

# First expeditious synthesis of 6, 11-diamino-[6]helicenes

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## Supporting Information

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## Table of contents

|   |    |
|---|----|
| Operating methods .....   | 4  |
| Procedure for the Suzuki-Miyaura Reaction .....                                     | 4  |
| Bromination/Cyanation .....   | 4  |
| Cyclisation (thermal activation)/Acetylation .....                                  | 5  |
| Cyclisation (ultrasonic activation)/Acetylation .....                               | 5  |
| Analytical data .....   | 6  |
| 1,8-di( <i>o</i> -tolyl)naphthalene <b>3</b> .....                                  | 6  |
| 1,8-Di(4-methoxy-2-methylphenyl)naphthalene <b>7</b> .....                          | 6  |
| 1,8-di(2-cyanomethylphenyl)naphthalene <b>2</b> .....                               | 7  |
| 1,8-di(2-cyanomethyl-4-methoxyphenyl)naphthalene <b>8</b> .....                     | 8  |
| 6,11-diacetamido-[6]-helicene <b>6</b> .....  | 8  |
| 3,14-dimethoxy-6,11-diacetamido-[6]-helicene <b>9</b> .....                         | 9  |
| NMR Spectrum .....  | 10 |
| <sup>1</sup> H NMR 1,8-di( <i>o</i> -tolyl)naphthalene <b>3</b> .....               | 10 |
| <sup>13</sup> C NMR 1,8-di( <i>o</i> -tolyl)naphthalene <b>3</b> .....              | 11 |
| <sup>1</sup> H NMR 1,8-di(4-methoxy-2-methylphenyl)naphthalene <b>7</b> .....       | 12 |
| <sup>13</sup> C NMR 1,8-di(4-methoxy-2-methylphenyl)naphthalene <b>7</b> .....      | 13 |
| <sup>1</sup> H NMR 1,8-di(2-cyanomethylphenyl)naphthalene <b>2</b> .....            | 14 |
| <sup>13</sup> C NMR 1,8-di(2-cyanomethylphenyl)naphthalene <b>2</b> .....           | 15 |
| <sup>1</sup> H NMR 1,8-di(2-cyanomethyl-4-methoxyphenyl)naphthalene <b>8</b> .....  | 16 |
| <sup>13</sup> C NMR 1,8-di(2-cyanomethyl-4-methoxyphenyl)naphthalene <b>8</b> ..... | 17 |
| <sup>1</sup> H NMR 6,11-diacetamido-[6]-helicene <b>6</b> .....                     | 18 |
| <sup>13</sup> C NMR 6,11-diacetamido-[6]-helicene <b>6</b> .....                    | 19 |
| <sup>1</sup> H NMR 3,14-dimethoxy,6,11-diacetamido-[6]-helicene <b>9</b> .....      | 20 |
| <sup>13</sup> C NMR 3,14-dimethoxy-6,11-diacetamido-[6]-helicene <b>9</b> .....     | 21 |
| X-Ray diffraction analysis .....  | 22 |

## General

Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without purification. Petroleum ether was distilled under Argon, DMF was distilled on CaH<sub>2</sub>, DMSO was distilled under reduced pressure, THF was dried on sodium/benzophenone and distilled under argon. Boronic acids were purchased from Aldrich and Alfa aesar and were used without purification. NMR spectra were recorded on a 300 MHz and 200 MHz Brucker spectrometer. Chemical shifts were reported in ppm relative to the residual solvent peak (7.26 ppm for CHCl<sub>3</sub>, 2.5 ppm DMSO-d6, 3.31 for CD<sub>3</sub>OD) for <sup>1</sup>H spectra and (77.00 ppm for CDCl<sub>3</sub>, 39.52 ppm for DMSO-d6, 49.00 ppm for CD<sub>3</sub>OD) for <sup>13</sup>C spectra. High Resolution Mass spectroscopy data were recorded on a Autospec Ultima (Waters/Micromass) device with a resolution of 5000 RP at 5%. UV spectra data were recorded on a Agilent 8453 UV-Visible Spectrometry system at 25 °C.

# Operating methods

## Procedure for the Suzuki-Miyaura Reaction

To a stirred suspension of 1,8-dibromonaphthalene<sup>[S1]</sup> **4** (285.9 mg; 1 mmol), boronic acid (2.4 mmol; 2.4 eq.), and Cs<sub>2</sub>CO<sub>3</sub> (1.6 g, 5 mmol; 5 eq.) in DMF/H<sub>2</sub>O (95:5, 2.5 mL) was added the palladium complex **5** (4.52 mg; 1% mol). The mixture was stirred at 100 °C for one night. Diethylether (50 mL) and water (50 mL) were then added, and the aqueous phase was extracted with diethylether (2x10 mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel (petroleum ether) to give the 1,8-di(*o*-tolyl)naphthalene **3** (245 mg; 80%) as a pale yellow solid.

Using the same procedure 1,8-di(4-methoxy-2-methylphenyl)naphthalene **7** was isolated in 85% yield.

## Bromination/Cyanation

To a solution of the 1,8-di(*o*-tolyl)naphthalene **3** (150 mg; 0.49 mmol) in CCl<sub>4</sub> (5 mL) was added *N*-Bromosuccinimide (181 mg; 1.03 mmol; 2.1 eq.) and a catalytic amount of AIBN. The solution was refluxed for 4 h and the solvent evaporated under reduced pressure. The crude product was filtered through a pad of silica gel (Petroleum ether/chloroform: 1/1) to give a white solid (230 mg). The white solid was dried under vacuum, and solubilized in DMSO (1 mL). Potassium cyanide (100 mg; 1.5 mmol; 3 eq.) was then added and the suspension was allowed to stir at room temperature overnight. The resulting redish solution was poured into water, the aqueous layer was extracted with dichloromethane (3x20 mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered, and concentrated under vacuum. The crude product was purified by gradient flash chromatography on silica gel (Petroleum ether/ethyl acetate: 95/5, then 80/20), to give 1,8-di(2-cyanomethylphenyl)naphthalene **2** as a white solid (105 mg; 60%).

Using the same procedure 1,8-di(2-cyanomethyl-4-methoxyphenyl)naphthalene **8** was isolated in 60% yield.

## Cyclisation (thermal activation)/Acetylation

The dinitrile product **2** (40 mg; 0.11 mmol) was solubilized in polyphosphoric acid (1 mL). The mixture was stirred at 100 °C overnight. The resulting greenish mixture was poured into ice (15 g) and basified with a K<sub>2</sub>CO<sub>3</sub> 1M solution until pH = 11-12. This aqueous layer was extracted with ethyl acetate (3x10 mL) and the combined organic layer was dried (MgSO<sub>4</sub>), filtered and concentrated under vacuum. To the resulting solid in THF (1 mL) at 0° were successively added triethylamine (20 µL; 2.1 eq.) and acetyl chloride (10 µL; 2 eq.). The suspension was stirred at room temperature overnight. Water (10 mL) was added and the aqueous phase was extracted with ethyl acetate (2x10 mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered, and concentrated under vacuum. The crude product was purified by thin layer chromatography (AcOEt) to give the 6,11-diacetamido-[6]-helicene **6** (20 mg; 40%) as a pale yellow solid.

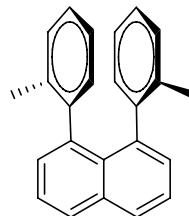
Using the same procedure 3,14-dimethoxy-6,11-diacetamido-[6]-helicene **9** was isolated in 30% yield.

## Cyclisation (ultrasonic activation)/Acetylation

The dinitrile product (40 mg; 0.095 mmol) was solubilized in polyphosphoric acid (1 mL) and sonoactivated at 40 °C overnight. The reddish mixture was poured into ice (15 g) and the suspension was stirred few minutes. See the thermal activation for work up procedure. The crude product was purified by thin layer chromatography (AcOEt) to give the 3,14-dimethoxy-6,11-diacetamido-[6]-helicene **9** (21 mg; 44%) as a white solid.

