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A new atom-transfer radical cyclization (ATRC) mediated by photocatalytically-generated aminyl radicals that do not have an α-C-H bond

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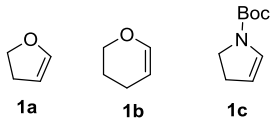
Part A: General methods, experimental procedures

General methods

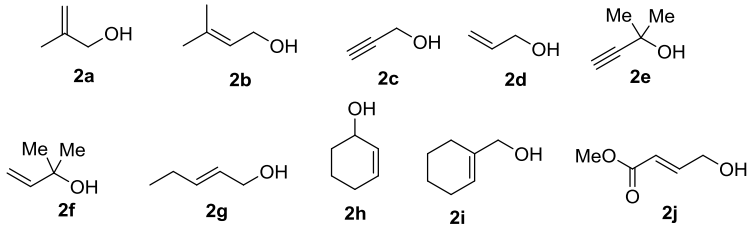
NMR data were obtained for ^{1}H at 500 MHz and for ^{13}C at 125 MHz. ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m), doublet of doublets (dd), triplet of doublets (td), doublet of quartets (dq), doublet of doublet of doublets (ddd) and broad (br). HRMS data was recorded on a Q-Exactive Plus Orbitrap MS, using ESI as ionization source.

Olefin substrates



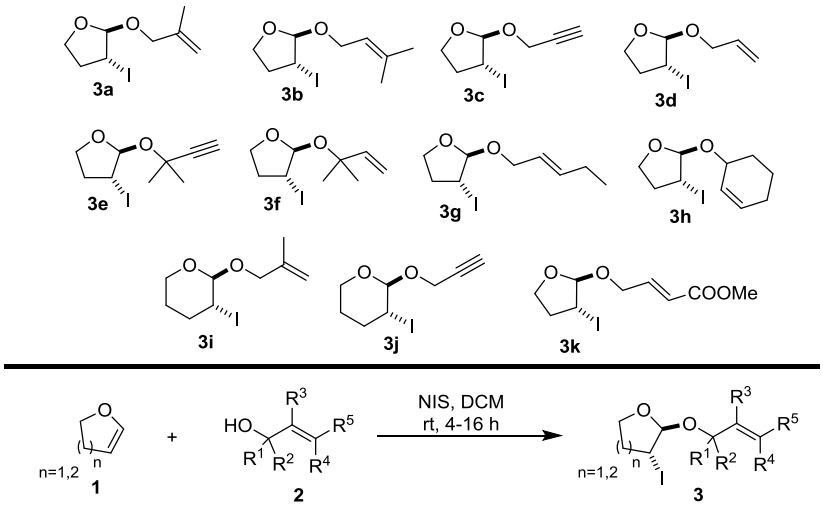
Compounds **1a-1c** are commercially available.

Starting alcohols



Compounds **2a**-**2g**, **2j** are commercially available and **2h**, **2i** were synthesized according to our previously published procedure.[1]

General experimental procedure for the synthesis of compounds of type 3

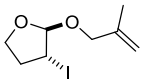


1 I. Papadopoulos, A. Bosveli, T. Montagnon, I. Zachilas, D. Kalaitzakis and G. Vassilikogiannakis, *Chem. Commun.*, 2024, **60**, 5494.

Compounds of type **1** (0.5 mmol, 37.8 μL for **1a**, 45.6 μL for **1b**) were dissolved in CH_2Cl_2 (2.5 mL). The corresponding alcohol (0.5 mmol, 42.1 μL for **2a**, 50.8 μL for **2b**, 29.1 μL for **2c**, 34.0 μL for **2d**, 48.5 μL for **2e**, 52.3 μL for **2f**, 50.9 μL for **2g**, 49.1 mg for **2h**, 58.1 mg for **2j**) was added followed by NIS (112.5 mg, 0.5 mmol). The solution was stirred in the dark at room temperature (except for the reactions of **3e** and **3f** which were heated to 40 ^oC for 48 h). After completion of the reaction (4-16 h), as was indicated by tlc analysis, a 10% aqueous solution of $Na_2S_2O_3$ (3 mL) was added and the mixture was extracted with CH_2Cl_2 (3× 4 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The products of type **3** were purified by flash column chromatography (silica gel, petroleum ether: EtOAc).

The trans stereochemistry of the products **3a-3k** was assigned according to previously reported analogues.[2]

3-iodo-2-((2-methylallyl)oxy)tetrahydrofuran (3a)



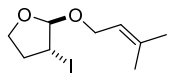
Product **3a** was synthesized according to the experimental procedure described above, with the reaction time being 16 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3a** as a pale-yellow oil (yield = 115.3 mg, 86%). The reaction was scaled up to 2 mmol scale and the results were almost identical (yield = 450.2 mg, 84%).

^1H NMR (500 MHz, $CHCl_3$) δ 5.36 (s, 1H), 4.95 (s, 1H), 4.89 (s, 1H), 4.20 (dd, J_1=6.3 Hz, J_2=2.3 Hz, 1H), 4.12 (dd, J_1=15.3 Hz, J_2=8.2 Hz, 1H), 4.06-4.01 (m, 2H), 3.89 (d, J=12.6 Hz, 1H), 2.64 (m, 1H), 2.20 (m, 1H), 1.72 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 112.4, 109.7, 70.9, 67.0, 35.7, 24.6, 19.6 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_8H_{14}IO_2$, 269.0033; found 269.0031.

3-iodo-2-((3-methylbut-2-en-1-yl)oxy)tetrahydrofuran (3b)



Product **3b** was synthesized according to the experimental procedure described above, with the reaction time being 16 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3b** as a yellow oil (yield = 77.6 mg, 55%).

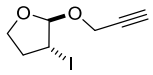
^1H NMR (500 MHz, $CHCl_3$) δ 5.37 (s, 1H), 5.30 (m, 1H), 4.17 (dd, J_1=6.3 Hz, J_2=2.1 Hz, 1H), 4.14-4.09 (m, 2H), 4.03 (td, J_1=8.4 Hz, J_2=3.7 Hz, 1H), 3.96 (dd, J_1=11.5 Hz, J_2=7.5 Hz, 1H), 2.63 (m, 1H), 2.19 (m, 1H), 1.75 (s, 3H), 1.68 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 120.1, 109.7, 66.9, 63.6, 35.6, 25.8, 24.9, 18.0 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_9H_{15}IO_2Na$, 305.0008; found 305.0008.

2 (a) S. H. Kyne, M. Clémancey, G. Blondin, E. Derat, L. Fensterbank, A. Jutand, G. Lefèvre and C. Ollivier, *Organometallics*, 2018, **37**, 761; (b) J. Y. Hwang, J. H. Baek, T. I. Shin, J. H. Shin, J. W. Oh, K. P. Kim, Y. You and E. J. Kang, *Org. Lett*., 2016, **18**, 4900; (c) A. Ekomié, G. Lefèvre, L. Fensterbank, E. Lacôte, M. Malacria, C. Ollivier and A. Jutand, *Angew. Chem. Int. Ed*., 2012, **51**, 6942; (d) S. Mayer., J. Prandi, *Tetrahedron Lett.*, 1996, **37**, 3117; (e) M. N. Matos, C. A. M. Afonso and R. A. Batey, *Tetrahedron*, 2005, **61**, 1221.

3-iodo-2-(prop-2-yn-1-yloxy)tetrahydrofuran (3c)



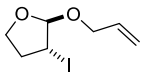
Product **3c** was synthesized according to the experimental procedure described above, with the reaction time being 16 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3c** as a yellow oil (yield = 78.2 mg, 62%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.50 (s, 1H), 4.25-4.19 (m, 3H), 4.15 (m, 1H), 4.04 (td, J_1=8.4 Hz, J_2=3.4 Hz, 1H), 2.63 (m, 1H), 2.44 (t, J=2.4 Hz, 1H), 2.20 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 108.8, 79.1, 74.5, 67.3, 53.9, 35.4, 24.1 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_7H_9IO_2Na$, 274.9539; found 274.9540.

2-(allyloxy)-3-iodotetrahydrofuran (3d)



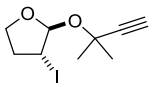
Product **3d** was synthesized according to the experimental procedure described above, with the reaction time being 16 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3d** as a pale-yellow oil (yield = 76.2 mg, 60%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.88 (m, 1H), 5.38 (s, 1H), 5.27 (dq, J_1=17.2 Hz, J_2=1.5 Hz, 1H), 5.19 (dq, J_1=10.3 Hz, J_2=1.2 Hz, 1H), 4.19-4.14 (m, 2H), 4.13 (dd, J_1=15.3 Hz, J_2=7.1 Hz, 1H), 4.03 (td, J_1=8.3 Hz, J_2=3.6 Hz, 1H), 3.97 (ddt, J_1=12.8 Hz, J_2=6.1 Hz, J_3=1.3 Hz, 1H), 2.64 (m, 1H), 2.20 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 134.1, 117.4, 109.8, 68.1, 67.0, 35.6, 24.6 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_7H_{11}IO_2Na$, 276.9695; found 276.9696.

3-iodo-2-((2-methylbut-3-yn-2-yl)oxy)tetrahydrofuran (3e)



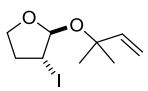
Product **3e** was synthesized according to the experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 80:1) to furnish **3e** as a yellow oil (yield = 70.1 mg, 50%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.81 (d, J=1.2 Hz, 1H), 4.15 (d, J=6.0 Hz, 1H), 4.07 (m, 2H), 2.57 (m, 1H), 2.53 (s, 1H), 2.17 (m, 1H), 1.50 (s, 3H), 1.45 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 107.3, 85.6, 72.9, 70.5, 67.0, 35.4, 30.3, 29.5, 26.6 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{14}IO_2$, 281.0033; found 281.0031.

3-iodo-2-((2-methylbut-3-en-2-yl)oxy)tetrahydrofuran (3f)



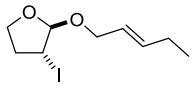
Product **3f** was synthesized according to the experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 80:1) to furnish **3f** as a yellow oil (yield = 71.9 mg, 51%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.86 (dd, J_1=17.6 Hz, J_2=10.8 Hz, 1H), 5.43 (d, J=0.5 Hz, 1H), 5.17 (dd, J_1=17.6 Hz, J_2=1.0 Hz, 1H), 5.14 (dd, J_1=10.8 Hz, J_2=1.0 Hz, 1H), 4.07-4.03 (m, 2H), 4.00 (dd, J_1=14.8 Hz, J_2=8.0 Hz, 1H), 2.57 (m, 1H), 2.16 (m, 1H), 1.31 (s, 3H), 1.27 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 114.0, 106.4, 66.6, 35.7, 27.5, 27.0, 26.1 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_9H_{15}IO_2Na$, 305.0008; found 305.0009.

(*E*)-3-iodo-2-(pent-2-en-1-yloxy)tetrahydrofuran[1] (3g)

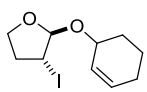


Product **3g** was synthesized according to the experimental procedure described above, with the reaction time being 4 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3g** as a yellow oil (yield = 76.9 mg, 55%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.75 (m, 1H), 5.50 (m, 1H), 5.37 (s, 1H), 4.17 (dd, J_1=6.3 Hz, J_2=2.1 Hz, 1H), 4.13-4.08 (m, 2H), 4.02 (td, J_1=8.3 Hz, J_2=3.7 Hz, 1H), 3.91 (m, 1H), 2.61 (m, 1H), 2.18 (m, 1H), 2.06 (quint, J=7.5 Hz, 2H), 0.99 (t, J=7.5 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 136.9, 124.4, 109.6, 68.0, 66.9, 35.6, 25.2, 24.8, 13.2 ppm.

2-(cyclohex-2-en-1-yloxy)-3-iodotetrahydrofuran (3h)



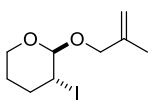
Product **3h** was synthesized according to the experimental procedure described above, with the reaction time being 5 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3h** as an inseparable mixture of two isomers 1:1 (see ^{1}H NMR integrations at 5.51 and 5.49 ppm) and as a pale-yellow oil (yield = 80.9 mg, 55%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.86 (m, 1H for both isomers), 5.72 (dq, J_1=10.0 Hz, J_2=2.5 Hz, 1H for one isomer), 5.67 (dq, J_1=10.5 Hz, J_2=2.6 Hz, 1H for one isomer), 5.51 (s, 1H for one isomer), 5.49 (s, 1H for one isomer), 4.15 (m, 2H for one isomer, 1H for the other), 4.12-4.08 (m, 2H for one isomer, 1H for the other), 4.06-4.02 (m, 1H for both isomers), 2.68-2.60 (m, 1H for both isomers), 2.21-2.17 (m, 1H for both isomers), 2.05-1.91 (m, 2H for both isomers), 1.84-1.79 (m, 1H for both isomers), 1.71-1.63 (m, 2H for both isomers), 1.57-1.53 (m, 1H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 131.6 (for one isomer), 131.0 (for one isomer), 128.2 (for one isomer), 127.0 (for one isomer), 109.7 (for one isomer), 108.8 (for one isomer), 71.0 (for one isomer), 70.2 (for one isomer), 66.8 (for one isomer), 66.7 (for one isomer), 35.7 (for one isomer), 35.6 (for one isomer), 29.9 (for one isomer), 28.3 (for one isomer), 25.7 (for one isomer), 25.4 (for one isomer), 25.0 (for both isomers), 19.1 (for one isomer), 19.0 (for one isomer) ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_{10}H_{15}IO_2Na$, 317.0008; found 317.0009.

3-iodo-2-((2-methylallyl)oxy)tetrahydro-2H-pyran[1] (3i)

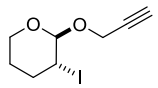


Product **3i** was synthesized according to the experimental procedure described above, with the reaction time being 4 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3i** as a yellow oil (yield = 100.2 mg, 71%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.01 (m, 1H), 4.91 (s, 1H), 4.64 (d, J=5.4 Hz, 1H), 4.14 (d, J=12.4 Hz, 1H), 4.11 (m, 1H), 3.99 (m, 1H), 3.94 (d, J=12.4 Hz, 1H), 3.58 (m, 1H), 2.39 (m, 1H), 2.03 (m, 1H), 1.78 (s, 3H), 1.75 (m, 1H), 1.58 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 141.3, 112.9, 101.5, 71.8, 63.6, 32.9, 29.1, 25.6, 19.7 ppm.

3-iodo-2-(prop-2-yn-1-yloxy)tetrahydro-2H-pyran (3j)



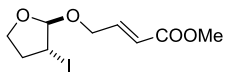
Product **3j** was synthesized according to the experimental procedure described above, with the reaction time being 5 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **3j** as a pale-yellow oil (yield = 80.9 mg, 70%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 4.88 (d, *J*=4.7 Hz, 1H), 4.33-4.26 (m, 2H), 4.12 (dt, J_1=7.4 Hz, J_2=4.4 Hz, 1H), 3.95 (m, 1H), 3.61 (m, 1H), 2.46 (t, *J*=2.5 Hz, 1H), 2.35 (m, 1H), 2.01 (m, 1H), 1.85 (m, 1H), 1.56 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 100.3, 78.8, 74.8, 63.1, 54.7, 31.8, 28.2, 24.8 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_8H_{11}IO_2Na$, 288.9695; found 288.9697.

methyl (E)-4-((3-iodotetrahydrofuran-2-yl)oxy)but-2-enoate (3k)



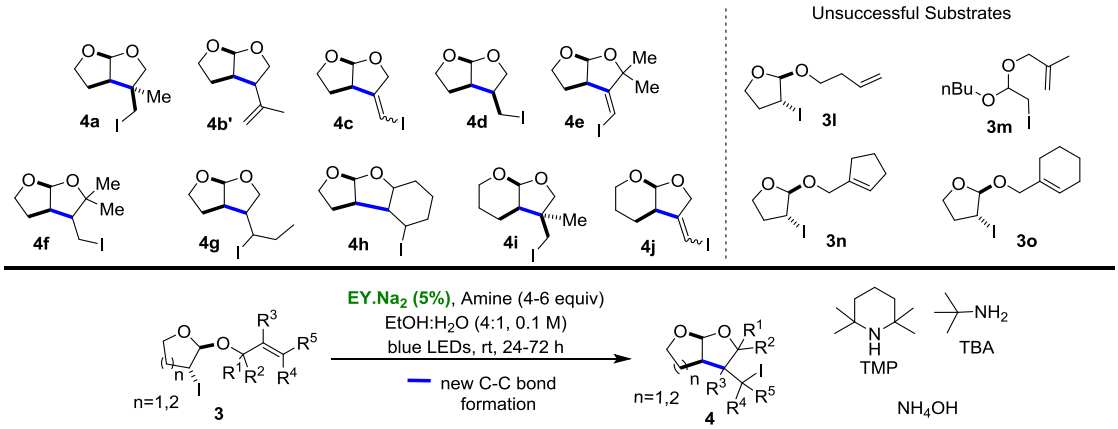
Product **3k** was synthesized according to the experimental procedure described above, with the reaction time being 16 h. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 40:1) to furnish **3k** as a yellow oil (yield = 78.0 mg, 50%).

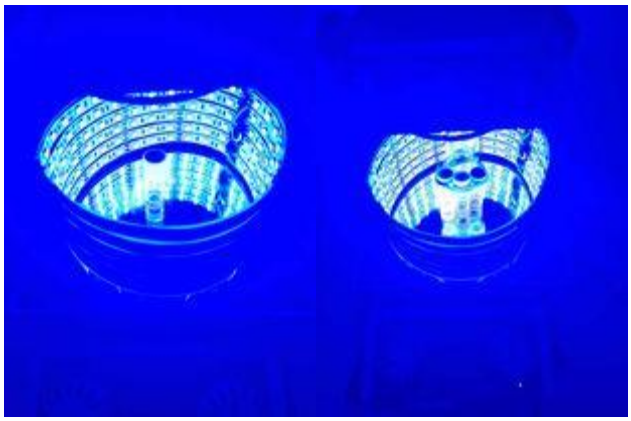
^{1}H NMR (500 MHz, $CHCl_3$) δ 6.91 (dt, J_1=14.2 Hz, J_2=4.4 Hz, 1H), 6.00 (dt, J_1=14.2 Hz, J_2=2.1 Hz, 1H), 5.36 (s, 1H), 4.31 (ddd, J_1=16.1 Hz, J_2=4.4 Hz, J_3=2.1 Hz, 1H), 4.18 (dd, J_1=6.3 Hz, J_2=2.1 Hz, 1H), 4.11 (m, 2H), 4.01 (td, J_1=8.4 Hz, J_2=3.6 Hz, 1H), 3.73 (s, 3H), 2.62 (m, 1H), 2.20 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 143.9, 120.8, 110.1, 67.2, 65.4, 51.6, 35.5, 23.9 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_9H_{13}IO_4Na$, 334.9750; found 334.9745.

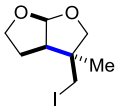
General experimental for the synthesis of substrates of type 4





To a solution of compounds of type **3** (0.1 mmol, 26.8 mg for **3a**, 28.2 mg for **3b**, 25.2 mg for **3c**, 25.4 mg for **3d**, 28.0 mg for **3e**, 28.2 mg for **3f**, 28.2 mg for **3g**, 28.2 mg for **4i**, 26.6 mg for **4j)** in EtOH: H_2O (4:1, 0.8 mL EtOH and 0.2 mL H_2O), the photocatalyst $EY.Na_2$ (5%, 3.5 mg, 0.005 mmol) was added and argon (balloon) was gently bubbled through the solution for 10 min at rt. Afterwards, under an argon atmosphere, the corresponding amine [101.3 μL, 0.6 mmol of TMP or 63.1 μL, 0.6 mmol of TBA or 27 μL of a 14.8 M aqueous solution of NH_4OH, (0.4 mmol)] was added and the solution was irradiated using blue LED light strips (60 LEDs/m, 10.8 w/m, 1000 lm/m, λ_{max} = 420 nm) at the same temperature. The LED light strips were placed in a circular formation with a circumference of 47 cm. If only one reaction vessel was used, it was placed at the center of the circle at a distance of 7 cm from the LED strips (see, photo above). If more than 1 reaction vessel was used then they were attached around an empty vial in order to prevent wobbling and to allow the light to pass through every vessel evenly (see photo above). After completion of the reaction, as indicated by tlc analysis and ^{1}H-NMR, the reactions were concentrated *in vacuo* and the products of type **4** were purified by flash column chromatography.

3-(iodomethyl)-3-methylhexahydrofuro[2,3-b]furan (4a)



Product **4a** was synthesized according to the experimental procedure described above, utilizing each one of the three amines (24 h for TBA & TMP, 48 h for NH_4OH). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4a** as a pale-

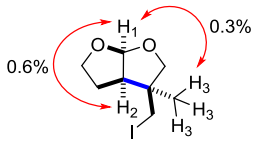
yellow oil (yield = 20.1 mg, 75% for NH_4OH, 22.0 mg, 82% for TMP, 20.6 mg, 77% for TBA). The procedure using NH_4OH as amine was scaled up to 1 mmol of starting material **3a** and the results were very similar (yield = 198.4 mg, 74%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.80 (d, *J*=5.0 Hz, 1H), 3.96 (dd, J_1=15.8 Hz, J_2= 7.0 Hz, 1H), 3.86 (m, 1H), 3.69 (d, *J*=8.4 Hz, 1H), 3.63 (d, *J*=8.4 Hz, 1H), 3.20 (d, *J*=10.0 Hz, 1H), 3.15 (d, *J*=10.0 Hz, 1H), 2.46 (m, 1H), 2.02 (m, 1H), 1.81 (m, 1H), 1.28 (s, 3H) ppm.

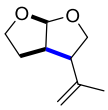
^{13}C NMR (125 MHz, $CDCl_3$) δ 109.6, 75.9, 68.8, 53.1, 45.8, 27.1, 26.4, 12.1 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_8H_{14}IO_2$, 269.0033; found 269.0031.

Representative NOE for compound **4a**



3-(prop-1-en-2-yl)hexahydrofuro[2,3-b]furan (4b′)



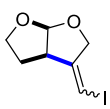
Product **4b′** was synthesized according to the experimental procedure described above, utilizing NH_4OH (72 h). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 40:1) to furnish **4b′** as an inseparable mixture of 1:1 diastereomers (see ^{13}C NMR) and as a yellow oil (yield = 14.2 mg, 46%).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.40 (s, 1H for one isomer), 5.38 (s, 1H for one isomer), 5.05 (s, 1H for one isomer), 5.04 (s, 1H for one isomer), 4.91 (s, 1H for both isomers), 4.18 (m, 2H for both isomers), 4.12 (m, 1H for both isomers), 4.06 (m, 1H for both isomers), 3.73 (dd, J_1=10.7 Hz, J_2=3 Hz, 1H for one isomer), 3.66 (dd, J_1=10.8 Hz, J_2=3 Hz, 1H for one isomer), 3.56 (dd, J_1=10.7 Hz, J_2=3 Hz, 1H for one isomer), 3.53 (dd, J_1=10.8 Hz, J_2=3 Hz, 1H for one isomer), 2.60 (m, 1H for both isomers), 2.20 (1H for both isomers), 1.73 (s, 3H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 143.5, 112.2, 111.9, 111.3, 111.1, 74.1, 74.0, 71.9, 71.4, 67.3, 67.2, 35.6, 35.5, 24.0, 23.9, 18.9, 18.8 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{15}O_2$, 155.1066; found 155.1064.

3-(iodomethylene)hexahydrofuro[2,3-b]furan (4c)



Product **4c** was synthesized according to the experimental procedure described above, utilizing TMP and TBA (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4c** as an inseparable mixture of 0.75:1 stereoisomers (see ^{1}H NMR integrations at 5.96 and 5.83 ppm) and as a yellow oil (yield = 16.9 mg, 67% for TBA, 17.1 mg, 68% for TMP).

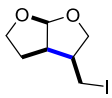
^{1}H NMR (500 MHz, $CHCl_3$) δ 6.16 (q, *J*=1.7 Hz, 1H for minor isomer), 6.13 (q, *J*=2.2 Hz, 1H for major isomer), 5.96 (d, *J*=4.8 Hz, 1H for major isomer), 5.83 (d, *J*=4.9 Hz, 1H for minor isomer), 4.46-4.37 (m, 2H for both isomers), 4.02-3.95 (m, 1H for both isomers), 3.84-3.77 (m, 1H for both isomers), 3.32 (dd, J_1=5.4 Hz, J_2=5.0 Hz, 1H for major isomer), 3.26 (m, 1H for minor isomer), 2.25-2.12 (m, 1H for both

isomers), 2.05 (m, 1H for minor isomer), 1.95 (dd, J_1=12.5 Hz, J_2=5.3 Hz, 1H for major isomer) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7 (major), 153.3 (minor), 110.9 (major), 108.9 (minor), 76.4 (major), 72.4 (minor), 70.5 (minor), 69.1 (major), 68.2 (minor), 67.5 (major), 51.3 (minor), 49.3 (major), 34.1 (major), 32.3 (minor) ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_7H_{10}IO_2$, 252.9720; found 252.9716.

3-(iodomethyl)hexahydrofuro[2,3-b]furan (4d)



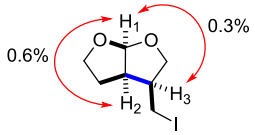
Product **4d** was synthesized according to the experimental procedure described above, utilizing TMP and TBA (24 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4d** as a yellow oil (yield = 17.8 mg, 70% for both amines).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.77 (d, J=5.0 Hz, 1H), 4.03 (dd, J_1=8.5 Hz, J_2=7.3 Hz, 1H), 3.90 (m, 2H), 3.45 (dd, J_1=11.0 Hz, J_2=8.7 Hz, 1H), 3.17 (dd, J_1=9.9 Hz, J_2=7.7 Hz, 1H), 3.08 (dd, J_1=9.8 Hz, J_2=8.6 Hz, 1H), 2.90 (m, 1H), 2.80 (m, 1H), 1.92 (m, 1H), 1.82 (m, 1H) ppm.

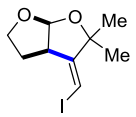
^{13}C NMR (125 MHz, $CDCl_3$) δ 109.7, 72.1, 69.1, 46.6, 45.4, 24.5, 0.3 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_7H_{12}IO_2$, 254.9876; found 254.9874.

Representative NOE for compound **4d**



***E*-3-(iodomethylene)-2,2-dimethylhexahydrofuro[2,3-b]furan (4e)**



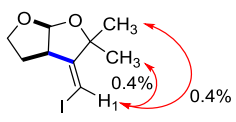
Product **4e** was synthesized according to the experimental procedure described above, utilizing TBA and TMP (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 40:1) to furnish **4e** as a yellow oil (yield = 13.7 mg, 49% for TBA, 15.1 mg, 54% for TMP).

^{1}H NMR (500 MHz, $CHCl_3$) δ 6.07 (d, J=2.3 Hz, 1H), 5.80 (d, J=5.0 Hz, 1H), 3.99 (td, J_1=8.7 Hz, J_2=2.8 Hz, 1H). 3.91 (m, 1H), 3.36 (m, 1H), 2.27 (m, 1H), 2.00 (m, 1H), 1.39 (s, 3H), 1.31 (s, 3H) ppm.

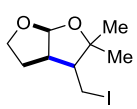
^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 106.4, 85.3, 71.1, 66.7, 52.3, 32.2, 30.0, 29.0 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_9H_{13}IO_2Na$, 302.9852; found 302.9851.

Representative NOE for compound **4e**



3-(iodomethyl)-2,2-dimethylhexahydrofuro[2,3-b]furan (4f)



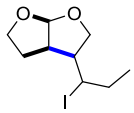
Product **4f** was synthesized according to the experimental procedure described above, utilizing TBA & TMP (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4f** as an inseparable mixture of 1:1 diastereomers (see ^{1}H NMR integrations at 5.67 and 5.59 ppm) and as a yellow oil (yield = 17.5 mg, 63% for both amines).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.67 (d, *J*=5.5 Hz, 1H for one isomer), 5.59 (d, *J*=5.3 Hz, 1H for one isomer), 4.10 (m, 1H for one isomer), 3.97 (m, 1H for one isomer), 3.86 (m, 1H for both isomers), 3.22 (dd, J_1=10 Hz, J_2=5 Hz, 1H for one isomer), 3.14 (m, 1H for both isomers), 3.09 (m, 1H for both isomers), 2.55 (m, 1H for both isomers), 2.03-1.96 (m, 2H for both isomers), 1.85 (m, 1H for one isomer), 1.35 (s, 3H for one isomer), 1.28 (s, 3H for one isomer), 1.17 (s, 3H for one isomer), 1.06 (s, 3H for one isomer) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 107.1, 106.2, 83.4, 82.8, 67.5, 66.1, 55.1, 53.9, 51.3, 48.4, 32.8, 30.4, 27.6, 24.9, 23.7, 21.9, 3.6, 1.2 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{16}IO_2$, 283.0189; found 283.0185.

3-(1-iodopropyl)hexahydrofuro[2,3-b]furan (4g)



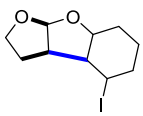
Product **4g** was synthesized according to the experimental procedure described above, utilizing each one of the three amines (48 h for NH_4OH, 24 h for TMP & TBA). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4g** as an inseparable mixture of 1:1 diastereomers (see ^{1}H NMR integrations at 5.85 and 5.68 ppm) and as a yellow oil (yield = 19.3 mg, 68% for NH_4OH; 22.9 mg, 81% for TMP; 20.9 mg, 74% for TBA).

