

## SUPPORTING INFORMATION

### Asymmetric Tandem Reactions of Dicyanoalkenes with Conjugated Sulfinyl Imino Esters

Francesc Ferrer-Pérez,<sup>a</sup> Marcos Escolano,<sup>a</sup> Daniel Gavina,<sup>a</sup> Santiago Díaz-Oltra,<sup>a</sup>  
Amparo Sanz-Marco,<sup>a</sup> María Sánchez-Roselló\*<sup>a</sup> and Carlos del Pozo\*<sup>a</sup>

<sup>a</sup> Departamento de Química Orgánica, Universidad de Valencia, 46100 Burjassot, España  
Fax: (+34)963544939; e-mail: [carlos.pozo@uv.es](mailto:carlos.pozo@uv.es); [maria.sanchez-rosello@uv.es](mailto:maria.sanchez-rosello@uv.es)

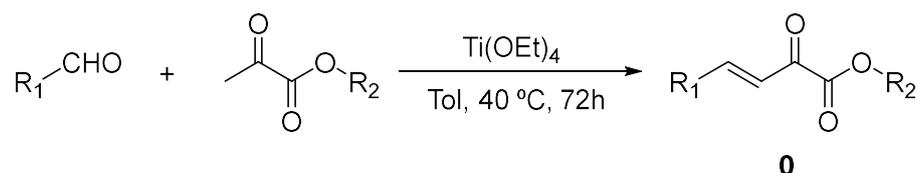
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## General remarks.

Solvents were purified prior to use: THF and toluene were distilled from sodium, and DCM was distilled from calcium hydride. The reactions were monitored by means of TLC on 0.25 mm precoated silica gel plates. Visualization was carried out with UV light and potassium permanganate stain. Flash column chromatography was performed with the indicated solvents on silica gel 60 (particle size 0.040–0.063 mm).  $^1\text{H}$ ,  $^{19}\text{F}$  and  $^{13}\text{C}$ -NMR spectra were recorded on a 300 MHz, 400 MHz or a 500 MHz spectrometer. Chemical shifts are given in ppm ( $\delta$ ), referenced to the residual proton resonances of the solvents. Coupling constants ( $J$ ) are given in hertz (Hz). The letters “m”, “s”, “d”, “t”, and “q” stand for multiplet, singlet, doublet, triplet, and quartet, respectively. The designation “b” indicates that the signal is broad. The abbreviations DCM and THF indicate dichloromethane and tetrahydrofuran, respectively. High-resolution mass spectra were carried out on VGmAutospec (VG Analytical, Micromass Instruments) by the Universidad de Valencia Mass Spectrometry Service using QTOF mass analyzer system. Enantiomeric ratios were determined with the aid of HPLC analysis with an appropriate chiral column (25cm x 0.46 cm) with mixtures of *n*-hexane: *i*-propanol as eluents.

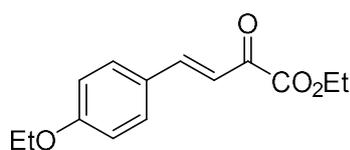
### General procedure A. Preparation of conjugated ketoesters **0**.



To a solution of the corresponding aldehyde and pyruvate (1.2 equiv.) in toluene (0.2M),  $\text{Ti(OEt)}_4$  (1.2 equiv.) was added. After stirring for 72 h at 40 °C, the reaction mixture was quenched with saturated  $\text{NaHCO}_3$  solution. The formed titanium precipitate was filtered over a Celite pad. The filtrate was added to a separatory funnel, and the two phases were separated. The aqueous phase was extracted 2 more times with  $\text{AcOEt}$ . Then, the organic phases were combined and dried over anhydrous sodium sulphate. The mixture was concentrated to dryness and purified by flash column chromatography on silica gel using mixtures of *n*-hexane and ethyl acetate as eluents. All conjugated ketoesters were previously reported, and their spectroscopic data are consistent with those described in the literature<sup>1</sup>, except **0f**.

(1) (a) R. Noël, V. Gembus, V. Levacher and J. -F. Brière, J.-F. *Org. Biomol. Chem.* **2014**, *12*, 1245. (b) S. Yu, Q. Cai, C. Wang, J. Hou, J. Liang, Z. Jiao, C. Yao and Y. -M. Li, *J. Org. Chem.* **2023**, *88*, 3046. (c) J. Mansaray, J. Sun, S. Huang and W. Yao, *Synlett.* **2019**, *30*, 809–812. (d) G. Dujardin, S. Leconte, A. Bénard, and E. Brown, *Synlett.* **2001**, *2001*, 0147.

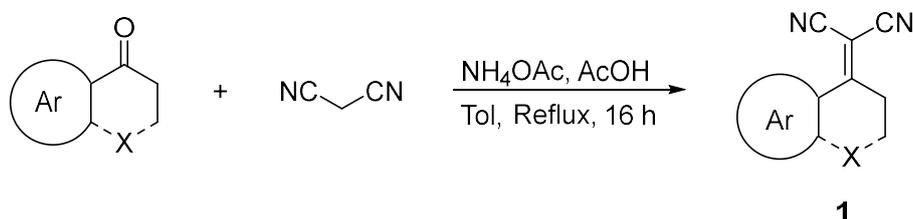
### Ethyl (*E*)-4-(4-ethoxyphenyl)-2-oxobut-3-enoate (**Of**)



**Of**

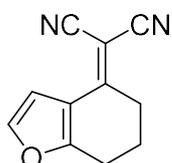
Starting from 4-ethoxybenzaldehyde (0.7 ml, 5 mmol) and ethyl pyruvate (0.66 ml, 6 mmol), following the **general procedure A**, ketoester **Of** (293 mg, 24 %) was obtained as a yellow oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 (d,  $J = 16.0$  Hz, 1H), 7.58 – 7.53 (m, 2H), 7.20 (d,  $J = 16.0$  Hz, 1H), 6.92 – 6.87 (m, 2H), 4.36 (q,  $J = 7.2$  Hz, 2H), 4.06 (q,  $J = 7.0$  Hz, 2H), 1.44 – 1.36 (m, 6H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  182.8, 162.6, 162.1, 148.5, 131.2 (2C), 126.7, 118.2, 115.1 (2C), 63.8, 62.4, 14.7, 14.2. HRMS (ESI/Q-TOF) calculated  $m/z$   $\text{C}_{14}\text{H}_{17}\text{O}_5^+$   $[\text{M}+\text{H}]^+$ : 249.1121 found 249.1128.

### General procedure B. Preparation of $\alpha,\alpha$ - dicyanoalkenes **1**.



To a stirred solution of the corresponding ketone (1 equiv.) and malononitrile (1.1 equiv.),  $\text{NH}_4\text{OAc}$  (0.25 equiv.) and  $\text{AcOH}$  (1.25 equiv.) were added. The reaction mixture was heated to reflux under nitrogen atmosphere using a Dean–Stark apparatus for 16 hours. After this time, the reaction was quenched with water, and the resulting mixture was transferred to a separatory funnel. The two phases were separated, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over anhydrous sodium sulphate, concentrated to dryness, and purified by crystallization using hot ethanol as solvent. The resulting crystals were washed with cold *n*-hexane. All dicyanoalkenes were previously reported, and their spectroscopic data are consistent with those described in the literature<sup>2</sup>, except **1i**.

### 2-(6,7-Dihydrobenzofuran-4(5H)-ylidene) malononitrile (**1i**)

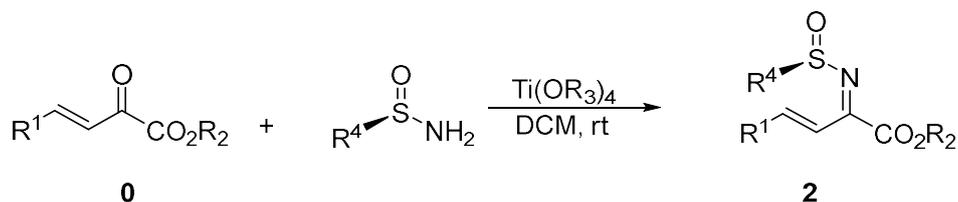


**1i**

Starting from 6,7-dihydro-4(5H)-benzofuranone (1.36 g, 10 mmol) and malononitrile (793 mg, 12 mmol) and following the **general procedure B**, dicyanoalkene **1i** (1.03 g, 55%) was obtained as yellow crystals. M.p. = 98.6 – 99.4 °C.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (d,  $J = 2.2$  Hz, 1H), 7.28 (d,  $J = 2.2$  Hz, 1H), 2.91 – 2.87 (m, 4H), 2.12 (q,  $J = 6.4$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 164.1, 143.6, 117.3, 114.0, 113.5, 107.5, 75.4, 30.7, 23.8, 22.5. HRMS (ESI/Q-TOF)  $m/z$  calculated for  $\text{C}_{11}\text{H}_9\text{N}_2\text{O}^+$   $[\text{M}+\text{H}]^+$ : 185.0709 found 185.0711.

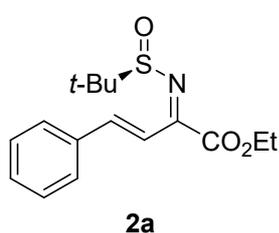
(2) (a) X. Li, X. Xu, W. Wei, A. Lin and H. Yao, *Org. Lett.* **2016**, *18*, 428. (b) S. Datta, S. and A. De, *J. Chem. Soc., Perkin Trans. 1.* **1989**, *3*, 603. (c) Y. Hayashi, X. Han and N. Mori, *Chem. Eur. J.* **2023**, *29*, e202301093. (d) J. Lu, F. Liu and T. Loh, *Adv. Synth. Catal.* **2008**, *350*, 1781–1784. (e) T. B. Poulsen, M. Bell and K. A. Jørgensen, *Org. Biomol. Chem.* **2006**, *4*, 63.

### General procedure C. Preparation of conjugated iminoesters 2.



To a stirred solution of the corresponding conjugated ketone (1 equiv.), enantiopure (*R*)-sulfinamide (1.1 equiv.) and the appropriate titanium alkoxide (4 equiv.) were added. The reaction mixture was stirred at rt for 18h under N<sub>2</sub> atmosphere. After that time, the reaction mixture was quenched with saturated NaHCO<sub>3</sub> solution. The formed titanium precipitate was filtered over a Celite pad. The filtrate was added to a separatory funnel, and the two phases were separated. The aqueous phase was extracted 2 more times with DCM. The organic phases were combined and dried over anhydrous sodium sulphate. The mixture was concentrated to dryness and purified by flash column chromatography on silica gel using mixtures of *n*-hexane and ethyl acetate as eluents. Conjugated iminoester **2b** was previously reported, and their spectroscopic data are consistent with those described in the literature<sup>3</sup>.

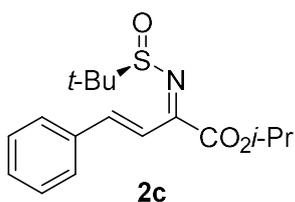
### Ethyl (2*E*,3*E*)-2-(((*R*)-*tert*-butylsulfinyl)imino)-4-phenylbut-3-enoate (**2a**)



Starting from the conjugated ketone ethyl (*E*)-2-oxo-4-phenylbut-3-enoate (376 mg, 1.8 mmol), *t*-butyl sulfinamide (246 mg, 2 mmol) and Ti(OEt)<sub>4</sub> (1.48 ml, 7.2 mmol), following the **general procedure C**, imine **2a** (0.26 g, 46 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_D = +240.6$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.53 – 7.50 (m, 2H), 7.39 – 7.37 (m, 3H), 7.16 (d, *J* = 16.6 Hz, 1H), 6.90 (d, *J* = 16.6 Hz, 1H), 4.51 – 4.35 (m, 2H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.31 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 165.7, 164.2, 142.2, 134.8, 130.6, 129.1 (2C), 128.2 (2C), 124.7, 62.4, 59.4, 23.0 (3C), 14.2. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>16</sub>H<sub>22</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 308.1315 found 308.1314.

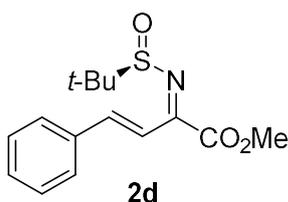
(3) D. Gaviña, M. Escolano, L. Sotorríos, E. Gómez-Bengoia, F. López-Ortiz, M. Sánchez-Roselló and C. del Pozo, *Adv. Synth. Catal.* **2024**, 366, 970.

### Isopropyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-phenylbut-3-enoate (2c)



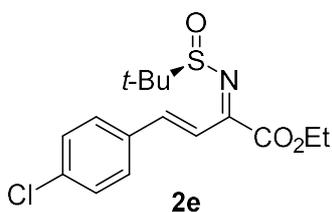
Starting from the conjugated ketone isopropyl (*E*)-2-oxo-4-phenylbut-3-enoate (1.0 g, 4.58 mmol), *t*-butyl sulfinamide (666 mg, 5.5 mmol) and Ti(*Oi-Pr*)<sub>4</sub> (5.44 ml, 18.3 mmol), following the **general procedure C**, imine **2c** (253 mg, 17 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = -239.9$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.52 – 7.49 (m, 2H), 7.39 – 7.37 (m, 3H), 7.14 (d, *J* = 16.6 Hz, 1H), 6.89 (d, *J* = 16.5 Hz, 1H), 5.36 – 5.30 (m, 1H), 1.42 (d, *J* = 7.1 Hz, 3H), 1.39 (d, *J* = 6.4 Hz, 3H), 1.30 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  165.1, 164.3, 142.0, 134.8, 130.5, 129.1 (2C), 128.2 (2C), 124.9, 70.6, 59.3, 23.0 (3C), 22.0, 21.8. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>17</sub>H<sub>24</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 322.1471 found 322.1479.

### Methyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-phenylbut-3-enoate (2d)



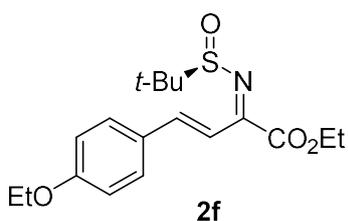
Starting from the conjugated ketone methyl (*E*)-2-oxo-4-phenylbut-3-enoate (675 g, 3.5 mmol), *t*-butyl sulfinamide (475 mg, 3.9 mmol) and Ti(OMe)<sub>4</sub> (2.47 g, 14 mmol), following the **general procedure C**, imine **2d** (268 mg, 26 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = +181.7$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.50 – 7.47 (m, 2H), 7.36 – 7.34 (m, 3H), 7.11 (d, *J* = 16.6 Hz, 1H), 6.89 (d, *J* = 16.5 Hz, 1H), 3.93 (s, 3H), 1.28 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  166.1, 163.7, 142.2, 134.6, 129.0 (2C), 128.1 (2C), 124.4, 59.4, 52.8, 22.9 (3C). HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>15</sub>H<sub>20</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 294.1158 found 294.1161.

### Ethyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-(4-chlorophenyl)but-3-enoate (2e)



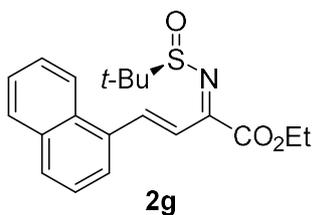
Starting from the conjugated ketone ethyl (*E*)-4-(4-chlorophenyl)-2-oxobut-3-enoate (375 mg, 1.57 mmol), *t*-butyl sulfinamide (210 mg, 1.73 mmol) and Ti(OEt)<sub>4</sub> (1.29 ml, 6.3 mmol) following the **general procedure C**, imine **2e** (0.24 g, 64 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = -198.3$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.42 – 7.39 (m, 2H), 7.33 – 7.30 (m, 2H), 7.06 (d, *J* = 16.6 Hz, 1H), 6.83 (d, *J* = 16.5 Hz, 1H), 4.43 – 4.34 (m, 2H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.27 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.5, 163.8, 140.5, 136.5, 133.3, 129.4 (2C), 129.3 (2C), 125.2, 62.5, 59.5, 23.0 (3C), 14.1. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>16</sub>H<sub>21</sub>ClNO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 342.0925 found 342.0919.

### Ethyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-(4-ethoxyphenyl)but-3-enoate (**2f**)



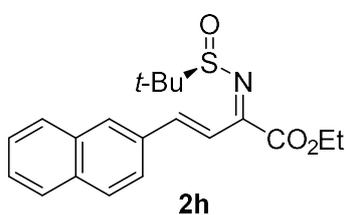
Starting from the conjugated ketone ethyl (*E*)-4-(4-ethoxyphenyl)-2-oxobut-3-enoate (300 mg, 1.2 mmol), *t*-butyl sulfinamide (162 mg, 1.33 mmol) and Ti(OEt)<sub>4</sub> (0.99 ml, 4.8 mmol), following the **general procedure C**, imine **2f** (0.17 g, 58 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = -239.8$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.45 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 16.5 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 16.5 Hz, 1H), 4.44 – 4.37 (m, 2H), 4.06 (q, *J* = 7.0 Hz, 2H), 1.42 (t, *J* = 6.9 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H) 1.29 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.9, 164.4, 161.2, 142.0, 129.9 (2C), 127.3, 122.4, 115.0 (2C), 63.8, 62.3, 59.2, 23.0 (3C), 14.9, 14.2. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>18</sub>H<sub>26</sub>NO<sub>4</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 352.1577 found 352.1579.

### Ethyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-(naphthalen-1-yl)but-3-enoate (**2g**)



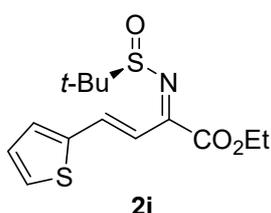
Starting from the conjugated ketone ethyl (*E*)-4-(naphthalen-1-yl)-2-oxobut-3-enoate (1.1 g, 4.36 mmol), *t*-butyl sulfinamide (582 mg, 4.8 mmol) and Ti(OEt)<sub>4</sub> (3.59 ml, 17.4 mmol), following the **general procedure C**, imine **2g** (541 mg, 35 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = +201.0$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.08 – 7.99 (m, 2H), 7.92 – 7.86 (m, 2H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.60 – 7.47 (m, 3H), 7.00 (d, *J* = 16.2 Hz, 1H), 4.55 – 4.44 (m, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.34 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.8, 164.1, 139.0, 133.8, 132.1, 131.4, 130.9, 129.0, 127.2, 127.1, 126.5, 125.6, 125.2, 123.2, 62.5, 59.5, 23.0 (3C), 14.3. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>20</sub>H<sub>24</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 358.1471 found 358.1479.

### Ethyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-(naphthalen-2-yl)but-3-enoate (**2h**)



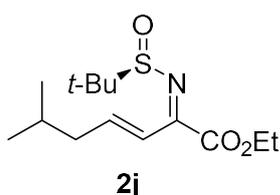
Starting from the conjugated ketone ethyl (*E*)-4-(naphthalen-2-yl)-2-oxobut-3-enoate (295 mg, 1.16 mmol), *t*-butyl sulfinamide (155 mg, 1.28 mmol) and Ti(OEt)<sub>4</sub> (0.95 ml, 4.6 mmol), following the **general procedure C**, imine **2h** (222 mg, 54 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent.  $[\alpha]^{25}_{\text{D}} = -139.5$  (*c* 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.89 (s, 1H), 7.84 – 7.79 (m, 3H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.32 (d, *J* = 16.5 Hz, 1H), 7.02 (d, *J* = 16.5 Hz, 1H), 4.51 – 4.41 (m, 2H), 1.44 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 164.1, 142.1, 134.3, 133.3, 132.2, 130.1, 128.8, 128.6, 127.8, 127.5, 126.9, 124.8, 123.3, 62.3, 59.4, 22.9 (3C), 14.1. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>20</sub>H<sub>24</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 358.1471 found 358.1479.

### Ethyl (2*E*,3*E*)-2-(((*R*)-tert-butylsulfinyl)imino)-4-(thiophen-2-yl)but-3-enoate (**2i**)



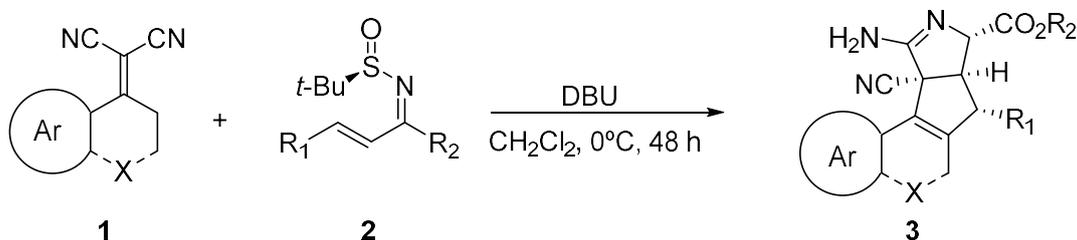
Starting from the conjugated ketone ethyl (*E*)-2-oxo-4-(thiophen-2-yl)but-3-enoate (300 mg, 1.42 mmol), *t*-butyl sulfinamide (191 mg, 1.56 mmol) and Ti(OEt)<sub>4</sub> (1.17 ml, 5.7 mmol), following the **general procedure C**, imine **2i** (221 mg, 50 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -147.6 (c 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.41 (d, *J* = 5.1 Hz, 1H), 7.30 (s, 1H), 7.23 (d, *J* = 3.4 Hz, 1H), 7.06 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.69 (d, *J* = 16.0 Hz, 1H), 4.45 – 4.36 (m, 2H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.29 (s, 9H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 163.7, 140.2, 134.6, 131.3, 129.2, 128.5, 123.6, 62.4, 59.4, 23.0 (3C), 14.1. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>14</sub>H<sub>20</sub>NO<sub>3</sub>S<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 314.0879 found 314.0871.

### Ethyl (2*E*,3*E*)-2-((tert-butylsulfinyl)imino)-6-methylhept-3-enoate (**2j**)



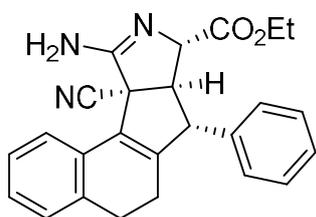
Starting from the conjugated ketone ethyl (*E*)-6-methyl-2-oxohept-3-enoate (500 mg, 2.71 mmol), *t*-butyl sulfinamide (365 mg, 2.98 mmol) and Ti(OEt)<sub>4</sub> (2.23 ml, 10.8 mmol), following the **general procedure C**, imine **2j** (228 mg, 30 %) was obtained as an orange oil after purification by column chromatography with Hex:EtOAc (20:1) as eluent. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +189.8 (c 0.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  6.45 – 6.35 (m, 1H), 6.24 (d, *J* = 16.2 Hz, 1H), 4.40 – 4.29 (m, 2H), 2.15 – 2.10 (m, 2H), 1.82 – 1.68 (m, 1H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.25 (s, 9H), 0.92 (d, *J* = 1.4 Hz, 3H), 0.90 (d, *J* = 1.5 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.7, 164.3, 146.3, 128.8, 62.1, 58.9, 42.4, 28.2, 22.9 (3C), 22.5, 22.5, 14.1. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>14</sub>H<sub>26</sub>NO<sub>3</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 288.1628 found 288.1624.

### General procedure D. Synthesis of rearranged polycycles **3**.



To a stirred solution of imine **2** (1 equiv.) and dicyanoalkene **1** (2 equiv.) in DCM (0.03 M), 2 equivalents of DBU was added. After stirring for 48h at 0 °C, the solvents were evaporated under vacuum and the crude product purified by means of flash column chromatography on silica gel using mixtures of *n*-hexane and ethyl acetate as eluents. Compounds **3** were obtained as inseparable mixtures of diastereoisomers.

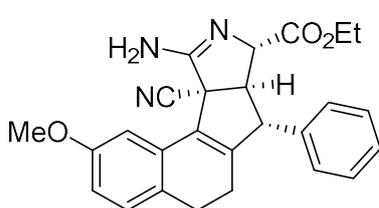
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (3a)**



**3a**

Starting from imine **2a** (61 mg, 0.2 mmol) and dicyanoalkene **1a** (78 mg, 0.4 mmol), following the **general procedure D**, **3a** was obtained as a non-separable 15:1 mixture of diastereoisomers (54 mg, 68% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 194.3 – 195 °C.  $[\alpha]^{25}_D = +50.6$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r = 92:8) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 90:10); flow rate = 1.0 mL/min,  $t_{major} = 29.5$  min,  $t_{minor} = 52.0$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.27 (m, 4H), 7.25 – 7.18 (m, 4H), 4.52 (d, *J* = 4.5 Hz, 1H), 4.26 – 4.19 (m, 2H), 4.03 (d, *J* = 3.1 Hz, 1H), 3.63 (dd, *J* = 4.5, 3.1 Hz, 1H), 2.95 – 2.76 (m, 2H), 2.17 (dd, *J* = 10.4, 5.5 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.0, 162.4, 147.4, 140.2, 136.6, 130.3, 129.6, 129.2 (2C), 128.8, 128.2, 127.7, 127.7 (2C), 127.1, 122.2, 118.9, 75.4, 62.8, 61.6, 60.6, 58.4, 28.3, 23.7, 14.2. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>25</sub>H<sub>24</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 398.1863 found 398.1859.

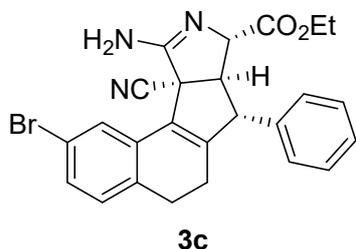
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-2-methoxy-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (3b)**



**3b**

Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1b** (147 mg, 0.65 mmol), following the **general procedure D**, **3b** was obtained as a 20:1 non-separable mixture of diastereoisomers (78 mg, 57% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 175.5 – 176.1 °C.  $[\alpha]^{25}_D = +42.2$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 90:10) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 80:20); flow rate = 1.0 mL/min,  $t_{major} = 31.0$  min,  $t_{minor} = 21.7$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.46 (d, *J* = 2.5 Hz, 1H), 7.38 – 7.28 (m, 3H), 7.21 – 7.13 (m, 2H), 7.14 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.53 (d, *J* = 4.3 Hz, 1H), 4.27 – 4.20 (m, 2H), 4.02 (d, *J* = 3.2 Hz, 1H), 3.85 (s, 3H), 3.64 (dd, *J* = 4.3, 3.3 Hz, 1H), 2.83 – 2.71 (m, 2H), 2.17 – 2.12 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.8, 162.2, 158.8, 148.4, 140.2, 131.2, 129.6, 129.4, 129.3 (2C), 128.5, 127.8, 127.7 (2C), 118.8, 112.6, 109.1, 75.4, 63.1, 61.8, 60.8, 58.3, 55.6, 27.4, 24.1, 14.3. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>26</sub>H<sub>26</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>: 428.1969 found 428.1971.

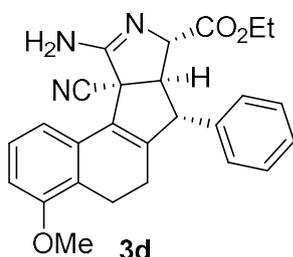
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-2-bromo-10a-cyano-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (3c)**



Starting from imine **2a** (63 mg, 0.2 mmol) and dicyanoalkene **1c** (113 mg, 0.4 mmol), following the **general procedure D**, **3c** was obtained as a non-separable 10:1 mixture of diastereoisomers (47 mg, 49% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 98.7 – 99.8 °C.  $[\alpha]^{25}_{\text{D}} = +42.8$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 97:3) was determined by HPLC

analysis using a Chiralcel OD-H column (hexane:isopropanol 70:30); flow rate = 1.0 mL/min,  $t_{\text{major}} = 17.3$  min,  $t_{\text{minor}} = 12.4$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.93 (d,  $J = 1.9$  Hz, 1H), 7.38 – 7.33 (m, 3H), 7.31 – 7.28 (m, 1H), 7.21 – 7.17 (m, 2H), 7.12 – 7.09 (m, 1H), 4.48 (d,  $J = 5.0$  Hz, 1H), 4.30 – 4.22 (m, 2H), 4.06 (s, 1H), 3.63 (dd,  $J = 5.0, 2.7$  Hz, 1H), 2.82 – 2.76 (m, 2H), 2.22 – 2.16 (m, 2H), 1.32 (t,  $J = 7.2$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  171.7, 161.7, 149.5, 139.6, 135.4, 132.3, 131.1, 130.2, 129.4 (2C), 128.6, 128.0, 127.6 (2C), 125.3, 120.7, 118.4, 75.3, 63.0, 61.9, 60.4, 58.2, 27.9, 23.7, 14.4 HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>25</sub>H<sub>23</sub>BrN<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 476.0944 found 476.0958.

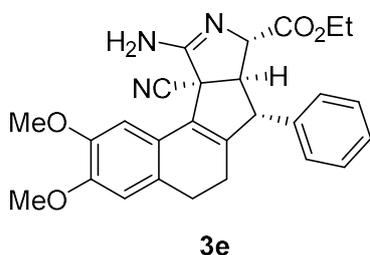
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-4-methoxy-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (3d)**



Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1d** (147 mg, 0.65 mmol), following the **general procedure D**, **3d** was obtained as a non-separable >20:1 mixture of diastereoisomers (78.4 mg, 57% yield, brown solid, 92:8 e.r.) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 64.9 – 65.5 °C.  $[\alpha]^{25}_{\text{D}} = +60.7$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 92:8) was determined by HPLC analysis using a Chiralcel OD-H column

(hexane:isopropanol 70:30); flow rate = 1.0 mL/min,  $t_{\text{major}} = 14.4$  min,  $t_{\text{minor}} = 78.2$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.52 (d,  $J = 7.7$  Hz, 1H), 7.37 – 7.27 (m, 4H), 7.21 – 7.17 (m, 2H), 6.87 (d,  $J = 8.3$  Hz, 1H), 5.61 (bs, 2H), 4.51 (d,  $J = 4.3$  Hz, 1H), 4.23 – 4.16 (m, 2H), 4.01 (d,  $J = 3.2$  Hz, 1H), 3.84 (s, 3H), 3.62 (dd,  $J = 4.3, 3.3$  Hz, 1H), 3.15 (ddd,  $J = 16.4, 7.0, 3.9$  Hz, 1H), 2.58 – 2.45 (m, 1H), 2.22 – 2.00 (m, 2H), 1.26 (t,  $J = 7.2$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  171.9, 162.5, 157.1, 147.6, 140.3, 131.3, 129.4, 129.2 (2C), 127.7 (3C), 127.6, 124.4, 119.1, 114.9, 110.9, 75.4, 62.9, 61.6, 60.8, 58.5, 55.7, 23.1, 20.2, 14.2. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>26</sub>H<sub>26</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>: 428.1969 found 428.1964

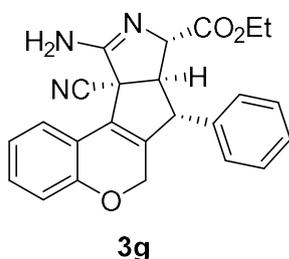
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-2,3-dimethoxy-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo [6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (**3e**)**



Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1e** (166 mg, 0.65 mmol), following the **general procedure D**, **3e** was obtained as a non-separable 18:1 mixture of diastereoisomers (82.9 mg, 57% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 118.1 – 118.9 °C.  $[\alpha]^{25}_D = +56.1$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 84:16) was

determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 70:30); flow rate = 1.0 mL/min,  $t_{\text{major}} = 20.3$  min,  $t_{\text{minor}} = 14.5$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.51 (s, 1H), 7.36 – 7.32 (m, 2H), 7.29 – 7.27 (m, 1H), 7.20 – 7.18 (m, 2H), 6.77 (s, 1H), 5.03 (bs, 2H), 4.53 (d,  $J = 3.9$  Hz, 1H), 4.20 (q,  $J = 7.1$  Hz, 2H), 3.98 (d,  $J = 3.5$  Hz, 1H), 3.95 (s, 3H), 3.89 (s, 3H), 3.61 (t,  $J = 3.7$  Hz, 1H), 2.87 – 2.68 (m, 2H), 2.15 – 2.10 (m, 2H), 1.26 (t,  $J = 7.2$  Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 171.8, 162.7, 148.7, 147.9, 144.8, 140.4, 129.6, 129.3 (2C), 129.1, 127.7 (3C), 122.7, 119.1, 112.6, 106.5, 75.1, 62.9, 61.7, 60.7, 58.3, 56.5, 56.2, 28.1, 23.7, 14.2. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>27</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub><sup>+</sup> [M+H]<sup>+</sup>: 458.2088 found 458.2074.

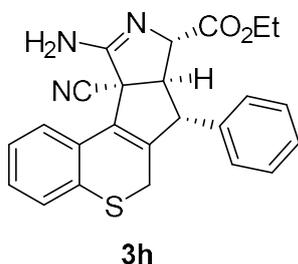
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-7,7*a*,8,10*a*-tetrahydro-6H chromeno[4',3':3,4] cyclopenta[1,2-*c*]pyrrole-8-carboxylate (**3g**)**



Starting from imine **2a** (51 mg, 0.17 mmol) and dicyanoalkene **1g** (66 mg, 0.33 mmol), following the **general procedure D**, **3g** was obtained as a non-separable 11:1 mixture of diastereoisomers (42 mg, 59% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 87.2 – 88.7 °C.  $[\alpha]^{25}_D = +34.2$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 95:5) was

determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 70:30); flow rate = 1.0 mL/min,  $t_{\text{major}} = 37.7$  min,  $t_{\text{minor}} = 28.9$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.72 (dd,  $J = 7.7, 1.6$  Hz, 1H), 7.39 – 7.28 (m, 3H), 7.23 – 7.20 (m, 3H), 7.05 – 7.00 (m, 1H), 6.91 (dd,  $J = 8.1, 1.2$  Hz, 1H), 5.30 (bs, 2H), 4.73 – 4.59 (m, 2H), 4.54 (d,  $J = 3.7$  Hz, 1H), 4.21 (q,  $J = 7.0$  Hz, 2H), 3.96 (d,  $J = 3.7$  Hz, 1H), 3.67 – 3.65 (m, 1H), 1.28 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.5, 161.6, 153.9, 139.4, 138.9, 130.5, 129.6 (2C), 128.2, 127.5 (2C), 127.2, 122.5, 122.2, 118.7, 117.9, 117.2, 74.9, 65.9, 63.6, 61.9, 58.6, 58.1, 14.3. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>: 400.1656 found 400.1663.

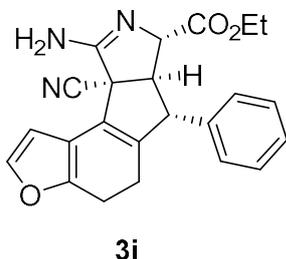
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-7,7*a*,8,10*a*-tetrahydro-6*H*-thiochromeno [4',3':3,4] cyclopenta[1,2-*c*] pyrrole-8-carboxylate (3*h*)**



Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1h** (168 mg, 0.65 mmol), following the **general procedure D**, **3h** was obtained as a non-separable 7:1 mixture of diastereoisomers (70 mg, 52% yield, brown solid, 78:22 e.r.) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 184.9 – 185.7 °C.  $[\alpha]^{25}_D = +61.7$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 78:22) was determined by HPLC analysis using a Chiralcel OD-

H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 25.8$  min,  $t_{\text{minor}} = 67.1$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.01 – 7.98 (m, 1H), 7.40 – 7.30 (m, 4H), 7.25 – 7.18 (m, 4H), 5.13 (bs, 2H), 4.53 (d,  $J = 4.6$  Hz, 1H), 4.24 – 4.16 (m, 2H), 4.10 (d,  $J = 3.2$  Hz, 1H), 3.63 (dd,  $J = 4.6, 3.2$  Hz, 1H), 3.43 (dd,  $J = 15.7, 1.5$  Hz, 1H), 2.98 (dd,  $J = 15.6, 0.8$  Hz, 1H), 1.26 (t,  $J = 7.0$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.7, 161.6, 141.2, 139.0, 133.7, 130.3, 129.5 (3C), 128.9, 128.5, 128.2, 127.7 (2C), 126.4, 124.1, 118.9, 75.0, 62.7, 61.7, 60.7, 58.7, 25.6, 14.3. HRMS (ESI/Q-TOF) m/z calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 416.1427 found 416.1427.

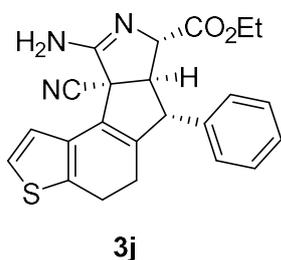
**Ethyl (6*R*,6*aS*,7*S*,9*aS*)-9-amino-9a-cyano-6-phenyl-4,5,6,6*a*,7,9*a*-hexahydrofuro[2',3':6,7]indeno[1,2-*c*] pyrrole-7-carboxylate (3*i*)**



Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1i** (120 mg, 0.65 mmol), following the **general procedure D**, **3i** was obtained as a non-separable 10:1 mixture of diastereoisomers (69.1 mg, 56% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 191.3 – 192.1 °C.  $[\alpha]^{25}_D = +33.6$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 79:21) was

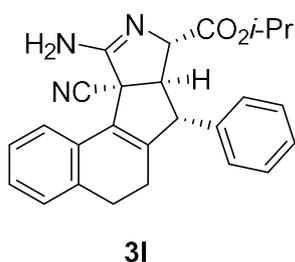
determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 28.8$  min,  $t_{\text{minor}} = 24.3$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.38 – 7.28 (m, 4H), 7.23 – 7.19 (m, 2H), 6.66 (d,  $J = 2.0$  Hz, 1H), 4.46 (d,  $J = 4.7$  Hz, 1H), 4.26 – 4.19 (m, 2H), 3.92 (d,  $J = 2.8$  Hz, 1H), 3.53 (dd,  $J = 4.7, 2.8$  Hz, 1H), 2.87 (t,  $J = 9.6$  Hz, 2H), 2.40 – 2.33 (m, 2H), 1.29 (t,  $J = 7.1$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.0, 161.8, 153.3, 142.3, 140.7, 138.6, 129.3 (2C), 127.7, 127.7 (2C), 126.2, 118.1, 112.9, 105.8, 75.5, 62.7, 61.7, 59.9, 58.9, 24.1, 21.3, 14.3. HRMS (ESI/Q-TOF) m/z calculated for C<sub>23</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>: 388.1656 found 388.1649.

**Ethyl (6*R*,6*aS*,7*S*,9*aS*)-9-amino-9a-cyano-6-phenyl-4,5,6,6*a*,7,9*a*-hexahydrothieno[2',3':6,7]indeno[1,2-*c*]pyrrole-7-carboxylate (**3j**)**



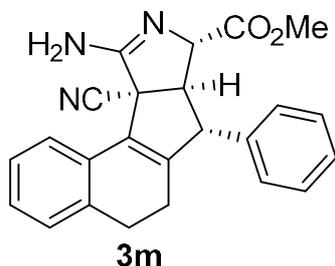
Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1j** (133 mg, 0.65 mmol), following the **general procedure D**, **3j** was obtained as a non-separable 10:1 mixture of diastereoisomers (58.1 mg, 45% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 77.1 – 78.2 °C.  $[\alpha]^{25}_{\text{D}} = +115.9$  (c 0.1, CHCl<sub>3</sub>). The e.r value of the major diastereoisomer (e. r. = 89:11) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 90:10); flow rate = 1.0 mL/min,  $t_{\text{major}} = 64.1$  min,  $t_{\text{minor}} = 51.2$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.44 (d, *J* = 5.1 Hz, 1H), 7.37 – 7.29 (m, 3H), 7.22 – 7.18 (m, 3H), 5.28 (bs, 2H), 4.49 (d, *J* = 4.4 Hz, 1H), 4.25 – 4.16 (m, 2H), 3.99 (d, *J* = 3.4 Hz, 1H), 3.56 (dd, *J* = 4.4, 3.1 Hz, 1H), 3.02 – 2.81 (m, 2H), 2.29 – 2.23 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.0, 162.4, 141.7, 140.4, 137.4, 130.2, 129.2 (2C), 127.7, 127.6 (2C), 127.6, 123.6, 122.0, 118.5, 75.2, 62.5, 61.6, 60.2, 59.1, 24.3, 23.2, 14.2. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>23</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 404.1427 found 404.1432.

**Isopropyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno [1,2-*c*]pyrrole-8-carboxylate (**3l**)**



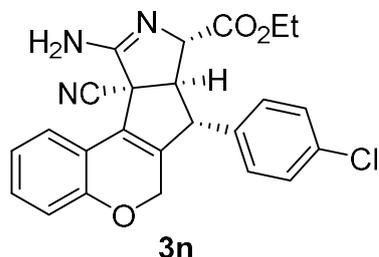
Starting from imine **2c** (100 mg, 0.31 mmol) and dicyanoalkene **1a** (120 mg, 0.62 mmol), following the **general procedure D**, **3l** was obtained as a non-separable >20:1 mixture of diastereoisomers (53.4 mg, 42% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 84.6 – 85.7 °C.  $[\alpha]^{25}_{\text{D}} = +58.4$  (c 0.1, CHCl<sub>3</sub>). The e.r. value (e. r. = 85:15) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 12.8$  min,  $t_{\text{minor}} = 22.8$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (d, *J* = 7.3 Hz, 1H), 7.36 – 7.31 (m, 3H), 7.30 – 7.27 (m, 1H), 7.25 – 7.22 (m, 2H), 7.21 – 7.19 (m, 2H), 5.07 (hept, *J* = 6.2 Hz, 1H), 4.47 (d, *J* = 4.8 Hz, 1H), 4.05 (d, *J* = 3.1 Hz, 1H), 3.57 (dd, *J* = 4.8, 2.9 Hz, 1H), 2.96 – 2.76 (m, 2H), 2.20 – 2.16 (m, 2H), 1.28 (dd, *J* = 6.3, 1.2 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 171.4, 162.2, 147.6, 140.2, 136.6, 130.3, 129.6, 129.3 (2C), 128.8, 128.3, 127.8, 127.7 (2C), 127.2, 122.3, 118.9, 75.5, 69.4, 63.0, 60.7, 58.3, 28.3, 23.8, 21.9, 21.9. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>26</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 412.2020 found 412.2027.

**Methyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno [1,2-*c*]pyrrole-8-carboxylate (3m)**



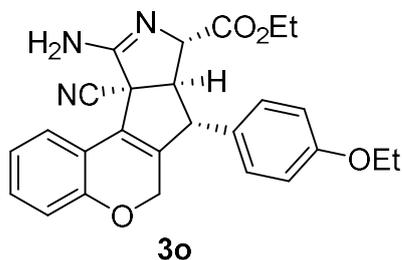
Starting from imine **2d** (100 mg, 0.34 mmol) and dicyanoalkene **1a** (135 mg, 0.68 mmol), following the **general procedure D**, **3m** was obtained as a non-separable 7:1 mixture of diastereoisomers (69.2 mg, 53% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 108.8 – 109.9 °C.  $[\alpha]^{25}_D = +43.6$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 90:10) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 24.9$  min,  $t_{\text{minor}} = 41.6$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.85 (d, *J* = 7.1 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.31 – 7.27 (m, 1H), 7.25 – 7.19 (m, 4H), 4.54 (d, *J* = 4.4 Hz, 1H), 4.02 (d, *J* = 3.4 Hz, 1H), 3.78 (s, 3H), 3.66 (dd, *J* = 4.4, 3.2 Hz, 1H), 2.93 – 2.77 (m, 2H), 2.19 – 2.15 (m, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 172.4, 162.2, 147.6, 140.1, 136.6, 130.3, 129.5, 129.3 (2C), 128.9, 128.3, 127.8, 127.7 (2C), 127.3, 122.2, 118.8, 75.4, 63.0, 60.7, 58.4, 52.7, 28.3, 23.7. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 384.1707 found 384.1707.

**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-7-(4-chlorophenyl)-10a-cyano-7,7*a*,8,10*a*-tetrahydro-6*H*-chromeno [4',3':3,4]cyclopenta[1,2-*c*]pyrrole-8-carboxylate (3n)**



Starting from imine **2e** (100 mg, 0.29 mmol) and dicyanoalkene **1g** (116 mg, 0.59 mmol), following the **general procedure D**, **3n** was obtained a non-separable 10:1 mixture of diastereoisomers (94.6 mg, 75% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 77.5 – 78.8 °C.  $[\alpha]^{25}_D = +31.1$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 91:9) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 70:30); flow rate = 1.0 mL/min,  $t_{\text{major}} = 56.3$  min,  $t_{\text{minor}} = 28.3$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.70 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.25 – 7.20 (m, 1H), 7.18 – 7.13 (m, 2H), 7.06 – 6.99 (m, 1H), 6.90 (dd, *J* = 8.1, 1.2 Hz, 1H), 5.41 (bs, 2H), 4.72 – 4.57 (m, 2H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.21 (q, *J* = 6.8 Hz, 2H), 3.95 (d, *J* = 3.8 Hz, 1H), 3.60 – 3.57 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.4, 161.3, 153.9, 138.8, 137.4, 134.2, 130.8, 129.8 (2C), 128.9 (2C), 127.7, 122.6, 122.3, 118.5, 117.7, 117.3, 74.7, 65.8, 63.6, 62.0, 58.0, 57.9, 14.3. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>24</sub>H<sub>21</sub>ClN<sub>3</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>: 434.1266 found 434.1253.

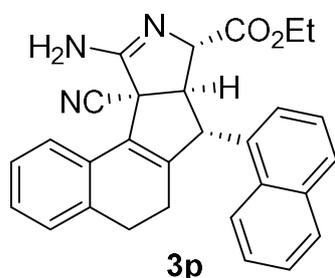
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-(4-ethoxyphenyl)-7,7*a*,8,10*a*-tetrahydro-6*H*-chromeno [4',3':3,4]cyclopenta[1,2-*c*]pyrrole-8-carboxylate (**3o**)**



Starting from imine **2f** (100 mg, 0.28 mmol) and dicyanoalkene **1g** (110 mg, 0.56 mmol), following the **general procedure D**, **3o** was obtained as a non-separable 10:1 mixture of diastereoisomers (77.1 mg, 62% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 82.7 – 83.4 °C.  $[\alpha]^{25}_{\text{D}} = +44.6$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 84:16)

was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 80:20); flow rate = 1.0 mL/min,  $t_{\text{major}} = 60.0$  min,  $t_{\text{minor}} = 49.9$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.71 (dd,  $J = 7.7, 1.6$  Hz, 1H), 7.23 – 7.19 (m, 1H), 7.11 (d,  $J = 8.7$  Hz, 2H), 7.03 – 6.99 (m, 1H), 6.91 – 6.85 (m, 3H), 5.77 (bs, 2H), 4.71 – 4.59 (m, 2H), 4.50 (d,  $J = 3.8$  Hz, 1H), 4.23 – 4.16 (m, 2H), 4.01 (q,  $J = 7.0$  Hz, 2H), 3.91 – 3.90 (m, 1H), 3.61 – 3.58 (m, 1H), 1.40 (t,  $J = 7.0$  Hz, 3H), 1.27 (t,  $J = 7.1$  Hz, 3H) <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.6, 161.7, 158.8, 153.9, 139.7, 130.7, 130.4, 128.5 (2C), 126.8, 122.5, 122.1, 118.8, 118.1, 117.1, 115.4 (2C), 74.8, 66.0, 63.8, 63.6, 61.8, 58.0, 57.8, 14.9, 14.2. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>26</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub><sup>+</sup> [M+H]<sup>+</sup>: 444.1918 found 444.1929.

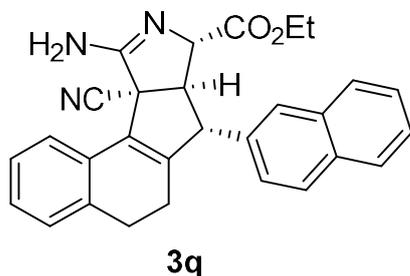
**Ethyl (7*S*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-(naphthalen-1-yl)-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno[1,2-*c*]pyrrole-8-carboxylate (**3p**)**



Starting from imine **2g** (100 mg, 0.28 mmol) and dicyanoalkene **1a** (109 mg, 0.56 mmol), following the **general procedure D**, **3p** was obtained as a non-separable 10:1 mixture of diastereoisomers (56.4 mg, 45% yield, brown solid, 83:17 e.r.) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 119.6 – 120.9 °C.  $[\alpha]^{25}_{\text{D}} = 75.6$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 83:17) was

determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 21.4$  min,  $t_{\text{minor}} = 40.7$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.26 (d,  $J = 8.2$  Hz, 1H), 7.93 – 7.90 (m, 1H), 7.84 – 7.79 (m, 2H), 7.61 – 7.50 (m, 2H), 7.44 – 7.28 (m, 4H), 7.22 – 7.10 (m, 1H), 4.96 – 4.83 (m, 3H), 4.66 (d,  $J = 5.0$  Hz, 1H), 4.24 – 4.16 (m, 2H), 3.59 (s, 1H), 2.94 – 2.84 (m, 2H), 2.35 – 2.17 (m, 2H), 1.30 – 1.25 (m, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.1, 162.2, 147.7, 136.7, 134.4, 131.8, 131.0, 130.2, 129.3, 128.9, 128.8, 128.4, 128.3, 127.1, 126.6, 126.0, 125.9, 124.2, 123.1, 122.4, 118.5, 75.3, 62.7, 61.8, 58.5, 54.0, 29.8, 28.3, 14.2. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>29</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 448.2020 found 448.2022.

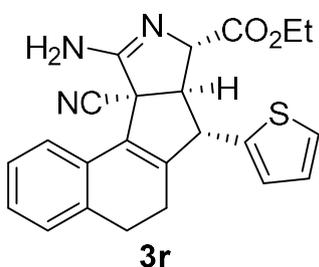
**Ethyl (7*R*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-(naphthalen-2-yl)-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7] indeno[1,2-*c*]pyrrole-8-carboxylate (3q)**



Starting from imine **2h** (100 mg, 0.28 mmol) and dicyanoalkene **1a** (109 mg, 0.56 mmol), following the **general procedure D**, **3q** was obtained as a non-separable 8:1 mixture of diastereoisomers as a brown solid (81.6 mg, 65% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 115.1 – 116.1 °C.  $[\alpha]^{25}_D = +24.2$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the

major diastereoisomer (e. r. = 92:8) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 90:10); flow rate = 1.0 mL/min,  $t_{\text{major}} = 42.7$  min,  $t_{\text{minor}} = 91.7$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.91 – 7.80 (m, 5H), 7.66 (d,  $J = 1.8$  Hz, 1H), 7.53 – 7.46 (m, 2H), 7.37 – 7.26 (m, 3H), 4.62 (d,  $J = 4.1$  Hz, 1H), 4.27 – 4.20 (m, 3H), 3.73 (dd,  $J = 4.1, 3.5$  Hz, 1H), 2.94 – 2.77 (m, 2H), 2.23 – 2.16 (m, 2H), 1.29 (t,  $J = 7.1$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.4, 162.7, 147.9, 137.3, 136.7, 133.7, 133.0, 130.1, 129.5, 129.4, 129.0, 128.6, 127.9, 127.9, 127.4, 126.8, 126.7, 126.3, 125.3, 122.2, 118.5, 74.3, 62.6, 62.0, 60.9, 58.1, 28.3, 23.7, 14.3. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>29</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 448.2020 found 448.2025.

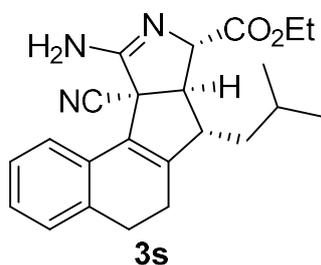
**Ethyl (7*S*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-(thiophen-2-yl)-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7] indeno[1,2-*c*]pyrrole-8-carboxylate (3r)**



Starting from imine **2i** (100 mg, 0.32 mmol) and dicyanoalkene **1a** (125 mg, 0.64 mmol), following the **general procedure D**, **3r** was obtained as a non-separable 11:1 mixture of diastereoisomers as a brown solid (60.9 mg, 47% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 91.9 – 92.7 °C.  $[\alpha]^{25}_D = +66.3$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 82:18) was determined by

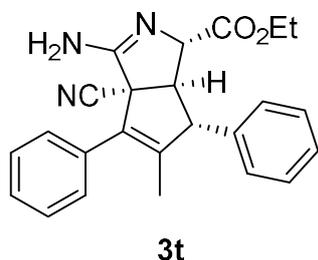
HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 22.3$  min,  $t_{\text{minor}} = 37.5$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.81 (d,  $J = 7.0$  Hz, 1H), 7.33 – 7.27 (m, 1H), 7.26 – 7.21 (m, 3H), 6.96 (dd,  $J = 5.1, 3.5$  Hz, 1H), 6.90 (ddd,  $J = 3.5, 1.2, 0.6$  Hz, 1H), 4.47 (d,  $J = 4.9$  Hz, 1H), 4.33 (d,  $J = 2.9$  Hz, 1H), 4.30 – 4.20 (m, 2H), 3.70 (dd,  $J = 4.9, 2.9$  Hz, 1H), 2.95 – 2.80 (m, 2H), 2.42 – 2.19 (m, 2H), 1.32 (t,  $J = 7.1$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 171.8, 161.8, 146.9, 143.3, 136.7, 130.1, 129.3, 128.9, 128.5, 127.5, 127.2, 125.2, 125.1, 122.4, 118.6, 75.0, 63.4, 61.8, 58.0, 54.8, 28.3, 23.7, 14.3. HRMS (ESI/Q-TOF)  $m/z$  calculated for C<sub>23</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 404.1427 found 404.1432.

**Ethyl (7*S*,7*aS*,8*S*,10*aS*)-10-amino-10a-cyano-7-isobutyl-5,6,7,7*a*,8,10*a*-hexahydrobenzo[6,7]indeno [1,2-*c*]pyrrole-8-carboxylate (3*s*)**



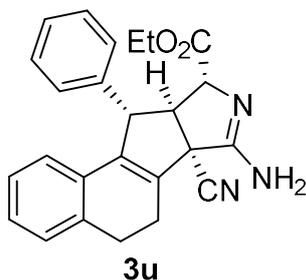
Starting from imine **2j** (150 mg, 0.53 mmol) and dicyanoalkene **1a** (206 mg, 1.06 mmol), following the **general procedure D**, **3s** was obtained as a non-separable >20:1 mixture of diastereoisomers (95.3 mg, 48% yield) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 176.9 – 177.8 °C.  $[\alpha]^{25}_{\text{D}} = +68.1$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 78:22) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 90:10); flow rate = 1.0 mL/min,  $t_{\text{major}} = 18.5$  min,  $t_{\text{minor}} = 24.8$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.68 (d, *J* = 7.3 Hz, 1H), 7.23 – 7.16 (m, 3H), 4.30 – 4.23 (m, 3H), 3.93 (bs, 2H), 3.41 (s, 1H), 2.95 – 2.80 (m, 4H), 2.41 – 2.23 (m, 2H), 1.85 – 1.78 (m, 1H), 1.48 – 1.40 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 1.7 Hz, 3H), 0.96 (d, *J* = 1.6 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.2, 162.2, 150.0, 136.5, 130.6, 128.7, 127.9, 127.2, 127.1, 121.8, 119.2, 75.1, 61.7, 60.0, 57.8, 52.3, 42.9, 28.3, 26.0, 24.0, 23.9, 21.8, 14.3. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>23</sub>H<sub>28</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 378.2176 found 378.2176.

**Ethyl (1*S*,3*aS*,6*R*,6*aS*)-3-amino-3a-cyano-5-methyl-4,6-diphenyl-1,3*a*,6,6*a*-tetrahydrocyclopenta[*c*] pyrrole-1-carboxylate (3*t*)**



Starting from imine **2a** (53 mg, 0.17 mmol) and dicyanoalkene **1l** (63 mg, 0.35 mmol), following the **general procedure D**, **3t** was obtained as a non-separable 10:1 mixture of diastereoisomers as a brown solid (34 mg, 52% yield, 61:39 e.r.) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 72.1 – 73.5 °C.  $[\alpha]^{25}_{\text{D}} = +35.8$  (c 0.1, CHCl<sub>3</sub>). The e.r. value of the major diastereoisomer (e. r. = 61:39) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min,  $t_{\text{major}} = 8.0$  min,  $t_{\text{minor}} = 10.9$  min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.47 – 7.37 (m, 8H), 7.32 – 7.29 (m, 2H), 4.46 (d, *J* = 6.3 Hz, 1H), 4.25 – 4.21 (m, 2H), 3.99 (s, 1H), 3.47 (dd, *J* = 6.3, 1.7 Hz, 1H), 1.57 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.3, 161.4, 144.4, 140.7, 133.5, 132.3, 129.5 (2C), 129.3 (2C), 129.1 (2C), 128.8, 127.7, 127.6 (2C), 118.9, 76.1, 62.8, 61.7, 61.6, 60.9, 14.4, 14.2. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>24</sub>H<sub>24</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 386.1863 found 386.1867.

**Ethyl (6*b*R,9*R*,9*a*R,10*S*)-7-amino-6*b*-cyano-10-phenyl-5,6,6*b*,9,9*a*,10-hexahydrobenzo[4,5]indeno[1,2-*c*]pyrrole-9-carboxylate (**3u**)**



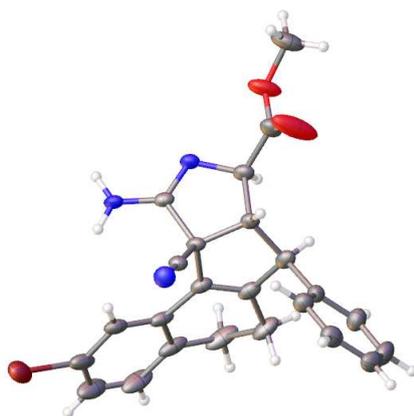
Starting from imine **2a** (100 mg, 0.32 mmol) and dicyanoalkene **1m** (130 mg, 0.65 mmol), following the **general procedure D**, **3u** was obtained as a non-separable >20:1 mixture of diastereoisomers (67.2 mg, 53% yield, brown solid) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. M.p.= 190.5 – 191.7 °C. [ $\alpha$ ]<sup>25</sup><sub>D</sub> = +41.7 (*c* 0.1, CHCl<sub>3</sub>). The e.r. value (e. r. = 87:13) was determined by HPLC analysis using a Chiralcel OD-H column (hexane:isopropanol 85:15); flow rate = 1.0 mL/min, *t*<sub>major</sub>= 22.8 min, *t*<sub>minor</sub>= 19.3 min. The spectroscopic data for the major diastereoisomer are reported below. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.46 – 7.45 (m, 3H), 7.39 – 7.34 (m, 1H), 7.18 – 7.11 (m, 2H), 7.04 – 6.95 (m, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.54 – 6.50 (m, 1H), 4.43 (d, *J* = 2.3 Hz, 1H), 4.18 – 4.07 (m, 3H), 3.57 – 3.52 (m, 3H), 3.05 (dd, *J* = 11.4, 9.1 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  171.1, 162.3, 141.2, 139.2, 136.4, 134.0, 129.7 (2C), 128.0 (2C), 128.0, 127.9, 126.9, 126.6, 125.9, 123.4, 118.7, 72.0, 62.8, 61.8, 56.0, 54.1, 48.9, 32.0, 14.1. HRMS (ESI/Q-TOF) *m/z* calculated for C<sub>25</sub>H<sub>24</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 398.1863 found 398.1867.

**X-Ray structure of compound ( $\pm$ )-**3m**<sup>4</sup>**

**Crystal Data and Structure Refinement for ( $\pm$ )-**3m****

Single crystal X-ray diffraction data was collected on Bruker D8 Venture diffractometer. Crystals suitable for X-ray single-crystal diffraction analysis were obtained through slowly cooling the mixture of a hot ethanol solution of **3m** (90:10 er) under air at room temperature. However, crystals of **3m** were racemic and the solution increased its er. Those crystals were analyzed to determine the unusual structure of compounds **3**. Therefore, the structure of compound ( $\pm$ )-**3m** was determined by anomalous dispersion with Mo K $\alpha$  radiation ( $\lambda$  = 0.7093 Å) as X-ray source for X ray diffraction experiment. CIF file for ( $\pm$ )-**3m** has been deposited at the Cambridge Crystallographic Data Centre with deposition number 2513043.

(4) CCDC 2513043 contains the supplementary crystallographic data of compound **3m**. These data can be obtained free of charge at [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44(1223)336-033, e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)].



**Figure S1.** Ortep diagram for compound ( $\pm$ )-**3m**

Crystal data and structure refinement for **3m**

Empirical formula	C <sub>24</sub> H <sub>20</sub> Br N <sub>3</sub> O <sub>2</sub>	
Formula weight	462.34	
Temperature	150K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2 <sub>1</sub> /c	
Unit cell dimensions	a = 13.1900(6) Å	$\alpha = 90^\circ$
	b = 17.5158(7) Å	$\beta = 91.1320(10)^\circ$
	c = 9.1469(4) Å	$\gamma = 90^\circ$
Volume	2112.83(16) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.453 Mg/m <sup>3</sup>	
F(000)	944	
Crystal size	1.00 x 0.75 x 0.35 mm <sup>-1</sup>	
Final R indices [I > 2 $\sigma$ (I)]	R1 = 0.0857	wR2 = 0.1645

**Electronic Circular Dichroism (ECD) of compound (+)-3c. Determination of the absolute configuration.**

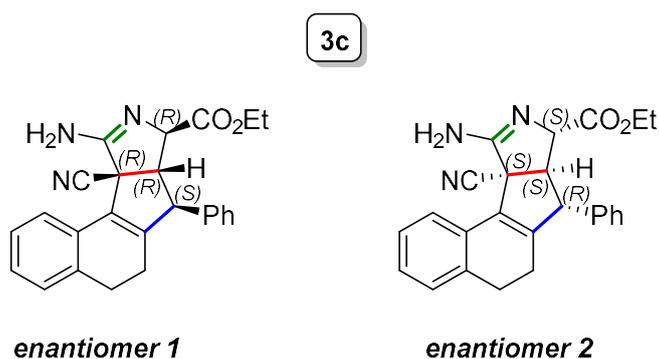
Compound **3c** was obtained with an er = 97:3. In order to determine the absolute configuration of compound **3c**, a theoretical prediction of the ECD spectra of both enantiomers of **3c** (Figure S2) was performed by TD-DFT studies. Figure S3 shows the experimental ECD spectrum of the enriched sample of **3c** with the predicted spectra for the enantiomer 1 (red curve) and the predicted spectra for enantiomer 2 (blue curve). Comparison of the prediction of both enantiomers with the enriched sample (black curve) led us to determine that the newly created stereocenter has the absolute configuration showed in enantiomer 2 (Figure S3).

**Similarity coefficient:**

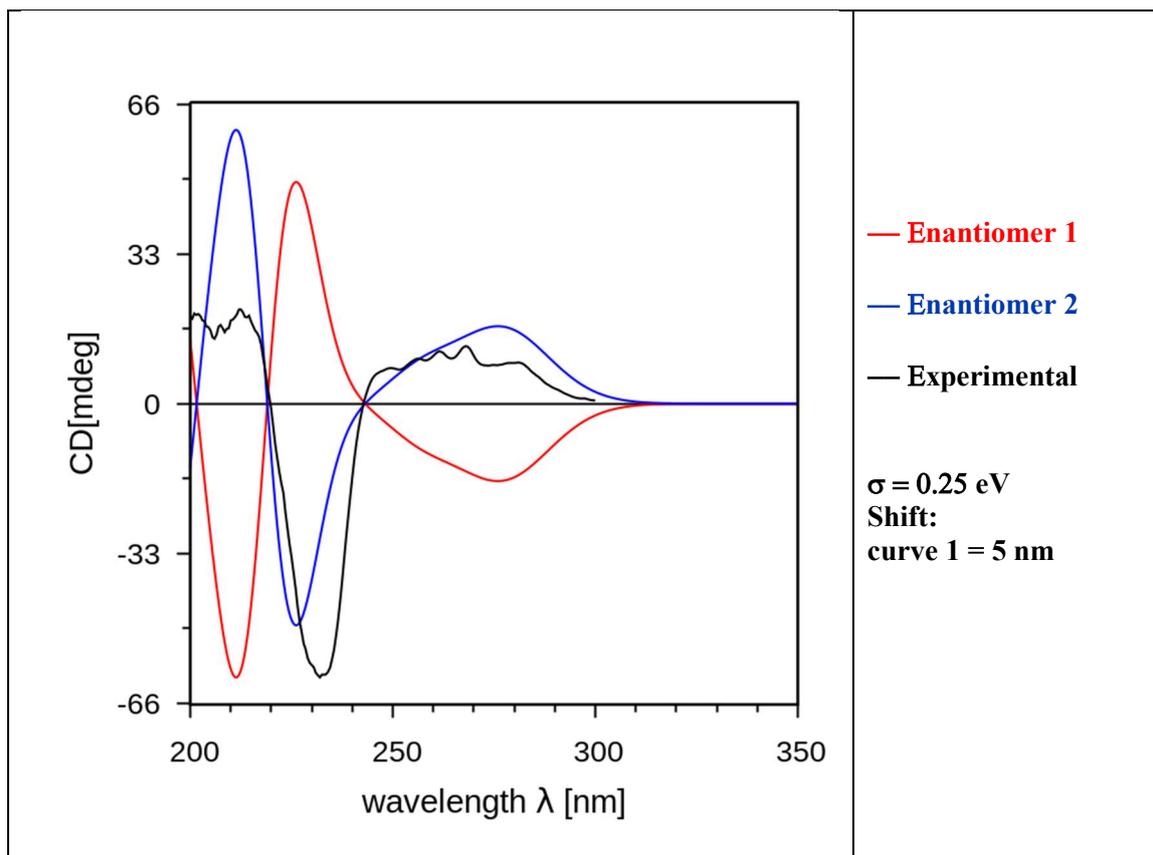
Similarity factor Enantiomer 1 = 0.0079

Similarity factor Enantiomer 2 = 0.8791

**Delta value:** 0.8712



**Figure S2**



**Figure S3**

**Technical details:** The equipment for the VCD experiment was a Jasco J-810. Analysis range was between 200 and 400 nm. A blank correction was performed with the pure solvent (acetonitrile). Final spectra of the sample were obtained with 0,0001M concentration with three accumulative scans.

**Theoretical model for the ECD prediction:**

**Conformational study.<sup>5</sup>**

Initially, the conformational space of the target molecule was evaluated through the following steps:

1. Seeking for the stable conformers with the XTB/ORCA 6.0 program through GOAT.
2. 34 conformers were found, occupying the 100% of the population following Boltzmann distribution. Energy limit to discard minor conformers was 10 Kcal/mol.

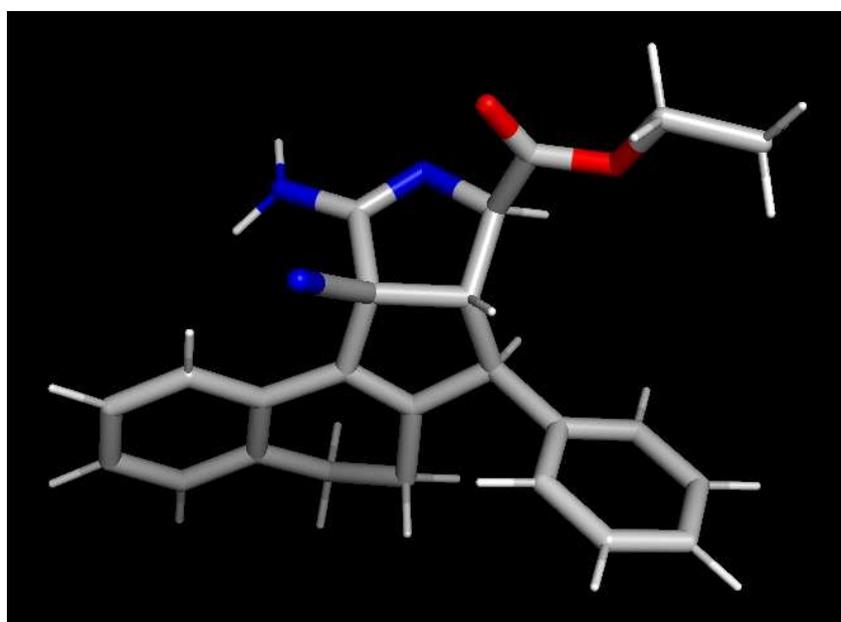
(5) (a) C. Bannwarth, S. Ehlert and S. Grimme, *J. Chem. Theory Comput.* **2019**, *15*, 1652. (b) C. Bannwarth, E. Caldeweyher, S. Ehlert, A. Hansen, P. Pracht, J. Seibert, S. Spicher and S. Grimme, *WIREs Comput. Molec. Sci.* **2020**, *11*, e1493. (c) F. Neese, F. Wennmohs, U. Becker and C. Riplinger, *J. Chem. Phys.* **2020**, *152*, L224108. (d) F. Neese, *Chem. Phys. Lett.* **2000**, *325*, 93.

3. The geometry of these 34 conformers was optimized using DFT ORCA 5.0.3 code,<sup>6</sup> using B3LYP/def2-TZVP method. In this optimization the contribution of the solvent (AcCN) was considered using CPCM method.

4. Once the geometry was optimized, a clustering for similarity factors was performed, what allowed us to detect several duplicated conformers, being the number reduced to 24. This clustering is based in a RMSD analysis considering a 0.1Å threshold.

5. The energy value of each conformer was revised using the double-hybrid functional B2PLYP and the base def2-TZVPP for the calculation. With those values, the population inside the conformational space of each conformer was updated.

The result of this study is shown in Figure S4 for enantiomer 1.



**Figure S4.** Optimized structure for enantiomer 1.

#### **Prediction of the ECD spectra.**

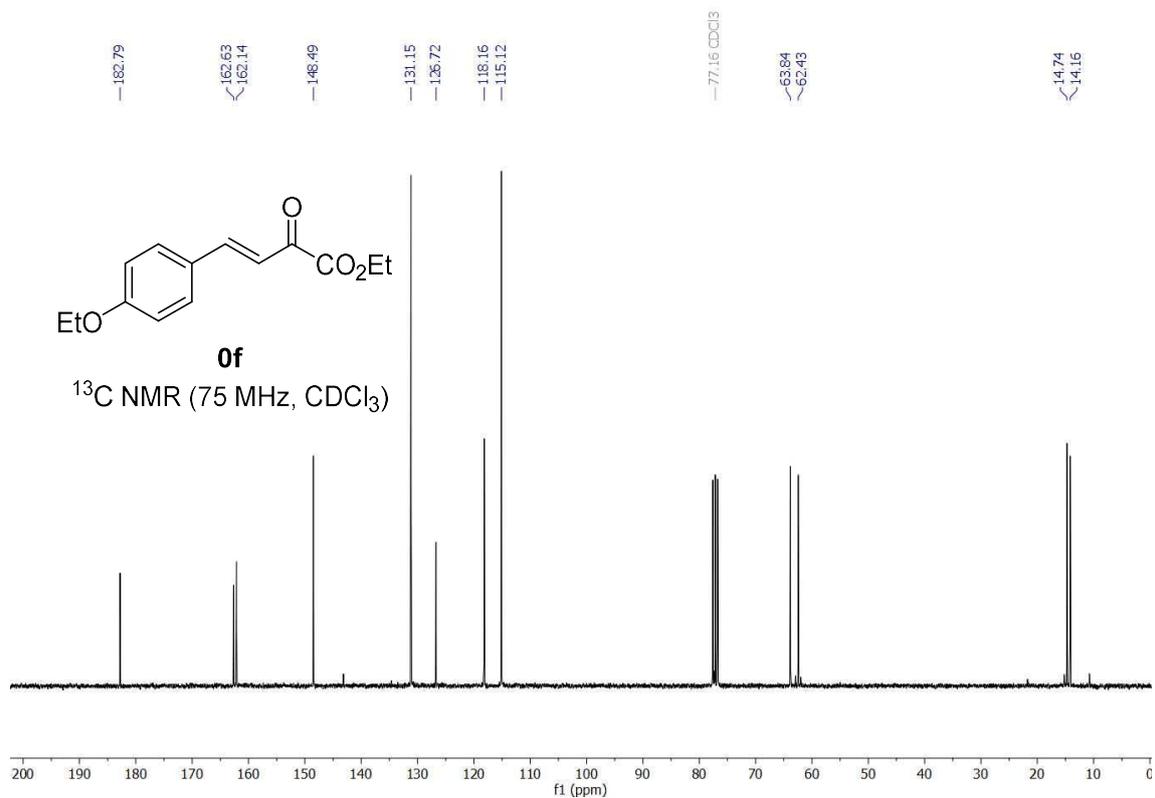
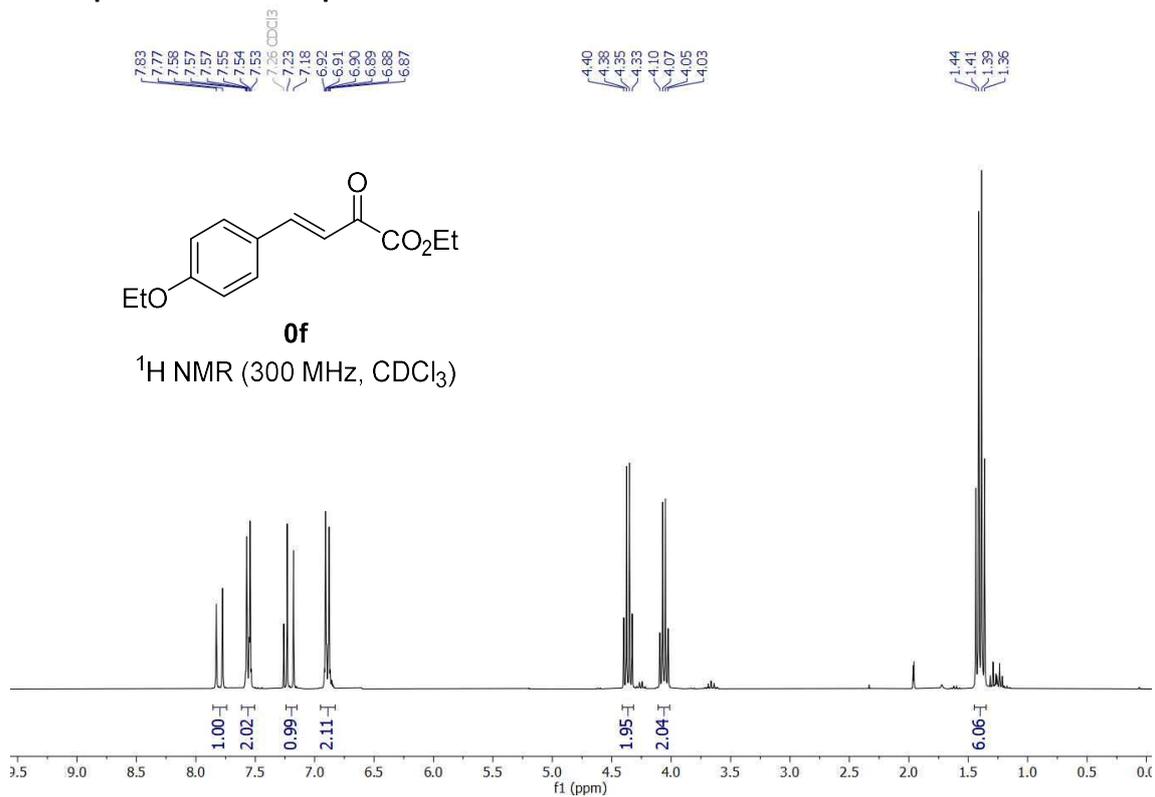
It was performed through TD-DFT theory with ORCA 5.0.3 program using CAM-B3LYP as density functional and def2-TZVPP as base. The first 30 excitations were calculated. In those calculations the presence of the solvent (MeCN) was considered. Tamm-Dancoffya approach was disabled, since it was described that produce wrong signals in the calculation of the spectra.<sup>7</sup> Spectra of each conformer were calculated and they were pondered using each relative population previously determined. A good consistency and similarity in the position, form and dichroism band width of all conformers was observed. Calculations were also performed with other density functionals (B3LYP, wBP87, B2PLYP, ...) with similar results.

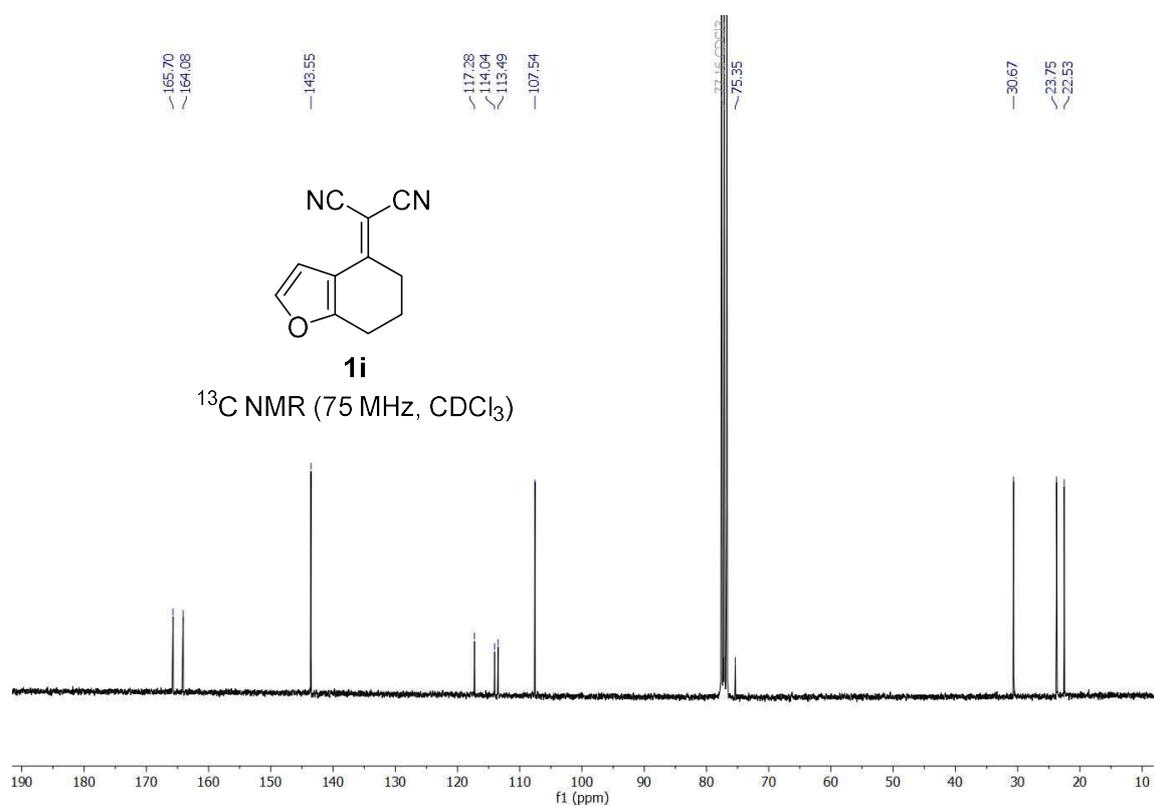
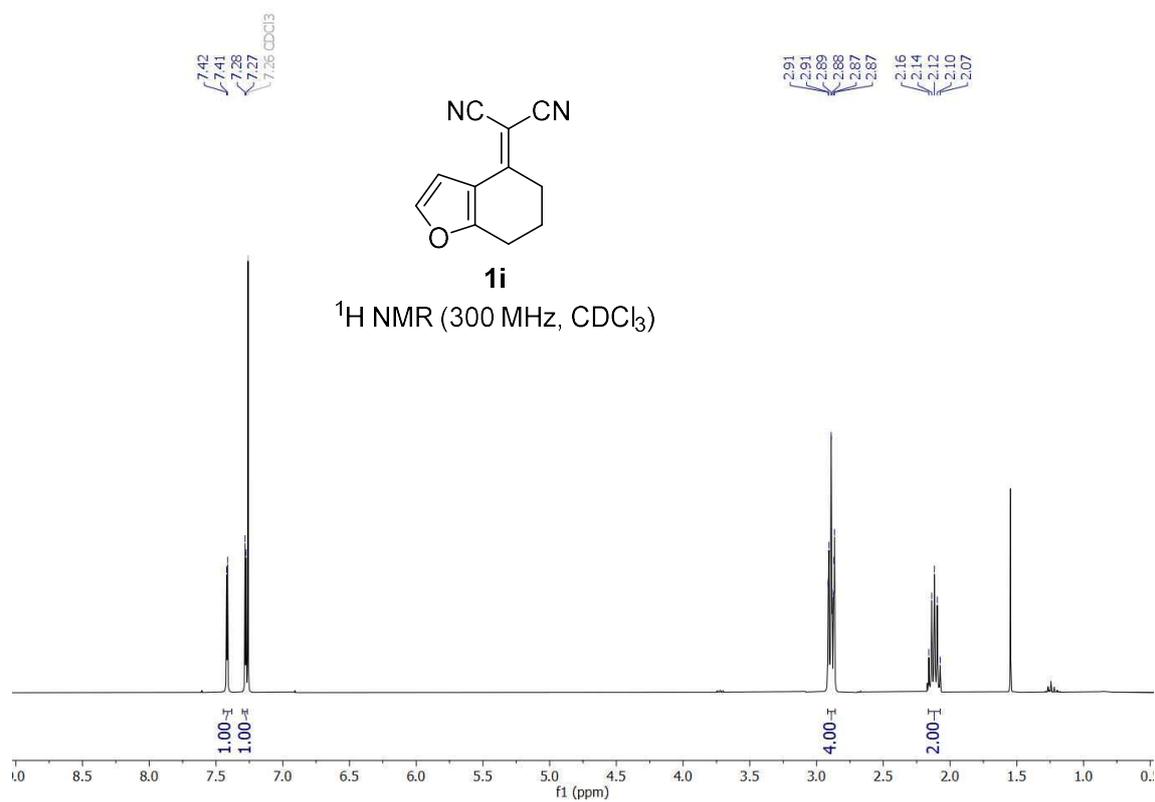
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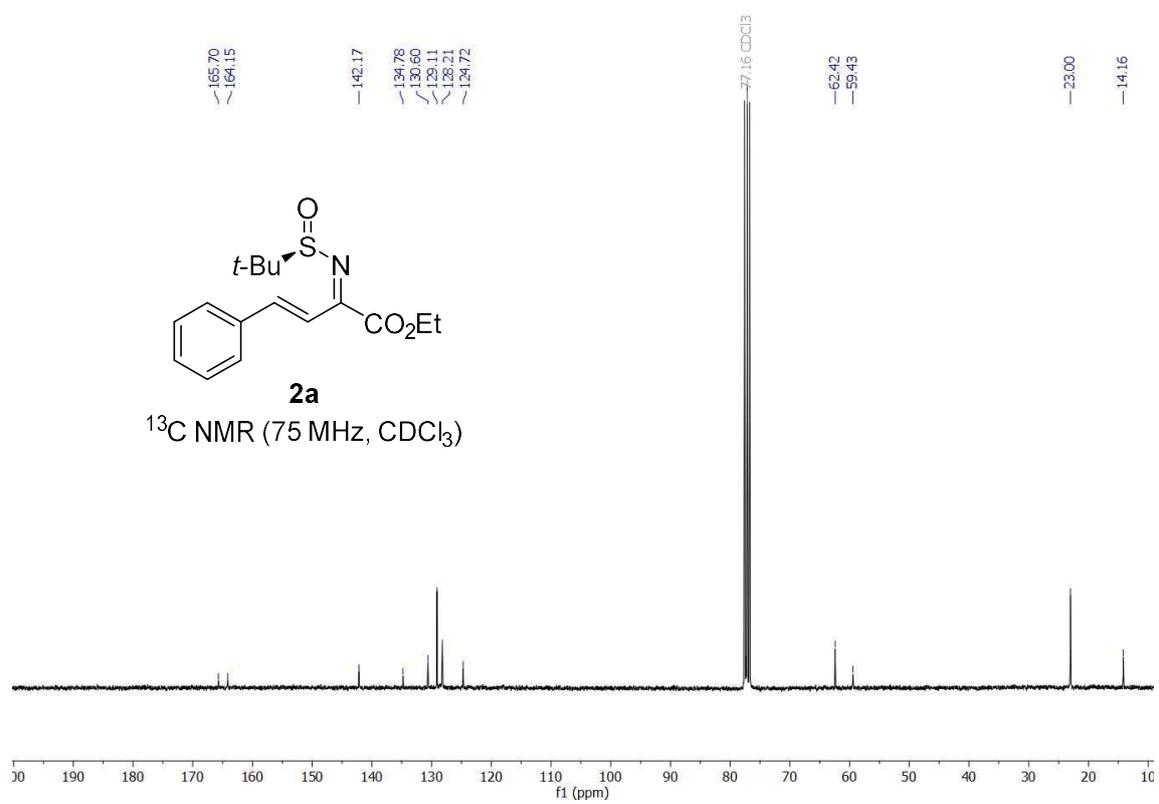
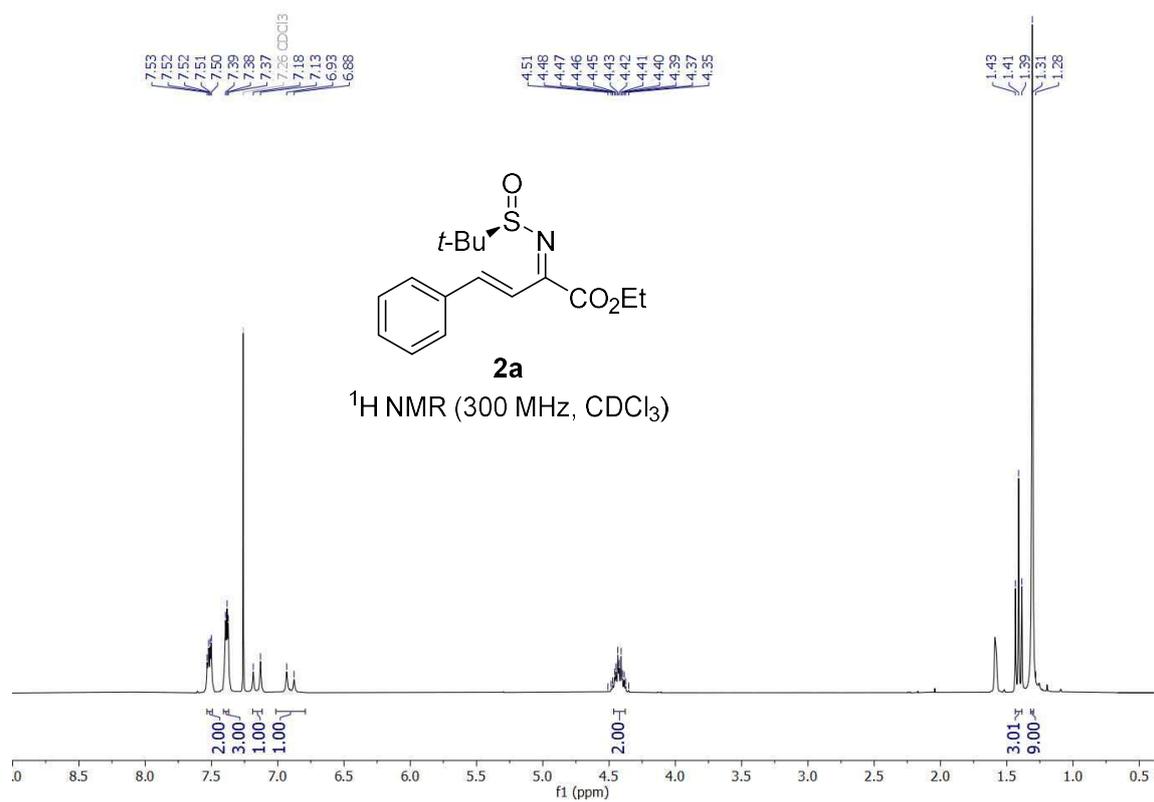
(6) F. Neese, *WIREs Comput. Molec. Sci.* **2012**, *2*, 73.

