

# European Journal of Organic Chemistry

Supporting Information

## **Photoinduced 1,3-Dipolar Cycloadditions of Cyclic Enones and 2,5-Disubstituted Tetrazoles: An Unprecedented Pathway to Polysubstituted Pyrazolines and Pyrazoles**

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Summary:

**Page 2:** General information, general procedure for pyrazole derivatives.

**Page 3-5:** Synthesis, characterization (NMR, mass spectrometry) of **8a**, in-progress absorption and emission curves for **8a**.

**Pages 6-8:** Synthesis, characterization (NMR, mass spectrometry) of **8b**, in-progress absorption and emission curves for **8b**.

**Pages 9-12:** Synthesis, characterization (NMR, mass spectrometry) of **9a**, in-progress absorption and emission curves for **9a**.

**Pages 13-15:** Synthesis, characterization (NMR, mass spectrometry) of **9b**, in-progress absorption and emission curves for **9b**.

**Pages 16-19:** Synthesis, characterization (NMR, mass spectrometry) of **10**, in-progress absorption and emission curves for **10**.

**Pages 20-22:** Synthesis, characterization (NMR, mass spectrometry) of **11**, in-progress absorption and emission curves for **11**.

**Pages 23-25:** Synthesis, characterization (NMR, mass spectrometry) of **12**, in-progress absorption and emission curves for **12**.

**General Information:**

Quartz tubes were used for the synthesis of pyrazole derivatives. Starting materials were purchased and used without further purification. Column chromatography purifications were performed using 400-mesh silica gel with a particle size of 40-63. Thin-layer chromatography (TLC) was carried out using silica gel 60 F254 plates, which were visualized under ultraviolet light. Spectroscopic measurements were performed using a UV-visible spectrophotometer and a fluorimeter. NMR spectra of samples in CDCl<sub>3</sub> or CD<sub>2</sub>Cl<sub>2</sub> were recorded on a 300 MHz spectrometer, and chemical shifts are reported relative to tetramethylsilane (TMS). <sup>13</sup>C NMR spectra were recorded on 75 MHz spectrometers with complete proton decoupling (CDCl<sub>3</sub>: δ = 77 ppm, CD<sub>2</sub>Cl<sub>2</sub>: δ = 53 ppm).

**General Procedure for Pyrazole Derivatives:**

In a quartz tube, 50 mg of tetrazole, 40 equivalents of cyclic enone, and 30 mL of anhydrous THF are introduced. The mixture is irradiated for 2 hours in a Rayonet® photoreactor equipped with 16 UV lamps emitting at 300 nm. After solvent evaporation, the product is purified by column chromatography on silica gel (heptane/ethyl ether).

**1-(4-methoxyphenyl)-3-phenyl-1,4,5,6-tetrahydro-7H-indazol-7-one: C<sub>20</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub> (**8a**)**

20.16 mg of **8a** (32%) were obtained as white crystals from 50 mg of tetrazole **3** and 40 eq of **7a** (0.8 mL).

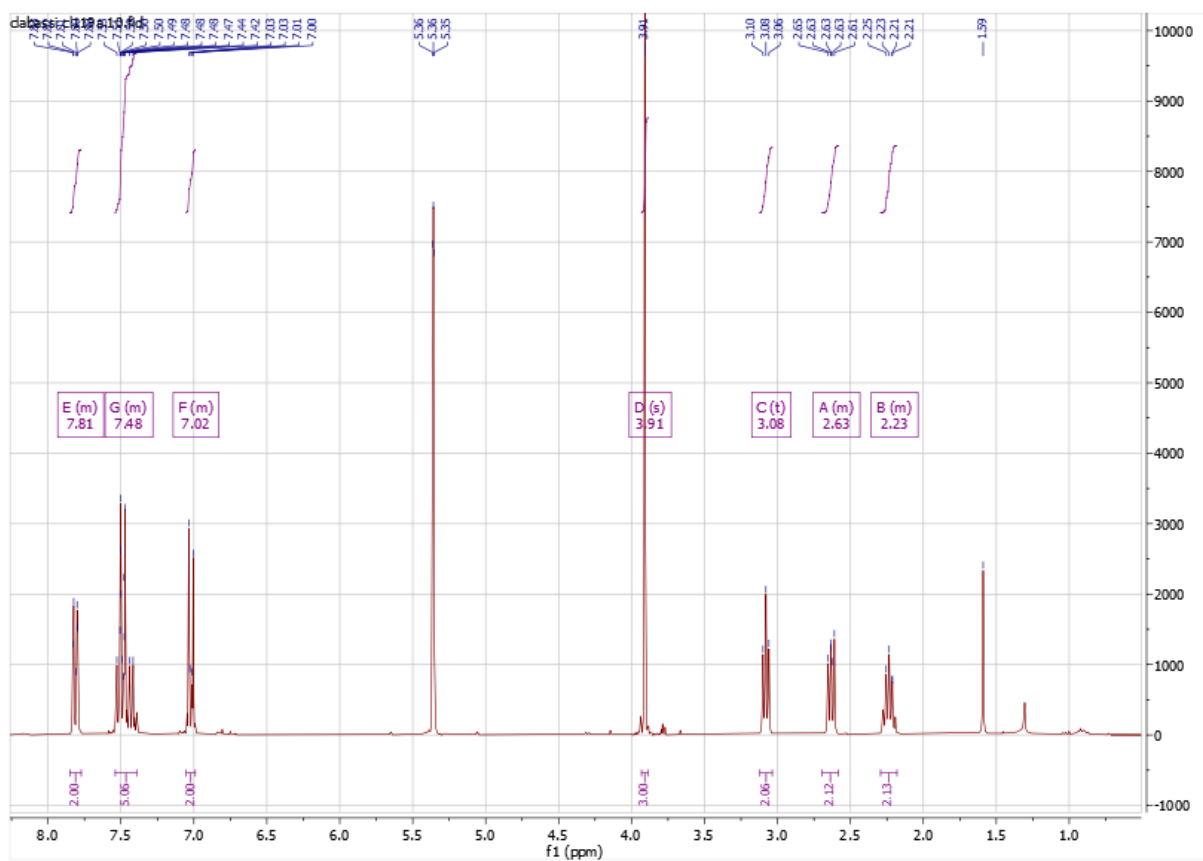
<sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.85 – 7.77 (m, 2H), 7.54 – 7.39 (m, 5H), 7.05 – 6.99 (m, 2H), 3.91 (s, 3H), 3.08 (t, J = 6.0 Hz, 2H), 2.69 – 2.58 (m, 2H), 2.29 – 2.18 (m, 2H).

<sup>13</sup>C NMR (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 190.2, 161.4, 150.1, 137.7, 135.4, 134.7, 130.5, 130.4, 129.9, 128.9, 128.6, 115.4, 57.4, 41.5, 26.6, 24.6.

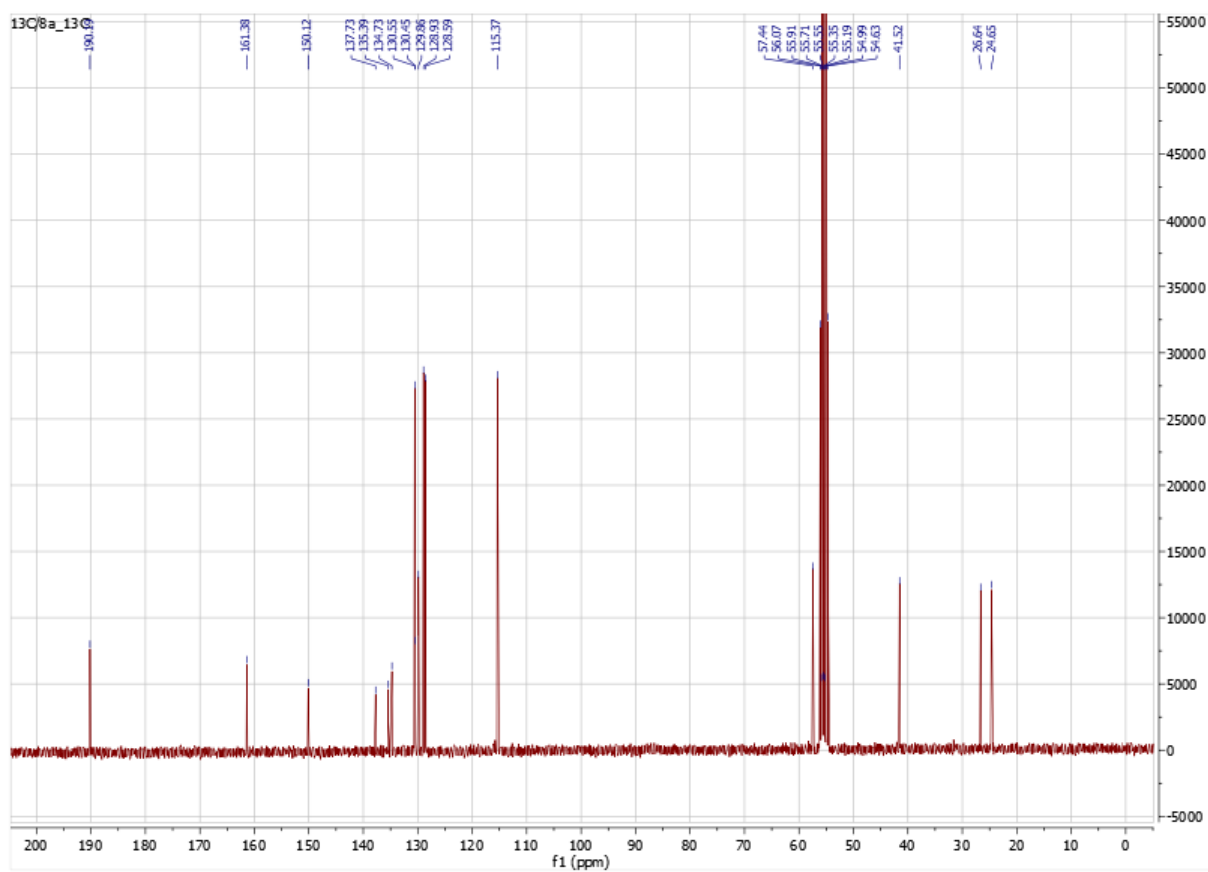
ESIMS: [M+H]<sup>+</sup> (C<sub>20</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>)

m/z Theoretical: 319.1441

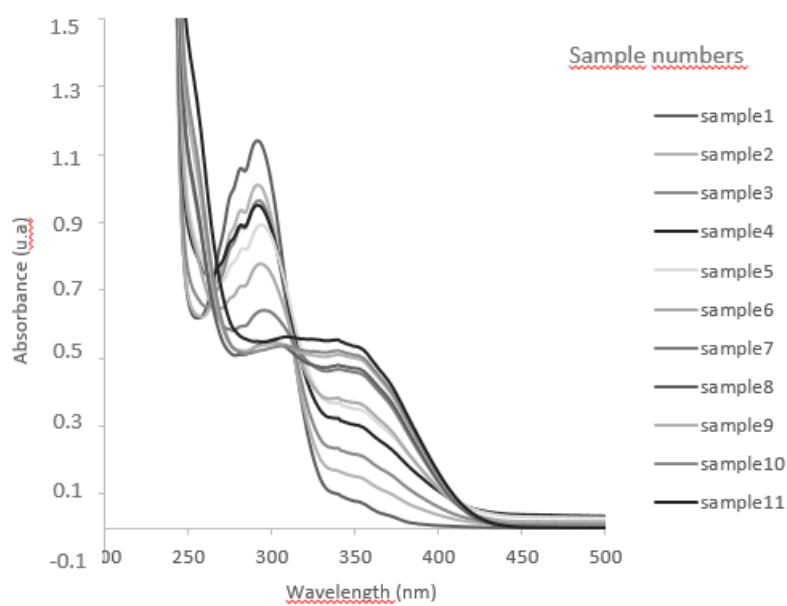
m/z Found: 319.1437



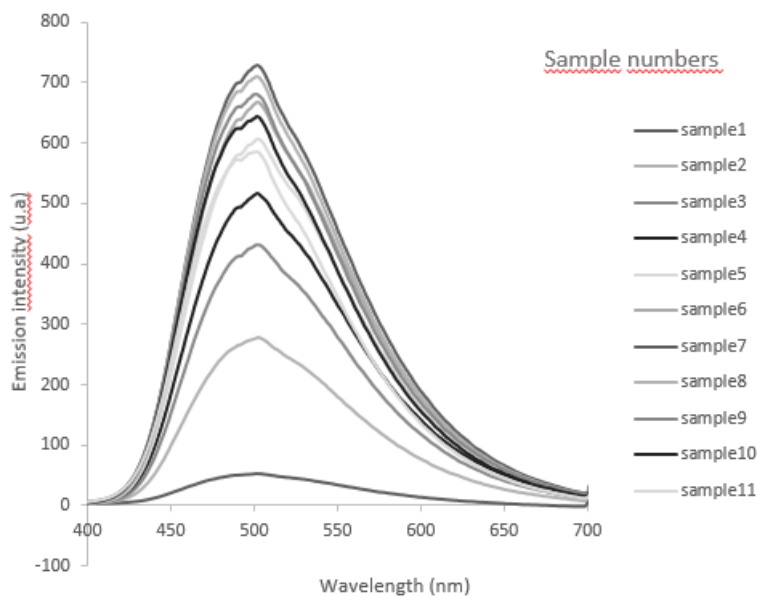
<sup>1</sup>H NMR spectrum (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) for **8a**.



