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### **Supporting Information**

## Flow Photolysis of Aryldiazoacetates Leading to Dihydrobenzofurans via Intramolecular C–H Insertion

### Katie S. O'Callaghan,<sup>a</sup> Denis Lynch,<sup>a</sup> Marcus Baumann,<sup>b</sup> Stuart G. Collins,<sup>a\*</sup> Anita R. Maguire<sup>a,c\*</sup>

 <sup>a</sup> School of Chemistry, Analytical and Biological Chemistry Research Facility, Synthesis and Solid State Pharmaceutical Centre, University College Cork, Ireland.
 <sup>b</sup> School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland.
 <sup>c</sup> School of Pharmacy, University College Cork, Ireland.
 \*E-mail: a.maguire@ucc.ie

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## **Experimental**

**General Procedures.** Solvents were distilled prior to use as follows: dichloromethane was distilled from phosphorous pentoxide, ethyl acetate was distilled from potassium carbonate, and hexane was distilled prior to use. Organic phases were dried using anhydrous magnesium sulfate. All commercial reagents were used without further purification.

<sup>1</sup>H (300 MHz) and <sup>13</sup>C (75.5 MHz) NMR spectra were recorded on a Bruker Avance 300 NMR spectrometer. <sup>1</sup>H (400 MHz) and <sup>13</sup>C (100.6 MHz) NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer. All spectra were recorded at 300 K in deuterated chloroform (CDCl<sub>3</sub>) unless otherwise stated, using tetramethylsilane (TMS) as an internal standard. Chemical shifts ( $\delta_{\rm H}$  and  $\delta_{\rm C}$ ) are reported in parts per million (ppm) relative to TMS and coupling constants (*J*) are expressed in hertz (Hz). Splitting patterns in <sup>1</sup>H spectra are designated as s (singlet), d (doublet), q (quartet), AB (AB system) or m (multiplet).

Infrared spectra were measured using universal ATR sampling accessories on a Perkin Elmer Spectrum Two Spectrometer. Flash column chromatography was carried out using silica gel 60, 0.040-0.063 mm (Merck). Thin layer chromatography (TLC) was carried out on pre-coated silica gel plates (Merck 60 PF<sub>254</sub>). Visualisation was achieved by UV (254 nm) light absorption or phosphomolybdic acid staining. Melting points were carried out on a Unimelt Thomas Hoover Capillary melting point apparatus and are uncorrected.

High resolution mass spectra (HRMS) recorded on a Waters Vion IMS instrument (SAA055 K) with Waters Acquity I-class UPLC in electrospray ionization (ESI) mode using 50% acetonitrile–water containing 0.1% formic acid as eluent and Leucine Enkephalin as reference solution. All samples were made up in acetonitrile.

All continuous processes were performed using a flow chemistry system consisting of four HPLC pumps or a flow chemistry system consisting of three peristaltic pumps. All continuous flow photoreactions were carried out in a 10 mL reactor with either a medium pressure mercury lamp (75 W), 365 nm LEDs (50 W) or 450 nm LEDs (12 W). Three wavelength filters with different cut-off wavelengths were used with the mercury lamp; 109–2000 nm, 250–390 nm or 300–2000 nm. To prepare the reactor for operation pumps were purged with the solvent to be used in the reaction prior to use. All reaction tubing, coils, inlets and connections were also purged thoroughly in a similar manner. All pumps were primed using appropriate solvents and pump backwash reservoirs were filled. The solvent that was to be used was flushed through all injectors and reactors. Pumps were run in advance at reaction flow rates to check for stability, in both reagent and solvent lines. General specifications of flow systems used: Material of tubing: PFA; Diameter of tubing: 1 mm; Working flow rates: 0.05 mL/min–9.99 mL/min; Tubular reactor working volume: 10 mL; Temperature range: –20 to +80 °C.

## **Details of Continuous Flow Platforms**

Continuous processes were performed using flow chemistry platforms, as previously described, consisting of a Vapourtec R-Series flow system consisting of four piston (HPLC) pumps and a Vapourtec E-Series flow system consisting of three peristaltic pumps.

