

University of Groningen

Asymmetric synthesis of N,O-heterocycles via enantioselective iridium-catalysed intramolecular allylic amidation

Zhao, Depeng; Fananas-Mastral, Martin; Chang, Mu-Chieh; Otten, Edwin; Feringa, Ben L.

Published in:
Chemical Science

DOI:
[10.1039/c4sc01940g](https://doi.org/10.1039/c4sc01940g)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2014

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Zhao, D., Fananas-Mastral, M., Chang, M-C., Otten, E., & Feringa, B. L. (2014). Asymmetric synthesis of N,O-heterocycles via enantioselective iridium-catalysed intramolecular allylic amidation. *Chemical Science*, 5(11), 4216-4220. <https://doi.org/10.1039/c4sc01940g>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Supporting Information

Asymmetric Synthesis of *N,O*-Heterocycles via Enantioselective Iridium-Catalysed Intramolecular Allylic Amidation

*Depeng Zhao, Martín Fañanás-Mastral, Mu-Chieh Chang, Edwin Otten, and Ben L. Feringa**

Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG, Groningen,

The Netherlands.

E-mail: b.l.feringa@rug.nl

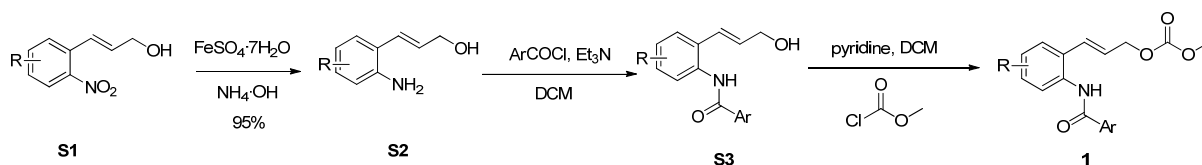
Table of Contents

General remarks	S2
Procedures for the synthesis of allylic carbonates 1	S2
General Procedure for the Iridium-catalyzed asymmetric allylic cyclization of 1a to 1n	S10-S16
General Procedure for the Iridium-catalyzed asymmetric allylic cyclization of 1o and 1p	S16-S17
Procedure for cross metathesis of 2a	S18
Procedure for the addition of organolithium reagent to benzoxazine	S18-S21
X-ray analysis of 2m and 4a: determination of relative and absolute configuration	S21-S22
Determination of the relative configuration of 4a and 4d by NOESY	S23
Copies of NMR spectra	S24-S44
Copies of HPLC results	S45-S62

General remarks

Column chromatography was performed on silica gel (Silica-P flash silica gel from Silicycle, size 40-63 μm). TLC was performed on silica gel 60/Kieselguhr F254. Components were visualized by UV and stained with a solution of a mixture of KMnO_4 (10 g) and K_2CO_3 (10 g) in H_2O (500 mL). Mass spectra were recorded on a AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). ^1H and ^{13}C NMR were recorded on a Varian AMX400 (400 and 100.6 MHz, respectively) or a Varian Unity Plus Varian-500 (500 and 125 MHz, respectively) using CDCl_3 as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl_3 : δ 7.26 for ^1H , δ 77.0 for ^{13}C ; acetone: δ 2.05 for ^1H , δ 29.8 ppm for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Optical rotations were measured in CHCl_3 on a *Schmidt + Haensch* polarimeter (Polartronic MH8) with a 10 cm cell (*c* given in g/100 mL). Conversions were determined by ^1H NMR. Enantioselectivities were determined by HPLC analysis using a Shimadzu LC-10ADVP HPLC equipped with a Shimadzu SPD-M10AVP diode array detector or by capillary GC analysis. Melting points were determined on a Buchi B-545 melting point apparatus. All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. CH_2Cl_2 was dried and distilled over calcium hydride. THF and Et_2O were dried and distilled over Na/benzophenone. $[\text{Ir}(\text{COD})\text{Cl}]_2$ was purchased from Strem Chemicals, Inc. Ligand L7 and L8 were prepared according to literature.¹

Procedures for the synthesis of allylic carbonates 1:



Representative procedure for the synthesis of allylic carbonate **1a**.

The amino alcohol **S2a** was prepared following a literature procedure.^[2] A mixture of o-nitrocinnamyl alcohol **S1a** (1.7 g, 9.5 mmol) and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (25.0 g, 90.9 mmol) in a mixture of methanol (100 mL) and conc. aqueous ammonium hydroxide (120 mL) was heated at 80 °C for 3 h. After cooling to room temperature, the mixture was extracted with DCM (6 \times 50 mL). The combined organic solution was dried over Na_2SO_4 and the solvent evaporated. The residue was purified by chromatography (3 : 7 pentane– EtOAc) to give **S2a** (1.41 g, 95%) as a light brown solid.

To a solution of **S2a** (1.49 g, 10 mmol) and Et_3N (4.2 mL, 30 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise benzoyl chloride (3.5 mL, 30 mmol) at 0 °C. The mixture was stirred at room temperature for 12 h. The solvent was removed under vacuum and the residue was dissolved in a mixture of THF (40 mL), MeOH (40 mL) and 1 N aq. NaOH (40 mL). The mixture was then stirred at room temperature for 2 h to hydrolyze the benzoic ester. After

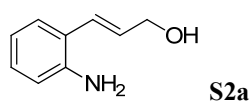
[1] W.-B. Liu, C. Zheng, C.-X. Zhuo, L.-X. Dai, S.-L. You, *J. Am. Chem. Soc.*, **2012**, *134*, 4812.

[2] J. M. Cuerva, D. J. Cárdenas, A. M. Echavarren, *J. Chem. Soc., Perkin Trans. 1*, **2002**, 1360.

extraction with CH₂Cl₂ (3 x 50 mL), the combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by chromatography (1 : 1 pentane–EtOAc) to give **S3a** as light brown solid in 85% yield.

To a solution of allyl alcohol **S3a** (1.68 g, 6.6 mmol) and pyridine (1.65 mL, 3 equiv) in CH₂Cl₂ (50 mL), methyl chloroformate (1.0 mL, 2 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and subsequently stirred for 1 h. Upon completion, the reaction mixture was diluted with CH₂Cl₂ (50 mL) and washed with aq. HCl (2N) (3 x 40 mL). The organic layer was dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by chromatography (3 : 1 pentane–EtOAc) to give **1a** as a light brown solid in 99% yield.

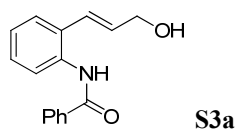
The other allylic carbonates **1** were synthesized in accordance with the representative procedures for **1a**.



(E)-3-(2-Aminophenyl)prop-2-en-1-ol (S2a)

¹H NMR (400 MHz, CDCl₃) δ = 7.25 (d, *J* = 8.2 Hz, 1H), 7.08 (td, *J* = 8.0, 1.4 Hz, 1H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.71 – 6.60 (m, 2H), 6.22 (dt, *J* = 15.7, 5.6 Hz, 1H), 4.30 (dd, *J* = 5.6, 1.5 Hz, 2H), 3.63 (brs, 2H).

¹³C NMR (101 MHz, CDCl₃) δ = 143.6, 130.2, 128.6, 127.4, 126.4, 123.1, 119.0, 116.2, 63.7.

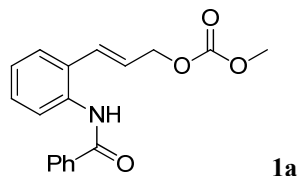


(E)-N-(2-(3-Hydroxyprop-1-en-1-yl)phenyl)benzamide (S3a)

¹H NMR (400 MHz, CDCl₃) δ 7.94 (s, 1H), 7.89 (d, *J* = 7.2 Hz, 3H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.32 (td, *J* = 8.1, 1.3 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.73 (d, *J* = 15.8 Hz, 1H), 6.29 (dt, *J* = 15.8, 5.3 Hz, 1H), 4.31 (dd, *J* = 5.3, 1.6 Hz, 2H), 2.11 (brs, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 166.0, 134.6, 134.4, 132.9, 131.9, 130.1, 128.2, 128.4, 127.2, 127.1, 125.7, 125.5, 124.1, 63.4.

HRMS (ESI⁺, *m/z*) calculated for C₁₆H₁₆NO₂ [M + H]⁺ 254.1176; found 254.1172.

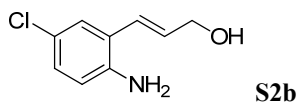


(E)-3-(2-Benzamidophenyl)allyl methyl carbonate (1a)

¹H NMR (400 MHz, CDCl₃) δ = 7.97 (d, *J* = 8.1 Hz, 1H), 7.96 – 7.85 (m, 3H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.42 (d, *J* = 7.8, 1H), 7.34 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 15.8 Hz, 1H), 6.22 (dt, *J* = 15.8, 6.3 Hz, 1H), 4.79 (dd, *J* = 6.3, 1.4 Hz, 2H), 3.77 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ = 165.6, 155.6, 134.7, 134.5, 131.9, 130.0, 129.2, 128.9, 128.8, 127.3, 127.2, 126.9, 125.5, 123.8, 68.1, 54.8.

HRMS (ESI+, m/z) calculated for $C_{18}H_{18}NO_4$ $[M + H]^+$ 312.1230; found 312.1229.

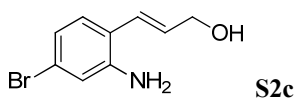


(E)-3-(2-Amino-5-chlorophenyl)prop-2-en-1-ol (S2b)

1H NMR (400 MHz, $CDCl_3$) δ = 7.22 (d, J = 2.4 Hz, 1H), 7.02 (dd, J = 8.5, 2.4 Hz, 1H), 6.62 (s, 1H), 6.59 (d, J = 5.7 Hz, 1H), 6.24 (dt, J = 15.7, 5.4 Hz, 1H), 4.34 (dd, J = 5.4, 1.6 Hz, 2H), 2.86 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 142.2, 131.5, 128.3, 127.0, 125.2, 124.5, 123.6, 117.2, 63.6.

HRMS (ESI+, m/z) calculated for $C_9H_{11}ClNO$ $[M + H]^+$ 184.0524; found 184.0528.

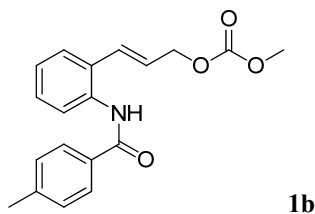


(E)-3-(2-Amino-4-bromophenyl)prop-2-en-1-ol (S2c)

1H NMR (400 MHz, $CDCl_3$) δ = 7.09 (d, J = 8.2 Hz, 1H), 6.86 (dd, J = 8.2, 1.9 Hz, 1H), 6.83 (d, J = 1.9 Hz, 1H), 6.58 (d, J = 15.7 Hz, 1H), 6.22 (dt, J = 15.7, 5.5 Hz, 1H), 4.32 (dd, J = 5.5, 1.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.9, 130.9, 128.8, 125.5, 122.0, 121.9, 121.8, 118.5, 63.7.

HRMS (ESI+, m/z) calculated for $C_9H_{11}BrNO$ $[M + H]^+$ 228.0019; found 228.0025.

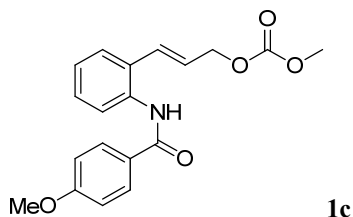


(E)-Methyl (3-(2-(4-methylbenzamido)phenyl)allyl) carbonate (1b)

1H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, J = 8.1 Hz, 1H), 7.82 (brs, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.42 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 6.84 (d, J = 15.8 Hz, 1H), 6.22 (dt, J = 15.8, 6.3 Hz, 1H), 4.79 (dd, J = 6.3, 1.2 Hz, 2H), 3.78 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.5, 155.6, 142.5, 134.9, 131.7, 130.1, 129.5, 129.1, 129.0, 127.3, 127.2, 126.9, 125.4, 123.7, 68.2, 54.9, 21.5.

HRMS (ESI+, m/z) calculated for $C_{19}H_{20}NO_4$ $[M + H]^+$ 326.1387; found 326.1385.

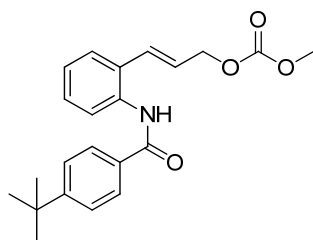


(E)-3-(2-(4-Methoxybenzamido)phenyl)allyl methyl carbonate (1c)

^1H NMR (400 MHz, CDCl_3) δ = 7.95 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.8 Hz, 2H), 7.82 (brs, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 15.8 Hz, 1H), 6.21 (dt, J = 15.8, 6.3 Hz, 1H), 4.78 (dd, J = 6.3, 1.2 Hz, 2H), 3.87 (s, 3H), 3.78 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ = 165.1, 162.6, 155.6, 135.0, 130.2, 129.0⁹, 129.0⁶, 128.9, 127.3, 126.7, 126.7, 125.3, 123.8, 114.0, 68.2, 55.4, 54.8.

HRMS (ESI+, m/z) calculated for $\text{C}_{19}\text{H}_{20}\text{NO}_5$ $[\text{M} + \text{H}]^+$ 342.1336; found 342.1333.



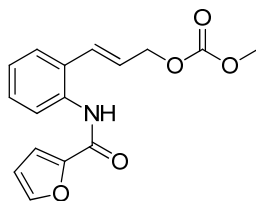
1d

(E)-3-(2-(4-(tert-butyl)benzamido)phenyl)allyl methyl carbonate (1d)

^1H NMR (400 MHz, CDCl_3) δ = 7.97 (d, J = 8.0 Hz, 1H), 7.89 (brs, 1H), 7.86 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.17 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 15.8 Hz, 1H), 6.22 (dt, J = 12.9, 6.1 Hz, 1H), 4.79 (d, J = 6.1 Hz, 2H), 3.78 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ = 165.5, 162.6, 155.5, 134.9, 131.6, 130.1, 129.1, 128.9, 127.3, 127.0, 126.8, 125.73, 125.4, 123.8, 68.2, 54.8, 35.0, 31.1.

HRMS (ESI+, m/z) calculated for $\text{C}_{22}\text{H}_{26}\text{NO}_4$ $[\text{M} + \text{H}]^+$ 368.1856; found 368.1852.



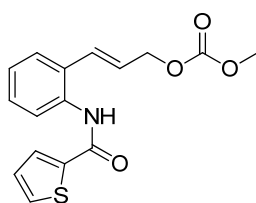
1e

(E)-3-(2-(Furan-2-carboxamido)phenyl)allyl methyl carbonate (1e)

^1H NMR (400 MHz, CDCl_3) δ = 8.11 (brs, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.54 (s, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 3.5 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 15.8 Hz, 1H), 6.57 (dd, J = 3.3, 1.6 Hz, 1H), 6.26 (dt, J = 15.8, 6.3 Hz, 1H), 4.82 (d, J = 6.3 Hz, 2H), 3.80 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ = 156.1, 155.5, 147.7, 144.4, 134.0, 129.6, 128.9, 128.7, 127.4, 126.9, 125.4, 123.4, 115.4, 112.6, 68.2, 54.9.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{16}\text{NO}_5$ $[\text{M} + \text{H}]^+$ 302.1023; found 302.1024.



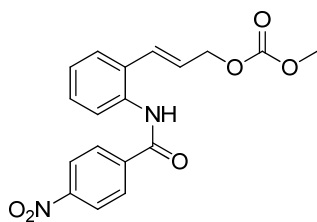
1f

(E)-Methyl (3-(2-(thiophene-2-carboxamido)phenyl)allyl) carbonate (1f)

^1H NMR (400 MHz, CDCl_3) δ 7.90 (d, $J = 8.0$ Hz, 1H), 7.83 (brs, 1H), 7.68 (d, $J = 3.4$ Hz, 1H), 7.55 (dd, $J = 5.0$, 0.8 Hz, 1H), 7.40 (d, $J = 7.7$ Hz, 1H), 7.31 (t, $J = 7.7$ Hz, 1H), 7.17 (t, $J = 7.4$ Hz, 1H), 7.12 (dd, $J = 4.9$, 3.8 Hz, 1H), 6.83 (d, $J = 15.8$ Hz, 1H), 6.20 (dt, $J = 15.8$, 6.3 Hz, 1H), 4.78 (dd, $J = 6.3$, 1.2 Hz, 2H), 3.78 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 160.0, 155.6, 139.0, 134.4, 130.9, 130.1, 129.1, 128.9, 128.6, 127.8, 127.3, 126.8, 125.6, 123.9, 68.1, 54.8$.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{16}\text{NO}_5$ $[\text{M} + \text{H}]^+$ 318.0795; found 318.0796.



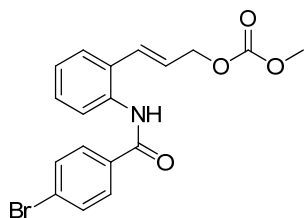
1g

(E)-Methyl (3-(2-(4-nitrobenzamido)phenyl)allyl) carbonate (1g)

^1H NMR (400 MHz, acetone) δ 9.65 (s, 1H), 8.42 (d, $J = 8.8$ Hz, 2H), 8.32 (d, $J = 8.7$ Hz, 2H), 7.70 (d, $J = 7.7$ Hz, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.40 (td, $J = 7.7$, 1.3 Hz, 1H), 7.33 (t, $J = 7.2$ Hz, 1H), 7.06 (d, $J = 15.9$ Hz, 1H), 6.39 (dt, $J = 15.8$, 6.3 Hz, 1H), 4.79 (dd, $J = 6.3$, 1.2 Hz, 2H), 3.76 (s, 3H).

^{13}C NMR (101 MHz, acetone) $\delta = 165.9, 157.1, 151.4, 142.3, 136.8, 133.6, 131.3, 130.7, 130.0, 128.4, 128.2, 128.0, 126.9, 125.1, 69.5, 55.8$.

HRMS (ESI+, m/z) calculated for $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 357.1081; found 357.1078.



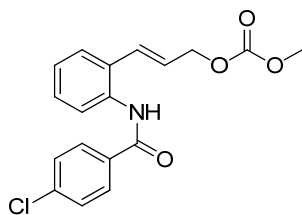
1h

(E)-3-(2-(4-Bromobenzamido)phenyl)allyl methyl carbonate (1h)

^1H NMR (400 MHz, CDCl_3) $\delta = 7.96$ (d, $J = 8.1$ Hz, 1H), 7.84 (brs, 1H), 7.79 (d, $J = 8.4$ Hz, 2H), 7.64 (d, $J = 8.4$ Hz, 2H), 7.41 (d, $J = 7.7$ Hz, 1H), 7.35 (t, $J = 7.8$ Hz, 1H), 7.19 (t, $J = 7.6$ Hz, 1H), 6.82 (d, $J = 15.8$ Hz, 1H), 6.20 (dt, $J = 15.8$, 6.3 Hz, 1H), 4.79 (dd, $J = 6.3$, 0.9 Hz, 2H), 3.78 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 164.7, 155.6, 134.5, 133.3, 132.0, 130.1, 129.2, 129.0, 128.8, 127.4, 127.2, 126.7, 125.7, 123.7, 68.1, 54.9$.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{13}\text{BrNO}$ $[\text{M} - \text{OCOOMe}]^+$ 314.0175; found 314.0178.



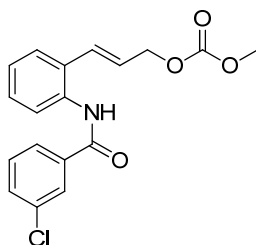
1i

(E)-3-(2-(4-Chlorobenzamido)phenyl)allyl methyl carbonate (1i)

^1H NMR (400 MHz, CDCl_3) δ 7.93 (d, $J = 8.1$ Hz, 1H), 7.88 (brs, 1H), 7.85 (d, $J = 8.5$ Hz, 2H), 7.46 (d, $J = 8.5$ Hz, 2H), 7.41 (d, $J = 7.7$ Hz, 1H), 7.34 (dd, $J = 11.1, 4.4$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 1H), 6.82 (d, $J = 15.8$ Hz, 1H), 6.20 (dt, $J = 15.8, 6.3$ Hz, 1H), 4.78 (dd, $J = 6.3, 1.1$ Hz, 2H), 3.78 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 164.6, 155.6, 138.2, 134.5, 132.8, 130.1, 129.3, 129.0, 129.0, 128.7, 127.3, 127.1, 125.7, 123.8, 68.1, 54.9$.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{13}\text{ClNO}$ [$\text{M} - \text{OCOOMe}$] $^+$ 270.0680; found 270.0682.



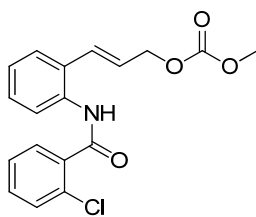
1j

(E)-3-(2-(3-Chlorobenzamido)phenyl)allyl methyl carbonate (1j)

^1H NMR (201 MHz, CDCl_3) δ 8.02 – 7.83 (m, 3H), 7.78 (d, $J = 7.6$ Hz, 1H), 7.61 – 7.27 (m, 4H), 7.20 (t, $J = 7.5$ Hz, 1H), 6.83 (d, $J = 15.8$ Hz, 1H), 6.20 (dt, $J = 15.8, 6.3$ Hz, 1H), 4.78 (d, $J = 6.2$ Hz, 3H), 3.77 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 164.7, 155.4, 134.8, 134.2, 131.7, 130.5, 130.4, 130.3, 129.6, 129.4, 128.8, 127.3, 127.0, 126.6, 125.9, 124.2, 68.0, 54.8$.

HRMS (ESI+, m/z) calculated for $\text{C}_{18}\text{H}_{17}\text{ClNO}_4$ [$\text{M} + \text{H}$] $^+$ 346.0841; found 346.0837.



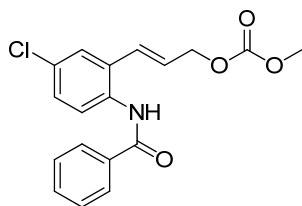
1k

(E)-3-(2-(2-chlorobenzamido)phenyl)allyl methyl carbonate (1k)

^1H NMR (400 MHz, CDCl_3) $\delta = 7.96$ (d, $J = 7.7$ Hz, 1H), 7.90 (s, 1H), 7.82 (d, $J = 5.1$ Hz, 1H), 7.53 – 7.30 (m, 5H), 7.21 (t, $J = 7.2$ Hz, 1H), 6.91 (d, $J = 15.6$ Hz, 1H), 6.23 (dt, $J = 15.5, 5.9$ Hz, 1H), 4.79 (d, $J = 5.8$ Hz, 2H), 3.77 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 164.5, 155.5, 136.2, 134.9, 134.3, 131.9, 129.9^9, 129.9^6, 129.7, 128.9, 127.6, 127.2, 126.7, 125.9, 125.2, 124.3, 68.1, 54.8$.

HRMS (ESI+, m/z) calculated for $C_{18}H_{17}ClNO_4$ $[M + H]^+$ 346.0841; found 346.0836.

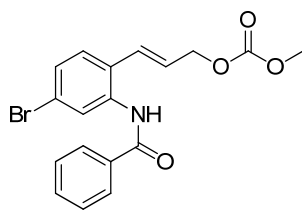


(E)-3-(2-Benzamido-5-chlorophenyl)allyl methyl carbonate (1l)

1H NMR (400 MHz, $CDCl_3$) δ = 7.97 – 7.82 (m, 4H), 7.57 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.38 (d, J = 2.4 Hz, 1H), 7.27 (dd, J = 8.6, 2.5 Hz, 1H), 6.75 (d, J = 15.8 Hz, 1H), 6.20 (dt, J = 15.7, 6.1 Hz, 1H), 4.76 (dd, J = 6.1, 1.4 Hz, 2H), 3.76 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.6, 155.5, 134.1, 133.3, 132.1, 130.9, 130.8, 128.8, 128.7, 128.6, 128.0, 127.2, 127.0, 125.2, 67.7, 54.9.

HRMS (ESI+, m/z) calculated for $C_{18}H_{17}ClNO_4$ $[M + H]^+$ 346.0841; found 346.0844.

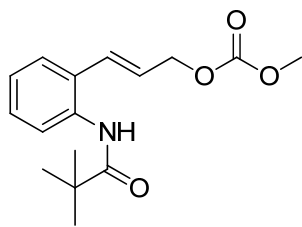


(E)-3-(2-Benzamido-4-bromophenyl)allyl methyl carbonate (1m)

1H NMR (400 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 8.00 – 7.81 (m, 3H), 7.58 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.3 Hz, 2H), 7.34 – 7.20 (m, 2H), 6.75 (d, J = 15.8 Hz, 1H), 6.20 (dt, J = 15.8, 6.2 Hz, 1H), 4.77 (dd, J = 6.1, 1.4 Hz, 2H), 3.77 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.4, 155.5, 135.8, 134.0, 132.2, 129.0, 128.9, 128.5, 128.4, 127.7, 127.7, 127.2, 126.3, 125.5, 122.4, 67.9, 54.9.

HRMS (ESI+, m/z) calculated for $C_{18}H_{17}BrNO_4$ $[M + H]^+$ 390.0335; found 390.0340.



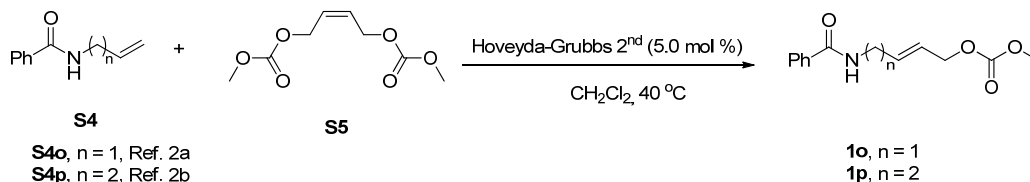
(E)-Methyl (3-(2-pivalamidophenyl)allyl) carbonate (1n)

1H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, J = 8.1 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.34 – 7.23 (m, 1H), 7.12 (d, J = 15.1 Hz, 1H), 6.72 (d, J = 15.7, 1H), 6.17 (dt, J = 15.8, 6.2 Hz, 1H), 4.78 (dd, J = 6.2, 1.4 Hz, 2H), 3.79 (s, 2H), 3.44 (s, 3H), 1.32 (s, 9H).

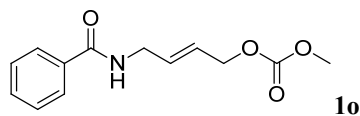
^{13}C NMR (101 MHz, CDCl_3) δ = 176.6, 155.5, 134.8, 129.7, 129.0, 128.8, 127.1, 126.6, 125.1, 123.7, 68.0, 54.8, 39.6, 27.6.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{22}\text{NO}_4$ $[\text{M} + \text{H}]^+$ 292.1543; found 292.1553.

General procedure for the synthesis of allylic carbonate **1o** and **1p**.



To a solution of **S4** (15.0 mmol)³ and **S5** (*Z*-but-2-ene-1,4-diyl dimethyl dicarbonate (30.0 mmol) in dry dichloromethane (50 mL), HG-II catalyst (5 mol%) was added and the mixture was heated at reflux for 2-3 h. After cooling down to room temperature, the solvent was removed under reduced pressure to yield the crude product which was purified by silica gel chromatography (EtOAc/Pentane 1:2) affording the pure compounds (**1o**, 76% yield; **1p**, 81% yield).

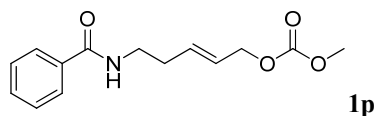


(*E*)-4-benzamidobut-2-en-1-yl methyl carbonate (**1o**)

^1H NMR (400 MHz, CDCl_3) δ = 7.77 (d, $J = 7.4$ Hz, 2H), 7.51 (t, $J = 7.3$ Hz, 1H), 7.43 (t, $J = 7.5$ Hz, 2H), 6.21 (brs, 1H), 5.93 (dt, $J = 15.4, 5.5$ Hz, 1H), 5.81 (dt, $J = 11.4, 6.0$ Hz, 1H), 4.63 (d, $J = 5.8$ Hz, 2H), 4.18 – 4.06 (m, 2H), 3.79 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ = 167.3, 155.4, 134.1, 131.5, 131.4, 128.4, 127.1, 126.9, 125.4, 67.4, 54.7, 41.0.

HRMS (ESI+, m/z) calculated for $\text{C}_{13}\text{H}_{15}\text{NO}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 272.0893; found 272.0896.



(*E*)-5-benzamidopent-2-en-1-yl methyl carbonate (**1p**)

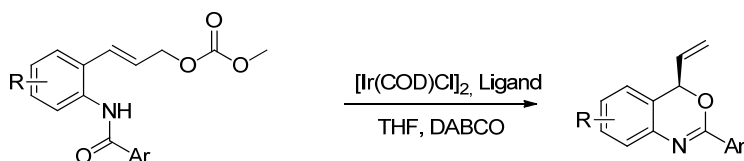
^1H NMR (400 MHz, CDCl_3) δ = 7.73 (d, $J = 7.2$ Hz, 2H), 7.48 (t, $J = 7.3$ Hz, 1H), 7.40 (t, $J = 7.4$ Hz, 2H), 6.31 (brs, 1H), 5.82 (dt, $J = 15.5, 7.3$ Hz, 1H), 5.69 (dt, $J = 15.5, 6.1$ Hz, 1H), 4.58 (d, $J = 5.9$ Hz, 2H), 3.75 (s, 3H), 3.52 (q, $J = 6.5$ Hz, 2H), 2.38 (q, $J = 6.6$ Hz, 2H).

^{13}C NMR (101 MHz, CDCl_3) δ = 170.0, 158.1, 137.2, 135.7, 133.9, 131.1, 129.4, 128.8, 70.6, 57.3, 41.4, 34.9.

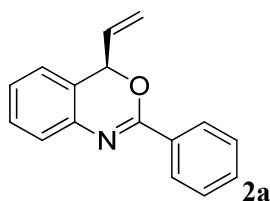
HRMS (ESI+, m/z) calculated for $\text{C}_{14}\text{H}_{17}\text{NO}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 286.1050; found 286.1053.

[3] **S4** were prepared according to literature procedures: a) X. Zhang, B. Cao, S. Yu, X. Zhang, *Angew. Chem. Int. Ed.* **2010**, *49*, 4047; b) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Médebielle, V. Gouverneur, *J. Am. Chem. Soc.* **2013**, *135*, 2505.

General Procedure for the Iridium-catalyzed asymmetric allylic cyclization of 1a to 1n:



To a suspension of [Ir(COD)Cl]₂ (3.3 mg, 2.5 mol%) and **L7** (4.47 mg, 5.0 mol%) in 2 mL dry THF was added 3.0 eq. DABCO (72.6 mg, 0.6 mmol) under a N₂ atmosphere. Then the reaction mixture was heated at 50 °C for 30 min to generate the catalyst. The corresponding allylic carbonate (2 mmol) was added and the reaction mixture was stirred until TLC showed full conversion. All volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography (Pentane/EtOAc = 10:1) to yield the desired product.



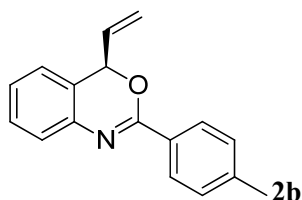
(*R*)-2-Phenyl-4-vinyl-4*H*-benzo[*d*][1,3]oxazine (**2a**)

Synthesized according to general procedure; 81% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiracel OD-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: *t*_R (major) 8.64 min, *t*_R (minor) 9.32 min, ee = 97%; [α]_D²⁰ = -8.2 (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.22 – 8.13 (m, 2H), 7.55 – 7.40 (m, 3H), 7.38 – 7.31 (m, 2H), 7.24 – 7.18 (m, 1H), 7.04 (d, *J* = 6.5 Hz, 1H), 6.11 (ddd, *J* = 17.4, 10.1, 6.4 Hz, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.35 (d, *J* = 6.2 Hz, 1H), 5.31 (d, *J* = 1.2 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 156.6, 139.1, 135.5, 132.5, 131.4, 129.1, 128.2, 128.0, 126.5, 125.0, 124.5, 124.1, 118.4, 77.2.

HRMS (ESI+, *m/z*) calculated for C₁₆H₁₄NO [M + H]⁺ 236.1070; found 236.1069.



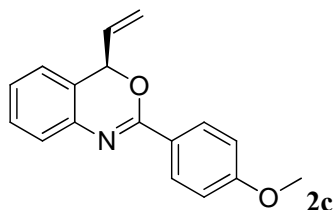
(*R*)-2-(*p*-Tolyl)-4-vinyl-4*H*-benzo[*d*][1,3]oxazine (**2b**)

Synthesized according to general procedure; 93% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OB-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: *t*_R (minor) 12.42 min, *t*_R (major) 36.83 min, ee = 94%; [α]_D²⁰ = -18.8 (c 1.0, CHCl₃).

^1H NMR (400 MHz, CDCl_3) δ = 8.07 (d, J = 8.2 Hz, 2H), 7.39 – 7.28 (m, 2H), 7.29 – 7.23 (m, 2H), 7.19 (ddd, J = 7.5, 5.9, 2.8 Hz, 1H), 7.04 (d, J = 7.1 Hz, 3H), 6.10 (ddd, J = 16.8, 10.3, 6.3 Hz, 1H), 5.86 (d, J = 1.3 Hz, 1H), 5.34 (d, J = 7.7 Hz, 1H), 5.31 (d, J = 1.2 Hz, 1H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ = 156.7, 141.8, 139.2, 135.5, 129.7, 129.0, 129.0, 128.0, 126.2, 124.8, 124.4, 124.1, 118.2, 77.3, 77.1, 77.0, 76.7, 21.6.

HRMS (ESI+, m/z) calculated for $\text{C}_{17}\text{H}_{16}\text{NO}$ $[\text{M} + \text{H}]^+$ 250.1226; found 250.1231.



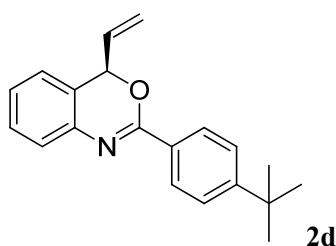
(R)-2-(4-Methoxyphenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2c)

Synthesized according to general procedure; 92% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak AS-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_{R} (major) 9.43 min, t_{R} (minor) 12.34 min, ee = 95%; $[\alpha]_{\text{D}}^{20}$ = -30.8 (c 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 8.12 (d, J = 8.9 Hz, 2H), 7.37 – 7.27 (m, 2H), 7.22 – 7.14 (m, 1H), 7.03 (d, J = 7.4 Hz, 1H), 6.95 (d, J = 8.9 Hz, 2H), 6.16 – 5.98 (m, 1H), 5.84 (d, J = 1.3 Hz, 1H), 5.34 (d, J = 6.8 Hz, 1H), 5.30 (d, J = 1.1 Hz, 1H), 3.86 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ = 162.3, 156.5, 139.4, 135.5, 129.8, 129.0, 126.0, 124.9, 124.6, 124.4, 124.1, 118.2, 113.6, 77.1, 55.4.

HRMS (ESI+, m/z) calculated for $\text{C}_{17}\text{H}_{16}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 266.1176; found 266.1182.



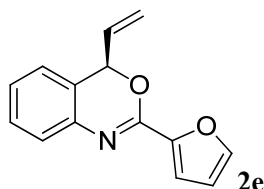
(R)-2-(4-(tert-Butyl)phenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2d)

Synthesized according to general procedure; 81% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_{R} (major) 11.68 min, t_{R} (minor) 15.36 min, ee = 96%; $[\alpha]_{\text{D}}^{20}$ = -20.0 (c 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 8.10 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.37 – 7.29 (m, 2H), 7.19 (ddd, J = 7.6, 5.2, 3.4 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 6.10 (ddd, J = 16.8, 10.3, 6.3 Hz, 1H), 5.85 (d, J = 6.2 Hz, 1H), 5.34 (d, J = 9.7 Hz, 1H), 5.32 – 5.28 (m, 1H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ = 31.2, 34.9, 77.1, 118.2, 124.2, 124.4, 124.9, 125.2, 126.2, 127.8, 129.0, 129.7, 135.5, 139.3, 154.9, 156.7.

