Rh(I)-Catalyzed Intermolecular Hydroacylation: Enantioselective Cross Coupling of Aldehydes and Ketoamides

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Supporting Information

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1. General Considerations

Commercial reagents were purchased from Sigma Aldrich, Strem, Acros Organics, ChemImpex, TCI and/or Alfa Aesar and used without further purification. Reaction progresses were monitored using a combination of LC/MS analysis,[1] GC/MS analysis,[2] and thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 plates. Visualization of the developed plates was performed under UV light (254 nm) and with $KMnO_4$ stain. Purification and isolation of products were performed via silica gel chromatography (both column and preparative thin-layer chromatography). Preparative thin-layer chromatography is preferred for isolating products from asymmetric catalysis because the UV-active band(s) can be completely identified and fully isolated, thus avoiding artificially enhanced ee's that can be due to self-disproportionation of enantiomers.[3] Enantiomeric excesses for stereoselective reactions were determined by chiral SFC analysis using an Agilent Technologies HPLC (1200 series) system and Aurora A5 Fusion. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Varian Mercury 400, VRX-S (Unity) 400, Bruker AV-III 400, Bruker DRX400, Bruker DRX500, Bruker DRX500 with TCI (three channel inverse) cryoprobe or a Bruker AVANCE600 spectrometer. ^{1}H NMR spectra were internally referenced to the residual solvent signal (δ 7.26 for $CDCl_3$) or to TMS when the δ 7.26 resonance cannot be distinguished amongst other signals. ^{13}C NMR spectra were internally referenced to the residual solvent signal (δ 77.16 for $CDCl_3$). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm).

High resolution mass spectra (HRMS) were obtained on a Waters LCT Premier spectrometer (using ESI-TOF). Infrared (IR) spectra were obtained on a Nicolet iS5 FT-IR spectrometer with an iD5 ATR, and are reported in terms of frequency of absorption (cm^{-1}). Melting point ranges were determined on a Fisher-Johns Melting Point Apparatus. Column chromatography was performed with Silicycle Silia-P Flash Silica Gel, using either glass columns or a Teledyne Isco Combiflash Rf 200 automated purification system. Solvents were purchased from Fisher

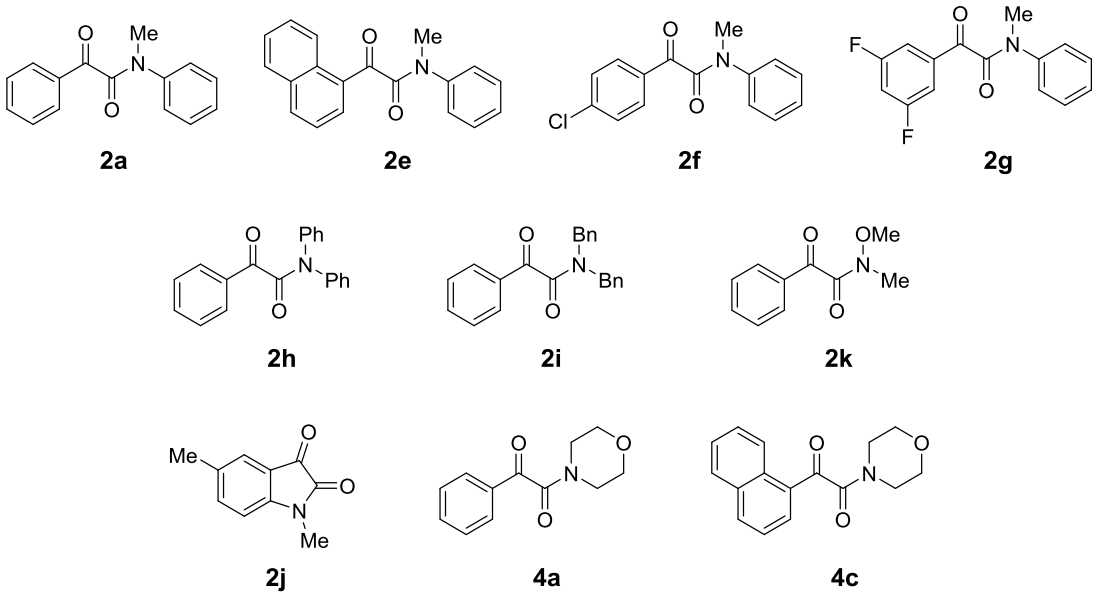
[1] Waters 2795 Separations Module equipped with Symmetry® C18 column (3.5 μm particle size; 4.6 × 75 mm), Waters micromass ZQ mass spectrometer and Waters 2996 Photodiode Array Detector

[2] Agilent Technologies 7890A GC system with Agilent Technologies 5975C inert XL EI/CI Mass Selective Detector

[3] Soloshonok, V. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 766.

Chemical and were purified according to standard procedures.[4] All solvents used for ligand synthesis and catalysis were degassed via a minimum of three cycles of 'freeze-pump-thaw'. DCE-d_4 was obtained from Cambridge Isotopes and degassed via'freeze-pump-thaw' prior to use. DFT calculations were performed using Gaussian09.[5] The DFT optimized intermediates presented in Section 7 were generated using CYLview.[6]

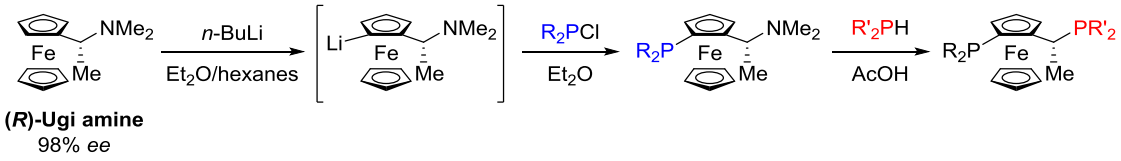
The following α-ketoamides have been previously synthesized and characterized: (**2a**),[7] (**2e**),[3] (**2f**),[3] (**2g**),[3] (**2h**),[3] (**2i**),[8] (**2j**),[9] (**4a**)[10] and (**4c**)[11]



[4] Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Butterworth-Heinemann: New York, 2003.
[5] Frisch, J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J. Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*; Gaussian Inc.: Wallingford, CT., 2010.
[6] CYLview, 1.0b, Legault, C. Y., Universit éde Sherbrooke, 2009 (http://www.cylview.org)
[7] Chiba, S.; Zhang, L.; Lee, J.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 7266.
[8] Wei, W.; Shao, Y.; Hu, H.; Zhang, F.; Zhang, C.; Xu, Y.; Wan, X. *J. Org. Chem.* **2012**, *77*, 7157.
[9] Tang, B.-X.; Song, R.-J.; Wu, C.-Y.; Liu, Y.; Zhou, M.-B.; Wei, W.-T.; Deng, G.-B.; Yin, D.-L.; Li, J.-H. *J. Am. Chem. Soc.* **2010**, *132*, 8900.
[10] Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 3280.
[11] Wei, W.; Shao, Y.; Hu, H.; Zhang, F.; Zhang, C.; Xu, Y.; Wan, X. *J. Org. Chem.* **2012**, *77*, 7157.

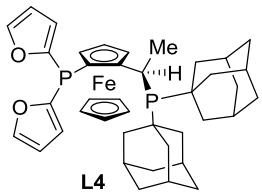
2. Synthesis of Josiphos Ligands L4 and L5

Enantioenriched (*R*)-Ugi amine was synthesized according to literature procedures.[12,13,14]



(*R*)-Ugi amine
98% *ee*

(*R*)-1-[(*S*$_P$)-2-(difuryl)ferrocenyl]ethylbis(1-adamantyl)phosphine (L4)



L4

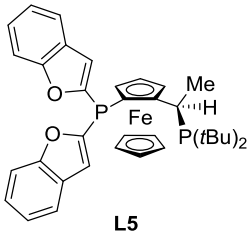
A flame-dried round bottom flask (equipped with a condenser) was charged with a suspension of (*R*)-Ugi amine (1.03 g, 4.00 mmol) in Et_2O (anhydrous, degassed, 6 mL) at rt and under a gentle flow of argon. To the resulting suspension was added a solution of *n*-BuLi (2.5 M in hexanes, 2.6 mL, 6.5 mmol), at which point the solution became homogeneous. The resulting red solution was stirred at rt for 1.5 h. Di-(2-furyl)-chlorophosphine was separately dissolved in Et_2O (anhydrous, degassed, 1 mL) and added to the reaction mixture dropwise. An orange precipitate formed and the reaction was heated to 40 ˚C for 18 h. The reaction mixture was cooled to rt and quenched with a solution of saturated $NaHCO_{3(aq)}$ (20 mL). The resulting mixture was extracted with benzene (3 × 15 mL). The combined organic fraction was washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to give a viscous reddish-brown oil. Purification by silica gel chromatography (eluting with 0–10% MeOH in DCM with 2% NH_4OH additive) gave the ferrocenyl monophosphine as a dark red oil (723 mg, 43%). This material was ~95% pure as judged by ^1H and ^{31}P NMR and was used in the subsequent substitution reaction without further purification.

A flame-dried round bottom flask was charged with ferrecenyl monophosphine (715 mg, 1.70 mmol), di-(1-adamanyl)phosphine (500 mg, 1.65 mmol) and glacial acetic acid (distilled, degassed, 17 mL). The resulting mixture was rapidly stirred at rt until all of the reagents dissolved. The homogeneous solution was heated at 105 ˚C for 16 h. The reaction mixture was cooled to rt and the majority of acetic acid was removed under reduced pressure. Purification of the resulting residue by silica gel chromatography (2 columns: first eluting with 20–50% EtOAc in hexanes, then 0–20% EtOAc in hexanes) gave the title product as an orange solid (606 mg, 54%

[12] Gokel, G. W.; Ugi, I. K. *J. Chem. Ed.* **1972**, *49*, 249.
[13] Wright, J.; Frambes, L.; Reeves, P. *J. Organomet. Chem.* **1994**, *476*, 215.
[14] Wu, Y.; Lu, C.; Shan, W.; Li, X. *Tetrahedron: Asymmetry* **2009**, *20*, 584.

yield). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.50 (s, 1H), 6.77 (s, 1H), 6.54 (s, 1H), 6.43 (s, 1H), 6.30 (s, 1H), 4.55 (s, 1H), 4.31 (s, 1H), 4.22 (s, 1H), 3.92 (s, 5H), 3.46 (q, *J* = 7.0 Hz, 1H), 2.02–2.12 (m, 6H), 1.99 (s, 3H), 1.83–1.90 (m, 3H), 1.68–1.83 (m, 9H), 1.64 (s, 6H), 1.56 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6 (d, *J* = 10.0 Hz), 154.5 (d, *J* = 10.0 Hz), 154.3_1–154.3_5 (m), 120.2 (d, *J* = 23.3 Hz), 119.1 (d, *J* = 4.5 Hz), 119.0 (d, *J* = 4.6 Hz), 110.7 (d, *J* = 6.1 Hz), 110.3 (d, *J* = 5.0 Hz), 102.0 (d, *J* = 22.8 Hz), 101.8 (d, *J* = 22.7 Hz), 73.5 (d, *J* = 5.7 Hz), 71.7_3 (d, *J* = 2.9 Hz), 71.7_0 (d, *J* = 3.0 Hz), 69.8_1 (d, *J* = 2.1 Hz), 69.7_6 (d, *J* = 2.2 Hz), 69.6, 68.2, 60.5, 42.5 (d, *J* = 2.1 Hz), 42.4 (d, *J* = 2.1 Hz), 42.0 (d, *J* = 11.6 Hz), 39.7 (d, *J* = 2.9 Hz), 39.4 (d, *J* = 2.9 Hz), 38.9 (d, *J* = 32.4 Hz), 37.2 (d, *J* = 17.9 Hz), 29.1_4 (d, *J* = 7.6 Hz), 29.0_8, 28.9 (d, *J* = 7.7 Hz), 28.8 (d, *J* = 2.4 Hz), 18.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 53.3 (d, *J* = 81.3 Hz), 71.8 (d, *J* = 80.7 Hz). HRMS (ESI-TOF) *m/z* calc'd for $C_{40}H_{48}FeO_2P_2Na$ $[M+Na]^+$: 701.2377, found: 701.2362. $[\alpha]^{26}_D$ −144 (*c* = 1.1, $CHCl_3$).

(*R*)-1-[(S_P)-2-(dibenzofuryl)ferrocenyl]ethylbis(*tert*-butyl)phosphine (L5)



L5

Di-(2-benzofuryl)-chlorophosphine was prepared by treatment of lithiated benzofuran [15] with Et_2NPCl_2. Benzofuran (2.0 mL, 18.6 mmol) was dissolved in Et_2O (anhydrous, degassed, 12 mL) and cooled to −78 ˚C under an argon atmosphere. A solution of *n*-BuLi (1.5 M in hexanes, 12.5 mL) was added dropwise to the cooled reaction mixture. The reaction mixture was stirred at −78 ˚C for 60 min, and then gradually allowed to warm and stir at rt for 60 min. Et_2NPCl_2 (1.35 mL, 9.28 mmol) was dissolved in Et_2O (25 mL) in a separate round-bottom flask under an argon atmosphere, and the resulting solution was cooled to −78 ˚C. The solution of lithiated benzofuran was transferred slowly via syringe pump (allowing the solution to run down the side of the flask) to the flask containing the Et_2NPCl_2 solution (−78 ˚C). The reaction mixture was stirred for 10 h, with gradual warming within the dry ice/acetone bath, then quenched with dH_2O (20 mL). The ethereal layer was separated and washed with brine (20 mL), dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give an orange liquid (3.08 g). The resulting 1,1-di(benzofuran-2-yl)-*N*,*N*-diethylphosphanamine was used without purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H),

[15] Yokoyama, M.; Akiba, T.; Ochiai, Y.; Momotake, A.; Togo, H. *J. Org. Chem.* **1996**, *61*, 6079.

7.32 (t, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.02 (s, 1H), 3.28 (dq, *J* = 11.1, 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 4H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.6 (p, *J* = 10.7 Hz).

1,1-di(benzofuran-2-yl)-*N*,*N*-diethylphosphanamine (3.08 g) was dissolved in Et_2O (5 mL) in a nitrogen-filled glovebox. A solution of anhydrous HCl (2 M, 20 mL, 40 mmol) was added and a white precipitate immediately formed. The suspension was left to stand at ambient temperature for 20 min, then filtered and rinsed with Et_2O. The orange filtrate was concentrated *in vacuo* to give di(benzofuran-2-yl)chlorophosphane as an orange solid (2.1 g, 70%), which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.63 (m, 4H), 7.27−7.37 (m, 3H), 7.15−7.25 (m, 3H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.9 (s).

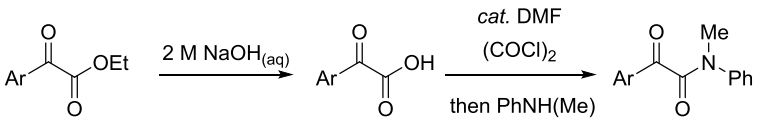
A flame-dried round bottom flask (equipped with a condenser) was charged with (*R*)-Ugi amine (864 mg, 3.36 mmol) and Et_2O (anhydrous, degassed, 10 mL) at rt, under a gentle flow of nitrogen. To the resulting suspension was added a solution of *n*-BuLi (1.5 M in hexanes, 2.3 mL, 4.3 mmol). The suspension gradually became homogeneous over the course of the addition. The resulting red solution was stirred at rt for 1.5 h, and then a solution of di-(2-benzofuryl)-chlorophosphine (10 mL 1:1 Et_2O/THF) was added. The resulting suspension was heated at 45 ˚C under argon for 20 h. The reaction mixture was cooled to rt and quenched with a solution of saturated $NaHCO_{3(aq)}$ (60 mL). The ethereal layer was separated and the aqueous layer was extracted with DCM (2 × 15 mL). The organic extracts were combined, washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to give a brown solid. Purification by silica gel chromatography (eluting with 5–65% acetone in DCM) gave the ferrocenyl monophosphine as an orange solid (634 mg). This material was used in the subsequent substitution reaction without further purification.

The ferrecenyl monophosphine (634 mg, 1.21 mmol) was reconstituted in glacial acetic acid (distilled, degassed, 10 mL) in a round bottom flask under nirogen, and to this was added a solution of di-(*tert*-butyl)phosphine (0.5 M in hexanes, 2.5 mL, 1.25 mmol). The resulting mixture was heated at 105 ˚C for 10 h. The reaction mixture was cooled to rt and the majority of acetic acid was removed under reduced pressure and by azeotropic distillation with toluene. Purification of the resulting residue by silica gel chromatography (eluting with 4% acetone in DCM for 2.5 column volumes, 8% acetone in DCM for 2 column volumes, then 20% EtOAc in hexanes for 5 column volumes) gave the title product as an orange solid (637 mg, 30% yield over 2 steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53–7.58 (m, 2H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J*

= 8.2, 0.7 Hz, 1H), 7.30 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.18–7.24 (m, 2H), 7.13–7.16 (m, 1H), 7.11 (dd, *J* = 2.2, 0.9 Hz, 1H), 6.83 (s, 1H), 4.65–4.67 (m, 1H), 4.36–4.39 (m, 1H), 4.29 (t, *J* = 2.5 Hz, 1H), 3.96 (s, 5H), 3.55 (q, *J* = 7.2 Hz, 1H), 1.82 (dd, *J* = 7.3, 3.3 Hz, 3H), 1.29 (d, *J* = 10.4 Hz, 9H), 0.84 (d, *J* = 10.5 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (s), 157.7 (d, *J* = 2.5 Hz), 157.3$_3$ (d, *J* = 4.1 Hz), 157.2 (d, *J* = 5.3 Hz), 157.1, 128.7 (d, *J* = 3.6 Hz), 128.2 (d, *J* = 6.3 Hz), 124.5 (d, *J* = 129 Hz), 122.6 (d, *J* = 58 Hz), 121.1 (d, *J* = 75 Hz), 117.1 (d, *J* = 21.4 Hz), 115.2 (d, *J* = 4.8 Hz), 115.1 (d, *J* = 4.7 Hz), 111.4 (d, *J* = 18.1 Hz), 102.1 (d, *J* = 23.3 Hz), 101.9 (d, *J* = 23.3 Hz), 69.9$_9$ (d, *J* = 1.9 Hz), 69.9$_5$ (d, *J* = 1.8 Hz), 69.8$_9$, 69.8$_5$, 69.8$_1$, 68.6, 34.8, 34.7, 34.2 (d, *J* = 3.3 Hz), 34.0, 33.9 (d, *J* = 3.1 Hz), 33.8, 31.7, 31.6 (d, *J* = 2.6 Hz), 31.5$_6$, 31.5$_2$, 31.4$_5$, 13.7 Hz), 30.7 (d, *J* = 2.3 Hz), 30.5 (d, *J* = 2.4 Hz), 28.2, 25.4, 22.8, 20.9, 16.5, 14.3, 11.6. ^{31}P NMR (162 MHz, $CDCl_3$) δ 55.0 (d, *J* = 84 Hz), −64.1 (d, *J* = 83.6 Hz). HRMS (ESI-TOF) *m/z* calc'd for $C_{36}H_{40}FeO_2P_2Na$ $[M+Na]^+$: 645.1751, found: 645.1753. $[\alpha]^{26}_D$ −418 (*c* = 1.0, $CHCl_3$).

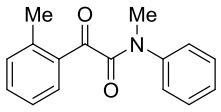
The enantiomer of this ligand, (*S*)-1-[(R_P)-2-(dibenzofuryl)ferrocenyl]ethylbis(*tert*-butyl)phosphine **L5**, was prepared from (*S*)-Ugi amine (99% ee) via an analogous route. ^{1}H, ^{13}C and ^{31}P NMR data are identical to those reported above for (S_P,*R*)-**L5**. $[\alpha]^{26}_D$ +438 (*c* = 0.99, $CHCl_3$).

3. Preparation of α-Ketoamides



2

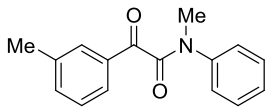
***N*-Methyl-2-oxo-*N*-phenyl-2-(*o*-tolyl)acetamide (2b)**



Ethyl 2-oxo-3-(o-tolyl)acetate (1.06 g, 5.51 mmol) was dissolved in 2 M $NaOH_{(aq)}$ (12 mL). The resulting suspension was maintained at rt with stirring for 48 h. The reaction mixture was quenched with 4 M $HCl_{(aq)}$ (~20 mL) and extracted with DCM (3 x 15 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give the oxo-acetic acid as a yellow liquid. This product appeared pure by ^{1}H NMR analysis and was used without purification. The oxo-acetic acid was dissolved in DCM (11 mL) under a N_2 atmosphere at rt. Oxalyl chloride (0.50 mL, 5.8 mmol) was added in one portion. To the resulting mixture was

added anhydrous DMF (4 drops), at which point gentle bubbling was observed. The mixture was allowed to stir at rt under gas evolution ceased (3 h). The reaction mixture was then cooled to 0 ˚C in an ice/water bath and successively added Et_3N (0.77 mL, 5.5 mmol) and *N*-methylaniline (0.90 mL, 8.3 mmol). The resulting mixture was stirred at 0 ˚C for an additional 20 min, then warmed to rt. The mixture was maintained at rt for 11 h, and then quenched with dH_2O (20 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 x 20 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the resulting residue by silica gel chromatography eluting with 4:1 hexanes/EtOAc gave the title product as a pale yellow solid (10:1 mixture of rotamers, 1.25 g, 90%, 3 steps). ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.38 (td, *J* = 7.5, 1.1 Hz, 1H), 7.17–7.30 (m, 4H), 7.07–7.17 (m, 3H), 3.45 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, rotameric mixture) δ 193.4, 193.3, 167.7, 167.5, 141.9, 141.31, 141.26, 140.9, 134.0, 133.2, 132.8, 132.4, 132.3, 131.9, 131.4, 129.6, 129.4, 128.2, 127.4, 127.2, 126.4, 125.9, 125.4, 38.3, 36.3, 22.0, 21.3. IR (ATR): 2926, 1666, 1641, 1595, 1496, 1118, 960, 859, 778, 734, 701, 665 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{16}H_{15}NO_2Na$ $[M+Na]^+$: 276.1000, found: 276.1006.

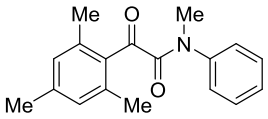
_N_-methyl-2-oxo-_N_-phenyl-2-(_m_-tolyl)acetamide (2c)



Ethyl 2-oxo-2-(*o*-tolyl)acetate (1.22 g, 6.35 mmol) was dissolved in 2 M $NaOH_{(aq)}$ (12 mL). The resulting suspension was maintained at rt with stirring for 48 h. The reaction mixture was quenched with 4 M $HCl_{(aq)}$ (~20 mL) and the resulting aqueous mixture was extracted with DCM (3 x 15 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give the oxo-acetic acid as a yellow liquid. This product appeared pure by ^{1}H NMR analysis and was used without purification. The oxo-acetic acid was dissolved in DCM (13 mL) under a N_2 atmosphere at rt. Oxalyl chloride (0.58 mL, 6.7 mmol) was added in one portion. To the resulting mixture was added anhydrous DMF (4 drops), at which point gentle bubbling was observed. The mixture was stirred at rt until gas evolution ceased (3 h). The reaction mixture was then cooled to 0 ˚C in an ice/water bath and successively added Et_3N (0.89 mL, 6.35 mmol) and *N*-methylaniline (1.03 mL, 9.53 mmol). The resulting mixture was stirred at 0 ˚C for an additional 20 min, then warmed to rt. The mixture was maintained at rt for 11 h, and

then quenched with dH_2O (20 mL). The organic layer was separated and the organic layer was extracted with DCM (2 x 20 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the resulting residue by silica gel chromatography eluting with 4:1 hexanes:EtOAc gave the title product as a pale yellow solid (9:1 mixture of rotamers, 1.11 g, 69%, 3 steps). ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer) δ 7.59–7.79 (m, 2H), 7.36–7.41 (m, 1H), 7.30–7.36 (m, 1H), 7.18–7.28 (m, 3H), 7.11–7.17 (m, 2H), 3.49 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, major rotamer) δ 191.6, 167.3, 141.4, 138.8, 135.3, 133.7, 129.9, 129.5, 128.8, 128.2, 127.0, 126.8, 36.4, 21.4. ^{13}C NMR (125 MHz, $CDCl_3$, minor rotamer) δ 191.1, 166.9, 141.2, 139.3, 135.9, 133.1, 130.2, 129.7, 129.2, 127.5, 127.2, 125.5, 38.3, 21.5. IR (ATR): 2921, 1669, 1641, 1583, 1493, 1392, 1259, 1192, 1125, 974, 760, 730, 777, 700, 661 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{16}H_{15}NO_2Na$ $[M+Na]^+$: 276.1000, found: 276.1001.

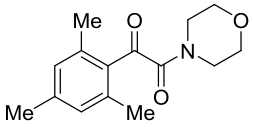
2-Mesityl-*N*-methyl-2-oxo-*N*-phenylacetamide (2d)



Mesityl glyoxylic acid (1.0 g, 5.2 mmol) was dissolved in DCM (5.2 mL) under a N_2 atmosphere at rt. Oxalyl chloride (0.47 mL, 5.5 mmol) was added in one portion. To the resulting mixture was added anhydrous DMF (2 drops), at which point gentle bubbling was observed. The mixture was allowed to stir at rt until gas evolution ceased (12 h). The reaction mixture was then cooled to 0 ˚C in an ice/water bath and successively added Et_3N (0.73 mL, 5.2 mmol) and *N*-methylaniline (0.85 mL, 7.8 mmol). The resulting mixture was stirred at 0 ˚C for an additional 20 min, then warmed to rt. The mixture was maintained at rt for 16 h, then quenched with dH_2O (20 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 x 20 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the resulting residue by silica gel chromatography eluting with 4:1 hexanes:EtOAc gave the title product as a pale yellow solid (4:1 mixture of rotamers, 993 mg, 68%, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer) δ 7.16–7.25 (m, 3H), 7.05 (d, J = 7.0 Hz, 2H), 6.69 (s, 2H), 3.37 (s, 3H), 2.21 (s, 3H), 2.18 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$, major) δ 184.4, 157.0, 131.6, 131.4, 127.8, 123.1, 119.7, 119.5, 118.2, 117.1, 27.9, 11.3, 10.8. ^{1}H NMR (500 MHz, $CDCl_3$, minor) δ 7.43 (t, J = 7.5 Hz, 2H), 7.37 (d, J = 7.7 Hz, 2H), 7.30 (t, J = 7.1 Hz, 1H), 6.90 (s, 2H), 3.52 (s, 3H), 2.43 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$,

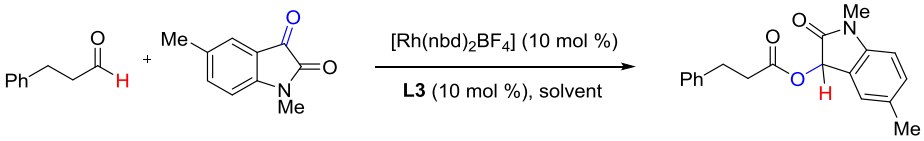
minor) δ 184.5, 156.7, 132.1, 131.8, 127.9, 123.1, 120.0, 119.4, 117.3, 115.5, 28.7, 11.4, 10.6. IR(ATR): 3065, 2920, 1672, 1659, 1648, 1606, 1594, 1495, 1375, 1220, 856, 799, 771, 703, 651 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{18}H_{19}NO_2Na$ $[M+Na]^+$: 304.1313, found: 304.1316.

1-Mesityl-2-morpholinoethane-1,2-dione (4b)



Mesityl glyoxylic acid (2.0 g, 10.4 mmol) was dissolved in DCM (48 mL) under a N_2 atmosphere at rt. Oxalyl chloride (0.93 mL, 11 mmol) was added in one portion. To the resulting mixture was added anhydrous DMF (2 drops), at which point gentle bubbling was observed. The mixture was allowed to stir at rt until gas evolution ceased (16 h). The reaction mixture was then cooled to 0 ˚C in an ice/water bath and successively added Et_3N (2.2 mL, 15.8 mmol) and morpholine (1.0 mL, 11.6 mmol). The resulting mixture was gradually warmed to rt over 6 h, then quenched with dH_2O (40 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 x 15 mL). The combined organic extract was washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was recrystallized in hot EtOAc/hexanes to give white needles (2.27 g, 84%, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 2H), 3.78 (broad s, 4H), 3.70 (dt, *J* = 14.6, 4.2 Hz, 4H), 2.32 (s, 6H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 165.6, 141.6, 137.3, 133.5, 129.8, 66.8, 66.7, 46.5, 42.3, 21.4, 20.4. IR (ATR): 2971, 2927, 2856, 1678, 1629, 1604, 1442, 1425, 1267, 1218, 1113, 980, 834, 781, 655, 618, 580. HRMS (ESI-TOF) *m/z* calc'd for $C_{15}H_{19}NO_3Na$ $[M+Na]^+$: 284.1263, found: 284.1252.

4. Solvent Optimization



Entry	Solvent	Time (h)	Yield (%)	ee (product)	Temp (℃)
1	DCE	7.5	88	69	32
2	DCE	19.5	94	47	50
3	DCE, 10 mol % CH_3CN	19.5	51	55	50
4	Acetone	19.5	30	53	50
5	EtOAc	19.5	50	57	50

Changing the solvent from DCE to other solvents generally resulted in decreased reactivity, although the effect on enantioselectivity is modest.

5. Enantioselective Ketone Hydroacylation

i) Standard Procedure

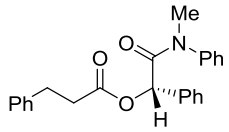
In a N_2-filled glovebox, Josiphos **L5** (3.1 mg, 0.005 mmol, 5 mol %) was dissolved in DCM (0.3 mL) and added to a vial containing $[Rh(cod)_2]BF_4$ (2.0 mg, 0.005 mmol, 5 mol %). The resulting solution was transferred to a 25 mL Schlenk tube. An additional 0.3 mL DCM was used to rinse the vial containing the ligand, and this liquid was also added to the Schlenk tube. The Schlenk tube was then connected to a Schlenk line (vacuum gas manifold), and the pre-catalyst solution was degassed via two cycles of 'freeze-pump-thaw'. The Schlenk tube was backfilled with H_2 gas and the solution was stirred at rt under a gentle flow of H_2 for 45−60 min. The DCM solvent was subsequently removed under reduced pressure to give the rhodium-catalyst as a dark red oil/film. To the catalyst residue was added a solution of α-ketoamide **2** (0.10 mmol) in DCE (0.4 mL), followed by aldehyde **1** (0.11 mmol). The reaction was stirred at rt (23 ˚C) for 24 h. The crude reaction mixture was purified by silica gel chromatography. While the majority of compounds can be adequately separated using column chromatography, preparative tlc is preferred because this allows us to completely identify and isolate the UV-active band, thus avoiding artificially enhanced ee's that can be due to self-disproportionation of enantiomers.[16] To demonstrate practicality, a 1.0 mmol scale reaction was performed (Table 1, entry 16, product **3p**). In this case, the product was purified by column chromatography.

For the racemic assay/reaction, an achiral catalyst derived from $[Rh(cod)_2]BF_4$ and 1,3-bis(dicyclohexyl)phosphinopropane was used.

[16] Soloshonok, V. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 766.

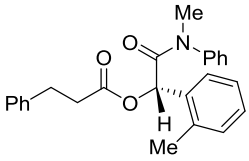
ii) Product Characterization

(*S*)-2-(Methyl(phenyl)amino)-2-oxo-1-phenylethyl 3-phenylpropanoate (3a, Table 1, entry 1)



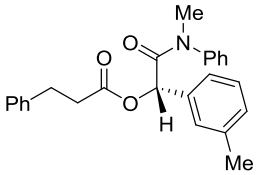
The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (24.2 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (br s, 3H), 7.29–7.33 (m, 1H), 7.22–7.28 (m, 4H), 7.15–7.21 (m, 3H), 7.10 (br. s, 2H), 7.05 (d, *J* = 7.3 Hz, 2H), 5.85 (s, 1H), 3.26 (s, 3H), 2.92–3.05 (m, 2H), 2.80 (ddd, *J* = 16.0, 9.2, 6.7 Hz, 1H), 2.69 (ddd, *J* = 16.4, 9.8, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 168.3, 142.5, 140.6, 134.1, 129.9, 129.3, 128.8, 128.7, 128.6, 128.5, 128.3, 126.4, 74.0, 38.1, 35.7, 30.9. HRMS (ESI+) *m/z* calc'd for $C_{20}H_{22}NO_3$ $[M+1]^+$: 374.17562; found: 374.17624. IR (ATR): 2923, 1733, 1671, 1595, 1495, 1454, 1385, 1245, 1151, 989, 911, 755, 730, 696. HRMS (ESI-TOF) *m/z* calc'd for $C_{24}H_{23}NO_3Na$ $[M+H]^+$: 374.17562; found: 374.17624. SFC analysis: 87% *ee*, 150 mm CHIRALPAK AD-H, 5% MeOH, 2.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 4.21 min, t_{R2} (major) = 5.09 min; $[\alpha]^{27}_D$ +88 (*c* = 1.3, $CHCl_3$).

(*S*)-Methyl(phenyl)amino)-2-oxo-1-(m-tolyl)ethyl 3-phenylpropanoate (3b, Table 1, entry 2)



The product was purified by preparative tlc as a colorless oil (34.1 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.13–7.33 (m, 10H), 6.80–7.10 (m, br, 3H), 6.10 (s, 1H), 3.28 (s, 3H), 2.93–3.04 (m, 2H), 2.79 (ddd, *J* = 15.9, 9.0, 6.8 Hz, 1H), 2.69 (ddd, *J* = 16.3, 9.5, 6.9 Hz, 1H), 1.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 168.6, 142.2, 140.5, 137.6, 132.3, 130.5, 129.8, 129.4, 129.0, 128.6, 128.4, 128.2, 126.5, 126.3, 70.8, 38.0, 35.6, 30.9, 18.2. IR (ATR): 3061, 3027, 2929, 1733, 1673, 1595, 1495, 1385, 1204, 759, 698 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{25}H_{25}NO_3Na$ $[M+Na]^+$: 410.1732, found: 410.1730. SFC analysis: 95% *ee*, 150 mm CHIRALPAK AD-H, 10% *i*PrOH, 3.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 2.48 min, t_{R2} (major) = 2.95 min; $[\alpha]^{26}_D$ +118 (*c* = 1.0, $CHCl_3$).

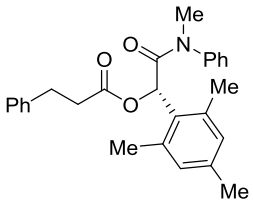
(*S*)-(Methyl(phenyl)amino)-2-oxo-1-(o-tolyl)ethyl 3-phenylpropanoate (3c, Table 1, entry 3)



The product was purified by preparative tlc (eluting with 4:1 hexanes/acetone) as a colorless oil (24.0 mg, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (br. s, 3H), 7.29–7.33 (m, 3H), 6.99–7.28 (m, 6H), 6.94 (s,

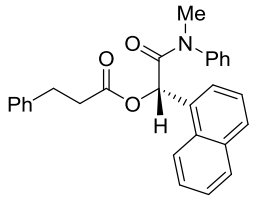
1H), 6.80–6.89 (m, 1H), 5.89 (s, 1H), 3.32 (s, 3H), 2.98–3.13 (m, 2H), 2.86 (ddd, *J* = 16.0, 9.2, 7.1 Hz, 1H), 2.75 (ddd, *J* = 16.5, 9.3, 7.1 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 168.3, 142.5, 140.6, 138.3, 133.9, 129.9, 129.7, 129.3, 128.6, 128.4_3, 128.4_0, 128.3_4, 126.2_6, 125.8, 74.1, 38.0, 35.6, 30.9, 21.4. IR (ATR): 3060, 3027, 2923, 2361, 2341, 1734, 1671, 1595, 1495, 1384, 1150, 772, 697 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{25}H_{25}NO_3Na$ $[M+Na]^+$: 410.1732, found 410.1721.SFC analysis: 86% *ee*, 150 mm CHIRALCEL OD-H, 6% *i*PrOH, 3.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 2.42 min, t_{R2} (minor) = 2.93 min; $[\alpha]^{27}_D$ +96 (*c* = 0.98, $CHCl_3$).

(*S*)-Mesityl-2-(methyl(phenyl)amino)-2-oxoethyl 3-phenylpropanoate (3d, Table 1, entry 4)



The product was purified by preparative tlc (eluting with 4:1 hexanes/acetone, 2 cycles) as a colorless oil (34.0 mg, 82%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.10–7.28 (m, 9H), 6.73–7.00 (br. s, 1H), 6.64 (s, 2H), 6.44 (s, 1H), 3.24 (s, 3H), 2.92–3.07 (m, 2H), 2.85–2.73 (m, 1H), 2.62–2.72 (m, 1H), 2.21 (s, 3H), 1.70–2.12 (br. s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 169.2, 142.3 (br. s), 140.7, 138.9, 138.6, 129.6, 128.9, 128.5, 128.4, 128.1, 128.0, 126.2, 70.7, 38.9, 35.8, 31.0, 21.0, 19.8. IR (ATR): 3027, 2920, 1735, 1674, 1595, 1495, 1377, 1142, 751, 697, 566 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{27}H_{29}NO_3Na$ $[M+Na]^+$: 438.2045, found: 438.2029. SFC analysis: 96% *ee*, 150 mm CHIRALCEL OD-H, 6% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 3.43 min, t_{R2} (minor) = 5.36 min; $[\alpha]^{27}_D$ +138 (*c* = 0.94, $CHCl_3$).

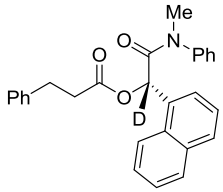
(*S*)-(Methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl 3-phenylpropanoate (3e, Table 1, entry 5)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (36.6 mg, 86%).^{1}H NMR (499 MHz, $CDCl_3$) δ 7.72–7.87 (m, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.35 (s, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.18–7.26 (m, 2H), 7.04–7.18 (m, 6H), 6.90 (br. s, 2H), 6.68 (s, 1H), 3.28 (s, 3H), 2.92–3.07 (m, 2H), 2.81 (dt, *J* = 15.9, 8.0 Hz, 1H), 2.64–2.75 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 168.5, 142.3, 140.5, 133.8, 131.3, 130.0, 129.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 126.6, 126.3, 125.9, 125.2, 123.2, 71.2,

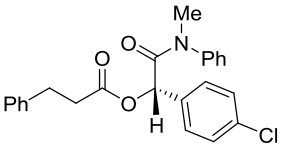
38.1, 35.6, 30.9. IR (ATR): 3061, 3028, 2929, 1733, 1671, 1595, 1495, 1411, 1237, 1149, 985, 799, 774, 697 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{28}H_{25}NO_3Na$ $[M+Na]^+$: 446.1732, found: 446.1716. SFC analysis: 95% *ee*, 150 mm CHIRALCEL OD-H, 10% *i*PrOH, 2.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 3.97 min, t_{R2} (minor) = 5.25 min; $[\alpha]^{26}_D$ +90 (*c* = 0.7, $CHCl_3$).

(*S*)-2-(methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl-1-d 3-phenylpropanoate (3e-D)



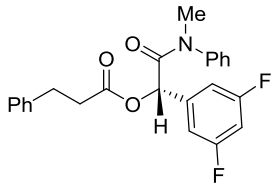
The product was purified by preparative TLC (eluting with 4:1 hexanes/EtOAc). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.78–7.84 (m, 2H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.34–7.39 (m, 2H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.19–7.25 (m, 2H), 7.06–7.19 (m, 6H), 6.91 (s, 2H), 3.29 (s, 3H), 2.94–3.07 (m, 2H), 2.82 (ddd, *J* = 15.9, 8.9, 6.9 Hz, 1H), 2.71 (ddd, *J* = 16.3, 9.5, 6.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 168.5, 142.3, 140.5, 133.8, 131.3, 130.0, 129.9, 129.7, 128.6, 128.6, 128.4, 128.2, 128.1, 127.9, 126.6, 126.3, 125.9, 125.2, 123.2, 38.1, 35.7, 30.9. IR (ATR): 3064, 3021, 2919, 1737, 1662, 1600, 1486, 1368, 1298, 1153, 1083, 899, 801, 765, 726, 691 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{28}H_{24}DNO_3Na$ $[M+Na]^+$: 447.1795, found: 447.1791.

(*S*)-1-(4-Chlorophenyl)-2-(methyl(phenyl)amino)-2-oxoethyl 3-phenylpropanoate (3f, Table 1, entry 6)



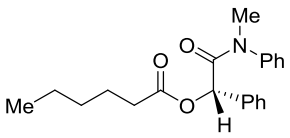
The product was purified by preparative tlc (eluting with 50:48:2 hexanes/DCM/acetone, 5 cycles, eluted at 4 ˚C) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 3H), 7.22 (ddd, *J* = 27.7, 15.8, 7.7 Hz, 9H), 6.98 (d, *J* = 8.4 Hz, 2H), 5.82 (s, 1H), 3.25 (s, 3H), 3.08 – 2.89 (m, 2H), 2.79 (ddd, *J* = 15.9, 9.0, 6.8 Hz, 1H), 2.68 (ddd, *J* = 16.3, 9.5, 6.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 167.9, 142.2, 140.4, 135.2, 132.6, 130.1, 129.9, 128.8, 128.6_5, 128.6_0, 128.4, 128.2, 126.4, 73.0, 38.0, 35.5, 30.8. IR (ATR): 3062, 3028, 2925, 2854, 2360, 2342, 1736, 1672, 1595, 1494, 1385, 1156, 805, 751, 698 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{24}H_{22}ClNO_3Na$ $[M+Na]^+$ = 430.1186, found: 430.1197. SFC analysis: 84% *ee*, 150 mm CHIRALPAK OD-H, 5% *i*PrOH, 2.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 6.87 min, t_{R2} (minor) = 7.69 min; $[\alpha]^{23}_D$ +46 (*c* = 1.5, $CHCl_3$).

(*S*)-1-(3,5-Difluorophenyl)-2-(methyl(phenyl)amino)-2-oxoethyl 3-phenylpropanoate (3g Table 1, entry 7)



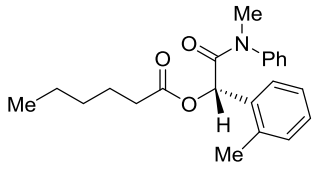
The product was purified by preparative tlc (eluting with 4:1 hexanes/Et_2O) as a colorless oil (27.5 mg, 67%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.41 (s, 3H), 7.22–7.32 (m, 3H), 7.04–7.22 (m, 4H), 6.75 (t, *J* = 8.8 Hz, 1H), 6.58 (d, *J* = 6.2 Hz, 2H), 5.82 (s, 1H), 3.27 (s, 3H), 2.90–3.06 (m, 2H), 2.79 (dt, *J* = 15.4, 7.8 Hz, 1H), 2.64–2.74 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 167.2, 162.8 (dd, *J* = 249.5, 12.5 Hz), 142.1, 140.3, 137.7 (t, *J* = 9.3 Hz), 130.0, 128.9, 128.6, 128.4, 128.1, 126.4, 111.6 (dd, *J* = 20.1, 6.3 Hz), 104.7 (t, *J* = 25.1 Hz), 72.5, 38.1, 35.5, 30.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.2 (t, *J* = 7.5 Hz). IR (ATR): 3063, 3029, 2925, 2854, 1739, 1674, 1624, 1597, 1496, 1157, 1120, 772, 698 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{24}H_{21}F_2NO_3Na$ $[M+Na]^+$: 432.1387, found: 432.1371. SFC analysis: 88% *ee*, 150 mm CHIRALPAK IC, 10% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 2.58 min, t_{R2} (minor) = 2.84 min; $[\alpha]^{26}_D$ +70 (*c* = 0.7, $CHCl_3$).

(*S*)-2-(Methyl(phenyl)amino)-2-oxo-1-phenylethyl hexanoate (3h, Table 1, entry 8)



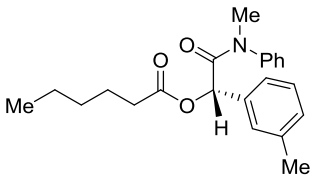
The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (29.3 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (br s, 3H), 7.28–7.33 (m, 1H), 7.22–7.28 (m, 2H), 7.12 (br s, 2H), 7.06 (d, *J* = 7.3 Hz, 2H), 5.83 (s, 1H), 3.25 (s, 3H), 2.46 (ddd, *J* = 15.4, 8.4, 6.9 Hz, 1H), 2.40–2.32 (m, 1H), 1.61–1.70 (m, 2H), 1.25–1.36 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.3, 142.5, 134.2, 129.8, 129.1, 128.7, 128.6, 128.4, 128.3, 73.7, 38.0, 34.0, 31.4, 24.5, 22.4, 14.0. IR(ATR): 3064, 3033, 2956, 2930, 2871, 1734, 1673, 1596, 1495, 1383, 1164, 757, 696, 557 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{21}H_{25}NO_3Na$ $[M+Na]^+$: 362.1732, found: 362.1736. SFC analysis: 89% *ee*, 150 mm CHIRALPAK AD-H, 10% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.31 min, t_{R2} (major) = 1.54 min; $[\alpha]^{27}_D$ +112 (*c* = 1.3, $CHCl_3$).

(*S*)-(Methyl(phenyl)amino)-2-oxo-1-(m-tolyl)ethyl hexanoate (3i, Table 1, entry 9)



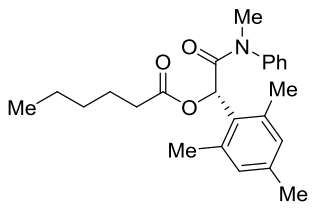
The product was purified by preparative tlc (4:1 hexanes/EtOAc) as a colorless oil (34.7 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.29 (m, br, 7.29, 3H), 7.20 (m, 2H), 6.99 (m, br, 3H), 6.09 (s, 1H), 3.27 (s, 3H), 2.44 (ddd, *J* = 15.4, 8.3, 6.9, 1H), 2.35 (m, 1H), 1.61–1.71 (m, 2H), 1.58 (s, 3H), 1.26–1.35 (m, 4H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 168.6, 142.3, 137.5, 132.4, 130.4, 129.8, 129.3, 129.0, 128.3, 128.2, 126.5, 70.5, 38.0, 34.0, 31.4, 24.6, 22.4, 18.2, 14.0. IR (ATR): 2955, 2930, 2871, 1734, 1675, 1595, 1495, 1384, 1162, 759, 726, 699 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{22}H_{27}NO_3Na$ $[M+Na]^+$: 376.1889, found: 376.1896. SFC analysis: 95% *ee*, 150 mm CHIRALCEL IA, 6% *i*PrOH, 5.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.85 min, t_{R2} (major) = 2.64 min; $[\alpha]^{26}_D$ +110 (*c* = 0.99, $CHCl_3$).

(*S*)-(Methyl(phenyl)amino)-2-oxo-1-(o-tolyl)ethyl hexanoate (3j, Table 1, entry 10)



The product was purified by preparative tlc (4:1 hexanes/EtOAc) as a colorless oil (27.9 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (br. s, 3H), 7.11 (br s, 4H), 6.88 (s, 1H), 6.79 (d, *J* = 5.6 Hz, 1H), 5.81 (s, 1H), 3.24 (s, 3H), 2.45 (dt, *J* = 15.5, 7.6 Hz, 1H), 2.3–2.40 (m, 1H), 2.27 (s, 3H), 1.60–1.72 (m, 2H), 1.28 (m, 4H), 0.88 (br s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.4, 142.5, 138.3, 134.0, 129.9, 129.6, 129.3, 128.4, 126.8, 73.8, 38.0, 34.0, 31.4, 24.6, 22.4, 21.4, 14.0 (2 signals likely overlapping); ^{13}C NMR (125 MHz, $(CD_3)CO$) δ 173.5, 168.4, 143.6, 138.7, 135.4, 130.4, 130.3, 130.0, 129.1, 129.0$_4$, 129.0, 126.4, 74.4, 37.8, 34.3, 31.9, 25.3, 23.0, 21.3, 14.2. IR (ATR): 2950, 2925, 2869, 1733, 1666, 1594, 1493, 1388, 1153, 1114, 778, 711 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{22}H_{27}NO_3Na$ $[M+Na]^+$: 376.1889, found: 376.1892. SFC analysis: 86% *ee*, 150 mm CHIRALPAK AD-H, 7.5% *i*PrOH, 4.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.07 min, t_{R2} (major) = 1.58 min; $[\alpha]^{27}_D$ +66 (*c* = 0.99, $CHCl_3$).

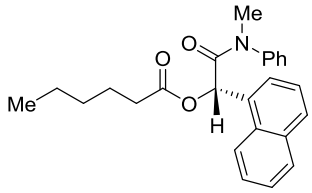
(*S*)-Mesityl-2-(methyl(phenyl)amino)-2-oxoethyl hexanoate (3k, Table 1, entry 11)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc, 2 elutions) as a colorless oil (29.1 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05–7.26 (m, 3H), 6.70–7.05 (br. s, 2H),

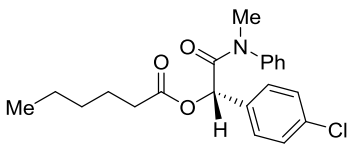
6.64 (s, 2H), 6.42 (s, 1H), 3.23 (s, 3H), 2.45 (ddd, *J* = 15.3, 8.1, 7.1 Hz, 1H), 2.40–2.29 (m, 1H), 2.21 (s, 3H), 1.75–2.12 (br. s, 5H), 1.61–1.75 (m, 3H), 1.23–1.37 (m, 4H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 169.3, 142.3, 138.8, 138.5, 129.6 (br. s), 129.0, 128.0 (br. s), 70.4, 38.9, 34.1, 31.4, 24.6, 22.4, 21.0, 19.8, 14.0. IR (ATR): 2956, 2928, 2861, 1736, 1677, 1595, 1495, 1377, 1163, 994, 851, 731, 698 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{24}H_{31}NO_3Na$ $[M+Na]^+$: 404.2202, found: 404.2211. SFC analysis: 96% *ee*, 150 mm CHIRALCEL OD-H, 6% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 1.54 min, t_{R2} (minor) = 2.05 min; $[\alpha]^{25}_D$ +188 (*c* = 1.0, $CHCl_3$). The reaction was also performed at 60˚C using 0.24 mmol aldehyde **1b** and 0.20 mmol ketone **2d**, in 0.4 mL DCE (64.3 mg, 84%, 94% ee).

(*S*)-2-(Methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl hexanoate (3l, Table 1, entry 12)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (28.6 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72–7.87 (m, 2H), 7.52 (d, *J* = 7.8 Hz, 1H) 7.41 (t, *J* = 7.3 Hz, 1H), 7.35 (s, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.05–7.22 (m, 3H), 6.91 (br. s, 2H), 6.66 (s, 1H), 3.27 (s, 3H), 2.47 (dt, *J* = 15.5, 7.5 Hz, 1H), 2.31–2.42 (m, 1H), 1.59–1.75 (m, 2H), 1.23–1.36 (m, 4H), 0.78–0.92 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 168.6, 142.4, 133.8, 131.3, 130.1, 129.9, 129.7, 128.6, 128.2, 128.1, 128.0, 126.6, 125.8, 125.2, 123.2, 71.0, 38.1, 34.1, 31.4, 24.6, 22.4, 14.0. IR (ATR): 3062, 2955, 2930, 2870, 1733, 1673, 1595, 1512, 1382, 1238, 1162, 1110, 798, 733, 698, 566 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{25}H_{27}NO_3Na$ $[M+Na]^+$: 412.1889, found: 412.1891. SFC analysis: 96% *ee*, 150 mm CHIRALCEL OJ-H, 5% *i*PrOH, 2.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 1.15 min, t_{R2} (minor) = 1.77 min; $[\alpha]^{26}_D$ +202 (*c* = 1.4, $CHCl_3$).

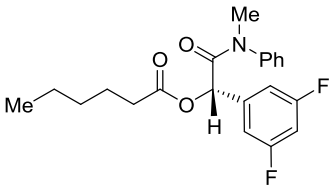
(*S*)-1-(4-Chlorophenyl)-2-(methyl(phenyl)amino)-2-oxoethyl hexanoate (3m, Table 2, entry 13)



This product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (19.8 mg, 53%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.38 (s, 3H), 7.10–7.30 (m, 3H), 7.13 (br. s, 1H),

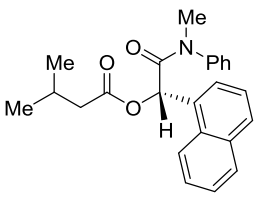
6.99 (d, *J* = 7.9 Hz, 2H), 5.81 (s, 1H), 3.24 (s, 3H), 2.40–2.49 (m, 1H), 2.30–2.40 (m, 1H), 1.57–1.72 (m, 2H), 1.26–1.36 (m, 4H), 0.82–0.93 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 168.0, 142.3, 135.2, 132.7, 130.1, 129.9, 128.8, 128.6, 128.2, 72.9, 38.0, 34.0, 31.4, 24.5, 22.4, 14.0. IR (ATR): 2956, 2929, 2871, 2859, 1737, 1674, 1595, 1494, 1384, 1241, 1263, 1105, 805, 773, 699 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{21}H_{24}ClNO_3Na$ $[M+Na]^+$ = 396.1342, found: 396.1331. SFC analysis: 87% *ee*, 150 mm CHIRALPAK AD-H, 7% *i*PrOH, 2.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 2.99 min, t_{R2} (major) = 4.36 min; $[\alpha]^{25}_D$ +54 (*c* = 1.76, $CHCl_3$). $[\alpha]^{25}_D$ +28 (*c* = 1.8, $CHCl_3$).

(*S*)-1-(3,5-Difluorophenyl)-2-(methyl(phenyl)amino)-2-oxoethyl hexanoate (3n, Table 1, entry 14)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a pale yellow oil (30.3 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (s, 3H), 7.00–7.35 (br. s, 2H), 6.75 (tt, *J* = 8.8, 2.3 Hz, 1H), 6.56–6.65 (m, 2H), 5.81 (s, 1H), 3.26 (s, 3H), 2.46 (ddd, *J* = 15.4, 8.2, 7.1 Hz, 1H), 2.33–2.40 (m, 1H), 1.61–1.71 (m, 2H), 1.27–1.37 (m, 4H), 0.89 (t, *J* = 0.89 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 167.3, 162.8 (dd, *J* = 249.5, 12.5 Hz), 142.1, 137.8 (t, *J* = 9.5 Hz), 130.0, 128.8, 128.1, 111.6 (dd, *J* = 20.0, 6.3 Hz), 104.6 (t, *J* = 25.2 Hz), 72.3, 38.1, 33.9, 31.3, 24.5, 22.4, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.2 (t, *J* = 7.5 Hz). IR (ATR): 2957, 2931, 2872, 2861, 1740, 1676, 1624, 1597, 1463, 1383, 1162, 1120, 984, 772, 700 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{21}H_{23}F_2NO_3Na$ $[M+Na]^+$: 398.1544, found: 398.1544. SFC analysis: 90% *ee*, 150 mm CHIRALPAK AD-H, 9% *i*PrOH, 3.25 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 0.62 min, t_{R2} (minor) = 0.82 min; $[\alpha]^{26}_D$ +100 (*c* = 1.5, $CHCl_3$).

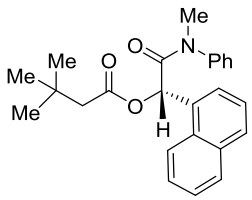
(*S*)-2-(methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl 3-methylbutanoate (3o, Table 1, entry 15)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (34.1 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.85 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.35 (s, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.04–7.22 (m, 3H), 6.76–7.14

(br. s, 2H), 6.66 (s, 1H), 3.27 (s, 3H), 2.34 (dd, *J* = 14.9, 6.9 Hz, 1H), 2.25 (dd, *J* = 14.9, 7.2 Hz, 1H), 2.10–2.21 (m, 1H), 0.93–1.01 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 168.5, 142.4, 133.8, 131.4, 130.2, 129.9, 129.7, 128.6, 128.1, 128.0, 126.6, 125.9, 125.2, 123.2, 71.0, 43.2, 38.1, 25.8, 22.6_1, 22.5_5. IR (ATR): 3061, 2967, 2926, 2872, 1723, 1667, 1594, 1494, 1387, 1248, 1199, 1090, 988, 803, 782, 774, 687 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{24}H_{25}NO_3Na$ $[M+Na]^+$: 398.1732, found: 398.1738. SFC analysis: 94% *ee*, 150 mm CHIRALCEL OD-H, 4% *i*PrOH, 2.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 5.50 min, t_{R2} (minor) = 6.68 min; $[\alpha]^{24}_D$ +232 (*c* = 0.98, $CHCl_3$).

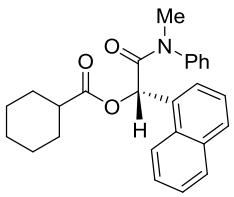
(*S*)-2-(methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl 3,3-dimethylbutanoate (3p, Table 1, entries 16 and 17)



To demonstrate scalability, this reaction was performed on 1.0 mmol scale, 5% Rh-catalyst loading, 3 mL DCE, 36 h reaction time. The product was purified by flash column chromatography (eluting with 0−45% EtOAc in hexanes) to give a pale yellow liquid (353.4 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (t, *J* = 7.0 Hz, 2H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.34 (d, *J* = 4.7 Hz, 2H), 7.28 (t, *J* = 4.5 Hz, 1H), 7.02–7.19 (m, 3H), 6.70–7.05 (br. s, 2H), 6.65 (s, 1H), 3.27 (s, 3H), 2.33 (d, *J* = 13.5 Hz, 1H), 2.27 (d, *J* = 13.5 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 168.5, 142.4, 133.8, 131.3, 130.2, 129.8, 129.7, 128.6, 128.1_5, 128.1_0, 128.0, 126.5, 125.8, 125.2, 123.2, 70.9, 47.8, 38.2, 31.1, 29.7. IR(ATR): 3061, 2955, 2869,1729, 1673, 1595, 1496, 1384, 1225, 1124, 994, 798, 774, 730, 698 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{25}H_{27}NO_3Na$ $[M+Na]^+$: 412.1889, found: 412.1890. SFC analysis: 93% *ee*, 150 mm CHIRALCEL OD-H, 5% *i*PrOH, 2.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 4.11 min, t_{R2} (minor) = 4.96 min; $[\alpha]^{27}_D$ +180 (*c* = 1.2, $CHCl_3$).

Also on 1.0 mmol scale, we demonstrate that the catalyst loading can be further reduced to 3.5 mol % by heating the reaction to 60˚C for 24 h in 2 mL DCE (359 mg, 92%, 87% ee).

