Supporting information

Color test for selective detection of secondary amines on resin and in solution

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Contents

1. General remarks. Polystyrene (aminomethylated, Indole aldehyde) and Tentagel resins were purchased from Sigma-Aldrich and Iris Biotech, amino-PEGA resin was purchased from Merck (Novabiochem). All chemicals were purchased from Sigma-Aldrich and solvents from Fischer Scientific and of HPLC grade. 2-methoxy-4-alkoxy-benzaldehyde (FMPB) resin was prepared as previously described. [1] The amine loading was determined by UV of the Dibenzofulvene-piperidine adduct at λ (290nm) as earlier described. [2] On-resin functional group determination was carried out by IR (attenuated technique of reflectance). Micrographs were taken on a Leica DMLS microscope with a 10x/0.22 PH1 lense. The microscope was equipped with a Leica DFC290 camera. The beads were suspended in NMP and dropped onto the microscope glass (no cover glass used). HPLC-MS analysis was performed on an equipment comprising of a Shimadzu Nexera X2 with diode array UV detection in conjunction with a Bruker MicrOTOF-Q III mass spectrometer (positive ionization mode), using a Ascentis Express Peptide ES-C18 column (2.7μm, 160Å) and a 1 mL/min linear gradient from 0 to 100% over 5.00 min (buffer A: 0.025% TFA in 10% aqueous acetonitrile; buffer B: 0.025% TFA in 90% aqueous acetonitrile) with buffer A and B.

2. Acetaldehyde/Fmoc-amino acid test: Sensitivity on solid-phase (method by Claerhout et al.[3])

Fmoc-Proline and Boc-Glycine were mixed in five ratios and coupled to Rink Amide aminomethylated polystyrene (loading 0.36mmol/g) or Tentagel S NH2 (loading 0.29mmol/g) using HBTU as the coupling agent. The resulting loadings of proline (secondary amine) on resin 1-5 were determined by Fmoc-quantization in triplicate (Table S1, measurement A, B and C)

Stock solutions:

Fmoc-Pro-OH stock (0.144mmol/mL): Fmoc-Pro-OH (972mg, 2.88mmol) in NMP (20mL)

Boc-Gly-OH stock(0.144mmol/mL): Boc-Gly-OH (505mg, 2.88mmol) in NMP (20mL)

HBTU stock solution: HBTU (1g, 2.6 mmol) was dissolved in NMP (10mL)

1) To Rink amide resin (deprotected) or Tentagel S NH2 (0.2g, approx. 0.072 mmol) was added Boc-Gly-OH (1mL, 0.144mmol) and Fmoc-Pro-OH (1mL, 0.144 mmol) followed by addition of DIPEA (97μL, 0.56 mmol) and HBTU stock solution (1 mL, 0.26 mmol) followed by shaking for 1 hr at r.t. Washing of the resin with NMP (5times) and DCM (5 times), shrinking with methanol. Secondary amine loading was determined by Fmoc-quantization to be: 172 μmol/g (Rink amide resin) and 87 μmol/g (Tentagel).

2) To Rink amide resin (deprotected) or Tentagel S NH2 (0.2g, approx. 0.072 mmol) was added Boc-Gly-OH (1.75 mL, 0.252mmol) and Fmoc-Pro-OH (250μL, 0.036 mmol) followed by addition of DIPEA (97μL, 0.56 mmol) and HBTU stock solution (1 mL, 0.26 mmol) followed by shaking for 1 hr at r.t. Washing of the resin with NMP (5times) and DCM (5 times), shrinking with methanol. Secondary

amine loading was determined by Fmoc-quantization to be: 63.1 μmol/g (Rink amide resin) and 33 μmol/g (Tentagel).

3) To Rink amide resin (deprotected) or Tentagel S NH2 (0.2g, approx. 0.072 mmol) was added Boc-Gly-OH (1.875 mL, 0.270mmol) and Fmoc-Pro-OH (125 μL, 0.018 mmol, mg) followed by addition of DIPEA (97μL, 0.56 mmol) and HBTU stock solution (1 mL, 0.26 mmol) followed by shaking for 1 hr at r.t. Washing of the resin with NMP (5times) and DCM (5 times), shrinking with methanol. Secondary amine loading was determined by Fmoc-quantization to be: 35.7 μmol/g (Rink amide resin) and 14.1 μmol/g (Tentagel).

4) To Rink amide resin (deprotected) or Tentagel S NH2 (0.2g, approx. 0.072 mmol) was added Boc-Gly-OH (1.94mL, 0.279mmol) and Fmoc-Pro-OH (63 μL, 0.009 mmol) followed by addition of DIPEA (97μL, 0.56 mmol) and HBTU stock solution (1 mL, 0.26 mmol) followed by shaking for 1 hr at r.t. Washing of the resin with NMP (5times) and DCM (5 times), shrinking with methanol. Secondary amine loading was determined by Fmoc-quantization to be: 16.1 μmol/g (Rink amide resin) and 6.2 μmol/g (Tentagel).

5) To Rink amide resin (deprotected) or Tentagel S NH2 (0.2g, approx. 0.072 mmol) was added Boc-Gly-OH (1.97 mL, 0.284mmol) and Fmoc-Pro-OH (31 μL, 0.0045 mmol, mg) followed by addition of DIPEA (97μL, 0.56 mmol) and HBTU stock solution (4 mL, 0.26 mmol) followed by shaking for 1 hr at r.t. Washing of the resin with NMP (5times) and DCM (5 times), shrinking with methanol. Secondary amine loading was determined by Fmoc-quantization to be: 7.3 μmol/g (Rink amide resin).

Table S1

Sample - Abs (Mass/mg)	Sample - Abs (Mass/mg)	Sample - Abs (Mass/mg)	Mean loading
	Rink amide-PS resin		
1A: 0.208(6.1)	1B: 0.207(5.5)	1C: 0.179(4.9)	172 μmol/g
2A: 0.078(6.1)	2B: 0.083(6.5)	2C: 0.081(5.7)	63.1 μmol/g
3A: 0.054(7.7)	3B: 0.061(8.0)	3C: 0.058(7.4)	35.7 μmol/g
4A: 0.037(10.3)	4B: 0.038(10.9)	4C: 0.034(11.0)	16.1 μmol/g
5A: 0.023(14.8)	5B: 0.018(12.3)	5C: 0.021(13.6)	7.3 μmol/g
	Tentagel resin		
1A: 0.120(6.5)	1B: 0.092(4.9)	1C: 0.109(6.2)	87 μmol/g
2A: 0.041(5.5)	2B: 0.055(8.5)	2C: 0.053(7.7)	33 μmol/g
3A: 0035(10.8)	3B: 0.035(11.5)	3C: 0.034(13.0)	14.1μmol/g
4A: 0.019(13.2)	4B: 0.020(13.3)	4C: 0.011(11.9)	6.2 μmol/g

After determination of loading the resins were Fmoc-deprotected to expose the various amounts of secondary amines present on the resins.

2. Acetaldehyde/Fmoc-amino acid test: Sensitivity on solid-phase (method by Yang et al.[4])

The sensitivity test was performed on Rink amide-PS resins 2A and 3A and Tentagel resins 1A and 2A from Table S1. Resins suspended in two drops of NMP were applied as references.

Fmoc removal was performed on all four derivatized resins with piperidine/NMP (1:4, 2mL) for 3 + 30 min.

