catalysts

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Supplementary Materials

Lipase Catalyzed Synthesis of Enantiopure Precursors and Derivatives for β-Blockers Practolol, Pindolol and Carteolol

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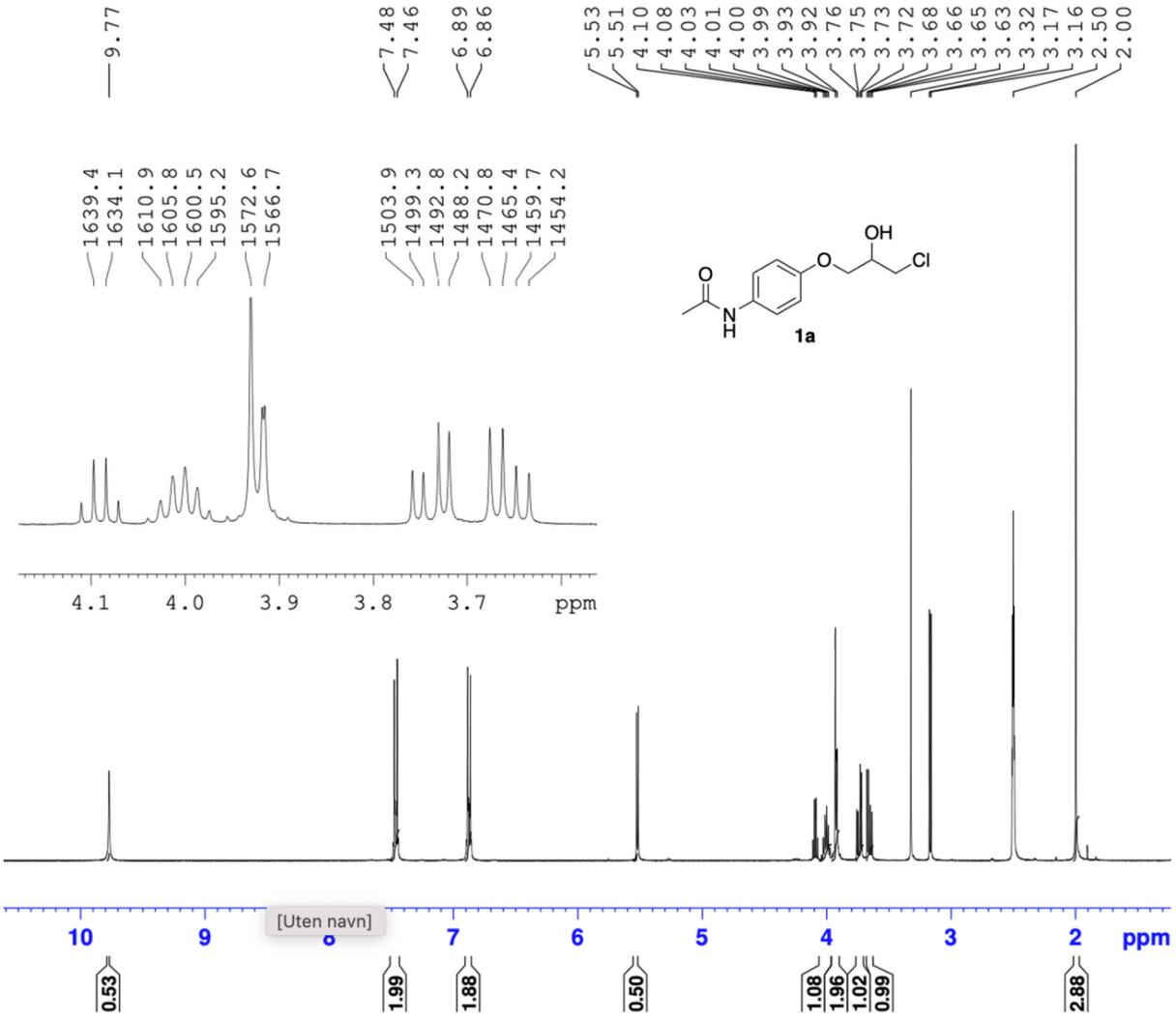
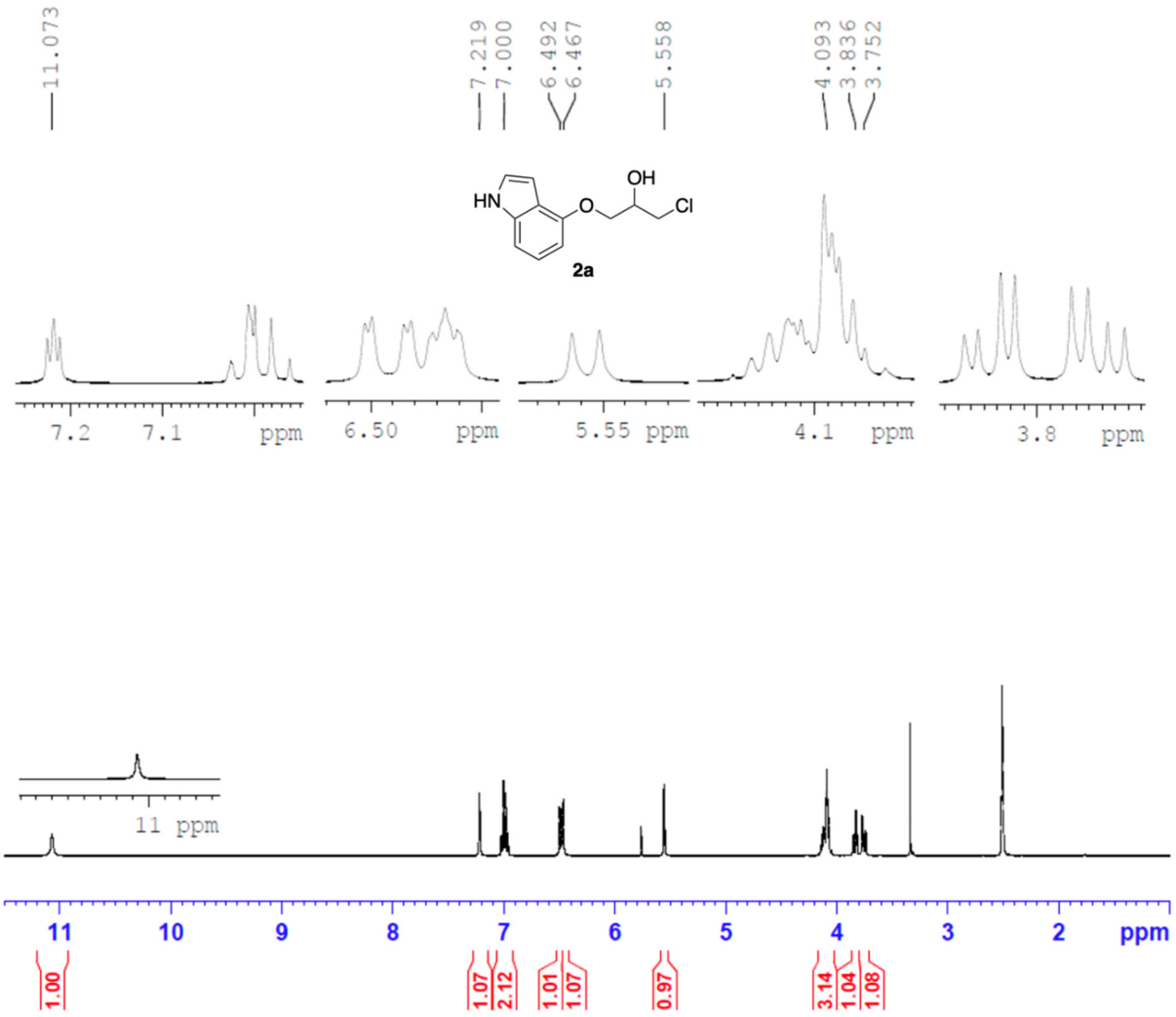
1.1. H NMR Spectra

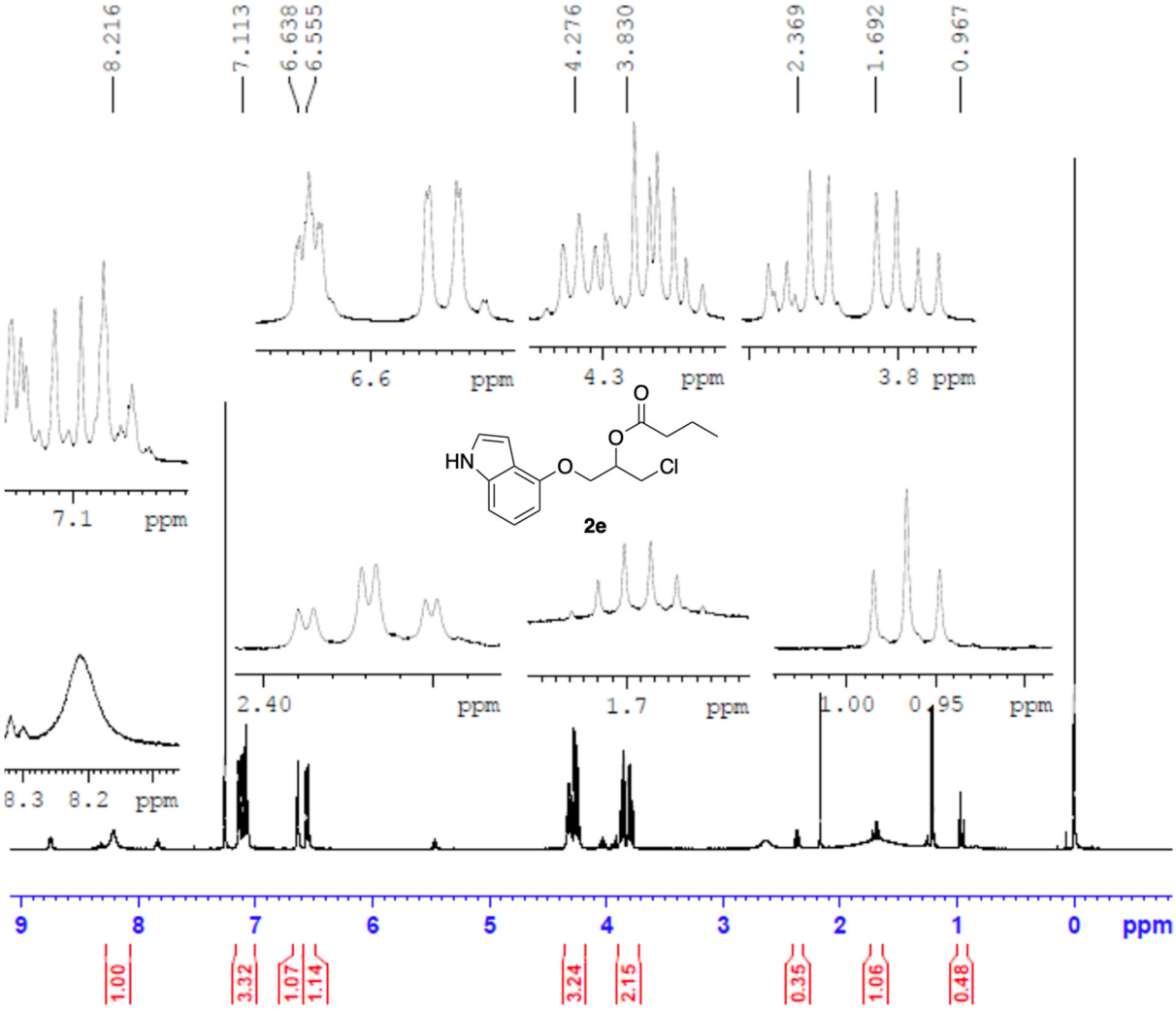
a) N-(4-(3-Chloro-2-hydroxypropoxy)phenyl)acetamide, 1a



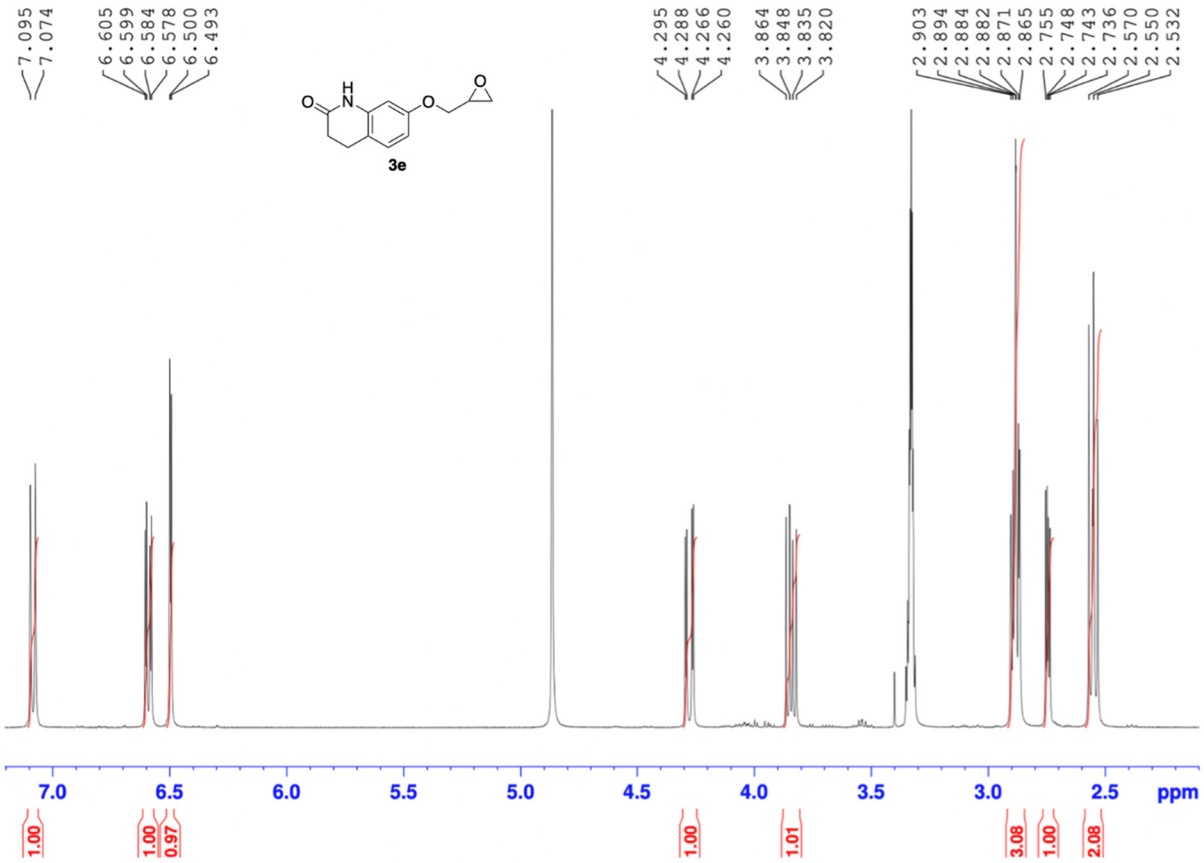
b) 1-((1H-Indol-4-yl)oxy)-3-chloropropan-2-ol, 2a