^{1}H NMR (500 MHz, $CHCl_3$) δ 5.85 (d, *J*=4.7 Hz, 1H for one isomer), 5.68 (d, *J*=4.8 Hz, 1H for one isomer), 4.15 (t, *J*=7.1 Hz, 1H for one isomer), 4.03-3.85 (m, 3H for one isomer plus 4H for the other), 3.56 (dd, J_1=11.2 Hz, J_2=8.9 Hz, 1H for one isomer), 3.46 (dd, J_1=11.2 Hz, J_2=6.5 Hz, 1H for one isomer), 2.95 (m, 1H for one isomer), 2.87 (m, 2H for one isomer), 2.82 (m, 1H for one isomer), 2.02 (m, 1H for one isomer), 1.87-1.74 (m, 2H for both isomers), 1.70 (m, 1H for one isomer), 1.65 (m, 1H for both isomers) 1.09-1.05 (m, 3H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 110.6, 108.2, 75.3, 68.9, 68.8, 66.7, 51.5, 50.4, 49.1, 44.7, 37.1, 35.4, 32.1, 31.8, 24.8, 23.8, 14.0, 13.6 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{16}IO_2$, 283.0189; found 283.0186.

4-iododecahydrofuro[2,3-b]benzofuran (4h)



Product **4h** was synthesized according to the experimental procedure described above, utilizing NH_4OH and TBA (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 40:1) to furnish **4h** as an inseparable mixture of 0.4:1 diastereomers (see ^{1}H NMR integrations at 5.70 and 5.54 ppm) and as a yellow oil (yield = 16.2 mg, 55% for NH_4OH; 16.8 mg, 57% for TBA).

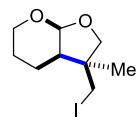
^{1}H NMR (500 MHz, $CHCl_3$) δ 5.70 (d, *J*=5.2 Hz, 1H for major isomer), 5.54 (d, *J*=5.6 Hz, 1H for minor isomer), 4.10 (s, 1H for major isomer), 4.03 (td, J_1=8.9 Hz, J_2=2.4

Hz, 1H for minor isomer), 3.98-3.77 (m 3H for both isomers), 2.99 (m, 1H for minor isomer), 2.79 (m, 1H for major isomer), 2.74 (m, 1H for minor isomer), 2.54 (m, 1H for minor isomer), 2.49 (m, 1H for minor isomer), 2.35 (m, 2H for major isomer), 2.22 (m, 1H for major isomer), 2.13 (m, 1H for major isomer), 2.02 (m, 2H for minor isomer), 1.92 (m, 1H for major isomer, 2H for minor), 1.65 (m, 1H for both isomers), 1.55 (m, 2H for major isomer), 1.38 (m, 1H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 108.1 (minor), 107.5 (major), 76.6 (both), 70.0 (minor), 68.4 (major), 57.1 (major), 51.0 (major), 49.9 (minor), 46.7 (minor), 39.8 (minor), 39.0 (major), 35.4 (major), 30.5 (major), 29.7 (minor), 27.1 (minor), 26.7 (major), 26.1 (minor), 22.7 (major), 22.5 (minor) ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_{10}H_{16}IO_2$, 295.0189; found 295.0187.

3-(iodomethyl)-3-methylhexahydro-4H-furo[2,3-b]pyran[1] (4i)

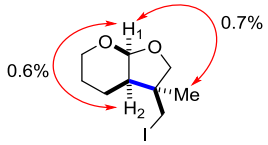


Product **4i** was synthesized according to the experimental procedure described above, utilizing TBA and TMP (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **4i** as a yellow oil (yield = 31.6 mg, 58% for both amines).

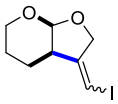
^{1}H NMR (500 MHz, $CHCl_3$) δ 5.42 (d, *J*=4.0 Hz, 1H), 3.97 (d, *J*=8.3 Hz, 1H), 3.75 (m, 1H), 3.61-3.57 (m, 2H), 3.36 (d, *J*=9.8 Hz, 1H), 3.20 (d, *J*=9.8 Hz, 1H), 1.91 (m, 1H), 1.80 (m, 1H), 1.61 (m, 1H), 1.51 (m, 2H), 1.28 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 101.8, 75.7, 61.4, 44.5, 43.8, 26.5, 22.7, 20.5, 14.6 ppm.

Representative NOE for compound **4i**



3-(iodomethylene)hexahydro-4H-furo[2,3-b]pyran (4j)



Product **4j** was synthesized according to the experimental procedure described above, utilizing TBA and TMP (72 h for both). The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 40:1) to furnish **4j** as an inseparable mixture of 0.3:1 stereoisomers (see ^{1}H NMR integrations at 5.33 and 5.26 ppm) and as a yellow oil. A small amount of the major isomer was also isolated and characterized as a single isomer (combined yield = 37.3 mg, 70% for TBA; 15.1 mg, 57% for TMP).

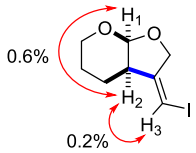
^{1}H NMR (500 MHz, $CHCl_3$) δ 5.95 (q, *J*=2.7 Hz, 1H for major isomer), 5.92 (q, *J*=1.8 Hz, 1H for minor isomer), 5.33 (d, *J*=3.7 Hz, 1H for major isomer), 5.27 (d, *J*=4.0 Hz, 1H for minor isomer), 4.55 (dt, J_1=13.3 Hz, J_2=1.8 Hz, 1H for minor isomer), 4.48 (dt, J_1=12.8 Hz, J_2=2.5 Hz, 1H for major isomer), 4.37 (ddd, J_1=14.3 Hz, J_2=2.6 Hz, J_3=1.5 Hz, 1H for major isomer), 4.28 (dd, J_1=13.3 Hz, J_2=1.8 Hz, 1H for minor isomer), 3.87 (m, 1H for both isomers), 3.70 (m, 1H for minor isomer), 3.45 (td, J_1=11.4 Hz, J_2=2.4 Hz, 1H for major isomer), 2.69 (s, 1H for major isomer), 2.66 (s, 1H for minor isomer), 2.09 (m, 1H for minor isomer), 2.01 (m, 1H for major isomer),

1.89 (m, 1H for major isomer), 1.64-1.55 (m, 1H for major isomer, 3H for minor), 1.34 (m, 1H for major isomer) ppm.

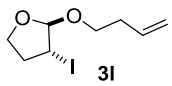
^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5 (minor), 150.6 (major), 102.3 (major), 99.9 (minor), 75.4 (major), 68.5 (minor), 67.1 (minor), 67.0 (major), 64.4 (major), 61.5 (minor), 44.9 (major), 43.9 (minor), 22.6 (major), 22.2 (minor), 22.0 (minor), 20.4 (major) ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_8H_{12}IO_2$, 266.9876; found 266.9872.

Representative NOE for the major isomer of compound **4j**

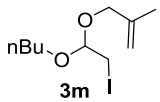


Unsuccessful Substrates



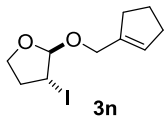
3l

NH_4OH: No Reaction
TMP & TBA: Reactions didn't reach completion. Up to 40% SM.



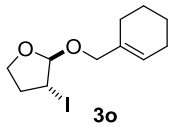
3m

NH_4OH: No Reaction
TMP & TBA: Slow reactions, low conversions & small amounts of the product where the iodine has been replaced by a hydrogen.



3n

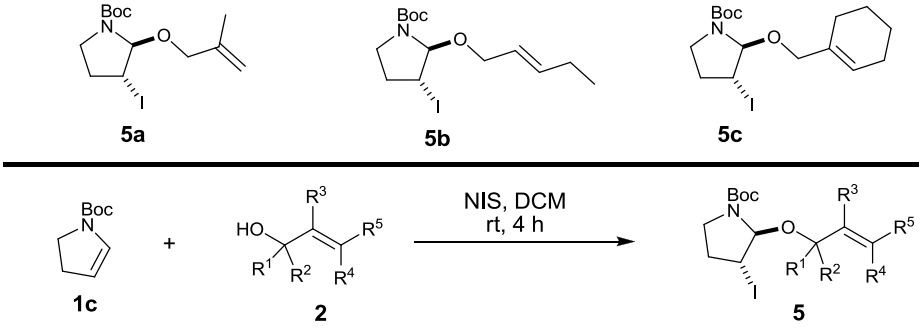
NH_4OH & TMP: Low conversions & many by-products
TBA: Reaction didn't reach completion & many by-products



3o

NH_4OH, TMP & TBA: Mixture of the iodo-product and the product where the iodine has been replaced by a hydrogen.

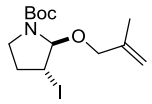
General experimental procedure for the synthesis of compounds of type 5



Compound **1c** (0.5 mmol, 86.3 μL) was dissolved in CH_2Cl_2 (2.5 mL). The corresponding alcohol (0.5 mmol, 42.1 μL for **2a**, 50.9 μL for **2g**, 56.1 mg for **2i**) was added followed by NIS (112.5 mg, 0.5 mmol). The solution was stirred in the dark at room temperature. After completion of the reaction (4 h), as was indicated by tlc analysis, a 10% aqueous solution of $Na_2S_2O_3$ (3 mL) was added and the mixture was extracted with CH_2Cl_2 (3× 4 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The products of type **5** were purified by flash column chromatography (silica gel neutralized with Et_3N, petroleum ether: EtOAc).

The stereochemistry of the corresponding products was assigned by comparison with previously synthesized compounds.[2]

tert-butyl 3-iodo-2-(2-methylallyloxy)pyrrolidine-1-carboxylate[1] (5a)

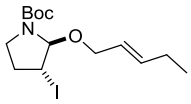


Product **5a** was synthesized according to the experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **5a** as a mixture of 1/1 Boc-isomers and as a yellow oil (yield = 112 mg, 61%). This reaction was scaled up to 2 mmol of the starting materials and the results were identical (yield = 445 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.48 (s, 1H for one Boc-isomer), 5.34 (s, 1H for one Boc-isomer), 4.94 (s, 1H for both Boc-isomers), 4.86 (m, 1H for both Boc-isomers), 4.23 (m, 1H for both Boc-isomers), 3.98 (m, 2H for both Boc-isomers), 3.62 (m, 1H for both Boc-isomers), 3.43 (m, 1H for both Boc-isomers), 2.53 (m, 1H for both Boc-isomers), 2.11 (m, 1H for both Boc-isomers), 1.71 (s, 3H for both Boc-isomers), 1.48 (s, 9H for both Boc-isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0 (one Boc-isomer), 154.2 (one Boc-isomer), 142.1 (one Boc-isomer), 141.8 (one Boc-isomer), 112.2 (one Boc-isomer), 112.0 (one Boc-isomer), 95.2 (one Boc-isomer), 94.8 (one Boc-isomer), 80.6 (one Boc-isomer), 80.2 (one Boc-isomer), 72.6 (one Boc-isomer), 72.4 (one Boc-isomer), 44.9 (one Boc-isomer), 44.3 (one Boc-isomer), 33.8 (one Boc-isomer), 32.9 (one Boc-isomer), 28.3 (both Boc-isomers), 27.5 (one Boc-isomer), 26.8 (one Boc-isomer), 19.5 (both Boc-isomers) ppm.

(*E*)-tert-butyl 3-iodo-2-(pent-2-en-1-yloxy)pyrrolidine-1-carboxylate[1] (5b)



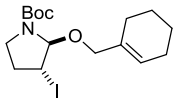
Product **5b** was synthesized according to the experimental procedure described above. The crude product was purified by flash column

chromatography (silica gel, petroleum ether: EtOAc = 20:1) to furnish **5b** as a mixture of 1/1 Boc-isomers and as a yellow oil (yield = 138.5 mg, 73%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 (m, 1H for both isomers), 5.51-5.45 (m, 1H for both isomers), 5.43 (s, 1H for one isomer), 5.29 (s, 1H for one isomer), 4.18 (m, 1H for both isomers), 4.00 (m, 2H for both isomers), 3.58 (m, 1H for both isomers), 3.40 (m, 1H for both isomers), 2.48 (m, 1H for both isomers), 2.09-2.01 (m, 3H for both isomers), 1.46 (s, 9H for both isomers), 0.98-0.94 (m, 3H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8 (one isomer), 154.1 (one isomer), 136.6 (one isomer), 136.4 (one isomer), 124.9 (one isomer), 124.8 (one isomer), 94.9 (one isomer), 94.7 (one isomer), 80.4 (one isomer), 80.1 (one isomer), 69.8 (one isomer), 69.4 (one isomer), 44.8 (one isomer), 44.3 (one isomer), 33.7 (one isomer), 32.8 (one isomer), 28.3 (one isomer), 28.3 (one isomer), 27.8 (one isomer), 27.1 (one isomer), 25.2 (both isomers), 13.2 (both isomers) ppm.

tert-butyl 2-(cyclohex-1-en-1-ylmethoxy)-3-iodopyrrolidine-1-carboxylate[1] (5c)

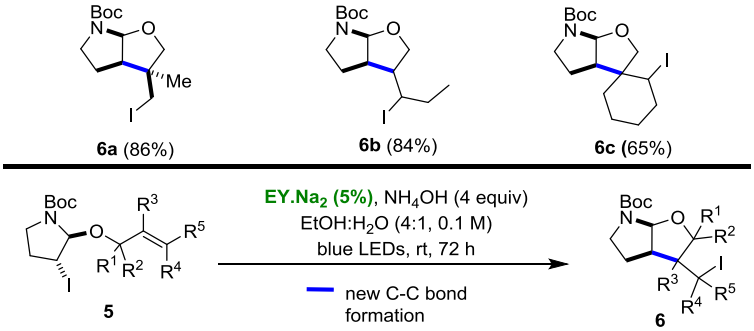


Product **5c** was synthesized according to the experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 60:1) to furnish **5c** as a mixture of 1.3/1 Boc-isomers (see ^{1}H NMR integrations at 5.43 and 5.29 ppm) and as a yellow oil (yield = 142.6 mg, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.67 (br, 1H for both isomers), 5.43 (s, 1H for minor isomer), 5.29 (s, 1H for major isomer), 4.19 (m, 1H for both isomers), 4.00-3.91 (m, 2H for major isomer and 1H for minor isomer), 3.83 (m, 1H for minor isomer), 3.58 (m, 1H for both isomers), 3.41 (m, 1H for both isomers), 2.49 (m, 1H for both isomers), 2.08 (m, 1H for both isomers), 2.00-1.95 (m, 4H for both isomers), 1.62-1.54 (m, 4H for both isomers), 1.47 (s, 9H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8 (minor), 154.2 (major), 134.8 (minor), 134.6 (major),125.2 (major), 125.1 (minor), 95.2 (major), 94.8 (minor), 80.4 (major), 80.0 (minor), 73.8 (minor), 73.5 (major), 44.8 (minor), 44.3 (major), 33.7 (minor), 32.8 (major), 28.3 (major), 28.3 (minor), 27.8 (major), 27.1 (minor), 25.9 (major), 25.9 (minor), 24.9 (both isomers), 22.4 (minor), 22.4 (major), 22.2 (minor), 22.2 (major) ppm.

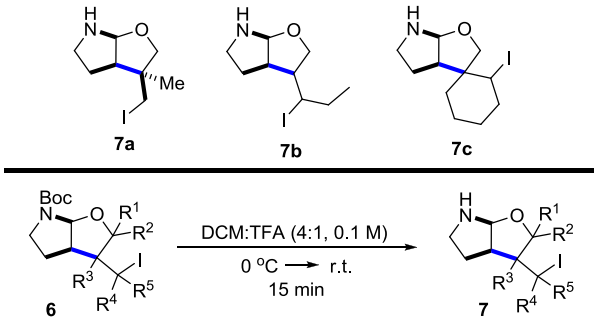
General experimental for the synthesis of substrates of type 6



To a solution of compounds of type **5** (0.2 mmol, 73.4 mg for **5a**, 76.3 mg for **5b**, 81.5 mg for **5c**) in EtOH: H_2O (4:1, 1.6 mL EtOH and 0.4 mL H_2O), the photocatalyst

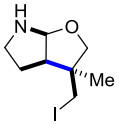
EY.Na_2 (5%, 7.0 mg, 0.01 mmol) was added and argon (balloon) was gently bubbled through the solution for 10 min at rt. Afterwards, under an argon atmosphere, NH_4OH (54 µL of a 14.8 M aqueous solution, 0.8 mmol) was added and the solution was irradiated using blue LED light strips (60 LEDs/m, 10.8 w/m, 1000 lm/m, λ_{max} = 420 nm) at the same temperature. After completion of the reaction, as indicated by ^{1}H-NMR (72 h), the reactions were concentrated *in vacuo* and the products of type **6** were purified by flash column chromatography (silica gel neutralized with Et_3N, petroleum ether: EtOAc = 20:1). Due to the complex ^{1}H & ^{13}C NMR spectrums of substrates of type **6** (attributed to the restricted rotation of the N-Boc group affording pseudo geometric isomers), we proceeded directly with deprotection, which is described below.

General experimental for the synthesis of substrates of type 7



Compounds of type **6** (0.1 mmol, 36.7 mg for **6a**, 38.1 mg for **6b**, 40.7 mg for **6c**) were dissolved in CH_2Cl_2 (0.8 mL) at 0 °C and TFA (0.2 mL) was added slowly. Afterwards, the reactions were warmed to room temperature and stirred. After completion of the reaction (15 min), as was indicated by tlc analysis, the crude mixtures were concentrated *in vacuo* and washed with a solution of *n*-Hexane: Et_2O (4 mL, 1:1) to give products **7a** & **7b**, without the need for further purification. In the case of substrate **7c**, the crude product was purified by flash column chromatography.

3-(iodomethyl)-3-methylhexahydro-2H-furo[2,3-b]pyrrole (7a)



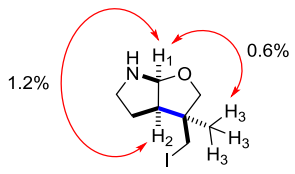
Product **7a** was synthesized and isolated according to the experimental procedure described above as a dark brown oil (yield = 20.3 mg, 76%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (d, *J*=6.3 Hz, 1H), 3.91 (d, *J*=8.8 Hz, 1H), 3.71 (d, *J*=8.8 Hz, 1H), 3.47 (m, 1H), 3.15 (s, 2H), 3.08 (m, 1H), 2.62 (m, 1H), 2.24 (m, 1H), 2.00 (m, 1H), 1.28 (s, 3H) ppm.

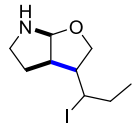
^{13}C NMR (125 MHz, $CDCl_3$) δ 95.1, 76.2, 52.7, 46.2, 45.1, 26.4, 25.3, 9.0 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_8H_{15}INO$, 268.0203; found 268.0189.

Representative NOE for compound **7a**



3-(1-iodopropyl)hexahydro-2H-furo[2,3-b]pyrrole (7b)



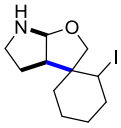
Product **7b** was synthesized and isolated according to the experimental procedure described above as inseparable mixture of 1:1 diastereomers (see ^{1}H NMR integrations at 5.77 and 5.61 ppm) and as a dark brown oil (yield = 21.1 mg, 75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (d, *J*=6.0 Hz, 1H for one isomer), 5.61 (d, *J*=6.4 Hz, 1H for one isomer), 4.26 (dd, J_1=8.8 Hz, J_2=7.1 Hz, 1H for one isomer), 4.06 (dd, J_1=8.5 Hz, J_2=7.5 Hz, 1H for one isomer), 3.97 (m, 1H for one isomer), 3.92 (m, 1H for one isomer), 3.76 (dd, J_1=11.4 Hz, J_2=9.2 Hz, 1H for one isomer), 3.70 (dd, J_1=11.4 Hz, J_2=8.9 Hz, 1H for one isomer), 3.45 (m, 1H for both isomers), 3.11 (m, 2H for both isomers), 2.92 (m, 1H for both isomers), 2.25 (m, 1H for one isomer), 2.02 (m, 1H for one isomer plus 2H for the other), 1.77-1.59 (m, 2H for both isomers), 1.07 (m, 3H for both isomers) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 96.2, 93.8, 76.2, 69.6, 51.4, 50.1, 48.7, 45.1, 45.0, 44.2, 33.8, 32.3, 31.9 (2 signals), 23.8, 22.9, 14.0, 13.6 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{17}INO$, 282.0349; found 282.0346.

2-iodotetrahydro-2'H,4'H-spiro[cyclohexane-1,3'-furo[2,3-b]pyrrole] (7c)



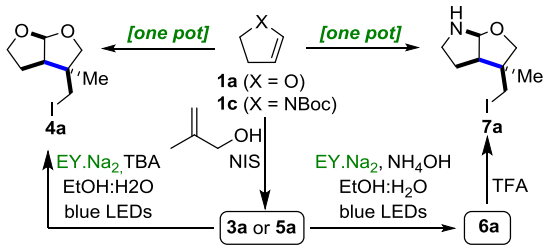
Product **7c** was synthesized according to the experimental procedure described above. The crude product was purified by flash column chromatography (silica gel neutralized with Et_3N, petroleum ether:EtOAc = 1:2) to furnish **7c** as inseparable mixture of 0.6:1 diastereomers (see ^{1}H NMR integrations at 5.50 and 5.30 ppm) and as a brown oil (yield = 22.4 mg, 73%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.50 (s, 1H for minor isomer), 5.30 (s, 1H for major isomer), 4.72 (s, 1H for minor isomer), 4.57 (s, 1H for major isomer), 4.06 (d, *J*=8.3 Hz, 1H for major isomer), 3.62 (d, *J*=8.2 Hz, 1H for minor isomer), 3.50 (d, *J*=8.3 Hz, 1H for major isomer), 3.41 (d, *J*=8.6 Hz, 1H for minor isomer), 3.15 (m, 1H for minor isomer), 3.09 (m 1H for major isomer), 2.96 (m, 1H for both isomers), 2.78 (m, 1H for major isomer), 2.69 (br, 1H for minor isomer), 2.11 (m, 1H for major isomer), 2.03-1.96 (m, 2H for major plus 1H for minor), 1.87-1.30 (m, 7H for major isomer plus 9H for minor).

^{13}C NMR (125 MHz, $CDCl_3$) δ 97.1 (minor), 93.7 (major), 81.9 (minor), 69.2 (major), 56.8 (major), 51.0 (minor), 48.9 (minor), 46.4 (major), 46.1 (minor), 45.5 (major), 42.0 (major), 40.2 (minor), 34.5 (major), 34.0 (minor), 31.0 (minor), 30.5 (major), 24.3 (minor), 23.8 (major), 22.4 (major), 22.0 (minor), 21.8 (major), 21.4 (minor) ppm.

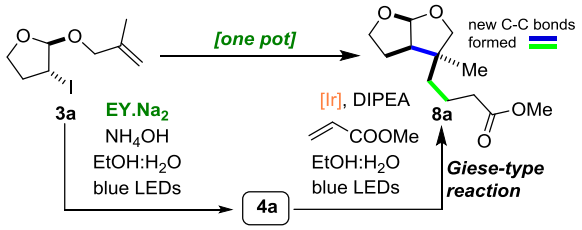
HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_{11}H_{19}INO$, 308.0505; found 308.0504.

One-pot synthesis of products 4a and 7a from starting materials of type 1 (1a and 1c, respectively) without intermediate purifications.



The corresponding starting material of type **1** (0.2 mmol, 15.1 μL for **1a** and 34.5 μL for **1c**) and alcohol **2a** (0.2 mmol, 16.8 μL) were dissolved in CH_2Cl_2 (1 mL), followed by NIS (0.2 mmol, 45.0 mg). The solutions were stirred in the dark at room temperature until full consumption of the starting compound of type **1** was indicated by tlc and ^{1}H NMR analysis (16 h for **1a** & 4 h for **1c**). Then, CH_2Cl_2 was removed under reduced pressure and the crude products **3a** and **5a** were re-dissolved in EtOH:H_2O (4:1, 1.6 mL EtOH and 0.4 mL H_2O) with the photocatalyst $EY.Na_2$ (0.01 mmol, 7.0 mg). Argon (balloon) was bubbled gently through the solution for 10 min at room temperature. Then, under argon atmosphere, the corresponding amine was added [TBA towards **4a** (126 μL, 1.2 mmol) and NH_4OH towards **7a** (54 μL of a 14.8 M aqueous solution, 0.8 mmol)] and the resulting solution was irradiated using blue LED strips (60 LEDs/m, 10.8 w/m, 1000 lm/m) at the same temperature. After completion of the reaction (72 h for both), indicated by ^{1}H NMR analysis, the solutions were concentrated under reduced pressure. The crude product **4a** was purified by flash column chromatography with an overall isolated yield of 20.2 mg (38 %). The crude product **6a** was dissolved in CH_2Cl_2 (1.6 mL) at 0 ^{o}C and TFA (0.4 mL) was added slowly. After consumption of the starting material, as was indicated by tlc analysis (15 min), the solution was concentrated under reduced pressure, washed with CH_2Cl_2 (10 mL) and concentrated again. Then, the residue was washed with a solution of n-Hexane: Et_2O (8 mL, 1:1) and afterwards with Et_2O (8 mL) to furnish compound **7a**, with an overall isolated yield of 21.2 mg (40 %).

One-pot Giese type reaction. Transformation of starting material 3a to compound 8a.



Starting material **3a** (0.1 mmol, 26.8 mg) and the photocatalyst $EY.Na_2$ (0.005 mmol, 3.5 mg) were dissolved in EtOH:H_2O (4:1, 0.8 mL EtOH and 0.2 mL H_2O). Argon (balloon) was then bubbled gently through the solution for 10 min at room temperature. Then, under argon atmosphere, NH_4OH was added (27 μL of a 14.8 M aqueous solution, 0.4 mmol) and the resulting solution was irradiated using blue LED

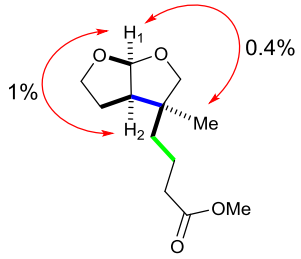
strips (60 LEDs/m, 10.8 w/m, 1000 lm/m) at the same temperature. After completion of the reaction (48 h), as was indicated by ^{1}H NMR analysis, the solution was concentrated under reduced pressure and the residue dissolved in EtOH:H_2O (4:1, 0.8 mL EtOH and 0.2 mL H_2O). $[Ir(ppy)_2(dtbbpy)]PF_6$ (1%, 0.9 mg, 0.001 mmol) was added. Argon was gently bubbled through the solution at room temperature, using a balloon for 10 min. Afterwards, DIPEA (69.7 µL, 0.4 mmol) was added followed by methyl acrylate (36 µL, 0.4 mmol) and the solution was irradiated using blue LED light strips (60 LEDs/m, 10.8 w/m, 1000 lm/m, λmax = 420 nm) until full consumption of the starting material **4a** was indicated by TLC analysis (4 h). The solution was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica gel, petroleum ether: EtOAc = 20:1) to yield **8a** as a single diastereomer and as a yellow oil (overall yield = 12.1 mg, 53%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (d, *J*=4.9 Hz, 1H), 3.90 (m, 1H), 3.82 (m, 1H), 3.67 (s, 3H), 3.56 (d, *J*=8.4 Hz, 1H), 3.53 (d, *J*=8.4 Hz, 1H), 2.39 (m, 1H), 2.32 (m, 2H), 1.86 (m, 2H), 1.64 (m, 2H), 1.41 (m, 1H), 1.31 (m, 1H), 1.10 (s, 3H) ppm.

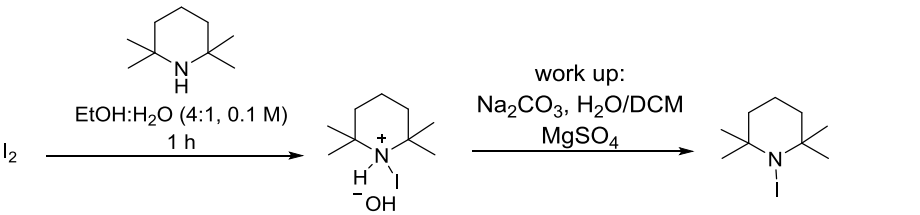
^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 109.6, 78.4, 68.8, 52.4, 51.6, 44.8, 34.4, 33.9, 26.1, 25.2, 20.5 ppm.

HRMS (Orbitrap ESI): $[M+Na]^+$ calcd. for $C_{12}H_{20}O_4Na$, 251.1253; found 251.1250.

Representative NOE for compound **8a**



Synthesis of 1-iodo-2,2,6,6-tetramethylpiperidine (1-iodo-TMP)



Iodine (0.2 mmol, 50.8 mg) was dissolved in EtOH: H_2O (4:1, 1.6 mL EtOH and 0.4 mL H_2O) and TMP was added (204.2 µL, 1.2 mmol). The solution was left stirring at room temperature and in the dark. After loss of colour (~1 h), the reaction was concentrated *in vacuo*. The **1-iodo-TMP salt** was taken up in Na_2CO_3 (3 mL of a 15% aqueous solution, pH~10-11) and was extracted with DCM (2x 4 mL). The combined organic phases were washed with H_2O (6 mL), dried over $MgSO_4$ and concentrated under reduced pressure to give the desired product **1-iodo-TMP** as orange solid.

1-iodo-TMP was also synthesized according to a published procedure[3] and was used to identify **1-iodo-TMP salt** (see Scheme above) in crude reaction mixtures (see **Optimization and Mechanistic Investigations** below).

1-iodo-TMP salt

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.75 (br, 6H), 1.63 (s, 12H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 58.1, 35.4, 27.6, 16.3 ppm.