HRMS (ESI+, m/z) calculated for $\text{C}_{20}\text{H}_{22}\text{NO}$ $[\text{M} + \text{H}]^+$ 292.1696; found 292.1703.



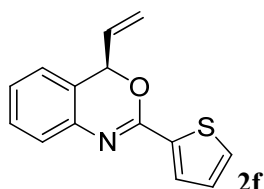
(R)-2-(Furan-2-yl)-4-vinyl-4H-benzo[d][1,3]oxazine (2e)

Synthesized according to general procedure; 87% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OB-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_{R} (minor) 17.31 min, t_{R} (major) 26.39 min, ee = 97%; $[\alpha]_{\text{D}}^{20}$ = -3.8 (c 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.59 (s, 1H), 7.39 – 7.26 (m, 2H), 7.18 (td, J = 7.3, 1.5 Hz, 1H), 7.09 (d, J = 3.4 Hz, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.51 (dd, J = 3.5, 1.7 Hz, 1H), 6.06 (ddd, J = 16.3, 10.8, 6.3 Hz, 1H), 5.80 (d, J = 6.4 Hz, 1H), 5.34 (d, J = 1.1 Hz, 1H), 5.31 (d, J = 7.0 Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3) δ = 149.5, 146.5, 145.6, 138.4, 135.0, 129.2, 126.5, 125.0, 124.5, 124.0, 118.7, 114.8, 111.8, 77.2.

HRMS (ESI+, m/z) calculated for $\text{C}_{14}\text{H}_{12}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 226.0863; found 226.0869.



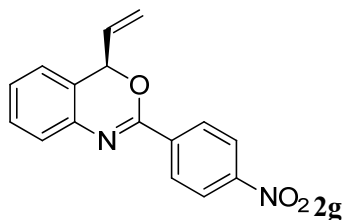
(R)-2-(Thiophen-2-yl)-4-vinyl-4H-benzo[d][1,3]oxazine (2f)

Synthesized according to general procedure; 83% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiracel OD-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_{R} (major) 10.37 min, t_{R} (minor) 14.00 min, ee = 95%; $[\alpha]_{\text{D}}^{20}$ = -21.6 (c 1.01, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.79 – 7.73 (m, 1H), 7.49 (dd, J = 5.1, 1.2 Hz, 1H), 7.37 – 7.26 (m, 2H), 7.18 (td, J = 7.2, 1.8 Hz, 1H), 7.10 (dd, J = 5.0, 3.7 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.08 (ddd, J = 16.8, 10.1, 6.2 Hz, 1H), 5.83 (d, J = 6.2 Hz, 1H), 5.35 (d, J = 3.8 Hz, 1H), 5.32 (d, J = 3.5 Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3) δ = 155.3, 138.7, 135.2, 134.4, 134.3, 131.3, 129.5, 129.2, 128.0, 126.8, 126.0, 125.1, 124.5, 124.0, 118.7, 77.4.

HRMS (ESI+, m/z) calculated for $\text{C}_{14}\text{H}_{12}\text{NOS}$ $[\text{M} + \text{H}]^+$ 242.0634; found 242.0640.



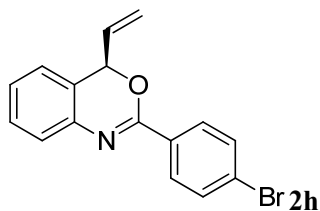
(R)-2-(4-Nitrophenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2g)

Synthesized according to general procedure; 93% yield; yellow solid, m.p. = 147-149 °C; enantiomeric excess was determined by HPLC (Chiralpak AS-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 14.73 min, t_R (minor) 17.73 min, ee = 92%; $[\alpha]_D^{20} = -18.6$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.32 (d, J = 8.9 Hz, 2H), 8.26 (d, J = 8.8 Hz, 2H), 7.41 – 7.30 (m, 2H), 7.25 (td, J = 6.9, 1.8 Hz, 1H), 7.05 (d, J = 7.4 Hz, 1H), 6.09 (ddd, J = 16.9, 10.3, 6.5 Hz, 1H), 5.91 (d, J = 6.5 Hz, 1H), 5.40 – 5.29 (m, 2H).

¹³C NMR (101 MHz, CDCl₃) δ = 154.3, 149.4, 138.4, 138.3, 135.1, 129.3, 128.7, 127.5, 125.4, 124.6, 123.8, 123.4, 119.0, 77.6.

HRMS (ESI+, m/z) calculated for C₁₆H₁₃N₂O₃ [M + H]⁺ 281.0921; found 281.0928.



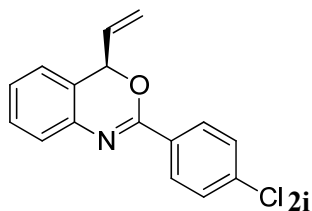
(R)-2-(4-Bromophenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2h)

Synthesized according to general procedure; 90% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 14.67 min, t_R (minor) 17.55 min, ee = 97%; $[\alpha]_D^{20} = -18.4$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.03 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.6 Hz, 2H), 7.38 – 7.28 (m, 2H), 7.21 (td, J = 7.1, 1.9 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.08 (ddd, J = 16.9, 10.4, 6.4 Hz, 1H), 5.86 (d, J = 6.4 Hz, 1H), 5.34 (d, J = 3.6 Hz, 1H), 5.31 (d, J = 10.3 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 155.7, 138.8, 135.3, 131.5, 129.5, 129.2, 126.7, 126.2, 125.0, 124.5, 124.0, 118.6, 77.3. (One resonance is missing due to coincidental overlap)

HRMS (ESI+, m/z) calculated for C₁₆H₁₃BrNO [M + H]⁺ 314.0175; found 314.0187.



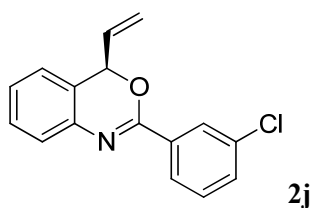
(R)-2-(4-Chlorophenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2i)

Synthesized according to general procedure; 90% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 15.29 min, t_R (minor) 19.18 min, ee = 95%; $[\alpha]_D^{20} = -3.8$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.11 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 8.6 Hz, 2H), 7.37 – 7.28 (m, 2H), 7.21 (td, J = 7.2, 1.9 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 6.09 (ddd, J = 16.9, 10.4, 6.4 Hz, 1H), 5.85 (d, J = 6.4 Hz, 1H), 5.34 (dd, J = 2.0, 1.2 Hz, 1H), 5.31 (d, J = 9.6 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 155.6, 138.8, 137.6, 135.3, 134.7, 131.0, 129.3, 129.2, 128.5, 126.7, 125.0, 124.5, 124.0, 118.5, 77.3.

HRMS (ESI+, m/z) calculated for C₁₆H₁₃ClNO [M + H]⁺ 270.0680; found 270.0688.



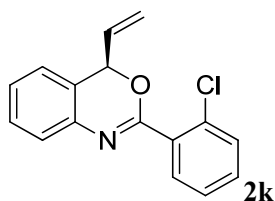
(R)-2-(3-Chlorophenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2j)

Synthesized according to general procedure; 67% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 12.85 min, t_R (minor) 17.61 min, ee = 83%; $[\alpha]_D^{20} = -2.0$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.15 (s, 1H), 8.05 (d, J = 7.8 Hz, 1H), 7.46 (ddd, J = 8.0, 2.1, 1.1 Hz, 1H), 7.41 – 7.29 (m, 3H), 7.22 (ddd, J = 7.5, 6.4, 2.2 Hz, 1H), 7.04 (d, J = 7.3 Hz, 1H), 6.09 (ddd, J = 16.9, 10.4, 6.4 Hz, 1H), 5.87 (d, J = 6.2 Hz, 1H), 5.35 (d, J = 5.1 Hz, 1H), 5.32 (d, J = 11.8 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 155.3, 138.7, 135.2, 134.4, 134.3, 131.3, 129.5, 129.2, 128.0, 126.8, 126.0, 125.1, 124.5, 124.0, 118.7, 77.4.

HRMS (ESI+, m/z) calculated for C₁₆H₁₃ClNO [M + H]⁺ 270.0680; found 270.0689.



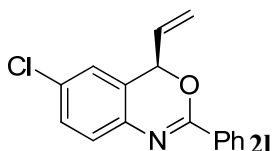
(R)-2-(2-Chlorophenyl)-4-vinyl-4H-benzo[d][1,3]oxazine (2k)

Synthesized according to general procedure; 67% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiracel OD-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 10.54 min, t_R (minor) 15.32 min, ee = 97%; $[\alpha]_D^{20} = +6.0$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.74 (dd, J = 7.5, 1.9 Hz, 1H), 7.44 (dd, J = 7.9, 1.4 Hz, 1H), 7.41 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 7.04 (d, J = 7.4 Hz, 1H), 6.21 (ddd, J = 17.2, 10.3, 7.1 Hz, 1H), 5.92 (d, J = 7.2 Hz, 1H), 5.41 (d, J = 4.5 Hz, 1H), 5.38 (d, J = 11.3 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 157.2, 138.7, 135.0, 133.3, 132.7, 131.3, 131.1, 130.5, 129.2, 127.1, 126.7, 125.0, 124.5, 123.8, 119.6, 78.1.

HRMS (ESI+, m/z) calculated for C₁₆H₁₃ClNO [M + H]⁺ 270.0680; found 270.0689.



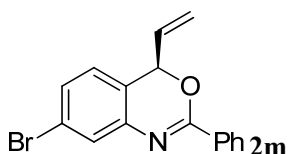
(R)-6-Chloro-2-phenyl-4-vinyl-4H-benzo[d][1,3]oxazine (2l)

Synthesized according to general procedure; 89% yield; yellow oil; enantiomeric excess was determined by HPLC (Chiralpak OB-H), *n*-heptane/*i*-propanol = 98:2, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (minor) 18.33 min, t_R (major) 21.89, ee = 90%; $[\alpha]_D^{20} = -4.4$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 8.15 (d, J = 7.0 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.3 Hz, 2H), 7.34 – 7.21 (m, 2H), 7.03 (d, J = 2.2 Hz, 1H), 6.07 (ddd, J = 16.9, 10.6, 6.5 Hz, 1H), 5.81 (d, J = 6.5 Hz, 1H), 5.39 (s, 1H), 5.35 (d, J = 7.6 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ = 156.8, 137.8, 134.7, 132.1, 131.6, 131.4, 129.1, 128.3, 128.0, 126.2, 125.6, 124.6, 119.1, 77.3, 77.0, 76.8, 76.7.

HRMS (ESI+, m/z) calculated for C₁₆H₁₃ClNO [M + H]⁺ 270.0680; found 270.0688.



(R)-7-Bromo-2-phenyl-4-vinyl-4H-benzo[d][1,3]oxazine (2m)

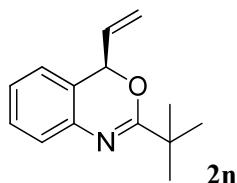
Synthesized according to general procedure; 81% yield; colorless solid, m.p. = 74-76 °C; enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 95:5, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (major) 18.40 min, t_R (minor) 23.22 min, ee = 93%; $[\alpha]_D^{20} = -11.4$ (c 1.0, CHCl₃). The absolute configuration of **2m** was determined as *R* by X-ray crystallographic analysis.^[4]

[4] CCDC 957091 contains the supplementary crystallographic data for **2m**.

^1H NMR (400 MHz, CDCl_3) δ = 8.15 (d, J = 7.0 Hz, 2H), 7.57 – 7.40 (m, 4H), 7.32 (dd, J = 8.0, 2.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.06 (ddd, J = 16.9, 10.4, 6.4 Hz, 1H), 5.82 (d, J = 6.4 Hz, 1H), 5.39 – 5.35 (m, 1H), 5.32 (d, J = 9.8 Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3) δ = 157.5, 140.7, 134.9, 132.1, 131.8, 129.2, 128.3, 128.3, 128.1, 127.9, 125.9, 123.0, 122.4, 118.9, 77.0.

HRMS (ESI+, m/z) calculated for $\text{C}_{16}\text{H}_{13}\text{BrNO}$ $[\text{M} + \text{H}]^+$ 314.0175; found 314.0186.



(*R*)-2-(*tert*-Butyl)-4-vinyl-4*H*-benzo[*d*][1,3]oxazine (2n)

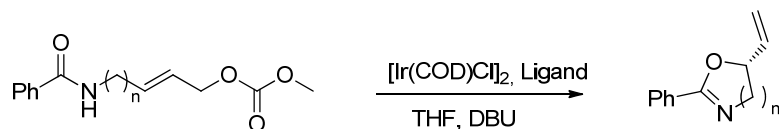
Synthesized according to general procedure; 63% yield; yellow oil; enantiomeric excess was determined by Chiralsil Dex CB (25 m x 0.25 mm x 0.25 μm), (initial temp. 40 $^\circ\text{C}$, gradient 10 $^\circ\text{C}/\text{min}$ to 120 $^\circ\text{C}$), retention time: t_{R} (minor) 35.48 min, t_{R} (major) 35.93 min, ee = 86%; $[\alpha]_{\text{D}}^{20}$ = +41.8 (c 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.31 – 7.23 (m, 1H), 7.19 (d, J = 7.7 Hz, 1H), 7.14 (td, J = 7.4, 1.3 Hz, 1H), 6.95 (d, J = 7.5 Hz, 1H), 6.03 (ddd, J = 17.0, 10.3, 6.7 Hz, 1H), 5.63 (d, J = 6.7 Hz, 1H), 5.28 (d, J = 10.2 Hz, 1H), 5.22 (d, J = 17.1 Hz, 1H), 1.26 (s, 9H).

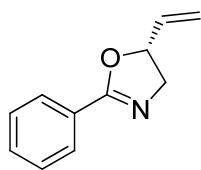
^{13}C NMR (101 MHz, CDCl_3) δ = 167.9, 138.9, 135.6, 128.9, 126.0, 124.6, 124.5, 123.7, 118.4, 76.7, 37.3, 27.6.

HRMS (ESI+, m/z) calculated for $\text{C}_{14}\text{H}_{18}\text{NO}$ $[\text{M} + \text{H}]^+$ 216.1383; found 216.1388.

General Procedure for the Iridium-catalyzed asymmetric allylic cyclization of 1o and 1p:



To a suspension of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.3 mg, 2.5 mol%) and **L7** (4.47 mg, 5.0 mol%) in 2.0 mL dry THF was added 0.5 eq. DBU (8 μL , 0.1 mmol) under a N_2 atmosphere. Then the reaction mixture was heated at 50 $^\circ\text{C}$ for 30 min to generate the catalyst. After cooling down to room temperature, the corresponding allylic carbonate (0.2 mmol) was added and the reaction mixture was stirred at rt for 24 h until TLC showed full conversion. The reaction was quenched by H_2O and extracted with ether. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column chromatography (Pentane/EtOAc = 10:1 to 4:1) to yield the desired product.



2o

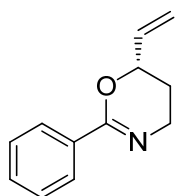
(R)-2-phenyl-5-vinyl-4,5-dihydrooxazole

Synthesized according to general procedure; 60% yield; pale yellow oil; enantiomeric excess was determined by HPLC (Chiracel OD-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (minor) 9.9 min, t_R (major) 18.5 min, ee = 95%; $[\alpha]_D^{20} = -56.0$ (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, $J = 7.3$ Hz, 2H), 7.47 (t, $J = 7.3$ Hz, 1H), 7.41 (t, $J = 7.4$ Hz, 2H), 5.96 (ddd, $J = 17.2, 10.3, 6.9$ Hz, 1H), 5.38 (d, $J = 17.1$ Hz, 1H), 5.25 (d, $J = 10.4$ Hz, 1H), 5.18 – 5.02 (m, 1H), 4.21 (dd, $J = 14.6, 9.9$ Hz, 1H), 3.78 (dd, $J = 14.6, 7.9$ Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 163.9, 136.3, 131.3, 128.3, 128.2, 127.6, 117.3, 80.5, 60.4.

HRMS (ESI+, m/z) calculated for C₁₁H₁₂NO [M + H]⁺ 174.09134; found 174.09135.



2p

(S)-2-phenyl-6-vinyl-5,6-dihydro-4H-1,3-oxazine

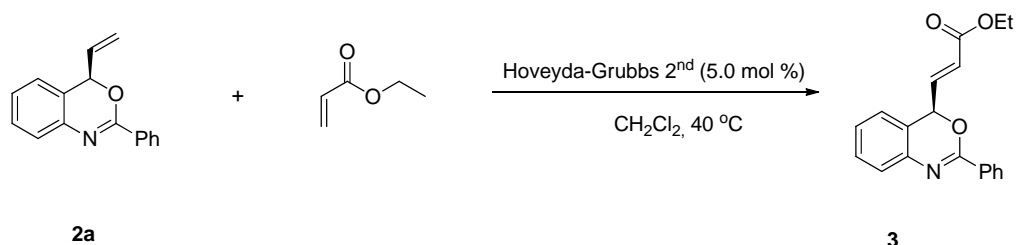
Synthesized according to general procedure; 67% yield; pale yellow oil; enantiomeric excess was determined by HPLC (Chiracel OD-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 1.0 mL/min, retention times: t_R (minor) 4.6 min, t_R (major) 6.3 min, ee = 92%; $[\alpha]_D^{20} = +25.1$ (c 2.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, $J = 6.8$ Hz, 2H), 7.42 – 7.23 (m, 3H), 5.89 (ddd, $J = 17.2, 10.6, 5.3$ Hz, 1H), 5.32 (dt, $J = 17.2, 1.3$ Hz, 1H), 5.21 (dt, $J = 10.6, 1.2$ Hz, 1H), 4.79 – 4.65 (m, 1H), 3.64 – 3.47 (m, 2H), 1.98 (dq, $J = 13.3, 4.7$, 1H), 1.72 (dtd, $J = 14.1, 8.6, 5.7$, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 155.4, 136.6, 133.8, 130.4, 128.0, 126.9, 116.3, 74.9, 41.9, 26.9.

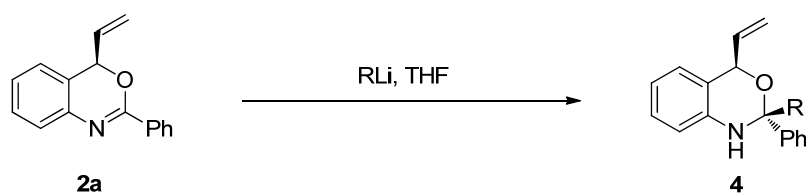
HRMS (ESI+, m/z) calculated for C₁₂H₁₄NO [M + H]⁺ 188.10699; found 188.10697.

Procedure for cross metathesis of **2a**.

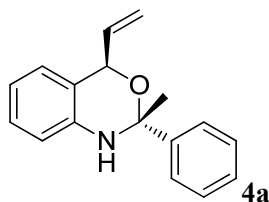


To a solution of **2a** (0.2 mmol, 47.5 mg) and ethyl acrylate (0.6 mmol, 64 μ L) in dry dichloromethane (2 mL), HG-II catalyst (6.3 mg, 0.01 mmol, 5 mol%) was added and the mixture was heated at reflux for 18 h. The mixture was cooled down to room temperature and the solvent was removed under reduced pressure to yield the crude product which was purified by silica gel chromatography (EtOAc/Pentane 1:10) affording **3** in 70 % yield as colorless oil. Enantiomeric excess was determined by HPLC (Chiralpak AD-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_r (minor) 11.16 min, t_r (major) 12.07 min, ee = 90%; $[\alpha]_D^{20} = -85.6$ (c 1.0, CHCl_3). ^1H NMR (400 MHz, CDCl_3) $\delta = 8.18$ (d, $J = 8.4$ Hz, 2H), 7.55 – 7.50 (m, 1H), 7.49 – 7.43 (m, 2H), 7.40 – 7.31 (m, 2H), 7.25 – 7.19 (m, 1H), 7.12 – 7.01 (m, 2H), 6.06 (d, $J = 5.4$ Hz, 1H), 5.99 (d, $J = 15.7$ Hz, 1H), 4.17 (q, $J = 7.1$ Hz, 2H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) $\delta = 165.7, 155.8, 143.4, 138.7, 132.0, 131.7, 129.6, 128.4, 128.3, 128.0, 126.8, 125.4, 124.4, 122.7, 122.4, 74.9, 60.8, 14.1$. HRMS (ESI+, m/z) calculated for $\text{C}_{19}\text{H}_{18}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 308.1282; found 308.1281.

Procedure for the addition of organolithium reagent to benzoxazine.

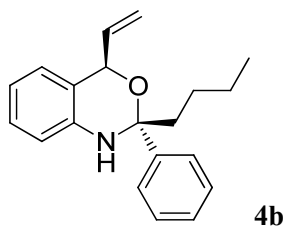


General procedure for the addition of organolithium reagents to benzoxazine: To a solution of the **2a** (40 mg, 0.17 mmol) in THF (2 mL) was added the corresponding organolithium reagent at -78 °C (-40 °C for MeLi·LiBr). The mixture was allowed to gradually warm to RT (0 °C for MeLi·LiBr). After the reaction is completed as monitored by TLC, the reaction was quenched with water (2 mL) and the mixture extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column chromatography (Pentane/EtOAc = 15:1) to yield the desired product.



(2*R*,4*R*)-2-Methyl-2-phenyl-4-vinyl-2,4-dihydro-1*H*-benzo[*d*][1,3]oxazine (4a)

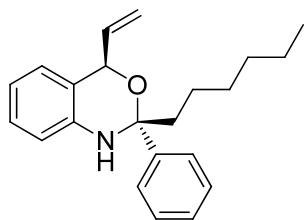
Synthesized according to the general procedure for the addition of organolithium reagents to benzoxazine. **2a** was treated with 1.5 eq of MeLi·LiBr and the mixture was allowed to gradually warm to 0 °C in 3 h. The product was obtained in 67% yield as white solid, m.p. = 122-124 °C. Enantiomeric excess was determined by HPLC (Chiralpak OJ-H), *n*-heptane/*i*-propanol = 90:10, 40 °C, 254 nm, 0.5 mL/min, retention times: t_R (minor) 13.0 min, t_R (major) 17.0 min, ee = 96%; $[\alpha]_D^{20} = +200.0$ (c 1.04, CHCl₃). The relative configuration of **4a** was determined by X-ray analysis^[5] and NOESY experiment. ¹H NMR (500 MHz, CDCl₃) δ = 7.54 (d, J = 7.3 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.3 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 8.0 Hz, 2H), 6.72 (t, J = 7.5 Hz, 1H), 6.03 – 5.83 (m, 1H), 5.39 (s, 1H), 5.36 (d, J = 5.9 Hz, 1H), 4.74 (d, J = 8.1 Hz, 1H), 4.47 (s, 1H), 1.75 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ = 144.1, 140.2, 137.3, 128.5, 127.8, 127.6, 126.7, 125.9, 123.3, 119.4, 119.0, 116.4, 85.5, 74.0, 31.9. HRMS (ESI+, m/z) calculated for C₁₇H₁₈NO [M + H]⁺ 252.1383; found 252.1383.



(2*R*,4*R*)-2-Butyl-2-phenyl-4-vinyl-2,4-dihydro-1*H*-benzo[*d*][1,3]oxazine (4b)

Synthesized according to the general procedure for the addition of organolithium reagents to benzoxazine. **2a** was treated with 1.1 eq of *n*BuLi at -78 °C and the reaction mixture was allowed to gradually warm to room temperature overnight. The product was obtained in 70% yield as a colorless oil. $[\alpha]_D^{20} = +262.0$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ = 7.50 (d, J = 7.1 Hz, 2H), 7.32 (t, J = 7.3 Hz, 2H), 7.25 (t, J = 7.2 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 6.80 (d, J = 8.2 Hz, 2H), 6.71 (t, J = 7.5 Hz, 1H), 5.94 (ddd, J = 11.3, 9.6, 8.1 Hz, 1H), 5.39 (d, J = 4.5 Hz, 1H), 5.35 (s, 1H), 4.79 (d, J = 8.1 Hz, 1H), 4.48 (brs, 1H), 2.10 – 1.99 (m, 1H), 1.99 – 1.88 (m, 1H), 1.56 – 1.38 (m, 1H), 1.38 – 1.23 (m, 2H), 1.22 – 1.09 (m, 1H), 0.87 (t, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ = 143.5, 140.3, 137.4, 128.4, 127.7, 127.5, 127.2, 125.9, 123.4, 119.1, 118.8, 116.3, 87.5, 73.7, 44.0, 25.4, 22.8, 13.9. HRMS (ESI+, m/z) calculated for C₂₀H₂₄NO₃ [M + H]⁺ 294.1852; found 294.1854.

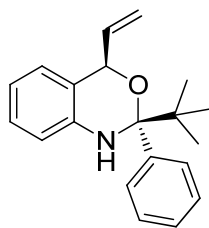
[5] CCDC 957090 contains the supplementary crystallographic data for **4a**.



4c

(2*R*,4*R*)-2-hexyl-2-phenyl-4-vinyl-2,4-dihydro-1*H*-benzo[*d*][1,3]oxazine (4c)

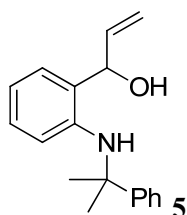
Synthesized according to the general procedure for the addition of organolithium reagents to benzoxazine. **2a** was treated with 1.1 eq of *n*-hexylLi at -78 °C and the mixture was allowed to gradually warm to room temperature overnight. The product was obtained in 73% yield as a colorless oil. $[\alpha]_D^{20} = +166.7$ (c 1.04, CHCl₃). ¹H NMR (400 MHz, CDCl₃) $\delta = 7.49$ (d, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 6.81 (t, *J* = 8.5 Hz, 2H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.01 – 5.80 (m, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 5.34 (s, 1H), 4.78 (d, *J* = 8.0 Hz, 1H), 4.47 (brs, 1H), 2.02 (ddd, *J* = 13.7, 11.8, 5.0 Hz, 1H), 1.97 – 1.87 (m, 1H), 1.53 – 1.39 (m, 1H), 1.37 – 1.02 (m, 7H), 0.85 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) $\delta = 143.5, 140.3, 137.4, 128.4, 127.7, 127.5, 127.2, 125.9, 123.4, 119.0, 118.8, 116.3, 87.5, 73.7, 44.2, 31.6, 29.4, 23.2, 22.5, 14.0$. HRMS (ESI+, *m/z*) calculated for C₂₂H₂₈NO [M + H]⁺ 322.2165; found 322.2166.



4d

(2*R*,4*R*)-2-(*tert*-Butyl)-2-phenyl-4-vinyl-2,4-dihydro-1*H*-benzo[*d*][1,3]oxazine (4d)

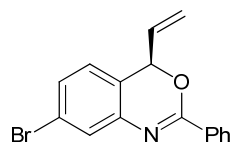
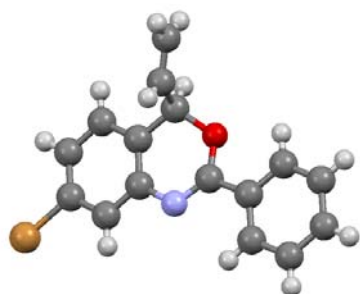
Synthesized according to the general procedure for the addition of organolithium reagents to benzoxazine. **2a** was treated with 1.1 eq of *t*BuLi at -78 °C and the mixture was allowed to gradually warm to room temperature overnight. The product was obtained in 42% yield as a colorless oil. $[\alpha]_D^{20} = +89.4$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) $\delta = 7.49$ (d, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 6.64 (t, *J* = 7.4 Hz, 1H), 5.99 (ddd, *J* = 17.5, 10.1, 7.6 Hz, 1H), 5.43 (dd, *J* = 17.1, 0.7 Hz, 1H), 5.35 (dd, *J* = 10.1, 1.5 Hz, 1H), 4.98 (d, *J* = 7.5 Hz, 1H), 4.74 (brs, 1H), 1.03 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) $\delta = 140.8, 140.7, 137.7, 129.5, 127.5, 127.4, 127.3, 125.5, 123.0, 118.0, 117.8, 115.6, 90.6, 73.3, 39.2, 25.1$. HRMS (ESI+, *m/z*) calculated for C₂₀H₂₄NO₃ [M + H]⁺ 294.1852; found 294.1855.



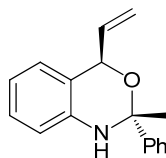
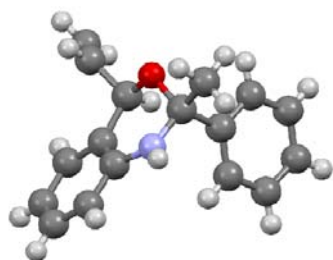
1-(2-((2-Phenylpropan-2-yl)amino)phenyl)prop-2-en-1-ol (**5**)

To a solution of the **2a** (40 mg, 0.17 mmol) in THF (2 mL) was added the MeLi·LiBr (0.51 mmol, 3.0 eq) at -40 °C. The mixture was allowed to gradually warm to RT. After stirring at RT for 3 h, the reaction was quenched with water (2 ml) and the mixture extracted with CH₂Cl₂ (3 x 5 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by silica gel column chromatography (Pentane/EtOAc = 10:1) to yield **5** as colorless oil in 40% yield. ¹H NMR (400 MHz, CHCl₃) δ = 7.46 (d, *J* = 7.1 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.07 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.86 (ddd, *J* = 8.2, 7.3, 1.7 Hz, 1H), 6.56 (td, *J* = 7.4, 1.1 Hz, 1H), 6.27 (ddd, *J* = 17.2, 10.5, 4.9 Hz, 1H), 6.09 (d, *J* = 8.3 Hz, 1H), 5.47 (d, *J* = 17.3 Hz, 1H), 5.35 (dt, *J* = 10.5, 1.6 Hz, 1H), 5.30 (d, *J* = 5.0 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H). ¹³C NMR (101 MHz, CHCl₃) δ = 147.6, 144.6, 138.4, 128.5, 128.3, 128.2, 126.2, 125.6, 125.4, 115.9, 115.3, 115.2, 75.3, 55.6, 30.9, 30.5. HRMS (ESI+, *m/z*) calculated for C₁₈H₂₂NO [M + H]⁺ 268.1689; found 268.1696.

X-ray analysis of **2m** and **4a**: Determination of Relative and Absolute Configuration



2m



4a

Crystal structure determination of 2m

Crystal data. $C_{16}H_{12}BrNO$, Fw = 314.18, colourless plate, 0.21 x 0.10 x 0.09 mm³, triclinic, P₁ (no. 1), a = 6.3154(5), b = 8.1371(7), c = 14.3362(12) Å, α = 85.222(3), β = 78.520(3), γ = 70.043°, V = 678.53(10) Å³, Z = 2, D_x = 1.538 g/cm³, μ = 3.019 mm⁻¹. 31603 Reflections were measured on a Bruker D8 Venture diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å) up to a resolution of $(\sin \theta/\lambda)_{\max}$ = 0.64 Å⁻¹ at a temperature of 293(2) K. Data collection and reduction was done using the Bruker software suite APEX2.^[6] Intensity data were integrated with the SAINT V8.27B software.^[4] Absorption correction and scaling was performed based on multiple measured reflections with SADABS (0.5697 – 0.7728 correction range).^[4] 5756 Reflections were unique (R_{int} = 0.0311), of which 4785 were observed [$I > 2\sigma(I)$]. The structure was solved with Direct Methods using the program SHELXS-97^[5] and refined with SHELXL-97^[7] against F^2 of all reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located in difference Fourier maps and refined with a riding model. 319 Parameters were refined with 17 restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0552 / 0.1339. R1/wR2 [all refl.]: 0.0675 / 0.1434. S = 1.046. Flack parameter^[8] x = 0.007(11). Residual electron density between –0.27 and 1.17 e/Å³. Geometry calculations and checking for higher symmetry was performed with the PLATON program.^[9]

Crystal structure determination of 4a

Crystal data. $C_{17}H_{17}NO$, Fw = 251.32, colourless plate, 0.27 x 0.10 x 0.03 mm³, orthorhombic, P2₁2₁2₁ (no. 19), a = 8.2349(3), b = 12.5658(4), c = 12.9900(5) Å, V = 1344.18(8) Å³, Z = 4, D_x = 1.242 g/cm³, μ = 0.077 mm⁻¹. 55490 Reflections were measured on a Bruker D8 Venture diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å) up to a resolution of $(\sin \theta/\lambda)_{\max}$ = 0.64 Å⁻¹ at a temperature of 100(2) K. Data collection and reduction was done using the Bruker software suite APEX2.^[4] Intensity data were integrated with the SAINT V8.27B software.^[4] Absorption correction and scaling was performed based on multiple measured reflections with SADABS (0.9796 – 0.9977 correction range). 2992 Reflections were unique (R_{int} = 0.0321), of which 2861 were observed [$I > 2\sigma(I)$]. The structure was solved with Direct Methods using the program SHELXS-97^[5] and refined with SHELXL-97^[5] against F^2 of all reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located in difference Fourier maps and refined with a riding model. 173 Parameters were refined with no restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0325 / 0.0820. R1/wR2 [all refl.]: 0.0347 / 0.836. S = 1.090. Residual electron density between –0.30 and 0.29 e/Å³. Geometry calculations and checking for higher symmetry was performed with the PLATON program.^[7]

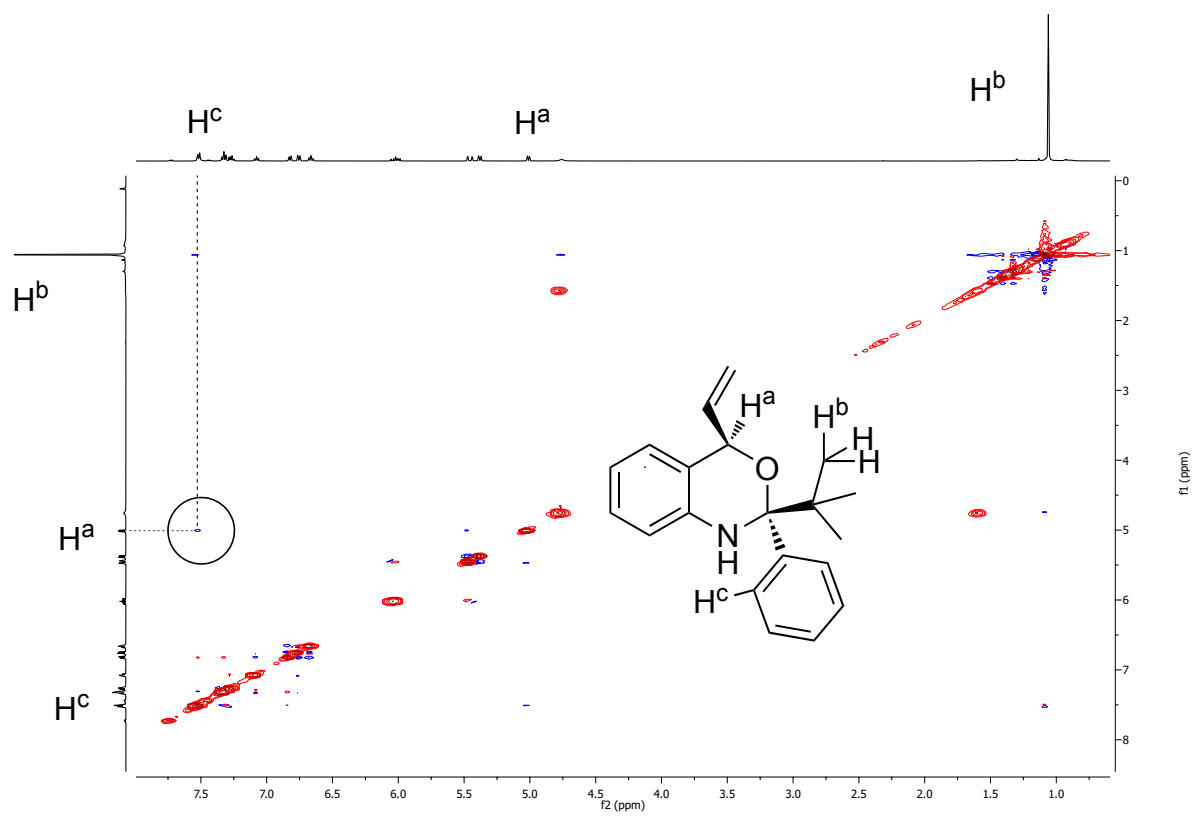
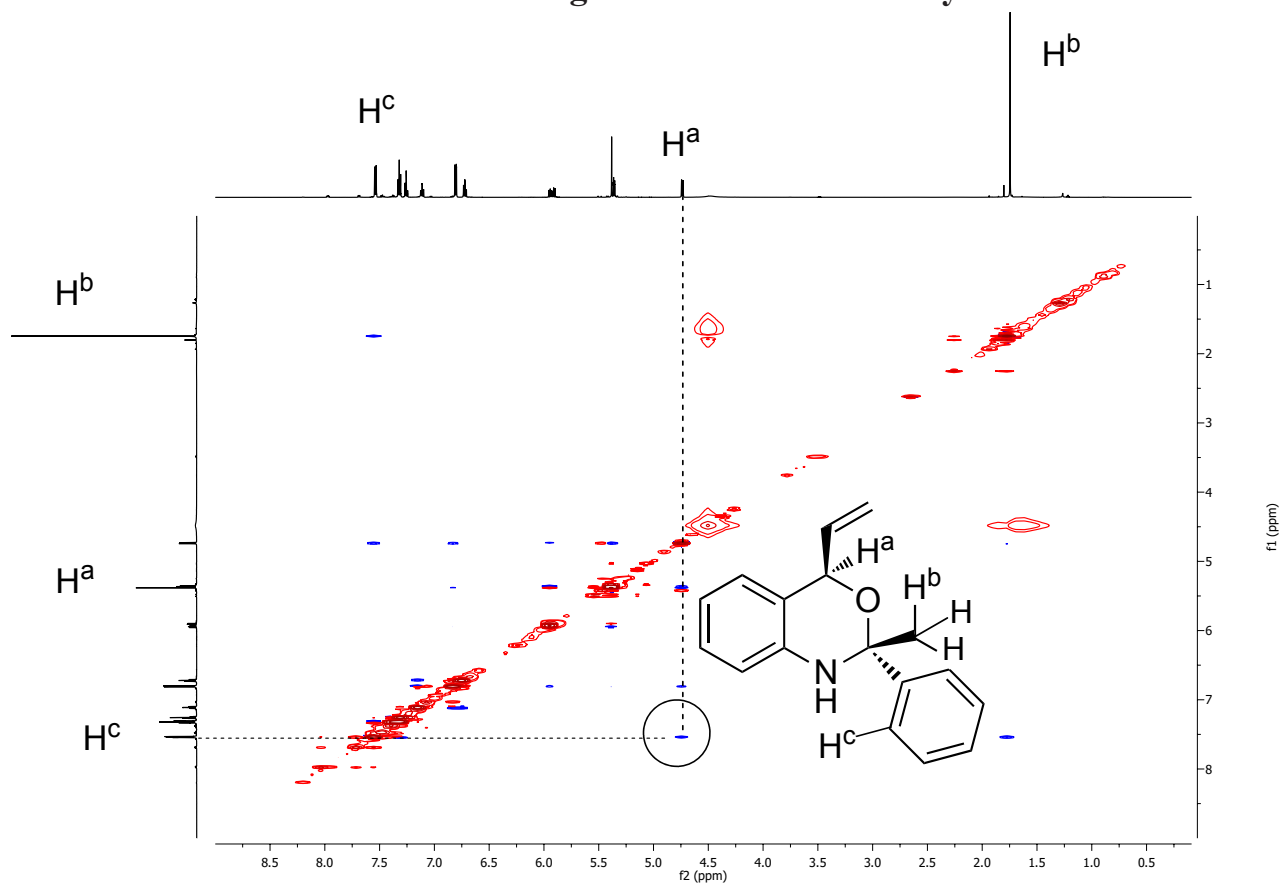
[6] Bruker, (2012). APEX2 (v2012.4-3), SAINT (Version 8.27B) and SADABS (Version 2012/1). Bruker AXS Inc., Madison, Wisconsin, USA.

