

The Optimization of the Synthesis Process and the Identification of Levobupivacaine Hydrochloride

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Table S1. Single crystal X-ray diffraction data of levobupivacaine hydrochloride (21).

Identification code	levobupivacaine hydrochloride (1)
Empirical formula	C ₃₇ H ₆₀ Cl ₄ N ₄ O ₂
Formula weight	734.69
Temperature/K	99.99(10)
Crystal system	tetragonal
Space group	P4 ₃
a/Å	15.56180(10)
b/Å	15.56180(10)
c/Å	34.3564(4)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	8320.08(14)
Z	8
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.173
μ/mm^{-1}	2.849
F(000)	3152.0
Crystal size/mm ³	0.42 × 0.23 × 0.13
Radiation	Cu K α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	5.144 to 134.118
Index ranges	-18 ≤ h ≤ 16, -18 ≤ k ≤ 7, -40 ≤ l ≤ 40
Reflections collected	28449
Independent reflections	13025 [R_{int} = 0.0270, R_{sigma} = 0.0340]
Data/restraints/parameters	13025/1280/860
Goodness-of-fit on F ²	1.035
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0495, wR_2 = 0.1255
Final R indexes [all data]	R_1 = 0.0512, wR_2 = 0.1269
Largest diff. peak/hole / e Å ⁻³	0.57/-0.54
Flack parameter	0.003(5)

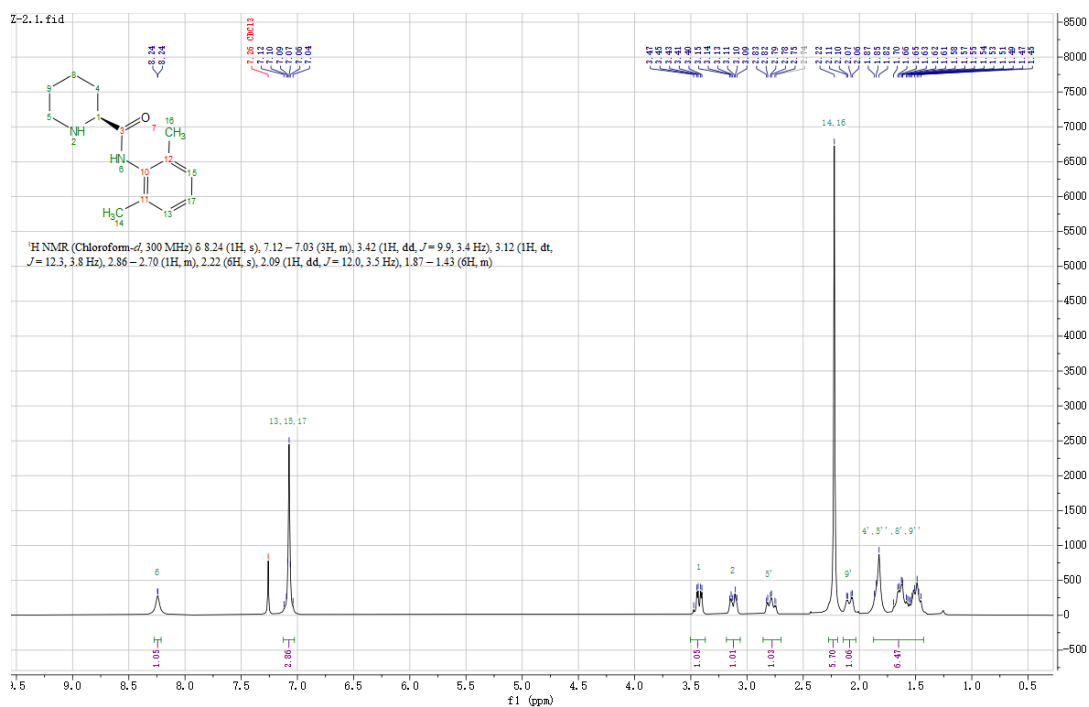


Figure S1 ¹H NMR of compound 5 (CDCl₃)