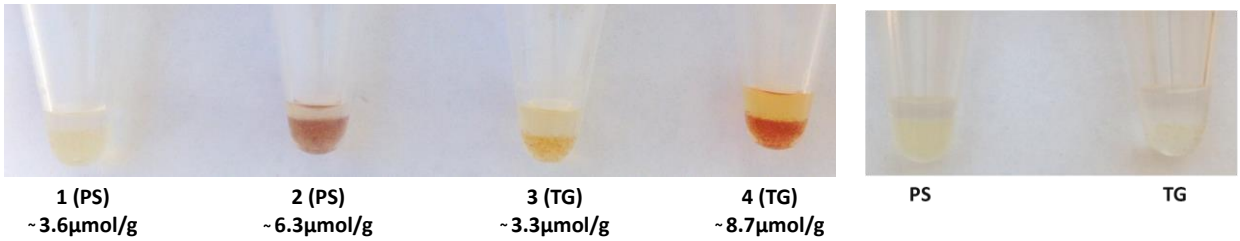
1) Rink amide-PS resin 3A (50mg, 1.8µmol, loading: 35.7µmol/g, 1 equiv.), Fmoc-Leu-OH (0.6mg, 1.6µmol, 0.9 equiv.), PyBOP (0.8mg, 1.6µmol, 0.9 equiv.), DIPEA (1.0µL, 6.4µmol, 3.6 equiv.) were suspended in NMP (1.0mL) and shaken at rt. After 1h the resin was washed with NMP (6x), DCM (5x) and MeOH (2x). Acetaldehyde/Fmoc-amino acid test was carried out as described and visualized after 5 min and 10 min. (see figure S1)

2) Rink amide-PS resin 2A (50mg, 3.2µmol, loading: 63.1µmol/g, 1 equiv.), Fmoc-Leu-OH (1.0mg, 2.8µmol, 0.9 equiv.), PyBOP (1.5mg, 2.8µmol, 0.9 equiv.), DIPEA (1.9µL, 11.4µmol, 3.6 equiv.) were suspended in NMP (0.5mL) and shaken at rt. After 1h the resin was washed with NMP (6x), DCM (5x) and MeOH (2x). Acetaldehyde/Fmoc-amino acid test was carried out as described and visualized after 5 min and 10 min. (see figure S1)

3) Tentagel resin 2A (50mg, 1.7µmol, loading: 33µmol/g, 1 equiv.), Fmoc-Leu-OH (0.5mg, 1.5µmol, 0.9 equiv.), PyBOP (0.8mg, 1.5µmol, 0.9 equiv.), DIPEA (1.0µL, 5.9µmol, 3.6 equiv.) were suspended in NMP (0.5mL) and shaken at rt. After 1h the resin was washed with NMP (6x), DCM (5x) and MeOH (2x). Acetaldehyde/Fmoc-amino acid test was carried out as described and visualized after 5 min and 10 min. (see figure S1)

4) Tentagel resin 1A (50mg, 4.4µmol, loading: 87µmol/g, 1 equiv.), Fmoc-Leu-OH (1.4mg, 3.9µmol, 0.9 equiv.), PyBOP (2.0mg, 3.9µmol, 0.9 equiv.), DIPEA (2.7µL, 15.7µmol, 3.6 equiv.) were suspended in NMP (0.5mL) and shaken at rt. After 1h the resin was washed with NMP (6x), DCM (5x) and MeOH (2x). Acetaldehyde/Fmoc-amino acid test was carried out as described and visualized after 5 min and 10 min. (see figure S1)

Acetaldehyde/Fmoc-Phenylalanine test after 5min.: References: Resins in NMP



Acetaldehyde/Fmoc-Phenylalanine test after 10min.:

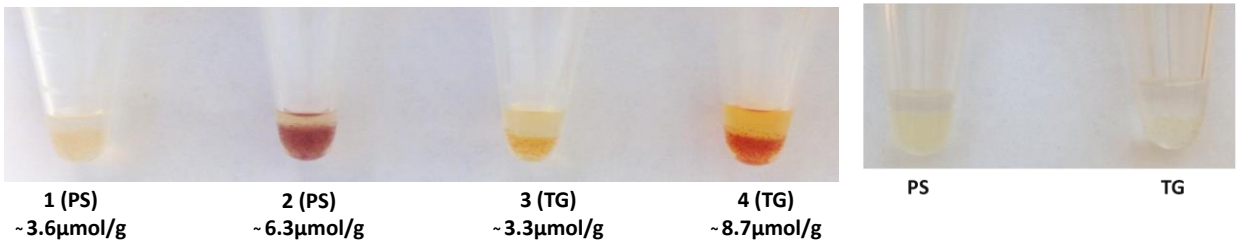


Figure S1. Sensitivity tests on polystyrene and tentagel

Preparation of Stock A, B and C used for the experiments below

Stock A: Acetaldehyde (1.1mL, 20mmol, d 0.79, MW 44) was dissolved in DMF (8mL)

Stock B: N-Benzylmethyl amine (0.52 mL, 4 mmol, d 0.94, MW 121.2) was dissolved in DMF (8mL)

Stock C: Benzyl amine (0.44mL, 4mmol, d 0.98, MW 107.2) in DMF (8mL)

3. Acetaldehyde/Fmoc-amino acid test in solution: N-Benzylmethyl amine compared to benzyl amine (Figure 3 in article)

1: Stock A (10µL) + Stock B (10µL) in DMF (5mL), shaking for 3 min
2: Stock A (10µL) + Fmoc-Gly-OH (1mg, 3.4 µmol) in DMF (5mL), to this solution is added Stock B (10µL), shaking for 3 min
3: Stock A (10µL) + Fmoc-Phe-OH (1.3mg, 3.4 µmol) in DMF (5mL), to this solution is added Stock B (10µL), shaking for 3 min
4: Stock A (10µL) in DMF (5mL), addition of Stock C (10µL), shaking for 3 min
5: Stock A (10µL) + Fmoc-Gly-OH (1mg, 3.4µmol) in DMF (5mL), to this solution is added Stock C (10µL) shaking for 3 min
6: Stock A (10µL) + Fmoc-Phe-OH (1.3mg, 3.4µmol) in DMF (5mL), to this solution is added Stock C (10µL), shaking for 3 min

4. Acetaldehyde/Fmoc-amino acid test: Sensitivity in solution

Stock B (5.2µL) was diluted in DMF (8mL) to give an amine concentration of 5mM. In the first well of the two rows diluted stock B (200 µL) was added and subjected to a two-fold dilution from 5mM-0.2mM concentration. In the first row, 40 µL of a test solution containing Fmoc-Glycine (2.0 mg, 7 µmol) in 2% Acetaldehyde in DMF (1mL) was added to each well. In the second row, 40 µL of a test solution containing Fmoc-Phenylalanine (2.6 mg, 7 µmol) in 2% Acetaldehyde in DMF (1mL) was added to each well. The total volume in each well was then 240 µL. Incubation for 5 minutes at room temperature (Figure S2).

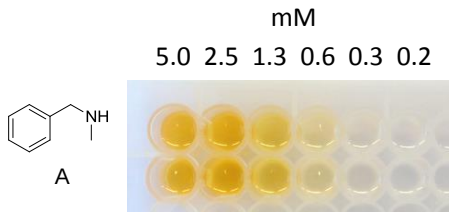


Figure S2. Two-fold dilution of amine **A** in DMF (total volume per well = 240 µL) visualized with acetaldehyde/Fmoc-Gly-OH (top row) and acetaldehyde/Fmoc-Phe-OH (bottom row)

5. 9-Methylfluorene compared to Fmoc-Phenylalanine in the acetaldehyde test solution.

1: Stock A (20uL) in DMF (10mL), addition of stock B (20uL)

2: Stock A (20uL) and 9-methylfluorene (1.2 mg, 6 µmol) in DMF (10mL), addition of stock B (20µL)

3: Stock A (20uL) and Fmoc-Phenylalanine (2.4mg, 6 µmol) in DMF (10mL), addition of Stock B (20µL)

4: Stock A (20uL) and 9-methylfluorene (1.2 mg, 6 µmol) in DMF (10mL), addition of Stock C (20µL)

5: Stock A (20uL) and Fmoc-Phenylalanine (2.4mg, 6 µmol) in DMF (10mL), addition of Stock C (20µL)

All the mixtures were shaken for 5 min before transfer to a 96 well plate. The results of the experiment and the structures of 9-methyl-fluorene and dibenzofulvene are shown in figure S3.

