Supplementary Information

Ternary Resin-Bound Dynamic Combinatorial Chemistry

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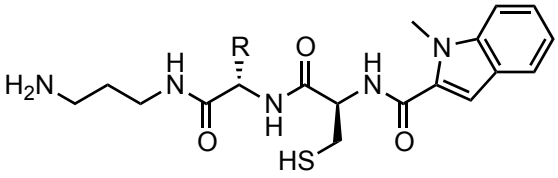
Materials and Methods

All reagents and solvents used in the synthesis were obtained from commercial sources (Sigma-Aldrich, Fisher Scientific or VWR), amino acids were purchased from Advanced ChemTech and Chem-Impex International and were used without further purification. *N*-(9-Fluorenylmethyloxycarbonyl)-3-amino-(2-nitrophenyl)propionic acid (AnpOH) was prepared according to a previously described protocol.[1] 4-Carboxybenzaldehyde benzoylhydrazone was synthesized by analogy to the previously published procedure for the synthesis of acylhydrazone derivatives.[2†] HPLC analysis was performed on a Shimadzu LC-2010A Liquid Chromatograph using a Shim-pack CLC-ODS-(M) C18 column. MALDI-MS data was recorded using Bruker Autoflex III MALDI-TOF spectrometer, using CHCA as a matrix.

Synthesis of library building blocks

Synthesis of thiol-containing building blocks A1 and A2.

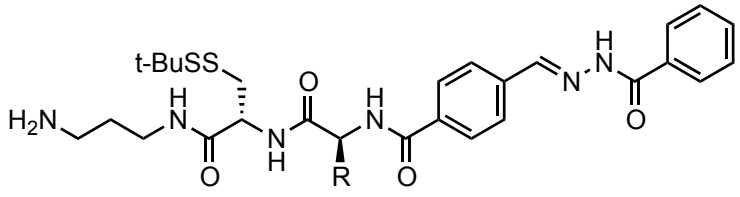


Wang resin (0.9 mmol/g, 100-200 mesh, 0.55 g, 0.5 mmol, 1 eq) was washed with DCM (x3), DMF (x3) and then resuspended in DMF. CDI (0.81 g, 5 mmol, 10 eq) was added to the reaction vessel, and the reaction mixture was allowed to rotate on a LabQuake rotator

† Reaction was allowed to proceed overnight.

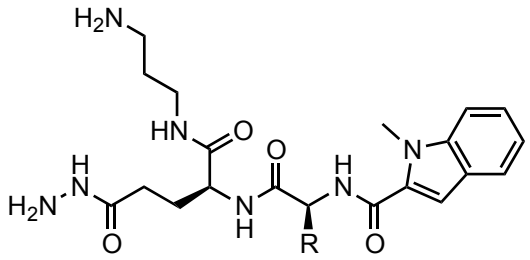
for 12 hours. Resin was then washed with DCM (x3), DMF (x3) and then resuspended in DMF. Diaminopropane (416 μL, 5 mmol, 10 eq) was then added, and the reaction mixture was allowed to rotate for an additional 12 h. Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Gly-OH or Fmoc-Pro-OH (1.5 mmol, 3 eq) was then added, followed by the addition of HBTU (0.57 g, 1.5 mmol, 3 eq), DIPEA (424 μL, 2.5 mmol, 5 eq). The coupling reaction was allowed to proceed on the LabQuake rotator for 1h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Cys(Trt)-OH (0.88 g, 1.5 mmol, 3 eq) was then added, followed by the addition of HBTU (0.57 g, 1.5 mmol, 3 eq), DIPEA (424 μL, 2.5 mmol, 5 eq). Coupling reaction was allowed to proceed for 1 h. Beads were then washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Lastly, indole-3-carboxylic acid (0.27 g, 1.5 mmol, 3 eq) was added, followed by the addition of HBTU (0.57 g, 1.5 mmol, 3 eq), DIPEA (424 μL, 2.5 mmol, 5 eq). Coupling reaction was allowed to proceed for 4 h, then washed with DMF (x3) and DCM (x3). Products were cleaved for 1 h in 15 mL of 1%TES/30%TFA solution in DCM. Filtrates were collected, dried and purified by precipitation in chilled ether (-20°C).

Synthesis of difunctional thiol, acyl hydrazone-containing building blocks B1 and B2.



Wang resin (0.9 mmol/g, 100-200 mesh, 0.55 g, 0.5 mmol, 1 eq) was washed with DCM (x3), DMF (x3) and then resuspended in DMF. CDI (0.81 g, 5 mmol, 10 eq) was added to the reaction vessel, and the reaction mixture was allowed to rotate on a LabQuake rotator for 12 h. Resin was then washed with DCM (x3), DMF (x3) and then resuspended in DMF. Diaminopropane (416 μL, 5 mmol, 10 eq) was then added and the reaction mixture was allowed to rotate for an additional 12 h. Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Cys(S-t-Bu)-OH (0.65 g, 1.5 mmol, 3 eq) was then added, followed by the addition of HBTU (0.57 g, 1.5 mmol, 3 eq), DIPEA (424 μL, 2.5 mmol, 5 eq). Coupling reaction was allowed to proceed on a LabQuake rotator for 1 h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Gly-OH or Fmoc-Pro-OH (1.5 mmol, 3 eq) was then added, followed by the addition of HBTU (0.57 g, 1.5 mmol, 3 eq), DIPEA (424 μL, 2.5 mmol, 5 eq). Coupling reaction was allowed to proceed for 1 h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Lastly, 4-carboxybenzaldehyde benzoylhydrazone hydrochloride (0.46 g, 1.5 mmol, 3 eq) was added, followed by HBTU (0.57 g, 1.5 mmol, 3 eq) and DIPEA (697 μL, 4.0 mmol, 8 eq). Coupling reaction was allowed to proceed for 12 h, washed with DMF (x3) and DCM (x3). Finally, peptides were cleaved for 1 h in 15 mL of 1%TES/30%TFA solution in DCM. Filtrates were collected, dried and purified by precipitation in chilled ether (-20°C).

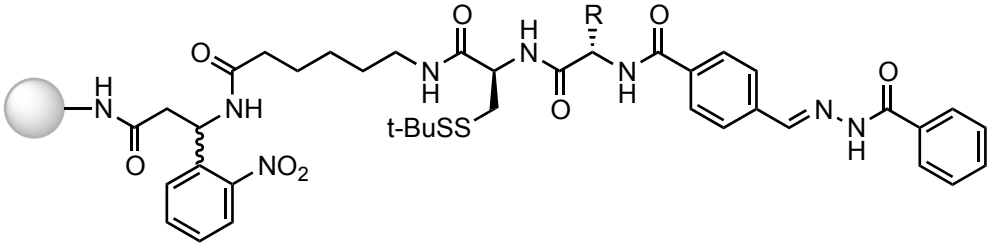
Synthesis of acyl hydrazine-containing building blocks C1 and C2.



