Supplementary Material (ESI) for Chemical Communications

Supporting Information

Chemical Synthesis on SU-8

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Collection of SU-8 particles (1)
SU-8 particles (round, diameter = 250 μm) were received on silicon wafers with Al as sacrificial layer. To collect the particles, the sacrificial layer was removed by submerging wafers in a 2.5% aqueous solution of tetramethylammonium hydroxide. The released microparticles were collected by filtration, washed with 10% TFA (aq), then repeatedly with excessive amounts of water, methanol and CH_2Cl_2, before being lyophilized to produce a dry SU-8 support.

Synthesis of aldehydo-SU-8 particles (2)
Sodium periodate (54 mg, 25 μmol) was dissolved in a mixture of water (150 μL) and CH_3CN (250 μL). This solution was transfered to a vial, containing SU-8 particles **1** (~ 7 mg). The vial was capped and agitated overnight (12 h) after which, the reaction mixture was filtered using a Brand Pipette Tip to collect the SU-8 particles. The particles contained in the tip were then washed with 10% TFA (aq), and repeatedly washed with water, methanol and CH_2Cl_2, before being lyophilized to produce a dry SU-8 support.

Synthesis of imino-SU-8 particles (3)
To a reaction vial containing aldehyde-functionalized SU-8 particles **2** (~ 7 mg), dry THF (200 μL) was added under argon. Ethylenediamine (80 μL) was added, the vial capped under argon, and the reaction left to agitate overnight (12 hr). The SU-8 particles was collected by filtering through a filter tip and washed repeatedly with THF, methanol and CH_2Cl_2, before being lyophilized.

Synthesis of amino-functionalized-SU-8 particles (4)
A solution of sodium cyanoborohydride (5 mg, 0.07 mmol) in dry MeOH (200 μL) was transferred to a vial containing imine-functionalized SU-8 particles **3** (7 mg) in dry MeOH (100 μL). Trifluoroacetic acid (5 μL, 0.07 mmol) was carefully added and the mixture allowed to agitate overnight (12 hr). The reaction was worked-up by filtering through a filter tip, followed washing of the isolated SU-8 particles with 10% DIPEA in DMF (2x), then with excessive amounts of water, methanol and CH_2Cl_2, before being lyophilized.

Attachment of Rink linker
Fmoc-Rink linker (24 mg, 45 μmol) was dissolved in DMF (200 μL), and DIPEA (12 μL, 68 μmol) was added. HATU (17 mg, 44 μmol) was added and the mixture was shaken for 5 min at room temperature. 100 μL of the mixture was added to amino-

functionalized SU-8 (~ 7 mg, 98 nmol based on available amino-groups) suspended in DMF (100 μL), and the mixture was shaken for 2 h at room temperature. The support was washed with DMF (5x 200 μL), and the procedure was repeated. The support was washed with DMF (8x 200 μL), followed by methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL), and lyophilized to afford a dry SU-8 support

Attachment of PLL linker
Fmoc-PLL-OH (24 mg, 45 μmol) was dissolved in DMF (200 μL), and DIPEA (12 μL, 68 μmol) was added. HATU (17 mg, 44 μmol) was added and the mixture was shaken for 5 min at room temperature. 100 μL of the mixture was added to amino-functionalized SU-8 (~ 7 mg, 98 nmol based on available amino-groups) suspended in DMF (100 μL), and the mixture was shaken for 2 h at room temperature. The support was washed with DMF (5x 200 μL), before the entire coupling procedure was repeated. The support was finally washed with DMF (8x 200 μL), followed by methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL) and lyophilized to afford a dry SU-8 support

Attachment of HMBA linker
HMBA (7 mg, 45 μmol) was dissolved in DMF (200 μL), and DIPEA (12 μL, 68 μmol) was added. HATU (17 mg, 44 μmol) was added and the mixture was shaken for 5 min at room temperature. 100 μL of the mixture was added to amino-functionalized SU-8 (~ 7 mg, 98 nmol) suspended in DMF (100 μL), and the mixture was shaken for 2 h at room temperature. The support was washed with DMF (5x 200 μL), before the entire coupling procedure was repeated. The support was finally washed with DMF (8x 200 μL), followed by methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL), and lyophilized to afford a dry SU-8 support.

Attachment of first amino acid to HMBA-functionalized SU-8 particles
Fmoc-phe-OH (18 mg, 45 μmol) was dissolved in dry CH_2Cl_2 (200 μL), and MeIm (4 μL, 73 μmol) was added followed by MSNT (13 mg, 45 μmol). The mixture was shaken for 5 min at RT before 100 μL of this solution was added to SU8-HMBA (~ 7 mg, 98 nmol) suspended in CH_2Cl_2 (100 μL); then, the mixture was shaken for 1 h at room temperature. The support was washed with DMF (5x 200 μL), before the entire coupling procedure was repeated. The support was finally washed with DMF (8x 200 μL), methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL) before being lyophilized.

