Supplementary information

Title: **Effective Construction of Quaternary Stereocenters by Highly Enanitioselective α-Amination of Branched Aldehydes**

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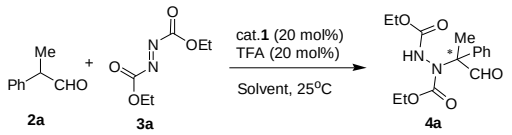
1.0. General information

All reagents were obtained from commercial supplier without further purification. Commercial grade solvent was dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997). NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 300 MHz, and ^{13}C NMR spectra were recorded at 75 MHz (Bruker Avance). Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) for ^{13}C NMR spectroscopy. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. Reactions were monitored by TLC and visualized with ultraviolet light. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. The enantiomeric excess (ee) of the products were determined by HPLC using Daicel Chiralpak AD or AS columns with *i*-PrOH/ hexane as eluent.

2.0 Screening reaction conditions

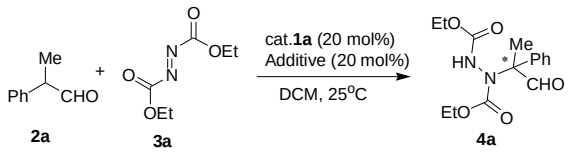
Table 1. Screening solvents [a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]	ee (%)[c]
1	**1a**	*o*-Xylene	11	91	77
2	**1a**	$CHCl_2CH_3$	21.5	76	84
3	**1a**	CCl_4	21.5	67	70
4	**1a**	$CHCl_2CH_2Cl$	26	58	83
5	**1a**	CCl_3CH_3	26	74	78
6	**1a**	DCM	8.5	96	87
7	**1a**	MTBE	6.5	86	77
8	**1a**	$CH_3OCH_2CH_2OCH_3$	6.5	90	80
9	**1a**	EtOAc	49	78	79

[a] Unless otherwise specified, all reactions were carried out with **2a** (0.30 mmol), **3a** (0.20 mmol), the catalyst (0.04 mmol) in the specified solvent (1.0 mL) at 25 °C. [b] Isolated yield . [c] Determined by HPLC with a Chiralpak-AS column

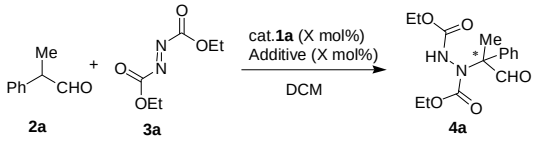
Table 2. The effect of additives.[a]



Entry	Additive	Time	Yield (%)[b]	Ee (%)[c]
1	---	4d	38	64
2	HCOOH	4 h	78	89
3	AcOH	50 h	39	90
4	PhCOOH	26 h	79	89
5	2-OHPhCOOH	1 h	99	90
6	4-ClPhCOOH	4 h	78	90
7	4-OHPhCOOH	20.5 h	67	91
8	4-COOHPhCOOH	26 h	48	63
9	4-NO_2PhCOOH	4 h	86	88
10	2,6-diFPhCOOH	3.5 h	56	83
11	3-OHPhCOOH	3.5 h	67	87
12	4-NO_2PhOH	51.5 h	61	94
13	2,4-diNO_2PhOH	6.5 h	71	90
14	3-OHPhOH	6.5 h	53	79
15	H_2O	4 d	29	47
16	DMAP	3.5 h	71	3
17	DIPEA	9 h	11	10

[a] Unless otherwise specified, all reactions were carried out with **2a**(0.30) mmol), **3a** (0.20 mmol), the catalyst **1a** (0.04 mmol) and additive (0.04 mmol) in DCM (1.0 mL) at 25 ºC. [b] Isolated yield. [c] Determined by HPLC with a Chiralpak-AS column.

Table 3. The effect of catalyst loading, amount of **2a** and temperture.[a]

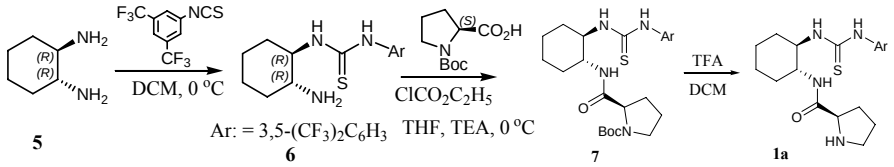


2a **3a** **4a**

Entry	Cat. Loading (X mol%)	**2a** (equiv)	Temp. (^oC)	Time (h)	Yield (%)[b]	Ee (%)[c]
1	20	1.5	25	1	99	90
2	20	1.5	0	6	91	93
3	20	1.5	-10	26	81	92
4	20	1.5	-40	98	77	94
5	15	1.5	0	6.5	78	93
6	10	1.5	0	21.5	88	95
7	5	1.5	0	47.5	77	96
8	10	2.0	0	29.5	57	96
9	10	3.0	0	14.5	75	92
10	10	4.0	0	14.5	75	93
11[d]	10	1.5	0	23	96	96
12[e]	10	1.5	0	37.5	92	94

[a] Unless otherwise specified, all reactions were carried out with **2a**, **3a** (0.20 mmol), the catalyst **1a** and additive in DCM (1.0 mL). [b] Isolated yield. [c] Determined by HPLC with a Chiralpak-AS column.. [d] additive (0.02 mmol). [e] additive (0.04 mmol)

3.0 The organocatalysts 1a-1d were synthesized as reported procedures.



N-((1R,2R)-2-aminocyclohexyl)-N'-(3,5-bis(trifluoromethyl)phenyl)thiourea (6).[1]

To a solution of compound **5** (1.23 g, 10.7 mmol, 1.0 eq) in CH_2Cl_2 (30 mL) was added isothiocyanate (2.33 g, 8.6 mmol, 0.8 eq). The reaction mixture was stirred at 0 °C for 20 hours. After the reaction was completed (monitored by TLC), the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (eluent PE:EtOAc = 8:1 to EtOAc) to afford pure products **6** (3.5 g) as a light yellow solid in 85.7% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.02 (s, 1H), 7.57 (s, 1H), 6.50 (s, 1H), 3.49 (s, 1H), 2.73-2.66 (m, 1H), 2.08-1.26 (m, 4H), 1.28-1.26 (m, 4H).

(S)-N-Boc-((1R,2R)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido) cyclohexyl-pyrrolidine-2-carboxamide (7).[1] The a solution of (S) Boc-proline (3.00 g, 14.1 mmol, 1.1 eq), TEA (1.41 mg, 14.3 mmol, 1.1 eq) in THF (40 mL) was stirred for 1 h at 0 °C, and ethyl chlorocarbonate (1.25 mL, 14.3 mmol, 1.1 eq) was added and stirred at 0 °C for 30 min. Then compound **6** (5.00 g, 13.0 mmol, 1.0 eq) was added, and the solution was stirred for 12 h at 0 °C. After the reaction was completed (monitored by TLC), the mixture was filtered, and the organic layer was removed under reduced pressure and the residue was purified by column chromatography on silica gel (eluent PE:EtOAc = 8:1 to EtOAc) to afford pure products **7** (6.06 g) as a white solid in 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 9.63 (s, 1H), 8.07 (s, 2H), 7.60-7.56 (m, 1H), 6.93-6.90 (m, 1H), 4.60 (m, 1H), 2.01-1.07 (m, 7H), 1.43-1.26 (m, 13H).

(S)-N((1R,2R)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)pyrrolidine-2-carb oxamide (1a).[1]

Trifluoroacetic acid (9.0 mL) was added dropwise to a solution of 7 (6.06 g, 10.4 mmol) in CH_2Cl_2 (20 mL) at ambient temperature, stirred for 2 hours (monitored by TLC), then adjust the pH value to 8.0 by aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 (30 mLx3), and the organic layer was combined and dried over anhydrous MgSO4, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent PE:tOAc = 10:1 to EtOAc) to afford 1a (4.11 g) as a white solid in 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.89 (s, 1H), 8.21 (d, J = 9.57 Hz, 1H), 8.12 (s, 2H), 7.80 (s, 1H), 7.55 (s, 1H), 4.63-4.60 (m, 1H), 3.74-3.67 (m, 2H), 3.01-2.96 (m, 2H), 1.99-1.94 (m,1H), 1.63-1.70 (m, 6H), 1.47-1.55 (m, 4H), 1.30-1.35 (m, 2H) ppm.

(S)-N((1S,2S)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido)cyclohexyl)pyrrolidine-2-carb oxamide (1b).[1]

white solid, 64% overall yield. ^{1}H NMR (300 MHz, $CDCl_3$): 9.90 (br, s, 1H), 8.21 (d, J = 9.84 Hz, 1H), 8.13 (s, 2H), 7.79 (d, J = 8.98 Hz, 1H), 7.55 (s, 1H), 4.59-4.62 (m, 1H), 3.69-3.73 (m, 2H),

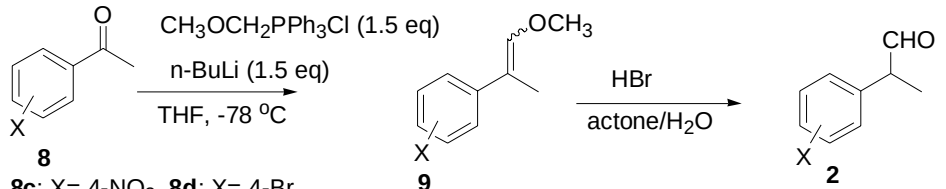
2.97-3.03 (m, 2H), 2.10-2.40 (m, 1H), 1.89-2.01 (m, 6H), 1.30-1.70 (m, 6H).

(S)-N-((1R,2R)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)-1,2-diphenylethl)pyrrolidine -2-carboxamide (1c). [1] ^{1}H NMR (300 MHz $CDCl_3$) δ (ppm): 10.11 (m, 1H), 8.97 (d, *J* = 9.96 Hz, 1H), 8.53 (d, *J* = 8.94 Hz,1H), 8.09 (s, 2H), 7.59 (s, 1H), 7.11-7.33 (m, 10 H), 6.44-6.47 (m, 1H), 5.41-5.48 (m, 1H), 3.67-3.71 (m, 1H), 3.12-3.15 (m, 1H), 2.98-3.03 (m, 1H), 1.60-1.96 (m, 4H), 1.60-1.63(m,1H).

(S)-N-((1S2S)-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)-1,2-diphenylethl)pyrrolidine-2-carboxamide (1d). [1]

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 1.25-1.63 (m, 2H), 1.83-1.85 (m, 1H), 2.09-2.13 (m, 2H), 2.74-2.78 (m, 1H), 2.98-3.02 (m, 1H), 3.83-3.88 (m, 1H), 5.23-5.29(m, 1H),5.35-5.37(m, 1H), 6.53-6.55 (d, *J* = 6 Hz, 1H), 7.08-7.19 (m, 13H), 7.43 (s, 1H), 8.65-8.68 (d, *J* = 9 Hz, 1H).

4.0 General procedure for branched aldehydes [2]



8c: X= 4-NO_2, **8d**: X= 4-Br
8e: X= 4-F, **8f**: X= 3-Cl
8g: X= 2-Cl, **8h**: X= 4-CH_3O
8i: X= 4-CH_3, **8j**: X= 2-CH_3
8k: X= 2-naph

9c: X= 4-NO_2, **9d**: X= 4-Br
9e: X= 4-F, **9f**: X= 3-Cl
9g: X= 2-Cl, **9h**: X= 4-CH_3O
9i: X= 4-CH_3, **9j**: X= 2-CH_3
9k: X= 2-naph

2c: X= 4-NO_2, **2d**: X= 4-Br
2e: X= 4-F, **2f**: X= 3-Cl
2g: X= 2-Cl, **2h**: X= 4-CH_3O
2i: X= 4-CH_3, **2j**: X= 2-CH_3
2k: X= 2-naph

General Procedure 1 for the Synthesis of 1-Methoxy-2-(3- Nitrophenyl) propene (9c):
A suspension of 1.5 equiv. of methoxymethyl(triphenyl)phosphonium chloride in abs. THF (12 mL/mmol acetophenone) is carefully treated under argon with 1.5 equiv. of a 2.5 M solution of *n*-butyllithium in hexane at –78 °C. The resulting orange to red suspension is stirred for 30 min at –78 °C, the cooling bath removed and the mixture stirred for another 30 min at room temperature. After cooling to –78 °C again 1 equiv. of the acetophenone is added as a solution in abs. THF. The reaction mixture is left stirring in the cooling bath to warm to room temperature (typically within 18 h) (monitored by TLC). The reaction is then quenched with water (5 mL/mmol acetophenone), the organic phase separated and the aqueous phase extracted twice with diethyl ether (3 mL/mmol acetophenone). The combined organic phases are washed with brine and dried with magnesium sulfate. The orgnic phases was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: PE) to afford pure products **9**. The known products were identified by spectroscopic data (MS, ^{1}H and ^{13}C NMR) which are in good agreement with those reported.[2]

General Procedure 2 for the Synthesis of 2-(4'-Nitrophenyl)propionaldehyde (2c)[2]:
A solution of the 2-aryl-1-nitrophenyl propene (**9c**) obtained by general procedure **1** in acetone/water, 4:1 is treated at 0°C with 10 mL of 48% aqueous hydrobromic acid and stirred for 1 d. The addition of hydrobromic acid and stirring at room temperature is repeated until the TLC indicates complete consumption of the enol ether. Most of the acetone was removed by

evaporation. The residue is then neutralized by addition of saturated aqueous sodium carbonate solution, and the aqueous phase extracted three times with diethyl ether. The combined organic phases are washed with brine, dried with magnesium sulfate, and the solvent is removed by evaporation. The residue is purified by flash chromatography on silica (eluent: PE).

2-(4'-Nitrophenyl)propionaldehyde (2c) [2]**:**

The product was synthesized according to GP 2, employing **9c** (2.70g, 13.97mmol). Flash chromatography on silica delivered 1.11g (Yield: 44%) of a yellow oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.49 (d, *J* = 7.2 Hz, 3H), 3.79 (q, *J* = 7.1 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 2H), 8.19 (d, *J* = 8.7 Hz, 2H), 9.69 (d, *J* = 1.1 Hz, 1H) ppm.

2-(4'-Bromophenyl)propionaldehyde (2d) [2]**:**

The product was synthesized according to GP 2, employing **9d** (2.50 g, 11.00 mmol). Flash chromatography on silica delivered 1.26 g (Yield: 55%) of a yellow oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.40 (d, *J* = 7.1 Hz, 3H), 3.58 (q, *J* = 7.0 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 9.62 (s, 1H) ppm..

2-(4'-Fluorophenyl)propionaldehyde (2e) [2]**:**

The product was synthesized according to GP 2, employing **9e** (2.00 g, 12.03 mmol). Flash chromatography on silica delivered 0.648 g (Yield: 35%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.42 (d, *J* = 7.1 Hz, 3H), 3.62 (q, *J* = 7.0 Hz, 1H), 7.02-7.19 (m, 4H), 9.65 (d, *J* = 1.1 Hz, 1H) ppm..

2-(3'-Chlorophenyl)propionaldehyde (2f):

The product was synthesized according to GP 2, employing **9f** (1.80 g, 9.85 mmol). Flash chromatography on silica delivered 0.875 g (Yield: 53%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.44 (d, *J* = 7.1 Hz, 3H), 3.63 (q, *J* = 7.1 Hz, 1H), 7.09-7.34 (m, 4H), 9.67 (t, *J* = 0.7 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.29, 52.33, 126.33, 127.50, 128.27, 130.11, 134.66, 139.65, 199.96 ppm. HRMS (ESI-TOF) calcd for C_9H_9OClNa ($[M+Na]^+$): 191.0240, found: 191.0240.