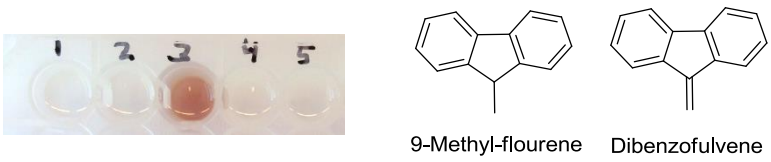


Figure S3. Effect of dibenzofulvene versus 9-methyl-fluorene in the formation colored solutions.

6. MS, UV and FT-IR analysis of colored dye precipitates

N-Benzylmethylamine (amine **A**, 130uL, 1mmol) was dissolved in DMF (2mL) and a mixture of acetaldehyde (280uL, 5mmol, MW 44, d 0.79) and Fmoc-amino acid (0.3mmol) dissolved in DMF (2mL) was added while stirring and the mixture turned rapidly dark brown. The mixture was stirred for 10 min. Acetonitrile (10mL) was added and the mixture was centrifuged and the dark brown/black

precipitate was isolated. The brown precipitate was wased 5 times with acetonitrile. A small amount of the precipitate was dissolved in DMF, filtered through a micro-filter and analyzed by MS (Figure S4, S5), which gave similar mass spectra regardless of using Fmoc-Gly-OH or Fmoc-Phe-OH in the color test indicative of the structure proposed in Figure S4. UV-VIS on the dye precipitated from Acetaldehyde/Fmoc-Phe-OH test showed UV absorption maxima at λ=198, 216 and 425nm (Figure S6). The solid precipitates were analyzed by FT-IR (attenuated technique of reflection) which showed a band at 1660 cm-1 characteristic for the presence of a dialkyliminium group (Figure S7).

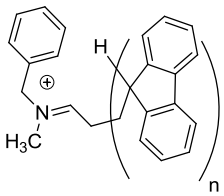


Figure S4. Proposed structure of DBF polymer formed by reaction between amine **A**, acetaldehyde and Fmoc-amino acid.

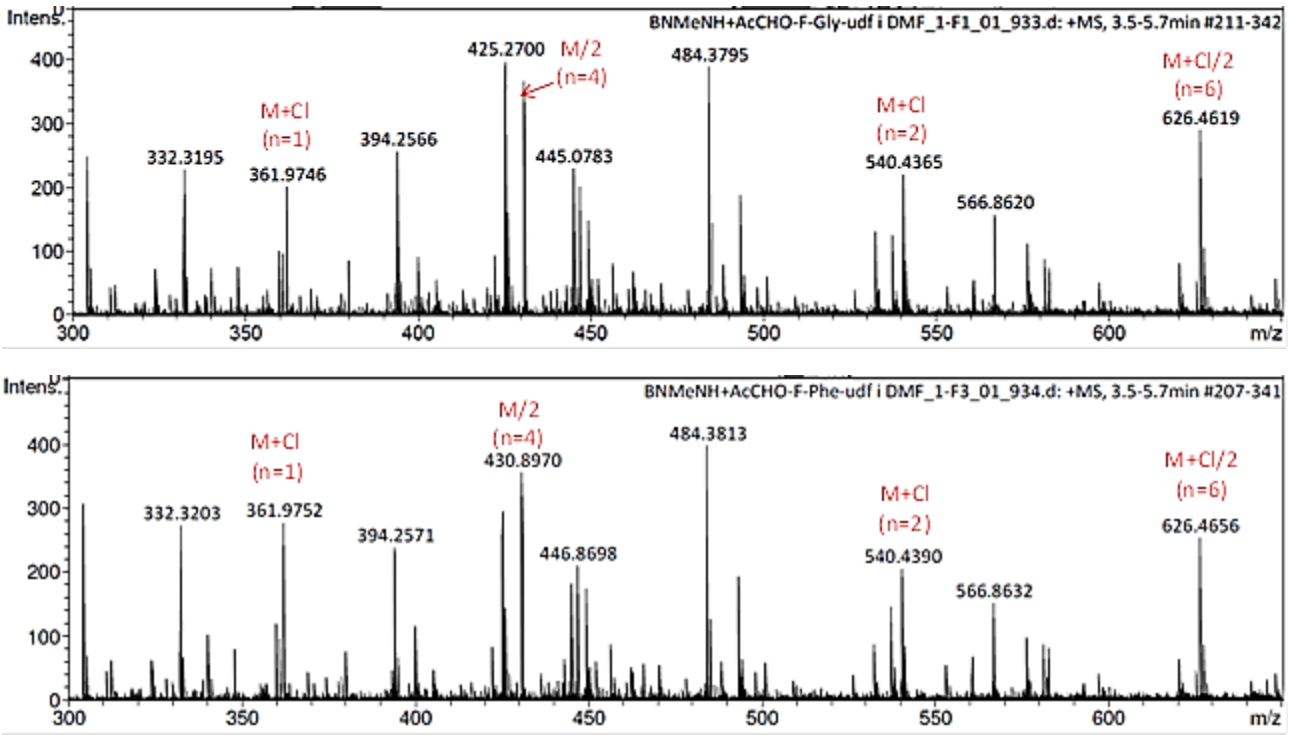


Figure S5. Interpreted MS spectra of dyes isolated as described above from: Amine **A** mixed with acetaldehyde/Fmoc-Gly-OH test mixture (top) and Amine **A** mixed with acetaldehyde/Fmoc-Phe-OH test mixture (bottom)

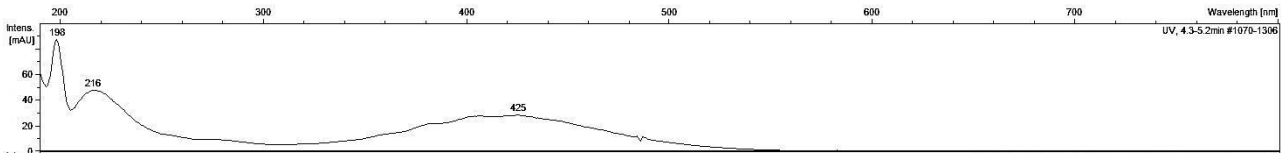
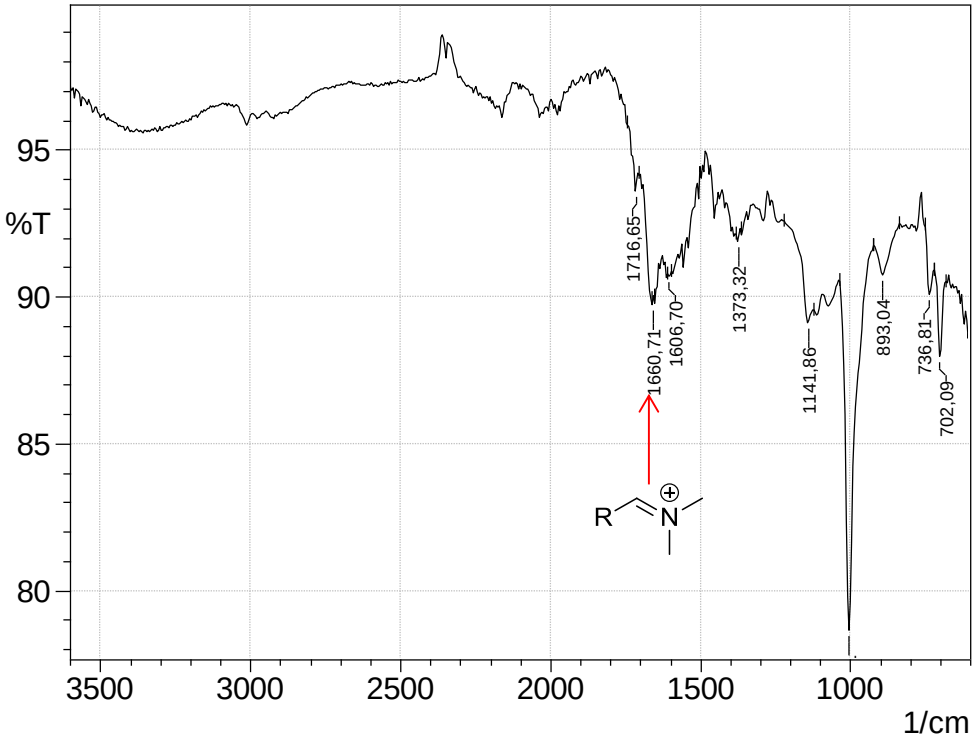


