Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Domino Michael/Michael reaction catalyzed by switchable modularly designed organocatalysts

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Supporting Information

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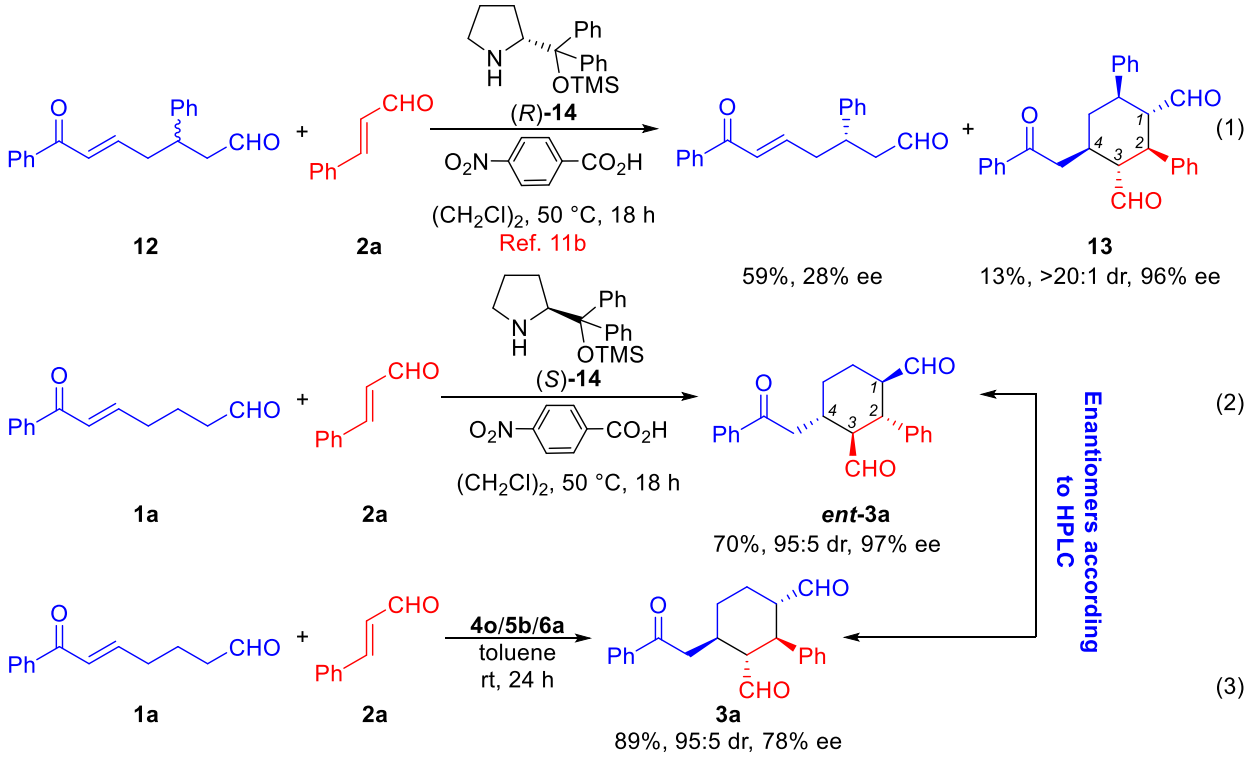
Determination of the Product Relative and Absolute Configuration

The relative stereochemistry of the product was determined by COSY experiments and the coupling constants using compound **3l** (please see Pages S-32-S-33 below for details).

The absolute stereochemistry of the domino Michael/Michael product was determined by comparing our product with that obtained with the Xu's catalytic system[11b] (Scheme S-1).

According to Xu report,[11b] the reaction of enonal **12** with **2a** under the catalysis of (*R*)-**14** gave the domino Michael/Michael product **13** with the absolute stereochemistry of **(1*S*,2*S*,3*R*,4*R*)** for the **newly formed four stereogenic centers** (Eq. 1, Scheme 1), which was assigned according to X-ray crystallography.[11b]

We conducted a similar reaction with enonal **1a** and **2a** with (*R*)-**14** as the catalyst (Eq. 2, Scheme 1) under otherwise identical conditions. Accordingly, the domino Michael/Michael product we obtained should have totally opposite stereochemistry for these four stereogenic centers [i.e., (1*R*,2*S*,3*S*,4*S*). Please note: The *R*/*S* designation is not totally flipped due to the removal of the 6-phenyl group]. According to the HPLC chromatograms, this product turned out to be the enantiomer of the major product in our study (Please see Page S-38 vs Page S-37 below), i.e., it is ***ent*-3a**, as shown in Eq. 2. Thus, the major enantiomer **3a** obtained in our study should have exactly the same absolute stereochemistry as that of compound **13** for the four stereogenic centers [i.e., (1*S*,2*R*,3*R*,4*R*) for **3a**, Eq. 3]. These results are not surprising, since compound **13** and compound **3a** are both obtained from catalysts that are based on D-proline.



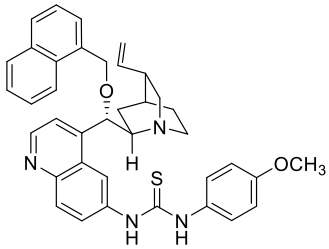
Scheme S-1. Determination of the absolute stereochemistry of the reaction product **3a**

Experimental Procedure for the Synthesis of *ent*-3a Using Catalyst (*S*)-14[11b]

Compound *ent-3a* was synthesized from enonal 1a and enal 2a using exactly the same conditions reported in Ref. 11b (Table 1, entry 3 of Ref. 11b) so that the results are comparable: Under the protection of nitrogen, to a flame dried 5-mL round bottom flask with a magnetic stirring bar was added catalyst (*S*)-**14** (6.5 mg, 0.020 mmol, 10 mol %) and 4-nitrobenzoic acid (1.7 mg, 0.010 mmol, 5 mol %). A solution of substrate **1a** (40.4 mg, 0.20 mmol) in dry dichloroethane (1.0 mL) and *trans*-cinnamaldehyde (**2a**, 26.4 mg, 0.20 mmol) was added by syringe, respectively. Then the reaction mixture was stirred at 50 °C for 18 h. After the reaction was completed, the solvent was evaporated in a rotavapor under reduced pressure and the crude product obtained was purified by flash column chromatography using 70:30 hexane/EtOAc to give product *ent*-**3a** (46.8 mg, 70%). The dr of the product was determined to be 95:5 according to the NMR of the crude product. The HPLC analysis of this product revealed that it was the enantiomer of the major enantiomer obtained in our study (i.e., ***ent*-3a**) with an ee value of 97% (Please see Page S-38 vs Page S-37 below).

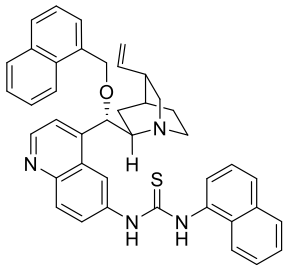
Characterization Data for New Cinchona Alkaloid Derivatives

1-(4-Methoxyphenyl)-3-(4-((*S*)-(naphthalen-1-ylmethoxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)thiourea (4d)



White solid; m.p. 118-119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.52 (s, 1H), 8.76 (d, *J* = 4.3 Hz, 1H), 8.61 (s, 1H), 8.29 (s, 1H), 7.89 (dd, *J* = 11.9, 8.6 Hz, 4H), 7.62 (dd, *J* = 16.9, 9.8 Hz, 2H), 7.55 – 7.42 (m, 5H), 6.75 (d, *J* = 8.1 Hz, 2H), 5.53 (ddd, *J* = 17.0, 10.3, 6.6 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.76 (d, *J* = 10.5 Hz, 1H), 4.58 (d, *J* = 17.1 Hz, 1H), 3.88 (d, *J* = 36.7 Hz, 2H), 3.76 (s, 3H), 3.68 (s, 1H), 3.07 (d, *J* = 78.0 Hz, 2H), 2.35 (d, *J* = 5.1 Hz, 1H), 2.08 (d, *J* = 14.3 Hz, 1H), 1.84 – 1.60 (m, 3H), 1.28 (s, 1H), 1.10 (s, 1H), 0.96 – 0.78 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.1, 157.5, 148.9, 145.8, 137.5, 133.7, 132.8, 131.5, 130.4, 129.1, 128.6, 127.1, 126.6, 126.5. 126.0, 125.3, 123.9, 116.1, 113.9, 77.3, 69.8, 60.0, 55.3, 49.8, 48.9, 37.4, 29.7, 27.4. ν_{max} (neat, cm^{-1}): 2931, 1526, 1457, 1235, 1167, 1030, 828, 799, 778. HRMS (ESI, m/z) calcd. for $C_{38}H_{39}N_4O_2S$ ($[M+H]^+$): 615.2788; found: 615.2780.

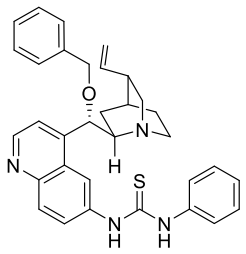
1-(Naphthalen-1-yl)-3-(4-((*S*)-(naphthalen-1-ylmethoxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)thiourea (4e)



White solid; m.p. 105-106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.82 (d, *J* = 4.4 Hz, 1H), 8.49 (s, 1H), 8.23 (d, *J* = 7.6 Hz, 1H), 8.12 (d, *J* = 7.3 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 4.3 Hz, 1H), 7.91 – 7.79 (m, 4H), 7.75 (d, *J* = 6.5 Hz, 1H), 7.49 (ddd, *J* = 30.3, 15.6, 7.5 Hz, 8H), 7.28 (s, 1H), 5.59 (ddd, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.07 (s, 1H), 4.94 (d, *J* = 11.2 Hz, 1H), 4.80 (d, *J* = 10.4 Hz, 1H), 4.68 (d, *J* = 17.2 Hz, 1H), 3.56 (s, 2H), 3.01 (s, 1H), 2.84 (s, 1H), 2.27 (d, *J* = 6.9 Hz, 1H), 2.10 (s, 1H), 1.77 (s, 1H), 1.66 – 1.48 (m, 2H), 1.28 (s, 1H), 1.16 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.7, 149.4, 146.4, 134.4, 133.6, 132.8, 131.4, 130.5, 129.9, 128.9, 128.6, 128.4, 127.2, 126.9, 126.6, 126.4, 125.9, 125.6, 125.2, 123.8, 122.7, 115.7, 69.8, 60.1, 49.7, 48.8, 38.0, 29.7, 27.5, 24.4. ν_{max} (neat, cm^{-1}): 2934, 1539, 1506,

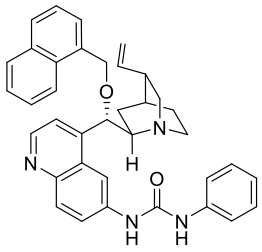
1267, 1117, 1016, 765. HRMS (ESI, m/z) calcd. for $C_{41}H_{39}N_4OS$ ($[M+H]^+$): 635.2839; found: 635.2831.

1-(4-((*S*)-(Benzyloxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylthiourea (4f)



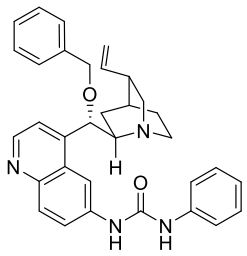
White solid; m.p. 90-91 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 8.73 (d, *J* = 4.4 Hz, 1H), 8.49 (s, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.45 (dd, *J* = 15.2, 6.2 Hz, 3H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.33 (s, 1H), 5.75 (ddd, *J* = 17.2, 10.5, 6.7 Hz, 1H), 5.03 (d, *J* = 10.5 Hz, 1H), 4.96 – 4.86 (m, 2H), 4.62 (d, *J* = 10.4 Hz, 1H), 4.10 (s, 1H), 3.87 (t, *J* = 9.0 Hz, 2H), 3.34 (dd, *J* = 20.5, 9.1 Hz, 1H), 3.08 (dd, *J* = 20.9, 9.7 Hz, 1H), 2.50 (dd, *J* = 16.2, 8.3 Hz, 1H), 2.20 (t, *J* = 11.6 Hz, 1H), 2.05 (d, *J* = 15.2 Hz, 1H), 1.89 (s, 1H), 1.82 – 1.64 (m, 2H), 1.08 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.8, 148.8, 145.5, 141.2, 138.5, 137.7, 136.8, 136.3, 130.1, 128.7, 128.5, 128.4, 128.3, 126.3, 125.2, 124.8, 124.2, 117.8, 117.0, 115.9, 72.1, 59.8, 49.7, 48.8, 37.2, 29.7, 27.3, 23.4, 18.7. ν_{max} (neat, cm^{-1}): 3030, 2926, 1545, 1542, 1539, 1506, 1312, 1236, 1122, 1053, 752. HRMS (ESI, m/z) calcd. for $C_{33}H_{35}N_4OS$ ($[M+H]^+$): 535.2526; found: 535.2528.

1-(4-((*S*)-(Naphthalen-1-ylmethoxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylurea (4h)



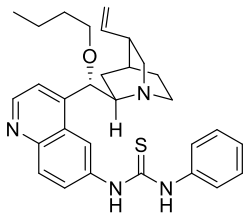
White solid; m.p. 121-123 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.65 (dd, *J* = 44.3, 20.3 Hz, 3H), 8.05 – 7.62 (m, 5H), 7.57 – 7.25 (m, 7H), 7.04 (t, *J* = 7.8 Hz, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.27 – 5.16 (m, 3H), 5.01 – 4.64 (m, 4H), 3.90 – 2.88 (m, 2H), 2.85 – 2.51 (m, 2H), 2.12 (dd, *J* = 16.4, 8.1 Hz, 2H), 1.71 (s, 1H), 1.55 – 0.97 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 147.8, 144.9, 144.2, 139.3, 138.6, 138.3, 133.5, 133.1, 131.2, 130.8, 128.7, 128.6, 128.5, 126.9, 126.4, 126.2, 125.8, 125.2, 123.6, 123.3, 122.9, 119.4, 115.0, 69.5, 59.6, 49.6, 49.1, 39.1, 27.7, 25.5. ν_{max} (neat, cm^{-1}): 2934, 1595, 1568, 1524, 1441, 1202, 791, 668. HRMS (ESI, m/z) calcd. for $C_{37}H_{37}N_4O_2$ ($[M+H]^+$): 569.2911; found: 569.2899.

1-(4-((*S*)-(Benzyloxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylurea (4j)



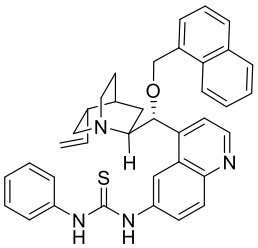
White solid; m.p. 114-116 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.4 Hz, 2H), 8.52 (s, 1H), 8.26 (s, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.57 – 7.44 (m, 2H), 7.32 (dd, *J* = 7.8, 6.0 Hz, 4H), 7.28 (s, 1H), 7.12 (t, *J* = 7.8 Hz, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 5.95 (ddd, *J* = 17.4, 10.0, 7.7 Hz, 1H), 5.45 (s, 1H), 4.99 (t, *J* = 13.1 Hz, 2H), 4.56 (s, 1H), 4.43 – 4.28 (m, 2H), 3.38 (s, 1H), 3.11 (s, 1H), 3.00 – 2.82 (m, 2H), 2.71 (dd, *J* = 14.9, 6.1 Hz, 1H), 2.27 – 2.06 (m, 2H), 1.73 (s, 1H), 1.58 – 1.37 (m, 2H), 1.26 (dd, *J* = 26.6, 19.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 148.2, 145.6, 144.9, 140.3, 138.3, 137.7, 137.6, 130.6, 128.9, 128.3, 127.8, 127.7, 127.2, 123.4, 120.1, 114.6, 71.4, 59.9, 49.8, 49.3, 39.8, 28.1, 26.2. ν_{max} (neat, cm^{-1}): 2939, 2859, 1595, 1545, 1525, 1515, 1205, 1026, 828, 743. HRMS (ESI, m/z) calcd. for $C_{33}H_{35}N_4O_2$ ($[M+H]^+$): 519.2755; found: 519.2741.

1-(4-((*S*)-Butoxy((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylthiourea (4l)



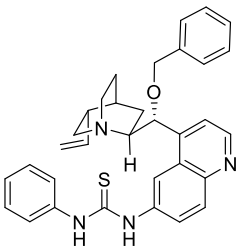
White solid; m.p. 79-81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.74 (d, *J* = 4.4 Hz, 1H), 8.34 (s, 1H), 7.91 – 7.81 (m, 2H), 7.48 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.38 (d, *J* = 4.4 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 5.99 (ddd, *J* = 17.5, 10.4, 7.4 Hz, 1H), 5.77 (s, 1H), 5.22 – 5.09 (m, 2H), 3.82 (s, 1H), 3.68 – 3.37 (m, 4H), 3.18 (t, *J* = 11.7 Hz, 1H), 2.93 (dt, *J* = 12.7, 9.3 Hz, 1H), 2.42 (dd, *J* = 17.4, 8.6 Hz, 1H), 2.24 – 2.12 (m, 1H), 1.84 (dt, *J* = 5.2, 2.4 Hz, 1H), 1.76 – 1.34 (m, 6H), 1.17 – 1.01 (m, 1H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.8, 149.1, 145.8, 143.2, 138.1, 137.9, 130.3, 128.8, 126.6, 125.7, 125.4, 124.4, 118.0, 116.4, 116.3, 69.6, 59.8, 49.8, 49.2, 38.3, 32.1, 27.6, 24.4, 19.5, 13.9. ν_{max} (neat, cm^{-1}): 2932, 2873, 1539, 1506, 1517, 1236, 1115, 828, 754, 693. HRMS (ESI, m/z) calcd. for $C_{30}H_{37}N_4OS$ ($[M+H]^+$): 501.2683; found: 501.2671.

1-(4-((*R*)-(Naphthalen-1-ylmethoxy)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylthiourea (4o)



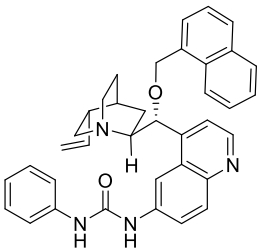
White solid; m.p. 116-118 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, *J* = 4.4 Hz, 1H), 8.58 (s, 1H), 8.07 – 7.96 (m, 3H), 7.90 – 7.80 (m, 2H), 7.61 – 7.41 (m, 8H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.14 (s, 1H), 5.64 (ddd, *J* = 17.3, 10.0, 7.6 Hz, 1H), 5.05 – 4.91 (m, 4H), 3.61 (d, *J* = 72.5 Hz, 2H), 3.23 – 2.97 (m, 2H), 2.81 (d, *J* = 11.4 Hz, 1H), 2.39 (s, 1H), 1.86 (t, *J* = 44.9 Hz, 3H), 1.55 (s, 2H), 1.29 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.9, 149.3, 146.2, 143.7, 139.3, 137.8, 137.4, 133.6, 132.9, 131.2, 130.6, 129.1, 128.8, 128.7, 126.9, 126.4, 126.2, 126.1, 125.3, 124.7, 123.4, 116.0, 69.5, 60.4, 55.8, 43.7, 38.5, 29.7, 27.3, 26.0. ν_{max} (neat, cm^{-1}): 2934, 2858, 2375, 1539, 1523, 1516, 1317, 1236, 1070, 751, 694. HRMS (ESI, m/z) calcd. for $C_{37}H_{37}N_4OS$ ($[M+H]^+$): 585.2683; found: 585.2668.

1-(4-((*R*)-(Benzyloxy)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylthiourea (4q)



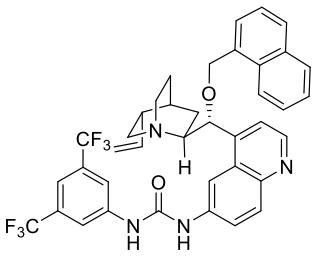
White solid; m.p. 95-97 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.81 (d, *J* = 4.4 Hz, 1H), 8.49 (s, 1H), 7.94 (q, *J* = 8.9 Hz, 2H), 7.48 (t, *J* = 6.7 Hz, 3H), 7.42 – 7.31 (m, 5H), 7.27 (dd, *J* = 12.9, 5.2 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 5.83 (s, 1H), 5.66 (ddd, *J* = 17.4, 10.3, 7.4 Hz, 1H), 4.97 (dd, *J* = 24.7, 13.7 Hz, 2H), 4.56 (d, *J* = 10.9 Hz, 1H), 4.46 (s, 1H), 3.75 (s, 1H), 3.53 (s, 1H), 3.22 (t, *J* = 11.7 Hz, 1H), 3.10 (s, 1H), 2.90 (s, 1H), 2.44 (s, 1H), 1.92 (d, *J* = 35.8 Hz, 3H), 1.60 (d, *J* = 38.8 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.9, 149.3, 146.1, 143.7, 139.4, 137.7, 137.2, 130.5, 129.1, 128.6, 128.0, 127. 7, 126.9, 126.1, 125.8, 124.8, 118.5, 117.0, 116.0, 71.5, 60.4, 56.0, 43.9, 38.6, 29.7, 27.4, 26.1. ν_{max} (neat, cm^{-1}): 2931, 1549, 1539, 1506, 1496, 1312,1238, 1025, 751, 726. HRMS (ESI, m/z) calcd. for $C_{33}H_{35}N_4OS$ ($[M+H]^+$): 535.2526; found: 535.2517.

1-(4-((*R*)-(Naphthalen-1-ylmethoxy)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylurea (4s)



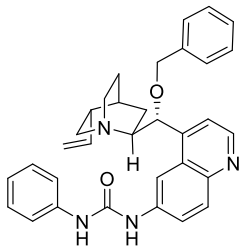
White solid; m.p. 111-113 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.75 (d, *J* = 4.5 Hz, 1H), 8.66 (s, 1H), 8.40 (s, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.80 (dd, *J* = 27.0, 8.2 Hz, 3H), 7.58 – 7.34 (m, 8H), 7.12 (t, *J* = 7.7 Hz, 2H), 6.90 (t, *J* = 7.2 Hz, 1H), 5.66 (ddd, *J* = 17.5, 10.1, 7.7 Hz, 1H), 5.16 (s, 1H), 4.96 – 4.74 (m, 4H), 3.39 (d, *J* = 7.3 Hz, 1H), 3.21 (s, 1H), 3.02 (t, *J* = 11.4 Hz, 1H), 2.72 – 2.51 (m, 2H), 2.20 (s, 1H), 1.96 – 1.51 (m, 4H), 1.41 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 148.2, 145.9, 145.0, 141.4, 138.5, 138.4, 137.9, 133.5, 133.3, 131.1, 130.7, 129.1, 128.9, 128.6, 128.5, 127.3, 126.3, 125.8, 125.3, 123.4, 120.0, 114.4, 69.3, 60.6, 56.7, 43.0, 39.7, 29.7, 27.9, 27.7, 27.4. ν_{max} (neat, cm^{-1}): 2939, 1549, 1506, 1456, 1362, 1312, 1204, 1083, 748. HRMS (ESI, m/z) calcd. for $C_{37}H_{37}N_4O_2$ ($[M+H]^+$): 569.2911; found: 569.2899.