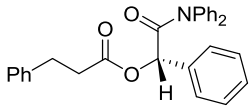
(*S*)-2-(methyl(phenyl)amino)-1-(naphthalen-1-yl)-2-oxoethyl cyclohexanecarboxylate (3q, Table 1, entry 18)



The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) as a colorless oil (22.8 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.85

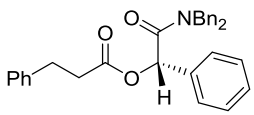
(m, 2H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.27–7.37 (m, 3H), 7.05–7.22 (m, 3H), 6.72–7.06 (br. s, 2H), 6.63 (s, 1H), 3.27 (s, 3H), 2.42 (tt, *J* = 11.3, 3.5 Hz, 1H), 2.09 (d, *J* = 12.7 Hz, 1H), 1.87 (d, *J* = 13.1 Hz, 1H), 1.74–1.83 (m, 1H), 1.66–1.74 (m, 1H), 1.38– 1.65 (m, 3H), 1.18–1.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 168.5, 142.3, 133.8, 131.4, 130.2, 129.9, 129.7, 128.6, 128.1_5, 128.1_2, 128.0, 126.6, 125.8, 125.2, 123.4, 71.0, 42.9, 38.1, 29.2, 28.9, 25.9, 25.5, 25.4. IR (ATR): 3061, 3013, 2930, 2854, 1728, 1672, 1595, 1495, 1382, 1244, 1163, 1127, 1024, 988, 799, 774, 698, 561. HRMS (ESI-TOF) *m/z* calc'd for $C_{26}H_{27}NO_3Na$ $[M+Na]^+$: 424.1889, found: 424.1877. SFC analysis: 90% *ee*, 150 mm CHIRALCEL OD-H, 8% *i*PrOH, 3.0 mL/min, 254 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 2.66 min, t_{R2} (minor) = 3.28 min; $[\alpha]^{25}_D$ +178 (*c* = 1.1, $CHCl_3$).

(*S*)-2-(diphenylamino)-2-oxo-1-phenylethyl 3-phenylpropanoate (3r, Table 1, entry 19)



The product was purified by preparative tlc (eluting with 4:1 hexanes/acetone) as a pale yellow oil (20.4 mg, 47%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09–7.42 (m, 20H), 6.01 (s, 1H), 2.94–3.07 (m, 2H), 2.80 (ddd, *J* = 16.0, 9.3, 6.6 Hz, 1H), 2.70 (ddd, *J* = 16.3, 9.8, 6.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 168.4, 140.6, 133.6, 129.7–129.9 (br. s), 129.5–129.7 (br. s), 129.4_6, 129.0–129.2 (br. s), 128.9, 128.8, 128.6, 128.4, 126.4–126.6 (br. s), 126.3_3, 126.1–126.3 (br. s), 74.7, 35.6, 30.9. IR (ATR): 3062, 3030, 2925, 2360, 1734, 1684, 1593, 1490, 1453, 1371, 1279, 1148, 1076, 753, 693, 633 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{29}H_{25}NO_3Na$ $[M+Na]^+$: 458.1732, found: 458.1718. SFC analysis: 78% *ee*, 150 mm CHIRALPAK AD-H, 20% *i*PrOH, 4.5 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.79 min, t_{R2} (major) = 2.28 min; $[\alpha]^{24}_D$ +30 (*c* = 0.3, $CHCl_3$).

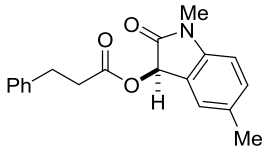
(*S*)-2-(dibenzylamino)-2-oxo-1-phenylethyl 3-phenylpropanoate (3s, Table 1, entry 20)



The yield was determined by ^{1}H NMR analysis of the crude reaction mixture (44%). We were unable to completely separate the starting material from the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05–7.53 (m, 20H), 6.25 (s, 1H), 4.94 (d, *J* = 14.9 Hz, 1H), 4.47 (d, *J* = 16.8 Hz, 1H), 4.17 (dd, *J* = 15.4, 13.2 Hz, 2H), 3.03 (qq, *J* = 14.3, 7.1 Hz, 2H), 2.82 (ddd, *J* = 15.9, 8.7, 7.1 Hz, 1H), 2.73 (ddd, *J* = 16.2, 9.4, 7.0 Hz, 1H). HRMS (ESI-TOF) *m/z* calc'd for $C_{31}H_{29}NO_3Na$ $[M+Na]^+$: 486.2045,

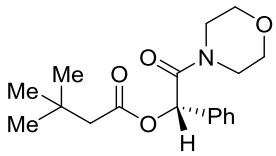
found: 486.2028. SFC analysis: 81% *ee*, 150 mm CHIRALPAK AD-H, 20% *i*PrOH, 4.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.94 min, t_{R2} (major) = 2.39 min.

1,5-dimethyl-2-oxoindolin-3-yl 3-phenylpropanoate (3t, Table 1, entry 21)



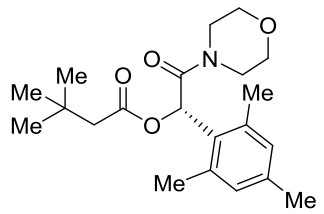
The product was purified by preparative tlc (eluting with 4:1 hexanes/EtOAc) and isolated as a white solid (16.7 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.33 (m, 3H), 7.21 (m, 3H), 7.13 (d, *J* = 7.9 Hz, 1H), 7.01 (s, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 3.19 (s, 1H), 2.93–3.09 (m, 1H), 2.68–2.87 (m, 1H), 2.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 172.2, 142.2, 140.2, 135.5, 132.9, 130.5, 128.9, 128.7, 128.5, 127.8, 127.4, 126.5$_1$, 126.4$_8$, 124.5, 108.3, 70.1, 35.6, 30.9, 26.5, 21.1. IR (ATR): 2923, 2854, 1725, 1624, 1603, 1497, 1454, 1363, 1139, 1097, 809, 751, 698. HRMS (ESI+) *m/z* calc'd for $C_{19}H_{20}NO_3$ $[M+H]^+$: 310.14432; found: 310.14395. SFC analysis: 54% *ee*, 150 mm CHIRALCEL OD-H, 10% MeOH, 3.0 mL/min, 254 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 1.6 min, t_{R2} (minor) = 2.2 min, t_{R3} (starting material) = 2.9min. This compound gradually racemizes in polar protic solvents (*i.e.* isopropanol). Subjecting this product to silica gel suspended in EtOAc at 80 ˚C for 4 h does not diminish the ee.

(*S*)-2-morpholino-2-oxo-1-phenylethyl 3,3-dimethylbutanoate (5a)



The product was purified by preparative tlc (eluting with 4:1 hexanes/acetone, 2 elutions) and isolated as a colorless solid (21.5 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.47 (m, 5H), 6.21 (s, 1H), 3.42–3.82 (m, 6H), 3.12–3.42 (m, 2H), 2.32 (d, *J* = 4.3 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 166.7, 134.3, 129.5, 129.2, 128.4, 73.0, 66.9, 66.2, 47.7, 46.0, 42.8, 31.1, 29.7. IR (ATR): 2958, 2862, 1732, 1660, 1436, 1228, 1115, 1014, 911, 729, 698. HRMS (ESI-TOF) *m/z* calc'd for $C_{18}H_{25}NO_4Na$ $[M+Na]^+$: 342.1681, found: 342.1685. SFC analysis: 80% *ee*, 250 mm, 10% *i*PrOH, 4.0 mL/min, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 2.18 min, t_{R2} (minor) = 3.40 min.

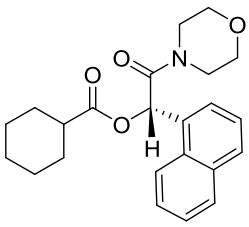
(*S*)-1-mesityl-2-morpholino-2-oxoethyl 3,3-dimethylbutanoate (5b)



The product was purified by preparative TLC (eluting with 4:1 hexanes/acetone) and isolated as a colorless oil (33.9 mg, 94%). ^{1}H

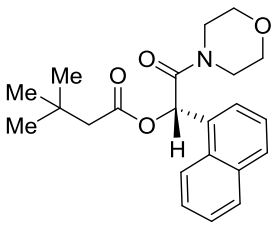
NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 2H), 6.50 (s, 1H), 3.73 (broad s, 2H), 3.47 (broad s, 3H), 2.85–3.29 (m, 3H), 2.36 (d, *J* = 13.5 Hz, 1H), 2.32 (s, 6H), 2.29 (d, *J* = 13.6 Hz, 1H), 2.27 (s, 3H), 1.07 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 167.6, 139.1, 137.8, 130.5, 129.3, 69.8, 66.8, 66.2, 47.9, 45.5, 43.1, 31.0, 29.7, 21.1, 20.3. IR (ATR): 2959, 2922, 2856, 1728, 1668, 1455, 1425, 1226, 1116, 1000, 863, 820, 726 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{21}H_{31}NO_4Na$ $[M+Na]^+$: 384.2151, found: 384.2140. SFC analysis: 95% *ee*, 150 mm CHIRALCEL OD-H, 5% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 1.35 min, t_{R2} (minor) = 1.83 min. $[\alpha]^{27}_D$ +204 (*c* = 1.3, $CHCl_3$).

(*S*)-2-morpholino-1-(naphthalen-1-yl)-2-oxoethyl cyclohexanecarboxylate (5c)



The product was purified by preparative TLC (eluting with 4:1 hexanes/acetone) and isolated as a colorless oil (22.4 mg, 59%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.5, 1.2 Hz, 1H), 7.88–7.96 (m, 2H), 7.52–7.62 (m, 3H), 7.44–7.51 (m, 1H), 6.94 (s, 1H), 3.52–3.84 (m, 4H), 3.46 (broad s, 1H), 3.31 (broad s, 1H), 3.07 (d, *J* = 26.3 Hz, 2H), 2.45 (tt, *J* = 11.3, 3.6 Hz, 1H), 2.02–2.09 (m, 1H), 1.87–1.95 (m, 1H), 1.65–1.80 (m, 2H), 1.56–1.63 (m, 1H), 1.44–1.56 (m, 2H), 1.12–1.35 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 167.0, 134.2, 131.3, 130.6, 129.8, 129.3, 127.5, 127.5, 126.5, 125.5, 122.8, 70.0, 66.9, 66.1, 45.8, 43.0, 42.7, 29.1, 29.0, 25.8, 25.5, 25.4. IR (ATR): 3005, 2927, 2857, 1729, 1658, 1439, 1247, 1224, 1161, 1114, 1000, 805, 781, 742 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{23}H_{27}NO_4Na$ $[M+Na]^+$: 404.1838, found: 404.1831. SFC analysis: 92% *ee*, 150 mm CHIRALCEL OD-H, 10% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 2.80 min, t_{R2} (minor) = 3.46 min. $[\alpha]^{23}_D$ +96 (*c* = 1.0, $CHCl_3$).

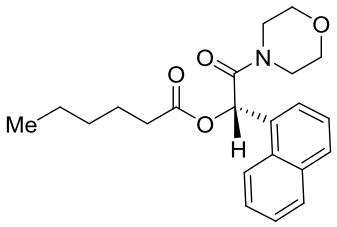
(*S*)-2-morpholino-1-(naphthalen-1-yl)-2-oxoethyl 3,3-dimethylbutanoate (5d)



The product was purified by preparative TLC (eluting with 3:2 hexanes/EtOAc) and isolated as a colorless oil (27.7 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 1H), 7.90–7.94 (m, 1H), 7.52–7.62 (m, 3H), 7.49 (dd, *J* = 8.2, 7.1 Hz, 1H), 6.96 (s, 1H), 3.52–3.89 (m, 4H), 3.45 (broad s, 1H), 3.31 (broad s, 1H), 2.94–3.13 (m, 2H), 2.25–2.39 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 167.0, 134.2, 131.1, 130.5,

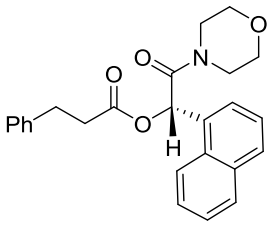
129.8, 129.3, 127.6, 127.4, 126.5, 125.5, 122.7, 69.9, 66.8, 66.0, 47.7, 45.8, 42.7, 31.1, 29.7. IR (ATR): 3064, 2955, 2853, 1725, 1662, 1455, 1431, 1224, 1118, 1004, 801, 773, 726 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{22}H_{27}NO_4Na$ $[M+Na]^+$: 392.1838, found: 392.1842. SFC analysis: 92% *ee*, 150 mm CHIRALPAK AD-H, 10% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 1.60 min, t_{R2} (major) = 1.92 min. $[\alpha]^{28}_D$ +124 (*c* = 1.5, $CHCl_3$).

(*S*)-2-morpholino-1-(naphthalen-1-yl)-2-oxoethyl hexanoate (5e)



The product was purified by preparative TLC (eluting with 3:2 hexanes/EtOAc) and isolated as a colorless oil (26.2 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.54–7.63 (m, 3H), 7.45–7.52 (m, 1H), 6.96 (s, 1H), 3.55–3.87 (m, 4H), 3.45 (broad s, 1H), 3.31 (broad s, 1H), 2.97–3.16 (m, 2H), 2.44 (dtd, *J* = 31.1, 15.6, 7.6 Hz, 2H), 1.56–1.79 (m, 2H), 1.18–1.37 (m, 4H), 0.75–0.91 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.0, 134.2, 131.2, 130.6, 129.6, 129.3, 127.6, 127.5, 126.5, 125.5, 122.7, 70.1, 66.9, 66.0, 45.8, 42.7, 34.1, 31.4, 24.6, 22.4, 14.0. IR (ATR): 3049, 2959, 2923, 2853, 1733, 1658, 1459, 1427, 1231, 1157, 1118, 1000, 801, 777, 730 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd for $C_{22}H_{27}NO_4Na$ $[M+Na]^+$: 392.1838, found: 392.1833. SFC analysis: 95% *ee*, 150 mm CHIRALCEL OD-H, 10% *i*PrOH, 4.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (major) = 1.34 min, t_{R2} (minor) = 2.10 min. $[\alpha]^{25}_D$ +132 (*c* = 1.4, $CHCl_3$).

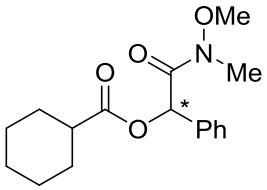
(*S*)-2-morpholino-1-(naphthalen-1-yl)-2-oxoethyl 3-phenylpropanoate (5f)



The product was purified by preparative TLC (eluting with 50:40:10 hexanes/EtOAc/Et_2O) and isolated as a colorless oil (36.3 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.85 (m, 3H), 7.62 – 7.53 (m, 3H), 7.50 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.20–7.29 (m, 2H), 7.17 (td, *J* = 6.9, 6.5, 1.6 Hz, 3H), 6.97 (s, 1H), 3.50–3.92 (m, 4H), 3.45 (broad s, 1H), 3.30 (broad s, 1H), 2.96–3.14 (m, 4H), 2.72–2.88 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 166.9, 140.4, 134.1, 131.2, 130.7, 129.4, 129.3, 128.5, 128.4, 127.6, 127.6, 126.5, 126.3, 125.4, 122.6, 70.3, 66.8, 66.0, 45.8, 42.7, 35.6, 30.8. IR (ATR): 3068, 3025, 2966, 2919, 2861, 1733, 1662, 1451, 1435, 1271, 1228, 1145, 997, 906, 797, 773, 730 cm^{-1}. HRMS (ESI-TOF) *m/z* calc'd

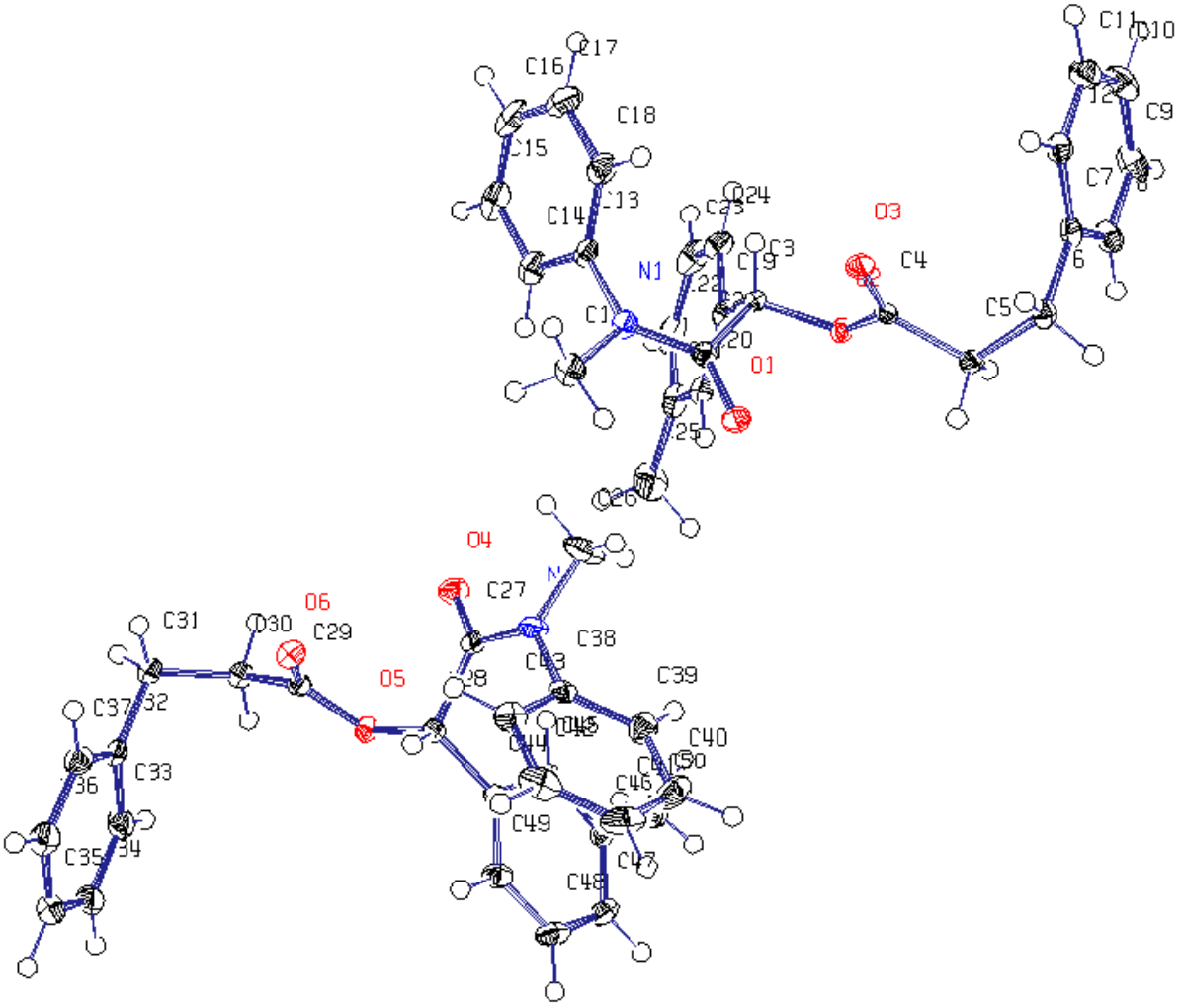
for $C_{25}H_{25}NO_4Na$ $[M+Na]^+$: 426.1681, found: 426.1687. SFC analysis: 94% *ee*, 250 mm CHIRALPAK IA, 10% *i*PrOH, 5.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 5.69 min, t_{R2} (major) = 6.42 min. $[\alpha]^{28}_D$ +98 (*c* = 1.7, $CHCl_3$).

2-(Methoxy(methyl)amino)-2-oxo-1-phenylethyl cyclohexanecarboxylate (6)



The product was purified by preparative tlc (eluting with 7:3 hexanes/EtOAc) and isolated as a colorless liquid (28.4 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.53 (m, 2H), 7.30–7.43 (m, 3H), 6.30 (s, 1H), 3.63 (s, 3H), 3.16 (s, 3H), 2.45 (tt, *J* = 11.3, 3.7 Hz, 1H), 2.05 (d, *J* = 12.8 Hz, 1H), 1.92 (d, *J* = 12.9 Hz, 1H), 1.67–1.82 (m, 2H), 1.58–1.66 (m, Hz, 1H), 1.42–1.57 (m, 2H), 1.15–1.35 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 169.0, 134.6, 129.1, 128.8, 128.4, 72.9, 61.1, 42.9, 32.3, 29.1, 28.9, 25.9, 25.5, 25.4. IR (ATR): 2932, 2855, 1731, 1678, 1451, 1386, 1245, 1163, 1130, 1040, 981, 915, 757, 731, 696. HRMS (ESI-TOF) *m/z* calc'd for $C_{17}H_{23}NO_4Na$ $[M+Na]^+$: 328.1525, found: 328.1517. SFC analysis: 51% *ee*, 250 mm CHIRALPAK IC, 10% *i*PrOH, 3.0 mL/min, 220 nm, 44 ℃, nozzle pressure = 200 bar CO_2, t_{R1} (minor) = 3.16 min, t_{R2} (major) = 3.89 min.

6. X-ray Crystallographic Data for 3c



A colorless crystal of approximate dimensions 0.407 x 0.310 x 0.196 mm was mounted on a glass fiber and transferred to a Bruker SMART APEX II diffractometer. The APEX2[17] program package was used to determine the unit-cell parameters and for data collection (25 sec/frame scan time for a sphere of diffraction data). The raw frame data was processed using SAINT[18] and SADABS[19] to yield the reflection data file. Subsequent calculations were carried out using the SHELXTL[20] program. The diffraction symmetry was 2/*m* and the systematic absences were

[17] APEX2 Version 2013.6-2, Bruker AXS, Inc.; Madison, WI 2013.
[18] SAINT Version 8.34a, Bruker AXS, Inc.; Madison, WI 2013.
[19] Sheldrick, G. M. SADABS, Version 2012/1, Bruker AXS, Inc.; Madison, WI 2012.
[20] Sheldrick, G. M. SHELXTL, Version 2013/4, Bruker AXS, Inc.; Madison, WI 2013.

consistent with the monoclinic space groups $P2_1$ and $P2_1/m$. It was later determined that space group $P2_1$ was correct.

The structure was solved by direct methods and refined on F^2 by full-matrix least-squares techniques. The analytical scattering factors[21] for neutral atoms were used throughout the analysis. There were two molecules per asymmetric unit. Hydrogen atoms were located from a difference-Fourier map and refined (x,y,z and U_{iso}).

At convergence, wR2 = 0.0865 and Goof = 1.054 for 723 variables refined against 10119 data (0.75 Å), R1 = 0.0334 for those 9473 data with $I > 2.0\sigma(I)$. *The absolute structure was assigned by refinement of the Flack[22] parameter*.

Table 1. Crystal data and structure refinement for vmd14.

Identification code	vmd14 (Kevin Kou)	
Empirical formula	$C_{25}\ H_{25}\ N\ O_3$	
Formula weight	387.46	
Temperature	88(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.0700(7) Å	α= 90 °.
	b = 10.0886(8) Å	β= 91.0402(9) °.
	c = 23.1150(18) Å	γ = 90 °.
Volume	2114.8(3) $Å^3$	
Z	4	
Density (calculated)	1.217 Mg/m^3	
Absorption coefficient	0.079 mm^{-1}	
F(000)	824	
Crystal color	colorless	
Crystal size	0.407 x 0.310 x 0.196 mm^3	
Theta range for data collection	0.881 to 28.305 °	
Index ranges	$-12 \le h \le 11$, $-13 \le k \le 13$, $-30 \le l \le 30$	

[21] International Tables for X-Ray Crystallography 1992, Vol. C., Dordrecht: Kluwer Academic Publishers.
[22] Flack, H. D., Parsons, S. *Acta. Cryst.* A60, s61, 2004.

Reflections collected	24823
Independent reflections	10119 [R(int) = 0.0167]
Completeness to theta = 25.242 °	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8621 and 0.8209
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10119 / 1 / 723
Goodness-of-fit on F^2	1.054
Final R indices [I>2sigma(I) = 9473 data]	R1 = 0.0334, wR2 = 0.0844
R indices (all data, 0.75 Å)	R1 = 0.0368, wR2 = 0.0865
Absolute structure parameter	0.0(2)
Largest diff. peak and hole	0.243 and -0.185 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for vmd14. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-992(1)	9095(1)	-3520(1)	19(1)
O(2)	-1617(1)	8153(1)	-4562(1)	14(1)
O(3)	-948(1)	10264(1)	-4736(1)	17(1)
N(1)	-3233(2)	10040(2)	-3386(1)	17(1)
C(1)	-2742(2)	10718(2)	-2856(1)	23(1)
C(2)	-2267(2)	9283(2)	-3682(1)	14(1)
C(3)	-2866(2)	8664(2)	-4251(1)	13(1)
C(4)	-673(2)	9095(2)	-4750(1)	13(1)
C(5)	735(2)	8483(2)	-4958(1)	15(1)
C(6)	1465(2)	9318(2)	-5429(1)	18(1)
C(7)	582(2)	9304(2)	-5990(1)	17(1)
C(8)	379(2)	8118(2)	-6293(1)	22(1)
C(9)	-446(3)	8088(2)	-6806(1)	27(1)
C(10)	-1070(2)	9241(2)	-7026(1)	28(1)
C(11)	-877(2)	10430(2)	-6728(1)	25(1)
C(12)	-59(2)	10458(2)	-6212(1)	20(1)
C(13)	-4757(2)	10197(2)	-3554(1)	17(1)
C(14)	-5820(2)	9412(2)	-3296(1)	22(1)
C(15)	-7301(2)	9585(2)	-3448(1)	28(1)
C(16)	-7704(2)	10521(2)	-3861(1)	31(1)
C(17)	-6644(2)	11298(2)	-4118(1)	31(1)
C(18)	-5161(2)	11149(2)	-3962(1)	24(1)
C(19)	-3900(2)	7514(2)	-4159(1)	15(1)
C(20)	-3602(2)	6576(2)	-3732(1)	17(1)
C(21)	-4537(2)	5495(2)	-3646(1)	23(1)
C(22)	-5778(2)	5373(2)	-4007(1)	28(1)
C(23)	-6093(2)	6306(2)	-4433(1)	28(1)
C(24)	-5159(2)	7379(2)	-4511(1)	21(1)
C(25)	-4209(3)	4506(2)	-3172(1)	35(1)
O(4)	-3904(1)	6304(1)	-1504(1)	21(1)
O(5)	-3323(1)	5620(1)	-415(1)	15(1)
O(6)	-4075(1)	7736(1)	-321(1)	18(1)

N(2)	-1663(2)	7206(2)	-1668(1)	19(1)
C(26)	-2063(3)	7420(3)	-2279(1)	35(1)
C(27)	-2650(2)	6558(2)	-1337(1)	15(1)
C(28)	-2080(2)	6106(2)	-735(1)	14(1)
C(29)	-4300(2)	6567(2)	-260(1)	15(1)
C(30)	-5676(2)	5957(2)	-21(1)	16(1)
C(31)	-6371(2)	6811(2)	450(1)	19(1)
C(32)	-5458(2)	6850(2)	1003(1)	18(1)
C(33)	-5085(2)	5683(2)	1295(1)	24(1)
C(34)	-4248(3)	5715(2)	1806(1)	27(1)
C(35)	-3794(2)	6912(2)	2040(1)	27(1)
C(36)	-4158(2)	8083(2)	1755(1)	25(1)
C(37)	-4972(2)	8052(2)	1238(1)	21(1)
C(38)	-162(2)	7445(2)	-1490(1)	17(1)
C(39)	961(2)	6718(2)	-1744(1)	24(1)
C(40)	2420(2)	6946(2)	-1574(1)	30(1)
C(41)	2745(2)	7881(2)	-1153(1)	31(1)
C(42)	1632(2)	8604(2)	-903(1)	29(1)
C(43)	163(2)	8401(2)	-1077(1)	22(1)
C(44)	-1002(2)	4971(2)	-780(1)	14(1)
C(45)	-1225(2)	3969(2)	-1184(1)	16(1)
C(46)	-248(2)	2900(2)	-1222(1)	19(1)
C(47)	973(2)	2868(2)	-847(1)	22(1)
C(48)	1209(2)	3873(2)	-445(1)	23(1)
C(49)	229(2)	4924(2)	-407(1)	19(1)
C(50)	-521(3)	1822(2)	-1663(1)	27(1)

Table 3. Bond lengths [Å] and angles [°] for vmd14.

O(1)-C(2)	1.224(2)
O(2)-C(4)	1.356(2)
O(2)-C(3)	1.447(2)
O(3)-C(4)	1.206(2)
N(1)-C(2)	1.357(2)
N(1)-C(13)	1.438(2)
N(1)-C(1)	1.466(2)
C(2)-C(3)	1.545(2)
C(3)-C(19)	1.509(2)
C(4)-C(5)	1.505(2)
C(5)-C(6)	1.535(2)
C(6)-C(7)	1.513(2)
C(7)-C(12)	1.395(3)
C(7)-C(8)	1.397(3)
C(8)-C(9)	1.391(3)
C(9)-C(10)	1.386(3)
C(10)-C(11)	1.393(3)
C(11)-C(12)	1.393(3)
C(13)-C(14)	1.390(3)
C(13)-C(18)	1.391(3)
C(14)-C(15)	1.393(3)
C(15)-C(16)	1.387(4)
C(16)-C(17)	1.383(4)
C(17)-C(18)	1.393(3)
C(19)-C(20)	1.390(3)
C(19)-C(24)	1.397(2)
C(20)-C(21)	1.398(3)
C(21)-C(22)	1.394(3)
C(21)-C(25)	1.507(3)
C(22)-C(23)	1.389(3)
C(23)-C(24)	1.389(3)
O(4)-C(27)	1.222(2)
O(5)-C(29)	1.355(2)
O(5)-C(28)	1.446(2)
O(6)-C(29)	1.206(2)

N(2)-C(27)	1.357(2)
N(2)-C(38)	1.436(2)
N(2)-C(26)	1.466(2)
C(27)-C(28)	1.545(2)
C(28)-C(44)	1.510(2)
C(29)-C(30)	1.506(2)
C(30)-C(31)	1.531(2)
C(31)-C(32)	1.512(3)
C(32)-C(33)	1.395(3)
C(32)-C(37)	1.396(3)
C(33)-C(34)	1.393(3)
C(34)-C(35)	1.383(3)
C(35)-C(36)	1.390(3)
C(36)-C(37)	1.394(3)
C(38)-C(43)	1.385(3)
C(38)-C(39)	1.394(3)
C(39)-C(40)	1.392(3)
C(40)-C(41)	1.384(4)
C(41)-C(42)	1.380(4)
C(42)-C(43)	1.399(3)
C(44)-C(45)	1.389(3)
C(44)-C(49)	1.398(2)
C(45)-C(46)	1.400(2)
C(46)-C(47)	1.394(3)
C(46)-C(50)	1.508(3)
C(47)-C(48)	1.389(3)
C(48)-C(49)	1.388(3)

C(4)-O(2)-C(3)	114.50(13)
C(2)-N(1)-C(13)	123.49(15)
C(2)-N(1)-C(1)	119.70(15)
C(13)-N(1)-C(1)	116.79(15)
O(1)-C(2)-N(1)	123.24(16)
O(1)-C(2)-C(3)	120.89(16)
N(1)-C(2)-C(3)	115.87(14)
O(2)-C(3)-C(19)	106.89(13)
O(2)-C(3)-C(2)	107.48(13)

C(19)-C(3)-C(2)	113.63(14)
O(3)-C(4)-O(2)	122.98(16)
O(3)-C(4)-C(5)	125.91(16)
O(2)-C(4)-C(5)	111.10(14)
C(4)-C(5)-C(6)	112.38(15)
C(7)-C(6)-C(5)	111.98(15)
C(12)-C(7)-C(8)	118.75(17)
C(12)-C(7)-C(6)	121.16(17)
C(8)-C(7)-C(6)	120.09(17)
C(9)-C(8)-C(7)	120.7(2)
C(10)-C(9)-C(8)	120.3(2)
C(9)-C(10)-C(11)	119.66(19)
C(10)-C(11)-C(12)	120.05(19)
C(11)-C(12)-C(7)	120.62(18)
C(14)-C(13)-C(18)	120.54(17)
C(14)-C(13)-N(1)	119.48(17)
C(18)-C(13)-N(1)	119.96(17)
C(13)-C(14)-C(15)	119.6(2)
C(16)-C(15)-C(14)	119.9(2)
C(17)-C(16)-C(15)	120.29(19)
C(16)-C(17)-C(18)	120.3(2)
C(13)-C(18)-C(17)	119.3(2)
C(20)-C(19)-C(24)	119.58(17)
C(20)-C(19)-C(3)	120.65(15)
C(24)-C(19)-C(3)	119.76(17)
C(19)-C(20)-C(21)	121.41(18)
C(22)-C(21)-C(20)	117.97(19)
C(22)-C(21)-C(25)	121.54(19)
C(20)-C(21)-C(25)	120.5(2)
C(23)-C(22)-C(21)	121.21(18)
C(24)-C(23)-C(22)	120.14(19)
C(23)-C(24)-C(19)	119.68(19)
C(29)-O(5)-C(28)	114.59(13)
C(27)-N(2)-C(38)	123.40(15)
C(27)-N(2)-C(26)	117.41(16)
C(38)-N(2)-C(26)	117.93(16)
O(4)-C(27)-N(2)	122.83(17)

O(4)-C(27)-C(28)	121.18(16)
N(2)-C(27)-C(28)	115.95(15)
O(5)-C(28)-C(44)	106.87(13)
O(5)-C(28)-C(27)	108.04(13)
C(44)-C(28)-C(27)	111.68(14)
O(6)-C(29)-O(5)	123.07(16)
O(6)-C(29)-C(30)	125.87(16)
O(5)-C(29)-C(30)	111.05(14)
C(29)-C(30)-C(31)	112.67(15)
C(32)-C(31)-C(30)	112.94(15)
C(33)-C(32)-C(37)	118.21(17)
C(33)-C(32)-C(31)	120.73(18)
C(37)-C(32)-C(31)	121.06(17)
C(34)-C(33)-C(32)	121.0(2)
C(35)-C(34)-C(33)	120.4(2)
C(34)-C(35)-C(36)	119.36(19)
C(35)-C(36)-C(37)	120.3(2)
C(36)-C(37)-C(32)	120.75(19)
C(43)-C(38)-C(39)	120.61(18)
C(43)-C(38)-N(2)	120.27(17)
C(39)-C(38)-N(2)	119.11(17)
C(40)-C(39)-C(38)	119.5(2)
C(41)-C(40)-C(39)	120.0(2)
C(42)-C(41)-C(40)	120.41(19)
C(41)-C(42)-C(43)	120.2(2)
C(38)-C(43)-C(42)	119.3(2)
C(45)-C(44)-C(49)	119.67(17)
C(45)-C(44)-C(28)	120.72(15)
C(49)-C(44)-C(28)	119.62(16)
C(44)-C(45)-C(46)	121.19(17)
C(47)-C(46)-C(45)	118.41(17)
C(47)-C(46)-C(50)	121.53(18)
C(45)-C(46)-C(50)	120.06(18)
C(48)-C(47)-C(46)	120.65(18)
C(49)-C(48)-C(47)	120.63(17)
C(48)-C(49)-C(44)	119.46(18)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for vmd14. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	13(1)	26(1)	18(1)	0(1)	-3(1)	0(1)
O(2)	15(1)	12(1)	16(1)	0(1)	3(1)	1(1)
O(3)	19(1)	13(1)	20(1)	2(1)	-1(1)	1(1)
N(1)	14(1)	20(1)	18(1)	-6(1)	-2(1)	-1(1)
C(1)	21(1)	27(1)	21(1)	-11(1)	-4(1)	-2(1)
C(2)	14(1)	14(1)	15(1)	1(1)	0(1)	-2(1)
C(3)	12(1)	14(1)	14(1)	0(1)	0(1)	2(1)
C(4)	15(1)	15(1)	10(1)	1(1)	-2(1)	1(1)
C(5)	16(1)	14(1)	15(1)	0(1)	0(1)	1(1)
C(6)	16(1)	19(1)	18(1)	-1(1)	2(1)	-3(1)
C(7)	16(1)	19(1)	15(1)	-1(1)	5(1)	-5(1)
C(8)	27(1)	19(1)	19(1)	0(1)	4(1)	-4(1)
C(9)	38(1)	25(1)	19(1)	-4(1)	4(1)	-11(1)
C(10)	30(1)	36(1)	17(1)	2(1)	-3(1)	-11(1)
C(11)	26(1)	26(1)	23(1)	4(1)	0(1)	-1(1)
C(12)	21(1)	18(1)	20(1)	-1(1)	4(1)	-2(1)
C(13)	13(1)	21(1)	18(1)	-9(1)	-2(1)	2(1)
C(14)	18(1)	22(1)	25(1)	-8(1)	1(1)	-1(1)
C(15)	18(1)	29(1)	37(1)	-16(1)	2(1)	-4(1)
C(16)	17(1)	34(1)	40(1)	-21(1)	-7(1)	7(1)
C(17)	27(1)	31(1)	33(1)	-7(1)	-9(1)	11(1)
C(18)	23(1)	22(1)	26(1)	-6(1)	-1(1)	4(1)
C(19)	12(1)	15(1)	18(1)	-4(1)	2(1)	1(1)
C(20)	16(1)	18(1)	19(1)	-2(1)	3(1)	-1(1)
C(21)	23(1)	17(1)	30(1)	-3(1)	11(1)	-1(1)
C(22)	19(1)	20(1)	46(1)	-12(1)	11(1)	-7(1)
C(23)	16(1)	27(1)	42(1)	-13(1)	-4(1)	-2(1)
C(24)	18(1)	21(1)	25(1)	-7(1)	-4(1)	1(1)
C(25)	41(1)	23(1)	40(1)	9(1)	13(1)	-5(1)
O(4)	15(1)	24(1)	24(1)	2(1)	-4(1)	-2(1)
O(5)	14(1)	14(1)	18(1)	0(1)	3(1)	-1(1)
O(6)	17(1)	14(1)	24(1)	-3(1)	-1(1)	-2(1)

N(2)	16(1)	24(1)	16(1)	5(1)	-4(1)	-2(1)
C(26)	30(1)	53(2)	22(1)	19(1)	-8(1)	-10(1)
C(27)	15(1)	13(1)	18(1)	0(1)	-1(1)	2(1)
C(28)	13(1)	14(1)	14(1)	0(1)	0(1)	-2(1)
C(29)	14(1)	16(1)	14(1)	-2(1)	-2(1)	0(1)
C(30)	15(1)	16(1)	19(1)	-2(1)	0(1)	-2(1)
C(31)	15(1)	21(1)	21(1)	0(1)	2(1)	3(1)
C(32)	16(1)	21(1)	18(1)	-1(1)	5(1)	4(1)
C(33)	32(1)	21(1)	21(1)	-1(1)	4(1)	4(1)
C(34)	36(1)	26(1)	20(1)	5(1)	3(1)	10(1)
C(35)	26(1)	35(1)	20(1)	-1(1)	1(1)	4(1)
C(36)	23(1)	25(1)	28(1)	-2(1)	1(1)	-2(1)
C(37)	19(1)	21(1)	24(1)	3(1)	3(1)	1(1)
C(38)	15(1)	18(1)	18(1)	8(1)	0(1)	-2(1)
C(39)	22(1)	24(1)	26(1)	2(1)	4(1)	-1(1)
C(40)	17(1)	29(1)	44(1)	12(1)	7(1)	2(1)
C(41)	19(1)	32(1)	41(1)	17(1)	-9(1)	-9(1)
C(42)	31(1)	25(1)	29(1)	5(1)	-8(1)	-13(1)
C(43)	22(1)	19(1)	24(1)	4(1)	0(1)	-4(1)
C(44)	13(1)	16(1)	14(1)	4(1)	1(1)	0(1)
C(45)	14(1)	17(1)	16(1)	2(1)	1(1)	-1(1)
C(46)	18(1)	18(1)	20(1)	3(1)	6(1)	0(1)
C(47)	15(1)	20(1)	30(1)	8(1)	4(1)	4(1)
C(48)	16(1)	24(1)	28(1)	8(1)	-6(1)	-2(1)
C(49)	18(1)	19(1)	20(1)	3(1)	-4(1)	-3(1)
C(50)	32(1)	22(1)	26(1)	-5(1)	5(1)	4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for vmd14.

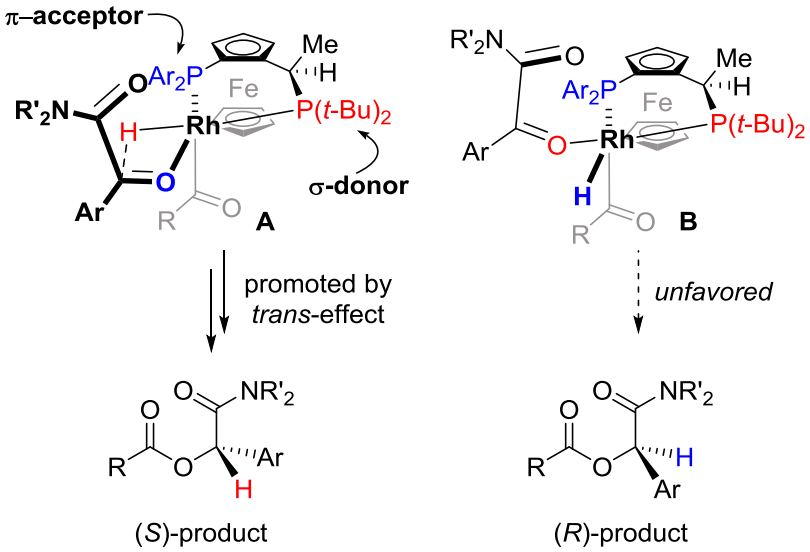
	x	y	z	U(eq)
H(1A)	-1690(30)	10560(30)	-2782(12)	36(7)
H(1B)	-3350(30)	10400(30)	-2513(11)	31(6)
H(1C)	-2980(30)	11600(30)	-2903(14)	49(8)
H(3A)	-3310(20)	9350(20)	-4483(9)	13(5)
H(5A)	540(20)	7620(20)	-5094(10)	18(5)
H(5B)	1360(30)	8420(30)	-4607(11)	25(6)
H(6A)	1620(30)	10220(30)	-5294(11)	29(6)
H(6B)	2460(30)	8960(30)	-5482(11)	27(6)
H(8A)	790(30)	7330(30)	-6143(11)	29(6)
H(9A)	-600(30)	7270(30)	-6998(12)	35(7)
H(10A)	-1660(30)	9220(30)	-7397(12)	34(7)
H(11A)	-1320(30)	11300(30)	-6863(11)	29(6)
H(12A)	50(30)	11320(30)	-5994(11)	29(6)
H(14A)	-5480(30)	8710(30)	-3012(11)	31(7)
H(15A)	-7990(30)	9110(30)	-3271(12)	36(7)
H(16A)	-8740(30)	10590(30)	-3947(11)	34(7)
H(17A)	-6910(30)	11960(30)	-4410(13)	43(8)
H(18A)	-4430(30)	11680(30)	-4142(12)	38(7)
H(20A)	-2750(30)	6650(30)	-3494(11)	27(6)
H(22A)	-6430(30)	4640(30)	-3931(12)	37(7)
H(23A)	-6940(30)	6200(30)	-4663(12)	33(7)
H(24A)	-5350(30)	8070(30)	-4797(11)	29(6)
H(25A)	-4880(30)	3700(30)	-3175(13)	47(8)
H(25B)	-4340(30)	4860(30)	-2803(14)	44(8)
H(25C)	-3120(40)	4200(30)	-3154(14)	57(9)
H(26A)	-3090(30)	7690(30)	-2306(13)	48(8)
H(26B)	-2000(50)	6540(50)	-2500(20)	103(16)
H(26C)	-1400(30)	7980(30)	-2429(13)	46(8)
H(28A)	-1690(20)	6820(20)	-535(10)	17(5)
H(30A)	-5470(20)	5030(20)	131(9)	13(5)
H(30B)	-6350(30)	5920(30)	-356(10)	23(6)

H(31A)	-6600(30)	7710(30)	312(11)	26(6)
H(31B)	-7340(30)	6470(20)	530(10)	23(6)
H(33A)	-5390(30)	4850(30)	1146(10)	20(6)
H(34A)	-4020(30)	4880(30)	1982(11)	29(6)
H(35A)	-3210(30)	6890(30)	2413(12)	32(7)
H(36A)	-3840(30)	9000(30)	1918(11)	33(7)
H(37A)	-5230(20)	8880(20)	1047(10)	18(6)
H(39A)	700(30)	6070(30)	-2014(12)	33(7)
H(40A)	3220(30)	6450(30)	-1768(12)	36(7)
H(41A)	3790(30)	8060(30)	-1049(11)	31(6)
H(42A)	1840(30)	9250(30)	-599(14)	51(9)
H(43A)	-650(30)	8920(20)	-916(11)	25(6)
H(45A)	-2110(30)	4000(20)	-1451(10)	22(6)
H(47A)	1670(20)	2140(20)	-872(10)	21(6)
H(48A)	2070(30)	3830(30)	-184(11)	29(7)
H(49A)	390(20)	5620(30)	-136(10)	23(6)
H(50A)	240(30)	1330(30)	-1716(13)	47(9)
H(50B)	-700(40)	2240(40)	-2056(17)	72(11)
H(50C)	-1450(40)	1310(30)	-1552(14)	57(9)

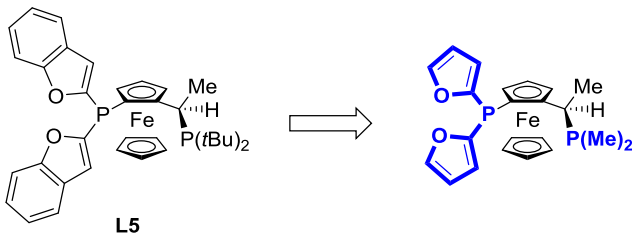
7. Mechanistic Studies

i) DFT

DFT was used to probe the relative stability of two acyl-Rh-hydride intermediates prior to product-determining ketone insertion. The intermediates are optimized at the M06/6-311G** level of theory (SDD for Rh) and verified by harmonic frequency analysis. We chose the M06 functional because it has been shown to be excellent for the study of organometallic chemistry[23] and better than the B3LYP functional.[24] Coordinates to the optimized structures are provided.

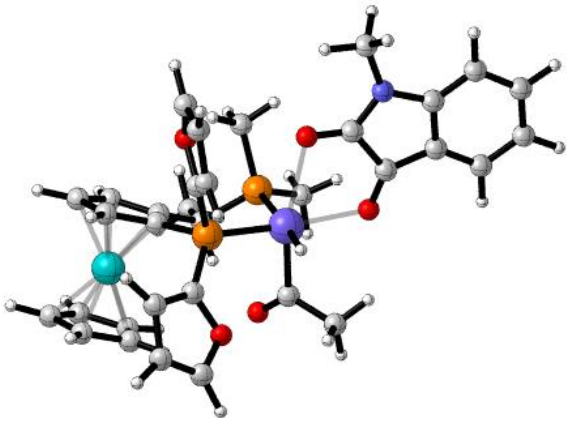


To ease computational demand, *N*-methylisatin and acetaldehyde were chosen as the model substrates and ligand **L5** was simplified as illustrated below:

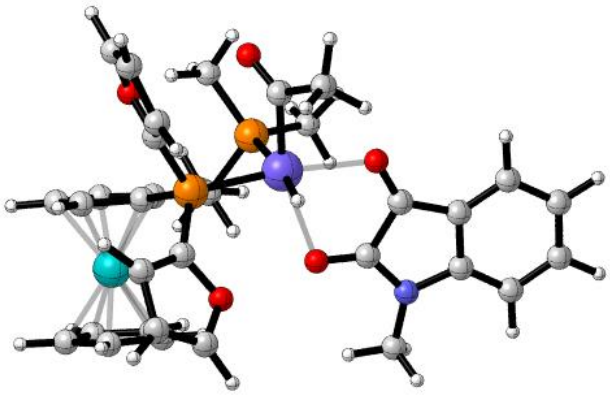


[23] Zhao, Y.; Truhlar, D. G. *Theor. Chem. Account* **2008**, *120*, 215.
[24] Peverati, R.; Truhlar, D. G. The Quest for a Universal Density Functional: The Accuracy of Density Functionals across a broad Spectrum of Databases in Chemistry and Physics, preprint (Dec. 5, 2012), arXiv:1212.0944, http://arxiv.org/pdf/1212.0944.pdf.

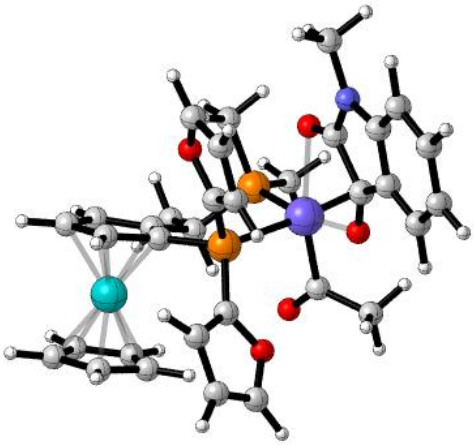
Optimized Structures



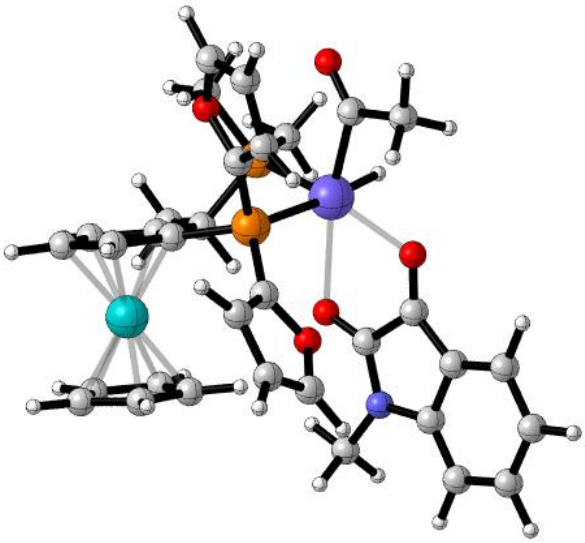
A (acyl "down")
5.6 kcal/mol



A' (acyl "up")
10.7 kcal/mol



B (acyl "down")
0 kcal/mol



B' (acyl "up")
1.4 kcal/mol

These computed data support our hypothesis. Complex B is indeed stabilized (less reactive) relative to complex A (See discussion in manuscript). *Although our model for enantioinduction correctly predicts the absolute configuration for the products obtained, it is limited such that it doesn't take into account the possibility of the involvement of a second molecule of Rh-catalyst.*

Rhodium complex A
M06 SCF Energy: -2625.7344686
M06 Free energy: -2625.201332

Cartesian coordinates

Atom	X	Y	Z
Rh	0.876573	-0.119131	0.705155
P	-0.957393	1.03686	0.171941
P	0.39549	-1.878254	-0.897367
C	-2.150833	0.253879	-0.932769
C	-2.200412	-1.106261	-1.419504
C	-1.410232	-2.292029	-0.937087

H	-1.63021	-2.431304	0.128597
O	2.946415	-0.912327	1.193338
O	2.53495	0.917993	-0.94435
C	3.632634	0.553577	-0.586326
C	3.875069	-0.443505	0.556455
N	4.855227	0.893052	-1.070572
C	5.298411	-0.620796	0.631668
C	5.85871	0.205184	-0.360756
C	6.102029	-1.391384	1.461476
C	7.475198	-1.330935	1.285838
H	8.133182	-1.918856	1.914926
C	8.015762	-0.511184	0.29818
H	9.09357	-0.475254	0.175623
C	7.221436	0.271370	-0.542243
H	7.670337	0.902895	-1.301018
C	5.085576	1.834867	-2.143619
H	4.11559	2.212468	-2.469755
H	5.696221	2.672707	-1.79478
H	5.585058	1.348399	-2.986621
C	0.840375	-1.530997	-2.635063
H	0.558059	-2.35505	-3.298309
H	0.341049	-0.611816	-2.957613
H	1.920640	-1.372268	-2.704692
C	1.226043	-3.466739	-0.536244
H	2.29897	-3.285922	-0.422754
H	0.847727	-3.856703	0.414608
H	1.072901	-4.211808	-1.322564
O	-1.039699	-1.678623	2.117193
C	-0.02007	-1.062268	2.214364
H	1.088987	1.133782	1.700117
C	0.767558	-0.973613	3.499258
H	1.84392	-1.004055	3.328827
H	0.528852	-0.009259	3.957866
H	0.455024	-1.783154	4.164715
H	5.652565	-2.019891	2.223648
C	-0.418049	2.453553	-0.809212
C	-1.862284	1.840303	1.506952
C	-0.009048	3.709957	-0.486317
H	-0.054696	4.160247	0.49451
C	-2.725887	2.891732	1.536112
C	-3.187219	2.993365	2.877381
C	-2.57093	1.997543	3.559459
O	-1.761732	1.287606	2.745754
O	-0.190767	2.210826	-2.127926
C	0.4849	4.286568	-1.689542
C	0.350342	3.333768	-2.644107
H	0.873395	5.284085	-1.826918
H	0.564893	3.310417	-3.701043
H	-2.596507	1.683153	4.591002
H	-2.994268	3.518417	0.697737
H	-3.878732	3.716615	3.281561
C	-3.143472	1.011359	-1.63852
C	-3.210455	-1.142065	-2.424199
C	-3.789819	0.147335	-2.550575
H	-4.610456	0.411394	-3.203401
H	-3.527671	-2.021221	-2.968384
H	-3.355524	2.062758	-1.489455
C	-1.751518	-3.570403	-1.684709
H	-2.825038	-3.775389	-1.603036
H	-1.505968	-3.507964	-2.751032
H	-1.232323	-4.433657	-1.26169
Fe	-3.979146	-0.532468	-0.628853
C	-5.259379	0.24544	0.75537
C	-4.324063	-0.620853	1.384197
C	-4.455390	-1.908155	0.800928
C	-5.972898	-0.510562	-0.21515
C	-5.475576	-1.842036	-0.186704
H	-6.733395	-0.131579	-0.884227
H	-5.792269	-2.652148	-0.830346
H	-3.857444	-2.775232	1.05207
H	-3.60321	-0.351341	2.145498
H	-5.381631	1.301257	0.957894

Rhodium complex A'

M06 SCF Energy: -2625.7291548

M06 Free energy: -2625.193168

Cartesian coordinates

Atom	X	Y	Z
Rh	0.796154	1.151548	0.106663
P	-1.386125	0.928682	0.625387
P	0.404434	0.538744	-2.215089
C	-2.341413	-0.105292	-0.513769
C	-1.904975	-0.837157	-1.682044
C	-0.49543	-1.088650	-2.147552
H	0.043142	-1.629614	-1.354315
O	3.027207	1.286746	-0.094264
O	1.782581	-1.233347	0.408011
C	2.983302	-1.067694	0.420033
C	3.671455	0.276649	0.133607
N	3.974028	-1.966742	0.650117
C	5.083157	0.021167	0.202167
C	5.230698	-1.340835	0.522834
C	6.189485	0.841329	0.026379
C	7.449547	0.283098	0.171122
H	8.335784	0.89266	0.039427
C	7.581275	-1.066455	0.48806
H	8.575624	-1.487204	0.598942
C	6.477852	-1.903402	0.670871
H	6.611977	-2.950463	0.9194
C	3.768265	-3.362049	0.970377
H	2.693531	-3.541948	1.011205
H	4.211779	-4.004765	0.204218
H	4.208657	-3.601182	1.942605
C	-0.599464	1.579658	-3.324583
H	-0.802348	1.068454	-4.271417
H	-1.539193	1.840483	-2.830242
H	-0.061656	2.51062	-3.51931
C	1.910032	0.203337	-3.204943
H	2.540362	1.097267	-3.190754
H	2.475600	-0.624252	-2.763605
H	1.676418	-0.047750	-4.244415
O	-0.058173	3.571382	-1.080989
C	0.593576	3.118387	-0.194719
H	0.928063	1.419543	1.685993
C	1.415911	3.950627	0.757653
H	0.876568	3.999696	1.708614
H	2.387819	3.496495	0.953075
H	1.527631	4.95707	0.345028
H	6.055768	1.890234	-0.218772
C	-2.320003	2.472929	0.621764
C	-1.723565	0.338194	2.296906
C	-2.449168	3.473073	1.537114
H	-2.119294	3.442127	2.565758
C	-2.760286	0.514232	3.161658

C	-2.472313	-0.290441	4.299072
C	-1.288492	-0.895503	4.037051
O	-0.818191	-0.525575	2.828439
O	-2.828552	2.865754	-0.573856
C	-3.091367	4.546797	0.861248
C	-3.290765	4.122092	-0.410104
H	-3.373879	5.504431	1.27055
H	-3.743988	4.574124	-1.278109
H	-0.670091	-1.580766	4.595387
H	-3.624099	1.143254	3.005485
H	-3.064304	-0.394285	5.195495
C	-3.770036	-0.186707	-0.45209
C	-3.082931	-1.321994	-2.321387
C	-4.218041	-0.932456	-1.564459
H	-5.243855	-1.198371	-1.779951
H	-3.11006	-1.943348	-3.206407
H	-4.389221	0.249675	0.321732
C	-0.438008	-1.908409	-3.425429
H	-0.966589	-2.859009	-3.291724
H	-0.902929	-1.387634	-4.269827
H	0.592142	-2.148183	-3.700286
Fe	-2.927438	-2.03615	-0.413094
C	-3.125334	-2.846258	1.447186
C	-1.798798	-3.032147	0.962583
C	-1.874952	-3.776546	-0.244063
C	-4.015430	-3.478123	0.538205
C	-3.244287	-4.050553	-0.508587
H	-5.094609	-3.485693	0.607245
H	-3.633493	-4.570221	-1.373785
H	-1.038470	-4.055042	-0.873197
H	-0.896004	-2.630159	1.405254
H	-3.409132	-2.29524	2.334352

Rhodium complex B

M06 SCF Energy: -2625.7458127

M06 Free energy: -2625.210286

Cartesian coordinates

Atom	X	Y	Z
Rh	0.546313	1.438939	-0.977239
P	-0.267826	-0.545212	0.154829
P	-1.046295	2.762544	-0.104809
C	-1.780609	-0.323732	1.110094
C	-2.677666	0.809091	1.055049
C	-2.693724	1.929221	0.050247
H	-2.803686	1.502506	-0.954305
O	2.393216	0.223216	-1.578519
O	2.287856	1.777203	0.816897
C	3.225885	1.0678	0.519696
C	3.291915	0.212941	-0.754605
N	4.391647	0.86569	1.183537
C	4.551053	-0.482139	-0.696073
C	5.180200	-0.072883	0.493032
C	5.147499	-1.406217	-1.541641
C	6.383023	-1.923349	-1.1818
H	6.879655	-2.645454	-1.819395
C	6.992783	-1.513698	0.000787
H	7.960492	-1.927868	0.26556
C	6.404814	-0.583631	0.861021
H	6.904303	-0.279149	1.774216
C	4.726237	1.452643	2.460592
H	3.94132	2.164785	2.718379
H	4.776933	0.679917	3.235136
H	5.683396	1.978163	2.402246
C	-0.576027	3.292064	1.571211
H	-1.356721	3.925489	2.00578
H	-0.421074	2.415714	2.206474
H	0.361486	3.851515	1.517282
C	-1.362998	4.310423	-1.006816
H	-0.412208	4.834595	-1.126821
H	-1.761248	4.080303	-1.999141
H	-2.065632	4.951626	-0.467644
O	-1.671272	1.224609	-2.782434
C	-0.482525	1.171259	-2.660602
H	1.038361	2.819212	-1.624065
C	0.442479	0.836427	-3.81067
H	1.268202	1.546709	-3.873142
H	0.865534	-0.15847	-3.654979
H	-0.141132	0.844281	-4.734731
H	4.648185	-1.70814	-2.456962
C	0.92232	-1.034151	1.437267
C	-0.361729	-2.097212	-0.764604
C	2.02376	-1.83933	1.436204
H	2.315953	-2.518025	0.647469
C	-0.403152	-3.410398	-0.407731
C	-0.55555	-4.151503	-1.611635
C	-0.594646	-3.236398	-2.610711
O	-0.474759	-1.985519	-2.118681
O	0.858114	-0.344273	2.60438
C	2.666468	-1.638880	2.694286
C	1.916069	-0.725937	3.355317
H	3.555035	-2.132016	3.060976
H	1.980518	-0.282486	4.336928
H	-0.692744	-3.315292	-3.682098
H	-0.33613	-3.796819	0.599398
H	-0.623932	-5.223152	-1.719712
C	-2.219762	-1.187549	2.164212
C	-3.63432	0.617681	2.094322
C	-3.358295	-0.603559	2.764015
H	-3.943975	-1.029448	3.567137
H	-4.474131	1.265288	2.307503
H	-1.753444	-2.124661	2.442148
C	-3.836471	2.907785	0.286648
H	-4.788673	2.367467	0.314796
H	-3.735124	3.449278	1.234631
H	-3.914283	3.637412	-0.521657
Fe	-3.666618	-0.937118	0.76449
C	-4.011422	-2.741388	-0.118904
C	-3.745418	-1.752888	-1.106568
C	-4.717918	-0.727822	-0.974646
C	-5.151456	-2.325001	0.621358
C	-5.587454	-1.079670	0.093043
H	-5.589015	-2.845541	1.462326
H	-6.414885	-0.488151	0.461815
H	-4.767901	0.173500	-1.572429
H	-2.921123	-1.746275	-1.808738
H	-3.429434	-3.635721	0.058027

Rhodium complex B′

M06 SCF Energy: -2625.7429411

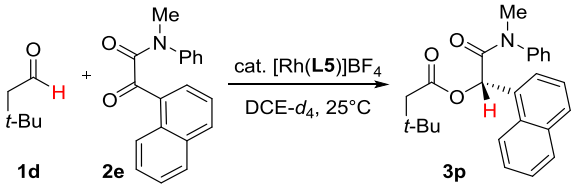
M06 Free energy: -2625.208109

Rh	0.09335	-1.730696	-1.030686
P	0.689022	-0.493928	0.973226
P	2.047635	-1.165934	-2.015252

C	1.916737	0.799157	0.675047
C	2.474467	1.176915	-0.605106
C	2.075336	0.695374	-1.978139
H	1.02374	0.954367	-2.157781
O	-2.107334	-1.999224	-0.441812
O	-1.215539	0.352252	-1.810291
C	-2.34656	0.200771	-1.401217
C	-2.842772	-1.059756	-0.672948
N	-3.397227	1.057252	-1.455501
C	-4.22457	-0.806693	-0.350677
C	-4.517697	0.484256	-0.8224
C	-5.176832	-1.554906	0.324388
C	-6.431765	-0.997054	0.52174
H	-7.201409	-1.555389	1.041851
C	-6.70904	0.282557	0.049127
H	-7.696695	0.702521	0.211136
C	-5.758713	1.048943	-0.629603
H	-5.999617	2.044339	-0.986673
C	-3.35654	2.387799	-2.020658
H	-2.380732	2.527764	-2.486627
H	-4.13386	2.504935	-2.780773
H	-3.491255	3.145248	-1.241154
C	3.655072	-1.678038	-1.342173
H	4.449217	-1.164515	-1.895348
H	3.729021	-1.438749	-0.280437
H	3.756612	-2.757719	-1.463438
C	2.162593	-1.672838	-3.758444
H	2.109834	-2.765397	-3.78085
H	1.315582	-1.277308	-4.324556
H	3.104928	-1.348293	-4.210206
O	1.850844	-3.941404	-0.573668
C	0.769271	-3.482256	-0.378636
H	-0.146743	-2.553112	-2.378966
C	-0.30259	-4.190023	0.425832
H	-0.772806	-3.525433	1.15344
H	-1.080707	-4.544582	-0.256125
H	0.159583	-5.03982	0.934663
H	-4.933833	-2.550355	0.682304

C	1.506936	-1.562758	2.186719
C	-0.600192	0.226571	2.025492
C	1.067696	-2.301925	3.242352
H	0.091964	-2.247296	3.702494
C	-0.658671	0.633836	3.321703
C	-1.961555	1.170219	3.526185
C	-2.606042	1.05196	2.341855
O	-1.800901	0.480248	1.416495
O	2.779681	-1.923106	1.869397
C	2.144438	-3.162679	3.603363
C	3.14902	-2.890127	2.739376
H	2.165833	-3.882236	4.407186
H	4.151056	-3.271385	2.623508
H	-3.606207	1.295528	2.012189
H	0.138930	0.552784	4.046201
H	-2.365219	1.581427	4.438826
C	2.592828	1.543992	1.69111
C	3.492589	2.136699	-0.334077
C	3.556118	2.367044	1.065406
H	4.204208	3.077862	1.559605
H	4.085810	2.654426	-1.075526
H	2.380661	1.492346	2.751802
C	2.921056	1.310497	-3.084356
H	2.873994	2.403704	-3.030665
H	3.975248	1.020097	-3.010899
H	2.555824	1.02027	-4.072152
Fe	1.675935	2.77437	0.355337
C	0.164784	3.754722	1.31081
C	-0.305637	3.174999	0.099366
C	0.451978	3.719229	-0.972897
C	1.210968	4.659447	0.983734
C	1.388374	4.637929	-0.425944
H	1.797154	5.234914	1.687115
H	2.133686	5.191907	-0.98071
H	0.361962	3.453173	-2.019001
H	-1.070536	2.412848	0.015227
H	-0.190091	3.522696	2.306416

ii) Kinetic Experiments

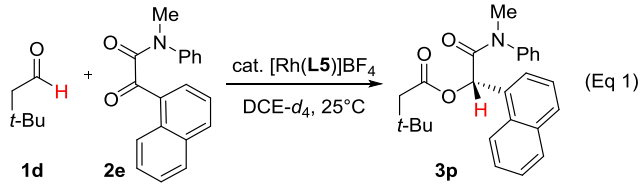


The kinetic profile of the reaction was studied by probing the initial rates of the reactions and varying the concentrations of **1d**, **2e** and Rh-catalyst. No products of decomposition were observed with this system. The rates were monitored by ^{1}H NMR using durene as an internal standard.