[7] G. M. Sheldrick, *Acta Cryst.* **2008**, A64, 112.

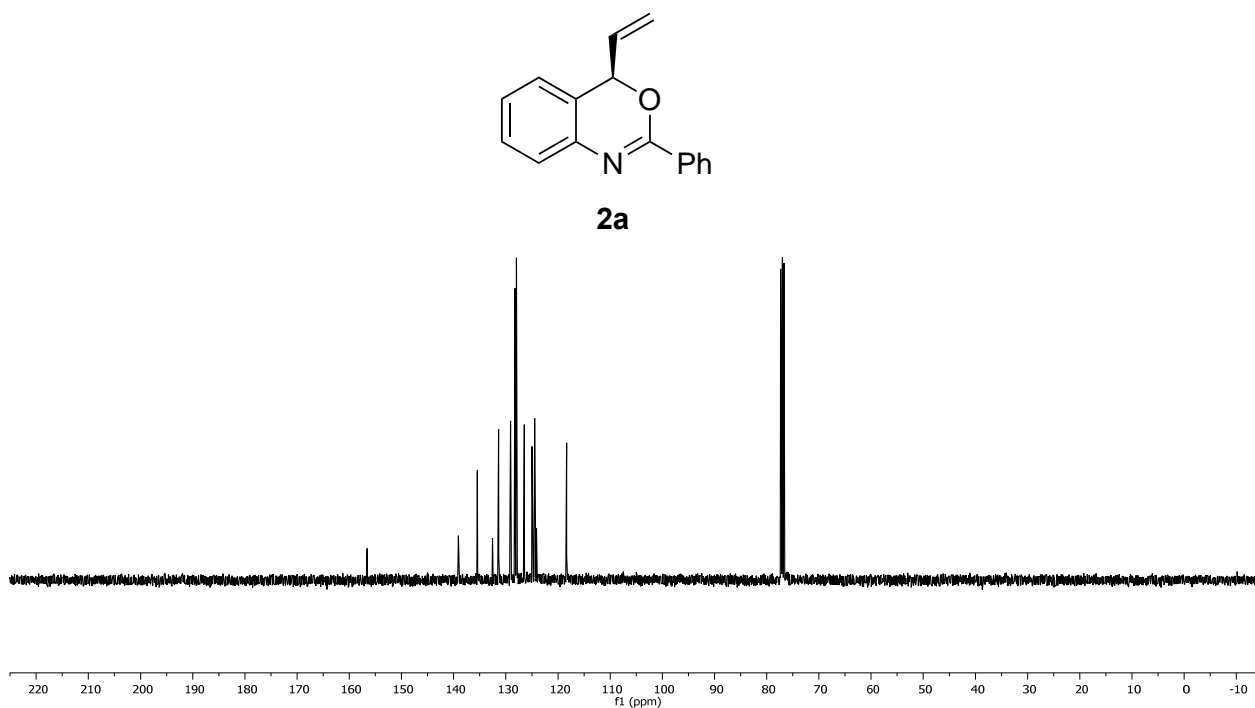
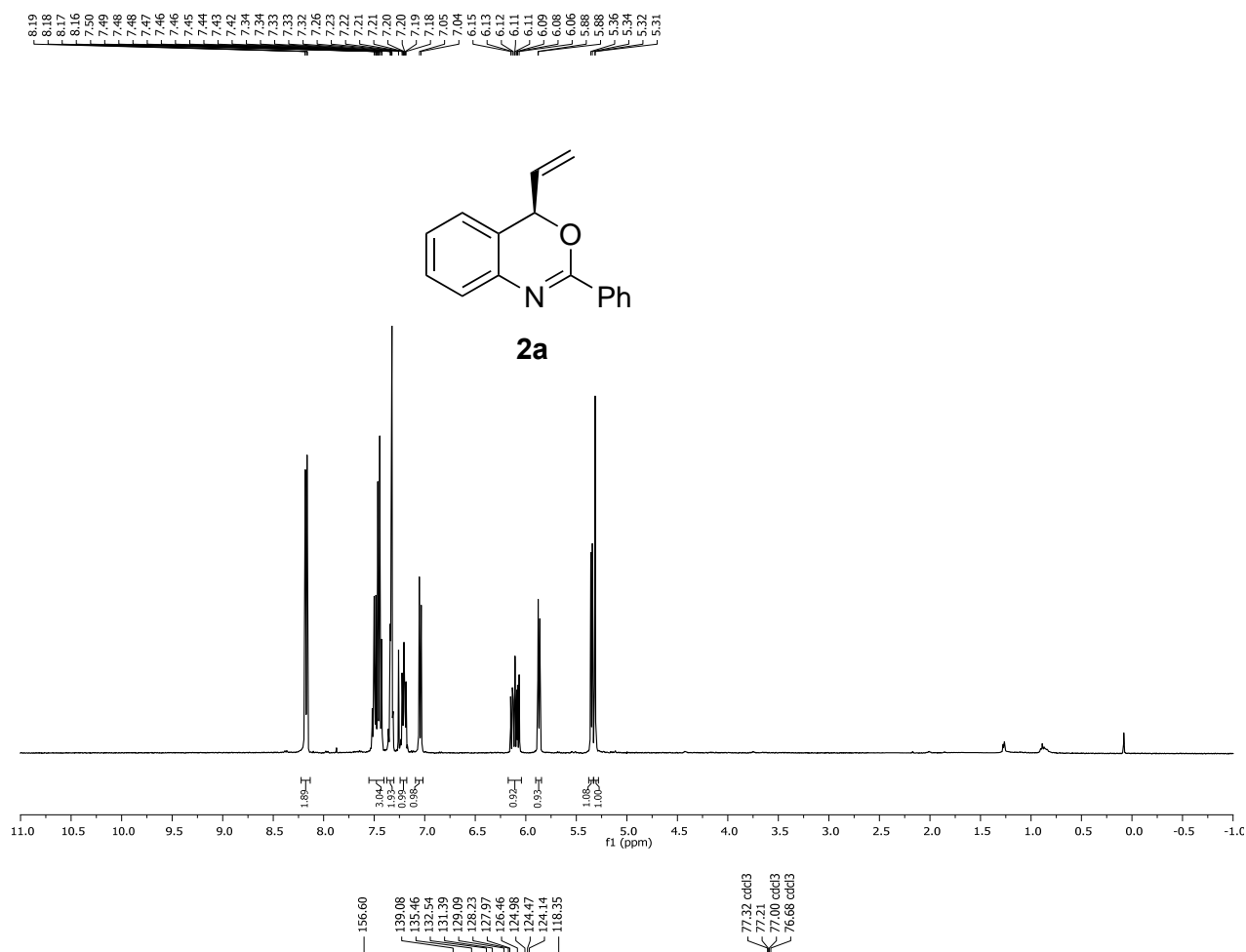
[8] H. D. Flack, *Acta Cryst.* **1983**, A39, 876.

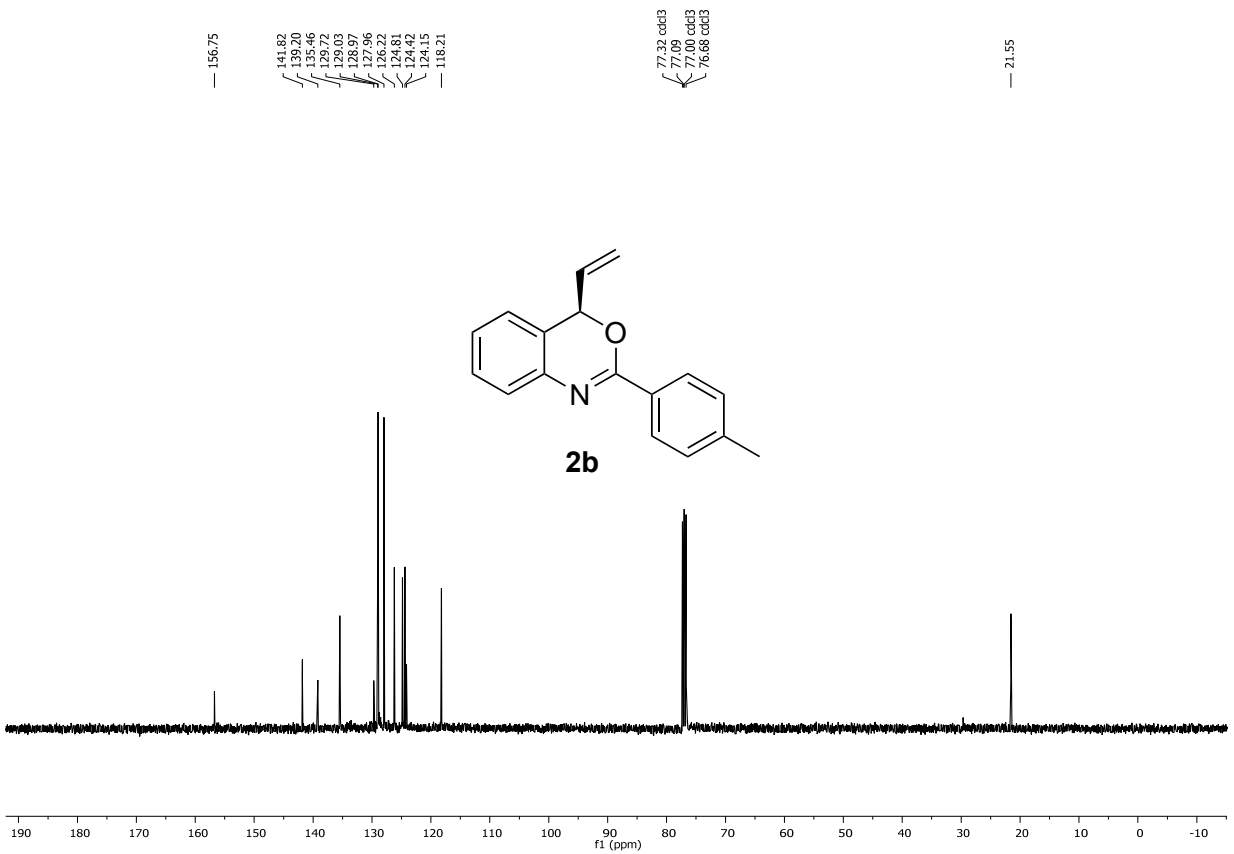
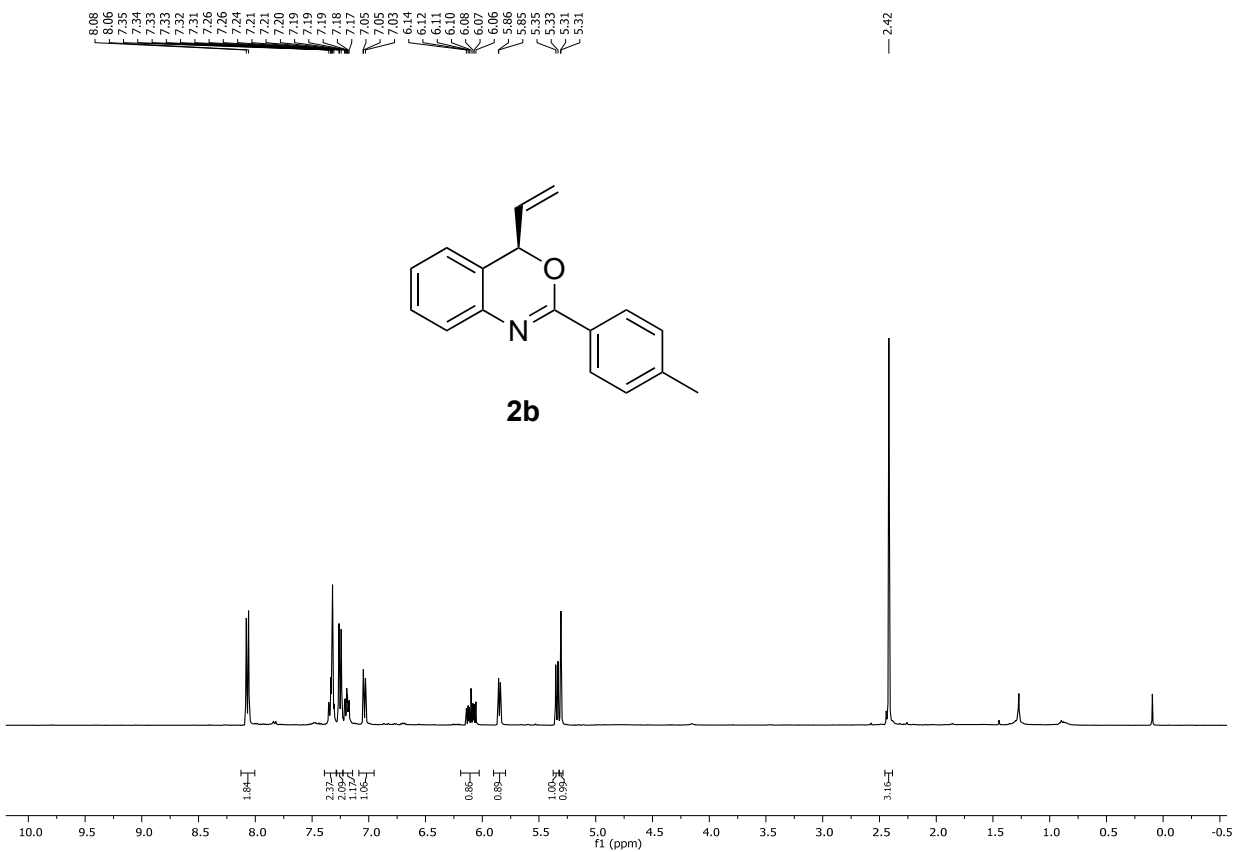
[9] A. L. Spek, *Acta Cryst.* **2009**, D65, 148.

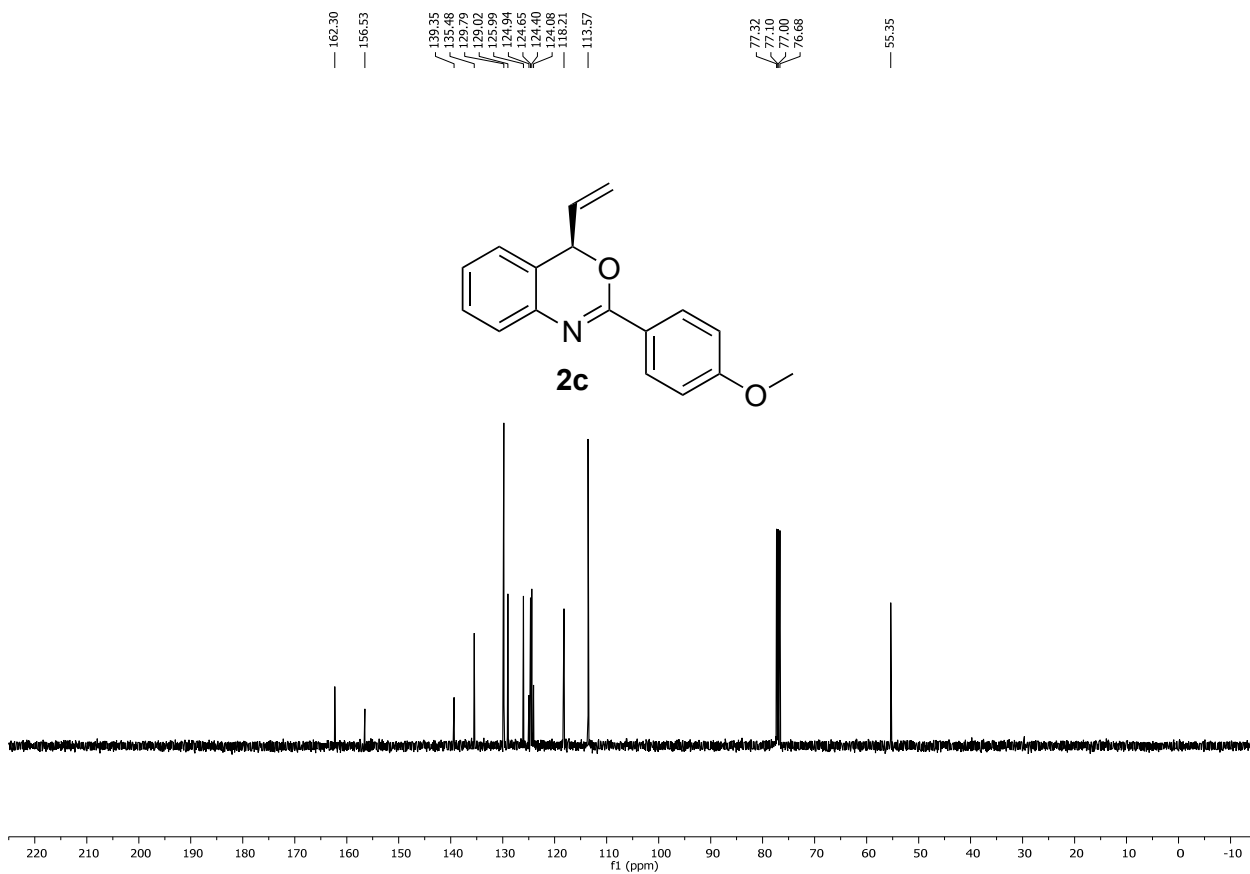
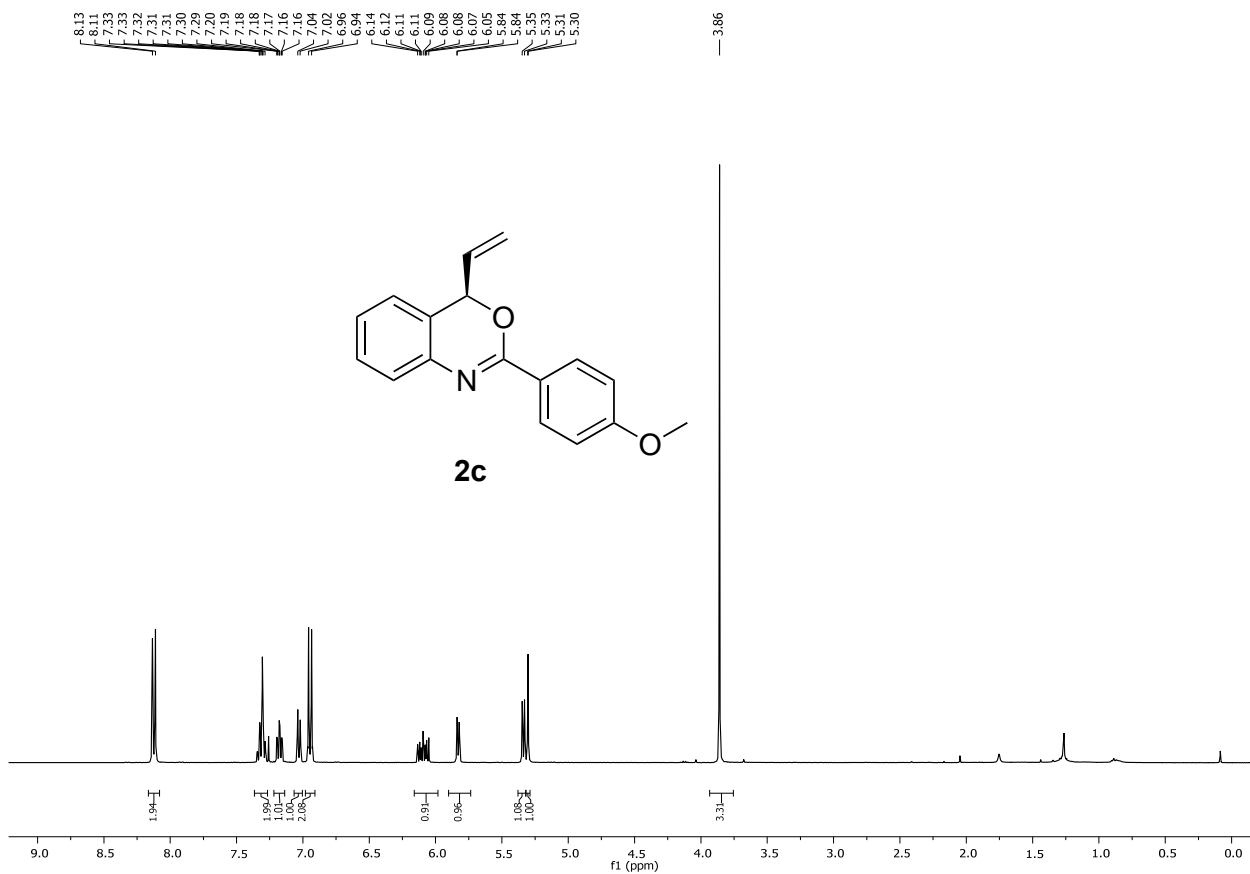
Determination of the relative configuration of 4a and 4d by NOESY

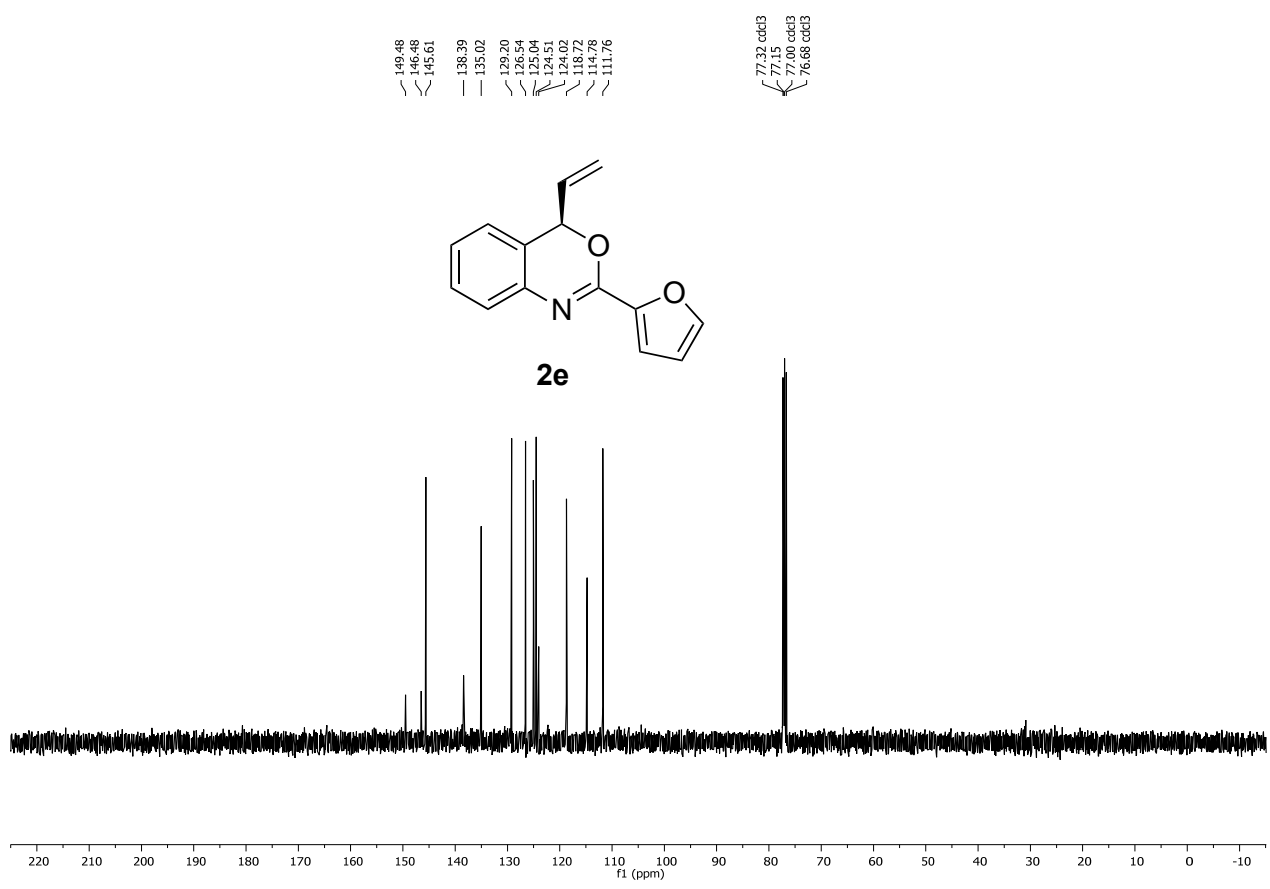
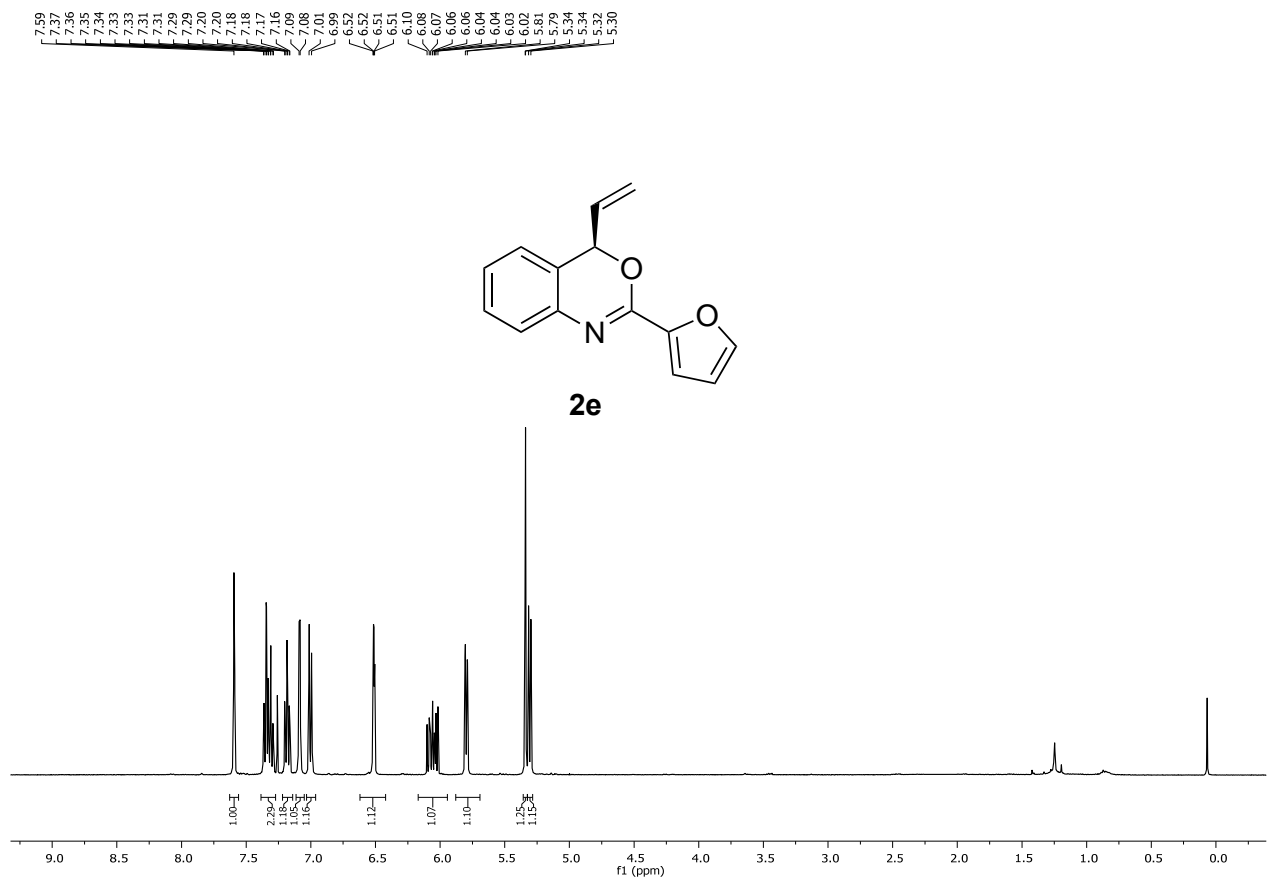


Copies of NMR spectra

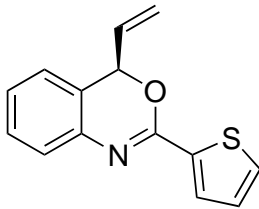




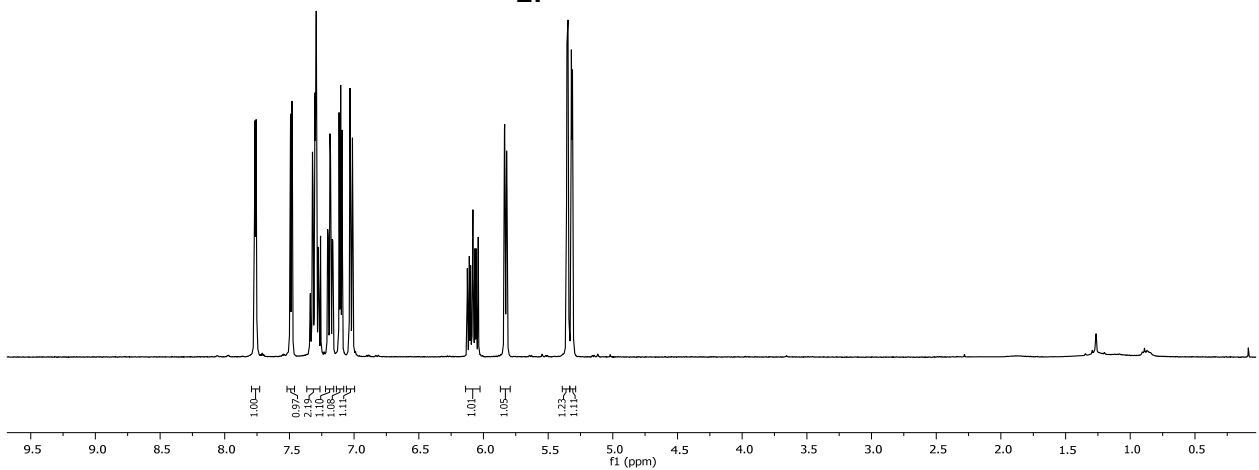




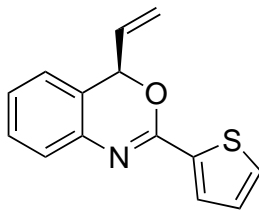
7.77
7.76
7.76
7.49
7.49
7.48
7.48
7.34
7.34
7.32
7.32
7.30
7.30
7.29
7.29
7.28
7.27
7.20
7.20
7.19
7.18
7.17
7.16
7.12
7.11
7.11
7.09
7.09
7.01
7.01
6.12
6.11
6.10
6.08
6.07
6.06
6.04
5.84
5.82
5.35
5.32
5.31