## Analytical data

### 1,8-di(*o*-tolyl)naphthalene **3**



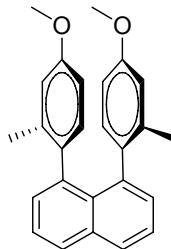
Chemical Formula: C<sub>24</sub>H<sub>20</sub>

**<sup>1</sup>H NMR:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 300 MHz): 7.95 (dd, 2H,  $J$  = 8.2, 1 Hz), 7.51 (dt, 2H,  $J$  = 8.2, 1 Hz), 7.20 (m, 2H), 7.10-6.75 (m, 8H), 1.91 (s, (syn form)), 1.88 (s, (anti form)).

**<sup>13</sup>C NMR:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 75 MHz): 142.3, 141.9, 139.7, 139.7, 135.4, 135.0, 135.0, 134.7, 131.4, 130.2, 130.0, 129.9, 128.9, 128.5, 128.4, 128.2, 126.6, 126.1, 124.9, 124.8, 124.3, 124.2, 20.6, 20.4.

Data in accordance with literature.<sup>[S2]</sup>

### 1,8-Di(4-methoxy-2-methylphenyl)naphthalene **7**



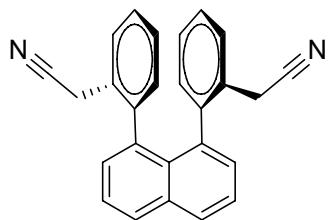
Chemical Formula: C<sub>26</sub>H<sub>24</sub>O<sub>2</sub>

**RMN <sup>1</sup>H :** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 300 MHz) : 7.91 (dd, 2H,  $J$  = 8.3, 1.3 Hz), 7.49 (dt, 2H,  $J$  = 8.3, 1.3 Hz), 7.19 (dd, 2H,  $J$  = 7, 1.3 Hz), 6.90 (d,  $J$  = 8.3 Hz (anti form)), 6.69 (d,  $J$  = 8.1 Hz (syn form)), 6.39 (dd, 2H,  $J$  = 8.3, 2.7 Hz), 6.34 (d,  $J$  = 2.7 Hz (syn form)), 6.29 (d,  $J$  = 2.7 Hz (anti form)) 3.73 (s, (syn form)), 3.72 (s, (antiform)), 1.85 (s, (syn form)), 1.78 (s, (anti form)).

**RMN <sup>13</sup>C :** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 75 MHz) : 158.0, 157.5, 139.4, 139.3, 136.8, 136.4, 135.3, 134.8, 134.7, 132.2, 130.9, 130.3, 130.1, 128.9, 128.5, 128.4, 124.9, 124.7, 114.3, 114.2, 110.2, 109.8, 56.1, 20.9, 20.8.

**Melting point :** 124 °C

1,8-di(2-cyanomethylphenyl)naphthalene **2**



Chemical Formula: C<sub>26</sub>H<sub>18</sub>N<sub>2</sub>

**<sup>1</sup>H NMR:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 200 MHz): 8.02 (dd, 2H,  $J$  = 8.2, 1.2 Hz), 7.57 (dt, 2H,  $J$  = 7.9, 1.2 Hz), 7.24 (m, 2H), 7.10-7.03 (m, 8H), 3.19 (s, 4H).

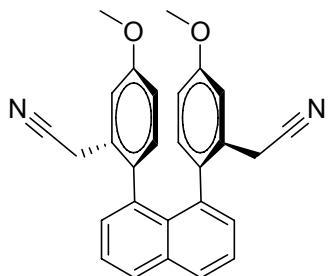
**<sup>13</sup>C NMR:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 75 MHz): 141.3, 136.4, 134.9, 130.9, 129.9, 128.6, 128.1, 127.9, 127.6, 127.4, 125.7, 117.7, 22.4.

**IR:** ( $\nu$  cm<sup>-1</sup>): 758, 775, 832, 1176, 1192, 1236, 1368, 1415, 1442, 1489, 2250 (CN), 2926, 2968, 3055.

**HRMS (ESI):**  $m/z$  calculated for C<sub>26</sub>H<sub>18</sub>N<sub>2</sub>Na ([M+Na]<sup>+</sup>): 381.1383; found: 381.1368.

**Melting point :** 176 °C

1,8-di(2-cyanomethyl-4-methoxyphenyl)naphthalene **8**



Chemical Formula: C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>

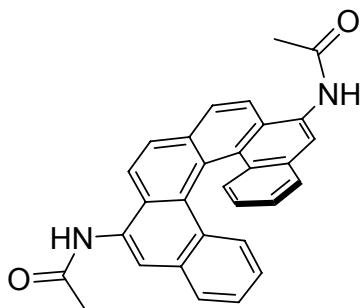
**RMN <sup>1</sup>H:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 300 MHz) : 7.99 (dd, 2H, J = 8.2, 1.2 Hz), 7.52 (dt, 2H, J = 8.1, 1.2 Hz), 7.23 (dd, 2H, J = 7, 1.3Hz), 6.95 (d, 2H, 8.3 Hz), 6.66 (dd, 2H, J = 8.3, 2.5 Hz), 6.58 (d, 2H, J = 2,5 Hz), 3.78 (s, 6H), 3.13 (s, 4H).

**RMN <sup>13</sup>C:** ( $\delta$  ppm, CDCl<sub>3</sub>, 300K, 100 MHz) : 158.9, 136.1, 135.0, 133.8, 131.0, 129.8, 129.5, 129.1, 125.6, 117.6, 113.1, 113.0, 55.3, 22.6.

**HRMS (ESI):** *m/z* calculated for C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Na ([M+Na]<sup>+</sup>): 441.1579; found: 441.1578.

**Melting point :** 147 °C

6,11-diacetamido-[6]-helicene **6**



Chemical Formula: C<sub>30</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>

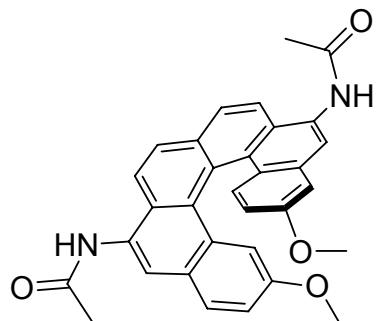
**<sup>1</sup>H NMR:** ( $\delta$  ppm, DMSO-d6, 300K, 200 MHz): 10.25 (s, 2H), 8.31 (d, 2H, J = 8.5 Hz), 8.20 (d, 2H, J = 8.5 Hz), 8.14 (s, 2H), 7.86 (d, 2H, J = 8.0 Hz), 7.34 (d, 2H, J = 8.5 Hz), 7.23 (t, 2H, J = 7.4 Hz), 6.65 (t, 2H, J = 7.5 Hz), 2.30 (s, 6H).

**<sup>13</sup>C NMR (Jmod):** ( $\delta$  ppm, DMSO-d6, 300K, 75 MHz): 169.4, 132.4, 131.5, 131.0, 128.3, 127.6, 127.5, 126.4, 126.3, 126.0, 124.3, 122.9, 122.7, 23.6.

**HRMS (ESI)**:  $m/z$  calculated for  $C_{30}H_{22}N_2O_2$  ( $[M+H]^+$ ): 443.1760; found: 443.1762.

**Melting point** : 315 °C (decomp.)

**3,14-dimethoxy-6,11-diacetamido-[6]-helicene 9**



Chemical Formula:  $C_{32}H_{26}N_2O_4$

**$^1H$  NMR**: ( $\delta$  ppm, CD<sub>3</sub>OD, 300K, 200 MHz): 8.11 (d, 2H,  $J = 8.5$  Hz), 7.94 (d, 2H,  $J = 8.5$  Hz), 7.92 (s, 2H), 7.38 (d, 2H,  $J = 9.5$  Hz), 7.19 (d, 2H,  $J = 2.6$  Hz), 6.28 (dd, 2H,  $J = 9.5, 2.6$  Hz), 3.78 (s, 6H), 2.36 (s, 6H).

