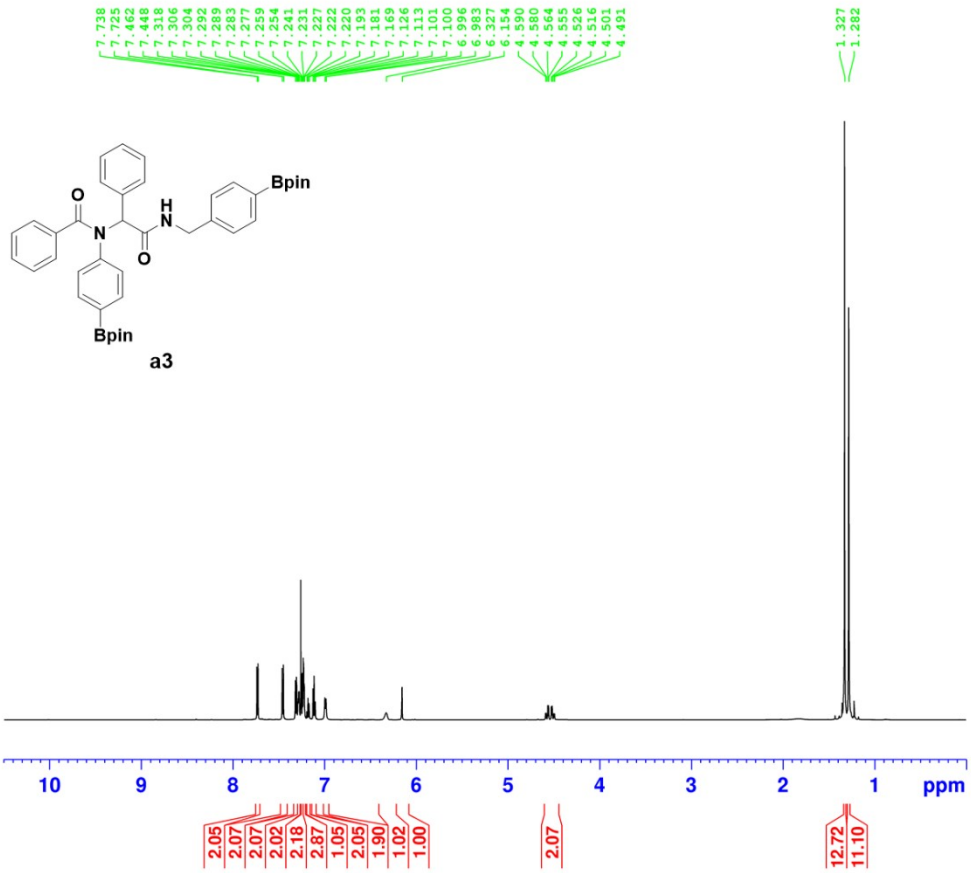


Figure S9. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **a3**

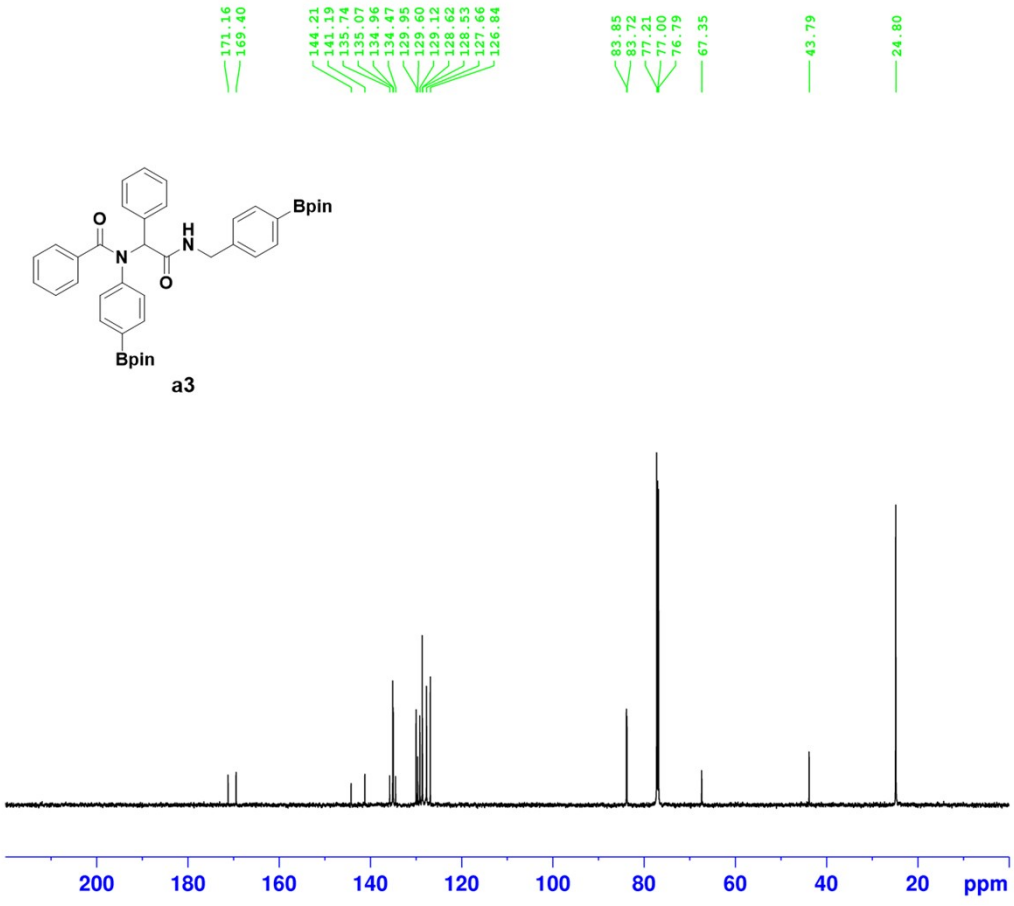


Figure S10. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **a3**

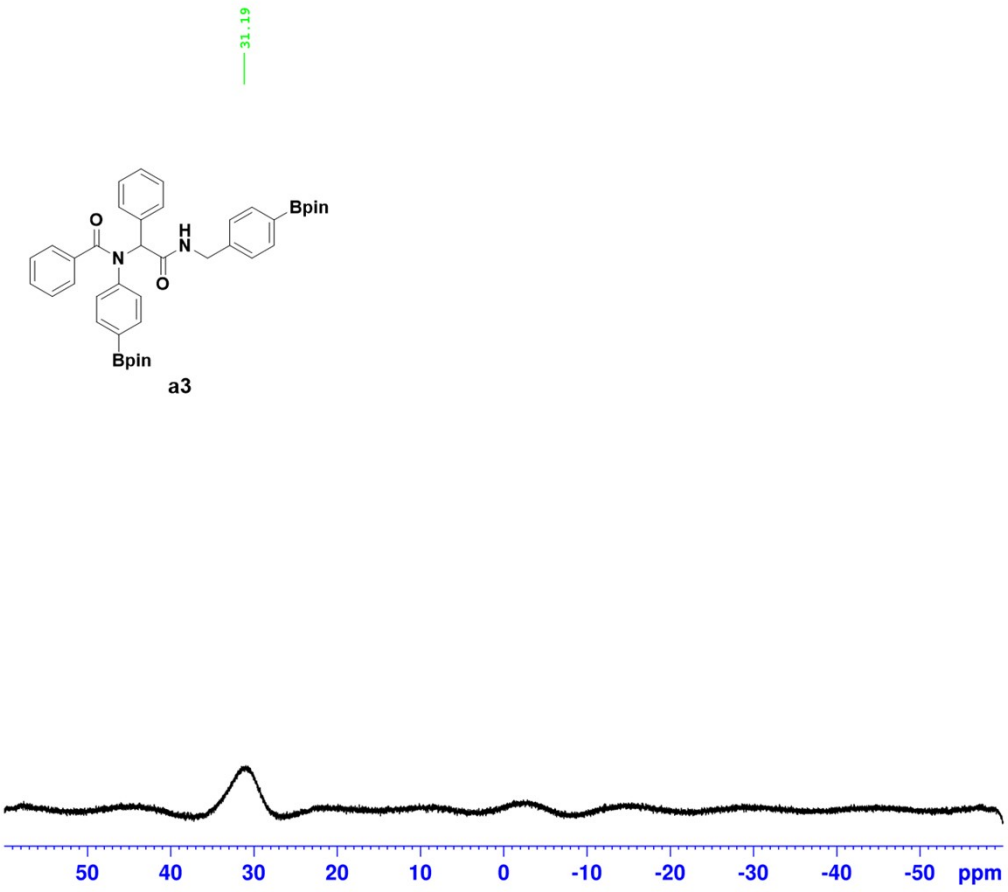


Figure S11. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound a3

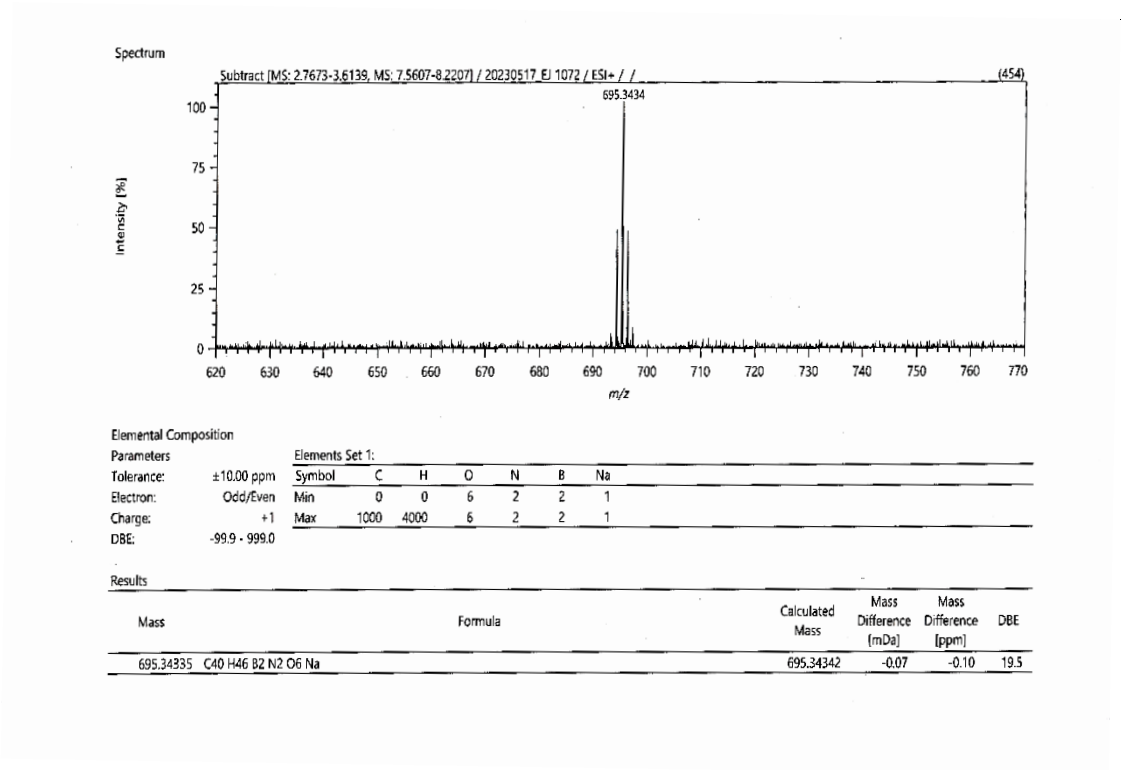


Figure S12. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **a3**

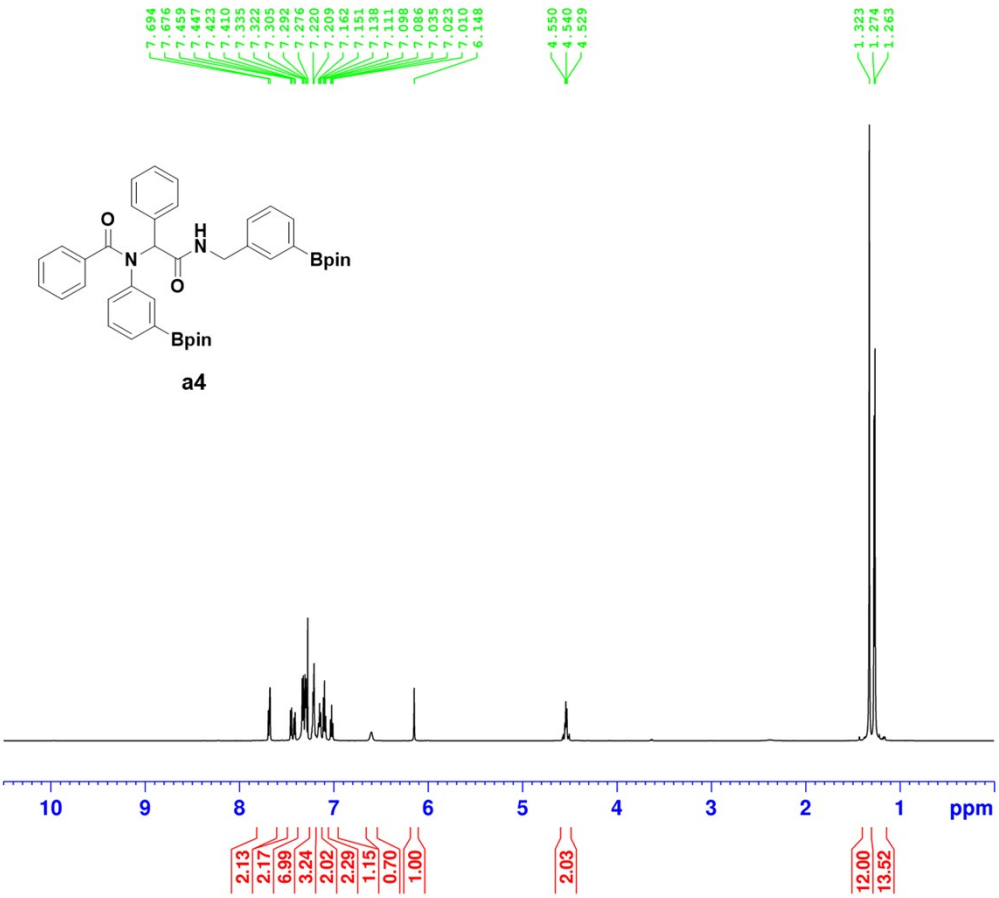


Figure S13. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **a4**

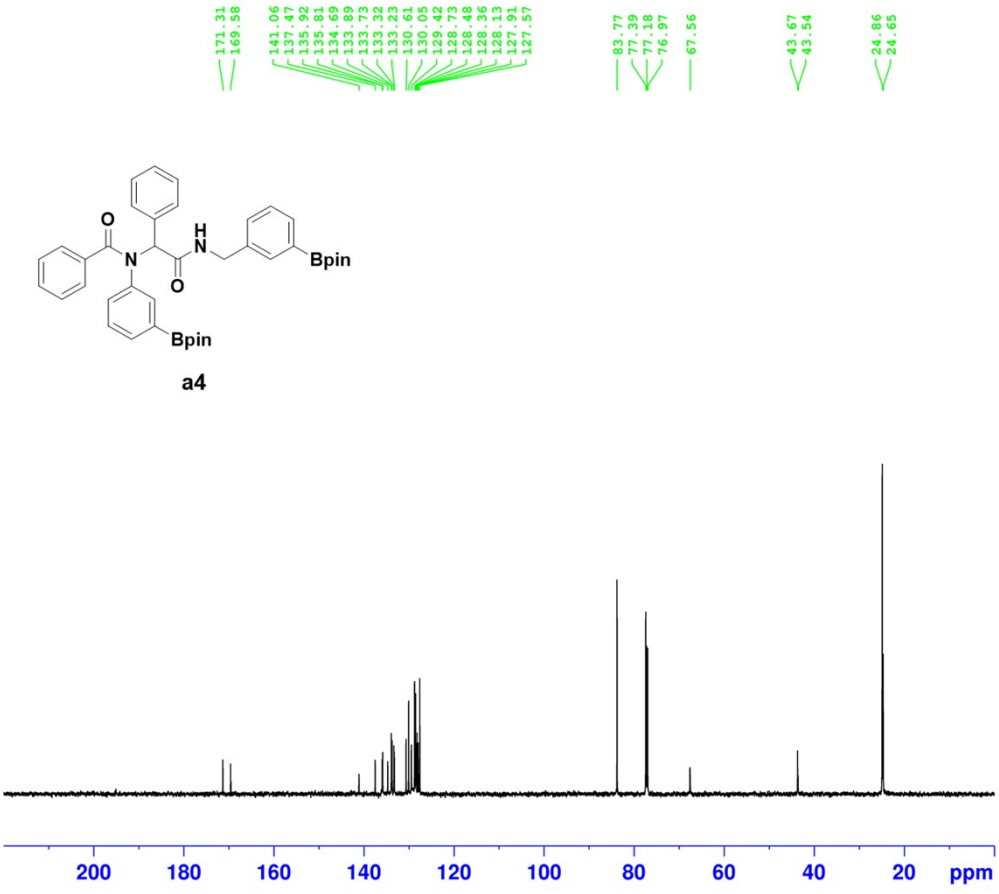
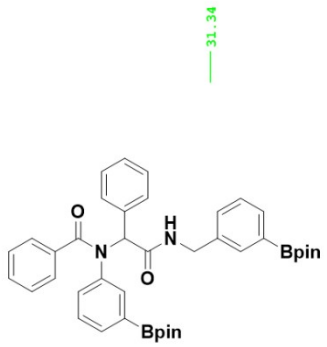


Figure S14. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **a4**



a4

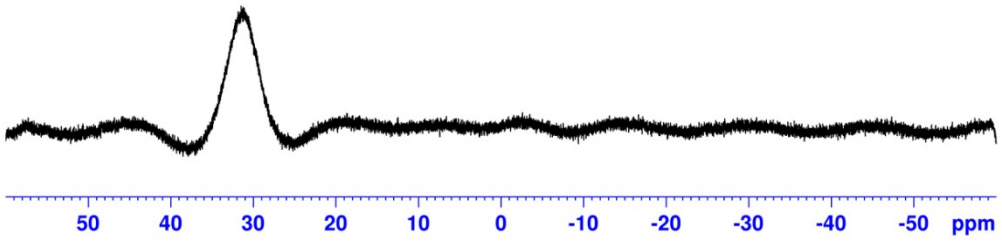
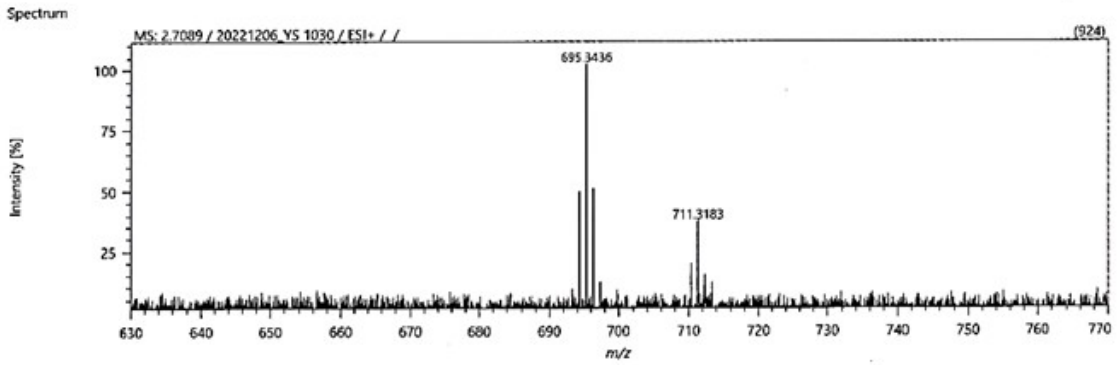


Figure S15. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound **a4**



Elemental Composition

Parameters		Elements Set 1:							
Tolerance:	±3.00 ppm	Symbol	C	H	O	N	B	Na	K
Electron:	Odd/Even	Min	0	0	6	2	2	0	0
Charge:	+1	Max	400	1000	6	2	2	1	1
DBE:	-99.0 - 999.0								

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
695.34356	C40 H46 B2 N2 O6 Na	695.34342	0.14	0.21	19.5
711.31833	C40 H46 B2 N2 O6 K	711.31736	0.97	1.36	19.5

Figure S16. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **a4**

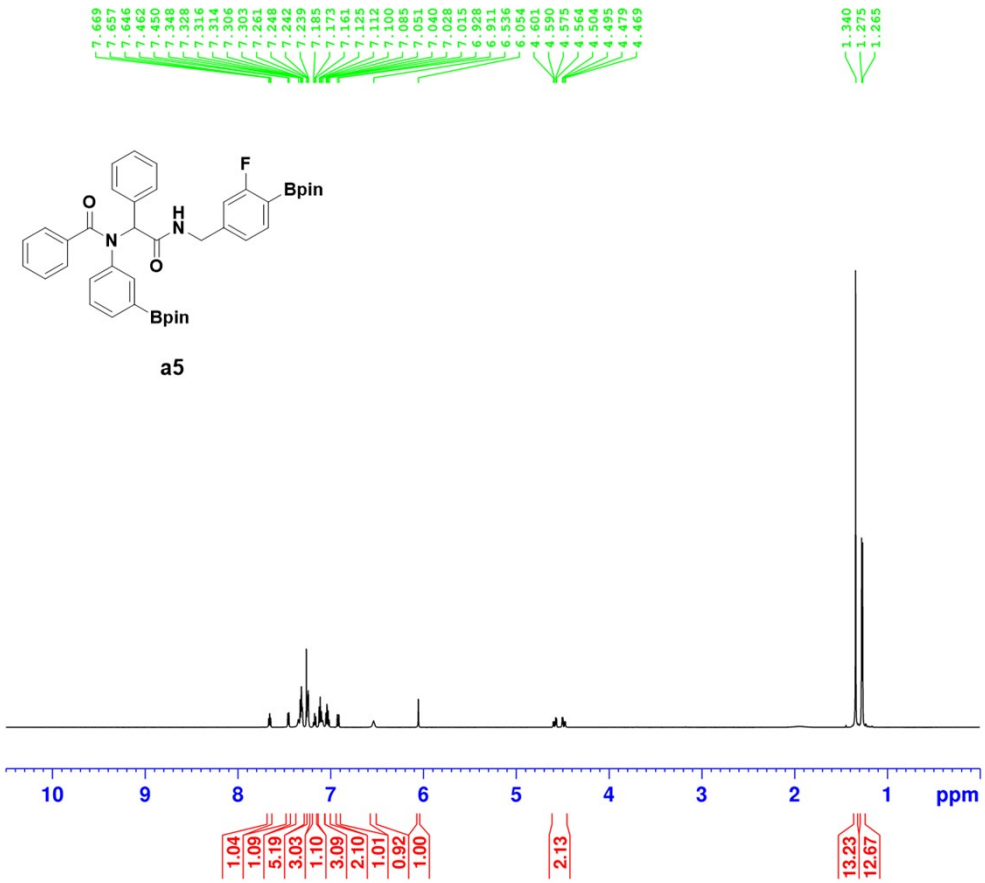


Figure S17. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **a5**

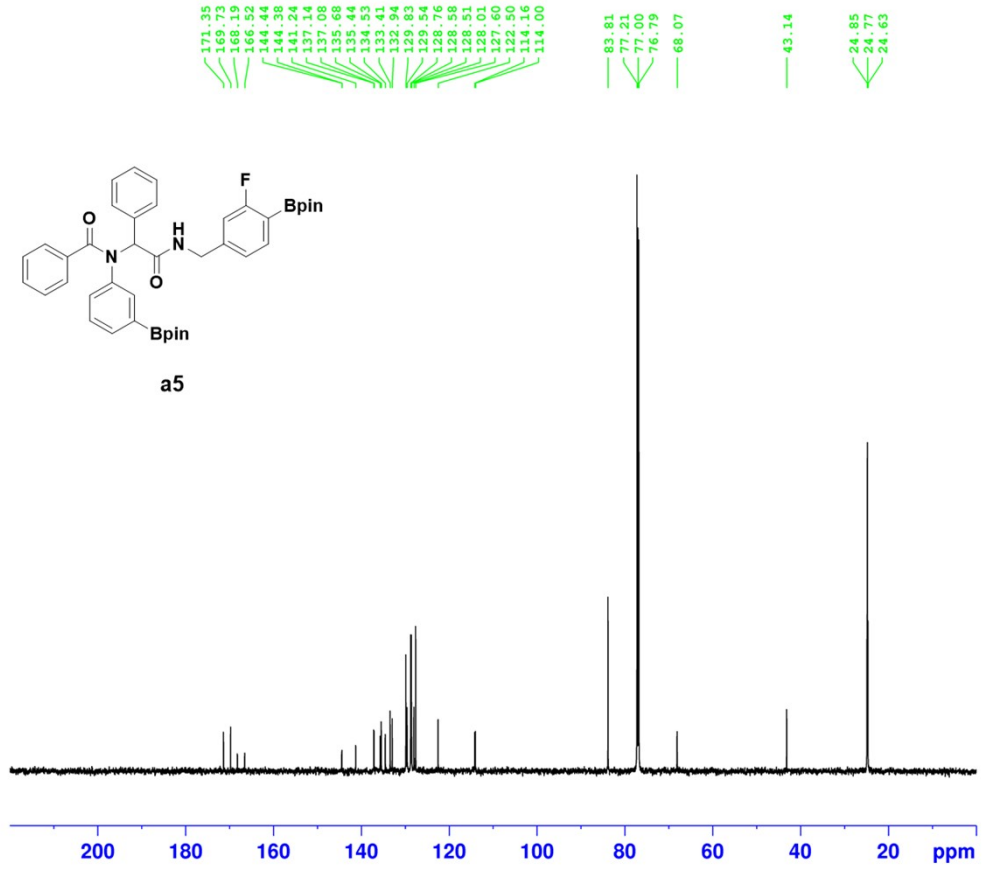


Figure S18. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **a5**

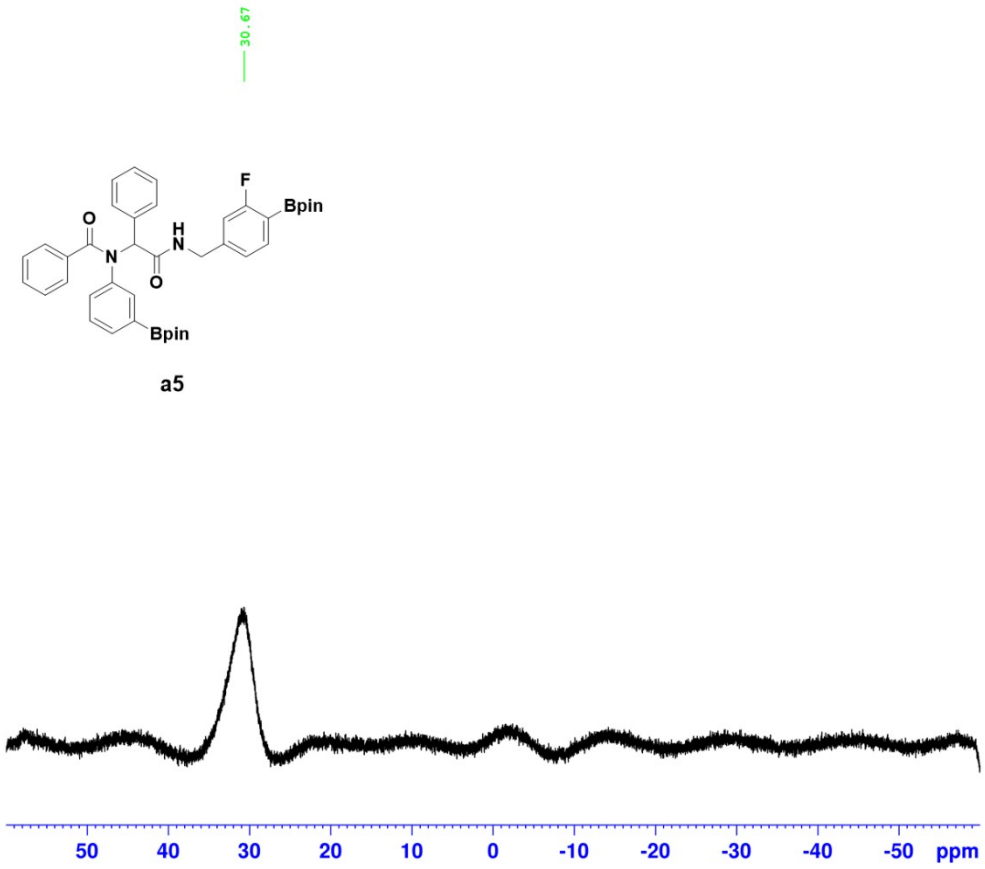


Figure S19. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound a5

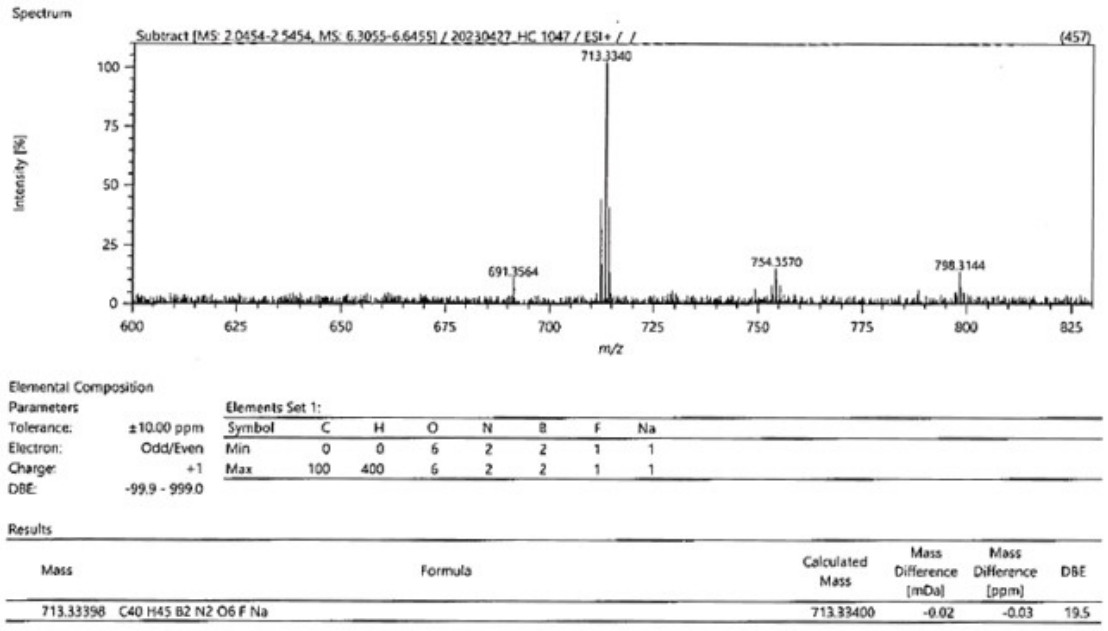


Figure S20. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **a5**

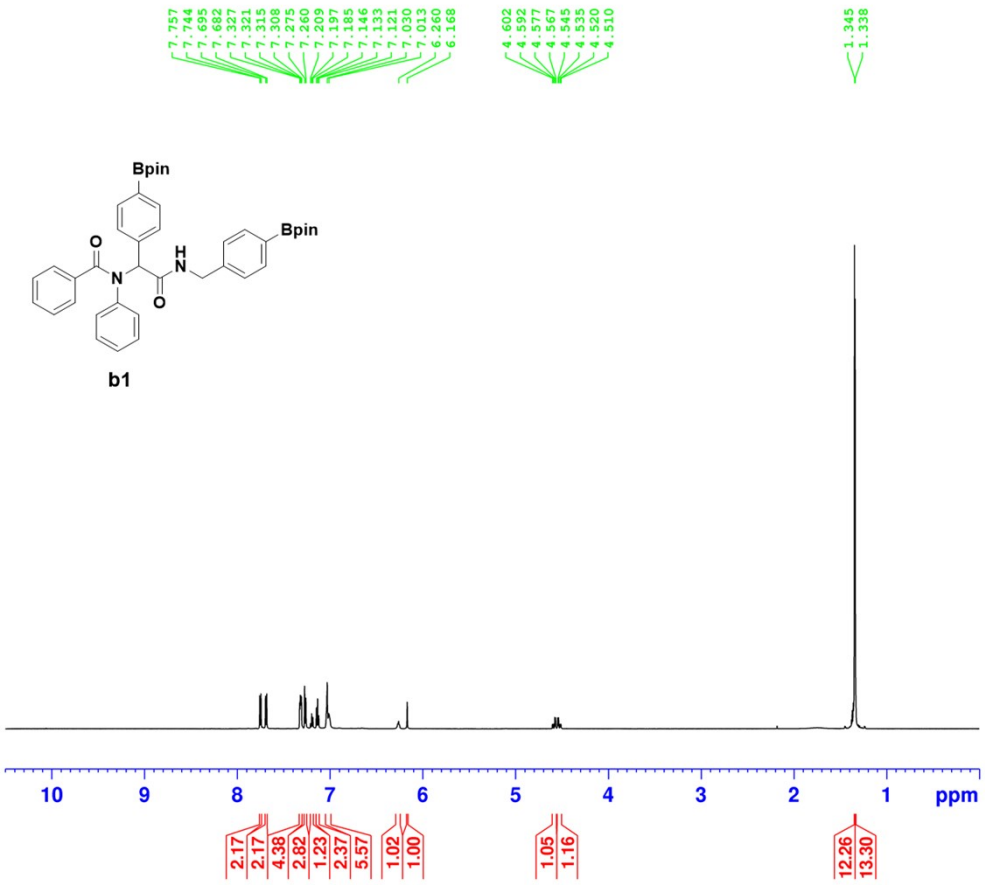


Figure S21. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **b1**

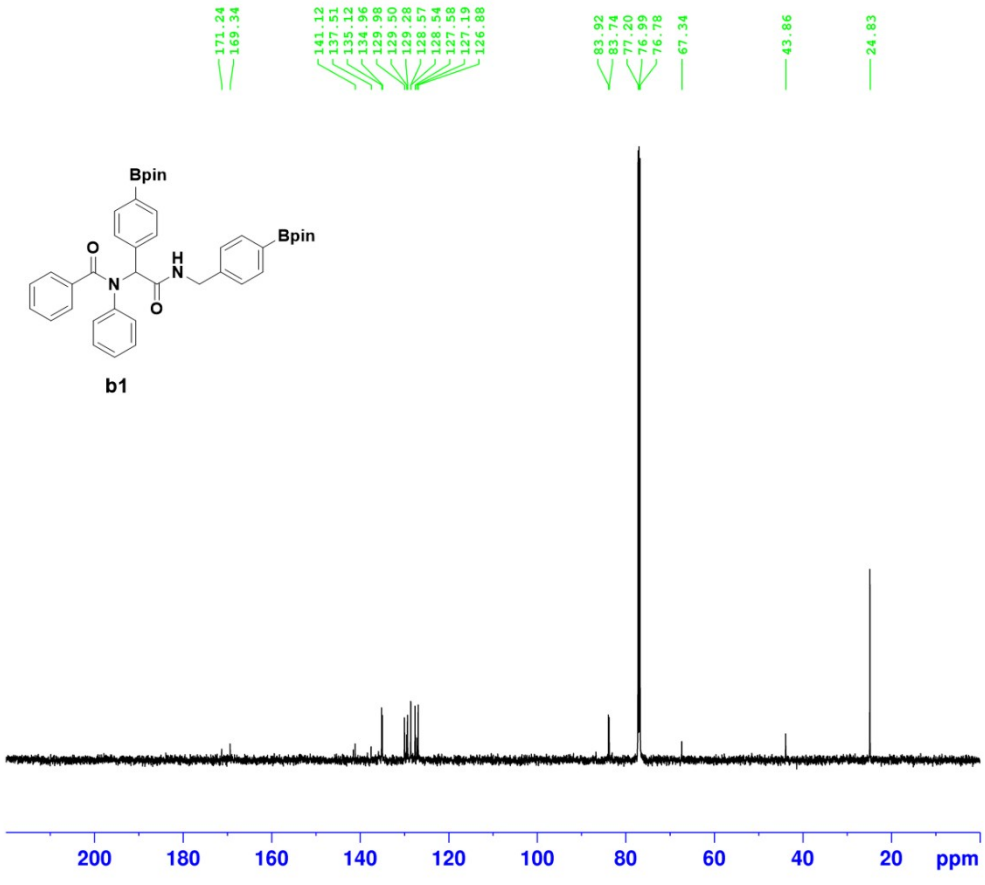
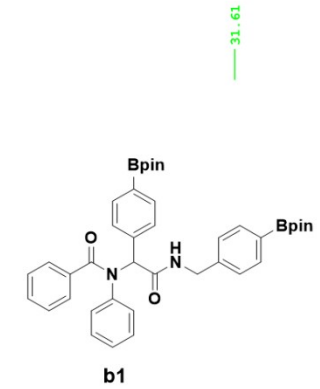