Wang resin (0.9 mmol/g, 100-200 mesh, 1.11 g, 1 mmol, 1 eq) was washed with DCM (x3), DMF (x3) and then resuspended in DMF. CDI (1.62 g, 10 mmol, 10 eq) was added to the reaction vessel and the reaction mixture was allowed to rotate on a LabQuake rotator for 12 h. Resin was then washed with DCM (x3), DMF (x3) and then resuspended in DMF. Diaminopropane (832 μL, 10 mmol, 10 eq) was then added and the reaction mixture was allowed to rotate for an additional 12 h. Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-L-GluOMe (1.15 g, 3 mmol, 3 eq) was then added, followed by the addition of HBTU (1.14 g, 3 mmol, 3 eq), DIPEA (848 μL, 5 mmol, 5 eq). The coupling reaction was allowed to proceed on a LabQuake rotator for 1 h, washed with DCM (x3), DMF (x3) and then deprotected for 1h using 20% piperidine/DMF solution (20 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Gly-OH or Fmoc-Pro-OH (3 mmol, 3 eq) was then added, followed by the addition of HBTU (1.14 g, 3 mmol, 3 eq), DIPEA (848 μL, 5 mmol, 5 eq). The coupling reaction was allowed to proceed for 1 h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (20 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Lastly, indole-3-carboxylic acid (0.53 g, 3 mmol, 3 eq) was added, followed by the

addition of HBTU (1.14 g, 5 mmol, 3 eq) and DIPEA (848 µL, 5 mmol, 5 eq). Coupling reaction was allowed to proceed for 4 h, washed with DMF (x3), DCM (x3), THF (x3) and then resuspended in THF. Hydrazine hydrate (0.5 mL, 10 mmol, 10 eq) was then added and reaction vessel was allowed to rotate for 12 h. Resin was then washed with DMF (x3), DCM (x3). Finally, peptides were cleaved for 1 h in 15 mL of 1% TES/30% TFA solution in DCM. Filtrates were collected, dried and purified by precipitation in chilled ether (-20 °C).

Synthesis of the resin-bound building blocks B1 and B2.



TentaGel Macrobead resin (MB300002, 0.27 mmol/g, 280-320 µm, 0.55 g, 0.15 mmol, 1 eq) was washed with DCM (x3), DMF (x3) and then resuspended in DMF. AnpOH (193 mg, 0.45 mmol, 3 eq) was then added, followed by the addition of HBTU (169 mg, 0.45 mmol, 3 eq), DIPEA (130 µL, 2.5 mmol, 5 eq). The reaction mixture was allowed to rotate for 4 h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Fmoc-6-Ahx-OH (158 mg, 0.45 mmol, 3 eq) was then added, followed by the addition of HBTU (169 mg, 0.45 mmol, 3 eq), DIPEA (130 µL, 2.5 mmol, 5 eq). The reaction mixture was allowed to rotate for 12 h, washed with DCM (x3), DMF (x3) and then deprotected for 1h using 20% piperidine/DMF solution (10 mL). Fmoc-Cys(S-t-Bu)-OH (193 mg, 0.45 mmol, 3 eq) was then added, followed by the addition of HBTU (169 mg, 0.45 mmol, 3 eq), DIPEA (130 µL, 2.5 mmol, 5 eq). Coupling reaction was allowed to proceed on a LabQuake rotator for 1 h, washed with

DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Fmoc-Gly-OH or Fmoc-Pro-OH (1.5 mmol, 3 eq) was then added, followed by the addition of HBTU (169 mg, 0.45 mmol, 3 eq), DIPEA (130 μL, 0.45 mmol, 5 eq). Coupling reaction was allowed to proceed for 1 h, washed with DCM (x3), DMF (x3) and then deprotected for 1 h using 20% piperidine/DMF solution (10 mL). Resin was then washed with DCM (x3) and DMF (x3) and resuspended in DMF. Lastly, 4-carboxybenzaldehyde benzoylhydrazone hydrochloride (152 mg, 0.45 mmol, 3 eq) was added, followed by the addition of HBTU (169 mg, 0.45 mmol, 3 eq), DIPEA (207 μL, 1.2 mmol, 8 eq). Coupling reaction was allowed to proceed for 12 h, washed with DMF (x3) and DCM (x3). Finally, compounds were cleaved for 1 h in 15 mL of 1% TES/30% TFA solution in DCM. Filtrates were collected, dried and purified by precipitation in chilled ether (-20 °C).

General protocols for exchange experiments

All exchange reactions were performed in 50 mM ammonium acetate buffer (pH=7.4) with 5.5% DMSO. Stock solutions of the building blocks were prepared as 200 mM stocks in DMSO and were stored in -20 ºC freezer in between the experiments. 1 M aniline stock solution was prepared in DMSO. 5% Thiopropanol stock solution was prepared in DMSO immediately before the experiment (for solution-phase disulfide exchange).

***Solution-phase hydrazone exchange*:**

To a 1.8 mL HPLC vial 1417.5 μL of the 50mM ammonium acetate buffer (pH=7.4) was added, followed by DMSO (63.5 μL), aniline (1 M, 15 μL, 10 mM, 37.5 eq), B1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), C1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), and C2 (200 mM, 1 μL, 0.13 mM, 0.5 eq). Vials were sealed, vortexed and allowed to equilibrate for 3 days.

***Solution-phase disulfide exchange*:**

To a 1.8 mL HPLC vial 1417.5 μL of the 50 mM ammonium acetate buffer (pH=7.4) was added, followed by DMSO (77.8 μL), A1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), A2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), and thiopropanol (5%, 0.7 μL, 0.267 mM, 1 eq). Vials were sealed, vortexed and allowed to equilibrate for 3 days.

Simultaneous disulfide and hyrazone exchange in solution (1:1:1:1:1:1 ratio):

To a 1.8 mL HPLC vial 1417.5 μL of the 50mM ammonium acetate buffer (pH=7.4) was added, followed by DMSO (61 μL), aniline (1 M,15 μL, 10 mM, 37.5 eq), A1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), A2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), C1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), C2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), and thiopropanol (5%, 0.7 μL, 0.267 mM, 1 eq). Vials were sealed, vortexed and allowed to equilibrate for 3 days.

Simultaneous disulfide and hyrazone exchange in solution (10:10:1:1:10:10 ratio):

To a 1.8 mL HPLC vial 1417.5 μL of the 50mM ammonium acetate buffer (pH=7.4) was added, followed by DMSO (24.8 μL), aniline (1 M,15 μL, 10 mM, 37.5 eq), A1 (200 mM, 10 μL, 1.3 mM, 0.5 eq), A2 (200 mM, 10 μL, 1.3 mM, 0.5 eq), B1 (200 mM, 1 μL, 0.13 mM, 0.5 eq), B2 (200 mM, 1 μL, 0.13 mM, 0.5 eq), C1 (200 mM, 10 μL, 1.3 mM, 0.5 eq), C2 (200 mM, 10 μL, 1.3 mM, 0.5 eq), and thiopropanol (5%, 0.7 μL, 0.267 mM, 1 eq). Vials were sealed, vortexed and allowed to equilibrate for 3 days.

RBDCC experiment (hydrazone exchange):

To a 1.5 mL eppendorf tube containing resin-bound B1 (1.69 mg, 0.4 mmol, 1 eq), 950 μL of the 50mM ammonium acetate buffer (pH=7.4) was added, and to this mixture aniline (1M, 15 μL, 15 mM, 37.5 eq) was added, followed by C1 (200 mM, 2 μL, 0.4 mM, 1 eq), and C2 (200 mM, 2 μL, 0.4 mM, 1 eq). Reaction vessel was allowed to rotate on LabQuake rotator for 1 week. Resin beads were then transferred into 1.2 mL peptide synthesis vessel and washed with water (x3), DMF (x3), THF (x3), CH_3CN (x3), and resuspended in 400 μL of a 4:1 mixture of acetonitrile:methanol. Resin beads along with the acetonitrile-methanol solution were transferred into 1.8 mL screw cap grass vials. Photolysis was carried out using 365 nm compact UV lamp (UVL-21, 4 watt) for 6-8 hours. In order to run HPLC analysis, sample (50 μL) was diluted with glass-distilled deionized water (150 μL).