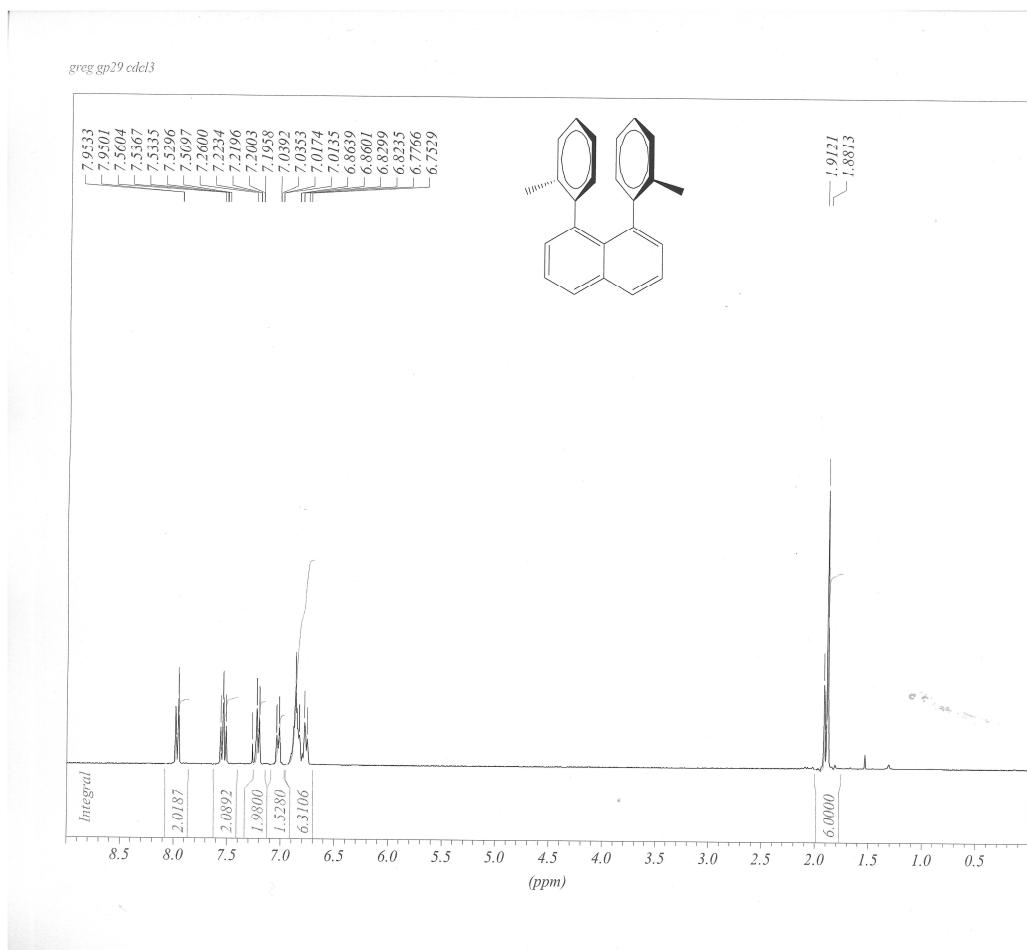
**$^{13}C$  NMR**: ( $\delta$  ppm, CD<sub>3</sub>OD, 300K, 75 MHz): 173.3, 159.0, 134.4, 132.5, 130.8, 130.2, 127.9, 126.8, 124.8, 124.7, 124.6, 123.1, 116.9, 107.8, 55.6, 24.1.