1-iodo-TMP

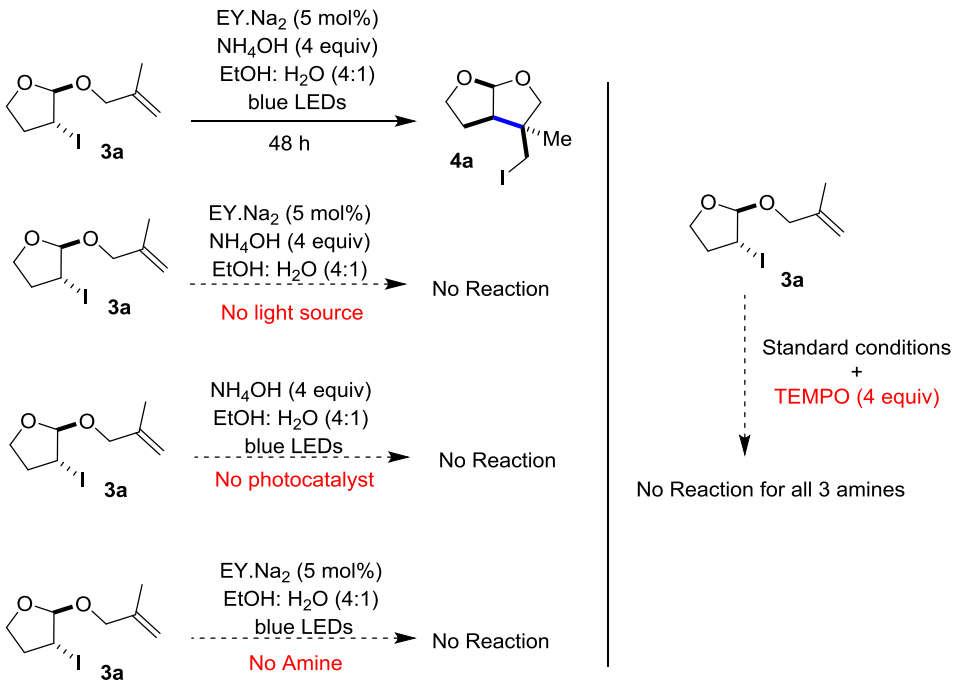
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.62 (br, 2H), 1.46 (br, 4H), 1.30 (s, 12H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2, 38.5, 30.5, 17.3 ppm.

HRMS (Orbitrap ESI): $[M+H]^+$ calcd. for $C_9H_{19}IN$, 268.0556; found 268.0552.

Optimization and Mechanistic Investigations

[1] Control and Trapping Experiments



[2] Emission Quenching Experiments – Stern-Volmer Plots

The emission spectra were measured on a JASCO FP-6500 fluorescence spectrophotometer equipped with a red-sensitive WRE-343 photomultiplier tube (wavelength range: 200-850 nm). All the $EY.Na_2$ solutions were excited at 400 nm and the emission intensity was collected at 560 nm.

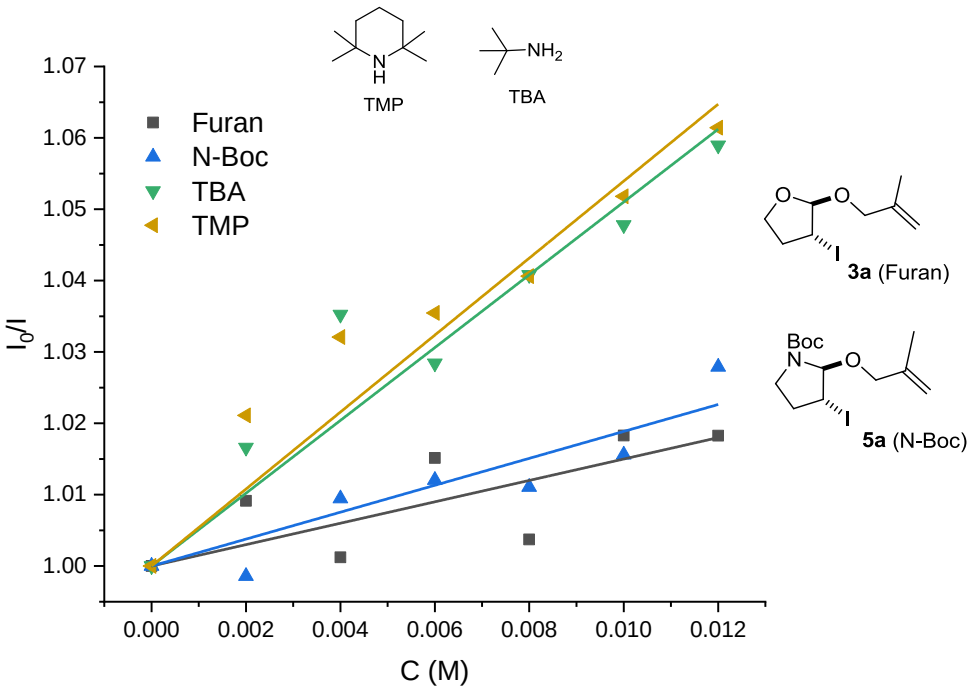
[3] L. Elmir, G. Bentabed-Ababsa, W. Erb, T. Roisnel and F. Mongin, *Eur. J. Org. Chem.*, 2023, **26**, e202300024.

Experimental procedure

A screw-top quartz cuvette was charged with a 0.1 mM of a degassed solution of EY.Na_2 in EtOH:H_2O (4:1, 2.0 mL) and the initial emission was collected. Then the appropriate amount of the quencher as a 0.2 M degassed solution in EtOH:H_2O (4:1) was added. The sample was shaken for 30 sec and then the emission spectra of the sample was collected.

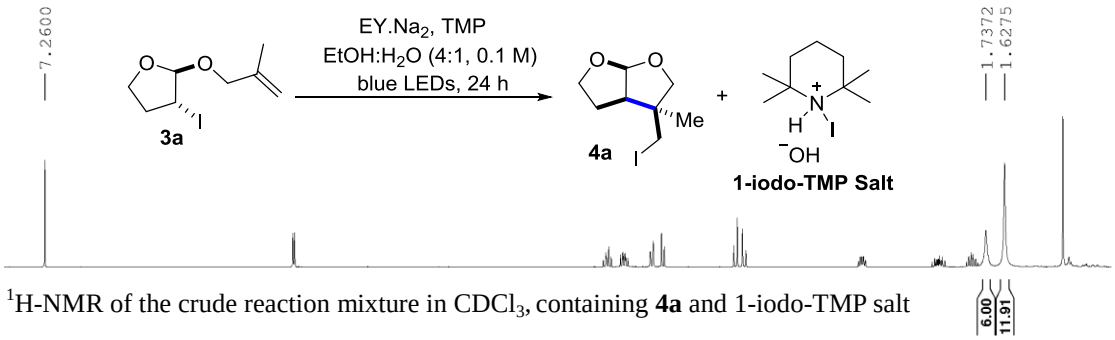
Combined Stern-Volmer plots

The Stern-Volmer quenching studies clearly illustrate that both TMP & TBA quench the excited state of eosin at a significantly higher rate than the reaction substrates (**3a** or **5a**). This supports the mechanistic analysis (Scheme 4, main paper) in which there is a SET step where an electron is transferred from the corresponding amine to the excited state of eosin; thus, reducing the latter (EY* → $EY^{\bullet-}$ and amine → $amine^{\bullet+}$).

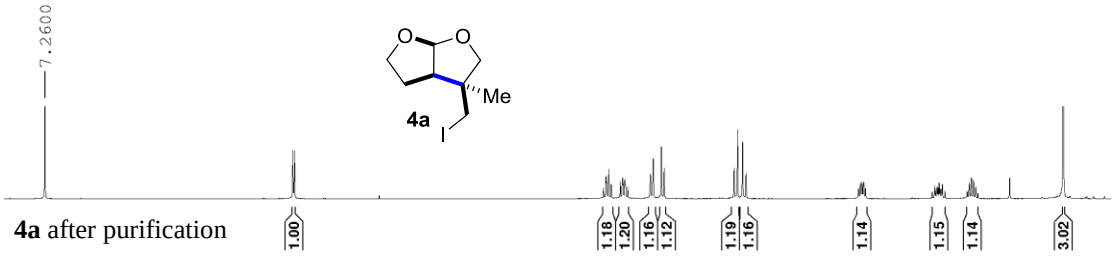


[3] Identification of 1-iodo-2,2,6,6-tetramethylpiperidin-1-ium hydroxide (1-iodo-TMP salt) in the crude reaction mixtures

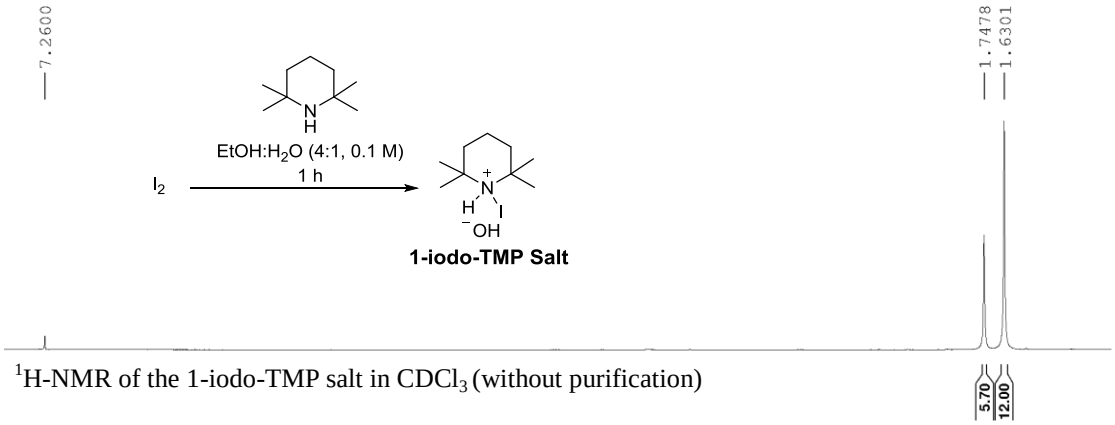
1-iodo-2,2,6,6-tetramethylpiperidin-1-ium hydroxide (**1-iodo-TMP salt**) was identified in crude ^{1}H-NMR spectra, as shown below. Mass spectrometry also confirmed this observation.



^{1}H-NMR of the crude reaction mixture in $CDCl_3$, containing **4a** and 1-iodo-TMP salt

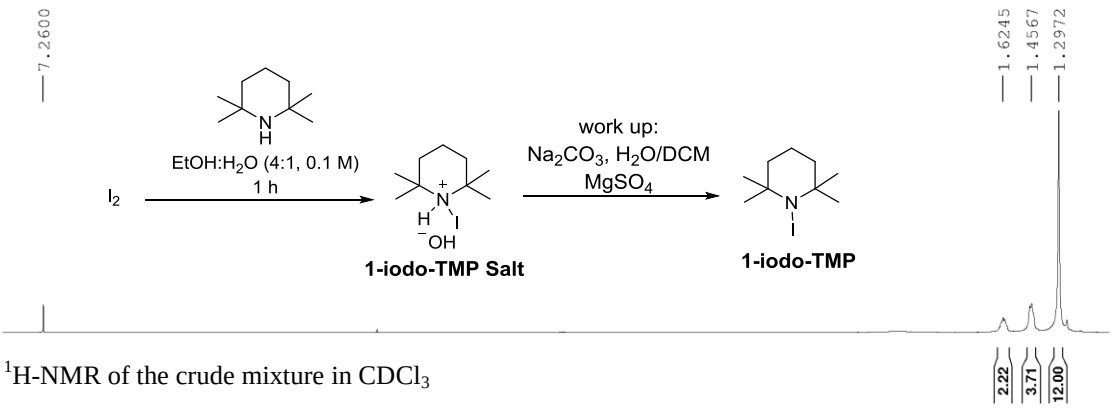


4a after purification

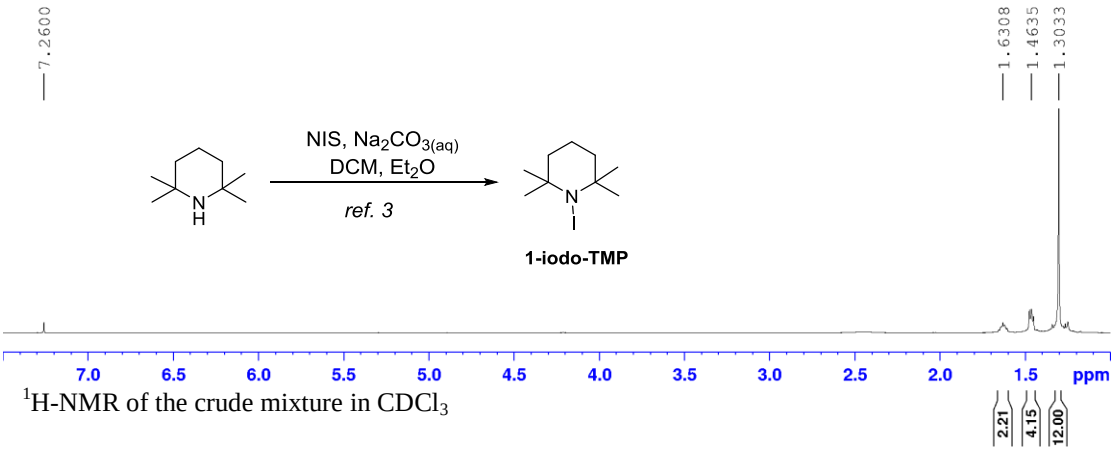


^{1}H-NMR of the 1-iodo-TMP salt in $CDCl_3$ (without purification)

^{1}H-NMR of pure TMP in $CDCl_3$

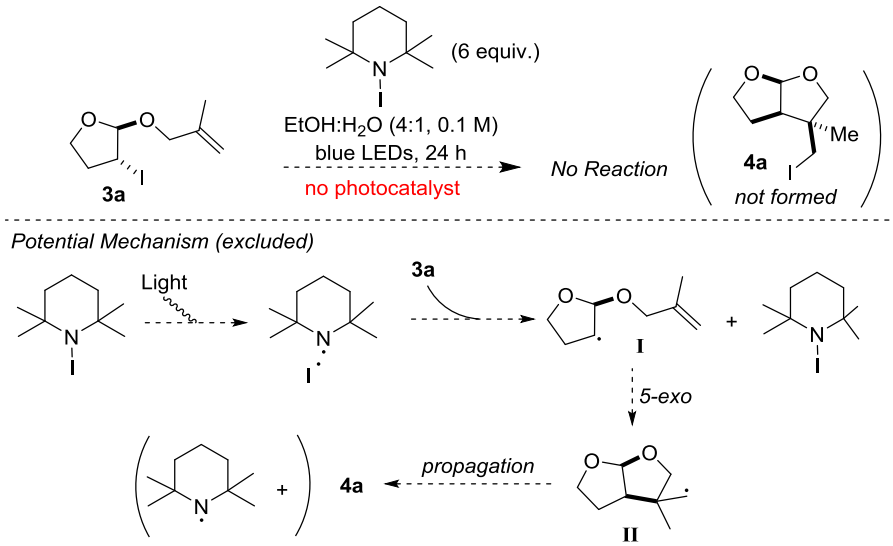


^{1}H-NMR of the crude mixture in $CDCl_3$



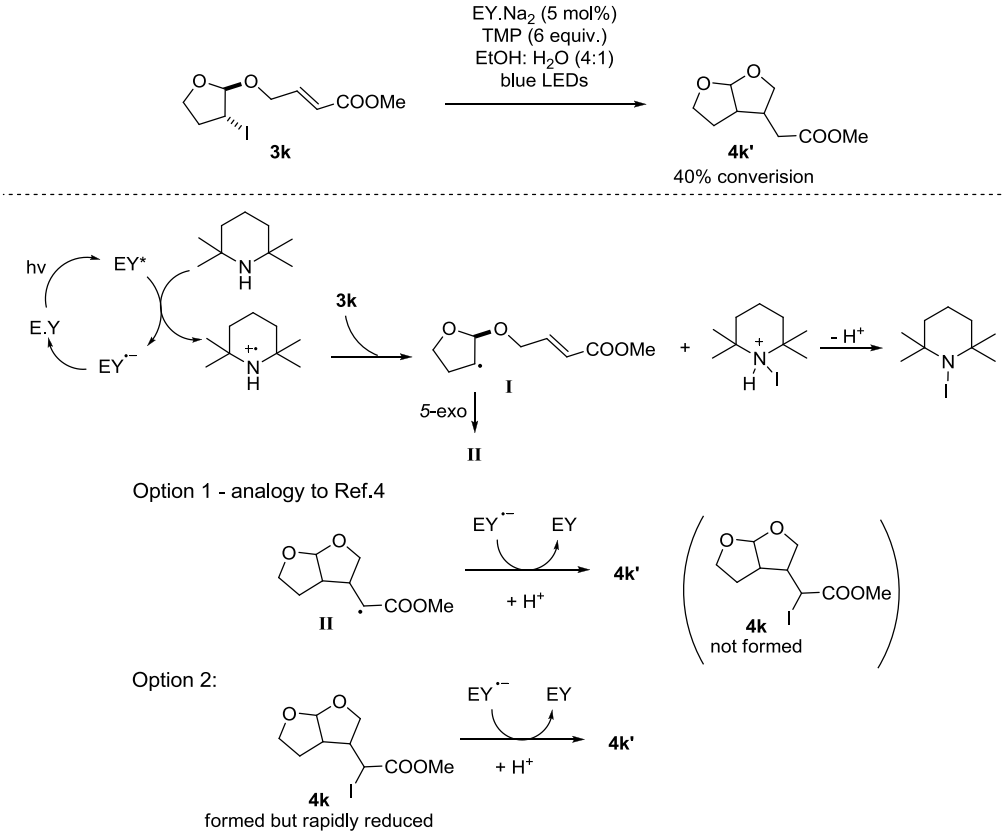
^{1}H-NMR of the crude mixture in $CDCl_3$

[4] Control experiment using 1-iodo-TMP



Given the weak nature of the N-I bond homolysis upon irradiation was a possibility. Thus, an experiment was carried out where **1-iodo-TMP** was used directly, without Eosin Y to test whether N-I bond homolysis occured. After 24 h, the starting material **3a** was recovered intact. This experiment proves that direct homolysis of the N-I bond upon irradiation is not the source of aminyl radicals in this methodology. The photocatalyst is absolutely necessary to generate the amino radical cation for the reaction to take place (see, Scheme 4 of the manuscript).

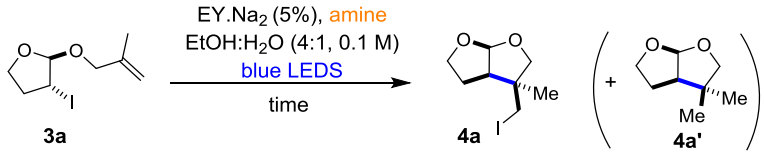
[5] Double bond change



This product is likely a result of either the radical adjacent to the ester group (**II**, after 5-exo cyclisation) being reduced by the photocatalyst radical anion ($EY^{\cdot-}$**,** Option 1)[4] or the α-iodoester product being reduced by the photocatalyst radical anion ($EY^{\cdot-}$, Option 2).

4 The radical anion of the photocatalyst 9,10-dicyanoanthracene (DCA) with a reduction potential lower than that of eosin's ($DCA^{\cdot-}$/DCA = -0.91, $EY^{\cdot-}$/EY = -1.08) has been used to reduce a radical adjacent to an ester, see; G. Gutenberger, E. Steckhan and S. Blechert, *Angew. Chem., Int. Ed*., 1998, **37**, 660.

[6] Amine screenings



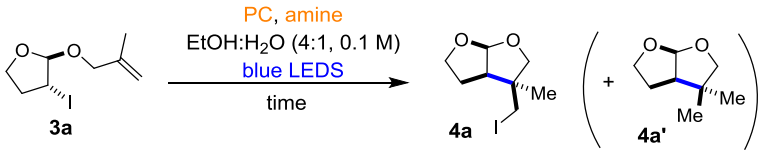
B1: NH_4OH
B2: *tert*-Butylamine
B3: 2,2,6,6-Tetramethylpiperidine
B4: 2,6-Lutidine
B5: Ph_2NH
B6: 1-Adamantylamine
B7: 4-Methoxy-*N*,*N*-diphenylamine
B8: $PhNH_2$
B9: $H_2NNH_2{\cdot}H_2O$

Entry	Base (eq.)	time (h)	conv. (%)[a]	**4a**:**4a'**	yield (%)
1	B1 (2)	48	83	10:1.4	NM
2	B1 (4)	24	85	1:0	NM
3	**B1 (4)**	**48**	**100**	**20:1.6**	**75**
4	B1 (6)	48	77	1:0	NM
5	B2 (2)	24	84	>10:1	NM
6	B2 (4)	24	91	10:1.3	NM
7	**B2 (6)**	**24**	**100**	**1:0**	**77**
8	B2 (8)	24	100	10:1.6	NM
9	B3 (2)	24	10	1:2	NM
10	B3 (4)	24	33	2:1	NM
11	**B3 (6)**	**24**	**100**	**1:0**	**82**
12	B3 (8)	24	49	4:1	NM
13	B4 (6)	24	<1	-	-
14	B5 (6)	24	NR	-	-
15	B6 (6)	24	100	4:1	NM
16	B7 (6)[b]	24	NR	-	-
17	B8 (6)	24	NR	-	-
18	B9 (6)	24	46	1:0	NM

a: As measured by ^{1}H-NMR
b: Dry ACN was used. insoluble in EtOH:H_2O & EtOH

NR: No Reaction
NM: Not Measured

[7] Photocatalyst changes



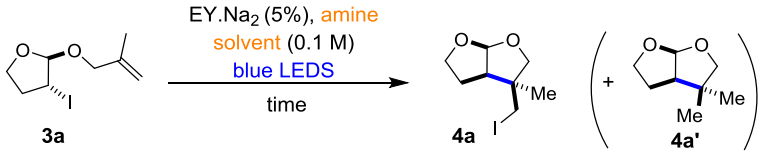
PC1: EY.Na_2 ($E_{EY/EY^{\cdot-}}$ = -1.06V)
PC2: 9,10-Dicyanoanthracene ($E_{DCA/DCA^{\cdot-}}$ = -0.91V)
PC3: Fluorescein.Na_2 ($E_{Fluo/Fluo^{\cdot-}}$ = -1.22V)
PC4: Riboflavin ($E_{R/R^{\cdot-}}$ = -0.79V)
PC5: Rhodamine 6G ($E_{Rh6G/Rh6G^{\cdot-}}$ = -1.14V)
PC6: Rose Bengal.Na_2 ($E_{RB/RB^{\cdot-}}$ = -0.99V)
PC7: 9-Mesityl-10-methylacridinium perchlorate ($E_{R/R^{\cdot-}}$ = -0.57V)

Entry	PC (mol %)	Base (eq.)	time (h)	conv. (%)[a]	**4a**:**4a'**	yield (%)
1	**PC1 (5)**	**B1 (4)**	**48**	**100**	**20:1.6**	**75**
2	PC2 (5)	B1 (4)	48	NR	-	-
3	PC3 (5)	B1 (4)	48	35	1:0	NM
4	PC4 (5)	B1 (4)	48	86	10:1	NM
5	PC5 (5)	B1 (4)	48	NR	-	-
6	PC6 (5)	B1 (4)	48	85	20:1	NM
7	PC7 (1)	B1 (4)	48	NR	-	-
8	**PC1 (5)**	**B2 (6)**	**24**	**100**	**1:0**	**77**
9	PC2 (5)	B2 (6)	24	87	1:0	NM
10	PC3 (5)	B2 (6)	24	71	20:1	NM
11	PC4 (5)	B2 (6)	24	86	10:1.3	NM
12	PC5 (5)	B2 (6)	24	10	1:0	NM
13	PC6 (5)	B2 (6)	24	100	10:1	65
14	PC7 (1)	B2 (6)	24	10	1:0	NM
15	**PC1 (5)**	**B3 (6)**	**24**	**100**	**1:0**	**82**
16	PC2 (5)	B3 (6)	24	NR	-	-
17	PC3 (5)	B3 (6)	24	NR	-	-
18	PC4 (5)	B3 (6)	24	100	10:1	59
19	PC5 (5)	B3 (6)	24	NR	-	-
20	PC6 (5)	B3 (6)	24	77	10:1.5	NM
21	PC7 (1)	B3 (6)	24	NR	-	-

a: As measured by ^{1}H-NMR
NR: No Reaction
NM: Not Measured

B1: NH_4OH **B2**: *tert*-Butylamine
B3: 2,2,6,6-Tetramethylpiperidine

[8] Solvent changes



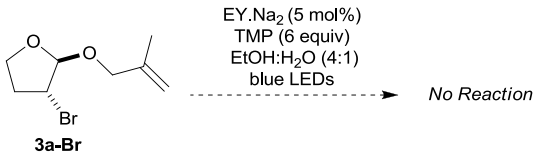
B1: NH_4OH **B2**: *tert*-Butylamine
B3: 2,2,6,6-Tetramethylpiperidine

S1: EtOH:H_2O (4:1) **S2**: dry EtOH
S3: ACN:H_2O (4:1) **S4**: dry ACN

Entry	Base (eq.)	time (h)	Solvent	conv. (%)[a]	**4a**:**4a'**	yield (%)
1	**B1 (4)**	**48**	**S1**	**100**	**20:1.6**	**75**
2	B1 (4)	48	S2	NR	-	-
3	B1 (4)	48	S3	70	1:0	NM
4	B1 (4)	48	S4	NR	-	-
5	**B2 (6)**	**24**	**S1**	**100**	**1:0**	**77**
6	B2 (6)	24	S2	75	10:1.3	NM
7	B2 (6)	24	S3	90	1:0	NM
8	B2 (6)	24	S4	40	1:0	NM
9	**B3 (6)**	**24**	**S1**	**100**	**1:0**	**82**
10	B3 (6)	24	S2	60	10:1	NM
11	B3 (6)	24	S3	80	1:0	NM
12	B3 (6)	24	S4	NR	-	-

a: As measured by ^{1}H-NMR
NR: No Reaction
NM: Not Measured

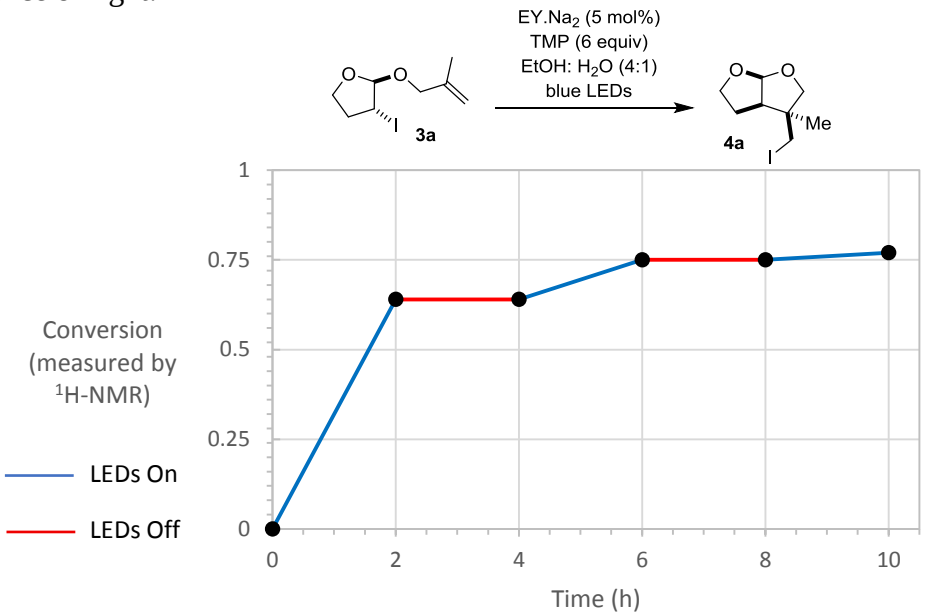
[9] Halogen change



Knowing that a key step of the reaction is the homolysis of the C-I bond of substrates of type **3**, starting material, **3a-Br** was synthesized and tested. Alkyl bromides have higher bond dissociation energies than the corresponding alkyl iodides,[5] which explains why the reaction didn't take place and **3a-Br** was recovered intact. In this case, the amino radical cation isn't strong enough to overcome the energy barrier and homolytically cleave the C-Br bond, even though the C-Br bond is weakened by the adjacent oxygen functionality.[1, 6]

[10] On-Off experiment

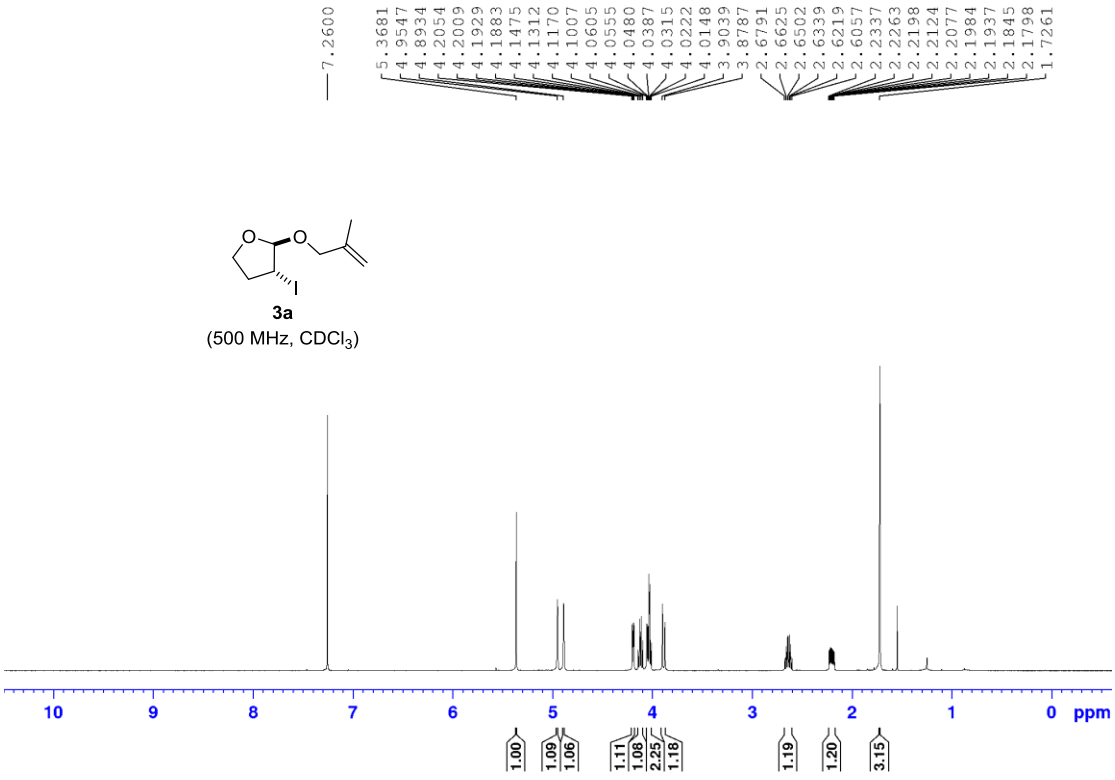
During our mechanistic studies, we conducted an on-off experiment with substrate **3a** to investigate the possibility that the reaction proceeds without the continuous presence of light.

