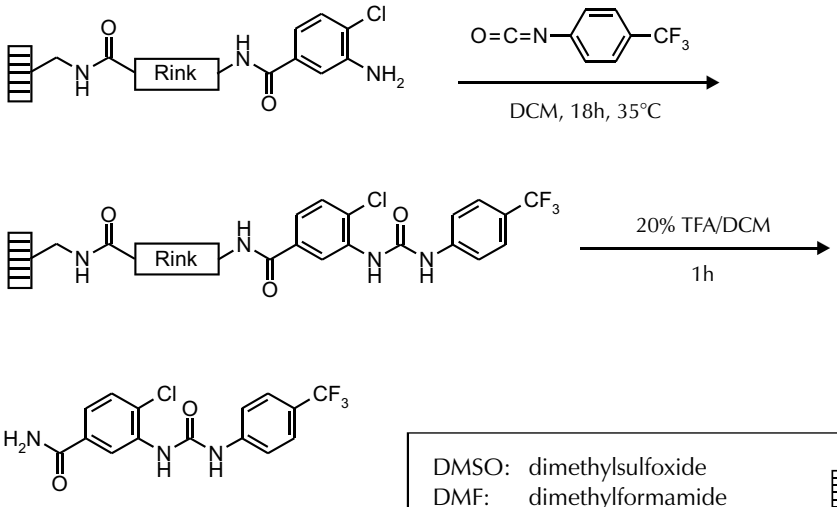
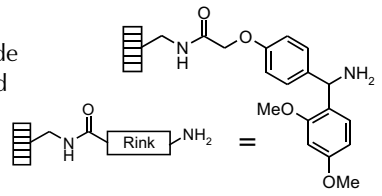
Acylation of a Support-Bound Amine with an Aryl Isocyanate

Acylation of primary or secondary amines with isocyanates gives rise to substituted ureas. In the following example, a support-bound aniline[1] on SynPhase™ PS Lanterns[2] is acylated with an aryl isocyanate, to form a diaryl urea.



DMSO: dimethylsulfoxide
DMF: dimethylformamide
TFA: trifluoroacetic acid
DCM: dichloromethane



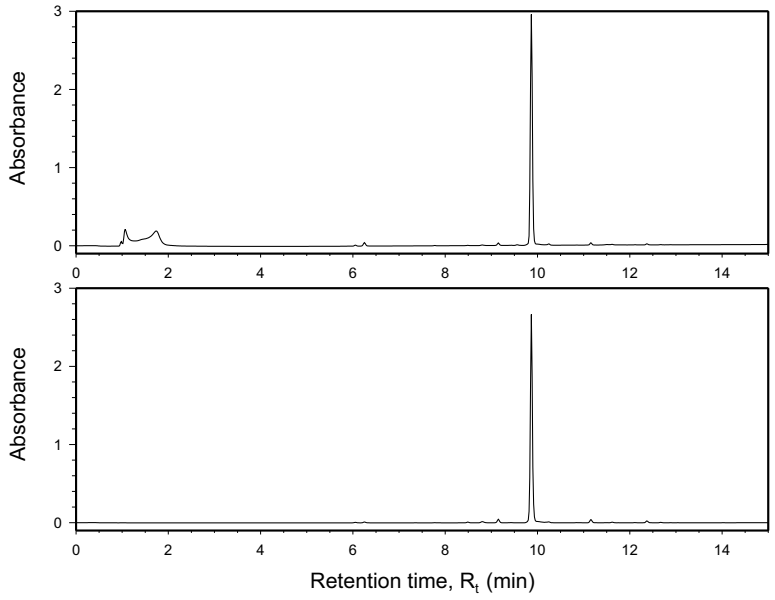
Urea Formation

Each D-Series Lantern derivatized with an aniline[1] (initial specified loading: 34μmol) is treated with 0.5mL of a 0.4M solution of 4-trifluoromethylphenylisocyanate (220μmol, 6.5 mole equivalents) in anhydrous DCM at 35°C for 18h. The reaction is allowed to cool to room temperature and the solution decanted. The Lanterns are washed with DCM (1×3min), DMF (3×3min) and DCM (3×3min) then air dried.

Cleavage

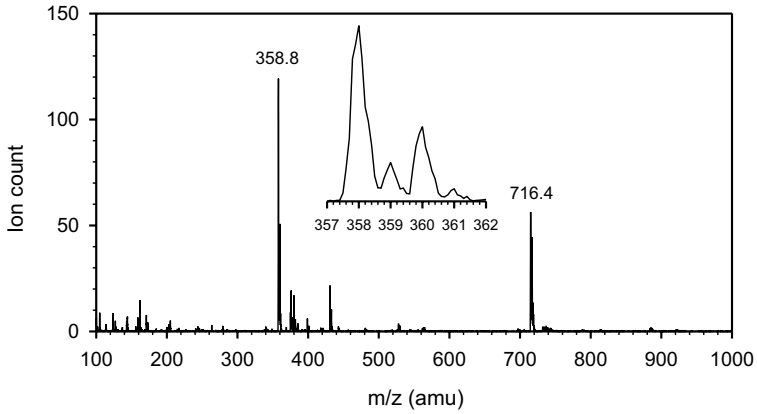
Individual Lanterns are placed in polypropylene tubes and treated with 20% TFA/DCM (0.6-0.8mL) for 1h. The Lanterns are removed and the cleaved products are concentrated using a centrifugal evaporator. Samples are dissolved in 90% CH_3CN/H_2O for HPLC and ES-MS analysis.

Analytical Data



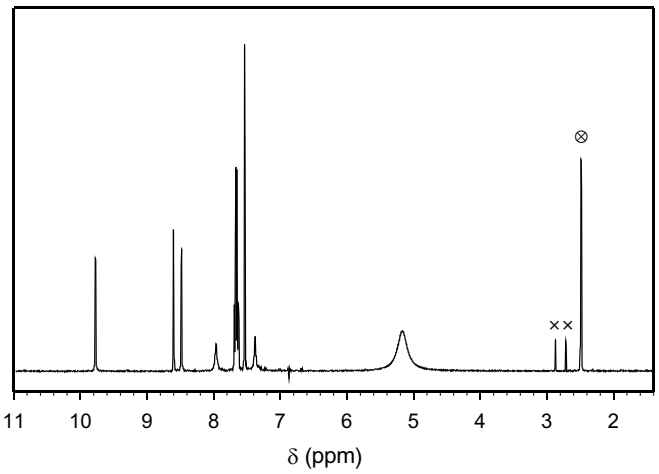
Reverse-phase HPLC traces of the crude urea

Top trace: detection at 214nm
Bottom trace: detection at 254nm



Electrospray MS trace of the crude urea

Molecular Formula: $C_{15}H_{11}ClF_3N_3O_2$
Monoisotopic Mol. Weight: 357.7amu
$[M+H]^+$ = 358.8amu
$[2M+H]^+$ = 716.4amu



400MHz ^{1}H NMR spectrum of the crude urea (D_6-DMSO)

(⊗) DMSO
(×) Residual DMF

References and Notes

1 See SynPhase Chemistry Note SCN 001-3.
2 The chemistry described here was performed using SynPhase PS Lanterns but is readily adaptable to SynPhase PA Lanterns.

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