Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

In depth analysis of heterogeneous catalysts for the chemoenzymatic dynamic kinetic resolution of beta-amino esters.

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Supplementary information

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1.0 Additional racemization data and figures

Figure 1: Racemization of beta-phenylalanine propyl ester with Pd/AlO(OH) (1 wt%) at various conditions. General reaction conditions: 72.5 mM substrate, 5 mol% catalyst, toluene, p(H_2) = 0.50 bar, p(total) = 5.0 bar (N2), 70 °C, 24 h.

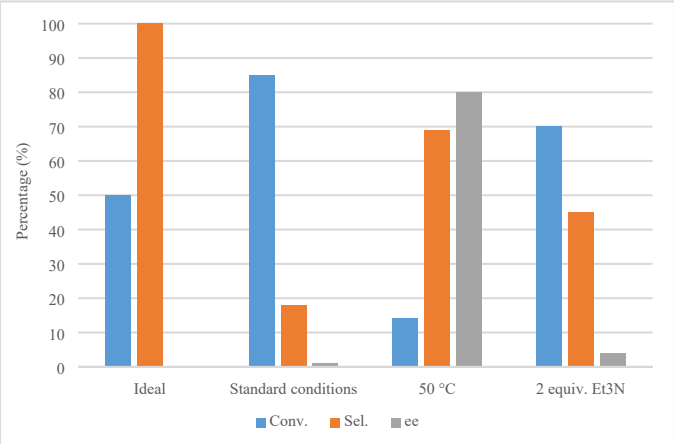
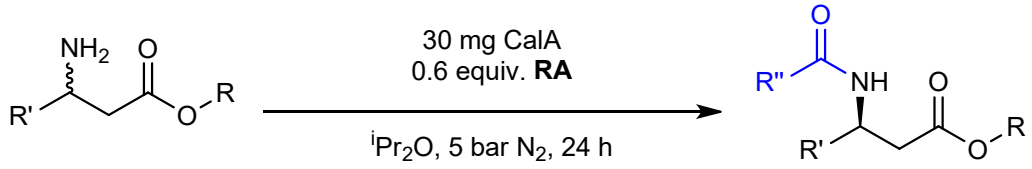


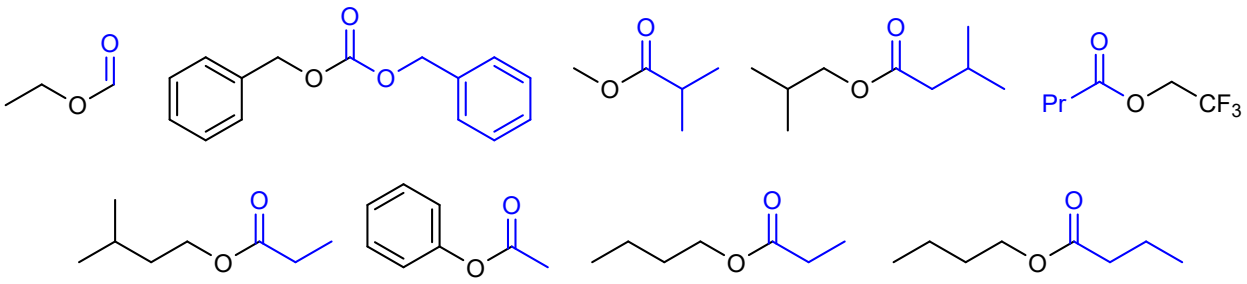
Table 1: Influence of base on the racemization of R-beta-phenylalanine propyl ester. General reaction conditions: 72.5 mM substrate, 5 mol% catalyst, toluene, p(H_2) = 0.50 bar, p(total) = 5.0 bar (N_2), 70 °C, 24 h. 2 equivalents of Et_3N with respect to the substrate were added. [1]: 5 equivalents instead of 2.

Entry	Catalyst	Additive	Conv. (%)	Sel. (%)	ee_R (%)
1	$Pd/CaCO_3$		59	70	1
2	$Pd/CaCO_3$	Cs_2CO_3	0	> 99	> 99
3	$Pd/CaCO_3$	K_2CO_3[1]	15	> 99	70
4	$Pd/CaCO_3$	KOH[1]	53	72	11
5	**$Pd/CaCO_3$**	**Et_3N**	**52**	**88**	**3**

2.0 Reaction scheme of the kinetic resolution



RA:



3.0 Derivation of kinetic equations

$$\frac{d[R]}{dt} = -k_1[R] + k_{-1}[imine] \quad (1)$$

$$\frac{d[S]}{dt} = -k_1[S] + k_{-1}[imine] \quad (2)$$

$$\frac{d[imine]}{dt} = -2k_{-1}[imine] + k_1([R] + [S]) \quad (3)$$

$$[R]_0 = [R] + [S] + [imine] \quad (4)$$

Assume equilibrium has been established so that $\frac{d[imine]}{dt} = 0$; this allows us to derive (3) to yield (5):

$$[imine] = \frac{k_1}{2k_{-1}}([R] + [S]) \quad (5)$$

$$[imine] = \frac{k_1}{2k_{-1}}([R]_0 - [imine]) \quad \textbf{substitute (4) into (5)} \quad (6)$$

$$[imine] = \frac{k_1}{k_1 + 2k_{-1}}[R]_0 \quad (7)$$

Enter (7) into (1) to yield:

$$\frac{d[R]}{dt} = -k_1[R] + \frac{k_1 k_{-1}}{k_1 + 2k_{-1}}[R]_0 \quad (8)$$

$$[R] = ce^{-k_1 t} + \frac{k_{-1}}{k_1 + 2k_{-1}}[R]_0 \quad \textbf{solve differential equation} \quad (9)$$

at t = 0, $[R] = [R]_0$; thus:

$$c = \frac{k_1 + k_{-1}}{k_1 + 2k_{-1}}[R]_0 \quad (10)$$

$$[R] = [R]_0 \frac{(k_{-1} + (k_1 + k_{-1})(e^{-k_1 t}))}{(k_1 + 2k_{-1})} \quad \textbf{enter (10) into (9)} \quad (11)$$

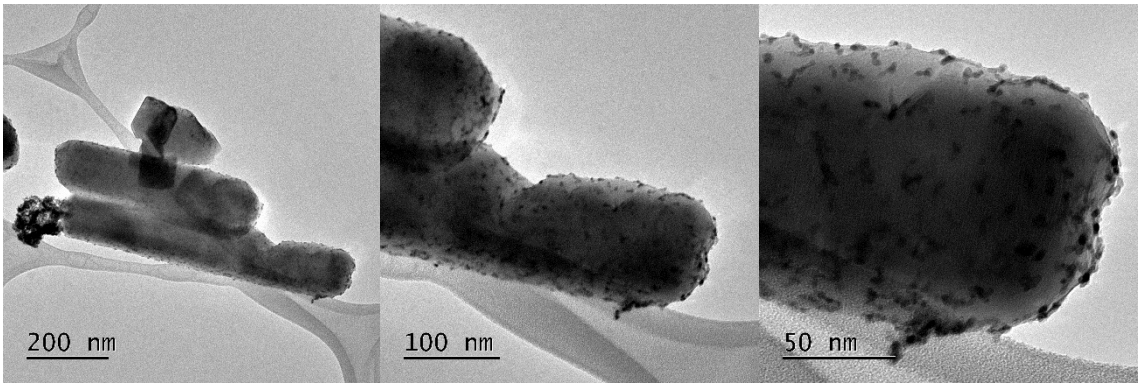
Correct for side reaction by introducing $(e^{-k_2 t})$:

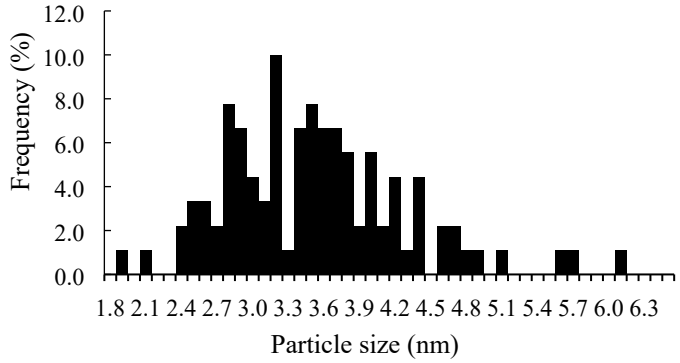
$$[R] = [R]_0 \frac{(k_{-1} + (k_1 + k_{-1})(e^{-k_1 t}))}{(k_1 + 2k_{-1})}(e^{-k_2 t})$$

(12)

4.0 Additional TEM images and particle distribution.

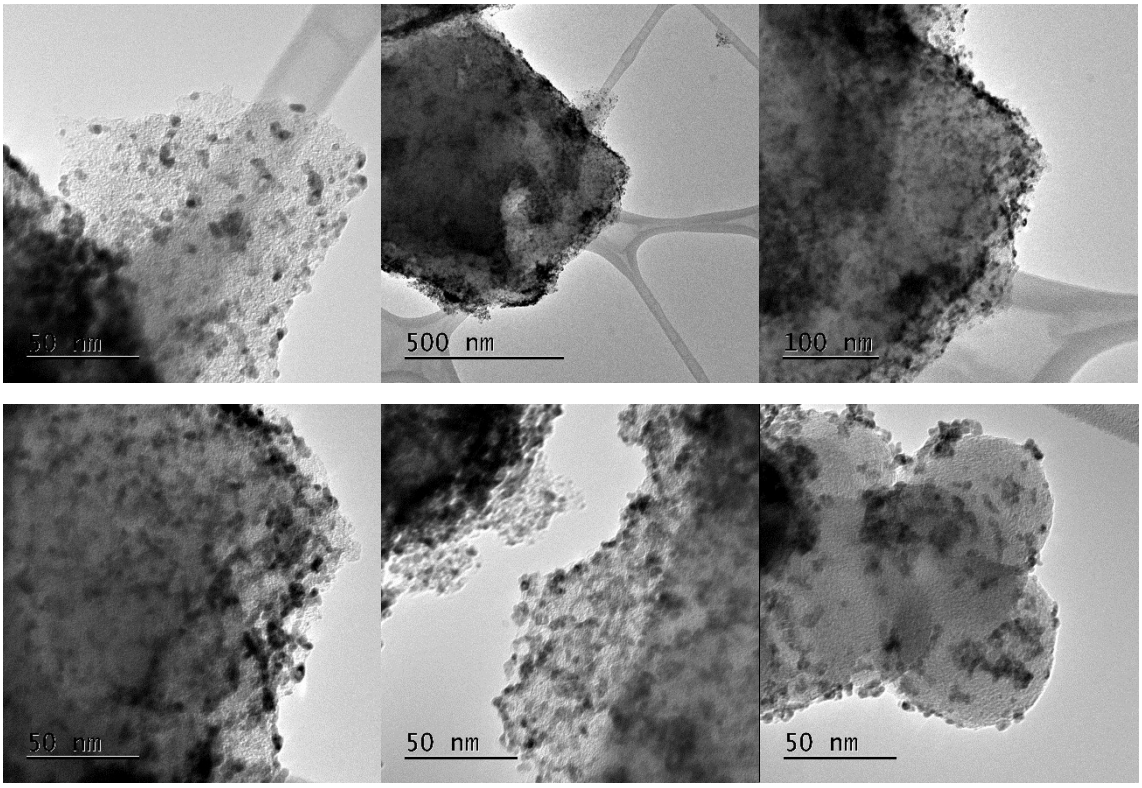
Pd/$CaCO_3$

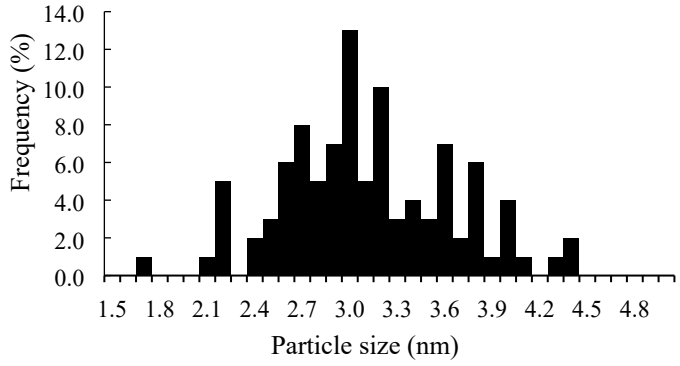




Median:	3.46 nm
Mean:	3.48 nm
Std deviation:	0.76

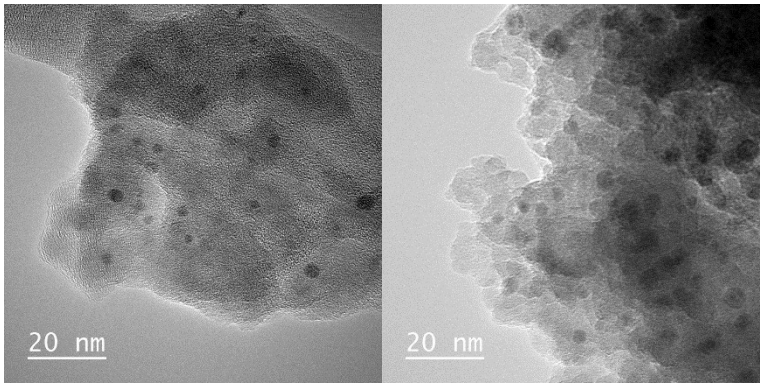
$Pd(OH)_2/C$

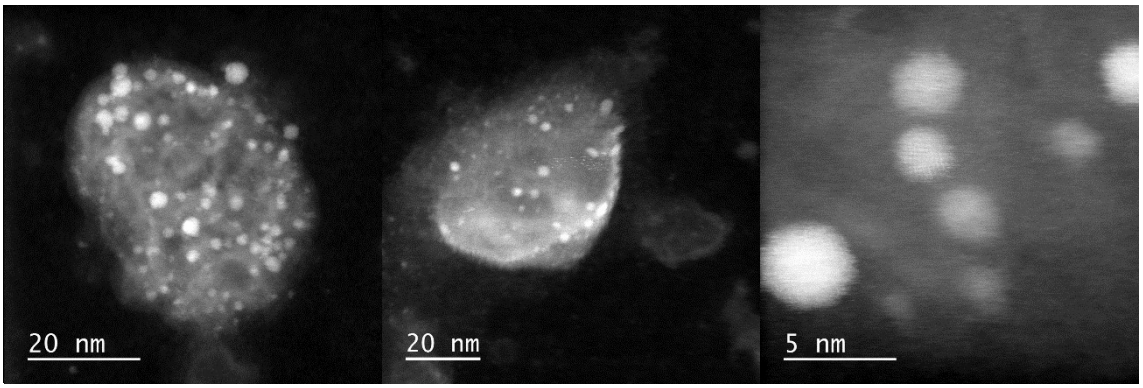


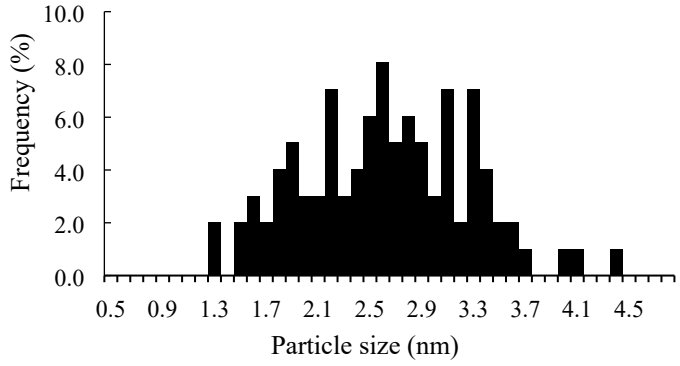


Median:	2.99 nm
Mean:	3.10 nm
Std deviation:	0.64

Pd/AlO(OH)



