Electronic Supplementary Information

Asymmetric Esterification of Ketenes Catalyzed by N-Heterocyclic Carbene

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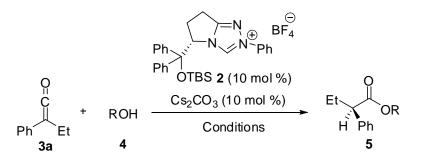
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Part I Experimental Part

1.1 General Information

Unless otherwise indicated, all starting materials were obtained from commercial supplies and used as received. Anhydrous toluene and Et₂O were distilled from sodium and benzophenone, Chiral triazolium salt 2 was synthesized according to previously report¹. 2-Phenylethanol was purified by shaking with a solution of ferrous sulfate, and the alcohol layer was washed with distilled water and fractionally distilled. Ketenes were prepared according to literature². All reactions were carried out under an argon atmosphere in oven-dried glassware with magnetic stirring. Column chromatograph was performed with silica gel 200~300 mesh. All ¹H NMR (300 MHz), ¹³C NMR (75 MHz) spectra were recorded on a Bruker-DMX 300 spectrometer in CDCl₃, with tetramethylsilane as an internal standard and reported in parts per million (ppm, δ). ¹H NMR spectroscopy splitting patterns were designated as singlet (s), doublet (d), triplet (t). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). Infrared spectra were recorded on a JASCO FT/IR-480 spectrophotometer and reported as wave number (cm⁻¹). Optical rotations were measured on Perkin Elmer/Model-343 digital polarimeter operating at the sodium D line with a 100 mm path cell, and reported as follows: $\left[\alpha\right]_{D}^{T}$ (concentration (g/100 mL), solvent).

1.2 Screening of alcohols and optimization of reaction conditions



General Procedure A (Method A). To the mixture of triazolium salt 2 (10 mol %), Cs_2CO_3 (10 mol %), and alcohol in toluene (9 mL) was added the solution of ketene in toluene (10 mL). The reaction mixture was stirred under N_2 at the specified temperature for the specified amount of time, and then it was quenched by the addition of silica gel, the mixture was further stirred for ten minutes. The reaction mixture was diluted with diethyl ether, and passed through a short silica pad. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel (Et₂O/petroleum ether, typically 1:90) to give the desired product.

General Procedure B (Method B). The same as Method A, except that the solution of ketene was added via a syringe pump over 30 min.

General Procedure C (Method C). To the mixture of ketene (0.5 mmol) and benzhydrol (184 .3 mg, 1.0 mmol) in toluene (2 mL) at -40° C was added the solution of NHC **2'**, which was freshly prepared from NHC precursor **2** (34.2 mg, 0.06 mmol) and Cs₂CO₃ (16.3 mg, 0.05 mol) in toluene/ether (1/1, 2 mL) at rt for 1 h. The

reaction mixture was stirred at -40 °C for specified time (See below). After quenched with silica gel and further stirred for 10 min, the reaction mixture was diluted with diethyl ether, and passed through a short silica pad. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel to give the desired product.

Racemic samples of esters for the standard of chiral HPLC spectra were prepared using 10 mol % Cs₂CO₃ as catalyst.

(R)-methyl 2-phenylbutanoate³

Table 1, entry 1. General Procedure A was followed: To the mixture of triazolium salt **2** (57.0 mg, 0.1 mmol), Cs₂CO₃ (32.6 mg, 0.1 mmol), methanol (40.5 μ L, 1.0 mmol) in toluene (9 mL) was added the solution of ketene (1.5 mmol) in toluene (10 mL) in one portion. Reaction temperature: -78 °C. Reaction time: 15 h. Yield: 149.6 mg, 84%; R_f = 0.24 (Et₂O/petroleum ether = 1:90); colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.29-7.16 (m, 5H), 3.57 (s, 3H), 3.44 (t, *J* = 7.7 Hz, 1H), 2.16-2.01 (m, 1H), 1.85-1.70 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 174.5, 139.1, 128.5, 127.9, 127.1, 53.3, 51.8, 26.7, 12.1; HPLC analysis: 13% ee [Daicel CHIRALPAK OD-H column; 20 °C; 0.5 mL/min; solvent system: 2-propanol/hexane = 0.5:99.5; retention times: 9.6 min (major), 10.4 min (minor)].

(R)-phenethyl 2-phenylbutanoate

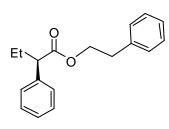


Table 1, entry 2. General Procedure A was followed: Tothe mixture of triazolium salt 2 (57.0 mg, 0.1 mmol), Cs_2CO_3 (32.6 mg, 0.1 mmol), 2-Phenylethanol (119.8 μ L ,

1.0 mmol) in toluene (9 mL) was added the solution of ketene (1.5 mmol) in toluene (10 mL) in one portion. Reaction temperature: -78 °C. Reaction time: 20 h. Yield: 284.0 mg, 99%; $R_f = 0.34$ (Et₂O/petroleum ether = 1:80); colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.24-7.13 (m, 8H), 7.04-7.02 (m, 2H), 4.23 (t, J = 6.8 Hz, 2H), 3.40 (t, J = 7.6 Hz, 1H), 2.80 (t, J = 6.8 Hz, 2H), 2.10-1.98 (m, 1H), 1.79-1.69 (m, 1H), 0.82 (t, J = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 173.5, 138.9, 137.6, 128.6, 128.3, 128.2, 127.8, 126.9, 126.2, 64.8, 53.39, 34.7, 26.4, 11.9; IR (KBr) v 3029, 2964, 2934, 1732, 1496, 1455, 1263, 1199, 1163, 799, 748, 698 cm⁻¹; MS (EI): m/z 268 (M⁺, 1.2), 119 (PhCH⁺C₂H₅, 9.6), 105 (PhCH₂CH₂⁺, 15.5), 104 (PhCH=CH⁺, 100), 91 (PhCH₂⁺, 26.9); HRMS (EI) calcd for C₁₈H₂₀O₂ [M]⁺ 268.1463, found 268.1465; HPLC analysis: 11% ce [Daicel CHIRALPAK OD-H column; 20 °C; 0.7 mL/min; solvent system: 2-propanol/hexane = 0.4:99.6; retention times: 21.6 min (major), 28.1 min (minor)].

(R)-benzyl 2-phenylbutanoate⁴

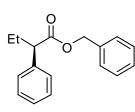


Table 1, entry 3. General Procedure A was followed: To the mixture of triazolium salt **2** (57.0 mg, 0.1 mmol), Cs_2CO_3 (32.6 mg, 0.1 mmol), benzyl alcohol (109.3 μ L, 1.0 mmol) in toluene

(9 mL) was added the solution of ketene (1.5 mmol) in toluene (10 mL) in one portion.

