Diastereoselective synthesis of epoxide-fused benzoquinolizidine derivatives using intramolecular domino aza-Michael addition/Darzens reaction

Jiajia Guo, Xiaoyang Sun and Shouyun Yu*

State Key Laboratory of Analytical Chemistry for Life Science, Institute of Chemical Biology and Drug Innovation, School of Chemistry and Chemical Engineering, Nanjing University.

22 Hankou Road, Nanjing 210093, China.

E-mail: yushouyun@nju.edu.cn; Tel: 86-25-83594717

Homepage: http://hysz.nju.edu.cn/yusy/

Electronic Supplementary Information

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1. General methods.

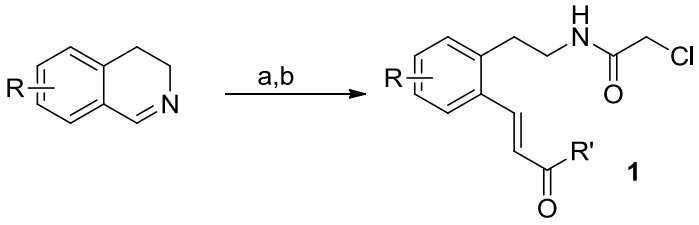
Thin layer chromatography (TLC) was performed on EMD precoated plates (silica gel 60 F254, Art 5715), Optical rotations were recorded on a A212000-T APIV/IW. Column chromatography was performed on Silica Gel 60 (300–400 Mesh) using a forced flow of 0.5–1.0 bar. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) were measured on a Bruker AVANCE Ⅲ–400 spectrometer. Chemical shifts are expressed in parts per million (ppm) with respect to the residual solvent peak. Coupling constants are reported as Hertz (Hz), signal shapes and splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; Infrared (IR) spectra were recorded on a Nicolet 6700 spectrophotometer and are reported as wavenumber (cm^{-1}).

1[1] were prepared according to published literature procedures. 1-(triphenylphosphoranylidene) propan-2-one, $CsOH.H_2O$, 2-chloroacetyl chloride were commercially available. Other Wittig reagents were prepared according to published literature procedures.[2, 3]

1. M. Ihara, T. Kirihara, A. Kawaguchi, K. Fukumoto and T. Kametani, *Tetrahedron Lett.* , 1984, **25**, 4541-4544.
2. E. Ruijter, H. Schültingkemper and L. A. Wessjohann, *J. Org.Chem.*, 2005, **70**, 2820-2823.
3. V. P. Balema, J. W. Wiench, M. Pruski and V. K. Pecharsky, *J. Am. Chem. Soc.* , 2002, **124**, 6244-6245.

2. General procedures and data for compounds

General procedure A : Preparation of amino α,β-unsaturated ketone 1

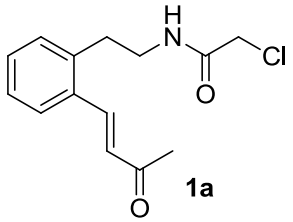


Reaction conditions : a). 2-chloroacetyl chloride, sat.$NaHCO_3$, CH_2Cl_2,0 ^oC ; b). Wittig reagents, toluene, reflux, 3-12h.

To a vigorously stirred mixture of 3,4-dihydroisoquinoline (1.0 mmol, 1.0 equiv), dichloromethane (10 ml), and saturated aqueous sodium hydrogen carbonate (10 ml) was added dropwise a solution of 2-chloroacetyl chloride (124.2 mg, 1.1 mmol, 1.1 equiv) in dichloromethane (2 ml) at 0 ℃, and the mixture was stirred vigorously at 0 ℃ until the reaction was completed, monitoring with TLC . The organic phase was seperated and the aqueous phase was extracted with dichloromethane (5.0 mL × 3). The combined organic phase was washed with brine, dried over Na_2SO_4. The solvent was removed under reduced presure to afford the crude product and the crude mixture purified by flash chromatography with hexanes / ethyl acetate to afford the intermediates.

Intermediate (0.5 mmol, 1.0 equiv) and the Wittig reagent (0.6 mmol, 1.2 equiv) were added to the flask, stirred vigorously at 110 ℃ until the reaction was completed, monitoring with TLC. The mixture was cool to room temperature, without removed the solvent under reduced pressure, the mixture was loaded on silica gel column and purified by flash chromatography (ethyl acetate /hexanes) to afford the pure product **1**.

Data for Compounds Afforded by General Procedure A:



1a

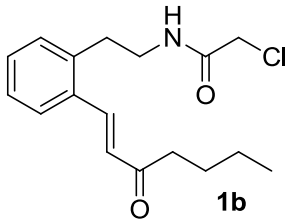
According to general procedure A, **1a** was obtained from 3,4-dihydroisoquinoline as a white solid in 56 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 16.0 Hz, 1H), 7.63 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.36 (td, *J* = 7.2, 1.2 Hz, 1H), 7.31-7.29 (m, 1H), 7.24 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.77 (brs, 1H), 6.68(d, *J* = 16.0 Hz, 1H), 4.03 (s, 2H), 3.53-3.47 (m, 2H), 3.04(t, *J* = 7.4, 2H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 198.64, 166.15, 140.12, 138.21, 133.57, 130.57, 130.51, 129.07, 127.51, 126.86, 42.61, 41.13, 32.93, 27.78.

FTIR (film): ν_{max} 3351, 3065, 2994, 2925, 1657, 1633, 1523, 1482, 1463, 1433, 1359, 974, 759, 675 cm^{-1}.

HRMS (ESI) calcd for $C_{14}H_{16}ClNO_2$ Na $(M+Na)^+$: 288.0767, found: 288.0765.



1b

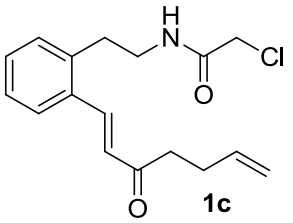
According to general procedure A, **1b** was obtained from 3,4-dihydroisoquinoline as a blue solid in 49 % yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 16.0 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.36 (td, *J* = 7.2, 1.2 Hz, 1H), 7.31-7.28 (m, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 6.72 (brs, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 4.02 (s, 1H), 3.54-3.49 (m, 2H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.73-2.69 (m, 2H), 1.72-1.64 (m, 2H), 1.43-1.36 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 200.63, 166.01, 138.86, 138.32, 133.67, 130.56, 130.35, 128.09, 127.42, 126.80, 42.61, 41.05, 40.97, 32.80, 26.45, 22.44, 13.93.

FTIR (film): ν_{max} 3352, 3022, 2954, 2919, 2868, 1645, 1524, 1482, 1435, 1376, 1183, 985, 779, 751 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{22}ClNNaO_2$ $(M+Na)^+$: 330.1237, found: 330.1240.



1c

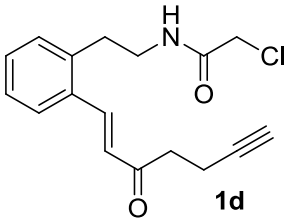
According to general procedure A, **1c** was obtained from 3,4-dihydroisoquinoline as a blue solid in 50 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 16.0 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.35 (td, *J* = 7.2, 1.2 Hz, 1H), 7.31-7.28 (m, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.72 (brs, 1H), 5.93-5.86 (m, 1H), 5.10 (dd, *J* = 16.8, 1.6 Hz, 1H), 5.02 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.02 (s, 2H), 3.54 - 3.49 (m, 2H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.83 (t, *J* = 7.4 Hz, 2H), 2.48-2.43 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): *δ* =199.50, 166.00, 139.14, 138.37, 137.25, 133.61, 130.59, 130.45, 128.02, 127.44, 126.83, 115.30, 42.62, 41.00, 40.25, 32.82, 28.17.

FTIR (film): ν_{max} 3369, 2999, 2943, 2919, 1664, 1647, 1639, 1519, 1482, 1431, 1182, 978, 925, 753, 674 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{20}ClNNaO_2$ $(M+Na)^+$: 328.1080, found: 328.1077



1d

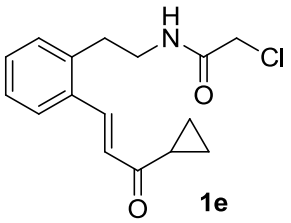
According to general procedure A, **1d** was obtained from 3,4-dihydroisoquinoline as a light blue solid in 42 % yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (d, *J* = 16.0 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.72 (brs, 1H), 4.02 (s, 2H), 3.50 (dd, *J* = 14.0, 6.8 Hz, 2H), 3.03 (t, *J* = 7.4 Hz, 2H), 2.98 (t, *J* = 7.2 Hz, 2H), 2.60-2.55 (m, 2H), 1.99 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 197.86, 166.14, 139.77, 138.54, 133.51, 130.69, 127.64, 127.55, 126.92, 83.38, 68.88, 42.70, 41.11, 39.77, 32.90, 13.33.

FTIR (film): ν_{max} 3317, 3280, 3022, 2961, 2915, 2846, 2117, 1686, 1645, 1605, 1536, 1481, 1364, 981, 775, 753 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{18}ClNNaO_2$ $(M+Na)^+$: 326.0924, found: 326.0922.



1e

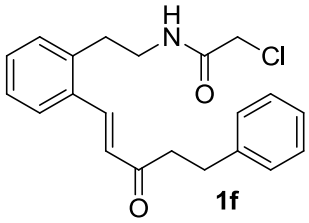
According to general procedure A, **1e** was obtained from 3,4-dihydroisoquinoline as a blue oil in 77% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 16.0 Hz, 1H), 7.67-7.65 (m, 1H), 7.36 (td, *J* = 7.2, 1.2 Hz, 1H), 7.29 (td, *J* = 7.2, 1.2 Hz, 1H), 7.24 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.70 (brs, 1H), 4.01 (s, 2H), 3.54-3.49 (m, 2H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.33-2.29 (m, 1H), 1.19-1.16 (m, 2H), 1.03-0.97 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 200.13, 166.05, 138.62, 138.43, 133.81, 130.60, 130.37, 128.36, 127.44, 126.82, 42.61, 41.04, 32.81, 19.88, 11.61.

FTIR (film): ν_{max} 3347, 3068, 3012, 2956, 1658, 1634, 1598, 1519, 1482, 1440, 1403, 977, 764 cm^{-1}.

HRMS (ESI) calcd for $C_{16}H_{18}ClNNaO_2$ $(M+Na)^+$: 314.0924, found: 314.0920.



1f

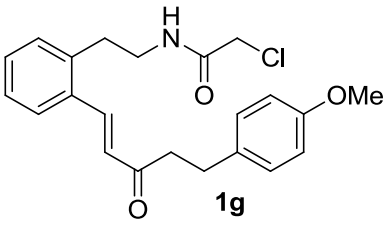
According to general procedure A, **1f** was obtained from 3,4-dihydroisoquinoline as a blue solid in 40% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 15.6 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.35 (td, *J* = 7.2, 1.2 Hz, 1H), 7.31-7.26 (m, 4H), 7.25-7.20 (m, 3H), 6.69 (d, *J* = 16.0 Hz, 1H), 6.62 (brs, 1H), 3.99 (s, 2H), 3.50-3.46 (m, 2H), 3.05-2.99 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.42, 166.06, 141.26, 139.34, 138.43, 133.66, 130.64, 130.53, 128.55, 128.14, 127.51, 126.90, 126.18, 42.67, 41.08, 32.87, 30.22.

FTIR (film): ν_{max} 3344, 2951, 2927, 2868, 1679, 1644, 1608, 1597, 1538, 1485, 1360, 980, 765, 753 cm^{-1}.

HRMS (ESI) calcd for $C_{21}H_{23}ClNO_2$ $(M+H)^+$: 356.1417, found: 356.1417.



1g

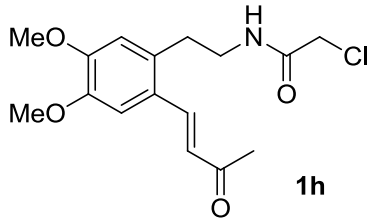
According to general procedure A, **1g** was obtained from 3,4-dihydroisoquinoline as a yellow solid in 43 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 15.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.77 (brs, 1H), 6.69 (d, *J* = 16.0 Hz, 1H), 3.99 (s, 2H), 3.78 (s, 3H), 3.49 (dd, *J* = 14.0, 6.8 Hz, 2H), 3.05-2.95 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.62, 166.09, 158.00, 139.28, 138.42, 133.59, 133.22, 130.58, 130.47, 129.42, 128.08, 127.43, 126.81, 113.92, 55.28, 42.88, 42.62, 41.04, 32.79, 29.33.

FTIR (film): ν_{max} 3337, 3012, 3000, 2919, 1678, 1670, 1647, 1608, 1596, 1541, 1512, 1436, 1361, 983, 754 cm^{-1}.

HRMS (ESI) calcd for $C_{22}H_{24}ClNNaO_3$ $(M+Na)^+$: 408.1342, found: 408.1337.



1h

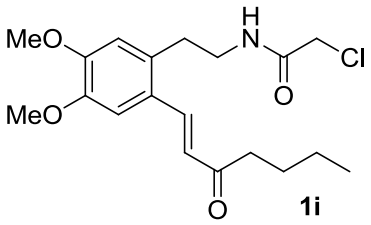
According to general procedure A, **1h** was obtained from 6,7-dimethoxy-3,4-dihydroisoquinoline as a white solid in 66 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 16.0 Hz, 1H), 7.12 (s, 1H), 6.71 (brs, 1H), 6.71 (s, 1H), 6.60 (d, *J* = 16.0 Hz, 1H), 4.04 (s, 2H), 3.91 (s, 6H), 3.49 (dd, *J* = 13.6, 6.8 Hz, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.43 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.54, 166.09, 151.31, 148.29, 139.73, 132.30, 126.76, 125.54, 113.01, 108.87, 56.06, 56.03, 42.66, 41.41, 32.53, 27.69.

FTIR (film): ν_{max} 3300, 3059, 2958, 2929, 2829, 1677, 1625, 1597, 1510, 1455, 1438, 1360, 974, 756 cm^{-1}.

HRMS (ESI) calcd for $C_{16}H_{20}ClNNaO_4$ $(M+Na)^+$: 348.0979, found: 348.0980.



1i

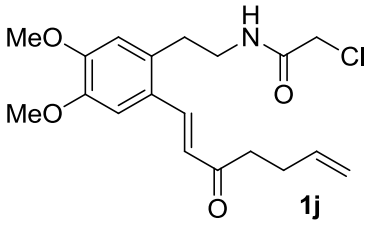
According to general procedure A, **1i** was obtained from 6,7-dimethoxy-3,4-dihydroisoquinoline as a yellow solid in 47 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 16.0 Hz, 1H), 7.09 (s, 1H), 6.73 (brs, 1H), 6.68 (s, 1H), 6.59 (d, *J* = 16.0 Hz, 1H), 3.99 (s, 2H), 3.88 (s, 3H), 3.88 (s, 3H), 3.46 (dd, *J* = 13.6, 6.8 Hz, 2H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 7.4 Hz, 2H), 1.68-1.60 (m, 2H), 1.41-1.32 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.69, 166.06, 151.24, 148.23, 138.61, 132.51, 125.79, 125.63, 113.08, 108.89, 56.06, 42.69, 41.31, 40.90, 32.45, 26.64, 22.53, 13.99.

FTIR (film): ν_{max} 3349, 2958, 2932, 2868, 1653, 1644, 1599, 1510, 1462, 1436, 1355, 979, 750 cm^{-1}.

HRMS (ESI) calcd for $C_{19}H_{26}ClNNaO_4$ $(M+Na)^+$: 390.1448, found: 390.1444.



1j

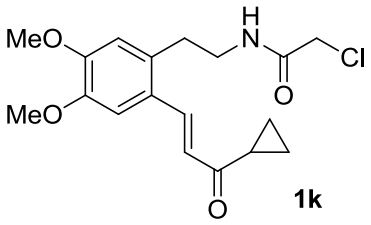
According to general procedure A, **1j** was obtained from 6,7-dimethoxy-3,4-dihydroisoquinoline as a white solid in 64 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 15.6 Hz, 1H), 7.10 (s, 1H), 6.69 (s, 1H), 6.69(brs, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 5.91-5.84 (m, 1H), 5.08 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.00 (d, *J* = 9.2 Hz, 1H), 4.01 (s, 2H), 3.90 (s, 3H), 3.90 (s, 3H), 3.48 (dd, *J* = 13.2, 6.8 Hz, 2H), 2.98 (t, *J* = 7.2 Hz, 2H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.46-2.41 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.57, 166.08, 151.36, 148.31, 138.90, 137.44, 132.60, 125.69, 125.59, 115.34, 113.12, 108.92, 56.12, 42.74, 41.38, 40.21, 32.52, 28.37.

FTIR (film): ν_{max} 3361, 3007, 2949, 2832, 1647, 1637, 1633, 1518, 1514, 1458, 1353, 978, 926, 749 cm^{-1}.

HRMS (ESI) calcd for $C_{19}H_{24}ClNNaO_4$ $(M+Na)^+$: 388.1292, found: 388.1290.



1k

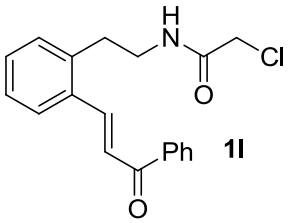
According to general procedure A, **1k** was obtained from 6,7-dimethoxy-3,4-dihydroisoquinoline as a light yellow solid in 63 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 15.6 Hz, 1H), 7.15 (s, 1H), 6.76 (d, *J* = 15.6 Hz, 1H), 6.71 (s, 1H), 6.69 (brs, 1H), 4.02 (s, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 3.50 (q , *J* = 6.8 Hz, 2H), 3.00 (t, *J* = 7.0 Hz, 2H), 2.33-2.28(m, 1H), 1.18-1.16 (m, 2H), 1.01-0.98 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.06, 166.03, 151.21, 148.22, 138.29, 132.54, 126.12, 125.75, 113.04, 108.87, 56.04, 42.65, 41.33, 32.43, 19.69, 11.48.

FTIR (film): ν_{max} 3359, 3073, 3000, 2956, 2861, 2827, 1658, 1632, 1598, 1513, 1464, 1438, 1324, 973, 750 cm^{-1}.

HRMS (ESI) calcd for $C_{18}H_{22}ClNNaO_4$ $(M+Na)^+$: 374.1135, found: 374.1135.



1l

According to general procedure A, **1l** was obtained from 3,4-dihydroisoquinoline as a white solid in 65% yield.