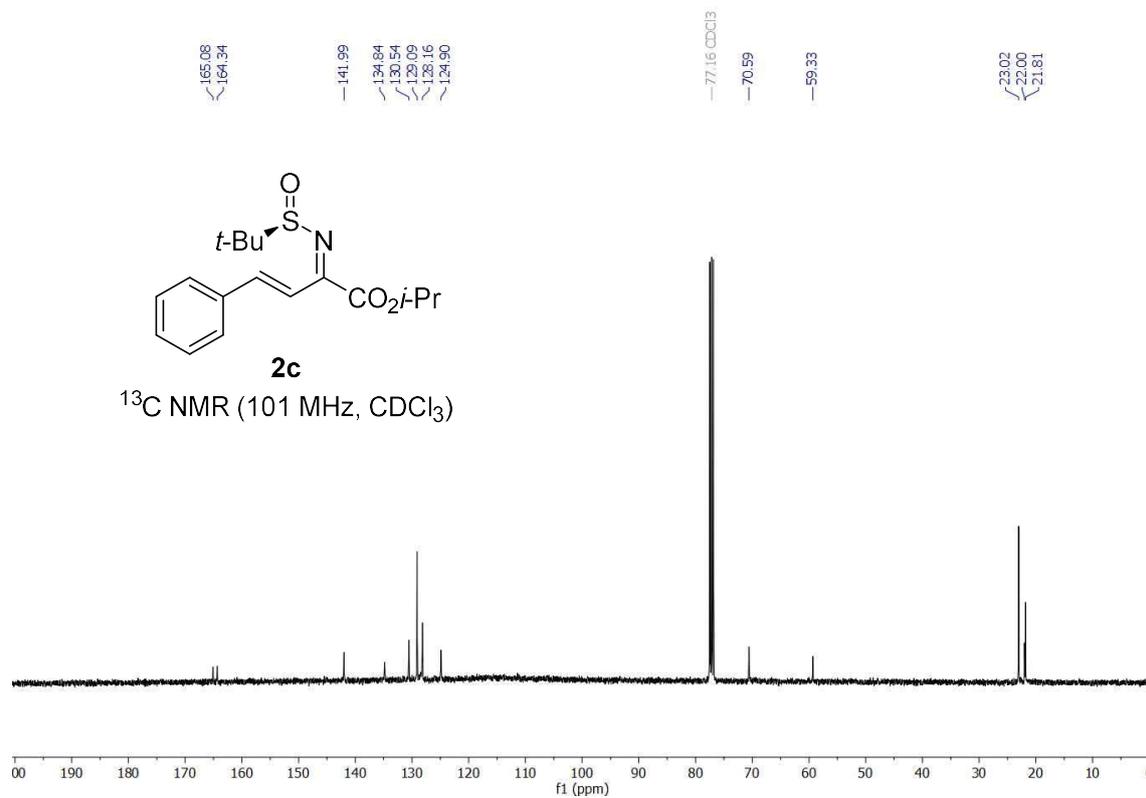
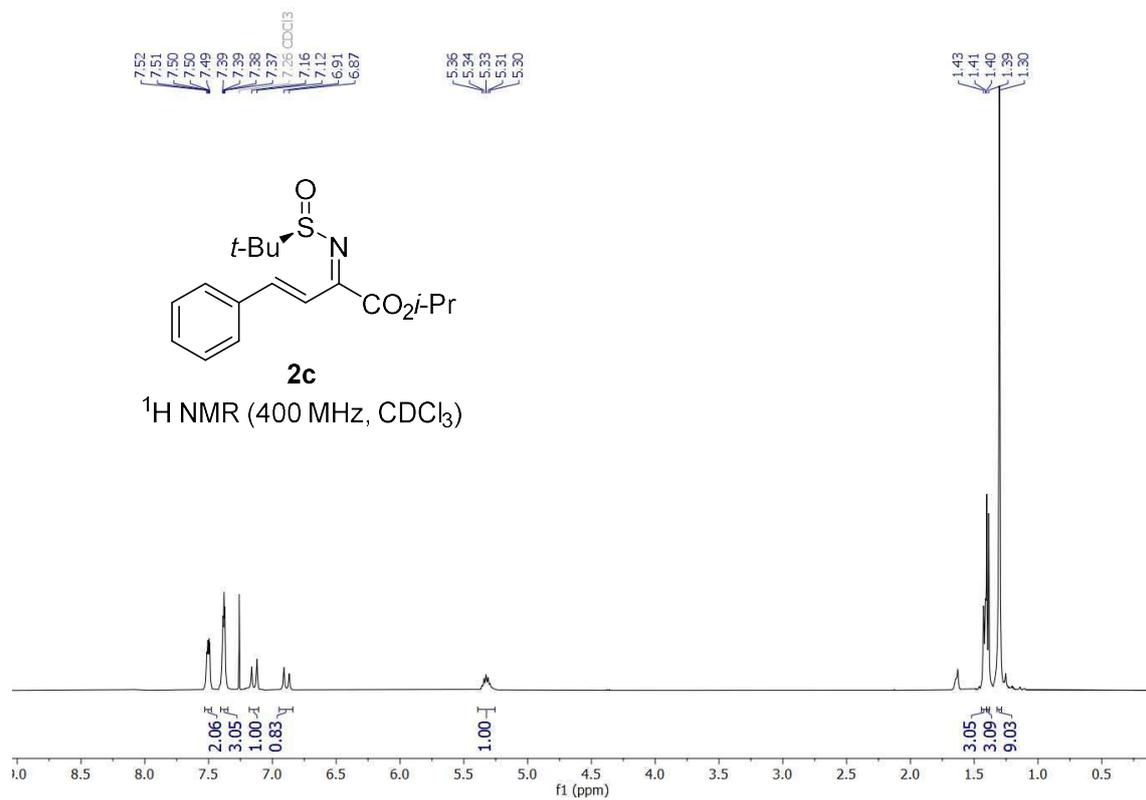
(7) C. Bannwarth and S. J. Grimme, *J. Phys. Chem. A* **2015**, *119*, 3653.

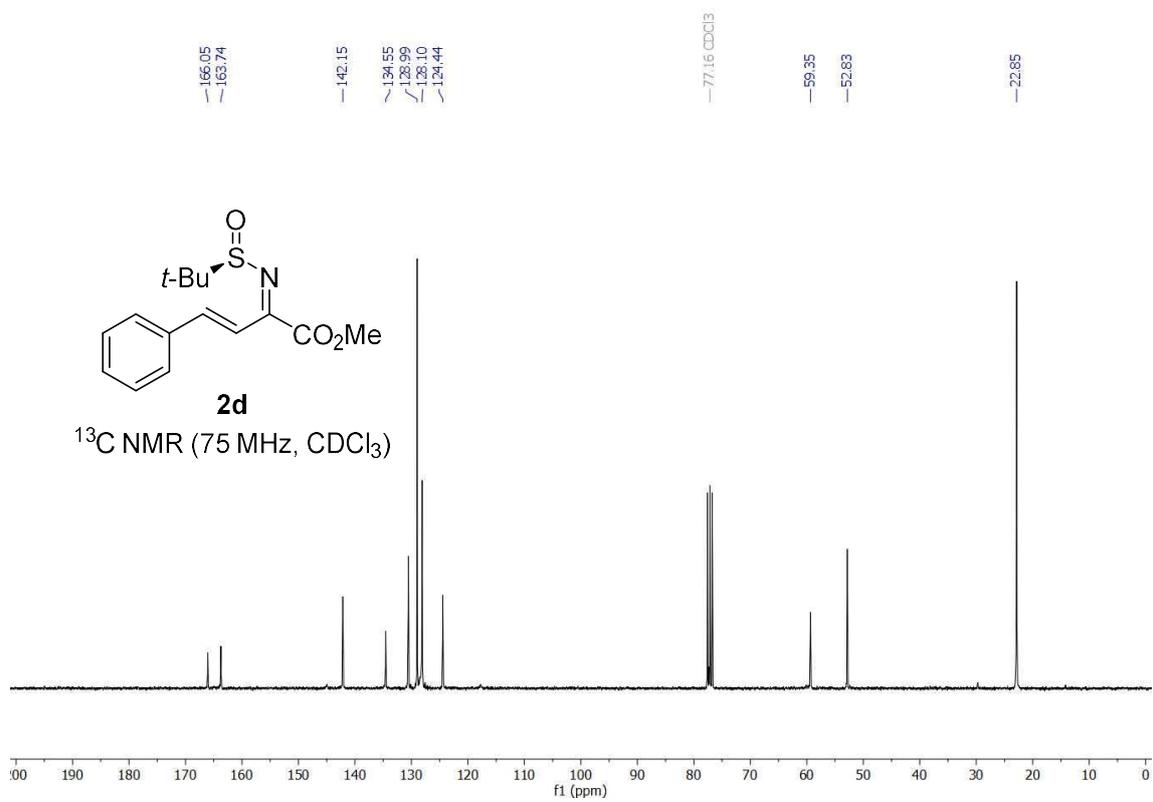
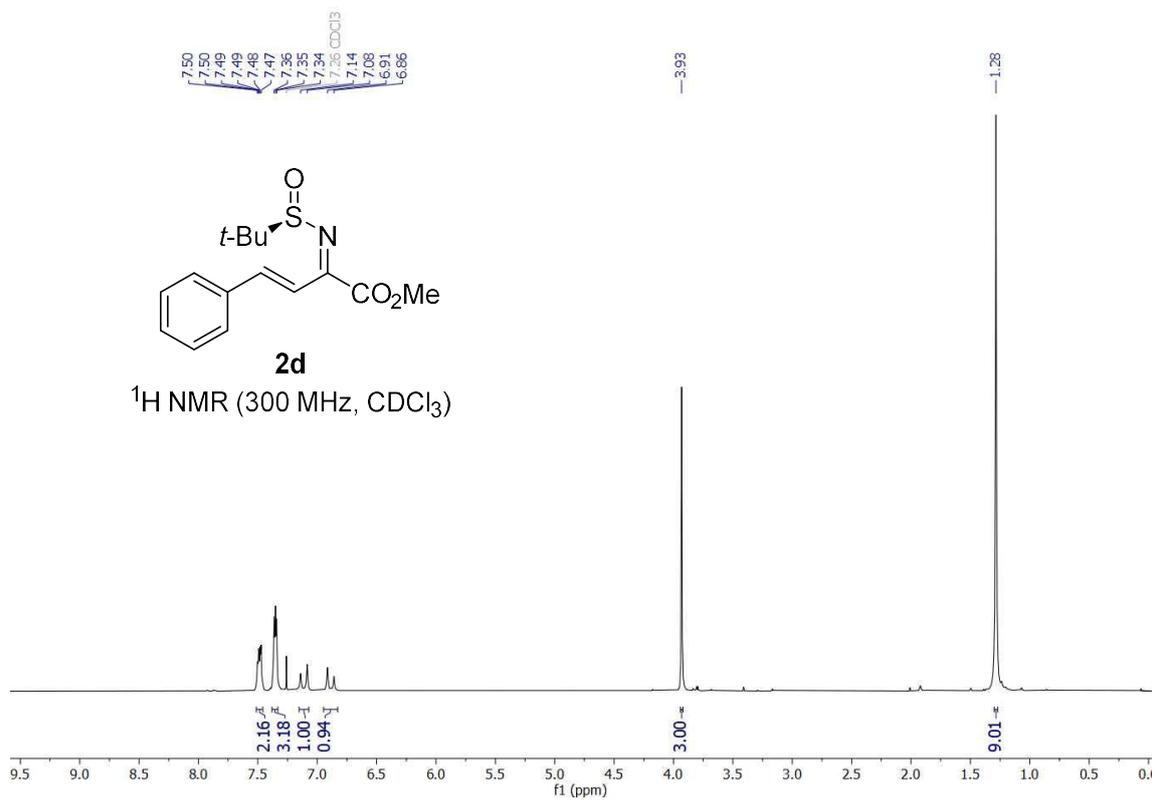
# NMR Spectra of new compounds

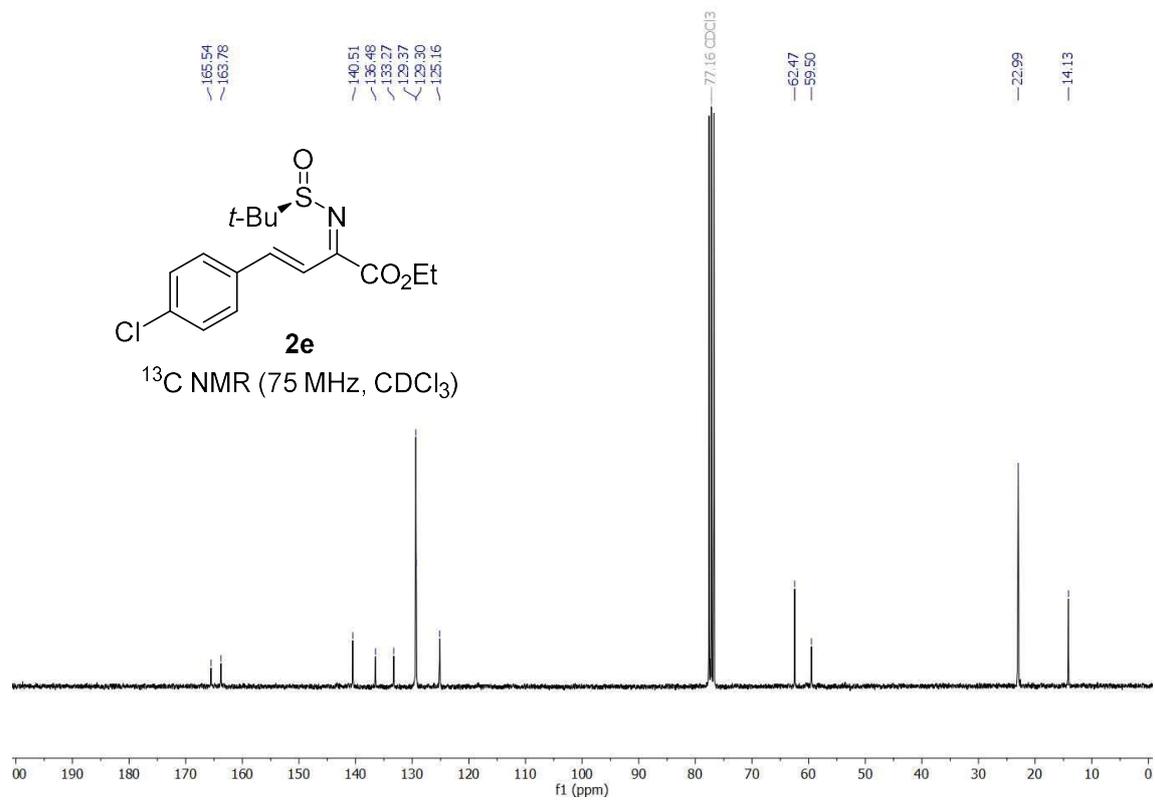
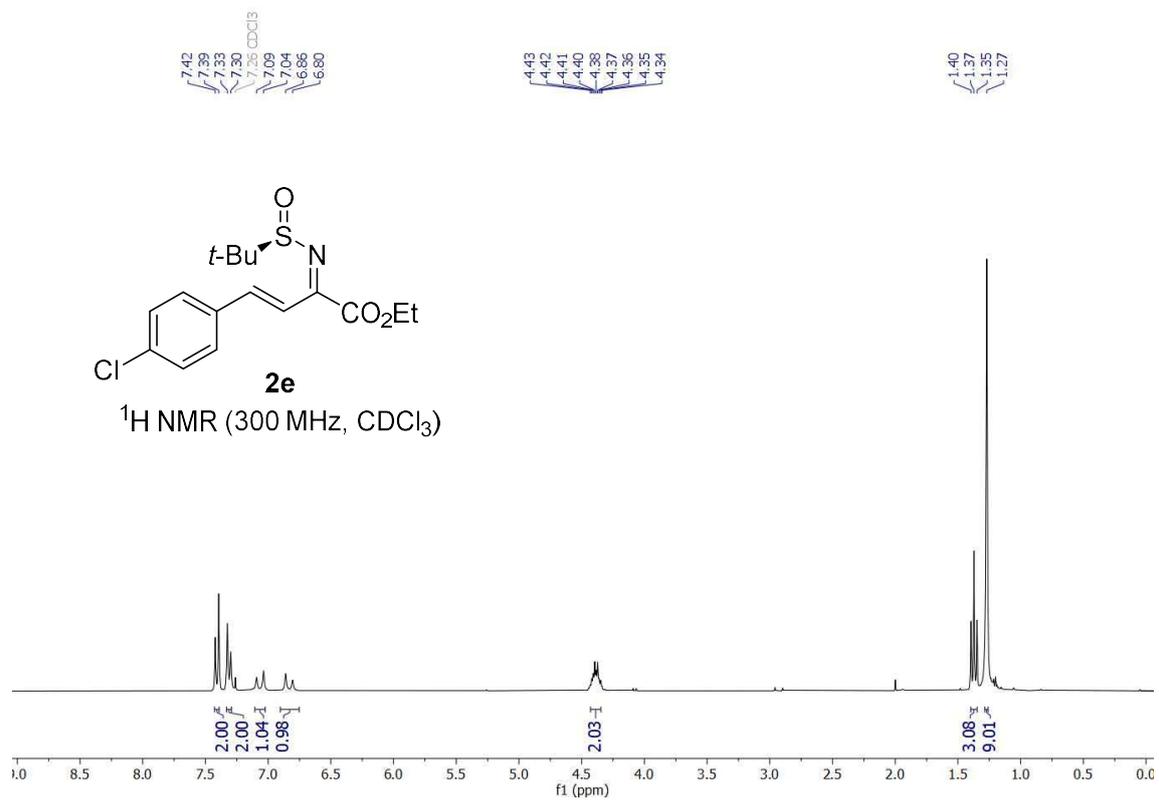


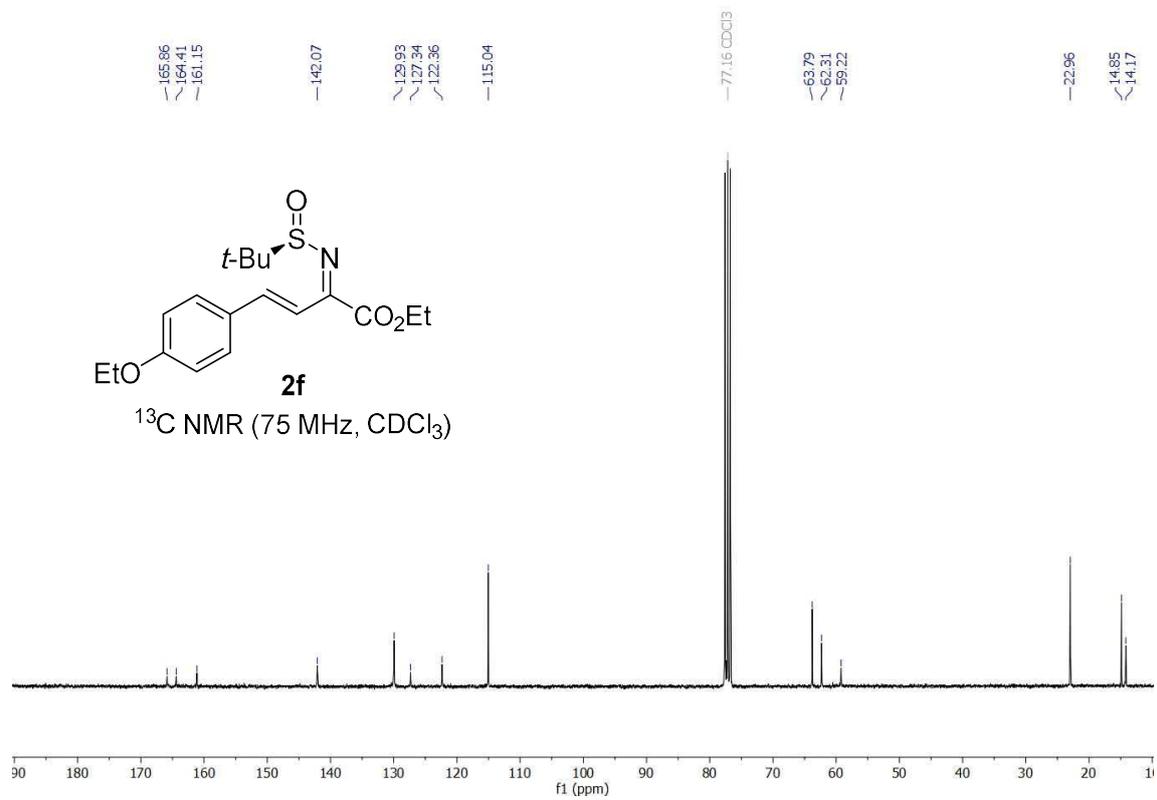
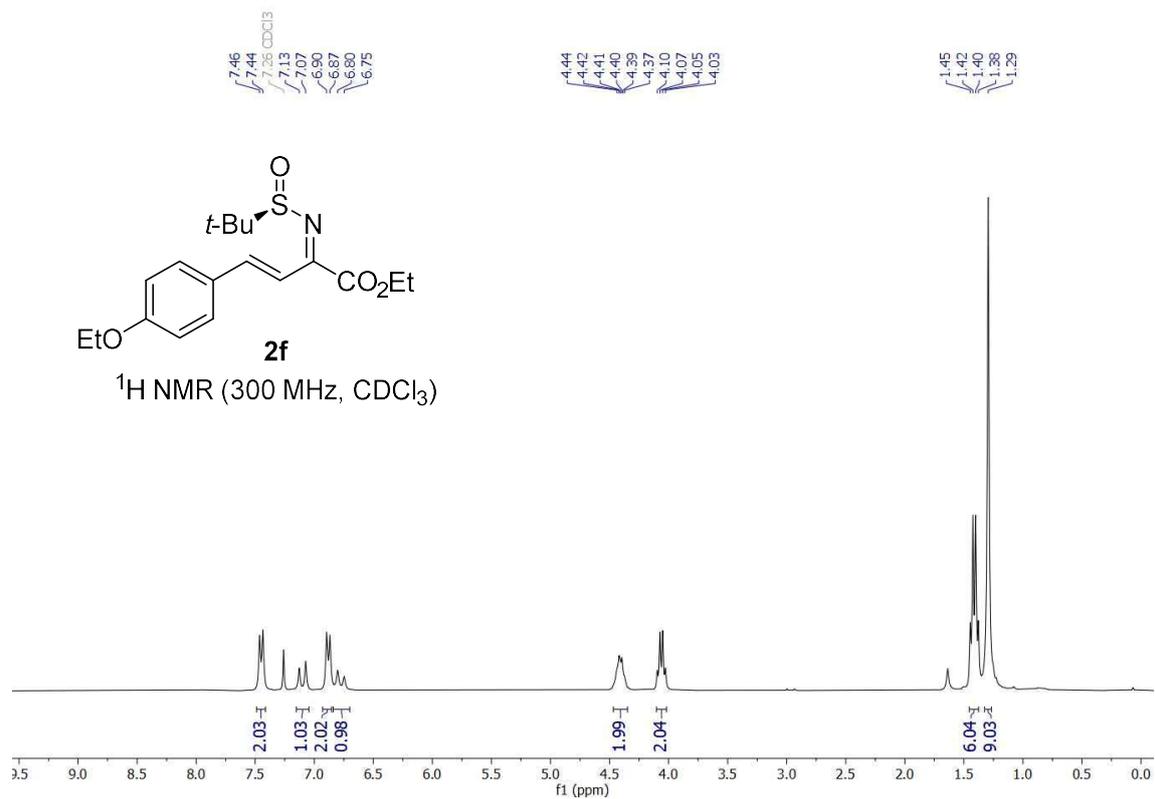


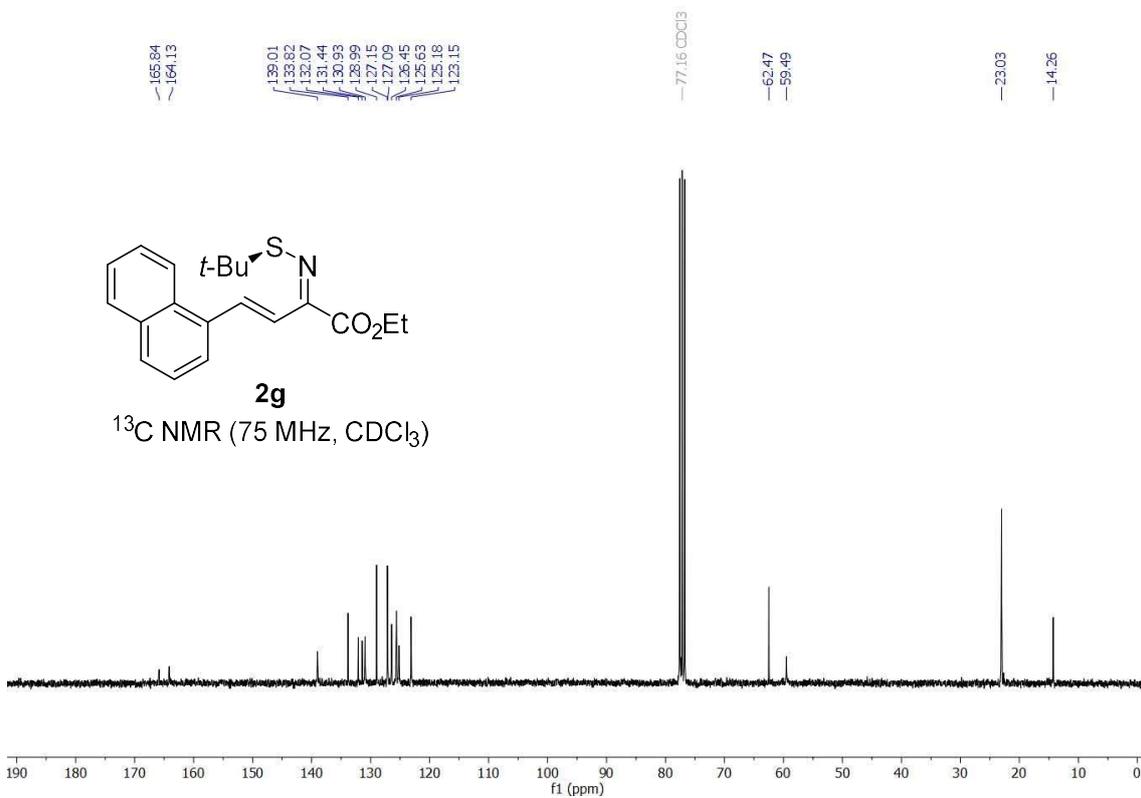
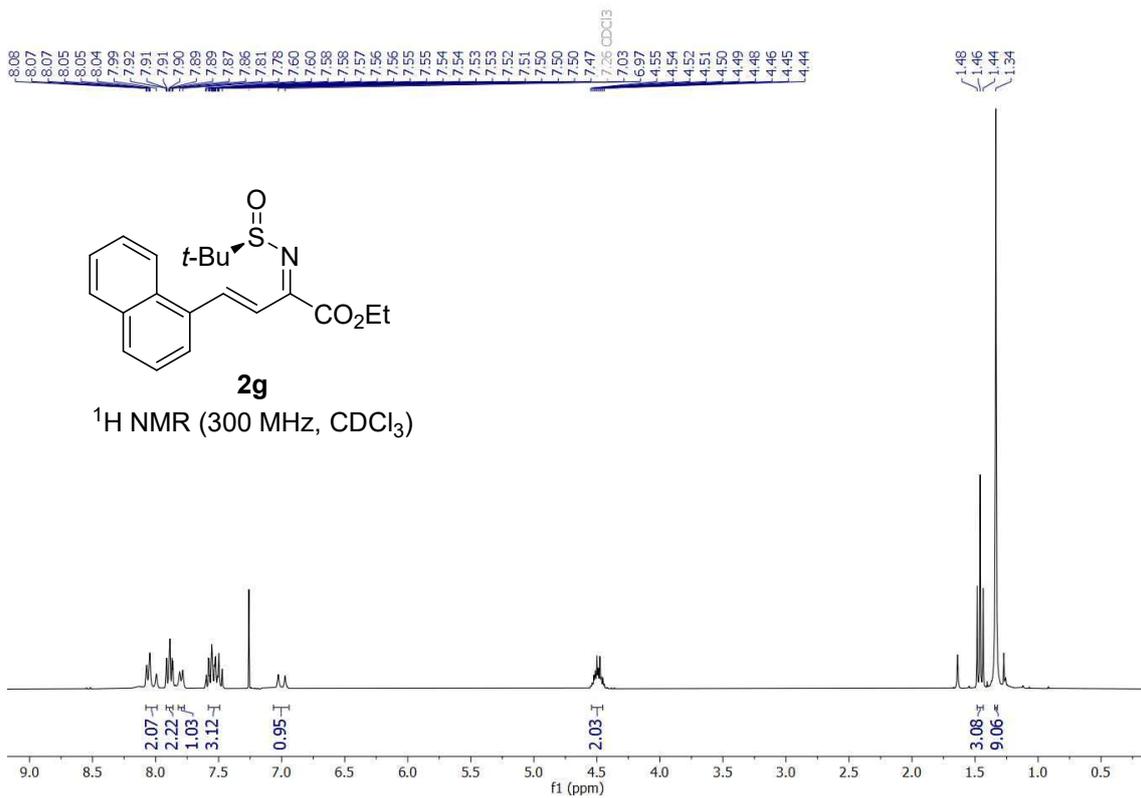


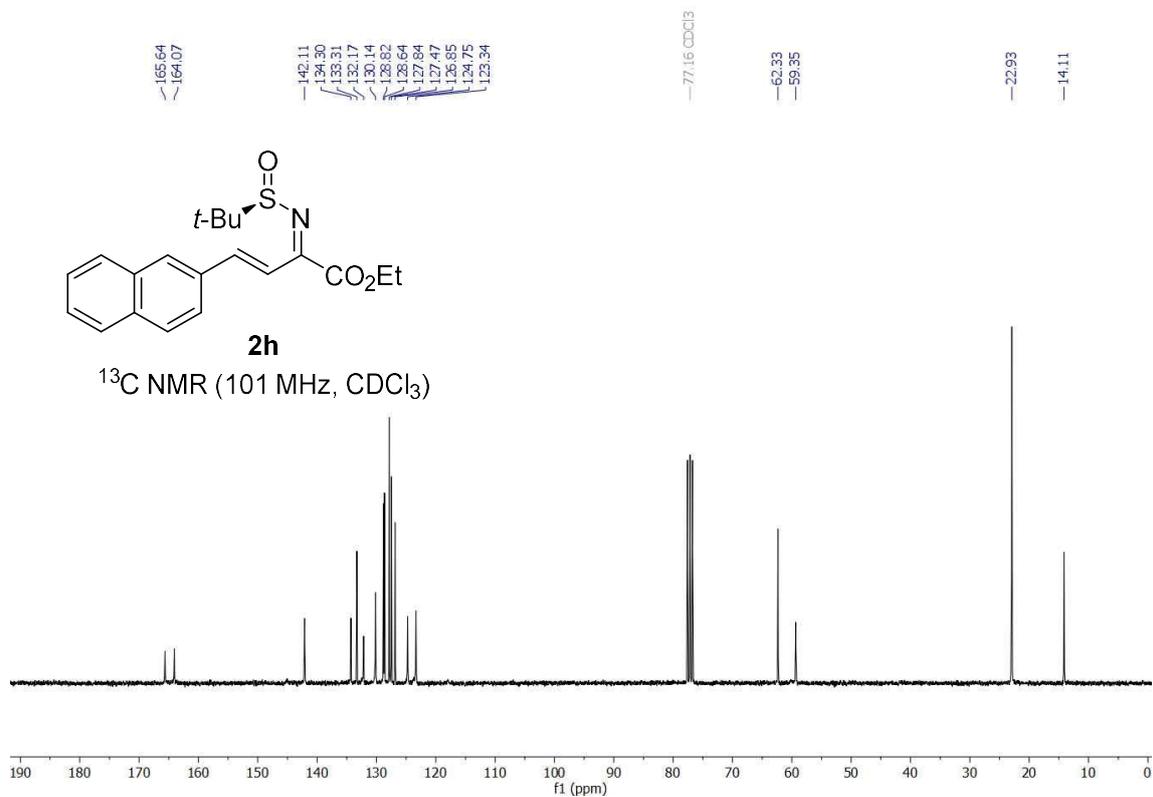
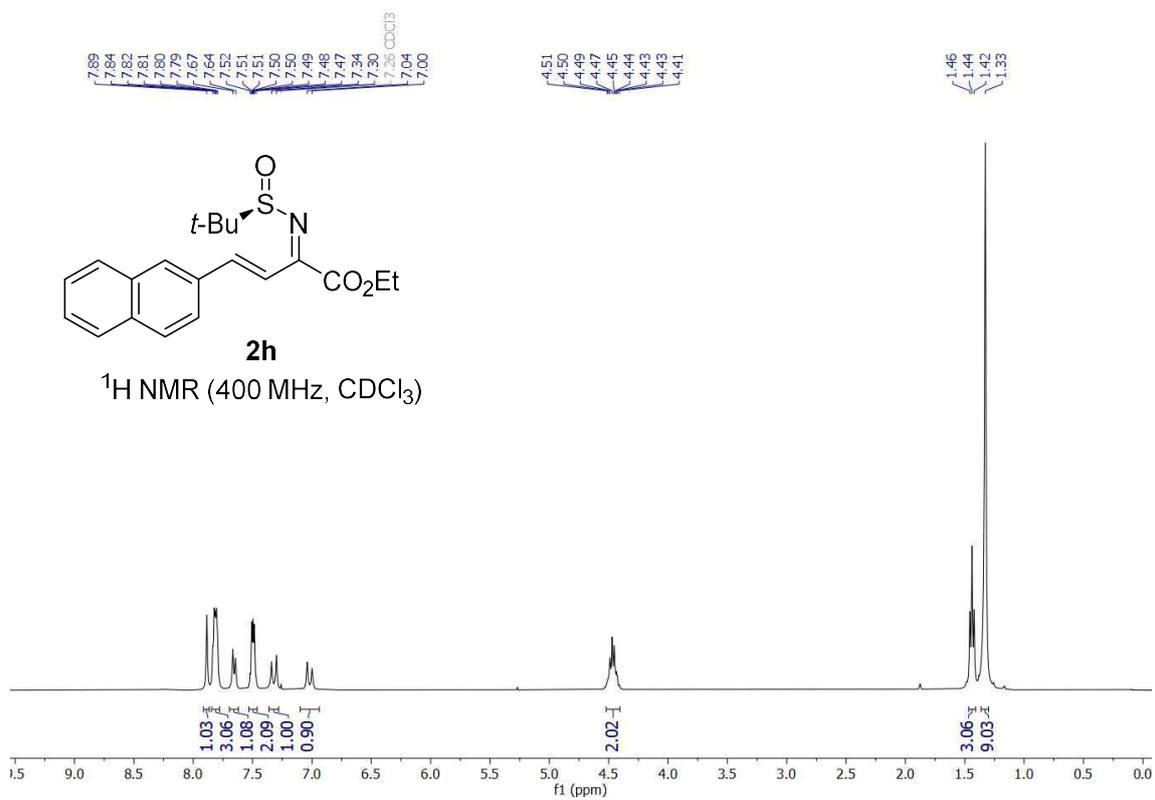