Figure S22. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **b1**



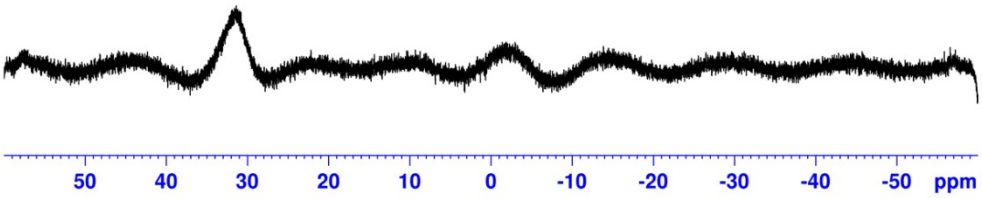


Figure S23. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound b1

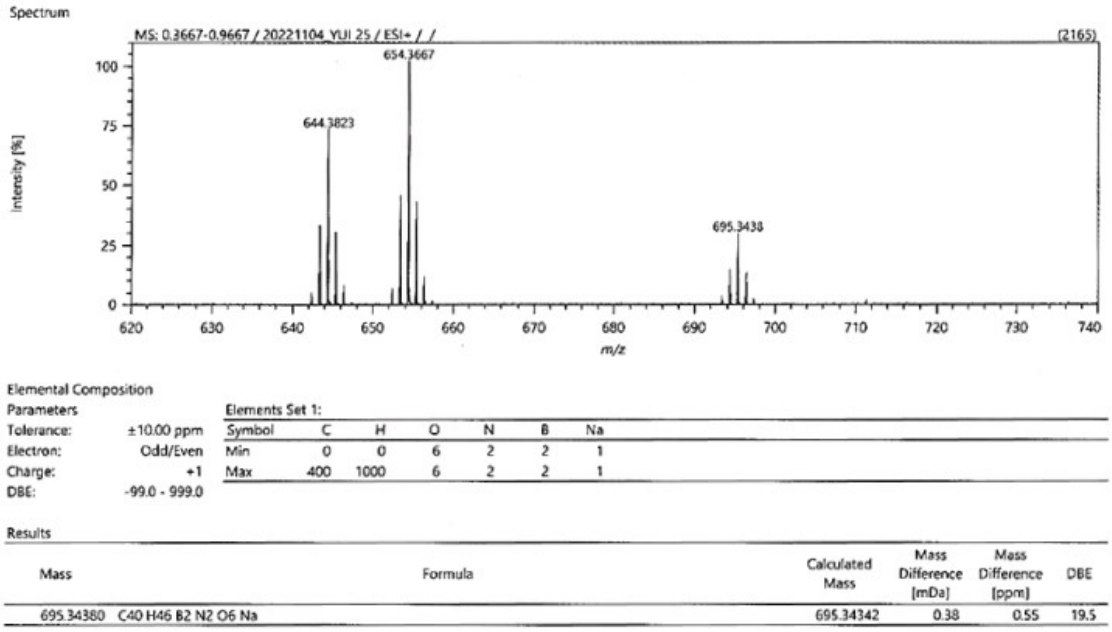


Figure S24. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **b1**

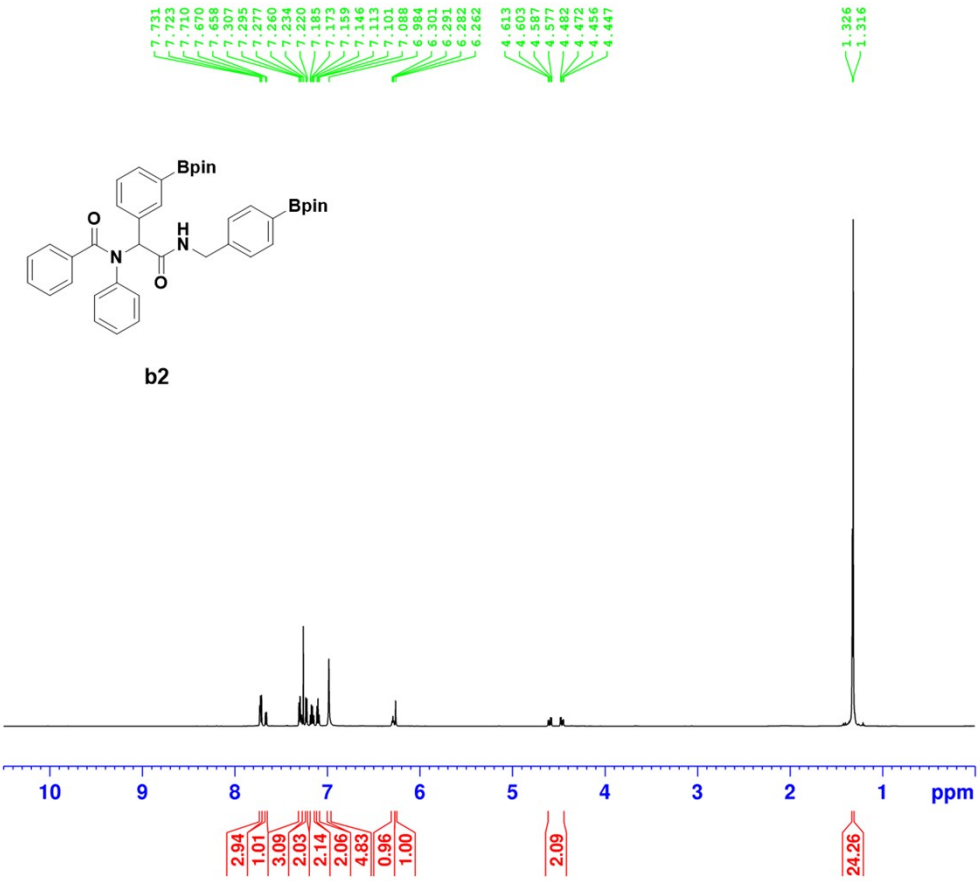


Figure S25. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **b2**

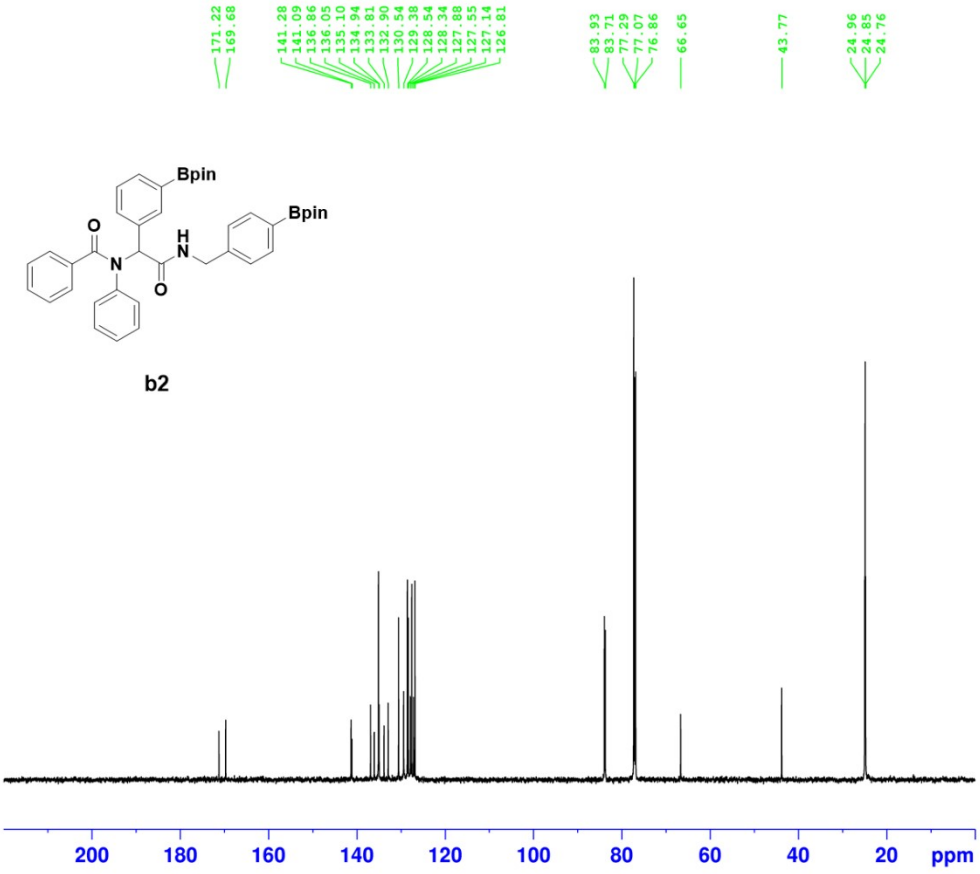


Figure S26. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **b2**

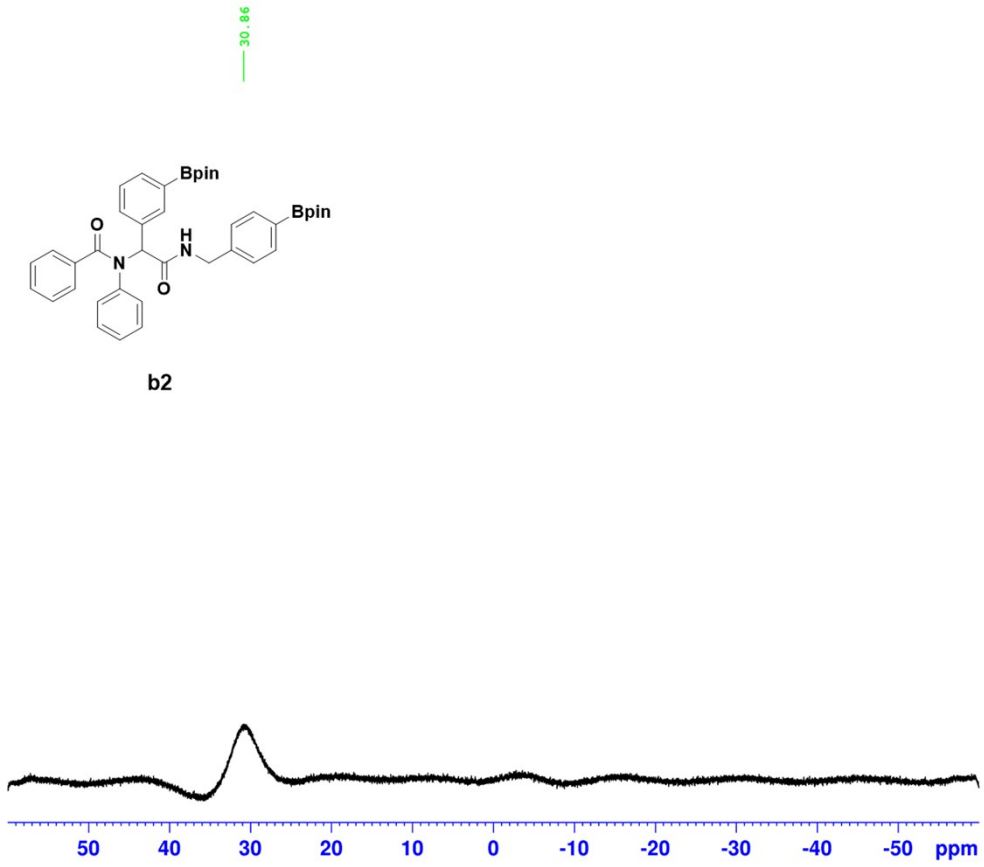


Figure S27. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound b2

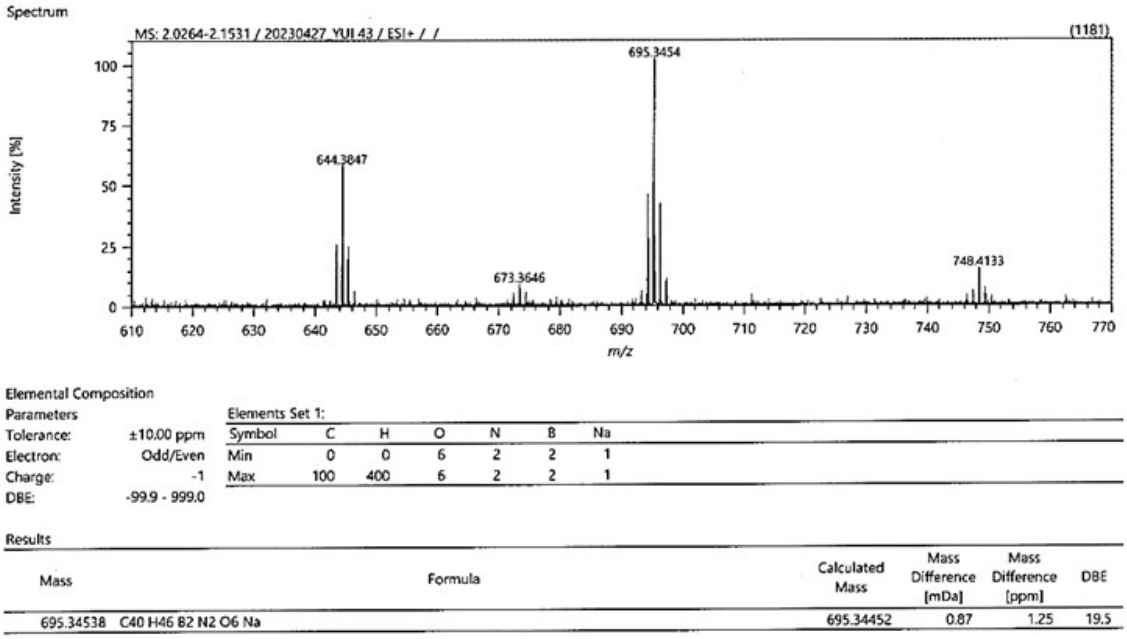


Figure S28. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **b2**

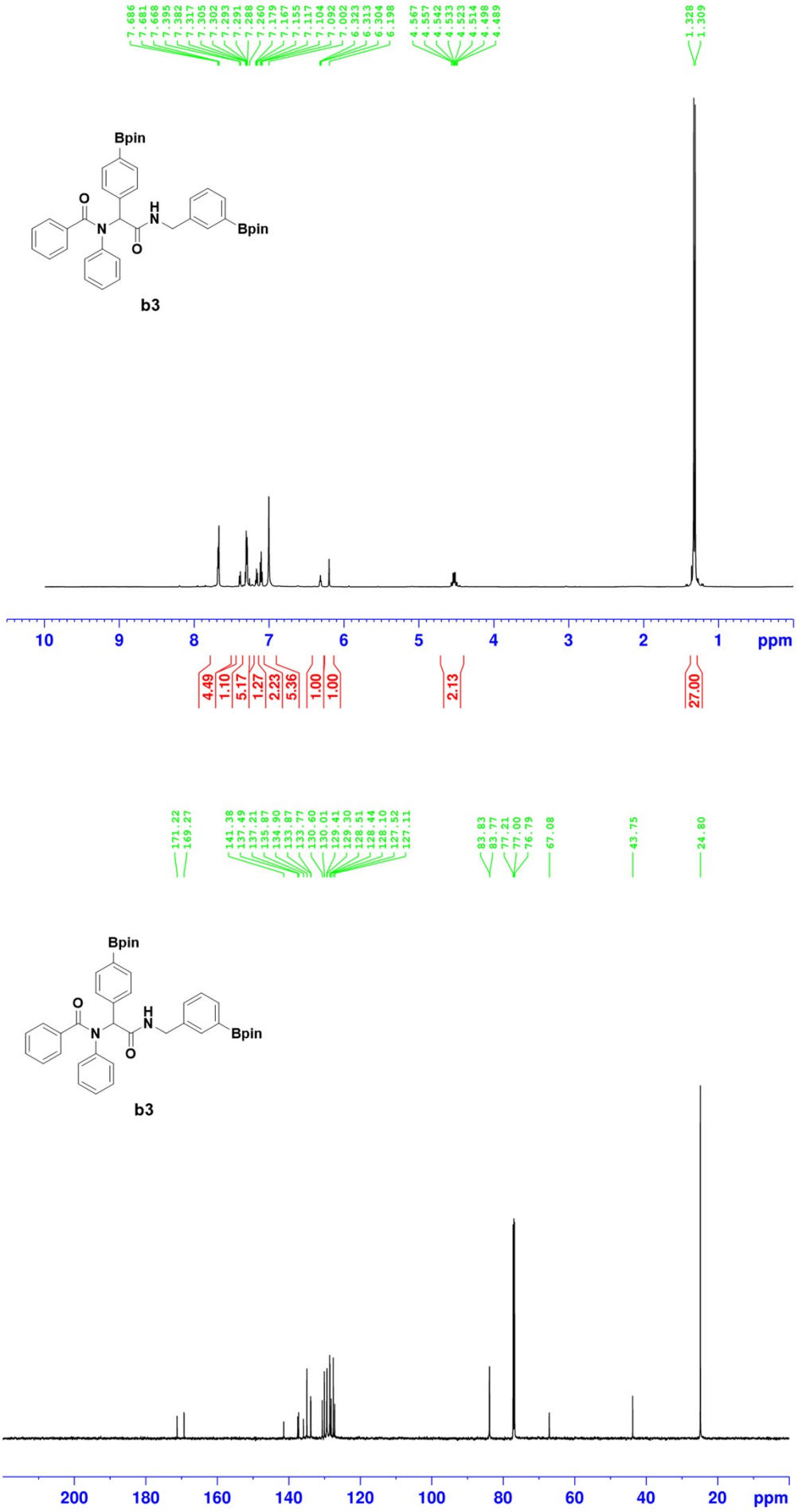


Figure S29. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **b3**

Figure S30. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **b3**

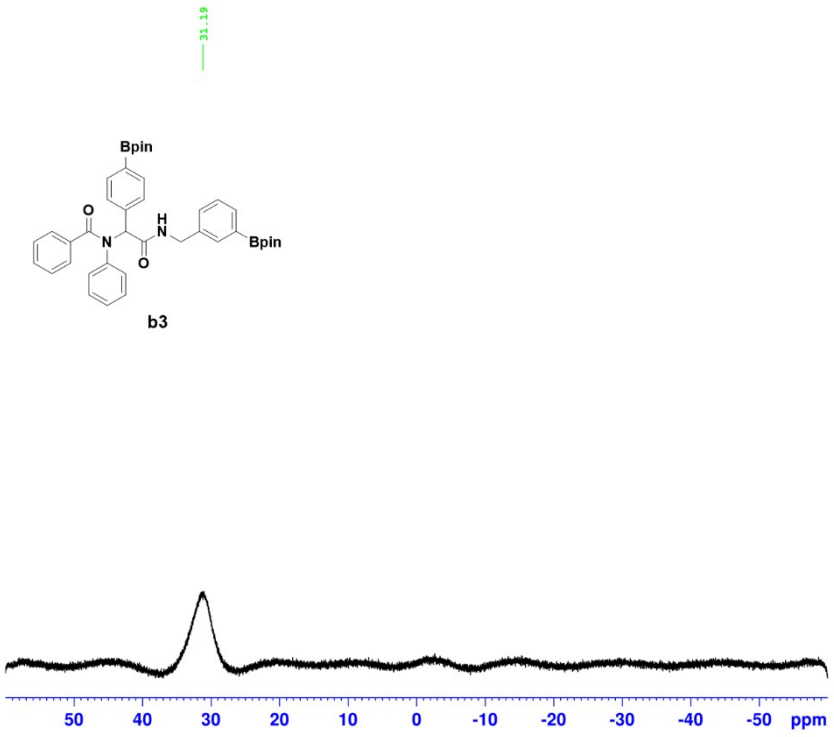
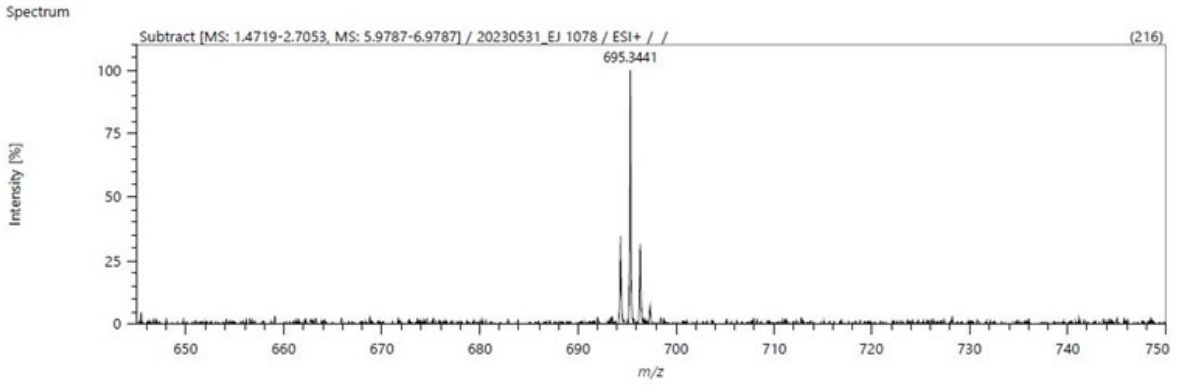


Figure S31. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound b3



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	6	2	2	1
Charge:	+1	Max	1000	4000	6	2	2	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
695.34407	C40 H46 B2 N2 O6 Na	695.34342	0.65	0.94	19.5

Figure S32. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **b3**

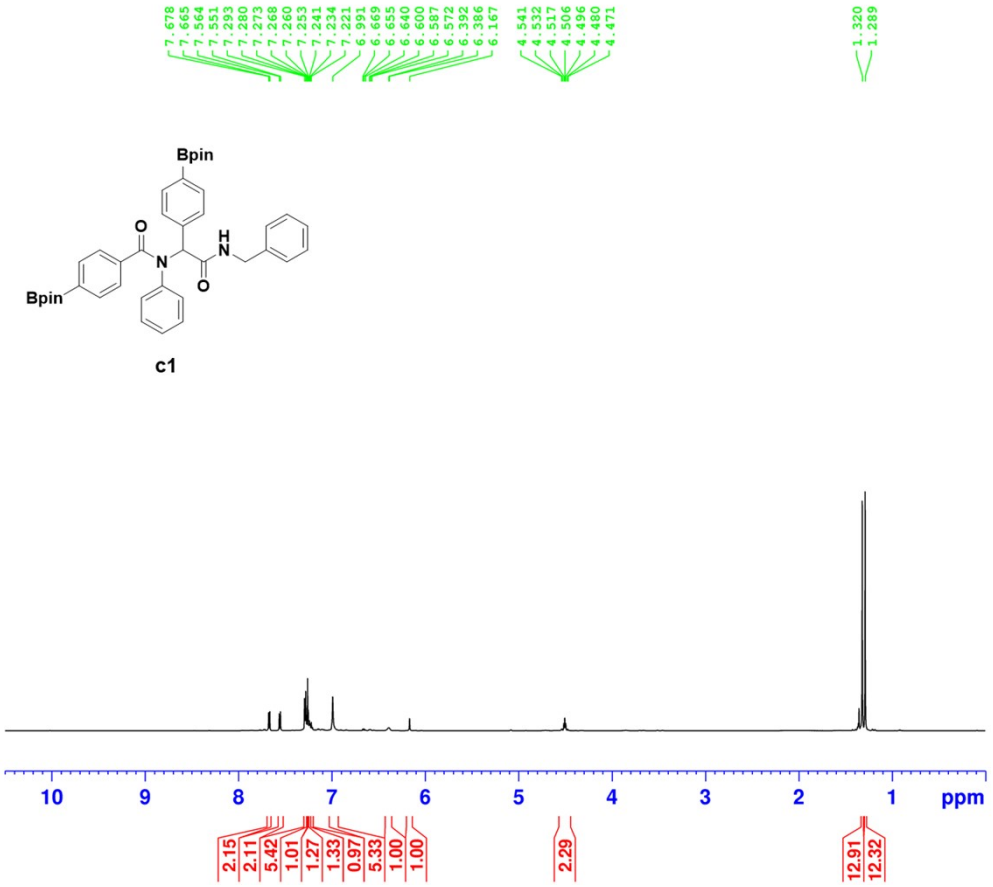


Figure S33. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **c1**

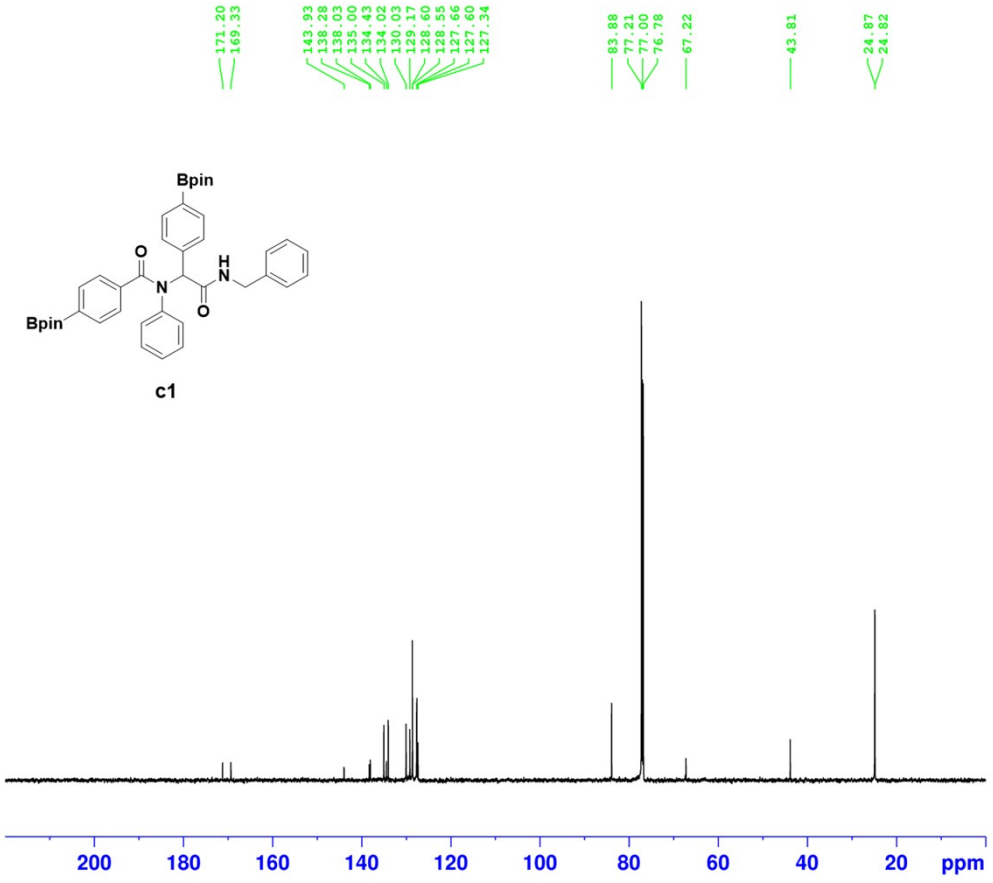
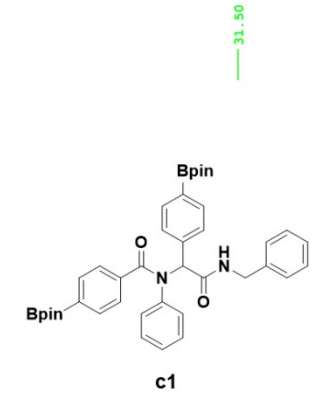


Figure S34. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **c1**



c1

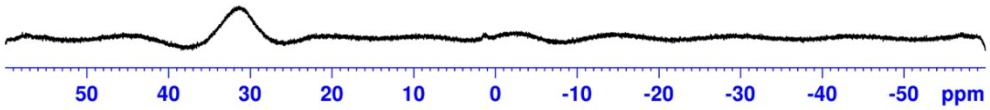
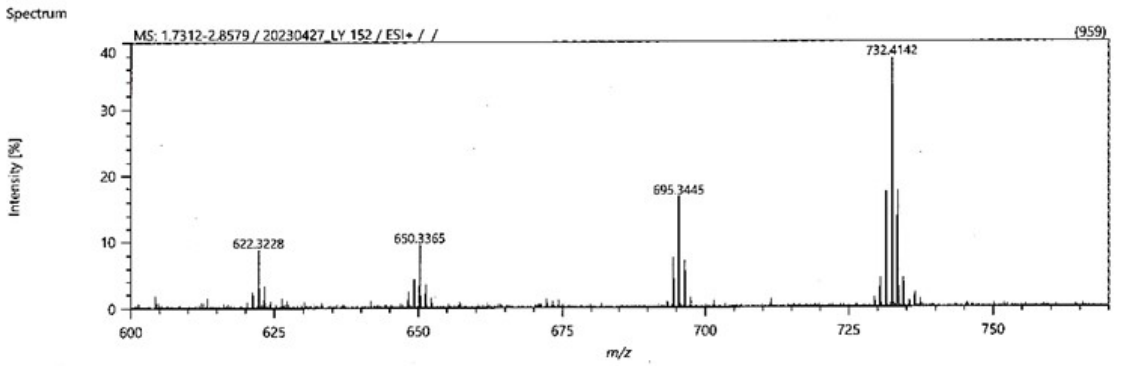


Figure S35. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound **c1**



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	0	2	2	1
Charge:	-1	Max	100	400	6	2	2	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
695.34451	C40 H46 B2 N2 O6 Na	695.34452	0.00	-0.01	19.5

Figure S36. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **c1**

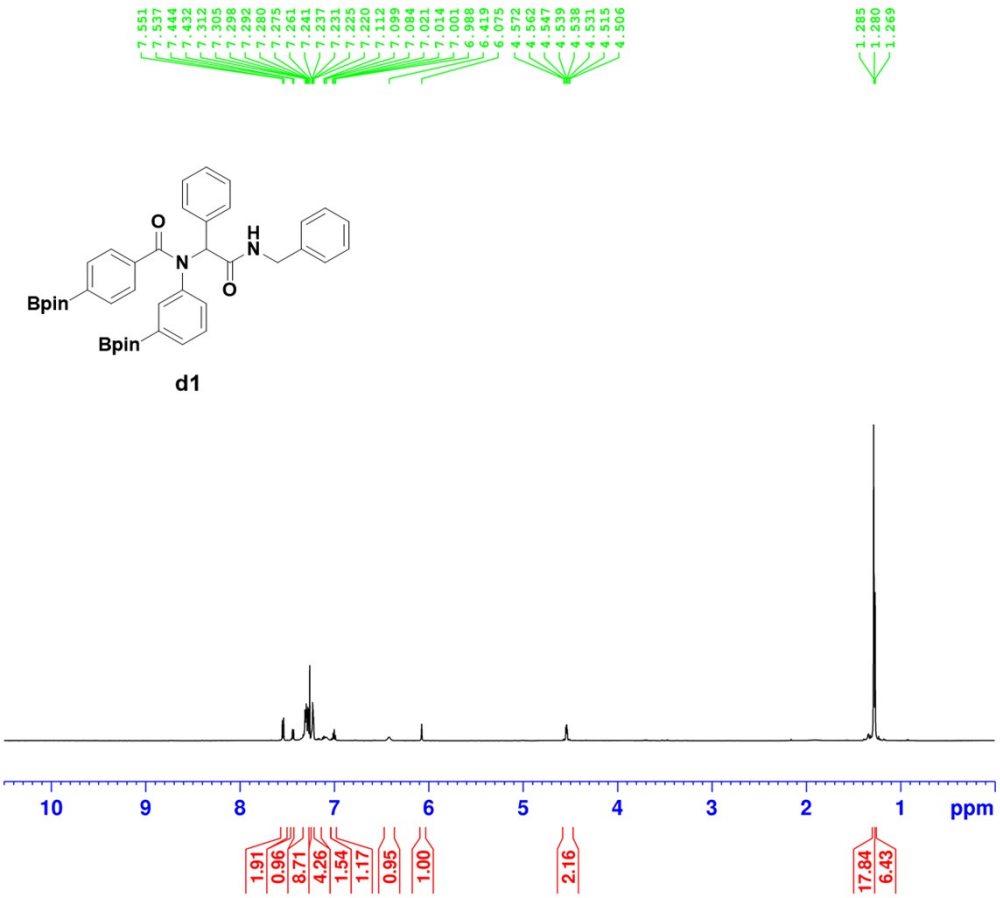


Figure S37. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **d1**

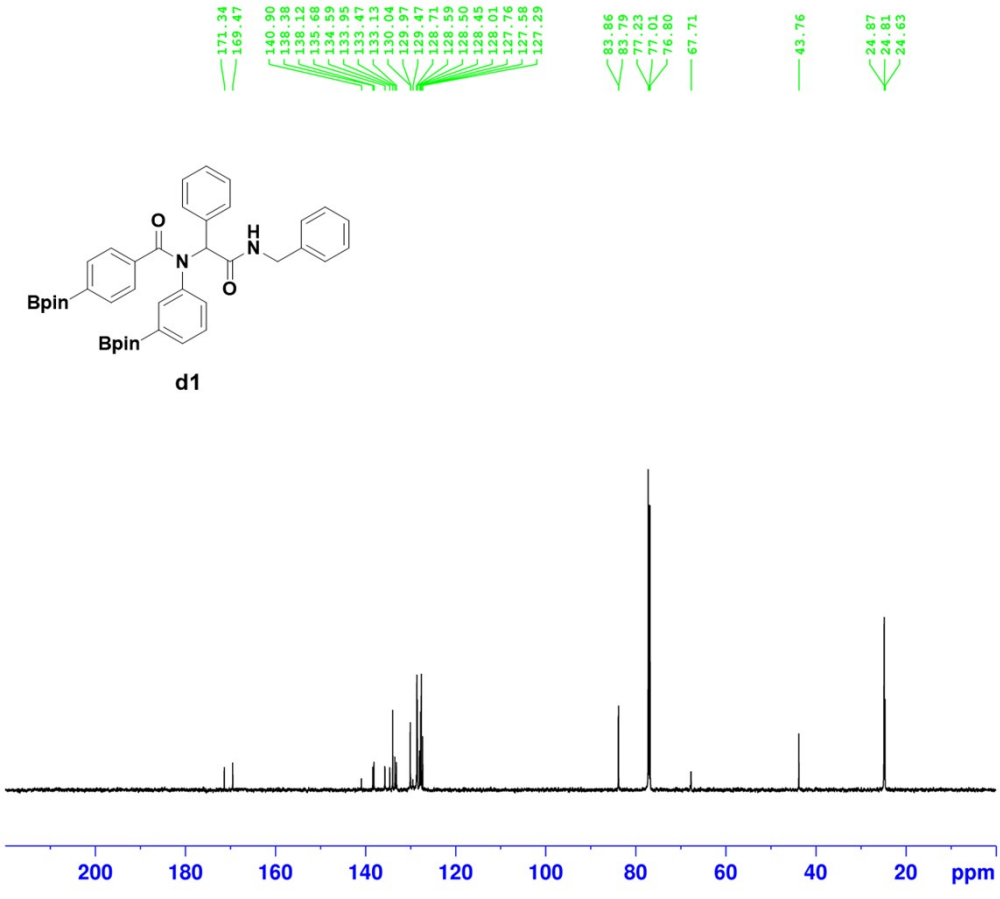


Figure S38. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **d1**

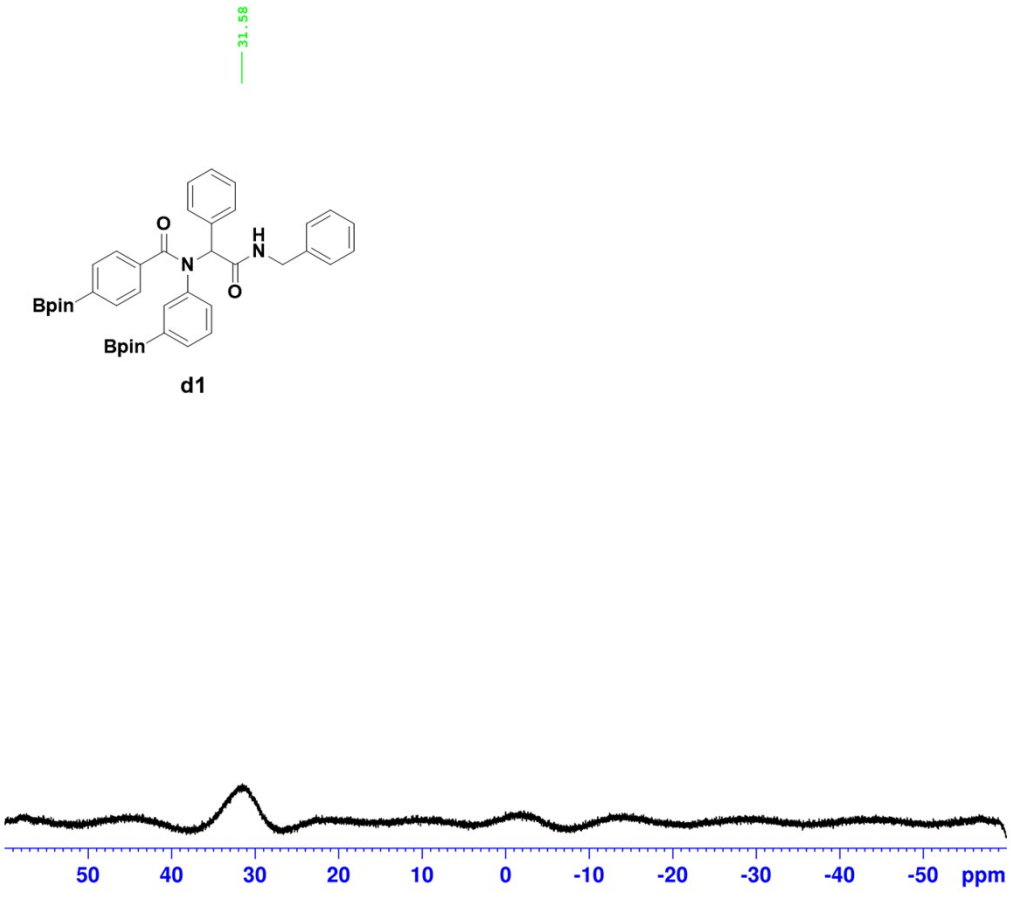


Figure S39. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound d1

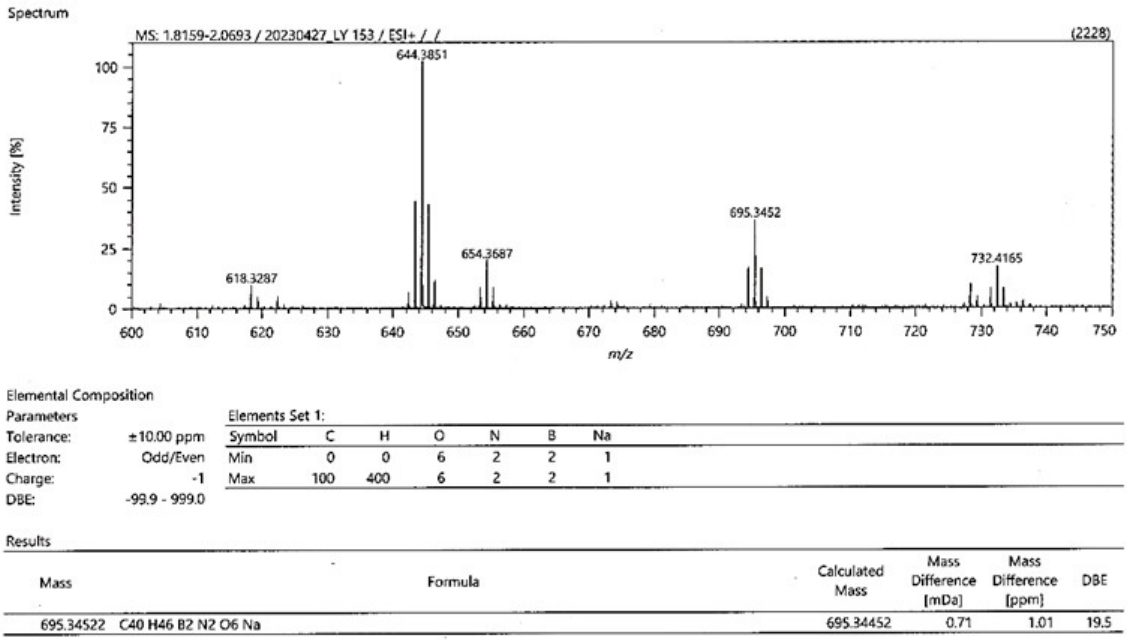


Figure S40. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **d1**

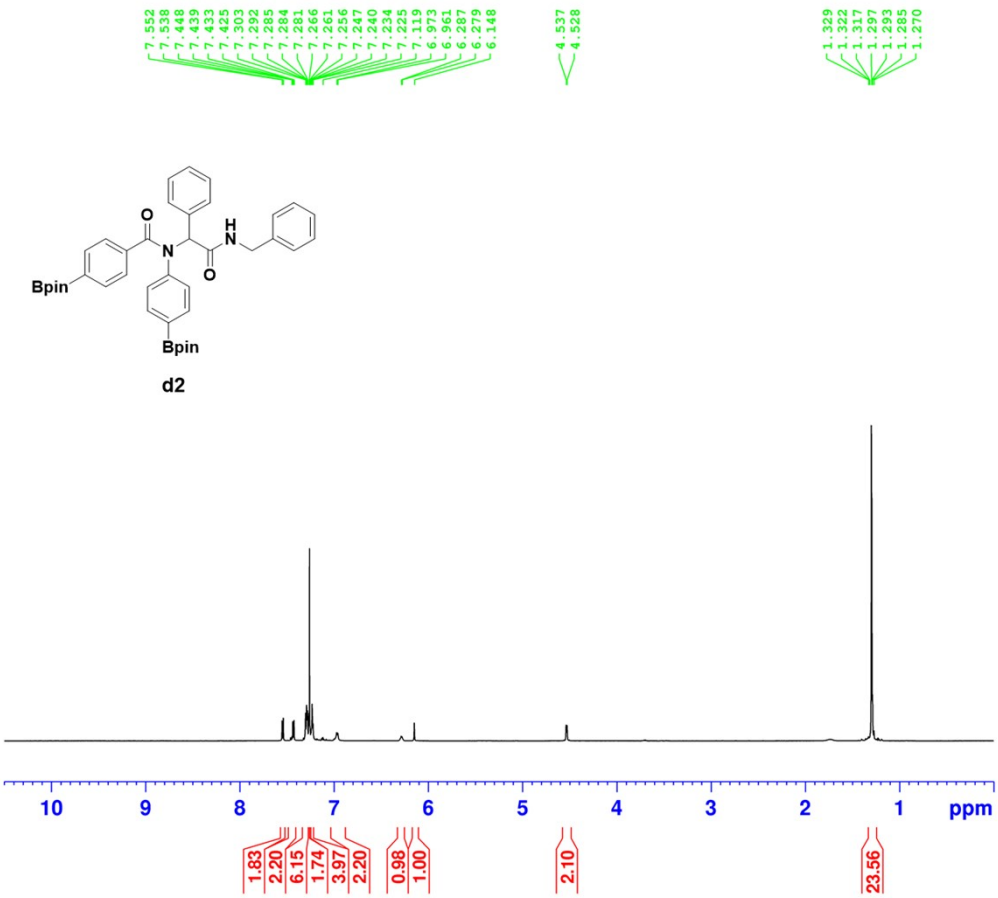


Figure S41. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **d2**

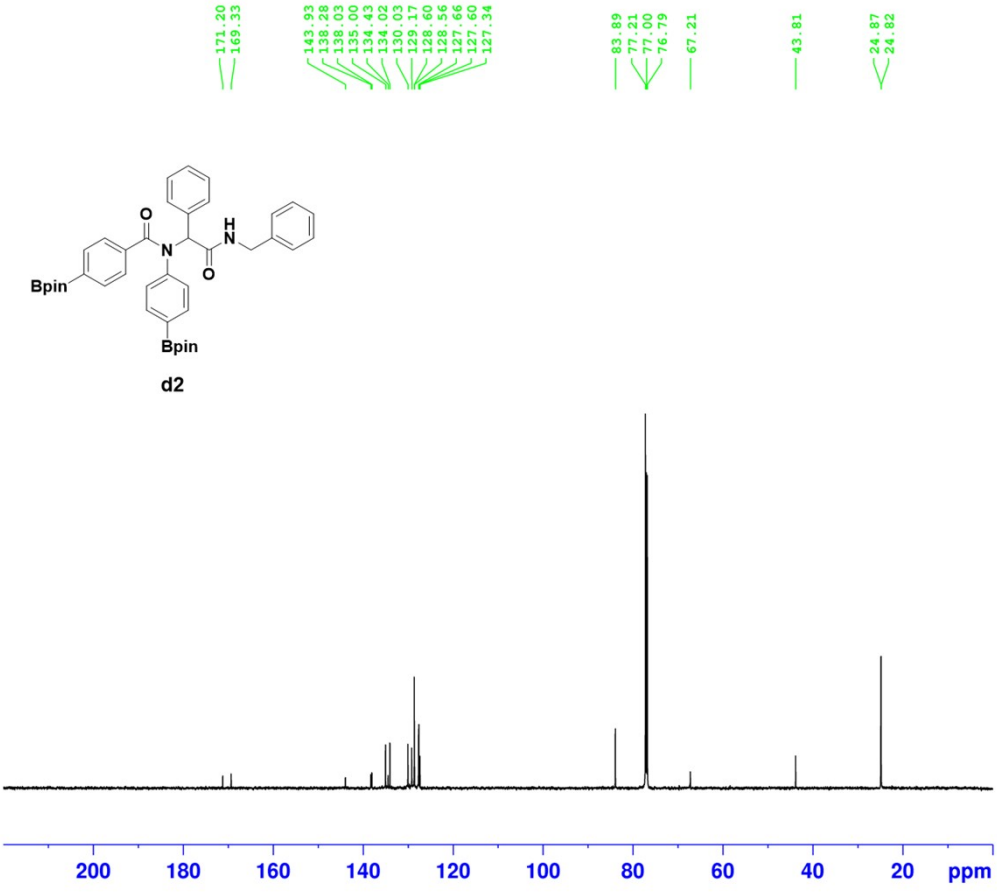
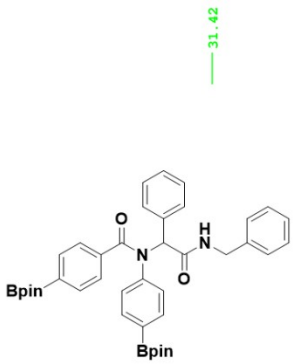


Figure S42. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **d2**



d2

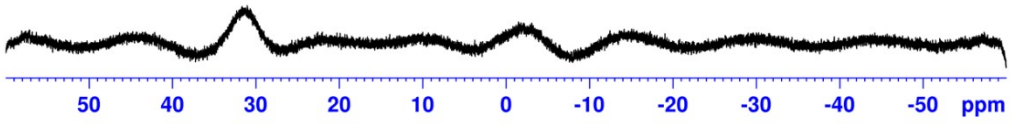
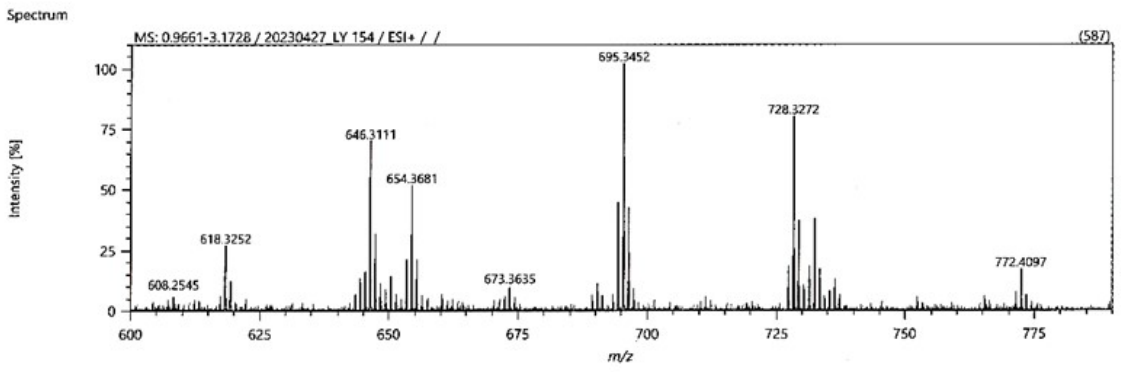


Figure S43. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound d2



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	6	2	2	1
Charge:	-1	Max	100	400	6	2	2	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
695.34518	C40 H46 B2 N2 O6 Na	695.34452	0.67	0.96	19.5