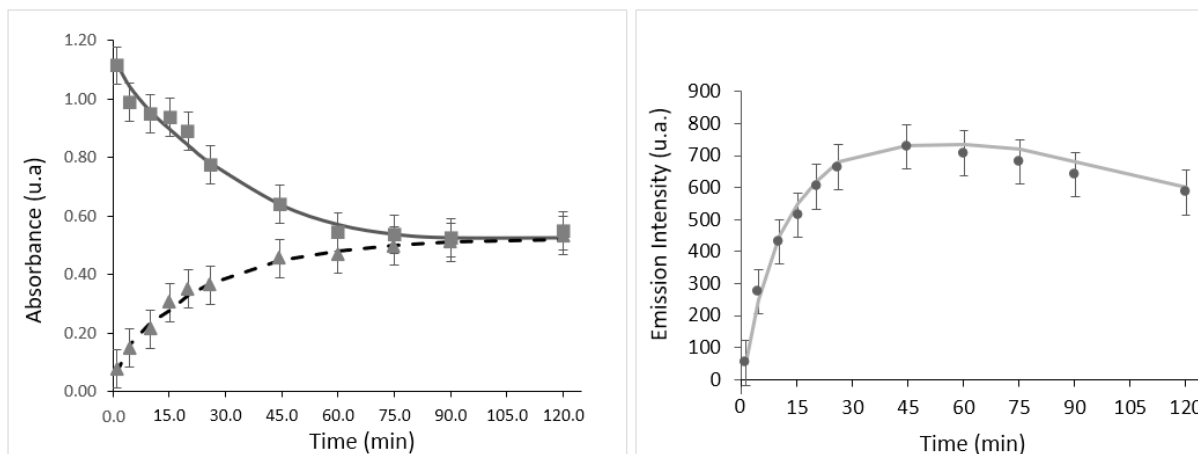
<sup>13</sup>C NMR spectrum (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>) for **8a**.



**Figure SI-1:** Evolution of absorption spectra during the synthesis of **8a**.



**Figure SI-2:** Evolution of emission spectra during synthesis of **8a**.



**Figure SI-3:** Curves obtained using samples taken during the synthesis of **8a**. On the left: evolution of the absorption maxima of tetrazole **3**(■) at 295 nm and of the reaction mixture ( $\Delta$ ) at 355 nm. Right figure: evolution of the emission maxima of the reaction mixture at 485 nm.

**1-(4-methoxyphenyl)-3-phenyl-4,5-dihydrocyclopenta[c]pyrazol-6(1H)-one: C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub> (8b)**

19.22 mg of **8b** (24%) were obtained as a brown powder from 50 mg of tetrazole **3** and 40 eq of **7b** (0.66 mL).

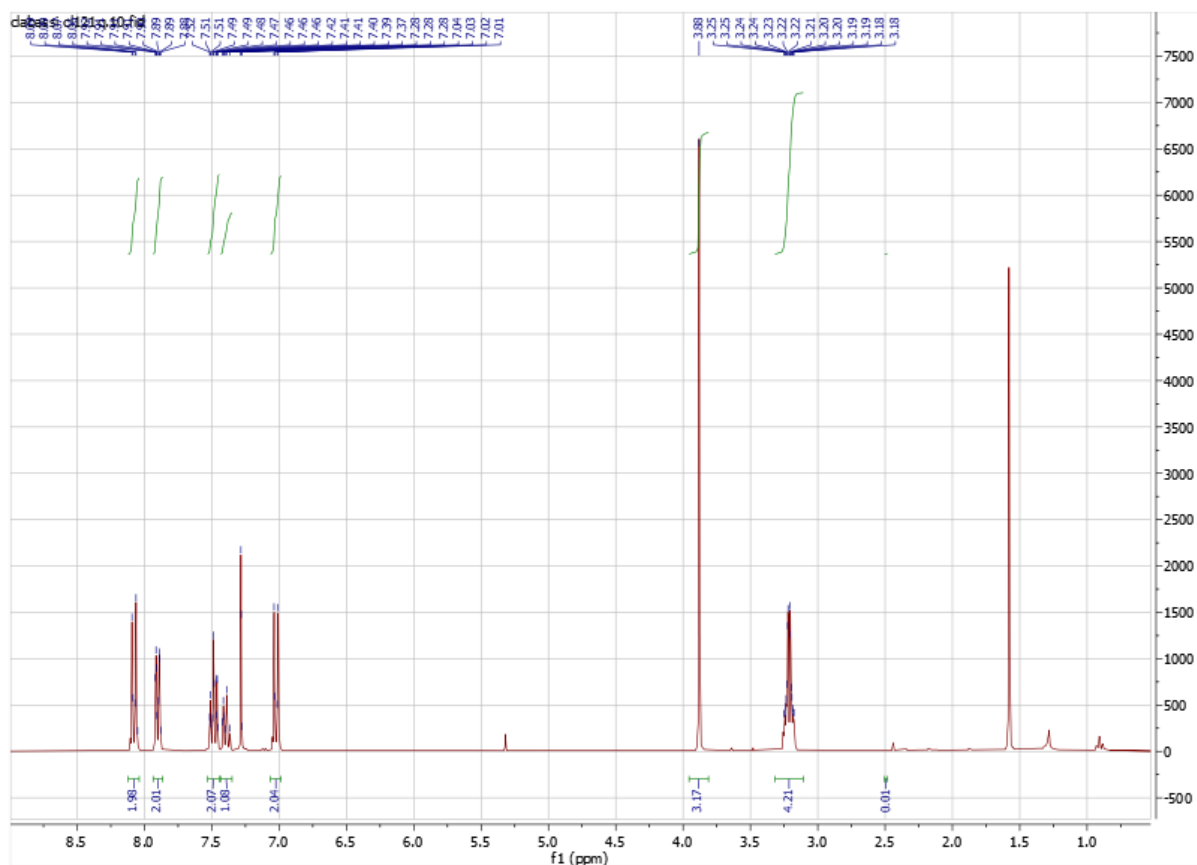
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.09 – 8.05 (m, 2H), 7.92 – 7.88 (m, 2H), 7.50 (tt, *J* = 6.7, 0.9 Hz, 2H), 7.41 – 7.36 (m, 1H), 7.04 – 6.99 (m, 2H), 3.88 (s, 3H), 3.27 – 3.17 (m, 4H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 189.2, 158.5, 145.6, 145.5, 144.0, 132.9, 132.25, 128.8, 128.2, 125.9, 121.6, 114.3, 55.5, 43.8, 19.6.

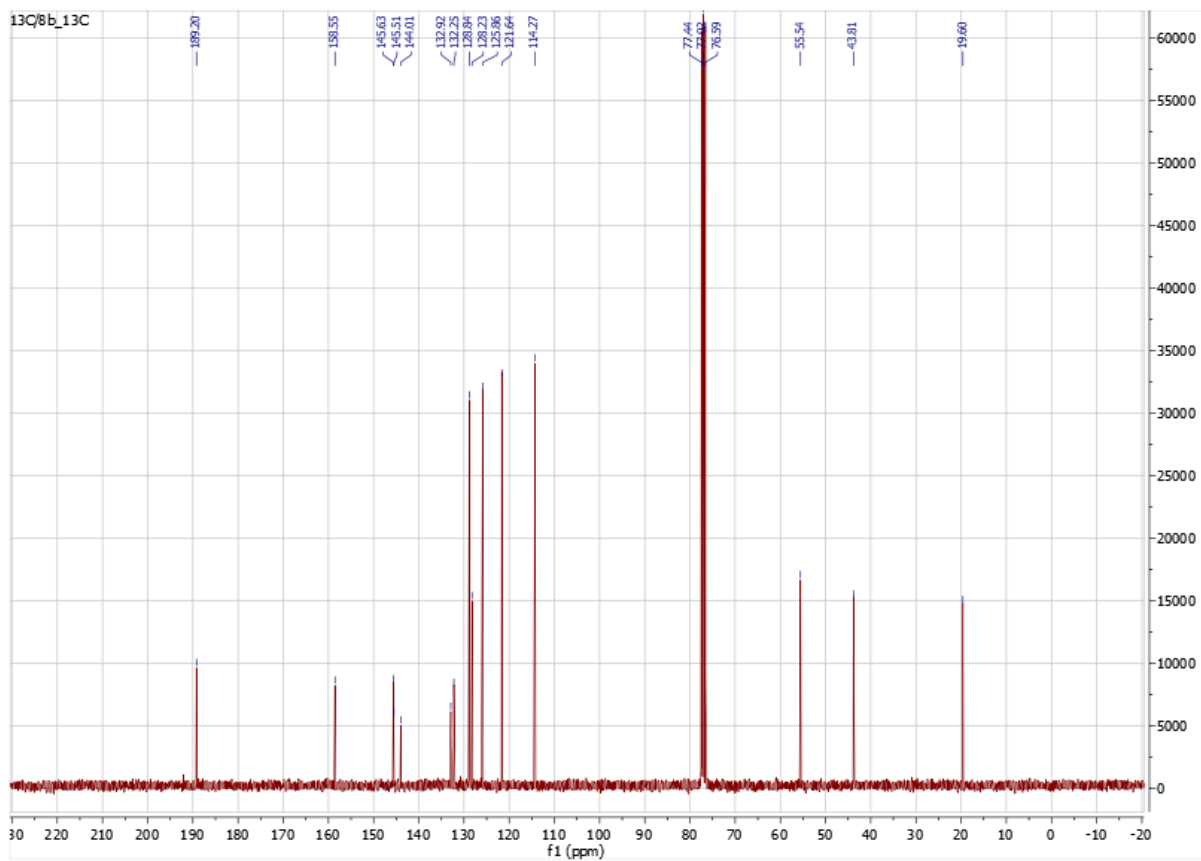
ESIMS: [M+Na]<sup>+</sup>: C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>Na

*m/z* Theoretical: 327.1104

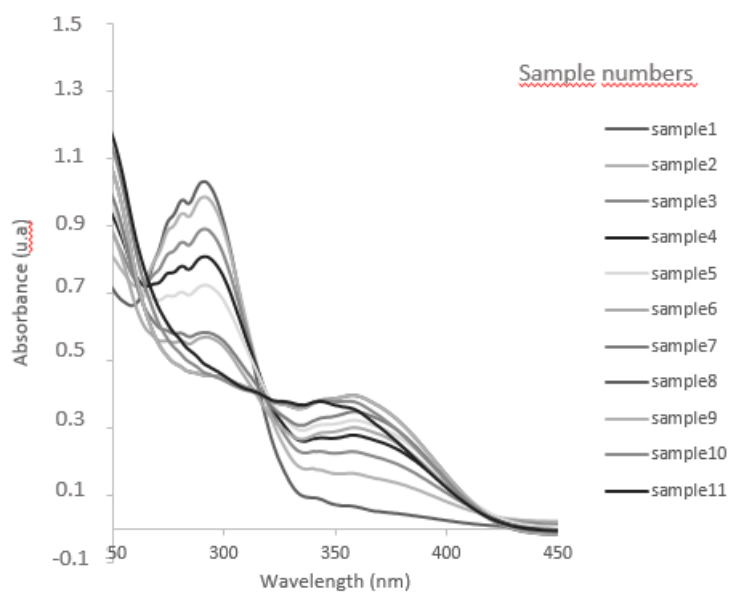
*m/z* Found: 327.1108



<sup>1</sup>H NMR spectrum (300 MHz, CDCl<sub>3</sub>) for **8b**.