RBDCC experiment (disulfide exchange):

To a 1.2 mL solid state peptide synthesis vessel containing resin-bound B1 (1.69 mg, 0.4 mmol, 1 eq), 950 μL of the 50 mM ammonium acetate buffer (pH=7.4) was added, followed by acetonitrile (50 μL), and thiopropanol (0.7 μL, 20 eq). Reaction vessel was allowed to rotate on a LabQuake rotator for 24 h. Resin beads were then washed with THF (x10), water (x10) and then resuspended in 950 μL of the 50 mM ammonium acetate buffer (pH=7.4). Resin beads along with the buffer were then transferred into 1.5 mL eppendorf tube, and to this mixture acetonitrile (48 μL) was added, followed A1 (200 mM, 2 μL, 0.4 mM, 1 eq). Reaction vessel was allowed to rotate on a LabQuake rotator for 1 week. Resin beads were then transferred into 1.2 mL peptide synthesis vessel and

washed with water (x3), DMF (x3), THF (x3), CH_3CN (x3), and resuspended in 400 μL of a 4:1 mixture of acetonitrile:methanol. Resin beads along with the acetonitrile-methanol solution were transferred into 1.8 mL screw cap grass vials. Photolysis was carried out using 365 nm compact UV lamp (UVL-21, 4 watt) for 6-8 hours. In order to run HPLC analysis, sample (50 μL) was diluted with glass-distilled deionized water (150 μL).

Simultaneous RBDCC experiment:

To a 1.2 mL solid state peptide synthesis vessel containing following resin beads: B1 (0.9 mg, 0.2 mmol, 0.5 eq), B2 (0.9 mg, 0.2 mmol, 0.5 eq), 950 μL of the 50 mM ammonium acetate buffer (pH=7.4) was added, followed by acetonitrile (50 μL), and thiopropanol (0.7 μL, 20 eq). Reaction vessel was allowed to rotate on LabQuake rotator for 24 h. Resin beads were then washed with THF (x10), water (x10) and then resuspended in 945 μL of the 50 mM ammonium acetate buffer (pH=7.4). Resin beads along with the buffer were then transferred into 1.5 mL eppendorf tube, and to this mixture aniline (1 M, 15 μL, 15 mM, 37.5 eq) was added, followed by A1 (200 mM, 10 μL, 2 mM, 5 eq), A2 (200 mM, 10 μL, 2 mM, 5 eq), C1 (200 mM, 10 μL, 2 mM, 5 eq), and C2 (200 mM, 10 μL, 2 mM, 5 eq). Reaction vessel was allowed to rotate on a LabQuake rotator for 1 week. Resin beads were then transferred into 1.2 mL peptide synthesis vessel and washed with water (x3), DMF (x3), THF (x3), CH_3CN (x3), and resuspended in 400 μL of a 4:1 mixture of acetonitrile:methanol. Resin beads along with the acetonitrile-methanol solution were transferred into 1.8 mL screw cap grass vials. Photolysis was carried out using a 365 nm compact UV lamp (UVL-21, 4 watt) for 6-8 hours. In order to run HPLC analysis, sample (50 μL) was diluted with glass-distilled deionized water (150 μL).

HPLC Parameters

Injection volume: 40 μL

Flow rate: 0.5 mL/min

Monitoring wavelength: 254 nm

Mobile phase:

Solvent A: Glass-distilled deionized water + 0.1% TFA

Solvent B: Acetonitrile + 0.1% TFA

Method setup:

Time, min	%B
0.01	15
15.00	30
30.00	100
35.00	100
40.00	10
45.00	0

HPLC and MALDI-MS results

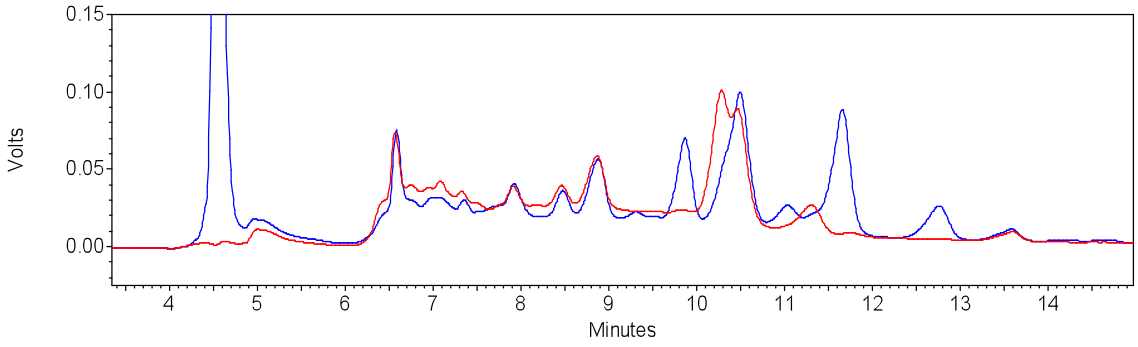


Fig. 1. Solution phase library constructed from B1, B2, C1, and C2 after 3 days of equilibration with aniline (blue trace) or without aniline (red trace) in ammonium acetate buffer (pH 7.4).

Product	[M+H]	[M+Na]
BC (Gly, Gly)	868.39	890.39‡
BC (Gly, Pro)	908.39	930.39
BC (Pro, Pro)	948.39	970.39

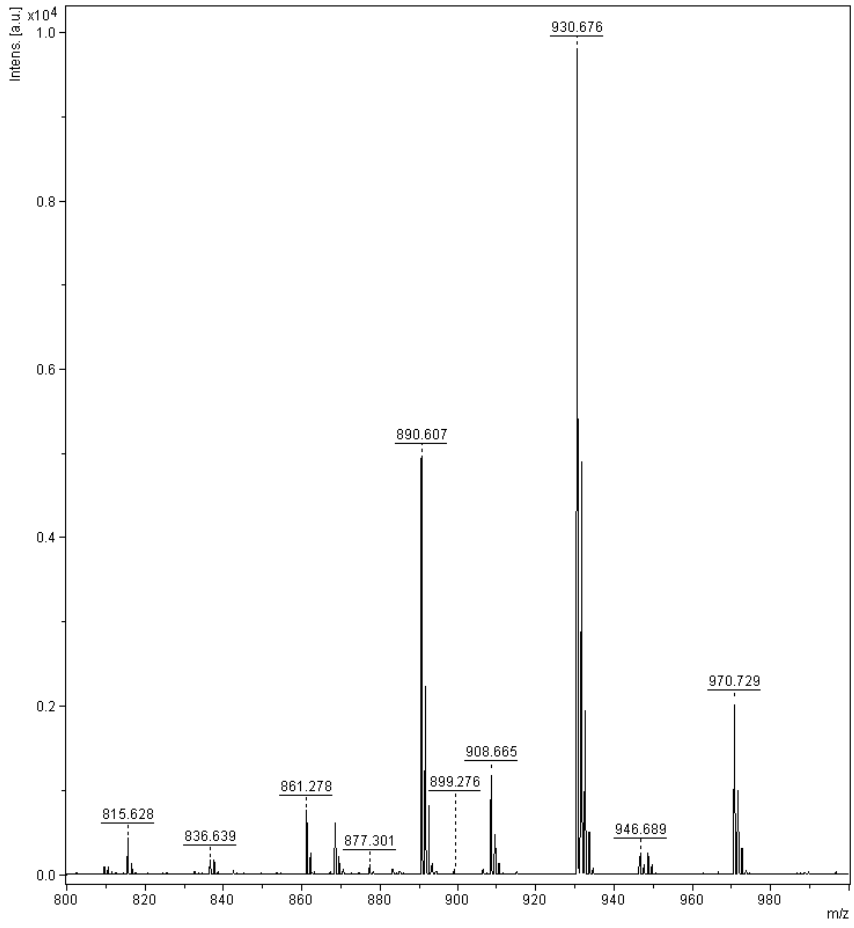


Fig. 2. Solution phase library constructed from B1, B2, C1, and C2 after 3 days of equilibration in the presence of aniline at pH 7.4