Figure S44. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **d2**

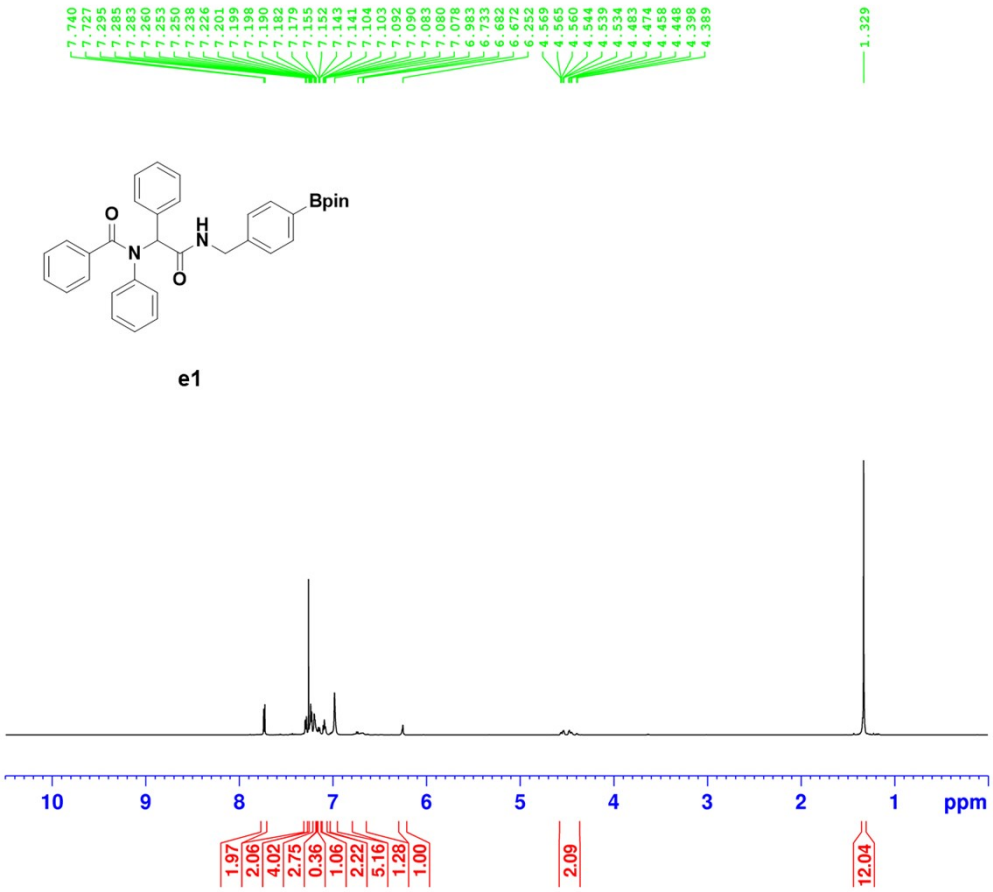


Figure S45. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **e1**

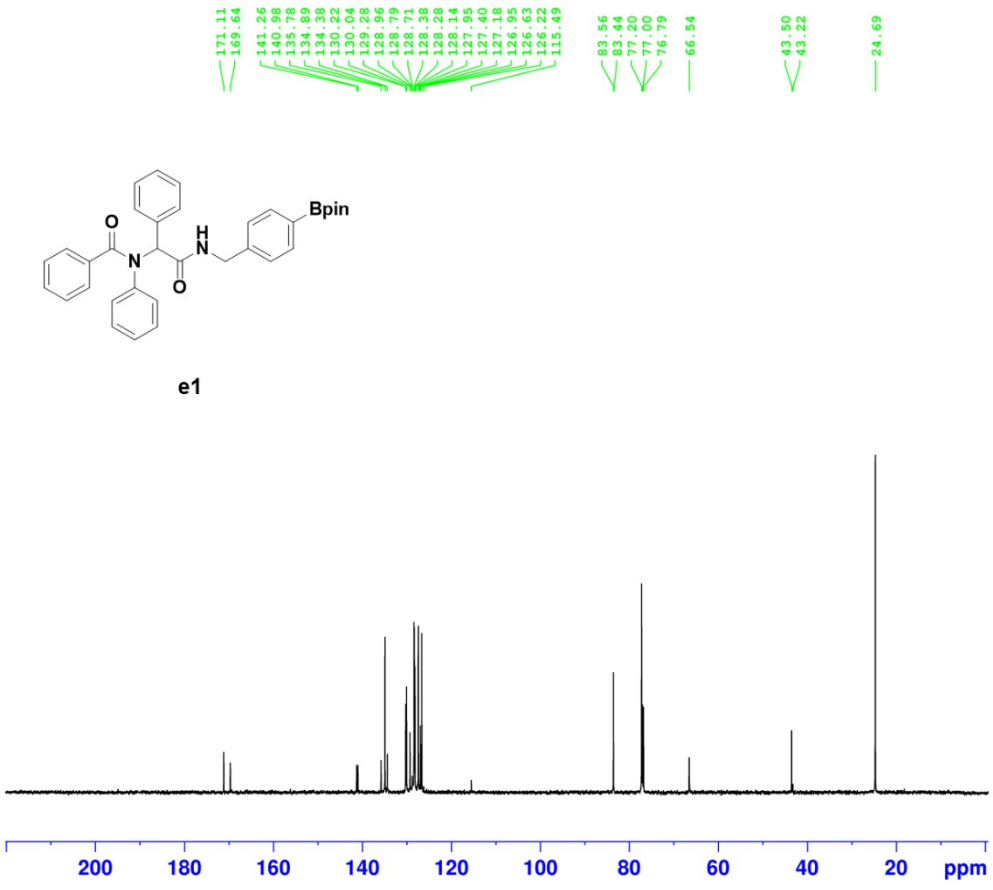
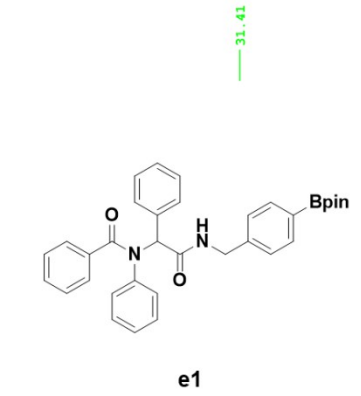


Figure S46. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **e1**



e1

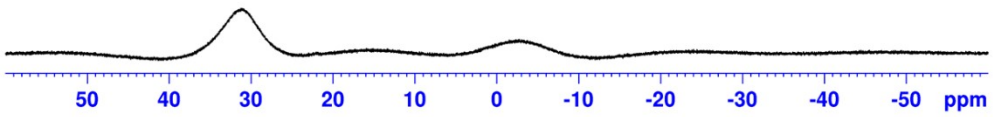
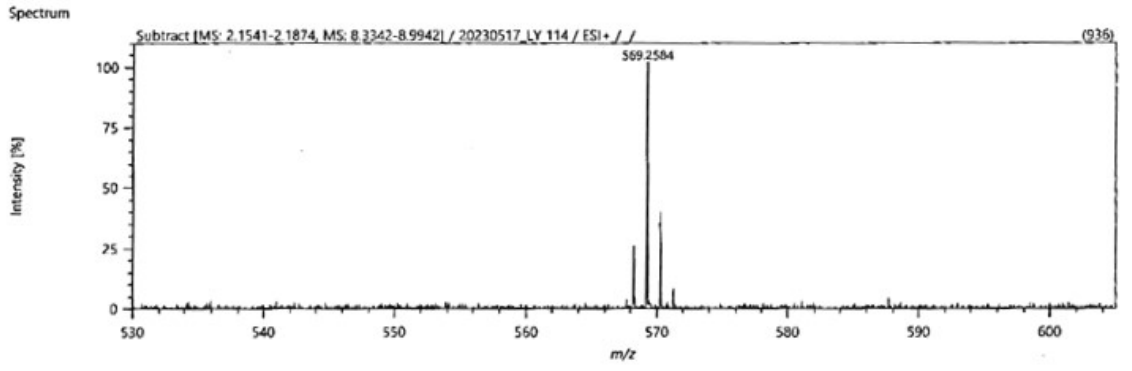


Figure S47. ^{11}**B NMR (192.5 MHz, CDCl$_3$) spectrum of compound e1**



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	4	2	1	1
Charge:	+1	Max	1000	4000	4	2	1	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
569.25839	C34 H35 B N2 O4 Na	569.25821	0.18	0.31	18.5

Figure S48. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **e1**

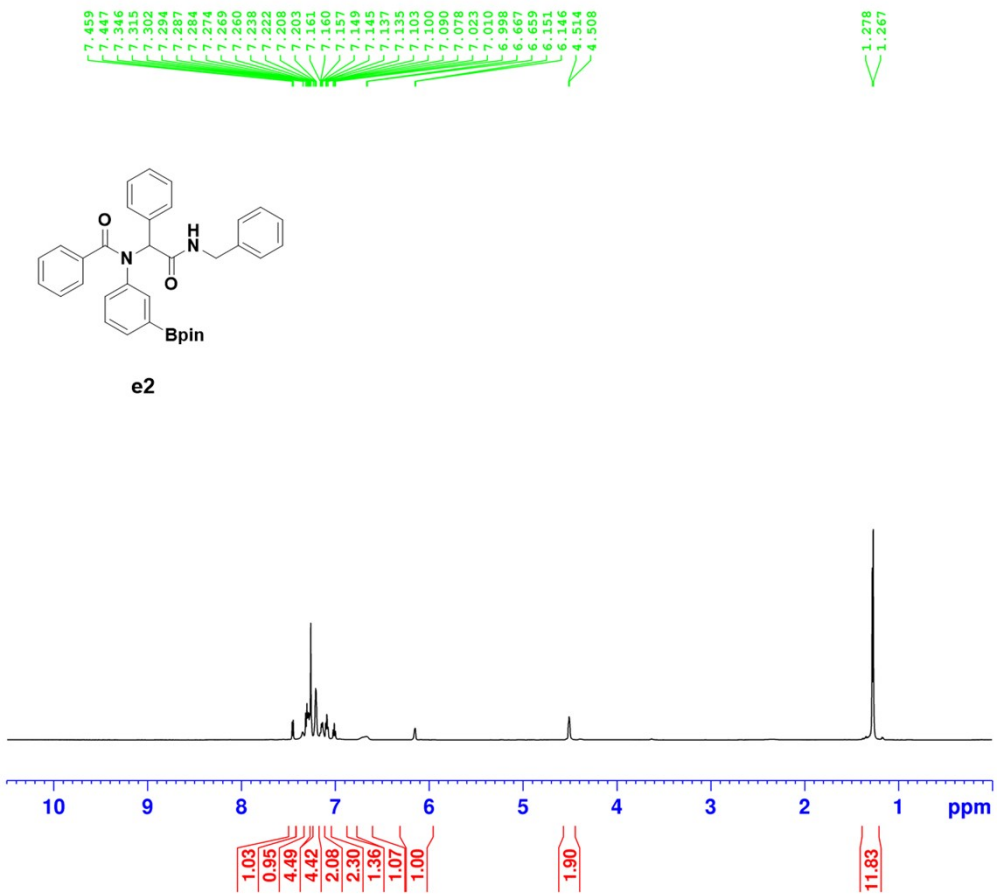


Figure S49. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **e2**

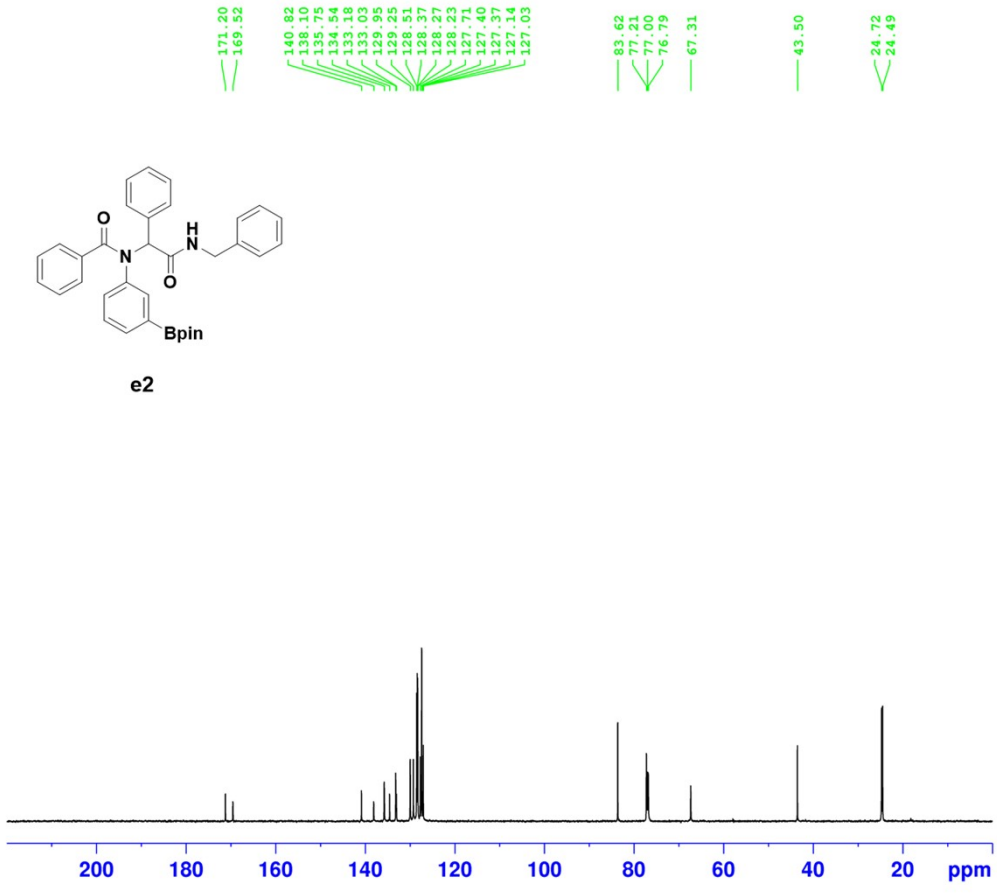
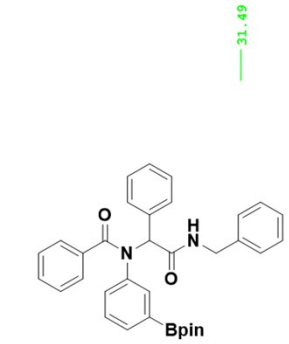


Figure S50. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **e2**



e2

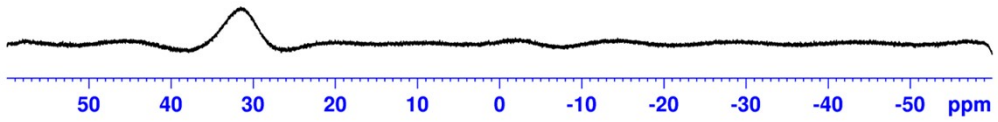
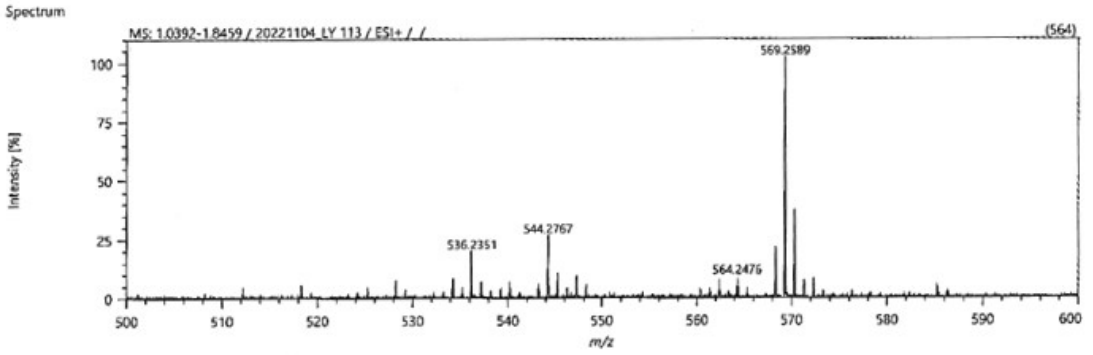


Figure S51. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound e2



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	4	2	1	1
Charge:	+1	Max	400	1000	4	2	1	1
DBE:	-99.0 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
569.25894	C34 H35 B N2 O4 Na	569.25821	0.73	1.29	18.5

Figure S52. HRMS (ESI, positive ion) $[M + Na]^+$ spectrum of compound **e2**

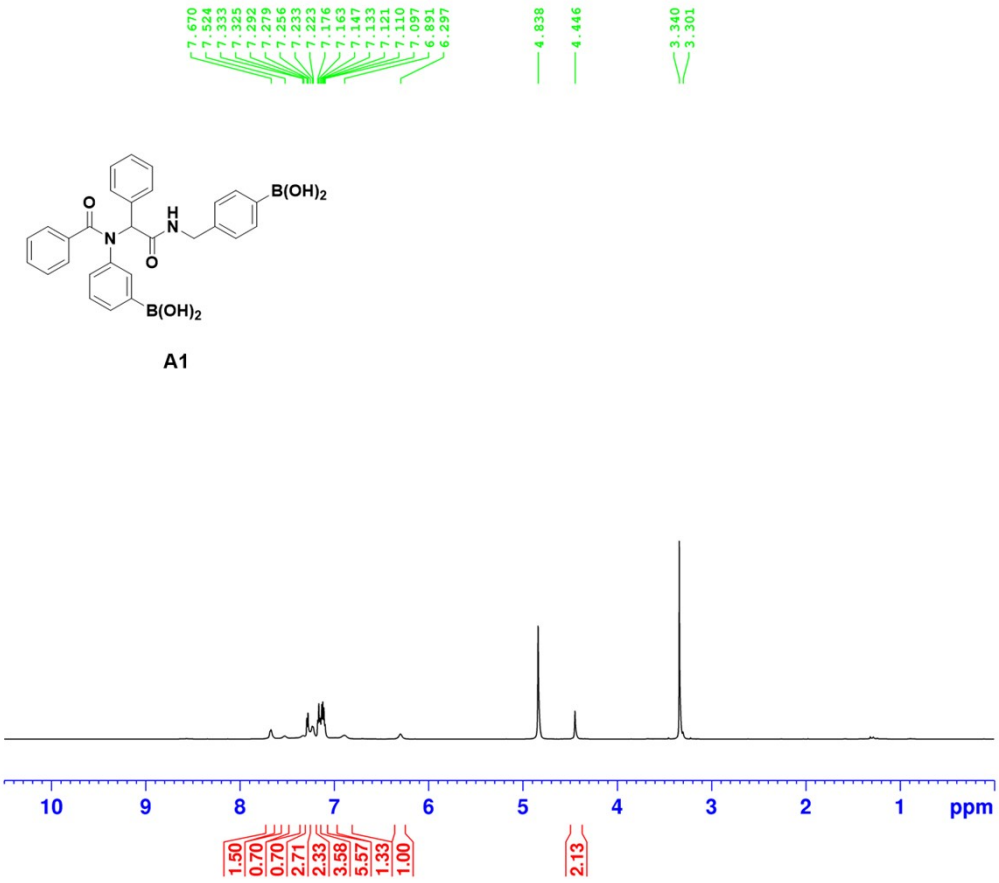


Figure S53. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **A1**

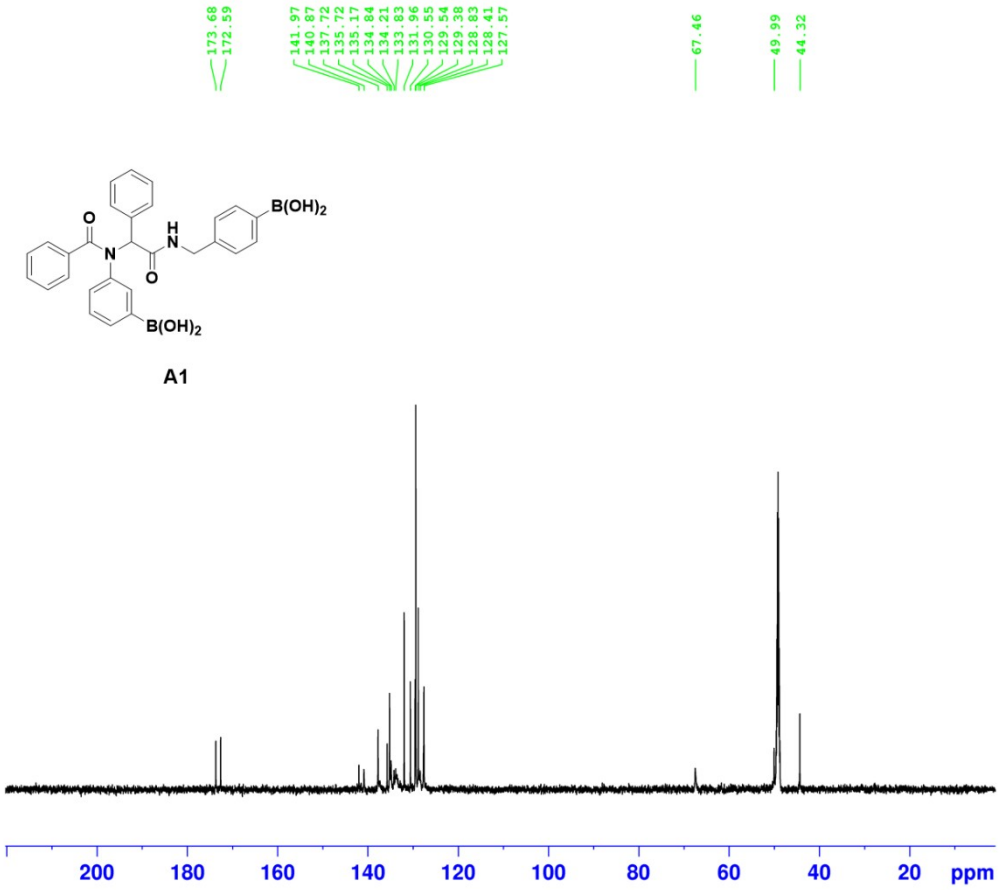


Figure S54. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **A1**

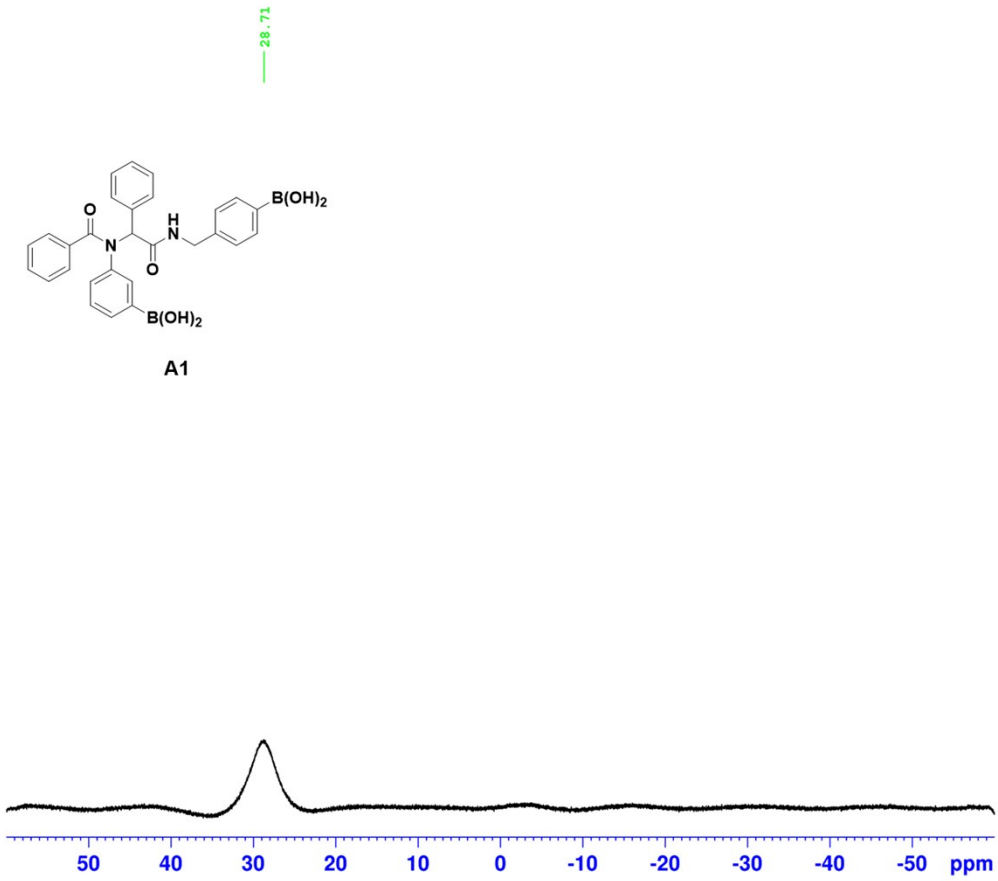


Figure S55. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound A1

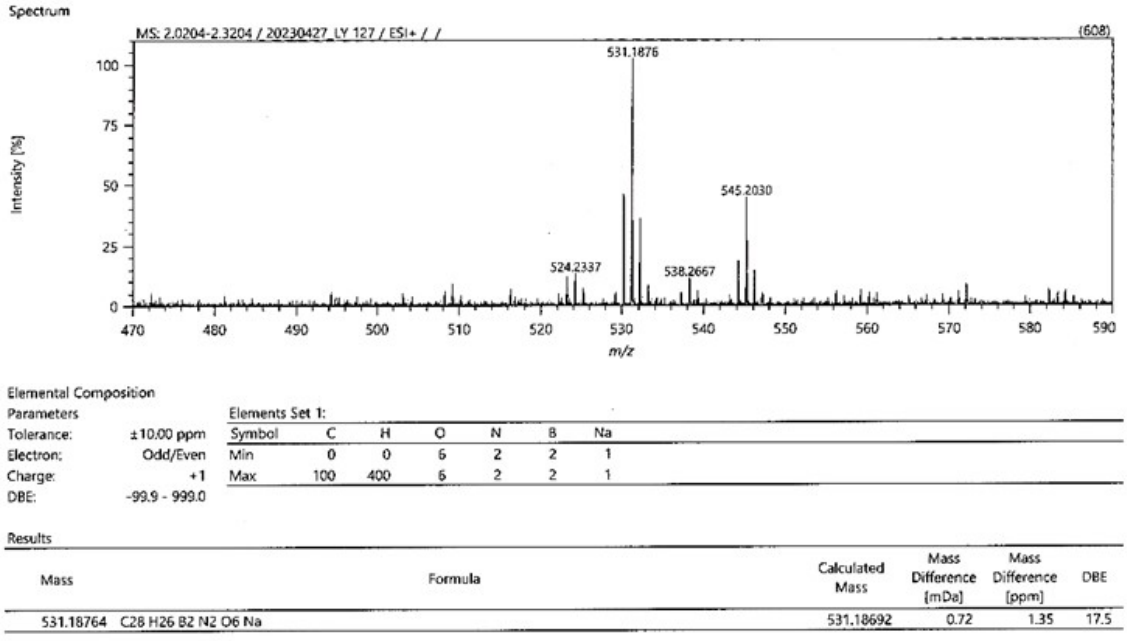


Figure S56. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **A1**

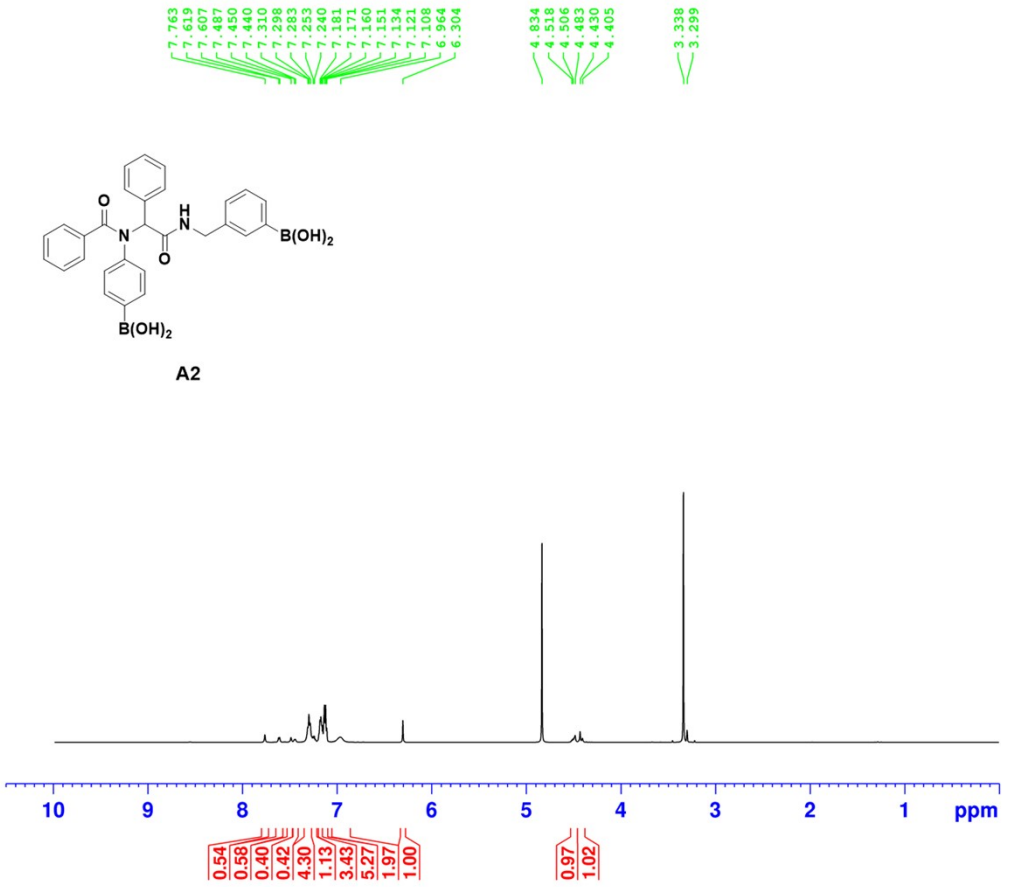


Figure S57. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **A2**

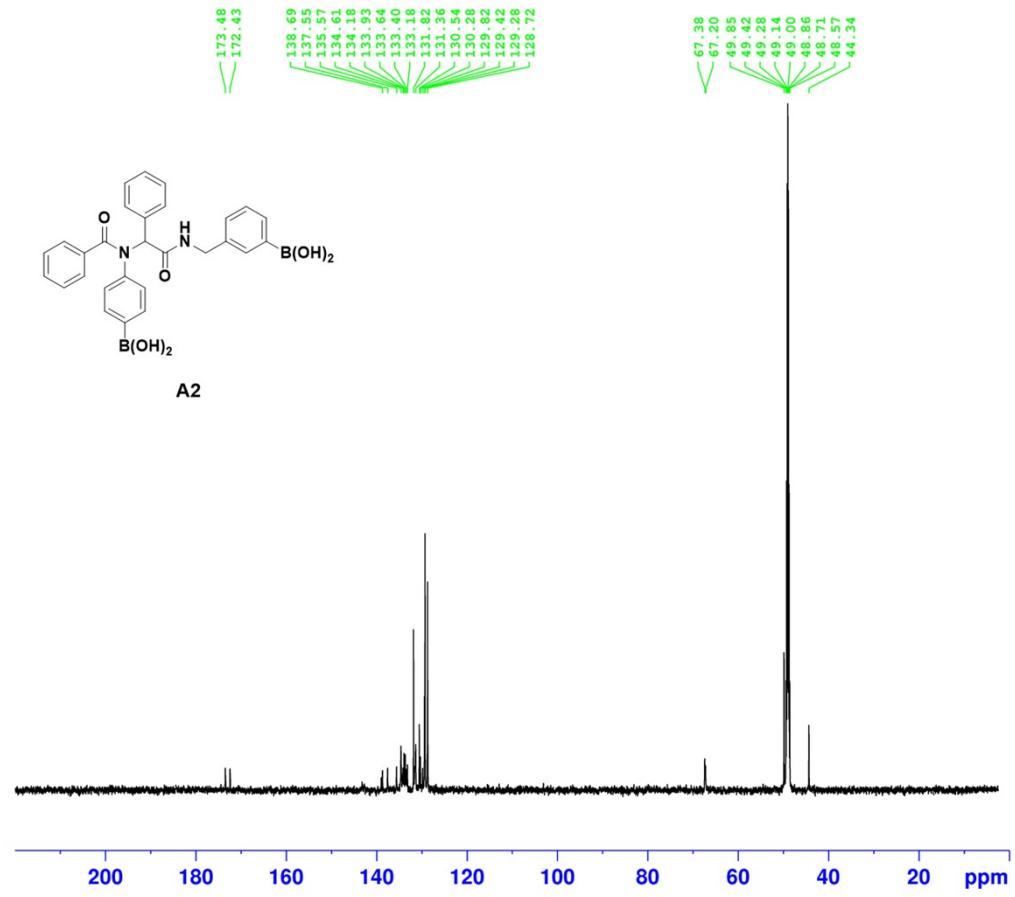
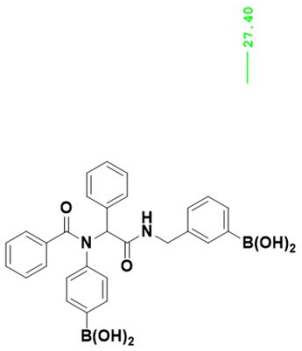


Figure S58. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **A2**



A2

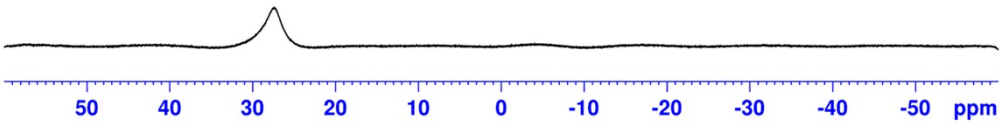
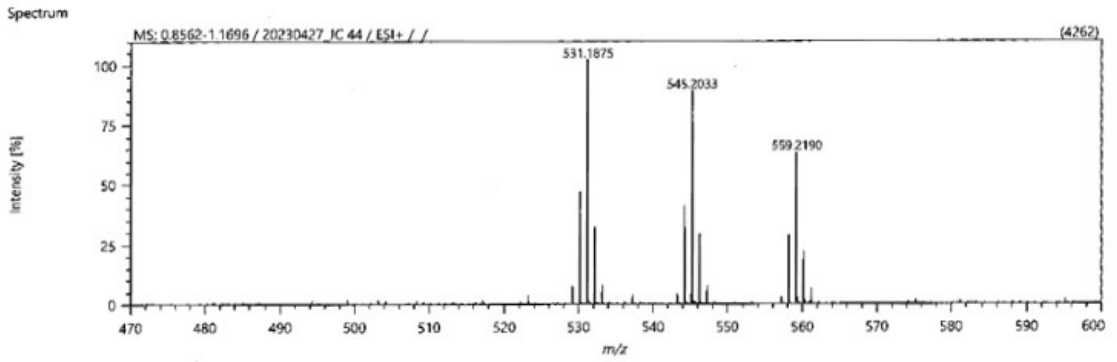


Figure S59. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound A2



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	6	2	2	1
Charge:	-1	Max	100	400	6	2	2	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
531.18754	C28 H26 B2 N2 O6 Na	531.18802	-0.47	-0.89	17.5