**HRMS (ESI)**:  $m/z$  calculated for  $C_{32}H_{27}N_2O_4$  ( $[M+H]^+$ ): 503.1971; found: 503.1982.

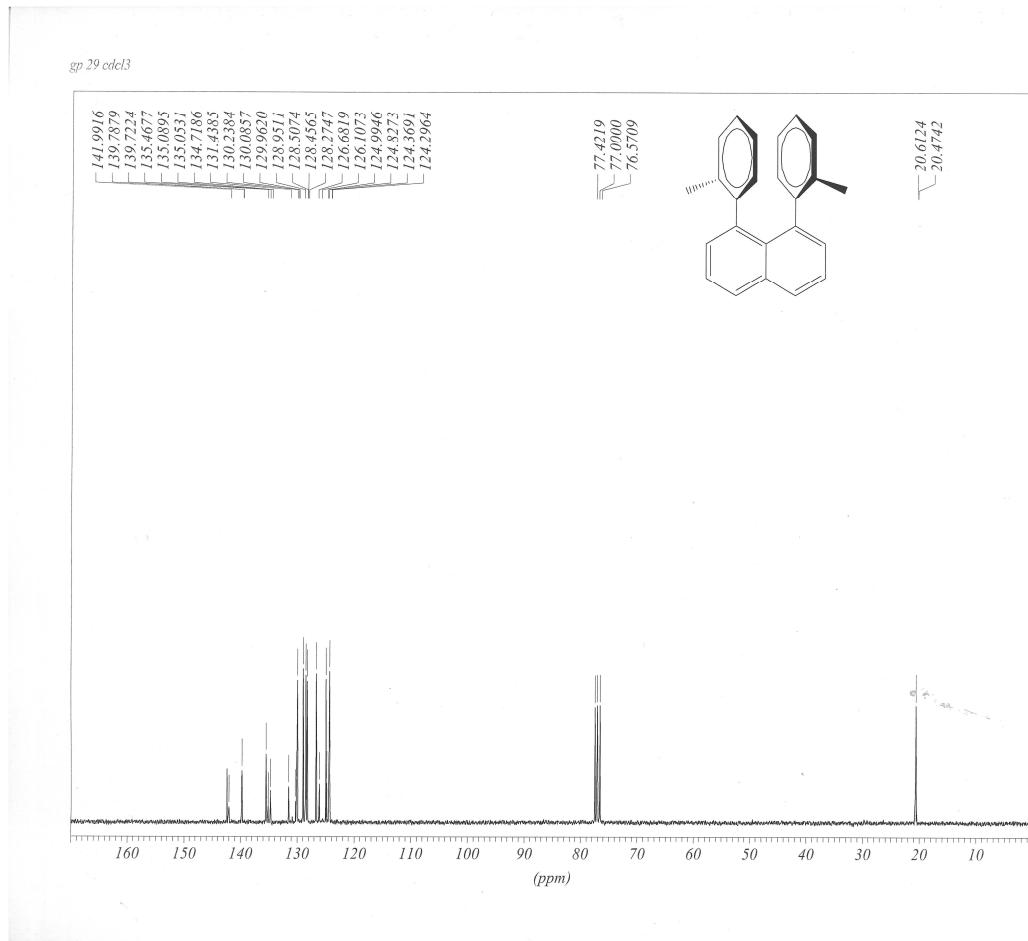
**Melting point** : 270 °C

# NMR Spectrum

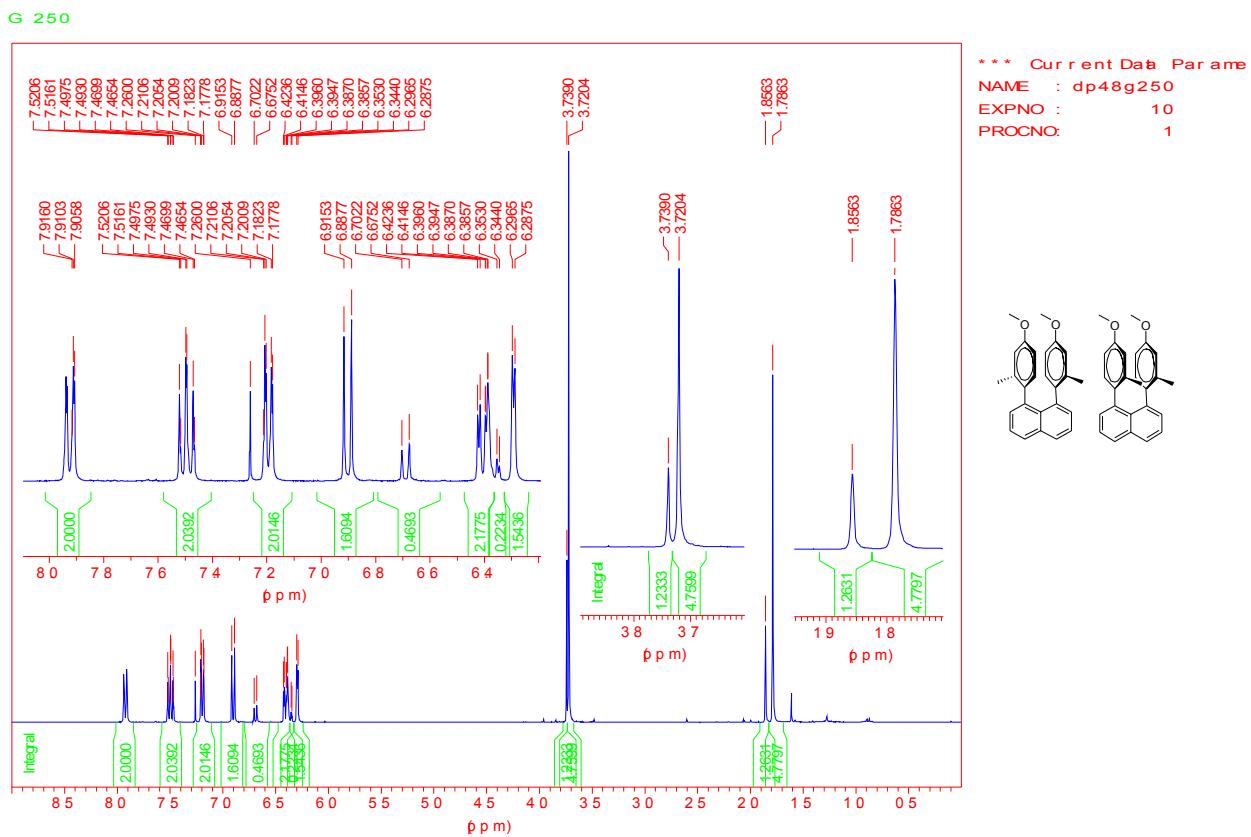
## <sup>1</sup>H NMR 1,8-di(*o*-tolyl)naphthalene 3



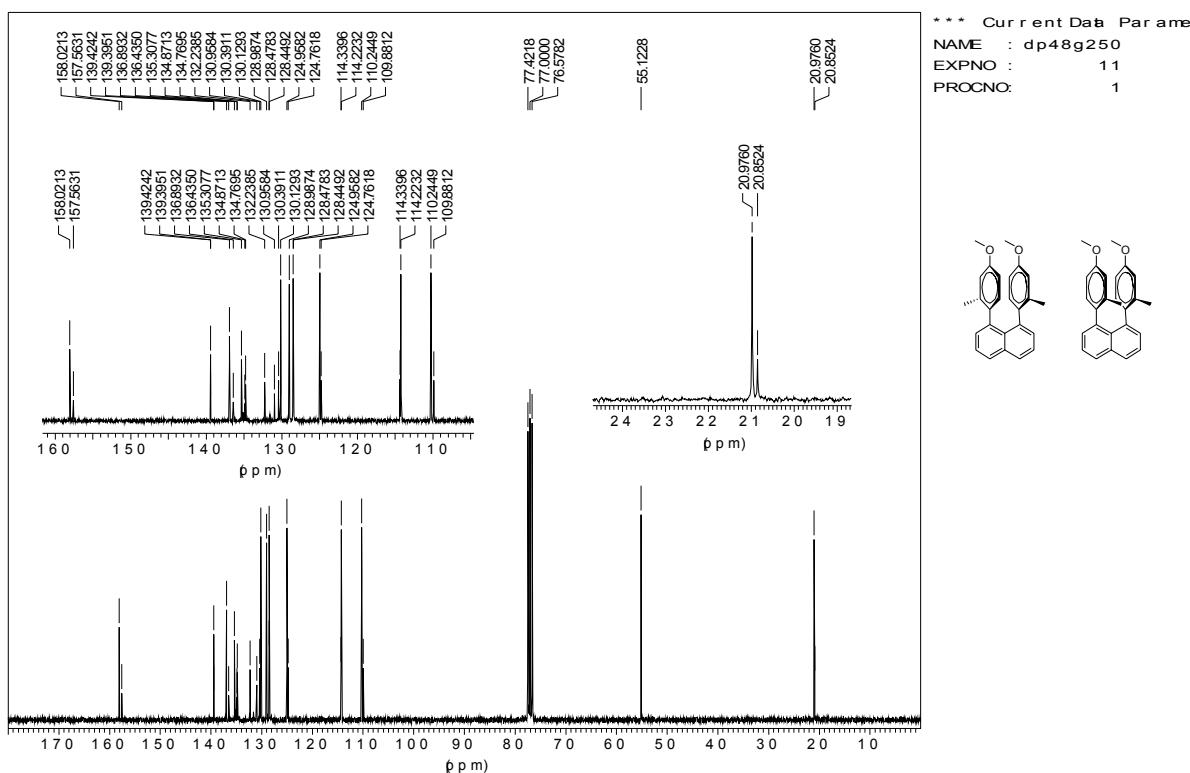
### **<sup>13</sup>C NMR 1,8-di(*o*-tolyl)naphthalene 3**



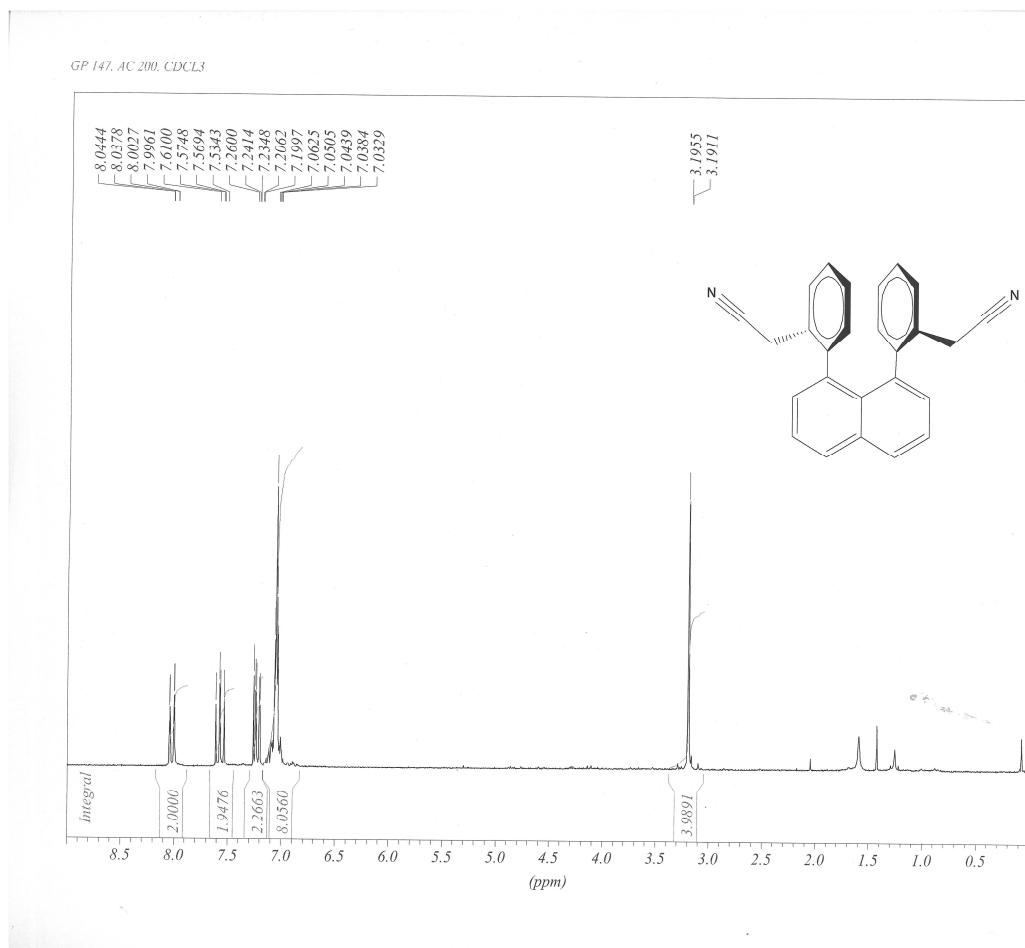
**<sup>1</sup>H NMR 1,8-di(*o*-tolyl) diMeOnaphthalene 7**