‡ Peaks observed by MALDI-MS are shown in yellow boxes

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	874.34	896.34	AA (Pro, Pro)	861.32	883.32
AB (Gly, Pro)	914.34	936.34	BB (Gly,Gly)	967.36	989.36
AB (Pro, Pro)	954.34	976.34	BB (Gly, Pro)	1007.36	1029.36
AA (Gly, Gly)	781.32	803.32	BB (Pro, Pro)	1047.36	1069.36
AA (Gly, Pro)	821.32	843.32			

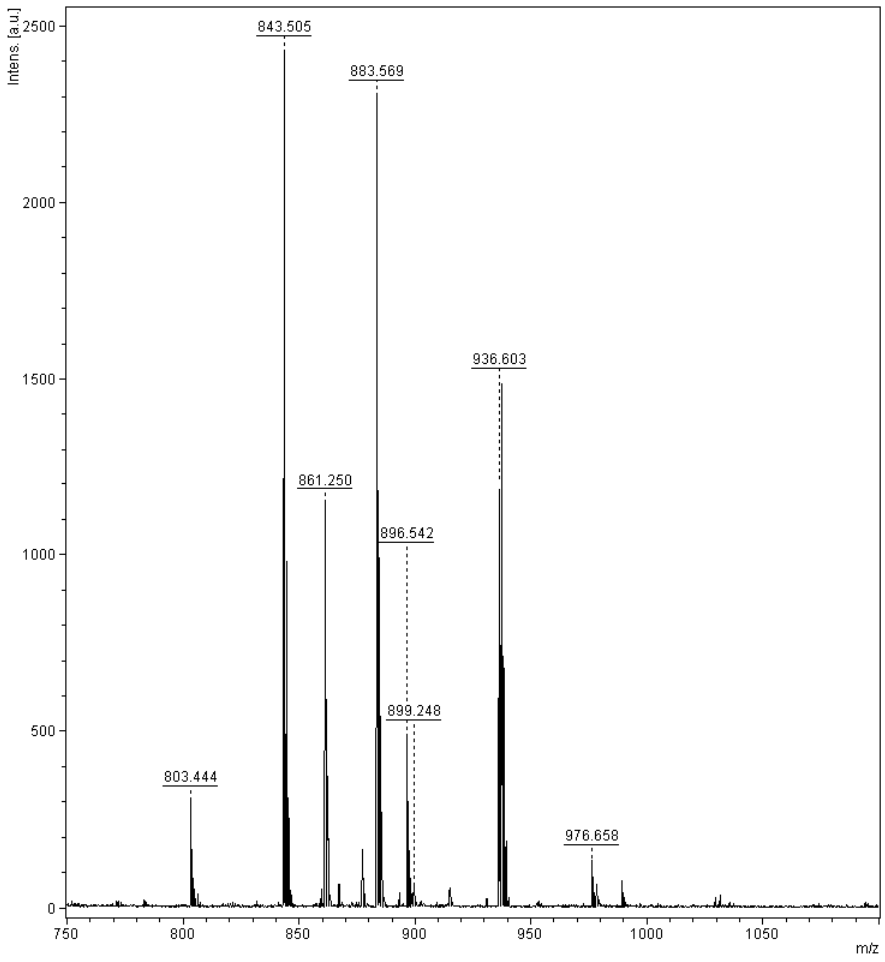


Fig. 3. Solution phase library constructed from A1, A2, B1 and B2 after 3 days of equilibration in the presence of thiopropanol at pH 7.4

Product	[M+H]	[M+Na]
AB (Gly, Gly)	874.34	896.34
BC (Gly, Gly)	868.39	890.39
ABC (Gly,Gly, Gly)	1169.5	1191.5

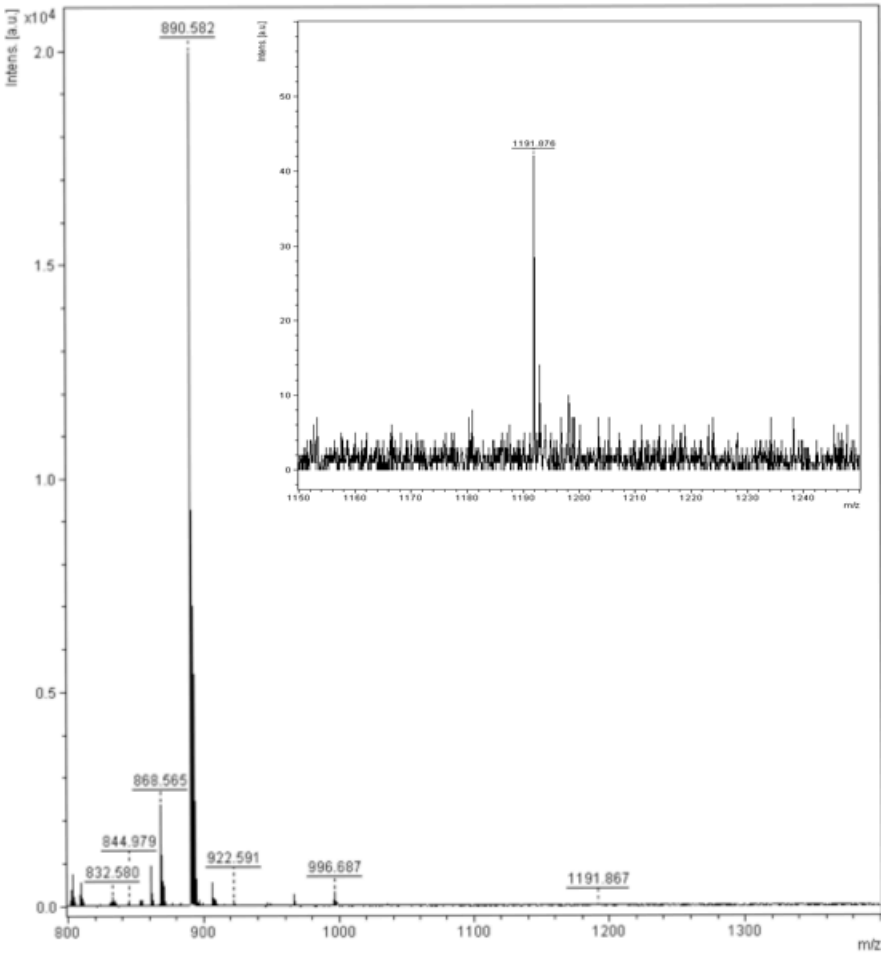


Fig. 4. Solution phase library constructed from A1, B1, and C1 after 3 days of equilibration in the presence of aniline and thiopropanol at pH 7.4

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	874.34	896.34	BC (Pro, Pro)	948.39	970.39
AB (Gly, Pro)	914.34	936.34	ABC (Gly,Gly, Gly)	1169.5	1191.5
AB (Pro, Pro)	954.34	976.34	ABC (Gly, Gly, Pro)	1209.5	1231.5
BC (Gly, Gly)	868.39	890.39	ABC (Gly, Pro, Pro)	1249.5	1271.5
BC (Gly, Pro)	908.39	930.39	ABC (Pro, Pro, Pro)	1289.5	1311.5

