Catalysis by Amino Acid-Derived Tetra-Coordinate Complexes: Enantioselective Addition of Dialkylzincs to Aliphatic and Aromatic Aldehydes.

Supplemental Information

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(66 pages)

Experimental Section:

General. All air- and moisture-sensitive reactions were performed under argon and in flame-dried glassware. Solvents were deoxygenated and distilled before use from an appropriate drying agent (THF – K°/ benzophenone, Toluene – CaH_2). Aldehydes were purchased from Aldrich, distilled and used immediately. The Schiff base ligands were synthesized from chiral amino acids purchased from Advanced Chem Tech. ^{1}H and ^{13}C NMR was used to confirm the structure and purity of the ligands. NMR spectra were measured on a Bruker WM 250 MHz spectrometer. For ^{13}C, spectra were taken at 62.5 MHz in the form of APT's (attached proton test spectra). Chemical shifts are reported in δ vs Me_4Si in ^{1}H spectra and vs $CDCl_3$ in ^{13}C spectra. Infrared spectra were taken on a Nicolet Impact-400D FT-IR. Enantiopurity was determined by optical rotation using a Jasco DIP-1000 polarimeter using the Na^D-line. The enantioselectivity of the products formed during the reaction were determined by capillary GC using Chiraldex chiral columns. Exact conditions are described in the appropriate experimental section.

L-{1-[2-(2-*tert*-Butoxycarbonylamino-3-phenyl-propionylamino)-phenylcarbamoyl]-2-phenyl-ethyl}-carbamic acid *tert*-butyl ester. In a flame-dried 250 ml glass round bottom flask equipped with a magnetic stir bar and a drying tube, phenylenediamine (2.5 g, 23.1 mmol) was dissolved in 200 ml of freshly distilled DMF. To the brown solution DIEA (8.9 g, 69 mmol, 3 equiv.) was added in a single portion. The reaction mixture was

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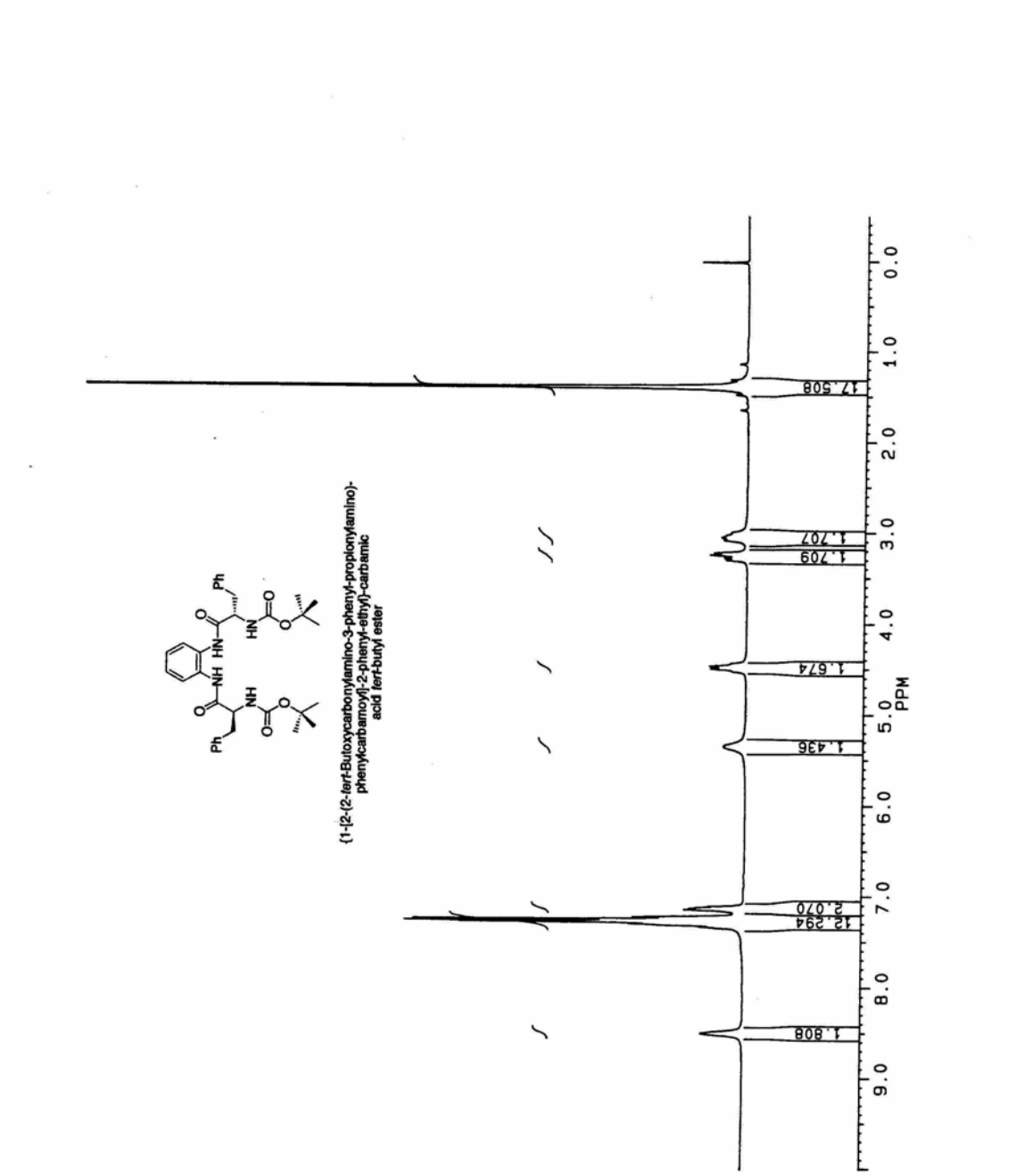
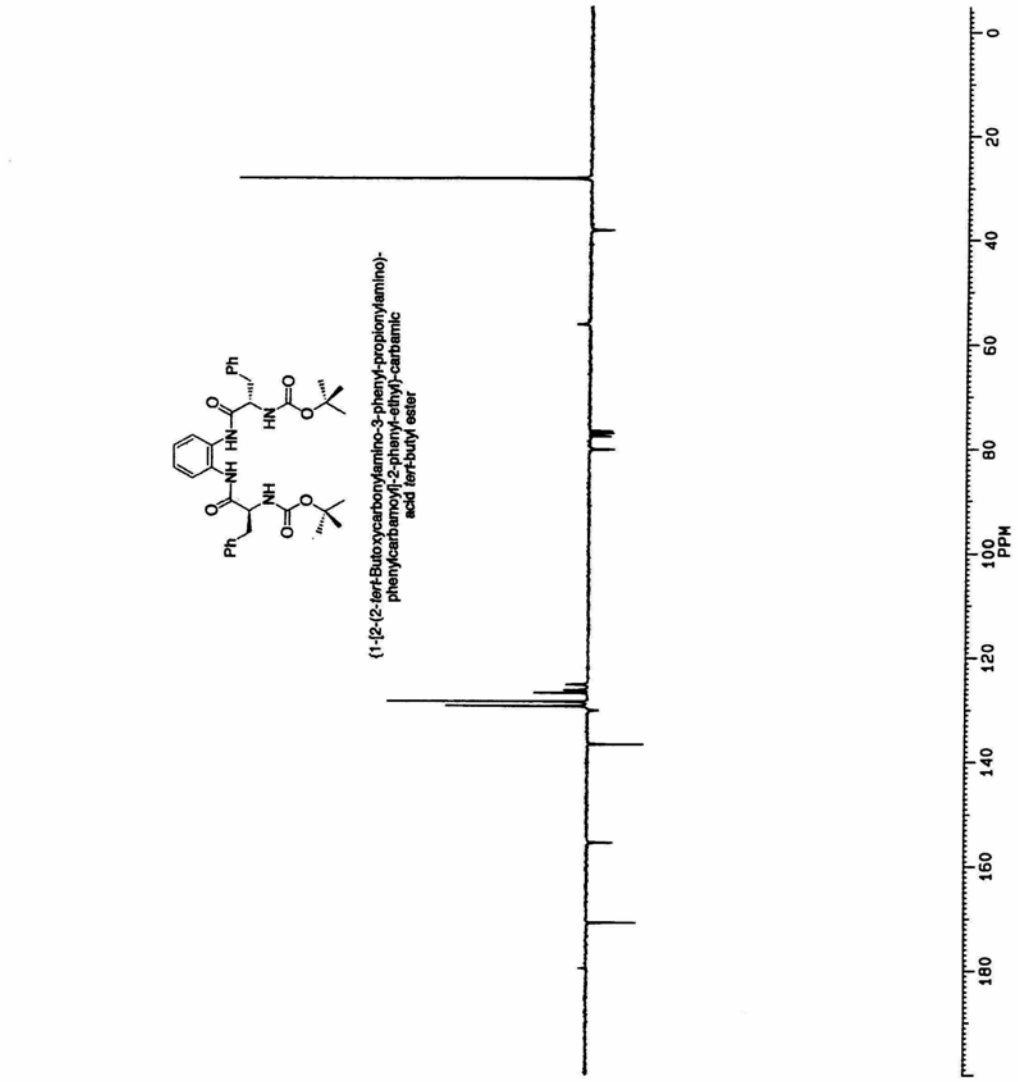
cooled to 0°C. Boc-L-Phe (13.5 g, 50.8 mmol, 2.2 equiv.) and BOP (25.5 g, 57.7 mmol, 2.5 equiv.) were added in a single portion. The solution was allowed to warm to room temperature and react for 24 hrs. The reaction progress was monitored by TLC (1:1 EtOAc-hexanes; ninhydrin development). The reaction was then diluted with EtOAc (300 ml) and washed appropriately: distilled H_2O (3 X 200 ml); 1M HCl (2 X 200 ml); H_2O (1 X 200 ml); sat. $NaHCO_3$ (2 X 200 ml); sat. NaCl (1 X 200 ml). The organic layer was dried over $MgSO_4$, filtered and concentrated to a light brown foam. This material was passed through a short plug of silica gel to remove polar compounds. Isolation gave 13.8 g of pure product in a 99% yield.

^{1}H NMR (250MHz, $CDCl_3$): δ 1.38 ppm, (s, 18H, *t*-butyl CH_3), (*ABMX* : δ 2.98-3.07 ppm, (dd, 2H, -$CH_A\underline{H}_B$-CH_X-NH_M-, J_{BX} = 7.30 Hz, J_{AB} = 13.3 Hz), δ 3.21-3.28 ppm, (dd, 2H, -$C\underline{H}_AH_B$-CH_X-NH_M-, J_{AX} = 5.82 Hz, J_{AB} = 13.7 Hz), δ 4.43-4.51 ppm, (dt, 2H, -CH_AH_B-$C\underline{H}_X$-NH_M-, J_{AX} = 6.71 Hz, J_{BX} = 6.96 Hz, J_{MX} = 6.6 Hz), δ 5.33 ppm, (broad s, 2H, -CH_AH_B-CH_X-$N\underline{H}_M$-)), δ 7.09-7.33 ppm, (m, 14H, aromatic CH), δ 8.49 ppm, (broad s, 2H, amide NH).

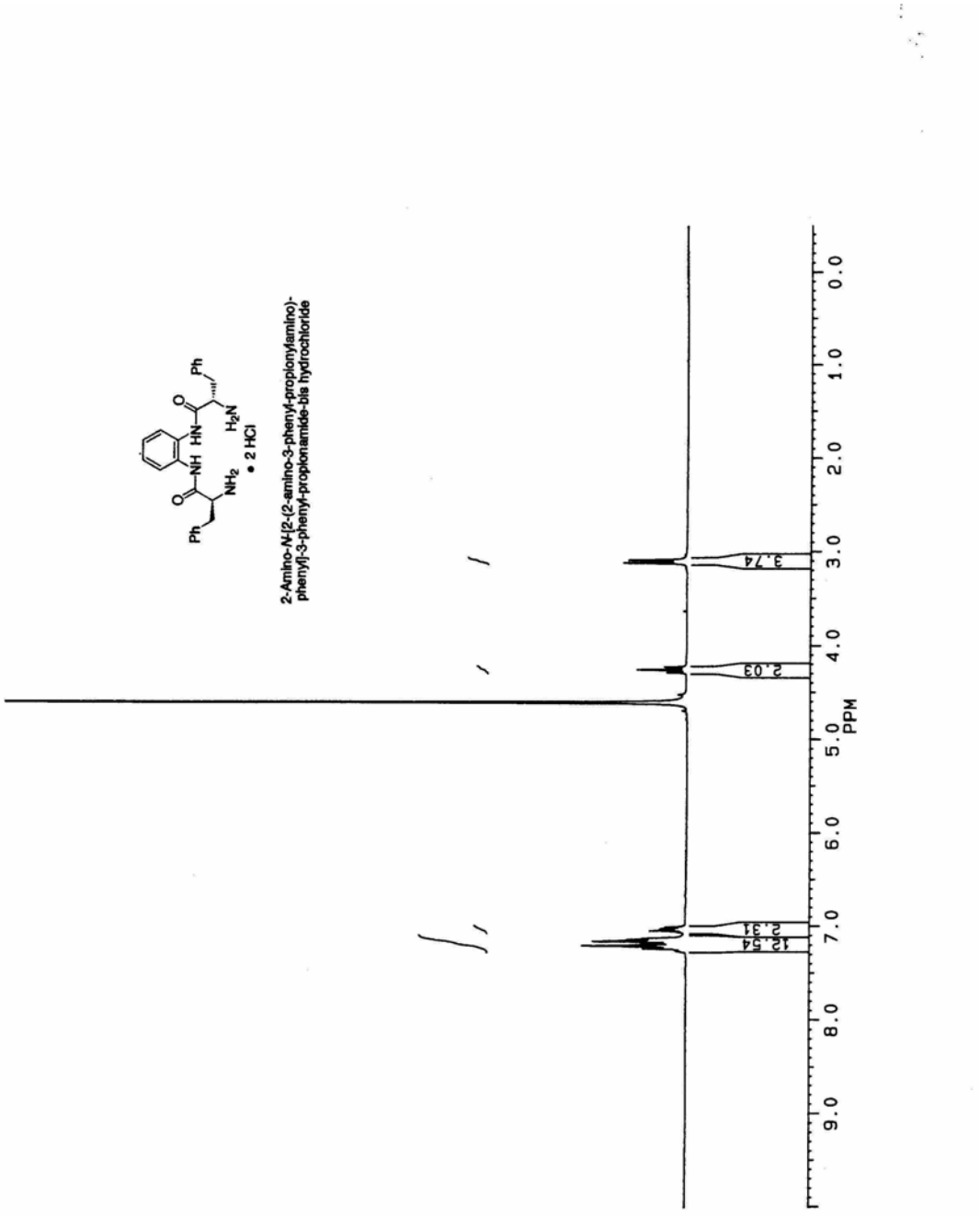
^{13}C-APT NMR (62.5 MHz, $CDCl_3$): CH_3 δ 28.1 ppm, CH_2 δ 38.1 ppm, CH_α δ 56.1 ppm, Me_3-C-OR δ 80.0 ppm, aromatic: CH δ 125.1, 126.1, 126.7, 128.4, 129.2 ppm; C δ 130.0, 136.5 ppm, -NH-CO-OR δ 155.4 ppm, -NH-CO-R δ 170.7 ppm.


{1-[2-(2-tert-Butoxycarbonylamino-3-phenyl-propionylamino)-phenylcarbamoyl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester
17.508
1.707
1.709
1.674
1.436
2.070
12.294
1.808
PPM


{1-[2-(2-tert-Butoxycarbonylamino-3-phenyl-propionylamino)-phenylcarbamoyl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester
PPM
0
20
40
60
80
100
120
140
160
180

L-2-Amino-*N*-[2-(2-amino-3-phenyl-propionylamino)-phenyl]-3-phenyl-propionamide-bis-hydrochloride. The Boc protected compound (13.8 g, 23.1 mmol) was dissolved in 50 ml of anhydrous MeOH. In a separate flask, 50 ml of MeOH was chilled to 0°C. AcCl (6.7 ml, 7.4 g, 92.4 mmol, 4 equiv.) was added slowly. The resultant methanolic HCl was stirred to 10 min. and then added to the chilled reaction mixture dropwise over 30 min. The reaction mixture was allowed to warm to RT for 24 hours. Disappearance of starting material was monitored by TLC (1:1 EtOAc-hexanes) and worked up in the following manner. MeOH was removed by rotary evaporation. The residual HCl was removed by dissolving the residue in MeOH and subsequent rotary evaporation (5 X 200 ml). This material was placed *in vacuo* until a brittle foam was obtained, then triturated in Et_2O until a fine suspension was achieved. The HCl salt was collected by filtration and dried *in vacuo* to provide a quantitative yield of the product (11 grams), which could be stored for extended periods as the HCl salt.

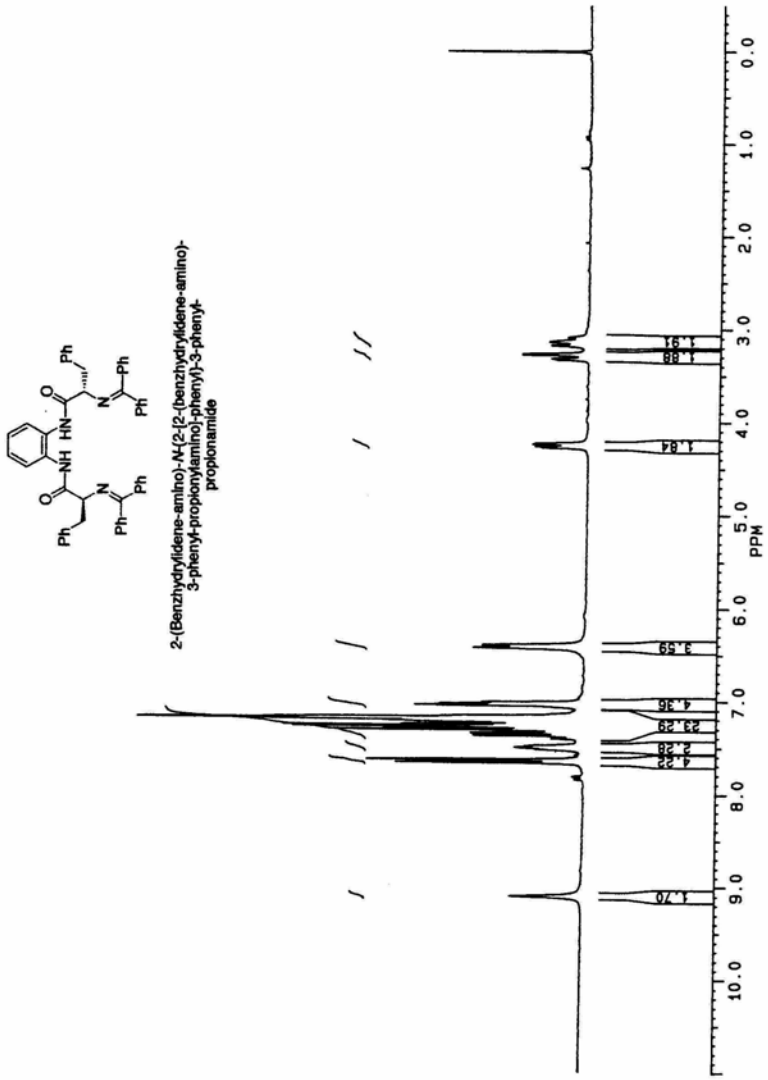
^{1}H NMR (250MHz D_2O): δ 3.07-3.11 ppm (d, 4H, J = 7.27 Hz), δ 4.22-4.27 ppm (t, 2H, J = 7.23 Hz), δ 6.99-7.26 ppm (m, 14 H, aromatics).

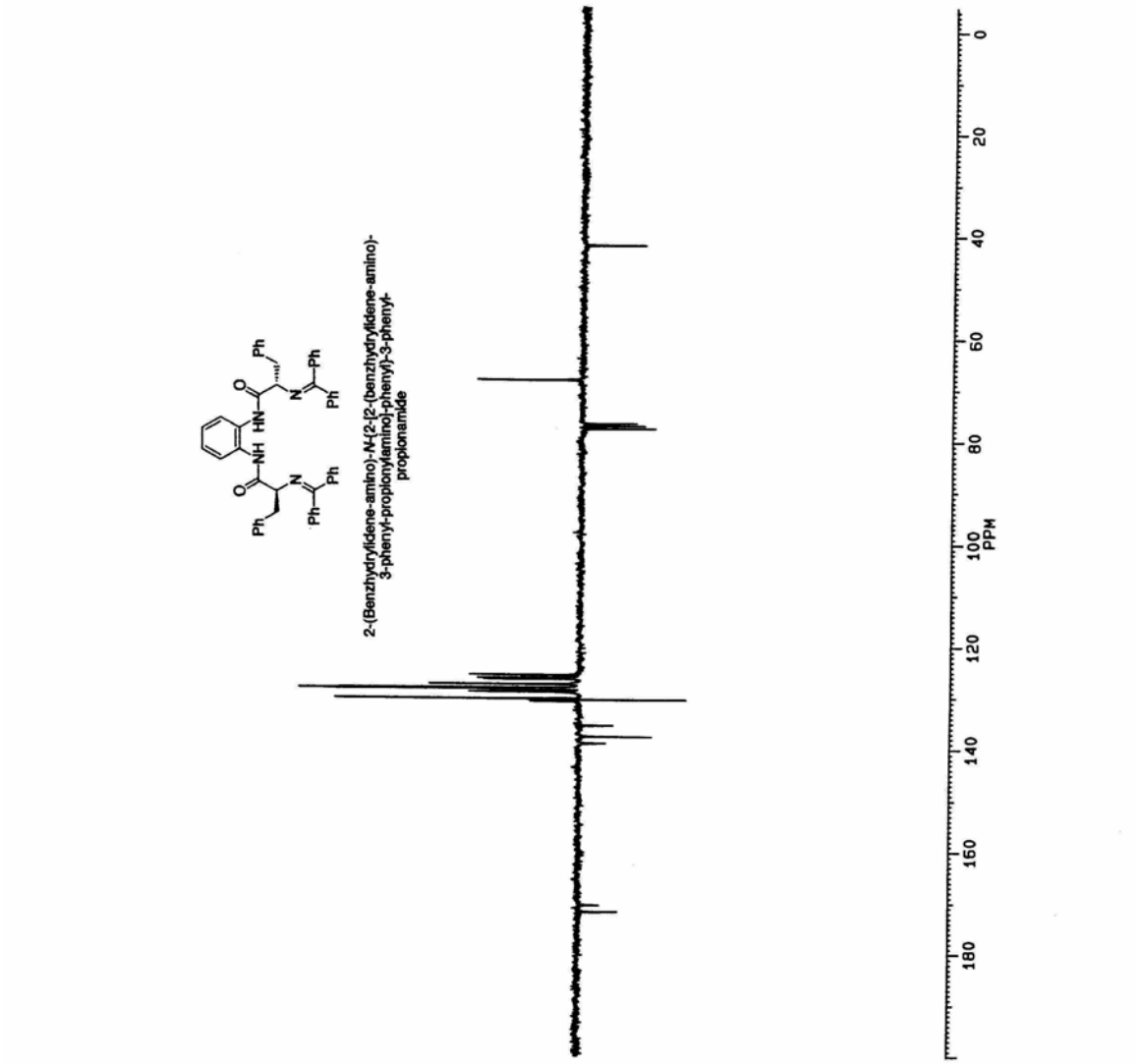

2-Amino-N-[2-(2-amino-3-phenyl-propionylamino)-phenyl]-3-phenyl-propionamide-bis hydrochloride
• 2 HCl
3.74
2.03
12.54
2.31
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

L-2-(Benzhydrylidene-amino)-*N*-{2-[2-(benzhydrylidene-amino)-3-phenyl-propionylamino]-phenyl}-3-phenyl-propionamide, **1**. In a 250 ml. 1-neck glass round bottom flask (previously flame-dried and purged with argon) the dry bis-HCl salt (2.5 g, 7.7 mmol) was suspended in 60 ml of dry CH_2Cl_2. Benzophenone imine (2.8 g, 2.65 ml, 15.8 mmol, 2.05 equiv.) was added in a single portion. The slurry was stirred at room temperature and allowed to react for 12 hr. The progress of the reaction was monitored by TLC (9:1 toluene-EtOAc; ninhydrin development). Upon completion, the reaction was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ (2 X 100 ml). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated. The crude oil was purified by silica gel flash column chromatography to provide 3.8 grams of a white crystalline foam in a 72% yield. Optical rotation: $[\alpha]_D$ = (-) 160.9° (c = 0.42; $CHCl_3$).

^{1}H NMR (500MHz, $CDCl_3$): (*ABX* : δ 3.09-3.14 ppm, (dd, 2H, -$CH_A\underline{H}_B$-CH_X-, J_{BX} = 9.39 Hz, J_{AB} = 13.0 Hz), δ 3.26-3.29 ppm, (dd, 2H, -$C\underline{H}_AH_B$-CH_X-, J_{AX} = 3.18 Hz, J_{AB} = 13.1 Hz), δ 4.21-4.24 ppm, (dt, 2H, -CH_AH_B-$C\underline{H}_X$-, J_{AX} = 3.26 Hz, J_{BX} = 9.39 Hz), (aromatics, 34 H): δ 6.39-6.41 ppm, (d, J = 7.23 Hz), δ 7.00-7.02 ppm, (dd, J = 1.88 Hz, J = 7.15 Hz), δ 7.15-7.29 ppm, m, δ 7.32-7.35 ppm, (t, J = 7.47 Hz), δ 7.46-7.48 ppm, m, δ 7.61-7.63 ppm, (dd, J = 1.29 Hz, J = 7.44 Hz), δ 9.06 ppm, (s, 2H, amide NH).