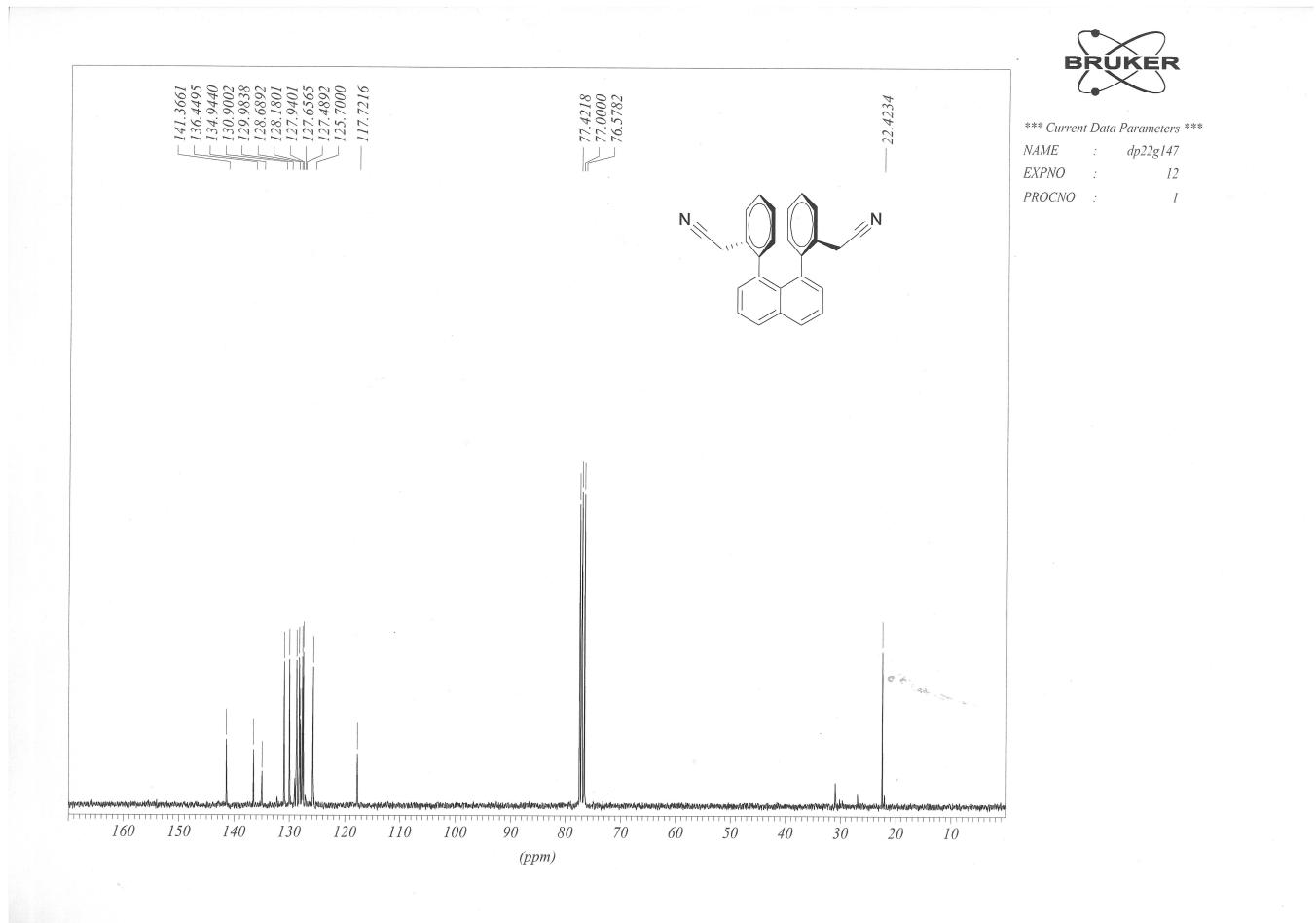
**<sup>13</sup>C NMR 1,8-di(*o*-tolyl)diMeOnaphthalene 7**



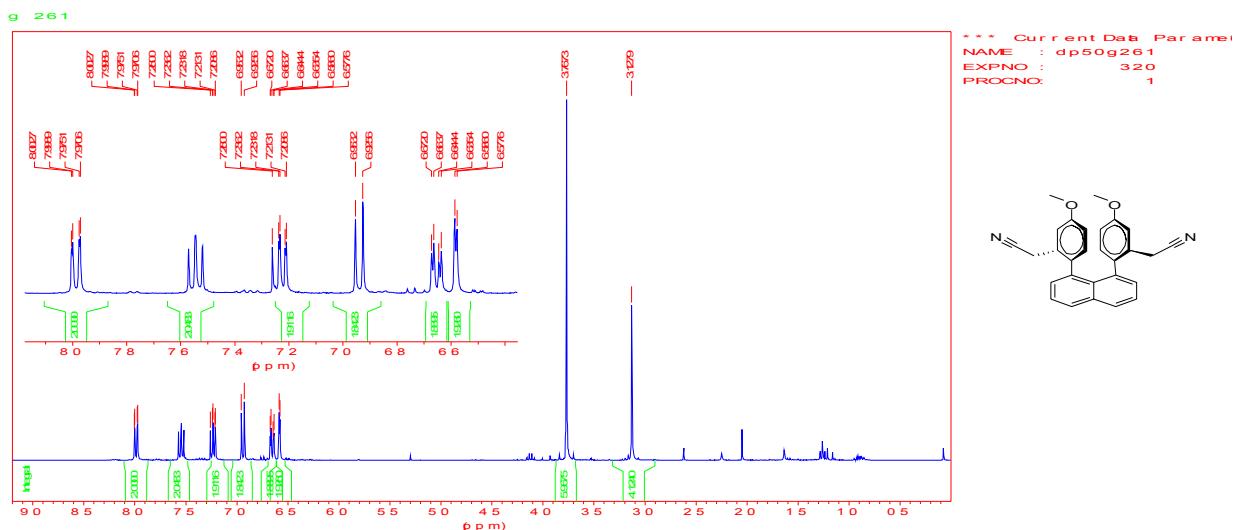
## **<sup>1</sup>H NMR 1,8-di(2-cyanomethylphenyl)naphthalene 2**