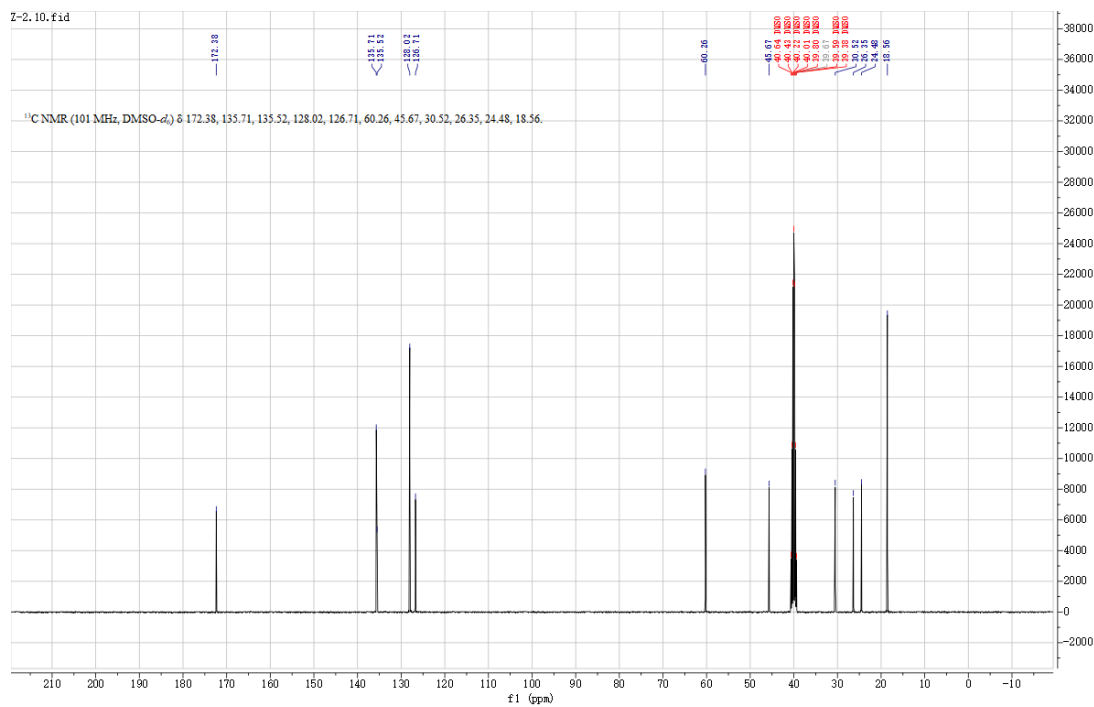


Figure S2 ¹³C NMR of compound 5 (DMSO-*d*₆)