# **Table S1.** General specifications for Vapourtec R-Series system

General Specifications for Continuous Flow System			
Material of tubing	PFA		
Diameter of tubing	1 mm		
Working flow rates	0.5 – 9.99 mL/min		
Tubular reactor working volume	10 mL		
Temperature range	-70 to 250 °C		

General Specifications for Continuous Flow System			
Material of tubing PFA			
Diameter of tubing	1 mm		
Working flow rates	0.02 – 10.0 mL/min		
Tubular reactor working volume	10 mL		
Temperature range	-70 to 250 °C		

Table S2. General specifications for Vapourtec E-Series system

For photochemical reactions using the medium pressure mercury lamp (75 W) the Vapourtec R-Series was used with a UV-150 reactor and one of three wavelength filters (300–2000 nm, 109–2000 nm or 250–390 nm)

For photochemical reactions using the 365 nm LEDs (50 W) the Vapourtec E-Series was used with a UV-150 photoreactor.

For photochemical reactions using the 450 nm LEDs (12 W), a LED flexible ribbon strip (84.5 cm) was used from Creative Lighting Solutions.

 $\alpha$ -Diazoesters **3**, **4** and **5** were prepared following reported procedures.

## Photochemical C–H insertion to form 2,3-Dihydrobenzofurans.

# Method A: General procedure for photochemical C–H insertion reactions using a mercury lamp (75 W).

A 25 mL solution of aryldiazoacetate (0.04 M) in TBME/MeCN (80:20) was prepared. The reaction solution (24 mL) was pumped (1.0 mL.min<sup>-1</sup>) to a 10 mL photoreactor coil [mercury lamp, (filter hv = 250–390 nm), 75 W, 10 min residence time] before passing through a back pressure regulator (8 bar). The product stream was collected in a round bottom flask. The mixture was then concentrated under reduced pressure to provide the crude product mixture; a <sup>1</sup>H NMR spectrum was obtained and following column chromatography on silica gel employing hexane/ethyl acetate (99:1) as the eluent, both isomers of the dihydrobenzofuran were isolated. The less polar *trans* isomers were isolated as colourless oils while the more polar *cis* isomers were isolated as white solids.

# Method B: General procedure for photosensitised C–H insertion reactions using a mercury lamp (75 W).

A 25 mL solution of aryldiazoacetate (0.04 M) and 4,4'-dimethoxybenzophenone **9** (0.05 M) in TBME/MeCN (80:20) was prepared. The reaction solution (24 mL) was pumped (3.33 mL.min<sup>-1</sup>) to a 10 mL photoreactor coil [mercury lamp, (filter hv = 250–390 nm), 75 W, 3 min residence time] before passing through a back pressure regulator (8 bar). The product stream was collected in a round bottom flask. The mixture was then concentrated under reduced pressure to provide the crude product mixture; a <sup>1</sup>H NMR spectrum was obtained and following column chromatography on silica gel employing hexane/ethyl acetate (99:1) as the eluent, both isomers of the dihydrobenzofuran were isolated. The less polar *trans* isomers were isolated as colourless oils while the more polar *cis* isomers were isolated as white solids.

# Method C: General procedure for photosensitised C–H insertion reactions using 365 nm LEDs (50 W).

A 25 mL solution of aryldiazoacetate (0.04 M) and 4,4'-dimethoxybenzophenone **9** (0.05 M) in TBME/MeCN (80:20) was prepared. The reaction solution (24 mL) was pumped (2.0 mL.min<sup>-1</sup>) to a 10 mL photoreactor coil (365 nm LEDs, 50 W, 5 min residence time) before passing through a back pressure regulator (8 bar). The product stream was collected in a round bottom flask. The mixture was then concentrated under reduced pressure to provide the crude product mixture; a <sup>1</sup>H NMR spectrum was obtained and following column chromatography on silica gel employing hexane/ethyl acetate (99:1) as the eluent, both isomers of the dihydrobenzofuran were isolated. The less polar *trans* isomers were isolated as colourless oils while the more polar *cis* isomers were isolated as white solids.