Figure S60. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **A2**

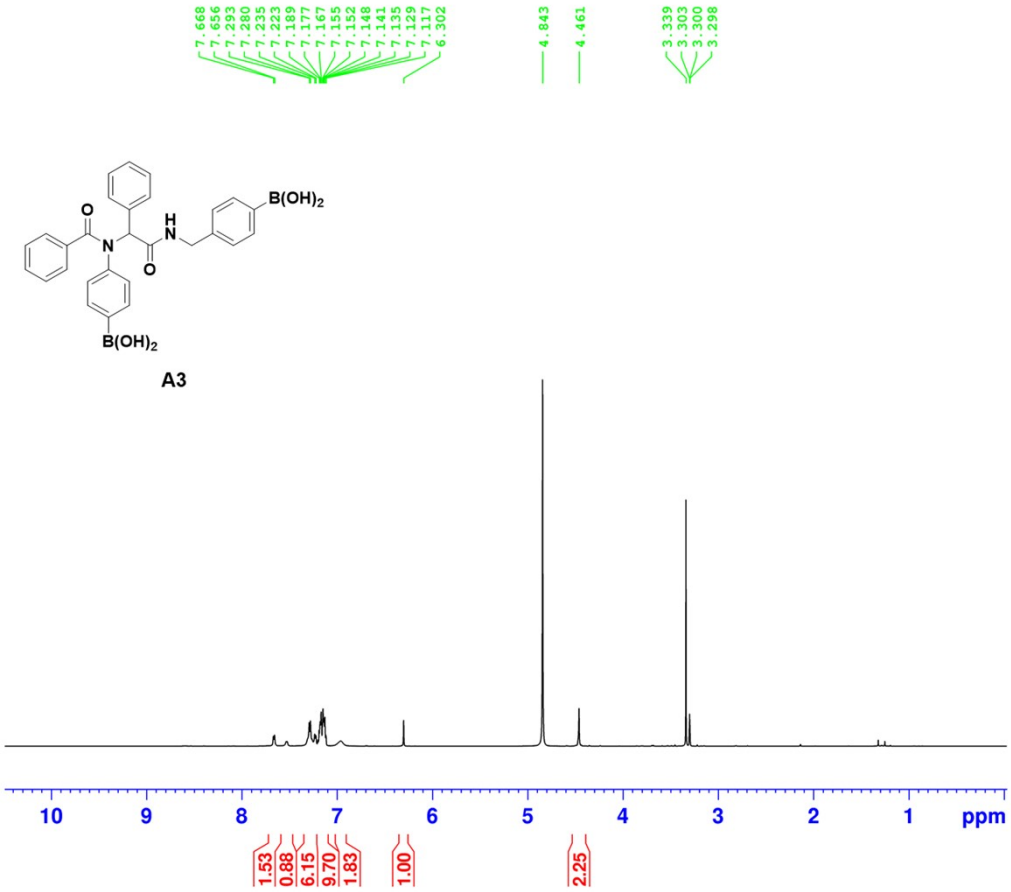


Figure S61. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **A3**

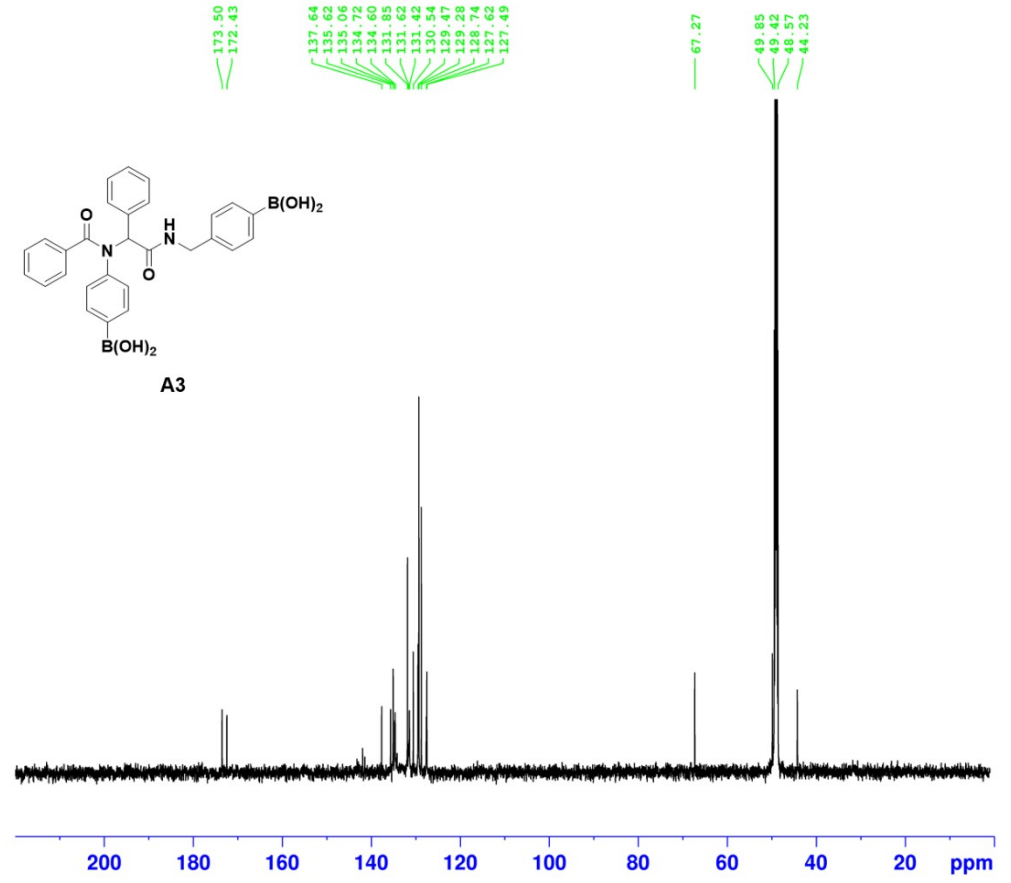


Figure S62. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **A3**

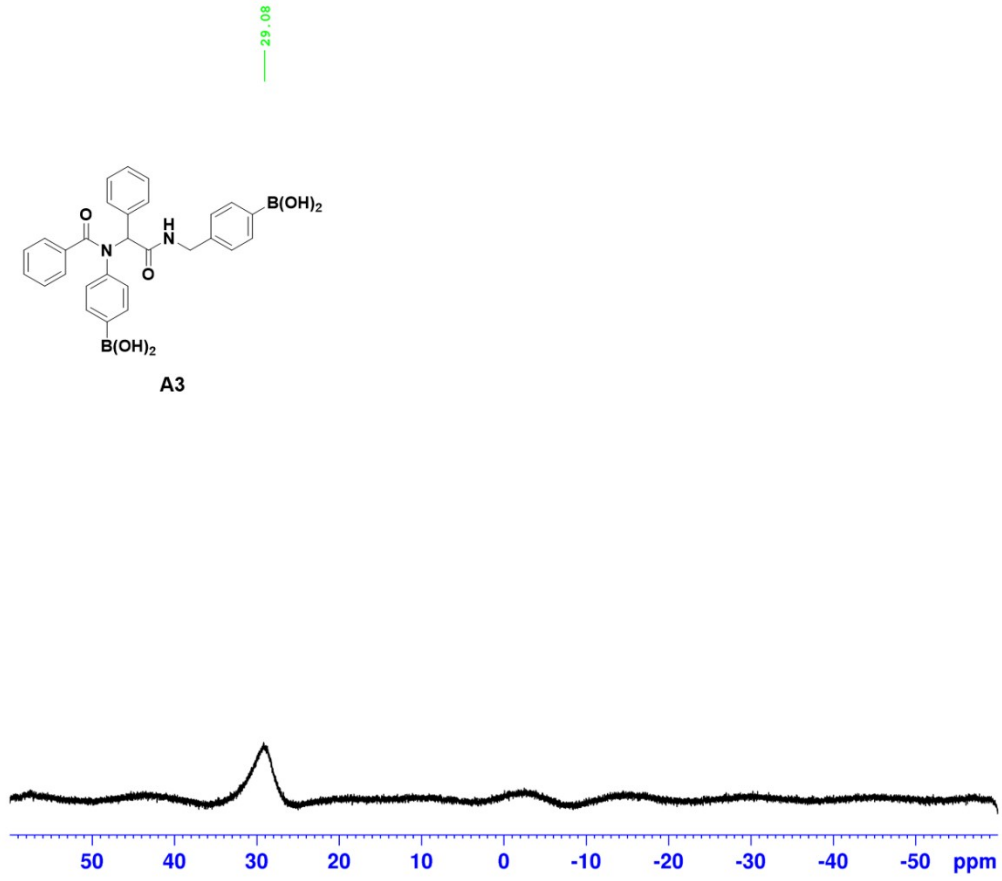


Figure S63. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound A3

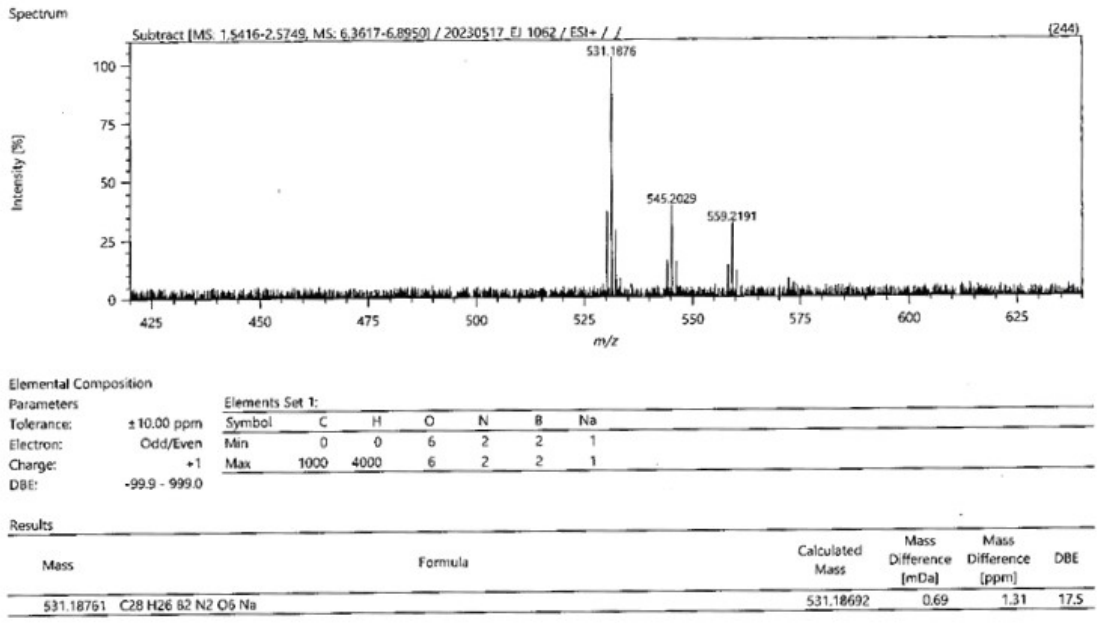


Figure S64. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **A3**

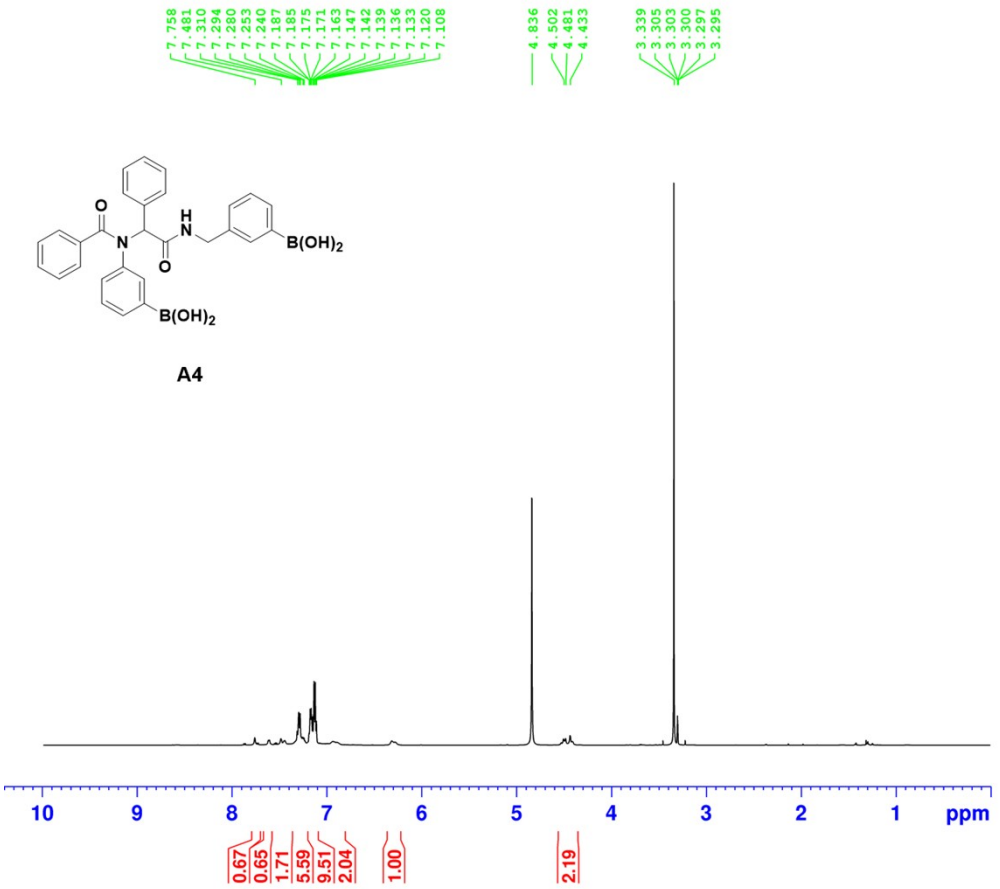


Figure S65. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **A4**

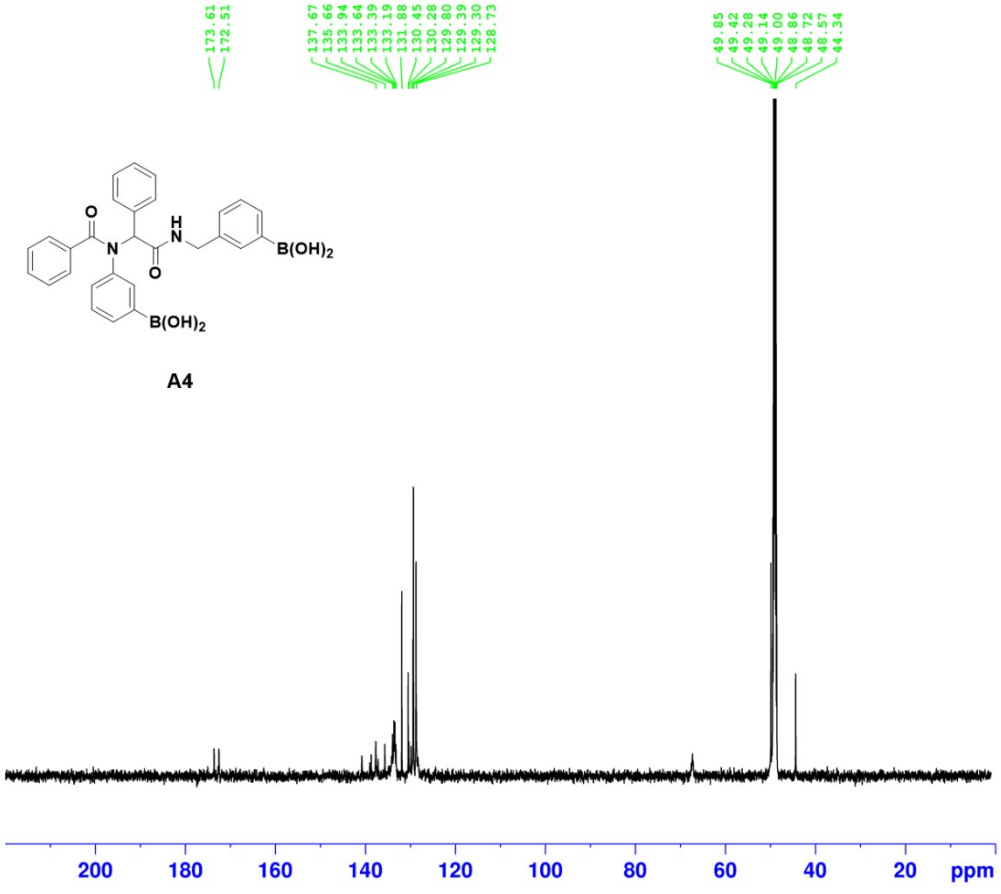


Figure S66. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **A4**

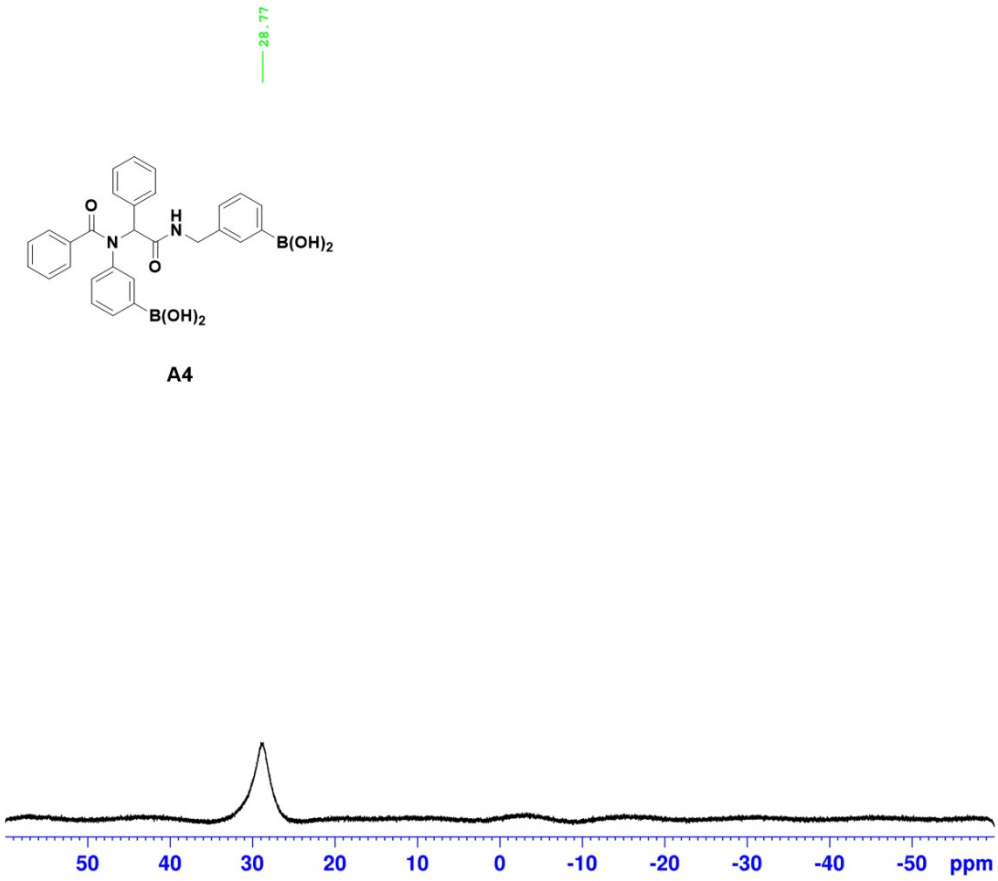


Figure S67. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound A4

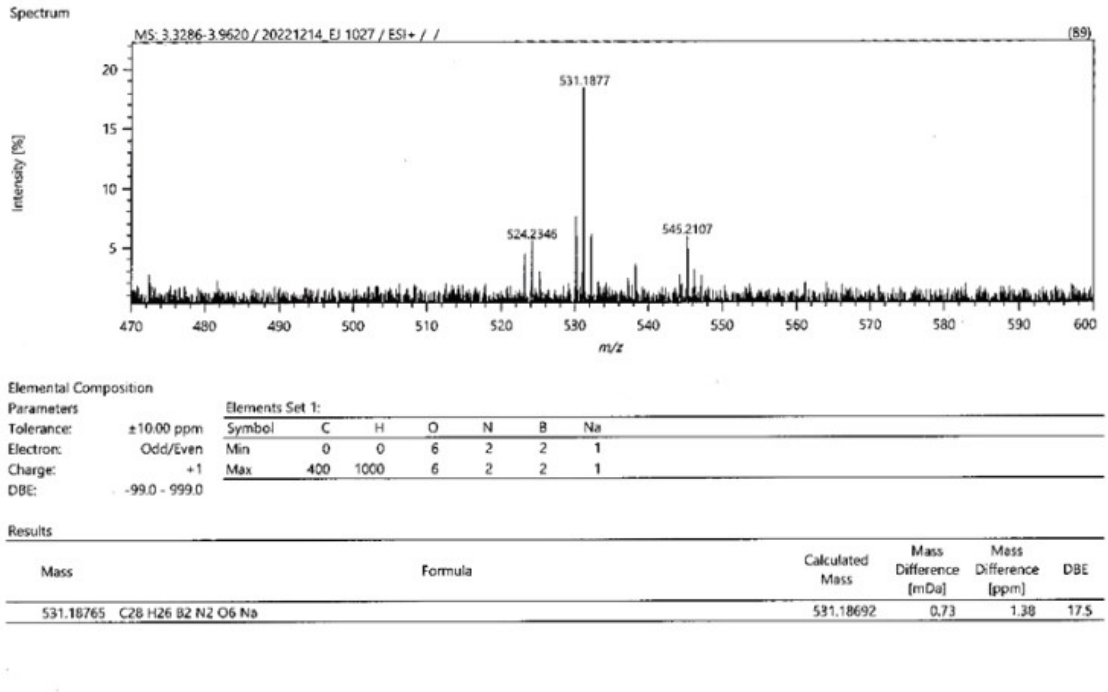


Figure S68. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **A4**

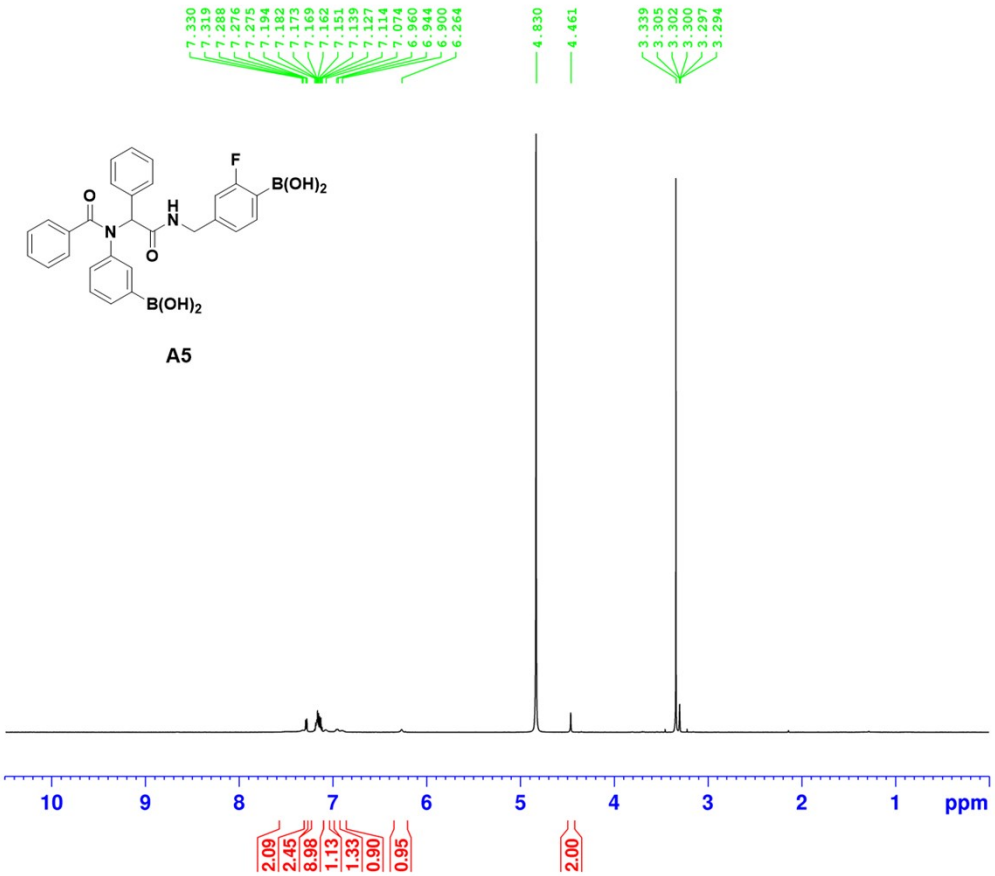


Figure S69. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **A5**

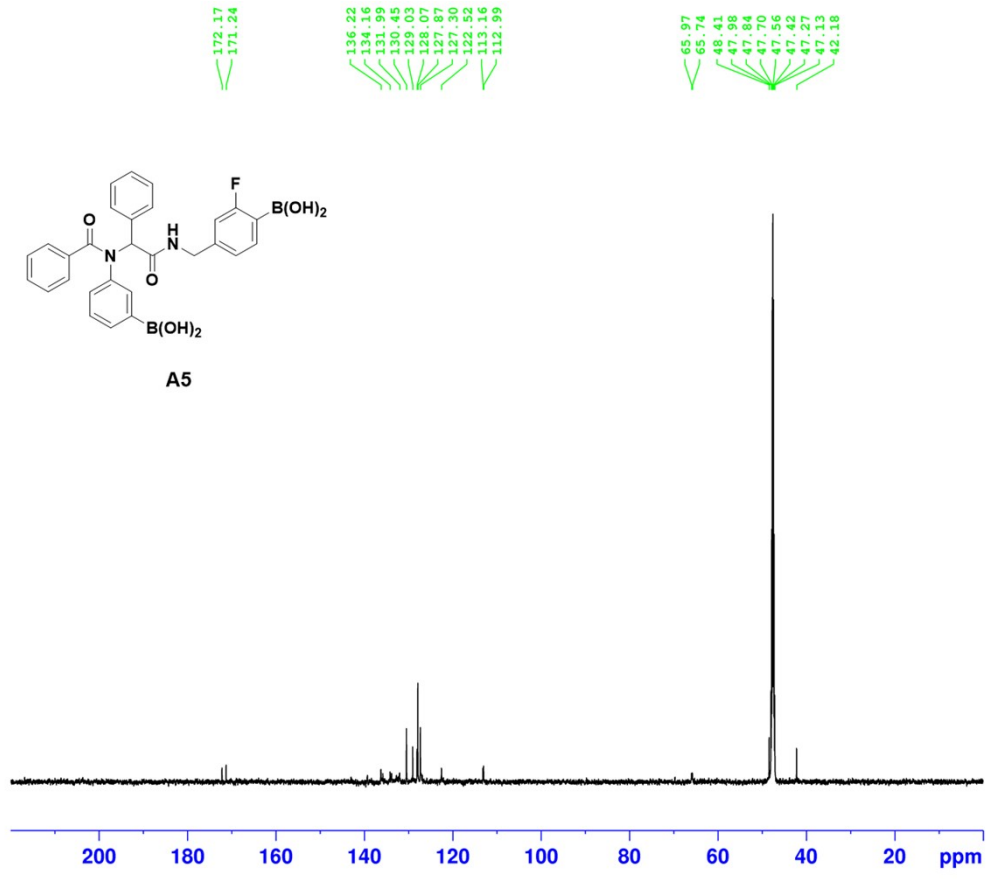


Figure S70. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **A5**

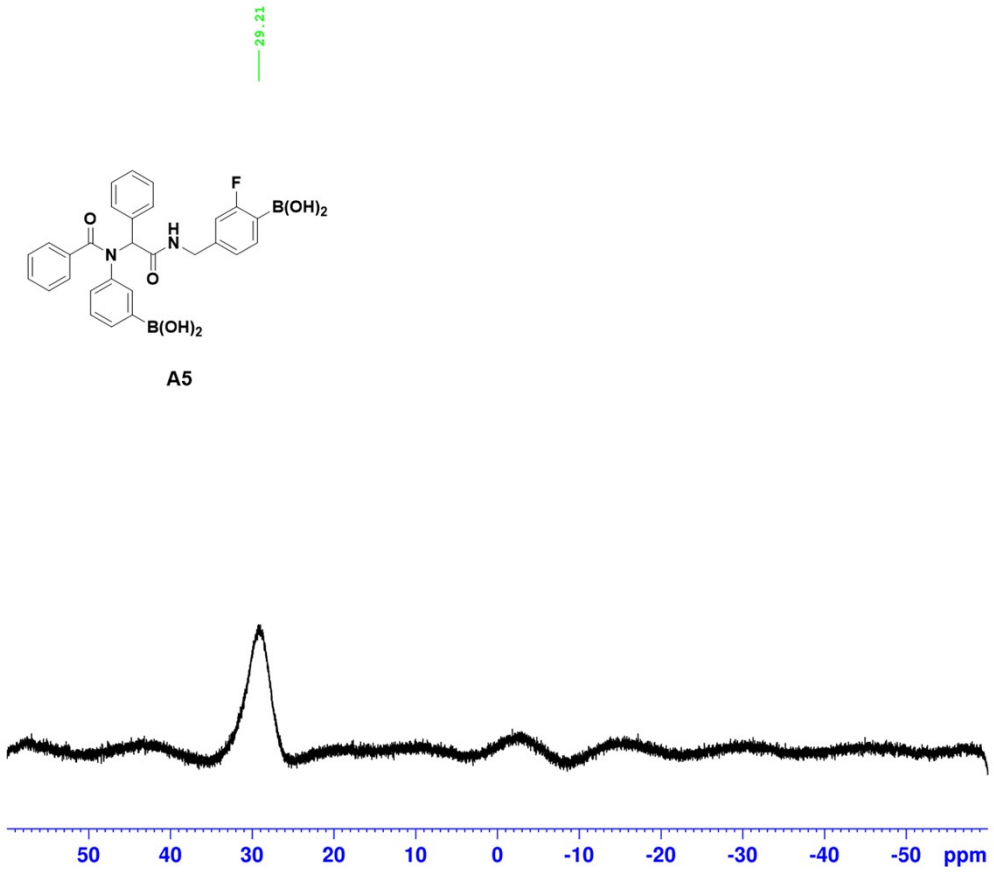


Figure S71. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound A5

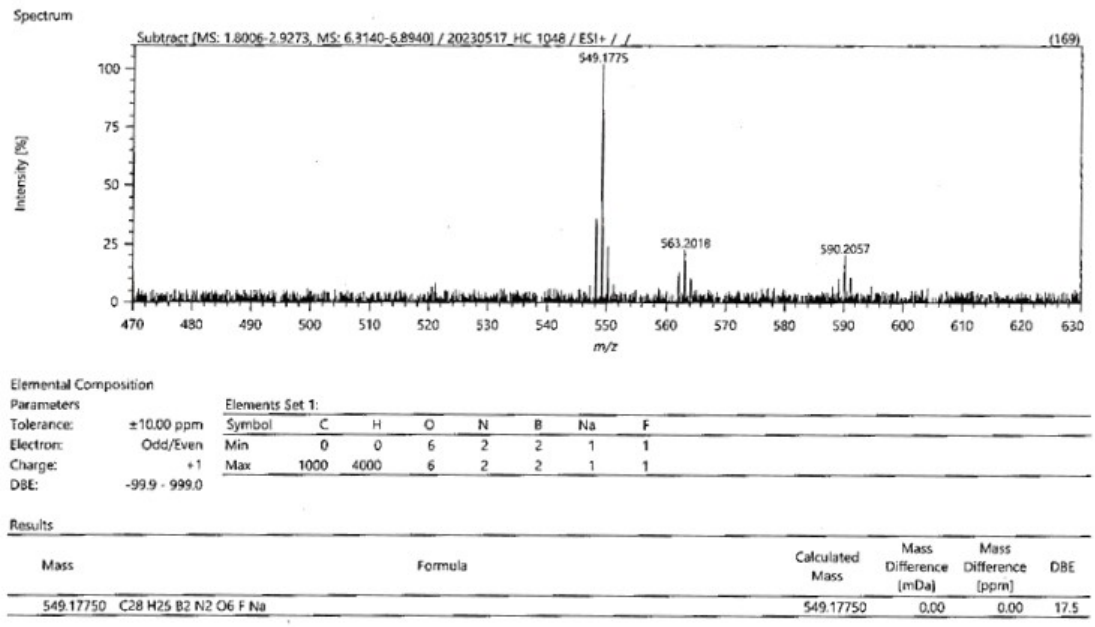


Figure S72. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **A5**

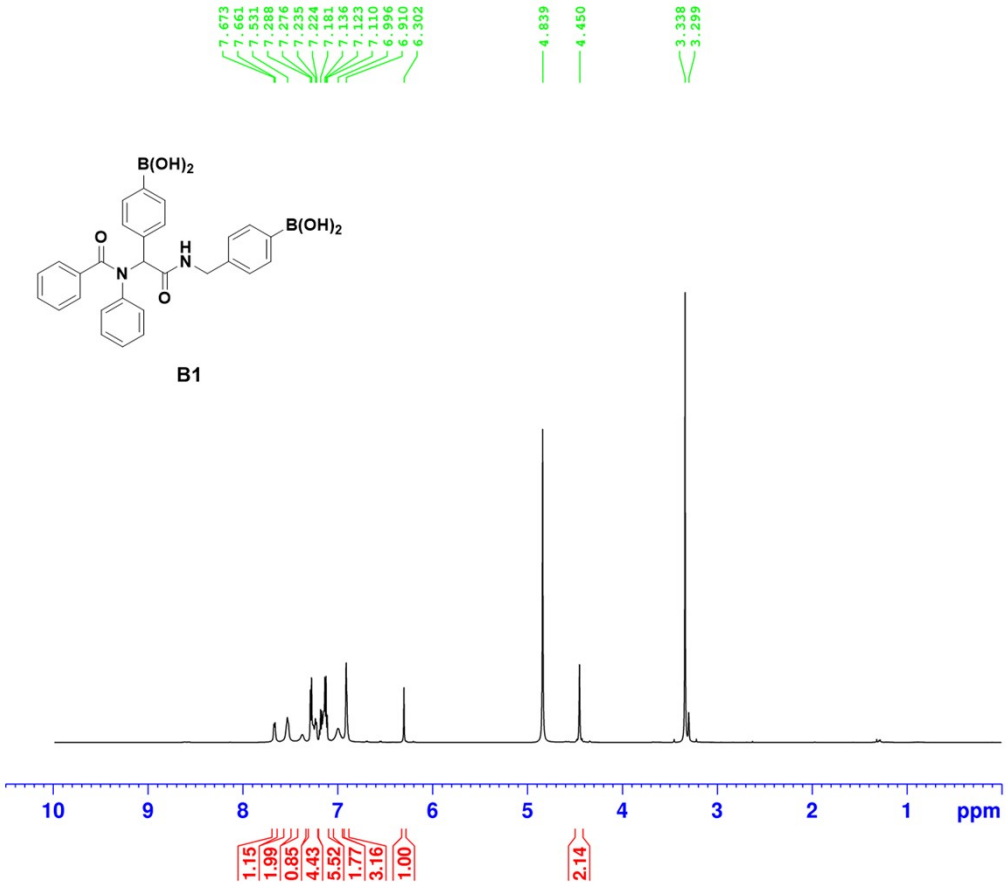


Figure S73. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **B1**

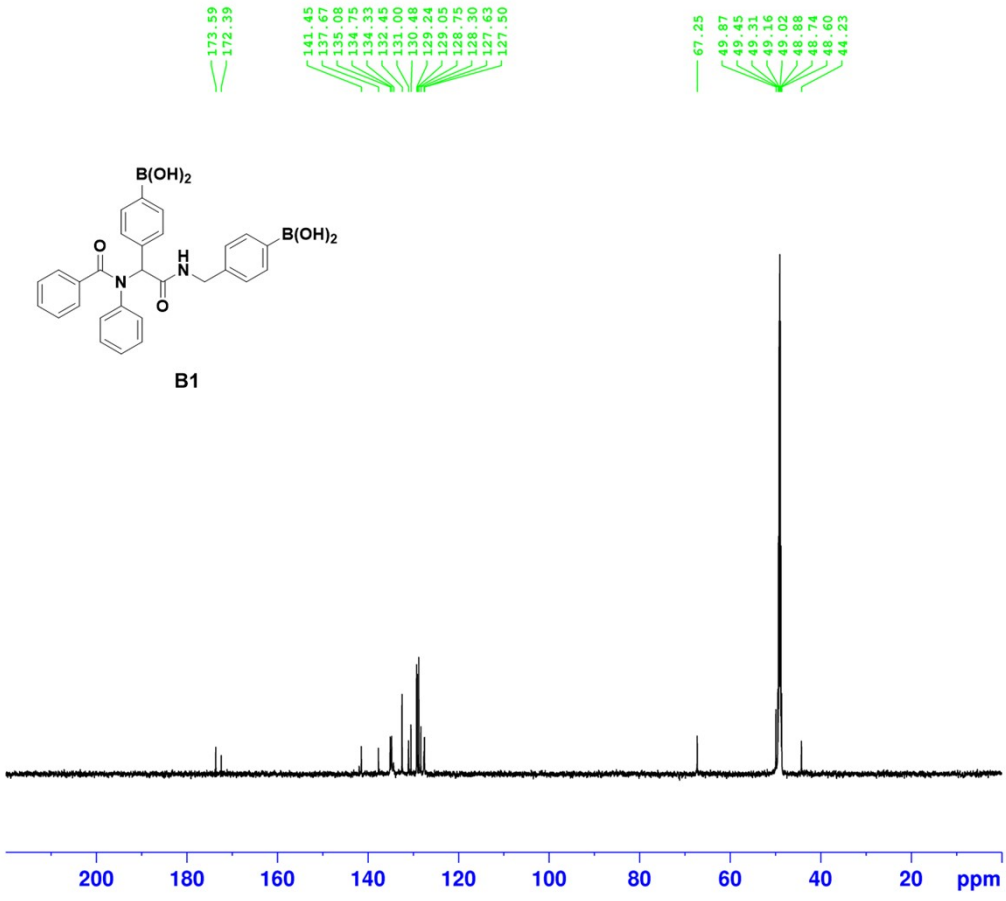


Figure S74. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **B1**

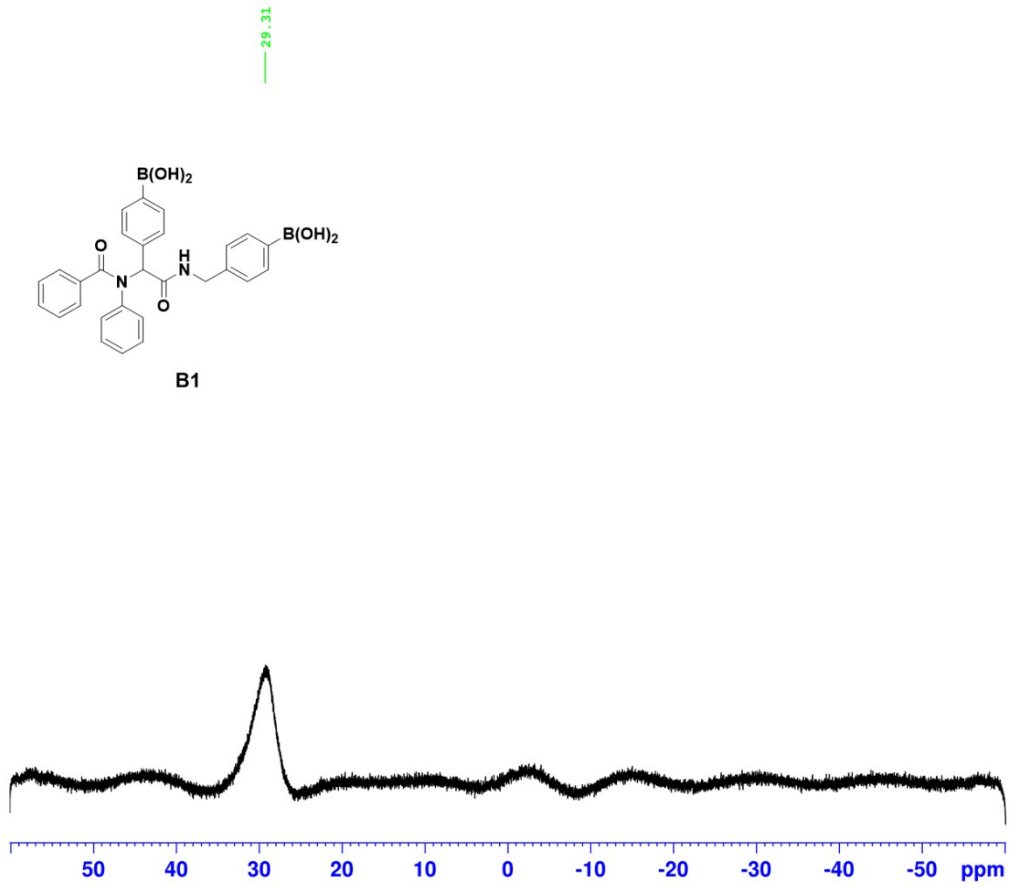


Figure S75. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound B1

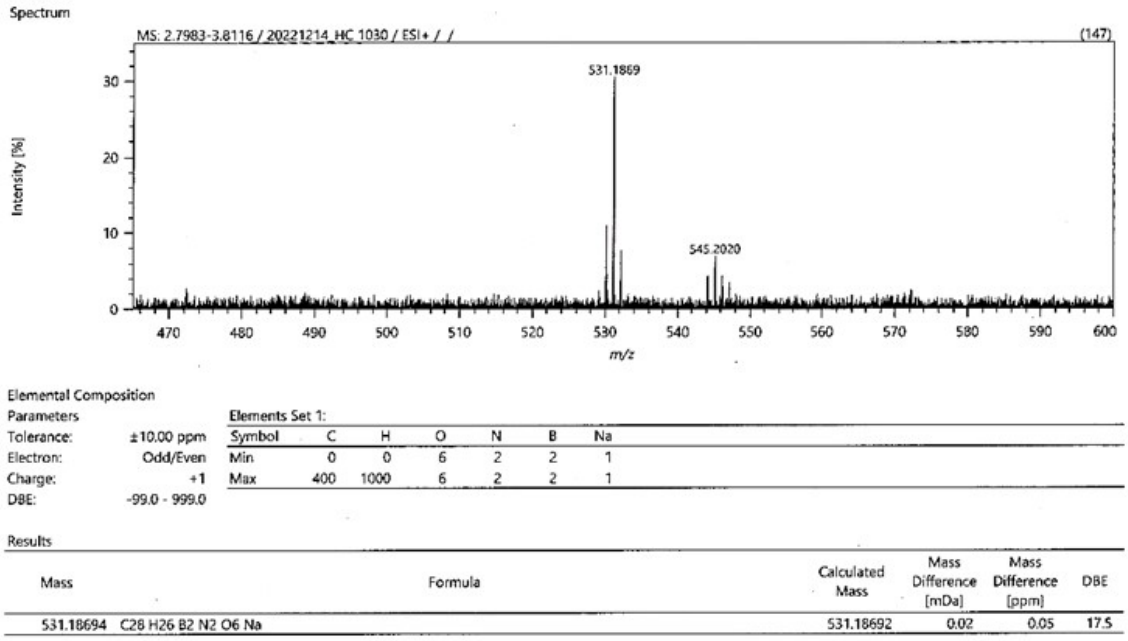


Figure S76. HRMS (ESI, positive ion)[M + Na]$^+$ spectrum of compound B1

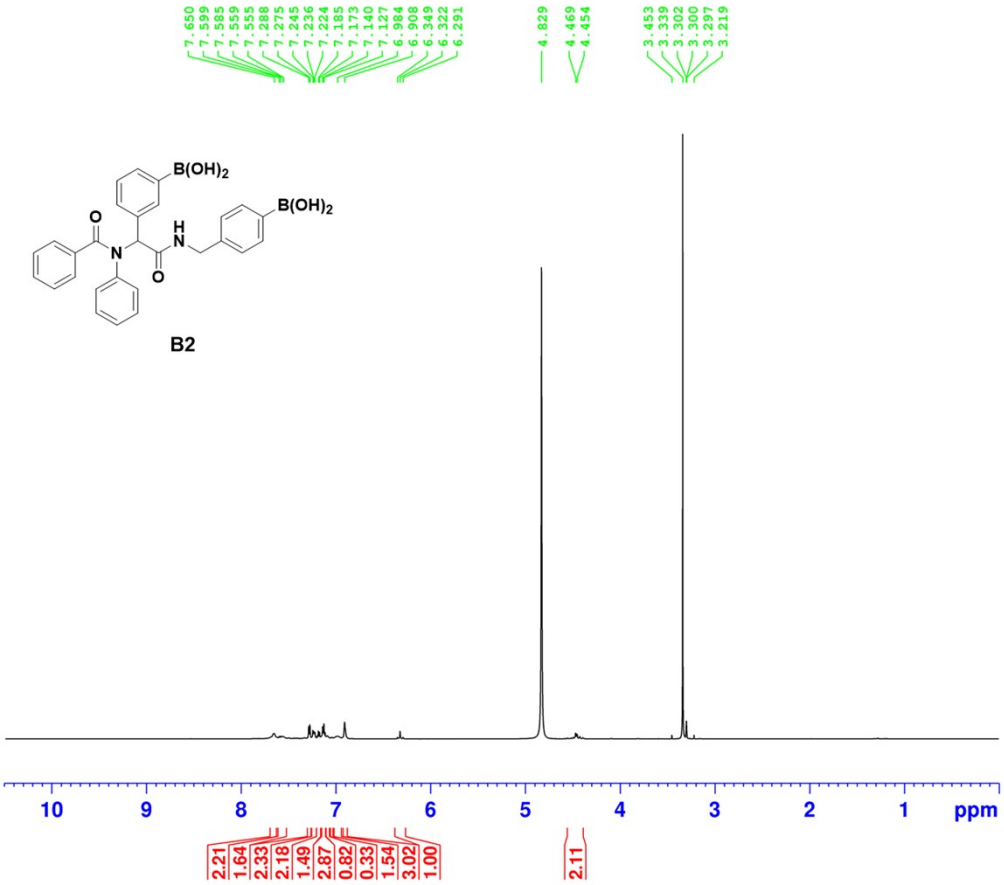


Figure S77. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **B2**

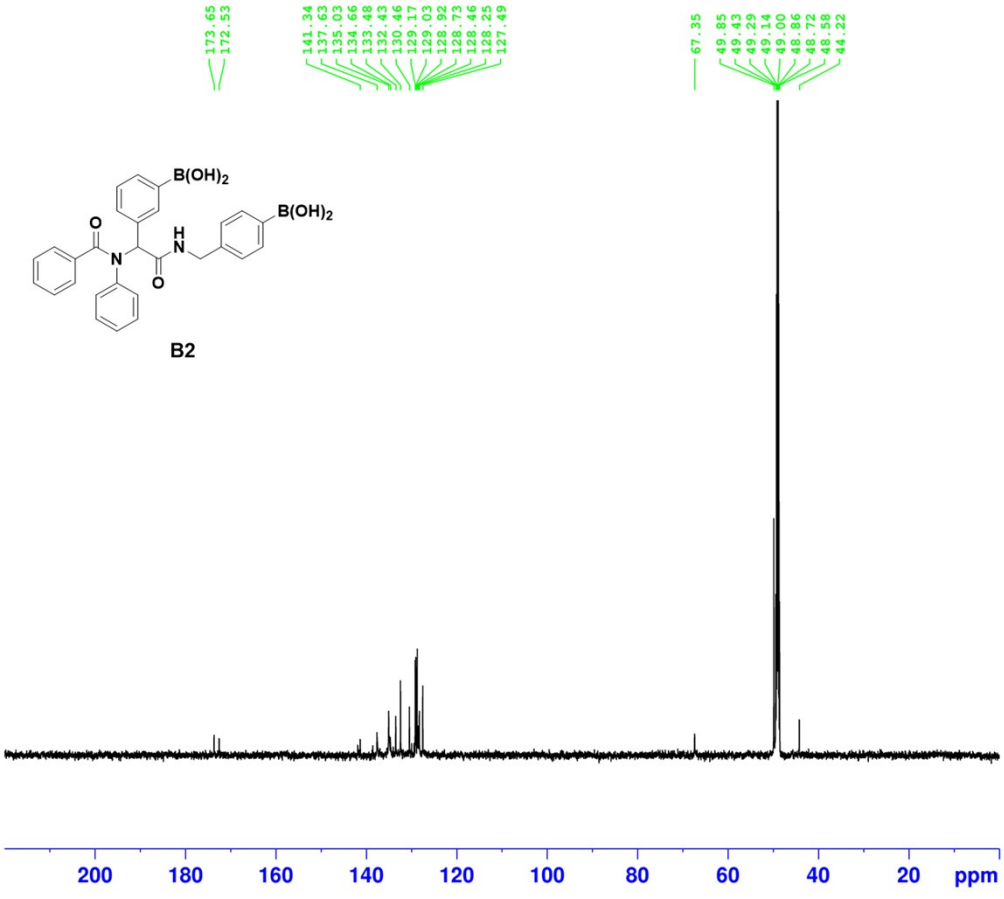


Figure S78. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **B2**

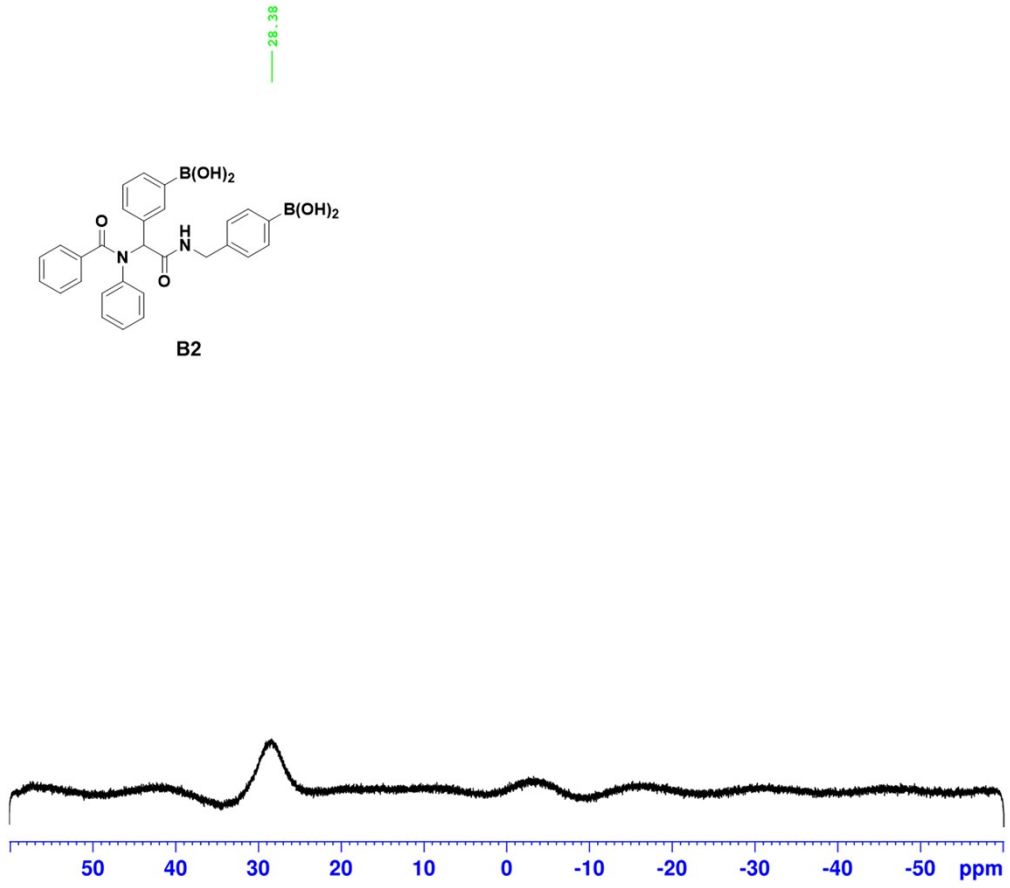


Figure S79. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound B2

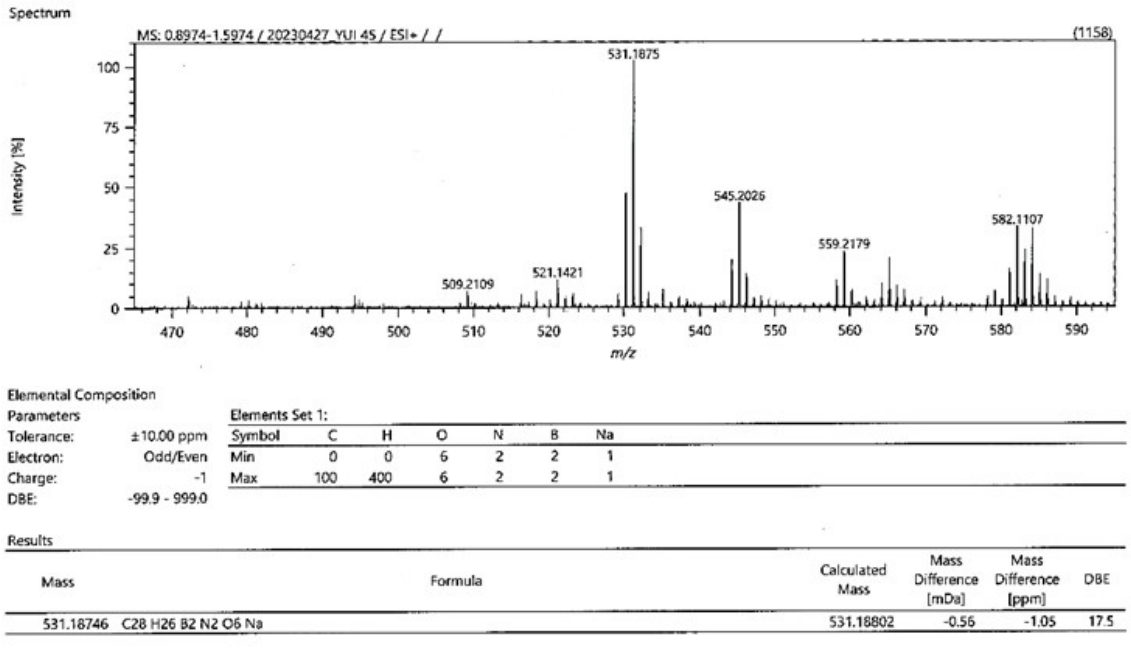


Figure S80. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **B2**

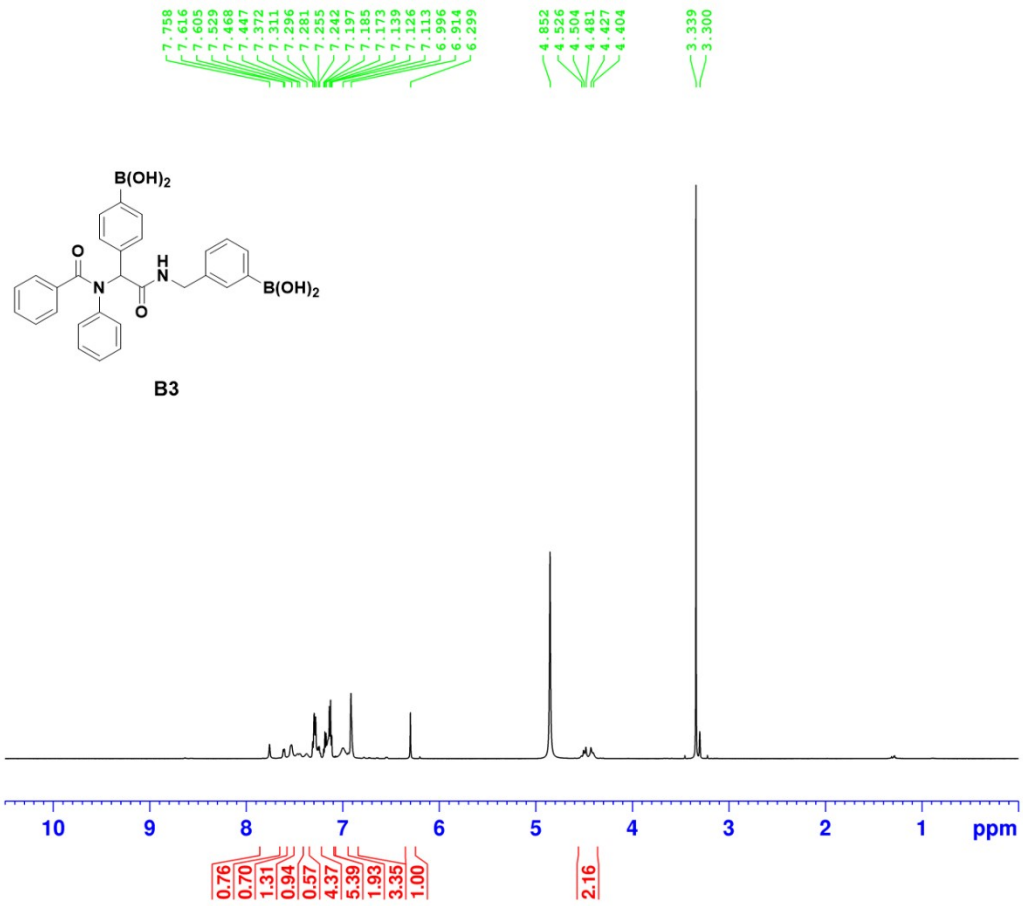


Figure S81. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **B3**

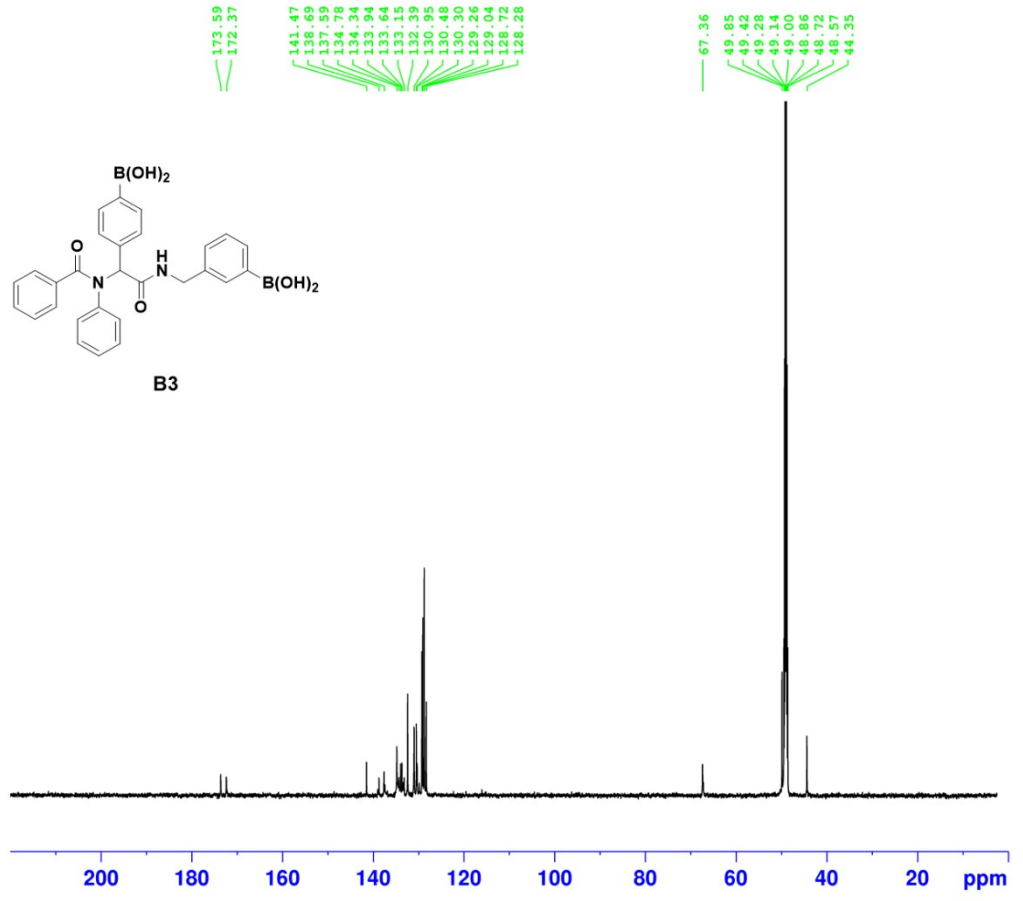
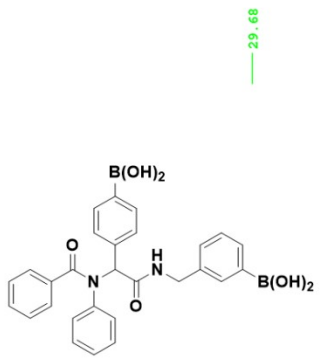