2-(2'-Chlorophenyl)propionaldehyde (2g)

The product was synthesized according to GP 2, employing **9g** (1.78 g, 9.74 mmol). Flash chromatography on silica delivered 0.600 g (Yield: 37%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.43 (d, *J* = 7.1 Hz, 3H), 4.13 (q, *J* = 7.0 Hz, 1H), 7.13 (dd, *J* = 2.2, 7.2 Hz, 1H), 7.23-7.28 (m, 2H), 7.43 (d, *J* = 1.1, 7.3 Hz, 1H), 9.71 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.71, 49.52, 127.37, 128.73, 129.16, 129.94, 134.30, 136.04, 200.11 ppm. HRMS (ESI-TOF) calcd for C_9H_8OCl ($[M-H]^+$): 167.0264, found: 167.0258.

2-(4'-Methoxyphenyl)propionaldehyde (2h) [2]**:**

The product was synthesized according to GP 2, employing **9h** (1.96 g, 11.00 mmol). Flash chromatography on silica delivered 0.815 g (Yield: 45%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.41 (d, *J* = 7.0 Hz, 3H), 3.79 (d, *J* = 5.4 Hz, 1H), 6.91(q, *J* = 2.1 Hz, 2H), 7.12 (q, *J* = 1.9 Hz, 2H), 9.64 (d, *J* = 1.5 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.61, 52.10, 55.24, 114.47, 129.30, 129.54, 158.99, 201.10 ppm.

2-(4'-Methylphenyl)propionaldehyde (2i):

The product was synthesized according to GP 2, employing **9i** (1.70 g, 10.47 mmol). Flash chromatography on silica delivered 1.10 g (Yield: 71%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.43 (d, *J* = 7.0 Hz, 3H), 2.34 (d, *J* = 7.6 Hz, 3H), 3.60 (m, 1H), 7.11 (d, *J* = 8.0 Hz,

2H), 7.19 (d, *J* = 7.9 Hz, 2H), 9.67 (d, *J* = 1.4 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.59, 21.00, 52.59, 128.17, 129.75, 134.64, 137.22, 201.14 ppm. HRMS (ESI-TOF) calcd for $C_{10}H_{12}ONa$ ($[M+Na]^+$): 171.0786, found: 171.0781.

2-(2'-Methylphenyl)propionaldehyde (2j):

The product was synthesized according to GP 2, employing **9j** (1.70 g, 10.47 mmol). Flash chromatography on silica delivered 0.90 g (Yield: 58%) of a colorless oil. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.65 (d, *J* = 7.0 Hz, 3H), 2.37 (s, 3H), 3.85 (q, *J* = 7.0 Hz, 1H), 7.05-7.09 (m, 1H), 7.18-7.26 (m, 3H), 9.66 (d, *J* = 1.1 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.29, 19.60, 49.27, 126.04, 127.43, 127.53, 130.91, 136.35, 136.60, 201.04 ppm. HRMS (ESI-TOF) calcd for $C_{10}H_{12}ONa$ ($[M+Na]^+$): 171.0786, found: 171.0786.

2-(2-naphthyl) propionaldehyde (2k) [2]**:**

The product was synthesized according to GP 2, employing **9k** (2.02 g, 10.18 mmol). Flash chromatography on silica delivered 1.62 g (Yield: 87%) of a white solid. ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.54 (d, *J* = 7.0 Hz, 3H), 3.81 (d, *J* = 7.0 Hz, 1H), 7.30-7.85 (m, 7H), 9.76 (d, *J* = 1.3 Hz, 1H) ppm. HRMS (ESI-TOF) calcd for $C_{13}H_{13}O$ ($[M+H]^+$): 185.0966, found: 185.0959.

5.0 General procedure for asymmetric α-Amination of branched aldehydes with azodicarboxylates.

Representative experimental procedure for the α-Amination: Typical experimental procedure for the amination of brached aldehydes with azodicarboxylates: to a stirred solution of catalyst **1a** (0.02 mmol), 2-OH-PhCOOH (0.04 mmol) and aldehydes **2** (0.3 mmol) in CH_2Cl_2 (1.0 mL) cooled to 0 °C, azodicarboxylates **3** (0.2 mmol) was added at the same temperature. The reaction mixture was stirred at 0 °C for the time indicated in Table 2. After the azodicarboxylate was consumed as indicated (monitored by TLC) (the decolorization of azodicarboxylate was also observed), the reaction solution was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent PE:EtOAc =8:1) to afford pure α-aminated products **4**. All products are known compounds and were identified by spectroscopic data (MS, ^{1}H and ^{13}C NMR) which are in good agreement with those reported.[2]

Spectroscopic data of final products 4.[2]

(-)-2-[*N*,*N*'-Bis(ethoxycarbonyl)hydrazino]-2-phenyl-propionaldehyde (4a-Et) [2]: The ee was determined by chiral HPLC analysis (AS-H, *i*-PrOH/ hexane = 20/80, t_r (major) = 15.670 min, t_r (minor) = 21.083 min). $[\alpha]_D^{20}$ = -19.3 (*c* 0.522, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.19-1.35 (m, 6H), 1.78-1.84 (m, 3 H), 4.08-4.29 (m, 4H), 6.54, 6.68 (2s, 1H), 7.23-7.42 (m, 5H), 10.09, 10.13 (2s, 1H) ppm.

(+)-2-[*N*,*N*'-Bis(isopropanoxycarbonyl)hydrazino]-2-phenyl-propionaldehyde (4a-*i*-Pr): The ee was determined by chiral HPLC analysis (AS-H, *i*-PrOH/ hexane = 10/90, t_r (major) = 17.585 min, t_r (minor) = 20.842 min). $[\alpha]_D^{20}$ = +49.0 (*c* 0.252, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21-1.31 (m, 12H), 1.71-1.81 (m, 3H), 4.93-4.97 (m, 2H), 6.49 (br, s, 1H), 7.28-7.47 (m, 5H), 9.61, 9.76 (2*s*, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.07, 21.68, 71.38, 73,00, 127.34, 128.05,128.86, 137.08, 155.63, 156.03, 192.84, 194.18 ppm. IR (Infrared film): ν = 3303, 3060, 2982, 2937, 2878, 2850, 1731, 1600, 1583, 1494, 1467, 1450, 1376, 1320, 1246, 1181, 1145, 1108, 1054, 1029, 938, 913, 873, 834, 764, 702 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{17}H_{25}N_2O_5$ ($[M+H]^+$): 337.1763, found: 337.1762.

(+)-2-[*N*,*N*'-Bis(ethoxycarbonyl)hydrazino]-2-(*n*-propyl)-propionaldehyde (4b-Et) [2]**:**

The ee could not be determined by chiral HPLC analysis or GC. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84-0.91 (m, 3H), 1.19-1.28 (m, 11H), 1.63-1.84 (m, 2H), 4.13-4.21 (m, 4H), 6.66 (br, s, 1H), 9.47, 9.50 (br, *s*, 1H) ppm.

(+)-2-[*N*,*N*'-Bis(isopropanoxycarbonyl)hydrazino]-2-(*n*-propyl)-propionaldehyde (4b-*i*-Pr): The ee could not be determined by chiral HPLC analysis or GC. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84-0.92 (m, 3H), 1.20-1.28 (m, 17H), 1.57-1.77 (m, 2H), 4.90-4.99 (m, 2H), 6.43 (br, 1H), 9.51(br, *s*, 1H) ppm.

(+)-2-[*N*,*N*'-Bis(ethoxycarbonyl)hydrazino]-2-(4'-nitrophenyl)-propionaldehyde (4c-Et) [2]**:** The ee was determined by chiral HPLC analysis (AS-H, *i*-PrOH/ hexane = 20/80, t_r (major) = 19.732 min, t_r (minor) = 26.365 min). $[\alpha]_D^{20}$ = +28.3 (*c* 0.430, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21-1.37 (m, 6H), 1.75 (s, 3H), 4.16-4.17 (m, 4H), 6.58 (s, 1H), 7.60-8.24 (m, 4H), 9.66, 9.78 (2s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.18, 14.36, 19.41, 20.48, 62.79, 63.68, 72.48, 123.76, 127.65, 147.49, 155.71, 156,72, 193.02, 194.28. ppm.

(+)-2-[*N*,*N*'-Bis(isopropanoxycarbonyl)hydrazino]-2-(4'-nitrophenyl)-propionaldehyde (4c-*i*-Pr): The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 10/90, t_r (major) = 16.567 min, t_r (minor) = 15.128 min). $[\alpha]_D^{20}$ = +29.0 (*c* 0.566, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25-1.27 (m, 12H), 2.51 (s, 3H), 4.89-5.03 (m, 2H), 5.41, 6.43 (2s, 1H), 7.56-7.62 (m, 2H), 8.18-8.24 (m, 2H). 9.66, 9.77 (2s, 1H) ppm. IR (Infrared film): ν = 3310, 3081, 2983, 2935, 2852, 2715, 1734, 1606, 1522, 1494, 1467, 1456, 1376, 1349, 1247, 1181, 1145, 1106, 1059, 1015, 931, 907, 857, 767 cm^{-1}. $C_{17}H_{24}N_3O_7$ ($[M+H]^+$): 382.1614, found: 382.1616.

(+)-2-[N,N-Bis(ethoxycarbonyl)hydrazino]-2-(4-bromophenyl)-propionaldehyde (4d-Et)[2]: The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 5/95, t_r (major) = 27.393 min, t_r (minor) = 25.737 min). $[\alpha]_D^{20}$ = +46.5 (*c* 0.550, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34-0.905 (m, 6H), 1.67-1.73 (m, 3H), 4.23-4.13 (m, 4H), 6.38, 6.52 (2s, 1H), 7.25-7.29 (m, 1H), 7.37-7.52 (m, 3H), 10.71, 10.75 (2s, 1H) ppm. HRMS (ESI-TOF) calcd for $C_{15}H_{20}N_2O_5Br$ ($[M+H]^+$): 387.0556, found: 387.0545 .

(+)-2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(4-bromophenyl)-propionaldehyde (4d-*i*-Pr): The ee was determined by chiral HPLC analysis (Whelk-01, *i*-PrOH/ hexane = 3/97, t_r (major) = 29.847 min, t_r (minor) = 27.418 min). $[\alpha]_D^{20}$ = +15.0 (*c* 0.610, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34-1.19 (m, 12H), 1.73-1.33 (m, 3H), 5.02-4.90 (m, 2H), 6.34, 6.15 (2s, 1H), 7.23-7.29 (m, 2H), 7.43-7.59 (m, 2H) 9.70, 9.57 (2s, 1H) ppm. IR (Infrared smear): ν = 3303, 2982, 2936, 2877, 1715, 1588, 1488, 1455, 1375, 1320, 1244, 1181, 1107, 1033, 1009, 913, 824, 766 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{17}H_{24}N_2O_5Br$ ($[M+H]^+$): 415.0869, found: 415.0880.

(+)-2-[N,N-Bis(ethoxycarbonyl)hydrazino]-2-(4-fluorophenyl)-propionaldehyde (4e-Et) [2]: The ee was determined by chiral HPLC analysis (AS-H, *i*-PrOH/ hexane = 20/80, t_r (major) = 12.798 min, t_r (minor) =15.532 min). $[\alpha]_D^{20}$ = +47.4 (*c* 0.540, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29-1.20 (m, 6H), 1.76-1.69 (m, 3H), 4.25-4.13 (m, 4H), 6.45 (br, s, 1H), 7.04-7.16 (m, 2H), 7.34-7.54 (m, 2H), 9.72, 966 (2s, 1H) ppm.

(+)-2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(4-fluorophenyl)-propionaldehyde (4e-*i*-Pr): The ee was determined by chiral HPLC analysis (Whelk-01, *i*-PrOH/ hexane = 3/97, t_r (major) = 25.988 min, t_r (minor) =24.338 min. $[\alpha]_D^{20}$ = +35.7 (*c* 0.400, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24-1.18 (m, 12H), 1.75-1.63 (m, 3H), 4.94-4.90 (m, 2H), 6.33 (br, s, 1H), 7.04-7.09 (m, 2H), 7.37-7.55 (m, 2H), 9.71, 9.58 (2s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

18.11, 18.55, 21.80, 21.92, 70.38, 71.59, 72.39, 115.46, 128.67, 133.21, 155.51, 156.12, 160.81, 164.10, 192.84, 193.74. IR (Infrared smear): ν = 3308, 3072, 2983, 2938, 2880, 1727, 1599, 1509, 1467, 1456, 1376, 1321, 1265, 1236, 1181, 1056, 931, 912, 839, 766 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{17}H_{24}FN_2O_5$ ($[M+H]^+$): 355.1669, found: 355.1677.

(+)-2-[N,N-Bis(enthoxycarbonyl)hydrazino]-2-(3-chlorophenyl)-propionaldehyde (4f-Et): The ee was determined by chiral HPLC analysis (AS, *i*-PrOH/ hexane = 20/80, t_r (major) = 12.898 min, t_r (minor) = 19.432 min). $[\alpha]_D^{20}$ = +34.0 (*c* 0.270, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35-1.20 (m, 6H), 1.74-1.69 (m, 3H), 4.25-4.17 (m, 4H), 6.53 (br, 1H), 7.39-7.22 (m, 4H), 9.72, 9.66 (br, 2s, 1H) ppm. IR (Infrared smear): ν = 3245, 3040, 2989, 2917, 2852, 2768, 1751, 1697, 1532, 1481, 1448, 1367, 1248, 1112, 1068, 1020 (w), 900, 795, 783, 760 cm.$^{-1}$. HRMS (ESI-TOF) calcd for $C_{15}H_{20}N_2O_5Cl$ ($[M+H]^+$): 343.1061, found: 343.1067.

(+)-2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(3-chlorophenyl)-propionaldehyde (4f-*i*-Pr): The ee was determined by chiral HPLC analysis (Whelk-01, *i*-PrOH/ hexane = 3/97, t_r (major) = 25.855 min, t_r (minor) = 23.823 min). $[\alpha]_D^{20}$ = +40.8 (*c* 0.660, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24-1.90 (m, 12H), 1.73-1.61 (m, 3H), 4.95-4.93 (m, 2H), 6.37 (br, s, 1H), 7.35-7.30 (m, 4H), 9.72, 9.55 (2s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.42, 21.07, 21.71, 21.80, 21.92, 70.89, 71.70, 72.51, 125.03, 126.96, 128.24, 129.30, 134.85, 139.70, 155.47, 156.31, 192.76, 193,89. IR (Infrared smear): ν = 3307, 3068, 2983, 2937, 2879, 1732, 1595, 1572, 1498, 1468, 1376, 1321, 1250, 1181, 1145, 1056, 999, 932, 834, 788 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{17}H_{24}N_2O_5Cl$ ($[M+H]^+$): 371.1374, found: 371.1369.

(-)-2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(2-chlorophenyl)-propionaldehyde (4g-*i*-Pr): The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 5/95, t_r (major) = 16.989 min, t_r (minor) = 15.482 min). $[\alpha]_D^{20}$ = -13.0 (*c* 0.306, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17-1.35 (m, 12H), 1.77-1.83 (m, 3H), 4.88-4.97 (m, 2H), 6.57, 6.40 (2s, 1H), 7.22-7.43 (m, 4H), 10.12, 10.08 (2s, 1H) ppm. HRMS (ESI-TOF) calcd for $C_{17}H_{24}N_2O_5Cl$ ($[M+H]^+$): 371.1374, found: 371.1379.