1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-((*R*)-(naphthalen-1-ylmethoxy)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)urea (4t)

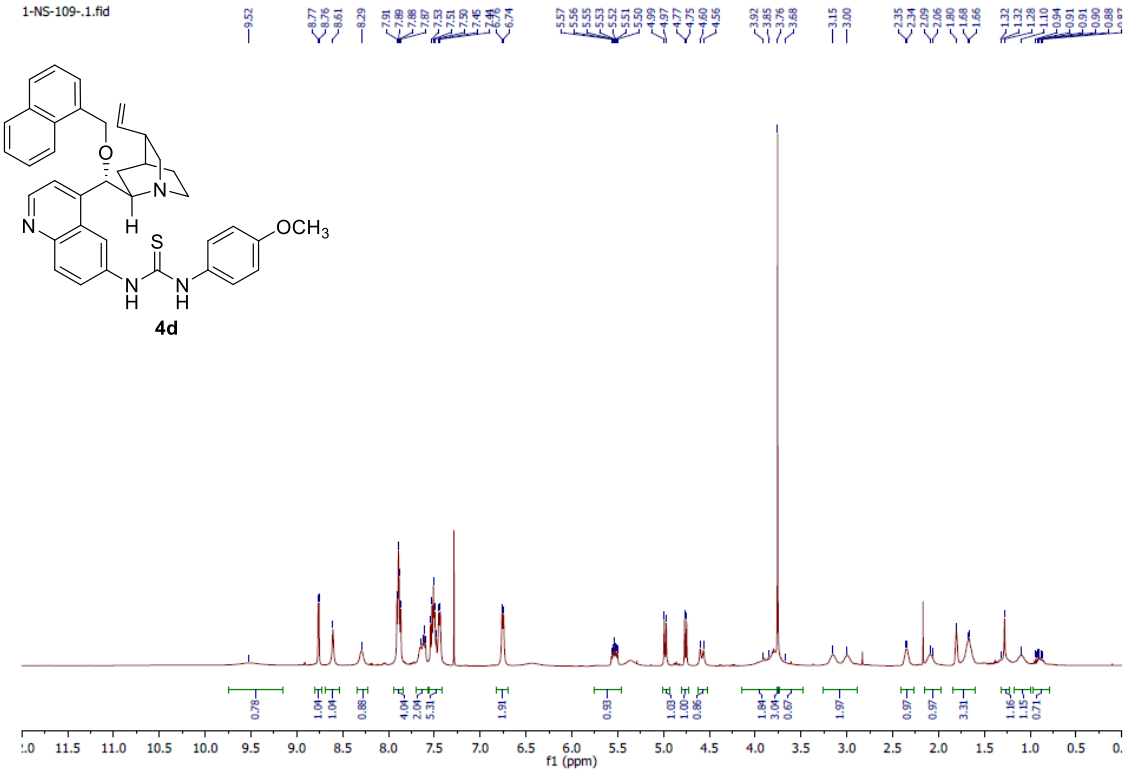


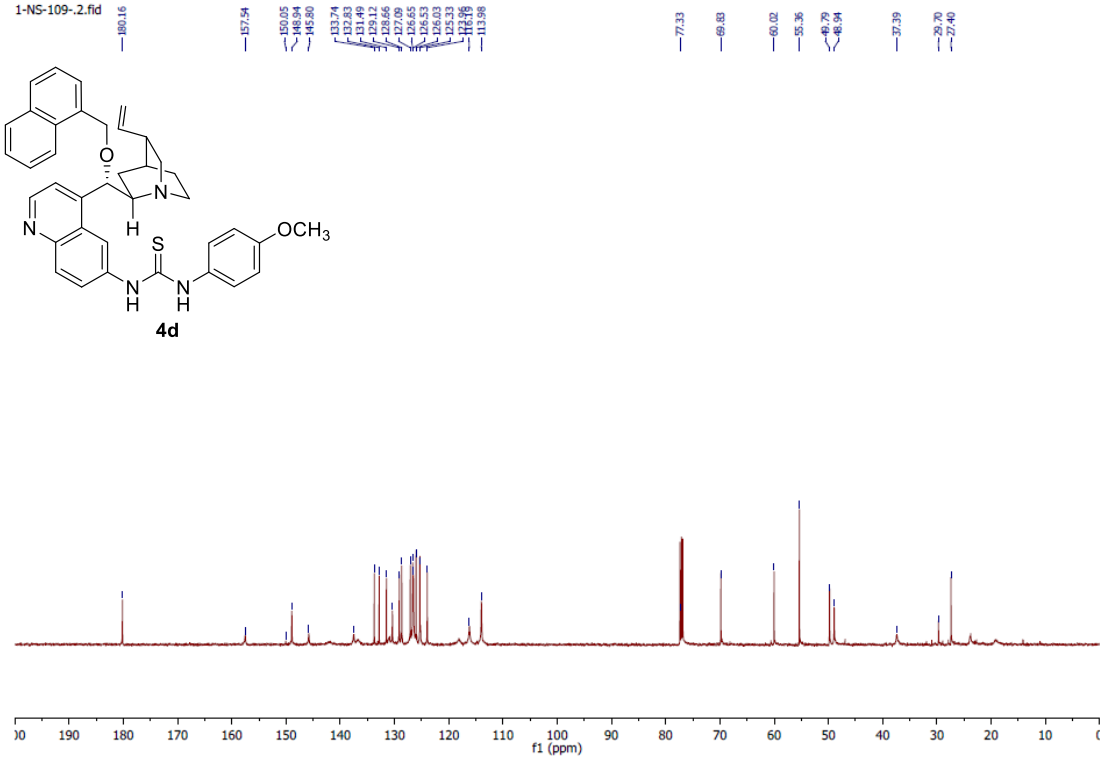
White solid; m.p. 127-129 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.77 (d, *J* = 4.4 Hz, 1H), 8.59 (s, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.94 – 7.72 (m, 5H), 7.63 – 7.31 (m, 7H), 5.74 – 5.60 (m, 1H), 4.99 – 4.78 (m, 4H), 4.45 (s, 1H), 3.39 (s, 1H), 3.21 (s, 1H), 3.02 (t, *J* = 11.7 Hz, 1H), 2.68 (d, *J* = 11.9 Hz, 1H), 2.53 (dd, *J* = 15.6, 7.6 Hz, 1H), 2.23 (d, *J* = 19.1 Hz, 1H), 1.99 – 1.17 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 148.4, 145.6, 145.0, 140.9, 140.4, 137.2, 133.5, 133.0, 132.3, 132.1, 131.8, 131.5, 131.1, 130.7, 128.6, 127.1, 126.1, 125.8, 125.2, 124.2, 123.3, 123.0, 122.0, 118.3, 115.7, 114.7, 69.3, 60.4, 56.4, 43.0, 39.4, 27.5, 27.1. ν_{max} (neat, cm^{-1}): 2945, 1558, 1521, 1386, 1278, 1174, 791, 701, 681. HRMS (ESI, m/z) calcd. for $C_{39}H_{35}F_6N_4O_2$ ($[M+H]^+$): 705.2659; found: 705.2640.

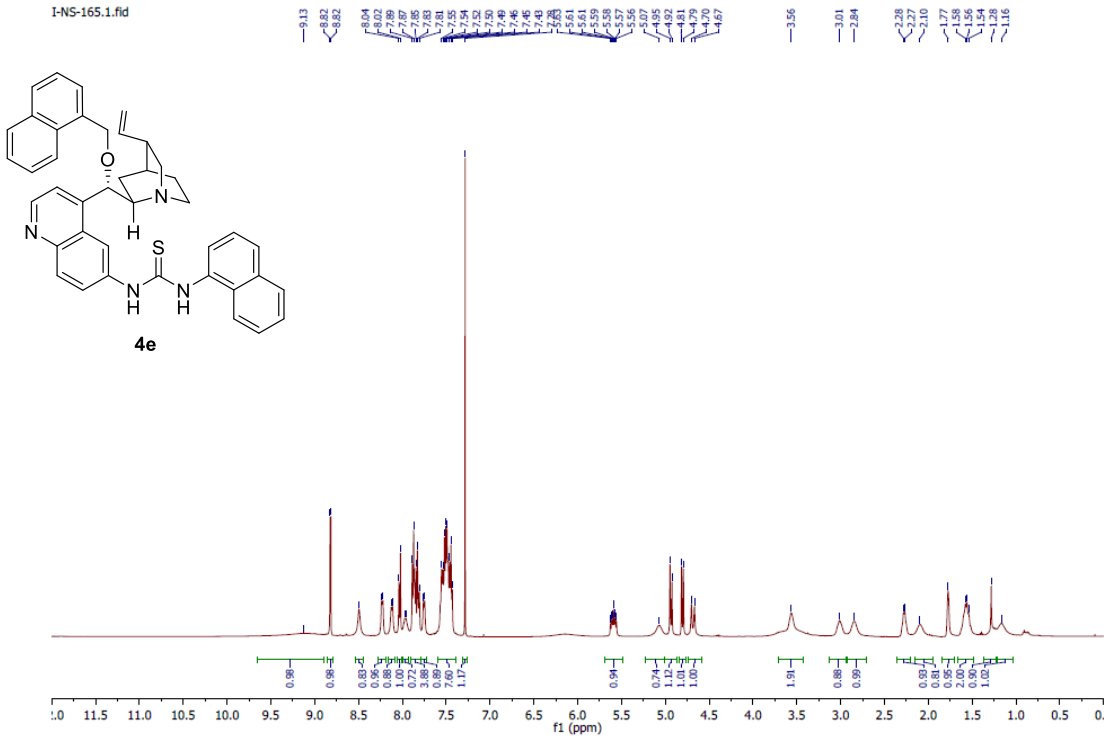
1-(4-((*R*)-(Benzyloxy)((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-yl)-3-phenylurea (4u)

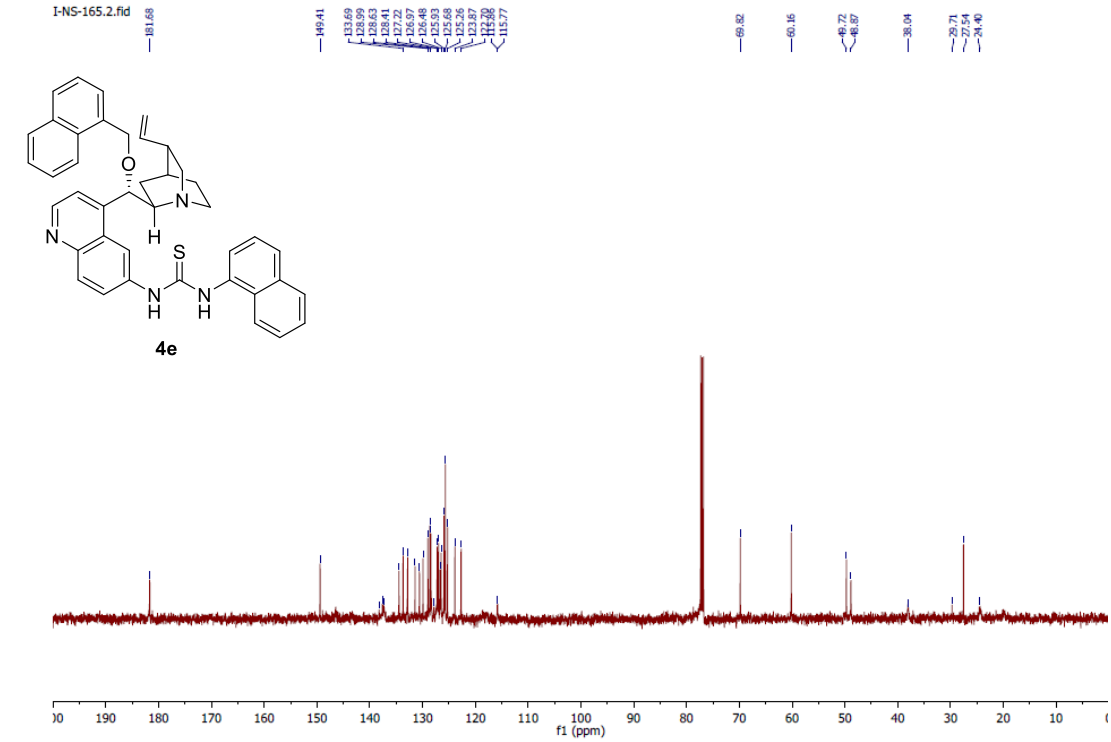


White solid; m.p. 98-100 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.74 (d, *J* = 4.4 Hz, 1H), 8.53 (s, 1H), 8.26 (dd, *J* = 27.4, 6.4 Hz, 1H), 8.18 – 8.08 (m, 1H), 7.96 (t, *J* = 8.3 Hz, 1H), 7.46 (t, *J* = 5.5 Hz, 3H), 7.40 – 7.34 (m, 4H), 7.15 (t, *J* = 7.9 Hz, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.03 (s, 1H), 5.57 (ddd, *J* = 17.2, 10.5, 6.8 Hz, 1H), 5.00 (dd, *J* = 46.5, 13.8 Hz, 2H), 4.62 (d, *J* = 11.0 Hz, 1H), 4.51 (d, *J* = 11.0 Hz, 1H), 3.91 (dd, *J* = 19.3, 8.4 Hz, 1H), 3.60 (dd, *J* = 10.3, 7.9 Hz, 1H), 3.35 (d, *J* = 9.1 Hz, 2H), 3.10 – 2.99 (m, 1H), 2.60 – 2.48 (m, 1H), 2.11 (dd, *J* = 13.7, 7.4 Hz, 1H), 2.05 – 1.92 (m, 2H), 1.73 (td, *J* = 7.1, 3.2 Hz, 1H), 1.52 (dd, *J* = 8.1, 5.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 147.8, 144.9, 141.1, 139.1, 139.0, 137.6, 136.8, 130.9, 128.7, 128.7, 128.2, 127.7, 125.9, 123.6, 122.6, 119.2, 117.7, 116.9, 109.1, 76.2, 71.6, 60.1, 54.9, 44.0, 37.5, 29.7, 26.9, 24.9. ν_{max} (neat, cm^{-1}): 2934, 1700, 1569, 1557, 1549, 1539, 1506, 1200, 1025, 1025, 745, 692. HRMS (ESI, m/z) calcd. for $C_{33}H_{35}N_4O_2$ ($[M+H]^+$): 519.2755; found: 519.2740.

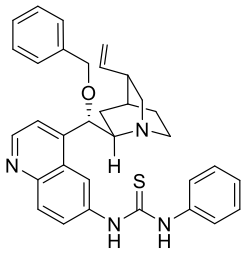

1-NS-109-.1.fid
OCH3
4d
f1 (ppm)


1-NS-109-.2.fid
OCH3
4d
f1 (ppm)

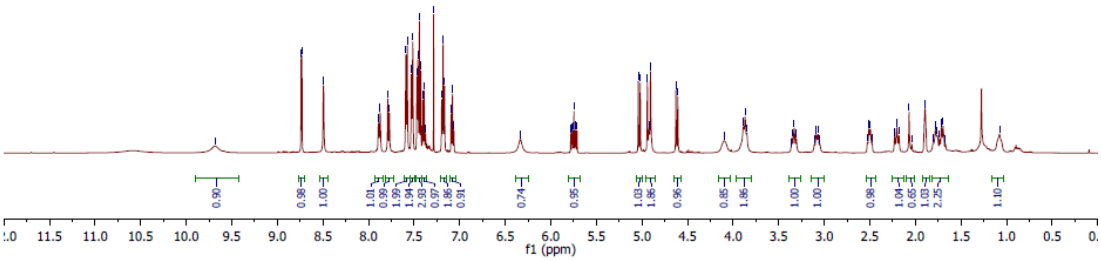

I-NS-165.1.fid
4e
f1 (ppm)


I-NS-165.2.fid
4e
f1 (ppm)