Reaction temperature: -78 °C. Reaction time: 21 h. Yield: 166.5 mg, 65%; $R_f = 0.33$ (Et₂O/petroleum ether = 1:80); colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.26-7.15 (m, 10H), 5.07 (d, J = 12.5 Hz, 1H), 4.99 (d, J = 12.5 Hz, 1H), 3.44 (t, J = 7.7 Hz, 1H), 2.10-2.00 (m, 1H), 1.80-1.70 (m, 1H), 0.81 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 173.8, 138.9, 136.0, 128.5, 128.4, 128.0, 128.0, 127.8, 127.1, 66.3, 53.4, 26.6, 12.1; HPLC analysis: 36% ee [Daicel CHIRALPAK OD-H column; 20 °C; 0.5 mL/min; solvent system: 2-propanol/hexane = 0.4:99.6; retention times: 11.2 min (major), 12.4 min (minor)].

1.3 References and notes

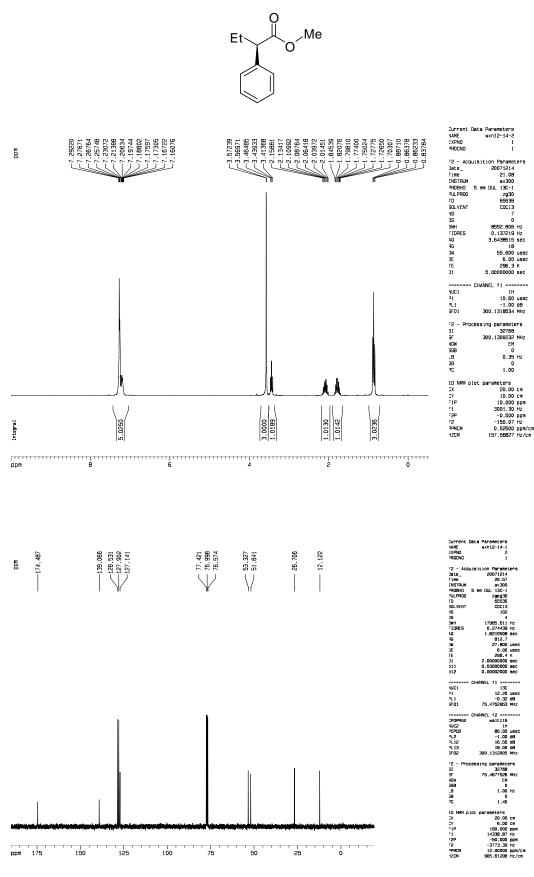
(1) Y.-R. Zhang, L. He, X. Wu, P.-L. Shao, Ye, S. Org. Lett. 2008, 10, 277-280.

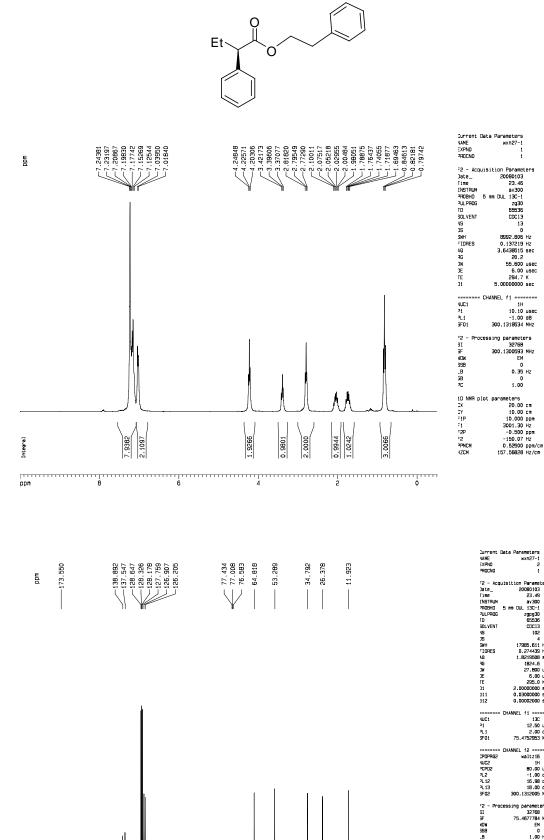
(2) (a) L. M. Baigrie, H. R. Seiklay, T. T. Tidwelll, J. Am. Chem. Soc. **1985**, 107, 5391-5396. (b) A. D. Allen, L. M. Baigrie, L. Gong, T. T. Tidwelll, Can. J. Chem. **1991**, 69, 138-145.

(3) B. L. Hodous, J. C. Ruble, G. C. Fu, J. Am. Chem. Soc. 1999, 121, 2637-2638.

(4) J. C. Ruble, G. C. Fu, J. Org. Chem. 1996, 61, 7230-723.





