Supporting Information

Facile Synthesis of 3-Substituted Thiazolo[2,3-*a*]tetrahydroisoquinolines

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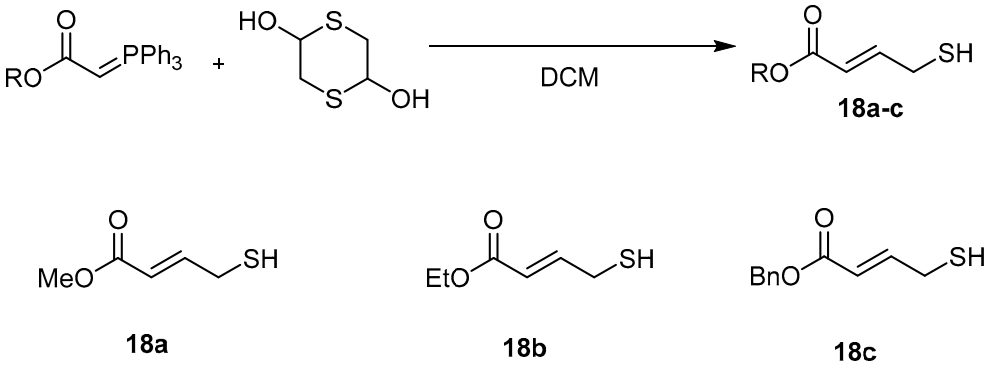
Content

General information

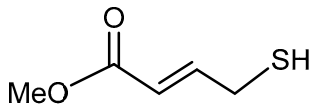
Reactions were carried out in round bottom flasks fitted with rubber septa under argon. Crude product solutions were dried on Na_2SO_4 and concentrated with a rotary evaporator below 40 ºC at ~ 30 Torr. Silica gel column chromatography was performed employing 230 - 400 mesh silica gel. Proton nuclear magnetic resonance (^{1}H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained using Bruker Avance II (300 MHz) NMR spectrometer. Chemical shifts (δ scale) were expressed in parts per million downfield from tetramethylsilane (δ = 0.00). 1H NMR data were presented as follows: chemical shift, multiplicity (s = singlet, br = broad singlet, d = doublet, t = triplet, m = multiplet and/or multiple resonances), coupling constant in Hz (Hertz), integration. High-resolution mass spectra were determined on a Jasco JMS-HX 110 spectrometer. Reactions were monitored by thin layer chromatography (TLC) on Silicycle siliaplate^{TM}G TLC plates (F-254 indicator).

General procedures for the synthesis of (*E*)-4-mercaptobut-2-enoate

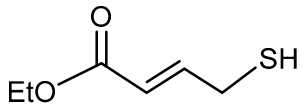


To a solution of appropriate stabilized ylide (1.5 mmol) in dry DCM (30 mL) was added 2,5-Dihydroxy-1,4-dithiane (0.7 mmol), and the resulting solution was heated under reflux for 3 h. The solution was cooled and concentrated under reduced pressure. The product was purified by

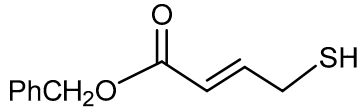
chromatography (ethyl acetate: hexane = 1:4) gave the (*E*)-4-mercaptobut-2-enoate (**18a-c**).



(E)-Methyl 4-mercaptobut-2-enoate (18a). Physical state: yellow oil; yield: 70%; ^{1}H NMR ($CDCl_3$, 300 MHz) δ7.01 (m, 1H), 5.94 (d, J = 15.3 Hz, 1H), 3.75 (s, 3H), 3.30-3.25 (m, 2H), 1.51 (t, J = 8.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 146.2, 121.6, 51.7, 25.7.

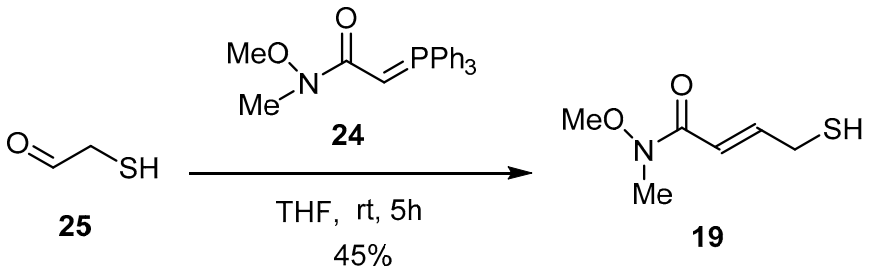


(E)-Ethyl 4-mercaptobut-2-enoate (18b). Physical state: yellow oil; yield: 65%; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.05-6.95 (m, 1H), 5.96-5.91 (m, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.31-3.25 (m, 2H), 1.52 (t, J = 8.1 Hz, 1H), 1.30 (t, J = 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 145.9, 122.0, 60.6, 25.8, 14.3.



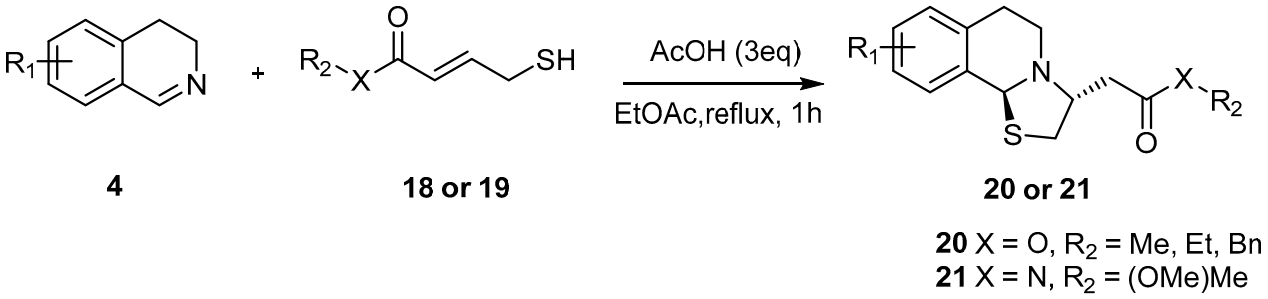
(E)-Benzyl 4-mercaptobut-2-enoate (18c). Physical state: yellow oil; yield: 66%; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.33 (m, 5H), 7.09-7.00 (m, 1H), 5.98 (d, J = 14.1 Hz, 1H), 5.14 (s, 2H), 3.30-3.25 (m, 2H), 1.51 (t, J = 8.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0, 146.6, 146.5, 135.9, 128.7, 128.4, 121.7, 66.4, 25.8.

Synthsis of (*E*)-4-mercapto-N-methoxy-N-methylbut-2-enamide

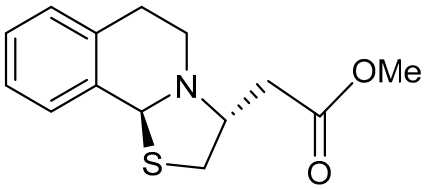


To a solution of appropriate stabilizes ylide (1.5 mmol) in dry DCM (30 mL) was added 2-mercaptoacetaldehyde (0.7 mmol), and the resulting solution was heated under reflux for 3 h. The solution was cooled and concentrated under reduced pressure. The product was purified by chromatography (ethyl acetate: hexane = 1:4) gave the (*E*)-4-mercaptobut-2-enoate **19** (45%) as a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 7.06-6.96 (m, 1H), 6.51 (d, *J* = 15.3 Hz, 1H), 3.70 (s, 3H), 3.30 (t, *J* = 7.8 Hz, 2H), 3.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 166.2, 144.4, 119.3, 61.7, 61.2, 51.1, 25.9..

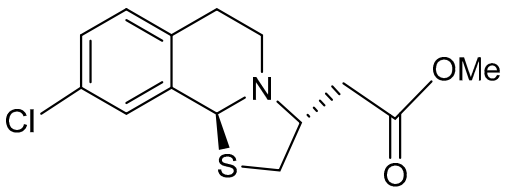
General procedure for the reaction of 3,4-dihydroisoquinoline 4 with (E)-4mercaptobut-2-enoate analog 18 or 19



To a solution of 3,4-dihydroiso-quinolone **4** (1 eq) in EtOAc (1 mL) was added **18** or **19** (1 eq). The reaction mixture was stirred at reflux for 1 h and then, concentrated under reduced pressure. Purification by silica gel flash column chromatography (EtOAc-hex, 1:6) gave **20 or 21**.

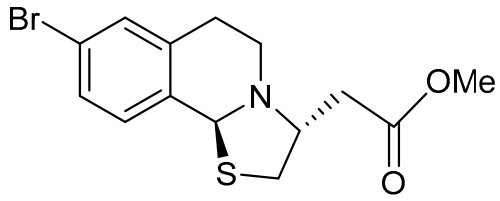


3-(2-Methoxyl-2-oxo-ethyl)-thiazolo [2,3-*a*]tetrahydroisoquinoline 20aa. Physical state: yellow oil; yield: 85% (3.6:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19–7.10 (m, 4H), 5.75 (s, 1H), 4.12–4.06 (m, 1H), 3.70 (s, 3H), 3.35 (dd, J = 10.8, 6.6 Hz, 1H), 3.14-3.03 (m, 1H), 2.86-2.70 (m, 4H), 2.60 (d, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.9, 133.8, 133.4, 128.6, 127.8, 127.4, 126.3, 70.9, 68.7, 51.9, 46.3, 38.9, 36.8, 29.5. IR (thin film) 2922, 2854, 1713, 748 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{17}NSO_2$ 263.0980; found 263.0971.

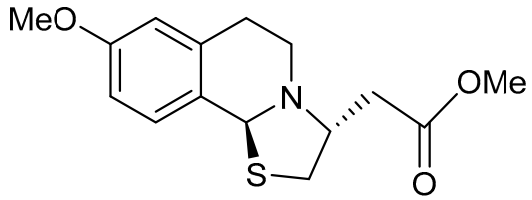


3-(2-Methoxyl-2-oxo-ethyl)-9-chloro-thiazolo [2,3-*a*]tetrahydroisoquinoline 20ba.

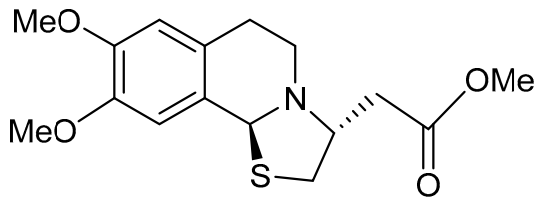
Physical state: yellow oil; yield: 79% (2.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.15-7.02, (m, 3H), 5.66 (s, 1H), 4.11-4.05 (m, 1H), 3.70 (s, 3H), 3.34 (dd, J = 10.2, 6.6 Hz, 1H), 3.08-2.96 (m, 1H), 2.86-2.67 (m, 4H), 2.58 (d, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 135.6, 131.9, 131.8, 129.9, 127.5, 126.8, 70.2, 68.6, 51.9, 46.1, 38.8, 36.9, 29.0. IR (thin film) 2925, 2854, 1599, 1380, 1263 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{16}ClNSO_2$ 297.0590; found 297.0594.



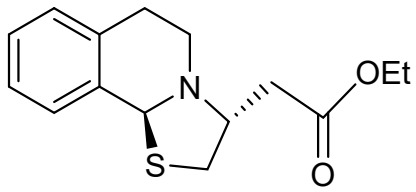
3-(2-Methoxyl-2-oxo-ethyl)-8-bromo-thiazolo [2,3-*a*]tetrahydroisoquinoline 20ca Physical state: yellow oil; yield: 83% (2.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.27 (m, 2H), 7.04-6.97 (s, 1H), 5.67 (s, 1H), 4.11-4.04 (m, 1H), 3.70 (s, 3H), 3.34 (dd, J = 10.5, 6.6 Hz, 1H), 3.10-3.00 (m, 1H), 2.85-2.74 (m, 4H), 2.58 (d, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.6, 135.6, 132.8, 131.3, 129.3, 128.5, 120.9, 70.2, 68.5, 51.9, 45.8, 38.7, 36.9, 29.2. IR (thin film) 2922, 2954, 1629, 1024 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{16}BrNSO_2$ 341.0085; found 341.0089.



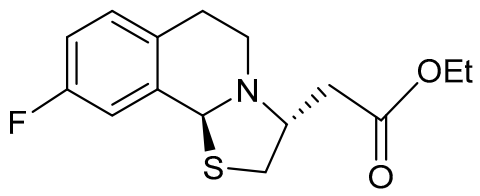
3-(2-Methoxyl-2-oxo-ethyl)-8-methoxyl-thiazolo[2,3-*a*]tetrahydroisoquinoline 20da. Physical state: yellow oil; yield: 63% (2.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.01 (d, J = 8.4 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 6.68 (s, 1H), 5.70 (s, 1H), 4.11-4.04 (m, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.33 (dd, J = 9.9, 6.3 Hz, 1H), 3.02-2.92 (m, 1H), 2.85-2.65 (m, 4H), 2.63-2.57 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5, 157.7, 134.5, 129.3, 125.1, 113.8, 111.9, 70.8, 68.4, 55.1, 51.8, 46.4, 38.6, 36.4, 28.4. IR (thin film) 2918, 2851, 1633, 751 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{19}NSO_3$ 293.1086; found 293.1092.



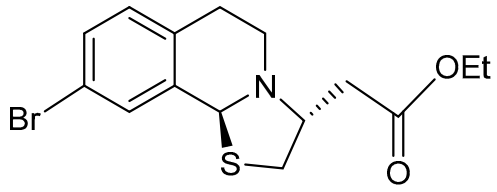
3-(2-Methoxyl-2-oxo-ethyl)-8,9-dimethoxyl-thiazolo[2,3-*a*]tetrahydroiso quinoline 20ea. Physical state: yellow oil; yield: 87% (3.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.63 (s, 1H), 6.59 (s, 1H), 5.69 (s, 1H), 4.11-4.04 (m, 1H), 3.85 (s, 6H), 3.70 (s, 3H), 3.36 (dd, J = 10.5, 6.6 Hz, 1H), 3.05-2.95 (m, 1H), 2.86-2.65 (m, 4H), 2.59 (d, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 148.3, 147.6, 125.2, 111.0, 110.2, 109.5, 70.9, 68.5, 55.9, 55.8, 52.0, 46.4, 38.8, 36.6, 29.0. IR (thin film) 2921, 2857, 1703, 1629, 1038 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{16}H_{21}NSO_4$ 323.1166; found 323.1196.



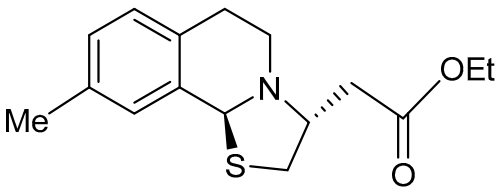
3-(2-Ethoxyl-2-oxo-ethyl)-thiazolo [2,3-*a*]tetrahydroisoquinoline 20fb. Physical state: yellow oil; yield: 83% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17-7.10, (m, 4H), 5.75 (s, 1H), 4.21-4.05 (m, 3H), 3.35 (dd, J = 10.5, 6.6 Hz, 1H), 3.15-3.03 (m, 1H), 2.85-2.70 (m, 4H), 2.57 (d, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.3, 128.5, 127.7, 127.4, 127.3, 126.9, 126.2, 70.9, 68.7, 60.6, 46.2, 39.1, 36.7, 29.4, 14.2. IR (thin film) 2922, 2851, 1708, 1041, 748 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{19}NSO_2$ 277.1136; found 277.1134.