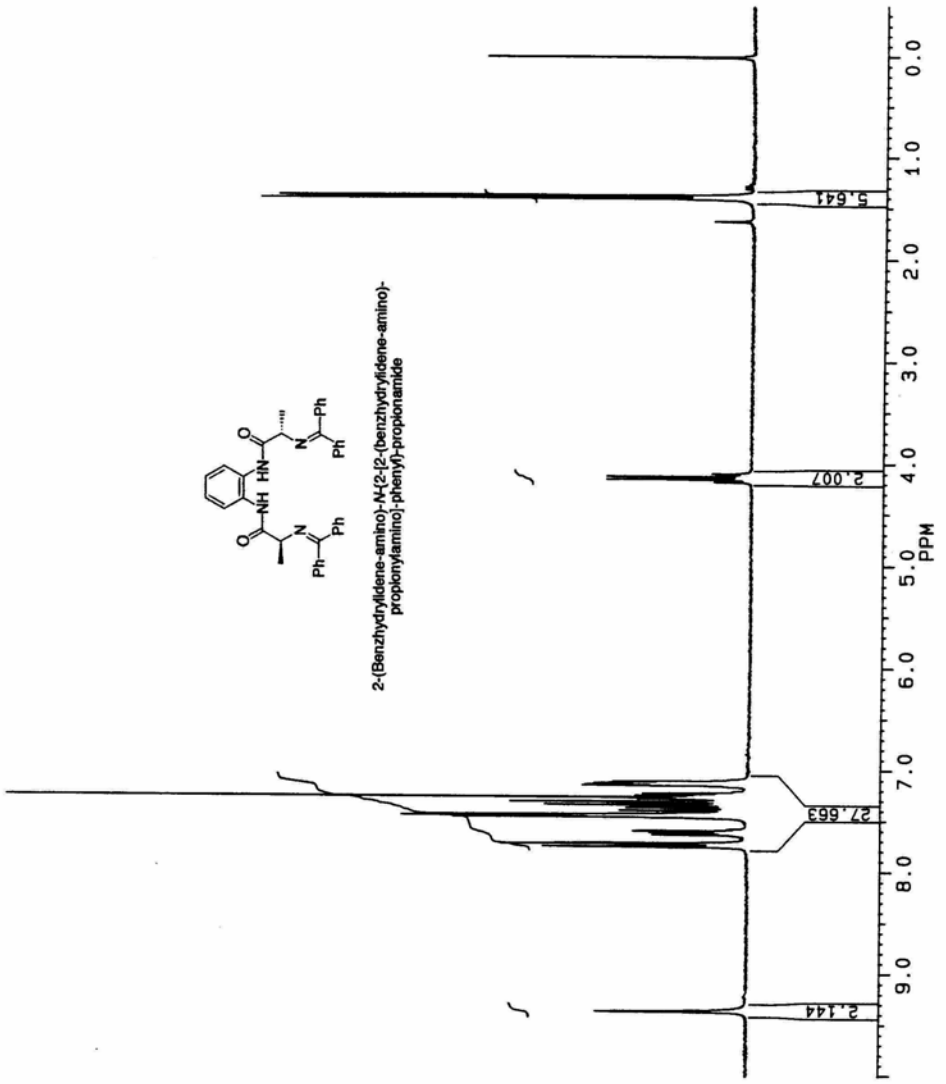
^{13}C-APT NMR (62.5 MHz, $CDCl_3$): CH_2 δ 41.7 ppm, CH_α δ 67.9 ppm, aromatic: CH δ 125.4, 126.0, 126.3, 127.2, 128.0, 128.1, 128.2, 128.7, 130.0, 130.5 ppm; C δ 130.2, 135.3, 137.5, 138.7 ppm, -NH-CO-R δ 170.4 ppm, -N=CPh_2 δ 171.7 ppm.

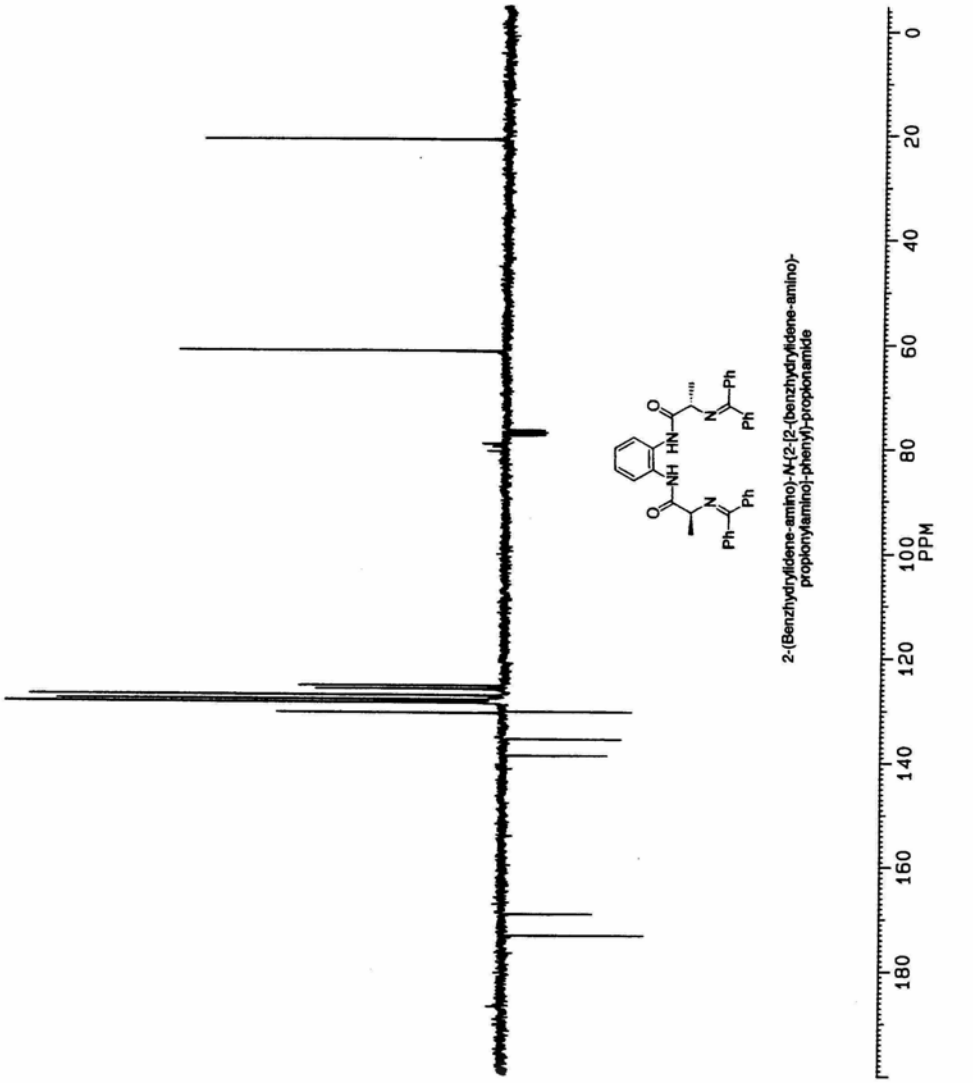

2-(Benzhydrylidene-amino)-N'-[2-[2-(benzhydrylidene-amino)-3-phenyl-propionylamino]-phenyl]-3-phenyl-propionamide
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
1.70
4.22
2.58
2.29
4.36
3.59
1.84
1.88
1.91


2-(Benzhydrylidene-amino)-N-[2-[2-(benzhydrylidene-amino)-3-phenyl-propionylamino]-phenyl]-3-phenyl-propionamide
0
20
40
60
80
100
120
140
160
180
PPM

L-2-(Benzhydrylidene-amino)-*N*-{2-[2-(benzhydrylidene-amino)-propionylamino]-phenyl}-propionamide, **3**. 45% yield. M.P. = 180 – 181°C. $[\alpha]_D$ = (+) 50.5° (c = 0.56; $CHCl_3$).

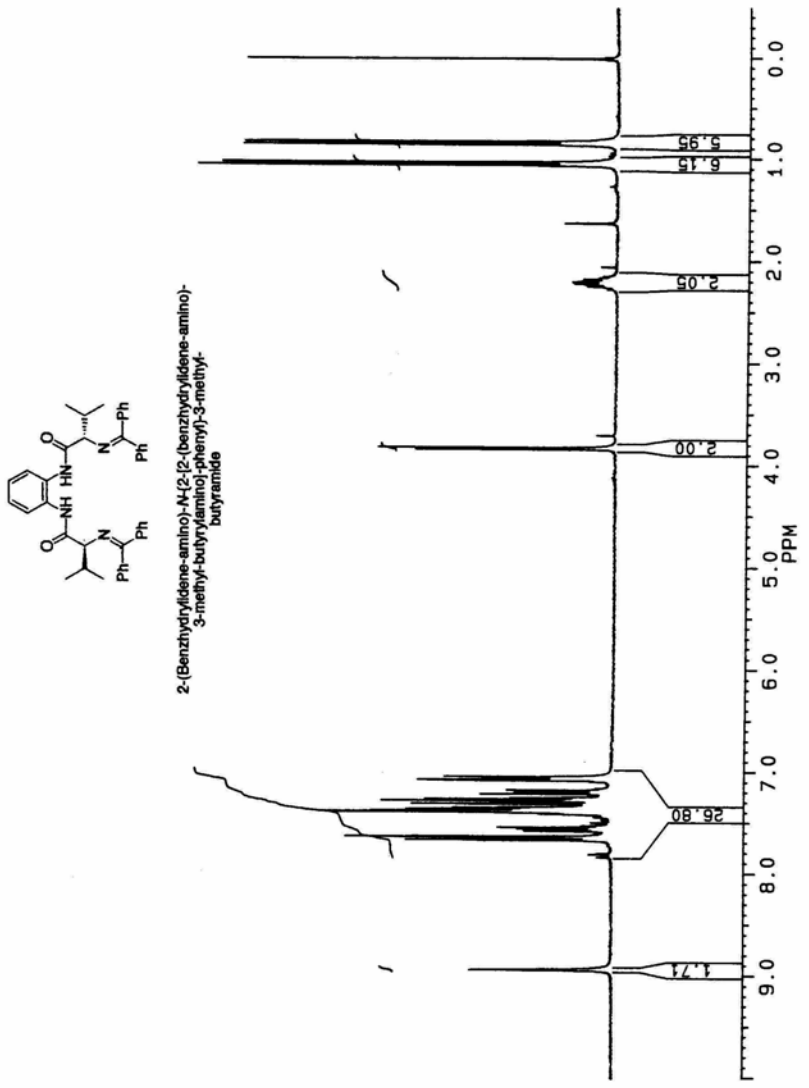
^{1}H NMR (250MHz, $CDCl_3$): δ 1.36 ppm, (d, 6H, CH_3, J = 6.9 Hz), δ 4.08 ppm, (q, 2H, CH_α, J = 6.9 Hz), δ 7.05 – 7.77 ppm, (aromatics, 24H), δ 9.35 ppm, (s, 2H, amide NH). ^{13}C-APT NMR (62.5 MHz, $CDCl_3$): CH_3 δ 20.9 ppm, CH_α δ 61.3 ppm, aromatic: CH δ 125.3, 126.0, 127.2, 128.0, 128.6, 130.5 ppm; C δ 130.2, 135.5, 138.7 ppm, -NH-CO-R δ 169.1 ppm, -N=CPh_2 δ 173.2 ppm.

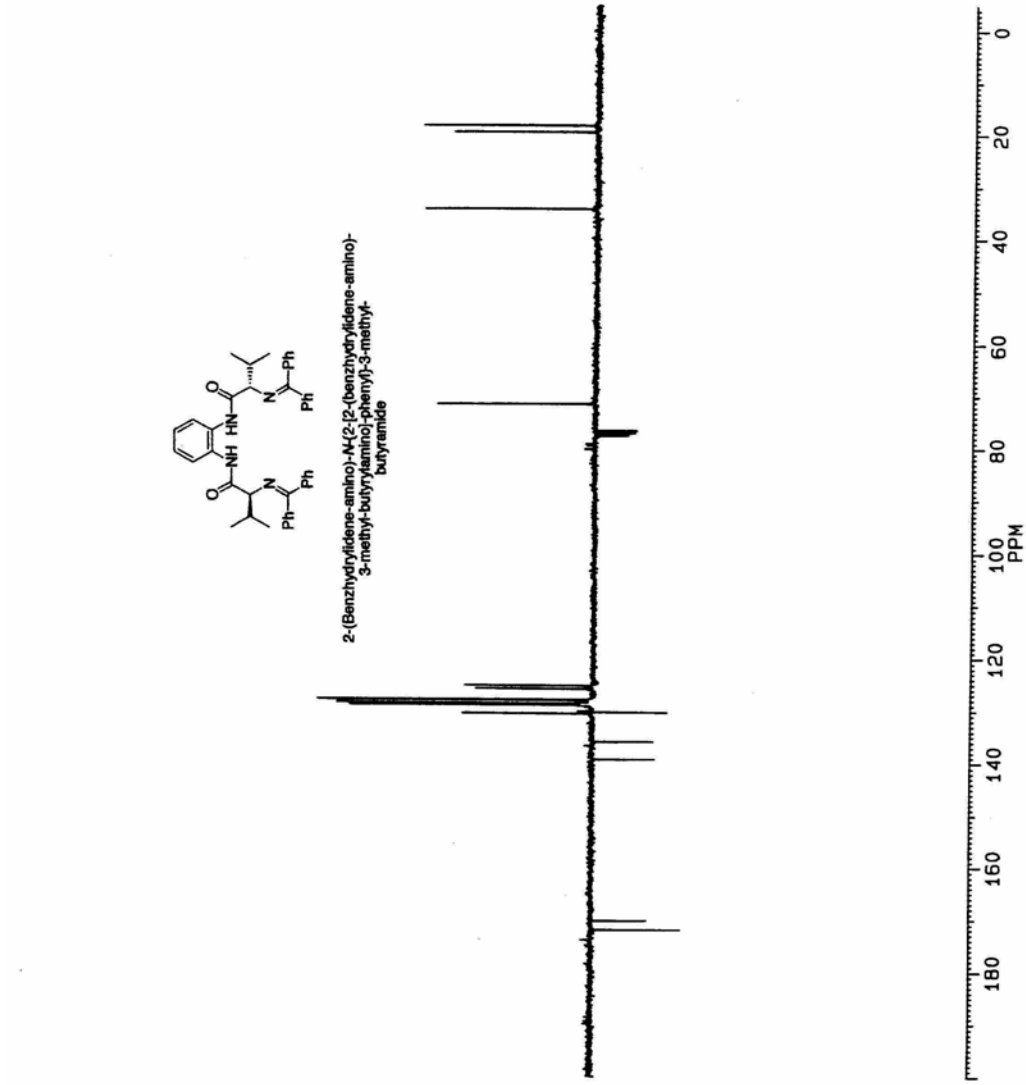

2-(Benzhydrylidene-amino)-N-{2-[2-(benzhydrylidene-amino)-propionylamino]-phenyl}-propionamide
5.641
2.007
27.663
2.144
PPM


2-(Benzhydrylidene-amino)-N-{2-[2-(benzhydrylidene-amino)-propionylamino]-phenyl}-propionamide
PPM
0
20
40
60
80
100
120
140
160
180

L-2-(Benzhydrylidene-amino)-*N*-{2-[2-(benzhydrylidene-amino)-3-methyl butyrylamino]-phenyl}-3-methyl-butyramide, **4**. 69% yield. $[\alpha]_D$ = (-) 20.2° (c = 0.82; $CHCl_3$)

^{1}H NMR (250MHz, $CDCl_3$): δ 0.82 ppm, (d, 6H, CH_3, J = 6.9 Hz), δ 1.02 ppm, (d, 6H, CH_3, J = 6.8 Hz), δ 2.13 ppm, (m, 2H, -C<u>H</u>$(CH_3)_2$), δ 3.81 ppm, (d, 2H, CH_α, J = 4.25 Hz), δ 7.1 – 7.85 ppm, (aromatics, 24H), δ 8.93 ppm, (s, 2H, amide NH).
^{13}C-APT NMR (62.5 MHz, $CDCl_3$): CH_3 δ 18.1, 19.4 ppm, CH δ 34.1 ppm, CH_α δ 71.3 ppm, aromatic: CH δ 125.1, 125.7, 127.8, 127.9, 128.5, 128.6, 128.8, 130.4 ppm; C δ 130.2, 135.8, 139.1 ppm, -NH-CO-R δ 170.1 ppm, -N=CPh_2 δ 171.8 ppm.


2-(Benzhydrylidene-amino)-N-[2-[2-(benzhydrylidene-amino)-3-methyl-butyrylamino]-phenyl]-3-methyl-butyramide
5.95
6.15
2.05
2.00
26.80
1.71
PPM

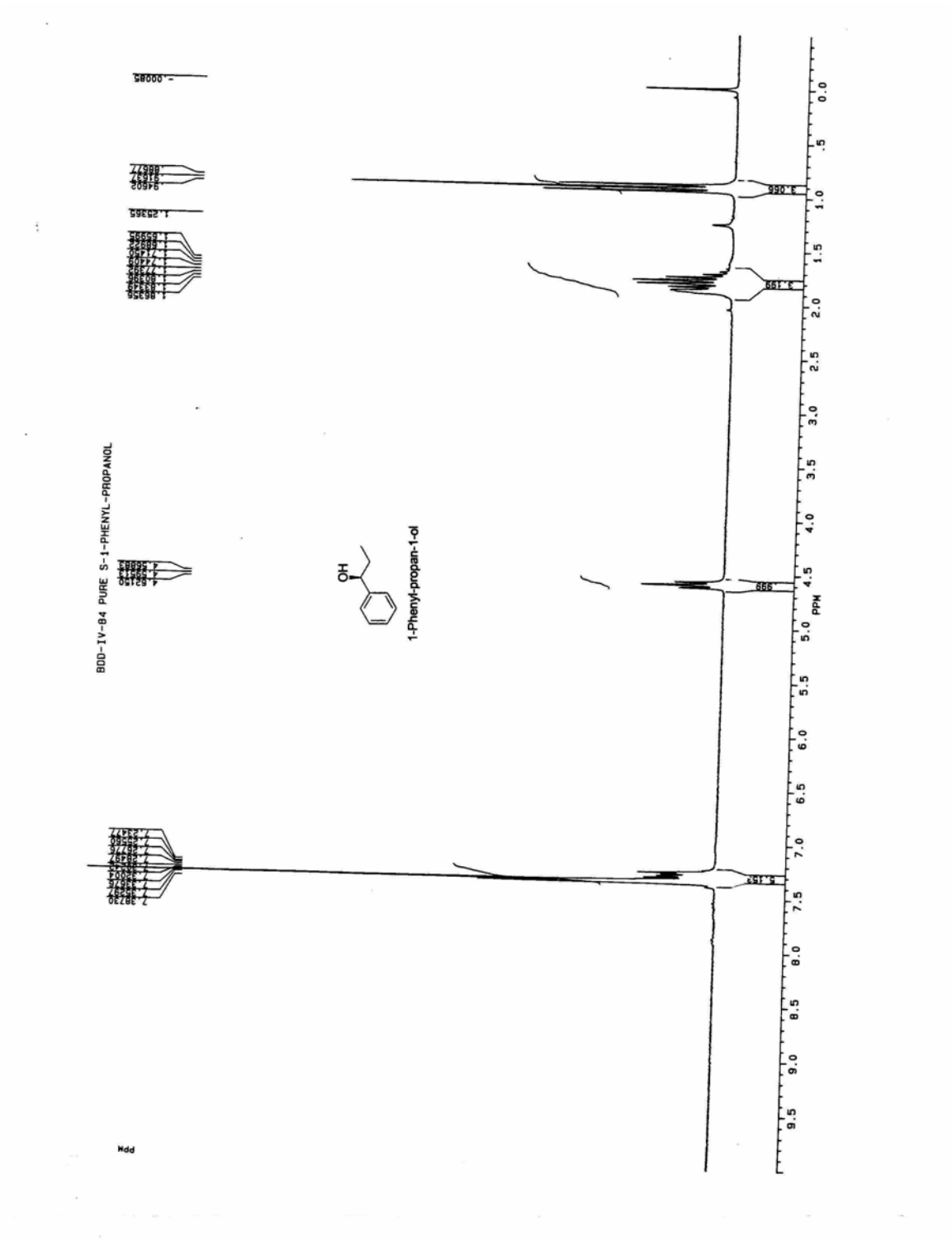

2-(Benzhydrylidene-amino)-N-{2-[2-(benzhydrylidene-amino)-3-methyl-butyrylamino]-phenyl}-3-methyl-butyramide
PPM
0
20
40
60
80
100
120
140
160
180

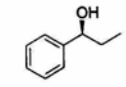
Diethyl Zinc Addition to Aldehydes Catalyzed by Chiral Zn(II)-L-(Phe)$_2$ Complex, 2. A general experimental for a typical catalyst study reaction is provided below. All reagents and solvents were freshly distilled and dried before use. The L-(Phe/Phe)-H_2 (219 mg, 0.3 mmol, 3 mole%) ligand was azeotropically dried with toluene. In a flame-dried 50 ml glass round bottom flask the ligand was dissolved in 3 ml of freshly distilled THF. To the clear homogeneous solution, a 0.5 M Et_2Zn solution in THF (0.64 ml, 0.32 mmol, 3.2 mole%) was added in a single portion. The resultant reaction mixture was heated to reflux for 1 hour. The Zn-complex is relatively stable and its formation can be monitored by TLC (8:2 hexanes / ethyl acetate). Two UV active spots are observed corresponding to the complex (R_f = 0.2) and the ligand (R_f = 0.75) which is generated from the hydrolysis of the complex during the TLC development. After complete insertion, the reaction mixture was cooled to –78°C and hydrocinnamyl aldehyde (1.34 g, 0.01 mole) was added in a single portion. A 0.5 M Et_2Zn solution in THF (26 ml, 0.013 mole, 1.3 equiv.) was then added dropwise over a 2 hour period. The reaction mixture was allowed to warm to room temperature where it reacted for 16 hours. The reaction was then cooled to 0°C and quenched with 1 M HCl. The THF was removed by rotary evaporation. The residue was diluted with ethyl acetate was washed twice with 1 M HCl. The organic layer was dried over $MgSO_4$, filtered and concentrated to an oil. The crude mixture was purified by flash column chromatography to provide the 2° alcohol as either a white solid or a clear colorless oil. In order to ensure that the material was pure for optical rotation, 1-phenyl-3-pentanol was sublimed and 3-undecanol was distilled under vacuum. If the alcohols could not be separated with the available chiral capillary GC's, the Mosher esters were formed. GC then proved to be an effective method for determining the enantioselectivities.

(S)-(-)-1-phenyl-propan-1-ol. The alcohol was isolated in an 85% yield. The conversion was monitored by capillary GC (Hewlett Packard 5890 series) using an SPB-5 column. GC conditions are as follows: Initial temperature – 100°C / 2 min. Final temperature – 275°C. Rate – 10°C / min. Injector – 200°C. Detector – 275°C. Flow – 80 psi. Retention times for the benzaldehyde and 1-phenyl-propan-1-ol are 5.32 min. and 7.99 min. respectively. The enantioselectivity was determined by capillary GC (Hewlett

Packard 5890 Series II Plus) using a Chiraldex β-pH column. GC conditions are as follows: 100°C isotherm. Injector – 220°C. Detector – 250°C. Flow – 1 ml/min. Retention times for R and S-1-phenyl-propan-1-ol are 64 min. and 68 min. respectively.

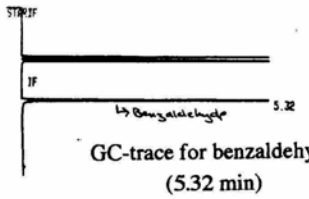
^{1}H NMR (250MHz, $CDCl_3$): δ 0.80 – 0.86 ppm, (t, 3H, CH_3, J = 7.42 Hz), δ 1.6 – 1.8 ppm, (m, 2H), δ 1.92 ppm, (broad s, 1H, -OH), δ 4.47 – 4.52 ppm, (t, 1H, CH, J = 6.6 Hz), δ 7.1 – 7.3 ppm, (m, aromatics 5H).