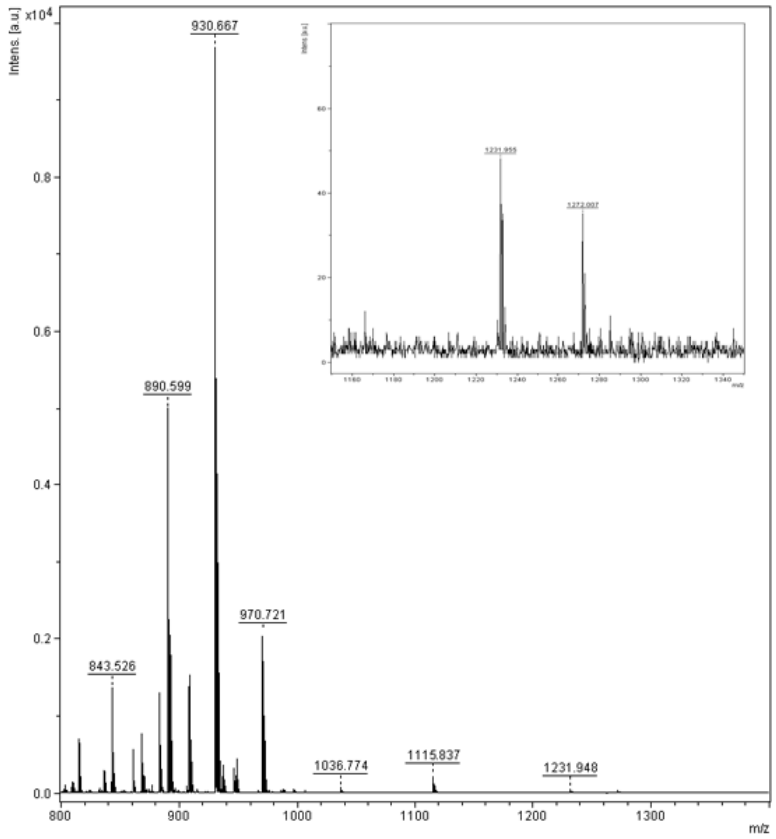


Fig. 5a. Solution phase library constructed from A1, A2, B1, B2, C1, and C2 (1:1:1:1:1:1 ratio) after 3 days of equilibration in the presence of aniline and thiopropanol at pH 7.4

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	874.34	896.34	BC (Pro, Pro)	948.39	970.39
AB (Gly, Pro)	914.34	936.34	ABC (Gly,Gly, Gly)	1169.5	1191.5
AB (Pro, Pro)	954.34	976.34	ABC (Gly, Gly, Pro)	1209.5	1231.5
BC (Gly, Gly)	868.39	890.39	ABC (Gly, Pro, Pro)	1249.5	1271.5
BC (Gly, Pro)	908.39	930.39	ABC (Pro, Pro, Pro)	1289.5	1311.5

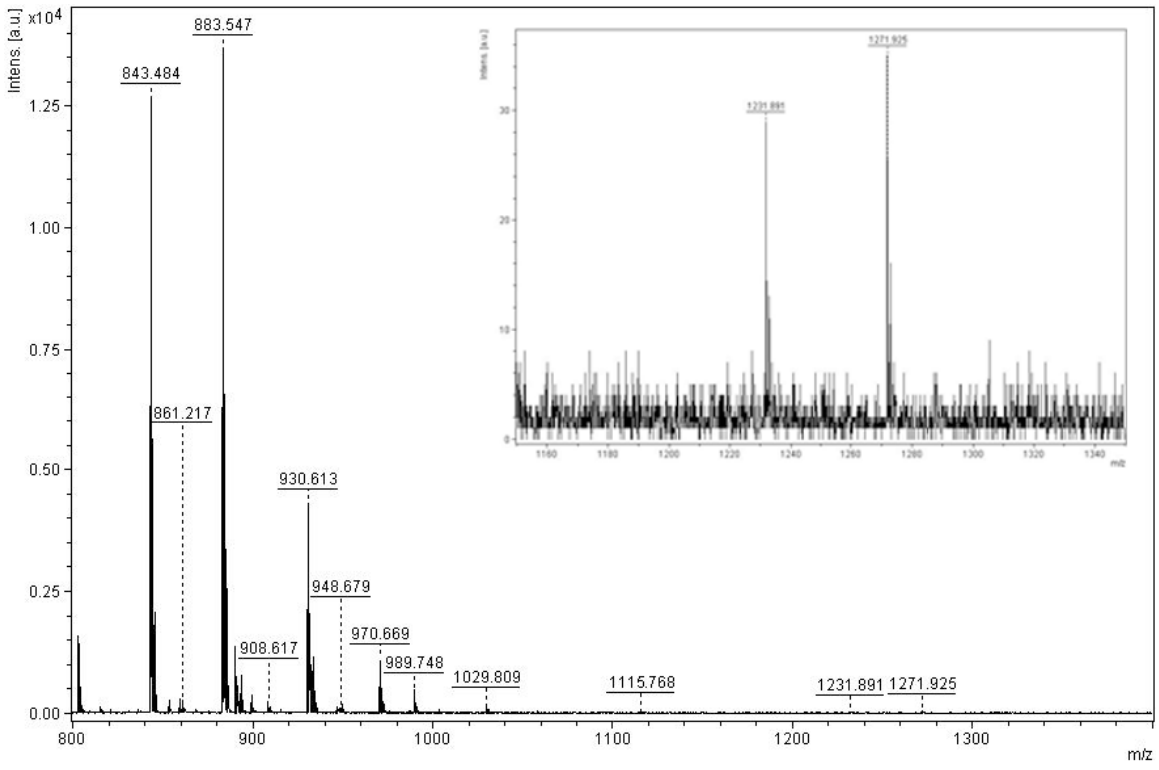


Fig. 5b. Solution phase library constructed from A1, A2, B1, B2, C1, and C2 (10:10:1:1:10:10 ratio) after 3 days of equilibration in the presence of aniline and thiopropanol at pH 7.4

Product	[M+H]	[M+Na]
BC (Gly, Gly)	924.41	946.41
BC (Gly, Pro)	964.41	986.41

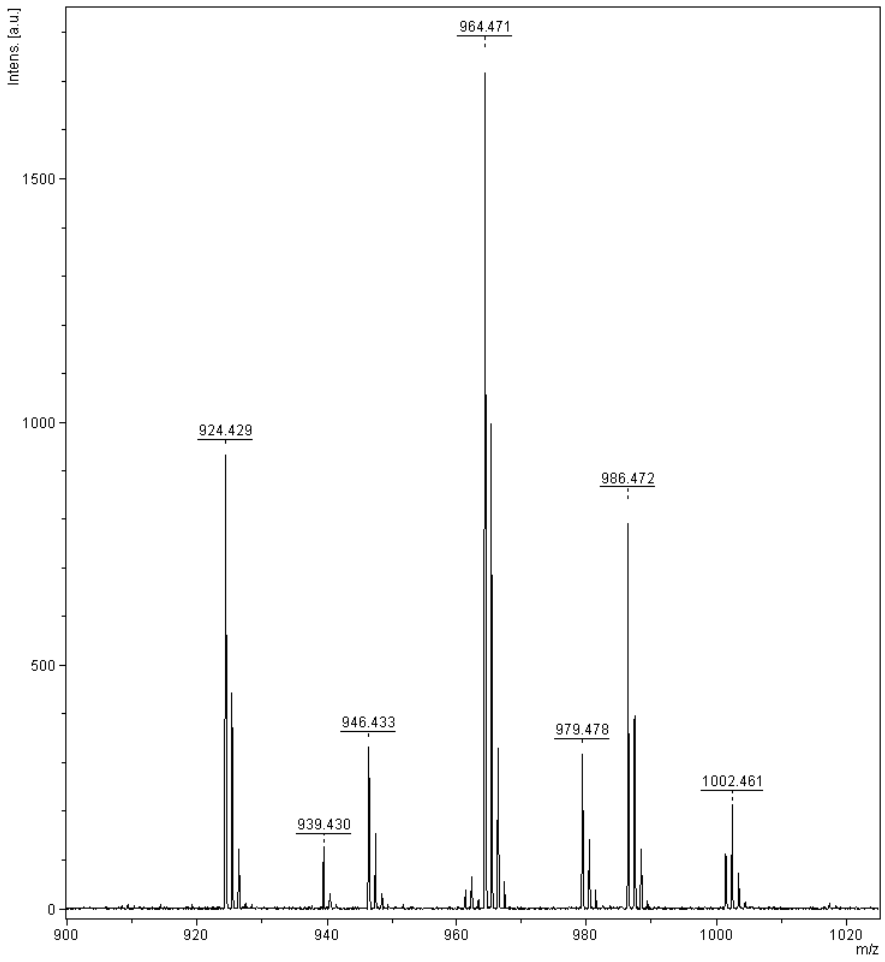


Fig. 6. Resin bound library constructed from C1 and C2 in solution and resin bound B1 after 6 days of equilibration in the presence of aniline at pH 7.4