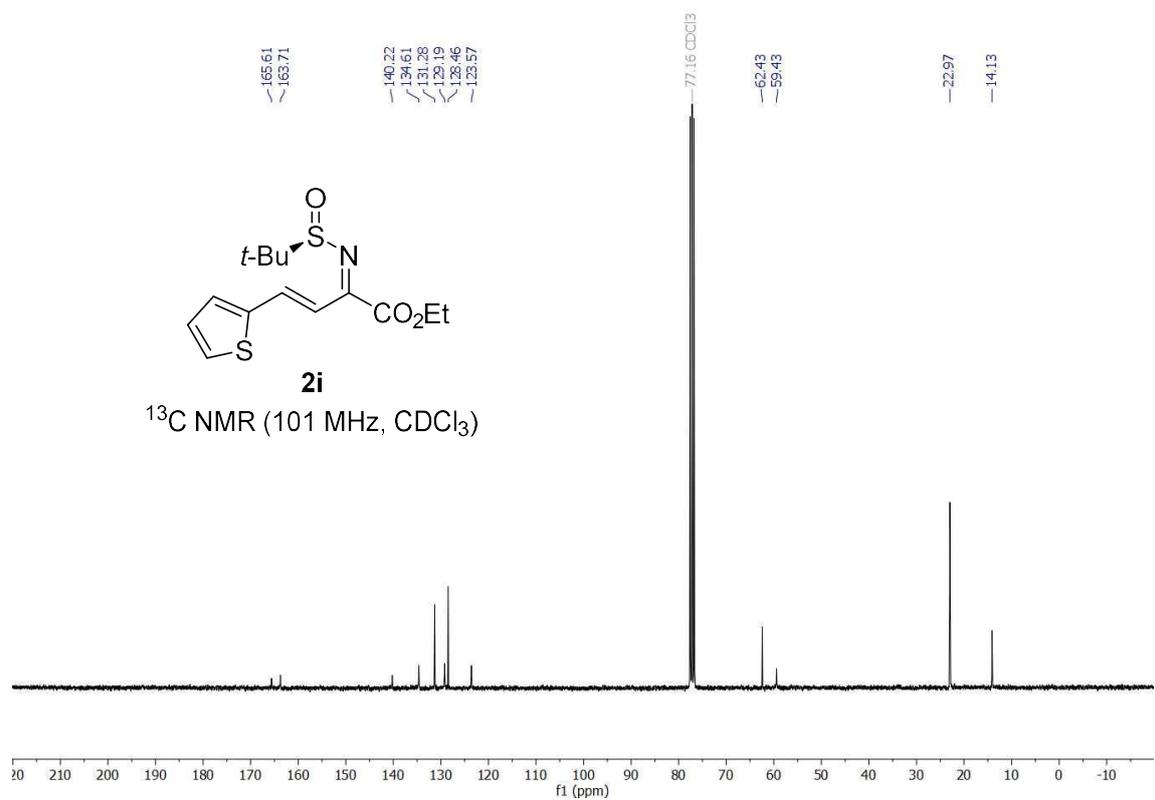
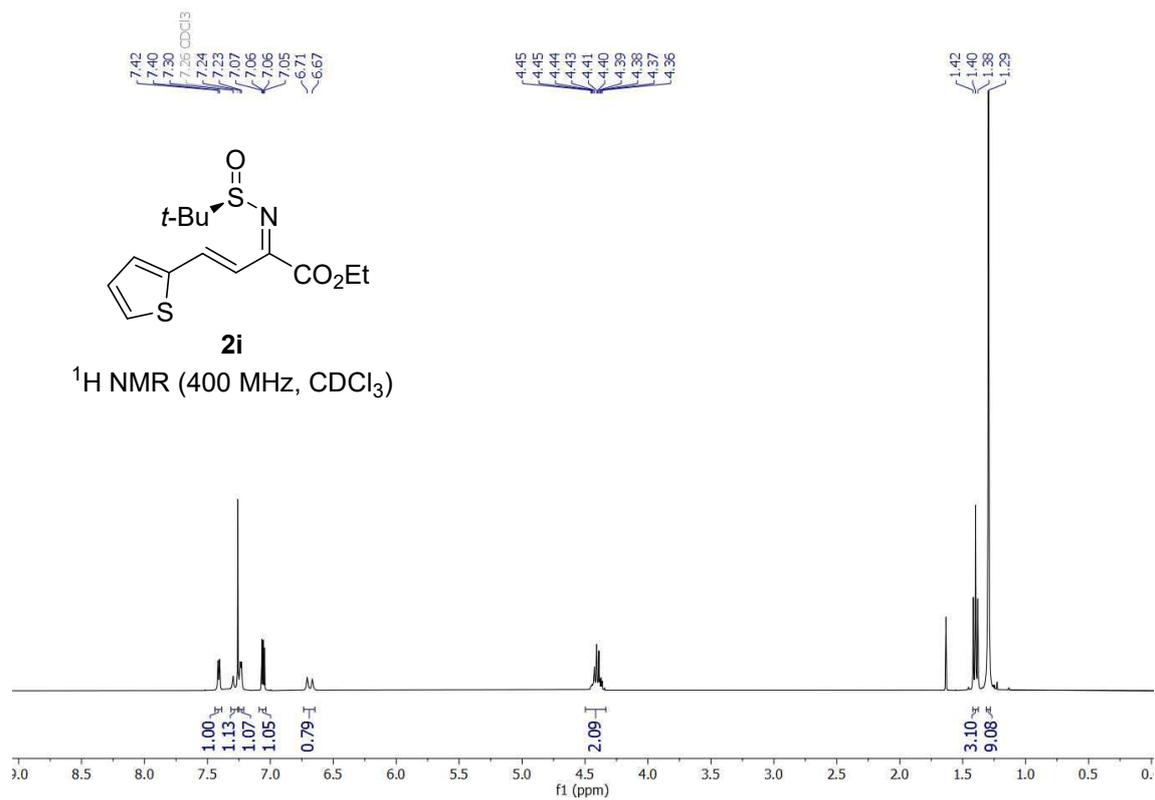


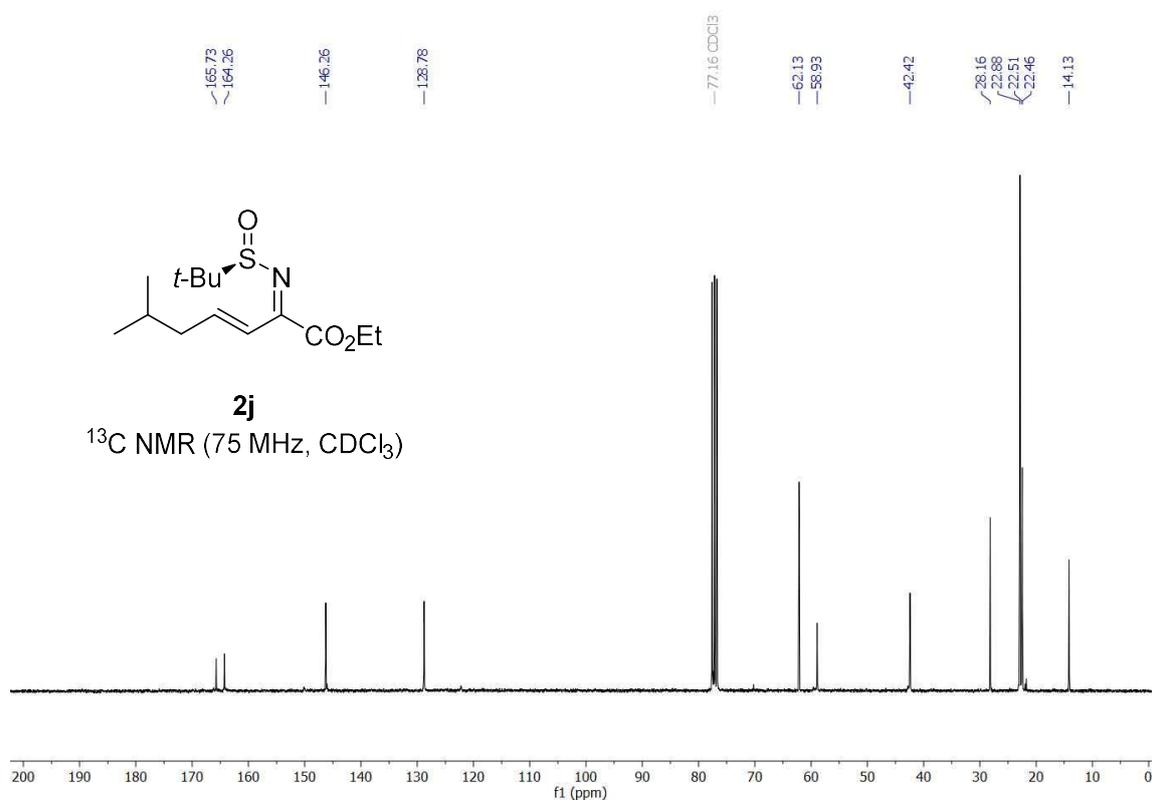
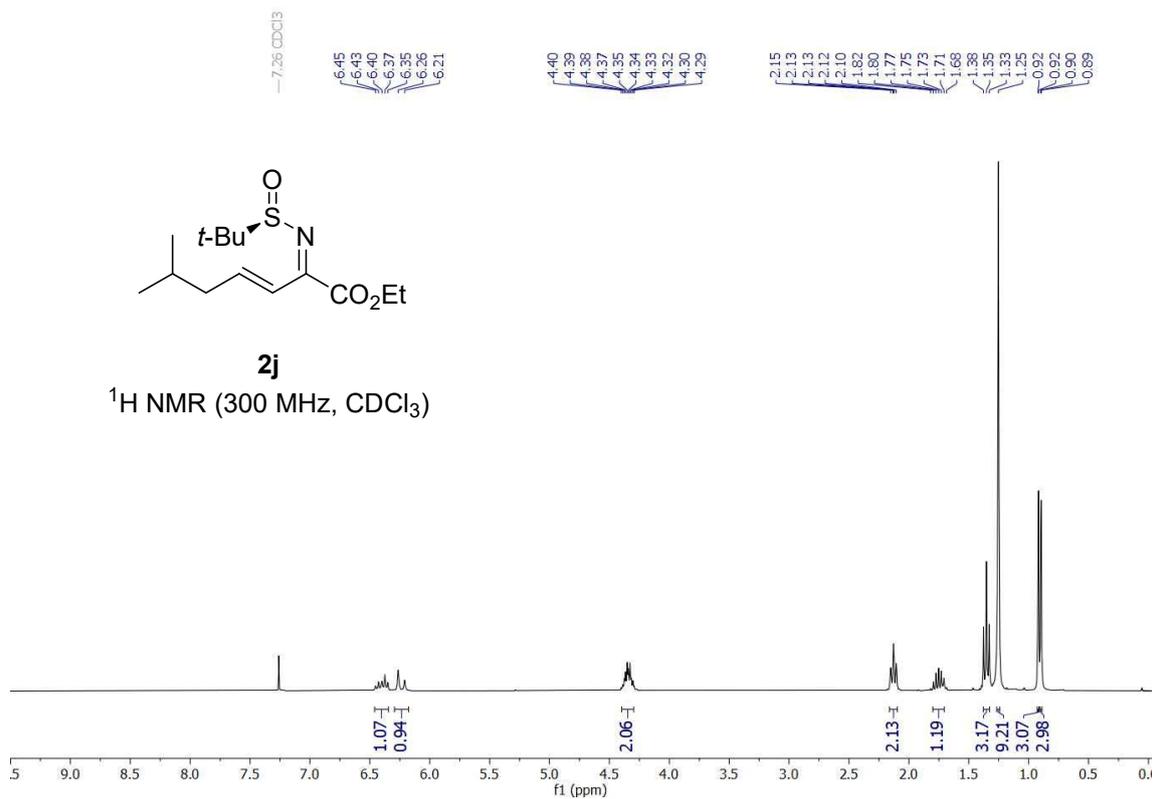


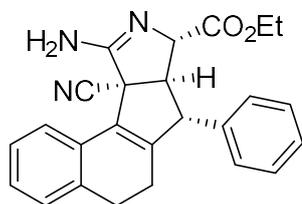
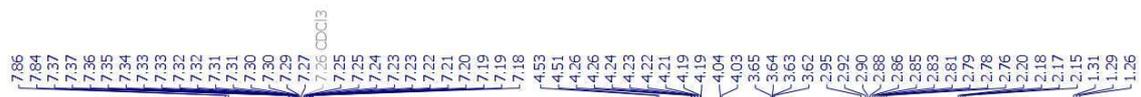






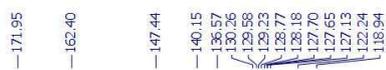
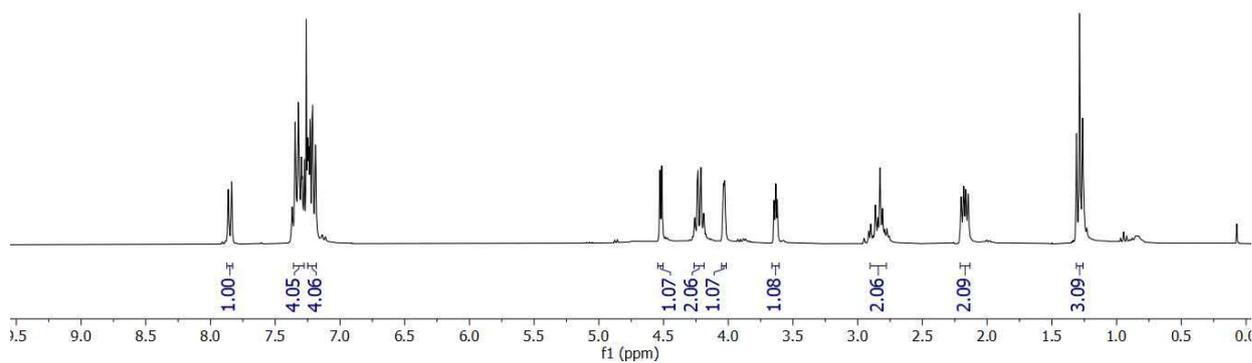






**3a**

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

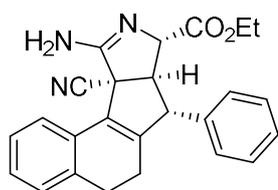


77.16 CDCl<sub>3</sub>  
75.39

62.82  
61.60  
60.59  
58.35

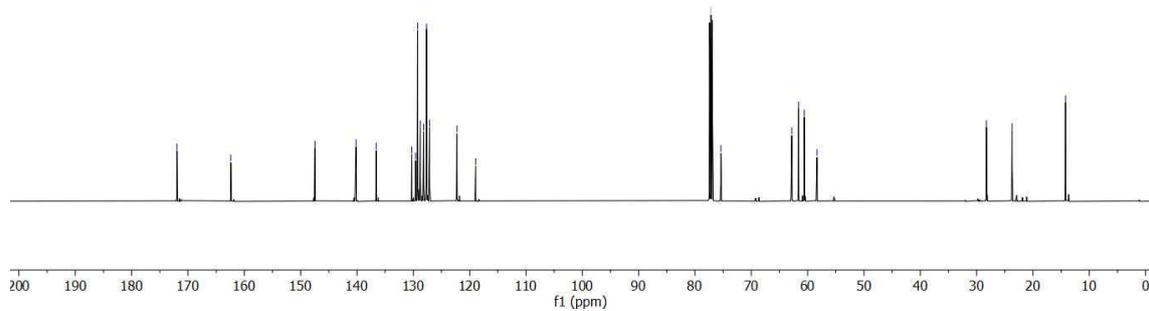
28.27  
23.70

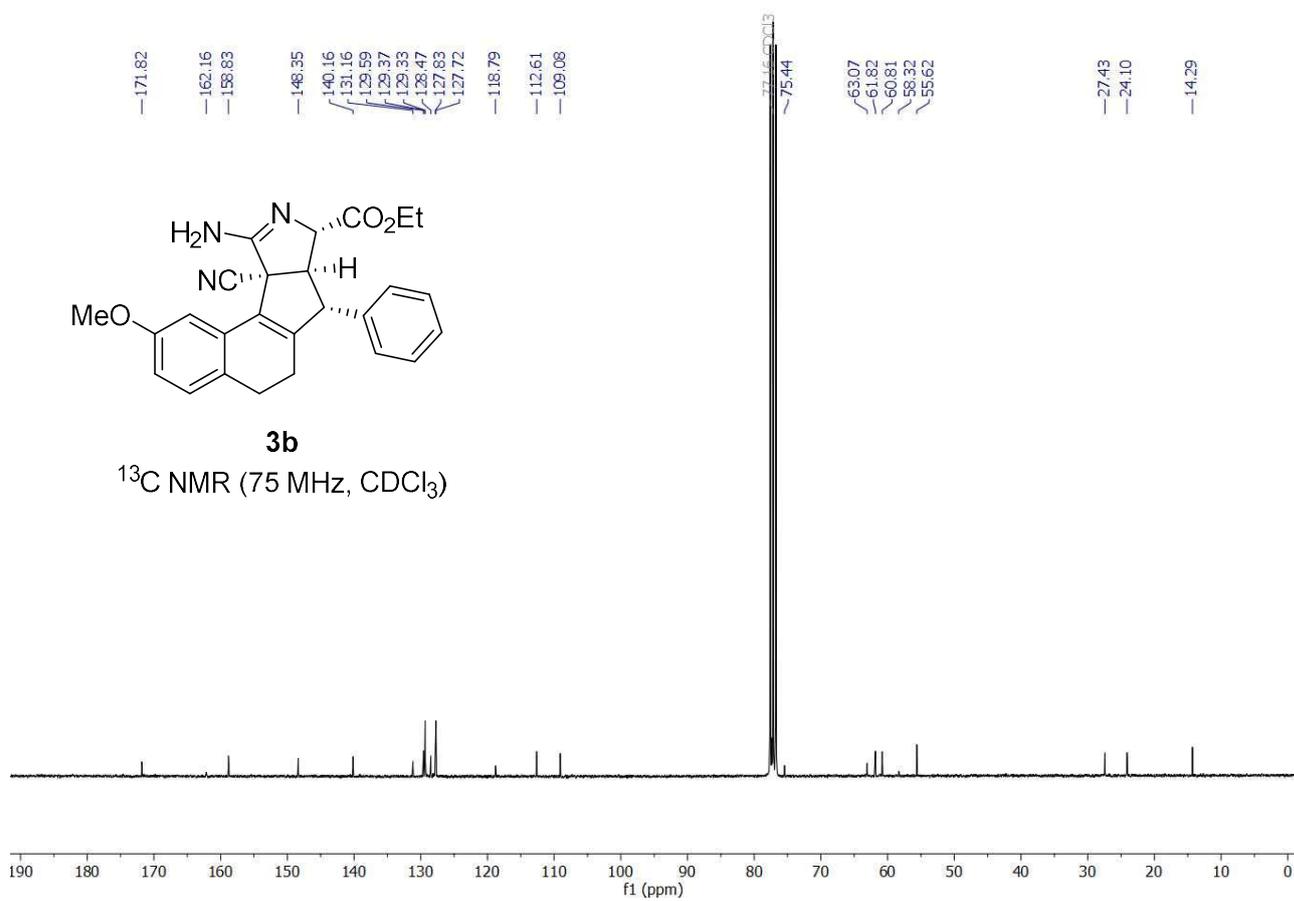
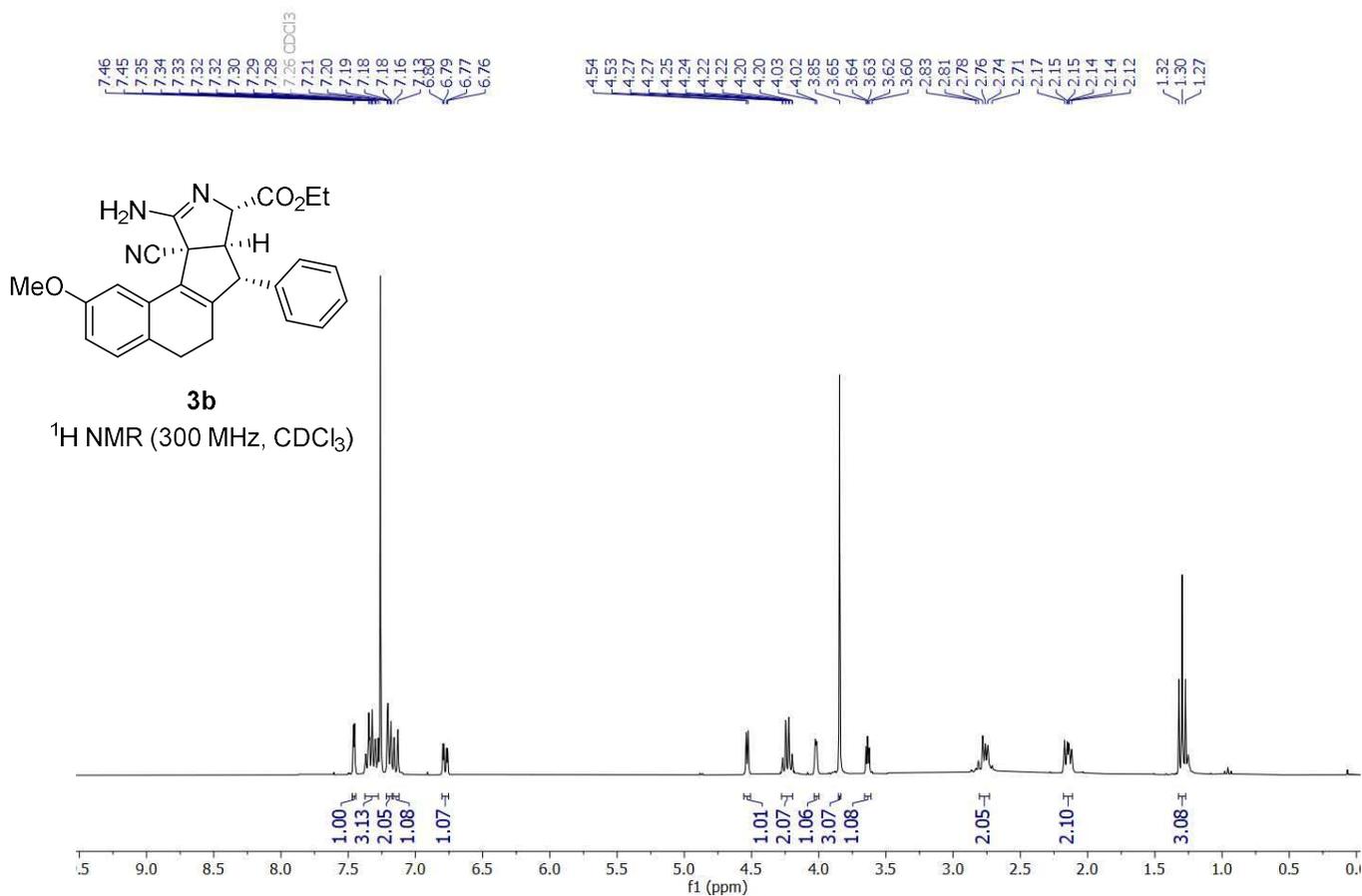
14.22

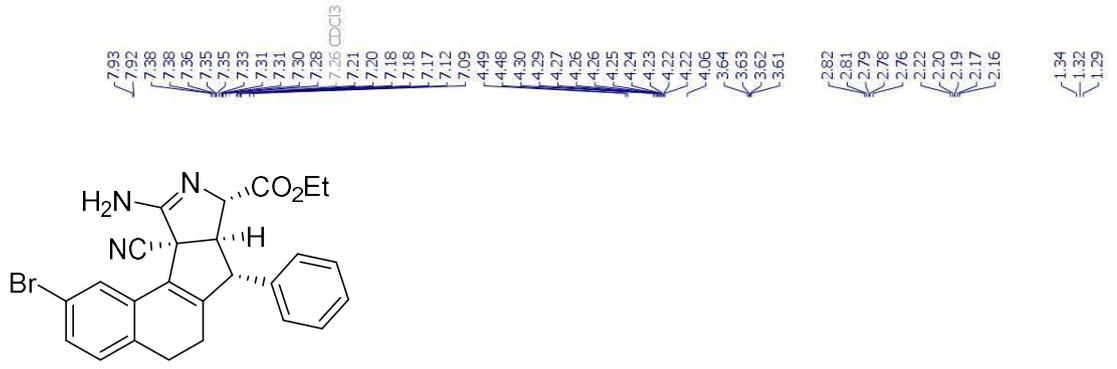


**3a**

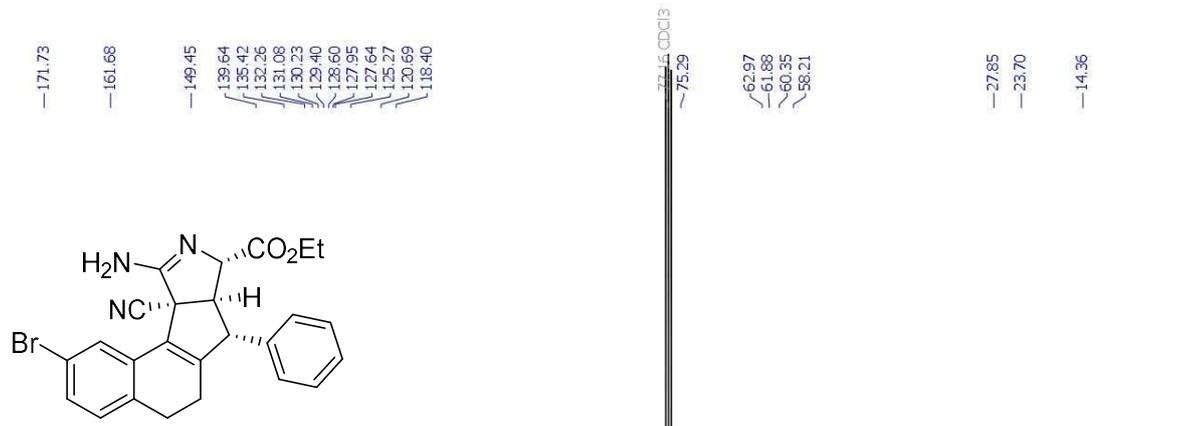
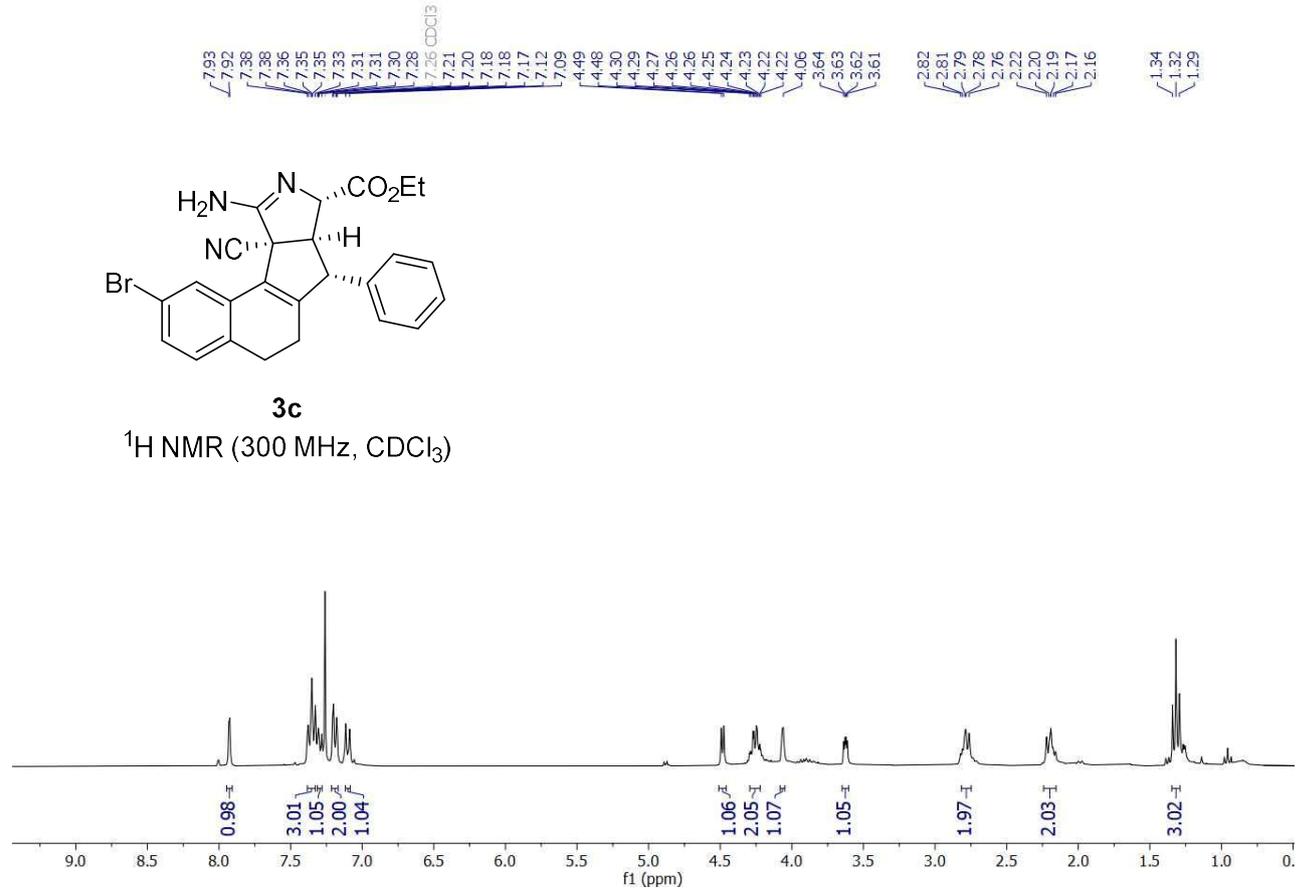
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



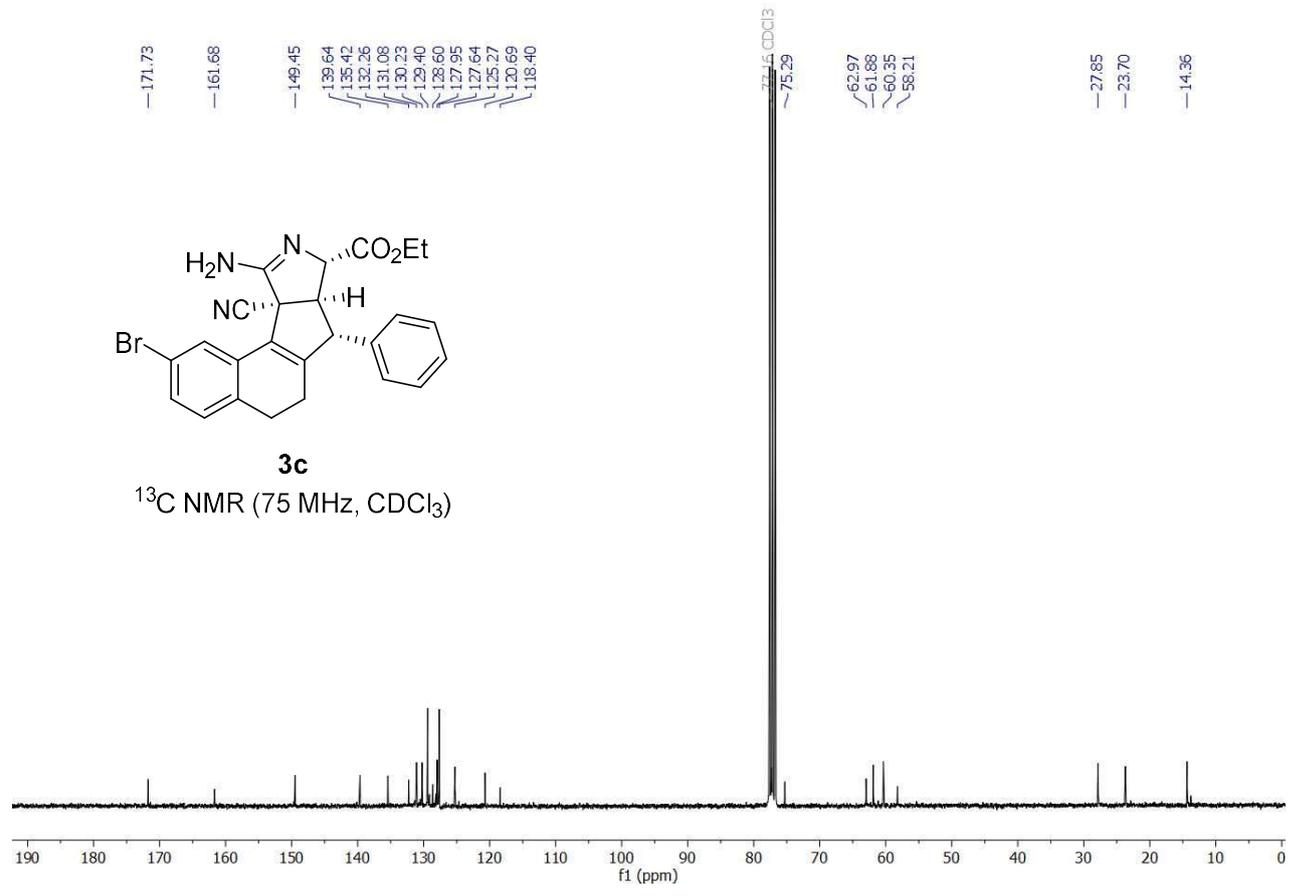


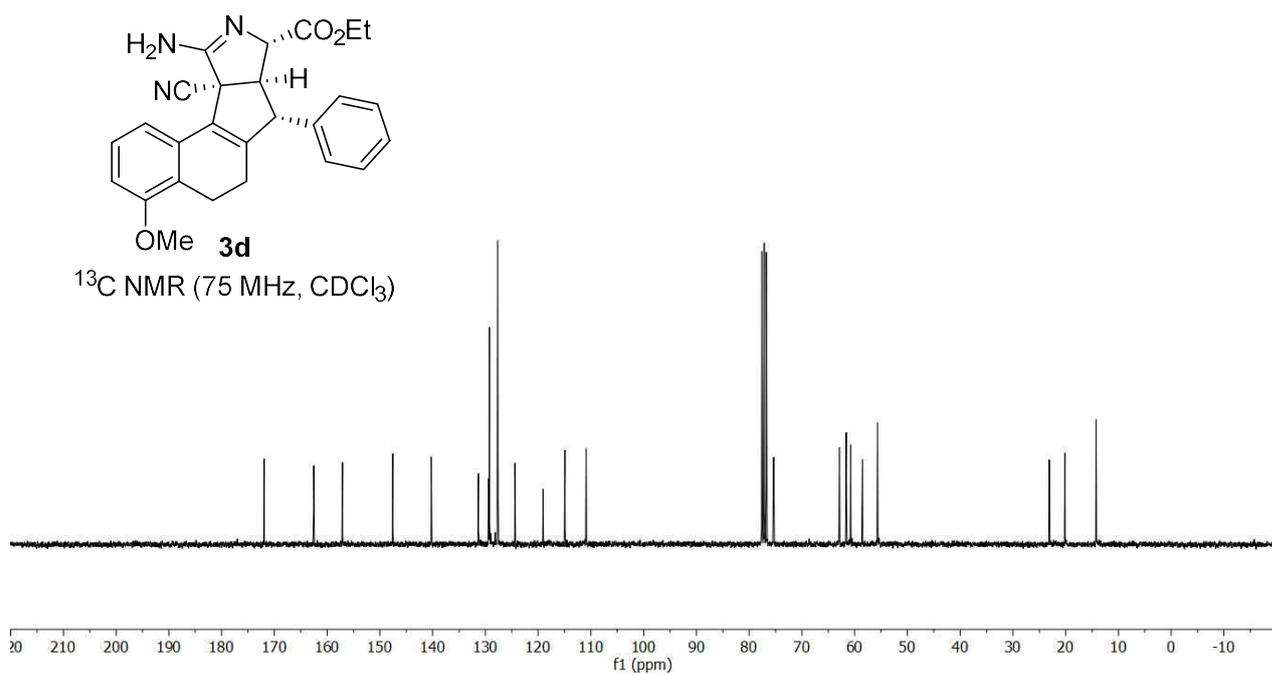
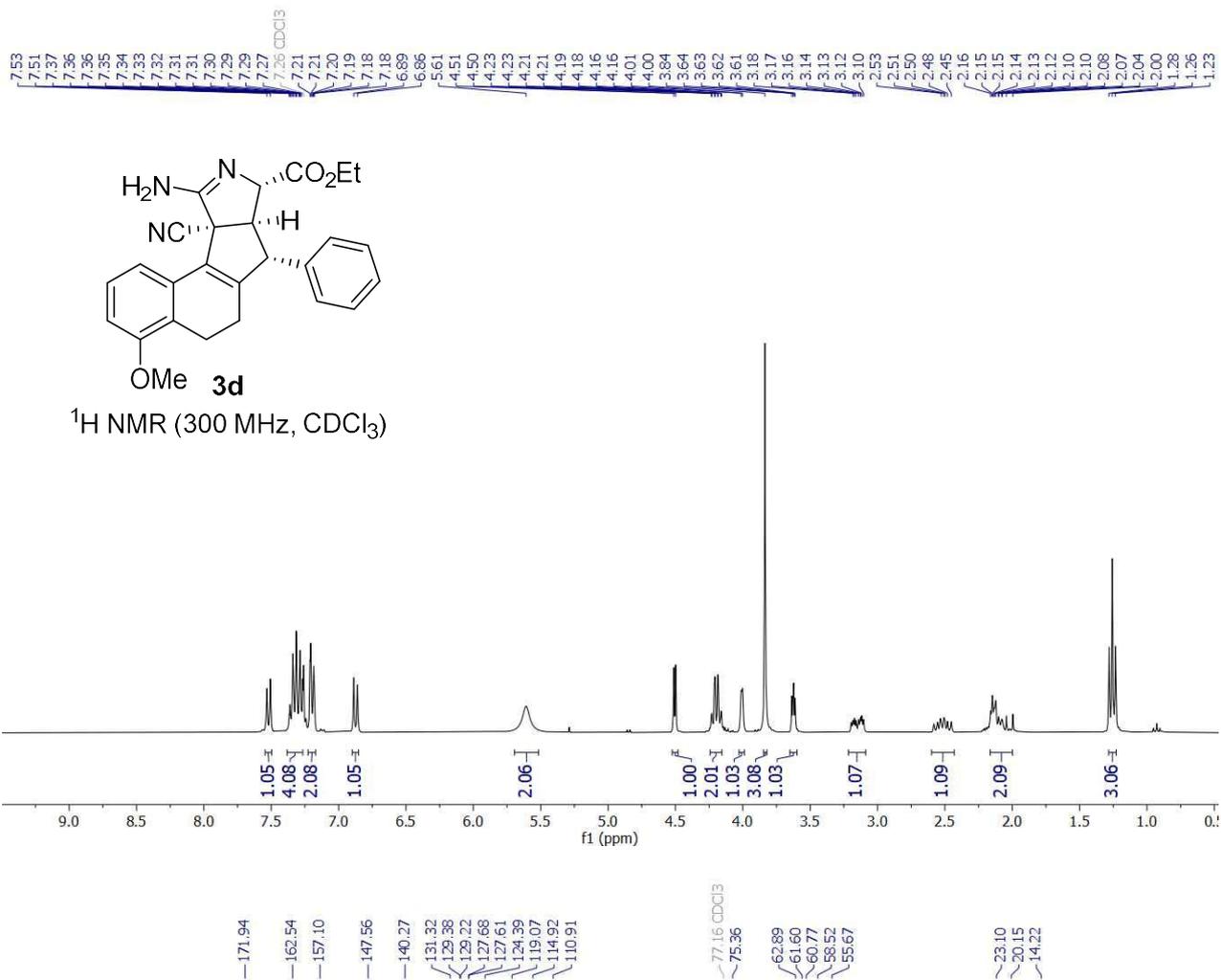


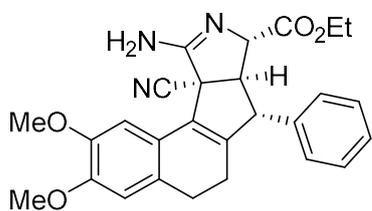
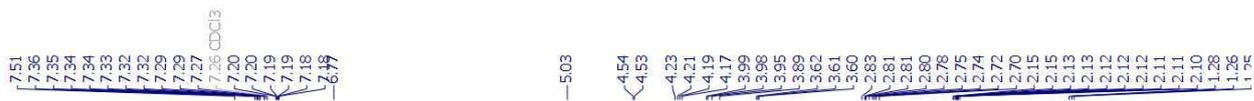
**3c**  
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



**3c**  
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

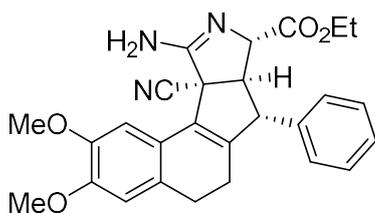
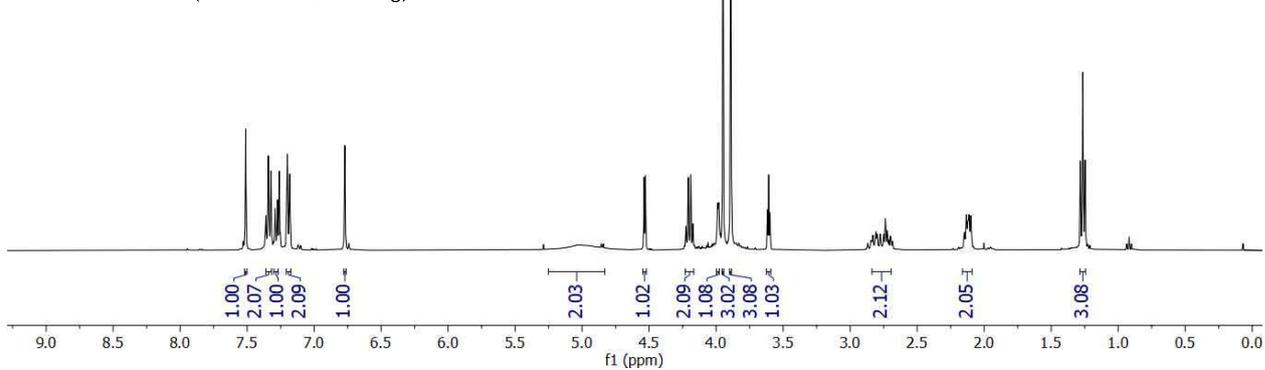