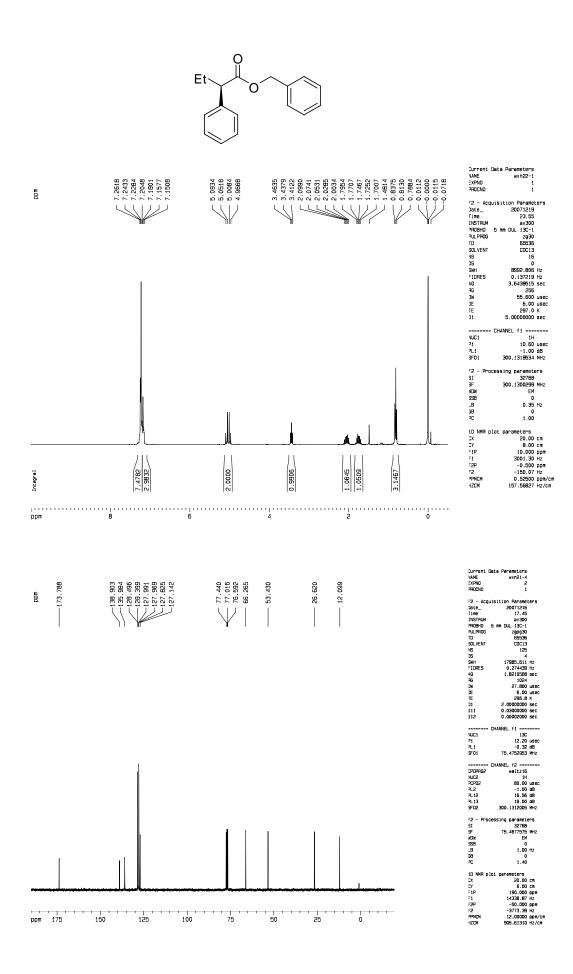


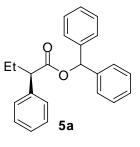
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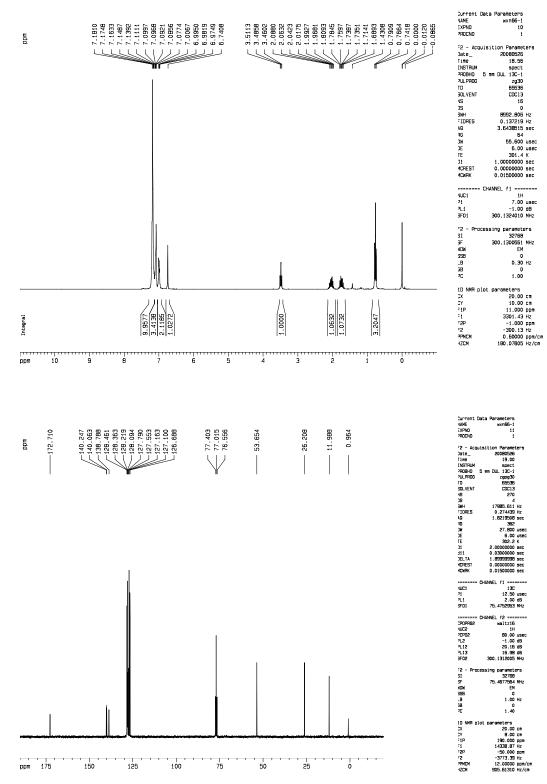
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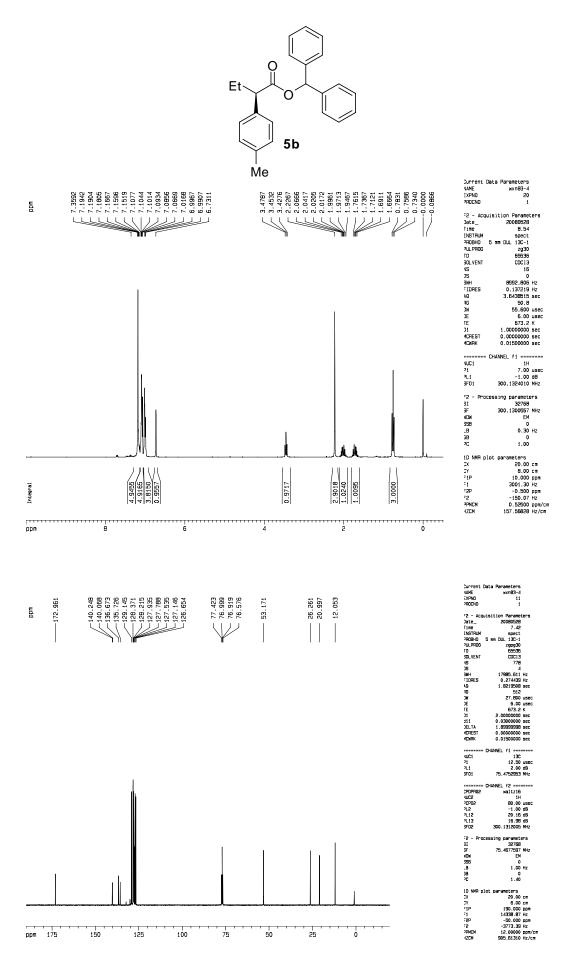
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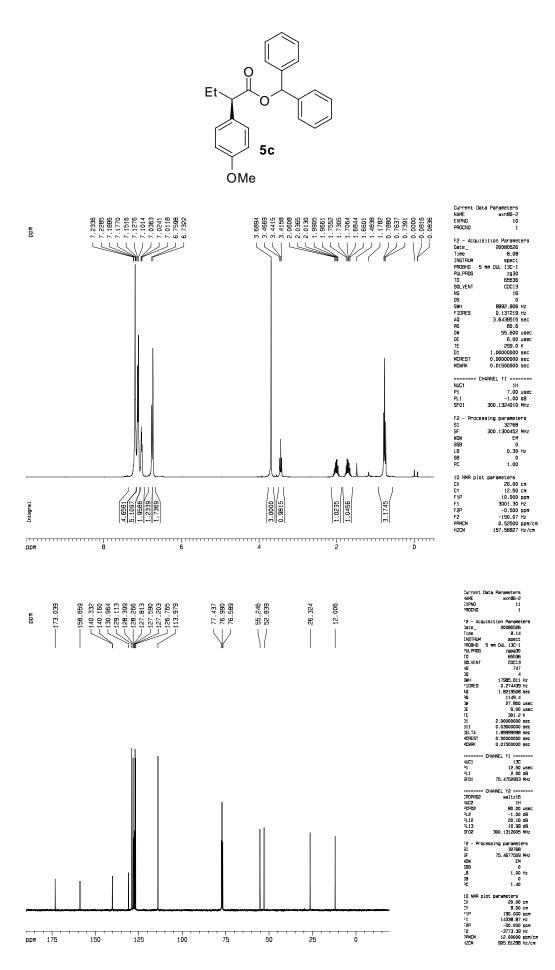
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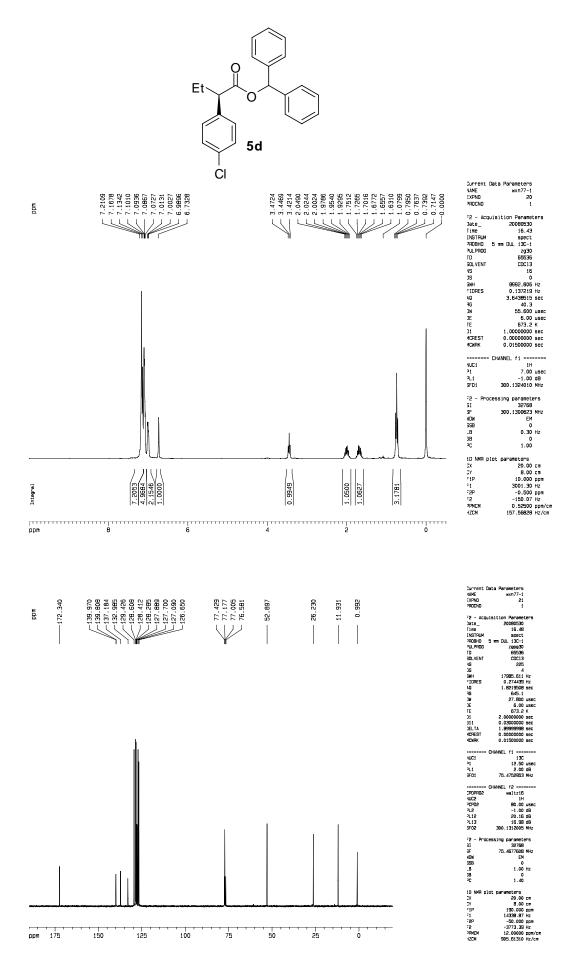