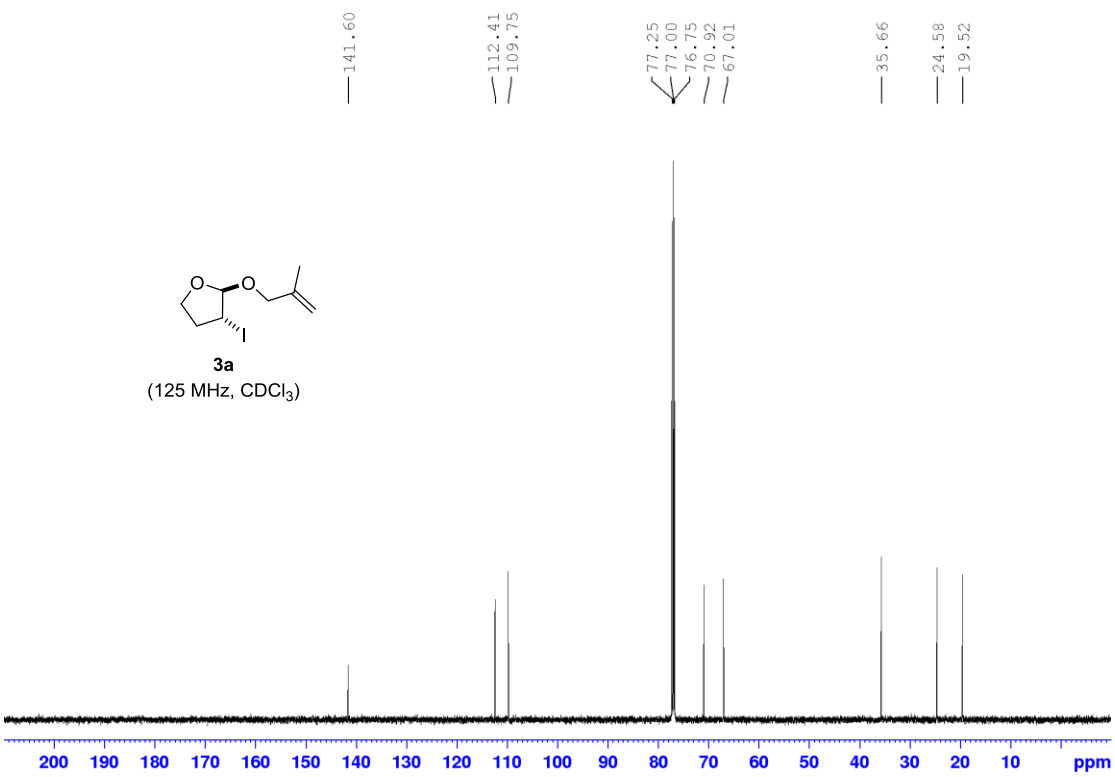


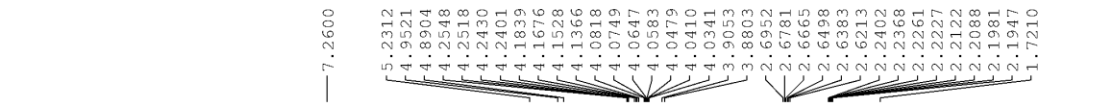
As we can see from the diagram above, whenever the LEDs were off, the conversion to product **4a** stayed the same. However, as soon as the LEDs were turned on, the reaction restarted towards completion (@24 h). It is known that light on/off experiments where yields do not grow in the dark phase do not conclusively disprove the involvement of a radical chain process.[7]

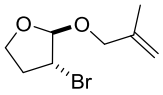
[5] S. K. Pagire, T. Föll and O. Reiser, *Acc. Chem. Res*., 2020, **53**, 782.
[6] D. Kalaitzakis, A. Bosveli, T. Montagnon and G. Vassilikogiannakis, *Chem.− Eur. J*., 2022, **28**, e202200322.
[7] M. A. Cismesia and T. P. Yoon, *Chem. Sci.*, 2015, **6**, 5426.

Part B: Copies of ^{1}H-NMR, ^{13}C-NMR and NOE spectra



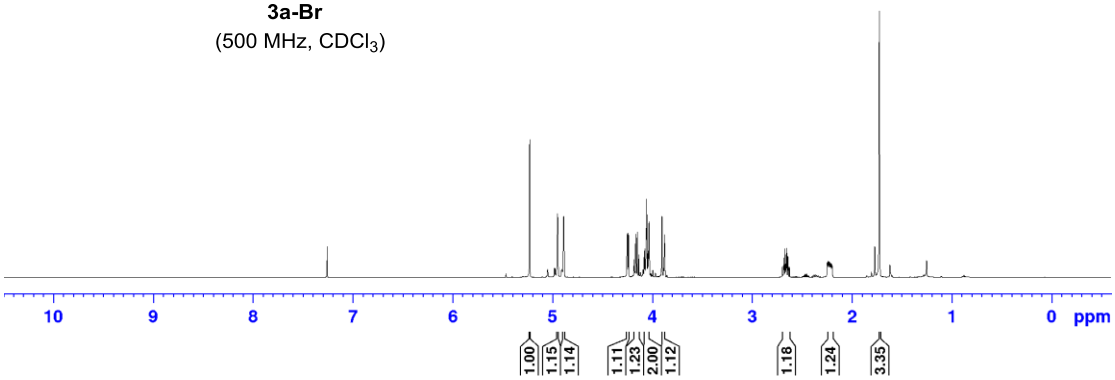


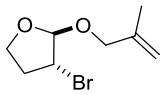




3a-Br

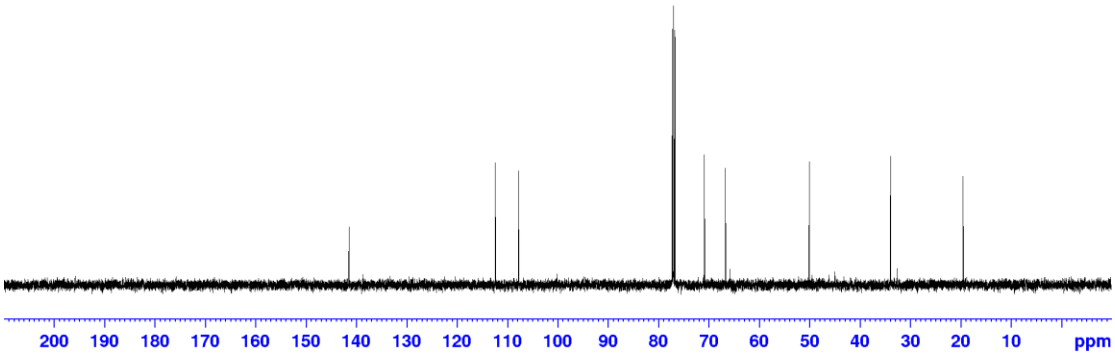
(500 MHz, $CDCl_3$)

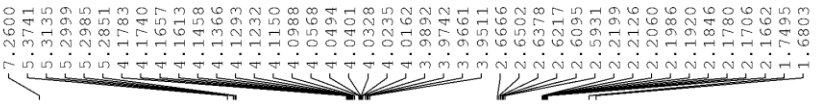


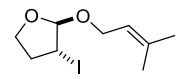


3a-Br

(125 MHz, $CDCl_3$)

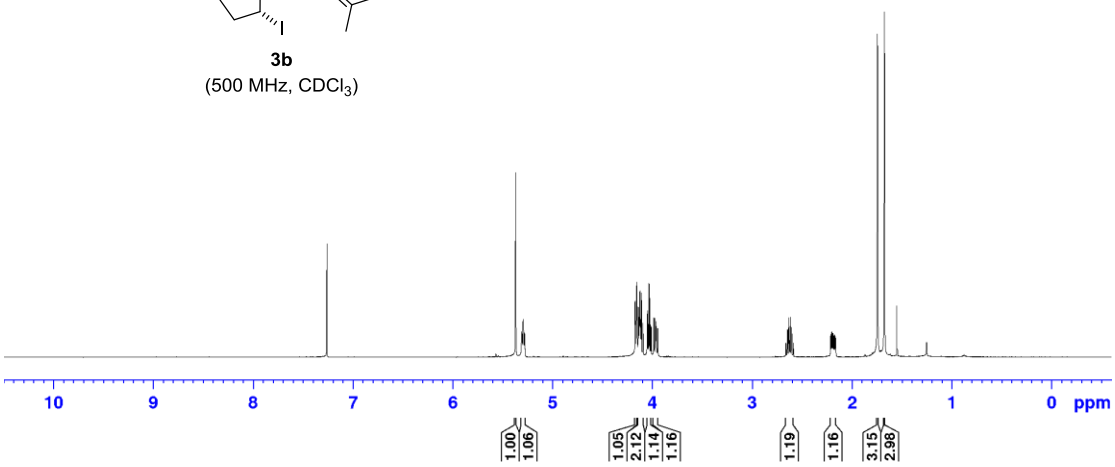


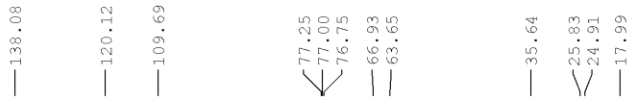


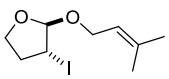


3b

(500 MHz, $CDCl_3$)

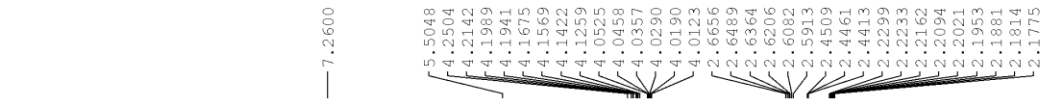


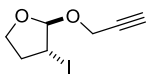




3b

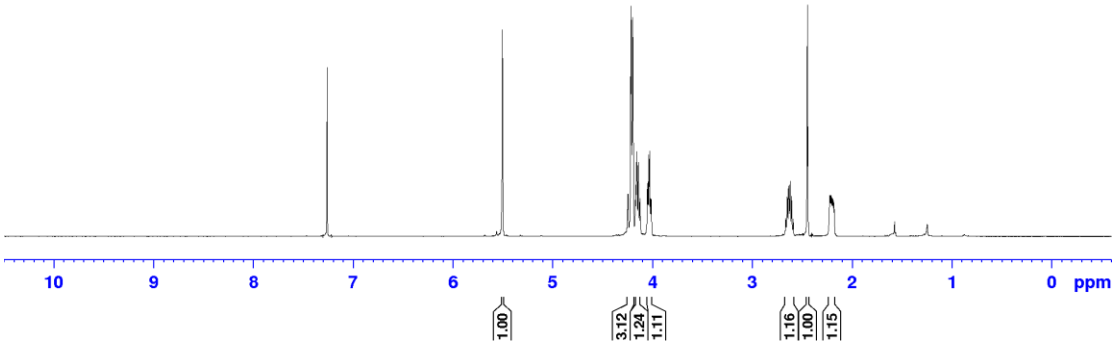
(125 MHz, $CDCl_3$)

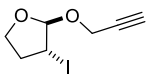




3c

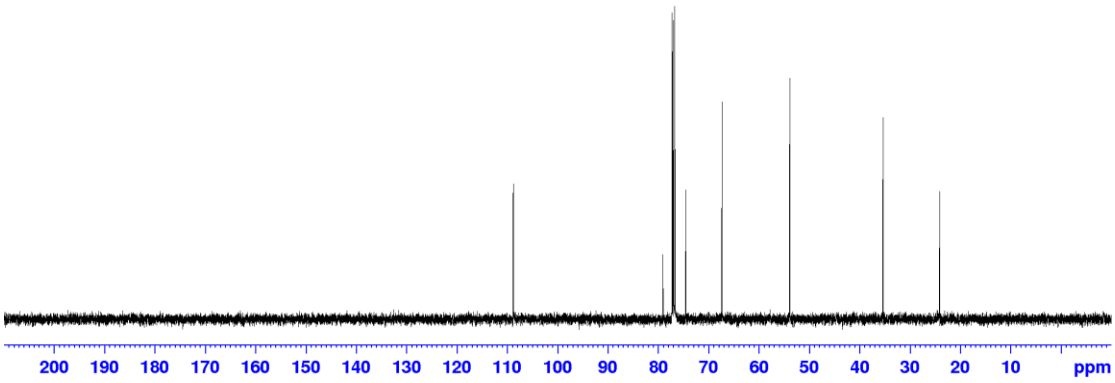
(500 MHz, $CDCl_3$)

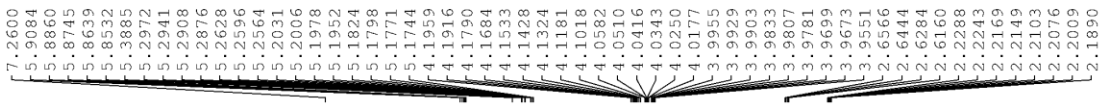


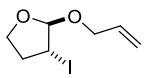


3c

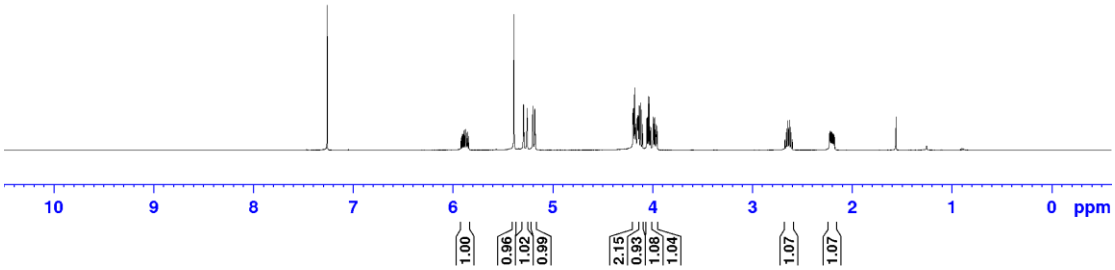
(125 MHz, $CDCl_3$)

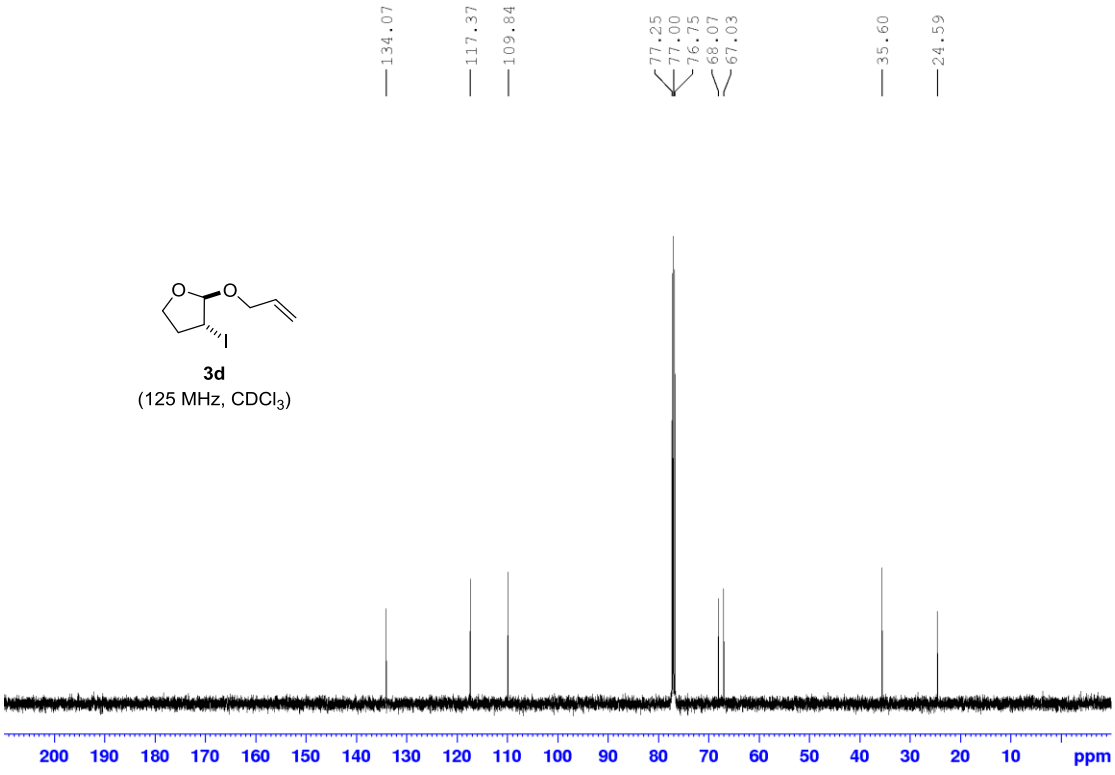




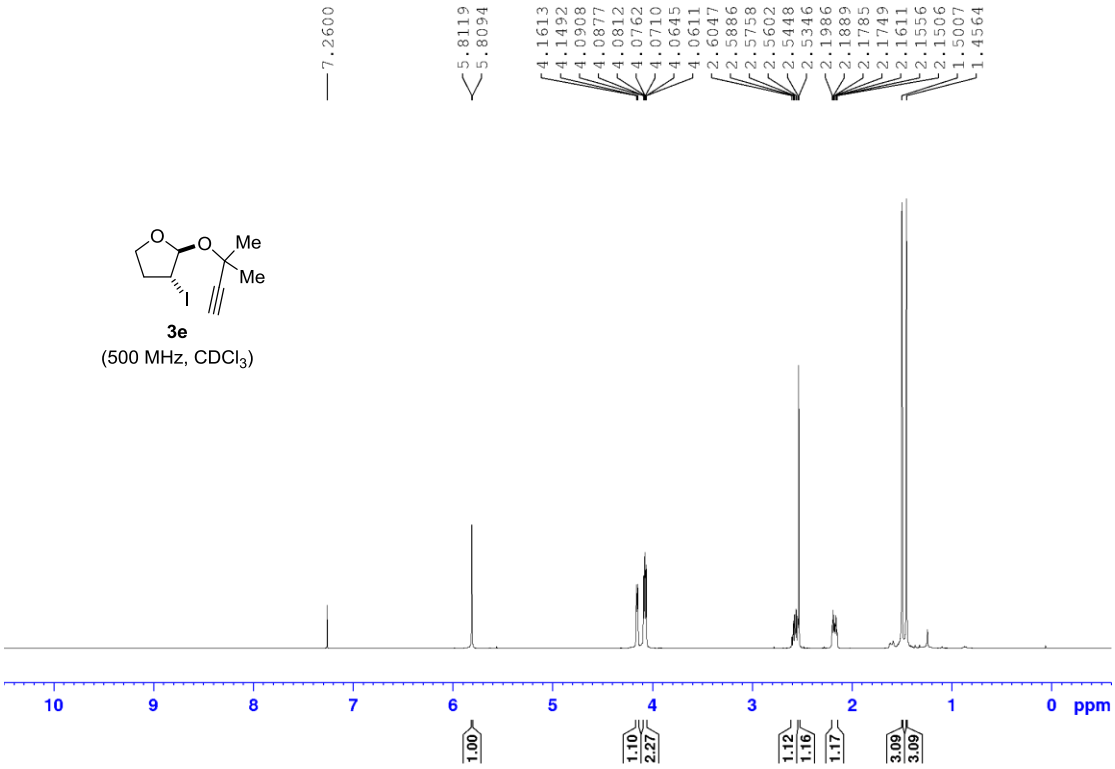


3d
(500 MHz, $CDCl_3$)





3d
(125 MHz, $CDCl_3$)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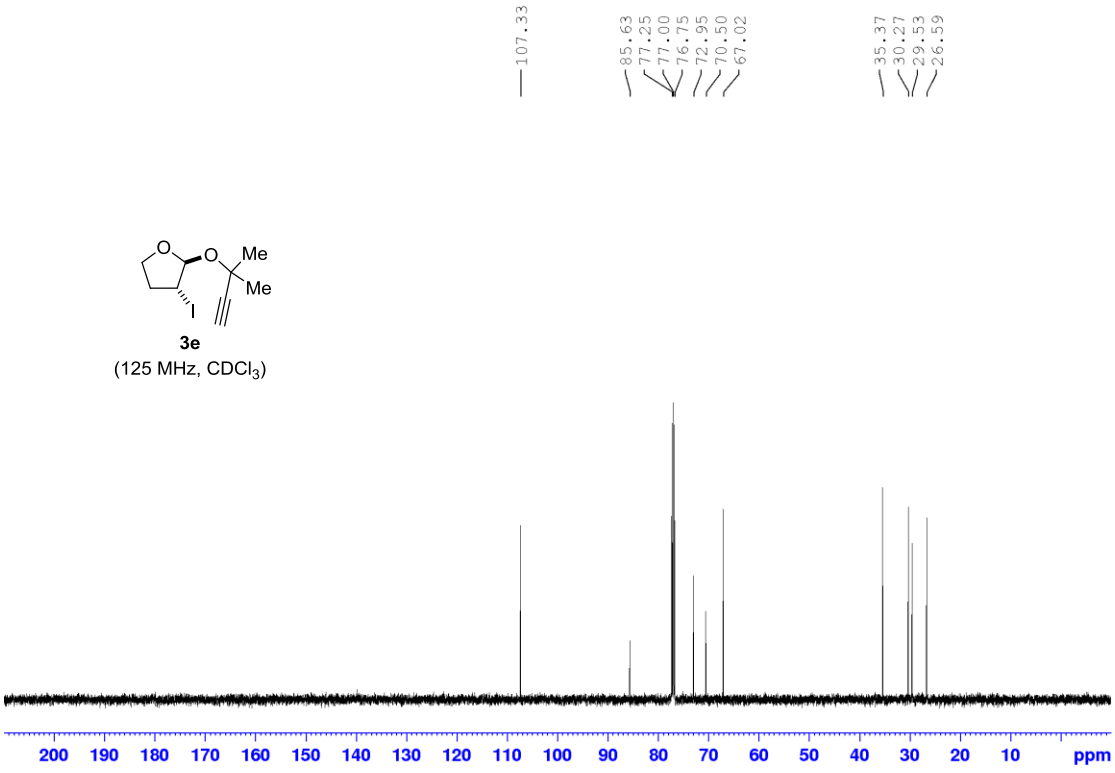
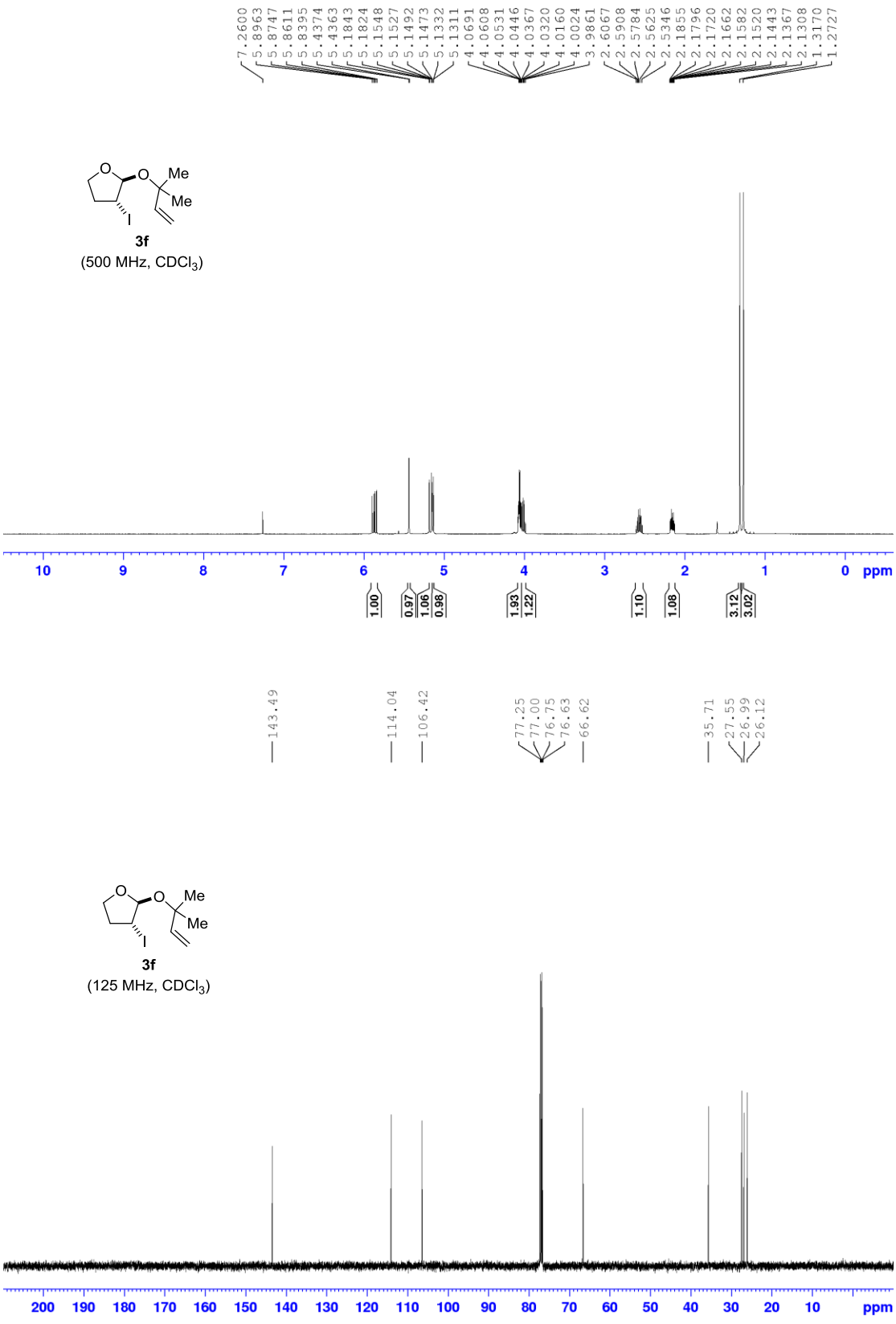
5.8094
4.1613
4.1492
4.0908
4.0877
4.0812
4.0762
4.0710
4.0645
4.0611
2.6047
2.5886
2.5758
2.5602
2.5448
2.5346
2.1986
2.1889
2.1785
2.1749
2.1611
2.1556
2.1506
1.5007
1.4564
Me
Me
O
O
I
3e
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.10
2.27
1.12
1.16
1.17
3.09
3.09


107.33
85.63
77.25
77.00
76.75
72.95
70.50
67.02
35.37
30.27
29.53
26.59
Me
Me
O
O
I
3e
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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5.8611
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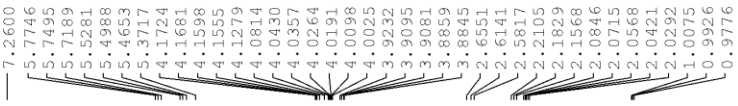
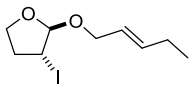
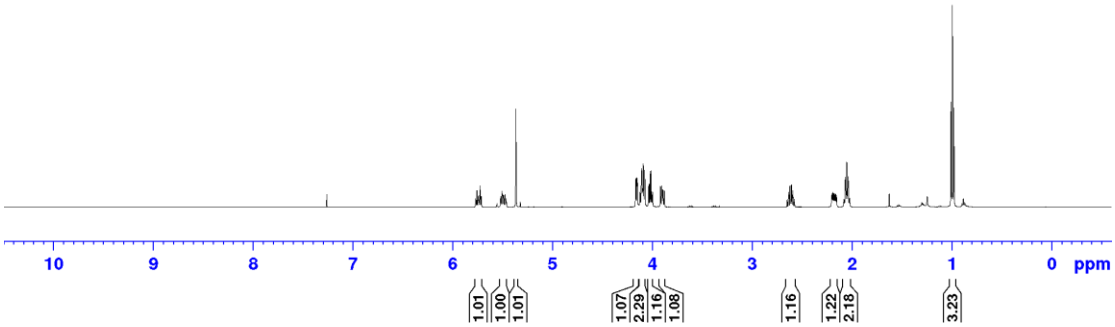
5.1824
5.1548
5.1527
5.1492
5.1473
5.1332
5.1311
4.0691
4.0608
4.0531
4.0446
4.0367
4.0320
4.0160
4.0024
3.9861
2.6067
2.5908
2.5784
2.5625
2.5346
2.1855
2.1796
2.1720
2.1662
2.1582
2.1520
2.1443
2.1367
2.1308
1.3170
1.2727
O
O
Me
Me
I
3f
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.97
1.06
0.98
1.93
1.22
1.10
1.08
3.12
3.02
143.49
114.04
106.42
77.25
77.00
76.75
76.63
66.62
35.71
27.55
26.99
26.12
O
O
Me
Me
I
3f
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