(+)-2-[N,N-Bis(enthoxycarbonyl)hydrazino]-2-(4-methoxyphenyl)-propionaldehyde (4h-Et) [2]:

The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 5/95, t_r (major) = 16.898 min, t_r (minor) = 15.482 min). $[\alpha]_D^{20}$ = +61.8 (*c* 0.390, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28-1.21 (m, 6H), 1.77-1.71 (m, 3H), 3.79 (s, 3H), 4.20-4.12 (m, 4H), 6.45 (br, s, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 7.28-7.46 (m, 2H), 9.69, 9.54 (2s, 1H).

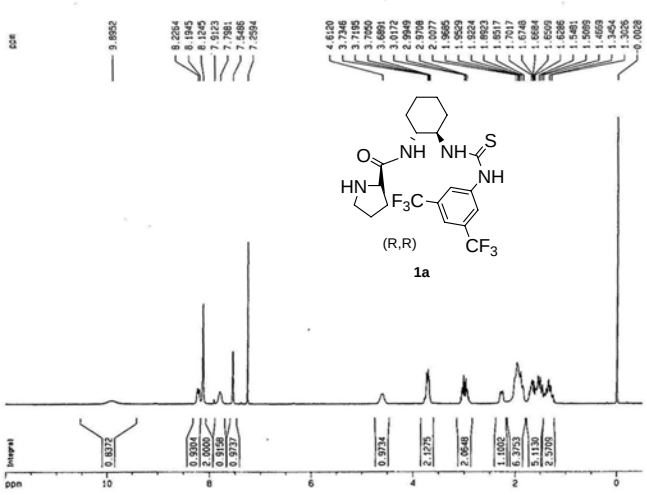
2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(4-methylphenyl)-propionaldehyde (4i-*i*-pr): The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 5/95, t_r (major) = 19.565 min, t_r (minor) = 21.498 min). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23-1.19 (m, 12H), 1.76-1.66 (m, 3H), 2.32 (s, 3H), 4.95-4.91 (m, 2H), 6.41 (br, 1H), 7.40-7.18 (m, 4H), 9.69, 9.55 (2s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.92, 21.53, 21.70, 21.77, 21.86, 70.07, 70.69, 70.55, 72.91, 127.36, 128.86, 133.89, 137.92, 155.67, 156.02, 192.71, 193.86 ppm. HRMS (ESI-TOF) calcd for $C_{18}H_{27}N_2O_6$ ($[M+H]^+$): 367.1869, found: 367.1877.

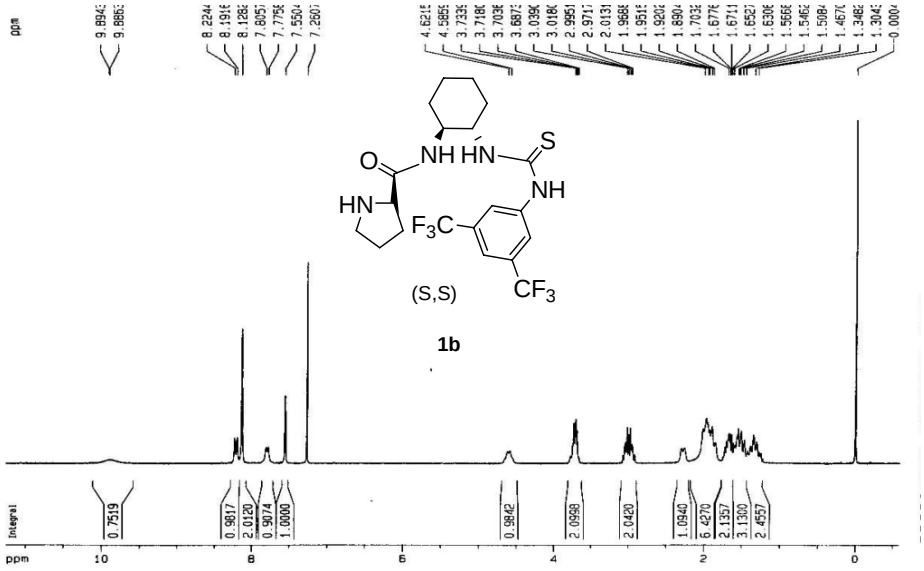
(+)-2-[N,N-Bis(enthoxycarbonyl)hydrazino]-2-(2-naphthyl)-propionaldehyde (4k-Et)[2]: The ee was determined by chiral HPLC analysis (OD-H, *i*-PrOH/ hexane = 10/90, t_r (major) = 11.440 min, t_r (minor) = 14.332 min). $[\alpha]_D^{20}$ = +28.9 (*c* 0.470, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39-1.21 (m, 6H), 1.92-1.85 (m, 3H), 4.20-4.13 (m, 4H), 6.51 (br, s, 1H), 7.50-7.44

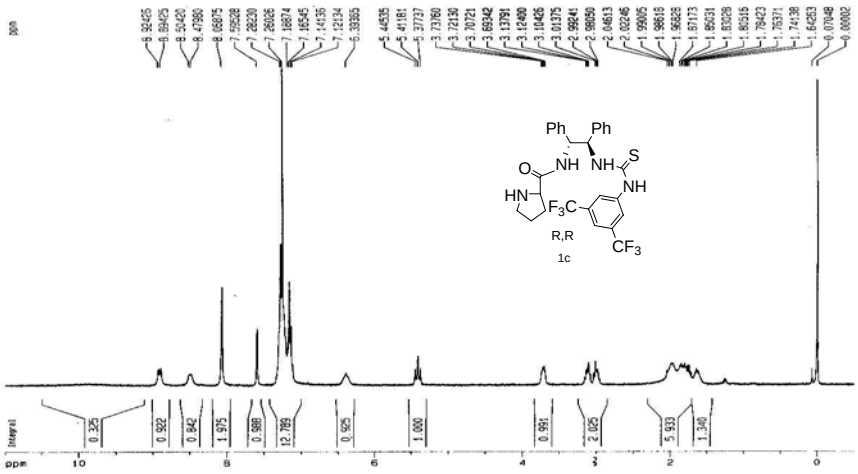
(m, 3H), 7.95-7.82(m, 4H), 9.87, 9.70 (2s, 1H) ppm. IR (Infrared smear): ν = 3300, 3057, 2983, 2933, 2852, 2768, 1731, 1627, 1598, 1508, 1444, 1377, 1240, 1130, 1064, 1017, 925, 861, 821, 751. HRMS (ESI-TOF) calcd for $C_{19}H_{23}N_2O_5$ ($[M+H]^+$): 359.1607, found: 369.1599.

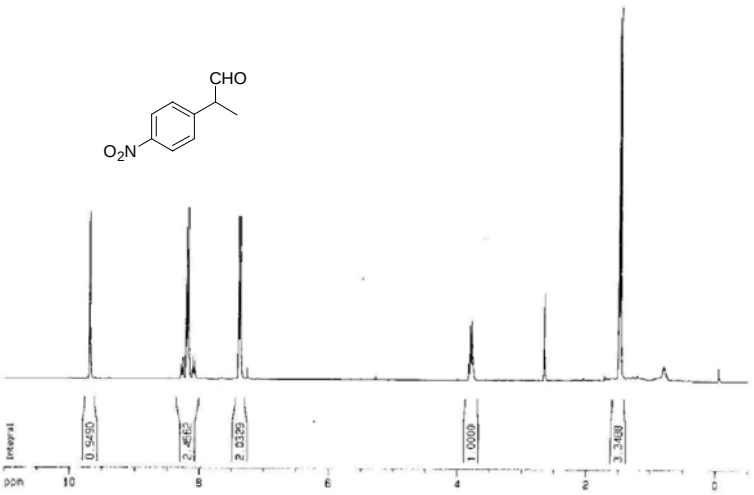
(+)-2-[N,N-Bis(isopropanoxycarbonyl)hydrazino]-2-(2-naphthyl)-propionaldehyde (4k-*i*-pr): The ee was determined by chiral HPLC analysis (AD-H, *i*-PrOH/ hexane = 10/90, t_r (major) = 12.782 min, t_r (minor) = 16.782 min). $[\alpha]_D^{20}$ = +38.0 (*c* 0.24, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40-1.25 (m, 12H), 2.23 (s, 3H), 4.97-4.93 (m, 2H), 6.27 (br, s, 1H), 7.55-7.50 (m, 3H), 7.98-7.82(m, 4H), 9.86, 9.70 (2s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.63, 21.74, 21.92, 47.15, 70.25, 71.56, 73.27, 124.33, 126.30, 126.49, 126.64, 127.52, 128.24, 128.71, 132.80, 133.30, 155.47, 156.31, 192.73. IR (Infrared smear): ν = 3303, 3057, 2982, 2934, 2875, 2853, 1731, 1628, 1600, 1506, 1467, 1375, 1320, 1243, 1181, 1145, 1106, 1078, 1030, 940, 911, 819, 750 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{21}H_{27}N_2O_5$ ($[M+H]^+$): 387.1920, found: 387.1923.

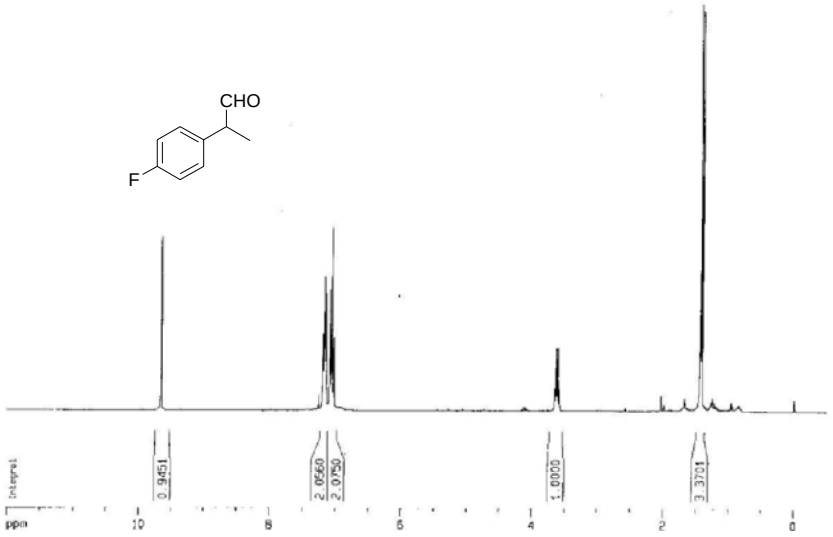
6.0 Selected ^{1}H NMR and ^{13}C NMR of the the catalysts and amination adducts