Ret. Time: 0.86

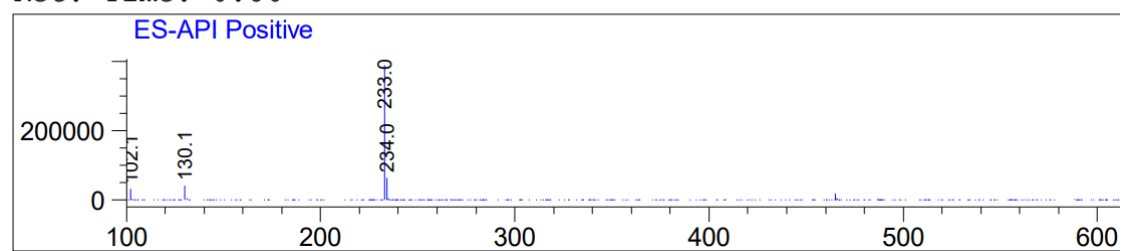
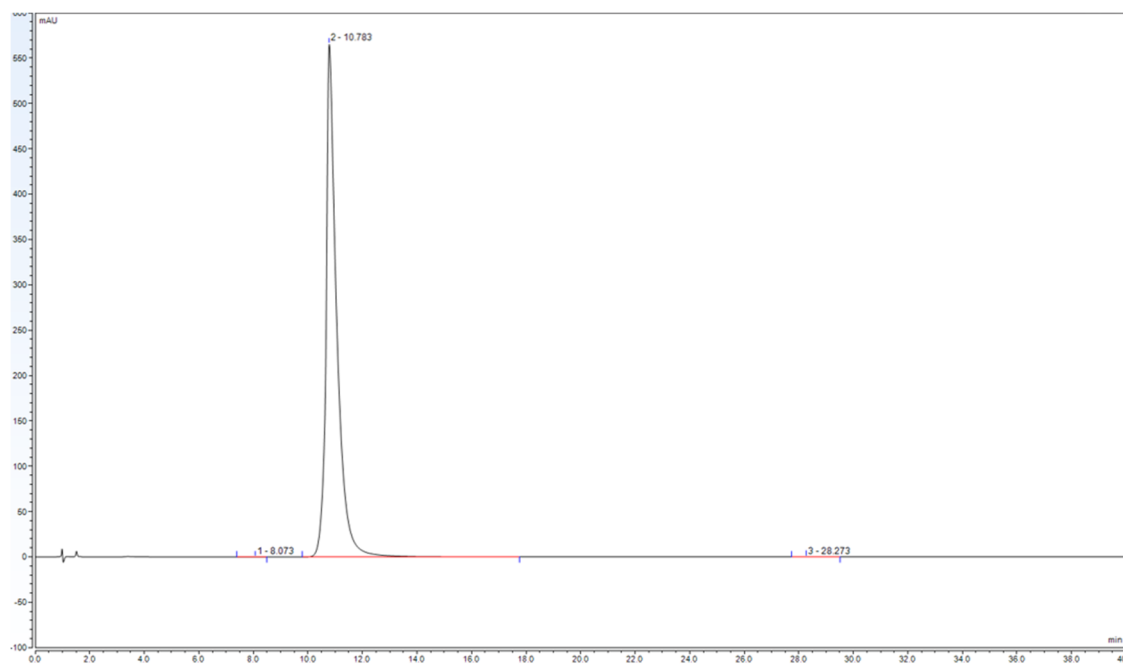


Figure S3 LC-MS of compound 5 (MW =232.2)



No.↵	Peak name↵	Retention Time↵ min↵	Relative Area↵ %↵	Area↵ mAU*min↵
1↵	↵	8.073↵	0.01↵	0.0192↵
2↵	↵	10.783↵	99.98↵	256.6985↵
3↵	↵	28.273↵	0.01↵	0.0262↵