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	930.37	952.37	BB (Gly,Gly)	1079	1101

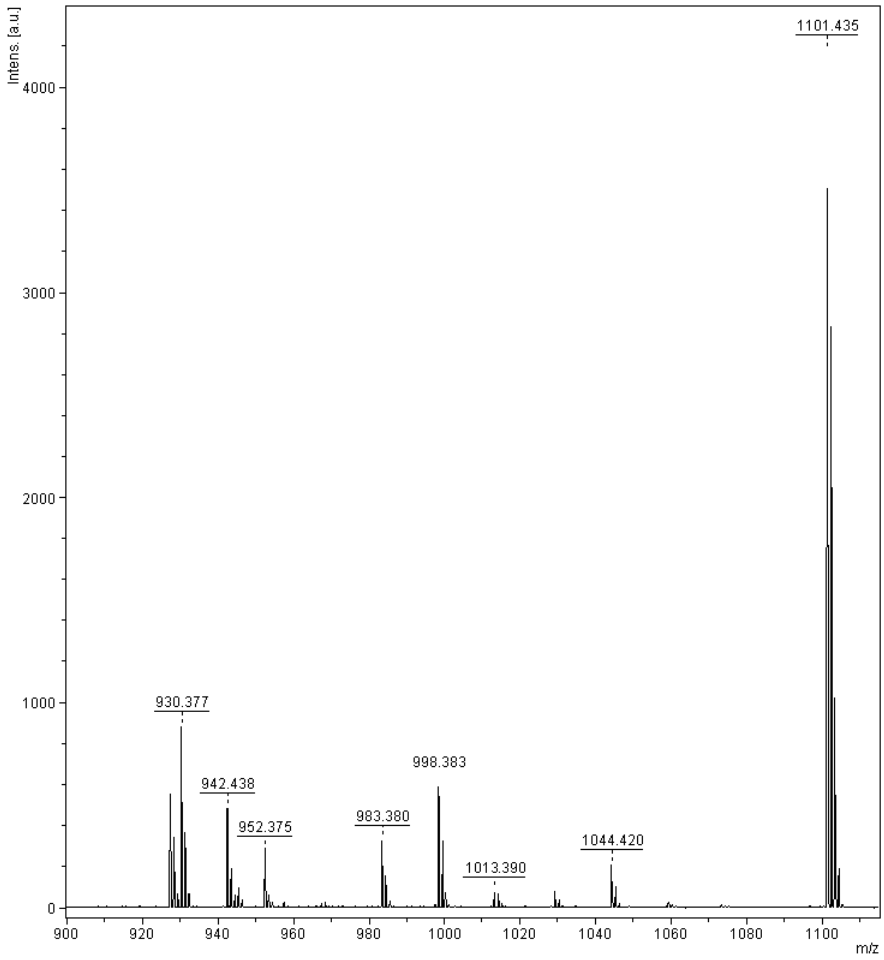


Fig. 7. Resin bound library constructed from A1 in solution and resin bound B1 after 6 days of equilibration in the presence of thiopropanol at pH 7.4

Product	[M+H]	[M+Na]
AB (Gly, Gly)	930.37	952.37
AB (Gly, Gly) hydrate	830.33	852.33
BB (Gly,Gly)	1079	1101
BC (Gly, Gly)	924.41	946.41
ABC (Gly,Gly, Gly)	1225.53	1247.53

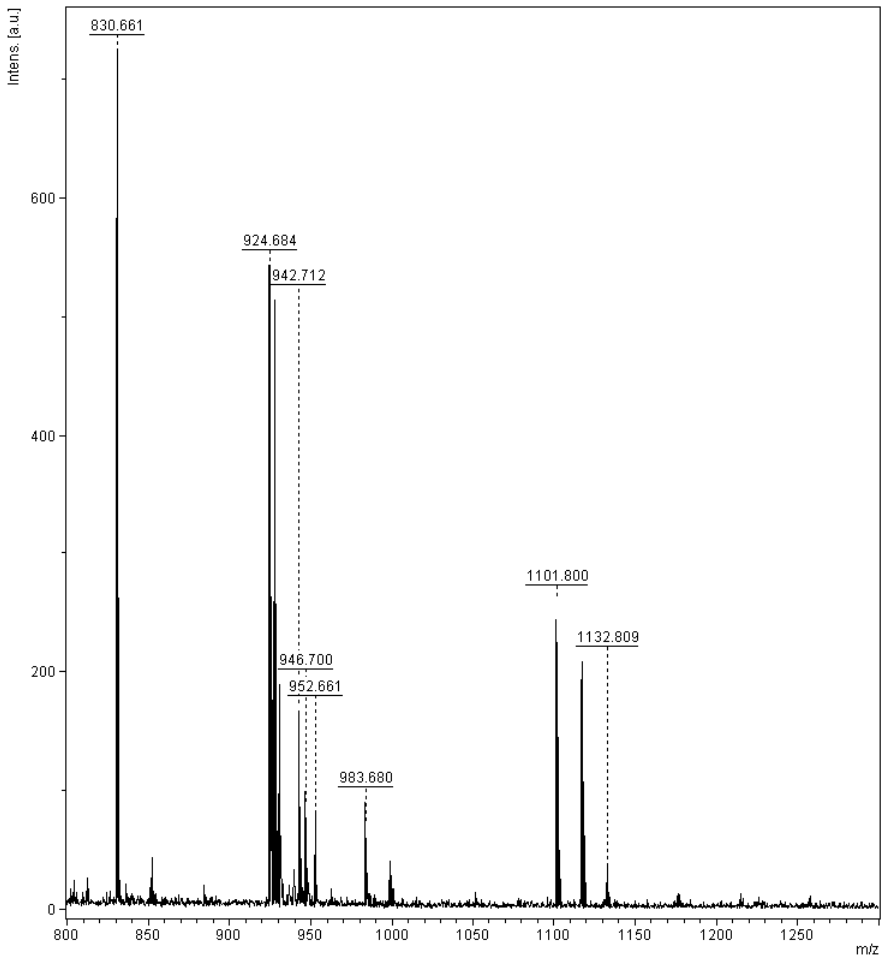


Fig. 8. Resin bound library constructed from A1 and C1 in solution and resin bound B1 (1:1:1 ratio) after 6 days of equilibration in the presence of thiopropanol at pH 7.4

Product	[M+H]	[M+Na]
AB (Gly, Gly)	930.37	952.37
AB (Gly, Gly) hydrate	830.33	852.33
BC (Gly, Gly)	924.41	946.41
ABC (Gly,Gly, Gly)	1225.53	1247.53