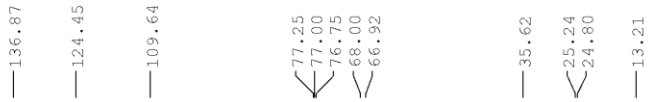


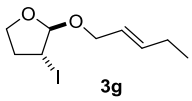


3g

(500 MHz, $CDCl_3$)

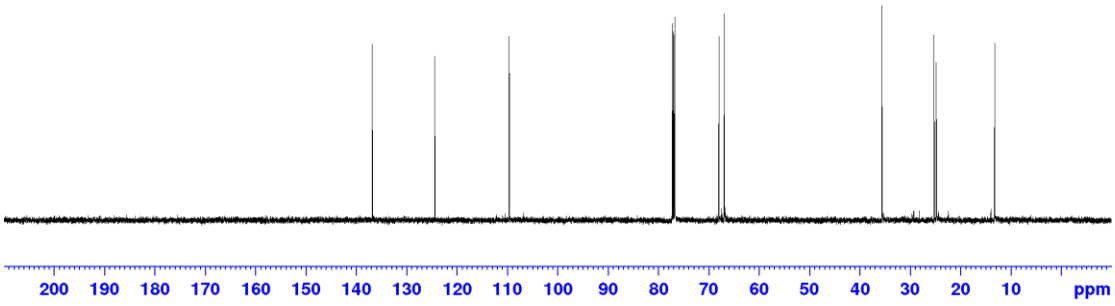


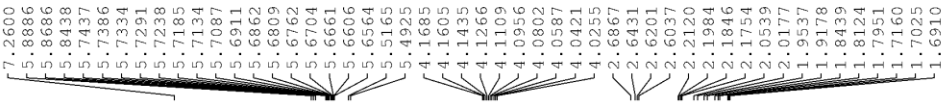


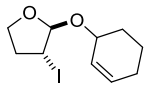


3g

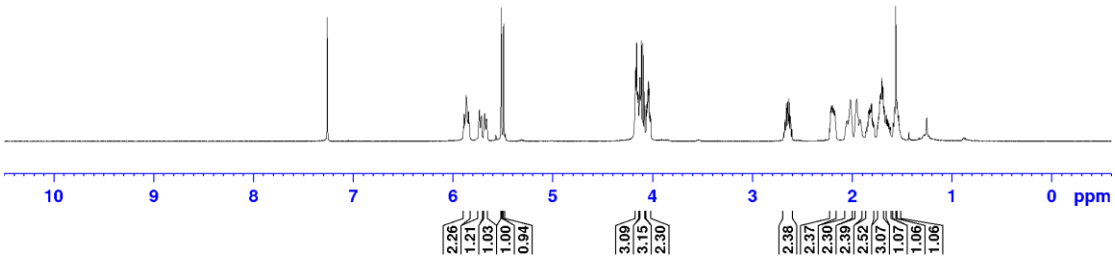
(125 MHz, $CDCl_3$)

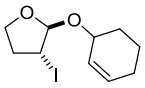




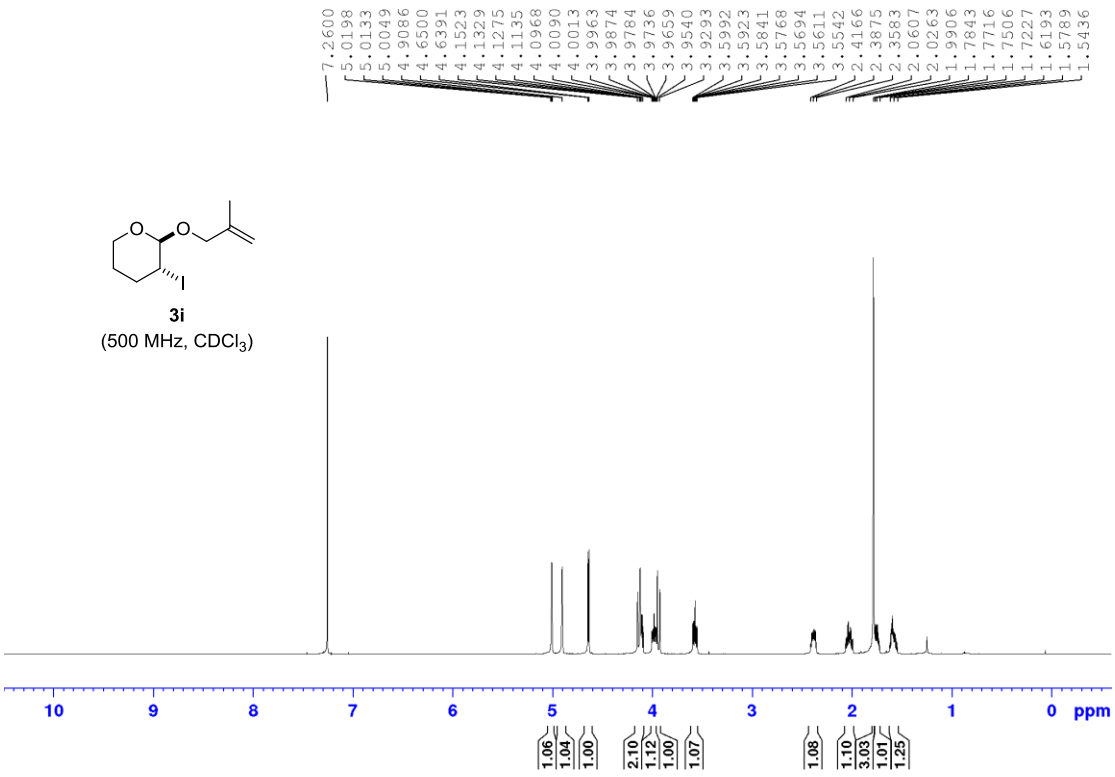


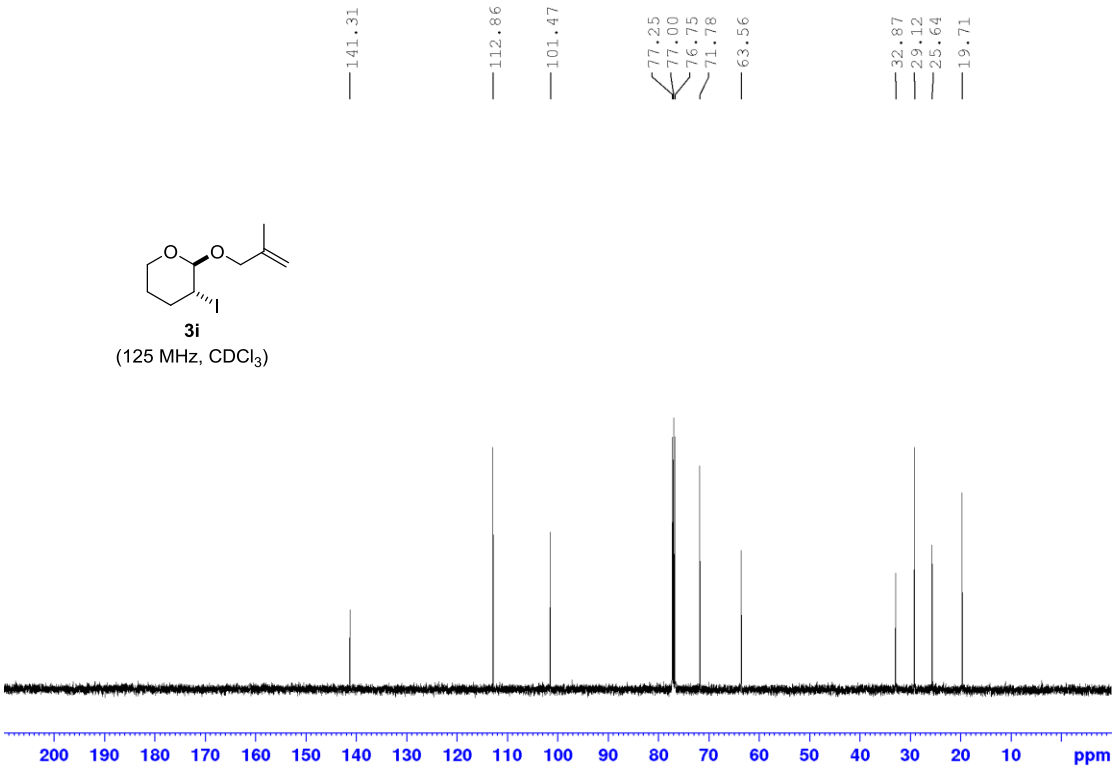
3h
(500 MHz, $CDCl_3$)

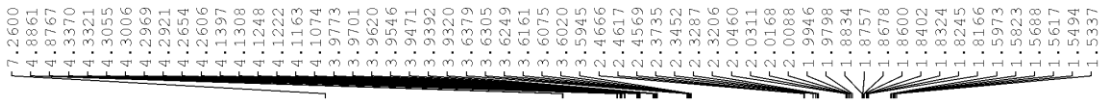


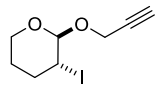


3h
(125 MHz, $CDCl_3$)

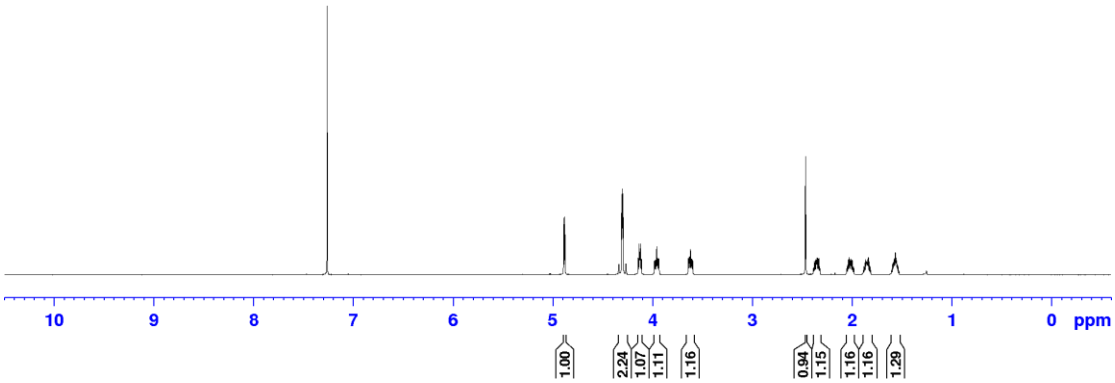

7.2600
5.0198
5.0133
5.0049
4.9086
4.6500
4.6391
4.1523
4.1329
4.1275
4.1135
4.0968
4.0090
4.0013
3.9963
3.9874
3.9784
3.9736
3.9659
3.9540
3.9293
3.5992
3.5923
3.5841
3.5768
3.5694
3.5611
3.5542
2.4166
2.3875
2.3583
2.0607
2.0263
1.9906
1.7843
1.7716
1.7506
1.7227
1.6193
1.5789
1.5436
O
O
I
3i
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.06
1.04
1.00
2.10
1.12
1.00
1.07
1.08
1.10
3.03
1.01
1.25

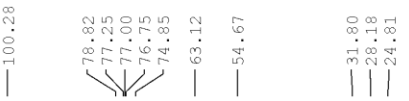

141.31
112.86
101.47
77.25
77.00
76.75
71.78
63.56
32.87
29.12
25.64
19.71
O
O
I
3i
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

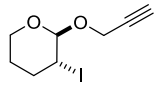




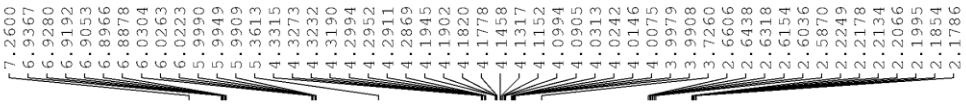
3j
(500 MHz, $CDCl_3$)

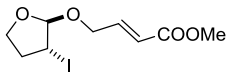






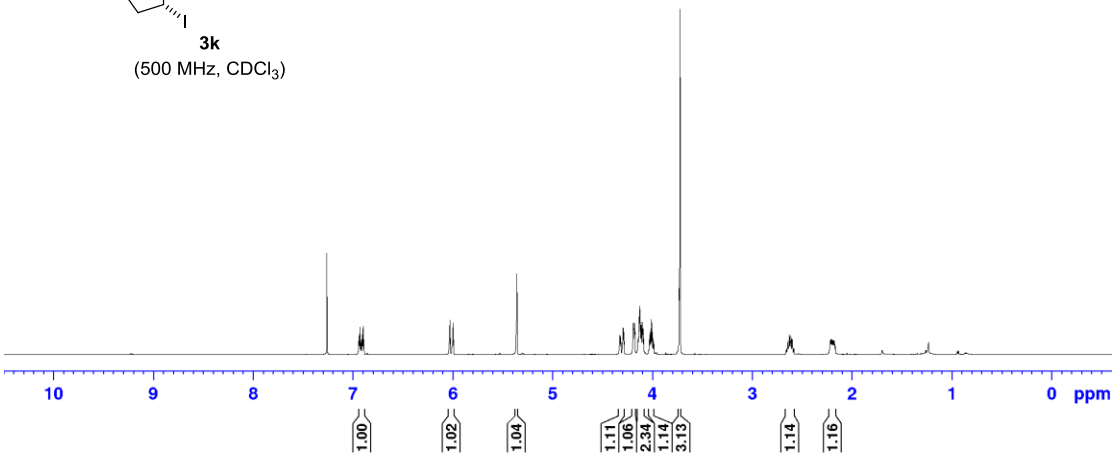
3j
(125 MHz, $CDCl_3$)

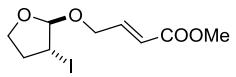




3k

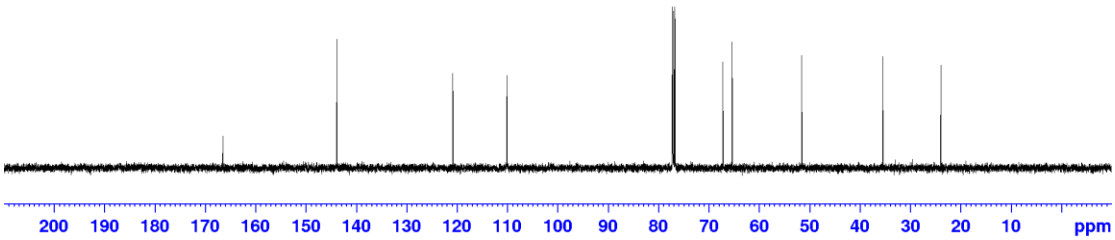
(500 MHz, $CDCl_3$)

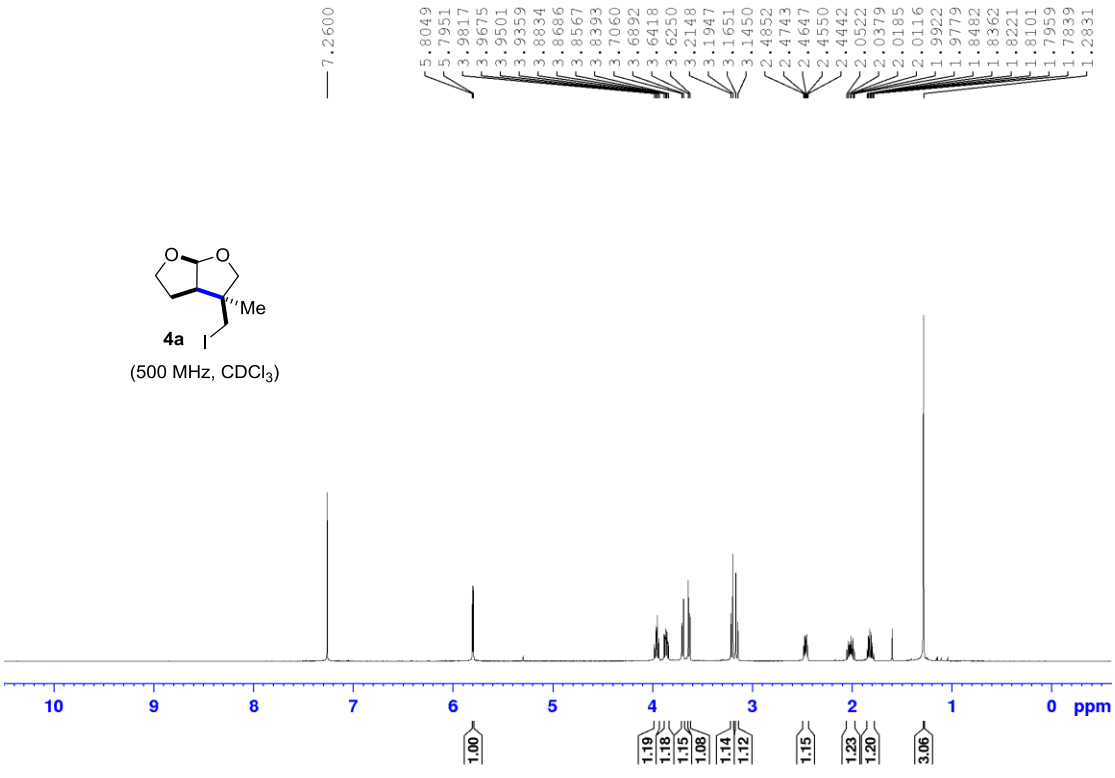


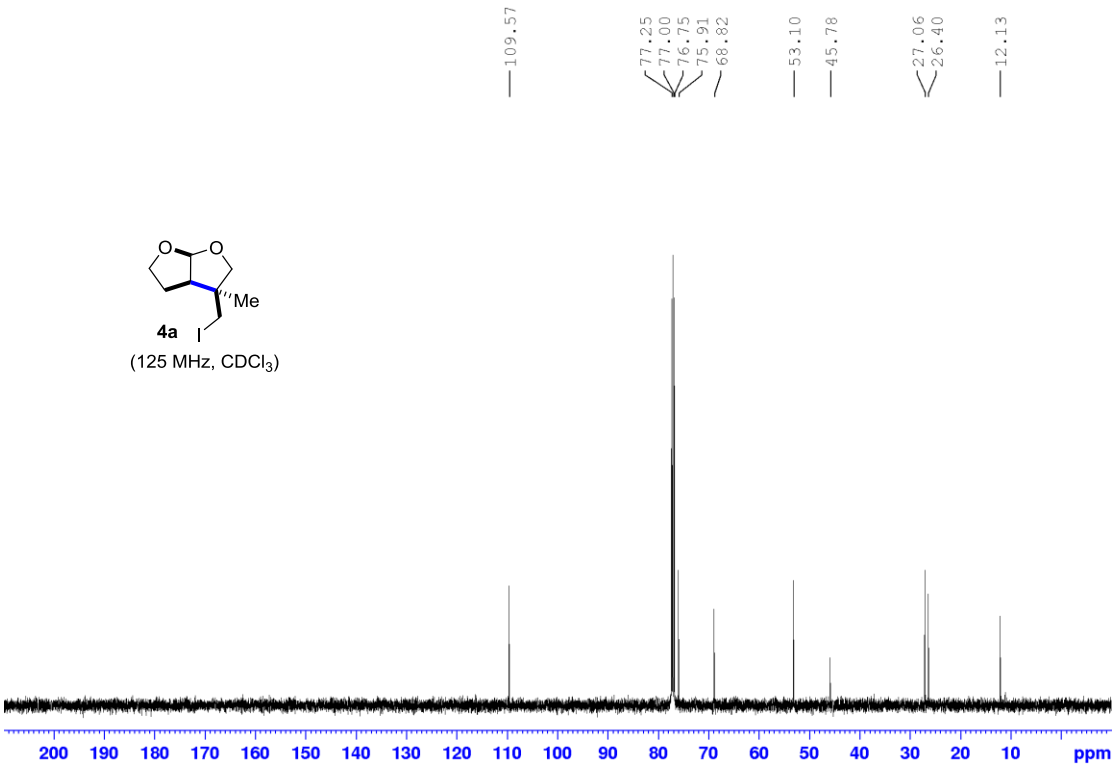


3k

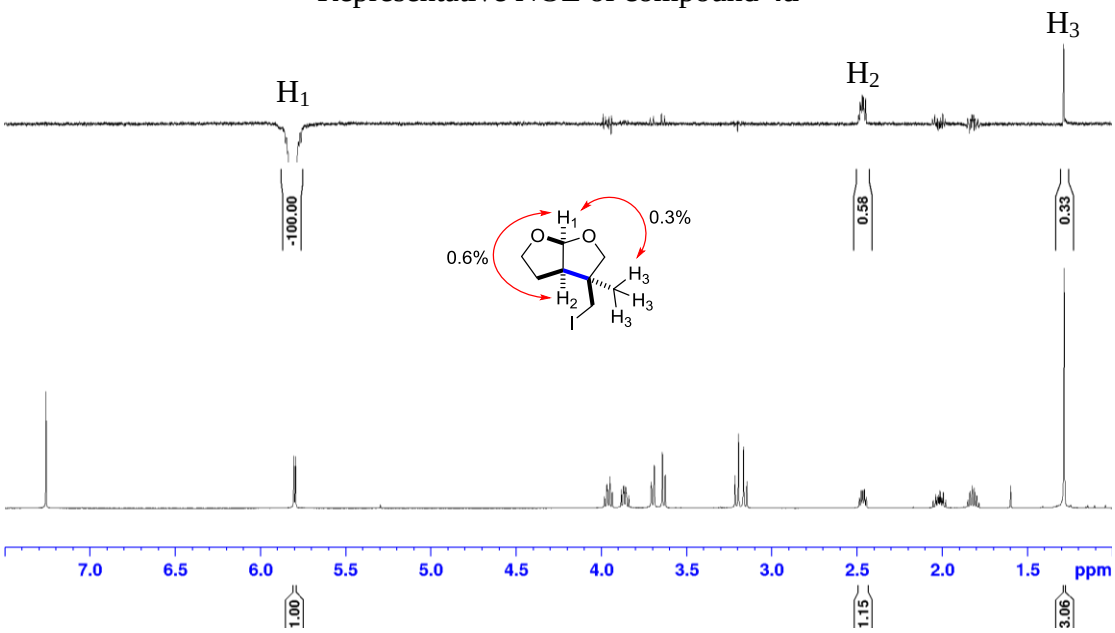
(125 MHz, $CDCl_3$)

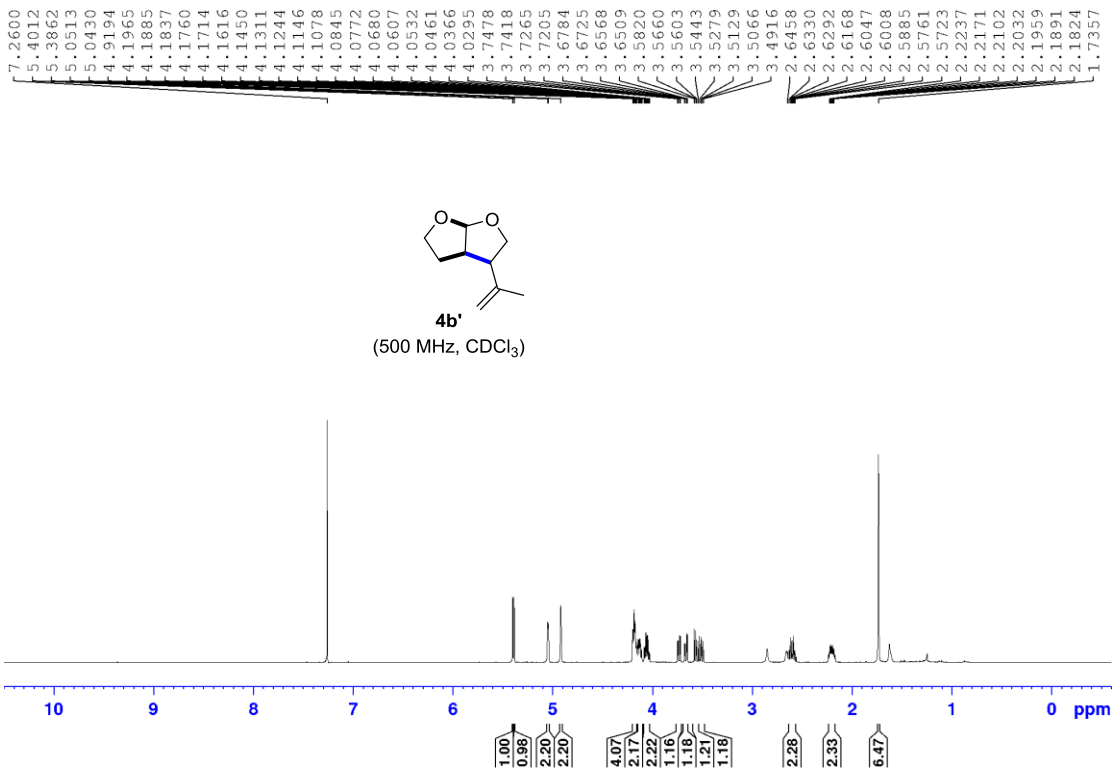


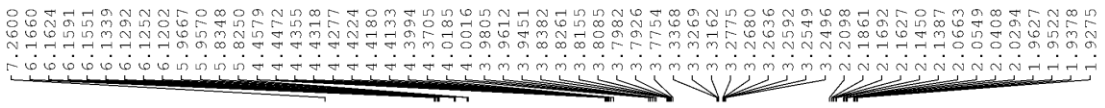

7.2600
5.8049
5.7951
3.9817
3.9675
3.9501
3.9359
3.8834
3.8686
3.8567
3.8393
3.7060
3.6892
3.6418
3.6250
3.2148
3.1947
3.1651
3.1450
2.4852
2.4743
2.4647
2.4550
2.4442
2.0522
2.0379
2.0185
2.0116
1.9922
1.9779
1.8482
1.8362
1.8221
1.8101
1.7959
1.7839
1.2831
Me
4a
(500 MHz, CDCl3)
10 9 8 7 6 5 4 3 2 1 0 ppm
1.00
1.19
1.18
1.15
1.08
1.14
1.12
1.15
1.23
1.20
3.06

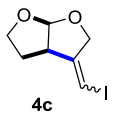

109.57
77.25
77.00
76.75
75.91
68.82
53.10
45.78
27.06
26.40
12.13
Me
4a
(125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Representative NOE of compound **4a**



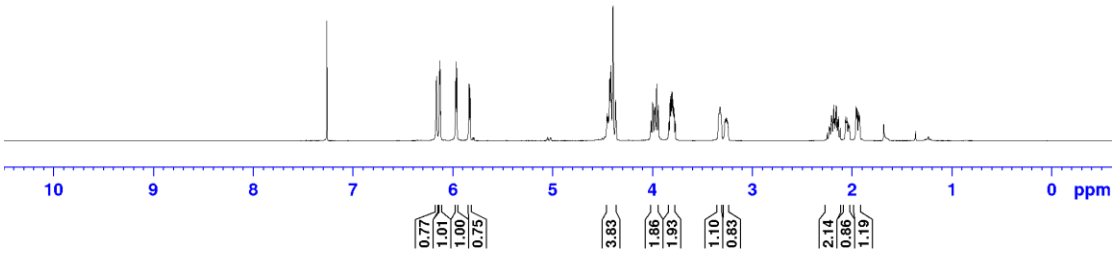

7.2600
5.4012
5.3862
5.0513
5.0430
4.9194
4.1965
4.1885
4.1837
4.1760
4.1714
4.1616
4.1450
4.1311
4.1244
4.1146
4.1078
4.0845
4.0772
4.0680
4.0607
4.0532
4.0461
4.0366
4.0295
3.7478
3.7418
3.7265
3.7205
3.6784
3.6725
3.6568
3.6509
3.5820
3.5660
3.5603
3.5443
3.5279
3.5129
3.5066
3.4916
2.6458
2.6330
2.6292
2.6168
2.6047
2.6008
2.5885
2.5761
2.5723
2.2237
2.2171
2.2102
2.2032
2.1959
2.1891
2.1824
1.7357
4b'
(500 MHz, CDCl3)
10 9 8 7 6 5 4 3 2 1 0 ppm
1.00 0.98 2.20 2.20 4.07 2.17 2.22 1.16 1.18 1.21 1.18 2.28 2.33 6.47
143.82
143.47
112.20
111.96
111.31
111.08
77.25
77.00
76.75
74.08
74.00
71.89
71.37
67.29
67.27
35.62
35.56
23.98
23.89
18.90
18.84
4b'
(125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

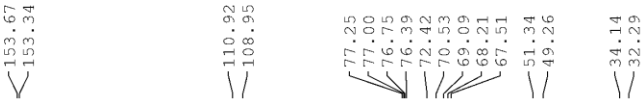


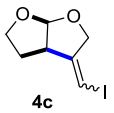


4c

(500 MHz, $CDCl_3$)