## Method D; General procedure for photochemical C–H insertion reactions using 450 nm LEDs (12 W).

A 25 mL solution of aryldiazoacetate (0.04 M) in TBME/MeCN (80:20) was prepared. The reaction solution (20 mL) was pumped (0.167 mL.min<sup>-1</sup>) to a 10 mL reactor coil fitted with a coiled strip of blue LEDs (450 nm LEDs, 12 W, 60 min residence time) before passing through a back pressure regulator (8 bar). The product stream was collected in a round bottom flask. The mixture was then concentrated under reduced pressure to provide the crude product mixture; a <sup>1</sup>H NMR spectrum was obtained. Signals in the <sup>1</sup>H NMR spectrum of the crude product mixture characteristic of the azine as mentioned by Hashimoto and coworkers<sup>1</sup> were seen at  $\delta_{\rm H} \sim 5.10$  ppm (apparent singlet) in the <sup>1</sup>H NMR spectra and an absorption at ~2108 cm<sup>-1</sup> in the IR spectra of the crude reaction mixtures of the photolysis of aryldiazoacetate **3**. Following column chromatography on silica gel employing hexane/ethyl acetate (99:1) as the eluent, *trans* isomers of the dihydrobenzofurans were isolated as colourless of the.

## 3-Methoxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 6<sup>1,2</sup>

This compound was prepared using **Methods A-D** above from aryldiazoacetate **3** (0.04 M). For **Methods B** and **C** 4,4'-dimethoxybenzophenone **9** (0.05 M) was also added to the 25 mL starting solution. Isolated yields from each method are outlined in **Table 6**.

Method	Input (3)	Mass <i>trans</i> (6a)	Yield <i>trans</i> (6a)	Mass <i>cis</i> (6b)	Yield <i>cis</i> (6b)
	(mg)	(mg)	(%)	(mg)	(%)
Α	277 (0.98 mmol)	64	26	53	21
В	287 (1.02 mmol)	130	50	51	20
С	288 (1.02 mmol)	95	37	30	12
D	236 (0.84 mmol)	54	25	48	23 <sup>a</sup>

#### Table 6.

<sup>a</sup> Isolated as a mixture of *cis* dihydrobenzofuran **6b** and aryldiazoacetate starting material **3**.

Spectral details below and spectra included in Supporting Information are for compounds from **Method B**.

# 2,3-trans-3-Methoxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 6a<sup>1,2</sup>



Spectroscopic characteristics were consistent with previously reported data<sup>1,2</sup> **6a**, Colourless oil;  $v_{max}/cm^{-1}$  (neat): 2953, 1736, 1478, 1234, 748; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.48–7.18 (7H, m), 7.28–7.19 (2H, m), 6.97–6.87 (2H, m), 6.11 (1H, d, *J* = 7.5 Hz), 4.28 (1H, d, *J* = 7.5 Hz), 3.81 (3H, s); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  171.3, 159.3, 140.7, 129.6, 128.7, 128.3, 125.7, 125.2, 123.7, 121.0, 109.9, 85.5, 55.7, 52.6.

### 2,3-cis-3-Methoxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 6b<sup>1,2</sup>



Spectroscopic characteristics were consistent with previously reported data.<sup>1,2</sup> **6b**, white solid; m.p. 90-92 °C (lit. 90-91 °C)<sup>1</sup>;  $\nu_{max}/cm^{-1}$  (neat): 2950, 1733, 1479, 1234, 748; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.39–7.18 (7H, m), 7.00–6.90 (2H, m), 5.98 (1H, d, *J* = 9.8 Hz), 4.61 (1H, d, *J* = 9.8 Hz), 3.20 (3H, s); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  170.3, 160.4, 137.1, 129.6, 128.3, 128.1, 126.2, 125.9, 124.7, 121.3, 110.0, 85.7, 54.0, 51.6.

#### 3-Benxyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 7<sup>2</sup>

This compound was prepared using **Methods A-D** above from aryldiazoacetate **4** (0.04 M). For **Methods B** and **C** 4,4'-dimethoxybenzophenone **9** (0.05 M) was also added to the starting solution. Isolated yields from each method are outlined in **Table 7**.