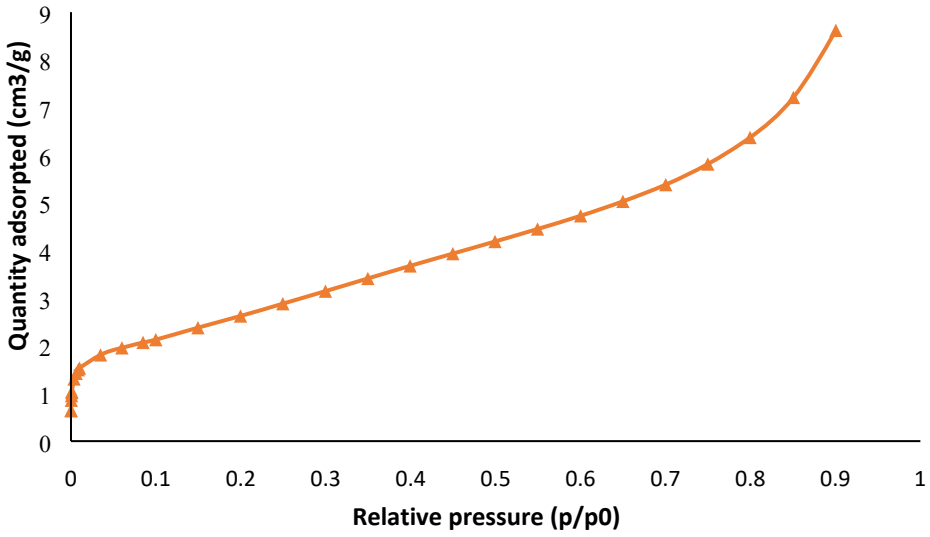




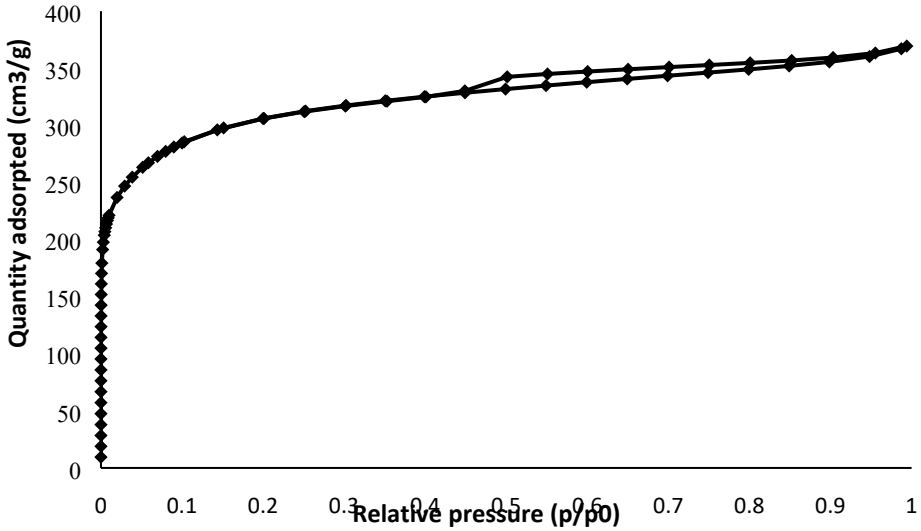
Median:	2.58 nm
Mean:	2.57 nm
Std deviation:	0.64

5.0 N_2 physisorption isotherms

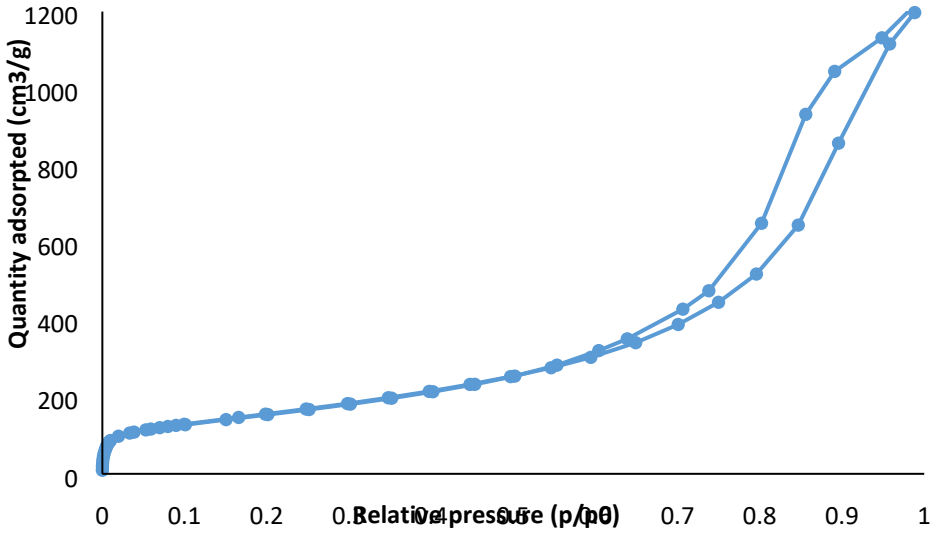
$Pd/CaCO_3$



$Pd(OH)_2/C$



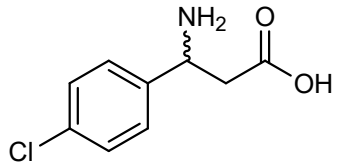
Pd/AlO(OH)

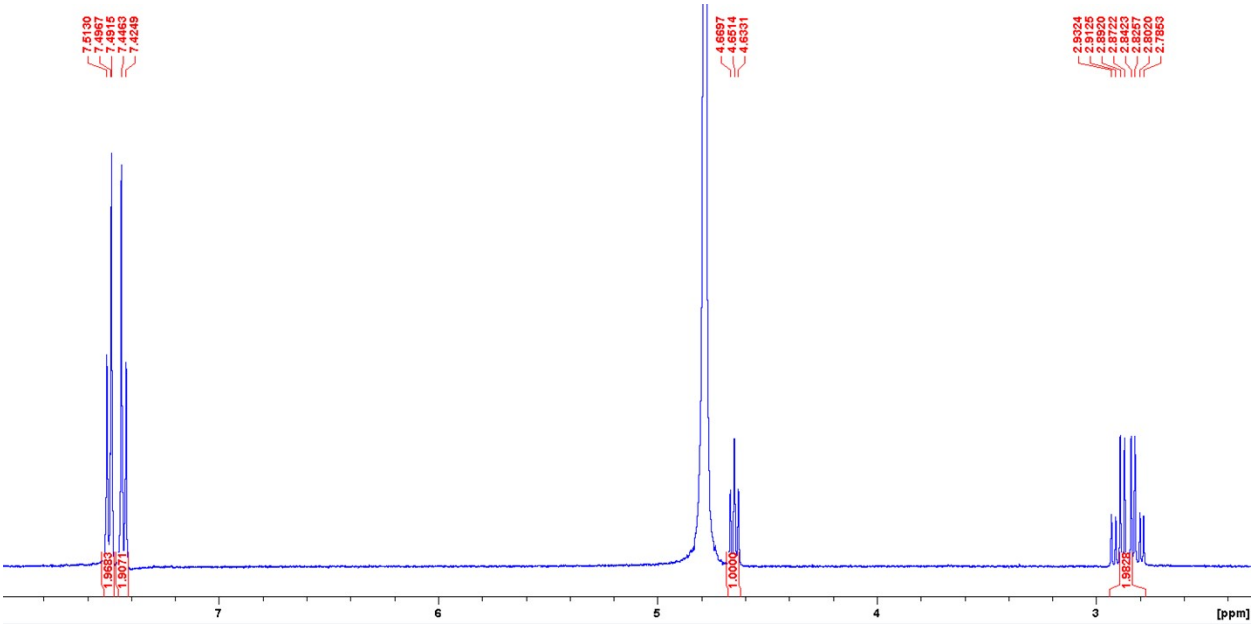

Quantity adsorpted (cm3/g)
1200
1000
800
600
400
200
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Relative pressure (p/p0)

6.0 Amino ester characterization

6.1 Synthesis of β-amino acids

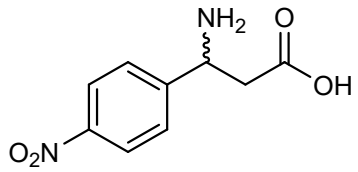
3-amino-3-(4'-chlorophenyl)propionic acid (199.63 g/mol)

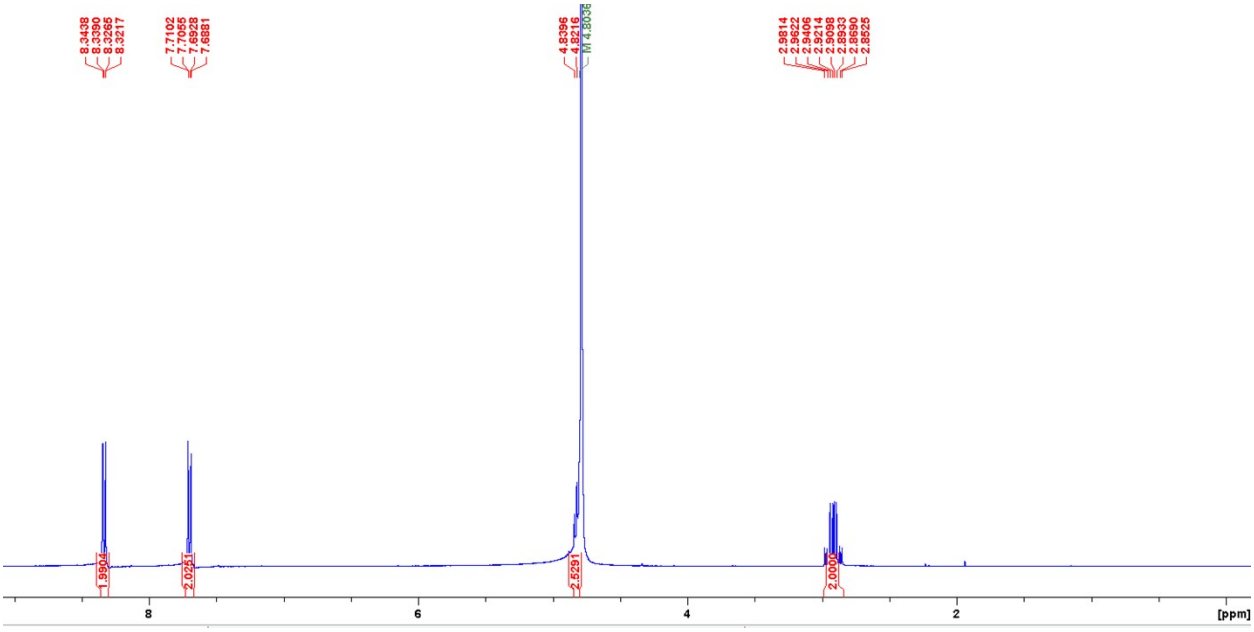




^{1}H NMR (300 MHz; D_2O): δ_H 2.77-2.95 (2 H, m (2 x dd)), 4.65 (1 H, m (dd)), 7.41-7.53 (4 H, m).

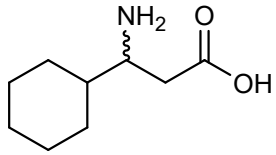
3-amino-3-(4'-nitrophenyl)propionic acid (210.19 g/mol)

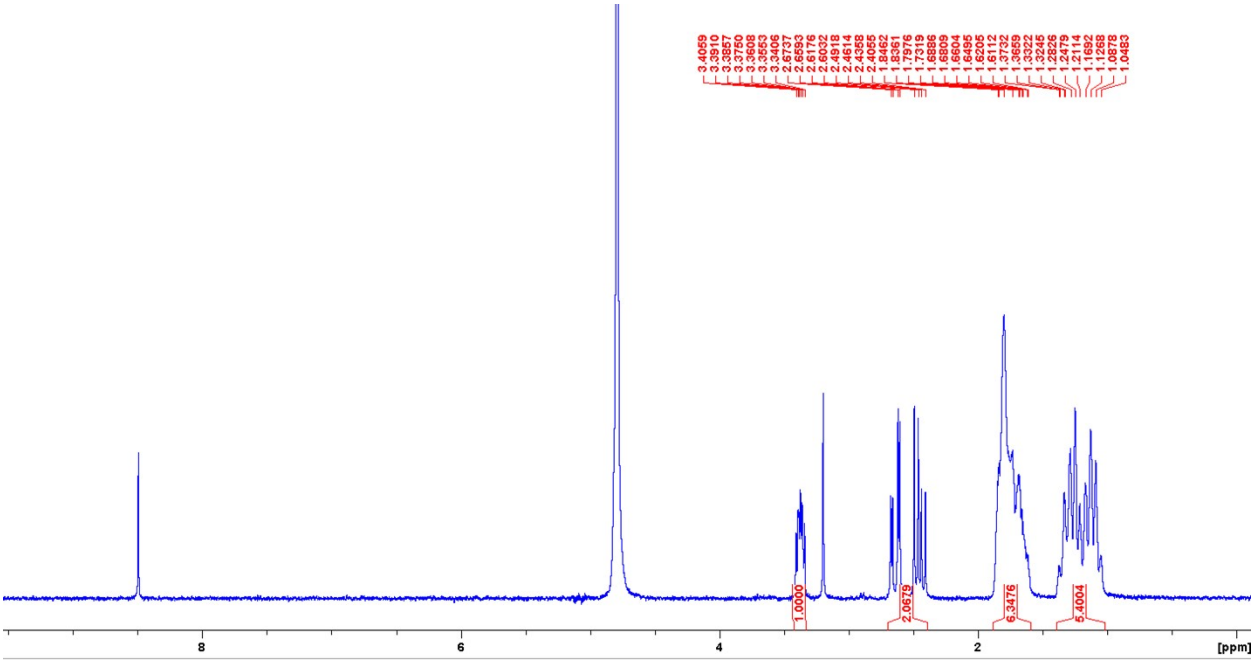




^{1}H NMR (300 MHz; D_2O): δ_H 2.82-2.99 (2 H, m (2 x dd)), 7.69 (2 H, d), 8.31 (2 H, d). (Ph-C**H**(NH_2)-CH_2-COOH signal probably underneath H_2O signal)

3-amino-3-cylohexanepropionic acid (171.24 g/mol)



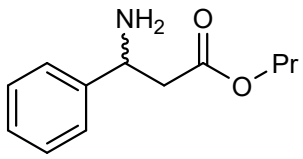


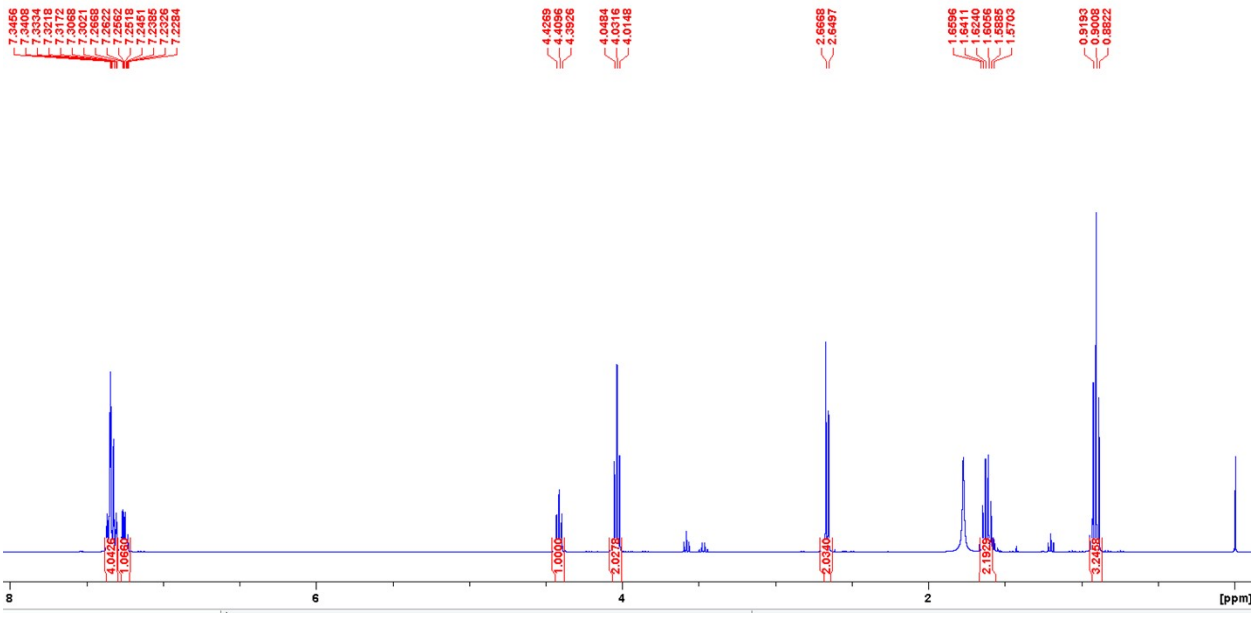
^{1}H NMR (300 MHz; D_2O): δ_H 1.04-1.40 (5 H, m), 1.60-1.88 (6 H, m), 2.39-2.70 (2 H, m (2 x dd)), 3.32-3.43 (1 H, m (dd)).