General procedure for HATU-mediated coupling of amino acids, iodobenzoic acid, 4-azidobenzoic acid and 5(6)-carboxyfluorescein to amino-functionalized SU-8 particles
The corresponding carboxylic acid (45 μmol) was dissolved in DMF (200 μL), and HATU (17 mg, 44 μmol), DIPEA (12 μL, 68 μmol) were added. The mixture was shaken for 5 min; then 100 μL of the mixture was added to amino-functionalized SU-8 (~ 7mg, 98 nmol based on available amino-groups) suspended in DMF (100 μL), and the mixture was shaken for 2 h at RT. The support was washed with DMF (5x 200 μL), before the entire coupling procedure was repeated. The support was finally washed with DMF (8x 200 μL), methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL) before being lyophilized.

Removal of Fmoc-protection group was accomplished with 20% piperidine in DMF (200 uL) for 5 min. After washing twice with DMF, the deprotection procedure was repeated with a reaction time of 30 min. The support was washed with DMF (8 x 200 μL), methanol (8 x 200 μL) and CH_2Cl_2 (8 x 200 μL) before being lyophilized.

Pd-catalyzed Sonogashira coupling: Synthesis of 8
A mixture of Fmoc-protected 4-ethynylaniline (15 mg, 45 μmol), DIPEA (7 μL, 40 μmol), CuI (2 mg, 10 μmol) and $PdCl_2(PPh_3)_2$ (6 mg, 9 μmol) in dry degassed THF (400 μL) was degassed with Argon for 5 min. The mixture was added to a vial containing iodo-functionalized SU-8 particles (~ 14 mg, 196 nmol) suspended in dry degassed THF (100 μL) under argon. The vial was capped under argon, and the reaction left to agitate overnight (approx. 12 hr). The SU-8 particles were collected by filtering through a filter tip and the isolated SU-8 particles washed with THF, 10% DIPEA (DMF), then with excessive amounts of DMF, water, methanol and CH_2Cl_2, before being lyophilized.

Cu-catalyzed azide-alkyne cycloaddition: Synthesis of 10
Fmoc-protected propargylamine (8,9 mg, 32 μmol), CuI (6.1 mg, 32 μmol), sodium ascorbate (6.3 mg, 32 μmol), and 2,6-lutidine (4 μL, 32 μmol) in NMP/H_2O (4:1) (800 μL) and shaken for 30 min before being added to azido-functionalized SU-8 particles (~ 14 mg, 196 nmol). The reaction mixture was shaken at rt for 12h, filtered, washed with 10 % DIPEA (DMF), then with excessive amounts of DMF, water, methanol and CH_2Cl_2, before being lyophilized.

General procedure for release of Rink-linked compounds from SU-8 particles
Before cleavage of material from the SU-8 support, the support was shaken overnight in DMF to remove excess reagent entrapped in the SU-8 polymer network. The support was washed with methanol (8 x 200 μL) and CH_2Cl_2 (8 x 200 μL) before being lyophilized. The peptide was cleaved from the SU-8 support (~ 7 mg) by treatment with 95% TFA (aq, 200 μL) for 2h at room temperature. The support was filtered and washed with CH_3CN and the combined filtrate used directly for analytically purposes.

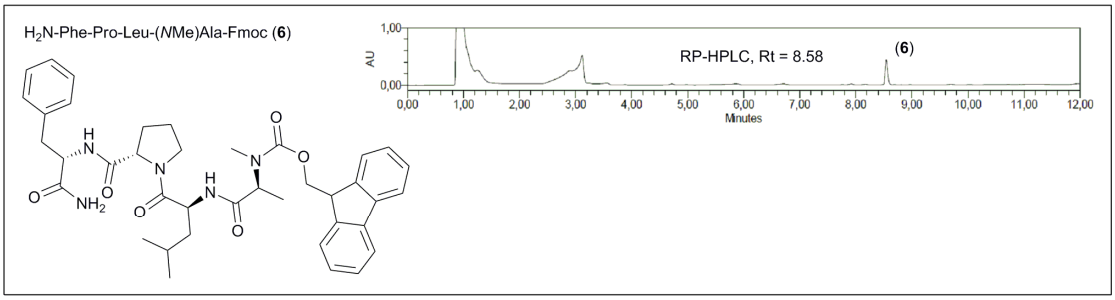
General procedure for release of HMBA-linked compounds from SU-8 particles
Before cleavage of material from the SU-8 support, the support was shaken overnight in DMF to remove excess reagent entrapped in the SU-8 polymer network. The support was washed with methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL) before being lyophilized. The peptide was cleaved from the SU-8 support (~ 7mg, 98 nmol) by treatment with 0.1% NaOH (aq, 200 μL) for 2h at room temperature followed by 0.1% HCl (aq, 200 μL). The support was filtered and washed with CH_3CN and the combined filtrate used directly for analytically purposes.