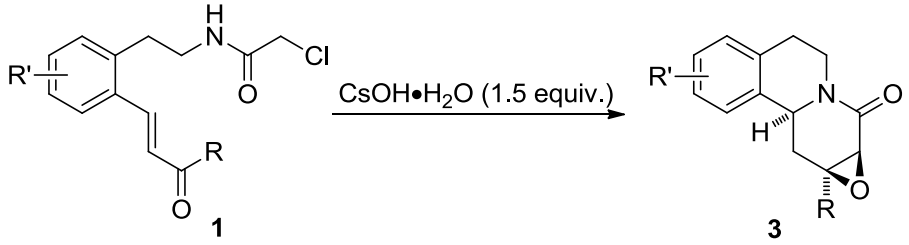
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 15.6 Hz, 1H), 8.05 (s, 1H), 8.03 (t, *J* = 1.6 Hz, 1H), 7.75 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.61 - 7.57 (m, 1H), 7.55 - 7.49 (m, 3H), 7.38 (td, *J* = 7.2, 1.2 Hz, 1H), 7.32 (td, *J* = 7.4, 1.2 Hz, 1H), 7.27 - 7.25 (m, 1H), 6.73 (brs, 1H), 4.01 (s, 2H), 3.54 (dd, *J* = 13.2, 6.8 Hz, 2H), 3.06 (t, *J* = 7.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.99, 165.99, 141.36, 138.76, 138.02, 133.91, 133.03, 130.74, 130.62, 128.72, 128.55, 127.43, 126.90, 123.80, 42.66, 40.92, 32.79.

FTIR (film): ν_{max} 3303, 2920, 2849, 1656, 1605, 1594, 1571, 1556，1481, 1447, 1331, 1214，1016，968, 749 cm^{-1}.

HRMS (ESI) calcd for $C_{19}H_{18}ClNNaO_2$ $(M+Na)^+$: 350.0924, found: 350.0922.

Preparation of expoxide-fused benzoquinolizidine 3



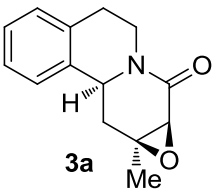
General procedure B:

To a solution of amino α,β-unsaturated ketone 1 (0.1 mmol, 1.0 equiv) in 1,4-dioxane (0.1M), the $CsOH.H_2O$ were added. The resulting solution was stirred for 2-4 h at room temperature until the reaction was completed, monitoring with TLC and then, solvent was removed under reduced presure , the crude mixture purified by flash chromatography with hexanes / ethyl acetate as eluents.

General procedure C:

To a solution of amino α,β-unsaturated ketone 1 (0.1 mmol, 1.0 equiv) in 1,4-dioxane:THF = 2:1 mixed solvent (0.1M) at 0 ℃, the $CsOH.H_2O$ were added quickly. The resulting solution was stirred overnight at 0 ℃ (TLC) and then, solvents were removed under reduced pressure, the crude mixture purified by flash chromatography with hexanes / ethyl acetate as eluents.

Data for Compounds Afforded by General Procedure B and C



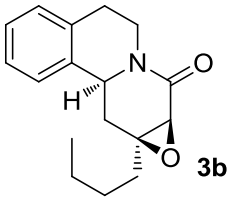
According to general procedure B, **3a** was obtained from **1a** as a white solid in 80 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.10 (m, 4H), 4.70 (t, J = 5.4 Hz, 1H), 4.66-4.56 (m, 1H), 3.20 (s, 1H), 3.09-3.01 (m, 2H), 2.76 (td, J = 11.8, 3.2 Hz, 1H), 2.70 (dd, J = 15.2, 4.8 Hz, 1H), 2.46 (dd, J = 15.2, 6.4 Hz, 1H), 1.52 (s, 3H).

^{13}C NMR (100MHz, $CDCl_3$): δ =167.62, 137.63, 134.22, 129.09, 126.87, 126.43, 123.52, 59.37, 55.65, 53.79, 41.75, 32.49, 28.31, 21.73.

FTIR (film): ν_{max} 2977, 2964, 2919, 2853, 1644, 1492, 1474, 1429, 1296, 1264, 859, 790, 752 cm^{-1}.

HRMS (ESI) calcd for $C_{14}H_{15}NNaO_2$ $(M+Na)^+$: 252.1000, found: 252.0998.



3b

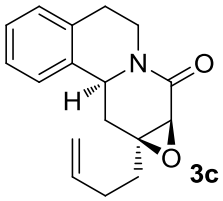
According to general procedure B, **3b** was obtained from **1b** as a white solid in 64 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.11 (m, 4H), 4.71 (t, *J* = 5.8 Hz, 1H), 4.62-4.59 (m, 1H), 3.21 (s, 1H), 3.07-2.99 (m, 1H), 2.77-2.73 (m, 1H), 2.63 (dd, *J* = 15.2, 5.6 Hz, 1H), 2.47 (dd, *J* = 15.2, 6.4 Hz, 1H), 1.76-1.70 (m, 2H), 1.48-1.32 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.77, 137.56, 134.25, 129.07, 126.87, 126.46, 123.65, 62.06, 54.64, 53.96, 41.50, 35.01, 31.41, 28.40, 26.54, 22.66, 13.96.

FTIR (film): ν_{max} 2949, 2920, 2851, 1658, 1493, 1461, 1376, 1255, 1160, 809, 751 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{22}NO_2$ $(M+H)^+$: 272.1651, found: 272.1655.



3c

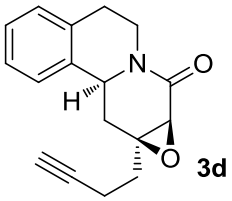
According to general procedure B, **3c** was obtained from **1c** as a white oil in 56 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.24-7.11 (m, 4H), 5.87-5.80 (m, 1H), 5.10 (dd, *J* =17.2, 1.2 Hz, 1H), 5.04 (dd, *J* =10.4, 1.2 Hz, 1H), 4.72 (t, *J* = 5.6 Hz, 1H), 4.63-4.60 (m, 1H), 3.23 (s, 1H), 3.07-2.99 (m, 2H), 2.79-2.73 (m, 1H), 2.65 (dd, *J* = 15.2, 5.4 Hz, 1H), 2.51-2.46 (m, 1H), 2.25 (dd, *J* = 14.4, 7.4 Hz, 2H), 1.88-1.83 (m, 2H).

^{13}C NMR (100MHz, $CDCl_3$): *δ* = 167.68, 137.56, 137.25, 134.34, 129.19, 127.00, 126.57, 123.78, 115.82, 61.78, 54.75, 53.98, 41.63, 34.59, 31.56, 28.78, 28.49.

FTIR (film): ν_{max} 3067, 2922, 2845, 1653, 1649, 1468, 1434, 1258, 1096, 1013, 914, 861, 796, 755 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{20}NO_2$ $(M+H)^+$: 270.1494, found: 270.1497.



3d

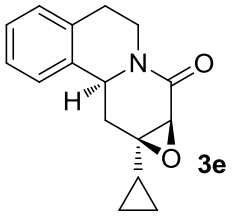
According to general procedure C, **3d** was obtained from **1d** as a white solid in 40 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23-7.12 (m, 4H), 4.78 (t, *J* = 5.8 Hz, 1H), 4.64-4.62 (m, 1H), 3.33 (s, 1H), 3.04-3.01 (m, 2H), 2.77-2.66 (m, 2H), 2.56 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.42-2.36 (m, 2H), 2.06-2.01 (m, 2H), 1.99-1.94 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.28, 137.30, 134.29, 129.14, 126.98, 126.53, 123.81, 82.81, 69.95, 61.13, 54.70, 53.97, 41.46, 33.95, 31.68, 28.44, 14.10.

FTIR (film): ν_{max} 3280, 3027, 2923, 2851, 2121, 1708, 1645, 1606, 1536, 1429, 1364, 1287, 1167, 1094, 981, 861, 754 cm^{-1}.

HRMS (ESI) calcd for $C_{17}H_{18}NO_2$ $(M+H)^+$: 268.1338, found: 268.1338.



3e

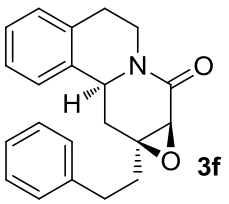
According to general procedure B, **3e** was obtained from **1e** as a white solid in 72 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22-7.09 (m, 4H), 4.71 (t, *J* = 5.4 Hz, 1H), 4.62-4.58 (m, 1H), 3.13 (s, 1H), 3.06-3.01 (m, 2H), 2.76-2.70 (m, 2H), 2.57 (dd, *J* = 15.2, 6.4 Hz, 1H), 1.29-1.25 (m, 1H), 0.59-0.57 (m, 1H), 0.46-0.32 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.56, 137.84, 134.28, 129.12, 126.95, 126.52, 123.49, 61.78, 54.42, 53.91, 41.81, 31.65, 28.38, 14.08, 1.98, 0.68.

FTIR (film): ν_{max} 3083, 3005, 2924, 2846, 1641, 1462, 1434, 1359, 1287, 1246, 1029, 861, 754 cm^{-1}.

HRMS (ESI) calcd for $C_{16}H_{18}NO_2$ $(M+H)^+$: 256.1338, found: 256.1337.



3f

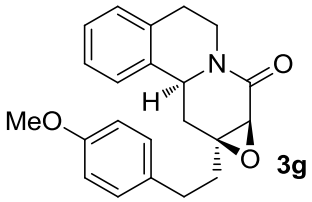
According to general procedure C, **3f** was obtained from **1f** as a white solid in 55 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t, *J* = 7.6 Hz, 2H), 7.25-7.17 (m, 5H), 7.10 (dd, *J* = 17.6, 7.2 Hz, 2H), 4.69 (t, *J* = 5.8 Hz, 1H), 4.63-4.60 (m, 1H), 3.24 (s, 1H), 3.05-2.98 (m, 2H), 2.82-2.73 (m, 3H), 2.64 (dd, *J* = 15.2, 5.6 Hz, 1H), 2.47 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.09 (t, *J* = 8.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.49, 140.61, 137.39, 134.23, 129.09, 128.68, 128.30, 126.91, 126.47, 126.39, 123.67, 61.74, 54.63, 53.88, 41.51, 36.91, 31.67, 30.64, 28.38.

FTIR (film): ν_{max} 3063, 3027, 2924, 2851, 1691, 1649, 1603, 1511, 1467, 1439, 1245, 1029, 795, 753 cm^{-1}.

HRMS (ESI) calcd for $C_{21}H_{22}NO_2$ $(M+H)^+$: 320.1651, found: 320.1651.



3g

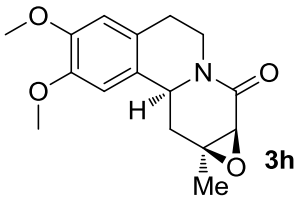
According to general procedure B, **3g** was obtained from **1g** as a yellow oil in 52 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.07 (m, 6 H), 6.86 (d, *J* = 7.6 Hz, 2H), 4.69 (s, 1H), 4.61 (d, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.24 (s, 1H), 3.04-2.99 (m, 2H), 2.76-2.61 (m, 4H), 2.49-2.45 (m, 1H), 2.05 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.55, 158.13, 137.40, 134.21, 132.59, 129.22, 129.09, 126.90, 126.45, 123.67, 114.06, 61.79, 55.31, 54.62, 53.86, 41.53, 37.11, 31.57, 29.76, 28.36.

FTIR (film): ν_{max} 2993, 2927, 2844, 1651, 1611, 1511, 1495, 1431, 1366, 1334, 1245, 1174, 1104, 1031, 841, 819, 769, 756 cm^{-1}.

HRMS (ESI) calcd for $C_{22}H_{24}NO_3$ $(M+H)^+$: 350.1756, found: 350.1756 .



3h

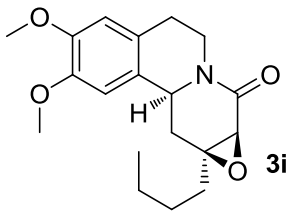
According to general procedure B, **3h** was obtained from **1h** as a white solid in 61 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (s, 1H), 6.61 (s, 1H), 4.71-4.64 (m, 2H), 3.89 (s, 3H), 3.84 (s, 3H), 3.20 (s, 1H), 2.98-2.94 (m, 2H), 2.66-2.62 (m, 1H), 2.54 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.44 (dd, *J* = 15.2, 6.0 Hz, 1H), 1.53 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.85, 148.11, 147.77, 129.27, 126.70, 112.12, 107.71, 59.29, 56.44, 56.08, 55.63, 53.96, 41.73, 34.01, 28.21, 22.08.

FTIR (film): ν_{max} 2961, 2919, 2849, 1656, 1633, 1513, 1462, 1441, 1257, 1116, 1082, 1015, 858, 811, 786 cm^{-1}.

HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ $(M+H)^+$: 290.1392, found: 290.1392 .



3i

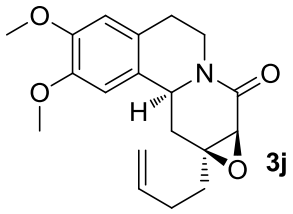
According to general procedure C, **3i** was obtained from **1i** as a white solid in 52 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (s, 2H), 4.70-4.64 (m, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.21 (s, 1H), 2.97-2.95 (m, 2H), 2.66-2.63 (m, 1H), 2.51-2.41 (m, 2H), 1.76-1.72 (m, 2H), 1.49 -1.36 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.88, 147.92, 147.57, 129.20, 126.50, 111.90, 107.44, 61.92, 56.24, 55.94, 54.57, 53.90, 41.54, 35.04, 32.25, 28.09, 26.58, 22.65, 14.01.

FTIR (film): ν_{max} 2956, 2927, 2854, 1655, 1601, 1512, 1463, 1439, 1358, 1254, 1228, 1209, 1118, 1024, 994, 855, 755 cm^{-1}.

HRMS (ESI) calcd for $C_{19}H_{26}NO_4$ $(M+H)^+$: 332.1862, found: 332.1860.



3j

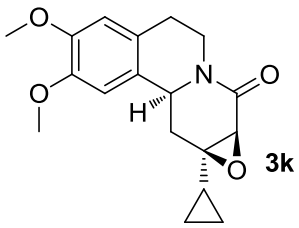
According to general procedure C, **3j** was obtained from **1j** as a white oil in 57 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (s, 1H), 6.60 (s, 1H), 5.89-5.82 (m, 1H), 5.11 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.04 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.71-4.63 (m, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.23 (s, 1H), 2,98-2.91 (m, 2H), 2.66-2.63 (m, 1H), 2.53 (dd, *J* = 15.2, 6.4 Hz, 1H), 2.46 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.29-2.23 (m, 2H), 1.88-1.85 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.65, 148.01, 147.67, 137.20, 129.08, 126.58, 115.73, 111.99, 107.63, 61.53, 56.31, 55.96, 54.57, 53.88, 41.48, 34.60, 32.52, 28.64, 28.10.

FTIR (film): ν_{max} 3073, 2995, 2924, 2844, 1655, 1649, 1611, 1513, 1463, 1438, 1357, 1256, 1227, 1209, 1117, 1026, 996, 914, 858, 814, 754 cm^{-1}.

HRMS (ESI) calcd for$C_{19}H_{24}NO_4$ $(M+H)^+$: 330.1705, found: 330.1707.



3k

According to general procedure B, **3k** was obtained from **1k** as a white oil in 80 % yield.

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 6.61 (s, 1H), 6.60 (s, 1H), 4.70 (t, *J* = 5.8 Hz, 1H), 4.65-4.63 (m, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.14 (s, 1H), 3.01-2.95 (m, 2H), 2.66-2.57 (m, 2H), 1.31-1.26 (m, 1H), 0.60-0.58 (m, 1H), 0.47-0.45 (m, 1H), 0.39-0.33 (m, 2H);

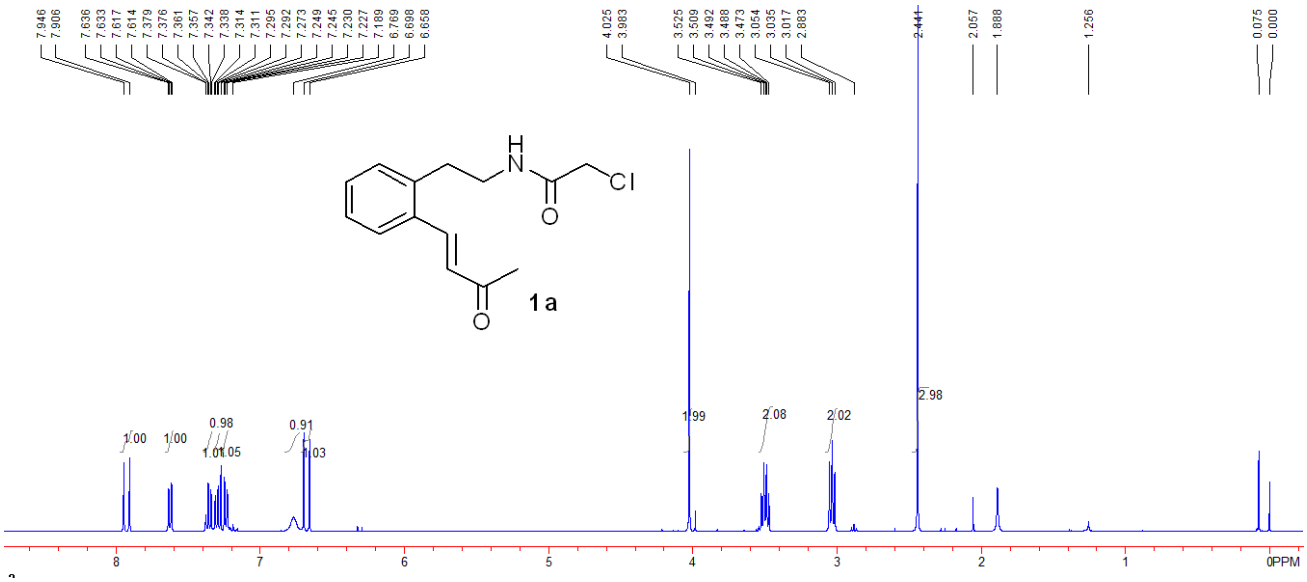
^{13}C NMR (100 MHz, $CDCl_3$) : δ = 167.68, 148.05, 147.69, 129.49, 126.55, 112.07, 107.49, 61.56, 56.37, 56.04, 54.36, 53.94, 41.82, 32.88, 28.12, 14.22, 2.01, 0.66;