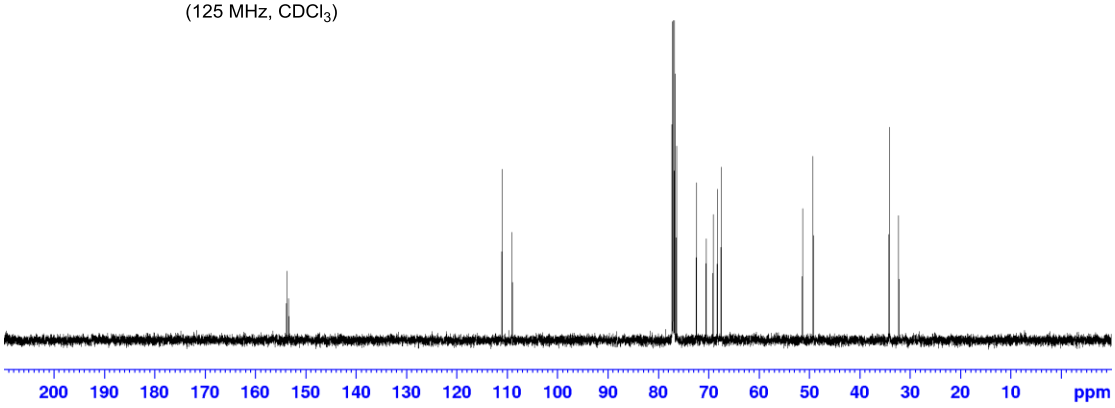


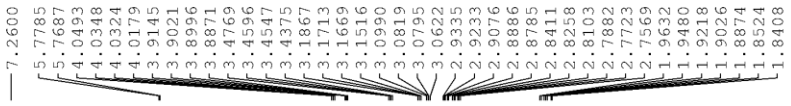


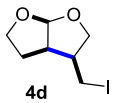


4c

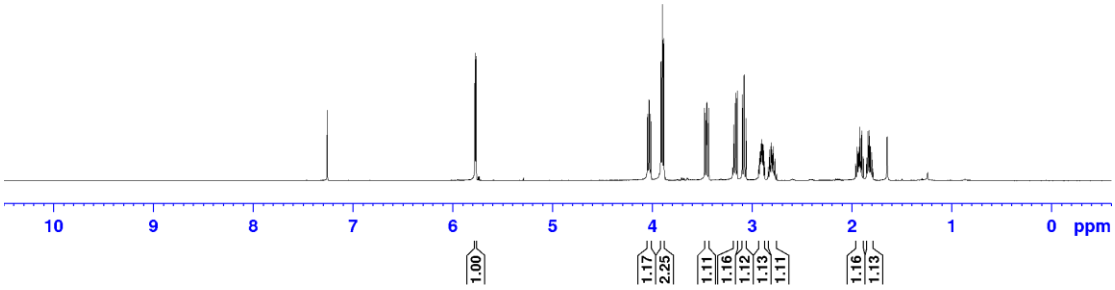
(125 MHz, $CDCl_3$)

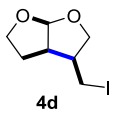




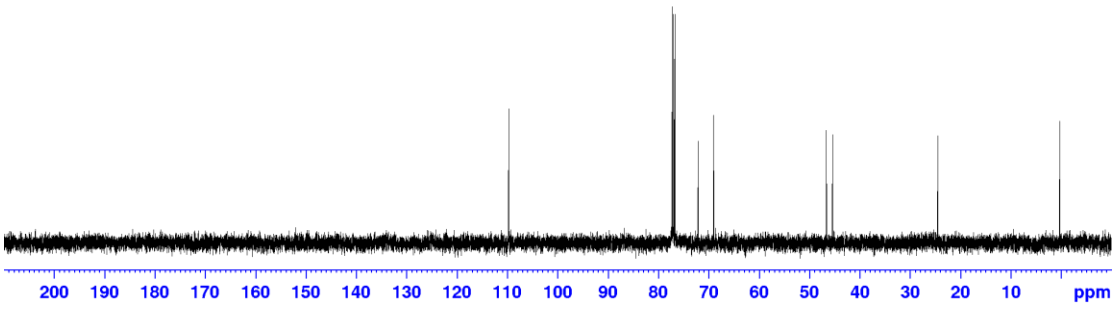


4d
(500 MHz, $CDCl_3$)

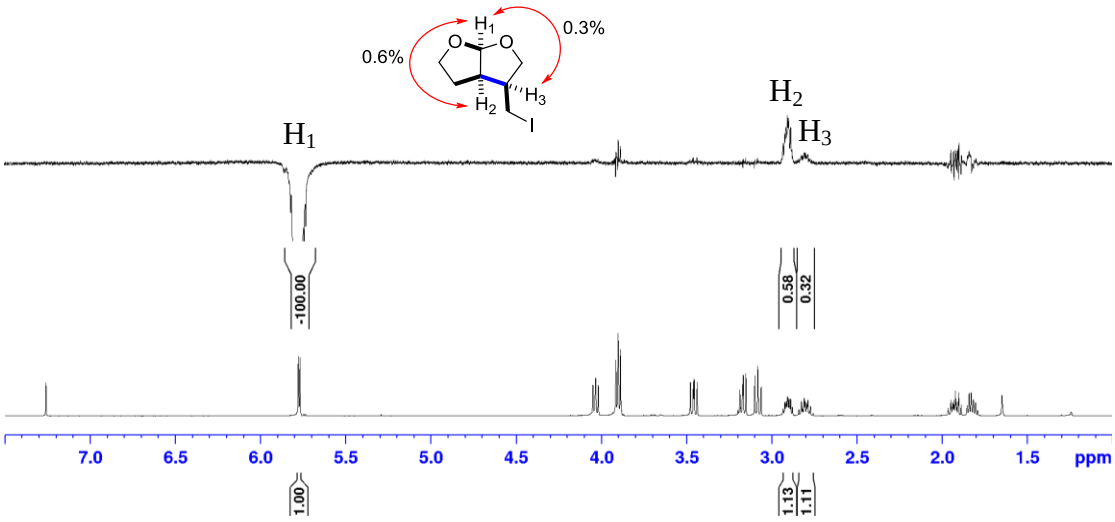


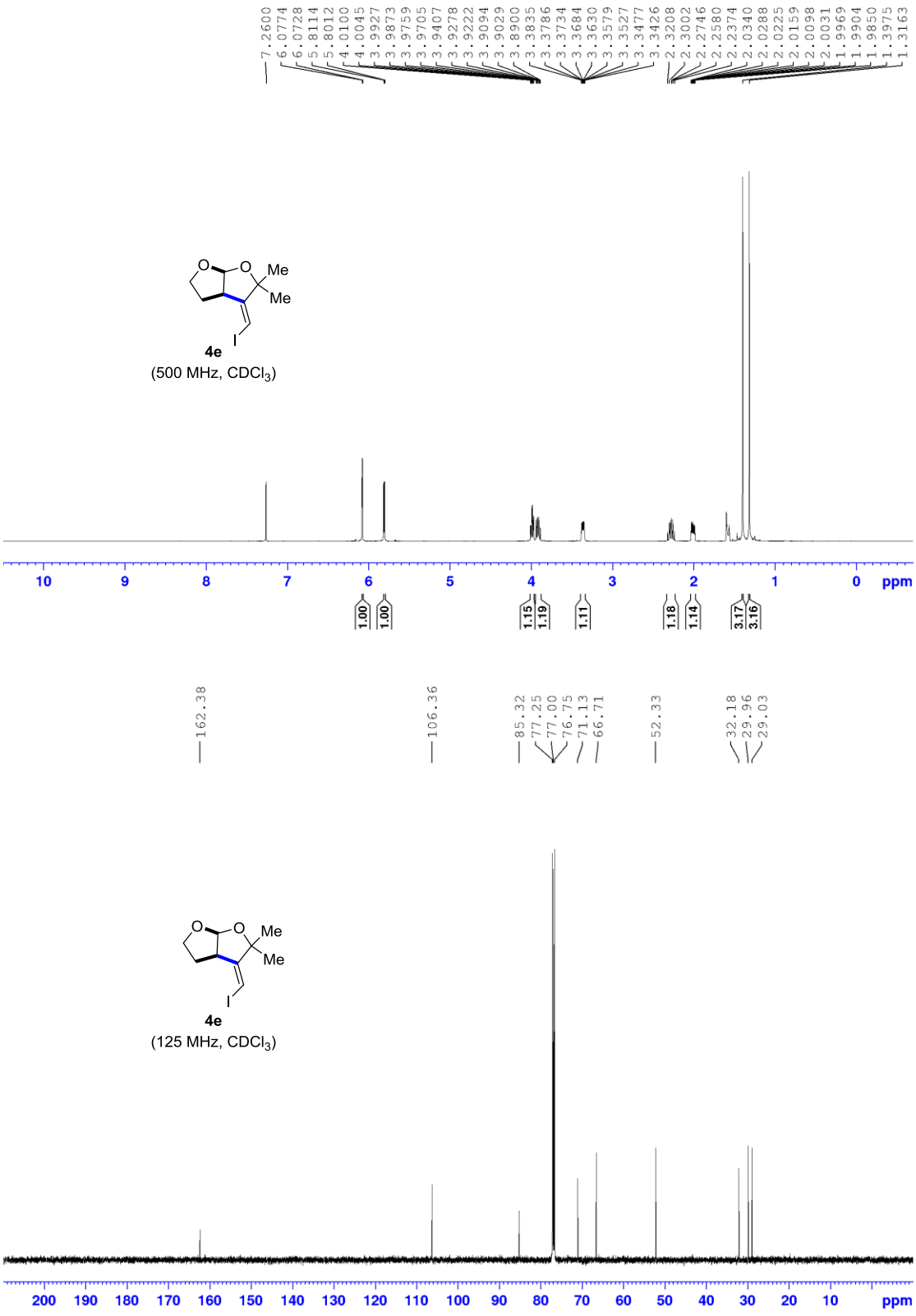


4d
(125 MHz, $CDCl_3$)

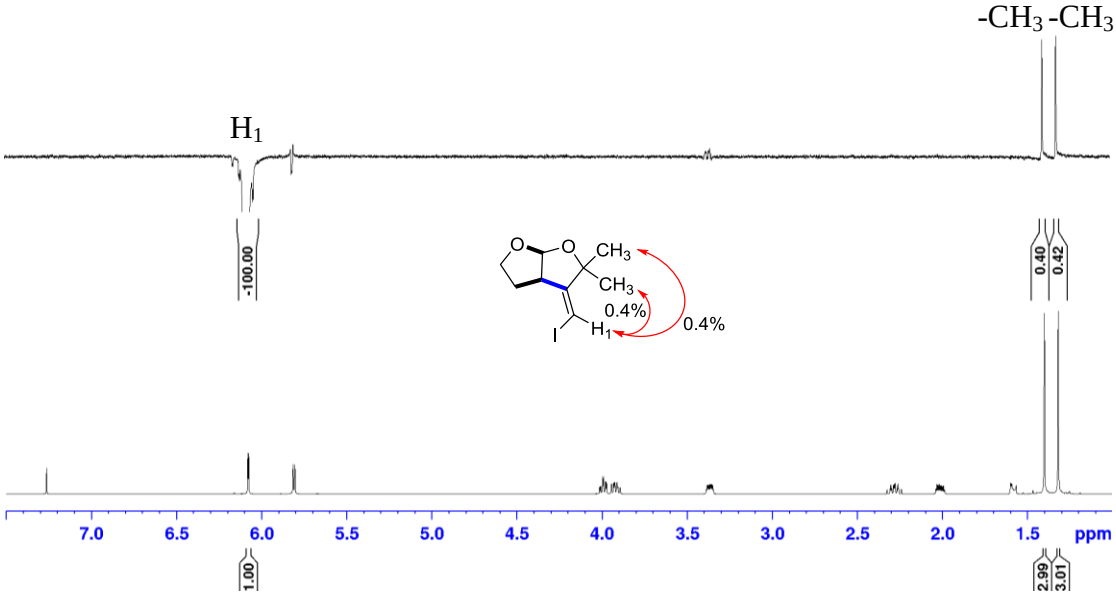


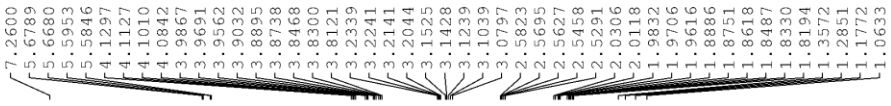
Representative NOE of compound **4d**

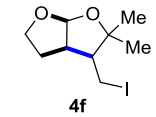



7.2600
6.0774
6.0728
5.8114
5.8012
4.0100
4.0045
3.9927
3.9873
3.9759
3.9705
3.9407
3.9278
3.9222
3.9094
3.9029
3.8900
3.3835
3.3786
3.3734
3.3684
3.3630
3.3579
3.3527
3.3477
3.3426
2.3208
2.3002
2.2746
2.2580
2.2374
2.0340
2.0288
2.0225
2.0159
2.0098
2.0031
1.9969
1.9904
1.9850
1.3975
1.3163
O
O
Me
Me
I
4e
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.00
1.15
1.19
1.11
1.18
1.14
3.17
3.16
162.38
106.36
85.32
77.25
77.00
76.75
71.13
66.71
52.33
32.18
29.96
29.03
O
O
Me
Me
I
4e
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Representative NOE of compound **4e**

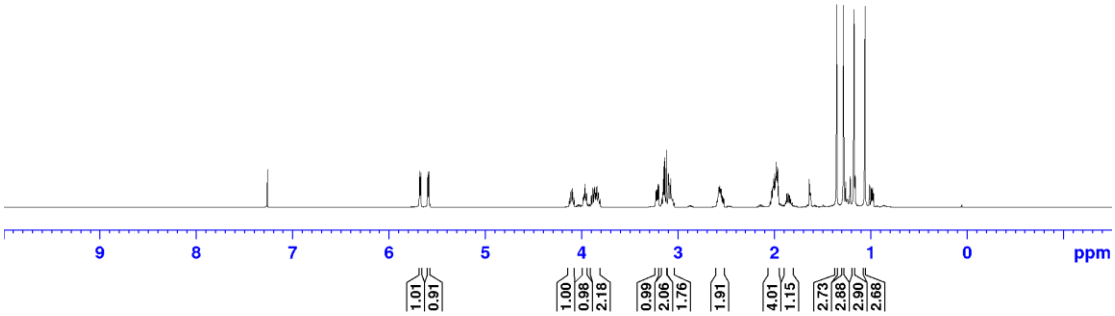


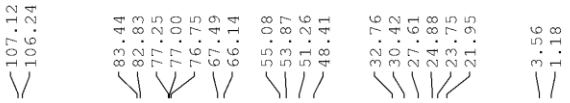


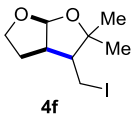


4f

(500 MHz, $CDCl_3$)

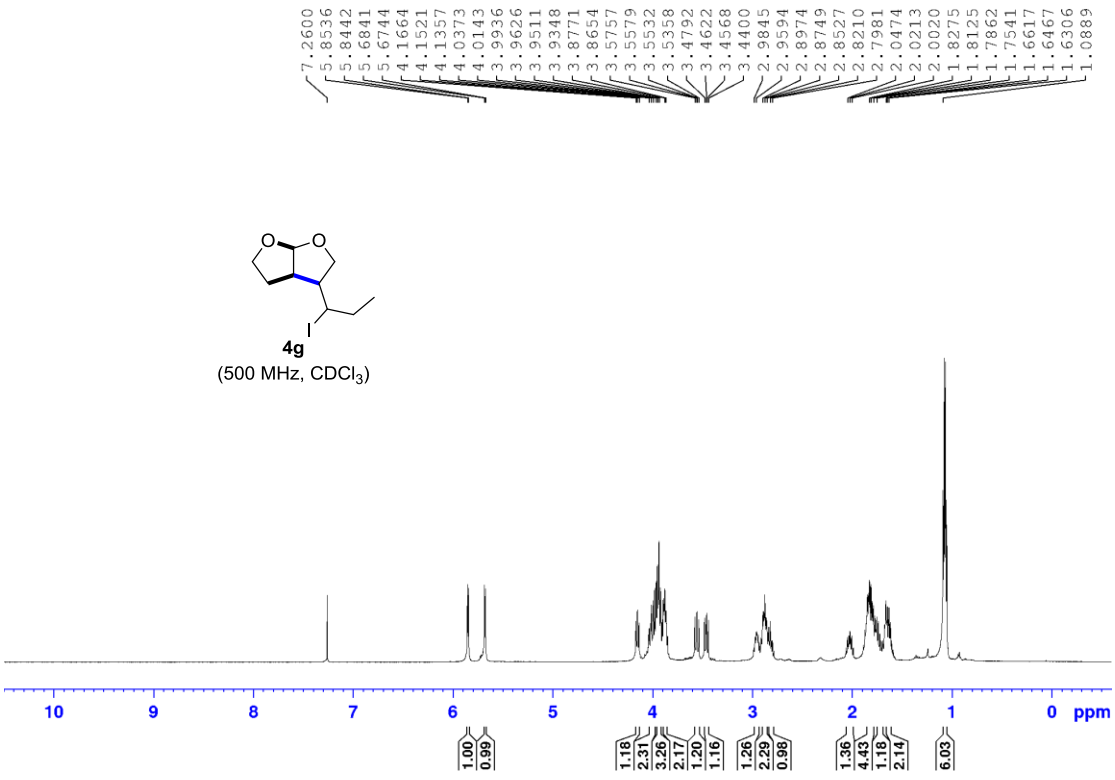


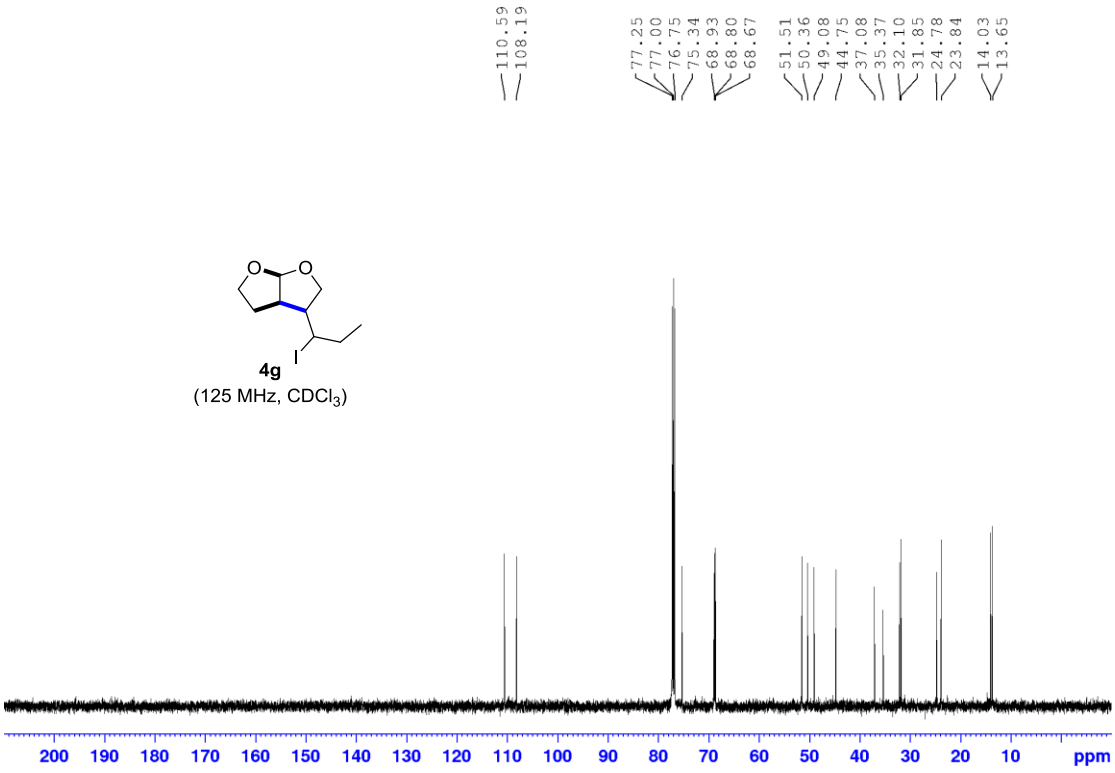


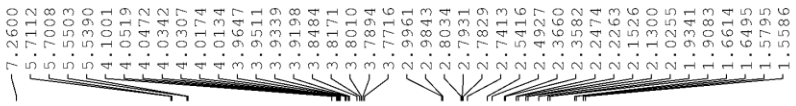


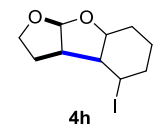
4f

(125 MHz, $CDCl_3$)


7.2600
5.8536
5.8442
5.6841
5.6744
4.1664
4.1521
4.1357
4.0373
4.0143
3.9936
3.9626
3.9511
3.9348
3.8771
3.8654
3.5757
3.5579
3.5532
3.5358
3.4792
3.4622
3.4568
3.4400
2.9845
2.9594
2.8974
2.8749
2.8527
2.8210
2.7981
2.0474
2.0213
2.0020
1.8275
1.8125
1.7862
1.7541
1.6617
1.6467
1.6306
1.0889
4g
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
1.18
2.31
3.26
2.17
1.20
1.16
1.26
2.29
0.98
1.36
4.43
1.18
2.14
6.03

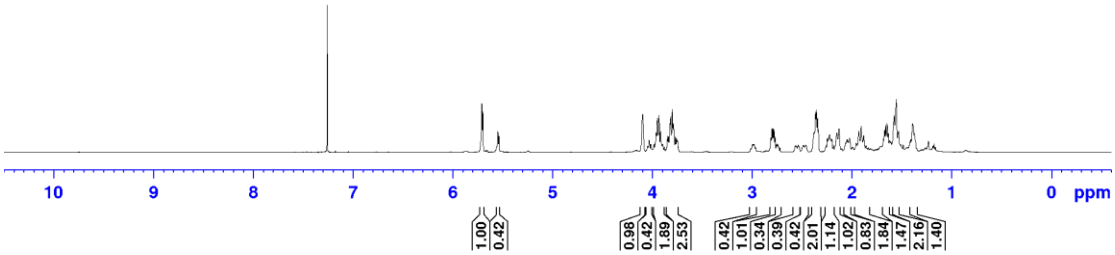

110.59
108.19
77.25
77.00
76.75
75.34
68.93
68.80
68.67
51.51
50.36
49.08
44.75
37.08
35.37
32.10
31.85
24.78
23.84
14.03
13.65
4g
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

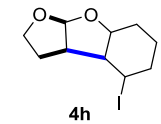




4h

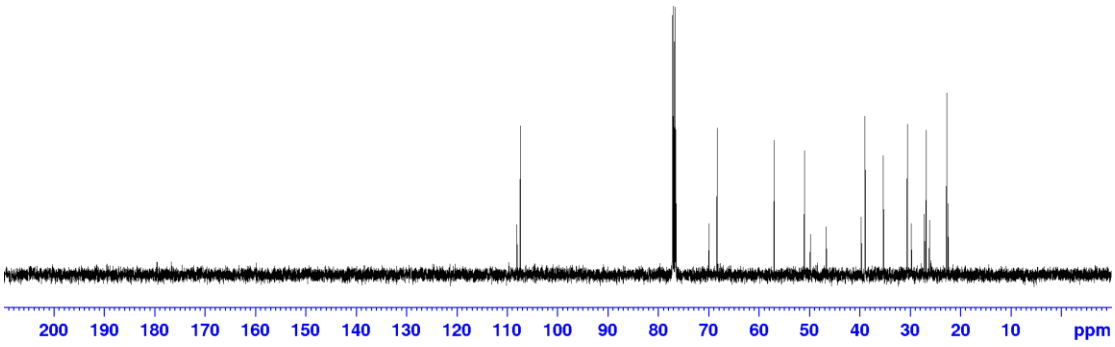
(500 MHz, $CDCl_3$)

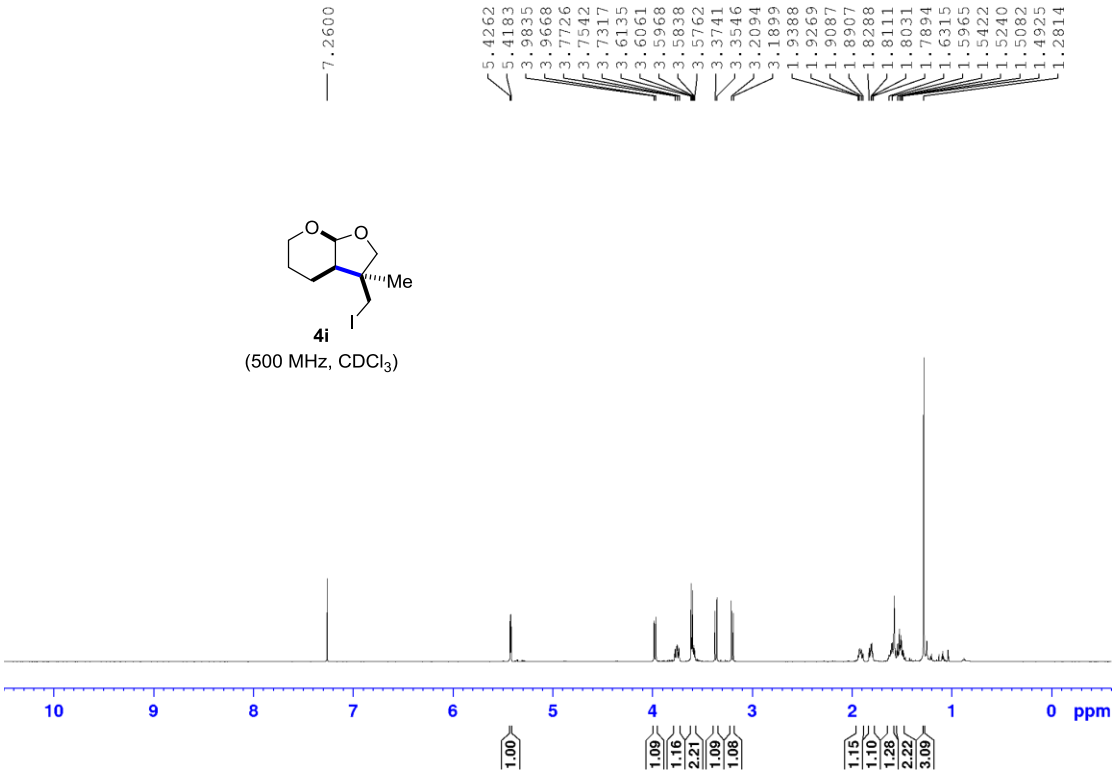


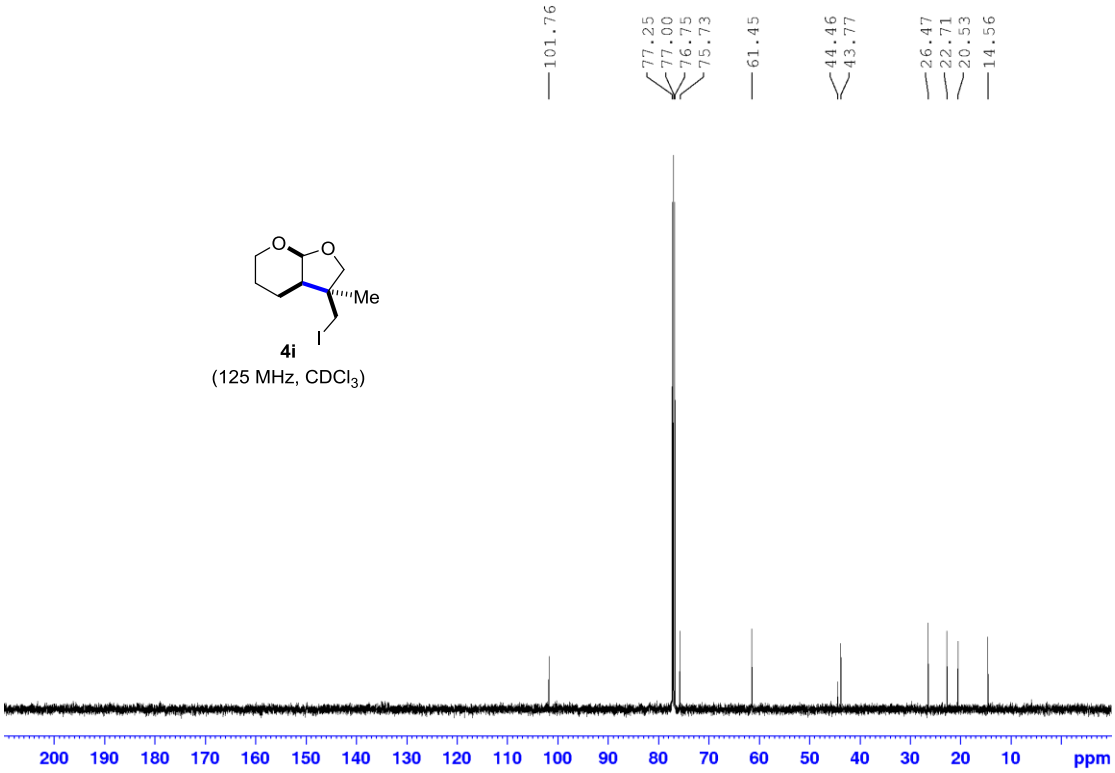


4h

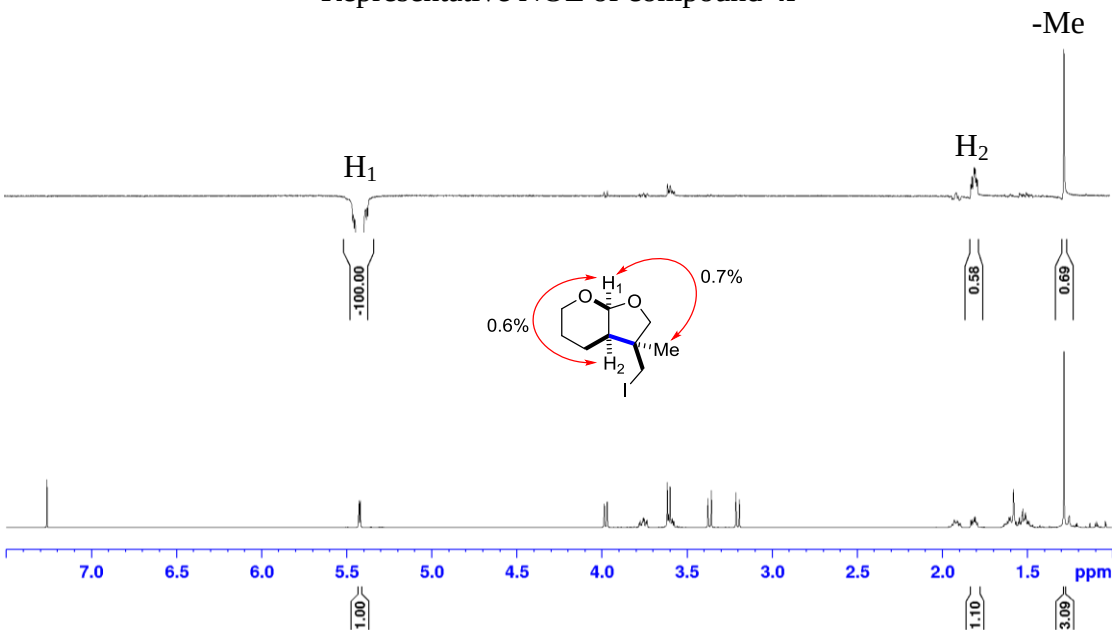
(125 MHz, $CDCl_3$)

