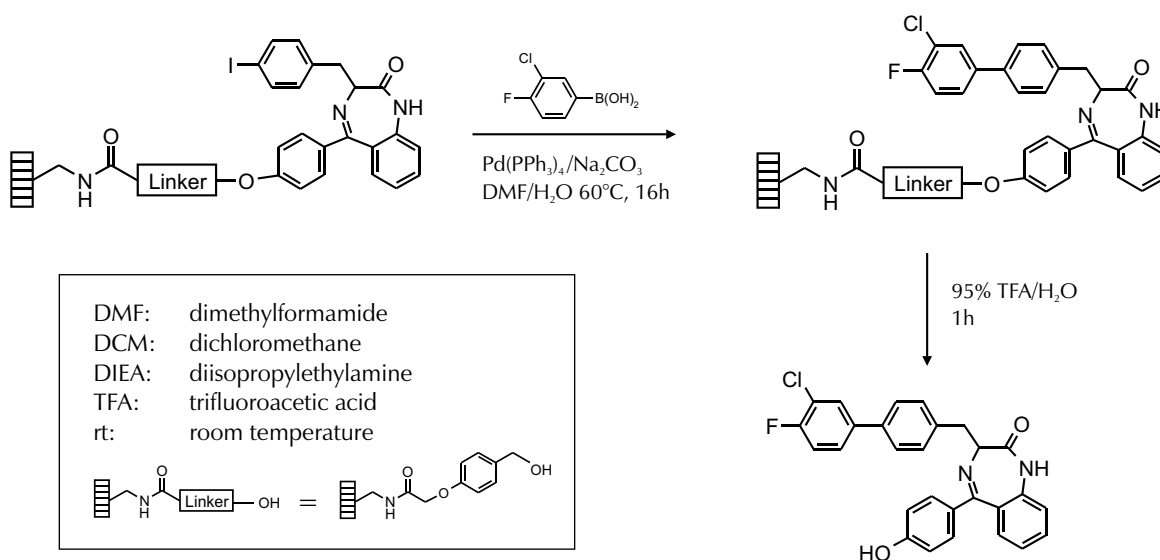




## Suzuki Coupling on a Support-Bound 1,4-Benzodiazepine

**1,4-Benzodiazepines containing an iodo-aryl moiety** may be further derivatised using a Suzuki coupling reaction. In the following example, the iodine substituent of a 1,4-benzodiazepine (generated from Fmoc-4-iodo-L-phenylalanine)<sup>1</sup> on SynPhase™ Lanterns is replaced with a 3-chloro-4-fluorophenyl group, yielding a biphenyl substituted 1,4-benzodiazepine upon cleavage from the solid support.



### Preparation of Stock Solutions

**Solutions of Pd(PPh<sub>3</sub>)<sub>4</sub>/DMF (0.09M), 3-chloro-4-fluorobenzeneboronic acid/DMF**

**(0.2M) and Na<sub>2</sub>CO<sub>3</sub>/H<sub>2</sub>O (5M)** are prepared in an N<sub>2</sub>-filled gloved bag using degassed solvents.

### Suzuki Coupling on 1,4-Benzodiazepine

**In the glove bag**, each 1,4-benzodiazepine substituted D-Series Lantern<sup>1</sup> (initial specified loading: 35μmol) is treated with Pd(PPh<sub>3</sub>)<sub>4</sub>/DMF (200μL, final concentration 0.036M, 18μmol, 0.5 mole equivalents), 3-chloro-4-fluorobenzeneboronic acid/DMF (250μL, final concentration 0.1M, 50μmol, 1.4 mole equivalents), and aqueous Na<sub>2</sub>CO<sub>3</sub> (50μL, final concentration 0.5M, 250μmol, 7 mole

equivalents). This gives ca. 0.5mL reaction volume/Lantern. The reaction vessel is sealed, removed from the glove bag, heated at 60°C for 16h, then cooled to rt and the reagent solution decanted. The Lanterns are washed with DMF (1×3 min), a solution of sodium diethyldithiocarbamate (5mg/mL)/DIEA (5μL/mL) in DMF (2×10min), DMF (3×3min), and DCM (3×3min).