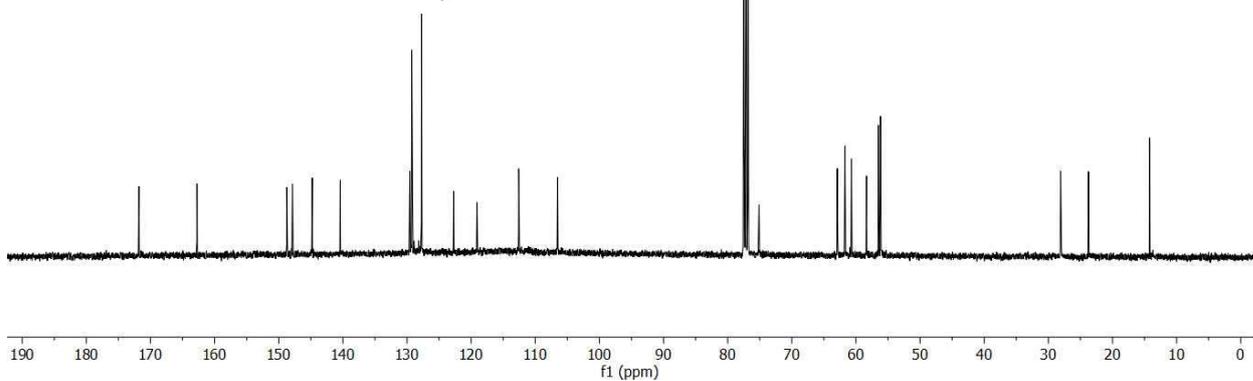
**3e**

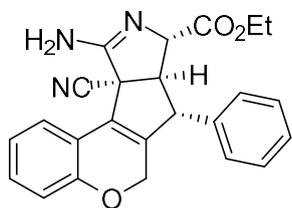
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



**3e**

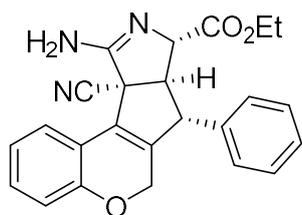
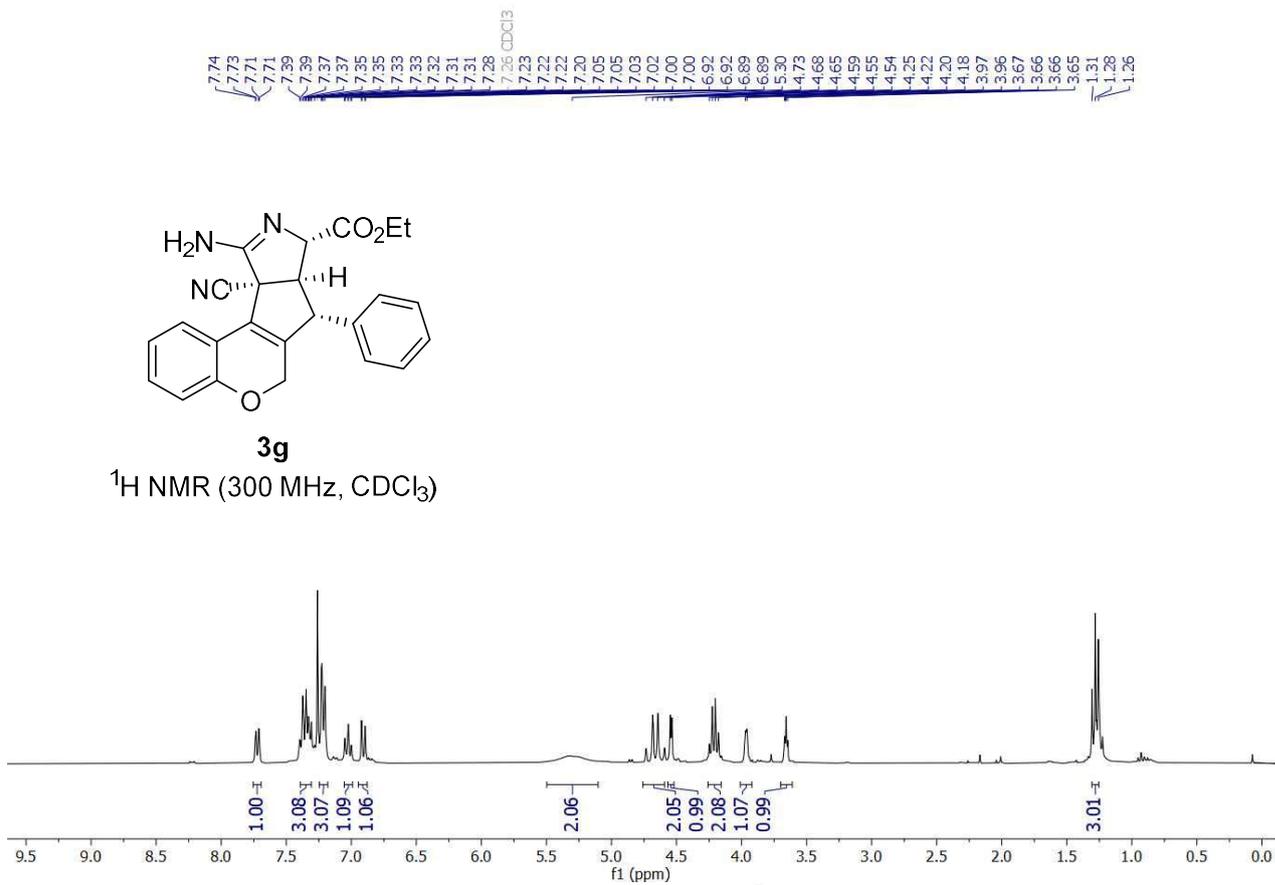
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)





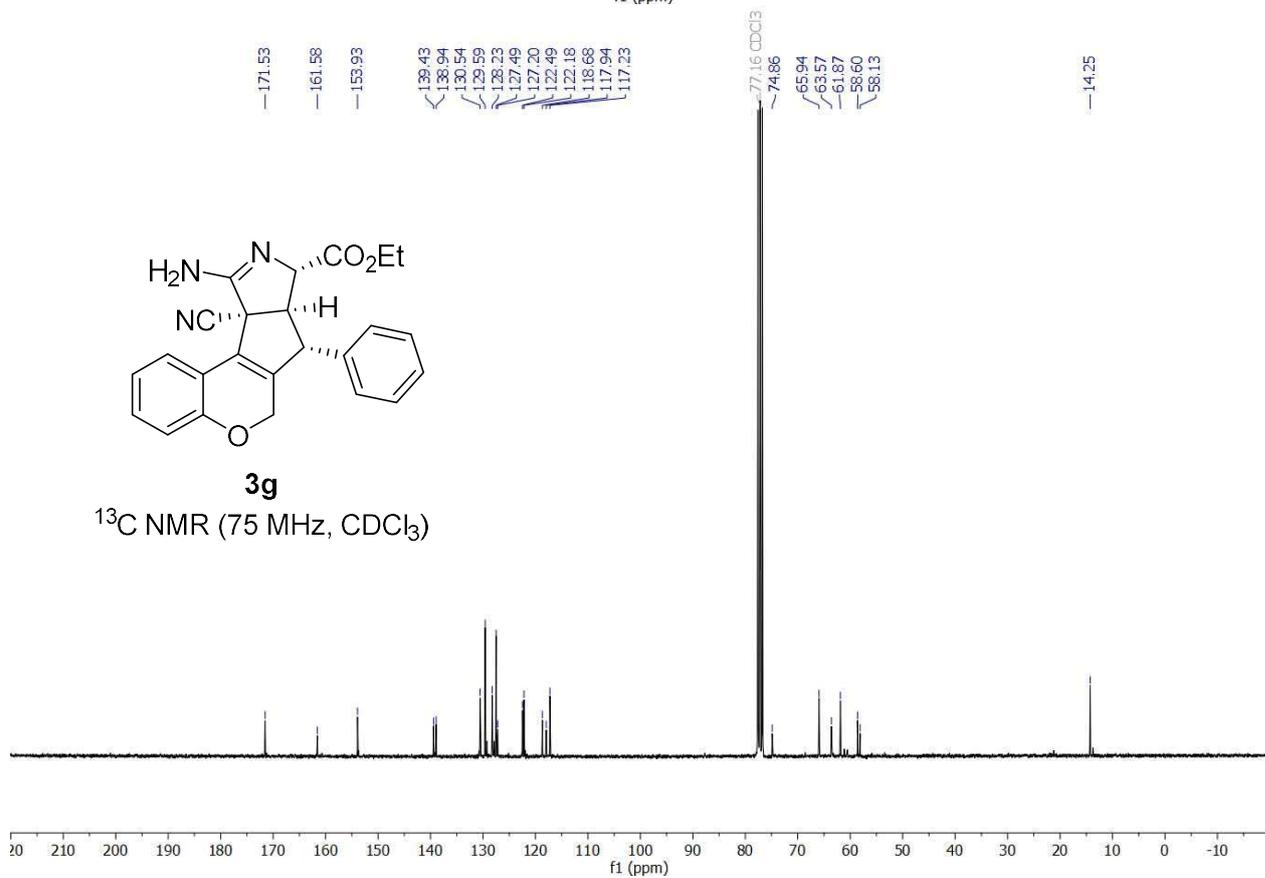
**3g**

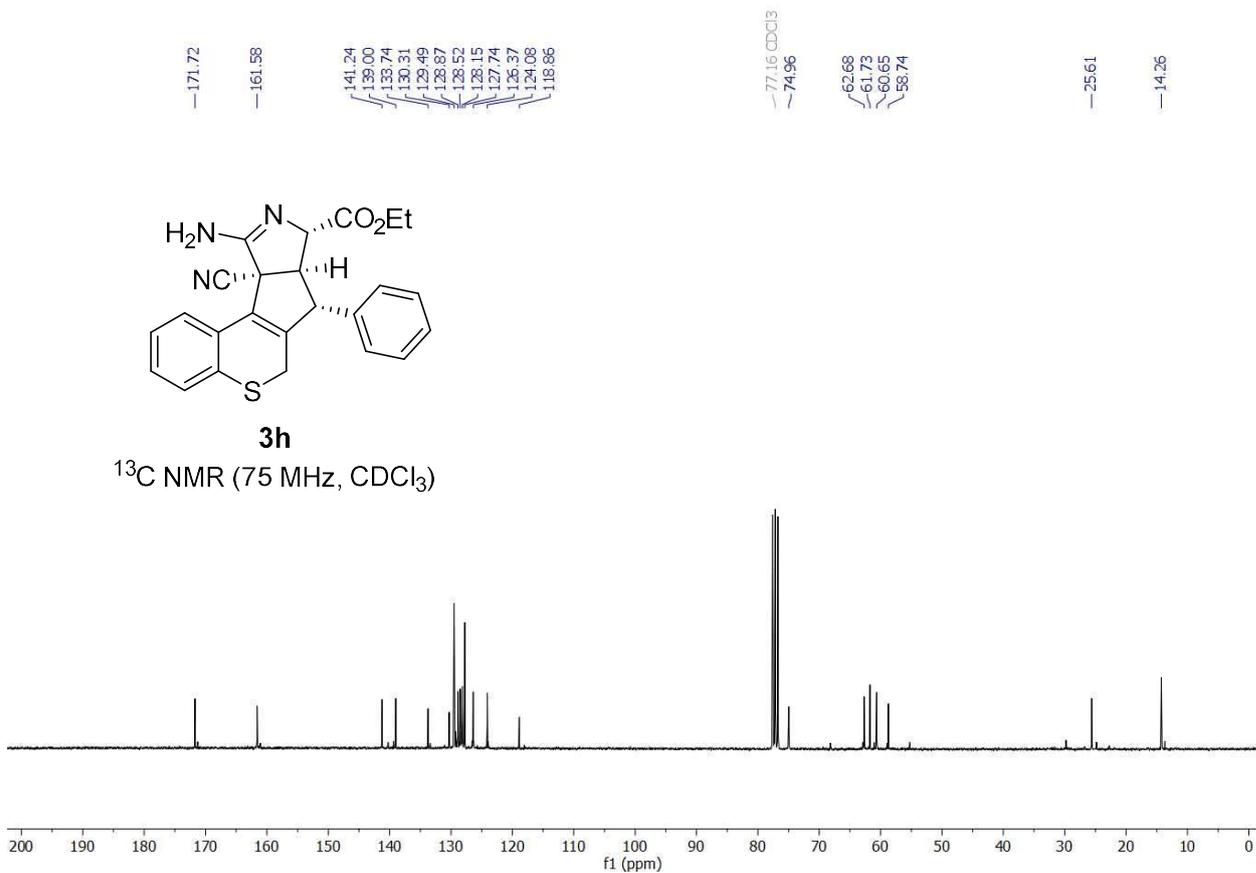
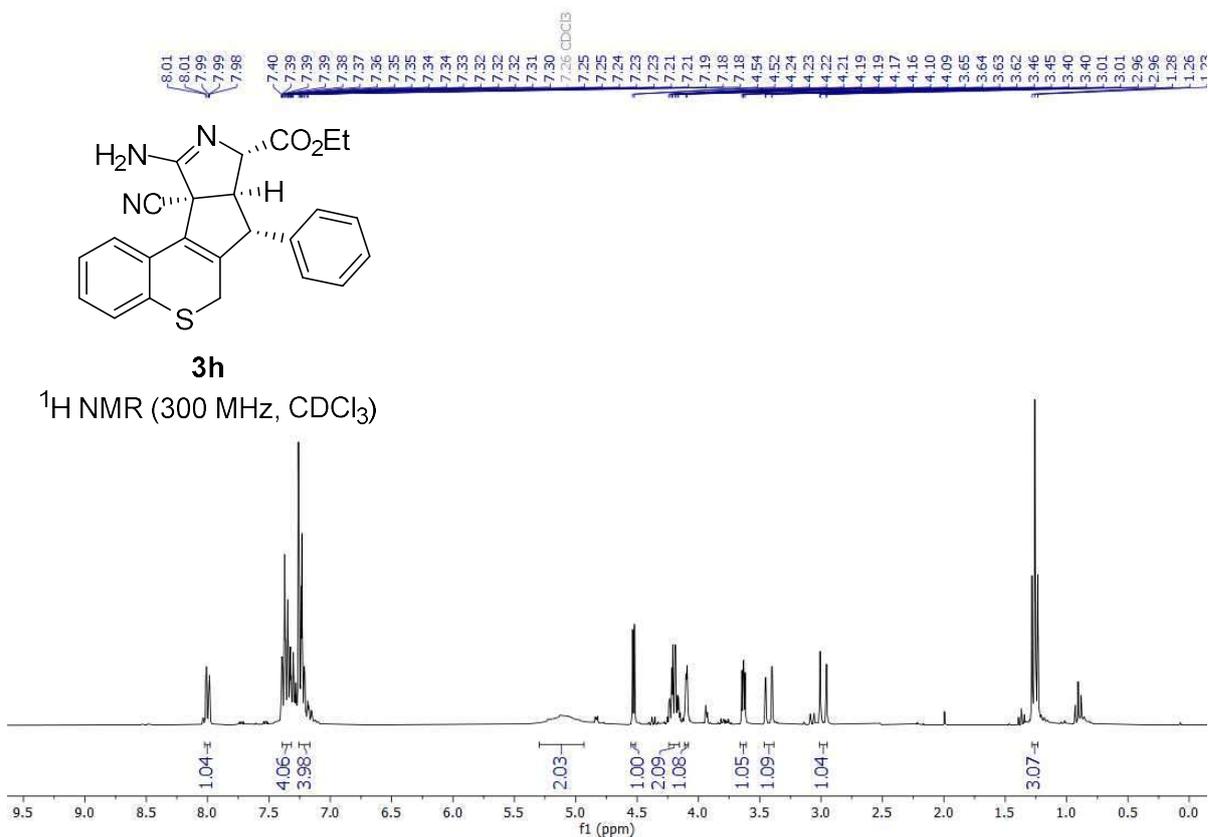
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

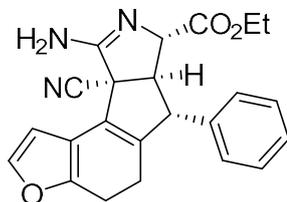
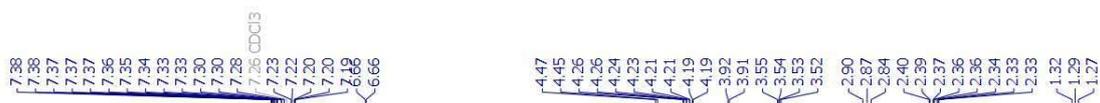


**3g**

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

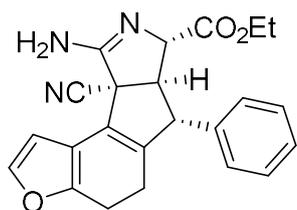
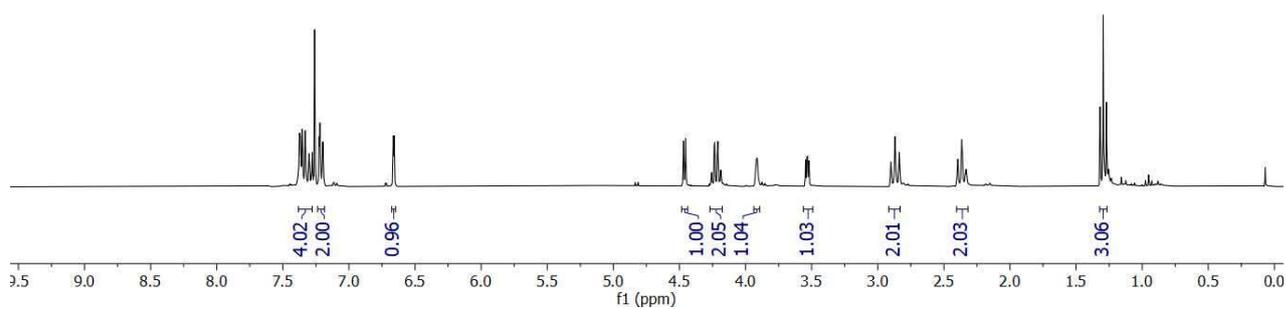






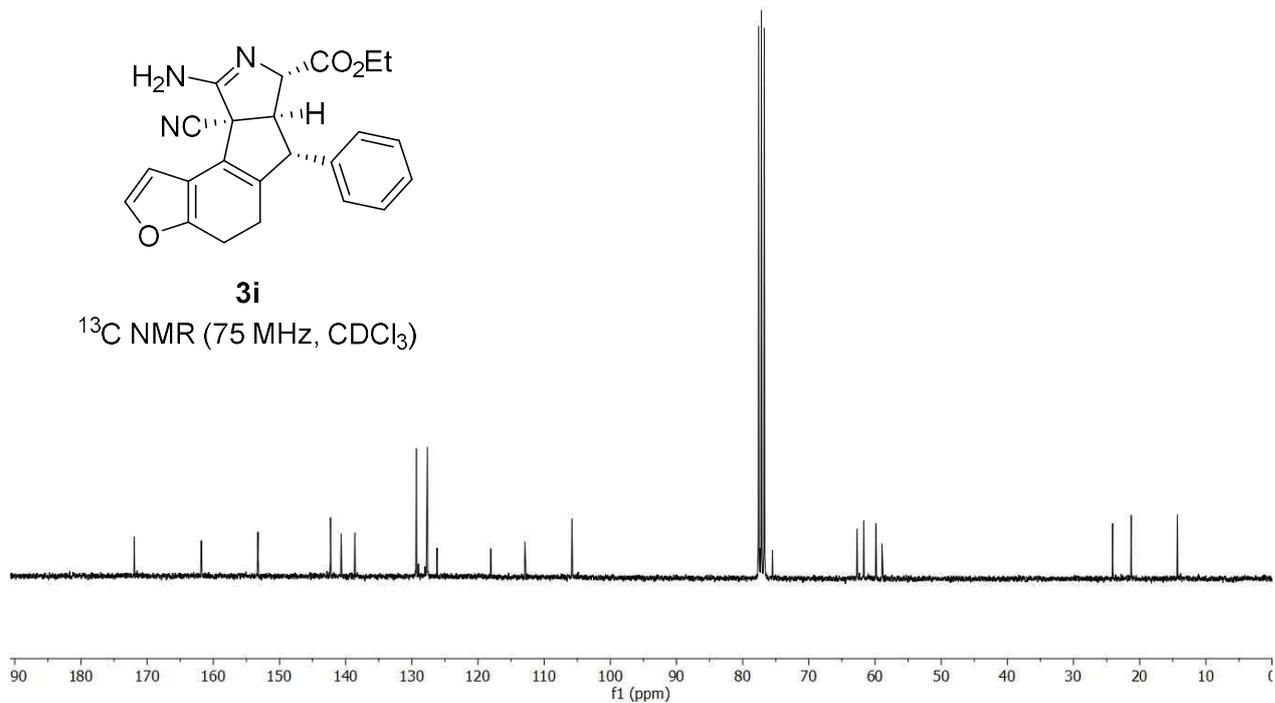
**3i**

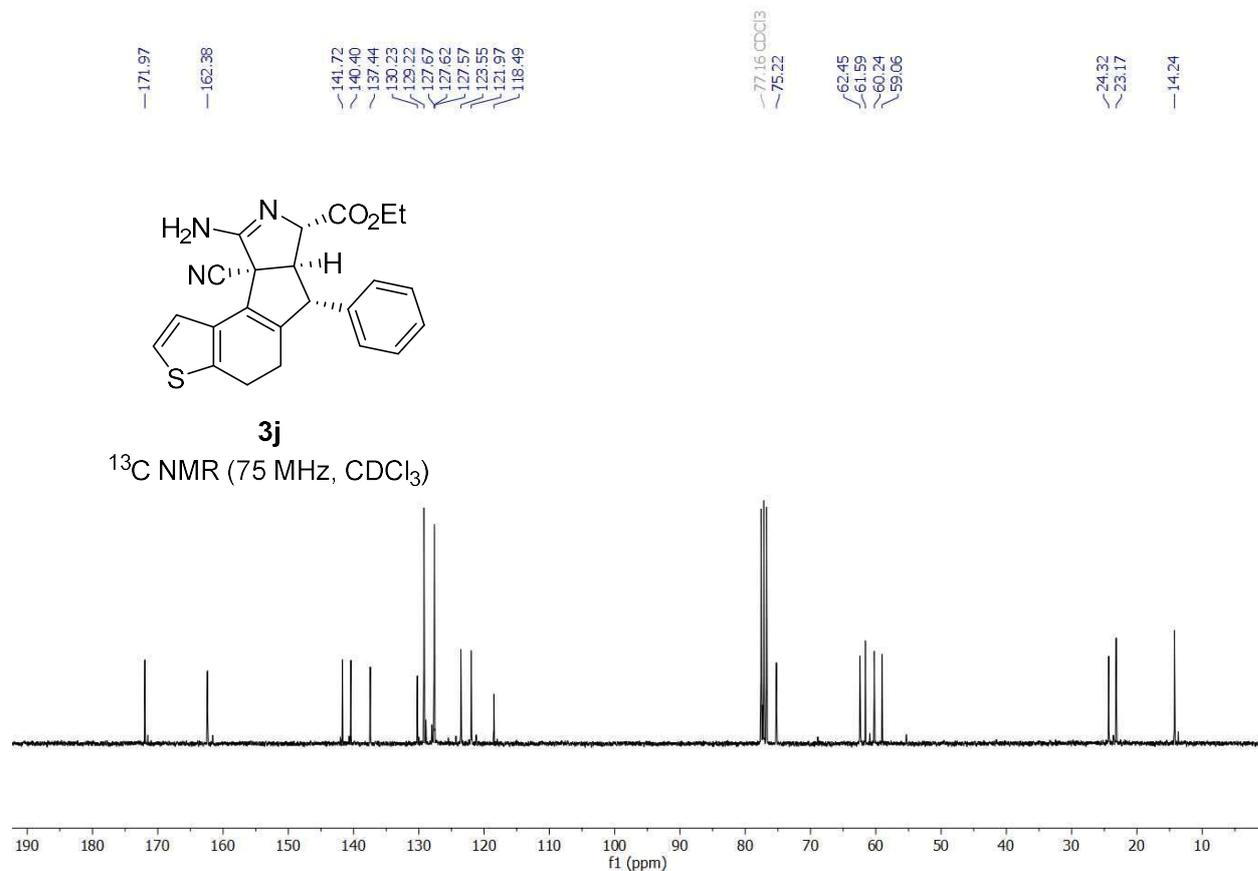
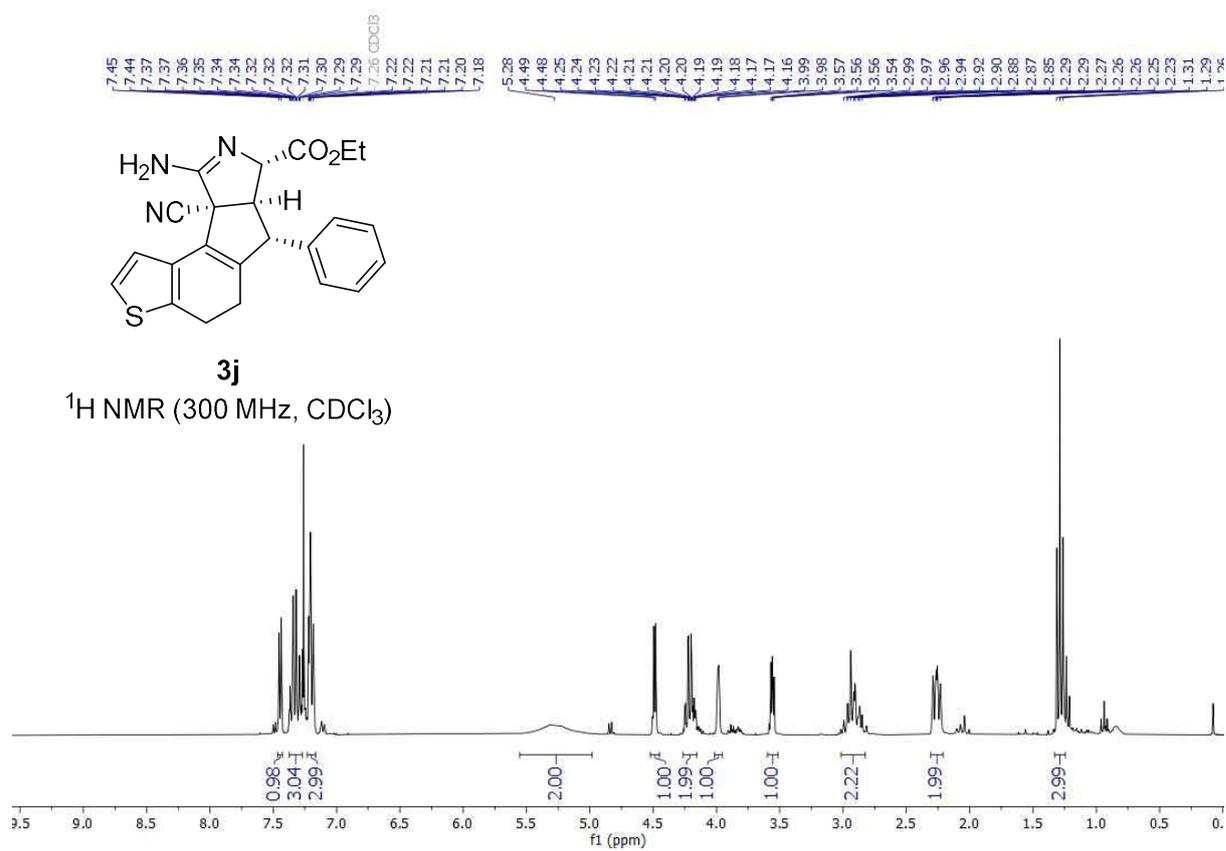
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)



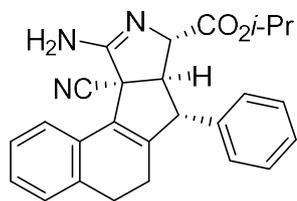
**3i**

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



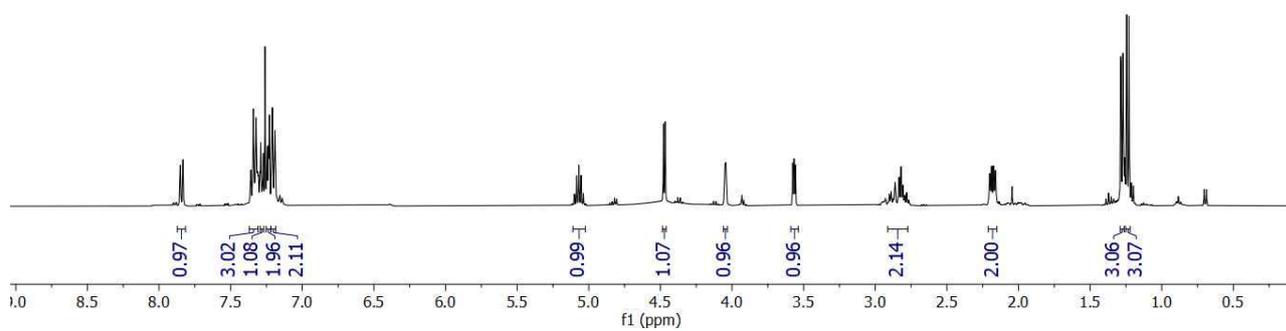


7.85  
7.83  
7.36  
7.36  
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7.28  
7.27  
7.27  
7.26 CDCl<sub>3</sub>  
7.25  
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7.23  
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7.22  
7.21  
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7.19  
5.08  
5.07  
5.05  
4.48  
4.47  
4.05  
4.04  
3.58  
3.57  
3.56  
3.56  
2.86  
2.86  
2.83  
2.82  
2.81  
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1.23

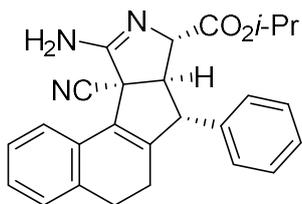


**3I**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

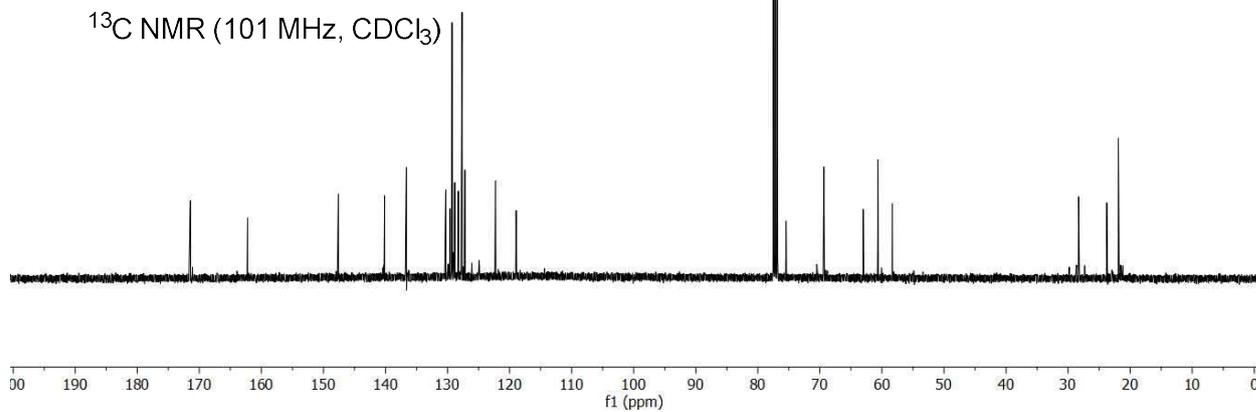


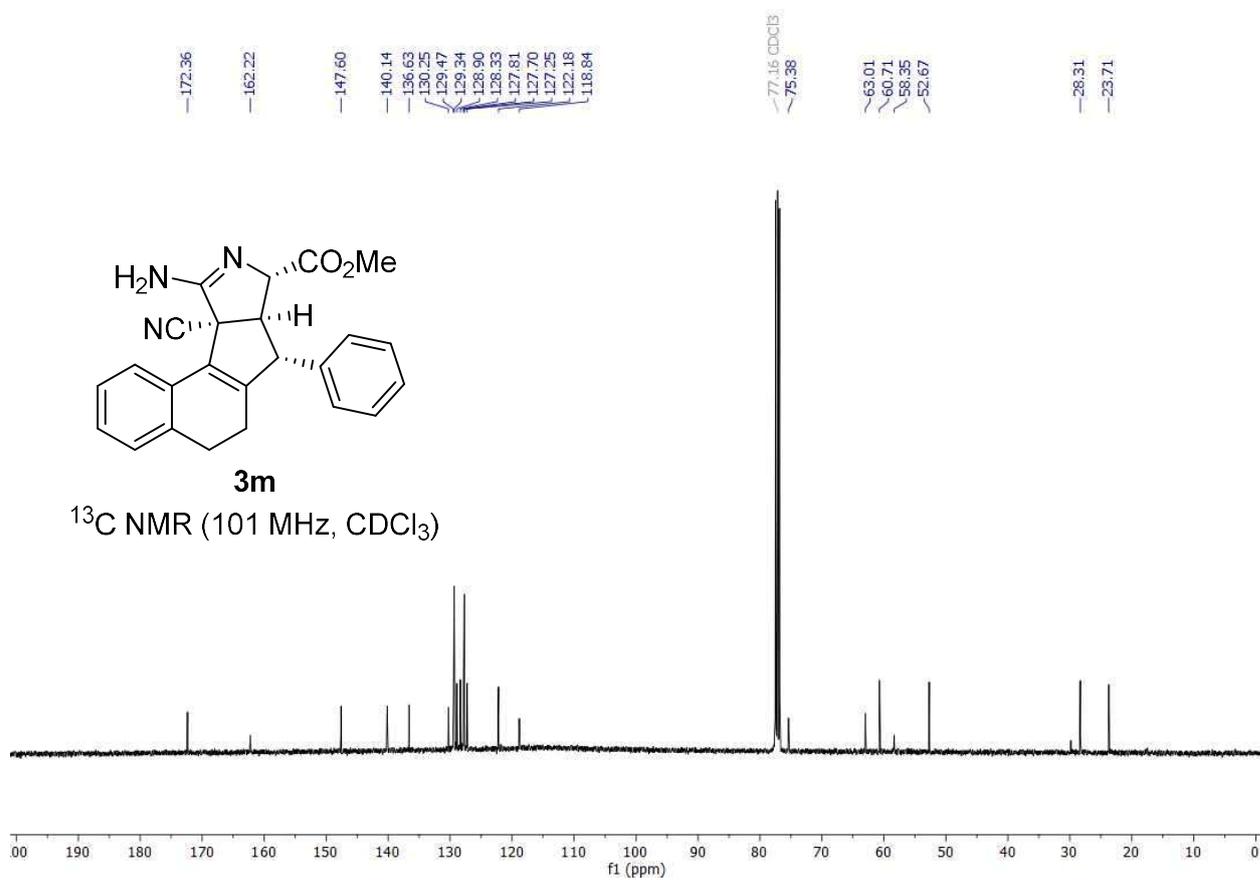
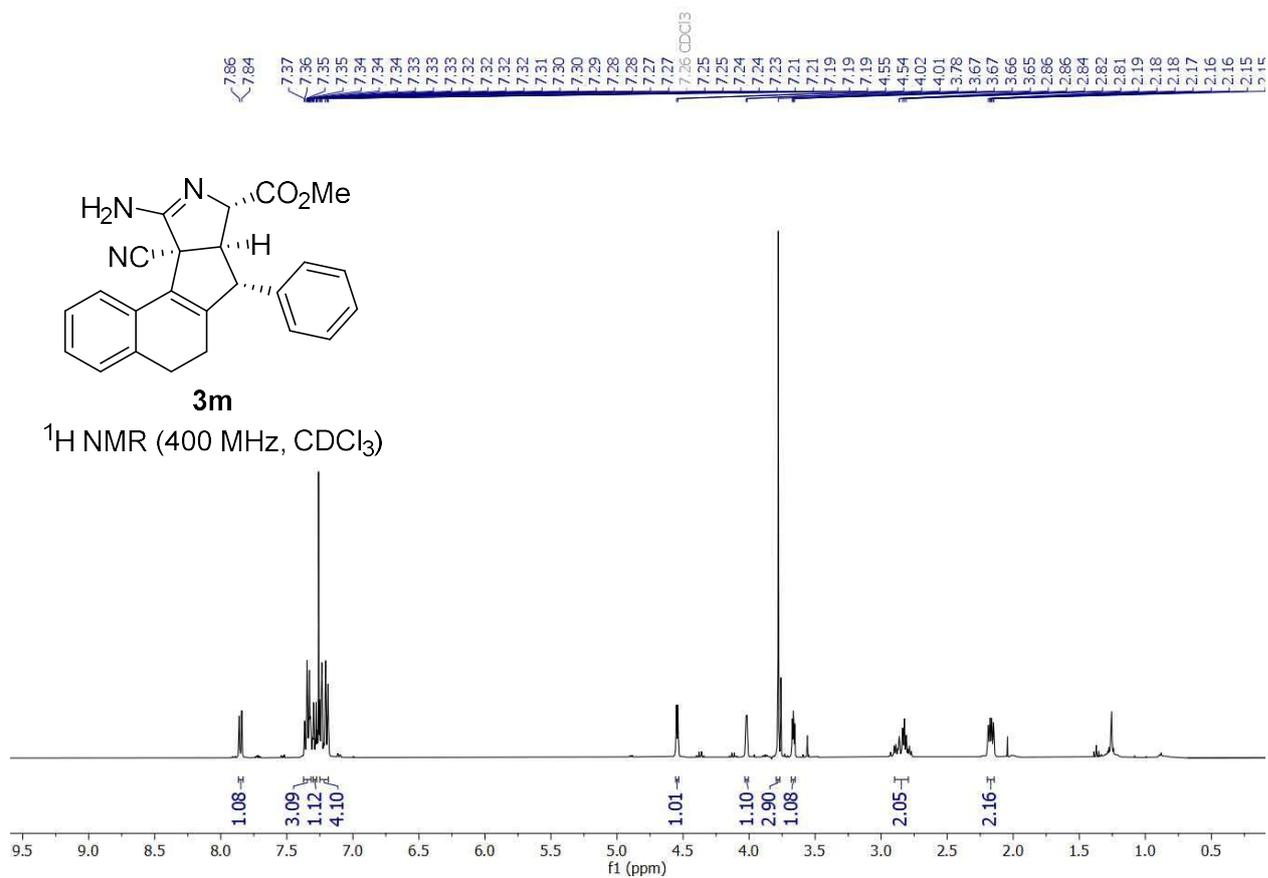
171.43  
162.22  
147.58  
140.15  
136.63  
130.27  
129.62  
129.27  
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128.26  
127.77  
127.67  
127.19  
122.27  
118.94  
77.16 CDCl<sub>3</sub>  
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69.37  
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60.67  
58.32  
28.31  
23.77  
21.90  
21.88