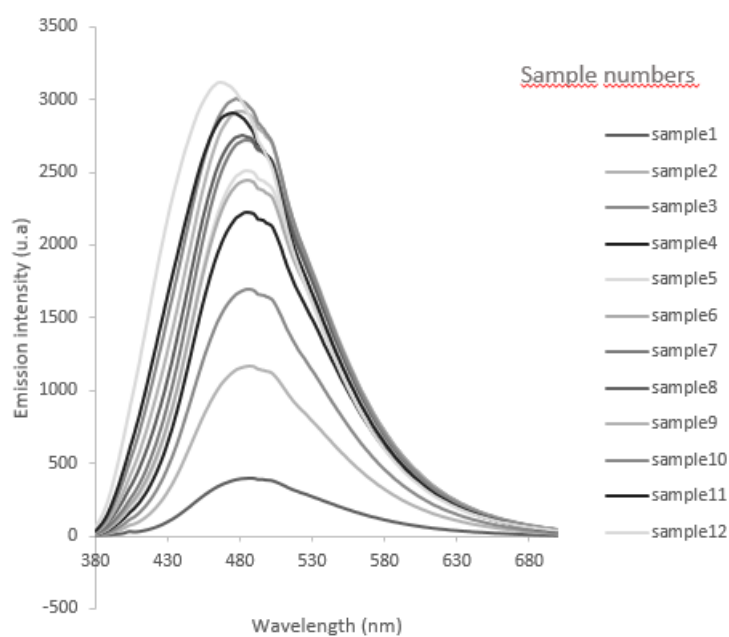


<sup>13</sup>C NMR spectrum (75 MHz, CDCl<sub>3</sub>) for **8b**.

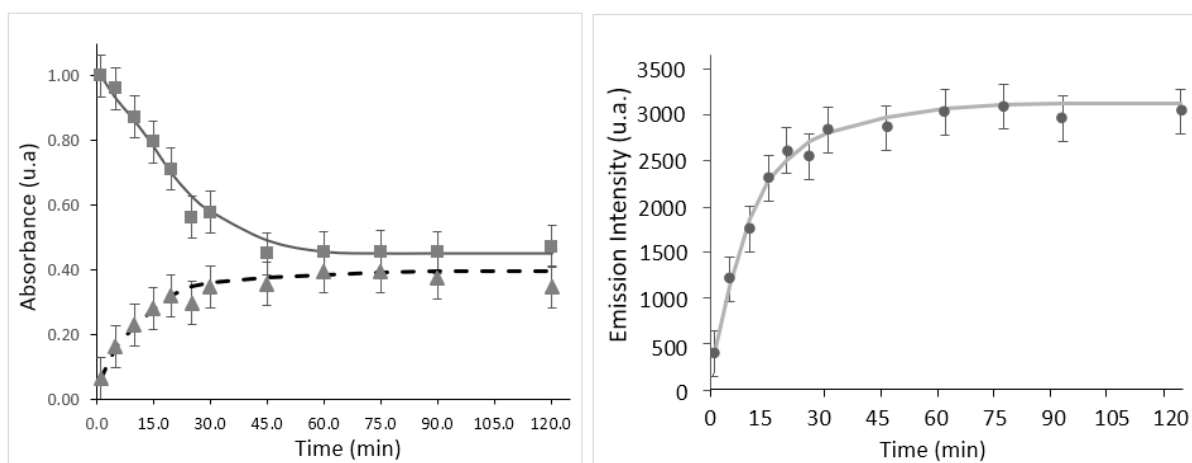


**Figure SI-4:** Evolution of absorption spectra during synthesis of **8b**.





**Figure SI-5:** Evolution of emission spectra during synthesis of **8b**.



**Figure SI-6:** Curves obtained using samples taken during the synthesis of **8b**. On the left: evolution of the absorption maxima of tetrazole **3** (■) at 295 nm and of the reaction mixture (Δ) at 360 nm. Right figure: evolution of the emission maxima of the reaction mixture at 485 nm.

**1-(6-methoxynaphthalen-2-yl)-3-(naphthalen-2-yl)-1,4,5,6-tetrahydro-7H-indazol-7-one:**  
**C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> (9a)**

27.9 mg of **9a** (47%) were obtained as a pink powder from 50 mg of tetrazole **6** and 40 eq of **7a** (0.55 mL).

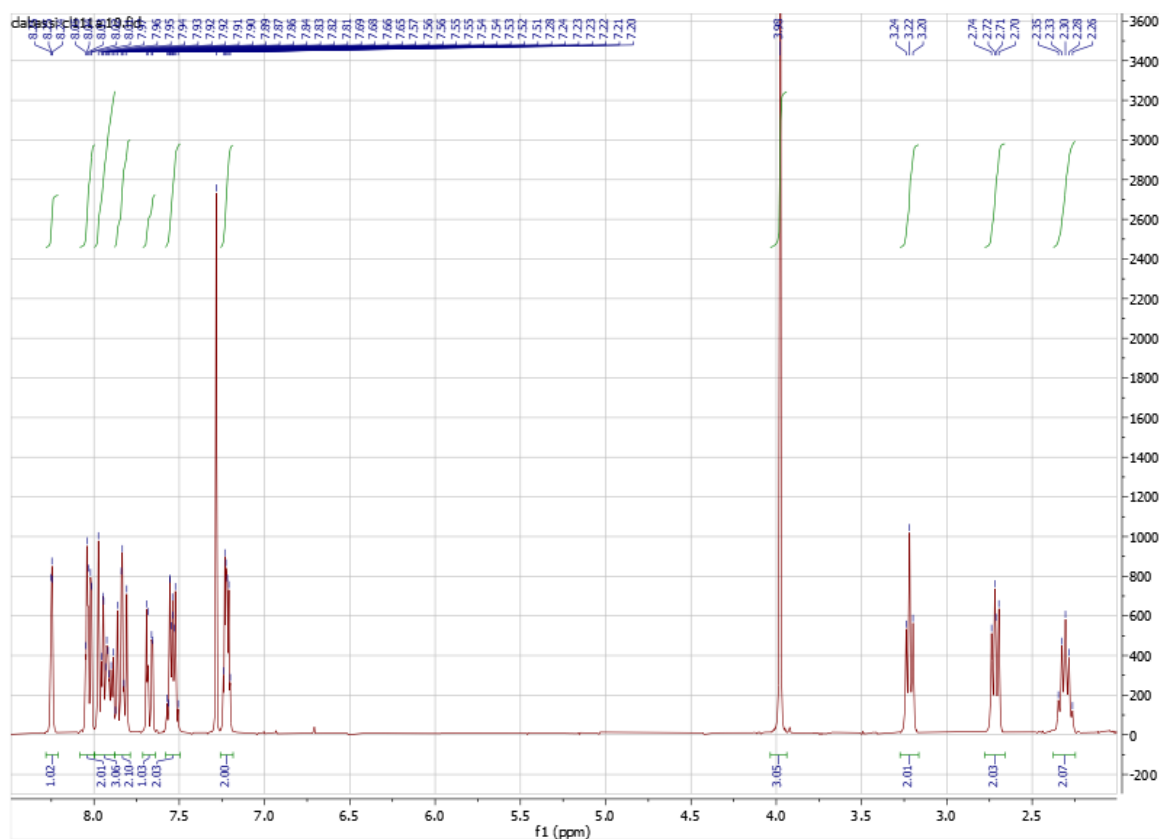
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.28 – 8.21 (m, 1H), 8.08 – 8.00 (m, 2H), 8.00 – 7.88 (m, 3H), 7.84 (dd, *J* = 9.1, 7.4 Hz, 2H), 7.67 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.22 (dq, *J* = 5.2, 2.5 Hz, 2H), 3.98 (s, 3H), 3.22 (t, *J* = 6.0 Hz, 2H), 2.72 (dd, *J* = 7.4, 5.5 Hz, 2H), 2.30 (p, *J* = 6.3 Hz, 2H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 188.3, 158.3, 148.7, 136.0, 135.8, 134.3, 133.4, 133.0, 130.1, 129.9, 129.1, 128.4, 128.4, 128.3, 127.8, 127.0, 126.4, 126.3, 126.2, 125.2, 124.3, 123.8, 119.5, 105.78, 55.4, 39.7, 24.8, 23.0.

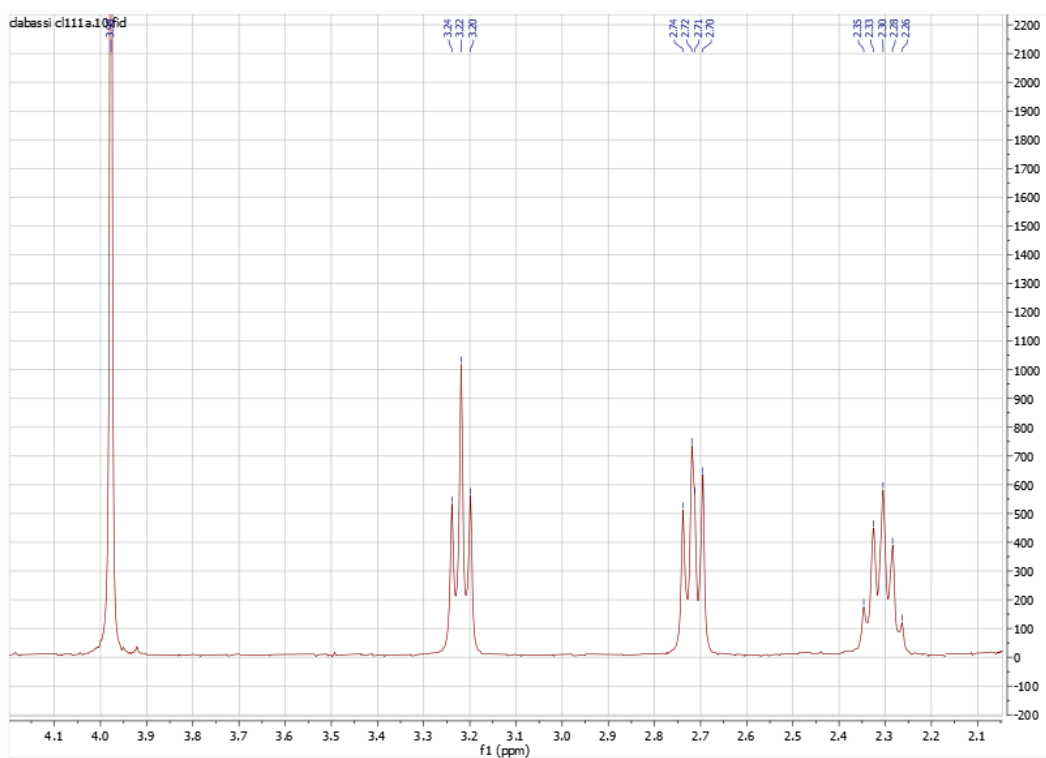
ESIMS: [M+H]<sup>+</sup> (C<sub>28</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>):