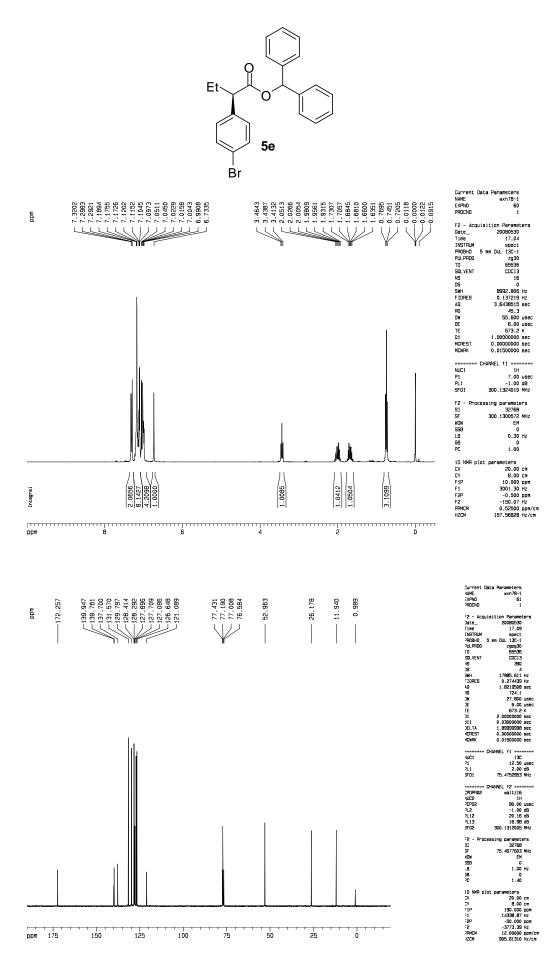


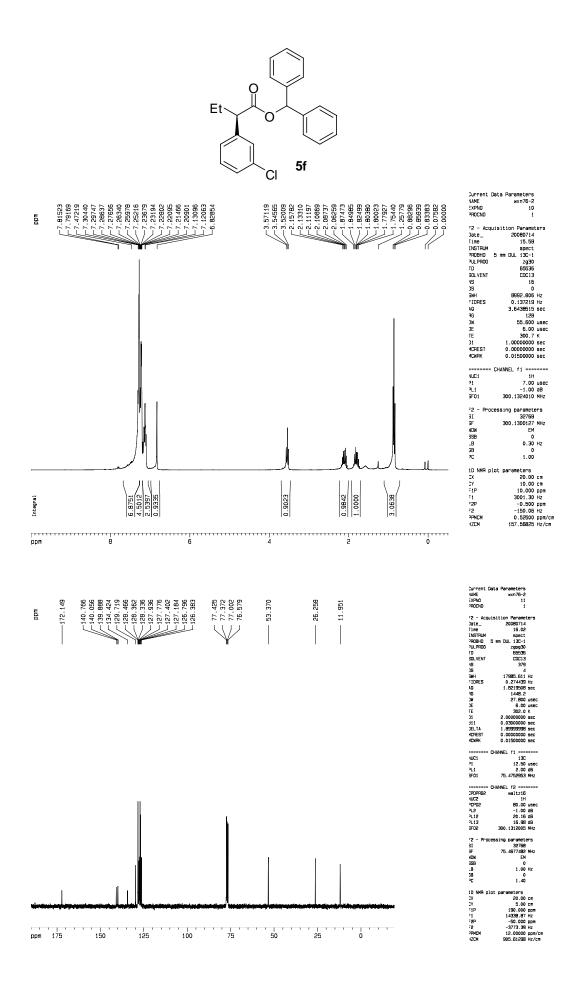


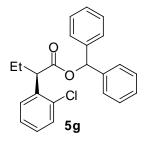


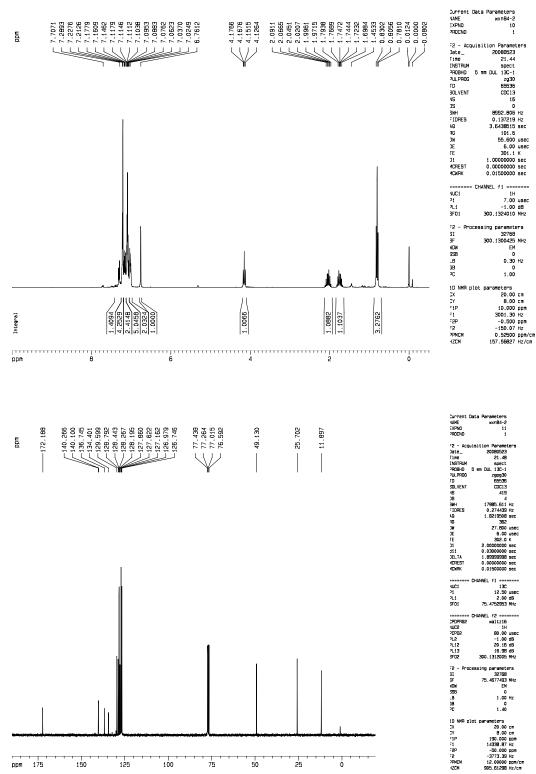


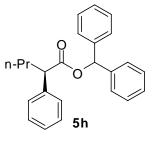


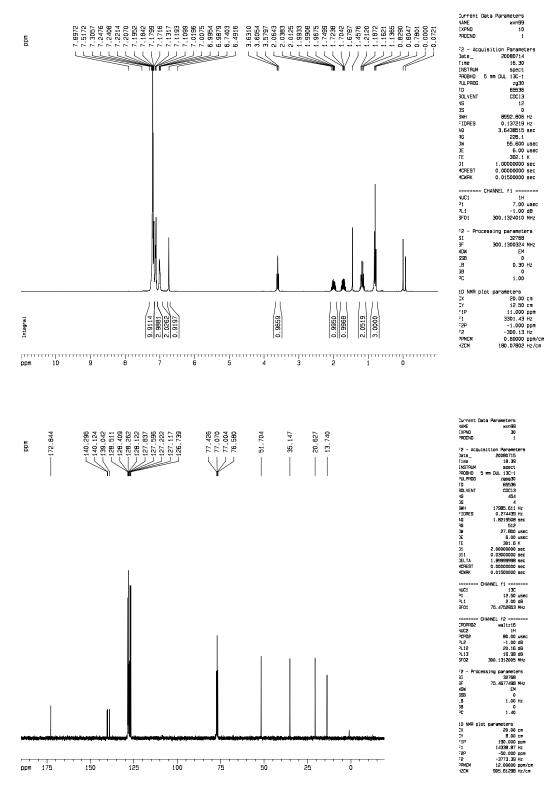


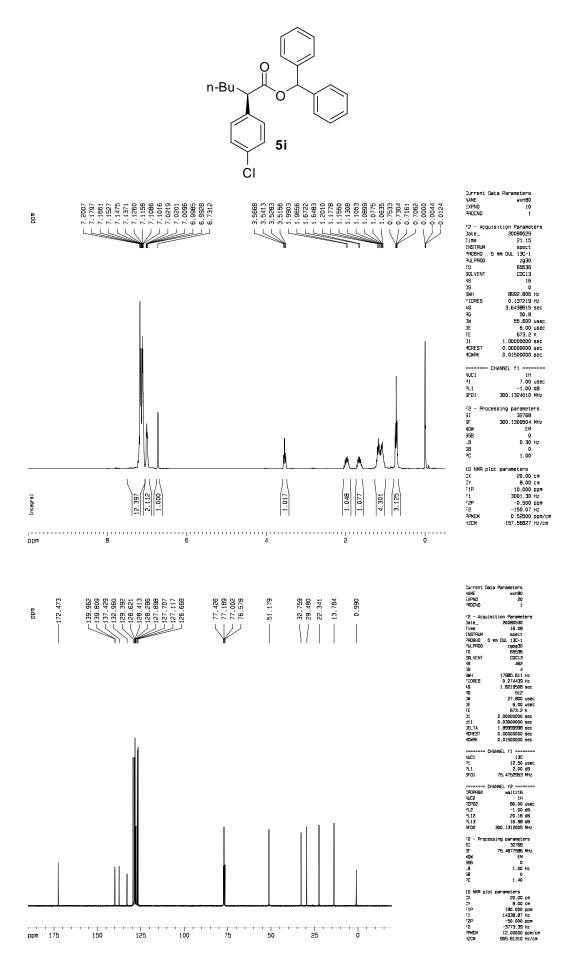