BDD-IV-84 PURE S-1-PHENYL-PROPANOL
1-Phenyl-propan-1-ol
OH
PPM



1-Phenyl-propan-1-ol

Capillary GC-traces for the synthesis of 1-phenyl-1-propanol.
-Determination of the extent of conversion (PhCHO —> 1-phenyl-1-propanol)



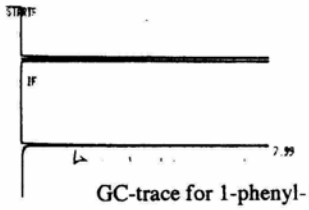
GC-trace for benzaldehyde
(5.32 min)

RUN # 435
WORKFILE ID: C
WORKFILE NAME:

AREA%

RT	AREA	TYPE	AR/HT	AREA%
5.32	387160	PB	0.044	100.000

TOTAL AREA= 387160
MUL FACTOR= 1.0000E+00



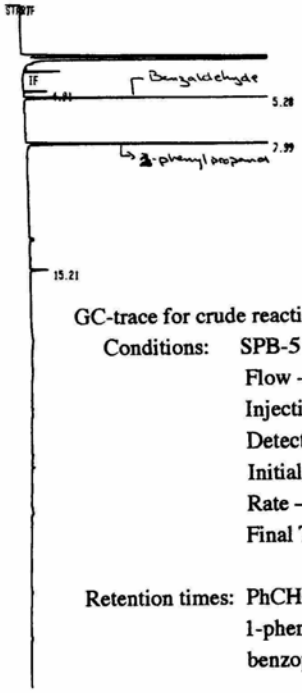
GC-trace for 1-phenyl-1-propanol
(7.99 min)

RUN # 436
WORKFILE ID: C
WORKFILE NAME:

AREA%

RT	AREA	TYPE	AR/HT	AREA%
7.99	122000	PB	0.046	100.000

TOTAL AREA= 122000
MUL FACTOR= 1.0000E+00



GC-trace for crude reaction mixture

Conditions: SPB-5 column
Flow – 80 psi
Injection Temp. – 200°C
Detector Temp. – 275°C
Initial Temp. – 100°C for 2 min
Rate – 10°C / min
Final Temp. – 275°C

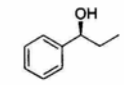
Retention times: PhCHO – 5.28 min
1-phenyl-1-propanol – 7.99 min
benzophenone – 15.21 min

RUN # 433
WORKFILE ID: C
WORKFILE NAME:

AREA%

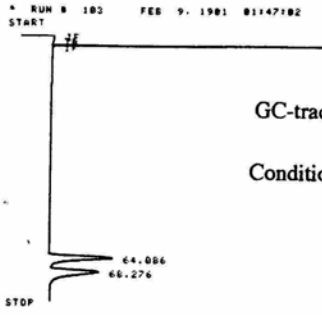
RT	AREA	TYPE	AR/HT	AREA%
4.91	1703	PB	0.037	0.721
5.28	33649	PB	0.043	14.242
7.99	198870	PB	0.050	84.170
15.21	2050	PB	0.058	0.868

TOTAL AREA= 236270
MUL FACTOR= 1.0000E+00



1-Phenyl-propan-1-ol

Capillary GC-traces for the synthesis of 1-phenyl-1-propanol.
–Determination of the enantioselectivity for the conversion of PhCHO to 1-phenyl-1-propanol



GC-trace for (±)-1-phenyl-1-propanol

Conditions: Chiraldex β-pH column
Flow – 1 ml / min
Injection Temp. – 220°C
Detector Temp. – 250°C
100°C Isotherm

Retention times: (R) - 1-phenyl-1-propanol – 64.1 min
(S) - 1-phenyl-1-propanol – 68.3 min

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RUN# 103 FEB 9. 1901 01:47:02

SIGNAL FILE: M:SIGNAL.BNC
AREA%

RT	AREA	TYPE	WIDTH	AREA%
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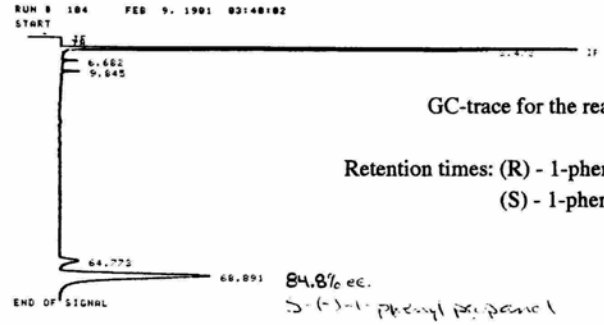
68.276	176492	VV	1.866	50.51302



GC-trace for the reaction mixture

Retention times: (R) - 1-phenyl-1-propanol – 64.7 min
(S) - 1-phenyl-1-propanol – 68.9 min

Closing signal file M:SIGNAL .BNA

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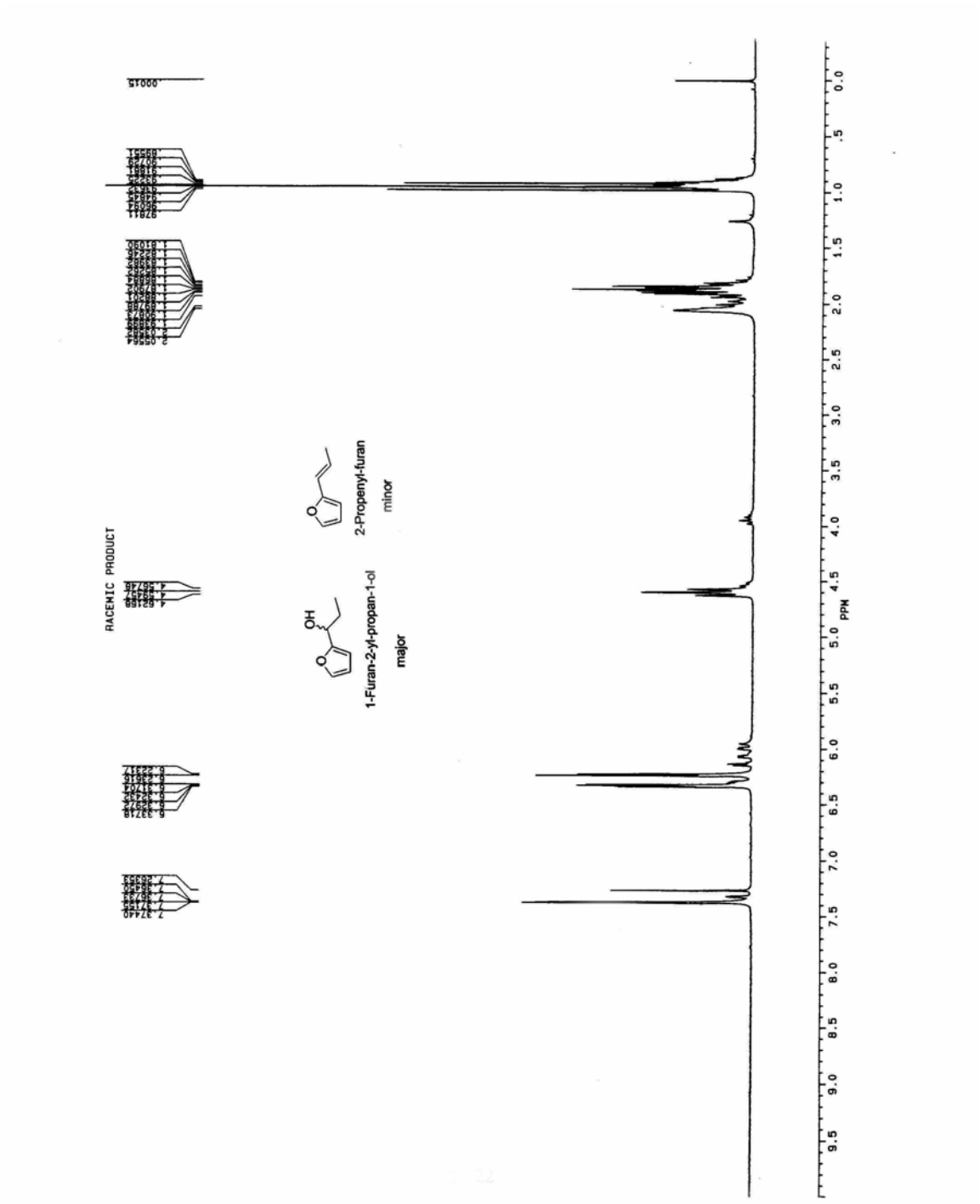
SIGNAL FILE: M:SIGNAL.BNA
AREA%

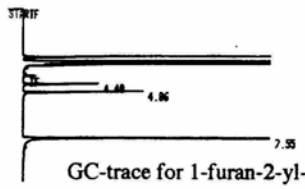
RT	AREA	TYPE	WIDTH	AREA%
3.473	6193	BB	.064	8.02316
6.682	941	PV	.261	1.21989
9.845	801	BP	.230	1.03771
64.773	5270	PV	1.107	6.82740
68.891	63964	VV	1.926	82.89264

(S)-1-furan-2-yl-propan-1-ol. The alcohol was isolated in a 30% yield. The conversion was monitored by capillary GC (Hewlett Packard 5890 series) using an SPB-5 column. GC conditions are as follows: Initial temperature – 100°C / 2 min. Final temperature – 275°C. Rate – 10°C / min. Injector – 200°C. Detector – 275°C. Flow – 80 psi. Retention times for the 2-furaldehyde and 1-furan-2-yl-propan-1-ol are 5.22 min. and 7.55 min. respectively. The enantioselectivity was determined by capillary GC (Varian 3800 Series) using a Chiraldex γ-TA (Gamma-cyclodextrin trifluoroacetyl) column. GC conditions are as follows: 60°C isotherm. Injector – 200°C. Detector – 200°C. Flow – 1.1 ml/min. Retention times for S and R-1-furan-2-yl-propan-1-ol are 63 min. and 66 min. respectively.

^{1}H NMR (250MHz, $CDCl_3$): δ 0.92 – 0.98 ppm, (t, 3H, CH_3, J = 7.42 Hz), δ 1.7 – 1.9 ppm, (m, 2H), δ 2.05 ppm, (broad s, 1H, -OH), δ 4.56 – 4.62 ppm, (t, 1H, CH, J = 6.78 Hz), δ 6.2 ppm, (d, 1H, CH, J = 3.25 Hz), δ 6.31 – 6.33 ppm, (dd, 1H, CH, J = 1.85 Hz, J = 3.19 Hz), δ 7.36 – 7.37 ppm, (dd, 1H, CH, J = 0.7 Hz, J = 1.76 Hz).


RACEMIC PRODUCT
1-Furan-2-yl-propan-1-ol
major
2-Propenyl-furan
minor
PPM

Capillary GC-traces for the synthesis of 1-furan-2-yl-propan-1-ol.
–Determination of the extent of conversion (2-furaldehyde —> 1-furan-2-yl-propan-1-ol).



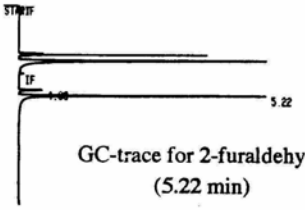
GC-trace for 1-furan-2-yl-propan-1-ol (7.55 min)

RUN # 687
WORKFILE ID: C
WORKFILE NAME:

AREA%

RT	AREA	TYPE	AR/HT	AREA%
4.40	5572	PB	0.038	3.511
4.86	8323	PB	0.036	5.245
7.55	144796	PB	0.045	91.243

TOTAL AREA= 158688
MUL FACTOR= 1.0000E+00



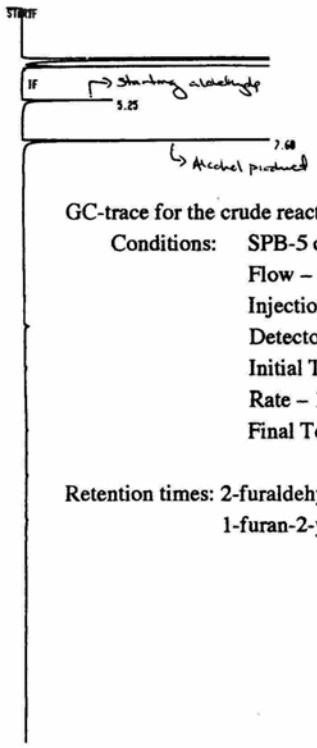
GC-trace for 2-furaldehyde (5.22 min)

RUN # 688
WORKFILE ID: C
WORKFILE NAME:

AREA%

RT	AREA	TYPE	AR/HT	AREA%
4.88	2168	PB	0.046	0.867
5.22	248238	PB	0.046	99.133

TOTAL AREA= 242338
MUL FACTOR= 1.0000E+00



GC-trace for the crude reaction mixture

Conditions: SPB-5 column
Flow – 80 psi
Injection Temp. – 200°C
Detector Temp. – 275°C
Initial Temp – 100°C for 2 min
Rate – 10°C / min
Final Temp. – 275°C

Retention times: 2-furaldehyde – 5.25 min
1-furan-2-yl-propan-1-ol – 7.60 min

RUN # 686
WORKFILE ID: C
WORKFILE NAME:

AREA%

RT	AREA	TYPE	AR/HT	AREA%
5.25	8729	PB	0.051	7.116
7.60	113950	PB	0.044	92.885

TOTAL AREA= 122680
MUL FACTOR= 1.0000E+00

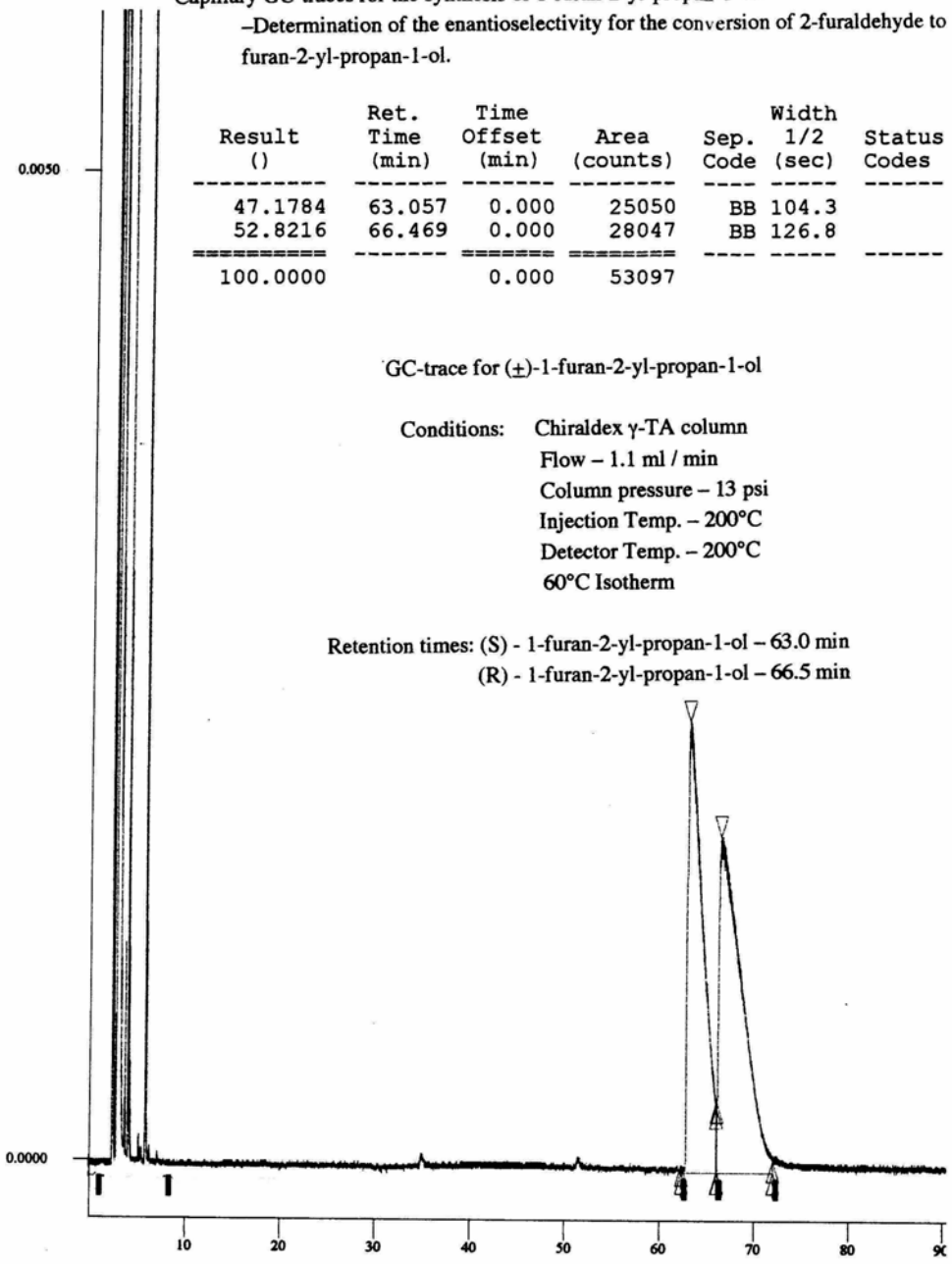
Capillary GC-traces for the synthesis of 1-furan-2-yl-propan-1-ol.
–Determination of the enantioselectivity for the conversion of 2-furaldehyde to 1-furan-2-yl-propan-1-ol.

Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
47.1784	63.057	0.000	25050	BB	104.3	
52.8216	66.469	0.000	28047	BB	126.8	
100.0000		0.000	53097			

GC-trace for (±)-1-furan-2-yl-propan-1-ol

Conditions: Chiraldex γ-TA column
Flow – 1.1 ml / min
Column pressure – 13 psi
Injection Temp. – 200°C
Detector Temp. – 200°C
60°C Isotherm

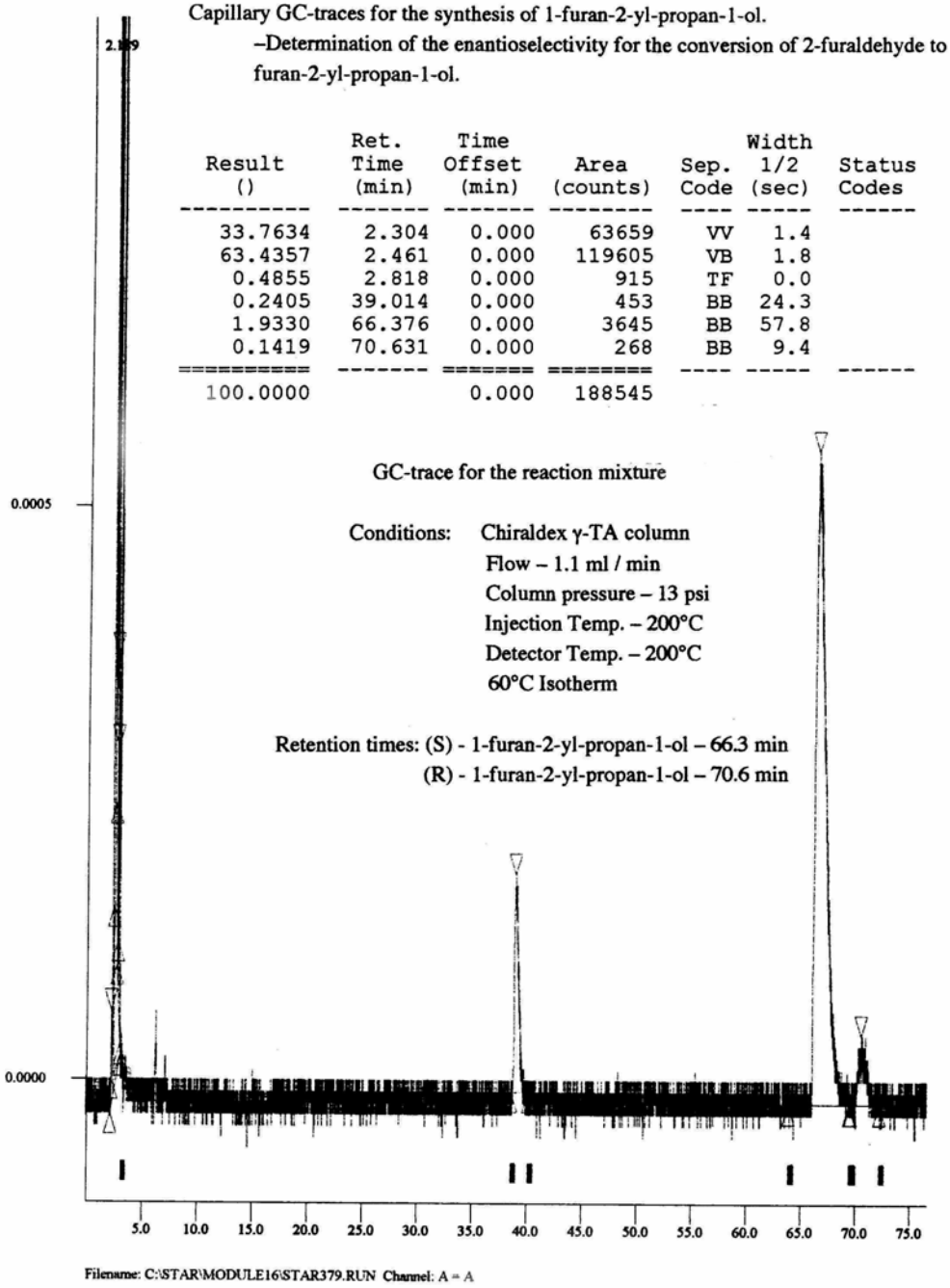
Retention times: (S) - 1-furan-2-yl-propan-1-ol – 63.0 min
(R) - 1-furan-2-yl-propan-1-ol – 66.5 min



Filename: C:\STAR\MODULE16\STAR384.RUN Channel: A = A

Capillary GC-traces for the synthesis of 1-furan-2-yl-propan-1-ol.
–Determination of the enantioselectivity for the conversion of 2-furaldehyde to 1-furan-2-yl-propan-1-ol.

Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
33.7634	2.304	0.000	63659	VV	1.4	
63.4357	2.461	0.000	119605	VB	1.8	
0.4855	2.818	0.000	915	TF	0.0	
0.2405	39.014	0.000	453	BB	24.3	
1.9330	66.376	0.000	3645	BB	57.8	
0.1419	70.631	0.000	268	BB	9.4	
100.0000		0.000	188545			



GC-trace for the reaction mixture

Conditions: Chiraldex γ-TA column
Flow – 1.1 ml / min
Column pressure – 13 psi
Injection Temp. – 200°C
Detector Temp. – 200°C
60°C Isotherm

Retention times: (S) - 1-furan-2-yl-propan-1-ol – 66.3 min
(R) - 1-furan-2-yl-propan-1-ol – 70.6 min

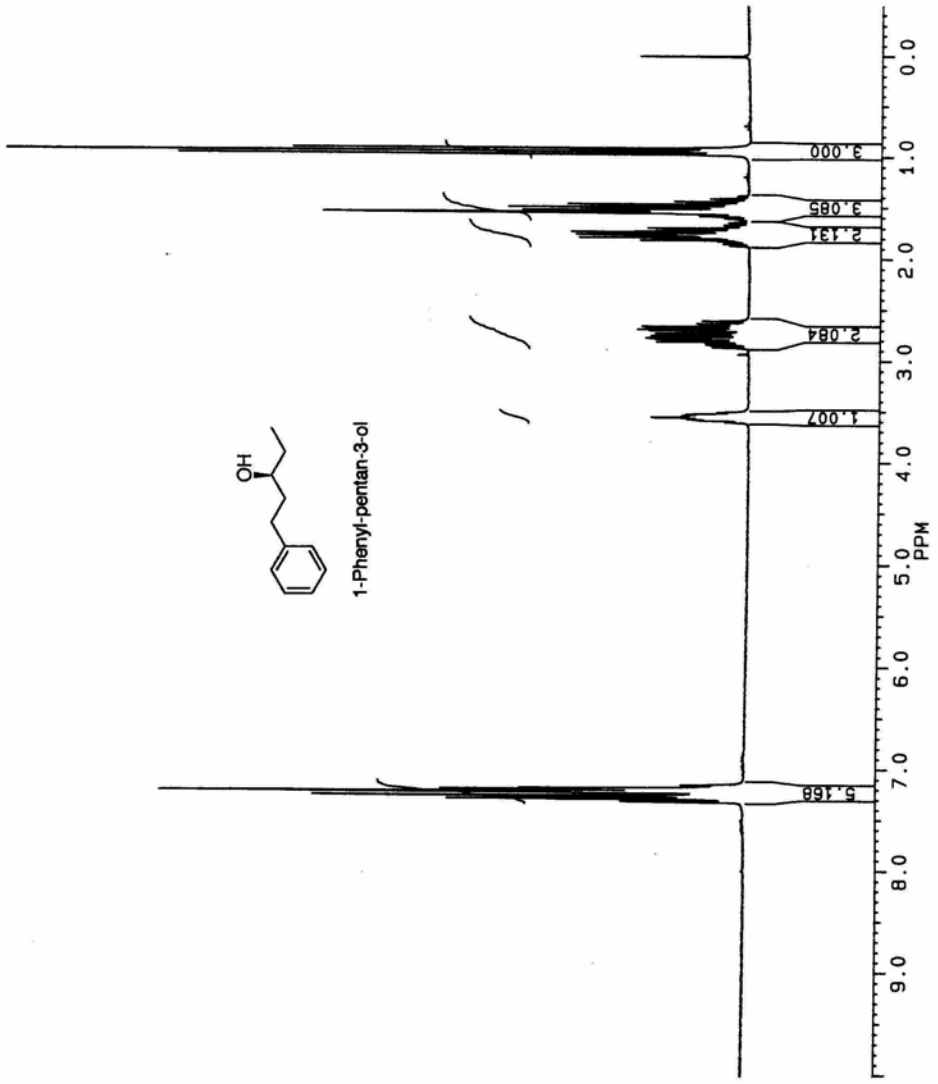
Filename: C:\STAR\MODULE16\STAR379.RUN Channel: A = A

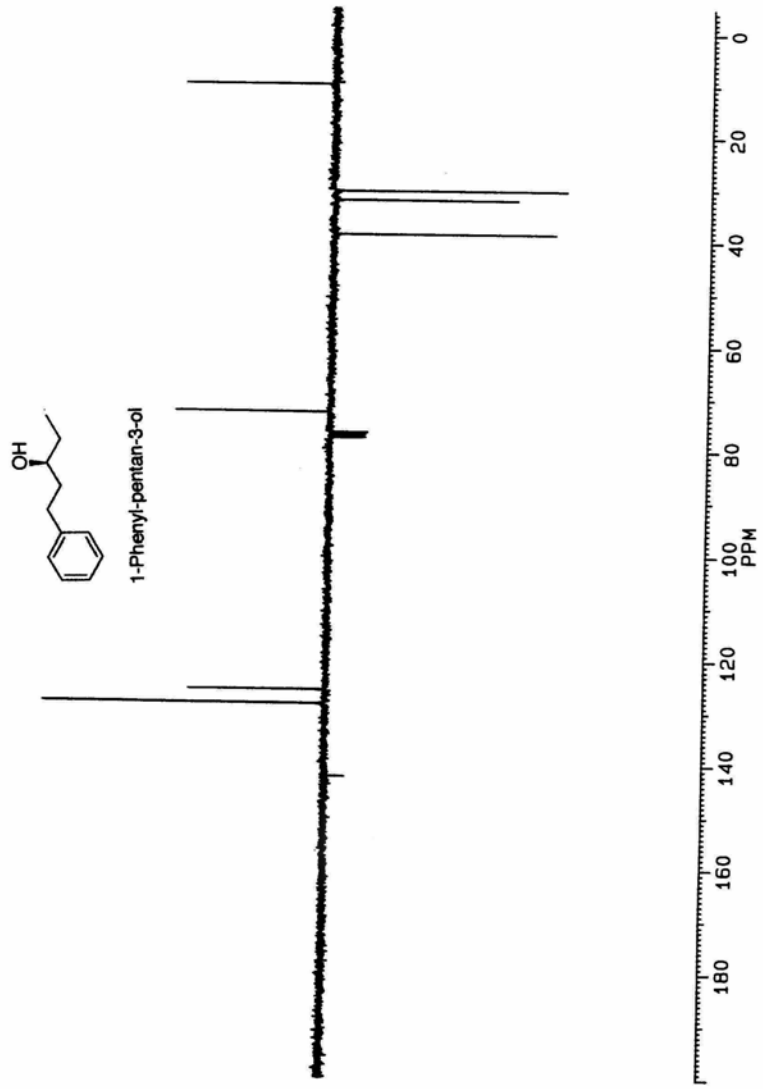
(S)-(+)-1-phenyl-pentan-3-ol. The alcohol was isolated in a 30% yield. The conversion was monitored by capillary GC (Hewlett Packard 5890 series) using an SPB-5 column. GC conditions are as follows: Initial temperature – 100°C / 2 min. Final temperature – 275°C. Rate – 10°C / min. Injector – 200°C. Detector – 275°C. Flow – 80 psi. Retention times for the hydrocinnamyl aldehyde and 1-phenyl-pentan-3-ol are 8.44 min. and 11.45 min. respectively. After purification of the crude reaction mixture, formation of the Mosher ester was achieved by treating a small portion of the alcohol with the corresponding R-(-)-Mosher acid chloride. The enantioselectivity of the ester was then determined by capillary GC (Varian 3800 Series) using a Chiraldex β-TA (Beta-cyclodextrin trifluoroacetyl) column. GC conditions are as follows: 140°C isotherm. Injector – 200°C. Detector – 200°C. Flow – 1.1 ml/min. Retention times for RR and RS Mosher esters of 1-furan-2-yl-propan-1-ol are 297 min. and 306 min. respectively.

