

# ***Supporting Information***

for

## **Expanding Access to Optically Active Non-steroidal Anti-inflammatory Drugs *via* Lipase-catalyzed KR of Racemic Acids Using Trialkyl Orthoesters as Irreversible Alkoxy Group Donors**

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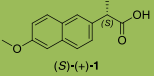
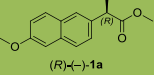
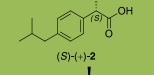
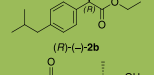
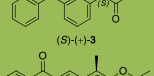
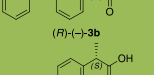
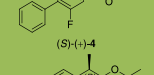
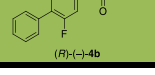
**Table S1. List of commercial enzyme preparations employed in these studies.**

Enzyme and its origin (microorganism/tissue)	Enzyme preparation <sup>[a]</sup> (brand name)	Usage form of enzyme preparation	Enzyme specified activity	Commercial supplier (Cat. No.)
Lipase from <i>Candida antarctica</i> B (CAL-B)	Novozym 435	immobilized on the macroporous acrylic resin [poly (methyl methacrylate-co-butyl methacrylate)]	>10000 U/g or 10 PLU/mg, water content 1.4%	Novozymes A/S (Bagsvaerd, Denmark)
	Lipozyme 435	immobilized on Lewatit VP OC 1600	unspecified	Novozymes A/S (Bagsvaerd, Denmark)
	Chirazyme L-2, c.-f., C2, Lyo.	immobilized on the carrier-fixed (carrier 2)	150 kU	Roche
	Chirazyme L-2, c.-f., C3, Lyo.	immobilized on the carrier-fixed (carrier 3)	150 kU	Roche
	CAL-B Sigma L4777	immobilized on the macroporous acrylic resin	≥5,000 U/g	Sigma Aldrich (cat. nr.: L4777)
	Novozym 435-STREM	immobilized on the macroporous acrylic resin	10000 PLU/g	STREM Chemicals, INC. (cat. nr.: 06-3123)
	CAL-B-Immobead 150	immobilized on Immobead 150	≥1800 U/g	Sigma Aldrich (cat. nr.: 54326)
Lipase from <i>Candida antarctica</i> A (CAL-A)	Chirazyme L-5	native	unspecified	Boehringer Mannheim <sup>[b]</sup>
Lipase from <i>Burkholderia</i> (formerly <i>Pseudomonas</i> ) <i>cepacia</i>	PS-Immobead 150	immobilized on Immobead 150	≥900 U/g	Sigma Aldrich (cat. nr.: 54327)
	Amano PS	native	>23.000 U/g	Amano Pharmaceutical Co., Ltd.
	Amano PS-IM	immobilized on diatomite	500 U/g	Amano Pharmaceutical Co., Ltd.
	Amano PS-C II	immobilized on ceramic	≥30.000 U/g	Amano Pharmaceutical Co., Ltd.
Lipase from <i>Pseudomonas fluorescens</i>	Amano AK	native	>20.000 U/g	Amano Pharmaceutical Co., Ltd.
Lipase from <i>Thermomyces lanuginosus</i>	TL-Immobead 150	immobilized on Immobead 150	≥3000 U/g	Sigma Aldrich (cat. nr.: 76546)
	Lipozyme TL IM	immobilized on a non-compressible silica gel carrier into an immobilized granulate (a silica granulated)	170 IUN/g	Novozymes A/S (Bagsvaerd, Denmark)
Lipase from <i>Rhizomucor miehei</i>	Lipozyme RM IM	immobilized (unspecified carrier)	150 IU/g	Novozymes A/S (Bagsvaerds, Denmark)
Lipase from <i>Alcaligenes</i> sp.	Chirazyme L-10	native	unspecified	Boehringer Mannheim <sup>[b]</sup>
Lipase from <i>Mucor javanicus</i>	Amano Lipase M	native	>10.000 U/g	Sigma Aldrich (cat. nr.: 534803)
Lipase from <i>Rhizopus oryzae</i>	Amano Lipase F-AP15	native	≥150.000 U/g	Sigma Aldrich (cat. nr.: 534811)
Lipase from <i>Penicillium camemberti</i>	Lipase G50 Amano	native	≥50 U/mg	Sigma Aldrich (cat. nr.: 96888)
Lipase from <i>Candida rugosa</i>	Lipase AY Amano 30	native	>30.000 U/g	Amano Pharmaceutical Co., Ltd.
	Lipase Type VII	native	≥700 unit/mg	Sigma Aldrich (cat. nr.: L1754)
	Chirazyme L-3	native	unspecified	Boehringer Mannheim <sup>[b]</sup>
Lipase from <i>Geotrichum candidum</i>	Chirazyme L-8	native	unspecified	Boehringer Mannheim <sup>[b]</sup>
Lipase A from <i>Aspergillus niger</i>	Amano A	native	≥120,000 U/g	Sigma Aldrich (cat. nr.: 534781)
Esterase from porcine liver	PLE	native	≥50 U/mg	Sigma Aldrich (cat. nr.: 46058)

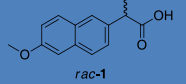
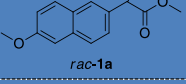
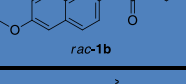
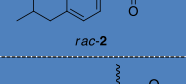
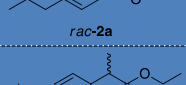
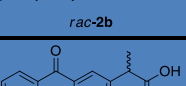
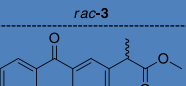
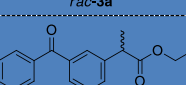
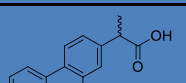
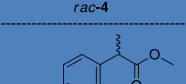
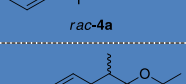
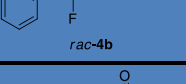
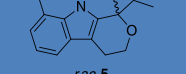
[a] All commercial formulations of enzymes studied herein were used without pre-treatment.

[b] Currently: Roche Diagnostics.

**Table S2. The results of specific rotation values for the EKR products.**

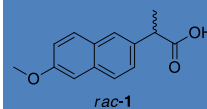
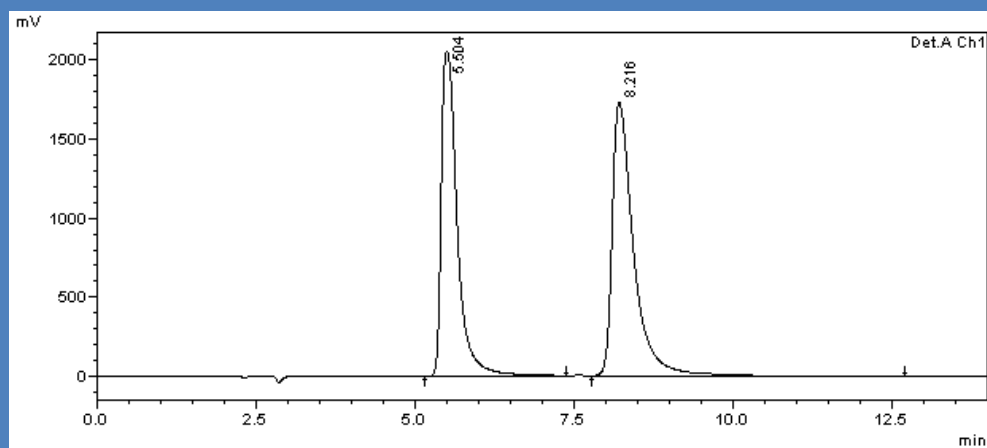
Product of EKR	ee [%]	Measured specific rotation $[\alpha]_D$	Literature specific rotation $[\alpha]_D^{\text{lit.}}$	Ref.
 (S)-(+)-1	57	$[\alpha]_D^{29} = +16.0$ (c 0.50, CHCl <sub>3</sub> )	$[\alpha]_D^{20} = +65.5$ (c 1.00, CHCl <sub>3</sub> , 99% ee)	[1]
 (R)-(-)-1a	29	$[\alpha]_D^{29} = -45.0$ (c 1.00, CHCl <sub>3</sub> )	$[\alpha]_D^{20} = -76.0$ (c 1.00, CHCl <sub>3</sub> , >95% ee)	[2]
 (S)-(+)-2	56	$[\alpha]_D^{24} = +28.5$ (c 1.00, EtOH)	$[\alpha]_D^{25} = +58.2$ (c 1.00, EtOH, 99% ee)	[1]
 (R)-(-)-2b	67	$[\alpha]_D^{25} = -30.0$ (c 0.95, CHCl <sub>3</sub> )	Lack of data	-
 (S)-(+)-3	53	$[\alpha]_D^{23} = +7.4$ (c 0.61, MeOH)	$[\alpha]_D^{25} = +46.3$ (c 1.00, MeOH, 99.4% ee)	[3]
 (R)-(-)-3b	21	$[\alpha]_D^{26} = -11.5$ (c 1.44, CHCl <sub>3</sub> )	Lack of data	-
 (S)-(+)-4	23	$[\alpha]_D^{25} = +8.9$ (c 1.02, CHCl <sub>3</sub> )	$[\alpha]_D^{20} = +37.2$ (c 1.00, CHCl <sub>3</sub> , 98% ee)	[4]
 (R)-(-)-4b	70	$[\alpha]_D^{25} = -17.7$ (c 1.44, CHCl <sub>3</sub> )	Lack of data	-

**Table S3. HPLC analytical separation conditions of NSAIDs and their esters by chiral columns – (S,S)-Whelk-O 1 or Chiralcel OJ-H or Chiralpak AD-H.**

Compound	HPLC Column	Mobile Phase		Flow Rate [mL/min]	Detection [nm]	Retention Time [min]
		<i>n</i> -Hexane/IPA [v/v]	Acidic Additive			
 <i>rac-1</i>	(S,S)-Whelk-O 1	70:30	0.1% AcOH	1.5	230	5.504 ( <i>R</i> ) and 8.216 ( <i>S</i> )
 <i>rac-1a</i>	(S,S)-Whelk-O 1	70:30	-	1.5	230	9.797 ( <i>R</i> ) and 12.541 ( <i>S</i> )
 <i>rac-1b</i>	(S,S)-Whelk-O 1	70:30	-	1.5	230	8.975 ( <i>R</i> ) and 11.542 ( <i>S</i> )
 <i>rac-2</i>	Chiralcel OJ-H	98:2	0.05% TFA	1.0	216	8.616 ( <i>R</i> ) and 9.415 ( <i>S</i> )
 <i>rac-2a</i>	Chiralcel OJ-H	99:1	-	0.7	217	10.393 ( <i>S</i> ) and 13.210 ( <i>R</i> )
 <i>rac-2b</i>	Chiralcel OJ-H	99:1	-	0.7	217	8.465 ( <i>S</i> ) and 10.159 ( <i>R</i> )
 <i>rac-3</i>	Chiralcel OJ-H	96:4	0.1% TFA	0.8	250	34.018 ( <i>S</i> ) and 44.343 ( <i>R</i> )
 <i>rac-3a</i>	Chiralpak AD-H	99:1	-	0.7	249	29.146 ( <i>S</i> ) and 30.214 ( <i>R</i> )
 <i>rac-3b</i>	Chiralcel OJ-H	99:1	-	0.7	249	30.411 ( <i>S</i> ) and 31.951 ( <i>R</i> )
 <i>rac-4</i>	Chiralcel OJ-H	96.5:3.5	0.2% TFA	0.5	246	40.346 ( <i>S</i> ) and 43.773 ( <i>R</i> )
 <i>rac-4a</i>	Chiralcel OJ-H	99:1	-	0.7	246	29.847 ( <i>S</i> ) and 35.927 ( <i>R</i> )
 <i>rac-4b</i>	Chiralcel OJ-H	99:1	-	0.7	246	19.916 ( <i>S</i> ) and 26.663 ( <i>R</i> )
 <i>rac-5</i>	Chiralcel OJ-H	95:5	0.05% TFA	1.0	230	10.252 and 11.657

## HPLC analytical separation for both enantiomers of naproxen (*rac*-1) using (*S,S*)-Whelk-O1

HPLC conditions: *n*-hexane-2-PrOH-AcOH (70:30:0.1, v/v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



1 Det.A Ch1/230nm

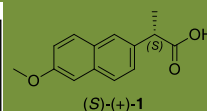
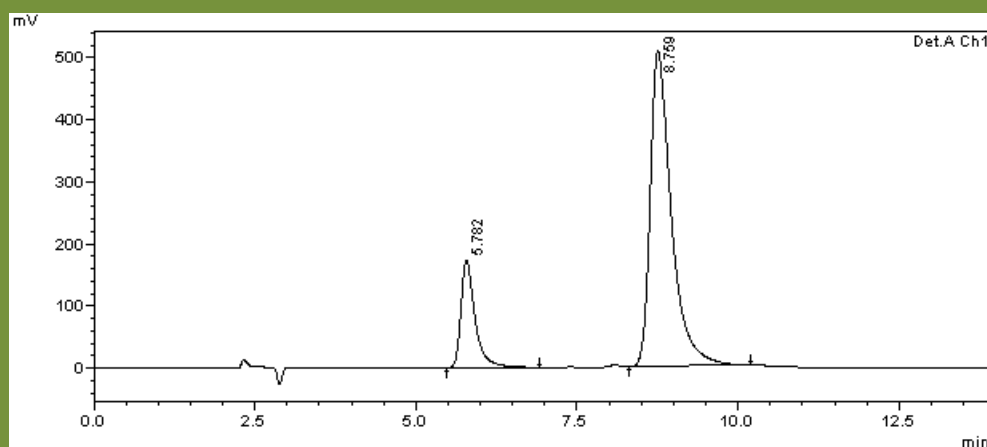
PeakTable

Detector A Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.504	35852166	2051776	46.942	54.352
2	8.216	40522687	1723233	53.058	45.648
Total		76374852	3775008	100.000	100.000

## HPLC analytical separation for (*S*)-(+)-1 (63% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH-AcOH (70:30:0.1, v/v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



1 Det.A Ch1/230nm

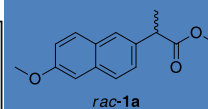
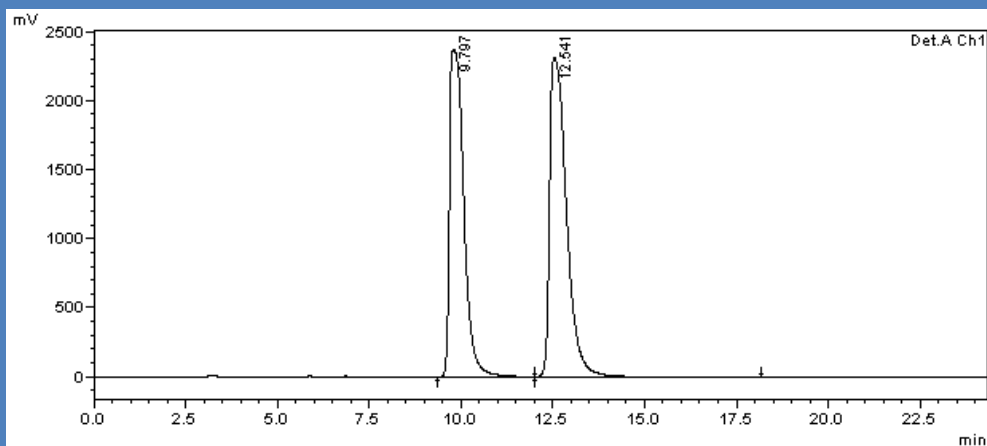
PeakTable

Detector A Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.782	2652284	172860	18.716	25.360
2	8.759	11518605	508759	81.284	74.640
Total		14170889	681619	100.000	100.000

## HPLC separation for both enantiomers of naproxen methyl ester (*rac*-1a) using (*S,S*)-Whelk-O1

HPLC conditions: *n*-hexane-2-PrOH (70:30, v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



1 Det.A Ch1/230nm

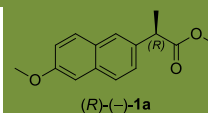
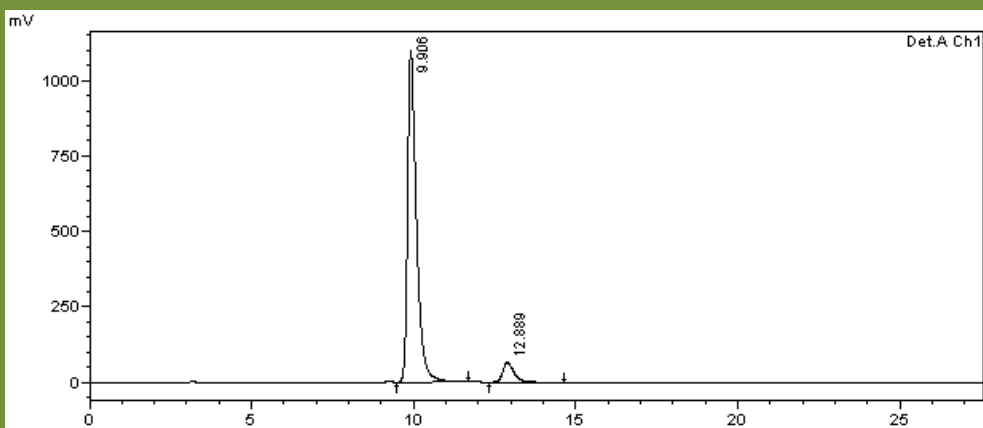
Peak Table

Detector A Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.797	64669521	2371479	46.635	50.643
2	12.541	74002036	2311214	53.365	49.357
Total		138671558	4682693	100.000	100.000

## HPLC analytical separation for (*R*)-(-)-1a (86% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (70:30, v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



1 Det.A Ch1/230nm

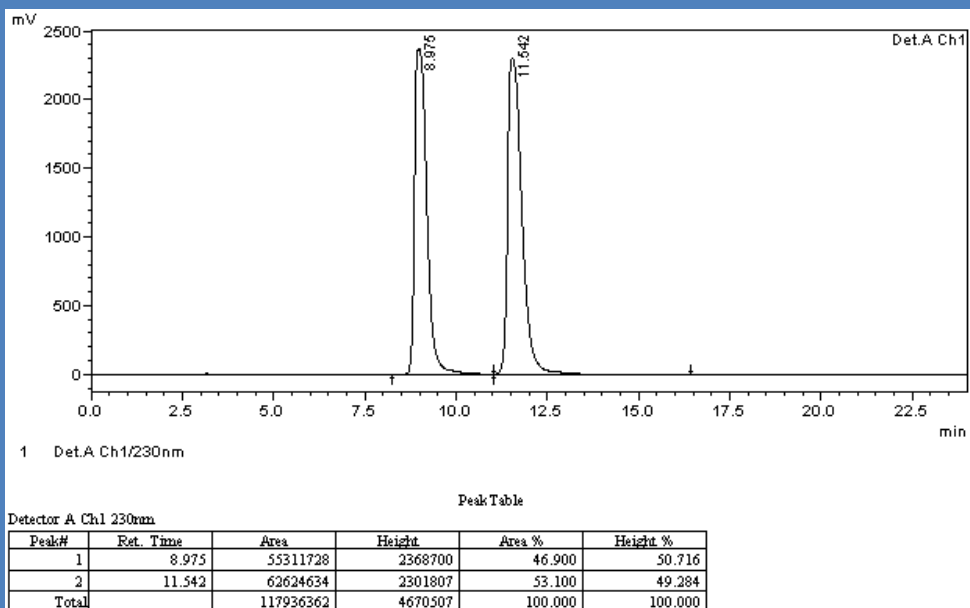
Peak Table

Detector A Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.906	20754586	1097430	92.880	94.387
2	12.889	1591074	65262	7.120	5.613
Total		22345661	1162692	100.000	100.000

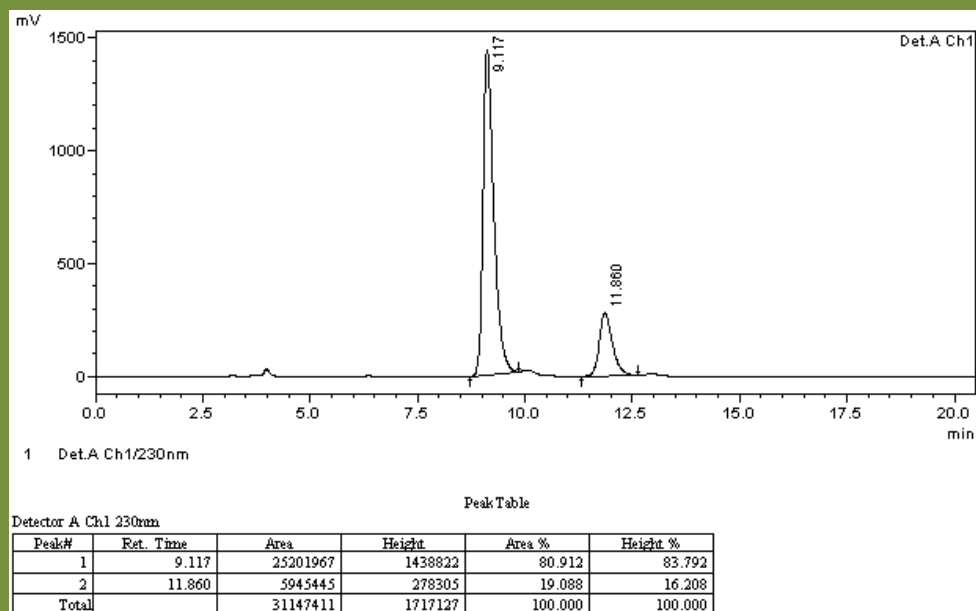
## HPLC analytical separation for both enantiomers of naproxen ethyl ester (*rac*-1b) using (*S,S*)-Whelk-O1

HPLC conditions: *n*-hexane-2-PrOH (70:30, v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



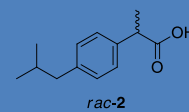
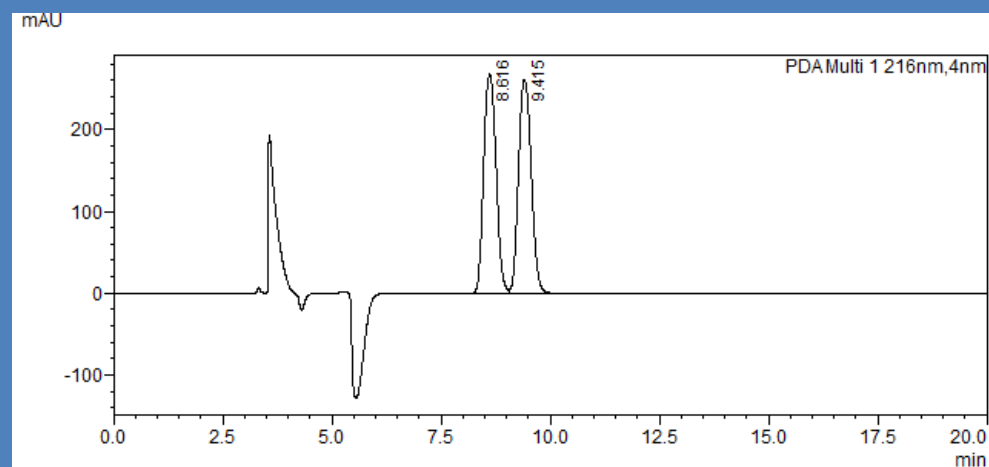
## HPLC analytical separation for (*R*)-(-)-1b (62% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (70:30, v/v); *f*=1.5 mL/min;  $\lambda$ =230 nm; *T*=30 °C.



## HPLC analytical separation for both enantiomers of ibuprofen (*rac*-2) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH-TFA (98:2:0.05, v/v/v); *f*=1.0 mL/min;  $\lambda$ =216 nm; *T*=30 °C.



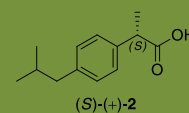
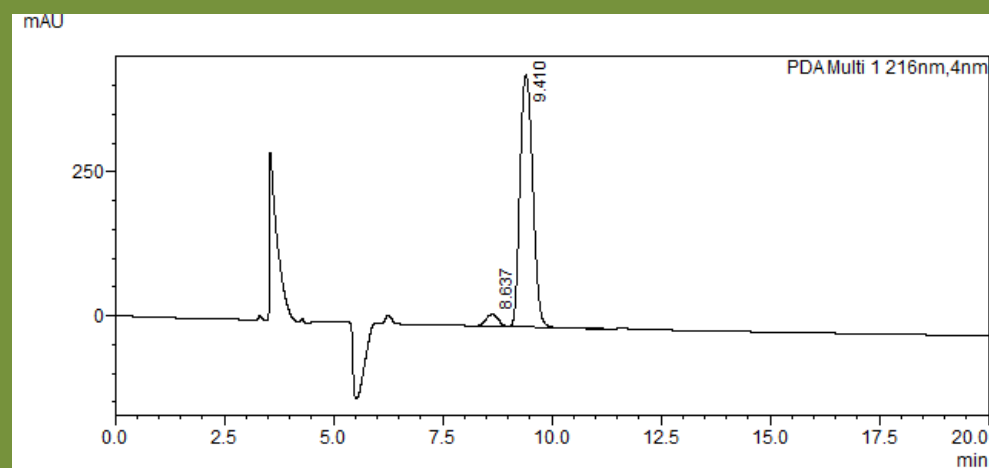
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PDA Ch1 216nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	8.616	5291757	267670	49.889	50.616
2	9.415	5315213	261152	50.111	49.384
Total		10606970	528821	100.000	100.000

## HPLC analytical separation for (*S*)-(+)-2 (91% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH-TFA (98:2:0.05, v/v/v); *f*=1.0 mL/min;  $\lambda$ =216 nm; *T*=30 °C.