Figure S4 HPLC of compound 5

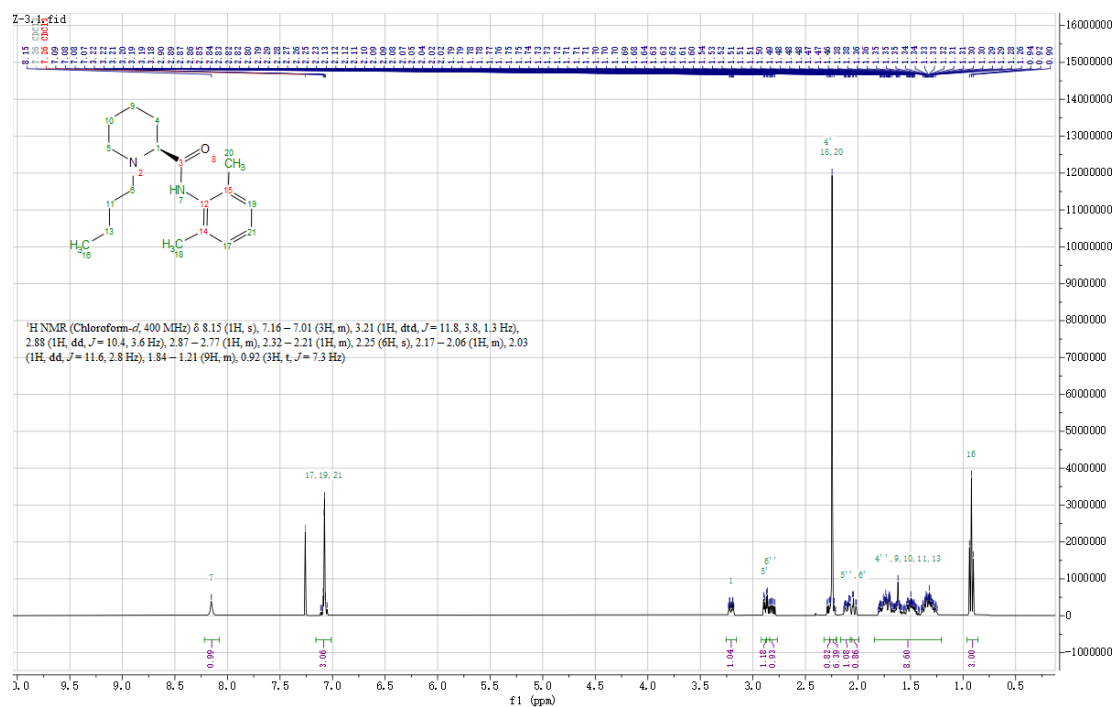


Figure S5 $^1\text{H NMR}$ of compound 6 (CDCl_3)

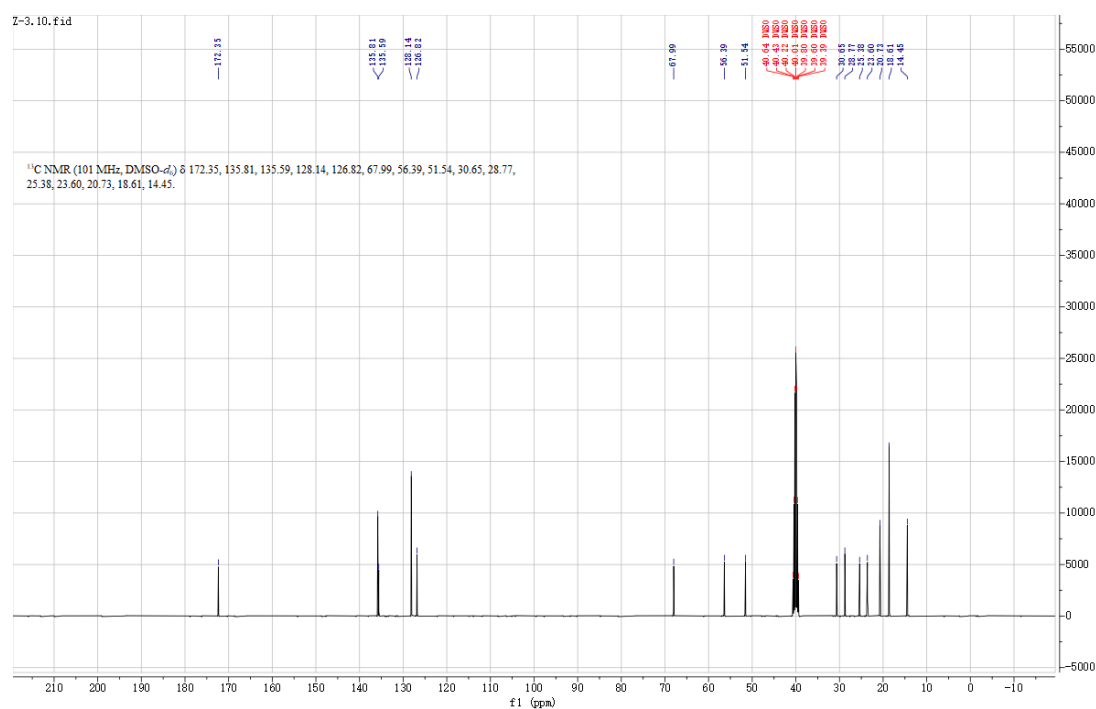


Figure S6 $^{13}\text{C NMR}$ of compound 6 ($\text{DMSO}-d_6$)