Representative procedure (Table 3, entry 2):

The catalyst was first prepared by mixing (S_P,*R*)-Josiphos (3.1 mg, 0.005 mmol) and $[Rh(cod)_2]BF_4$ (2.0 mg, 0.005 mmol) in protio-DCE (0.5 mL) in a N_2-filled glovebox and transferring the solution to a J-Young NMR tube. The J-Young NMR tube was connected to a Schlenk/gas line and degassed via 'freeze-pump-thaw'. Hydrogen gas was introduced into the J-Young NMR tube, and the content was thoroughly mixed by continuously inverting the tube (~20 min). Upon hydrogenation, the catalyst solution turns from dark red to a very dark brown color. The DCE solvent was then carefully removed under reduced pressure, leaving behind a brown residue. In a separate 1-dram vial, α-ketoamide **2e** (28.9 mg, 0.100 mmol) was dissolved in 0.1 mL DCE-d_4 and transferred to the J-Young NMR tube containing catalyst (in a N_2-filled glovebox). The 1-dram vial was rinsed with DCE-d_4 (5 × 0.1 mL), and this liquid was also transferred to the J-Young NMR tube (for a total of 0.6 mL solvent). Aldehyde **1d** (15.0 μL, 0.12 mmol) was subsequently added via microsyringe. The J-Young tube was sealed, thoroughly mixed by inverting the sample at least 10 times, and immediately subjected to ^{1}H NMR analysis (T = 298K). Time points were taken every 5 minutes.

Table S1. Kinetic Data For Intermolecular Ketone Hydroacylation[a]



Entry	[**1d**] / M	[**2e**] / M	[catalyst] / M	Initial rate[b] / M·min^{-1}
1	1.0×10^{-1}	1.7×10^{-1}	8.3×10^{-3}	$(0.87 \pm 0.06) \times 10^{-4}$
2	2.0×10^{-1}	1.7×10^{-1}	8.3×10^{-3}	$(2.40 \pm 0.02) \times 10^{-4}$
3	3.0×10^{-1}	1.7×10^{-1}	8.3×10^{-3}	$(3.03 \pm 0.06) \times 10^{-4}$
4	5.0×10^{-1}	1.7×10^{-1}	8.3×10^{-3}	$(4.41 \pm 0.06) \times 10^{-4}$
5	6.0×10^{-1}	1.7×10^{-1}	8.3×10^{-3}	$(6.0 \pm 0.1) \times 10^{-4}$
6	2.0×10^{-1}	0.83×10^{-1}	8.3×10^{-3}	$(0.80 \pm 0.02) \times 10^{-4}$
7	2.0×10^{-1}	2.5×10^{-1}	8.3×10^{-3}	$(3.92 \pm 0.07) \times 10^{-4}$
8	2.0×10^{-1}	4.2×10^{-1}	8.3×10^{-3}	$(6.3 \pm 0.2) \times 10^{-4}$
9	2.0×10^{-1}	5.0×10^{-1}	8.3×10^{-3}	$(7.7 \pm 0.4) \times 10^{-4}$
10	2.0×10^{-1}	1.7×10^{-1}	2.1×10^{-3}	$(0.099 \pm 0.002) \times 10^{-4}$
11	2.0×10^{-1}	1.7×10^{-1}	4.2×10^{-3}	$(0.49 \pm 0.01) \times 10^{-4}$
12	2.0×10^{-1}	1.7×10^{-1}	4.8×10^{-3}	$(0.91 \pm 0.03) \times 10^{-4}$
13	2.0×10^{-1}	1.7×10^{-1}	6.8×10^{-3}	$(1.69 \pm 0.04) \times 10^{-4}$
14	2.0×10^{-1}	1.7×10^{-1}	7.2×10^{-3}	$(1.91 \pm 0.09) \times 10^{-4}$

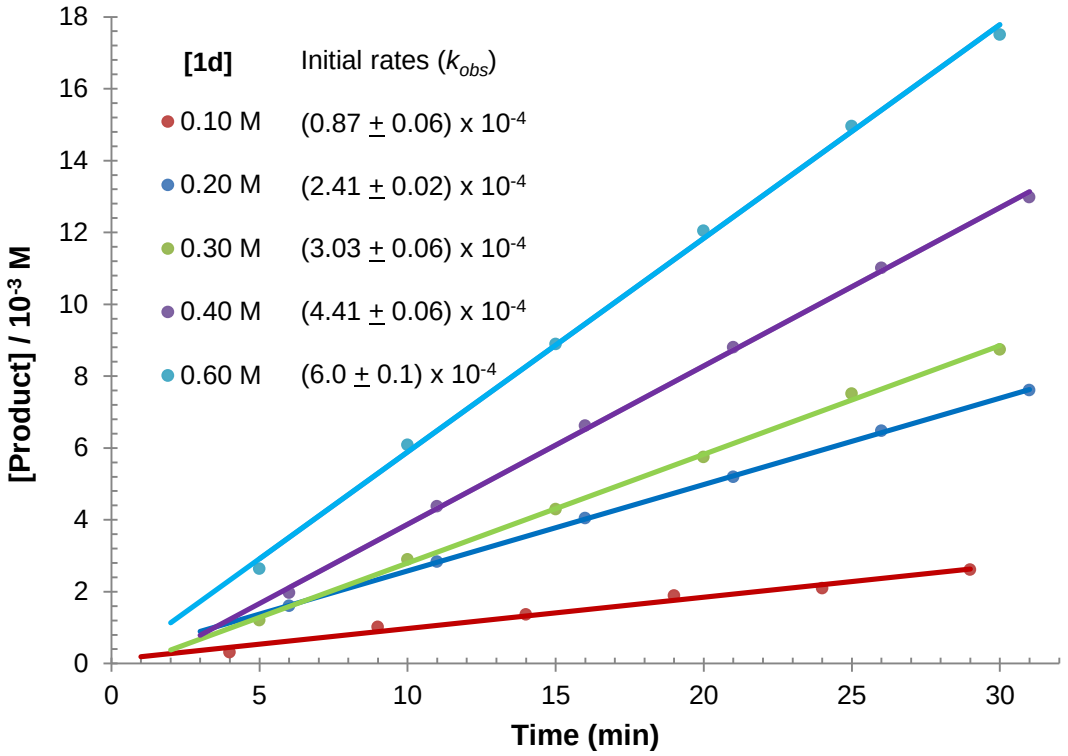


Figure S1. Plot of initial rates with various aldehyde concentrations.

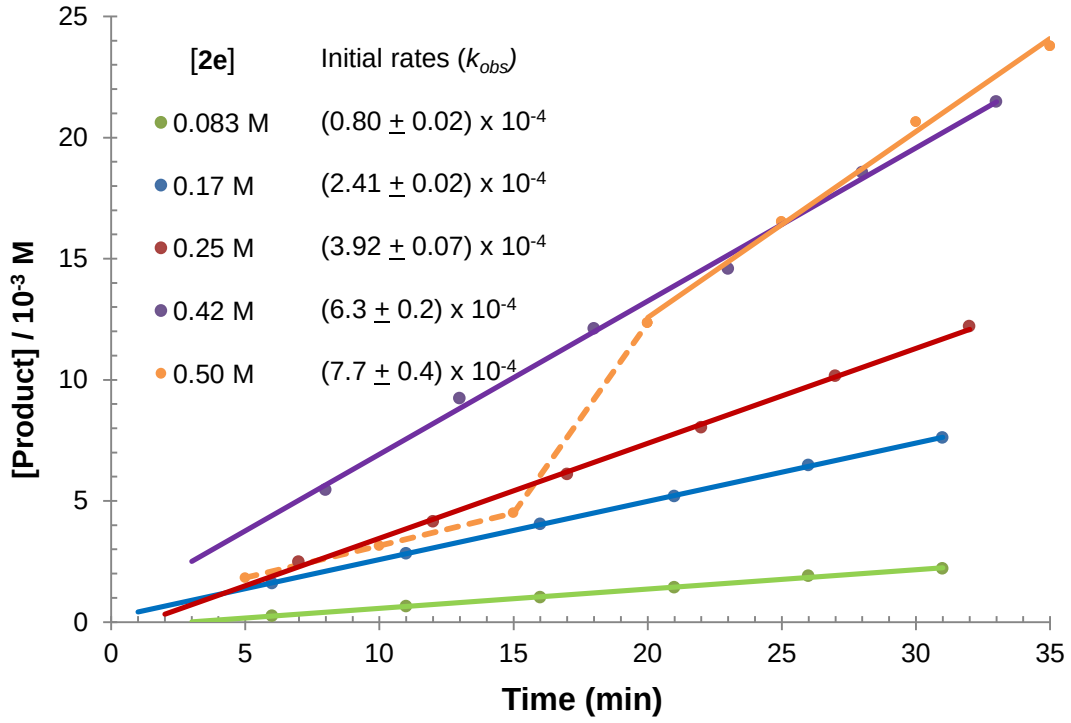


Figure S2. Plot of initial rates with various ketone concentrations.[25]

[25] An induction period is observed when a large excess of ketone **2e** was used (orange line, Figure S2). This data set was not used for the determination of the kinetic order.

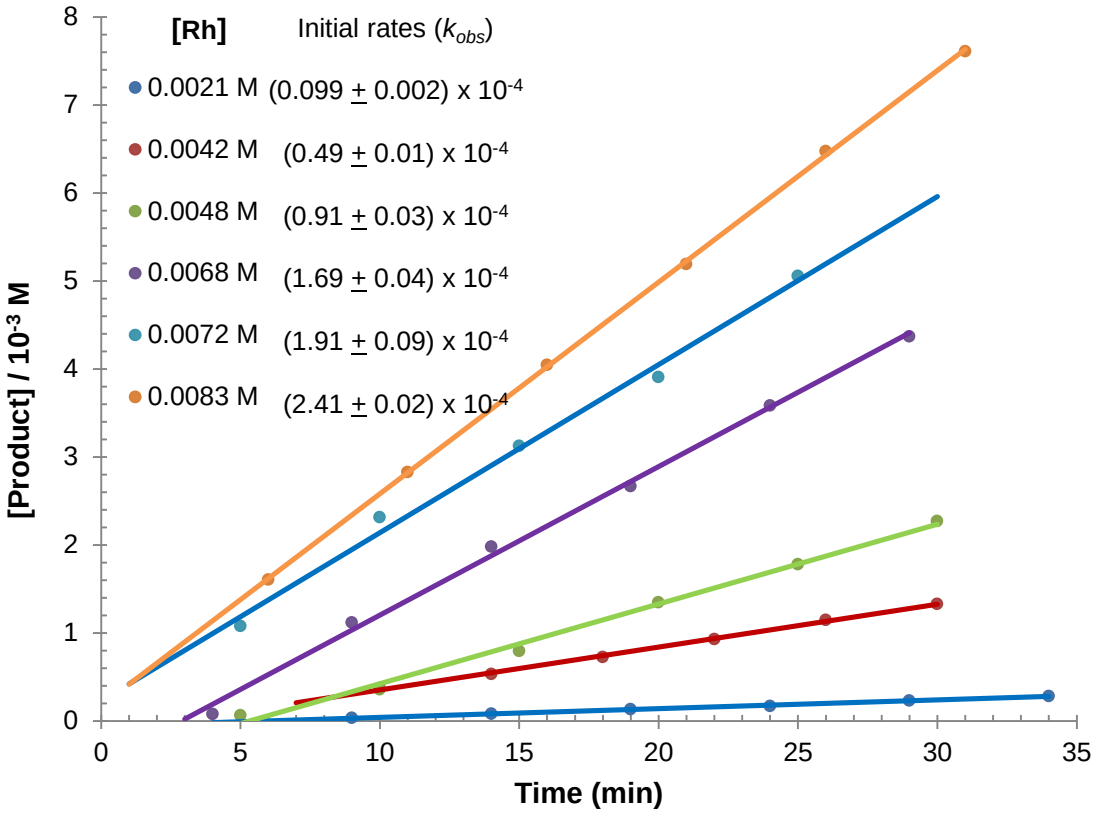


Figure S3. Plot of initial rates with various catalyst concentrations.

Second-order dependence of the rate on catalyst order is observed in the regime between 1.25 mol % and 5 mol % [Rh(Josiphos)]BF_4.

Based on this study, the following rate law is obtained:

rate = *k*[aldehyde]^1[α-ketoamide]^1[catalyst]^2

iii) Non-Linear Experiments

To study the relationship between the ee of the catalyst and the ee of the product, stock solutions of [Rh((*S*$_P$,*R*)-**L5**)]BF_4 and [Rh((*R*$_P$,*S*)-**L5**)]BF_4 were prepared. Varying volumes of these stock solutions were mixed together to obtain a catalyst with a certain ee. The reactions were run using standard procedure (see section 4) and 5 mol % catalyst.

Preparation of [Rh((*S*P,*R*)-**L5**)]BF_4 stock solution. In a N_2-filled glovebox, (*S*P,*R*)-**L5** (9.4 mg, 0.015 mmol) and [Rh(cod)$_2$]BF_4 (6.2 mg, 0.015 mmol) were dissolved in DCE (0.6 mL) and transferred to a 25 mL Schlenk tube. The content within the Schlenk tube was degassed via 2 cycles of 'freeze-pump-thaw', then backfilled with hydrogen gas. The catalyst solution was hydrogenated under a gentle flow of hydrogen gas at rt for 45 min, at which point the solvent was carefully removed under reduced pressure. The resulting catalyst residue was redissolved in DCE (1.0 mL), providing a solution containing 0.0015 mmol [Rh((*S*P,*R*)-**L5**)]BF_4 per 0.1 mL solution.

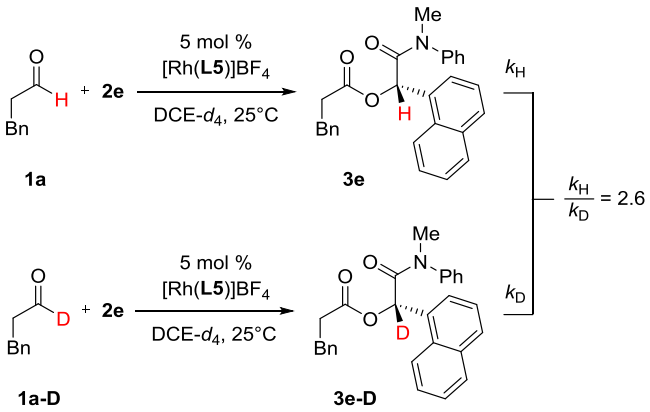
Preparation of [Rh((*R*P,*S*)-**L5**)]BF_4 stock solution. In a N_2-filled glovebox, (*R*P,*S*)-**L5** (6.3 mg, 0.010 mmol) and [Rh(cod)$_2$]BF_4 (4.1 mg, 0.010 mmol) were dissolved in DCE (0.6 mL) and transferred to a 25 mL Schlenk tube. The content within the Schlenk tube was degassed via 2 cycles of 'freeze-pump-thaw', then backfilled with hydrogen gas. The catalyst solution was hydrogenated under a gentle flow of hydrogen gas at rt for 45 min, at which point the solvent was carefully removed under reduced pressure. The resulting catalyst residue was redissolved in DCE (1.0 mL), providing a solution containing 0.0010 mmol [Rh((*R*P,*S*)-**L5**)]BF_4 per 0.1 mL solution.

[Rh((*S*P,*R*)-**L5**)]BF_4 solution (*x* mL) and [Rh((*R*P,*S*)-**L5**)]BF_4 (*y* mL) were added to a vial containing α-ketoamide **2e**. The final volume was made to 0.4 mL DCE and the resulting mixture was stirred at ambient glovebox temperature (35˚C) for 5 min. Aldehyde **1d** was subsequently introduced via microsyringe and the reaction was stirred at rt (23˚C) for 40 h. The crude reaction mixtures were directly loaded onto preparative tlc-plates, which were eluted with 4:1 hexanes/EtOAc. The product band was isolated and extracted with EtOAc. Using enantiopure (*S*P,*R*)-catalyst (≥98% ee), 93% ee in product is obtained (Table S1, entry 5). Similarly, enantiopure (*R*P,*S*)-catalyst (≥99% ee) gave the product in −93% ee (Table S1, entry 10). Therefore, the theoretical maximum ee was adjusted to 93% ee. Entries 6−9 are duplicate experiments. The values are averaged together to yield a small positive non-linear relationship.

Table S2. Data from Non-Linear Relationship Experiment

Entry	*x*	*y*	ee (cat)	ee (product)
1	0.20 mL	0.20 mL	20.4	24.5
2	0.23 mL	0.15 mL	40.3	45.3
3	0.27 mL	0.10 mL	60.3	61.3
4	0.30 mL	0.05 mL	80.1	78.4
5	--	--	≥98	93
6	0.20 mL	0.20 mL	20.4	18.6
7	0.23 mL	0.15 mL	40.3	41.5
8	0.27 mL	0.10 mL	60.3	59.2
9	0.30 mL	0.05 mL	80.1	77.6
10	--	0.50 mL	≥99	−93

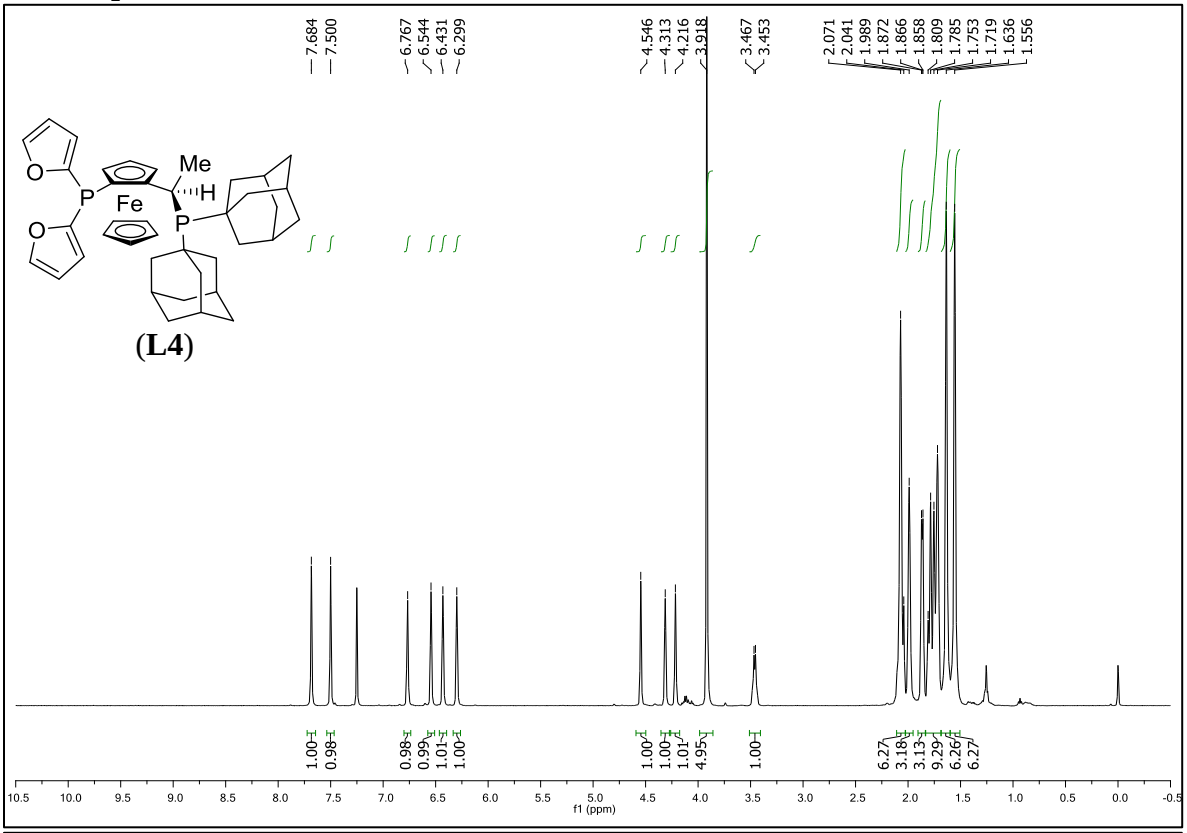
iv) KIE experiment

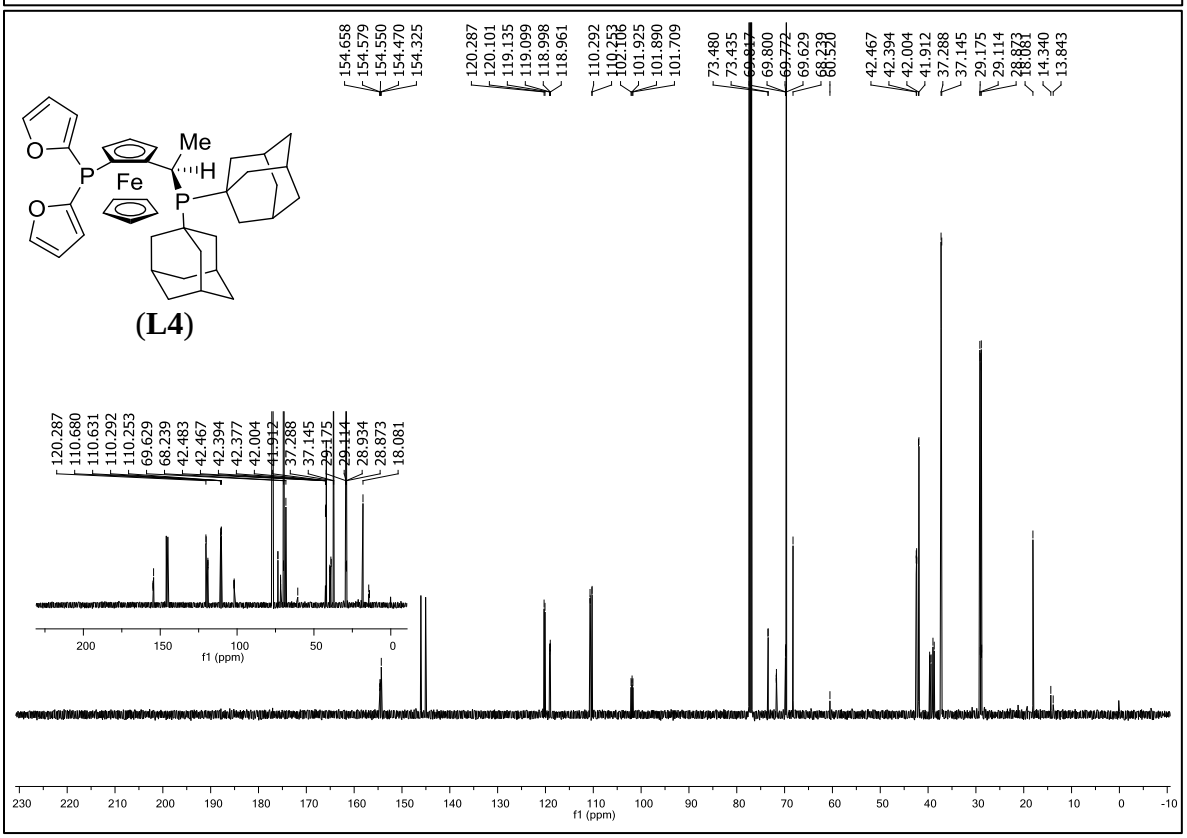


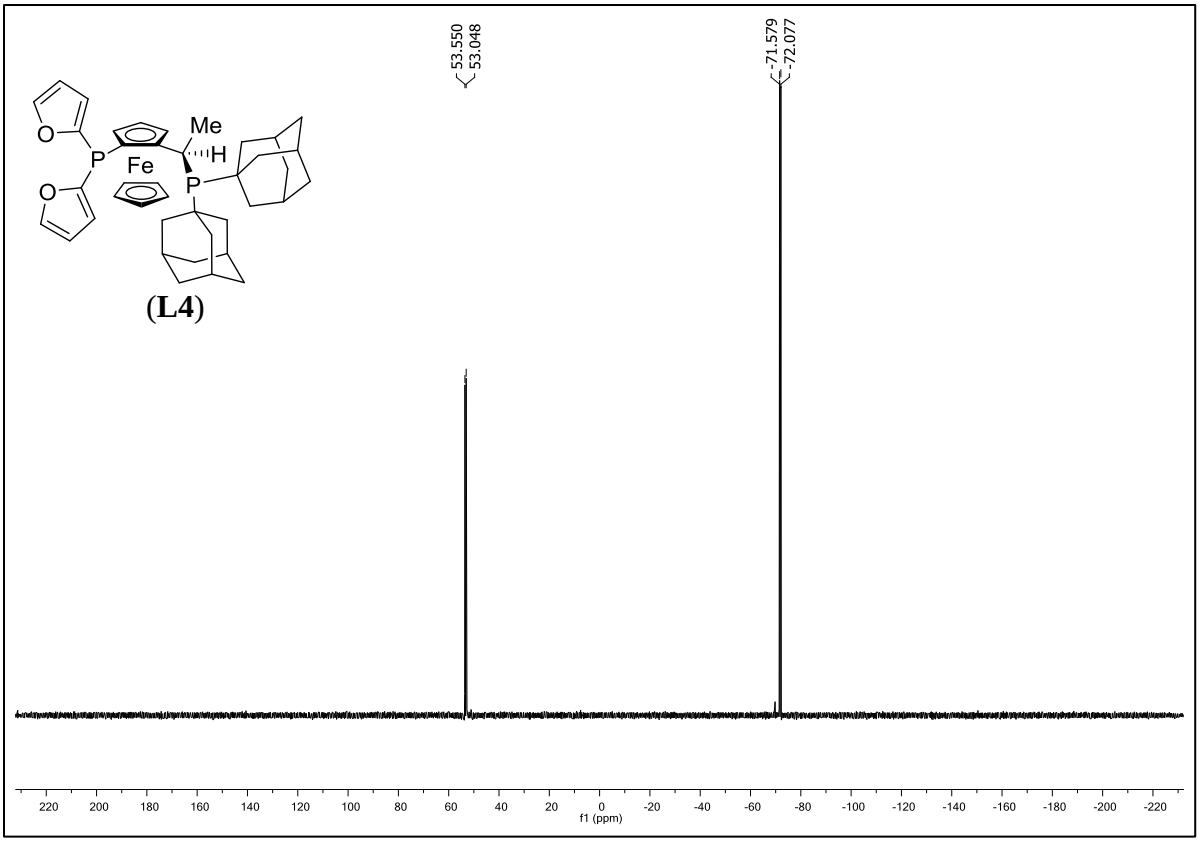
The KIE was obtained by measuring the initial rates of two independent experiments. Hydrocinnamaldehyde **1a** and **1a-D** was chosen for this study because the larger molecular weight of **1a-D**[26] relative to all other aldehydes in this study renders it more convenient to prepare and isolate (via distillation). The catalyst was prepared as described in the standard procedure and the reaction was monitored by ^{1}H NMR (T = 298K). The following initial rates were measured: $k_{H\,=}$ (4.6 ± 0.1) × 10^{-4} M^{-1}·min^{-1}; k_D = (1.78 ± 0.05) × 10^{-4} M^{-1}·min^{-1}.

[26] Campaña, A. G.; Carlone, A.; Chen, K.; Dryden, D. T. F.; Leigh, D. A.; Lewandowska, U.; Mullen, K. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 5480.

8. NMR Spectra



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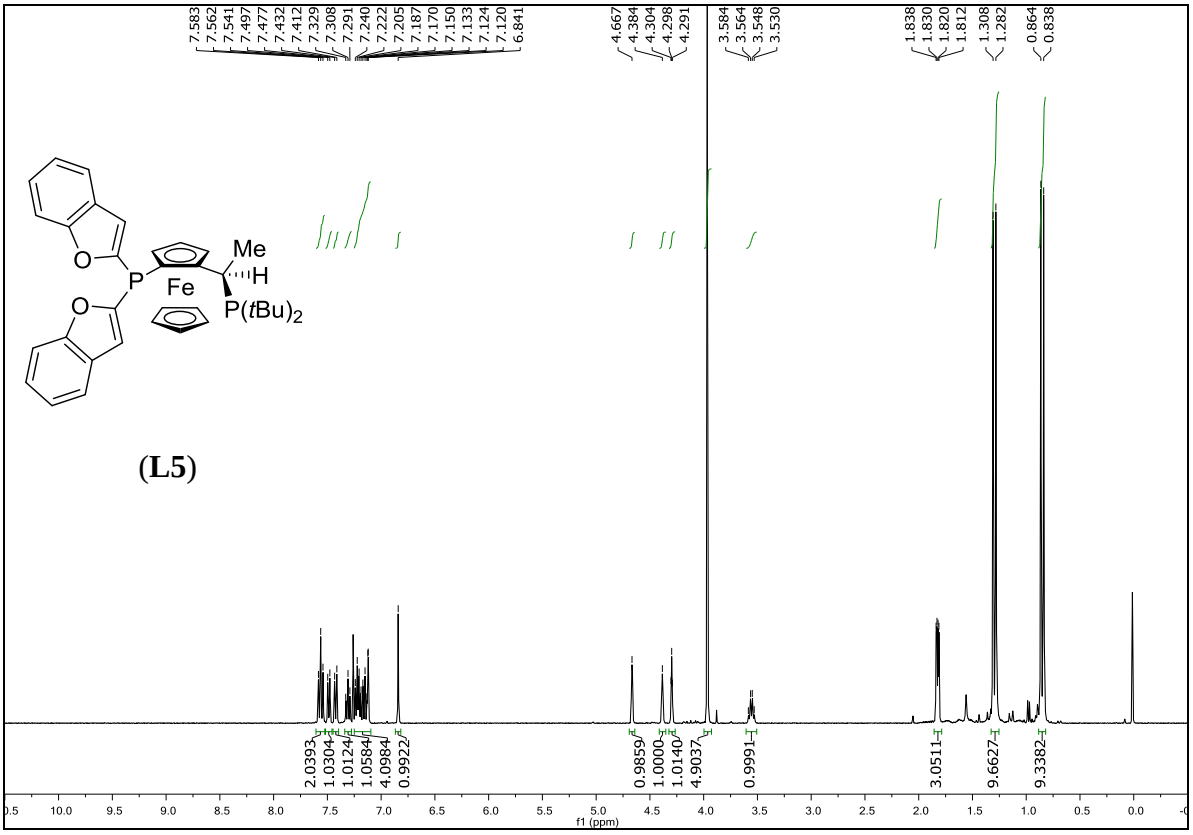
53.048
-71.579
-72.077
Me
H
Fe
P
P
O
O
220 200 180 160 140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

(**L4**)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7.541
7.497
7.477
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7.412
7.329
7.308
7.291
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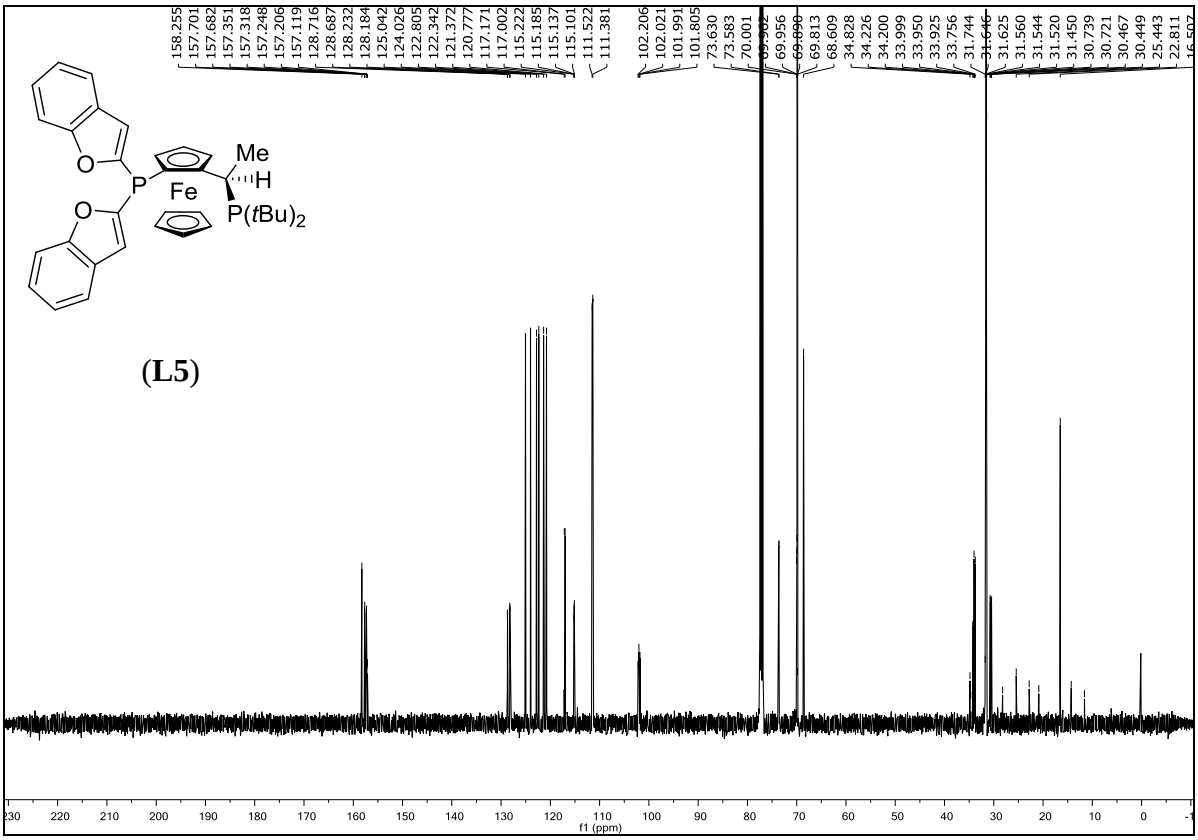
7.205
7.187
7.170
7.150
7.133
7.124
7.120
6.841
4.667
4.384
4.304
4.298
4.291
3.584
3.564
3.548
3.530
1.838
1.830
1.820
1.812
1.308
1.282
0.864
0.838
Me
H
Fe
P
P(tBu)2
O
O
2.0393
1.0304
1.0124
1.0584
4.0984
0.9922
0.9859
1.0000
1.0140
4.9037
0.9991
3.0511
9.6627
9.3382
f1 (ppm)

(**L5**)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157.248
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128.687
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125.042
124.026
122.805
122.342
121.372
120.777
117.171
117.002
115.222
115.185
115.137
115.101
111.522
111.381
102.206
102.021
101.991
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70.001
69.956
69.890
69.813
68.609
34.828
34.226
34.200
33.999
33.950
33.925
33.756
31.744
31.646
31.625
31.560
31.544
31.520
31.450
30.739
30.721
30.467
30.449
25.443
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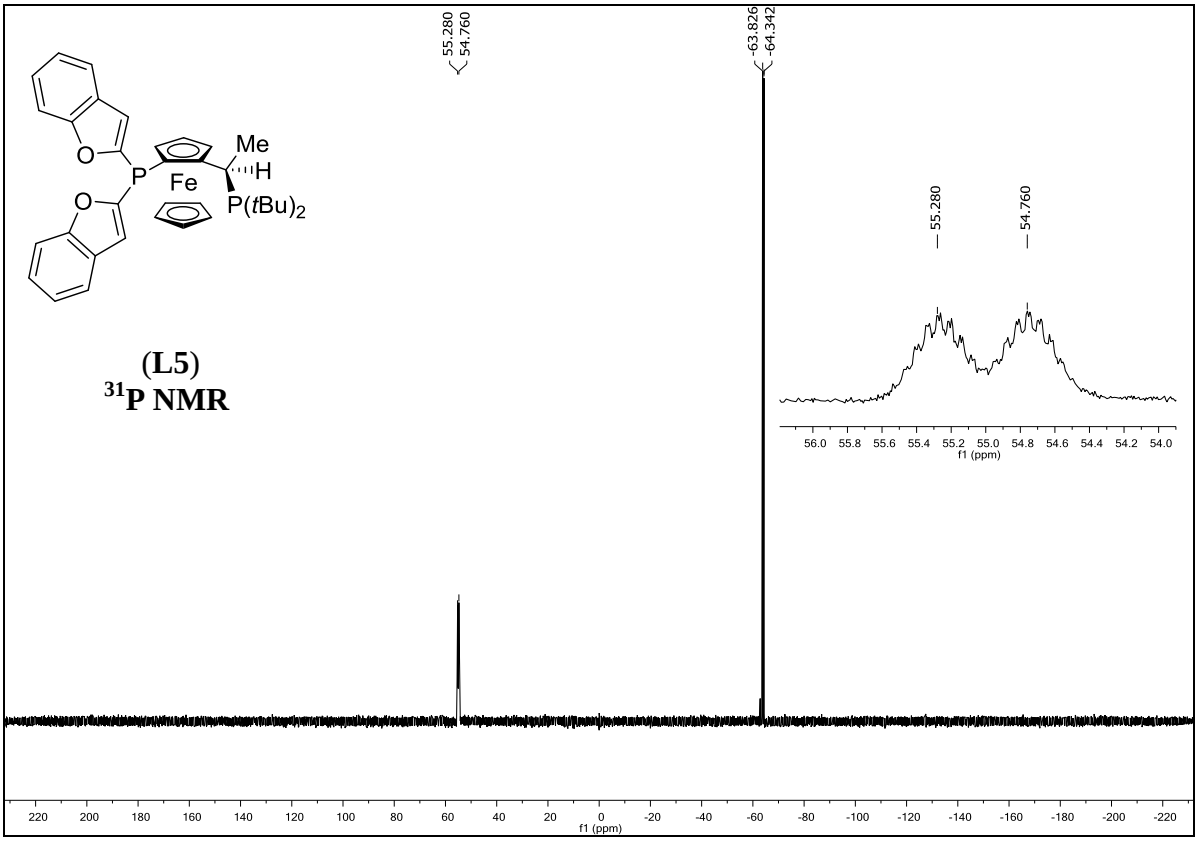
O
P
Fe
O
Me
H
P(tBu)2
(L5)
f1 (ppm)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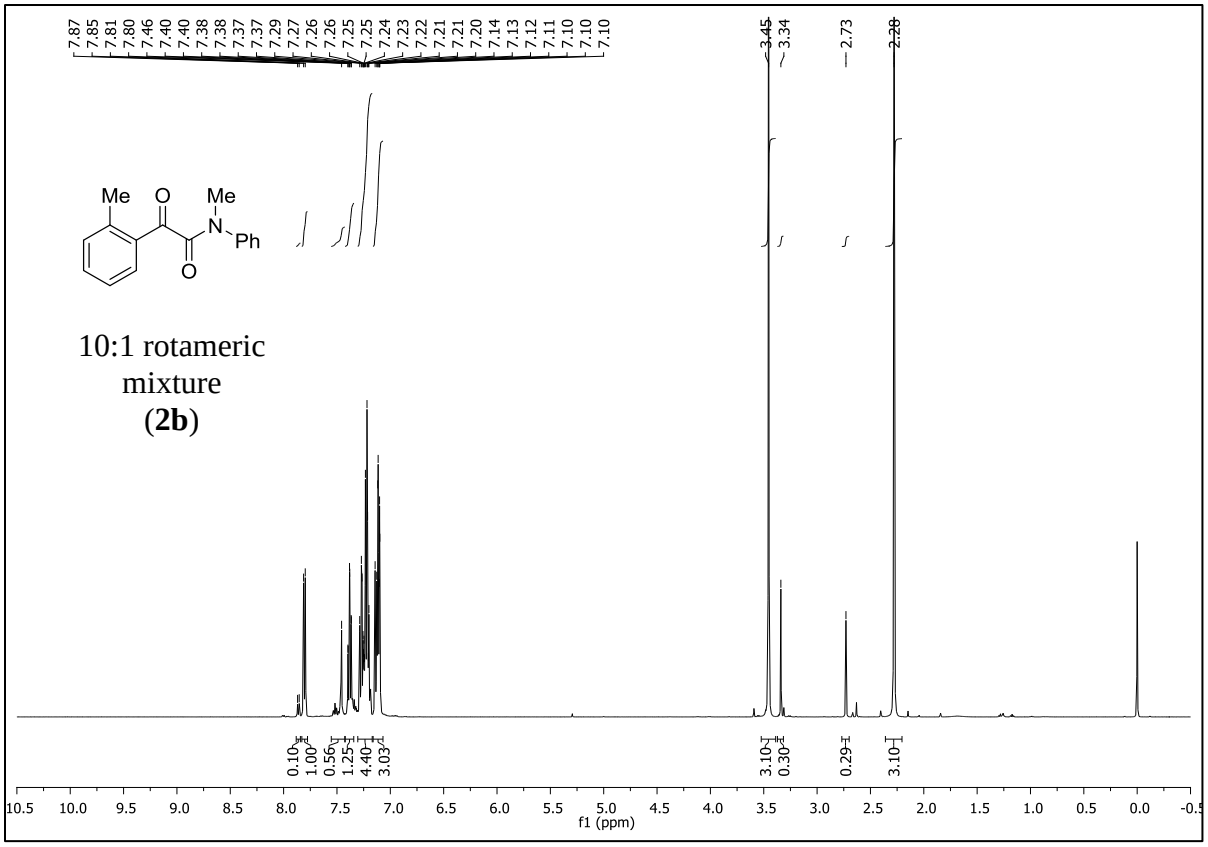
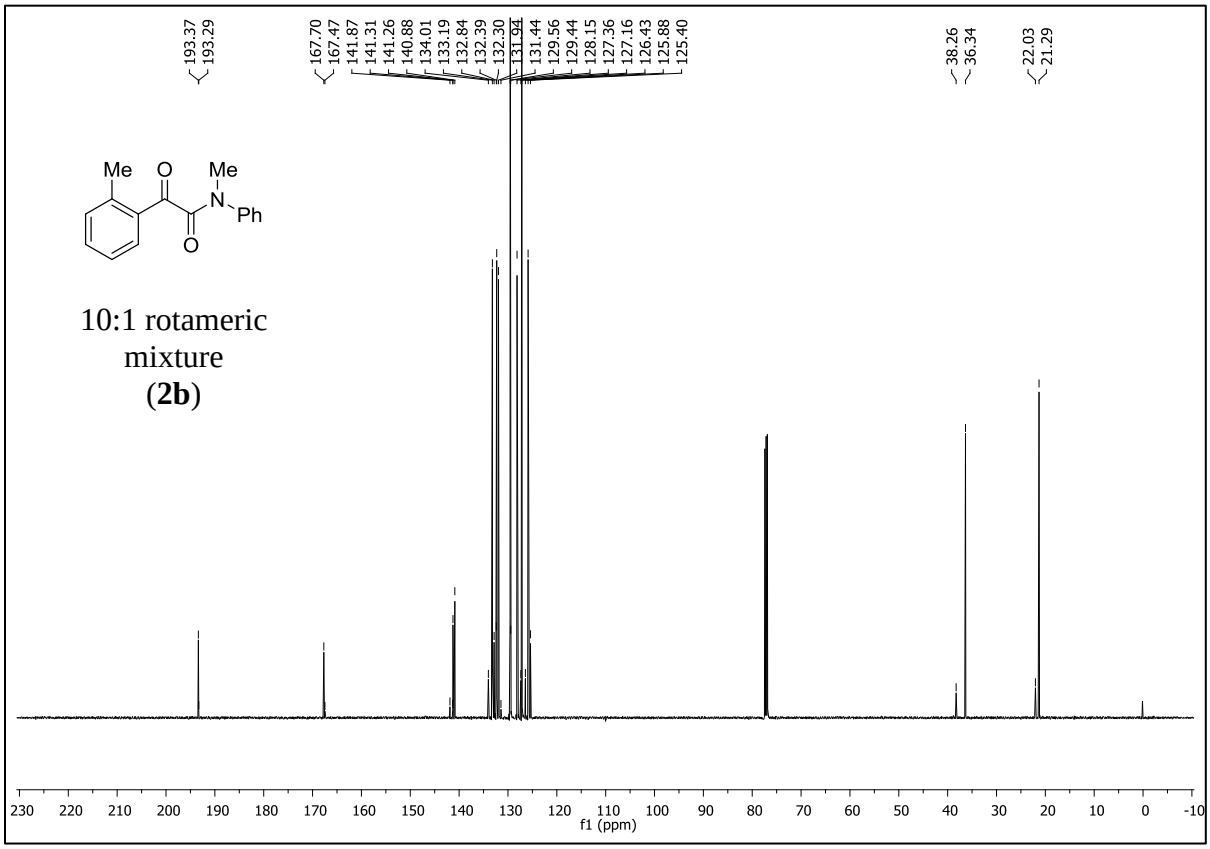
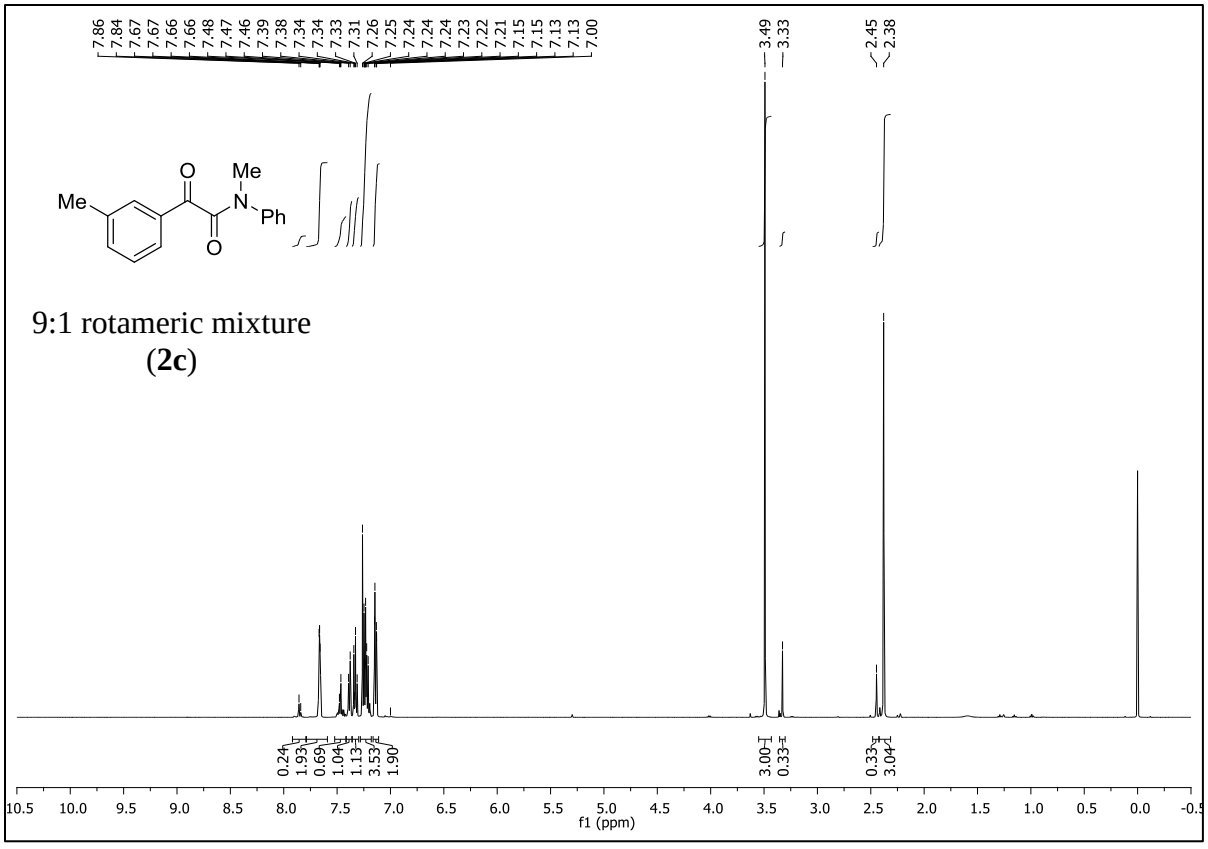
-64.342
O
P
Fe
O
Me
H
P(tBu)2
(L5)
31P NMR
55.280
54.760
f1 (ppm)
f1 (ppm)



10:1 rotameric mixture (**2b**)

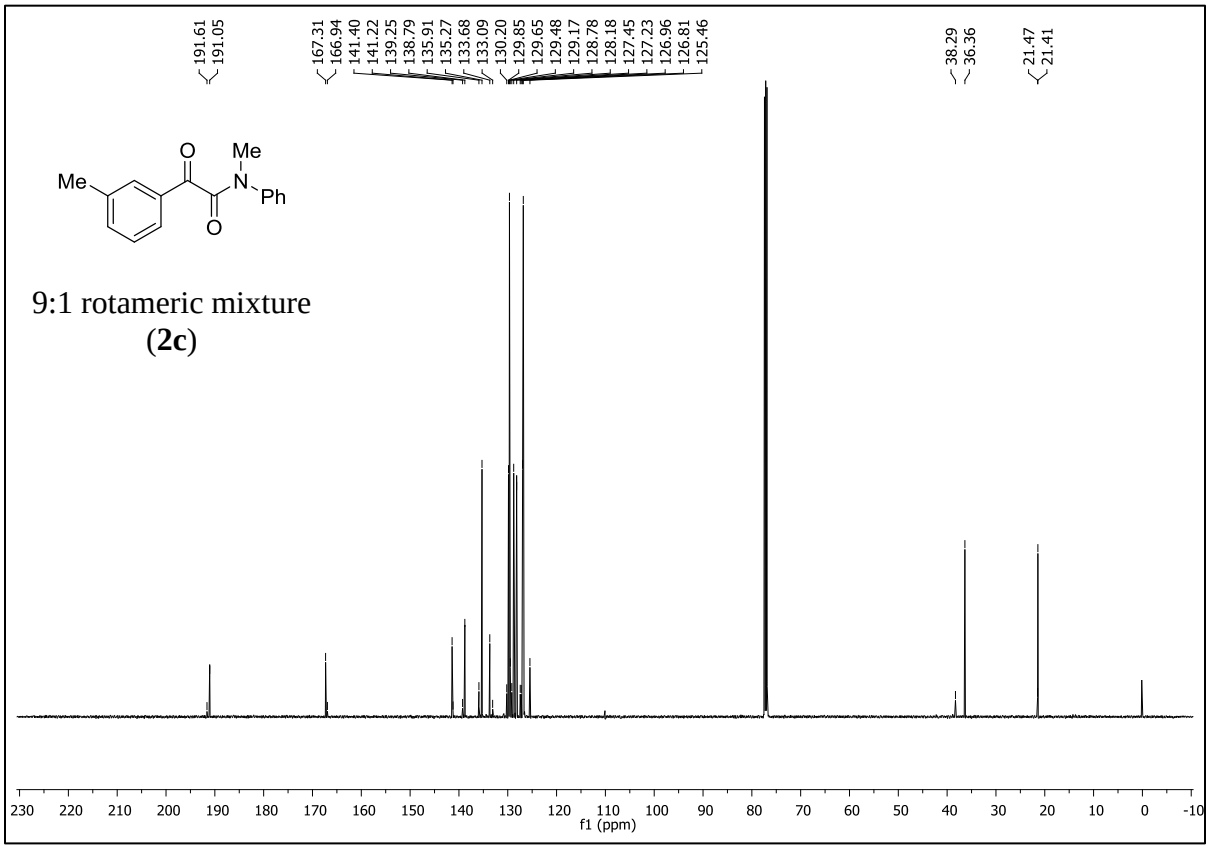


10:1 rotameric mixture (**2b**)



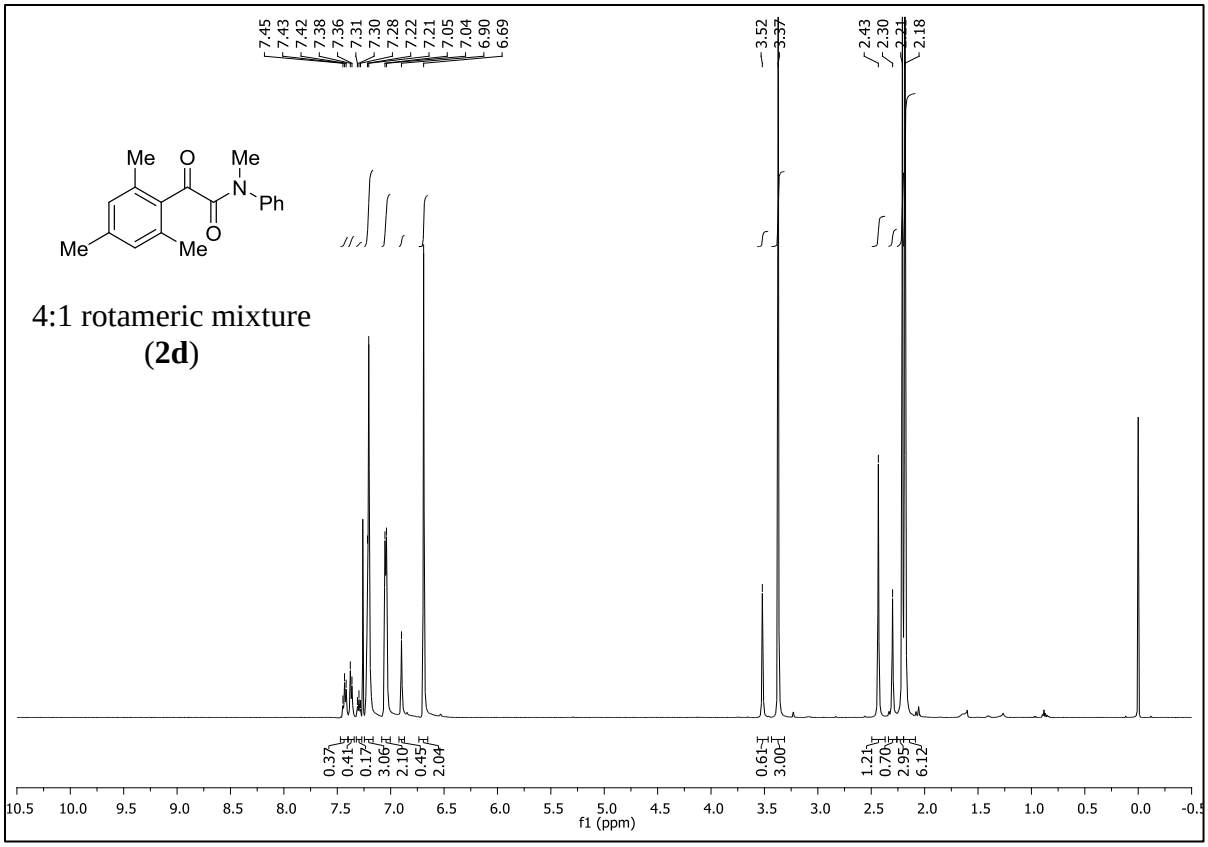
9:1 rotameric mixture

(**2c**)