### <Peak Table>

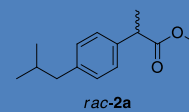
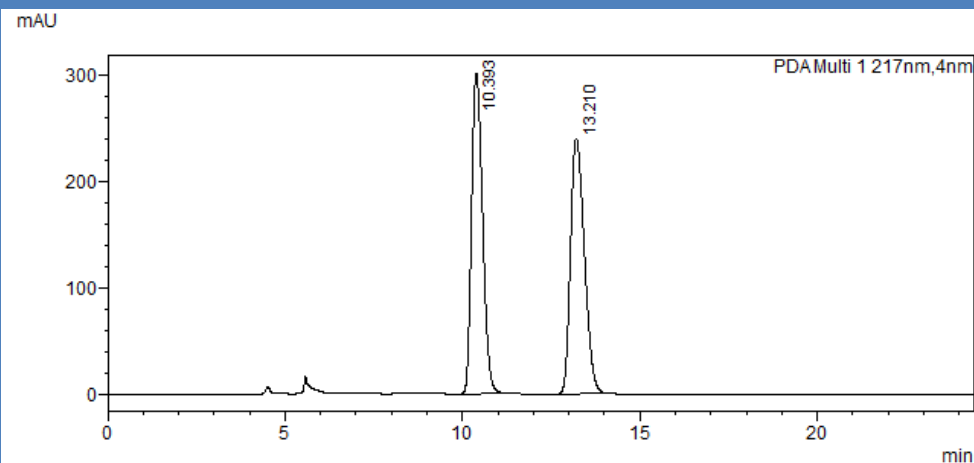
PDA Ch1 216nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	8.637	408944	20594	4.383	4.494
2	9.410	8921888	437698	95.617	95.506
Total		9330832	458292	100.000	100.000



## HPLC separation for both enantiomers of ibuprofen methyl ester (*rac*-2a) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =217 nm; *T*=30 °C.



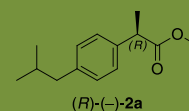
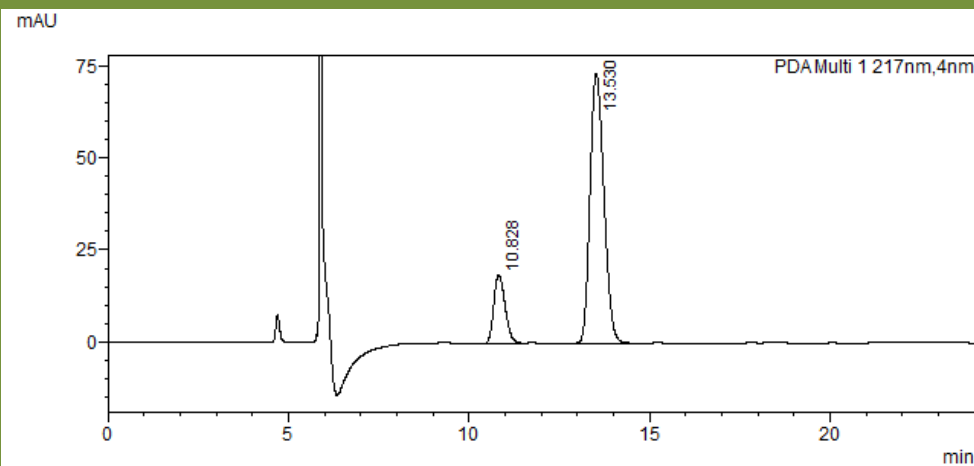
### <Peak Table>

PDA Ch1 217nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	10.393	6500700	300668	49.987	55.606
2	13.210	6504064	240045	50.013	44.394
Total		13004765	540713	100.000	100.000

## HPLC analytical separation for (*R*)-(-)-2a (66% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =217 nm; *T*=30 °C.



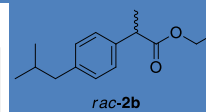
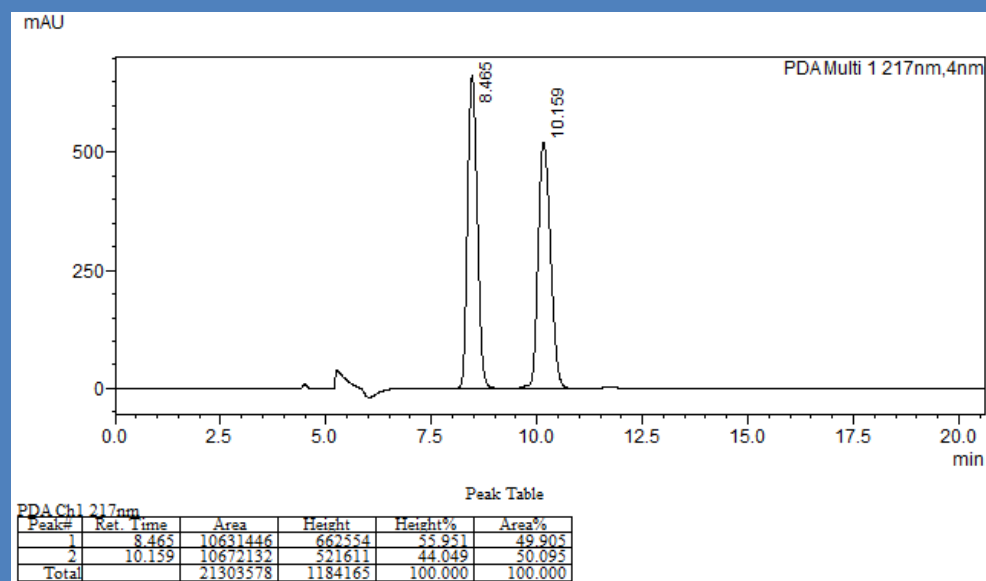
### <Peak Table>

PDA Ch1 217nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	10.828	405083	18690	17.158	20.367
2	13.530	1955843	73076	82.842	79.633
Total		2360926	91767	100.000	100.000

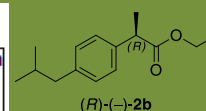
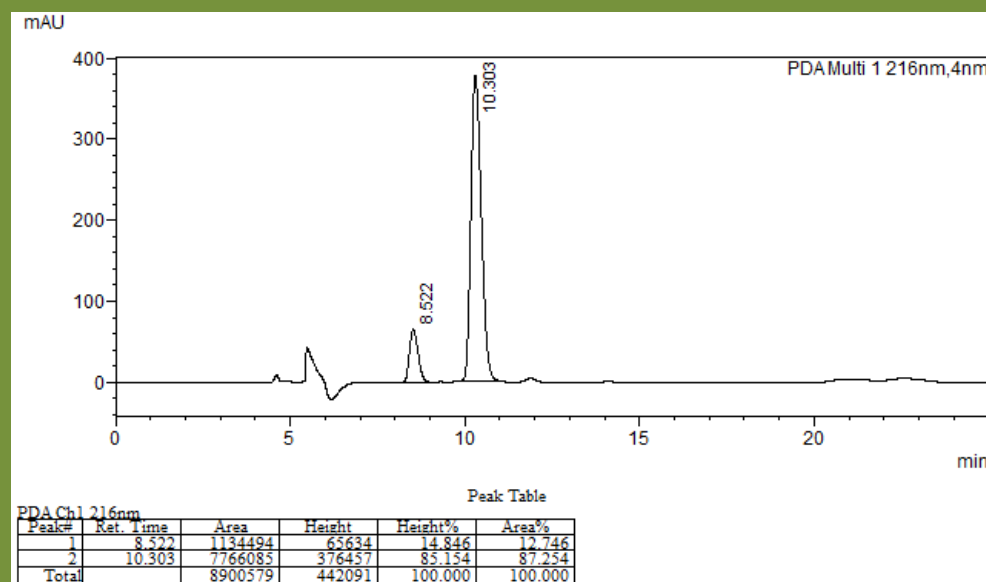
# HPLC analytical separation for both enantiomers of ibuprofen ethyl ester (*rac*-2b) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =217 nm; *T*=30 °C.



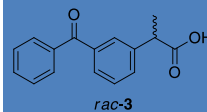
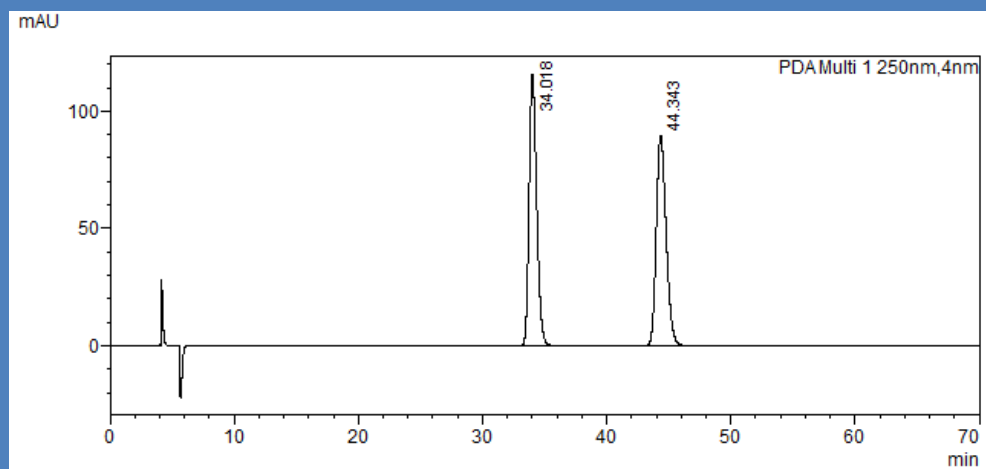
## HPLC analytical separation for (*R*)-(-)-2b (75% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =217 nm; *T*=30 °C.



## HPLC analytical separation for both enantiomers of ketoprofen (*rac*-3) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH-TFA (96:4:0.1, v/v/v); *f*=0.8 mL/min;  $\lambda$ =250 nm; *T*=30 °C.



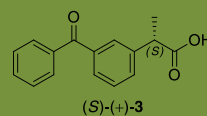
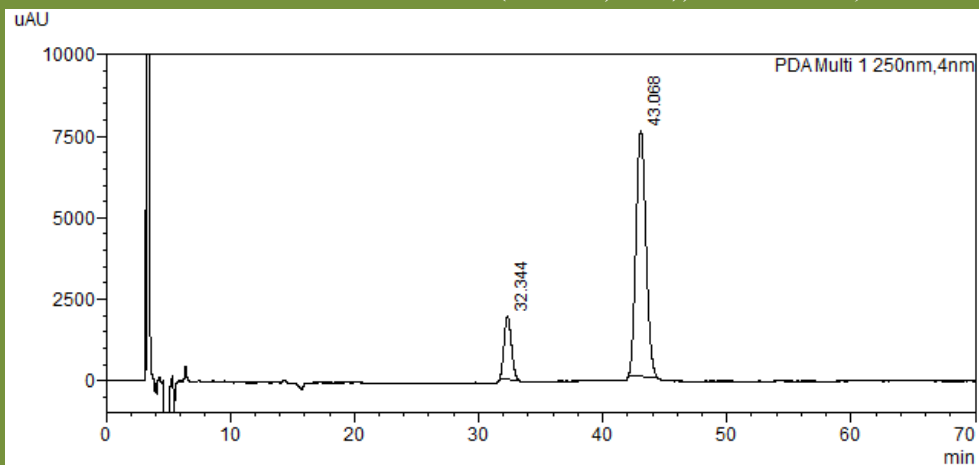
### <Peak Table>

PDA Ch1 250nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	34.018	4909515	115394	49.993	56.307
2	44.343	4910983	89544	50.007	43.693
Total		9820498	204938	100.000	100.000

## HPLC analytical separation for (*S*)-(+)-3 (69% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH-TFA (96:4: 0.1, v/v/v); *f*=0.8 mL/min;  $\lambda$ =250 nm; *T*=30 °C.

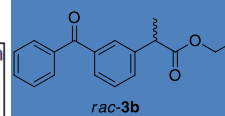
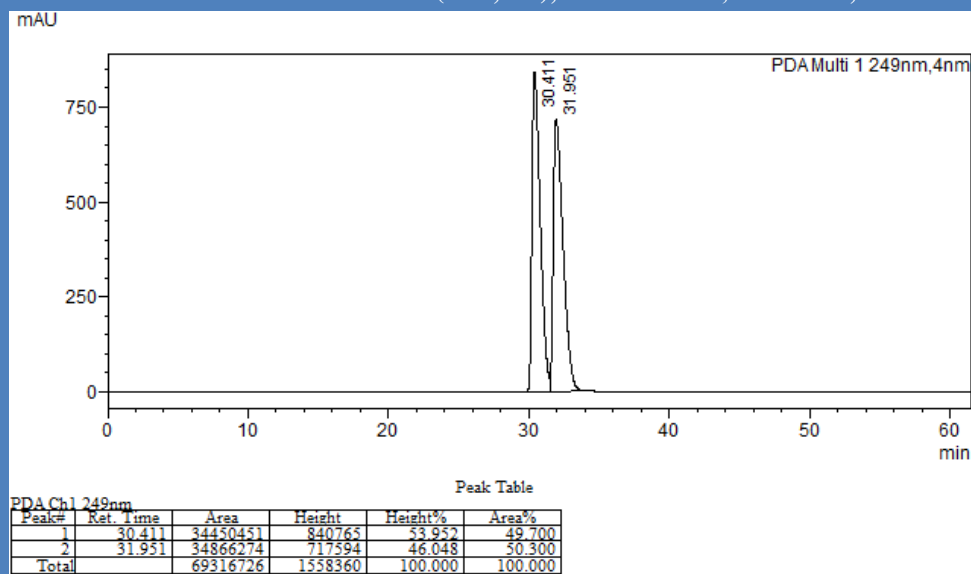


PDA Ch1 250nm

Peak#	Ret. Time	Area	Height	Height%	Area%
1	32.344	78033	1927	20.282	15.582
2	43.068	422754	7573	79.718	84.418
Total		500786	9500	100.000	100.000

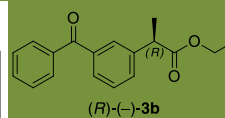
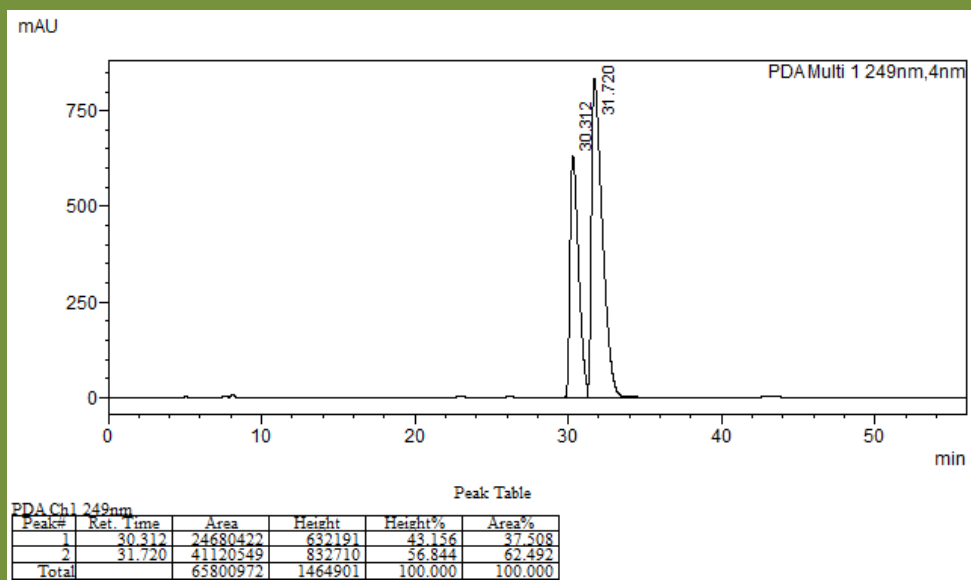
## HPLC separation for both enantiomers of ketoprofen ethyl ester (*rac*-3b) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =249 nm; *T*=30 °C.



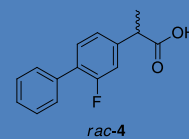
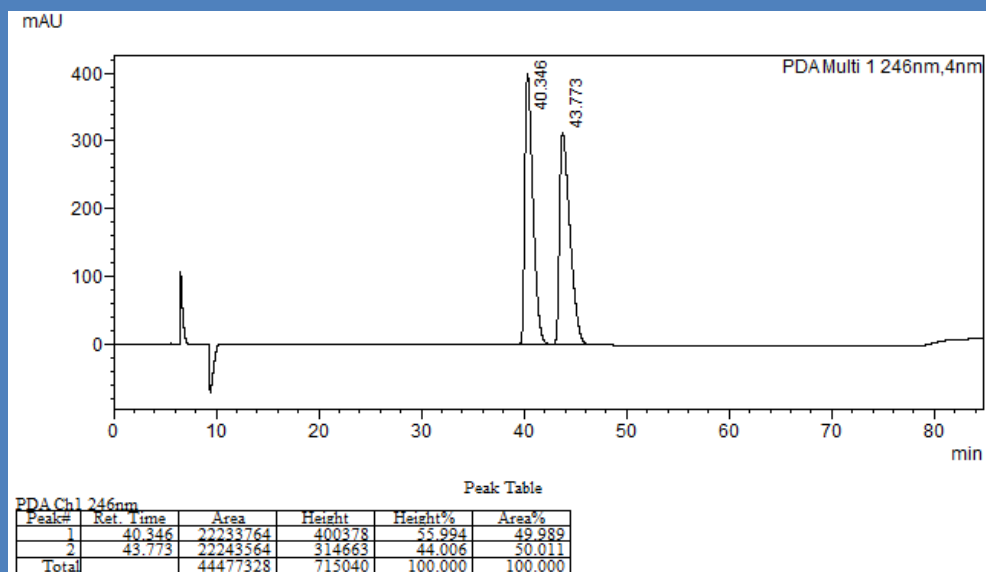
## HPLC analytical separation for (*R*)-(-)-3b (25% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =249 nm; *T*=30 °C.



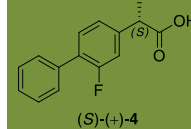
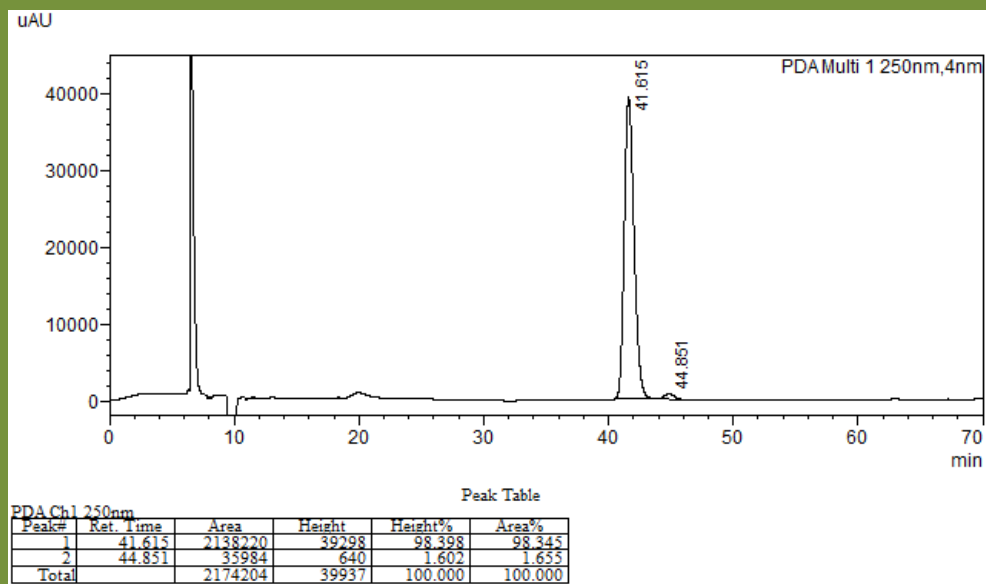
## HPLC analytical separation for both enantiomers of flurbiprofen (*rac*-4) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH-TFA (96.5:3.5:0.2, v/v/v); f=0.5 mL/min;  $\lambda$ =246 nm;  $T$ =30 °C.



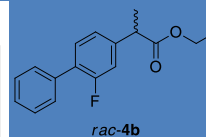
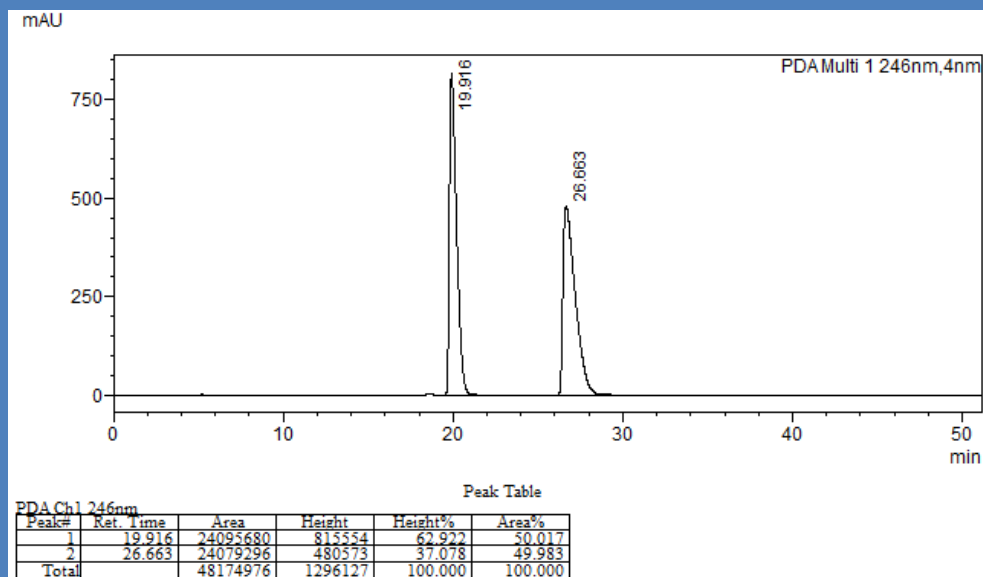
## HPLC analytical separation for (*S*)-(+)-4 (97% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH-TFA (96.5:3.5:0.2, v/v/v); f=0.5 mL/min;  $\lambda$ =246 nm;  $T$ =30 °C.



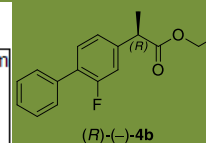
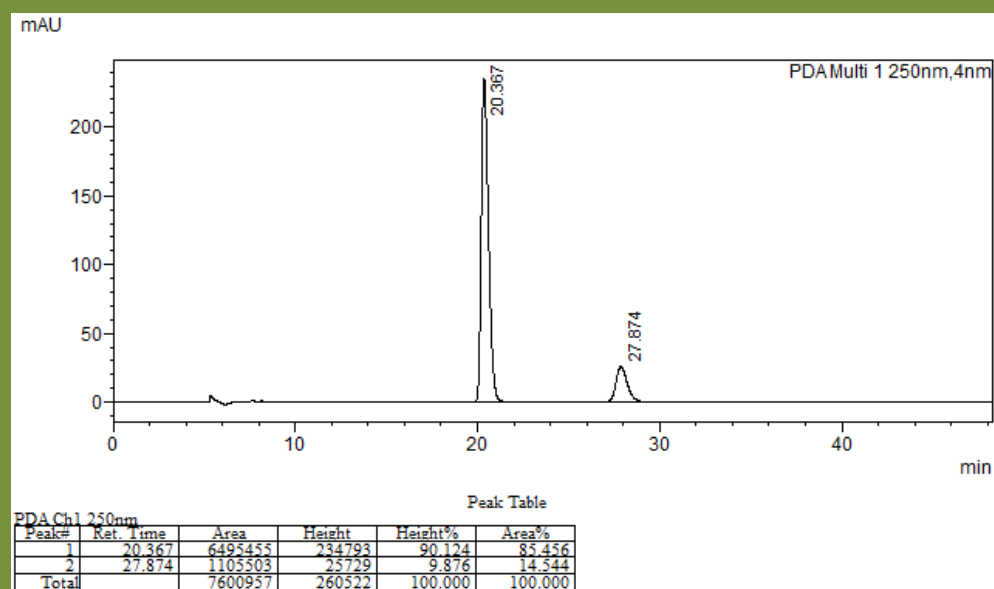
## HPLC separation for both enantiomers of flurbiprofen ethyl ester (*rac*-4b) using Chiralcel OJ-H

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =246 nm; *T*=30 °C.