6.2 Synthesis of β-amino esters

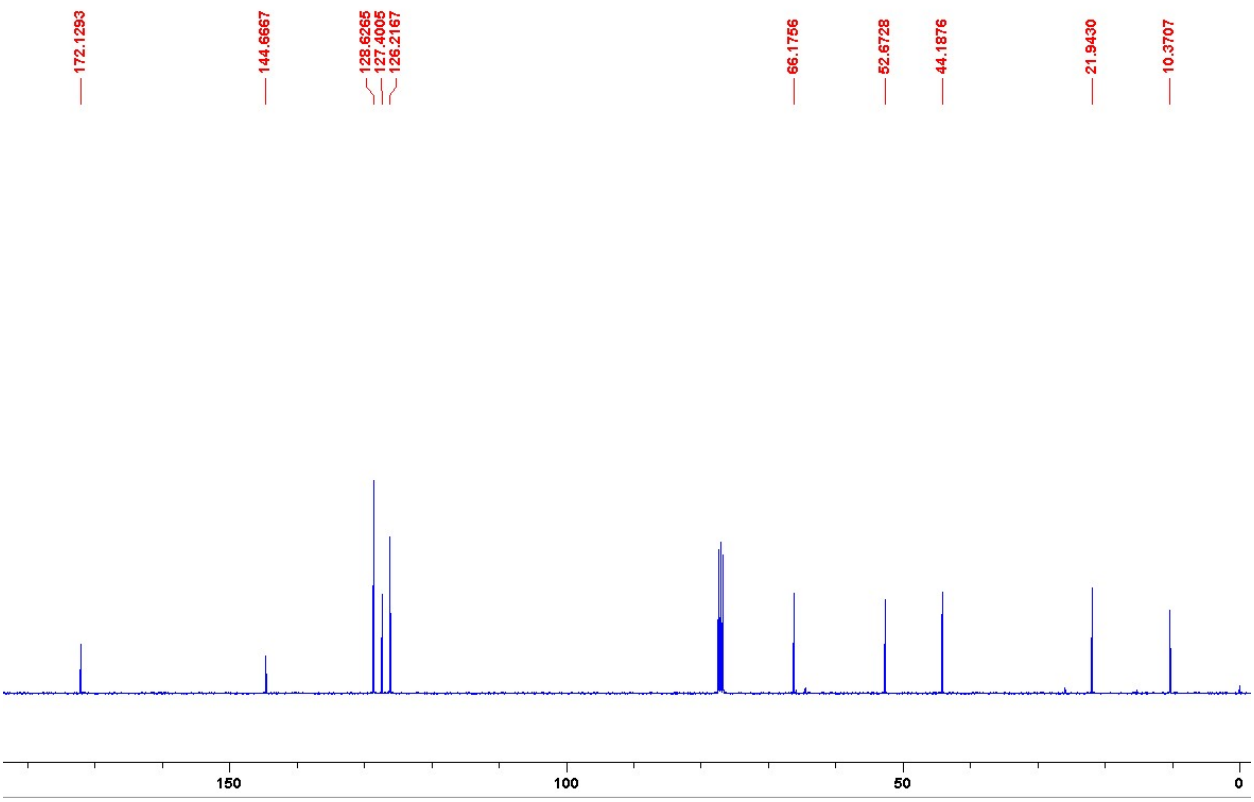
A notation of "CH" and "Cq" is used in the description of ^{13}C-NMR signals to denote protonated carbons (CH, CH_2 or CH_3) and quaternary carbons, respectively.

propyl 3-aminobenzenepropanoate (207.27 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.58-1.68 (2 H, sext), 2.65-2.69 (2 H, m (2 x dd)), 4.04 (2 H, t), 4.42 (1 H, t (dd)), 7.23-7.29 (1 H, m), 7.30-7.39 (4 H, m).



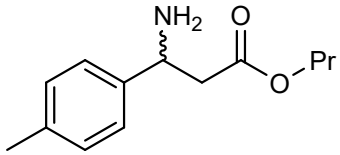
^{13}C NMR (400 MHz, $CDCl_3$): δ_C 10.4 (CH), 21.9 (CH), 44.2 (CH), 52.7 (CH), 66.2 (CH), 126.2 (CH), 127.4 (Cq), 128.6 (CH), 144.7 (Cq), 172.1 (Cq).

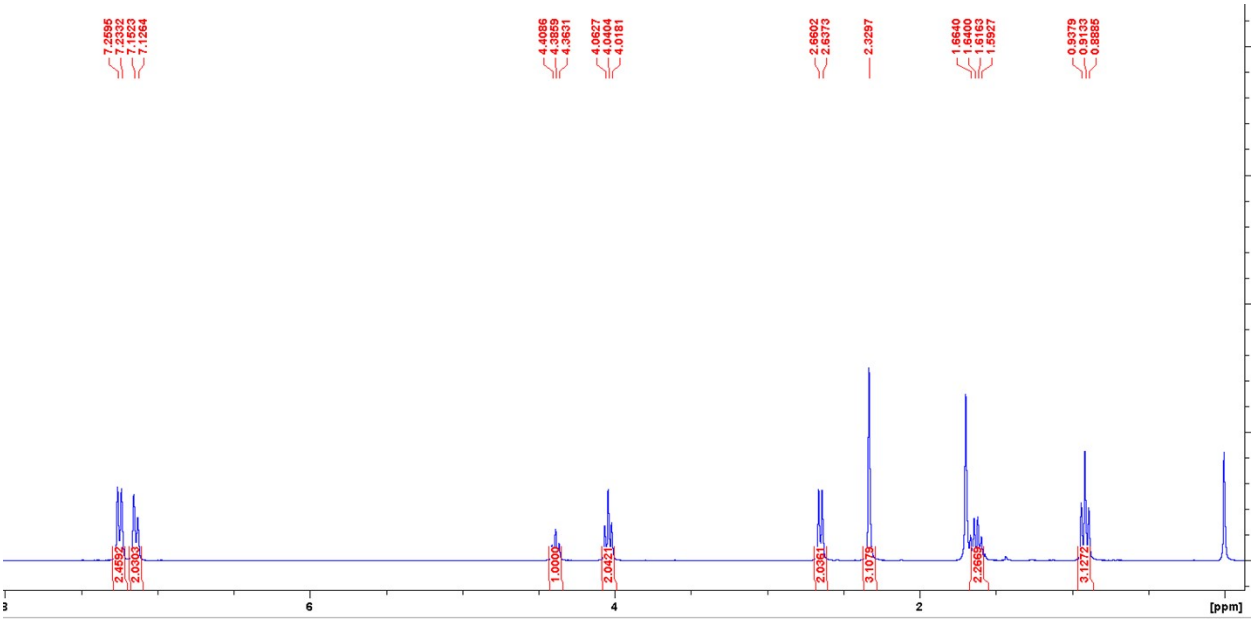
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

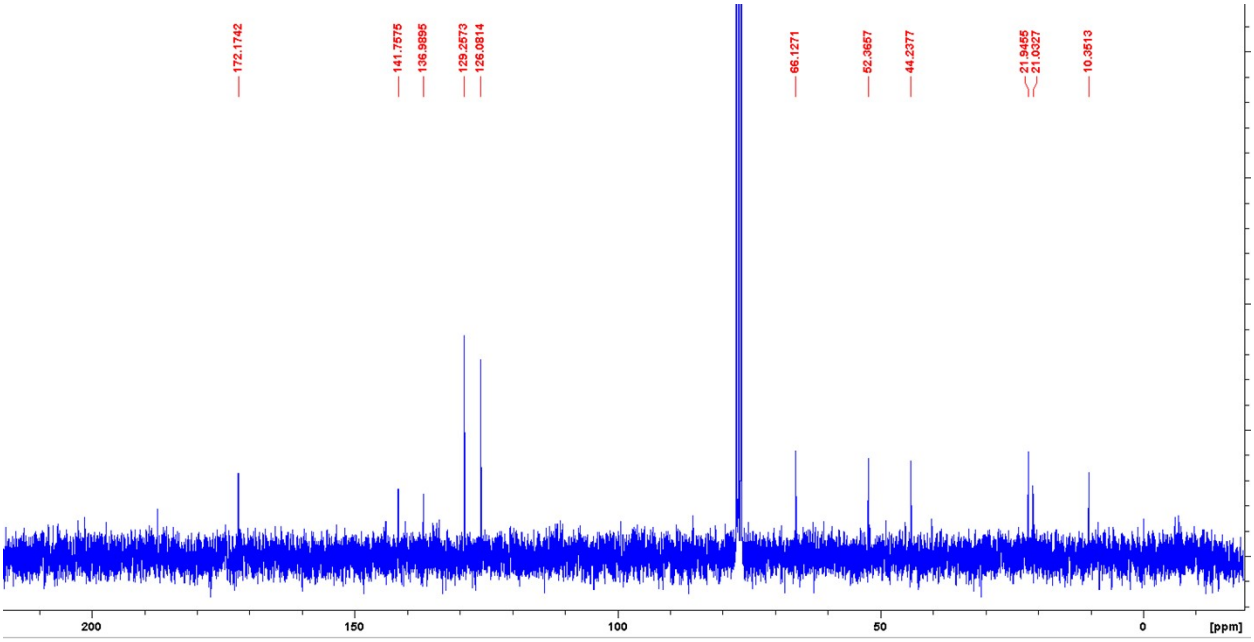
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4'-methylbenzenepropanoate (221.30 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.55-1.70 (2 H, sext), 2.33 (3 H, s), 2.65 (2 H, d (2 x dd)), 4.04 (2 H, t), 4.39 (1 H, t (dd)), 7.14 (2 H, d), 7.25 (2 H, d).



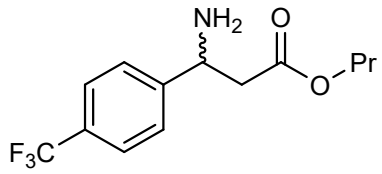
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 21.0 (CH), 21.9 (CH), 44.2 (CH), 52.4 (CH), 66.1 (CH), 126.1 (CH), 129.3 (CH), 137.0 (Cq), 141.8 (Cq), 172.2 (Cq).

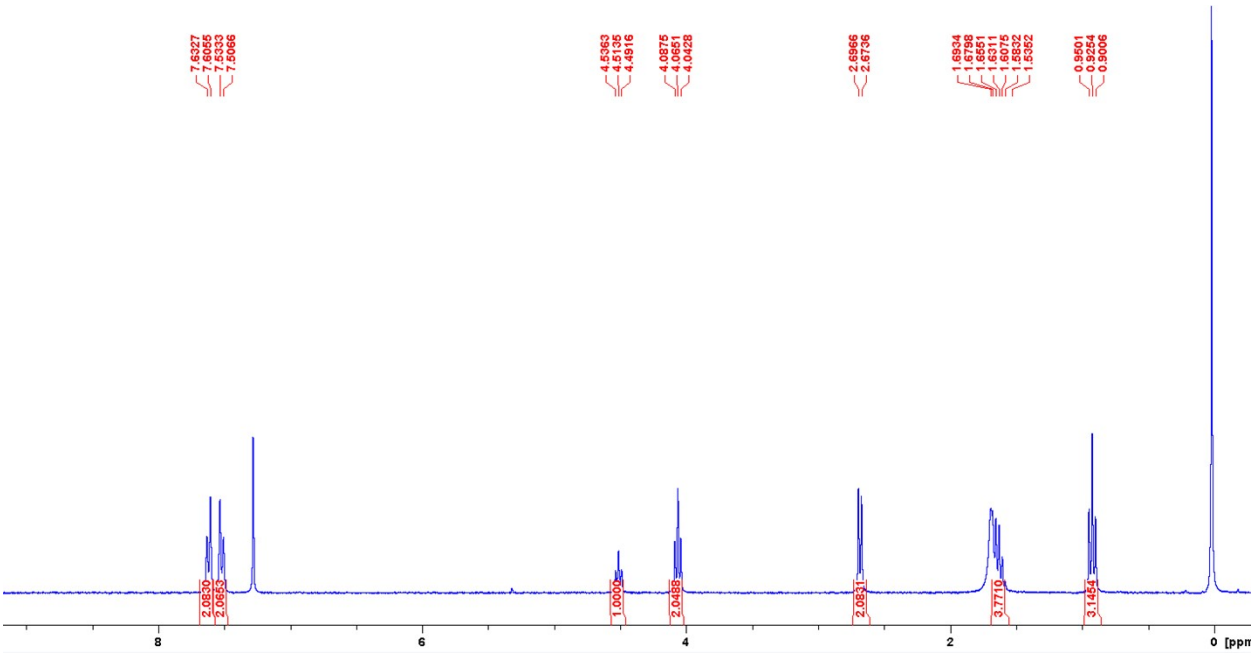
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

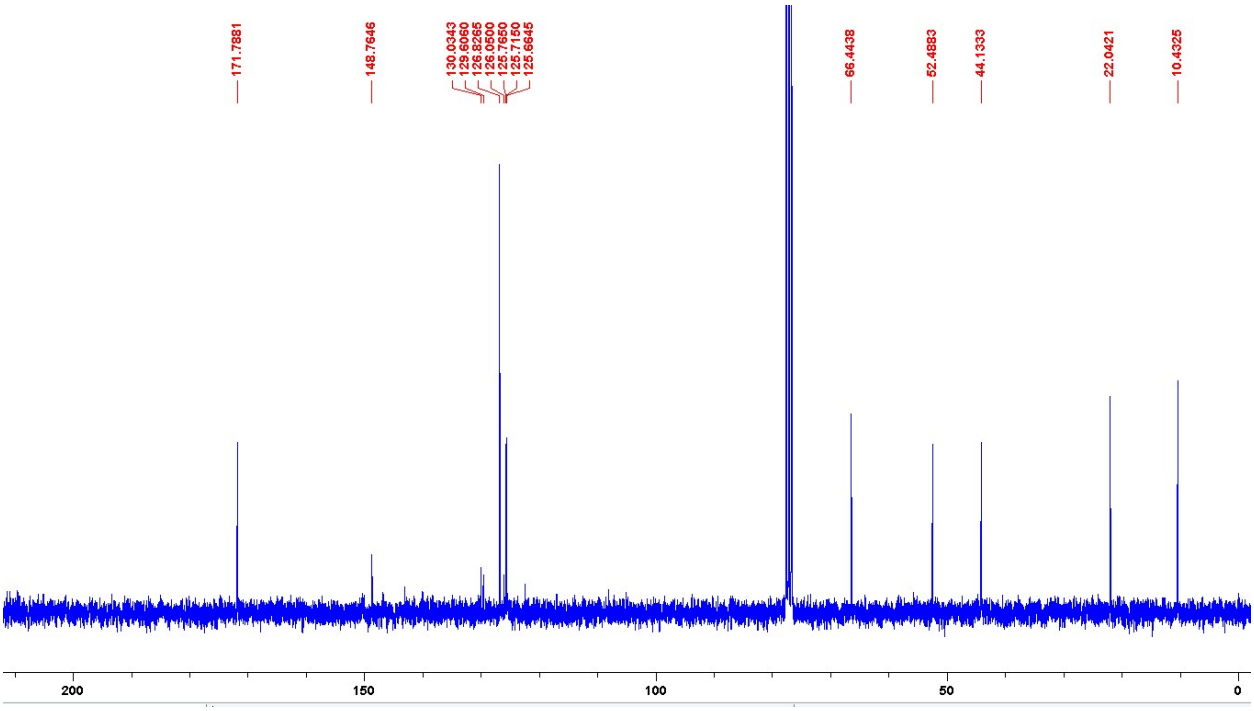
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4'-(trifluoromethyl)benzenepropanoate (275.27 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.92 (3 H, t), 1.56-1.70 (2 H, sext), 2.67 (2 H, d (2 x dd)), 4.04 (2 H, t), 4.48 (1 H, t (dd)), 7.49-7.65 (4 H, m (dd)).