Table 7.	
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Method	Input (4)	Mass <i>trans</i> (7a)	Yield <i>trans</i> (7a)	Mass <i>cis</i> (7b)	Yield <i>cis</i> (7b)
	(mg)	(mg)	(%)	(mg)	(%)
Α	368 (1.03 mmol)	59	18	50	14
В	322 (0.90 mmol)	136	46	52	17
С	302 (0.84 mmol)	84	30	13	5
D	309 (0.86 mmol)	41	14	43	15 <sup><i>a</i></sup>

<sup>a</sup> Isolated as a mixture of *cis* dihydrobenzofuran **7b** and aryldiazoacetate starting material **4**.

Spectral details below and spectra included in Supporting Information are for compounds from **Method B**.

#### 2,3-trans-3-Benzyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 7a<sup>2</sup>



Spectroscopic characteristics were consistent with previously reported data.<sup>2</sup> **7a**, colourless oil;  $v_{max}/cm^{-1}$  (neat): 3033, 1733, 1478, 1232, 748, 695. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.41–7.28 (11H, m), 7.27–7.16 (1H, m), 6.95– 6.84 (2H, m), 6.12 (1H, d, *J* = 7.5 Hz), 5.29–5.18 (2H, fine AB q, *J* = 12.4 Hz), 4.32 (1H, d, *J* = 7.5 Hz); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  170.7, 159.4, 140.7, 135.4, 129.7, 128.8, 128.7, 128.5, 128.4, 128.3, 125.8, 125.3, 123.8, 121.0, 110.0, 85.5, 67.5, 55.9.

## 2,3-cis-3-Benzyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 7b<sup>2</sup>



Spectroscopic characteristics were consistent with previously reported data.<sup>2</sup> **7b**, white solid; m.p. 88-90 °C (lit. 89-90 °C)<sup>2</sup>;  $\nu_{max}/cm^{-1}$  (neat): 2973, 1736, 1479, 1228, 749, 694; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.40–7.18 (10H, m), 7.04–6.90 (4H, m), 5.98 (1H, d, *J* = 9.8 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 4.64 (1H, d, *J* = 9.8 Hz), 4.50 (1H, d, *J* = 12.2 Hz); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  169.8, 160.4, 137.0, 135.2, 129.6, 128.43, 128.39, 128.3, 128.2, 128.1, 126.4, 125.9, 124.8, 121.3, 110.0, 85.7, 66.7, 53.8.

## 3-Isopropyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 8<sup>2</sup>

This compound was prepared using **Methods A-D** above from aryldiazoacetate **5** (0.04 M). For **Methods B** and **C** 4,4-dimethoxybenzophenone **9** (0.05 M) was also added to the starting solution. Isolated yields from each method are outlined in **Table 8**.

Tabl	e 8.
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Method	Input (5)	Mass <i>trans</i> (8a)	Yield <i>trans</i> (8a)	Mass <i>cis</i> (8b)	Yield <i>cis</i> (8b)
	(mg)	(mg)	(%)	(mg)	(%)
Α	296 (0.95 mmol)	46	17	44	16
В	297 (0.96 mmol)	117	44	40	15
С	297 (0.96 mmol)	86	32	-	-
D	240 (0.77 mmol)	22	10	28	13 <sup><i>a</i></sup>

<sup>a</sup> Isolated as a mixture of *cis* dihydrobenzofuran **8b** and aryldiazoacetate starting material **5**.

Spectral details below and spectra included in Supporting Information are for compounds from **Method B**.

#### 2,3-trans-3-Isopropyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 8a<sup>2</sup>



Spectroscopic characteristics were consistent with previously reported data.<sup>2</sup> **8a**, colourless oil;  $v_{max}/cm^{-1}$  (neat): 2981, 1729, 1478, 1234, 748, 697; <sup>1</sup>H NMR (**300** MHz, CDCl<sub>3</sub>):  $\delta$  7.45–7.27 (6H, m), 7.27–7.19 (1H, m), 6.97–6.86 (2H, m), 6.11 (1H, d, *J* = 7.7 Hz), 5.13 (1H, septet, *J* = 6.3 Hz), 4.22 (1H, d, *J* = 7.7 Hz), 1.25–1.18 (6H, containing 2 × d at 1.31 and 1.29, *J* = 6.2 Hz); <sup>13</sup>C NMR (**75.5** MHz, CDCl<sub>3</sub>):  $\delta$  170.3, 159.3, 140.9, 129.6, 128.8, 128.3, 125.8, 125.0, 124.2, 120.9, 109.9, 85.5, 69.3, 56.0, 21.88, 21.86.