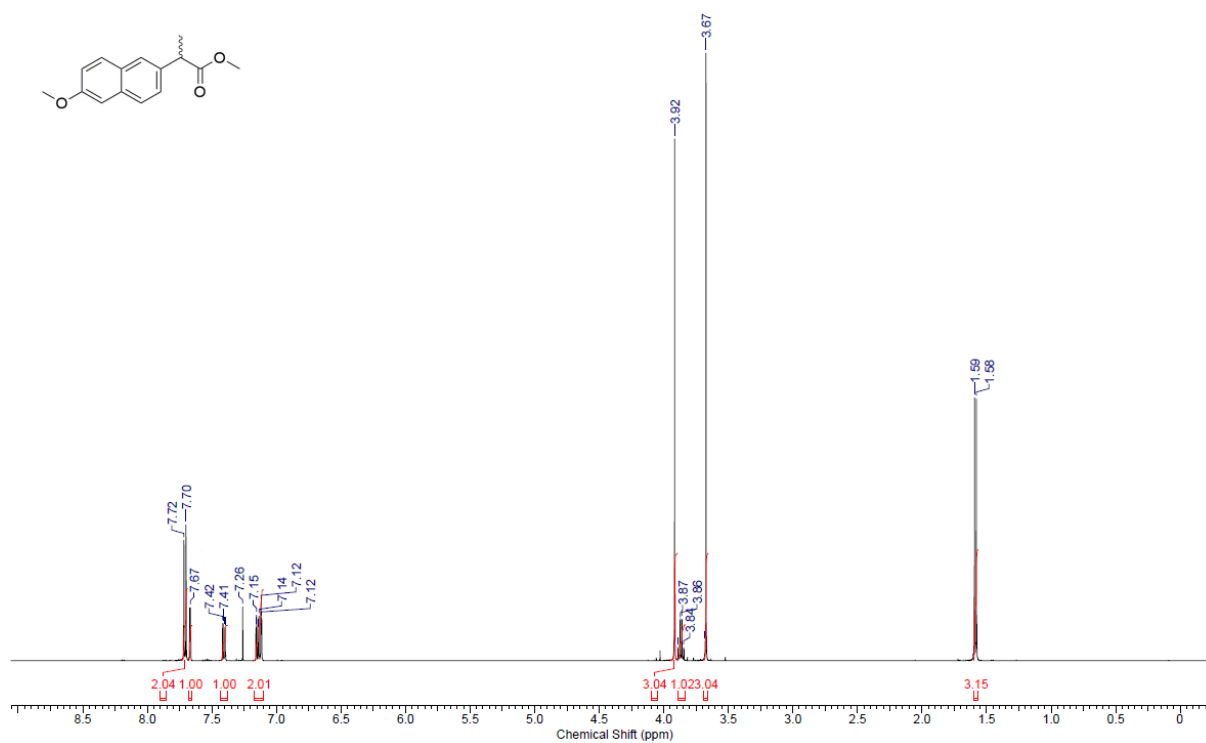
## HPLC analytical separation for (*R*)-(-)-4b (71% ee) obtained from EKR.

HPLC conditions: *n*-hexane-2-PrOH (99:1, v/v); *f*=0.7 mL/min;  $\lambda$ =246 nm; *T*=30 °C.

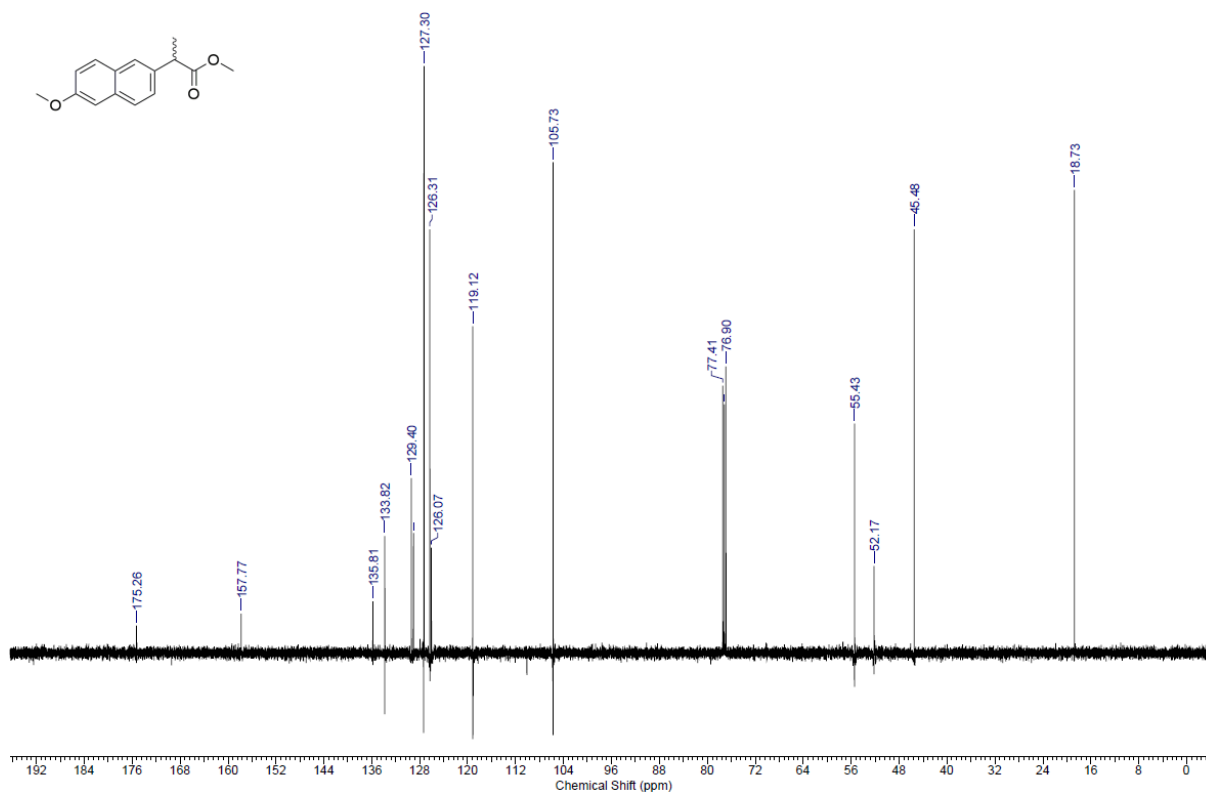


**Methyl 2-(6-methoxynaphthalen-2-yl)propanoate (Naproxen methyl ester, *rac*-1a)**

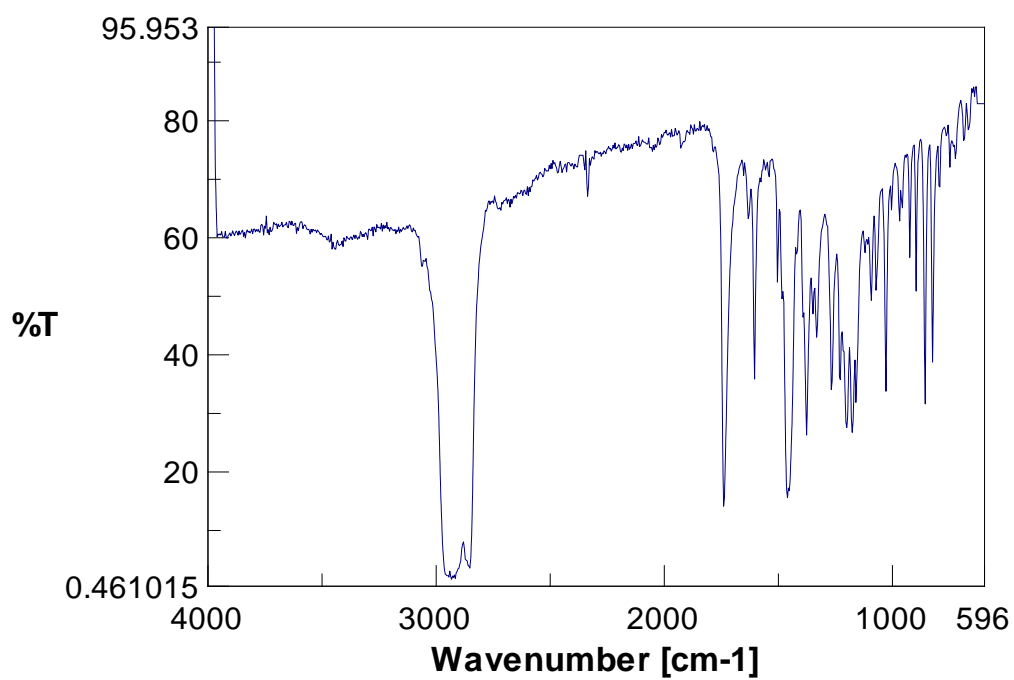
$^1\text{H}$  NMR spectrum of *rac*-1a (500 MHz,  $\text{CDCl}_3$ )



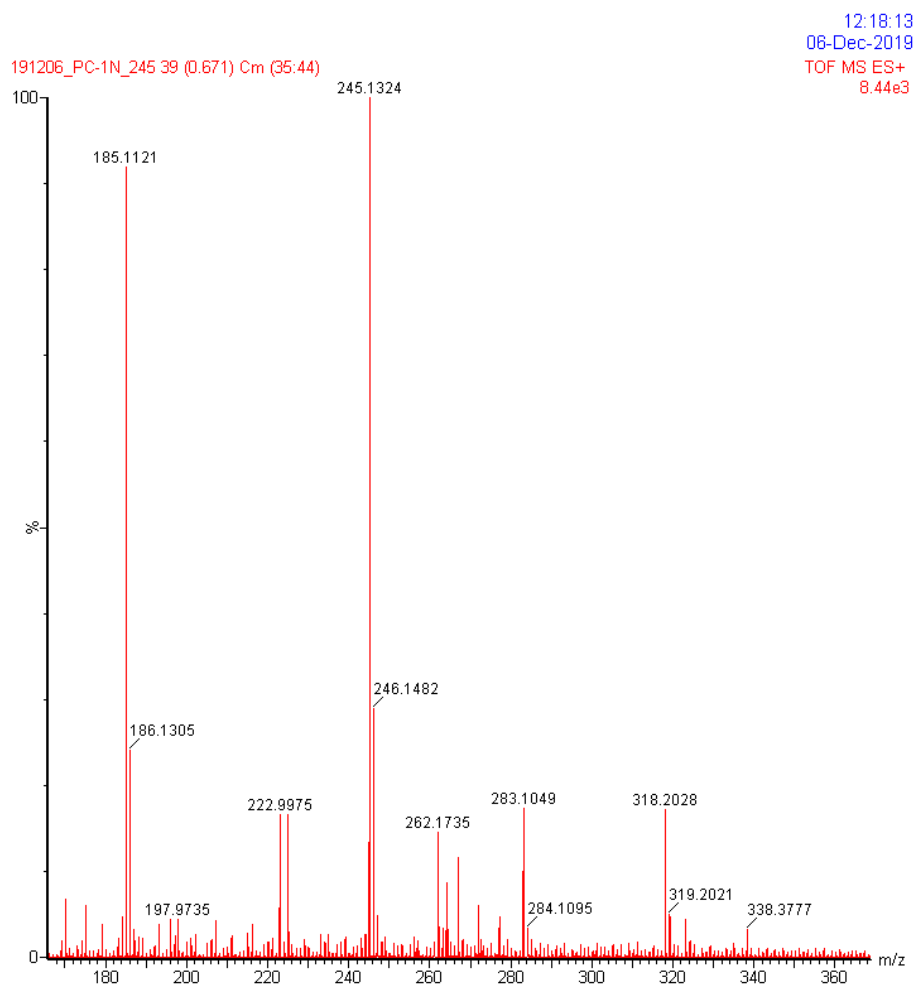
$^{13}\text{C}$  NMR spectrum of *rac*-1a (126 MHz,  $\text{CDCl}_3$ )



FTIR spectrum of *rac*-**1a** (Mineral oil, Nujol)

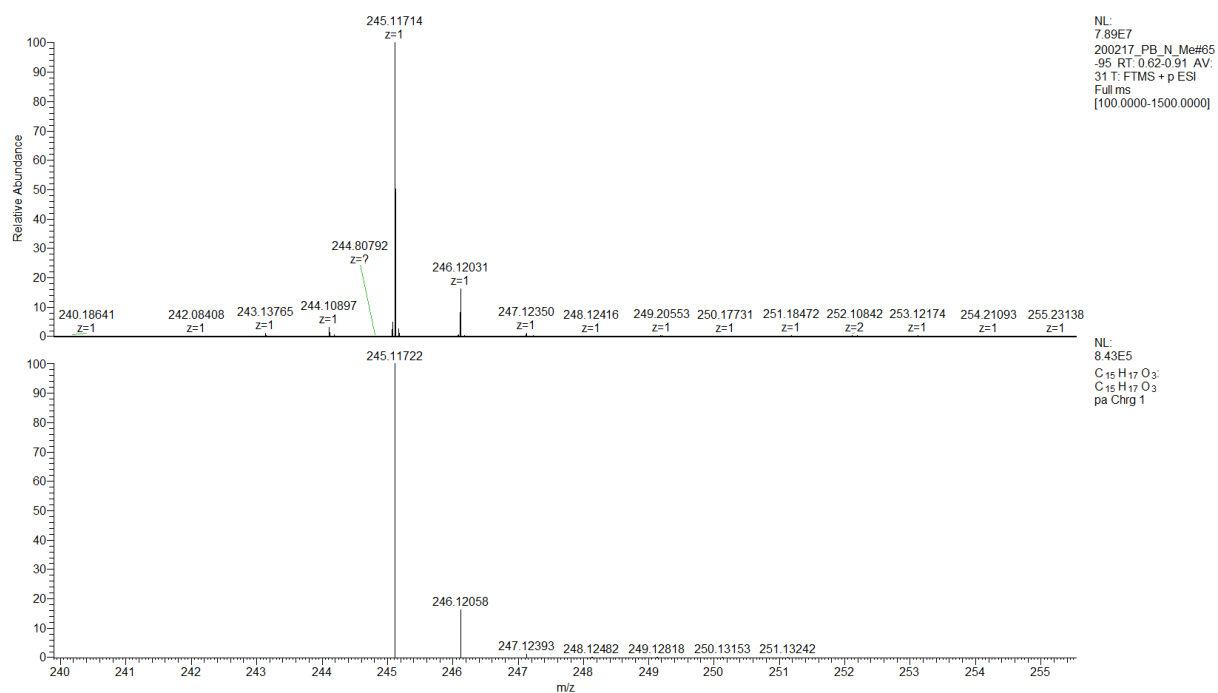


MS spectrum of *rac*-**1a** (ESI-TOF)



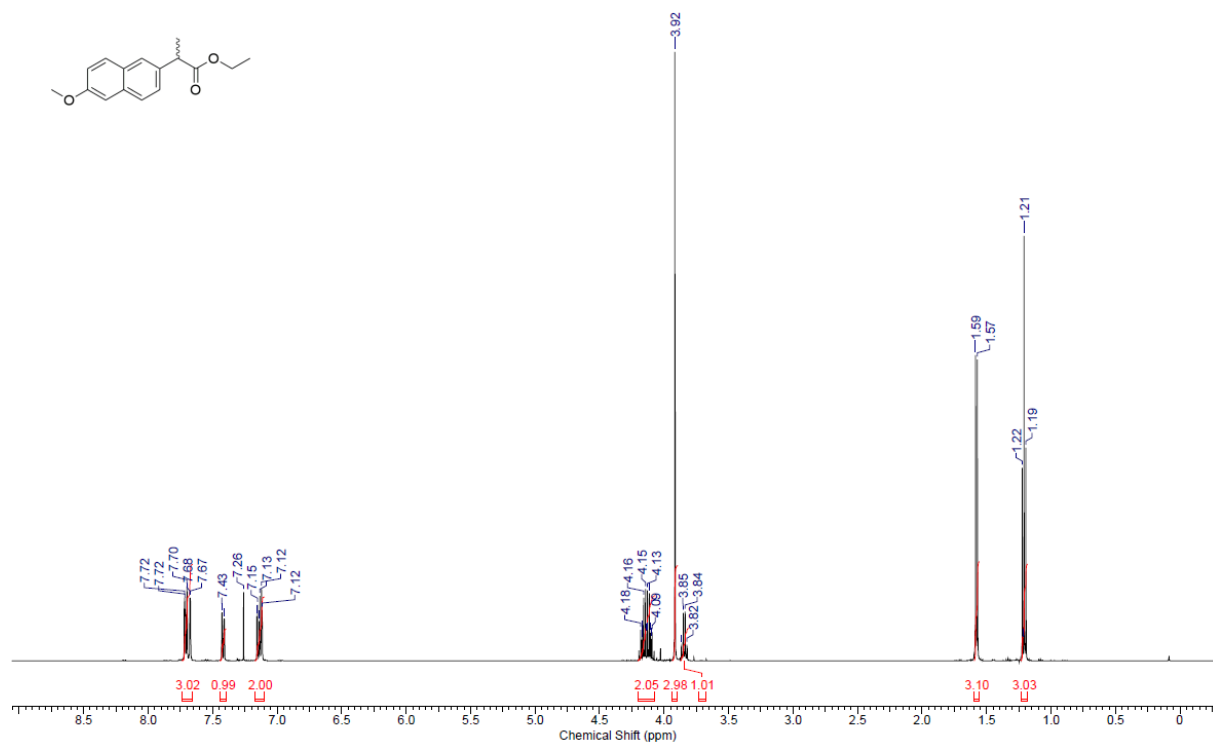


# FTMS spectrum of *rac*-**1a** (ESI-TOF)

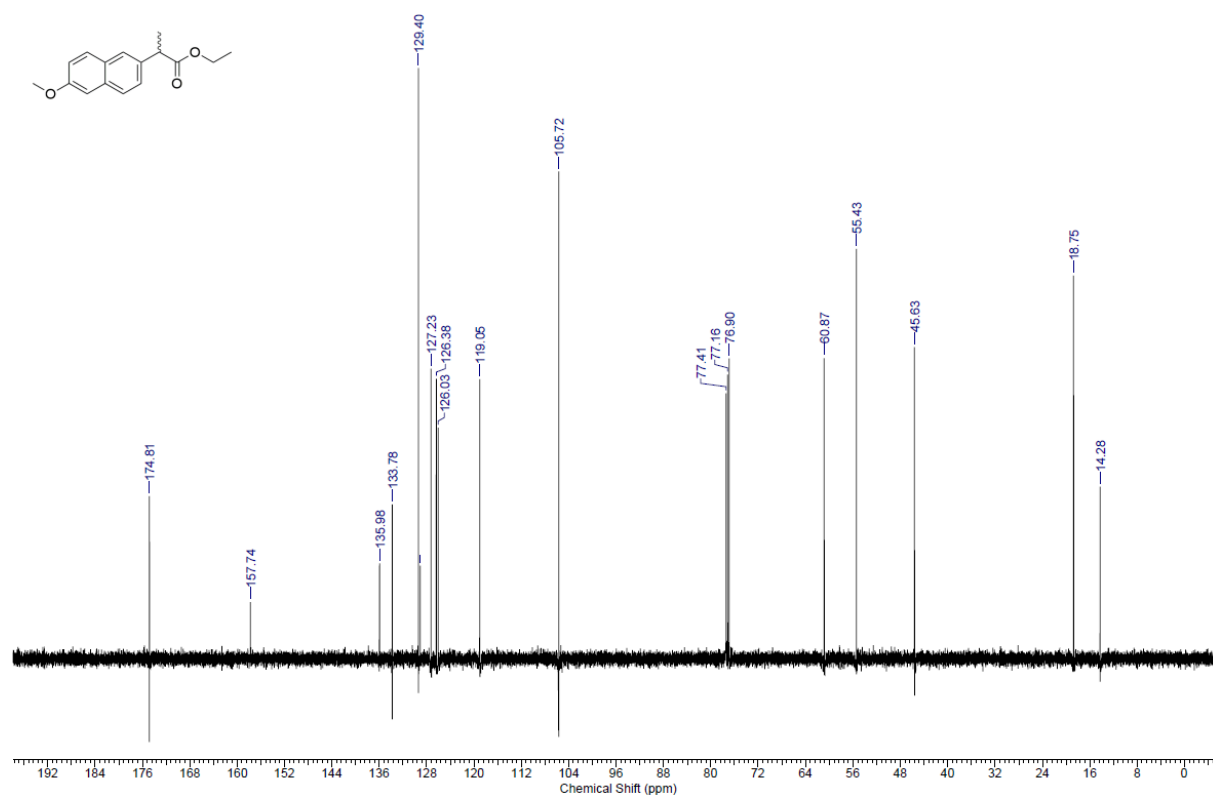


***Ethyl 2-(6-methoxynaphthalen-2-yl)propanoate (Naproxen ethyl ester, rac-1b)***

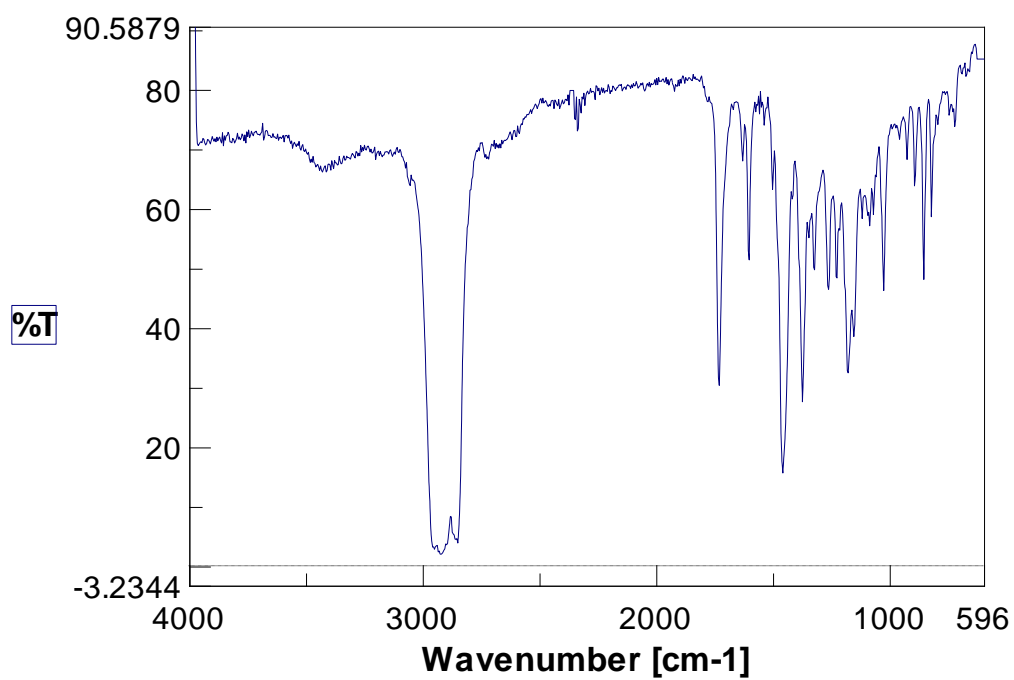
$^1\text{H}$  NMR spectrum of *rac-1b* (500 MHz,  $\text{CDCl}_3$ )