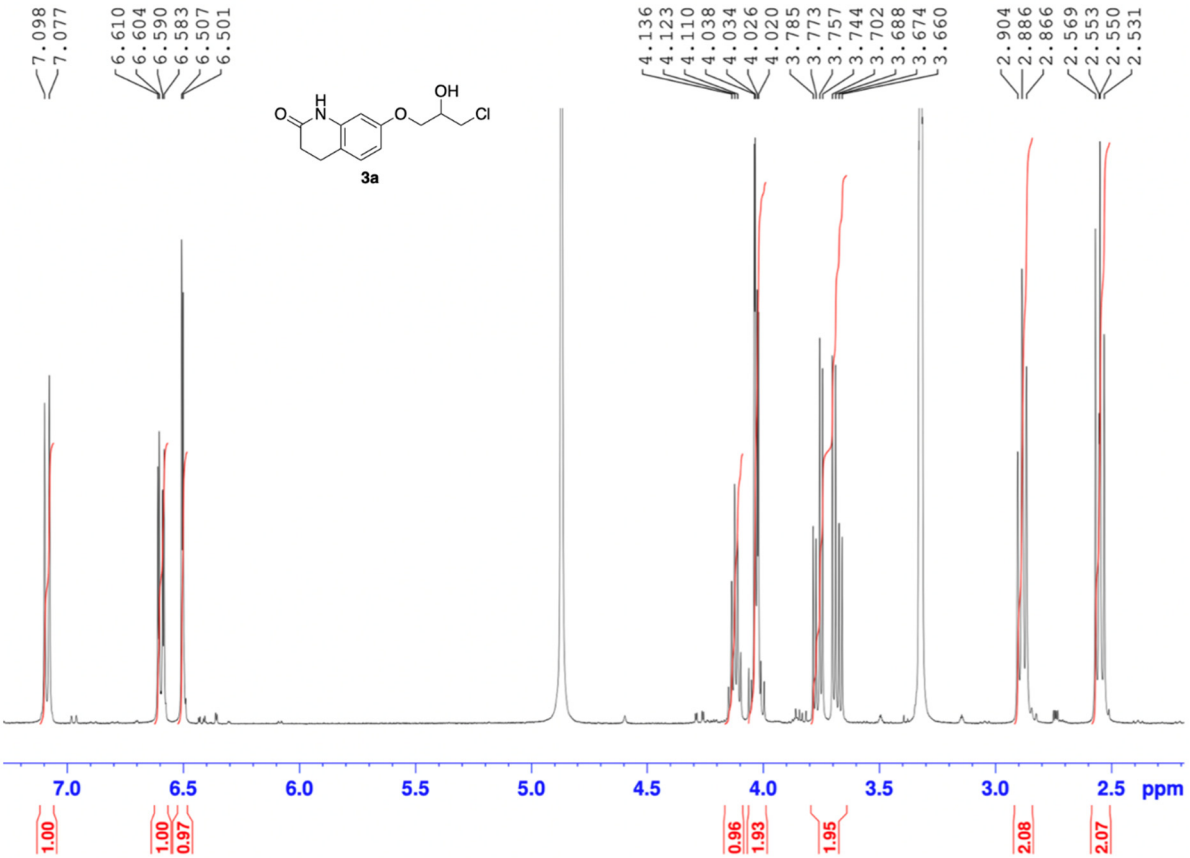
c) 1-((1H-Indol-4-yl)oxy)-3-chloropropan-2-yl butanoate, 2e



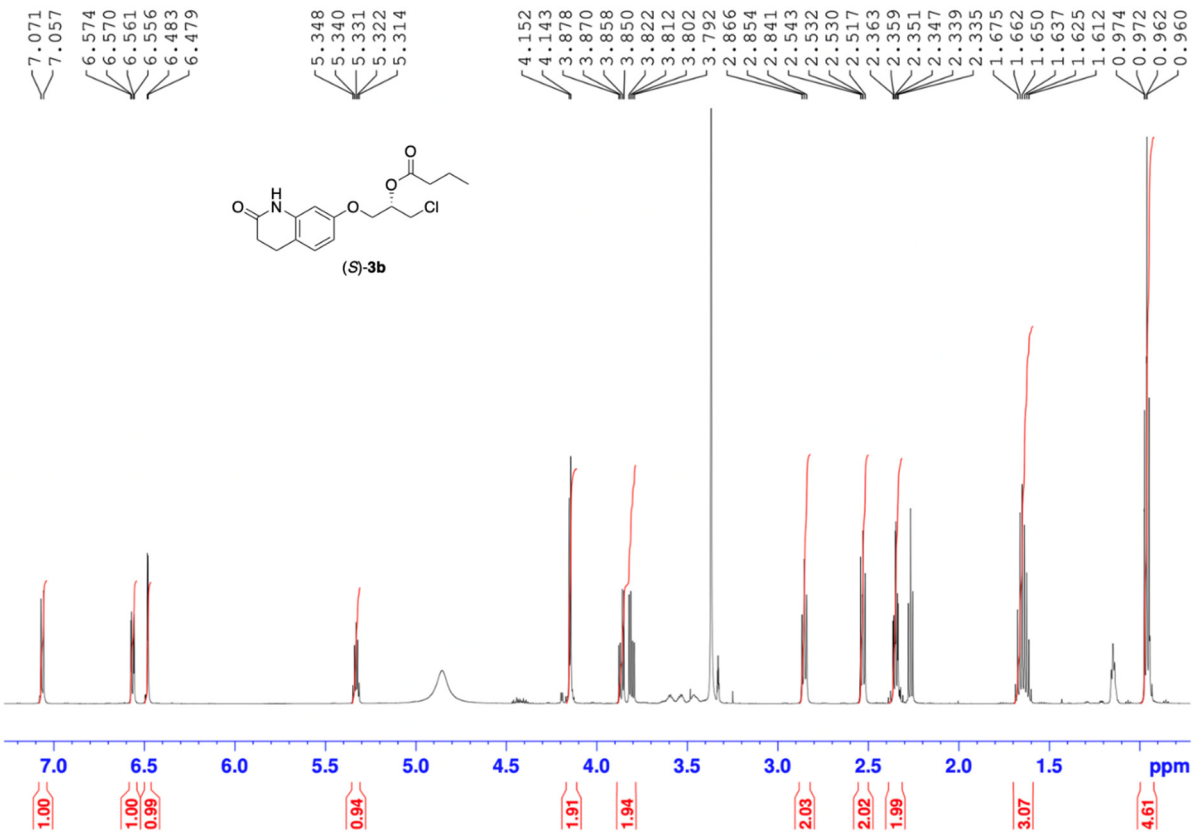
d) 7-(Oxiran-2-ylmethoxy)-3,4-dihydroquinolin-2(1H)-one, 3e



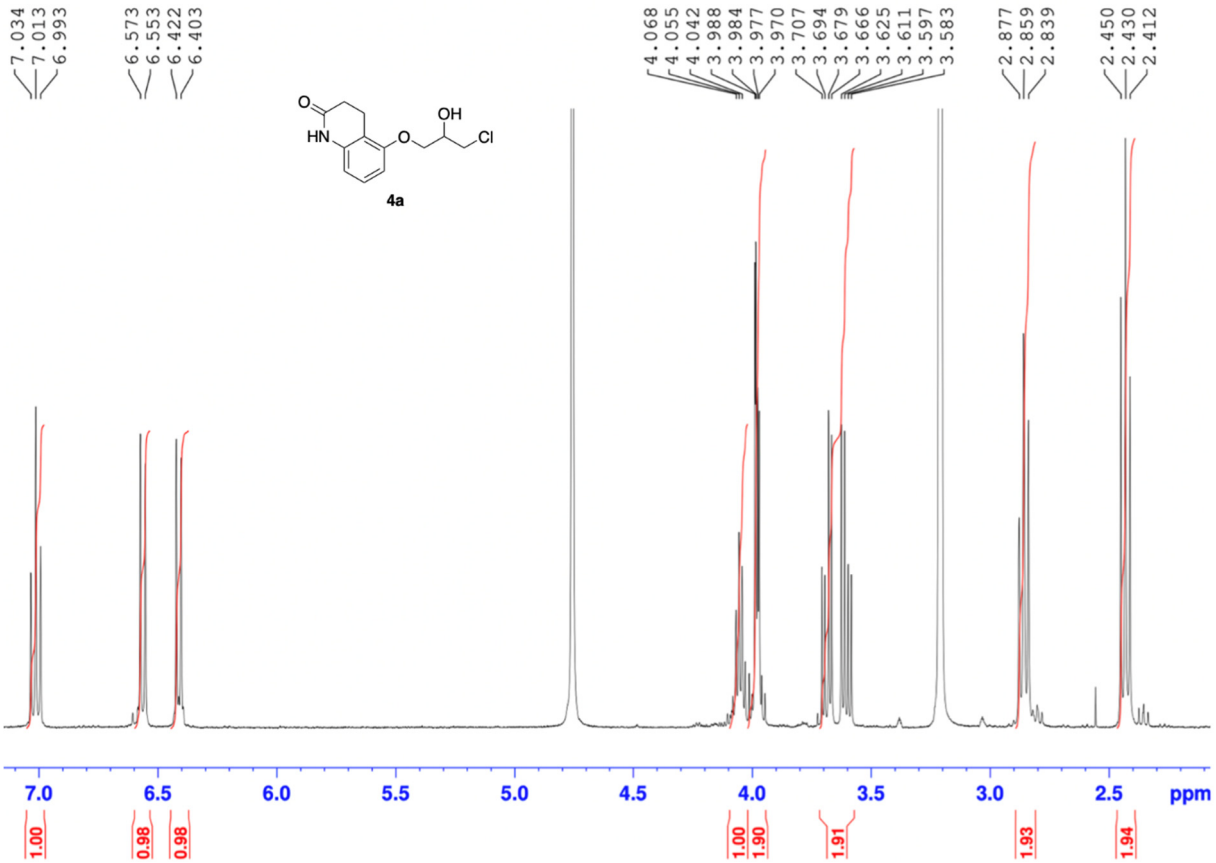
e) 7-(3-Chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, 3a



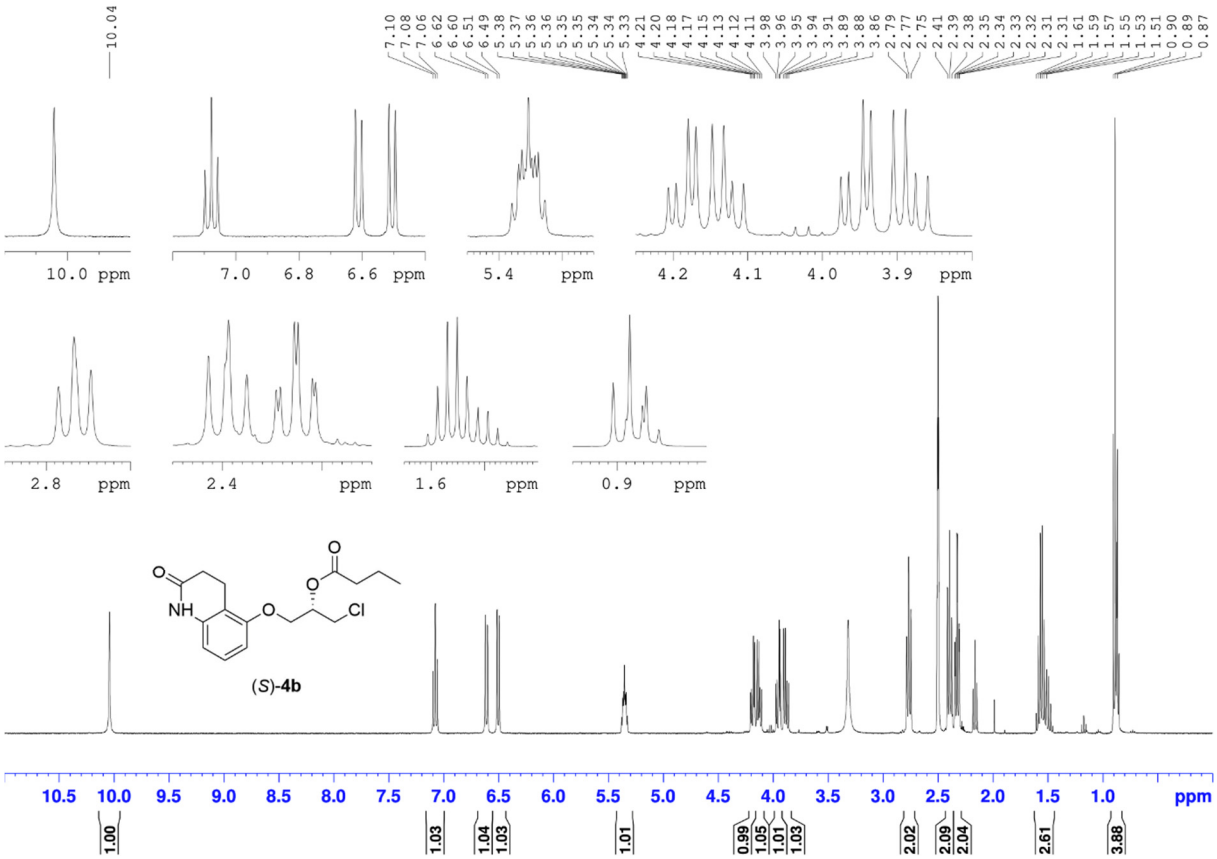
f) (S)-1-Chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)propan-2-yl butanoate, (S)-3b



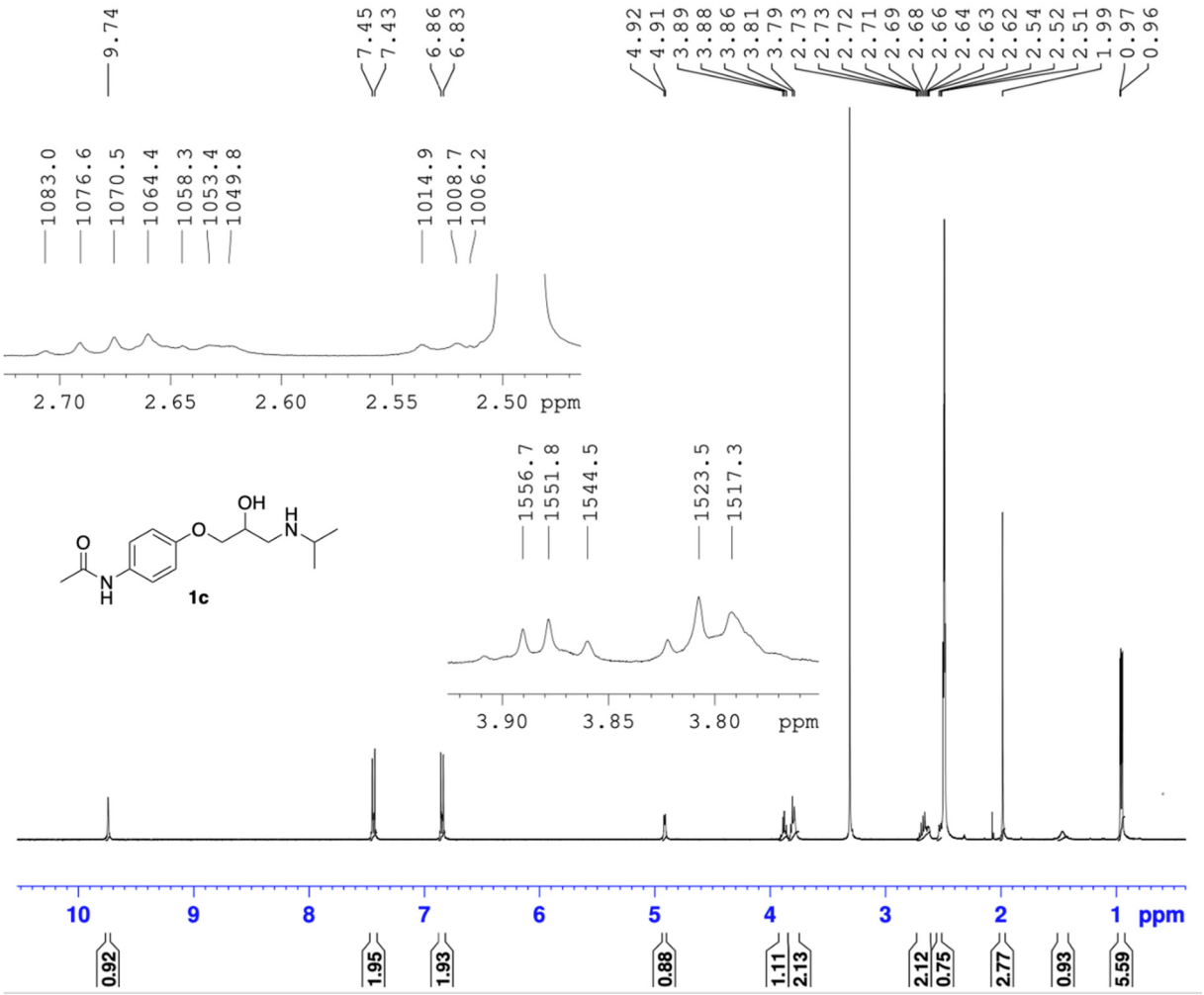
g) 5-(3-Chloro-2-hydroxypropoxy)-3,4-dihydroquinolin- 2(1H)-one, 4a