Figure S82. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **B3**



B3

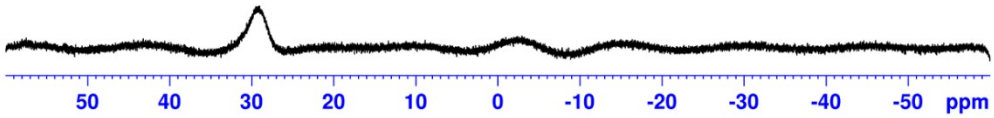
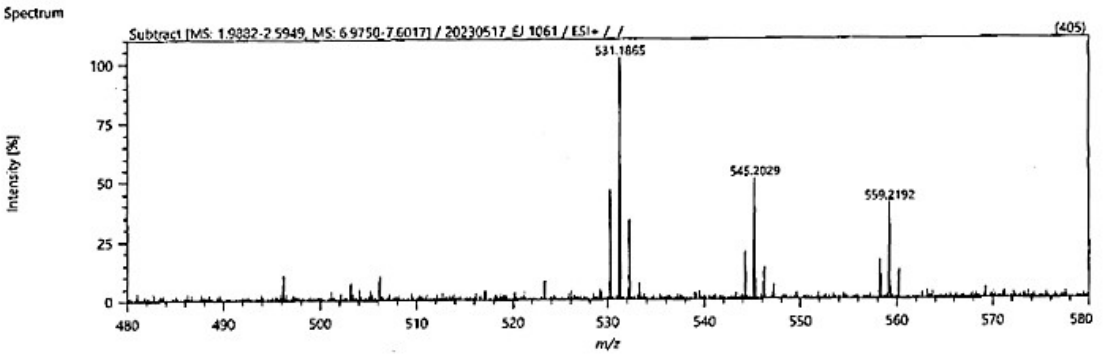


Figure S83. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound B3



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B	Na
Electron:	Odd/Even	Min	0	0	6	2	2	1
Charge:	+1	Max	1000	4000	6	2	2	1
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
531.18653	C28 H26 B2 N2 O6 Na	531.18692	-0.39	-0.73	17.5

Figure S84. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **B3**

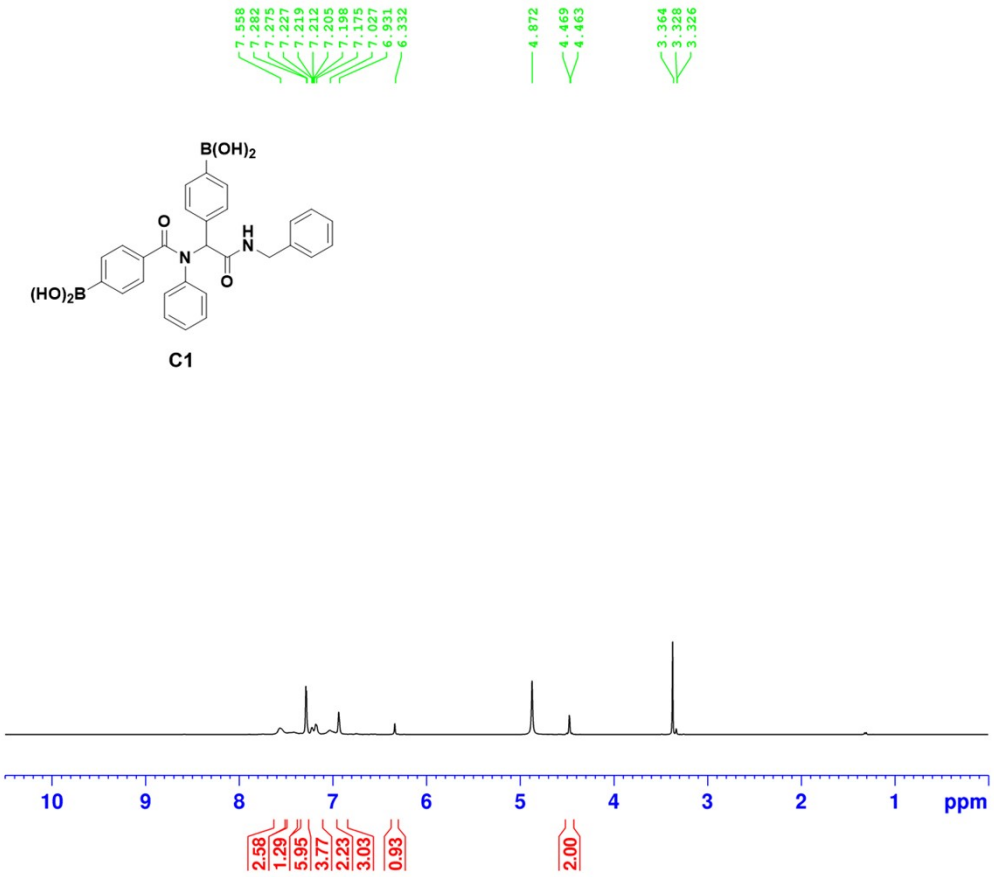


Figure S85. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **C1**

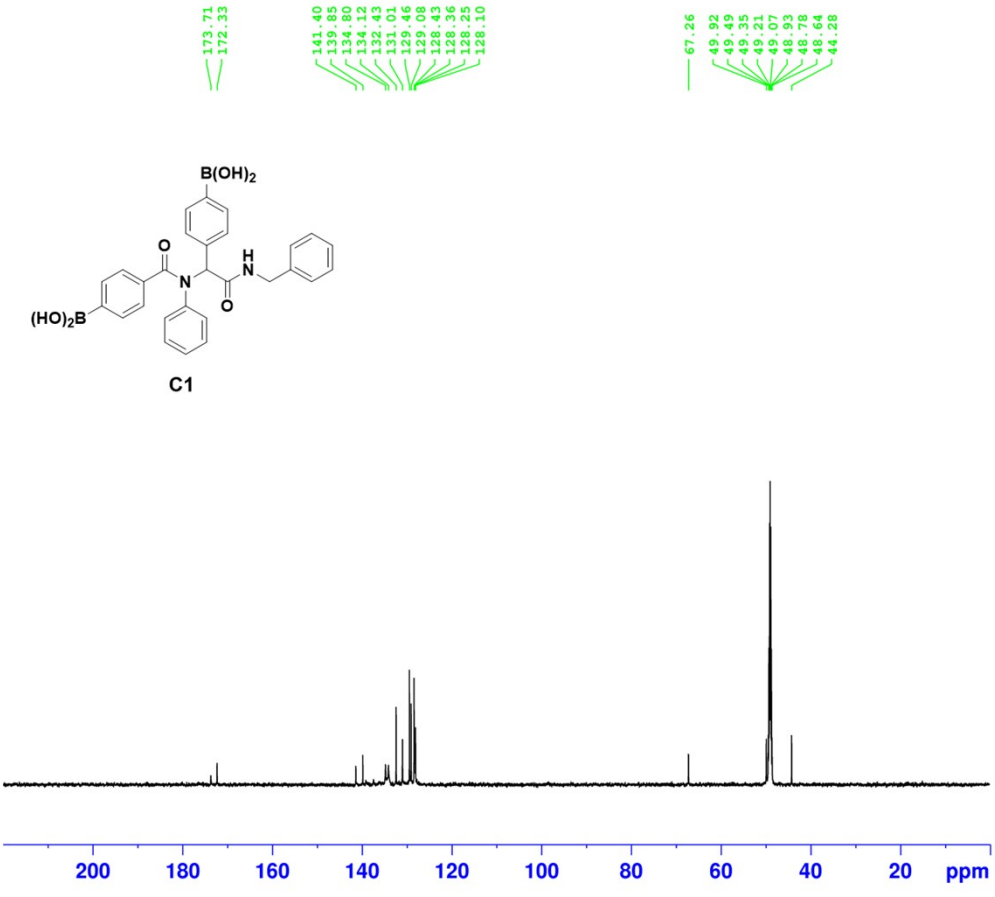
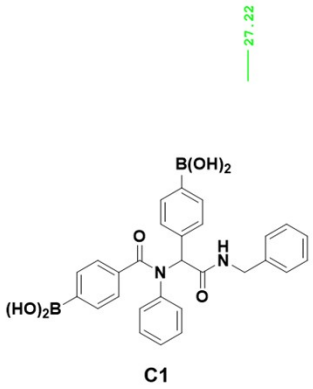


Figure S86. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **C1**



C1

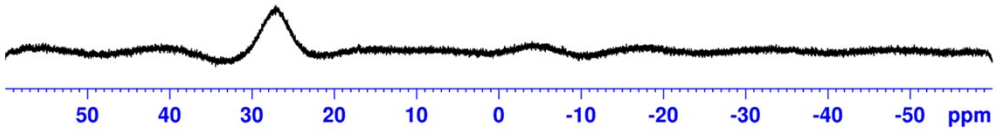
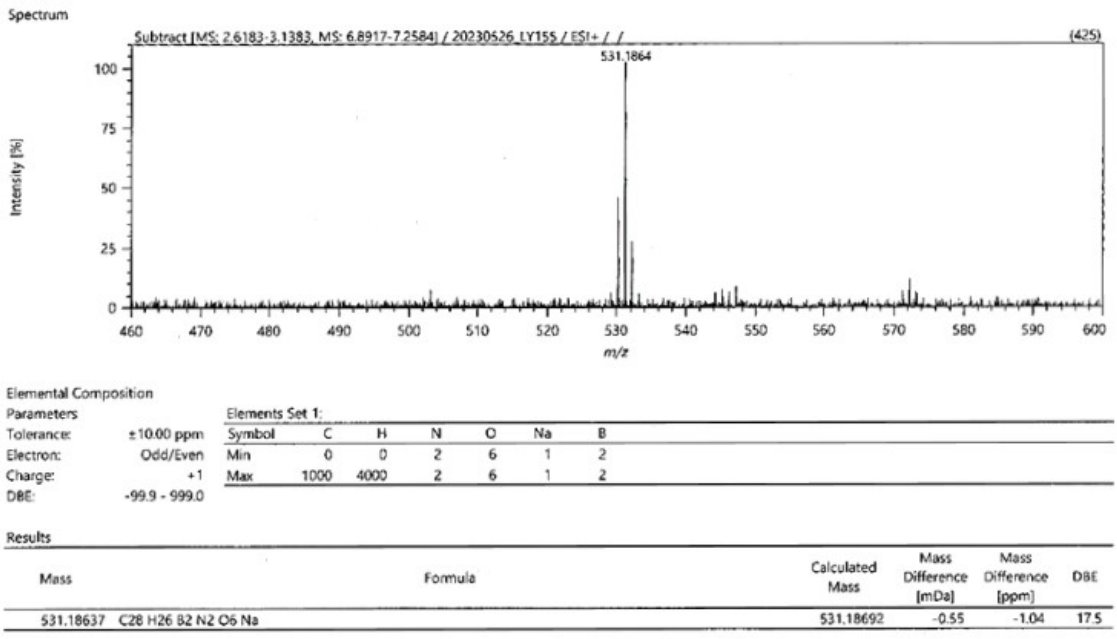


Figure S87. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound C1



Elemental Composition

Parameters		Elements Set 1:						
Tolerance:	±10.00 ppm	Symbol	C	H	N	O	Na	B
Electron:	Odd/Even	Min	0	0	2	6	1	2
Charge:	+1	Max	1000	4000	2	6	1	2
DBE:	-99.9 - 999.0							

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
531.18637	C28 H26 B2 N2 O6 Na	531.18692	-0.55	-1.04	17.5

Figure S88. HRMS (ESI, positive ion)[M + Na]$^+$ spectrum of compound **C1**

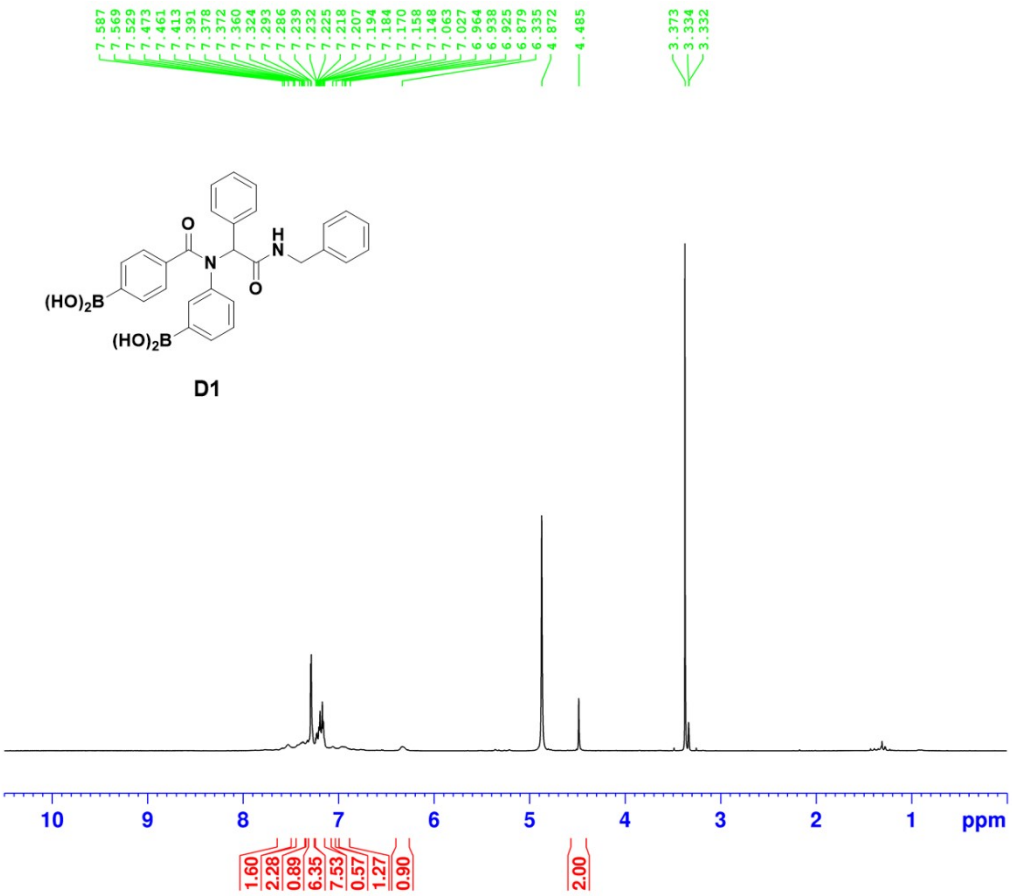


Figure S89. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **D1**

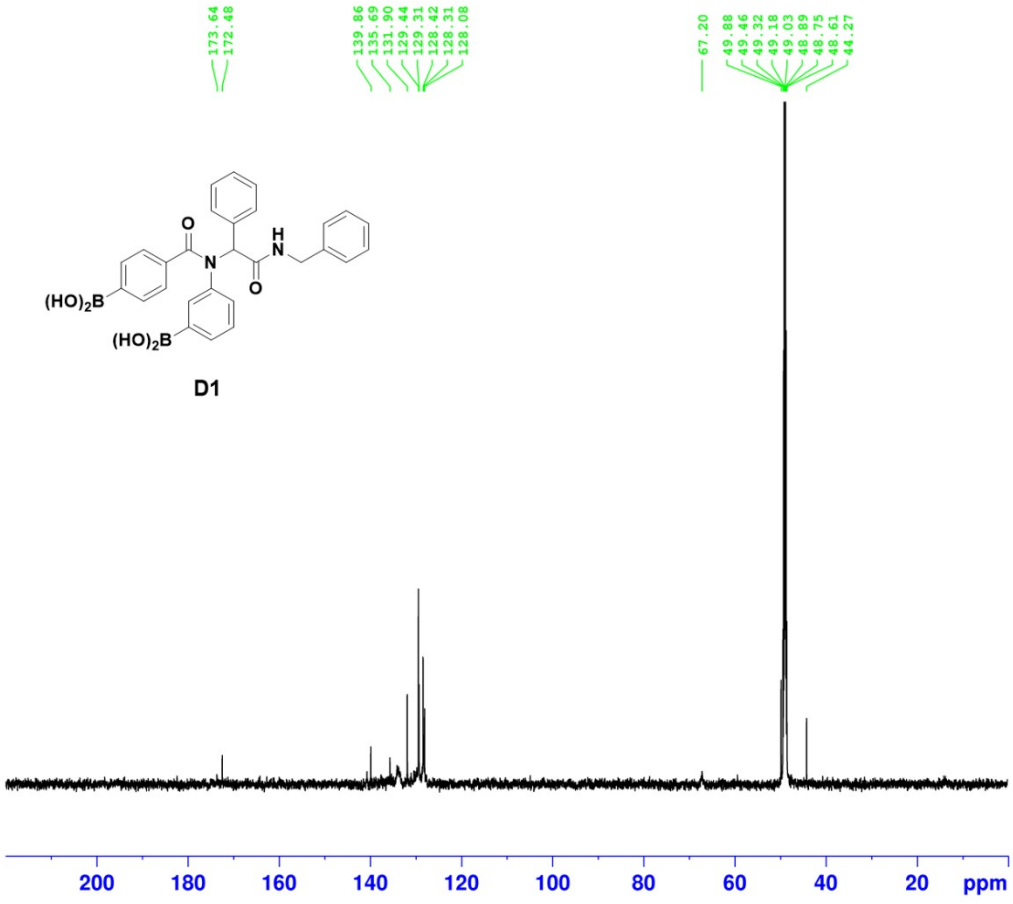
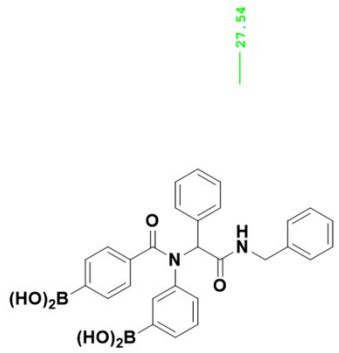


Figure S90. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **D1**



D1

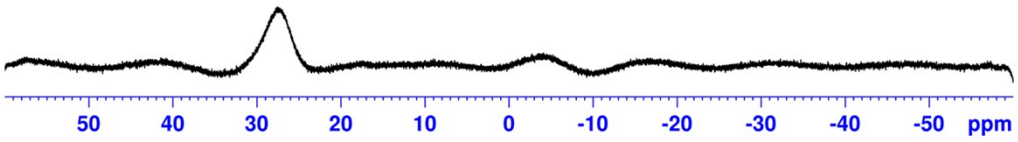
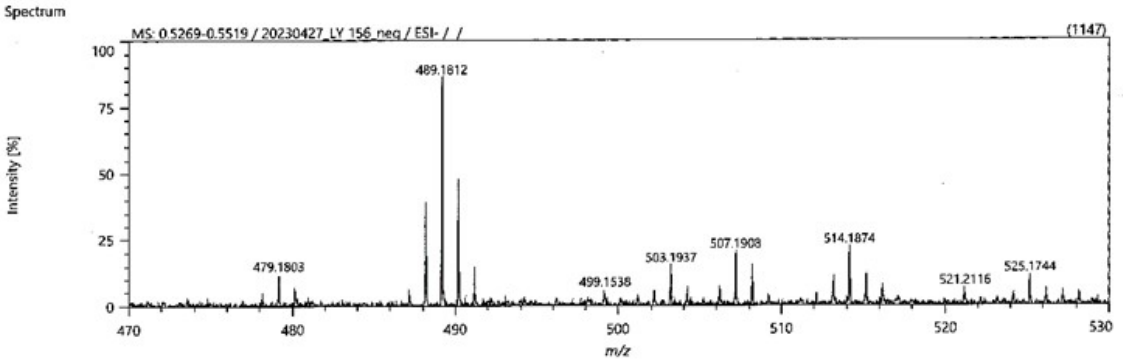


Figure S91. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound D1



Elemental Composition

Parameters		Elements Set 1:					
Tolerance:	±10.00 ppm	Symbol	C	H	O	N	B
Electron:	Odd/Even	Min	0	0	6	2	2
Charge:	-1	Max	100	400	6	2	2
DBE:	-99.9 - 999.0						

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]	DBE
507.19079	C28 H25 B2 N2 O6	507.19042	0.37	0.74	18.5

