

## Supplementary information

for

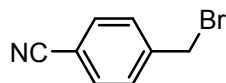
# Extending Molecular Computational Identification into the Near-infrared for Populations of Small Objects

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Compounds **1**,<sup>53</sup> **2**,<sup>54</sup> and **8**<sup>57,58</sup> are all known, but the multi-step preparation of **2** is collected here in one location for easy reference.

### Synthesis of $\alpha$ -bromo-p-tolunitrile<sup>S1</sup>

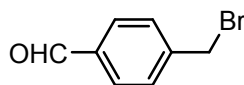
p-Tolunitrile (30.0 g, 0.256 mol), N-bromosuccinimide, (45.6 g, 0.256 mmol), and benzoyl peroxide (0.6 g, 2.5 mmol) were added to DCM (dichloromethane, 180 mL). This mixture was heated under reflux for 3 days, after which time all solids floated to the surface. The mixture was filtered when hot and the solvent was removed by rotary evaporation. The orange coloured solid was dissolved in DCM (200 mL) and washed with water (200 mL X 3). The organic layer which became pale yellow was dried by anhydrous MgSO<sub>4</sub>. Then the solvent was removed by rotary evaporation. The product was recrystallized from cyclohexane (1200 mL) and dried under vacuum at room temperature overnight. The product appeared as white crystals. (White solid, 27.0 g, yield 53.8%).



<sup>1</sup>H NMR (300 MHz, Chloroform-*d*)  $\delta$  7.65 (d,  $J$  = 8.3 Hz, 2H, ortho-H-Ar-CN), 7.50 (d,  $J$  = 8.2 Hz, 2H, meta-H-Ar-CN), 4.48 (s, 2H, Ar-CH<sub>2</sub>Br).

### Synthesis of 4-bromomethyl-benzaldehyde<sup>S2</sup>

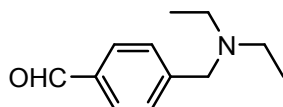
$\alpha$ -bromo-p-tolunitrile (20.0 g, 0.102 mol) was dissolved in toluene (200 mL) and cooled to 0 °C in a 2-litre three-necked flask. DIBAL-H (diisobutylaluminium hydride, 25% w/w in hexane, 115.9 mL, 0.143 mol) was added dropwise under N<sub>2</sub>. The solution was stirred for another hour at 0 °C. Chloroform (250 mL) was then added followed by hydrochloric acid (10% HCl, 600 mL), and the solution was stirred at room temperature for one hour. The organic layer was separated, washed with distilled water (300 mL X 3), dried over anhydrous MgSO<sub>4</sub>, and filtered. The solvent was almost completely removed from the filtrate by rotary evaporation, and the residue was cooled, filtered, washed with cold hexane (300 mL), and dried at room temperature under vacuum overnight. The product appeared as white crystals. (White solid, 17.3 g, yield 85%).



<sup>1</sup>H NMR (300 MHz, Chloroform-*d*)  $\delta$  10.02 (s, 1H, Ar-CHO), 7.87 (d,  $J$  = 8.2 Hz, 2H, ortho-H-Ar-CHO), 7.56 (d,  $J$  = 8.1 Hz, 2H, meta-H-Ar-CHO), 4.52 (s, 2H, Ar-CH<sub>2</sub>Br).

### Synthesis of 4-diethylaminomethyl-benzaldehyde<sup>55</sup>

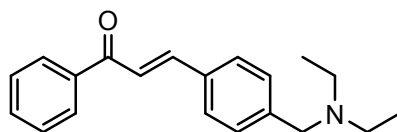
To a stirred solution of 4-bromomethyl-benzaldehyde (17 g, 85.4 mmol) in THF (400 mL) was added diethylamine (26.5 mL, 0.256 mol) and the resulting mixture was heated at reflux for two hours. The solvent was removed by rotary evaporation and the resulting oil was partitioned between diethyl ether (400 mL) and water (400 mL). The organic layer was extracted with hydrochloric acid (1M, 400 mL, 33.3 mL 36.5% HCl in 366.7 mL water), the aqueous layer was neutralised with sodium hydroxide solution (2M, 200 mL, 16 g NaOH in 200 mL water) and extracted with diethyl ether (400 mL X 2). The organic layer was washed with saturated NaCl solution (400 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent removed by rotary evaporation giving a pale yellow colour liquid. (Pale yellow oil, 13.9 g, yield 85%).



<sup>1</sup>H NMR (300 MHz, Chloroform-*d*) δ 9.99 (s, 1H, Ar-CHO), 7.82 (d, *J* = 8.1 Hz, 2H, ortho-H-Ar-CHO), 7.52 (d, *J* = 7.9 Hz, 2H, meta-H-Ar-CHO), 3.62 (s, 2H, Ar-CH<sub>2</sub>NEt<sub>2</sub>), 2.52 (q, *J* = 7.1 Hz, 4H, Ar-CH<sub>2</sub>N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 1.04 (t, *J* = 7.1 Hz, 6H, Ar-CH<sub>2</sub>N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>).