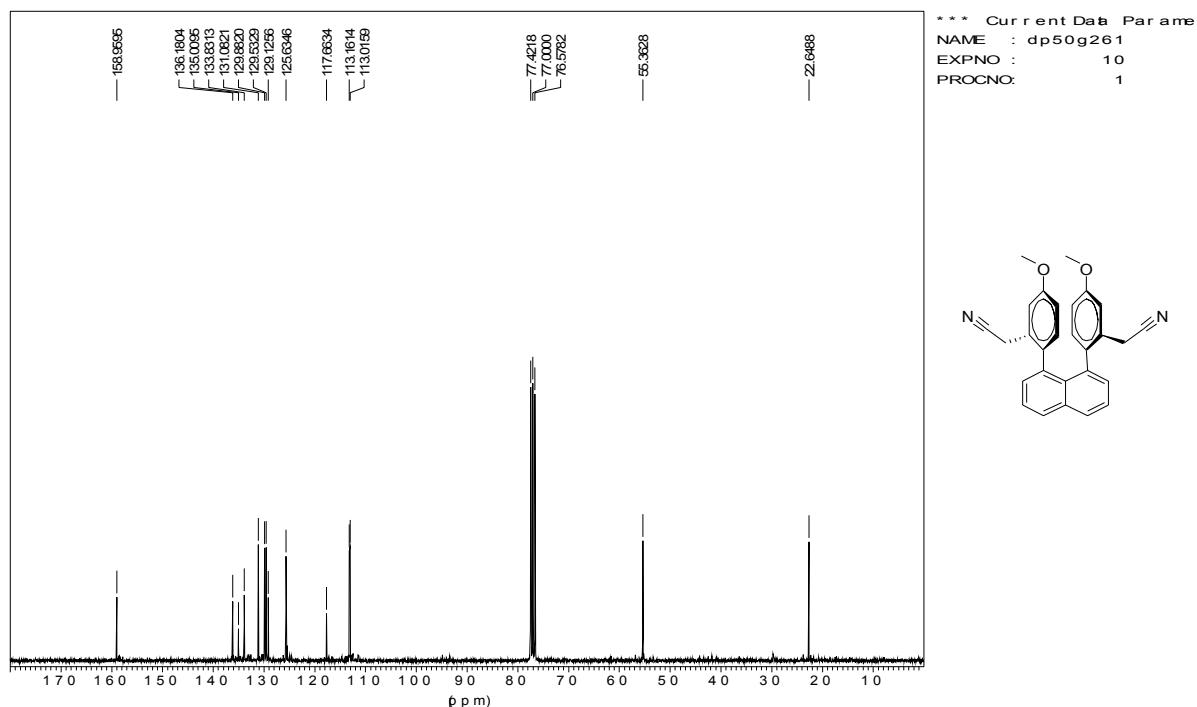
**<sup>13</sup>C NMR 1,8-di(2-cyanomethylphenyl)naphthalene 2**



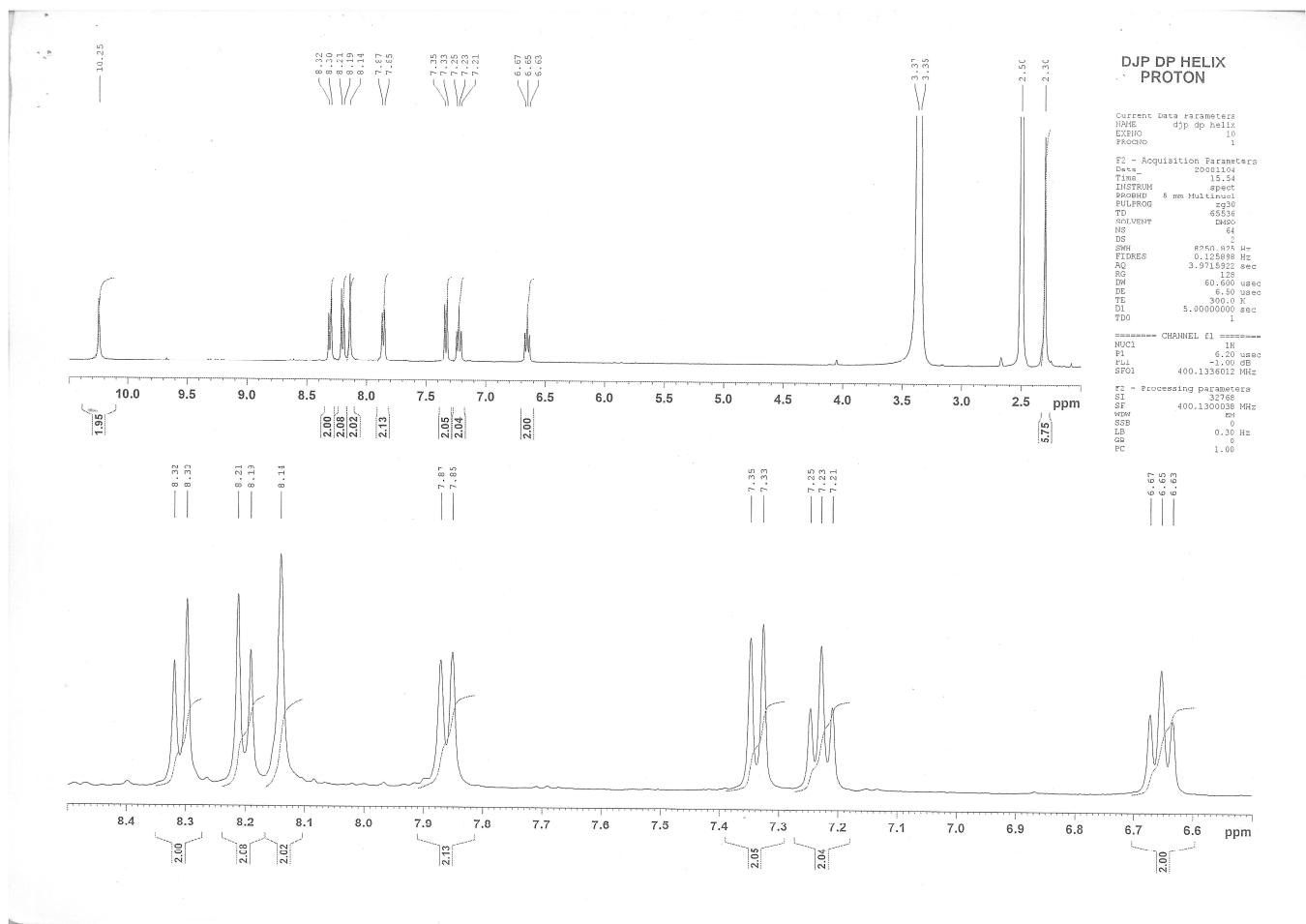
**<sup>1</sup>H NMR 1,8-di(2-cyanomethylphenyl)diMeOnaphthalene 8**