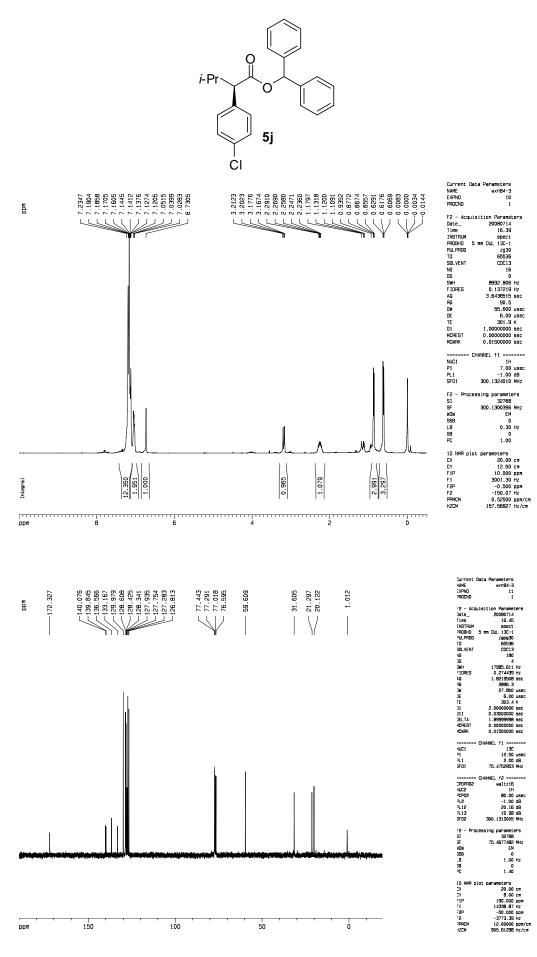




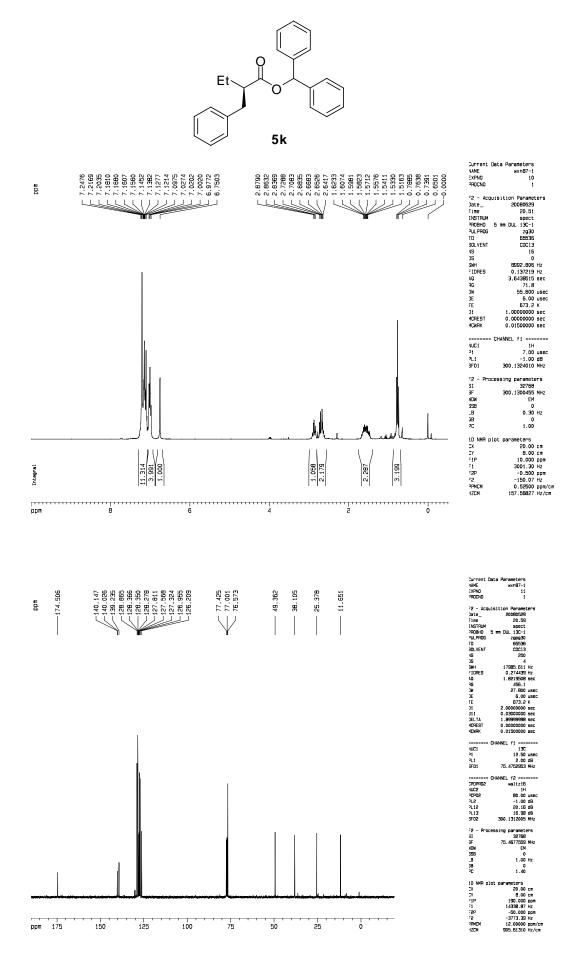


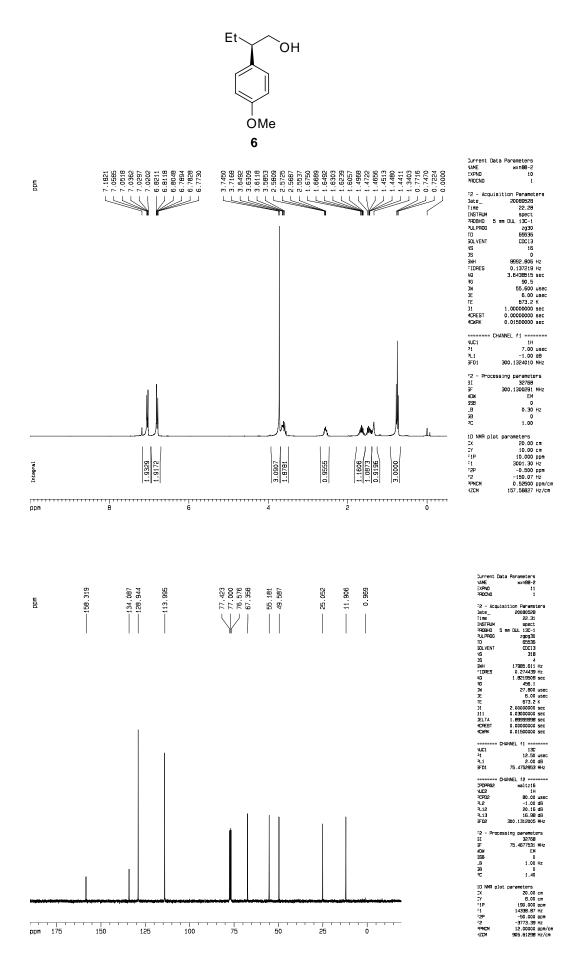


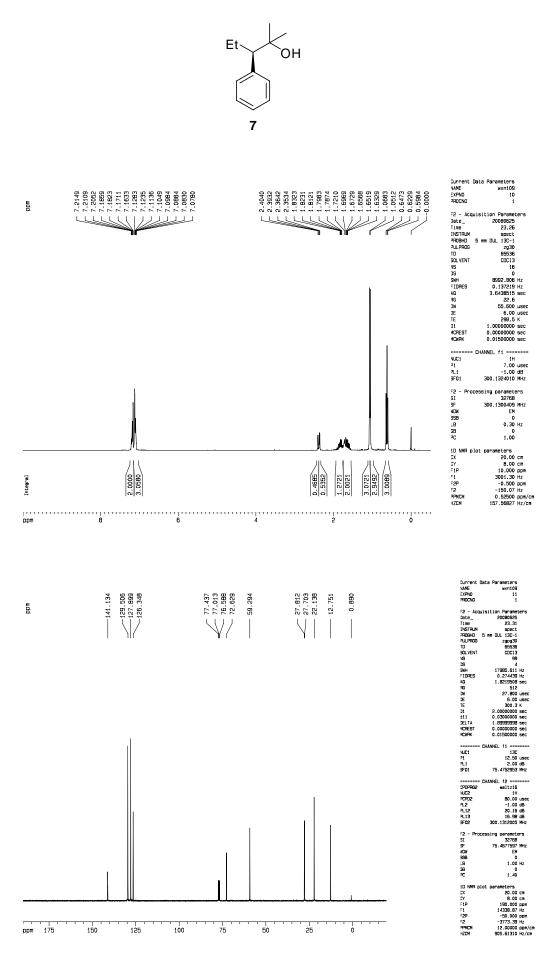






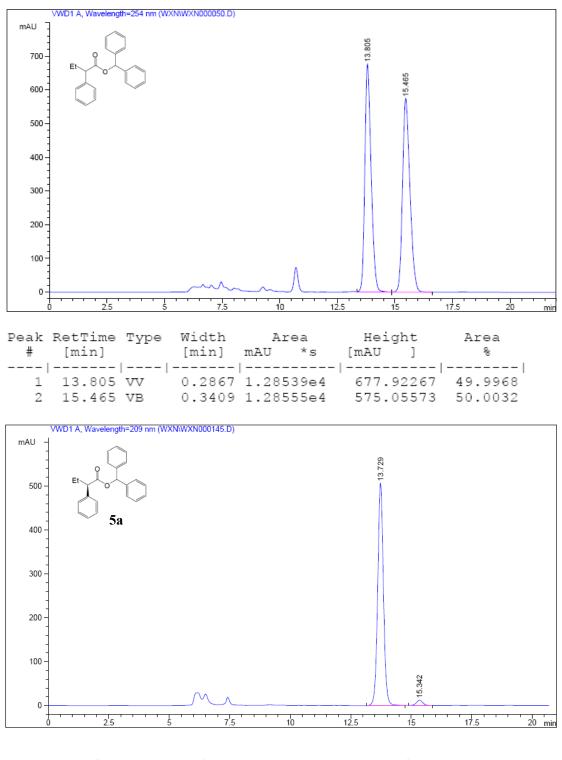






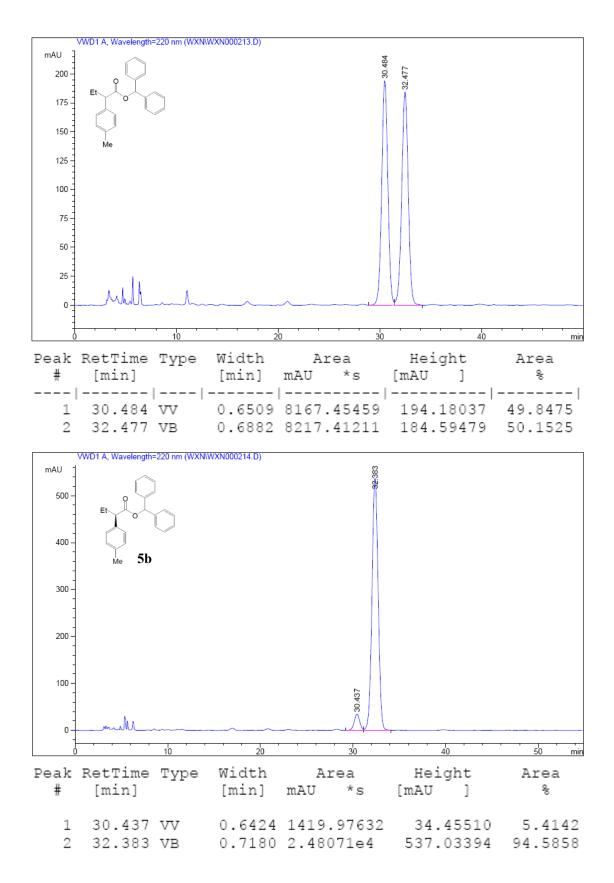
Part III Copies of HPLC spectra