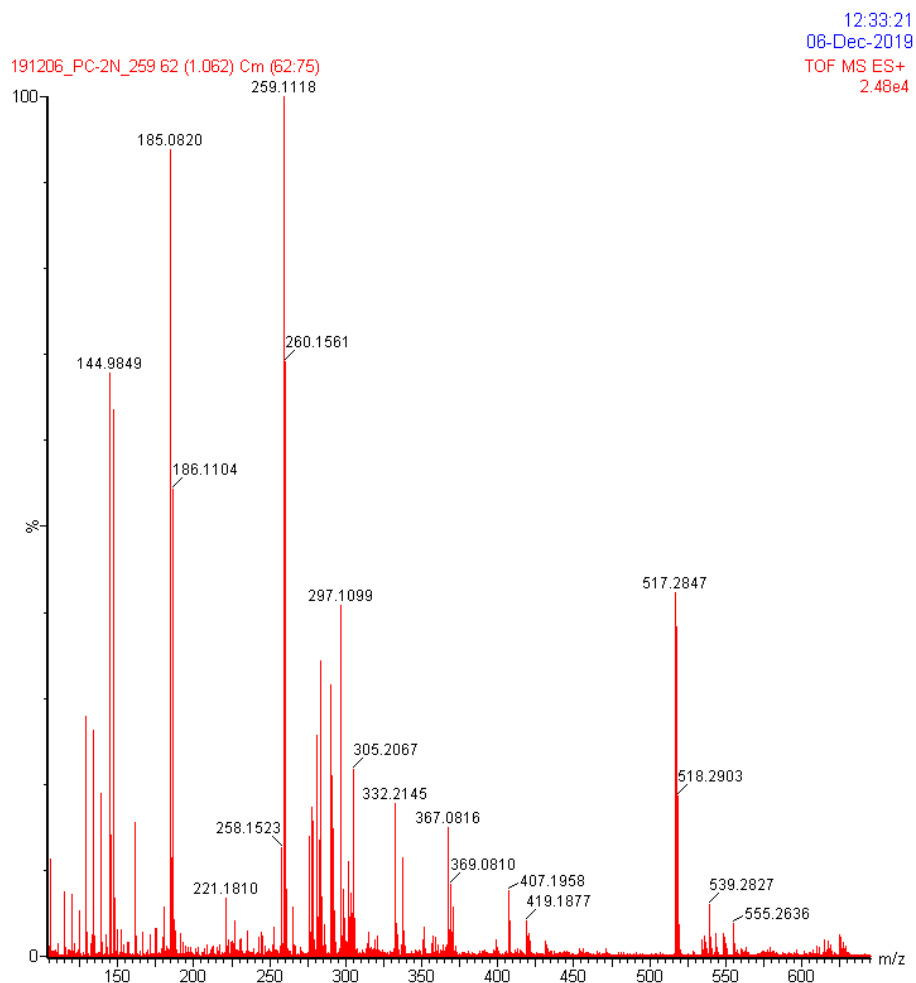
$^{13}\text{C}$  NMR spectrum of *rac-1b* (126 MHz,  $\text{CDCl}_3$ )



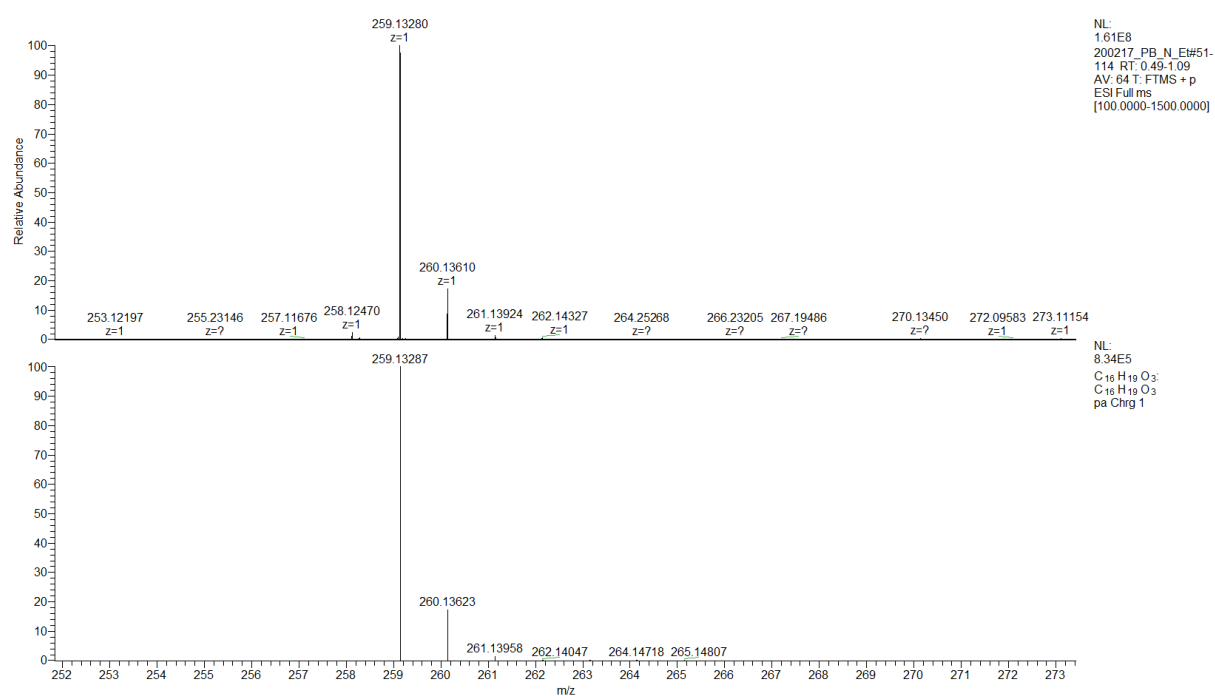
FTIR spectrum of *rac*-**1b** (Mineral oil, Nujol)



MS spectrum of *rac*-**1b** (ESI-TOF)

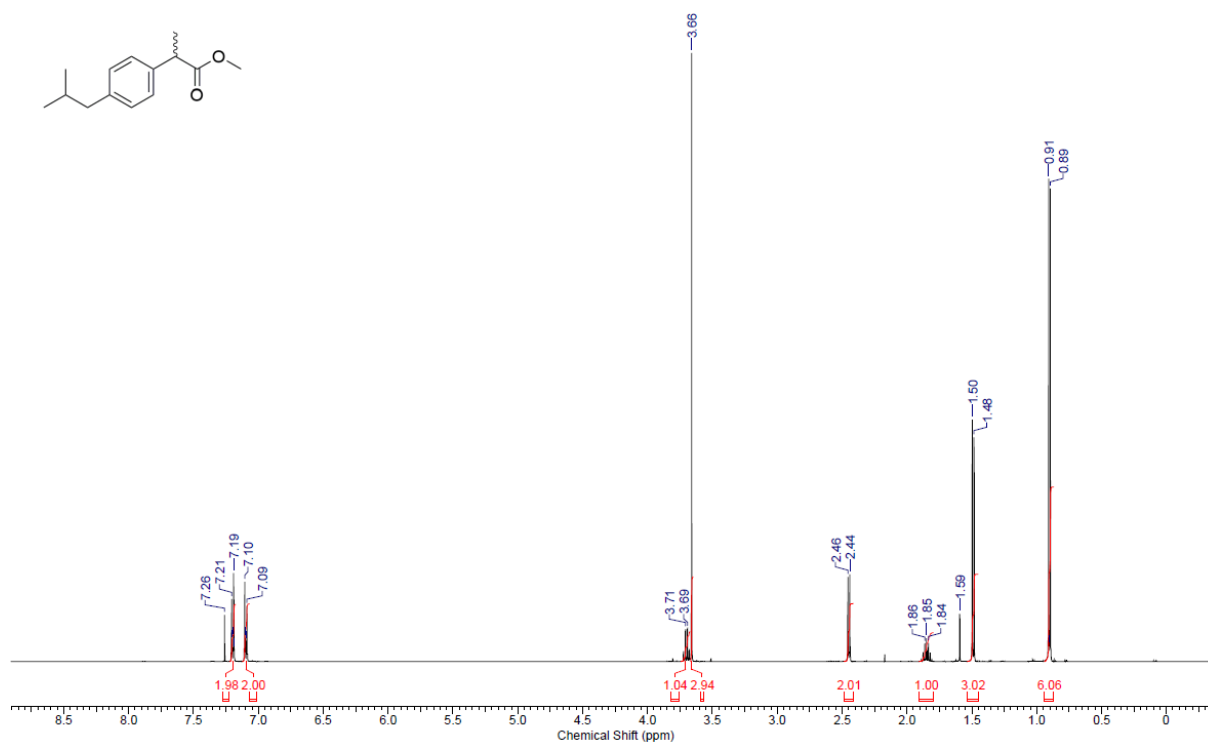


# FTMS spectrum of *rac*-**1b** (ESI-TOF)

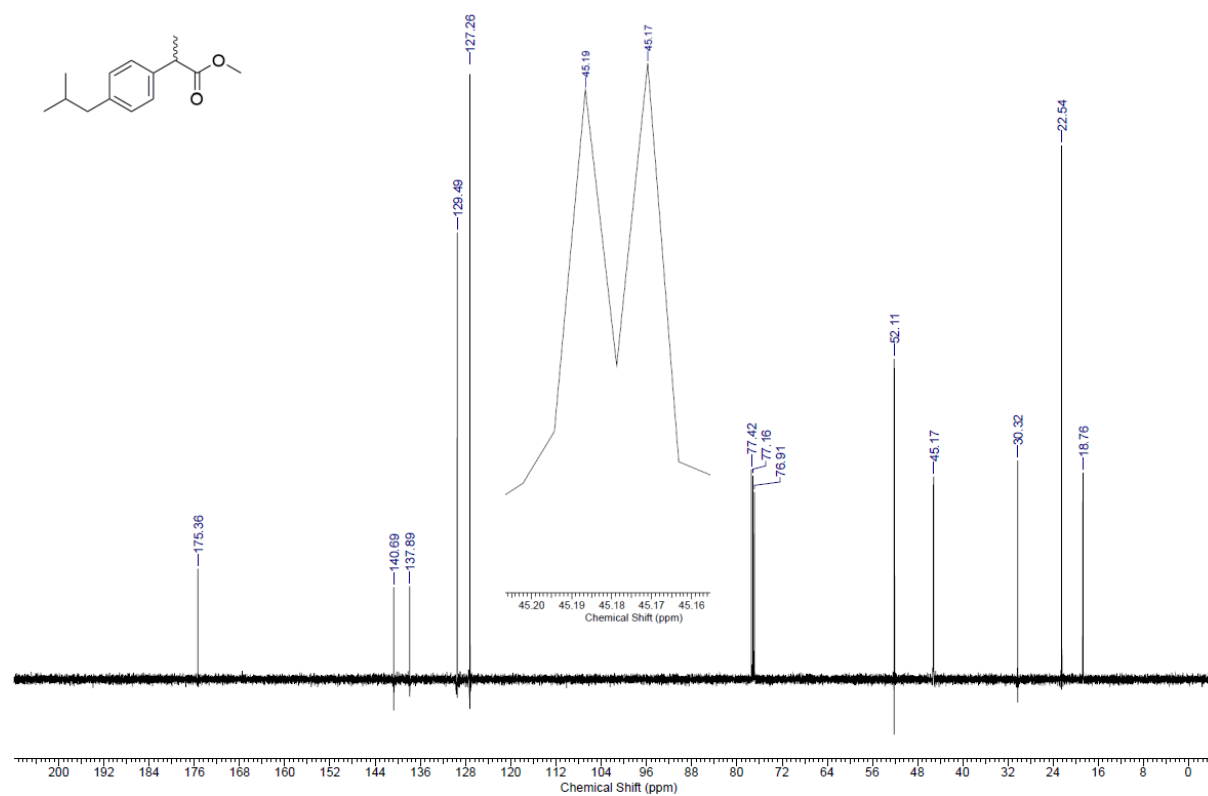


**Methyl 2-[4-(2-methylpropyl)phenyl]propanoate (Ibuprofen methyl ester, *rac*-2a)**

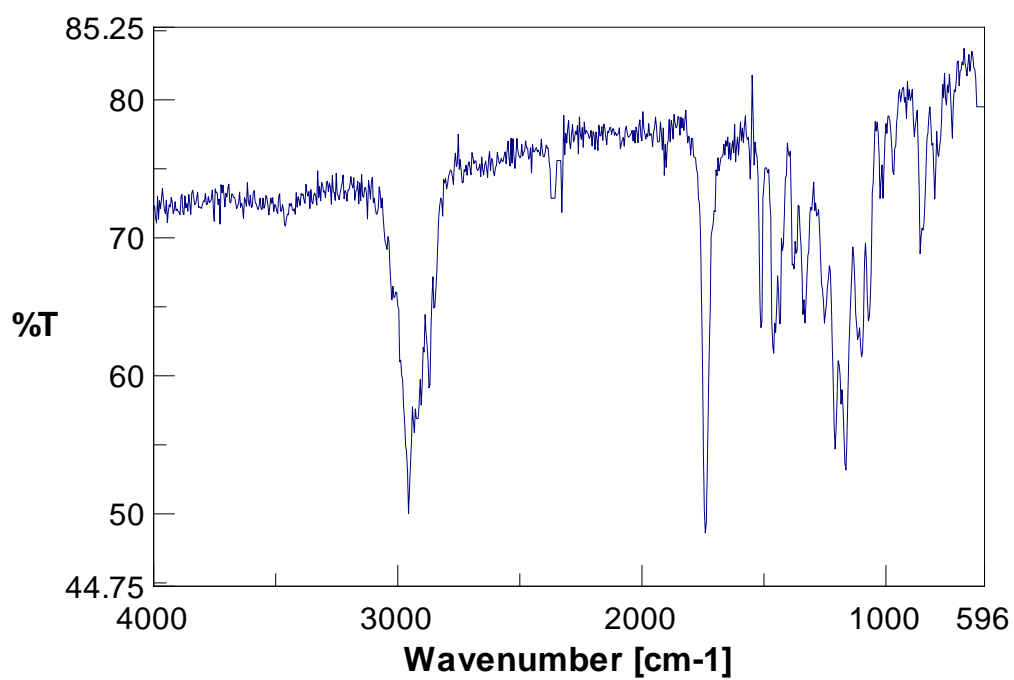
$^1\text{H}$  NMR spectrum of *rac*-2a (500 MHz,  $\text{CDCl}_3$ )



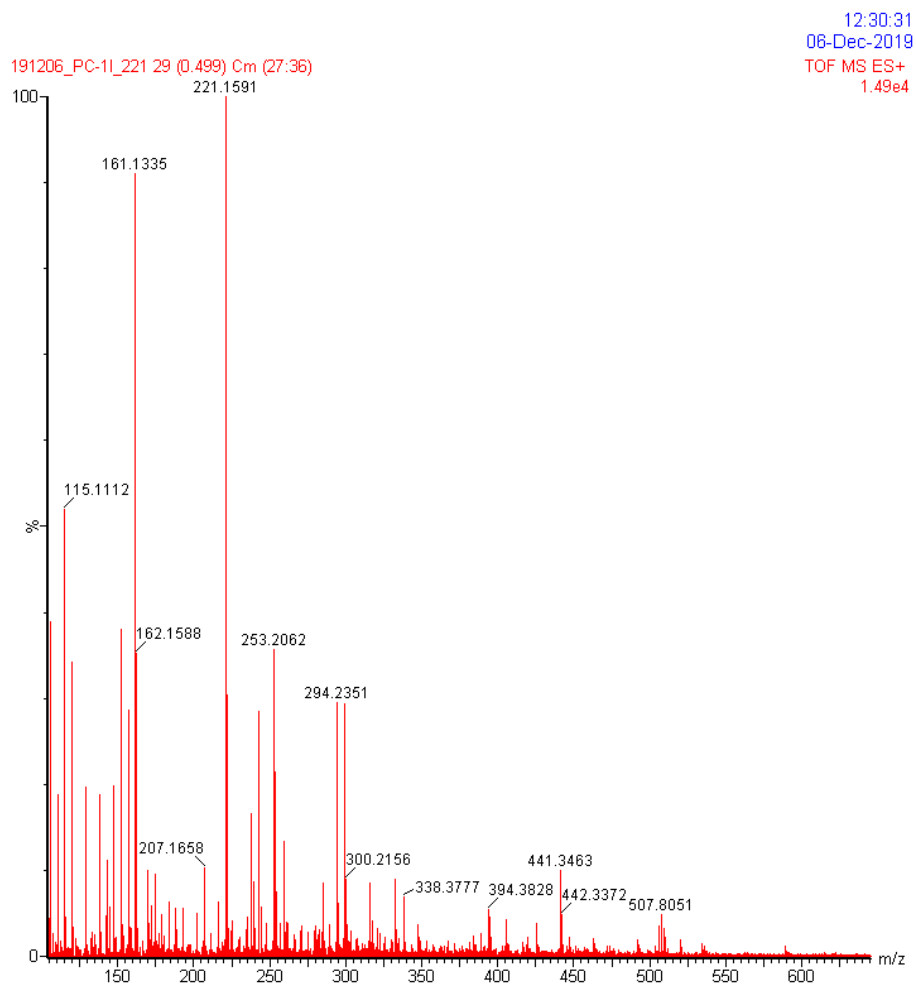
$^{13}\text{C}$  NMR spectrum of *rac*-2a (126 MHz,  $\text{CDCl}_3$ )



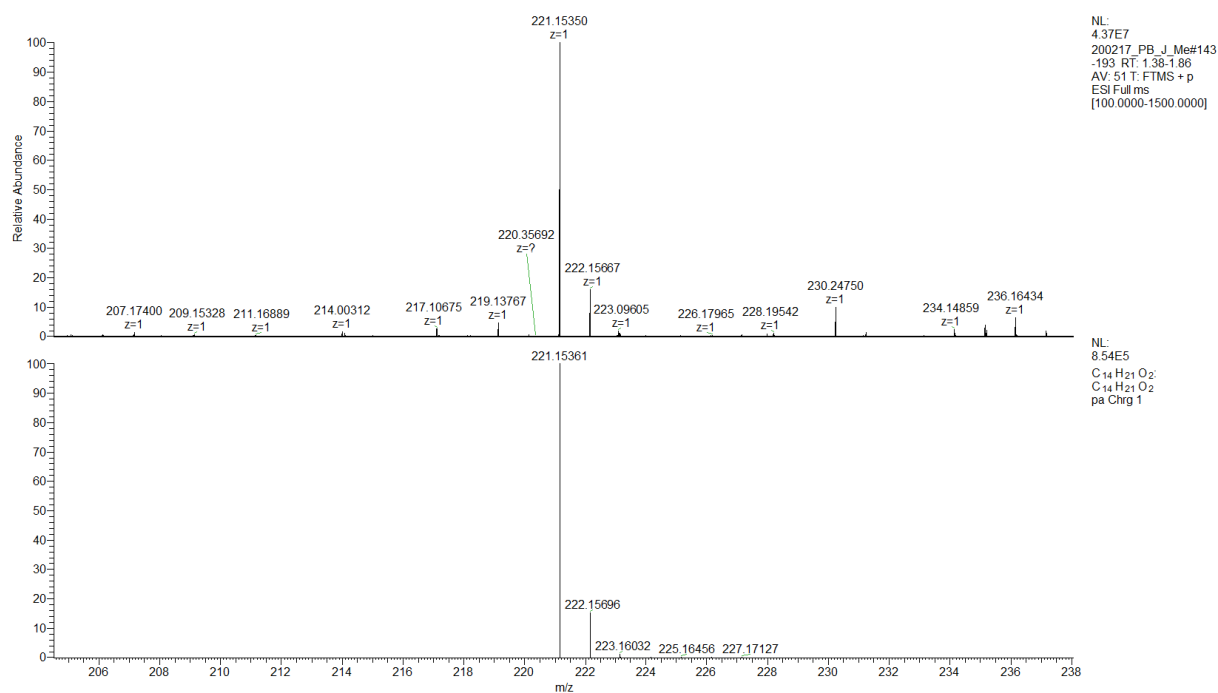
FTIR spectrum of *rac*-**2a** (Mineral oil, Nujol)



MS spectrum of *rac*-**2a** (ESI-TOF)



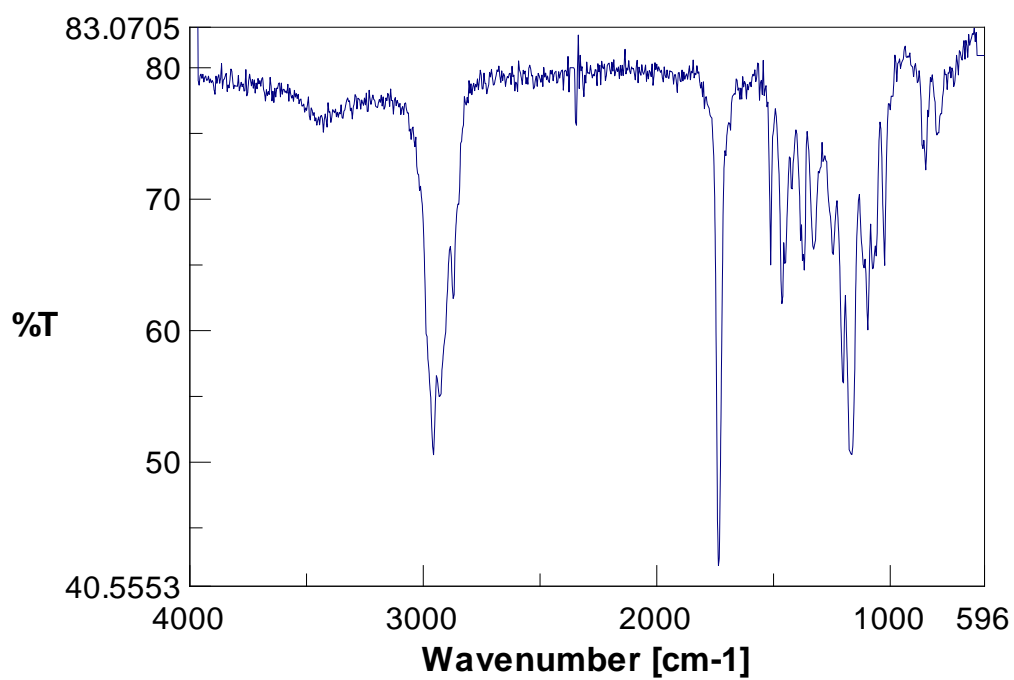
# FTMS spectrum of *rac*-**2a** (ESI-TOF)



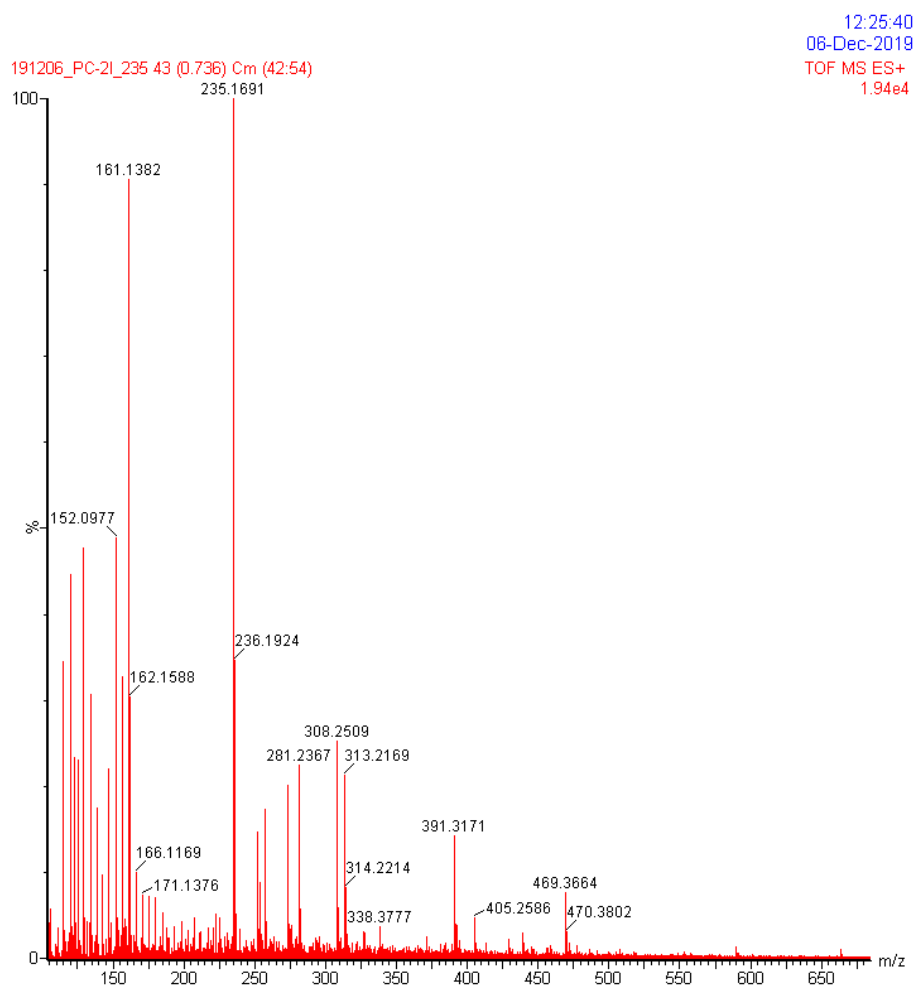




FTIR spectrum of *rac*-**2b** (Mineral oil, Nujol)