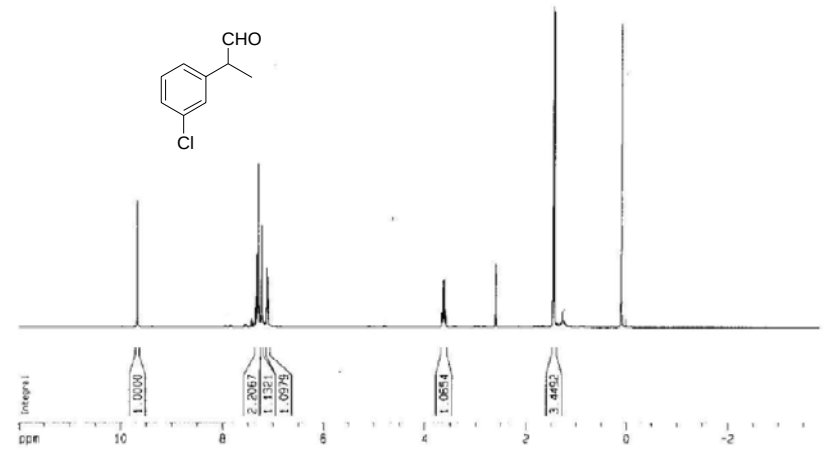


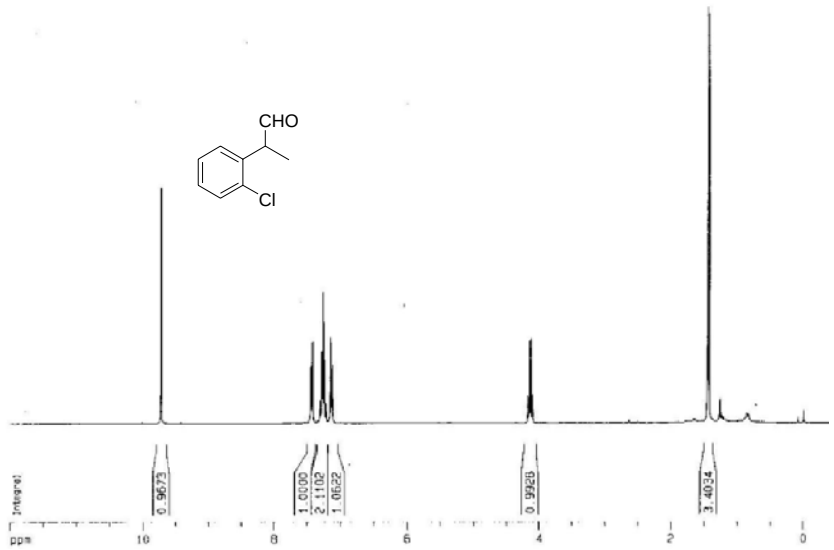


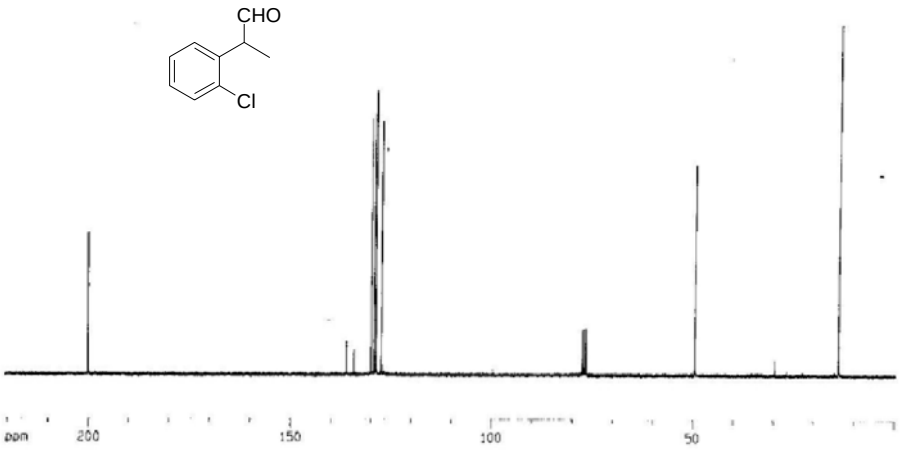


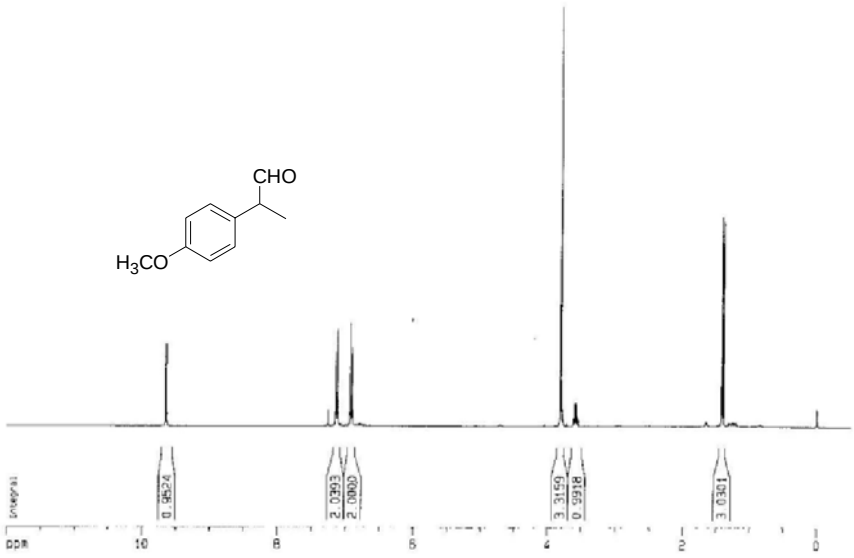


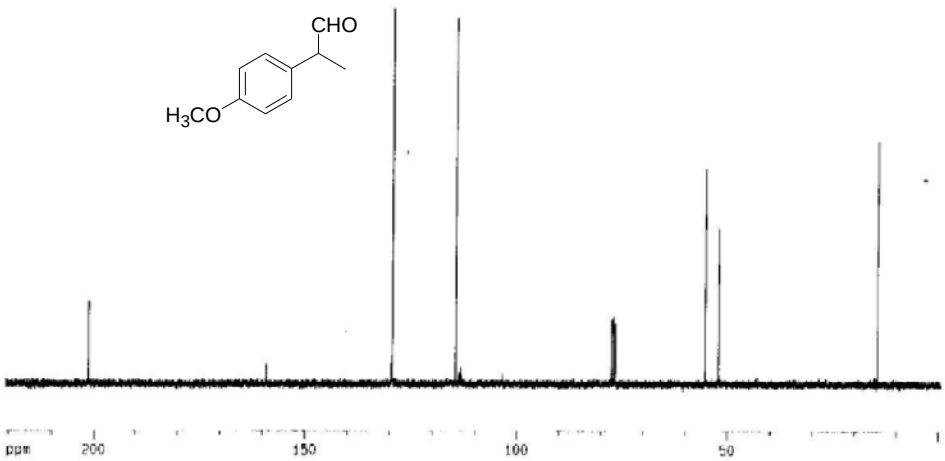


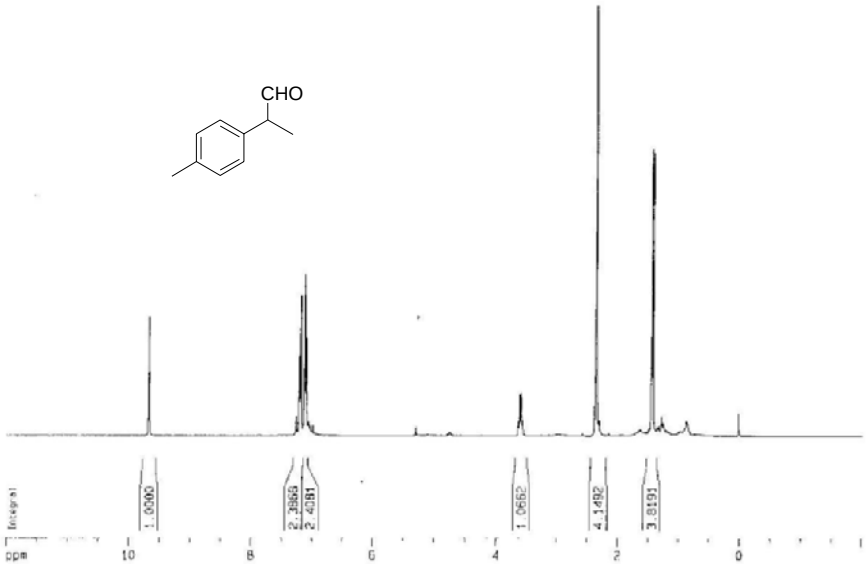


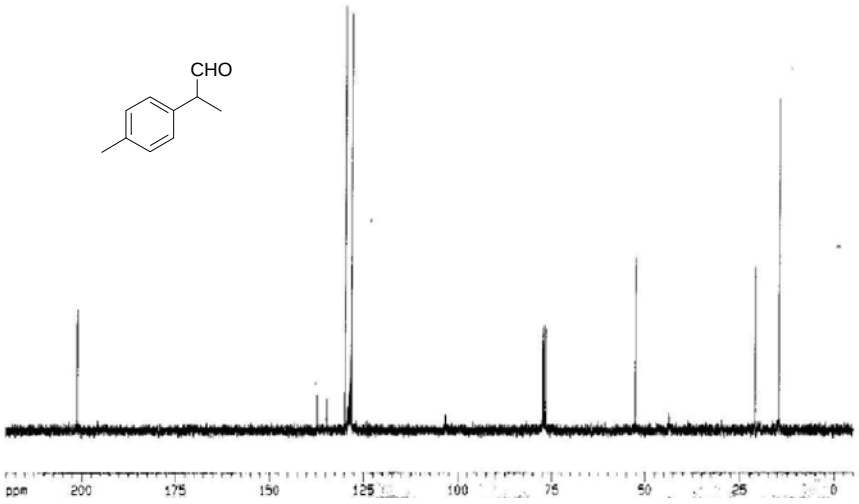


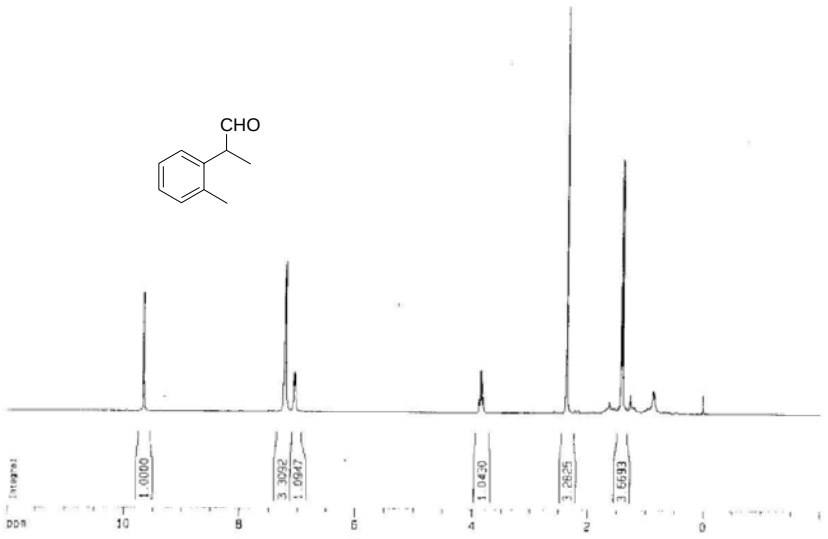


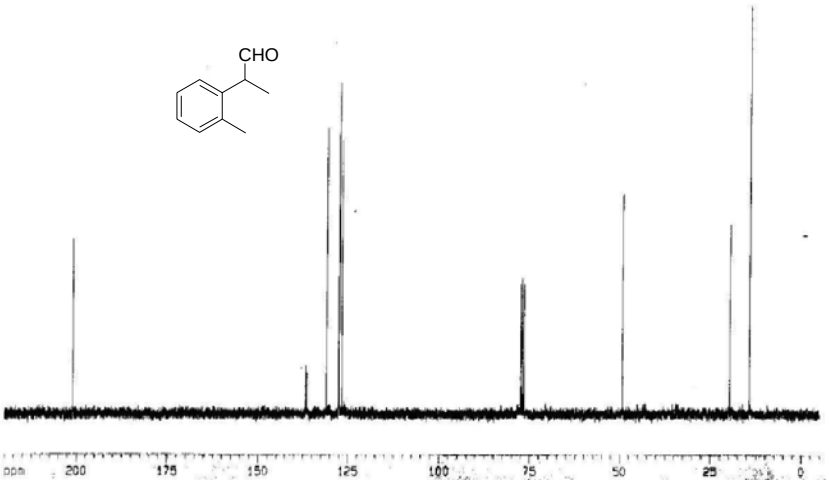


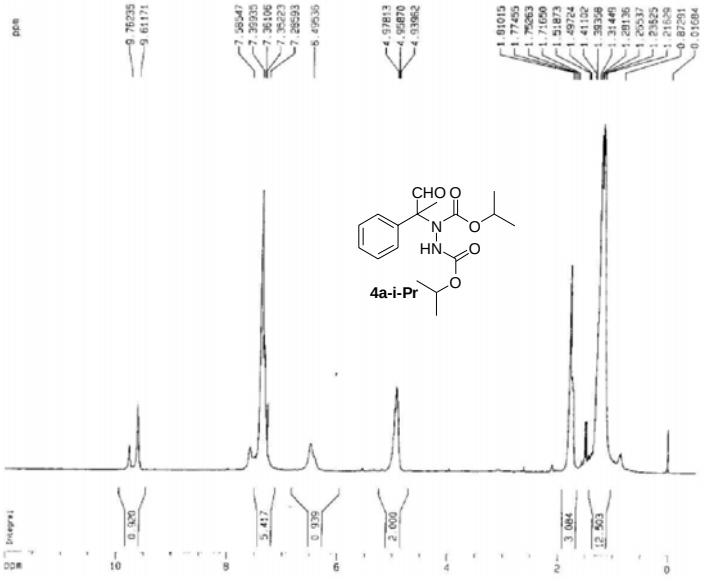


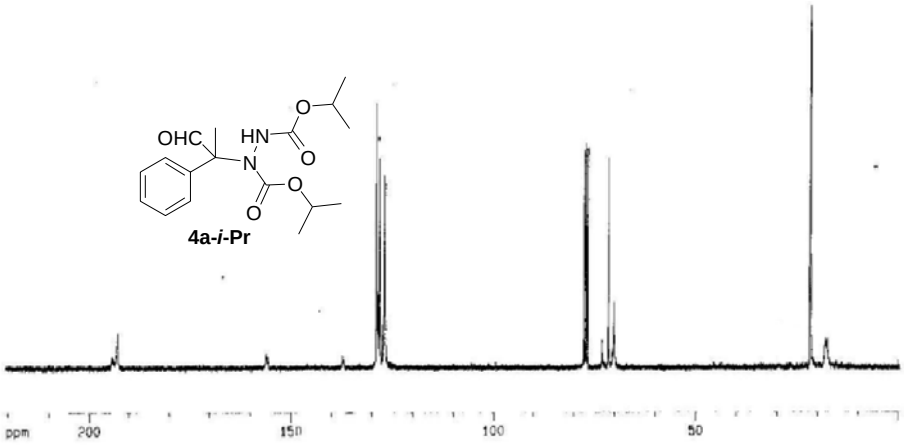


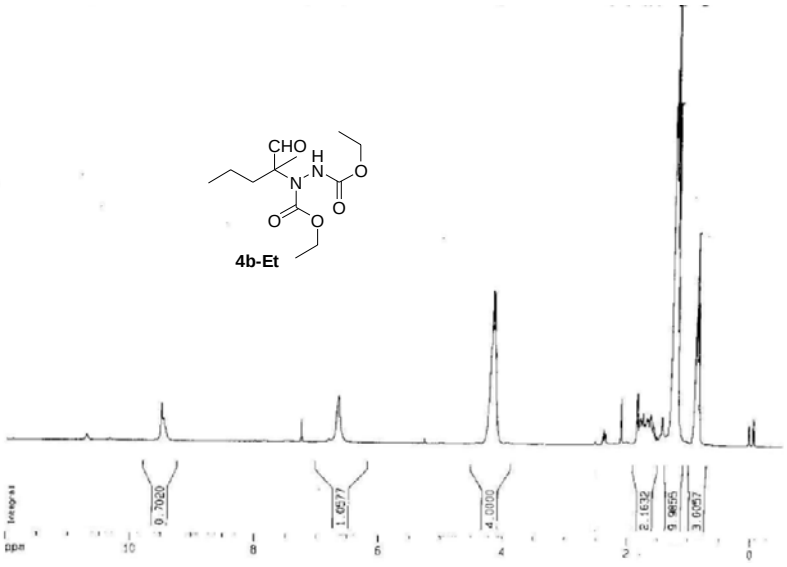


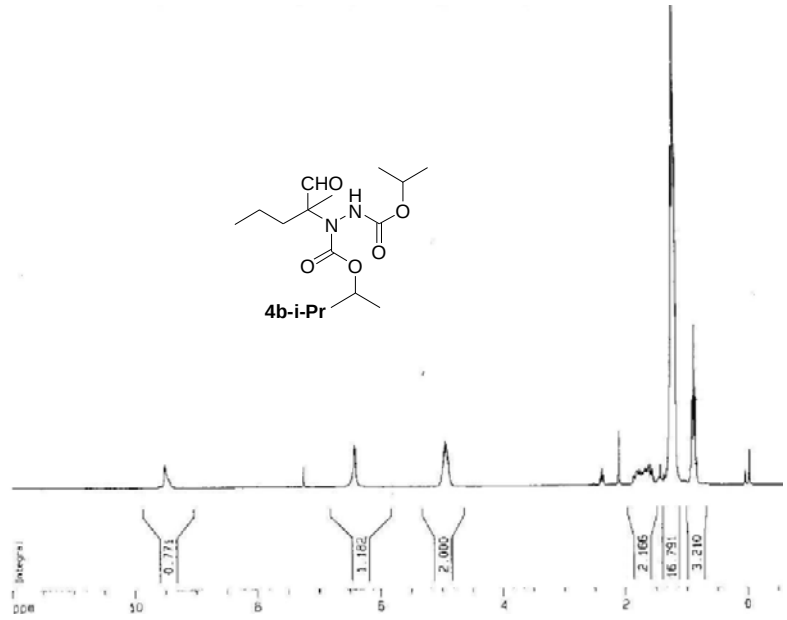


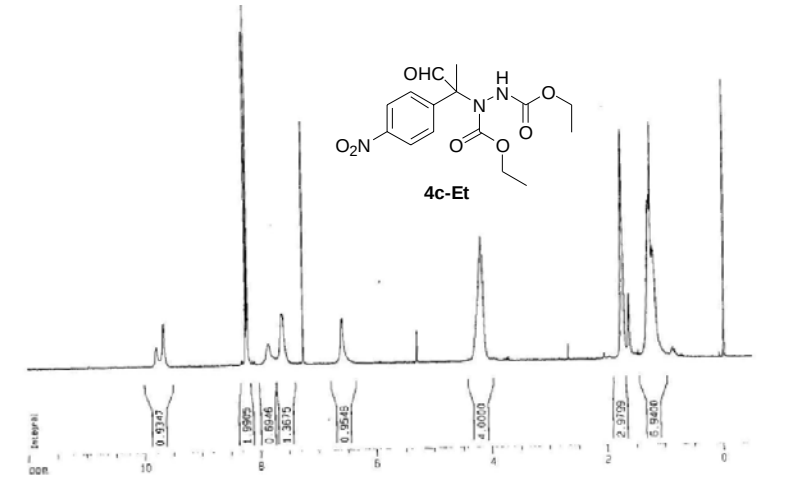


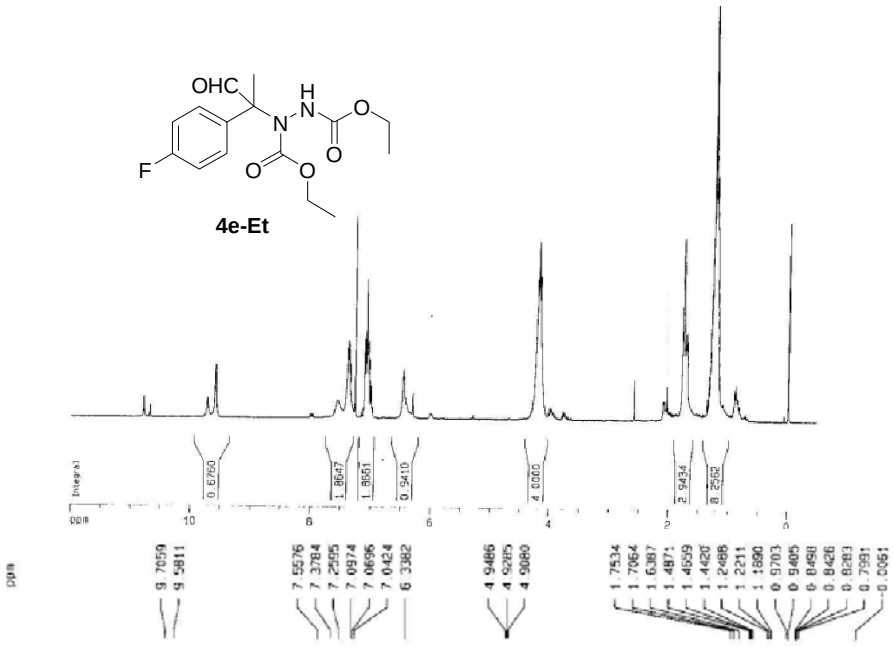




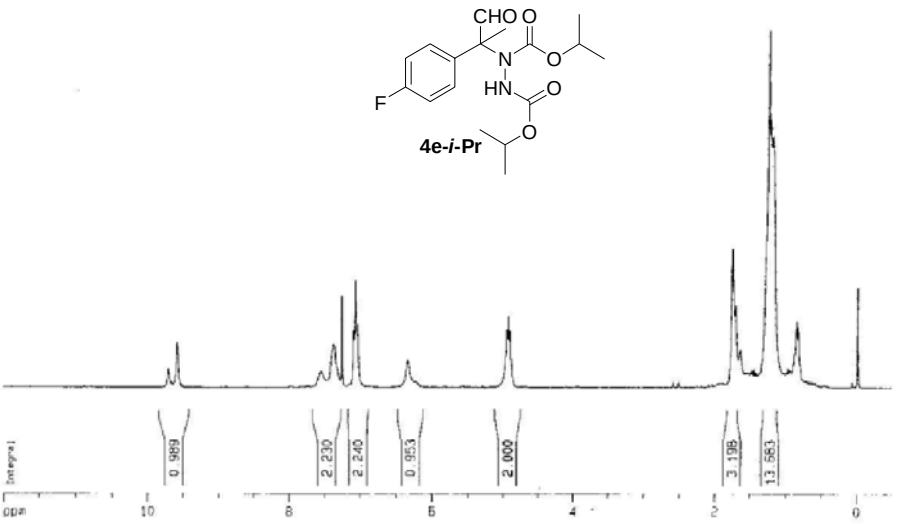