Figure S6. UV-VIS (diode array) spectrum of dye isolated as above from: Amine **A** mixed with acetaldehyde/Fmoc-Phe-OH test mixture



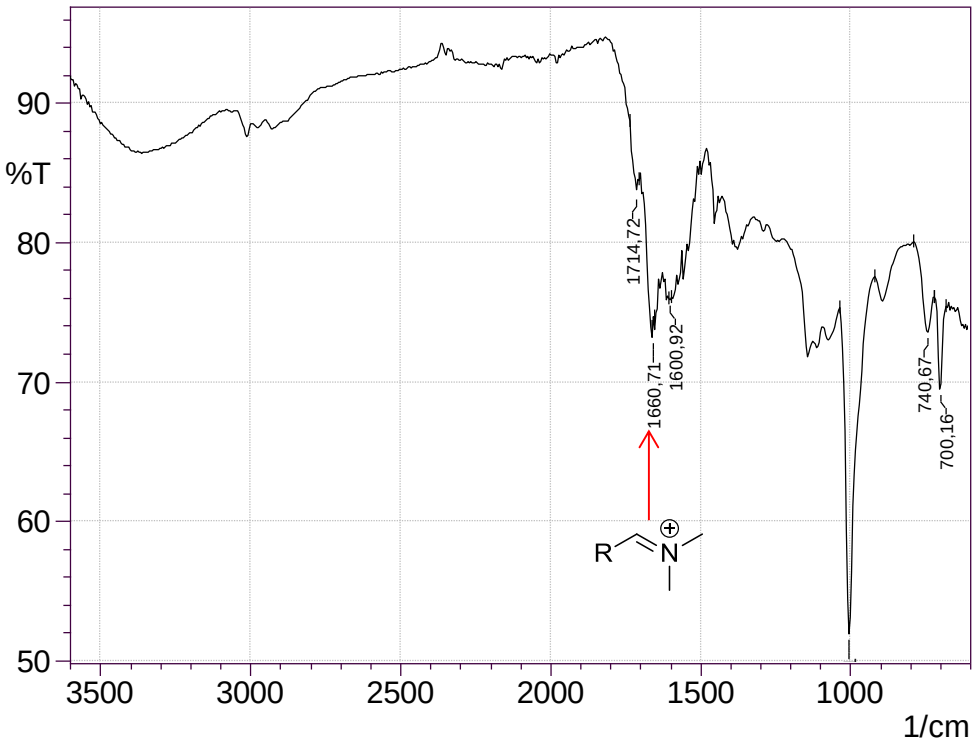
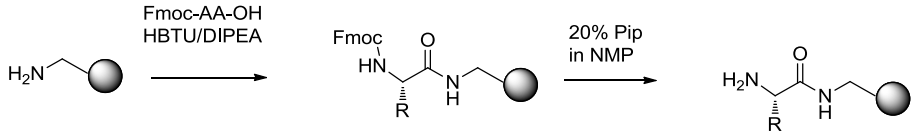


Figure S7. Analysis of dye precipitates by FT-IR of dyes isolated as described above from: Amine **A** mixed with acetaldehyde/Fmoc-Gly-OH mixture (top) and Amine **A** mixed with acetaldehyde/Fmoc-Phe-OH mixture (bottom)

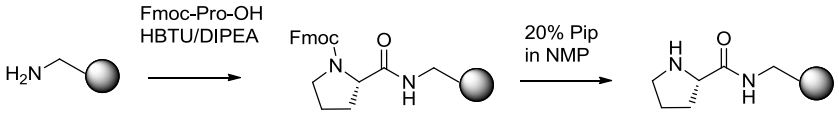
7. Procedures for the synthesis of resin substrates

Proline/lysine/alanine on aminomethylated polystyrene resin (compounds 5, 10 and 11, respectively)



Procedure: Aminomethylated polystyrene resin (0.3g, 0.6mmol, load 2mmol/g) was swelled in dry NMP (5mL). PyBOP (1.24g, 4equiv., 2.4mmol, MW 520.4) and dry DIPEA (0.82mL, 4equiv., 4.8mmol, MW129.3) were added followed by Fmoc protected aa (4equiv., 2.4mmol). The resin suspension was shaken for 1h at r.t. and washed with 6x NMP, 5x DCM and 3x MeOH. Ninhydrin test, negative. Cleavage of Fmoc group by 20% Piperidine in NMP (5mL, 3+20min), wash (6x NMP, 5x DCM, 2x MeOH). Ninhydrin test was positive. IR-(ATR) ν (Cm^{-1}). Alanine: 2922 (C-H stretch), 1668 (C=O stretch, amide), 758 (N-H bend). Lysine: 2922 (C-H stretch), 1660 (C=O stretch, amide), 758 (N-H bend). Proline: 2922 (C-H stretch), 1668 (C=O stretch, amide), 759 (N-H bend)

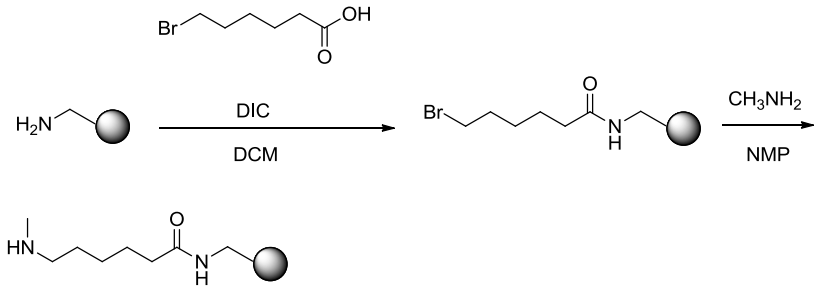
Proline on Tentagel S NH2 and Amino PEGA resins (compound 5a and 5b)



Procedure (Tentagel S NH2): Fmoc-Pro-OH (0.4 mmol, 135mg, MW 337.4) was suspended in dry NMP (4 mL) and HBTU (0.4mmol, 152 mg, MW 379) was added followed by DIPEA (0.8mmol, 138 uL, MW 129.3, d 0.75) the mixture was stirred for 5 minutes and added to tentagel resin (0.3g, 0.09 mmol, load 0.29mmol/g) was swelled in NMP (3mL). The resin suspension was shaken for 2 hr at r.t. and washed (DCM x5, NMP x5), Ninhydrin test, negative Cleavage of Fmoc group by 20% Piperidine in NMP(3mL, 3+20min), wash (5xDCM, 5x NMP, 2xmethanol), Ninhydrin test (should be negative). IR (ATR) ν (Cm^{-1}) 3468 (N-H stretch, amide), 2870 (C-H, stretch), 1667 (C=O, amide),