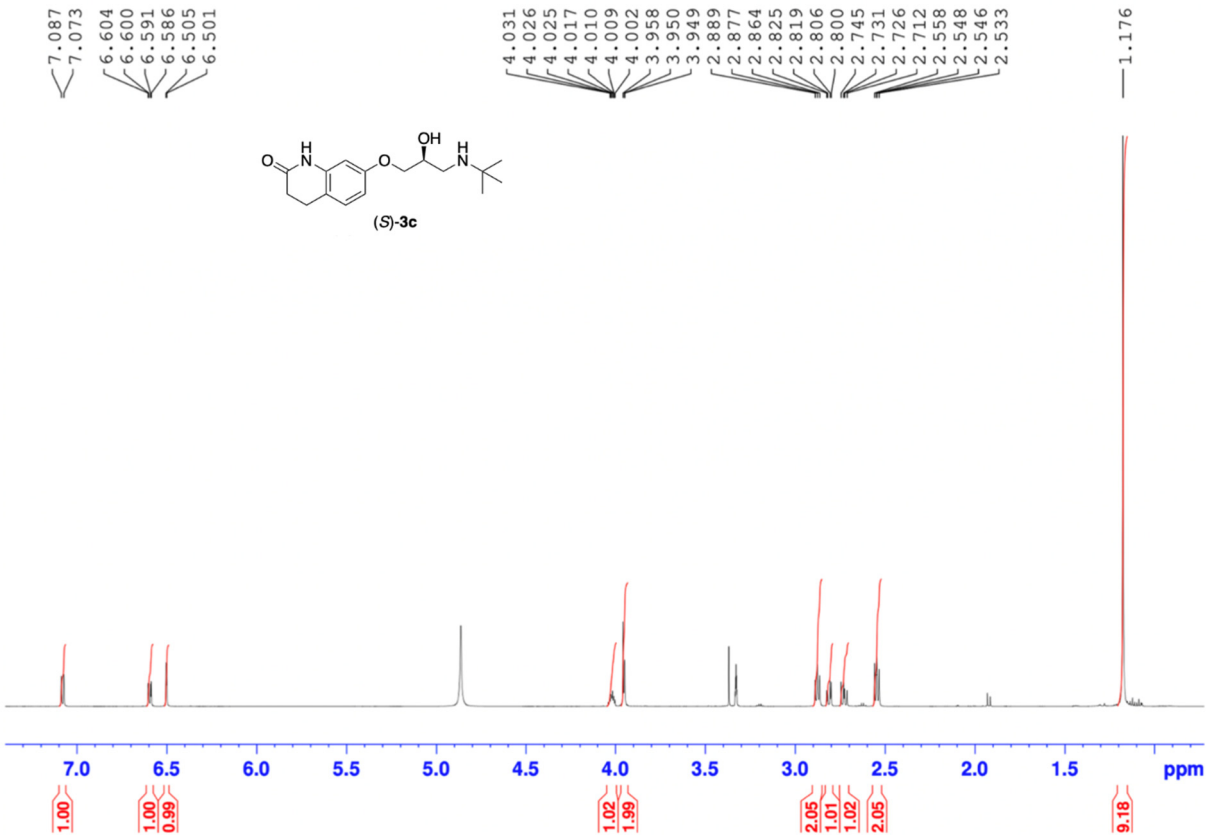
h) (S)-1-Chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)oxy)propan-2-yl butanoate, (S)-4b



i) Practolol, (N-(4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)acetamide), 1c

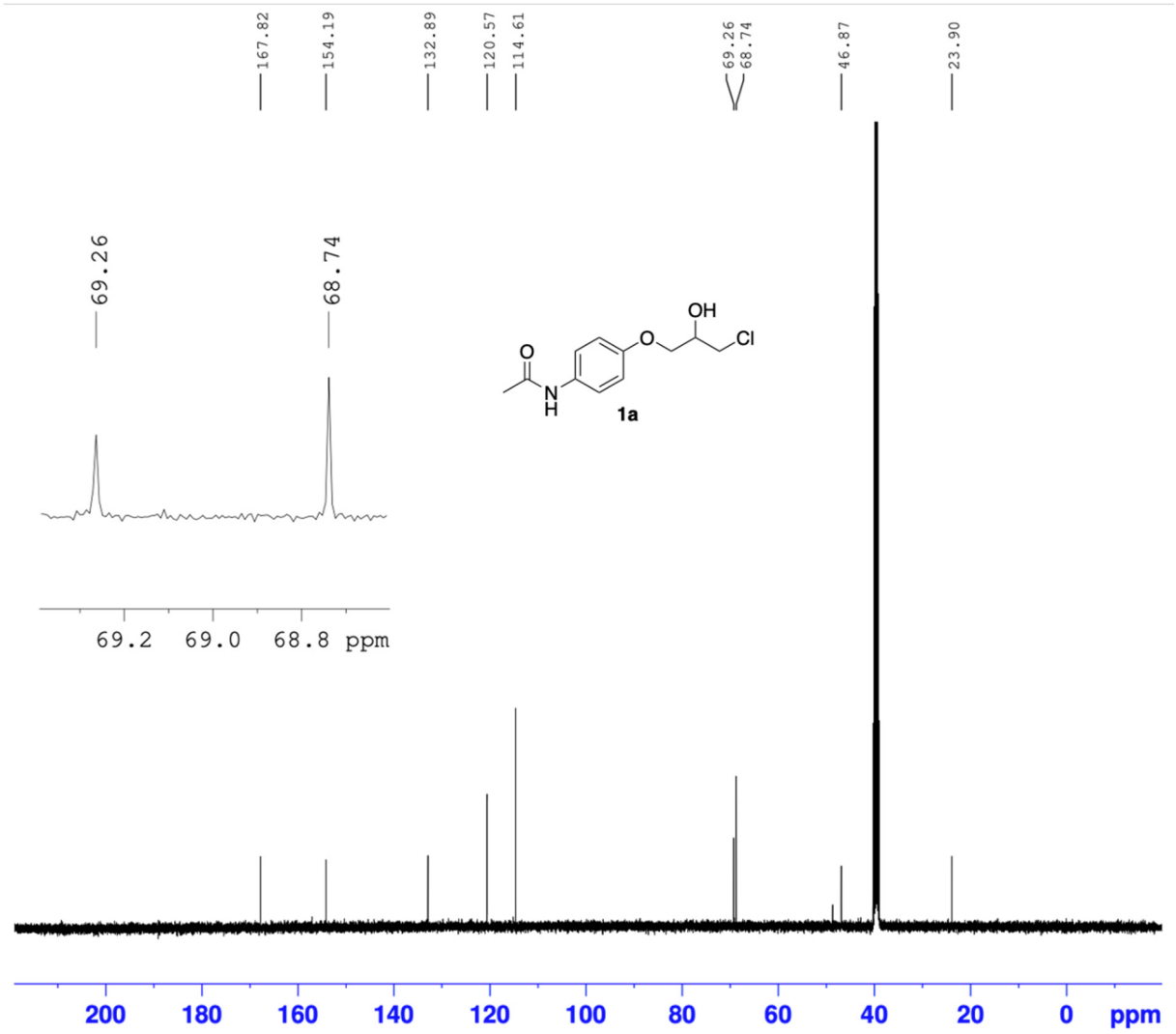


j) (S)-7-(3-(tert-Butylamino)-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, (S)-3c

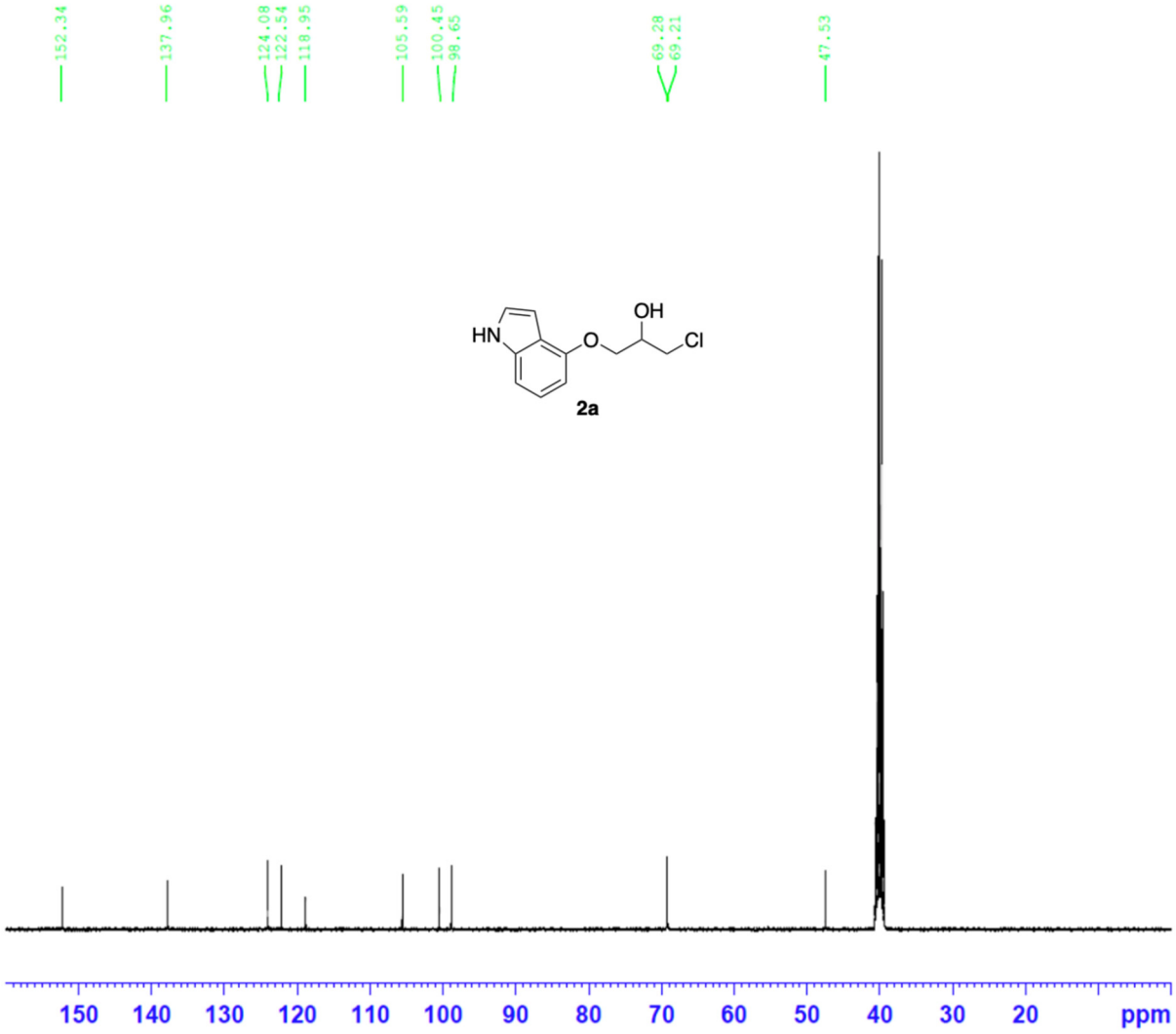


2. ^{13}C NMR Spectra

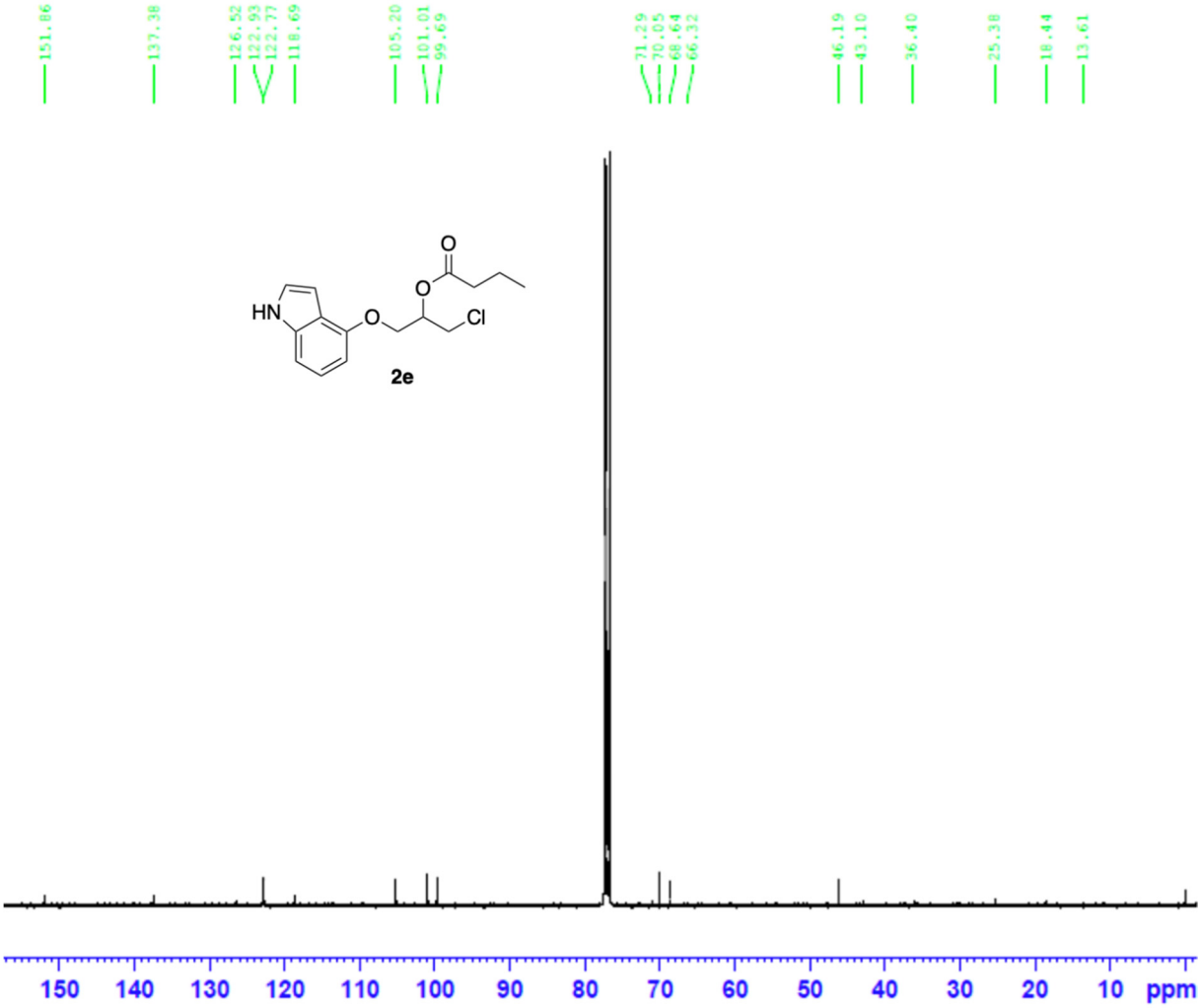
a) N-(4-(3-Chloro-2-hydroxypropoxy)phenyl)acetamide, 1a