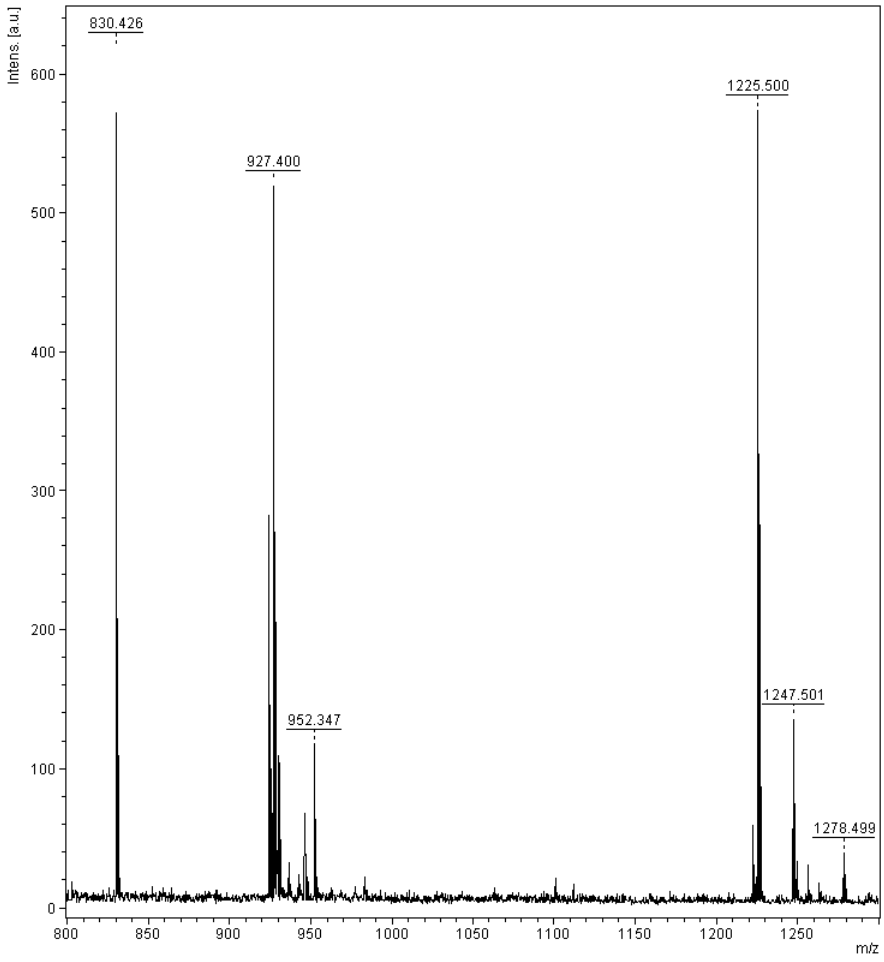


Fig. 9. Resin bound library constructed from A1 and C1 in solution and resin bound B1 (10:1:10 ratio) after 6 days of equilibration in the presence of aniline at pH 7.4

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	930.37	952.37	BC (Pro, Pro)	1004.41	1026.41
AB (Gly, Pro)	970.37	992.37	ABC (Gly,Gly, Gly)	1225.53	1247.53
AB (Pro, Pro)	1010.37	1032.37	ABC (Gly, Gly, Pro)	1265.53	1287.53
BC (Gly, Gly)	924.41	946.41	ABC (Gly, Pro, Pro)	1305.53	1327.53
BC (Gly, Pro)	964.41	986.41	ABC (Pro, Pro, Pro)	1345.53	1367.53

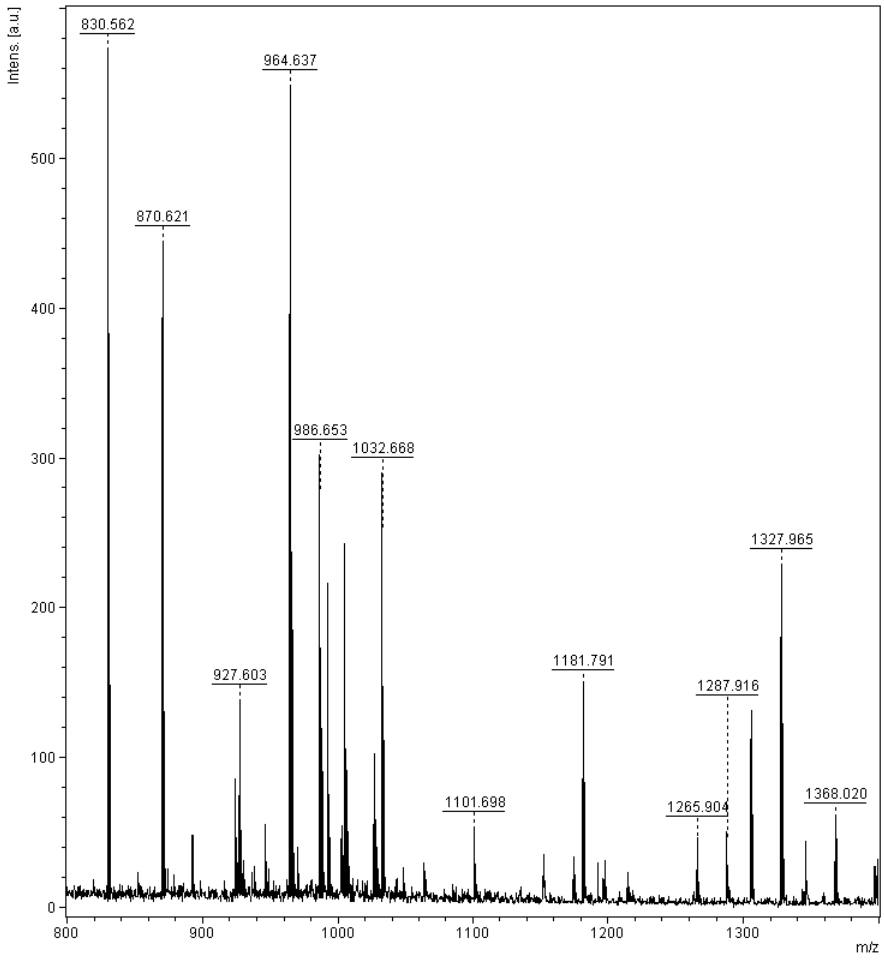


Fig. 10 a. Resin bound library constructed from A1, A2, C1, C2 in solution and resin bound B1 and B2 (10:10:10:10:1:1 ratio) after 1 week of equilibration in the presence of aniline at pH 7.4

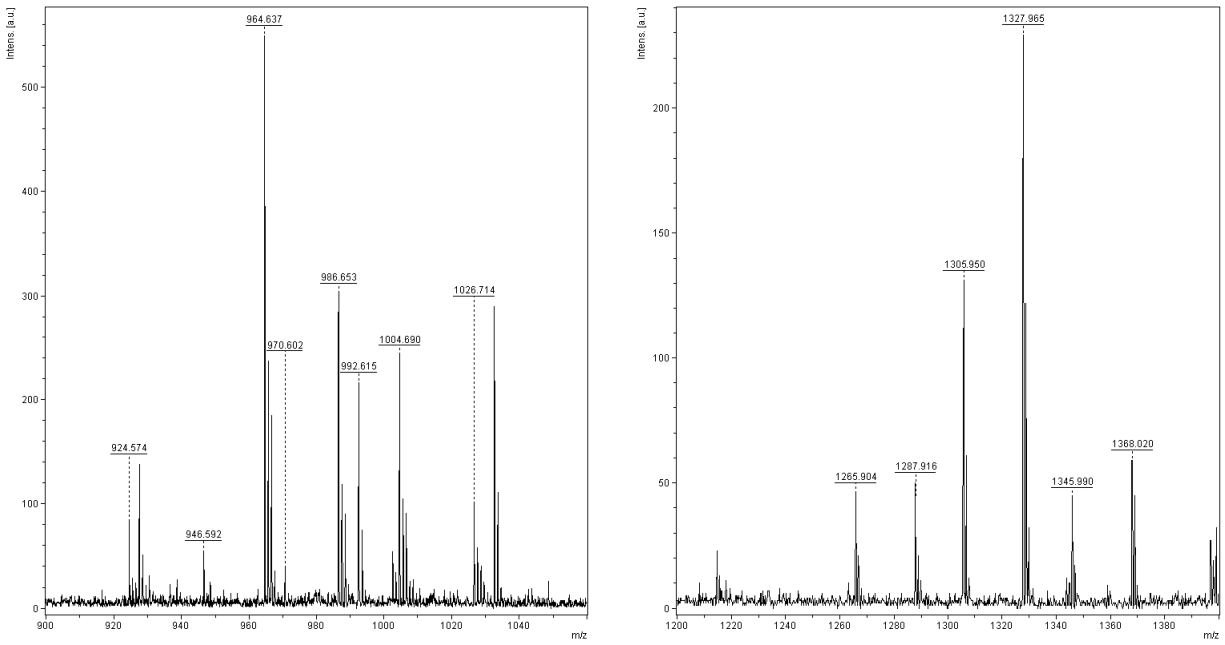


Fig. 10 b. Resin bound library constructed from A1, A2, C1, C2 in solution and resin bound B1 and B2 (10:10:10:10:1:1 ratio) after 1 week of equilibration in the presence of aniline at pH 7.4