Figure S92. HRMS (ESI, negative ion)[M + H^+]$^-$ spectrum of compound **D1**

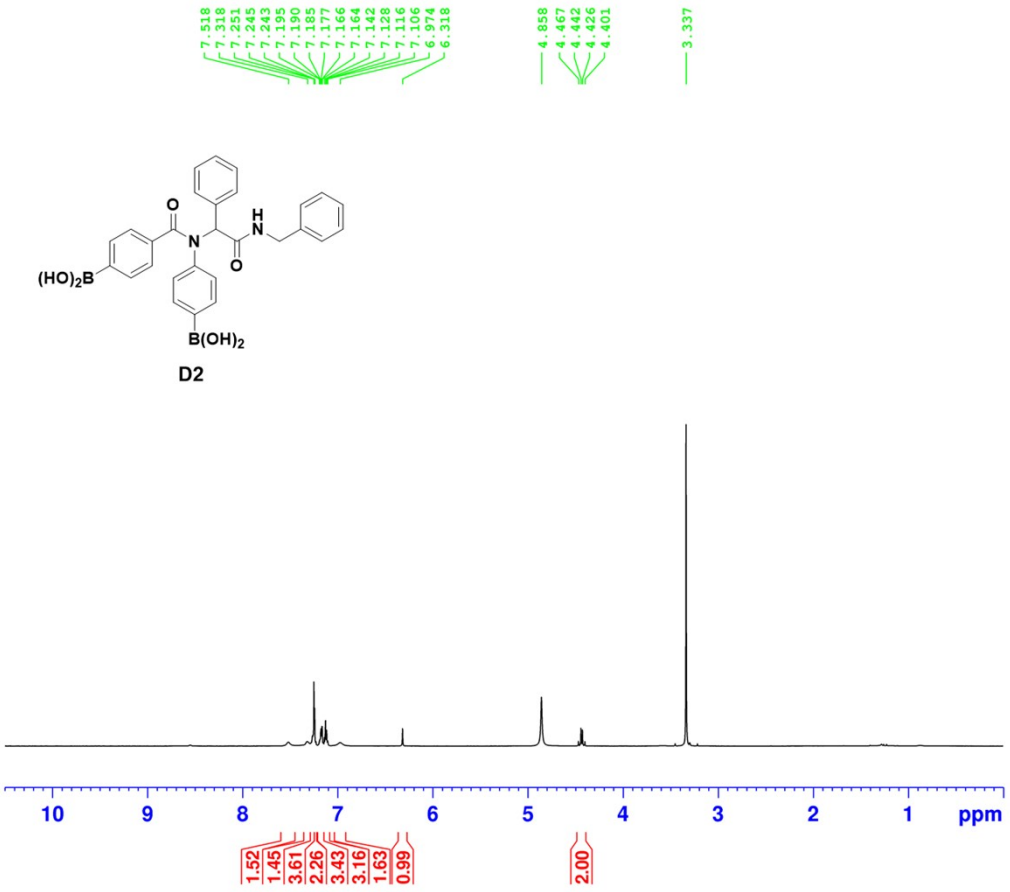


Figure S93. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **D2**

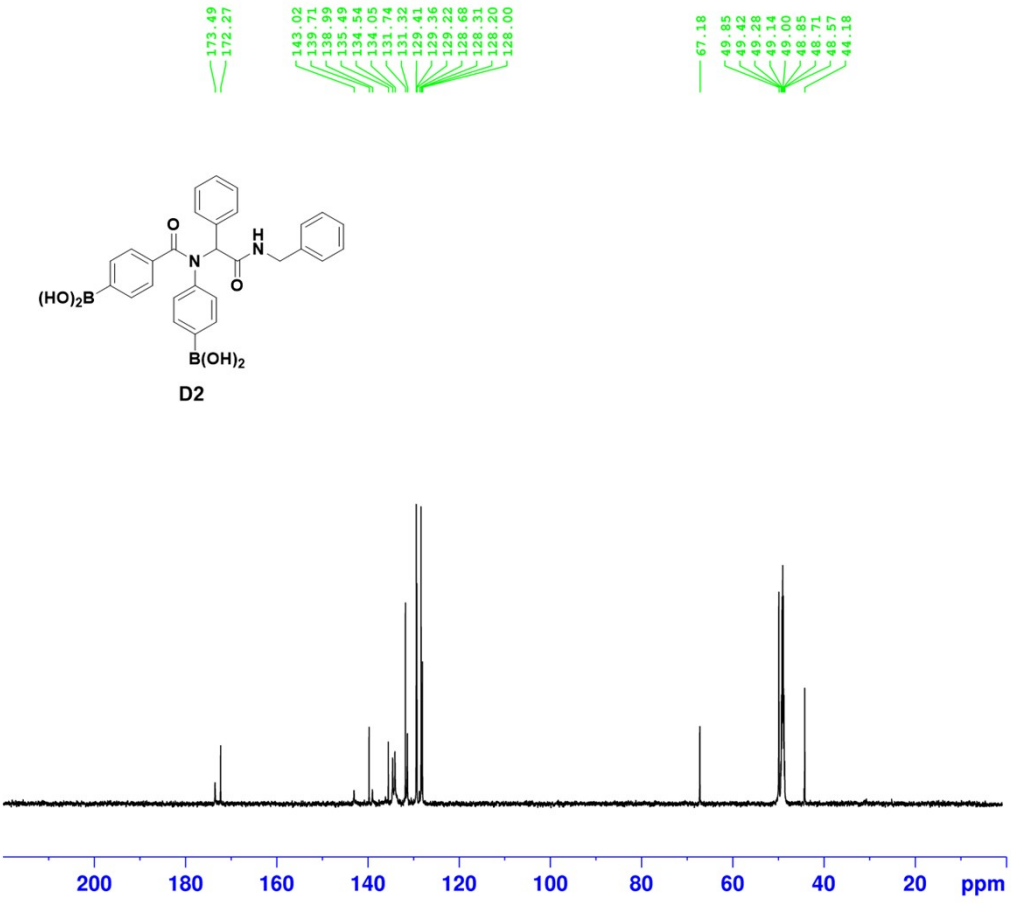


Figure S94. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **D2**

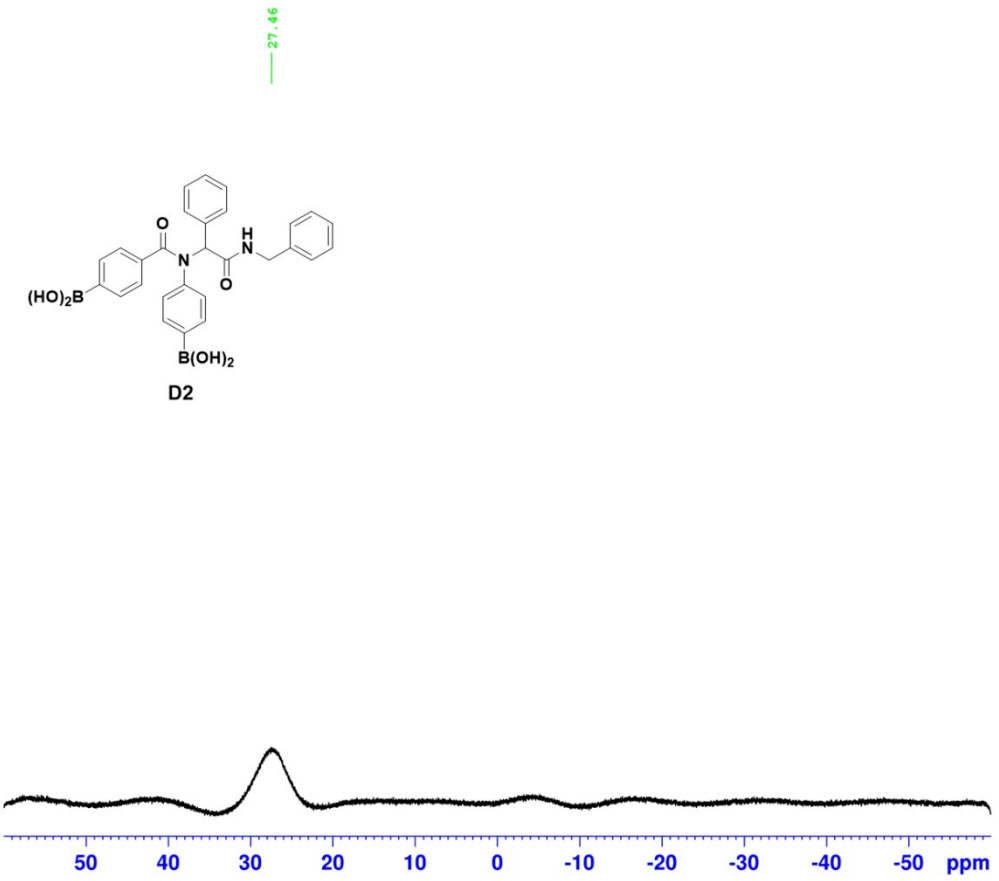


Figure S95. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound D2

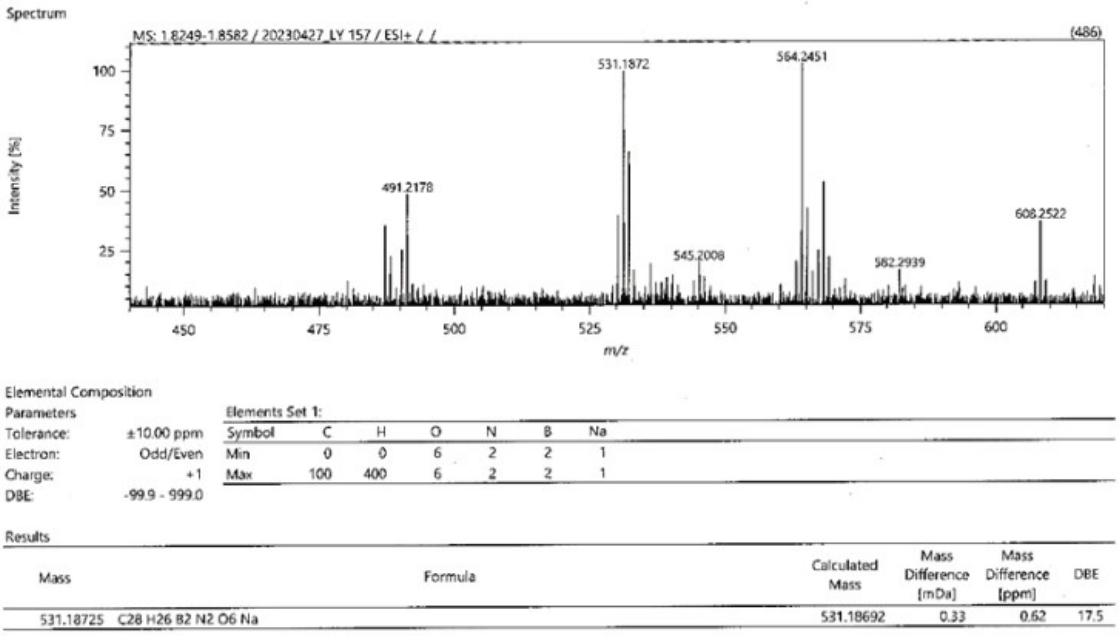


Figure S96. HRMS (ESI, positive ion)[M + Na]$^+$ spectrum of compound **D2**

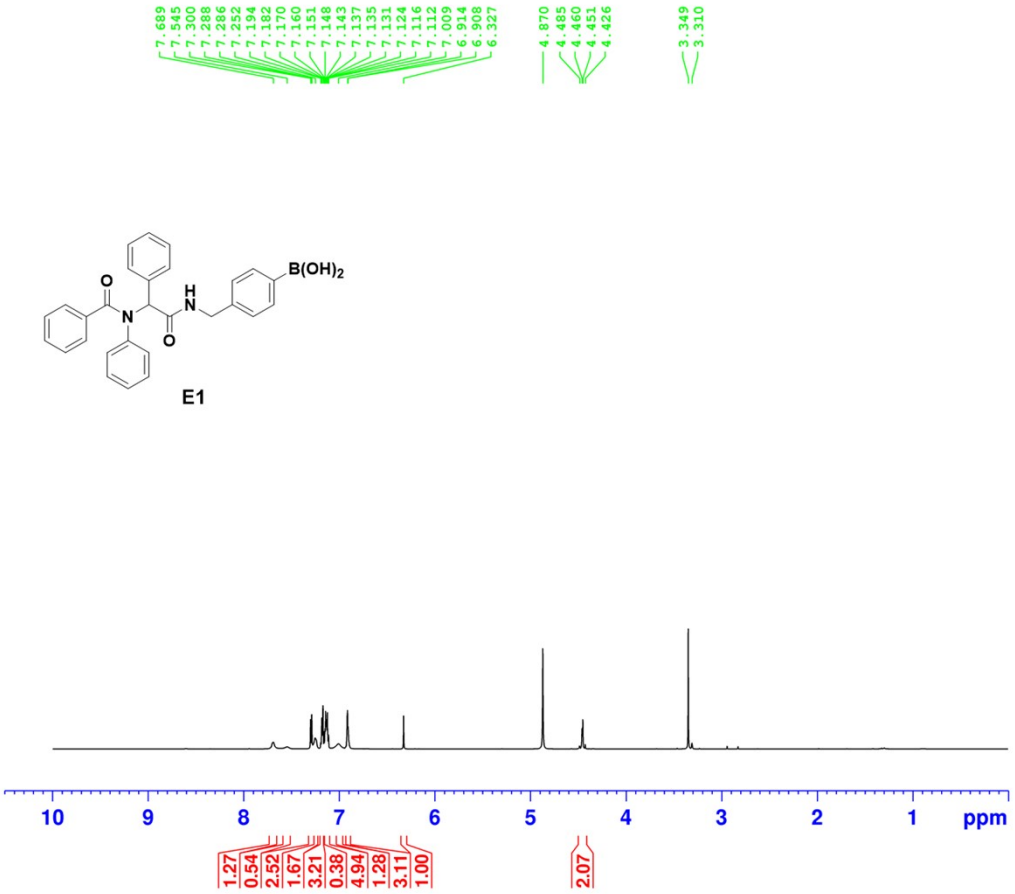


Figure S97. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **E1**

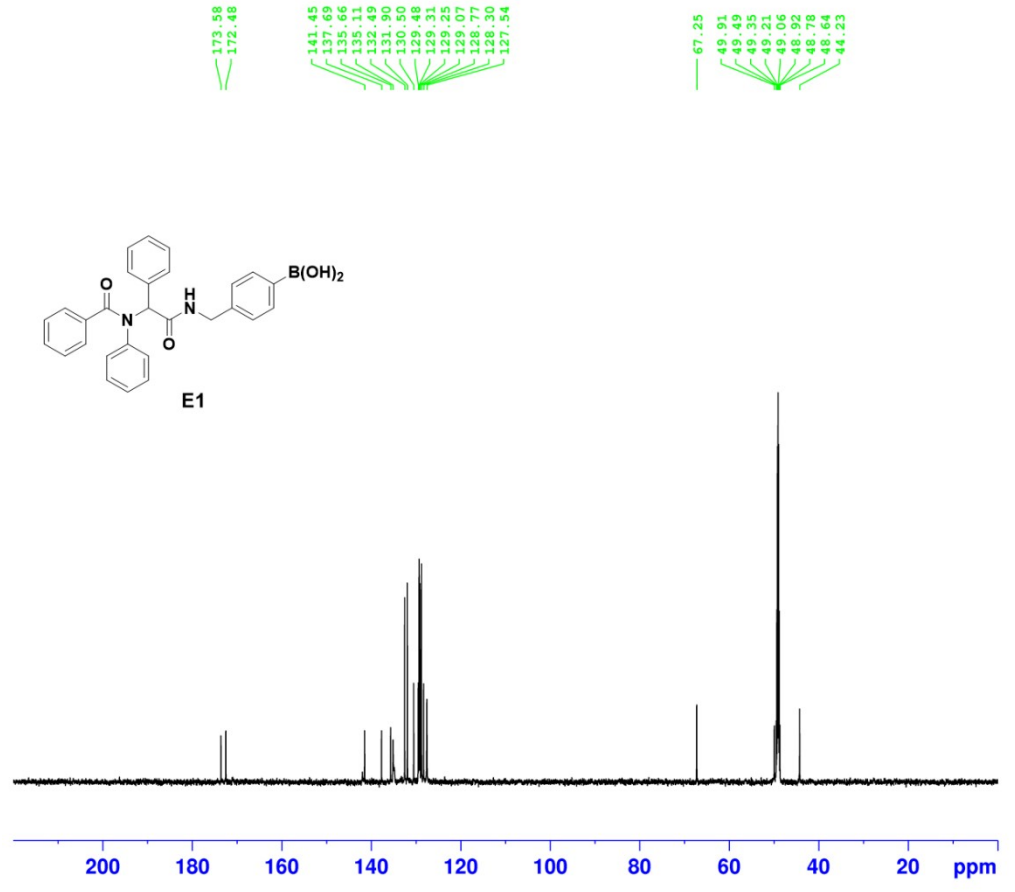


Figure S98. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **E1**

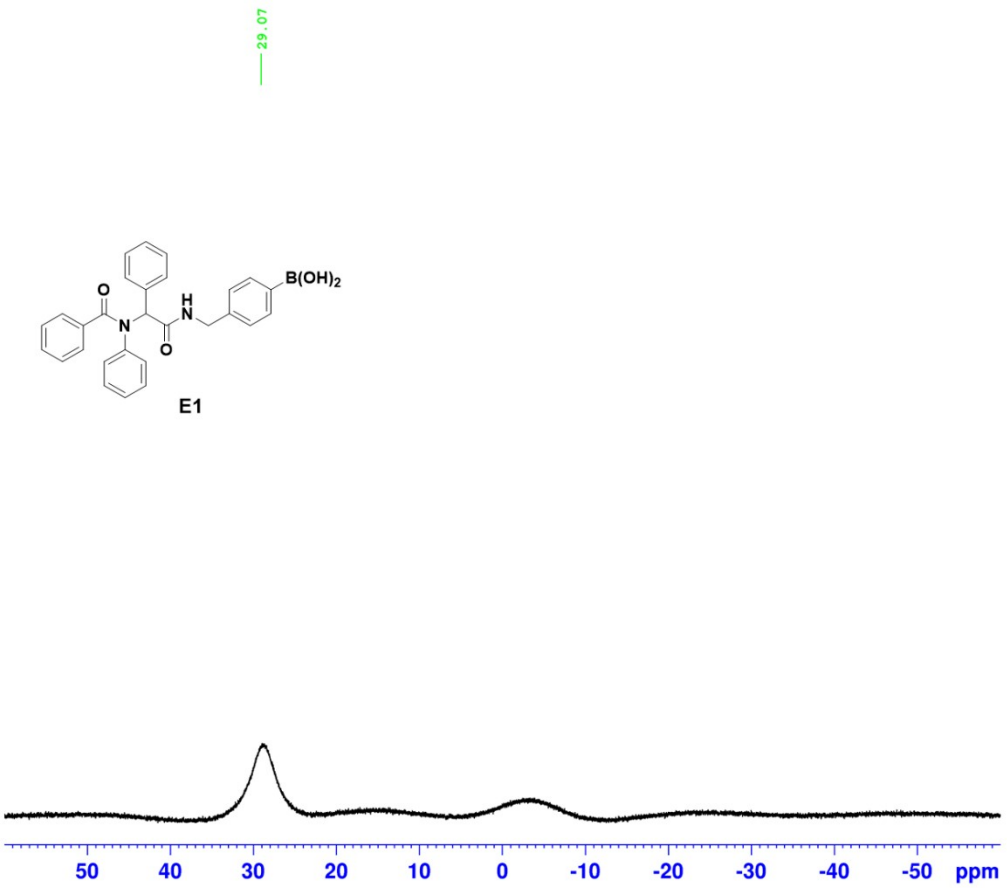


Figure S99. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound E1

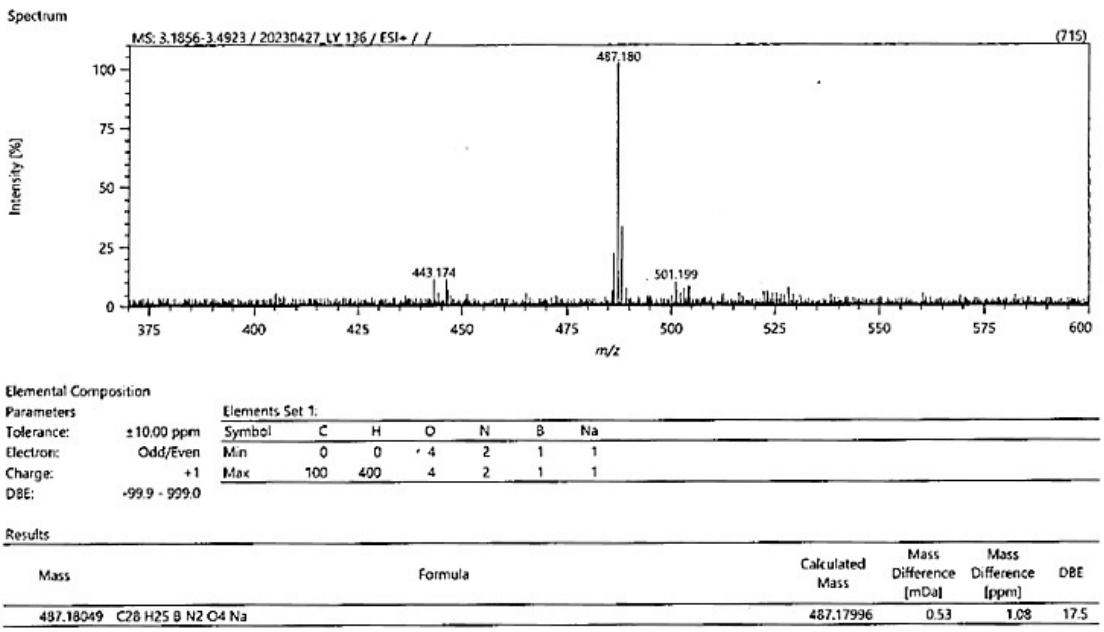


Figure S100. HRMS (ESI, positive ion)$[M + Na]^+$ spectrum of compound **E1**

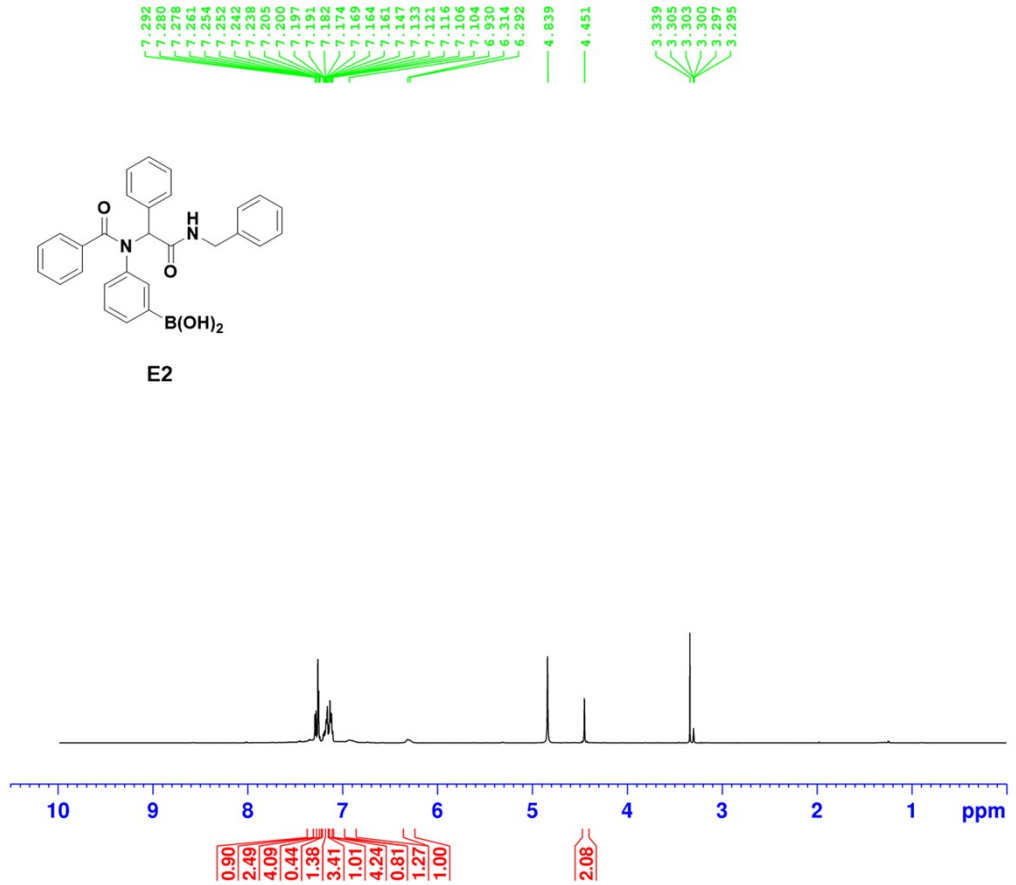


Figure S101. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **E2**

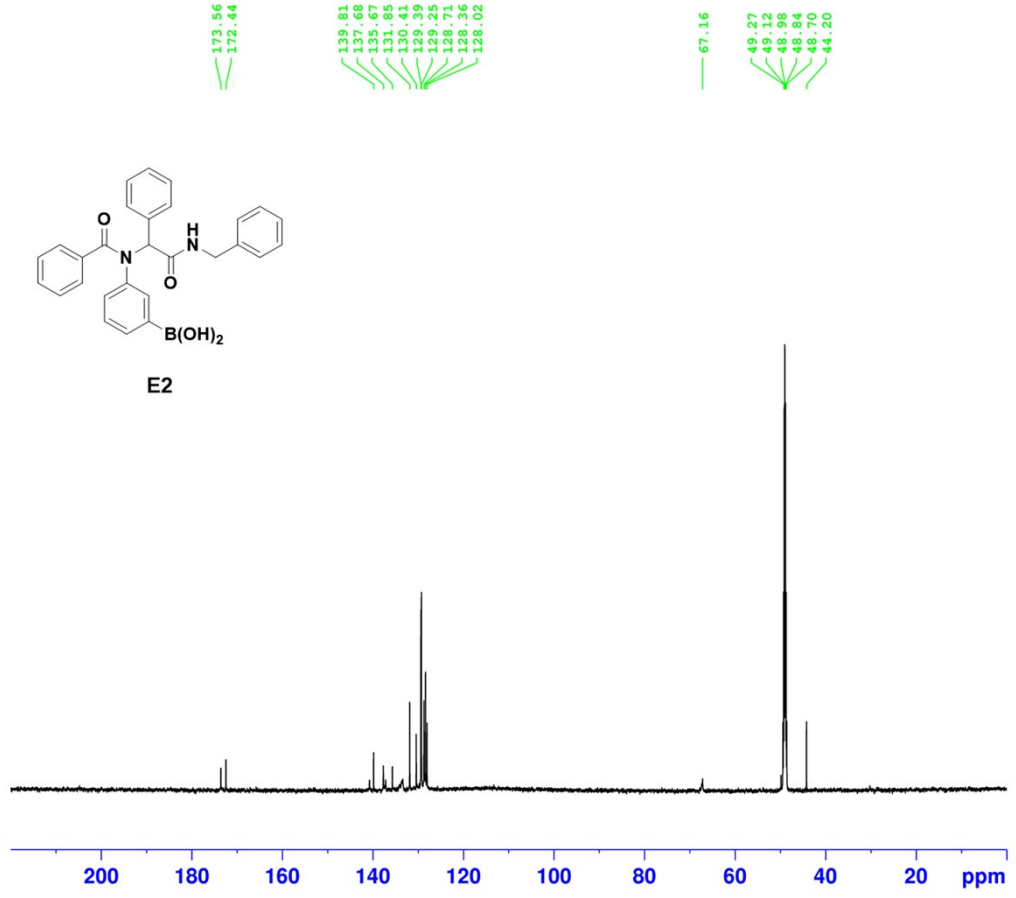


Figure S102. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound **E2**

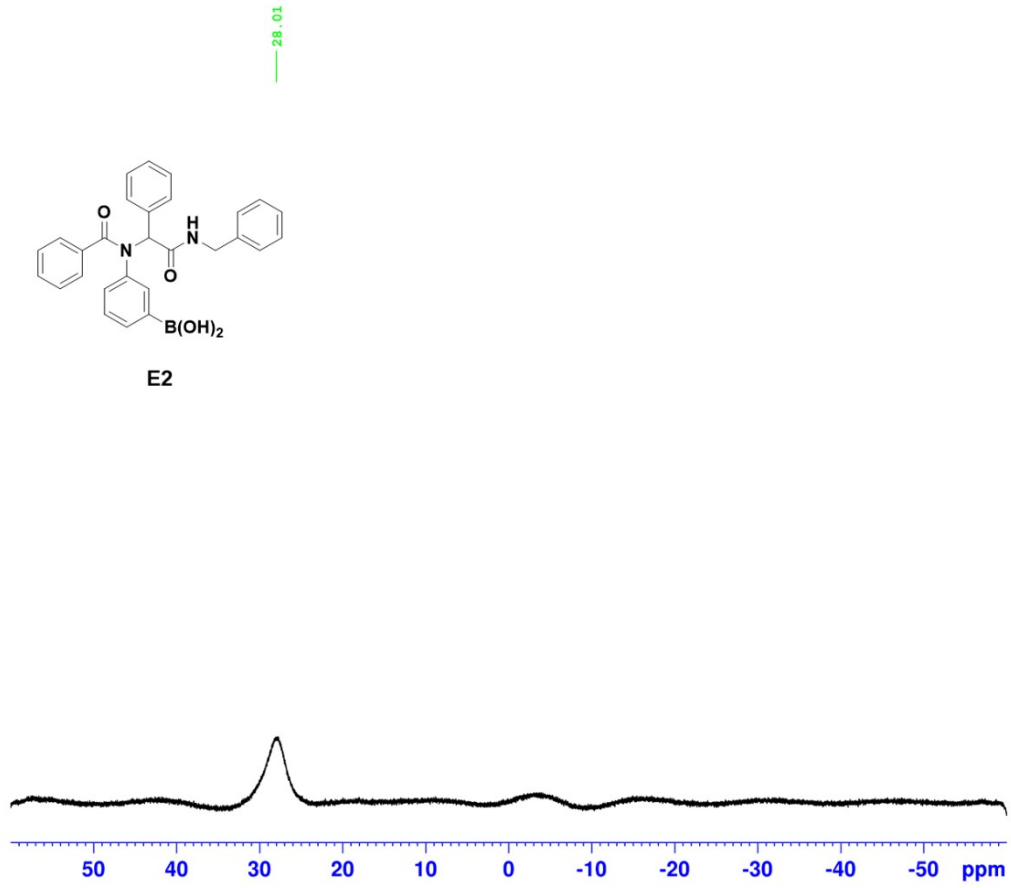


Figure S103. ^{11}B NMR (192.5 MHz, $CDCl_3$) spectrum of compound E2

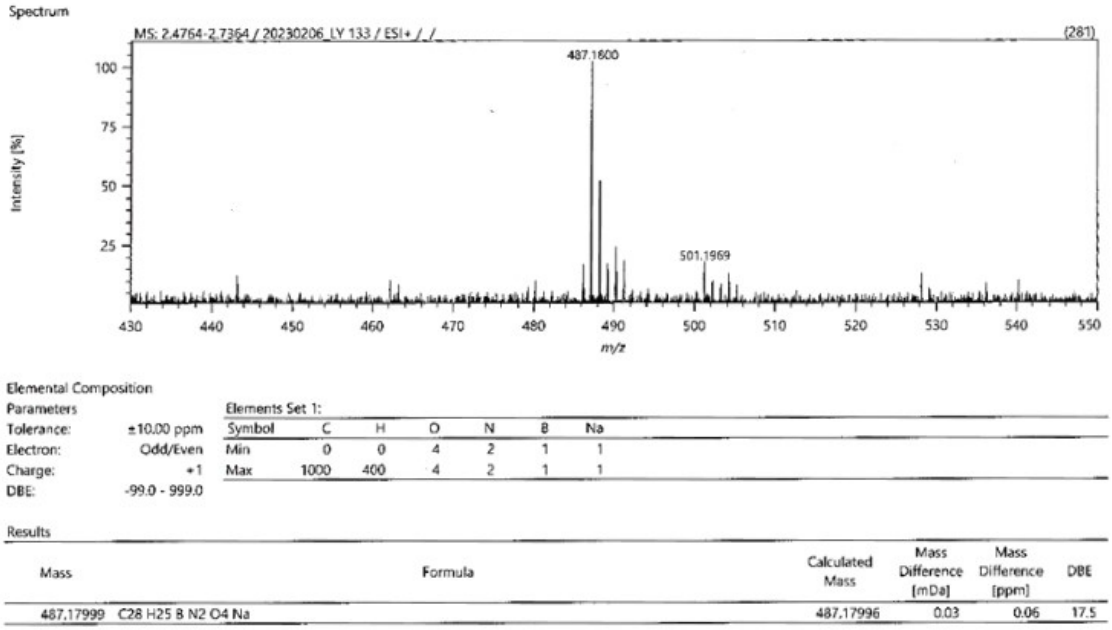


Figure S104. HRMS (ESI, positive ion)[M + Na]$^+$ spectrum of compound **E2**

K_{ARS} and K_{eq} (Sialic acid) titration curve at pH 6.0 and pH 6.5

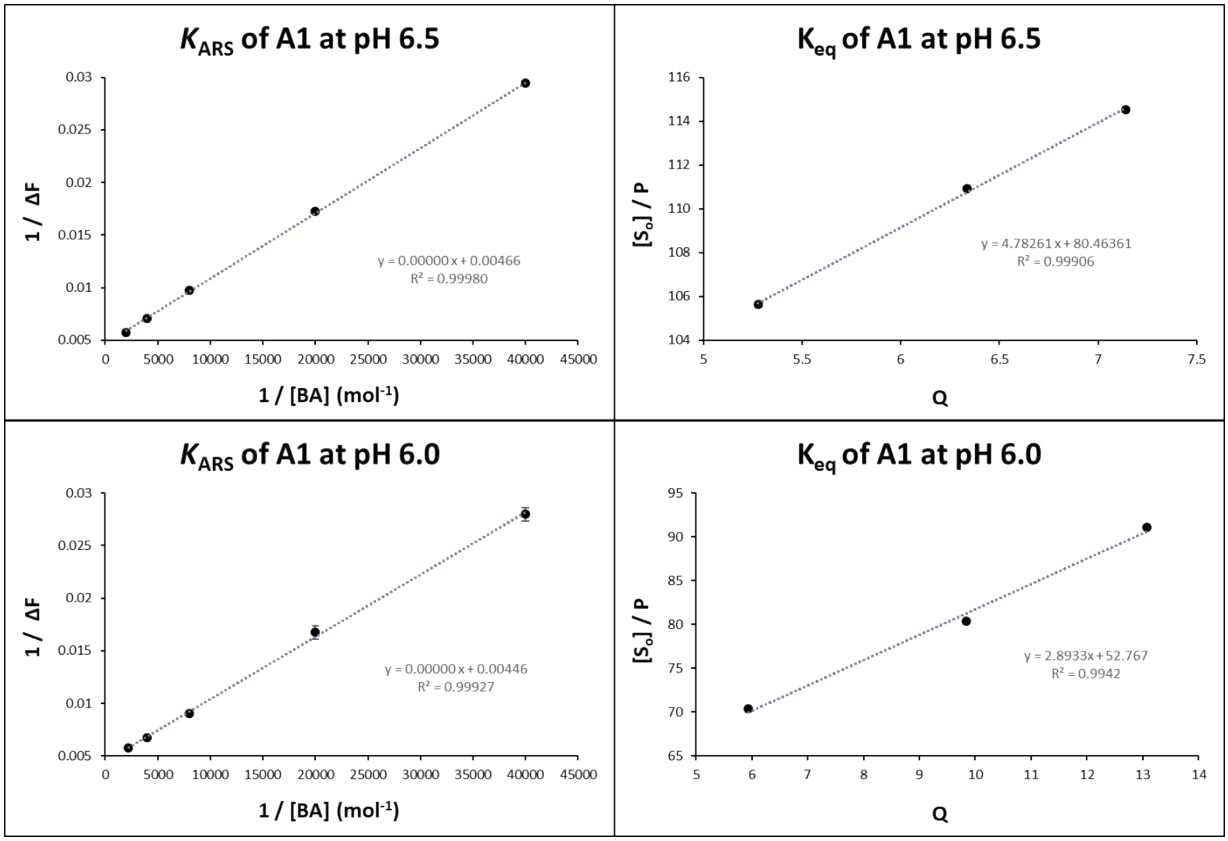


Figure S105. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A1** at pH 6.0 and pH 6.5 (three repetitions)

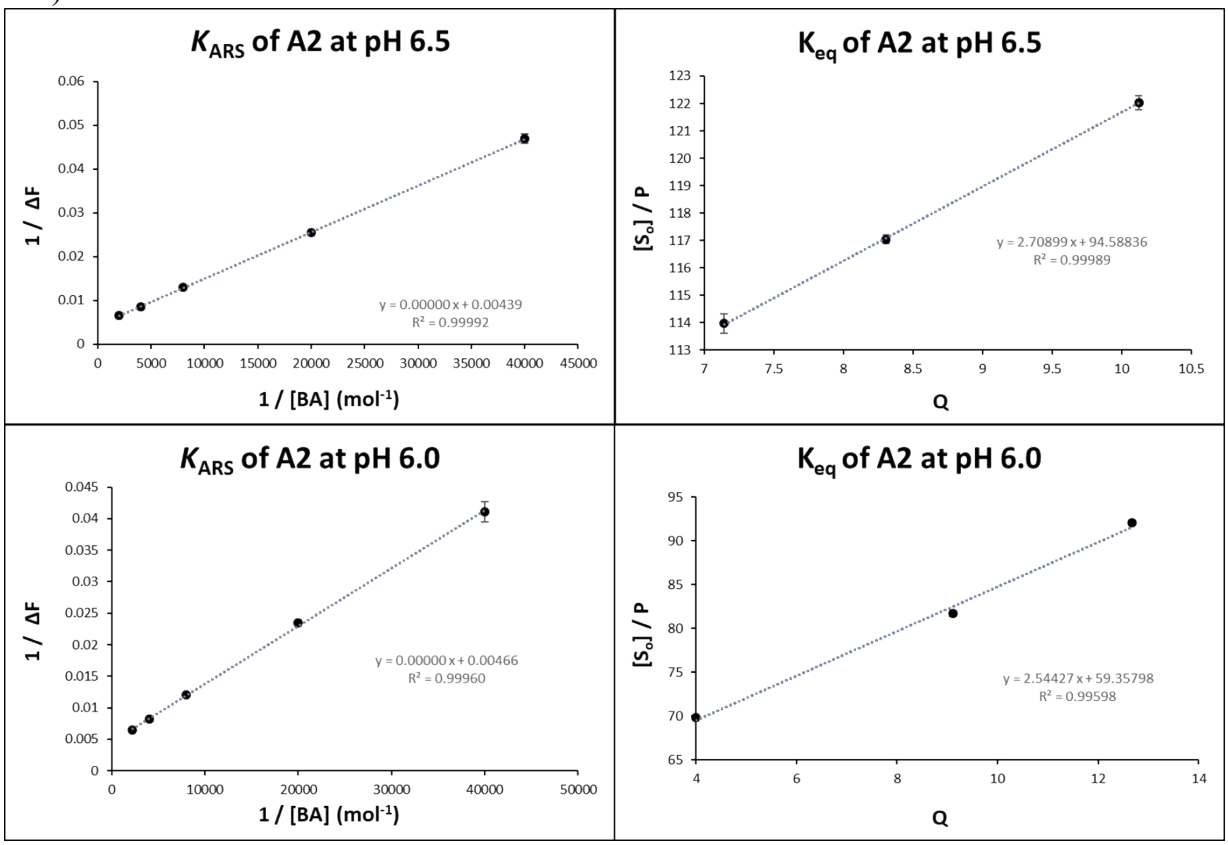


Figure S106. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A2** at pH 6.0 and pH 6.5 (three repetitions)

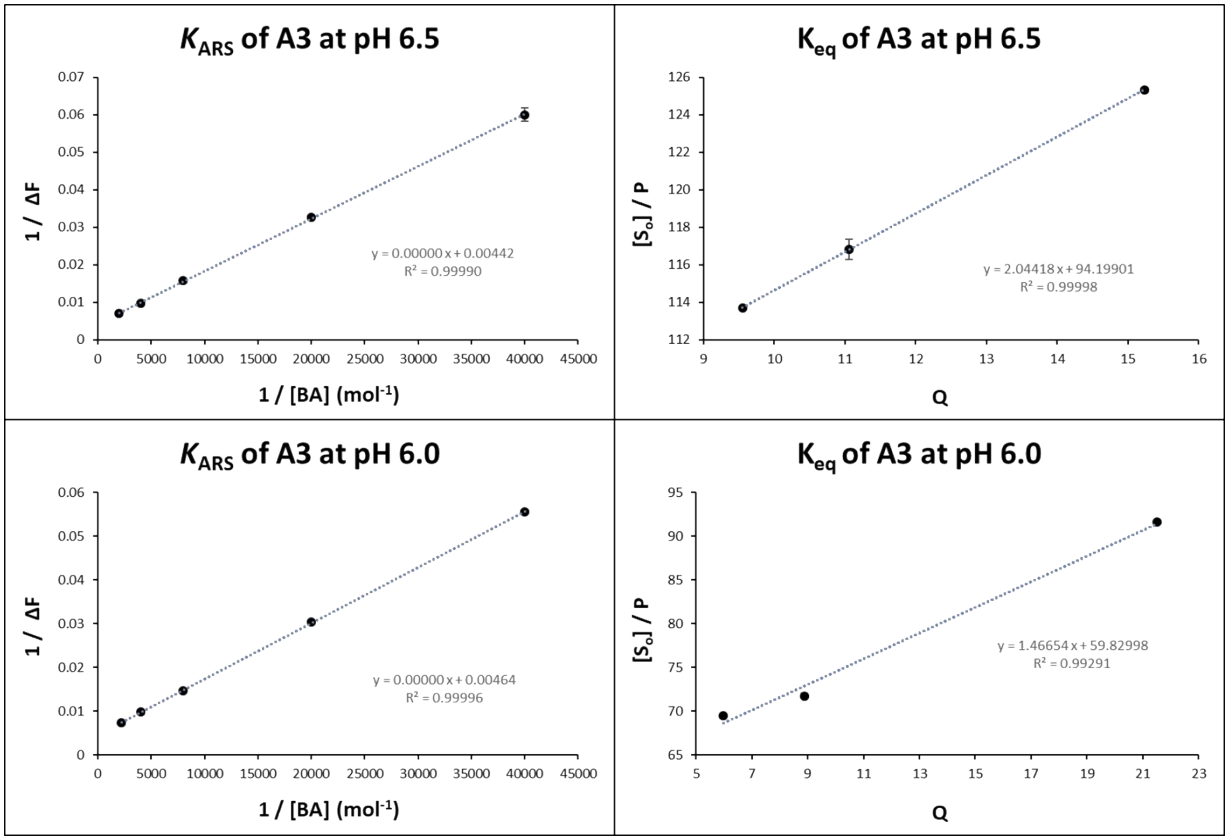


Figure S107. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A3** at pH 6.0 and pH 6.5 (three repetitions)

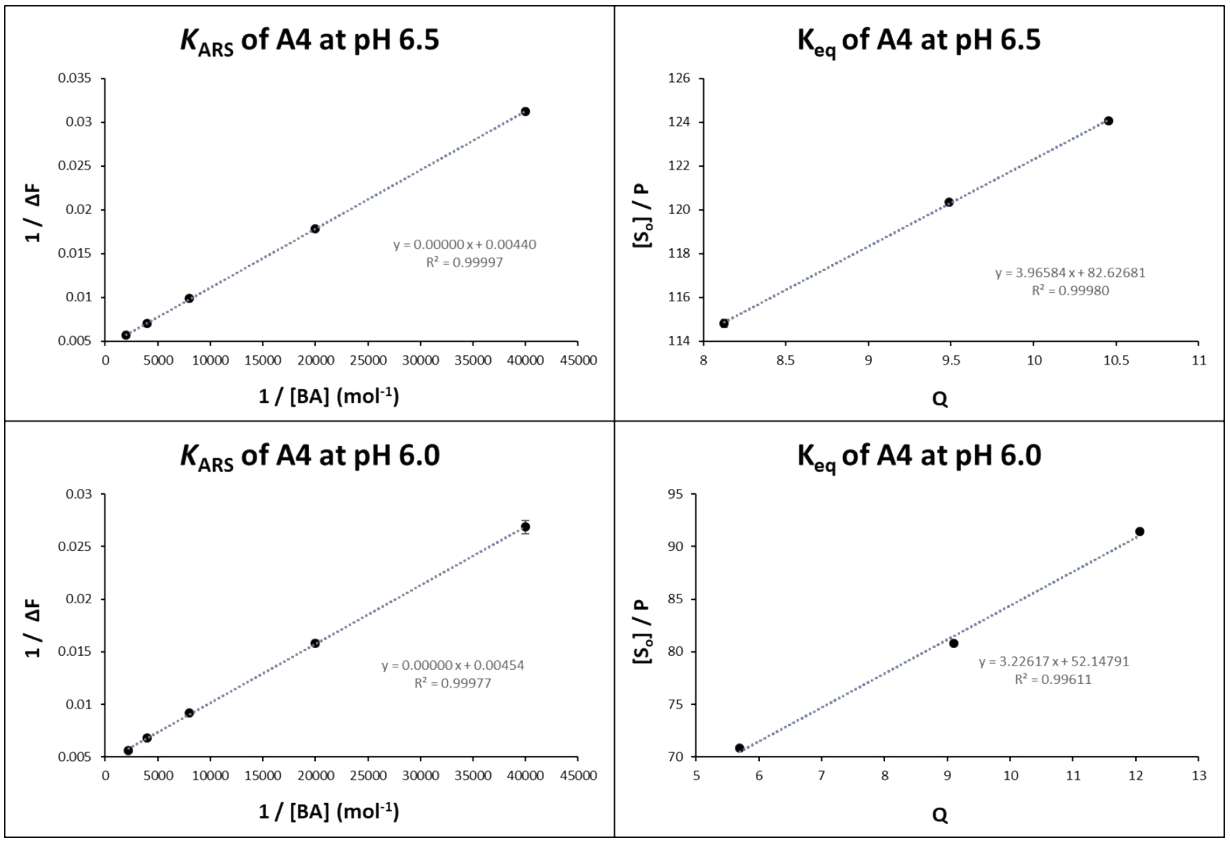


Figure S108. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A4** at pH 6.0 and pH 6.5 (three repetitions)

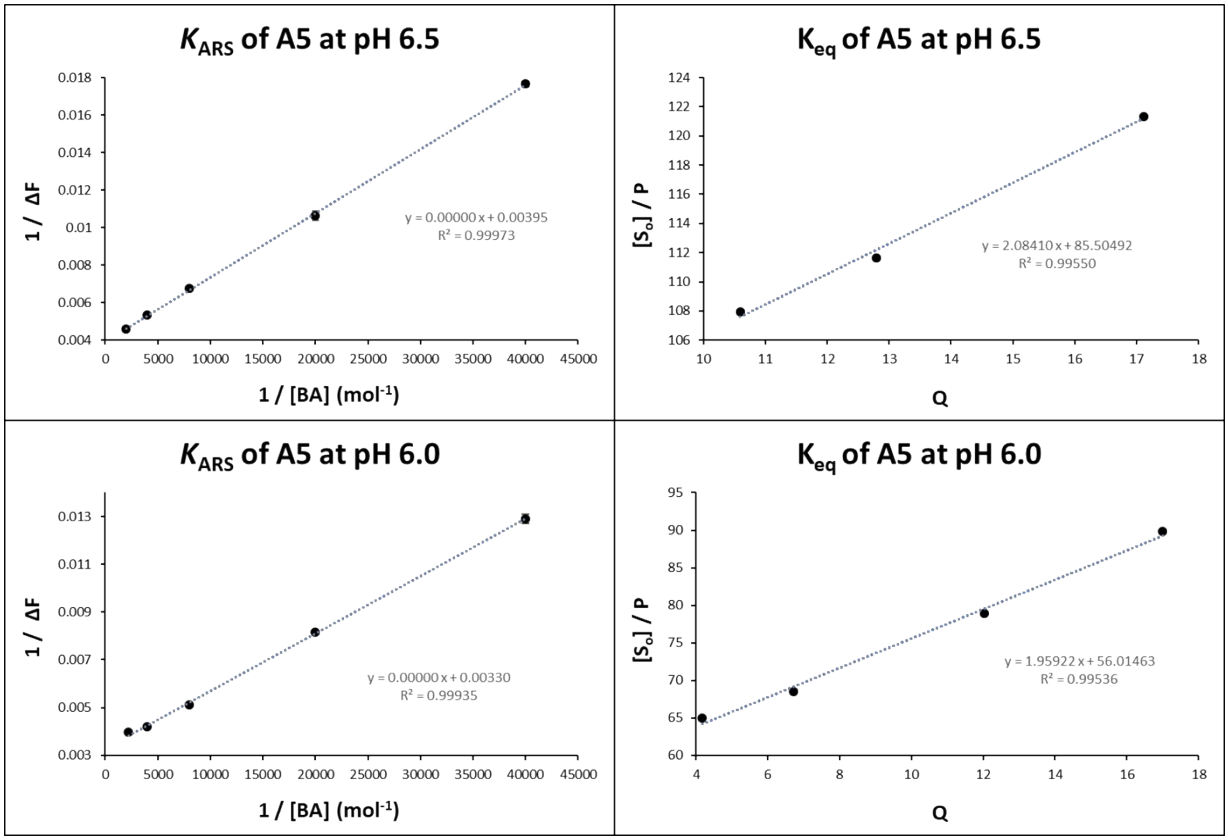


Figure S109. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A5** at pH 6.0 and pH 6.5 (three repetitions)

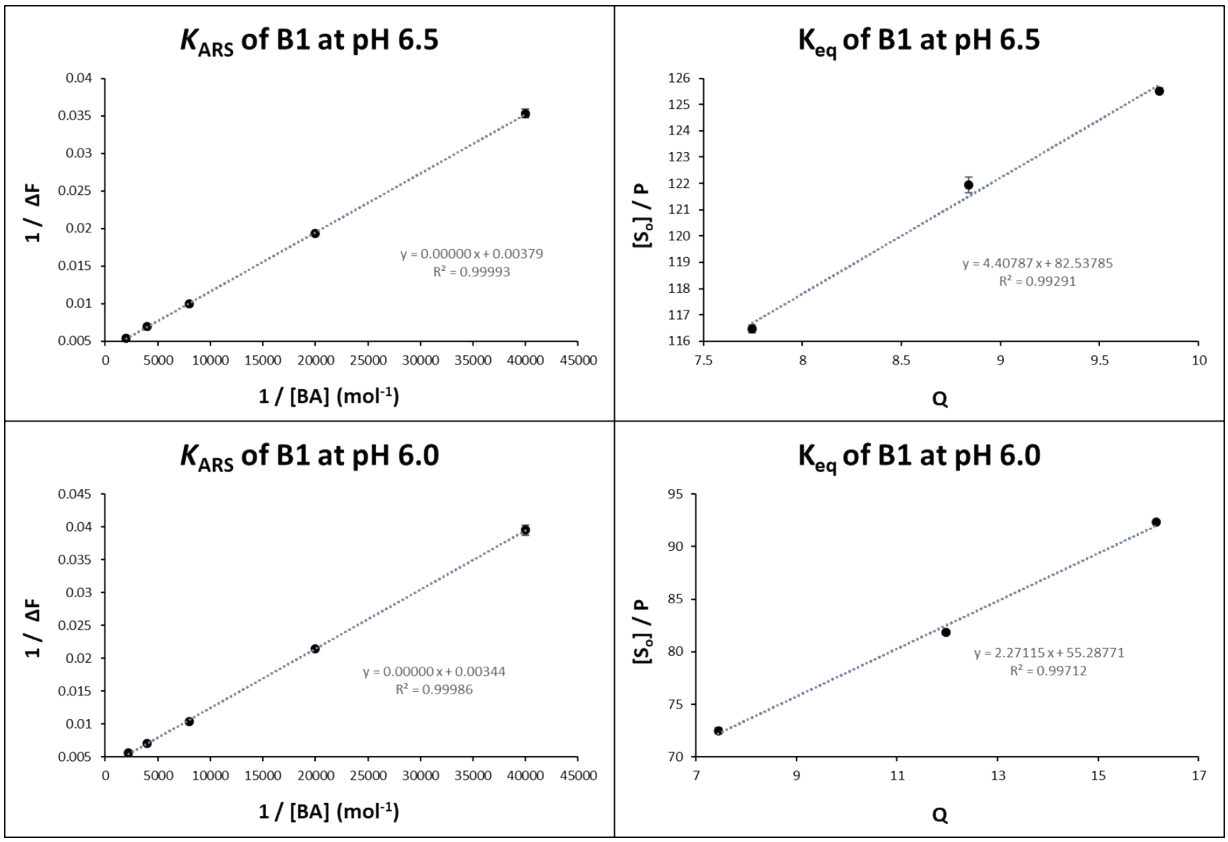


Figure S110. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **B1** at pH 6.0 and pH 6.5 (three repetitions)

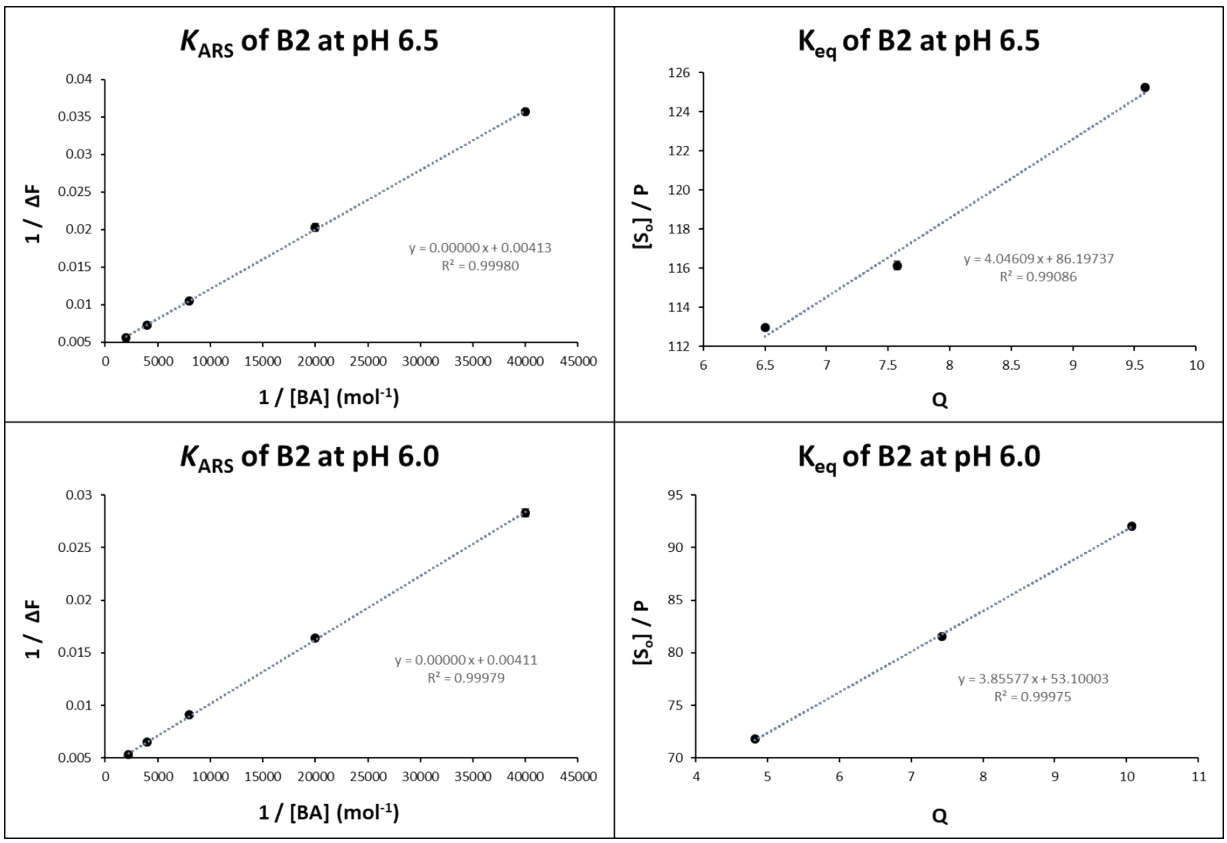


Figure S111. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **B2** at pH 6.0 and pH 6.5 (three repetitions)

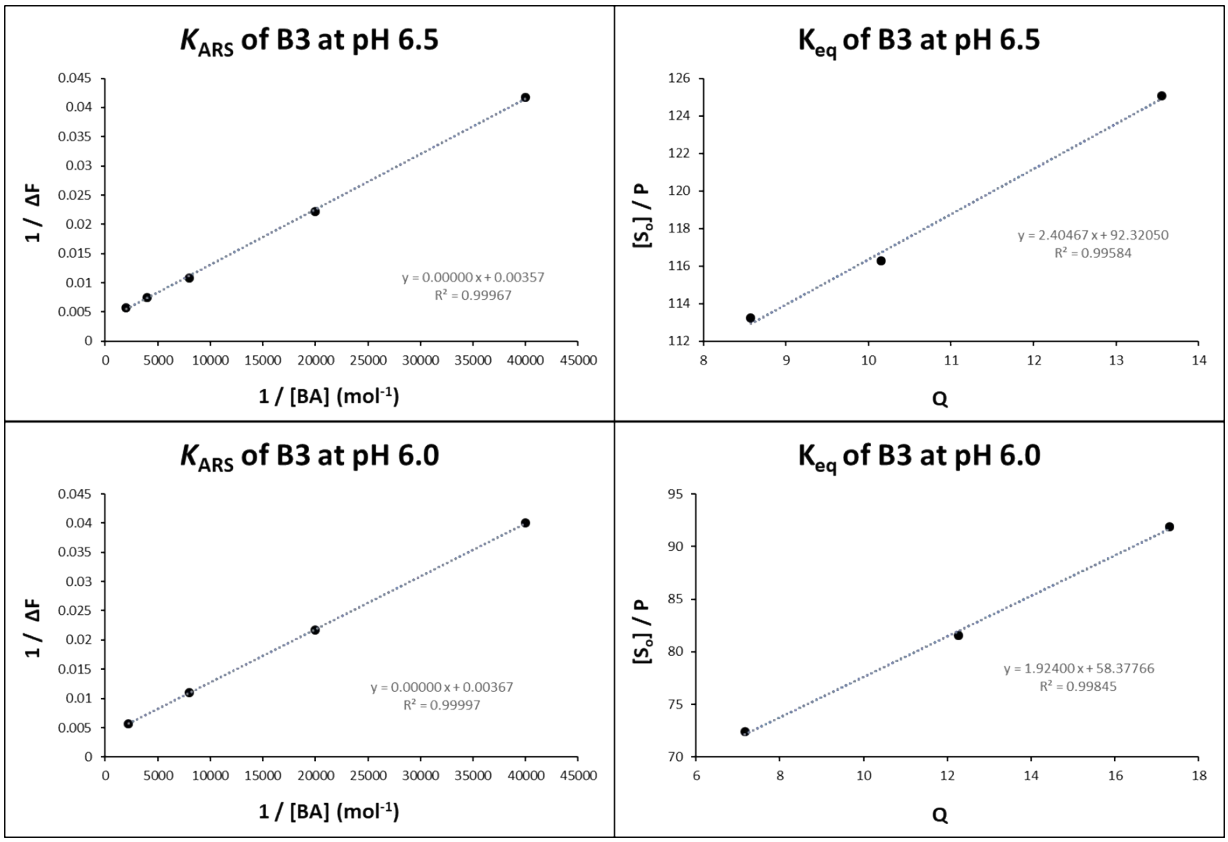


Figure S112. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **B3** at pH 6.0 and pH 6.5 (three repetitions)

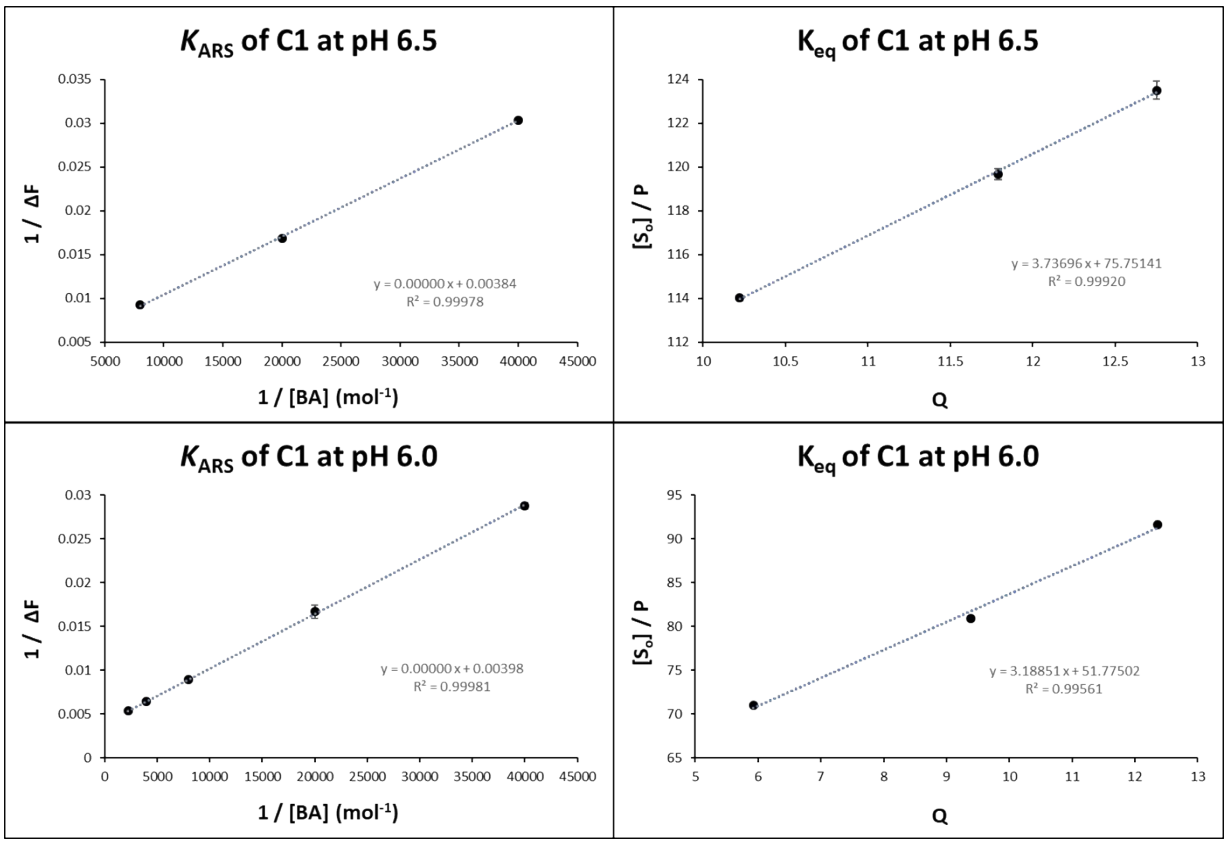


Figure S113. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **C1** at pH 6.0 and pH 6.5 (three repetitions)