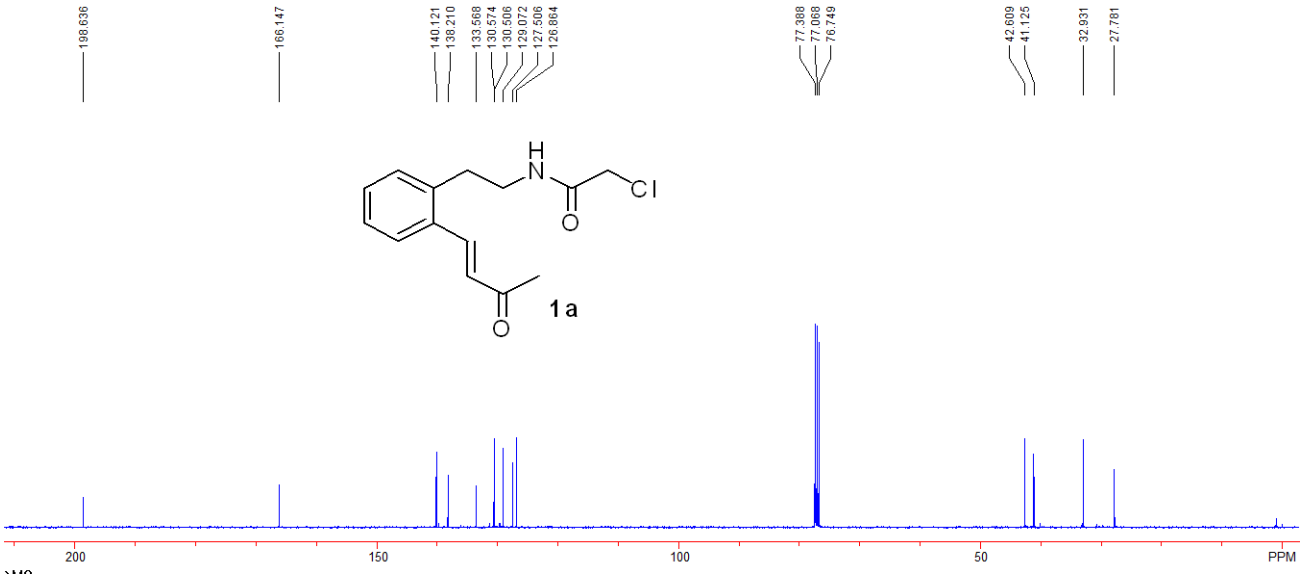
FTIR (film): ν_{max} 3007, 2954, 2922, 2841, 1649, 1513, 1462, 1440, 1355, 1257, 1227, 1204, 1117, 1021, 855, 808, 755 cm^{-1};

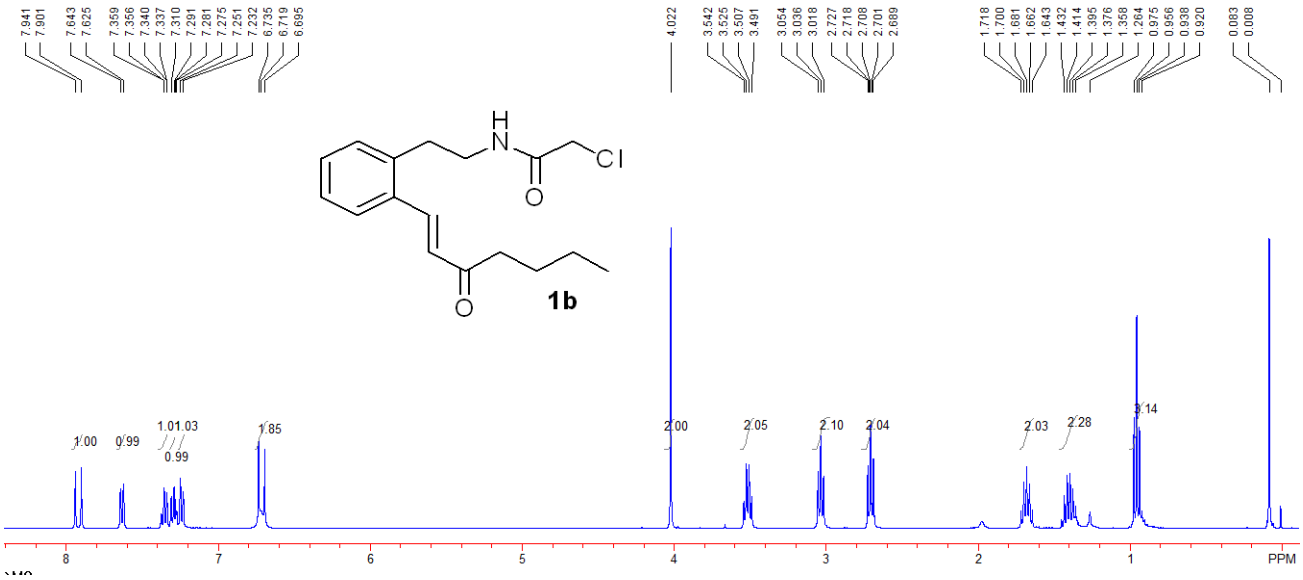
HRMS (ESI) calcd for $C_{18}H_{22}NO_4$ $(M+H)^+$: 316.1549, found: 316.1552.

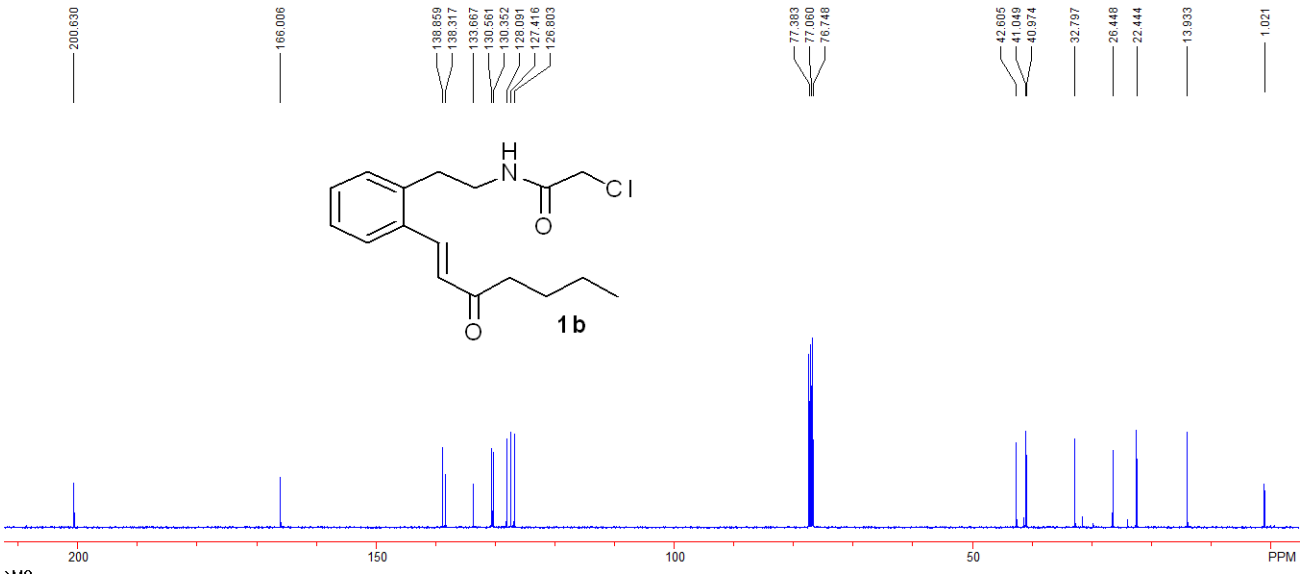
3. ^{1}H NMR and ^{13}C NMR Spectra

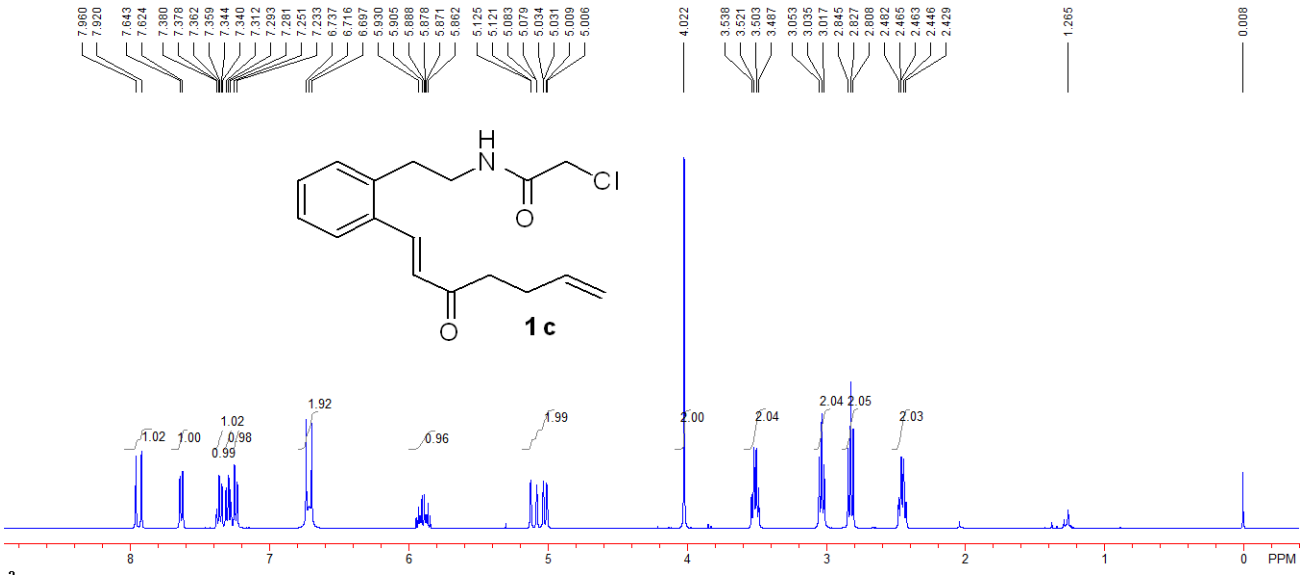
NMR Spectra for Compounds Afforded by General Procedure A:

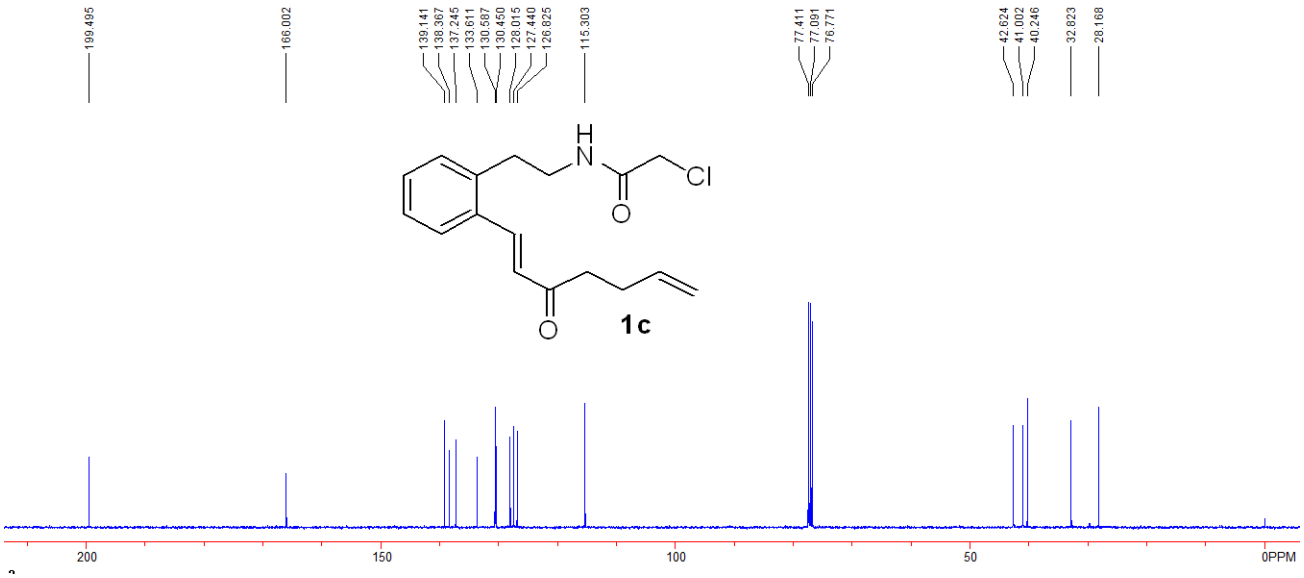


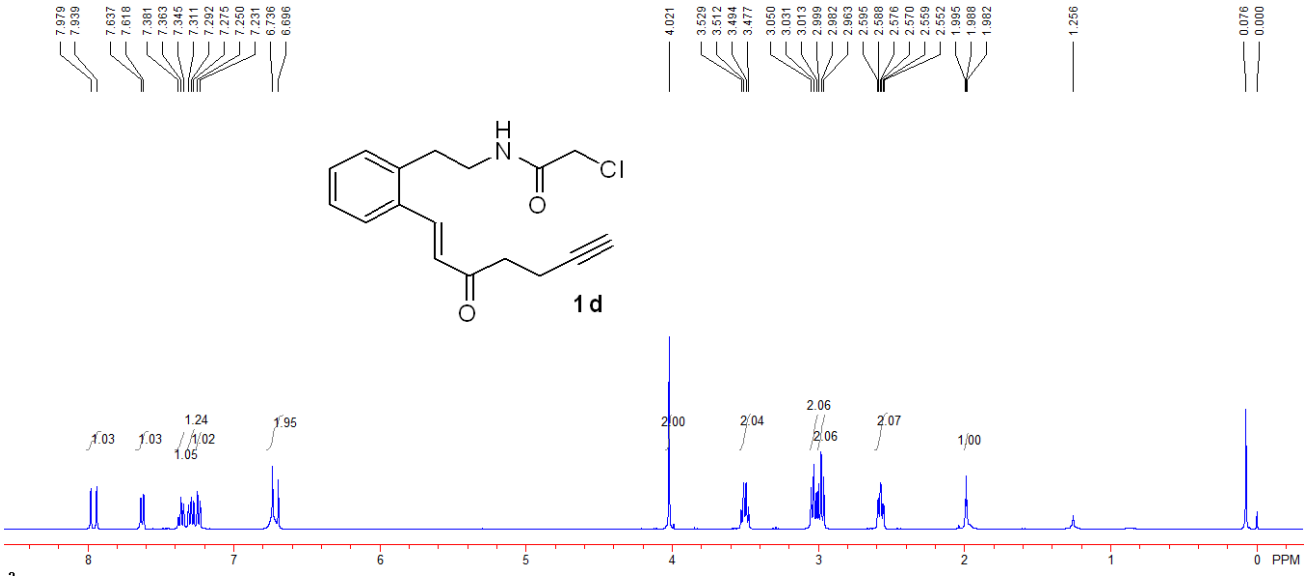


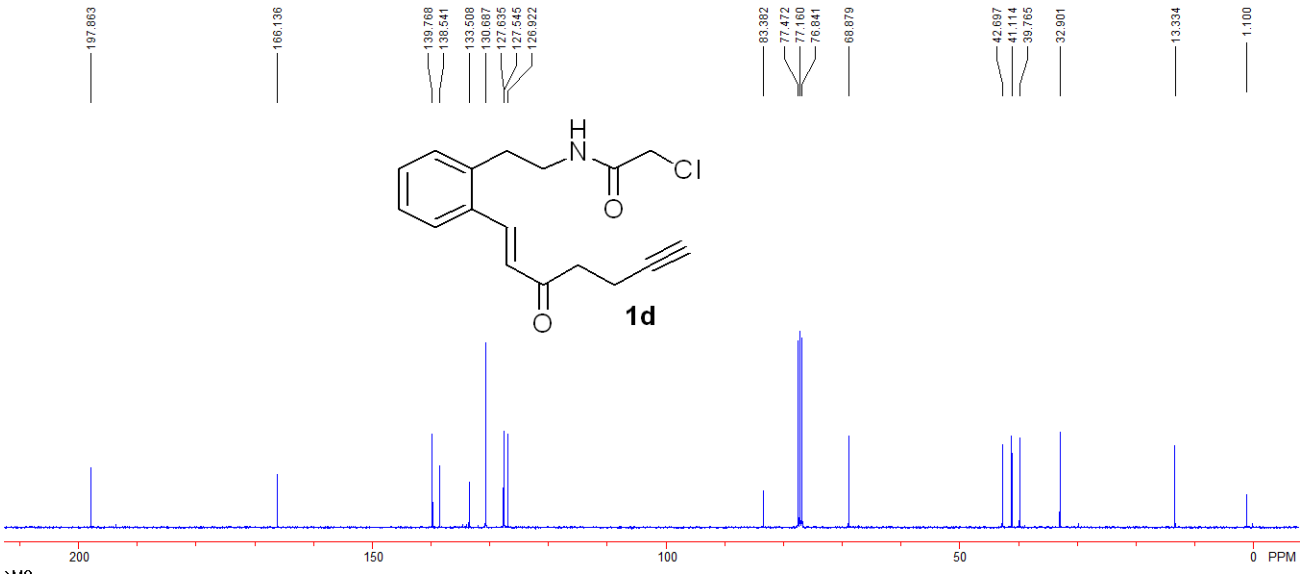


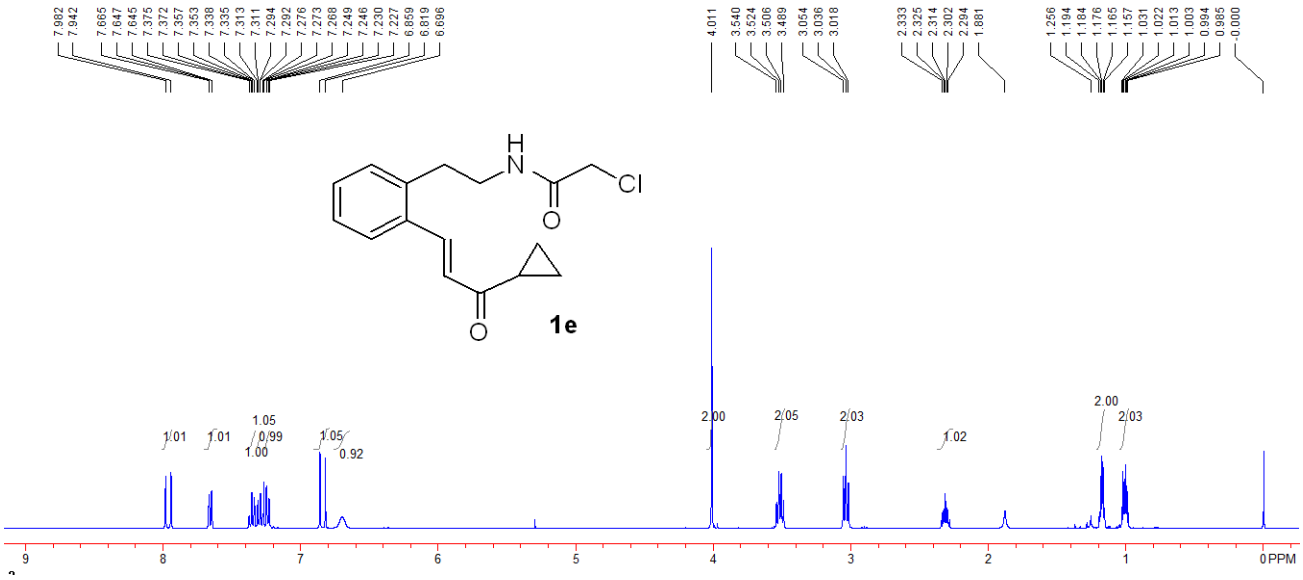








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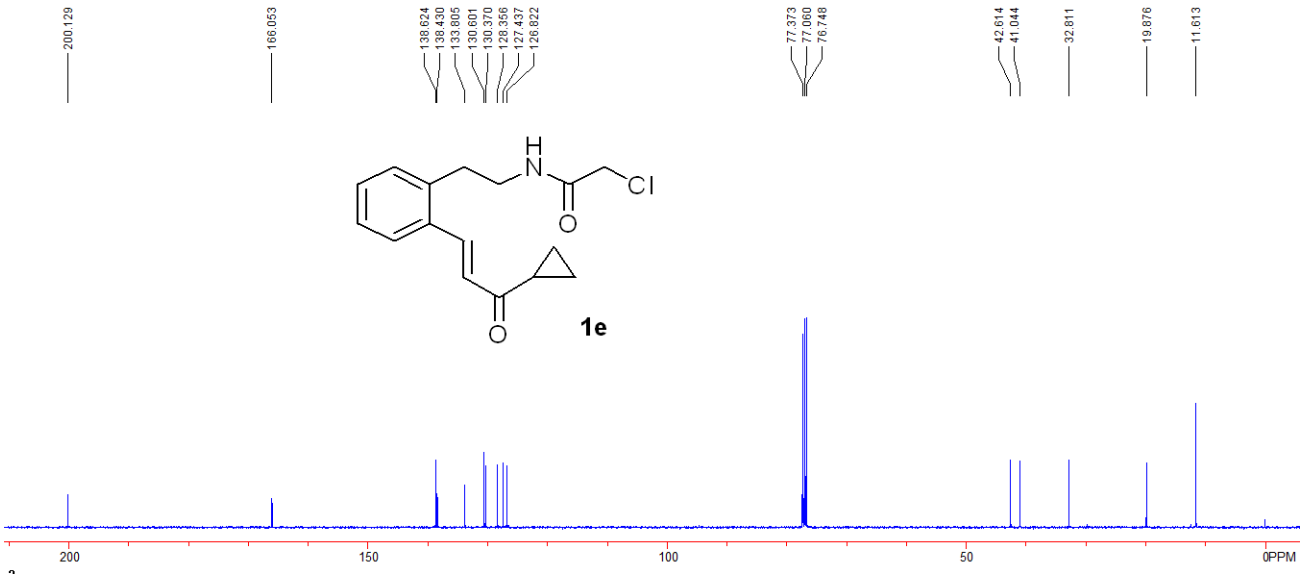
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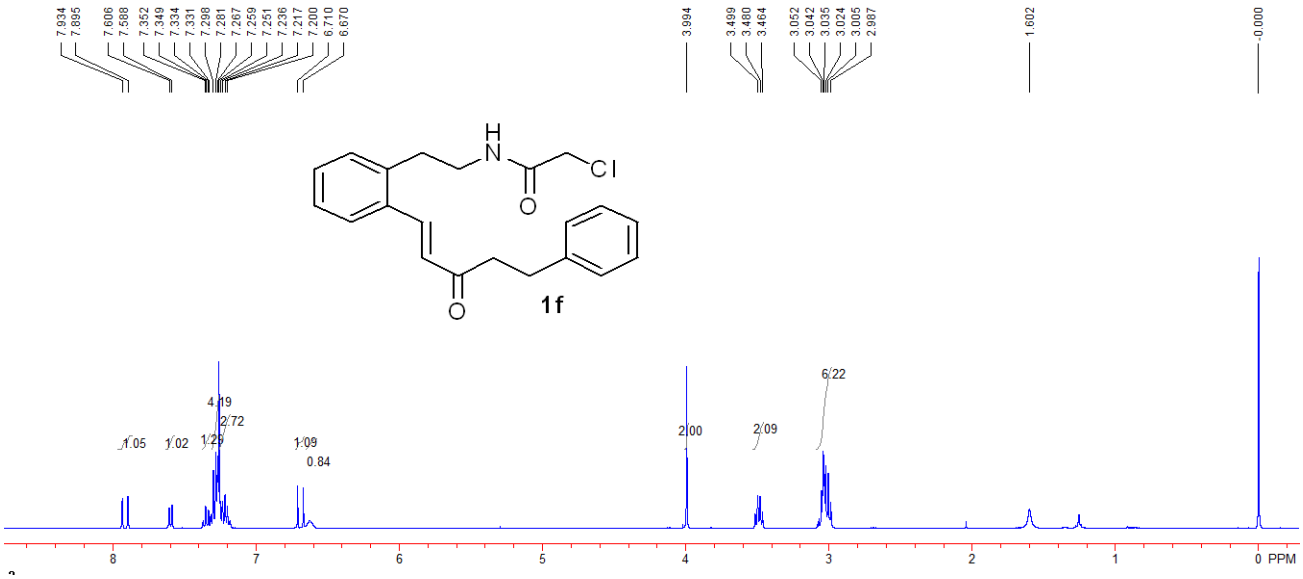

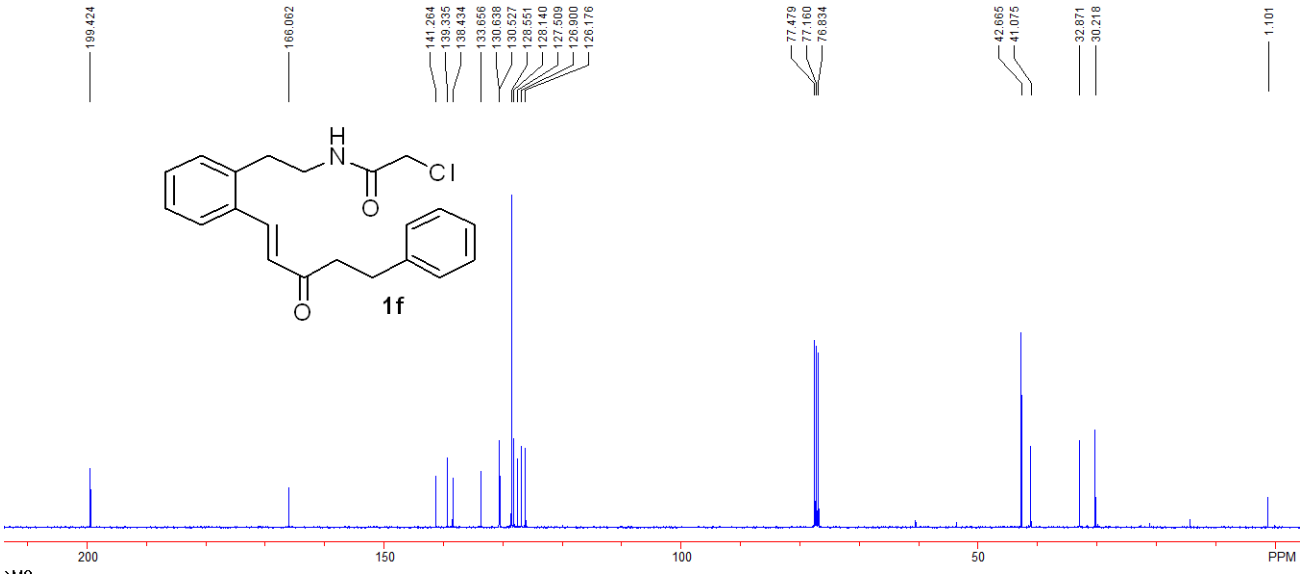

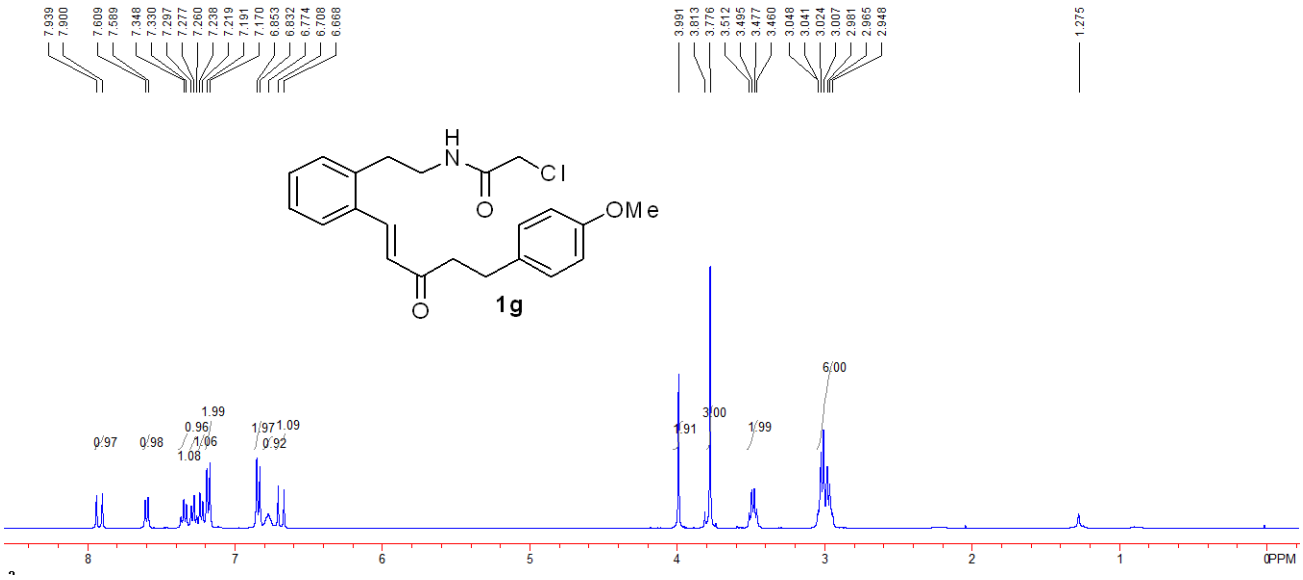
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7.238
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7.191
7.170
6.853
6.832
6.774
6.708
6.668
3.991
3.813
3.776
3.512
3.495
3.477
3.460
3.048
3.041
3.024
3.007
2.981
2.965
2.948
1.275
H
N
Cl
O
OMe
O
1g
0.97
0.98
1.99
0.96
1.06
1.08
1.97
1.09
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6.00
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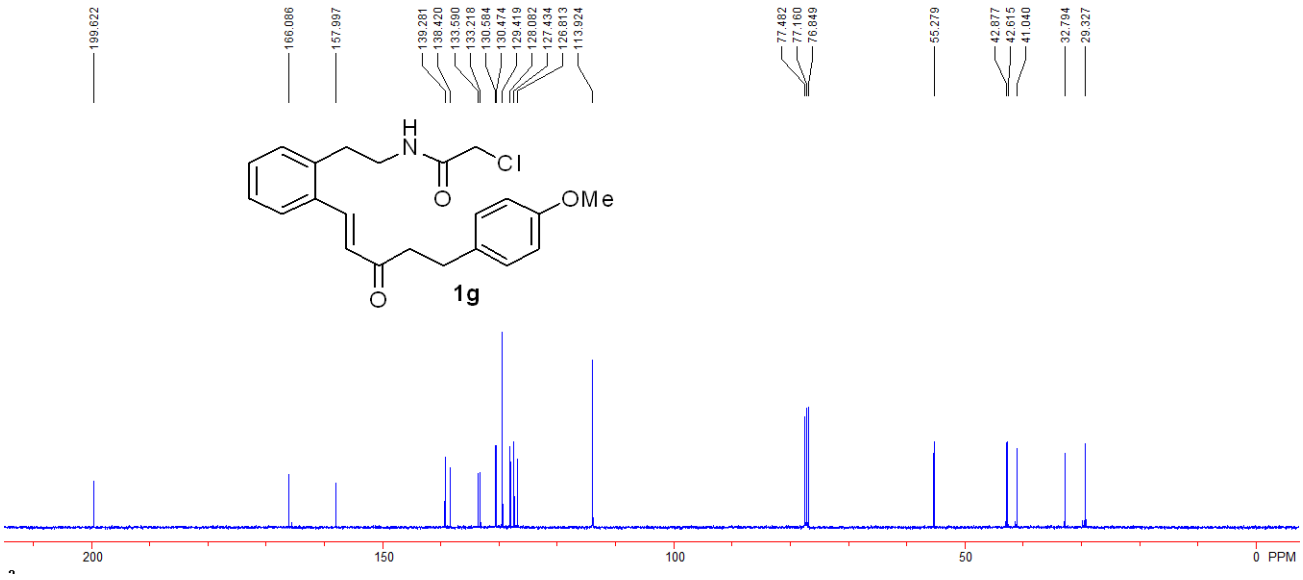
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133.590
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130.584
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129.419
128.082
127.434
126.813
113.924
77.482
77.160
76.849
55.279
42.877
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41.040
32.794
29.327
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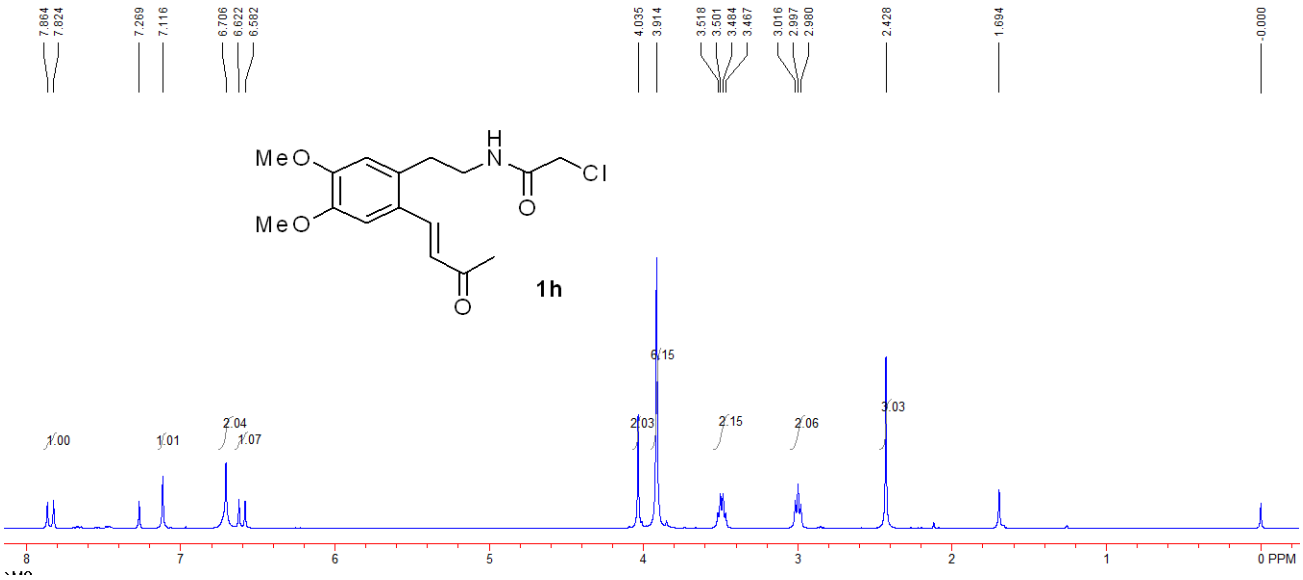
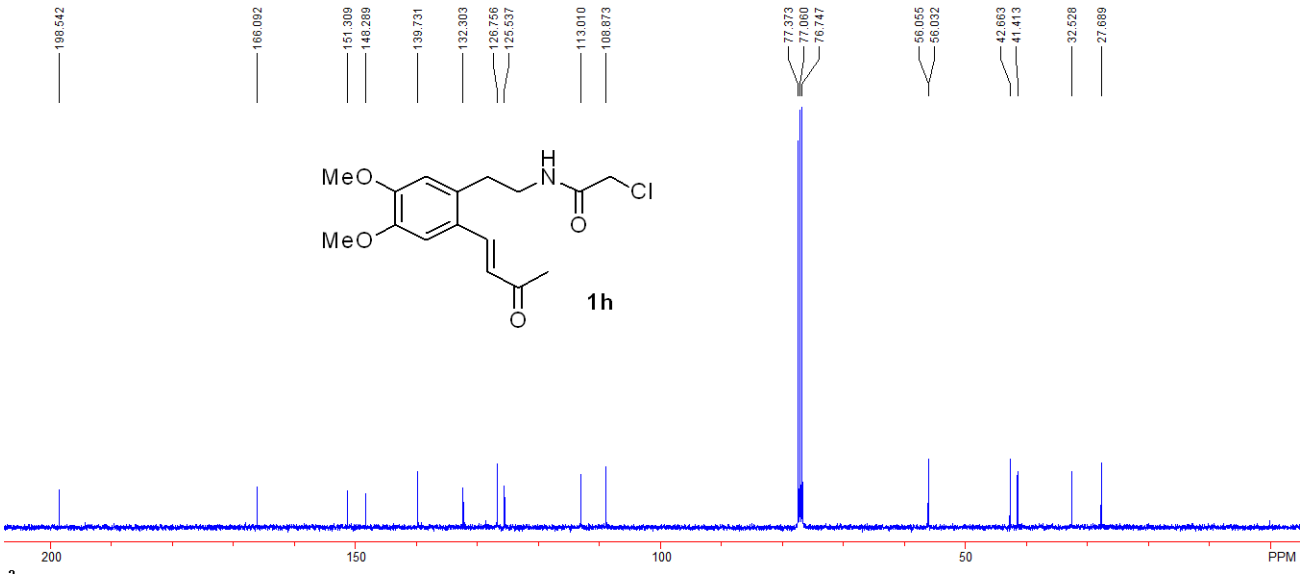
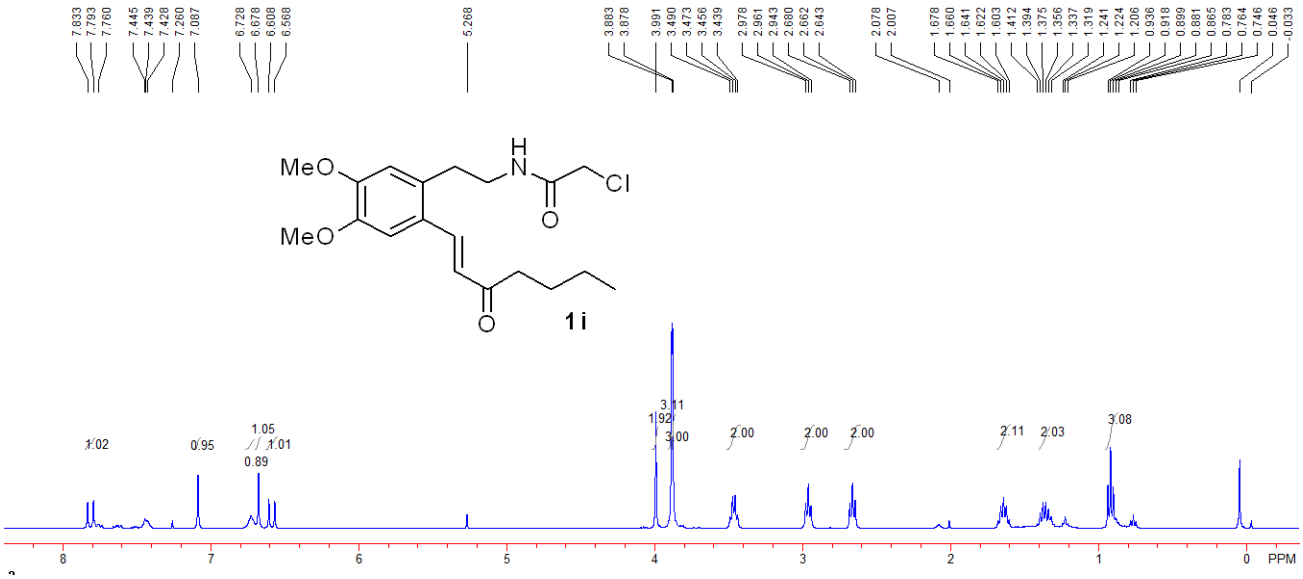
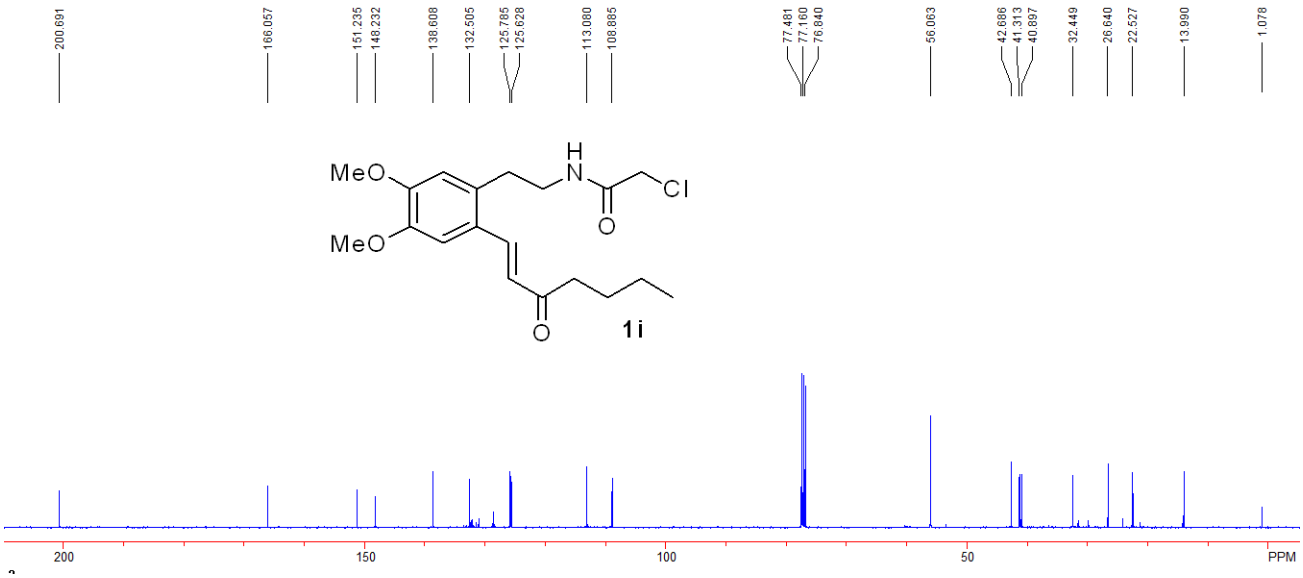
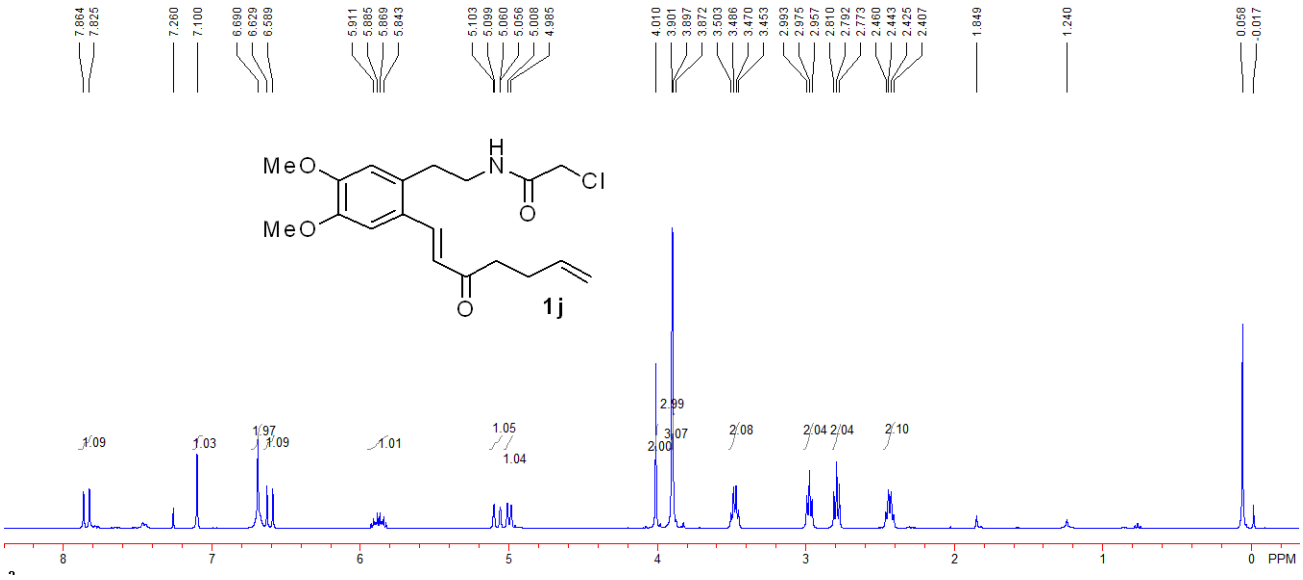
N
Cl
O
OMe
O
1g
200
150
100
50
0 PPM