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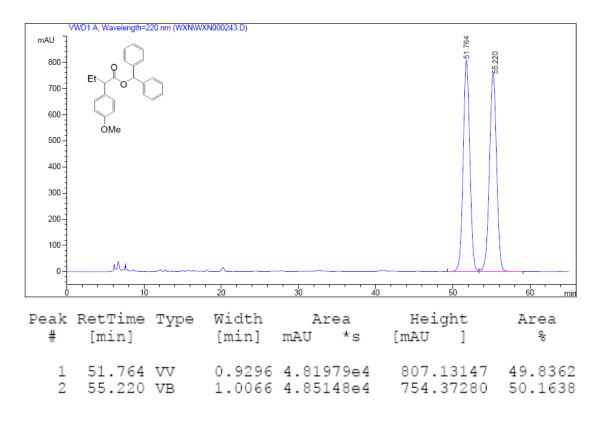


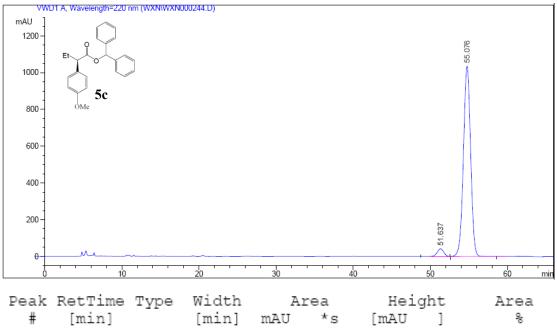
Peak	RetTime	Туре	Width	Ar	ea	Hei	ght	Area	
#	[min]		[min]	mAU	*s	[mAU]	웅	
1	13.729	BB	0.2509	8303.	67969	506.	62173	97.4700	
2	15.342	BB	0.2818	215.	53758	11.	78757	2.5300	