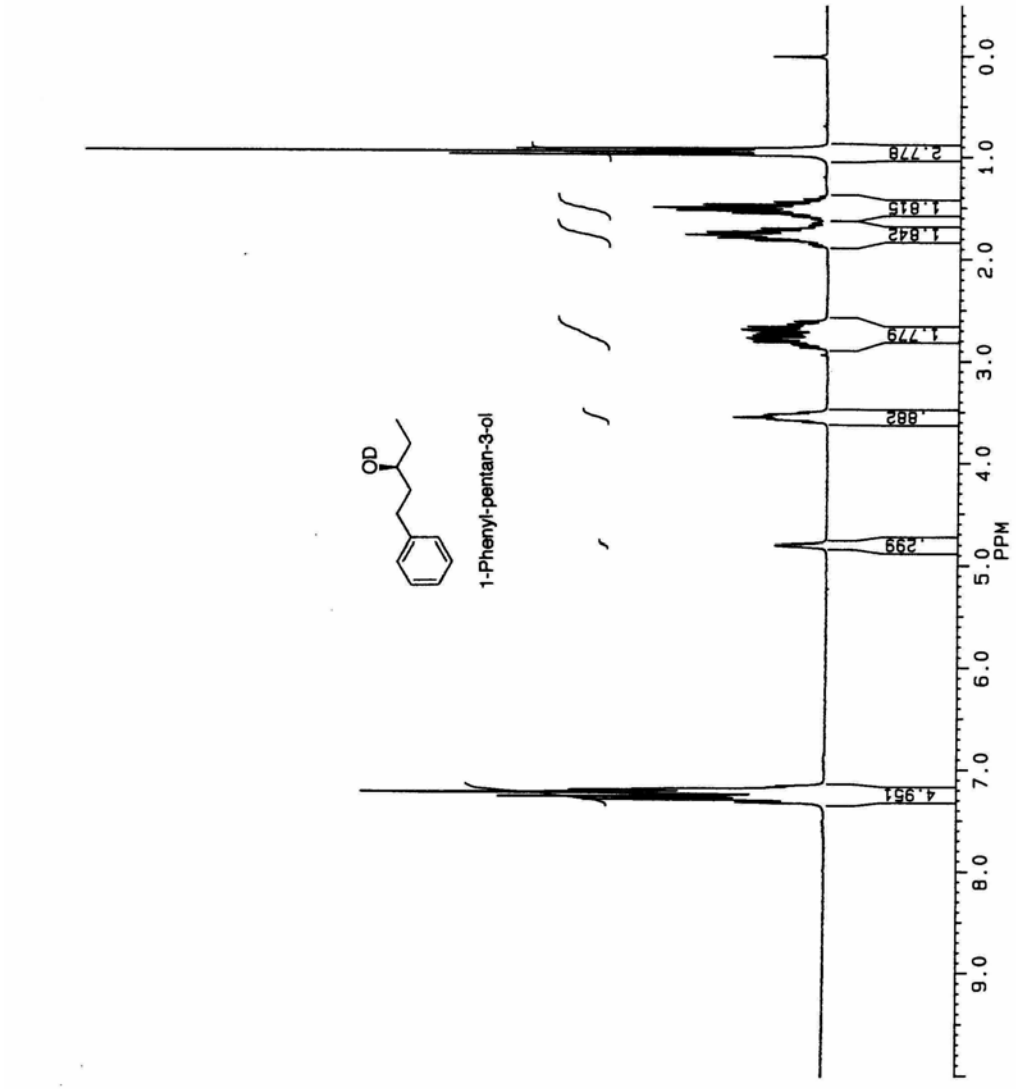
^{1}H NMR (250MHz, $CDCl_3$) of (S)-(+)-1-phenyl-pentan-3-ol (94% e.e. S enantiomer): δ 0.90 – 0.97 ppm, (t, 3H, CH_3, J = 7.42 Hz), δ 1.4 – 1.57 ppm, (m, 2H, CH_2), δ 1.66 – 1.82 ppm, (m, 2H, CH_2), δ 2.59 – 2.85 ppm, (m, 2H, CH_2, δ 3.49 – 3.58 ppm, (m, 1H, CH), aromatics: (5H) δ 7.14 – 7.31 ppm.

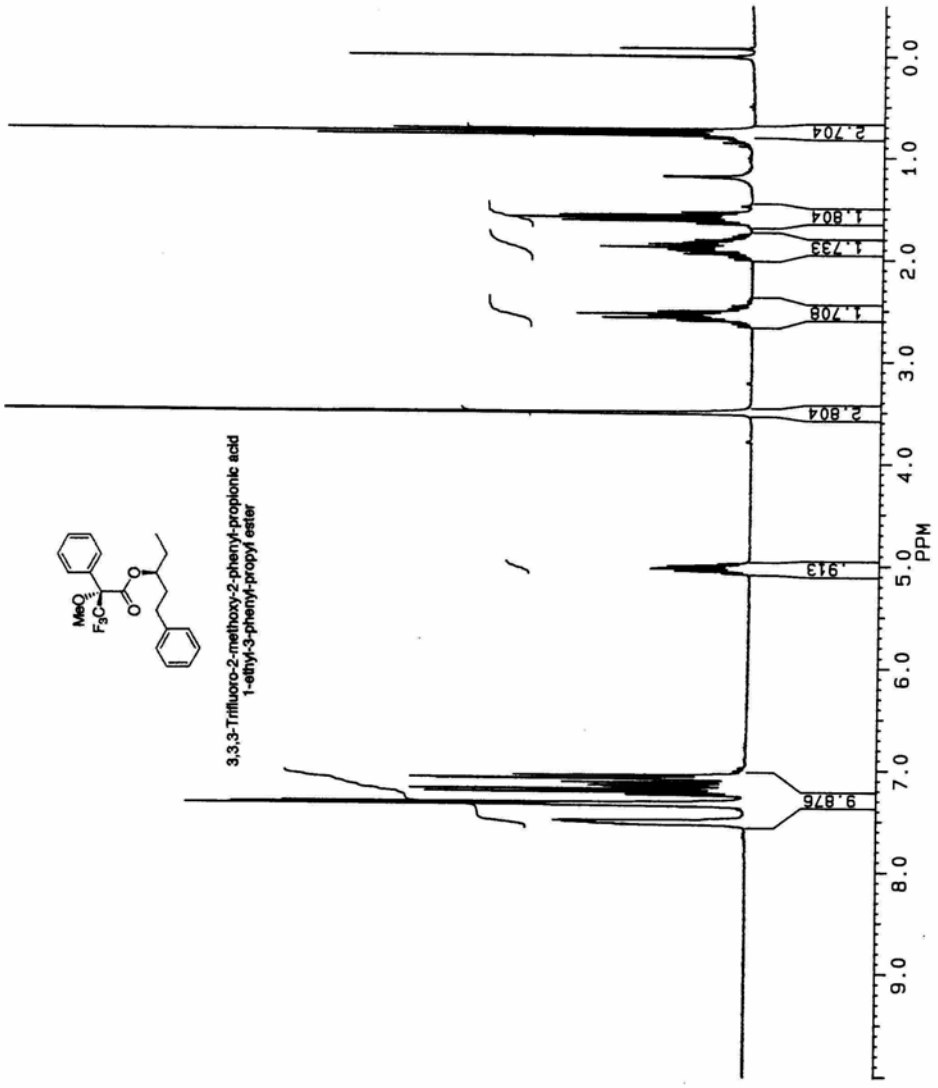
^{13}C-APT NMR (62.5 MHz, $CDCl_3$) of (S)-(+)-1-phenyl-pentan-3-ol (94% e.e. S enantiomer): CH_3 δ 9.8 ppm, CH_2 δ 30.2, 32.0, 38.5 ppm, CH δ 72.5 ppm, aromatic: CH δ 125.7, 128.32, 128.35 ppm, C δ 142.2 ppm.

^{1}H NMR (250MHz, $CDCl_3$) of (R)-3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid-(S)-1-ethyl-3-phenyl-propyl ester (94% e.e. S enantiomer): δ 0.72 – 0.78 ppm, (t, 3H, CH_3, J = 7.42 Hz), δ 1.53 – 1.64 ppm, (apparent pentet, 2H, CH_2, J = 7.33 Hz), δ 1.78 – 1.96 ppm, (m, 2H, CH_2), δ 2.47 – 2.59 ppm, (m, 2H, CH_2), δ 5.02 ppm, (s, 3H, -OCH_3), δ 4.97 – 5.06 ppm, (p, 1H, CH, J = 6.0 Hz), aromatics: (10H) δ 7.04 – 7.23 ppm, (m), δ 7.3 – 7.34 ppm, (m), δ 7.48 – 7.52 ppm, (m).

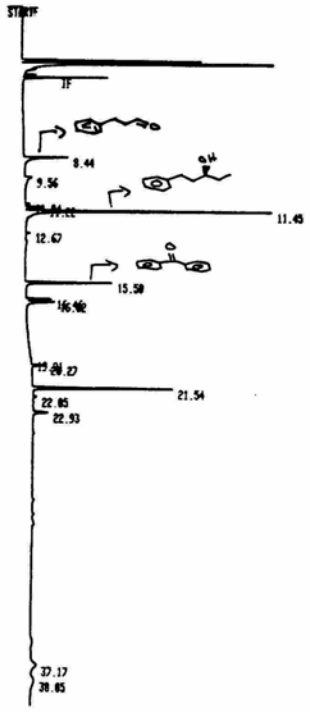

OH
1-Phenyl-pentan-3-ol
3.000
3.085
2.131
2.084
1.007
5.168
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
PPM


OH
1-Phenyl-pentan-3-ol
0
20
40
60
80
100
120
140
160
180
PPM


OD
1-Phenyl-pentan-3-ol
2.778
1.815
1.842
1.779
.882
.299
4.951
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
PPM


3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-3-phenyl-propyl ester
MeO
F3C
O
O
2.704
1.804
1.733
1.708
2.804
.913
9.876
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
PPM

Capillary GC-traces for the synthesis of 1-phenyl-3-pentanol.
–Determination of the extent of conversion (hydrocinnamyl aldehyde —> 1-phenyl-3-pentanol).



GC-trace for the crude reaction mixture
Conditions: SPB-5 column
Flow – 80 psi
Injection Temp. – 200°C
Detector Temp. – 275°C
Initial Temp – 100°C for 2 min
Rate – 10°C / min
Final Temp. – 275°C

Retention times: hydrocinnamyl aldehyde – 8.44 min
1-phenyl-3-pentanol – 11.45 min
benzophenone – 15.5 min

RUN # 182
WORKFILE ID: C
WORKFILE NAME:

AREA%:

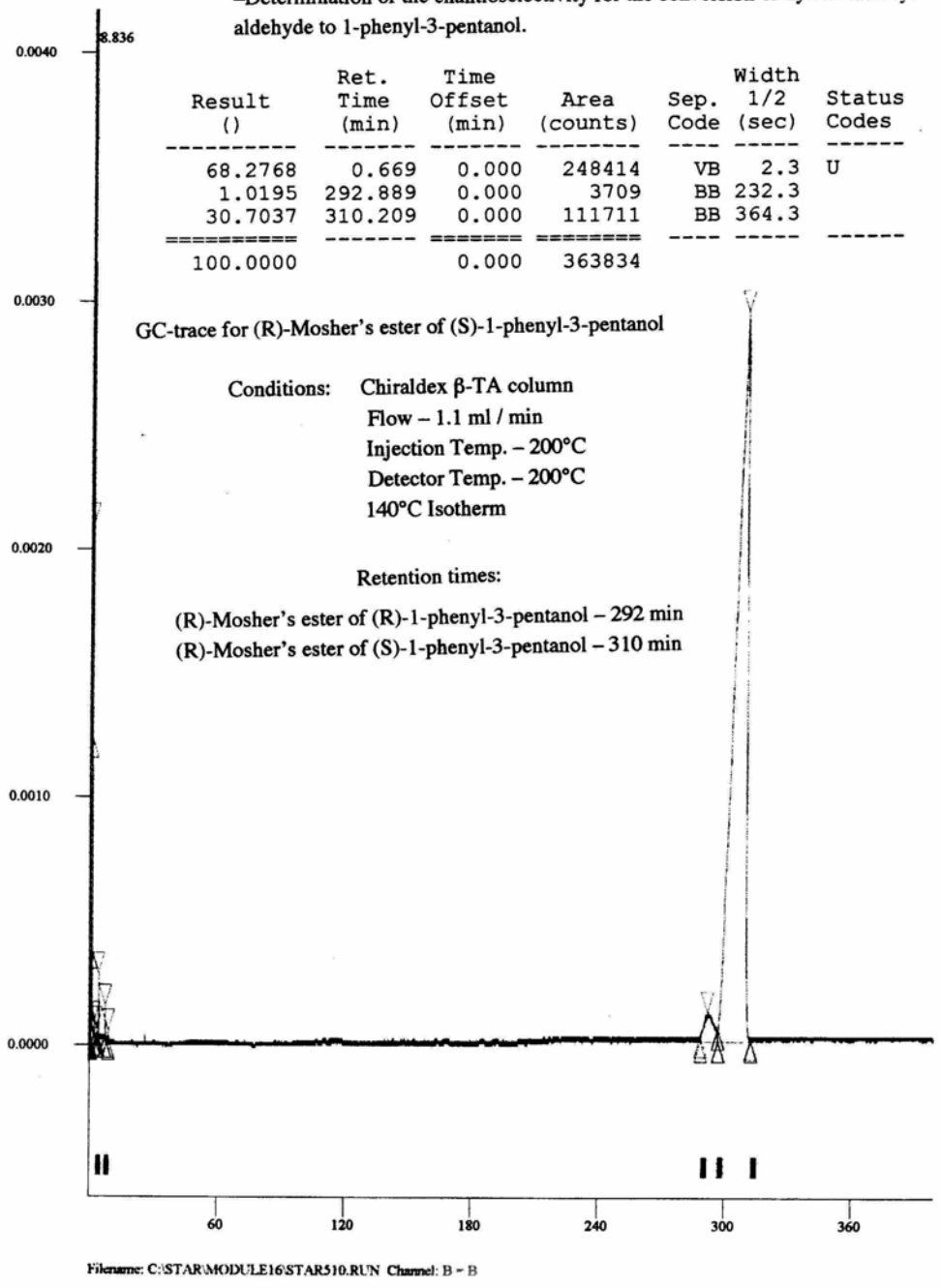
RT	AREA	TYPE	AR/HT	AREA%
8.44	6462	PB	0.079	4.815
9.56	3285	PB	0.244	2.388
11.04	452	PP	0.054	0.337
11.22	2251	PP	0.064	1.677
11.45	72082	PB	0.052	53.714
12.67	469	BB	0.068	0.350
15.50	10376	PB	0.063	7.732
16.46	3236	PV	0.068	2.411
16.62	4985	VB	0.093	3.715
19.91	291	PV	0.269	0.217
20.27	2038	VB	0.077	1.519
21.54	18859	PB	0.070	14.053
22.85	609	BB	0.091	0.454
22.93	2517	BB	0.092	1.876
37.17	3232	BV	0.354	2.408
38.85	3131 I	VP	0.512	2.333

TOTAL AREA= 134200
MUL FACTOR= 1.0000E+00

Capillary GC-traces for the synthesis of 1-phenyl-3-pentanol.

–Determination of the enantioselectivity for the conversion of hydrocinnamyl aldehyde to 1-phenyl-3-pentanol.

Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
68.2768	0.669	0.000	248414	VB	2.3	U
1.0195	292.889	0.000	3709	BB	232.3	
30.7037	310.209	0.000	111711	BB	364.3	
100.0000		0.000	363834			



GC-trace for (R)-Mosher's ester of (S)-1-phenyl-3-pentanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

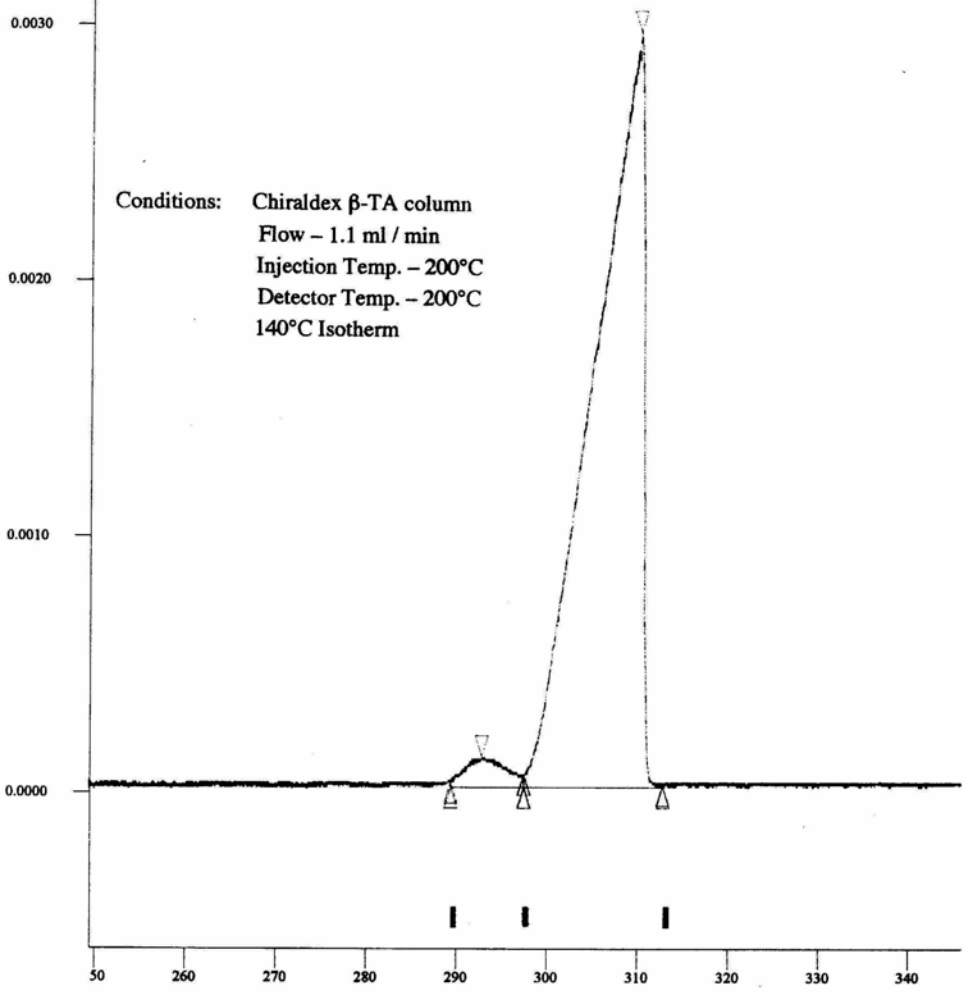
Retention times:

(R)-Mosher's ester of (R)-1-phenyl-3-pentanol – 292 min
(R)-Mosher's ester of (S)-1-phenyl-3-pentanol – 310 min

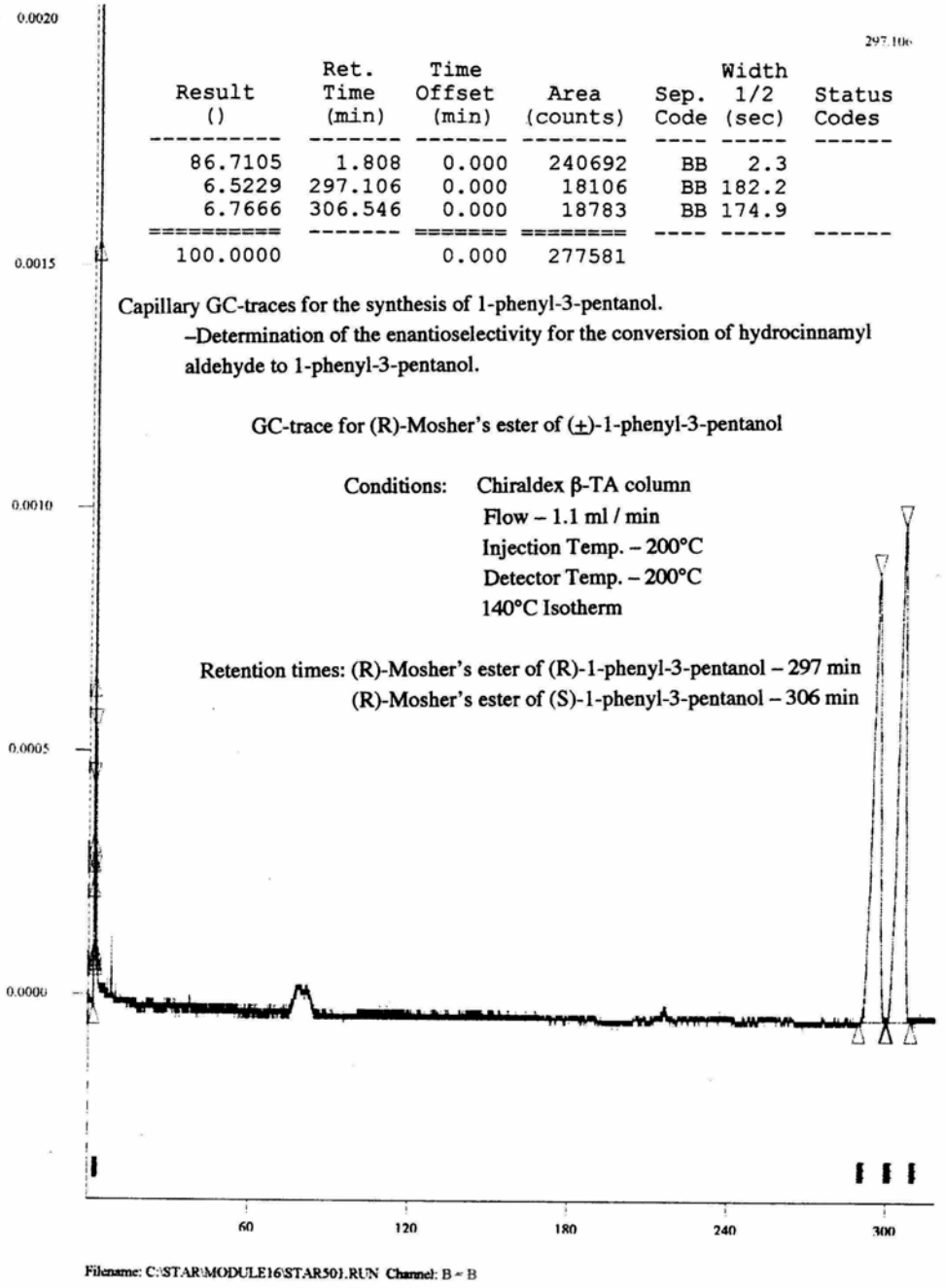
Capillary GC-traces for the synthesis of 1-phenyl-3-pentanol.
–Determination of the enantioselectivity for the conversion of hydrocinnamyl aldehyde to 1-phenyl-3-pentanol.

GC-trace for (R)-Mosher's ester of (S)-1-phenyl-3-pentanol

Retention times: (R)-Mosher's ester of (R)-1-phenyl-3-pentanol – 292 min
(R)-Mosher's ester of (S)-1-phenyl-3-pentanol – 310 min



Filename: C:\STAR\MODULE16\STAR510.RUN Channel: B = B



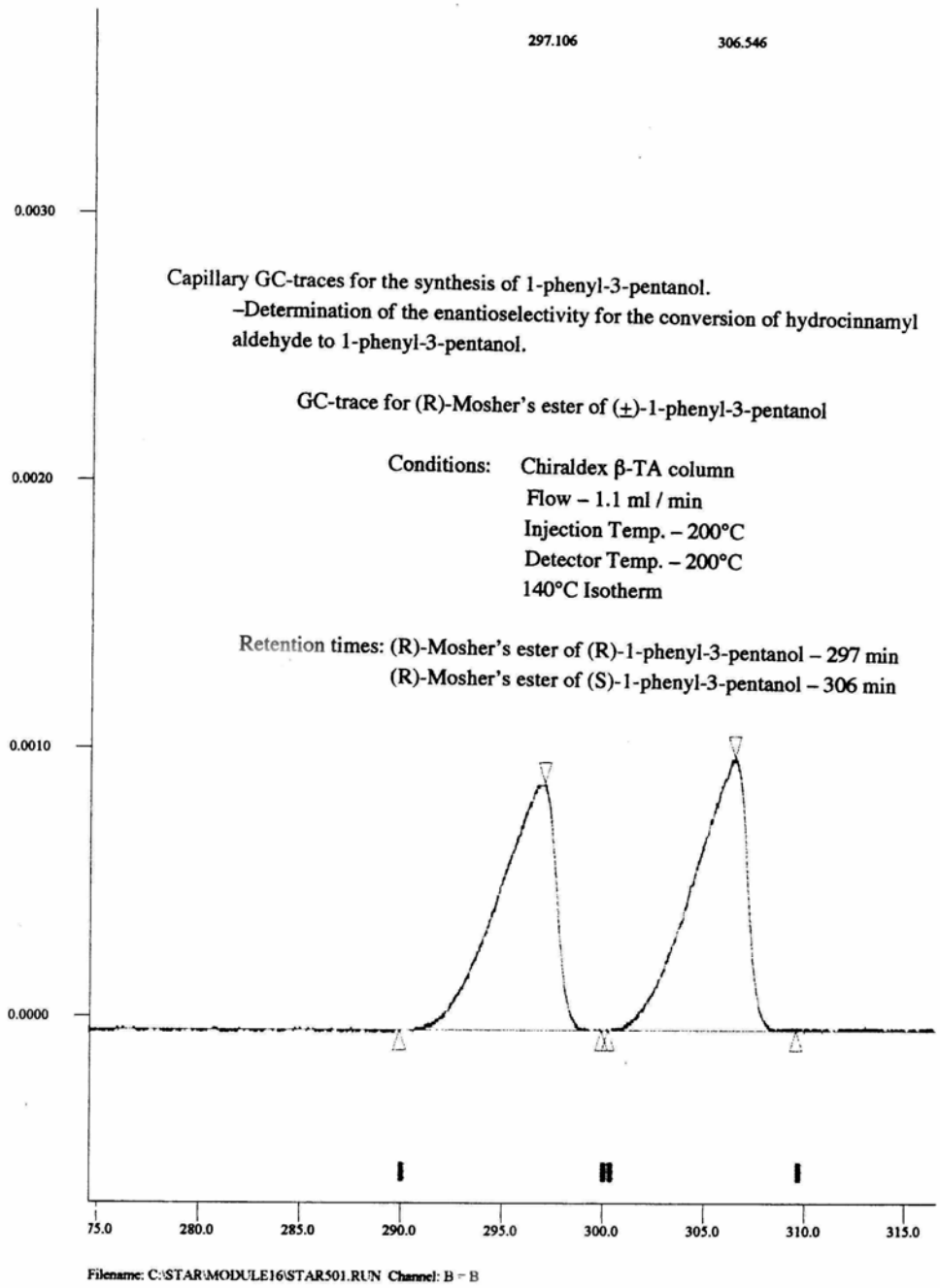
Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
86.7105	1.808	0.000	240692	BB	2.3	
6.5229	297.106	0.000	18106	BB	182.2	
6.7666	306.546	0.000	18783	BB	174.9	
100.0000		0.000	277581			

Capillary GC-traces for the synthesis of 1-phenyl-3-pentanol.
–Determination of the enantioselectivity for the conversion of hydrocinnamyl aldehyde to 1-phenyl-3-pentanol.