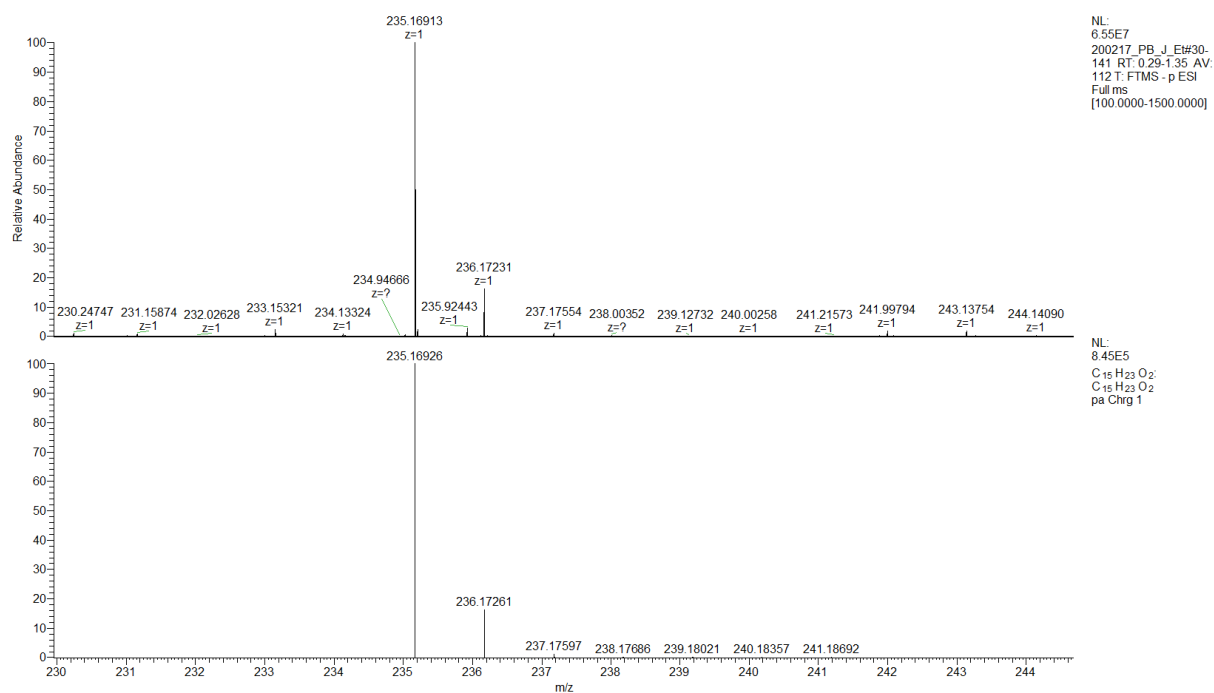


MS spectrum of *rac*-**2b** (ESI-TOF)



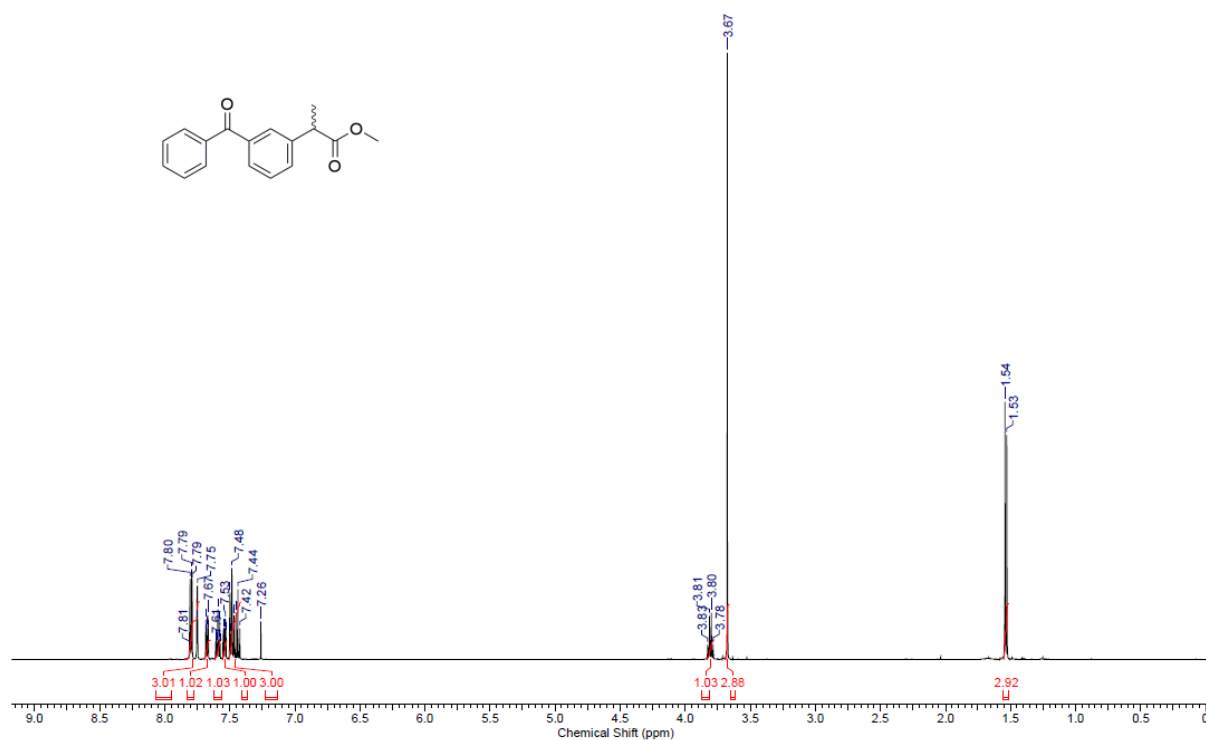
12:25:40  
08-Dec-2019  
TOF MS ES+  
1.94e4

# FTMS spectrum of *rac*-**2b** (ESI-TOF)

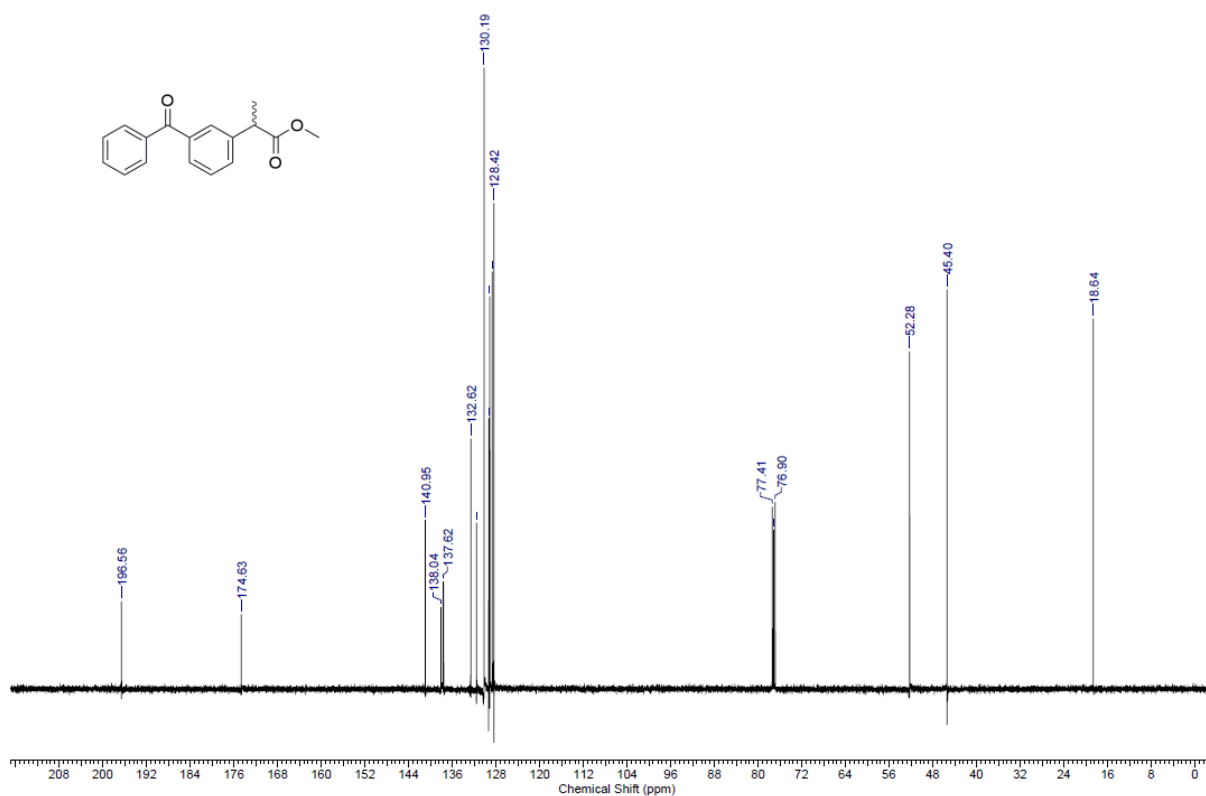


**Methyl 2-(3-benzoylphenyl)propanoate (Ketoprofen methyl ester, *rac*-3a)**

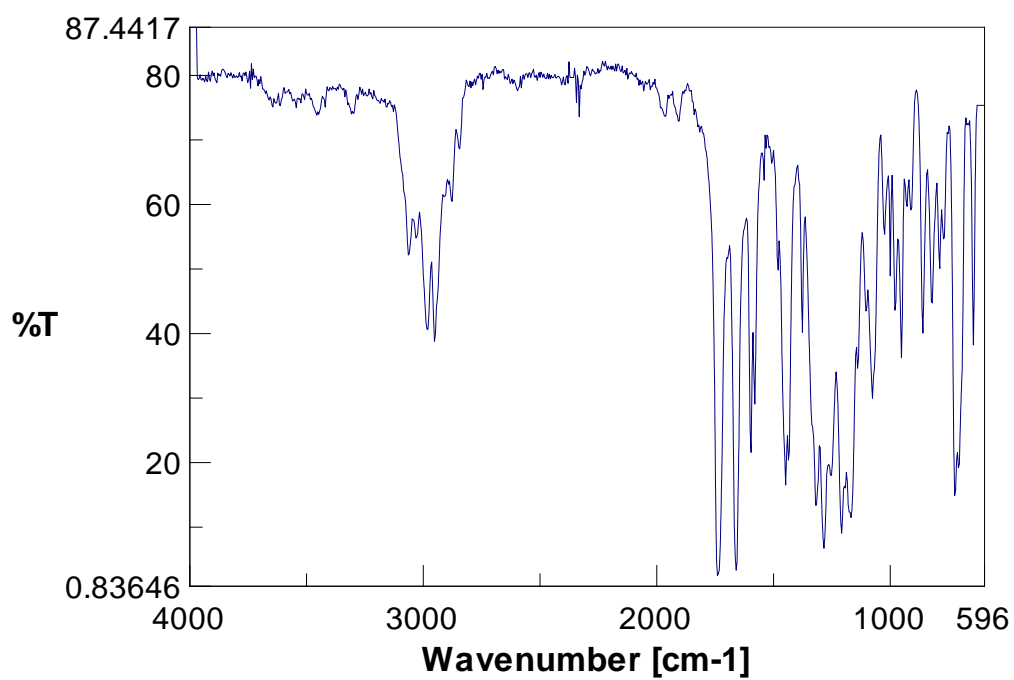
$^1\text{H}$  NMR spectrum of *rac*-3a (500 MHz,  $\text{CDCl}_3$ )



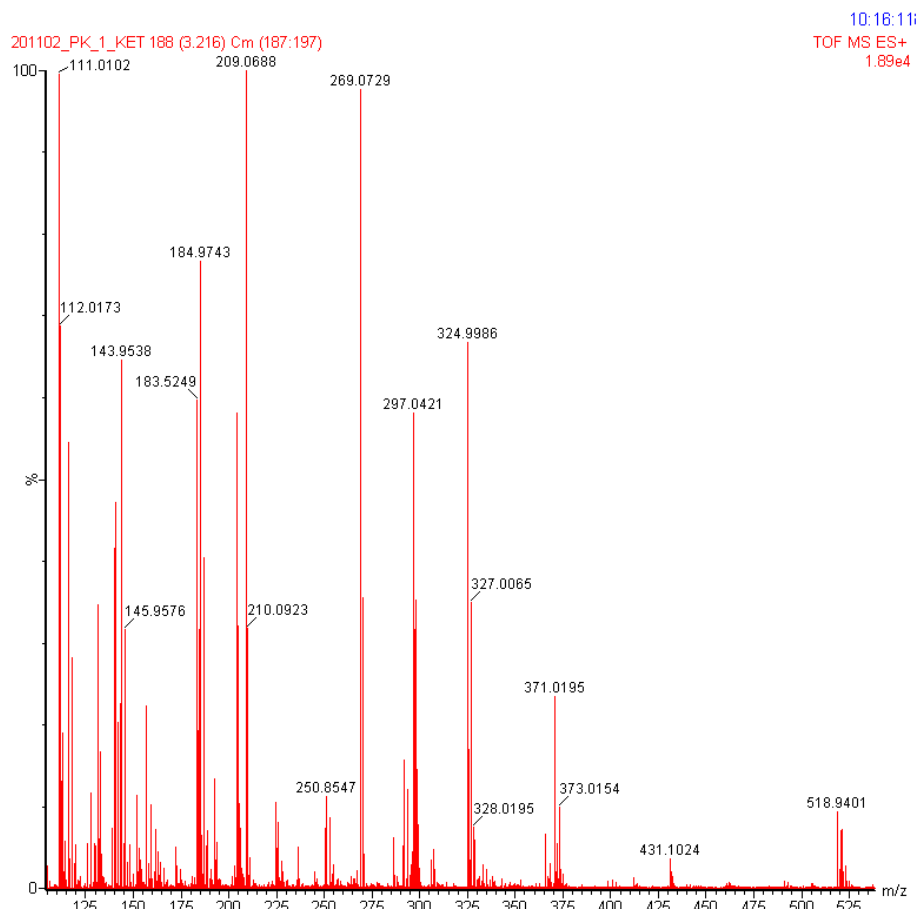
$^{13}\text{C}$  NMR spectrum of *rac*-3a (126 MHz,  $\text{CDCl}_3$ )



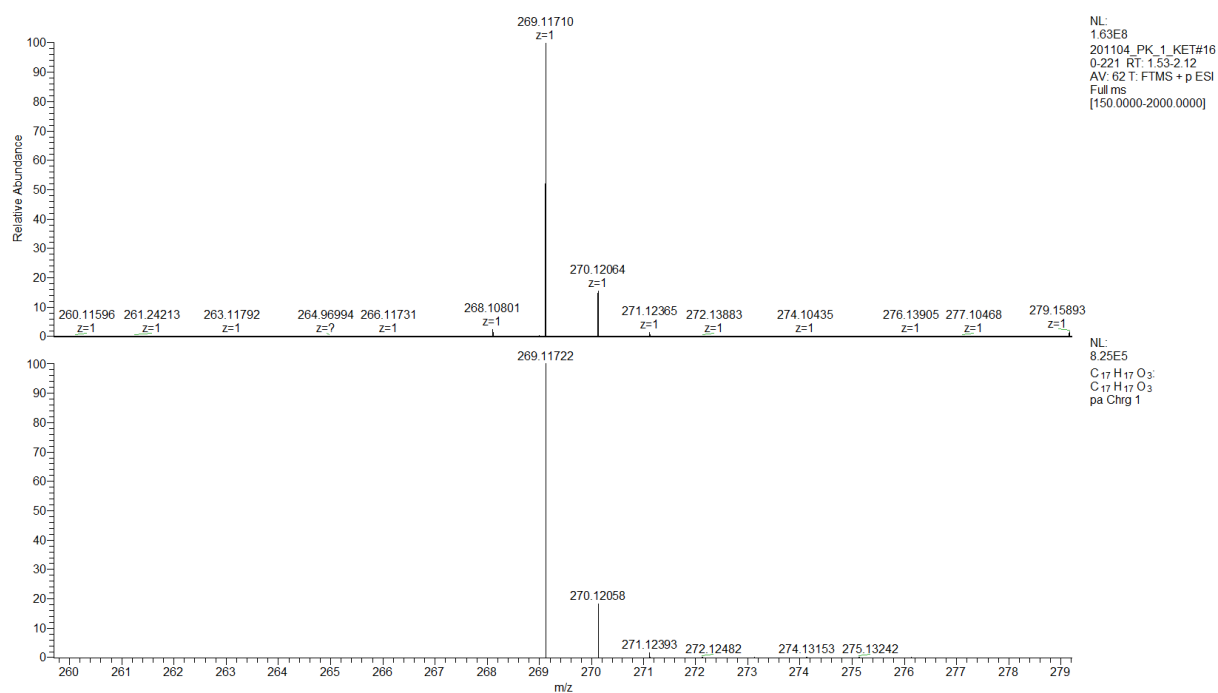
FTIR spectrum of *rac*-**3a** (Mineral oil, Nujol)



MS spectrum of *rac*-**3a** (ESI-TOF)

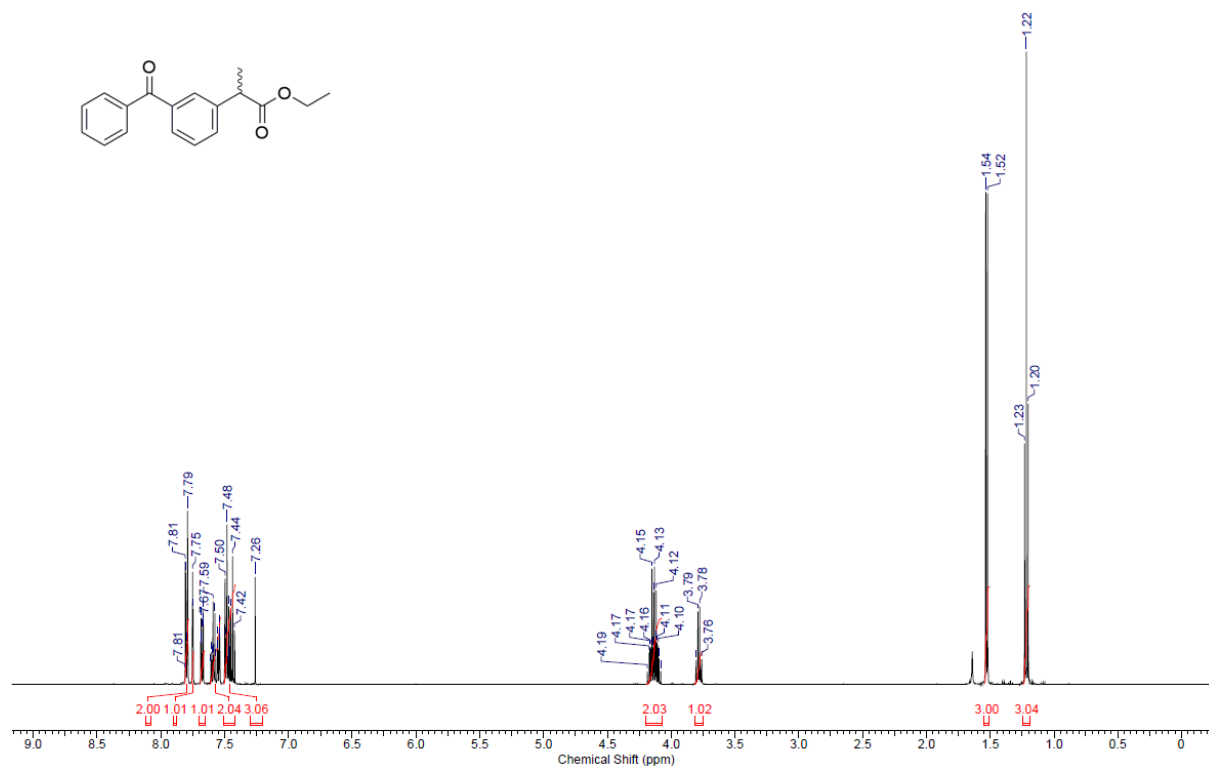


# FTMS spectrum of *rac*-**3a** (ESI-TOF)

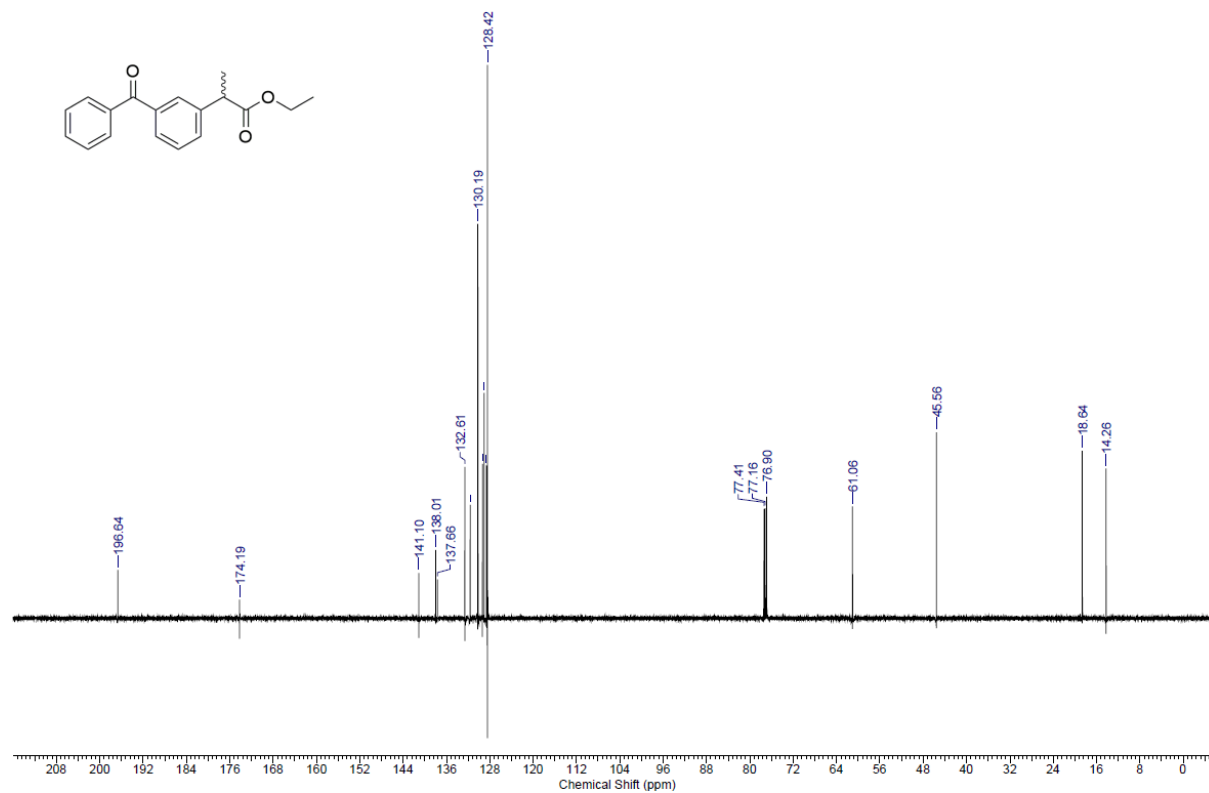


***Ethyl 2-(3-benzoylphenyl)propanoate (Ketoprofen ethyl ester, rac-3b)***

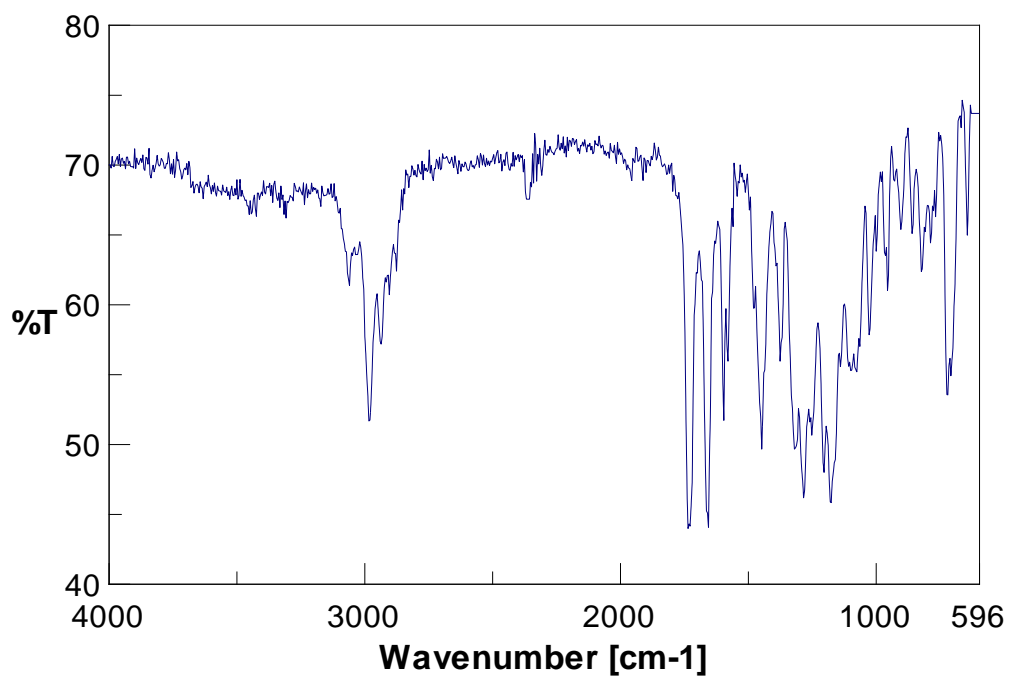
$^1\text{H}$  NMR spectrum of *rac*-**3b** (500 MHz,  $\text{CDCl}_3$ )