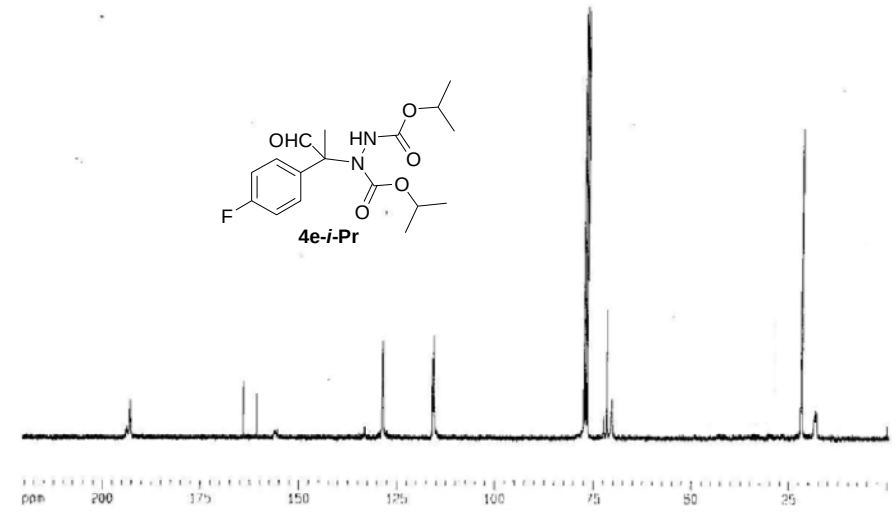




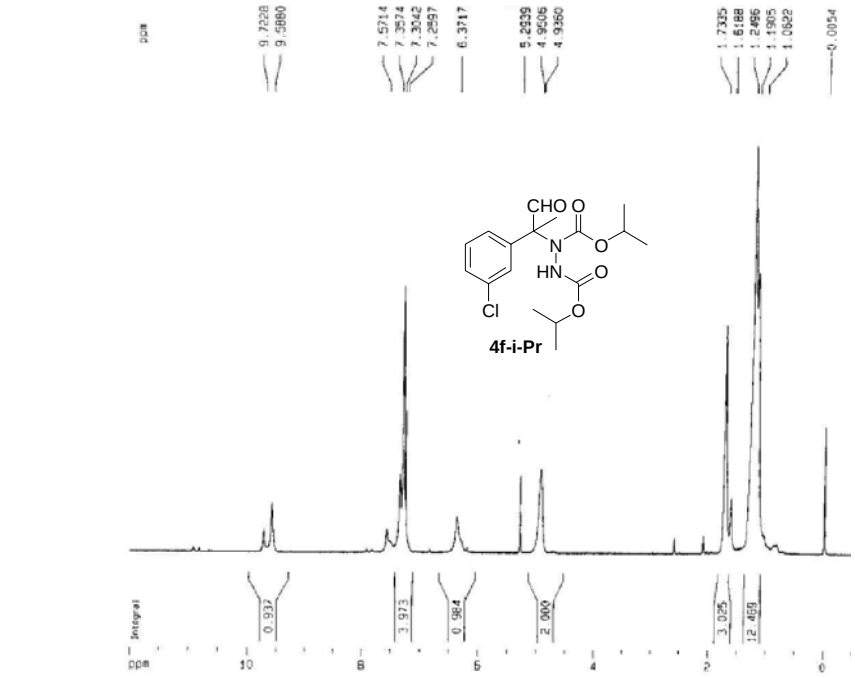
4e-Et

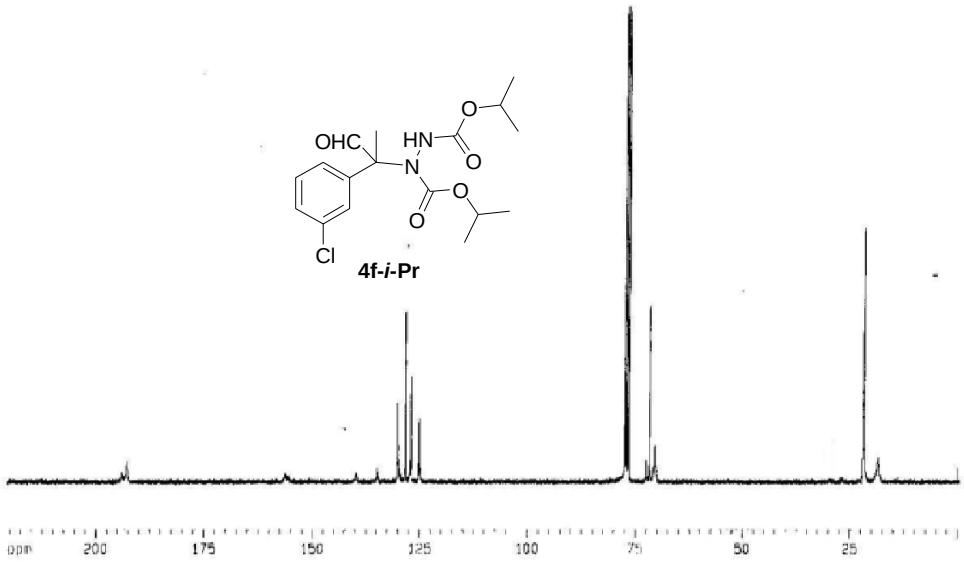


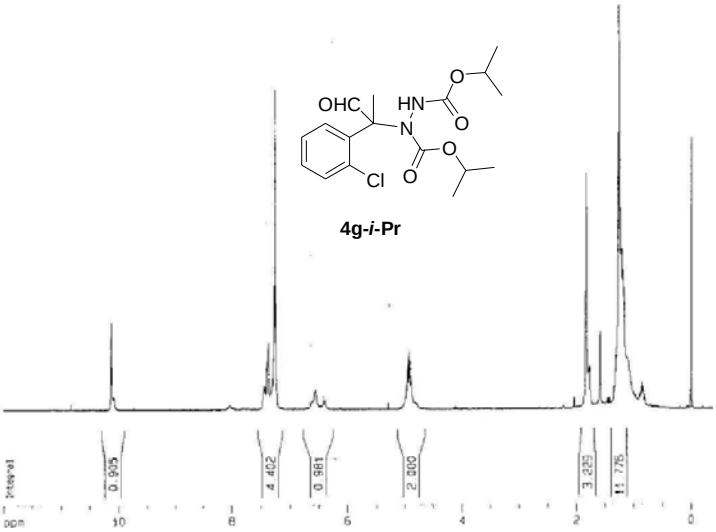
4e-*i*-Pr

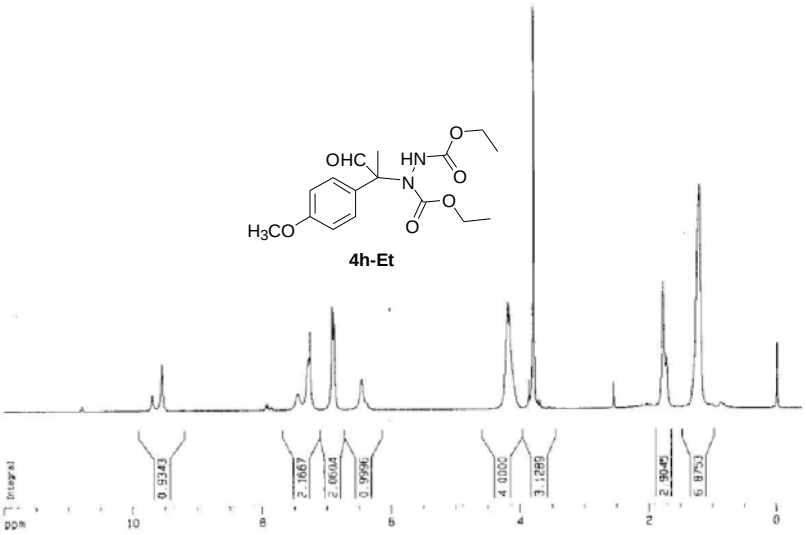


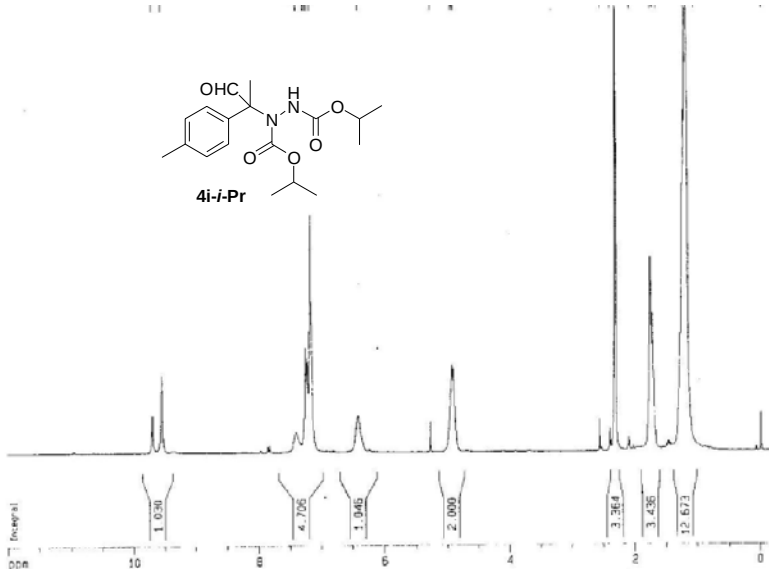
4e-*i*-Pr

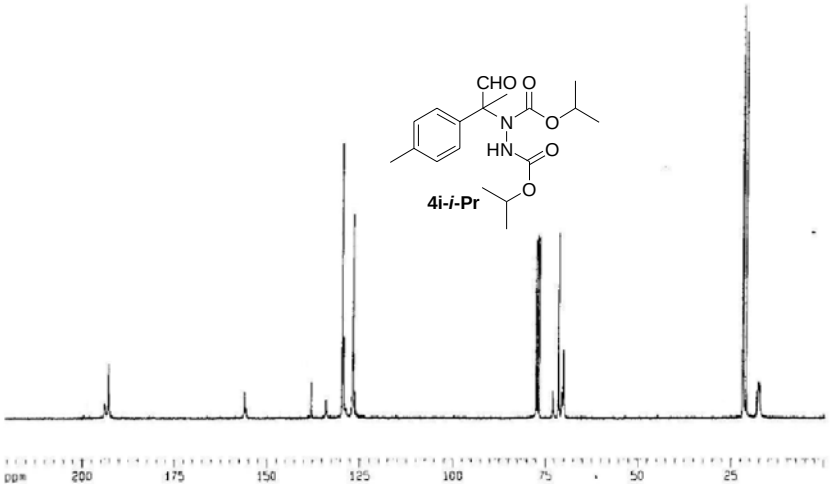


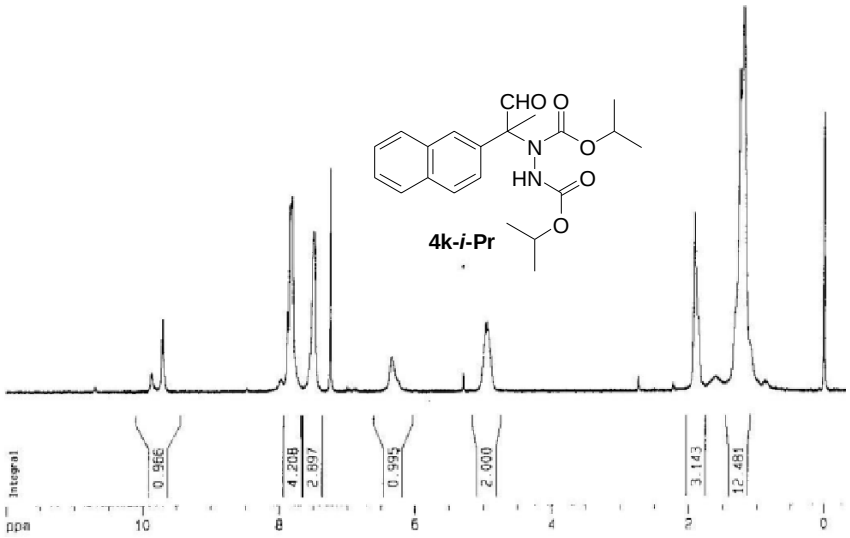


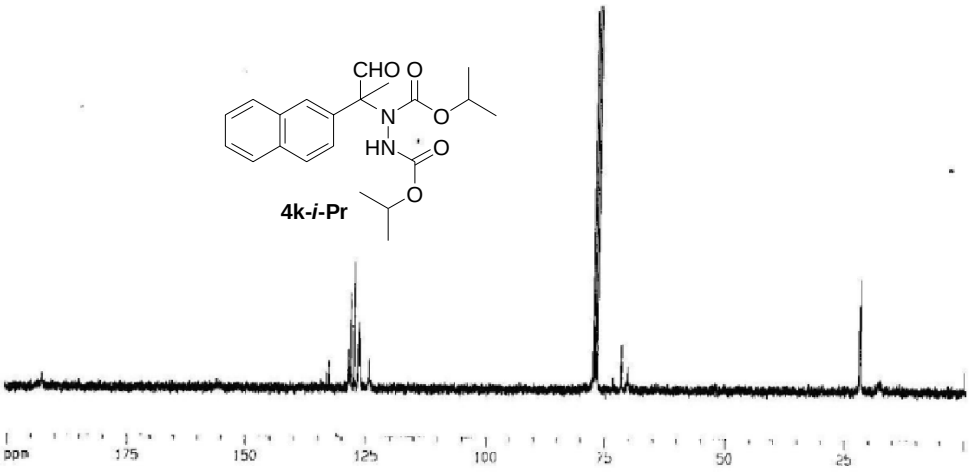




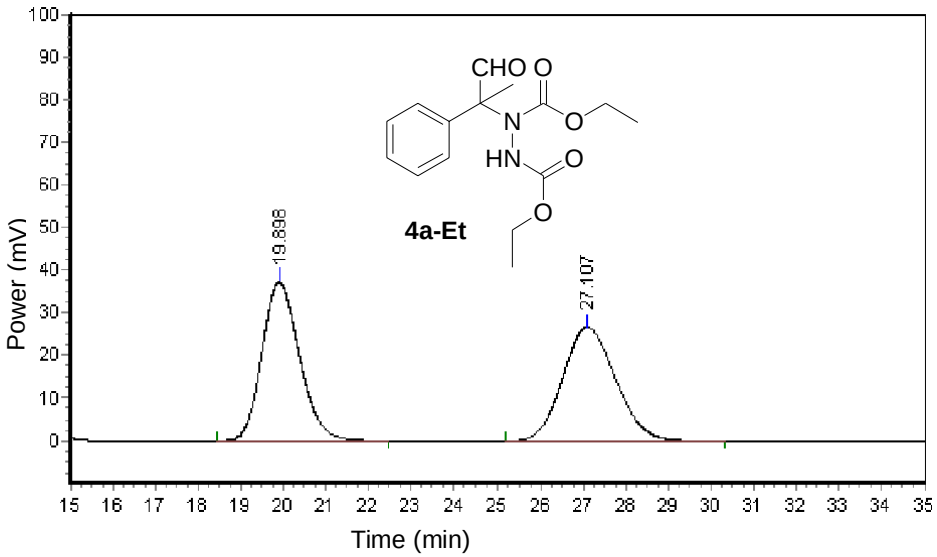




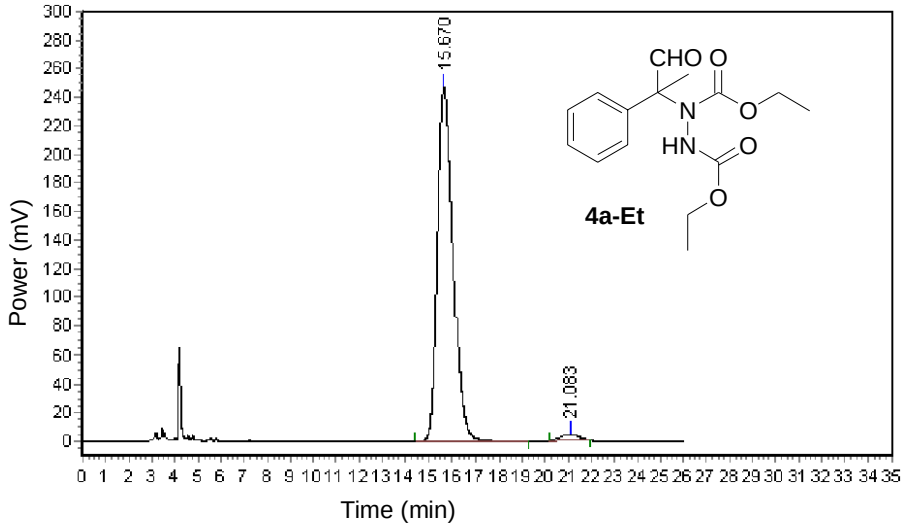




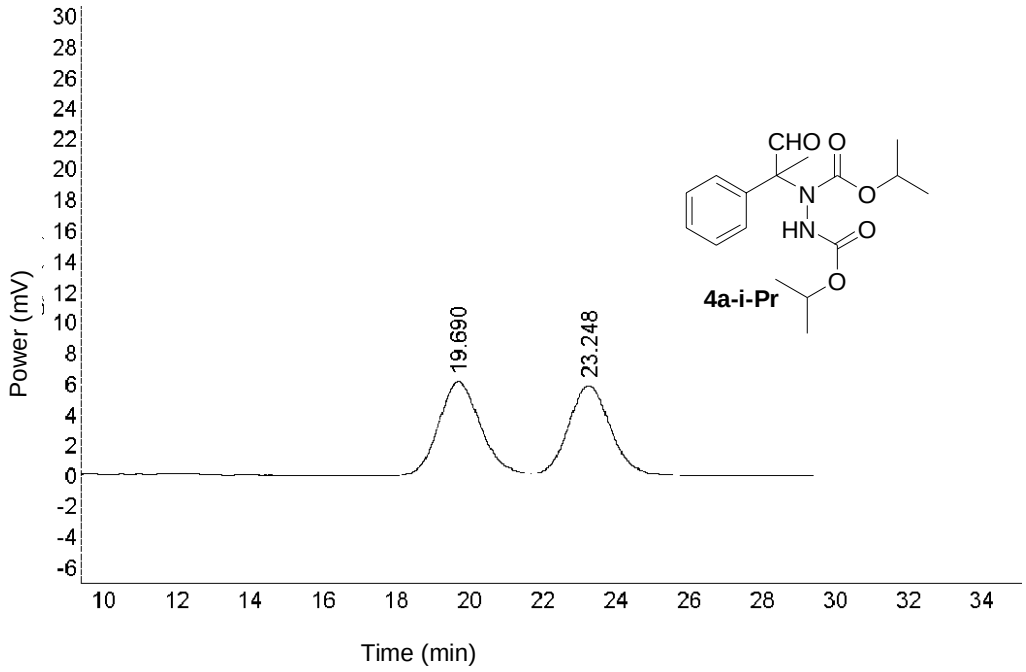
7.0 HPLC data



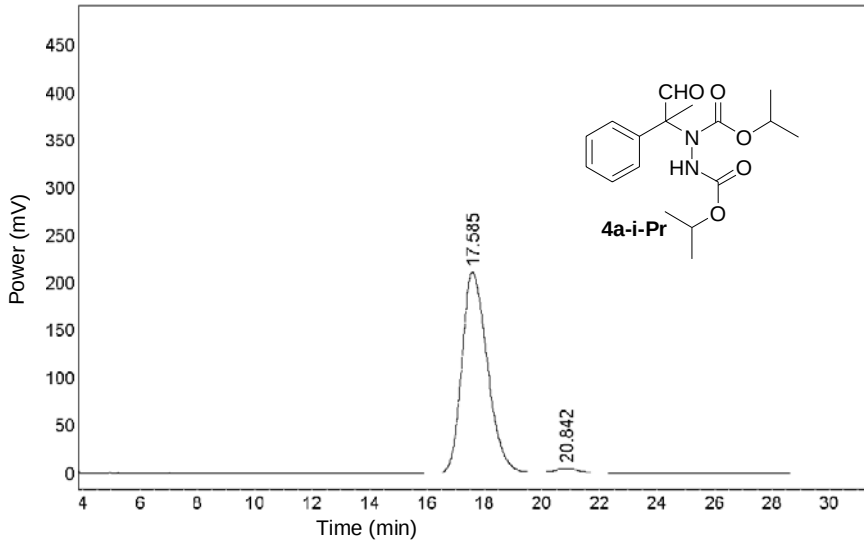
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.898	36949.930	2251085.750	49.7245
2	27.107	26513.504	2276029.500	50.2755