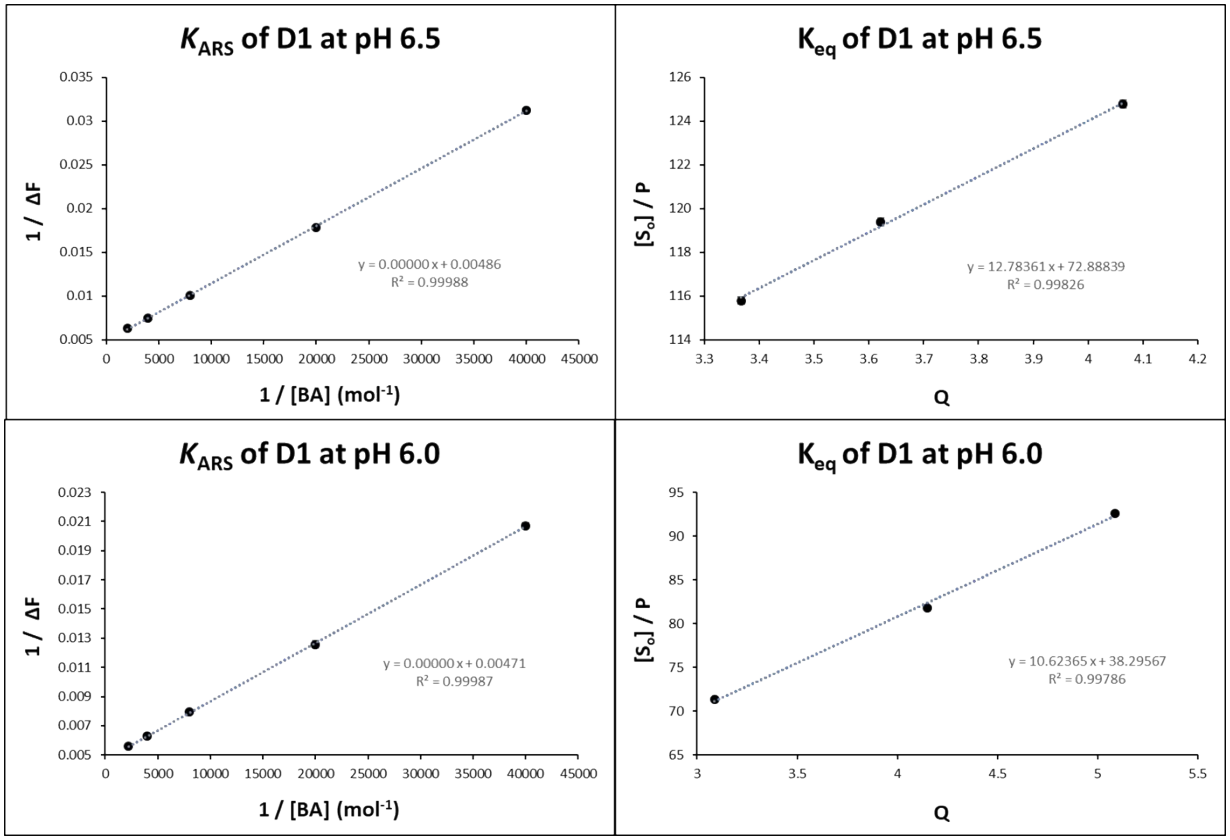


Figure S114. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **D1** at pH 6.0 and pH 6.5 (three repetitions)

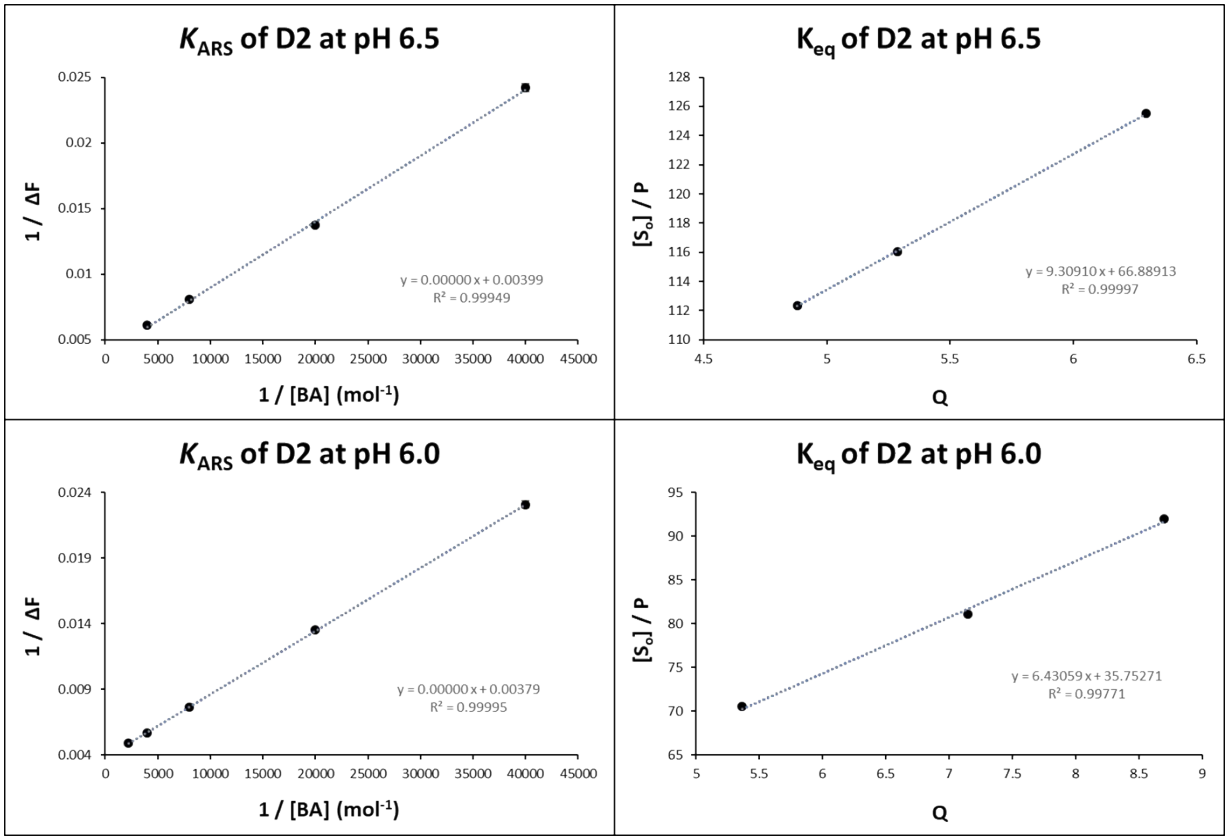


Figure S115. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **D2** at pH 6.0 and pH 6.5 (three repetitions)

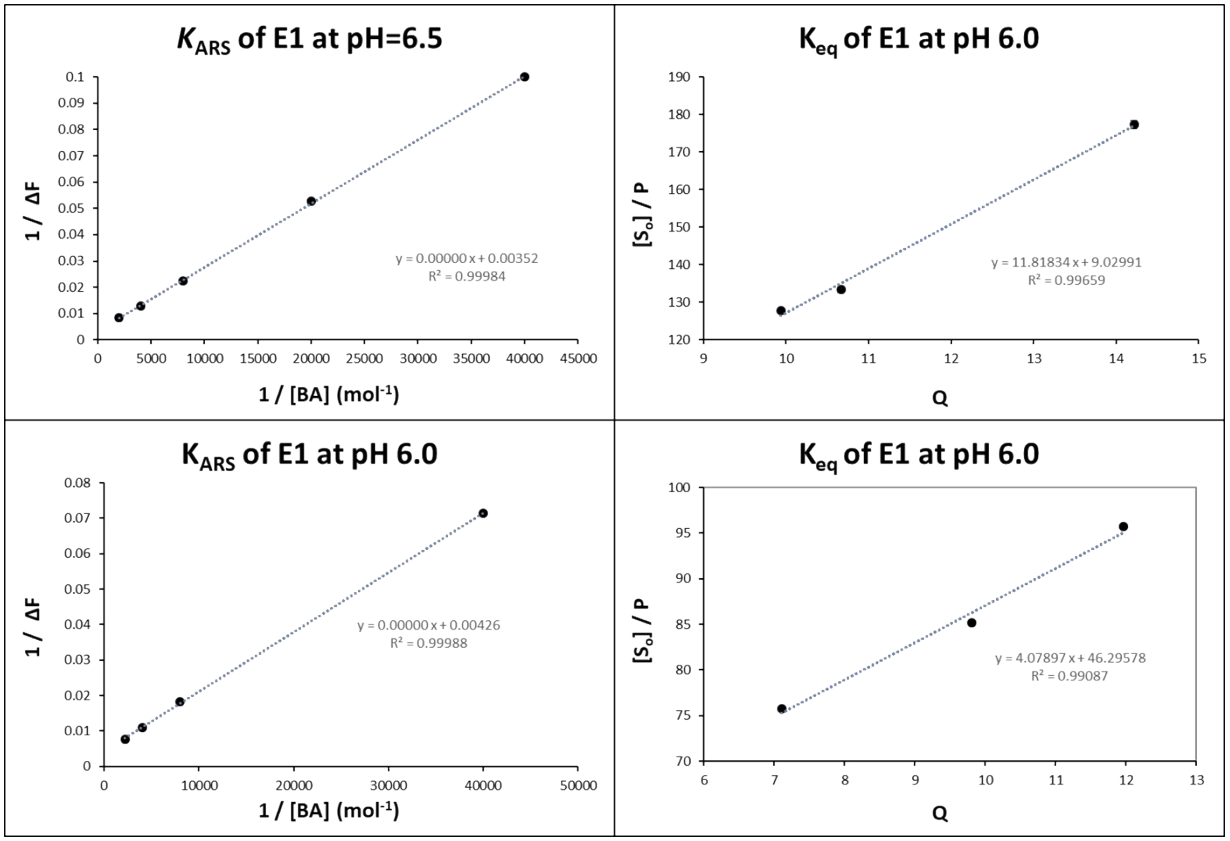


Figure S116. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **E1** at pH 6.0 and pH 6.5 (three repetitions)

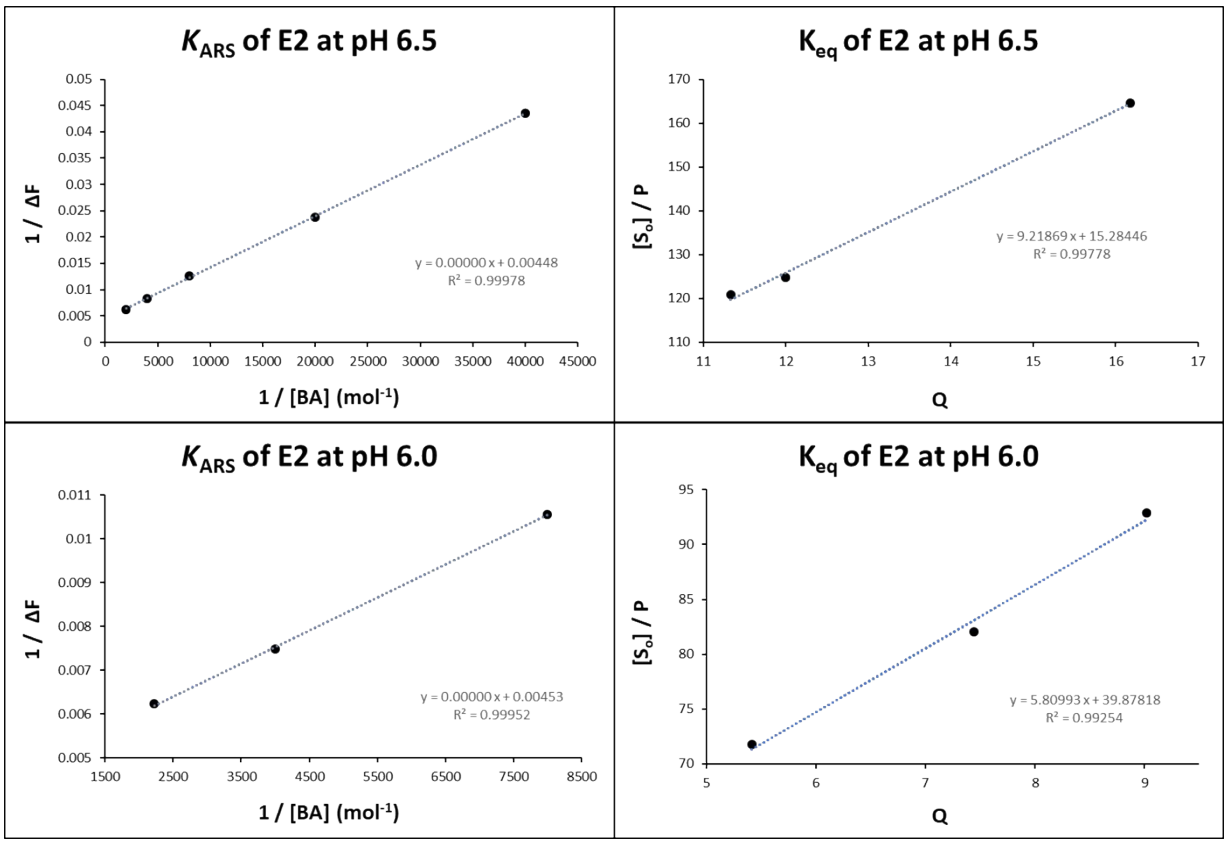
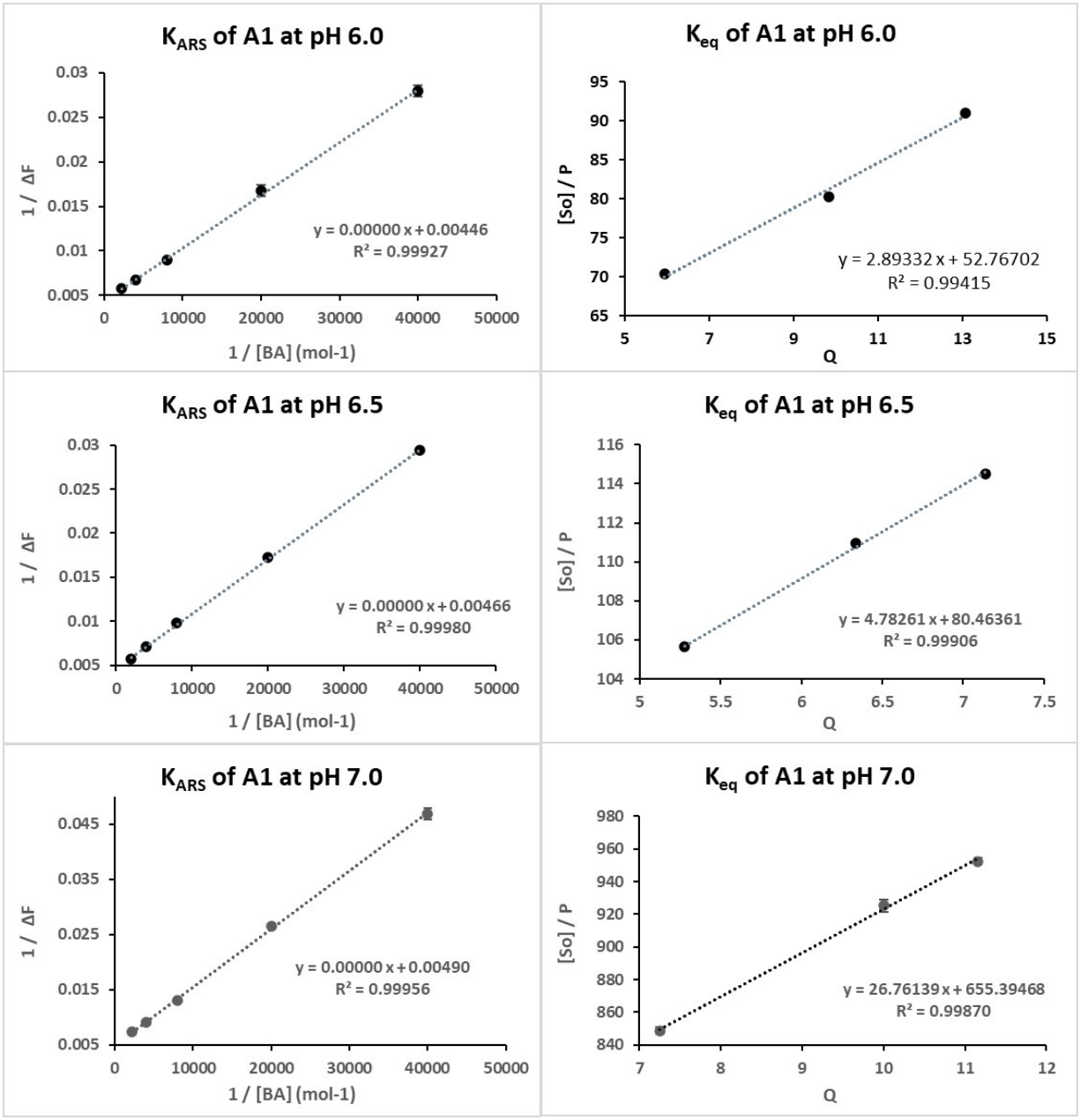


Figure S117. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **E2** at pH 6.0 and pH 6.5 (three repetitions)

Table S1. The binding constant (M^{-1}) of boron-containing Ugi compounds to sialic acid at pH 6.0 and pH 6.5

Series	cpd	K_{eq} with SA (M^{-1})	
		pH 6.0	pH 6.5
A	A1	2602±100	1570±146
	A2	2071±165	1527±79
	A3	2485±34	1552±153
	A4	2152±72	1551±69
	A5	7015±5	5559±35
B	B1	1686±104	1094±229
	B2	1756±25	1286±23
	B3	2102±151	1565±26
C	C1	2008±20	1556±190
D	D1	1112±86	577±16
	D2	1249±16	823±13
E	E1	652±2	123±17
	E2	1035±11	499±34

3.3 K_{ARS} and K_{eq} (Sialic acid, Fructose, Galactose and Glucose) titration



curve at pH 6.0, pH 6.5, pH 7.0, and pH 7.5

Figure S118. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A1** at pH 6.0, pH 6.5, and pH 7.0 (three repetitions)

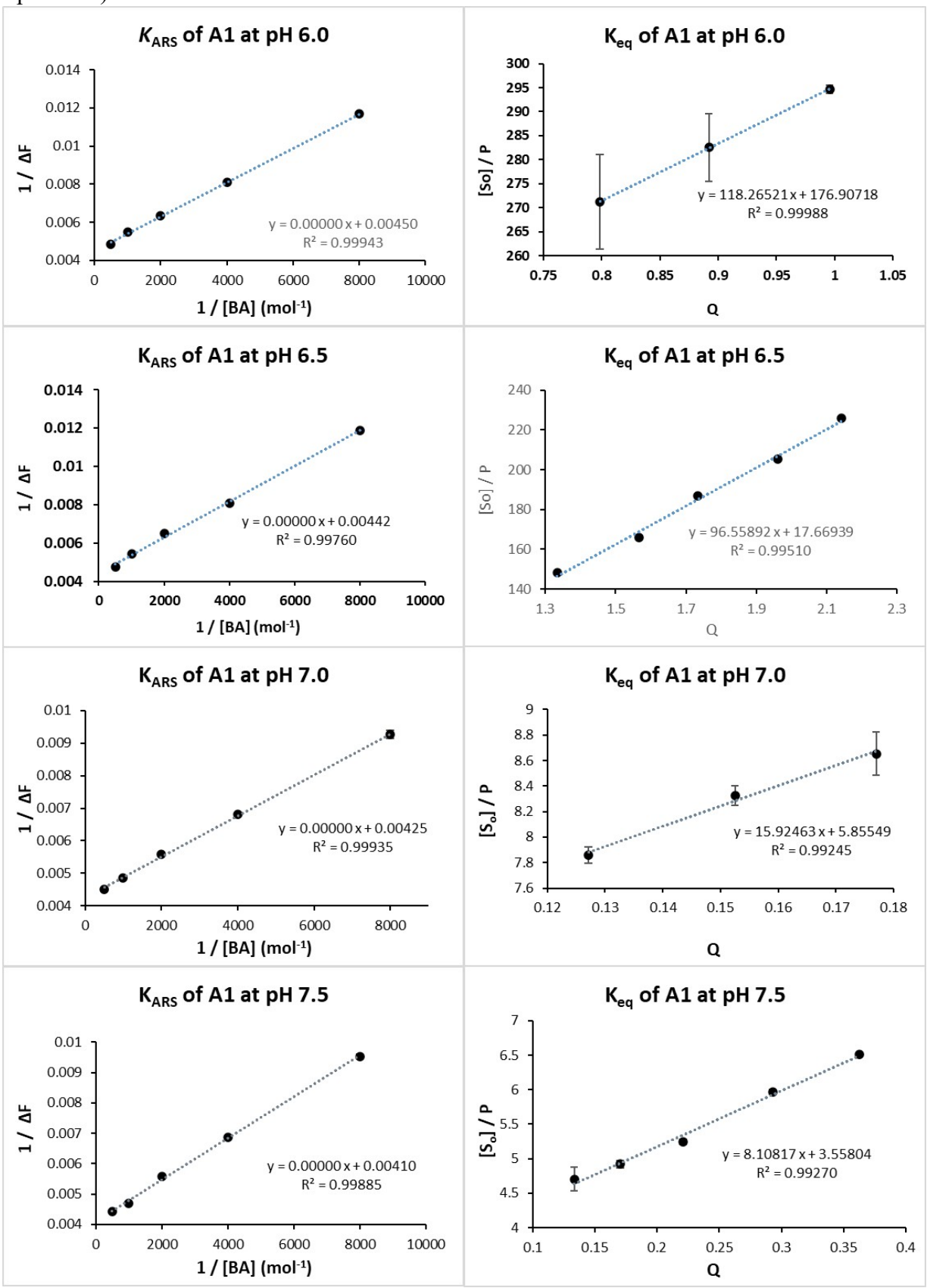


Figure S119. K_{ARS} and K_{eq} (Fructose) titration curves of compound **A1** at pH 6.0, pH 6.5, pH 7.0, and pH 7.5 (three repetitions)

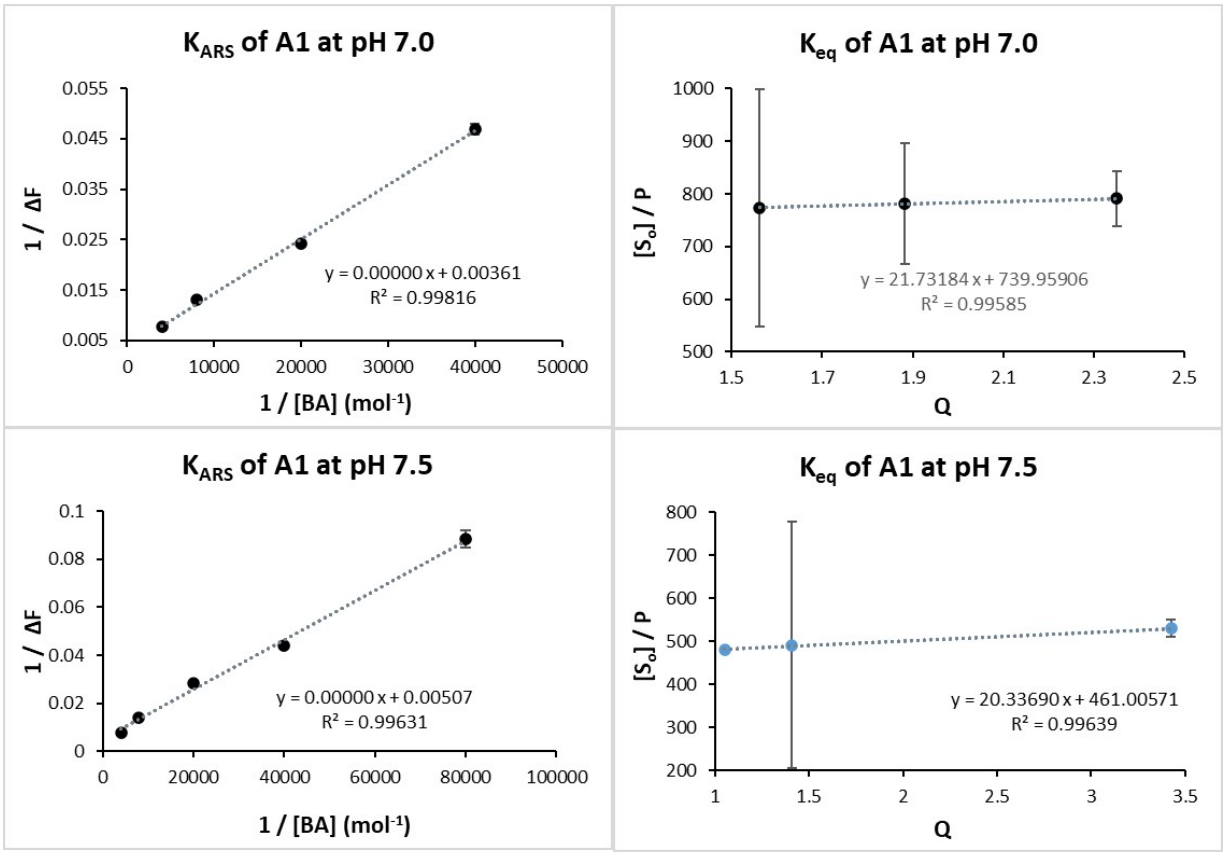
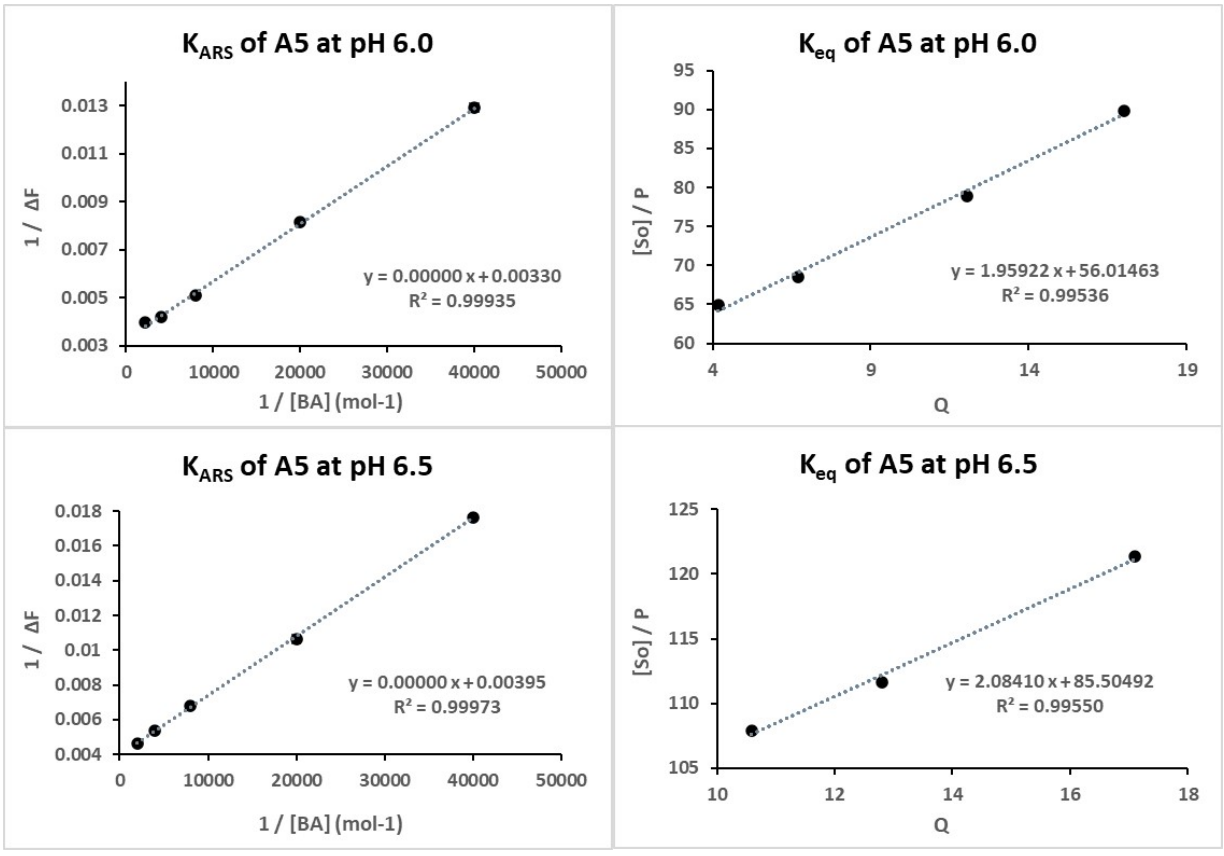


Figure S120. K_{ARS} and K_{eq} (Galactose) titration curves of compound **A1** at pH 7.0 and pH 7.5 (three repetitions)



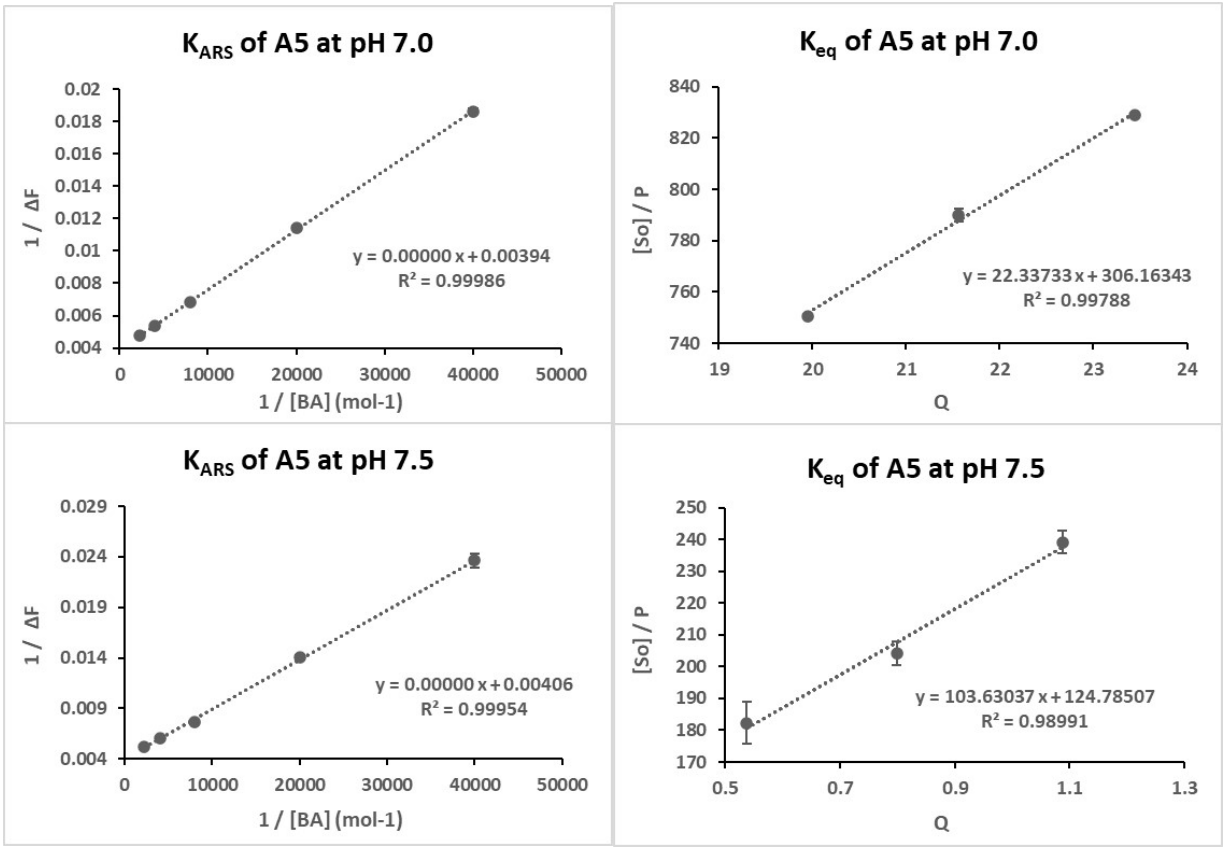
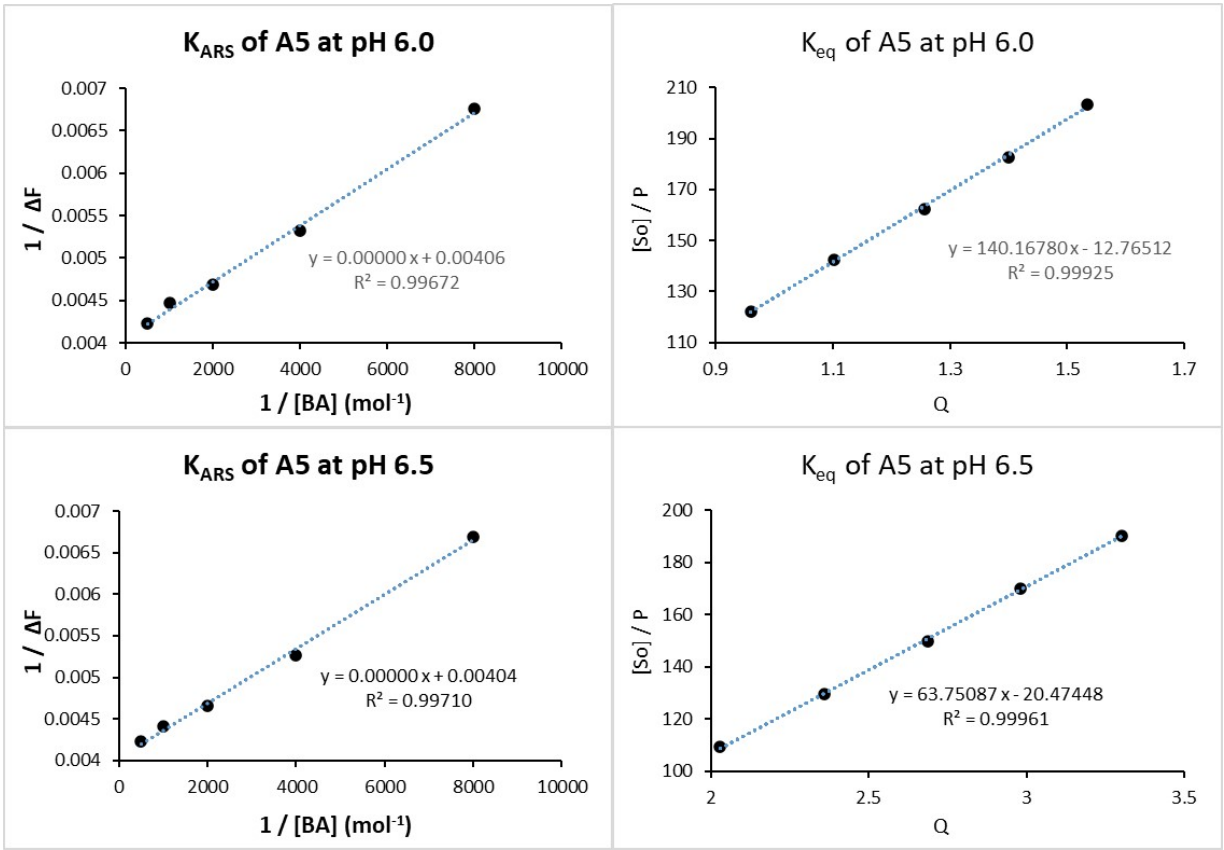


Figure S121. K_{ARS} and K_{eq} (Sialic acid) titration curves of compound **A5** at pH 6.0, pH 6.5, pH 7.0, and pH 7.5 (three repetitions)



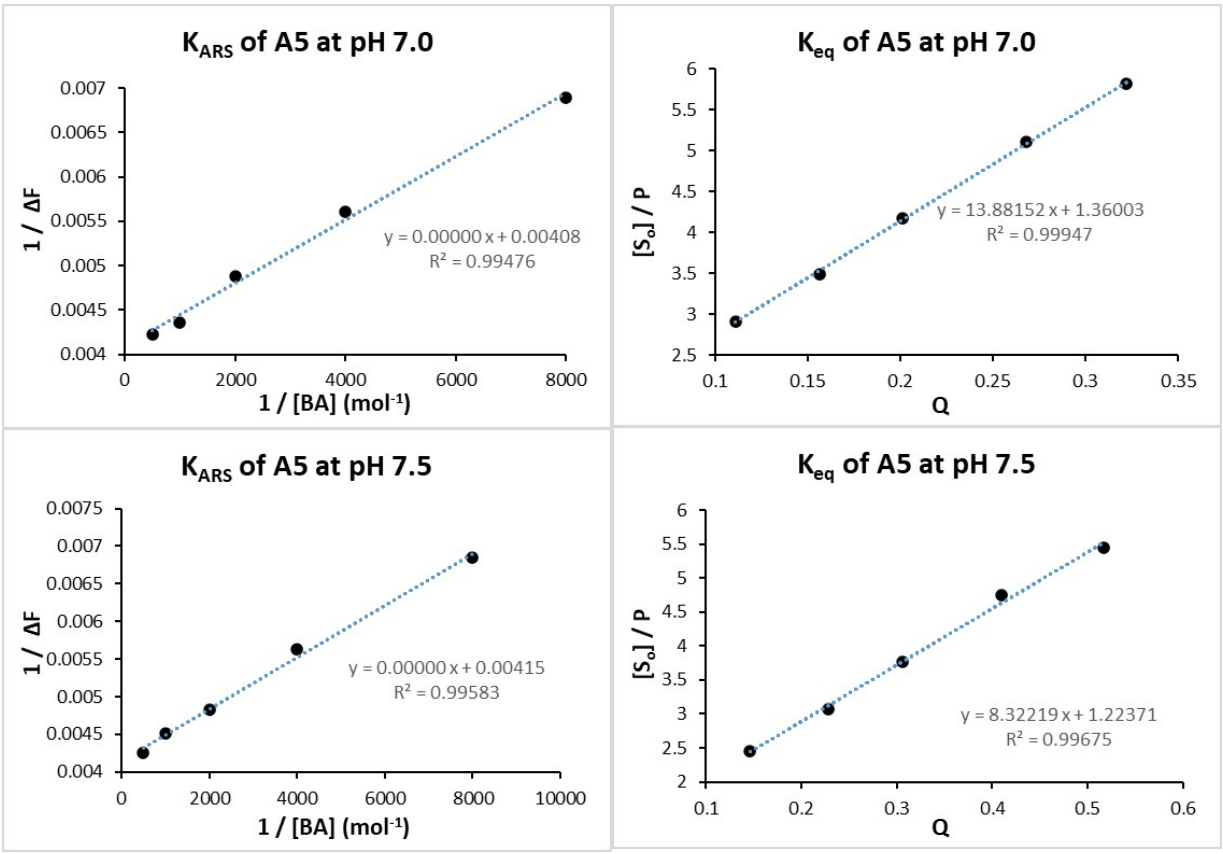


Figure S122. K_{ARS} and K_{eq} (Fructose) titration curves of compound **A5** at pH 6.0, pH 6.5, pH 7.0, and pH 7.5 (three repetitions)

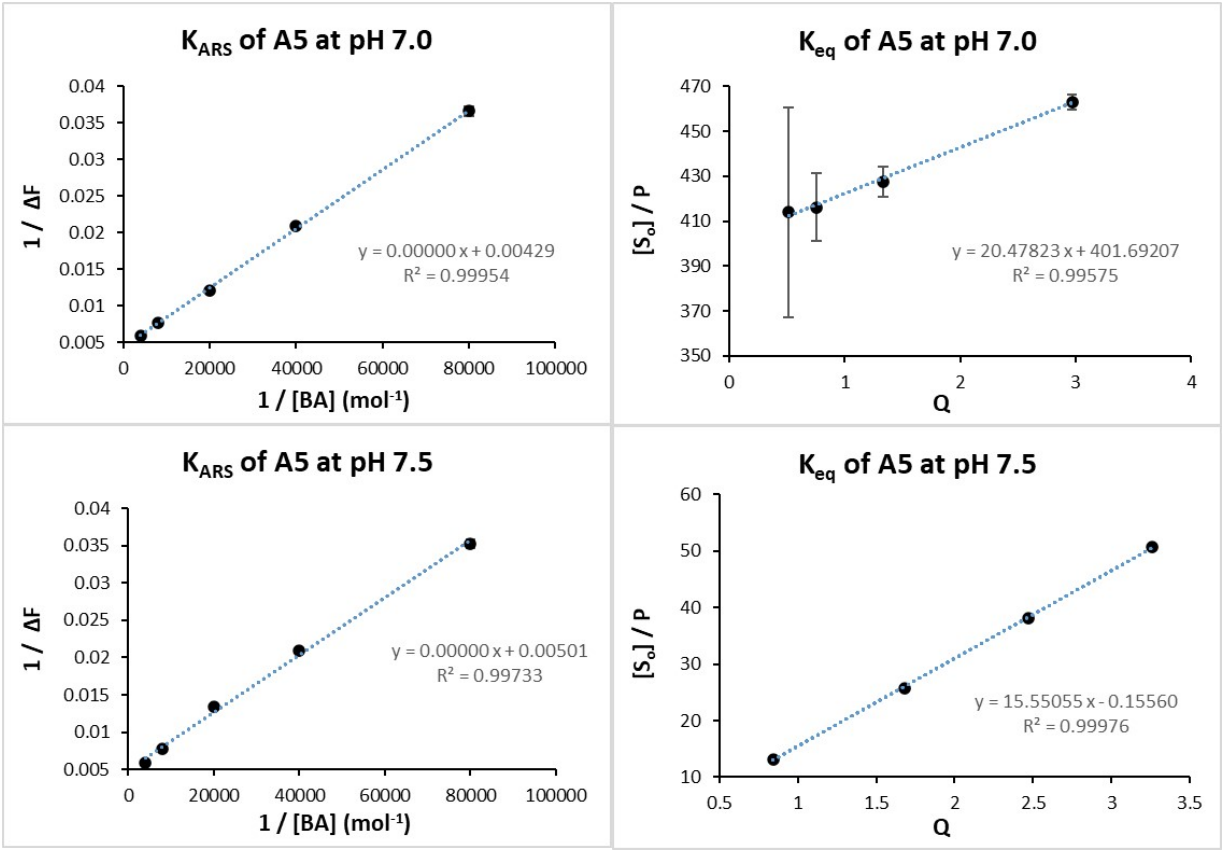


Figure S123. K_{ARS} and K_{eq} (Galactose) titration curves of compound **A5** at pH 7.0 and pH 7.5 (three repetitions)

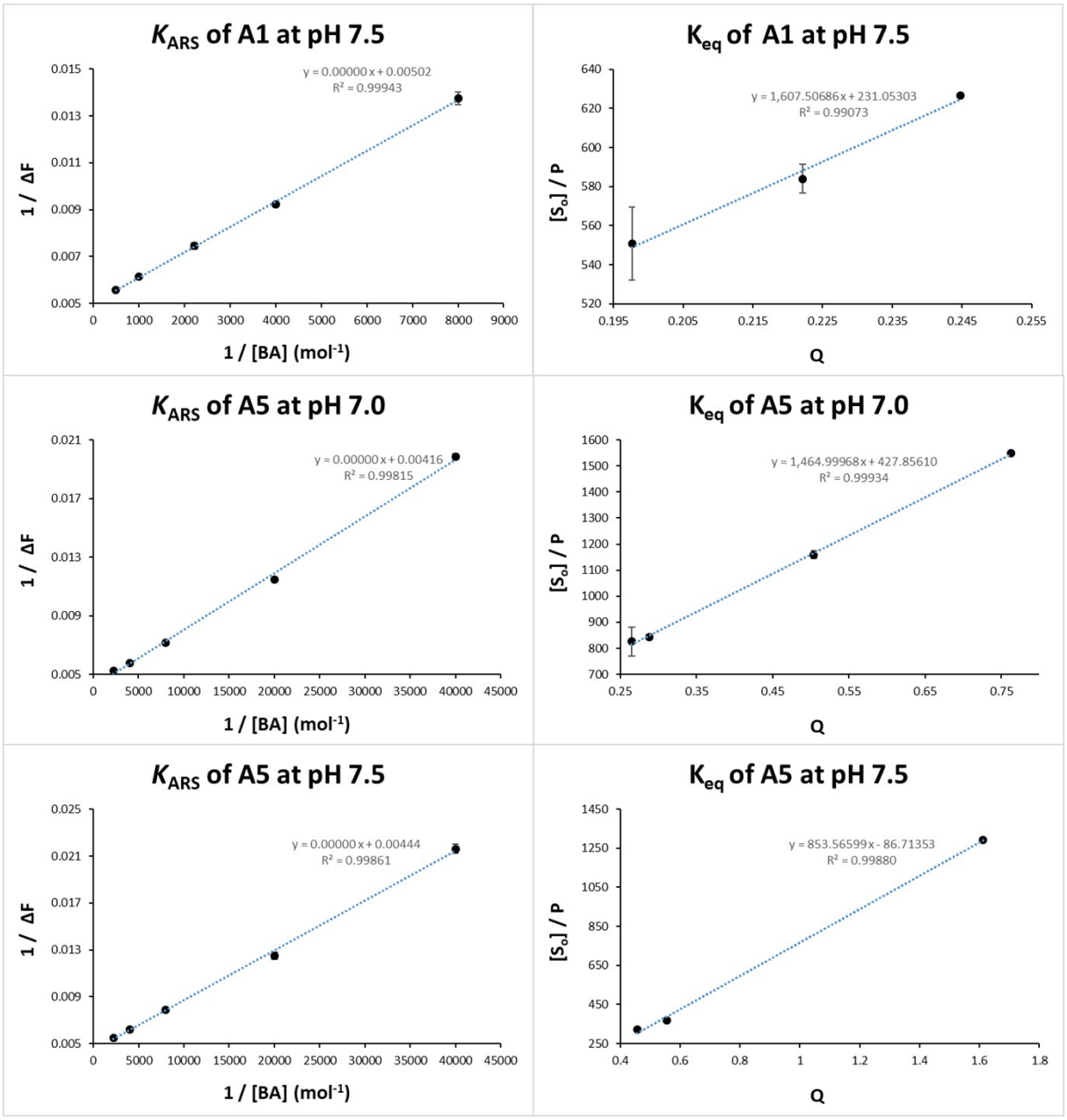


Figure S124. K_{ARS} and K_{eq} (Glucose) titration curves of compound **A5** and A1 at pH 7.0 and pH 7.5 (three repetitions)

Table S2. The binding constant (M^{-1}) of boron-containing Ugi compounds to sialic acid, Fructose, Galactose and Glucose at pH 6.0, pH 6.5, pH 7.0, and pH 7.5

cpd	pH value	K_{eq} with sialic acid (M^{-1})	K_{eq} with Fructose (M^{-1})	K_{eq} with Galactose (M^{-1})	K_{eq} with Glucose (M^{-1})
A1	pH 6.0	2602±100	45±22	n/d	n/d
	pH 6.5	1570±146	49±0	n/d	n/d
	pH 7.0	174±5	424±74	162±17	n/d
	pH 7.5	n/d	741±56	241±64	3±0
A5	pH 6.0	7016±5	87±1	n/d	n/d
	pH 6.5	5559±35	193±1	n/d	n/d
	pH 7.0	479±9	821±0	518±391	7±0
	pH 7.5	80±1	1455±5	755±13	22±0

4. Computational details

Reaction energy

The following are the calculated energies of sialic acid, A1, H_2O and their complexes. The reaction energy in this article is judged by kcal/mole in the last line.