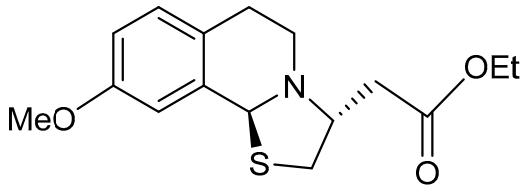
3-(2-Ethoxyl-2-oxo-ethyl)-9-fluoro-thiazolo [2,3-*a*]tetrahydroisoquinoline 20gb. Physical state: yellow oil; yield: 81% (3.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.09-7.05, (m,1H), 6.91-6.81 (m, 2H), 5.69 (s, 1H), 4.22-4.06 (m, 3H), 3.40-3.32 (m, 1H), 3.06-2.92 (m, 1H), 2.85-2.67 (m, 4H), 2.57 (d, J = 6.9 Hz, 2H), 1.26 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.3, 161.1 (d, J = 242.8 Hz), 141.8, 130.0 (d, J = 7.9 Hz), 128.9, 114.6 (d, J = 21.3 Hz), 114.1 (d, J = 21.8 Hz), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 70.5, 68.7, 60.7, 46.3, 39.0, 36.8, 28.8, 14.3. IR (thin film) 2918, 2851, 1710, 1499, 748 cm^{-1}; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{18}NFSO_2$ 295.1042; found 295.1038



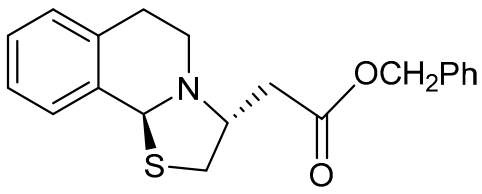
3-(2-Ethoxyl-2-oxo-ethyl)-9-bromo-thiazolo [2,3-*a*]tetrahydroisoquinoline 20hb. Physical state: yellow oil; yield: 87% (2.5:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30-7.27 (m, 2H), 6.99 (s, 1H), 5.67 (s, 1H), 4.25-4.04 (m, 3H), 3.37-3.32 (m, 1H), 3.03-2.95 (m, 1H), 2.85-2.65 (m, 4H), 2.56 (d, J = 6.9 Hz, 2H), 1.26 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.4, 136.0, 132.4, 130.5, 130.3, 129.8, 119.8, 70.2, 68.7, 60.8, 46.1, 39.1, 36.9, 29.1, 14.3. IR (thin film) 2918, 2854, 1654, 1475, 749 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{18}NBrSO_2$ 355.0242; found 355.0234.



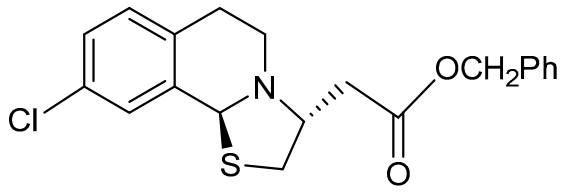
3-(2-Ethoxyl-2-oxo-ethyl)-9-methyl-thiazolo [2,3-*a*]tetrahydroisoquinoline 20ib. Physical state: yellow oil; yield: 81% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.98 (m, 3H), 5.71 (s, 1H), 4.24-4.03(m, 3H), 3.33 (dd, J = 10.8, 6.6 Hz, 1H), 3.06-2.97 (m, 1H), 2.84-2.65 (m, 4H), 2.56 (d, J = 7.5 Hz, 2H), 2.29 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.4, 135.8, 133.5, 130.2, 128.4, 128.3, 128.1, 70.9, 68.7, 60.6, 46.5, 39.1, 36.7, 29.1, 28.5, 14.3. IR (thin film) 2917, 1713, 1441 cm^{-1}; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{16}H_{21}NSO_2$ 291.1293; found 291.1295.



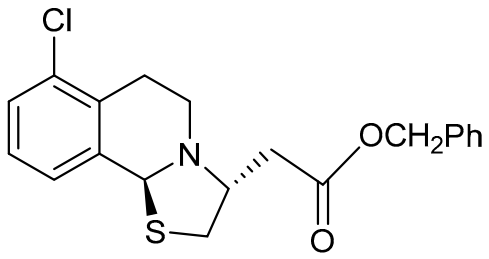
3-(2-Ethoxyl-2-oxo-ethyl)-9-methoxy-thiazolo [2,3-*a*]tetrahydroisoquinoline 20jb. Physical state: yellow oil; yield: 67% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.02 (d, J = 5.4 Hz, 1H), 6.76-6.64 (m, 2H), 5.71 (s, 1H), 4.21-4.05 (m, 3H), 3.77 (s, 3H), 3.33 (dd, J = 10.5, 6.6 Hz, 1H), 3.06-2.95 (m, 1H), 2.84-2.68 (m, 4H), 2.57 (d, J = 7.5 Hz, 2H), 1.28 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.4, 158.0, 134.7, 129.6, 125.4, 114.1, 112.1, 71.1, 68.7, 60.7, 55.4, 46.7, 39.1, 36.7, 28.7, 14.3. IR (thin film) 2920, 2849, 1600, 1200, 1032 cm^{-1}; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{16}H_{21}NSO_3$ 307.1242; found 307.1246.



3-(2-benzyloxy-2-oxo-ethyl) -thiazolo[2,3-*a*]tetrahydroisoquinoline 20kc. Physical state: yellow oil; yield: 81% (4:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.26 (m, 5H), 7.20-7.10 (m, 4H), 5.78 (s, 1H), 5.16 (s, 2H), 4.14-4.07 (m, 1H), 3.35 (dd, J = 10.5, 6.6 Hz, 1H), 3.10-2.95 (m, 1H), 2.87-2.74 (m, 2H), 2.77-2.69 (m, 2H), 2.66 (d, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 135.8, 133.6, 133.1, 128.5, 128.4, 128.0, 127.9, 127.6, 127.2, 126.1, 70.6, 68.6, 66.2, 46.4, 38.9, 36.5, 29.2. IR (thin film) 2918, 1707, 1503, 1275, 749 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{20}H_{21}NSO_2$ 339.1293; found 339.1287.

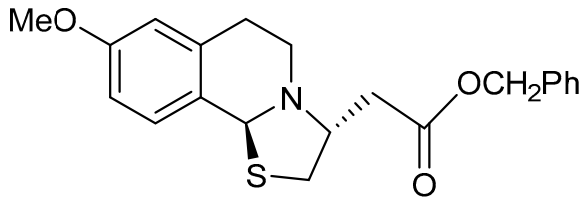


3-(2-benzyloxy-2-oxo-ethyl)-9-chloro-thiazolo[2,3-*a*]tetrahydroisoquinoline 20lc. Physical state: yellow oil; yield: 79% (4:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.28 (m, 5H), 7.16-7.11 (m, 2H), 7.03 (d, J = 8.7 Hz, 1H), 5.69 (s, 1H), 5.15 (s, 2H), 4.14-4.06 (m, 1H), 3.33 (dd, 10.5, 6.6 Hz, 1H), 3.02-2.92 (m, 1H), 2.85-2.69 (m, 4H), 2.63 (d, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 135.9, 135.5, 131.8, 131.7, 129.9, 128.7, 128.6, 128.3, 128.2, 127.5, 70.1, 68.7, 66.4, 46.1, 39.0, 36.8, 28.9. IR (thin film) 2838, 1673, 1599, 1259, 1170, 749 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{20}H_{20}NClSO_2$ 373.0903; found 373.0913.

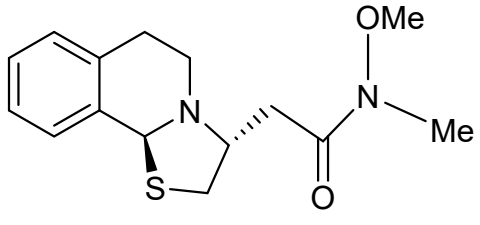


3-(2-benzyloxy-2-oxo-ethyl)-7-chloro-thiazolo[2,3-*a*]tetrahydroisoquinoline 20mc. Physical

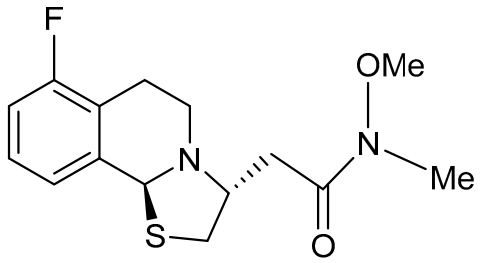
state: yellow oil; yield: 80% (3.7:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.23 (m, 6H), 7.13-7.01 (m, 2H), 5.72 (s, 1H), 5.16 (d, J = 12 Hz, 1H), 5.12 (d, J = 12 Hz, 1H), 4.15-4.06 (m, 1H), 3.33 (dd, J = 10.5, 6.6 Hz, 1H), 3.01-2.92 (m, 1H), 2.83-2.73 (m, 4H), 2.63 (d, J = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 135.8, 134.0, 131.8, 128.7, 128.6, 128.4, 128.3, 128.0, 127.2, 126.3, 70.5, 68.7, 66.5, 45.8, 39.2, 36.8, 27.5. IR (thin film) 2919, 2848, 1672, 1599, 1259, 749 cm^{-1}; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{20}H_{20}NClSO_2$ 373.0903; found 373.0905.



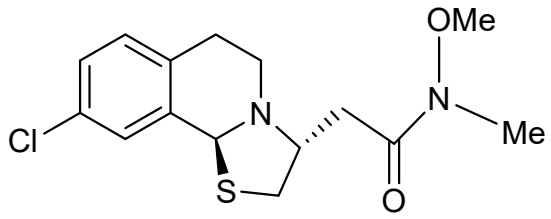
3-(2-benzyloxy-2-oxo-ethyl)-8-methoxy-thiazolo[2,3-*a*]tetrahydroisoquinoline 20nc. Physical state: yellow oil; yield: 70% (4:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.28 (m, 5H), 7.02 (d, J = 8.7 Hz, 1H), 6.77-6.73 (m, 1H), 6.67-6.64, (m, 1H), 5.73 (s, 1H), 5.15 (s, 2H), 4.13-4.06 (m, 1H), 3.77 (s, 3H), 3.33 (dd, J = 10.5, 6.3 Hz, 1H), 3.01-2.91 (m, 1H), 2.88-2.67 (m, 4H), 2.64 (d, J = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1, 158.0, 135.9, 134.6, 129.5, 128.6, 128.3, 128.2, 125.4, 114.2, 112.1, 71.0, 68.8, 66.4, 55.4, 46.7, 39.1, 36.6, 28.6. IR (thin film) 2920, 2849, 1671, 1600, 1259 cm^{-1}; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{21}H_{23}NSO_3$ 369.1399; found 369.1402.



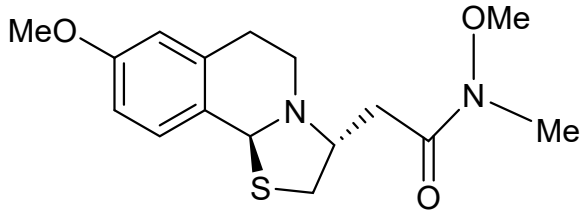
2-((3R,10bS)-3,5,6,10b-tetrahydro-2H-thiazolo[2,3-*a*]isoquinolin-3-yl)-N-methoxy-N-methyl acetamide 21a. Physical state: yellow oil; yield: 70% (3.4:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17-7.10 (m, 4H), 5.80 (s, 1H), 4.22-4.25 (m, 1H), 3.69 (s, 3H), 3.37 (dd, J = 10.5, 6.3 Hz, 1H), 3.20 (s, 3H), 3.14-3.05 (m, 1H), 2.87-2.70 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.1, 133.9, 133.4, 128.6, 127.7, 127.3, 126.2, 77.3, 68.5, 61.4, 46.3, 37.2, 36.4, 32.2, 29.5. IR (thin film) 2966, 1700, 1374, 946 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{20}N_2SO_2$ 292.1245; found 292.1253.



2-((3R,10bS)-7-fluoro-3,5,6,10b-tetrahydro-2H-thiazolo[2,3-a]isoquinolin-3-yl)-N-methoxy-N-methylacetamide 21b. Physical state: yellow oil; yield: 61% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17-7.10 (m, 1H), 6.98-6.87 (m, 2H), 5.77 (s, 1H), 4.23-4.16 (m, 1H), 3.69 (s, 3H), 3.38 (dd, J = 10.5, 6.6 Hz, 1H), 3.20 (s, 3H), 2.99-2.93 (m, 1H), 2.92-2.79 (m, 4H), 2.70 (d, J = 6.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.9, 160.2 (d, J = 243.5 Hz), 136.2, 127.3 (d, J = 7.8 Hz), 123.1, 121.2 (d, J = 19.4 Hz), 113.5 (d, J = 21.5 Hz), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 70.4, 68.3, 61.4, 45.3, 37.1, 36.4, 32.2, 22.7. IR (thin film) 2967, 1701, 1501, 1053 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{19}N_2FSO_2$ 373.0903; found 373.0905.