### Synthesis of 3-(4-diethylaminomethyl-phenyl)-1-phenyl-propenone<sup>54</sup>

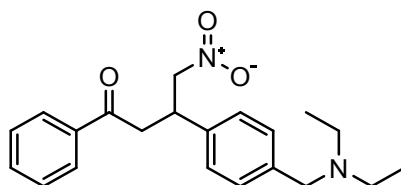
A stirred solution of 4-diethylaminomethyl-benzaldehyde (13 g, 68.0 mmol), acetophenone (7.93 mL, 68.0 mmol) and NaOH (6.80 mmol) in methanol (300 mL) was heated at reflux for 16 hours. The solvent was removed by rotary evaporation and the yellow material was purified by flash column chromatography (40% hexanes in ethyl acetate to ethyl acetate). (Yellow oil, 11.0 g, yield 55%).



<sup>1</sup>H NMR (300 MHz, Chloroform-*d*) δ 8.06 – 7.98 (m, 2H, ortho-H-Ar-CO), 7.81 (d, *J* = 15.6 Hz, 1H, Ar-CO-CH=CH), 7.64 – 7.46 (m, 6H, para&meta-H-Ar-CO, Ar-CO-CH=CH, meta-H-Ar-CH<sub>2</sub>NEt<sub>2</sub>), 7.40 (d, *J* = 8.0 Hz, 2H, ortho-H-Ar-CH<sub>2</sub>NEt<sub>2</sub>), 3.59 (s, 2H, Ar-CH<sub>2</sub>NEt<sub>2</sub>), 2.53 (q, *J* = 7.1 Hz, 4H, Ar-CH<sub>2</sub>N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 1.05 (t, *J* = 7.1 Hz, 6H, Ar-CH<sub>2</sub>N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>).

### Synthesis of 3-(4-Diethylaminomethyl-phenyl)-4-nitro-1-phenyl-butan-1-one<sup>54</sup>

A solution of 3-(4-diethylaminomethyl-phenyl)-1-phenyl-propenone (2.5 g, 8.52 mmol) in methanol (500 mL) was treated with diethylamine (8.81 mL, 85.2 mmol) and nitromethane (4.57 mL, 85.2 mmol) in a 1-litre round-bottomed flask and heated under reflux for 16 hours. The solution was cooled and all the solvent was removed by rotary evaporation. The resulting oil was purified by crystallization from ethanol. (White solid, 1.8 g, yield 59.6%).

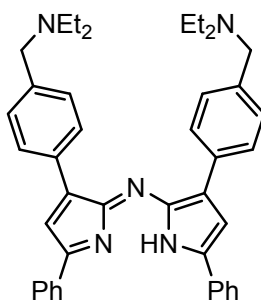


<sup>1</sup>H NMR (300 MHz, Chloroform-*d*) δ 7.96 – 7.85 (m, 2H, ortho-H-Ar-CO), 7.58 (t, *J* = 7.4 Hz, 1H, para-H-Ar-CO), 7.45 (t, *J* = 7.4 Hz, 2H, meta-H-Ar-CO), 7.32 – 7.17 (m, 6H, meta&ortho-H-Ar-CH<sub>2</sub>NEt<sub>2</sub>), 4.87 – 4.62 (m, 2H, Ar-CO-CH<sub>2</sub>CH-CH<sub>2</sub>NO<sub>2</sub>), 4.21 (p, *J* = 7.2, 6.8 Hz, 1H, Ar-CO-CH<sub>2</sub>CH-CH<sub>2</sub>NO<sub>2</sub>), 3.51 (s, 2H, Ar-

$\text{CH}_2\text{NEt}_2$ ), 3.48 – 3.36 (m, 2H, Ar-CO- $\text{CH}_2\text{CH}-\text{CH}_2\text{NO}_2$ ), 2.49 (q,  $J = 7.1$  Hz, 4H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 1.02 (t,  $J = 7.1$  Hz, 6H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ).