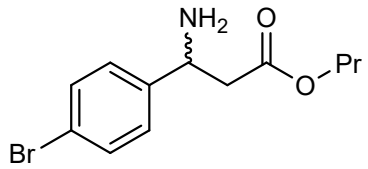
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 22.0 (CH), 44.1 (CH), 52.5 (CH), 66.4 (CH), 125.7 (q, CF_3), 126.8 (CH), 130.0 (Cq), 148.8 (Cq), 171.8 (Cq).

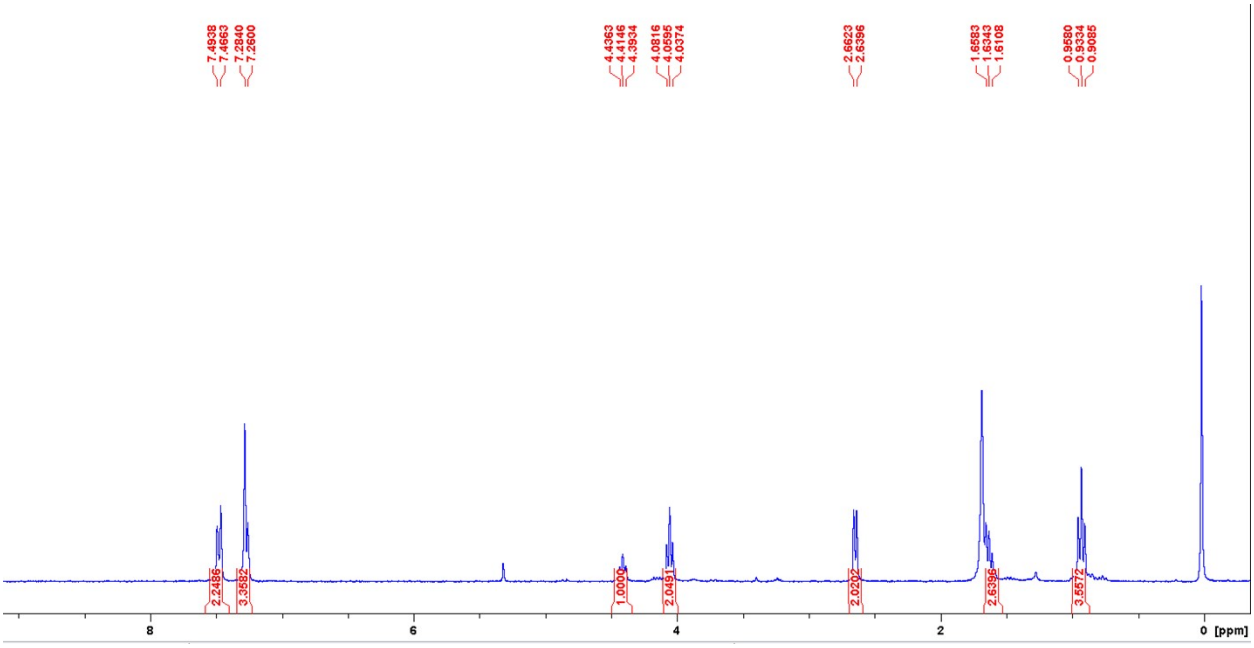
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

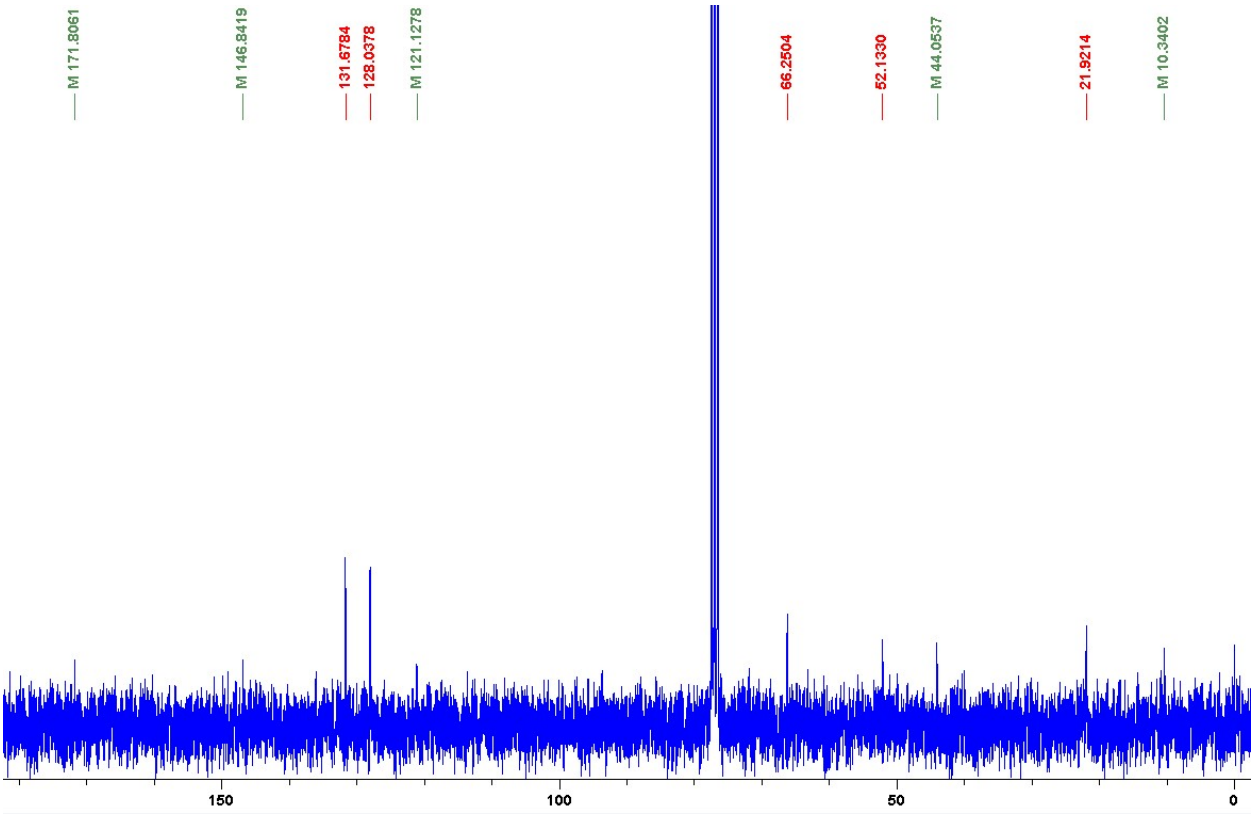
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4'-bromobenzenepropanoate (286.16 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.55-1.70 (2 H, sext), 2.62 (2 H, d (2 x dd)), 4.04 (2 H, t), 4.39 (1 H, t (dd)), 7.21-7.28 (2 H, m), 7.42-7.49 (2 H, m).



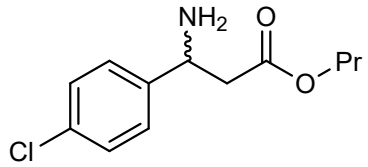
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.2 (CH), 21.9 (CH), 44.1 (CH), 52.1 (CH), 66.3 (CH), 121,1 (Cq), 128.0 (CH), 131.7 (CH), 146.8 (Cq), 171.8 (Cq).

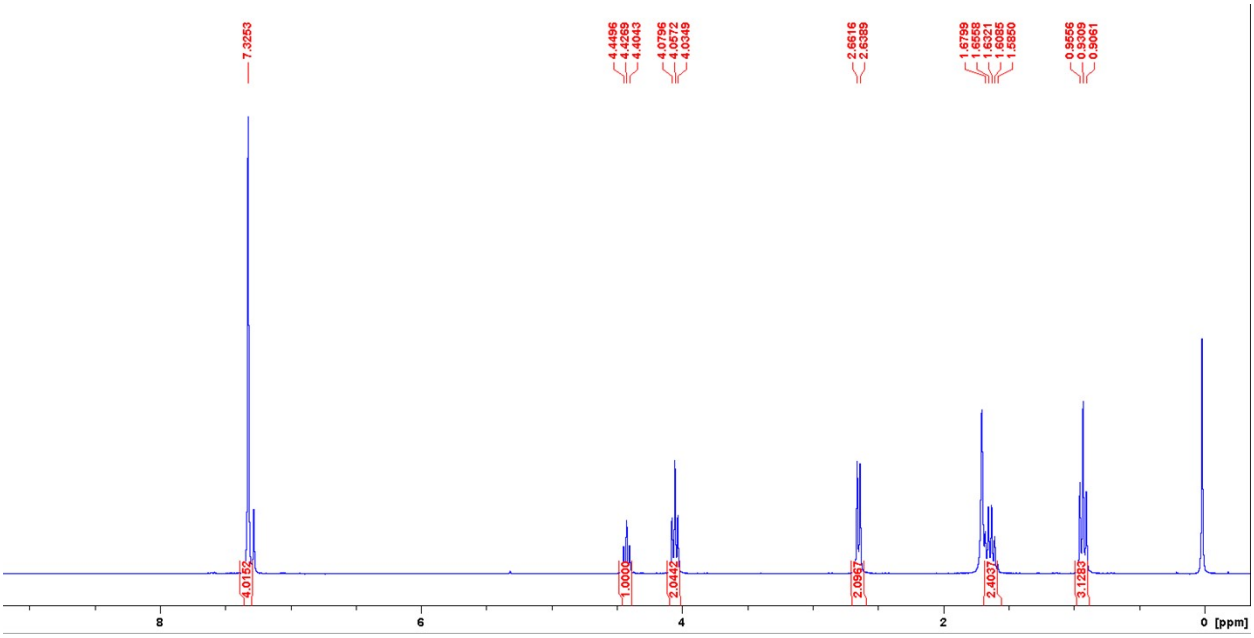
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

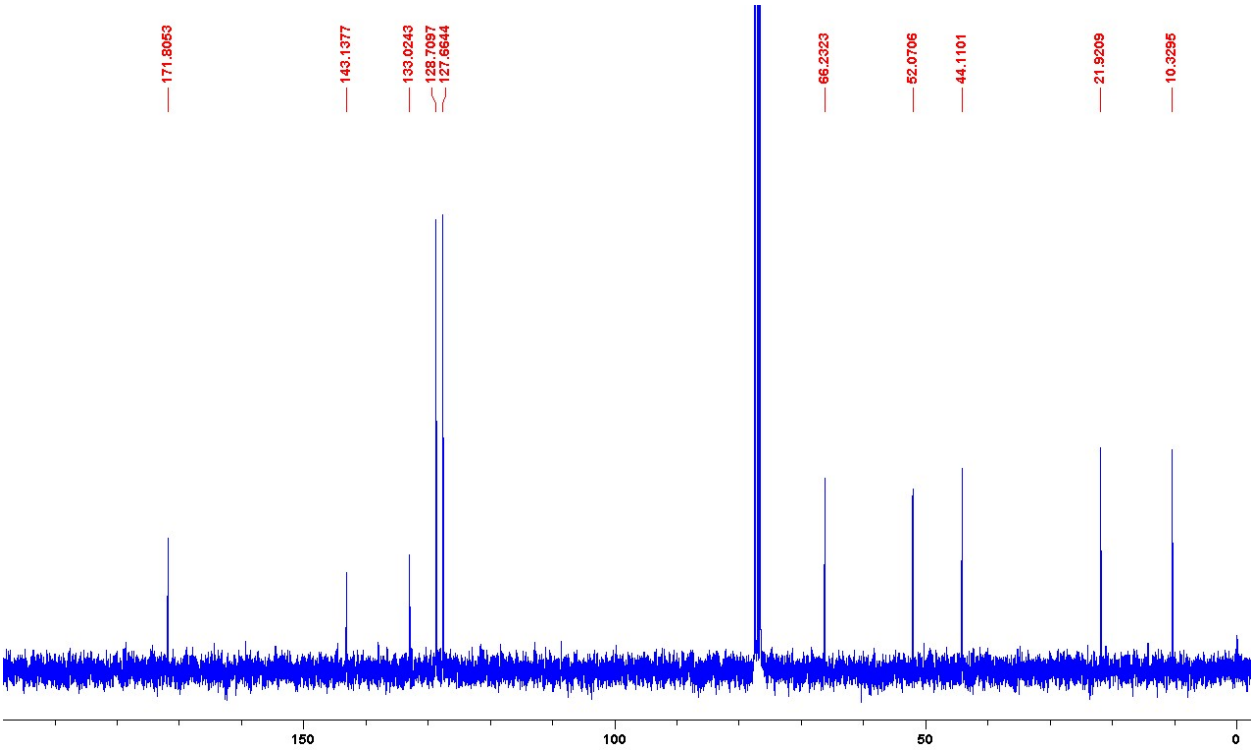
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4’-chlorobenzenepropanoate (241.71 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.55-1.70 (2 H, sext), 2.63 (2 H, d (2 x dd)), 4.04 (2 H, t), 4.41 (1 H, t (dd)), 7.33 (4 H, s).



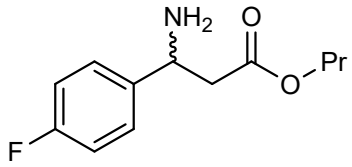
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.3 (CH), 21.9 (CH), 44.1 (CH), 52.1 (CH), 66.2 (CH), 127,7 (Cq), 128.7 (CH), 133.0 (CH), 143.1 (Cq), 171.8 (Cq).