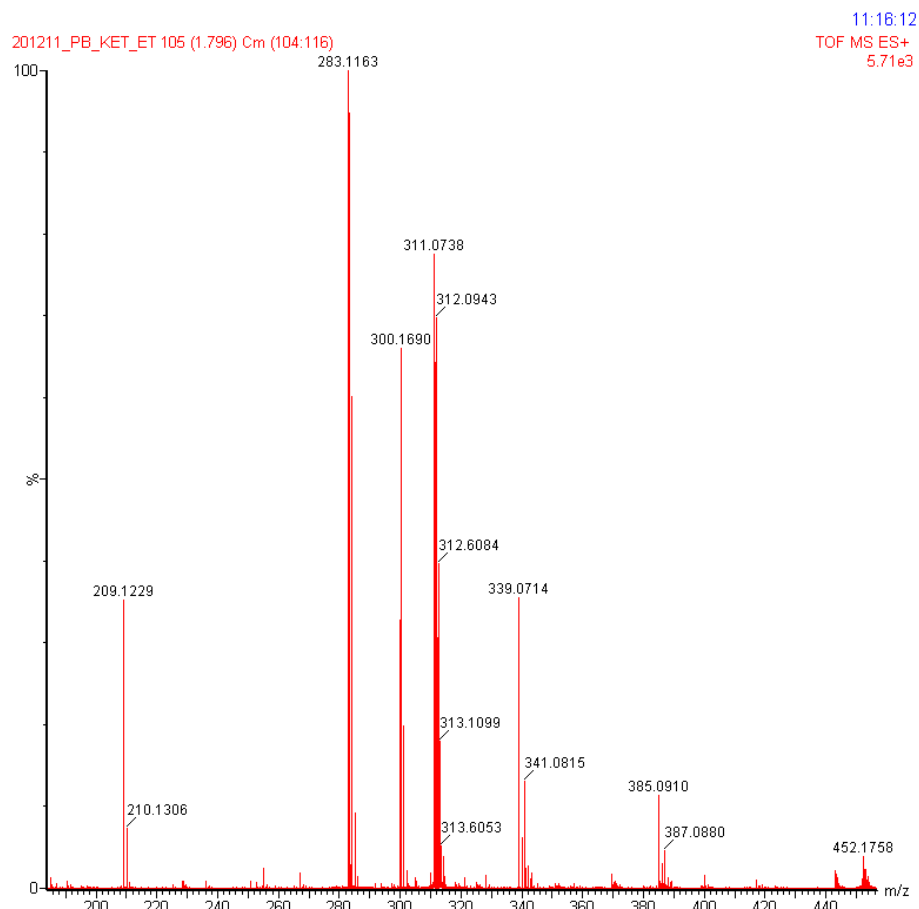
$^{13}\text{C}$  NMR spectrum of *rac*-**3b** (126 MHz,  $\text{CDCl}_3$ )



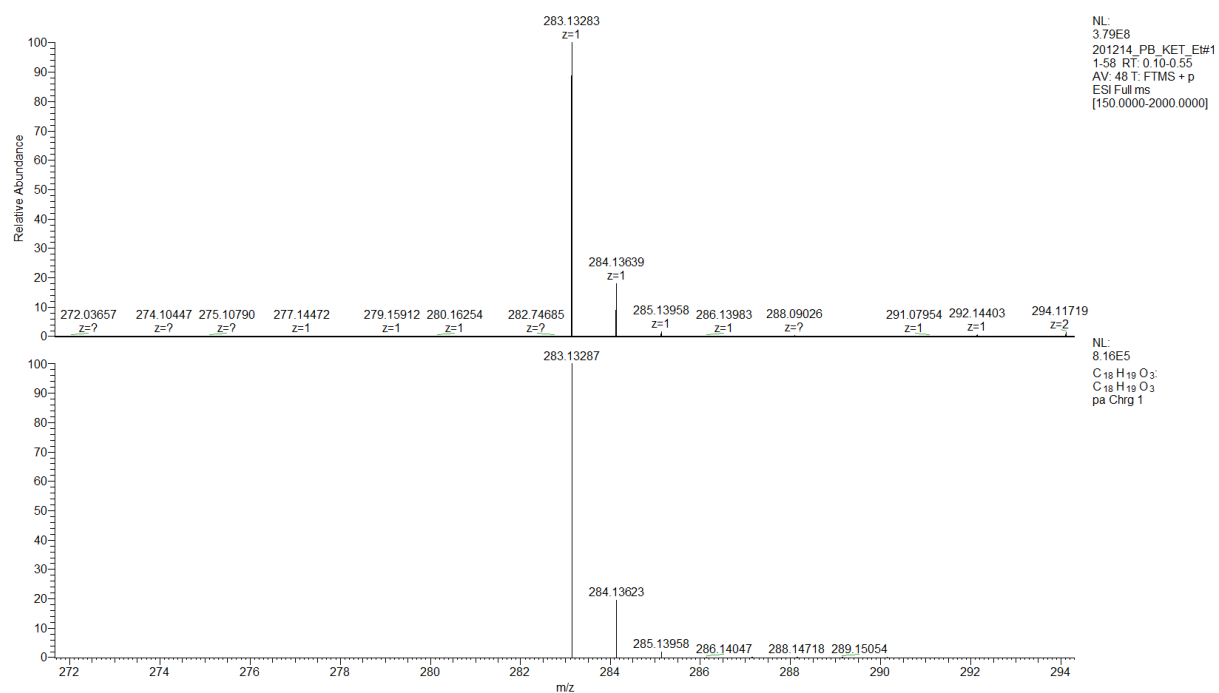
FTIR spectrum of *rac*-**3b** (Mineral oil, Nujol)



MS spectrum of *rac*-**3b** (ESI-TOF)



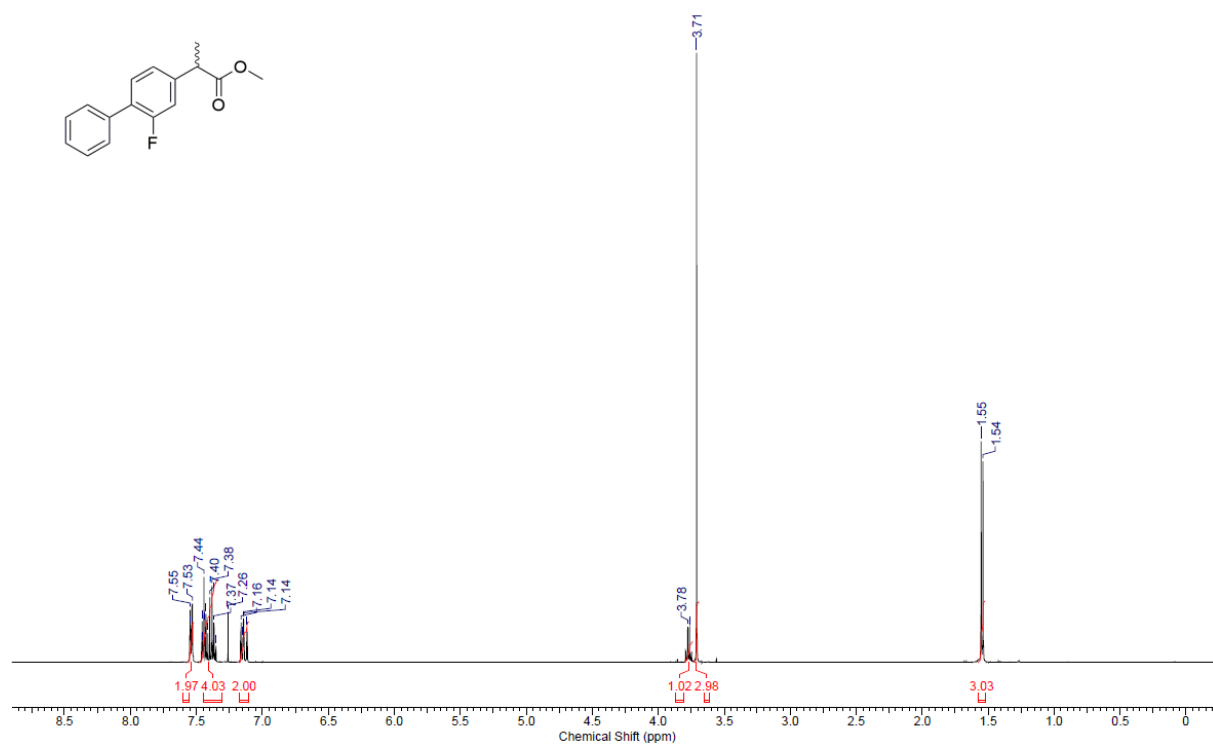
# FTMS spectrum of *rac*-**3b** (ESI-TOF)



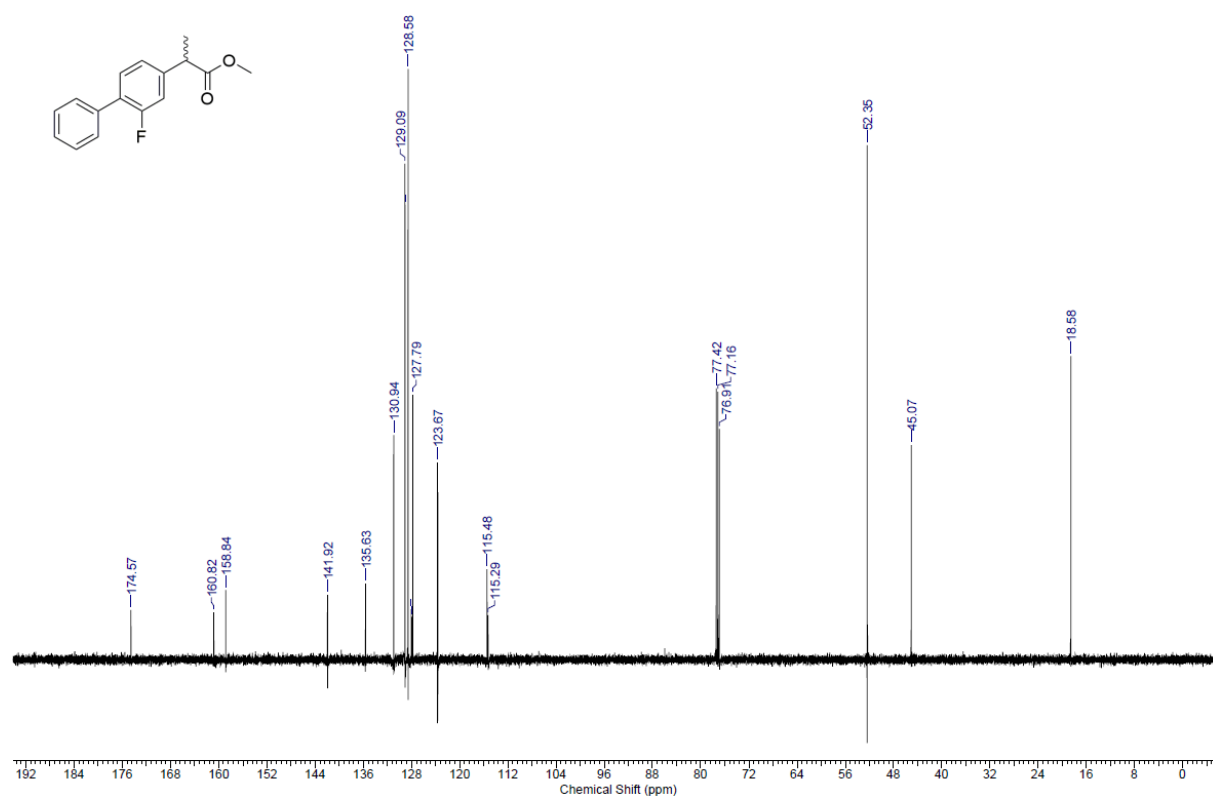


**Methyl 2-(2-fluoro[1,1'-biphenyl]-4-yl)propanoate (Flurbiprofen methyl ester, *rac*-4a)**

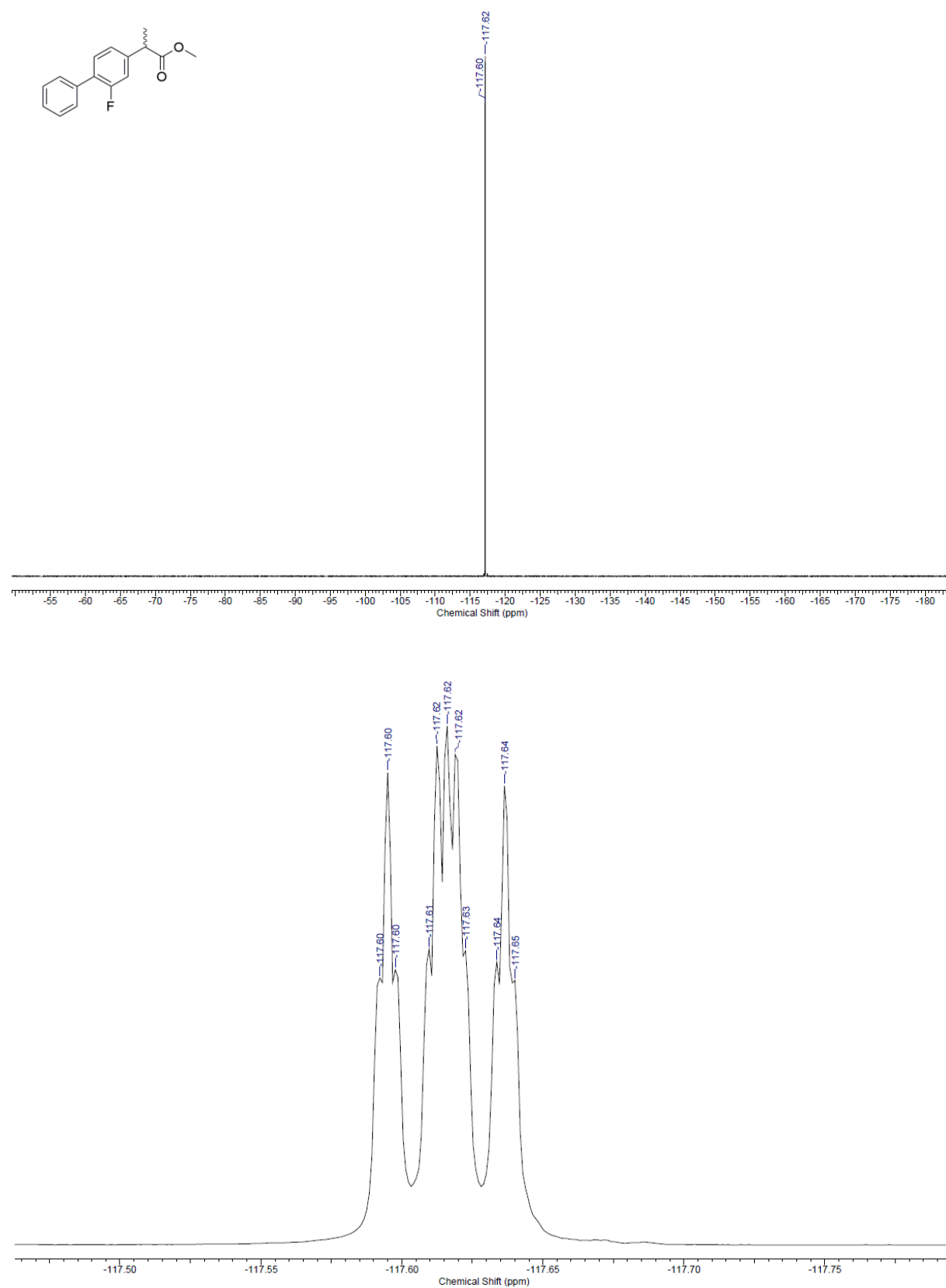
$^1\text{H}$  NMR spectrum of *rac*-4a (500 MHz,  $\text{CDCl}_3$ )



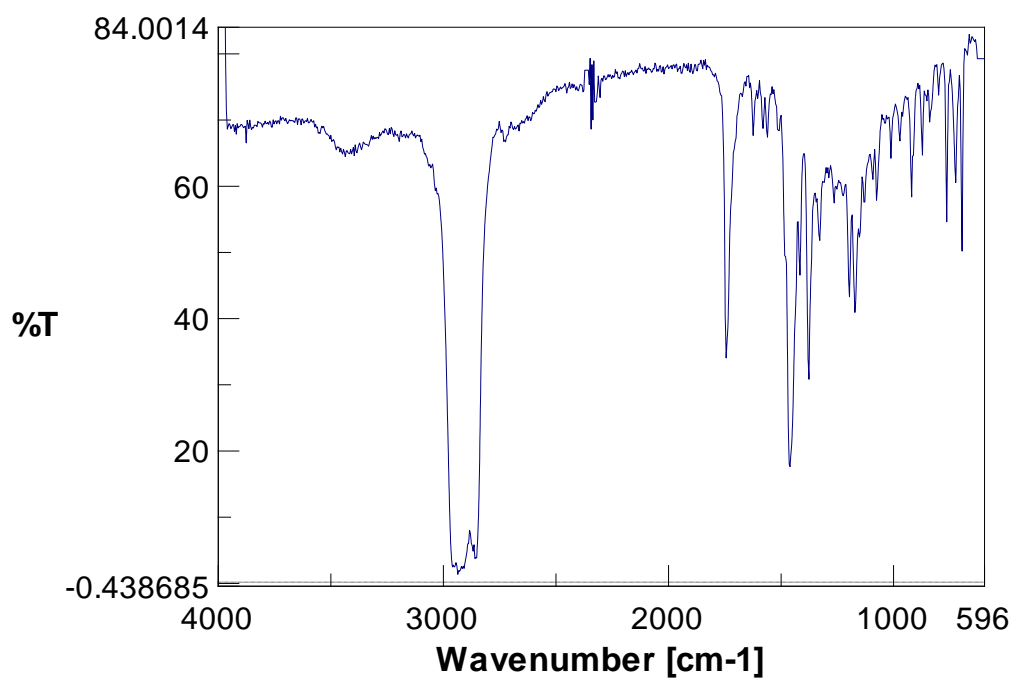
$^{13}\text{C}$  NMR spectrum of *rac*-4a (126 MHz,  $\text{CDCl}_3$ )



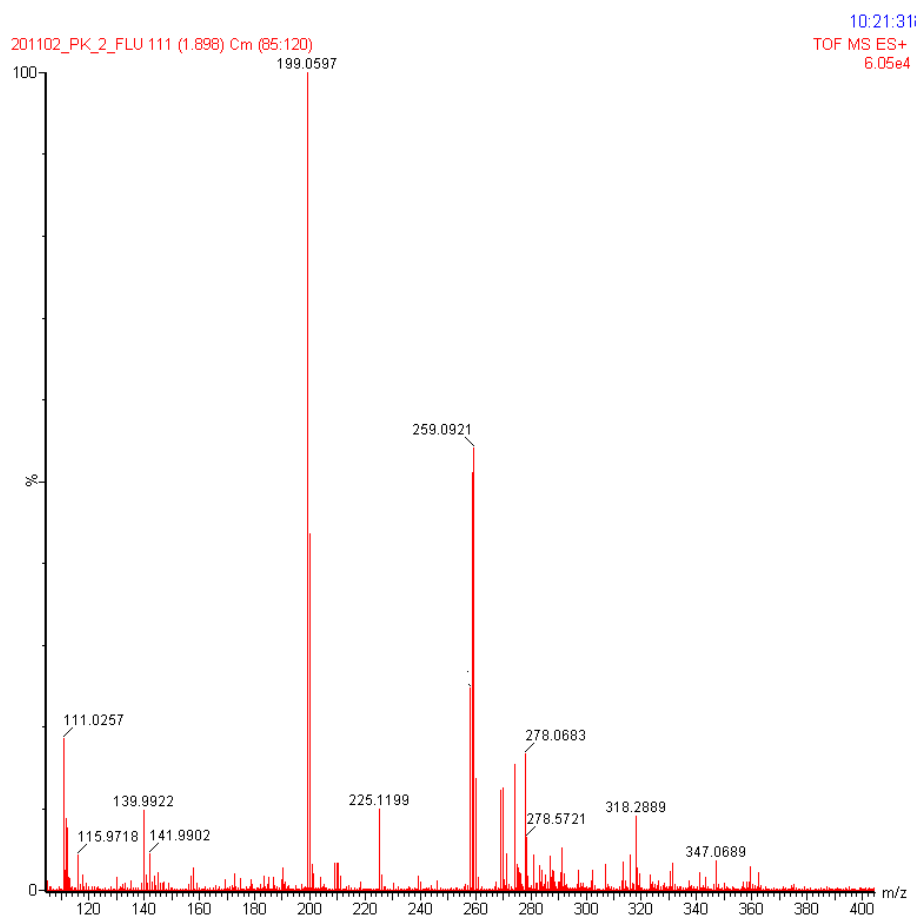
$^{19}\text{F}$  NMR spectrum of *rac*-**4a** (470 MHz,  $\text{CDCl}_3$ )



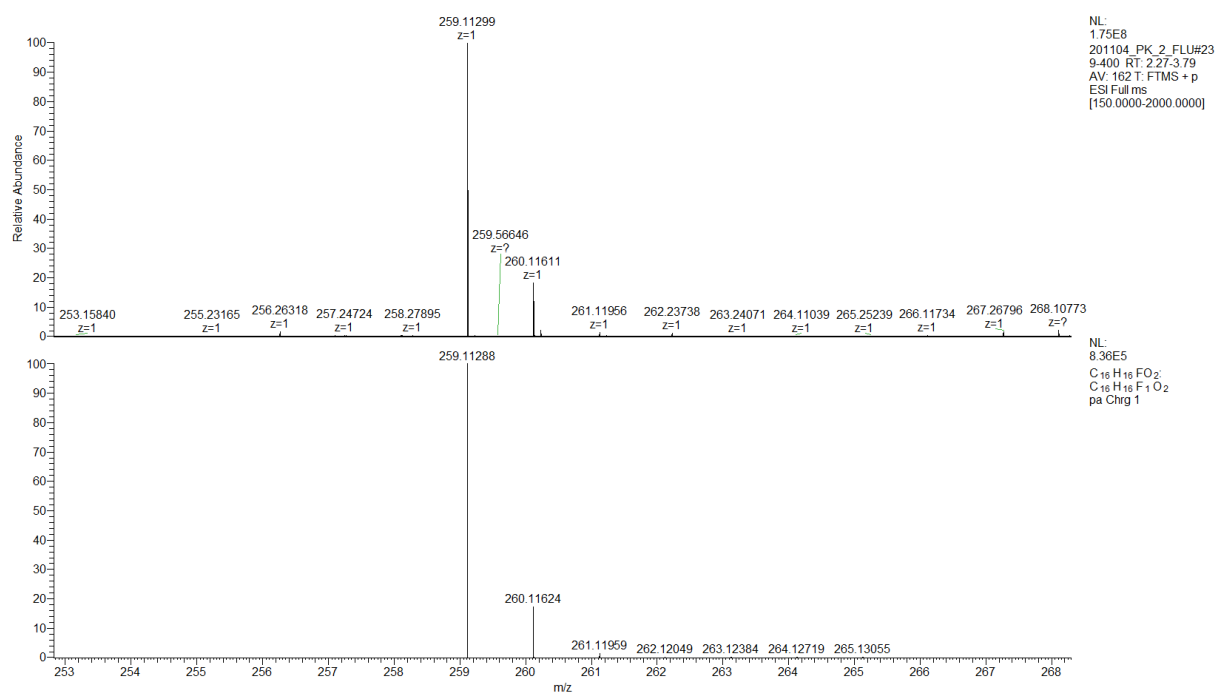
FTIR spectrum of *rac*-**4a** (Mineral oil, Nujol)



MS spectrum of *rac*-**4a** (ESI-TOF)