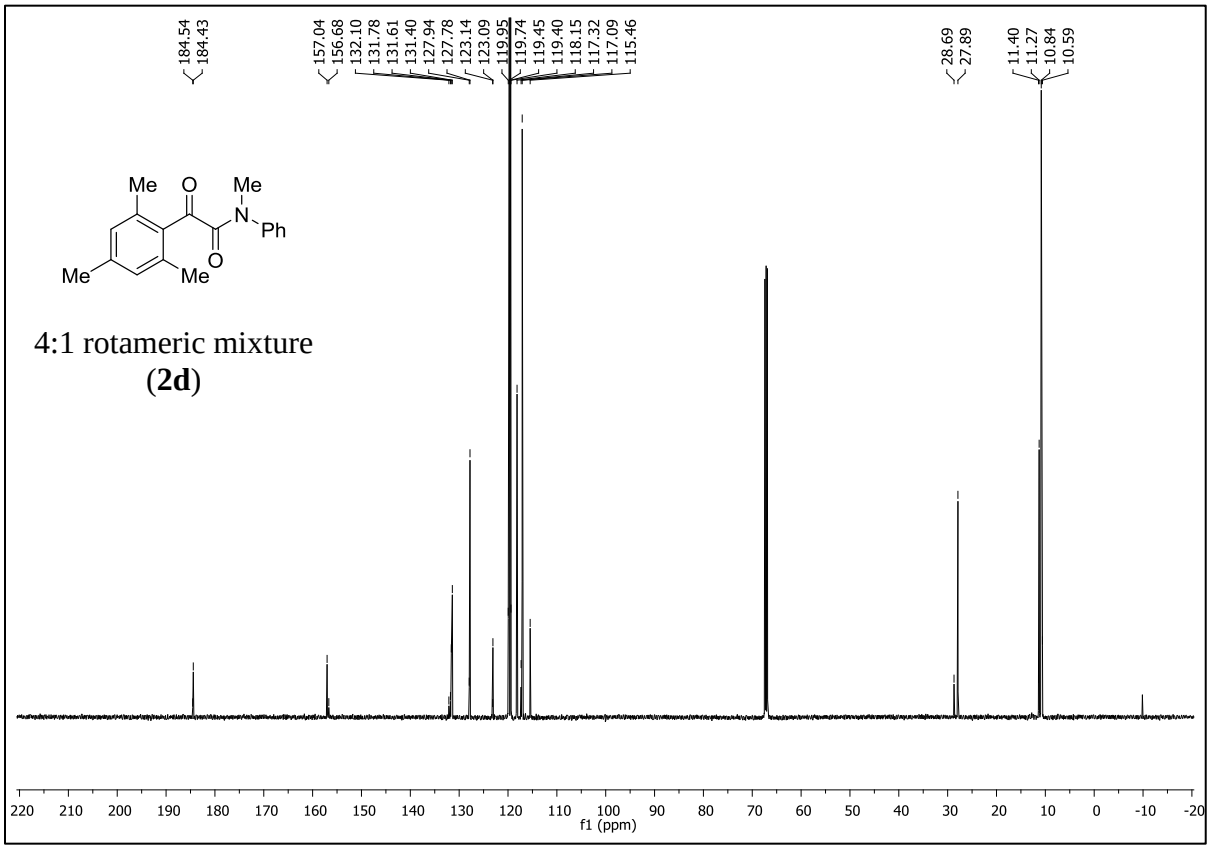


9:1 rotameric mixture

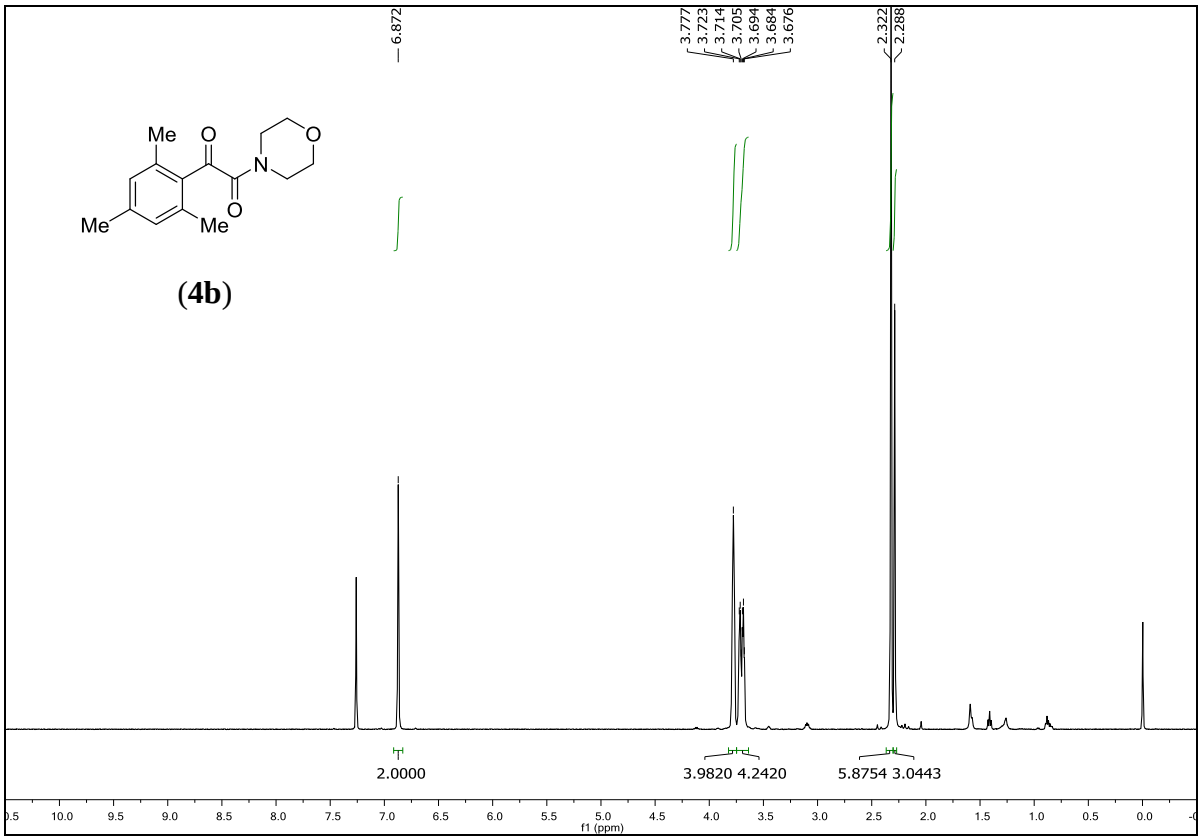
(**2c**)



4:1 rotameric mixture
(**2d**)



4:1 rotameric mixture
(**2d**)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3.705
3.694
3.684
3.676
2.322
2.288
Me
O
N
O
Me
O
Me
(4b)
2.0000
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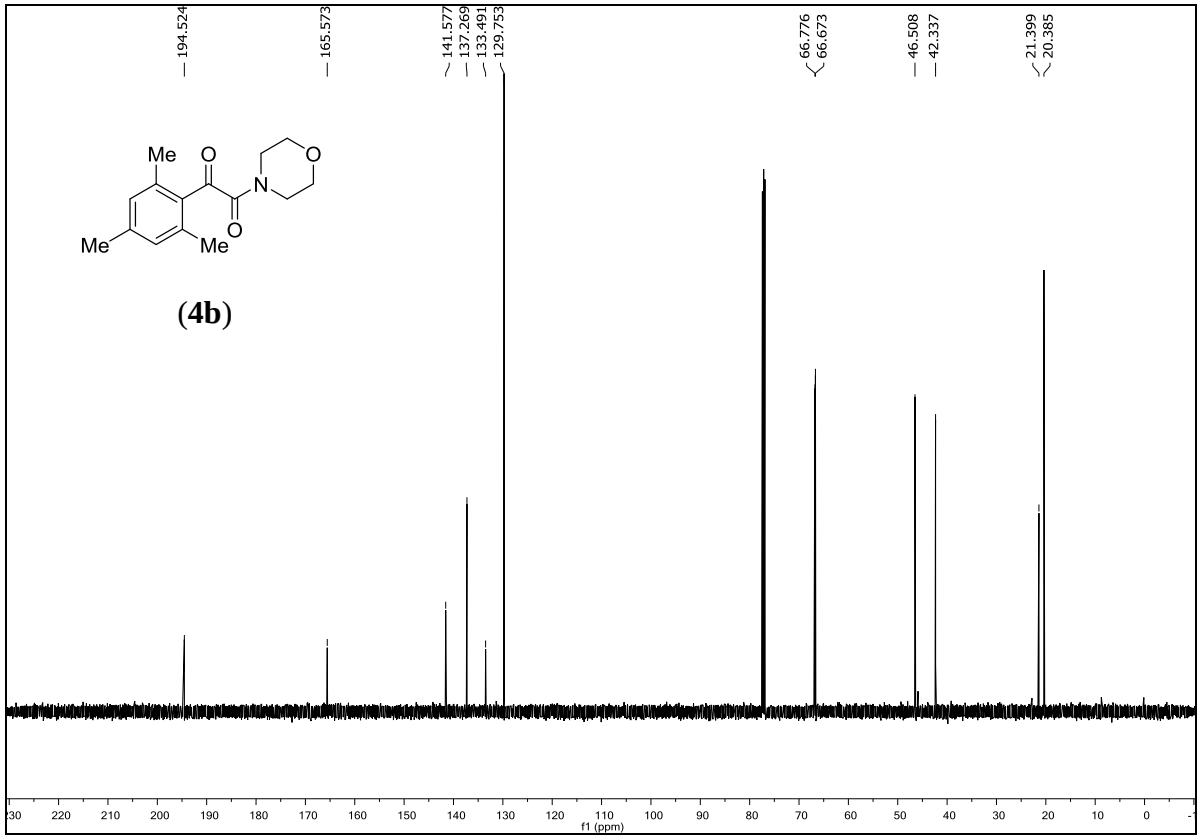
f1 (ppm)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133.491
129.753
66.776
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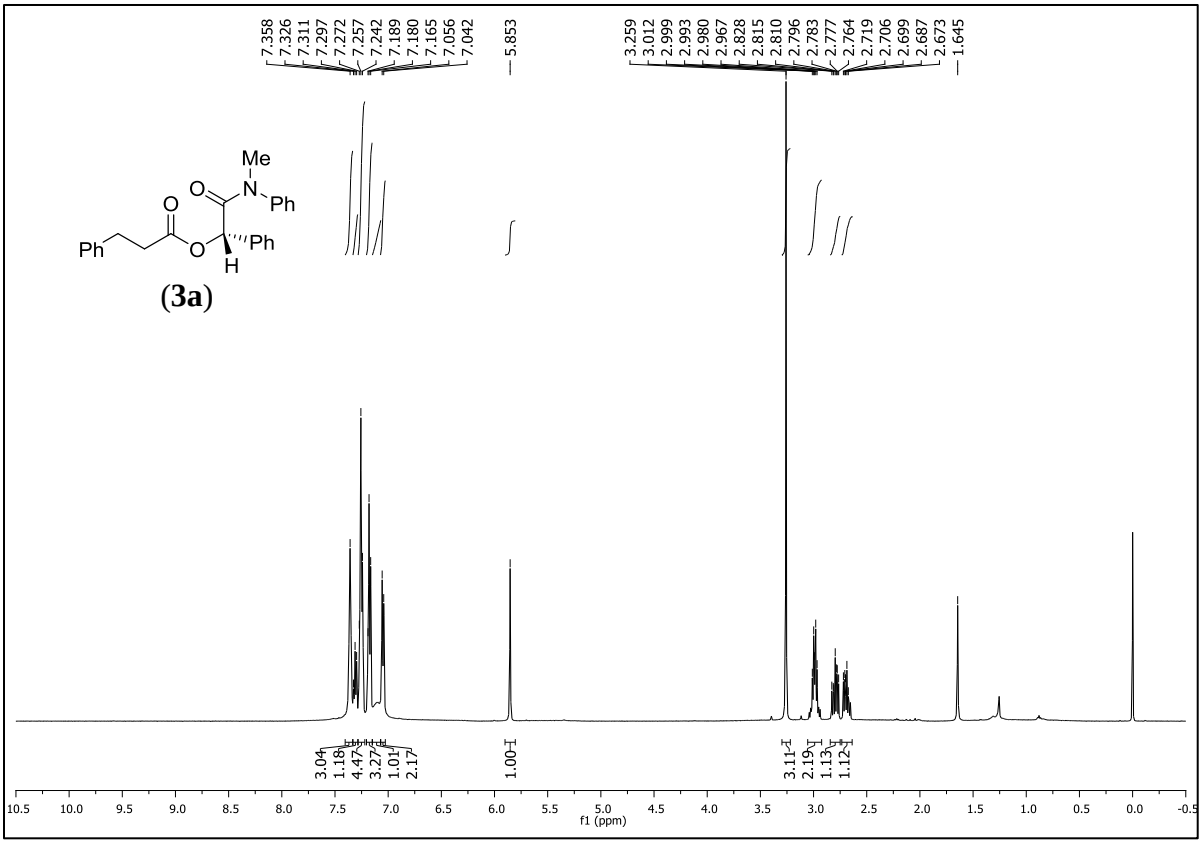
N
O
Me
O
Me
(4b)
f1 (ppm)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3.259
3.012
2.999
2.993
2.980
2.967
2.828
2.815
2.810
2.796
2.783
2.777
2.764
2.719
2.706
2.699
2.687
2.673
1.645
Me
N
Ph
O
O
Ph
O
Ph
H
(3a)
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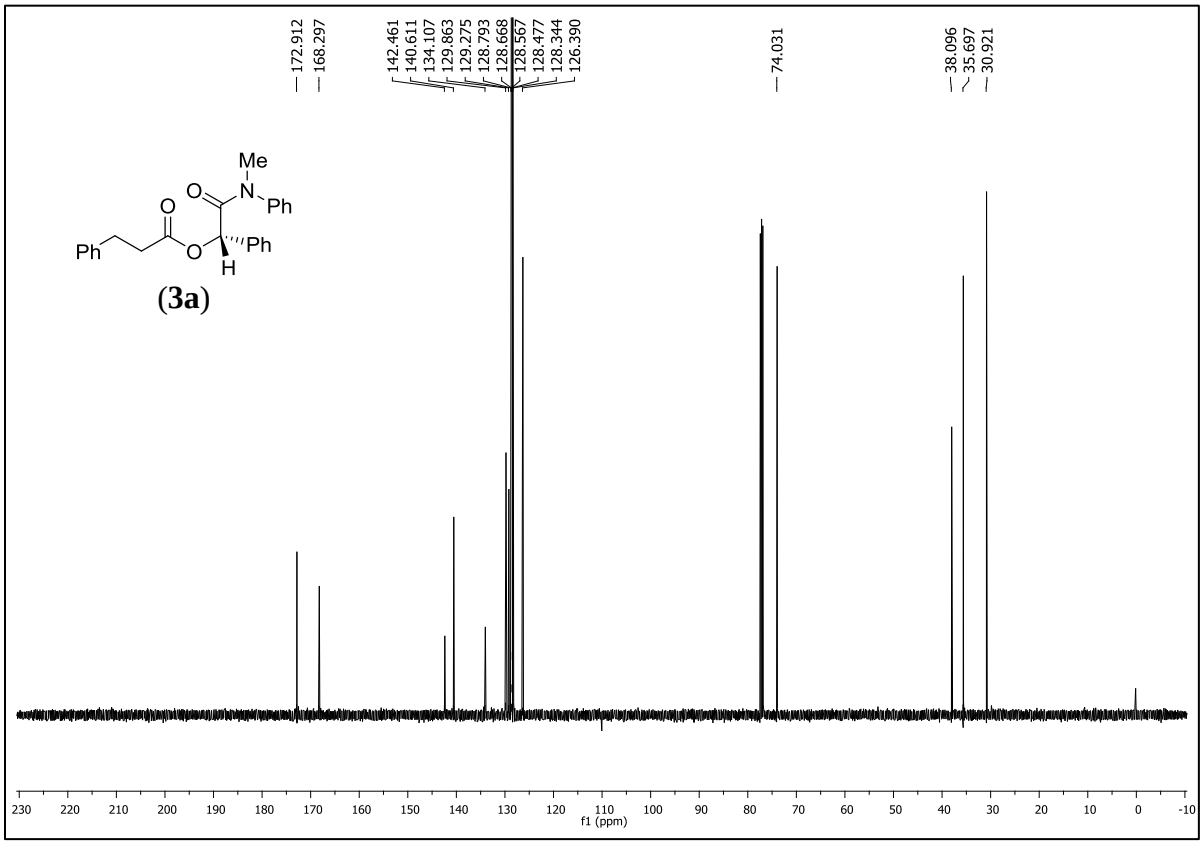
1.13
1.12
f1 (ppm)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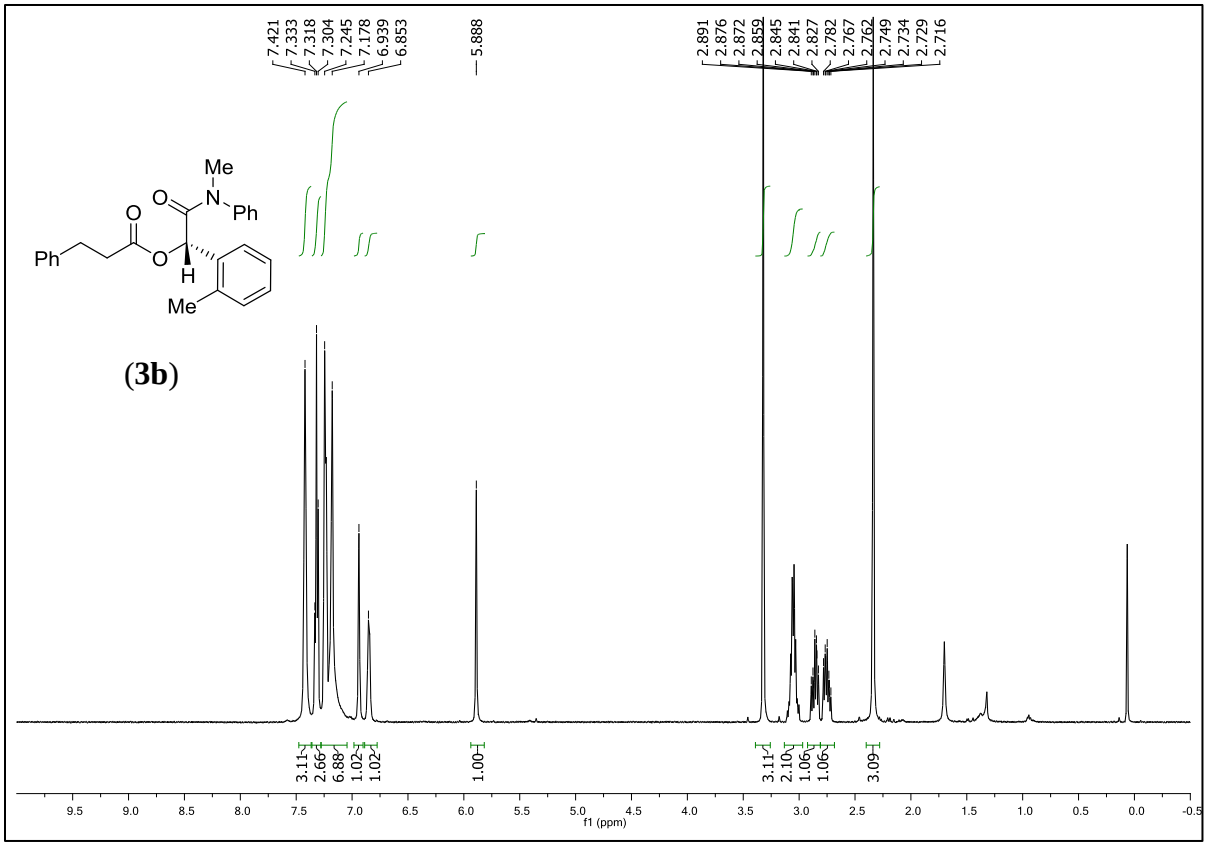
Ph
O
Ph
H
(3a)
f1 (ppm)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2.845
2.841
2.827
2.782
2.767
2.762
2.749
2.734
2.729
2.716
Me
N
Ph
O
O
Ph
O
H
Me
(3b)
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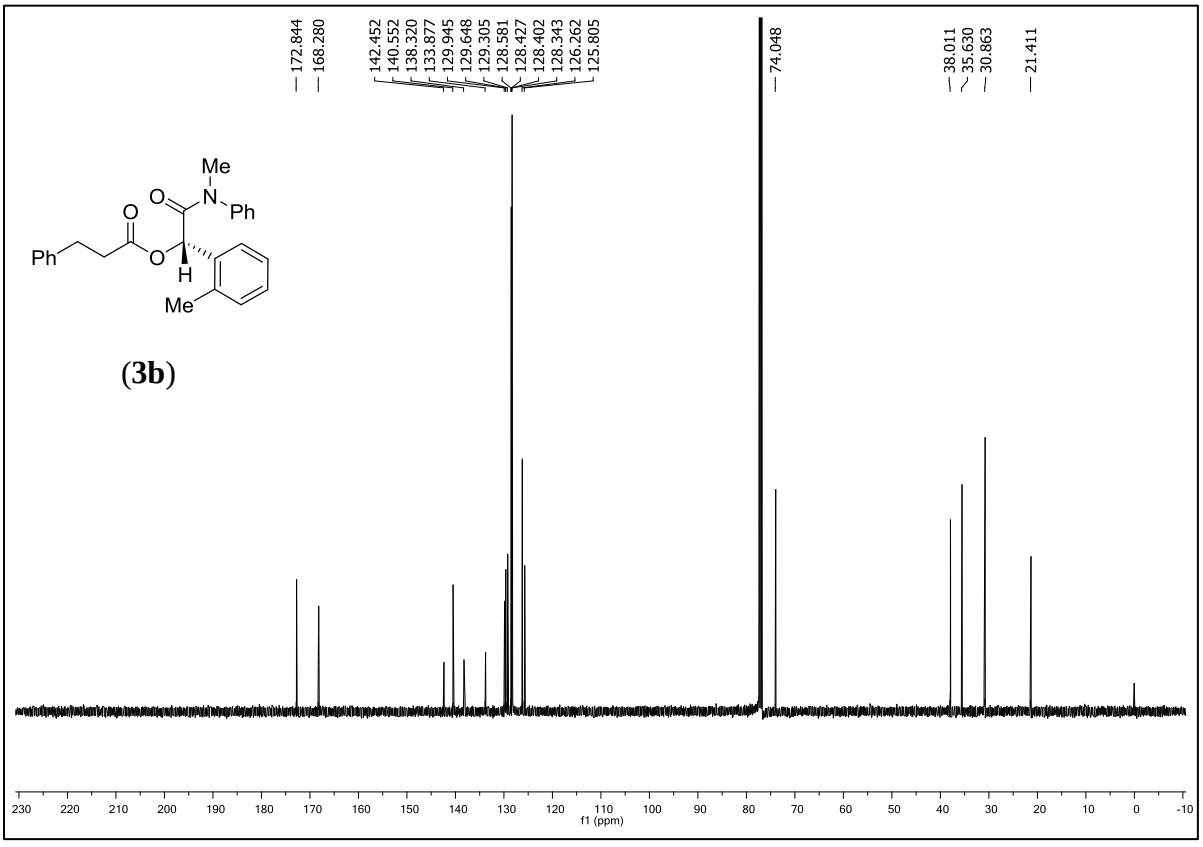
1.02
1.02
1.00
3.11
2.10
1.06
1.06
3.09
f1 (ppm)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125.805
74.048
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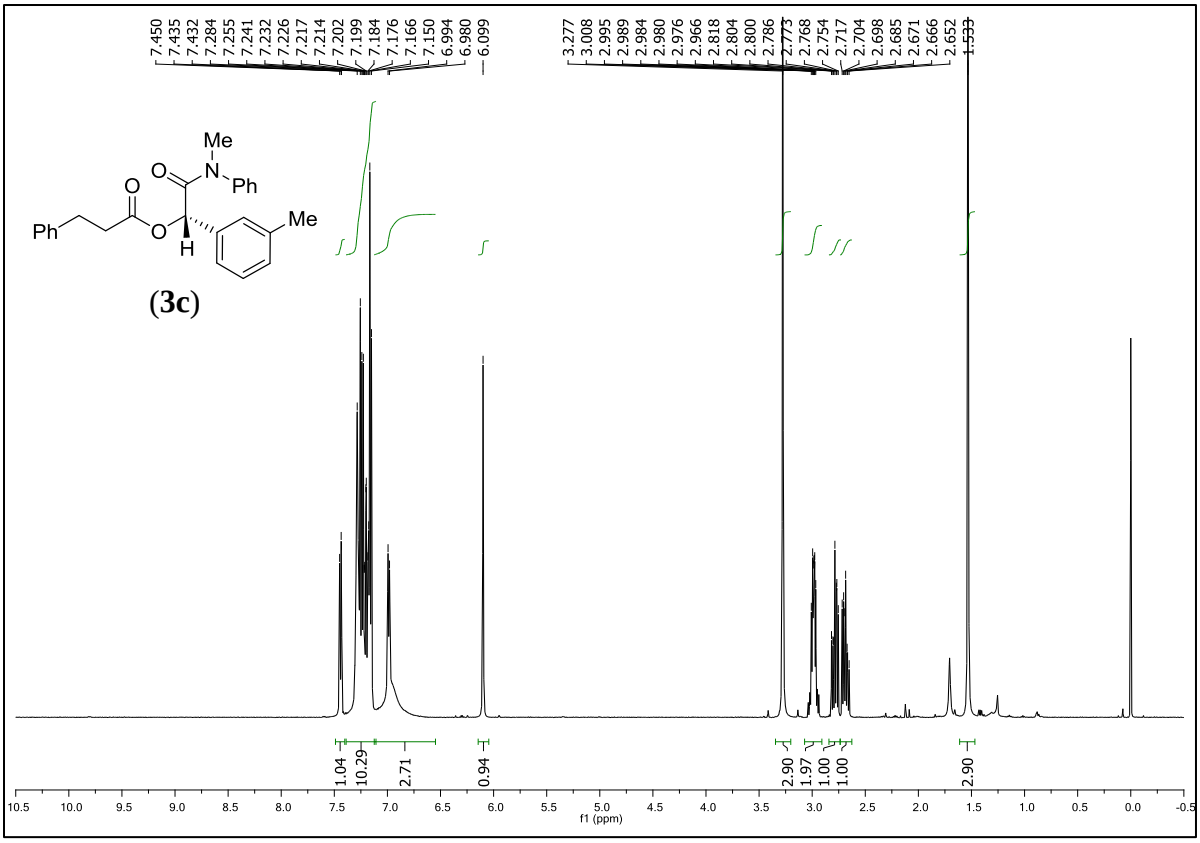
Ph
O
H
Me
(3b)
f1 (ppm)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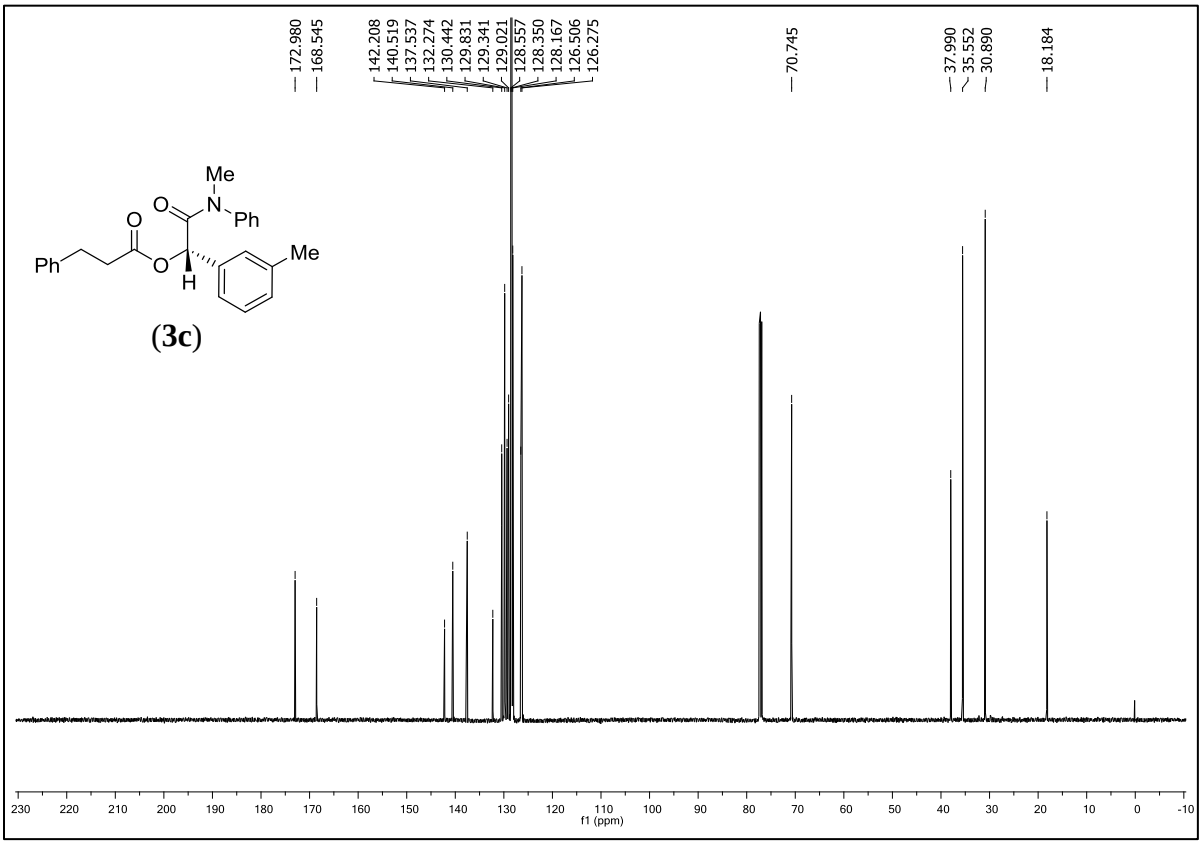
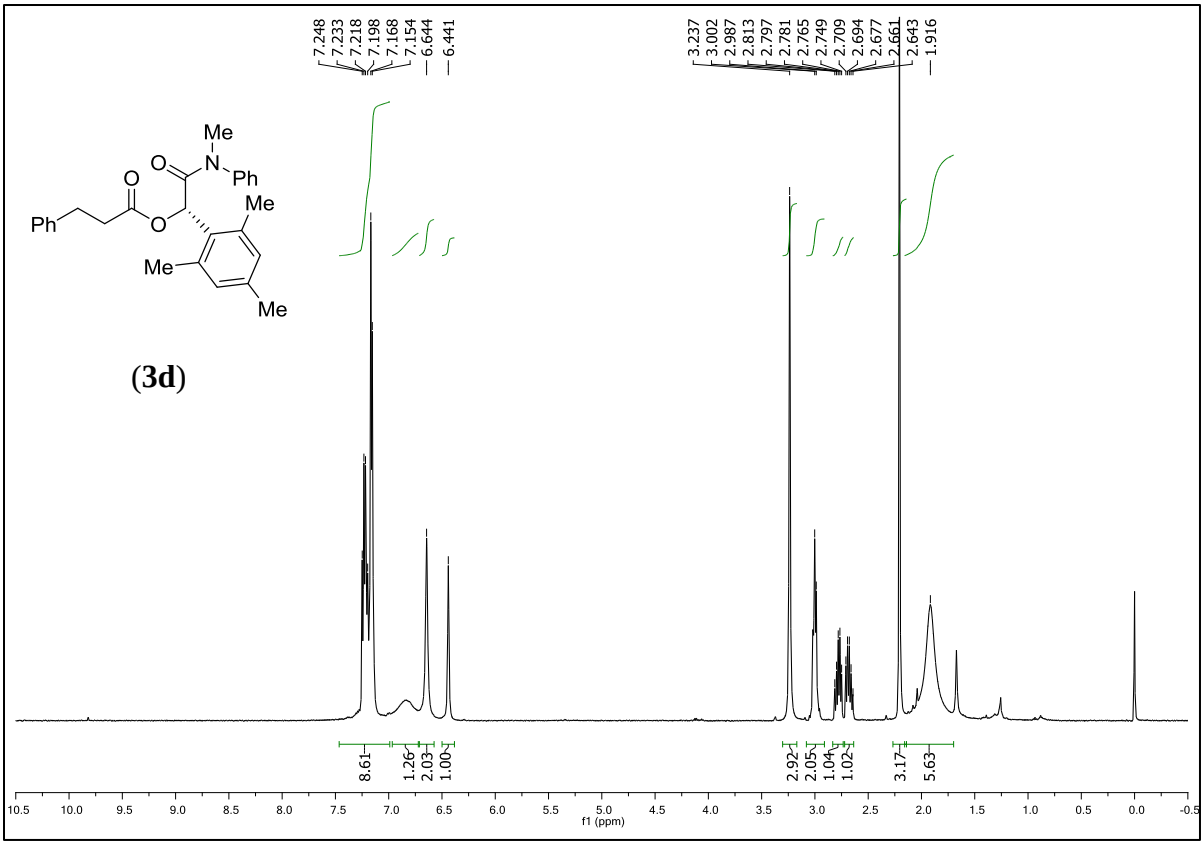
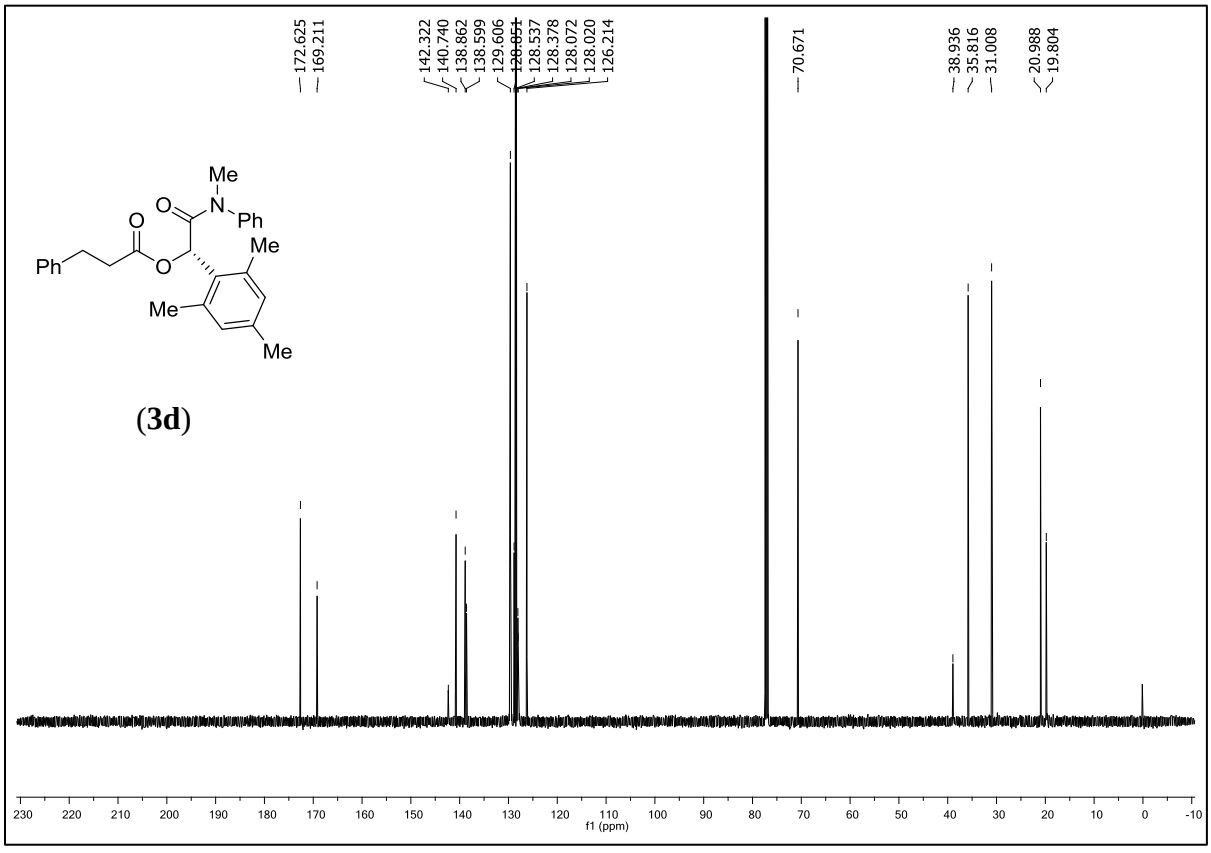
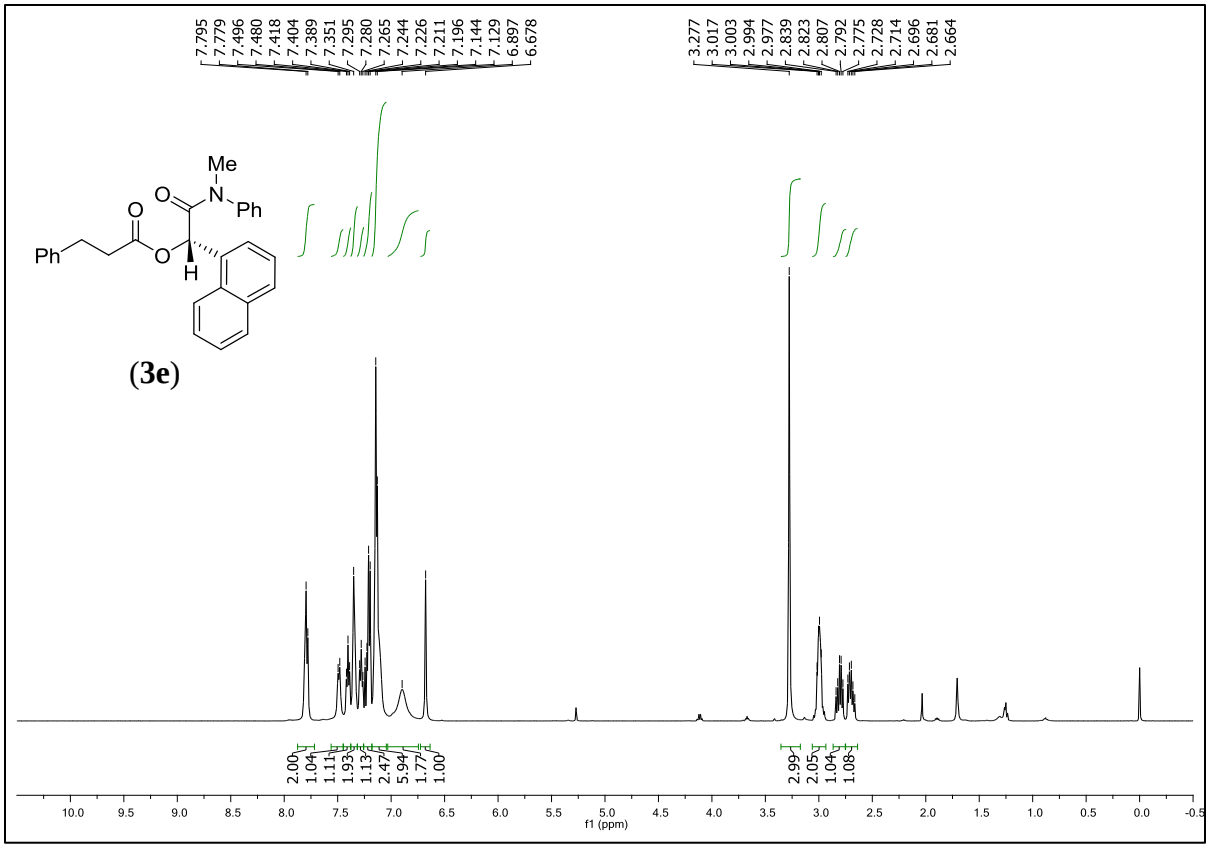
7.166
7.150
6.994
6.980
6.099
3.277
3.008
2.995
2.989
2.984
2.980
2.976
2.966
2.818
2.804
2.800
2.786
2.773
2.768
2.754
2.717
2.704
2.698
2.685
2.671
2.666
2.652
1.533
Me
N
Ph
O
O
Ph
O
H
Me
(3c)
1.04
10.29
2.71
0.94
2.90
1.97
1.00
1.00
2.90
f1 (ppm)

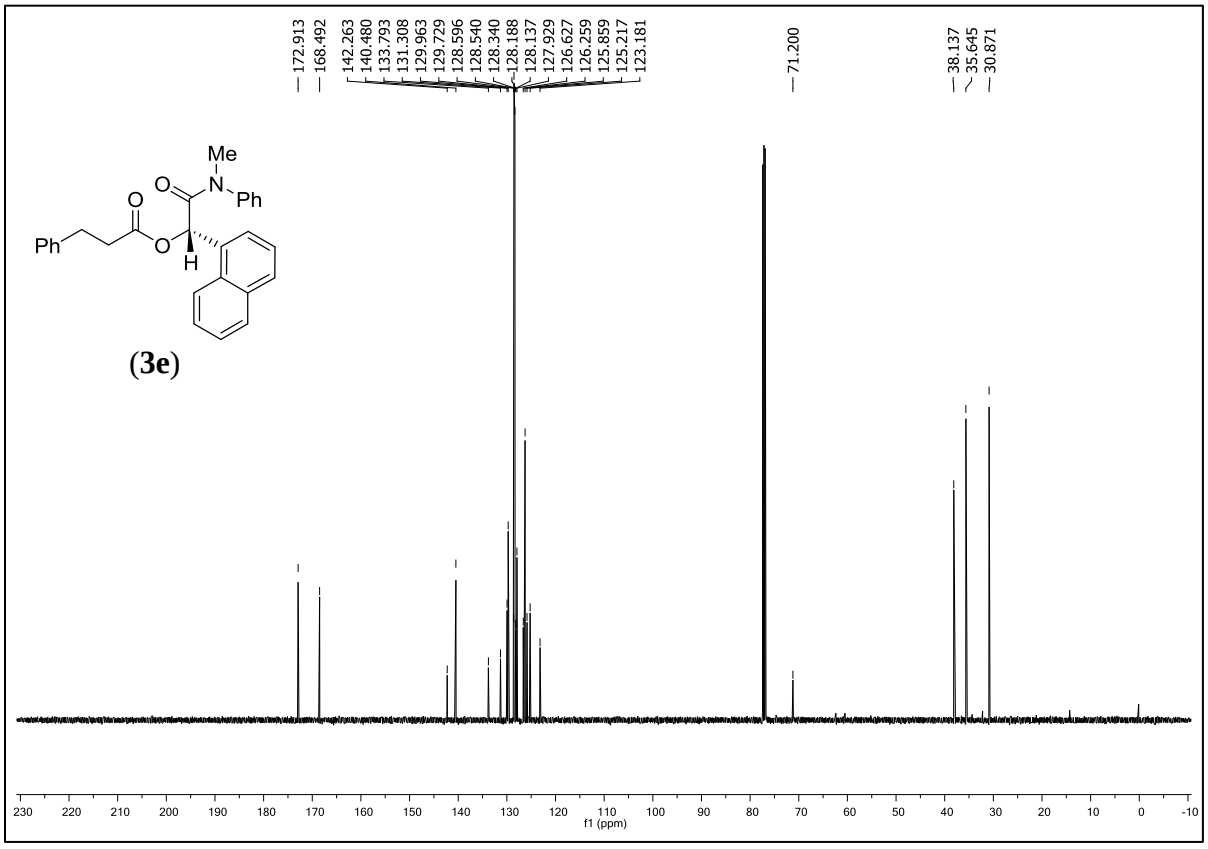

172.980
168.545
142.208
140.519
137.537
132.274
130.442
129.831
129.341
129.021
128.557
128.350
128.167
126.506
126.275
70.745
37.990
35.552
30.890
18.184
Me
N
Ph
O
O
Ph
O
H
Me
(3c)
f1 (ppm)


7.248
7.233
7.218
7.198
7.168
7.154
6.644
6.441
3.237
3.002
2.987
2.813
2.797
2.781
2.765
2.749
2.709
2.694
2.677
2.661
2.643
1.916
Me
N
Ph
O
O
Ph
Me
Me
Me
(3d)
8.61
1.26
2.03
1.00
2.92
2.05
1.04
1.02
3.17
5.63
f1 (ppm)

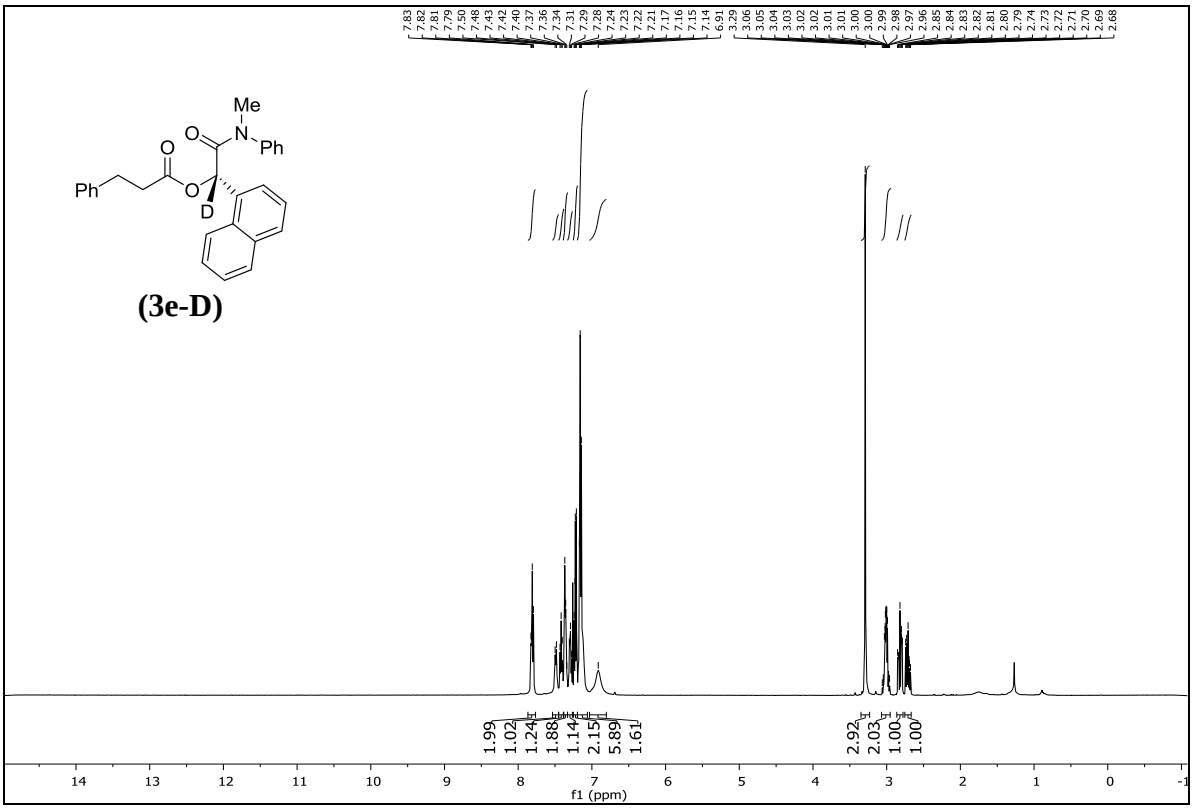

172.625
169.211
142.322
140.740
138.862
138.599
129.606
128.537
128.378
128.072
128.020
126.214
70.671
38.936
35.816
31.008
20.988
19.804
Me
N
Ph
O
O
Ph
Me
Me
Me
(3d)
f1 (ppm)

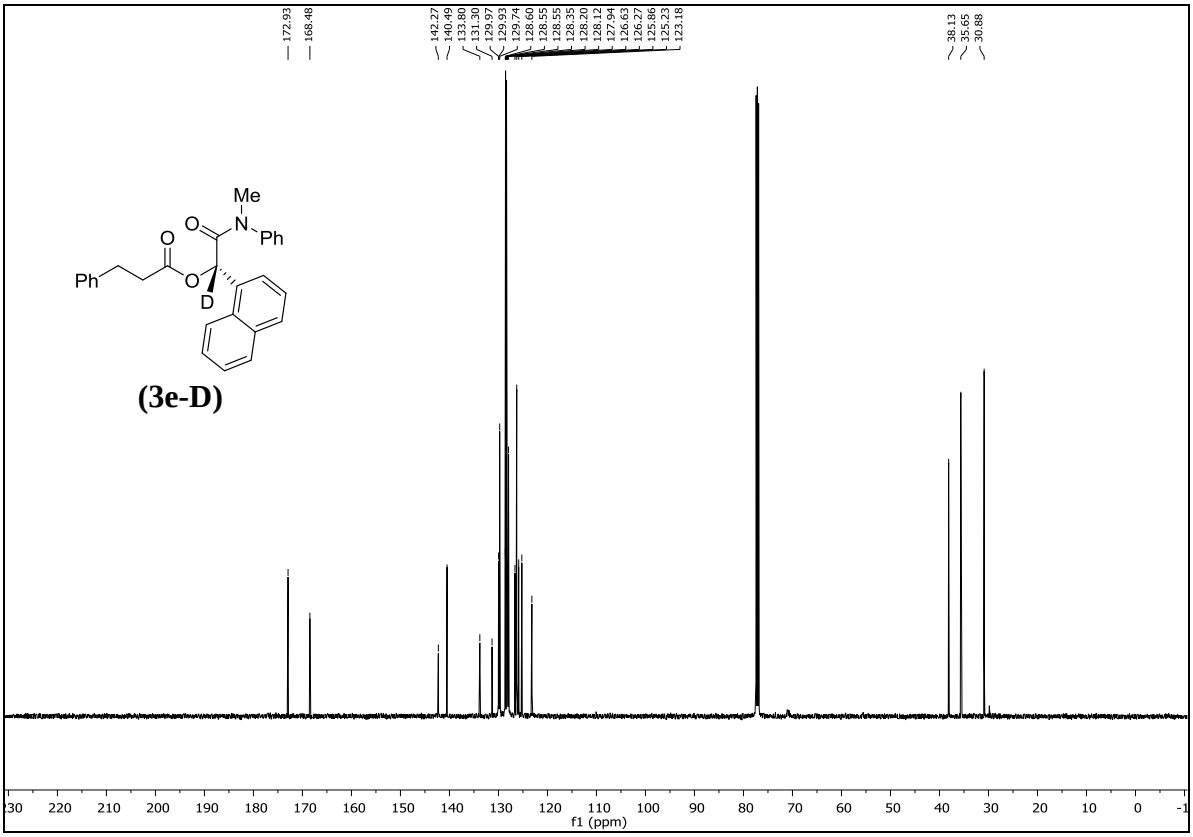

7.795
7.779
7.496
7.480
7.418
7.404
7.389
7.351
7.295
7.280
7.265
7.244
7.226
7.211
7.196
7.144
7.129
6.897
6.678
3.277
3.017
3.003
2.994
2.977
2.839
2.823
2.807
2.792
2.775
2.728
2.714
2.696
2.681
2.664
Me
N
Ph
O
O
Ph
O
H
2.00
1.04
1.11
1.93
1.13
2.47
5.94
1.77
1.00
2.99
2.05
1.04
1.08
f1 (ppm)

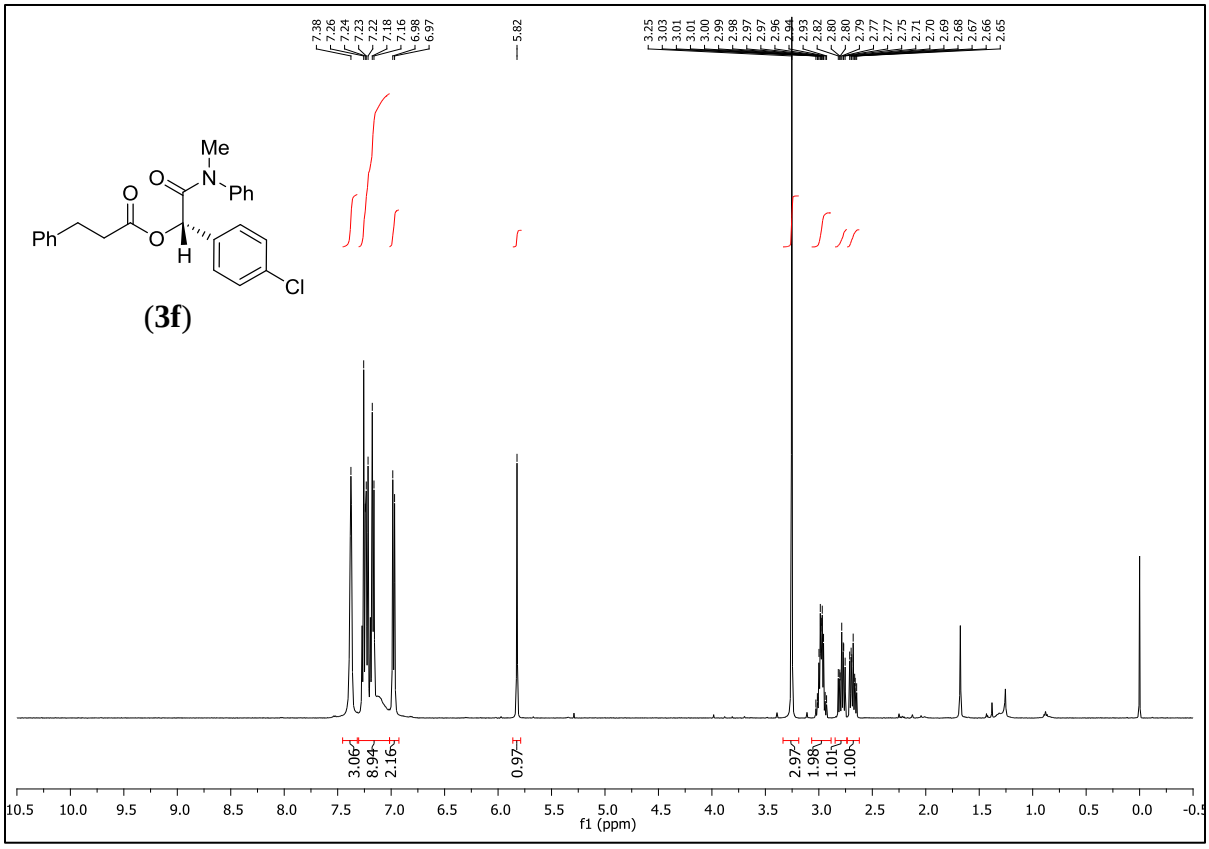
(**3e**)

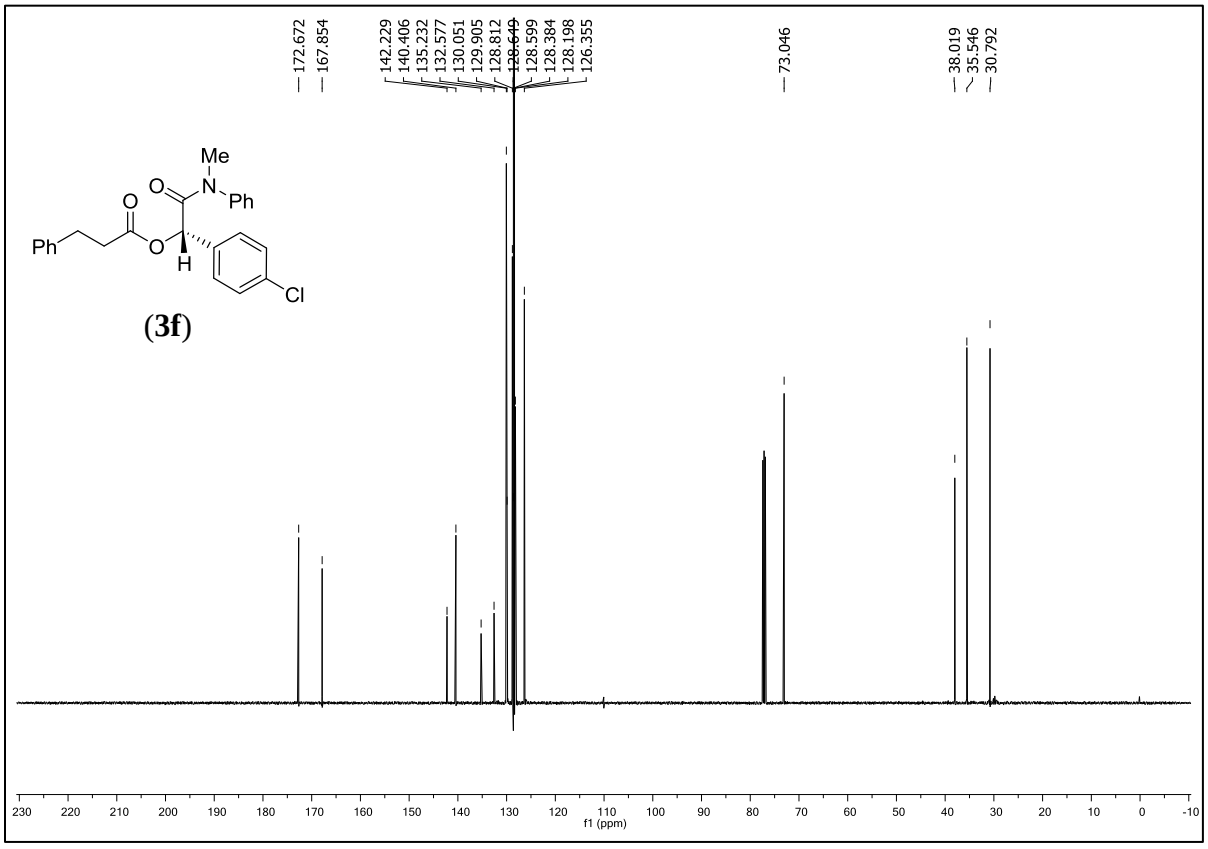

172.913
168.492
142.263
140.480
133.793
131.308
129.963
129.729
128.596
128.540
128.340
128.188
128.137
127.929
126.627
126.259
125.859
125.217
123.181
71.200
38.137
35.645
30.871
Me
N
Ph
O
O
Ph
O
H
f1 (ppm)