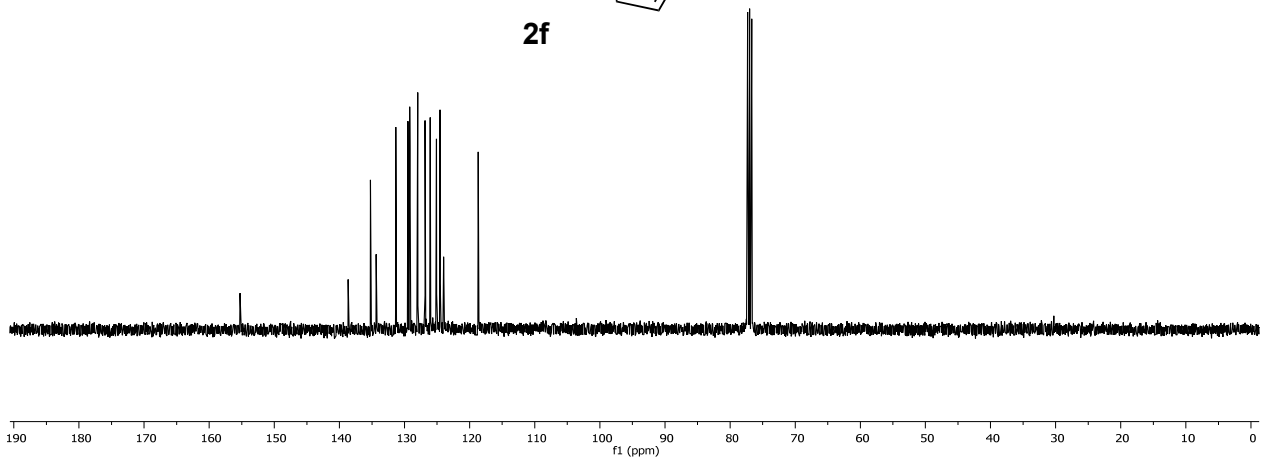
2f



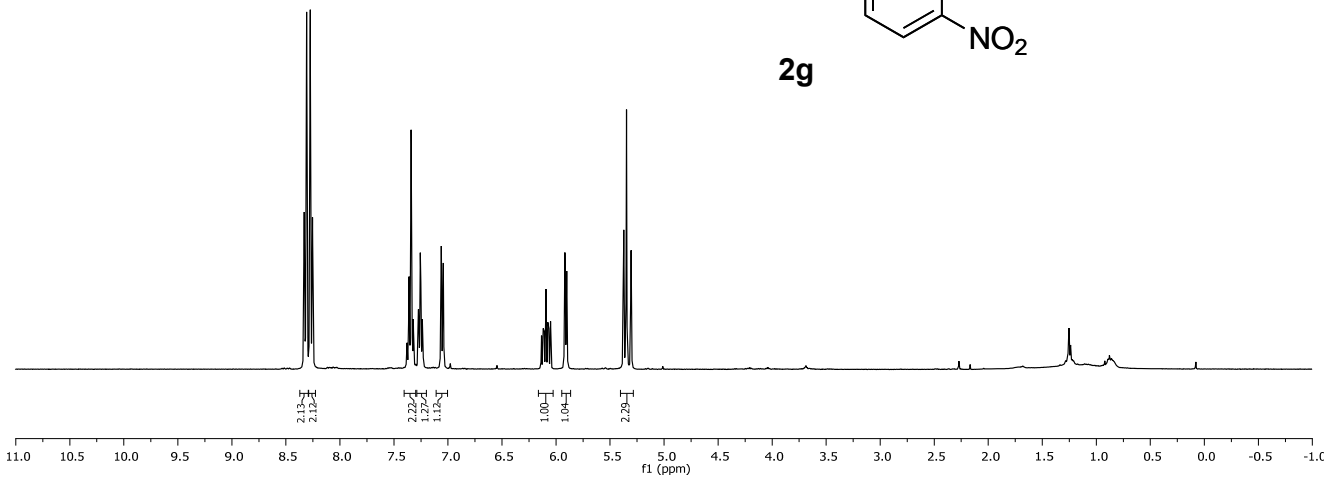
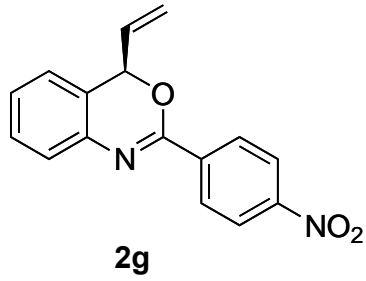
155.28
138.65
137.22
136.74
134.34
131.34
129.49
129.19
127.97
126.85
126.04
125.09
124.54
123.99
116.68
77.41
77.32 cd13
77.00 cd13
76.68 cd13



2f

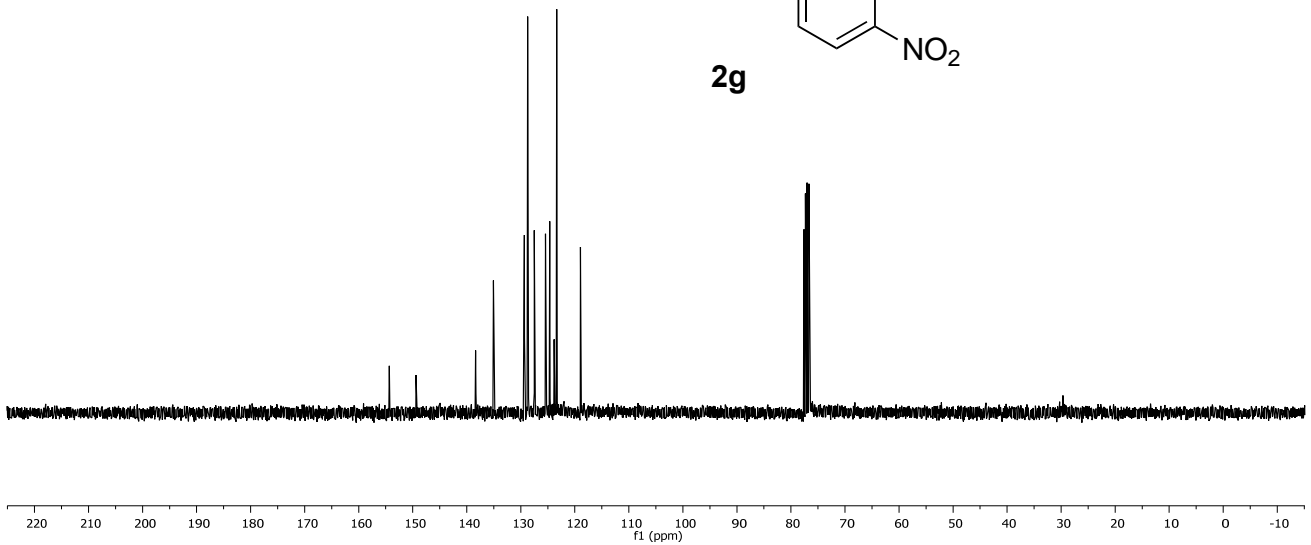
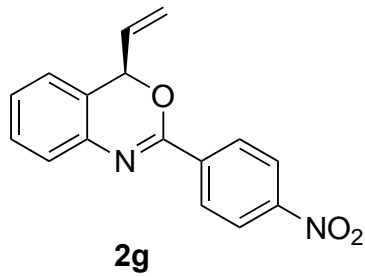


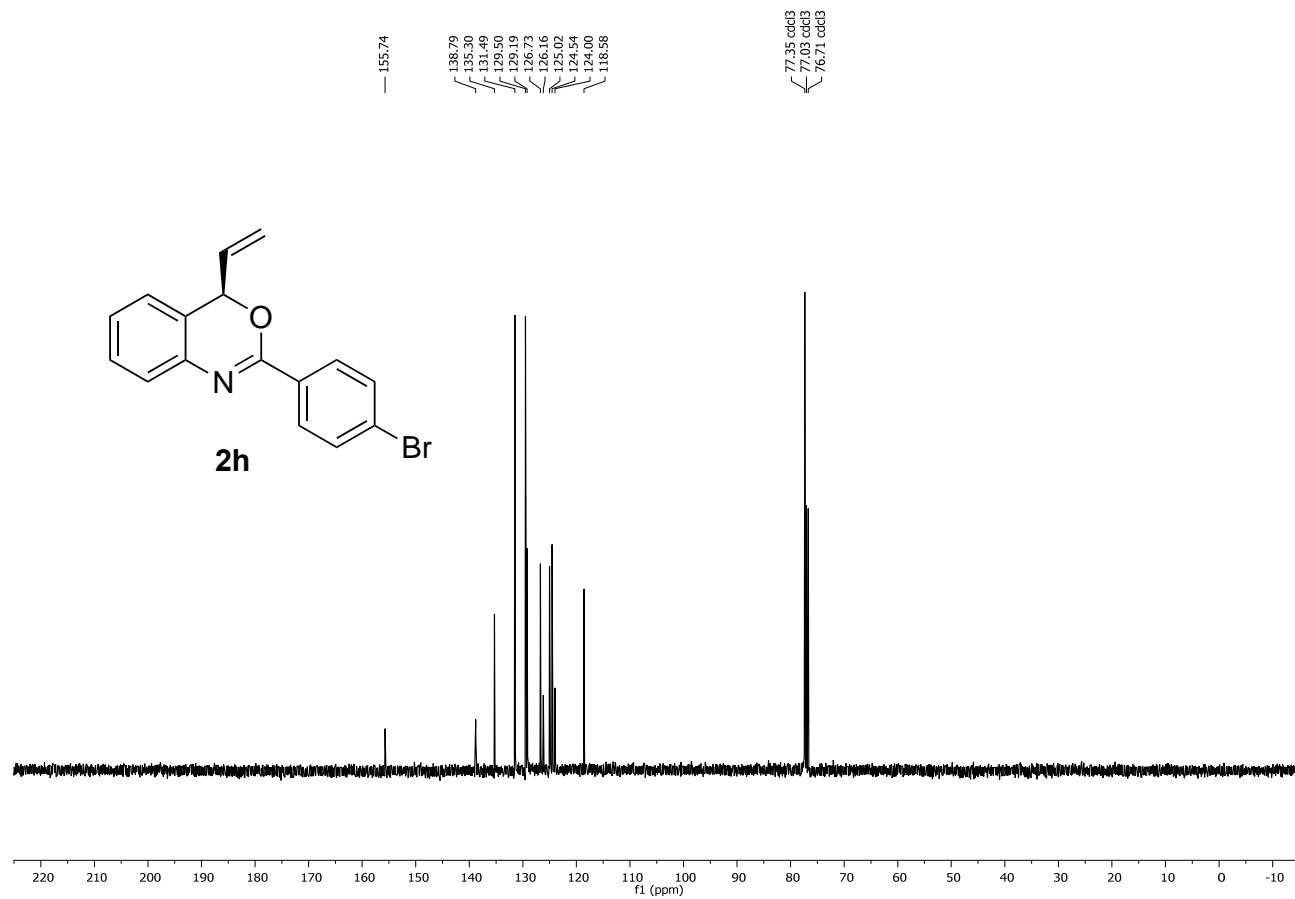
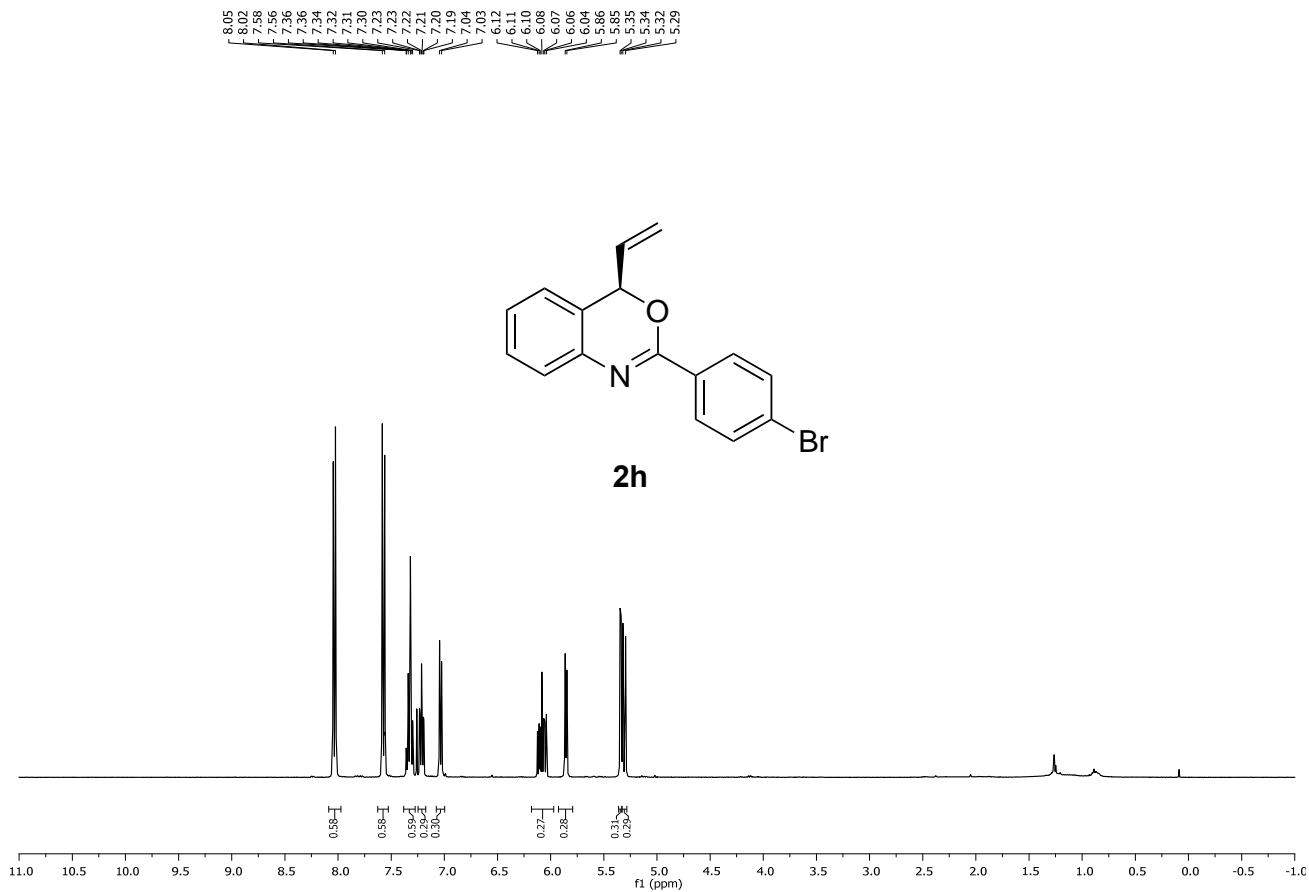
8.33
8.31
8.28
8.25
7.38
7.36
7.34
7.33
7.27
7.27
7.26
7.25
7.24
7.23
7.06
7.04
6.14
6.12
6.11
6.09
6.08
6.07
6.05
5.92
5.90
5.37
5.35
5.30

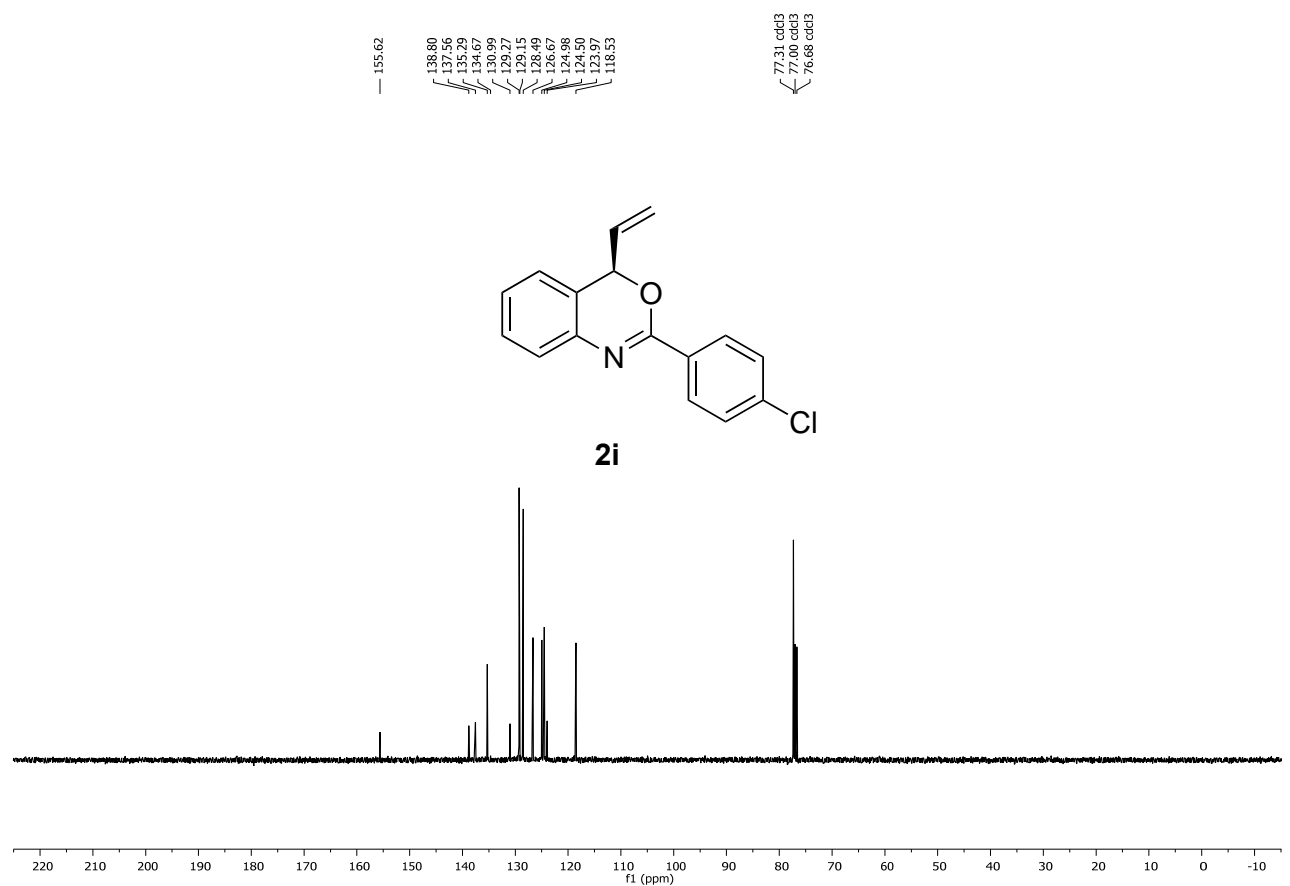
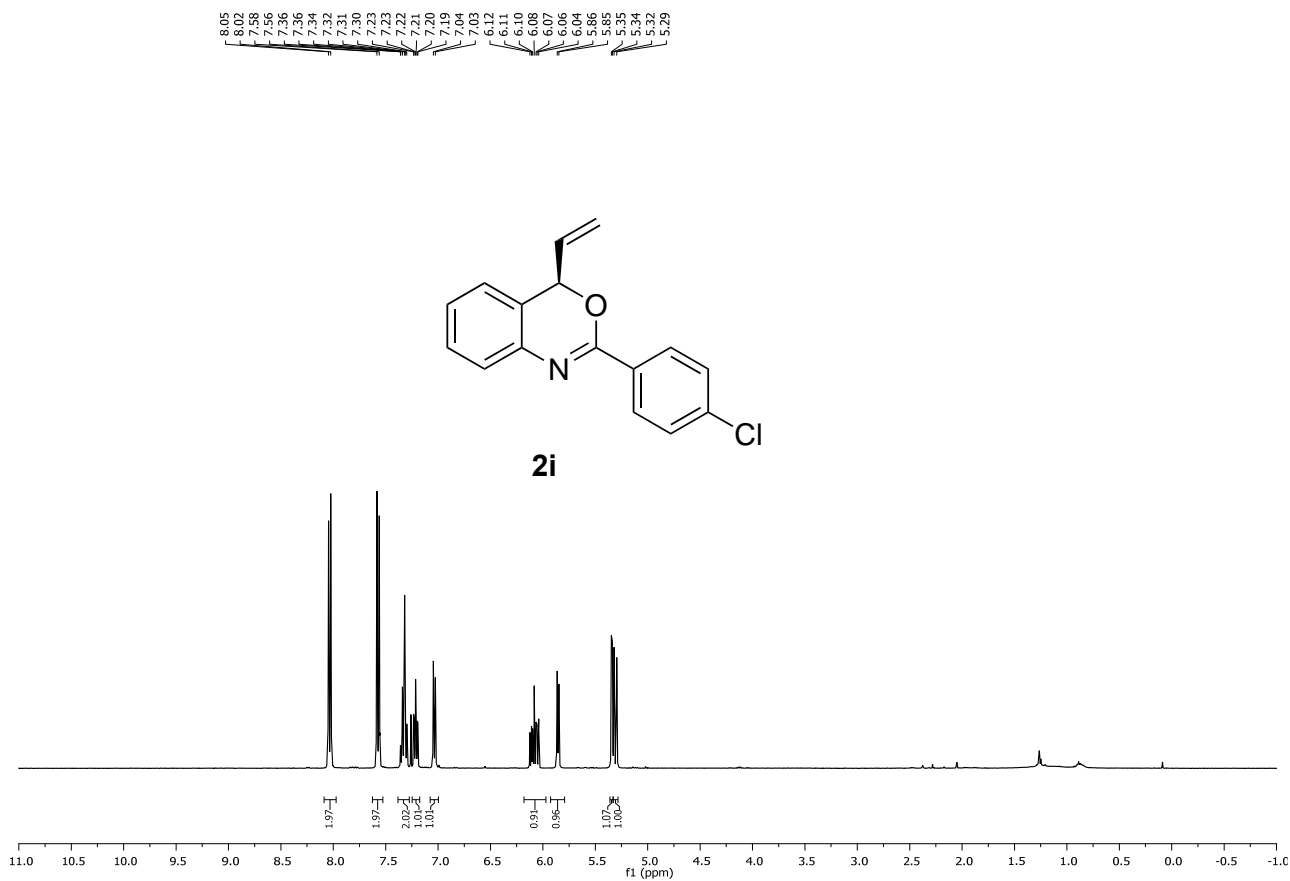


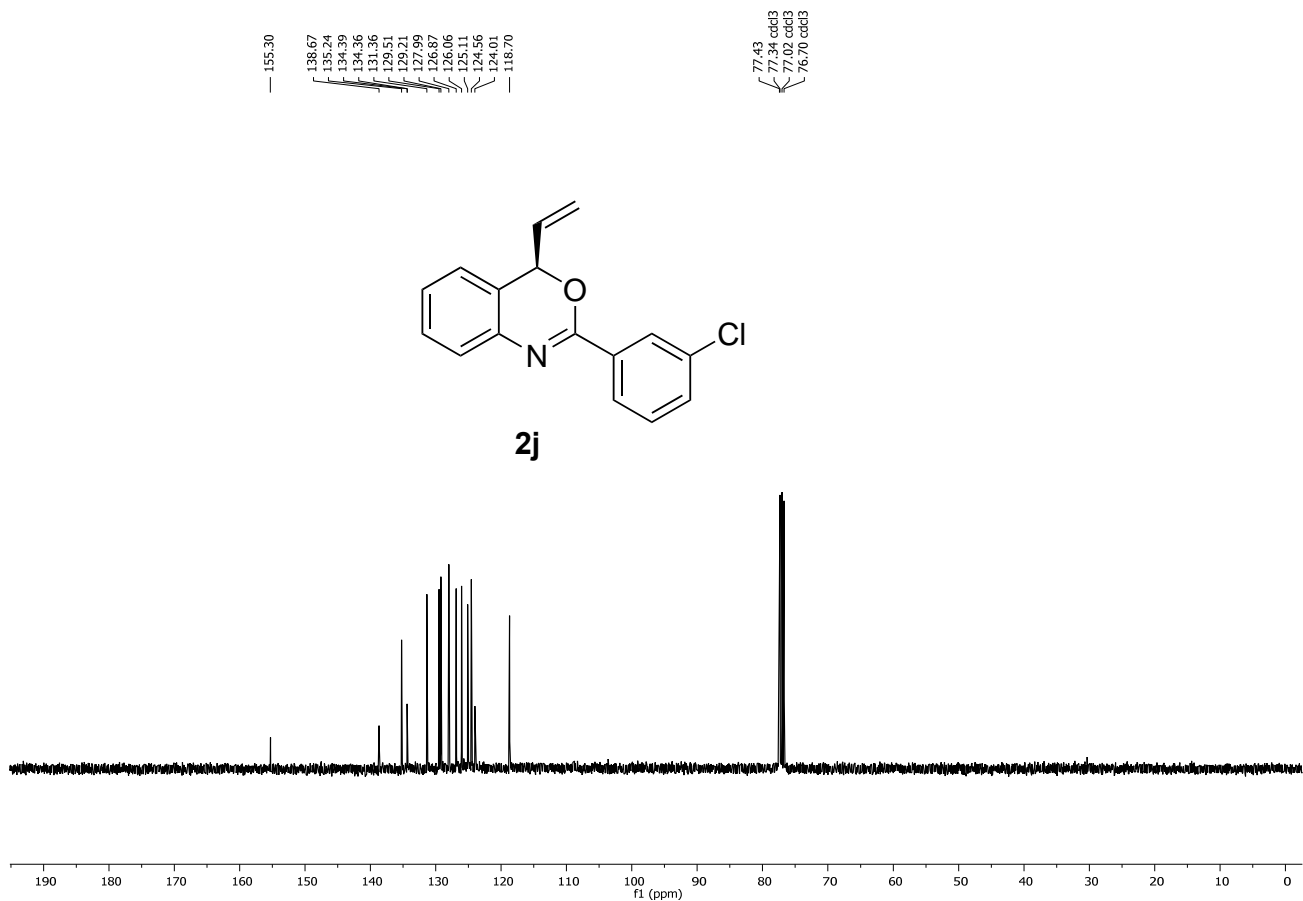
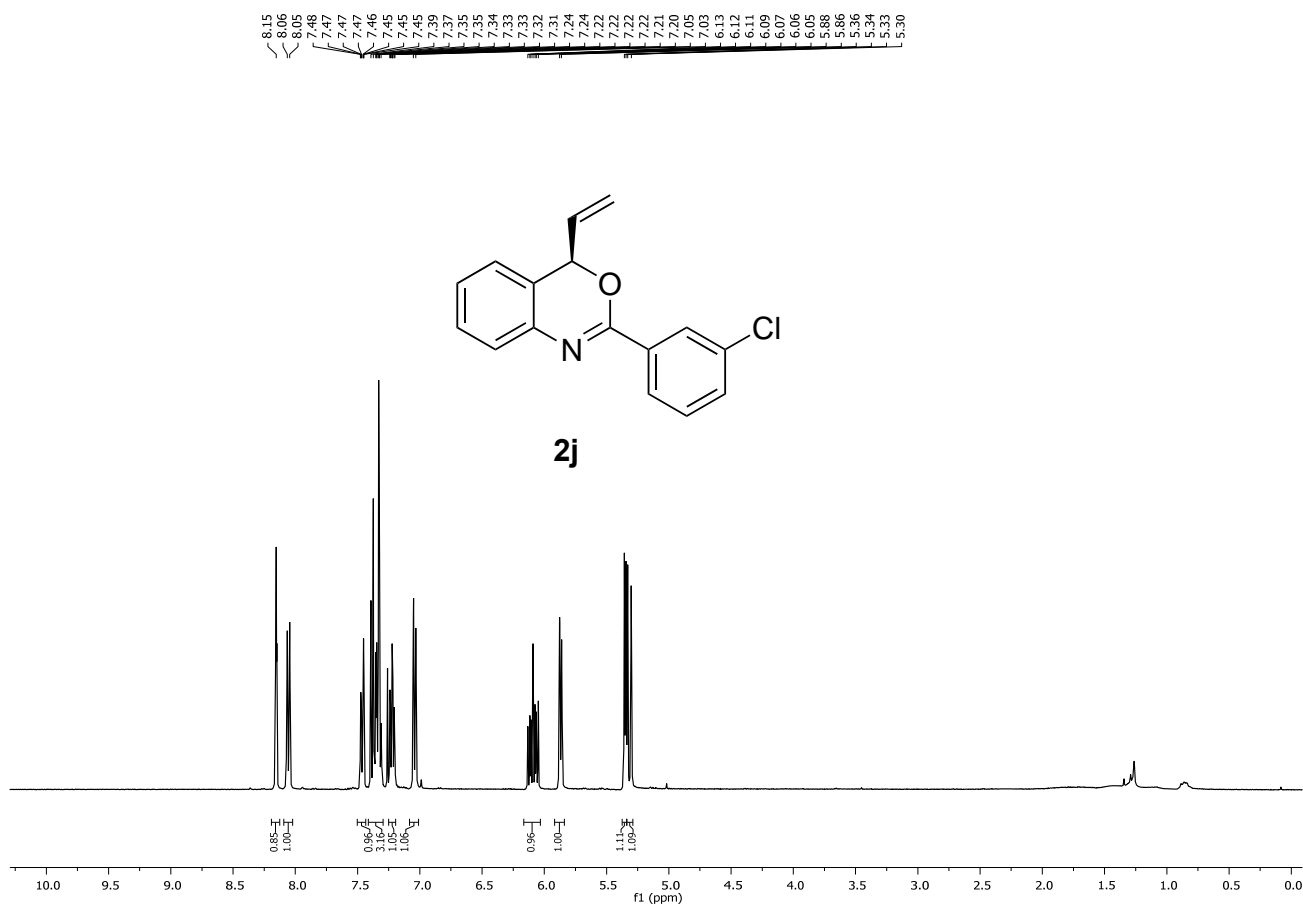
154.33
149.40
138.36
138.32
135.08
129.33
128.73
127.50
125.43
124.64
123.83
123.36
118.96

77.61
77.32 cdcl3
77.00 cdcl3
76.68 cdcl3

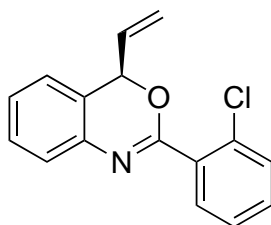




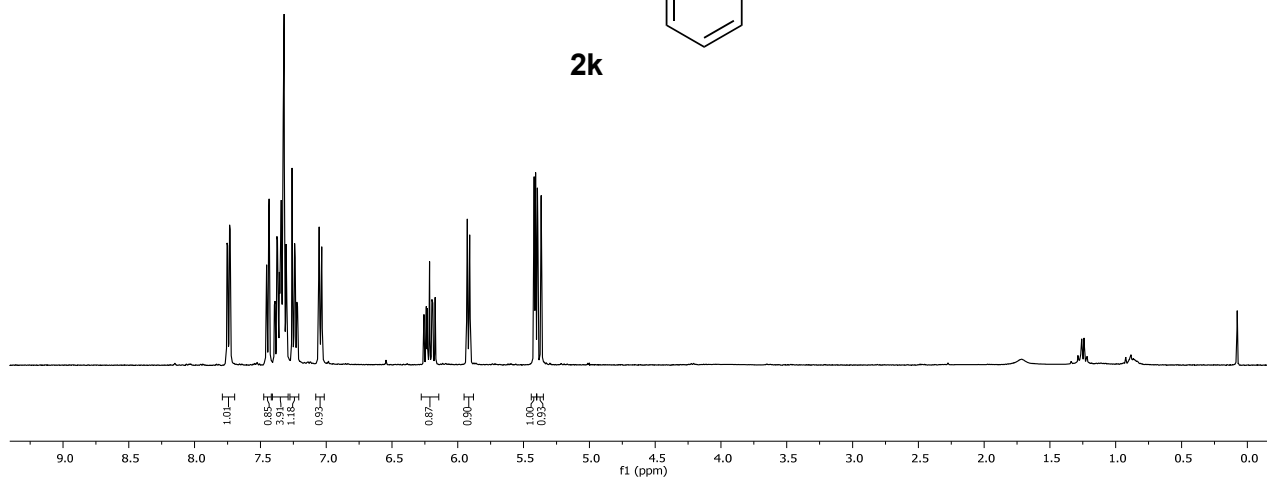




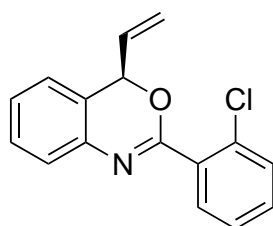
7.75
7.75
7.73
7.73
7.46
7.45
7.44
7.43
7.39
7.39
7.37
7.37
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.30
7.30
7.26
7.25
7.24
7.24
7.22
7.22
7.05
7.03
6.26
6.24
6.24
6.23
6.21
6.20
6.19
6.17
5.93
5.91
5.92
5.91
5.41
5.39
5.37



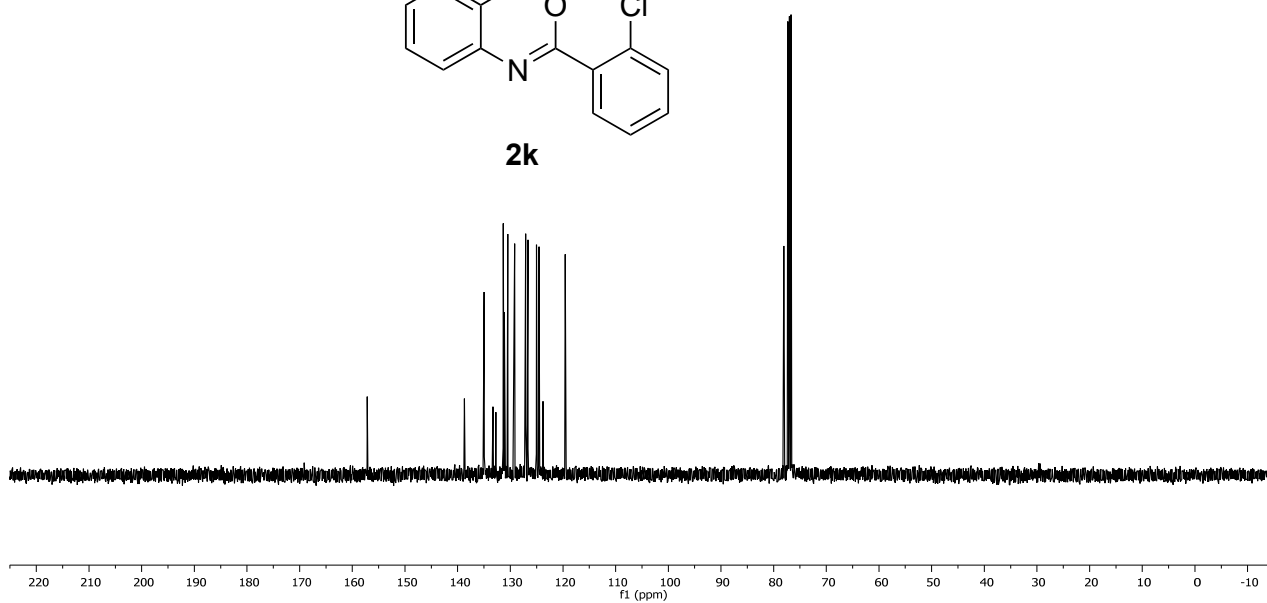
2k



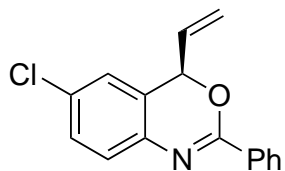
157.17
138.70
134.97
133.29
132.74
131.33
131.13
130.48
129.19
127.10
126.65
125.04
124.55
124.55
119.58
78.06
77.31 cdCl3
77.00 cdCl3
76.68 cdCl3