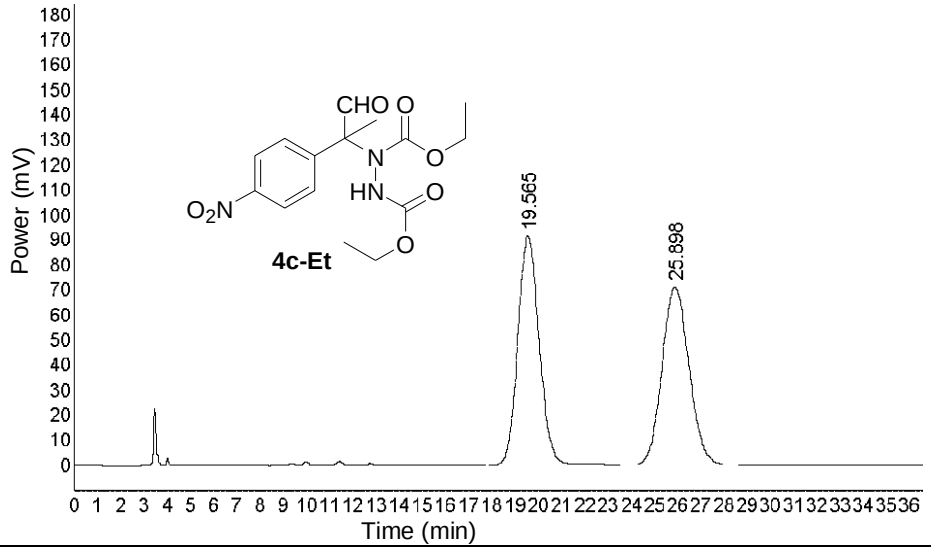
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	15.670	247446.109	11223906.000	97.9791
2	21.083	4346.950	231496.609	2.0209



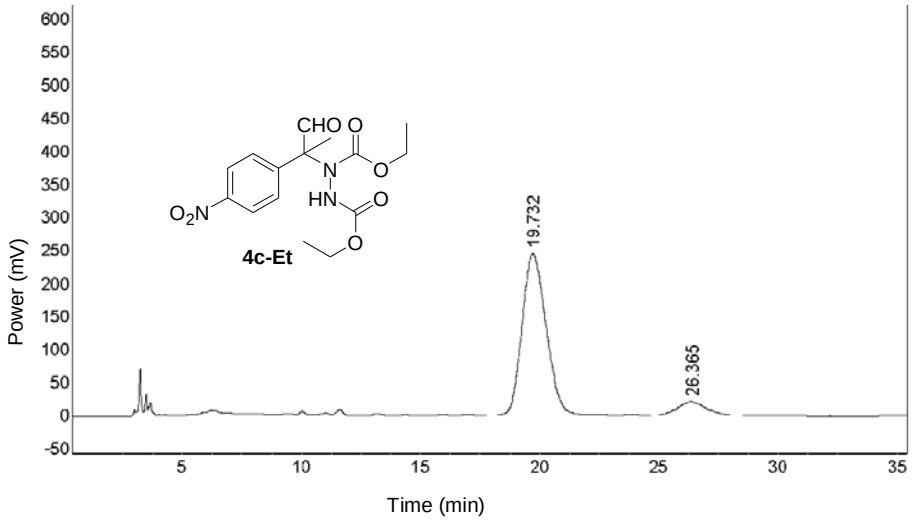
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.690	5993.741	465066.438	51.1464
2	23.248	5764.809	444217.906	48.8536



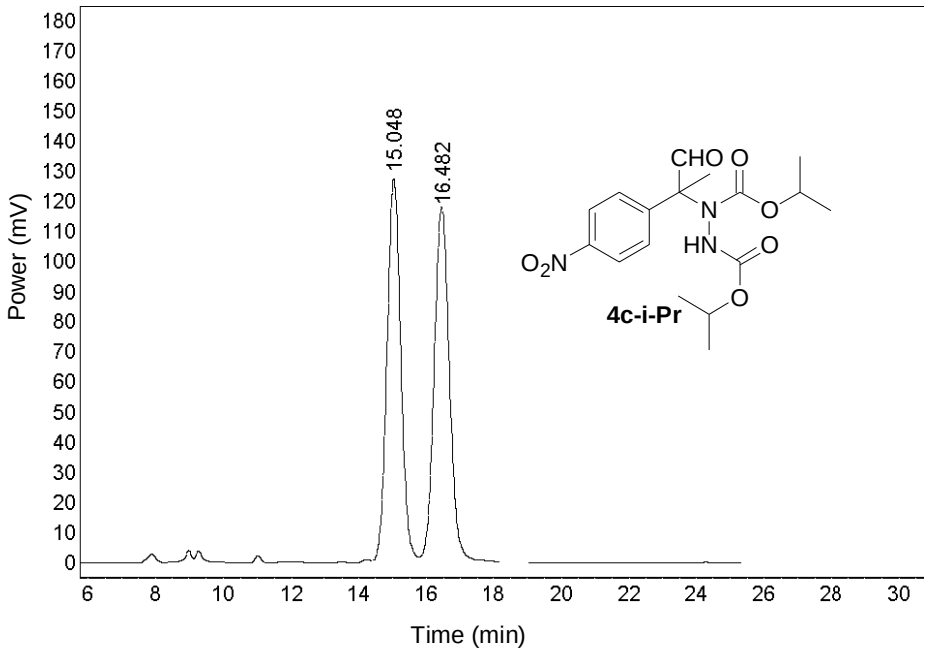
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	17.585	210575.953	12881603.000	98.2505
2	20.842	4020.373	231330.031	1.7495



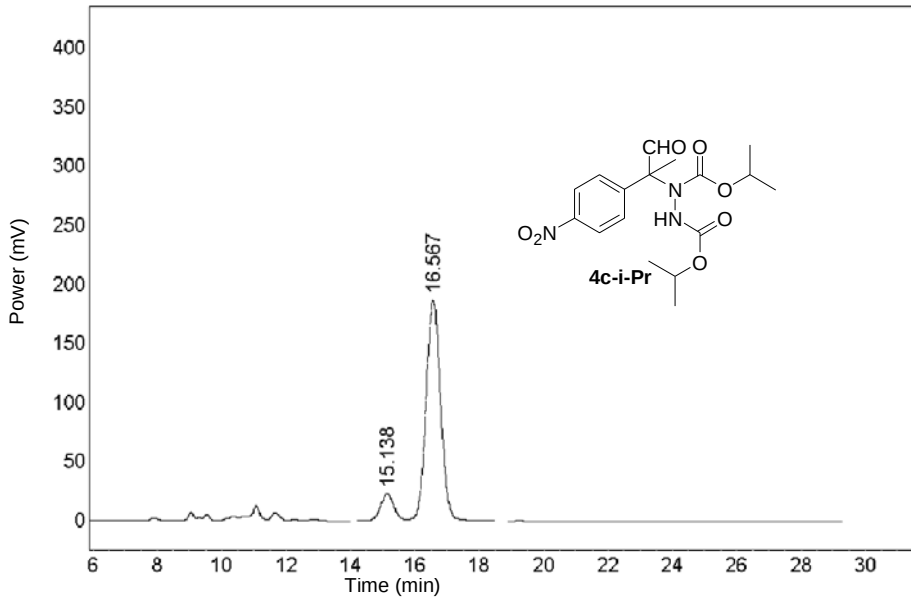
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.565	91461.797	5834918.000	50.4062
2	25.898	71058.102	5740871.500	49.5938