## Cleavage

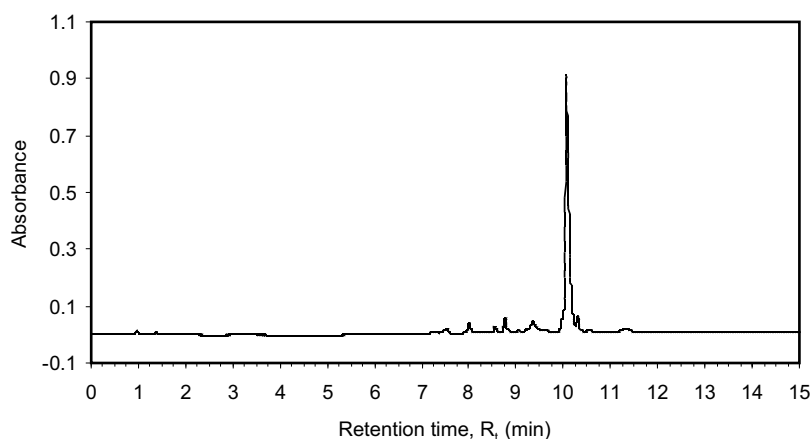
**Individual Lanterns are placed** in polypropylene tubes and treated with 95% TFA/H<sub>2</sub>O (0.6-0.8mL) for 1h. The Lanterns are removed and the cleaved products are concentrated using a centrifugal evaporator. The residue is freeze-dried from 90%

CH<sub>3</sub>CN/H<sub>2</sub>O to afford the benzodiazepine product (yield 80%, based on the initial Lantern loading). Samples are dissolved in 90% CH<sub>3</sub>CN/H<sub>2</sub>O for HPLC and ES-MS analysis.

## Analytical Data

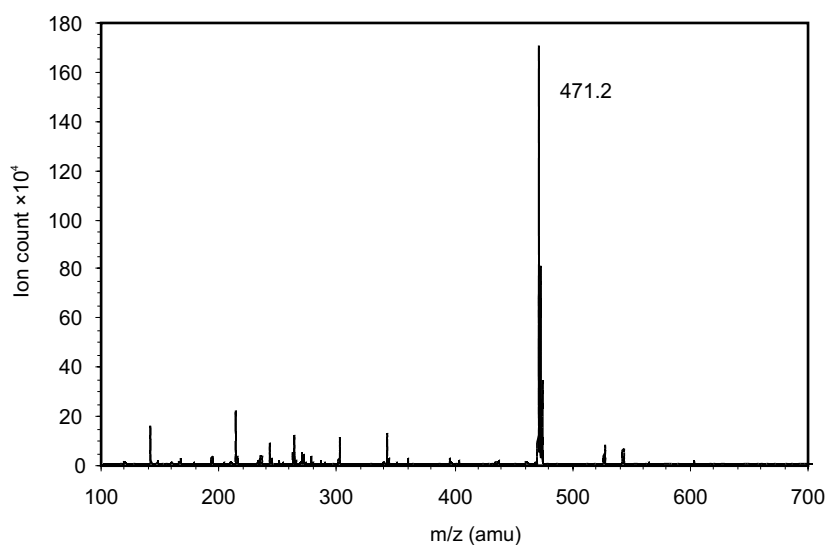
### Reverse phase HPLC trace of the crude benzodiazepine

Detection at 214nm



### Electrospray MS trace of LC peak at $R_t = 10.07$ min

Molecular Formula: C<sub>28</sub>H<sub>20</sub>ClFN<sub>2</sub>O<sub>2</sub>  
Monoisotopic Mol. Weight: 470.12amu  
[M+H]<sup>+</sup> peak at 471.2amu



### Reference

1 See Mimotopes SynPhase Chemistry Note SCN 011-2.



**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