Ret. Time: 1.58

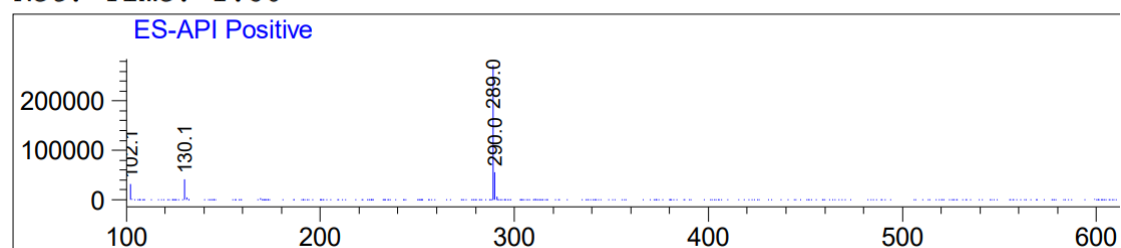
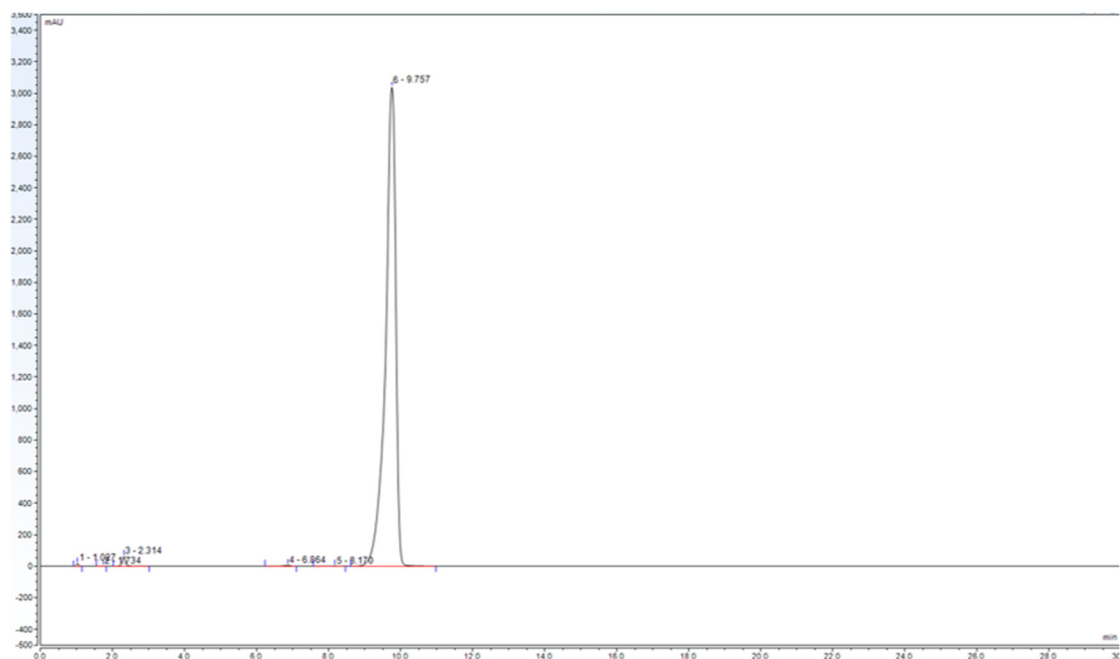


Figure S7 LC-MS of compound 6 (MW =288.2)



No.	Peak name	Retention Time min	Relative Area %	Area mAU*min
1		1.027	0.11	1.0715
2		1.734	0.01	0.0853
3		2.314	0.62	6.2272
4		6.864	0.11	1.134
5		8.17	0.03	0.2979
6		9.757	99.12	998.6678