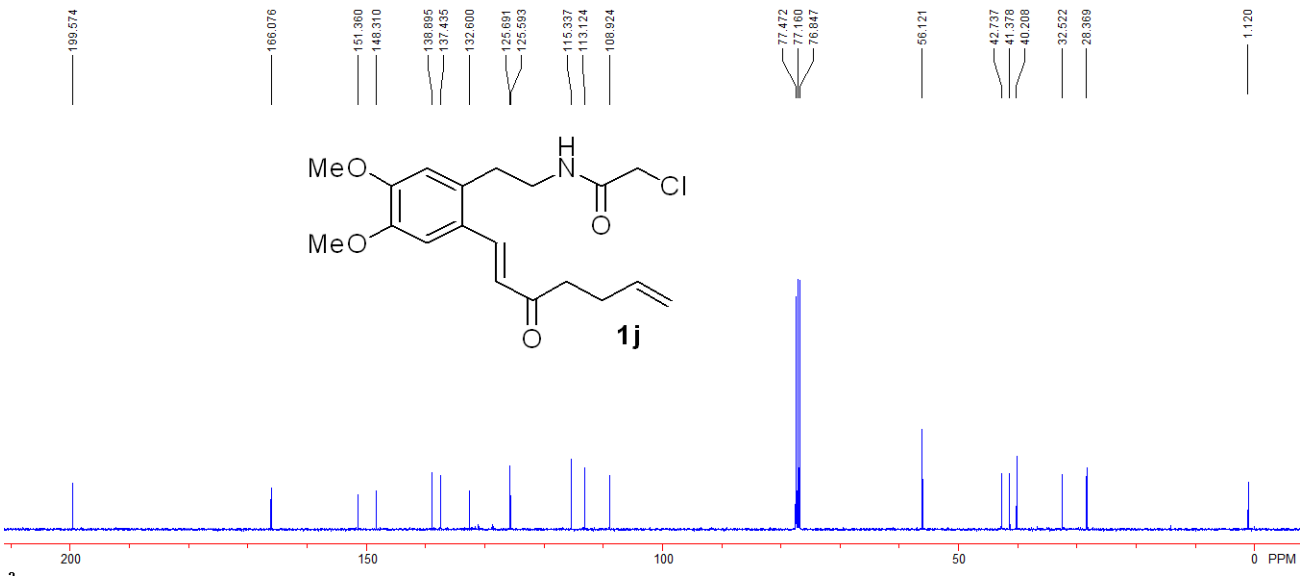


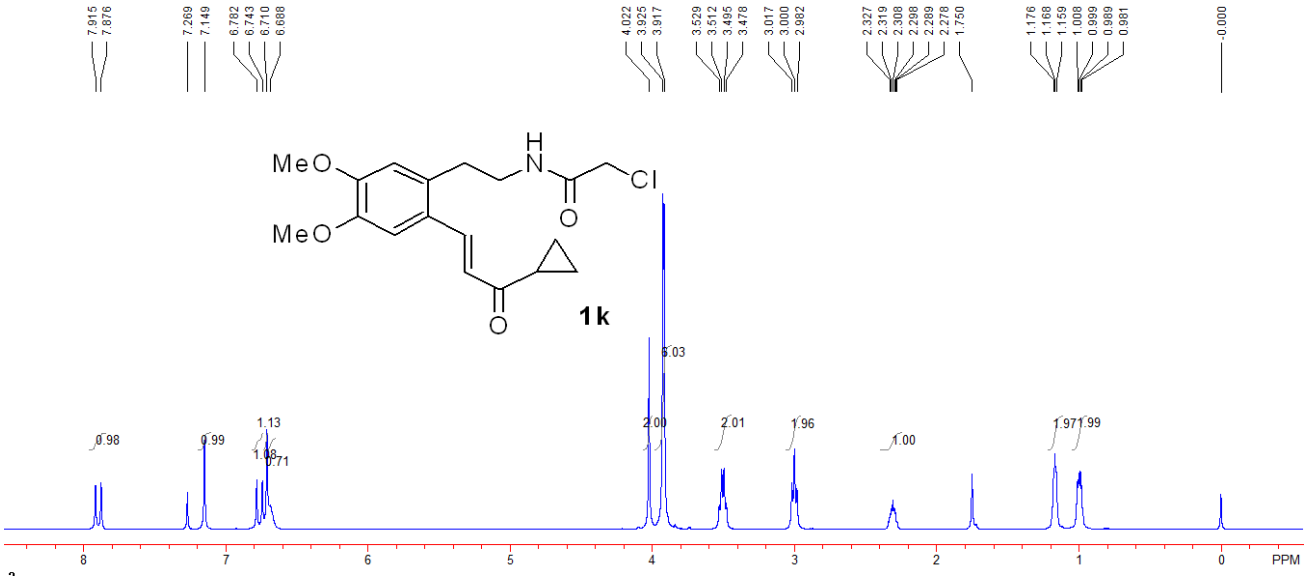








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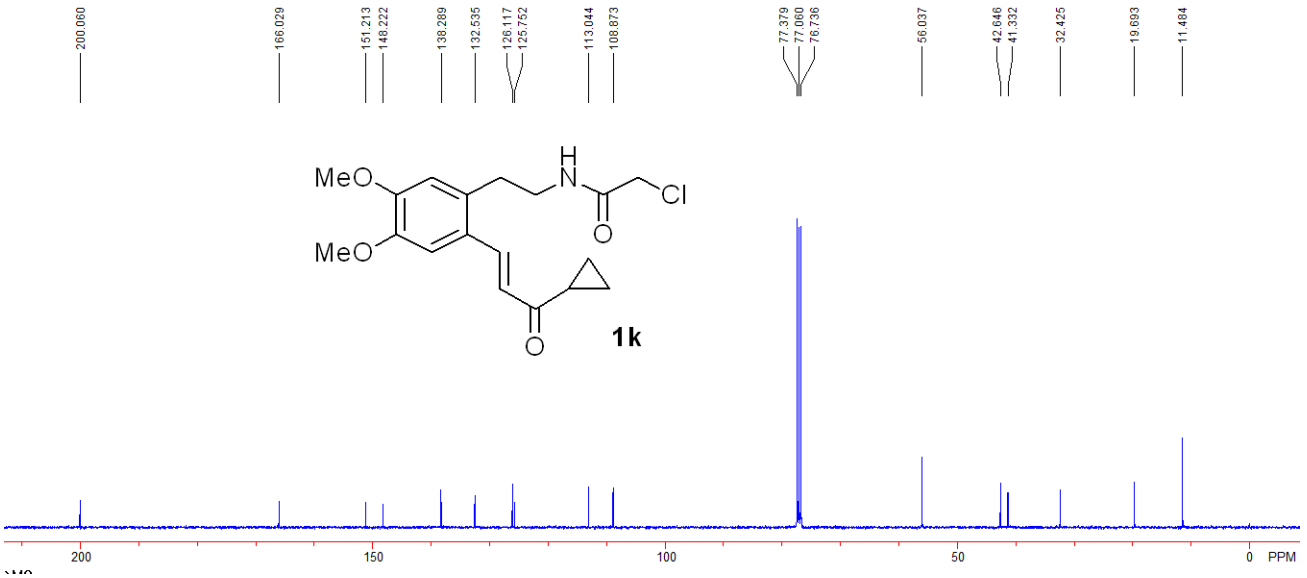
6.743
6.710
6.688
4.022
3.925
3.917
3.529
3.512
3.495
3.478
3.017
3.000
2.982
2.327
2.319
2.308
2.298
2.289
2.278
1.750
1.176
1.168
1.159
1.008
0.999
0.989
0.981
0.000
MeO
MeO
H
N
Cl
O
O
1k
6.03
0.98
0.99
1.13
1.08
0.71
2.00
2.01
1.96
1.00
1.97
1.99
8
7
6
5
4
3
2
1
0
PPM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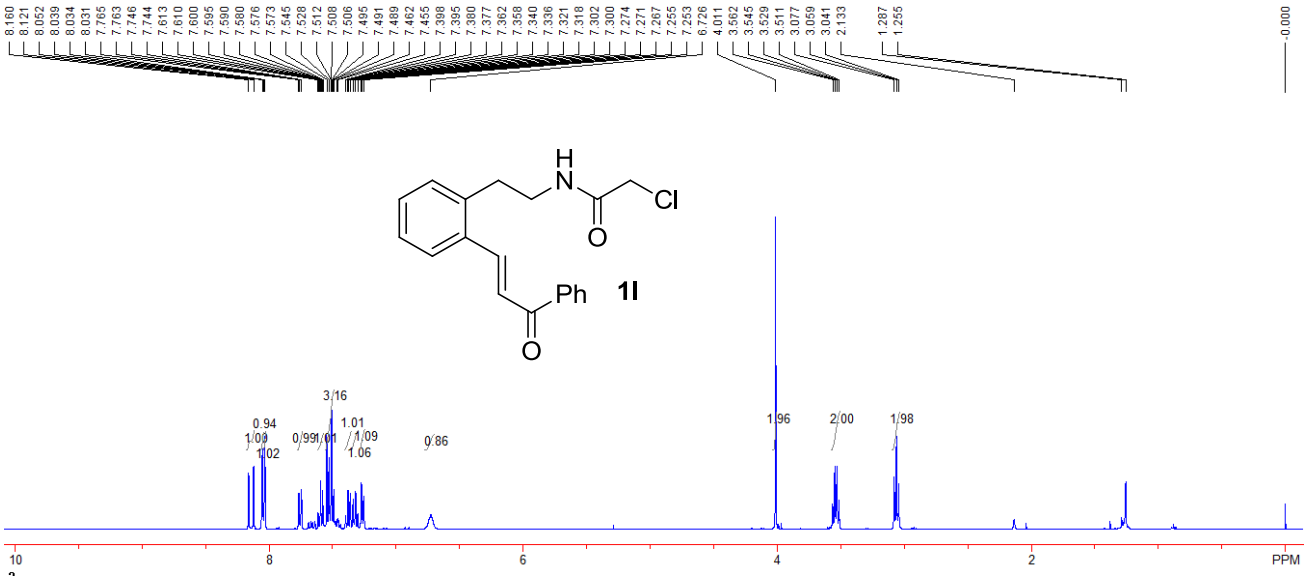
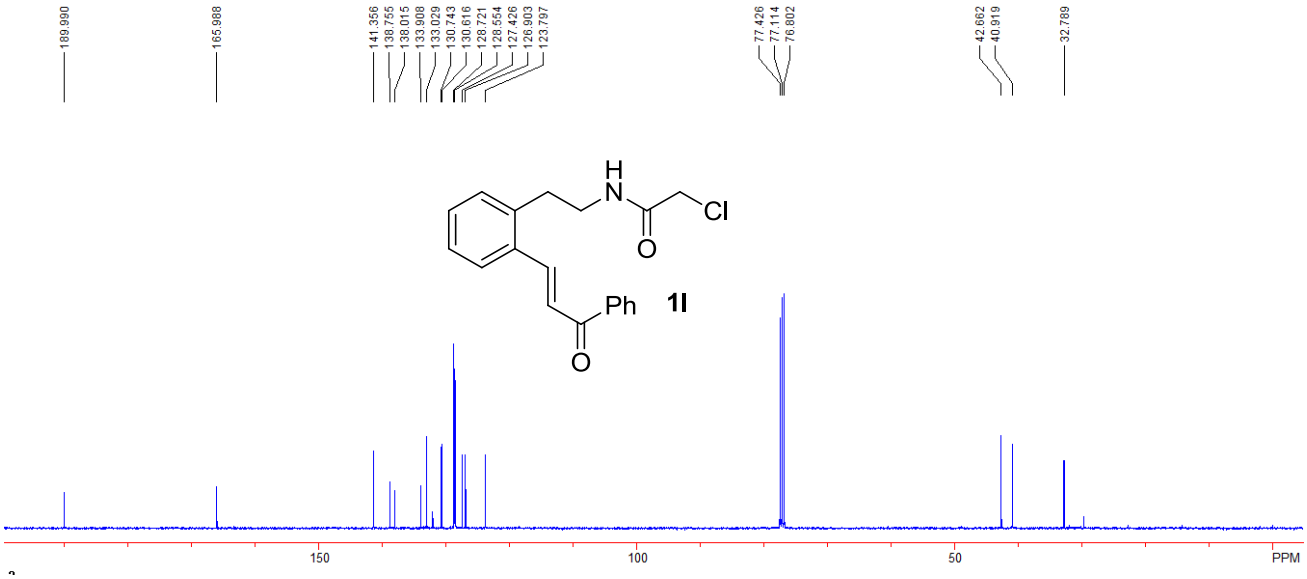
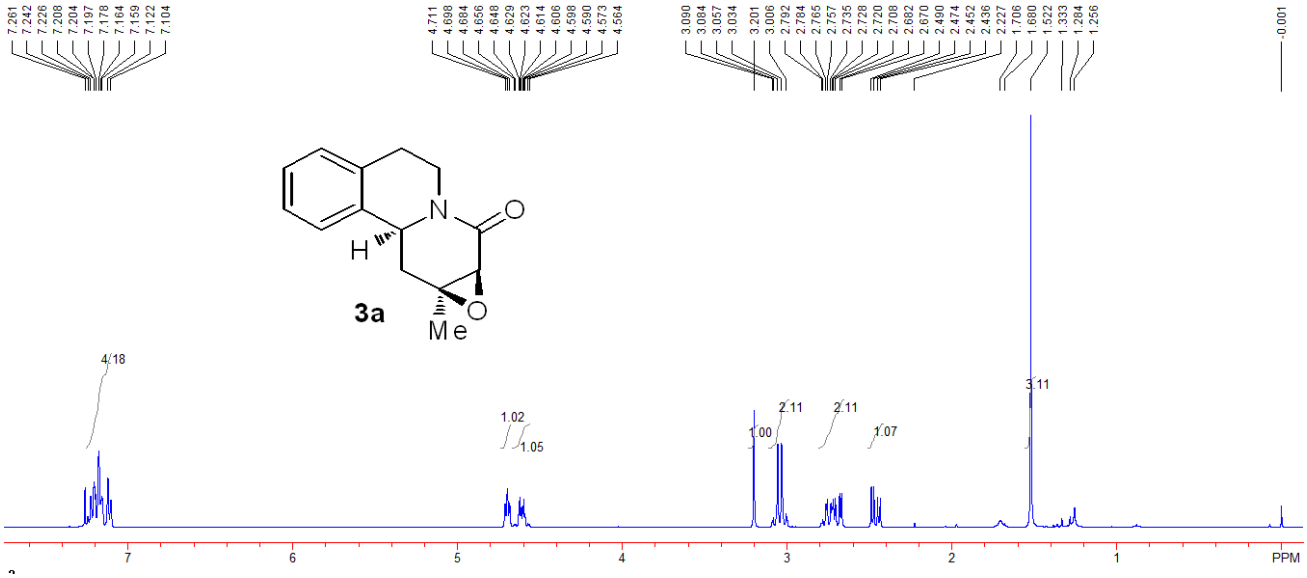
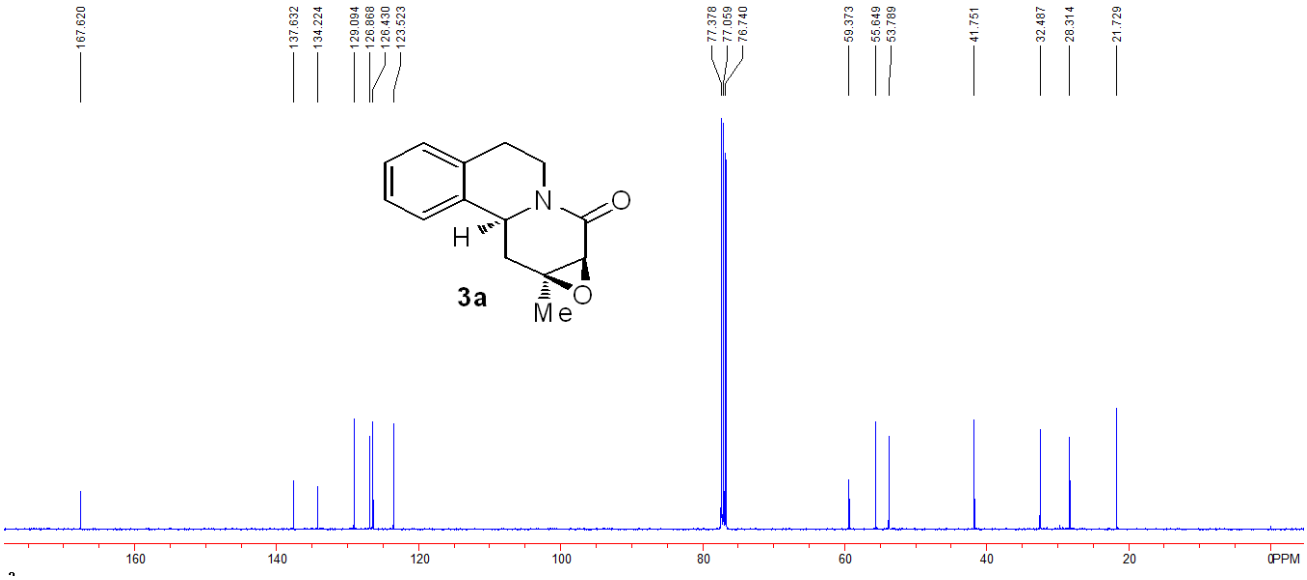
151.213
148.222
138.289
132.535
126.117
125.752
113.044
108.873
77.379
77.060
76.736
56.037
42.646
41.332
32.425
19.693
11.484
MeO
MeO
H
N
Cl
O
O
1k
200
150
100
50
0
PPM