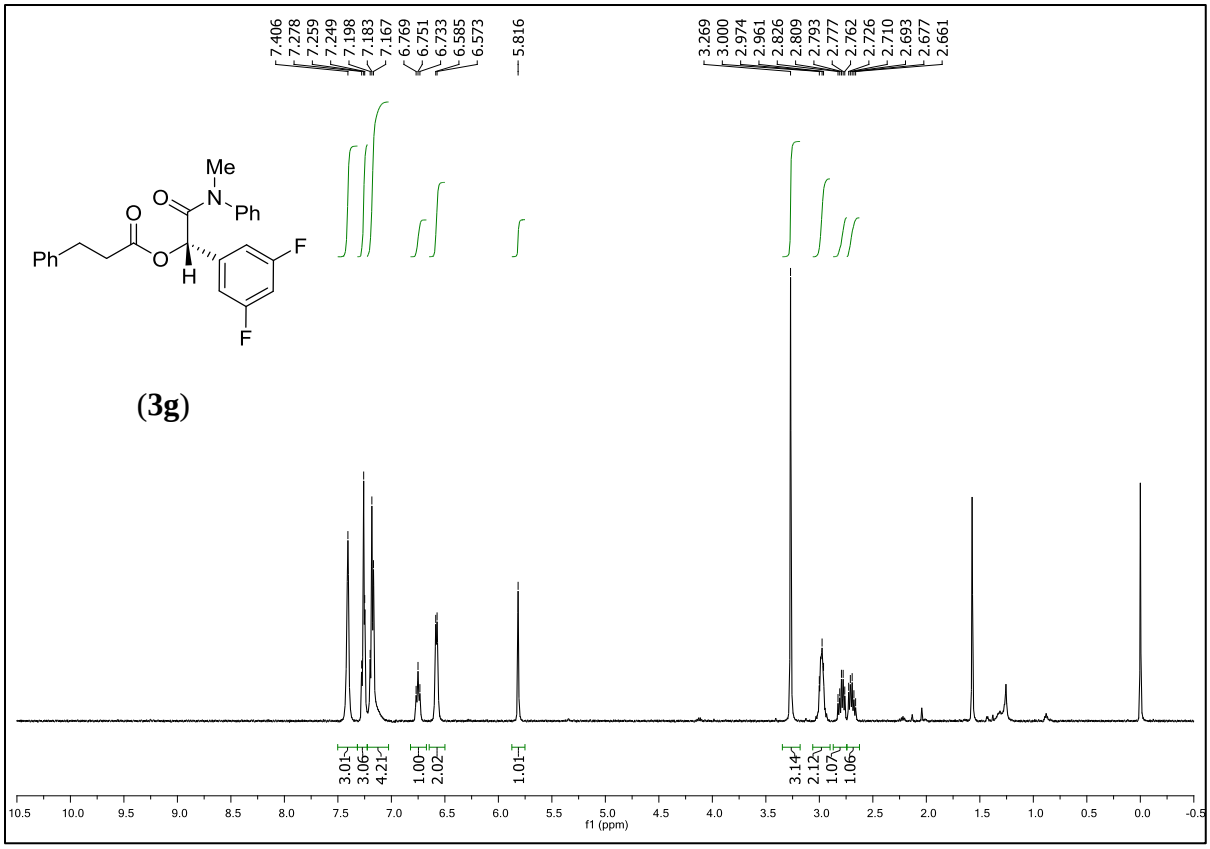
(**3e**)

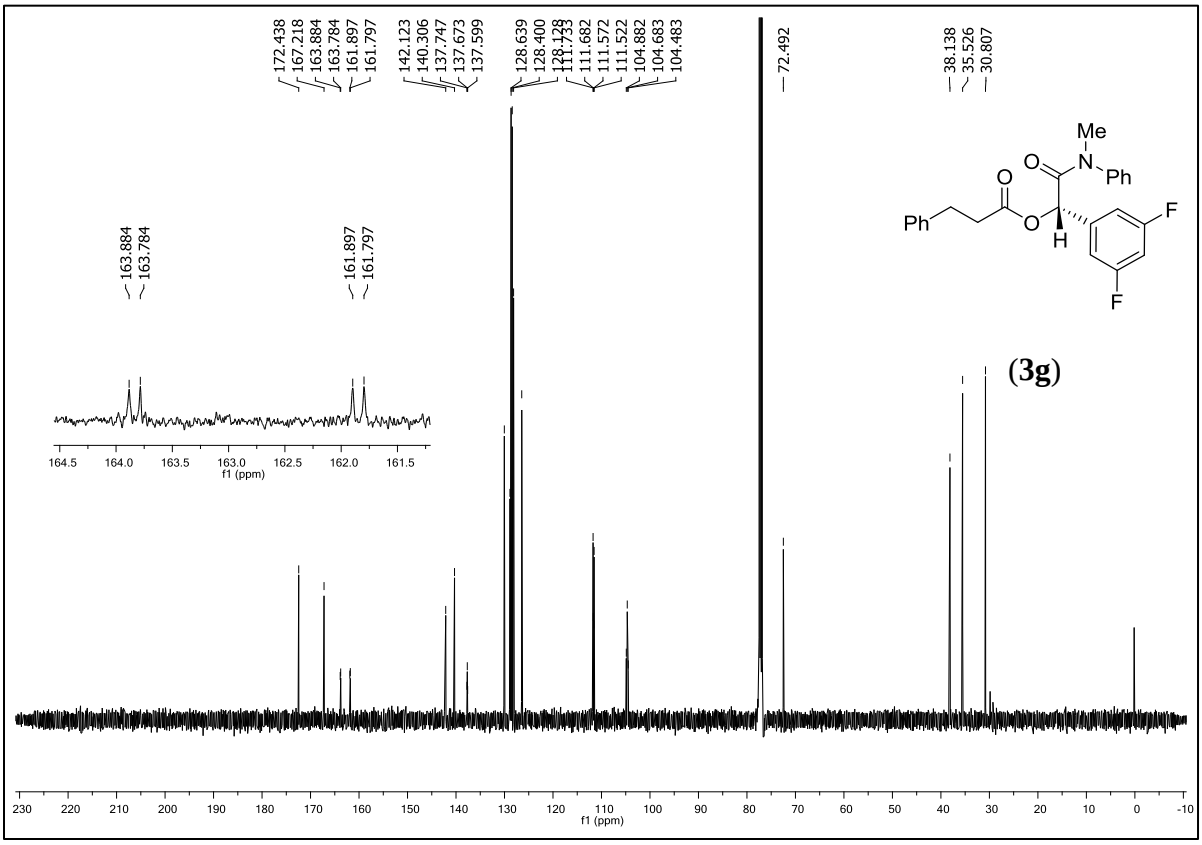

Me
N
Ph
O
O
Ph
O
D
(3e-D)
f1 (ppm)

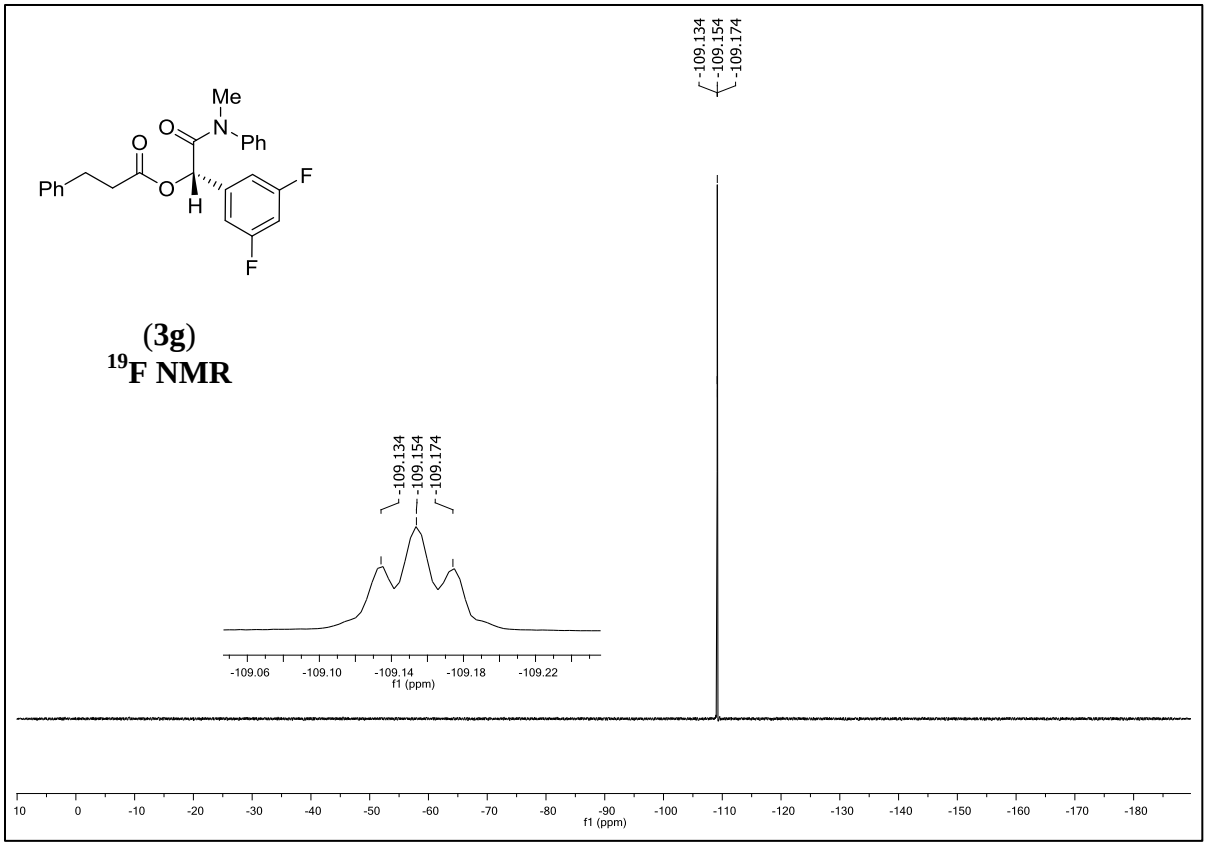

Me
N
Ph
O
O
Ph
O
D
(3e-D)
f1 (ppm)

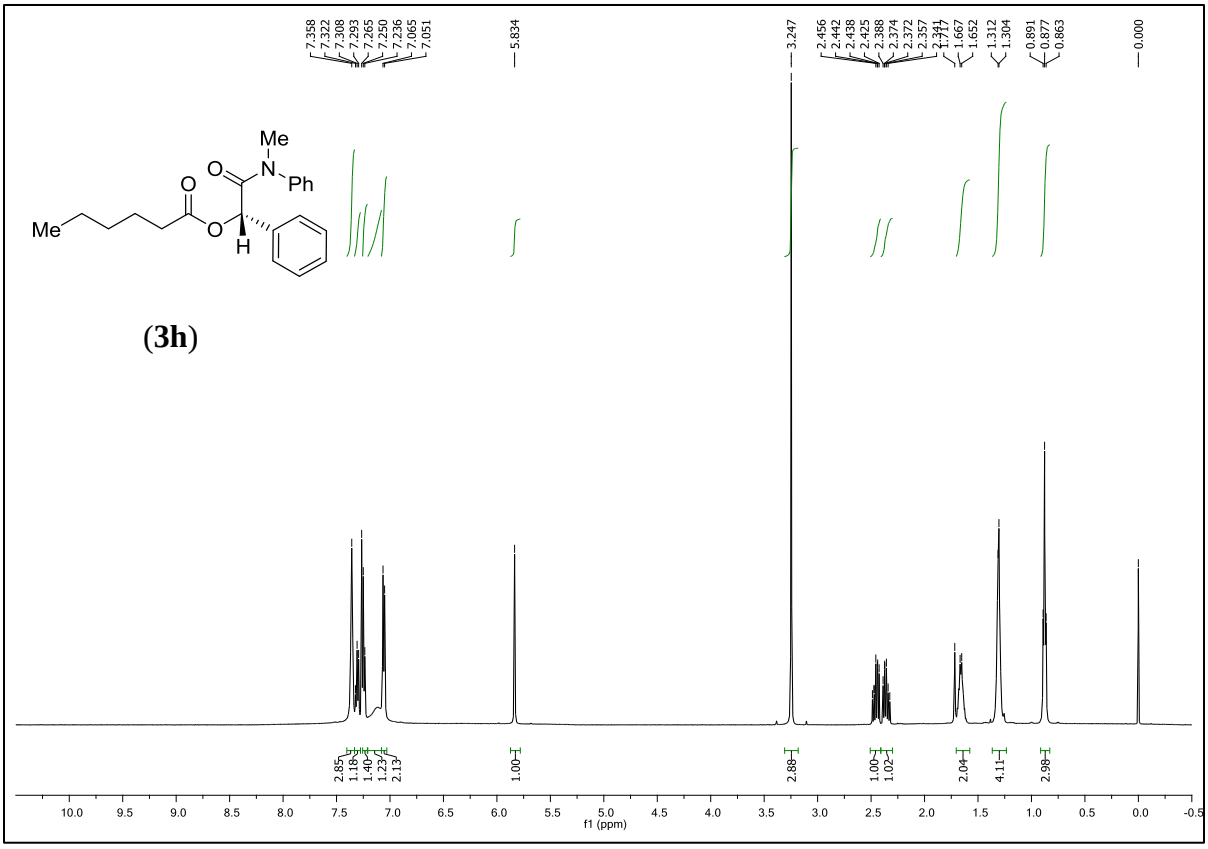

7.38
7.26
7.24
7.23
7.22
7.18
7.16
6.98
6.97
5.82
3.25
3.03
3.01
3.01
3.00
2.99
2.98
2.97
2.97
2.96
2.94
2.93
2.82
2.80
2.80
2.79
2.77
2.77
2.75
2.71
2.70
2.69
2.68
2.67
2.66
2.65
Me
N
Ph
O
O
Ph
O
H
Cl
(3f)
3.06
8.94
2.16
0.97
2.97
1.98
1.01
1.00
f1 (ppm)

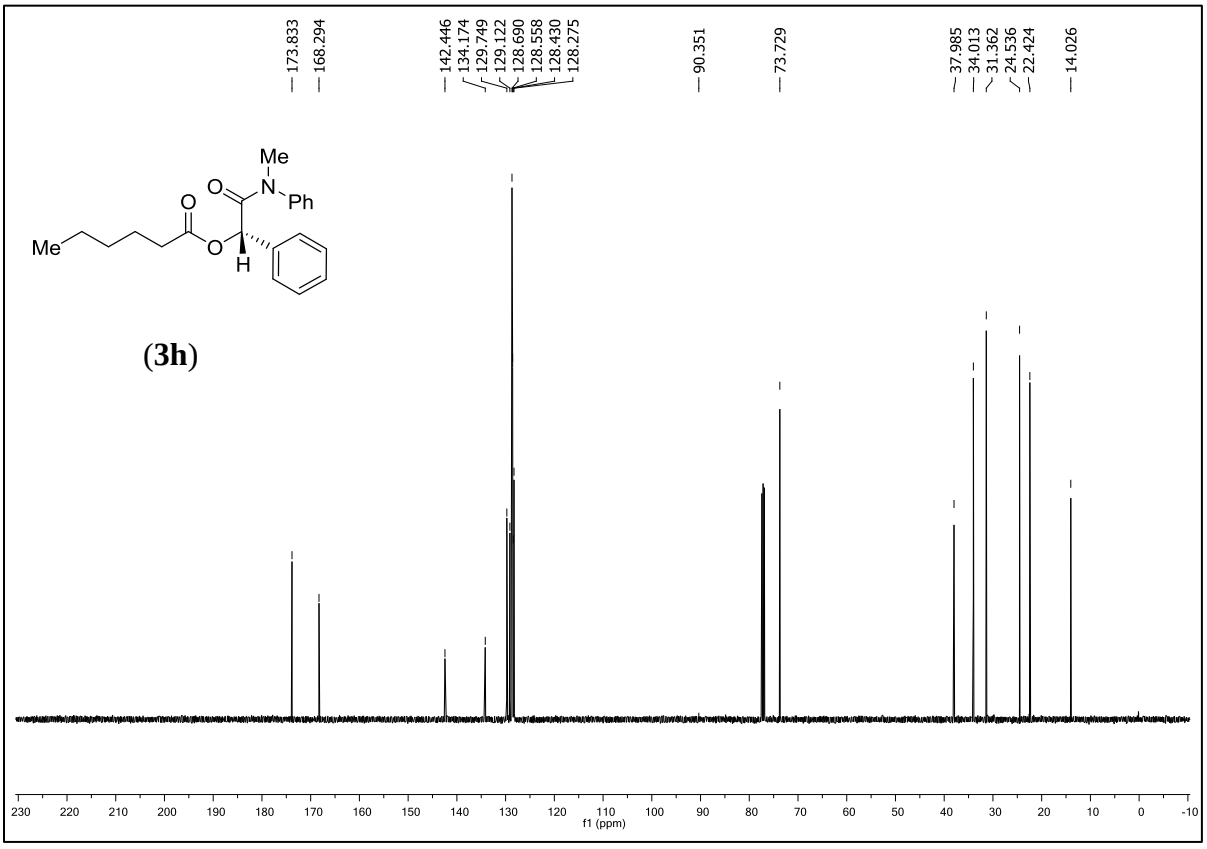

172.672
167.854
142.229
140.406
135.232
132.577
130.051
129.905
128.812
128.640
128.599
128.384
128.198
126.355
73.046
38.019
35.546
30.792
Me
N
Ph
O
O
Ph
O
H
Cl
(3f)
f1 (ppm)

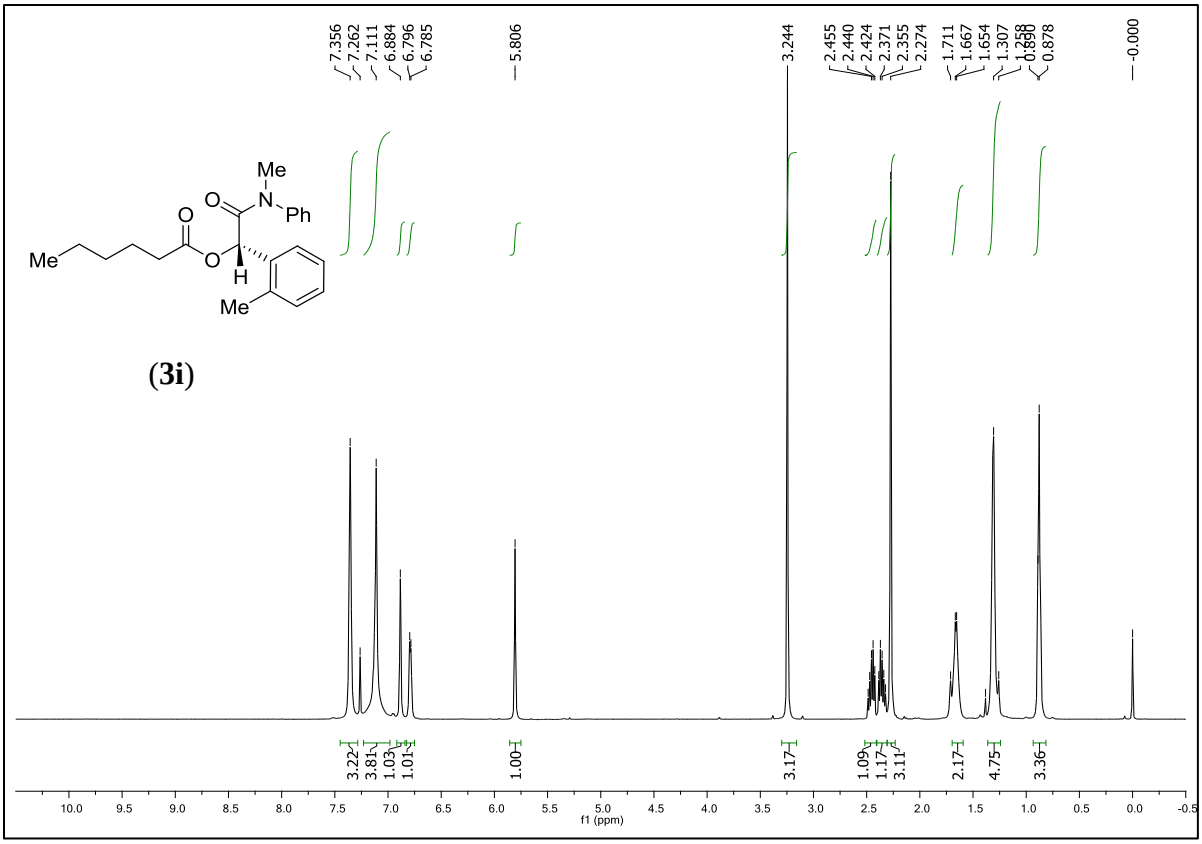

7.406
7.278
7.259
7.249
7.198
7.183
7.167
6.769
6.751
6.733
6.585
6.573
5.816
3.269
3.000
2.974
2.961
2.826
2.809
2.793
2.777
2.762
2.726
2.710
2.693
2.677
2.661
Me
N
Ph
O
O
Ph
O
H
F
F
(3g)
3.01
3.06
4.21
1.00
2.02
1.01
3.14
2.12
1.07
1.06
f1 (ppm)

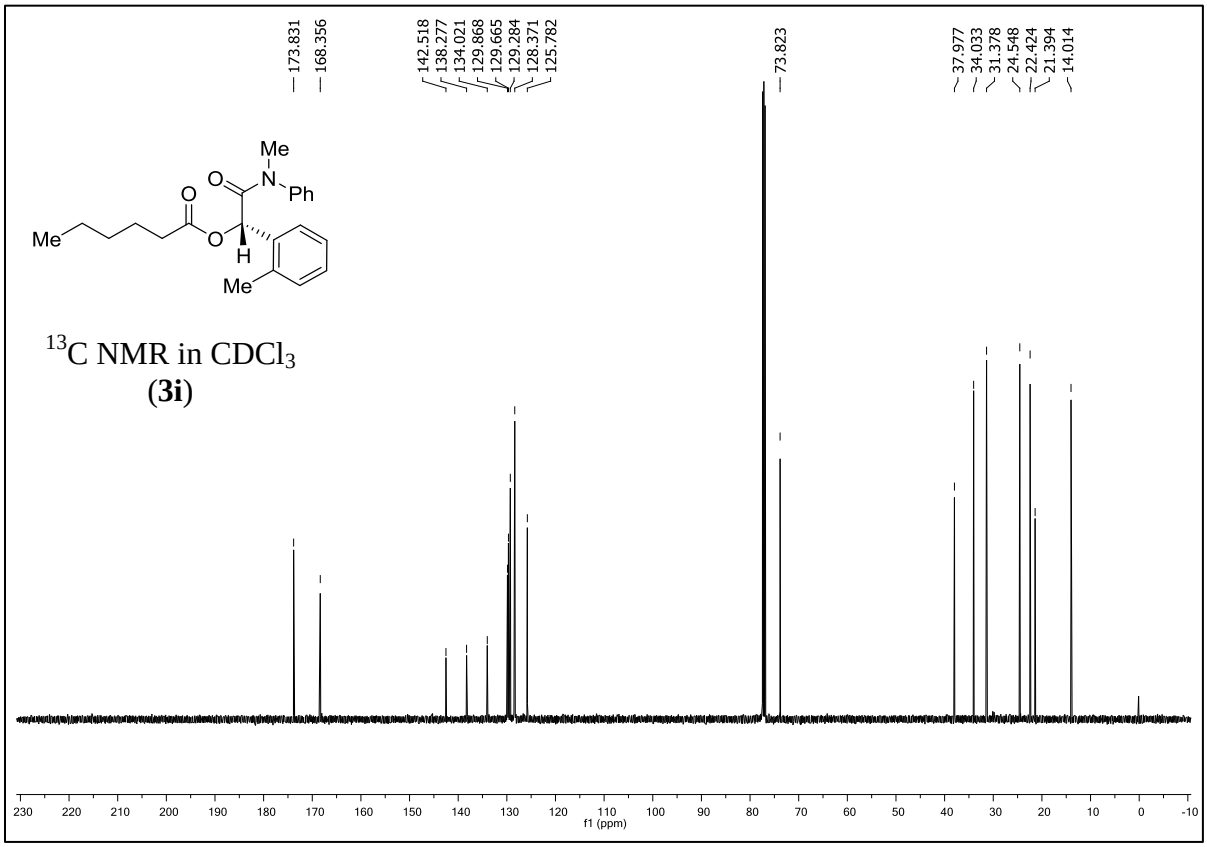

172.438
167.218
163.884
163.784
161.897
161.797
142.123
140.306
137.747
137.673
137.599
128.639
128.400
111.682
111.572
111.522
104.882
104.683
104.483
72.492
38.138
35.526
30.807
163.884
163.784
161.897
161.797
Me
N
Ph
O
O
Ph
O
H
F
F
(3g)
f1 (ppm)

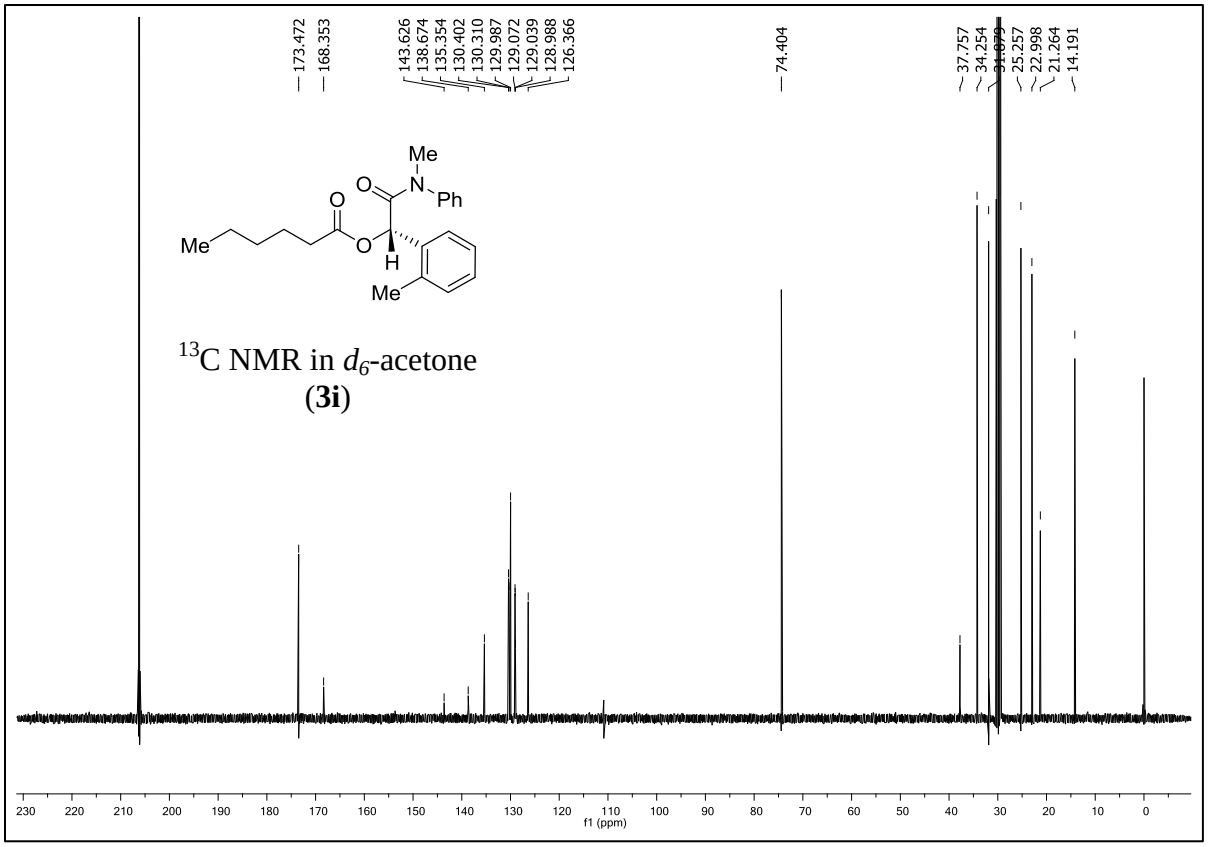

Me
N
Ph
O
O
Ph
O
H
F
F
(3g)
19F NMR
-109.134
-109.154
-109.174
-109.06
-109.10
-109.14
-109.18
-109.22
f1 (ppm)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)


7.358
7.322
7.308
7.293
7.265
7.250
7.236
7.065
7.051
5.834
3.247
2.456
2.442
2.438
2.425
2.388
2.374
2.372
2.357
1.741
1.667
1.652
1.312
1.304
0.891
0.877
0.863
0.000
Me
N
Ph
O
O
Me
H
(3h)
2.85
1.18
1.40
1.23
2.13
1.00
2.88
1.00
1.02
2.04
4.11
2.98
f1 (ppm)

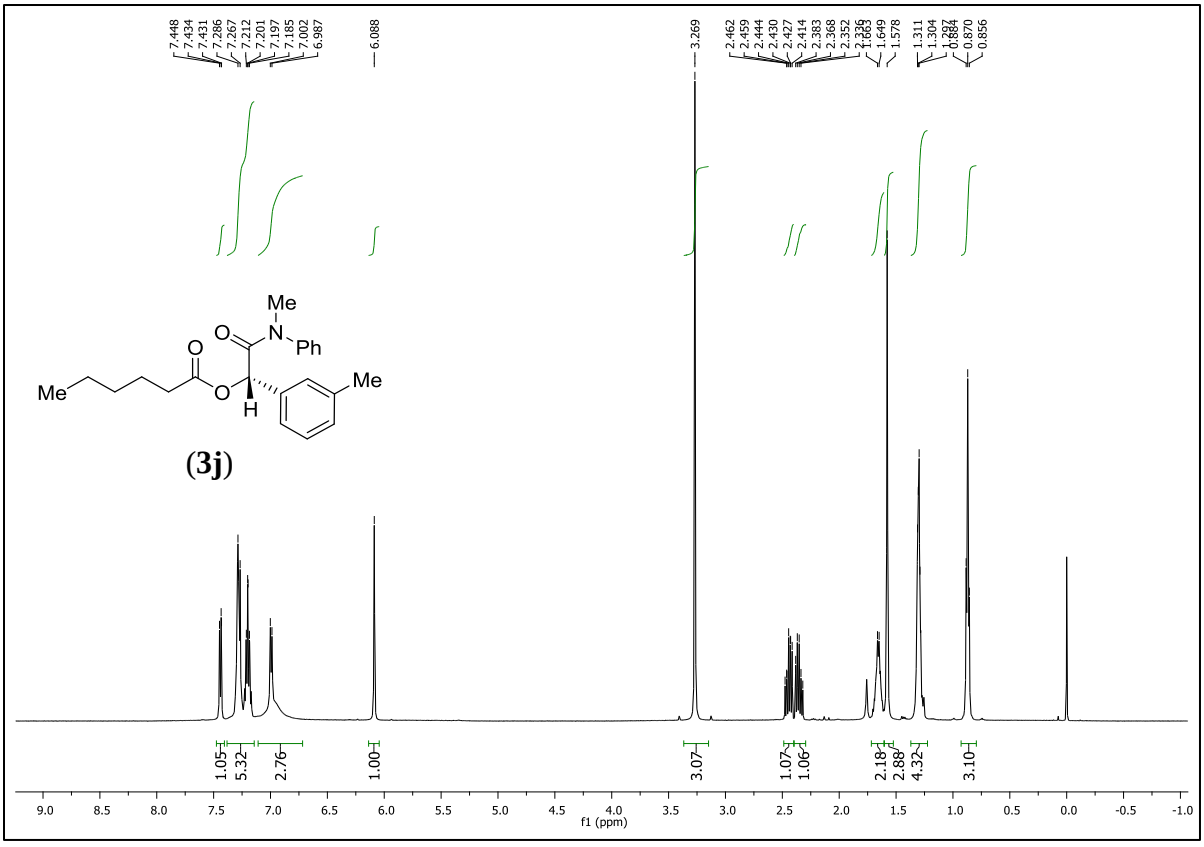

173.833
168.294
142.446
134.174
129.749
129.122
128.690
128.558
128.430
128.275
90.351
73.729
37.985
34.013
31.362
24.536
22.424
14.026
Me
N
Ph
O
O
Me
H
(3h)
f1 (ppm)

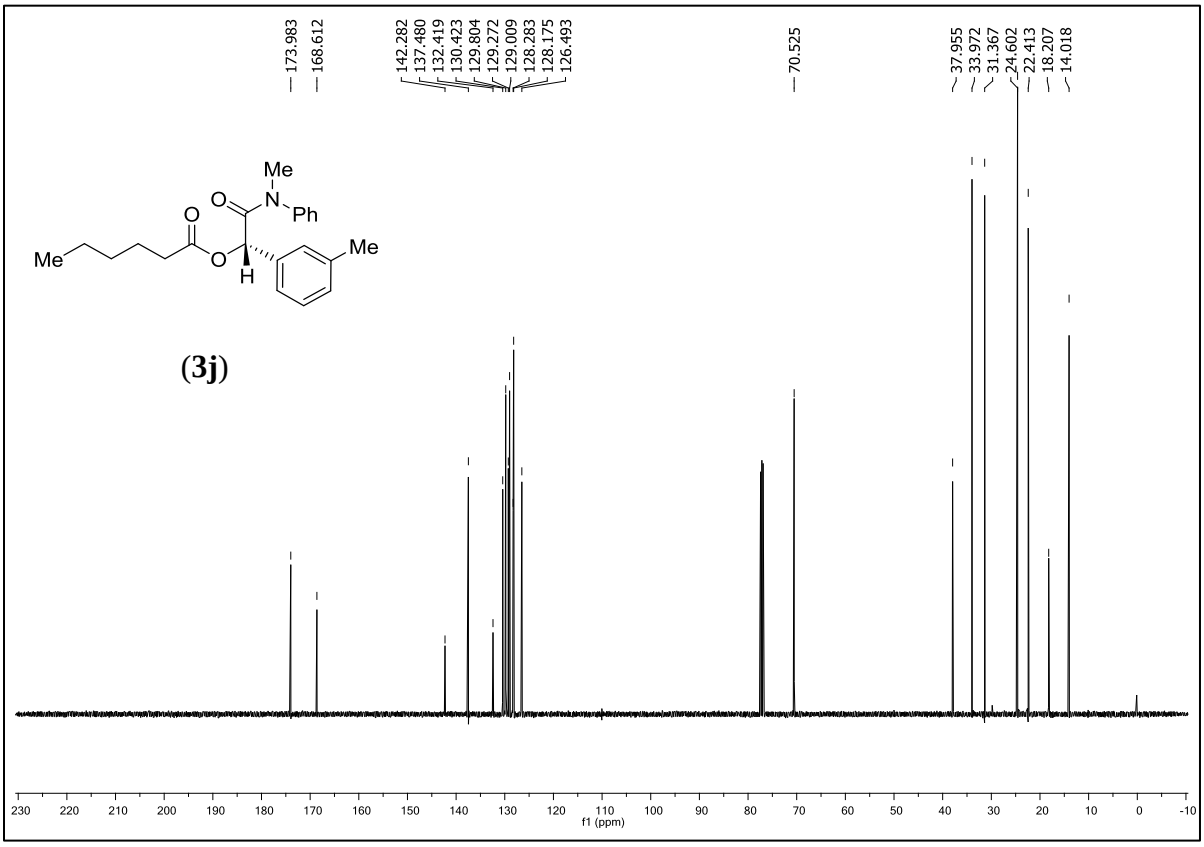

7.356
7.262
7.111
6.884
6.796
6.785
5.806
3.244
2.455
2.440
2.424
2.371
2.355
2.274
1.711
1.667
1.654
1.307
0.878
-0.000
Me
N
Ph
O
O
O
H
Me
Me
(3i)
3.22
3.81
1.03
1.01
1.00
3.17
1.09
1.17
3.11
2.17
4.75
3.36
f1 (ppm)

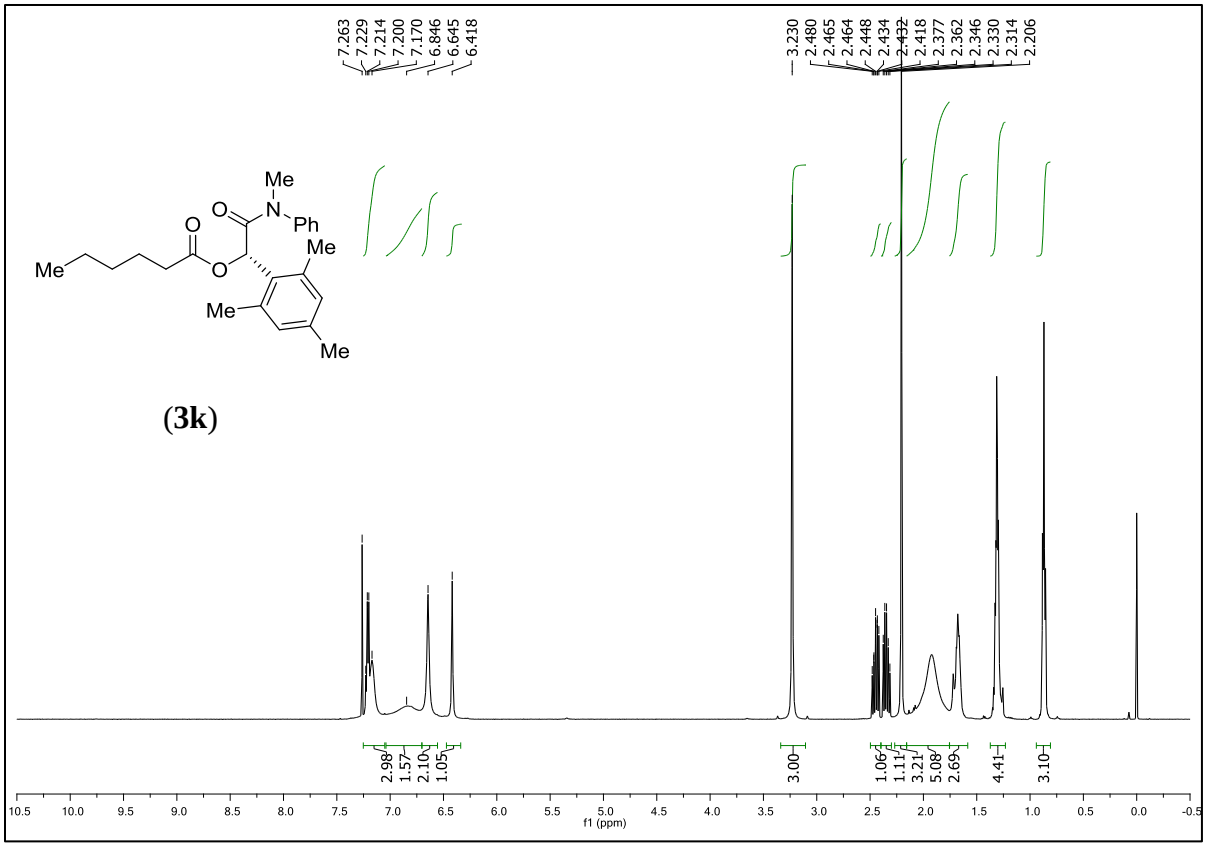

173.831
168.356
142.518
138.277
134.021
129.868
129.665
129.284
128.371
125.782
73.823
37.977
34.033
31.378
24.548
22.424
21.394
14.014
Me
N
Ph
O
O
O
H
Me
Me
13C NMR in CDCl3
(3i)
f1 (ppm)



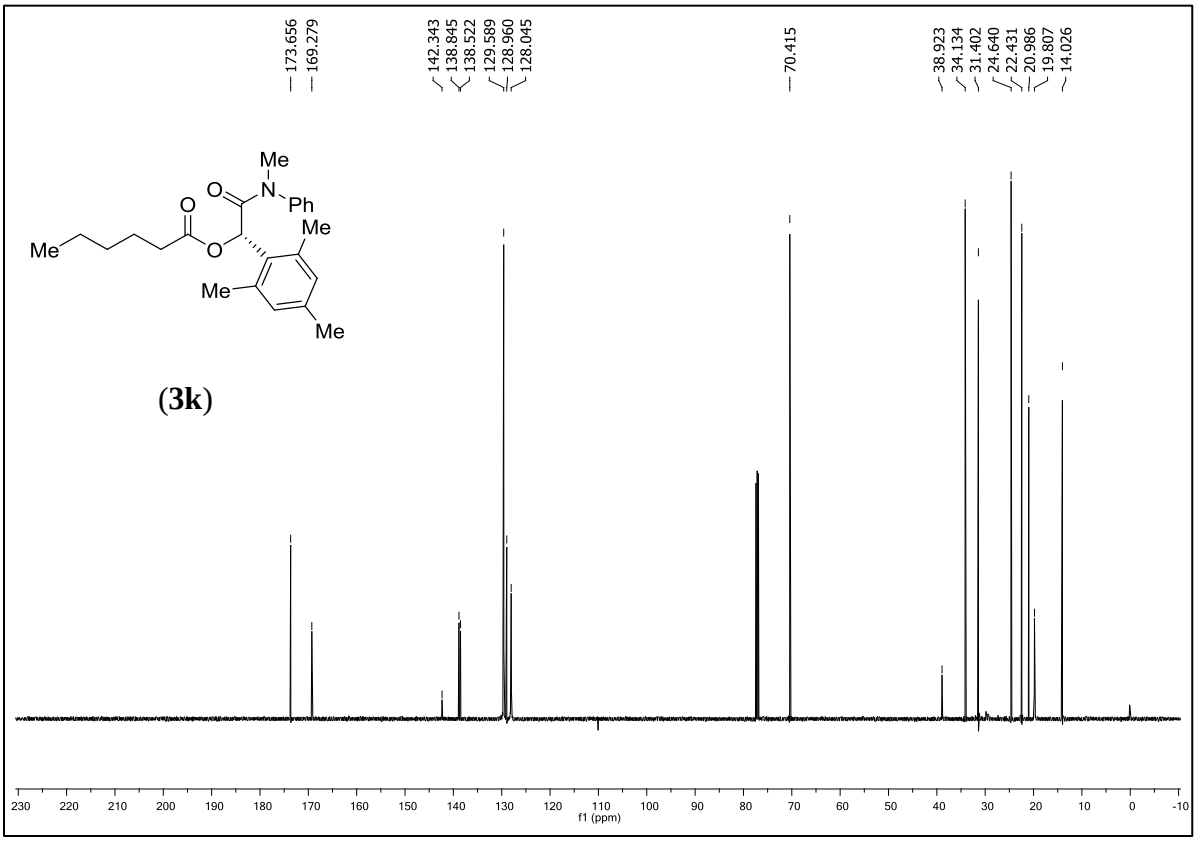
^{13}C NMR in d_6-acetone
(**3i**)


7.448
7.434
7.431
7.286
7.267
7.212
7.201
7.197
7.185
7.002
6.987
6.088
3.269
2.462
2.459
2.444
2.430
2.427
2.414
2.383
2.368
2.352
2.336
1.663
1.649
1.578
1.311
1.304
1.287
0.884
0.870
0.856
Me
N
Ph
O
O
Me
O
H
Me
(3j)
1.05
5.32
2.76
1.00
3.07
1.07
1.06
2.18
2.88
4.32
3.10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

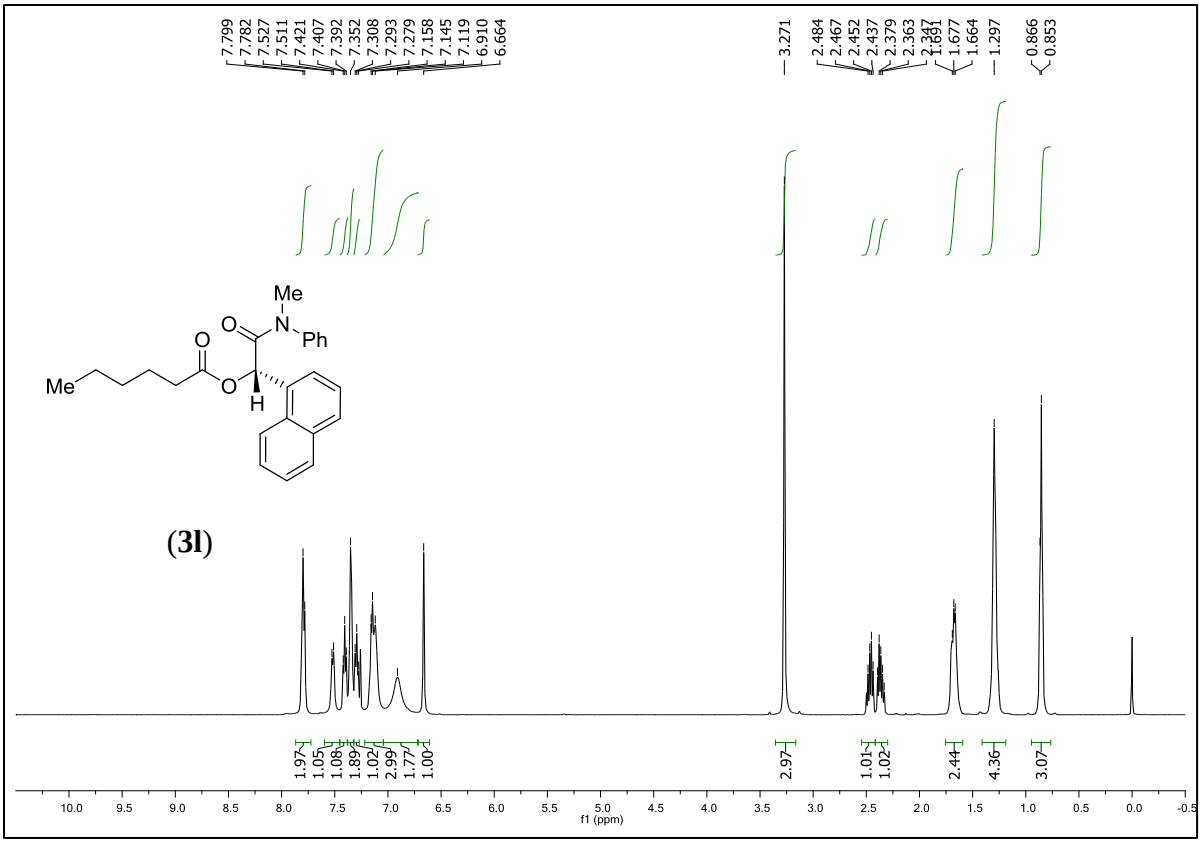

173.983
168.612
142.282
137.480
132.419
130.423
129.804
129.272
129.009
128.283
128.175
126.493
70.525
37.955
33.972
31.367
24.602
22.413
18.207
14.018
Me
N
Ph
O
O
Me
O
H
Me
(3j)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

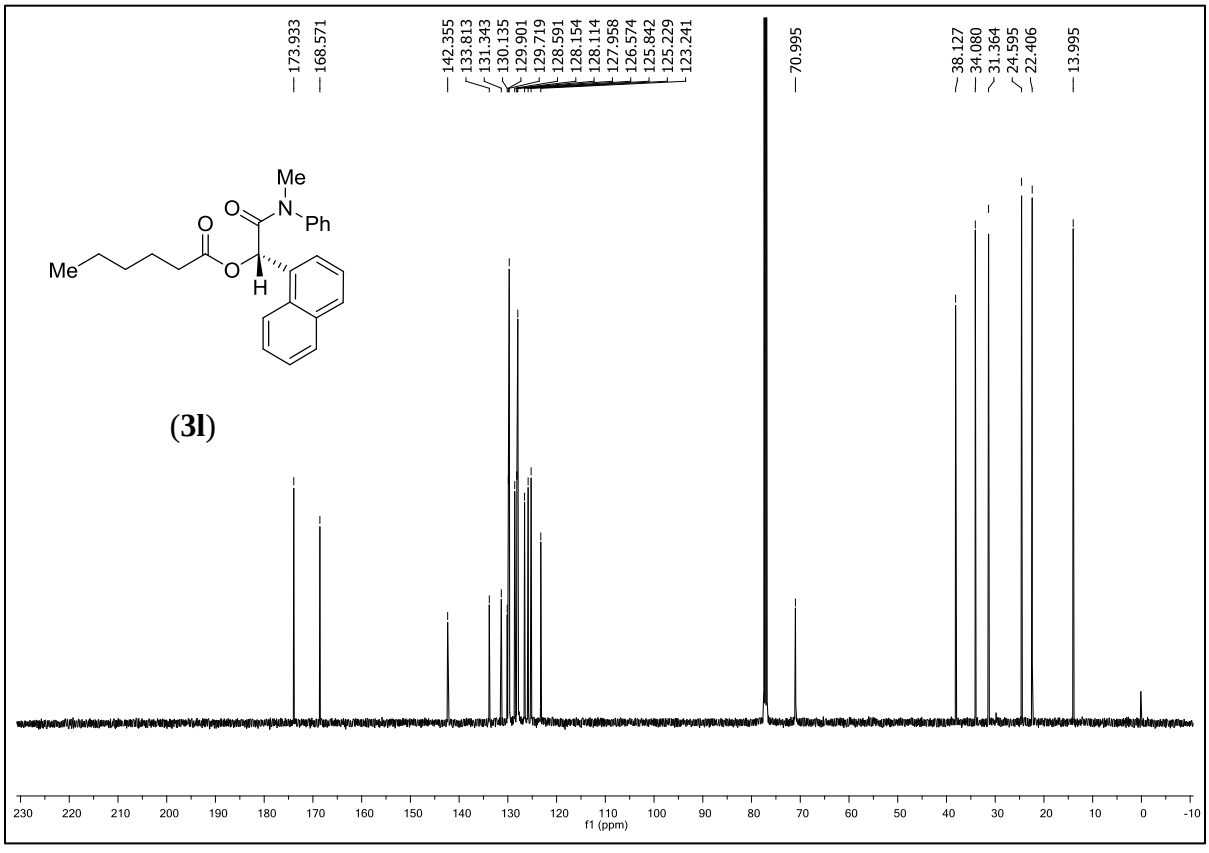

7.263
7.229
7.214
7.200
7.170
6.846
6.645
6.418
3.230
2.480
2.465
2.464
2.448
2.434
2.432
2.418
2.377
2.362
2.346
2.330
2.314
2.206
Me
N
Ph
O
O
Me
Me
Me
Me
2.98
1.57
2.10
1.05
3.00
1.06
1.11
3.21
5.08
2.69
4.41
3.10
f1 (ppm)

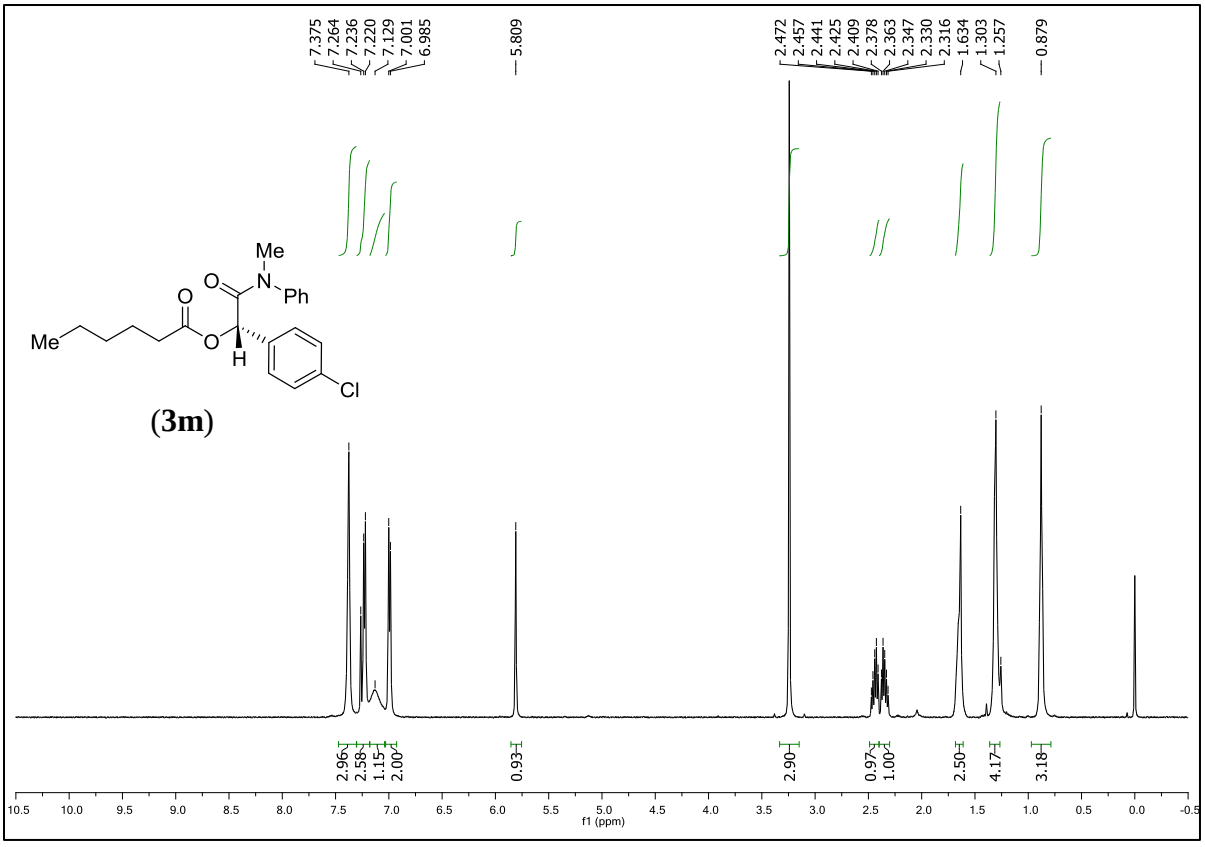
(3k)

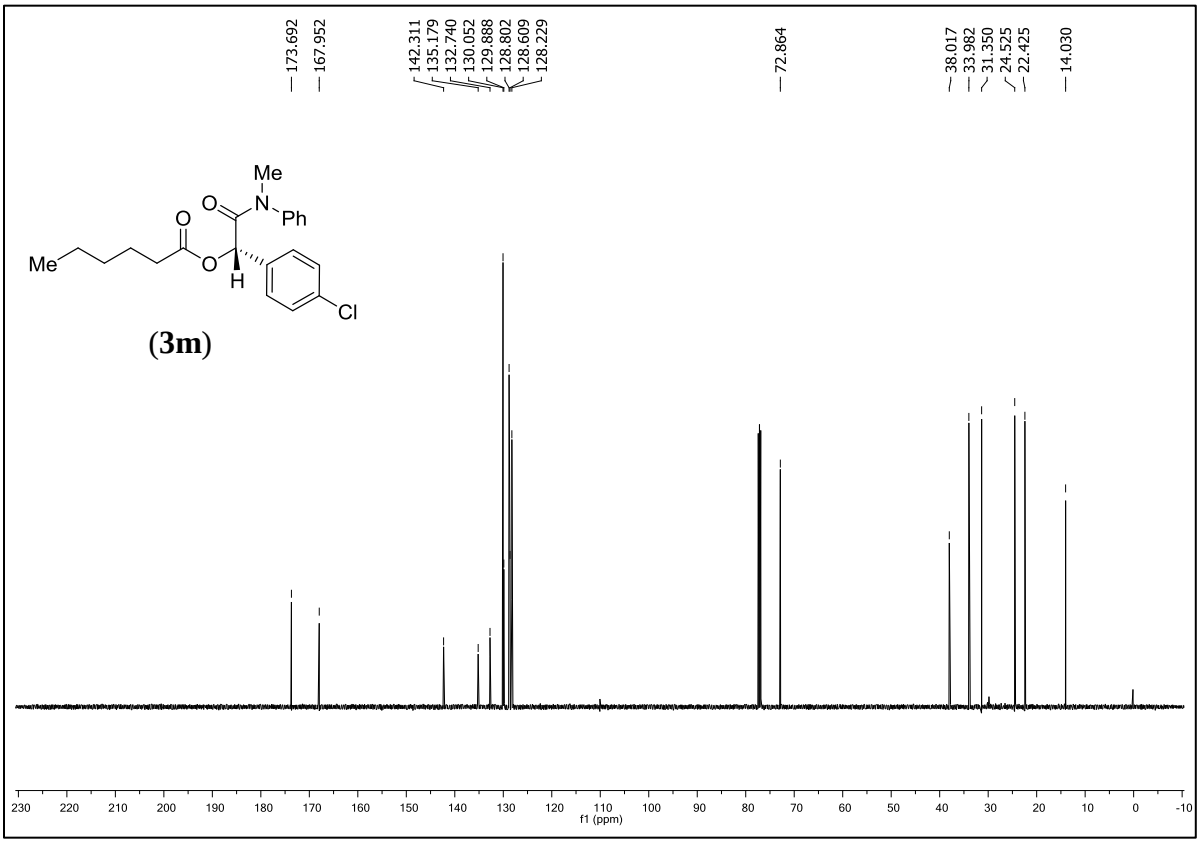

173.656
169.279
142.343
138.845
138.522
129.589
128.960
128.045
70.415
38.923
34.134
31.402
24.640
22.431
20.986
19.807
14.026
Me
N
Ph
O
O
Me
Me
Me
f1 (ppm)

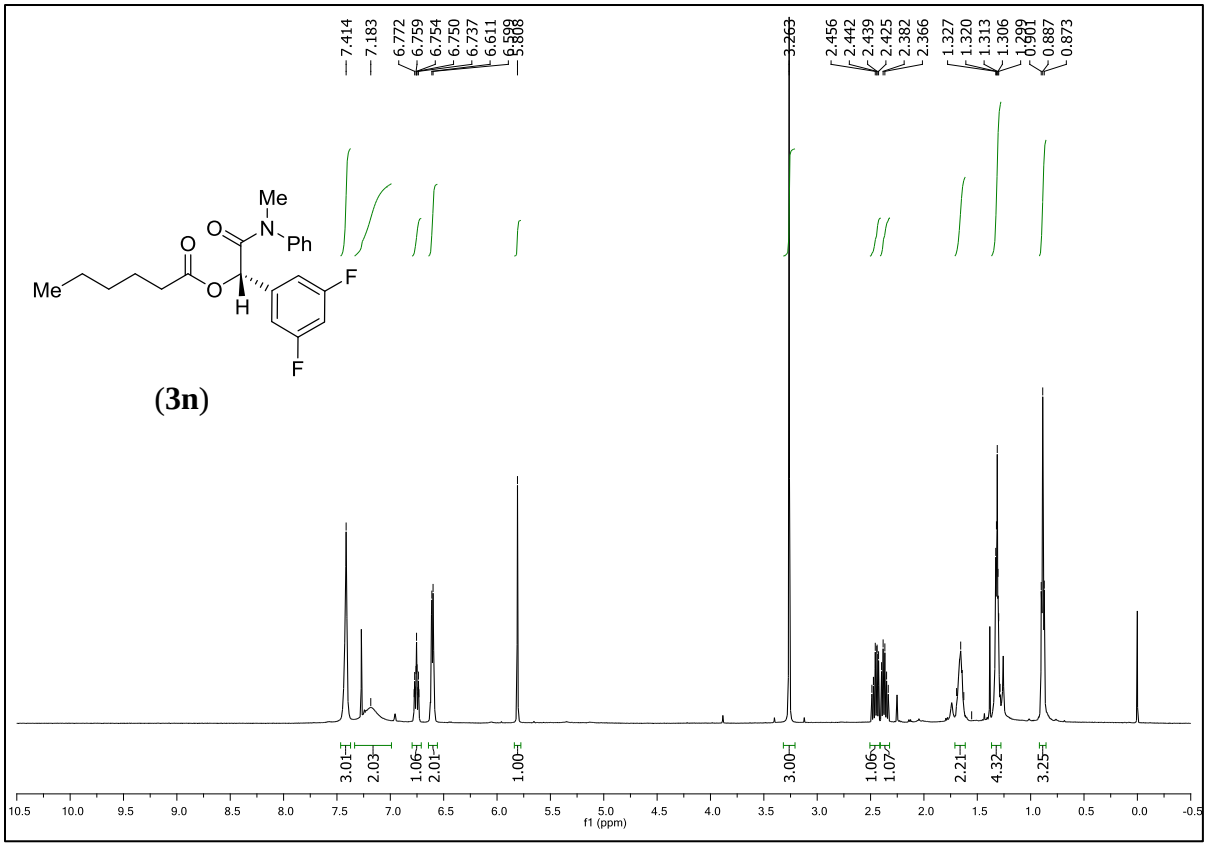
(3k)