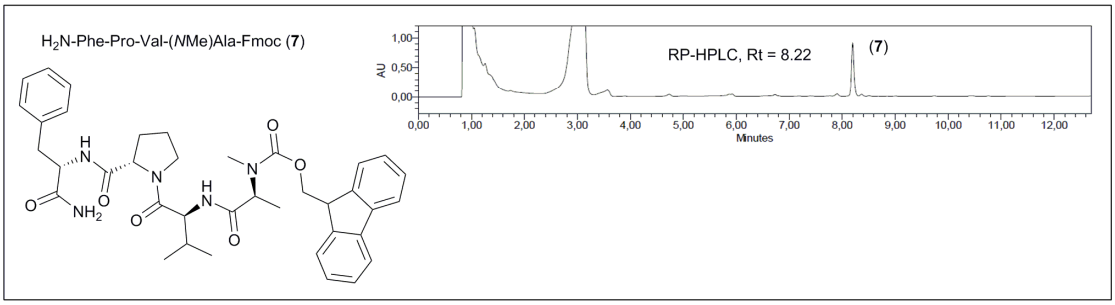
General procedure for release of PLL-linked compounds from SU-8 particles
Before cleavage of material from the SU-8 support, the support was shaken overnight in DMF to remove excess reagent entrapped in the SU-8 polymer network. The support was washed with methanol (8x 200 μL) and CH_2Cl_2 (8x 200 μL) before being lyophilized.

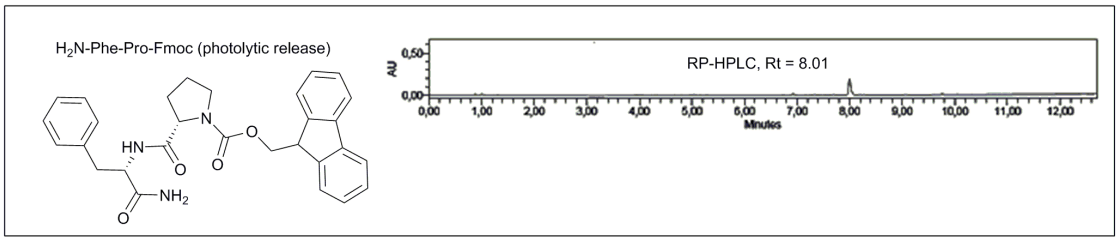
Photolysis was conducted by irradiating the SU-8 sample (~ 7mg, 98 nmol) suspended in MeOH/H2O (1:4, 500 µL) with an Omnilux UV-lamp 400W E40 for 2h. The support was filtered and washed with CH_3CN and the combined filtrate used directly for analytically purposes.