Figure S8 HPLC of compound 6

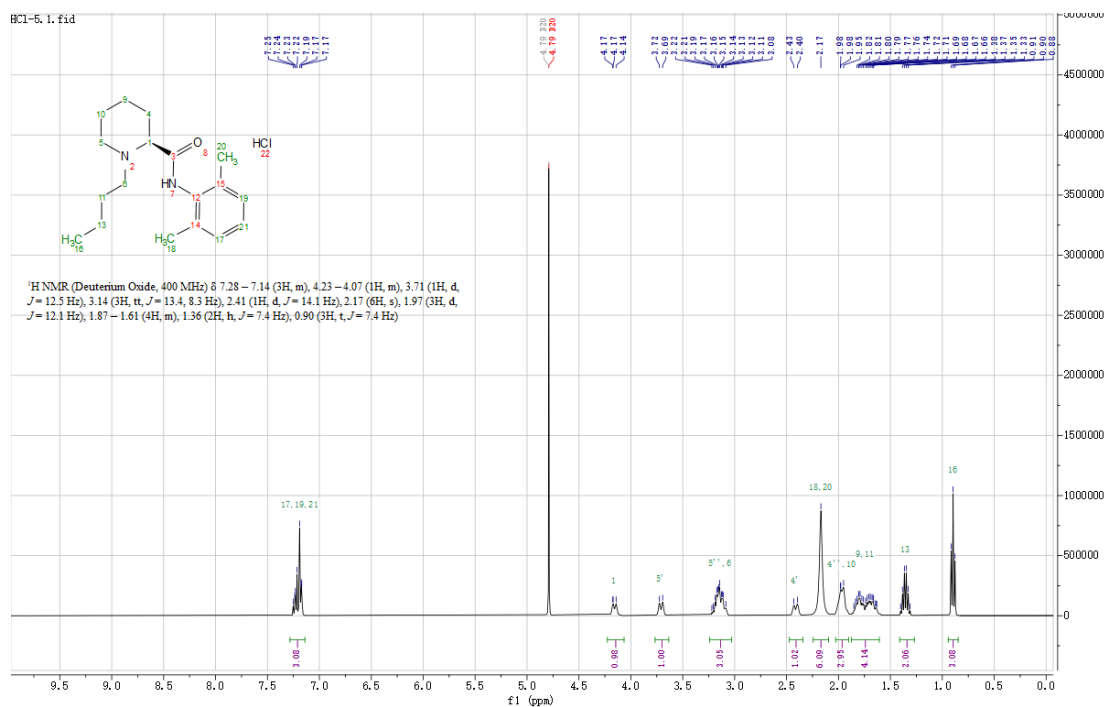


Figure S9 ¹H NMR of compound 21 (D₂O)

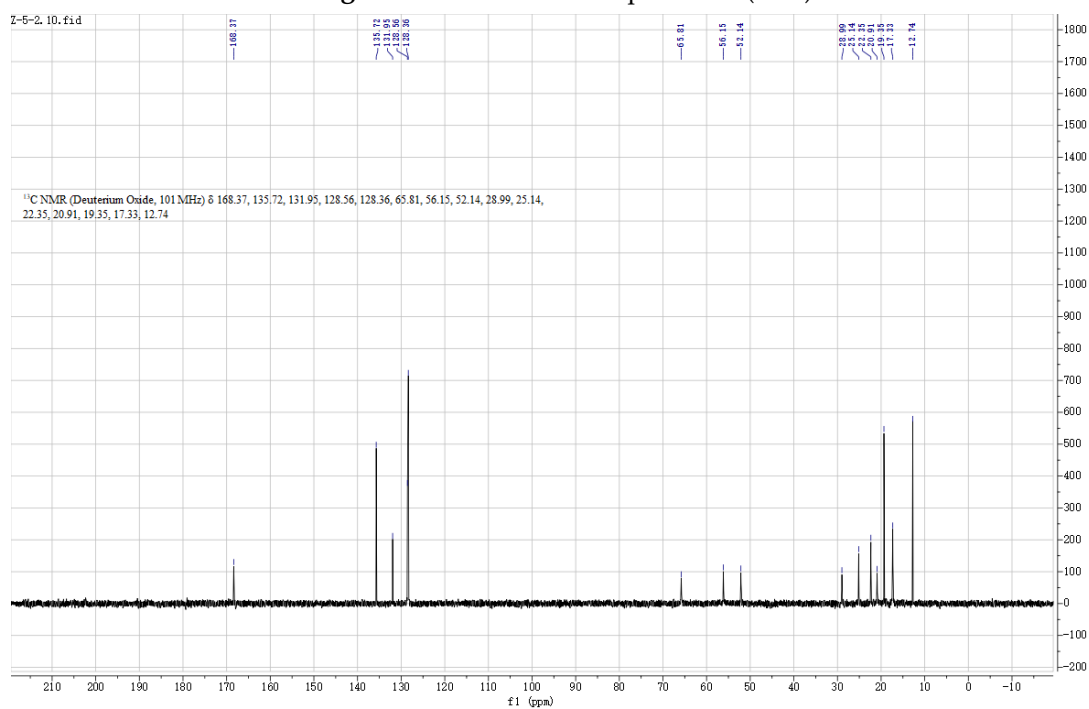


Figure S10 ¹³C NMR of compound 21 (D₂O)