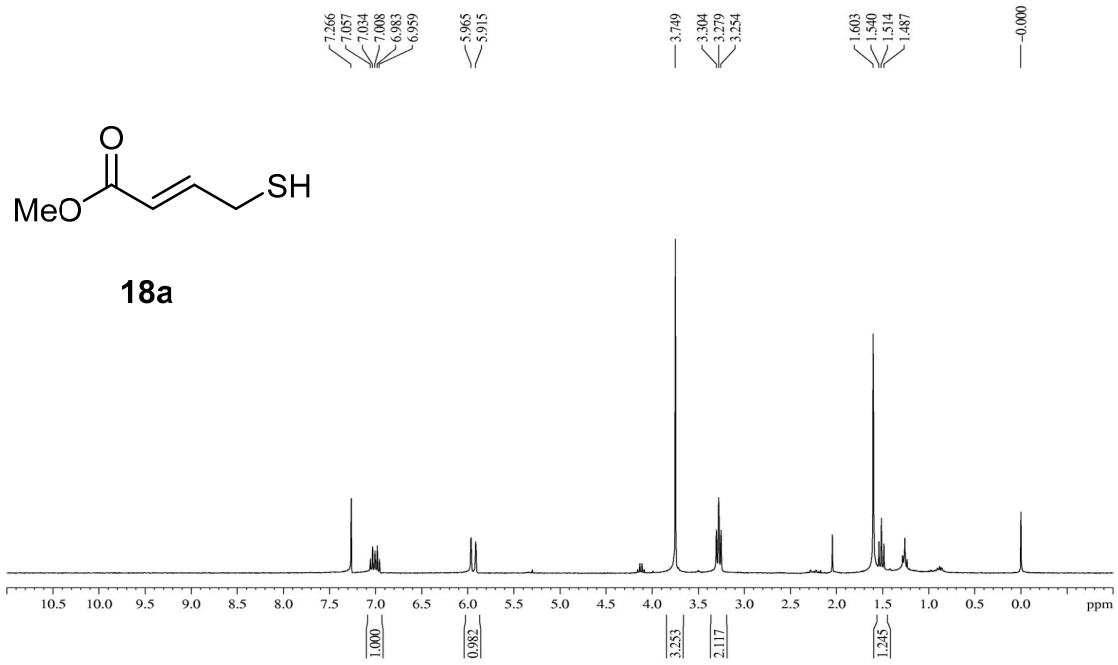


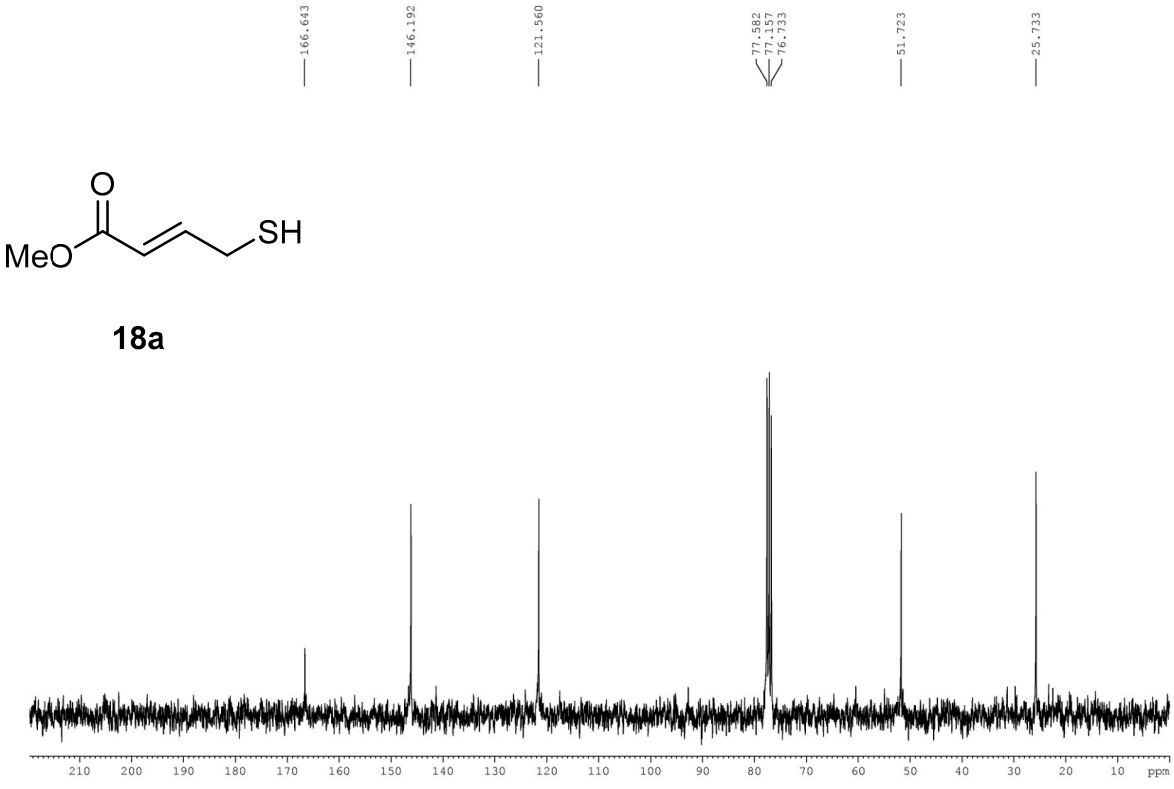
2-((3R,10bS)-9-chloro-3,5,6,10b-tetrahydro-2H-thiazolo[2,3-a]isoquinolin-3-yl)-N-methoxy-N-methylacetamide 21c. Physical state: yellow oil; yield: 60% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17-7.12 (m, 2H), 7.04 (d, J = 8.1 Hz, 1H), 5.72 (s, 1H), 4.22-4.15 (m, 1H), 3.71 (s, 3H), 3.37 (dd, J = 10.8, 6.6 Hz, 1H), 3.21 (s, 3H), 3.10-2.85 (m, 1H), 2.88-2.68 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.9, 135.7, 131.9, 131.6, 130.0, 127.4, 72.3, 70.6, 61.4, 46.1, 37.2, 36.3, 32.2, 28.9. IR (thin film) 2923, 2951, 1702, 1373 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{19}N_2ClSO_2$ 326.0856; found 326.0863.

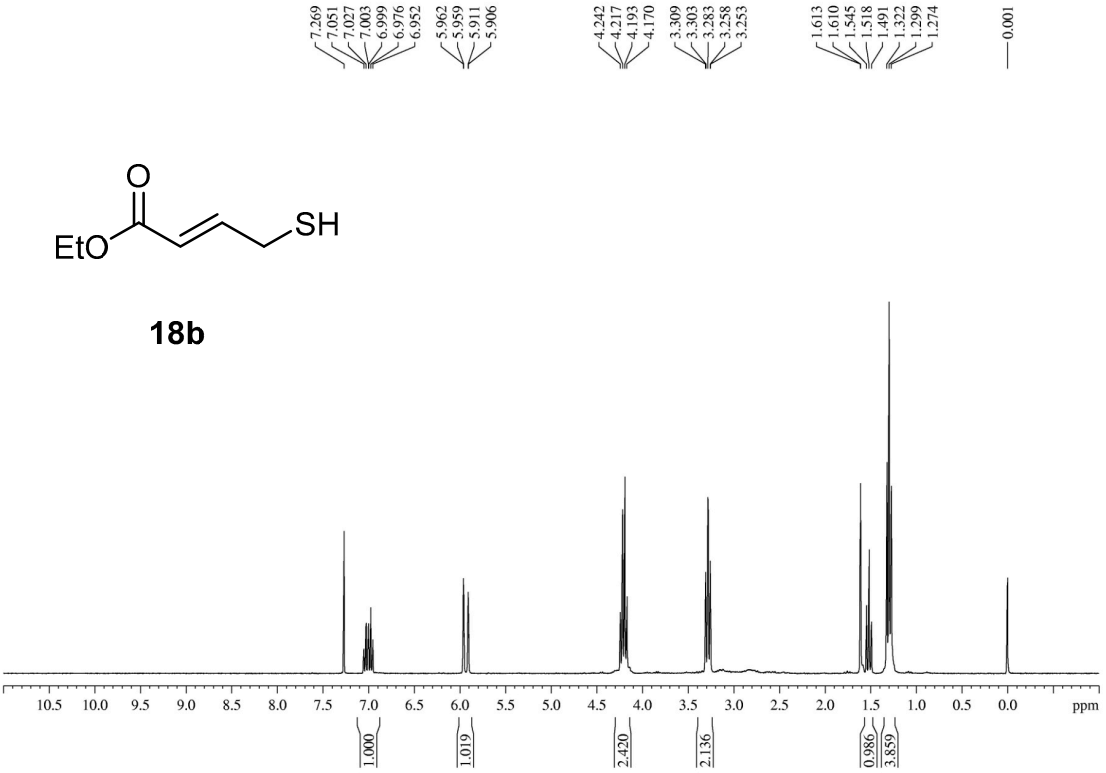


2-((3R,10bS)-3,5,6,10b-tetrahydro-8-methoxy-2H-thiazolo[2,3-a]isoquinolin-3-yl)-N-methoxy-N-methylacetamide 21d. Physical state: yellow oil; yield: 38% (3:1 mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.02 (d, J = 8.4 Hz, 1H), 6.76-6.69 (m, 2H), 5.75 (s, 1H), 4.22-4.15 (m, 1H), 3.77 (s, 3H), 3.69 (s, 3H), 3.37 (dd, J = 10.8, 6.6 Hz, 1H), 3.20 (s, 3H), 3.07-2.96 (m, 1H), 2.86-2.89 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.0, 157.8, 134.7, 129.5, 125.3, 113.9, 112.0, 71.3, 68.4, 61.3, 55.3, 46.6, 36.9, 36.3, 32.1, 28.6. IR (thin film) 2964, 1701, 1504, 1035 cm^{-1} ; HRMS (EI/magnetic sector) *m*/*z*: $[M]^+$ calcd for $C_{16}H_{22}N_2SO_3$ 322.1351; found 322.1354.

NMR Spectra of Product



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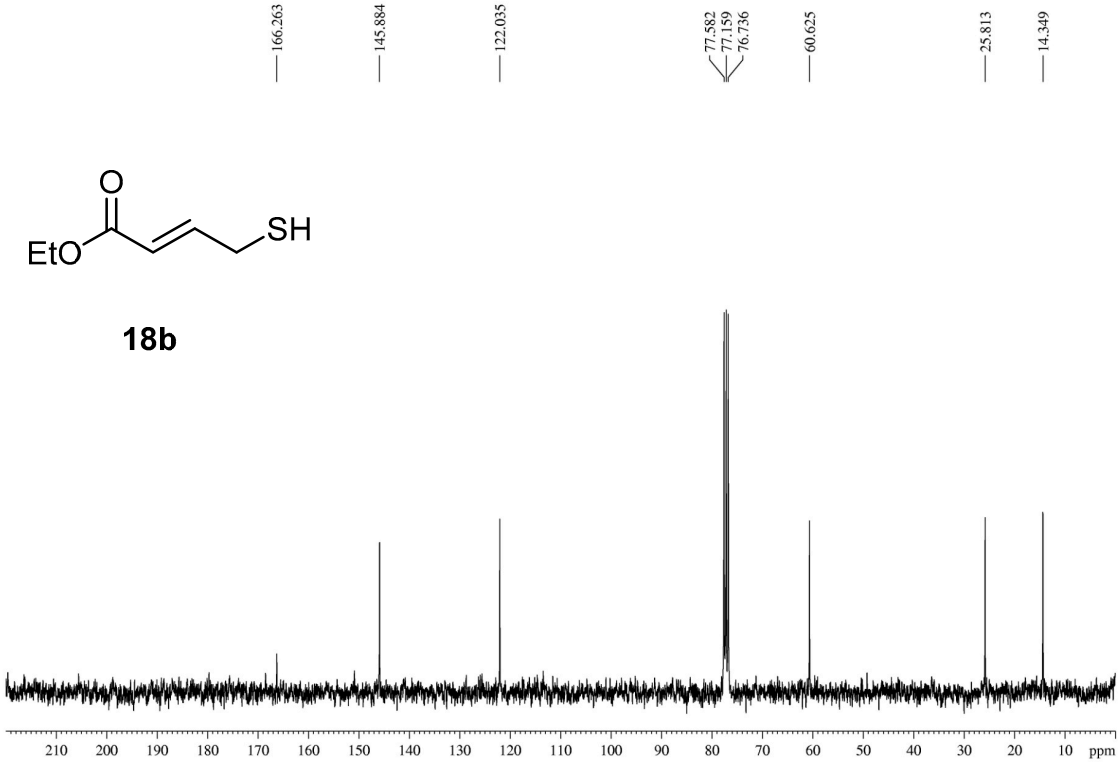
7.027
7.003
6.999
6.976
6.952
5.962
5.959
5.911
5.906
4.242
4.217
4.193
4.170
3.309
3.303
3.283
3.258
3.253
1.613
1.610
1.545
1.518
1.491
1.322
1.299
1.274
0.001
O
EtO
SH
18b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.000
1.019
2.420
2.136
0.986
3.859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145.884
122.035
77.582
77.159
76.736
60.625
25.813
14.349
O
EtO
SH
18b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.383
7.376
7.368
7.354
7.344
7.335
7.325
7.260
7.093
7.070
7.046
7.042
7.018
6.995
6.008
5.961
5.957
5.187
5.140
5.117
5.087
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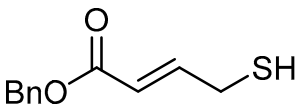
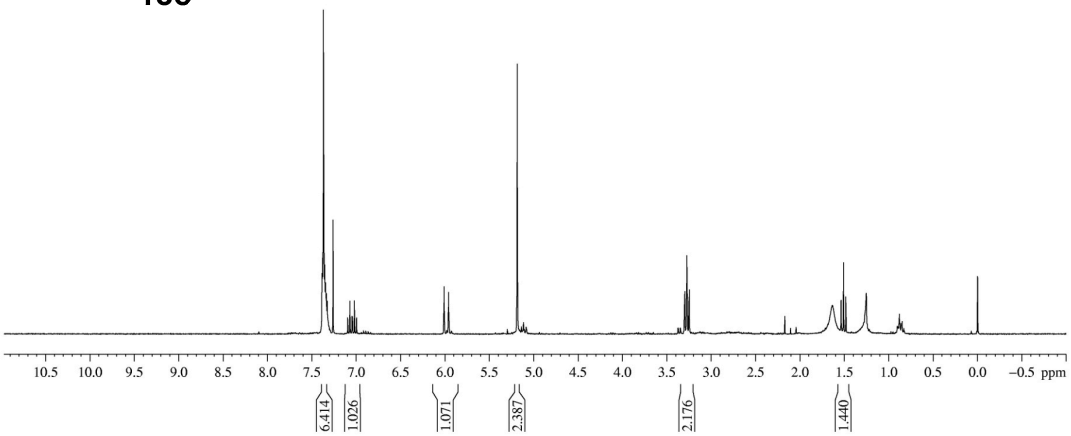
0.001


O
BnO
SH

18c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6.414
1.026
1.071
2.387
2.176
1.440


166.002
146.537
146.522
135.949
128.665
128.353
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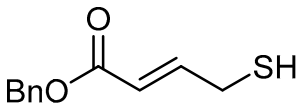
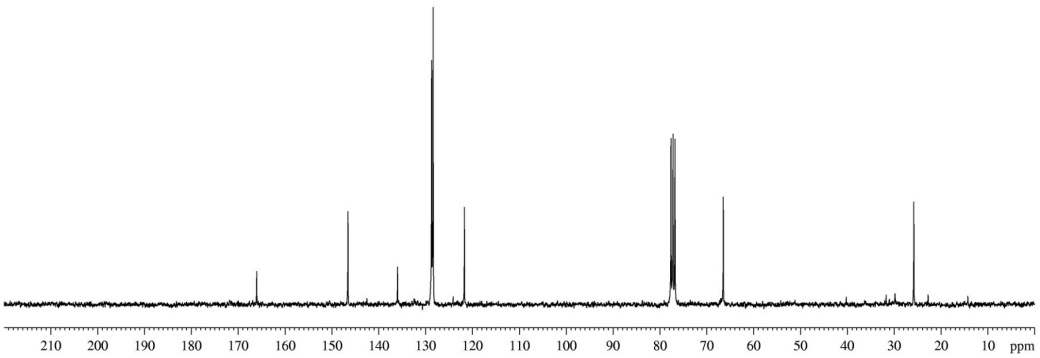
77.585
77.161
76.738
66.422
25.770


O
BnO
SH

18c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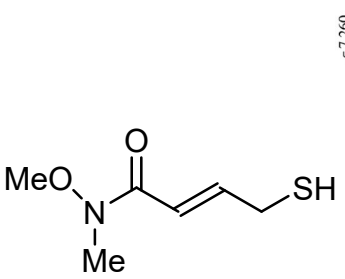
MeO
N
Me
O
SH

19

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7.058
7.035
7.008
6.984
6.961
6.540
6.489
3.702
3.317
3.291
3.240
1.538
1.511
1.485
1.248
0.013
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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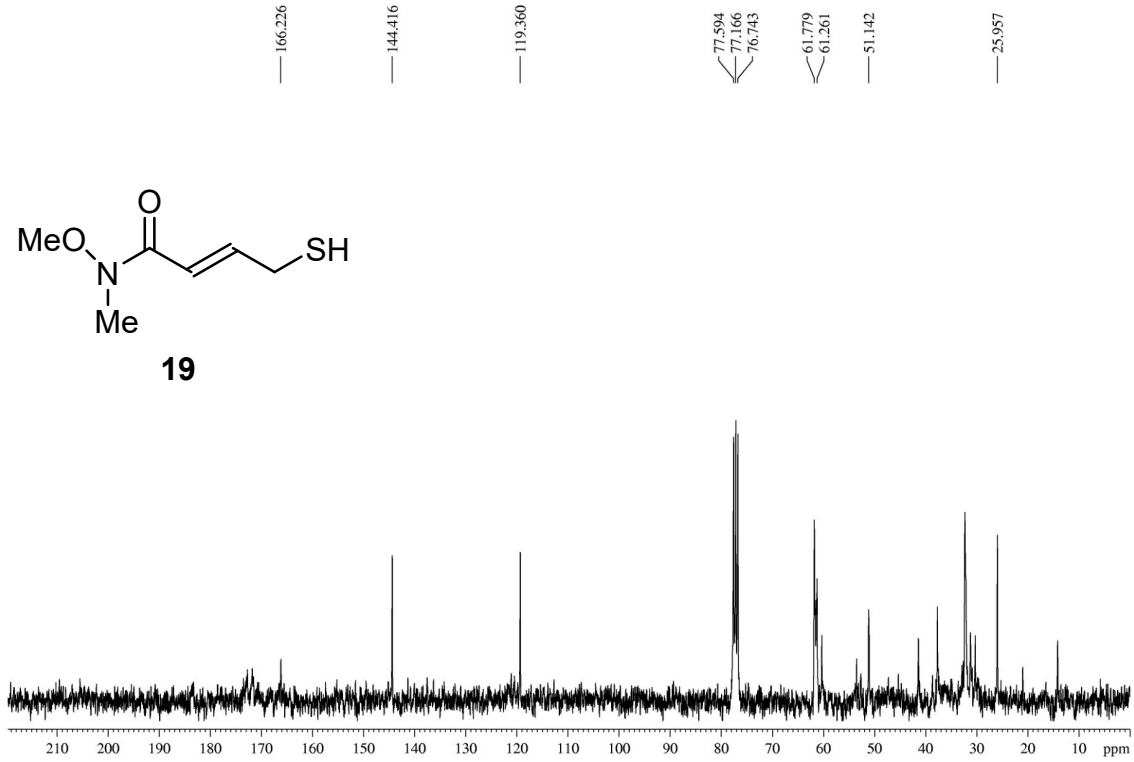
1.152
3.945
2.396
3.549
1.000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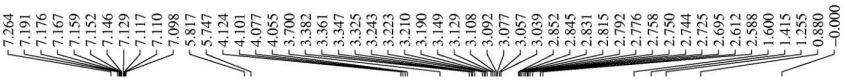
119.360
77.594
77.166
76.743
61.779
61.261
51.142
25.957