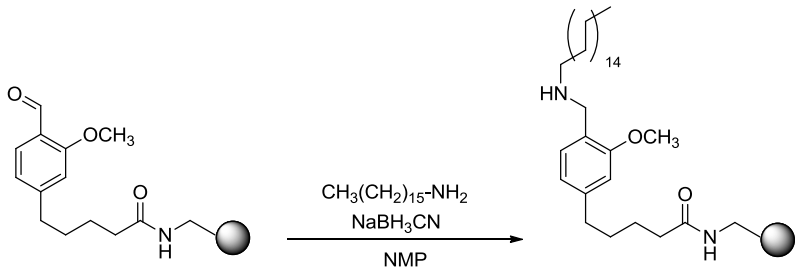
Procedure (Amino PEGA): Fmoc-Pro-OH (0.4 mmol, 135mg, MW 337.4) was suspended in dry NMP (4 mL) and HBTU (0.4mmol, 152 mg, MW 379) was added followed by DIPEA (0.8mmol, 138 uL, MW 129.3, d 0.75) the mixture was stirred for 5 minutes and added to Amino PEGA resin (0.2g, 0.08 mmol, load 0.4mmol/g, Novabiochem) was swelled in NMP (3mL). The resin suspension was shaken for 2 hr at r.t. and washed (DCM x5, NMP x5), Ninhydrin test? Cleavage of Fmoc group by 20% Piperidine in NMP(3mL, 3+20min), wash (5xDCM, 5x NMP, 2xmethanol), Ninhydrin test (should be negative). IR (ATR) ν (Cm^{-1}) 3446 (N-H stretch, amide)2927, 2875 (C-H stretch), 1659 (C=O stretch, amide)

N,N-methyl-(6-amidohexyl)amine on aminomethylated polystyrene resin (Compound 3)



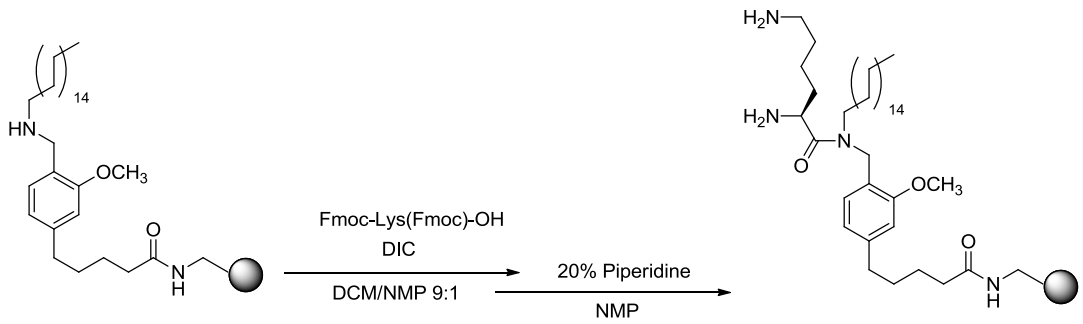
Procedure: 6-Bromohexanoic acid (3.9 g, 20 mmol, MW 195.05) was suspended in dry DCM (15mL) and the mixture was cooled on an icebath. After 5 minutes DIC (1.6 mL, 10 mmol, d=0.81, MW 126.2) was added and the mixture was stirred for 30 minutes on ice. The stirring bar was removed and Aminomethylated polystyrene resin (1g, 2 mmol, loading 2 mmol/g) was added and the resin mixture was shaken 3 h in the round bottomed flask. The resin suspension was transferred to a filter syringe and washed with NMP (x5) and DCM (x5) and methanol (x2). Ninhydrin test was performed and was negative (otherwise capping with acetic anhydride (5%Ac2O/10% DIPEA in DCM for 30 min). The bromo resin was suspended in dry NMP (10 mL) and 2M methyl amine in THF (10 mmol, 5 mL) and the suspension was shaken 16 h. The resin was washed with NMP (5x), DCM (5x) and shrunk with methanol (2x) and kept under vacuum (oilpump). IR (ATR) ν (Cm^{-1}) 2922 (C-H stretch), 1668 (C=O stretch, amide), 1367 (methyl, bend), 758 (N-H, bend)

Secondary amine substrate on aminomethylated polystyrene resin (Compound 4)



Procedure: Aldehyde (FMPB) derivatized resin (0.5g, 1mmol, 1 equiv.) was swelled in 5% acetic acid in dry NMP/THF (1:9) (14mL). $NaBH_3CN$ (0.63g, 10 equiv., 10mmol, MW 62.84) and hexadecylamine (2.41g, 10equiv., 10mmol, MW 241.46) were added. The resin suspension was shaken for 24h at r.t. and washed with 3x MeOH, 6x NMP, 5x DCM. DNPH test, positive. Reaction repeated 2h at r.t. and washed as above. DNPH test, negative. IR (ATR) ν (Cm^{-1}) 2922 (C-H stretch), 1651 (C=O stretch, amide), 1375 (methyl, bend), 759 (N-H, bend), 698 (C-H bend, aromatic)

Primary amine substrate on aminomethylated polystyrene resin (Compound 6)

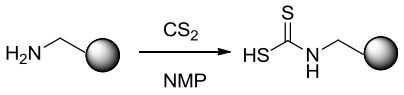


Procedure: Secondary amine-FMPB derivatized resin, (0.5g, 1mmol, 1 equiv.) was swelled in dry NMP (5mL). Et_3N (1.40mL, 10mmol, 10 equiv., MW 101.2, d=0.73), DMAP (0.12g, 1mmol, 1 equiv., MW 122.2) and TFFH (1.32g, 5mmol, 5 equiv., MW 264.1) were added followed by Fmoc-Lys(Fmoc)-OH (2.95g, 5mmol, 5 equiv., MW 590.7). The resin suspension was shaken 22.5h at r.t. and washed with 6x NMP, 5x DCM, 2x MeOH. Cleavage of Fmoc groups by 20% Piperidine in NMP (10mL, 3+30min), wash (6x NMP, 5x DCM, 2x MeOH). Ninhydrin test was positive. IR (ATR) ν (Cm^{-1}) 2922 (C-H stretch), 1651 (C=O stretch, amide), 1375 (methyl, bend), 759 (N-H, bend), 698 (C-H bend, aromatic)

Resin bound dithiocarbamate (Compound 8)

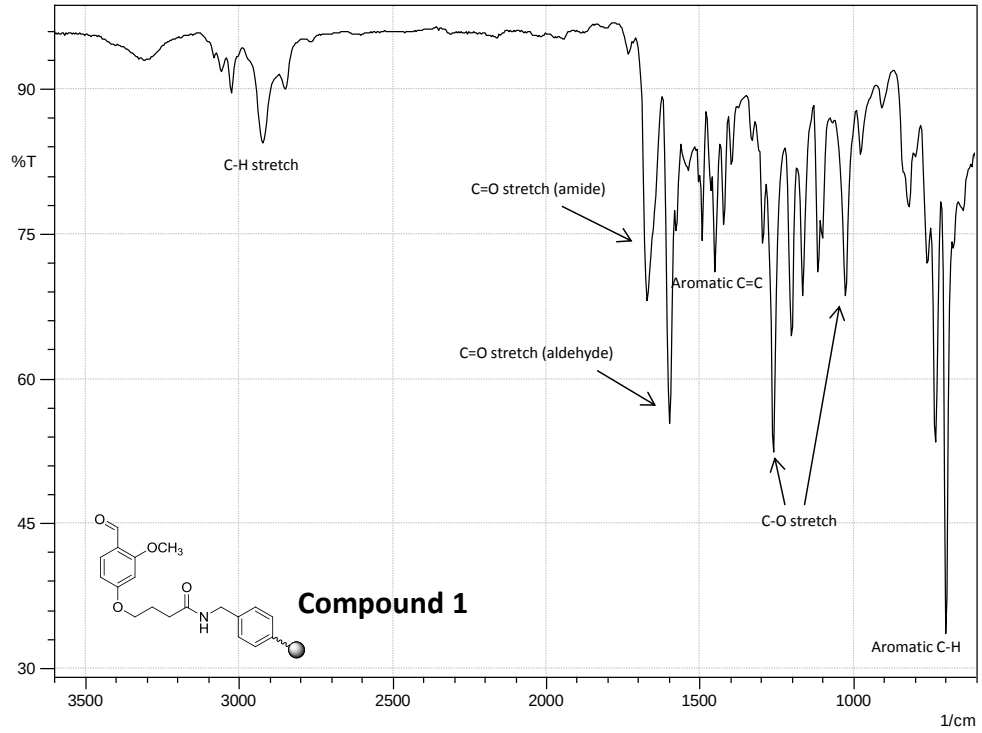
Procedure: N-methyl-(6-amidohexyl)amine on polystyrene (20 mg, 0.04mmol, loading 2 mmol/g) was put in an Eppendorf test tube and swelled in NMP (0.1 mL). Carbon disulfide (0.2mL) was added and the mixture was shaken for 1 h at r.t. The yellow resin suspension was transferred to a syringe equipped with a filter and washed with NMP (5 times), DCM (5 times) and methanol and air dried. IR (ATR) ν (cm^{-1}) 2922 (C-H stretch), 1651 (C=O stretch, amide), 1512 (C=S stretch), 1371 (methyl, bend), 758 (N-H bend)