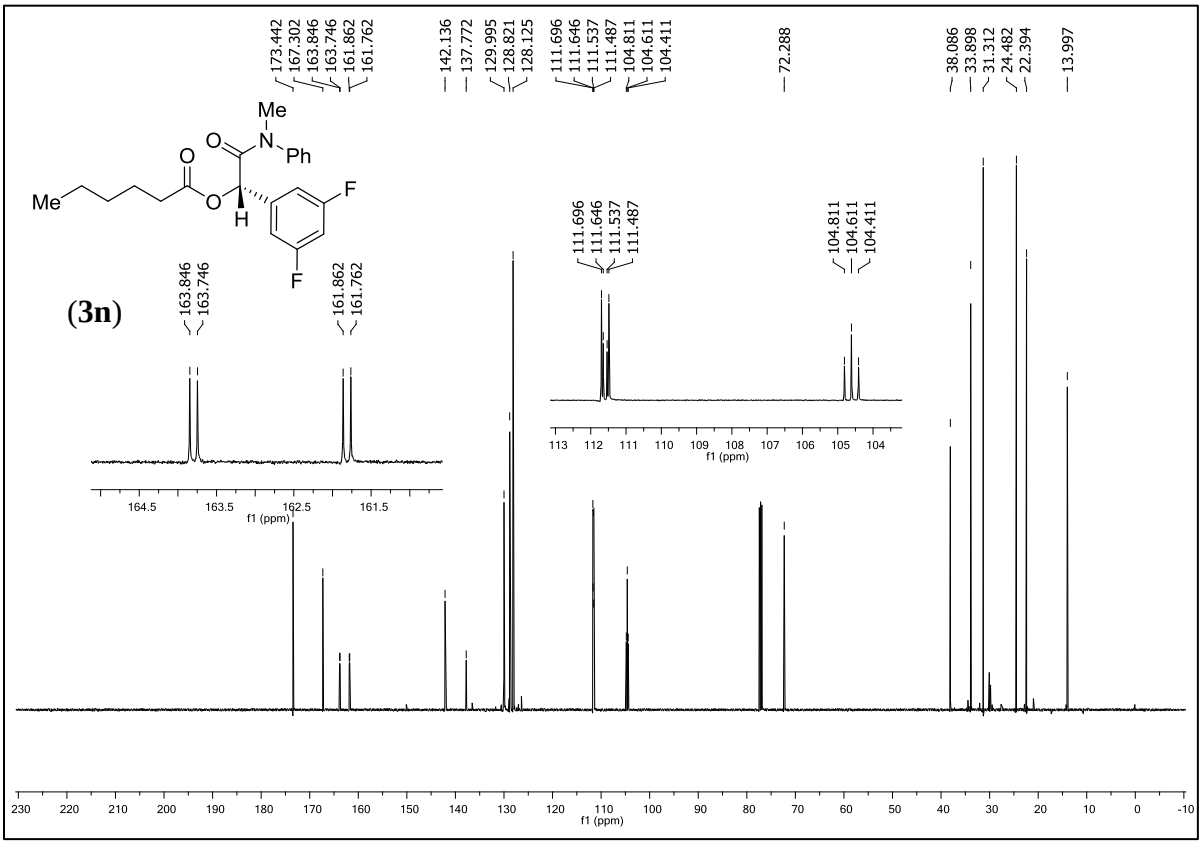

7.799
7.782
7.527
7.511
7.421
7.407
7.392
7.352
7.308
7.293
7.279
7.158
7.145
7.119
6.910
6.664
3.271
2.484
2.467
2.452
2.437
2.379
2.363
2.347
1.691
1.677
1.664
1.297
0.866
0.853
Me
N
Ph
O
O
Me
O
H
(3l)
1.97
1.05
1.08
1.89
1.02
2.99
1.77
1.00
2.97
1.01
1.02
2.44
4.36
3.07
f1 (ppm)

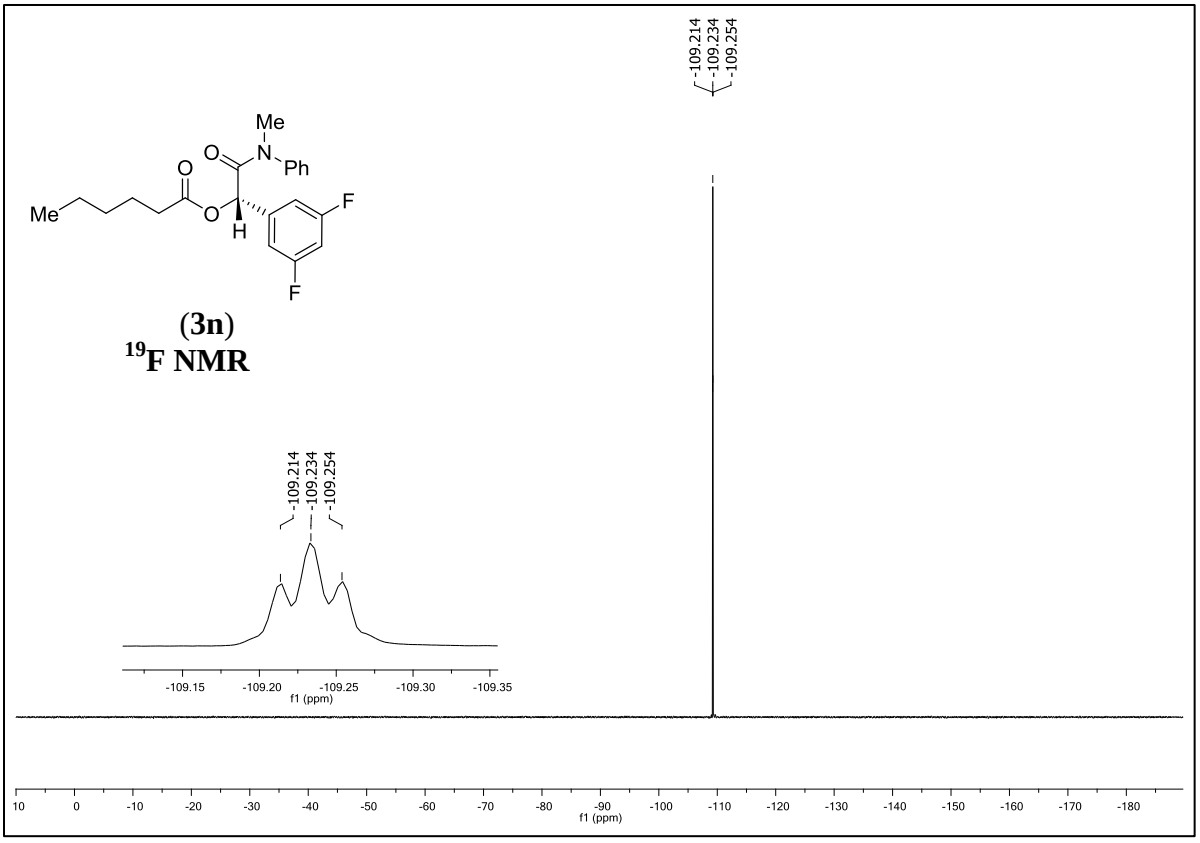

173.933
168.571
142.355
133.813
131.343
130.135
129.901
129.719
128.591
128.154
128.114
127.958
126.574
125.842
125.229
123.241
70.995
38.127
34.080
31.364
24.595
22.406
13.995
Me
N
Ph
O
O
Me
O
H
(3l)
f1 (ppm)

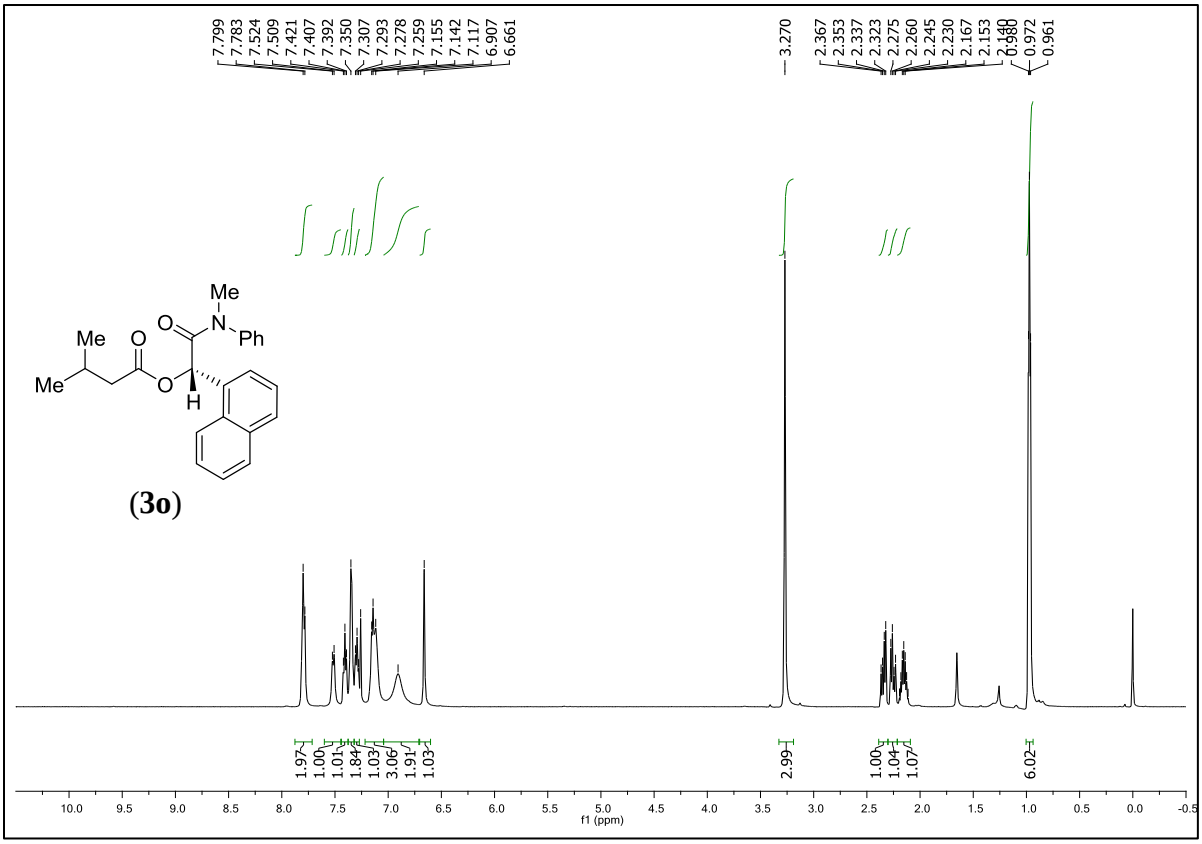

7.375
7.264
7.236
7.220
7.129
7.001
6.985
5.809
2.472
2.457
2.441
2.425
2.409
2.378
2.363
2.347
2.330
2.316
1.634
1.303
1.257
0.879
Me
N
Ph
O
O
O
H
Me
Cl
(3m)
2.96
2.58
1.15
2.00
0.93
2.90
0.97
1.00
2.50
4.17
3.18
f1 (ppm)

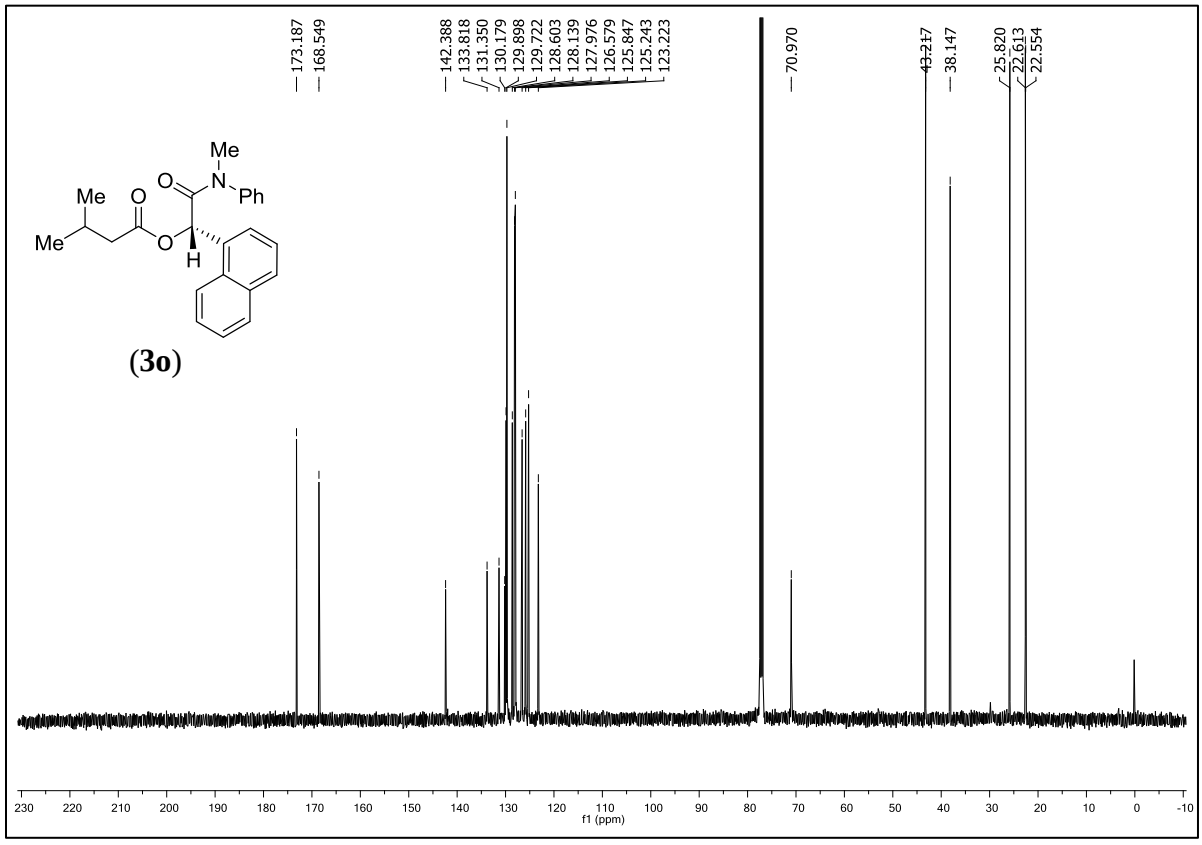

173.692
167.952
142.311
135.179
132.740
130.052
129.888
128.802
128.609
128.229
72.864
38.017
33.982
31.350
24.525
22.425
14.030
Me
N
Ph
O
O
O
H
Me
Cl
(3m)
f1 (ppm)

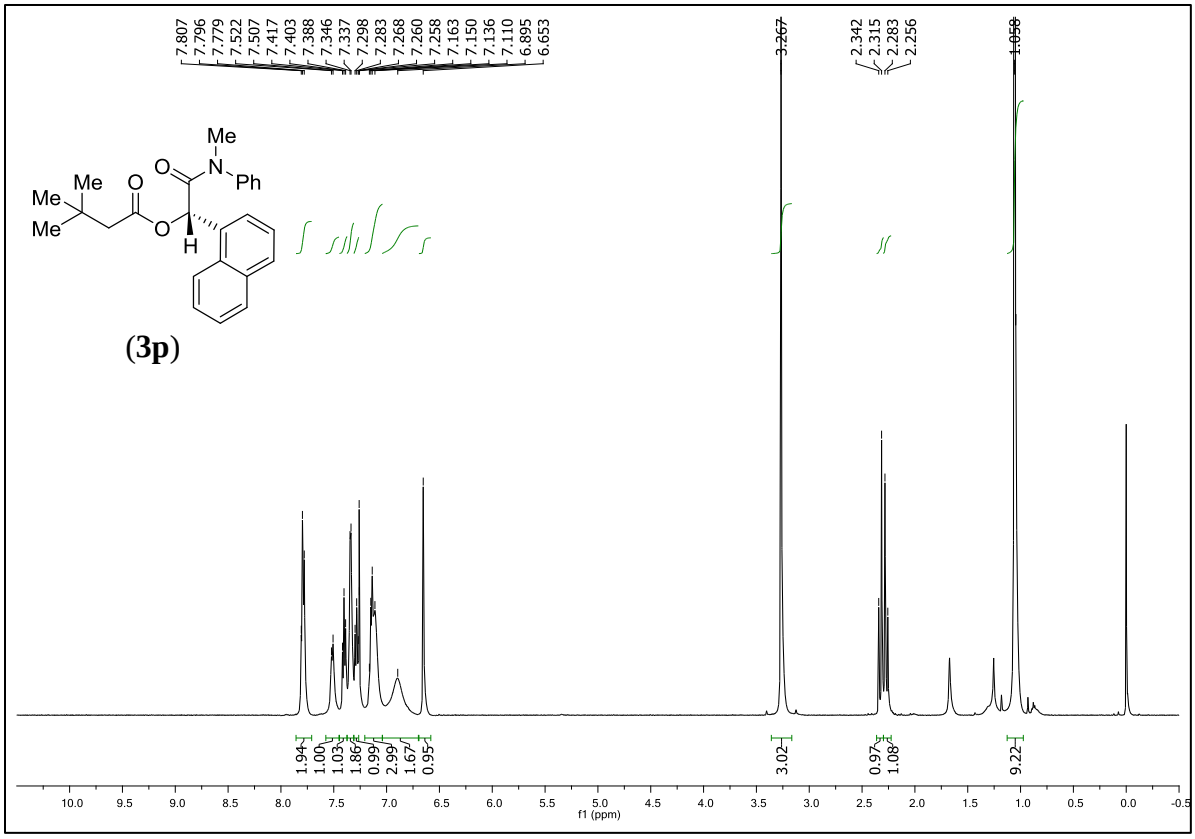

(3n)


(3n)

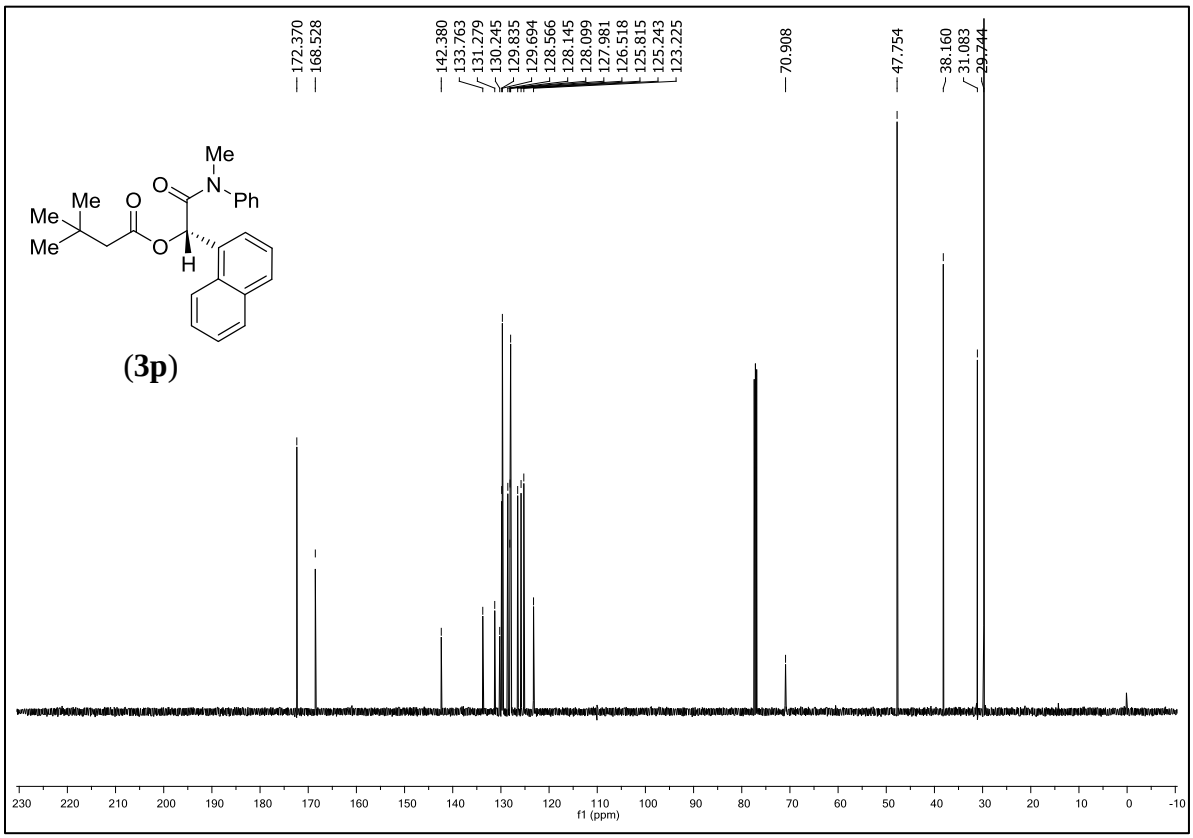

-109.214
-109.234
-109.254
Me
O
N
Ph
O
Me
O
H
F
F
(3n)
19F NMR
-109.214
-109.234
-109.254
-109.15
-109.20
-109.25
-109.30
-109.35
f1 (ppm)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)


7.799
7.783
7.524
7.509
7.421
7.407
7.392
7.350
7.307
7.293
7.278
7.259
7.155
7.142
7.117
6.907
6.661
3.270
2.367
2.353
2.337
2.323
2.275
2.260
2.245
2.230
2.167
2.153
0.972
0.961
Me
N
Ph
O
Me
O
Me
O
H
(3o)
1.97
1.00
1.01
1.84
1.03
3.06
1.91
1.03
2.99
1.00
1.04
1.07
6.02
f1 (ppm)

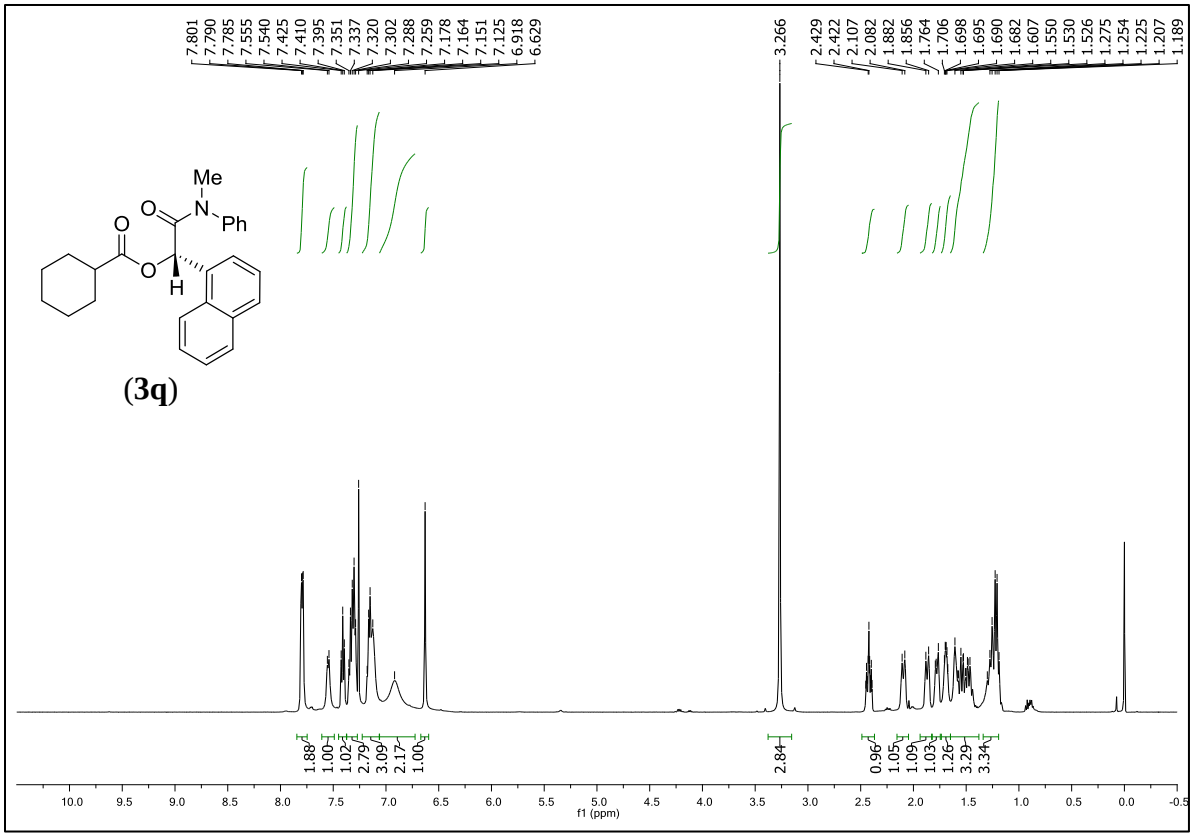

173.187
168.549
142.388
133.818
131.350
130.179
129.898
129.722
128.603
128.139
127.976
126.579
125.847
125.243
123.223
70.970
43.217
38.147
25.820
22.613
22.554
Me
N
Ph
O
Me
O
Me
O
H
(3o)
f1 (ppm)


7.807
7.796
7.779
7.522
7.507
7.417
7.403
7.388
7.346
7.337
7.298
7.283
7.268
7.260
7.258
7.163
7.150
7.136
7.110
6.895
6.653
3.267
2.342
2.315
2.283
2.256
1.058
Me
N
Ph
O
Me
Me
O
O
H
1.94
1.00
1.03
1.86
0.99
2.99
1.67
0.95
3.02
0.97
1.08
9.22
f1 (ppm)

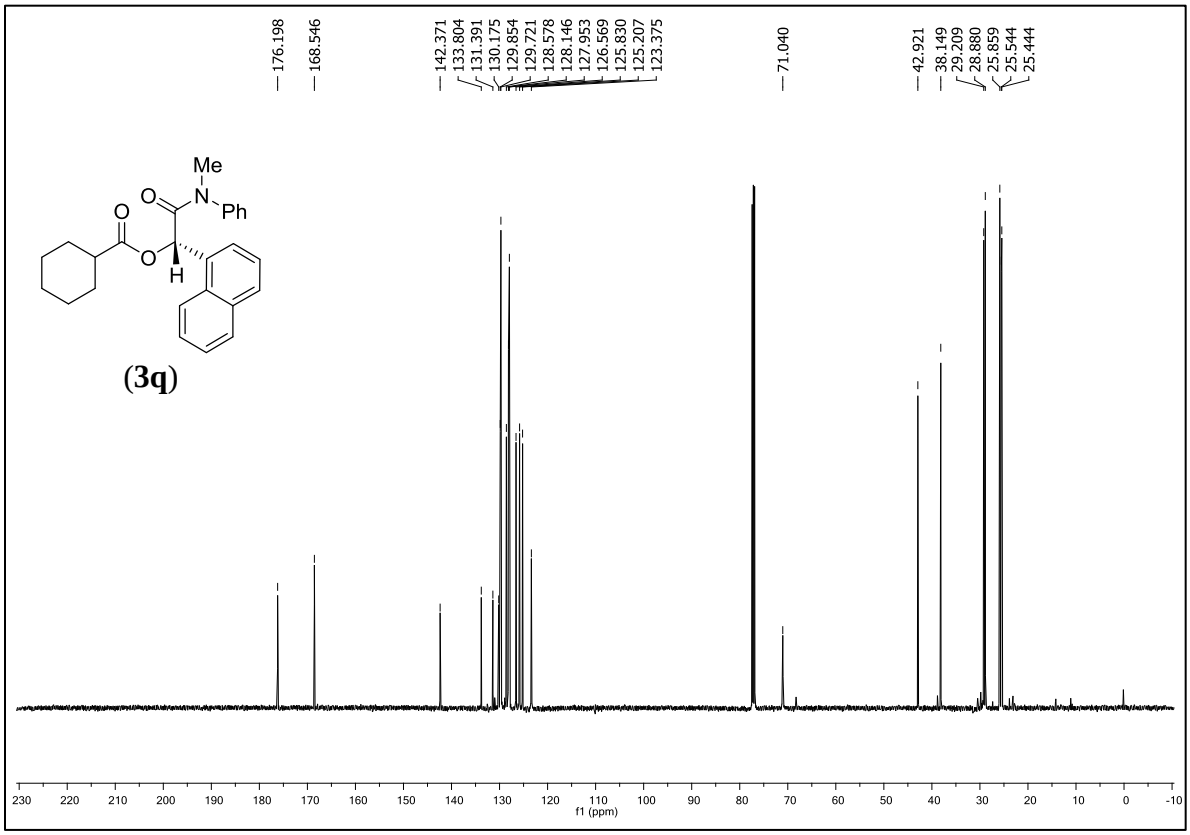
(3p)


172.370
168.528
142.380
133.763
131.279
130.245
129.835
129.694
128.566
128.145
128.099
127.981
126.518
125.815
125.243
123.225
70.908
47.754
38.160
31.083
29.744
Me
N
Ph
O
Me
Me
O
O
H
f1 (ppm)

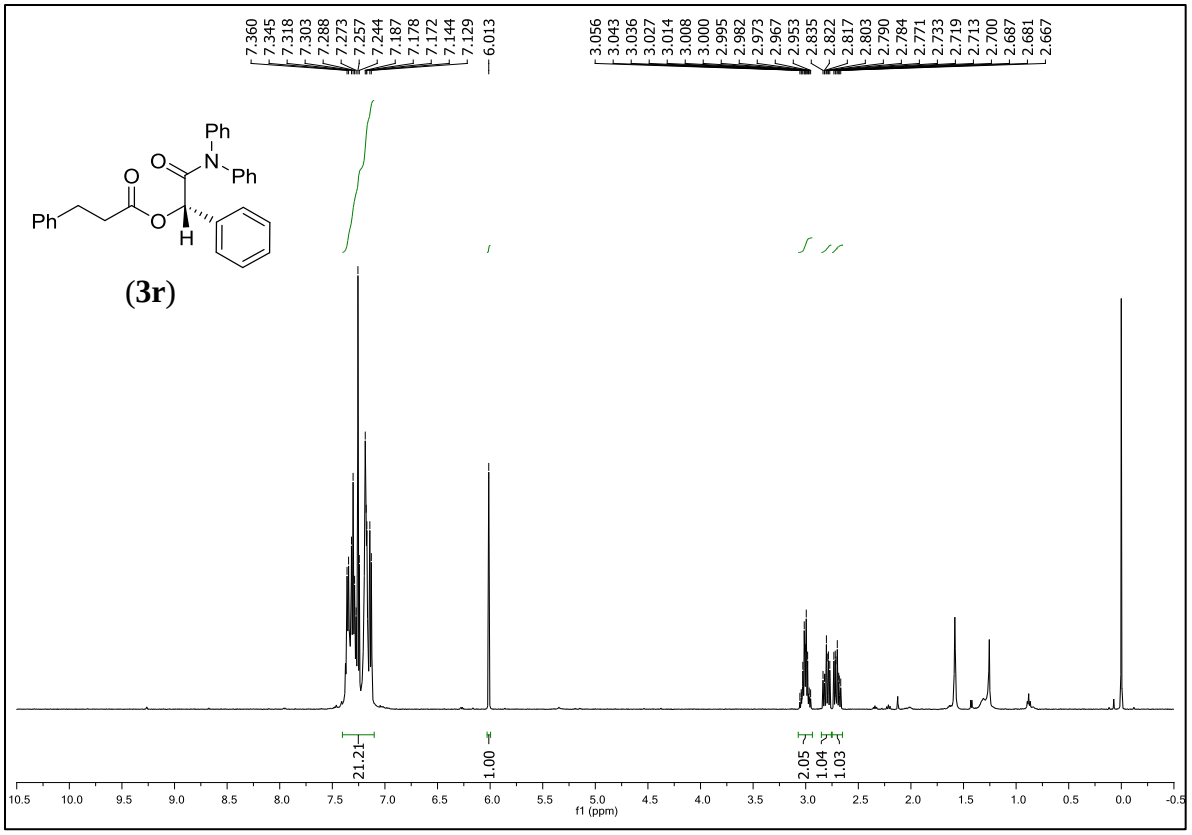
(3p)


7.801
7.790
7.785
7.555
7.540
7.425
7.410
7.395
7.351
7.337
7.320
7.302
7.288
7.259
7.178
7.164
7.151
7.125
6.918
6.629
3.266
2.429
2.422
2.107
2.082
1.882
1.856
1.764
1.706
1.698
1.695
1.690
1.682
1.607
1.550
1.530
1.526
1.275
1.254
1.225
1.207
1.189
Me
N
Ph
O
O
O
H
1.88
1.00
1.02
2.79
3.09
2.17
1.00
2.84
0.96
1.05
1.09
1.03
1.26
3.29
3.34
f1 (ppm)

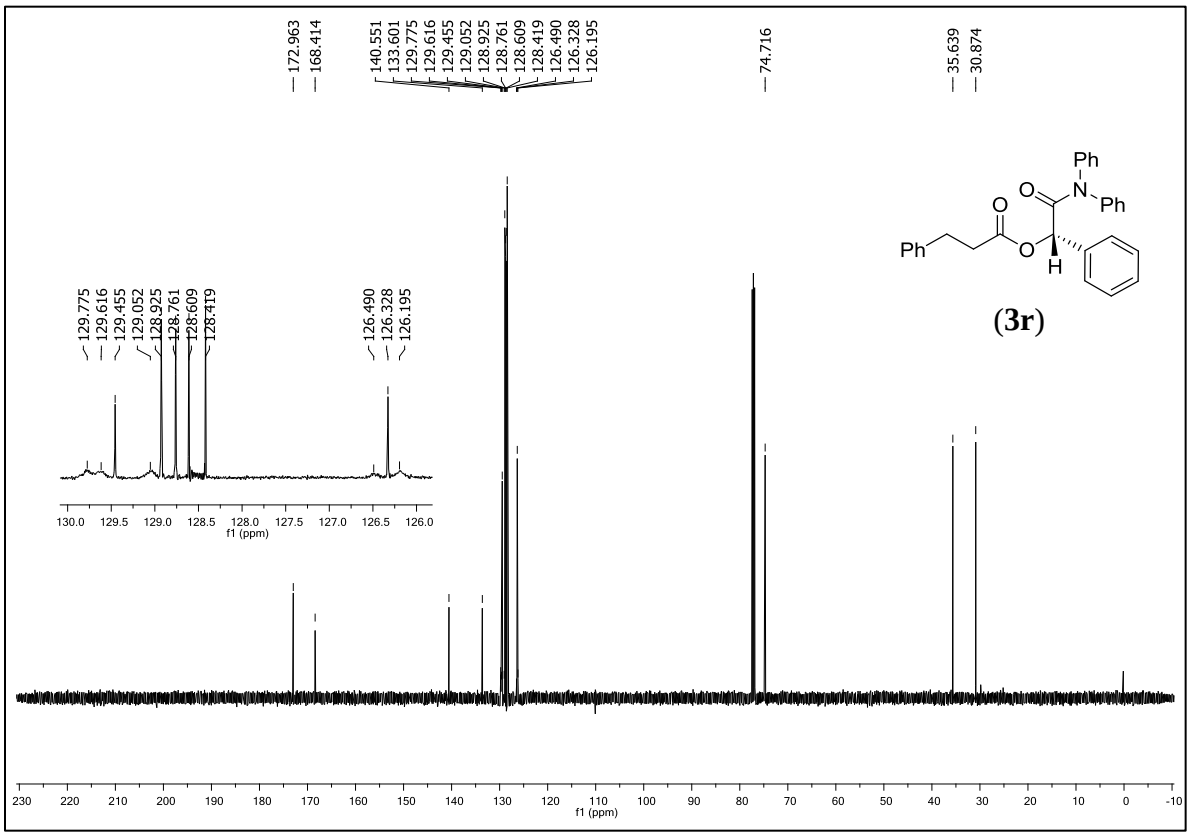
(3q)


176.198
168.546
142.371
133.804
131.391
130.175
129.854
129.721
128.578
128.146
127.953
126.569
125.830
125.207
123.375
71.040
42.921
38.149
29.209
28.880
25.859
25.544
25.444
Me
N
Ph
O
O
O
H
f1 (ppm)

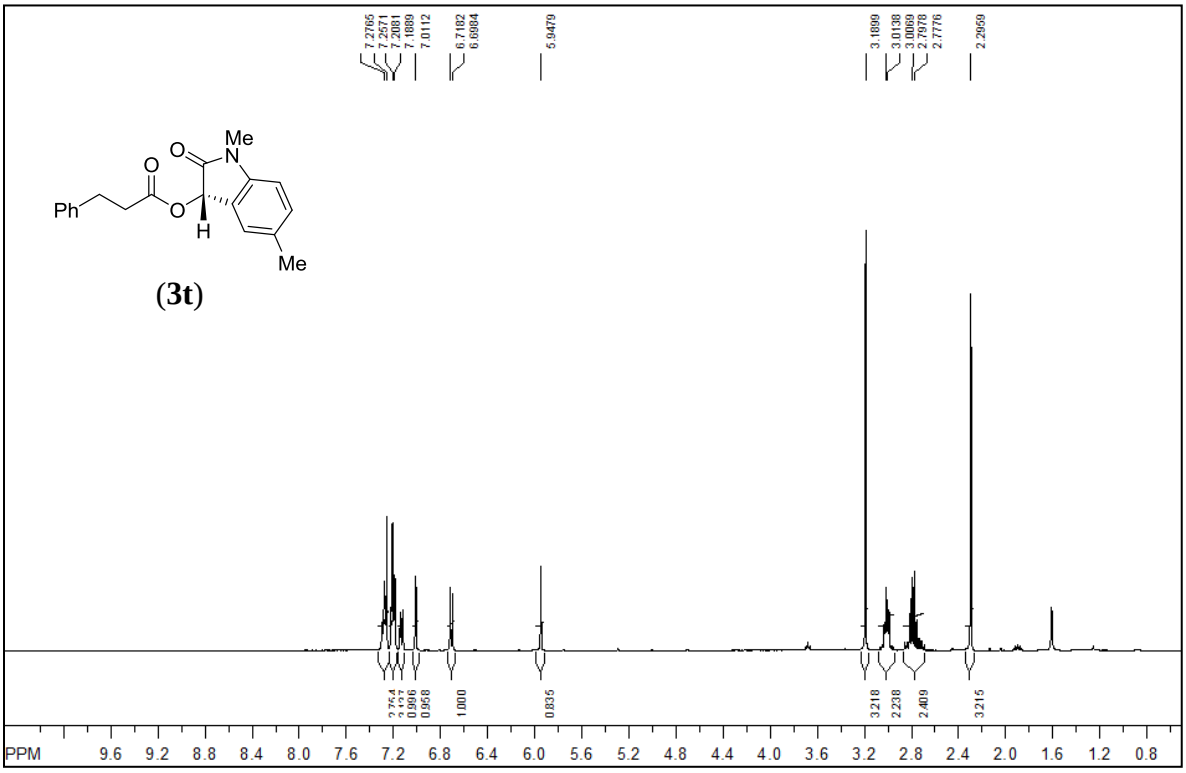
(3q)

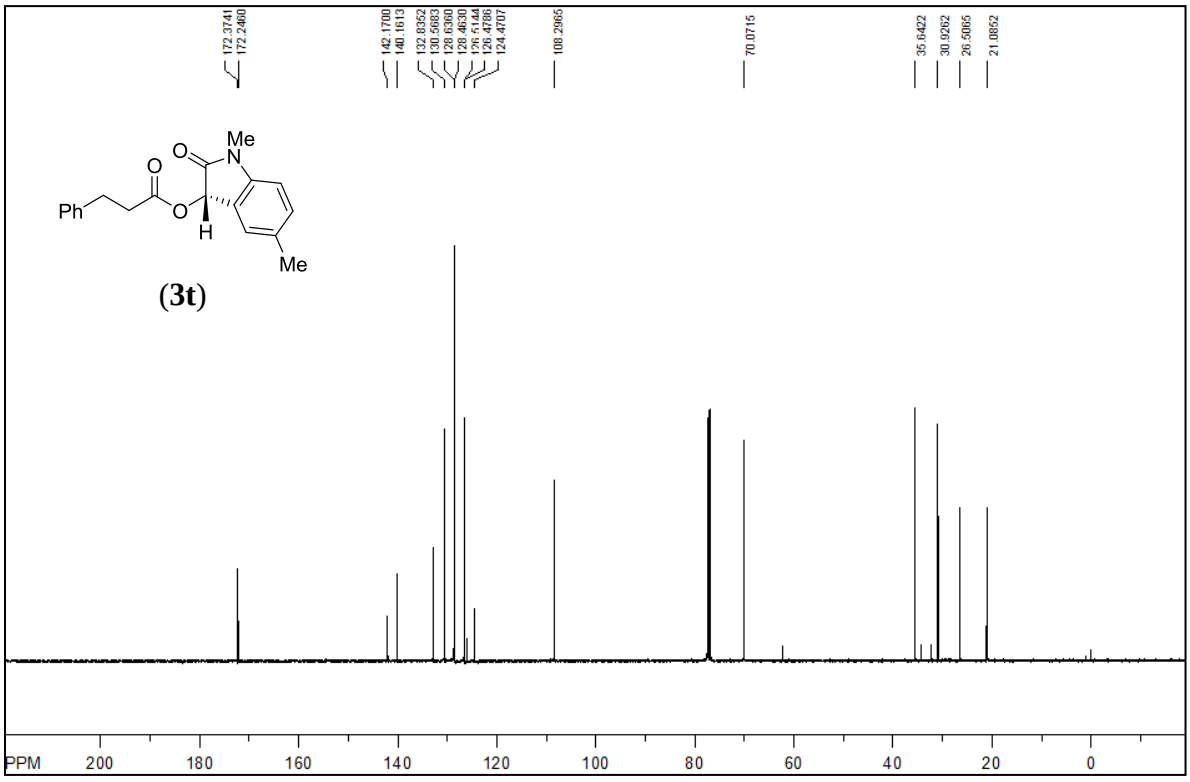

7.360
7.345
7.318
7.303
7.288
7.273
7.257
7.244
7.187
7.178
7.172
7.144
7.129
6.013
3.056
3.043
3.036
3.027
3.014
3.008
3.000
2.995
2.982
2.973
2.967
2.953
2.835
2.822
2.817
2.803
2.790
2.784
2.771
2.733
2.719
2.713
2.700
2.687
2.681
2.667
Ph
N
Ph
O
O
Ph
O
H
21.21
1.00
2.05
1.04
1.03
f1 (ppm)

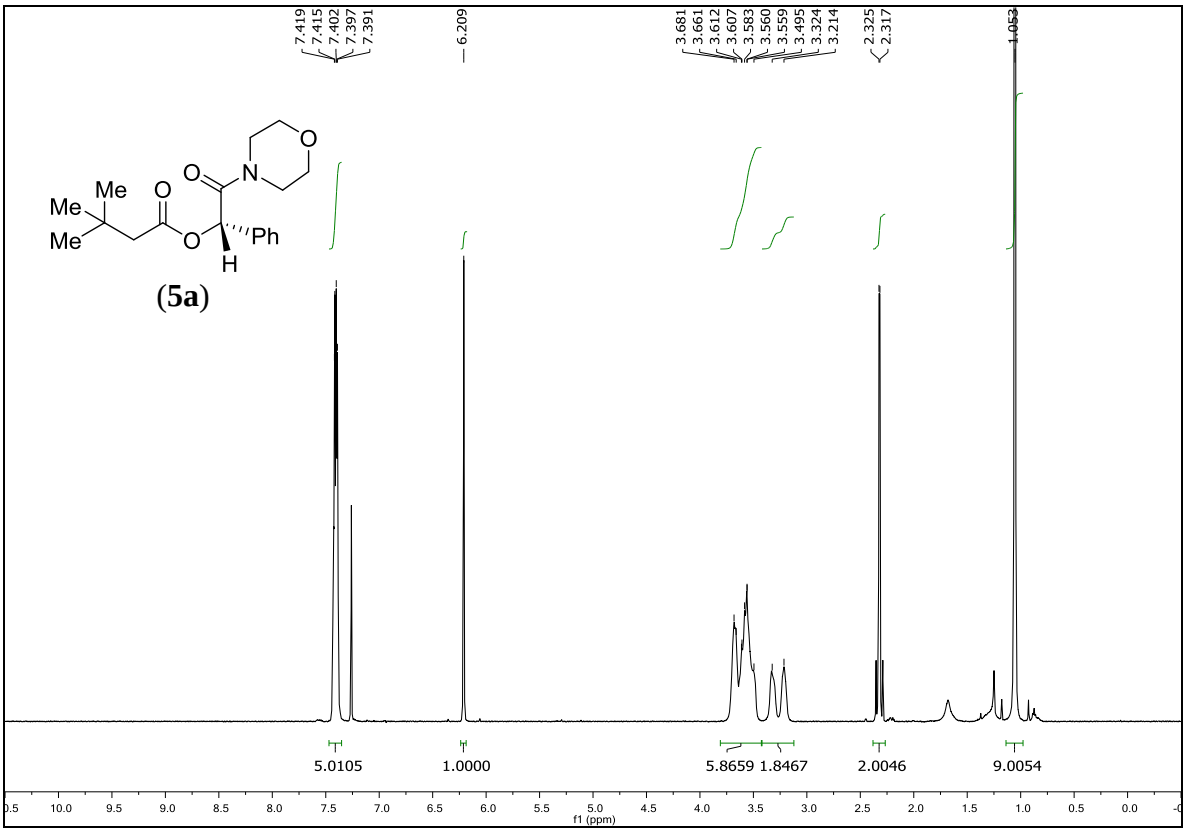
(3r)

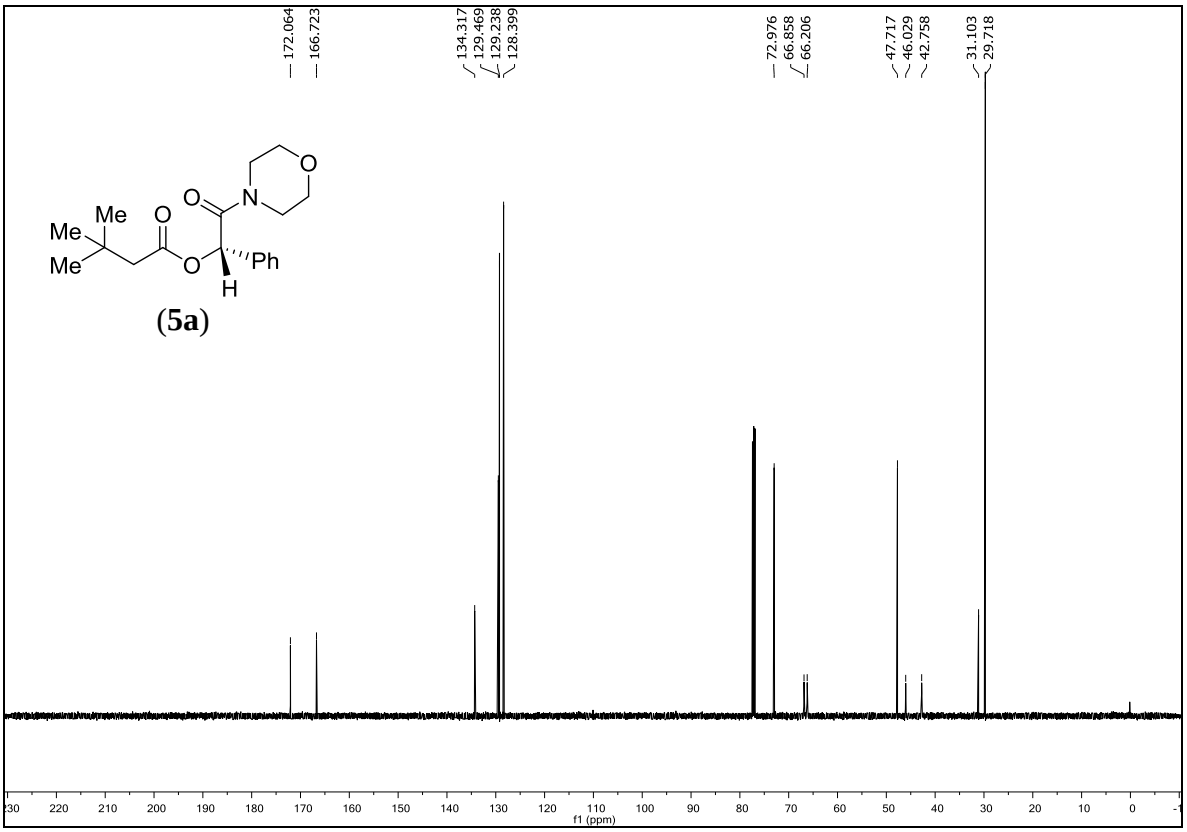

172.963
168.414
140.551
133.601
129.775
129.616
129.455
129.052
128.925
128.761
128.609
128.419
126.490
126.328
126.195
74.716
35.639
30.874
Ph
N
Ph
O
O
Ph
O
H
f1 (ppm)

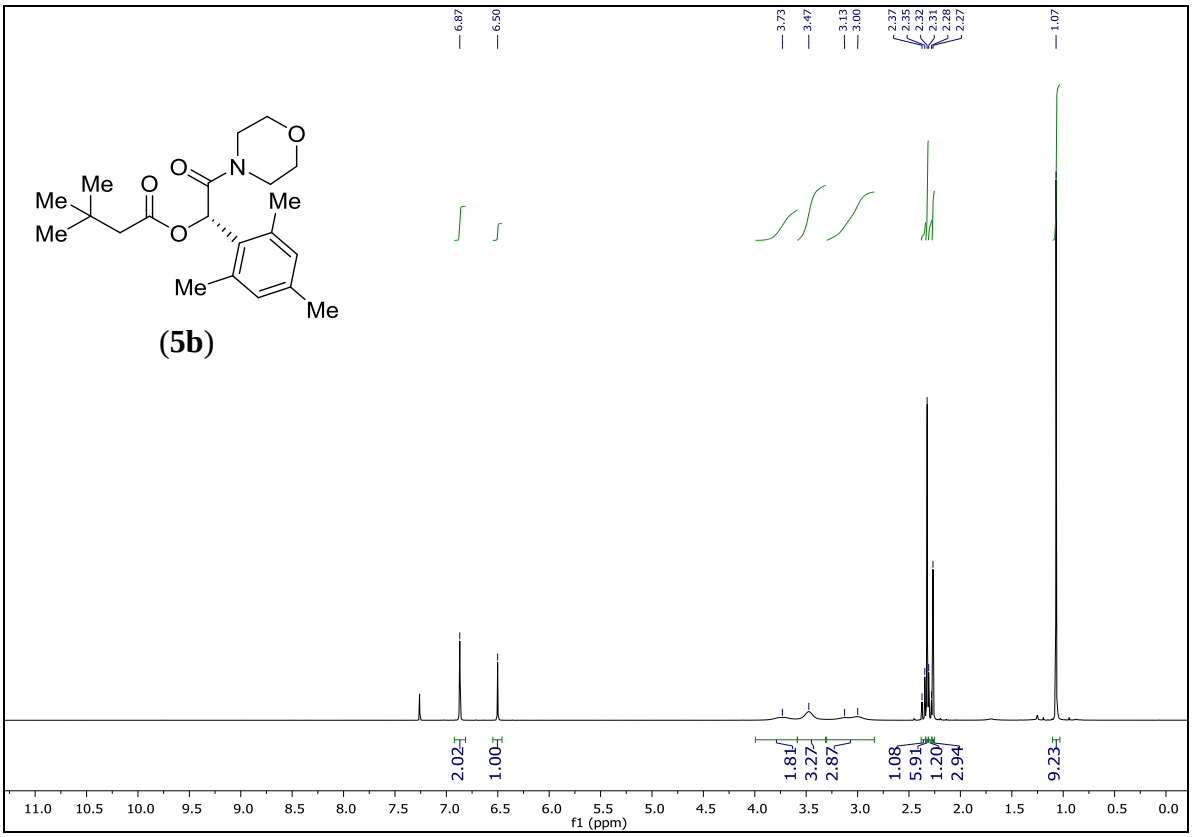
(3r)


7.2765
7.2571
7.2081
7.1889
7.0112
6.7182
6.6984
5.9479
3.1899
3.0138
3.0069
2.7978
2.7776
2.2959
Me
O
N
O
Ph
O
H
Me
(3t)
2.764
3.137
0.996
0.958
1.000
0.835
3.218
2.238
2.409
3.215
PPM
9.6 9.2 8.8 8.4 8.0 7.6 7.2 6.8 6.4 6.0 5.6 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8

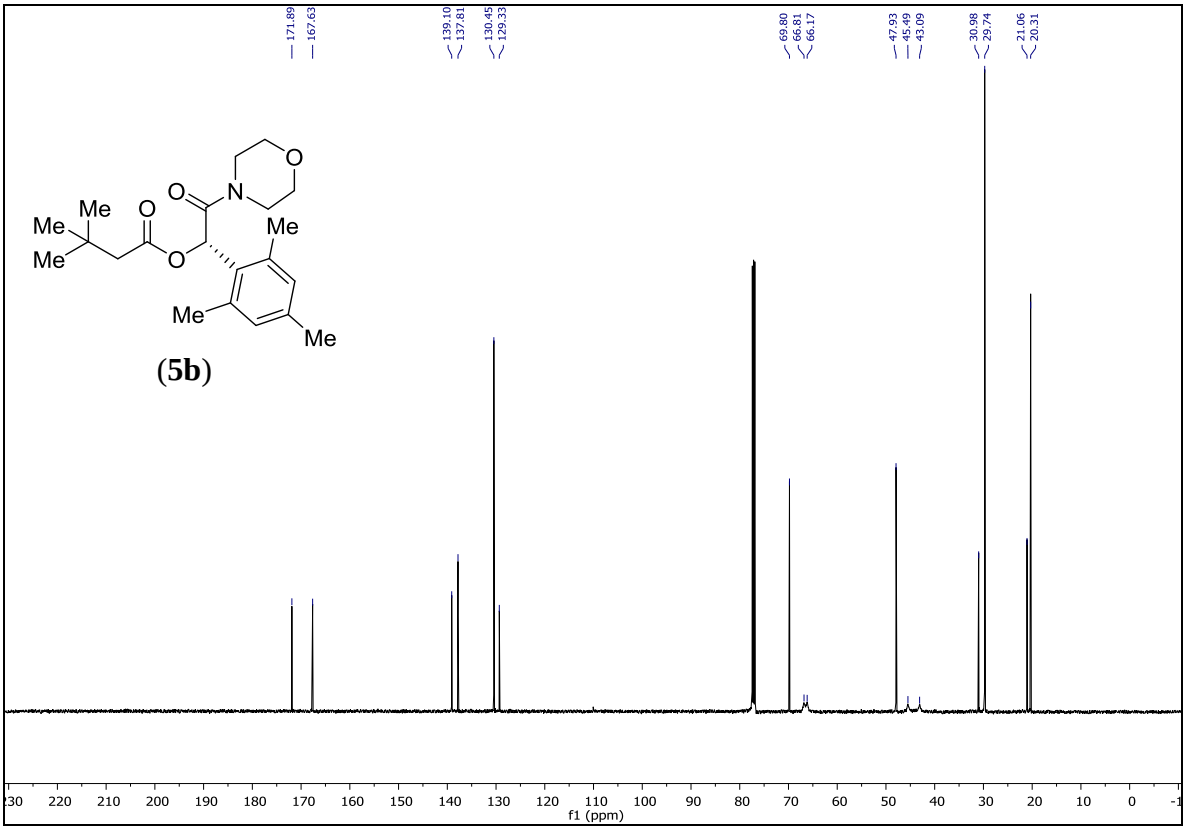

172.3741
172.2460
142.1700
140.1613
132.8352
130.5683
128.6360
128.4630
126.5144
126.4786
124.4707
108.2965
70.0715
35.6422
30.9262
26.5065
21.0852
Me
O
N
O
Ph
O
H
Me
(3t)
PPM
200 180 160 140 120 100 80 60 40 20 0


7.419
7.415
7.402
7.397
7.391
6.209
3.681
3.661
3.612
3.607
3.583
3.560
3.559
3.495
3.324
3.214
2.325
2.317
1.053
Me
Me
O
O
N
O
O
Ph
H
(5a)
5.0105
1.0000
5.8659
1.8467
2.0046
9.0054
f1 (ppm)

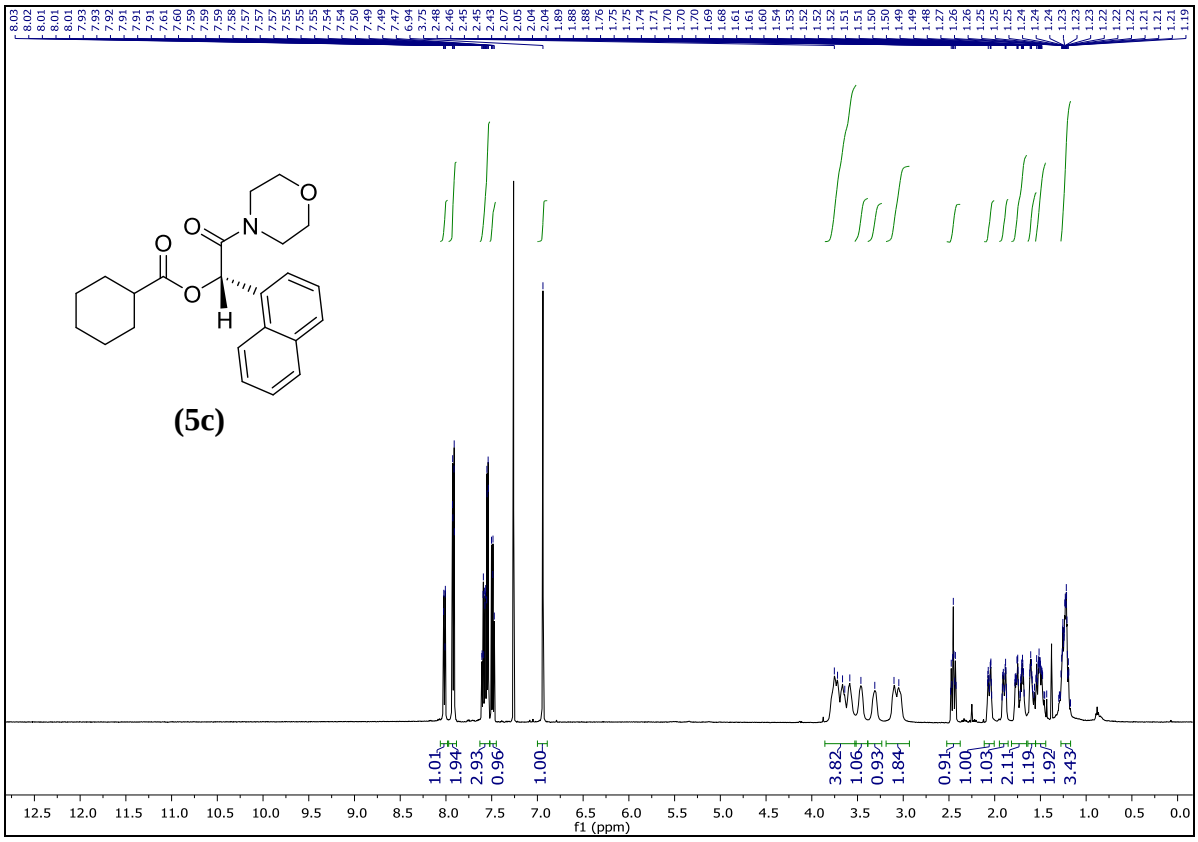

172.064
166.723
134.317
129.469
129.238
128.399
72.976
66.858
66.206
47.717
46.029
42.758
31.103
29.718
Me
Me
O
O
N
O
O
Ph
H
(5a)
f1 (ppm)