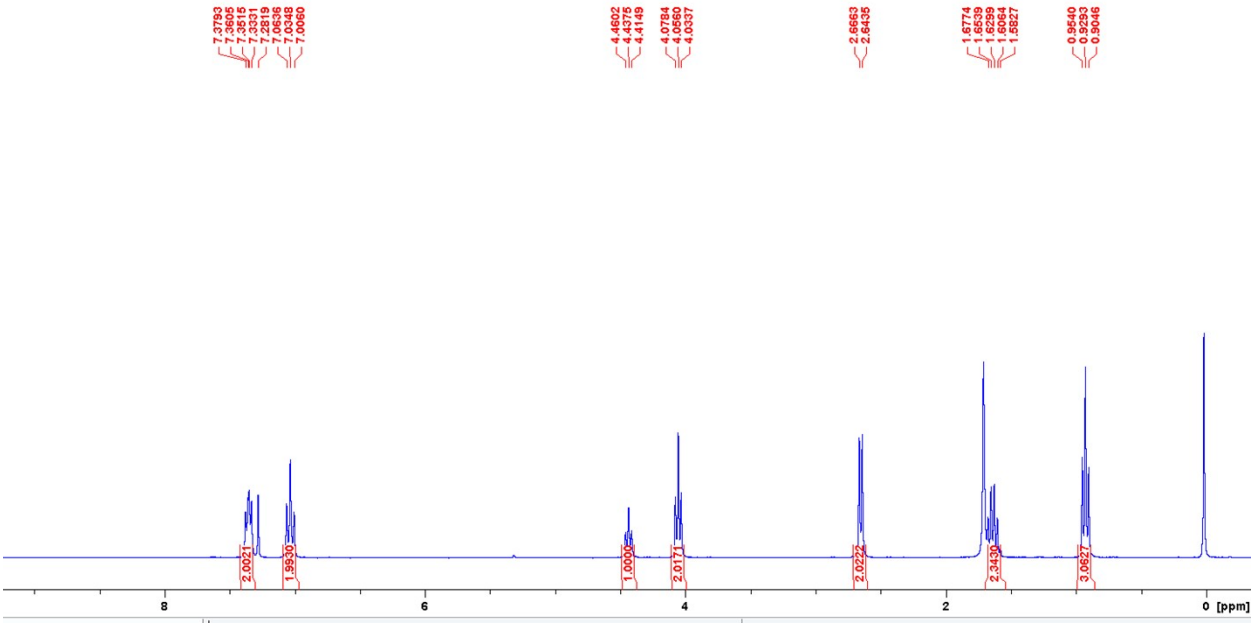
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

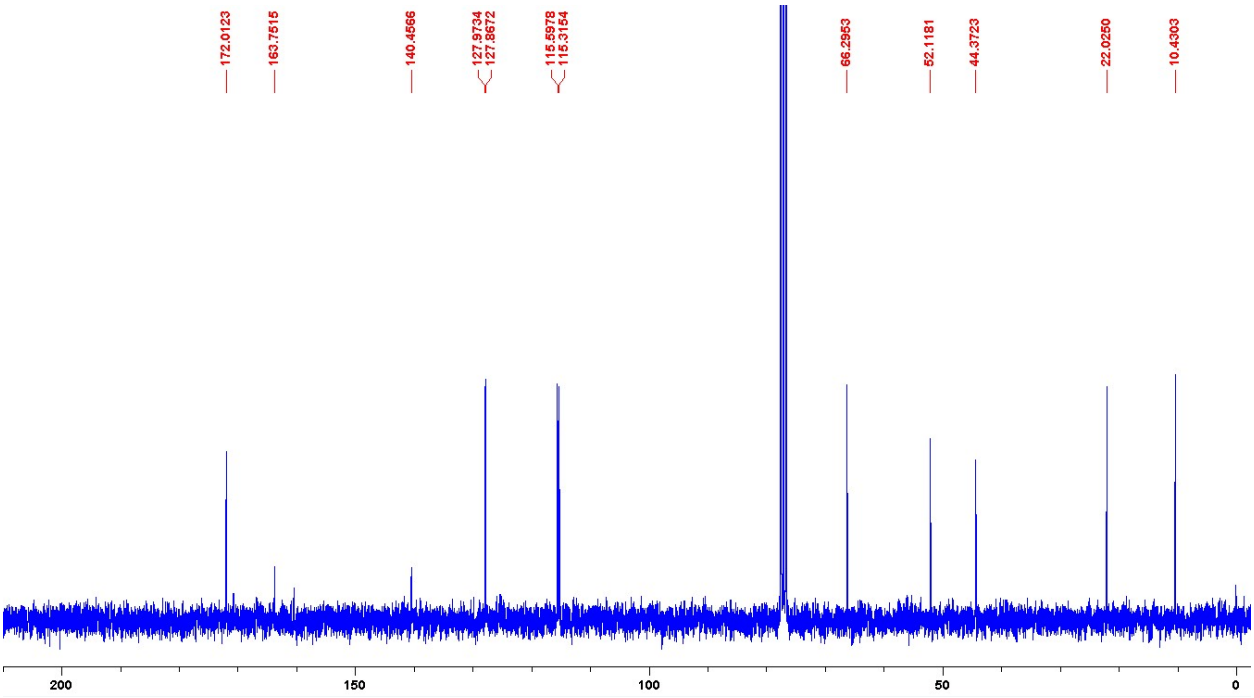
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4'-fluorobenzenepropanoate (225.26 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.92 (3 H, t), 1.57-1.71 (2 H, sext), 2.66 (2 H, d (2 x dd)), 4.05 (2 H, t), 4.44 (1 H, t (dd)), 6.99-7.08 (2 H, m), 7.31-7.40 (2 H, m).



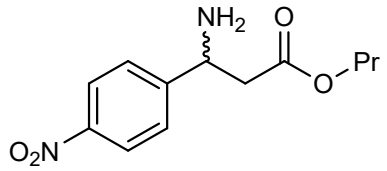
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 22.0 (CH), 44.4 (CH), 52.1 (CH), 66.3 (CH), 115.3 (CH), 115.6 (CH), 127.9 (CH), 128.0 (CH), 140.5 (Cq), 163.8 (Cq), 172.0 (Cq).

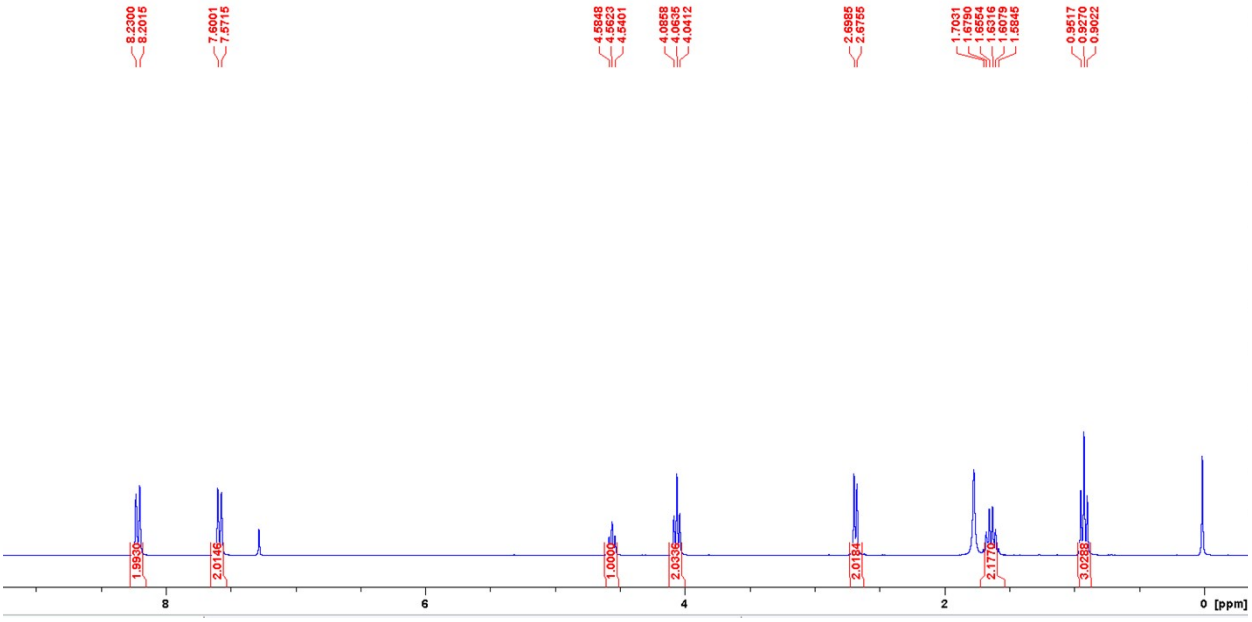
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

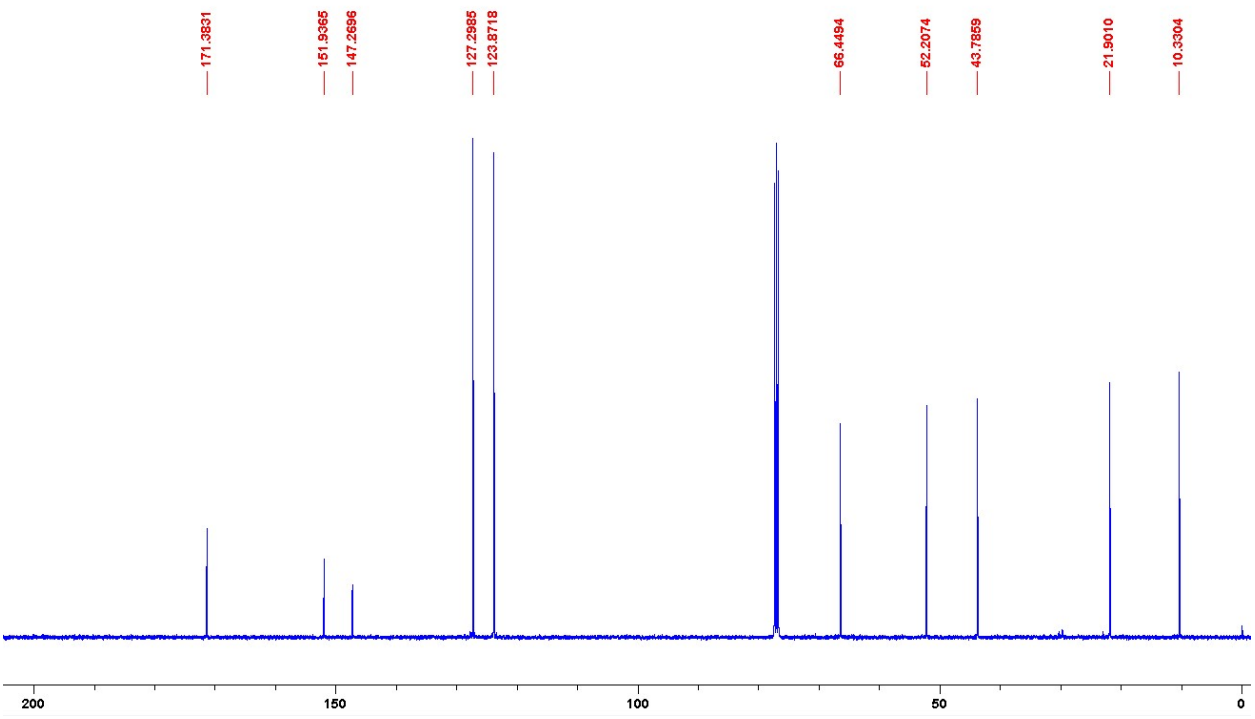
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4’-nitrobenzenepropanoate (252.27 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.54-1.70 (2 H, sext), 2.67 (2 H, d (2 x dd)), 4.05 (2 H, t), 4.55 (1 H, t (dd)), 7.57 (2 H, d), 8.21 (2 H, d).



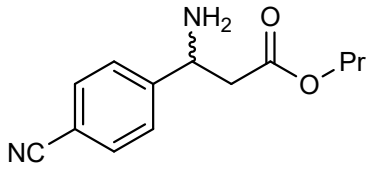
^{13}C NMR (400 MHz, $CDCl_3$): δ_C 10.3 (CH), 21.9 (CH), 43.8 (CH), 52.2 (CH), 66.4 (CH), 123.9 (CH), 127.3 (CH), 147.3 (Cq), 151.9 (Cq), 171.4 (Cq).

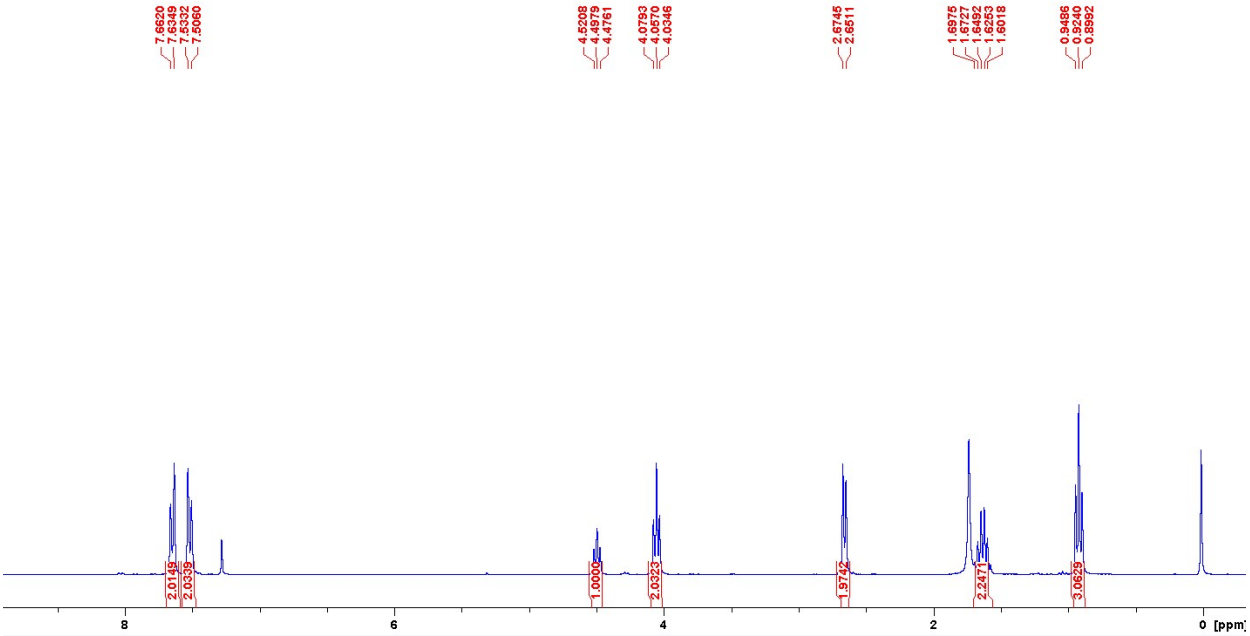
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

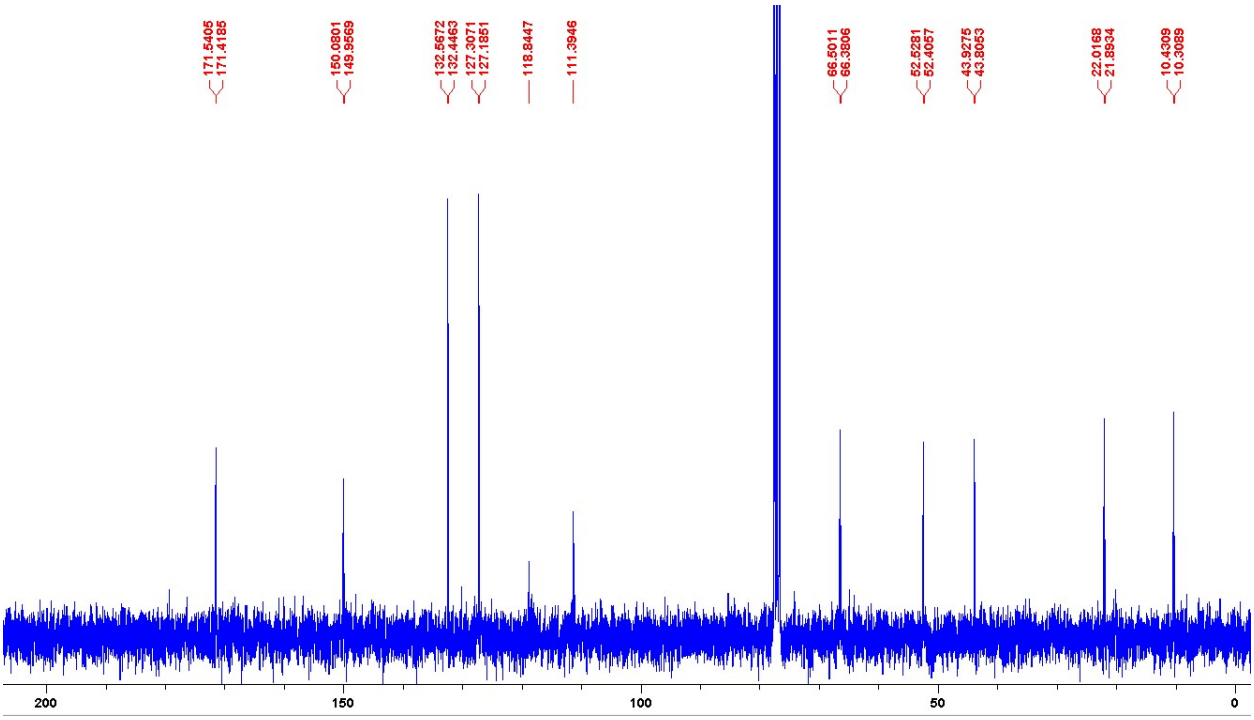
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 45 min, end.

propyl 3-amino-4’-cyanobenzenepropanoate (232.28 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.55-1.68 (2 H, sext), 2.66 (2 H, d (2 x dd)), 4.02 (2 H, t), 4.48 (1 H, t (dd)), 7.45-7.67 (4 H, m).



