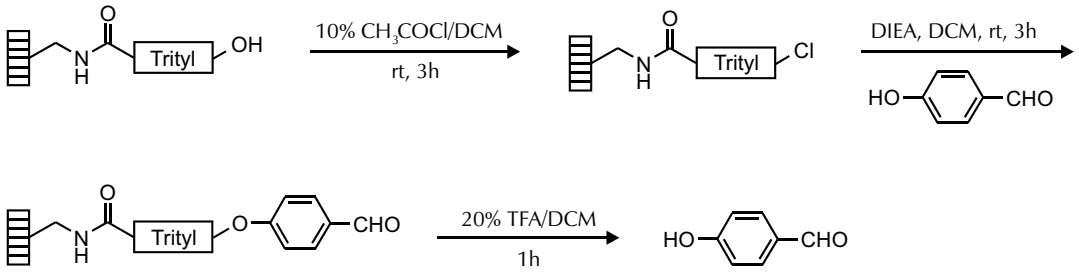
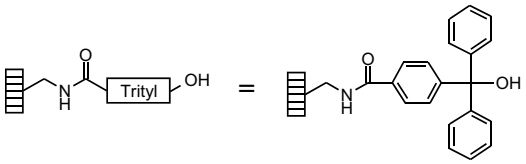
Attachment of a Phenol onto SynPhase™ Lanterns *via* the Trityl Linker

A common method for the attachment of phenols onto solid supports, is to react a phenol with freshly prepared solid-bound trityl chloride in the presence of a base, such as DIEA. In the following example, 4-hydroxybenzaldehyde is attached to SynPhase™ PS Lanterns[1] in a two step process, then cleaved in good yield (*ca.* 80%). Similar results are obtained for carboxylic acids (*e.g.* Fmoc protected amino acids).



DCM: dichloromethane
DIEA: diisopropylethylamine
TFA: trifluoroacetic acid
rt: room temperature



Trityl Chloride Formation[2]

Each D-Series trityl alcohol Lantern (initial specified loading: 36μmol) is treated with a 0.5mL solution of 10% (V/V) acetyl chloride in dry DCM at rt for 3h. The reagent solution is decanted and the Lanterns washed with DCM (3×3min) and used immediately in the next reaction without drying.

Attachment of Phenol

Each Lantern is treated with 0.5 mL of a solution of 4-hydroxybenzaldehyde (0.2M, 100μmol, 2.75 mole equivalents) and DIEA (0.4M, 200μmol, 5.5 mole equivalents) in DCM at rt for two hours. The reagent solution is decanted and the Lanterns washed with DMF (3×3min), DCM (3×3min) and then air dried.

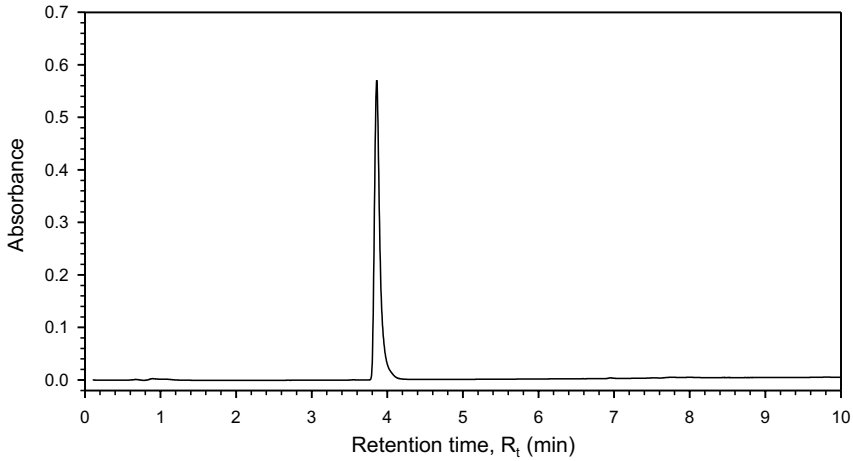
Cleavage

Individual Lanterns are placed in polypropylene tubes and treated with 1% TFA/DCM (0.6-0.8mL) for 1h. The Lanterns are removed and the cleaved products are concentrated using a centrifugal evaporator. The yield of 4-hydroxybenzaldehyde is *ca.* 80% (based on the initial loading). Samples are dissolved in 90% CH_3CN/H_2O for HPLC analysis.

Analytical Data

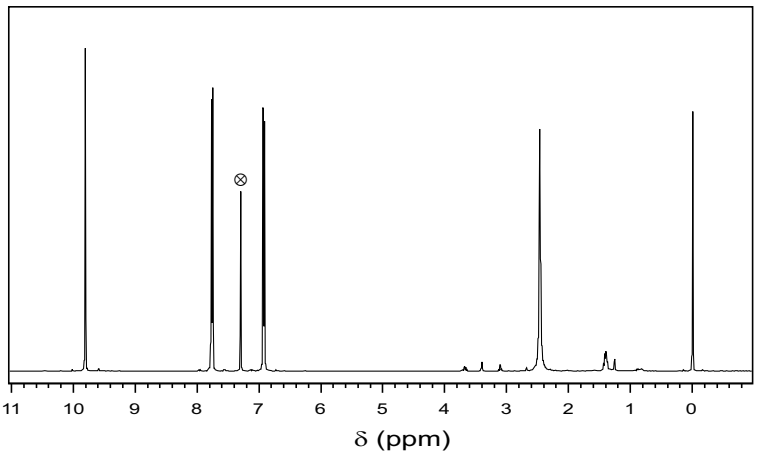
Reverse phase HPLC trace of the crude product

Detection at 214nm



400MHz ^{1}H NMR spectrum of the crude product ($CDCl_3/D_4$-methanol)

(⊗) $CHCl_3$



Notes

1 The chemistry described here was performed using SynPhase PS Lanterns but is readily adaptable to SynPhase PA Lanterns.

2 Trityl chloride formation and any subsequent chemistry is sensitive to atmospheric moisture. The solvent and reagents used in this preparation must be anhydrous, otherwise poor loading levels will be obtained. It is strongly recommended that all glassware be dried. Also, it is recommended that the trityl chloride Lanterns be prepared only as required, and used immediately.

MIMOTOPES

International
Tel : + 61 3 9565 1111
Fax : + 61 3 9565 1199
mimotopes@mimotopes.com

France
Tel : + 33 1 5858 0002
Fax : + 33 1 5858 0006
europe@mimotopes.com

United Kingdom
Tel: +44 151 648 3343
Fax: +44 151 648 3328
uk@mimotopes.com

USA West
Tel : + 1 858 558 5800
Fax : + 1 858 558 5810
Tel : 800 644 1866
Fax : 800 655 1866
uswest@mimotopes.com

USA East
Tel : + 1 919 873 1123
Fax : + 1 919 873 1127
Tel : 800 633 8161
Fax : 800 424 3970
useast@mimotopes.com

http://www.synphase.com http://www.mimotopes.com