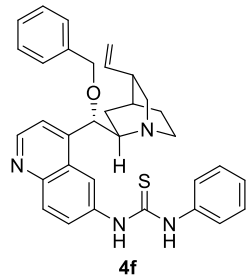
1-NS-91-PP1.1.fid



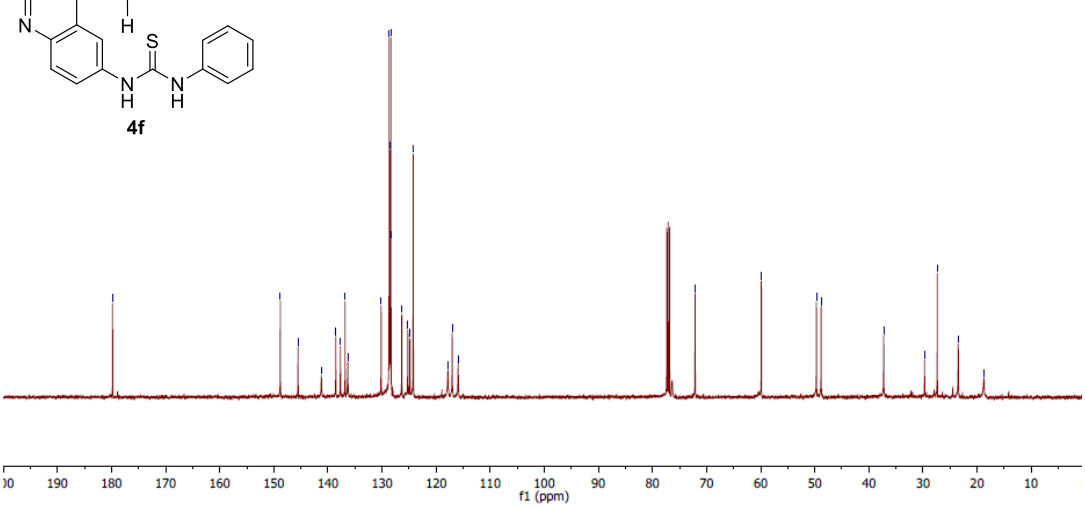
4f



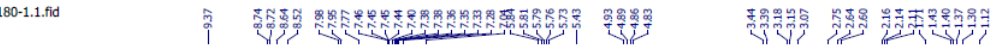
1-NS-91-P2.fid

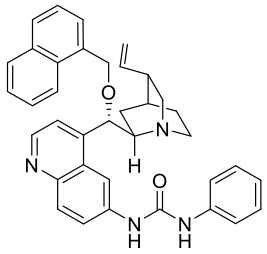


4f

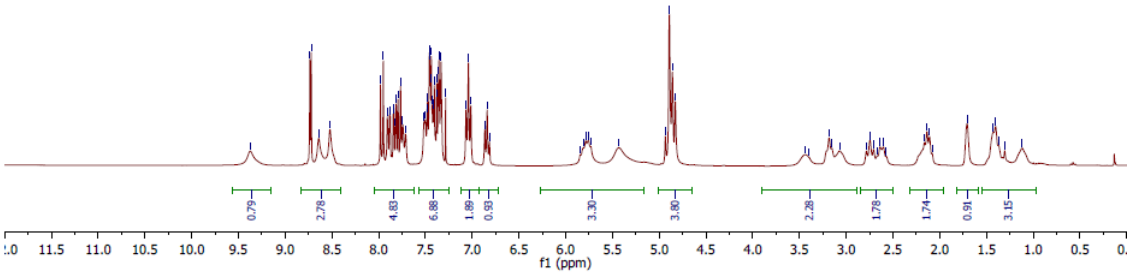


1-NS-180-1.1.fid

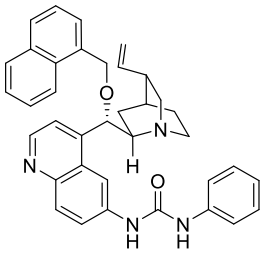




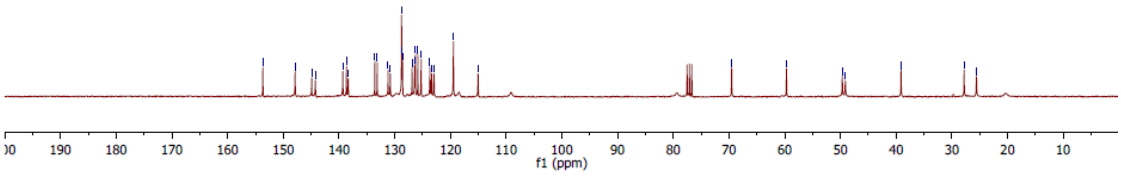
4h



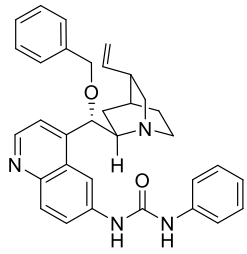
1-NS-180-1.2.fid



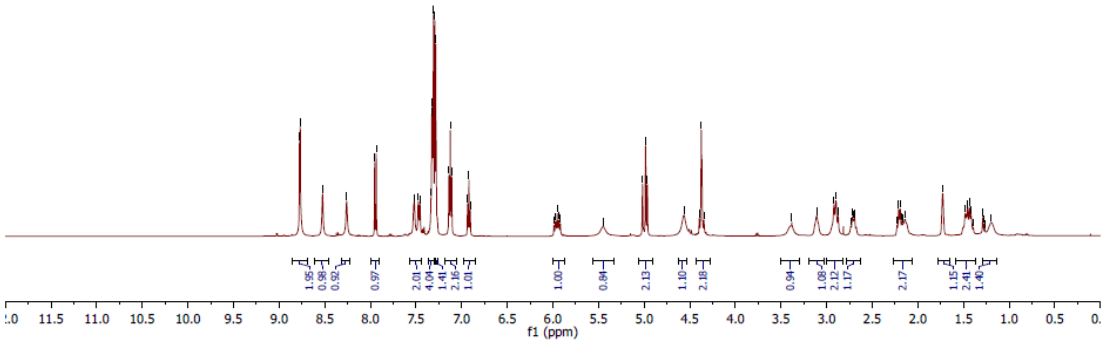
4h



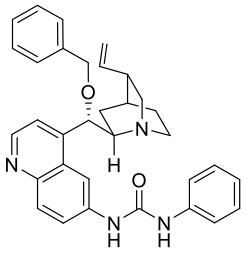
II-NS-365-1.1.fid



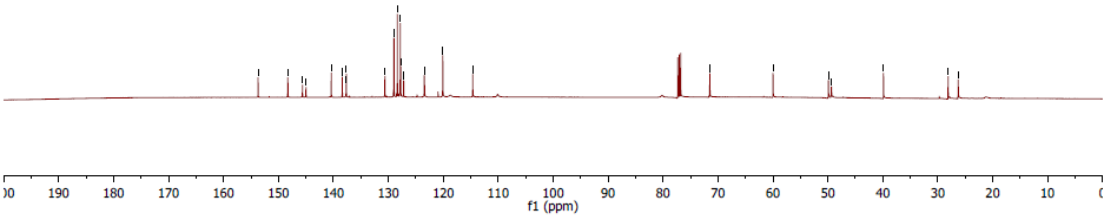
4j

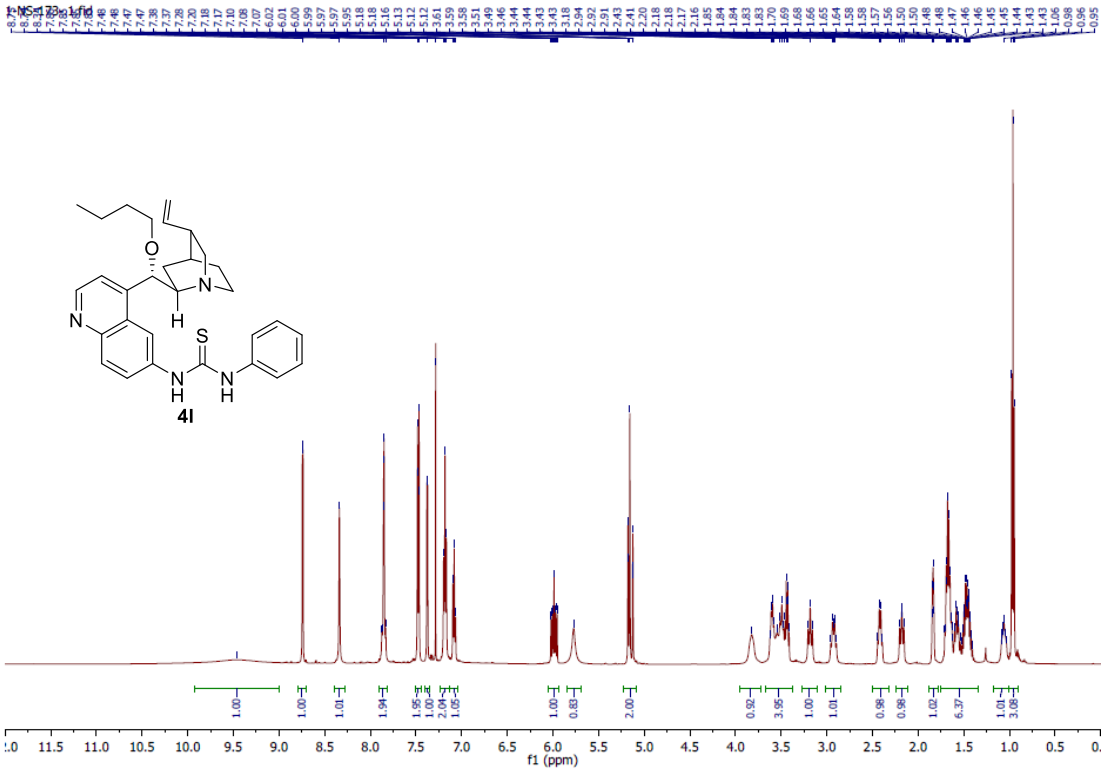


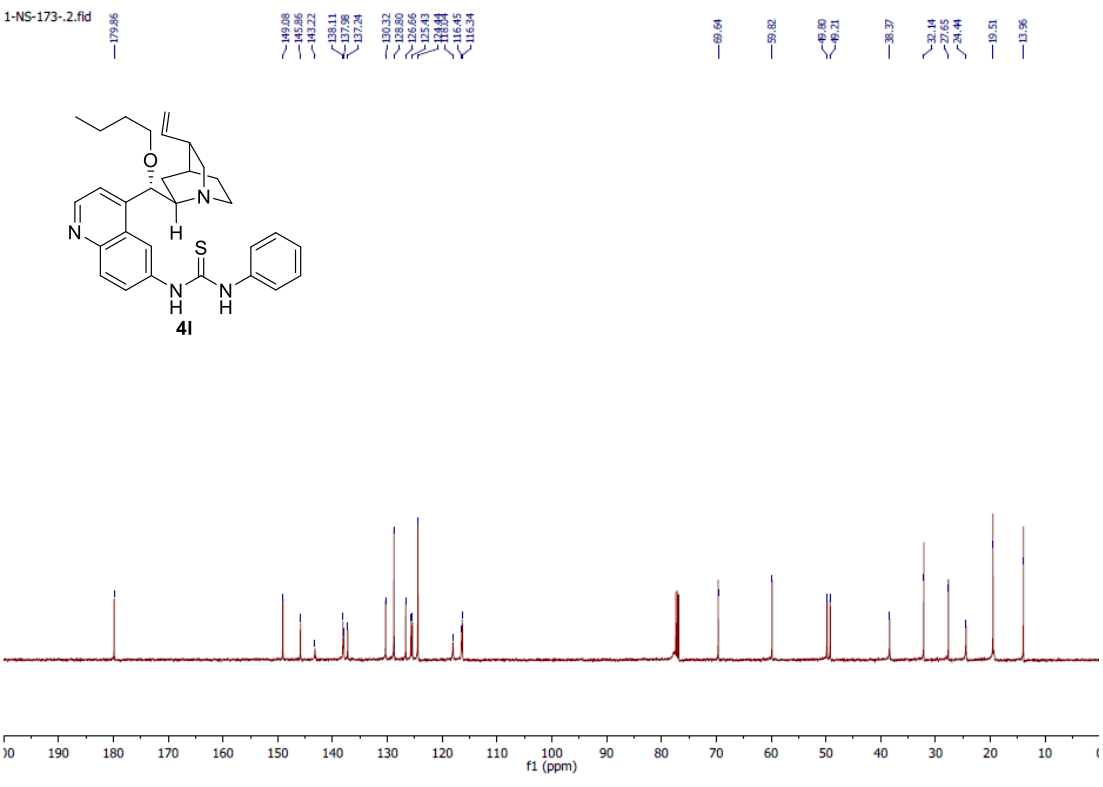
II-NS-365-1.2.fid



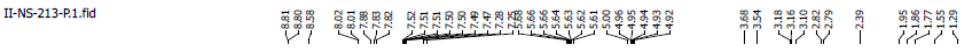
4j

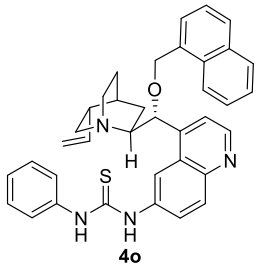



1-NS-173-.1.fid
4l
f1 (ppm)

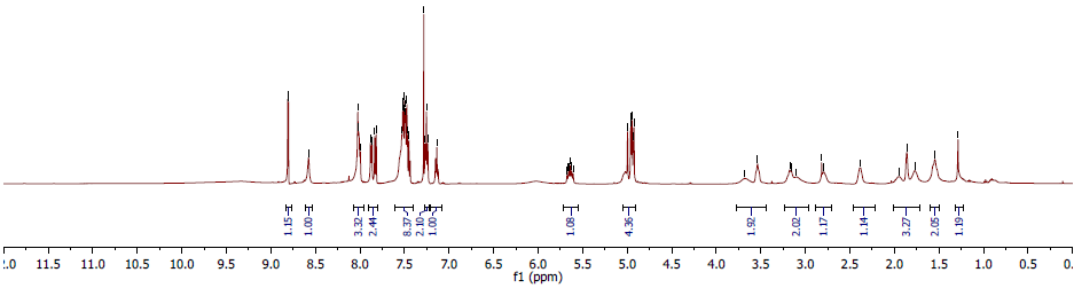

1-NS-173-.2.fid
4l
f1 (ppm)

II-NS-213-P.1.fid

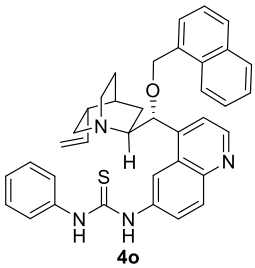




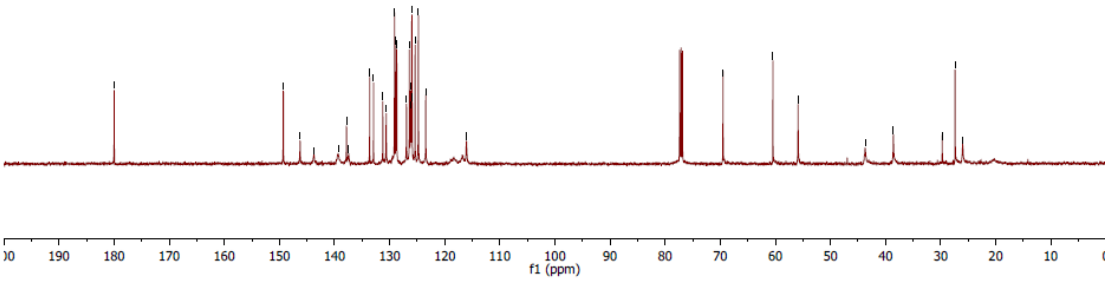
4o

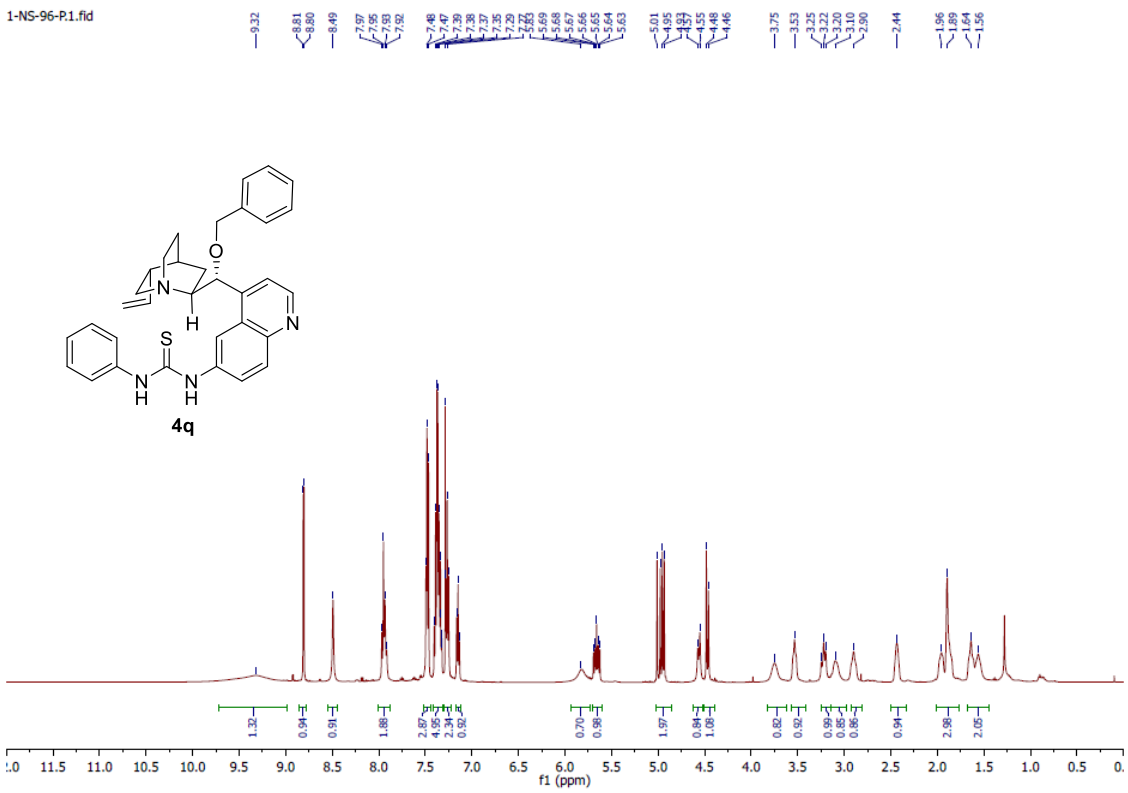


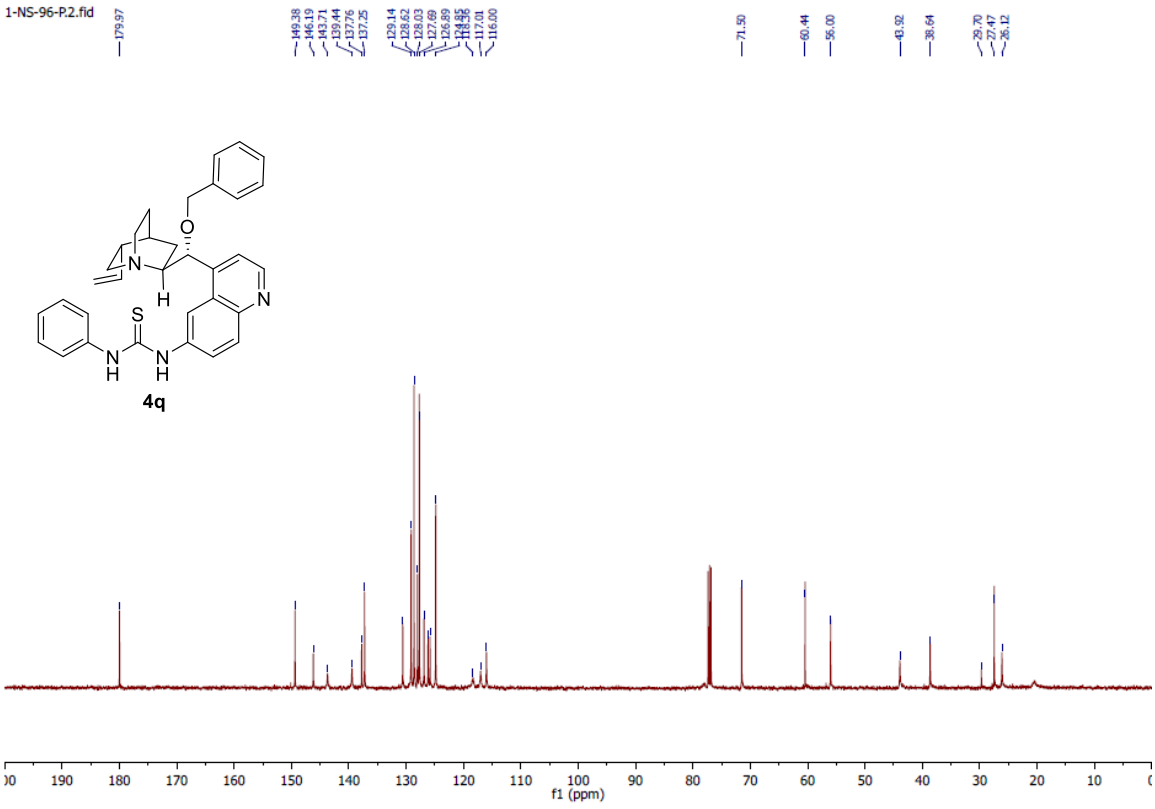
II-NS-213-P.2.fid



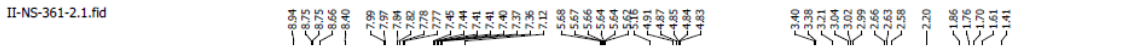
4o

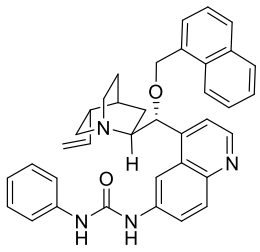



1-NS-96-P.1.fid
4q
f1 (ppm)

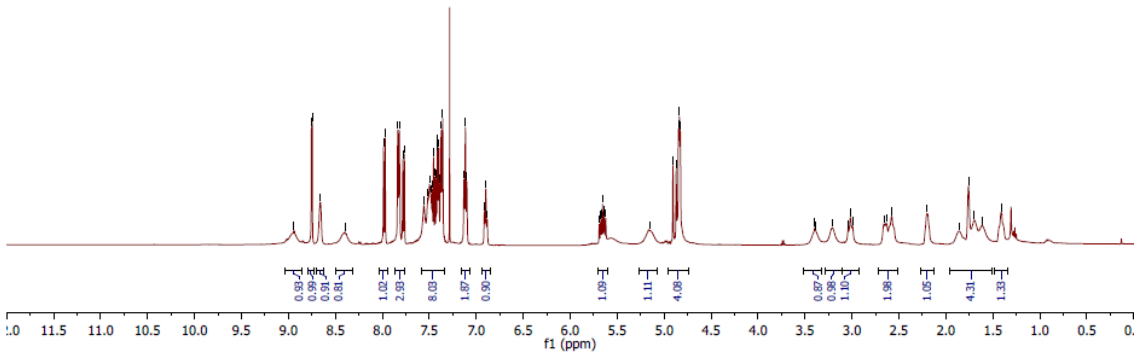

1-NS-96-P.2.fid
4q
f1 (ppm)

II-NS-361-2.1.fid

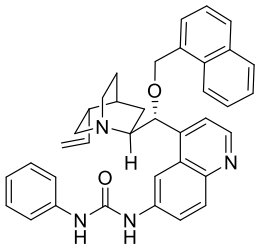




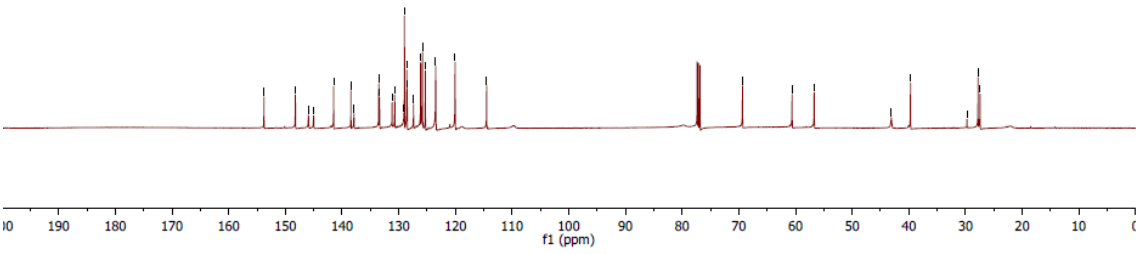
4s



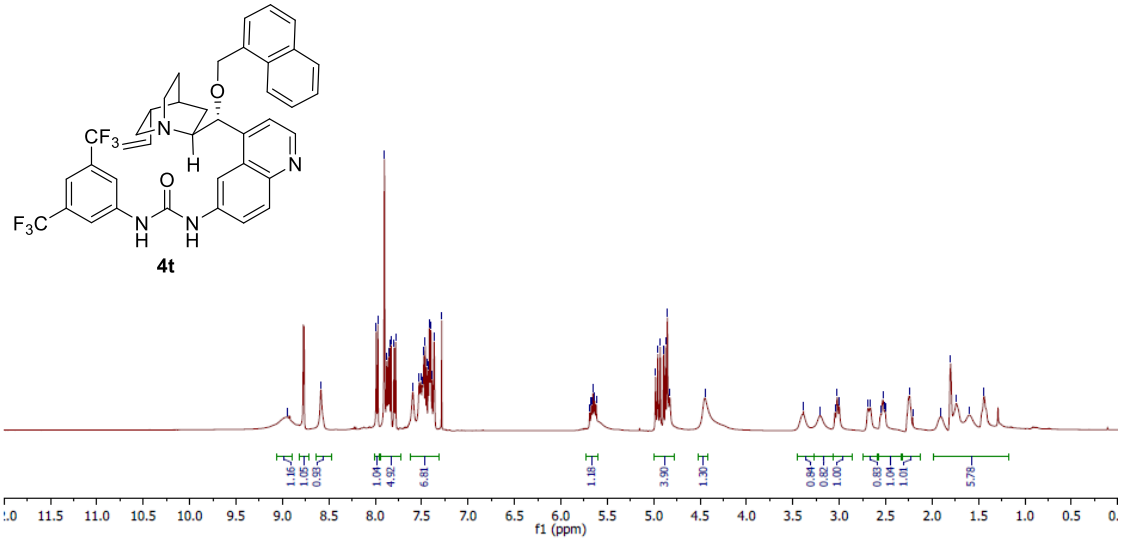
II-NS-361-1.2.fid



4s

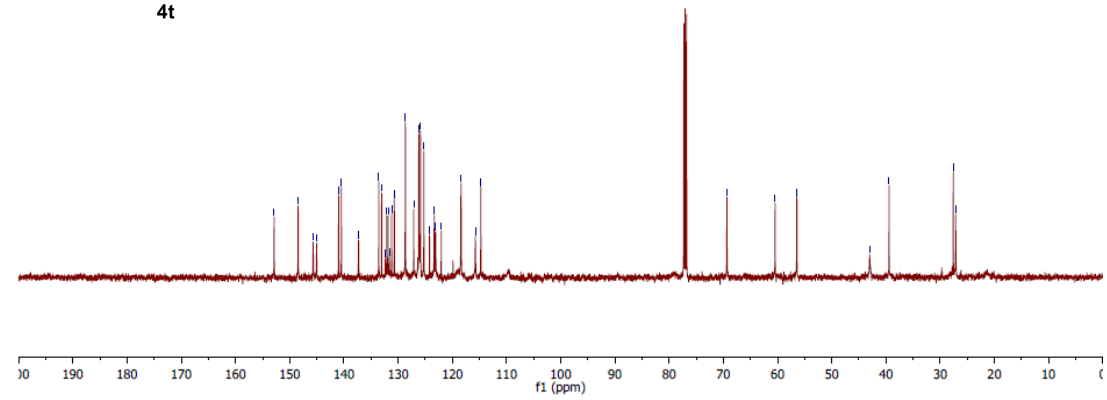


1-NS-179-1.1.fid



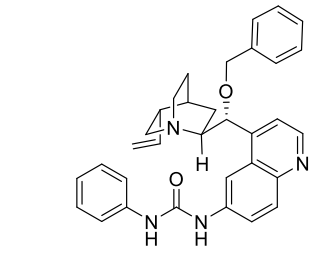
4t

1-NS-179-1.2.fid

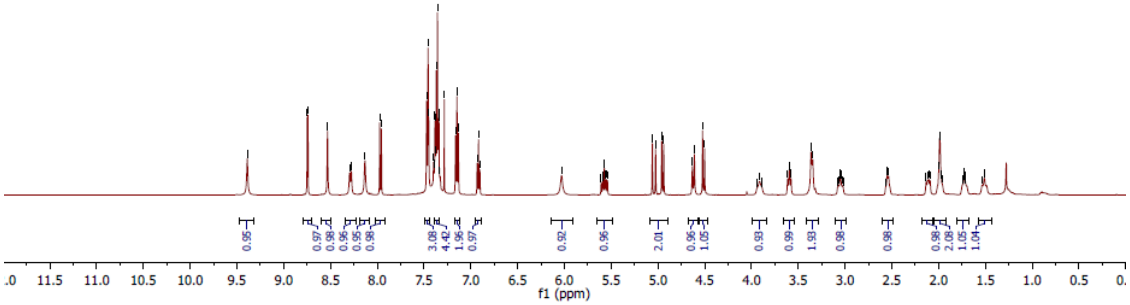


4t

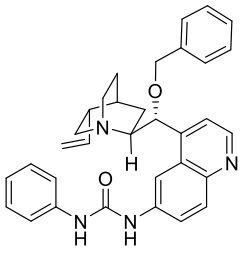
II-NS-358-1.1.fid



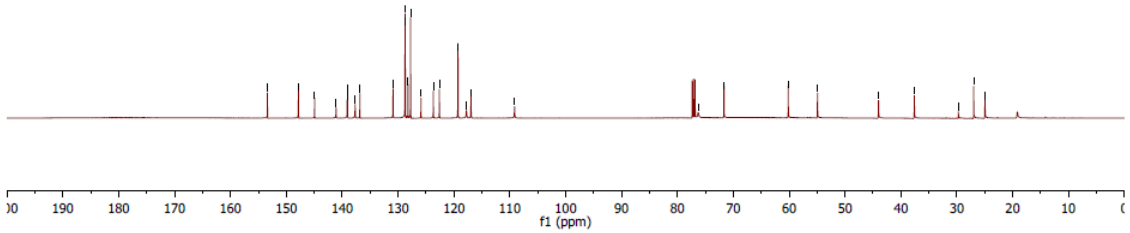
4u

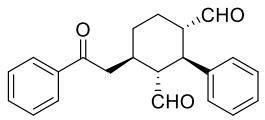


II-NS-358-1.2.fid

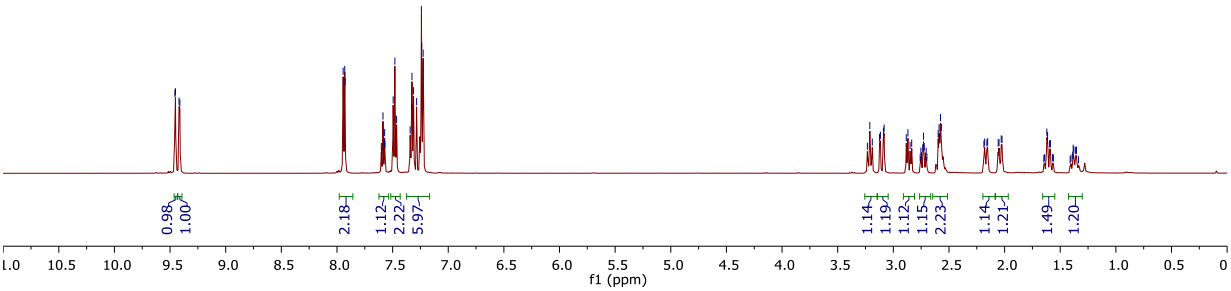


4u

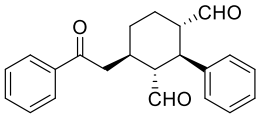



O
CHO
CHO

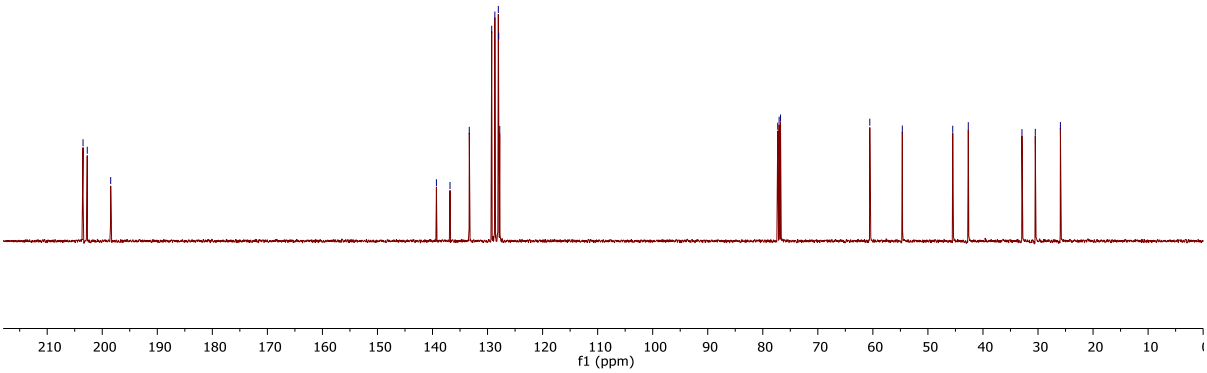
3a


0.98
1.00
2.18
1.12
2.22
5.97
1.14
1.19
1.12
1.15
2.23
1.14
1.21
1.49
1.20
f1 (ppm)