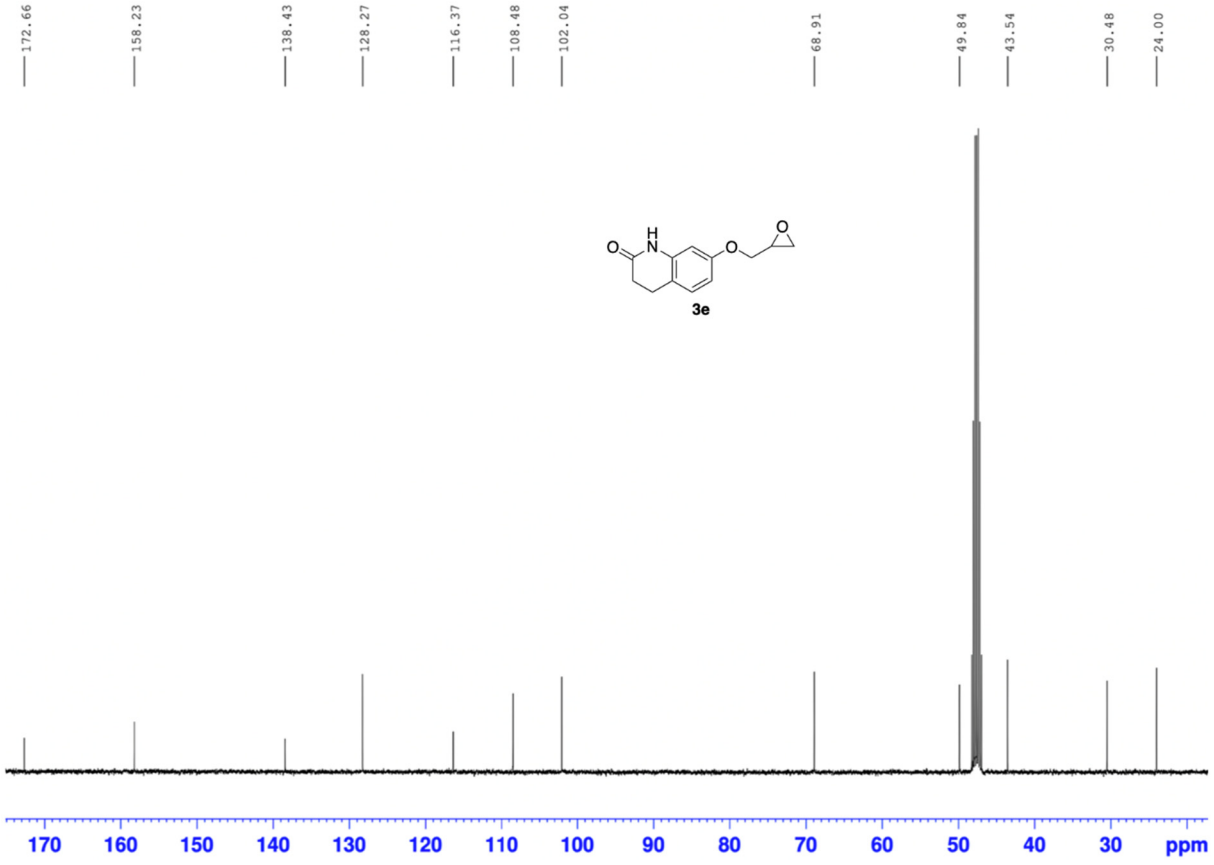
b) 1-((1H-Indol-4-yl)oxy)-3-chloropropan-2-ol, 2a



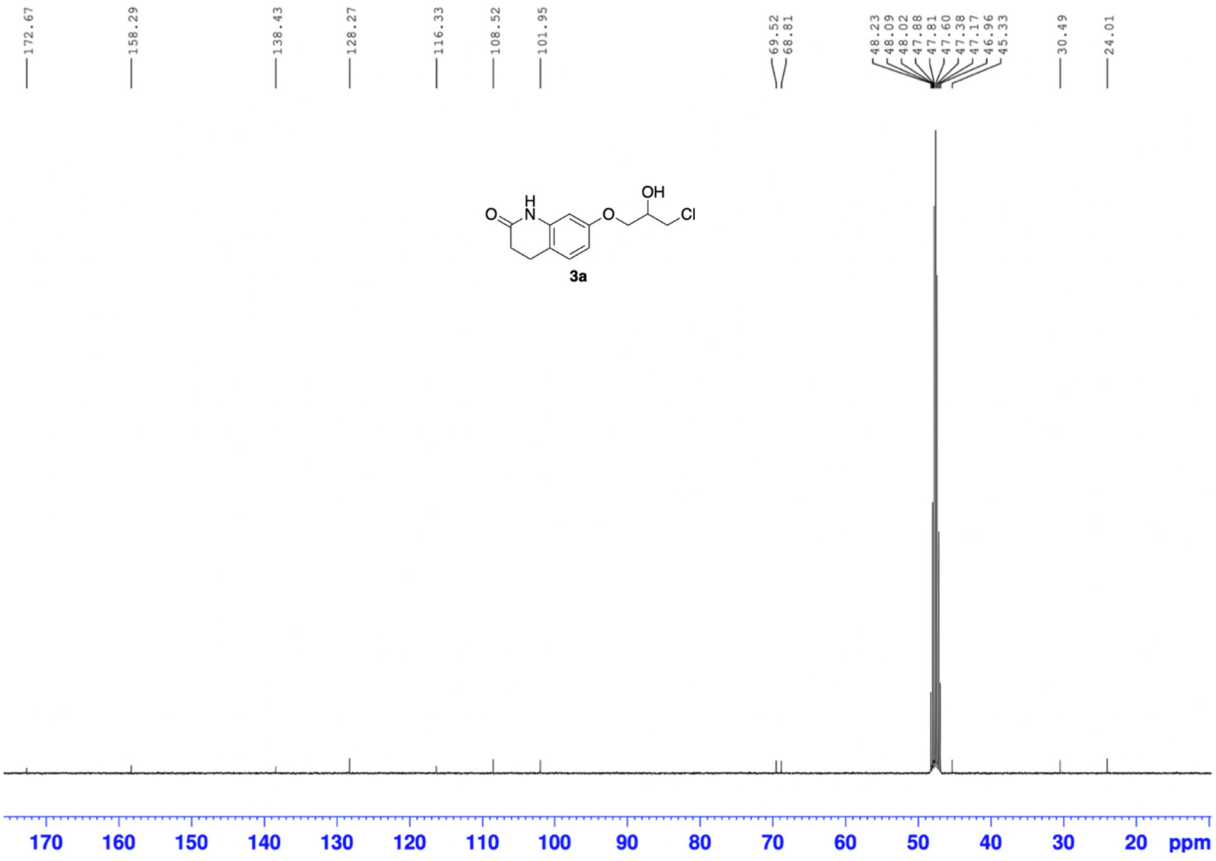
c) 1-((1H-Indol-4-yl)oxy)-3-chloropropan-2-yl butanoate, 2e



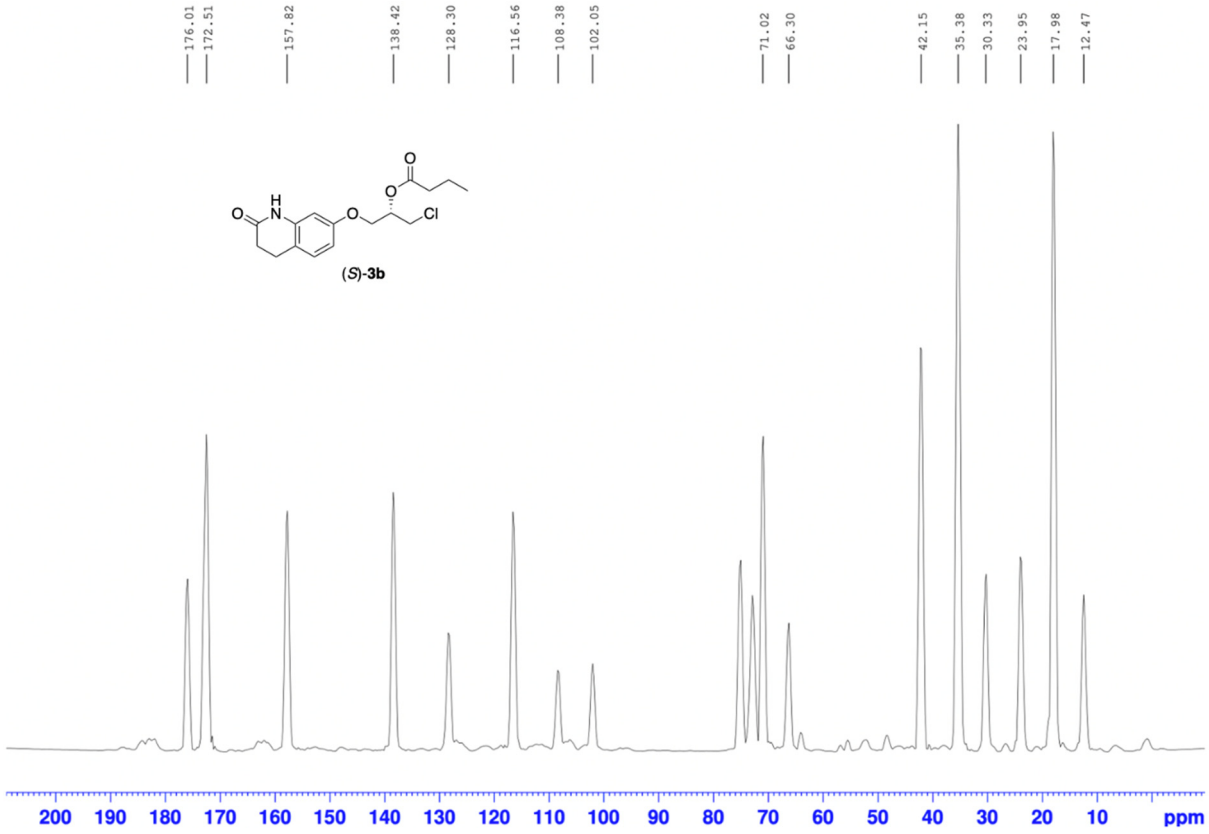
d) 7-(Oxiran-2-ylmethoxy)-3,4-dihydroquinolin-2(1H)-one, 3e



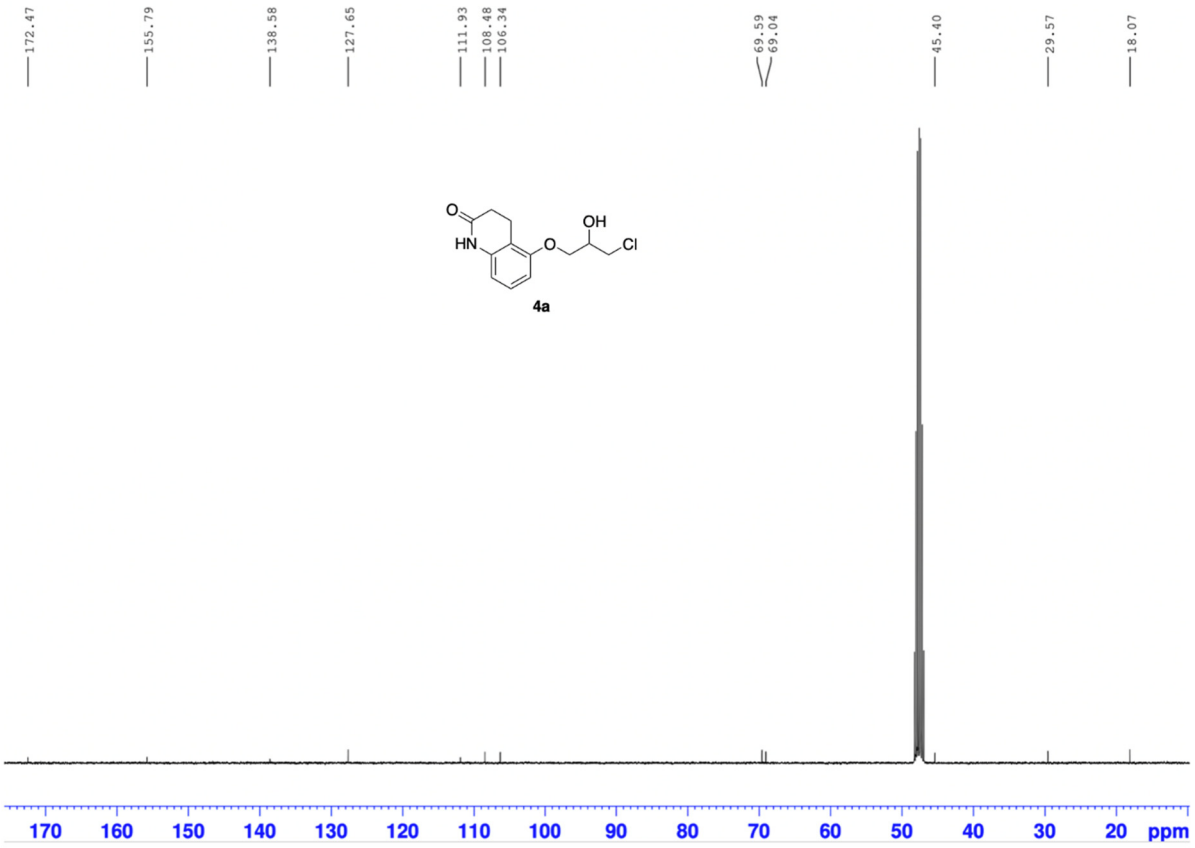
e) 7-(3-Chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, 3a



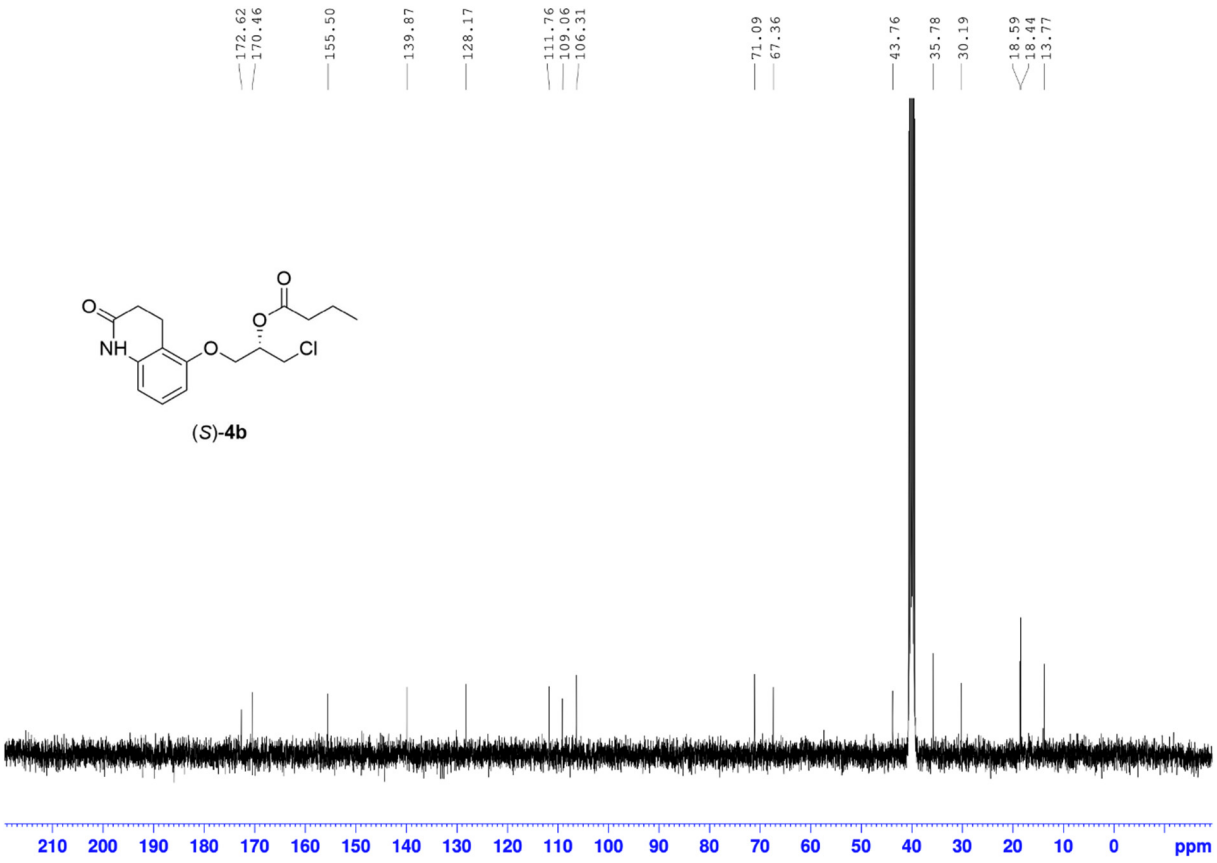
f) (S)-1-Chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)propan-2-yl butanoate, (S)-3b