Table S3. DFT calculation of the reaction energy of two binding site on A1 structure relative to sialic acid

Solvent Effect			
T (K)	298.15	G_A1 Binding Sites (kcal/mol)	
P (atm)	1	A1(S) - R^2	-2.18246
G_H_2O (Hartree)	-76.41	A1(S) - R^4	-1.87372
G_SA(Hartree)	-1161.31	A1(R) -R^2	-1.05734
G_A1-S(Hartree)	-1692.321	A1(S) - R^2 + R^4	-5.96065
G_A1-R(Hartree)	-1692.322	A1(R) - R^2 +R^4	-5.39966
ε	67.2		

Coordinate files

The following are the Cartesian coordinates of the optimized geometries :

- A1(R) (the number of imaginary frequencies = 0)

C	-5.04813400	-2.59301600	0.47604400
H	-4.77024900	-3.15197800	1.36357800
C	-6.37157700	-2.56788500	0.04911200
C	-6.71867500	-1.86897300	-1.10508900
C	-5.73849600	-1.19346900	-1.82795000
C	-4.41750100	-1.19811600	-1.38999800
C	-4.06848500	-1.89441100	-0.23191600
H	-7.13037000	-3.09990300	0.61358800
H	-7.74970700	-1.85545100	-1.44340200
H	-6.00133500	-0.65915300	-2.73505300
H	-3.66059300	-0.66796800	-1.95681100
C	-2.64512200	-2.01864500	0.22591500
O	-2.14675300	-3.13942900	0.36641700
N	-1.92181700	-0.88929300	0.48095200
C	-2.48432600	0.43184100	0.42726000
C	-0.51798100	-1.09565400	0.87229400
C	-3.37389000	0.84495300	1.41456800
C	-3.91803300	2.12451600	1.35888800
C	-3.55787300	2.98906500	0.33067200
C	-2.65016600	2.59591600	-0.66288700
C	-2.12352900	1.30137800	-0.59655100
H	-3.63801700	0.16471200	2.21746400
H	-4.61742700	2.44603000	2.12365000
H	-3.98230100	3.98710500	0.29547200
H	-1.42318100	0.92606500	-1.33693000
O	-2.84684600	4.82697700	-1.81866700
O	-1.35244700	3.31946300	-2.79547800
H	-0.94393700	2.44742900	-2.76044300
H	-2.54623600	5.38132100	-2.55065400
C	0.02551600	0.00878900	1.76113900
C	0.35980000	-1.34327700	-0.36895800
C	-0.15881600	-0.08982300	3.14157900
C	0.31895300	0.90109600	3.99382300
C	0.99523600	2.00126100	3.47236600
C	1.19009700	2.10311300	2.09737500
C	0.70684400	1.11267200	1.24712400
H	1.37302300	2.77335100	4.13479000
H	0.16807200	0.81002200	5.06458200
H	-0.68058100	-0.94928500	3.55265400
H	1.71958000	2.95503400	1.68324800
H	0.86206500	1.20629000	0.17714900
O	0.04259400	-0.93923500	-1.48705400
N	1.49337300	-2.02406600	-0.11535800
H	1.67668300	-2.31985400	0.83408000
C	2.48392800	-2.35782400	-1.13019300
C	3.80063200	-1.64133400	-0.92828800
C	4.96784900	-2.35711800	-0.66654400
C	6.18002700	-1.69417000	-0.48875000
C	6.26179600	-0.29951600	-0.56382100
C	5.08012500	0.40938900	-0.82797000
C	3.87033300	-0.24746300	-1.00901700
H	4.92927900	-3.44098100	-0.60094600
H	2.97039400	0.32395200	-1.21741600
H	5.11441200	1.49237400	-0.89588300
H	7.07741600	-2.27044700	-0.28551000
H	2.64370300	-3.43915300	-1.12408900
H	2.04440300	-2.08919800	-2.09227300
O	8.74294200	-0.30281700	-0.12250000

H	9.56633400	0.18558800	-0.00196500
B	-2.25557500	3.59520100	-1.80528800
B	7.62229100	0.44620100	-0.36229300
O	7.62423700	1.81329100	-0.43558900
H	8.47591000	2.24783200	-0.30735200
H	-0.51281300	-2.02298000	1.44881700

● A1(S) (the number of imaginary frequencies = 0)

C	-3.63058400	-3.42151700	0.53718900
H	-2.96236400	-3.78283300	1.31162200
C	-4.85139000	-4.04840900	0.31276400
C	-5.69262300	-3.59267900	-0.70011100
C	-5.31079400	-2.50673400	-1.48445400
C	-4.10026300	-1.86370400	-1.24628400
C	-3.25690100	-2.31672700	-0.23007800
H	-5.14293100	-4.89661400	0.92338900
H	-6.64181200	-4.08644800	-0.88155800
H	-5.95638200	-2.15806300	-2.28377900
H	-3.80910400	-1.01927900	-1.86057200
C	-1.89974300	-1.72585500	0.00056900
O	-0.91624800	-2.46320700	0.09670600
N	-1.77058600	-0.36805100	0.06802900
C	-2.87499700	0.51796700	0.30488800
C	-0.42973700	0.23582200	0.10863700
C	-3.61457000	0.41593800	1.47952400
C	-4.67582600	1.28867200	1.70191300
C	-4.97905800	2.26977900	0.76514500
C	-4.23344200	2.40116500	-0.41572400
C	-3.18012900	1.50647000	-0.62699800
H	-3.36097900	-0.34408500	2.21092500
H	-5.25793200	1.20527100	2.61373200
H	-5.80427800	2.94996800	0.94778400
H	-2.58057800	1.55058600	-1.53264600
O	-5.66233700	4.33456100	-1.16313600
O	-3.94307900	3.74216000	-2.62846100
H	-3.19813000	3.16094900	-2.81602600
H	-5.82675900	4.99649300	-1.84749700
C	0.13773600	0.39349700	1.50937400
C	0.48567000	-0.41801700	-0.94782600
C	0.18714300	-0.66127100	2.42711000
C	0.72010500	-0.46377200	3.69749400
C	1.21273500	0.78538400	4.06923900
C	1.16723200	1.84027000	3.16277400
C	0.63002500	1.64333300	1.89326700
H	1.62755400	0.93506100	5.06081300
H	0.75152500	-1.29121600	4.39916700
H	-0.18445000	-1.63786000	2.14022800
H	1.54337500	2.81886600	3.44291800
H	0.59094400	2.47346000	1.19342400
O	0.07607300	-0.56197500	-2.09983600
N	1.74572600	-0.68541900	-0.57020200
H	1.97512700	-0.62983700	0.41250000
C	2.73155100	-1.25167400	-1.47677700
C	4.12859800	-0.77193300	-1.16149800
C	5.18007500	-1.68284100	-1.06399300
C	6.47581500	-1.24321000	-0.80807100
C	6.76059900	0.11598100	-0.63381400
C	5.69397000	1.02133900	-0.72983600
C	4.39968100	0.58852400	-0.99052900
H	4.98376300	-2.74428900	-1.18695900
H	3.59050700	1.30965500	-1.06074100
H	5.88426900	2.08228100	-0.59974600
H	7.27965800	-1.96929100	-0.73588500
H	2.69636800	-2.34590300	-1.44047600
H	2.44094800	-0.95403100	-2.48736600
O	9.21095500	-0.33335900	-0.27045900
H	10.09960000	-0.00605700	-0.08646200
B	-4.60444900	3.52047400	-1.45206400
B	8.21687900	0.60560600	-0.33852000
O	8.42438300	1.94741200	-0.16269100
H	9.33124800	2.22177800	0.01955300
H	-0.56056800	1.24582000	-0.28857000

● Sialic acid (the number of imaginary frequencies = 0)

C	1.10217300	1.54502000	-0.15105100
C	-0.20504200	2.21724000	-0.56065800
C	-1.27980800	1.23278500	-0.99738500
C	-1.44885600	0.19787800	0.12165700
C	-0.10744200	-0.53055900	0.37408800
O	0.89623400	0.43261000	0.70302300
C	2.01501000	2.54236600	0.64549400
O	1.58846400	2.99693200	1.72042400
O	3.10990000	2.79024100	0.06531100
H	-0.57633700	2.77282300	0.30792400
H	0.00713700	2.93346300	-1.35798200
O	-2.49874300	1.90092800	-1.29619100
H	-2.61730200	2.64323300	-0.68885400
H	-0.99843600	0.73012000	-1.92743300
O	1.83645000	1.15054100	-1.29410000
H	2.64933700	1.71565600	-1.19805400
N	-2.53752000	-0.73094500	-0.10088400
H	-2.32751300	-1.54476900	-0.66915000
H	-1.65384300	0.74696100	1.04463400
H	-0.23259300	-1.12162200	1.28529400
C	1.75555100	-2.14296500	-0.47248900
O	2.83669000	-1.35914100	-0.95596600
H	2.55341800	-0.42325100	-1.02244300
H	1.76599200	-3.06890500	-1.06242400
O	3.28844600	-3.19884000	1.05769500
H	3.92749400	-2.63606000	0.59609400
O	-0.60611500	-2.54122400	-0.78324800
H	-0.43484900	-3.09814000	-1.55396300
C	0.37480800	-1.50230900	-0.72775000
H	0.42596200	-0.99224000	-1.69602500
C	2.03444300	-2.53052700	0.97452100
H	1.27708100	-3.22753000	1.34150200
H	2.04167200	-1.63901300	1.61090400
C	-3.78223000	-0.69567100	0.42256200
O	-4.60701600	-1.57074700	0.12422000
C	-4.14039300	0.41083400	1.38503300
H	-3.49409800	0.39252500	2.26693200
H	-4.04177400	1.39101000	0.91508200
H	-5.17245100	0.26740400	1.70068700

● A1(R)-R^2 binding site with sialic acid (the number of imaginary frequencies = 0)

C	-2.35569500	4.22060900	-2.12919100
H	-2.42452000	4.81110800	-1.22278900
C	-2.10158300	4.84750300	-3.34517500
C	-2.00656900	4.09611500	-4.51423100
C	-2.18554600	2.71524500	-4.46791700
C	-2.46228400	2.08981600	-3.25691900

C	-2.53281200	2.83686700	-2.07982100
H	-1.97616600	5.92485700	-3.37832300
H	-1.79849900	4.58619400	-5.45992100
H	-2.11578100	2.12533700	-5.37600500
H	-2.62033100	1.01722100	-3.21770200
C	-2.91285300	2.12523900	-0.81676700
O	-3.89411600	1.37285500	-0.81085700
N	-2.19407000	2.33366400	0.32234200
C	-0.89566000	2.95713700	0.31915100
C	-2.73836100	1.66876100	1.52123300
C	-0.71658000	4.18643800	0.95049300
C	0.54189700	4.77365900	0.94631200
C	1.60535900	4.14258000	0.30037900
C	1.44727500	2.91563900	-0.35382100
C	0.17269000	2.33462500	-0.31720000
H	-1.55579500	4.67279200	1.43579800
H	0.69182900	5.72928000	1.43953400
H	2.58094200	4.62113500	0.30527500
H	-0.00062800	1.37503400	-0.79380300
O	3.76917300	3.09118300	-1.45776700
H	3.45883300	3.92524300	-1.82515400
C	-2.09542300	2.09737800	2.82748600
C	-2.65709300	0.13999900	1.37854100
C	-2.80042300	2.94954300	3.67797000
C	-2.25437000	3.34868700	4.89545600
C	-0.99593400	2.89100500	5.27471600
C	-0.29016900	2.03444100	4.43156300
C	-0.83375100	1.63670000	3.21410400
H	-0.56712900	3.19825000	6.22330300
H	-2.81388500	4.01349200	5.54564100
H	-3.78331400	3.30791600	3.38553000
H	0.69195800	1.67427300	4.72148500
H	-0.26155400	0.98165900	2.56378500
O	-1.71397300	-0.40928500	0.80291700
N	-3.64855600	-0.53563100	1.98233800
H	-4.41505500	-0.01079500	2.38048200
C	-3.73004700	-1.98395100	2.01842000
C	-4.70968100	-2.57823500	1.02578400
C	-5.09361500	-1.89960200	-0.13105200
C	-5.96869400	-2.49680900	-1.03461600
C	-6.48314200	-3.78116600	-0.81910700
C	-6.08758100	-4.44928500	0.34817900
C	-5.21982900	-3.85786900	1.25826800
H	-4.71347800	-0.90125200	-0.32547800
H	-4.93587700	-4.39385100	2.16032800
H	-6.47178100	-5.44487300	0.54836000
H	-6.25832200	-1.95242300	-1.92848800
H	-2.72684700	-2.36914200	1.82183000
H	-4.00114900	-2.29101200	3.03193000
O	-7.83570200	-3.71935100	-2.94200000
H	-8.44088700	-4.15093600	-3.55669600
B	2.67803900	2.20609900	-1.12132100
B	-7.46405400	-4.44354900	-1.84050200
C	3.55889000	0.02055700	-1.32777200
C	5.03673500	0.04147900	-1.72334100
C	5.93419900	-0.62611500	-0.68923800
C	5.40225100	-2.03978800	-0.45988000
C	3.94668000	-1.97849600	0.05662500
O	3.13974000	-1.24880200	-0.87139500
C	2.67570200	0.34767400	-2.55439100
O	2.52287900	-0.38808800	-3.51463200
O	2.14710400	1.52912700	-2.40858800
H	5.15650500	-0.49961200	-2.66744300
H	5.32540700	1.08289000	-1.88221300
O	7.26672700	-0.73429200	-1.17416900
H	7.64865900	0.14987900	-1.24319300
H	5.93499400	-0.06500200	0.25306700
O	3.23953000	1.02105500	-0.40191400
N	6.23987200	-2.85835900	0.39313300
H	6.05813400	-2.80998800	1.39043000
H	5.34384000	-2.52029300	-1.44010300
H	3.55269400	-2.99738100	0.01783800
C	2.26822500	-1.29611300	1.93041300
O	1.78815500	0.00954900	1.67530400
H	2.20400600	0.37115500	0.86360100
H	2.26241400	-1.40481400	3.02304900
O	0.04046000	-2.27992700	1.99808800
H	-0.46763800	-1.55614600	1.58738600
O	4.35452300	-2.46654600	2.33741300
H	4.36650000	-2.14760300	3.24931600
C	3.74236100	-1.47686500	1.50392400
H	4.24065000	-0.51179200	1.65087100
C	1.31675500	-2.35727200	1.38249400
H	1.71692800	-3.35143600	1.60602900
H	1.22335700	-2.25436800	0.29668600
C	7.18939200	-3.74186500	0.01302800
O	7.83318200	-4.36739500	0.86725800
C	7.42916900	-3.96128900	-1.46026000
H	6.54687900	-4.40423000	-1.93224700
H	7.64784800	-3.01911000	-1.96533700
H	8.26806000	-4.64638400	-1.57251300
O	-7.90293700	-5.71579500	-1.58478000
H	-8.50277200	-6.10286300	-2.23375400
H	-3.79694100	1.93497100	1.56196600

- A1(S)-R^2 binding site with sialic acid (the number of imaginary frequencies = 0)

C	-3.70585300	4.16487000	-0.99559300
H	-4.53384200	3.92919100	-0.33538500
C	-3.71741700	5.33493700	-1.74713900
C	-2.66200500	5.61794700	-2.61164500
C	-1.59483000	4.72930700	-2.71855200
C	-1.57028700	3.56953800	-1.95000400
C	-2.62509800	3.28506000	-1.08106800
H	-4.55324400	6.02183600	-1.66360500
H	-2.67386600	6.52647100	-3.20510000
H	-0.77769500	4.93852700	-3.40110600
H	-0.73614500	2.88315300	-2.03744200
C	-2.69875900	2.00536800	-0.30440600
O	-3.72424300	1.31764500	-0.35188900
N	-1.62162500	1.61375500	0.42643800
C	-0.51881100	2.47552300	0.76600000
C	-1.62607600	0.31325200	1.11661400
C	-0.69993800	3.52623400	1.66089500
C	0.40467900	4.28065700	2.04351000
C	1.67140700	3.96511300	1.55449900
C	1.87472100	2.91484500	0.65012700
C	0.74469200	2.18944500	0.26169400
H	-1.68743200	3.73859400	2.05727100
H	0.27863700	5.10303500	2.74100700
H	2.52083500	4.54912600	1.89770400

H	0.83961100	1.36636200	-0.43972700	C	4.53588500	-1.77003600	-0.62644300	C	8.78763500	0.73290900	4.22002800
O	4.42157600	3.34519300	0.57168000	O	4.01076200	-0.61813400	-1.29333500	C	9.56523100	1.74001100	3.65219700
H	4.25388400	4.28842100	0.47629000	C	3.95322500	1.63978200	-2.00574800	C	9.20224600	2.28942200	2.42469300
C	-2.21360100	0.36541900	2.51662000	O	4.18964500	1.48832700	-3.19223200	C	8.07609500	1.82151500	1.75509700
C	-2.14396000	-0.80294300	0.19395300	O	3.30301800	2.63960700	-1.48023100	C	7.29701500	0.81022300	2.32044100
C	-3.46375700	0.93078900	2.78967400	H	6.41358500	0.76210900	-1.65571800	H	9.06430800	0.30513400	5.17805600
C	-3.95746000	0.95248700	4.09068300	H	6.12463200	1.74309000	-0.20432200	H	10.44955700	2.10000500	4.16802600
C	-3.21278500	0.40983100	5.13598200	O	7.89974300	-0.31779700	0.18881300	H	9.79689200	3.08398900	1.98608300
C	-1.96794600	-0.15426500	4.87345300	H	8.17087500	0.46000200	0.69284300	H	7.79902900	2.25270200	0.79983400
C	-1.47317000	-0.17281000	3.57178000	H	6.08472600	-0.34694500	1.17147300	C	6.01996900	0.34430000	1.69030300
H	-3.60076600	0.42906000	6.14932300	O	3.68375700	1.09758200	0.23861900	O	4.99604900	0.25491000	2.37183600
H	-4.92896800	1.39456900	4.28764300	N	6.66125800	-2.86035000	0.03864900	N	6.00557800	0.06100600	0.35478700
H	-4.05197100	1.34564100	1.97936000	H	6.15254000	-3.28990700	0.80439200	C	7.19371000	-0.20563000	-0.40690400
H	-1.37711300	-0.57480300	5.68077700	H	6.41787400	-1.59691000	-1.57927400	C	4.72602600	-0.20138500	-0.32184200
H	-0.49727300	-0.60692400	3.37340700	H	4.31157200	-2.60137700	-1.29922100	C	8.02973300	-1.26041100	-0.04884800
O	-1.64580700	-0.93474100	-0.93159200	C	2.23649300	-2.03916900	0.54989400	C	9.17397100	-1.51825700	-0.79831800
N	-3.01944800	-1.67094000	0.71600900	O	1.67323400	-0.74882400	0.71441500	C	9.46676700	-0.73958500	-1.91275600
H	-3.39871500	-1.47015200	1.63119800	H	2.33373900	-0.06150700	0.48581700	C	8.62496000	0.31212900	-2.29907500
C	-3.50462400	-2.84520400	0.01360400	H	1.86271500	-2.64270200	1.38783600	C	7.48724300	0.56644100	-1.52715600
C	-4.97281600	-2.77536800	-0.35051800	O	0.33419200	-2.96728800	-0.66492800	H	7.78551000	-1.87183900	0.81342500
C	-5.59272800	-1.56237900	-0.65635100	H	-0.17200000	-2.14396400	-0.78460900	H	9.82889500	-2.33540500	-0.51411000
C	-6.93330900	-1.53727700	-1.02890700	O	4.20128800	-3.33010000	1.13092300	H	10.35752700	-0.94930600	-2.49606200
C	-7.69484400	-2.71050600	-1.11014200	H	3.85426400	-3.49269700	2.01787000	H	6.82853600	1.38652700	-1.79677000
C	-7.05802100	-3.91898800	-0.79812300	C	3.77500000	-2.03826700	0.69050700	C	4.30273100	-1.66060400	-0.30230600
C	-5.72032200	-3.95246300	-0.42023000	H	4.03593000	-1.28572200	1.44336800	C	3.66729600	0.83644200	0.10602700
H	-5.02649000	-0.63790400	-0.59656300	C	1.72655000	-2.70086700	-0.72707600	C	4.26023300	-2.41700600	0.87366500
H	-5.25222000	-4.90207300	-0.17447600	H	2.22039200	-3.66906300	-0.85437900	C	3.86142800	-3.74991100	0.83889500
H	-7.62155100	-4.84583700	-0.84541200	H	1.95972200	-2.07110700	-1.59222900	C	3.49800000	-4.34597500	-0.36692600
H	-7.40020500	-0.58503500	-1.26256000	C	7.78554200	-3.50085600	-0.35182400	C	3.53800400	-3.60116200	-1.54175700
H	-2.89861000	-2.94304500	-0.88996700	O	8.17494600	-4.50313900	0.26388900	C	3.94104700	-2.26863000	-1.50695300
H	-3.31897500	-3.72932500	0.62987500	C	8.53516000	-2.98436200	-1.55505400	H	3.18739200	-5.38555600	-0.38976600
O	-9.76543700	-1.45817300	-1.81035400	H	7.92191700	-3.06642100	-2.45750000	H	3.83318600	-4.32436200	1.75935300
H	-10.69539600	-1.46589300	-2.06700000	H	8.80787500	-1.93592200	-1.42371600	H	4.53102600	-1.95578500	1.81605500
B	3.33281100	2.54041300	0.06818600	H	9.43234000	-3.58764700	-1.68440200	H	3.26182400	-4.05609100	-2.48749000
B	-9.20084200	-2.67378300	-1.52828200	O	-9.88307300	-3.85978000	-1.59260500	H	3.97656300	-1.69549600	-2.42924700
H	-0.56929600	0.04426900	1.21816300	H	-10.81018600	-3.80737000	-1.85384400	O	3.95216800	2.03519300	0.10636800
C	4.40844100	0.67412600	-0.88608700	●	A1(S)-R⁴ binding site with sialic acid (the			N	2.43068200	0.37871300	0.34417600
C	5.92036600	0.78104800	-0.67840100		number of imaginary frequencies = 0)			H	2.28187800	-0.61808600	0.41332600
C	6.47925600	-0.36942200	0.14821000	C	7.64882200	0.27992000	3.56298700	C	1.32995900	1.27103600	0.69613000
C	6.07605300	-1.66982800	-0.54349600	H	7.02822800	-0.49055800	4.00799100	C	0.00807500	0.54990400	0.61680100

C	-0.68377700	0.19454100	1.77372800	H	-5.55365400	3.54434500	0.36262100	C	5.18894300	2.20890200	-0.16844100
C	-1.89971600	-0.48274500	1.69242900	O	-4.66622800	3.83890600	-2.07840700	H	4.41372200	4.91863600	1.72486500
C	-2.47342700	-0.82807700	0.46281000	H	-3.88636700	3.32991000	-1.81118000	H	6.74045400	4.52468000	2.49918500
C	-1.76194700	-0.46404400	-0.68941500	O	-7.86410700	2.81497100	0.69354400	H	8.06231100	2.67151000	1.54838400
C	-0.54734200	0.21082900	-0.61979400	H	-7.54995200	3.36298300	1.42463700	H	4.72137500	1.56594700	-0.90725300
H	-0.26905600	0.44953900	2.74569100	C	-6.84995400	1.86731600	0.34799200	O	8.81862100	0.93287500	-0.25115600
H	-0.02357300	0.48015200	-1.53381700	H	-6.50399700	1.34982100	1.24898500	H	9.11007700	1.82992800	-0.44428700
H	-2.16997100	-0.71330400	-1.66489000	C	-5.79620300	3.06470000	-1.69131300	C	2.22377900	2.96582700	2.22524900
H	-2.41361700	-0.74681500	2.61339400	H	-6.67660400	3.69999200	-1.81592900	C	1.28683000	1.79763100	0.22403900
H	1.48439900	1.66899600	1.70487300	H	-5.88989600	2.18855000	-2.34225000	C	1.80554700	3.97888100	3.08857400
H	1.35555100	2.11913500	0.00664300	C	-11.09109200	0.67173400	0.29636600	C	2.03805300	3.88523500	4.45867800
O	-4.08771400	-2.57696400	1.43420600	O	-11.89209200	1.46649800	0.80812800	C	2.68821100	2.76938200	4.97738900
H	-3.27216200	-3.04573100	1.63805400	C	-11.57105800	-0.50542200	-0.51620900	C	3.10219800	1.75139900	4.12001500
B	8.94891400	1.19129300	-3.55527000	H	-11.25864000	-0.40750700	-1.56028800	C	2.87234200	1.84469700	2.75093400
B	-3.89473100	-1.58433400	0.40326700	H	-11.16499200	-1.44020500	-0.12607000	H	2.86964100	2.69115100	6.04465700
H	4.90021500	0.05862300	-1.36926600	H	-12.65893500	-0.52843900	-0.47596400	H	1.70812100	4.68192600	5.11763700
O	10.09324500	0.91856500	-4.25224800	H	10.26997900	1.47480100	-5.02064300	H	1.29632600	4.85065700	2.68759000
O	8.06835500	2.18368300	-3.88662300	H	8.28650000	2.70989500	-4.66538300	H	3.60939500	0.87837900	4.51872600
C	-6.04535400	-1.07781000	-0.46449900	●	A1(R)-R^2 and R^4 binding sites with sialic acids			H	3.21631000	1.04806300	2.09750200
C	-7.15197700	-1.87706300	0.22728400		(the number of imaginary frequencies = 0)			O	1.95601100	0.89377400	-0.28835500
C	-8.15969500	-0.99068400	0.94939500	C	4.71939300	5.39204500	-1.89336500	N	-0.03300300	1.69804100	0.42406600
C	-8.68878700	0.02719300	-0.05961400	H	4.65842300	5.81606300	-0.89764200	H	-0.53107100	2.47404000	0.83758000
C	-7.52136900	0.86988800	-0.62200100	C	5.64142400	5.89757100	-2.80475900	C	-0.80097300	0.50780600	0.05485800
O	-6.55651600	0.00127000	-1.22170900	C	5.73021100	5.35567500	-4.08486900	C	-2.27789400	0.76670900	0.20751500
C	-5.27957400	-1.98458100	-1.45408600	C	4.88013900	4.31721700	-4.45907100	C	-2.99049000	1.43577500	-0.78998700
O	-5.73998600	-2.42021600	-2.49568800	C	3.94255400	3.82608500	-3.55675600	C	-4.34629500	1.70609100	-0.62890300
O	-4.08805100	-2.22895500	-0.98755700	C	3.86818700	4.35003700	-2.26498200	C	-5.04841100	1.31616600	0.52080900
H	-7.69530400	-2.45178600	-0.52961400	H	6.29222100	6.71541100	-2.51294400	C	-4.31828400	0.64197100	1.50702200
H	-6.67884100	-2.57797900	0.91910000	H	6.45683300	5.74502200	-4.79072500	C	-2.95903800	0.37253600	1.35943100
O	-9.26287800	-1.75841400	1.41415500	H	4.94284100	3.89334000	-5.45601700	H	-2.47896500	1.74602300	-1.69784100
H	-8.96725500	-2.33098400	2.13329300	H	3.26633100	3.02957400	-3.84893500	H	-2.42165900	-0.15054400	2.14653500
H	-7.69425400	-0.47381300	1.79722800	C	2.78622100	3.84201000	-1.35990800	H	-4.82224000	0.32207200	2.41455400
O	-5.06226600	-0.64200500	0.42981300	O	1.62221500	3.78614800	-1.77176400	H	-4.87301800	2.23192600	-1.42139300
N	-9.76108500	0.86024000	0.44472400	N	3.08950500	3.47386600	-0.08287300	H	-0.55558200	0.25094900	-0.97971700
H	-9.48644200	1.70319300	0.93812300	C	4.44182600	3.25493700	0.36228200	H	-0.49044000	-0.33317300	0.68218900
H	-9.07209600	-0.53944900	-0.91219900	C	1.92757000	3.09581000	0.74214400	O	-7.01247300	2.93593500	0.18009800
H	-7.92371700	1.45248800	-1.45466900	C	4.99806200	4.09847600	1.32204400	H	-6.33668400	3.59978300	0.35022100
C	-5.64369900	2.62957500	-0.23843200	C	6.30060200	3.87513200	1.74845000	B	7.39074900	0.78054100	-0.40921100
O	-4.41139700	1.94238700	-0.09220400	C	7.04324200	2.82682200	1.20459400	B	-6.62151400	1.63270900	0.66516500
H	-4.57081100	0.97828000	0.01169900	C	6.51238400	1.97540400	0.22904500	C	7.06063600	-1.49079600	-0.98188500

C	8.37978500	-2.26435500	-1.01741300	C	-10.84915300	-0.92819600	-0.49767000	C	4.18240200	7.20516100	-2.28822600
C	8.41867600	-3.40200500	-0.00532500	C	-9.54140300	-1.68816800	-0.17890600	C	5.29245600	6.75145500	-2.99764400
C	7.20551200	-4.29368700	-0.26497600	O	-8.86799200	-1.03962400	0.90295500	C	5.59462000	5.39192700	-3.01861800
C	5.90357700	-3.47607300	-0.10284800	C	-8.16606300	0.79776800	2.22749100	C	4.80234400	4.48818900	-2.31727700
O	5.93596500	-2.34557600	-0.97820100	O	-8.78294900	0.57269200	3.25475100	C	3.69125200	4.94053400	-1.60343300
C	6.92521400	-0.60736700	-2.24384400	O	-7.05483000	1.47173800	2.13912300	H	3.94028800	8.26279600	-2.27223000
O	6.75008200	-1.03287000	-3.37310400	H	-10.56191900	1.16030900	1.20224900	H	5.91756100	7.45533900	-3.53762300
O	7.04961600	0.64658900	-1.91355900	H	-9.52577700	2.16699000	0.17200200	H	6.44983800	5.03240000	-3.58142600
H	8.50824100	-2.69797300	-2.01441300	O	-11.76815900	1.19150100	-1.09425700	H	5.04405400	3.43178700	-2.33639100
H	9.18987300	-1.55300200	-0.84229100	H	-11.58356200	2.08507800	-1.41031400	C	2.74857100	4.00042900	-0.91429500
O	9.58757000	-4.19325600	-0.18002100	H	-9.89870800	0.58406200	-1.72238000	O	1.53454700	4.08322500	-1.12674400
H	10.36060700	-3.67187400	0.07102500	O	-7.49585900	0.60321400	0.01115500	N	3.25572500	3.05322300	-0.08059500
H	8.39047200	-3.01653800	1.02103300	N	-11.63923500	-1.61252600	-1.50056800	C	4.59522100	3.07581500	0.44688400
O	7.00566800	-0.57939000	0.07923900	H	-11.12821700	-2.05013900	-2.26010100	C	2.36969400	2.04204100	0.52067400
N	7.17983500	-5.50530500	0.52895000	H	-11.41616100	-0.92583700	0.43685100	C	4.97247900	4.05525900	1.36134100
H	6.73261300	-5.44371800	1.43787100	H	-9.83080400	-2.66335500	0.22121700	C	6.24272000	3.99454300	1.92561200
H	7.24069100	-4.57935800	-1.31965300	C	-7.25278400	-2.63387800	-0.97975500	C	7.10567700	2.95038500	1.59660100
H	5.08988400	-4.09592000	-0.48802700	O	-6.23548300	-1.72329000	-0.59545900	C	6.74708900	1.95650300	0.67689500
C	4.27842500	-2.13989800	1.43394000	H	-6.63377100	-0.88398300	-0.27468900	C	5.47641900	2.05690100	0.10300200
O	4.62964700	-0.76992000	1.40779700	H	-6.89511300	-3.11513000	-1.89987300	H	4.27693000	4.84282200	1.63227000
H	5.42187600	-0.63541800	0.84535200	O	-6.09555000	-4.33945000	0.26746900	H	6.55051900	4.75195800	2.63996800
H	3.85428200	-2.31826200	2.43105700	H	-5.46170500	-3.61693500	0.38966100	H	8.07790100	2.90845700	2.07977900
O	1.98106100	-1.73994000	0.72722900	O	-9.29679500	-2.80783200	-2.25493300	H	5.14511100	1.31772300	-0.61975000
H	2.06427000	-0.82351800	0.40170800	H	-8.80728000	-2.88019200	-3.08472900	O	9.00607000	0.73580100	0.96713100
O	5.22869400	-4.29555400	2.01476600	C	-8.58194400	-1.95012700	-1.36099500	H	9.46335400	1.57990800	0.89426100
H	5.09147600	-4.11152000	2.95324000	H	-8.33328500	-1.01139600	-1.86736800	C	1.74969000	2.47420100	1.83821500
C	5.51038300	-3.06787600	1.33485600	C	-7.36540800	-3.72466900	0.07910000	C	1.40934000	1.45778600	-0.52753000
H	6.34247400	-2.55468600	1.83020200	H	-8.05531000	-4.50858400	-0.24297400	C	1.08226900	3.69344100	1.99498500
C	3.17166300	-2.45082900	0.42906500	H	-7.71943100	-3.30019200	1.02492300	C	0.52717400	4.03932000	3.22363000
H	2.92659100	-3.51665700	0.48098400	C	-12.97975200	-1.78377200	-1.51757800	C	0.62918900	3.17443500	4.31132000
H	3.51058400	-2.21974800	-0.58594100	O	-13.51764700	-2.38338300	-2.45901700	C	1.29272800	1.95982100	4.16450300
C	7.61700600	-6.73359200	0.17331300	C	-13.79381000	-1.25112300	-0.36425500	C	1.85020700	1.61578300	2.93565800
O	7.53614400	-7.67702000	0.97270300	H	-13.53693100	-1.77257200	0.56284300	H	0.19544100	3.44767000	5.26788600
C	8.17942400	-6.93074000	-1.21275400	H	-13.61116800	-0.18547900	-0.21666700	H	0.01194900	4.98864800	3.33053200
H	7.40557600	-6.76752600	-1.96906500	H	-14.84734800	-1.42003500	-0.58136000	H	0.99190100	4.36670700	1.15036900
H	8.99569700	-6.23287800	-1.40592500	H	1.19097300	3.89162000	0.61214800	H	1.38287200	1.28095000	5.00639900
H	8.53940500	-7.95517800	-1.29461600	●	A1(S)-R^2 and R^4 binding sites with sialic acids			H	2.37417500	0.67024400	2.82807500
C	-8.61014900	0.34764100	0.81750800		(the number of imaginary frequencies = 0)			O	1.86855500	0.99509200	-1.58200200
C	-9.84203900	1.14169200	0.37773200	C	3.37619500	6.30066000	-1.60563000	N	0.12077900	1.34705000	-0.19907800
C	-10.53715700	0.52957000	-0.83238800	H	2.49984000	6.64572900	-1.06719900	H	-0.21029500	1.79410100	0.64452700

C	-0.86012800	0.74352800	-1.10071000
C	-2.21465500	0.67905700	-0.44300200
C	-3.08607500	1.76841100	-0.49950100
C	-4.32438500	1.71663700	0.13498700
C	-4.74975700	0.58009600	0.83703500
C	-3.86319900	-0.50330800	0.88031700
C	-2.61802100	-0.45847300	0.25743800
H	-2.79325100	2.66151800	-1.04616800
H	-1.95336800	-1.31709300	0.31140400
H	-4.15274800	-1.40427300	1.41361500
H	-4.97967000	2.58213800	0.07509100
H	-0.90608600	1.33323500	-2.02228600
H	-0.51146700	-0.25672300	-1.37028300
O	-6.57279300	1.76534700	2.20596200
H	-5.81424700	2.18494800	2.62414900
B	7.73336900	0.74119000	0.28375100
B	-6.20538700	0.54507000	1.52592700
H	3.01962600	1.18673700	0.73263700
C	7.56210900	-1.43840500	-0.59355800
C	8.77490000	-2.26941800	-0.17050100
C	8.38951900	-3.47828300	0.67172700
C	7.37526500	-4.29149300	-0.12938000
C	6.12726300	-3.43160200	-0.43272300
O	6.51746000	-2.23453400	-1.11248000
C	7.95586500	-0.45392600	-1.72028700
O	8.21907100	-0.77869600	-2.86566000
O	7.98203600	0.76047200	-1.24784300
H	9.28390400	-2.63467300	-1.06843600
H	9.45634800	-1.61101500	0.37208100
O	9.52030700	-4.30592600	0.91397100
H	10.14023000	-3.83103100	1.48202400
H	7.95380300	-3.16755600	1.62920300
O	7.10102300	-0.60457600	0.43658800
N	7.02044900	-5.56045200	0.47275800
H	6.25636800	-5.55023700	1.14035100
H	7.83005800	-4.49492600	-1.10238800
H	5.53739600	-3.98402100	-1.16825400
C	4.00843600	-2.17841100	0.39354200
O	4.33786300	-0.80715900	0.53720600
H	5.30471800	-0.68084200	0.43674000
H	3.23112400	-2.38402800	1.14162200
O	2.13021000	-1.80836800	-1.12140500
H	2.25646300	-0.85563900	-1.27939000
O	4.66744200	-4.37022300	1.18594100
H	4.16773300	-4.24050300	2.00258100
C	5.18695000	-3.11163900	0.74988200
H	5.74487700	-2.63850300	1.56601100
C	3.38538400	-2.45302500	-0.97217700
H	3.19516300	-3.52597400	-1.07262200
H	4.07398900	-2.14286000	-1.76527000
C	7.55130300	-6.77457800	0.20683800
O	7.15166500	-7.77486500	0.81918400
C	8.61607700	-6.88349800	-0.85675700
H	8.20954600	-6.62104200	-1.83820500
H	9.44997900	-6.21256400	-0.64406700
H	8.96750900	-7.91366300	-0.88682100
C	-8.21514000	-0.66829600	1.17909200
C	-9.43693000	0.07496900	1.72287700
C	-10.44091500	0.43168800	0.63339100
C	-10.80158100	-0.85648000	-0.10473500
C	-9.53092800	-1.48914900	-0.71738700
O	-8.57414100	-1.73018800	0.31763400
C	-7.41559800	-1.29705800	2.34277500
O	-7.79453500	-2.23958600	3.01700300
O	-6.29804800	-0.64678800	2.50363800
H	-9.94522800	-0.56658700	2.44978200
H	-9.08421100	0.97064900	2.23957200
O	-11.63348700	0.95908900	1.20097900
H	-11.44418000	1.82679500	1.58028400
H	-10.01820000	1.16180900	-0.06720500
O	-7.30035100	0.19147900	0.56255700
N	-11.85338300	-0.70179100	-1.08875600
H	-11.56498100	-0.42187300	-2.02045500
H	-11.14460100	-1.56989400	0.64911800
H	-9.81170300	-2.48464000	-1.07090800
C	-7.57771000	-1.37320900	-2.43244500
O	-6.41992500	-0.90438000	-1.76058900
H	-6.65750300	-0.57270000	-0.86655100
H	-7.48238900	-1.03239900	-3.47208500
O	-6.33493000	-3.34265100	-3.05026900
H	-5.62414200	-2.86145300	-2.60096000
O	-9.86123800	-0.78961200	-2.96038100
H	-9.57791800	-0.20868500	-3.67864300
C	-8.88895800	-0.74912500	-1.91188700
H	-8.67363900	0.29140400	-1.64645500
C	-7.55079700	-2.89709900	-2.45928700
H	-8.36616800	-3.28887400	-3.07237700
H	-7.64093500	-3.29621400	-1.44314400
C	-13.17395900	-0.94078900	-0.92920700
O	-13.95823500	-0.74610600	-1.86847100
C	-13.66175800	-1.46474400	0.39895000
H	-13.25745500	-2.46315700	0.59162000
H	-13.35319700	-0.80947900	1.21510500
H	-14.74830600	-1.52742400	0.36440900