1-rp-891-pure2.10d
203.19
202.29
198.48
139.29
136.82
133.32
129.24
128.67
128.05
127.97
127.79
77.29
77.03
76.78
60.56
54.65
45.49
42.67
32.91
30.49
25.93


O
CHO
CHO

3a


f1 (ppm)


1-rp-2095-pure.1.fid
9.46
9.46
9.42
9.41
7.94
7.93
7.93
7.60
7.59
7.58
7.57
7.50
7.48
7.47
7.15
7.14
6.86
6.85
3.79
3.17
3.15
3.11
3.11
3.08
3.07
2.88
2.86
2.84
2.83
2.69
2.68
2.67
2.66
2.65
2.55
2.54
2.53
2.17
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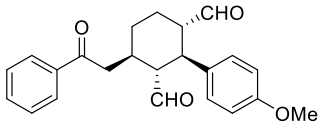
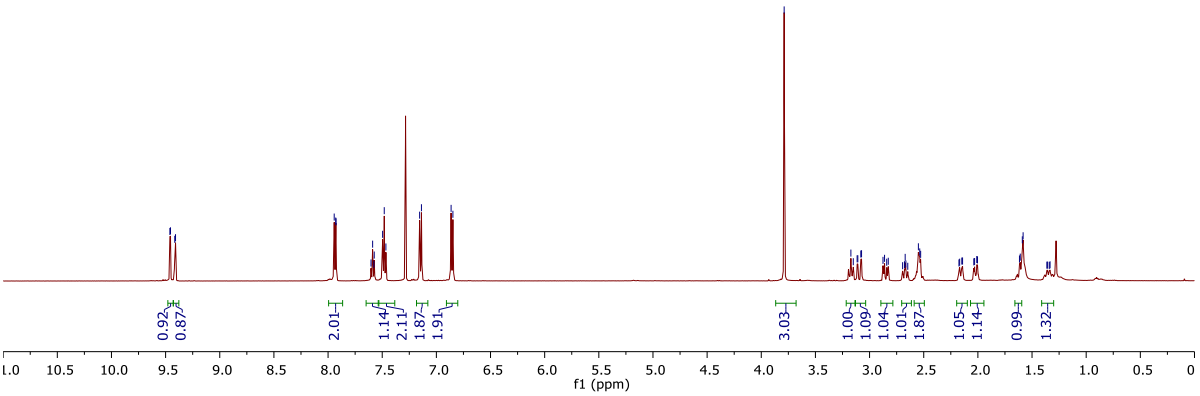
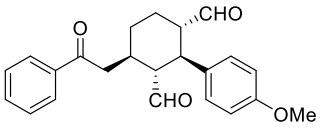
2.00
1.62
1.61
1.59
1.58
1.36


O
CHO
CHO
OMe

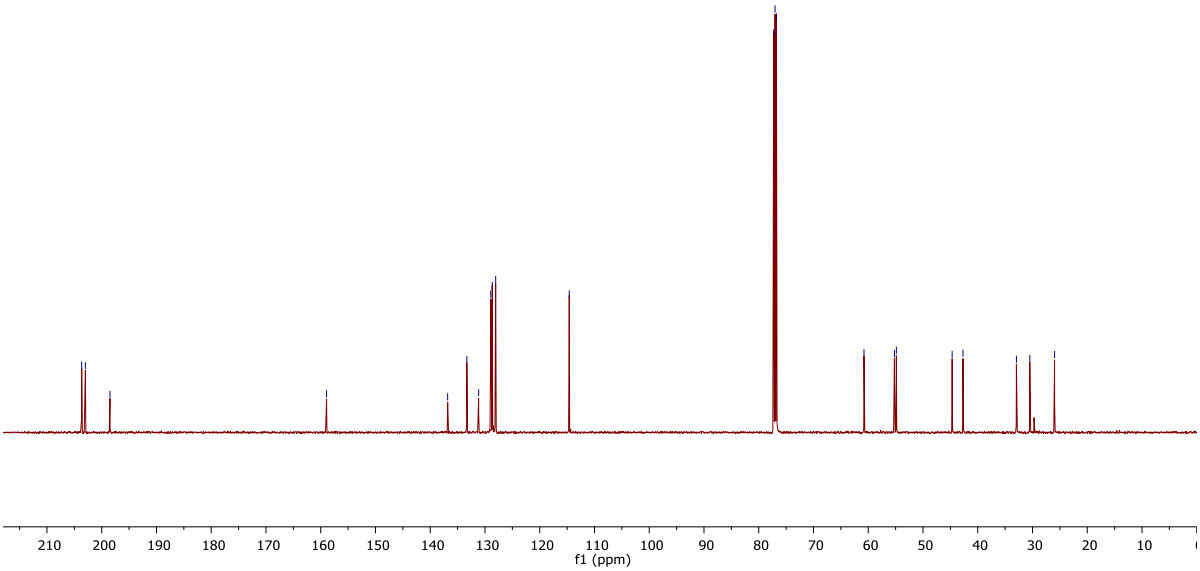
3b

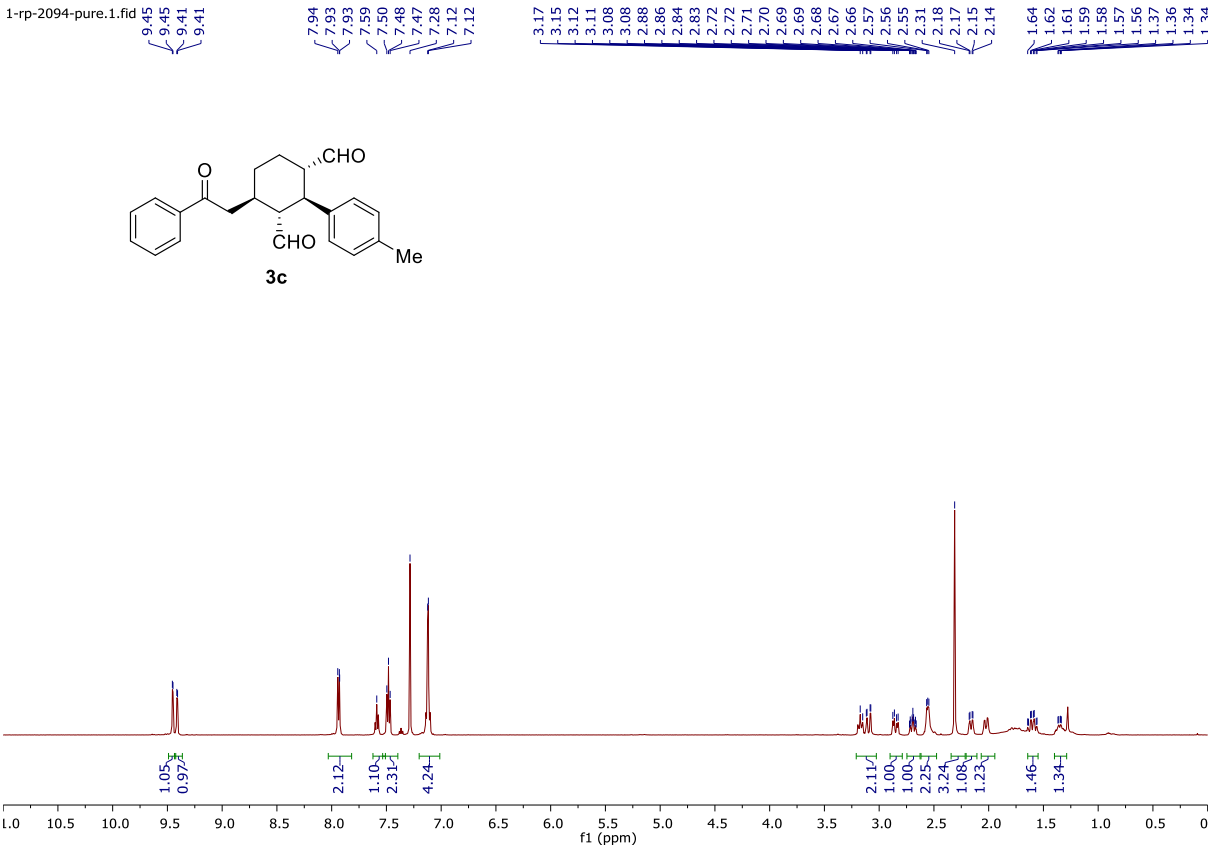

0.92
0.87
2.01
1.14
2.11
1.87
1.91
3.03
1.00
1.09
1.04
1.01
1.87
1.05
1.14
0.99
1.32
f1 (ppm)

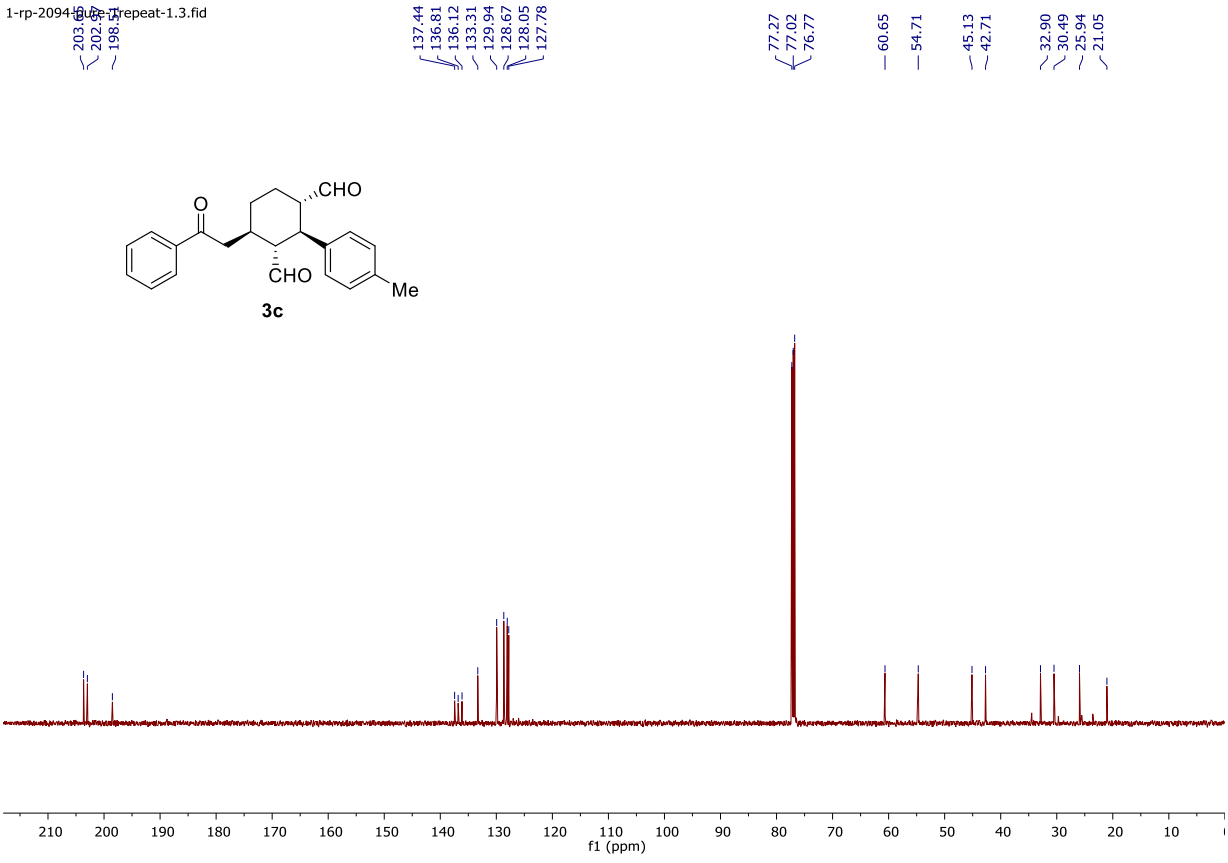

1-rp-2095-pure.3.fid
203.68
202.37
198.31
158.93
136.82
133.31
131.15
128.94
128.67
128.05
114.61
77.27
77.02
76.76
60.78
55.22
54.86
44.67
42.69
32.94
30.49
25.97


O
CHO
CHO
OMe

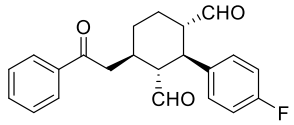
3b


f1 (ppm)

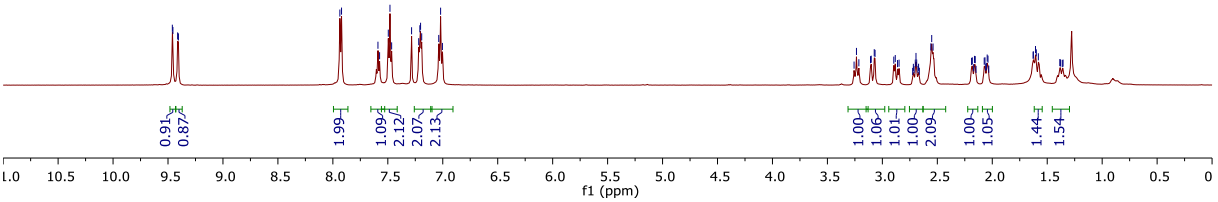

1-rp-2094-pure.1.fid
9.45
9.45
9.41
9.41
7.94
7.93
7.93
7.59
7.50
7.48
7.47
7.28
7.12
7.12
3.17
3.15
3.12
3.11
3.08
3.08
2.88
2.86
2.84
2.83
2.72
2.72
2.71
2.70
2.69
2.69
2.68
2.67
2.66
2.57
2.56
2.55
2.31
2.18
2.17
2.15
2.14
1.64
1.62
1.61
1.59
1.58
1.57
1.56
1.37
1.36
1.34
O
CHO
CHO
Me
3c
1.05
0.97
2.12
1.10
2.31
4.24
2.11
1.00
1.00
2.25
3.24
1.08
1.23
1.46
1.34
f1 (ppm)


1-rp-2094-pure-1repeat-1.3.fid
203.16
202.59
198.47
137.44
136.81
136.12
133.31
129.94
128.67
128.05
127.78
77.27
77.02
76.77
60.65
54.71
45.13
42.71
32.90
30.49
25.94
21.05
O
CHO
CHO
Me
3c
f1 (ppm)

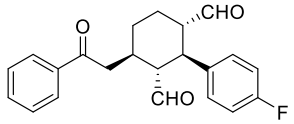

1-rp-2118-pure.1.fid
9.46 9.46 9.41 9.41
7.94 7.92 7.59 7.57 7.50 7.48 7.47 7.28 7.22 7.21 7.20 7.19 7.04 7.02 7.00
3.26 3.24 3.21 3.11 3.10 3.07 3.07 2.90 2.88 2.86 2.85 2.72 2.72 2.71 2.70 2.69 2.69 2.68 2.67 2.66 2.56 2.55 2.54
2.19 2.18 2.16 2.15 2.07 2.07 2.05 2.04 1.63 1.63 1.61 1.60 1.58


O
CHO
CHO
F

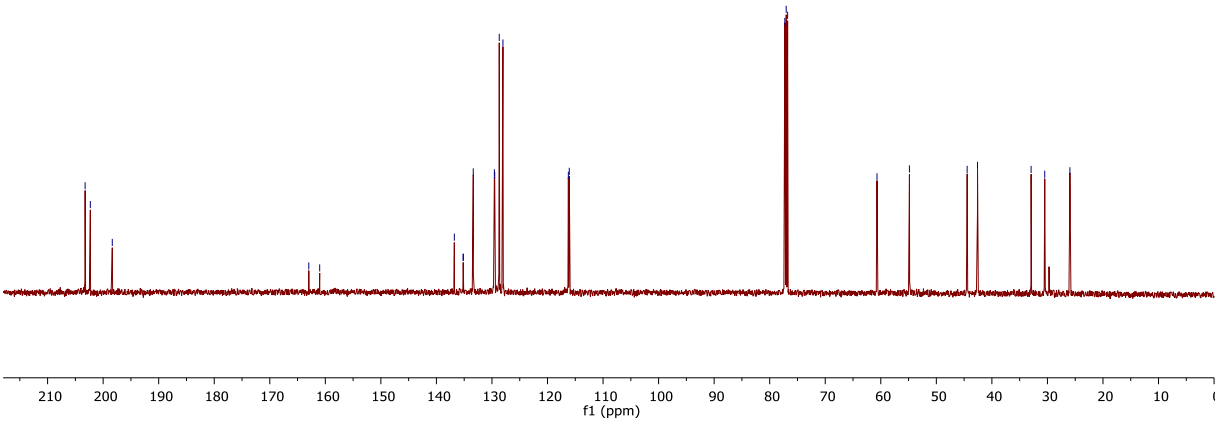
3d


0.91 0.87 1.99 1.09 2.12 2.07 2.13 1.00 1.06 1.01 1.00 2.09 1.00 1.05 1.44 1.54
f1 (ppm)

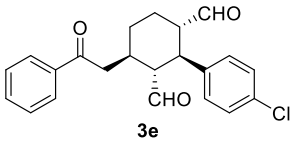

1-rp-2118-pure.3.fid
203.71 202.38 198.34
162.98 161.02
136.78 135.19 135.16 133.37 129.57 129.50 128.69 128.02
116.25 116.08
77.28 77.03 76.77
60.68 54.84
44.45 42.58
32.94 30.48 25.96


O
CHO
CHO
F

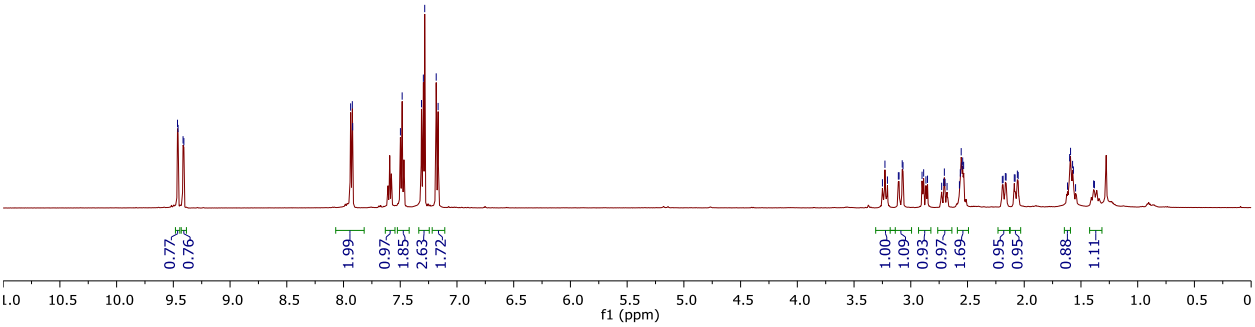
3d


f1 (ppm)

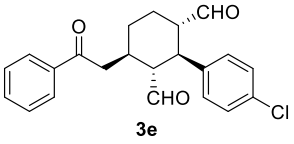

1-rp-2103-pure-1.1.fid
9.46
9.41
9.41
7.94
7.92
7.92
7.50
7.48
7.31
7.30
7.28
7.18
7.17
3.25
3.23
3.21
3.11
3.10
3.08
3.07
2.90
2.89
2.87
2.85
2.73
2.71
2.70
2.70
2.68
2.57
2.56
2.56
2.55
2.54
2.53
2.19
2.19
2.17
2.16
2.09
2.08
2.06
2.05
1.62
1.60
1.59
1.57
1.57
1.55
1.39
1.38


O
CHO
CHO
Cl

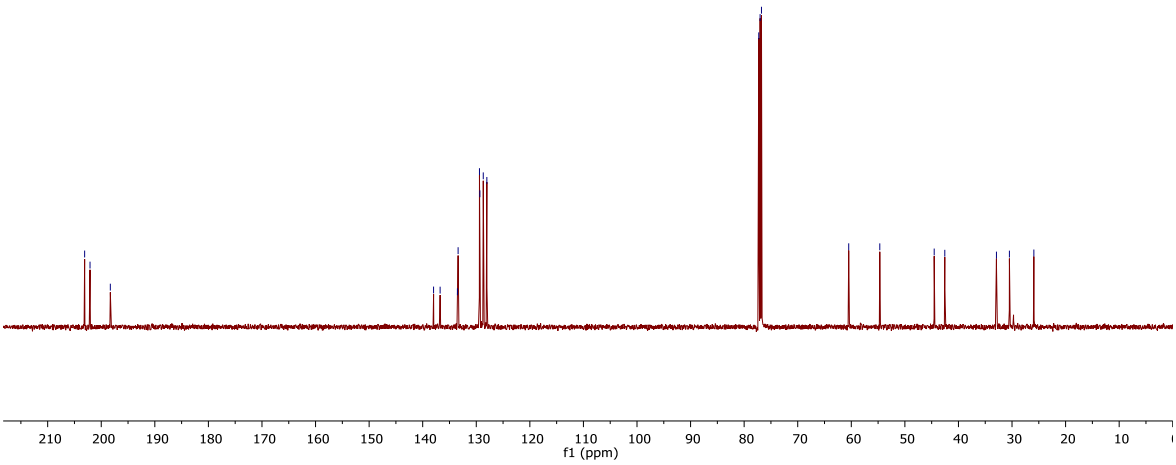
3e

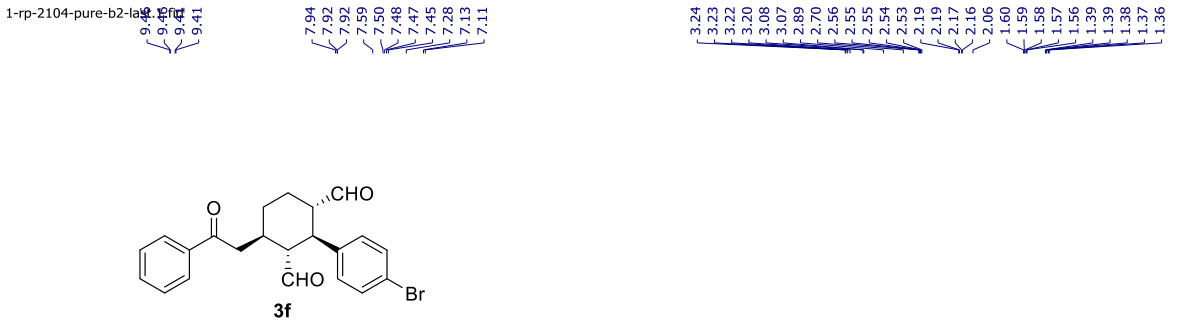

0.77
0.76
1.99
0.97
1.85
2.63
1.72
1.00
1.09
0.93
0.97
1.69
0.95
0.95
0.88
1.11
f1 (ppm)


1-rp-2103-pure-C2.fid
203.50
202.58
198.31
137.97
136.75
133.52
133.39
129.40
129.33
128.70
128.03
77.27
77.02
76.77
60.48
54.68
44.53
42.55
32.91
30.49
25.92


O
CHO
CHO
Cl

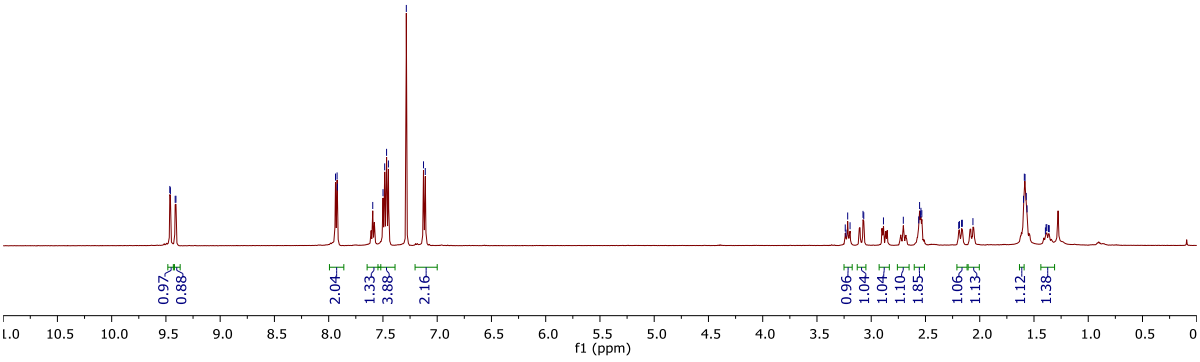
3e

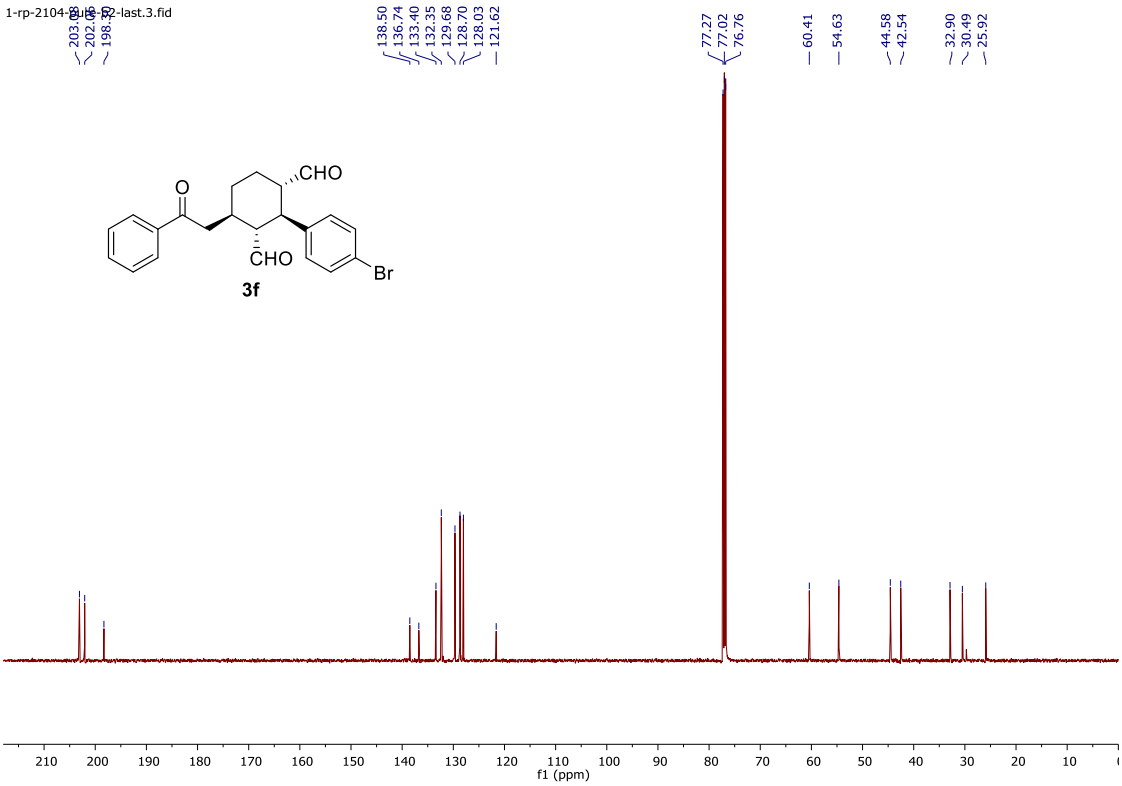

f1 (ppm)


1-rp-2104-pure-b2-last.1.fid
9.44
9.41
7.94
7.92
7.59
7.50
7.48
7.47
7.45
7.28
7.13
7.11
3.24
3.23
3.22
3.20
3.08
3.07
2.89
2.70
2.56
2.55
2.55
2.54
2.53
2.19
2.19
2.17
2.16
2.06
1.60
1.59
1.58
1.57
1.56
1.39
1.39
1.38
1.37
1.36

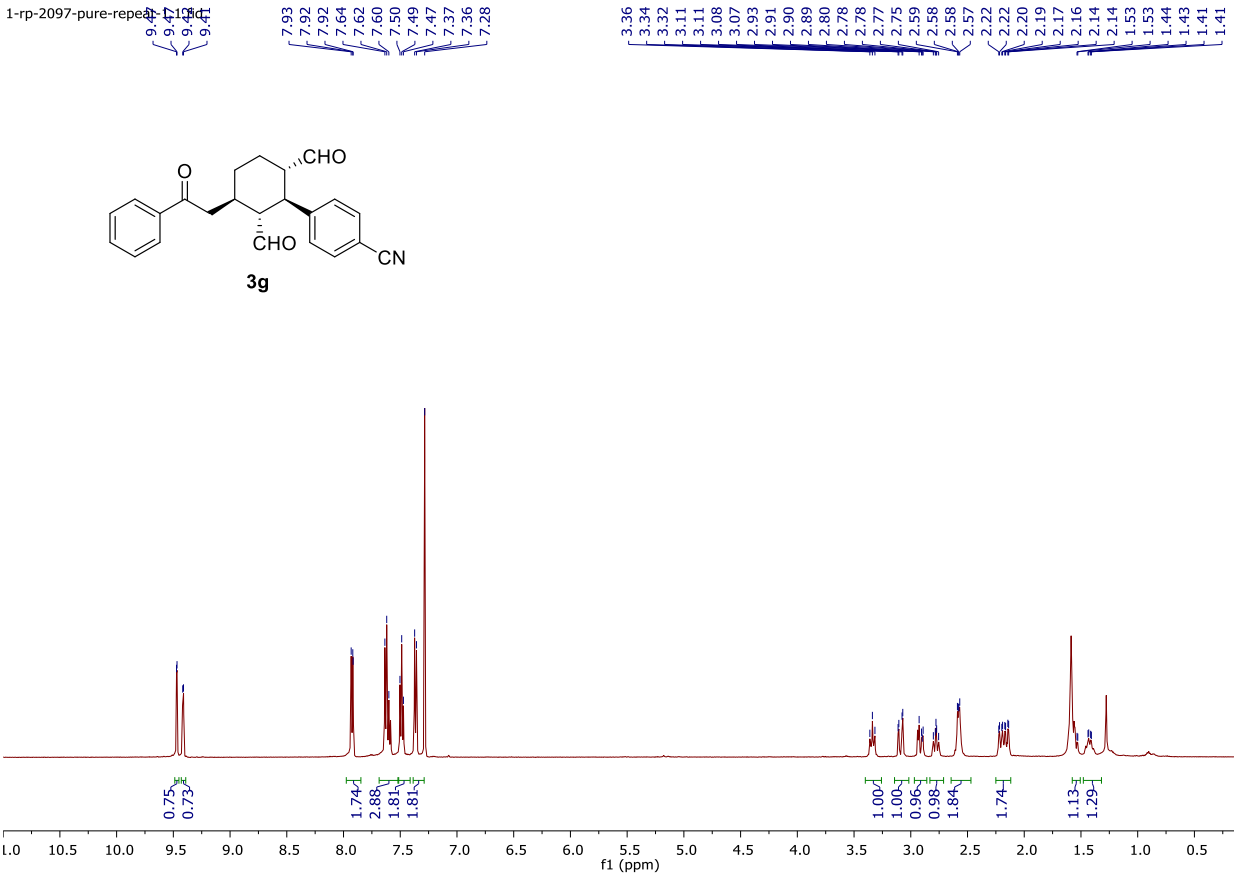
O
CHO
CHO
Br

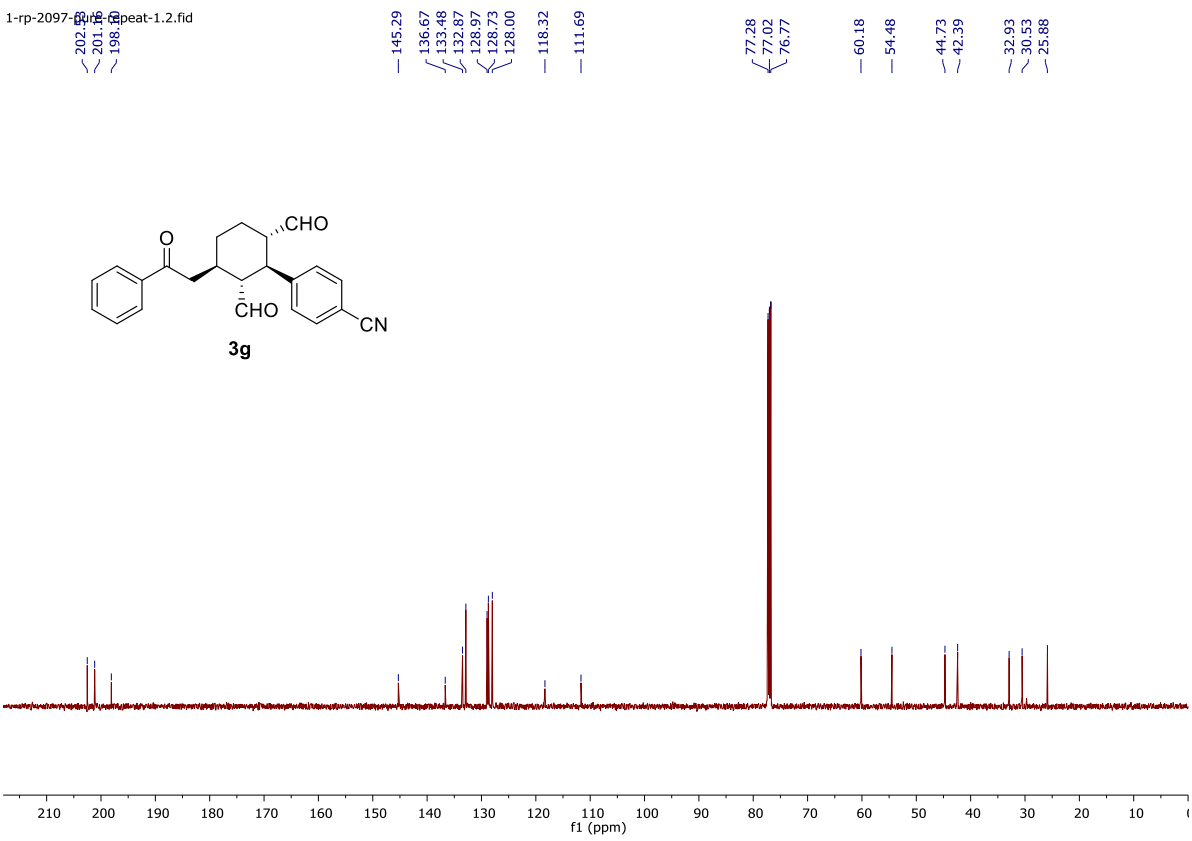
3f

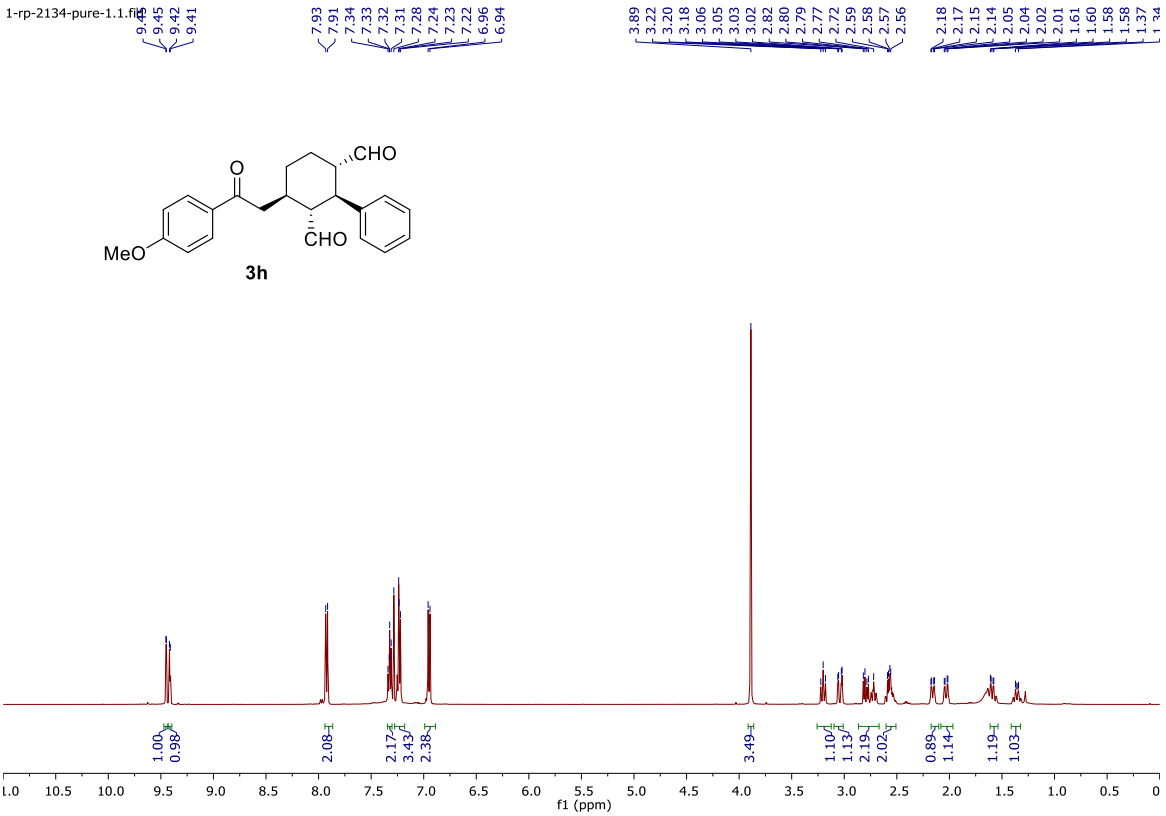

0.97
0.88
2.04
1.33
3.88
2.16
0.96
1.04
1.04
1.10
1.85
1.06
1.13
1.12
1.38
f1 (ppm)

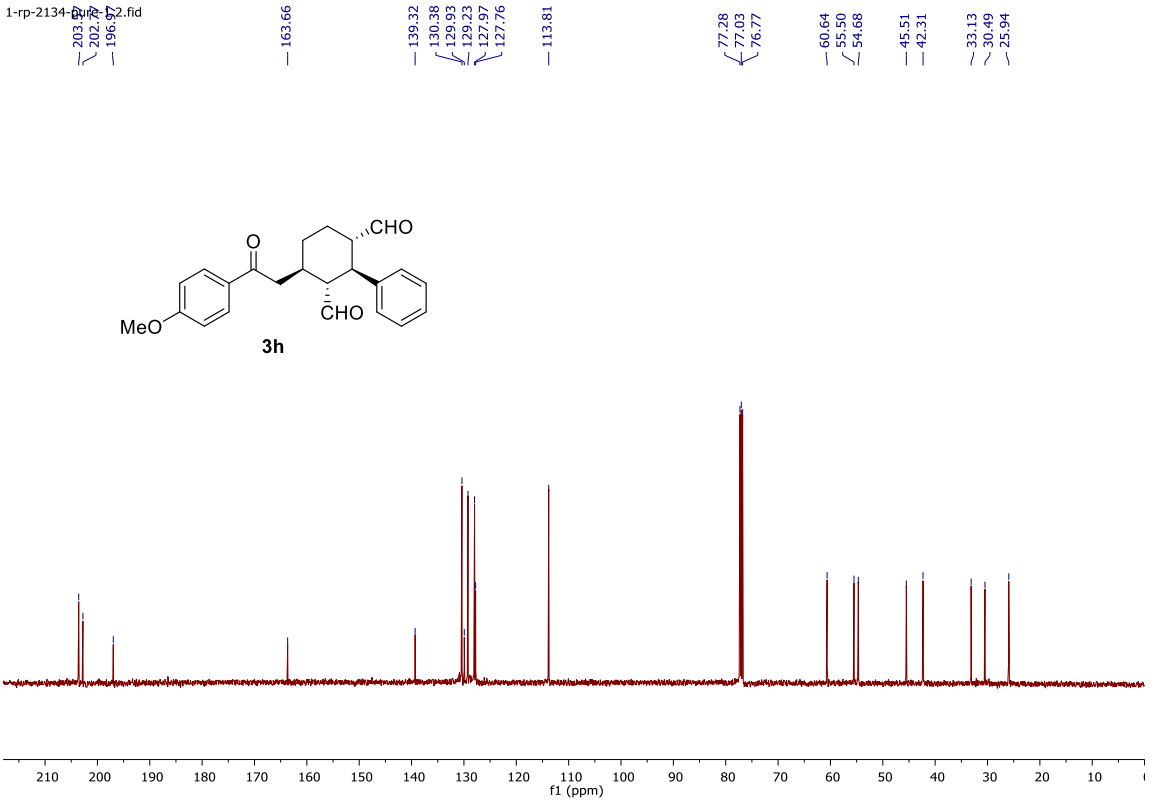

1-rp-2104-pure-b2-last.3.fid
203.01
202.68
198.72
138.50
136.74
133.40
132.35
129.68
128.70
128.03
121.62
77.27
77.02
76.76
60.41
54.63
44.58
42.54
32.90
30.49
25.92
O
CHO
CHO
Br
f1 (ppm)

3f

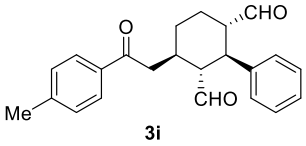

1-rp-2097-pure-repeat-1.1.fid
9.47
9.47
9.41
9.41
7.93
7.92
7.92
7.64
7.62
7.60
7.50
7.49
7.47
7.37
7.36
7.28
3.36
3.34
3.32
3.11
3.11
3.08
3.07
2.93
2.91
2.90
2.89
2.80
2.78
2.78
2.77
2.75
2.59
2.58
2.58
2.57
2.22
2.22
2.20
2.19
2.17
2.16
2.14
2.14
1.53
1.53
1.44
1.43
1.41
1.41
O
CHO
CHO
CN
3g
0.75
0.73
1.74
2.88
1.81
1.81
1.00
1.00
0.96
0.98
1.84
1.74
1.13
1.29
f1 (ppm)


1-rp-2097-pure-repeat-1.2.fid
202.18
201.16
198.46
145.29
136.67
133.48
132.87
128.97
128.73
128.00
118.32
111.69
77.28
77.02
76.77
60.18
54.48
44.73
42.39
32.93
30.53
25.88
O
CHO
CHO
CN
3g
f1 (ppm)

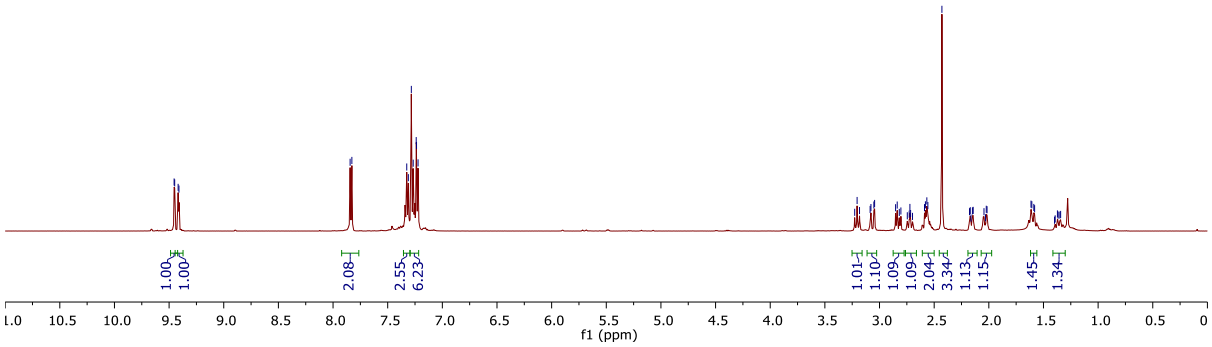

1-rp-2134-pure-1.1.fid
9.44
9.45
9.42
9.41
7.93
7.91
7.34
7.33
7.32
7.31
7.28
7.24
7.23
7.22
6.96
6.94
3.89
3.22
3.20
3.18
3.06
3.05
3.03
3.02
2.82
2.80
2.79
2.77
2.72
2.59
2.58
2.57
2.56
2.18
2.17
2.15
2.14
2.05
2.04
2.02
2.01
1.61
1.60
1.58
1.58
1.37
O
CHO
CHO
MeO
3h
1.00
0.98
2.08
2.17
3.43
2.38
3.49
1.10
1.13
2.19
2.02
0.89
1.14
1.19
1.03
f1 (ppm)


1-rp-2134-pure-2.2.fid
203.32
202.77
196.97
163.66
139.32
130.38
129.93
129.23
127.97
127.76
113.81
77.28
77.03
76.77
60.64
55.50
54.68
45.51
42.31
33.13
30.49
25.94
O
CHO
CHO
MeO
3h
f1 (ppm)

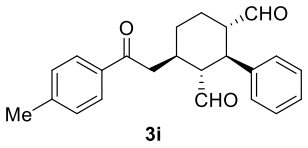

1-rp-2107-pure.1.fid
9.45
9.45
9.42
9.41
7.84
7.83
7.33
7.31
7.28
7.27
7.24
7.24
7.22
3.23
3.21
3.18
3.09
3.08
3.05
3.04
2.85
2.84
2.82
2.80
2.75
2.73
2.72
2.72
2.70
2.59
2.58
2.57
2.56
2.43
2.18
2.17
2.16
2.15
2.14
2.04
2.03
2.02
2.02
1.61
1.61
1.59
1.58
1.40
1.39
1.37
1.37
1.35
1.34


O
CHO
CHO
Me

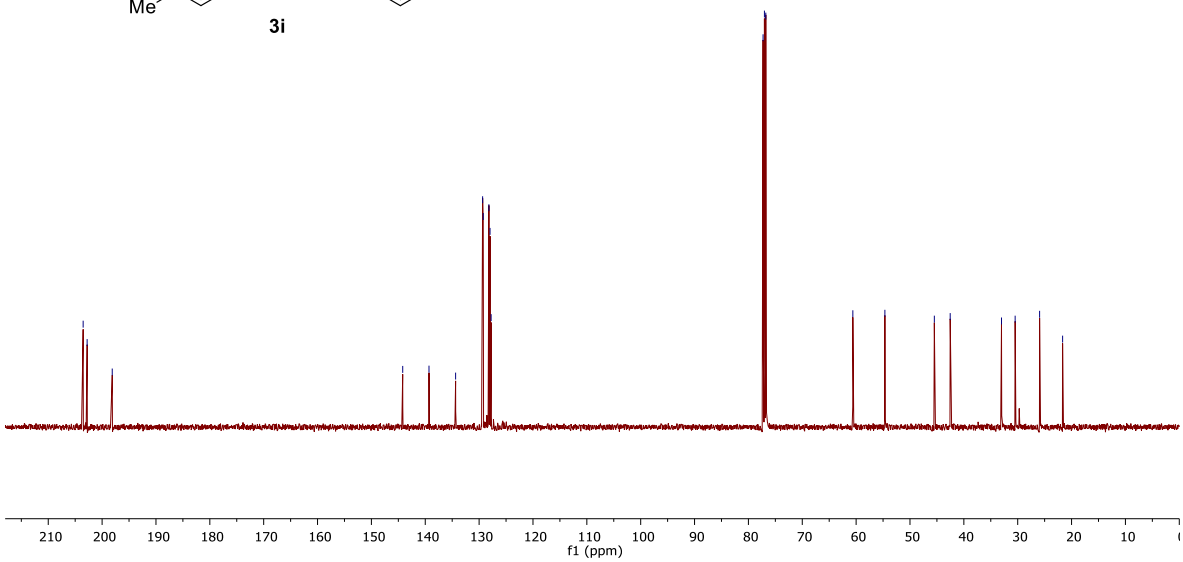
3i


1.00
1.00
2.08
2.55
6.23
1.01
1.10
1.09
1.09
2.04
3.34
1.13
1.15
1.45
1.34
f1 (ppm)

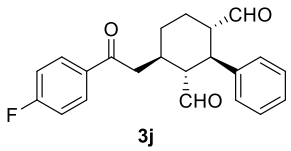

1-rp-2107-pure.2.fid
203.12
202.72
198.12
144.19
139.31
134.36
129.35
129.24
128.19
127.97
127.77
77.28
77.03
76.77
60.61
54.66
45.48
42.53
33.01
30.47
25.93
21.66


O
CHO
CHO
Me

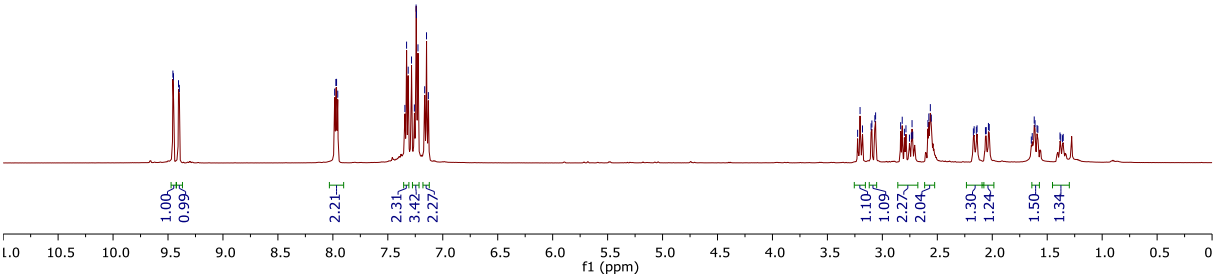
3i


f1 (ppm)

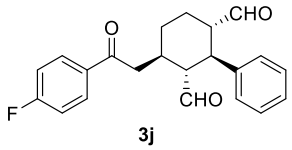

1-rp-2109-pure.1.fid
9.46
9.45
9.40
9.40
7.98
7.97
7.97
7.96
7.34
7.33
7.31
7.28
7.26
7.24
7.24
7.23
7.16
7.15
7.13
3.23
3.20
3.18
3.10
3.10
3.07
3.06
2.83
2.82
2.80
2.79
2.75
2.74
2.73
2.72
2.59
2.58
2.56
2.55
2.17
2.16
2.15
2.14
2.06
2.05
2.03
2.03
1.64
1.62
1.61
1.59
1.59


O
CHO
CHO
F

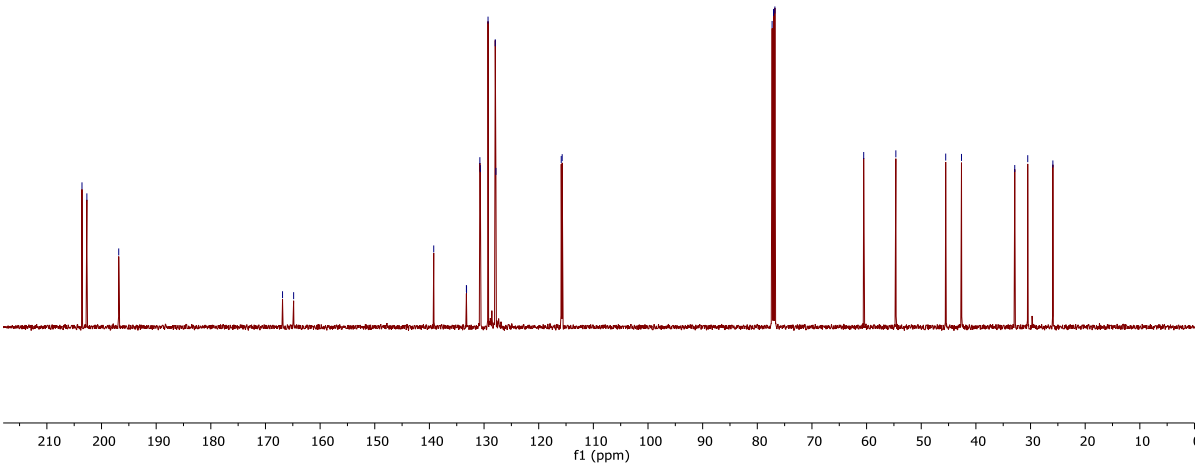
3j


1.00
0.99
2.21
2.31
3.42
2.27
1.10
1.09
2.27
2.04
1.30
1.24
1.50
1.34
f1 (ppm)


1-rp-2109-pure.2.fid
203.18
202.88
196.22
166.88
164.85
139.21
133.23
133.20
130.77
130.69
129.27
127.95
127.83
115.88
115.70
77.29
77.04
76.78
60.53
54.65
45.52
42.64
32.89
30.51
25.91


O
CHO
CHO
F

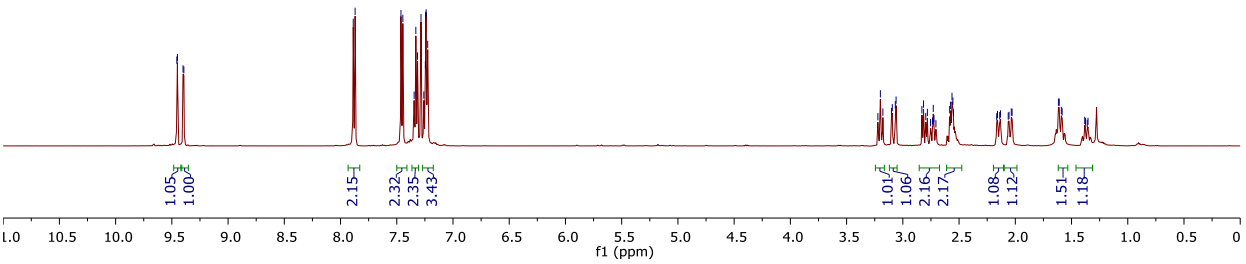
3j


f1 (ppm)

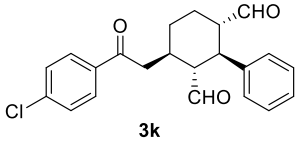

1-rp-2110-pure.1.fid
9.46
9.45
9.40
9.39
7.89
7.87
7.46
7.45
7.35
7.33
7.32
7.28
7.26
7.25
7.24
7.24
7.22
3.22
3.20
3.18
3.10
3.09
3.07
3.06
2.83
2.82
2.80
2.78
2.75
2.74
2.73
2.72
2.71
2.58
2.58
2.56
2.56
2.55
2.17
2.16
2.14
2.13
2.06
2.06
2.04
2.03
1.62
1.61
1.59
1.58
1.38

O
CHO
CHO
Cl

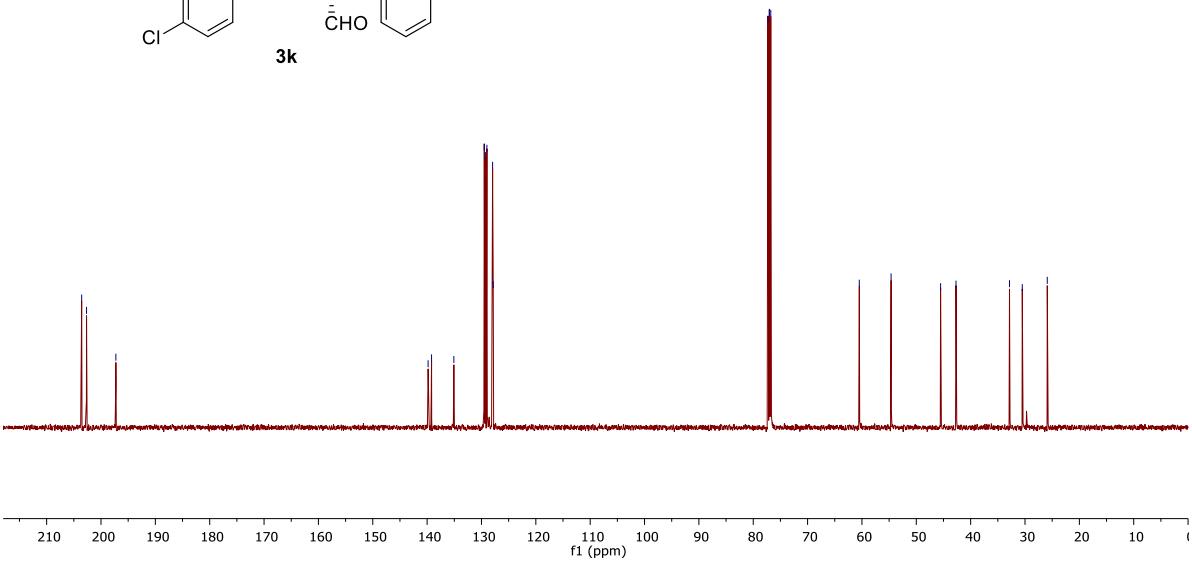
3k

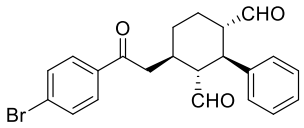

1.05
1.00
2.15
2.32
2.35
3.43
1.01
1.06
2.16
2.17
1.08
1.12
1.51
1.18
f1 (ppm)


1-rp-2110-pure.2.fid
203.34
202.42
197.42
139.82
139.18
135.08
129.48
129.28
129.00
127.95
127.84
77.28
77.03
76.77
60.49
54.64
45.53
42.69
32.85
30.50
25.90

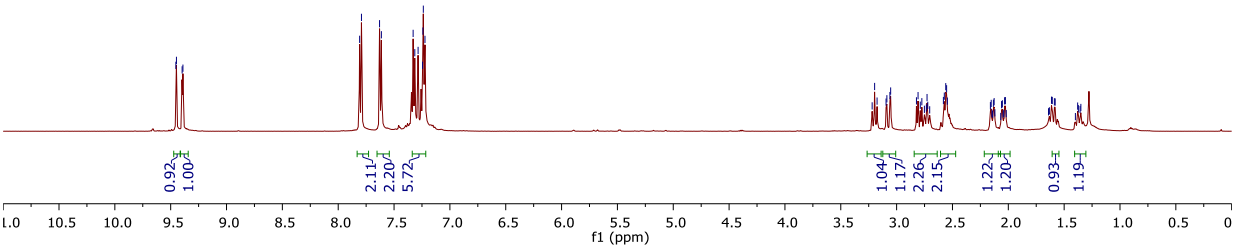

O
CHO
CHO
Cl

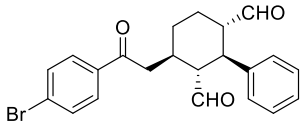
3k


f1 (ppm)

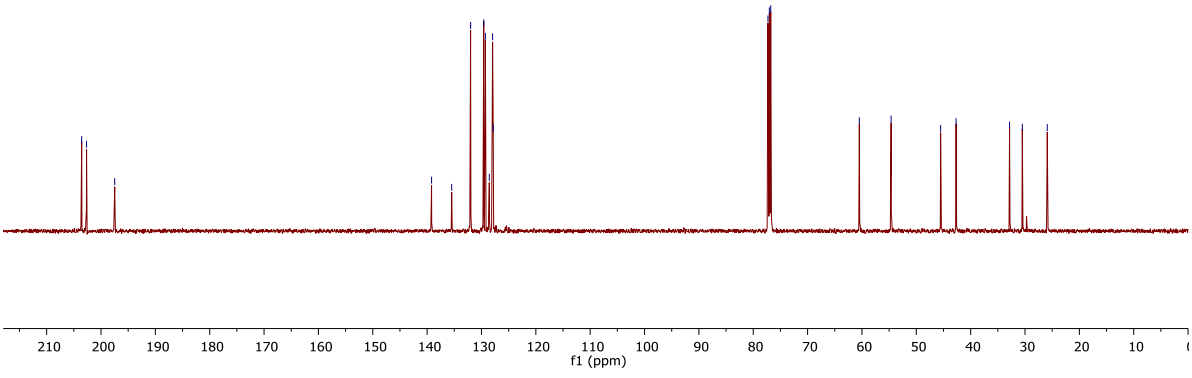


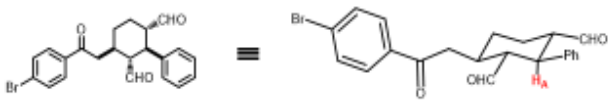
3l





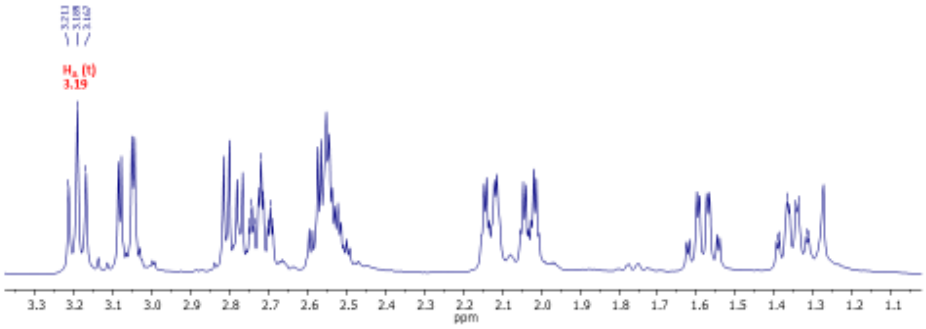
3l

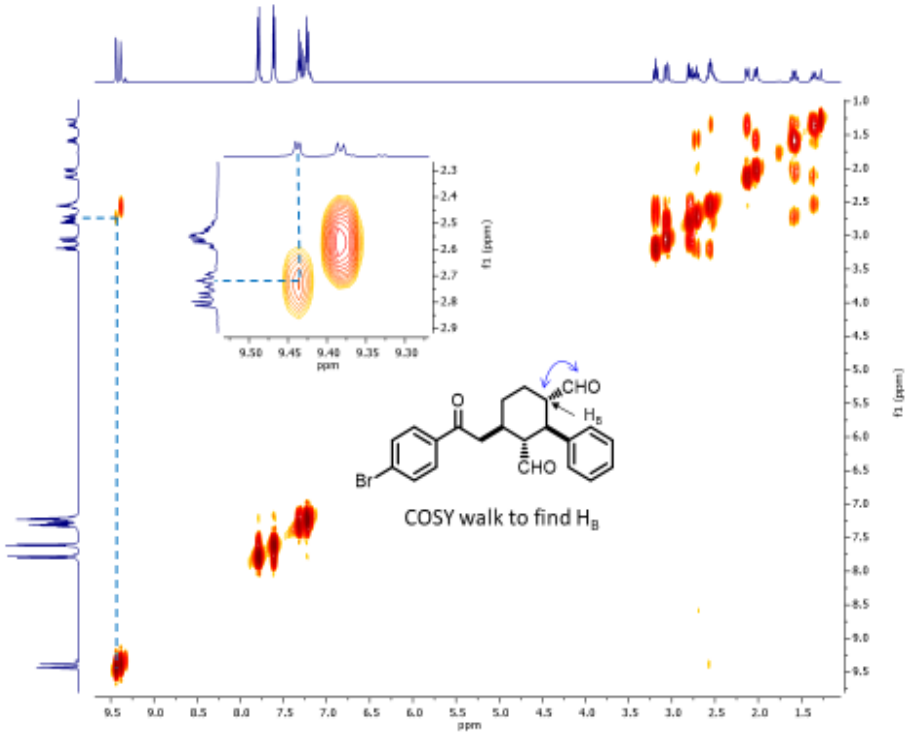




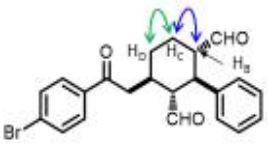
H_A δ 3.19 (t, J = 11.1 Hz, 1H)

2 – axial-axial couplings, substituents must be equatorial

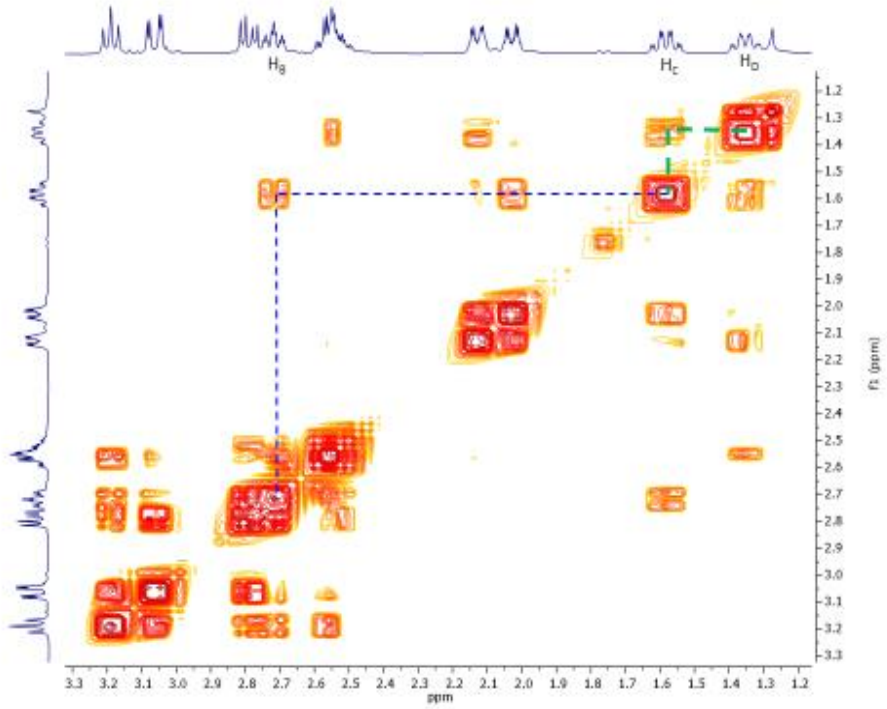


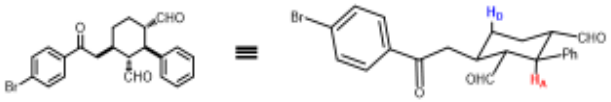


Relative stereochemistry assignment of compound 3I



COSY walk to find H_D



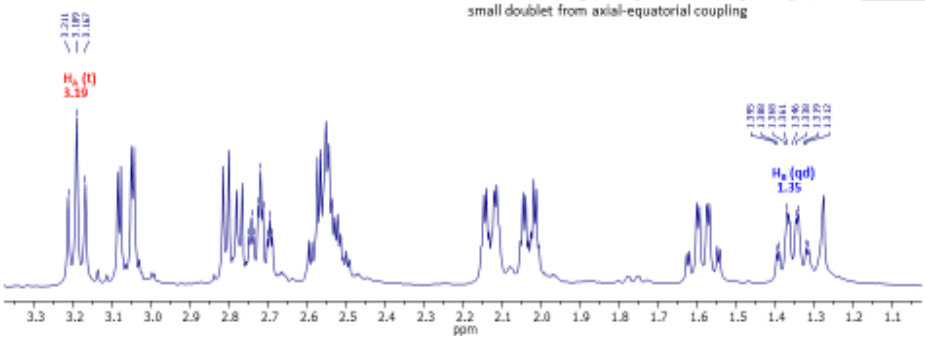


H_A δ 3.19 (t, *J* = 11.1 Hz, 1H)

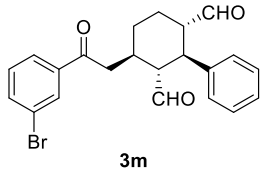
2 – axial-axial couplings, substituents must be equatorial

H_D 1.35 (qd, *J* = 13.3, 3.6 Hz, 1H)

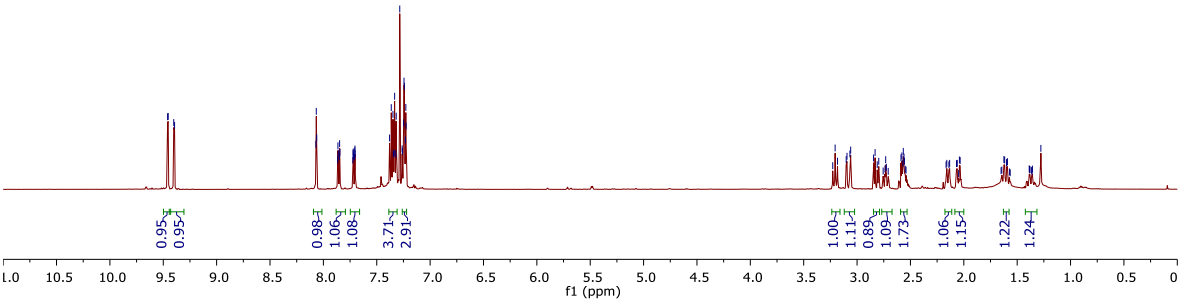
2 – axial-axial couplings and 1 germinal coupling for large quartet, substituent must be equatorial
small doublet from axial-equatorial coupling

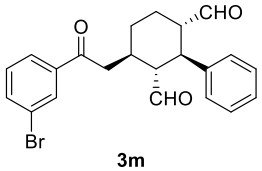


Relative stereochemistry assignment of compound 3I

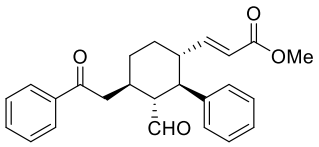


3m





3m



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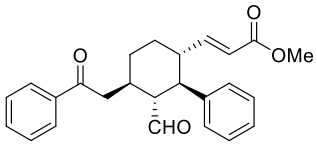

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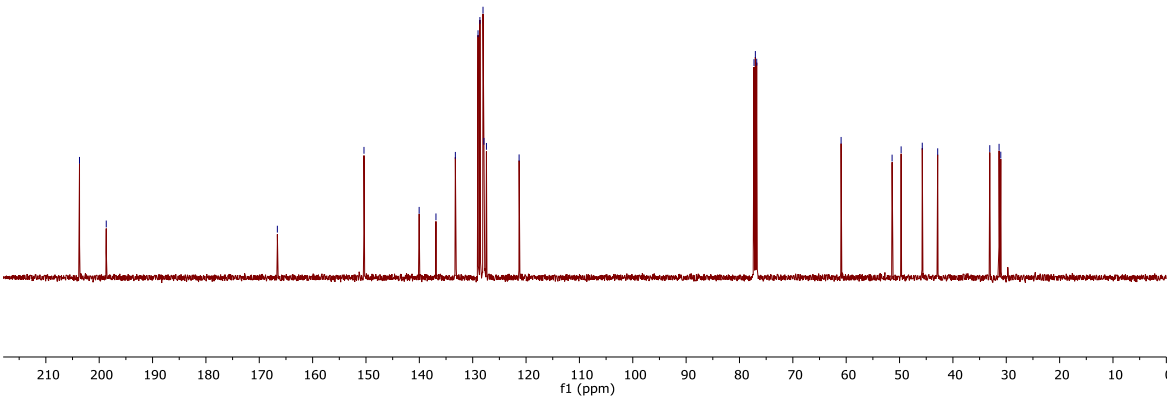
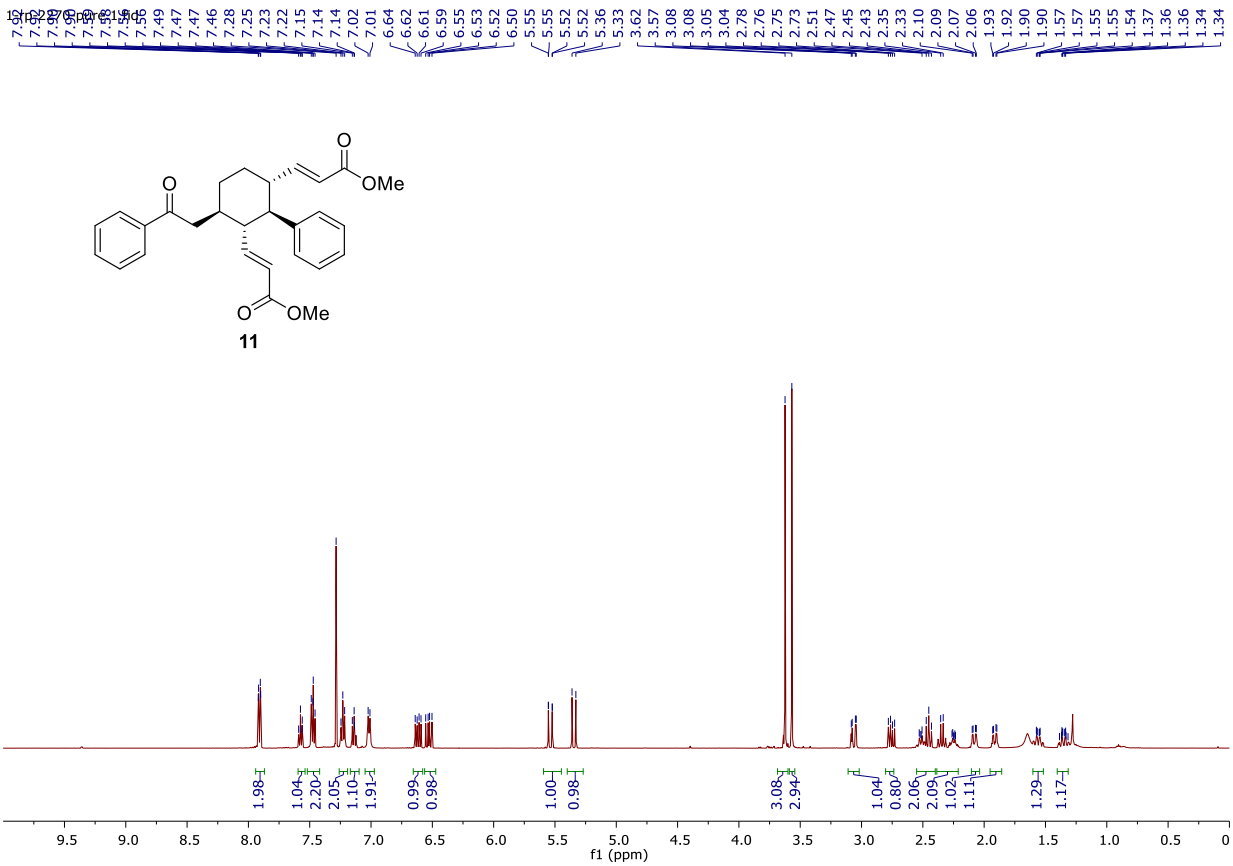
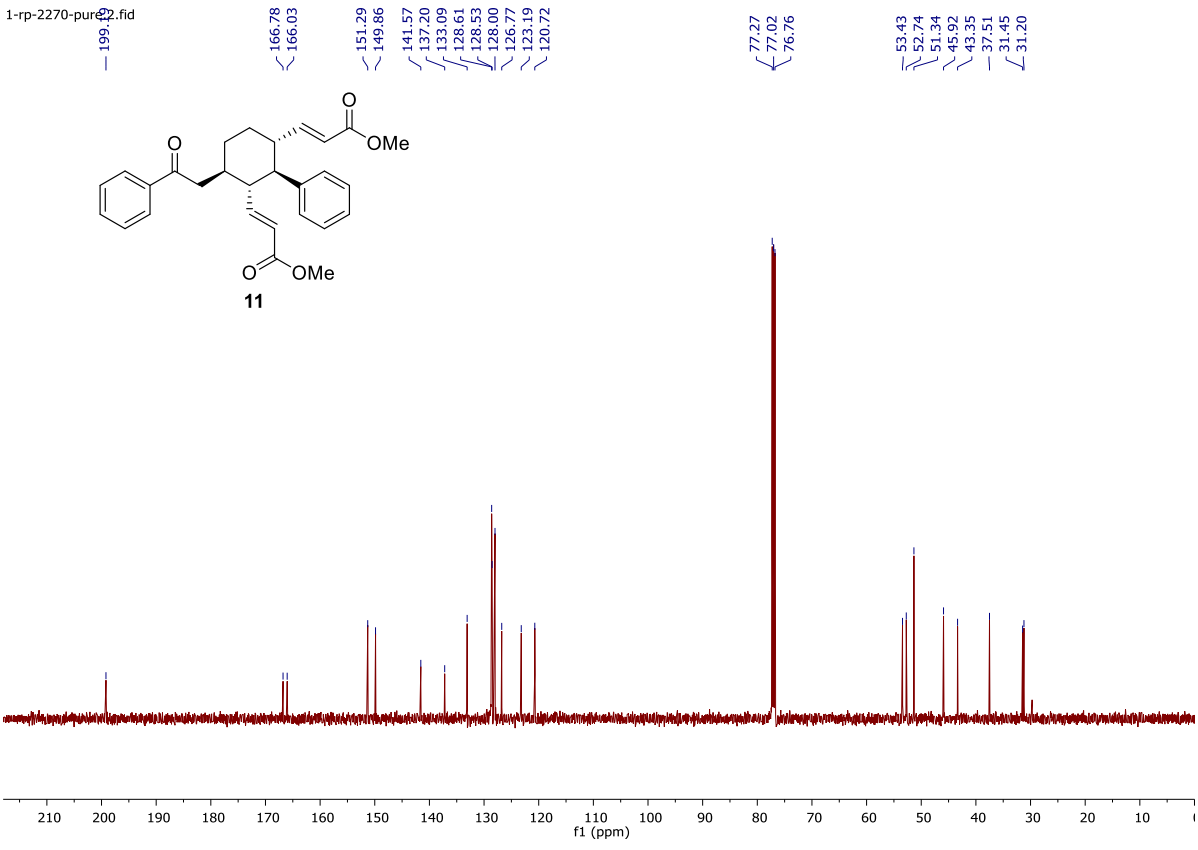



1-rp-2270-pure1.fid
OMe
OMe
11
1.98
1.04
2.20
2.05
1.10
1.91
0.99
0.98
1.00
0.98
3.08
2.94
1.04
0.80
2.06
2.09
1.02
1.11
1.29
1.17
f1 (ppm)


1-rp-2270-pure2.fid
199.12
166.78
166.03
151.29
149.86
141.57
137.20
133.09
128.61
128.53
128.00
126.77
123.19
120.72
77.27
77.02
76.76
53.43
52.74
51.34
45.92
43.35
37.51
31.45
31.20
OMe
OMe
11
f1 (ppm)

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-1687-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-1687-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 10/1/2019 12:52:08 PM
Data Processed	: 10/1/2019 1:20:20 PM

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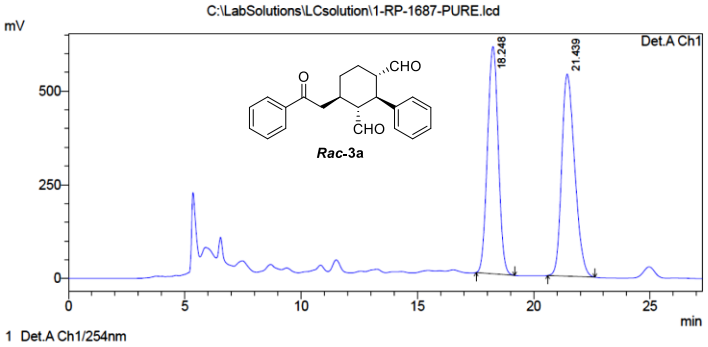


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.248	19604482	606349	48.285	52.939
2	21.439	20997316	539026	51.715	47.061
Total		40601798	1145374	100.000	100.000

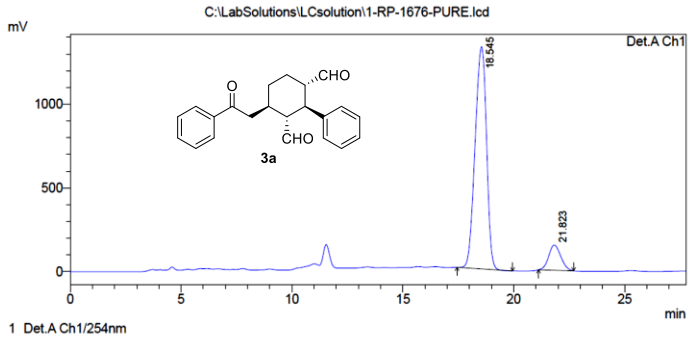
HPLC of racemic **3a**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-1676-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-1676-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 9/30/2019 9:00:20 AM
Data Processed	: 8/28/2020 1:30:54 PM

<Chromatogram>



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.545	47552058	1326525	89.259	89.801
2	21.823	5722264	150662	10.741	10.199
Total		53274322	1477187	100.000	100.000

HPLC of **3a**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-rp-2339-pure.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-rp-2339-pure.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 9/22/2020 10:34:13 AM
Data Processed	: 9/22/2020 11:11:35 AM

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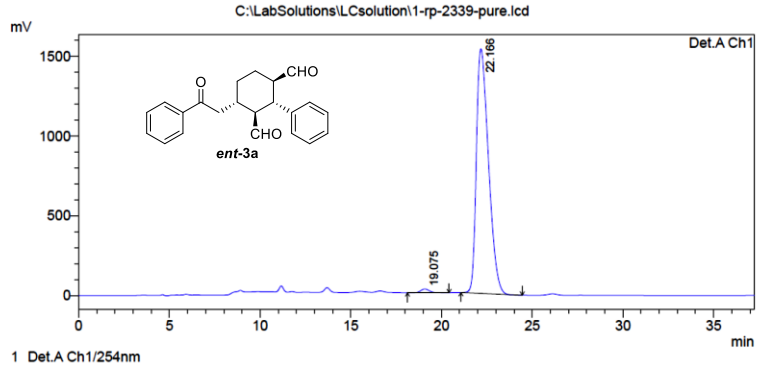
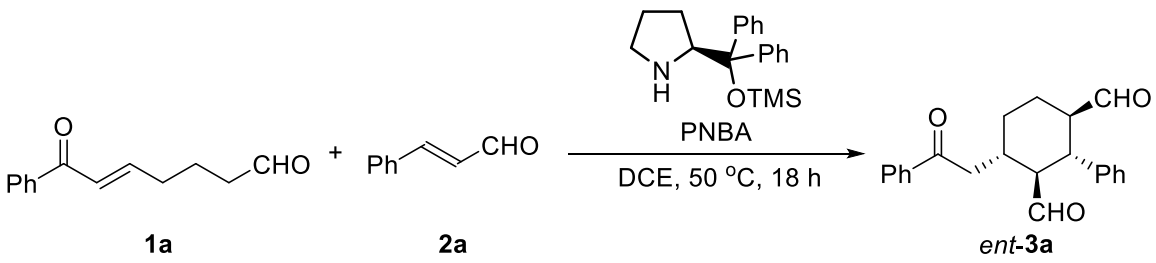


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.075	784257	23960	1.091	1.537
2	22.166	71114163	1534921	98.909	98.463
Total		71898419	1558881	100.000	100.000

HPLC of ***ent*-3a** obtained by using the Xu's catalytic system:



1a **2a** ***ent*-3a**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2088-C2-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2088-C2-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
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Data Processed	: 3/9/2020 3:19:30 PM

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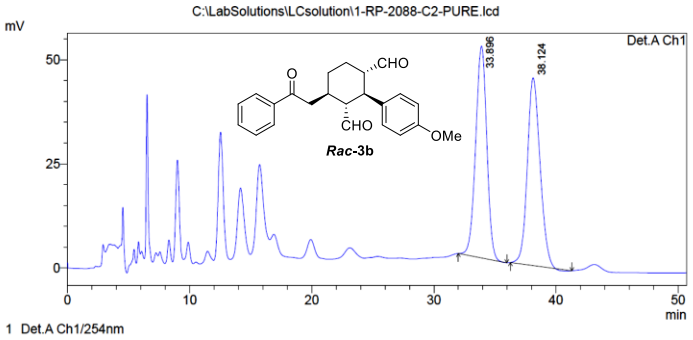

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.896	3225498	50860	49.799	53.022
2	38.124	3251525	45062	50.201	46.978
Total		6477022	95922	100.000	100.000

HPLC of racemic **3b**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2095-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2095-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/13/2020 11:28:43 AM
Data Processed	: 3/17/2020 9:38:00 AM

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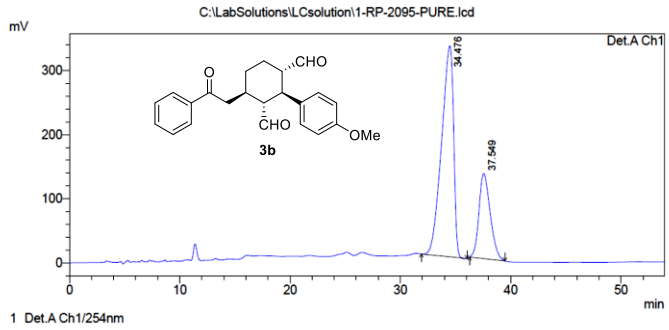

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.476	24895414	329444	72.477	71.265
2	37.549	9453943	132839	27.523	28.735
Total		34349357	462283	100.000	100.000

HPLC of **3b**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2087-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2087-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/9/2020 11:52:40 AM
Data Processed	: 3/9/2020 3:20:01 PM

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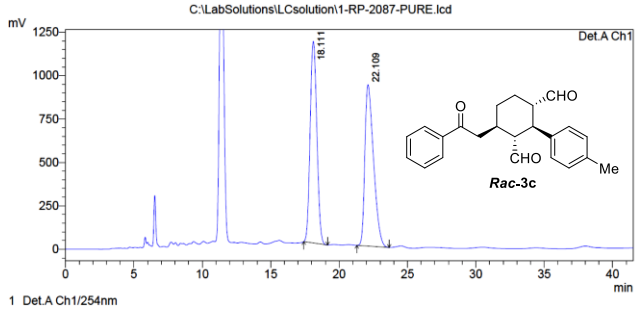

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.111	39691542	1161294	49.160	55.541
2	22.109	41048378	929584	50.840	44.459
Total		80739920	2090877	100.000	100.000

HPLC of racemic **3c**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2094-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2094-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/12/2020 10:25:56 AM
Data Processed	: 3/12/2020 11:33:43 AM

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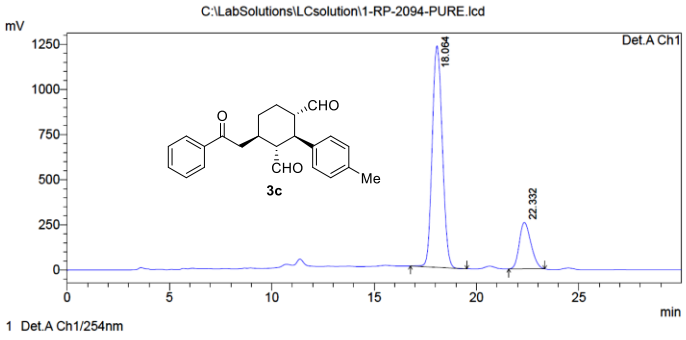

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.064	42199887	1227048	80.479	82.632
2	22.332	10236144	257901	19.521	17.368
Total		52436030	1484949	100.000	100.000

HPLC of **3c**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2096-PURE-RM-1.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2096-PURE-RM-1.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/3/2020 12:01:43 PM
Data Processed	: 6/3/2020 12:33:16 PM

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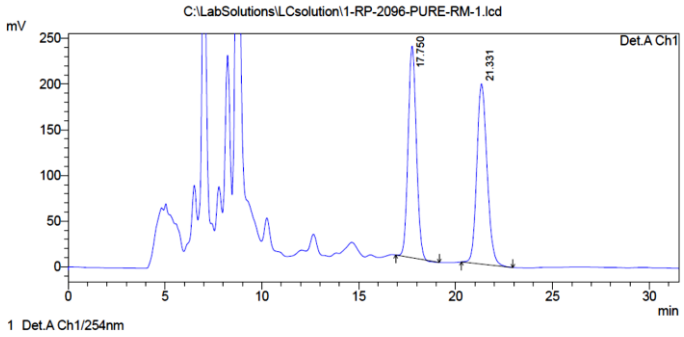

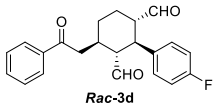

***Rac*-3d**

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.750	6848247	231994	48.437	54.036
2	21.331	7290299	197338	51.563	45.964
Total		14138546	429332	100.000	100.000

HPLC of racemic **3d**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2118-PURE-1.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2118-PURE-1.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/3/2020 11:29:22 AM
Data Processed	: 6/3/2020 12:02:45 PM

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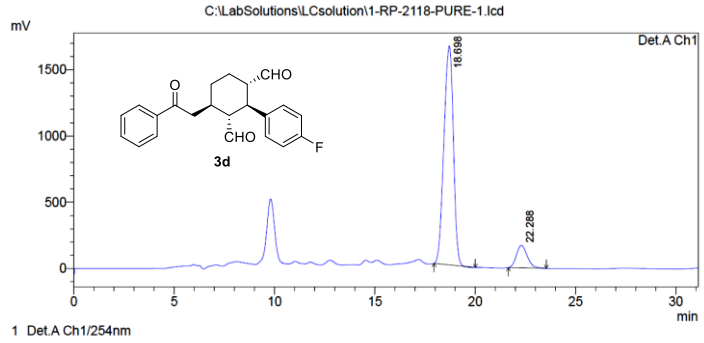

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.698	54053120	1650555	89.430	90.658
2	22.288	6388863	170075	10.570	9.342
Total		60441983	1820631	100.000	100.000

HPLC of **3d**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2092-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2092-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
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Data Processed	: 3/10/2020 12:04:37 PM

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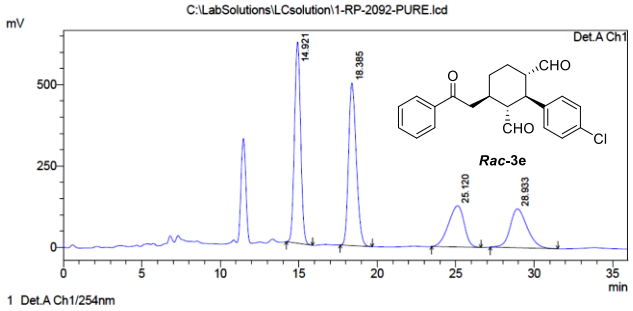


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.921	16920203	619417	32.584	45.356
2	18.385	17174390	499906	33.074	36.605
3	25.120	8820279	126713	16.986	9.278
4	28.933	9013032	119650	17.357	8.761
Total		51927904	1365687	100.000	100.000