m/z Theoretical: 419.1754

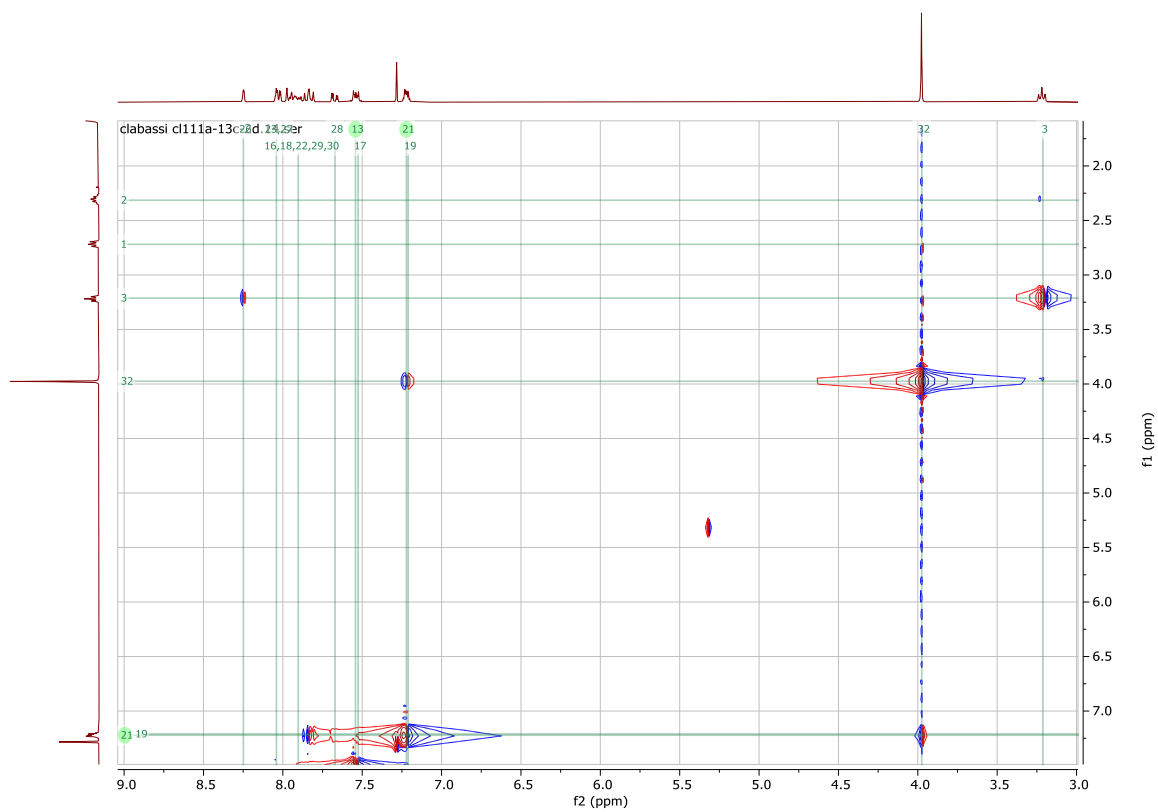
m/z Found: 419.1754



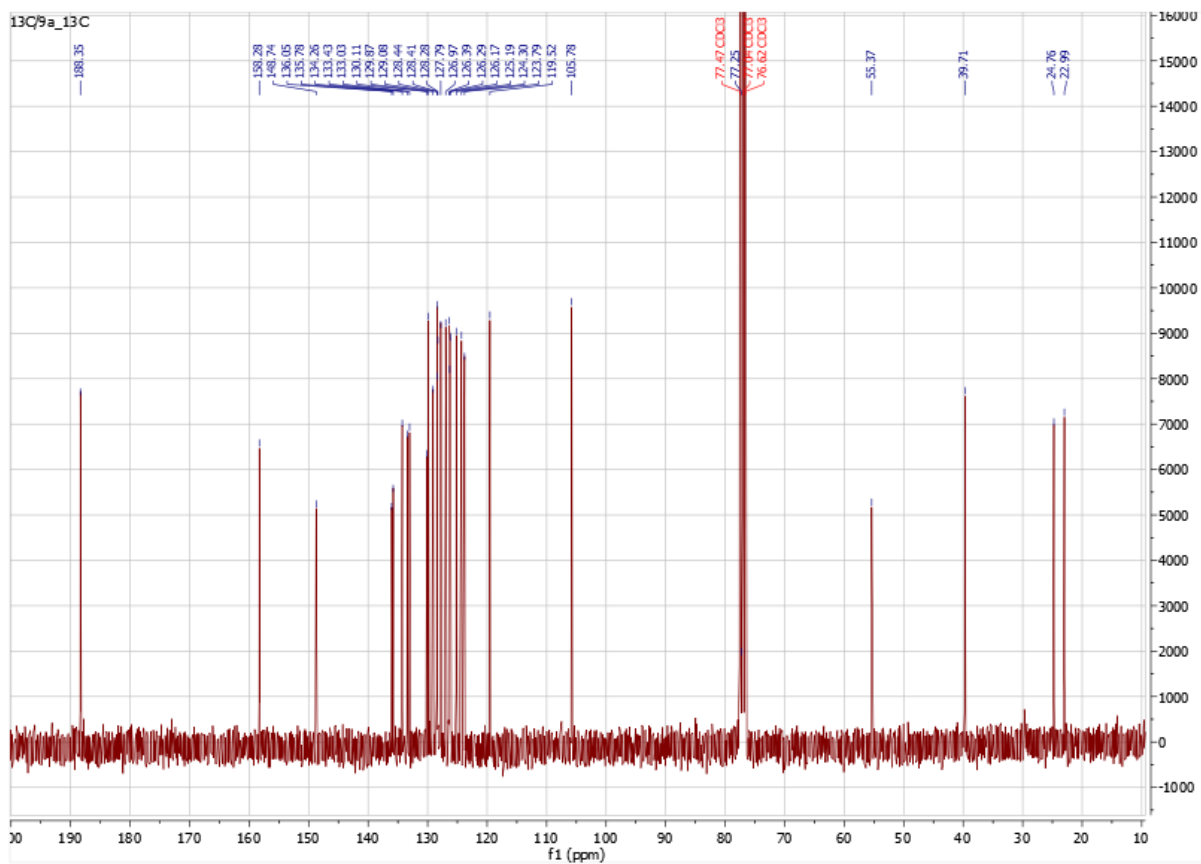
<sup>1</sup>H NMR spectrum (300 MHz, CDCl<sub>3</sub>) for **9a**.



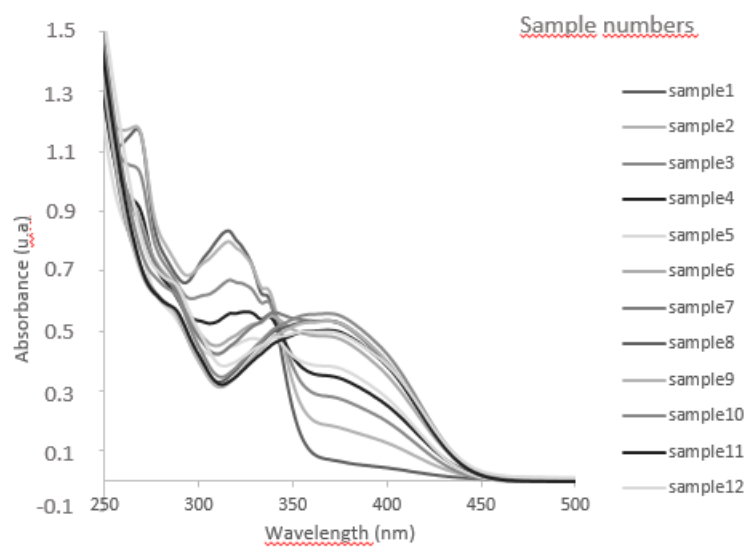
**Figure SI-7:**  $^1\text{H}$  NMR spectrum of **9a** (zoom in on the aliphatic protons).



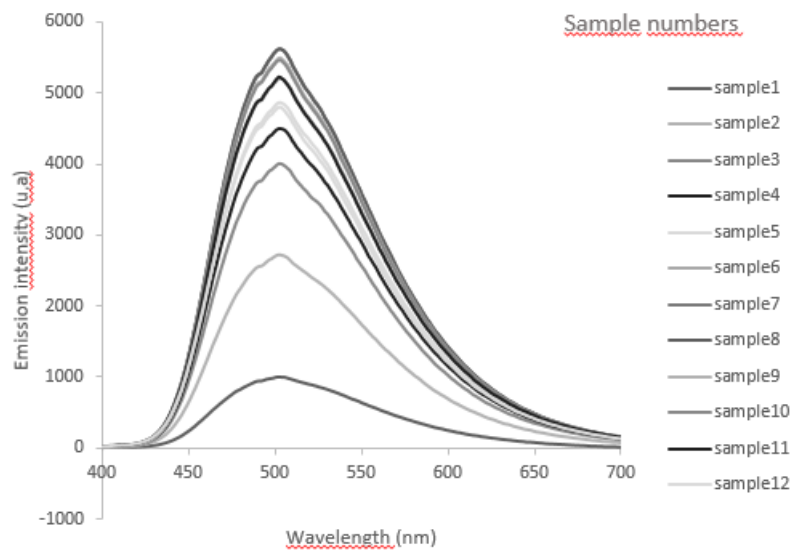
**Figure SI-8:** NOESY 2D NMR map of pyrazole **9a**



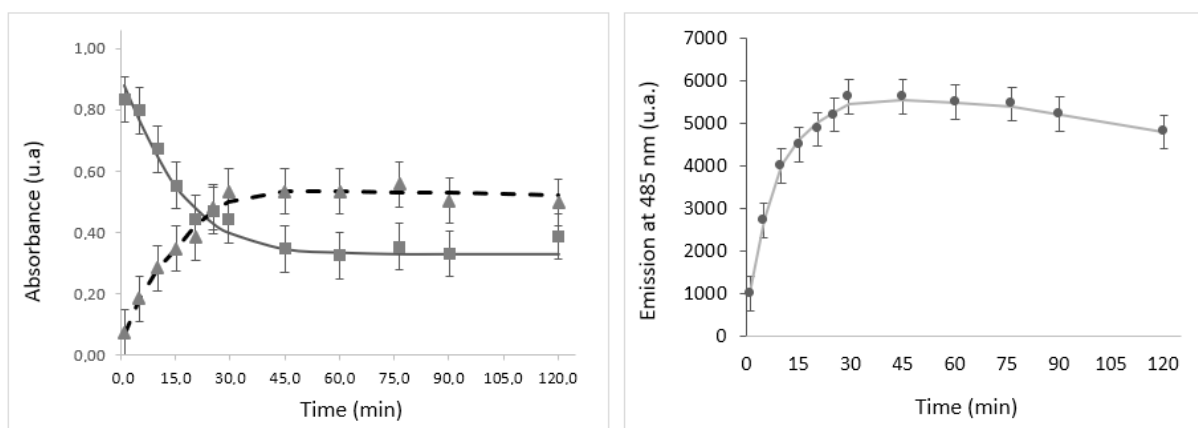
<sup>13</sup>C NMR spectrum (75 MHz, CDCl<sub>3</sub>) for **9a**.



**Figure SI-9:** Evolution of absorption spectra during synthesis of **9a**.



**Figure SI-10:** Evolution of emission spectra during the synthesis of **9a**.



**Figure SI-11:** Curves obtained using samples taken during the synthesis of **9a**. On the left: evolution of the absorption maxima of tetrazole **6** (■) at 316 nm and of the reaction mixture (Δ) at 360 nm. Right figure: evolution of the emission maxima of the reaction mixture at 500 nm.

**1-(6-methoxynaphthalen-2-yl)-3-(naphthalen-2-yl)-4,5-dihydrocyclopenta[c]pyrazol-6(1H)-one: C<sub>27</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> (9b)**

9.29 mg of **9b** (27%) were obtained as a brown powder from 30 mg of tetrazole **6** and 40 eq of **7b** (0.28mL).