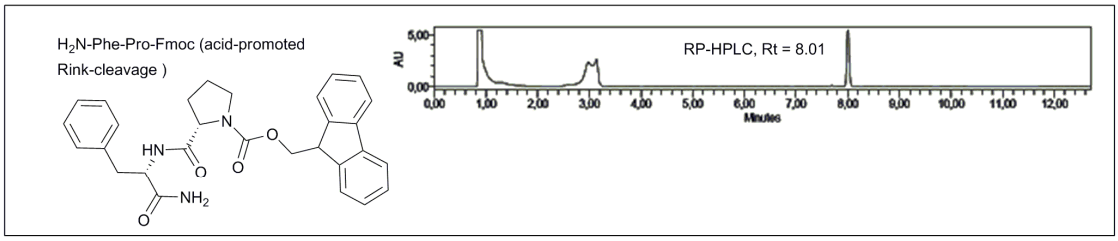
Analysis of Peptides

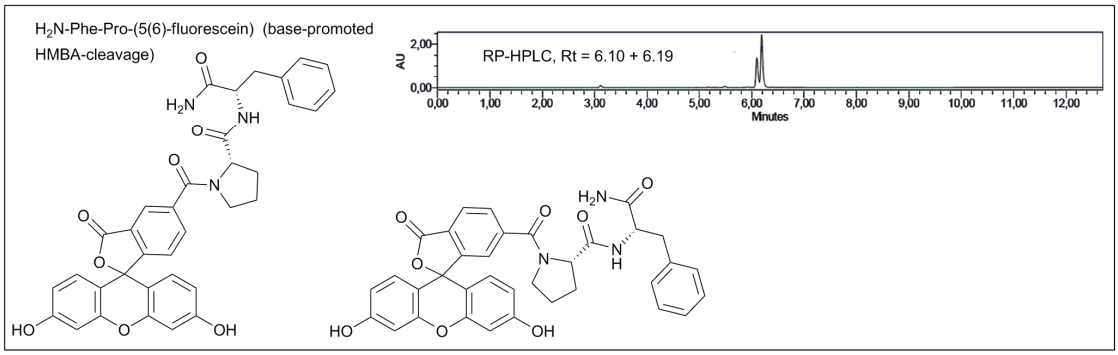
Analytical HPLC was performed by RP-HPLC at 215 and 254 nm using a XBridge™ C-18 column (2.5 µm, 4.6 x 75 mm, 1 mL/min). The gradient was 0-100% B in A gradient in a run time of 12.70 min, where A was 0.1% TFA in water and B was 0.1% TFA in acetonitrile. See below for UV-HPLC results. Reactions were further analyzed by analytically LC-MS on a Waters AQUITY UPLC system equipped with PDA and SQD MS detector; column: AQUITY UPLC BEH C18 1.7µm, 2.1 x 50mm; column temp: 65 °C; solvent A: 0.1% formic acid (aq); solvent B: 0.1% formic acid (acetonitrile); gradient: 5% B to 100% B in 2.4 min, hold for 0.1 min, total runtime ca. 2.6 min.

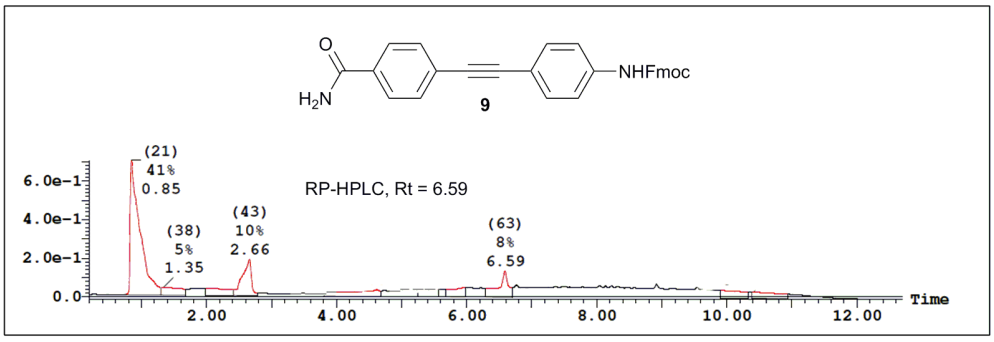


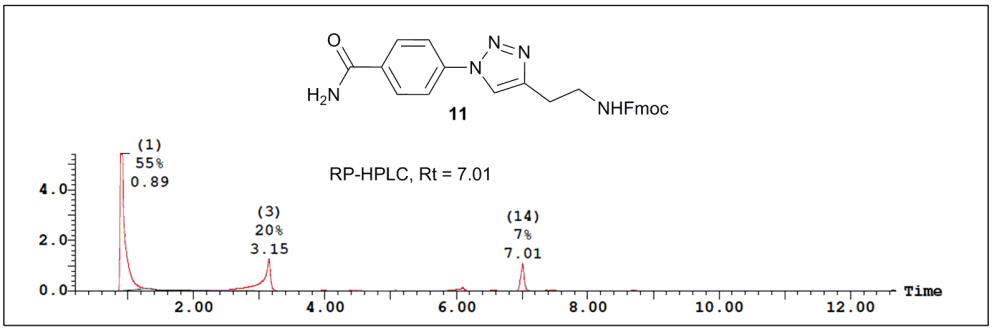



H2N-Phe-Pro-Fmoc (photolytic release)
RP-HPLC, Rt = 8.01
AU
Minutes


H2N-Phe-Pro-Fmoc (acid-promoted
Rink-cleavage)
RP-HPLC, Rt = 8.01
AU
Minutes


H2N-Phe-Pro-(5(6)-fluorescein) (base-promoted
HMBA-cleavage)
RP-HPLC, Rt = 6.10 + 6.19
AU
Minutes


NHFmoc
9
RP-HPLC, Rt = 6.59
(21) 41% 0.85
(38) 5% 1.35
(43) 10% 2.66
(63) 8% 6.59
Time


NHFmoc
11
RP-HPLC, Rt = 7.01
(1) 55% 0.89
(3) 20% 3.15
(14) 7% 7.01
Time