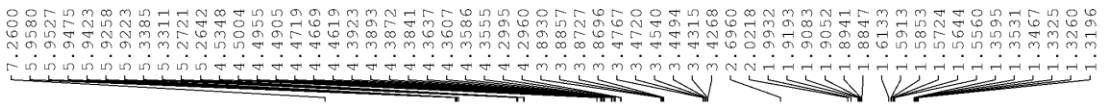


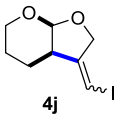

7.2600
5.4262
5.4183
3.9835
3.9668
3.7726
3.7542
3.7317
3.6135
3.6061
3.5968
3.5838
3.5762
3.3741
3.3546
3.2094
3.1899
1.9388
1.9269
1.9087
1.8907
1.8288
1.8111
1.8031
1.7894
1.6315
1.5965
1.5422
1.5240
1.5082
1.4925
1.2814
O
O
Me
I
4i
(500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.09
1.16
2.21
1.09
1.08
1.15
1.10
1.28
2.22
3.09


101.76
77.25
77.00
76.75
75.73
61.45
44.46
43.77
26.47
22.71
20.53
14.56
O
O
Me
I
4i
(125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

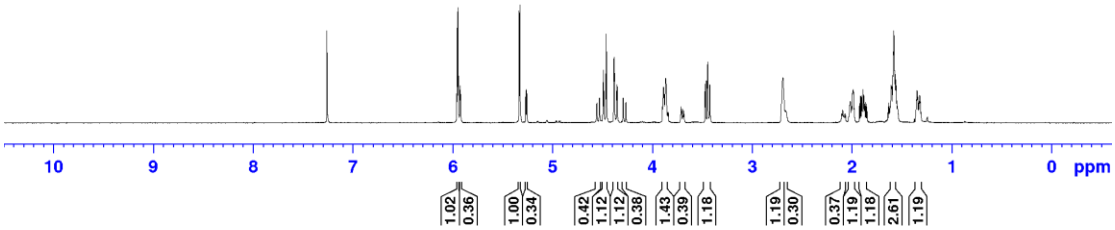
Representative NOE of compound **4i**

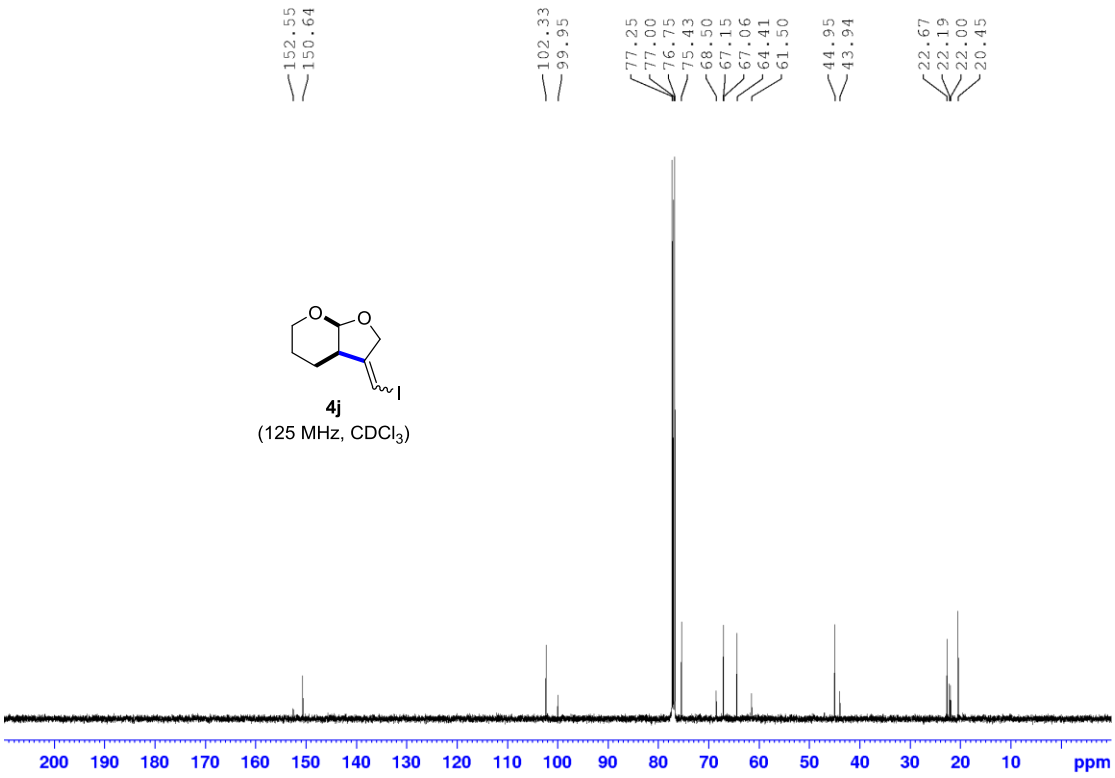




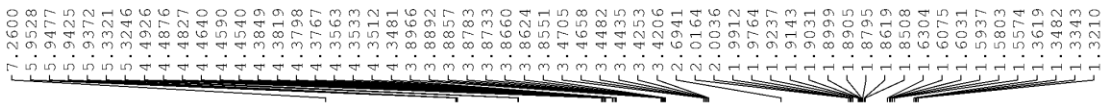


4j
(500 MHz, $CDCl_3$)

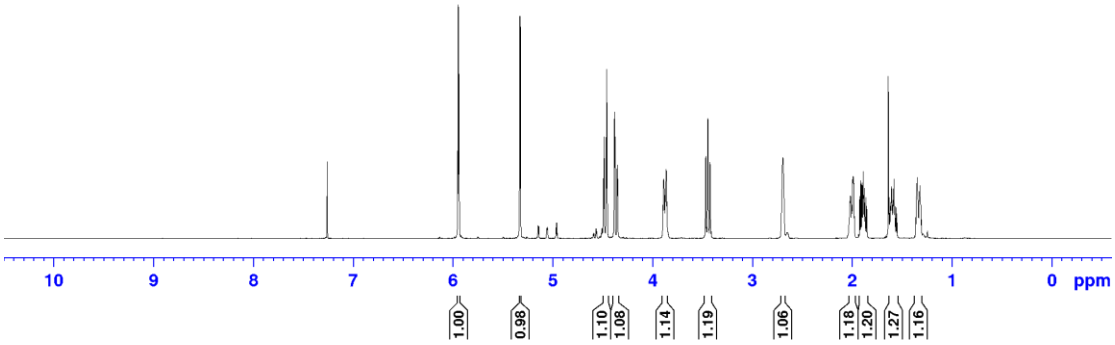




4j
(125 MHz, $CDCl_3$)

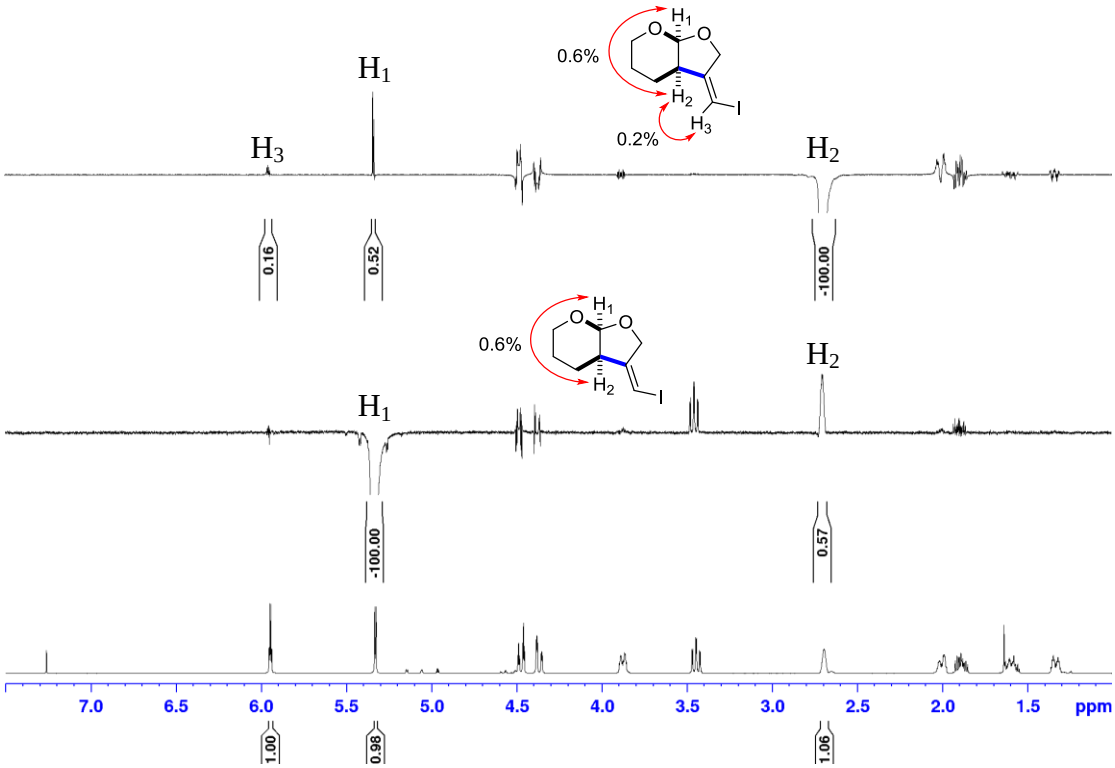


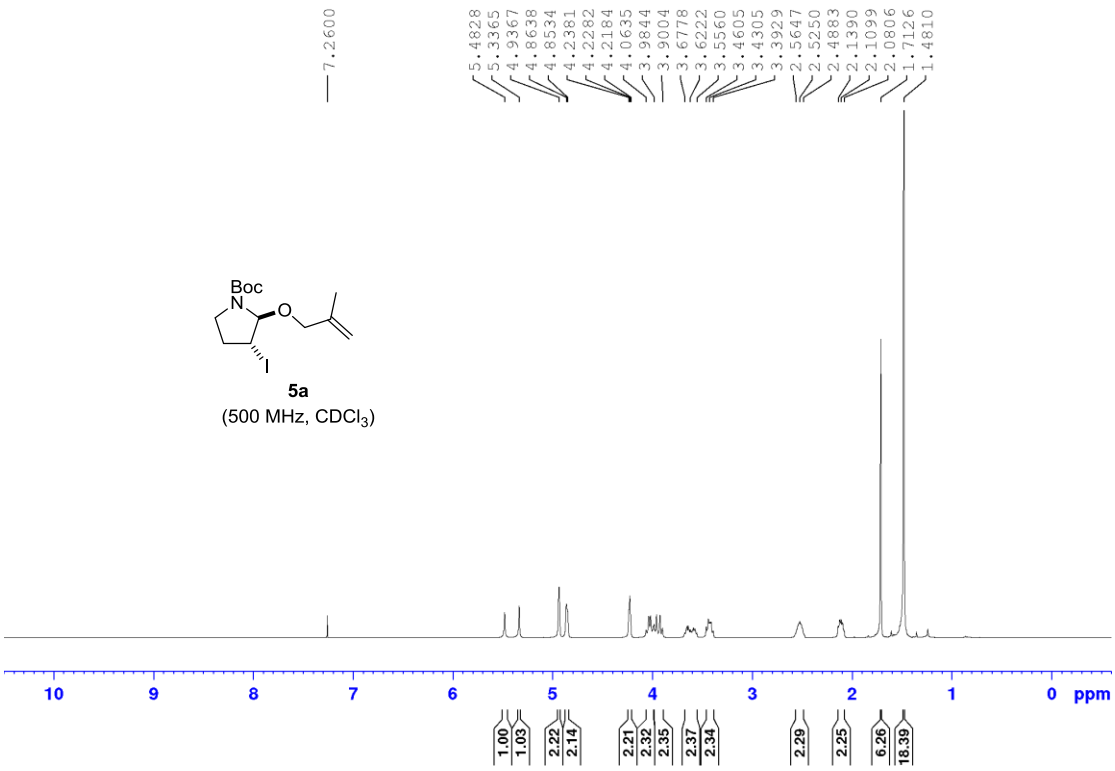
4j-major
(500 MHz, $CDCl_3$)



4j-major
(125 MHz, $CDCl_3$)

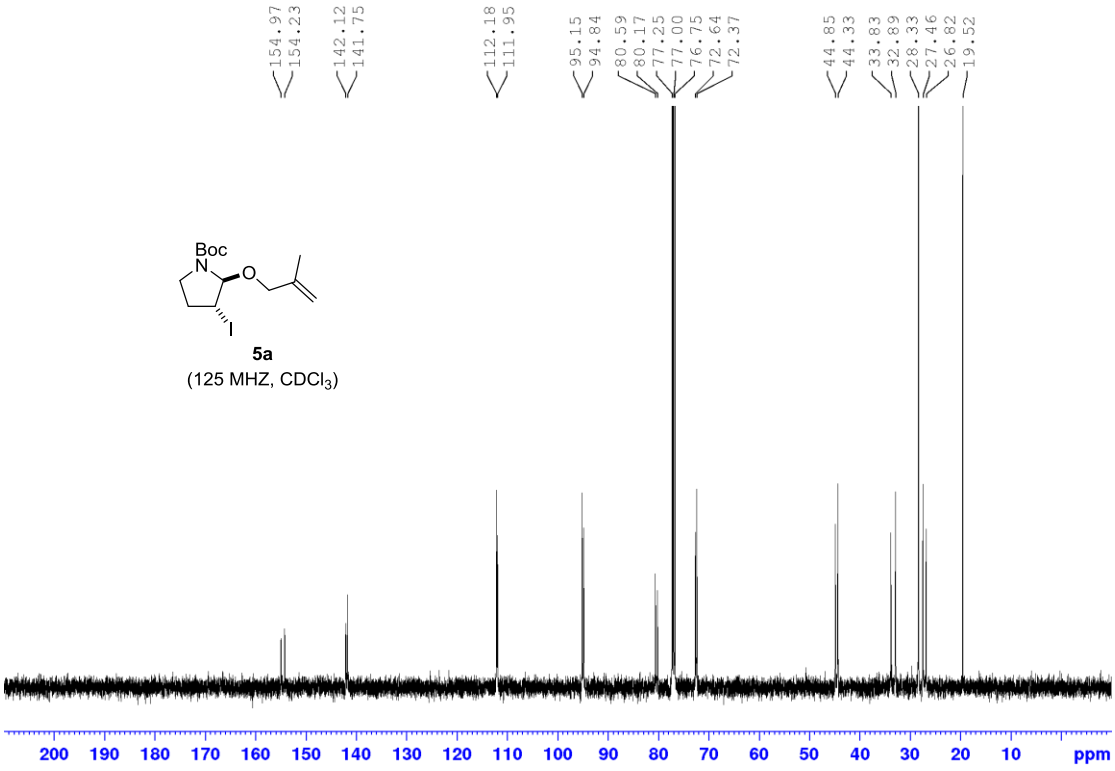
Representative NOEs of compound **4j-major**





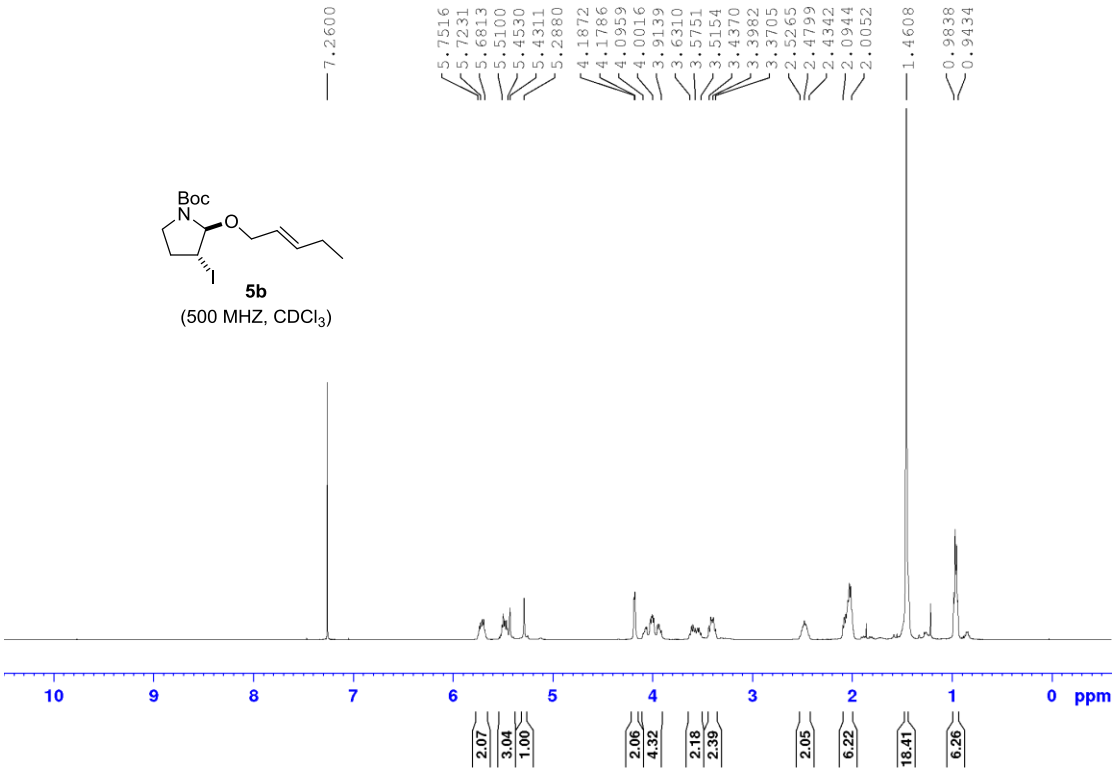
5a

(500 MHz, $CDCl_3$)



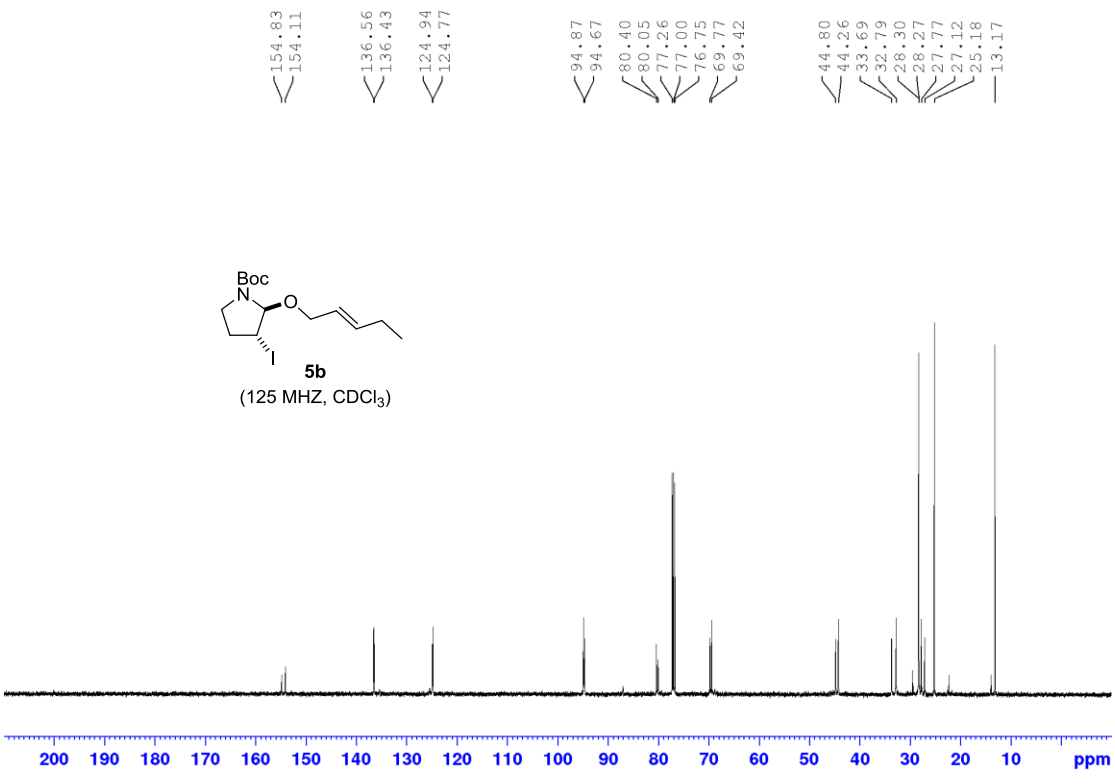
5a

(125 MHZ, $CDCl_3$)



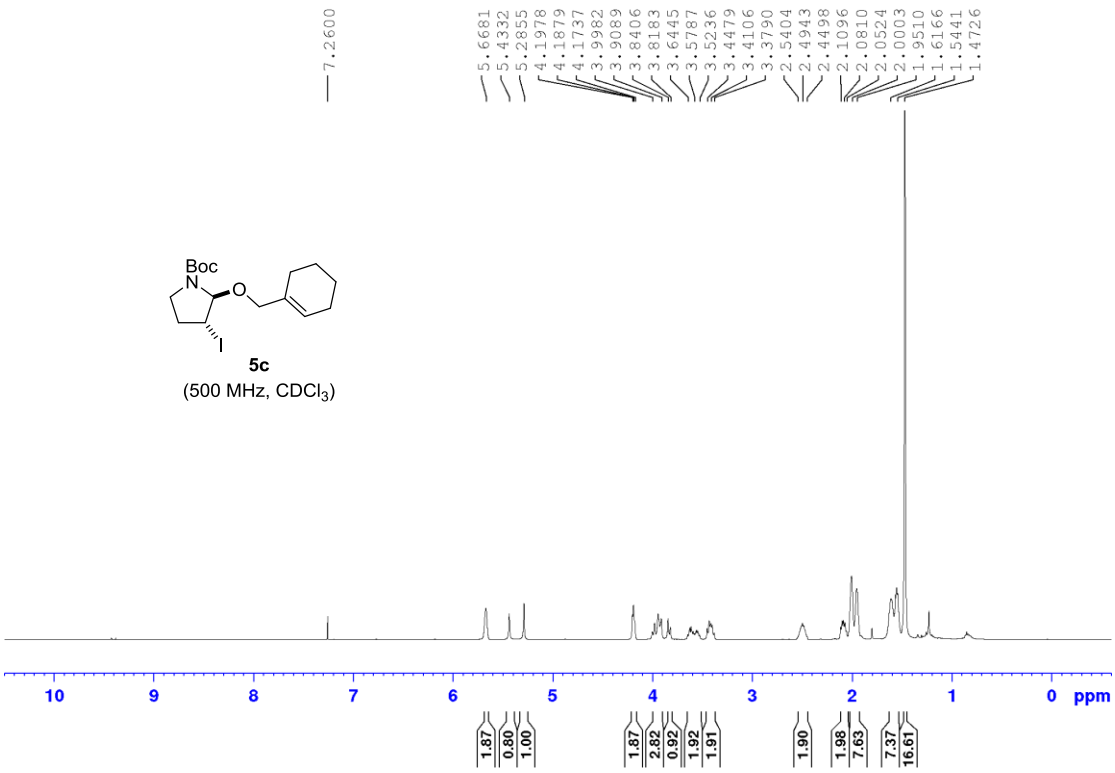
5b

(500 MHZ, $CDCl_3$)

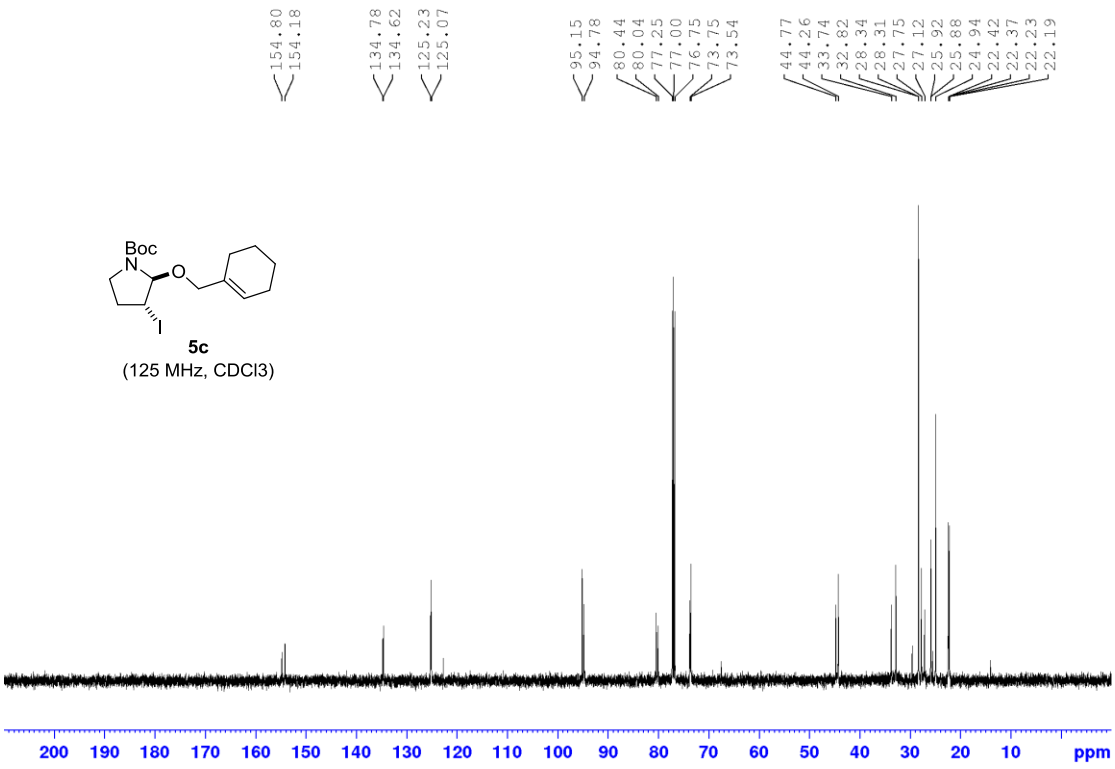


5b

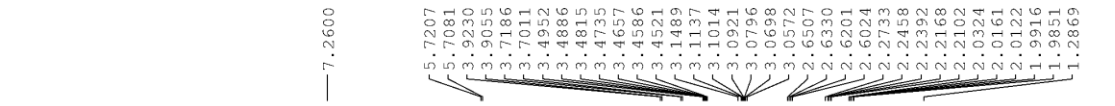
(125 MHZ, $CDCl_3$)

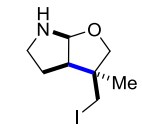


5c
(500 MHz, $CDCl_3$)

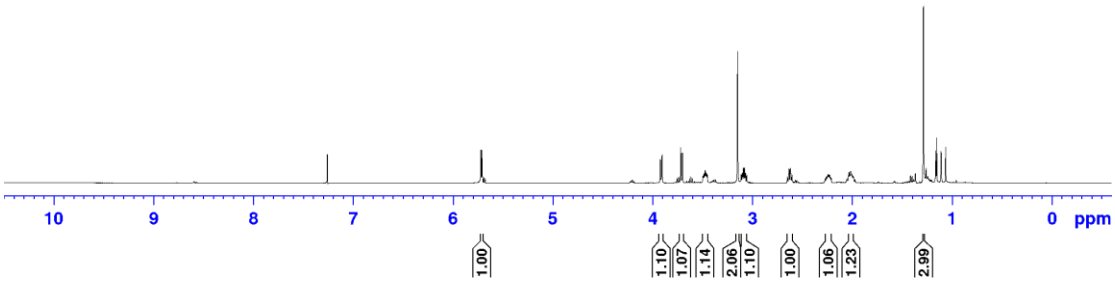


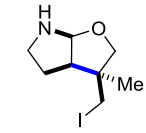
5c
(125 MHz, CDCl3)



