# Communication

# **Electronic Supplementary Material**

## One "Click" access to self-complementary molecular modules for halogen bonding

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## S.1 General procedures

All syntheses were performed under nitrogen atmosphere. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer, chemical shifts are reported in  $\delta$  vs. TMS. <sup>19</sup>F NMR spectra were recorded on a Bruker 200 AC equipped with a QNP probe. IR spectra were recorded in KBr pellets on a Perkin Elmer Spectrum-One spectrophotometer.

UV-vis spectra absorption spectra were recorded in solution using a Perkin Elmer Lambda 40 spectrophotometer. Emission spectra were recorded on a Perkin-Elmer LS 55 fluorescence spectrometer.

Elemental analyses were performed in the Microanalytical Laboratory of the Dipartimento di Scienze del Farmaco, University of Padova (Italy). Melting points (M.p.) were determined in glass capillaries on a Büchi 535 apparatus.

4-Ethynyl-dimethylaniline was purchased by Aldrich. 4-Iodo-2,3,5,6-tetrafluoroaniline and the fluorinated azides **1a-c** were prepared according to the literature. <sup>[S1]</sup>

## S.2 Synthesis

## Synthesis of 2c (procedure A)

Procedure (A): The synthesis was carried out under inert atmosphere (nitrogen). In a 50 mL round bottomed flask 291 mg (0.92 mmol) of 1-azido-2,3,5,6-tetrafluoro-4-iodobenzene and 160 mg (1.1 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine were dissolved in 50 mL of freshly distilled tetrahydrofuran. Under stirring, to the resulting solution was drop wise added a H<sub>2</sub>O solution (2 mL) of 25 mg (0.1 mmol) of CuSO<sub>4</sub>·5H<sub>2</sub>O and 40 mg (0.2 mmol) of sodium ascorbate. The mixture was stirred at room temperature for 72 h, then 20 mL of were added. The organic phase was washed with water (2 × 15 mL), then dried on MgSO<sub>4</sub> and rotoevaporated to dryness. The solid residue was dissolved in a small amount of CH<sub>2</sub>Cl<sub>2</sub> and precipitated with *n*-hexane. Following this procedure, **2c** was obtained as a buff microcrystalline solid in 49% yield.

## Synthesis of 2c (Procedure B)

Procedure (B): The synthesis was carried out under inert atmosphere (nitrogen). In a 50 mL round bottomed flask were sequentially added 634 mg (2.0 mmol) of 1-azido-2,3,5,6-tetrafluoro-4-iodobenzene, 145 mg (1.0 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine, 3.45 mL (19.8 mmol) of *N*-ethyl-diisopropylamine and 15 mL of acetonitrile. The mixture was stirred at room temperature for 15 min, then 65 mg (0.346 mmol) of CuI were added.

The resulting mixture was stirred at room temperature for 24 hours, then diluted with 20 mL of dichloromethane. The organic phase was washed with water ( $2 \times 15$  mL), dried on MgSO<sub>4</sub>, filtered and rotevaporated. The solid residue was purified by flash chromatography (silica gel and dichloromethane as the eluent) to give 376 mg (0.81 mmol, 81% yield) of the coupling product as a pale brown microcrystalline solid.

### Synthesis of **2a**

The synthesis was carried out according to the above reported Procedure (A). The pale brown coupling product was obtained in 53% yield.

### Synthesis of 2b

The synthesis was carried out according to the above reported Procedure (A). The pale pale brown coupling product was obtained in 61% yield.

4-(1-(2,3,5,6-tetrafluorophenyl)-1H-1,2,3-triazol-4-yl)-N,N-dimethylbenzenamine (2a)



<sup>1</sup>H NMR (300 MHz,  $CD_2Cl_2$ )  $\delta$ : 7.98 (t, 1H,  ${}^4J_{H-F} = 1.0 \text{ Hz}$ ), 7.75 (d, 2H, J = 8.7 Hz), 7.34 (m, 1H), 6.80 (d, 2H), 3.01 (s, 6H).