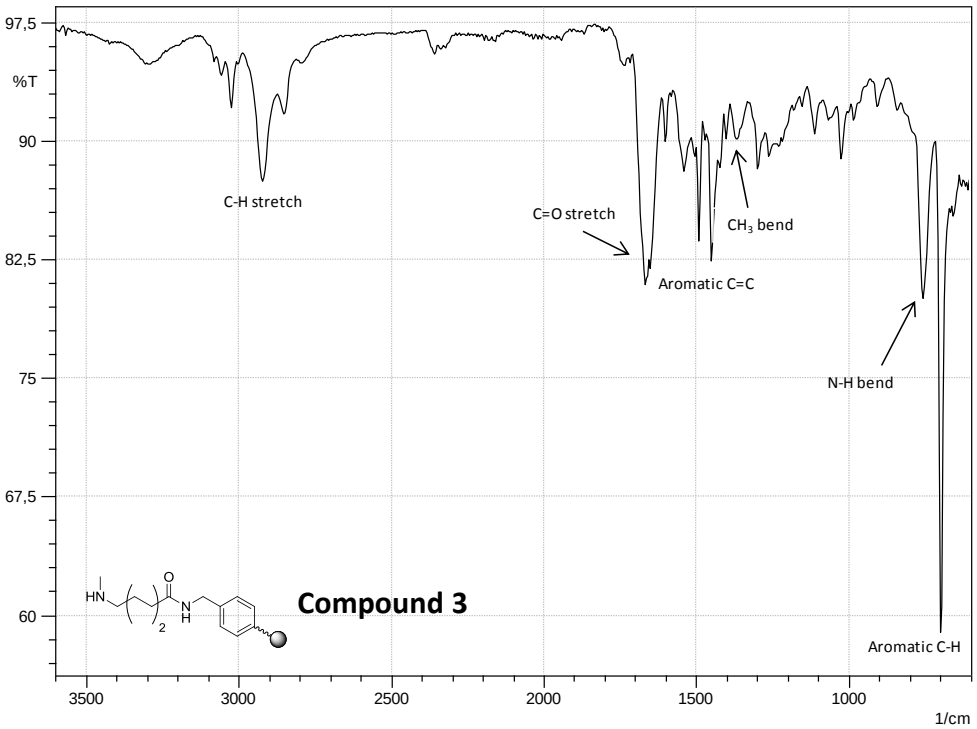
Resin bound dithiocarbamate (Compound 9)

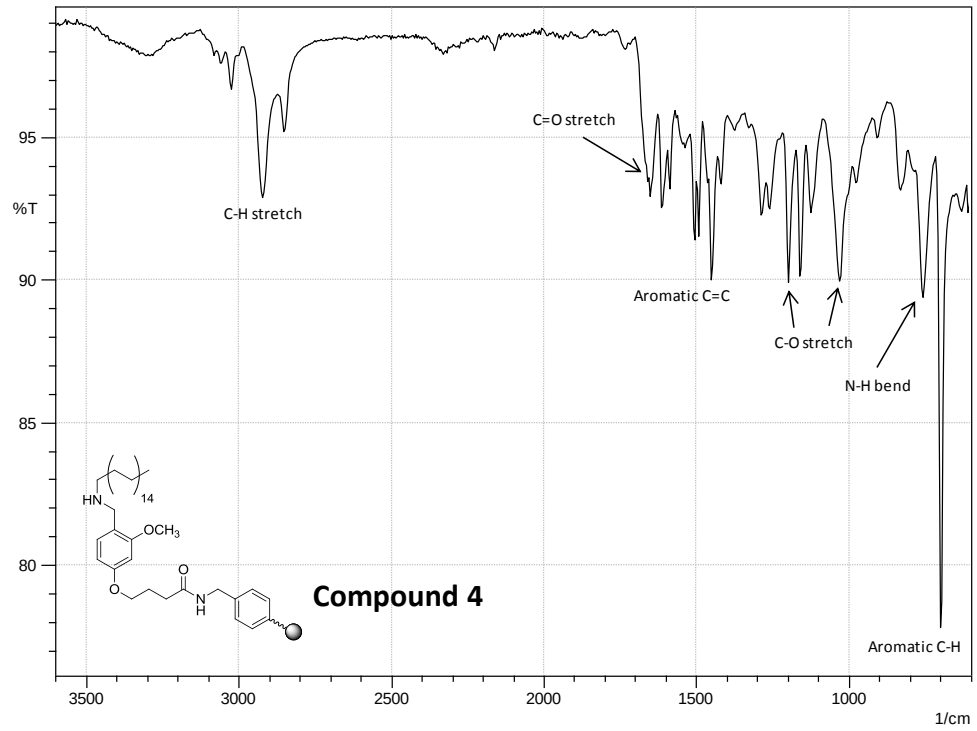


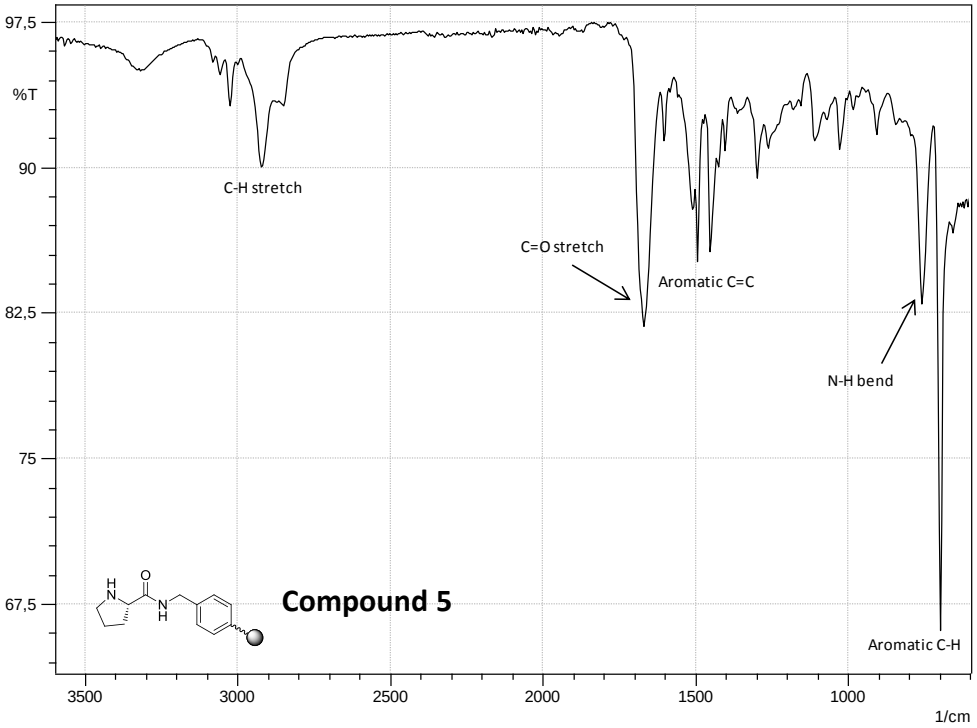
Procedure: Aminomethylated polystyrene (20 mg, 0.04mmol, loading 2 mmol/g) was put in an Eppendorf test tube and swelled in NMP (0.1 mL). Carbon disulfide (0.2mL) was added and the mixture was shaken for 1 h at r.t. The yellow resin suspension was transferred to a syringe equipped with a filter and washed with NMP (5 times), DCM (5 times) and methanol and air dried. IR (ATR) ν (cm^{-1}) 2920 (C-H stretch), 1506 (C=S stretch), 758 (N-H bend)