Sample Infomation: AD-H Hex: Ipr=99.5:0.5,1.0ml/min

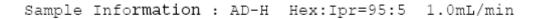


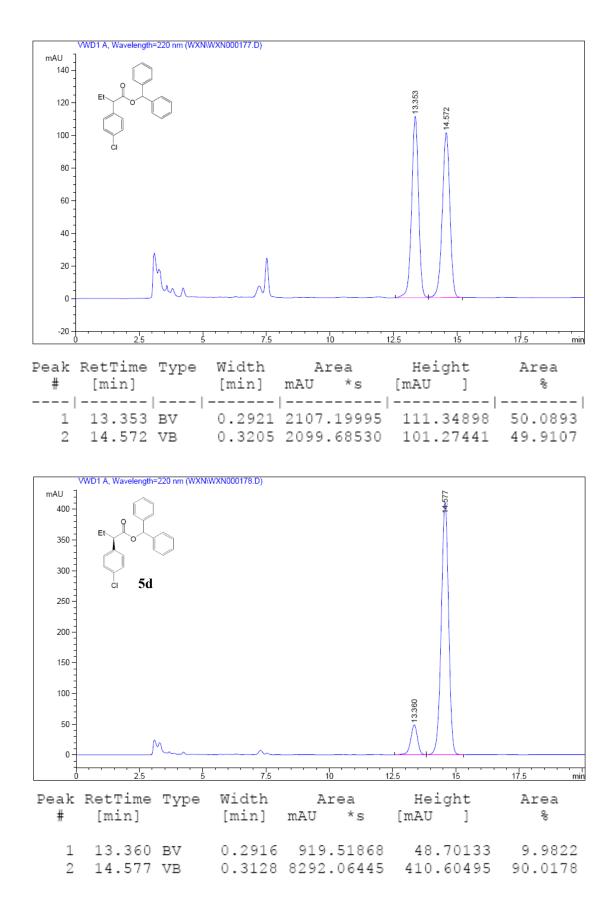
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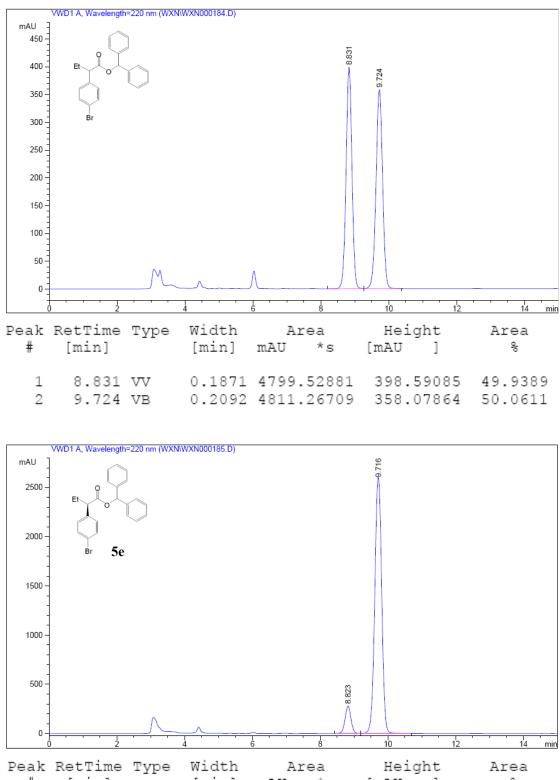




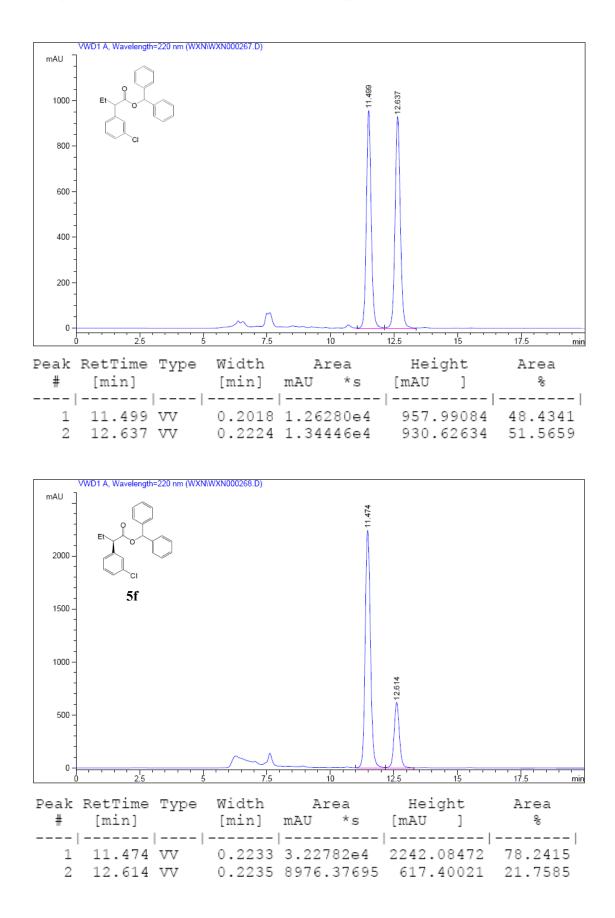
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2	55.076	VB	1.0076	6.71390e4	1034.49780	96.3732



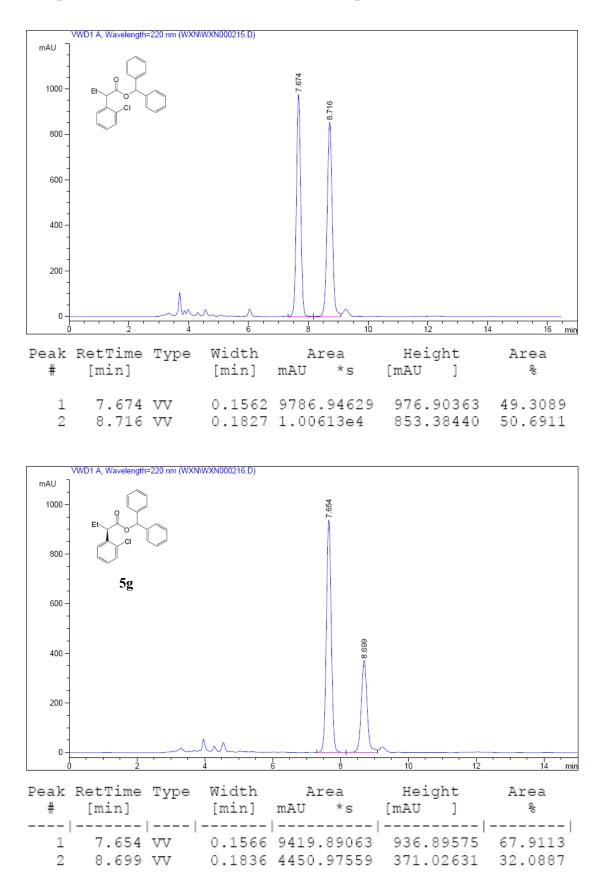




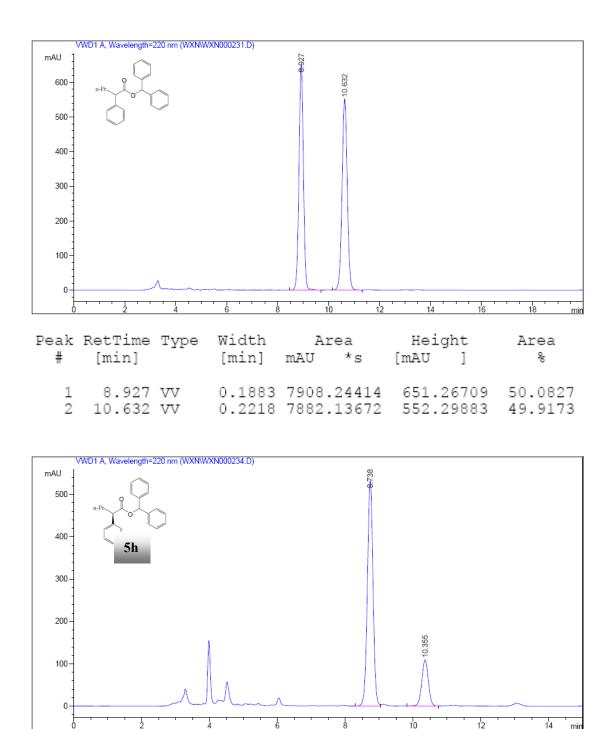
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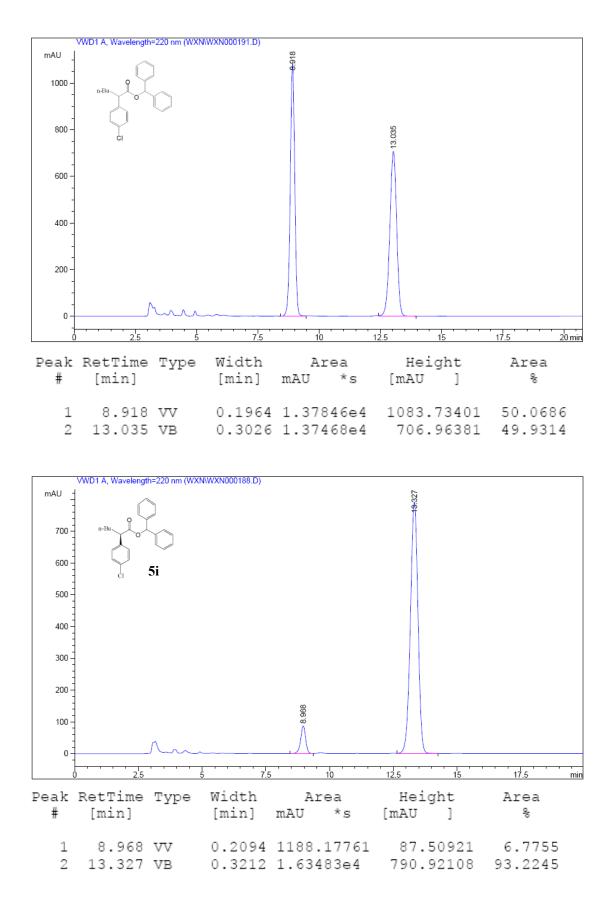
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Sample Information : AD-H Hex: Ipr=95:5 1mL/min