<sup>13</sup>C NMR (75 MHz,  $CD_2CI_2$ )  $\delta$ : 151.5, 149.0, 146.9 (m, <sup>1</sup> $J_{CF}$  = 250.7 Hz), 142.2 (m, 2C, <sup>1</sup> $J_{CF}$  = 255.7 Hz), 127.4, 120.7, 118.3 (t, <sup>2</sup> $J_{CF}$  = 13.0 Hz), 117.8, 112.8, 107.7 (t, <sup>2</sup> $J_{CF}$  = 22.7 Hz), 40.7.

<sup>19F</sup>NMR (188.05 MHz, CDCl<sub>3</sub>) δ: –136.40 (m, 2F), –146.16 (m, 2F).

IR (KBr): 2917 (br, w), 1645 (m) 1615 (s), 1572 (w), 1523 (s), 1499 (s), 1448 (m), 1353 (m), 1195 (m), 1176 (s), 1017 (m), 936 (s), 824 (m), 792 (m) cm<sup>-1</sup>.

C<sub>16</sub>H<sub>12</sub>F<sub>4</sub>N<sub>4</sub> (336.29), calcd: C, 57.15; H, 3.60; N, 16.66 found: C, 57.3; H, 3.5; N, 16.5. M.p. 143 °C.

MS/ESI: m/z 336.2 found 337.2 (M+H<sup>+</sup>) 359.2 (M+Na<sup>+</sup>)

4-(1-(2,3,5,6-tetrafluoro-4-bromophenyl)-1H-1,2,3-triazol-4-yl)-N,N-dimethylbenzenamine (2b)



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<sup>1</sup>H NMR (300 MHz,  $CD_2Cl_2$ )  $\delta$ : 7.98 (t, 1H, <sup>4</sup> $J_{H-F}$  = 1.0 Hz), 7.74 (d, 2H, J = 9.0 Hz), 6.80 (d, 2H), 3.01 (s, 6H).

<sup>13</sup>C NMR (75 MHz,  $CD_2CI_2$ )  $\delta$ : 151.5, 149.2, 146.0 (m, <sup>1</sup> $J_{CF}$  = 248.3 Hz), 142.3 (m, 2C, <sup>1</sup> $J_{CF}$  = 259.9 Hz), 127.4, 120.6, 117.5, 117.2 (t, <sup>2</sup> $J_{CF}$  = 12.7 Hz), 112.8, 102.3 (t, <sup>2</sup> $J_{CF}$  = 22.5 Hz), 40.7. <sup>19F</sup>NMR (188.05 MHz, CDCI<sub>3</sub>)  $\delta$ : –130.46 (m, 2F), –144.78 (m, 2F).

IR (KBr): 2890 (br, w), 1615 (s), 1506 (s), 1492 (s), 1352 (s), 1196 (s), 1072 (m), 1017 (s), 973 (s), 812 (s), 790 (s) cm<sup>-1</sup>.

C<sub>16</sub>H<sub>11</sub>BrF<sub>4</sub>N<sub>4</sub> (415.18), calcd: C, 46.29; H, 2.67; N, 13.49; found: 46.1; H, 2.80; N, 13.7. M.p. 168 °C.

MS/ESI: m/z 415.2 found 415.1

4-(1-(2,3,5,6-tetrafluoro-4-iodophenyl)-1H-1,2,3-triazol-4-yl)-N,N-dimethylbenzenamine (**2c**)



<sup>1</sup>H NMR (300 MHz,  $CD_2CI_2$ )  $\delta$ : 8.01 (t, 1H,  ${}^4J_{H-F} = 1.0 \text{ Hz}$ ), 7.77 (d, 2H, J = 8.9 Hz), 6.83 (d, 2H), 3.04 (s, 6H).