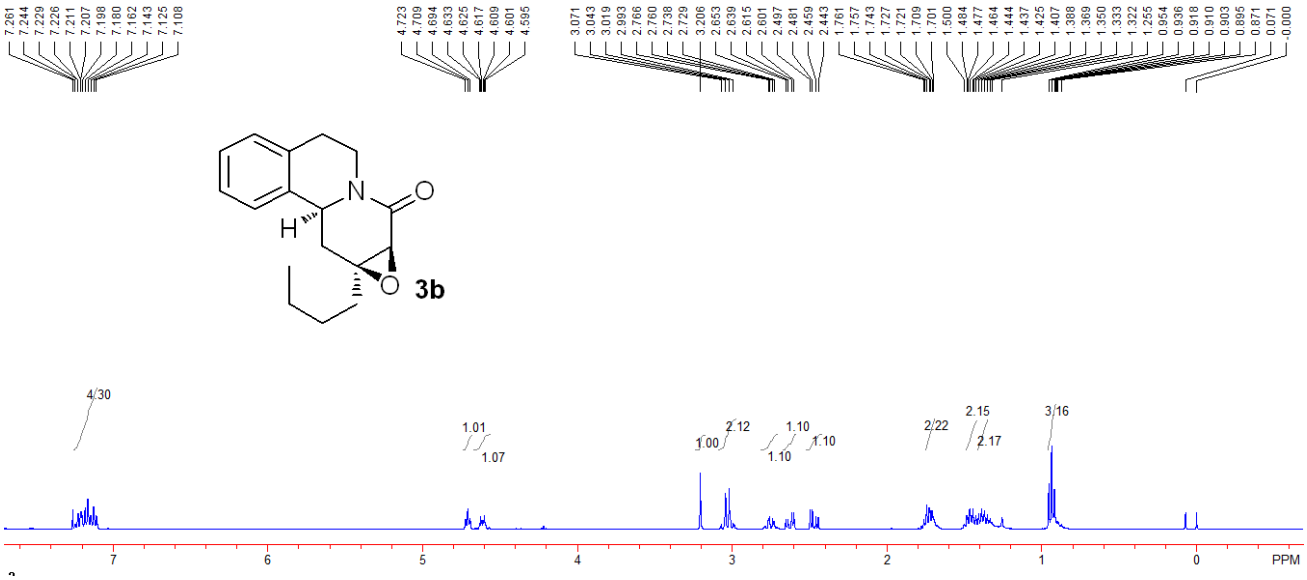


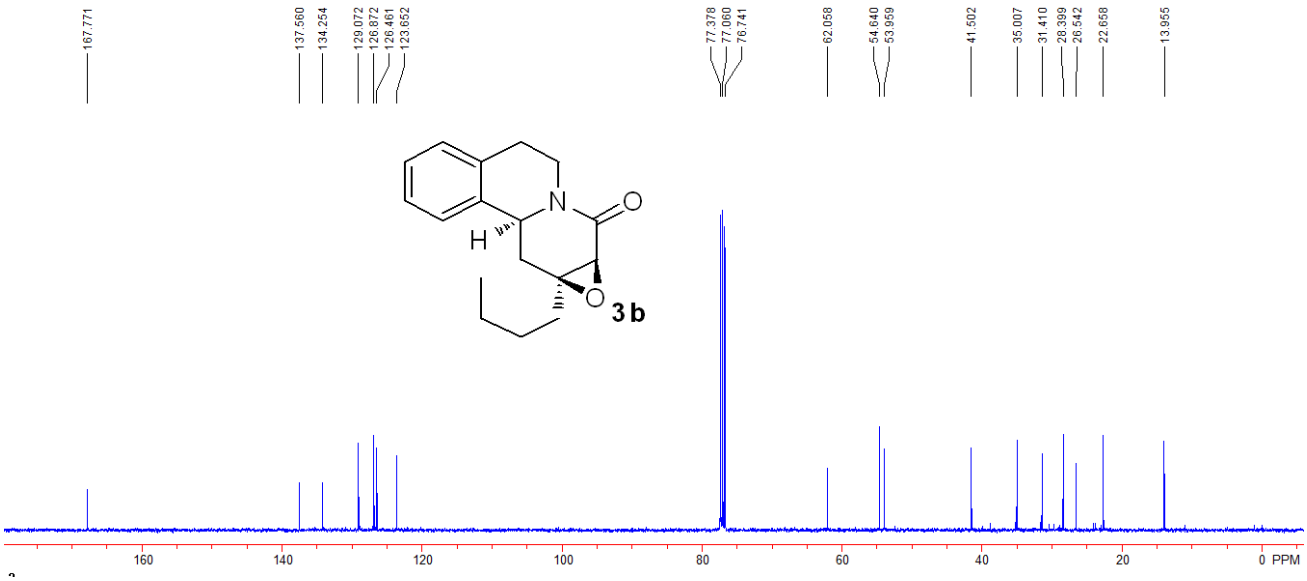


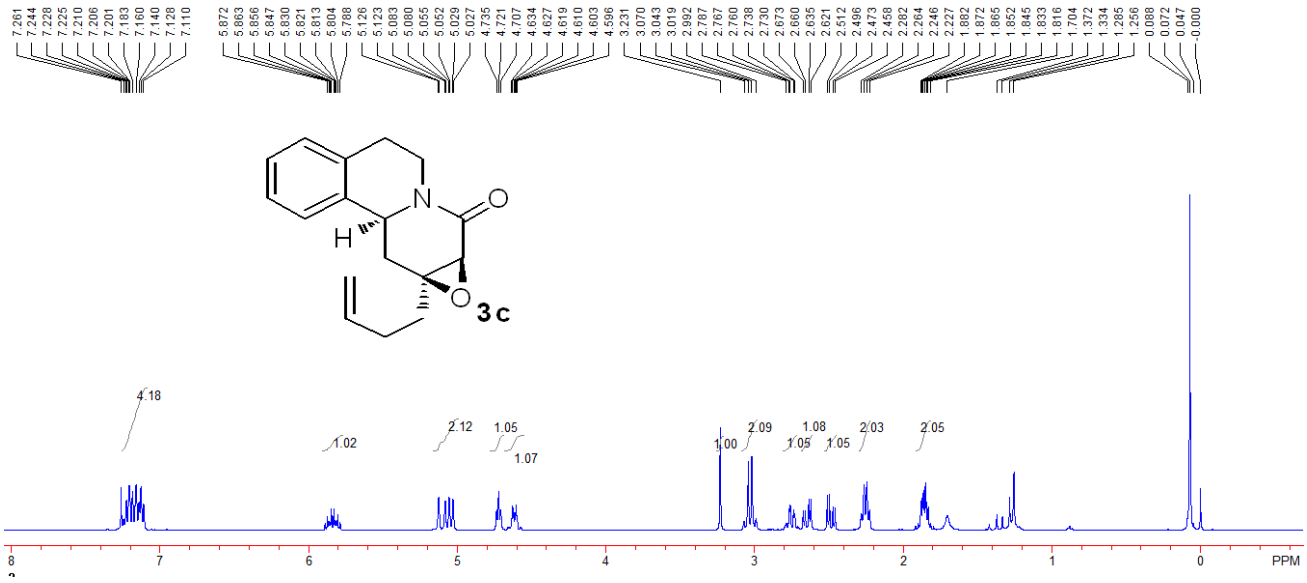
NMR Spectra for Compounds Afforded by General Procedure B and C.