Product	[M+H]	[M+Na]	Product	[M+H]	[M+Na]
AB (Gly, Gly)	930.37	952.37	BC (Pro, Pro)	1004.41	1026.41
AB (Gly, Pro)	970.37	992.37	ABC (Gly,Gly, Gly)	1225.53	1247.53
AB (Pro, Pro)	1010.37	1032.37	ABC (Gly, Gly, Pro)	1265.53	1287.53
BC (Gly, Gly)	924.41	946.41	ABC (Gly, Pro, Pro)	1305.53	1327.53
BC (Gly, Pro)	964.41	986.41	ABC (Pro, Pro, Pro)	1345.53	1367.53

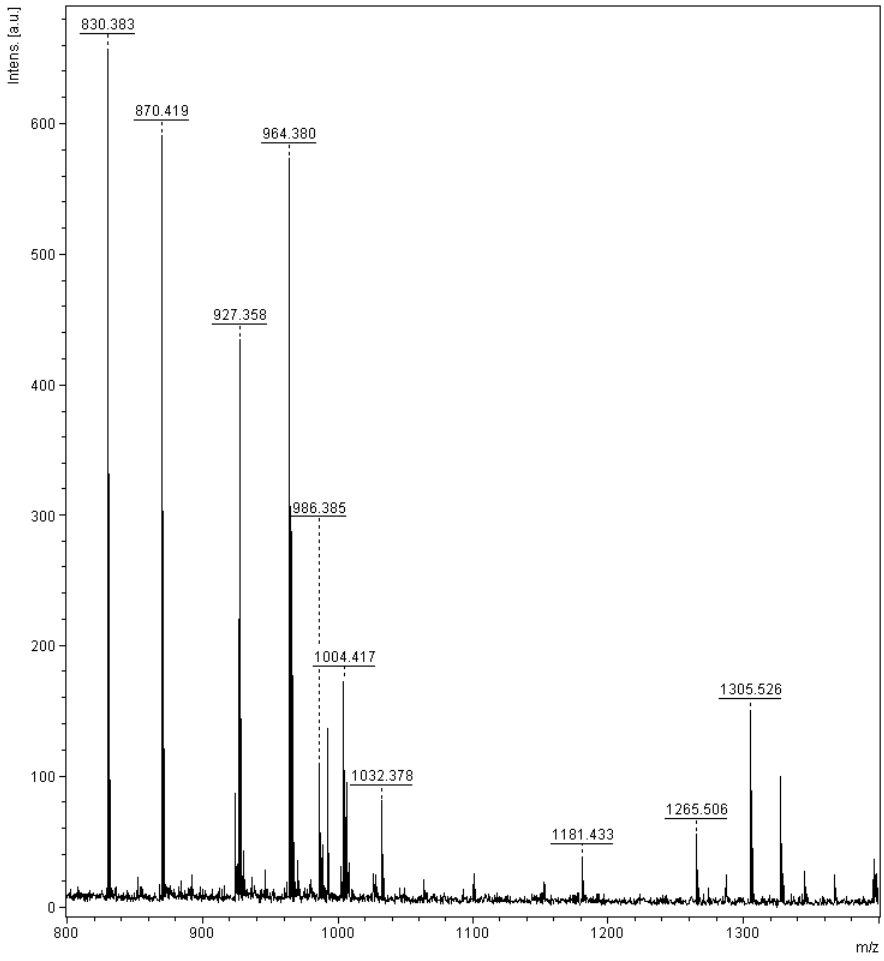


Fig. 11 a. Resin bound library constructed from A1, A2, C1, C2 in solution and resin bound B1 and B2 (10:10:10:10:1:1) after 2 weeks of equilibration in the presence of aniline at pH 7.4

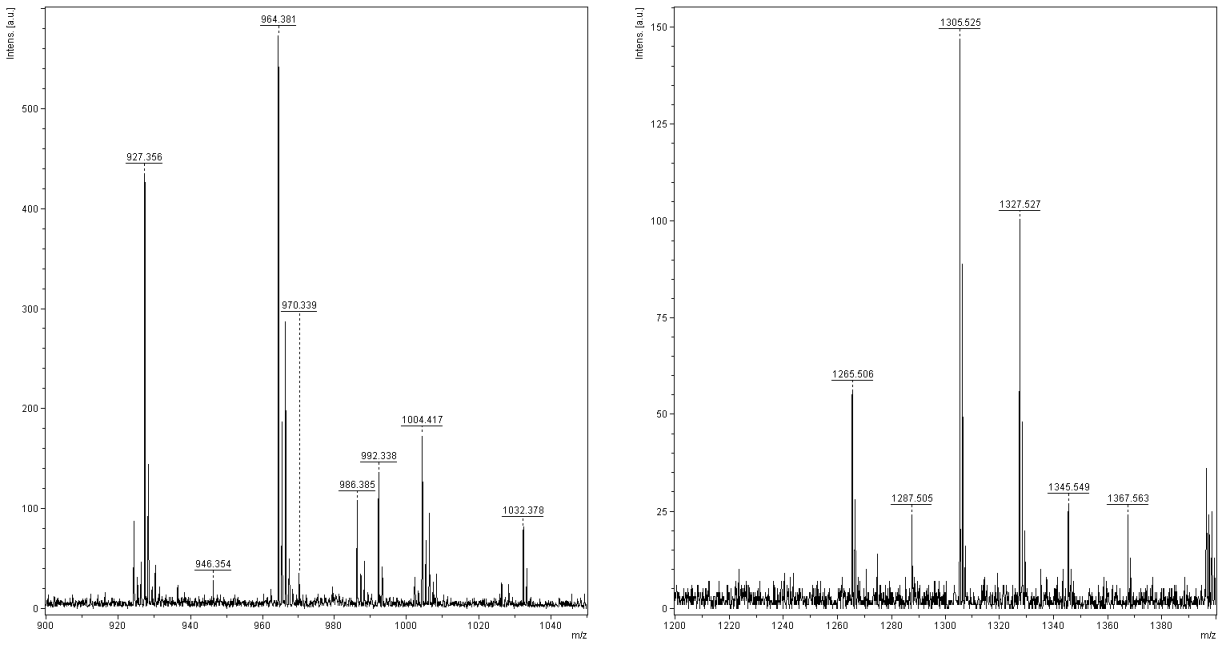


Fig. 11 b. Resin bound library constructed from A1, A2, C1, C2 in solution and resin bound B1 and B2 (10:10:10:10:1:1) after 2 weeks of equilibration in the presence of aniline at pH 7.4

References

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[2] G. A. Silva, L. M. M. Costa, F. C. F. Brito, A. L. P. Miranda, E. J. Barreiro, C. A. M. Fraga, *Bioorg. Med. Chem*. 2004, **12**, 3149.