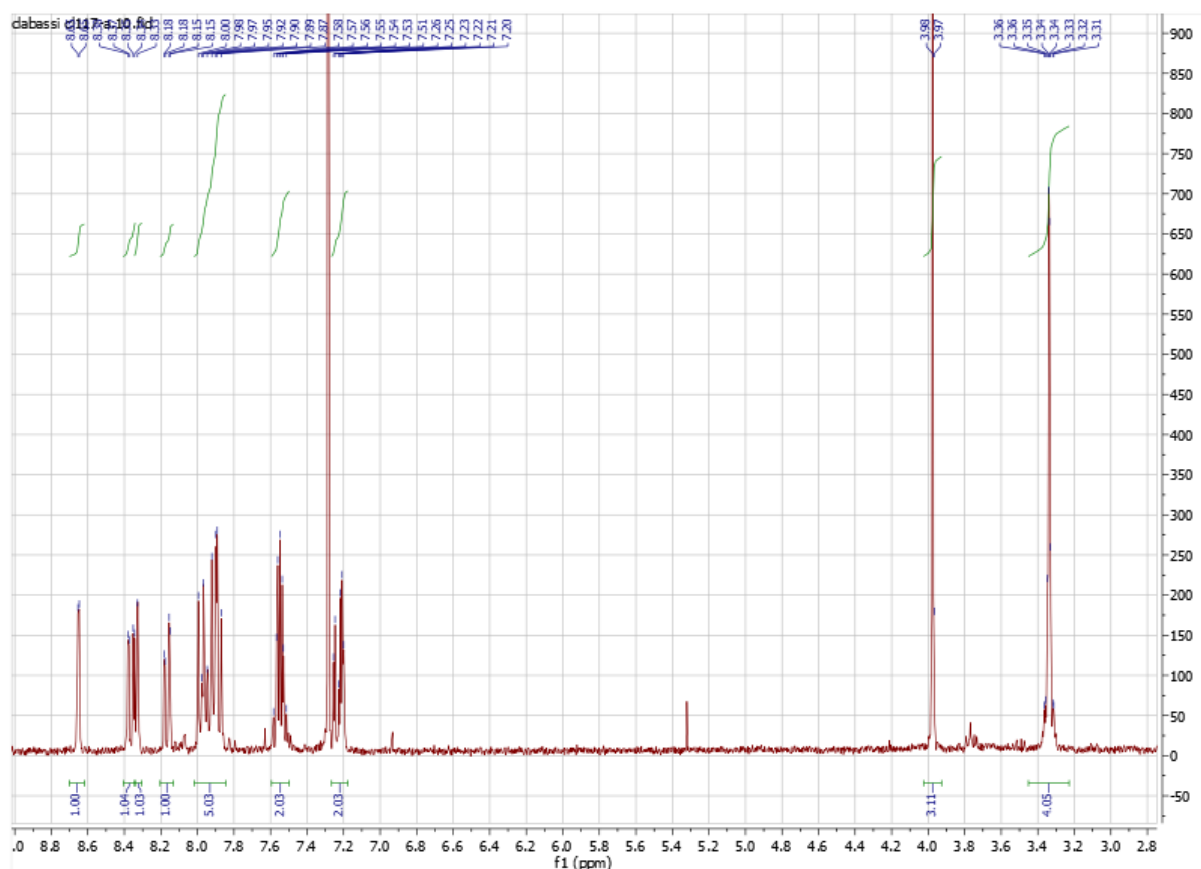
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.65 (d, *J* = 2.2 Hz, 1H), 8.36 (dd, *J* = 9.0, 2.3 Hz, 1H), 8.33 (s, 1H), 8.17 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.93 (ddd, *J* = 23.2, 8.8, 6.2 Hz, 5H), 7.59 – 7.50 (m, 2H), 7.27 – 7.18 (m, 2H), 3.98 (s, 3H), 3.34 (q, *J* = 1.8 Hz, 4H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 189.2, 158.0, 146.5, 145.9, 144.6, 135.2, 133.5, 133.4, 129.9, 129.7, 128.8, 128.7, 128.3, 127.8, 126.5, 126.3, 125.0, 123.8, 119.7, 119.6, 118.8, 117.9, 105.8, 55.3, 43.9, 19.9.

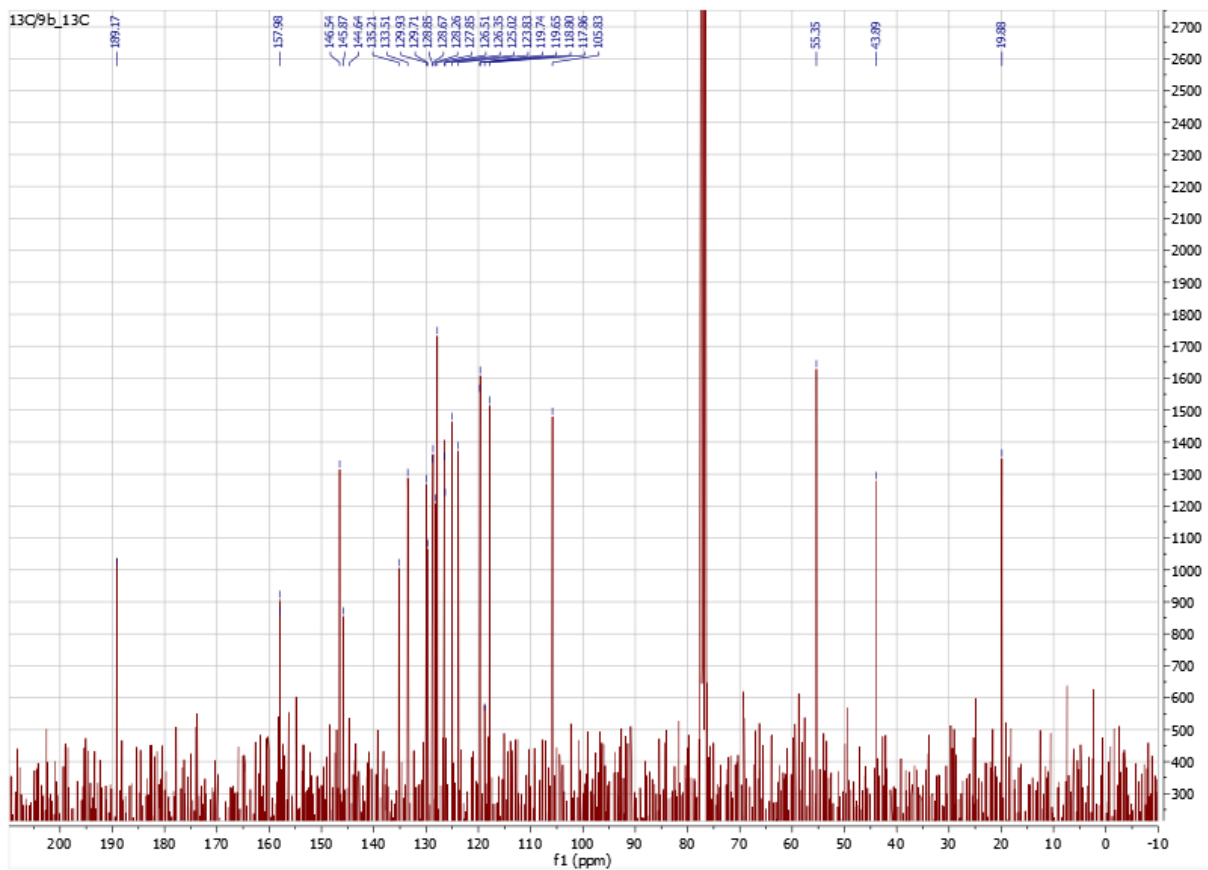
ESIMS: [M+H]<sup>+</sup> (C<sub>27</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub>)

m/z Theoretical : 405.15975

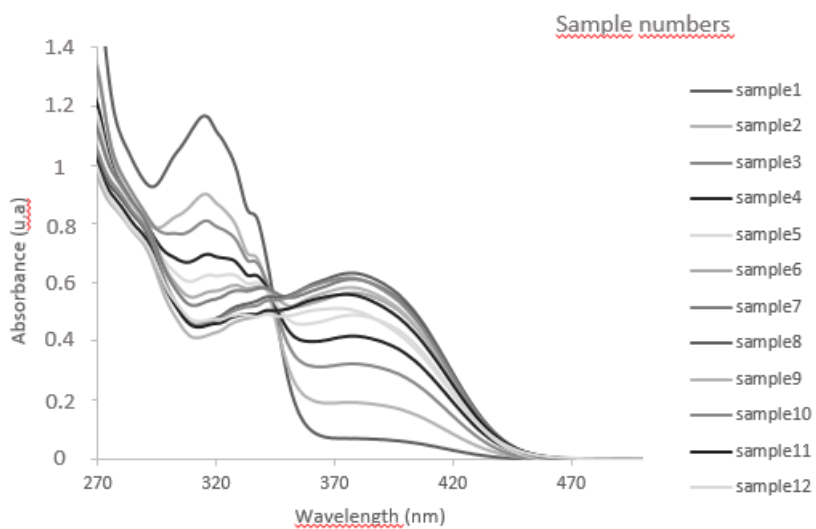
m/z Found : 405.1597



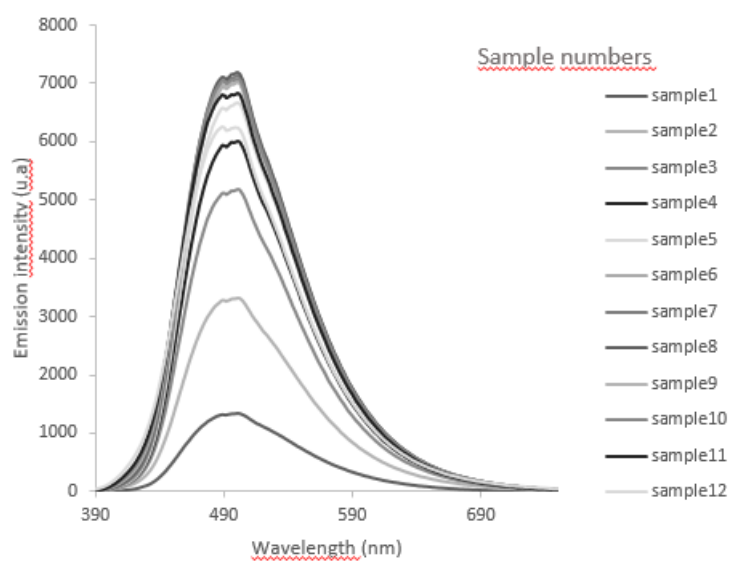
<sup>1</sup>H NMR spectrum (300 MHz, CDCl<sub>3</sub>) for **9b**.



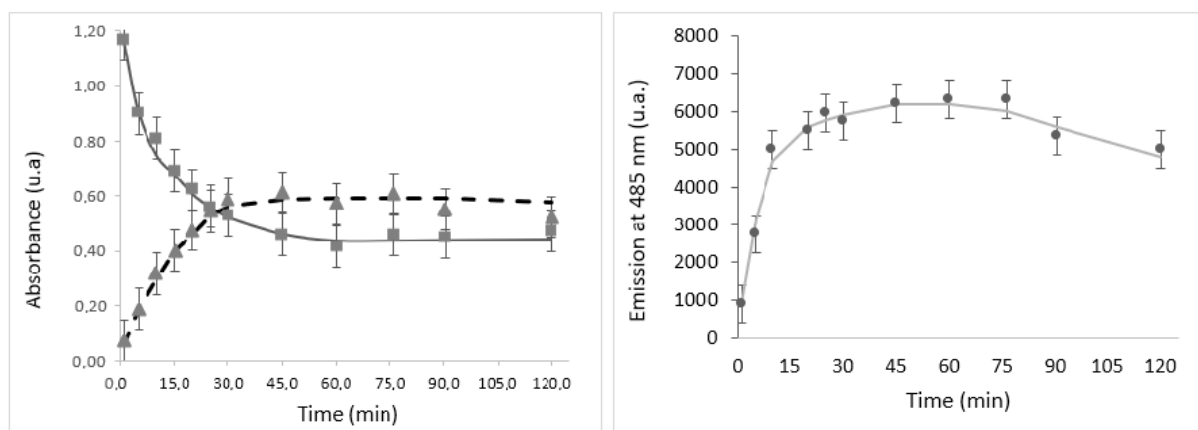
<sup>13</sup>C NMR spectrum (75 MHz, CDCl<sub>3</sub>) for **9b**.



**Figure SI-12:** Evolution of absorption spectra during the synthesis of **9b**.



**Figure SI-13:** Evolution of emission spectra during the synthesis of **9b**.



**Figure SI-14:** Curves obtained using samples taken during the synthesis of **9b**. On the left: evolution of the absorption maxima of tetrazole **6** (■) at 316 nm and of the reaction mixture (Δ) at 370 nm. Right figure: evolution of the emission maxima of the reaction mixture at 500 nm.



**7a-(hydroxymethyl)-1-(6-methoxynaphthalen-2-yl)-3-(naphthalen-2-yl)-1,3a,4,5,6,7a-hexahydro-7H-indazol-7-one: C<sub>29</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> (10)**

53.18 mg of **10** (52%) were obtained as a yellow powder from 80 mg of tetrazole **6** and 40 eq of **7c** (1.154 mL).