GC-trace for (R)-Mosher's ester of (±)-1-phenyl-3-pentanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

Retention times: (R)-Mosher's ester of (R)-1-phenyl-3-pentanol – 297 min
(R)-Mosher's ester of (S)-1-phenyl-3-pentanol – 306 min



Capillary GC-traces for the synthesis of 1-phenyl-3-pentanol.
–Determination of the enantioselectivity for the conversion of hydrocinnamyl aldehyde to 1-phenyl-3-pentanol.

GC-trace for (R)-Mosher's ester of (±)-1-phenyl-3-pentanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

Retention times: (R)-Mosher's ester of (R)-1-phenyl-3-pentanol – 297 min
(R)-Mosher's ester of (S)-1-phenyl-3-pentanol – 306 min

(S)-(+)-undecan-3-ol. The alcohol was isolated in a 30% yield. The conversion was monitored by capillary GC (Hewlett Packard 5890 series) using an SPB-5 column. GC conditions are as follows: Initial temperature – 100°C / 2 min. Final temperature – 275°C. Rate – 10°C / min. Injector – 200°C. Detector – 275°C. Flow – 80 psi. Retention times for the nonyl aldehyde and undecan-3-ol are 7.41 min. and 10.37 min. respectively. After purification of the crude reaction mixture, formation of the Mosher ester was achieved by treating a small portion of the alcohol with the corresponding R-(-)-Mosher acid chloride. The enantioselectivity of the ester was then determined by capillary GC (Varian 3800 Series) using a Chiraldex β-TA (Beta-cyclodextrin trifluoroacetyl) column. GC conditions are as follows: 140°C isotherm. Injector – 200°C. Detector – 200°C. Flow – 1.1 ml/min. Retention times for RR and RS Mosher esters of undecan-3-ol are 143 min. and 146 min. respectively.

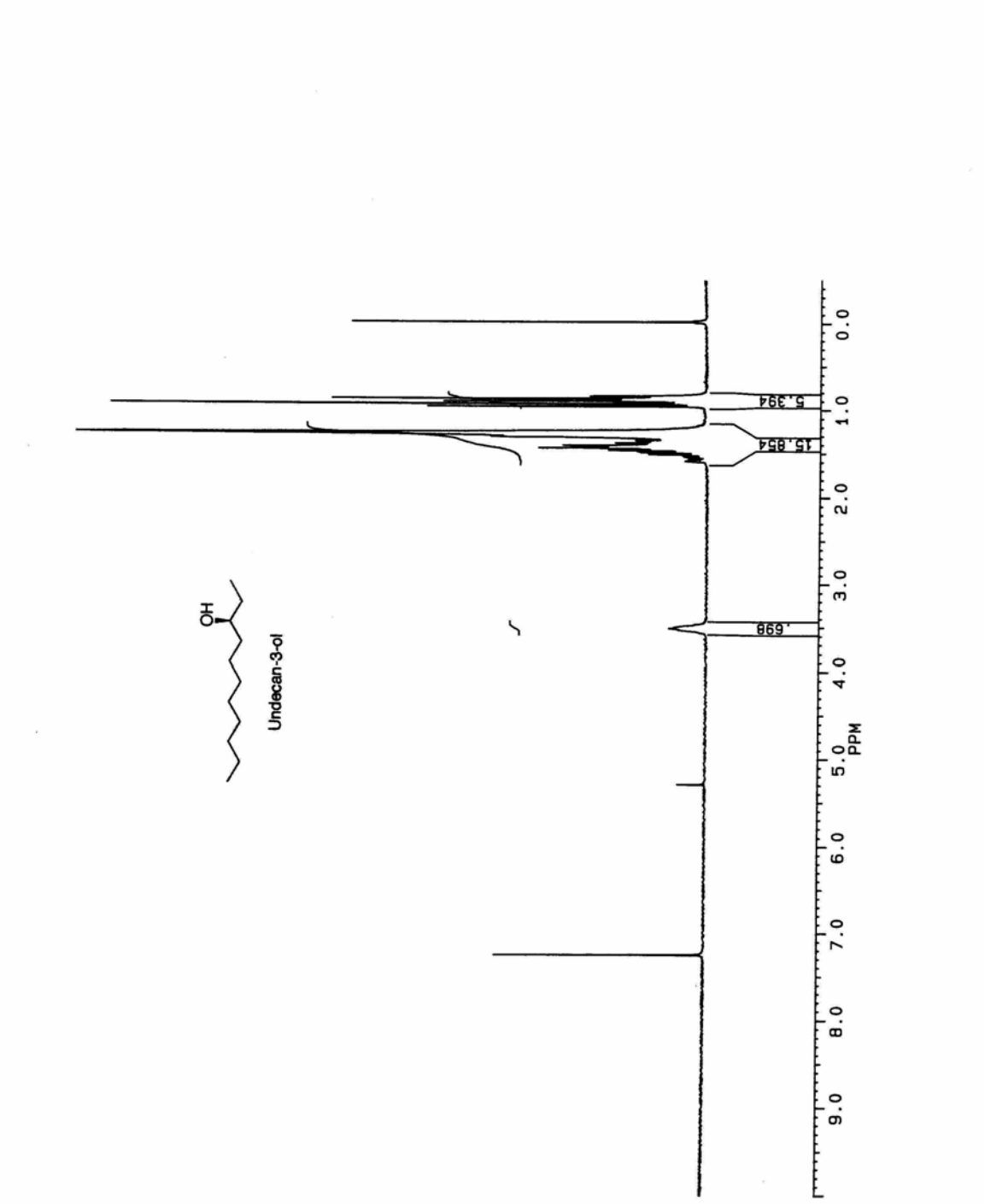
^{1}H NMR (250MHz, $CDCl_3$) of (S)-(+)-undecan-3-ol (96% e.e. S-enantiomer): δ 0.82 – 0.94 ppm, (m, 6H, CH_3), δ 1.25 – 1.49 ppm, (m, 16H, CH_2), δ 3.51 ppm, (m, 1H, CH).
^{13}C-APT NMR (62.5 MHz, $CDCl_3$) of (S)-(+)-undecan-3-ol (96% e.e. S-enantiomer): CH_3 δ 9.85, 14.1 ppm, CH_2 δ 22.6, 25.6, 29.2, 29.5, 29.7, 30.1, 31.8, 36.9 ppm, CH δ 73.3 ppm.

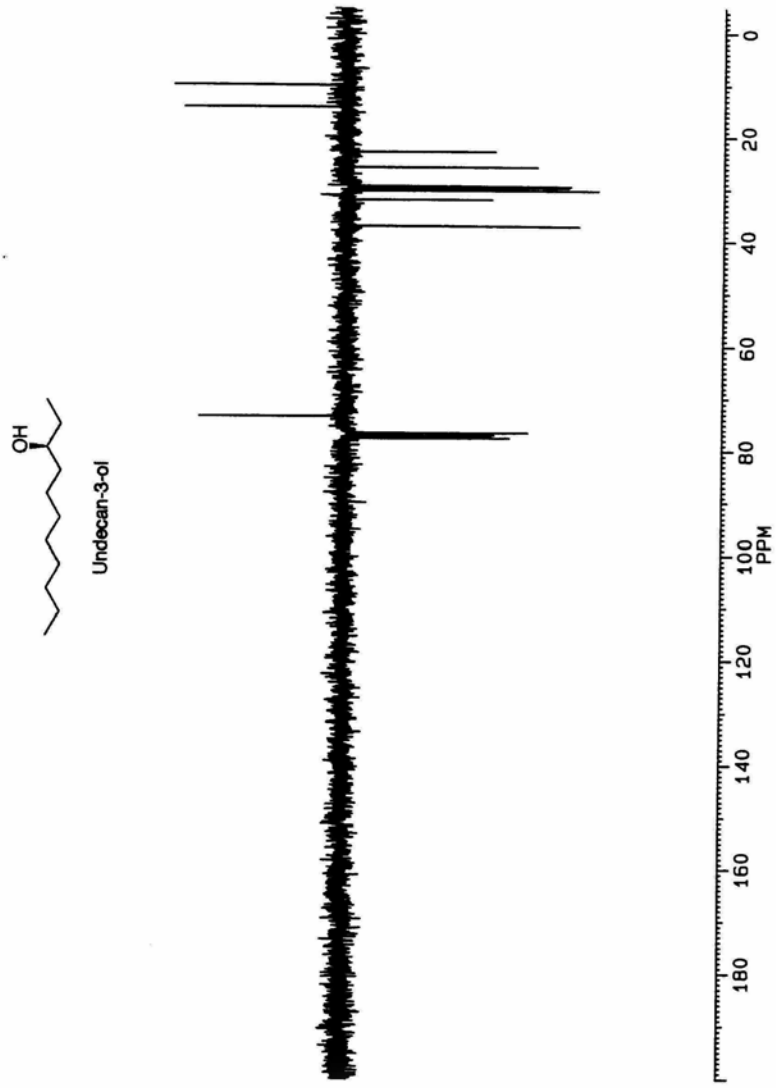
^{1}H NMR (250 MHz, $CDCl_3$) of (R)-3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid-1-ethyl-nonyl ester (racemic undecan-3-ol): δ 0.77 – 0.95 ppm, (m, 6H, CH_3), δ 1.1 – 1.25 ppm, (m, 12H, CH_2), δ 1.55 – 1.72 ppm, (m, 4H, CH_2), δ 3.55 – 3.57 ppm, (dd, 3H. –OCH_3, J = 1.15 Hz, J = 1.3 Hz), δ 4.99 – 5.08 ppm, (p, 1H, CH, J = 6.09 Hz), aromatics: (5H) δ 7.36 – 7.42 ppm (m), δ 7.53 – 7.56 ppm, (m).
^{13}C-APT NMR (62.5 MHz, $CDCl_3$) of (R)-3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid-1-ethyl-nonyl ester (racemic undecan-3-ol): CH_3 δ 9.1, 9.5, 14.0 ppm, CH_2 δ 22.6, 24.8, 25.2, 26.3, 26.6, 29.12, 29.14, 29.3, 29.4, 31.8, 32.9, 33.1 ppm, CH δ 55.3, 78.71, 78.76 ppm, C δ 121.1, 125.6, 132.4, 166.2 ppm, aromatic: CH δ 127.3, 128.2, 129.4 ppm.

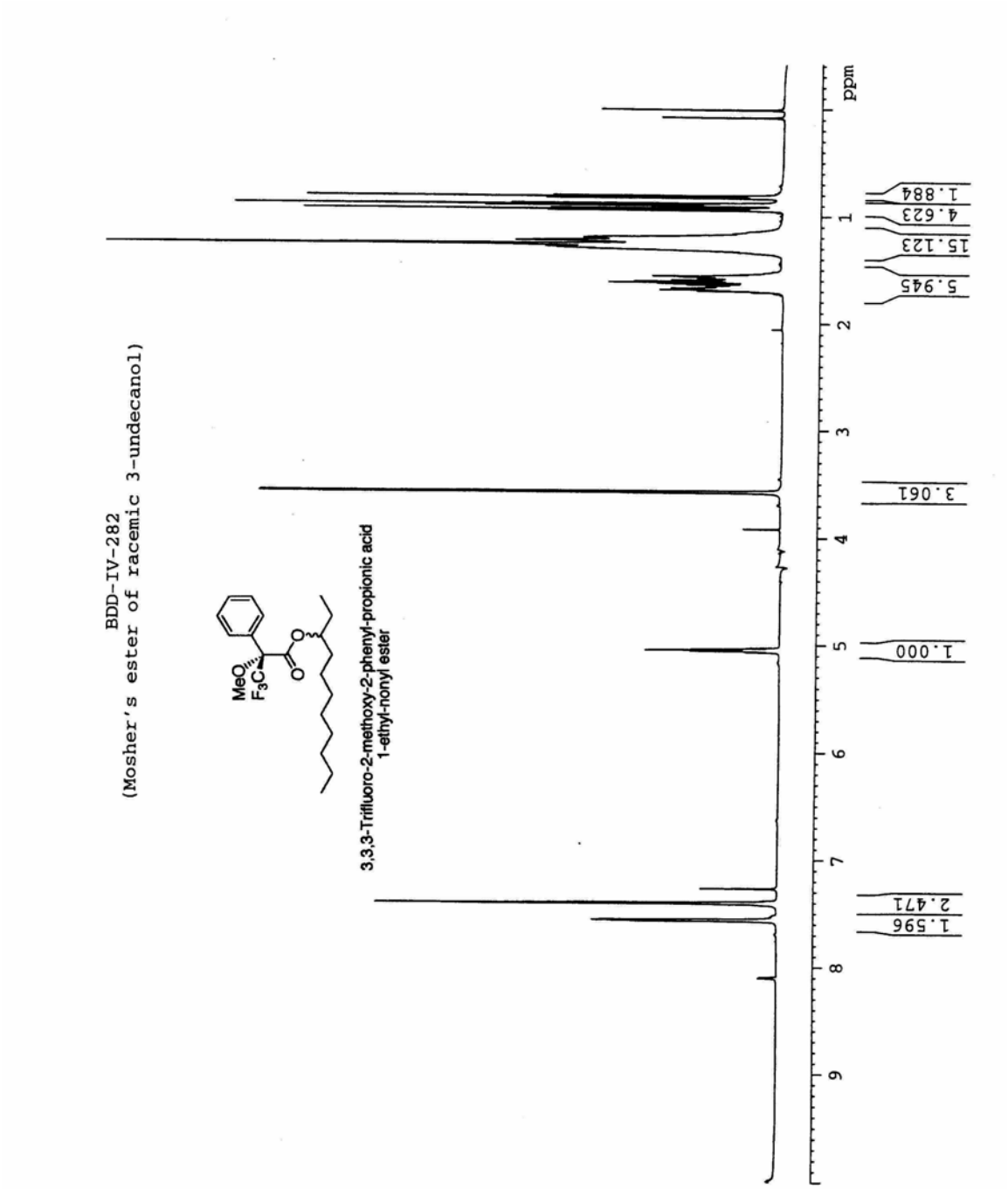
^{1}H NMR (250 MHz, $CDCl_3$) of (R)-3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid-(S)-1-ethyl-nonyl ester (96% e.e. S-enantiomer): δ 0.77 – 0.95 ppm, (m, 6H, CH_3), δ 1.1

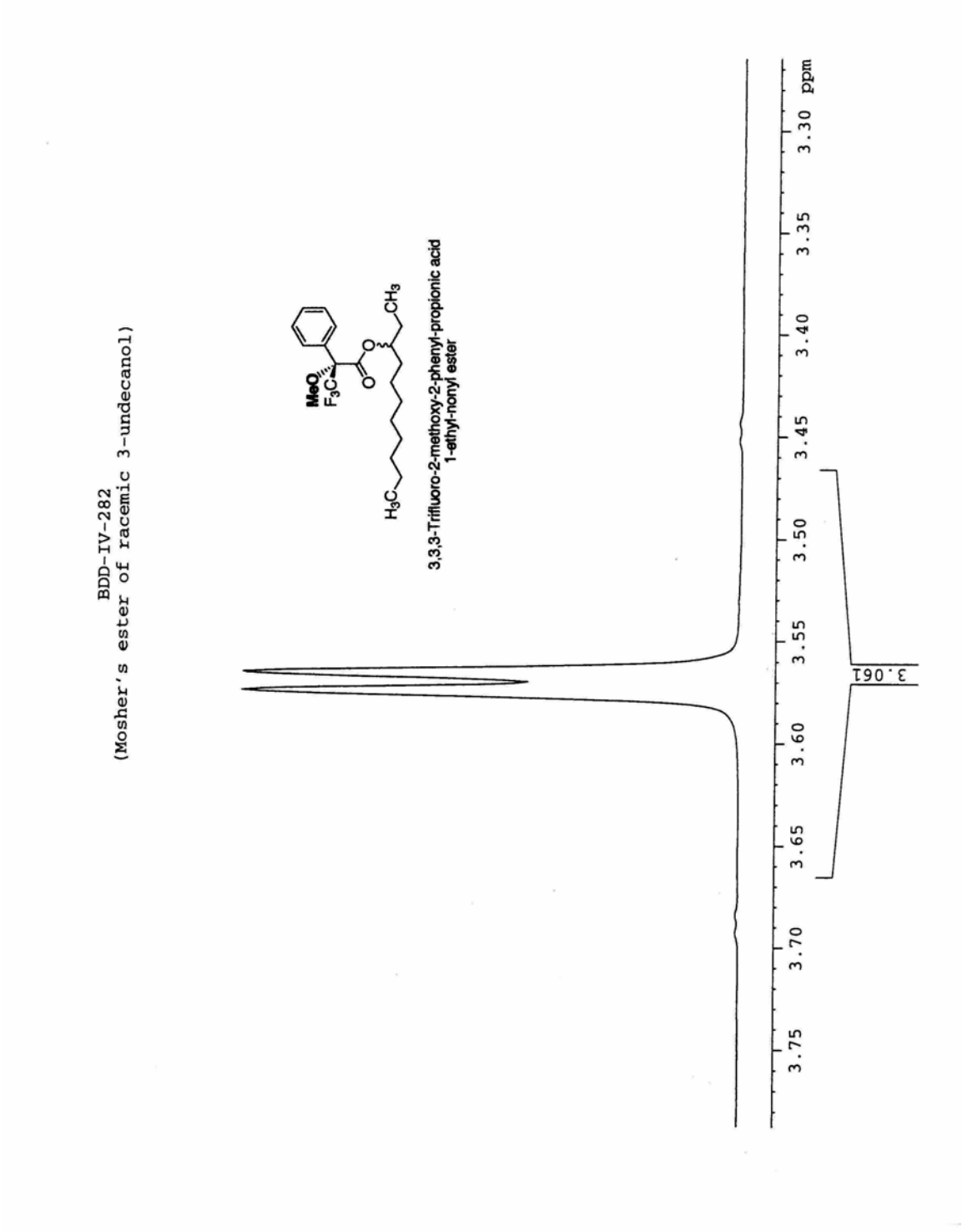
– 1.25 ppm, (m, 12H, CH_2), δ 1.52 – 1.69 ppm, (m, 4H, CH_2), δ 3.55 – 3.56 ppm, (d, 3H. –OCH_3, J = 1.15 Hz), δ 4.99 – 5.08 ppm, (p, 1H, CH, J = 6.09 Hz), aromatics: (5H) δ 7.36 – 7.42 ppm (m), δ 7.53 – 7.57 ppm, (m).

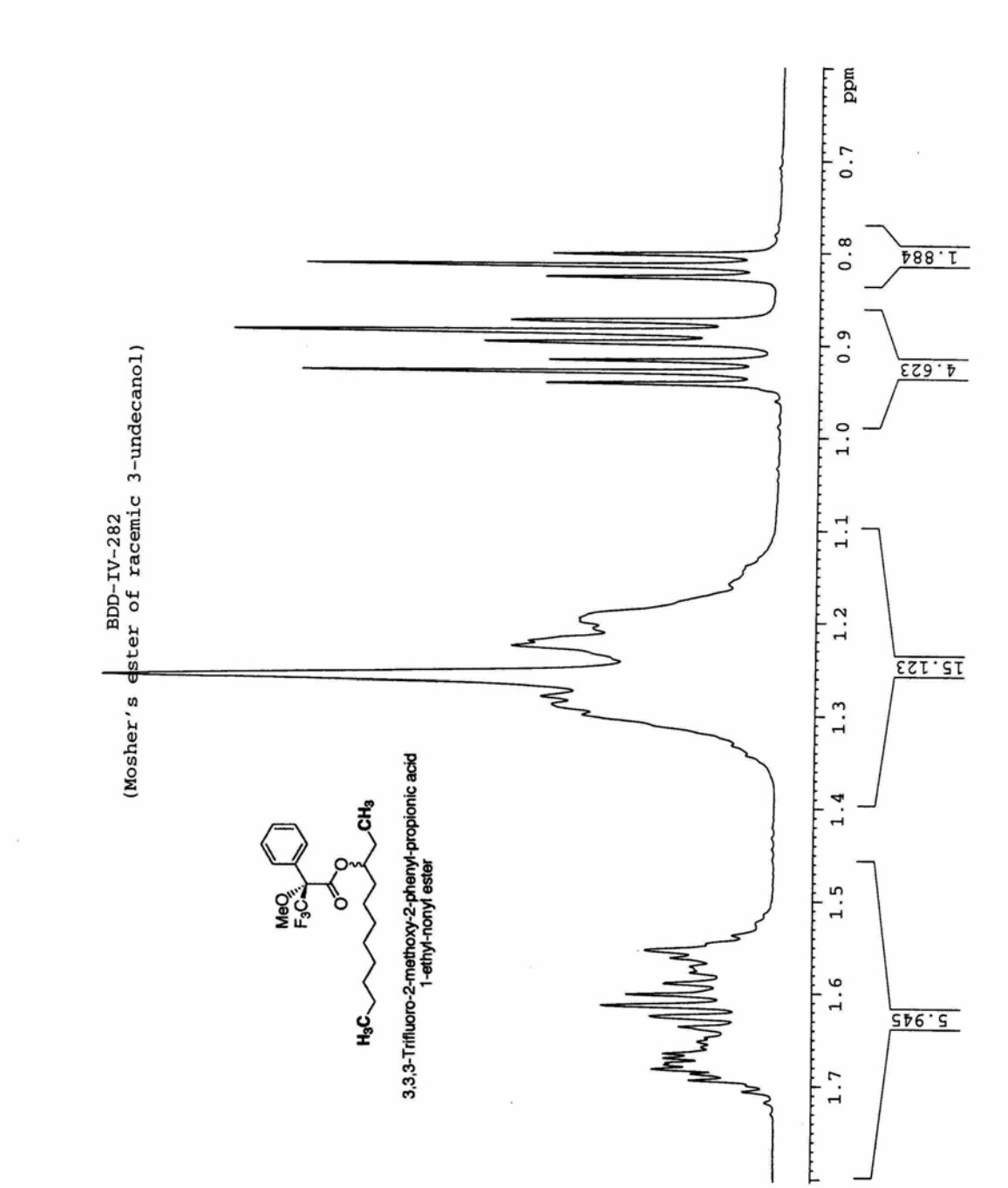
^{13}C-APT NMR (62.5 MHz, $CDCl_3$) of (R)-3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid-(S)-1-ethyl-nonyl ester (96% e.e. S-enantiomer): CH_3 δ 9.1, 14.0 ppm, CH_2 δ 22.6, 24.8, 25.2, 26.3, 29.14, 29.4, 31.8, 32.9, 33.2 ppm, CH δ 55.3, 79.7 ppm, C δ 121.1, 125.6, 132.5, 166.3 ppm, aromatic: CH δ 127.3, 128.2, 129.4 ppm.

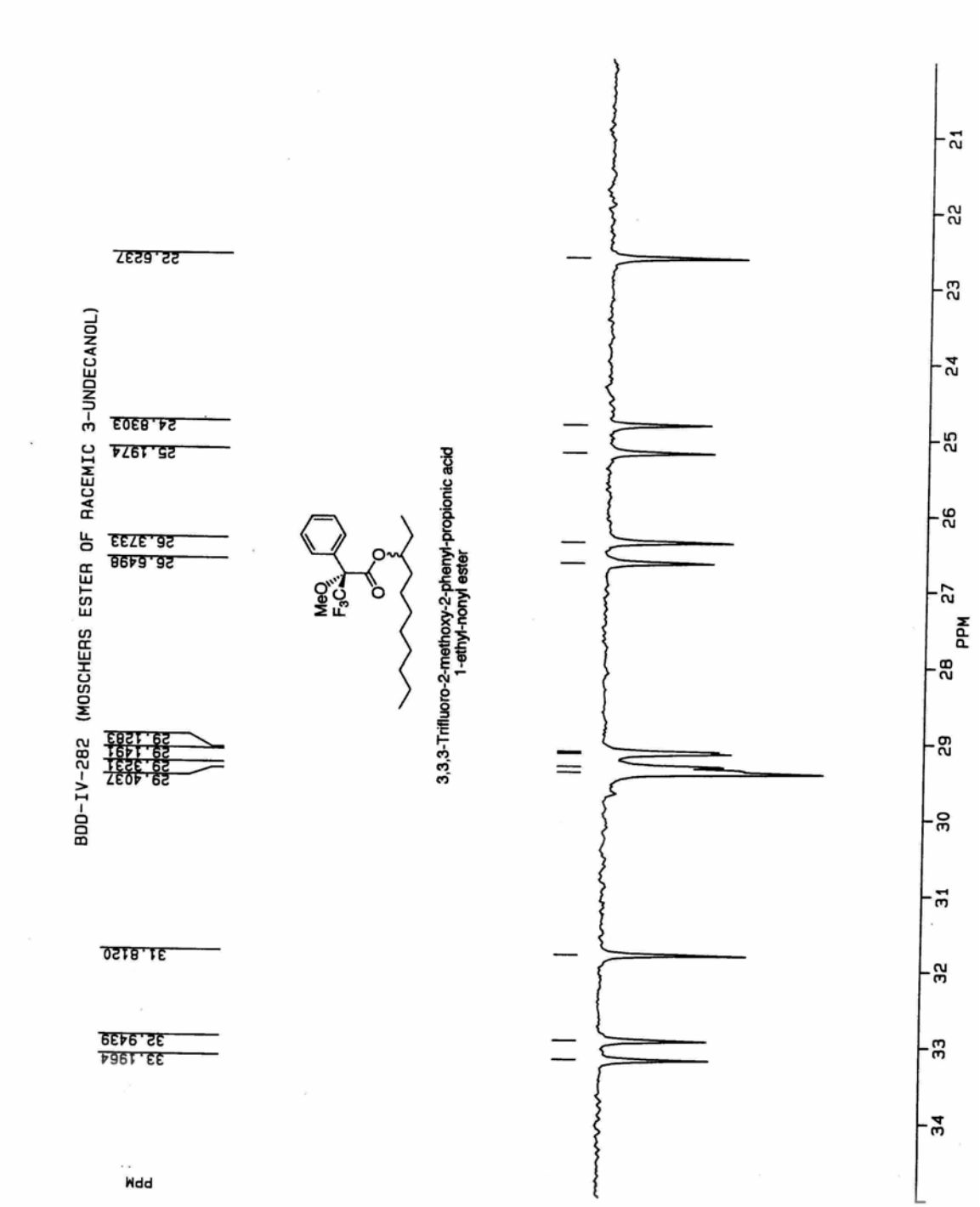

OH
Undecan-3-ol
15.854
5.394
.698
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
PPM