**Synthesis of [3-(4-Diethylamino-methyl-phenyl)-5-phenyl-pyrrol-2-ylidene]-[3-(4-diethylamino-methyl-phenyl)-5-phenyl-1H-pyrrol-2-yl]-amine<sup>54</sup>**

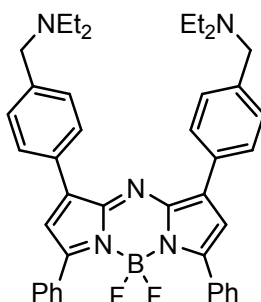
A 500 mL round-bottomed flask was charged with 3-(4-Diethylaminomethyl-phenyl)-4-nitro-1-phenylbutan-1-one (1.8 g, 6.13 mmol), ammonium acetate (18.9 g, 0.245 mol), and ethanol (80 mL) and heated under reflux for two days. The reaction was cooled to room temperature and filtered, and the isolated solid was collected. (Blue-black solid, 0.8 g, yield 42.1%)



$^1\text{H}$  NMR (300 MHz, Chloroform-*d*)  $\delta$  8.05 (d,  $J = 8.1$  Hz, 4H, ortho-H-Ar- $\text{CH}_2\text{-NEt}_2$ ), 7.95 (d,  $J = 7.8$  Hz, 4H, meta-H-Ar- $\text{CH}_2\text{-NEt}_2$ ), 7.51 (dt,  $J = 20.2, 7.3$  Hz, 10H, H-Ar-pyrrole), 7.20 (s, 2H, H-pyrrole), 4.03 (s, 4H, Ar- $\text{CH}_2\text{NEt}_2$ ), 2.89 (q,  $J = 7.2$  Hz, 8H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 1.23 (t,  $J = 7.2$  Hz, 12H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ).

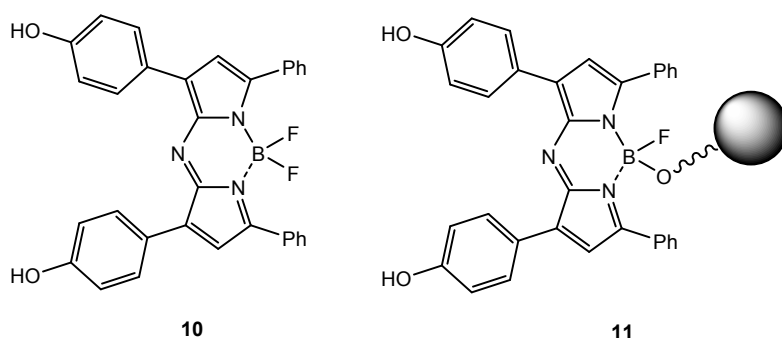
**Synthesis of  $\text{BF}_2$ -chelated-[3-(4-Diethylamino-methyl-phenyl)-5-phenyl-pyrrol-2-ylidene]-[3-(4-diethylamino-methyl-phenyl)-5-phenyl-1H-pyrrol-2-yl]-amine (2)<sup>54</sup>**

[3-(4-Diethylamino-methyl-phenyl)-5-phenyl-pyrrol-2-ylidene]-[3-(4-diethylamino-methyl-phenyl)-5-phenyl-1H-pyrrol-2-yl]-amine (700 mg, 1.13 mmol) was dissolved in dry DCM (300 mL), treated with diisopropylethylamine (2.4 mL, 13.6 mmol) and boron trifluoride diethyl etherate (2.5 mL, 20.3 mmol), and stirred at room temperature under  $\text{N}_2$  for 24 hours. The mixture was washed with water (300 mL X 2), and organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to dryness. Purification by flash column chromatography eluting with 5% MeOH in DCM gave the product as a copper coloured solid. (Copper coloured solid, 0.26 g, 35%).



$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.08 – 7.99 (m, 8H, H-Ar- $\text{CH}_2\text{-NEt}_2$ ), 7.52 – 7.41 (m, 10H, H-Ar-pyrrole), 7.04 – 7.00 (m, 2H, H-pyrrole), 3.66 (s, 4H, Ar- $\text{CH}_2\text{NEt}_2$ ), 2.58 (q,  $J = 7.1$  Hz, 8H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 1.09 (t,  $J = 7.1$  Hz, 12H, Ar- $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$ ).

Compound **10** (which is a known intermediate in a solar energy conversion material)<sup>88</sup> and its bead-bound version **11** were also prepared and tested.