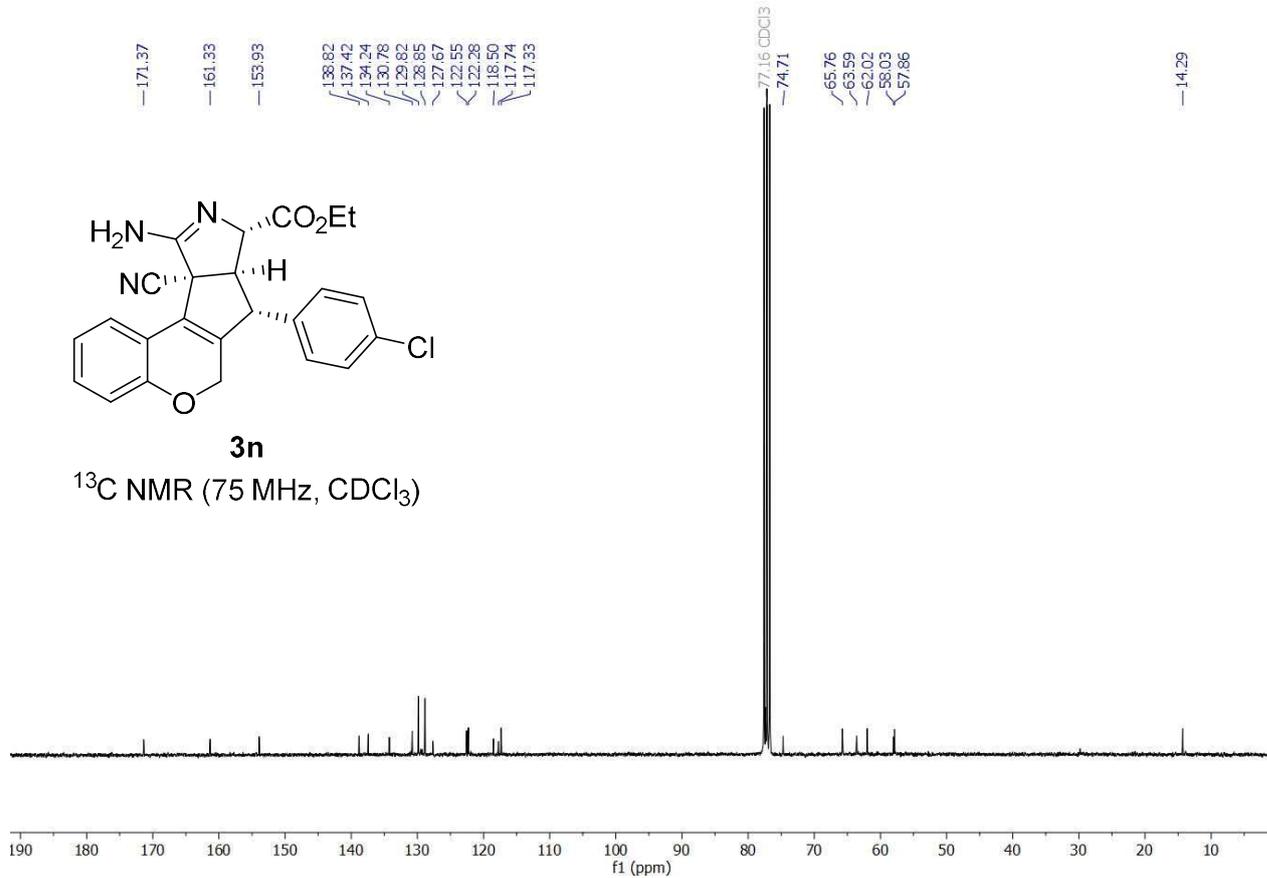
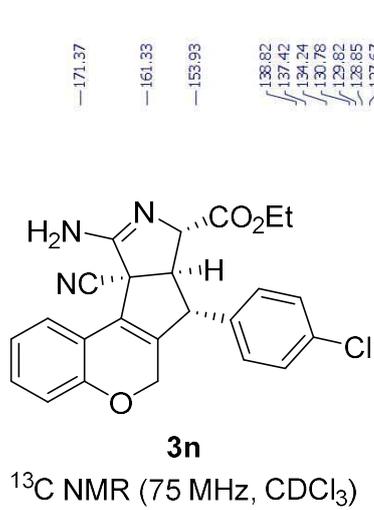
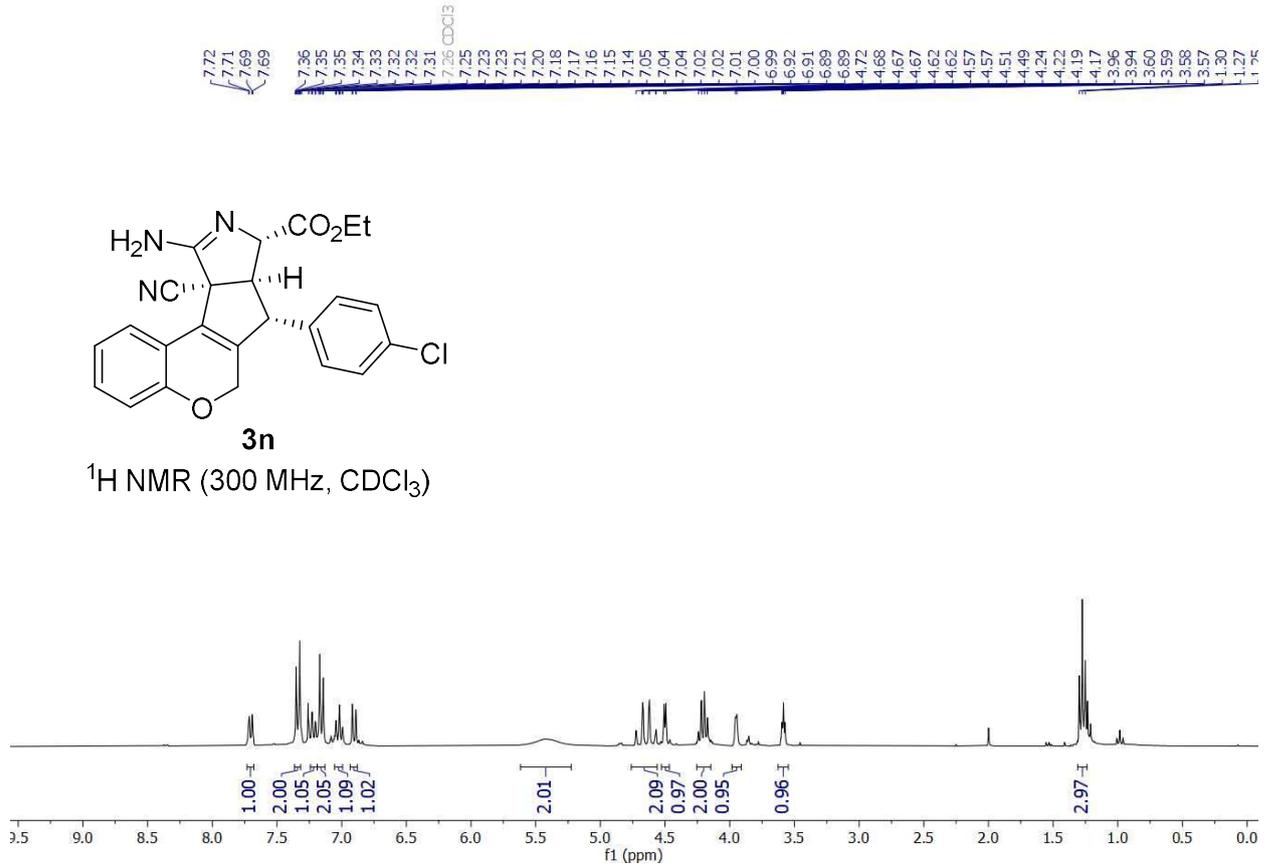
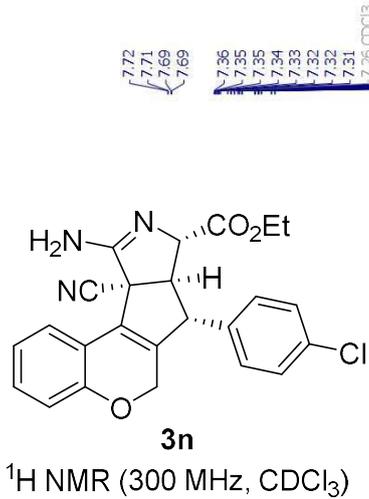


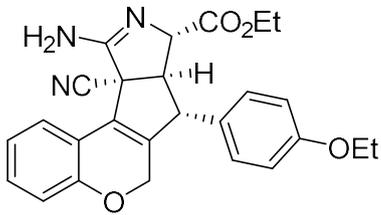
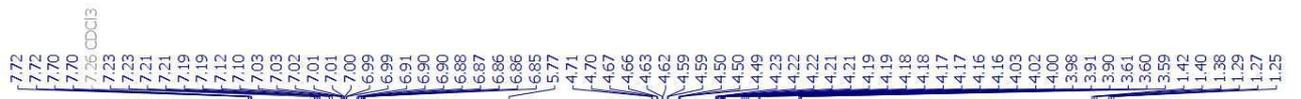
**3I**

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



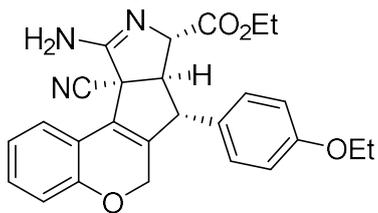
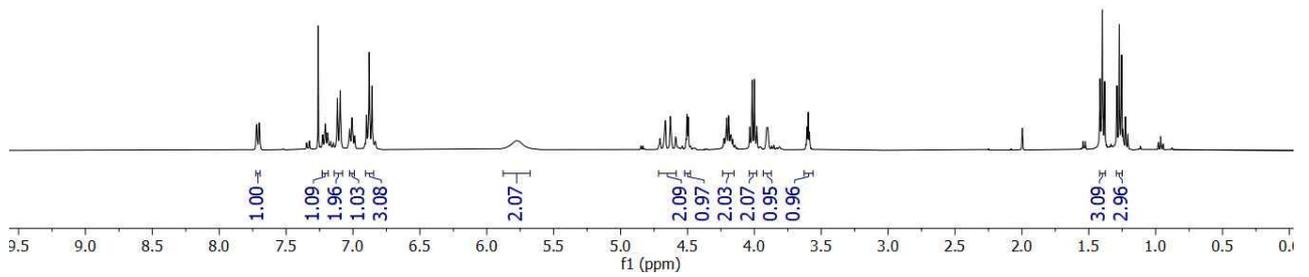






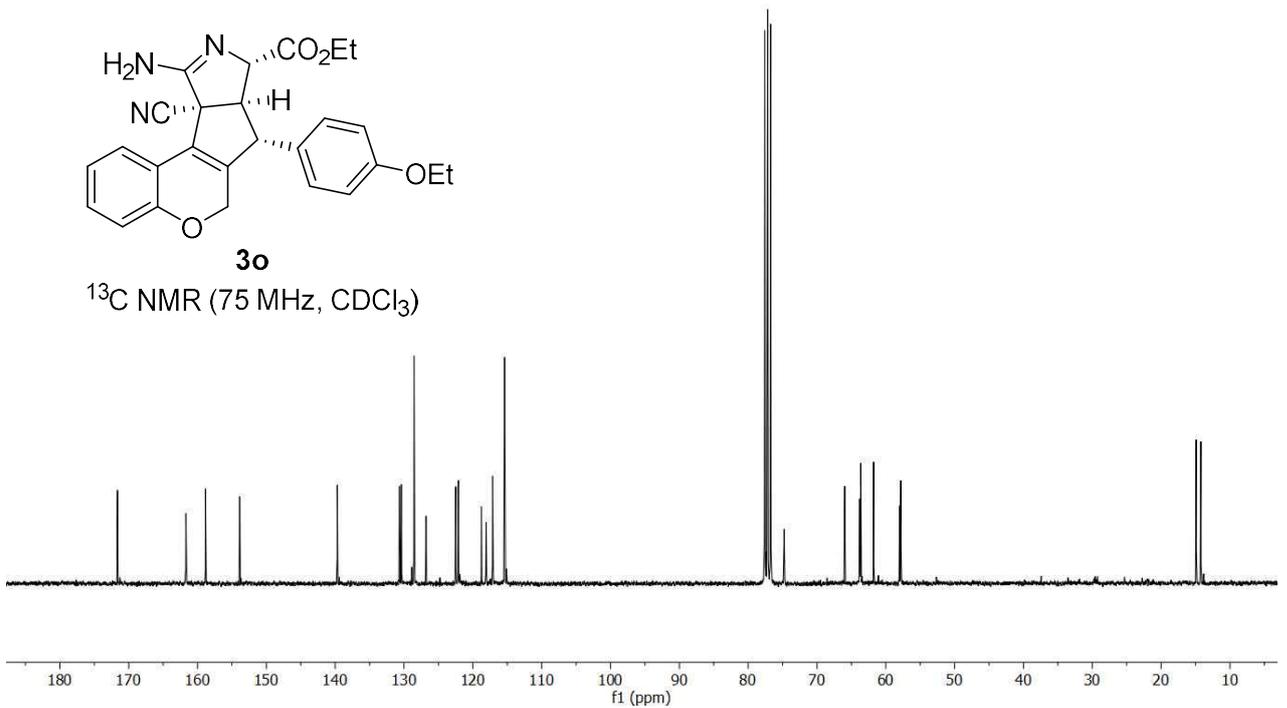
**3o**

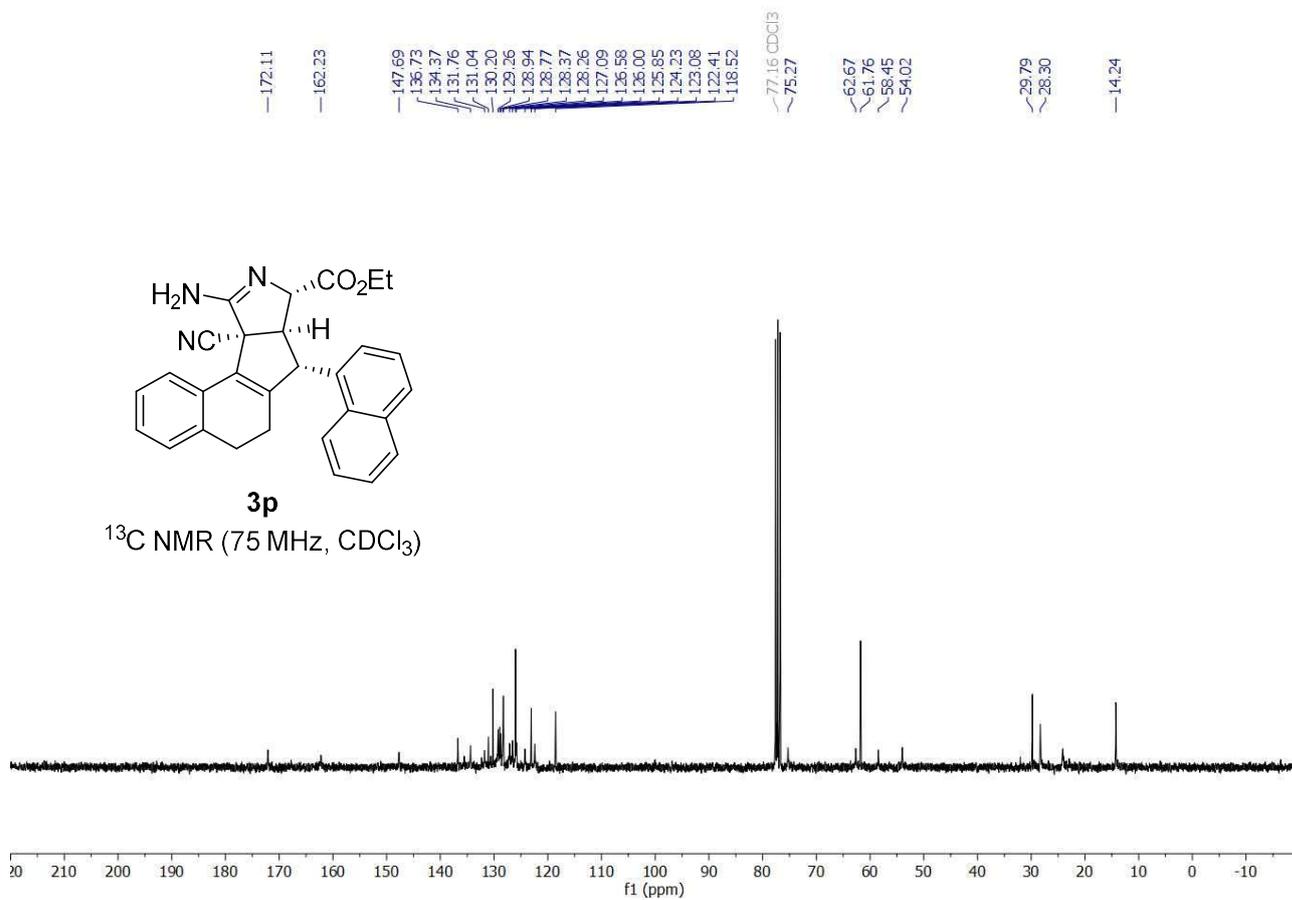
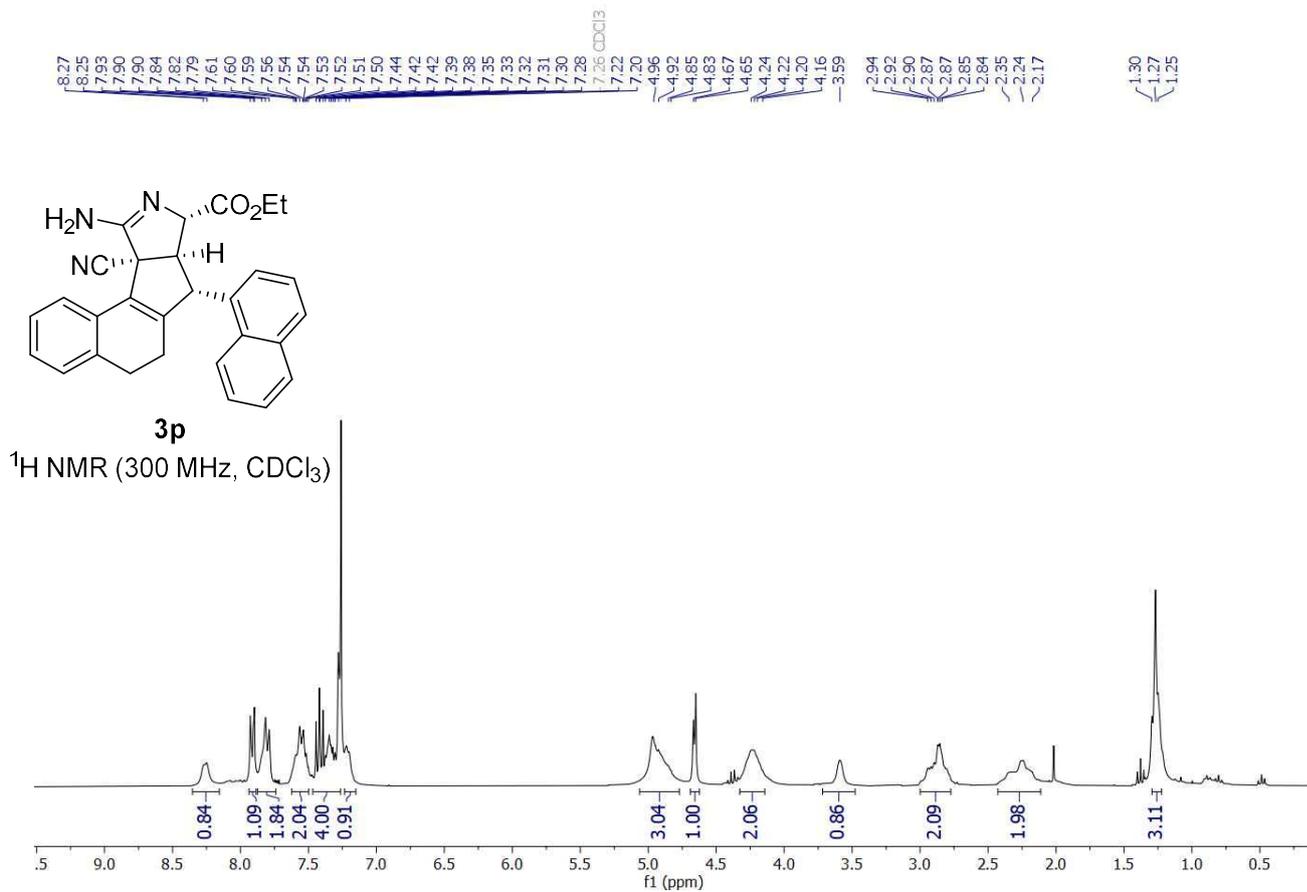
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



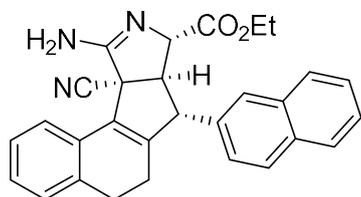
**3o**

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



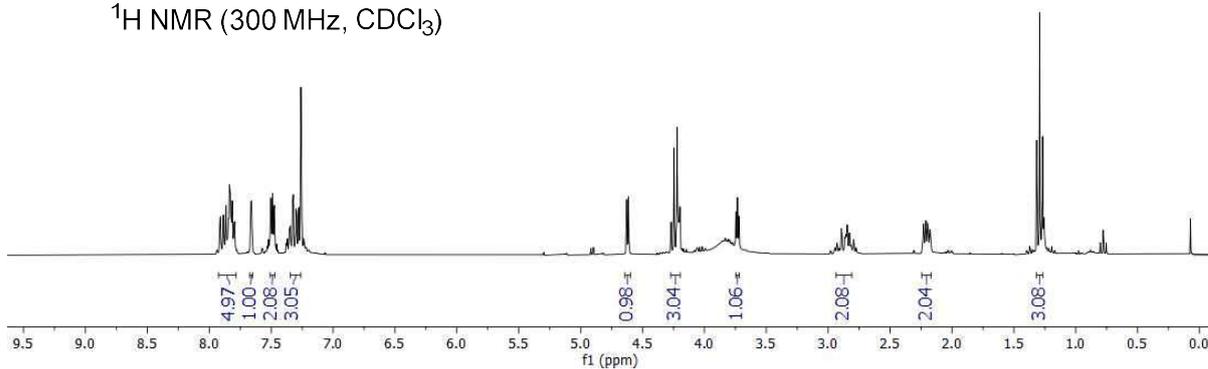


7.91  
7.91  
7.89  
7.87  
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1.27

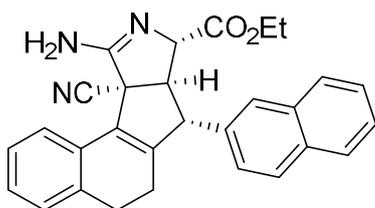


**3q**

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )

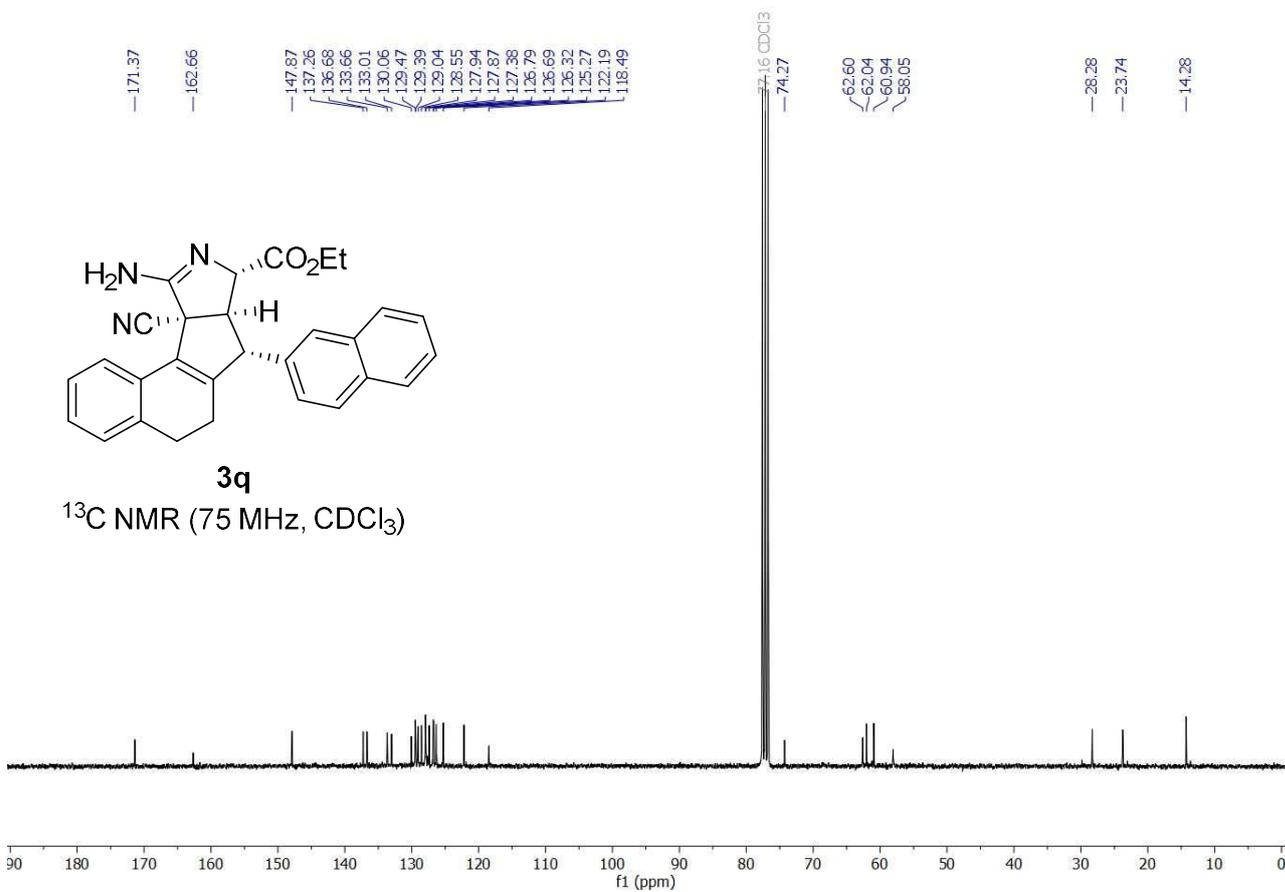


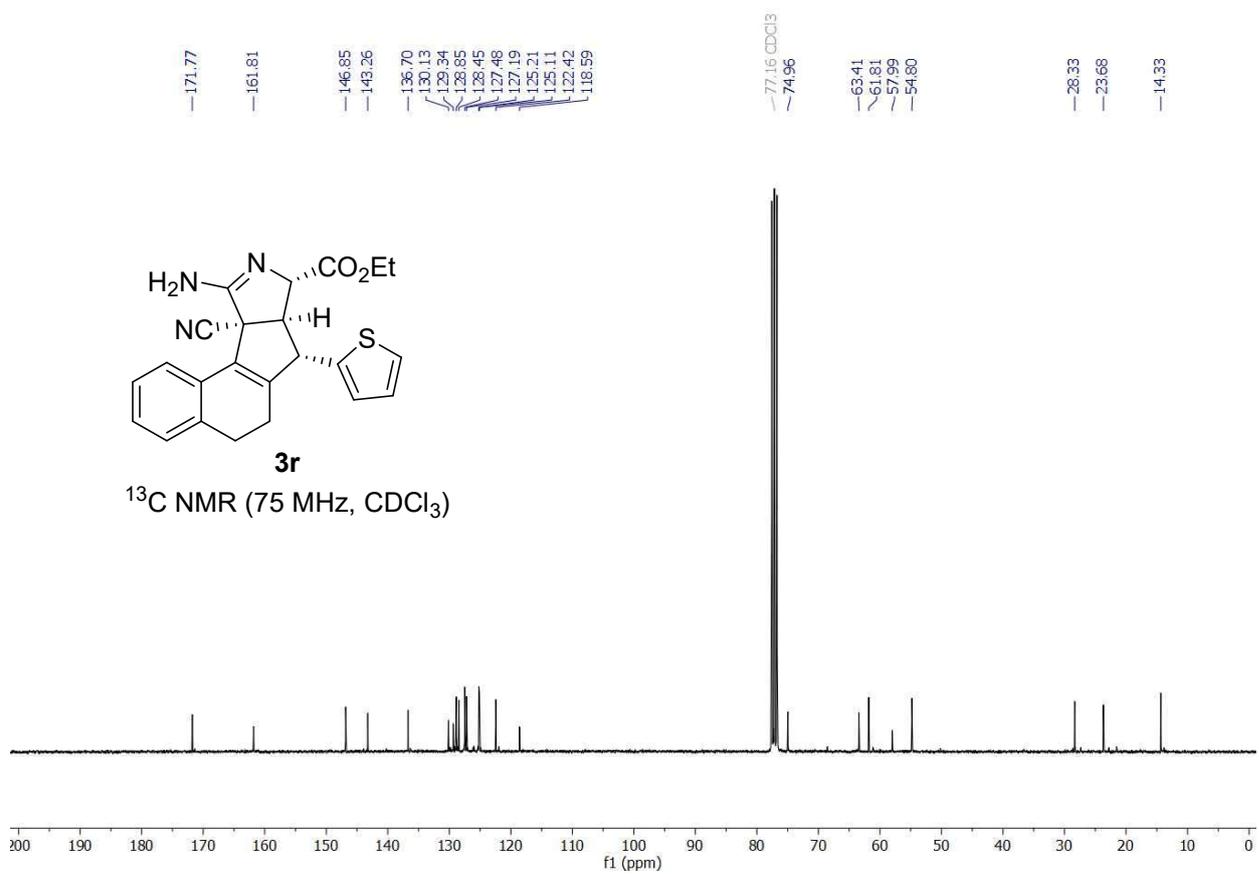
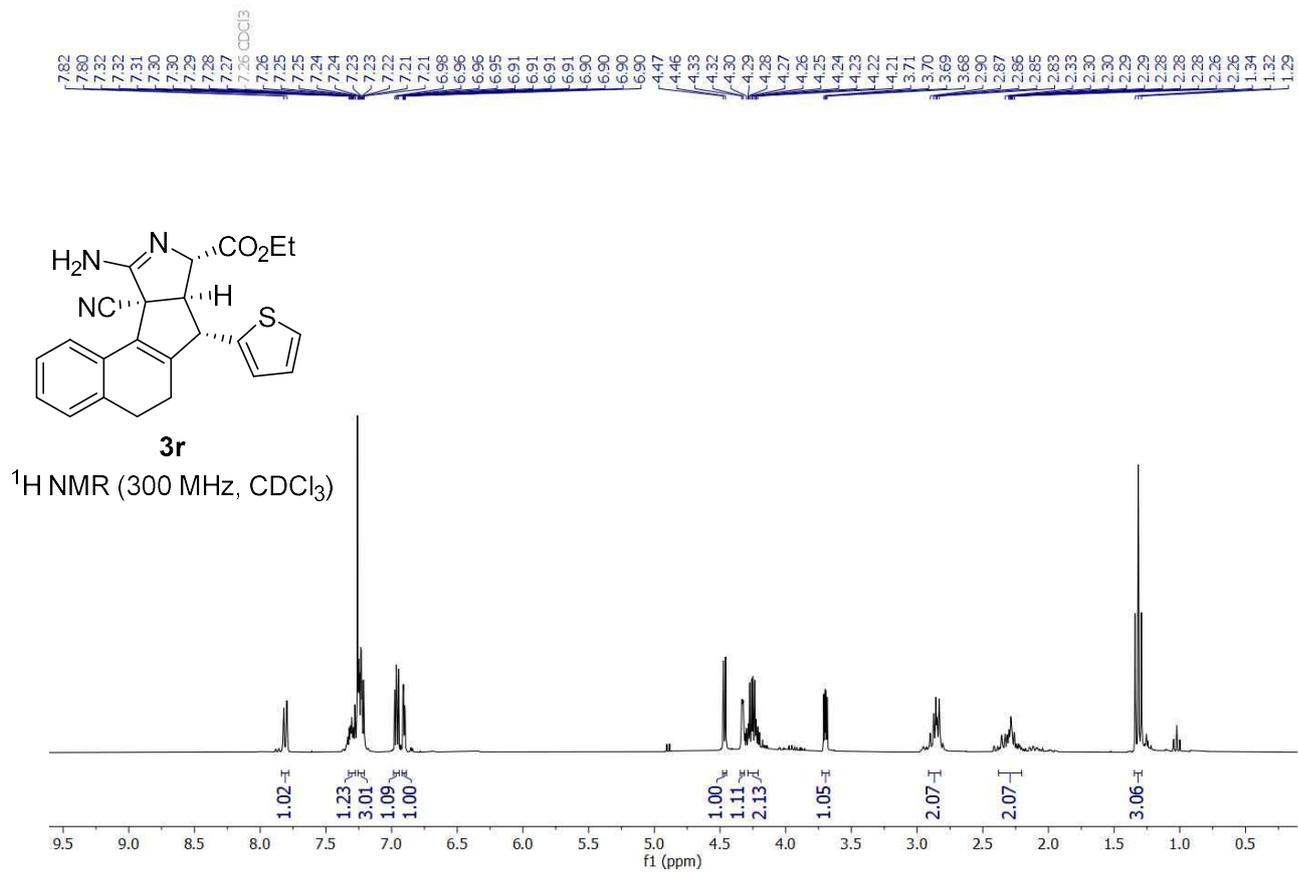
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—147.87  
—137.26  
—136.68  
—133.66  
—133.01  
—130.06  
—129.47  
—129.39  
—129.04  
—128.55  
—127.94  
—127.87  
—127.38  
—126.79  
—126.69  
—126.32  
—125.27  
—122.19  
—118.49  
—74.27  
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—62.04  
—60.94  
—58.05  
—28.28  
—23.74  
—14.28

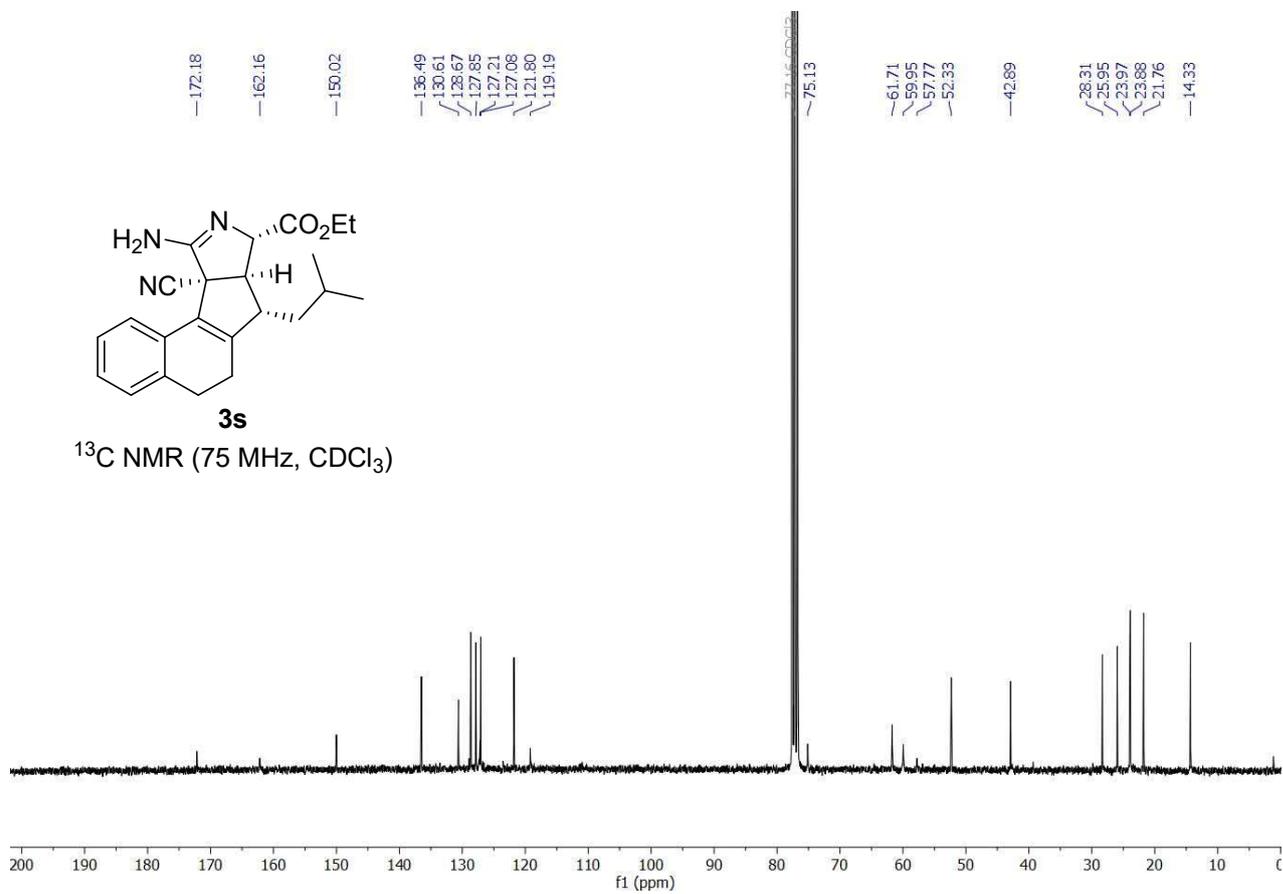
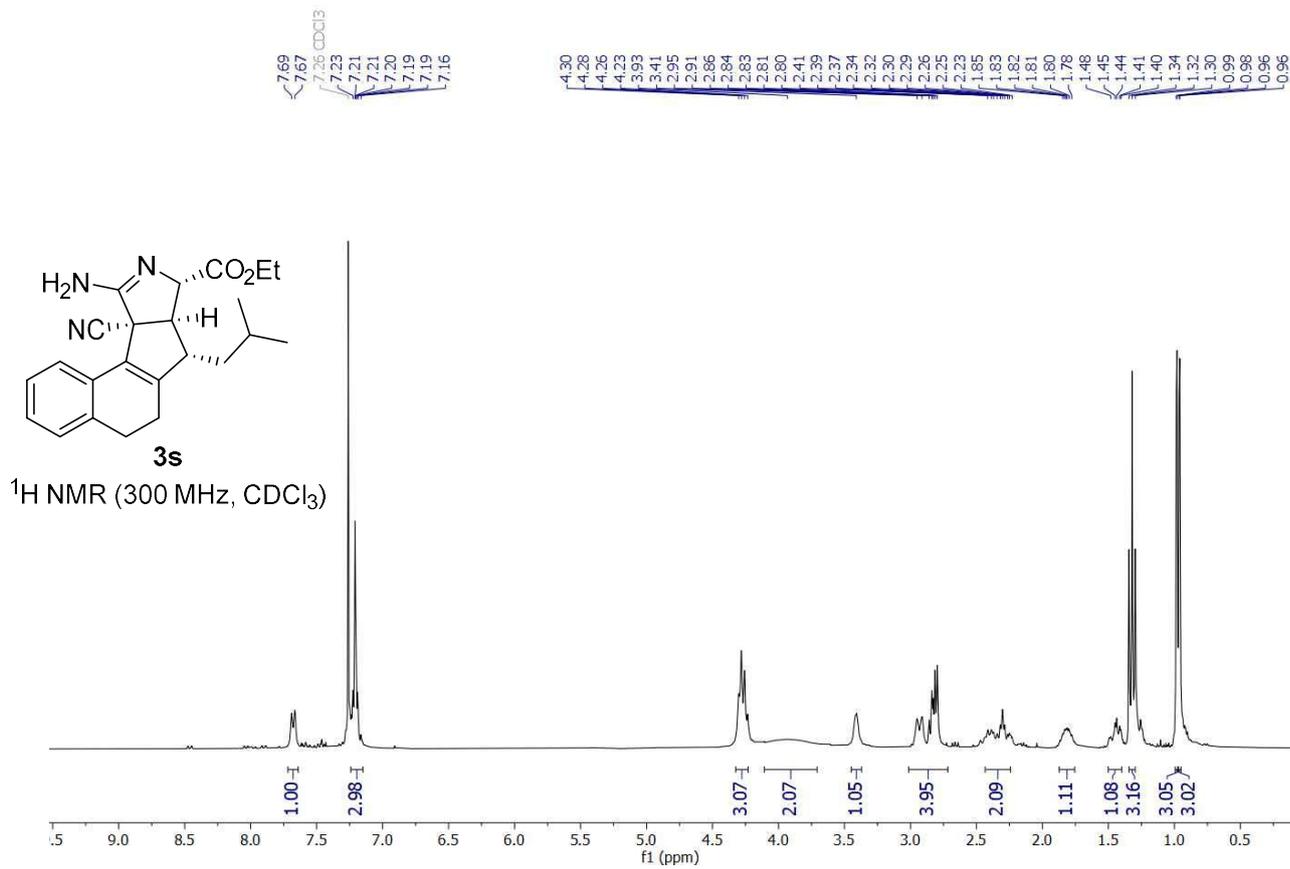


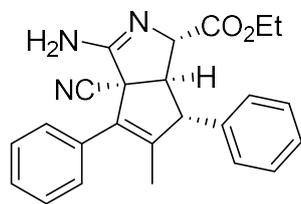
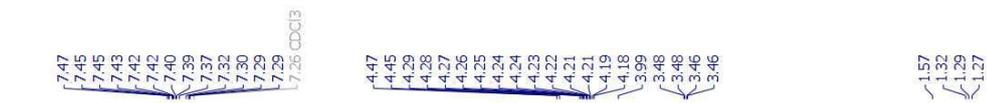
**3q**

$^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )



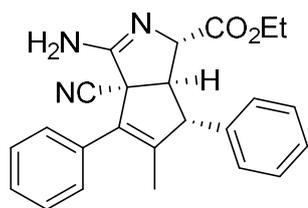
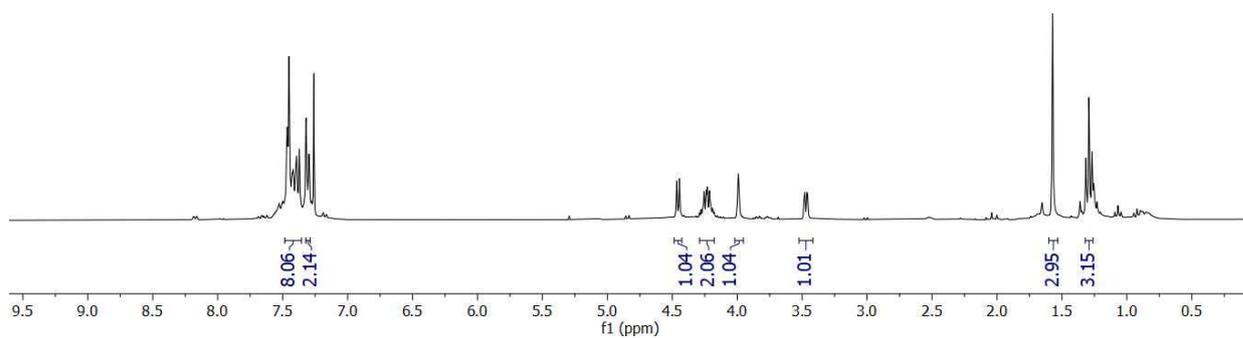