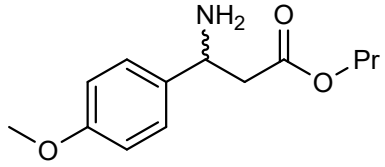
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 22.1 (CH), 43.9 (CH), 52.5 (CH), 66.5 (CH), 111,4 (Cq), 118.8 (Cq), 127.3 (CH), 132.6 (CH), 150.1 (Cq), 171.5 (Cq).

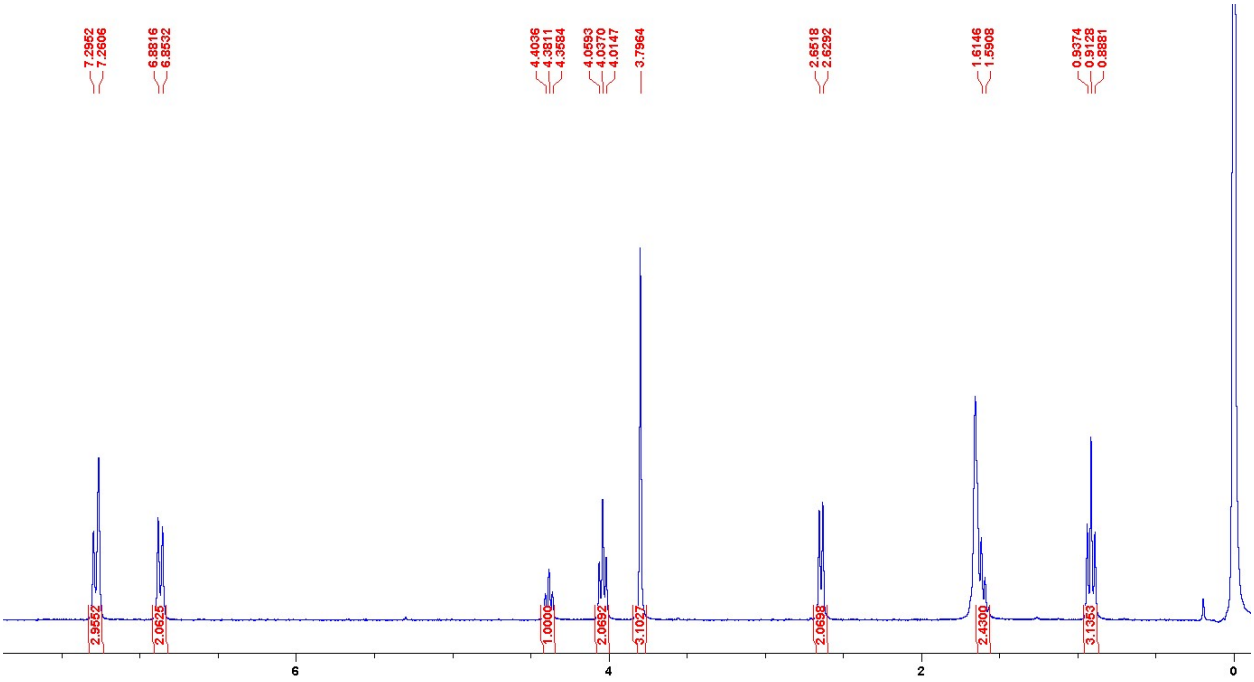
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

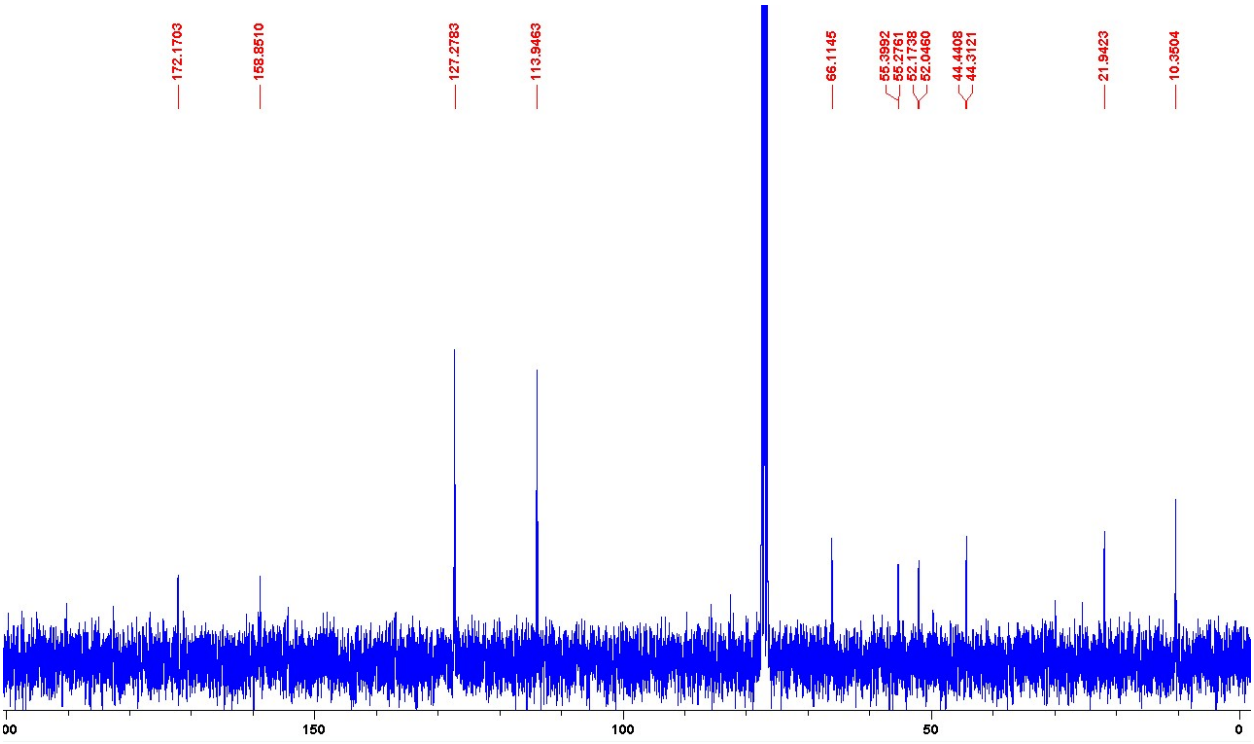
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4'-methoxybenzenepropanoate (237.29 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.91 (3 H, t), 1.56-1.70 (2 H, sext), 2.61-2.67 (2 H, d (2 x dd)), 3.80 (3 H, s), 4.04 (2 H, t), 4.38 (1 H, t (dd)), 6.87 (2 H, d), 7.28 (2 H, d).



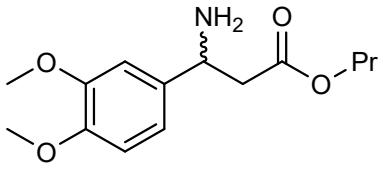
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 21.9 (CH), 44.4 (CH), 52.1 (CH), 55.3 (CH), 66.1 (CH), 113.9 (CH), 127.3 (CH), 137.0 (Cq), 158.9 (Cq), 172.2 (Cq).

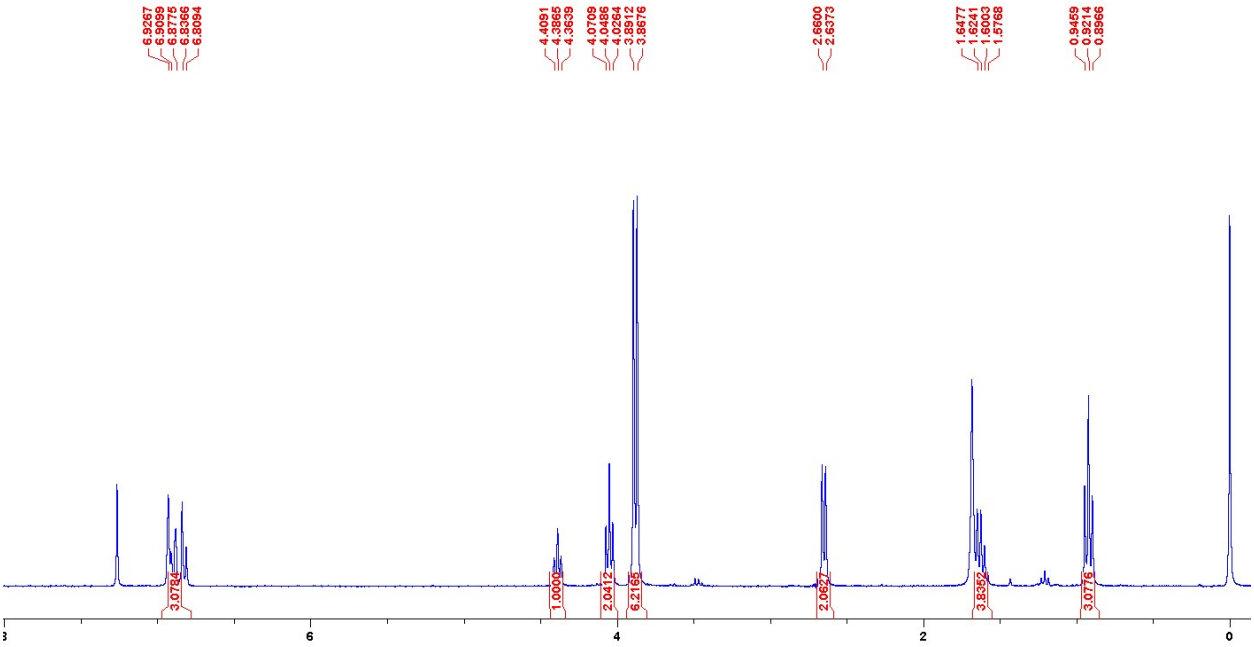
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

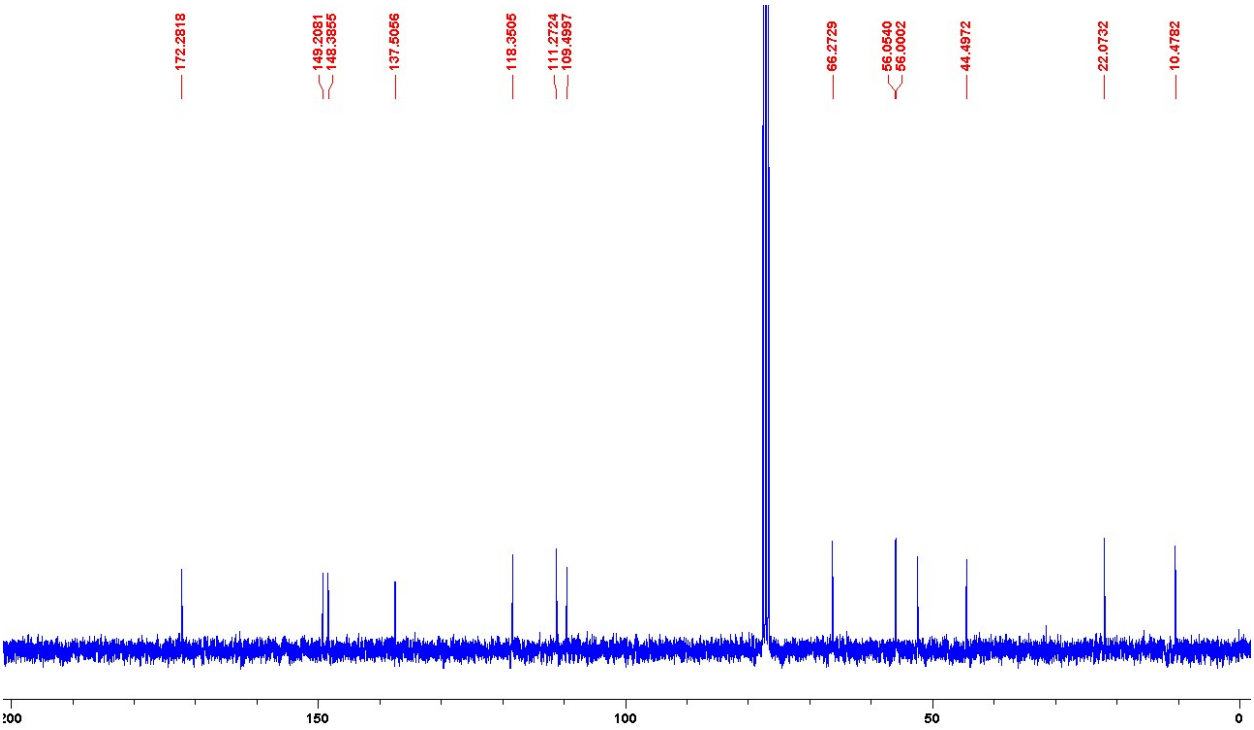
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-3',4'-dimethoxybenzenepropanoate (267.32 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.92 (3 H, t), 1.56-1.69 (2 H, sext), 2.65 (2 H, d (2 x dd)), 3.87 (3 H, s), 3.89 (3 H, s), 4.04 (2 H, t), 4.39 (1 H, t (dd)), 6.78-6.95 (3 H, m).



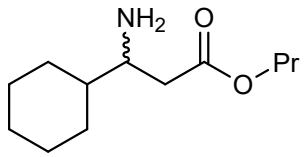
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.4 (CH), 22.1 (CH), 44.5 (CH), 52.5 (CH), 56.0 (CH), 56.1 (CH), 66.3 (CH), 109.5 (CH), 111.3 (CH), 118.4 (CH), 137.5 (Cq), 148.4 (Cq), 149.2 (Cq), 172.3 (Cq).