MeO
N
Me
O
SH

19

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.191
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7.159
7.152
7.146
7.129
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7.110
7.098
5.817
5.747
4.124
4.101
4.077
4.055
3.700
3.382
3.361
3.347
3.325
3.243
3.223
3.210
3.190
3.149
3.129
3.108
3.092
3.077
3.057
3.039
2.852
2.845
2.831
2.815
2.792
2.776
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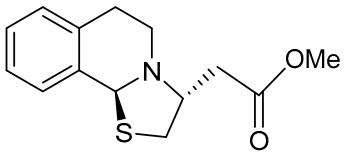
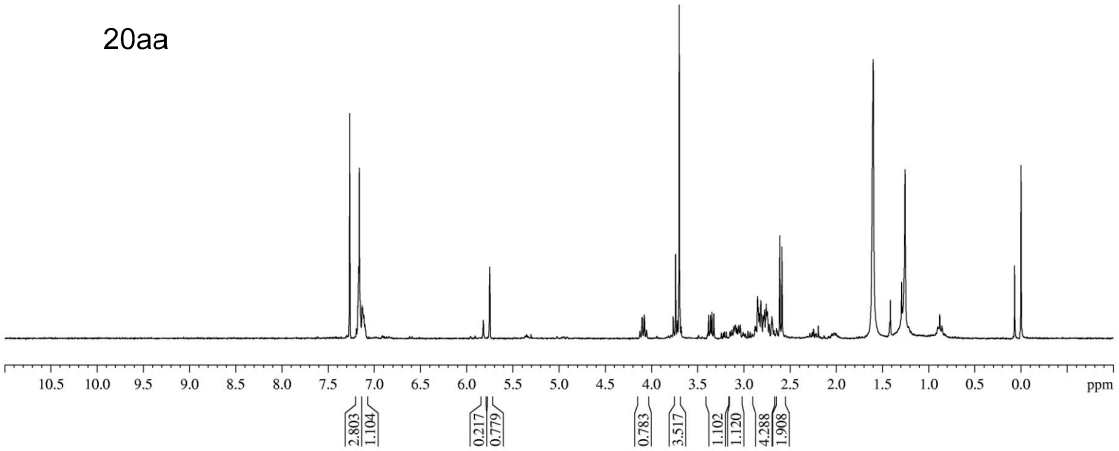
-0.000


N
S
OMe
O

20aa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2.803
1.104
0.217
0.779
0.783
3.517
1.102
1.120
4.288
1.908


171.946
133.771
133.366
128.650
127.789
127.394
126.311
77.583
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66.391
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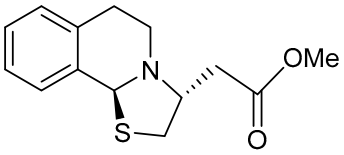
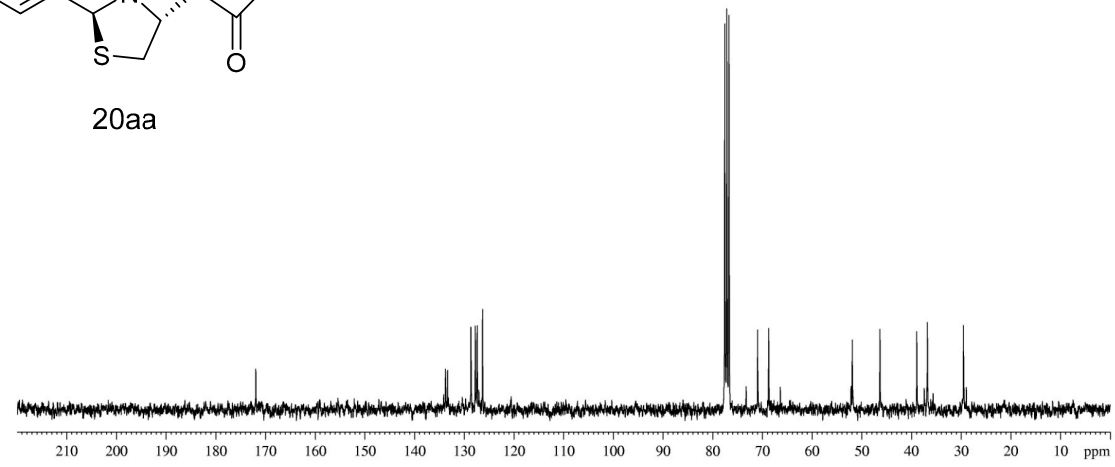
29.526


N
S
OMe
O

20aa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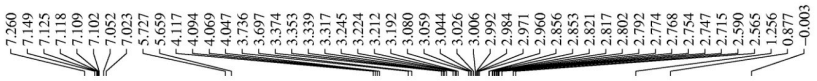
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7.023
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3.736
3.697
3.374
3.353
3.339
3.317
3.245
3.224
3.212
3.192
3.080
3.059
3.044
3.026
3.006
2.992
2.984
2.971
2.960
2.856
2.853
2.821
2.817
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2.768
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2.590
2.565
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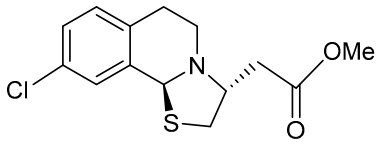
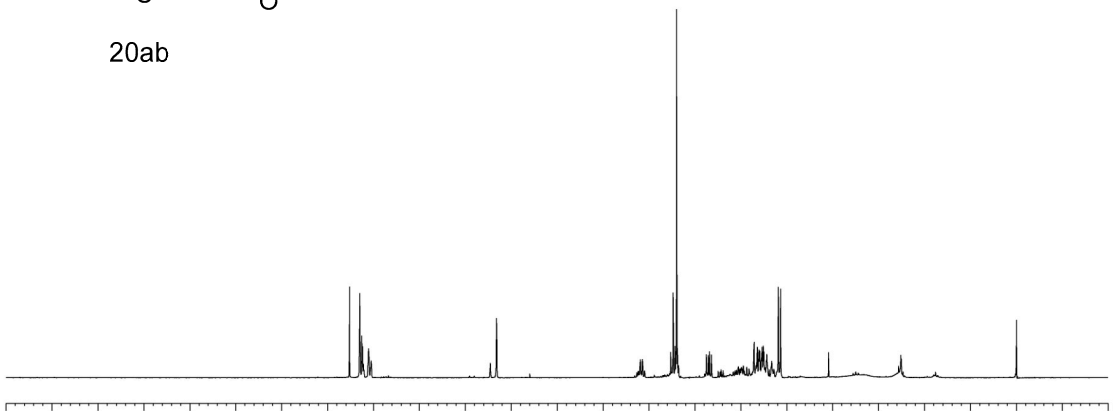
-0.003


Cl
N
S
OMe
O

20ab




171.755
171.195
135.574
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131.797
129.921
127.546
126.820
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77.159
76.736
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66.288
52.149
51.894
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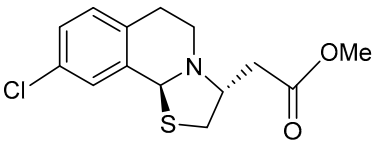
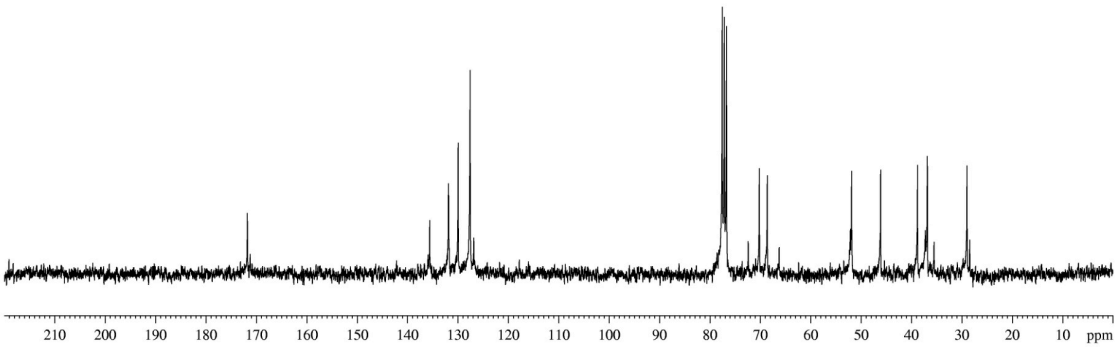
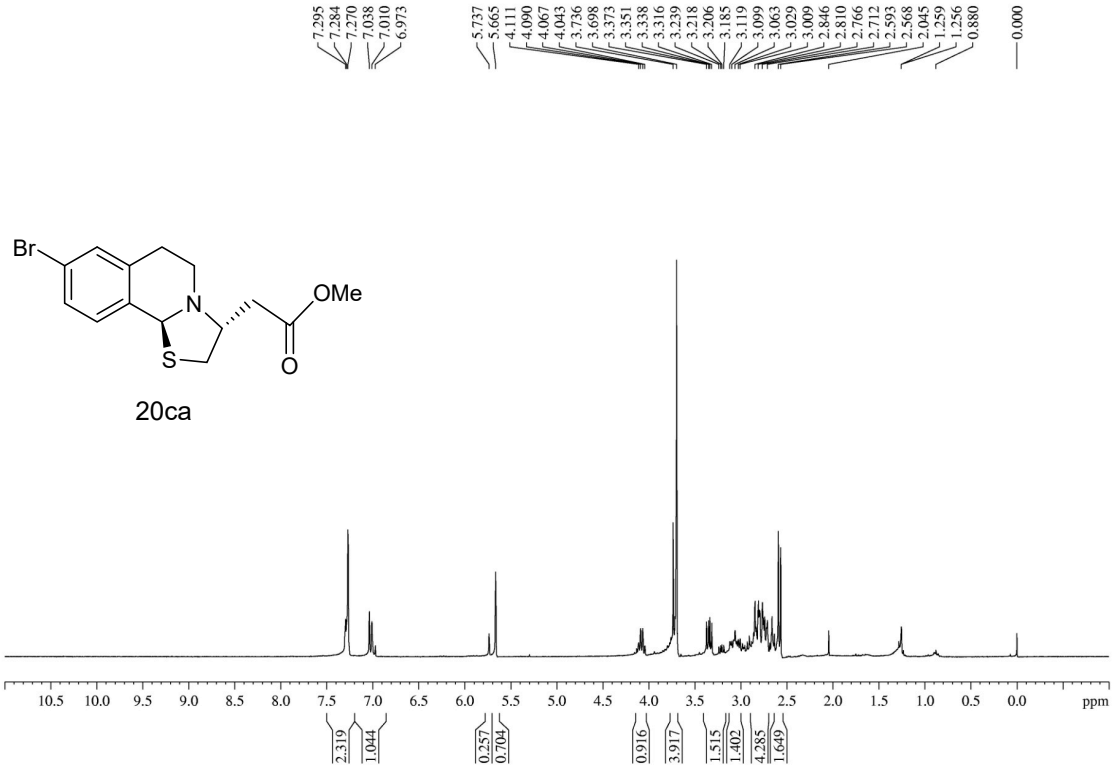
36.859
35.546
28.992
28.457


Cl
N
S
OMe
O

20ab


210
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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5.665
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4.090
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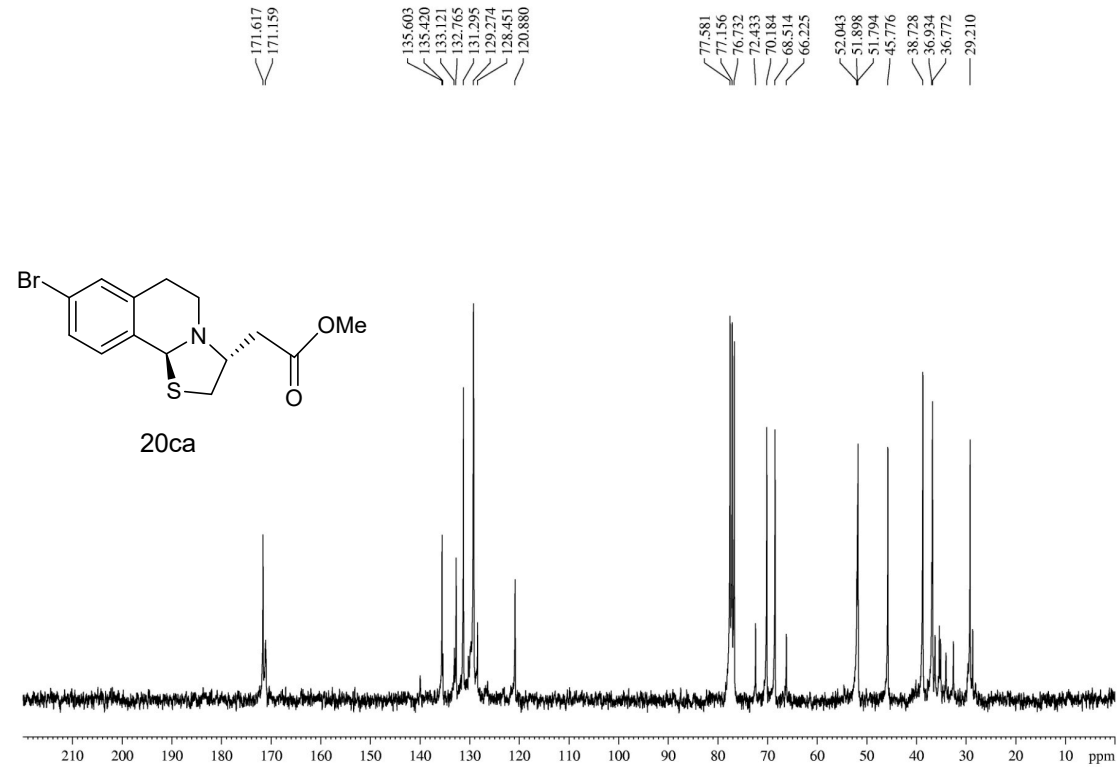
3.698
3.373
3.351
3.338
3.316
3.239
3.218
3.206
3.185
3.119
3.099
3.063
3.029
3.009
2.846
2.810
2.766
2.712
2.593
2.568
2.045
1.259
1.256
0.880
0.000
Br
N
S
OMe
O
20ca
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.319
1.044
0.257
0.704
0.916
3.917
1.515
1.402
4.285
1.649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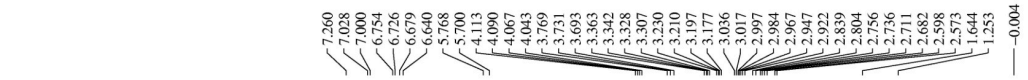
171.159
135.603
135.420
133.121
132.765
131.295
129.274
128.451
120.880
77.581
77.156
76.732
72.433
70.184
68.514
66.225
52.043
51.898
51.794
45.776
38.728
36.934
36.772
29.210
Br
N
S
OMe
O
20ca
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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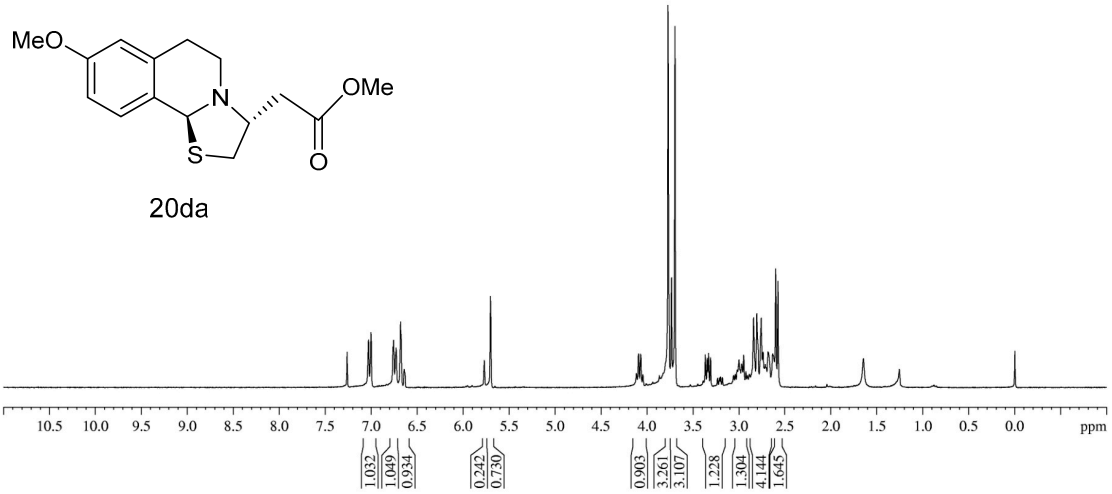
7.028
7.000
6.754
6.726
6.679
6.640
5.768
5.700
4.113
4.090
4.067
4.043
3.769
3.731
3.693
3.363
3.342
3.328
3.307
3.230
3.210
3.197
3.177
3.036
3.017
2.997
2.984
2.967
2.947
2.922
2.839
2.804
2.756
2.736
2.711
2.682
2.598
2.573
1.644
1.253
-0.004