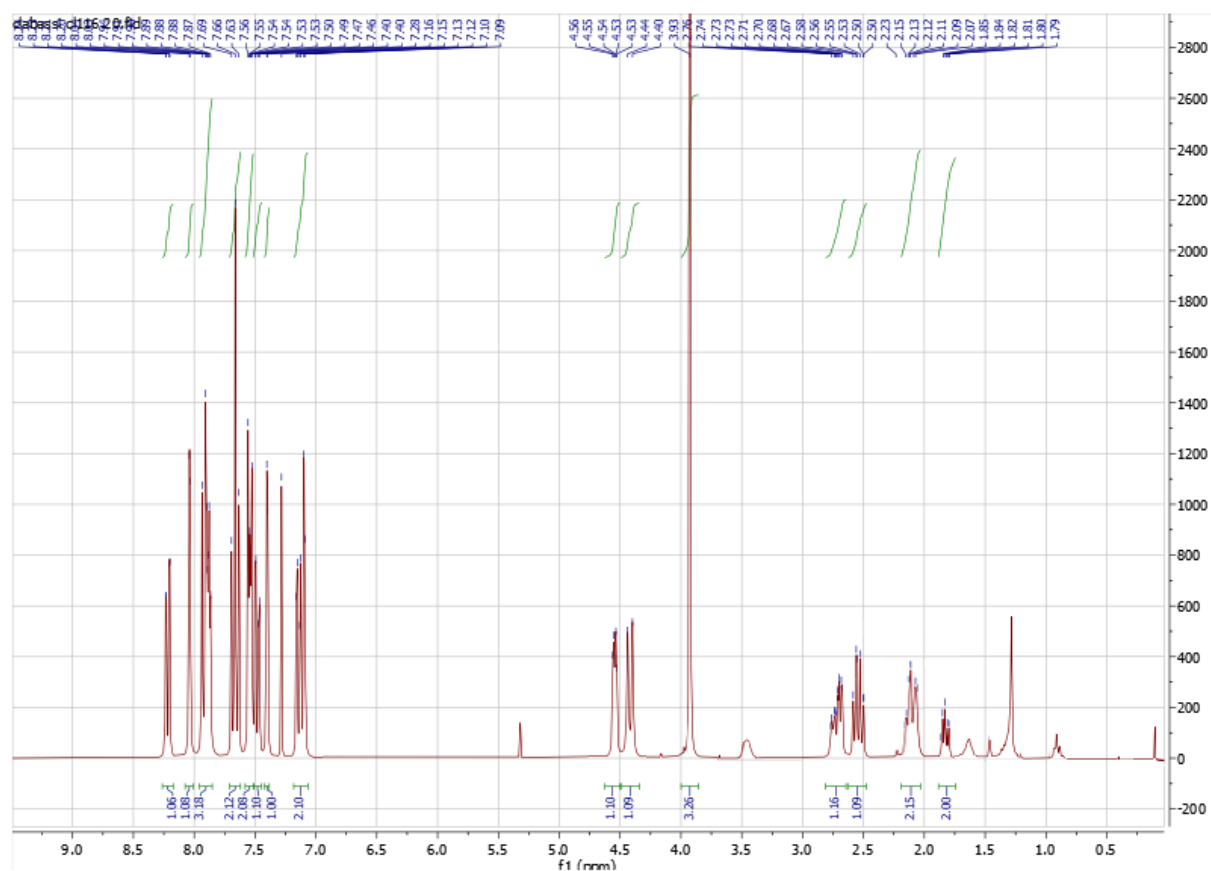
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.22 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.04 (d, *J* = 1.7 Hz, 1H), 7.97 – 7.84 (m, 3H), 7.66 (t, *J* = 9.1 Hz, 2H), 7.59 – 7.46 (m, 3H), 7.40 (d, *J* = 2.4 Hz, 1H), 7.19 – 7.05 (m, 2H), 4.59 – 4.50 (m, 1H), 4.42 (d, *J* = 11.9 Hz, 1H), 3.93 (s, 3H), 3.56 – 3.38 (m, 1H), 2.80 – 2.65 (m, 1H), 2.61 – 2.24 (m, 2H), 2.22 – 2.01 (m, 2H), 1.81 (tdd, *J* = 14.0, 6.7, 2.9 Hz, 2H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 214.8, 156.3, 150.6, 140.0, 133.6, 133.3, 130.0, 129.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.8, 126.7, 126.7, 125.8, 124.1, 119.4, 117.5, 110.2, 105.8, 60.5, 55.3, 53.5, 39.0, 25.7, 20.4.

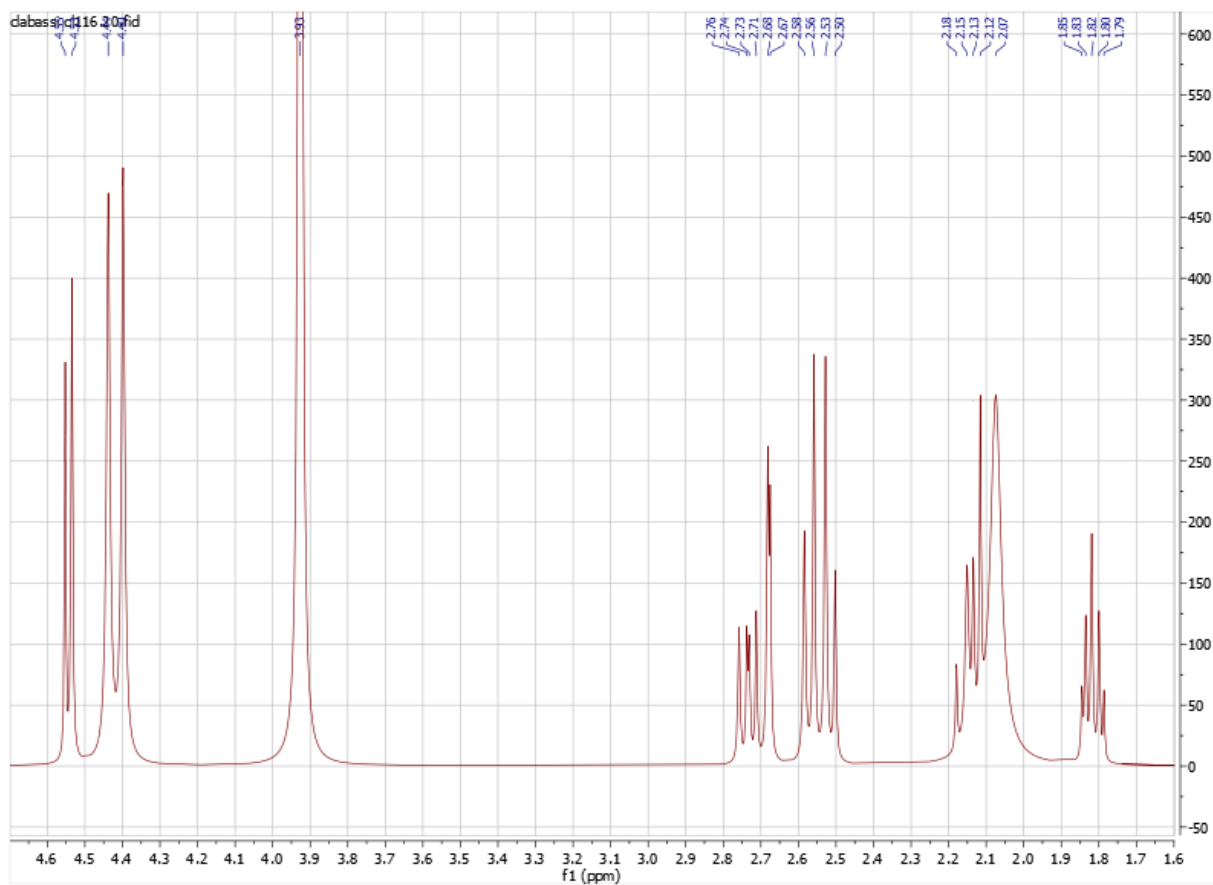
ESIMS: M<sup>+</sup>(C<sub>29</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>)

m/z Theoretical: 450.19379

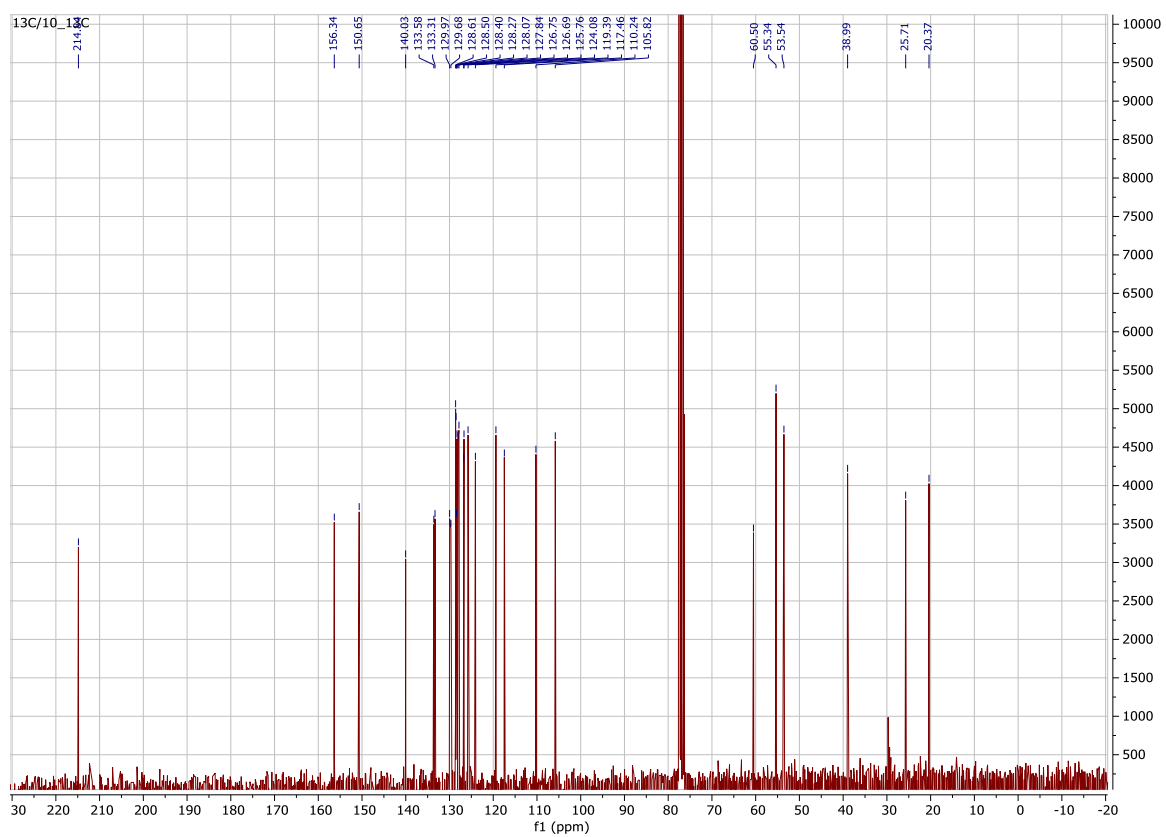
m/z Found: 450.1944



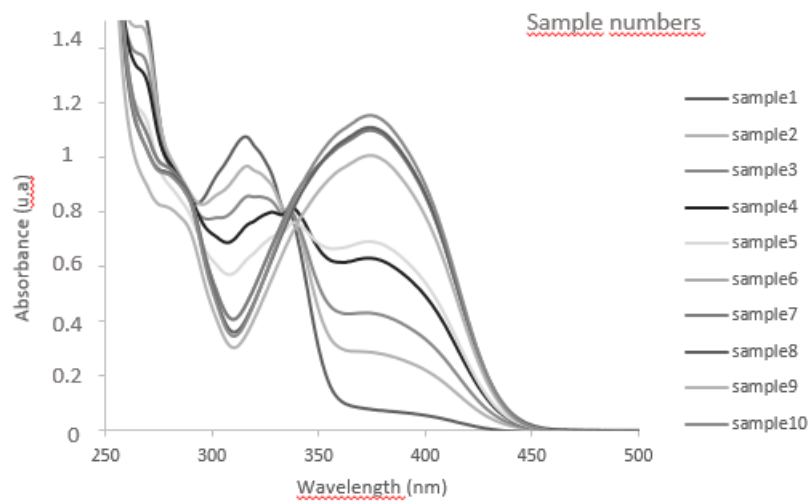
<sup>1</sup>H NMR spectrum (300 MHz, CDCl<sub>3</sub>) for **10**.



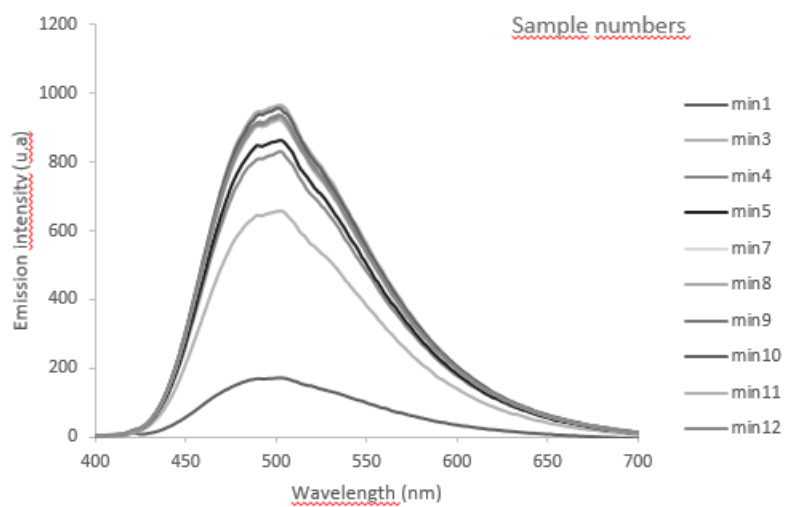
**Figure SI-15:**  $^1\text{H}$  NMR spectrum of **10** (zoom in on the aliphatic protons).