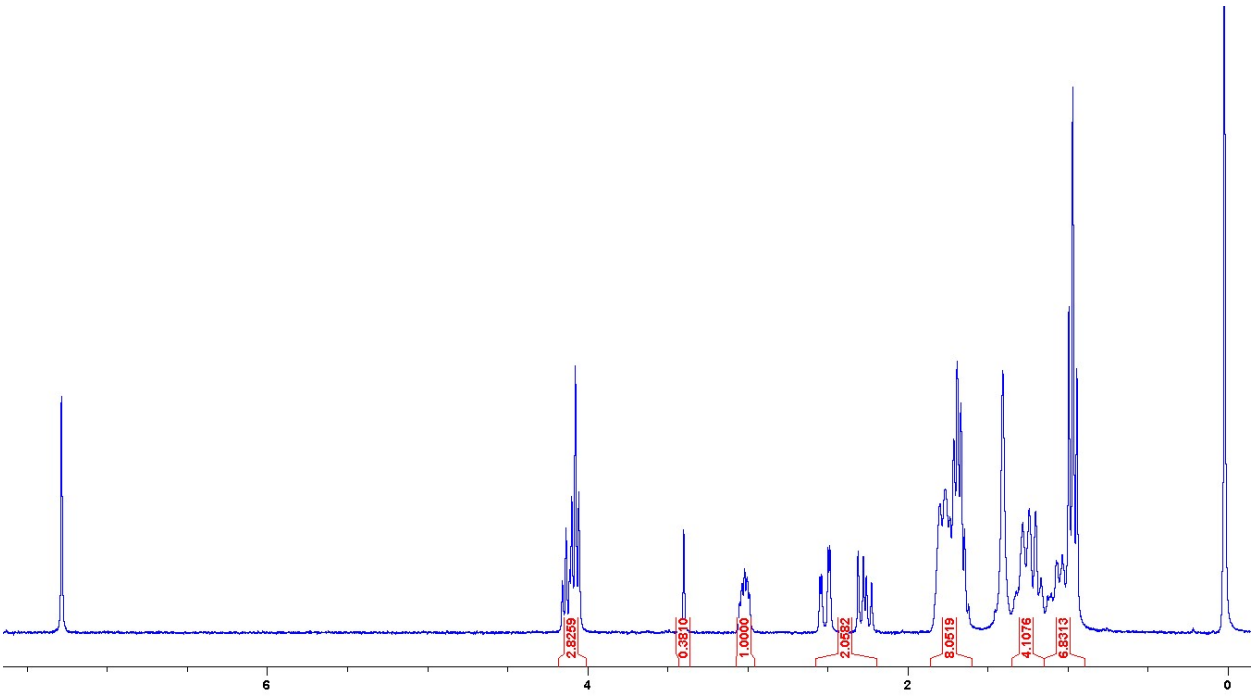
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

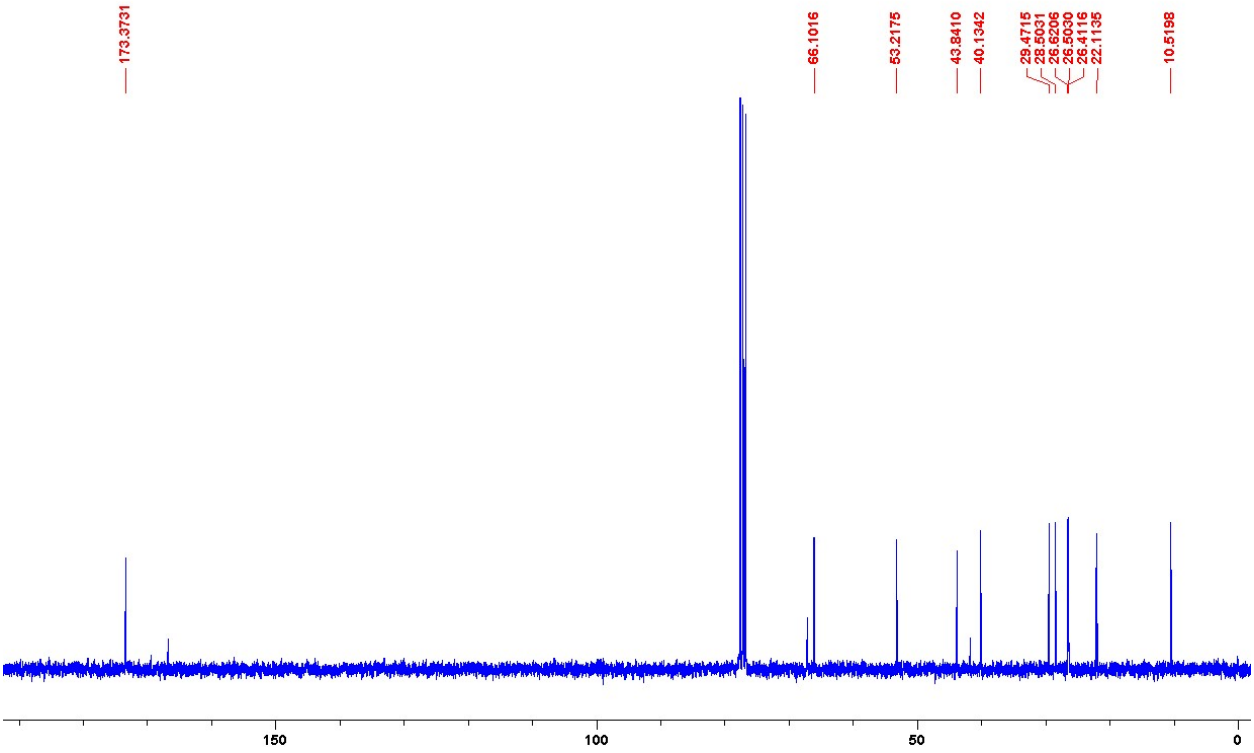
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-3-cylohexanepropanoate (213.24 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.89-1.11 (6 H, m), 1.11-1.33 (4 H, m), 1.58-1.83 (8 H, m), 2.18-2.56 (2 H, m (2 x dd)), 2.95-3.04 (1 H, m (dd)), 4.06 (2 H, t).



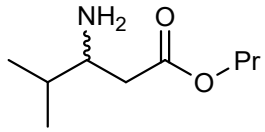
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.5 (CH), 22.1 (CH), 26.4 (CH), 26.5 (CH), 26.6 (CH), 28.5 (CH), 29.5 (CH), 40.1 (Cq), 43.8 (CH), 53.2 (CH), 66.1 (CH), 173.4 (Cq).

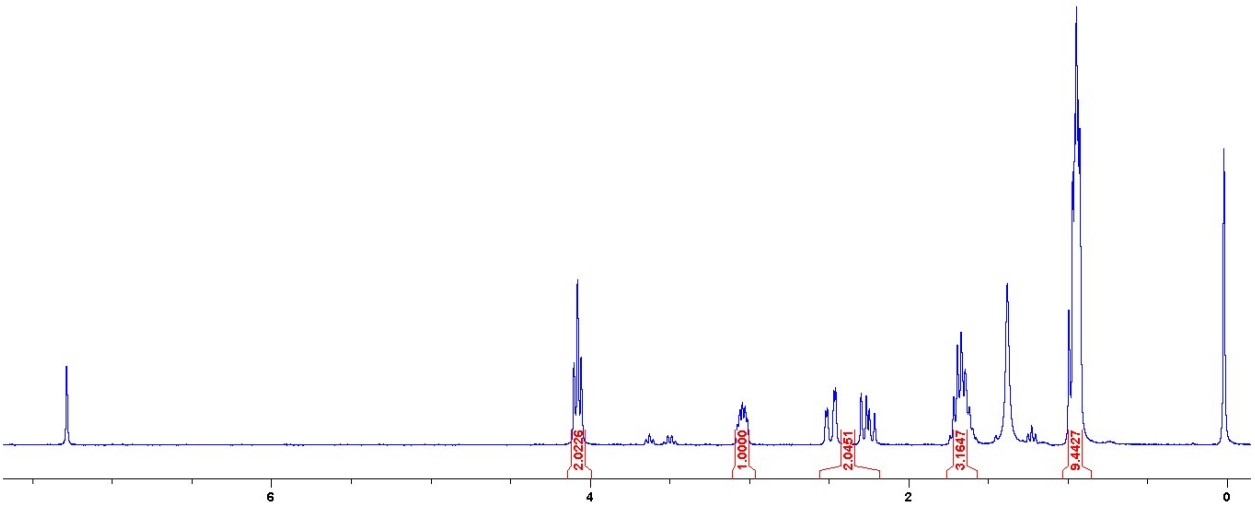
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

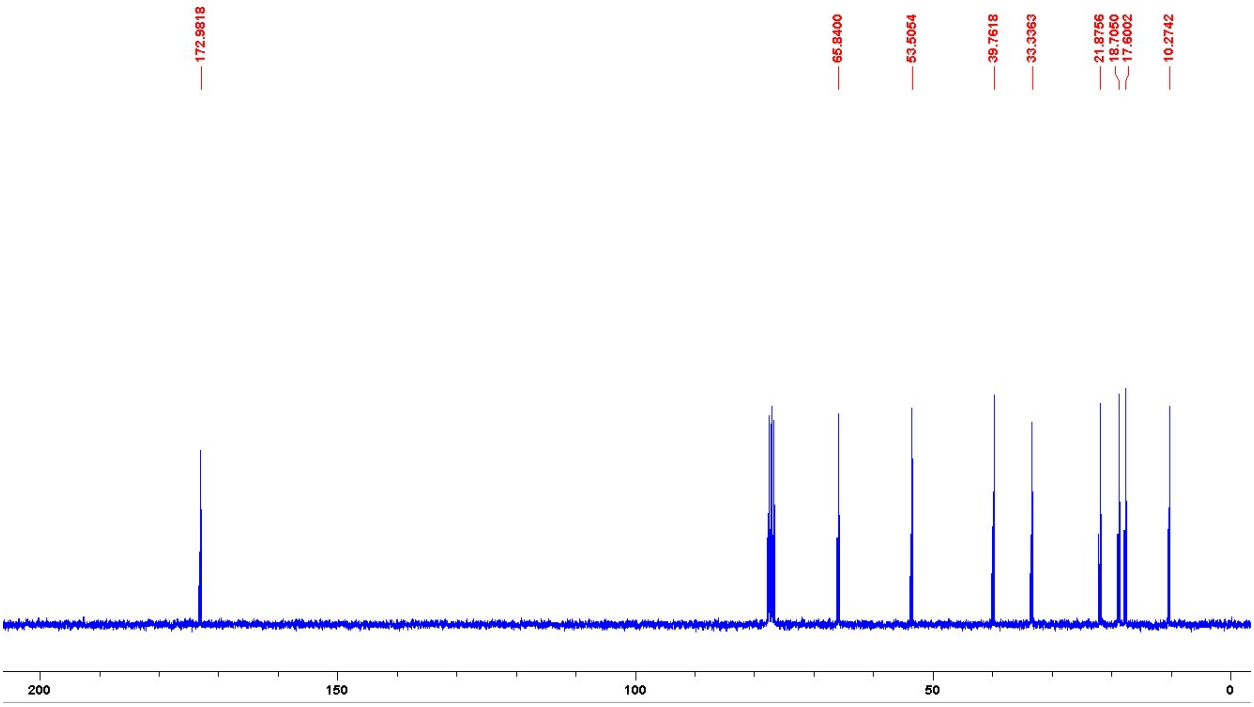
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-4-methylpentanoate (173.25 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.84-1.00 (9 H, m), 1.55-1.74 (3 H, m), 2.17-2.53 (2 H, m (2 x dd)), 2.97-3.07 (1 H, m (dd)), 4.06 (2 H, t).



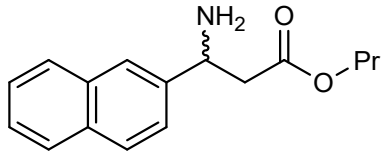
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.3 (CH), 17.6 (CH), 18.7 (CH), 21.9 (CH), 33.3 (CH), 39.8 (CH), 53.5 (CH), 65.8 (CH), 173.0 (Cq).

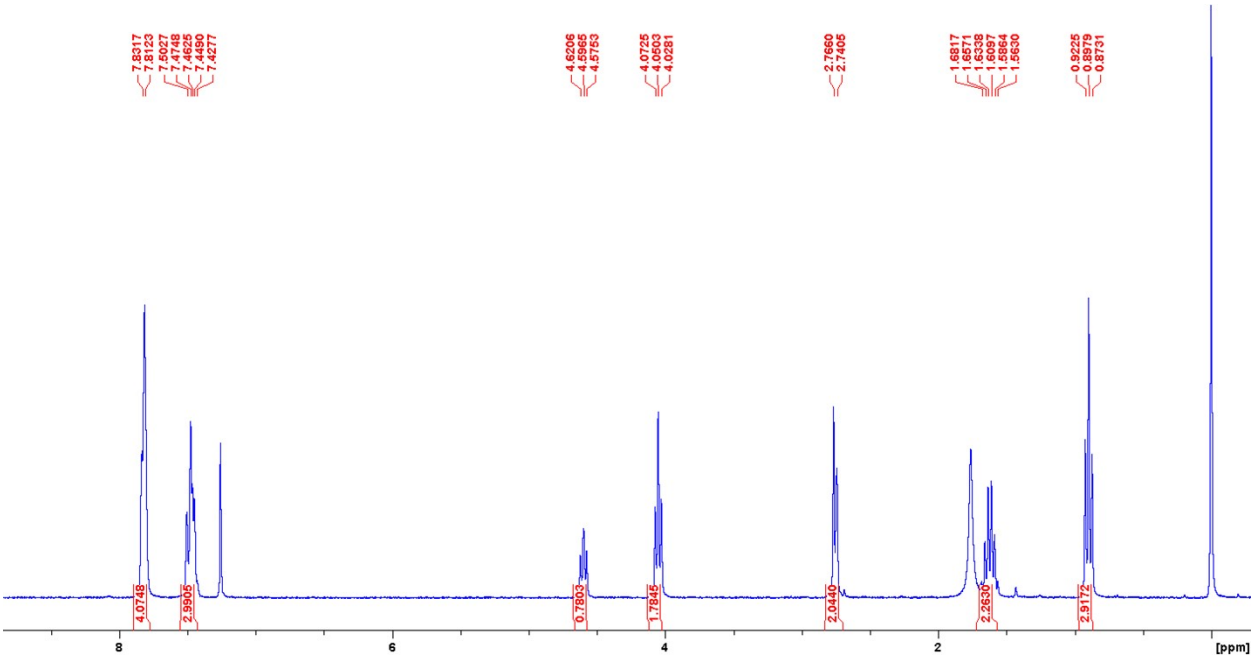
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

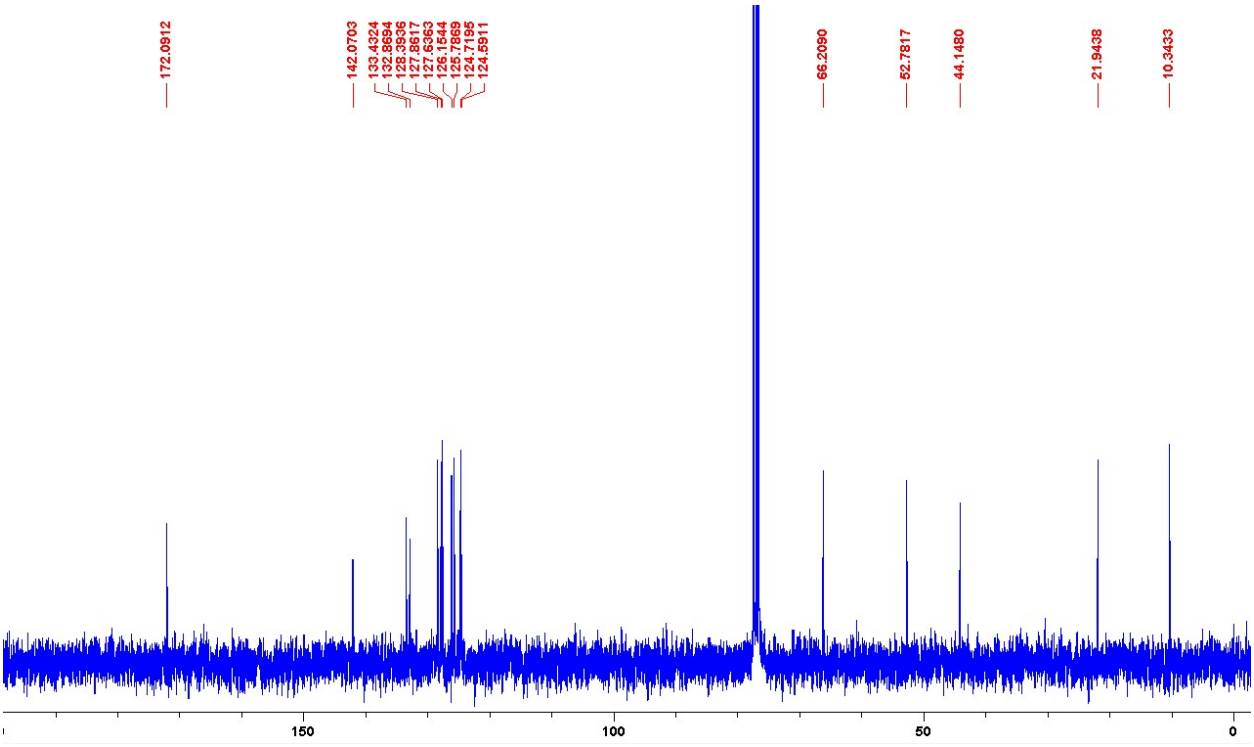
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 25 min, end.

propyl 3-amino-3-anthracenepropanoate (257.33 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.90 (3 H, t), 1.55-1.70 (2 H, sext), 2.75 (2 H, d (2 x dd)), 4.05 (2 H, t), 4.60 (1 H, t (dd)), 7.40-7.53 (3 H, m), 7.77-7.87 (4 H, m).