<sup>13</sup>C NMR (75 MHz,  $CD_2Cl_2$ )  $\delta$ : 151.4, 149.1, 148.2 (m, <sup>1</sup> $J_{CF}$  = 245.8 Hz), 141.4 (m, <sup>1</sup> $J_{CF}$  = 259.3 Hz), 127.4 , 120.6, 118.0 (t, <sup>2</sup> $J_{CF}$  = 13.7 Hz), 117.6, 112.8, 74.7 (t, <sup>2</sup> $J_{CF}$  = 28.2 Hz), 40.7.

<sup>19</sup>F NMR (188.05 MHz, CDCl<sub>3</sub>) δ: –117.41 (m, 2F), –144.36 (m, 2F).

IR (KBr): 2891 (br, w), 2852 (w), 1618 (s), 1500 (s), 1480 (s), 1240 (m), 1198 (s), 1072 (m), 1020 (s), 971 (s), 955 (s), 828 (m), 808 (s), 778 (s) cm<sup>-1</sup>.

 $C_{16}H_{11}F_4IN_4$  (462.18), calcd: C, 41.58; H, 2.40; N, 12.12%; found: C, 41.4; H, 2.5; N, 12.4.

M.p. 182 °C.

MS/ESI *m*/z 462.2 found 463.2 (M+H<sup>+</sup>) 485.2 (M+Na<sup>+</sup>)

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## <sup>1</sup>H NMR spectrum of **2a**

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<sup>13</sup>C NMR spectrum of 2a



<sup>19</sup>F NMR spectrum of **2a** 

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<sup>1</sup>H NMR spectrum of **2b** 

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<sup>13</sup>C NMR spectrum of **2b** 

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<sup>19</sup>F NMR spectrum of **2c** 

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## S.3 Single-crystal X-ray diffraction analysis

Data were collected on a Bruker KAPPA APEX II diffractometer with Mo-K $\alpha$  radiation and CCD detector, at room temperature. The structure was resolved by SIR200465<sup>[S2]</sup> and refined by SHELXL-97<sup>[S3]</sup> programs, respectively. The refinement was carried on by full-matrix least-squares on F<sup>2</sup>. Hydrogen atoms were placed using standard geometric models and with their thermal parameters riding on those of their parent atoms. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via <u>www.ccdc.cam.ac.uk/data\_request/cif</u>.

The crystals were extremely thin plate and several attempts to find good quality single crystals suitable for data collection failed, both for lack of intensity and for twinning. At last we decided to collect data on the thickest crystal found, although it was twinned with a large mosaicity. An initial fast data collection allowed to solve the structure, then we carried on an accurate data collection on this crystal.

Two reflections were omitted from all the calculation, being obscured by the beam stop, while 12 more reflections were omitted because affected by the twinning. CCDC no. 1453398, contains the supplementary crystallographic data for **2c** and the list of omitted reflections.

CCDC	1453398
Chemical Formula	C <sub>16</sub> H <sub>11</sub> F <sub>4</sub> I N <sub>4</sub>
M <sub>r</sub>	346.64
Crystal system, space group	P2 <sub>1</sub> /n
Temperature (K)	100 K
a, b, c (Å)	5.9494(6), 22.142(2), 36.396(4)
$\alpha, \beta, \gamma$ (°)	90.00, 91.449(3), 90.00
V (ų)	4792.97
Ζ	4
Radiation type	Μο Κα λ = 0.71073 Å
μ (mm <sup>-1</sup> )	2.054
Crystal size	0.40x0.20x0.02
Data collection	
Diffractometer	Bruker APEX-II CCD area detector
Radiation type	Mo Kα, λ = 0.71073 Å
Absorption correction	0.6255 – 0.7416
No. of measured, independent and observed $[I > 2\sigma(I)]$ reflections	38811, 11514, 8816
R <sub>int</sub>	0.1045
θmax , θ(completeness) (°)	28.00, 0.996
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.0619, 15.47, 1.045
No. of reflections	11514
No. of parameters	682
No. of restraints	0
$\Delta  ho_{max}$ , $\Delta  ho_{min}$ (e Å <sup>-3</sup> )	1.68, -1.06

Table S1. Single-crystal X-ray data collection, structure solution, and refinement of a single crystal of 2c.

### S.4 References

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