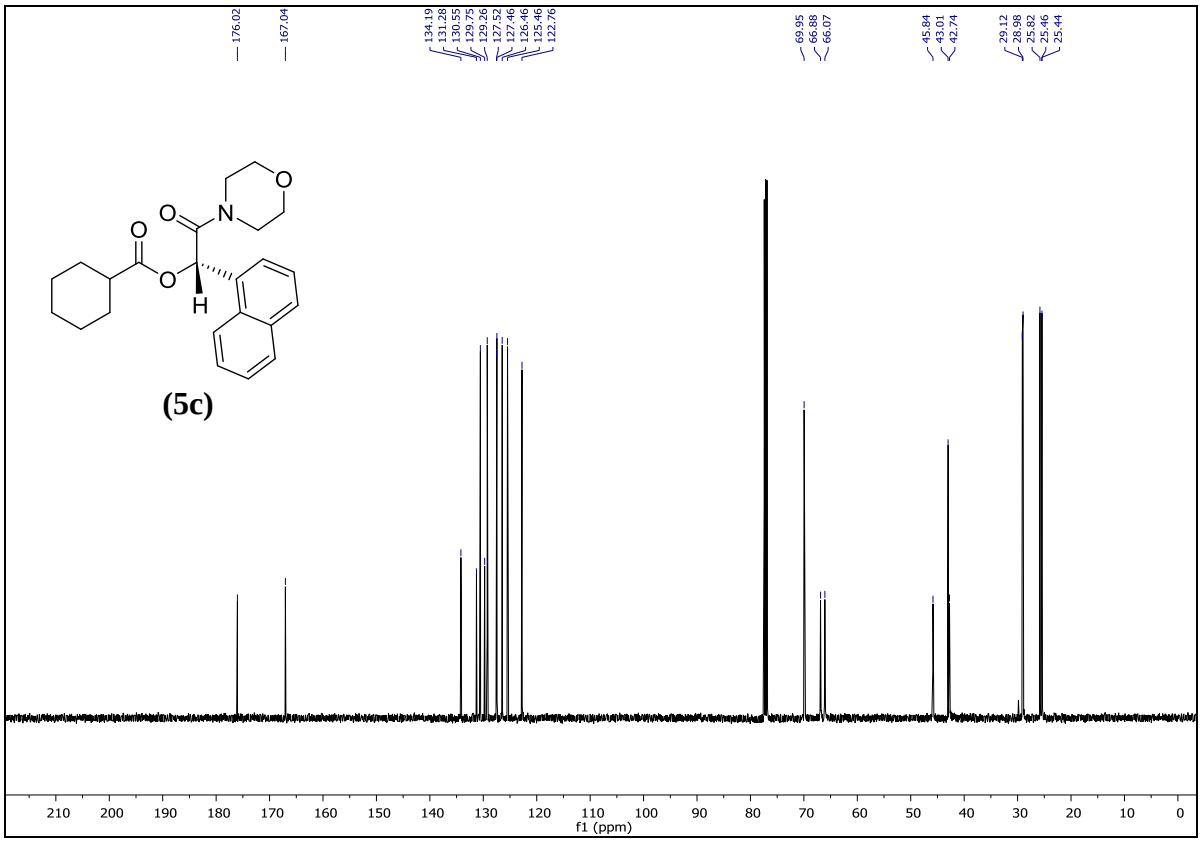

6.87
6.50
3.73
3.47
3.13
3.00
2.37
2.35
2.32
2.31
2.28
2.27
1.07
2.02
1.00
1.81
3.27
2.87
1.08
5.91
1.20
2.94
9.23
f1 (ppm)

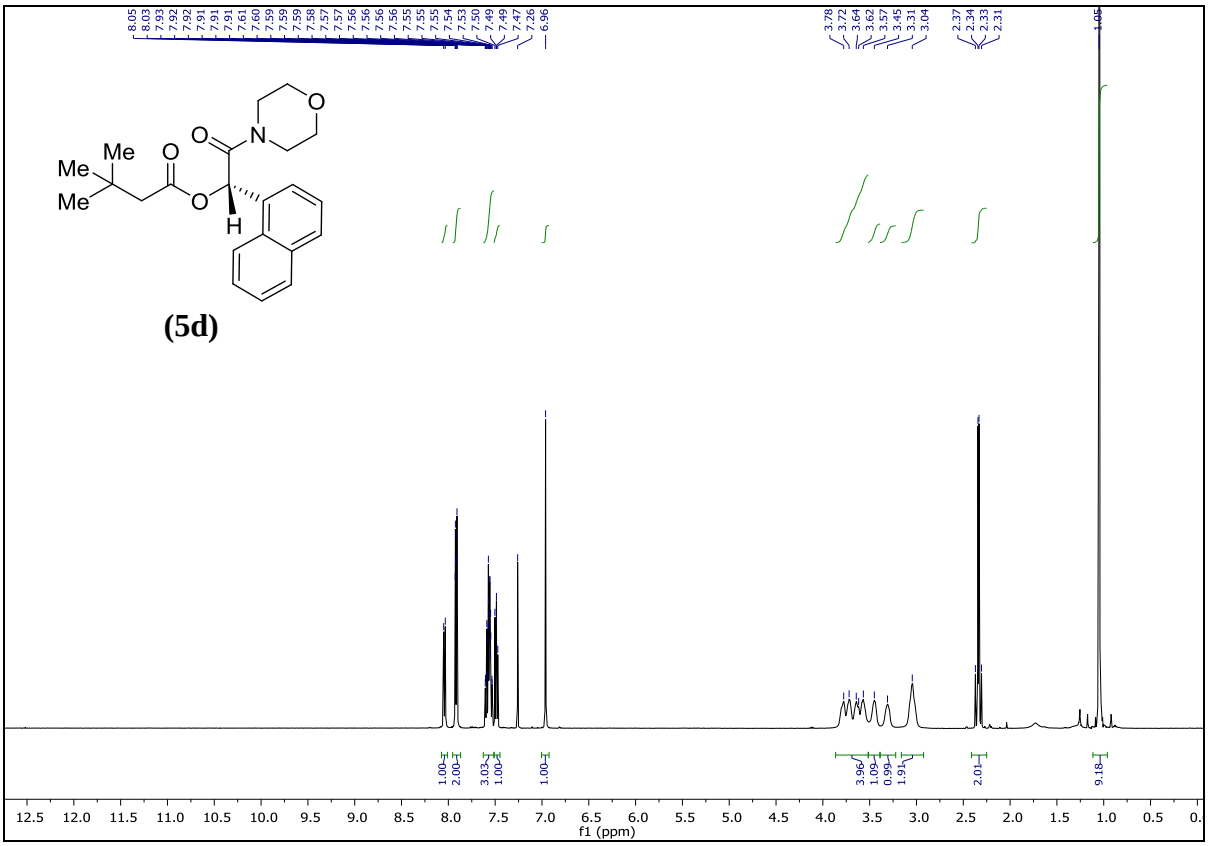
(5b)

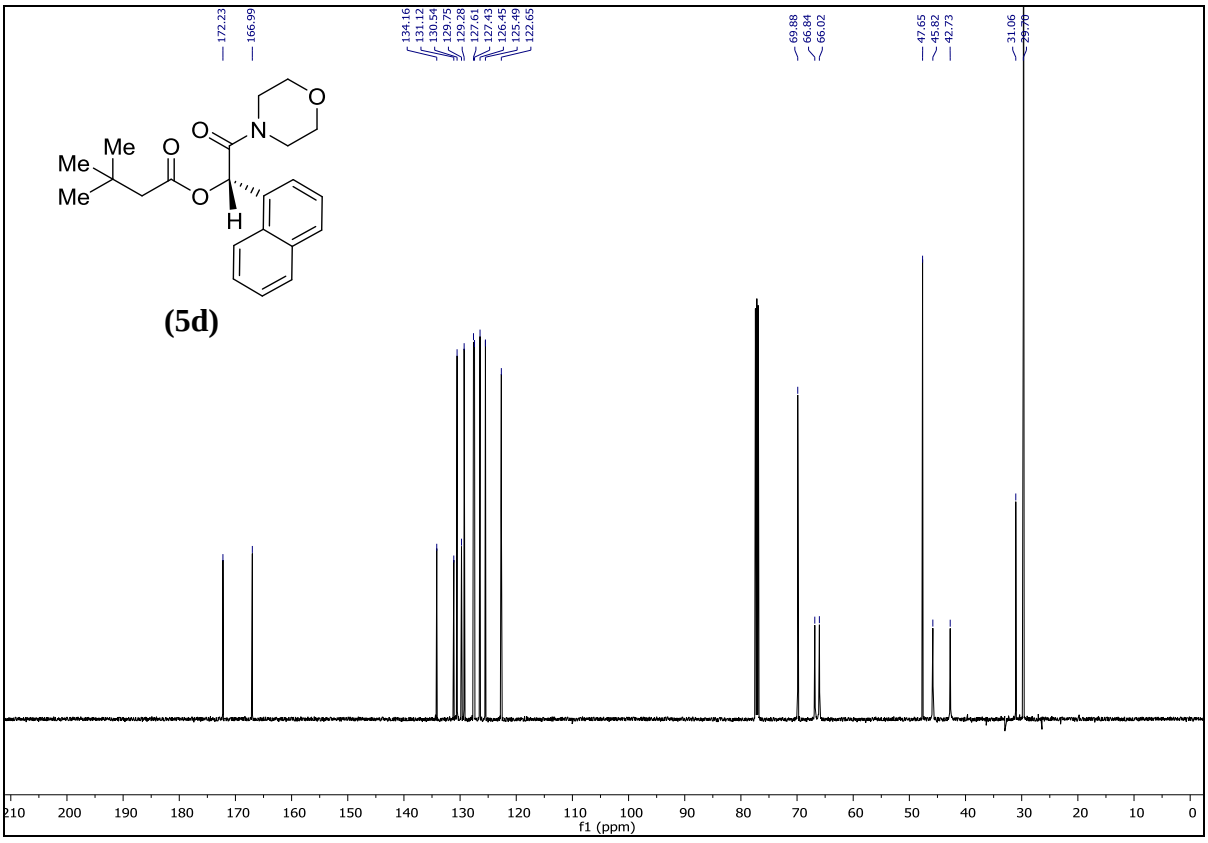

171.89
167.63
139.10
137.81
130.45
129.33
69.80
66.81
66.17
47.93
45.49
43.09
30.98
29.74
21.06
20.31
f1 (ppm)

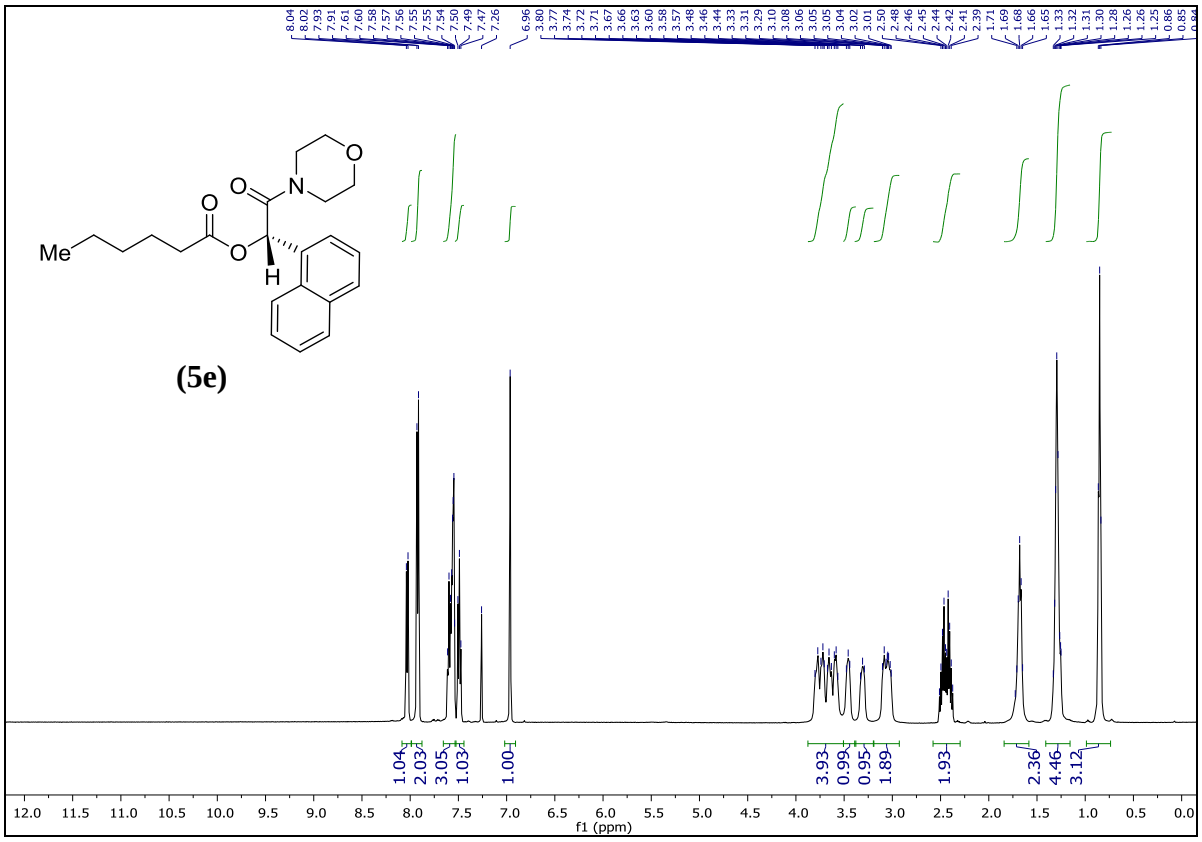
(5b)

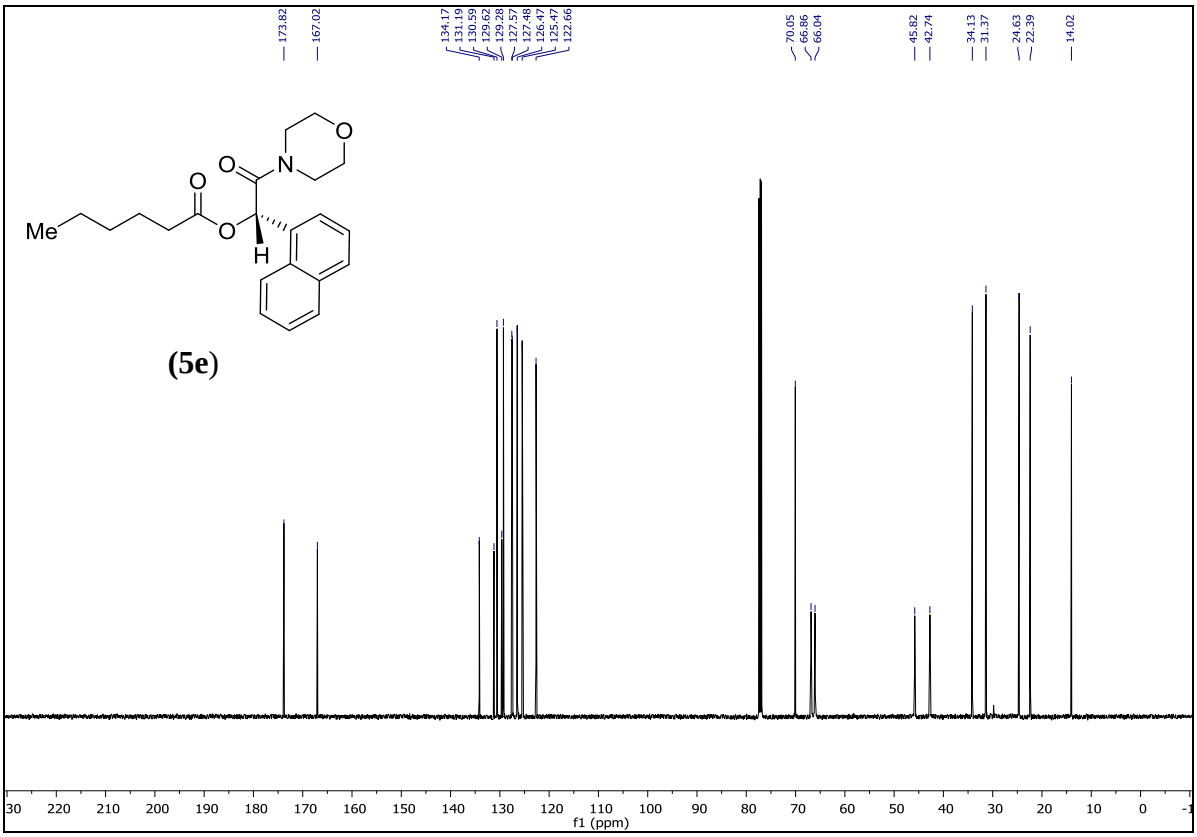

(5c)
f1 (ppm)

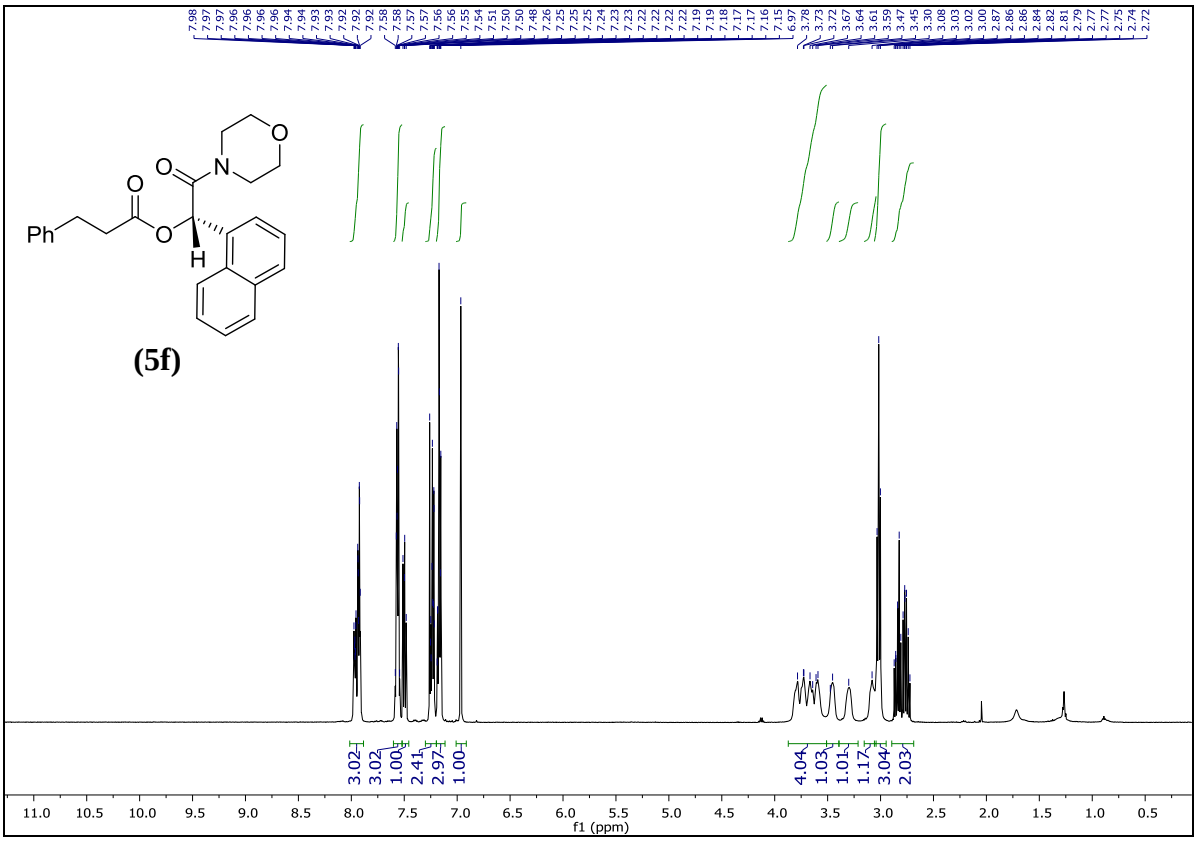

(5c)
f1 (ppm)

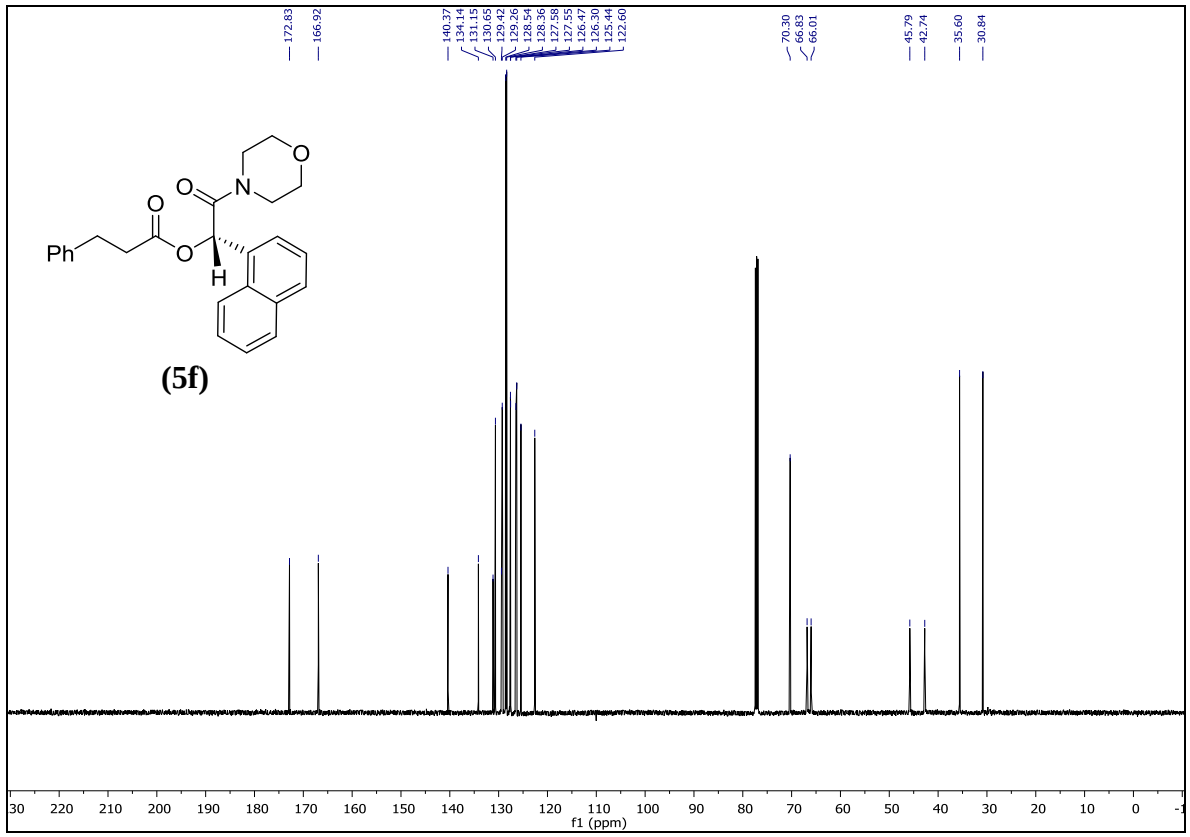

(5d)
f1 (ppm)


(5d)
f1 (ppm)

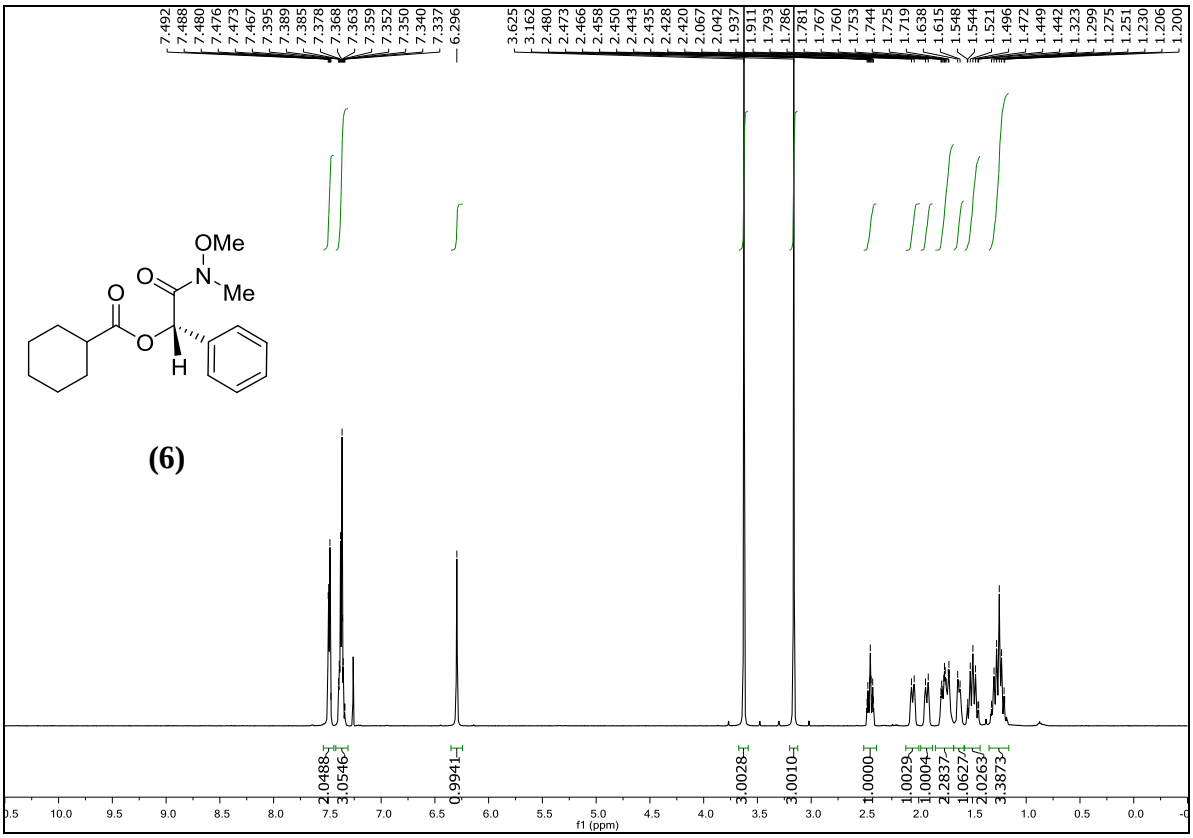

Me
O
N
O
O
O
H
(5e)
1.04
2.03
3.05
1.03
1.00
3.93
0.99
0.95
1.89
1.93
2.36
4.46
3.12
f1 (ppm)


Me
O
N
O
O
O
H
(5e)
173.82
167.02
134.17
131.19
130.59
129.62
129.28
127.57
127.48
126.47
125.47
122.66
70.05
66.86
66.04
45.82
42.74
34.13
31.37
24.63
22.39
14.02
f1 (ppm)

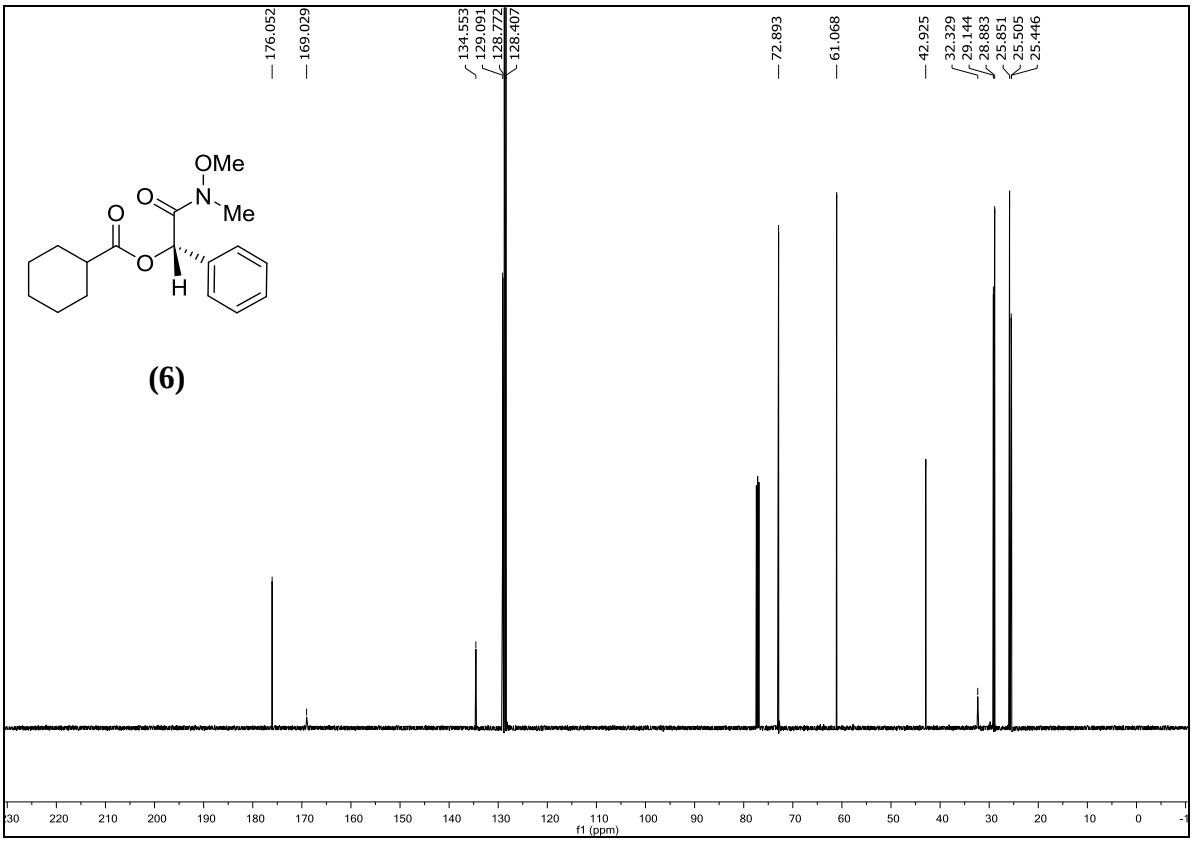

(5f)
f1 (ppm)


172.83
166.92
140.37
134.14
131.15
130.65
129.42
129.26
128.54
128.36
127.58
127.55
126.47
126.30
125.44
122.60
70.30
66.83
66.01
45.79
42.74
35.60
30.84
O
O
N
O
Ph
O
H
f1 (ppm)

(5f)


7.492
7.488
7.480
7.476
7.473
7.467
7.395
7.389
7.385
7.378
7.368
7.363
7.359
7.352
7.350
7.340
7.337
6.296
3.625
3.162
2.480
2.473
2.466
2.458
2.450
2.443
2.435
2.428
2.420
2.067
2.042
1.937
1.911
1.793
1.786
1.781
1.767
1.760
1.753
1.744
1.725
1.719
1.638
1.615
1.548
1.544
1.521
1.496
1.472
1.449
1.442
1.323
1.299
1.275
1.251
1.230
1.206
1.200
OMe
O
N
Me
O
O
H
2.0488
3.0546
0.9941
3.0028
3.0010
1.0000
1.0029
1.0004
2.2837
1.0627
2.0263
3.3873
f1 (ppm)

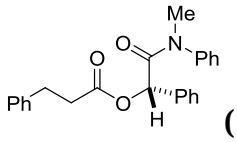
(6)



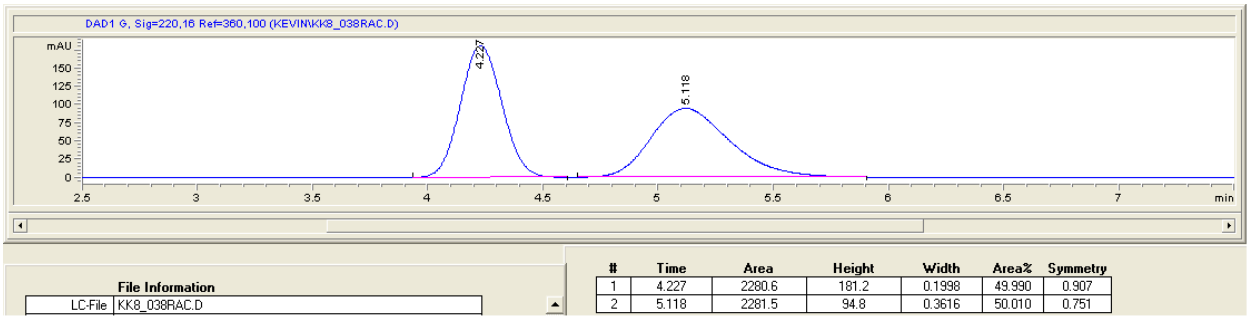
(6)

9. Determination of Enantioselectivity by Chiral SFC Analysis

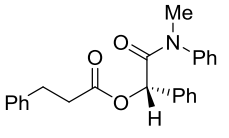
See Product Characterization (Section 4) for chromatography conditions.



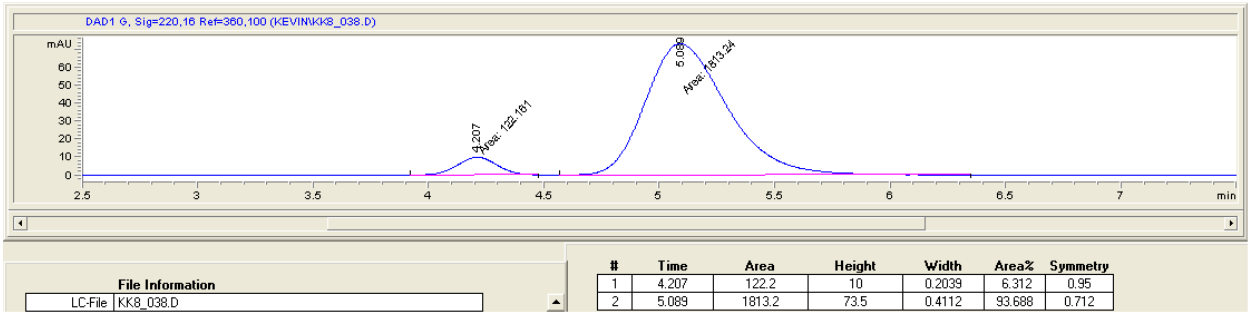
(±)-3a



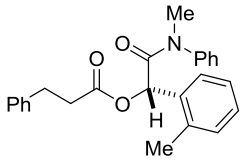
#	Time	Area	Height	Width	Area%	Symmetry
1	4.227	2280.6	181.2	0.1998	49.990	0.907
2	5.118	2281.5	94.8	0.3616	50.010	0.751



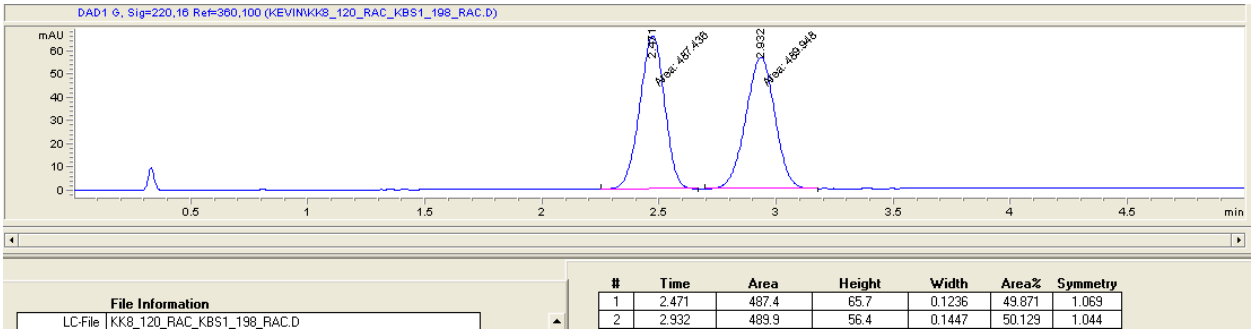
(+)-3a



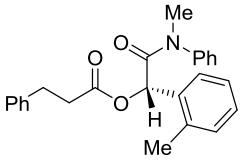
#	Time	Area	Height	Width	Area%	Symmetry
1	4.207	122.2	10	0.2039	6.312	0.95
2	5.089	1813.2	73.5	0.4112	93.688	0.712



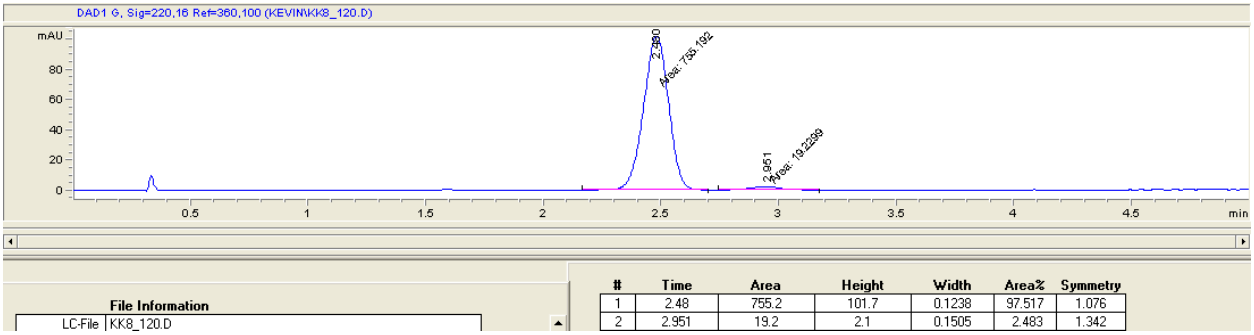
(±)-3b



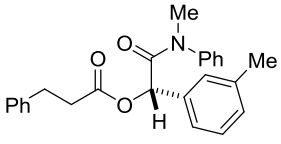
#	Time	Area	Height	Width	Area%	Symmetry
1	2.471	487.4	65.7	0.1236	49.871	1.069
2	2.932	489.9	56.4	0.1447	50.129	1.044



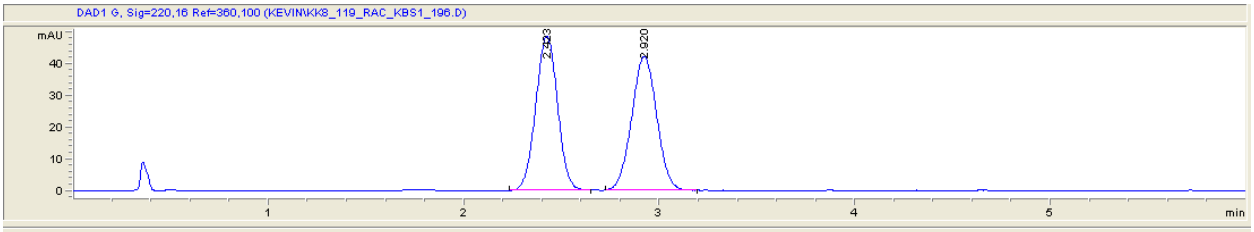
(+)-3b



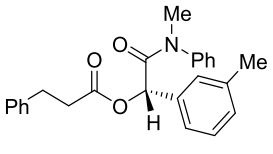
#	Time	Area	Height	Width	Area%	Symmetry
1	2.48	755.2	101.7	0.1238	97.517	1.076
2	2.951	19.2	2.1	0.1505	2.483	1.342



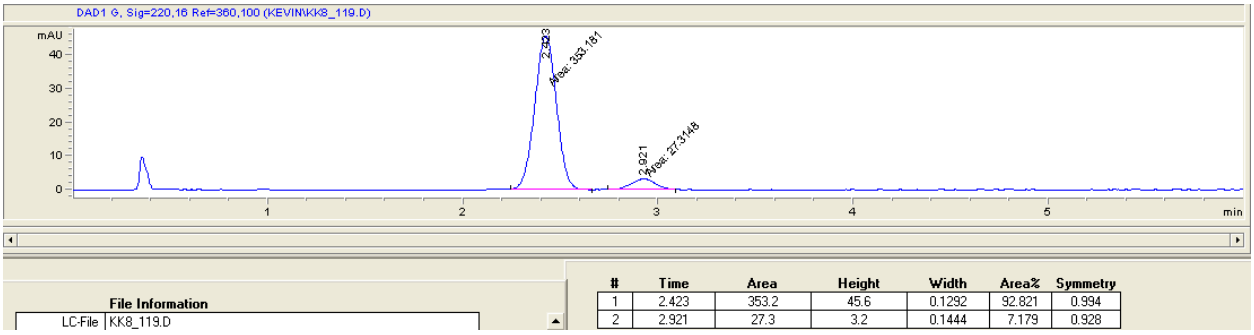
(±)-3c



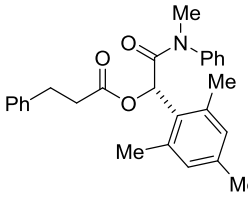
#	Time	Area	Height	Width	Area%	Symmetry
1	2.423	379.5	48.7	0.1219	50.097	1.007
2	2.92	378	42.3	0.1393	49.903	0.964



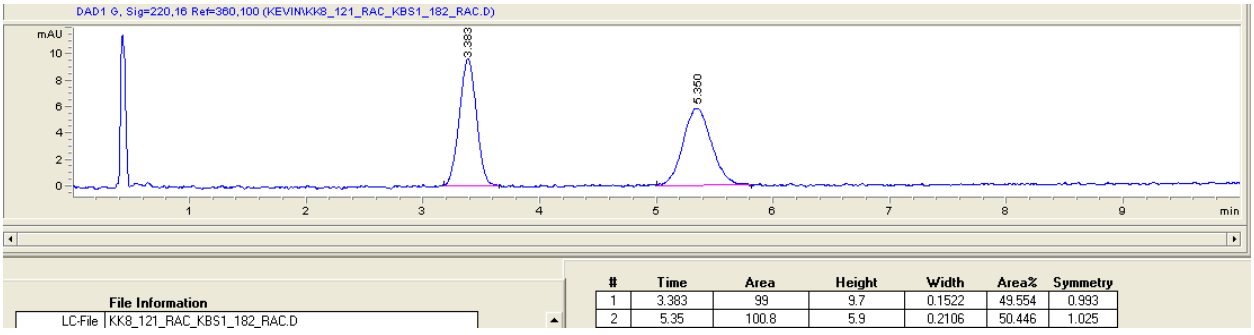
(+)-3c



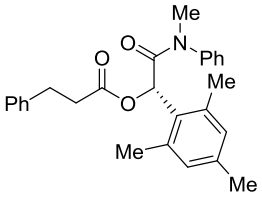
#	Time	Area	Height	Width	Area%	Symmetry
1	2.423	353.2	45.6	0.1292	92.821	0.994
2	2.921	27.3	3.2	0.1444	7.179	0.928



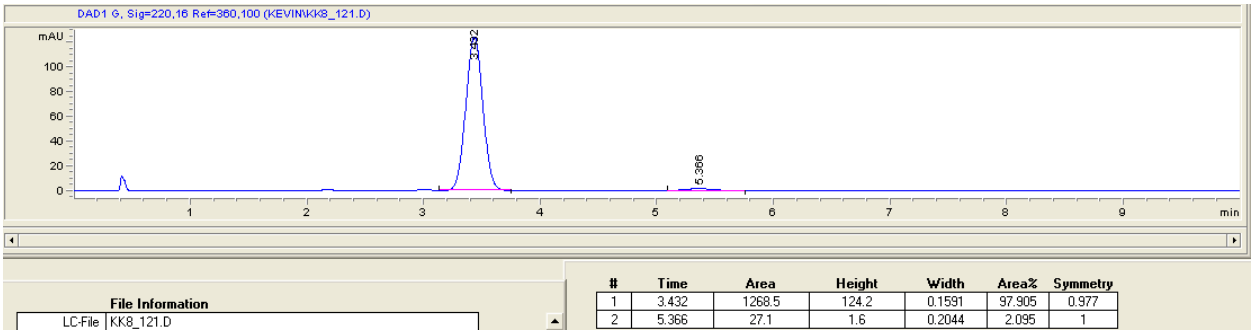
(±)-3d



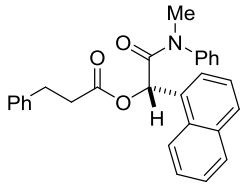
#	Time	Area	Height	Width	Area%	Symmetry
1	3.383	99	9.7	0.1522	49.554	0.993
2	5.35	100.8	5.9	0.2106	50.446	1.025



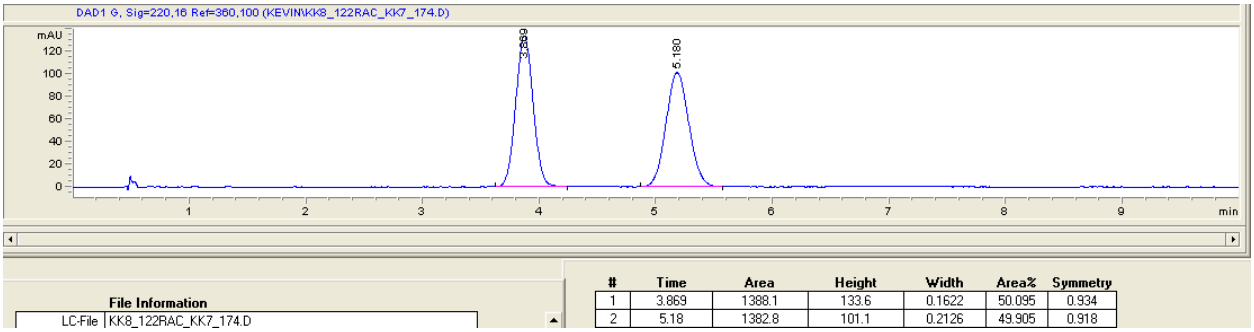
(+)-3d



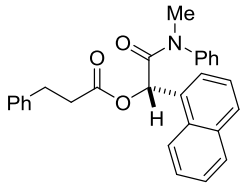
#	Time	Area	Height	Width	Area%	Symmetry
1	3.432	1268.5	124.2	0.1591	97.905	0.977
2	5.366	27.1	1.6	0.2044	2.095	1



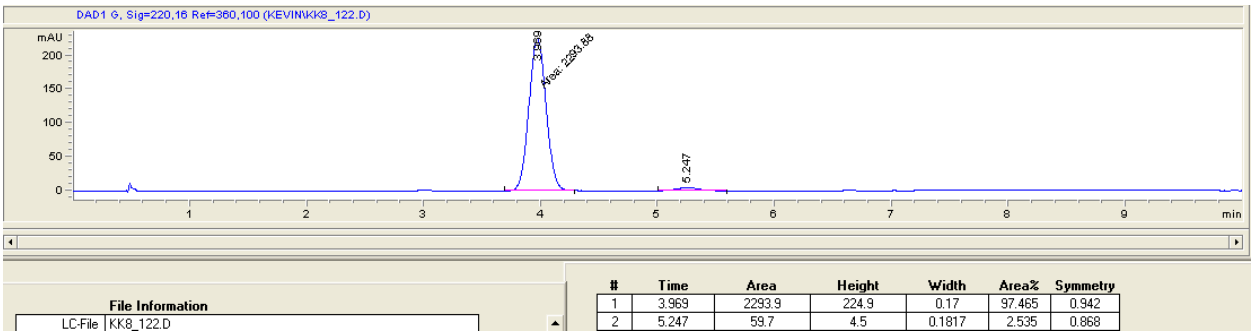
(±)-3e



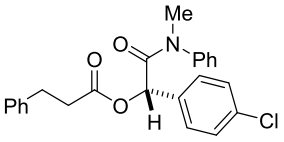
#	Time	Area	Height	Width	Area%	Symmetry
1	3.869	1388.1	133.6	0.1622	50.095	0.934
2	5.18	1382.8	101.1	0.2126	49.905	0.918



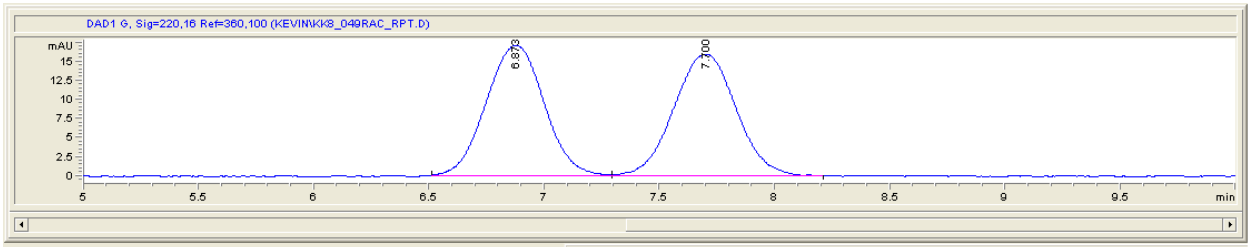
(+)-3e



#	Time	Area	Height	Width	Area%	Symmetry
1	3.969	2293.9	224.9	0.17	97.465	0.942
2	5.247	59.7	4.5	0.1817	2.535	0.868



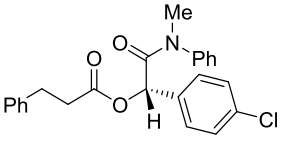
(±)-3f



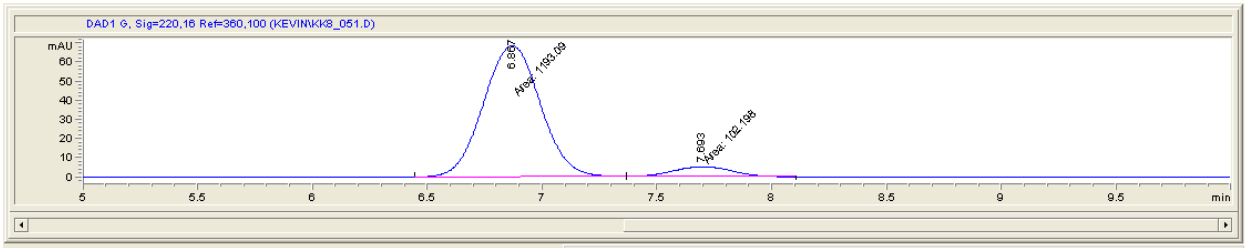
File Information

LC-File	KK8_049RAC_RPT.D

#	Time	Area	Height	Width	Area%	Symmetry
1	6.873	301.2	17.1	0.2676	49.998	0.983
2	7.7	301.2	16	0.2631	50.002	1.024



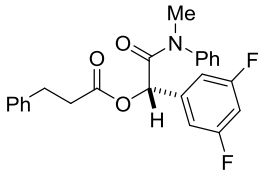
(+)-3f



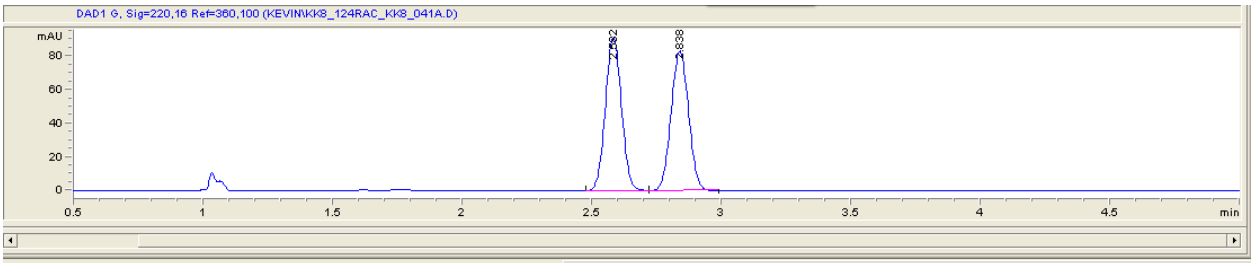
File Information

LC-File	KK8_051.D

#	Time	Area	Height	Width	Area%	Symmetry
1	6.867	1193.1	68.7	0.2896	92.110	0.972
2	7.693	102.2	5.3	0.3186	7.890	0.959



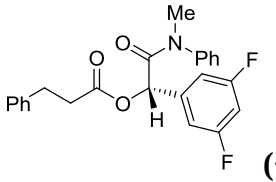
(±)-3g



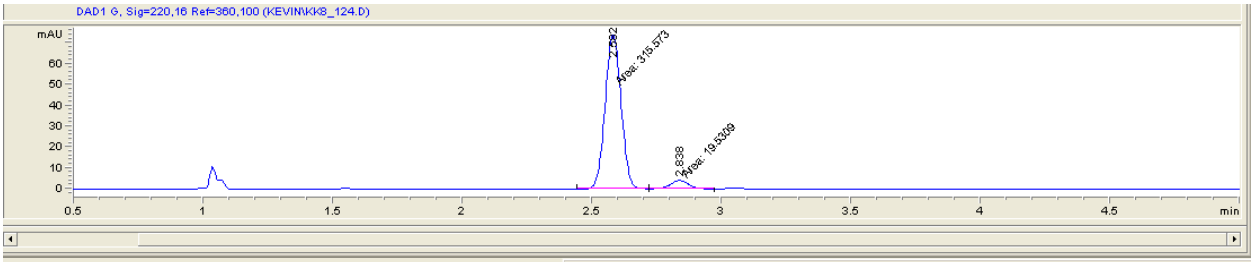
File Information

LC-File	KK8_124RAC_KK8_041A.D

#	Time	Area	Height	Width	Area%	Symmetry
1	2.582	393.5	91.6	0.0671	50.211	0.948
2	2.838	390.2	83.2	0.0737	49.789	0.96



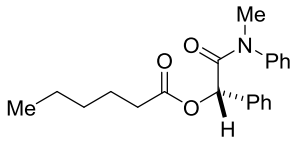
(+)-3g



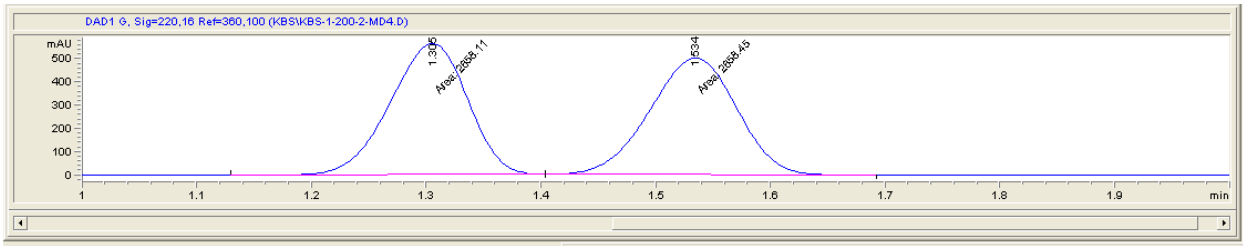
File Information

LC-File | KK8_124.D

#	Time	Area	Height	Width	Area%	Symmetry
1	2.582	315.6	74	0.0711	94.172	0.966
2	2.838	19.5	4	0.0807	5.828	1.05



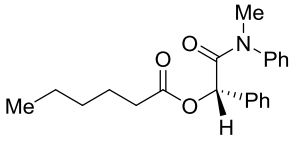
(±)-3h



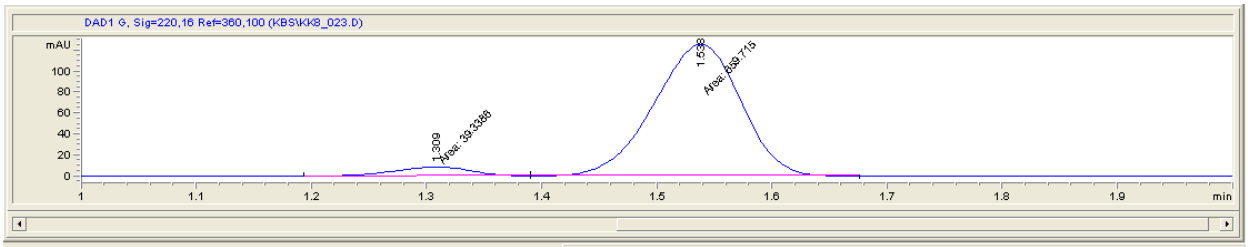
File Information

LC-File | KBS-1-200-2-MD4.D

#	Time	Area	Height	Width	Area%	Symmetry
1	1.305	2658.1	565.9	0.0783	49.997	1.181
2	1.534	2658.4	503.3	0.088	50.003	1.088



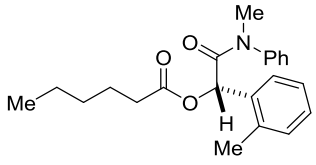
(+)-3h



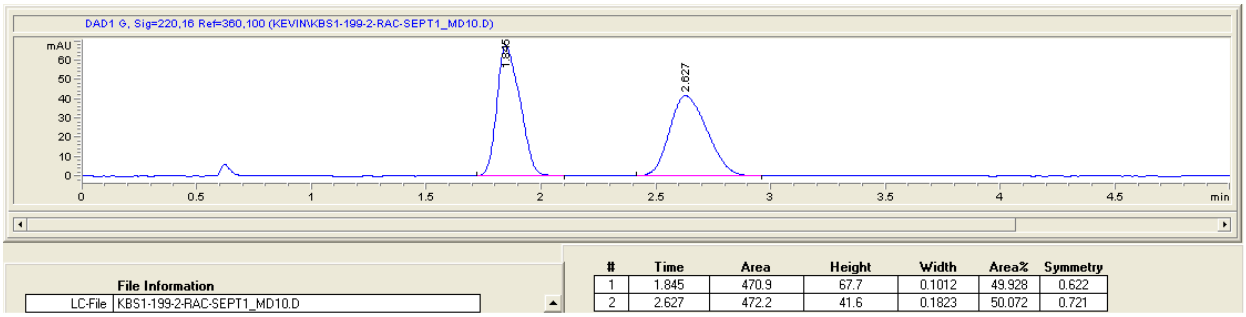
File Information

LC-File | KK8_023.D

#	Time	Area	Height	Width	Area%	Symmetry
1	1.309	39.3	8.5	0.0772	5.627	1.258
2	1.538	659.7	125.5	0.0876	94.373	1.15



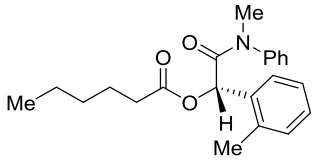
(±)-3i



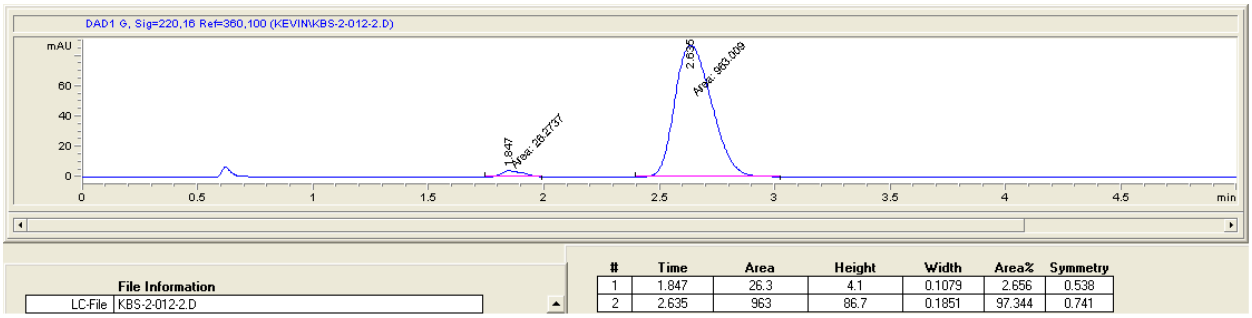
File Information

LC-File	KBS1-199-2-RAC-SEPT1_MD10.D

#	Time	Area	Height	Width	Area%	Symmetry
1	1.845	470.9	67.7	0.1012	49.928	0.622
2	2.627	472.2	41.6	0.1823	50.072	0.721



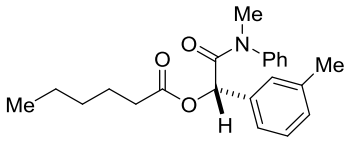
(+)-3i



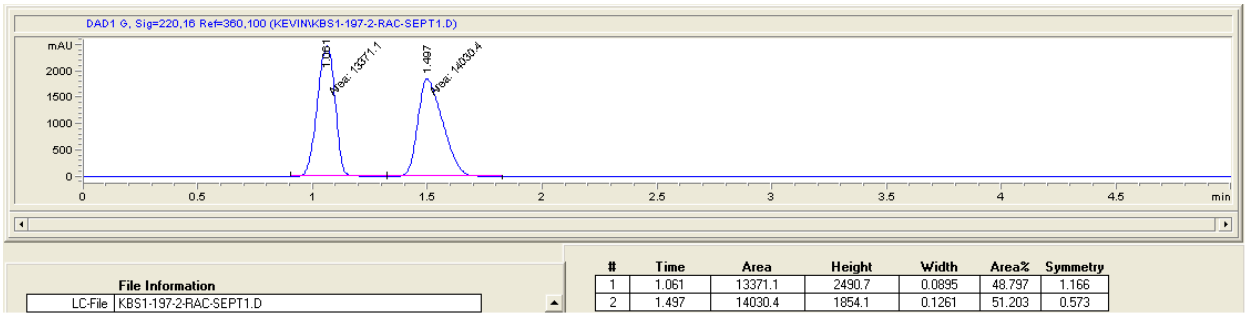
File Information

LC-File	KBS-2-012-2.D

#	Time	Area	Height	Width	Area%	Symmetry
1	1.847	26.3	4.1	0.1079	2.656	0.538
2	2.635	963	86.7	0.1851	97.344	0.741



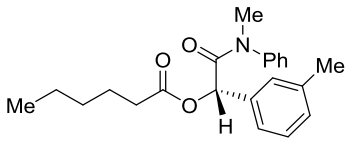
(±)-3j



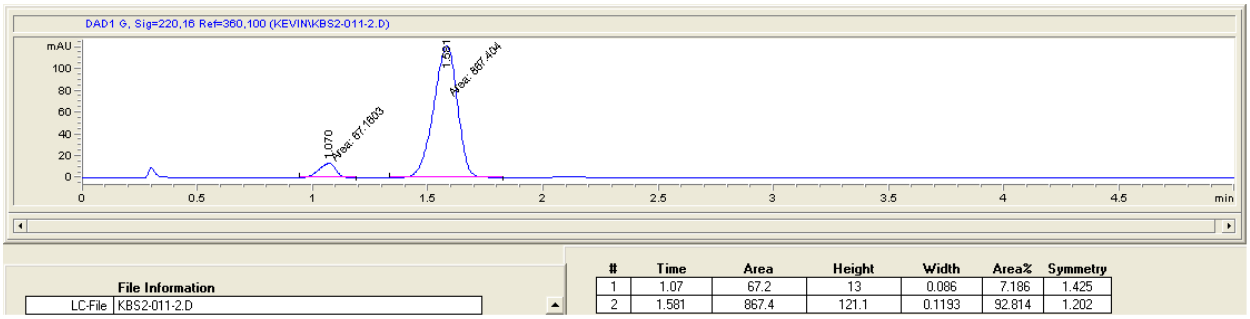
File Information

LC-File	KBS1-197-2-RAC-SEPT1.D

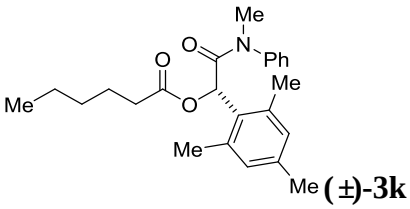
#	Time	Area	Height	Width	Area%	Symmetry
1	1.061	13371.1	2490.7	0.0895	48.797	1.166
2	1.497	14030.4	1854.1	0.1261	51.203	0.573