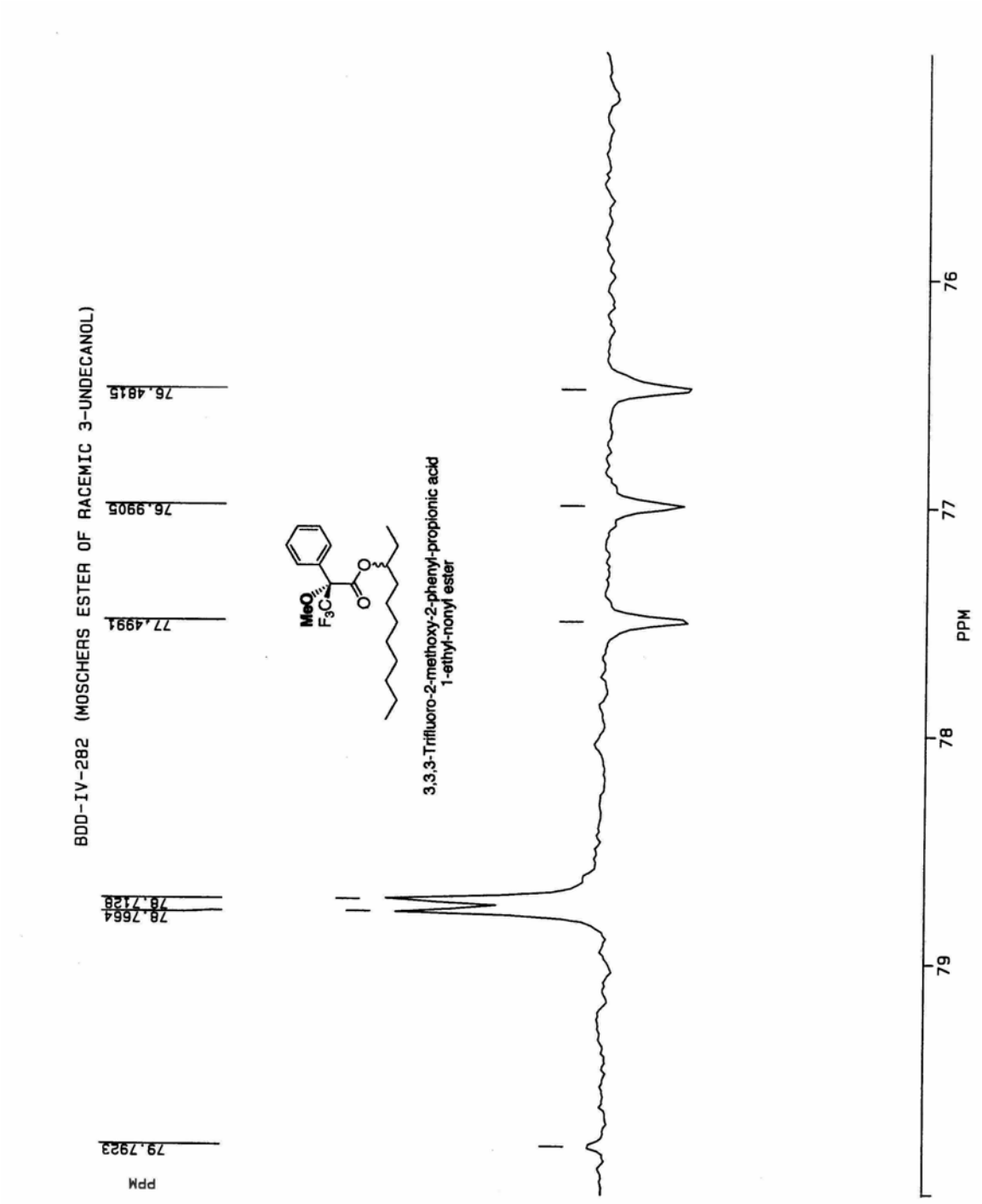

OH
Undecan-3-ol
0
20
40
60
80
100
120
140
160
180
PPM

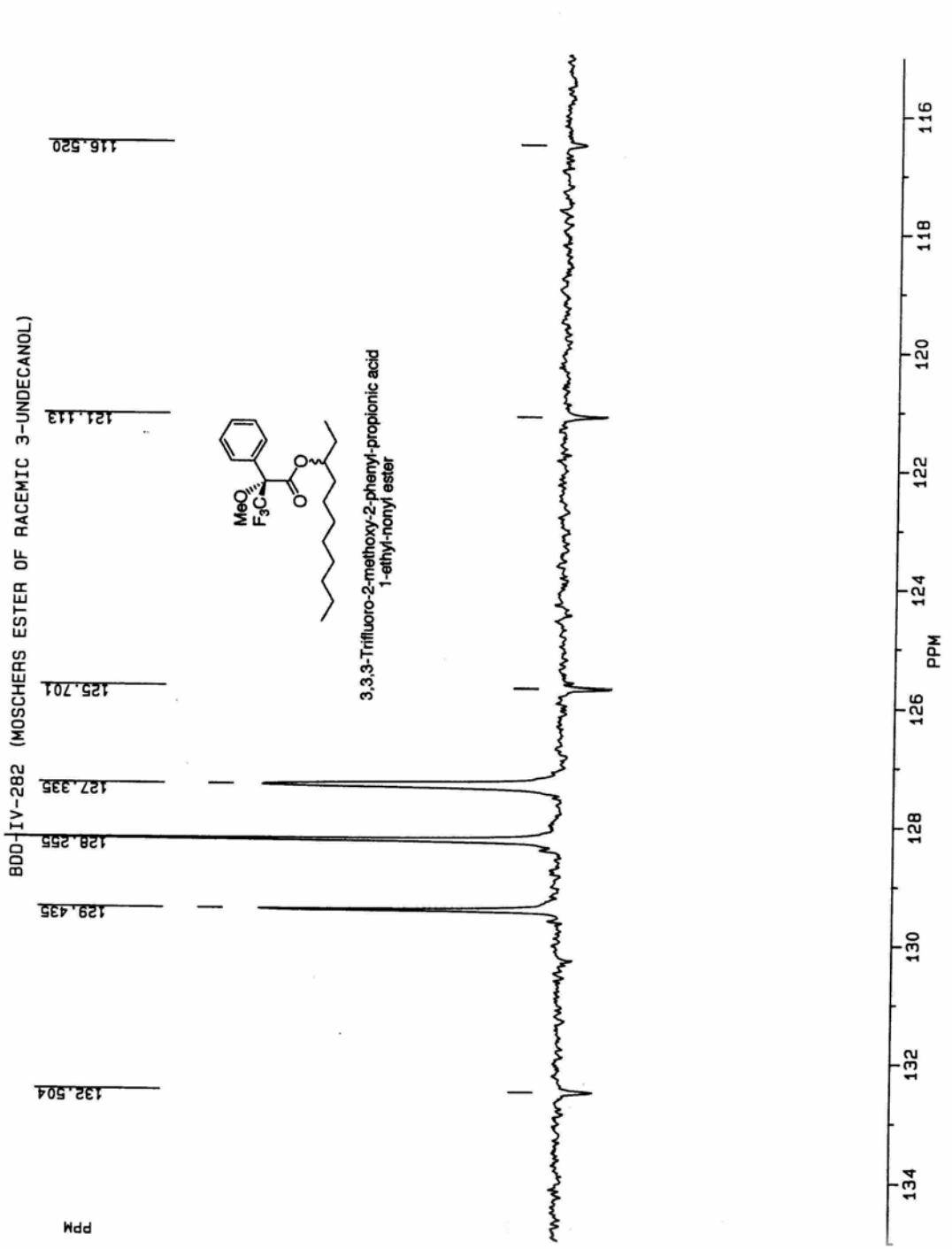

BDD-IV-282
(Mosher's ester of racemic 3-undecanol)
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
MeO
F3C
ppm
1.884
4.623
15.123
5.945
3.061
1.000
1.596
2.471

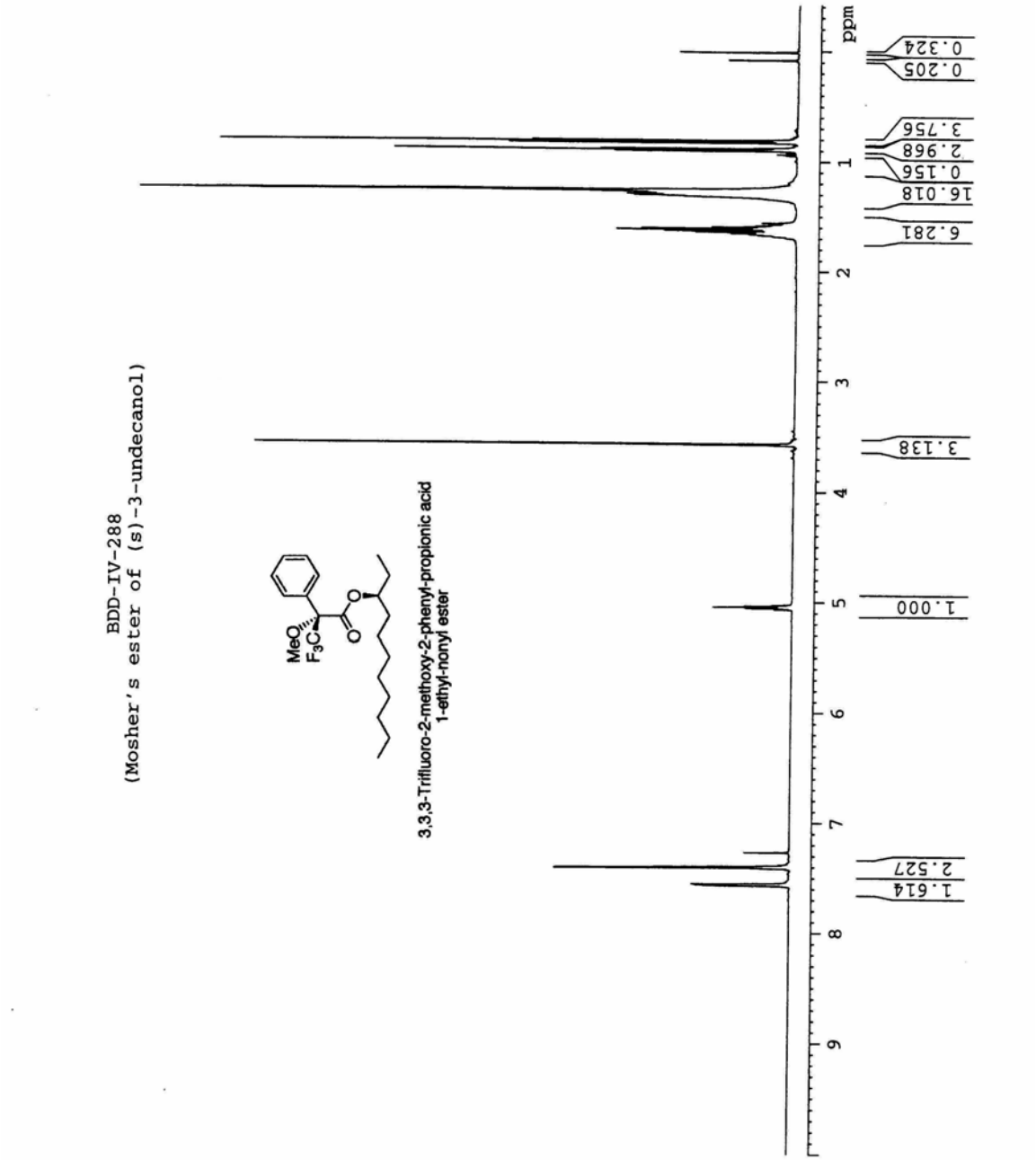

BDD-IV-282
(Mosher's ester of racemic 3-undecanol)
MeO
F3C
CH3
H3C
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
3.75
3.70
3.65
3.60
3.55
3.50
3.45
3.40
3.35
3.30 ppm
3.061

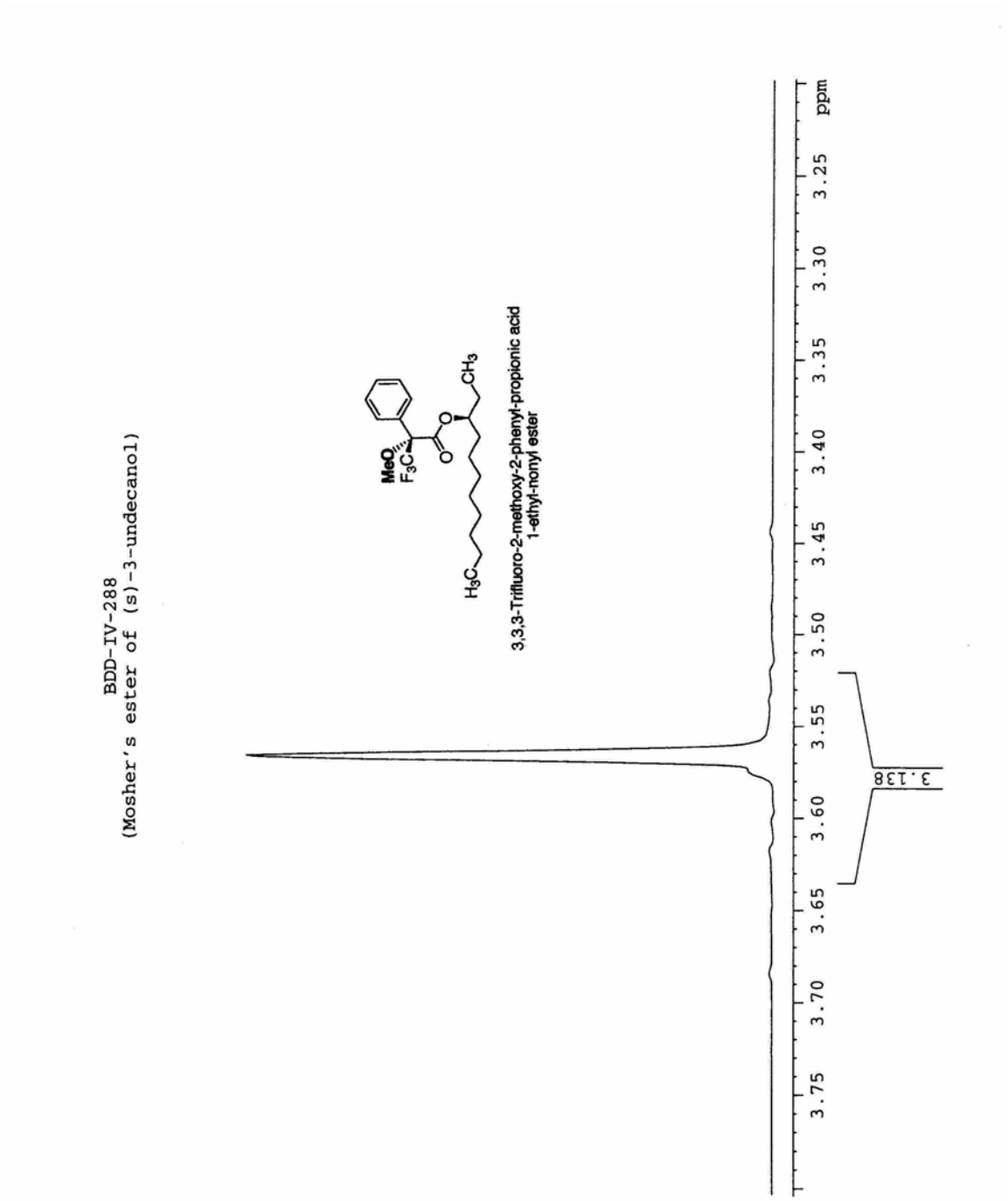

BDD-IV-282
(Mosher's ester of racemic 3-undecanol)
MeO
F3C
O
O
CH3
H3C
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
5.945
15.123
4.623
1.884
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
ppm

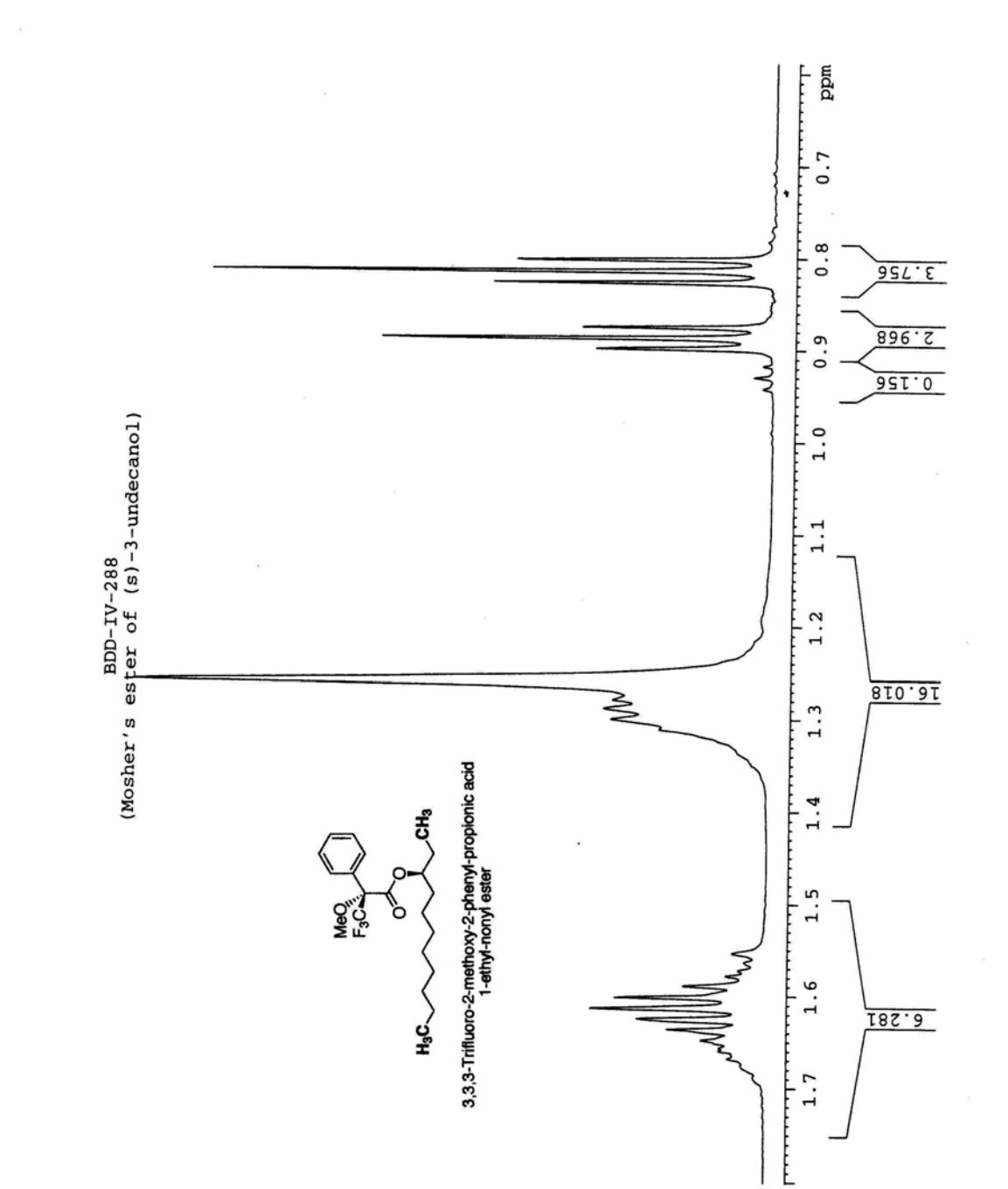

BDD-IV-282 (MOSCHERS ESTER OF RACEMIC 3-UNDECANOL)
22.6237
24.8303
25.1974
26.3733
26.6498
29.1283
29.1491
29.3231
29.4037
31.8120
32.9439
33.1964
PPM
MeO
F3C
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
21
22
23
24
25
26
27
28
29
30
31
32
33
34
PPM

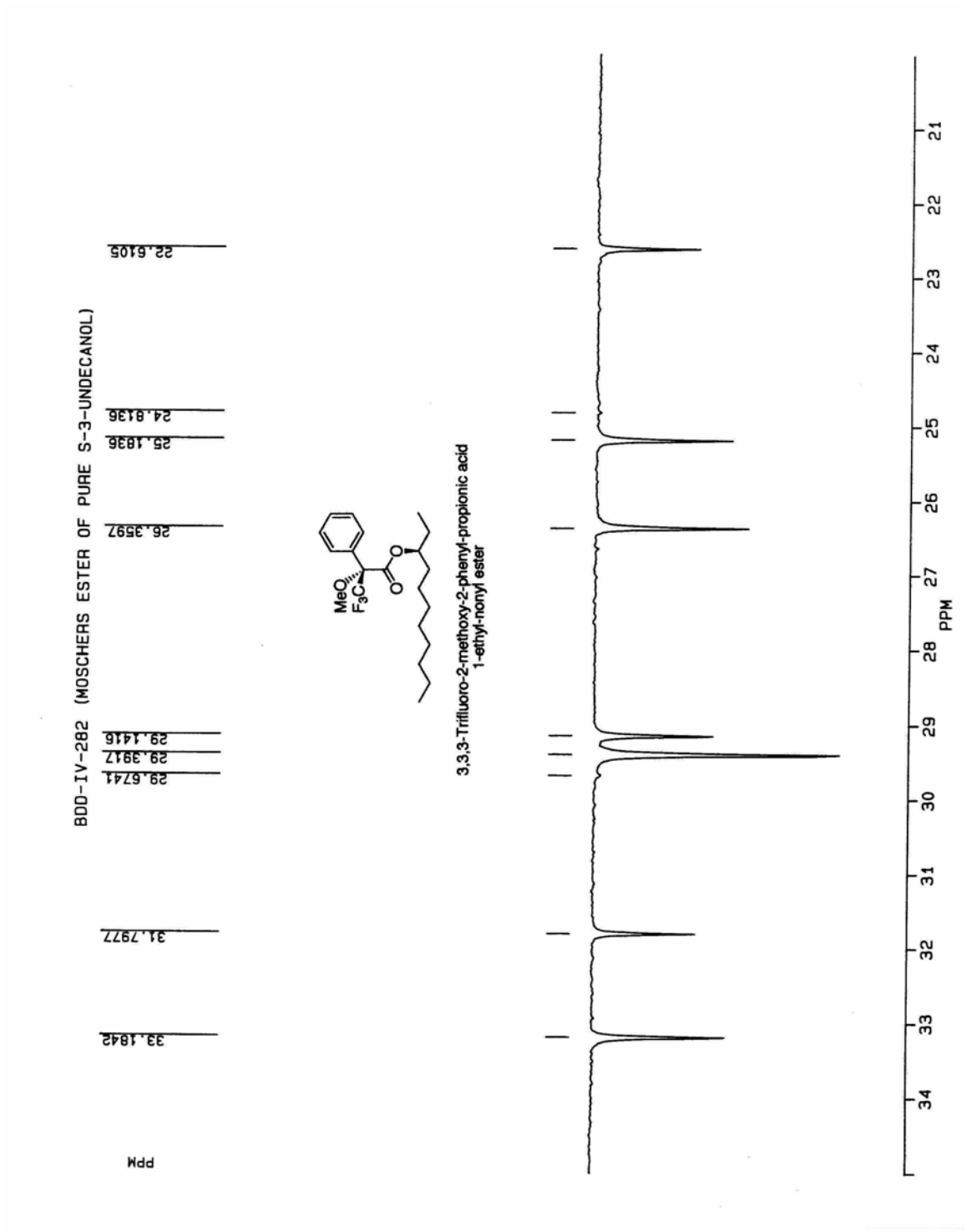

BDD-IV-282 (MOSCHERS ESTER OF RACEMIC 3-UNDECANOL)
79.7923
78.7664
78.7128
77.4991
76.9905
76.4815
PPM
MeO
F3C
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
76
77
78
79
PPM

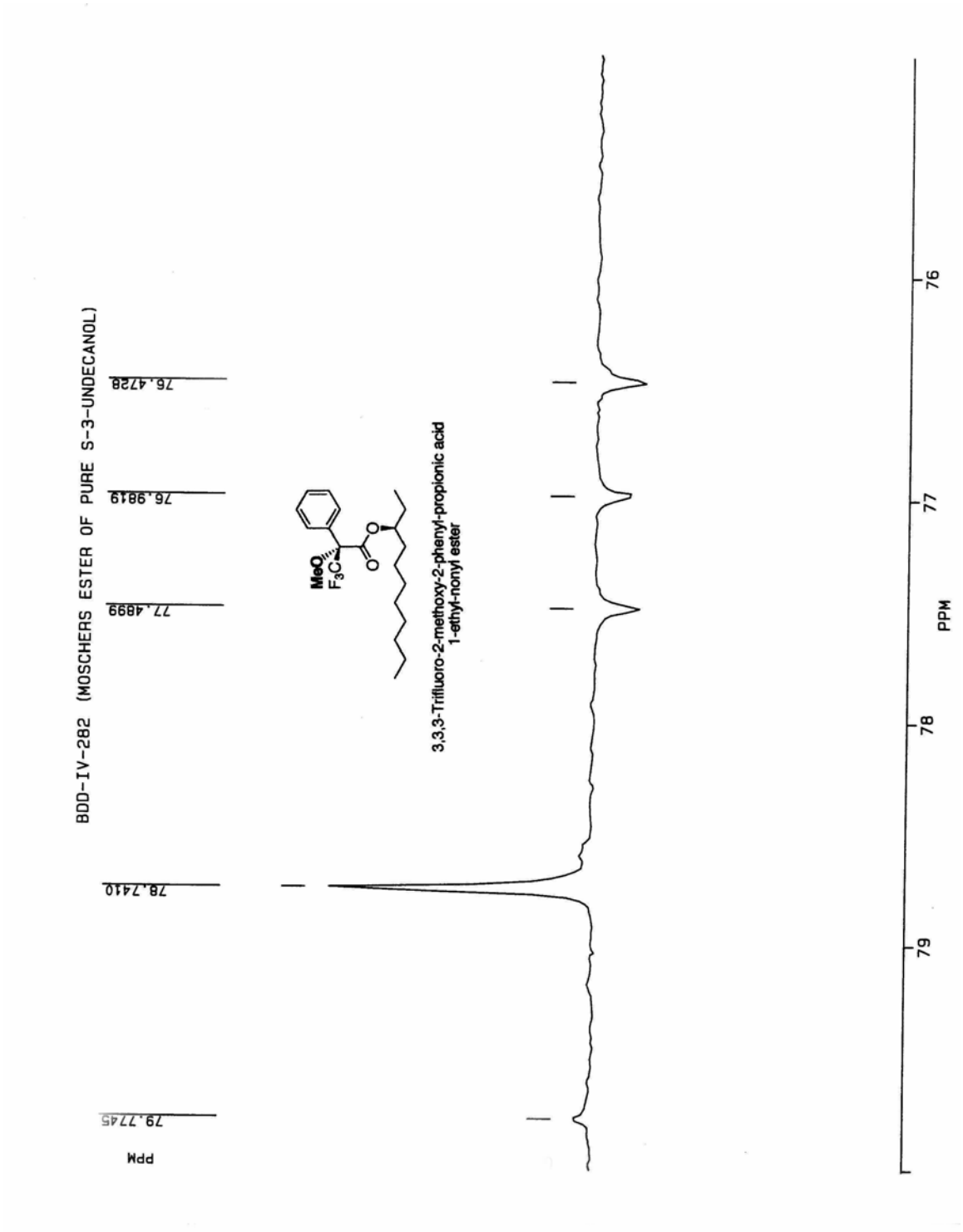

BDD-IV-282 (MOSCHERS ESTER OF RACEMIC 3-UNDECANOL)
116.520
121.113
125.701
127.335
128.255
129.435
132.504
PPM
MeO
F3C
O
O
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
116
118
120
122
124
126
128
130
132
134
PPM