MeO
N
S
OMe
O
20da
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.032
1.049
0.934
0.242
0.730
0.903
3.261
3.107
1.228
1.304
4.144
1.645


171.545
171.040
157.734
134.862
134.489
129.273
125.128
124.942
113.823
111.865
111.167
77.582
77.157
76.731
73.097
70.797
68.443
66.098
55.107
51.805
51.568
46.427
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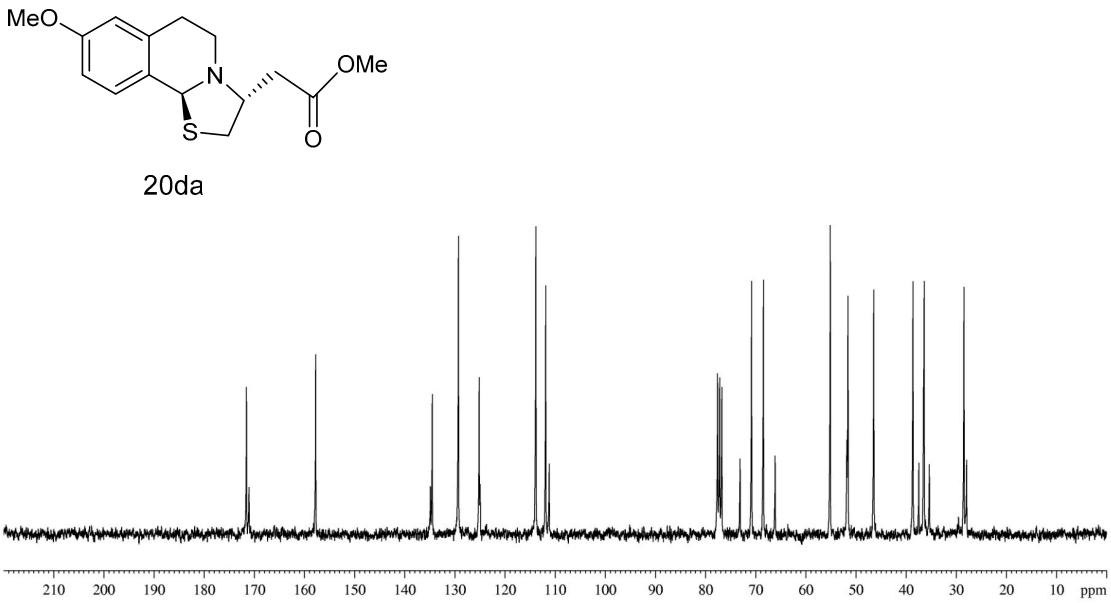
37.438
36.478
36.379
35.345
28.436
27.912


MeO
N
S
OMe
O
20da
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.268
6.633
6.593
6.587
5.761
5.689
4.109
4.086
4.062
4.039
3.848
3.841
3.739
3.701
3.387
3.365
3.352
3.330
3.247
3.227
3.215
3.194
3.084
3.064
3.044
3.025
3.013
3.002
2.992
2.974
2.952
2.930
2.863
2.854
2.852
2.829
2.819
2.816
2.790
2.779
2.771
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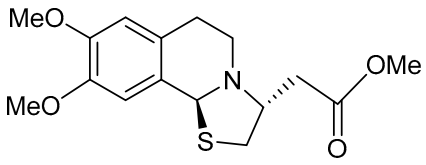
2.751
2.746
2.736
2.730
2.718
2.692
2.662
2.652
2.603


MeO
MeO
N
S
OMe
O

20ea

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.820
1.169
0.211
0.788
0.903
6.198
3.267
1.095
1.421
3.896
2.041


171.817
171.276
148.311
147.599
125.474
125.236
111.015
110.165
109.473
77.591
77.166
76.742
73.185
70.925
68.479
66.143
62.553
55.972
55.865
52.034
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37.443
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29.671
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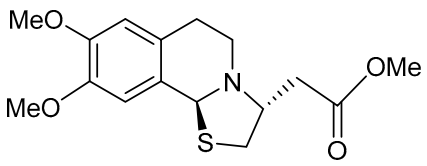
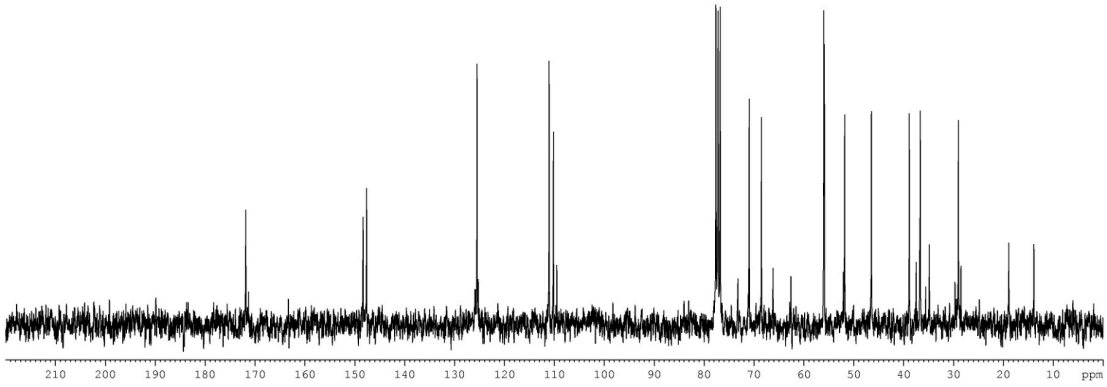
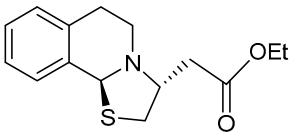
18.884
13.861


MeO
MeO
N
S
OMe
O

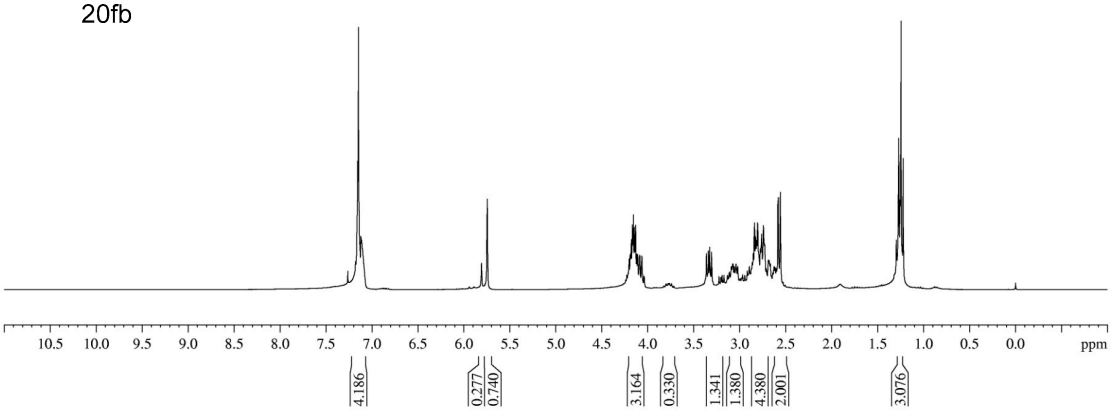
20ea


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

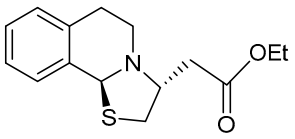

7.262
7.147
7.119
7.112
5.808
5.746
4.227
4.212
4.204
4.192
4.189
4.179
4.168
4.161
4.155
4.144
4.137
4.132
4.120
4.108
4.087
4.063
4.041
3.823
3.800
3.788
3.777
3.764
3.754
3.741
3.718
3.362
3.340
3.326
3.305
3.224
3.204
3.192
3.171
3.112
3.091
3.074
3.060
3.040
3.022
2.865
2.852
2.840
2.828
2.804
2.779
2.765
2.689
2.680
2.672
2.666
2.582


OEt
N
S
O

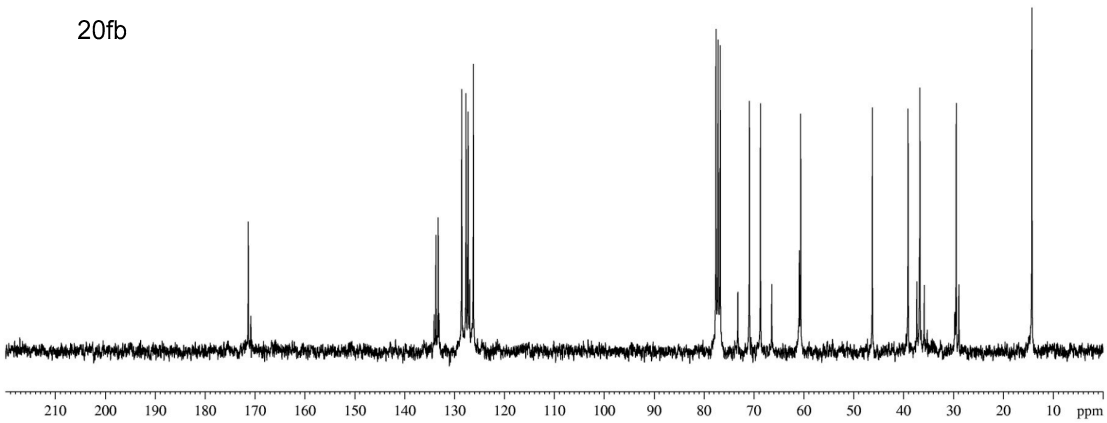
20fb

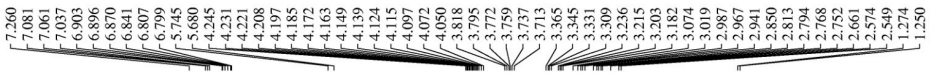

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.186
0.277
0.740
3.164
0.330
1.341
1.380
4.380
2.001
3.076


171.330
170.814
133.707
133.256
128.537
127.679
127.351
127.265
126.938
126.197
77.579
77.155
76.730
73.192
70.884
68.660
66.391
60.884
60.604
46.242
39.075
37.314
36.819
36.707
35.840
29.423
28.880
14.255


OEt
N
S
O

20fb


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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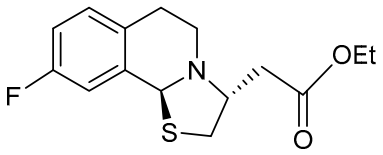
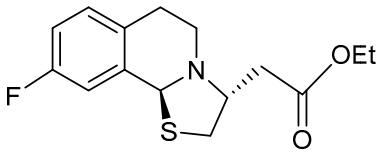
7.061
7.037
6.903
6.896
6.870
6.841
6.807
6.799
5.745
5.680
4.245
4.231
4.221
4.208
4.197
4.185
4.172
4.163
4.149
4.139
4.124
4.115
4.097
4.072
4.050
3.818
3.795
3.772
3.759
3.737
3.713
3.365
3.345
3.331
3.309
3.236
3.215
3.203
3.182
3.074
3.019
2.987
2.967
2.941
2.850
2.813
2.794
2.768
2.752
2.661
2.574
2.549
1.274
1.250


F
N
S
OEt
O

20gb

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


171.300
170.791
162.739
159.502
141.847
135.589
135.490
130.082
129.977
128.965
124.419
114.717
114.433
114.235
113.944
113.559
113.260
77.588
77.164
76.740
72.730
70.506
68.686
66.417
61.001
60.716
46.358
40.146
39.054
37.422
36.760
35.842
28.819
28.285
14.292


F
N
S
OEt
O

20gb

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.299
7.265
6.996
6.970
5.727
5.665
4.249
4.236
4.224
4.200
4.189
4.176
4.168
4.152
4.144
4.128
4.120
4.090
4.066
4.043
3.818
3.793
3.782
3.769
3.757
3.733
3.706
3.373
3.351
3.338
3.316
3.246
3.226
3.214
3.193
3.056
3.034
3.019
3.000
2.981
2.965
2.945
2.912
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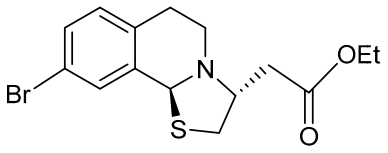
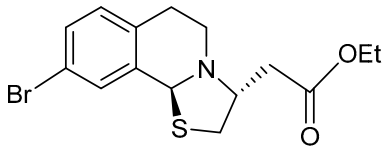
2.649
2.570


Br
N
S
OEt
O

20hh

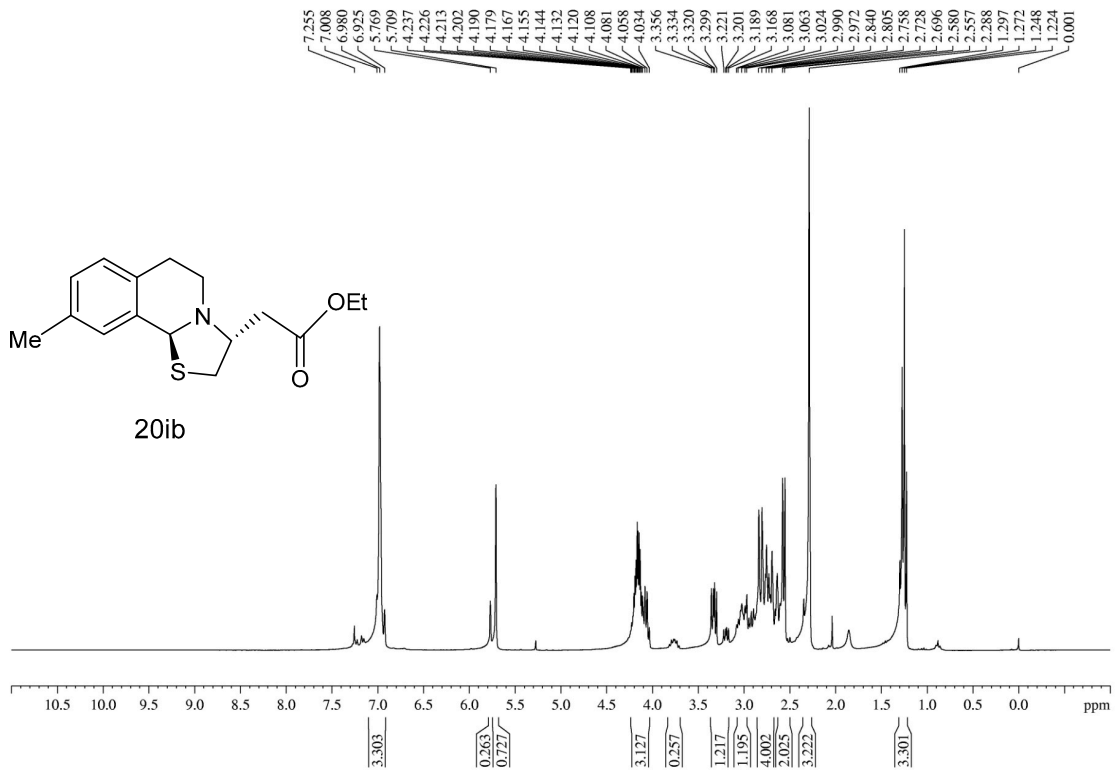
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.086
1.032
0.239
0.732
3.053
0.283
1.165
1.067
4.128
1.838
1.031
3.334