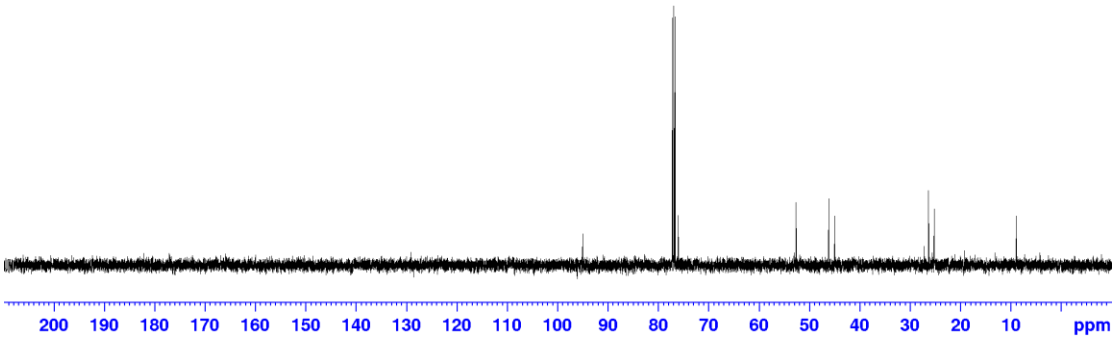


7a
(500 MHz, $CDCl_3$)

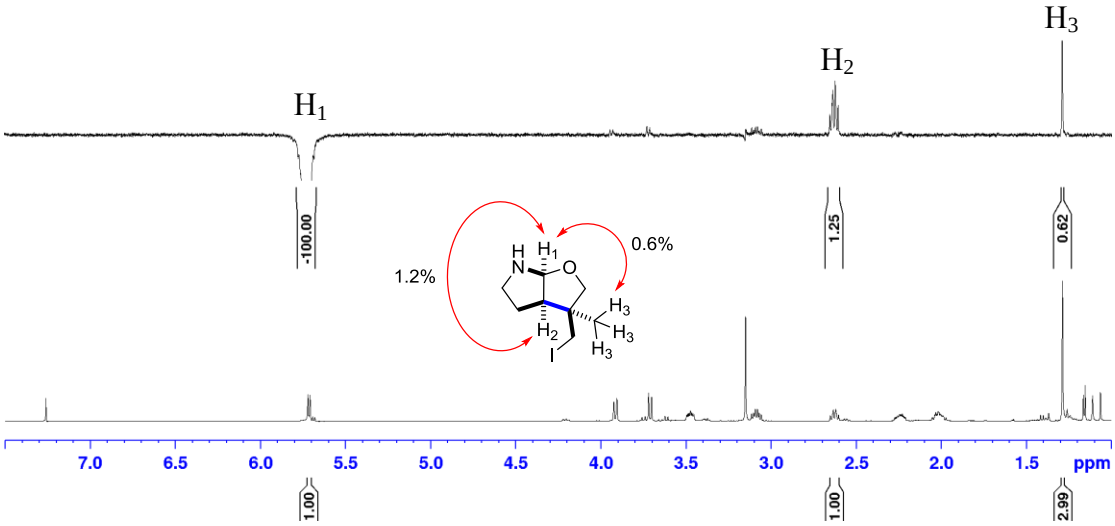


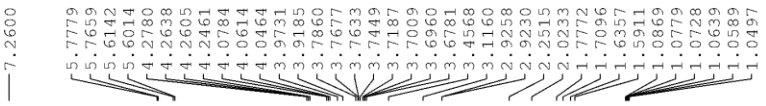


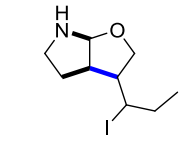
7a
(125 MHz, $CDCl_3$)



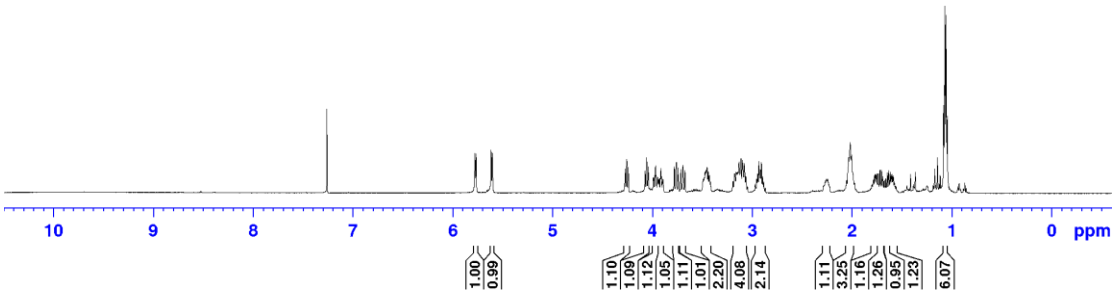
Representative NOE of compound **7a**

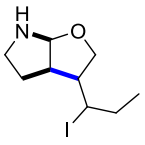




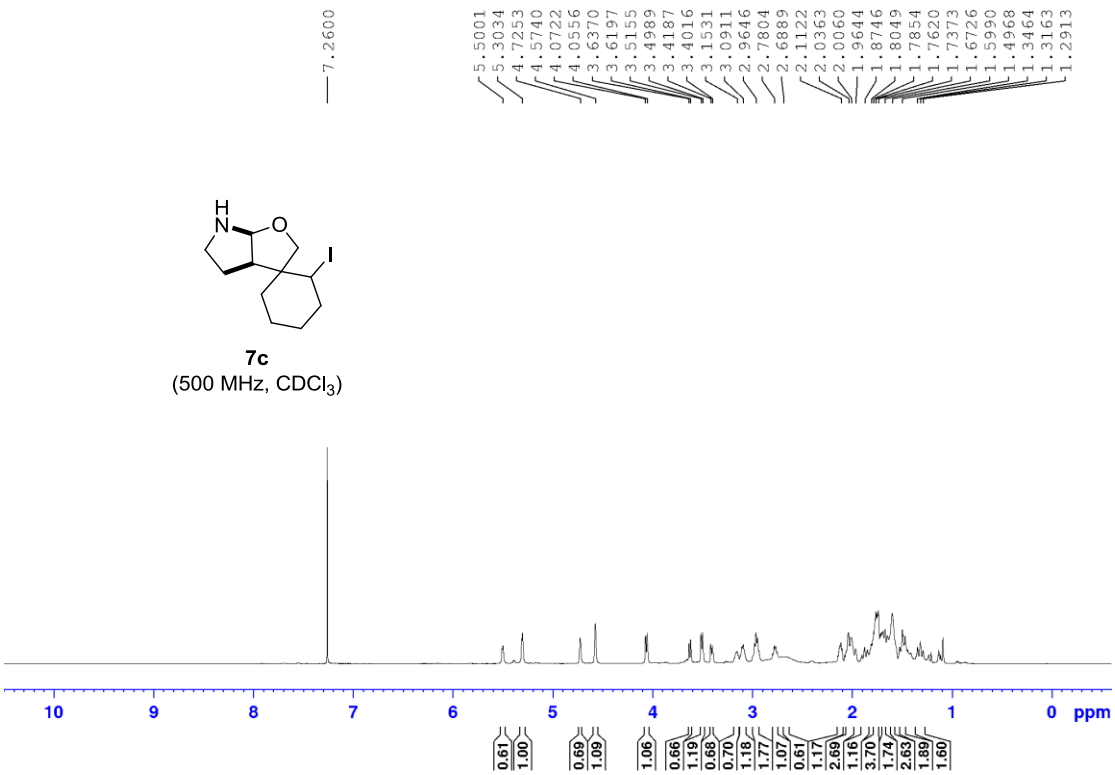


7b
(500 MHz, $CDCl_3$)

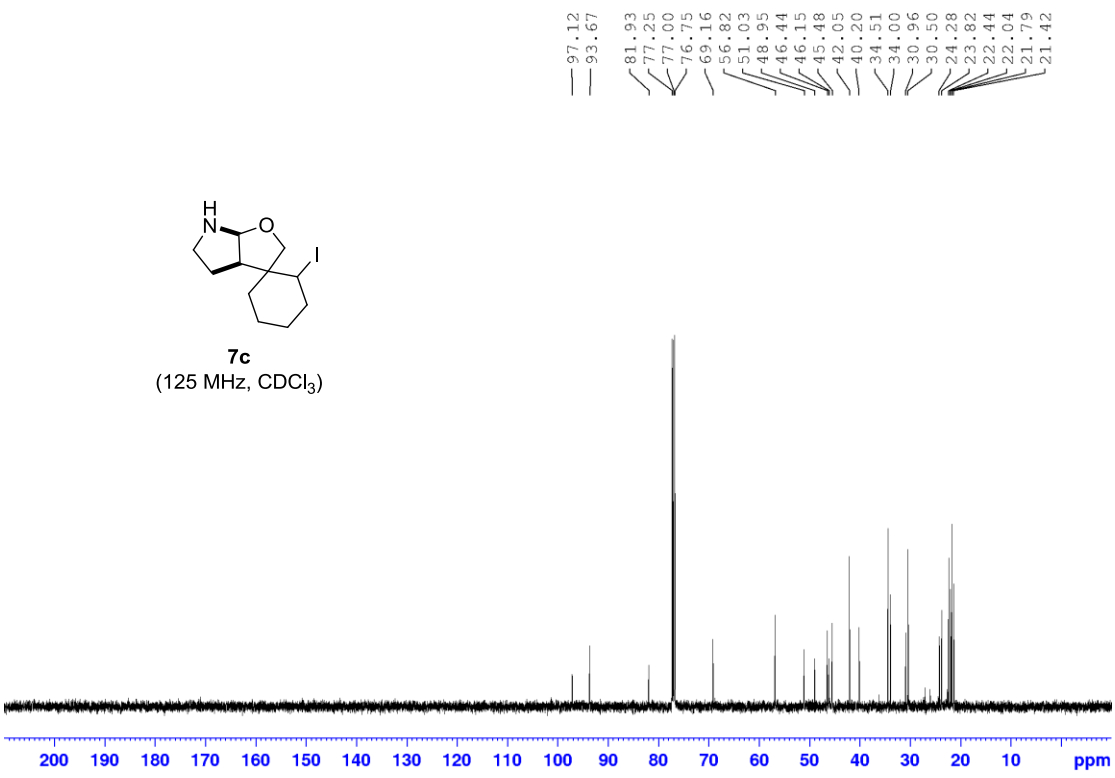




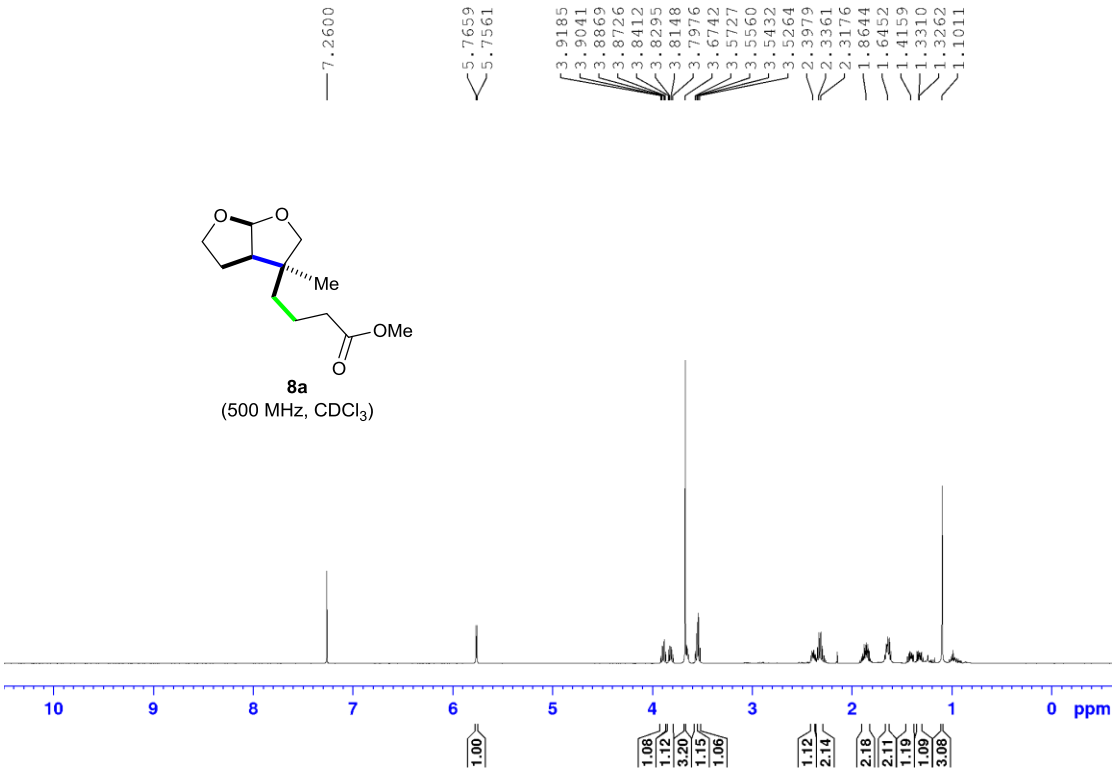
7b
(125 MHz, $CDCl_3$)



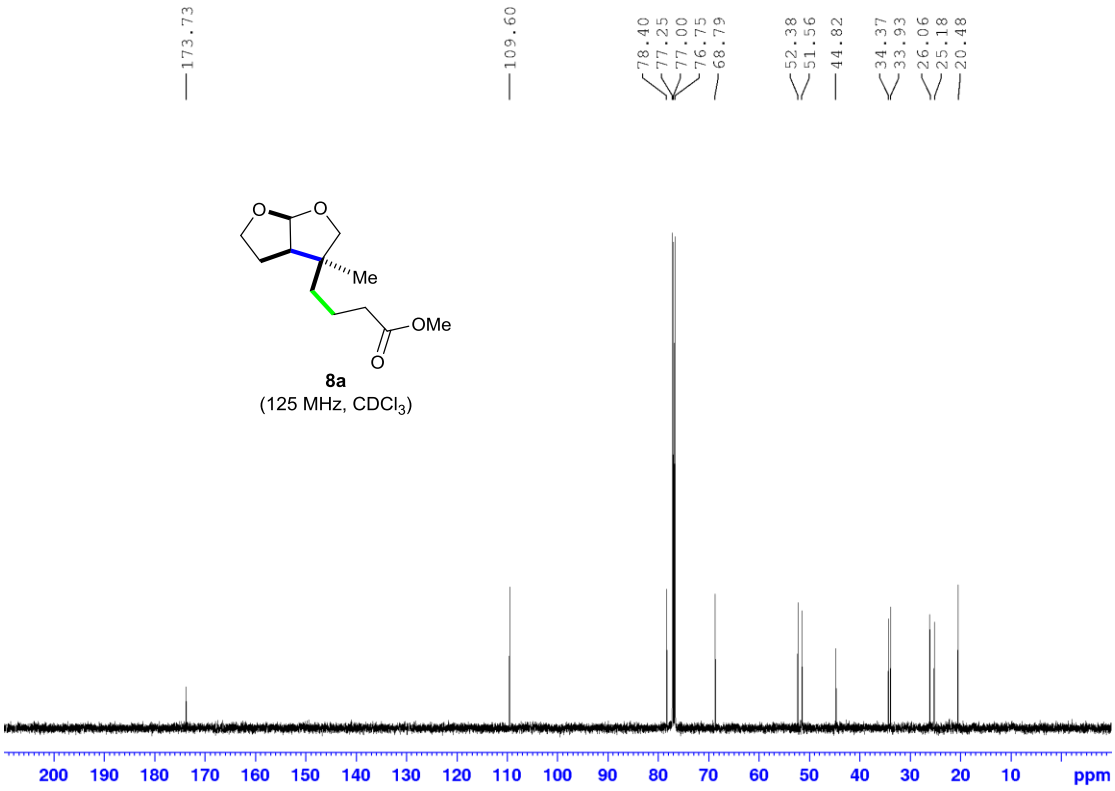
7c
(500 MHz, $CDCl_3$)



7c
(125 MHz, $CDCl_3$)

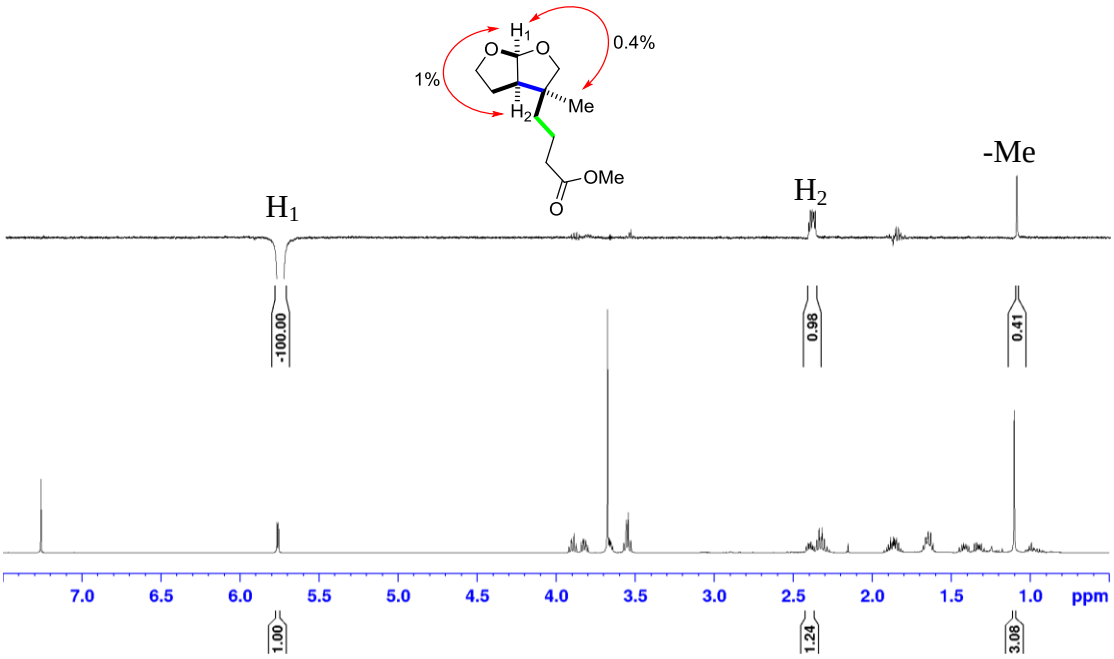


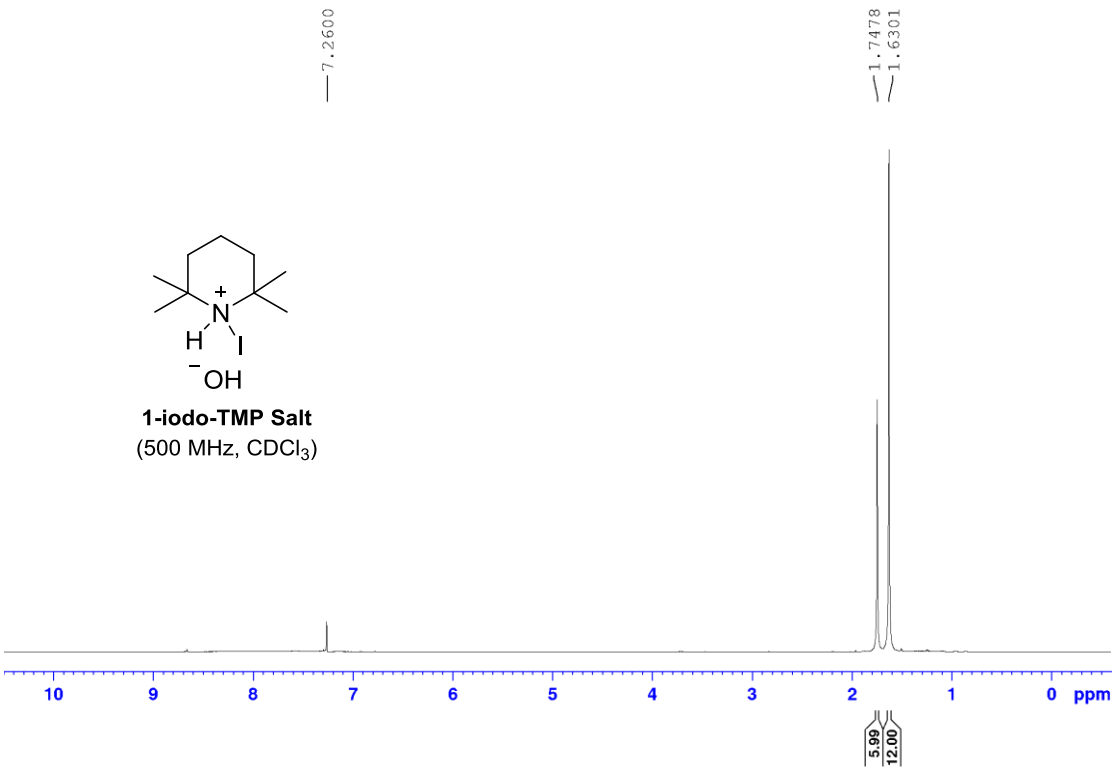
8a
(500 MHz, $CDCl_3$)



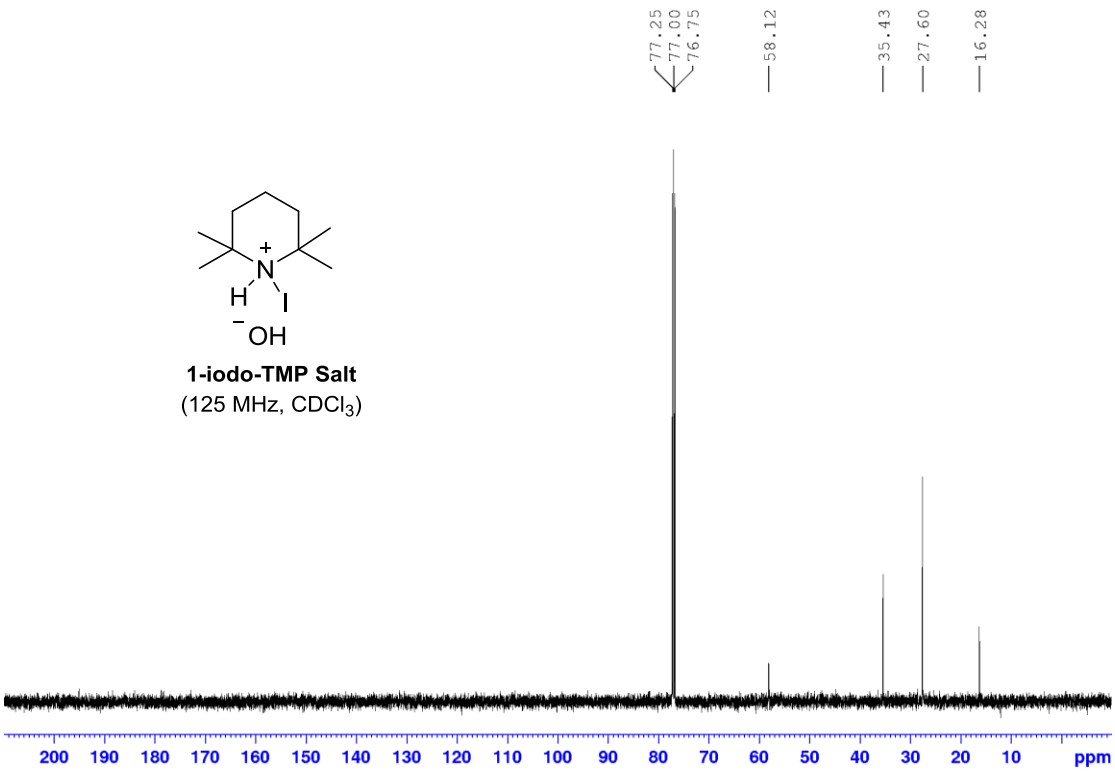
8a
(125 MHz, $CDCl_3$)

Representative NOE of compound **8a**

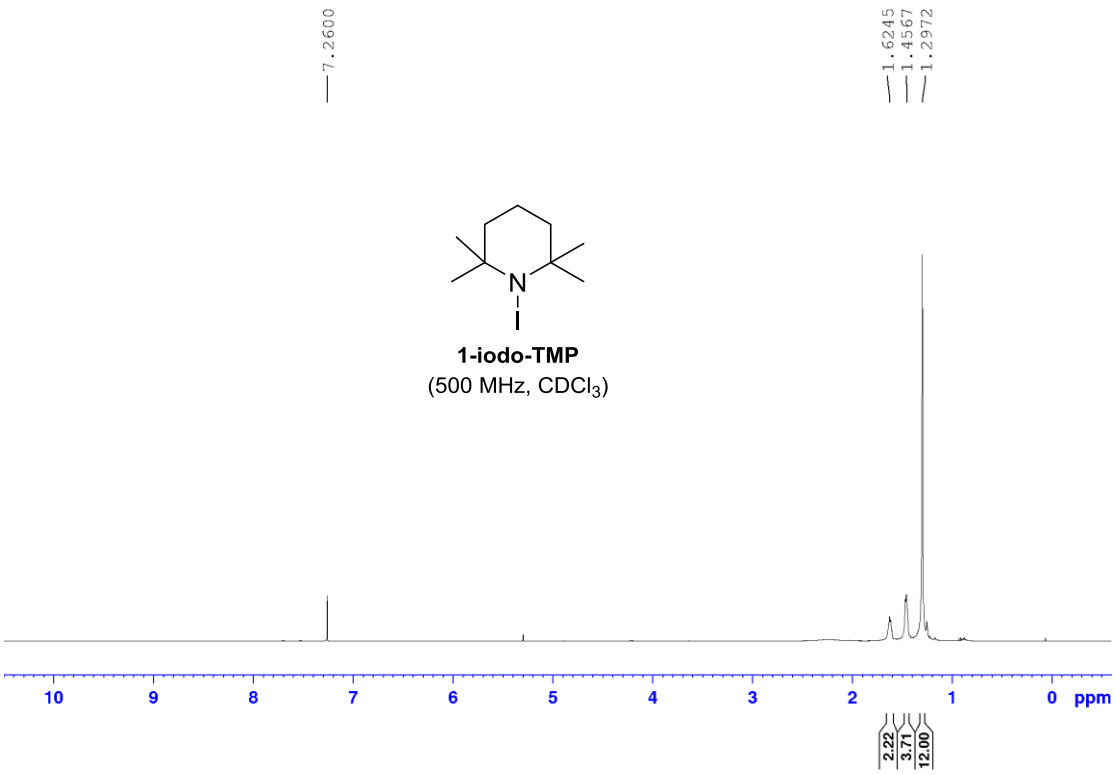




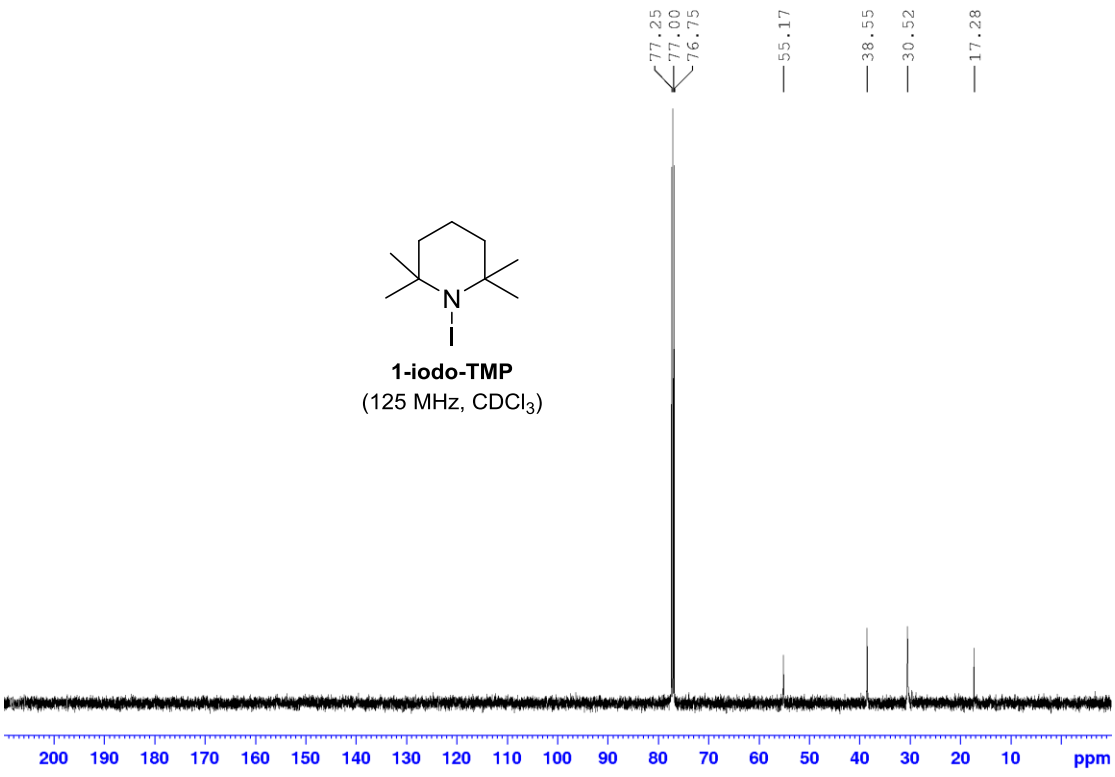
1-iodo-TMP Salt
(500 MHz, $CDCl_3$)



1-iodo-TMP Salt
(125 MHz, $CDCl_3$)



1-iodo-TMP
(500 MHz, $CDCl_3$)



1-iodo-TMP
(125 MHz, $CDCl_3$)