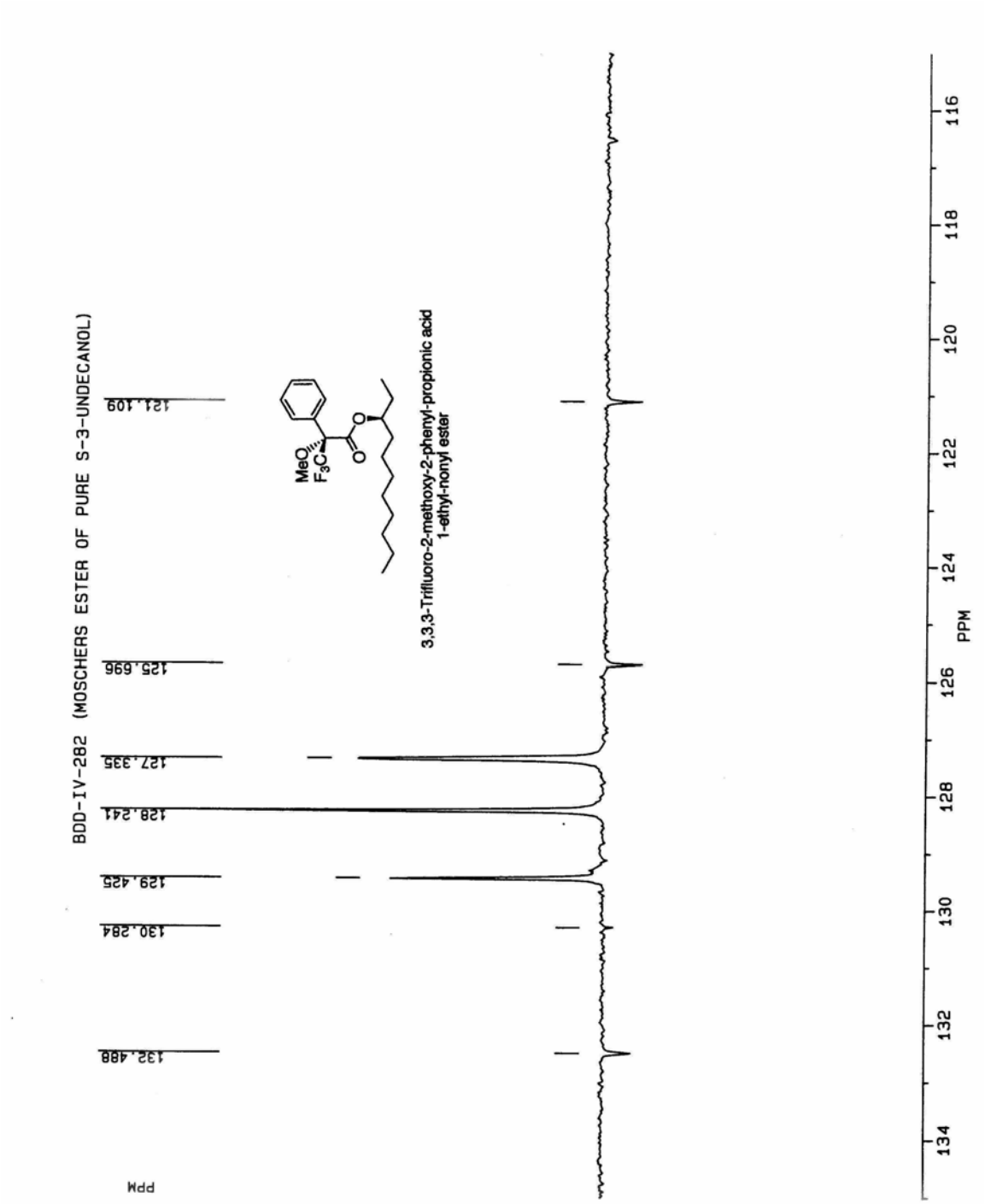

BDD-IV-288
(Mosher's ester of (s)-3-undecanol)
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
MeO
F3C
O
O
ppm
1
2
3
4
5
6
7
8
9
0.324
0.205
3.756
2.968
0.156
16.018
6.281
3.138
1.000
2.527
1.614


BDD-IV-288
(Mosher's ester of (s)-3-undecanol)
MeO
F3C
O
O
CH3
H3C
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
3.75
3.70
3.65
3.60
3.55
3.50
3.45
3.40
3.35
3.30
3.25
ppm
3.138

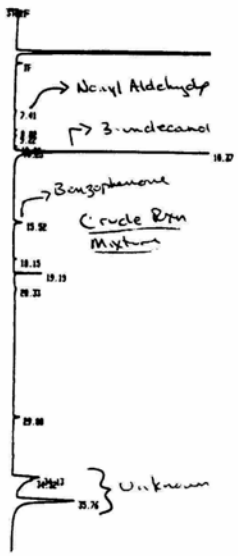

BDD-IV-288
(Mosher's ester of (s)-3-undecanol)
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
MeO
F3C
H3C
CH3
ppm
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
3.756
2.968
0.156
16.018
6.281


BDD-IV-282 (MOSCHERS ESTER OF PURE S-3-UNDECANOL)
22.6105
24.8136
25.1836
26.3597
29.1416
29.3917
29.6741
31.7977
33.1842
PPM
MeO
F3C
O
O
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
21
22
23
24
25
26
27
28
29
30
31
32
33
34
PPM


BDD-IV-282 (MOSCHERS ESTER OF PURE S-3-UNDECANOL)
76.4728
76.9819
77.4899
78.7410
79.7745
PPM
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
MeO
F3C
76
77
78
79
PPM


BDD-IV-282 (MOSCHERS ESTER OF PURE S-3-UNDECANOL)
121.109
125.696
127.335
128.241
129.425
130.284
132.488
PPM
MeO
F3C
O
O
3,3,3-Trifluoro-2-methoxy-2-phenyl-propionic acid
1-ethyl-nonyl ester
116
118
120
122
124
126
128
130
132
134
PPM

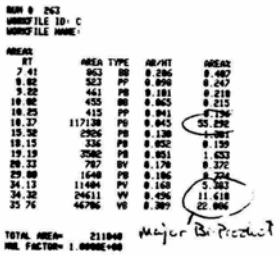
Capillary GC-traces for the synthesis of 3-undecanol.
–Determination of the extent of conversion (nonyl aldehyde —> 3-undecanol).



GC-trace for the crude reaction mixture

Conditions: SPB-5 column
Flow – 80 psi
Injection Temp. – 200°C
Detector Temp. – 275°C
Initial Temp – 100°C for 2 min
Rate – 10°C / min
Final Temp. – 275°C

Retention times: nonyl aldehyde – 7.41 min
3-undecanol – 10.37 min
benzophenone – 15.5 min



Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
80.7562	1.795	0.000	250696	BB	2.4	
0.3653	142.806	0.000	1134	BB	68.4	
18.8785	148.511	0.000	58605	BB	132.0	
100.0000		0.000	310435			

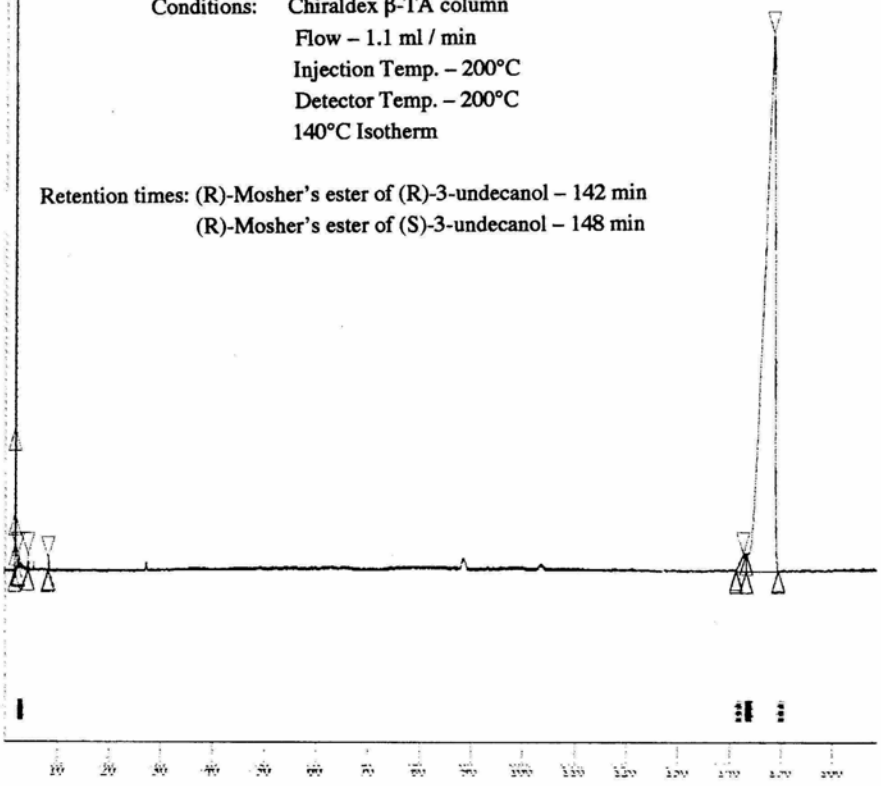
Capillary GC-traces for the synthesis of 3-undecanol.

–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

GC-trace for (R)-Mosher's ester of (S)-3-undecanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

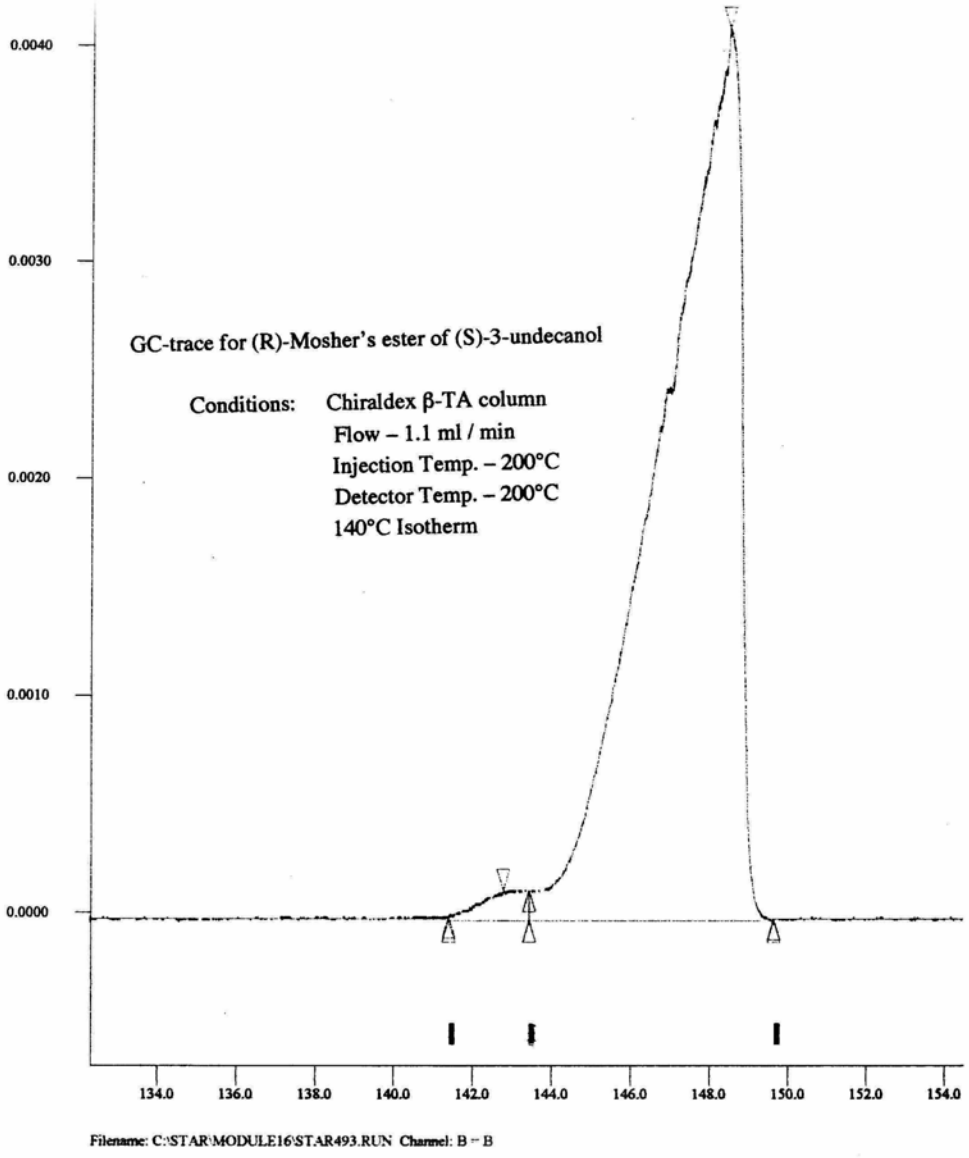
Retention times: (R)-Mosher's ester of (R)-3-undecanol – 142 min
(R)-Mosher's ester of (S)-3-undecanol – 148 min

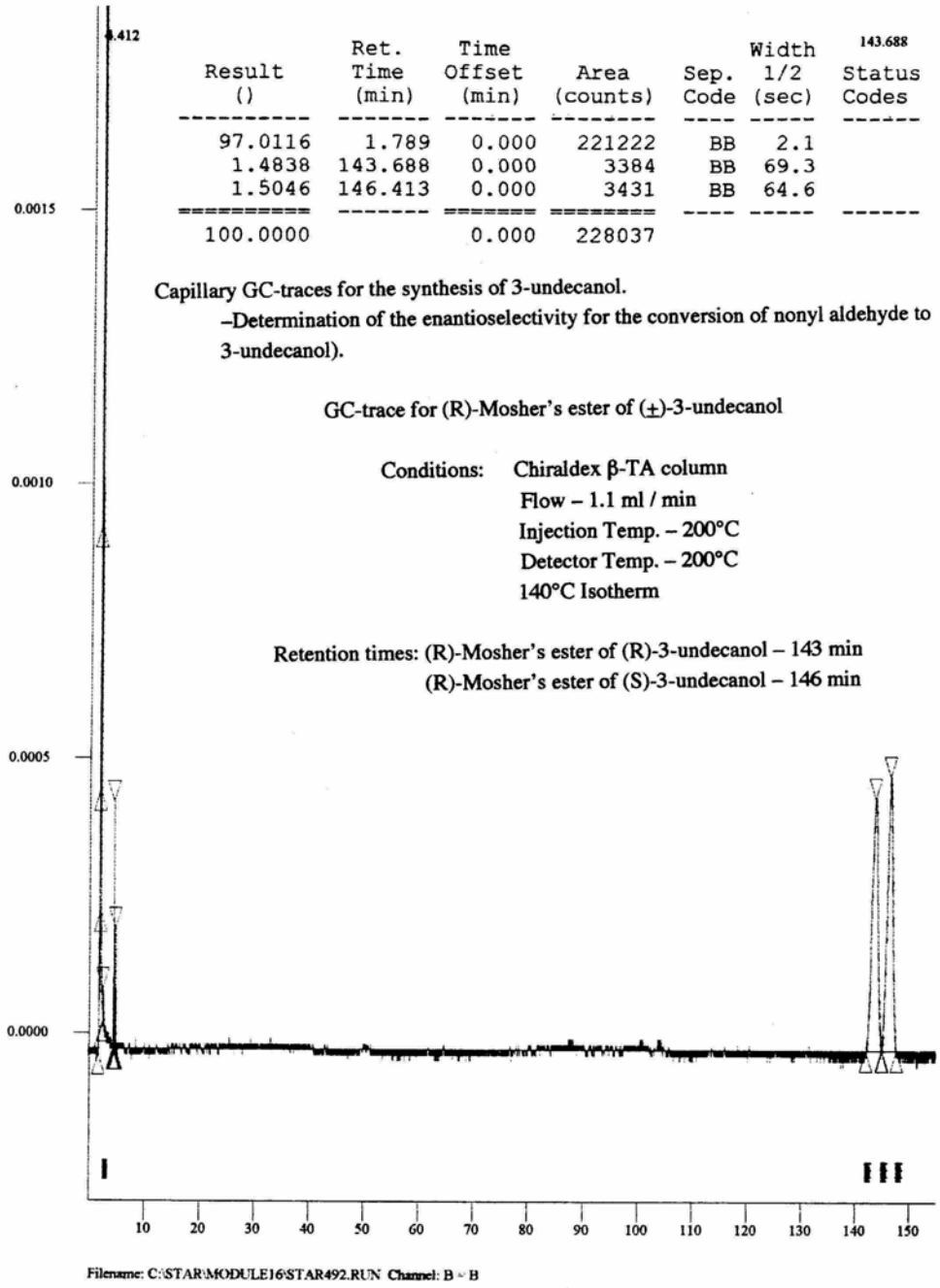


Filename: C:\STAR\MODULE16\STAR493.RUN Channel: B = B

Capillary GC-traces for the synthesis of 3-undecanol.
–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

Retention times: (R)-Mosher's ester of (R)-3-undecanol – 142 min
(R)-Mosher's ester of (S)-3-undecanol – 148 min





Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
97.0116	1.789	0.000	221222	BB	2.1	
1.4838	143.688	0.000	3384	BB	69.3	
1.5046	146.413	0.000	3431	BB	64.6	
100.0000		0.000	228037			

Capillary GC-traces for the synthesis of 3-undecanol.
–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

GC-trace for (R)-Mosher's ester of (±)-3-undecanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

Retention times: (R)-Mosher's ester of (R)-3-undecanol – 143 min
(R)-Mosher's ester of (S)-3-undecanol – 146 min

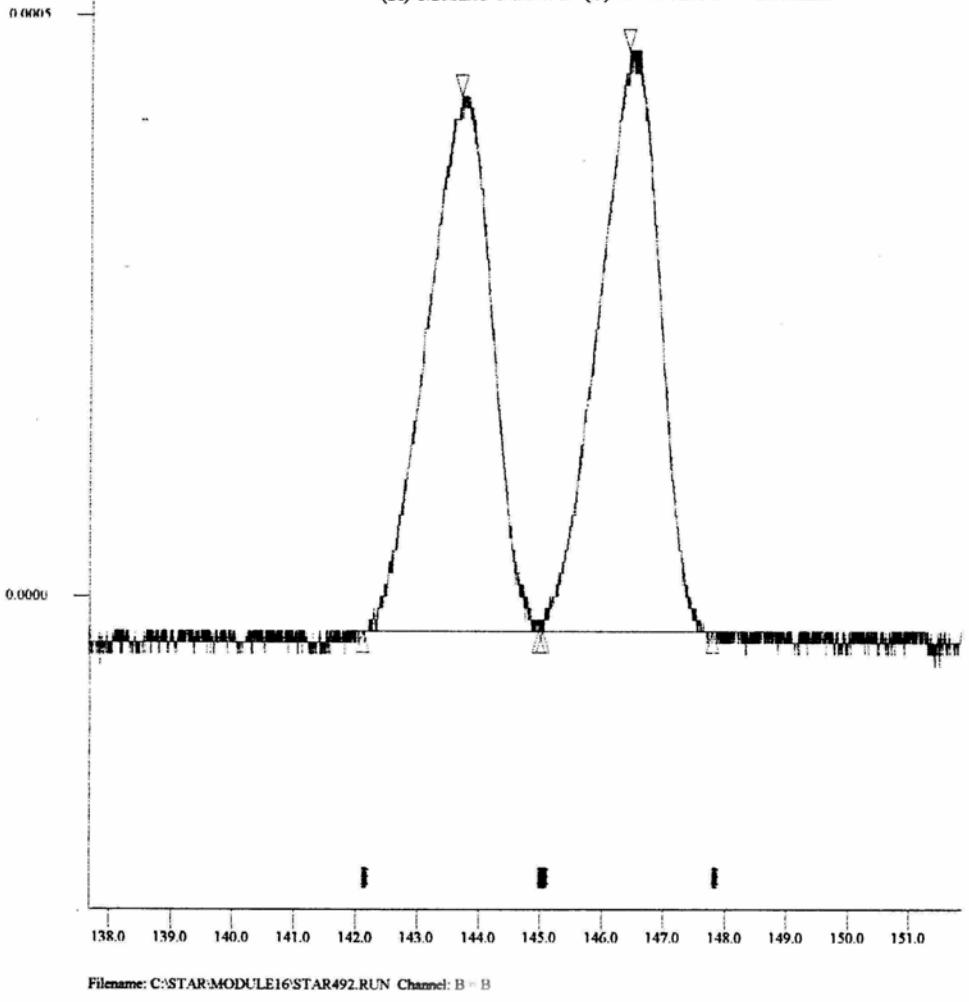
Capillary GC-traces for the synthesis of 3-undecanol.

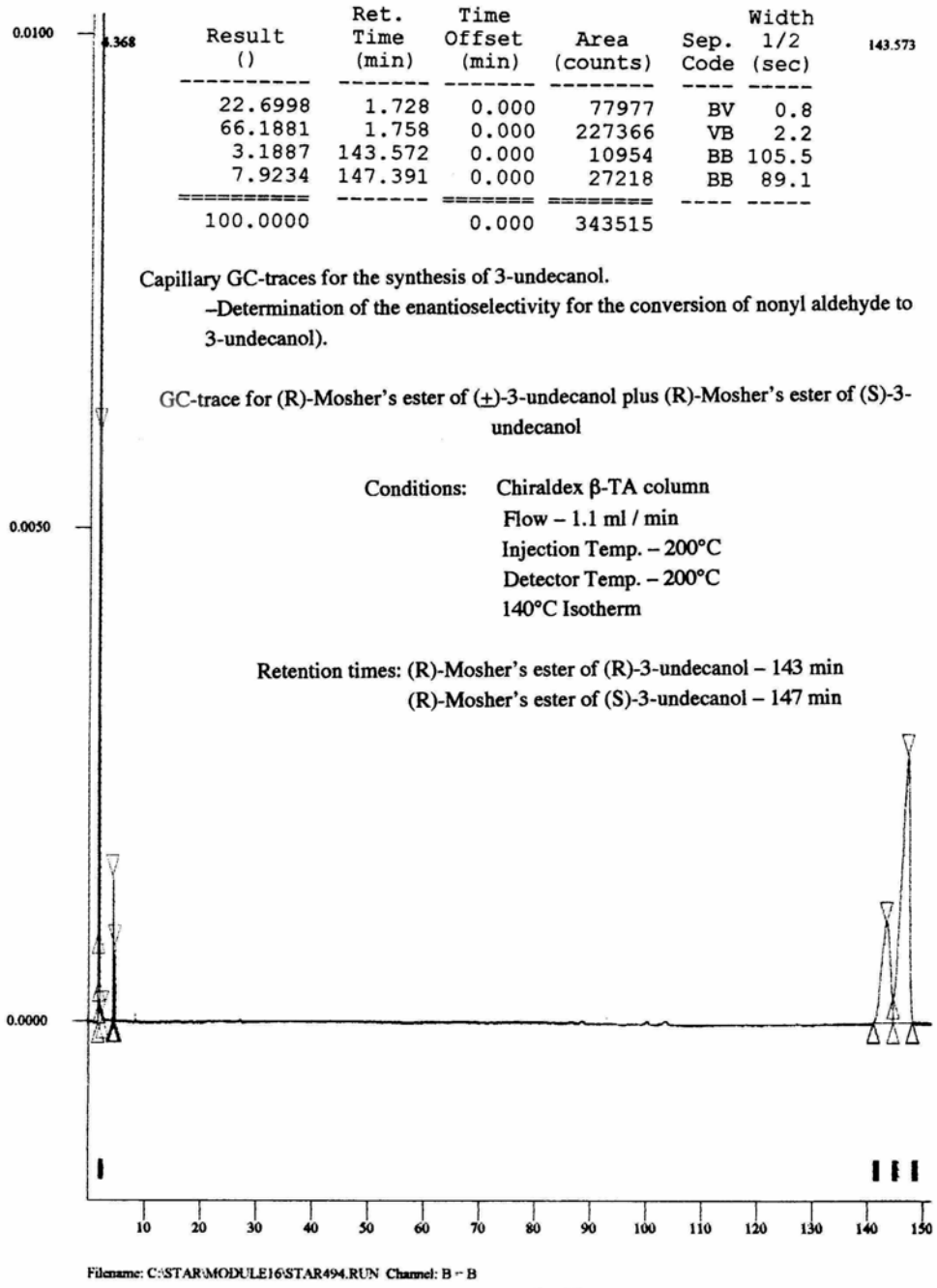
–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

GC-trace for (R)-Mosher's ester of (±)-3-undecanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

Retention times: (R)-Mosher's ester of (R)-3-undecanol – 143 min
(R)-Mosher's ester of (S)-3-undecanol – 146 min





Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)
22.6998	1.728	0.000	77977	BV	0.8
66.1881	1.758	0.000	227366	VB	2.2
3.1887	143.572	0.000	10954	BB	105.5
7.9234	147.391	0.000	27218	BB	89.1
100.0000		0.000	343515		

Capillary GC-traces for the synthesis of 3-undecanol.