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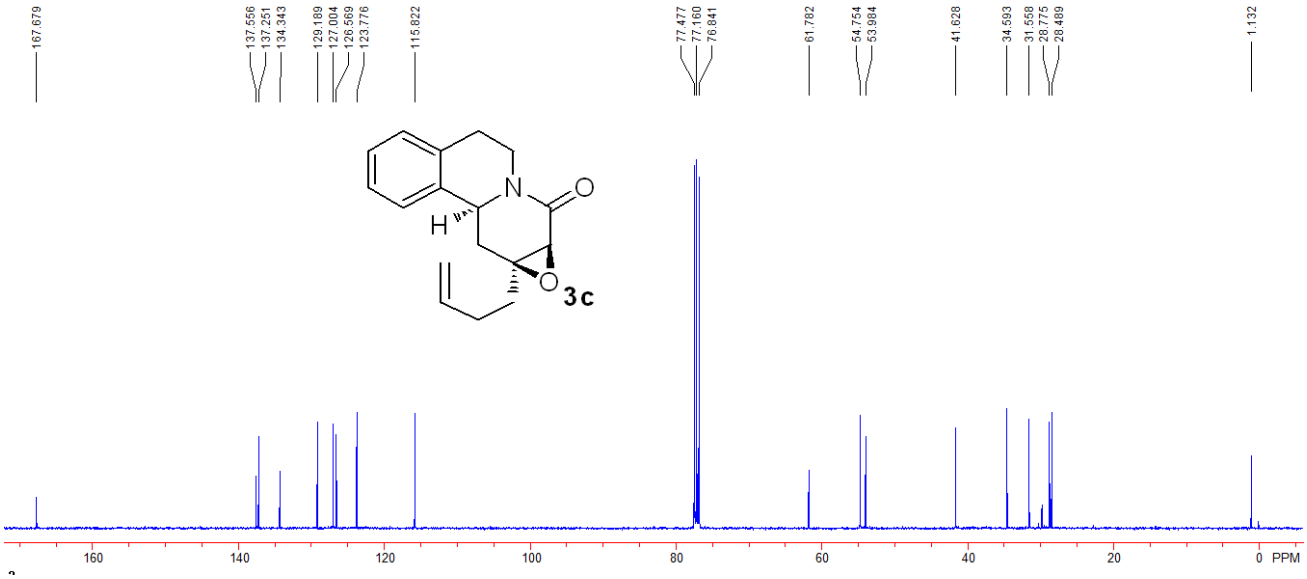
7.228
7.225
7.210
7.206
7.201
7.183
7.160
7.140
7.128
7.110
5.872
5.863
5.856
5.847
5.830
5.821
5.813
5.804
5.788
5.126
5.123
5.083
5.080
5.055
5.052
5.029
5.027
4.735
4.721
4.707
4.634
4.627
4.619
4.610
4.603
4.596
3.231
3.070
3.043
3.019
2.992
2.787
2.767
2.760
2.738
2.730
2.673
2.660
2.635
2.621
2.512
2.496
2.473
2.458
2.282
2.264
2.246
2.227
1.882
1.872
1.865
1.852
1.845
1.833
1.816
1.704
1.372
1.334
1.285
1.256
0.088
0.072
0.047
-0.000
N
O
H
O
3c
4.18
1.02
2.12
1.05
1.07
1.00
2.09
1.08
1.05
1.05
2.03
2.05
8
7
6
5
4
3
2
1
0
PPM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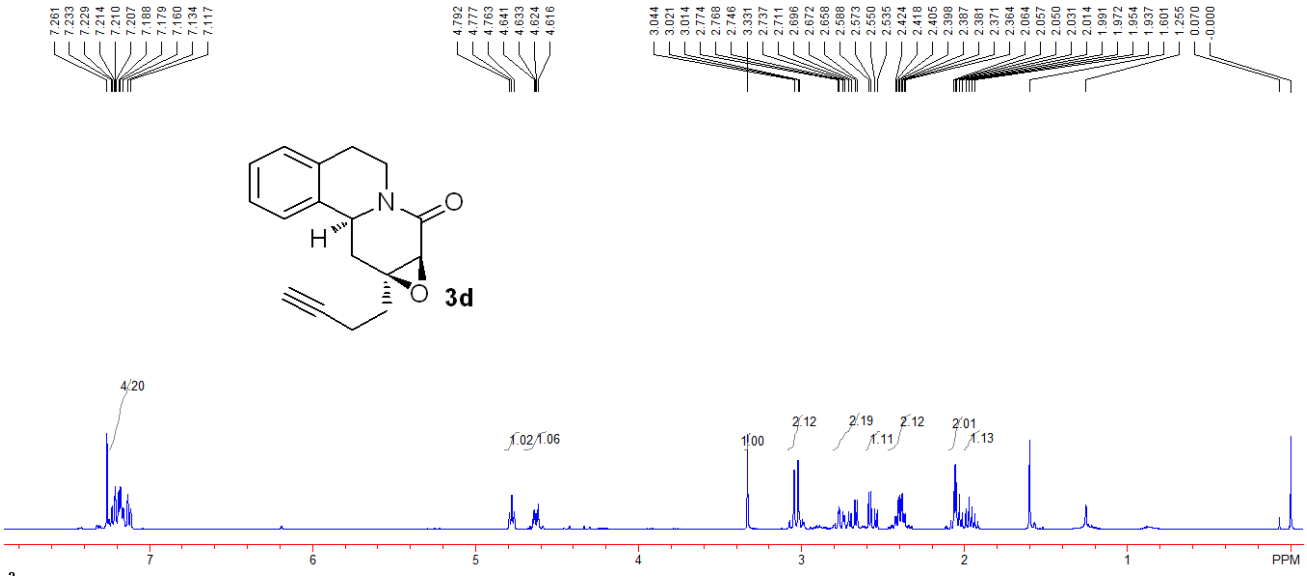
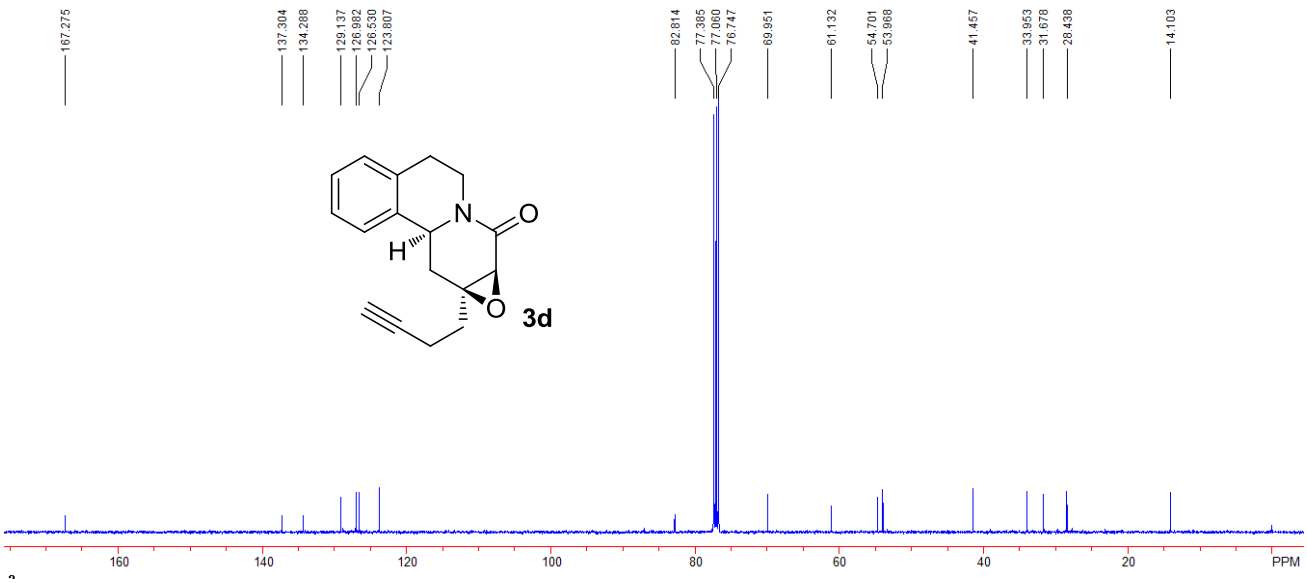
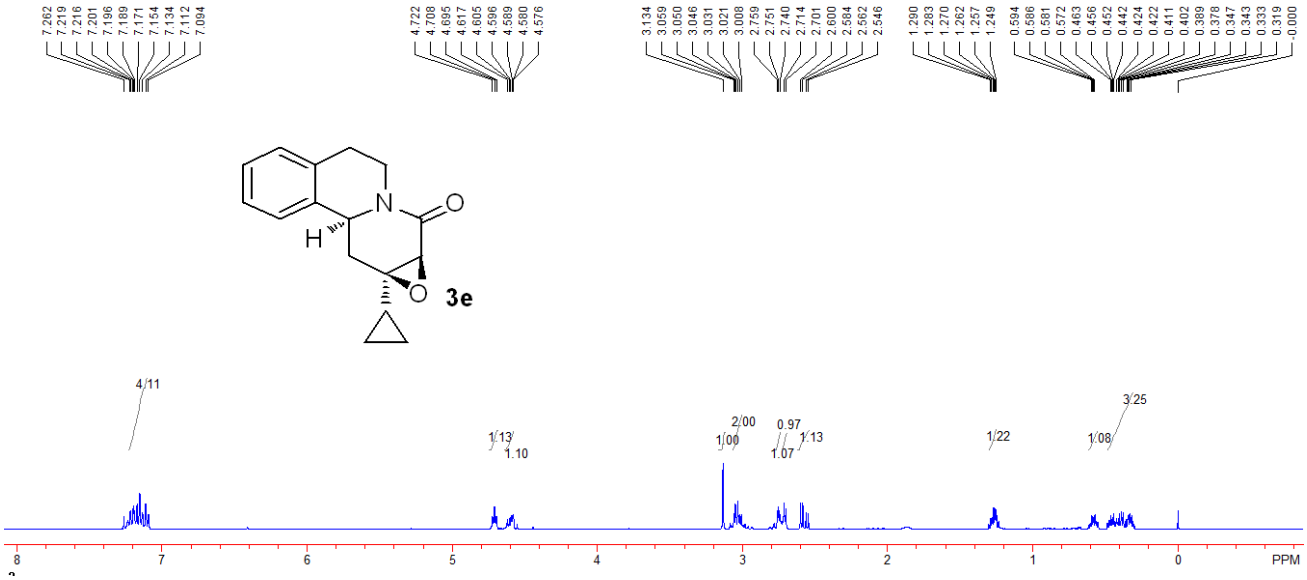
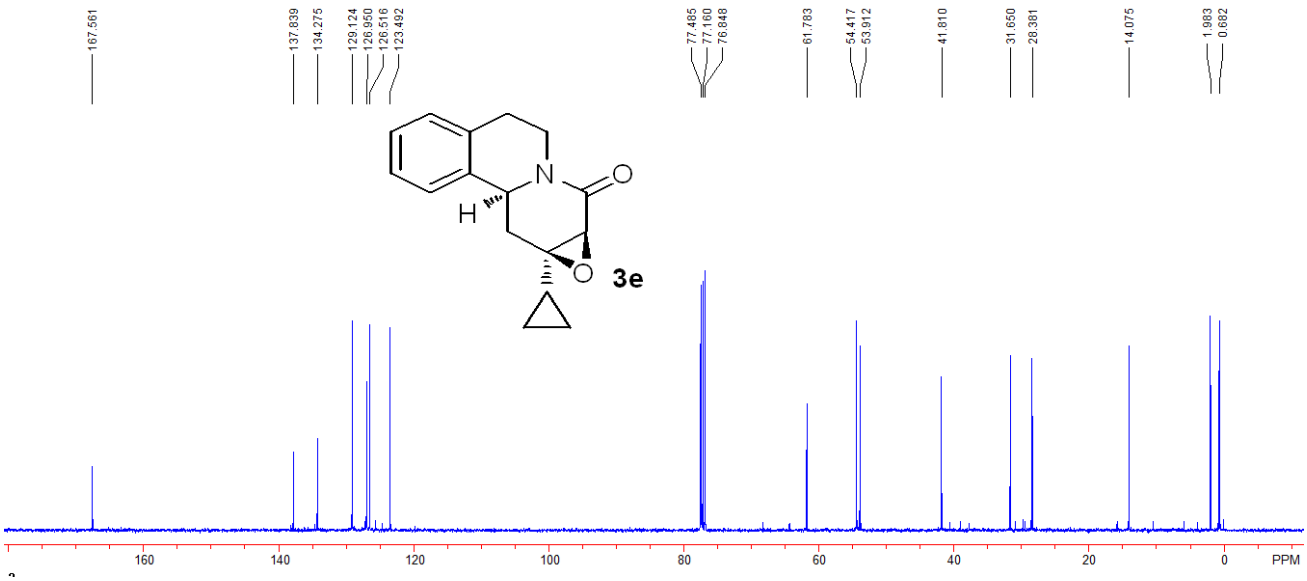
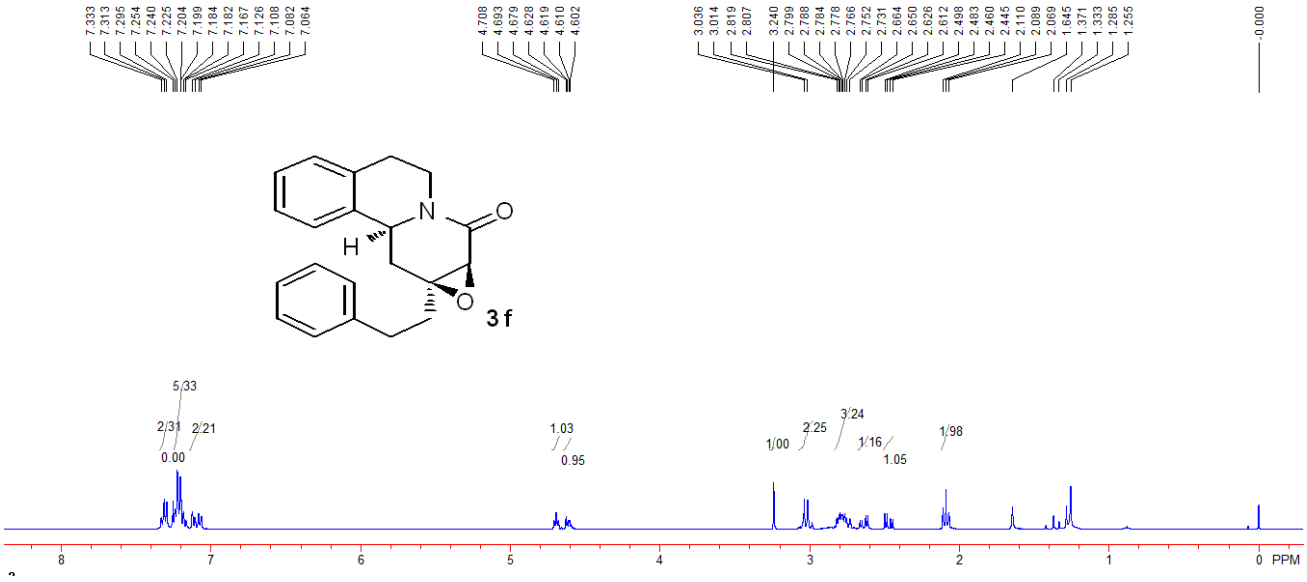
129.189
127.004
126.569
123.776
115.822
77.477
77.160
76.841
61.782
54.754
53.984
41.628
34.593
31.558
28.775
28.489
1.132
N
O
H
O
3c
160
140
120
100
80
60
40
20
0
PPM







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7.225
7.204
7.199
7.184
7.182
7.167
7.126
7.108
7.082
7.064
4.708
4.693
4.679
4.628
4.619
4.610
4.602
3.036
3.014
2.819
2.807
3.240
2.799
2.788
2.784
2.778
2.766
2.752
2.731
2.664
2.650
2.626
2.612
2.498
2.483
2.460
2.445
2.110
2.089
2.069
1.645
1.371
1.333
1.285
1.255
0.000
N
O
H
O
3f
5.33
2.31
2.21
0.00
1.03
0.95
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1.98
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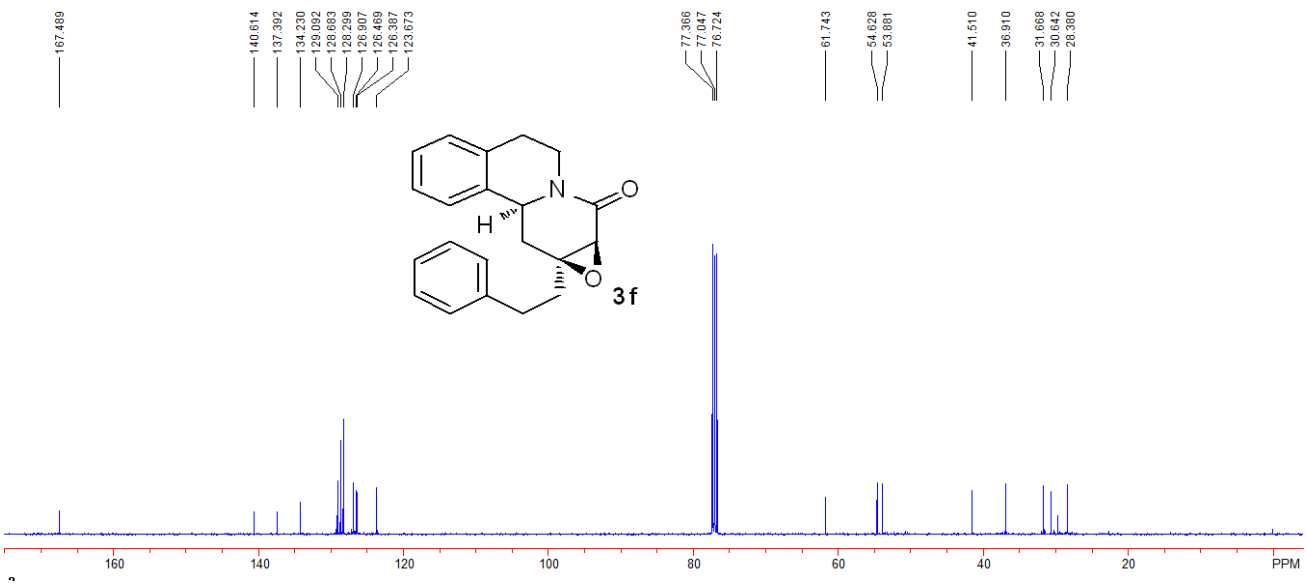
PPM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123.673
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77.047
76.724
61.743
54.628
53.881
41.510
36.910
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28.380
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O
3f
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120
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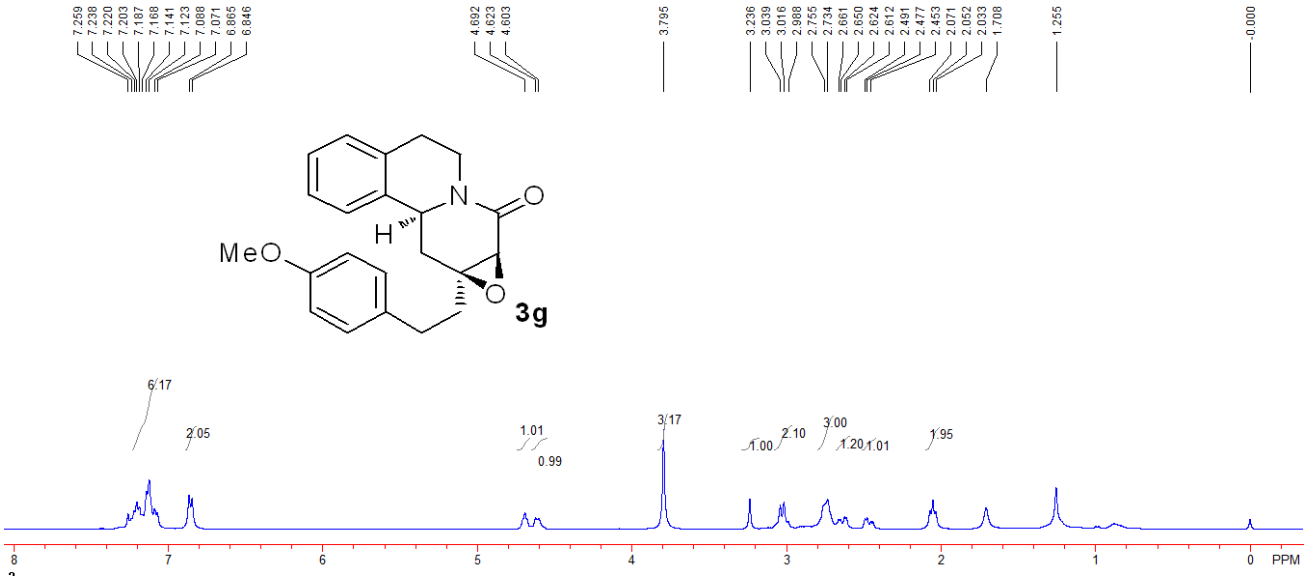
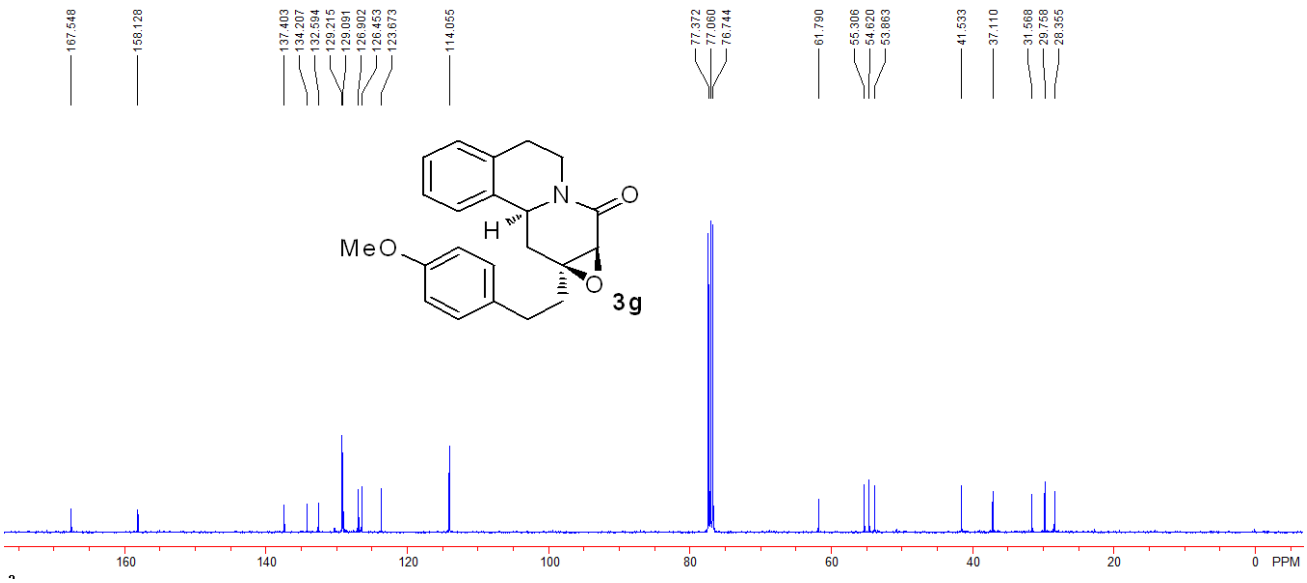
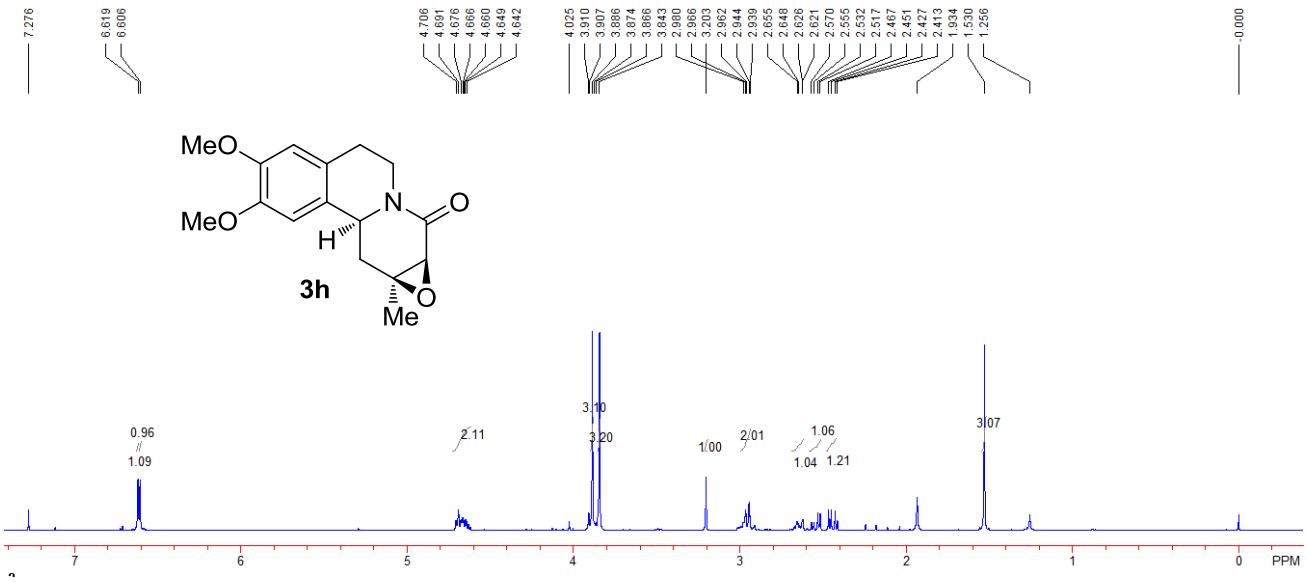
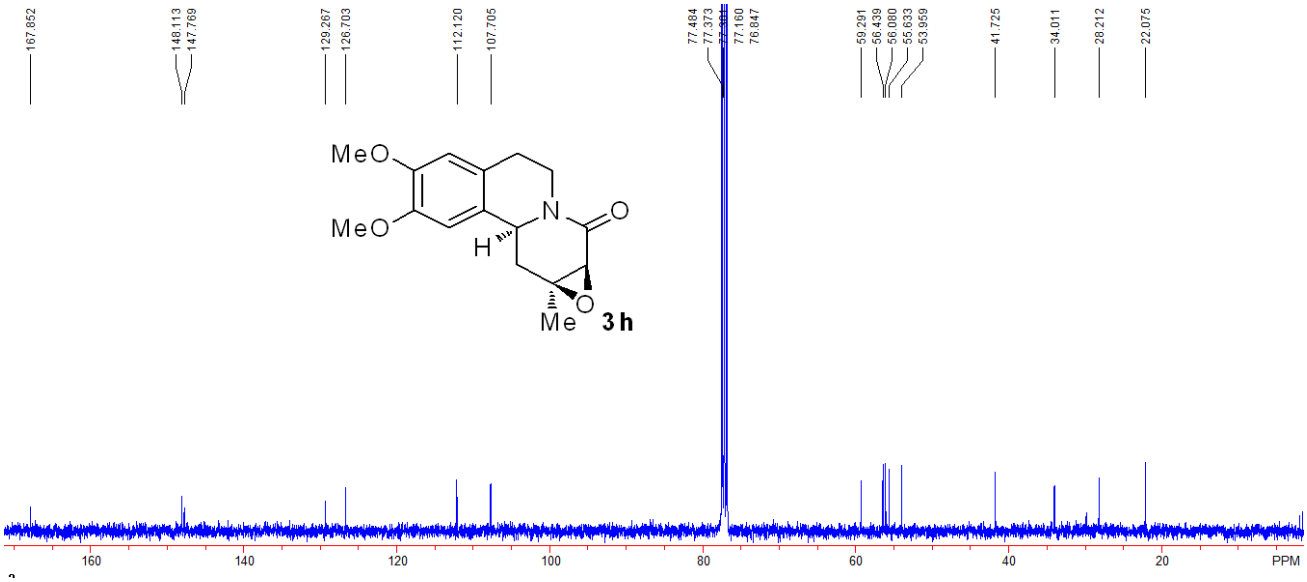
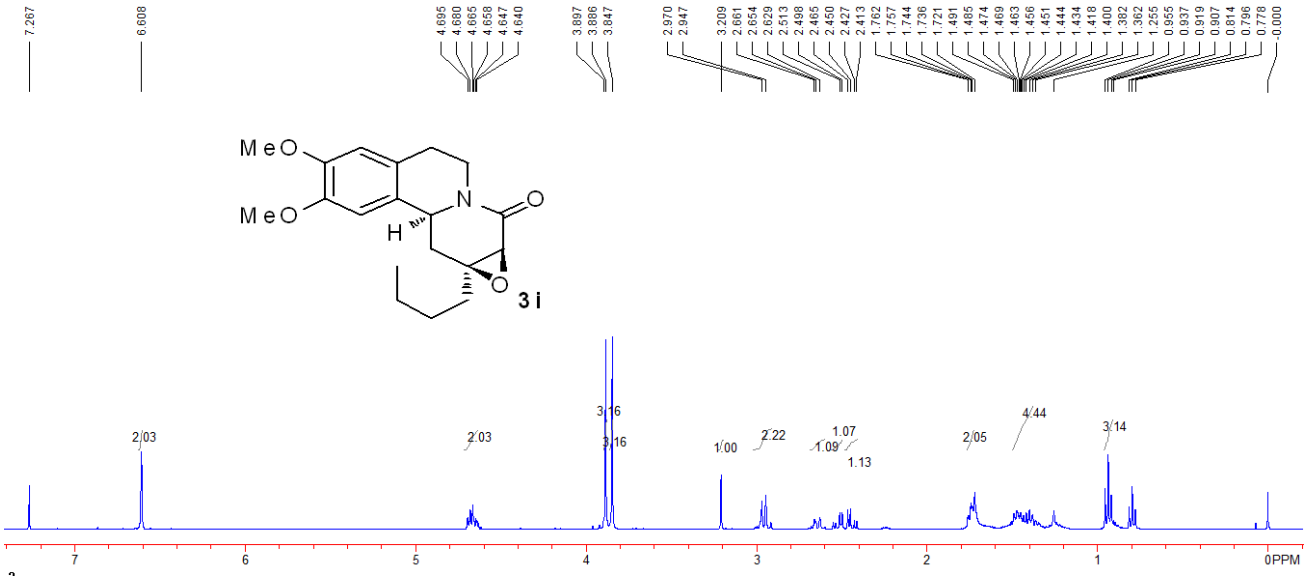
80
60
40
20
PPM