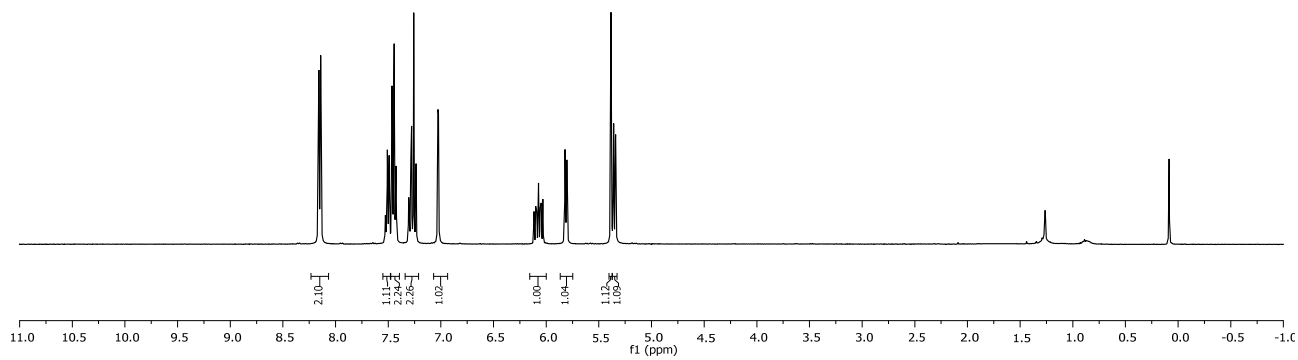
2k



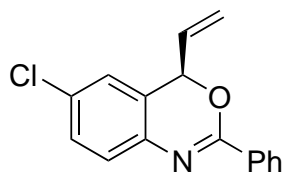
8.16
8.14
7.53
7.51
7.49
7.46
7.44
7.43
7.31
7.30
7.28
7.28
7.26
7.24
7.03
7.02
6.12
6.10
6.09
6.07
6.06
6.05
6.03
5.82
5.80
5.39
5.36
5.34



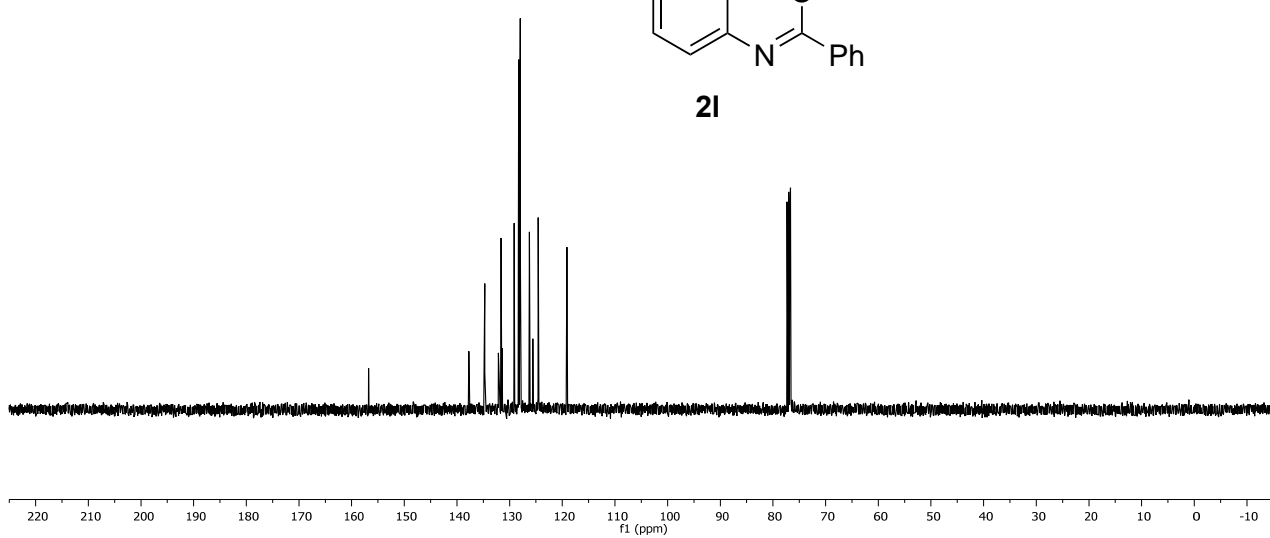
21

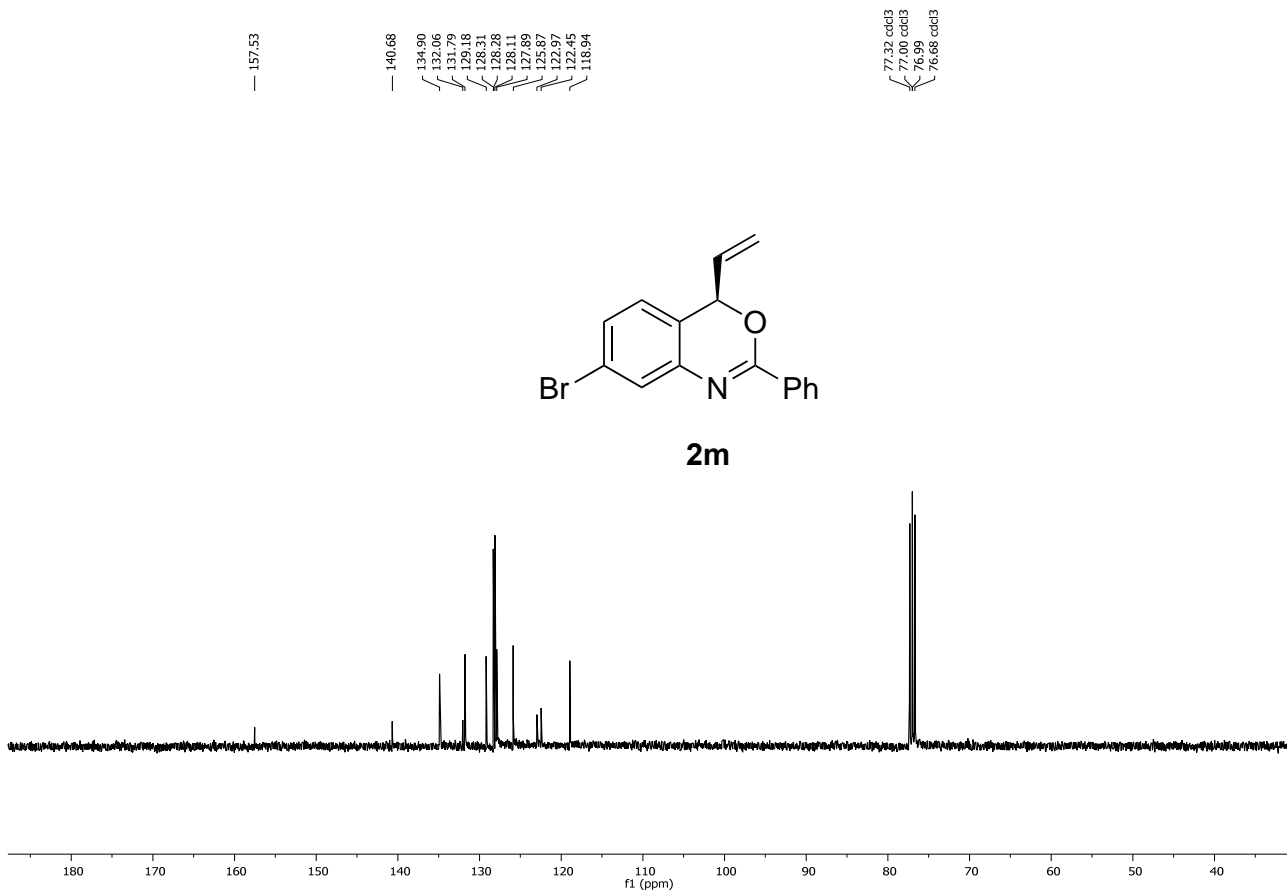
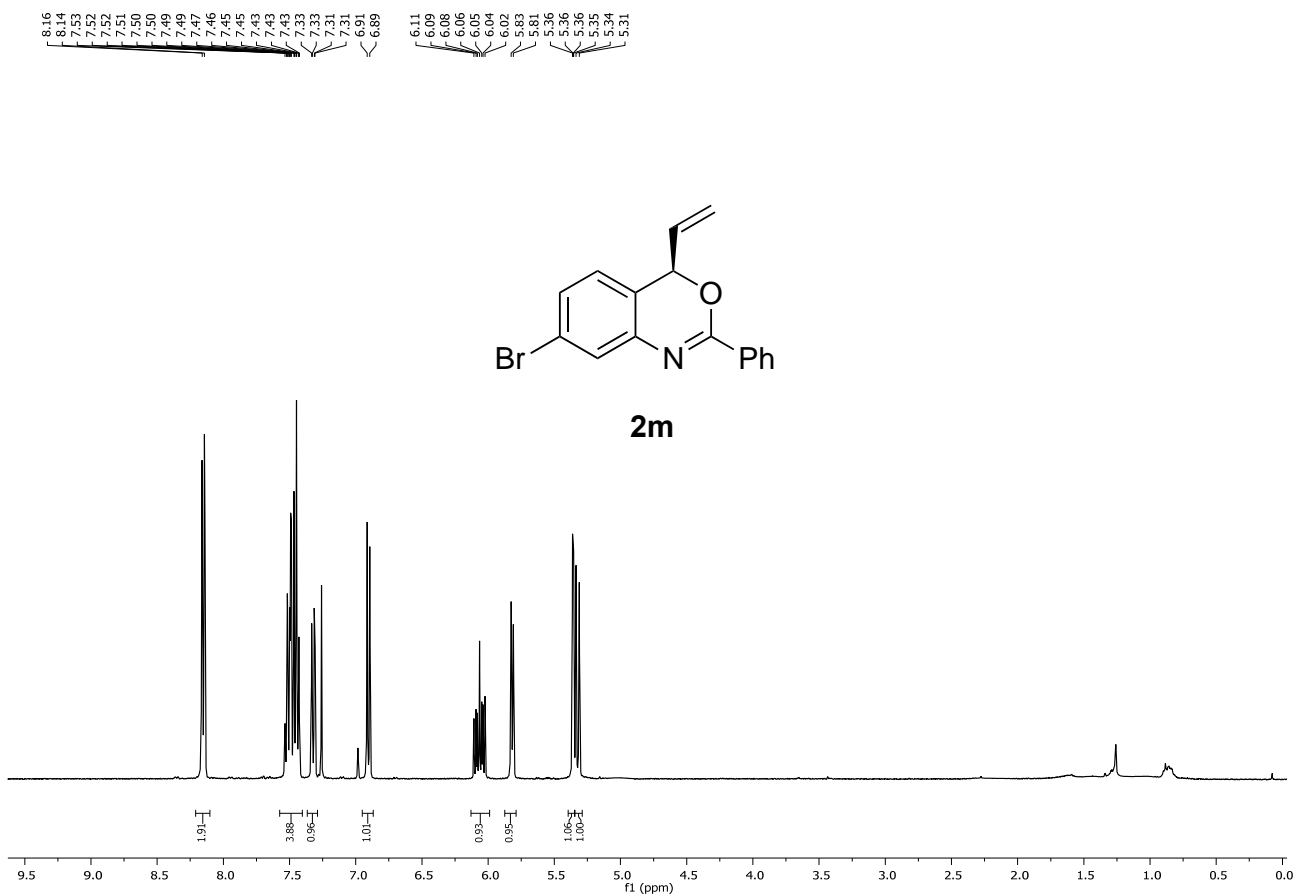


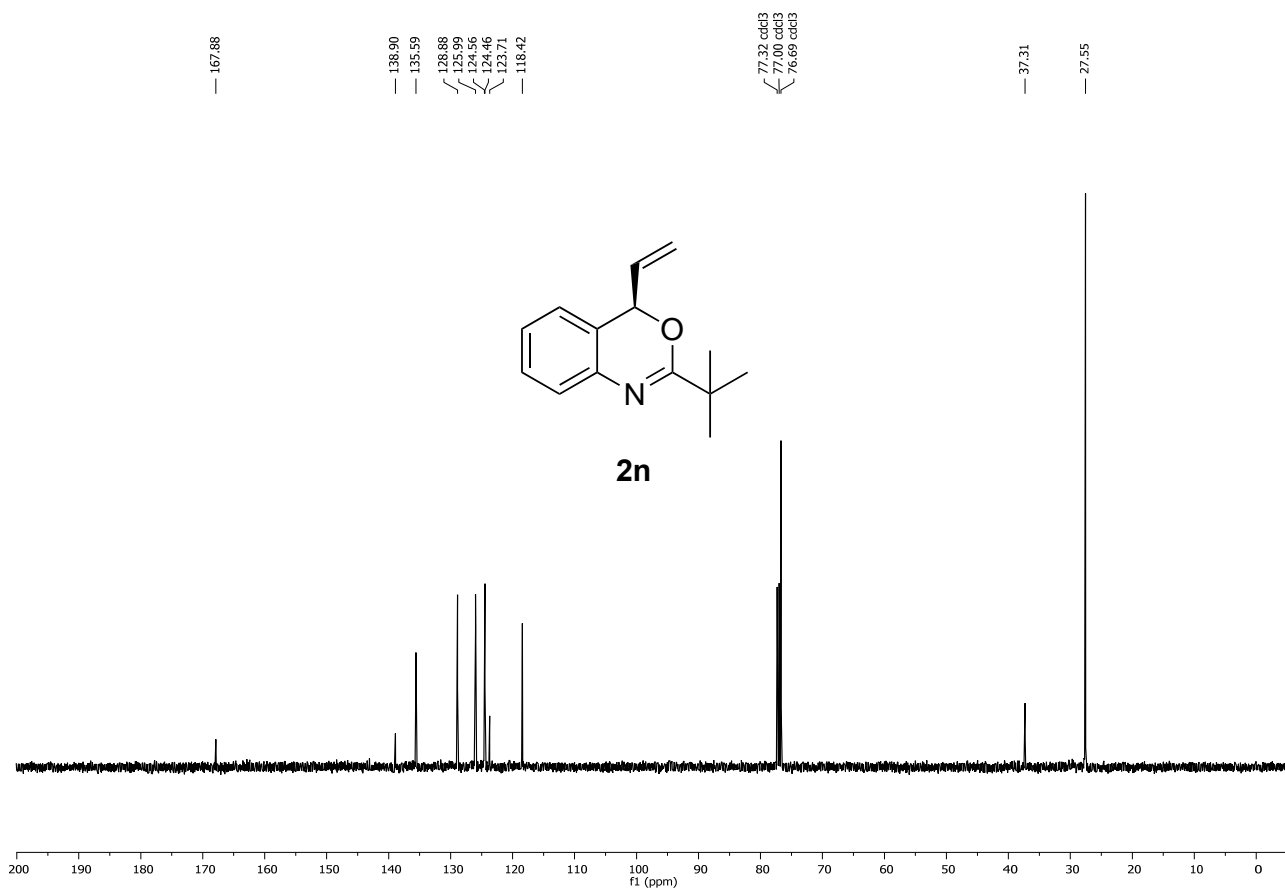
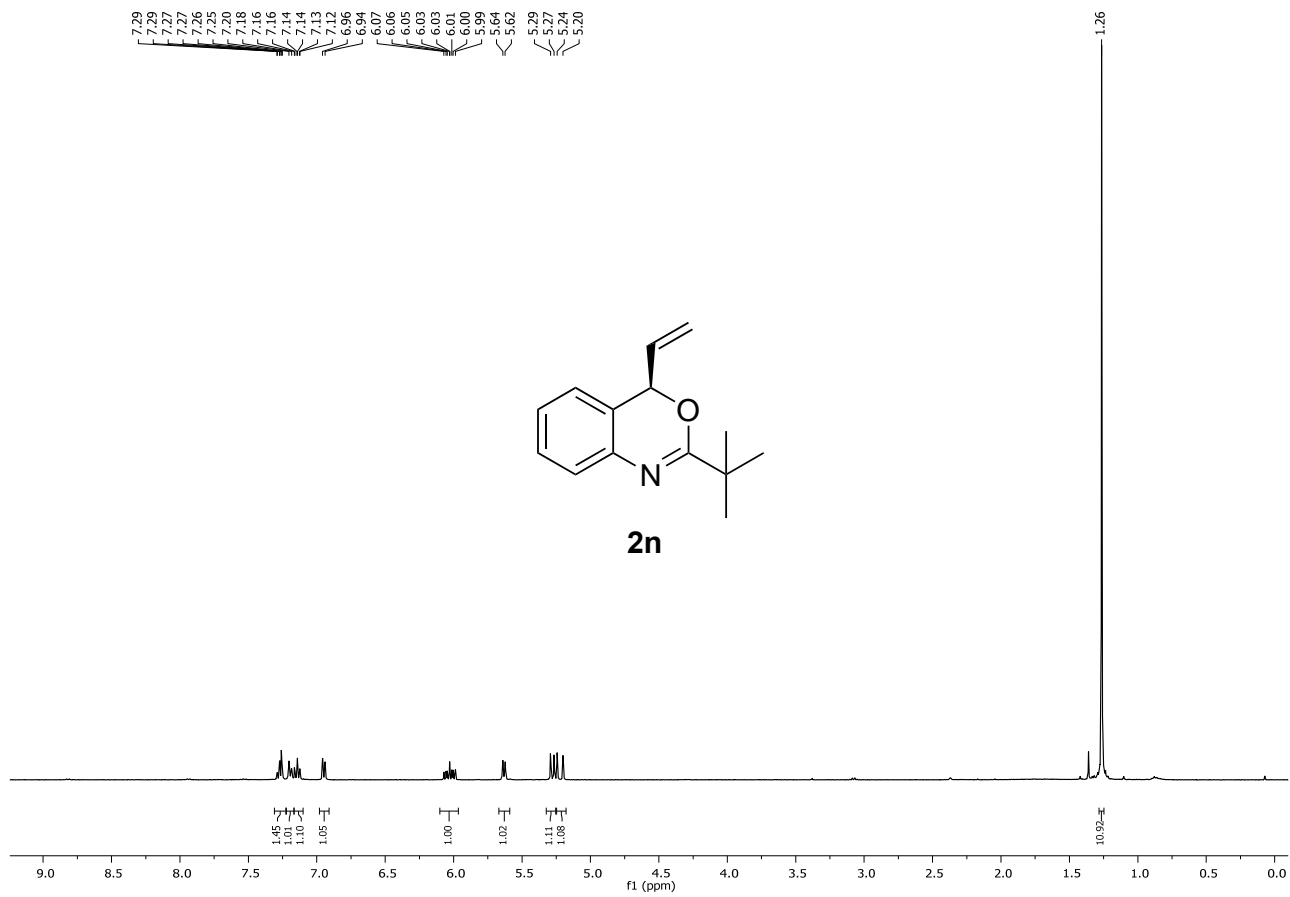
156.78
137.75
134.72
132.13
131.61
129.91
129.14
128.27
127.97
126.25
125.61
124.57
119.12
77.32 cdCl3
77.06 cdCl3
76.80 cdCl3
76.68 cdCl3



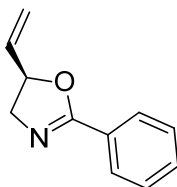
21



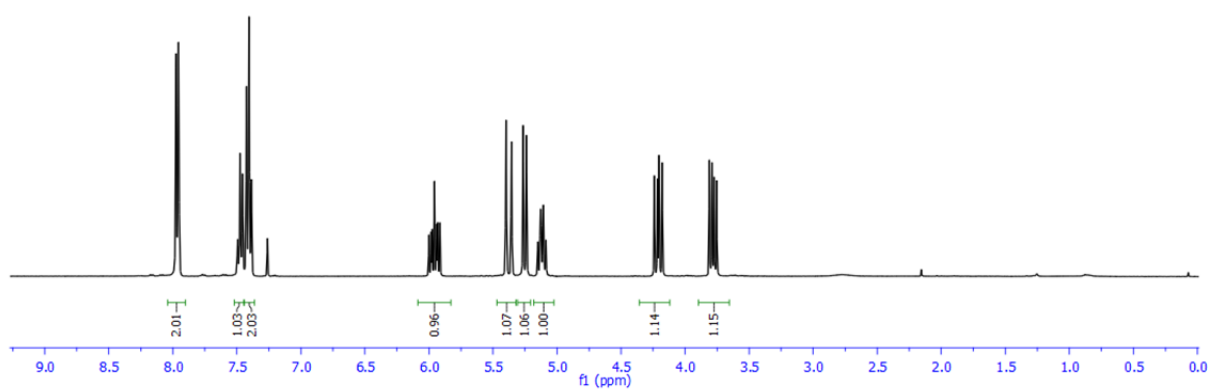




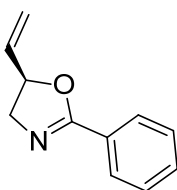
7.97
7.96
7.49
7.48
7.47
7.46
7.45
7.40
7.39
6.00
5.98
5.97
5.96
5.94
5.93
5.91
5.40
5.37
5.24
5.15
5.13
5.11
5.09
4.24
4.22
4.19
4.18
3.81
3.79
3.77
3.75



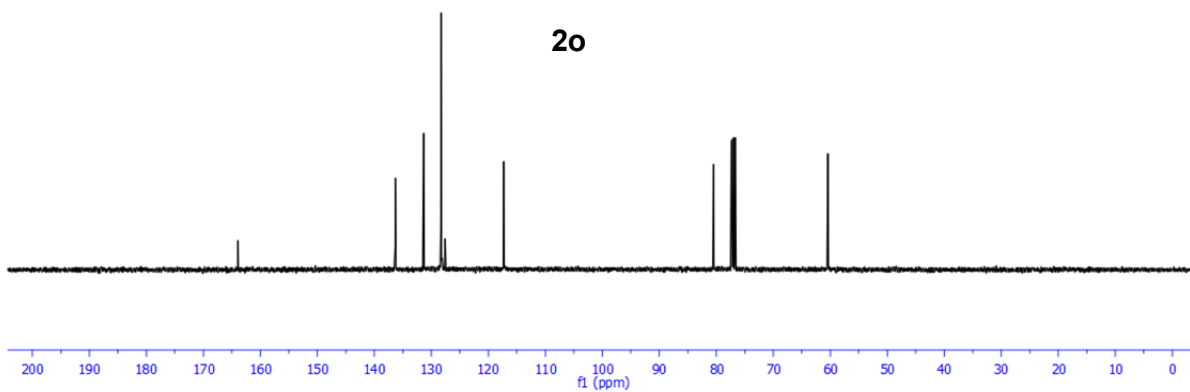
2o

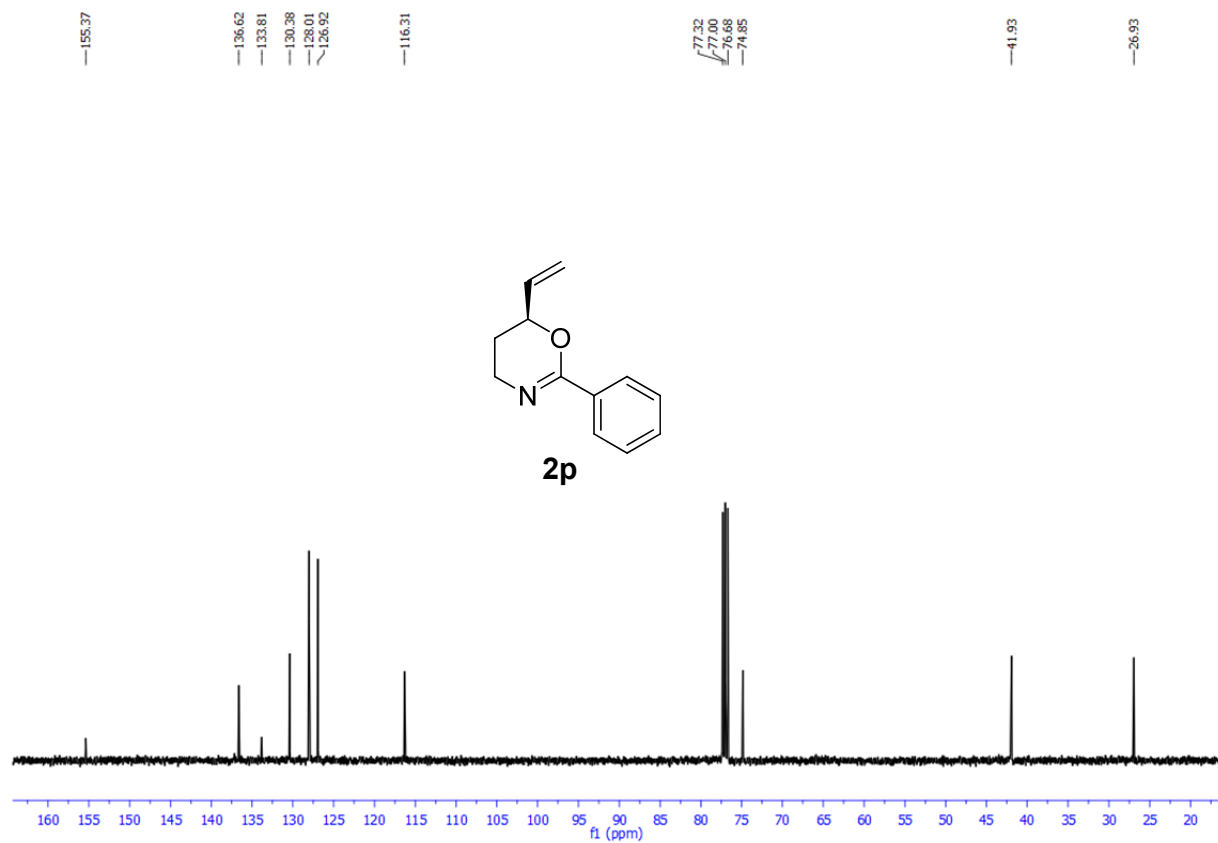
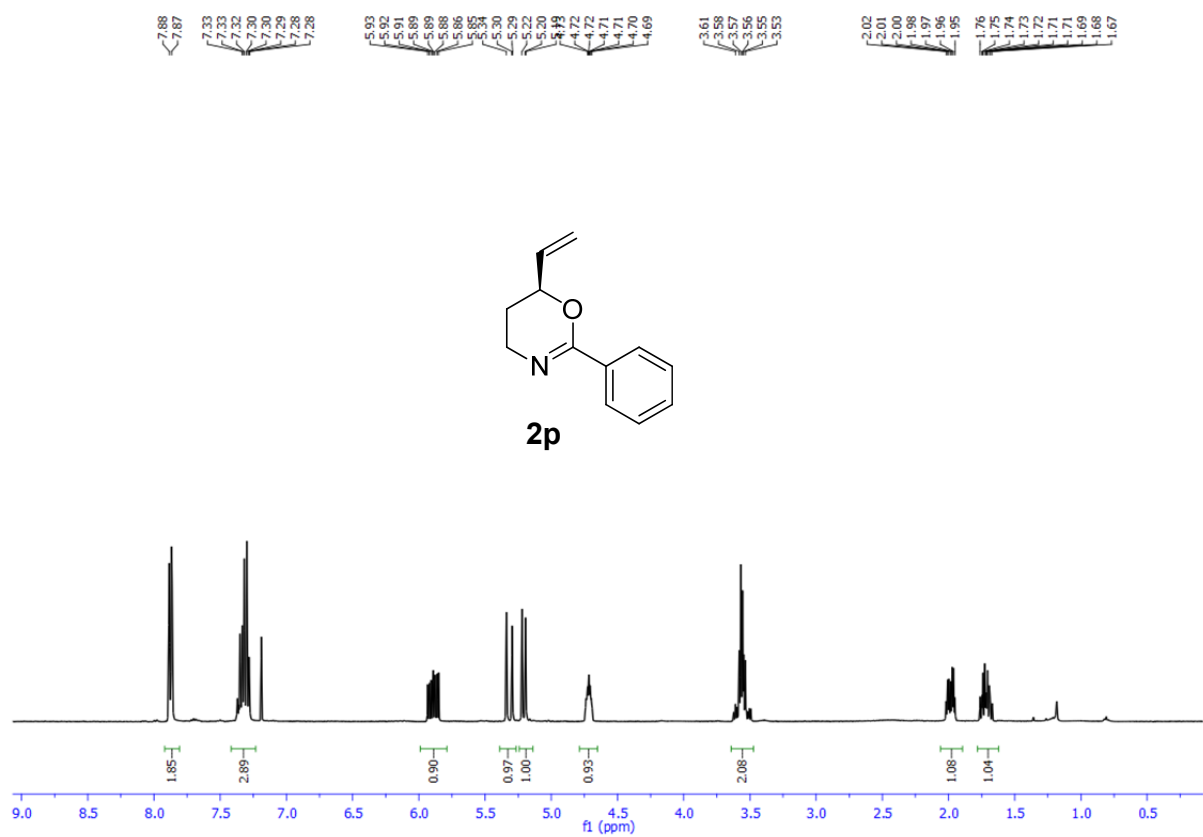


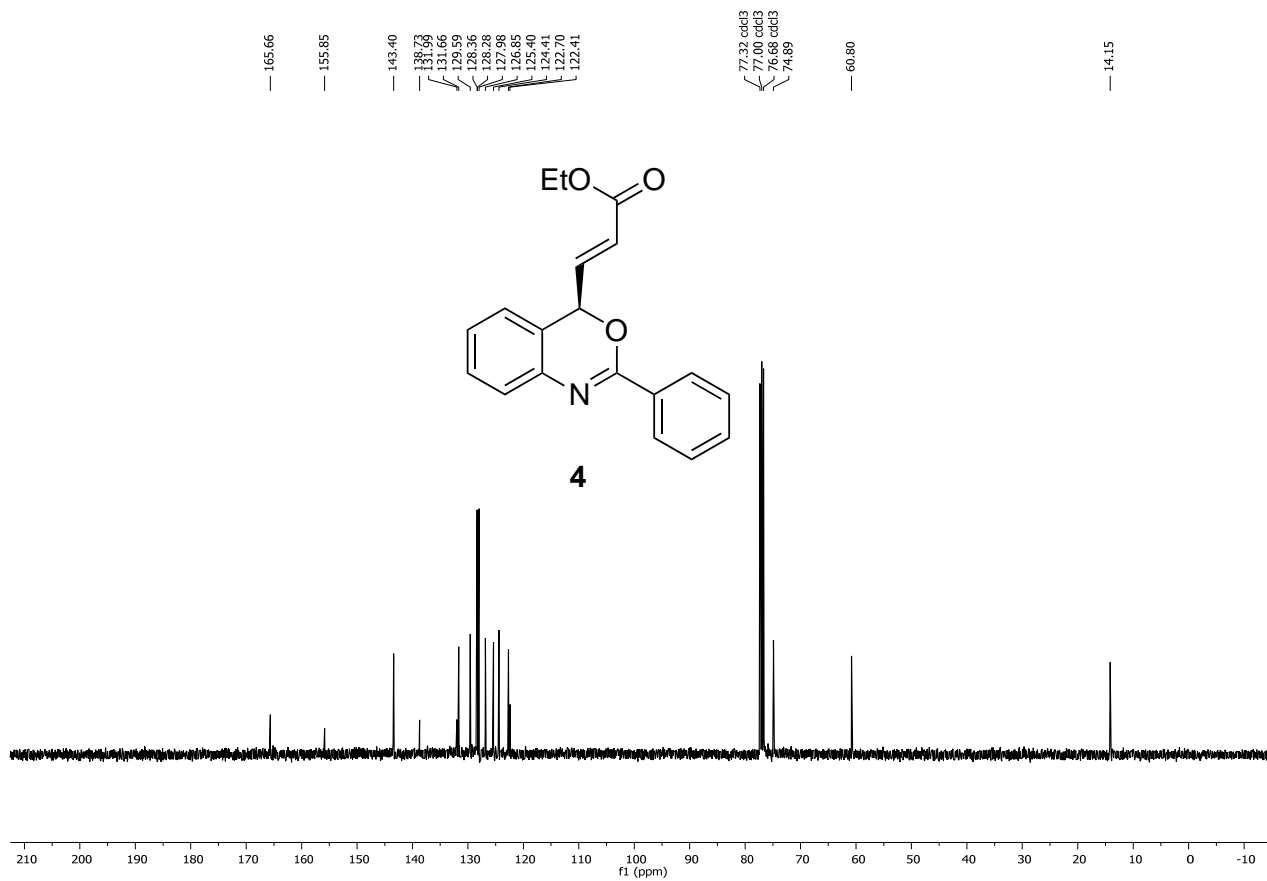
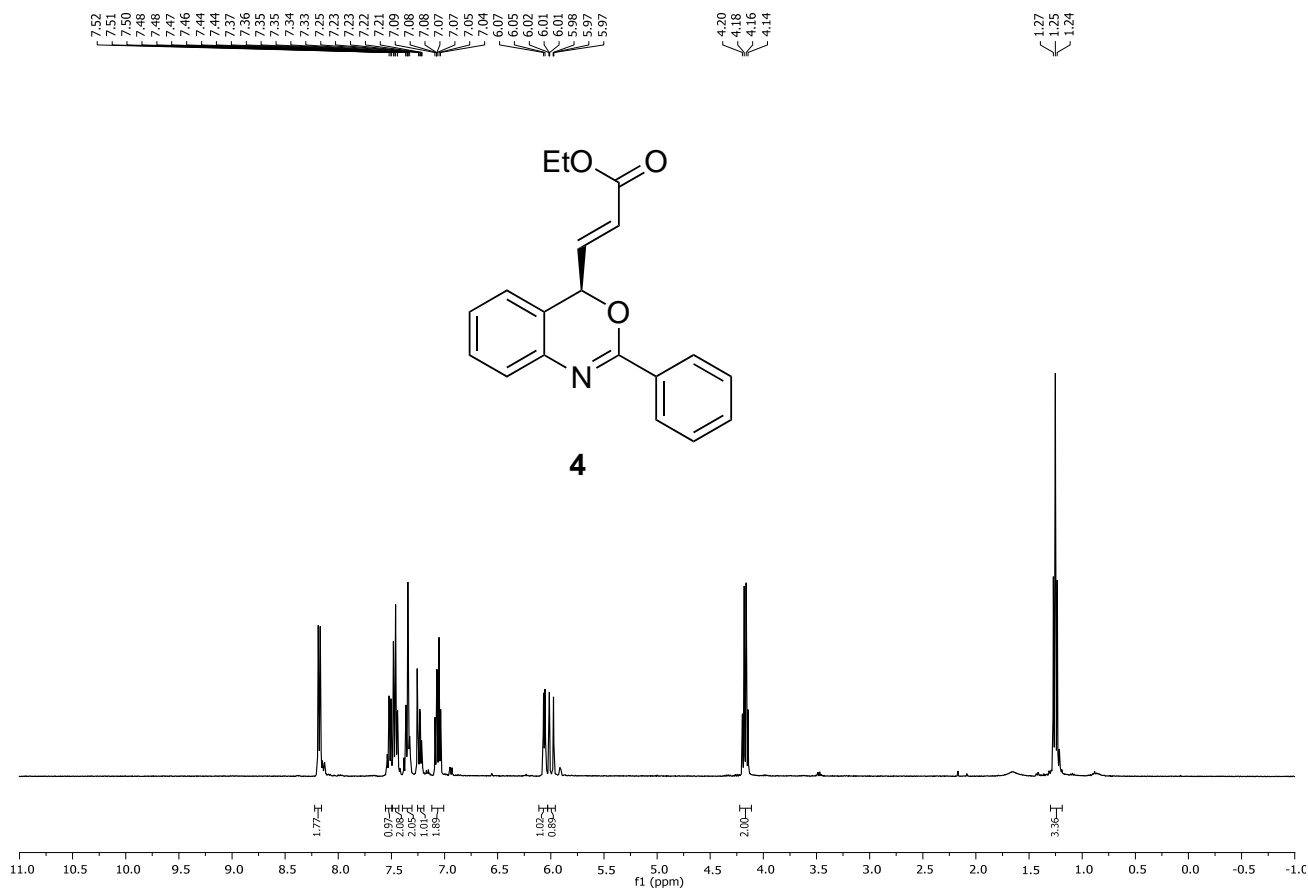
163.92
136.31
131.33
128.30
128.15
127.58
117.31
80.47
77.32
77.00
76.68
60.43



2o







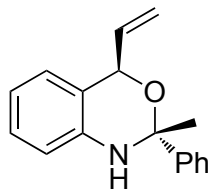
7.55
7.53
7.34
7.32
7.31
7.27
7.24
7.13
7.12
7.10
6.82
6.80
6.74
6.72
6.71