Ret. Time: 1.54

<<<< POSITIVE SPECTRA >>>>

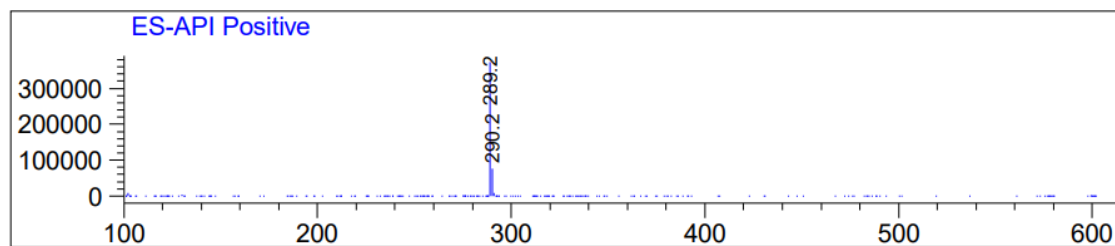


Figure S11 LC-MS of compound **21** (MW-HCl =288.2)

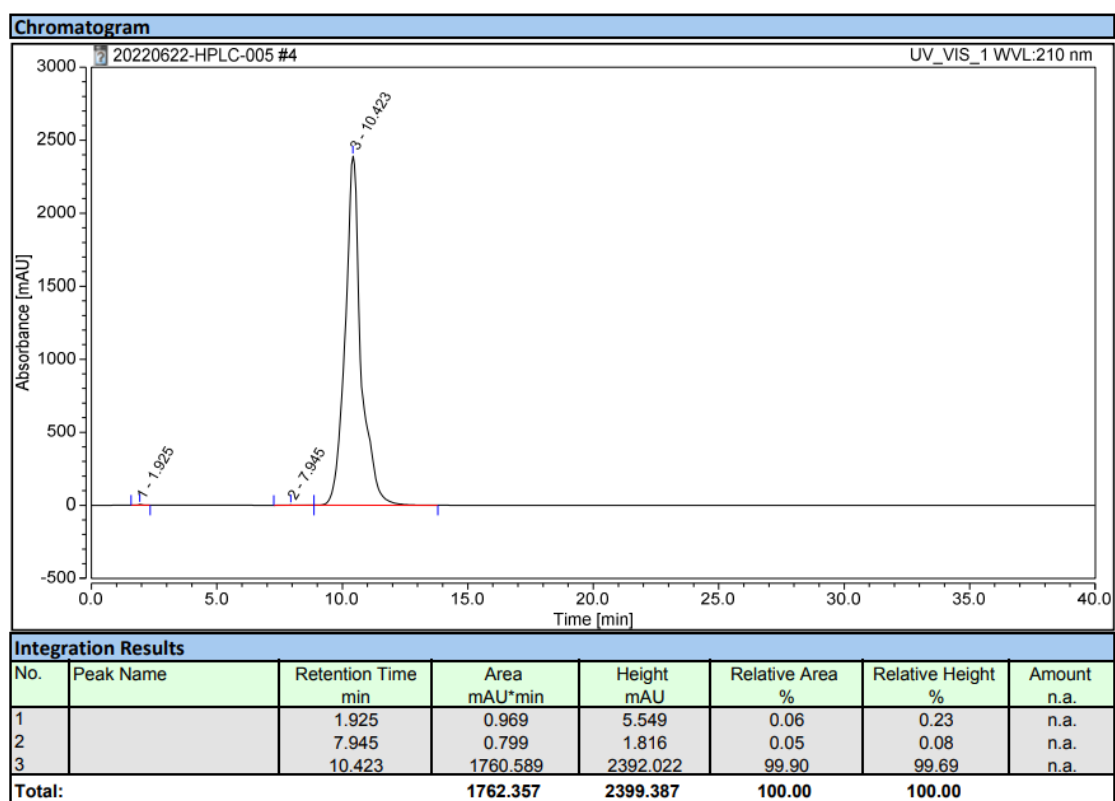
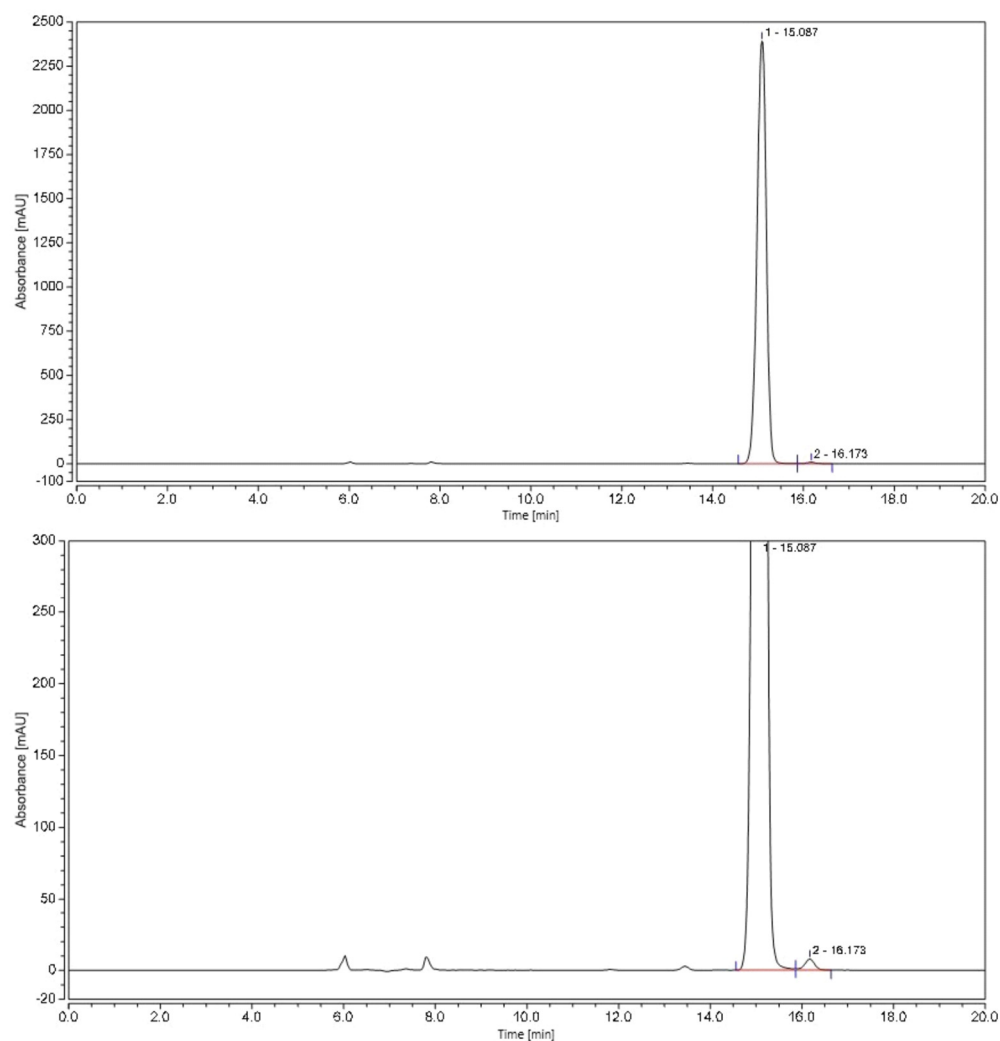


Figure S12 HPLC of compound **21** (chemically pure)



No.	Peak name	Retention Time min	Relative Area %	Area mAU*min	Resolution
1	levobupivacaine hydrochloride	15.087	99.65	569.9299	2.93
2	dextrobupivacaine hydrochloride	16.173	0.35	2.0292	n.a.

Figure S13 HPLC of compound **21** (optical pure)