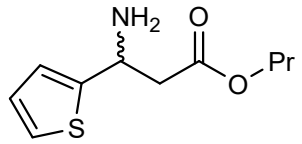
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.3 (CH), 21.9 (CH), 44.1 (CH), 52.8 (CH), 66.2 (CH), 124.6 (CH), 124.7 (CH), 125.8 (CH), 126.2 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 132.9 (Cq), 133.4 (Cq), 142.1 (Cq), 172.1 (Cq).

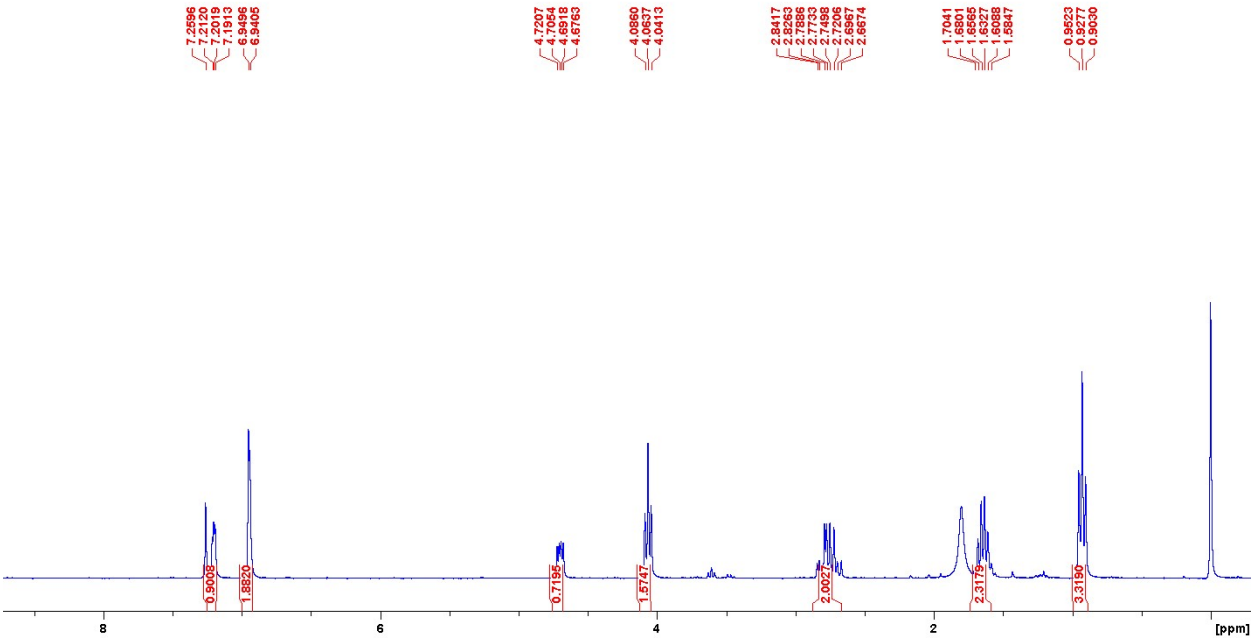
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

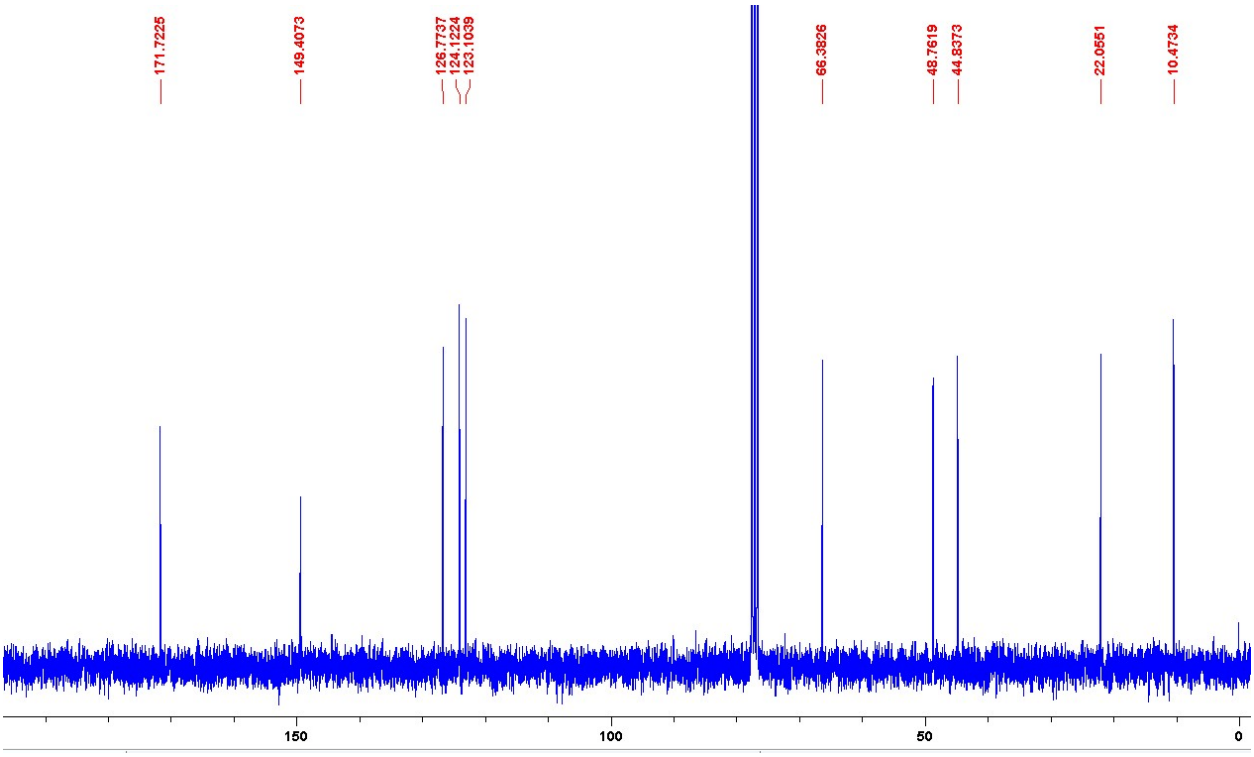
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 45 min, end.

propyl 3-amino-2'-thiophenepropanoate (213.30 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.93 (3 H, t), 1.54-1.72 (2 H, sext), 2.65-2.87 (2 H, m (2 x dd)), 4.06 (2 H, t), 4.65-4.74 (1 H, m (dd)), 6.90-6.98 (2 H, m), 7.17-7.23 (1 H, m).



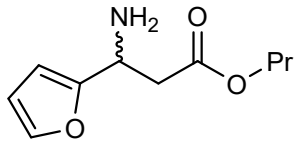
^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.5 (CH), 22.1 (CH), 44.8 (CH), 48.8 (CH), 66.4 (CH), 123.1 (CH), 124.1 (CH), 126.8 (CH), 149.4 (Cq), 171.7 (Cq).

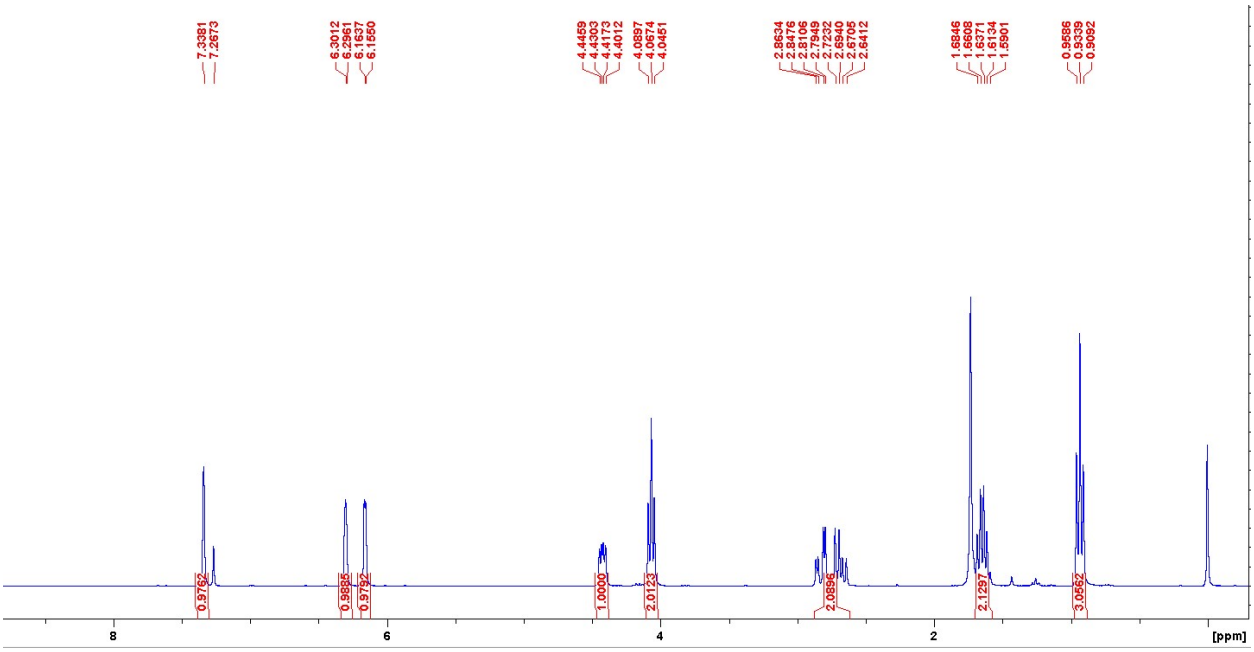
Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

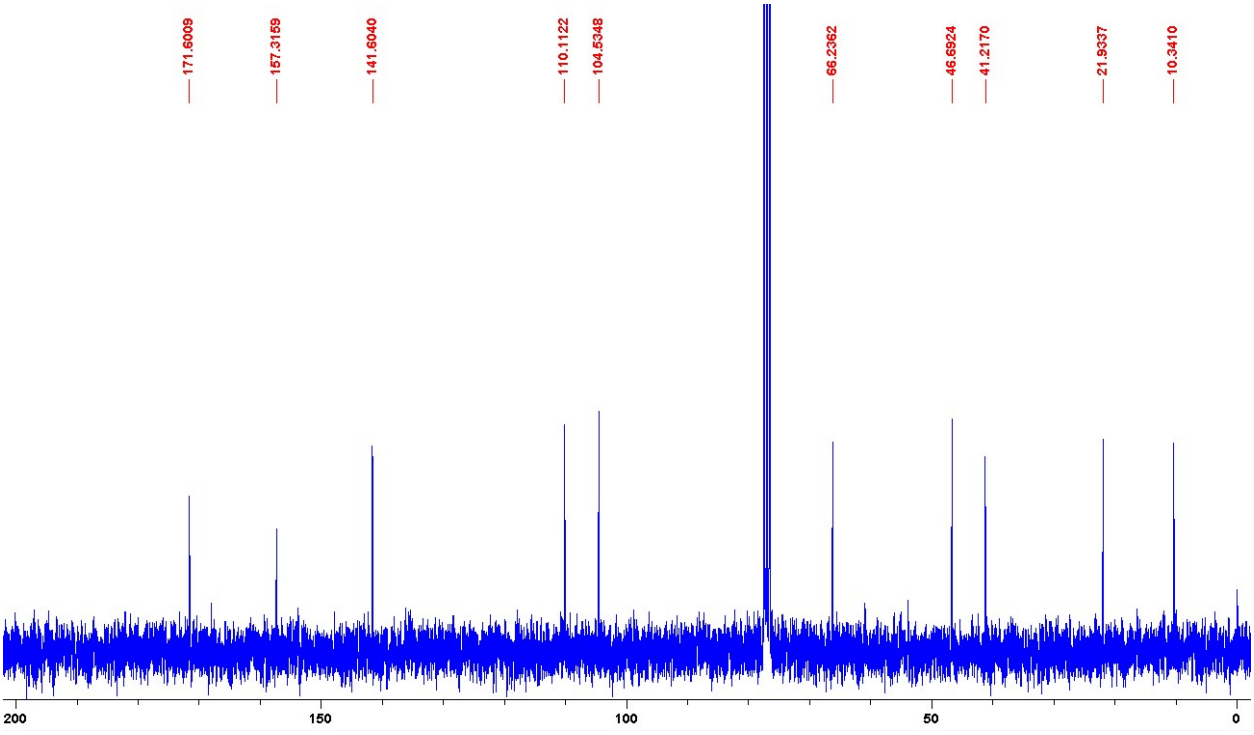
Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 45 min, end.

propyl 3-amino-2'-furanpropanoate (197.23 g/mol)





^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.93 (3 H, t), 1.57-1.71 (2 H, sext), 2.62-2.89 (2 H, m (2 x dd)), 4.07 (2 H, t), 4.38-4.48 (1 H, m (dd)), 6.16 (1 H, d), 6.30 (1 H, d), 7.34 (1 H, s (t)).



^{13}C NMR (300 MHz, $CDCl_3$): δ_C 10.3 (CH), 21.9 (CH), 41.2 (CH), 46.7 (CH), 66.2 (CH), 104.5 (CH), 110.1 (CH), 141.6 (CH), 157.3 (Cq), 171.6 (Cq).

Chiral GC (*ee* determination):

Method (CP-CHIRASIL-DEX CB 25m column):

Start at 85 °C, hold for 20min, heat until 200 °C at a rate of 1.00 °C/min, hold 200°C for 45 min, end.