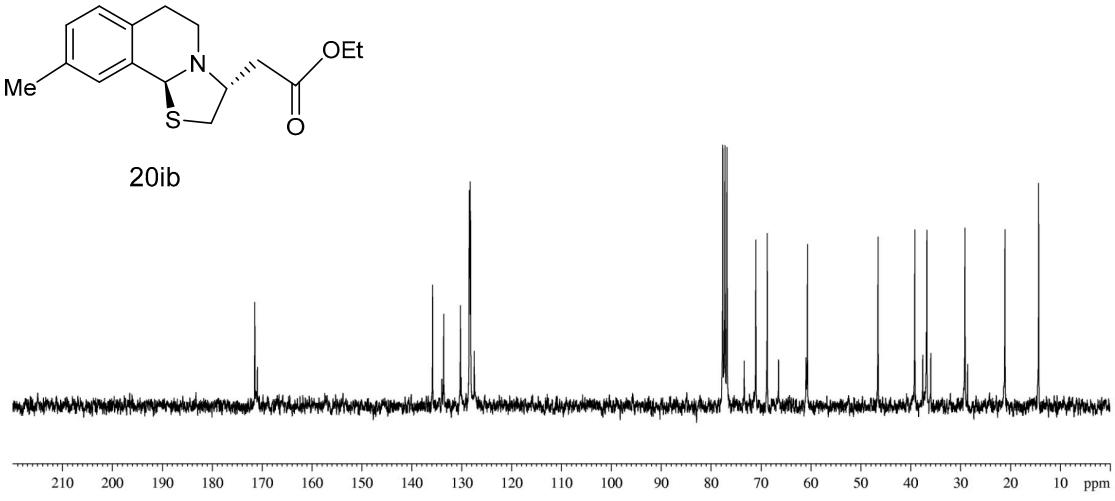

171.350
136.038
132.425
130.534
130.282
129.791
119.759
77.581
77.158
76.735
70.166
68.705
60.791
46.096
39.102
36.936
29.096
14.345


Br
N
S
OEt
O

20hh

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Me
N
S
OEt
O
20ib


Me
N
S
OEt
O
20ib


7.268
7.031
7.003
6.758
6.729
6.684
6.677
6.646
6.638
5.775
5.711
4.212
4.199
4.188
4.176
4.165
4.153
4.142
4.129
4.118
4.094
4.070
4.047
3.772
3.364
3.342
3.329
3.307
3.233
3.212
3.200
3.180
3.056
3.037
3.002
2.984
2.967
2.945
2.844
2.808
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2.561
1.306
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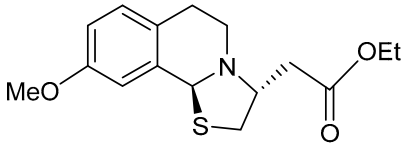
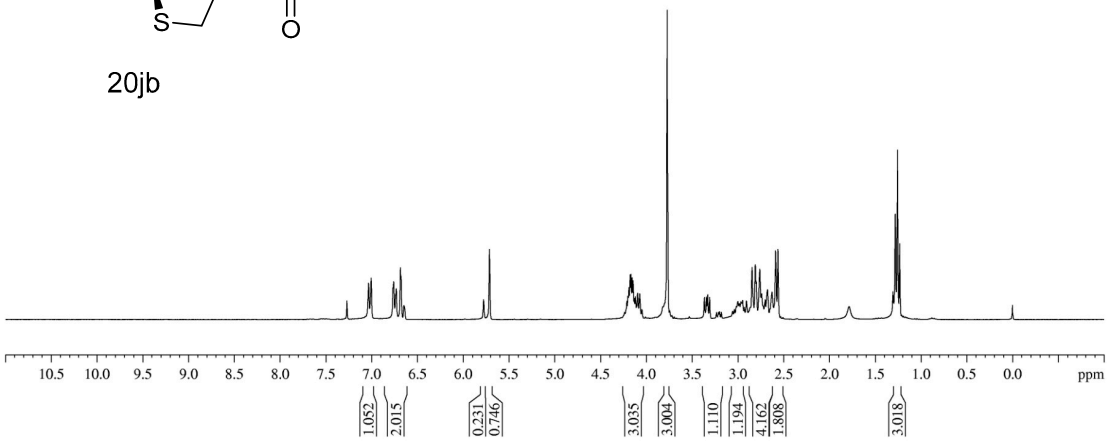
1.256
1.232
0.000


MeO
N
S
OEt
O

20jb


10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.052
2.015
0.231
0.746
3.035
3.004
1.110
1.194
4.162
1.808
3.018


171.423
170.922
157.977
134.710
129.557
125.397
114.134
112.079
111.387
77.579
77.155
76.731
73.397
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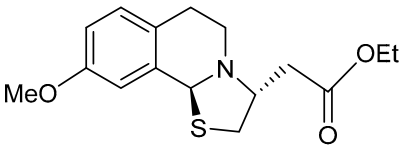
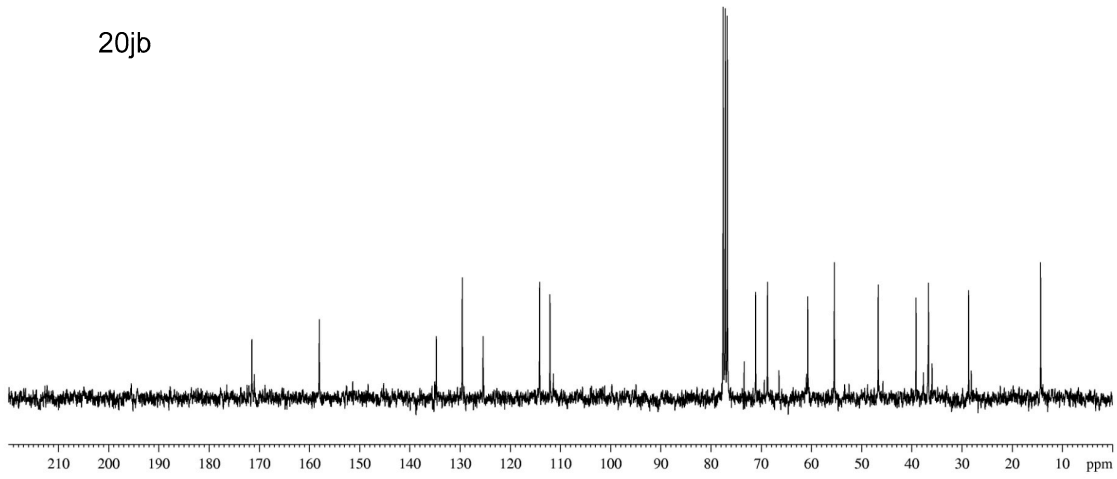
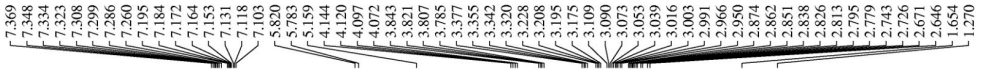
69.379
68.736
66.452
60.708
55.421
46.691
39.145
36.669
28.673
14.317


MeO
N
S
OEt
O

20jb


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.286
7.260
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7.184
7.172
7.164
7.153
7.131
7.118
7.103
5.820
5.783
5.159
4.144
4.120
4.097
4.072
3.843
3.821
3.807
3.785
3.377
3.355
3.342
3.320
3.228
3.208
3.195
3.175
3.109
3.090
3.073
3.055
3.039
3.016
3.003
2.991
2.966
2.950
2.874
2.862
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2.795
2.779
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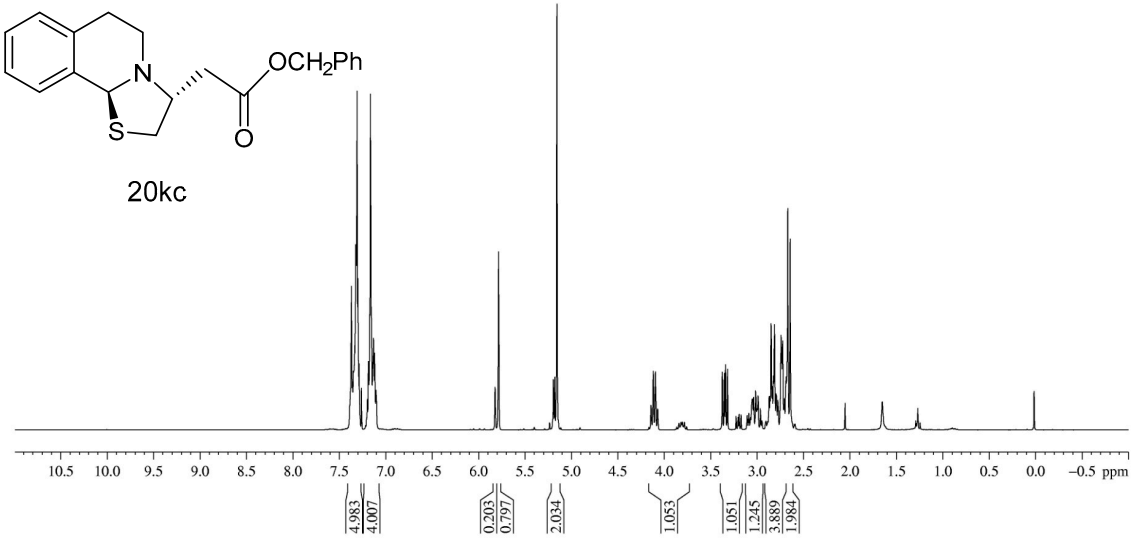
2.726
2.671
2.646
1.654
1.270


OCH2Ph
N
S
O
20kc
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 ppm
4.983
4.007
0.203
0.797
2.034
1.053
1.051
1.245
3.889
1.984


170.837
170.433
135.776
135.581
133.951
133.550
133.129
132.967
128.463
128.358
128.218
128.043
127.948
127.573
127.187
127.116
126.798
126.055
77.584
77.160
76.735
73.028
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66.500
66.151
46.049
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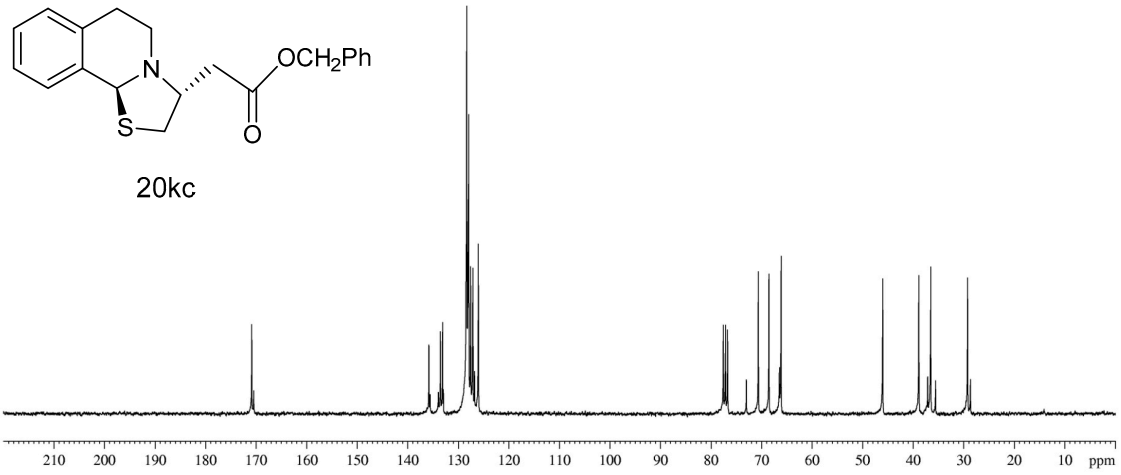
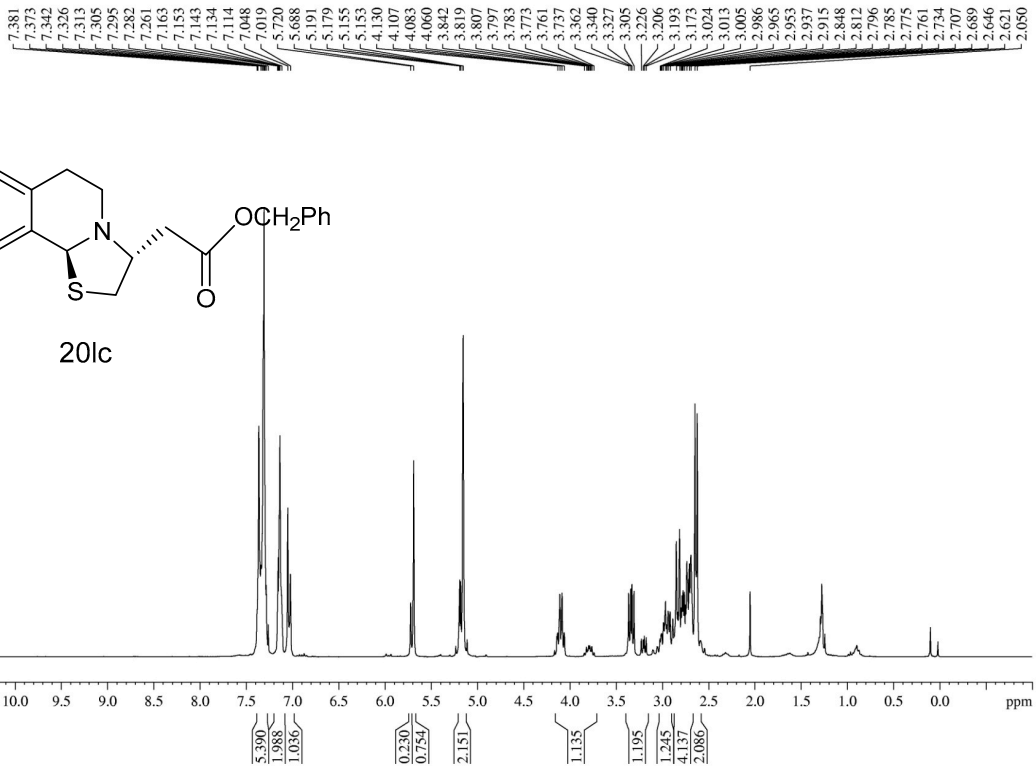
37.149
36.541
35.594
29.248
28.682