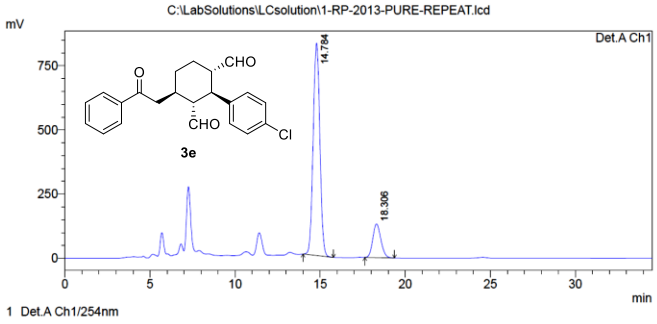
HPLC of racemic **3e**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2013-PURE-REPEAT.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2013-PURE-REPEAT.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/19/2020 11:11:47 AM
Data Processed	: 3/19/2020 11:47:52 AM

<Chromatogram>



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.784	22566147	826880	83.878	86.307
2	18.306	4337383	131184	16.122	13.693
Total		26903530	958064	100.000	100.000

HPLC of **3e**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2265-IC-RM.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2265-IC-RM.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/21/2020 3:07:36 PM
Data Processed	: 8/21/2020 3:33:21 PM

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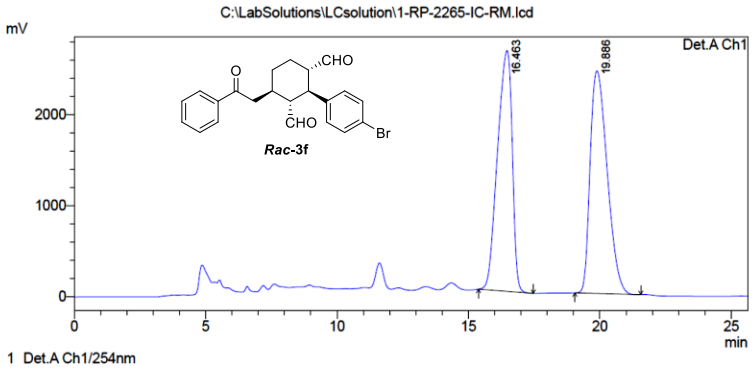

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.463	102983647	2646662	48.290	51.971
2	19.886	110276034	2445956	51.710	48.029
Total		213259682	5092617	100.000	100.000

HPLC of racemic **3f**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2266-PURE-11.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2266-PURE-11.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/21/2020 4:28:43 PM
Data Processed	: 8/24/2020 9:44:46 AM

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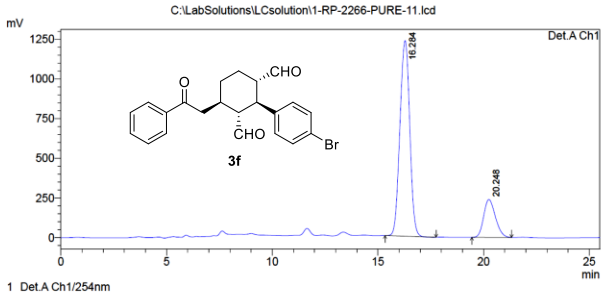

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.284	39811360	1232791	81.214	83.773
2	20.248	9208904	238792	18.786	16.227
Total		49020265	1471583	100.000	100.000

HPLC of **3f**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2097RMM.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2097RMM.lcd
Method File Name	: ChiralPak ID-40%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/4/2020 11:34:52 AM
Data Processed	: 6/4/2020 12:38:02 PM

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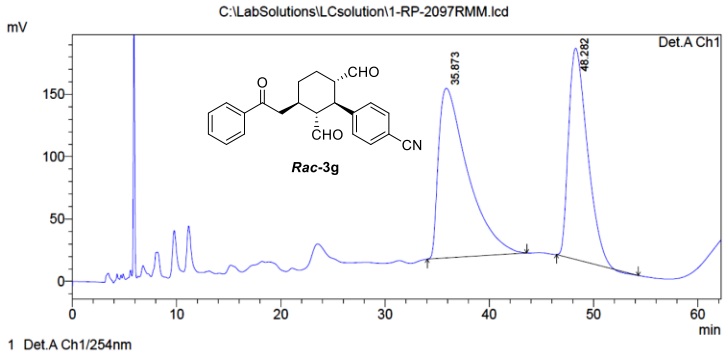

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.873	26645845	136126	55.499	44.532
2	48.282	21365452	169556	44.501	55.468
Total		48011297	305682	100.000	100.000

HPLC of racemic **3g**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2119-CHIRAL.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2119-CHIRAL.lcd
Method File Name	: ChiralPak ID-40%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/4/2020 1:59:07 PM
Data Processed	: 6/4/2020 3:02:11 PM

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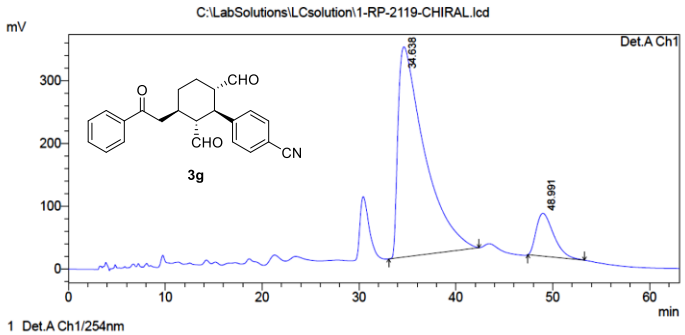

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.638	63957369	334991	88.165	83.051
2	48.991	8585128	68364	11.835	16.949
Total		72542497	403355	100.000	100.000

HPLC of **3g**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-rp-2134-ic-11.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-rp-2134-ic-11.lcd
Method File Name	: ChiralPak IC 40%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/16/2020 10:41:13 AM
Data Processed	: 7/16/2020 11:41:17 AM

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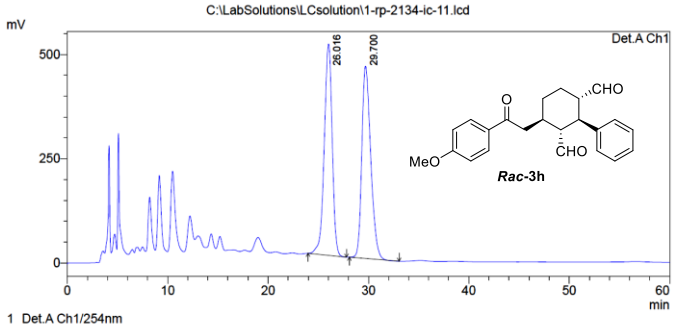

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.016	27897036	507174	49.507	52.359
2	29.700	28453183	461479	50.493	47.641
Total		56350219	968653	100.000	100.000

HPLC of racemic **3h**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-rp-2193-pure.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-rp-2193-pure.lcd
Method File Name	: ChiralPak IC-40%-1 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/20/2020 3:25:57 PM
Data Processed	: 7/20/2020 4:06:02 PM

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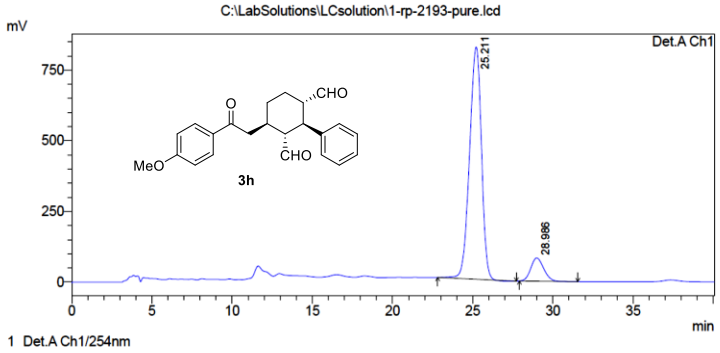

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.211	42241214	821392	90.173	90.904
2	28.986	4603643	82191	9.827	9.096
Total		46844857	903583	100.000	100.000

HPLC of **3h**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-rp-2133-pure.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-rp-2133-pure.lcd
Method File Name	: ChiralPak ID-40%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/16/2020 2:35:09 PM
Data Processed	: 7/24/2020 10:04:32 AM

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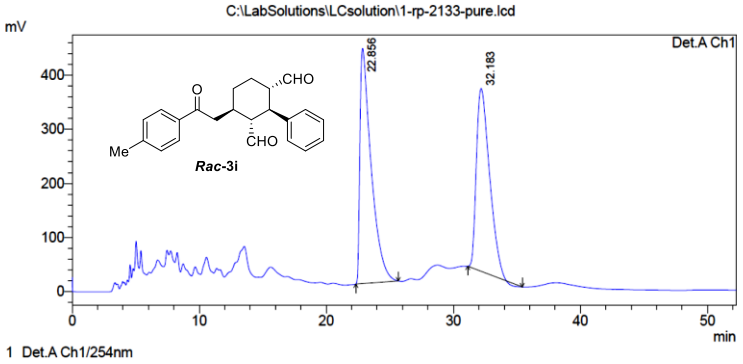

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.856	26693989	434202	52.341	56.263
2	32.183	24305891	337536	47.659	43.737
Total		50999880	771738	100.000	100.000

HPLC of racemic **3i**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-rp-2203-pure-4-me.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-rp-2203-pure-4-me.lcd
Method File Name	: ChiralPak ID-40%-1 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/24/2020 10:55:07 AM
Data Processed	: 7/24/2020 11:42:21 AM

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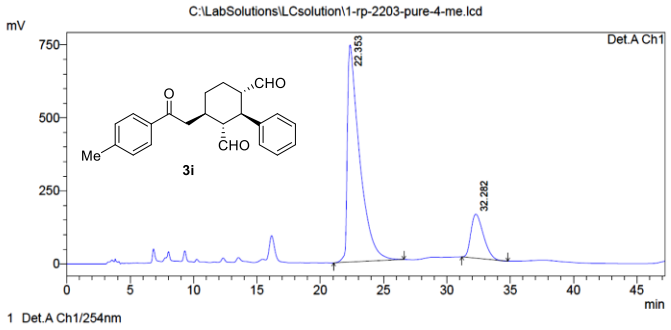

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.353	49911331	743044	82.911	83.165
2	32.282	10287335	150416	17.089	16.835
Total		60198666	893460	100.000	100.000

HPLC of **3i**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2129-PURE.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2129-PURE.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/15/2020 11:21:31 AM
Data Processed	: 6/15/2020 4:07:10 PM

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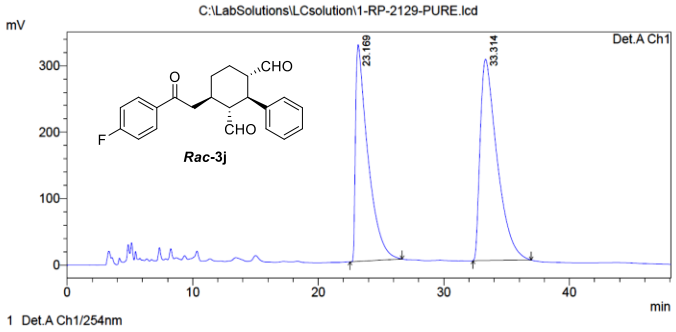

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.169	22432180	326443	44.114	51.867
2	33.314	28418221	302945	55.886	48.133
Total		50850401	629388	100.000	100.000

HPLC of racemic **3j**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2126-PURE.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2126-PURE.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/12/2020 3:37:16 PM
Data Processed	: 6/15/2020 4:08:29 PM

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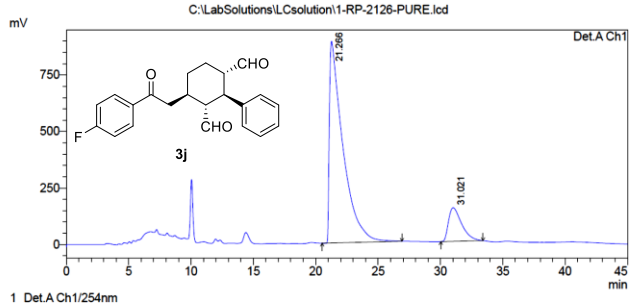

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.266	67302377	892398	86.046	85.702
2	31.021	10914799	148882	13.954	14.298
Total		78217176	1041280	100.000	100.000

HPLC of **3j**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2130-ID.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2130-ID.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/18/2020 2:04:52 PM
Data Processed	: 6/18/2020 3:01:00 PM

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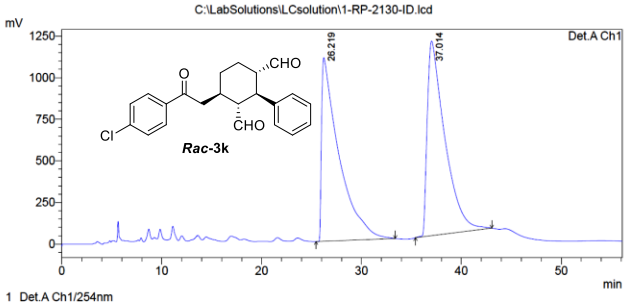

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.219	133972179	1102885	48.385	48.542
2	37.014	142914722	1169152	51.615	51.458
Total		276886901	2272037	100.000	100.000

HPLC of racemic **3k**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2131-PURE-CHIRAL.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2131-PURE-CHIRAL.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/19/2020 10:14:00 AM
Data Processed	: 6/19/2020 11:10:27 AM

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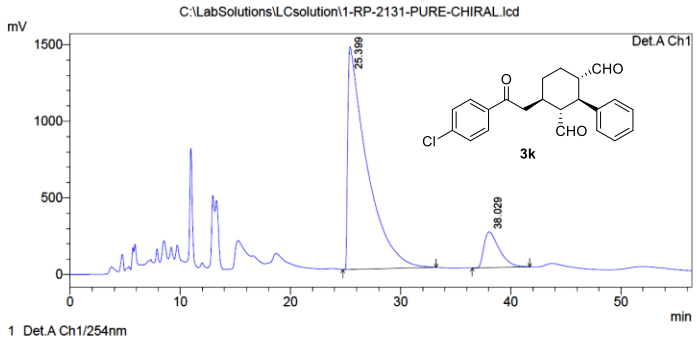

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.399	175599254	1454379	88.613	86.141
2	38.029	22564423	233984	11.387	13.859
Total		198163677	1688363	100.000	100.000

HPLC of **3k**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2124-RM-PURE.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2124-RM-PURE.lcd
Method File Name	: ChiralPak ID-20.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/10/2020 11:52:39 AM
Data Processed	: 6/10/2020 2:11:01 PM

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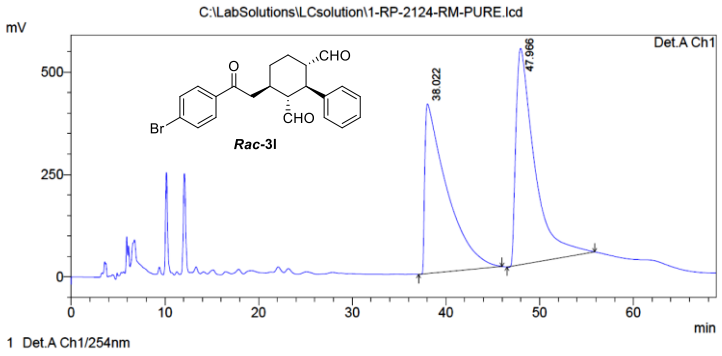

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	38.022	68060127	414164	47.980	43.961
2	47.966	73790837	527949	52.020	56.039
Total		141850964	942114	100.000	100.000

HPLC of racemic **3l**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2123-C-PURE.lcd

Acquired by	: Admin
Sample Name	: baseline
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2123-C-PURE.lcd
Method File Name	: ChiralPak ID-20.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/10/2020 1:01:55 PM
Data Processed	: 6/10/2020 2:12:56 PM

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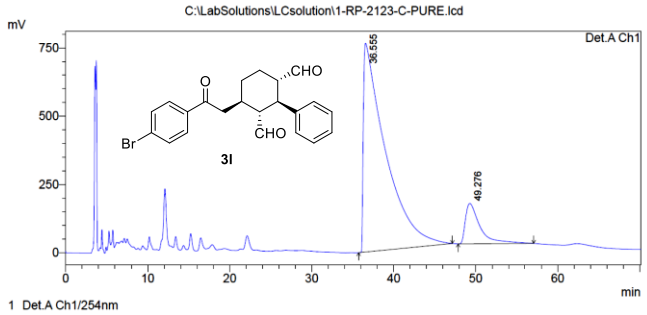

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.555	142940647	764211	88.599	83.790
2	49.276	18394634	147846	11.401	16.210
Total		161335281	912058	100.000	100.000

HPLC of **3l**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2299-PURE-RM.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2299-PURE-RM.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 9/4/2020 2:46:37 PM
Data Processed	: 9/7/2020 2:06:14 PM

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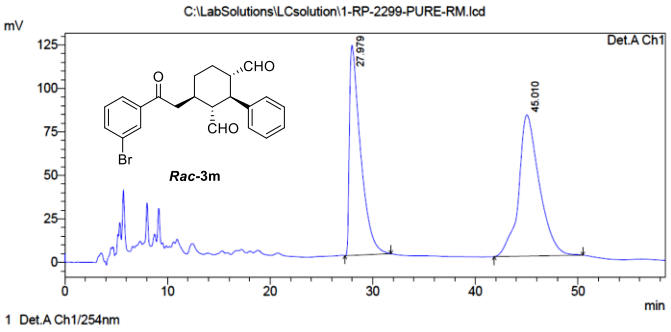

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.979	9084693	120714	44.328	59.789
2	45.010	11409789	81186	55.672	40.211
Total		20494481	201900	100.000	100.000

HPLC of racemic **3m**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2300-PURE-CHIRAL.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2300-PURE-CHIRAL.lcd
Method File Name	: ChiralPak ID-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 9/7/2020 1:52:39 PM
Data Processed	: 9/7/2020 2:54:59 PM

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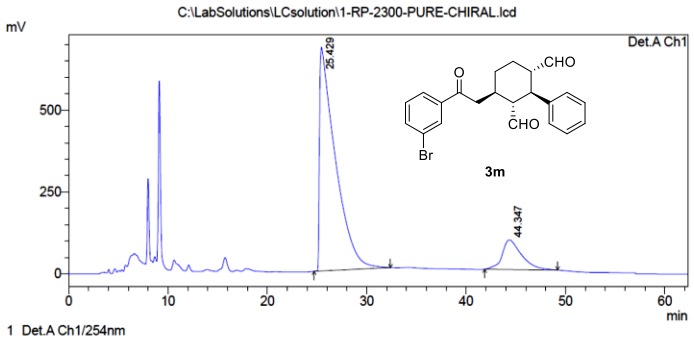

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.429	75803084	683346	86.089	88.325
2	44.347	12248993	90328	13.911	11.675
Total		88052077	773674	100.000	100.000

HPLC of **3m**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2268-RM.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2268-RM.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/21/2020 11:56:12 AM
Data Processed	: 8/21/2020 12:40:29 PM

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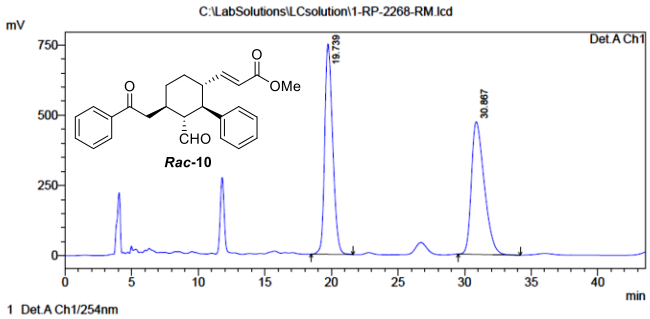

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.739	31121470	748912	49.534	61.340
2	30.867	31707053	472014	50.466	38.660
Total		62828523	1220926	100.000	100.000

HPLC of racemic **10**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2267-CHIRAL.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2267-CHIRAL.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/21/2020 12:41:26 PM
Data Processed	: 8/21/2020 1:48:12 PM

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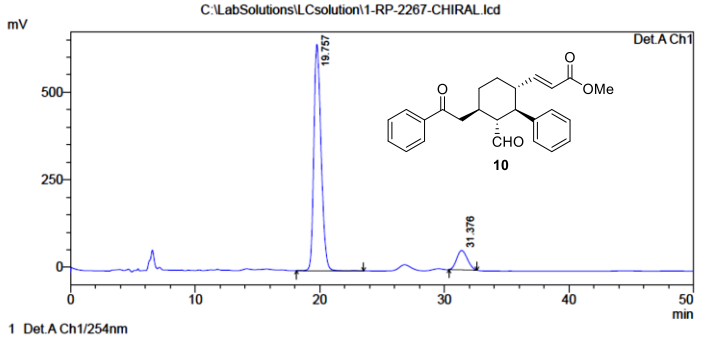

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.757	26191817	646643	88.796	92.118
2	31.376	3304958	55330	11.204	7.882
Total		29496775	701972	100.000	100.000

HPLC of **10**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2233-1-PURE-1RM.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2233-1-PURE-1RM.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/20/2020 12:37:26 PM
Data Processed	: 8/20/2020 1:52:34 PM

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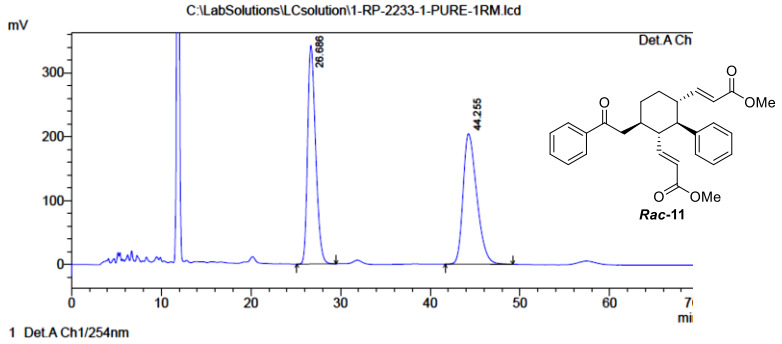


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.686	21203762	342433	49.406	62.637
2	44.255	21713456	204263	50.594	37.363
Total		42917218	546696	100.000	100.000

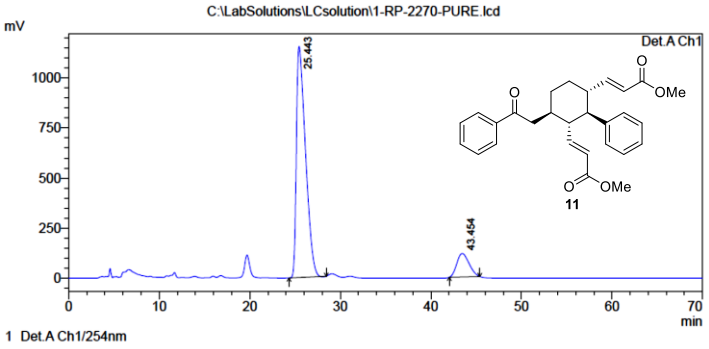
HPLC of racemic **11**

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-RP-2270-PURE.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-RP-2270-PURE.lcd
Method File Name	: ChiralPak IC-30.0%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 8/24/2020 11:40:50 AM
Data Processed	: 8/24/2020 12:57:15 PM

<Chromatogram>



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.443	80454704	1153739	87.949	90.776
2	43.454	11024351	117240	12.051	9.224
Total		91479055	1270978	100.000	100.000

HPLC of **11**