–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

GC-trace for (R)-Mosher's ester of (±)-3-undecanol plus (R)-Mosher's ester of (S)-3-undecanol

Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm

Retention times: (R)-Mosher's ester of (R)-3-undecanol – 143 min
(R)-Mosher's ester of (S)-3-undecanol – 147 min

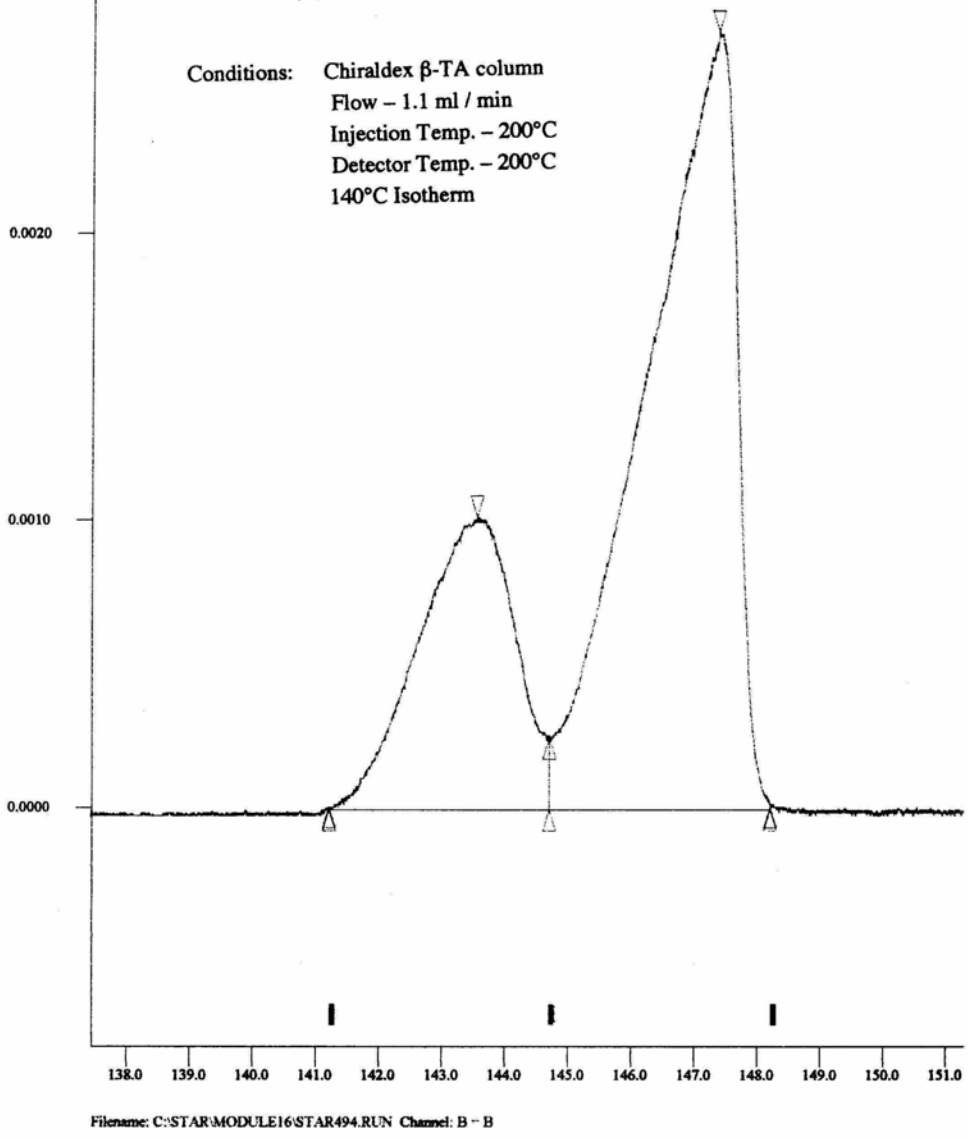
Capillary GC-traces for the synthesis of 3-undecanol.

–Determination of the enantioselectivity for the conversion of nonyl aldehyde to 3-undecanol).

GC-trace for (R)-Mosher's ester of (±)-3-undecanol plus (R)-Mosher's ester of (S)-3-undecanol

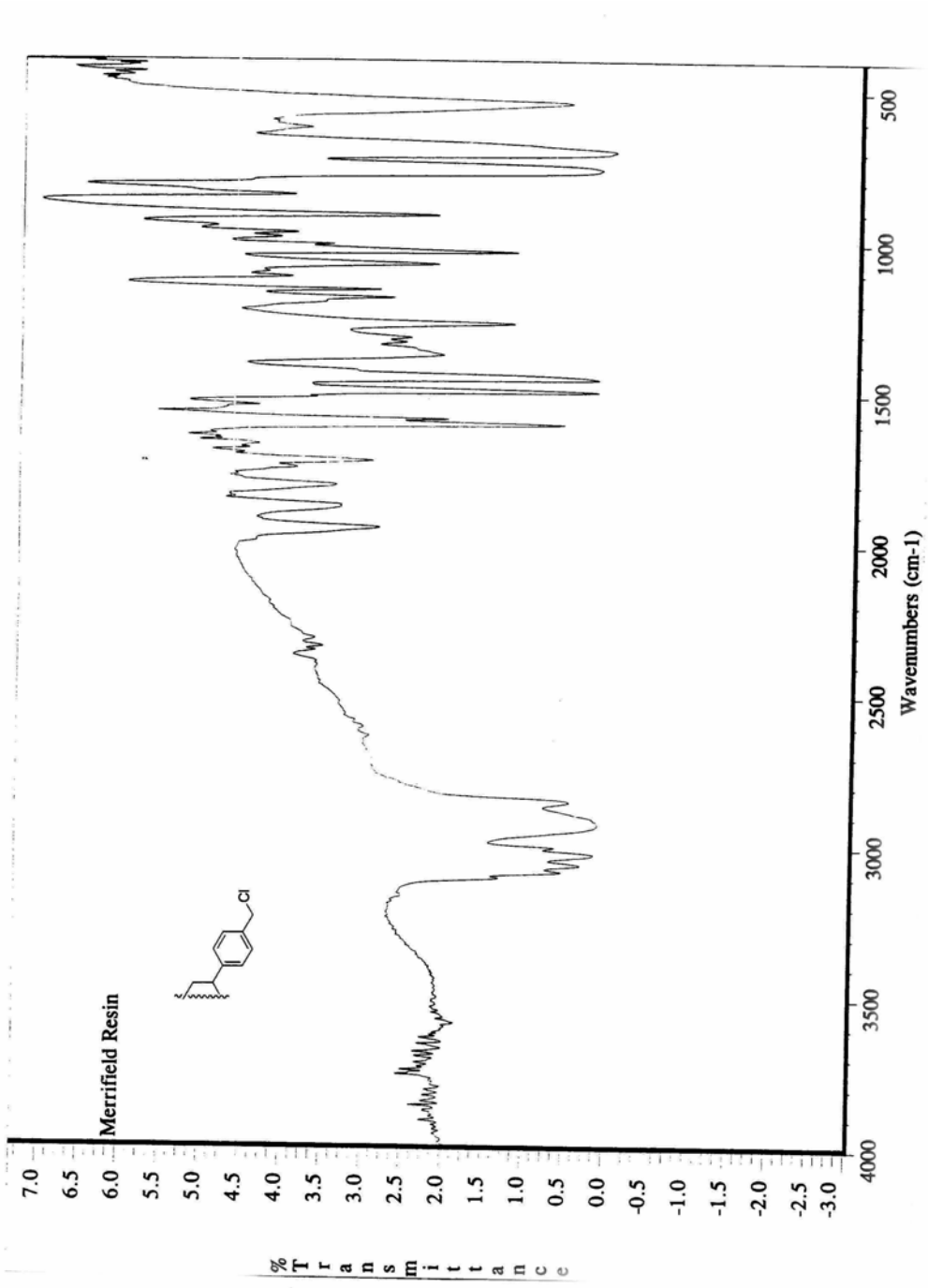
Retention times: (R)-Mosher's ester of (R)-3-undecanol – 143 min
(R)-Mosher's ester of (S)-3-undecanol – 147 min

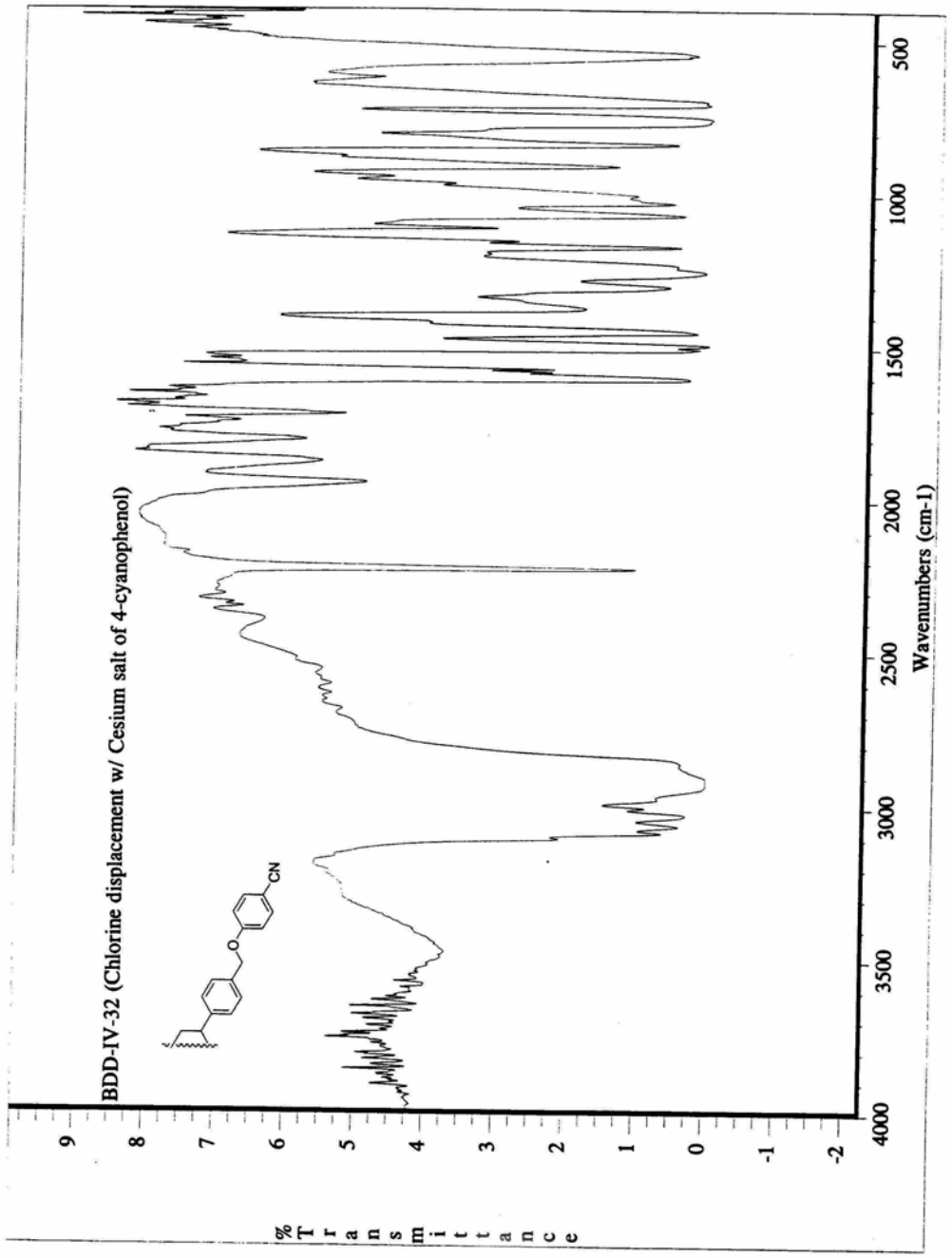
Conditions: Chiraldex β-TA column
Flow – 1.1 ml / min
Injection Temp. – 200°C
Detector Temp. – 200°C
140°C Isotherm



Phenol Attachment to Merrifield resin. In a jacketed sintered glass reactor equipped with a cold water condenser, argon line and a heating bath, Merrifield resin (10 g, 1 mmol/g, 10 mmol) was swelled in 60 ml of freshly distilled DMF for 1 hr. Solid $CsCO_3$ (9.77 g, 30 mmol, 3 equiv.) and 4-cyanophenol (3.57 g, 30 mmol, 3 equiv.) were added in a single portion. The resulting suspension was agitated with a stream of argon while being heated to 60°C for 24 hrs.

The resulting gray resin was washed with dioxane (2 X 80ml); 1:1 dioxane-water (4 X 80 ml); dioxane (4 X 80 ml); methanol (4 X 80ml); CH_2Cl_2 (2 X 80ml); and dried *in vacuo* at 60°C for 5 hours. Elemental analysis showed >96% displacement (Cl analysis). FT-IR (KBr Pellet) nitrile stretch at 2224 cm^{-1}.

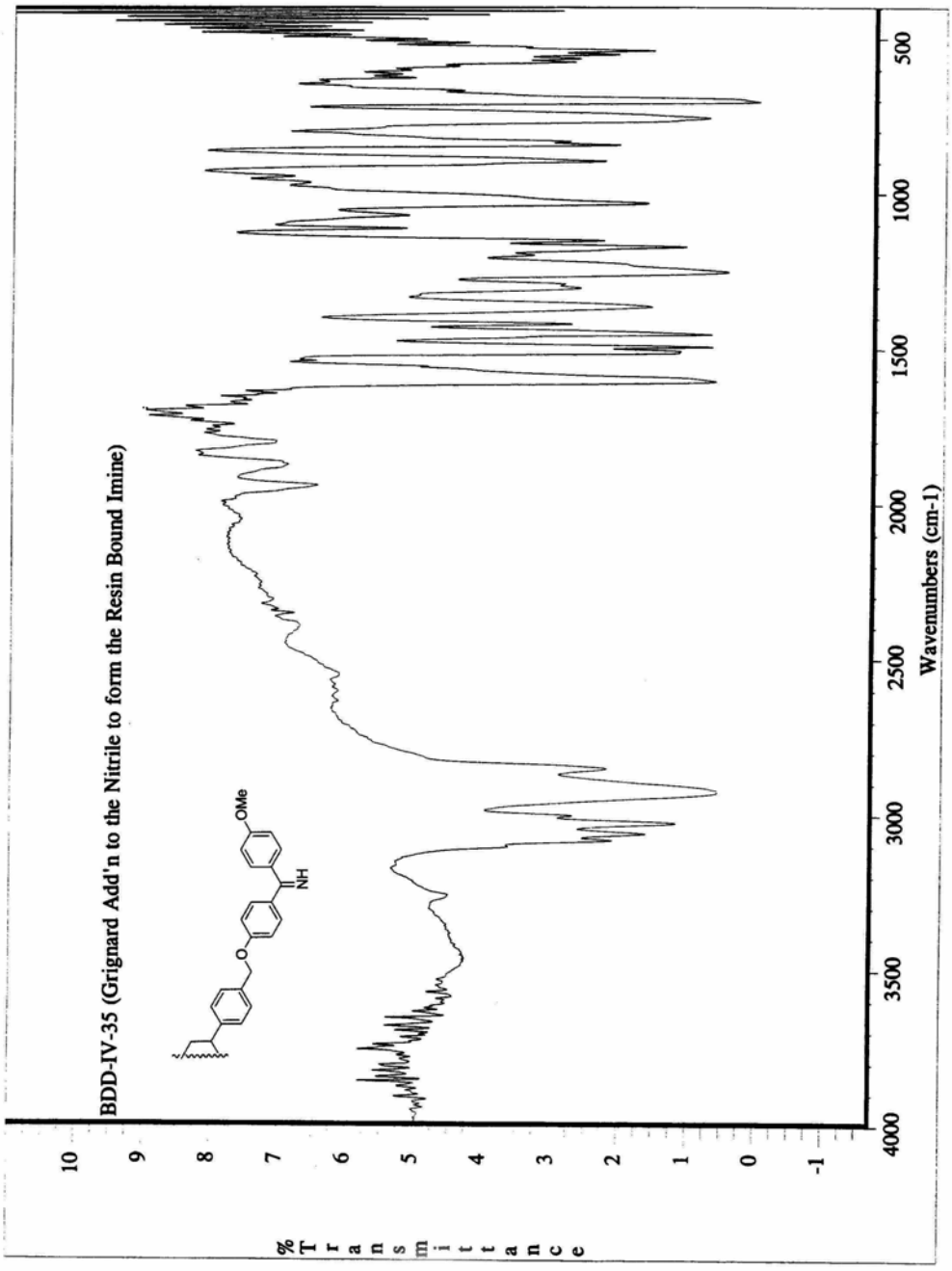

Merrifield Resin
Cl
% Transmittance
Wavenumbers (cm-1)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
4000
3500
3000
2500
2000
1500
1000
500


BDD-IV-32 (Chlorine displacement w/ Cesium salt of 4-cyanophenol)
CN
O
% Transmittance
9
8
7
6
5
4
3
2
1
0
-1
-2
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

Resin-Bound Ketimine. In a jacketed sintered glass funnel equipped with a cold water condenser, and an argon line the polymer bound nitrile resin (~10 g, 1 mmol/g, 10 mmol) was swelled in 60 ml of freshly distilled THF. In a separate 250 ml, flask (flame-dried and purged with argon) containing magnesium turnings (1.25 g, 50 mmol, 5 equiv.), para-bromoanisole (5.61g, 30 mmol, 3 equiv.), diluted with 20 ml of dry THF, was added to in a dropwise fashion *via* syringe, then stirred at 40°C for 1 hr. This brown Grignard reagent was then added dropwise to the suspended resin with argon agitation. Agitation was continued for 24 hrs at 40·C°, at which time the resin was washed with anhydrous MeOH (3 X 100 ml); CH_2Cl_2 (3 X 100 ml); MeOH (3 X 100 ml); and CH_2Cl_2 (3 X 100 ml) for a final time. The resin was dried at 50°C for 24 hours *in vacuo*. FT-IR (KBr Pellet) showed the absence of nitrile stretch at 2224 cm-1. ^{13}C-NMR ($CDCl_3$; 125 MHz) data for the ketimine resin is provided in **Table 1**.

Carbon	Chemical Shift (ppm)
Resin backbone	40.4 – 45.5
	113.7 – 114.2
	125.7 – 133.8
	144.3 – 145.3
	160.8 – 161.7
aromatic methoxy	55.3
benzylic CH_2	70.1

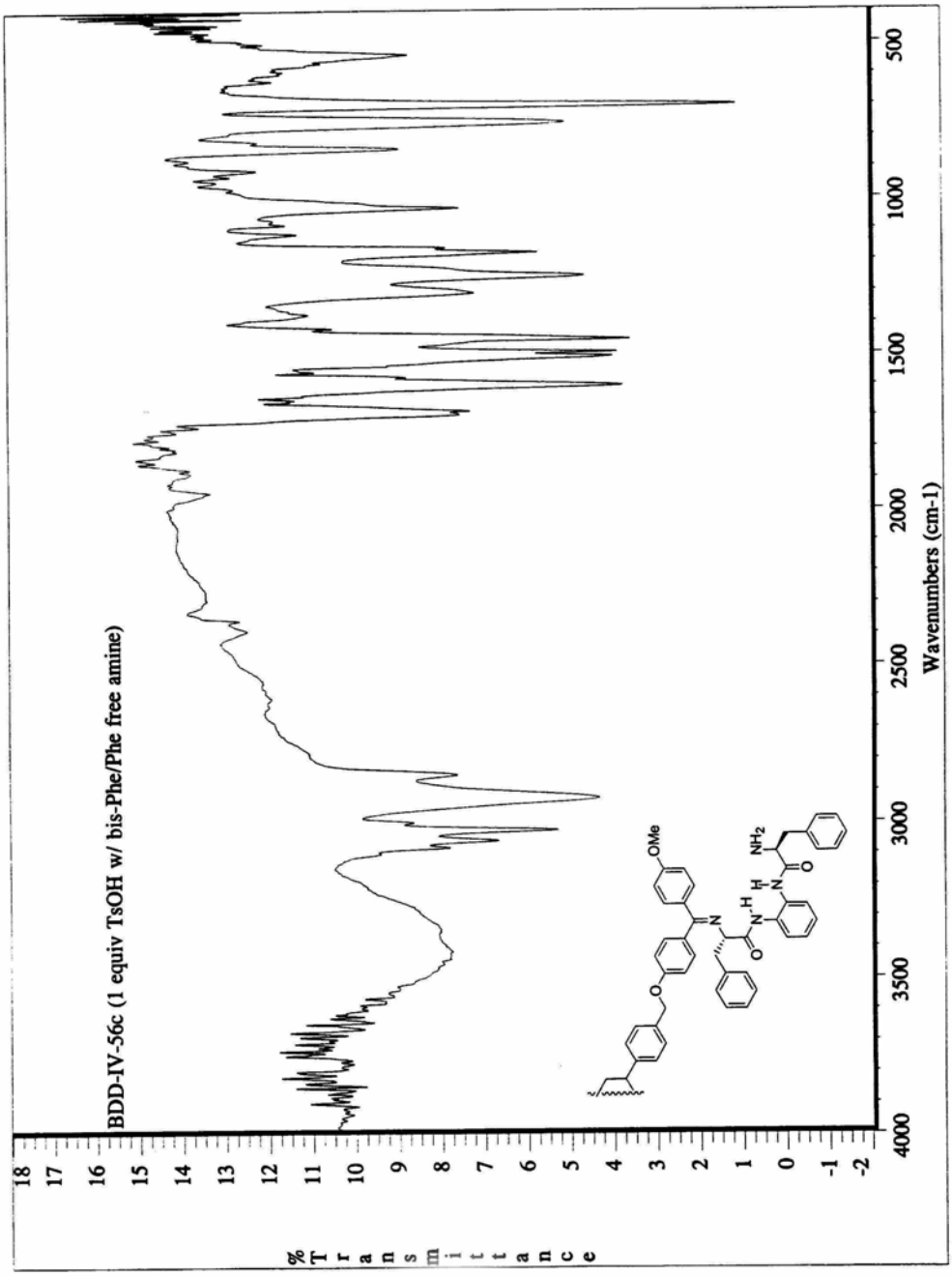
Table 1: ^{13}C-NMR ($CDCl_3$; 125 MHz) data for resin bound ketimine.

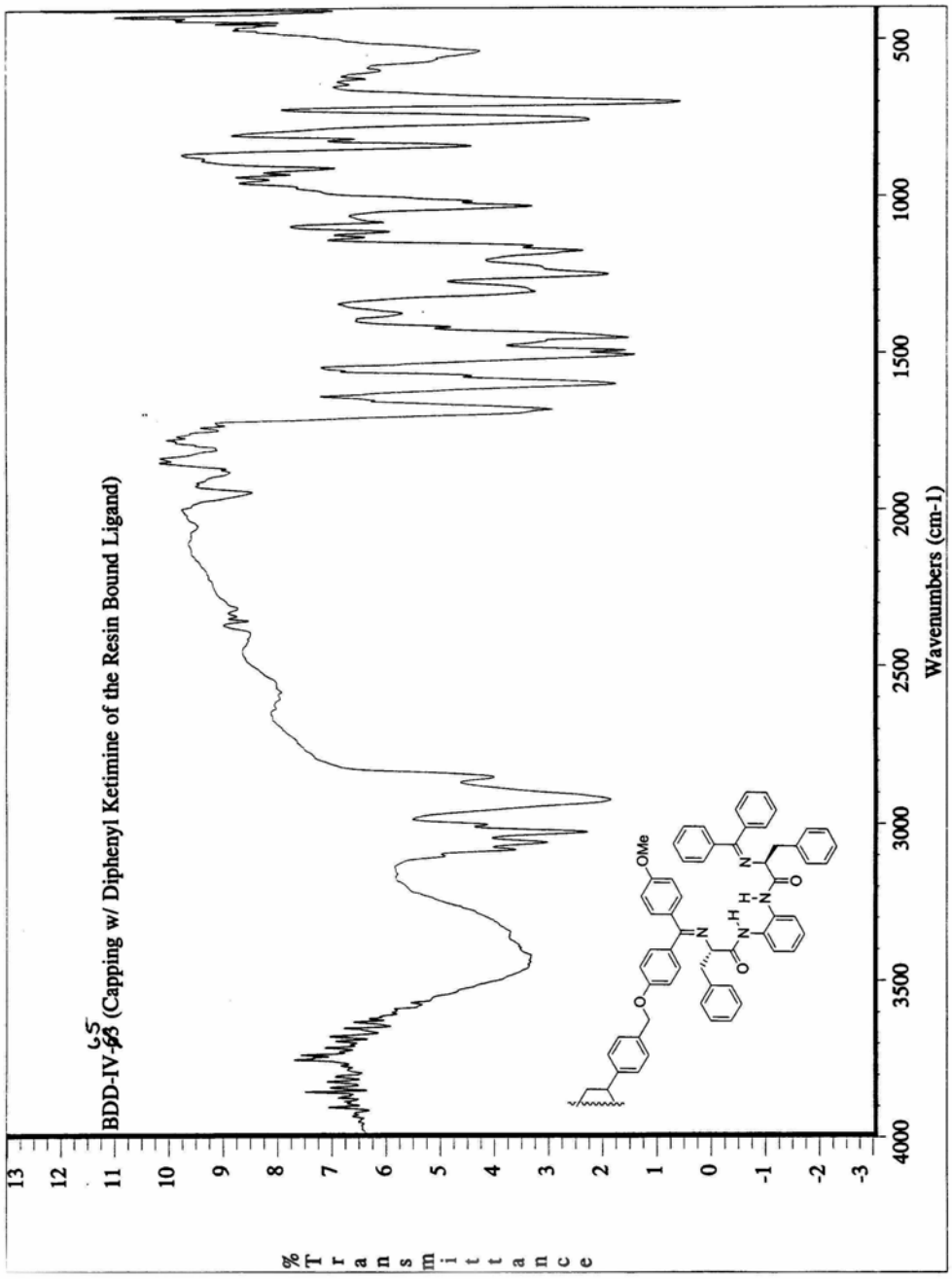

BDD-IV-35 (Grignard Add'n to the Nitrile to form the Resin Bound Imine)
OMe
NH
O
% Transmittance
10
9
8
7
6
5
4
3
2
1
0
-1
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

Resin-Bound (Wang) Phe/Phe Ligand, **5**. In a jacketed sintered glass funnel, the Wang-based ketimine resin (1.09 g, 1.28 mmol/g. 1.39 mmol) was suspended in 80 ml of freshly distilled toluene. The Phe/Phe bis-HCl salt (2g, 4.2 mmol, 3 equiv.) was free based and azeotropically dried before use. The free amine and dry TsOH (240 mg, 1.39 mmol, 1 equiv.) were added to the suspension in a single portion. The reaction mixture was heated to 90°C and agitated with a stream of argon for 24 hours. The resin was then cooled and worked up by filtering the resin and washing with CH_2Cl_2 (3 X 100 ml). A portion of the resin was analyzed by FT-IR (KBr Pellet) to show the presence of the amide carbonyl at 1681 cm^{-1}.

The resin was then re-suspended in 80 ml of dry toluene. TsOH (240 mg, 1.39 mmol. 1 equiv.) and benzophenone imine (1.17 ml, 1.26 g, 6.97 mmol, 5 equiv.) were added in a single portion. The reaction mixture was heated to 60°C for 24 hours. The resin was then cooled and worked up in the following manner.

The resin was filtered and washed with anhydrous methanol (3x50ml); CH_2Cl_2 (3x50ml); methanol (2x50ml); dried resin under vacuum at 60°C for 16 hours. Analysis of the resin bound ligand by FT-IR (KBr Pellet) showed no significant change in the spectrum.


BDD-IV-56c (1 equiv TsOH w/ bis-Phe/Phe free amine)
%Transmittance
Wavenumbers (cm-1)
OMe
NH2


BDD-IV-65 (Capping w/ Diphenyl Ketimine of the Resin Bound Ligand)
% Transmittance
Wavenumbers (cm-1)
OMe