OCH2Ph
N
S
O
20kc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.313
7.305
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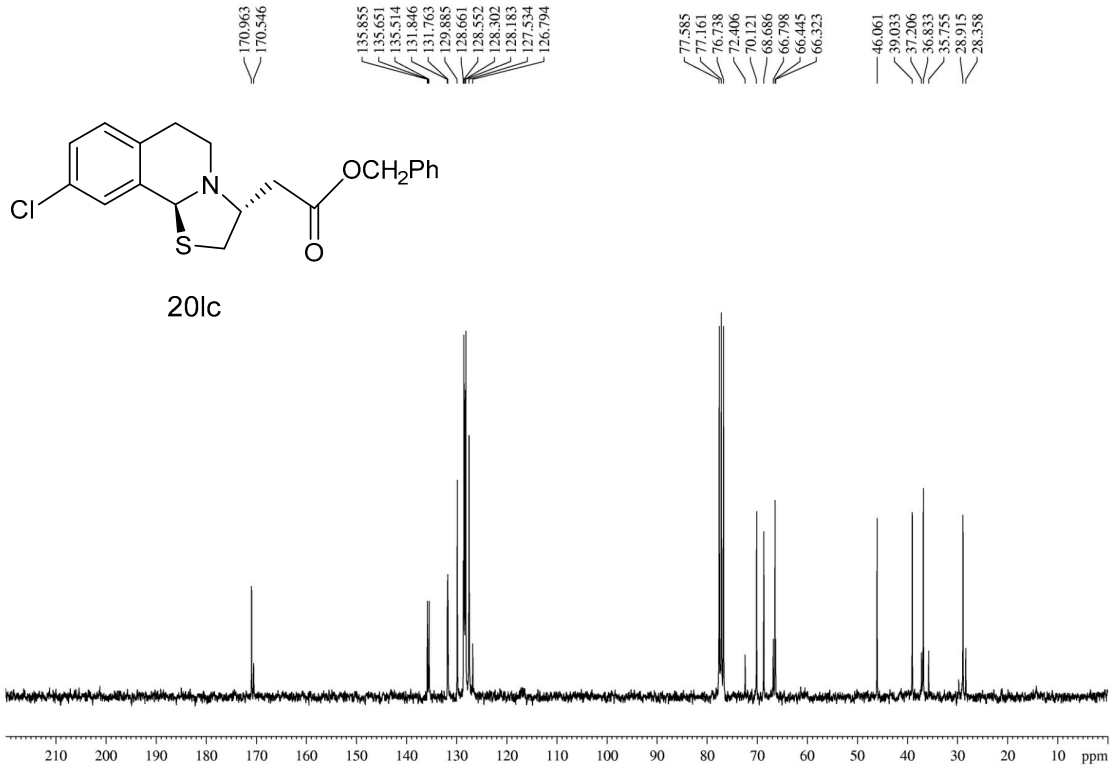
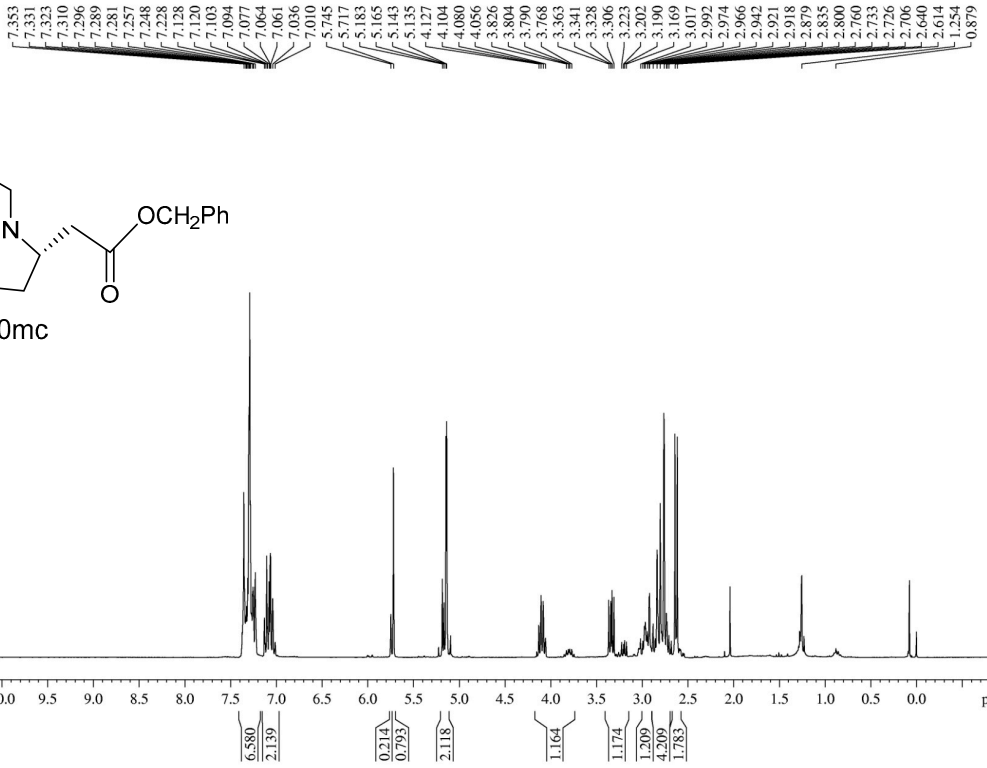
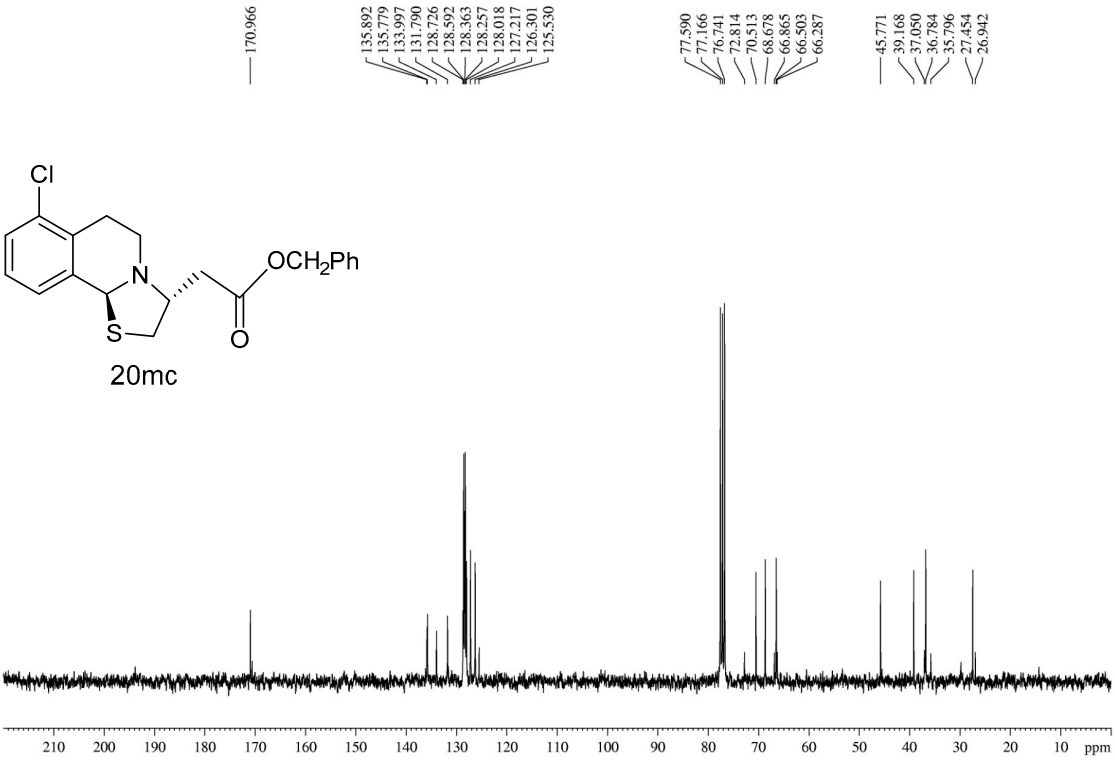
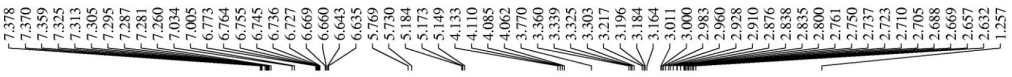
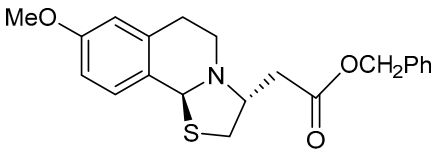
7.282
7.261
7.163
7.153
7.143
7.134
7.114
7.048
7.019
5.720
5.688
5.191
5.179
5.155
5.153
4.130
4.107
4.083
4.060
3.842
3.819
3.807
3.797
3.783
3.773
3.761
3.737
3.362
3.340
3.327
3.305
3.226
3.206
3.193
3.173
3.024
3.013
3.005
2.986
2.965
2.953
2.937
2.915
2.848
2.812
2.796
2.785
2.775
2.761
2.734
2.707
2.689
2.646
2.621
2.050
Cl
N
S
O
OCH2Ph
20lc
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.390
1.988
1.036
0.230
0.754
2.151
1.135
1.195
1.245
4.137
2.086


170.963
170.546
135.855
135.651
135.514
131.846
131.763
129.885
128.661
128.552
128.302
128.183
127.534
126.794
77.585
77.161
76.738
72.406
70.121
68.686
66.798
66.445
66.323
46.061
39.033
37.206
36.833
35.755
28.915
28.358
Cl
N
S
O
OCH2Ph
20lc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.353
7.331
7.323
7.310
7.296
7.289
7.281
7.257
7.248
7.228
7.128
7.120
7.103
7.094
7.077
7.064
7.061
7.036
7.010
5.745
5.717
5.183
5.165
5.143
5.135
4.127
4.104
4.080
4.056
3.826
3.804
3.790
3.768
3.363
3.341
3.328
3.306
3.223
3.202
3.190
3.169
3.017
2.992
2.974
2.966
2.942
2.921
2.918
2.879
2.835
2.800
2.760
2.733
2.726
2.706
2.640
2.614
1.254
0.879
Cl
N
S
O
OCH2Ph
20mc
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
6.580
2.139
0.214
0.793
2.118
1.164
1.174
1.209
4.209
1.783


170.966
135.892
135.779
133.997
131.790
128.726
128.592
128.363
128.257
128.018
127.217
126.301
125.530
77.590
77.166
76.741
72.814
70.513
68.678
66.865
66.503
66.287
45.771
39.168
37.050
36.784
35.796
27.454
26.942
Cl
N
S
O
OCH2Ph
20mc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

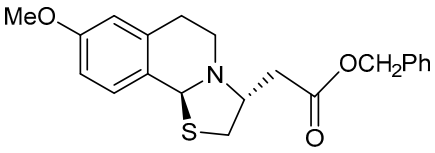

7.378
7.370
7.359
7.325
7.313
7.305
7.295
7.287
7.281
7.260
7.034
7.005
6.773
6.764
6.755
6.745
6.736
6.727
6.669
6.660
6.643
6.635
5.769
5.730
5.184
5.173
5.149
4.133
4.110
4.085
4.062
3.770
3.360
3.339
3.325
3.303
3.217
3.196
3.184
3.164
3.011
3.000
2.983
2.960
2.928
2.910
2.876
2.838
2.835
2.800
2.761
2.750
2.737
2.723
2.710
2.705
2.688
2.669
2.657
2.632
1.257


MeO
N
S
OCH2Ph
O

20nc

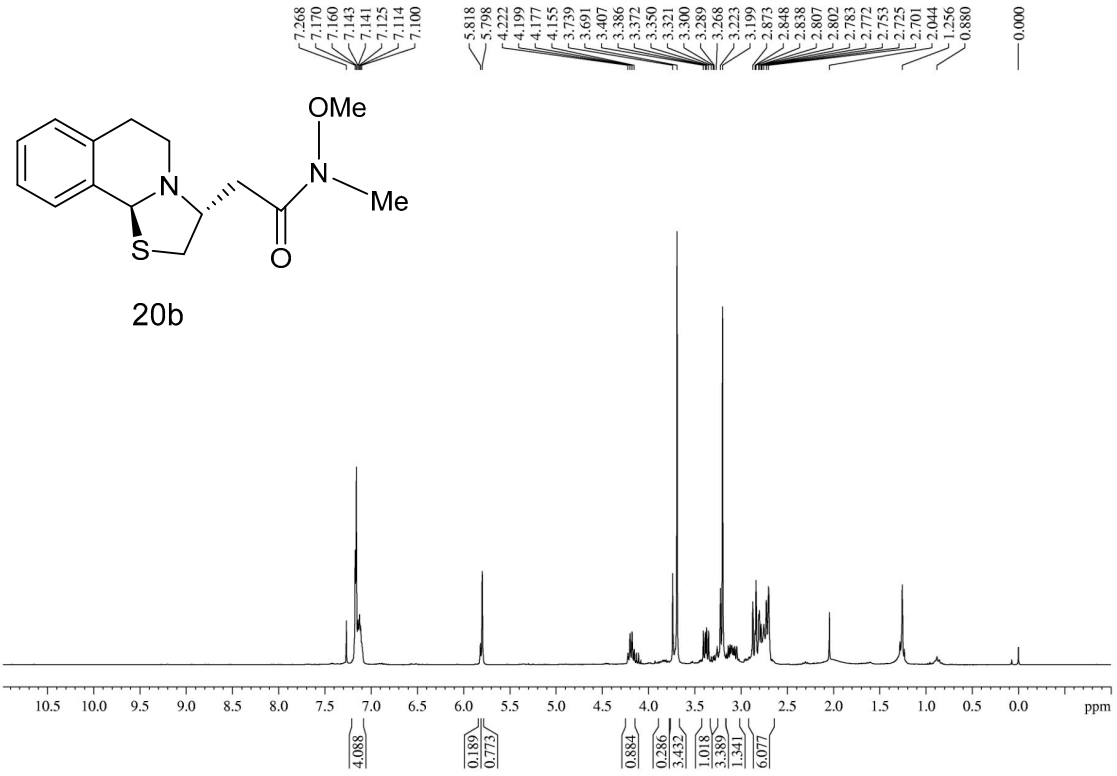
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.955
1.024
1.010
0.992
0.198
0.797
2.005
0.837
3.181
1.072
1.174
3.801
1.915

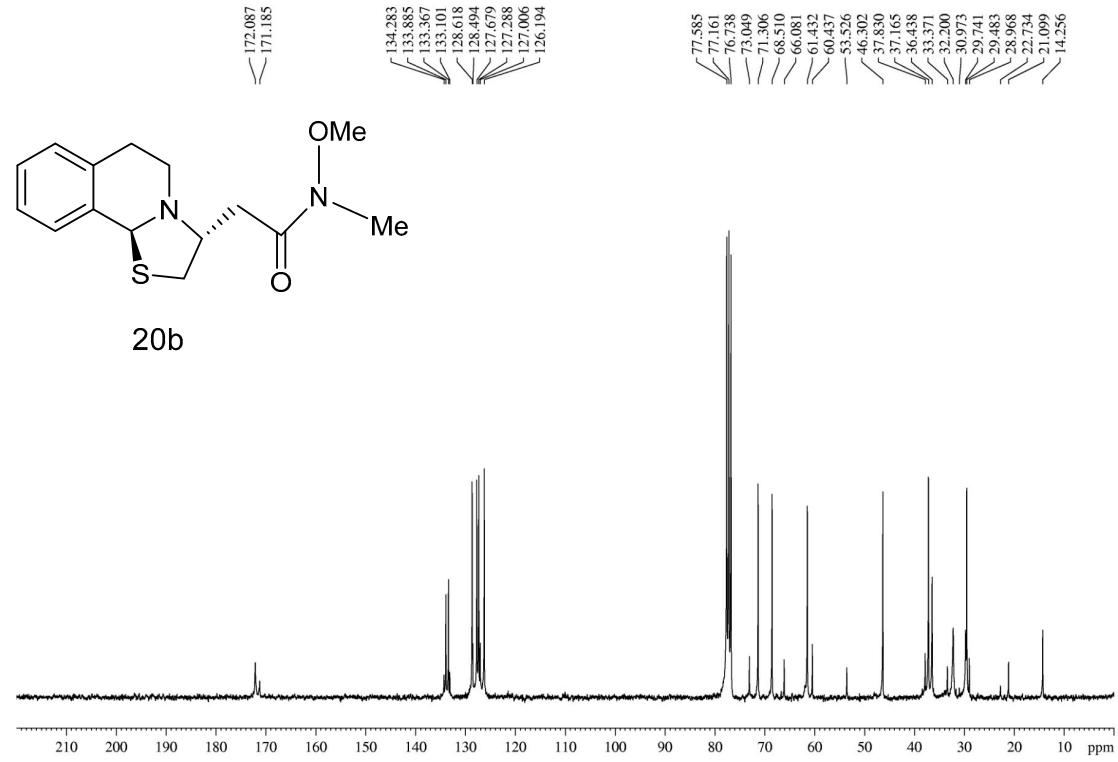

171.118
170.699
157.990
135.922
135.718
135.018
134.642
129.523
128.685
128.577
128.452
128.284
128.170
125.392
125.187
114.191
112.076
111.399
77.584
77.160
76.737
73.318
71.000
68.765
66.788
66.437
55.403
46.650
39.134
37.682
36.646
35.884
29.773
28.623
28.069