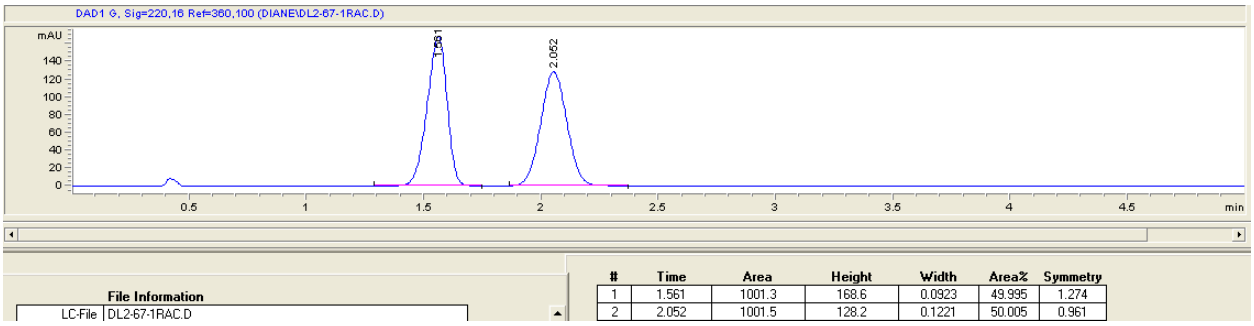
(+)-3j



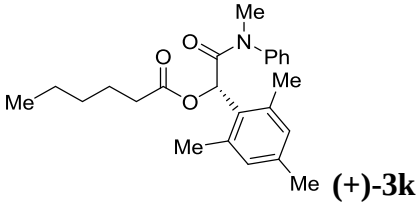
#	Time	Area	Height	Width	Area%	Symmetry
1	1.07	67.2	13	0.086	7.186	1.425
2	1.581	867.4	121.1	0.1193	92.814	1.202



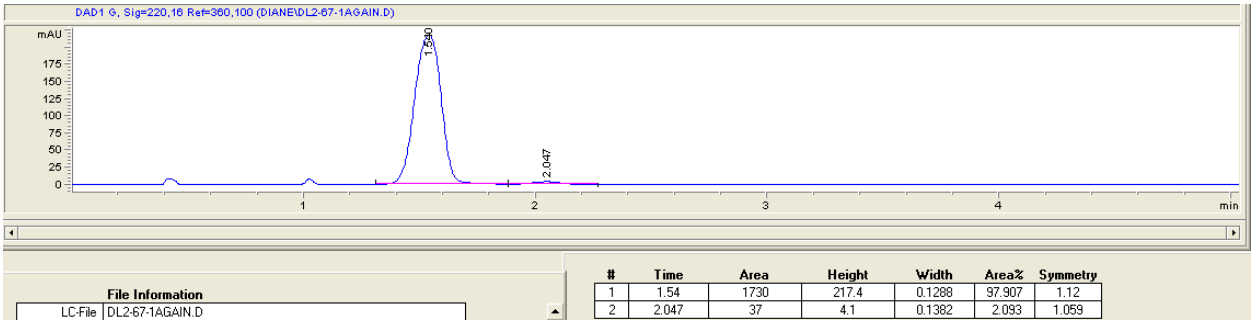
(±)-3k



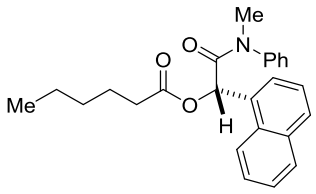
#	Time	Area	Height	Width	Area%	Symmetry
1	1.561	1001.3	168.6	0.0923	49.995	1.274
2	2.052	1001.5	128.2	0.1221	50.005	0.961



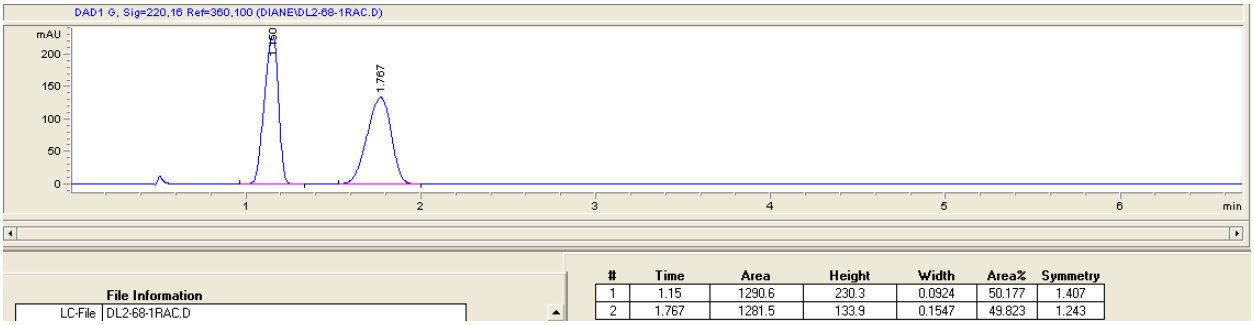
(+)-3k



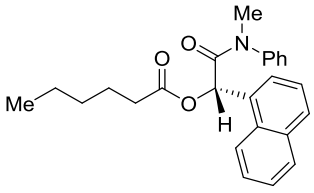
#	Time	Area	Height	Width	Area%	Symmetry
1	1.54	1730	217.4	0.1288	97.907	1.12
2	2.047	37	4.1	0.1382	2.093	1.059



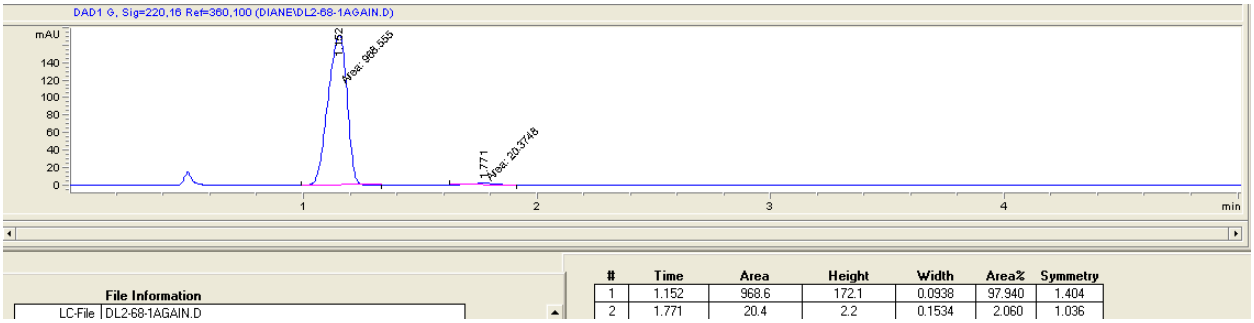
(±)-3l



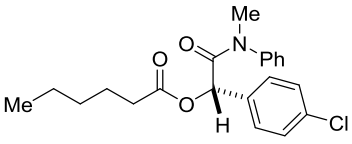
#	Time	Area	Height	Width	Area%	Symmetry
1	1.15	1290.6	230.3	0.0924	50.177	1.407
2	1.767	1281.5	133.9	0.1547	49.823	1.243



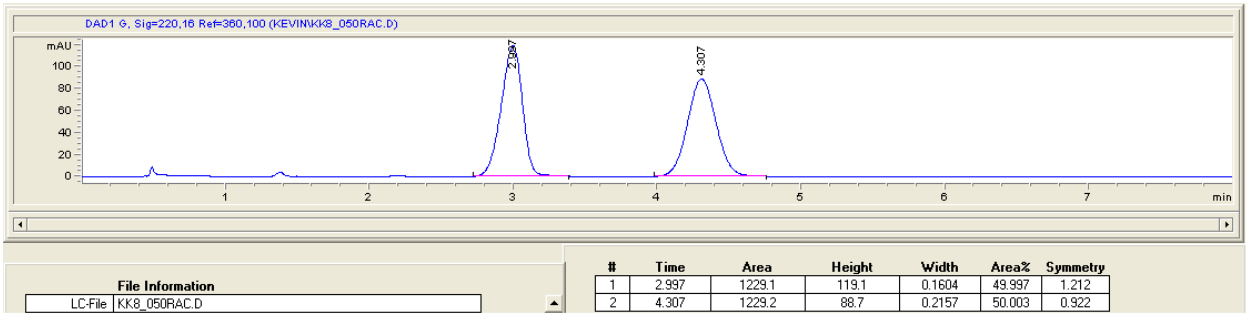
(+)-3l



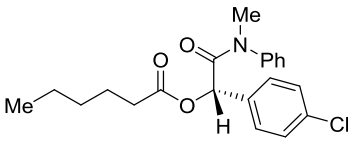
#	Time	Area	Height	Width	Area%	Symmetry
1	1.152	968.6	172.1	0.0938	97.940	1.404
2	1.771	20.4	2.2	0.1534	2.060	1.036



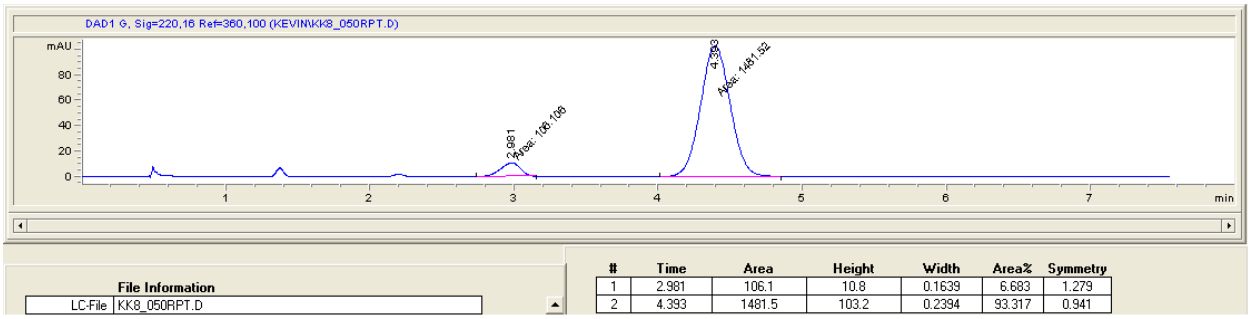
(±)-3m



#	Time	Area	Height	Width	Area%	Symmetry
1	2.997	1229.1	119.1	0.1604	49.997	1.212
2	4.307	1229.2	88.7	0.2157	50.003	0.922



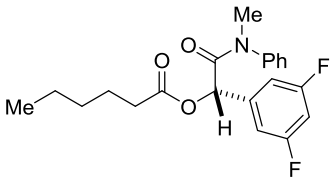
(+)-3m



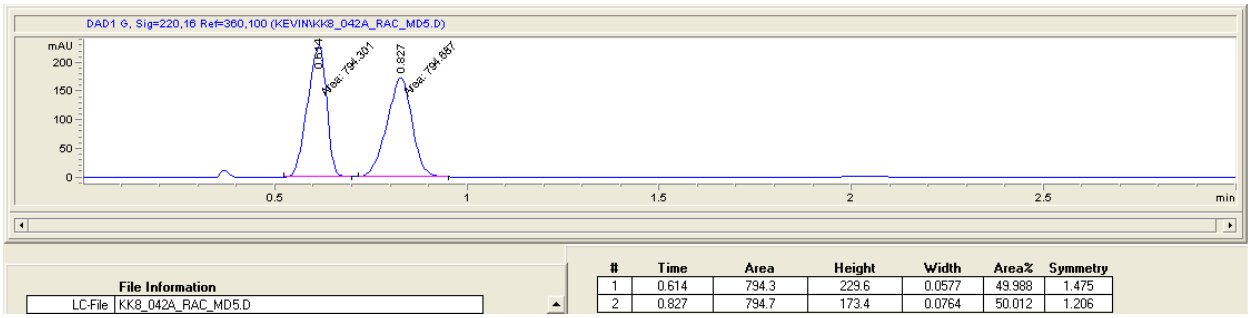
File Information

LC-File | KK8_050RPT.D

#	Time	Area	Height	Width	Area%	Symmetry
1	2.981	106.1	10.8	0.1639	6.683	1.279
2	4.393	1481.5	103.2	0.2394	93.317	0.941



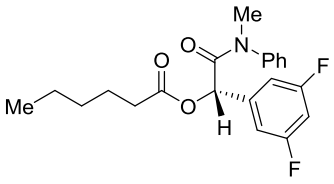
(±)-3n



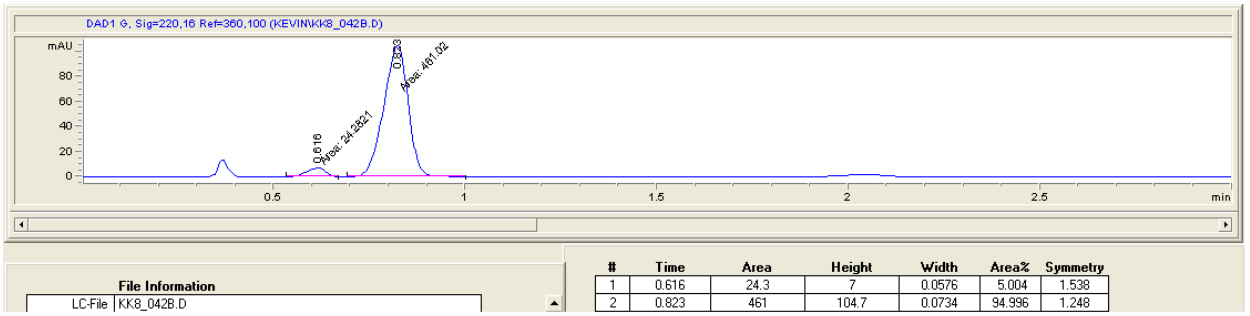
File Information

LC-File | KK8_042A_RAC_MD5.D

#	Time	Area	Height	Width	Area%	Symmetry
1	0.614	794.3	229.6	0.0577	49.988	1.475
2	0.827	794.7	173.4	0.0764	50.012	1.206



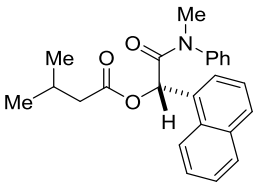
(+)-3n



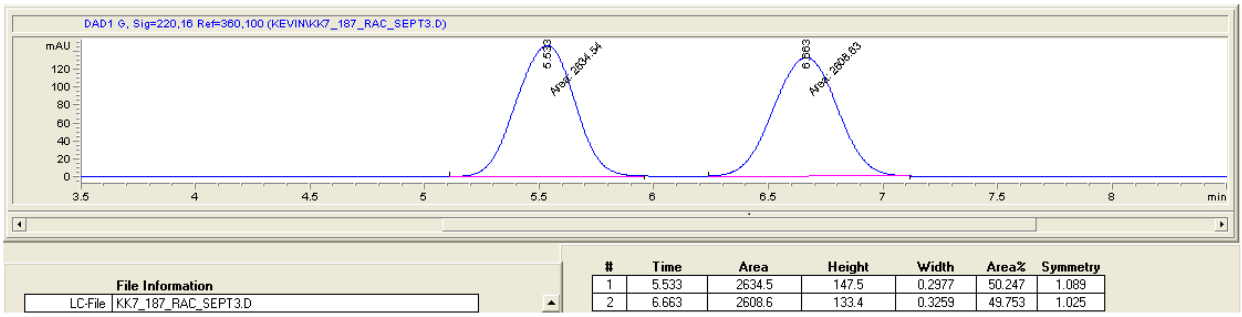
File Information

LC-File | KK8_042B.D

#	Time	Area	Height	Width	Area%	Symmetry
1	0.616	24.3	7	0.0576	5.004	1.538
2	0.823	461	104.7	0.0734	94.996	1.248



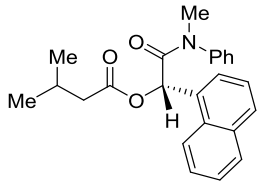
(±)-3o



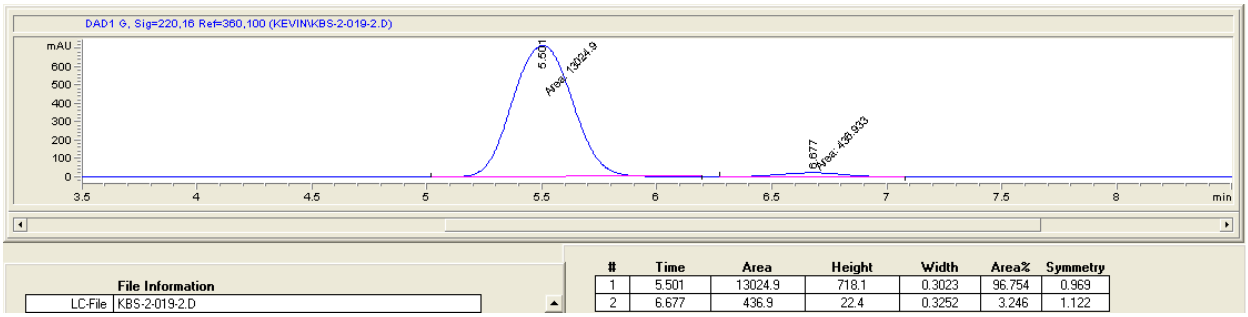
File Information

LC-File	KK7_187_RAC_SEPT3.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.533	2634.5	147.5	0.2977	50.247	1.089
2	6.663	2608.6	133.4	0.3259	49.753	1.025



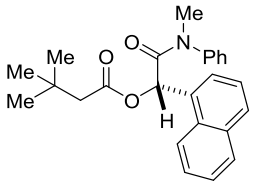
(+)-3o



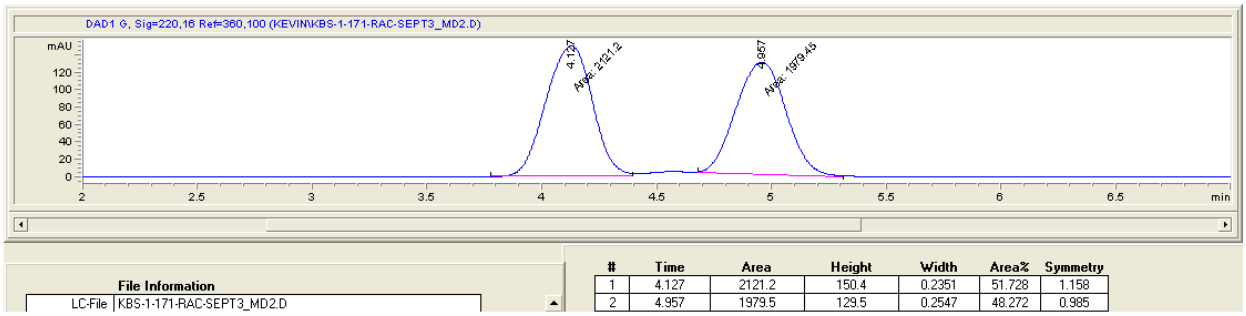
File Information

LC-File	KBS-2-019-2.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.501	13024.9	718.1	0.3023	96.754	0.969
2	6.677	436.9	22.4	0.3252	3.246	1.122



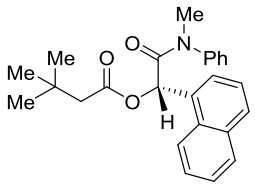
(±)-3p



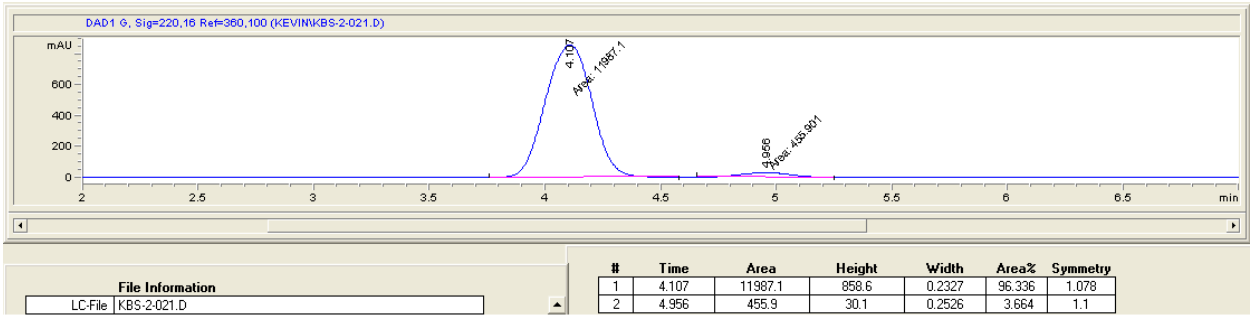
File Information

LC-File	KBS-1-171-RAC-SEPT3_MD2.D

#	Time	Area	Height	Width	Area%	Symmetry
1	4.127	2121.2	150.4	0.2351	51.728	1.158
2	4.957	1979.5	129.5	0.2547	48.272	0.985



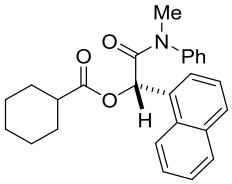
(+)-3p



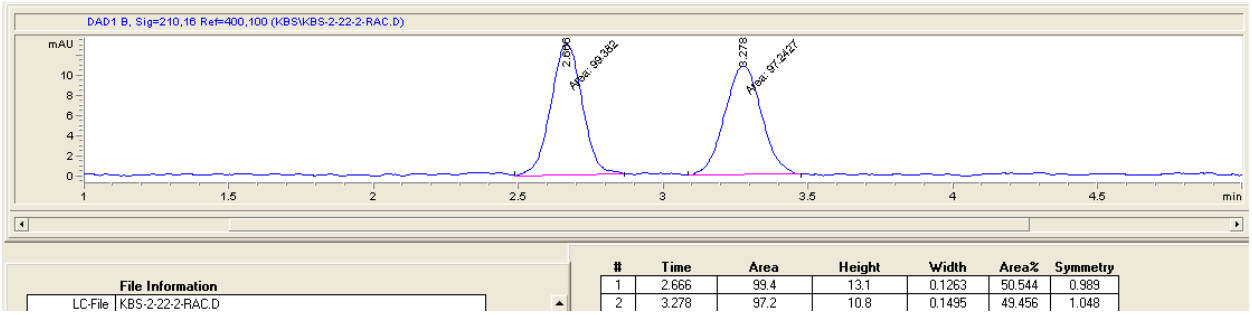
File Information

LC-File | KBS-2-021.D

#	Time	Area	Height	Width	Area%	Symmetry
1	4.107	11987.1	858.6	0.2327	96.336	1.078
2	4.956	455.9	30.1	0.2526	3.664	1.1



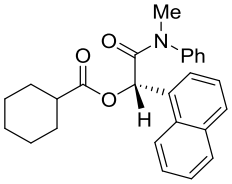
(±)-3q



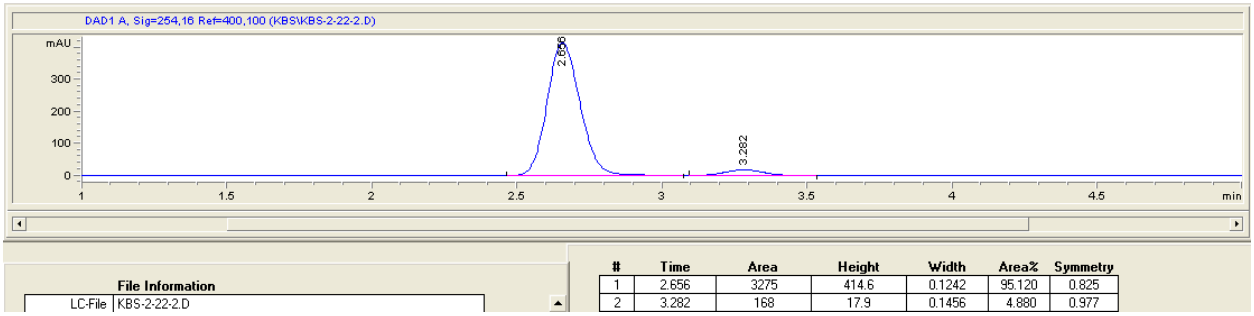
File Information

LC-File | KBS-2-22-2-RAC.D

#	Time	Area	Height	Width	Area%	Symmetry
1	2.666	99.4	13.1	0.1263	50.544	0.989
2	3.278	97.2	10.8	0.1495	49.456	1.048



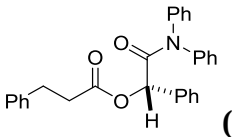
(+)-3q



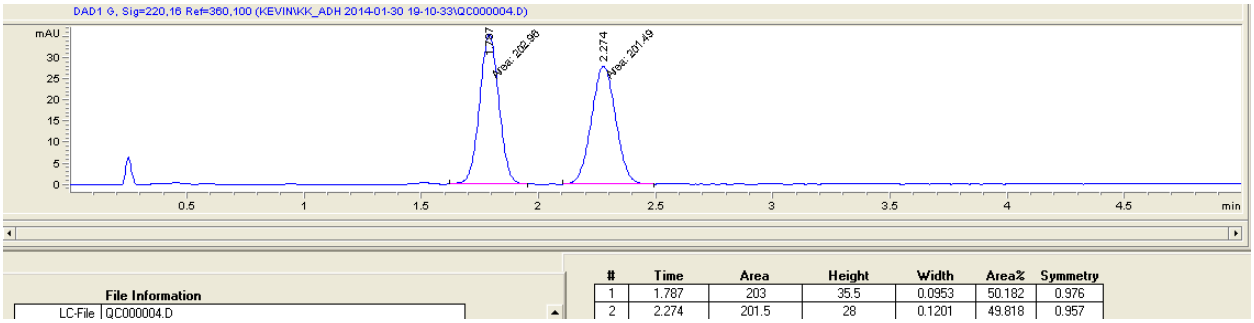
File Information

LC-File | KBS-2-22-2.D

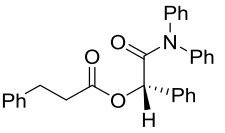
#	Time	Area	Height	Width	Area%	Symmetry
1	2.656	3275	414.6	0.1242	95.120	0.825
2	3.282	168	17.9	0.1456	4.880	0.977



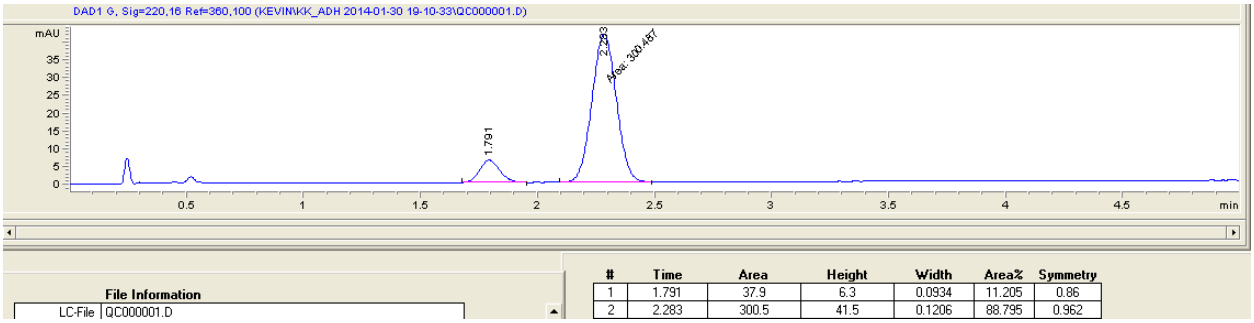
(±)-3r



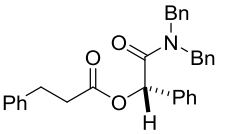
#	Time	Area	Height	Width	Area%	Symmetry
1	1.787	203	35.5	0.0953	50.182	0.976
2	2.274	201.5	28	0.1201	49.818	0.957



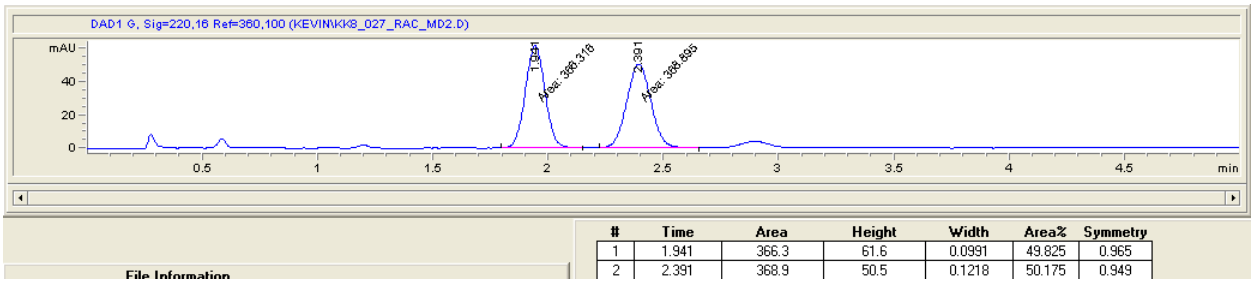
(+)-3r



#	Time	Area	Height	Width	Area%	Symmetry
1	1.791	37.9	6.3	0.0934	11.205	0.86
2	2.283	300.5	41.5	0.1206	88.795	0.962

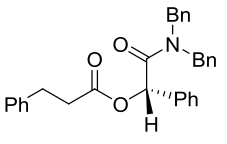


(±)-3s

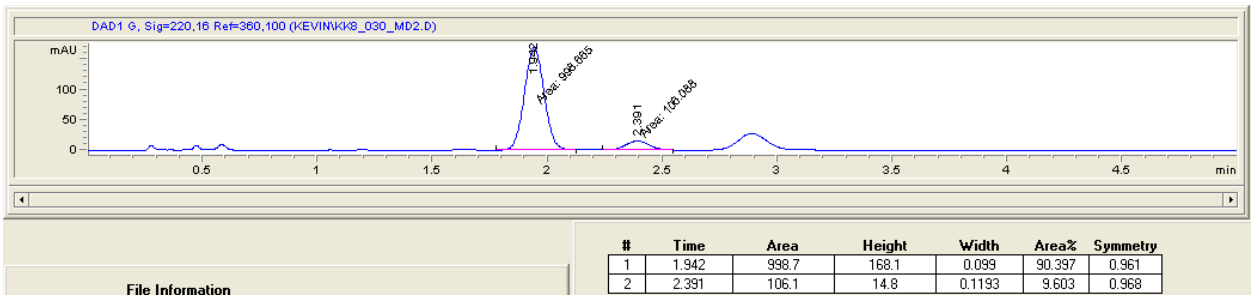


#	Time	Area	Height	Width	Area%	Symmetry
1	1.941	366.3	61.6	0.0991	49.825	0.965
2	2.391	368.9	50.5	0.1218	50.175	0.949

* peak at 2.9 min is residual α-ketoamide starting material that were not completely separated from product

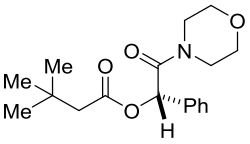


(+)-3s

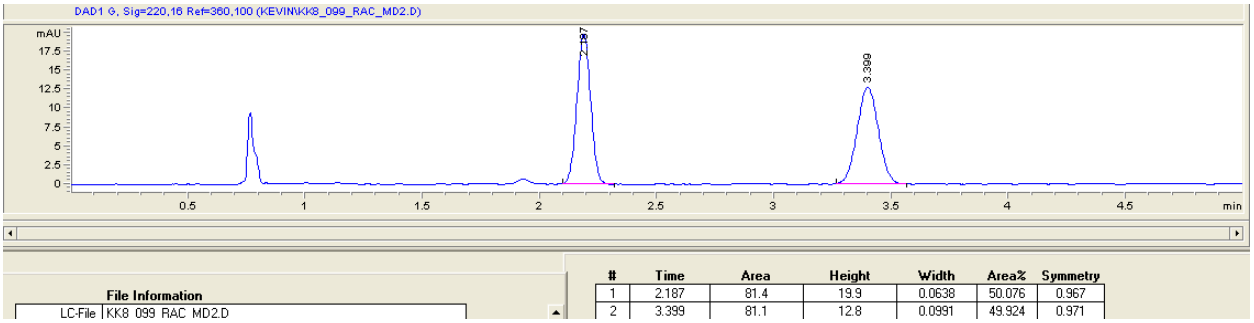


#	Time	Area	Height	Width	Area%	Symmetry
1	1.942	998.7	168.1	0.099	90.397	0.961
2	2.391	106.1	14.8	0.1193	9.603	0.968

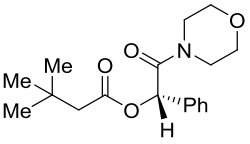
* peak at 2.9 min is residual α-ketoamide starting material that were not completely separated from product



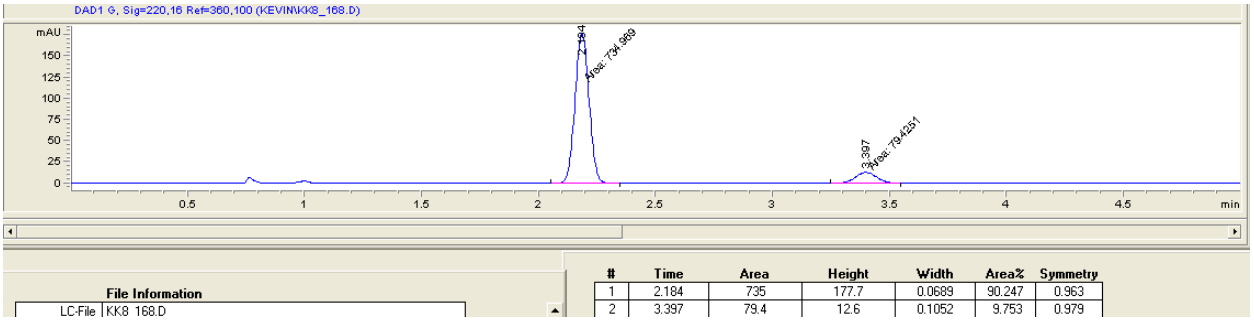
(±)-5a



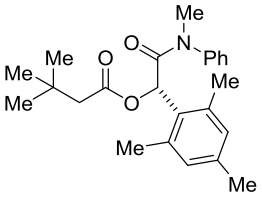
#	Time	Area	Height	Width	Area%	Symmetry
1	2.187	81.4	19.9	0.0638	50.076	0.967
2	3.399	81.1	12.8	0.0991	49.924	0.971



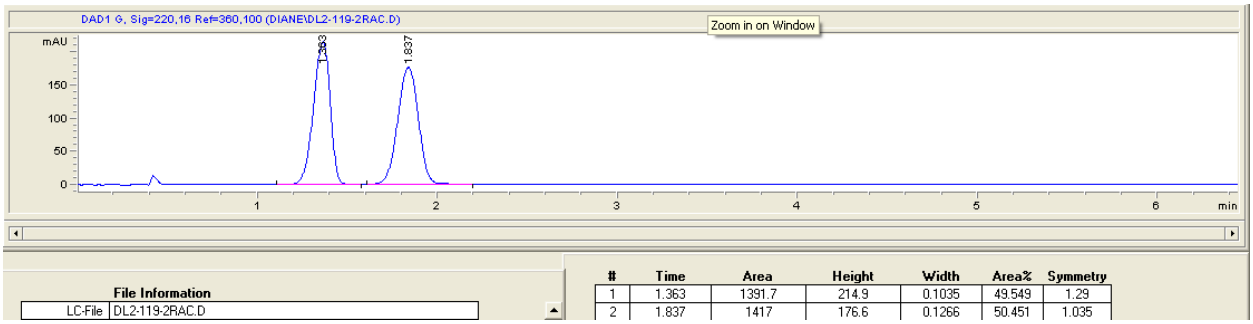
(+)-5a



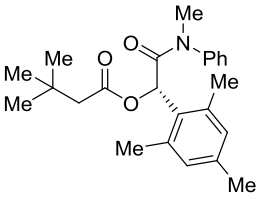
#	Time	Area	Height	Width	Area%	Symmetry
1	2.184	735	177.7	0.0689	90.247	0.963
2	3.397	79.4	12.6	0.1052	9.753	0.979



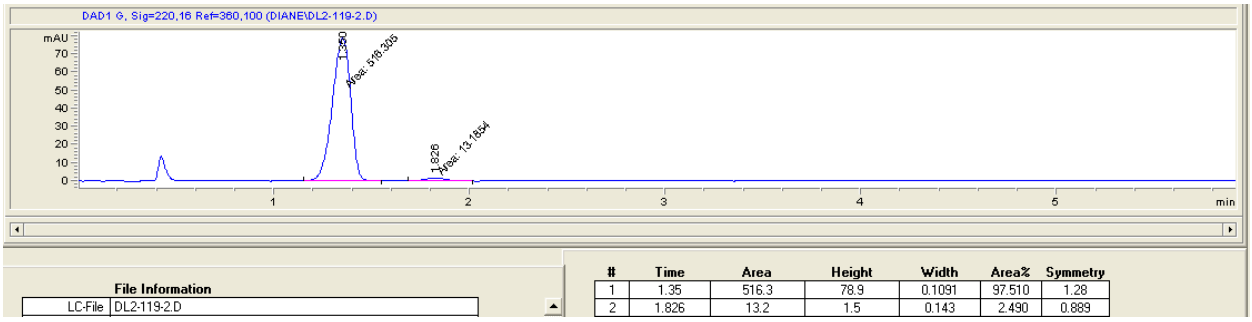
(±)-5b



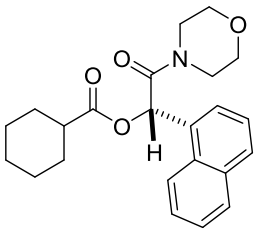
#	Time	Area	Height	Width	Area%	Symmetry
1	1.363	1391.7	214.9	0.1035	49.549	1.29
2	1.837	1417	176.6	0.1266	50.451	1.035



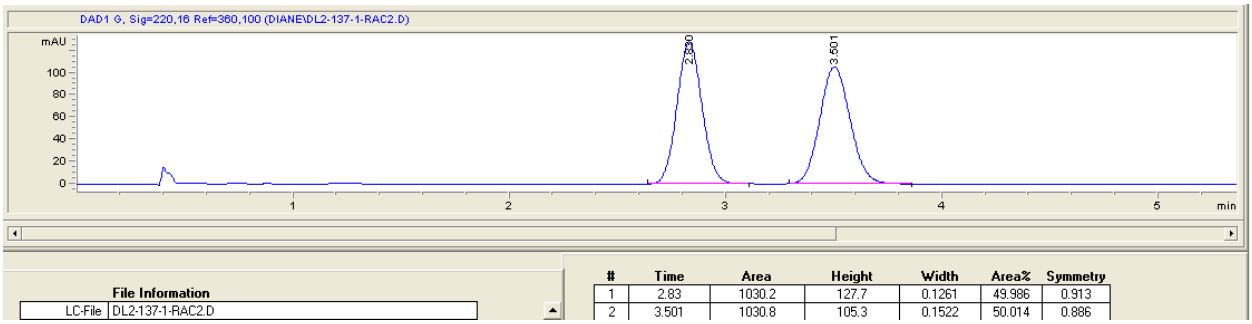
(+)-5b



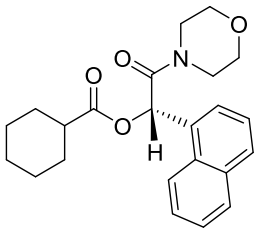
#	Time	Area	Height	Width	Area%	Symmetry
1	1.35	516.3	78.9	0.1091	97.510	1.28
2	1.826	13.2	1.5	0.143	2.490	0.889



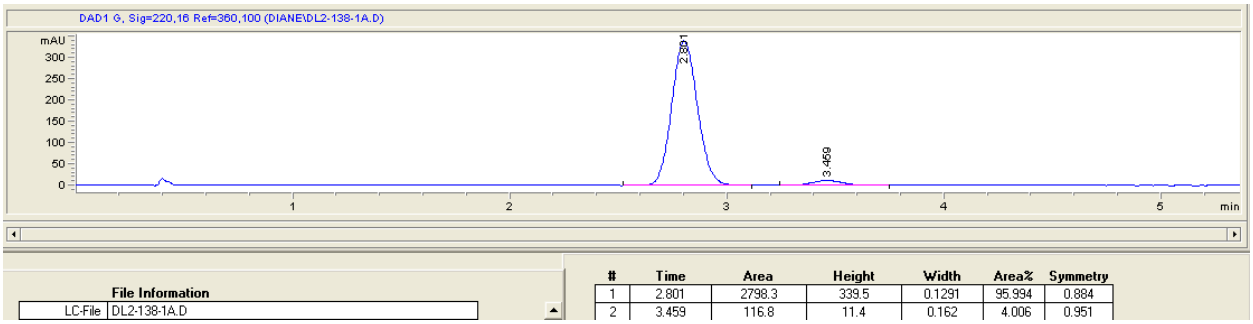
(±)-5c



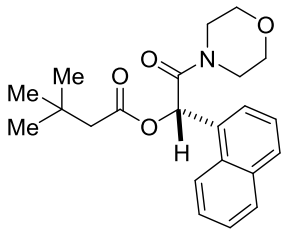
#	Time	Area	Height	Width	Area%	Symmetry
1	2.83	1030.2	127.7	0.1261	49.986	0.913
2	3.501	1030.8	105.3	0.1522	50.014	0.886



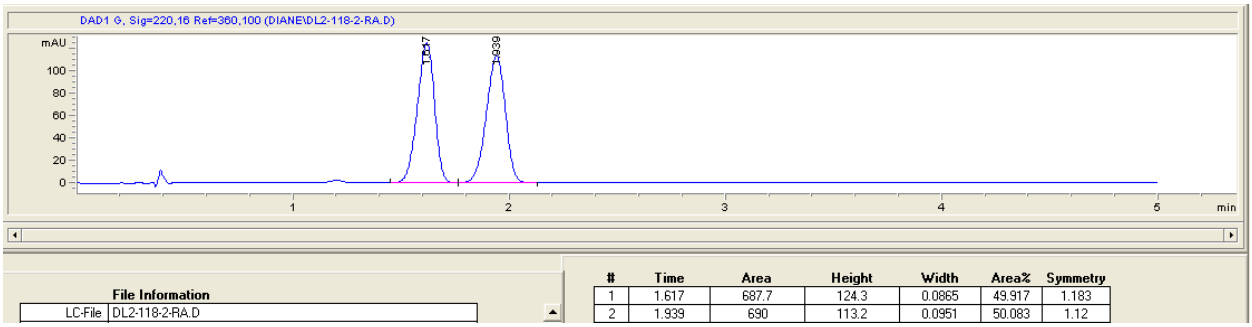
(+)-5c



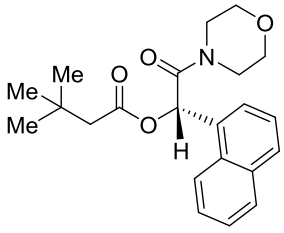
#	Time	Area	Height	Width	Area%	Symmetry
1	2.801	2798.3	339.5	0.1291	95.994	0.884
2	3.459	116.8	11.4	0.162	4.006	0.951



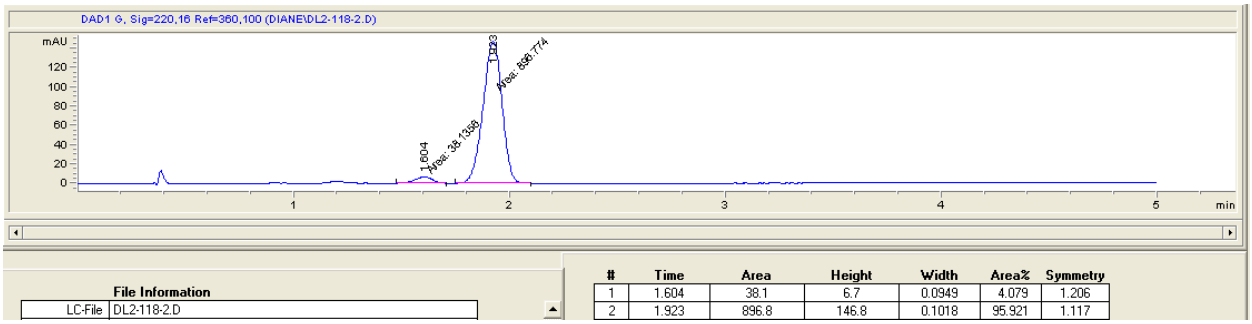
(±)-5d



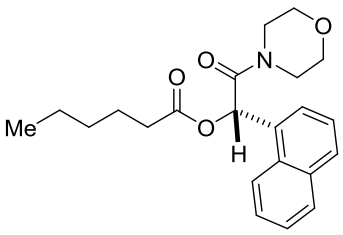
#	Time	Area	Height	Width	Area%	Symmetry
1	1.617	687.7	124.3	0.0865	49.917	1.183
2	1.939	690	113.2	0.0951	50.083	1.12



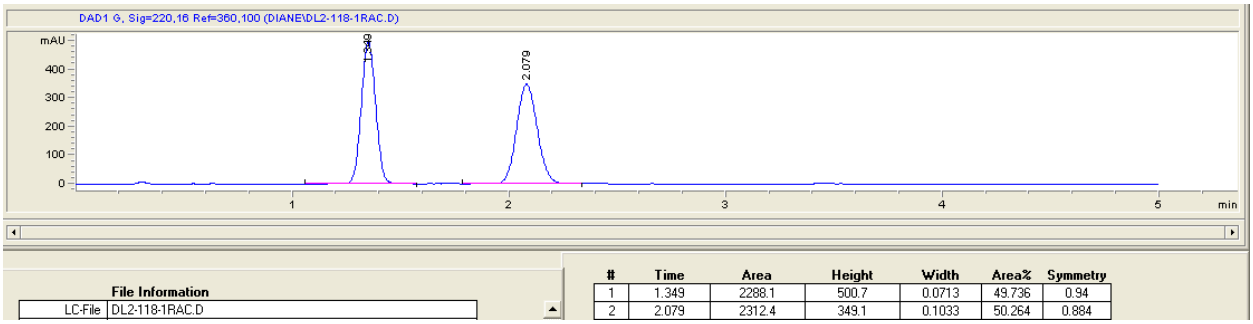
(+)-5d



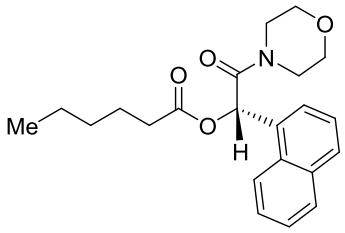
#	Time	Area	Height	Width	Area%	Symmetry
1	1.604	38.1	6.7	0.0949	4.079	1.206
2	1.923	896.8	146.8	0.1018	95.921	1.117



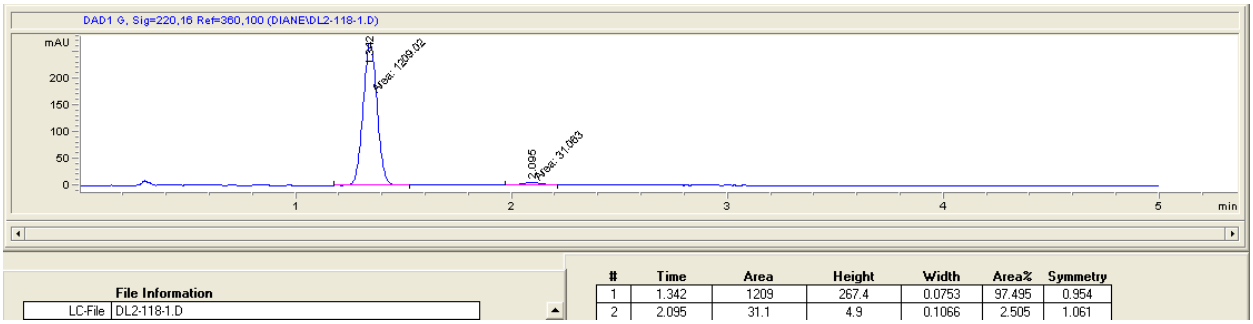
(±)-5e



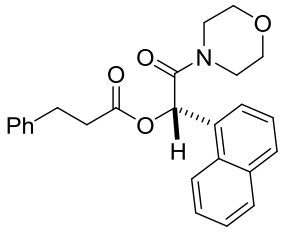
#	Time	Area	Height	Width	Area%	Symmetry
1	1.349	2288.1	500.7	0.0713	49.736	0.94
2	2.079	2312.4	349.1	0.1033	50.264	0.884



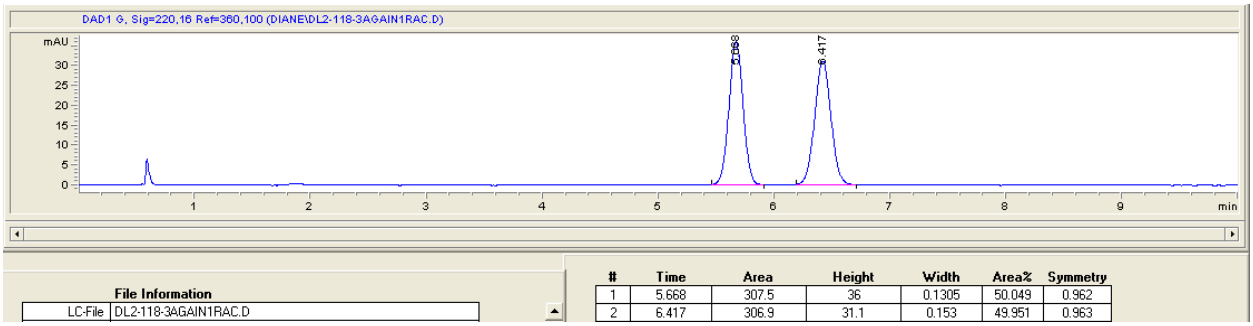
(+)-5e



#	Time	Area	Height	Width	Area%	Symmetry
1	1.342	1209	267.4	0.0753	97.495	0.954
2	2.095	31.1	4.9	0.1066	2.505	1.061



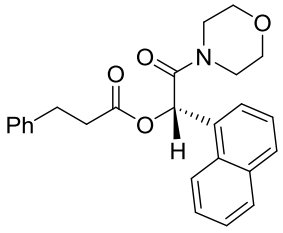
(±)-5f



File Information

LC-File	DL2-118-3AGAIN1RAC.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.668	307.5	36	0.1305	50.049	0.962
2	6.417	306.9	31.1	0.153	49.951	0.963



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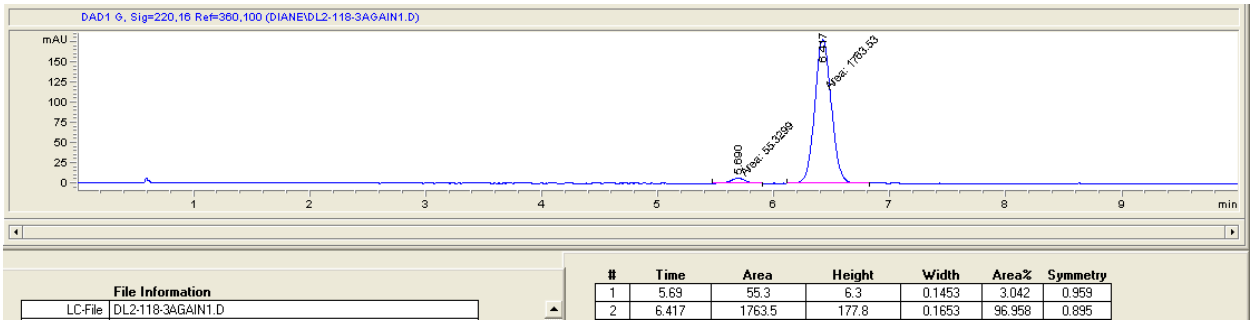
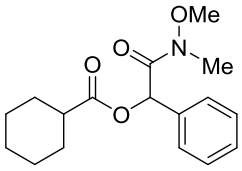


File Information

LC-File	DL2-118-3AGAIN1.D

#	Time	Area	Height	Width	Area%	Symmetry
1	5.69	55.3	6.3	0.1453	3.042	0.959
2	6.417	1763.5	177.8	0.1653	96.958	0.895



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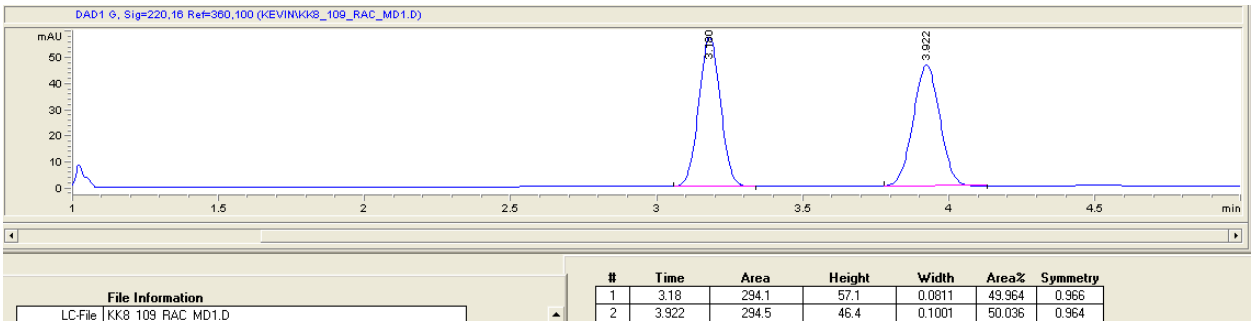
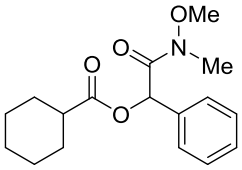


#	Time	Area	Height	Width	Area%	Symmetry
1	3.18	294.1	57.1	0.0811	49.964	0.966
2	3.922	294.5	46.4	0.1001	50.036	0.964



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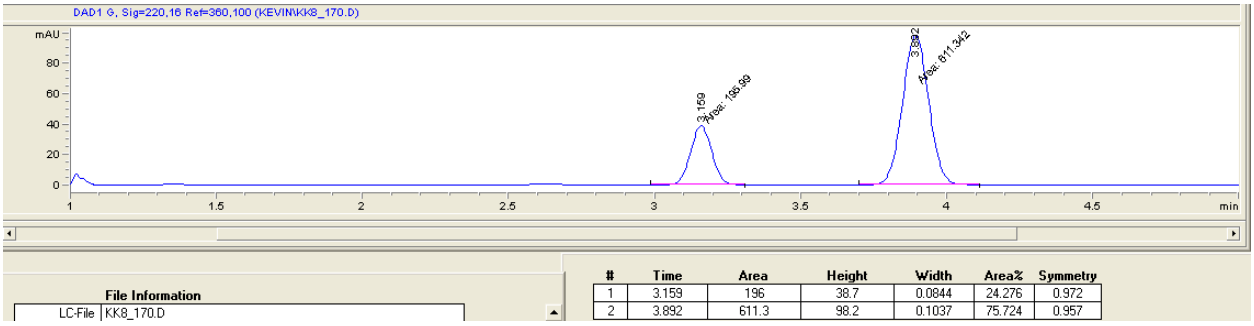

#	Time	Area	Height	Width	Area%	Symmetry
1	3.159	196	38.7	0.0844	24.276	0.972
2	3.892	611.3	98.2	0.1037	75.724	0.957