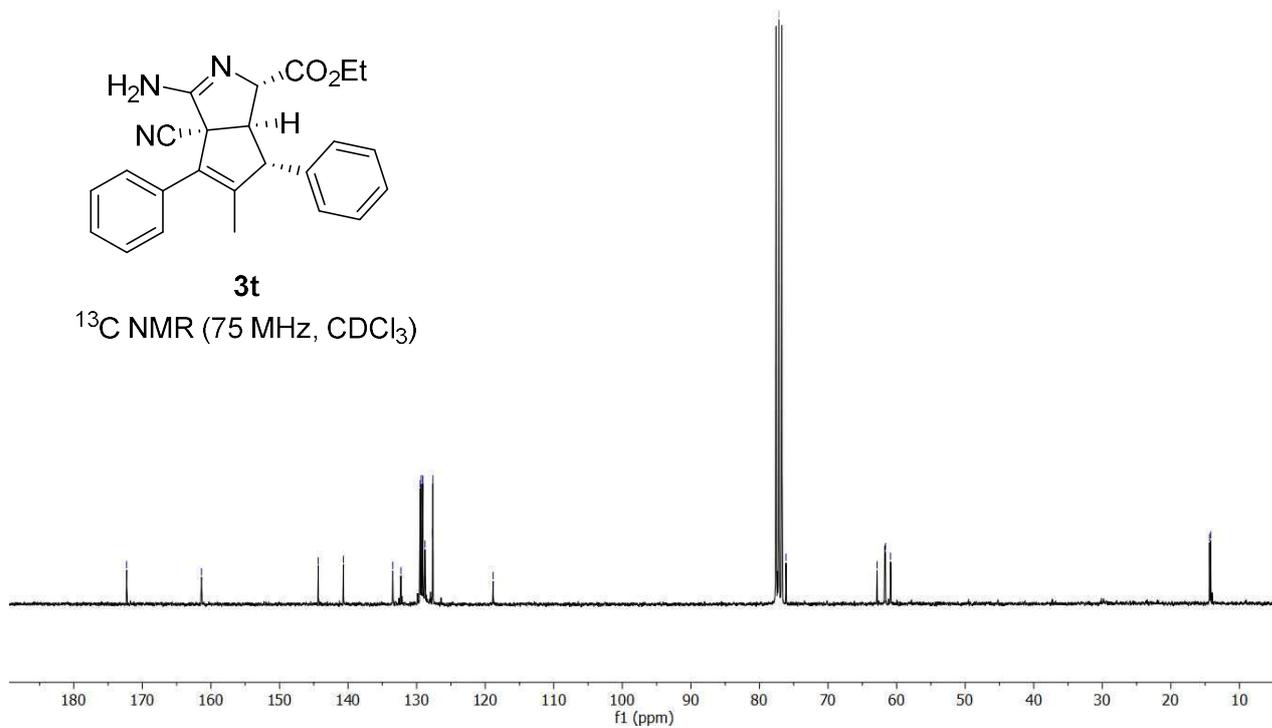
**3t**

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

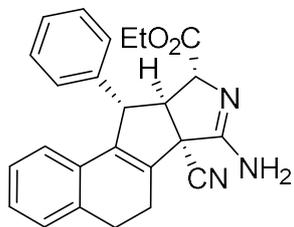


**3t**

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

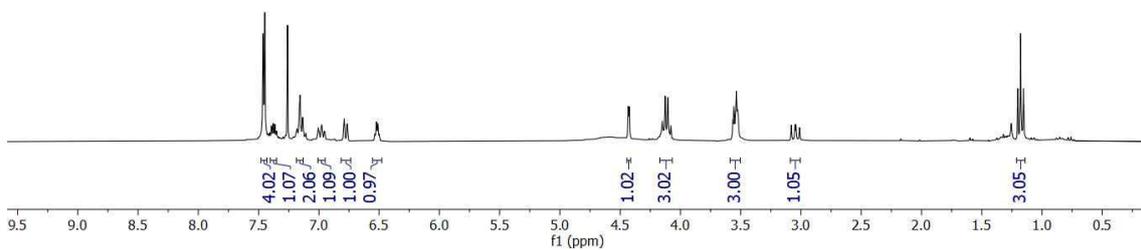


7.46  
7.45  
7.39  
7.38  
7.37  
7.36  
7.35  
7.34  
7.26 CDCl<sub>3</sub>  
7.18  
7.16  
7.15  
7.13  
7.11  
7.11  
7.04  
7.01  
7.00  
6.98  
6.96  
6.95  
6.79  
6.76  
6.54  
6.52  
6.51  
6.51  
6.50  
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4.42  
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4.15  
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3.01

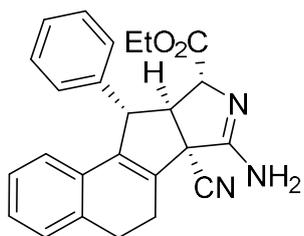


**3u**

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

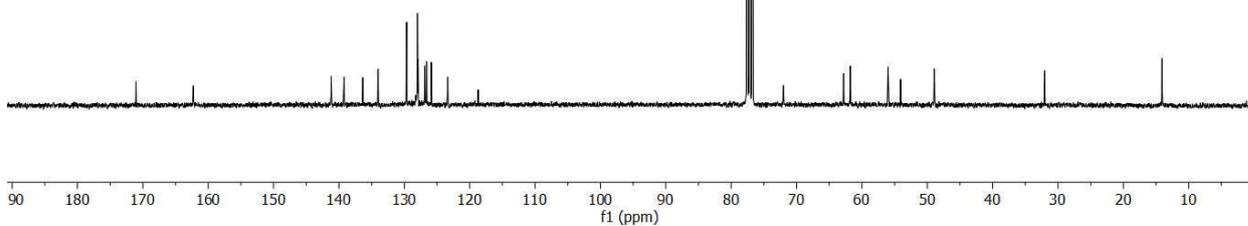


—171.07  
—162.27  
141.20  
139.22  
136.35  
134.03  
133.65  
133.00  
127.95  
127.89  
136.89  
136.60  
125.87  
123.38  
118.70  
72.16 CDCl<sub>3</sub>  
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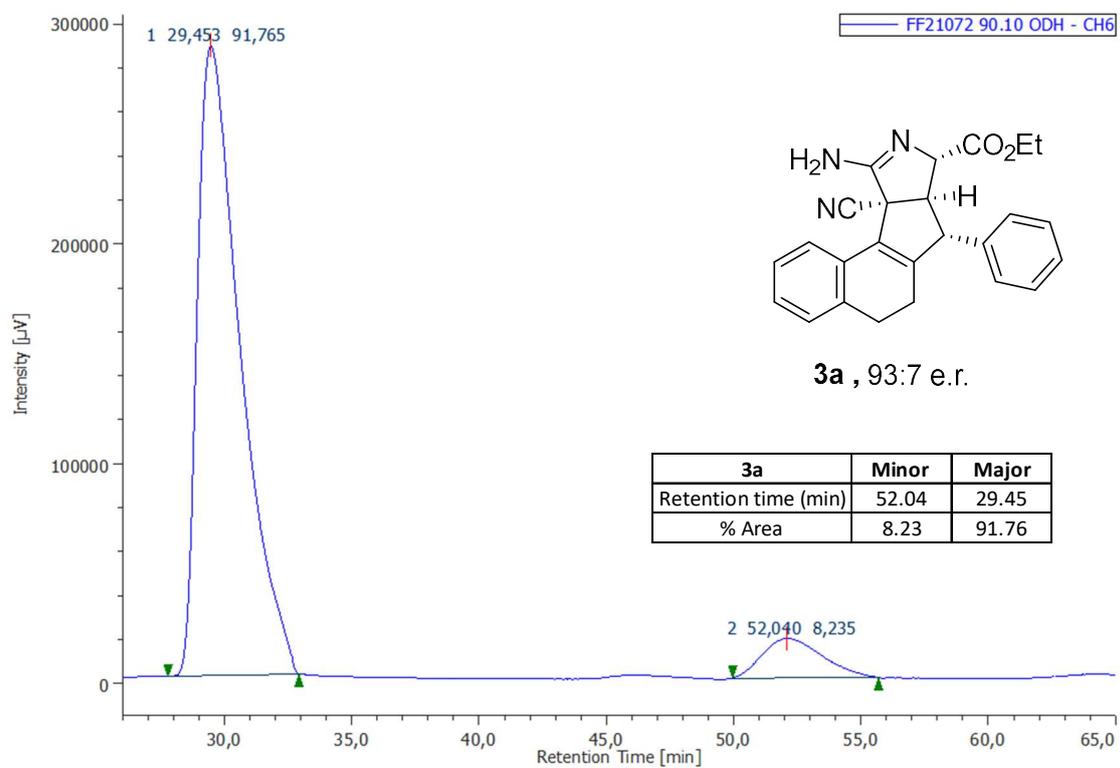
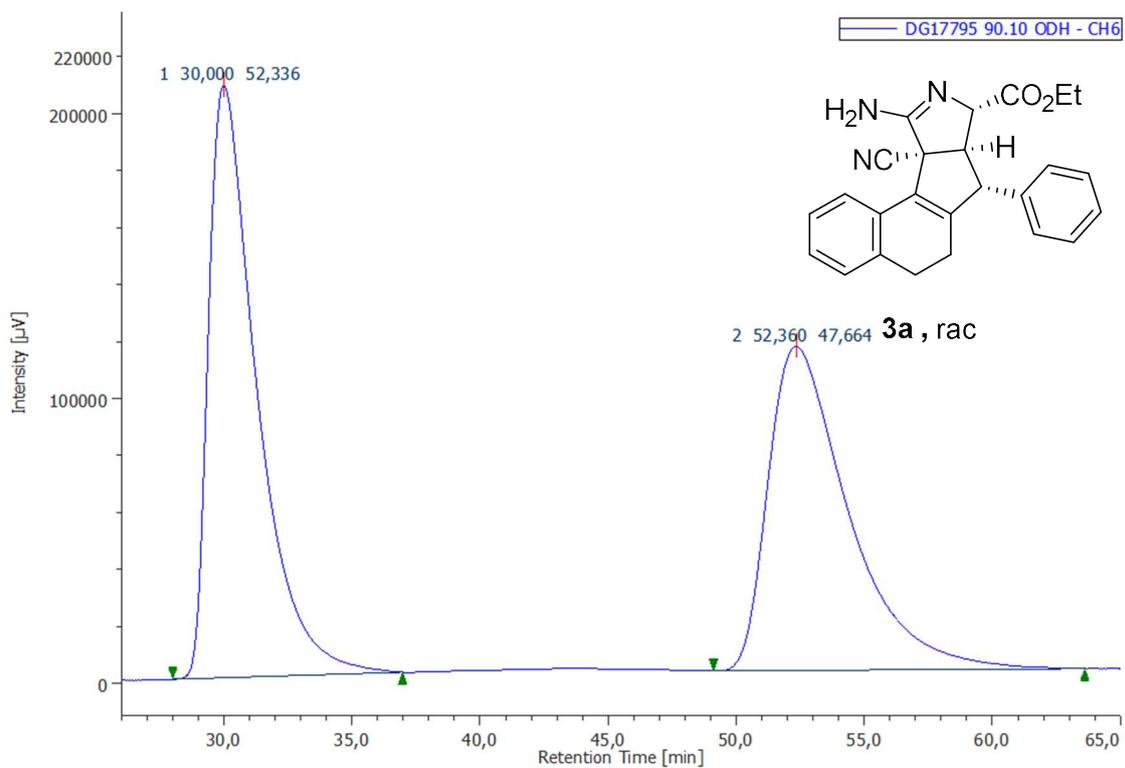


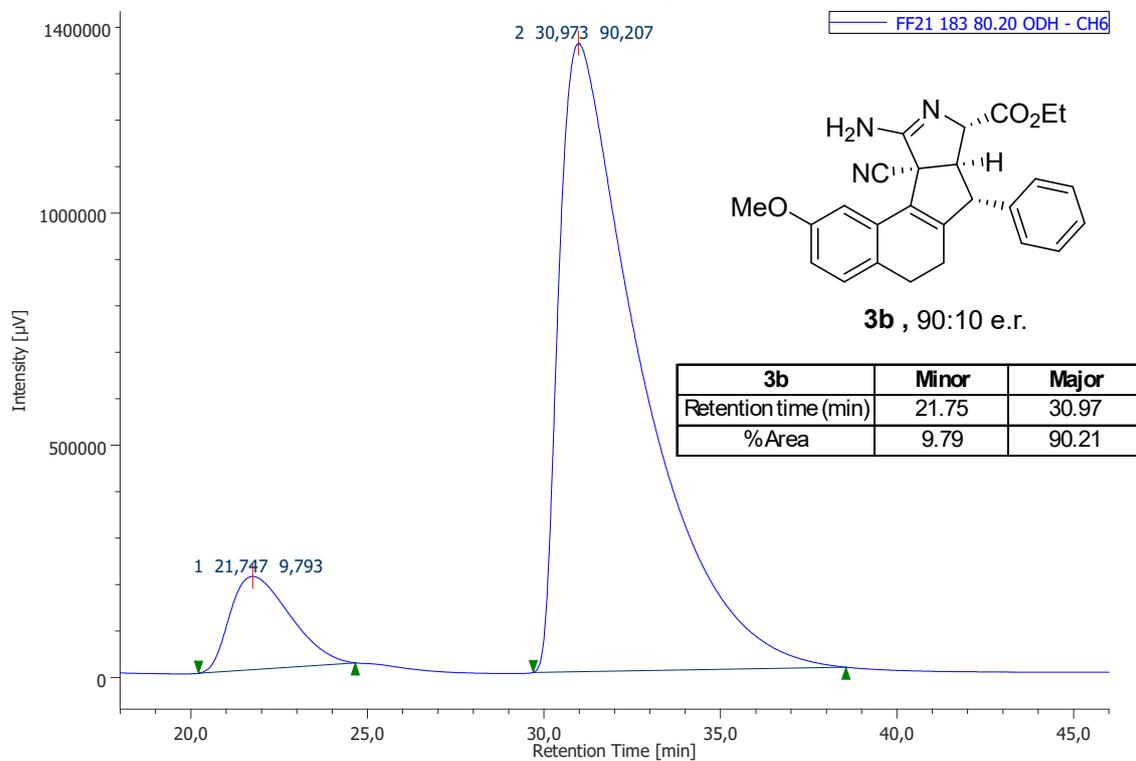
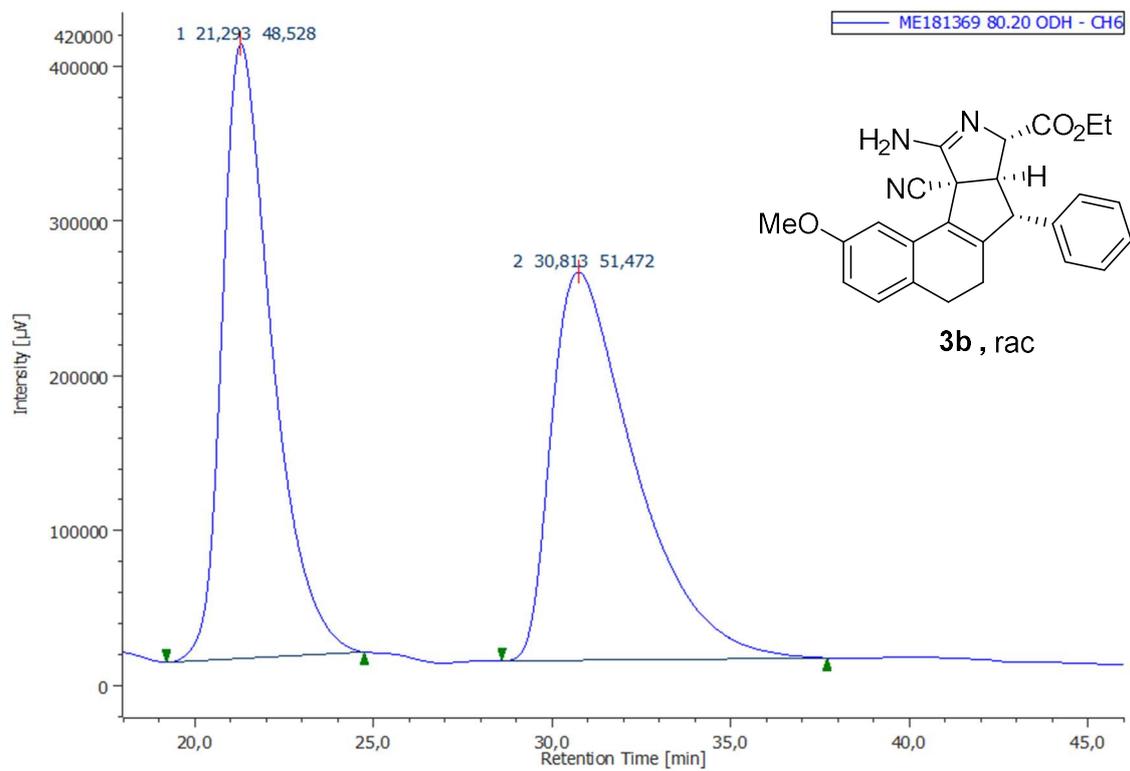
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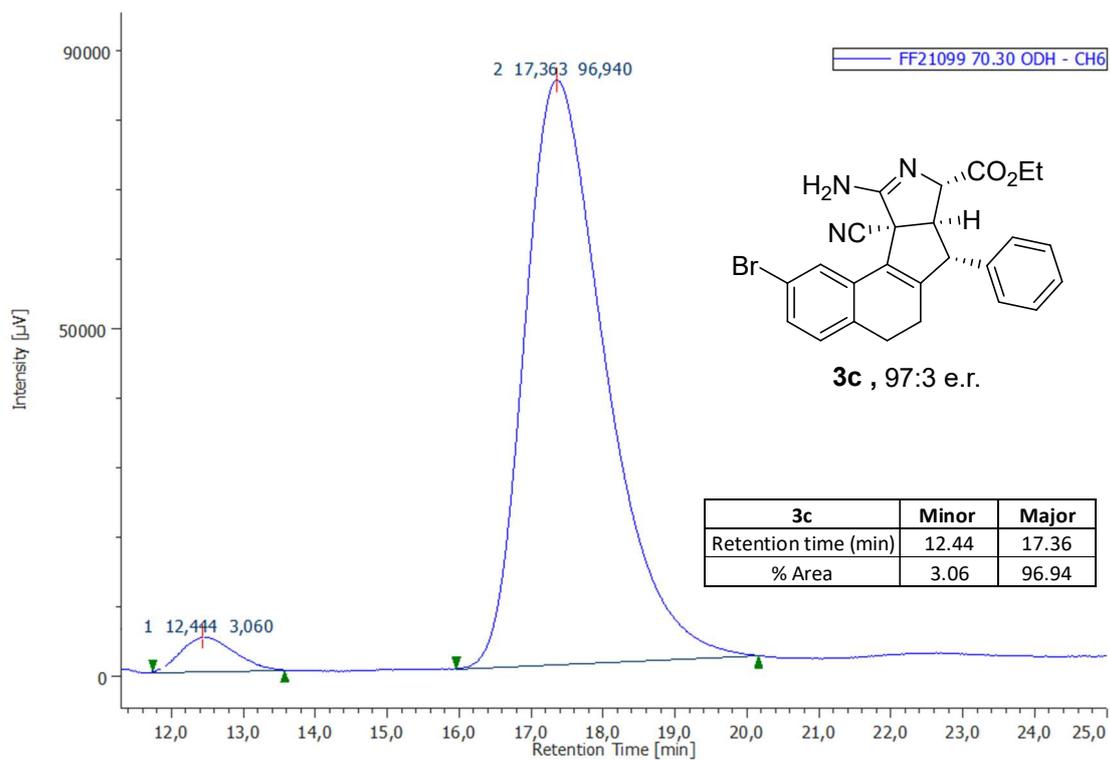
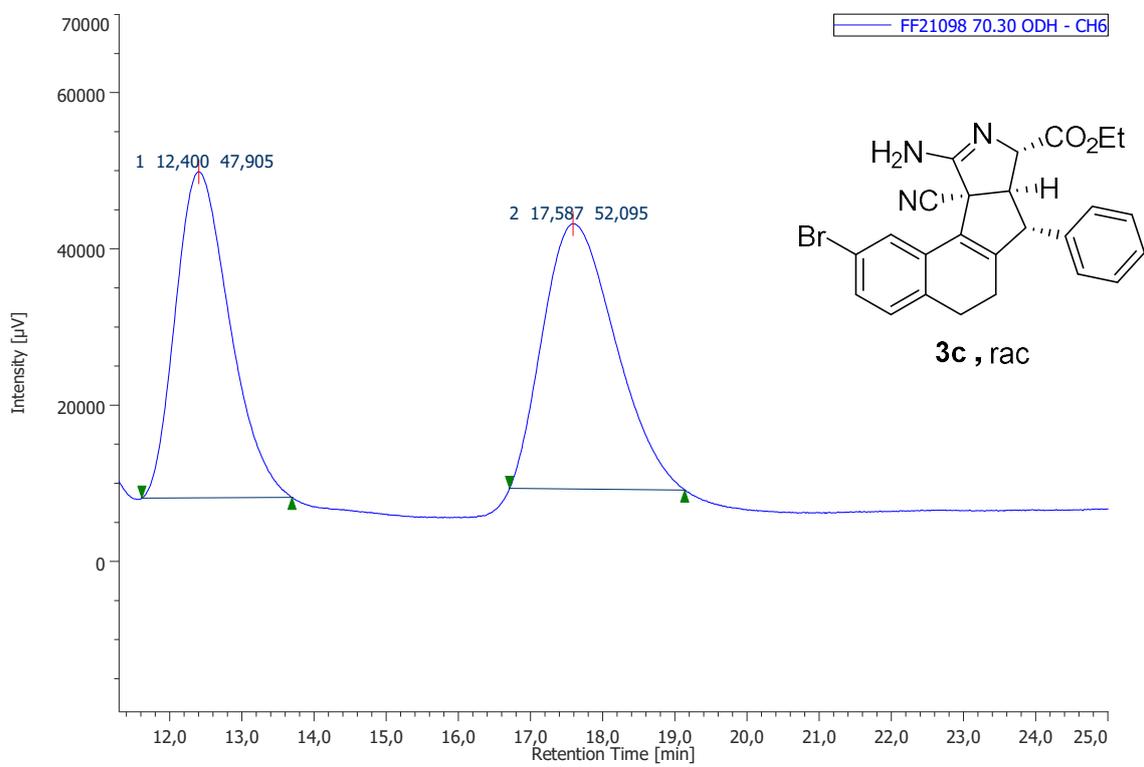
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

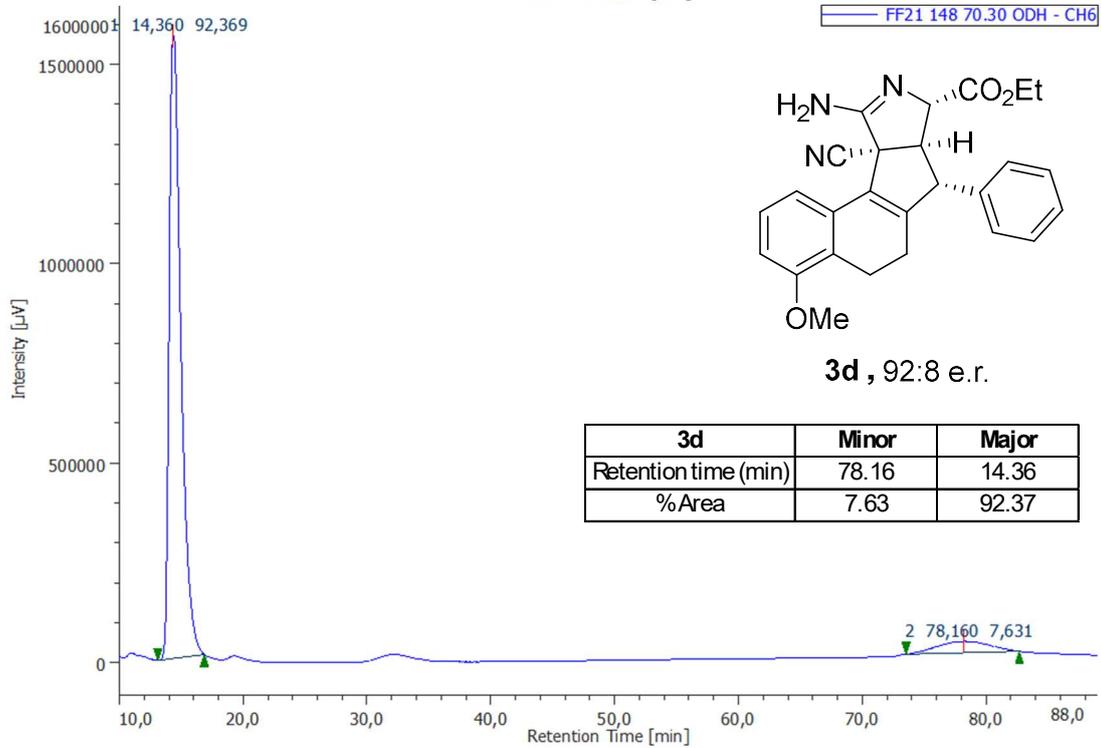
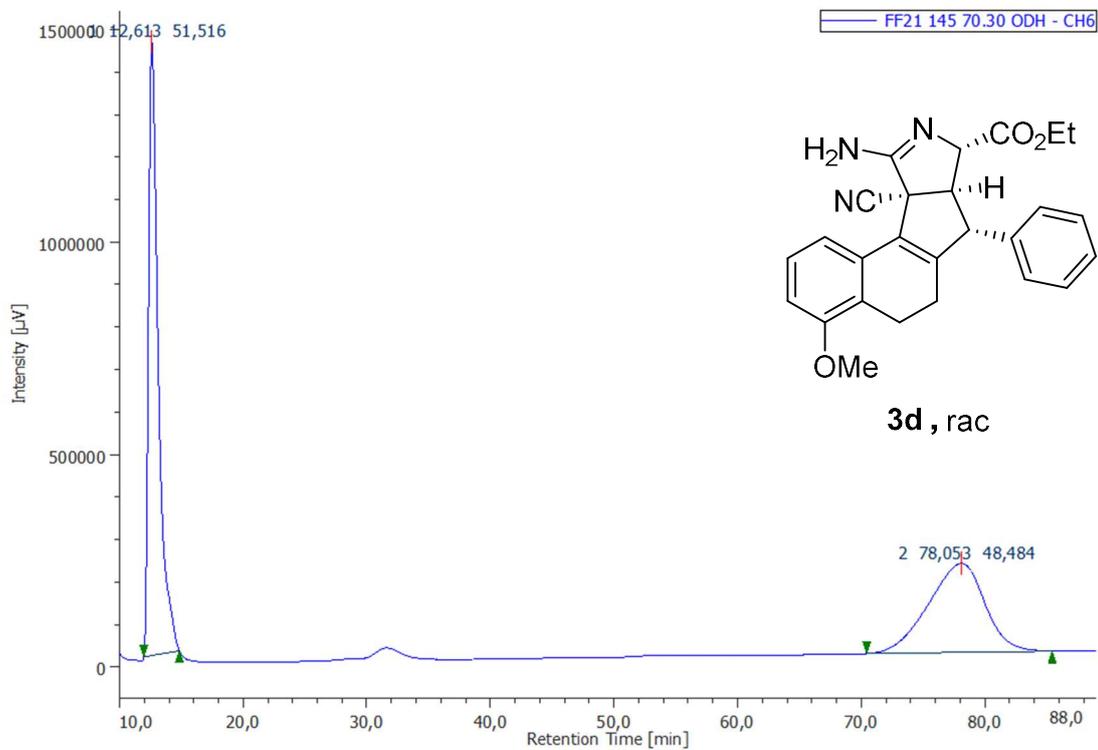


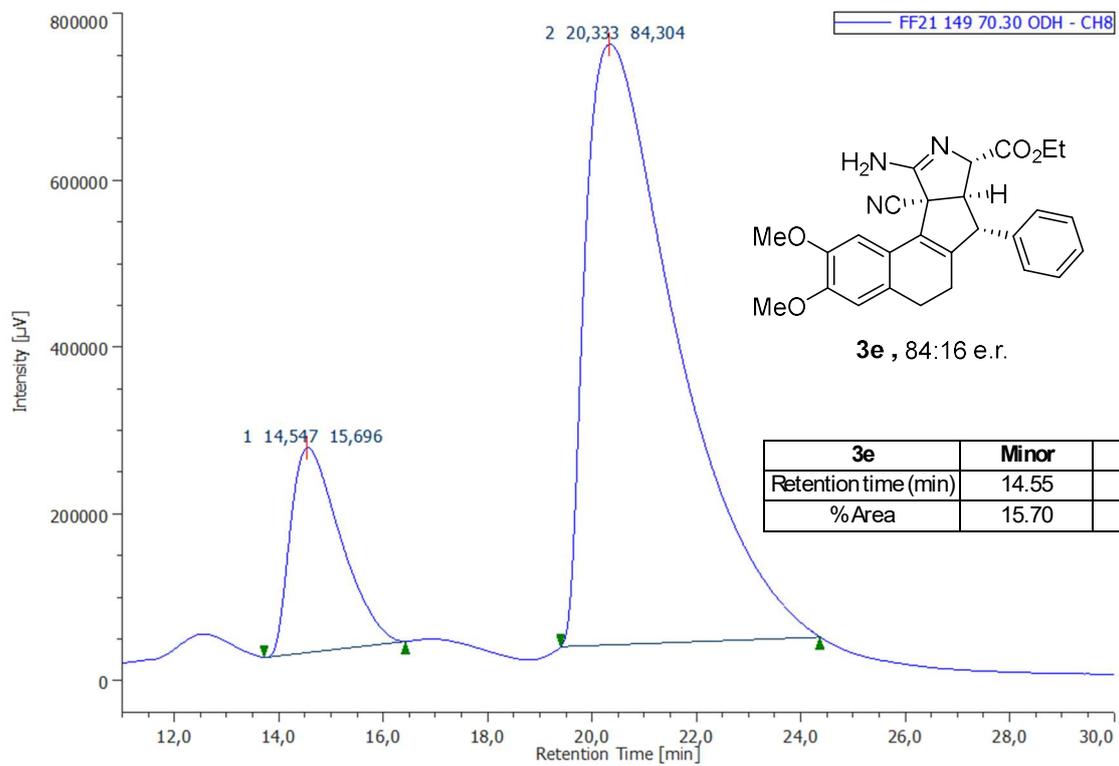
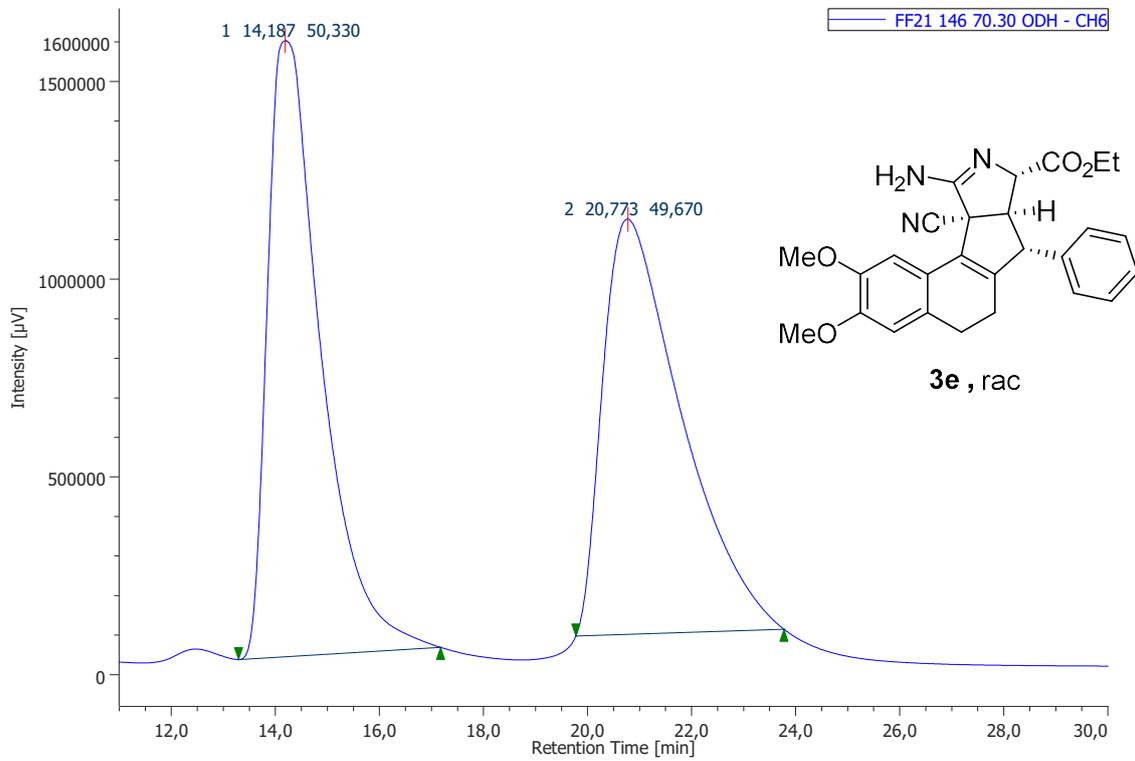
### HPLC traces of enantioenriched compounds 3

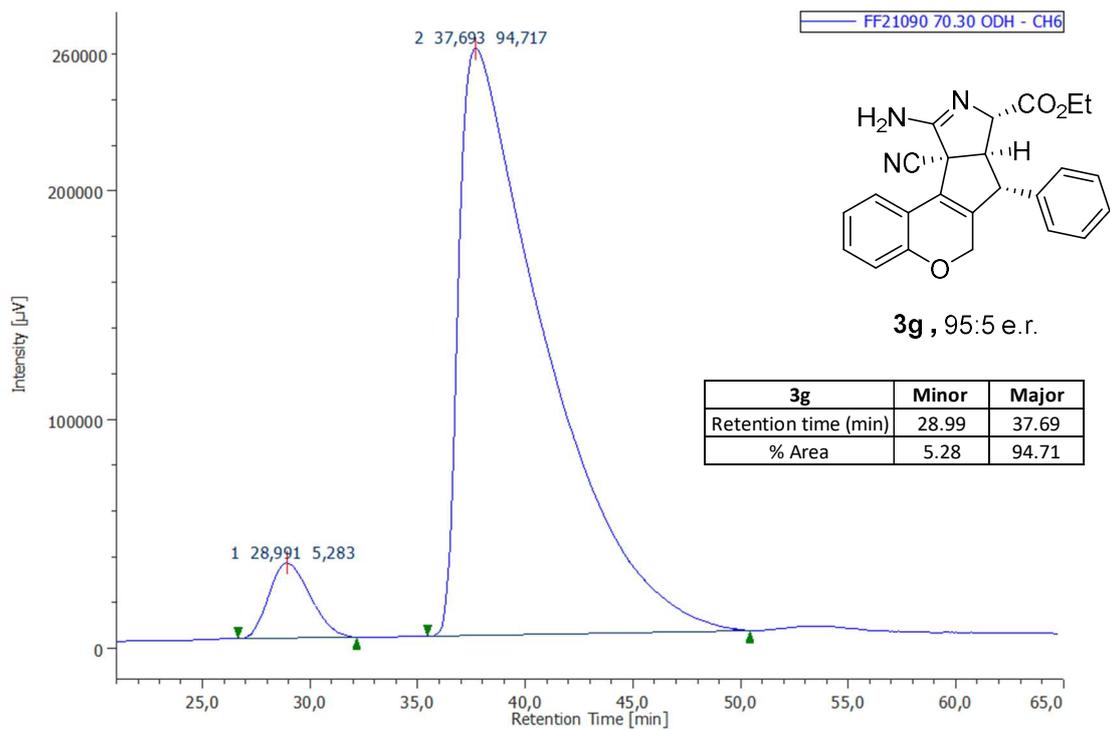
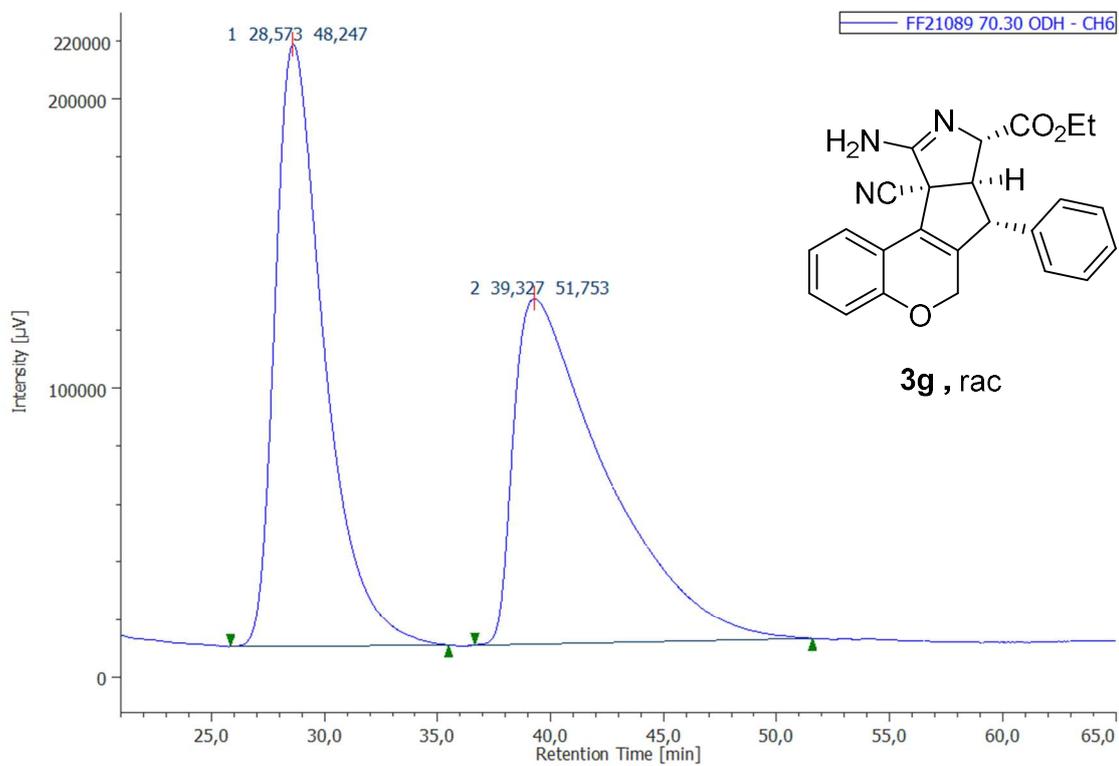


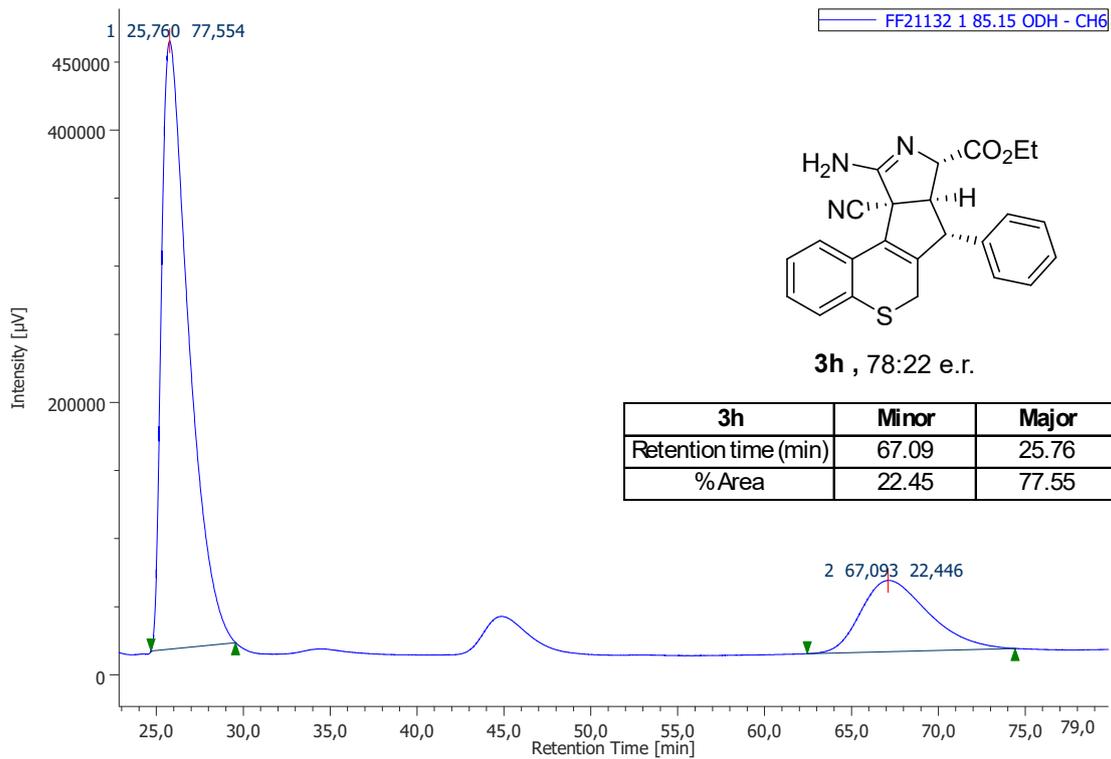
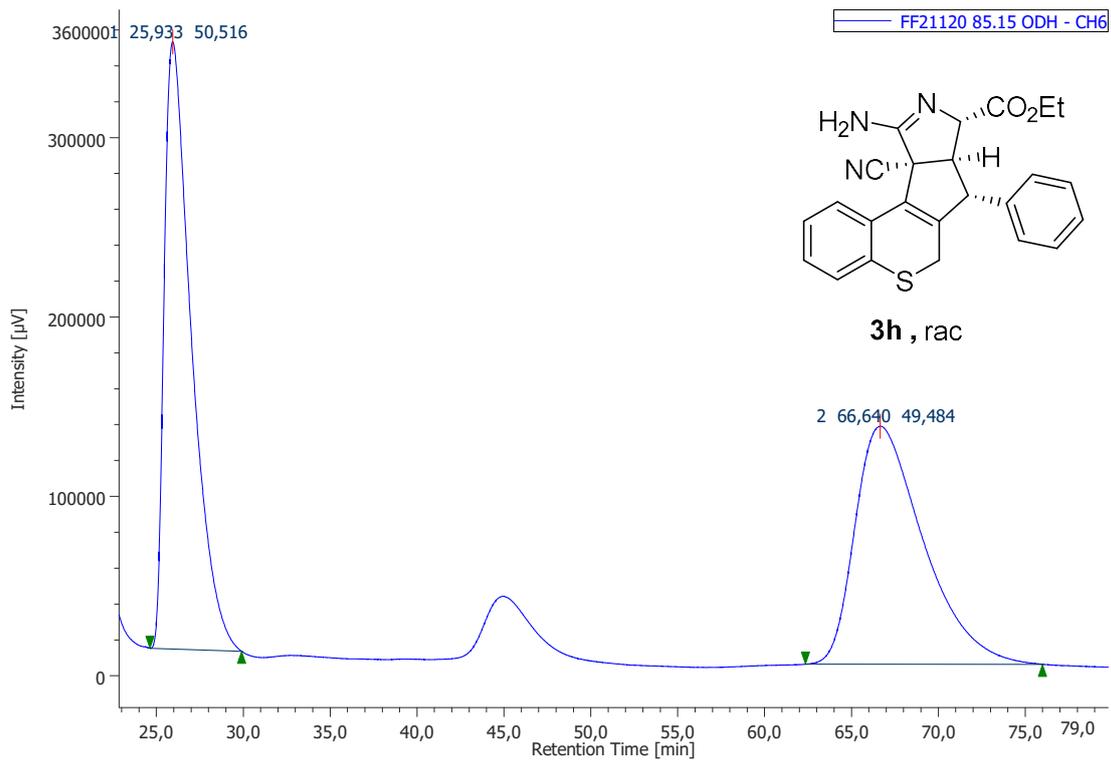