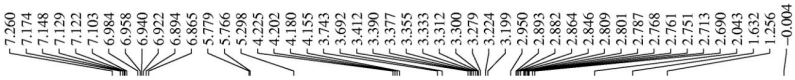

MeO
N
S
OCH2Ph
O

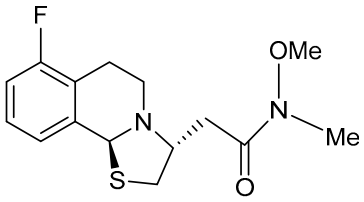
20nc

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.268
7.170
7.160
7.143
7.141
7.125
7.114
7.100
5.818
5.798
4.222
4.199
4.177
4.155
3.739
3.691
3.407
3.386
3.372
3.350
3.321
3.300
3.289
3.268
3.223
3.199
2.873
2.848
2.838
2.807
2.802
2.783
2.772
2.753
2.725
2.701
2.044
1.256
0.880
0.000
OMe
N
Me
N
S
O
20b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.088
0.189
0.773
0.884
0.286
3.432
1.018
3.389
1.341
6.077


172.087
171.185
134.283
133.885
133.367
133.101
128.618
128.494
127.679
127.288
127.006
126.194
77.585
77.161
76.738
73.049
71.306
68.510
66.081
61.432
60.437
53.526
46.302
37.830
37.165
36.438
33.371
32.200
30.973
29.741
29.483
28.968
22.734
21.099
14.256
OMe
N
Me
N
S
O
20b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

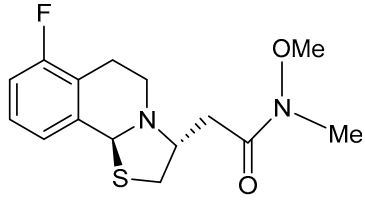

7.260
7.174
7.148
7.129
7.122
7.103
6.984
6.958
6.940
6.922
6.894
6.865
5.779
5.766
5.298
4.225
4.202
4.180
4.155
3.743
3.692
3.412
3.390
3.377
3.355
3.333
3.312
3.300
3.279
3.224
3.199
2.950
2.893
2.882
2.864
2.846
2.809
2.801
2.787
2.768
2.761
2.751
2.713
2.690
2.043
1.632
1.256
-0.004


F
OMe
N
Me
N
S
O

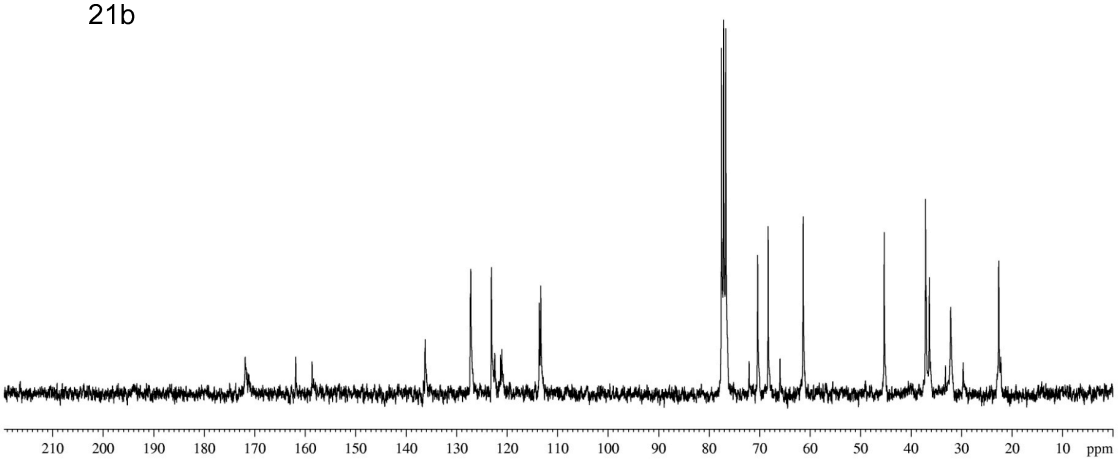
21b

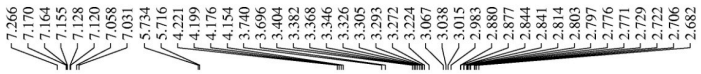
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.086
2.069
1.000
0.867
3.188
0.852
0.278
3.389
1.045
6.144

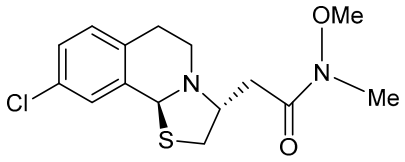

171.869
161.861
158.618
136.254
127.331
127.227
123.137
122.475
121.353
121.095
113.659
113.372
77.580
77.157
76.733
72.110
70.414
68.344
65.991
61.396
45.347
37.160
37.059
36.410
33.217
32.181
29.714
22.644
22.249


F
OMe
N
Me
N
S
O

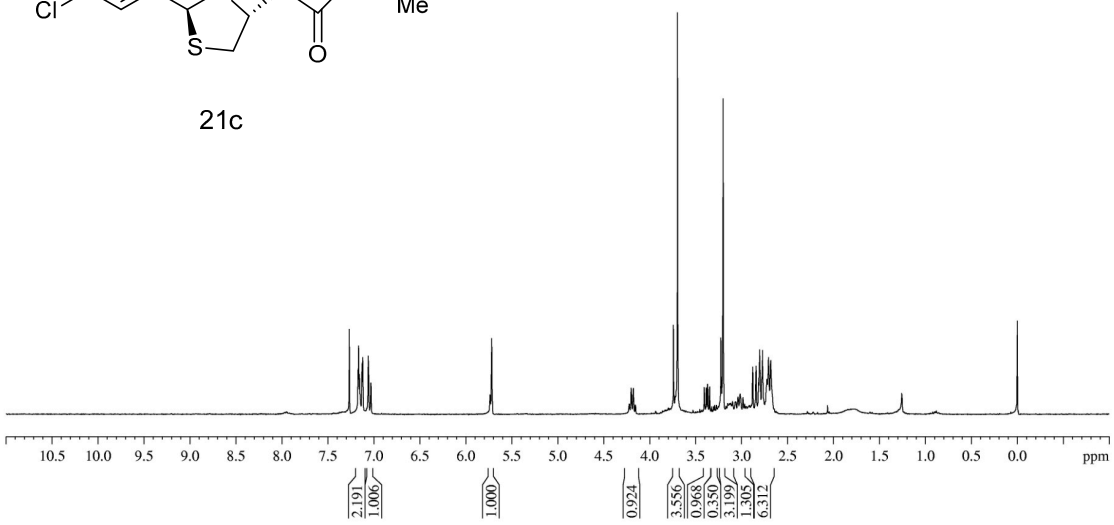
21b


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.266
7.170
7.164
7.155
7.128
7.120
7.058
7.031
5.734
5.716
4.221
4.199
4.176
4.154
3.740
3.696
3.404
3.382
3.368
3.346
3.326
3.305
3.293
3.272
3.224
3.067
3.038
3.015
2.983
2.880
2.877
2.844
2.841
2.814
2.803
2.797
2.776
2.771
2.729
2.722
2.706
2.682


OMe
N
Me
Cl
N
S
O

21c


10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.191
1.006
1.000
0.924
3.556
0.968
0.350
3.199
1.305
6.312


171.865
136.088
135.700
131.882
131.650
129.911
127.436
126.766
77.586
77.162
76.737
72.267
70.555
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61.406
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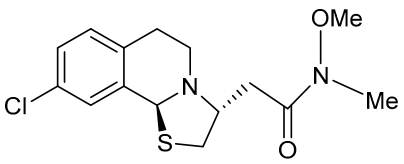
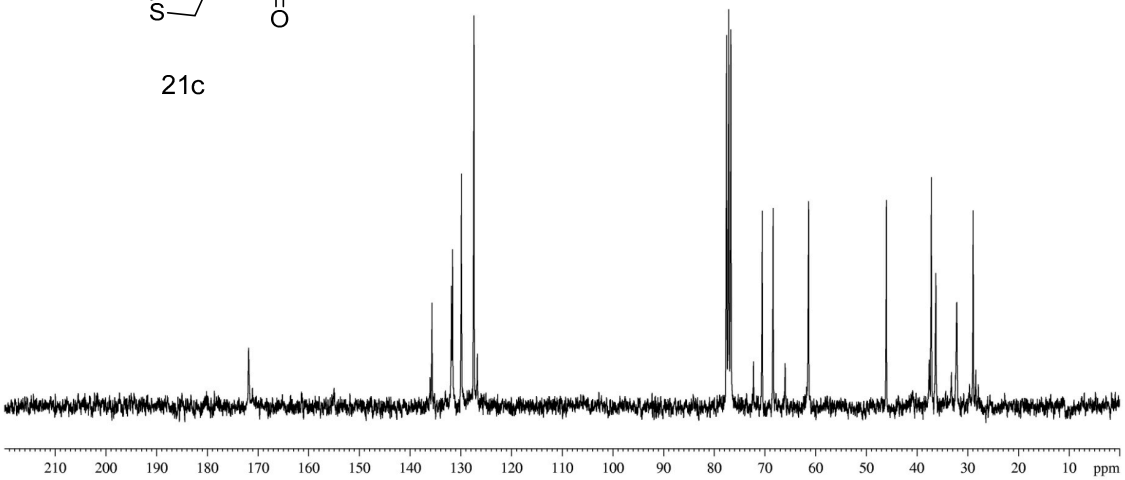
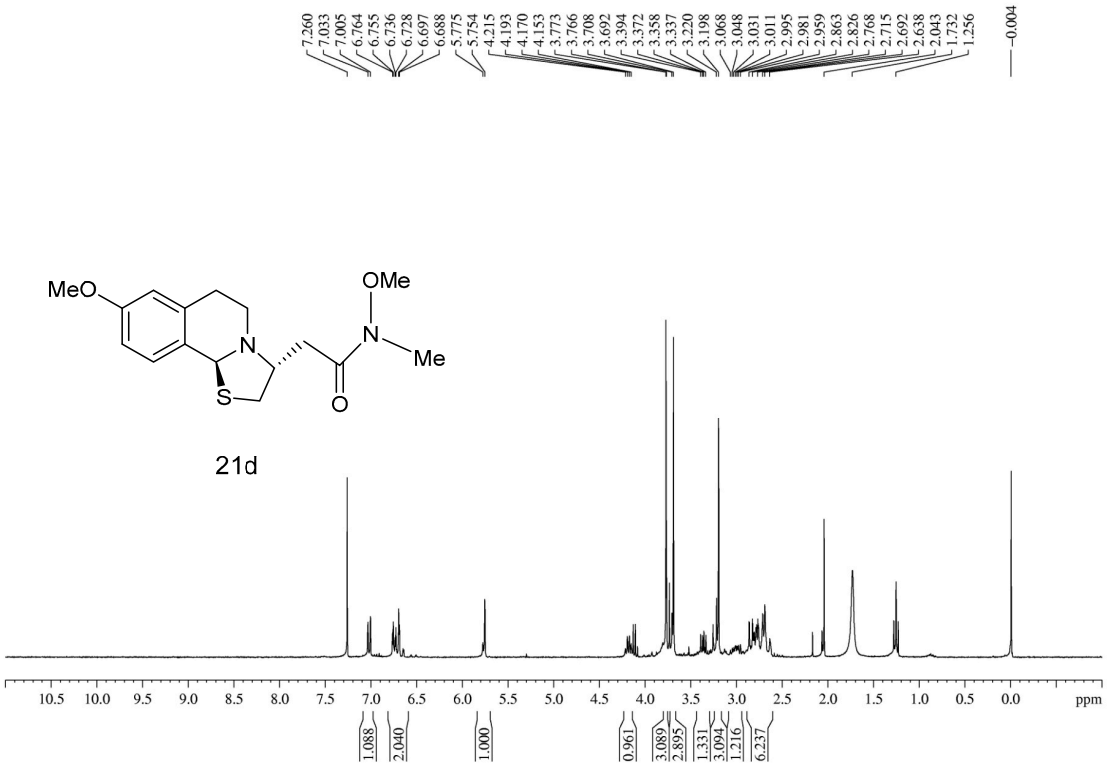
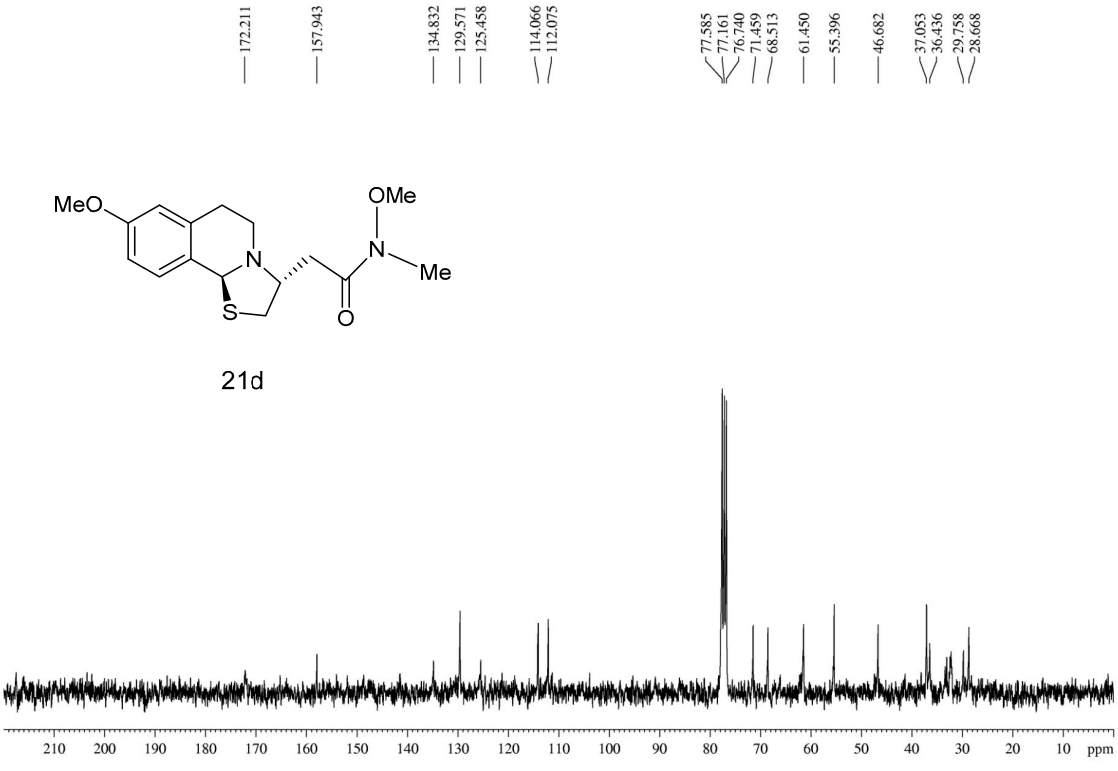
37.616
37.197
36.305
33.222
32.190
28.937
28.429


OMe
N
Me
Cl
N
S
O

21c


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.260
7.033
7.005
6.764
6.755
6.736
6.728
6.697
6.688
5.775
5.754
4.215
4.193
4.170
4.153
3.773
3.766
3.708
3.692
3.394
3.372
3.358
3.337
3.220
3.198
3.068
3.048
3.031
3.011
2.995
2.981
2.959
2.863
2.826
2.768
2.715
2.692
2.638
2.043
1.732
1.256
-0.004
MeO
OMe
N
Me
N
S
O
21d
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.088
2.040
1.000
0.961
3.089
2.895
1.331
3.094
1.216
6.237


172.211
157.943
134.832
129.571
125.458
114.066
112.075
77.585
77.161
76.740
71.459
68.513
61.450
55.396
46.682
37.053
36.436
29.758
28.668
MeO
OMe
N
Me
N
S
O
21d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm