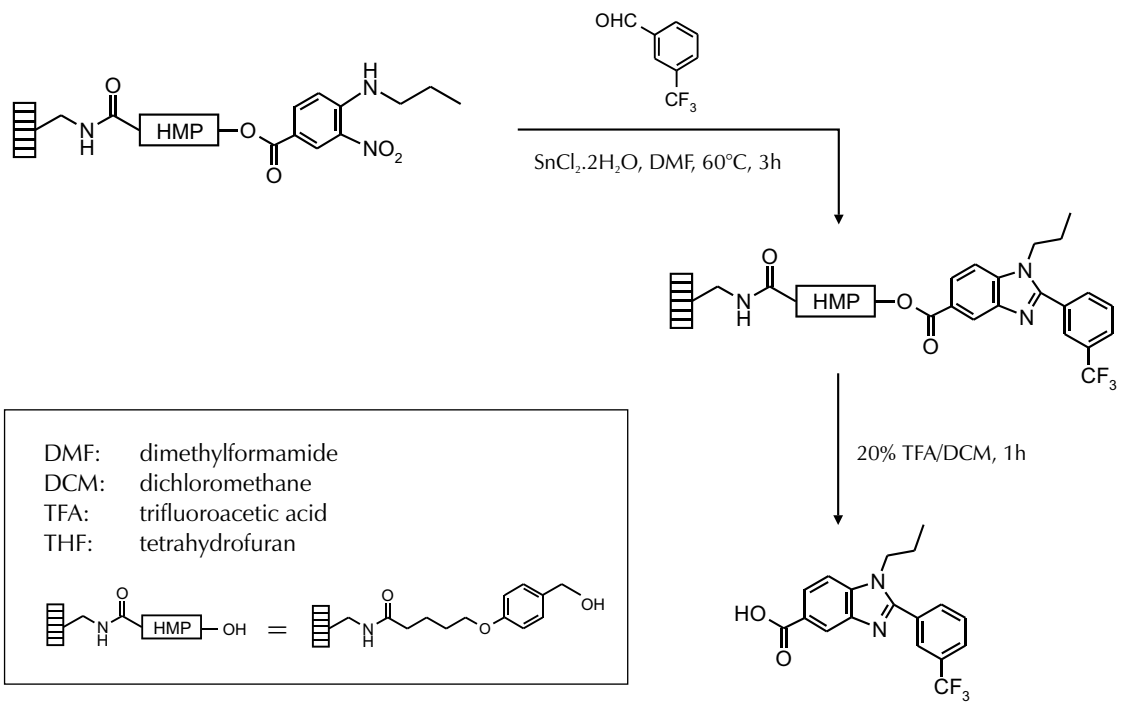
One-Pot Synthesis of a Benzimidazole from a Solid-Bound *o*-Nitroaniline

Benzimidazoles may be generated efficiently by heating a solid-bound *o*-nitroaniline and an aldehyde in the presence of tin(II) chloride dihydrate.[1] In the following example, an *o*-nitroaniline prepared[2] on hydroxymethylphenoxy derivatized SynPhase™ Lanterns is converted to a benzimidazole in a one-pot procedure.



Synthesis of Benzimidazole

Each *o*-nitroaniline derivatised-HMP D-Series Lantern is treated with a 0.5mL solution of 3-(trifluoromethyl)benzaldehyde (0.15M, 75μmol, 2.1 mole equivalents) and tin(II) chloride dihydrate (0.75M, 375μmol, 10.7 mole equivalents) and heated at 60°C for 3h.[3] The reagent solution is then decanted and the Lanterns are washed with DMF (3×3min), 80% THF/H_2O[4] (60°C, 2×1h), MeOH (2×3min) and DCM (3×3min).

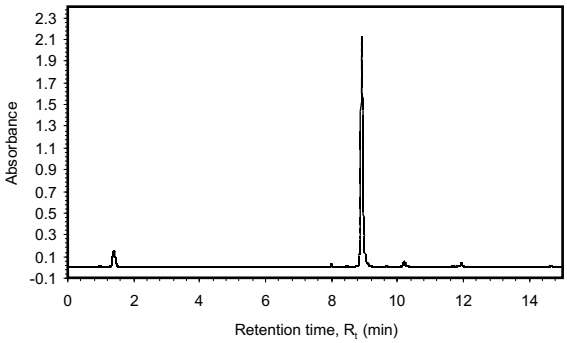
Cleavage

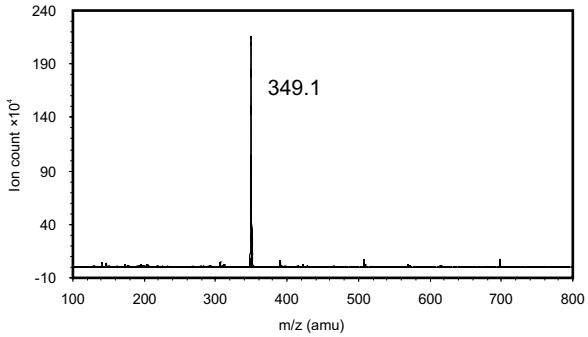
Individual Lanterns are placed in polypropylene tubes and treated with 20% TFA/DCM (0.6-0.8mL) for 1h. The Lanterns are removed and the cleaved products are concentrated using a centrifugal evaporator. The residue is freeze-dried from 90% CH_3CN/H_2O. The benzimidazole product was obtained in *ca.* 85% yield, based on the initial Lantern loading. Samples are dissolved in 90% CH_3CN/H_2O for HPLC and ES-MS analysis.

Analytical Data

Reverse phase HPLC trace of the crude benzimidazole

Detection at 214nm



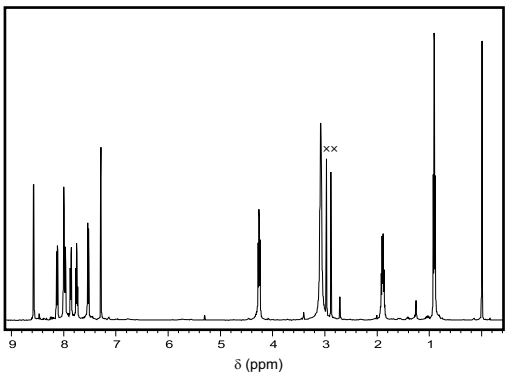


Electrospray MS trace of LC peak at R_t = 8.91min

Molecular Formula: $C_{18}H_{15}F_3N_2O_2$
Monoisotopic Mol. Weight: 348.1amu
$[M+H]^+$ peak at 349.1amu

400MHz ^{1}H NMR spectrum of the crude benzimidazole ($CDCl_3$)

(×) Residual DMF



References & Notes

1 Wu, Z., Rea, P. and Wickham, G., *Tetrahedron Lett.*, 2000, **41**, 9871-9874.
2 See Mimotopes SynPhase Chemistry Note SCN 014-2.
3 If the solid supported species is *N*-diphenyl substituted, then a longer reaction time may be required.
4 THF/H_2O washing assists in the removal of tin residues.

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