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2.947
3.209
2.661
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2.498
2.465
2.450
2.427
2.413
1.762
1.757
1.744
1.736
1.721
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1.485
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1.469
1.463
1.456
1.451
1.444
1.434
1.418
1.400
1.382
1.362
1.255
0.955
0.937
0.919
0.907
0.814
0.796
0.778
0.000
MeO
MeO
N
O
H
O
3 i
2.03
2.03
3.16
3.16
1.00
2.22
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1.13
2.05
4.44
3.14
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2
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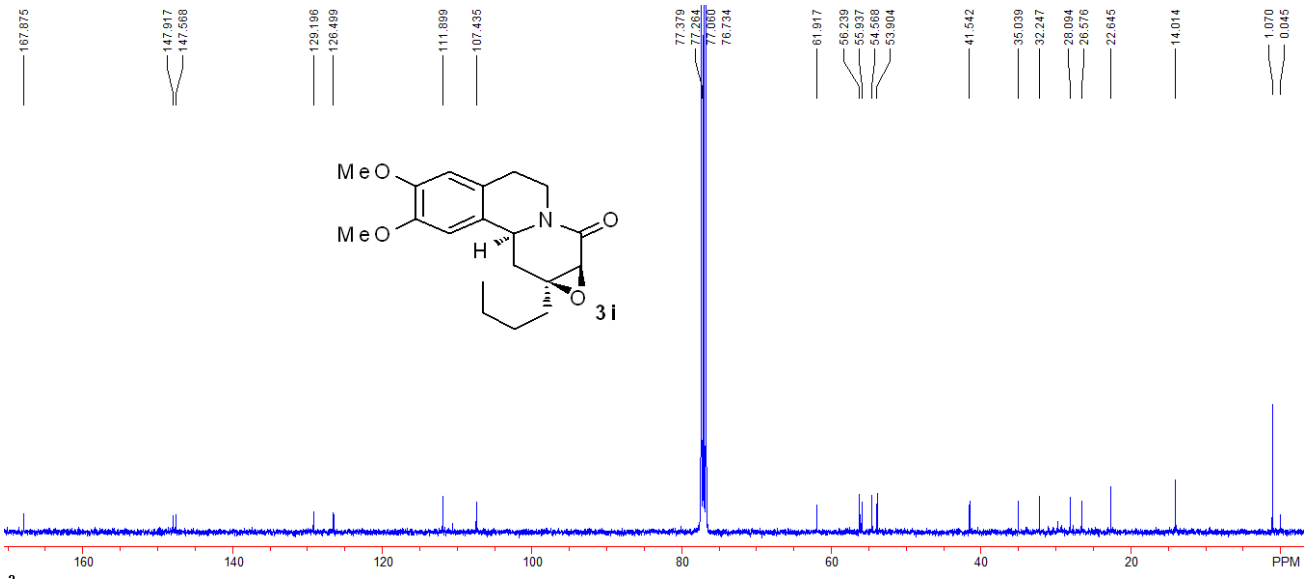
0PPM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111.899
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77.060
76.734
61.917
56.239
55.937
54.568
53.904
41.542
35.039
32.247
28.094
26.576
22.645
14.014
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MeO
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H
O
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120
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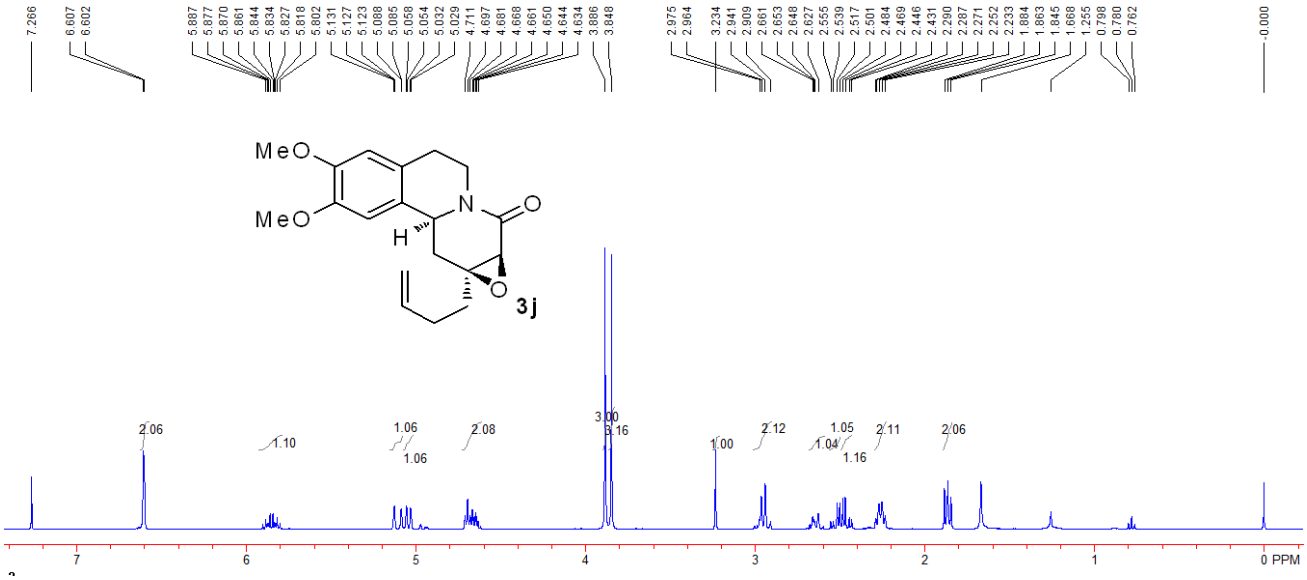
40
20
PPM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5.131
5.127
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5.088
5.085
5.058
5.054
5.032
5.029
4.711
4.697
4.681
4.668
4.661
4.650
4.644
4.634
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3.848
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3.234
2.941
2.909
2.661
2.653
2.648
2.627
2.555
2.539
2.517
2.501
2.484
2.469
2.446
2.431
2.290
2.287
2.271
2.252
2.233
1.884
1.863
1.845
1.668
1.255
0.798
0.780
0.762
0.000
MeO
MeO
N
O
H
O
3j
2.06
1.10
1.06
1.06
2.08
3.00
3.16
1.00
2.12
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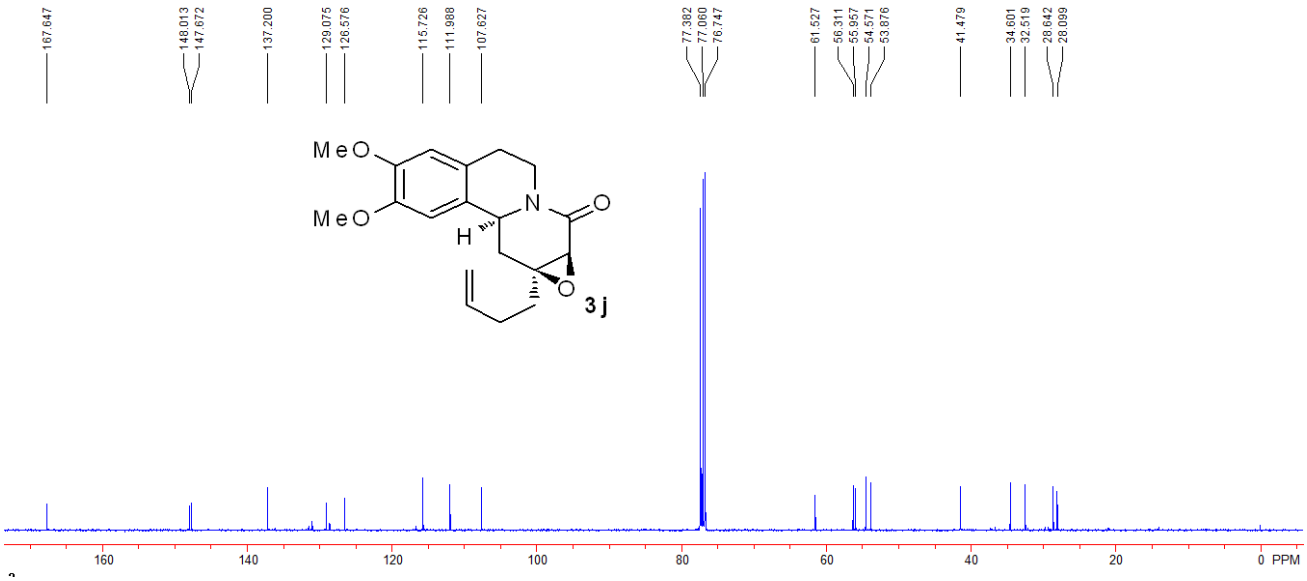
1.04
1.16
2.11
2.06
7
6
5
4
3
2
1
0 PPM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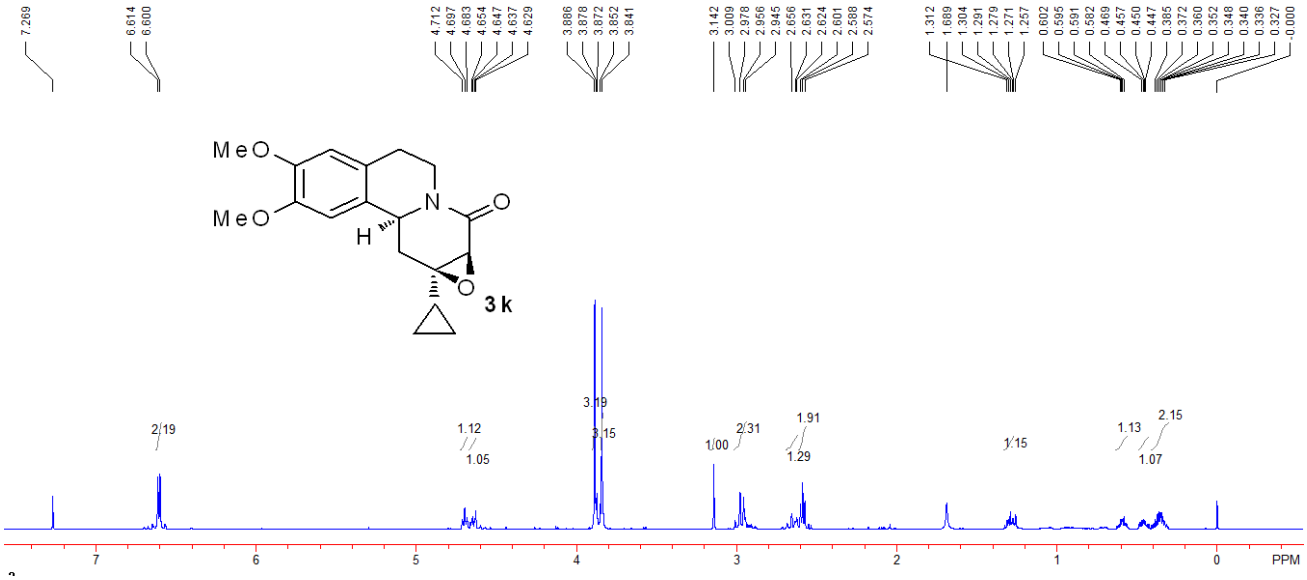
129.075
126.576
115.726
111.988
107.627
77.382
77.060
76.747
61.527
56.311
55.957
54.571
53.876
41.479
34.601
32.519
28.642
28.099
MeO
MeO
N
O
H
O
3j
160
140
120
100
80
60
40
20
0 PPM



4. X-ray Spectra of 3a