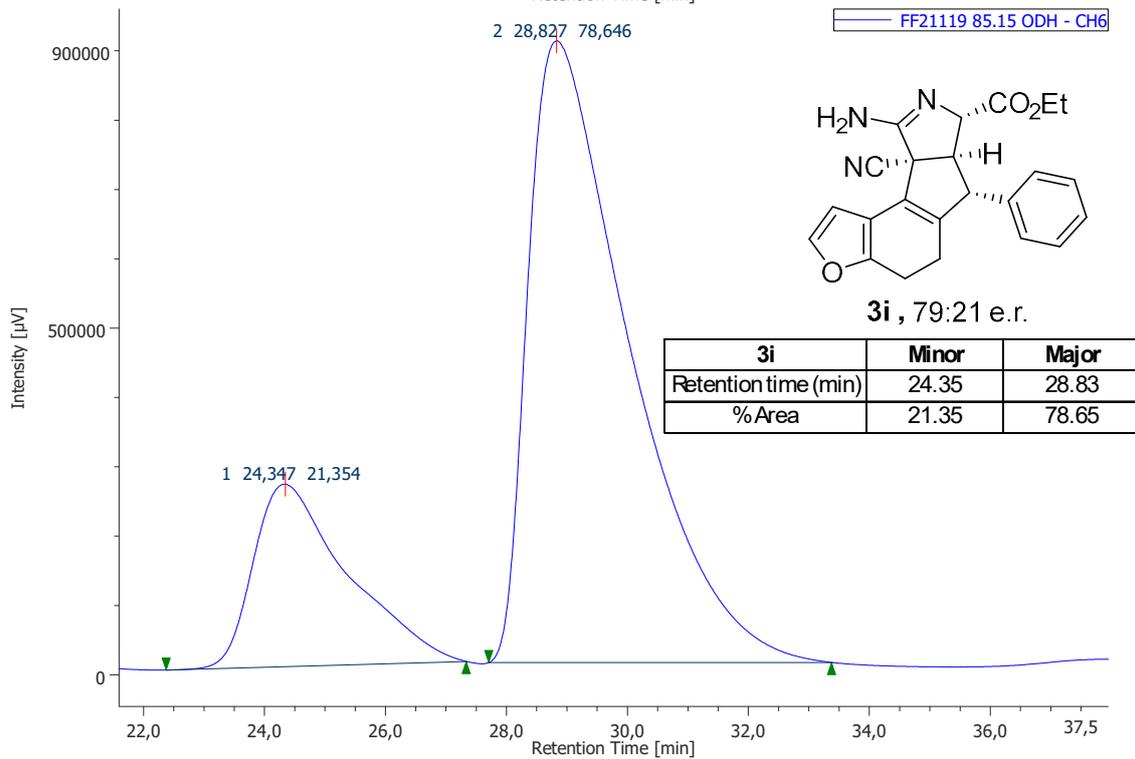
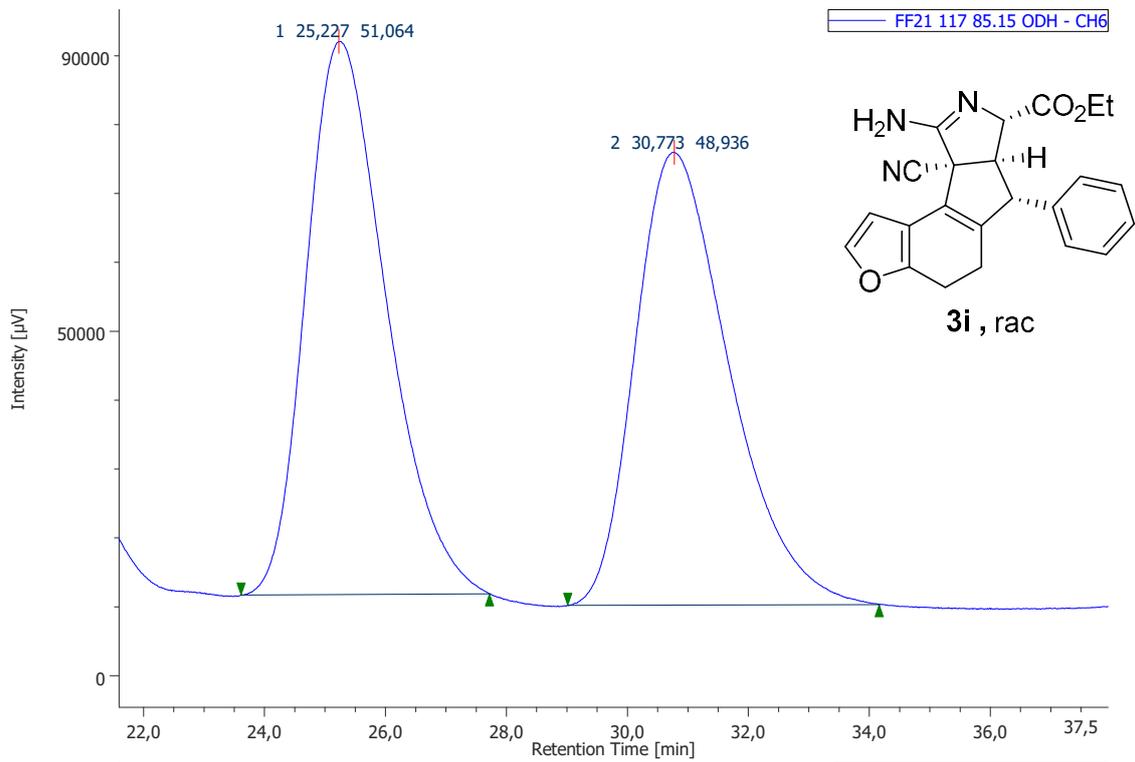


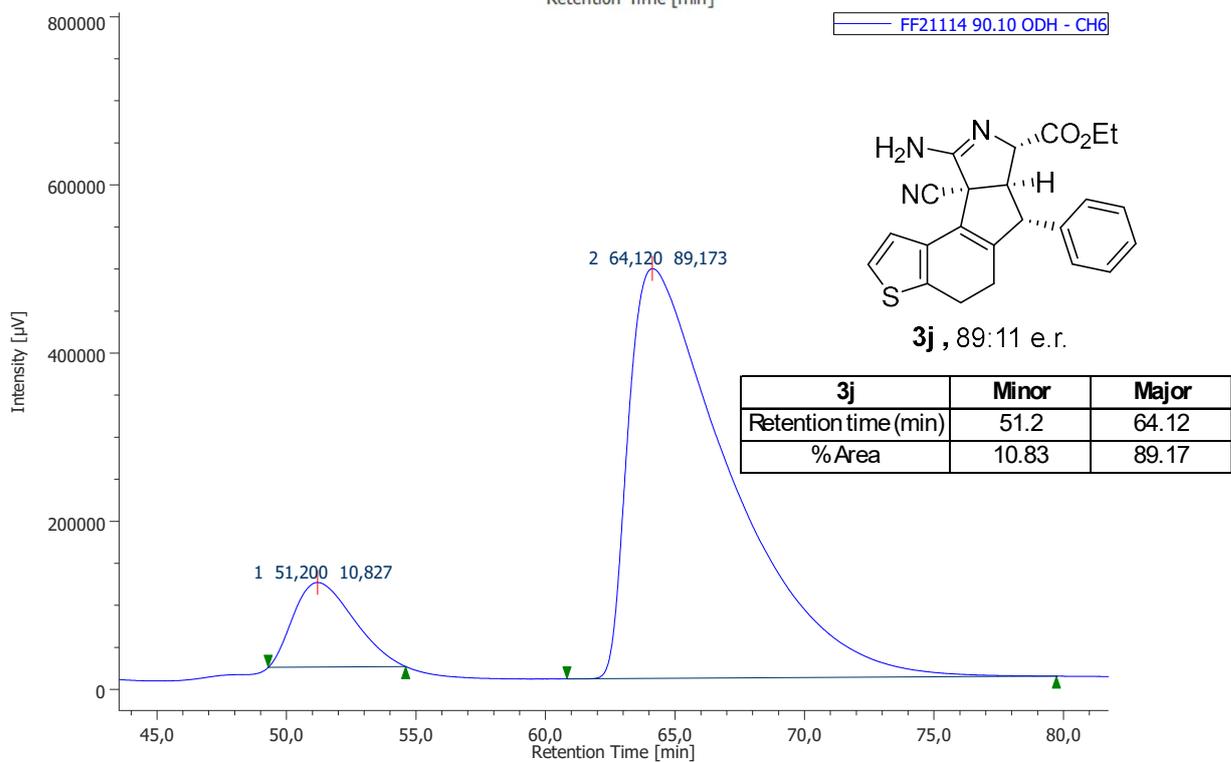
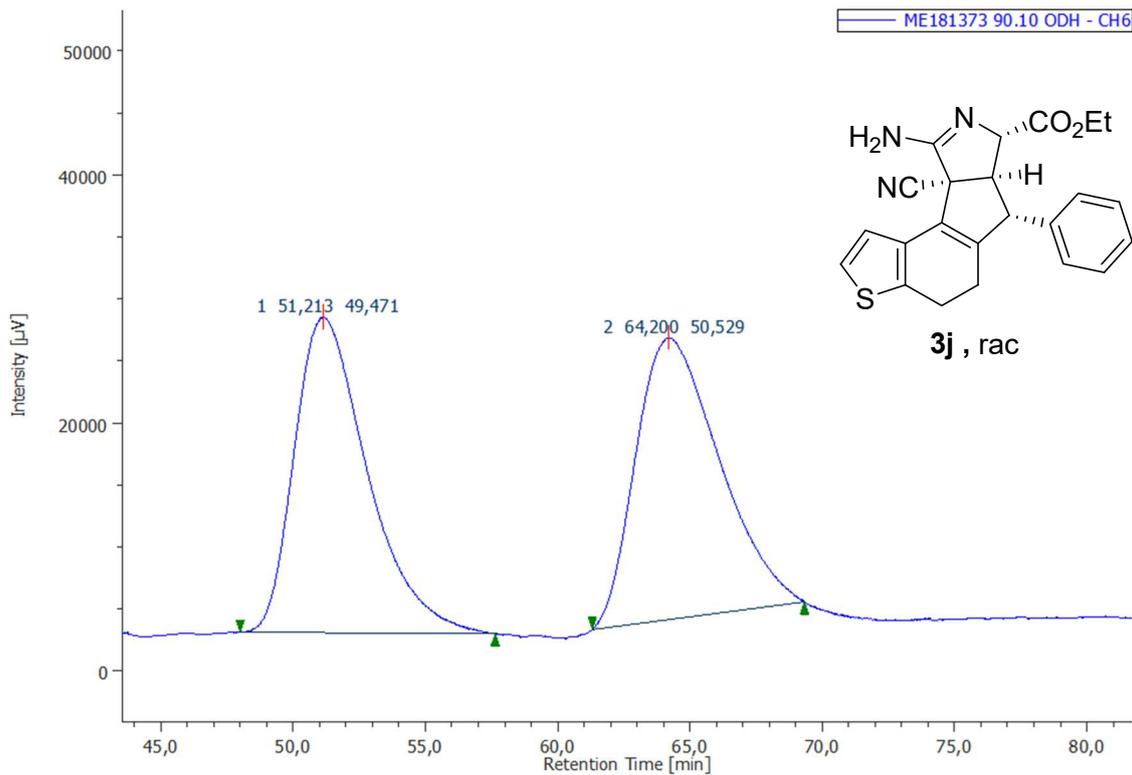


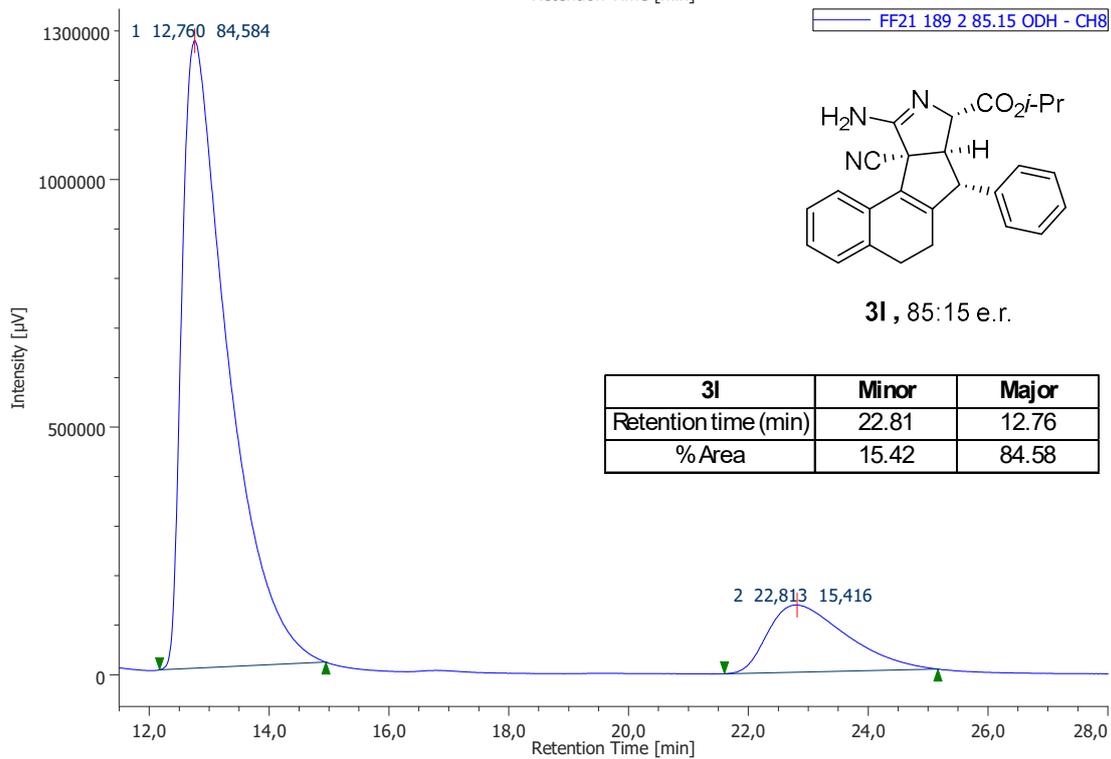
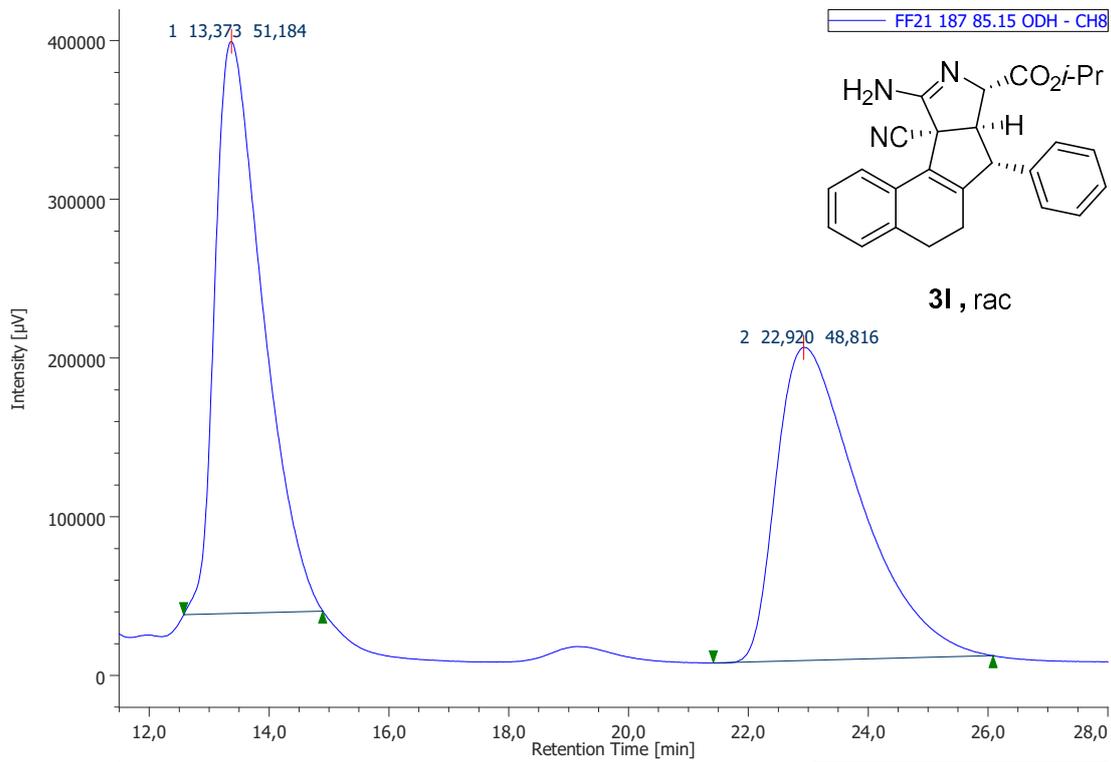


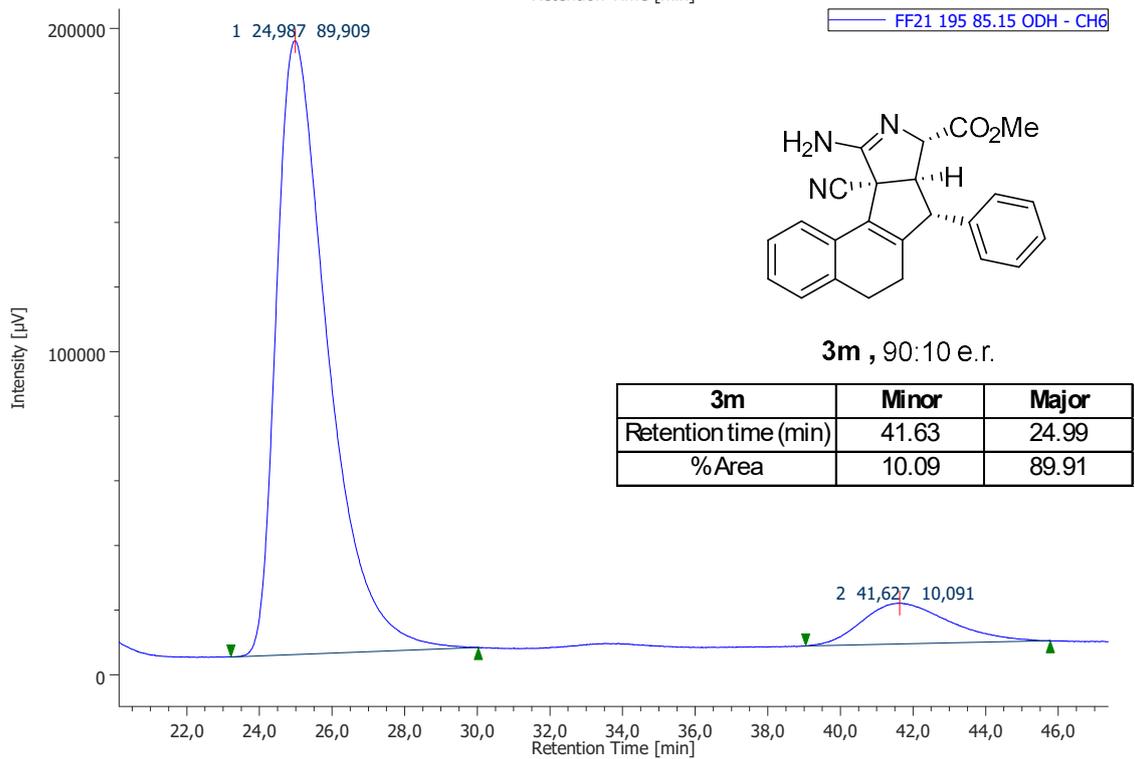
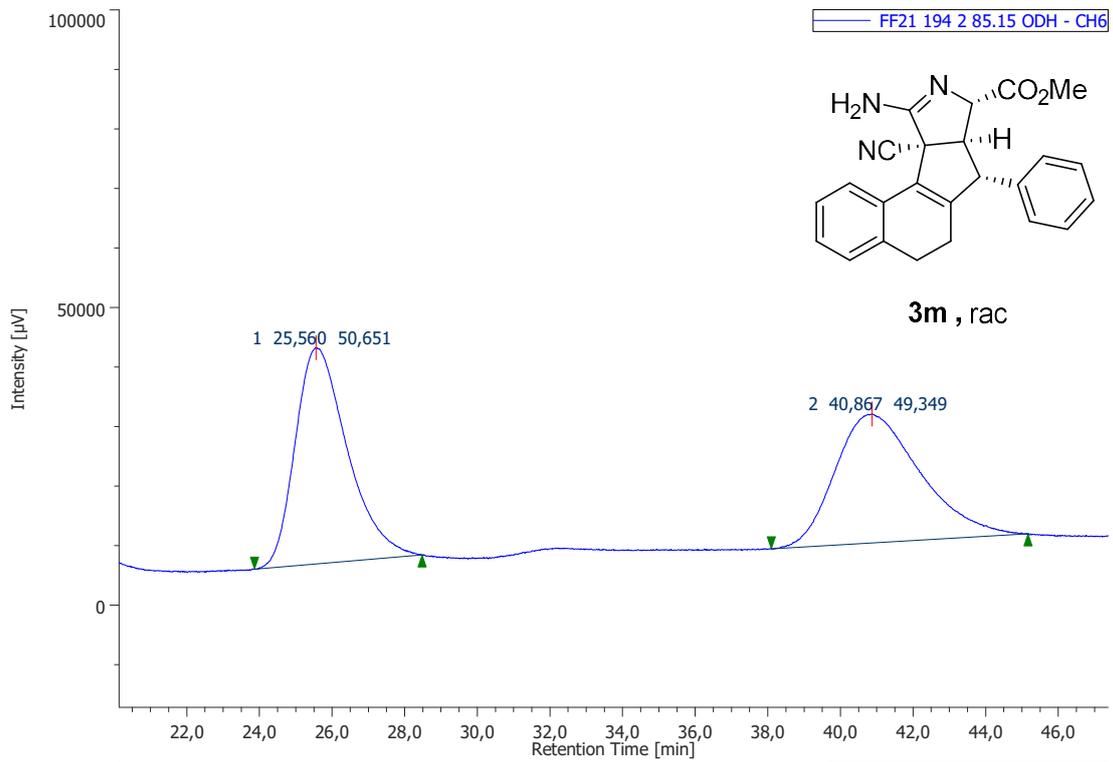


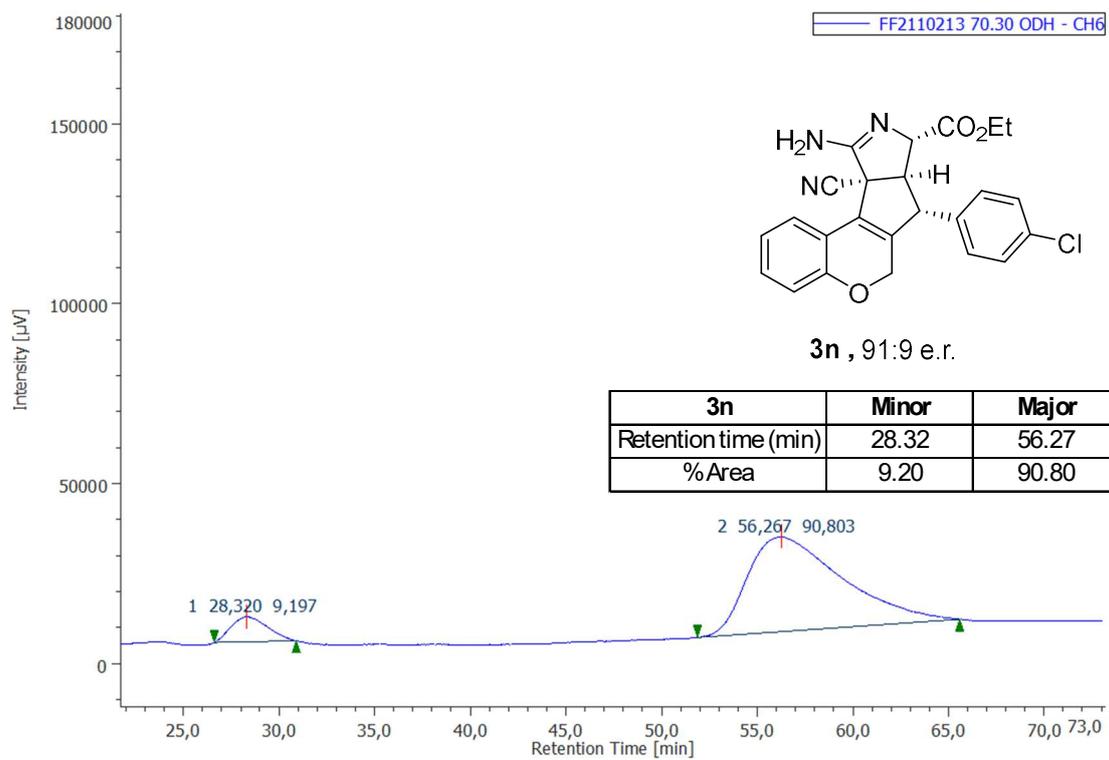
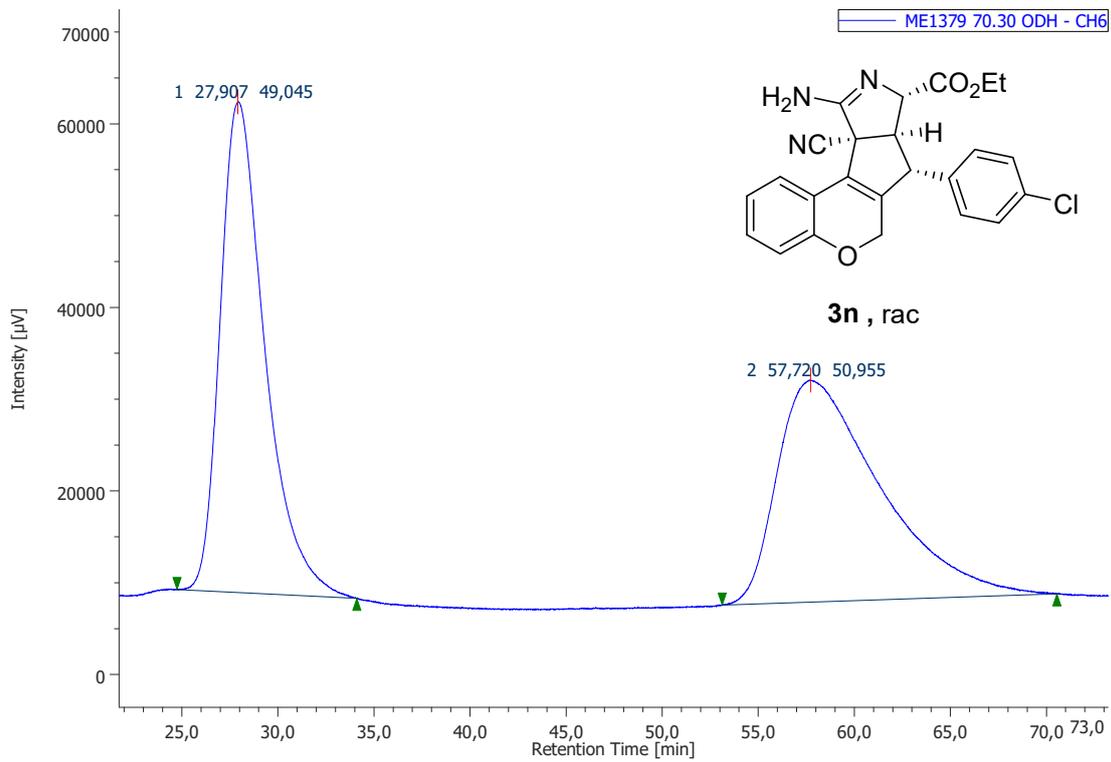


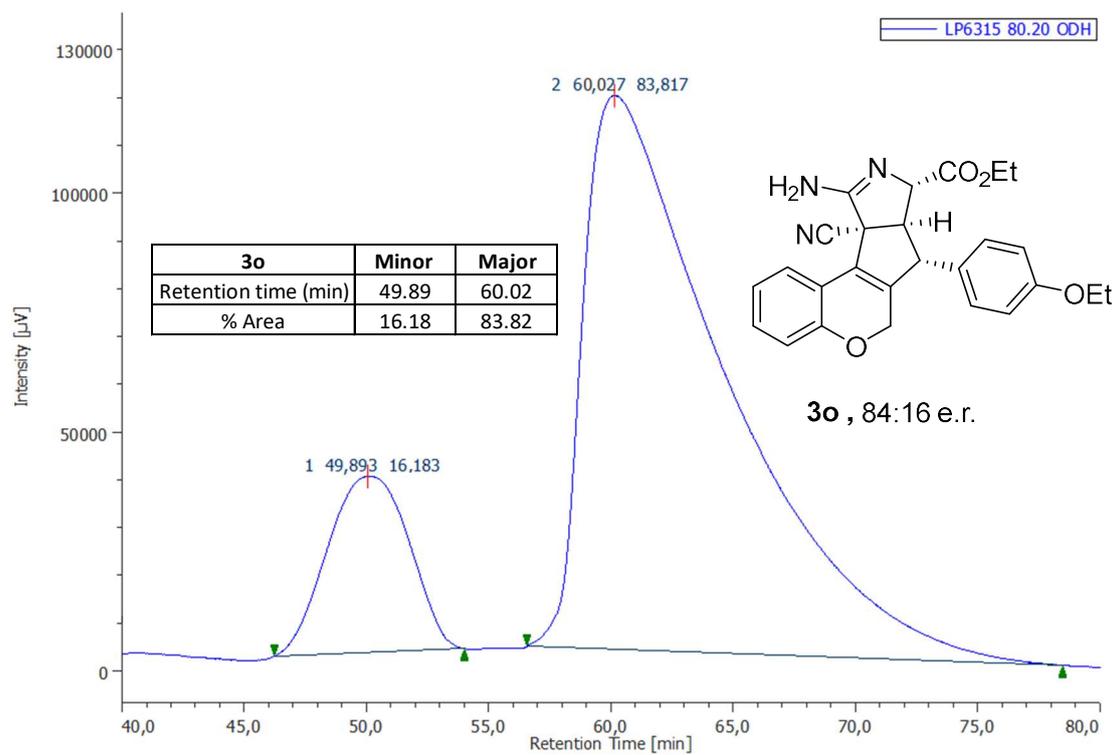
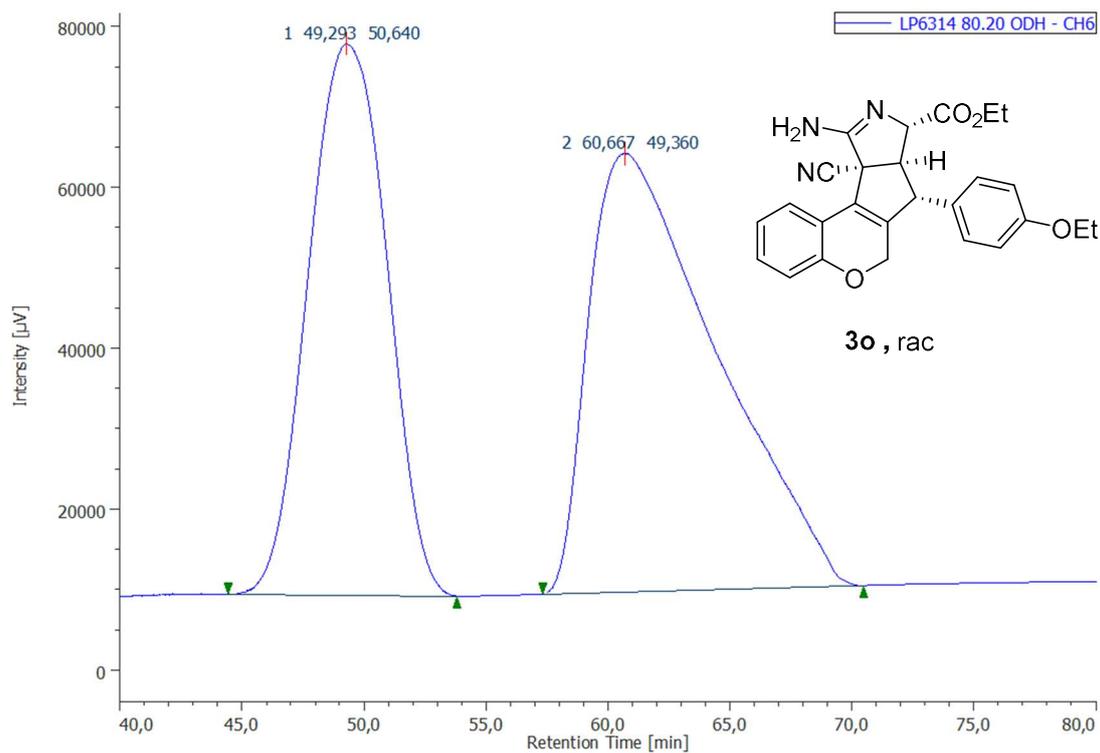


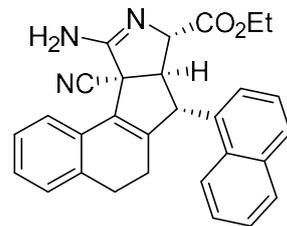
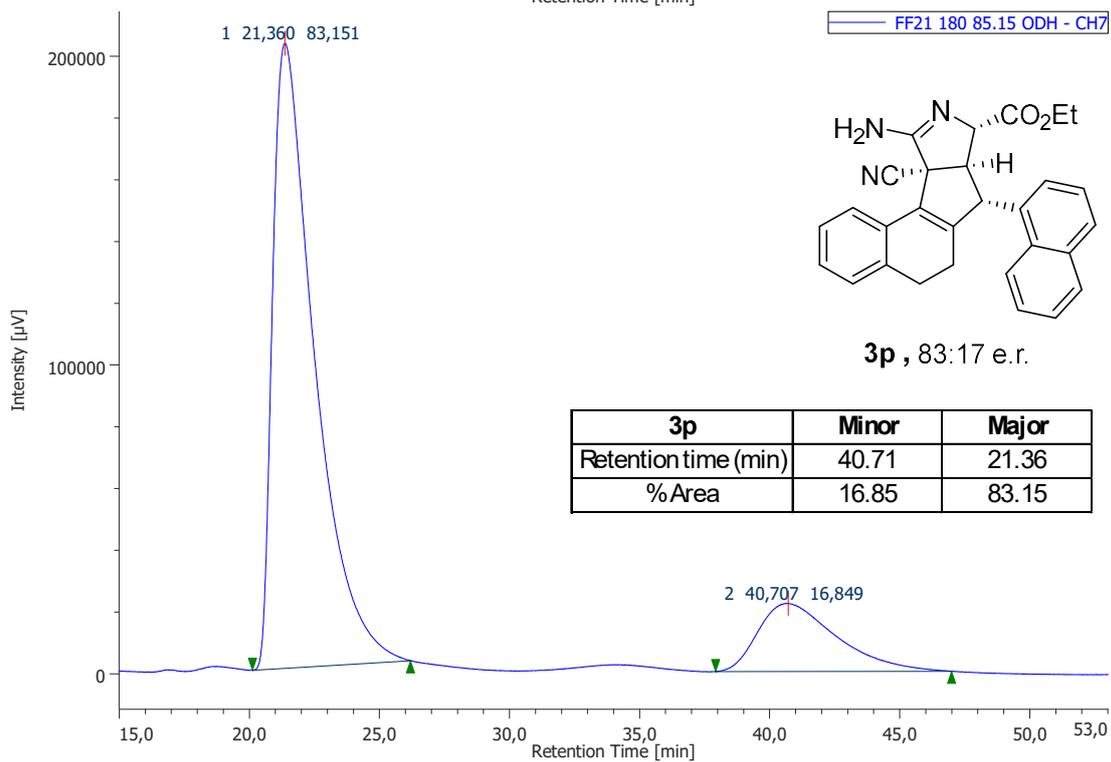
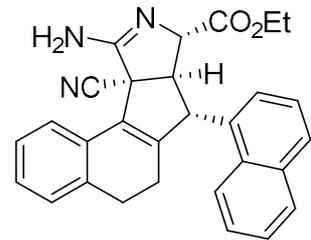
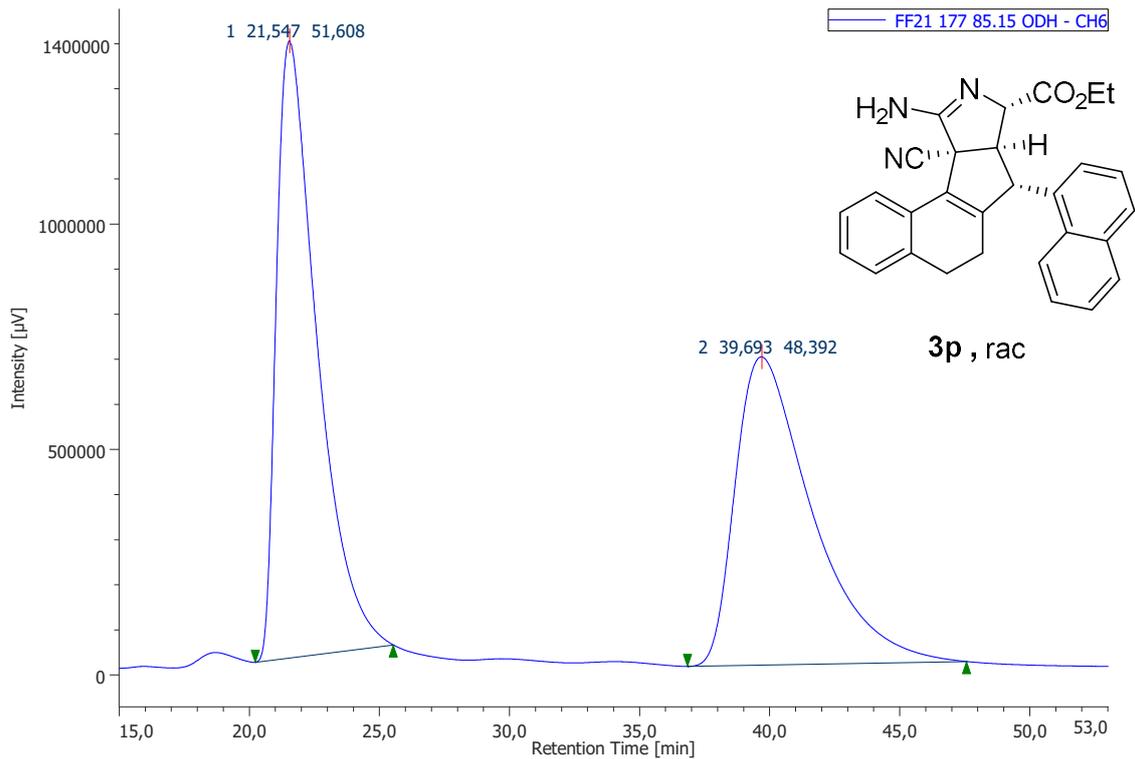












<b>3p</b>	<b>Minor</b>	<b>Major</b>
Retention time (min)	40.71	21.36
%Area	16.85	83.15