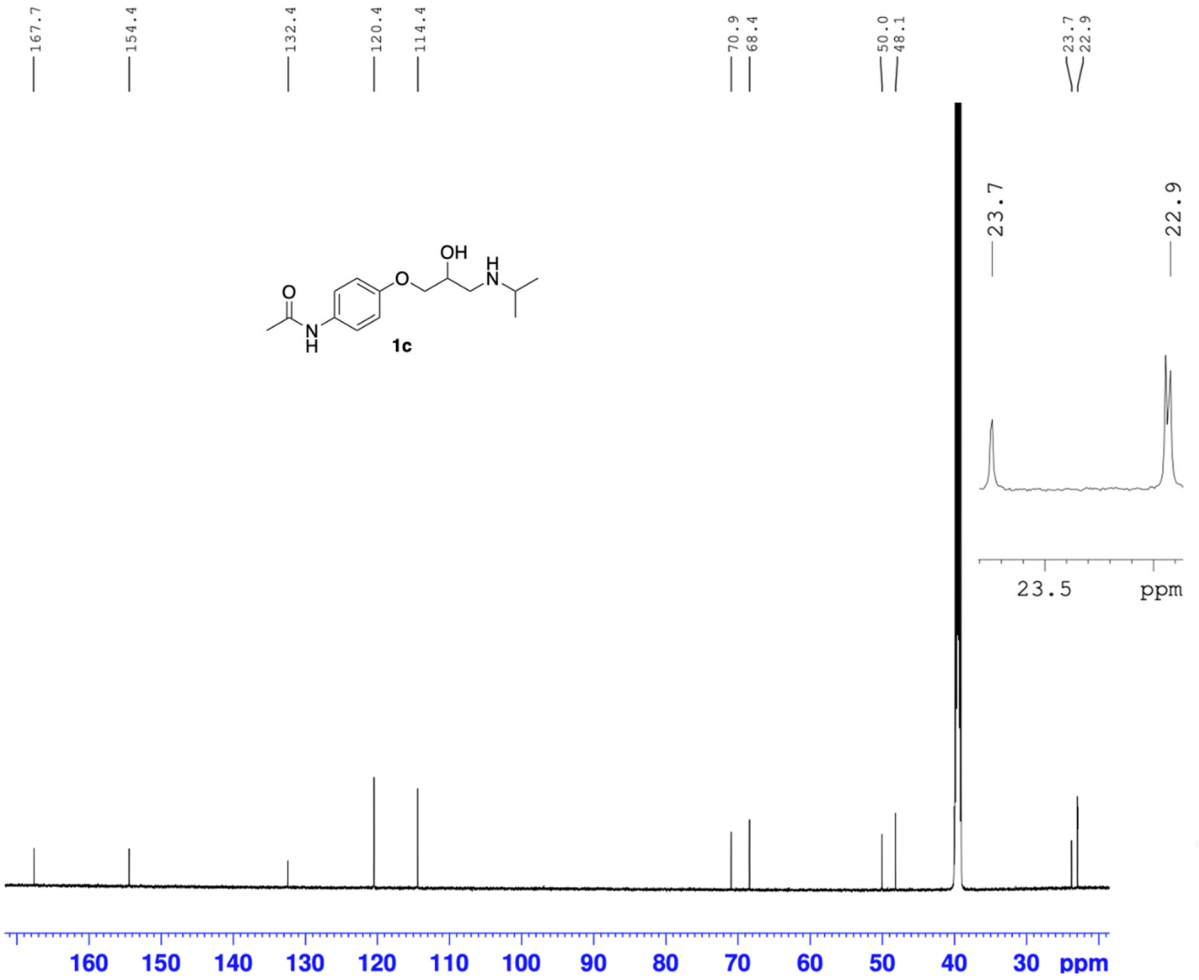
g) 5-(3-Chloro-2-hydroxypropoxy)-3,4-dihydroquinolin- 2(1H)-one, 4a



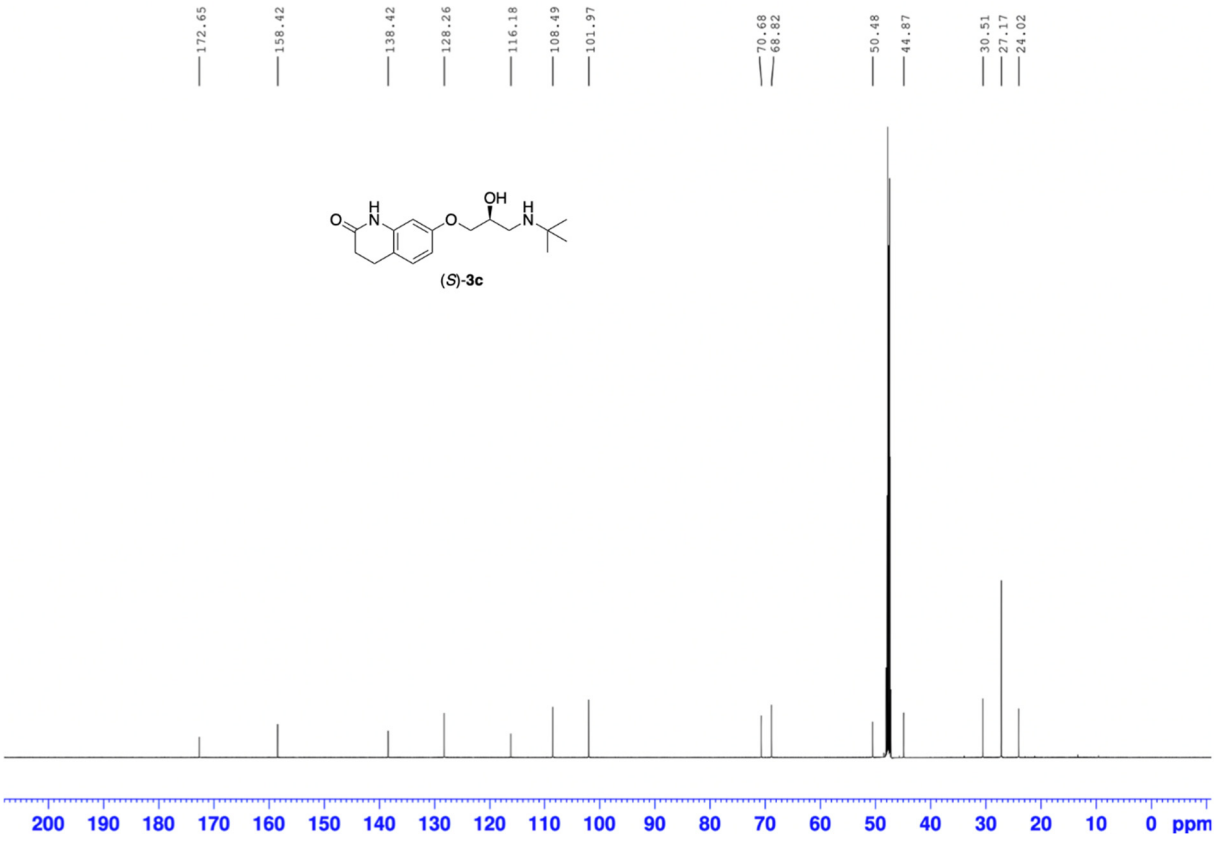
h) (S)-1-Chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)oxy)propan-2-yl butanoate, (S)-4b



i) Practolol, (N-(4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)acetamide), 1c



j) (S)-7-(3-(tert-Butylamino)-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, (S)-3c



3. Mass Spectra

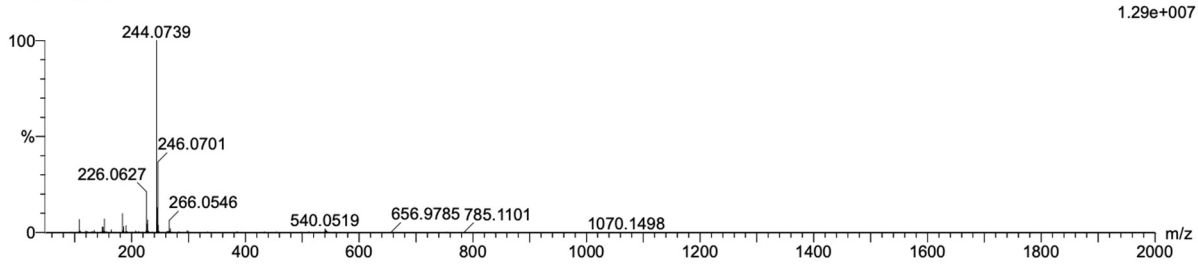
a) N-(4-(3-chloro-2-hydroxypropoxy)phenyl)acetamide, 1a

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
2735 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-500 H: 0-1000 N: 0-200 O: 0-200 S: 0-6 Cl: 0-8 Br: 0-8

SVG_20180201_LCMS_guro28 261 (4.814) AM2 (Ar,20000.0,0.00,0.00); Cm (261:262)
1: TOF MS ES+



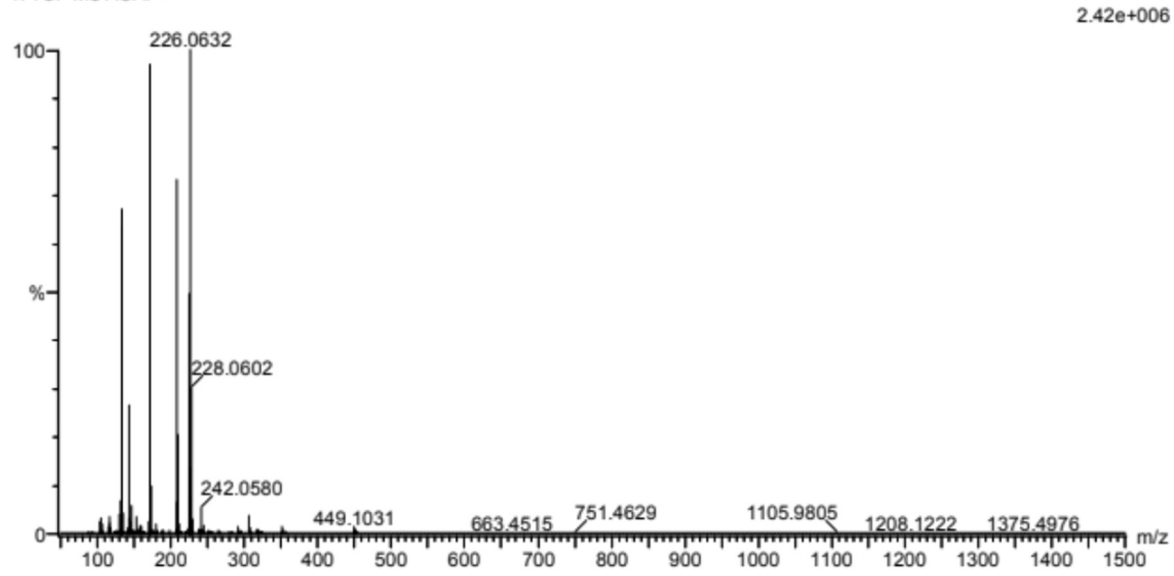
Minimum:				-1.5				
Maximum:		5.0	5.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
244.0739	244.0740	-0.1	-0.4	4.5	942.8	0.007	99.30	C11 H15 N O3 Cl
	244.0747	-0.8	-3.3	0.5	947.9	5.138	0.59	C4 H15 N7 O S Cl
	244.0732	0.7	2.9	0.5	949.6	6.792	0.11	C6 H16 N5 O Cl2
	244.0729	1.0	4.1	5.5	953.3	10.479	0.00	C5 H10 N9 O S

b) 1-((1H-indol-4-yl)oxy)-3-chloropropan-2-ol, 2a

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -2.0, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions
462 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-500 N: 0-10 O: 0-20 Cl: 0-1
2018-465 104 (2.032) AM2 (Ar,35000.0,0.00,0.00); Cm (103:106)
1: TOF MS ASAP+



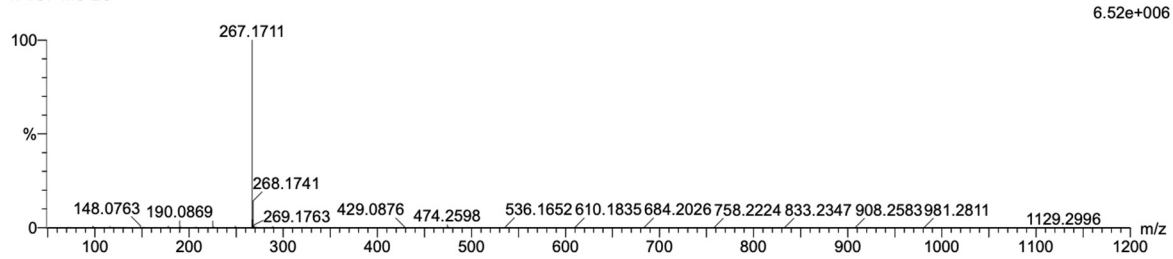
Minimum:				-2.0				
Maximum:		5.0	5.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
226.0632	226.0635	-0.3	-1.3	5.5	1073.1	n/a	n/a	C11 H13 N O2 Cl

c) Practolol, (N-(4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)acetamide), 1c

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1921 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-500 H: 0-1000 N: 0-10 O: 0-10 Na: 0-1 S: 0-5
2018-162 45 (0.837) AM2 (Ar,35000.0,0.00,0.00); Cm (45:46)
1: TOF MS ES+