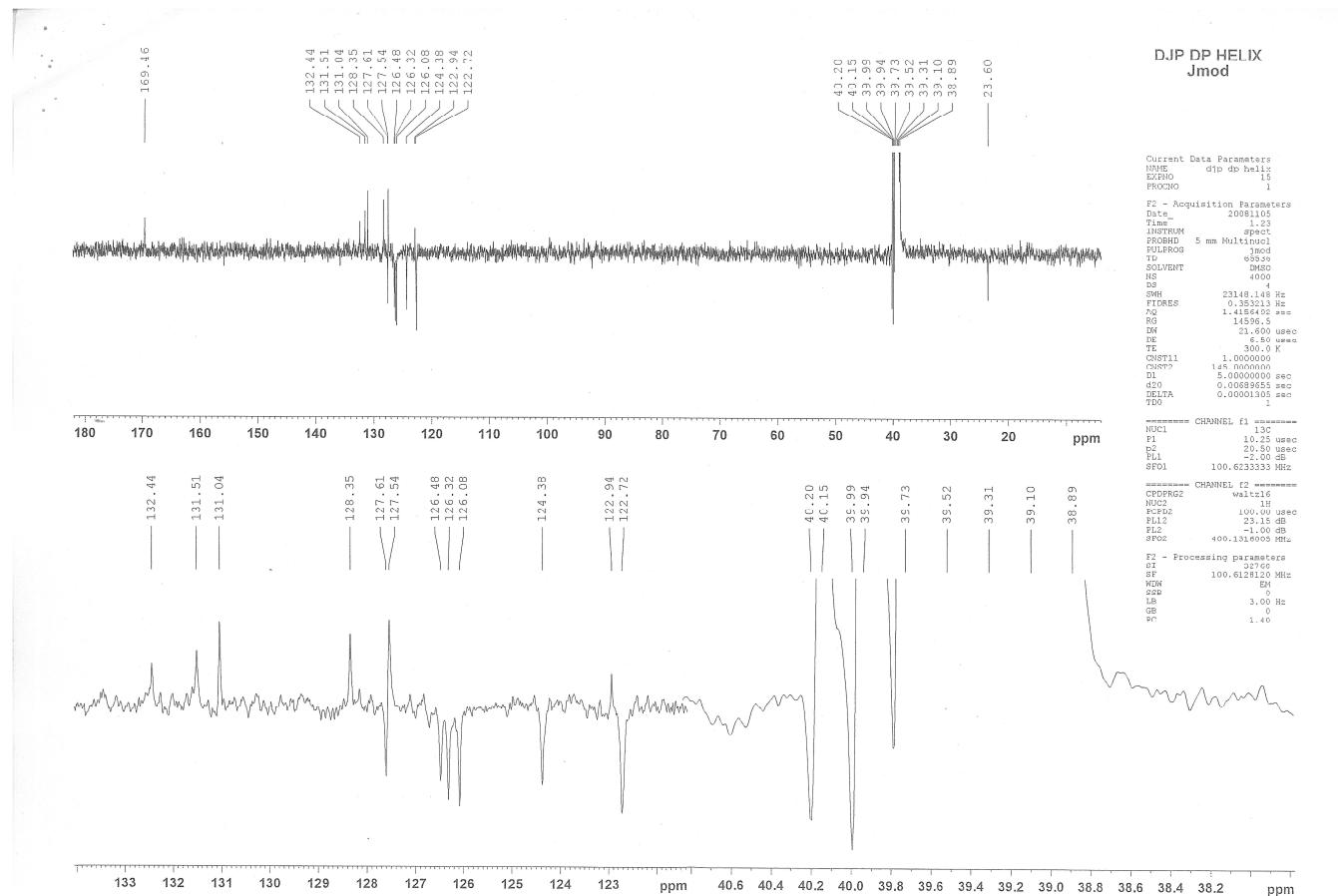
**<sup>13</sup>C NMR 1,8-di(2-cyanomethylphenyl)diMeOnaphthalene 8**



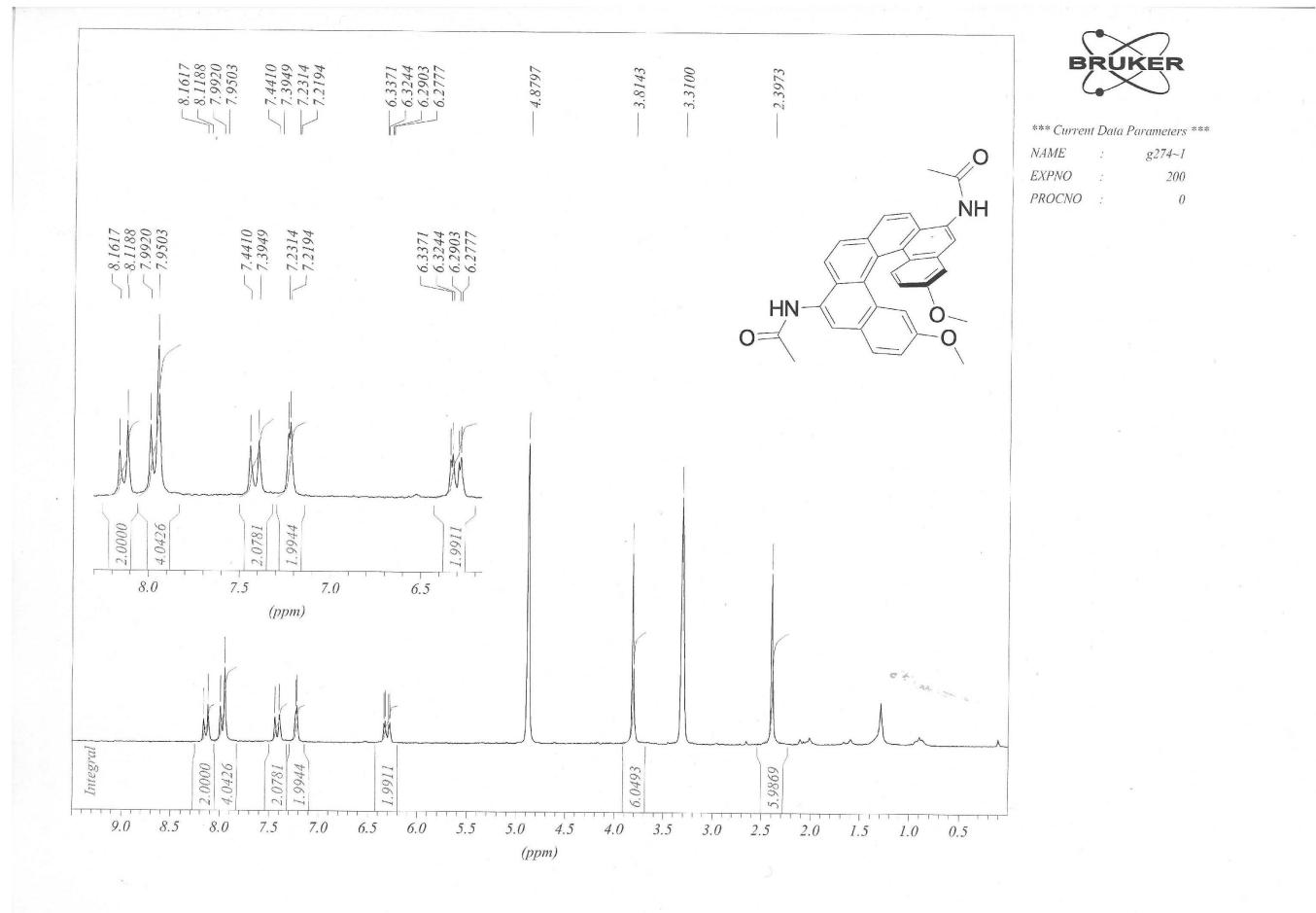
**<sup>1</sup>H NMR 6,11-diacetamido-[6]-helicene 6**