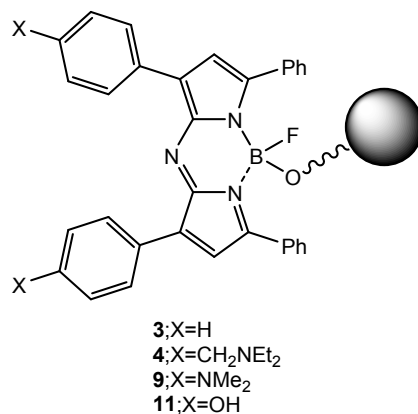


The pH-dependent fluorescence of **10** has an ICT origin like that of **8**, and gives  $\lambda_{\text{acid}} = 713$  nm,  $FE_{\text{H}^+} > 50$  and  $\text{p}K_{\text{a}}^* = 8.7$  in free solution. While the  $\text{p}K_{\text{a}}^*$  value is useful and the switching factor is excellent for our purpose, the emission band is red-shifted and very broad compared to that of the PASS 1 case (**1**). This is a potential incompatibility for creating multi-valued logic tags, e.g. YES + PASS 1. Furthermore, the on-bead version of **10** (**11**) results in  $\lambda_{\text{acid}} = 780$  &  $827$  nm,  $\lambda_{\text{base}} = 730$  nm,  $FE_{\text{H}^+} = 37$  and  $\text{p}K_{\text{a}}^* = 6.5$ . The incompatibility with **3** is rather pronounced in this situation, with the dual emission suggesting some domain formation on the bead surface. Although **10** and **11** are easier to synthesize, these incompatibilities prevent them from being useful MCID tags at present. Nevertheless we report them here for completeness.

### Bead-tagging

#### Single tagged beads **3**, **4**, **9** and **11**

TentaGel S-OH beads (300 mg, 0.078 mmol) were suspended in dry THF (10 mL) and treated with NaH (60% dispersion in mineral oil, 3.12 mg, 0.078 mmol) for 20 minutes. azaBODIPY derivative **1** (3.9 mg, 0.0078 mmol) or **2** (5.2 mg, 0.0078 mmol) or **8** (4.6 mg, 0.0078 mmol) or **10** (4.1 mg, 0.0078 mmol) was dissolved in dry THF in a 10 mL volumetric flask. 1 mL of the azaBODIPY solution was added and the suspension was agitated for 5 hours at room temperature. Ethanol (10 mL) was added and stirred for another 30 minutes. The resin was filtered, washed with dry  $\text{CH}_2\text{Cl}_2$  (10 mL) and agitated in dry  $\text{CH}_2\text{Cl}_2$  (10 mL) for 20 minutes, following by a wash with dry THF (10 mL) and agitated for a further 20 minutes in dry THF (10 mL). The washing sequence was repeated three times and the beads were filtered and air-dried.



#### Double tagged beads **5**, **6** and **7**

TentaGel S-OH beads (300 mg, 0.078 mmol) were suspended in dry THF (10 mL) and treated with NaH (60% dispersion in mineral oil, 3.12 mg, 0.078 mmol) for 20 minutes. azaBODIPY derivative **1** (3.9 mg, 0.0078 mmol) and **2** (5.2 mg, 0.0078 mmol) were dissolved in dry THF in a 10 mL volumetric flask respectively. 0.33 mL of the azaBODIPY **1** solution and 0.67 mL of the azaBODIPY **2** were added and the suspension was agitated for 5 hours at room temperature to give the YES + 2 PASS 1 logic type beads **5**. Similarly, 0.50 mL of the azaBODIPY **1** solution and 0.50 mL of the azaBODIPY **2** gave the YES + PASS 1 logic type beads **6** while 0.67 mL of the azaBODIPY **1** solution and 0.33 mL of the azaBODIPY **2** gave the 2 YES + PASS 1 logic type beads **7**. Ethanol (10 mL) was added and stirred for another 30 minutes. The resin was filtered, washed with dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and agitated in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) for 20 minutes, following by a wash with dry THF (10 mL) and agitated for a further 20 minutes in dry THF (10 mL). The washing sequence was repeated three times and the beads were filtered and air-dried.

### Full version of Figure 2

All the pH values studied are given below.

**Figure 2. pH-dependent fluorescence spectra of five types of logic gates when tagged onto TentaGel™ S-OH beads.** The pH values (in order of decreasing intensity at the peak wavelength) are; a) 3.0, 3.9, 5.1, 6.1, 7.1, 8.2, 9.1 and 10.1. b) 4.0, 4.6, 5.2, 5.5, 5.8, 6.0, 6.2, 6.4, 6.7, 6.9, 7.2, 7.6, 8.0, 8.4, 9.0, 11.0, 10.3 and 9.7. c) 3.9, 4.6, 5.0, 5.2, 5.5, 5.7, 5.9, 6.1, 6.3, 6.5, 6.7, 7.0, 7.1, 7.6, 8.0, 9.8, 9.0, 8.0, 11.0 and 8.5. d) 3.8, 4.1, 4.6, 5.1, 5.6, 5.8, 5.9, 6.1, 6.3, 6.5, 6.7, 7.0, 7.2, 7.4, 8.5, 11.1, 7.98, 9.1 and 9.9. e) 3.6, 4.0, 4.6, 5.0, 5.5, 5.7, 5.9, 6.2, 6.4, 6.7, 7.0, 7.3, 11.0, 9.8, 8.1 and 9.2.

S1. V. Ashokkumar and A. Siva, *Org. Biomol. Chem.* 2017, **15**, 2551.

S2. X. –Z. Wang and T. R. Burke, *Synlett* 2004, 469.