#### 2,3-cis-3-Isopropyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran 8b<sup>2</sup>



Spectroscopic characteristics were consistent with previously reported data.<sup>2</sup> **8b**, white solid; m.p. 55-57 °C (lit. 56-58 °C)<sup>2</sup>;  $v_{max}/cm^{-1}$  (neat): 2980, 1727, 1480, 1104, 747, 695. <sup>1</sup>H NMR (**300** MHz, CDCl<sub>3</sub>):  $\delta$ 7.40–7.21 (7H, m), 6.99–6.89 (2H, m), 5.96 (1H, d, *J* = 9.9 Hz), 4.65–4.50 (2H, m), 0.92 (3H, d, *J* = 6.3 Hz), 0.68 (3H, d, *J* = 6.2 Hz); <sup>13</sup>C NMR (**75.5** MHz, CDCl<sub>3</sub>):  $\delta$  169.4, 160.3, 137.3, 129.4, 128.3, 128.2, 126.6, 125.9, 125.1, 121.1, 109.9, 85.6, 68.5, 53.7, 21.4, 20.9.

#### 3-(2-(Benzyloxy)phenyl)-4,4-dimethyloxetan-2-one 13

The title compound was isolated from the reaction of aryldiazoacetate **5** (297 mg, 0.96 mmol, 0.04 M) and 4,4-dimethoxybenzophenone **9** (294 mg, 1.21 mmol, 0.05 M) using **Method C**.



White solid (101 mg, 37% yield); m.p. 69-70 °C;  $v_{max}/cm^{-1}$  (neat): 2979, 2932, 1805, 1729, 1453, 1238, 1104, 752, 697; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.18-7.48 (7H, m), 6.88-7.05 (2H, m), 5.04 (2H, s), 4.73 (1H, s), 1.53 (3H, s), 1.17 (3 H, s); <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>):  $\delta$  169.7, 155.9, 136.2, 129.3, 128.8, 128.7, 128.4, 128.0, 121.2, 120.9, 111.3, 82.3, 70.4, 59.6, 27.1, 22.6; HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for  $C_{18}H_{19}O_3$  283.1329; Found 283.1324.

# trans-3-Methoxycarbonyl-2-phenyl-2,3-dihydrobenzofuran (6a)





<sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)

# *cis*-3-Methoxycarbonyl-2-phenyl-2,3-dihydrobenzofuran (6b)

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)









# *cis*-3-Benzyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran (7b)

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)





# *trans*-3-Isopropyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran (8a)





# cis-3-Isopropyloxycarbonyl-2-phenyl-2,3-dihydrobenzofuran (8b)





# 3-(2-(Benzyloxy)phenyl)-4,4-dimethyloxetan-2-one (13)







**Figure S1.** <sup>1</sup>H NMR spectra of crude product mixtures from the photolysis of aryldiazoacetate **3** in the presence of photosensitiser **9** using method **B** for a small scale reaction (287 mg **3**, black spectrum) and a larger scale reaction (2.00 g **3**, red spectrum).

UV/Vis Spectrum of Methyl 2-(2-(benzyloxy)phenyl)-2-diazoacetate (3) (100  $\mu$ M) in TMBE/MeCN (80:20)



UV/Vis Spectrum of Benzyl 2-(2-(benzyloxy)phenyl)-2-diazoacetate (4) (100  $\mu\rm M$ ) in TBME/MeCN (80:20)



# UV/Vis Spectrum of Isopropyl 2-(2-(benzyloxy)phenyl)-2-diazoacetate (5) (100 $\mu$ M) in TBME/MeCN (80:20)



UV/Vis Spectrum 4,4'-Dimethoxybenzophenone (9) (100  $\mu$ M) in TBME/MeCN (80:20)



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