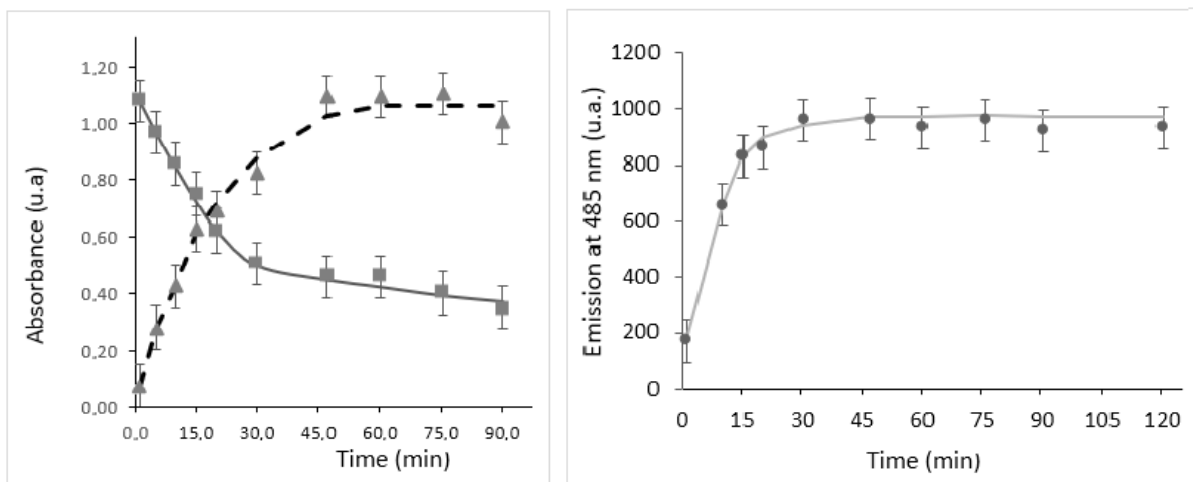
$^{13}\text{C}$  NMR spectrum (75 MHz,  $\text{CDCl}_3$ ) for **10**.



**Figure SI-16:** Evolution of absorption spectra during the synthesis of **10**.



**Figure SI-17:** Evolution of emission spectra during the synthesis of **10**.



**Figure SI-18: Curves obtained using samples taken during the synthesis of 10.** On the left: evolution of the absorption maxima of tetrazole 6(■) at 316 nm and of the reaction mixture (Δ) at 380 nm. Right figure: evolution of the emission maxima of the reaction mixture at 500 nm.

**1-(6-methoxynaphthalen-2-yl)-7a-methyl-3-(naphthalen-2-yl)-5-(prop-1-en-2-yl)-1,3a,4,5,6,7a-hexahydro-7H-indazol-7-one: C<sub>32</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub> (**11**)**

28.95 mg de **11** (43%) were obtained as a yellow powder from 50 mg of tetrazole **6** and 40 eq of **7d** (0.9 mL).

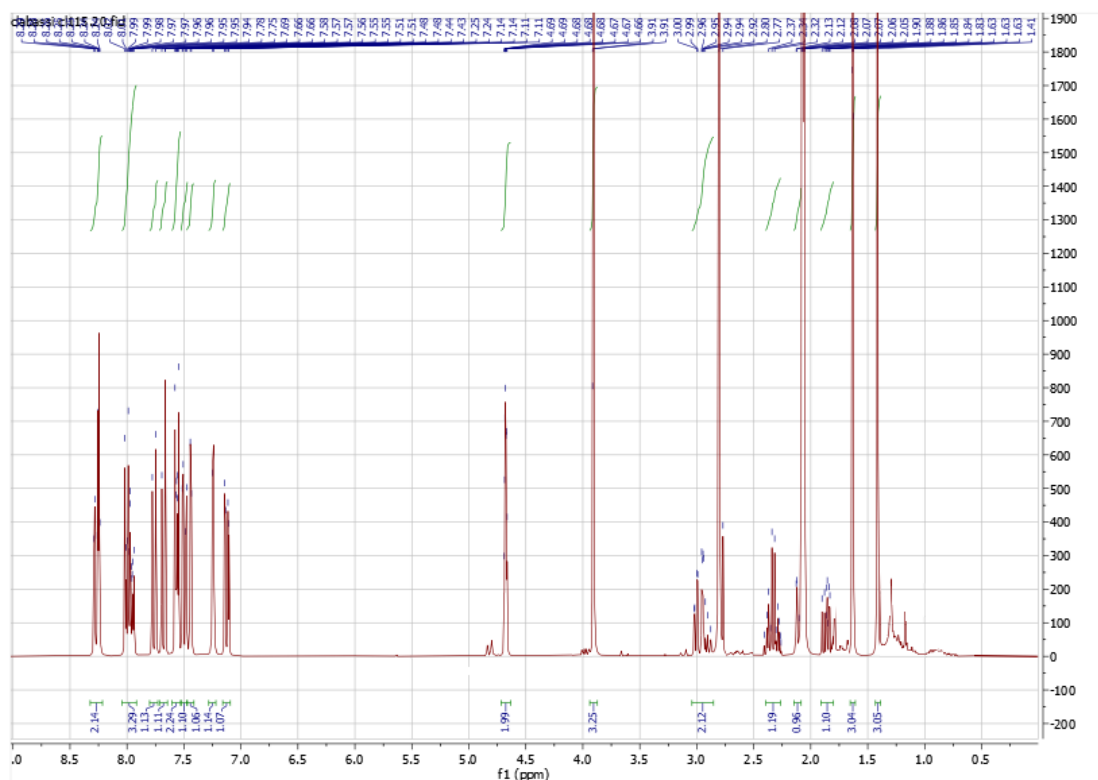
<sup>1</sup>H NMR (300 MHz, Acetone) δ 8.33 – 8.22 (m, 2H), 8.05 – 7.91 (m, 3H), 7.76 (d, *J* = 9.4 Hz, 1H), 7.72 – 7.63 (m, 1H), 7.60 – 7.53 (m, 2H), 7.50 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.44 (d, *J* = 2.8 Hz, 1H), 7.24 (d, *J* = 2.7 Hz, 1H), 7.12 (dd, *J* = 8.9, 2.6 Hz, 1H), 4.72 – 4.61 (m, 2H), 3.91 (d, *J* = 2.5 Hz, 3H), 3.11 – 2.86 (m, 2H), 2.80 – 2.74 (m, 1H), 2.41 – 2.27 (m, 1H), 2.14 – 2.08 (m, 1H), 1.91 – 1.80 (m, 1H), 1.66 – 1.61 (m, 3H), 1.41 (s, 3H).

<sup>13</sup>C NMR (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 211.2, 156.3, 150.1, 147.3, 140.0, 133.5, 133.4, 129.9, 129.7, 128.8, 128.4, 128.3, 128.1, 127.7, 127.7, 126.6, 125.3, 124.0, 119.1, 117.7, 110.2, 109.6, 105.8, 73.6, 56.7, 55.2, 53.9, 44.1, 37.8, 29.6, 20.2, 17.6.

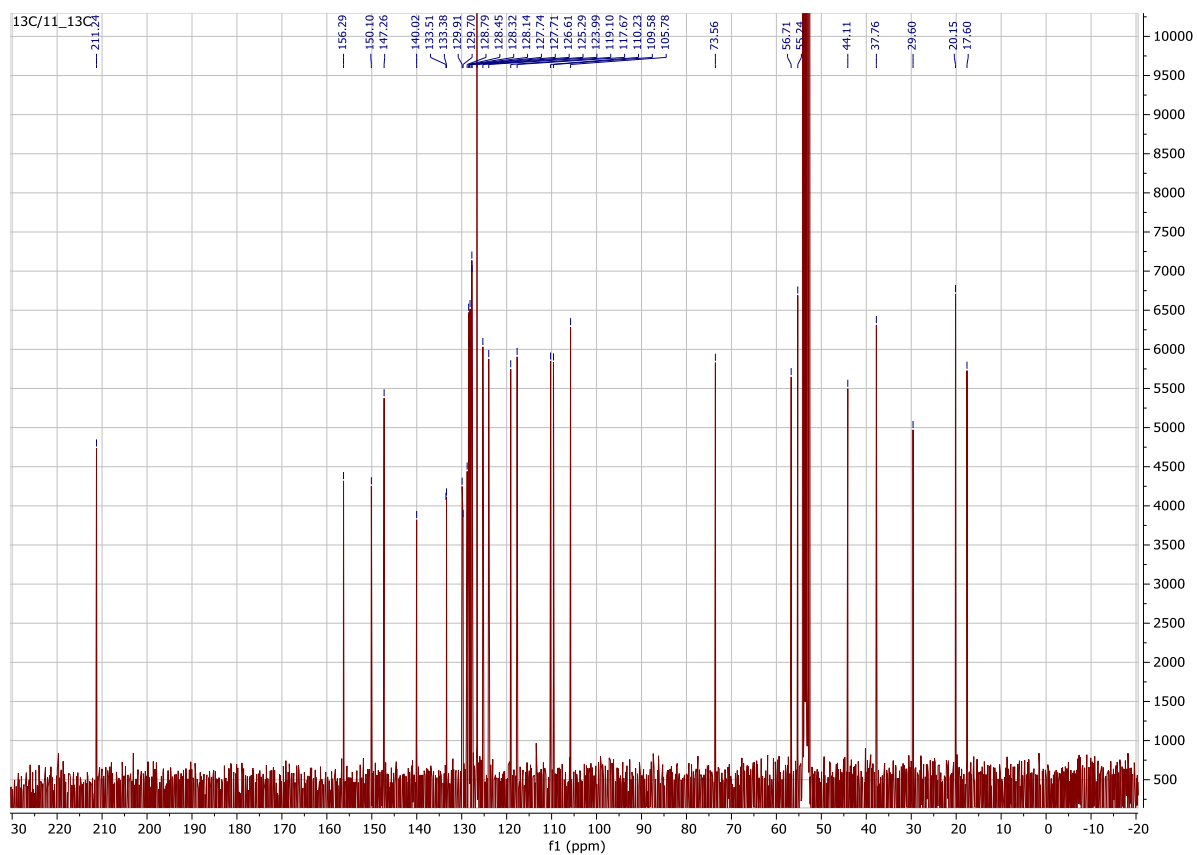
ESIMS: M<sup>+</sup>(C<sub>32</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub>)

*m/z* Theoretical: 474.23018

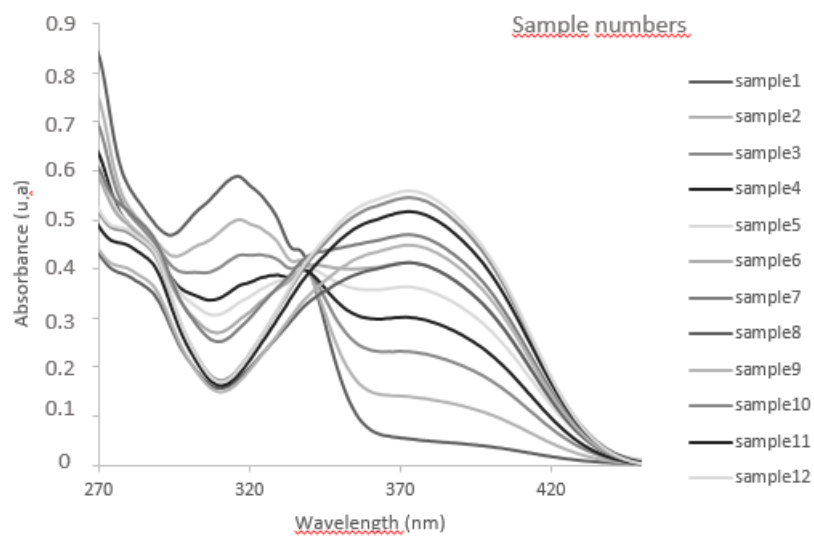
*m/z* Found: 474.2298



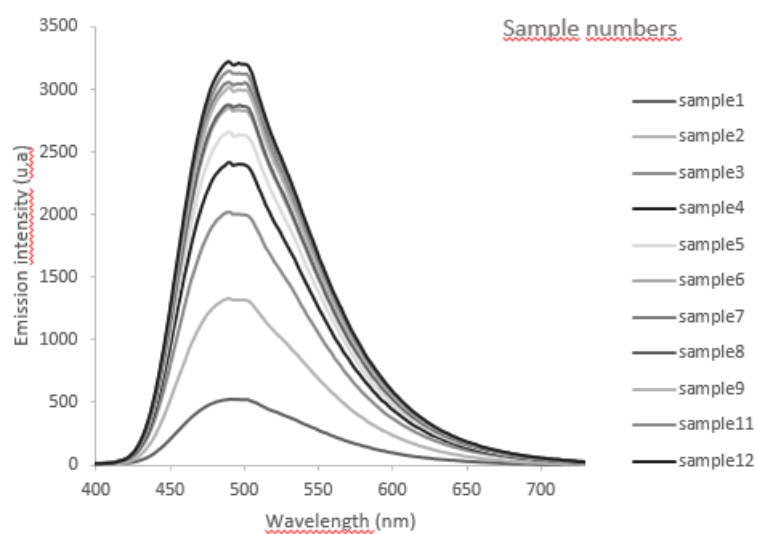
<sup>1</sup>H NMR spectrum (300 MHz, Acetone) for **11**.