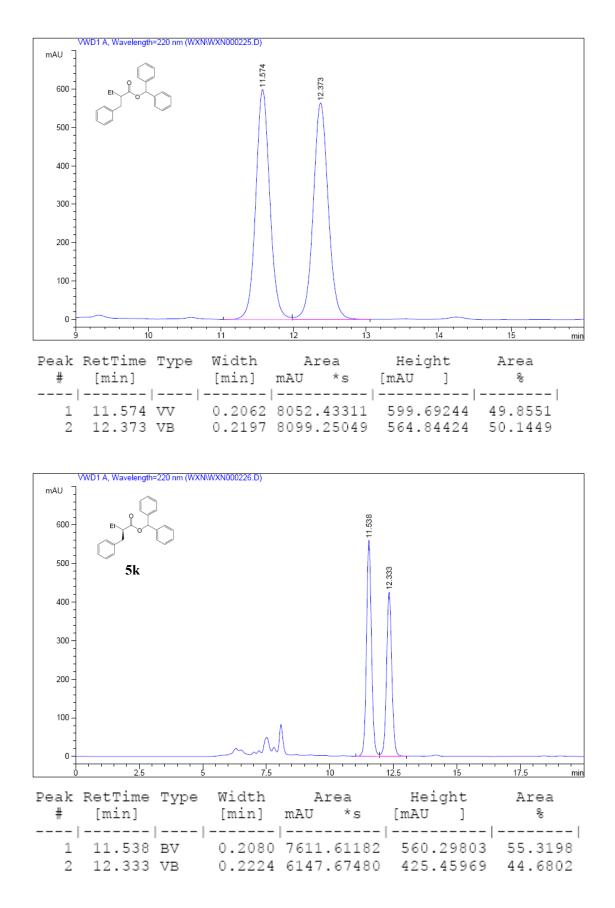


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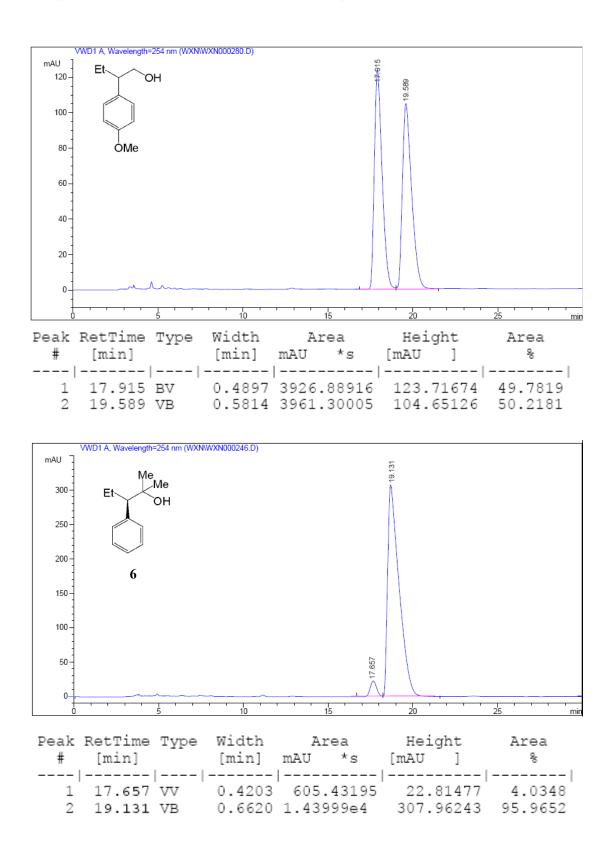


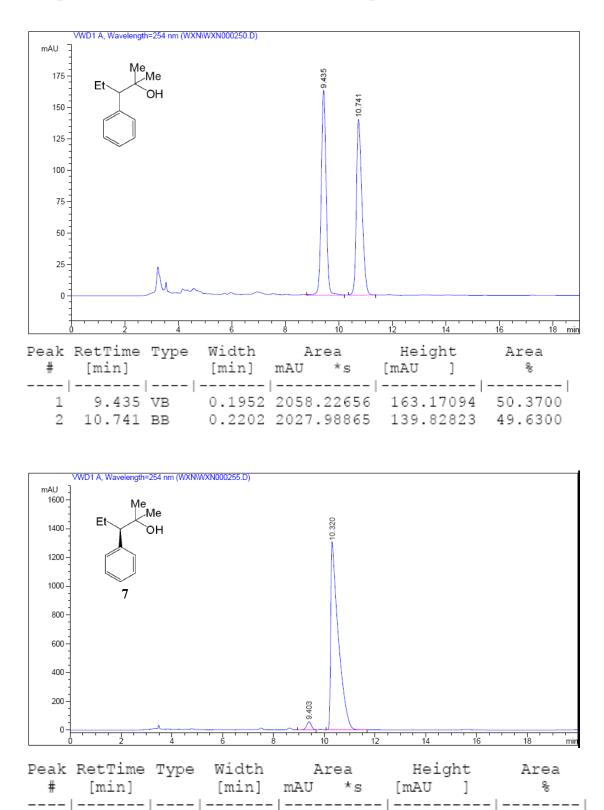
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Sample Information : AD-H Hex: Ipr=95:5 , 1ml/min



Sample Information : OD-H Hex: Ipr=99:1 1mL/min





ъ	3	5

9.403 VV

10.320 VV

1

2

0.2097 776.27460 57.57655

0.2805 2.71298e4 1304.20923 97.2183

2.7817