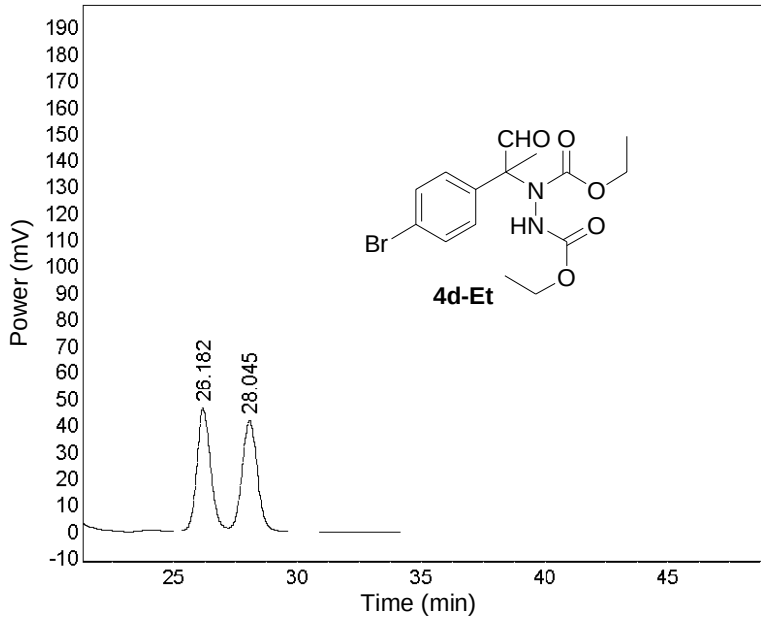
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.732	245664.156	17194096.000	90.5585
2	26.365	20696.715	1792633.500	9.4415



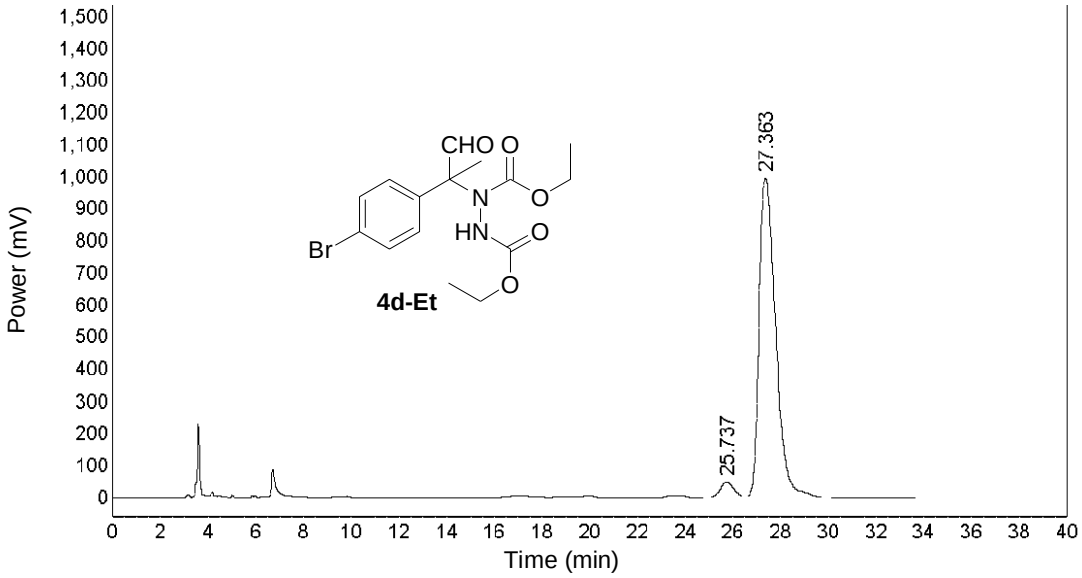
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	15.048	127817.570	3643324.250	49.3885
2	16.482	117583.656	3733537.000	50.6115



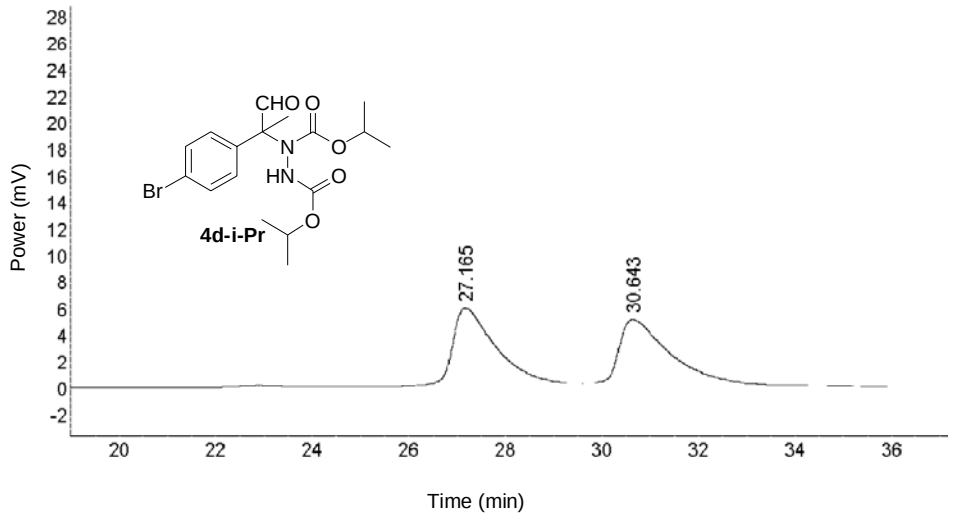
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	15.138	22618.656	646693.000	9.9716
2	16.567	186866.031	5838664.000	90.0284



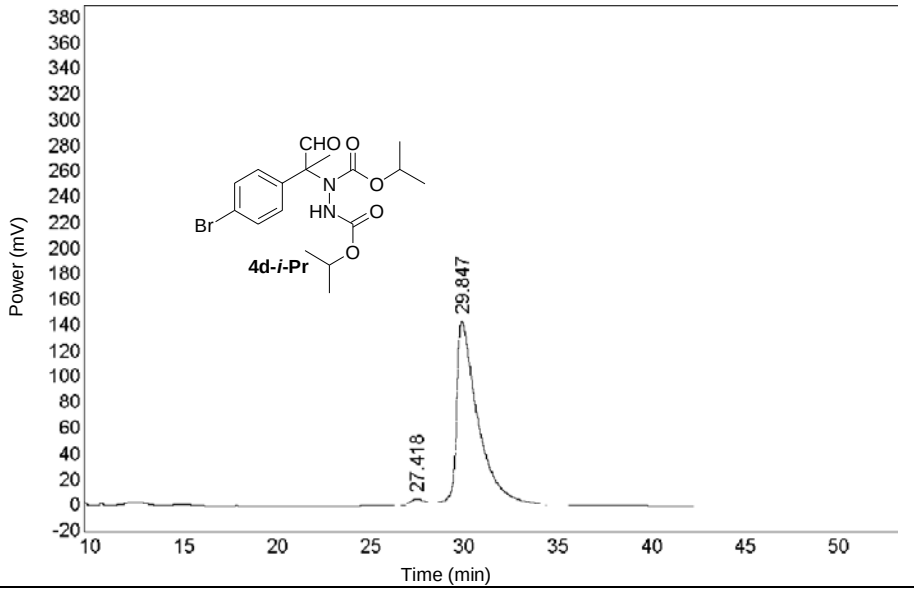
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	26.182	46415.039	1828043.375	50.8578
2	28.045	41836.621	1802068.125	49.6422



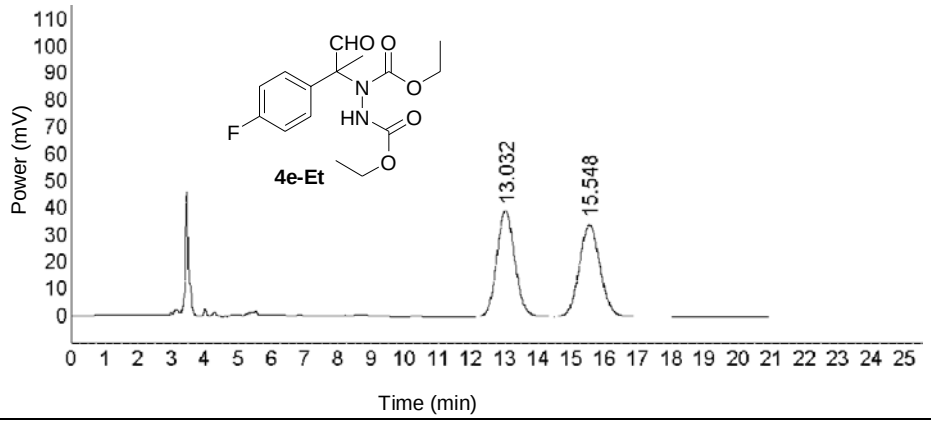
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	25.737	44878.973	1718290.875	3.4939
2	27.363	994909.375	47461632.000	96.5061



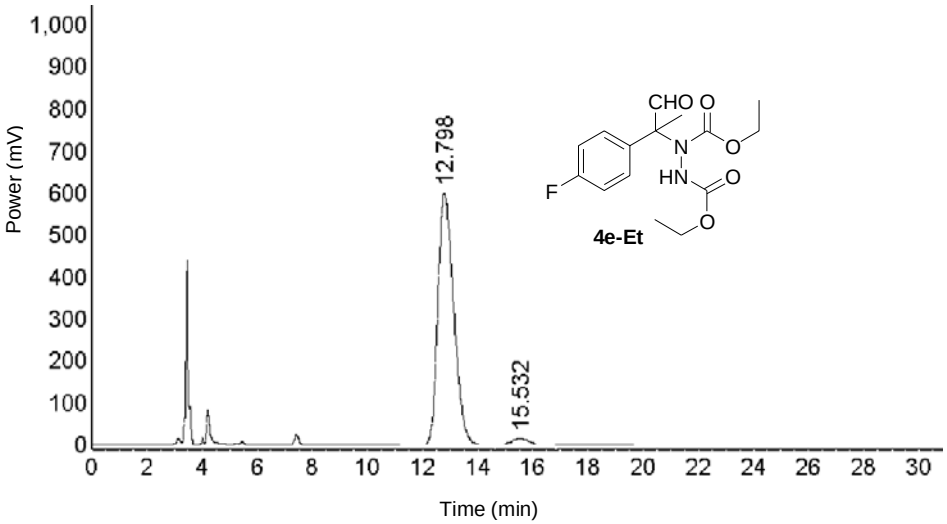
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	27.165	5796.416	357120.313	50.1228
2	30.643	4864.795	355370.469	49.8772



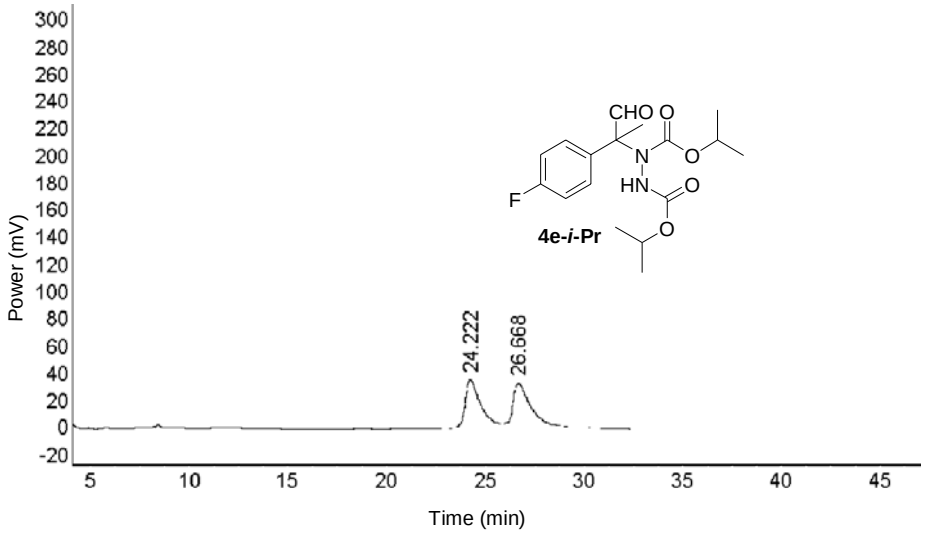
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	27.418	3978.087	165205.000	1.4679
2	29.847	141825.453	11089276.000	98.5321



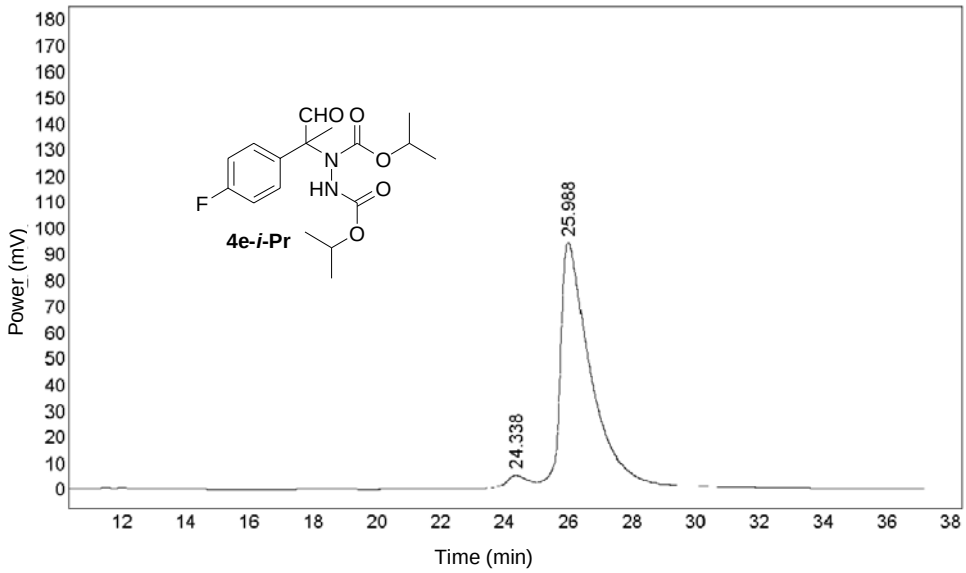
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	13.032	39335.023	1466937.125	49.8620
2	15.548	34051.426	1475056.000	50.1380



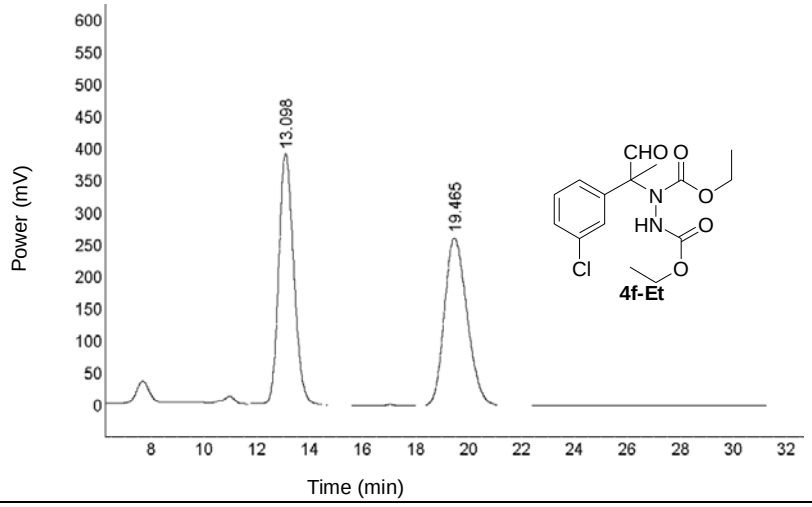
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	12.798	599564.688	23999914.000	97.0500
2	15.532	16281.000	729505.313	2.9499