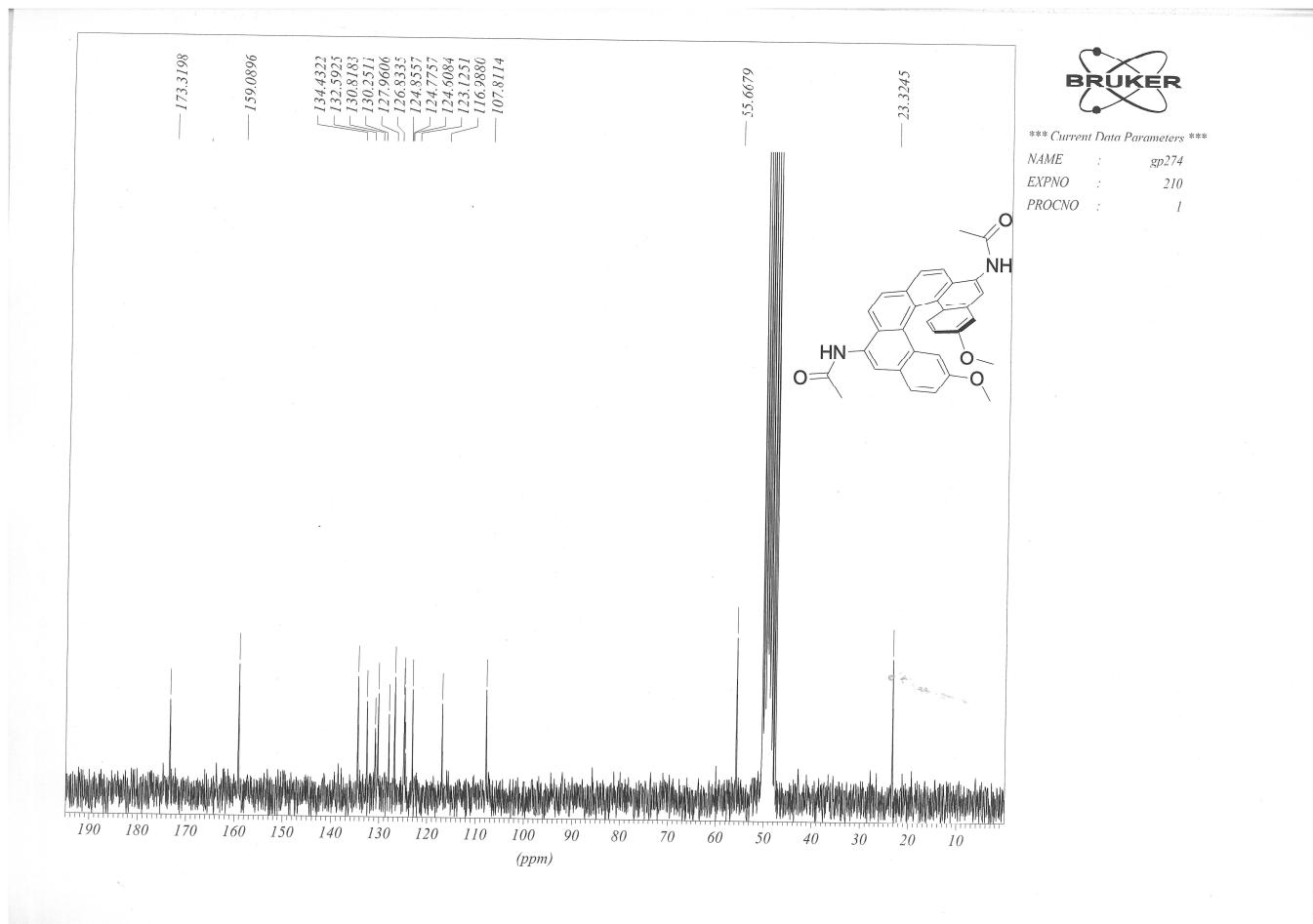
**<sup>13</sup>C NMR 6,11-diacetamido-[6]-helicene 6**



**<sup>1</sup>H NMR 3,14-dimethoxy,6,11-diacetamido-[6]-helicene 9**



**<sup>13</sup>C NMR 3,14-dimethoxy-6,11-diacetamido-[6]-helicene 9**



## X-Ray diffraction analysis

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Crystal of dimensions 0.24 x 0.12 x 0.06 mm<sup>3</sup> was mounted with Paratone-N oil (Hampton Research) coating and immediately placed in a nitrogen cold stream.

X-ray intensity data were collected on a Bruker X8-APEX2 CCD area-detector diffractometer using Mo- $K_{\alpha}$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). Nine sets of narrow data frames (30 s per frame) were collected at different values of  $\theta$ , for 8 and 1 initial values of  $\phi$  and  $\omega$ , respectively, using 0.5° increments of  $\phi$  or  $\omega$ . Data reduction was accomplished using SAINT V7.03 [S3]. The substantial redundancy (5.0) in data allowed a semi-empirical absorption correction (SADABS V2.10) [S3] to be applied, on the basis of multiple measurements of equivalent reflections. The structure was solved by direct methods, developed by successive difference Fourier syntheses, and refined by full-matrix least-squares on all F<sup>2</sup> data using SHELXTL V6.12[S4]. Hydrogen atoms were included in calculated positions and allowed to ride on their parent atoms.

Table 1. Crystal data and structure refinement for CCDC 719176.

|                                   |  |
|-----------------------------------|--|
| Identification code               | CCDC 719176  |
| Empirical formula                 | C <sub>34</sub> H <sub>29</sub> N <sub>3</sub> O <sub>4</sub>  |
| Formula weight                    | 543.60   |
| Temperature                       | 100(2) K   |
| Wavelength                        | 0.71073 Å  |
| Crystal system, space group       | Triclinic, P-1   |
| Unit cell dimensions              | a = 9.4922(14) Å alpha = 79.913(7)°<br>b = 11.5758(16) Å beta = 75.844(7)°<br>c = 13.5860(18) Å gamma = 73.560(7)° |
| Volume                            | 1379.3(3) Å <sup>3</sup>   |
| Z, Calculated density             | 2, 1.309 Mg/m <sup>3</sup>   |
| Absorption coefficient            | 0.087 mm <sup>-1</sup>   |
| F(000)                            | 572  |
| Crystal size                      | 0.24 x 0.12 x 0.06 mm  |
| Theta range for data collection   | 1.56 to 30.17 deg.   |
| Limiting indices                  | -13<=h<=13, -16<=k<=16, 19<=l<=18  |
| Reflections collected / unique    | 40142 / 8030 [R(int) = 0.0345]   |
| Completeness to theta = 30.17     | 98.2 %   |
| Absorption correction             | Semi-empirical from equivalents  |
| Max. and min. transmission        | 0.9948 and 0.9795  |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>  |
| Data / restraints / parameters    | 8030 / 0 / 375   |
| Goodness-of-fit on F <sup>2</sup> | 1.062  |
| Final R indices [I>2sigma(I)]     | R1 = 0.0469, wR2 = 0.1267  |
| R indices (all data)              | R1 = 0.0630, wR2 = 0.1397  |
| Largest diff. peak and hole       | 0.447 and -0.212 e.Å <sup>-3</sup>   |

Table 2. Hydrogen bonds for **9** [Å and deg.] .

| D-H...A<br>< (DHA)  | d (D-H) | d (H...A) | d (D...A)         |
|---------------------|---------|-----------|-------------------|
| N(1)-H(1')...O(2)#1 | 0.88    | 2.08      | 2.8923 (15) 153.7 |
| N(2)-H(2')...O(1)#2 | 0.88    | 2.01      | 2.8750 (15) 168.4 |

Symmetry transformations used to generate equivalent atoms:  
#1 x,y+1,z    #2 x+1,y-1,z

## References

- [S1]: For preparation of this compounds see: Š. Vyskočil, L. Meca, I. Tišlerová, I. Císařová, M. Polášek, S. R. Harutyunyan, Y. N. Belokon, R. M. J. Stead, L. Farrugia, S. C. Lockhart, W. L. Mitchell, P. Kočovský, *Chem. Eur. J.* **2002**, *8*, 4633-4648
- [S2]: R. L. Clough, J. D. Roberts, *J. Am. Chem. Soc.* **1976**, *98*, 1018-1020
- [S3]: APEX2 version 1.0-8; Bruker AXS: Madison, WI, 2003
- [S4]: SHELXTL version 6.12; Bruker AXS: Madison, WI, 2001