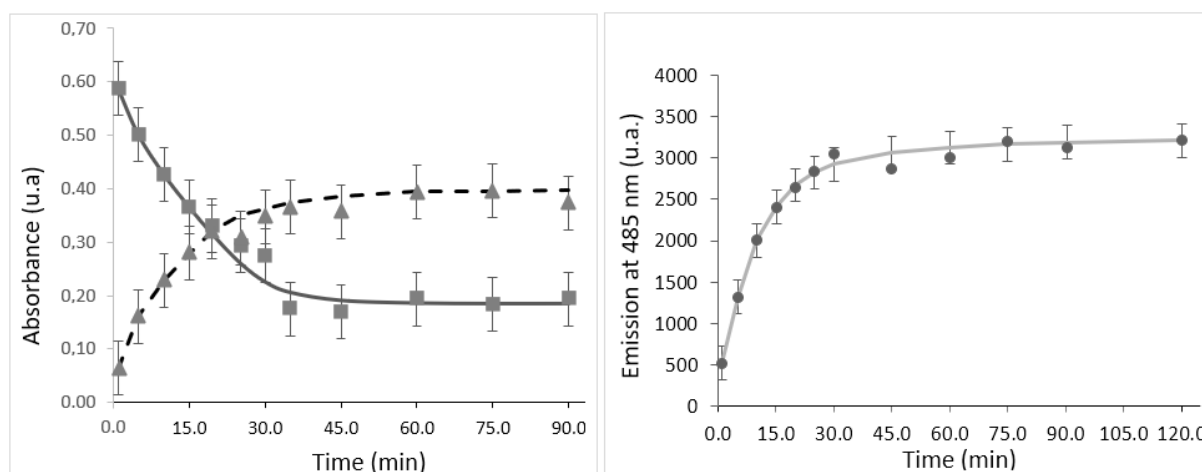
$^{13}\text{C}$  NMR spectrum (75 MHz,  $\text{CD}_2\text{Cl}_2$ ) for **11**.



**Figure SI-19:** Evolution of absorption spectra during the synthesis of **11**.



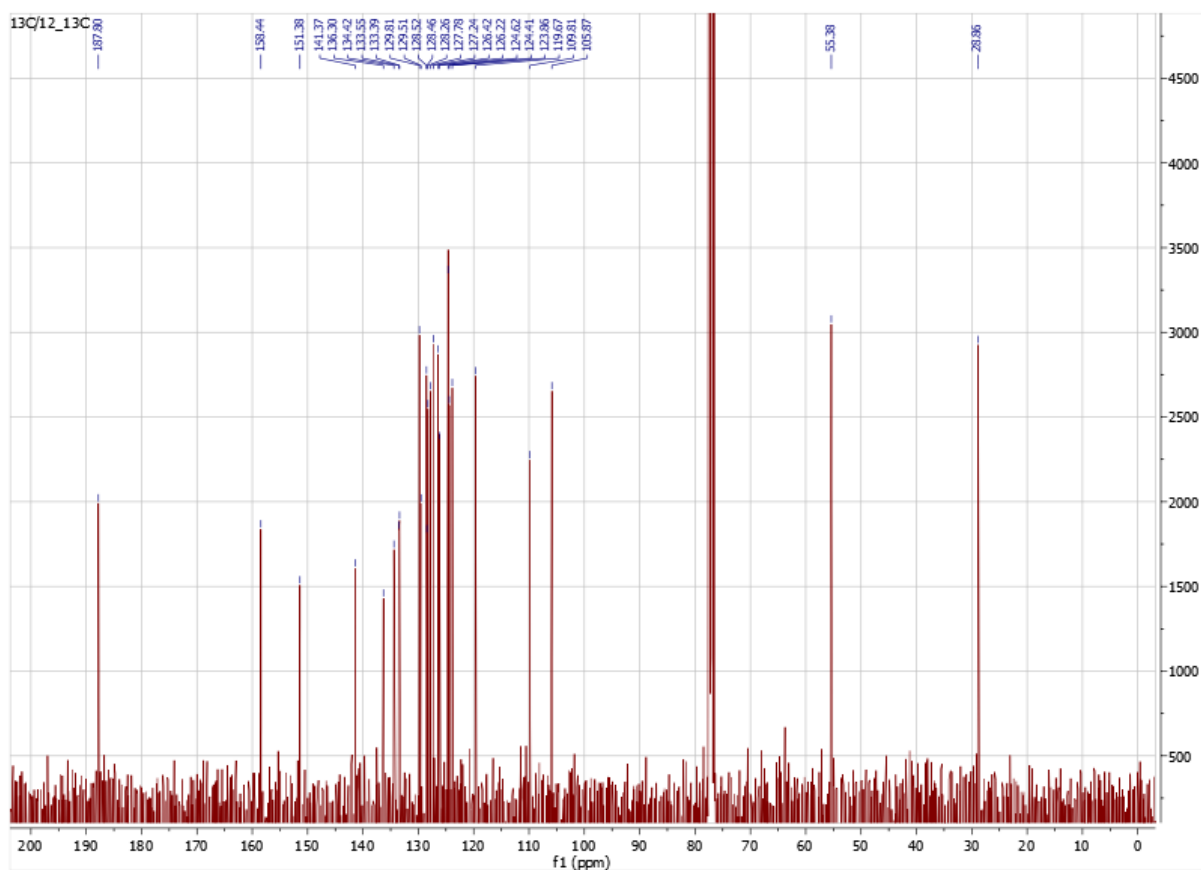
**Figure SI-20:** Evolution of emission spectra during the synthesis of **11**.



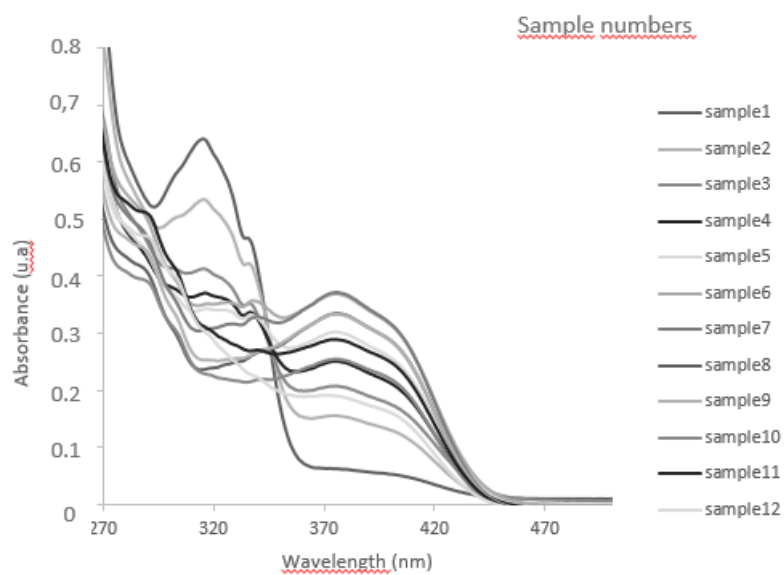
**Figure SI-21:** Curves obtained using samples taken during the synthesis of **11**. On the left: evolution of the absorption maxima of tetrazole **6** (■) at 316 nm and of the reaction mixture (Δ) at 375 nm. Right figure: evolution of the emission maxima of the reaction mixture at 500 nm.



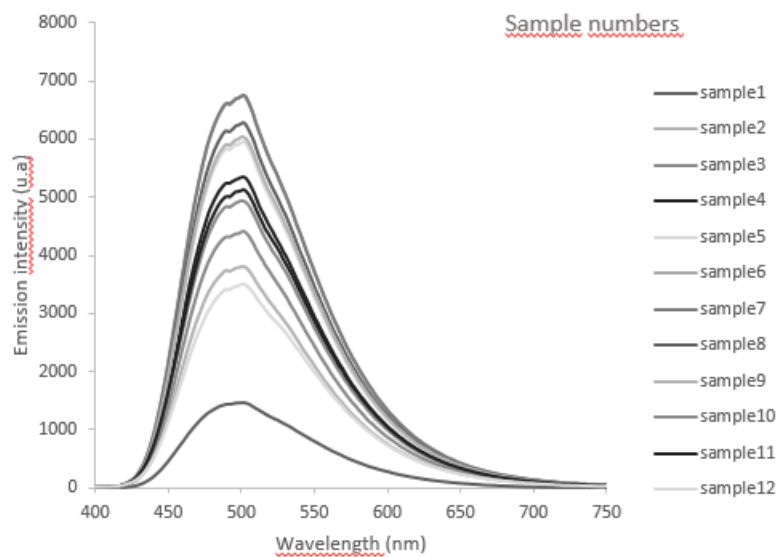




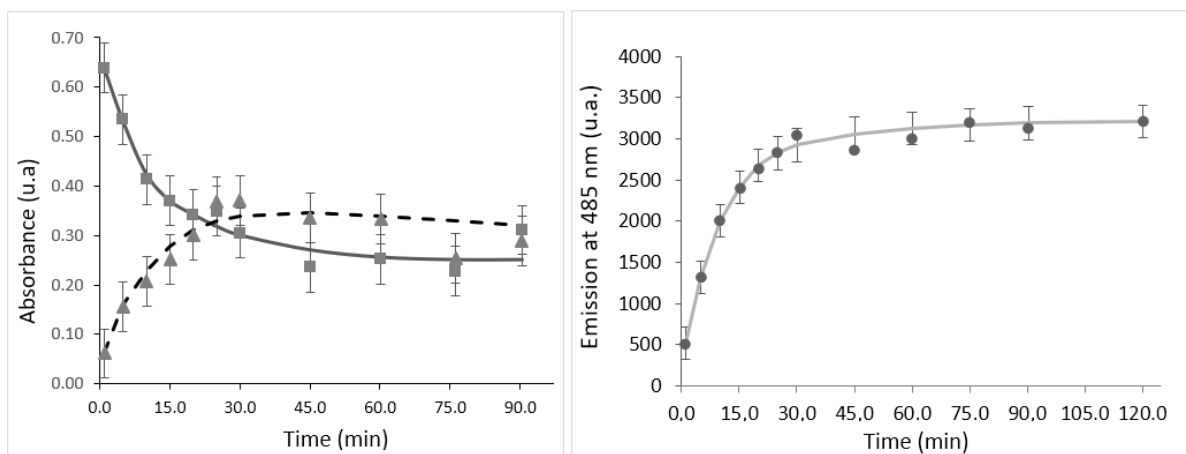
<sup>13</sup>C NMR spectrum (75 MHz, CDCl<sub>3</sub>) for **12**.



**Figure SI-22:** Evolution of absorption spectra during the synthesis of **12**.



**Figure SI-23:** Evolution of emission spectra during the synthesis of **12**.



**Figure SI-24:** Curves obtained using samples taken during the synthesis of **12**. On the left: evolution of the absorption maxima of tetrazole **6** (■) at 316 nm and of the reaction mixture (Δ) at 375 nm. Right figure: evolution of the emission maxima of the reaction mixture at 500 nm.