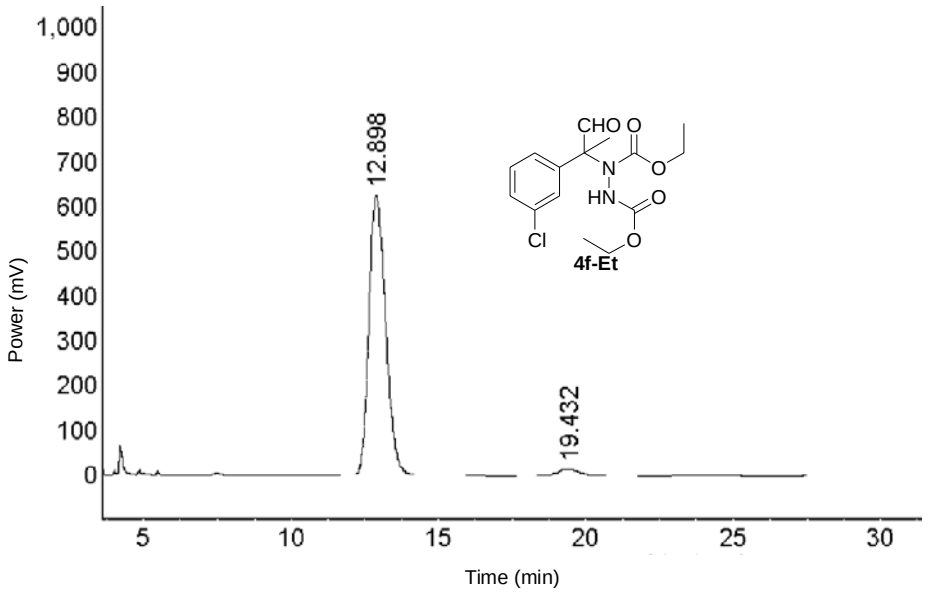
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	24.222	34406.371	1703902.625	49.1436
2	26.668	30517.092	1763289.375	50.8564



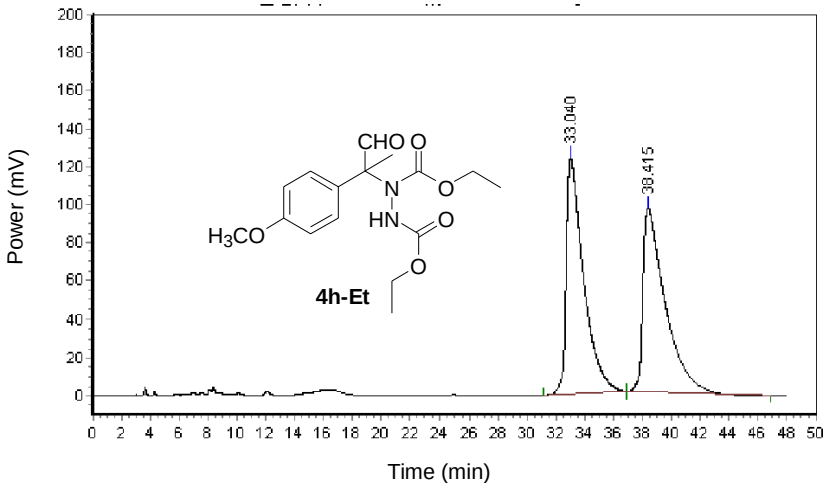
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	24.338	3556.925	122013.000	2.0650
2	25.988	92150.953	5786511.500	97.9350



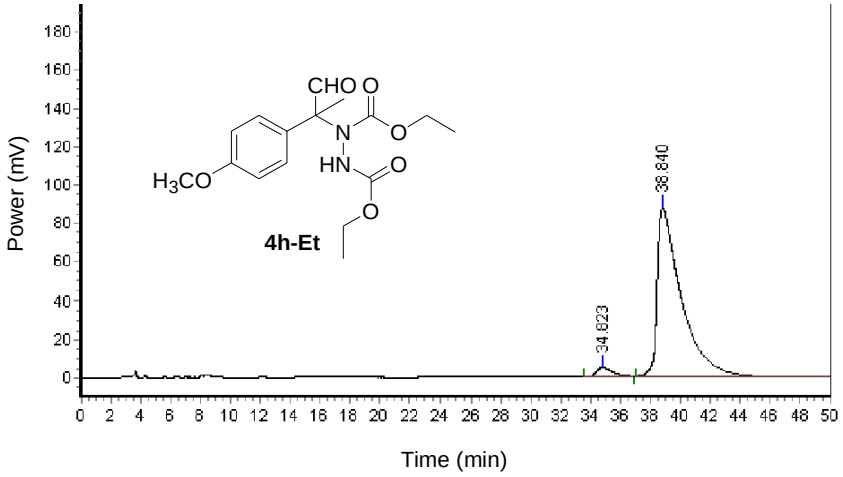
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	13.098	390812.156	15434799.000	49.7881
2	19.465	261586.500	15566192.000	50.2119



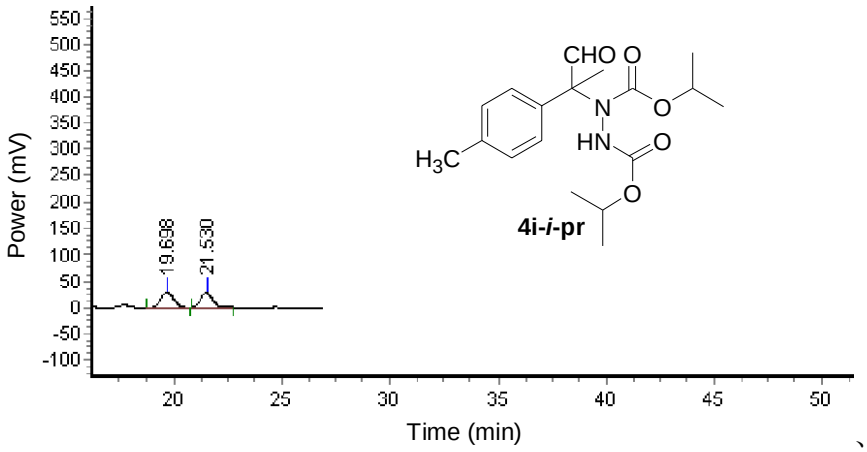
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	12.898	626101.813	24819724.000	96.7187
2	19.432	14787.179	842047.625	3.2813



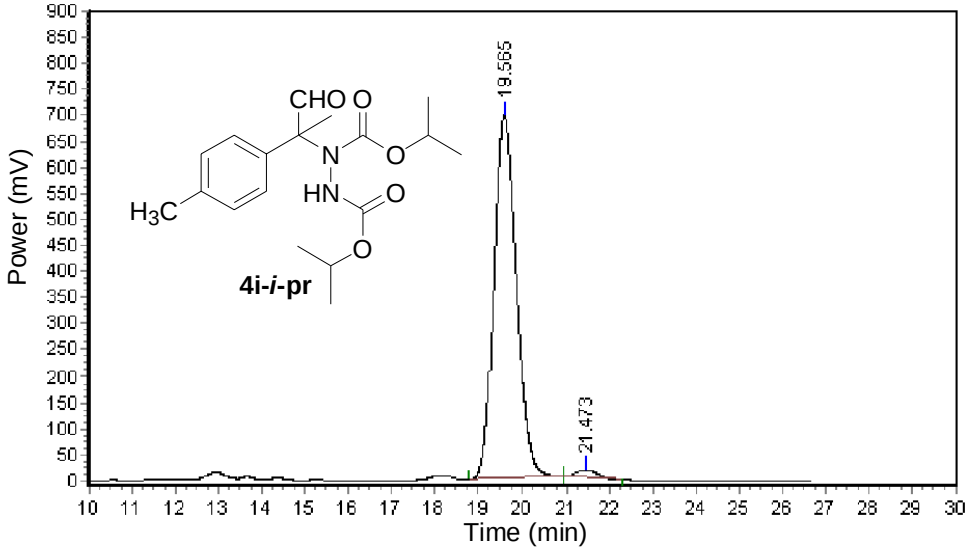
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	33.040	123767.141	10390154.000	50.2115
2	38.415	96217.289	10302613.000	49.7885



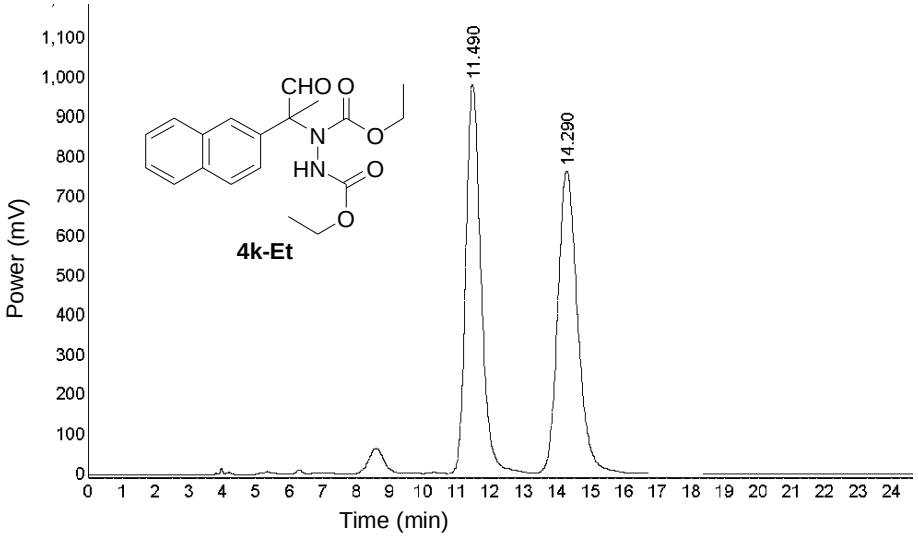
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	34.823	4702.979	376982.875	3.6689
2	38.840	87777.141	9898182.000	96.3311



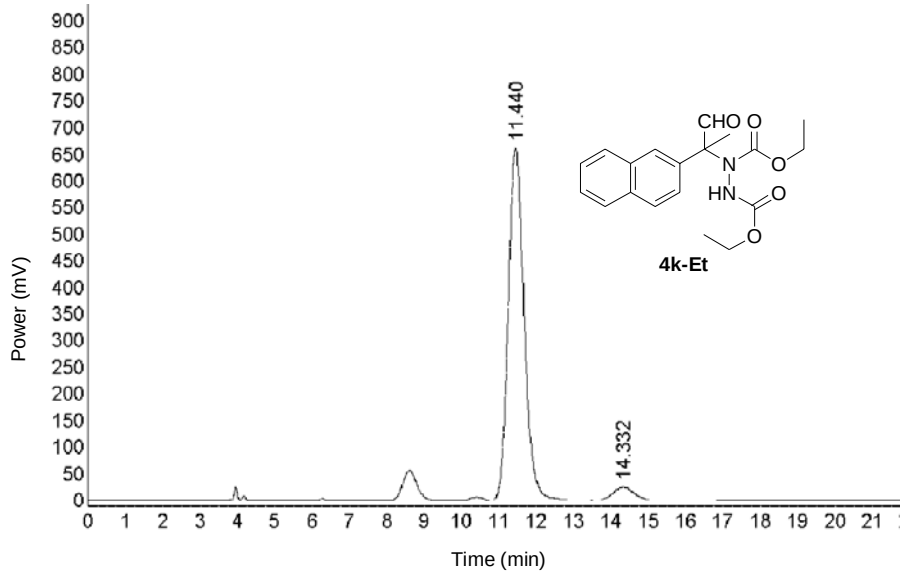
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.698	28959.748	1137386.375	51.7902
2	21.530	27395.191	1058753.500	48.2097



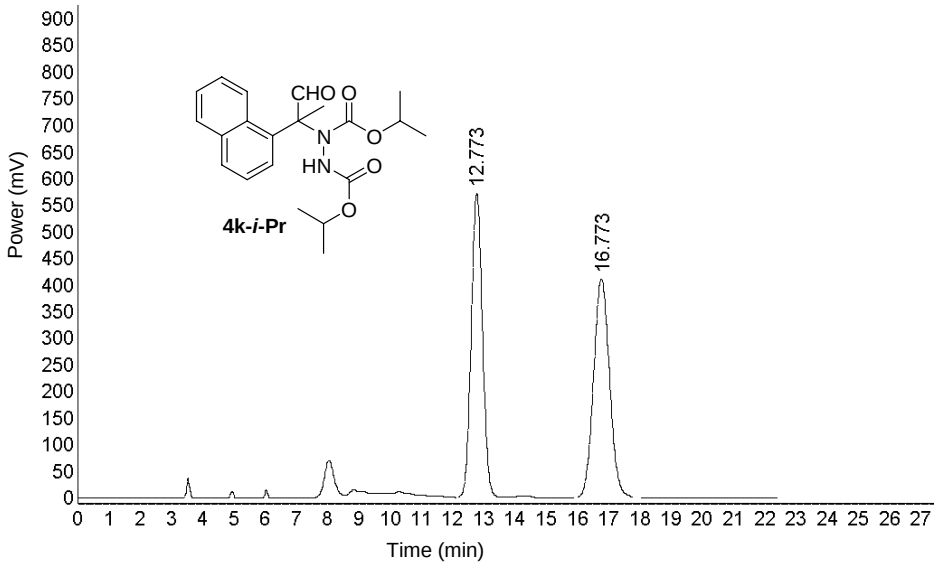
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	19.565	697480.375	24904548.000	98.0389
2	21.473	15086.172	498169.594	1.9611



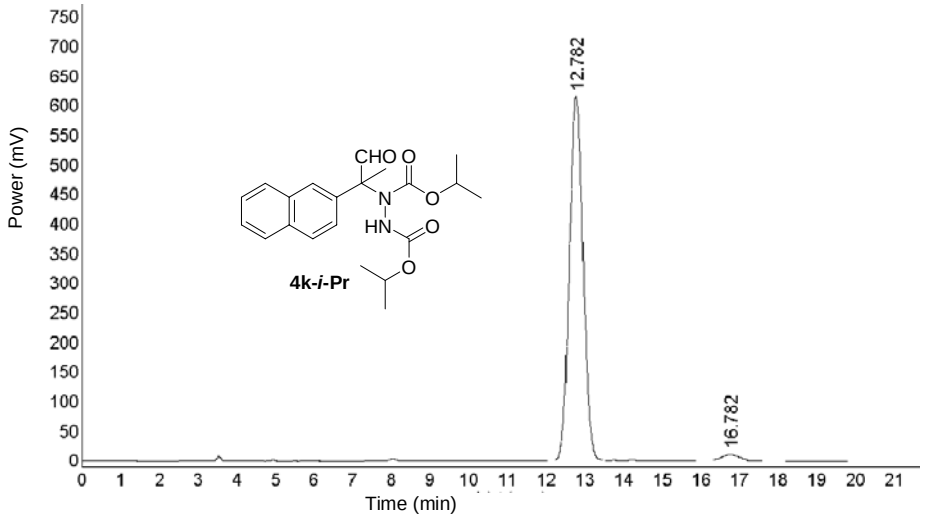
Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	11.490	982317.125	30805248.000	49.5425
2	14.290	761978.938	31374244.000	50.4575



Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	11.440	661414.188	19433784.000	95.1613
2	14.332	25453.750	988151.000	4.8387



Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	12.773	570520.375	14287302.000	49.2924
2	16.773	411469.000	14697471.000	50.7076



Peak	Ret Time [min]	Height [mV*sec]	Area [mV]	Aear [%]
1	12.782	616569.938	15356280.000	97.3276
2	16.782	11901.761	421643.063	2.6724

Reference:

[1] (a) Q.-W., Wang, L. Peng, J.-Y. Fu, Q.-C. Huang, L.-X. Wang and X.-Y. Xu, *ARKIVOC(ii)***,** 2010, 340-351; (b) J.-F. Bai, X.-Y. Xu, Q.-C. Huang, L. Peng and L.–X. Wang, *Tetrahedron Lett*. 2010, **51**, 2803-2805.

[2] T. Baumann, H. Vogt and S. Bräse, *Eur. J. Org. Chem*. **2007**, 266-282.