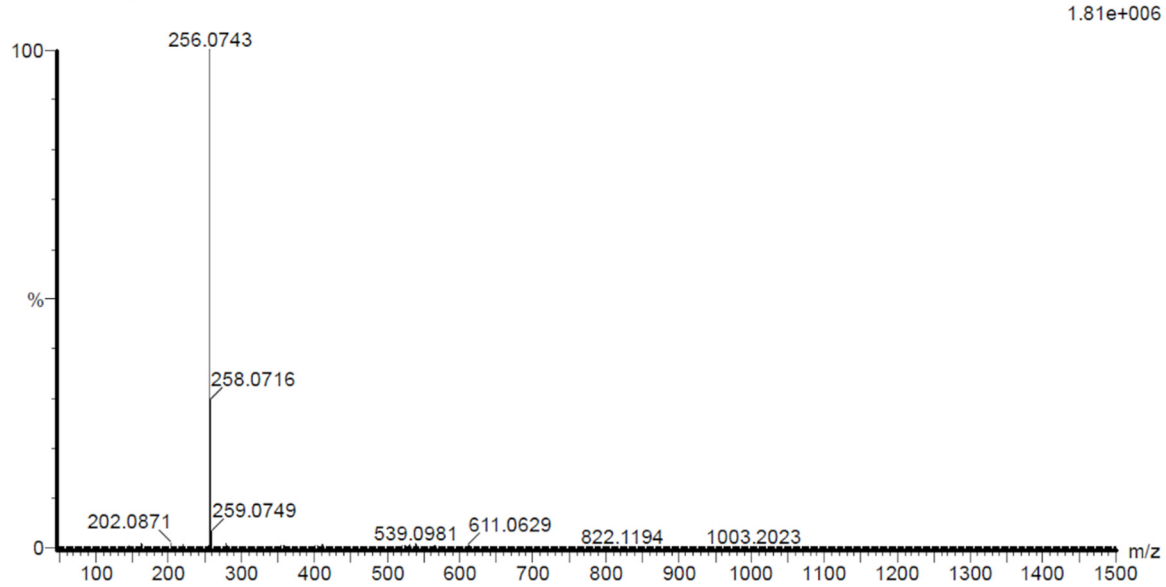
Minimum:				-1.5				
Maximum:		5000.0	2.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
267.1711	267.1709	0.2	0.7	4.5	1681.8	0.000	100.00	C14 H23 N2 O3
	267.1716	-0.5	-1.9	0.5	1699.8	17.988	0.00	C7 H23 N8 O S

d) 5-(3-Chloro-2-hydroxypropoxy)-3,4-dihydroquinolin- 2(1H)-one, 4a

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -50.0, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 6

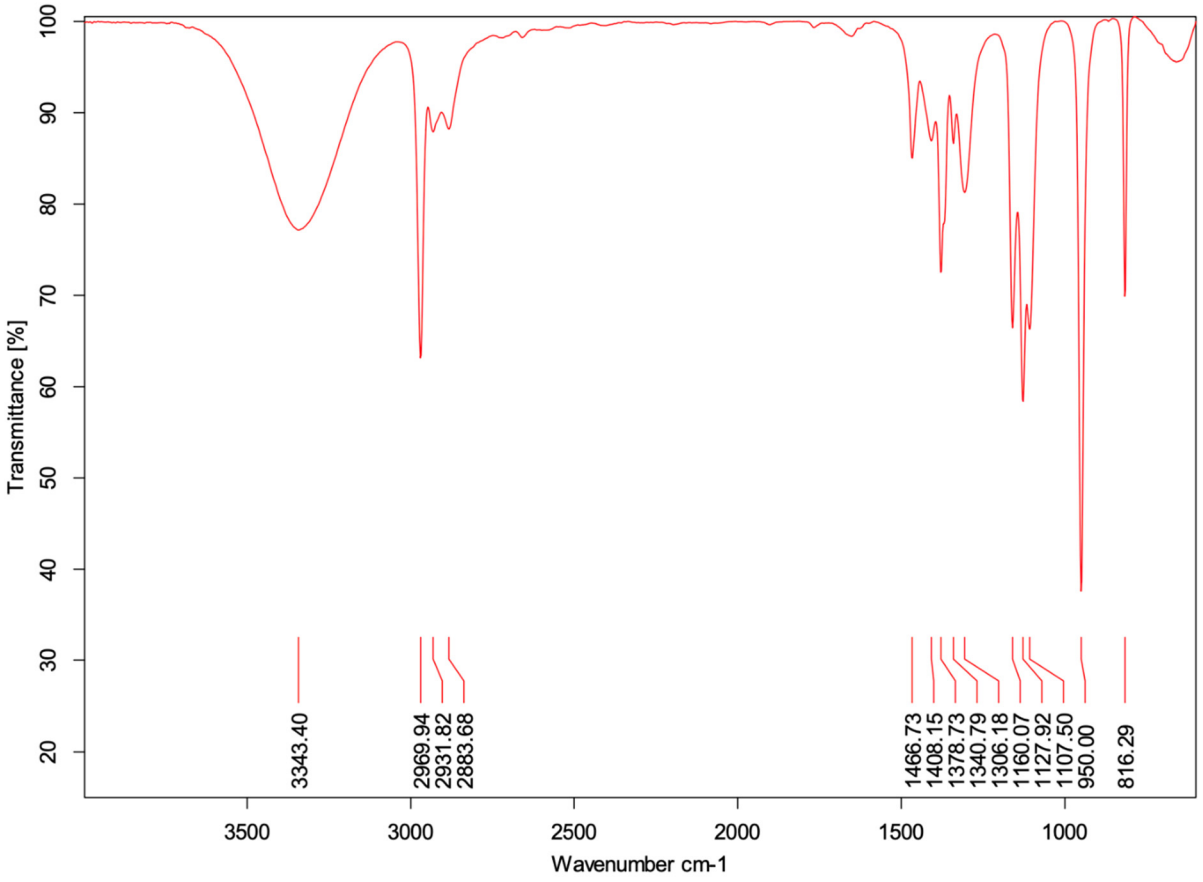
Monoisotopic Mass, Even Electron Ions
3565 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-8 O: 0-8 Na: 0-1 Cl: 0-3
SVG_20201029_S2F3 147 (2.723) AM2 (Ar,35000.0,0.00,0.00)
1: TOF MS ES+



Minimum:				-50.0				
Maximum:		5.0	2.0	100.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
256.0743	256.0740	0.3	1.2	5.5	2797.0	0.000	100.00	C12 H15 N O3 Cl
	256.0738	0.5	2.0	11.5	2819.6	22.647	0.00	C16 H11 N O Na

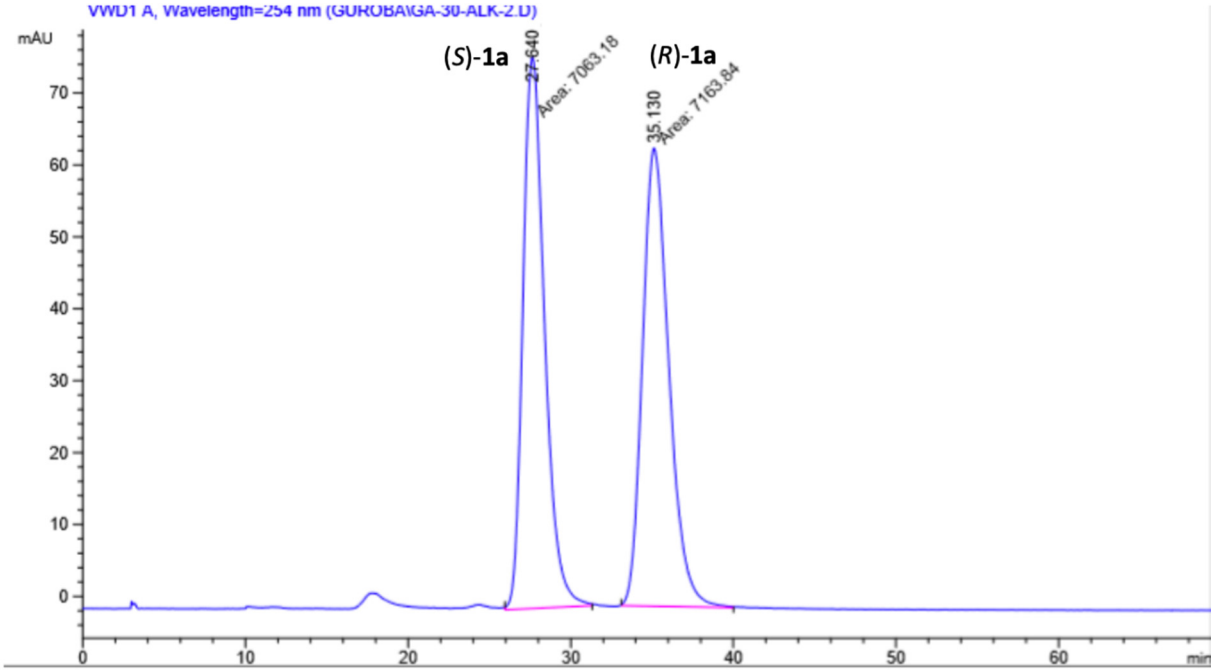
4. IR spectra

a) Practolol, (N-(4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)acetamide), 1c

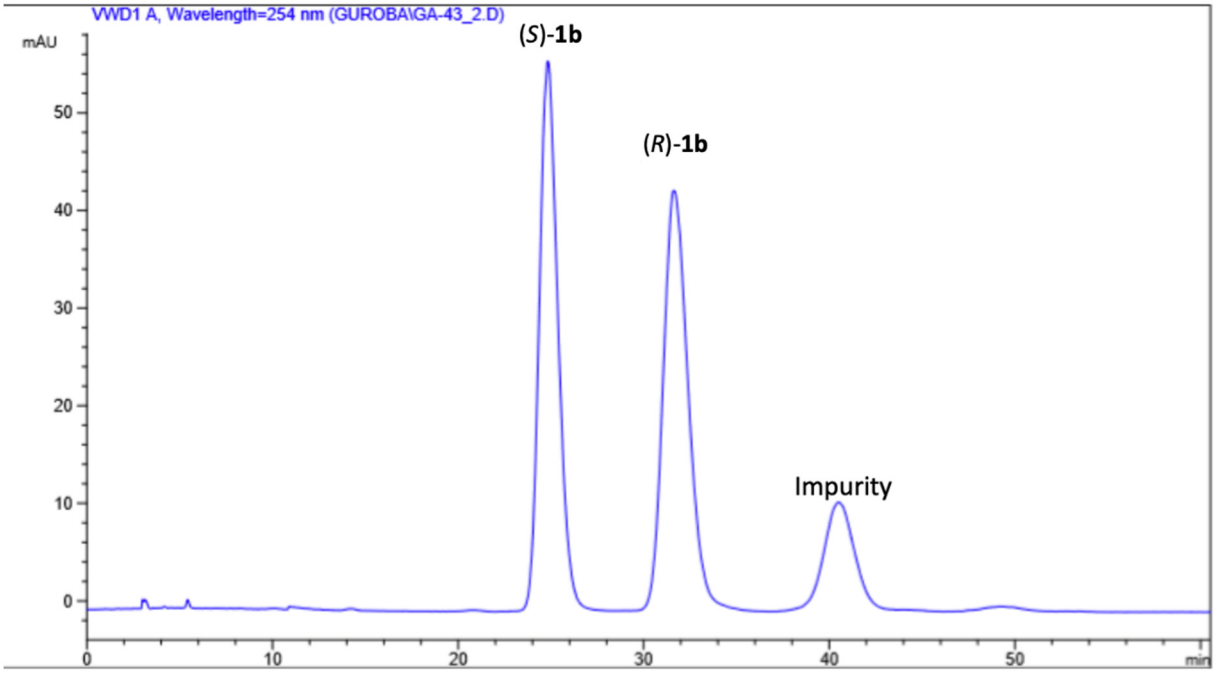


5. Chromatograms from kinetic resolution of *N*-(4-(3-chloro-2-hydroxypropoxy)phenyl)acetamide, 1a

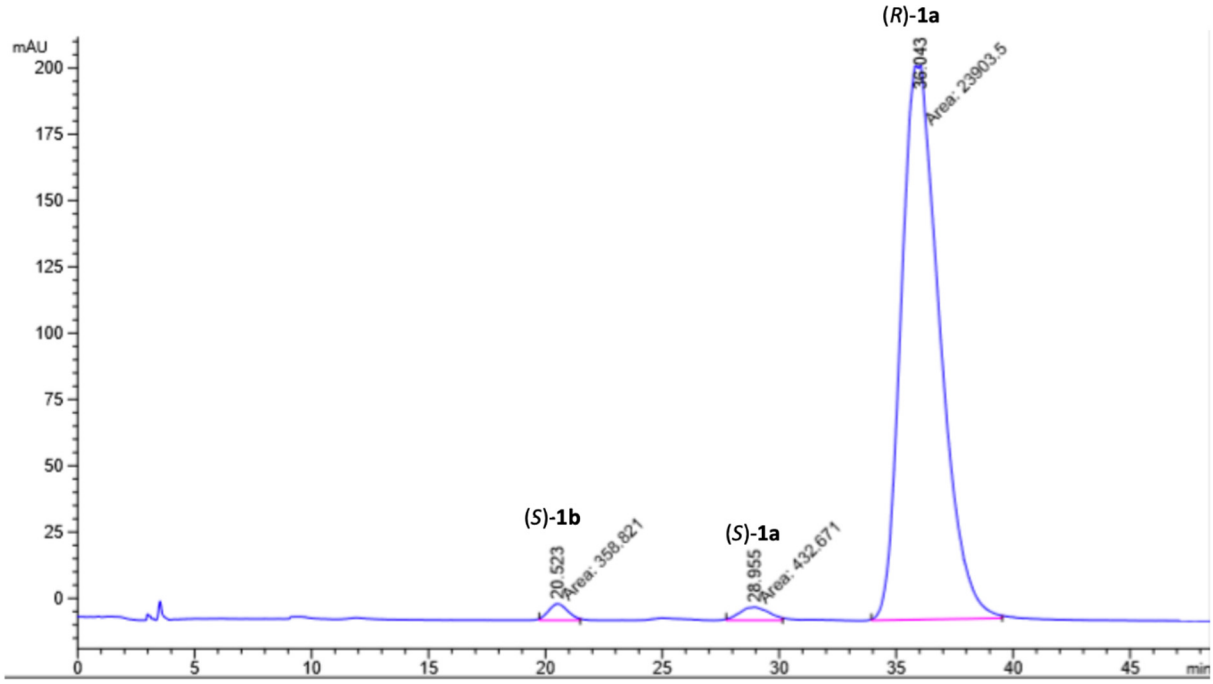
a) N-(4-(3-Chloro-2-hydroxypropoxy)phenyl)acetamide, 1a



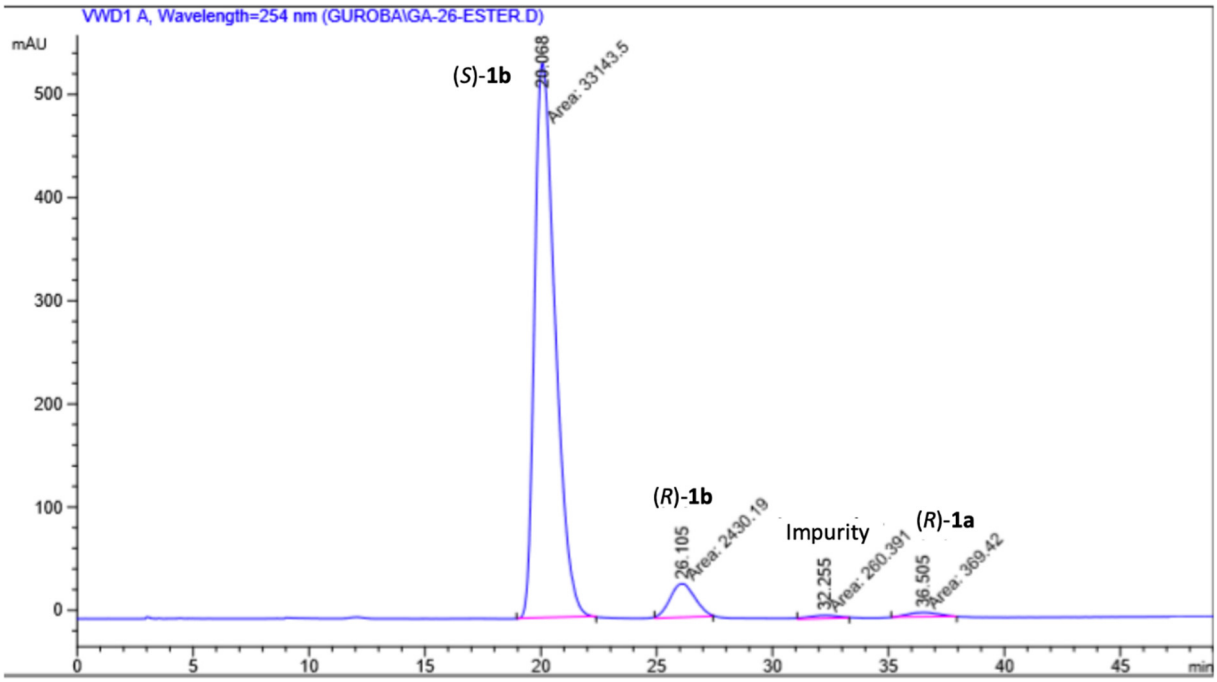
b) 1-(4-Acetamidophenoxy)-3-chloropropan-2-yl butanoate, 1b



