N-Heterocyclic Carbene-Catalyzed Enantioselective Annulations: A Dual Activation Strategy for a Formal [4+2] Addition for Dihydrocoumarins

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Supporting Information

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General Information

All reactions were carried out under a nitrogen atmosphere in oven-dried glassware with magnetic stirring. All organic solvents were purified by passage through a bed of activated alumina.[1] Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.[2] Purification of reaction products was carried out by flash chromatography using EM Reagent or Silicycle silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and ceric ammonium nitrate stain, potassium permanganate stain or ninhydrin stain followed by heating. Infrared spectra were recorded on a Bruker Tensor 37 FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Bruker Avance 500 MHz w/ direct cryoprobe (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz, integration). Proton-decoupled ^{13}C-NMR spectra were recorded on a Bruker Avance 500 MHz w/ direct cryoprobe (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). Mass spectra data were obtained on a Waters Acquity-H UPLC-MS with a single quadrupole ESI Spectrometer or on a Gas Chromatography Mass Spectrometer (Agilent 7890A/5975C GCMS System).

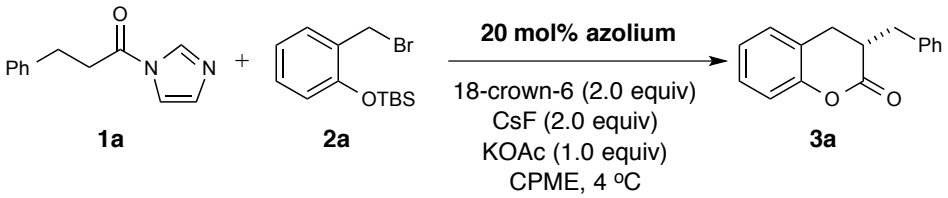
[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers F. J., *Organometallics* **1996**, *15*, 1518.

[2] D. D. Perrin, W. L. Armarego, *Purification of Laboratory Chemicals;* 3rd Ed., Pergamon Press, Oxford. 1988.

1. Optimization Experiments

We investigated various reaction conditions, of which selected examples are summarized in Table 1.

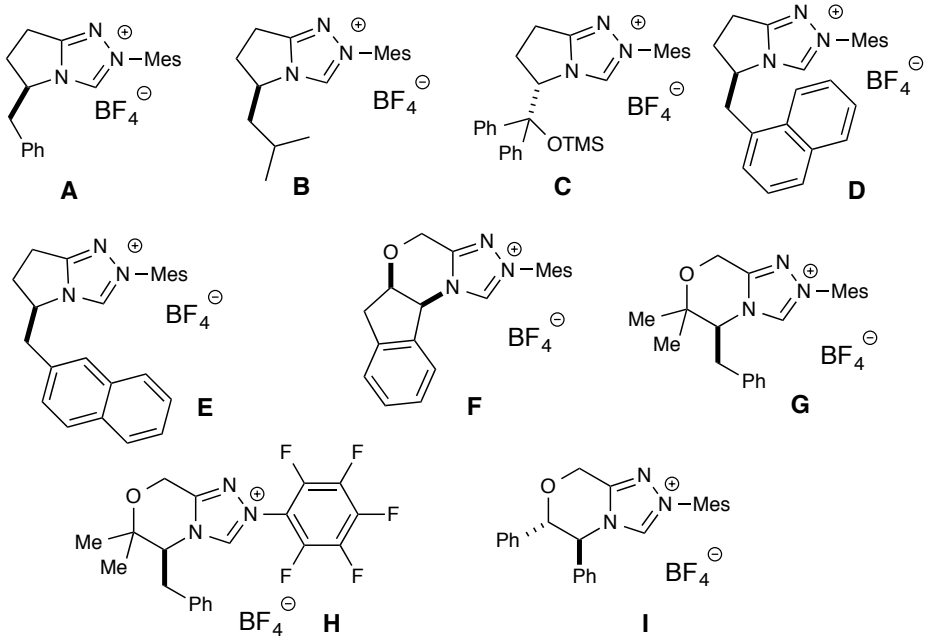
<Table 1> Catalyst optimization experiments.[a]



1a **2a** **3a**

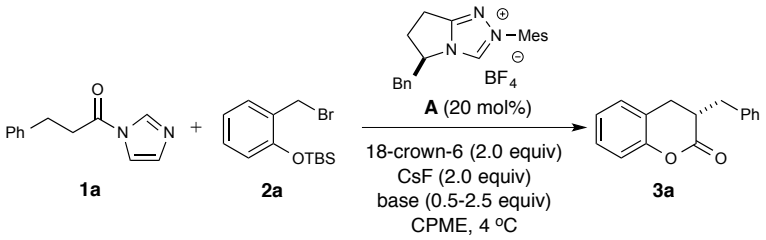
entry	azolium	% yield[b]	er[c]
1	**A**	75	85:15
2	**B**	55	79:21
3	**C**	No Rxn	-
4	**D**	57	80:20
5	**E**	47	65:35
6	**F**	No Rxn	-
7	**G**	No Rxn	-
8	**H**	No Rxn	-
9	**I**	10	75:25

[a]Conditions: **1a** (0.05 mmol, 1 equiv), **2a** (2.0 equiv), azolium (0.2 equiv), 18-crown-6 (2.0 equiv), CsF (2.0 equiv), KOAc (1.0 equiv) in CPME (0.125 M) at 4 °C for 15 h. [b]Determined by NMR. [c]Determined by HPLC analysis on a chiral stationary phase. CPME=cyclopentyl methyl ether)



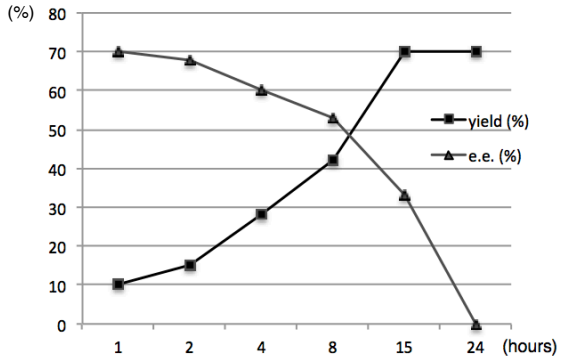
We observed racemization in the presence of strong bases such as CsOAc and Cs_2CO_3 under the reaction conditions. Therefore, a weak base (KOAc) was selected for further studies. The optimization result was summarized in Table 2, and the comparison of the reaction with CsOAc and KOAc were shown in Figure 1.

<Table 2> Optimization of asymmetric conditions.

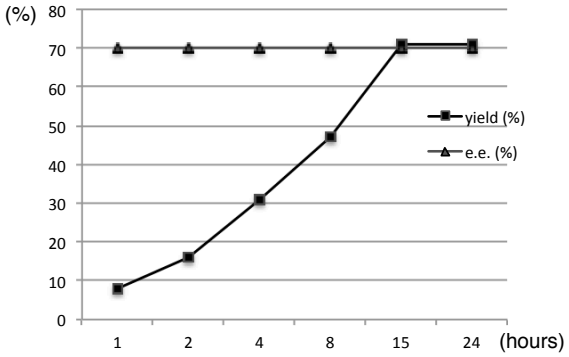


Entry	Base	Equiv.	Yield (%)[b]	e.r.[c]
1	Cs_2CO_3	2.5	65	50:50
2	CsOAc	2.5	70	50:50
3	CsOAc	1.0	68	67:33
4	CsOAc	0.5	32	84:16
5	K_2CO_3	1.0	60	59:41
6	KOAc	1.5	74	67:33
7	**KOAc**	**1.0**	**75**	**85:15**
8	KOAc	0.5	40	85:15
9	NaOAc	1.0	40	85:15
10	NaOAc	0.5	11	85:15
11	NaOAc	2.5	44	85:15
12[d]	KOAc	1.0	no rxn	-
13[e]	KOAc	1.0	no rxn	-

[a] Conditions: **1a** (0.05 mmol, 1.0 equiv), **2a** (2.0 equiv), triazolium **A** (0.2 equiv), 18-crown-6 (2.0 equiv), CsF (2.0 equiv) at 4 °C for 15 h. [b] Determined by NMR analysis with 1,3,5- trimethoxybenzene as an internal standard. [c] Determined by HPLC analysis. [d] Reaction conducted in the absence of CsF and 18-crown-6. [e] Reaction conducted in the absence of 18-crown-6. CPME=cyclopentyl methyl ether.

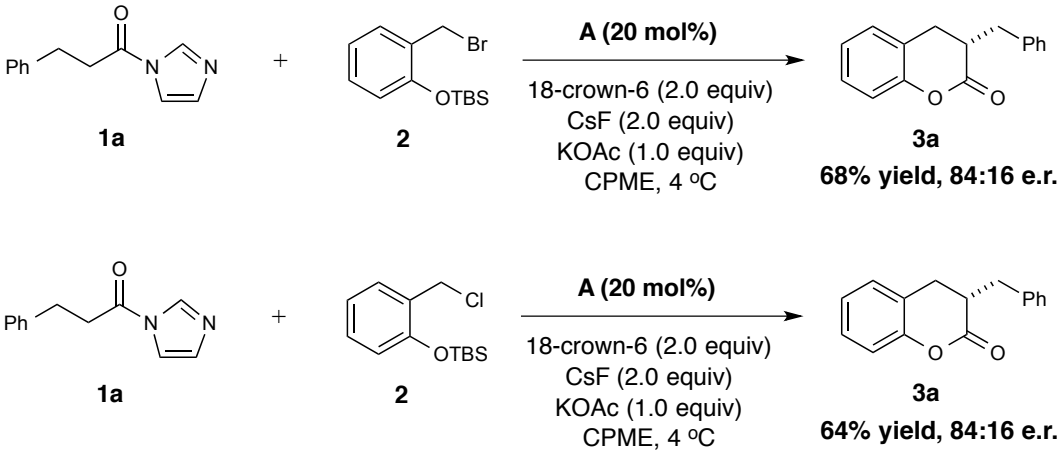


<Figure 1a> Racemization in the presence of 1.0 equiv of CsOAc as the base.



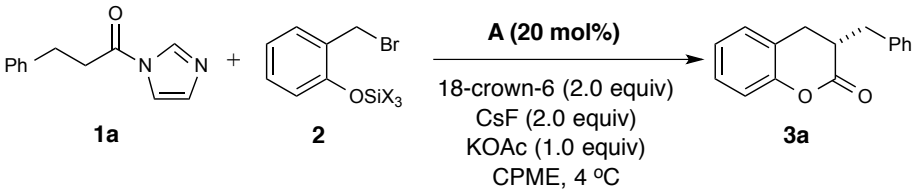
<Figure 1b> The reaction trends in the presence of 1.0 equiv of KOAc as the base.

We also checked the leaving group effect, interestingly, the choice of chloride and bromide leaving groups on substrate **2a** was found to be inconsequential in terms of reactivity and enantioselectivity.



Next, various silyl groups on substrate **2** were evaluated under the reaction conditions, and it was found that the proper rate of *ortho*-quinone methide (*o*-QM) production was achieved by the use of an equimolar combination of crown ether and cesium fluoride in conjunction with the *tert*-butyldimethylsilyl (TBS)-protected phenol substrate (Table 3).

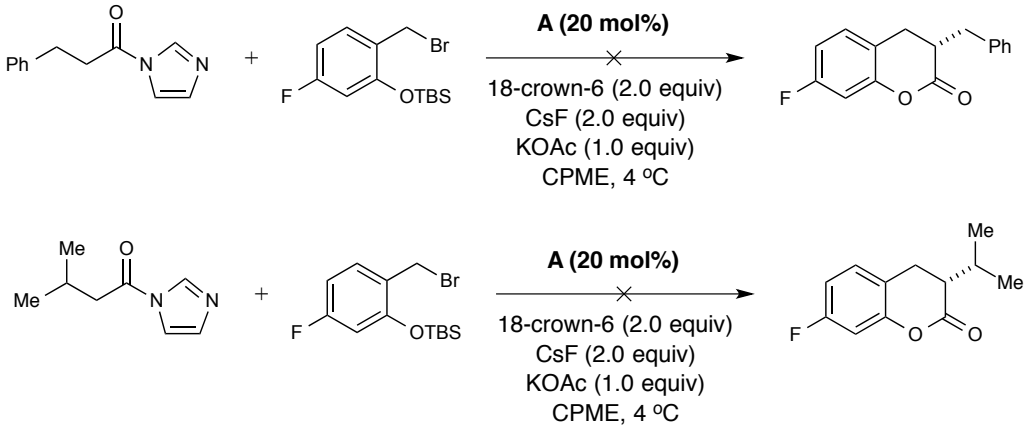
<Table 3> Silyl group effects.[a]



entry	SiX_3	% yield[b]	er[c]
1	**TMS**	No Rxn	-
2	**TES**	No Rxn	-
3	**TIPS**	55	75:25
4	**TBS**	75	85:15

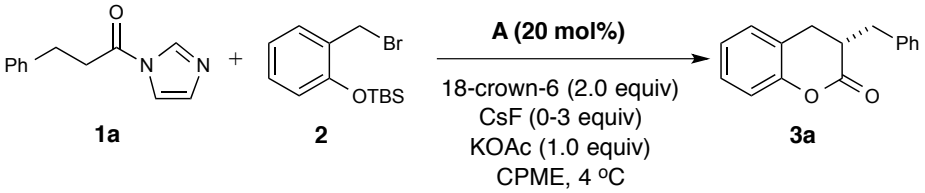
[a]Conditions: **1a** (0.05 mmol, 1 equiv), **2a** (2.0 equiv), azolium (0.2 equiv), 18-crown-6 (2.0 equiv), CsF (2.0 equiv), KOAc (1.0 equiv) in CPME (0.125 M) at 4 ºC for 15 h. [b]Determined by NMR. [c]Determined by HPLC analysis on a chiral stationary phase.

For substrate screening experiments, tolerance to substitution on the benzyl bromide derivative **2** was also investigated. Various substituents were tolerated at the C-3, C-4, and C-5 positions affording the desired products in good to high yields and high enantioselectivities. However, the bromides including electron-withdrawing groups at C-5 positions were not suitable substrates, and no desired products were obtained. The SM (*o*-QM precursor) was mostly recovered, this indicates that the generation of *o*-QM did not take place properly.



Additionally, we found that the ratio of CsF and the *o*-QM precursor would be important in the reaction. We employed 2.0 equiv of CsF and 2.0 equiv of *o*-QM precursor, no racemization was observed in this case. However, in the presence of more than 2.0 equiv of CsF (with 2.0 equiv of *o*-QM), we observed reduced enantioselectivity, this indicates additional CsF could act as the base under the reaction condition. The additional information for this issue is summarized in Table 4.

<Table 4> CsF optimization experiment.



1a **2** **3a**

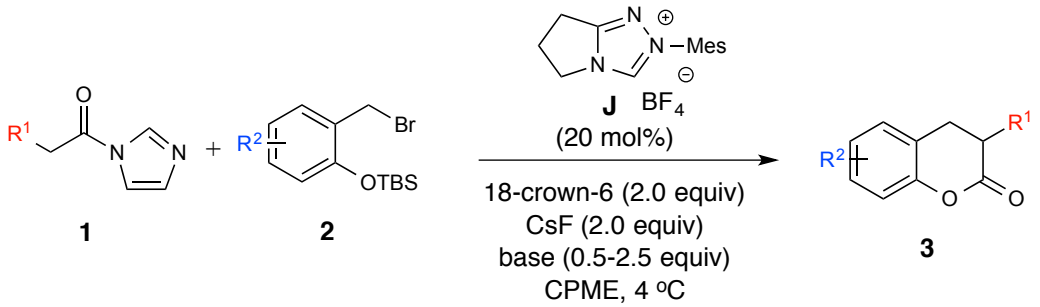
entry	**2** (equiv)	CsF (equiv)	% yield[b]	er[c]
1	**2**	**2**	75	85:15
2	**2**	**1**	40	85:15
3	**2**	**3**	78	75:25
4	**2**	**0**	No Rxn	-
5	**3**	**3**	77	84:16
6	**1**	**1**	31	n.d.

[a]Conditions: **1a** (0.05 mmol, 1 equiv), **2a** (1-3 equiv), azolium (0.2 equiv), 18-crown-6 (2.0 equiv), CsF (0-3 equiv), KOAc (1.0 equiv) in CPME (0.125 M) at 4 °C for 15 h. [b]Determined by NMR. [c]Determined by HPLC analysis on a chiral stationary phase.

2. General Procedure for the [4+2] Annulation Reaction via NHC Catalysis

The starting acyl imidazoles **1** were prepared based on the previous procedure[3]: The appropriate acid (1.0 equiv) was dissolved in dry dichloromethane (0.3 M), and CDI (carbonyldiimidazole, 1.5 equiv) was added at 0 ºC. The resulting mixture was stirred for 2 h at RT, washed with dichloromethane and sat. sodium bicarbonate solution. After drying over $MgSO_4$, residue solvent was removed under reduced pressure, the resulting acyl imidazole was used for the reaction without further purification.

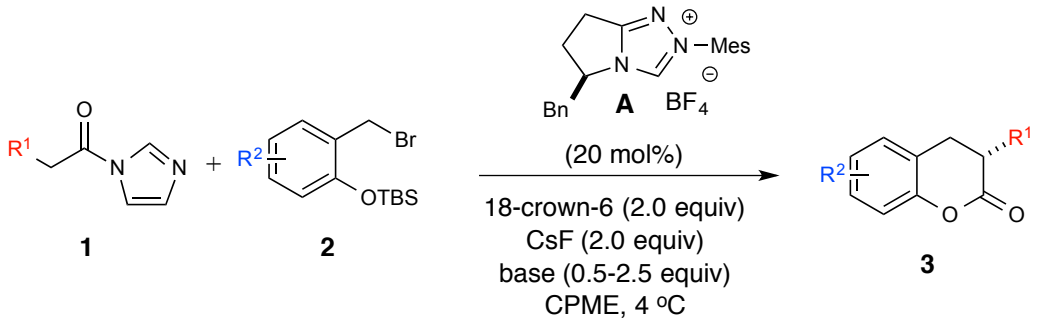
2.1. General Procedure for Racemate Preparation



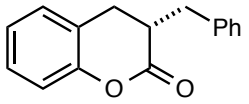
An oven-dried screw-capped tube-vial equipped with a magnetic stirbar was taken into a nitrogen-filled drybox at which time achiral 5,5-mesityl triazolium NHC pre-catalyst **J** (0.04 mmol, 0.2 equiv.), acylimidazole **1** (0.2 mmol, 1 equiv.), 18-crown-6 (0.4 mmol, 2.0 equiv.), cesium fluoride (0.4 mmol, 2.0 equiv.), and potassium acetate (0.2 mmol, 1.0 equiv) were added. The vial was capped with a septum cap, removed from the drybox and put under positive nitrogen pressure. The mixture was dissolved in 1.0 mL of dry CPME (cyclopentyl methyl ether) and stirred for 10 min at 4 ºC. Then, benzyl bromide **2** (0.4 mmol, 2.0 equiv.) dissolved in 0.6 mL of dry CPME was added slowly. After 15 hours at 4 ºC, the reaction mixture was filtered ovr a pad of silica washing with ethyl acetate and concentrated under reduced pressure. Purification by flash chromatography with ethyl acetate/hexanes afforded the corresponding racemic dihydrocoumarin **3**.

[3] T. B. Durham, M. J. Miller, *J. Org. Chem.* **2003**, *68*, 27-34.

2.2. General Procedure for the Asymmetric [4+2] Annulation Reaction *via* NHC catalysis



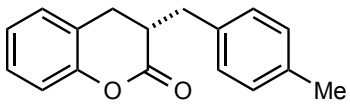
An oven-dried screw-capped tube-vial equipped with a magnetic stirbar was taken into a nitrogen-filled drybox at which time chiral NHC pre-catalyst **A** (0.04 mmol, 0.2 equiv.), acylimidazole **1** (0.2 mmol, 1 equiv.), 18-crown-6 (0.4 mmol, 2.0 equiv.), cesium fluoride (0.4 mmol, 2.0 equiv.), and potassium acetate (0.2 mmol, 1.0 equiv) were added. The vial was capped with a septum cap, removed from the drybox and put under positive nitrogen pressure. The mixture was dissolved in 1.0 mL of dry CPME (cyclopentyl methyl ether) and stirred for 10 min at 4 ºC. Then, benzyl bromide **2** (0.4 mmol, 2.0 equiv.) dissolved in 0.6 mL of dry CPME was added slowly. After 15 hours at 4 ºC, the reaction mixture was filtered over a pad of silica washing with ethyl acetate and concentrated under reduced pressure. Purification by flash chromatography with ethyl acetate/hexanes afforded the corresponding enantioenriched dihydrocoumarin **3**.



3a

(*S*)-3-benzylchroman-2-one (3a): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-phenylpropan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (34 mg, 71% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.0, 6.6 Hz, 2H), 7.29 – 7.23 (m, 2H), 7.23 – 7.16 (m, 2H), 7.14 – 7.01 (m, 3H), 3.41 (dd, *J* = 13.9, 4.5 Hz, 1H), 3.01 – 2.91 (m, 1H), 2.85 (dd, *J* = 15.8, 5.9 Hz, 1H), 2.80 – 2.68 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 151.6, 138.0, 129.2, 128.7, 128.3, 128.2, 126.8, 124.4, 122.4, 116.6, 40.8, 35.6, 28.3; IR (film) 3028, 1760, 1589, 1488, 1458, 1361, 1229, 1124, 1078, 1031, 979, 919, 754, 700, 622 cm^{-1}; LRMS (EI); Mass calcd for $C_{16}H_{14}O_2$ $[M]^+$: 238.1; found 238.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 5%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 22.5 min, Rt_2 (minor) = 28.9 min; er = 85:15.

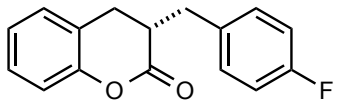


3b

(*S*)-3-(4-methylbenzyl)chroman-2-one (3b): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-(*p*-tolyl)propan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (36 mg, 70% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.12 – 7.02 (m, 5H), 3.36 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.93 (tdd, *J* = 10.4, 5.9, 4.5 Hz, 1H), 2.85 (dd, *J* = 15.8, 5.9 Hz, 1H), 2.71 (dt, *J* = 14.0, 10.4 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 151.6, 136.4, 134.9, 129.4, 129.0, 128.3, 124.4, 122.4, 116.6, 40.9, 35.2, 28.2, 21.1; IR (film)

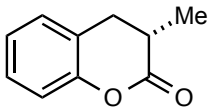
3128, 2250, 1761, 1489, 1459, 1230, 1132, 905, 808, 725, 649 cm^{-1}; LRMS (EI); Mass calcd for $C_{17}H_{16}O_2$ $[M]^+$: 252.1; found 252.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 16.2 min, Rt_2 (minor) = 18.3 min; er = 85:15.



3c

(*S*)-3-(4-fluorobenzyl)chroman-2-one (3c): Prepared according to the general procedure using 3-(4-fluorophenyl)-1-(1*H*-imidazol-1-yl)propan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (37 mg, 71% yield) as a white solid.

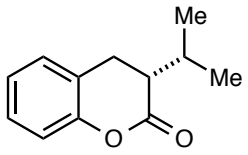
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (ddd, J = 10.2, 6.1, 2.3 Hz, 1H), 7.20 – 7.13 (m, 2H), 7.12 – 6.96 (m, 5H), 3.34 (dd, J = 14.0, 4.8 Hz, 1H), 2.96 – 2.88 (m, 1H), 2.84 (dd, J = 15.7, 5.9 Hz, 1H), 2.80 – 2.69 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 161.8 (d, J_{CF} = 245.1 Hz), 151.5, 133.6, 133.5, 130.6 (d, J_{CF} = 7.9 Hz), 128.3 (d, J_{CF} = 21.4 Hz), 124.4, 122.2, 116.6, 115.6, 115.4, 40.9, 34.8, 28.3; IR (film) 2923, 1758, 1588, 1510, 1488, 1457, 1357, 1280, 1230, 1194, 1159, 1128, 1109, 1024, 976, 918, 847, 758, 737, 644 cm^{-1}; LRMS (EI); Mass calcd for $C_{16}H_{13}FO_2$ $[M]^+$: 256.1; found 256.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 18.9 min, Rt_2 (minor) = 22.9 min; er = 85:15.



3d

(*S*)-3-methylchroman-2-one (3d): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)propan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (21 mg, 65% yield) as a white solid.

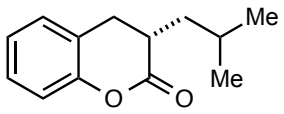
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 1H), 7.17 (dt, *J* = 7.5, 1.4 Hz, 1H), 7.09 (td, *J* = 7.5, 1.2 Hz, 1H), 7.04 (dd, *J* = 8.1, 1.2 Hz, 1H), 2.98 (dd, *J* = 14.5, 5.0 Hz, 1H), 2.88 – 2.72 (m, 2H), 1.38 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 151.8, 128.2, 127.9, 124.3, 122.9, 116.6, 34.3, 31.7, 15.4; IR (film) 3120, 1763, 1489, 1459, 1265, 1228, 1146, 1085, 732, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{10}H_{10}O_2$ $[M]^+$: 162.1; found 162.0. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H, 2%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (minor) = 26.9 min, Rt_2 (major) = 28.5 min; er = 88:12.



3e

(*R*)-3-isopropylchroman-2-one (3e): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-methylbutan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (26 mg, 67% yield) as a colorless oil.

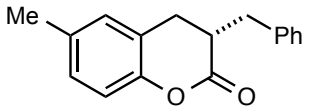
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 2H), 7.09 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.02 (dd, *J* = 8.1, 1.1 Hz, 1H), 2.93 (qd, *J* = 15.8, 7.9 Hz, 2H), 2.54 (dt, *J* = 9.6, 6.0 Hz, 1H), 2.21 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.06 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.23, 151.55, 128.15, 128.13, 124.21, 122.76, 116.43, 45.43, 26.94, 25.43, 20.60, 18.73; IR (film) 3120, 1763, 1489, 1459, 1265, 1228, 1146, 1085, 732, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{12}H_{14}O_2$ $[M]^+$: 190.1; found 190.0. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 5%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (minor) = 26.9 min, Rt_2 (major) = 28.5 min; er = 92:8.



3f

(*S*)-3-isobutylchroman-2-one (3f): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-4-methylpentan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (29 mg, 71% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 1H), 7.18 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.08 (td, *J* = 7.5, 1.2 Hz, 1H), 7.03 (dd, *J* = 8.2, 1.2 Hz, 1H), 3.04 (q, *J* = 10.5 Hz, 1H), 2.81 – 2.69 (m, 2H), 1.86 – 1.71 (m, 2H), 1.42 – 1.31 (m, 1H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 151.6, 128.2, 128.2, 124.2, 122.5, 116.5, 38.7, 37.1, 29.5, 25.3, 22.9, 21.9; IR (film) 2957, 1764, 1589, 1489, 1458, 1368, 1232, 1188, 1137, 1105, 980, 946, 916, 757, 735, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{13}H_{16}O_2$ $[M]^+$: 204.1; found 204.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 5%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (major) = 12.5 min, Rt_2 (minor) = 13.8 min; er = 88:12.

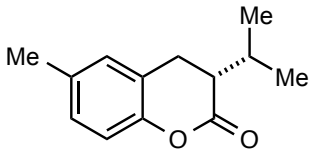


3g

(*S*)-3-benzyl-6-methylchroman-2-one (3g): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-phenylpropan-1-one and (2-(bromomethyl)-4-methylphenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (40 mg, 80% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.1, 6.6 Hz, 2H), 7.27 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.04 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.89 (d, *J* = 2.0 Hz, 1H), 3.40 (dd, *J* = 13.9, 4.6 Hz, 1H), 2.98 – 2.86 (m, 1H), 2.83 – 2.64 (m, 3H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 149.5, 138.1, 133.9, 129.2, 128.7, 128.7, 128.6, 126.7, 122.0, 116.2, 40.9, 35.6, 28.2, 20.7; IR (film) 2957, 1764, 1589, 1489, 1458, 1368, 1232, 1188, 1137, 1105,

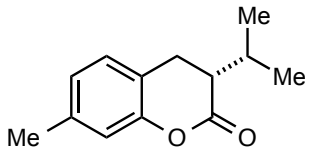
980, 946, 916, 757, 735, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{17}H_{16}O_2$ $[M]^+$: 252.1; found 252.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (minor) = 19.5 min, Rt_2 (major) = 21.6 min; er = 88:12.



3h

(*R*)-3-isopropyl-6-methylchroman-2-one (3h): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-methylbutan-1-one and (2-(bromomethyl)-4-methylphenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (27 mg, 65% yield) as a pale yellow oil.

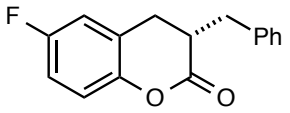
^1H NMR (500 MHz, $CDCl_3$) δ 7.08 – 6.95 (m, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 2.88 (qd, *J* = 15.8, 7.8 Hz, 2H), 2.50 (dt, *J* = 9.5, 6.0 Hz, 1H), 2.31 (s, 3H), 2.23 – 2.13 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 149.4, 133.7, 128.6, 128.5, 122.4, 116.1, 45.5, 26.9, 25.4, 20.7, 20.6, 18.8; IR (film) 2957, 1762, 1580, 1455, 1264, 1180, 978, 731, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{13}H_{16}O_2$ $[M]^+$: 204.1; found 204.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 5%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (major) = 14.6 min, Rt_2 (minor) = 17.4 min; er = 93:7.



3i

(*R*)-3-isopropyl-7-methylchroman-2-one (3i): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-methylbutan-1-one and (2-(bromomethyl)-5-methylphenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (27 mg, 67% yield) as a pale yellow oil.

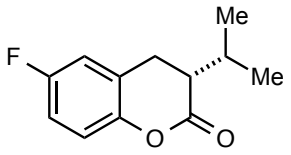
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.6 Hz, 1H), 6.89 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.83 (d, *J* = 1.6 Hz, 1H), 2.96 – 2.79 (m, 2H), 2.50 (dt, *J* = 9.5, 6.0 Hz, 1H), 2.33 (s, 3H), 2.19 (dq, *J* = 13.4, 6.7 Hz, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 151.4, 138.3, 127.9, 124.9, 119.5, 116.8, 45.6, 26.9, 25.1, 21.1, 20.6, 18.7; IR (film) 2962, 1768, 1627, 1585, 1509, 1416, 1370, 1258, 1229, 1140, 1120, 1092, 1012, 962, 856, 811, 735 cm^{-1}; LRMS (EI); Mass calcd for $C_{13}H_{16}O_2$ $[M]^+$: 204.1; found 204.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 5%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (minor) = 23.1 min, Rt_2 (major) = 24.6 min; er = 89:11.



3j

(*S*)-3-benzyl-6-fluorochroman-2-one (3j): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-phenylpropan-1-one and (2-(bromomethyl)-4-fluorophenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (40 mg, 78% yield) as a colorless solid.

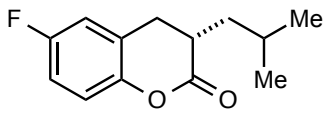
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 2H), 7.27 (dd, *J* = 9.0, 3.1 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.01 (dd, *J* = 8.9, 4.7 Hz, 1H), 6.95 (dd, *J* = 8.4, 3.0 Hz, 1H), 6.80 (dd, *J* = 8.2, 3.0 Hz, 1H), 3.40 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.99 – 2.87 (m, 1H), 2.82 (dd, *J* = 16.0, 5.9 Hz, 1H), 2.78 – 2.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 158.9 (d, J_{CF} = 243.7 Hz), 147.6, 147.5, 137.7, 129.1, 128.8, 126.9, 124.0 (d, J_{CF} = 8.1 Hz), 117.8 (d, J_{CF} = 8.5 Hz), 114.8 (dd, J_{CF} = 23.6, 11.1 Hz), 40.4, 35.5, 28.3; IR (film) 3120, 2880, 1763, 1601, 1489, 1434, 1360, 1266, 1202, 1124, 1078, 982, 957, 890, 816, 773, 738, 698, 673, 656 cm^{-1}; LRMS (EI); Mass calcd for $C_{16}H_{13}FO_2$ $[M]^+$: 256.1; found 256.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 280 nm), Rt_1 (major) = 20.4 min, Rt_2 (minor) = 25.6 min; er = 84:16.



3k

(*R*)-6-fluoro-3-isopropylchroman-2-one (3k): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-methylbutan-1-one and (2-(bromomethyl)-4-fluorophenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (27 mg, 65% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 – 6.87 (m, 3H), 2.91 (qd, J = 16.0, 7.8 Hz, 2H), 2.52 (dt, J = 9.6, 6.0 Hz, 1H), 2.20 (dq, J = 13.4, 6.7 Hz, 1H), 1.06 (d, J = 6.9 Hz, 3H), 1.00 (d, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 158.9 (d, J_{CF} = 243.3 Hz), 147.5, 128.3, 124.4 (d, J_{CF} = 8.2 Hz), 117.6 (d, J_{CF} = 8.6 Hz), 114.7 (dd, J_{CF} = 23.7, 6.7 Hz), 44.9, 26.9, 25.5, 20.5, 18.7; IR (film) 3071, 2962, 1749, 1600, 1490, 1456, 1437, 1369, 1340, 1265, 1236, 1187, 1163, 1141, 1099, 972, 944, 910, 884, 844, 821, 797, 723, 701, 638 cm^{-1}; LRMS (EI); Mass calcd for $C_{12}H_{13}FO_2$ $[M]^+$: 208.1; found 208.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 12.7 min, Rt_2 (minor) = 14.0 min; er = 86:14.

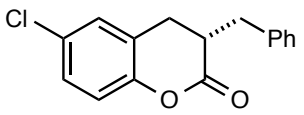


3l

(*S*)-6-fluoro-3-isobutylchroman-2-one (3l): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-4-methylpentan-1-one and (2-(bromomethyl)-4-fluorophenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (31 mg, 70% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 – 6.83 (m, 3H), 3.02 (q, J = 10.4 Hz, 1H), 2.79 – 2.68 (m, 2H), 1.85 – 1.70 (m, 2H), 1.40 – 1.31 (m, 1H), 0.96 (d, J = 6.3 Hz, 3H), 0.90 (d, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 158.9 (d, J_{CF} = 243.3 Hz), 147.6 (d, J_{CF} = 2.6 Hz), 124.1

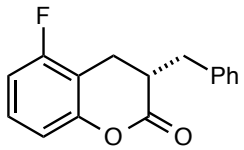
(d, J_{CF} = 8.1 Hz), 117.7 (d, J_{CF} = 8.5 Hz), 114.8 (dd, J_{CF} = 23.0, 6.0 Hz), 38.6, 36.7, 29.6, 25.3, 22.8, 21.8; IR (film) 2959, 1754, 1490, 1435, 1368, 1221, 1189, 1140, 1112, 973, 955, 891, 817, 742, 701, 676 cm^{-1}; LRMS (EI); Mass calcd for $C_{13}H_{15}FO_2$ $[M]^+$: 222.1; found 222.0. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 12.1 min, Rt_2 (minor) = 14.4 min; er = 88:12.



3m

(*S*)-3-benzyl-6-chlorochroman-2-one (3m): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-phenylpropan-1-one and (2-(bromomethyl)-4-chlorophenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (31 mg, 56% yield) as a white solid.

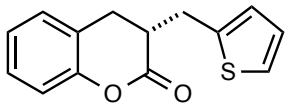
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.1, 6.6 Hz, 2H), 7.30 – 7.24 (m, 1H), 7.24 – 7.16 (m, 3H), 7.09 (d, *J* = 2.5 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 3.40 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.98 – 2.88 (m, 1H), 2.82 (dd, *J* = 16.0, 5.9 Hz, 1H), 2.78 – 2.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 150.1, 137.6, 129.4, 129.1, 128.7, 128.3, 128.1, 126.9, 124.0, 117.9, 40.4, 35.5, 28.1; IR (film) 2959, 2161, 1766, 1480, 1454, 1416, 1234, 1194, 1128, 1081, 850, 818, 741, 701 cm^{-1}; LRMS (EI); Mass calcd for $C_{16}H_{13}ClO_2$ $[M]^+$: 272.1; found 272.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 250 nm), Rt_1 (major) = 20.1 min, Rt_2 (minor) = 22.1 min; er = 82:18.



3n

(*S*)-3-benzyl-5-fluorochroman-2-one (3n): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-phenylpropan-1-one and (2-(bromomethyl)-3-fluorophenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (31 mg, 60% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.0, 6.6 Hz, 2H), 7.30 – 7.25 (m, 1H), 7.24 – 7.18 (m, 3H), 6.95 – 6.75 (m, 2H), 3.39 (dd, *J* = 13.9, 4.6 Hz, 1H), 3.06 – 2.89 (m, 2H), 2.78 (dd, *J* = 13.9, 9.3 Hz, 1H), 2.66 (dd, *J* = 15.9, 10.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 159.6 (d, J_{CF} = 246.7 Hz), 152.6 (d, J_{CF} = 6.8 Hz), 137.5, 129.1, 128.7, 128.6, 126.9, 112.3, 111.2 (d, J_{CF} = 21.6 Hz), 110.5 (d, J_{CF} = 22.6 Hz), 53.4, 40.0, 35.7, 21.7, 21.6; IR (film) 2899, 2060, 1764, 1467, 1444, 1416, 1264, 1124, 1081, 731, 701 cm^{-1}; LRMS (EI); Mass calcd for $C_{16}H_{13}FO_2$ [M]$^+$: 256.1; found 256.1. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-PrOH/Hexanes, 0.5 mL/min, 230 nm), Rt_1 (major) = 15.8 min, Rt_2 (minor) = 17.2 min; er = 82:18.

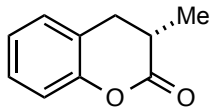


3o

(*R*)-3-(thiophen-2-ylmethyl)chroman-2-one (3o): Prepared according to the general procedure using 1-(1*H*-imidazol-1-yl)-3-(thiophen-2-yl)propan-1-one and (2-(bromomethyl)phenoxy)(*tert*-butyl)dimethylsilane. The reaction mixture was purified by flash chromatography using 5% EtOAc/hexane to afford the product (32 mg, 65% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 1H), 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.16 – 7.10 (m, 1H), 7.12 – 7.02 (m, 2H), 6.97 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.89 (dd, *J* = 3.4, 1.0 Hz, 1H), 3.55 (ddd, *J* = 15.2, 4.4, 1.0 Hz, 1H), 3.11 (dd, *J* = 15.1, 8.6 Hz, 1H), 3.02 – 2.89 (m, 2H), 2.80 (dd, *J* = 17.1, 13.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 151.5, 139.9, 128.3, 128.2, 127.0, 126.5, 124.4, 122.3, 116.6, 41.0, 29.7, 28.4; IR (film) 3310, 3150, 2460, 1850, 1768, 1469, 1416, 1264, 1124, 1081, 974, 731, 703 cm^{-1}; LRMS (EI); Mass calcd for $C_{14}H_{12}O_2S$[M]$^+$: 244.1; found 244.0. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 10%, *i*-

PrOH/Hexanes, 0.5 mL/min, 254 nm), Rt_1 (major) = 21.5 min, Rt_2 (minor) = 24.4 min; er = 75:25.



3d

Determiation of the absolute configuration of compound 3d:

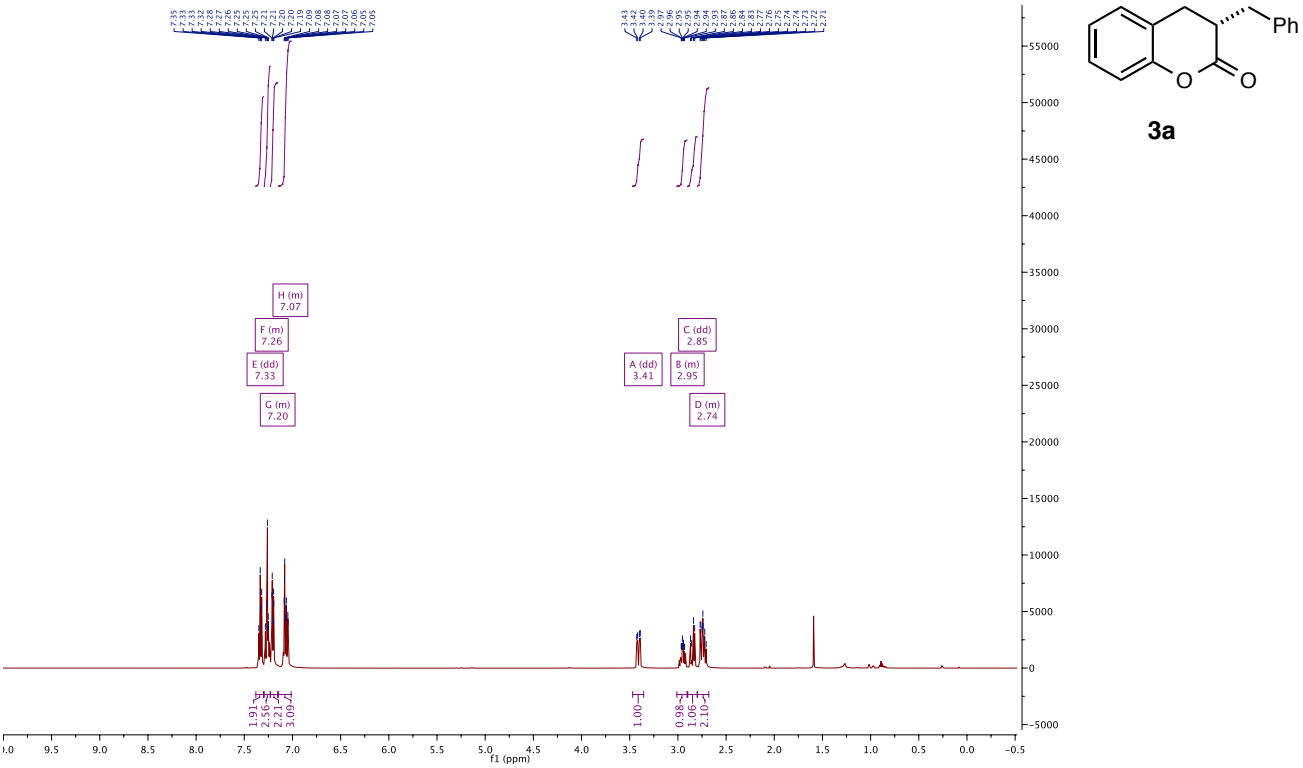
The absolute configuration of compound **3d** was determined to be (*S*)-configuration by comparison with the reported optical rotation value.[4]

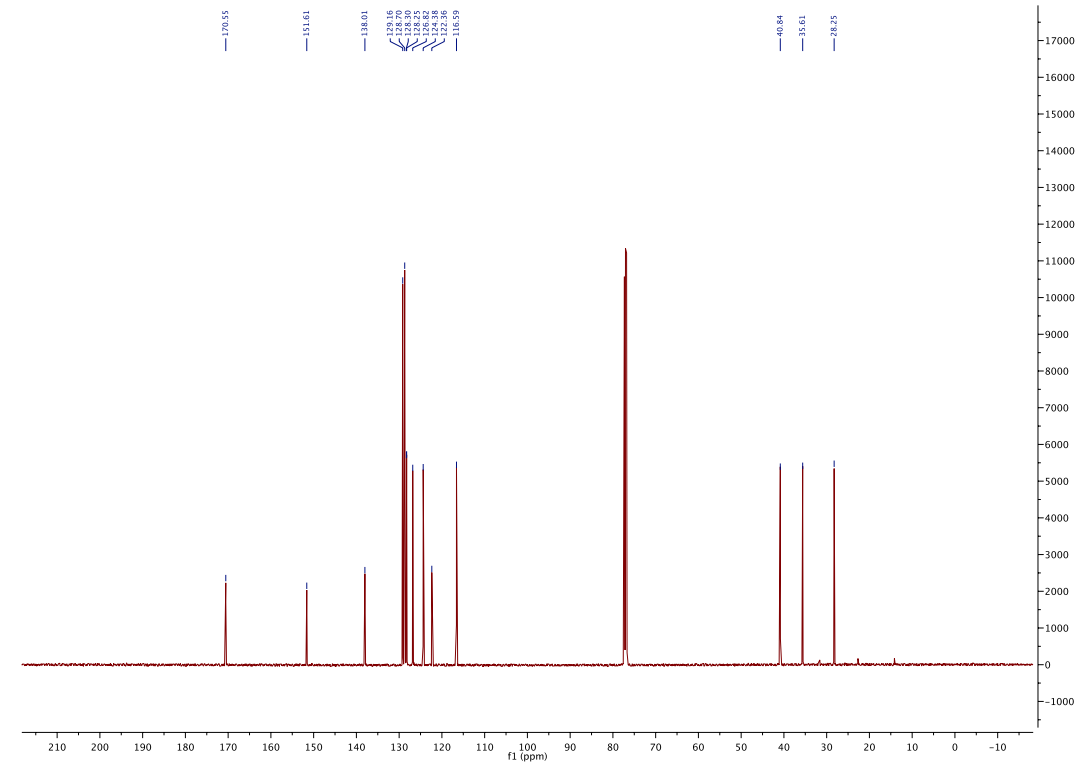
$[\alpha]_D^{25}$ = -12.3 (c = 0.8, benzene, 88:12 e.r.): (*S*)-configuration

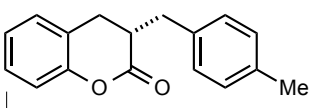
Literature value: $[\alpha]_D^{25}$ = -3.4 (c = 1.03 benzene, 66.5:33.5 e.r.)

[4] M. Murakata, H. Tsutsui, N. Takeuchi, O. Hoshino Tetrahedron 1999, 55, 10295-10304.

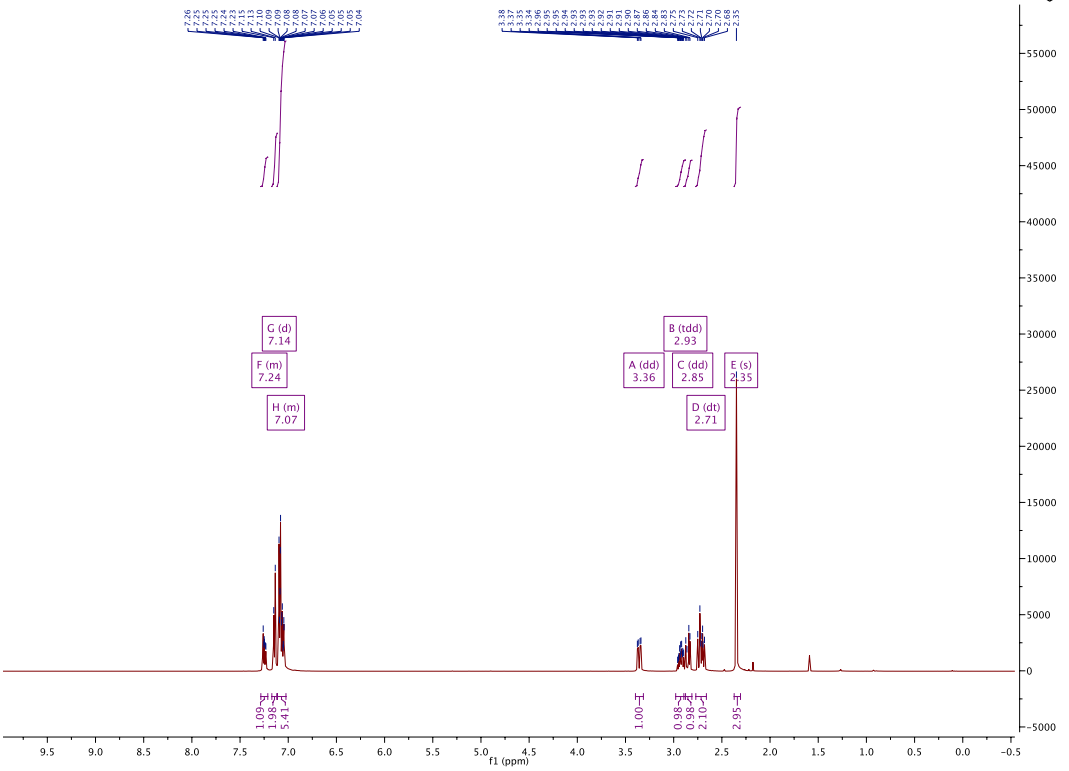
Selected NMR Spectra






O
O
Me

3b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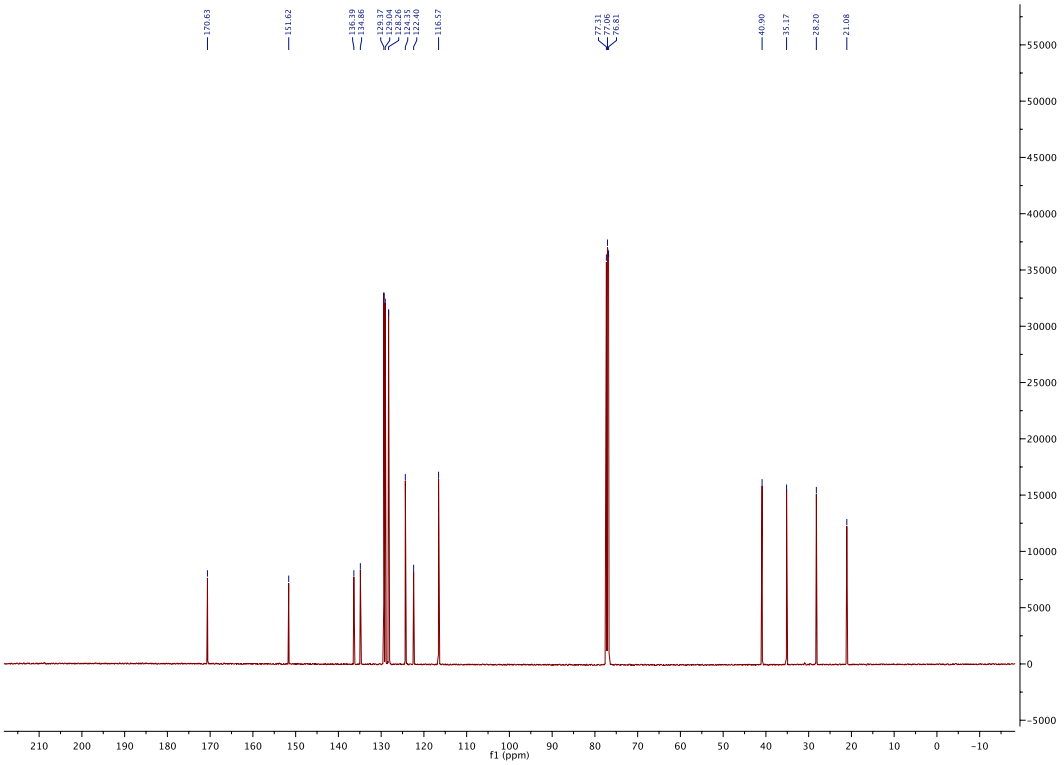
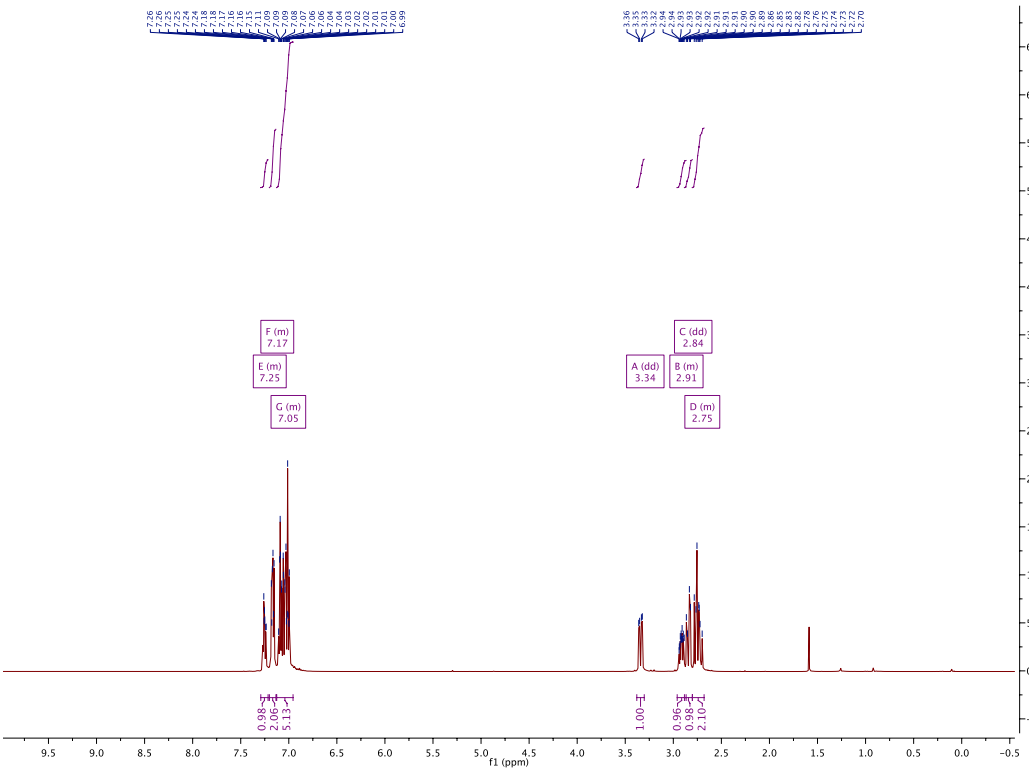
F (m) 7.24
H (m) 7.07
B (tdd) 2.93
A (dd) 3.36
C (dd) 2.85
E (s) 2.35
D (dt) 2.71
f1 (ppm)


170.63
151.62
136.19
134.86
129.37
129.04
128.26
124.15
122.40
116.57
77.31
77.06
76.80
40.90
35.17
28.20
21.08
f1 (ppm)


F (m)
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E (m)
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G (m)
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C (dd)
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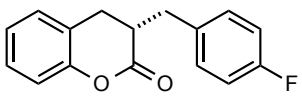
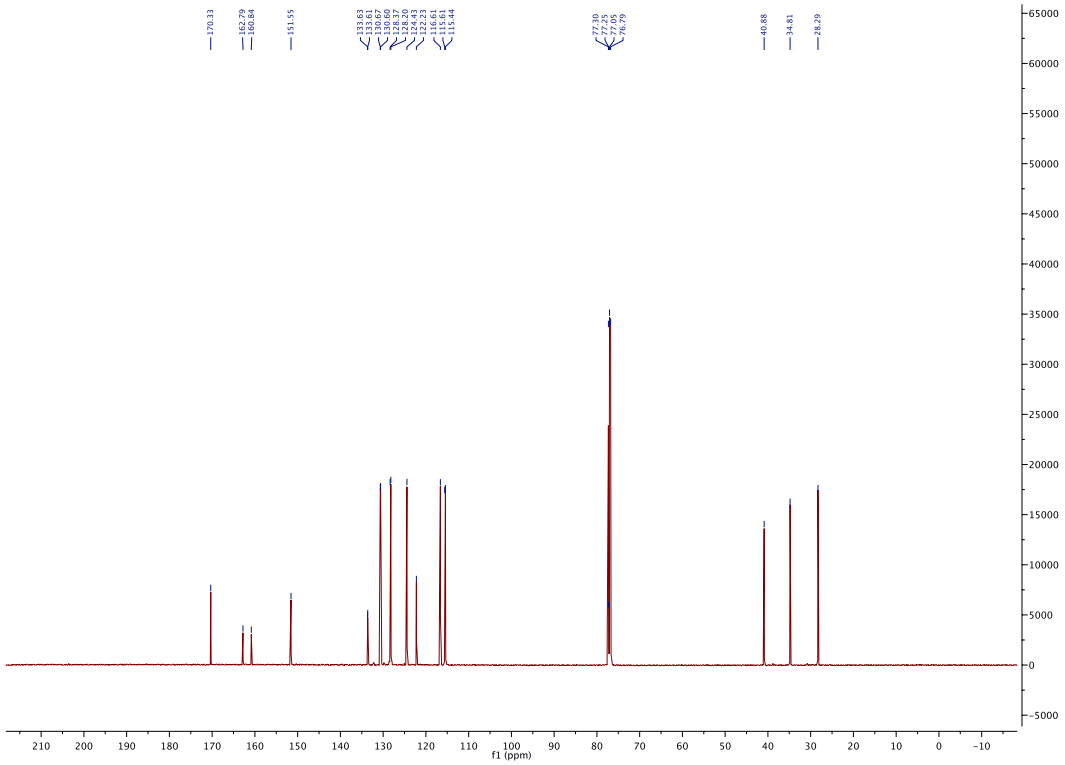
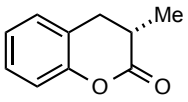
A (dd)
3.34
B (m)
2.91
D (m)
2.75
f1 (ppm)

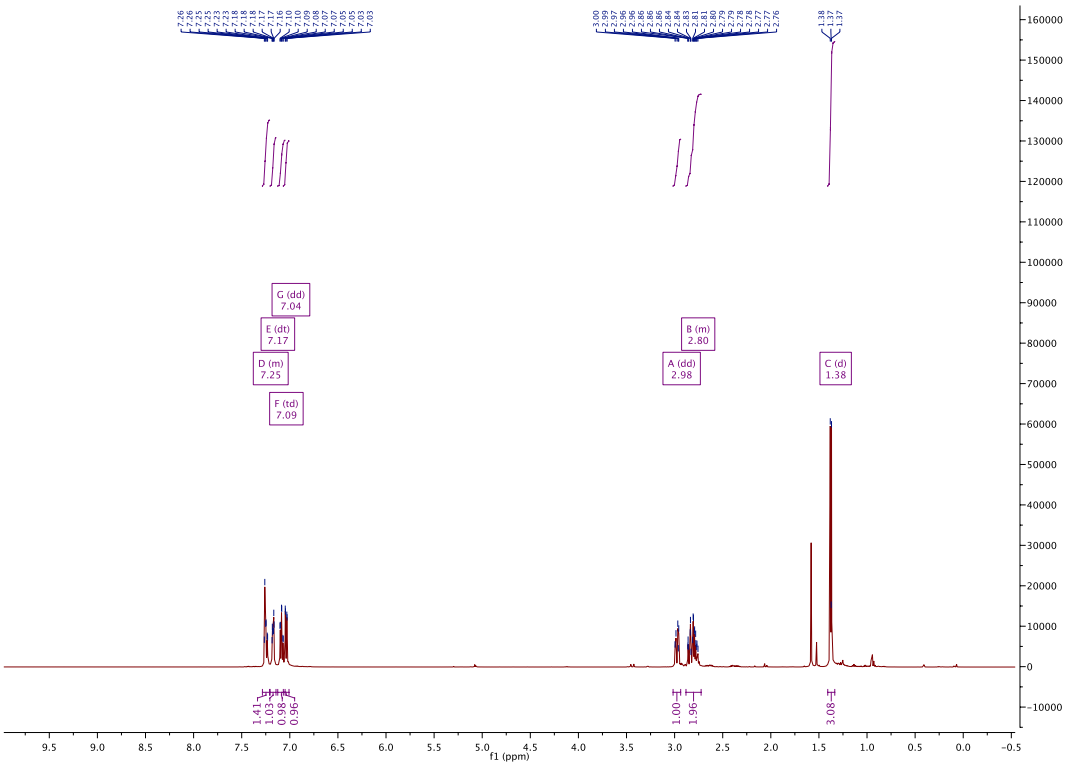

O
O
F

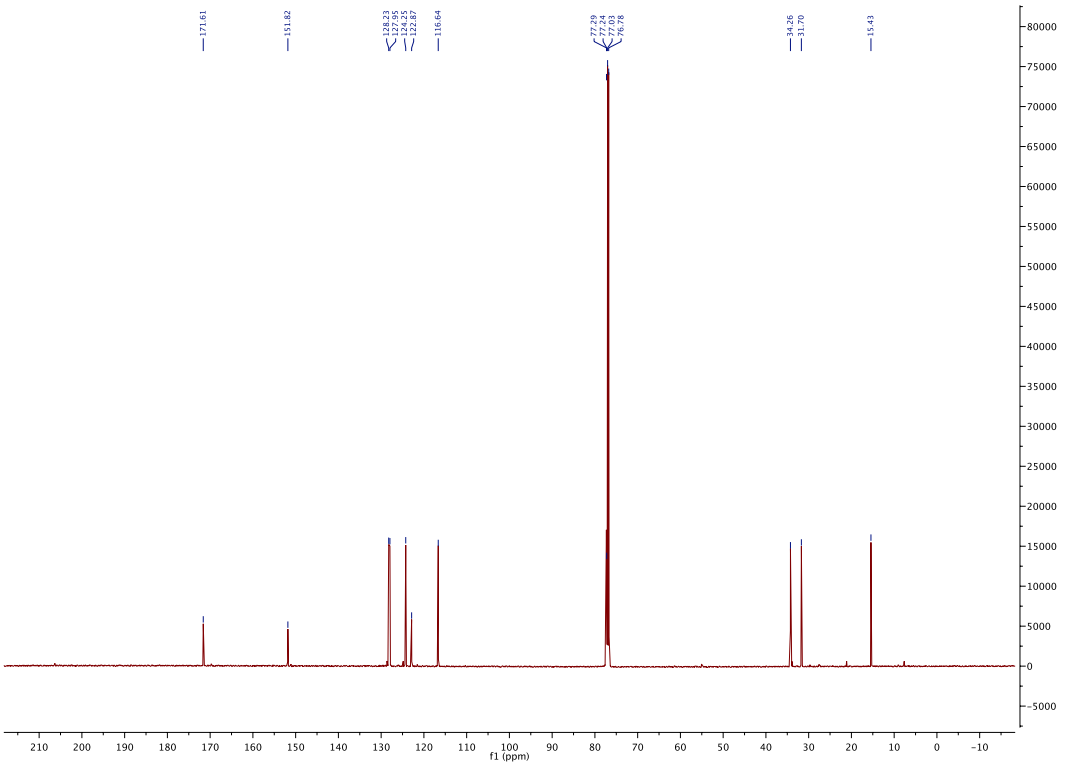
3c

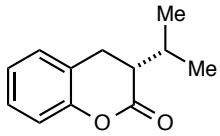

f1 (ppm)


Me
O
O

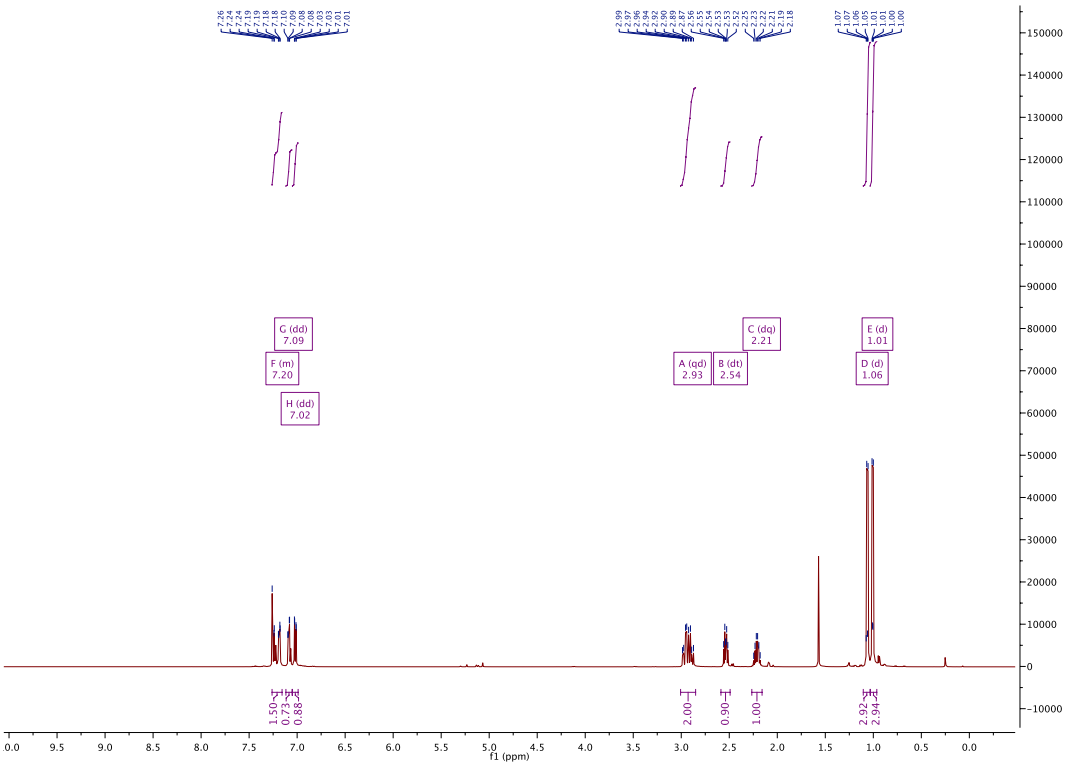
3d

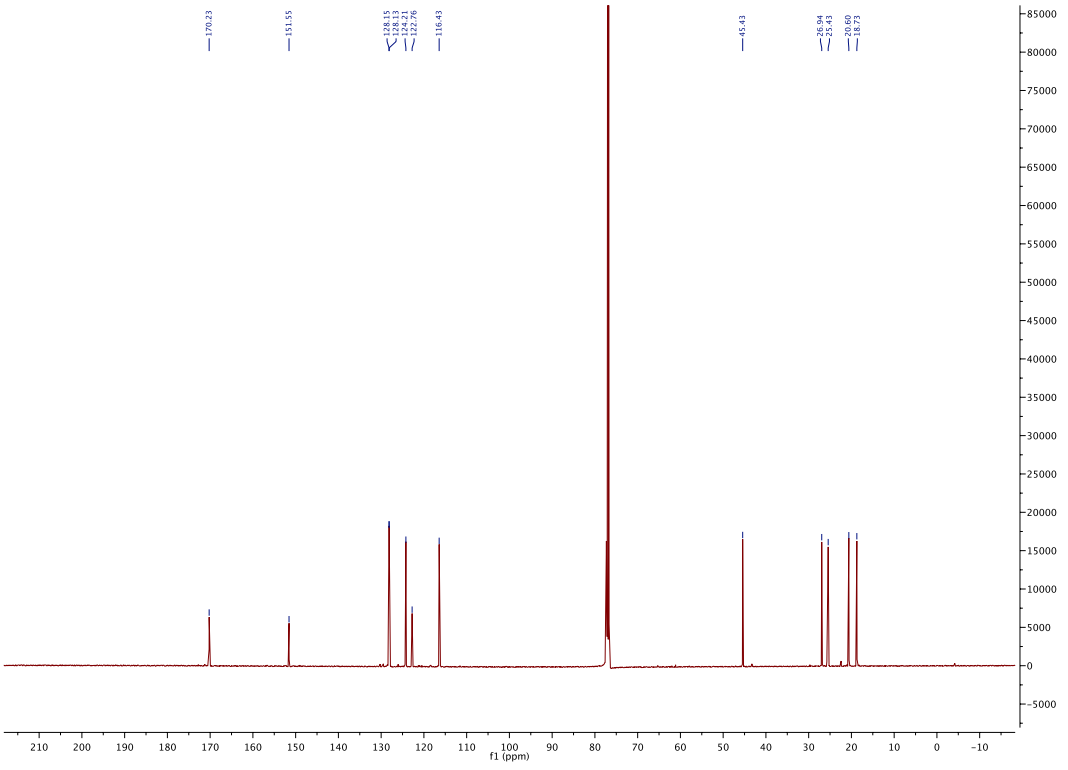

G (dd)
7.04
E (dt)
7.17
D (m)
7.25
F (td)
7.09
B (m)
2.80
A (dd)
2.98
C (d)
1.38
1.41
1.03
0.98
0.96
1.00
1.96
3.08
f1 (ppm)

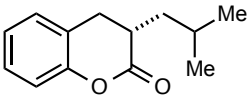

171.61
151.82
128.23
127.65
124.25
122.87
116.64
77.29
77.04
77.03
76.78
34.26
31.70
15.43
f1 (ppm)


Me
Me
O
O

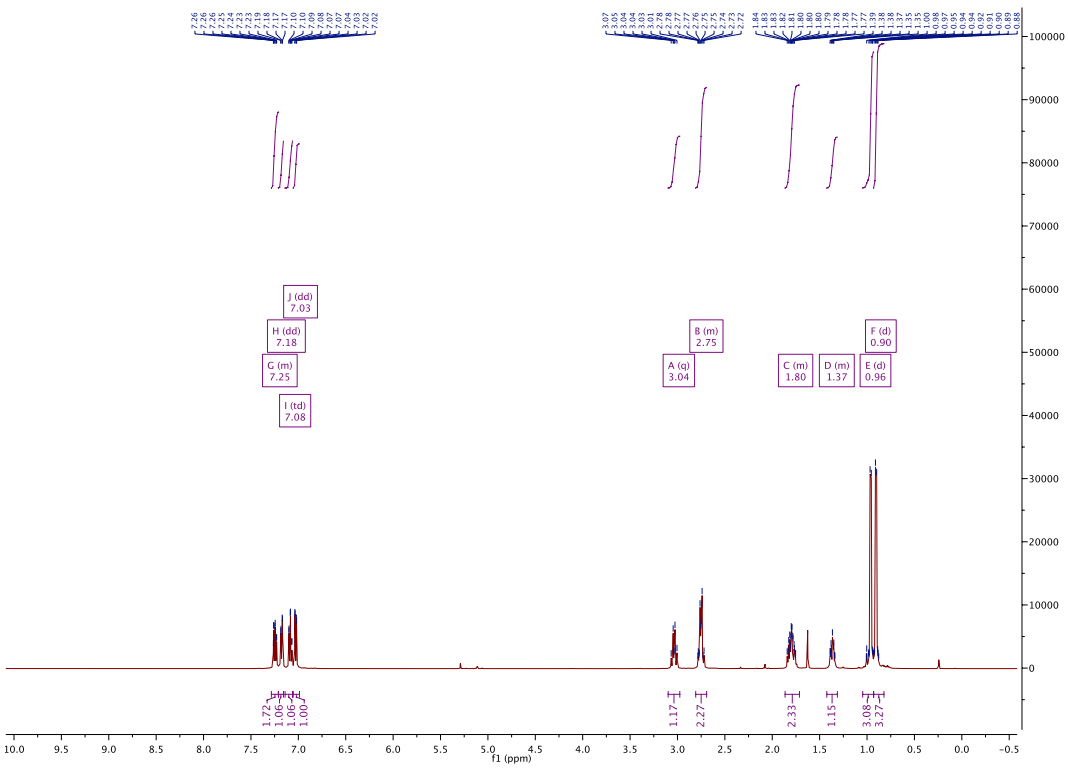
3e

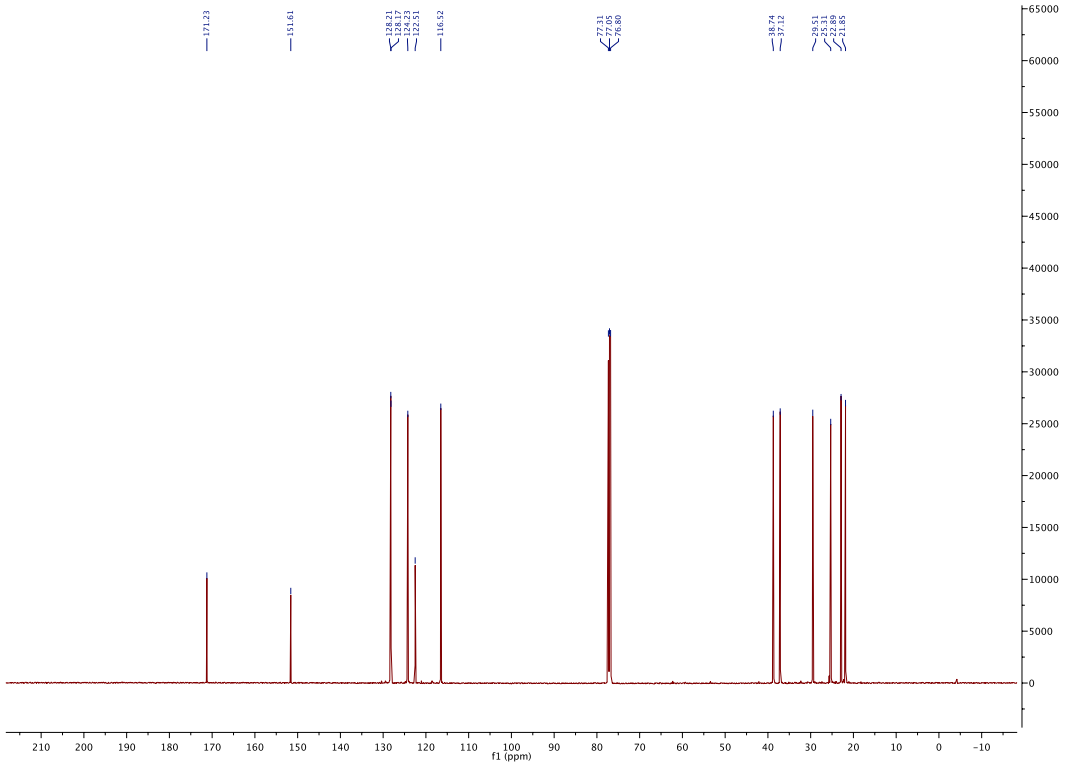

G (dd) 7.09
F (m) 7.20
H (dd) 7.02
C (dq) 2.21
A (qd) 2.93
B (dt) 2.54
E (d) 1.01
D (d) 1.06
f1 (ppm)

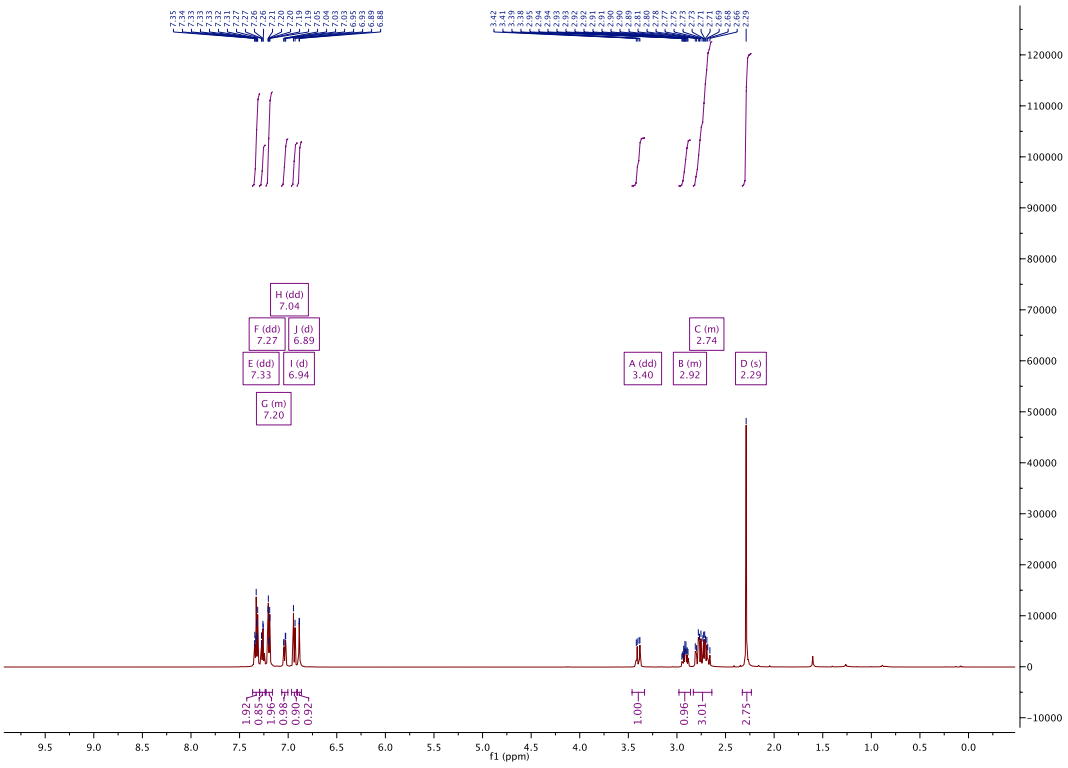

170.23
151.55
128.15
127.13
124.21
122.76
116.43
45.43
26.94
25.43
20.60
18.73
f1 (ppm)

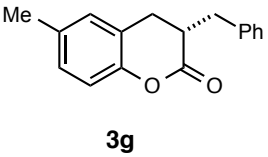

Me
Me
O
O

3f

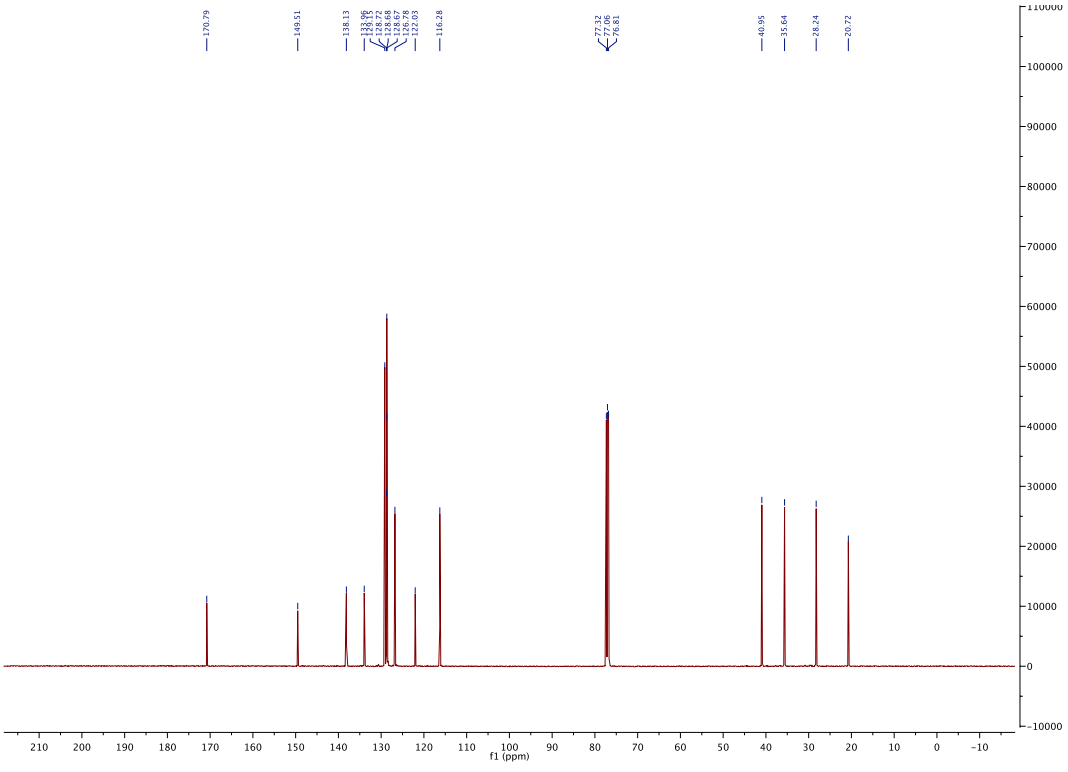

J (dd) 7.03
H (dd) 7.18
G (m) 7.25
I (td) 7.08
A (q) 3.04
B (m) 2.75
C (m) 1.80
D (m) 1.37
E (d) 0.96
F (d) 0.90
1.72
1.06
1.06
1.00
1.17
2.27
2.33
1.15
3.08
3.27
f1 (ppm)

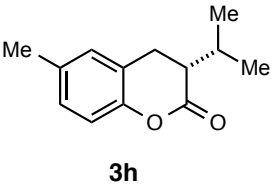

171.23
151.61
128.21
127.77
124.23
122.51
116.52
77.31
77.05
76.80
38.74
37.12
29.51
25.31
21.89
21.83
f1 (ppm)


H (dd) 7.04
F (dd) 7.27
J (d) 6.89
E (dd) 7.33
I (d) 6.94
G (m) 7.20
C (m) 2.74
A (dd) 3.40
B (m) 2.92
D (s) 2.29
1.92
0.85
1.96
0.96
0.92
1.00
0.96
3.01
2.75
f1 (ppm)

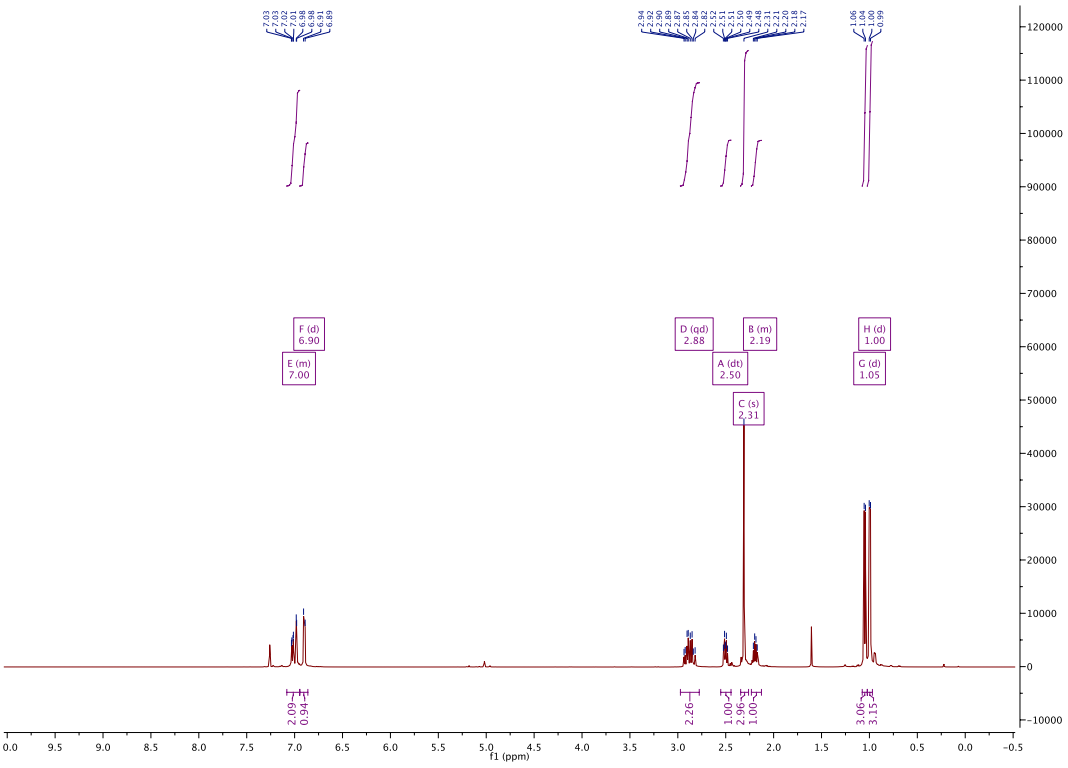

Me
Ph
O
O

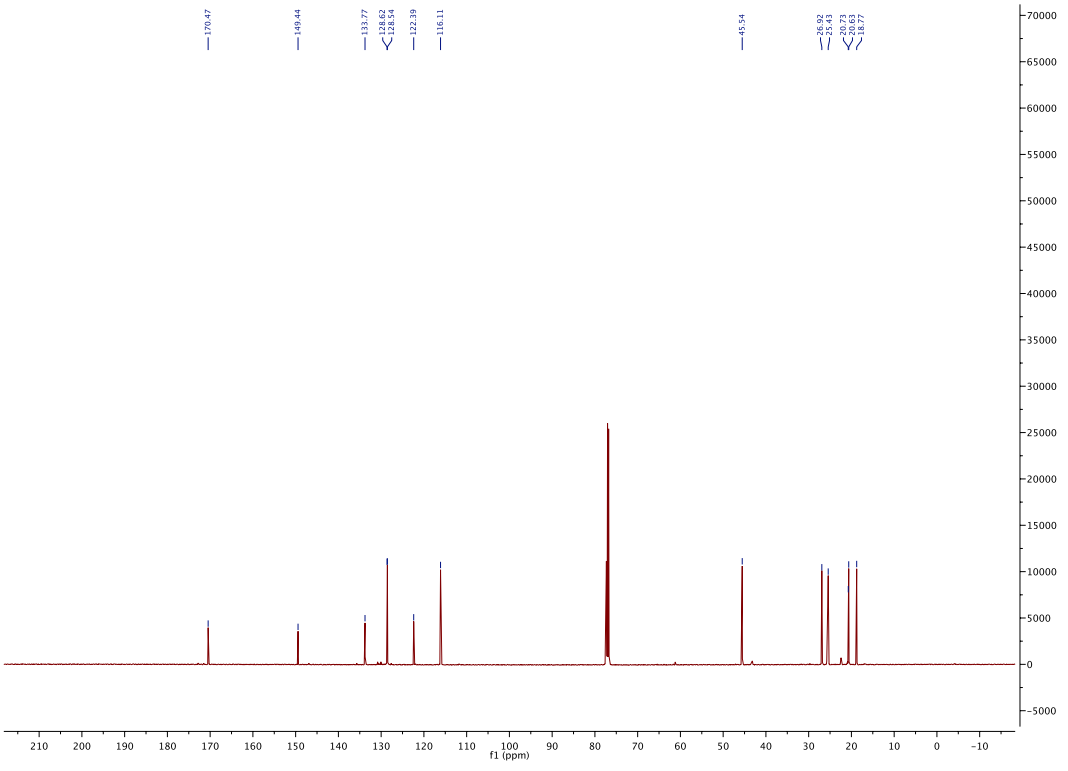
3g

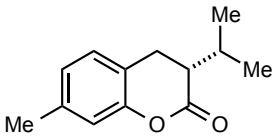

170.79
149.51
138.13
133.96
129.75
129.22
128.68
126.87
126.80
122.03
116.28
77.32
77.06
76.81
40.95
35.64
28.24
20.72
f1 (ppm)


Me
Me
Me
O
O

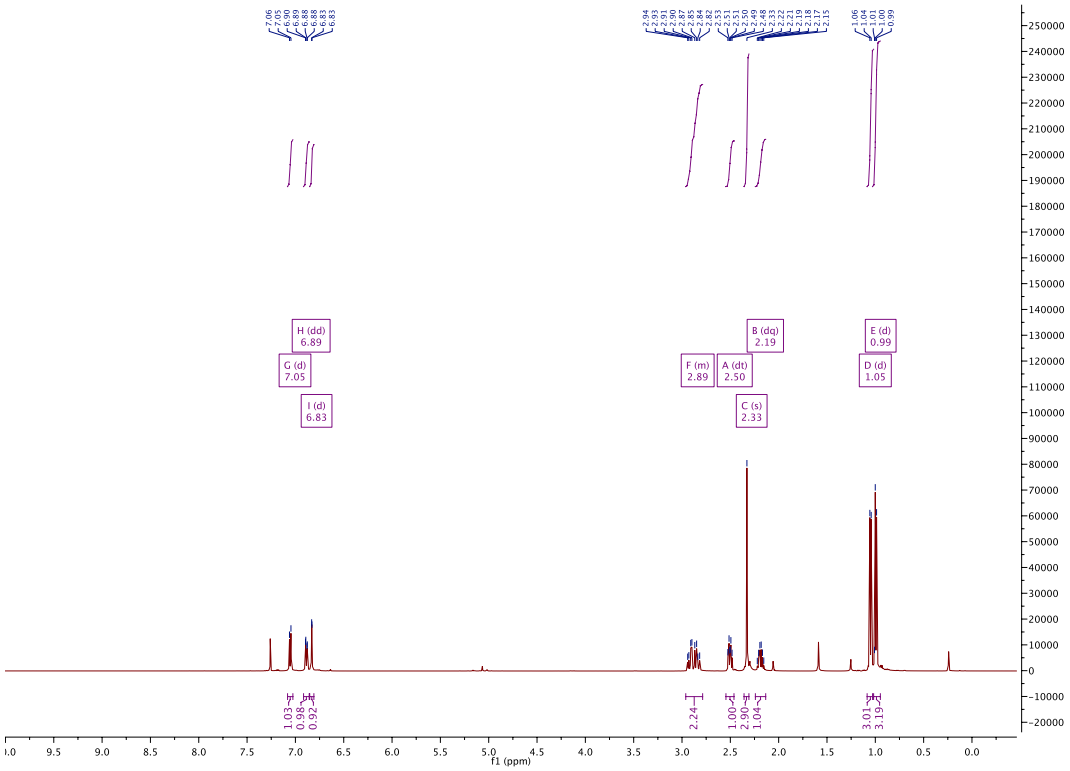
3h

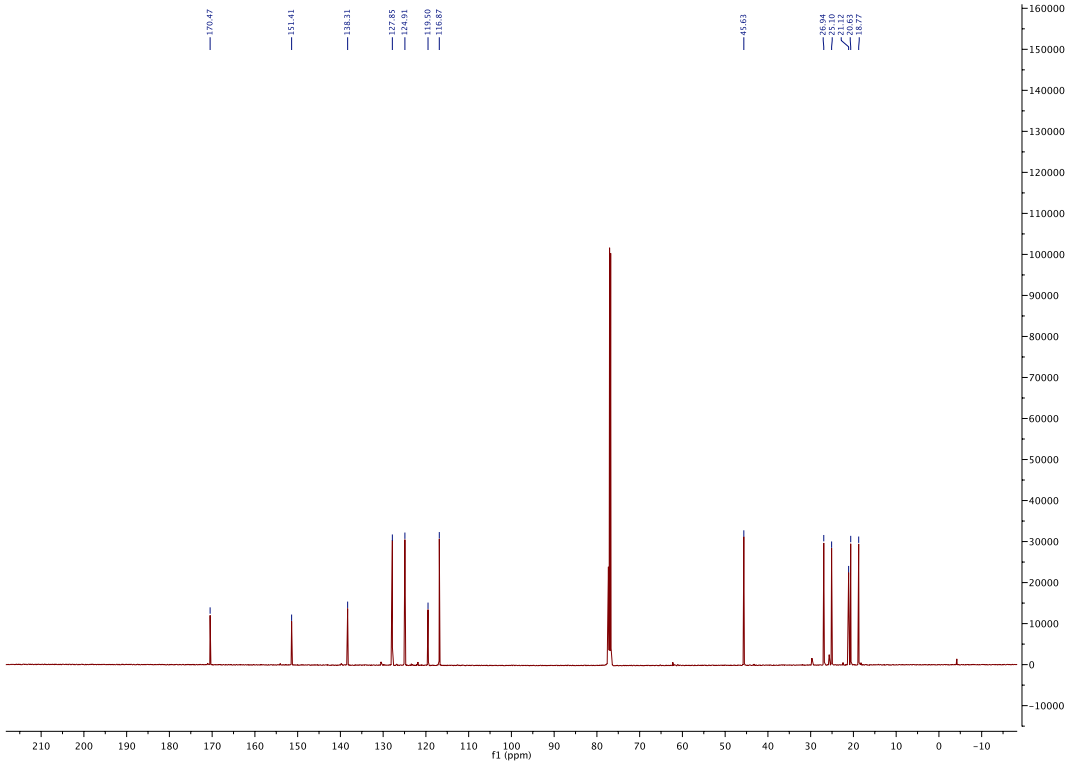

F (d) 6.90
E (m) 7.00
D (qd) 2.88
B (m) 2.19
A (dt) 2.50
C (s) 2.31
H (d) 1.00
G (d) 1.05
f1 (ppm)

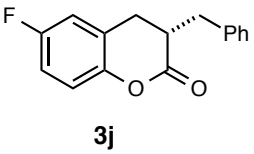

170.47
149.44
133.77
128.62
128.54
122.39
116.11
45.54
26.92
25.43
21.73
20.63
18.77
f1 (ppm)


Me
Me
Me
O
O

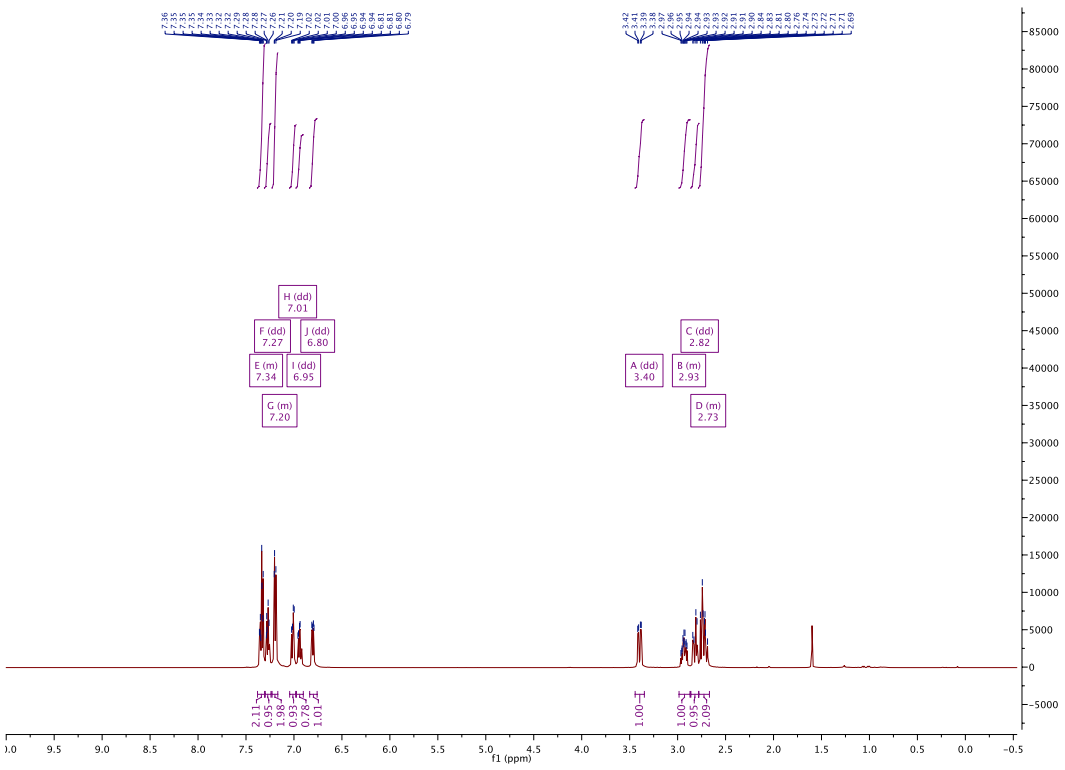
3i

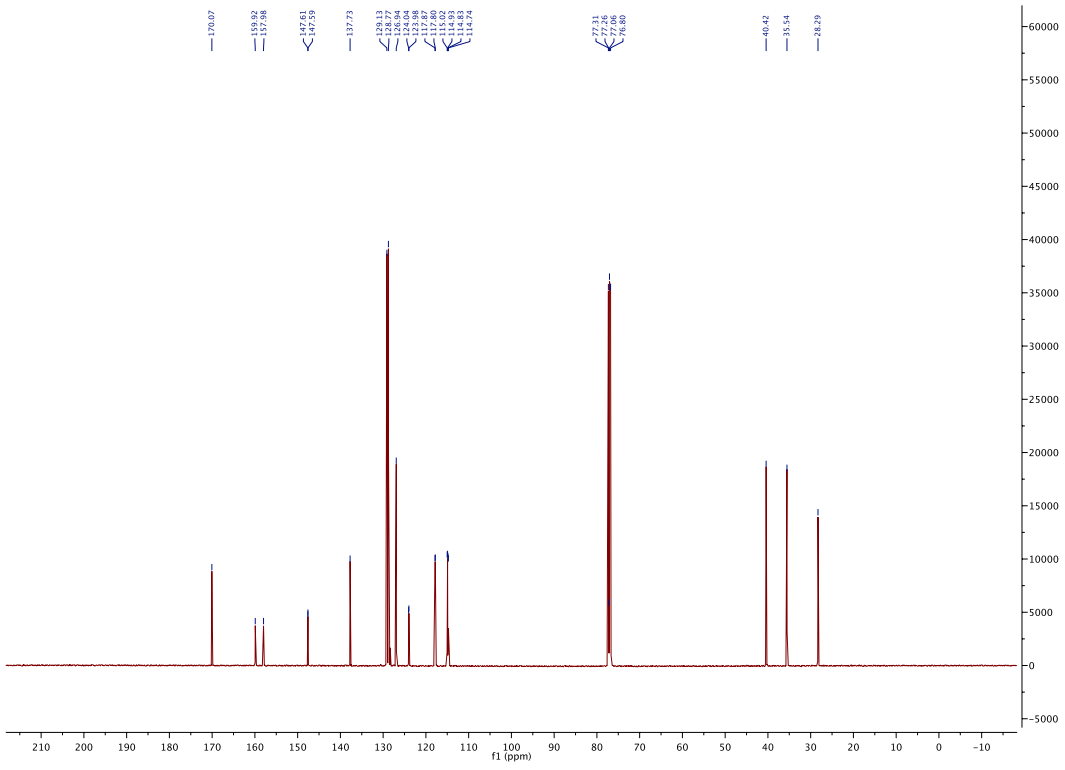

H (dd) 6.89
G (d) 7.05
I (d) 6.83
B (dq) 2.19
F (m) 2.89
A (dt) 2.50
C (s) 2.33
E (d) 0.99
D (d) 1.05
f1 (ppm)

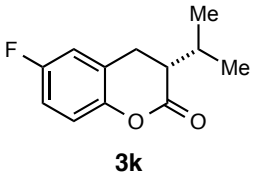

170.47
151.41
138.31
127.85
124.91
119.50
116.87
45.63
26.94
25.10
21.12
20.63
18.77
f1 (ppm)


F
Ph
O
O

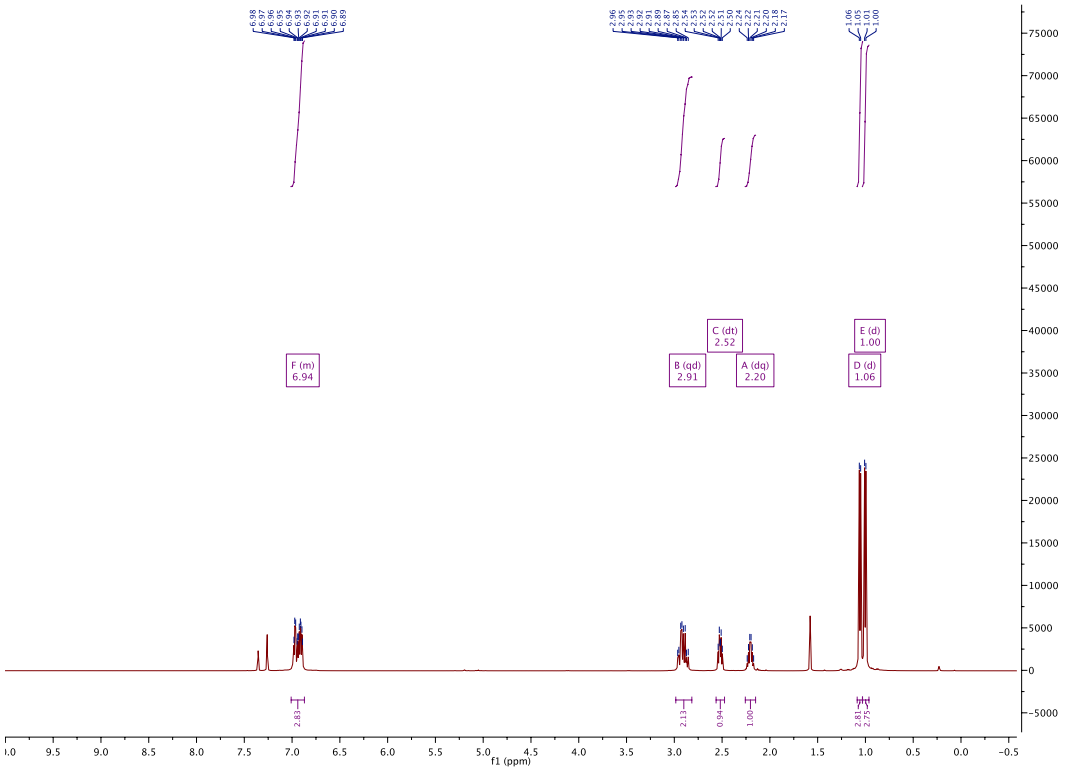
3j

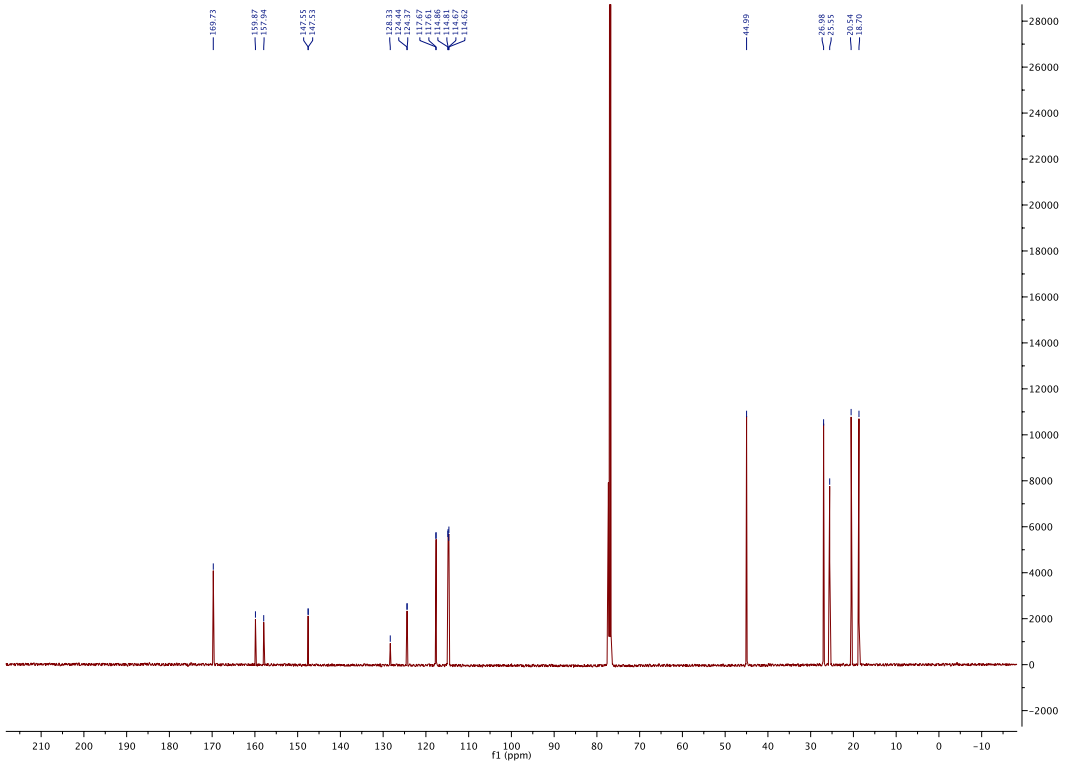

H (dd) 7.01
F (dd) 7.27
J (dd) 6.80
E (m) 7.34
I (dd) 6.95
G (m) 7.20
C (dd) 2.82
A (dd) 3.40
B (m) 2.93
D (m) 2.73
f1 (ppm)

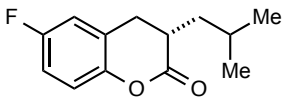

f1 (ppm)


Me
F
Me
O
O

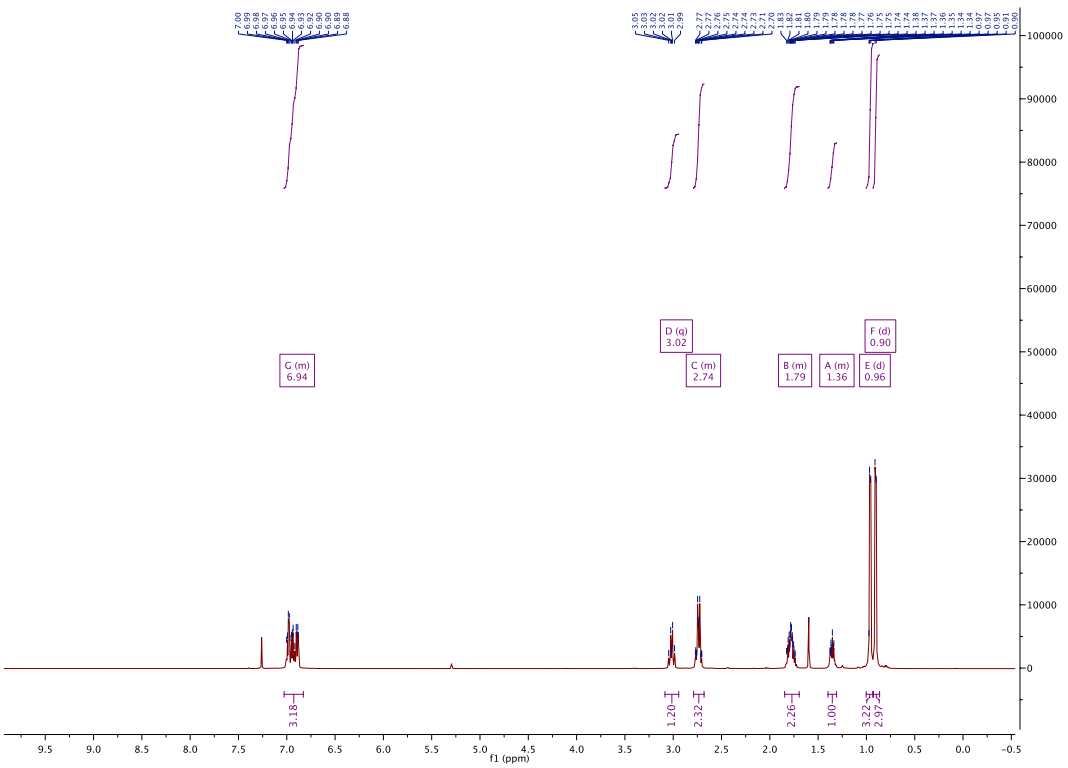
3k

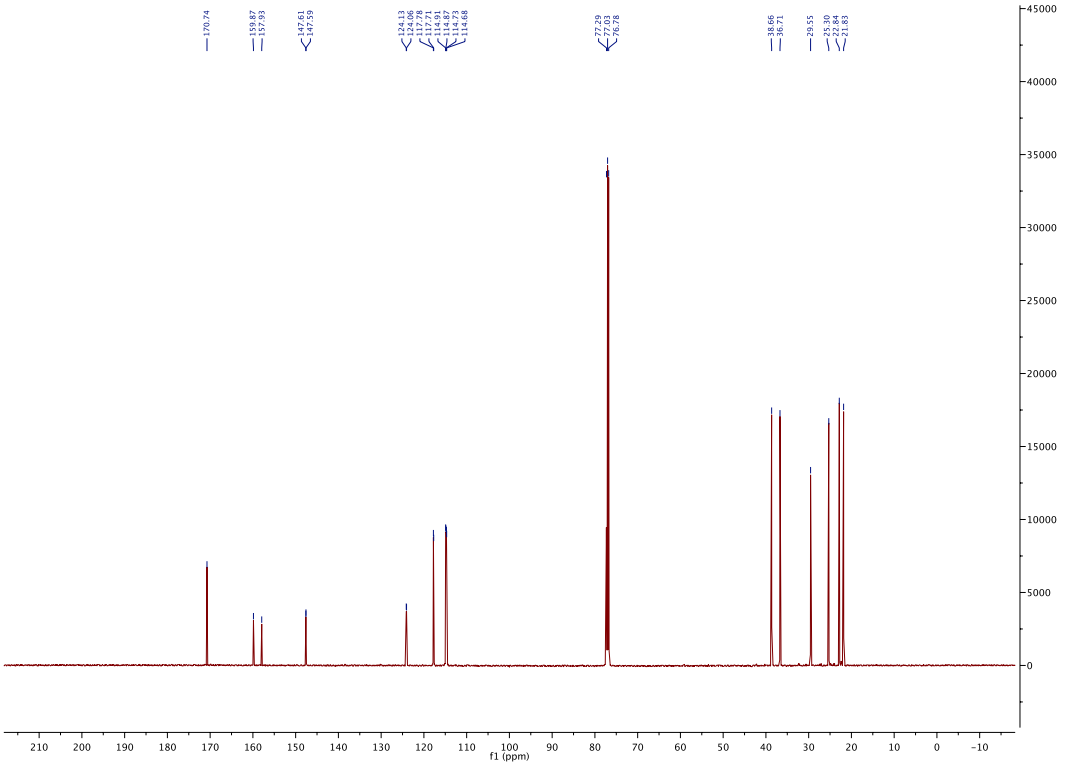

F (m)
6.94
B (qd)
2.91
C (dt)
2.52
A (dq)
2.20
D (d)
1.06
E (d)
1.00
f1 (ppm)

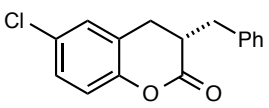

169.73
159.87
157.94
147.55
147.53
128.33
128.24
124.37
117.67
117.61
114.86
114.81
114.67
114.62
44.99
26.98
25.55
20.54
18.70
f1 (ppm)


F
Me
Me
O
O

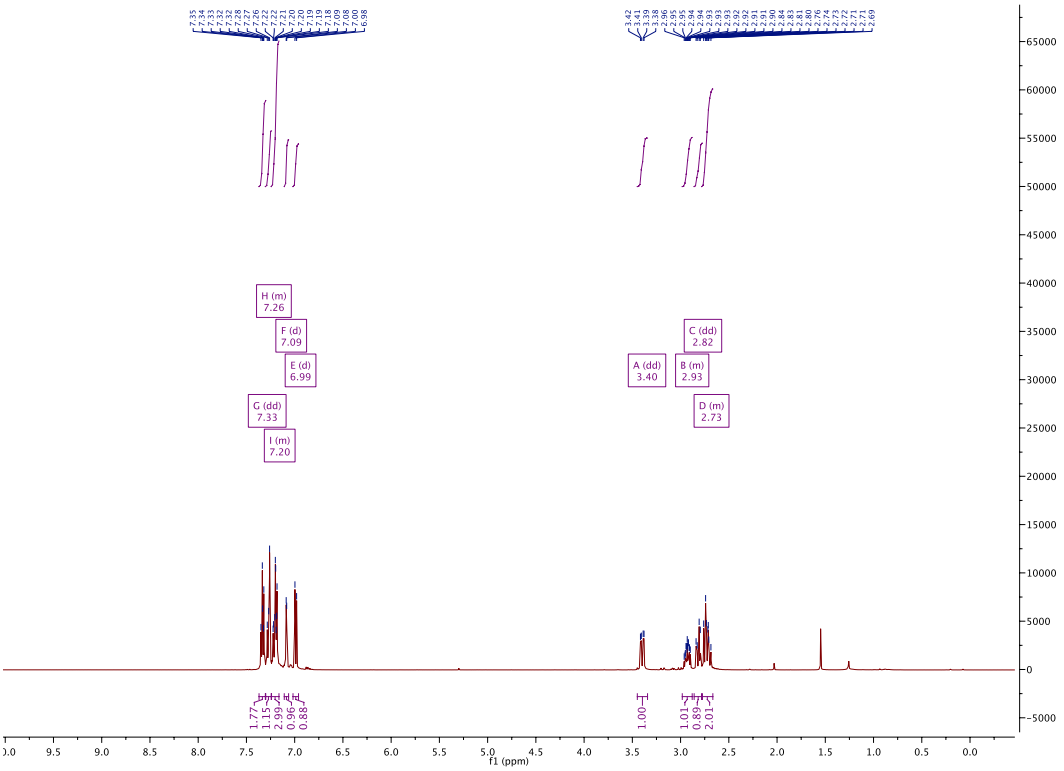
3l

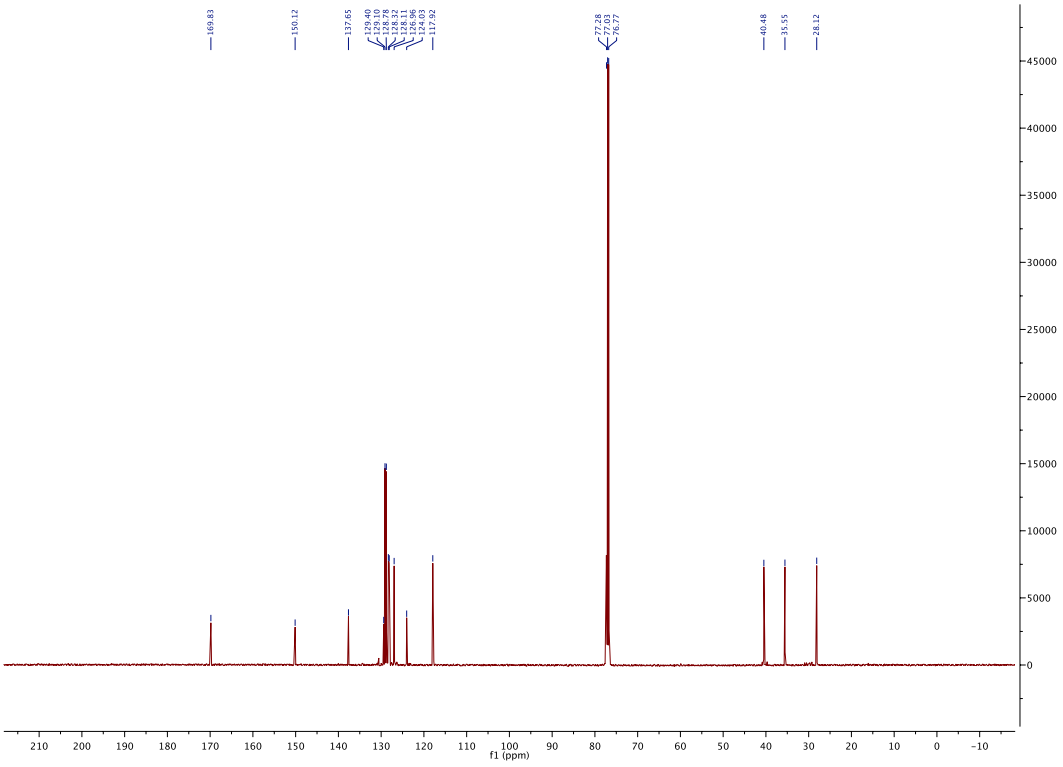

G (m) 6.94
D (q) 3.02
C (m) 2.74
B (m) 1.79
A (m) 1.36
F (d) 0.90
E (d) 0.96
3.18
1.20
2.32
2.26
1.00
3.22
2.97
f1 (ppm)

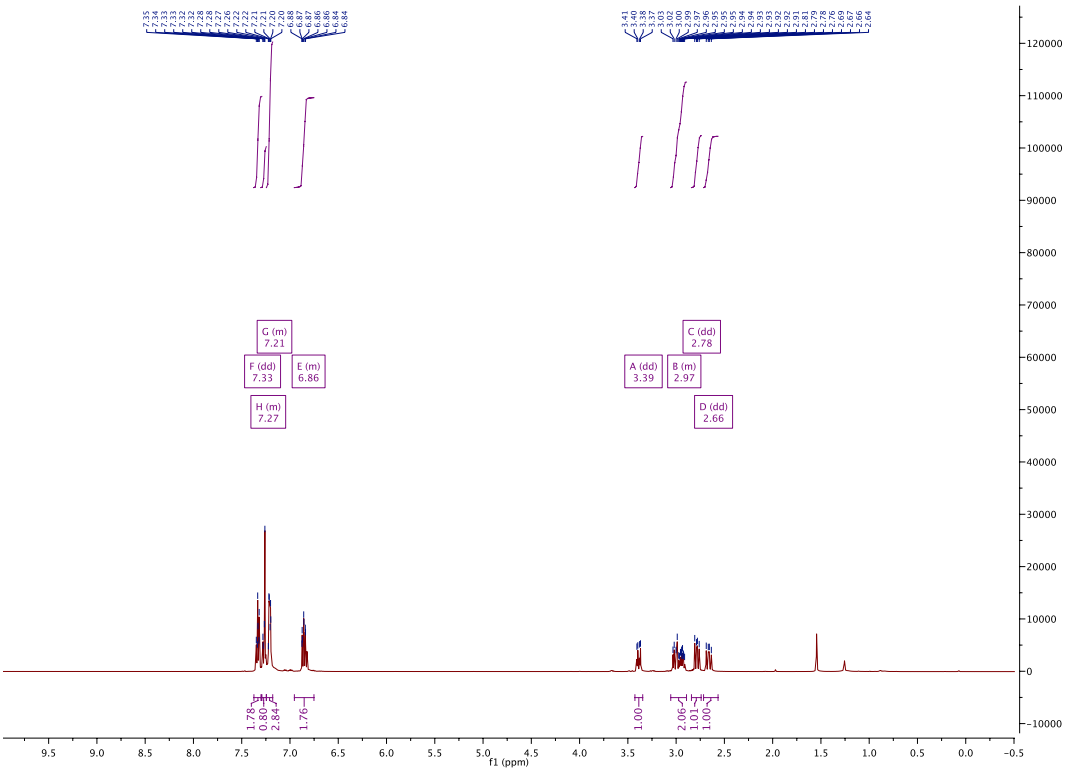

170.74
159.87
157.93
147.61
147.59
124.13
124.06
117.96
117.71
114.91
114.87
114.73
114.68
77.29
77.03
76.78
38.66
36.71
29.55
25.30
22.84
21.83
f1 (ppm)

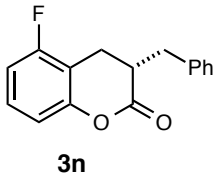

Cl
Ph
O
O

3m

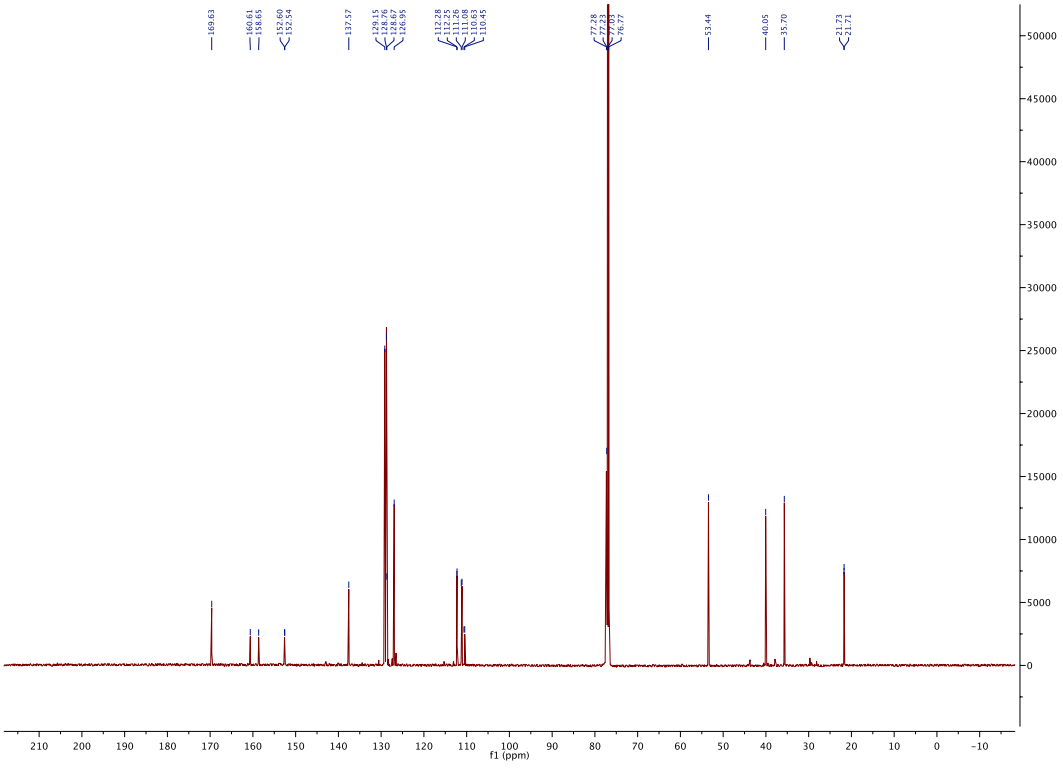

H (m) 7.26
F (d) 7.09
E (d) 6.99
G (dd) 7.33
I (m) 7.20
A (dd) 3.40
B (m) 2.93
C (dd) 2.82
D (m) 2.73
f1 (ppm)

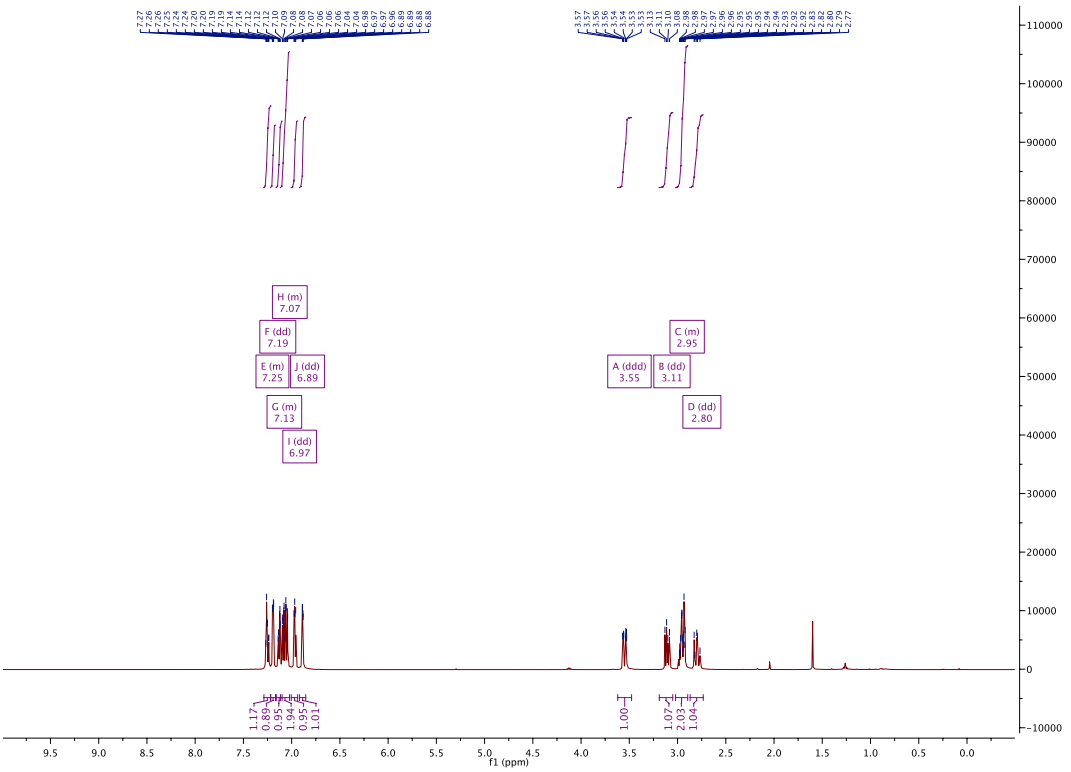

169.83
150.12
137.65
129.40
129.10
128.78
128.32
128.11
126.96
124.03
117.92
77.28
77.03
76.77
40.48
35.55
28.12
f1 (ppm)

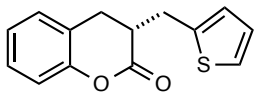

G (m)
7.21
F (dd)
7.33
E (m)
6.86
H (m)
7.27
C (dd)
2.78
A (dd)
3.39
B (m)
2.97
D (dd)
2.66
f1 (ppm)


F
Ph
O
O

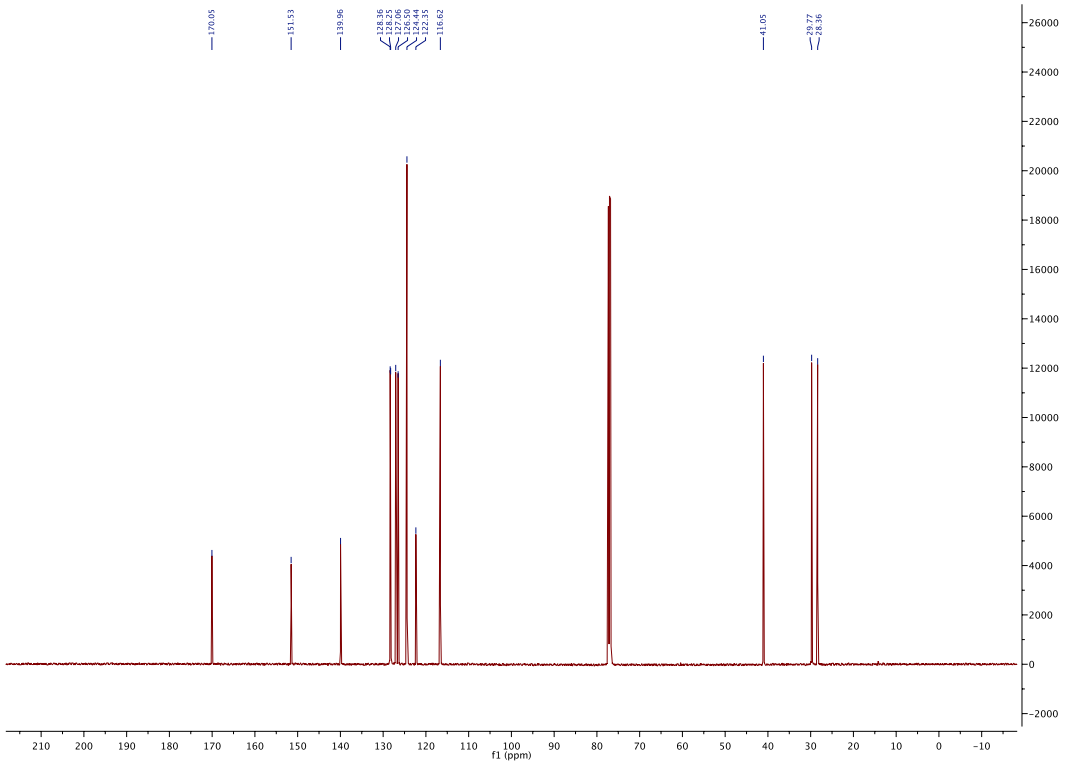
3n


f1 (ppm)

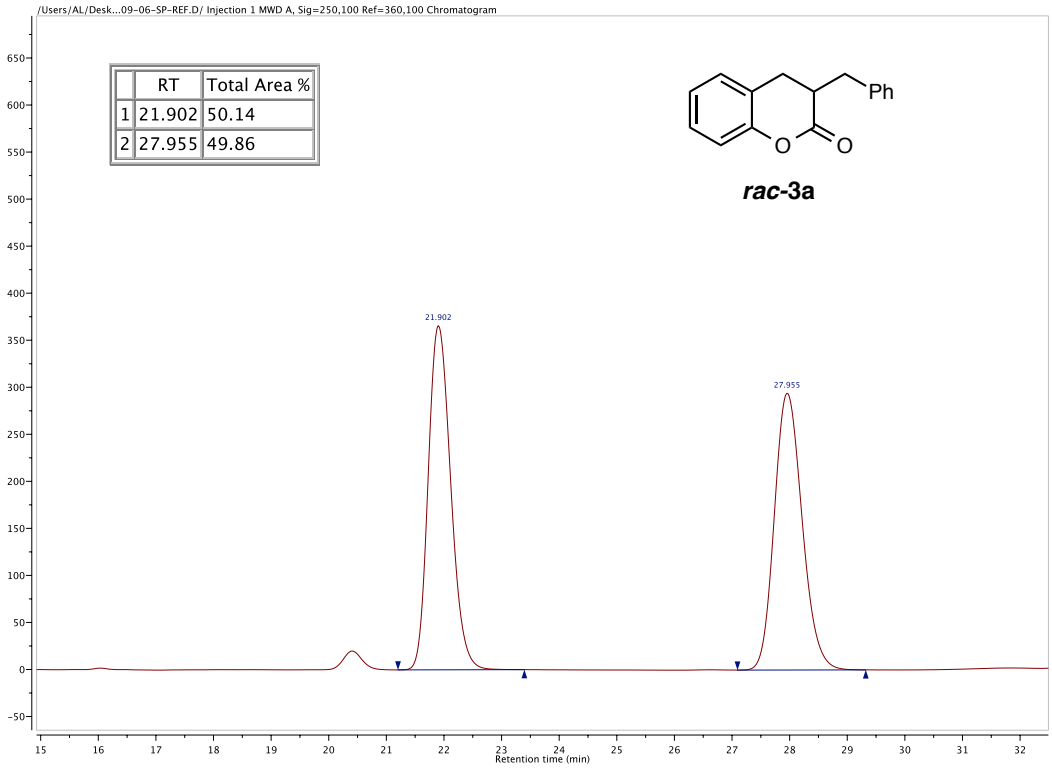

H (m)
7.07
F (dd)
7.19
E (m)
7.25
J (dd)
6.89
G (m)
7.13
I (dd)
6.97
C (m)
2.95
A (ddd)
3.55
B (dd)
3.11
D (dd)
2.80
f1 (ppm)

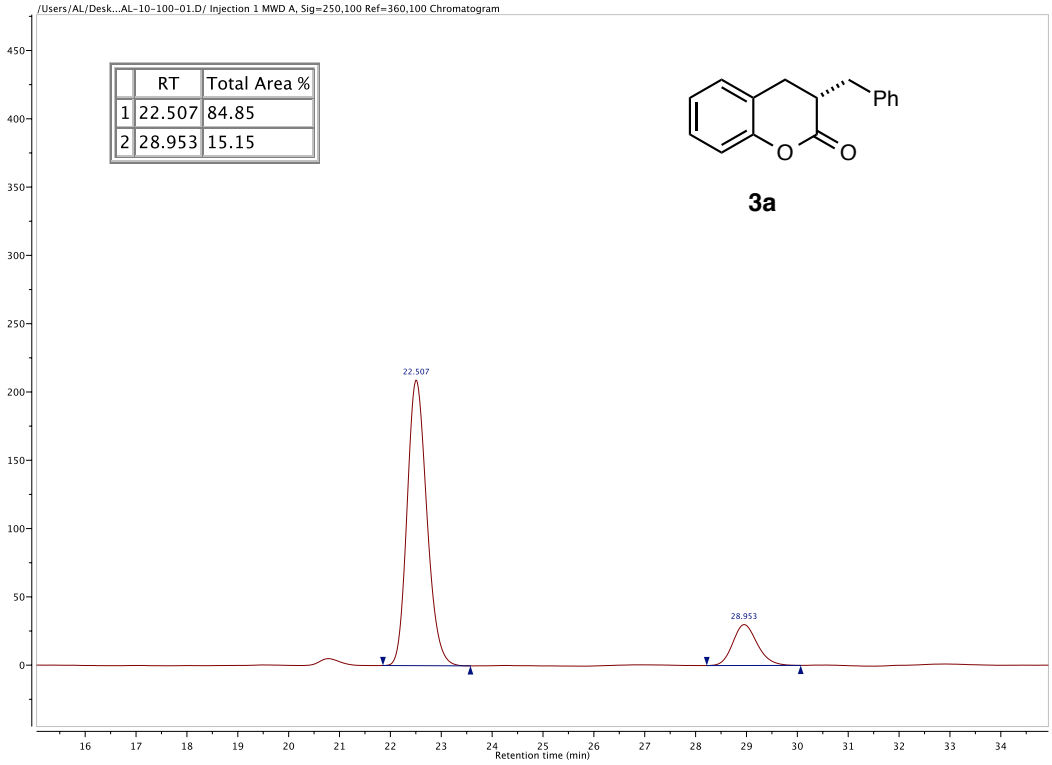


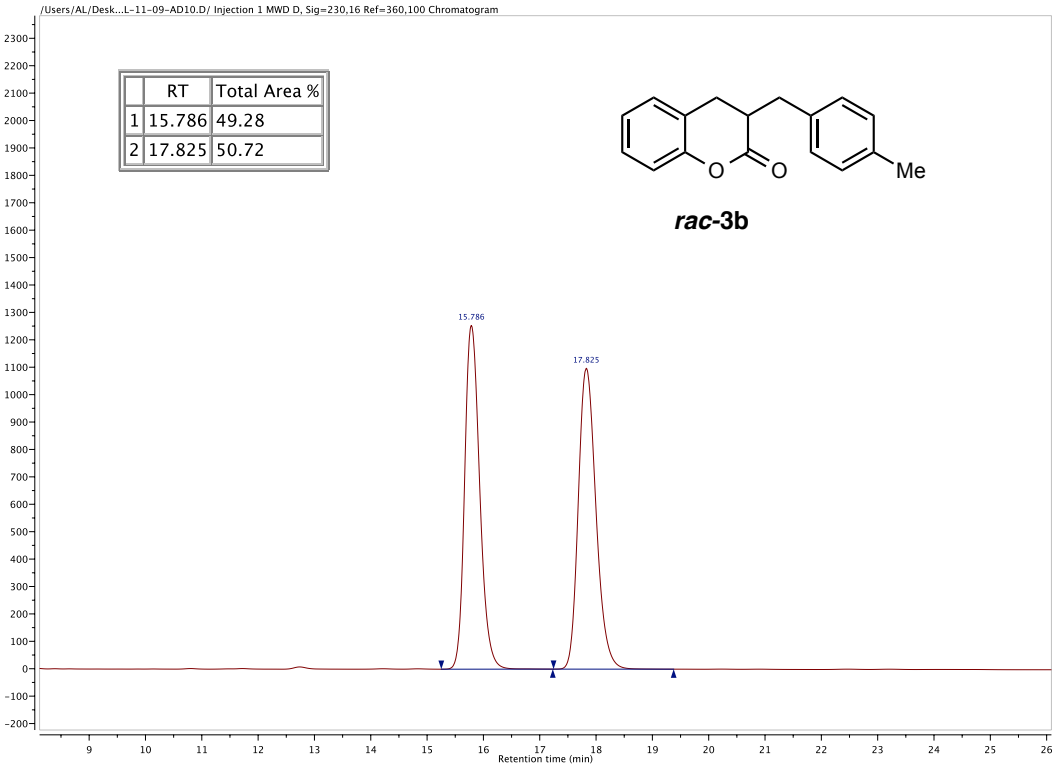
3o


170.05
151.53
139.96
128.36
128.25
127.66
126.90
124.44
122.35
116.62
41.05
29.77
28.36
f1 (ppm)

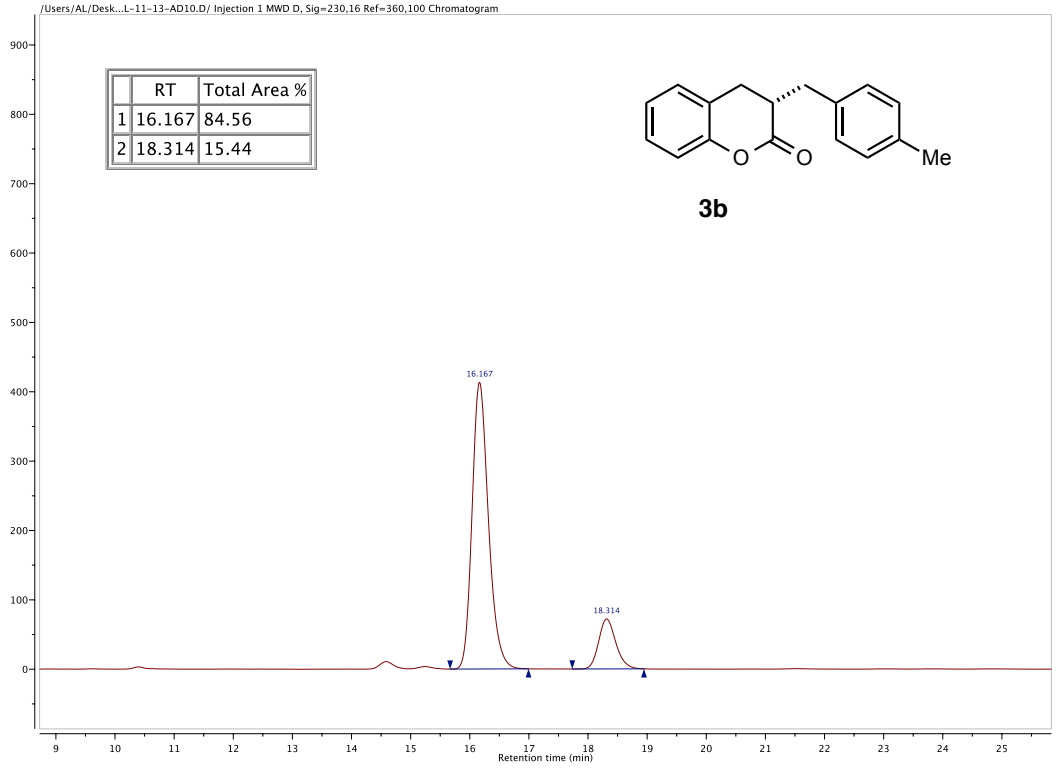
HPLC Traces of Racemic and Enantioenriched Compounds



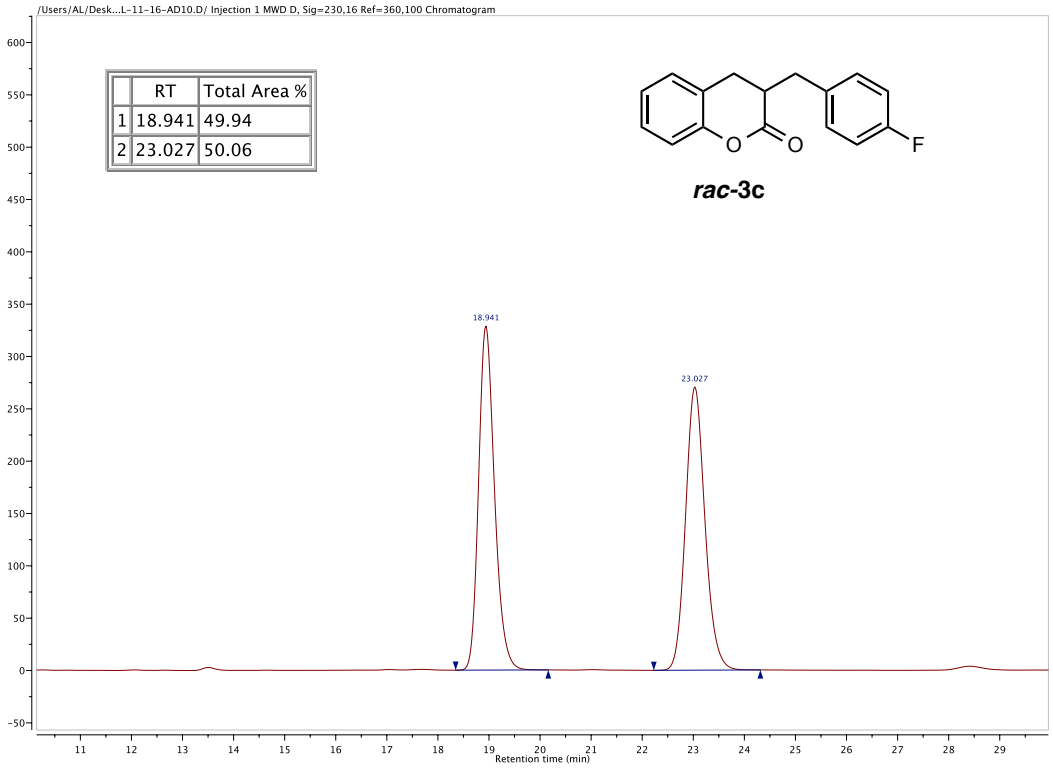


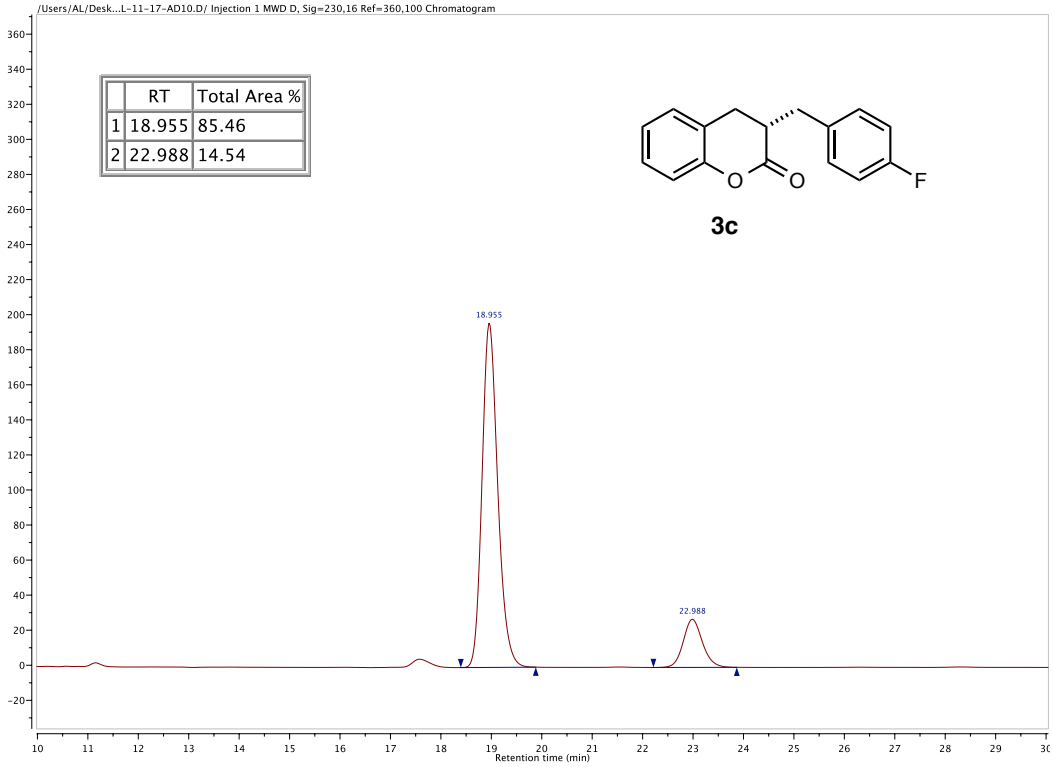

/Users/AL/Desk...L-11-09-AD10.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 15.786 49.28
2 17.825 50.72
15.786
17.825
Retention time (min)

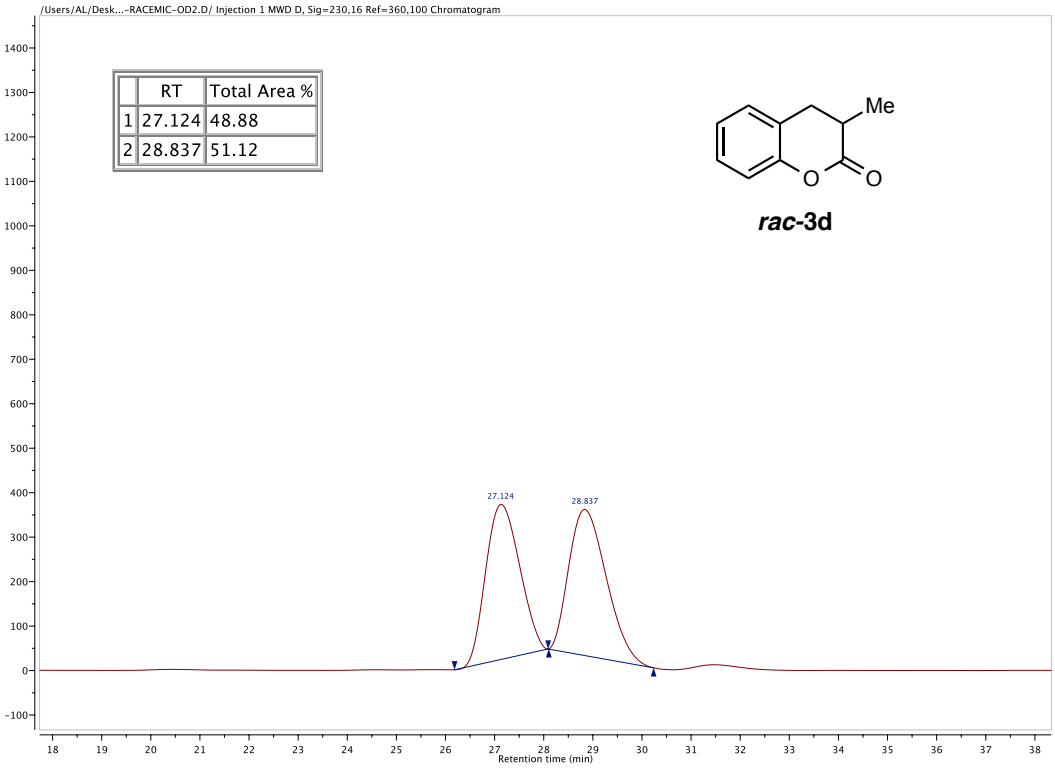
***rac*-3b**

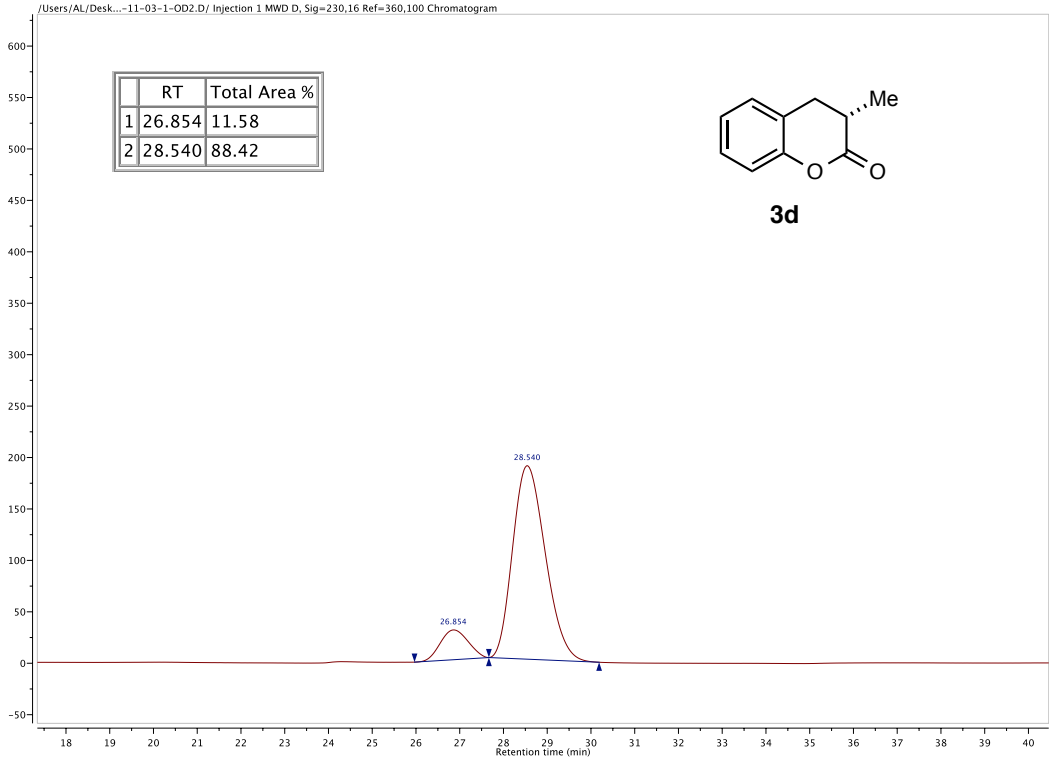

/Users/AL/Desk...L-11-13-AD10.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 16.167 84.56
2 18.314 15.44
16.167
18.314
Retention time (min)

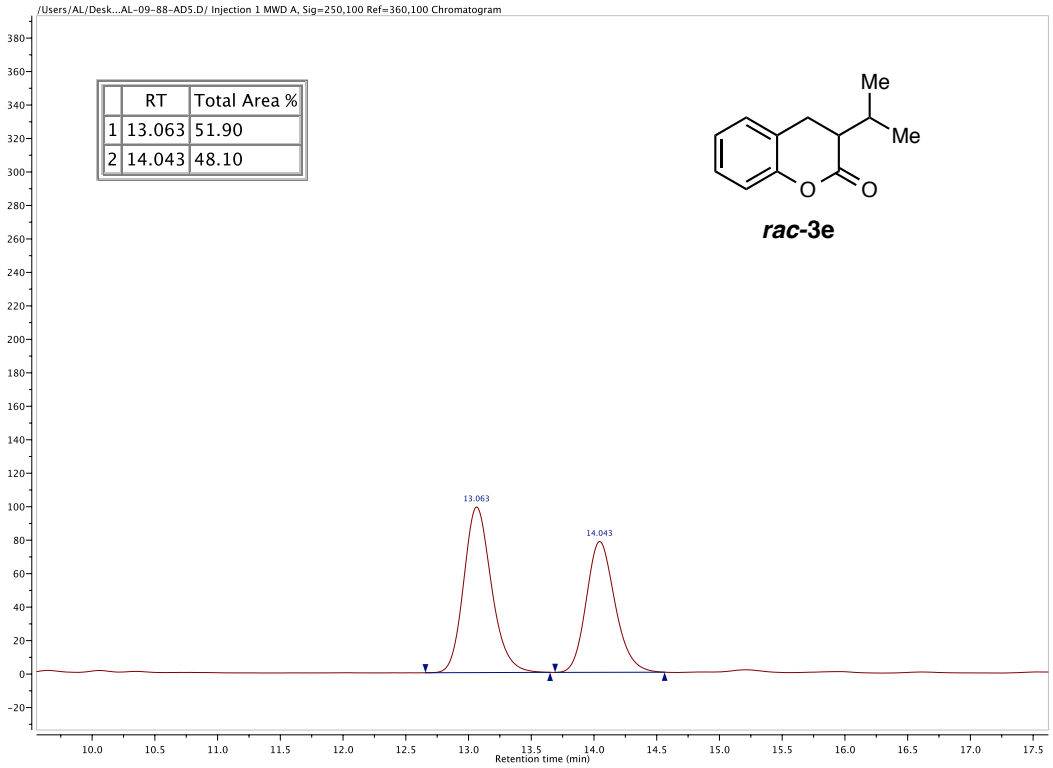
3b

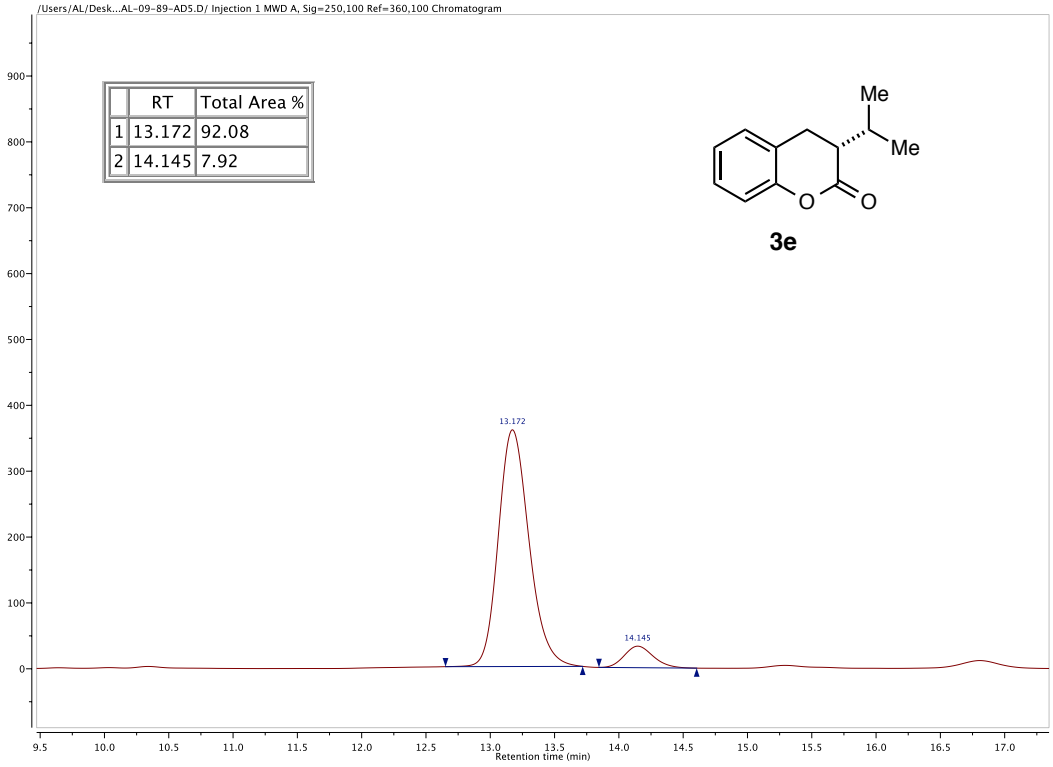

/Users/AL/Desk...L-11-16-AD10.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT Total Area %
1 18.941 49.94
2 23.027 50.06
rac-3c
18.941
23.027
Retention time (min)

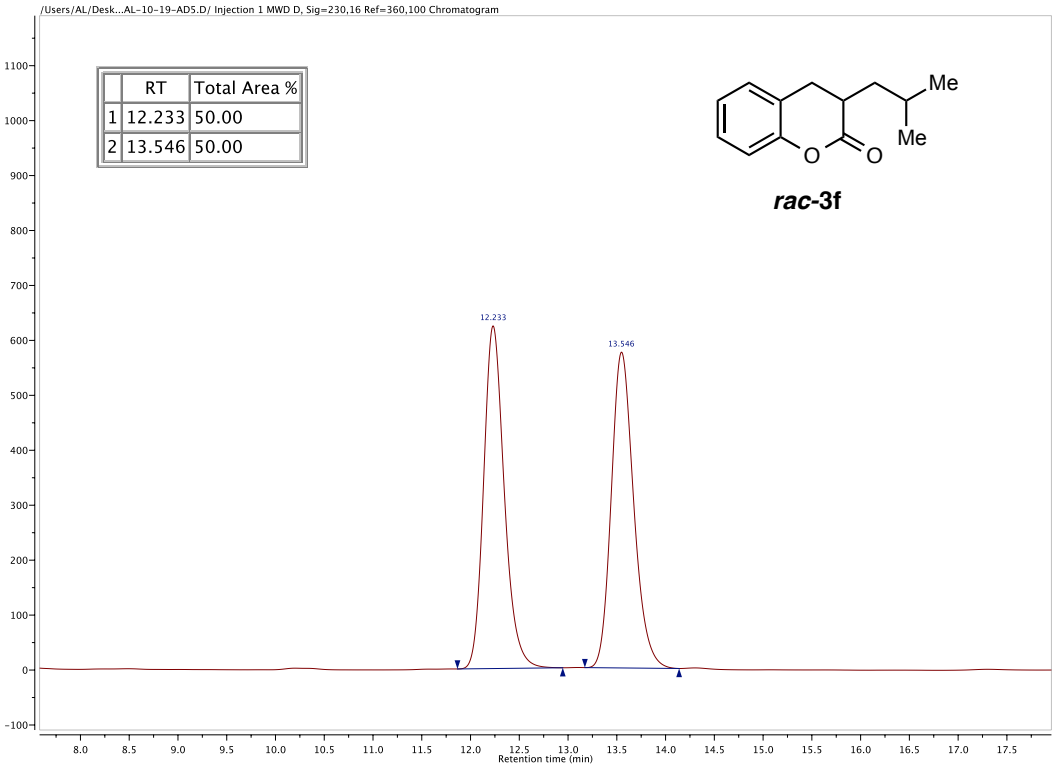

/Users/AL/Desk...L-11-17-AD10.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT Total Area %
1 18.955 85.46
2 22.988 14.54
3c
18.955
22.988
Retention time (min)

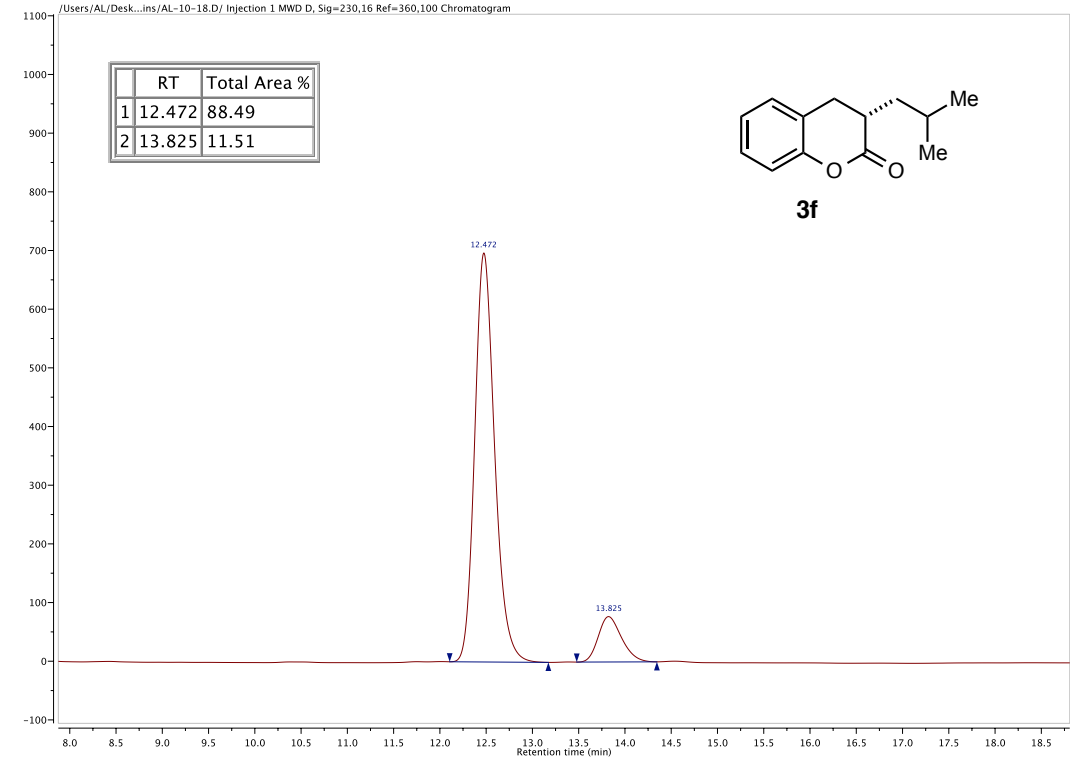

/Users/AL/Desk...-RACEMIC-OD2.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 27.124 48.88
2 28.837 51.12
Me
O
O
rac-3d
27.124
28.837
Retention time (min)

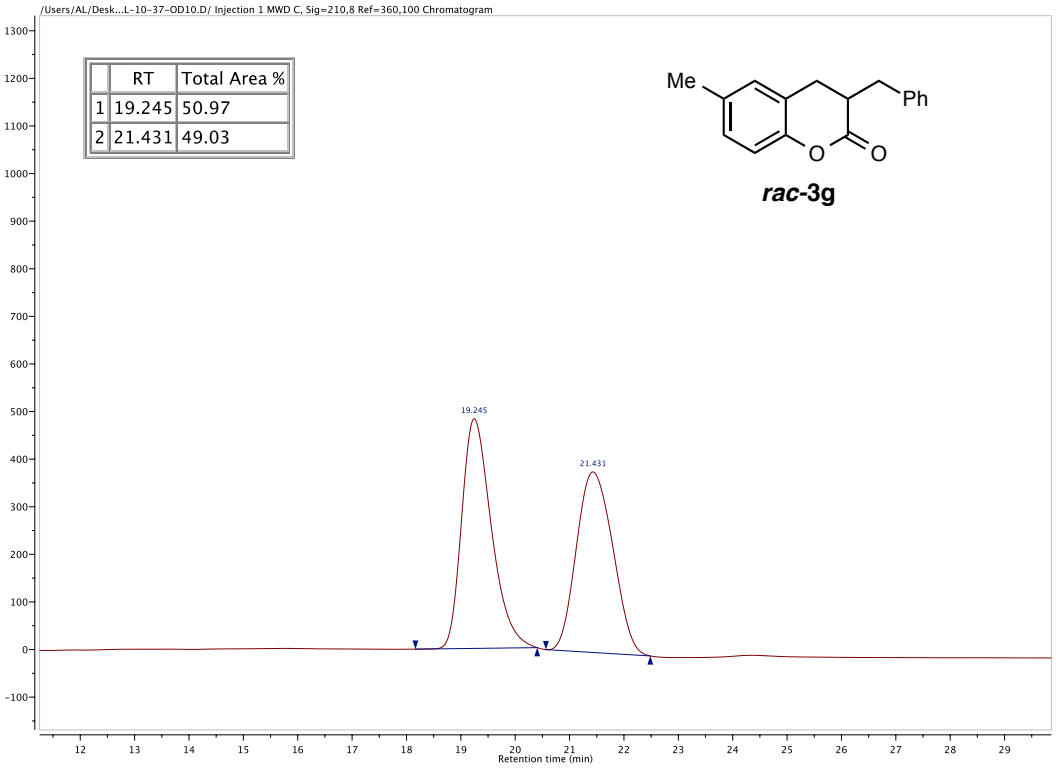

/Users/AL/Desk...-11-03-1-OD2.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 26.854 11.58
2 28.540 88.42
Me
O
O
3d
28.540
26.854
Retention time (min)

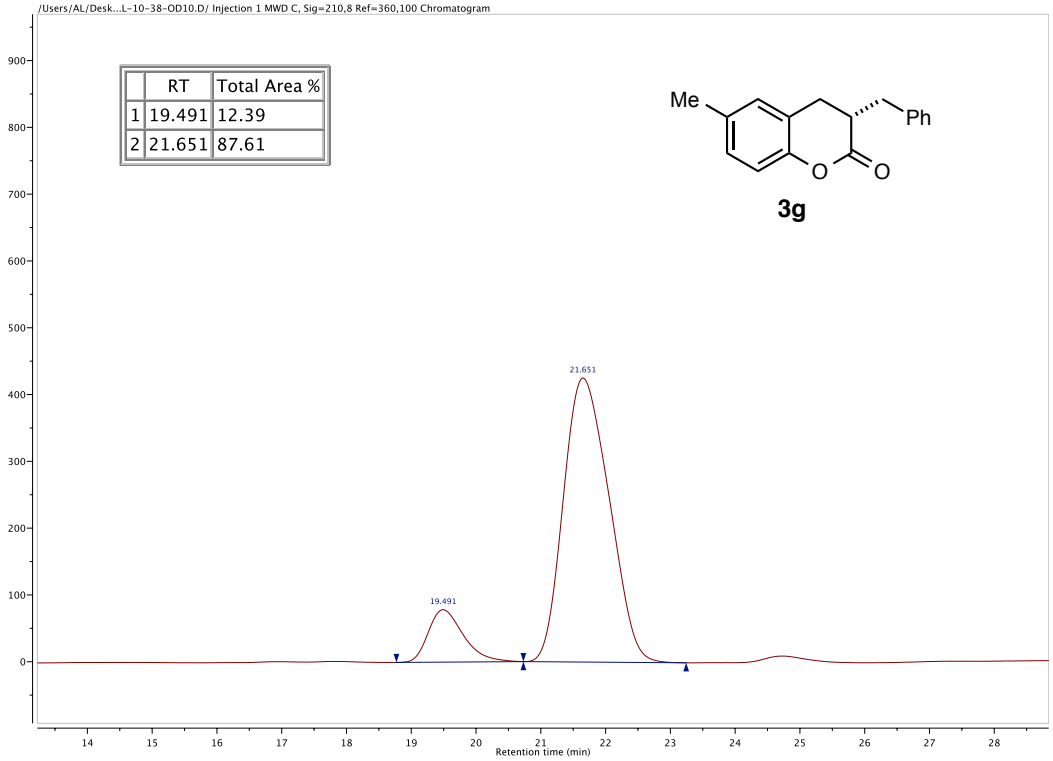

/Users/AL/Desk...AL-09-88-AD5.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT Total Area %
1 13.063 51.90
2 14.043 48.10
Me
Me
O
O
rac-3e
13.063
14.043
Retention time (min)

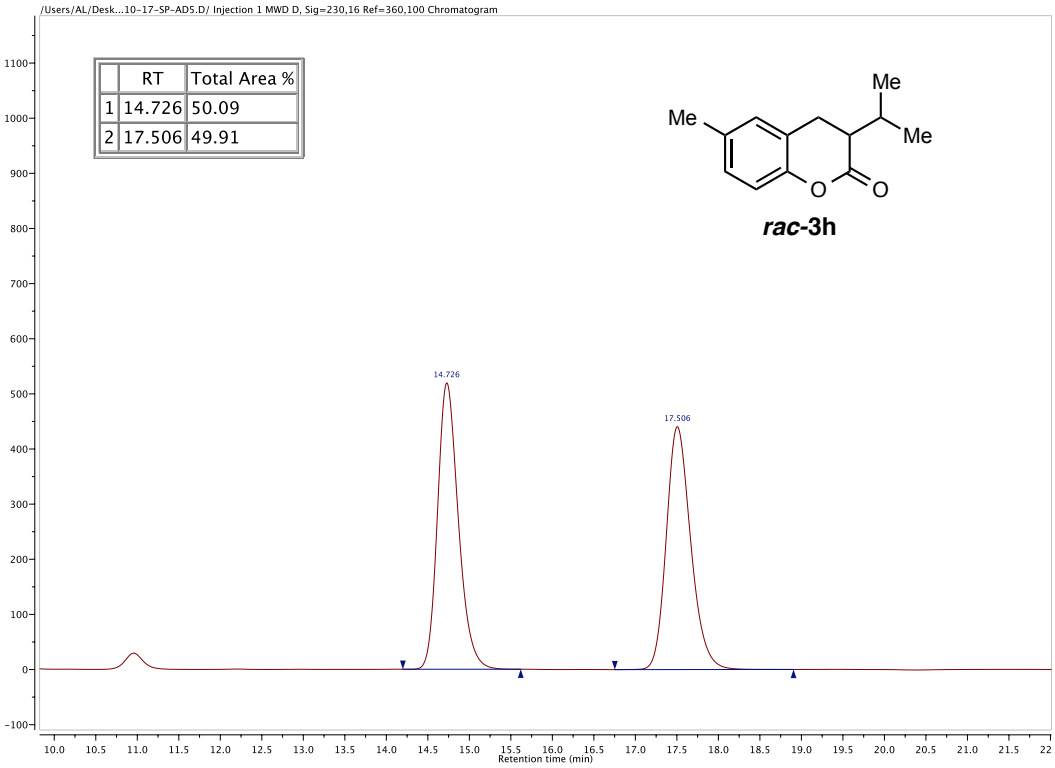

/Users/AL/Desk...AL-09-89-AD5.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT Total Area %
1 13.172 92.08
2 14.145 7.92
Me
Me
O
O
3e
13.172
14.145
Retention time (min)

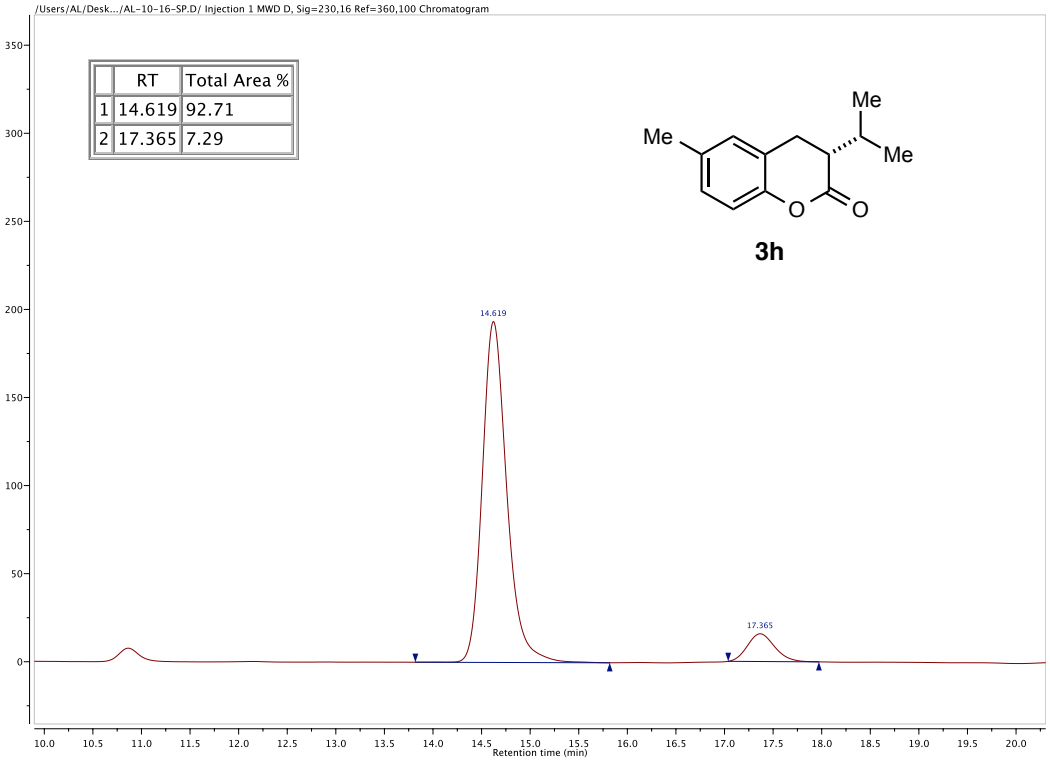

/Users/AL/Desk...AL-10-19-AD5.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT | Total Area %
1 | 12.233 | 50.00
2 | 13.546 | 50.00
Me
Me
O
O
rac-3f
12.233
13.546
Retention time (min)

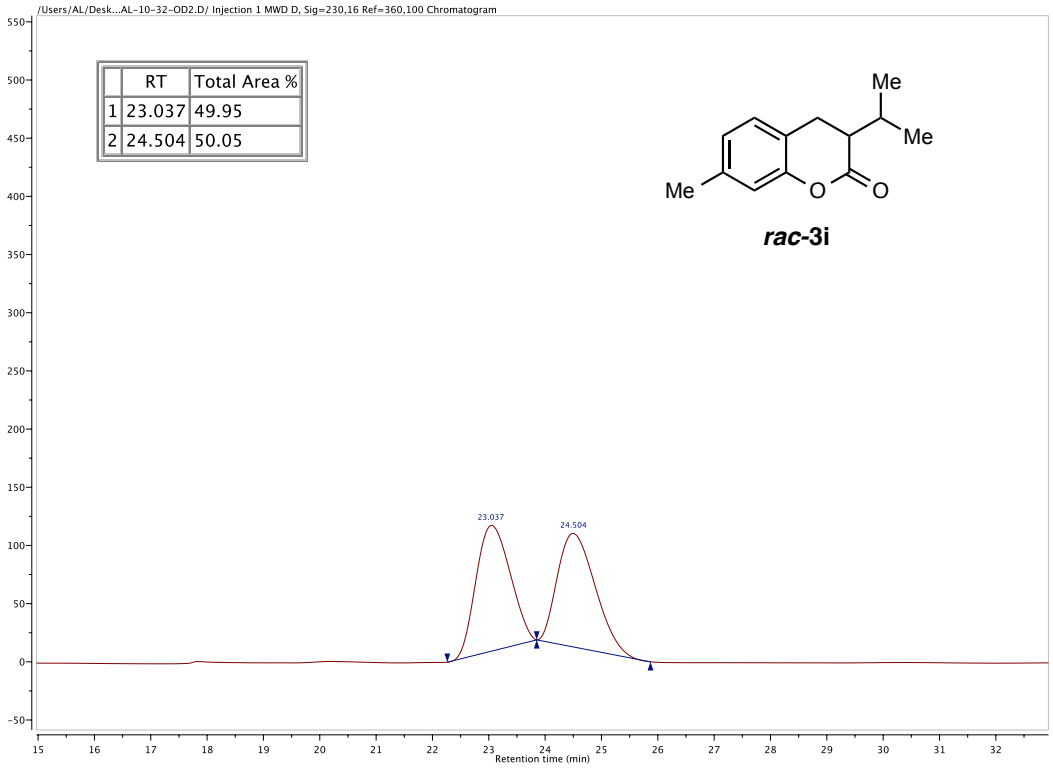

/Users/AL/Desk...ins/AL-10-18.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT | Total Area %
1 | 12.472 | 88.49
2 | 13.825 | 11.51
Me
Me
O
O
3f
12.472
13.825
Retention time (min)


/Users/AL/Desk...L-10-37-OD10.D/ Injection 1 MWD C, Sig=210,8 Ref=360,100 Chromatogram
RT
Total Area %
1 19.245 50.97
2 21.431 49.03
Me
Ph
O
O
rac-3g
19.245
21.431
Retention time (min)

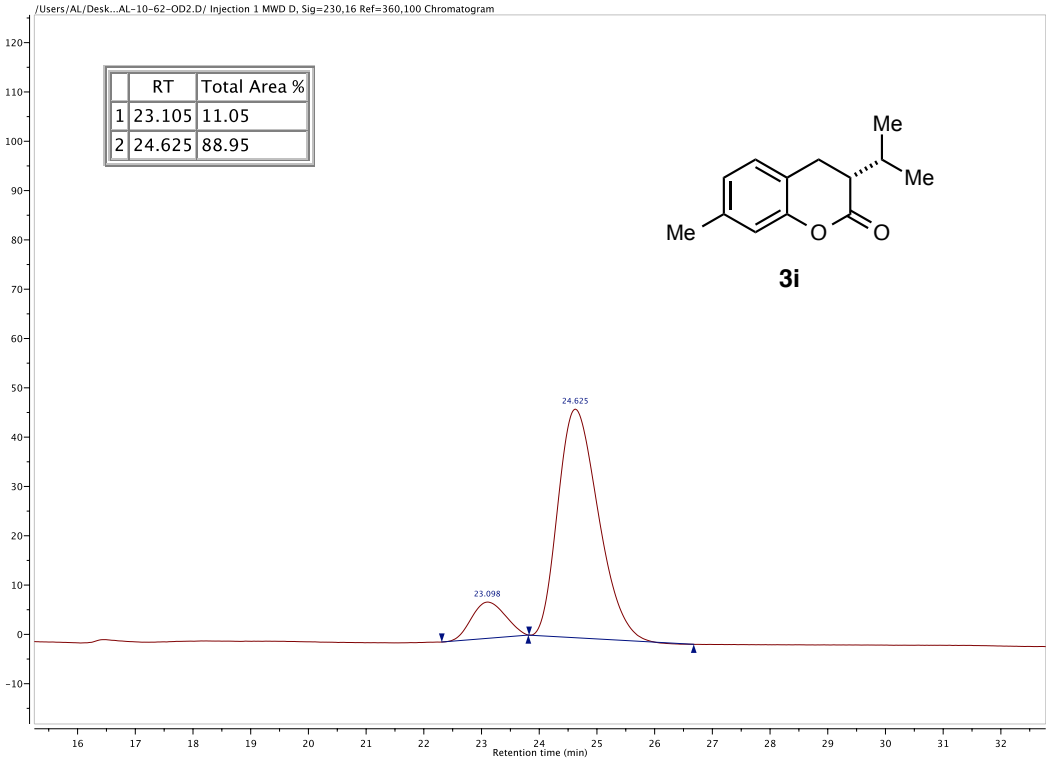

/Users/AL/Desk...L-10-38-OD10.D/ Injection 1 MWD C, Sig=210,8 Ref=360,100 Chromatogram
RT
Total Area %
1 19.491 12.39
2 21.651 87.61
Me
Ph
O
O
3g
19.491
21.651
Retention time (min)


/Users/AL/Desk...10-17-SP-ADS.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 14.726 50.09
2 17.506 49.91
Me
Me
Me
O
O
rac-3h
14.726
17.506
Retention time (min)

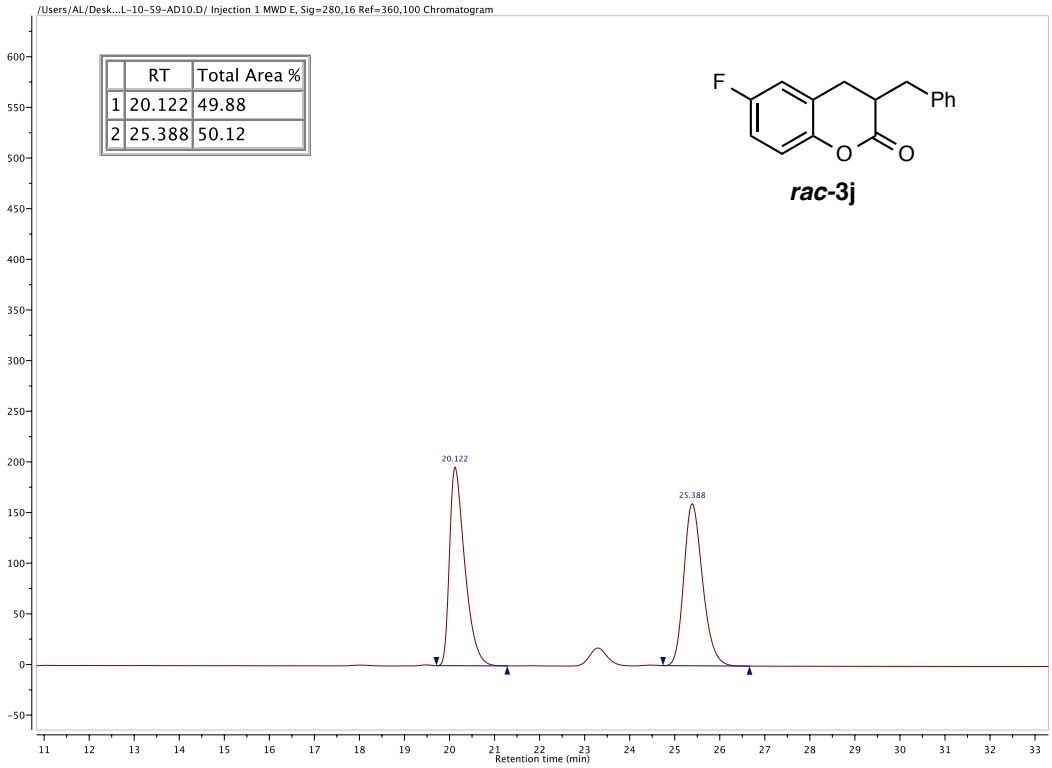

/Users/AL/Desk.../AL-10-16-SP.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1 14.619 92.71
2 17.365 7.29
Me
Me
Me
O
O
3h
14.619
17.365
Retention time (min)

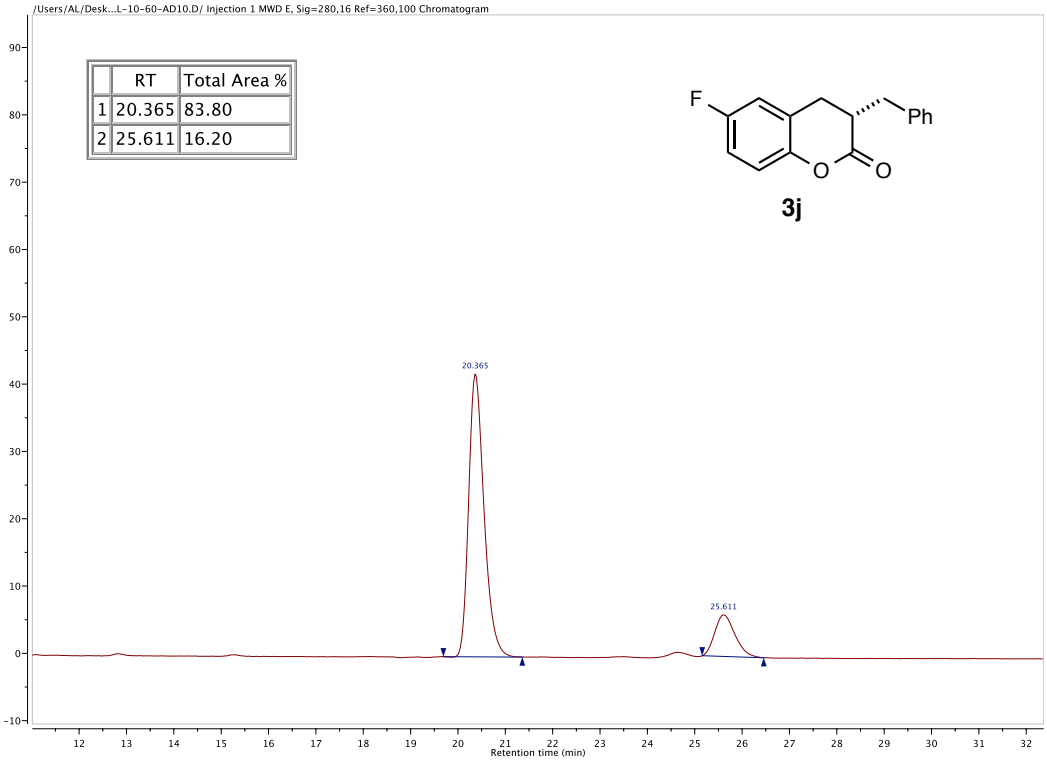

/Users/AL/Desk...AL-10-32-OD2.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT | Total Area %
1 | 23.037 | 49.95
2 | 24.504 | 50.05
Me
Me
Me
O
O
23.037
24.504
Retention time (min)

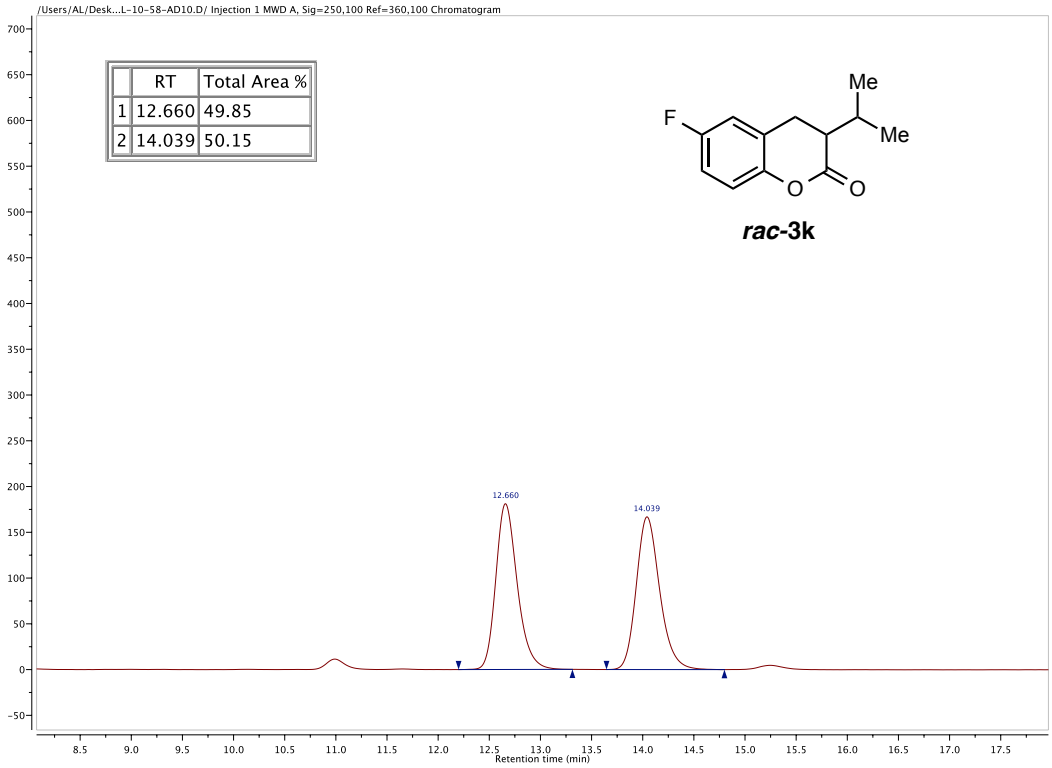
***rac*-3i**

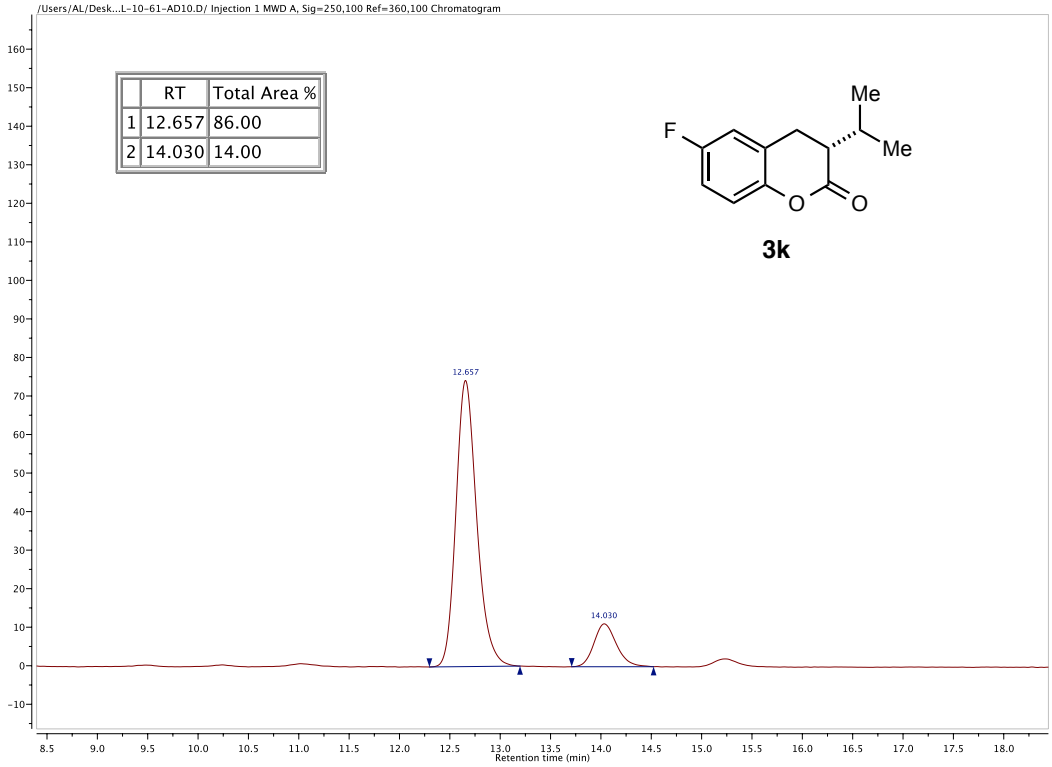

/Users/AL/Desk...AL-10-62-OD2.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT | Total Area %
1 | 23.105 | 11.05
2 | 24.625 | 88.95
Me
Me
Me
O
O
24.625
23.098
Retention time (min)

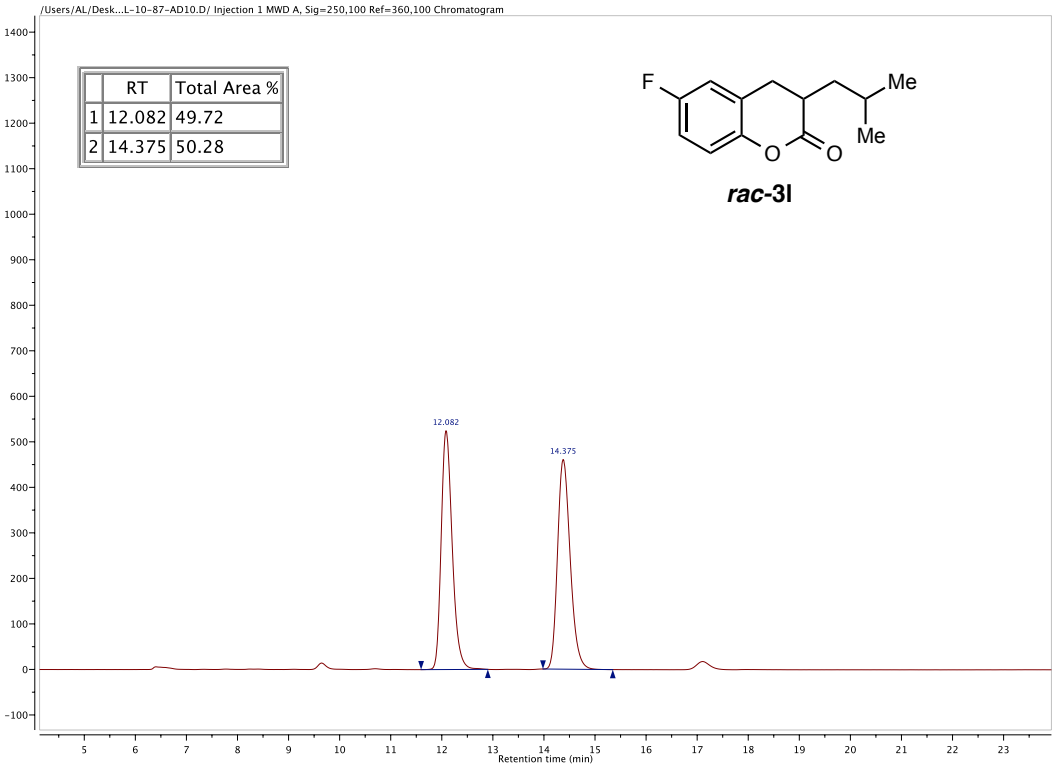
3i

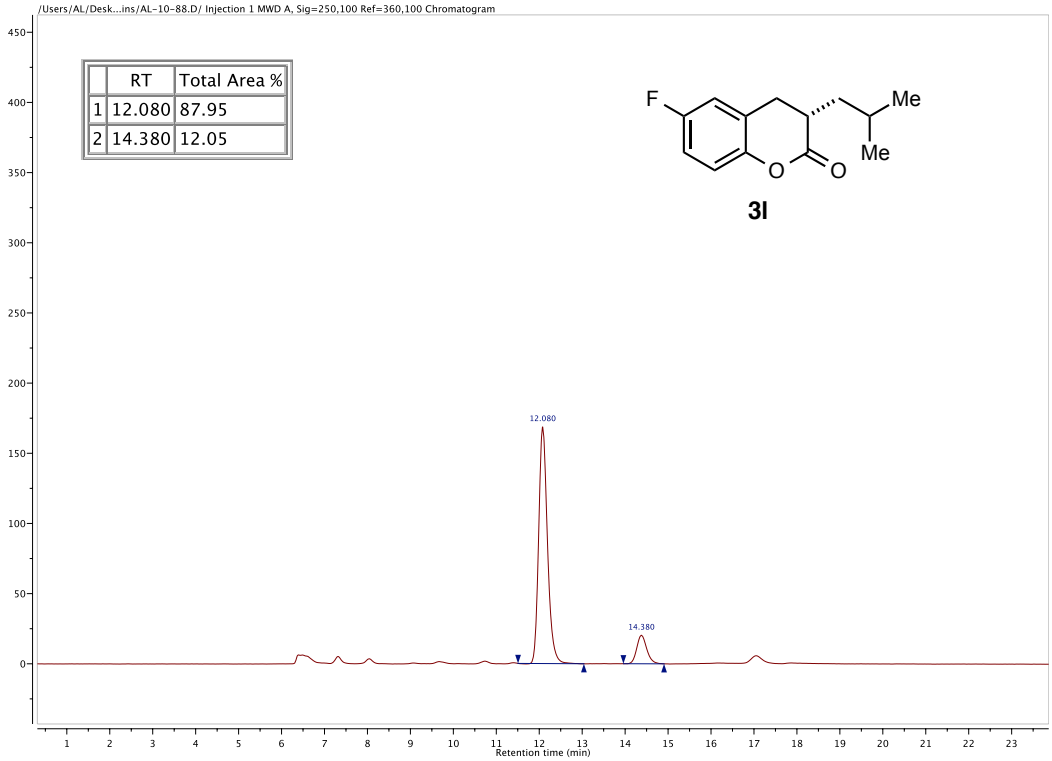

/Users/AL/Desk...L-10-59-AD10.D/ Injection 1 MWD E, Sig=280,16 Ref=360,100 Chromatogram
RT
Total Area %
1 20.122 49.88
2 25.388 50.12
F
Ph
O
O
rac-3j
20.122
25.388
Retention time (min)

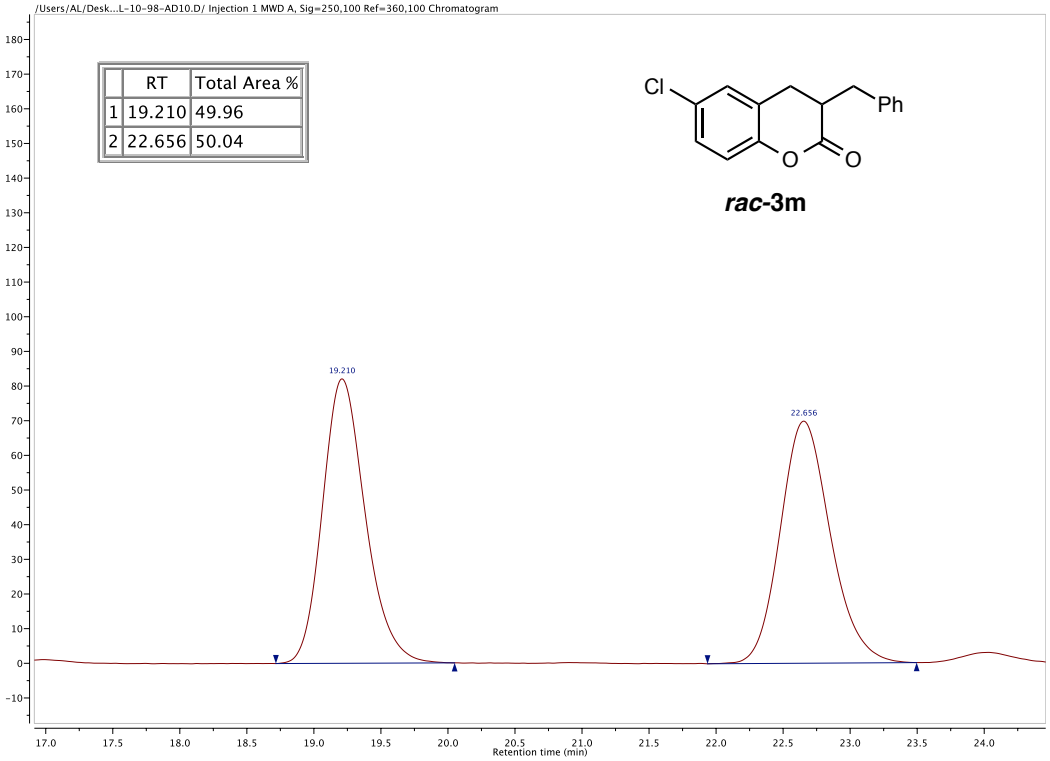

/Users/AL/Desk...L-10-60-AD10.D/ Injection 1 MWD E, Sig=280,16 Ref=360,100 Chromatogram
RT
Total Area %
1 20.365 83.80
2 25.611 16.20
F
Ph
O
O
3j
20.365
25.611
Retention time (min)

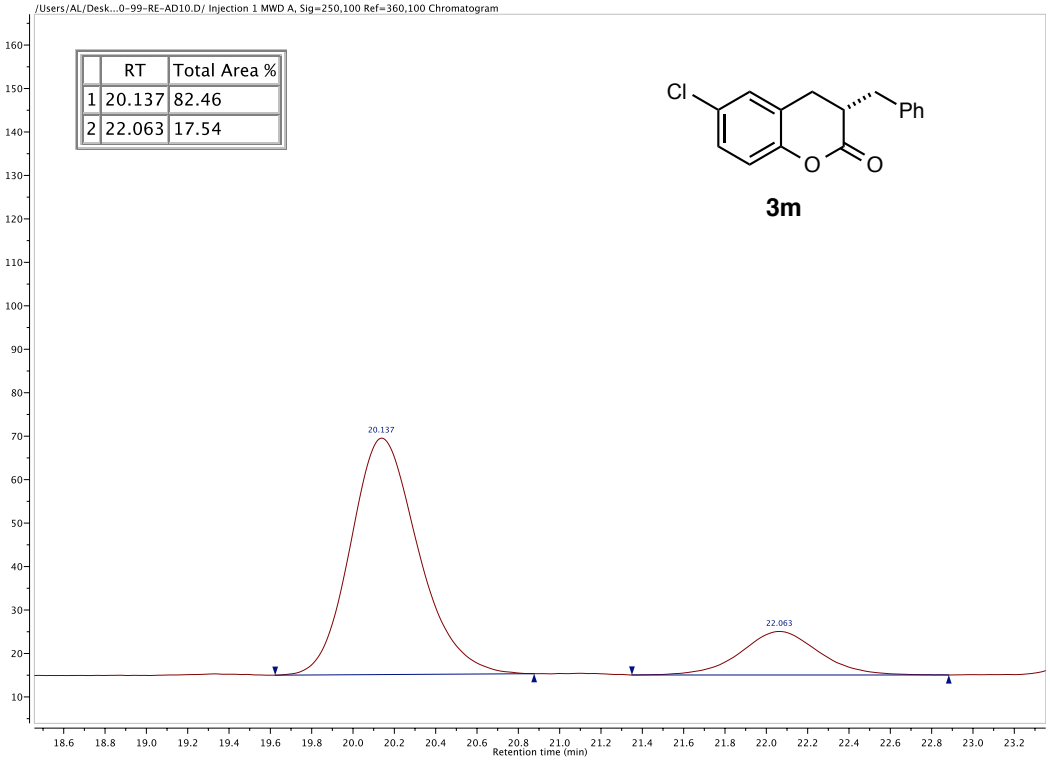

/Users/AL/Desk...L-10-58-AD10.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT
Total Area %
1 12.660 49.85
2 14.039 50.15
Me
F
Me
O
O
rac-3k
12.660
14.039
Retention time (min)

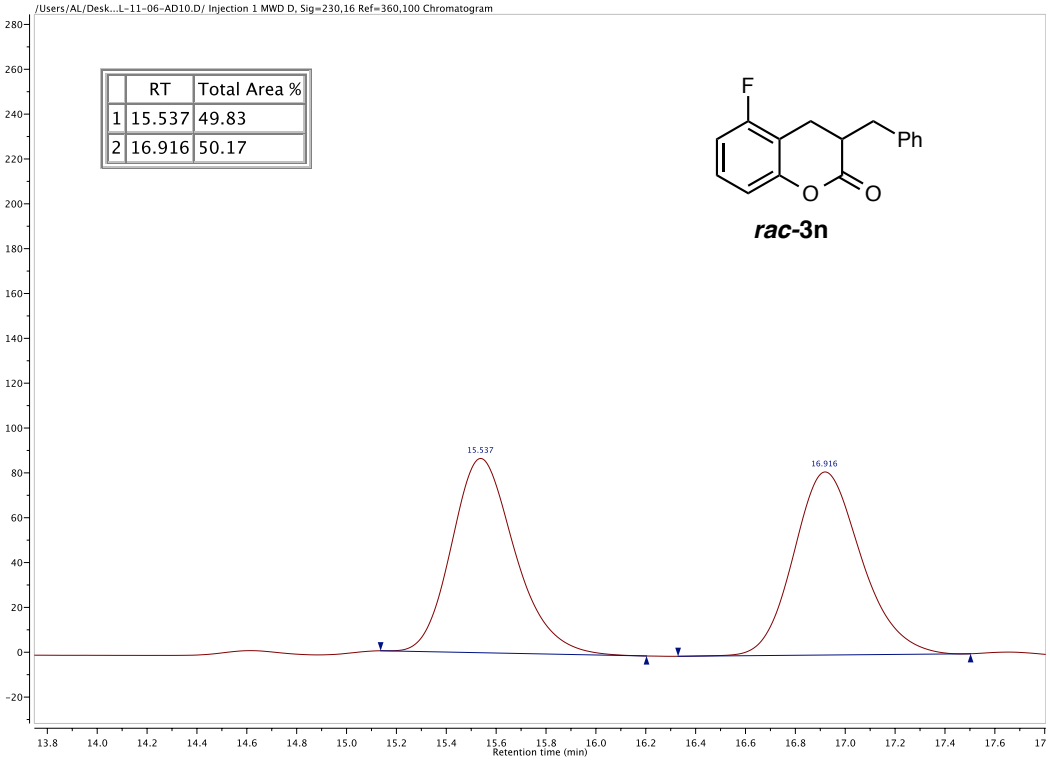

/Users/AL/Desk...L-10-61-AD10.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT
Total Area %
1 12.657 86.00
2 14.030 14.00
Me
F
Me
O
O
3k
12.657
14.030
Retention time (min)

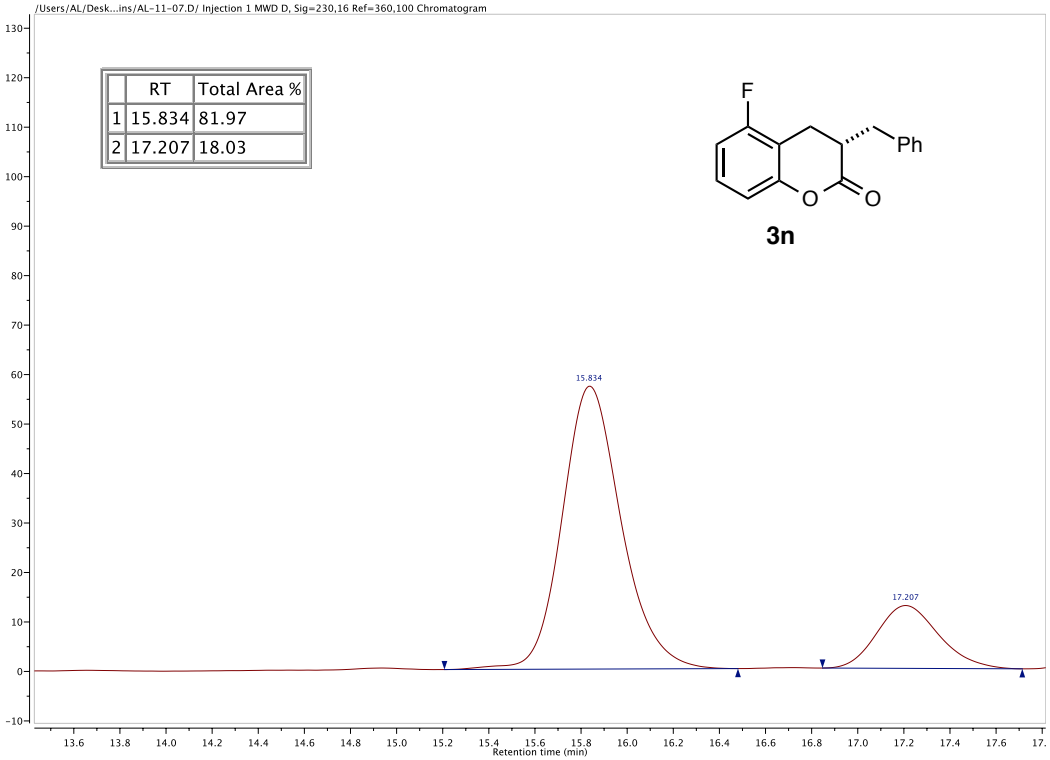

/Users/AL/Desk...L-10-87-AD10.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT
Total Area %
1 12.082 49.72
2 14.375 50.28
F
Me
Me
O
O
rac-3l
12.082
14.375
Retention time (min)

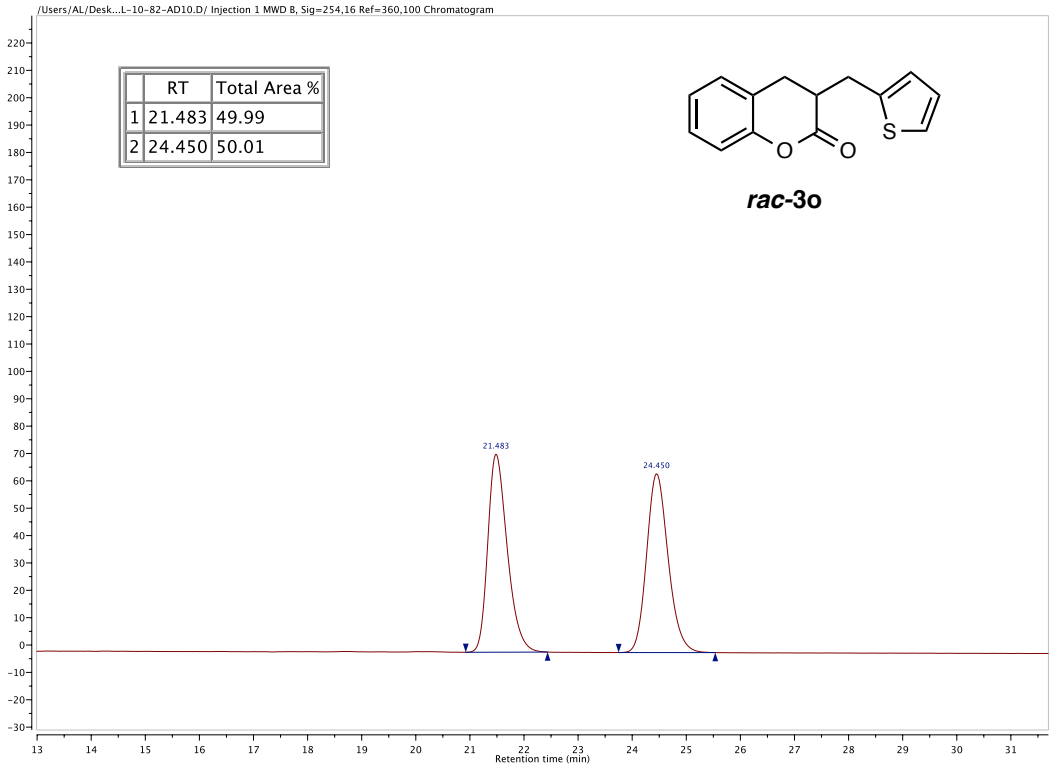

/Users/AL/Desk...ins/AL-10-88.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT
Total Area %
1 12.080 87.95
2 14.380 12.05
F
Me
Me
O
O
3l
12.080
14.380
Retention time (min)

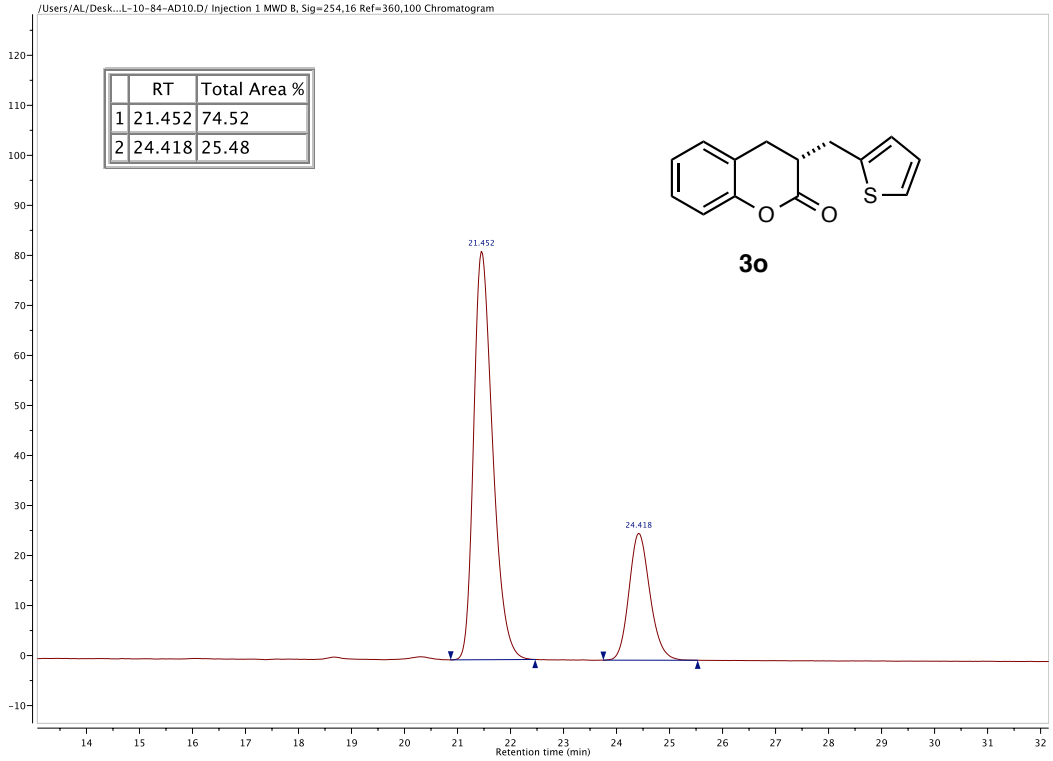

/Users/AL/Desk...L-10-98-AD10.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT | Total Area %
1 | 19.210 | 49.96
2 | 22.656 | 50.04
Cl
Ph
O
O
rac-3m
19.210
22.656
Retention time (min)


/Users/AL/Desk...0-99-RE-AD10.D/ Injection 1 MWD A, Sig=250,100 Ref=360,100 Chromatogram
RT | Total Area %
1 | 20.137 | 82.46
2 | 22.063 | 17.54
Cl
Ph
O
O
3m
20.137
22.063
Retention time (min)


/Users/AL/Desk...L-11-06-AD10.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1
15.537
49.83
2
16.916
50.17
F
Ph
O
O
rac-3n
15.537
16.916
Retention time (min)


/Users/AL/Desk...ins/AL-11-07.D/ Injection 1 MWD D, Sig=230,16 Ref=360,100 Chromatogram
RT
Total Area %
1
15.834
81.97
2
17.207
18.03
F
Ph
O
O
3n
15.834
17.207
Retention time (min)


/Users/AL/Desk...L-10-82-AD10.D/ Injection 1 MWD B, Sig=254,16 Ref=360,100 Chromatogram
RT
Total Area %
1 21.483 49.99
2 24.450 50.01
21.483
24.450
Retention time (min)
rac-3o


/Users/AL/Desk...L-10-84-AD10.D/ Injection 1 MWD B, Sig=254,16 Ref=360,100 Chromatogram
RT
Total Area %
1 21.452 74.52
2 24.418 25.48
21.452
24.418
Retention time (min)
3o