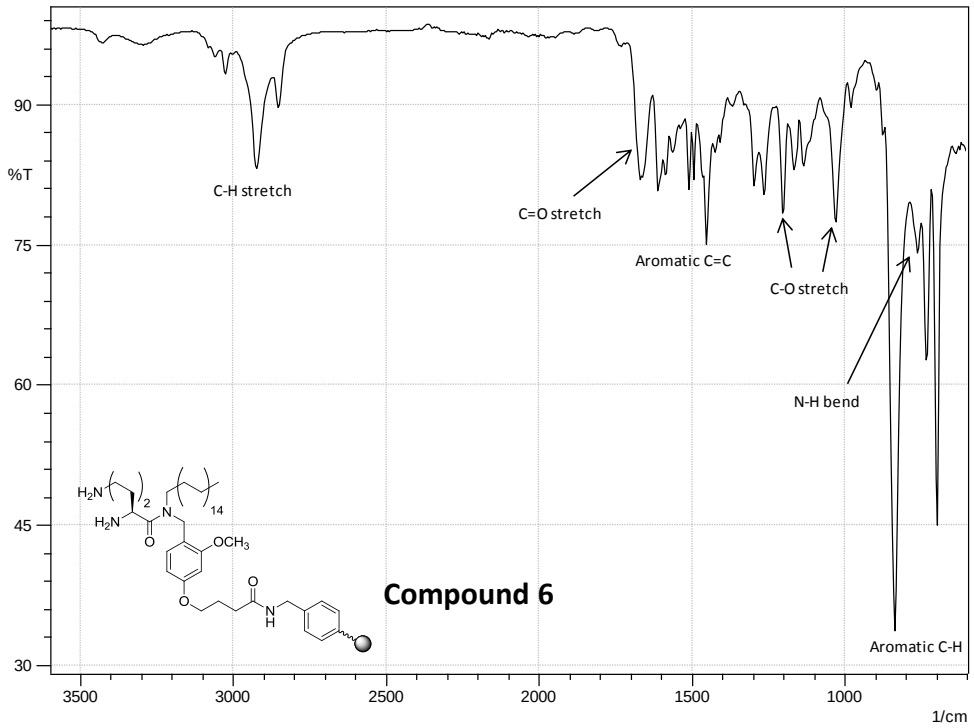
8. Selected FT-IR spectra for resin substrates