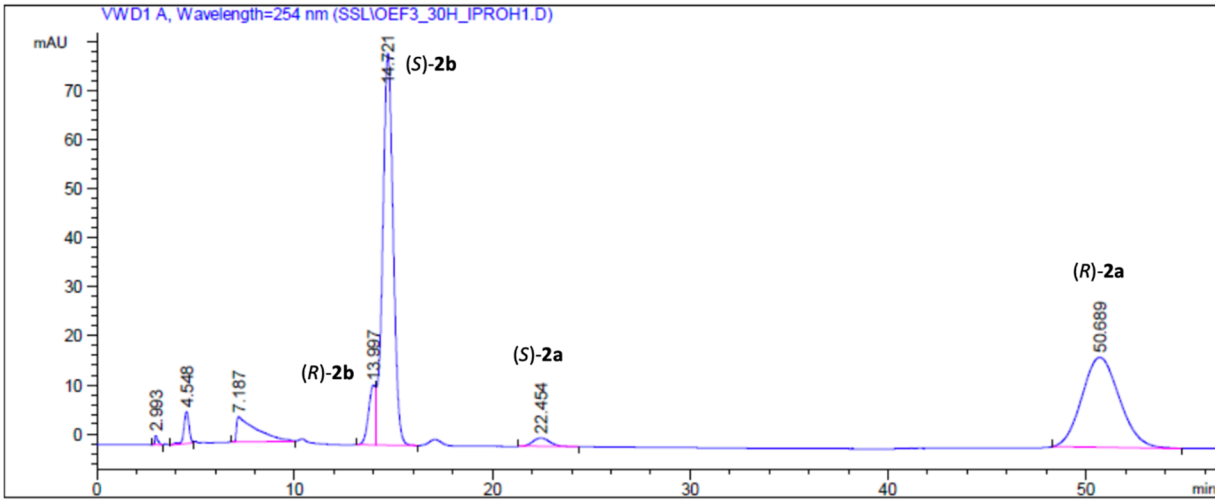
c) (R)-N-(4-(3-Chloro-2-hydroxypropoxy)phenyl)acetamide, (R)-1a



d) (S)-1-(4-Acetamidophenoxy)-3-chloropropan-2-yl butanoate, (S)-1b

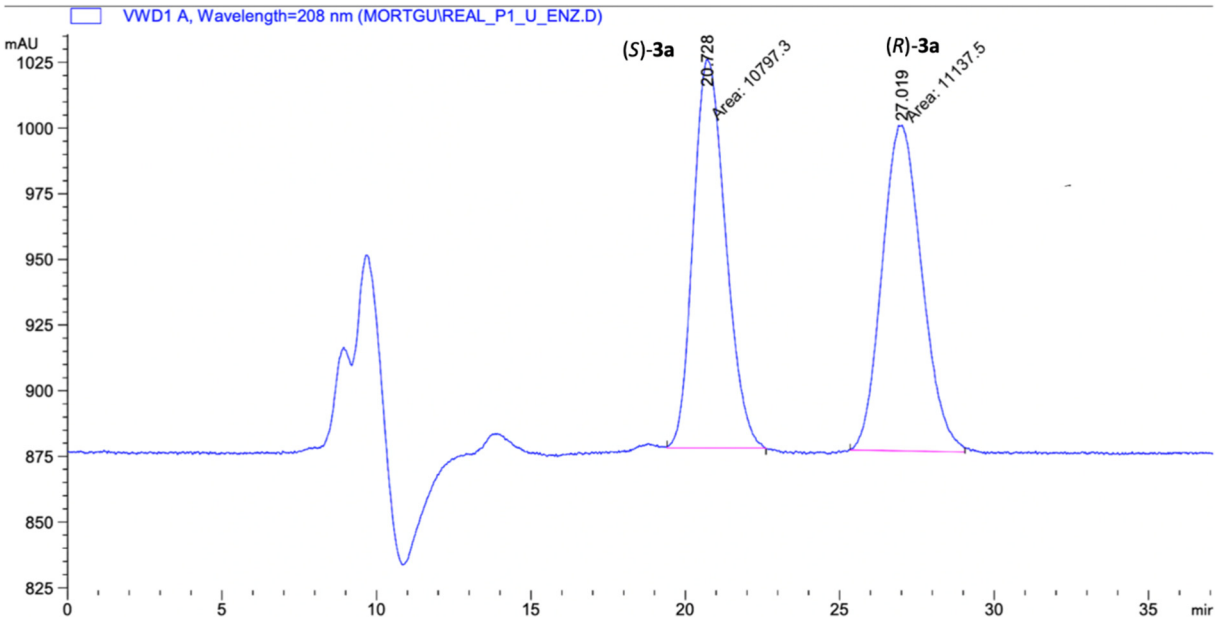


6. Chromatogram of kinetic resolution of (*R*)-1-chloro-3-(1*H*-indol-4-yloxy)-propan-2-ol, (*R*)-2a, at optimal reaction time

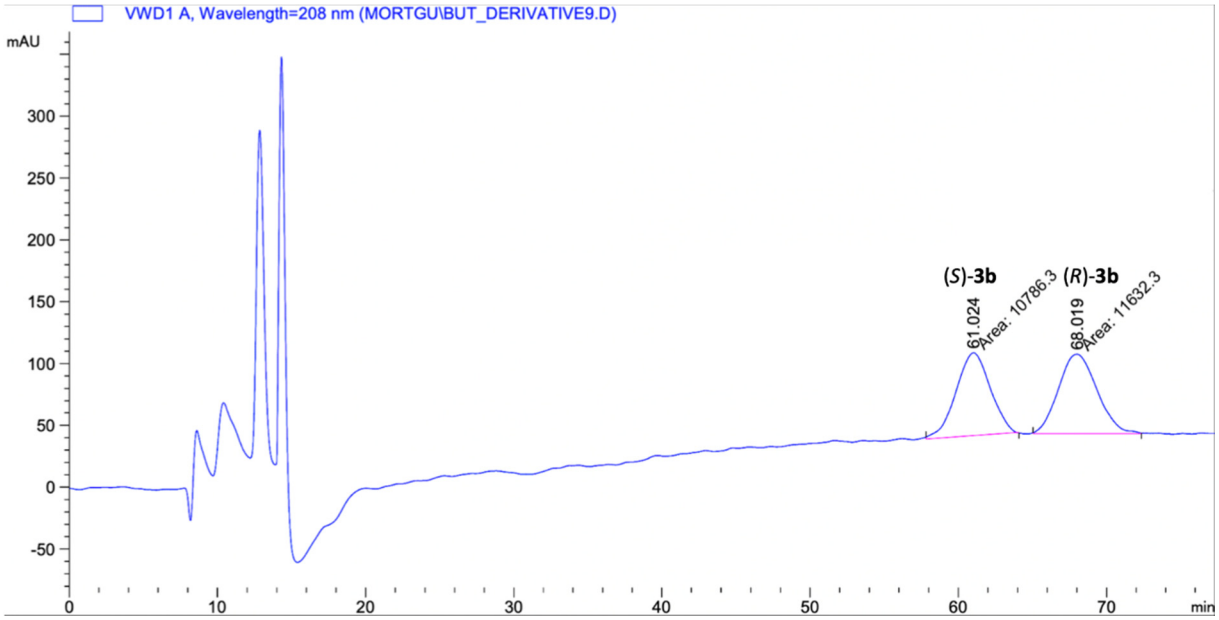


7. Chromatogram from kinetic resolution of 7-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1*H*)-one, 3a

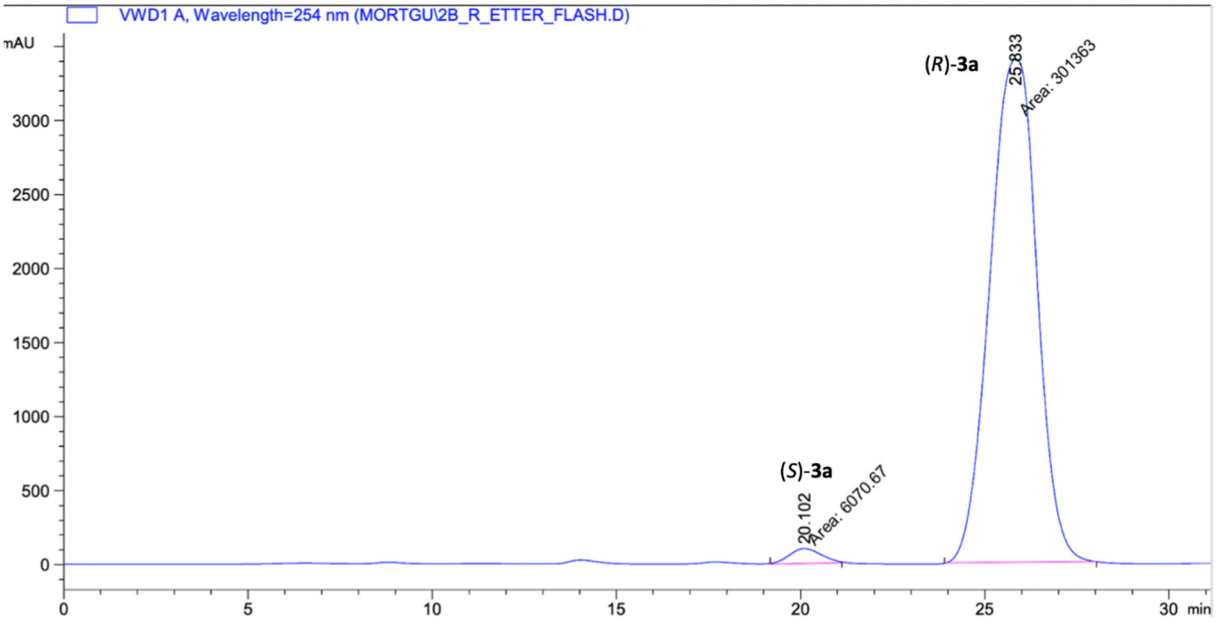
a) 7-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, 3a



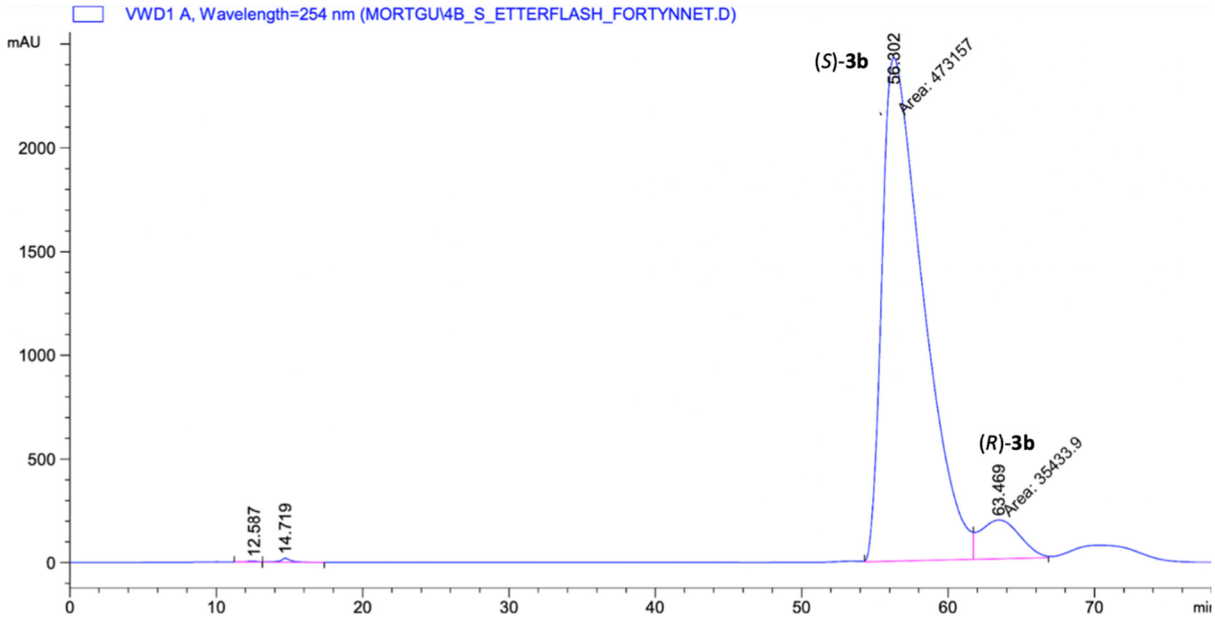
b) 1-chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)propan-2-yl butanoate, 3b



c) (R)-7-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, (R)-3a

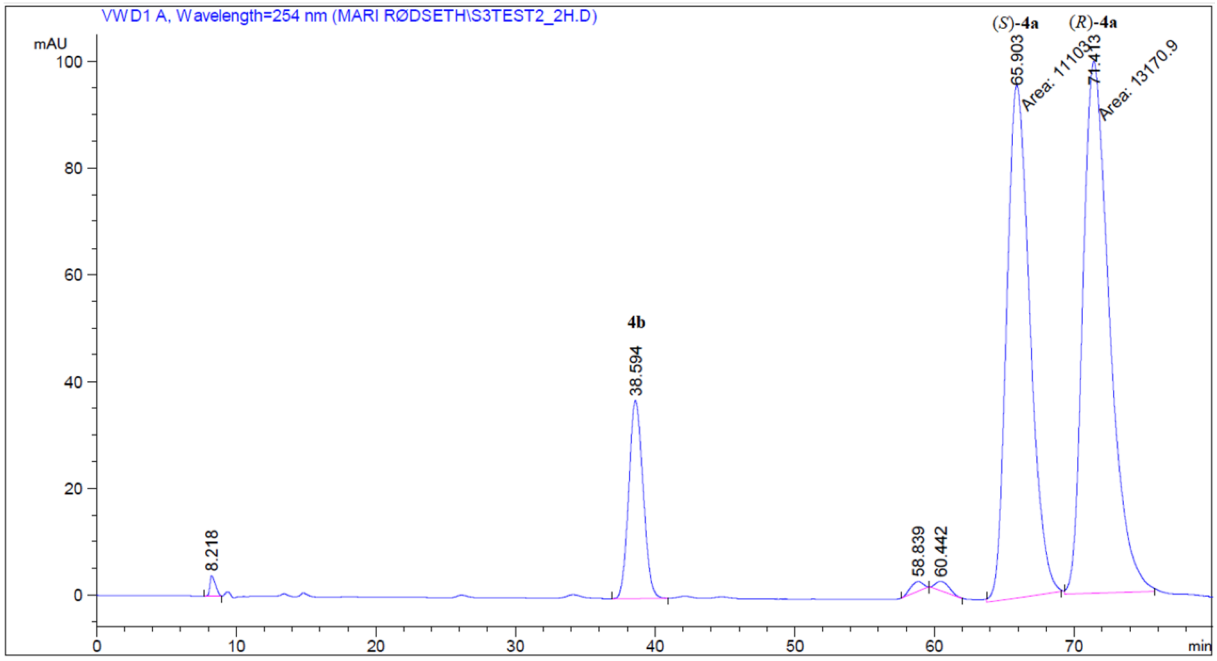


d) (S)-1-chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)propan-2-yl butanoate, (S)-3b