5.97
5.95
5.94
5.93
5.90

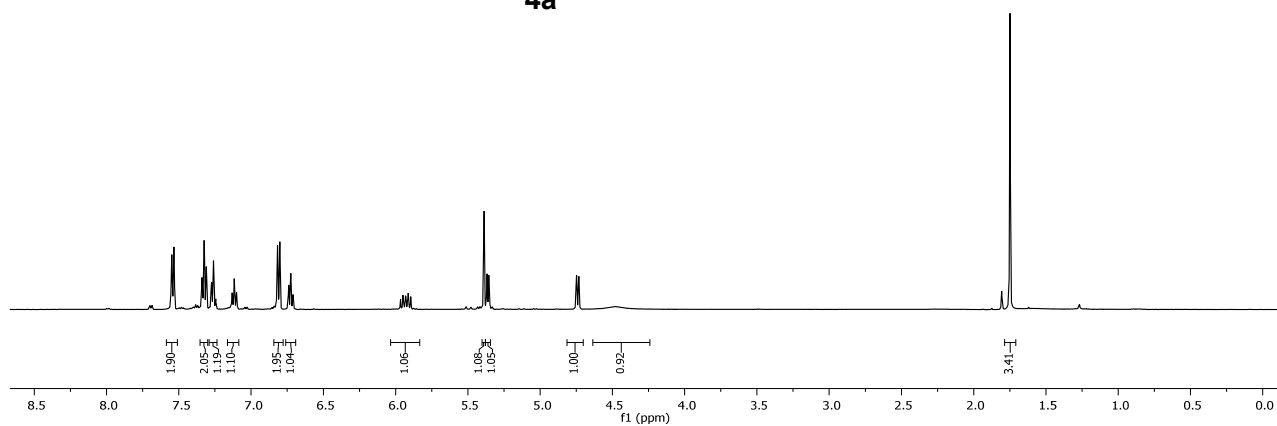
5.39
5.37
5.35

4.75
4.73
4.47

1.75



4a



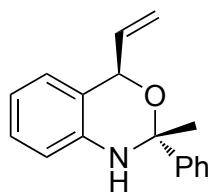
144.15
140.15
137.33

128.53
127.77
127.59
126.73
125.91
123.26
119.36
118.99
116.38

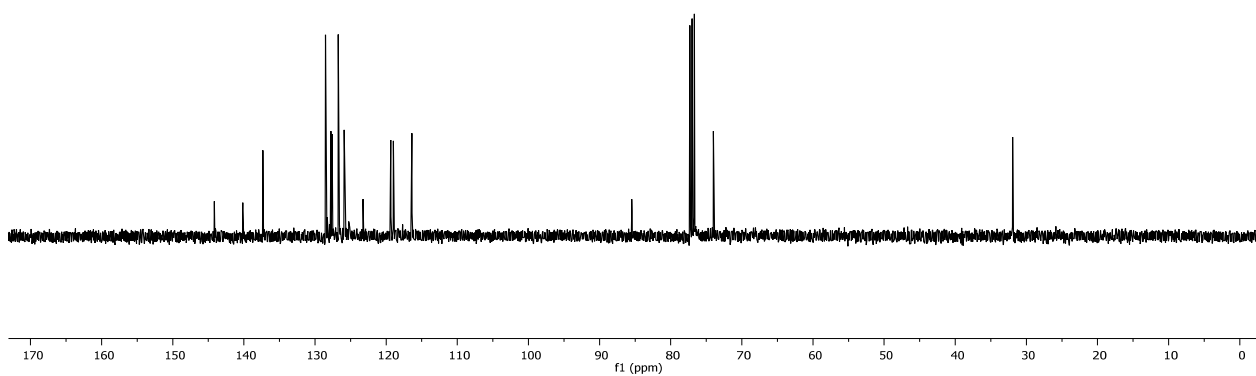
85.47

77.32
77.00
76.68
74.00

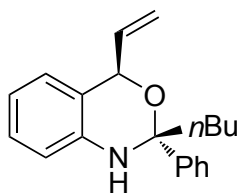
31.93



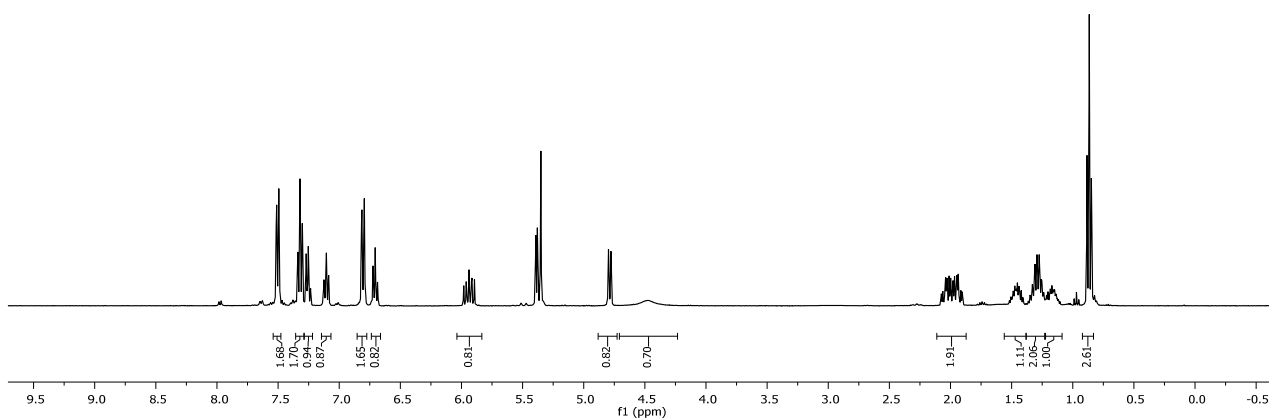
4a



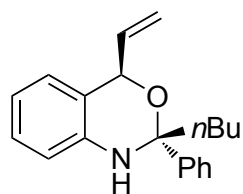
7.51, 7.49, 7.34, 7.32, 7.30, 7.27, 7.25, 7.12, 7.11, 7.10, 7.09, 7.08, 6.82, 6.79, 6.72, 6.71, 6.69, 5.98, 5.96, 5.96, 5.94, 5.92, 5.91, 5.89, 5.39, 5.38, 5.35, 4.80, 4.78, 4.48, 2.07, 2.06, 2.04, 2.03, 2.01, 2.00, 1.98, 1.97, 1.95, 1.94, 1.91, 1.90, 1.89, 1.47, 1.47, 1.46, 1.45, 1.44, 1.42, 1.33, 1.31, 1.29, 1.27, 1.26, 0.88, 0.87



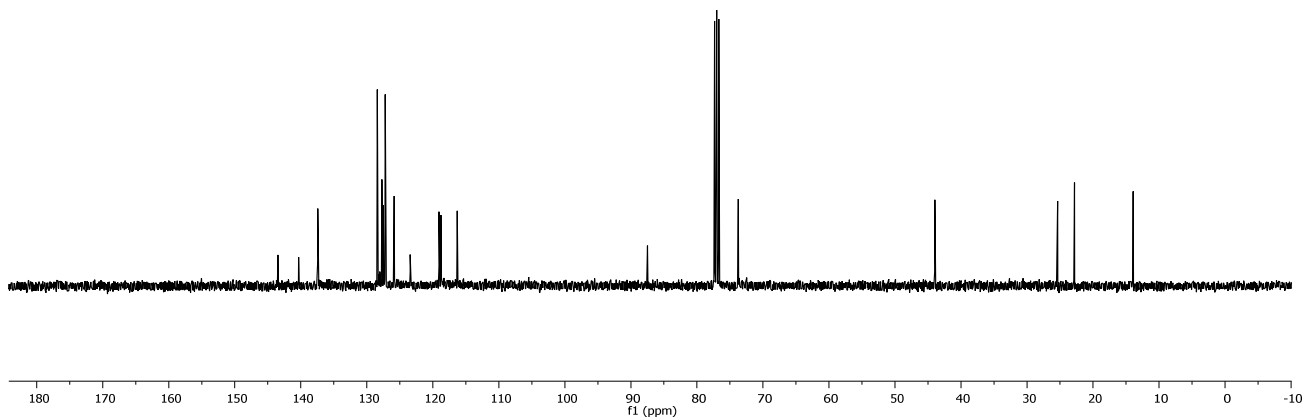
4b



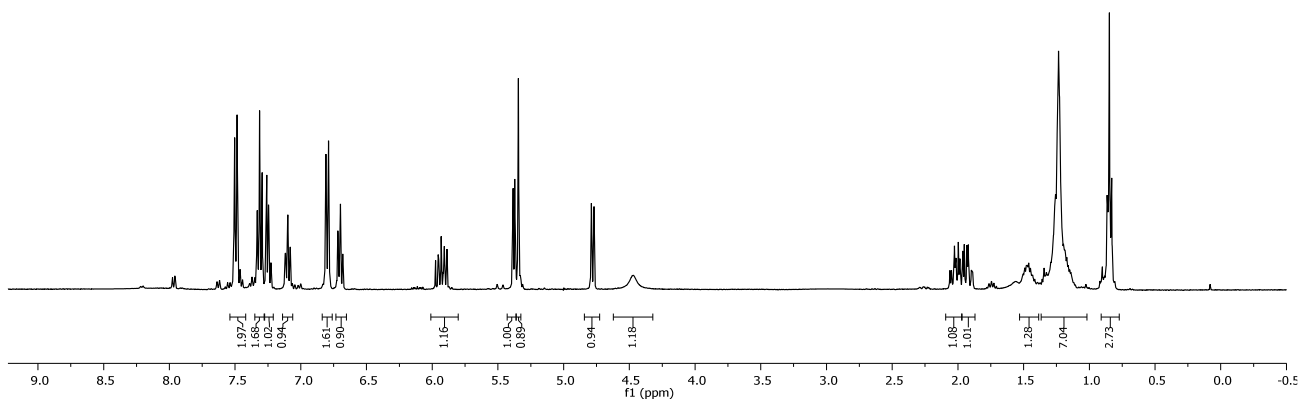
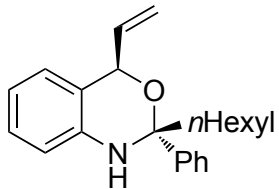
143.48, 140.33, 137.42, 128.40, 127.72, 127.49, 127.21, 125.86, 123.62, 119.96, 118.96, 116.29, 87.50, 77.32 cdd3, 77.00 cdd3, 76.68 cdd3, 73.73, 43.96, 25.36, 22.81, 13.92



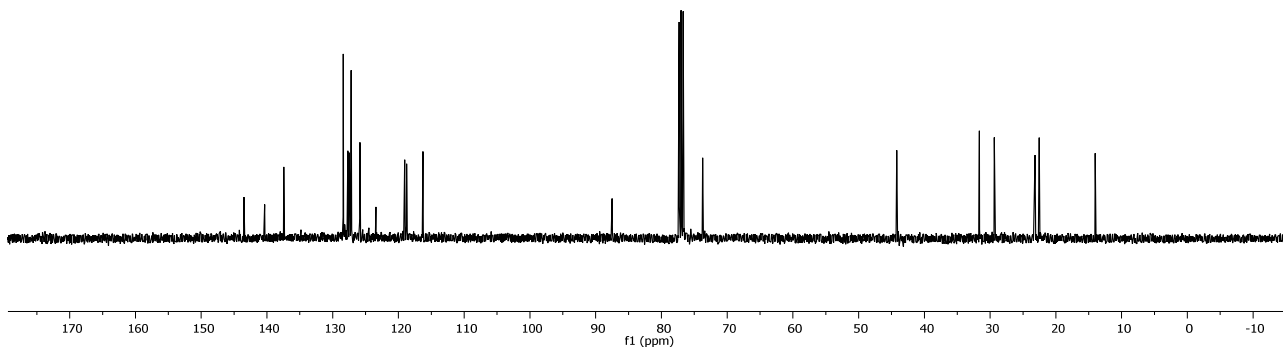
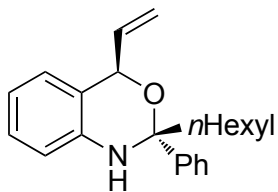
4b

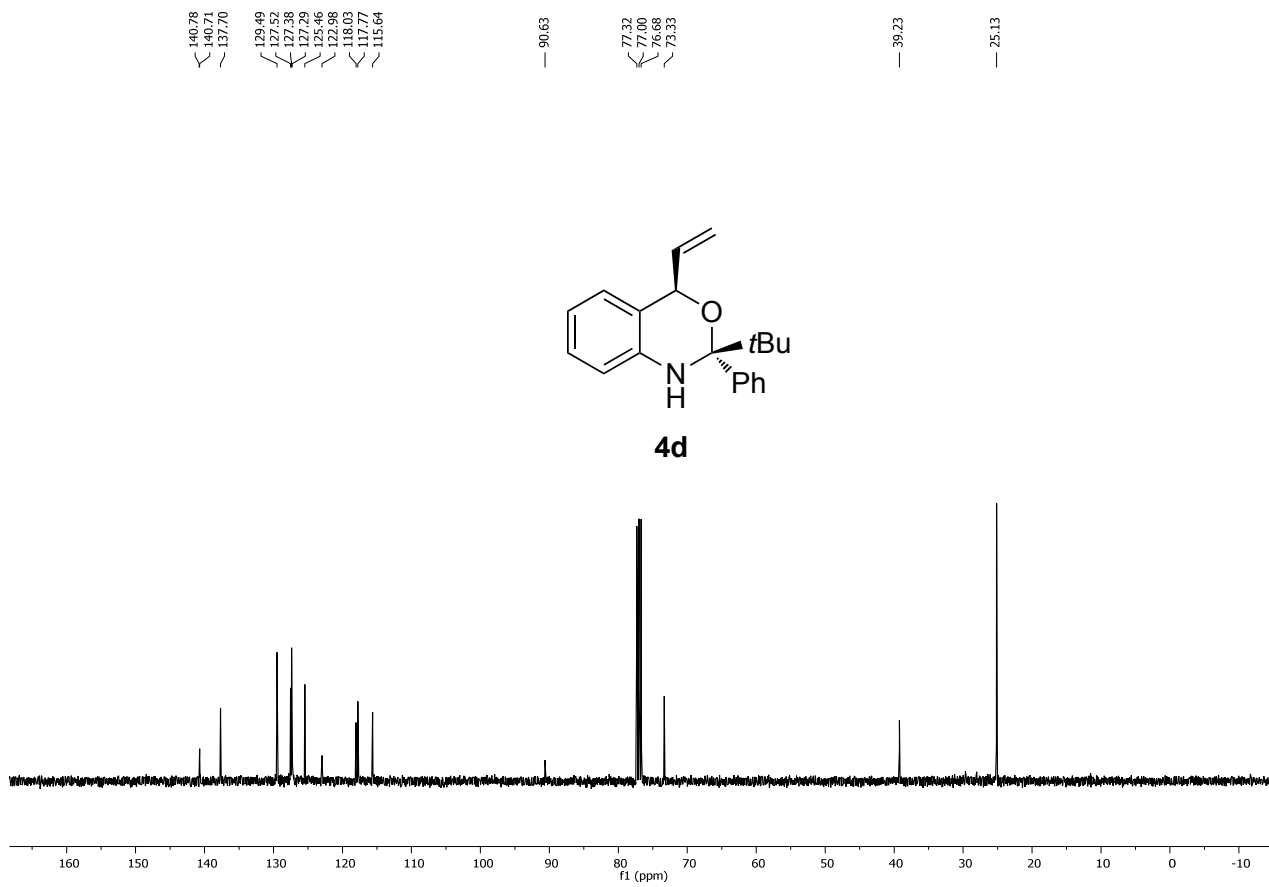
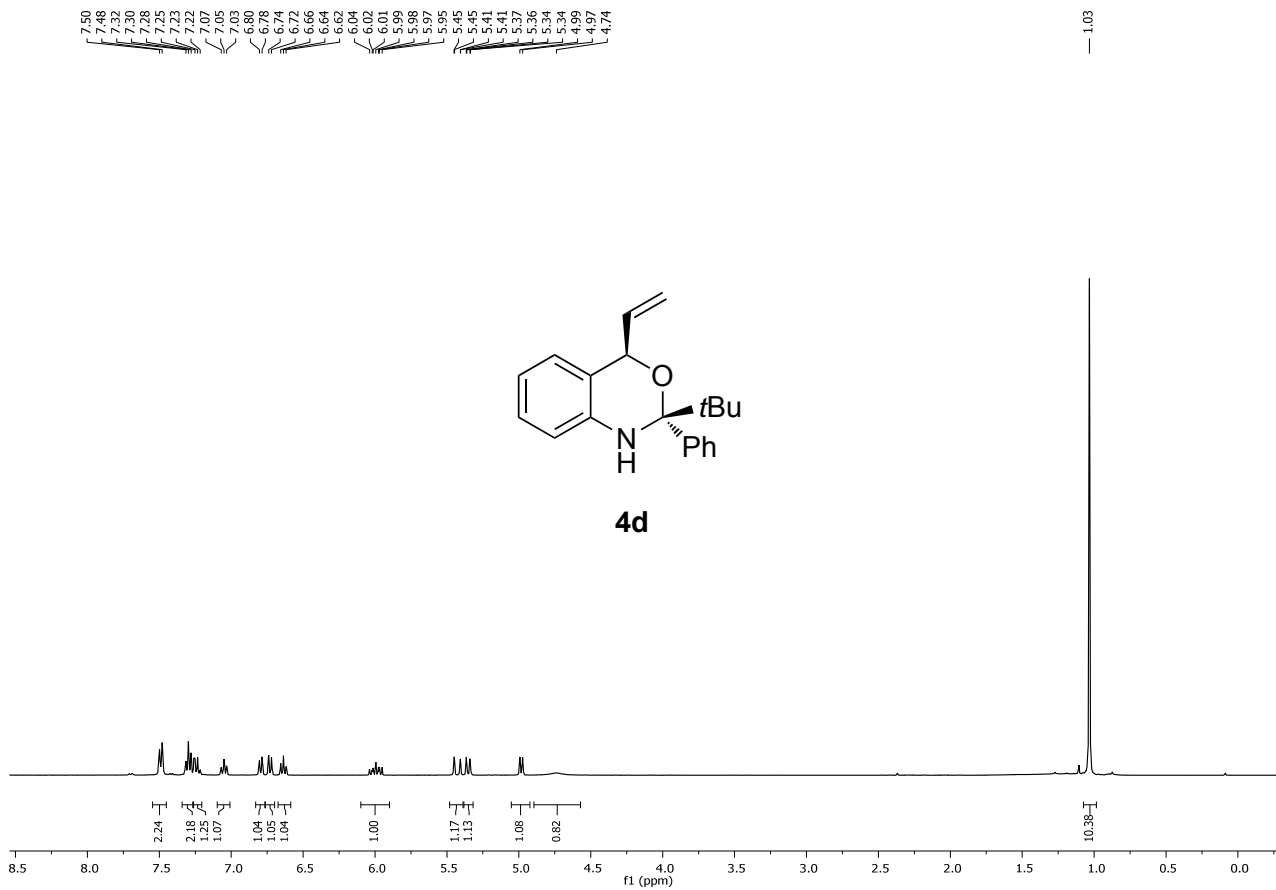


7.50
7.48
7.33
7.31
7.29
7.26
7.25
7.23
7.10
7.08
5.97
5.95
5.93
5.91
5.89
5.38
5.37
5.34
4.79
4.77
4.47
2.06
2.05
2.03
2.02
2.01
2.00
1.98
1.96
1.95
1.93
1.92
1.90
1.89
1.49
1.48
1.47
1.46
1.45
1.44
1.43
1.26
1.23
1.20
1.18
1.17
0.86
0.85

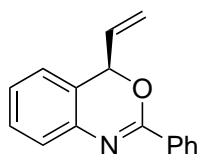


143.50
140.34
137.43
128.40
127.71
127.49
127.20
125.86
123.42
119.04
118.75
116.29
87.50
77.31
77.00
76.68
73.73
44.21
31.63
29.36
23.17
22.54
14.02



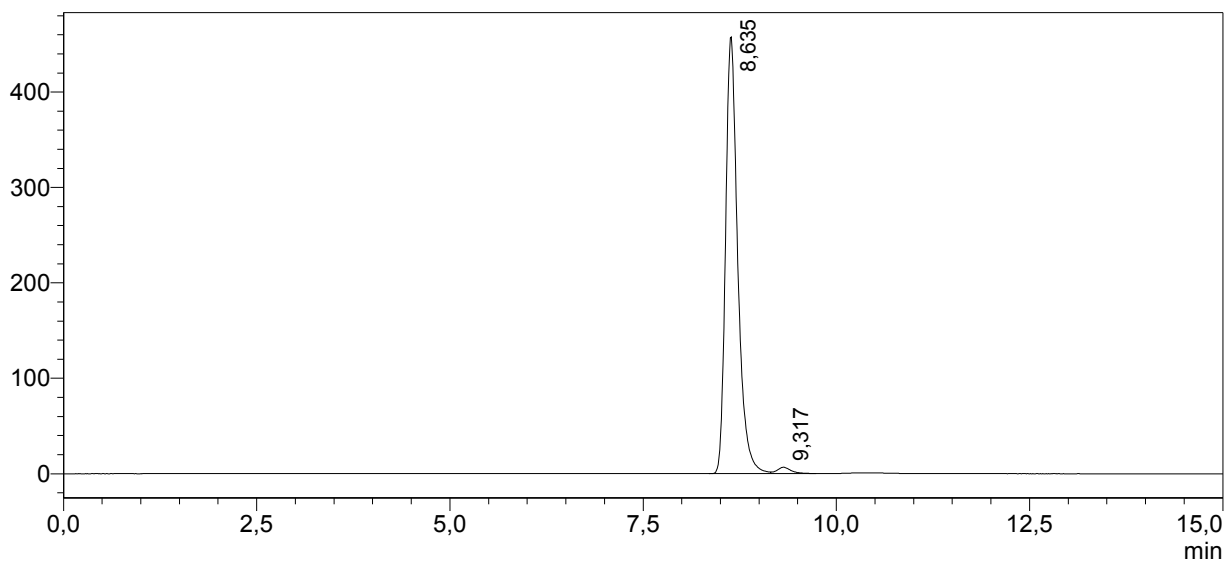


Copies of HPLC results



2a

mAU

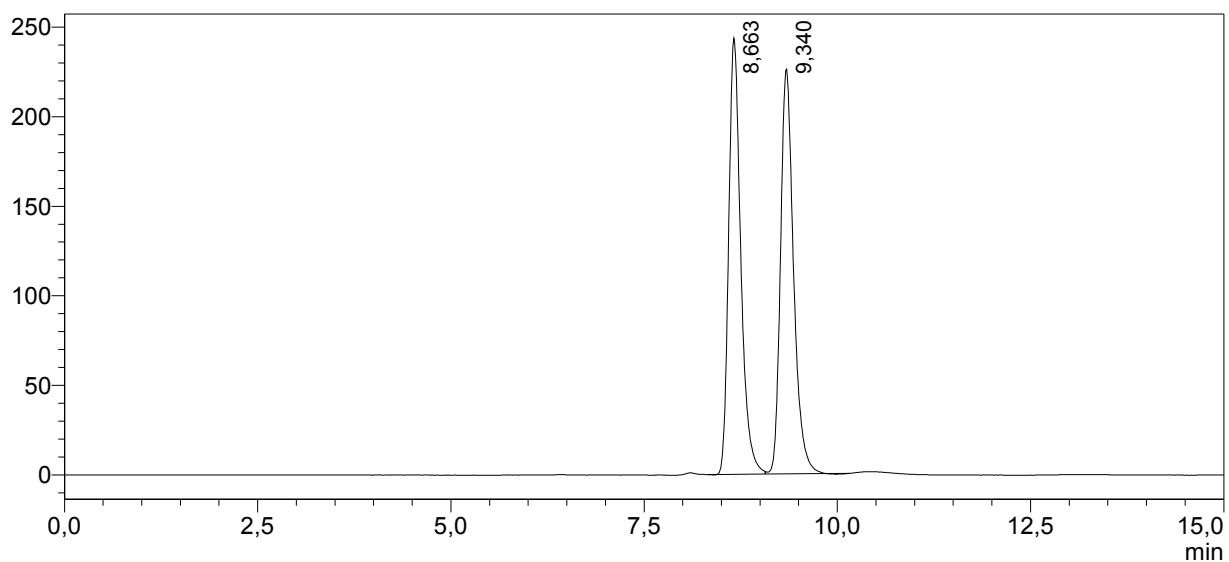


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8,635	5000450	457494	0,000	98,399
2	9,317	81383	6572	0,000	1,601
Total		5081832	464066		100,000

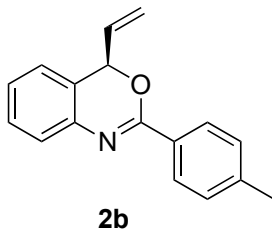
mAU

Racemic mixture:

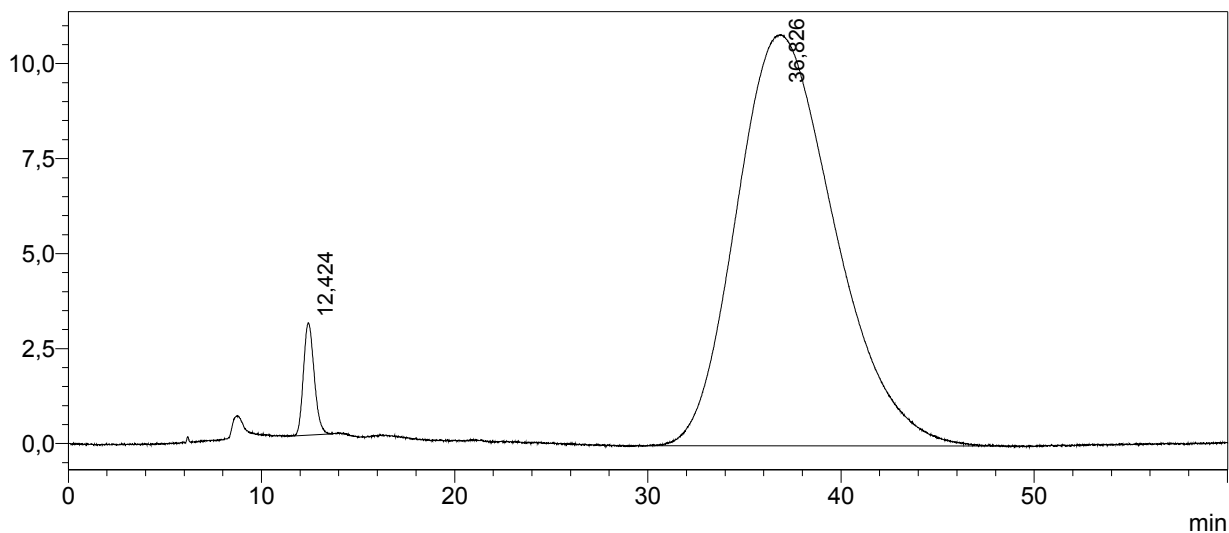


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	8,663	2654392	243343	0,000	49,991
2	9,340	2655308	226029	0,000	50,009
Total		5309701	469372		100,000



mAU

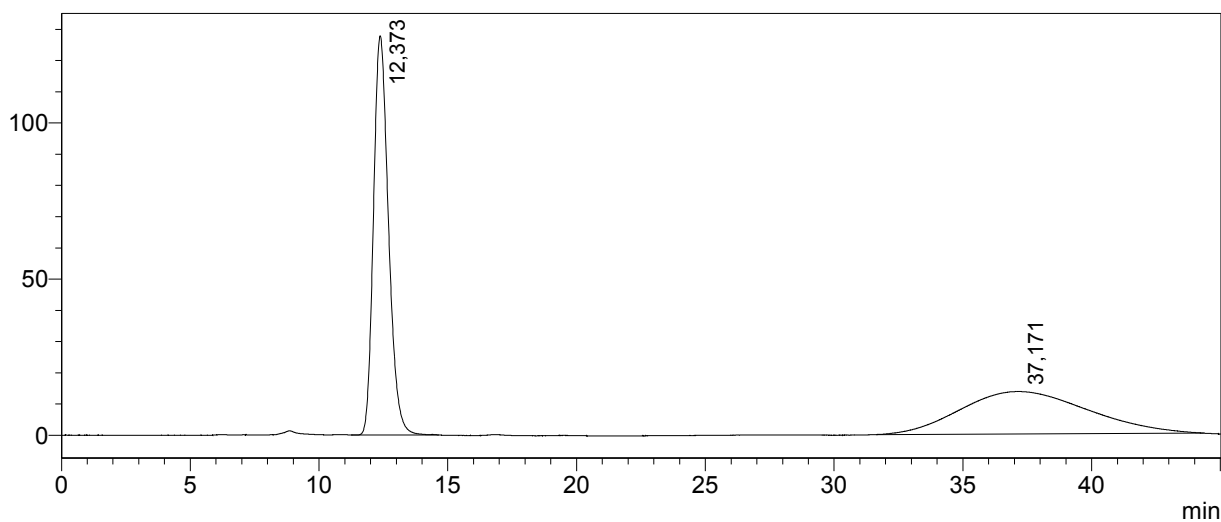


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12,424	114792	2956	0,000	2,918
2	36,826	3819775	10822	0,000	97,082
Total		3934567	13779		100,000

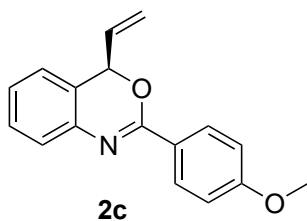
mAU

Racemic mixture:

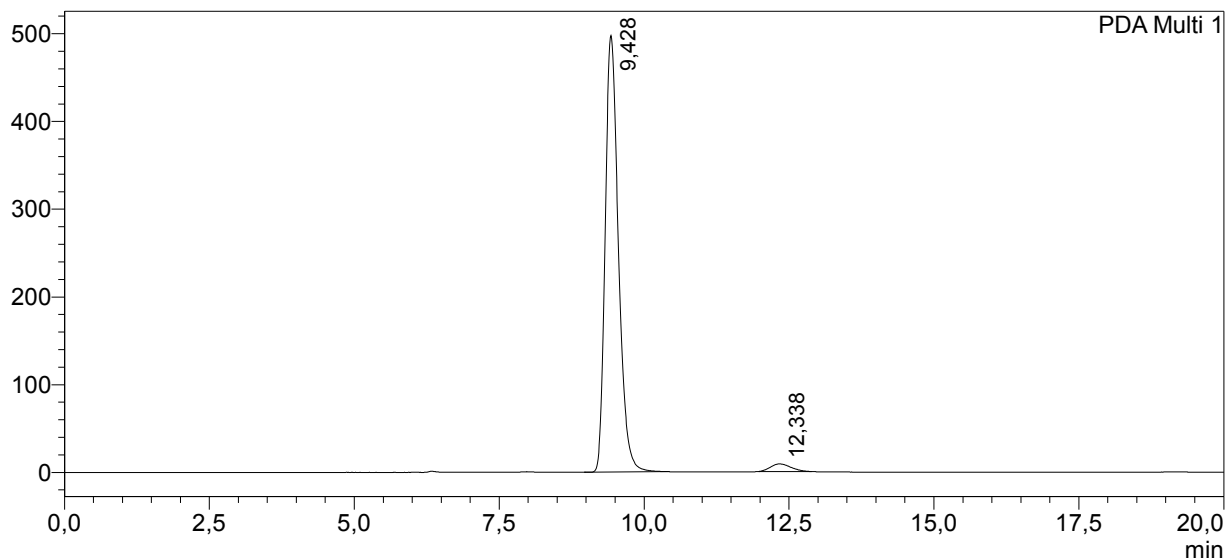


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12,373	5183488	127892	0,000	52,600
2	37,171	4671073	13579	0,000	47,400
Total		9854560	141471		100,000



mAU

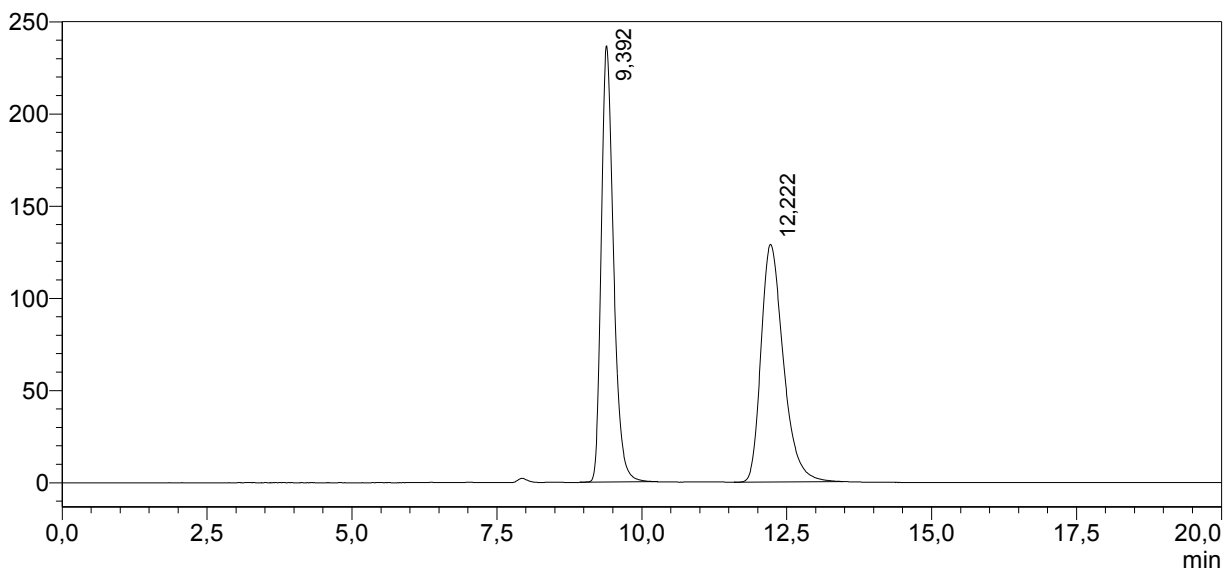


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9,428	7893858	497459	0,000	97,384
2	12,338	212040	8665	0,000	2,616
Total		8105898	506124		100,000

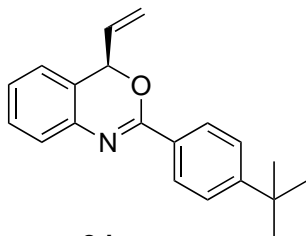
mAU

Racemic mixture:

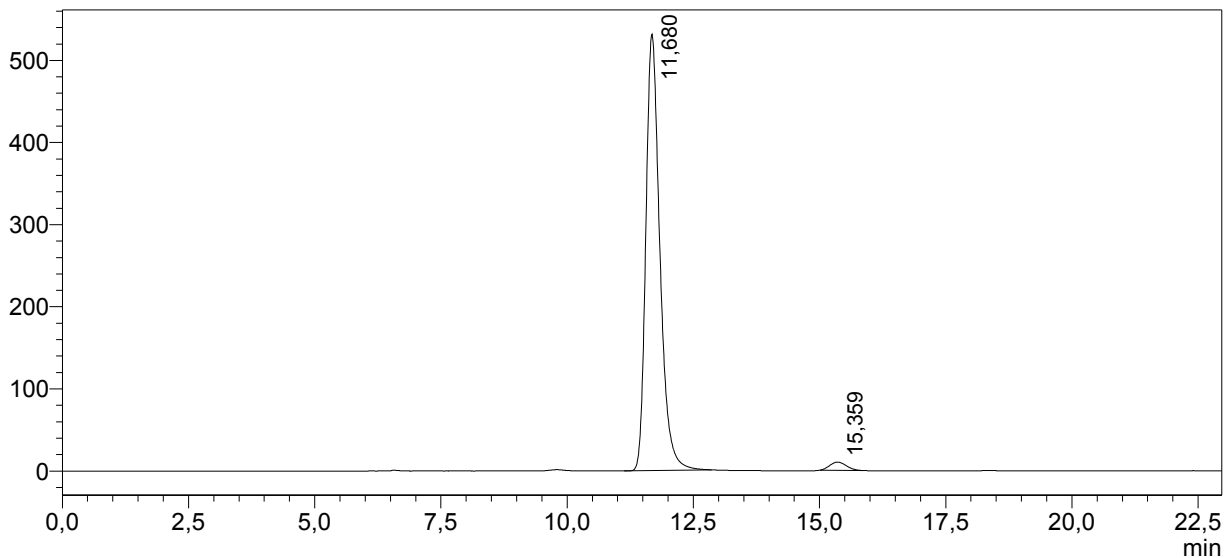


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9,392	3496560	236474	0,000	50,335
2	12,222	3449968	128820	0,000	49,665
Total		6946528	365295		100,000



mAU

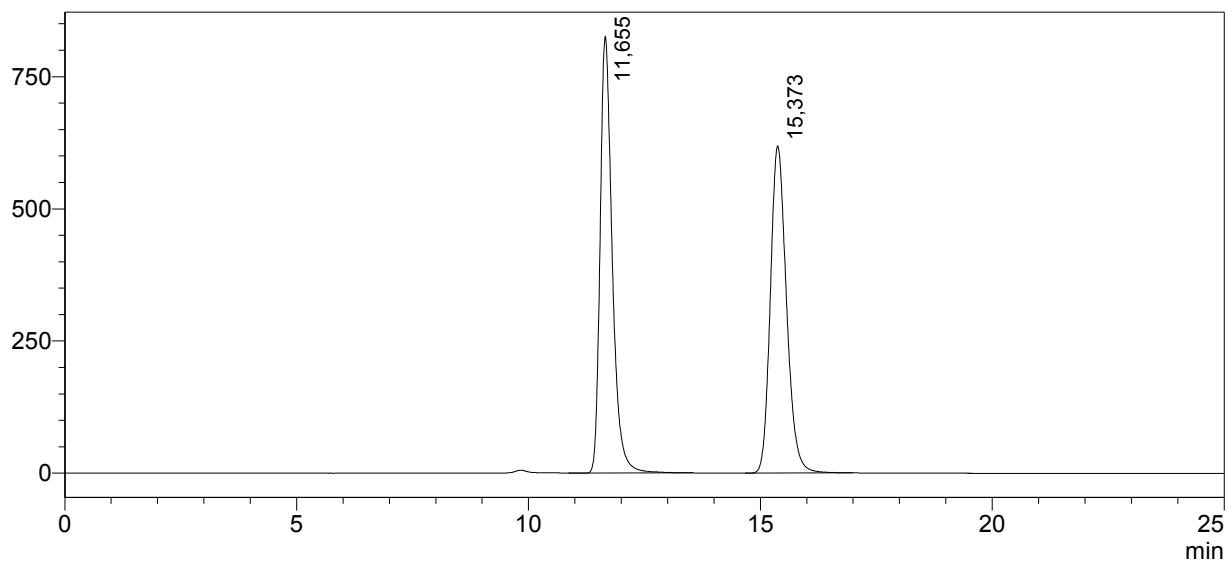


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11,680	10248972	531158	0,000	97,864
2	15,359	223685	9927	0,000	2,136
Total		10472657	541085		100,000

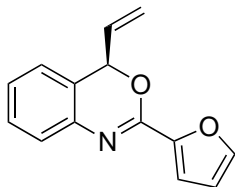
mAU

Racemic mixture:



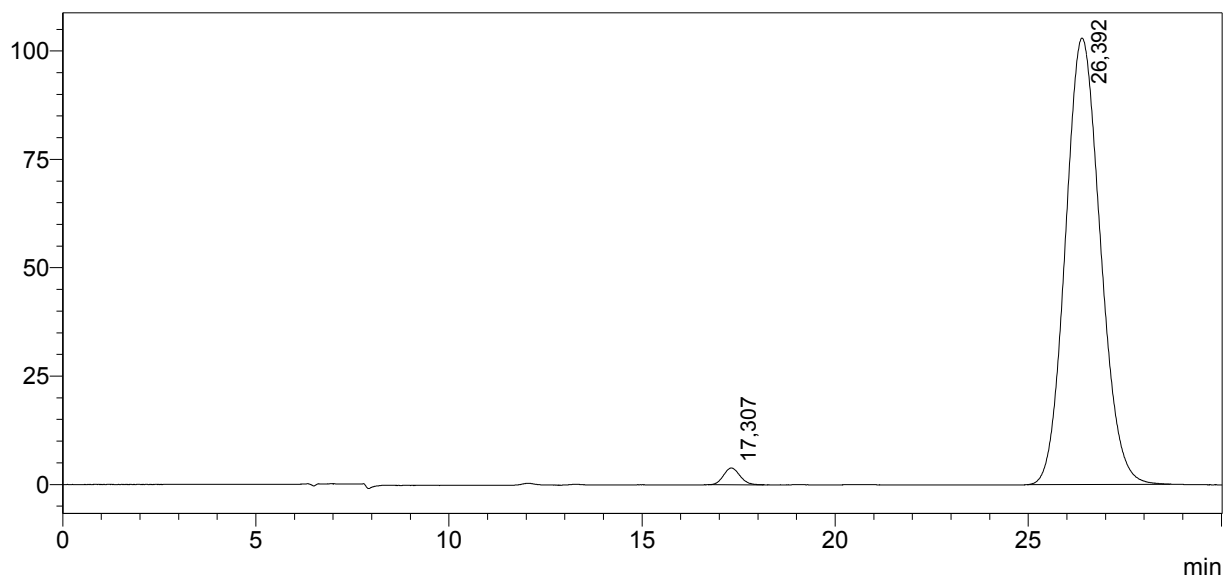
<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11,655	14975247	825387	0,000	50,003
2	15,373	14973385	618688	0,000	49,997
Total		29948631	1444075		100,000



mAU

2e

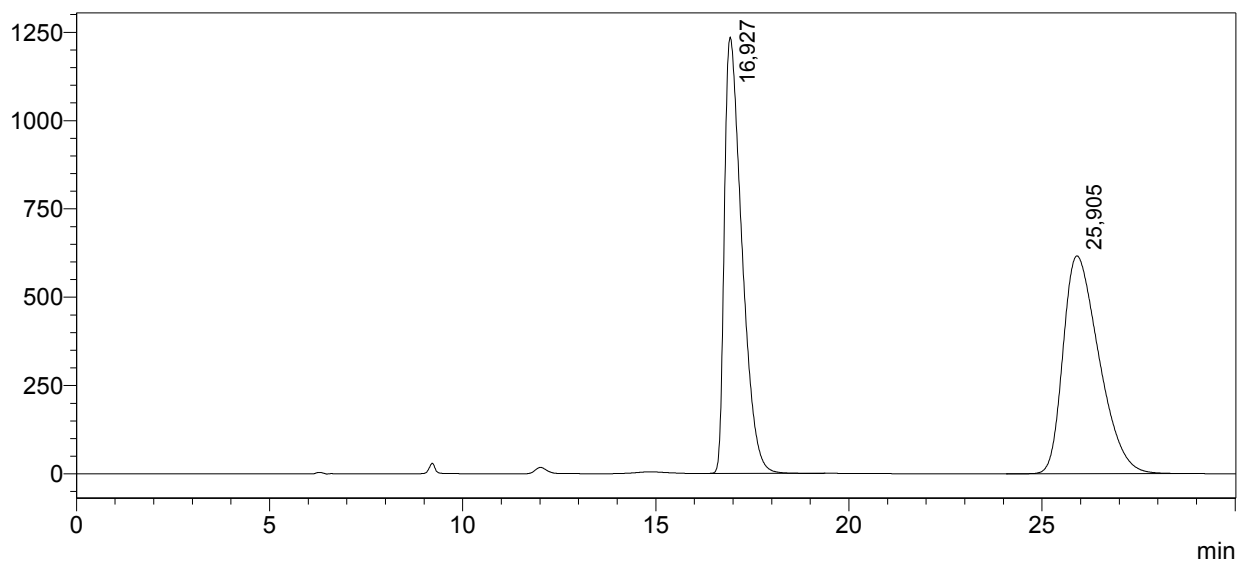


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17,307	114187	3864	0,000	1,736
2	26,392	6463193	102988	0,000	98,264
Total		6577379	106852		100,000

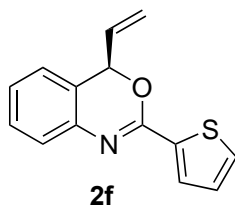
mAU

Racemic mixture:

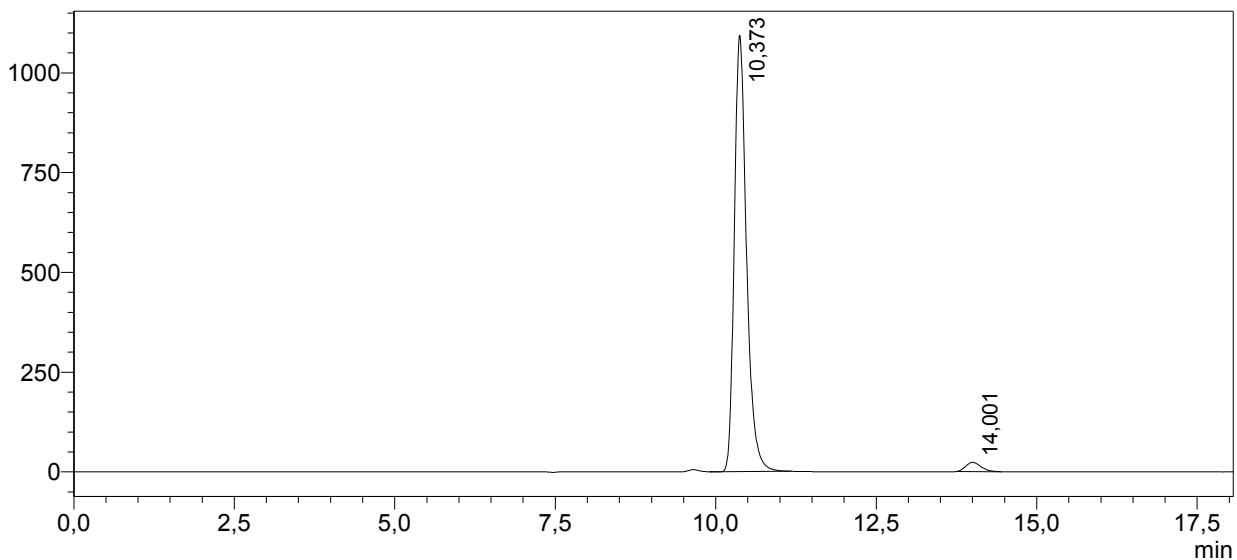


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	16,927	38877482	1234613	0,000	49,411
2	25,905	39803930	616442	0,000	50,589
Total		78681412	1851055		100,000



mAU

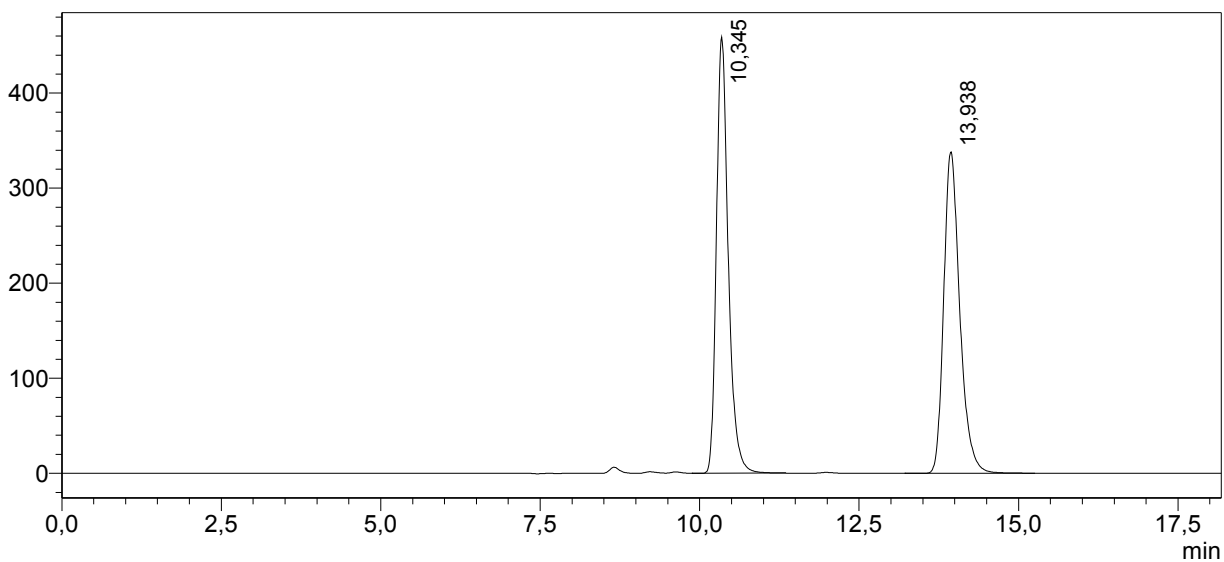


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10,373	14438329	1092586	0,000	97,427
2	14,001	381240	23141	0,000	2,573
Total		14819569	1115727		100,000

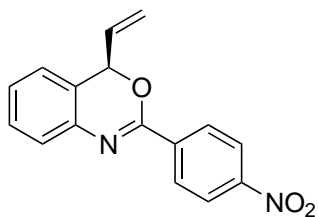
mAU

Racemic mixture:

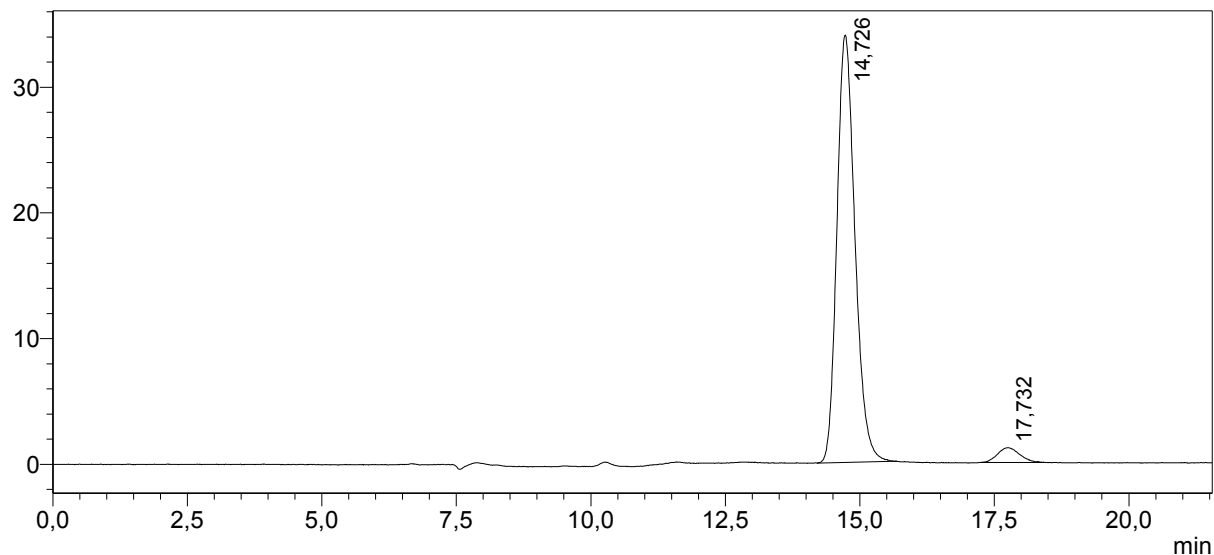


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10,345	5921901	458883	0,000	49,975
2	13,938	5927932	338186	0,000	50,025
Total		11849833	797069		100,000



mAU

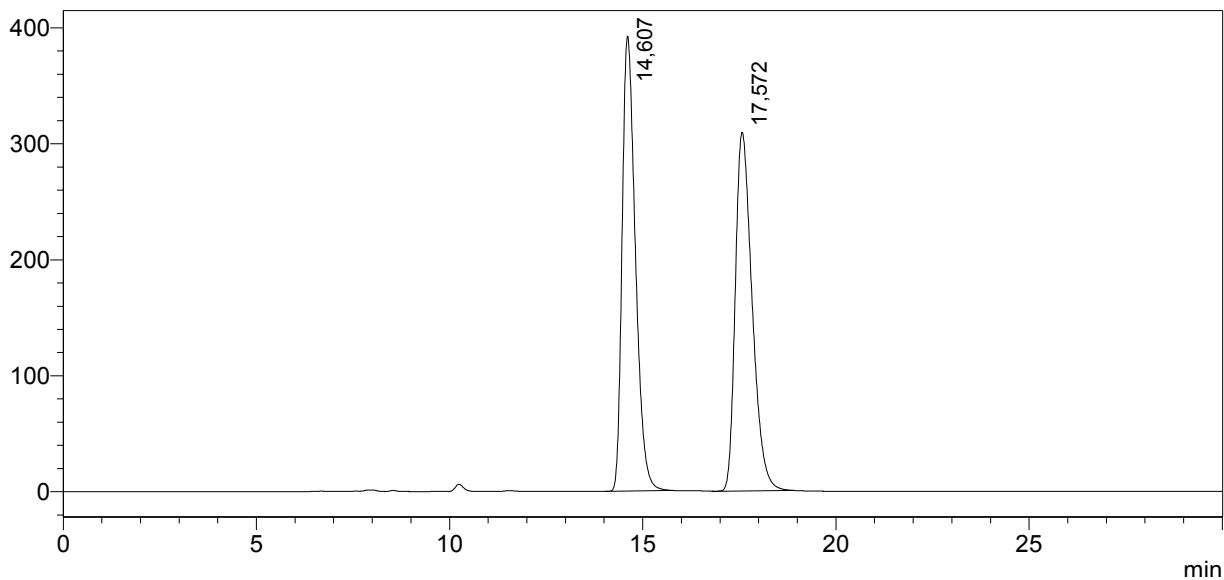


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14,726	793930	33998	0,000	95,952
2	17,732	33498	1179	0,000	4,048
Total		827428	35177		100,000

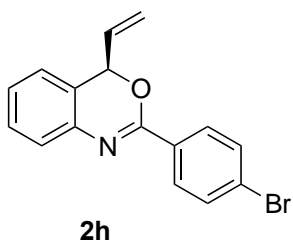
mAU

Racemic mixture:

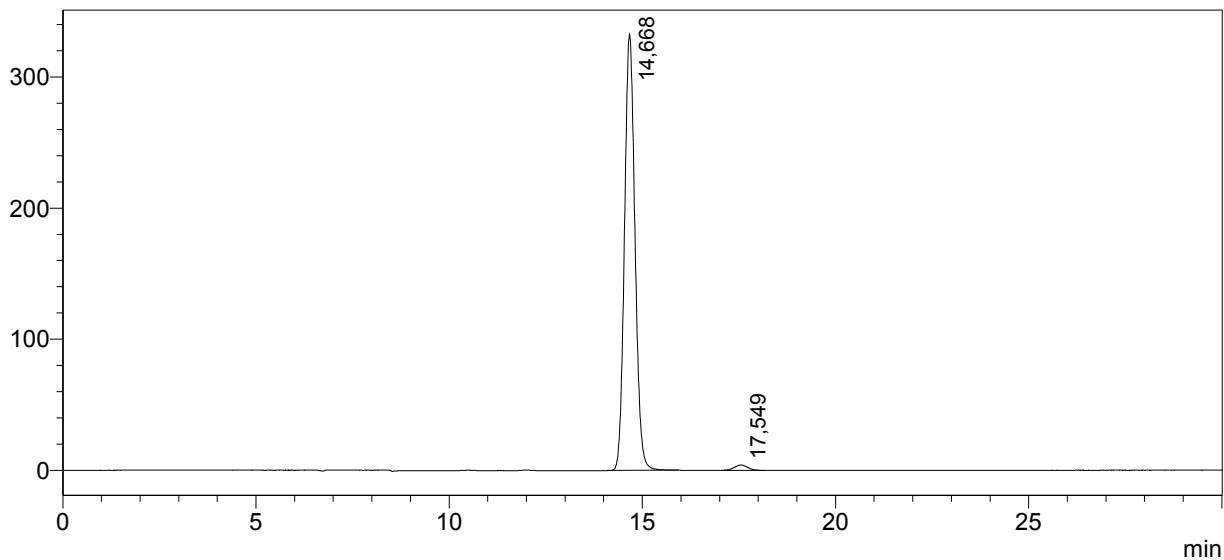


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14,607	9371156	392257	0,000	50,012
2	17,572	9366490	309231	0,000	49,988
Total		18737646	701489		100,000



mAU

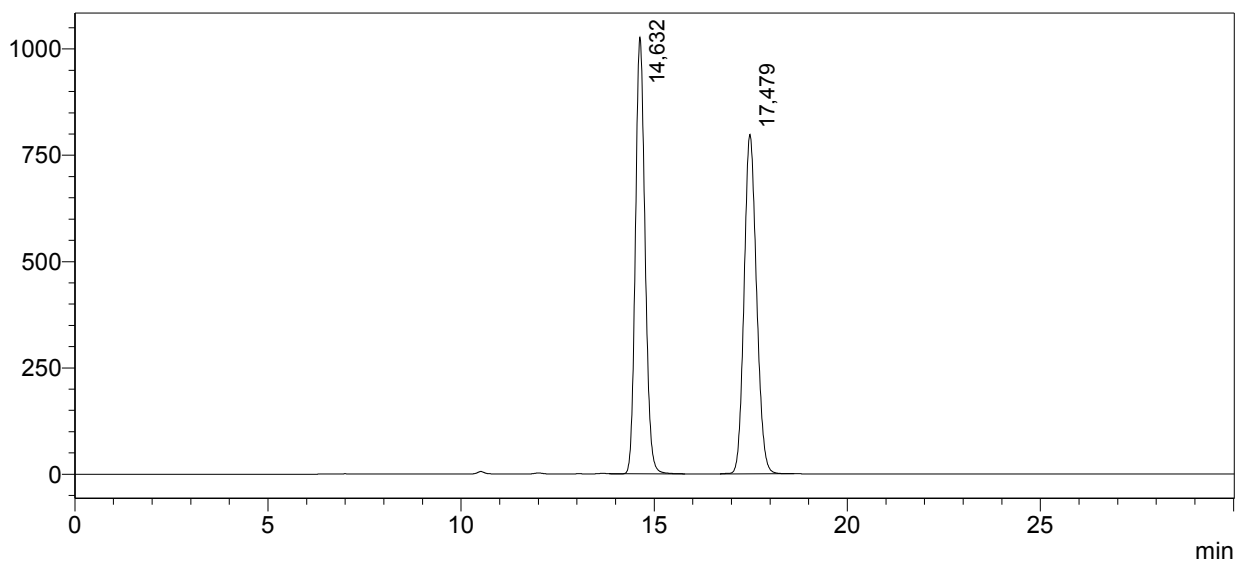


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14,668	6279017	332542	0,000	98,475
2	17,549	97211	4075	0,000	1,525
Total		6376228	336617		100,000

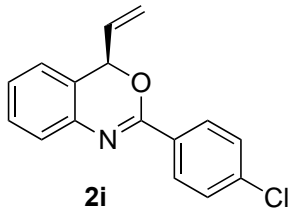
mAU

Racemic mixture:

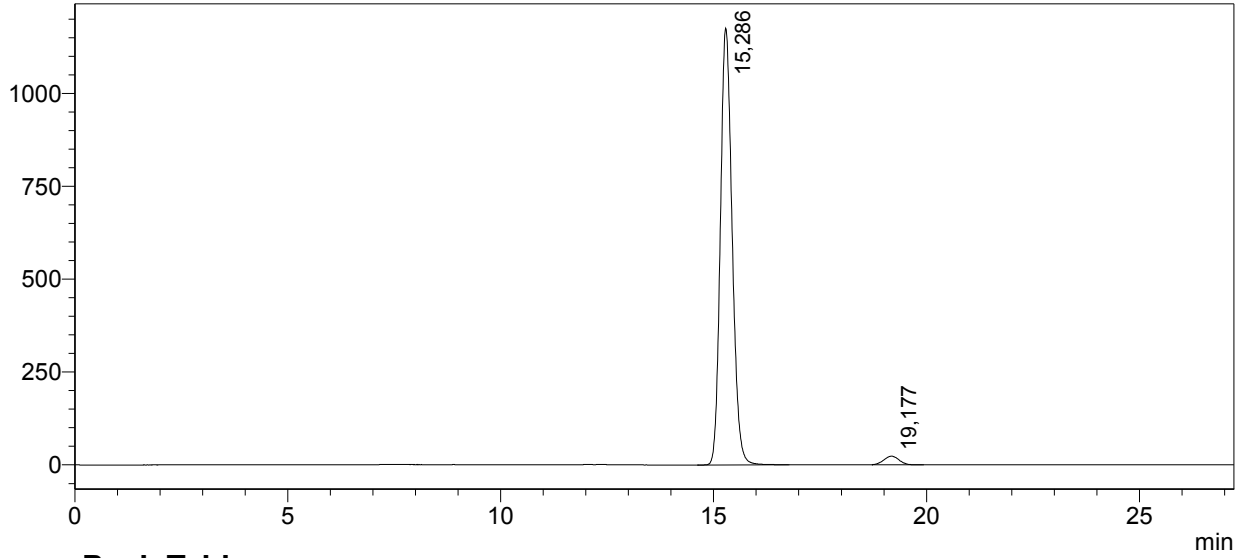


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	14,632	17814047	1026175	0,000	49,877
2	17,479	17901784	798480	0,000	50,123
Total		35715831	1824655		100,000



mAU

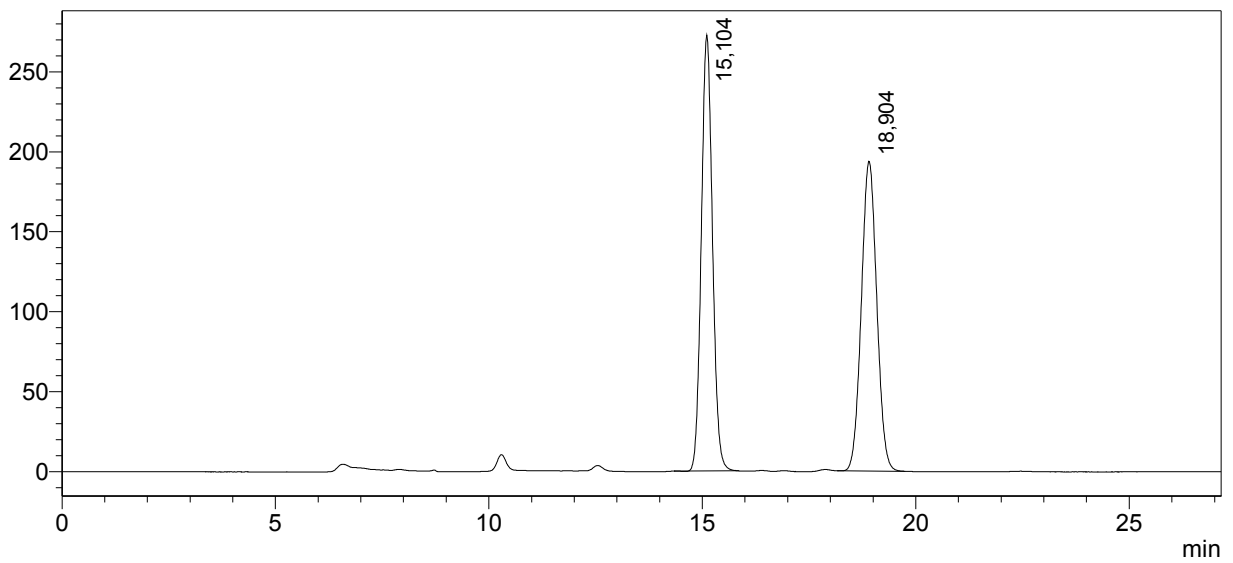


<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	15,286	22568719	1175212	97,524
2	19,177	573086	23159	2,476
Total		23141805	1198371	100,000

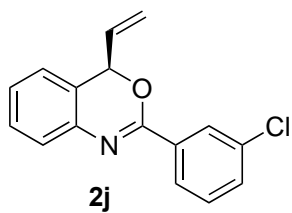
mAU

Racemic mixture:

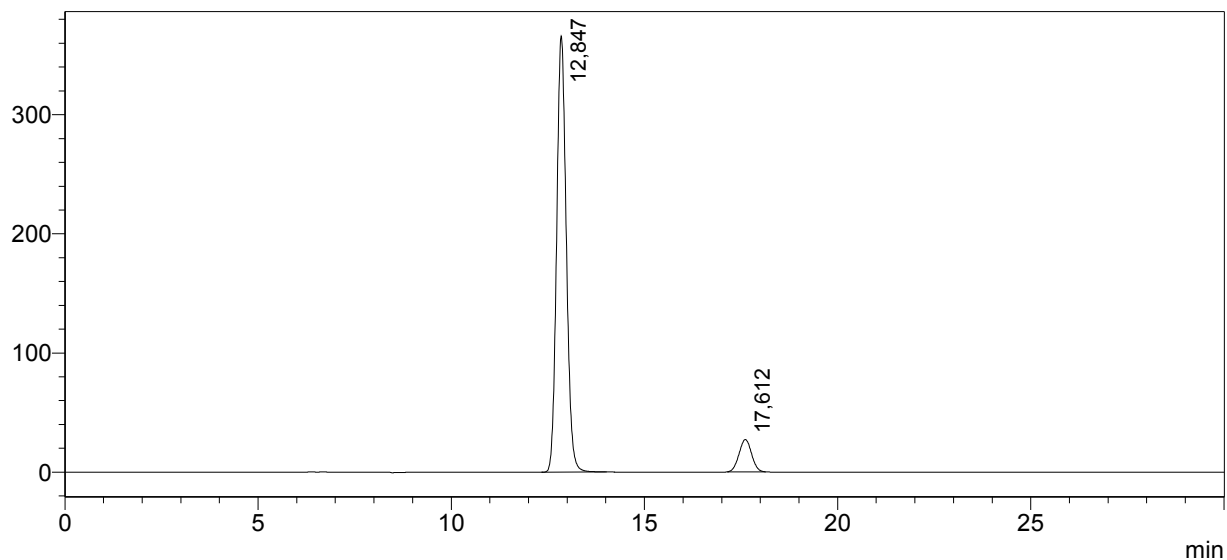


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	15,104	4950049	272552	0,000	50,431
2	18,904	4865498	193843	0,000	49,569
Total		9815547	466394		100,000



mAU

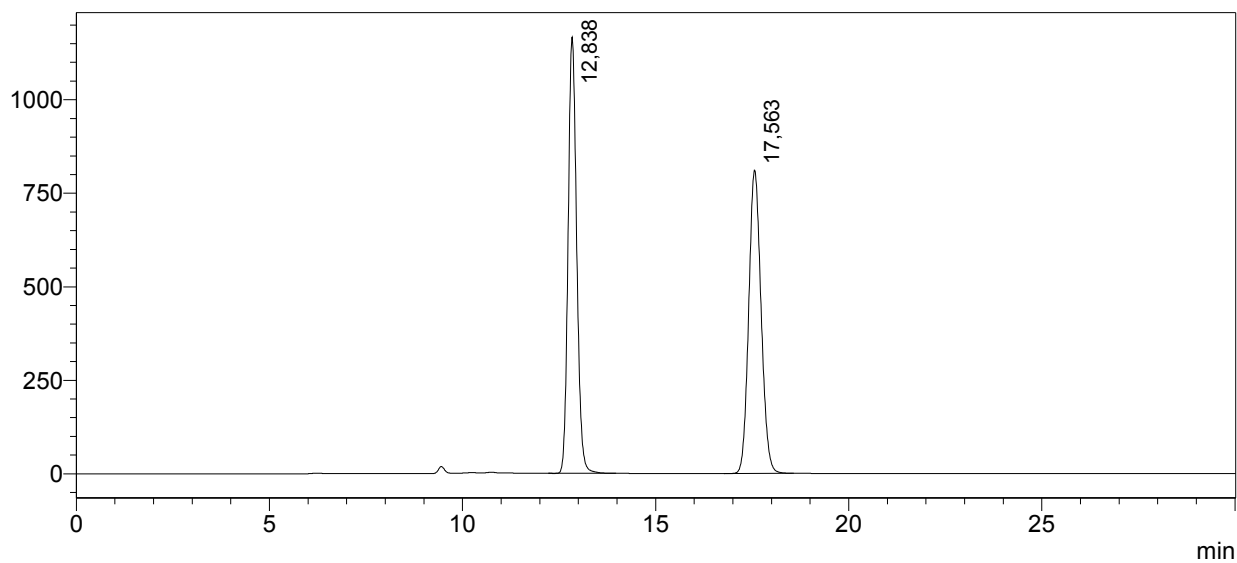


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12,847	6346912	366096	0,000	91,226
2	17,612	610430	27139	0,000	8,774
Total		6957343	393235		100,000

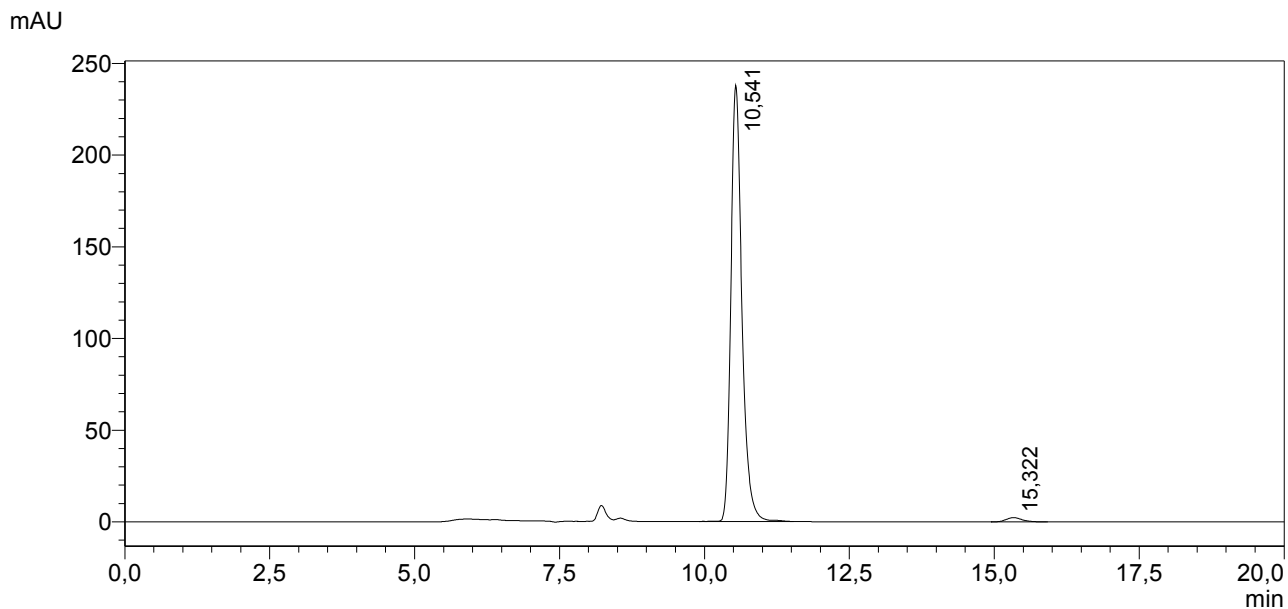
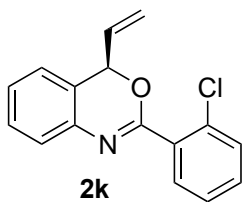
mAU

Racemic mixture:



<Peak Table>

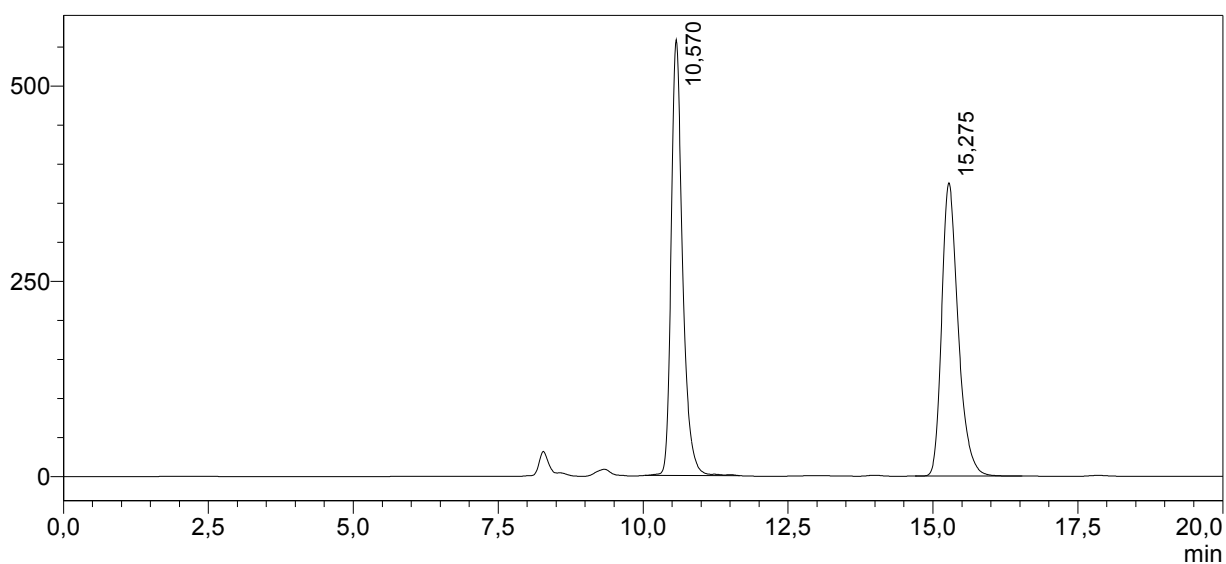
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	12,838	17957826	1166602	0,000	49,884
2	17,563	18041292	810857	0,000	50,116
Total		35999118	1977459		100,000



<Peak Table>

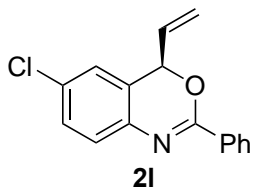
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10,541	3140940	237782	0,000	98,585
2	15,322	45097	2353	0,000	1,415
Total		3186037	240135		100,000

mAU Racemic mixture:

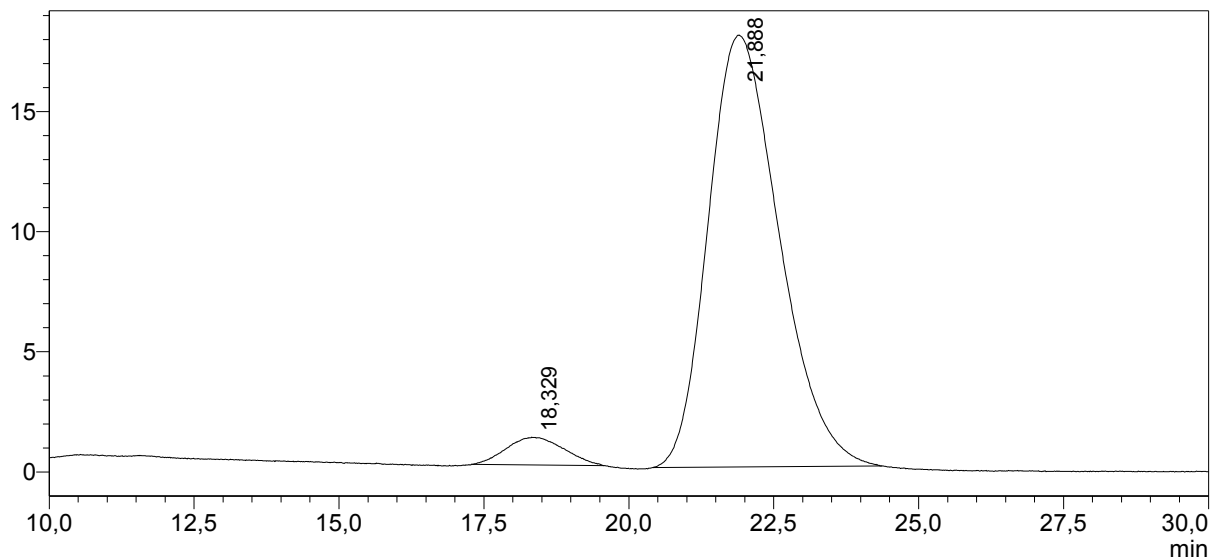


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	10,570	7592347	558030	0,000	50,547
2	15,275	7428137	375487	0,000	49,453
Total		15020484	933517		100,000



mAU

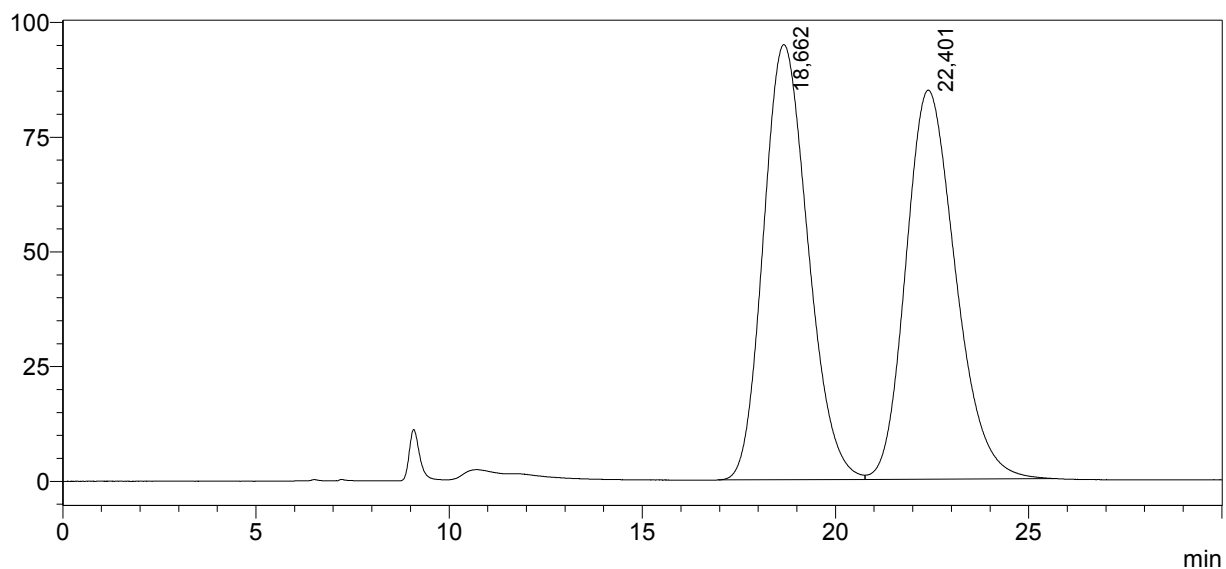


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	18,329	79752	1151	0,000	4,949
2	21,888	1531598	17970	0,000	95,051
Total		1611350	19121		100,000

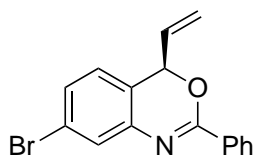
mAU

Racemic mixture:



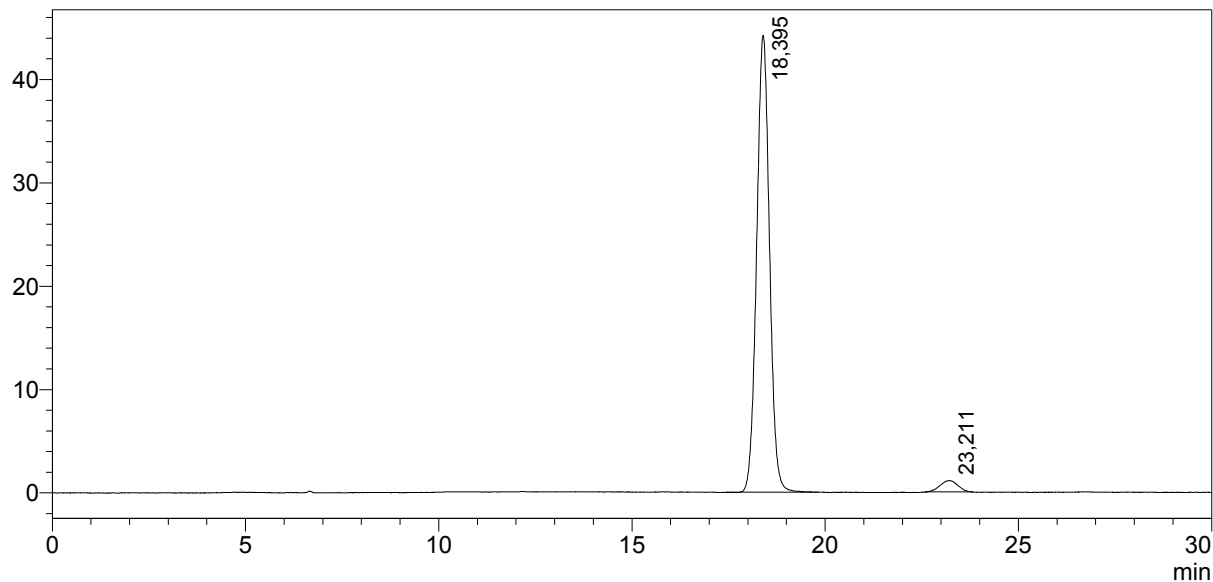
<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	18,662	7608786	94844	0,000	50,095
2	22,401	7580061	84805	0,000	49,905
Total		15188846	179649		100,000



2m

mAU

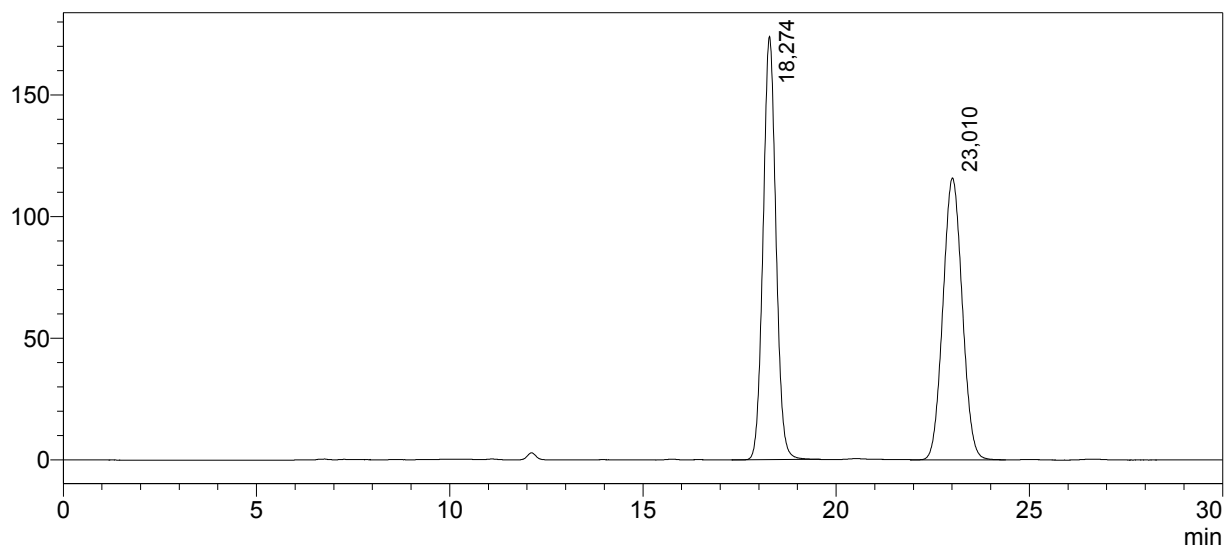


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	18,395	1021895	44211	0,000	96,663
2	23,211	35273	1101	0,000	3,337
Total		1057168	45313		100,000

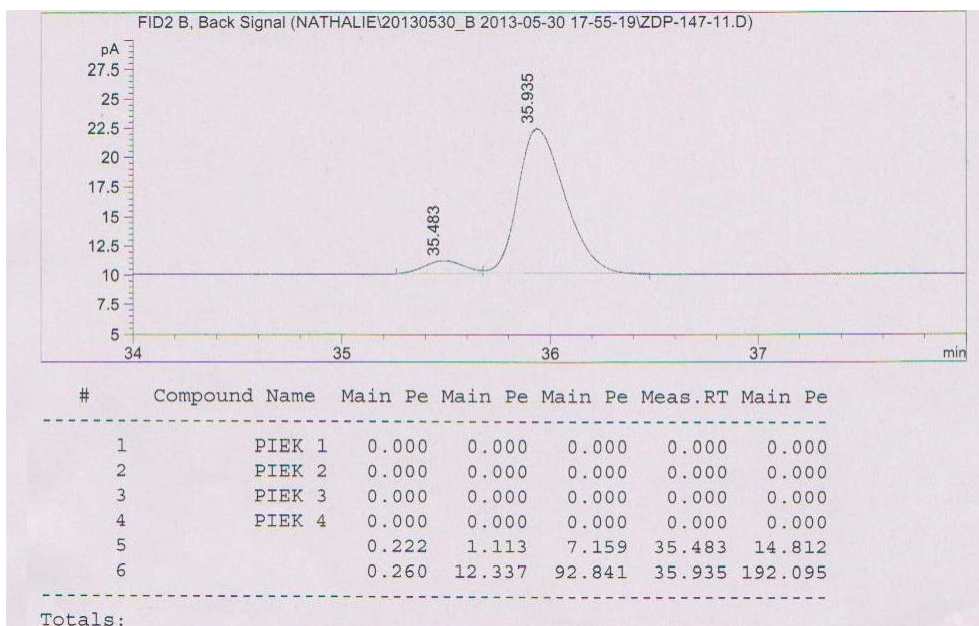
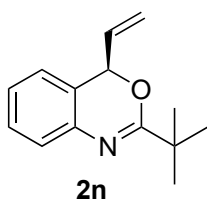
mAU

Racemic mixture:

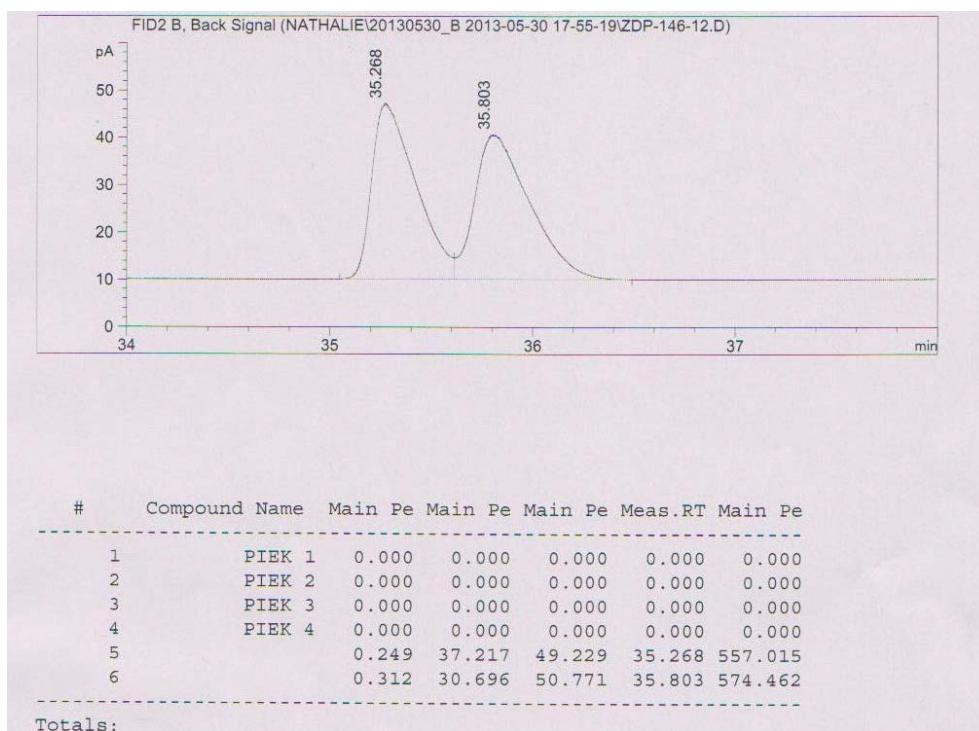


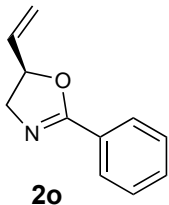
<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	18,274	4028174	173979	0,000	50,062
2	23,010	4018149	115855	0,000	49,938
Total		8046323	289833		100,000

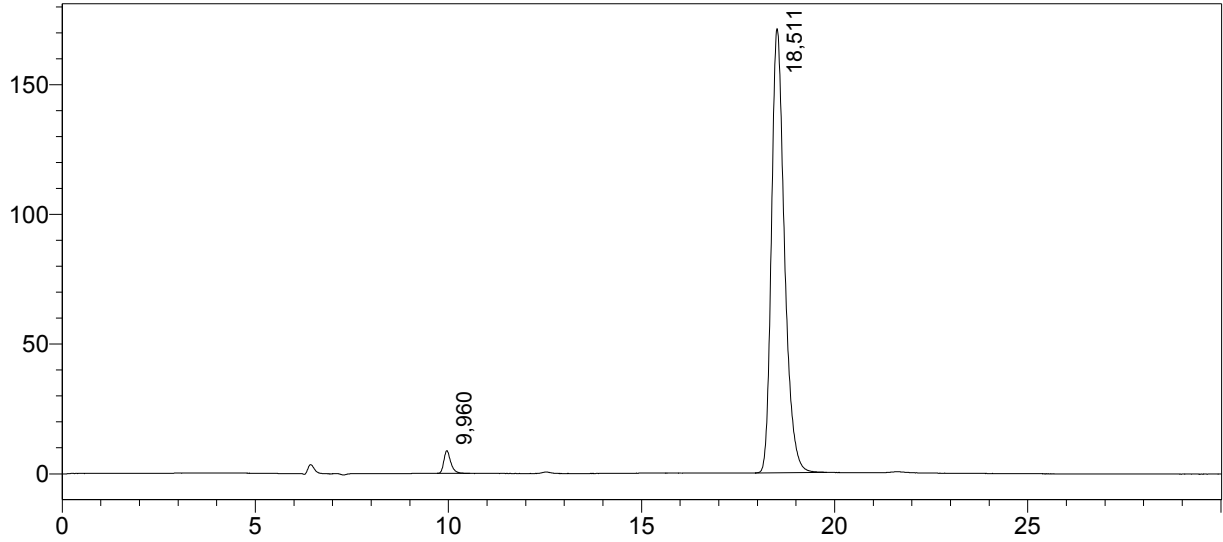


Racemic mixture:





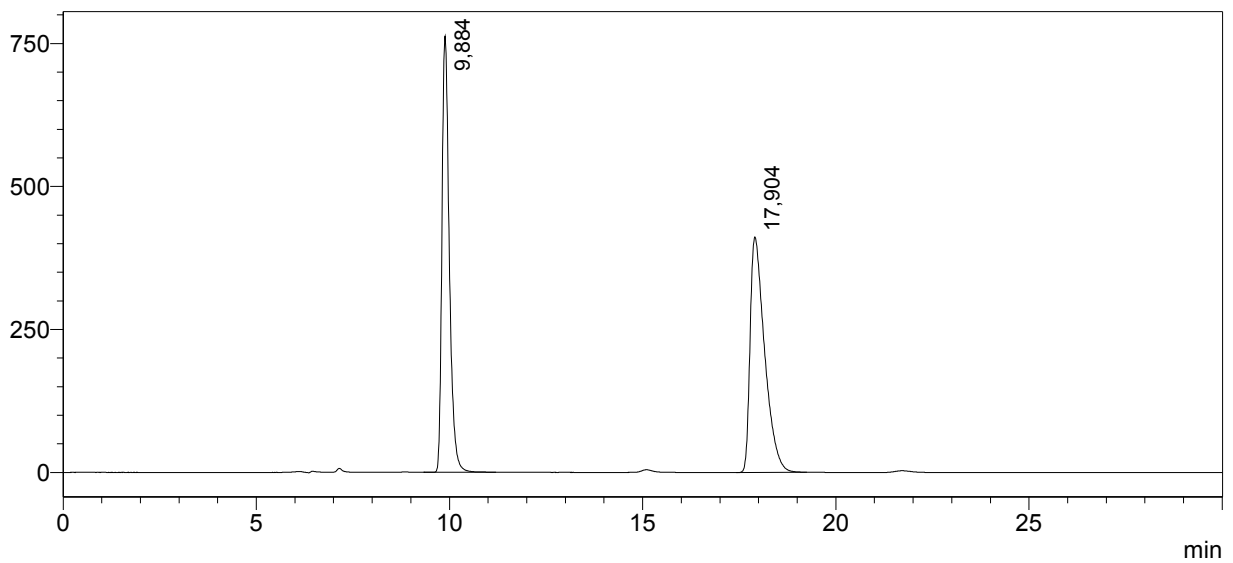
mAU



<Peak Table>

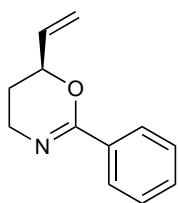
Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9,960	109722	8759	0,000	2,660
2	18,511	4014628	171201	0,000	97,340
Total		4124351	179960		100,000

mAU

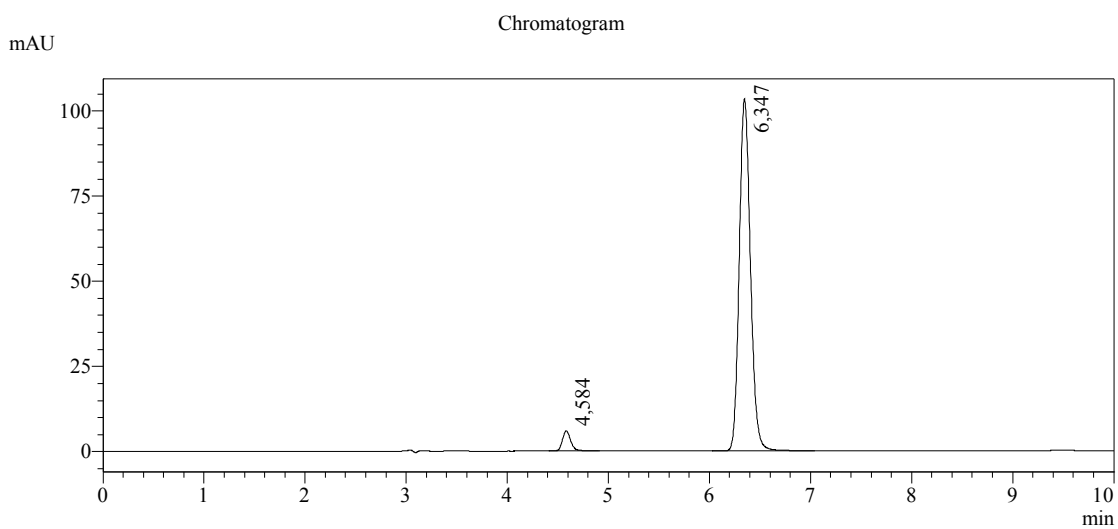


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9,884	10113248	762754	0,000	48,467
2	17,904	10752962	411477	0,000	51,533
Total		20866209	1174231		100,00

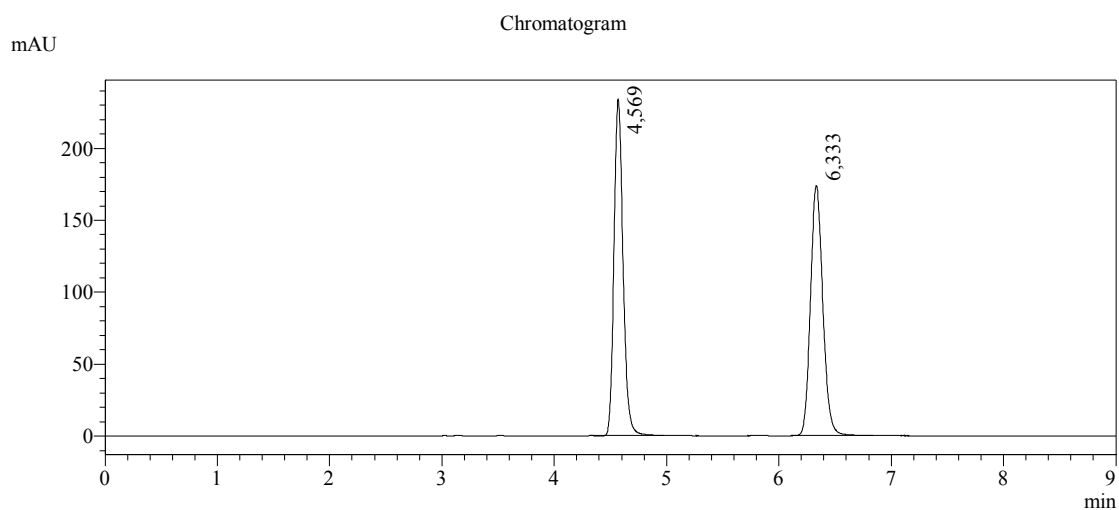


2p



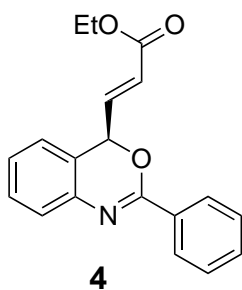
Peak Table

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	4.584	33695	5880	0,000	4,073
2	6.347	793654	103077	0,000	95,927
Total		827348	108957		100,000

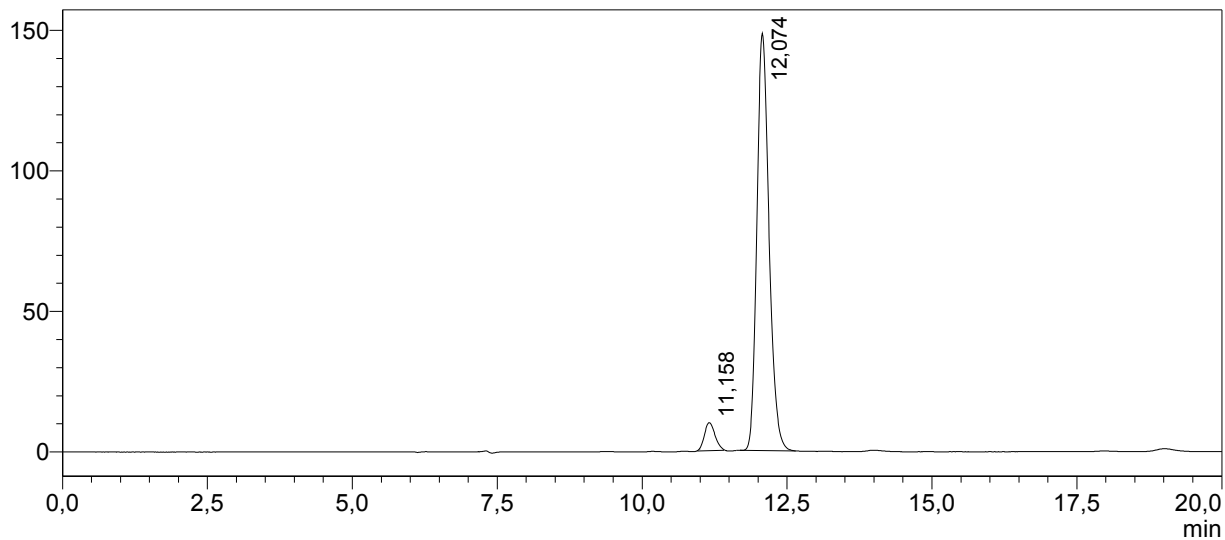


Peak Table

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	4.569	1312628	232328	0,000	49,734
2	6.333	1326650	173579	0,000	50,266
Total		2639278	405907		100,000



mAU

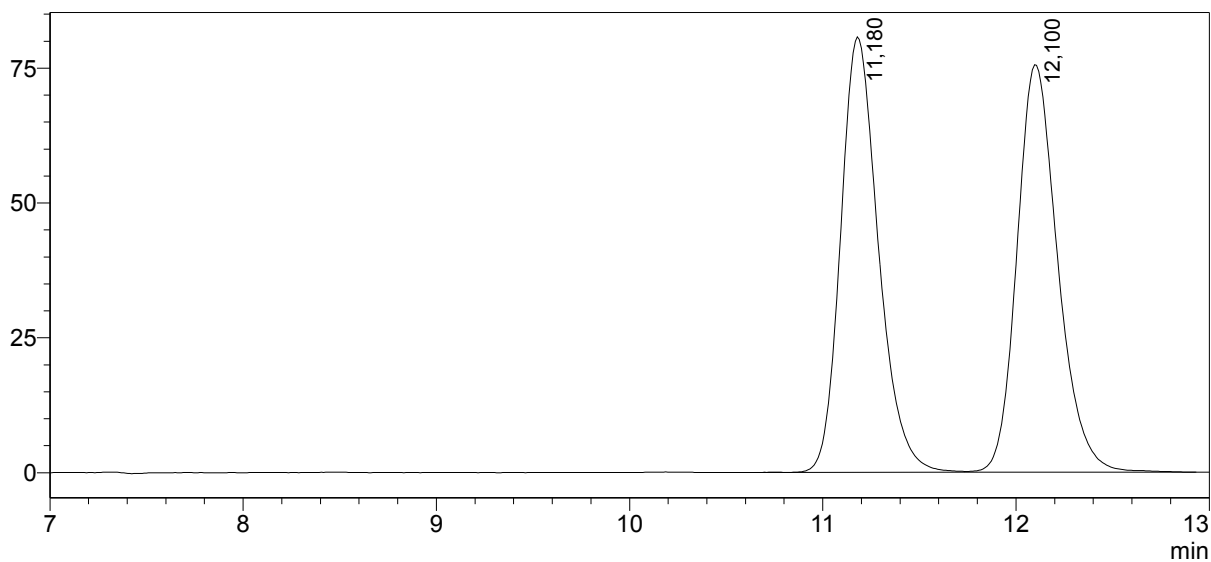


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11,158	118009	9564	0,000	5,166
2	12,074	2166551	148436	0,000	94,834
Total		2284561	158000		100,000

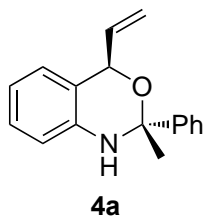
mAU

Racemic mixture:

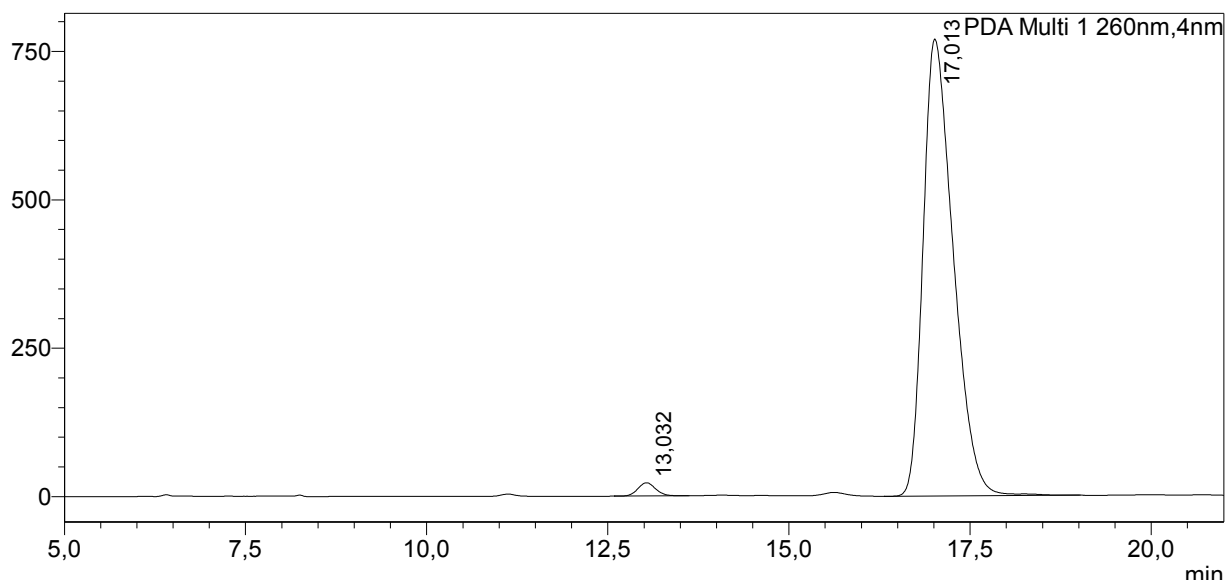


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11,180	1100178	80722	0,000	49,830
2	12,100	1107681	75540	0,000	50,170
Total		2207858	156263		100,000



mAU

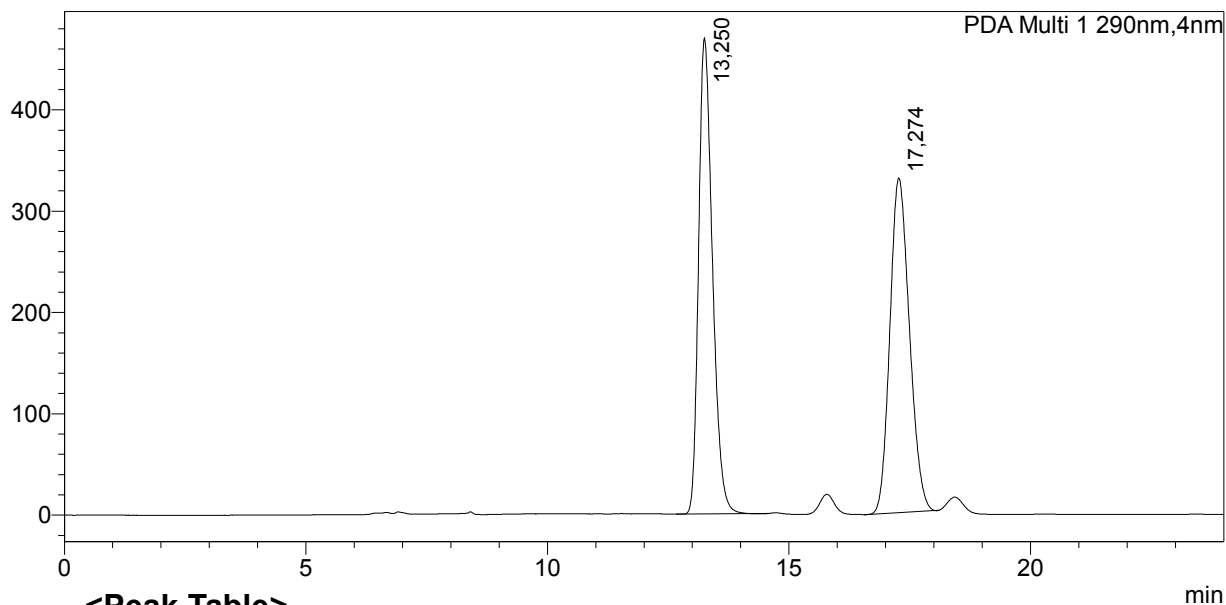


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13,032	378233	22205	0,000	1,669
2	17,013	22286251	770040	0,000	98,331
Total		22664484	792244		100,000

mAU

Racemic mixture:



<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	13,250	9365003	469565	0,000	50,196
2	17,274	9291971	330225	0,000	49,804
Total		18656974	799790		100,000