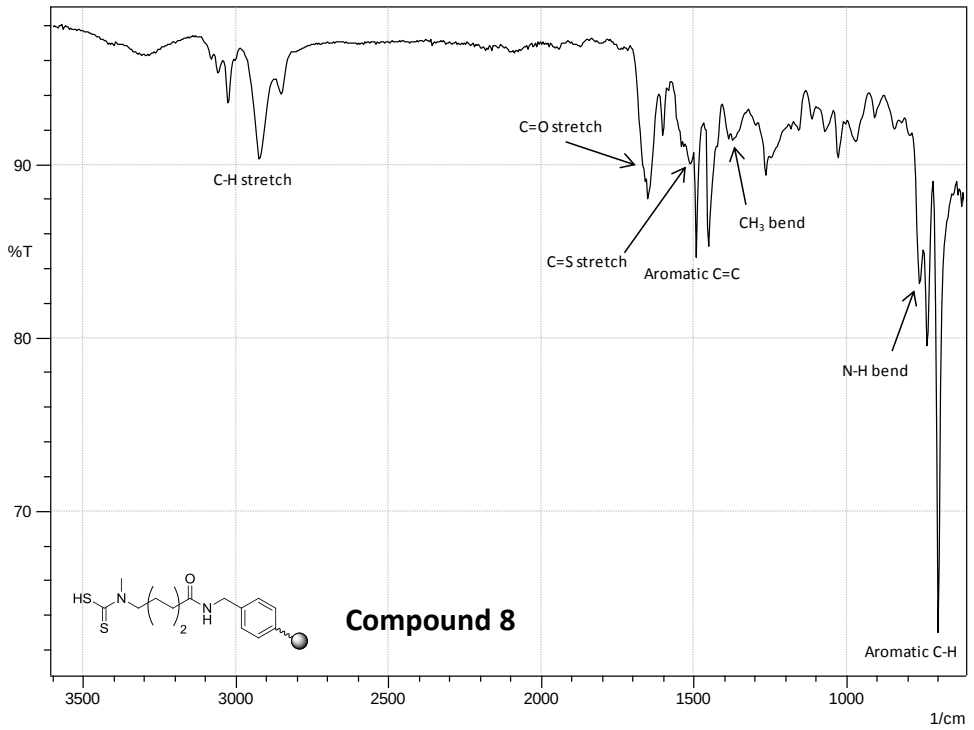


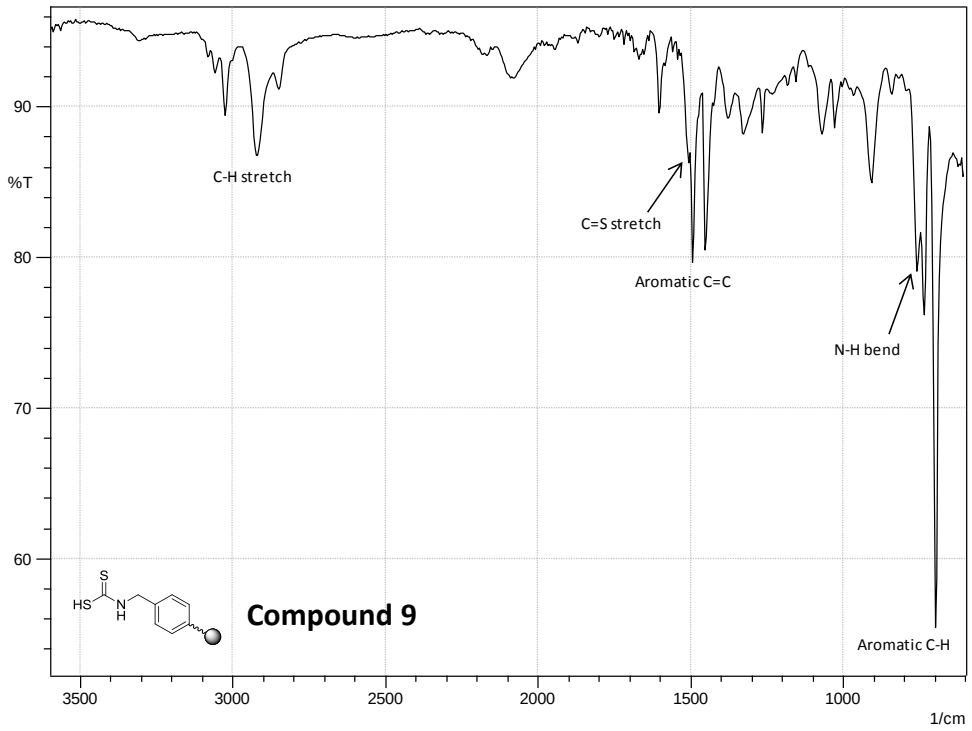


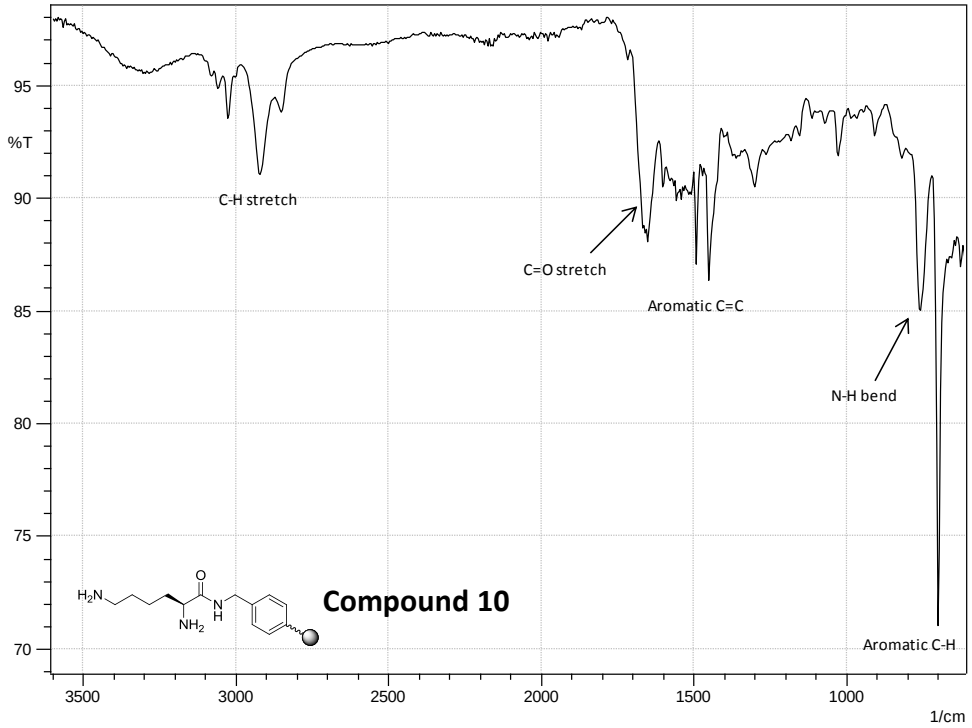

95
%T
90
85
80
C=O stretch
C-H stretch
Aromatic C=C
C-O stretch
N-H bend
Aromatic C-H
HN
14
OCH3
O
O
N
H
Compound 4
3500
3000
2500
2000
1500
1000
1/cm

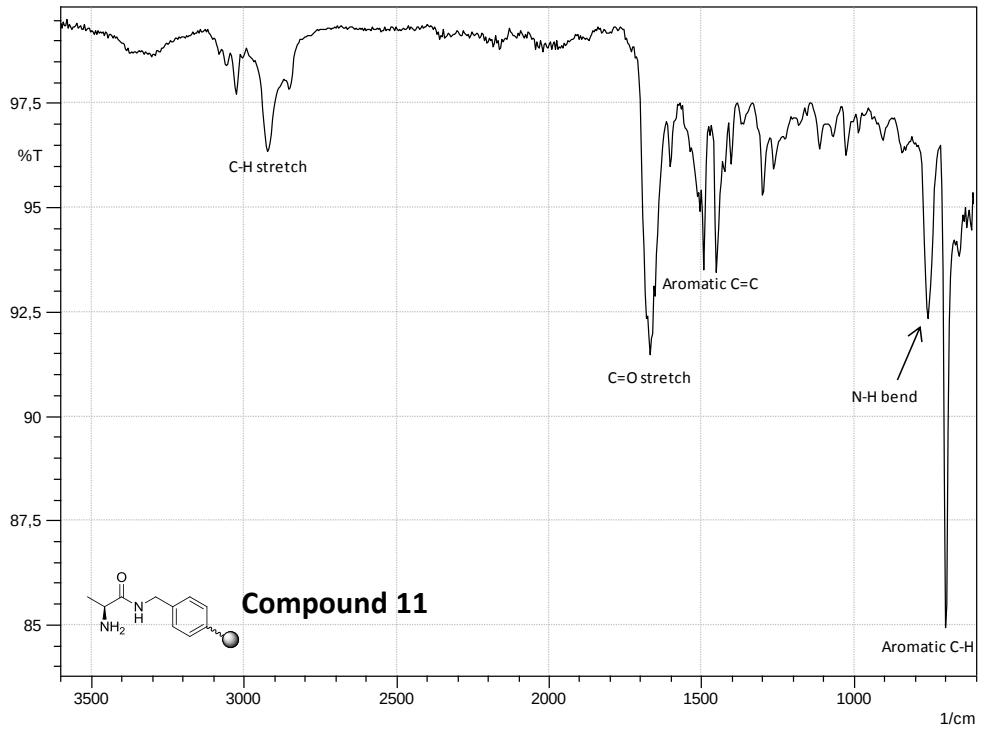

97,5
%T
90
82,5
75
67,5
C-H stretch
C=O stretch
Aromatic C=C
N-H bend
Aromatic C-H
H
N
O
N
H
Compound 5
3500
3000
2500
2000
1500
1000
1/cm


%T
90
75
60
45
30
C-H stretch
C=O stretch
Aromatic C=C
C-O stretch
N-H bend
Aromatic C-H
Compound 6
3500
3000
2500
2000
1500
1000
1/cm

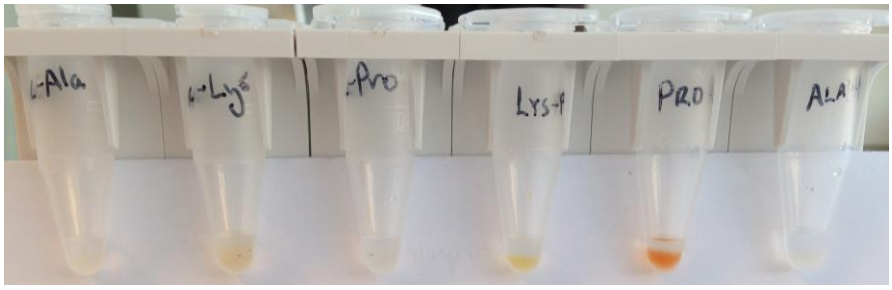

%T
90
80
70
C-H stretch
C=O stretch
C=S stretch
Aromatic C=C
CH3 bend
N-H bend
Aromatic C-H
Compound 8
3500
3000
2500
2000
1500
1000
1/cm


90
%T
80
70
60
C-H stretch
C=S stretch
Aromatic C=C
N-H bend
Aromatic C-H
Compound 9
3500
3000
2500
2000
1500
1000
1/cm

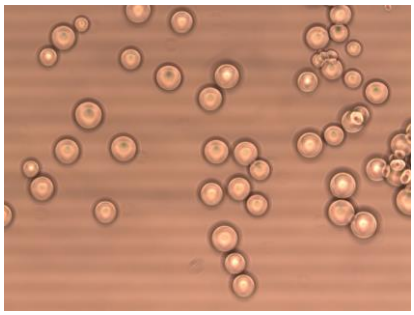

95
%T
90
85
80
75
70
C-H stretch
C=O stretch
Aromatic C=C
N-H bend
Aromatic C-H
Compound 10
3500
3000
2500
2000
1500
1000
1/cm



9. Test carried out on Fmoc-protected amines (primary and secondary) and alkyl chlorides



Picture S1: The acetaldehyde test performed on Fmoc-protected amino acids, alanine, lysine and proline (three tubes to the left) and unprotected amino acids (three tubes to the right)



Picture S2: Micrograph of the colorless beads of chloromethylated polystyrene after performing the acetaldehyde test.

10. References

1) Svenssen, D. K.; Mirsharghi, S.; Boas. U. *Tetrahedron Lett.* **2014**, *55*, 3942-3945

2) Boas, U.; Gertz, H.; Christensen, J. B.; Heegaard, P. M. H. *Tetrahedron Lett.* **2004**, *45*, 269-272

3) Claerhout, S.; Ermolat'ev, D. S.; Van der Eycken, E. V. *J. Comb. Chem.* **2008**, *10*, 580-585

4) Yang, S.-J-; Tian, X. Z.; Shin, I. *Org. Lett.* **2009**, *11*, 3438-3441