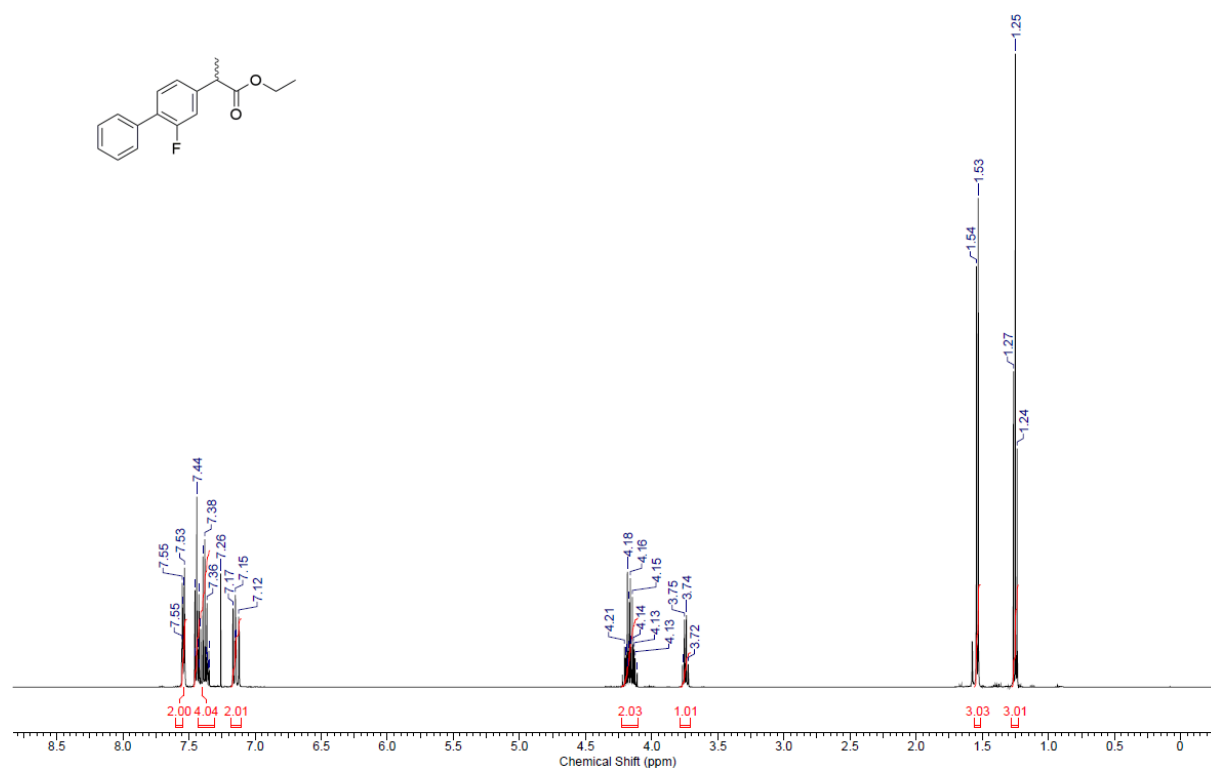


# FTMS spectrum of *rac*-**4a** (ESI-TOF)

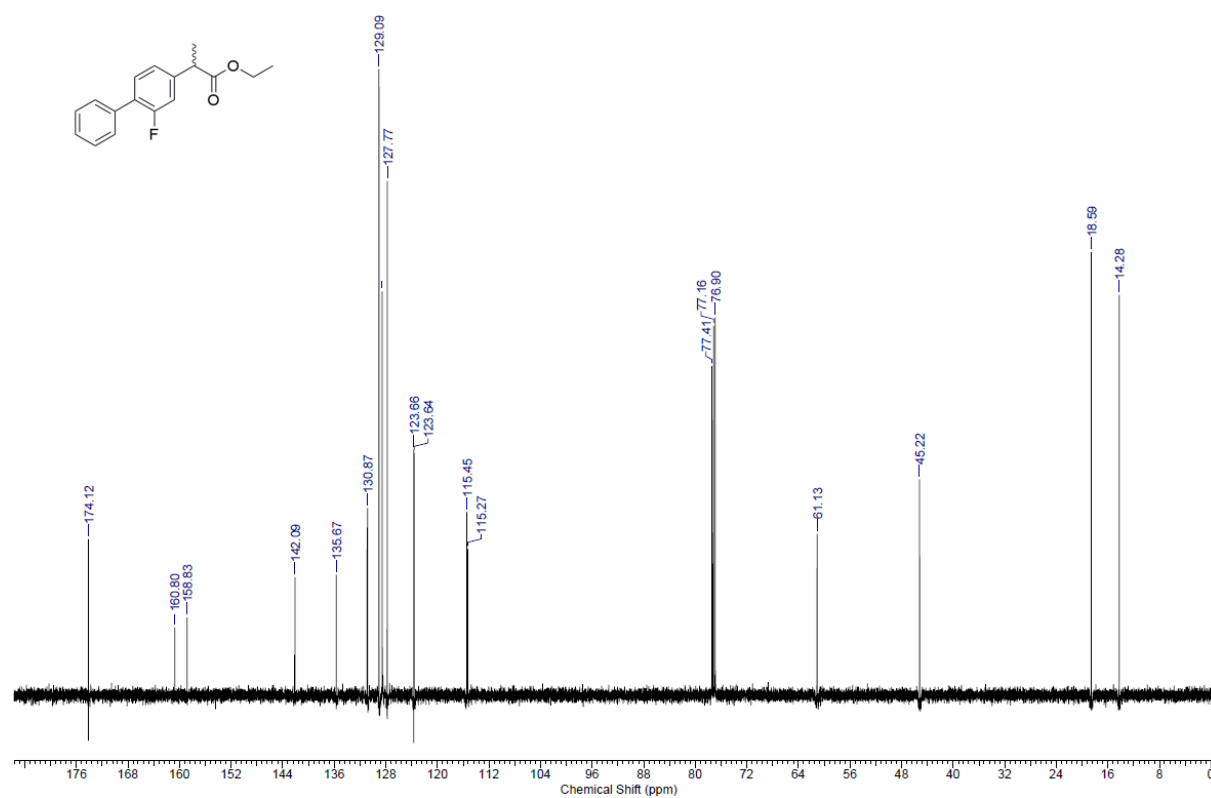


***Ethyl 2-(2-fluoro[1,1'-biphenyl]-4-yl)propanoate (Flurbiprofen ethyl ester, rac-4b)***

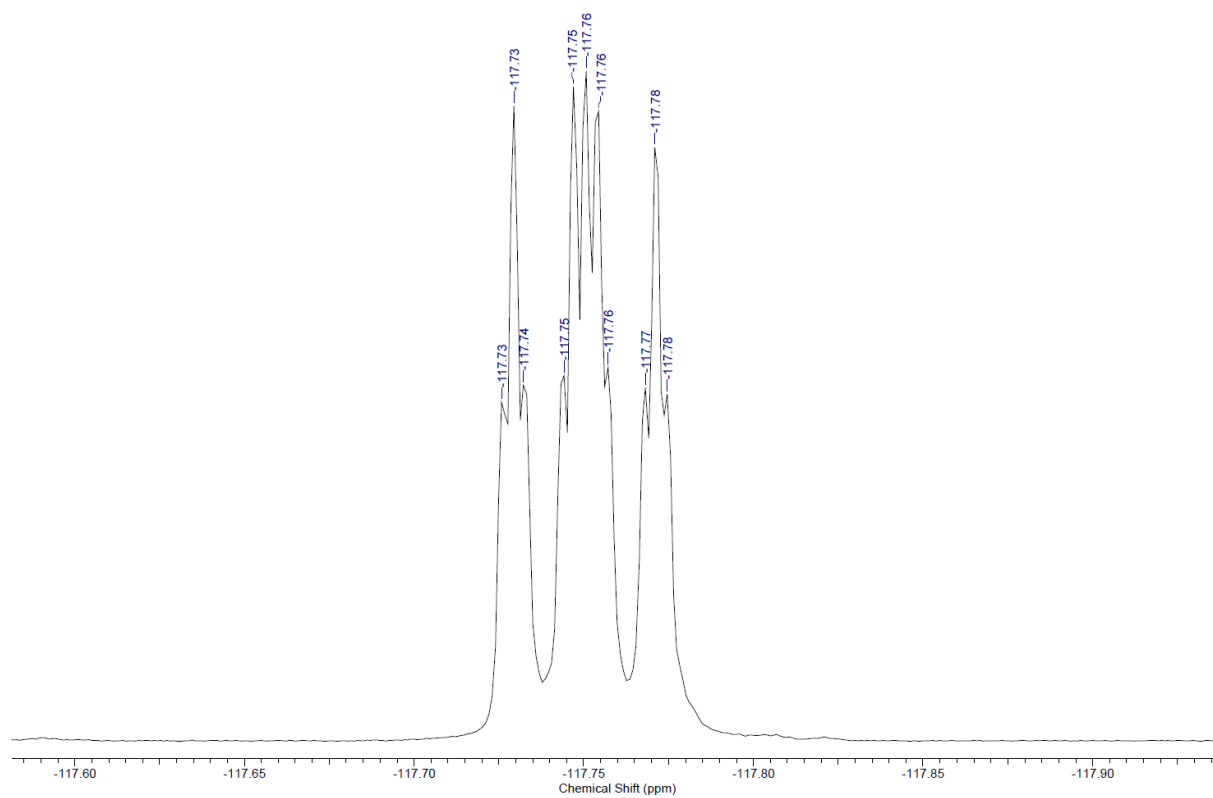
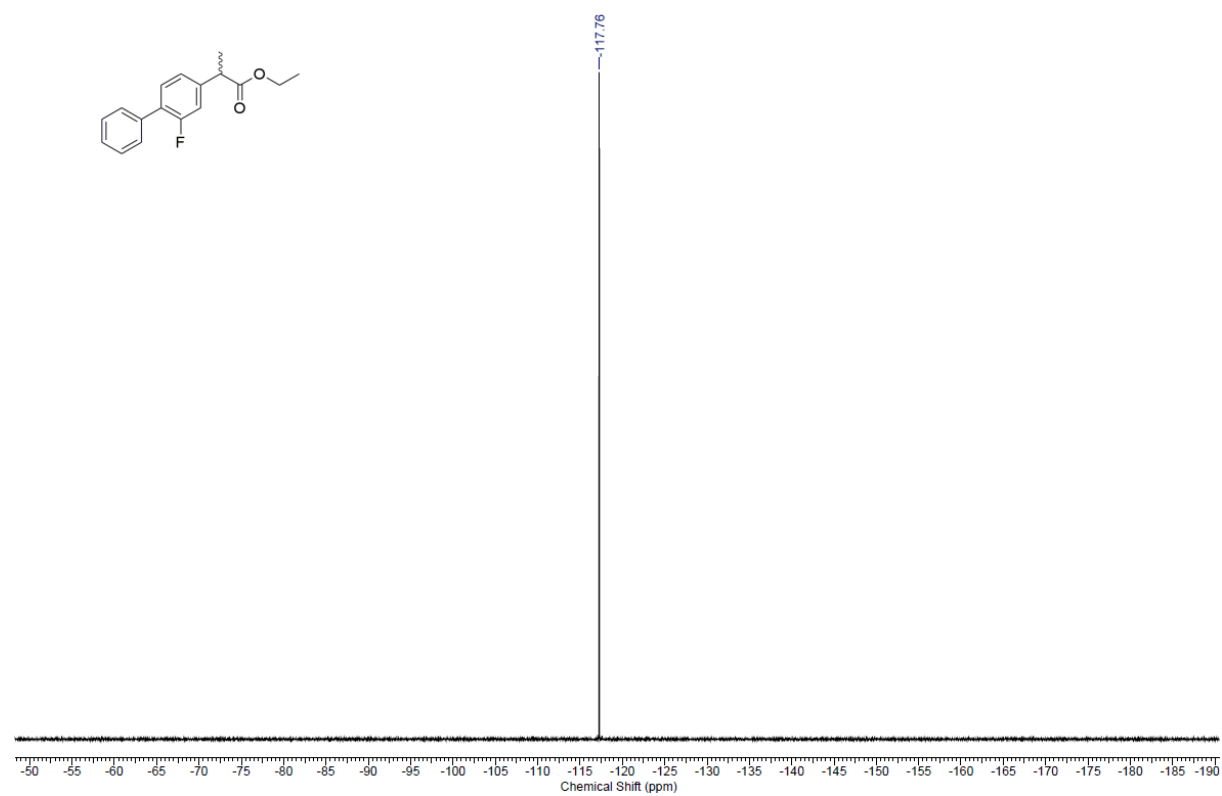
$^1\text{H}$  NMR spectrum of *rac*-**4b** (500 MHz,  $\text{CDCl}_3$ )



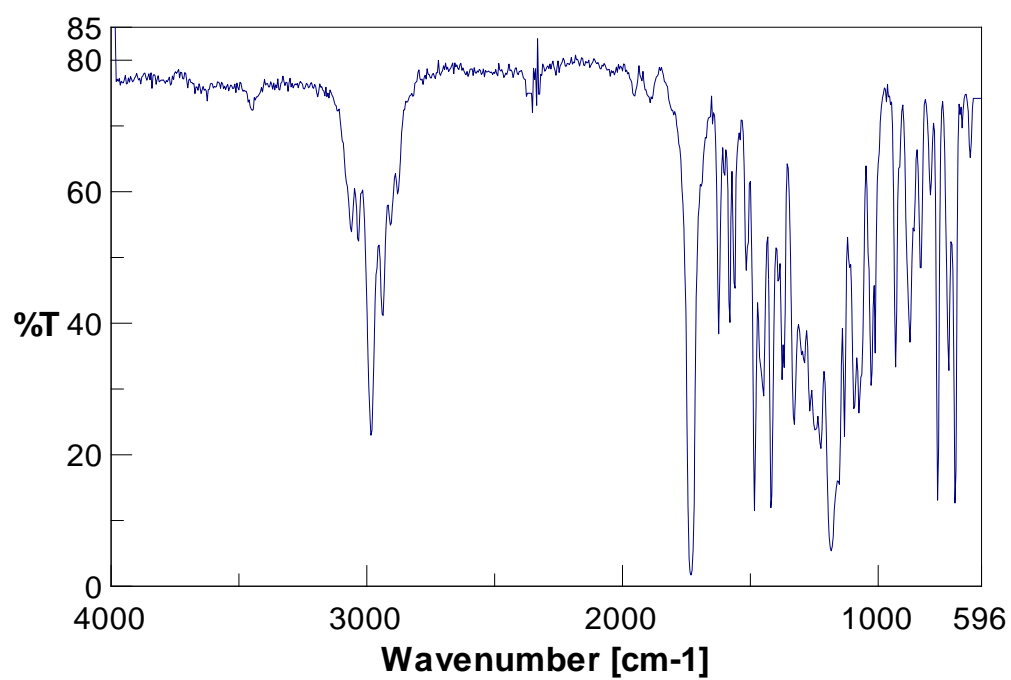
$^{13}\text{C}$  NMR spectrum of *rac*-**4b** (126 MHz,  $\text{CDCl}_3$ )



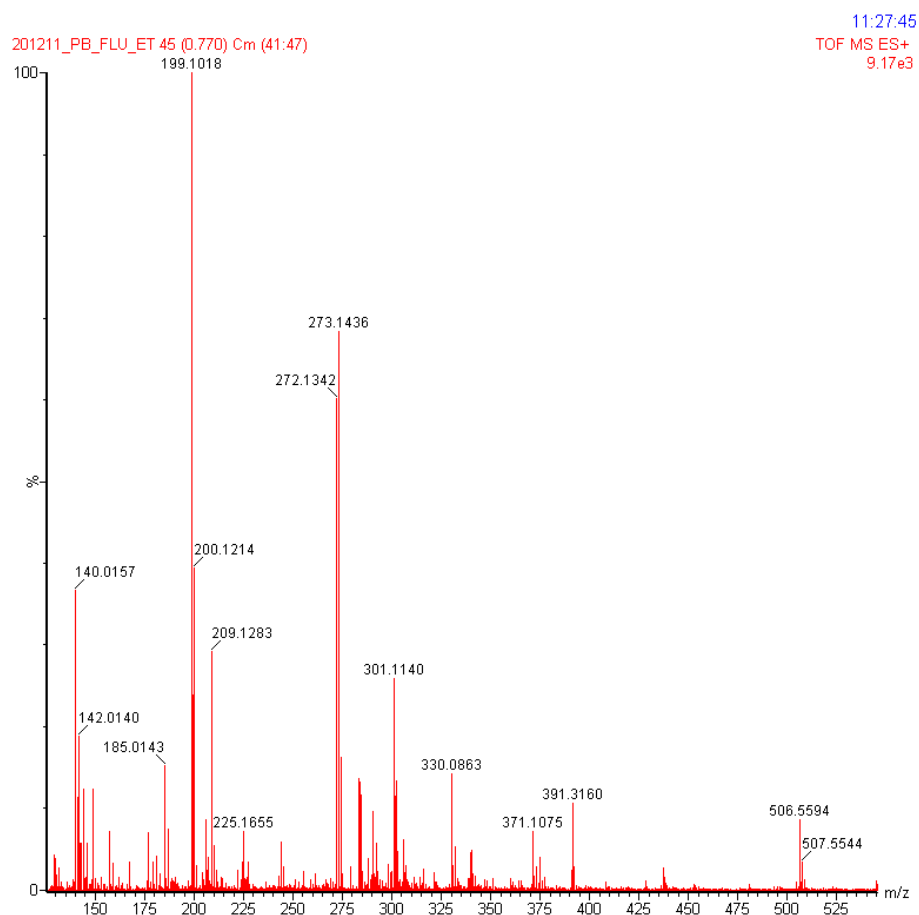
$^{19}\text{F}$  NMR spectrum of *rac*-**4b** (470 MHz,  $\text{CDCl}_3$ )



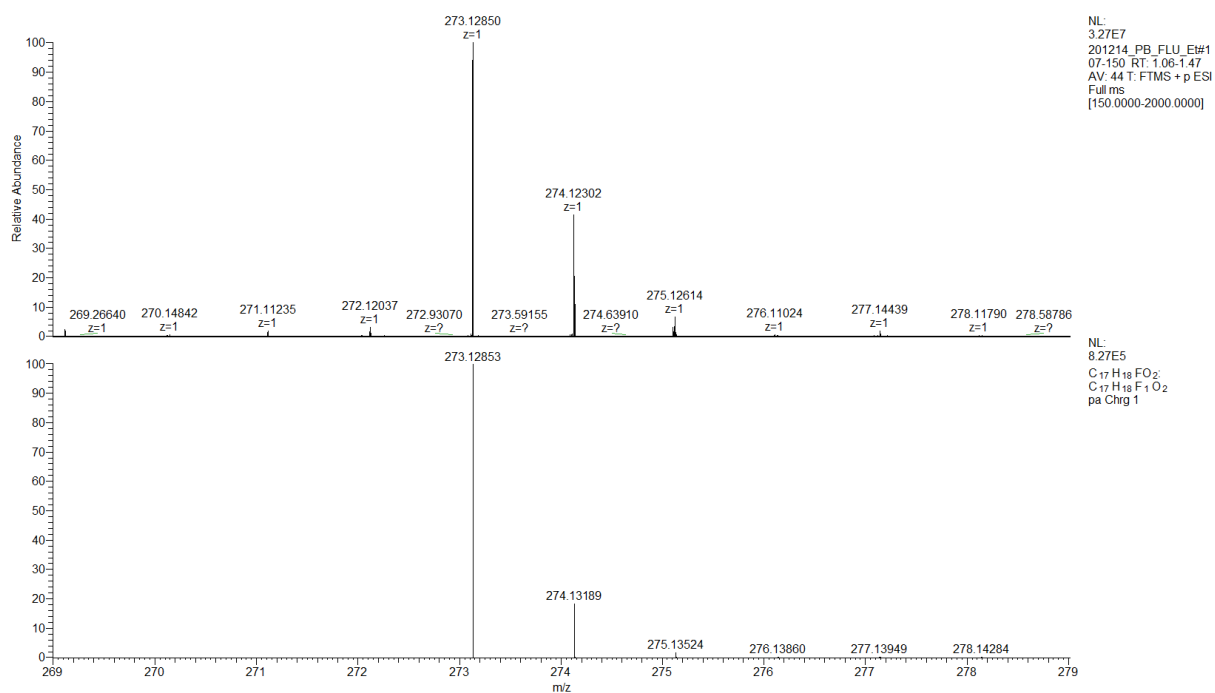
FTIR spectrum of *rac*-**4b** (Mineral oil, Nujol)



MS spectrum of *rac*-**4b** (ESI-TOF)



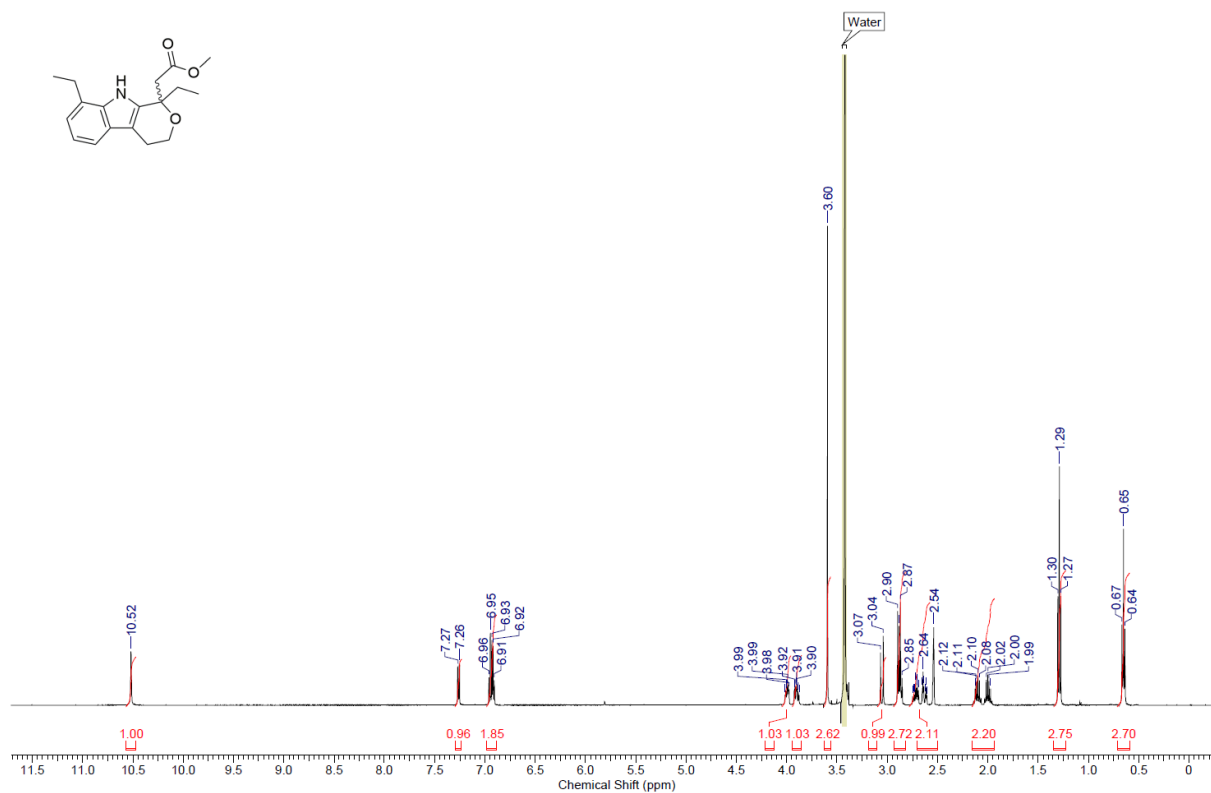
# FTMS spectrum of *rac*-**4b** (ESI-TOF)