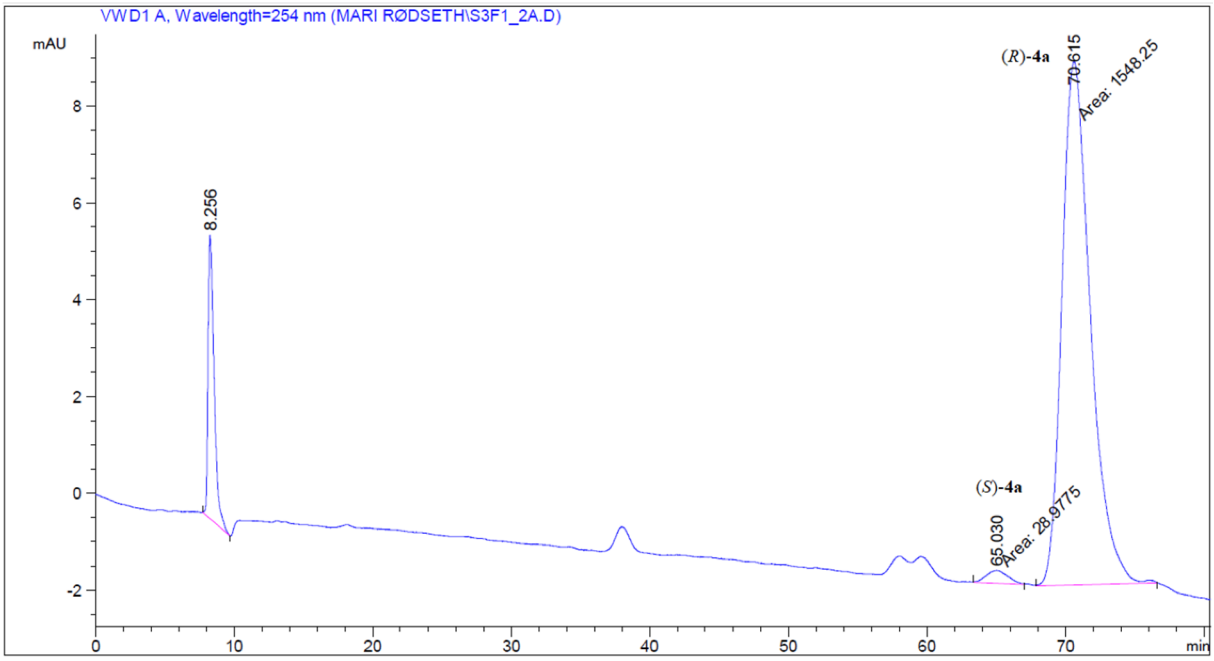


8. Chromatogram from kinetic resolution of 5-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1*H*)-one, 4a

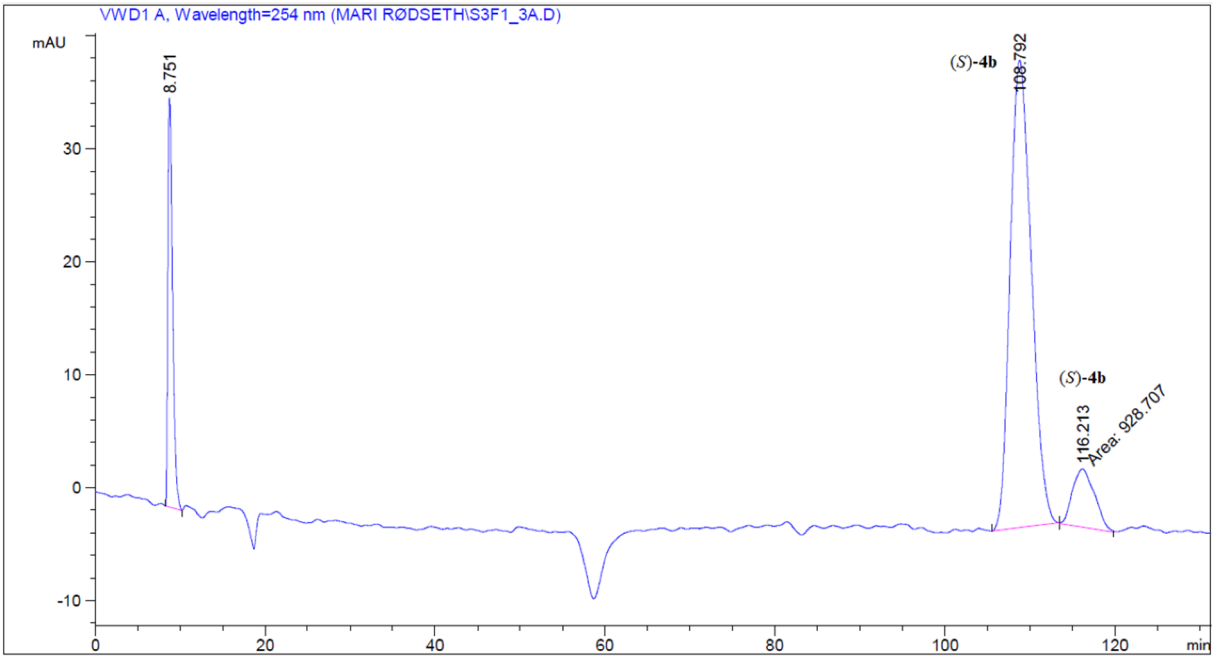
a) 5-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, 4a



b) (R)-5-(3-chloro-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, (R)-4a

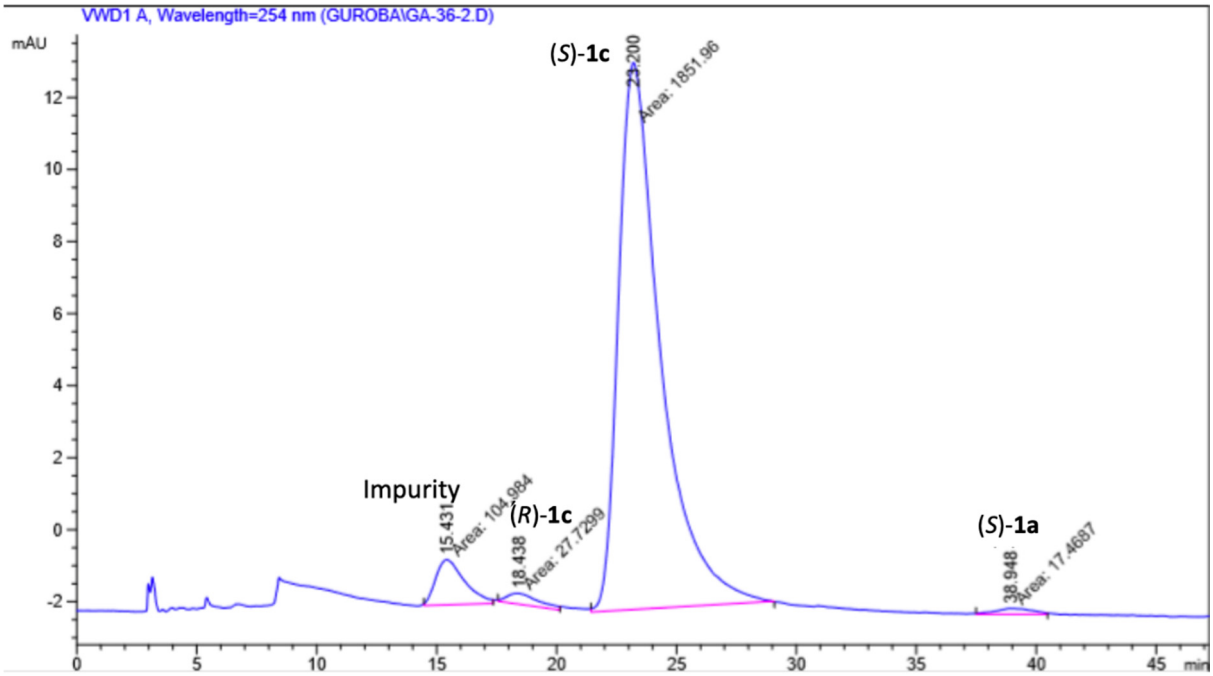


c) (S)-1-chloro-3-((2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)oxy)propan-2-yl butyrate, (S)-4b

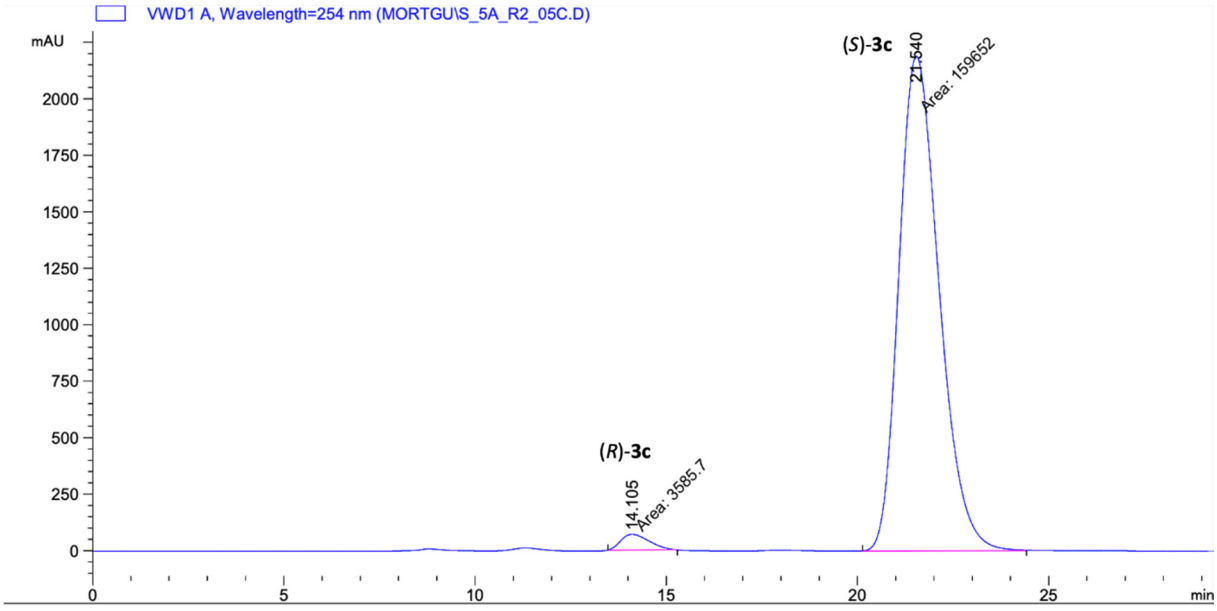


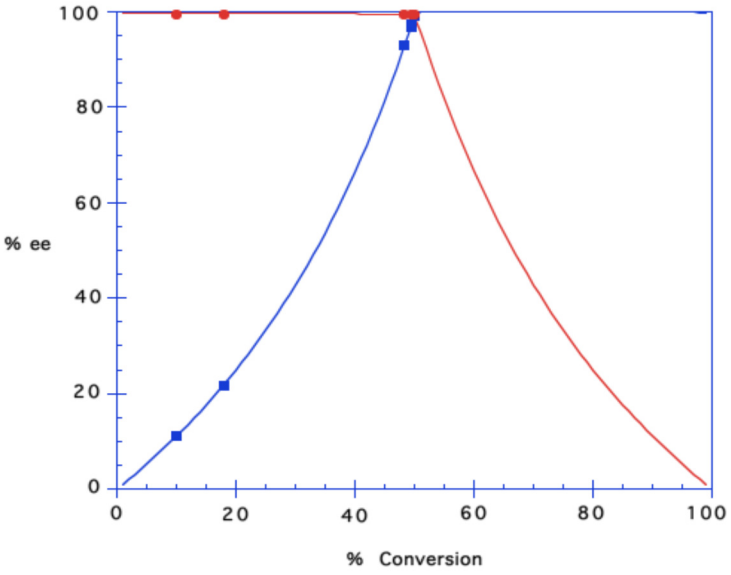
9. Chromatogram of enantiopure drugs

a) (S)-Practolol, (S)-(N-(4-(2-hydroxy-3-(isopropylamino)propoxy)phenyl)-acetamide), (S)-1c



b) (S)-7-(3-(tert-Butylamino)-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1H)-one, (S)-3c




100
80
60
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20
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% ee
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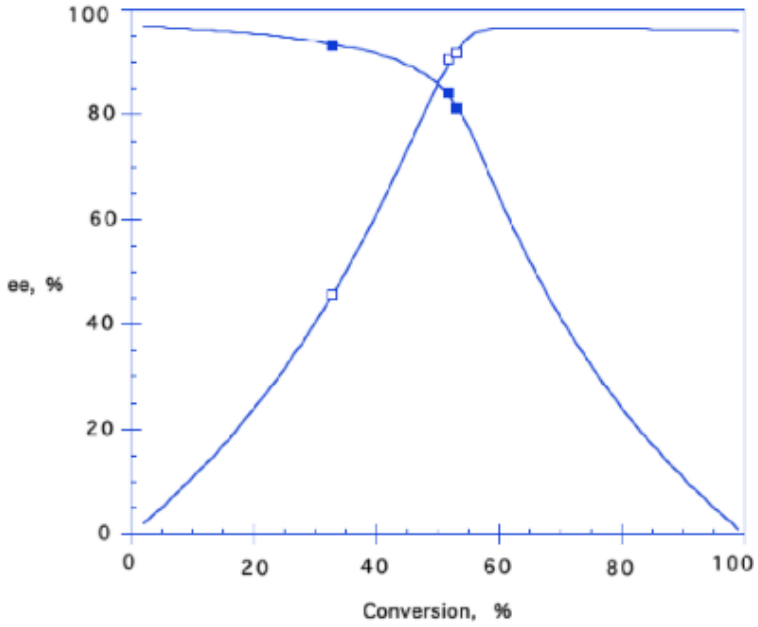
80
100
% Conversion


100
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20
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ee, %
0
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40
60
80
100
Conversion, %

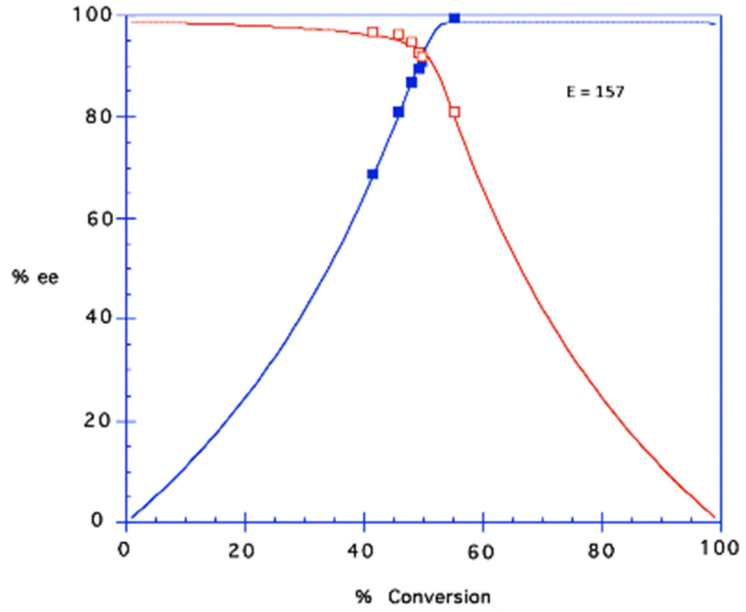

Figure 1. Graphical illustration of reaction progress of kinetic resolution at different degrees of conversion. Upper panel: **1a** ee_P (red filled squares) and ee_S (blue filled squares); *E*-value >200. Middle panel: kinetic resolution of **2a** ee_P (filled squares) and ee_S (open squares) $E = 66$. Lower panel: **3a** ee_P (open red squares) and ee_S (filled blue squares); $E = 157$. All three reactions used CALB from SyncoZymes as catalyst and vinyl butanoate as acyl donor in different solvents. All reactions were performed at 30 °C. *E*-values calculated from *E&K Calculator* 2.1b0 PPC [24].