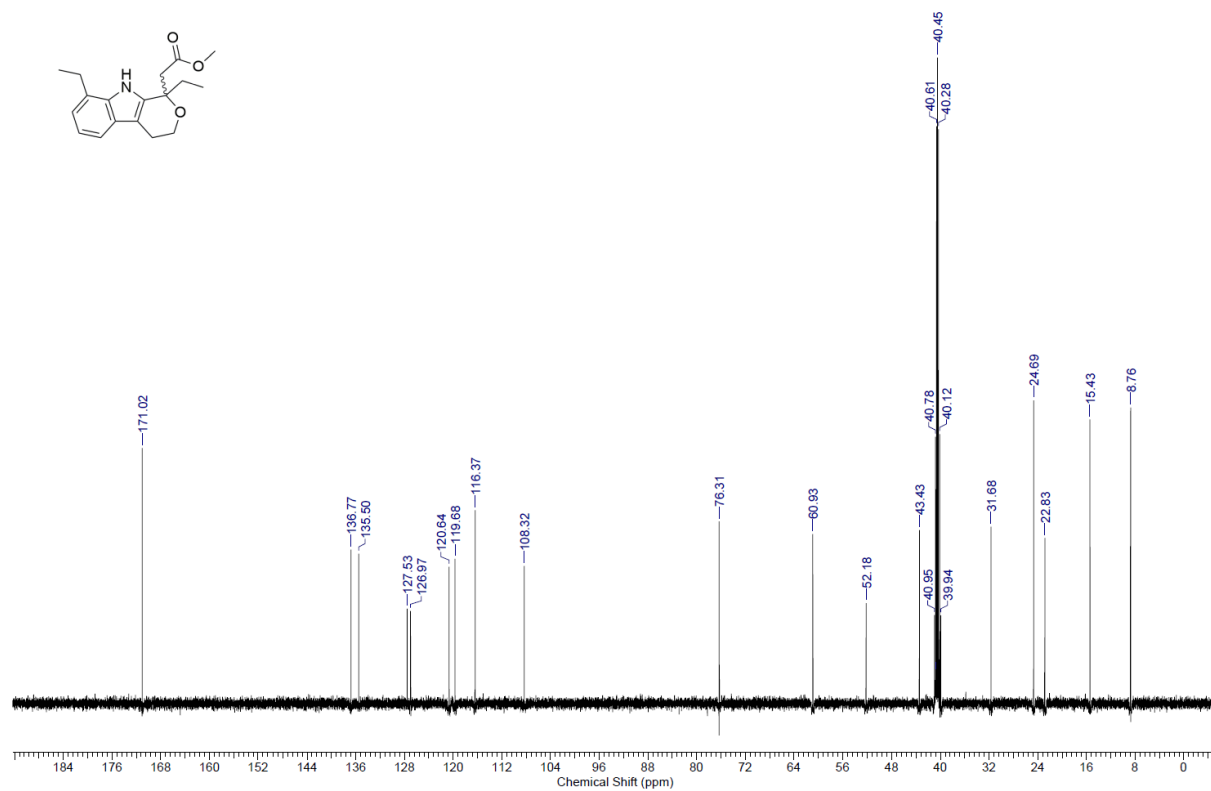


**Methyl (1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-b]indol-1-yl)acetate (Etodolac methyl ester, *rac*-5a)**

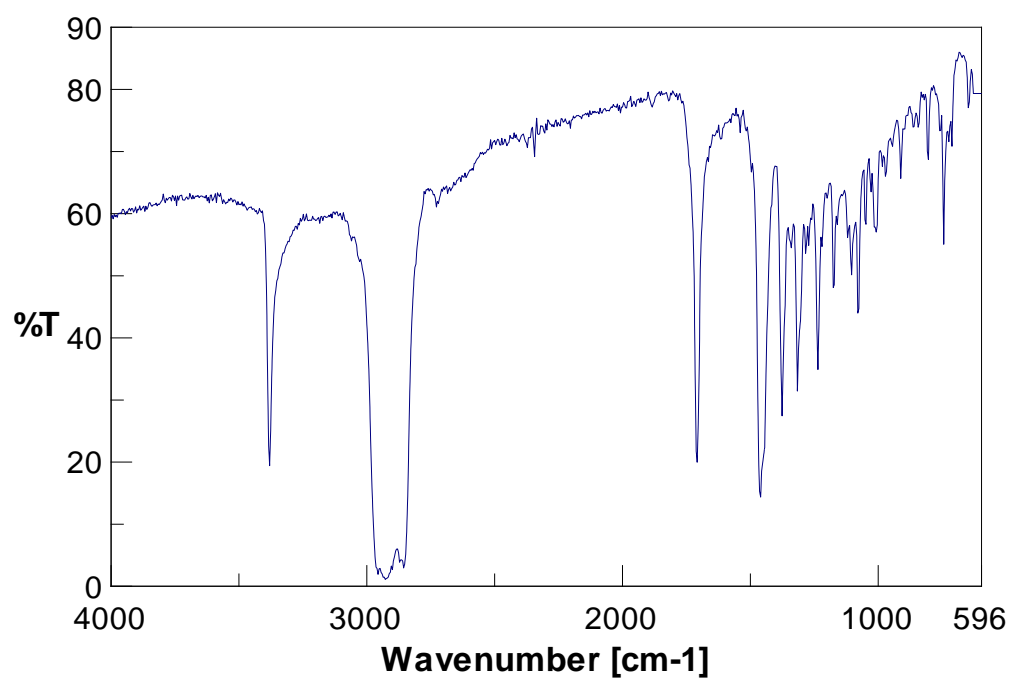
<sup>1</sup>H NMR spectrum of *rac*-5a (500 MHz, DMSO-*d*<sub>6</sub>)



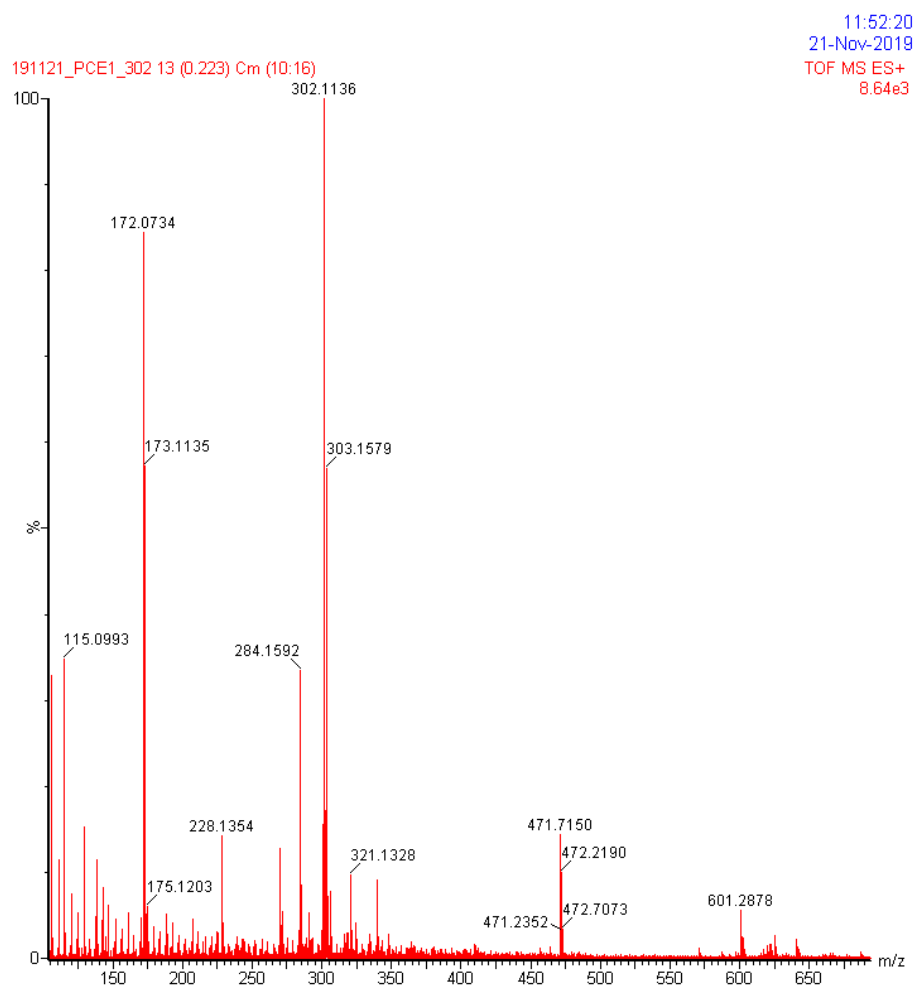
<sup>13</sup>C NMR spectrum of *rac*-5a (126 MHz, DMSO-*d*<sub>6</sub>)



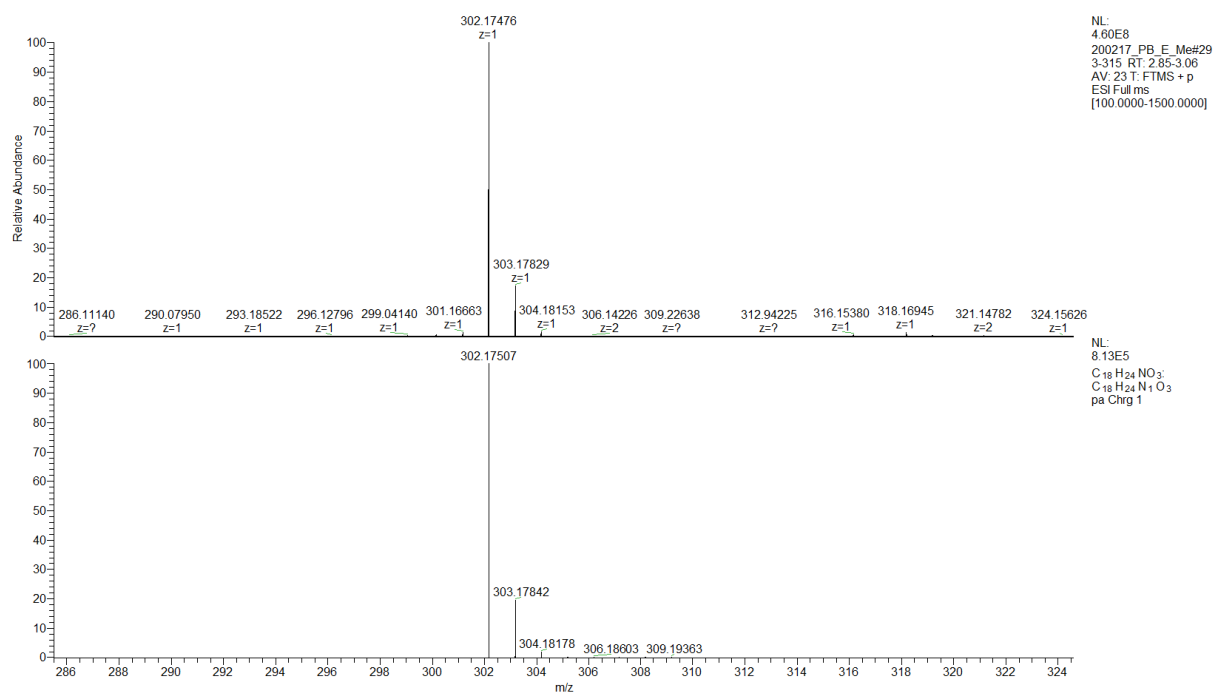
FTIR spectrum of *rac*-**5a** (Mineral oil, Nujol)



MS spectrum of *rac*-**5a** (ESI-TOF)

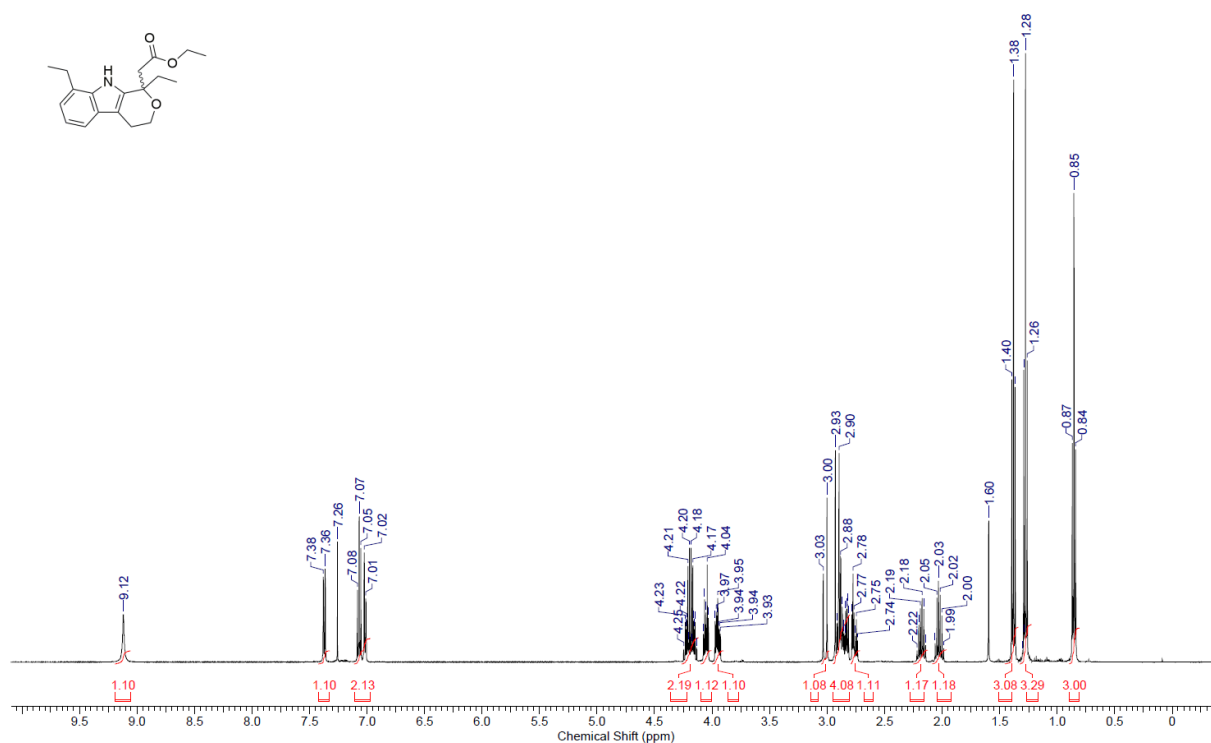


# FTMS spectrum of *rac*-5a (ESI-TOF)

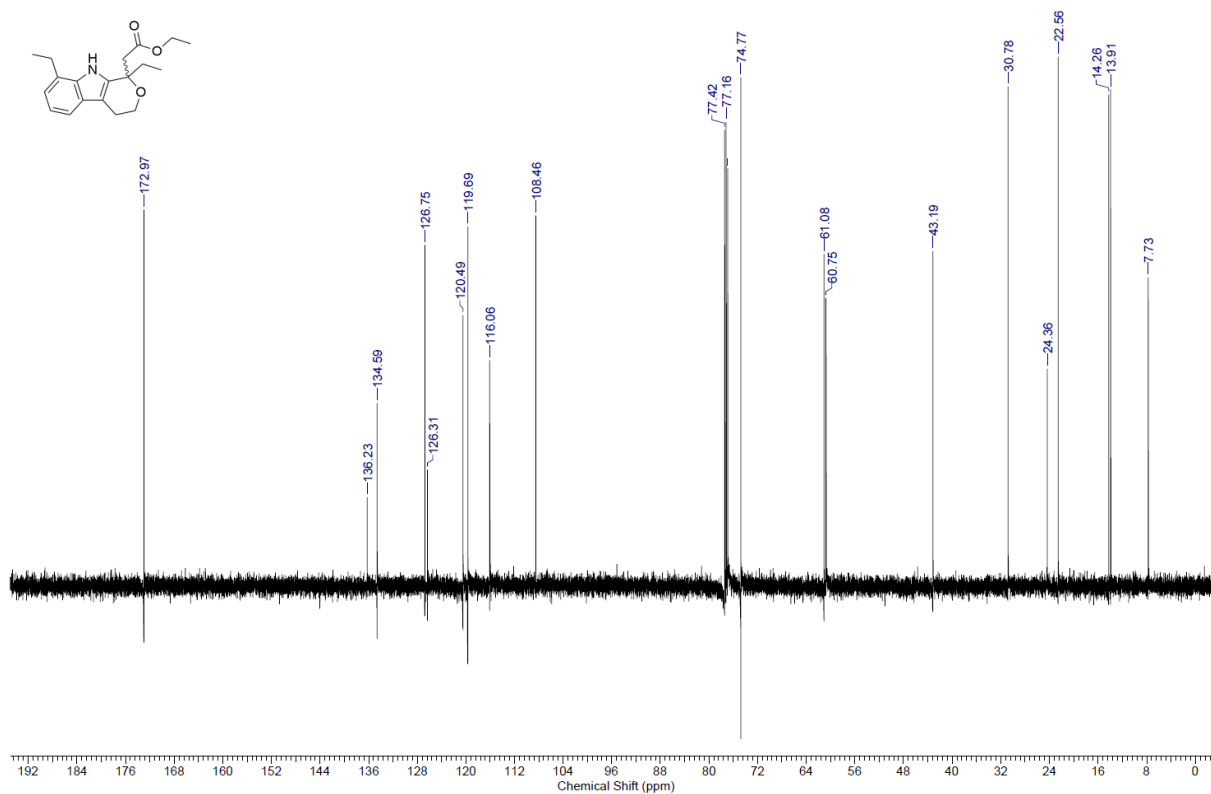


***Ethyl (1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-b]indol-1-yl)acetate (Etodolac ethyl ester, rac-5b)***

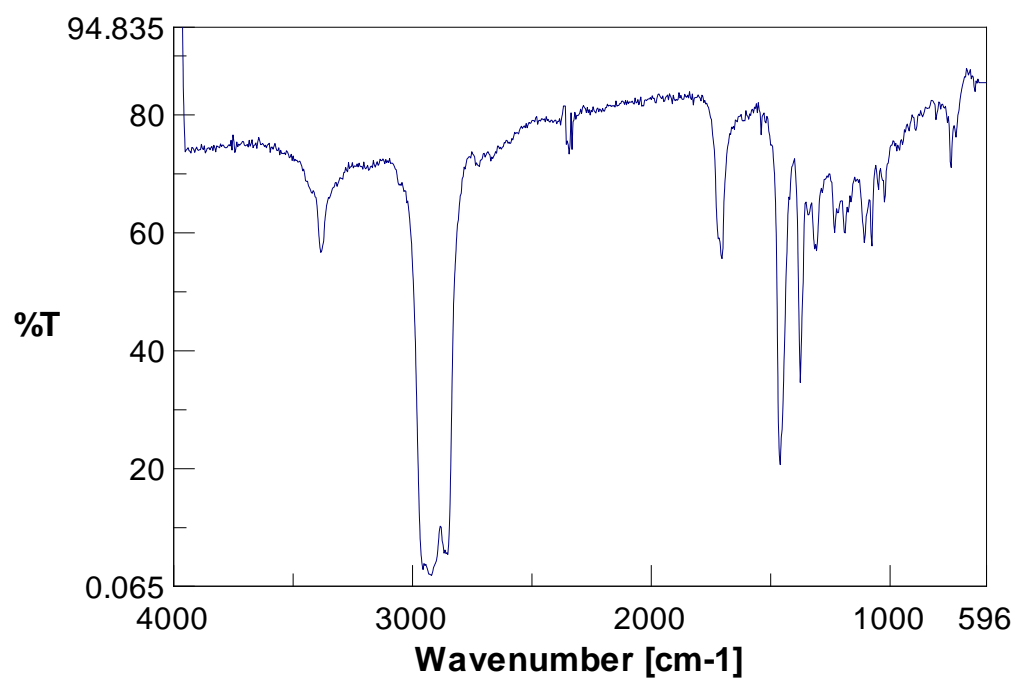
<sup>1</sup>H NMR spectrum of *rac-5b* (500 MHz, CDCl<sub>3</sub>)



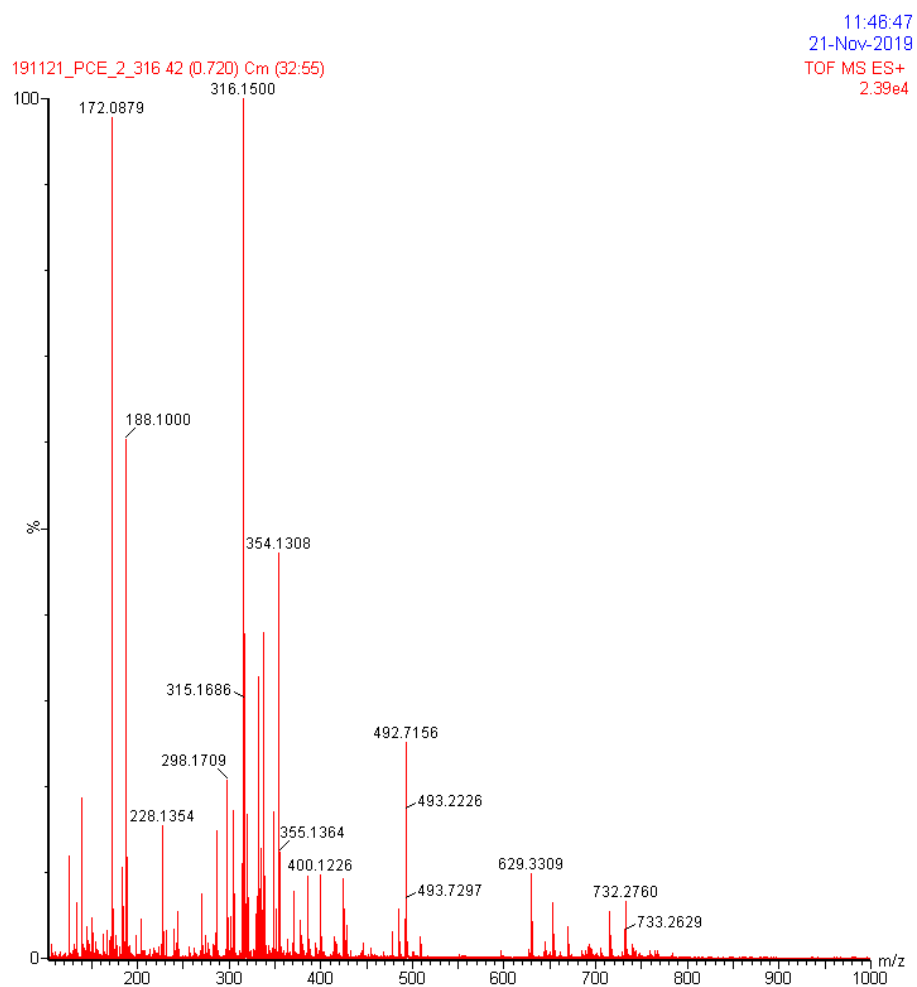
<sup>13</sup>C NMR spectrum of *rac-5b* (126 MHz, CDCl<sub>3</sub>)



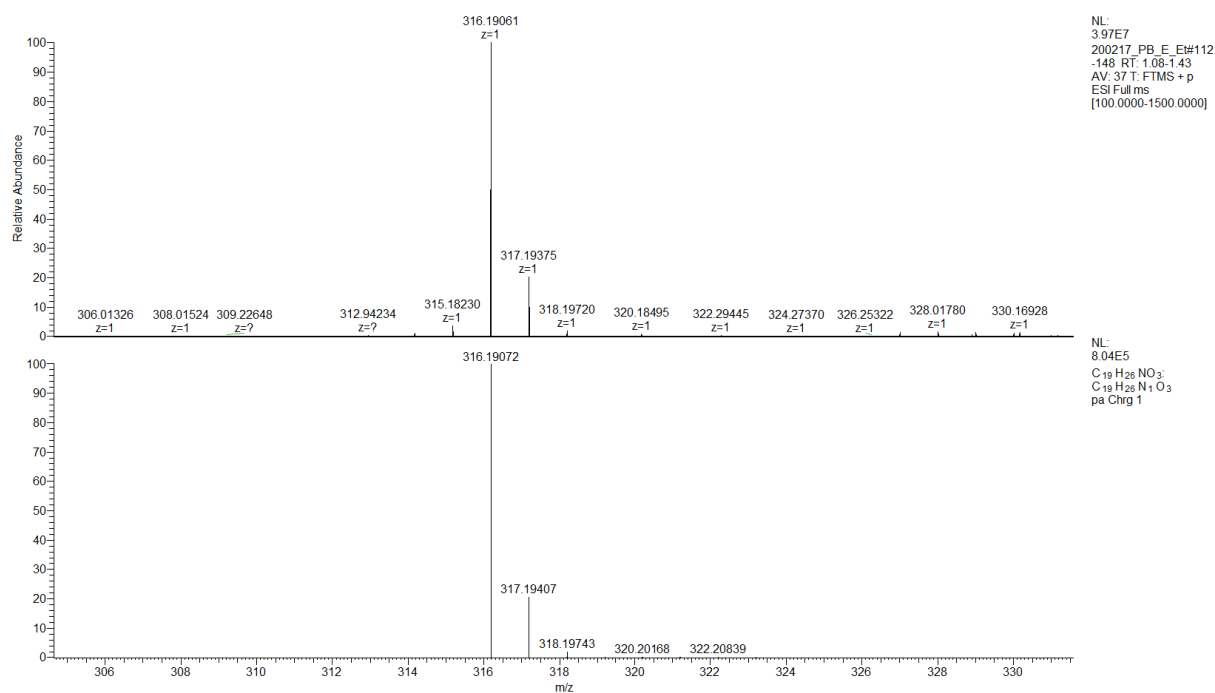
FTIR spectrum of *rac*-**5b** (Mineral oil, Nujol)



MS spectrum of *rac*-**5b** (ESI-TOF)



# FTMS spectrum of *rac*-**5b** (ESI-TOF)



## References

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