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Supplementary Materials

Lipase-catalysed Kinetic Resolution of Alcohols as Intermediates for the Synthesis of Heart-rate Reducing Agent Ivabradine

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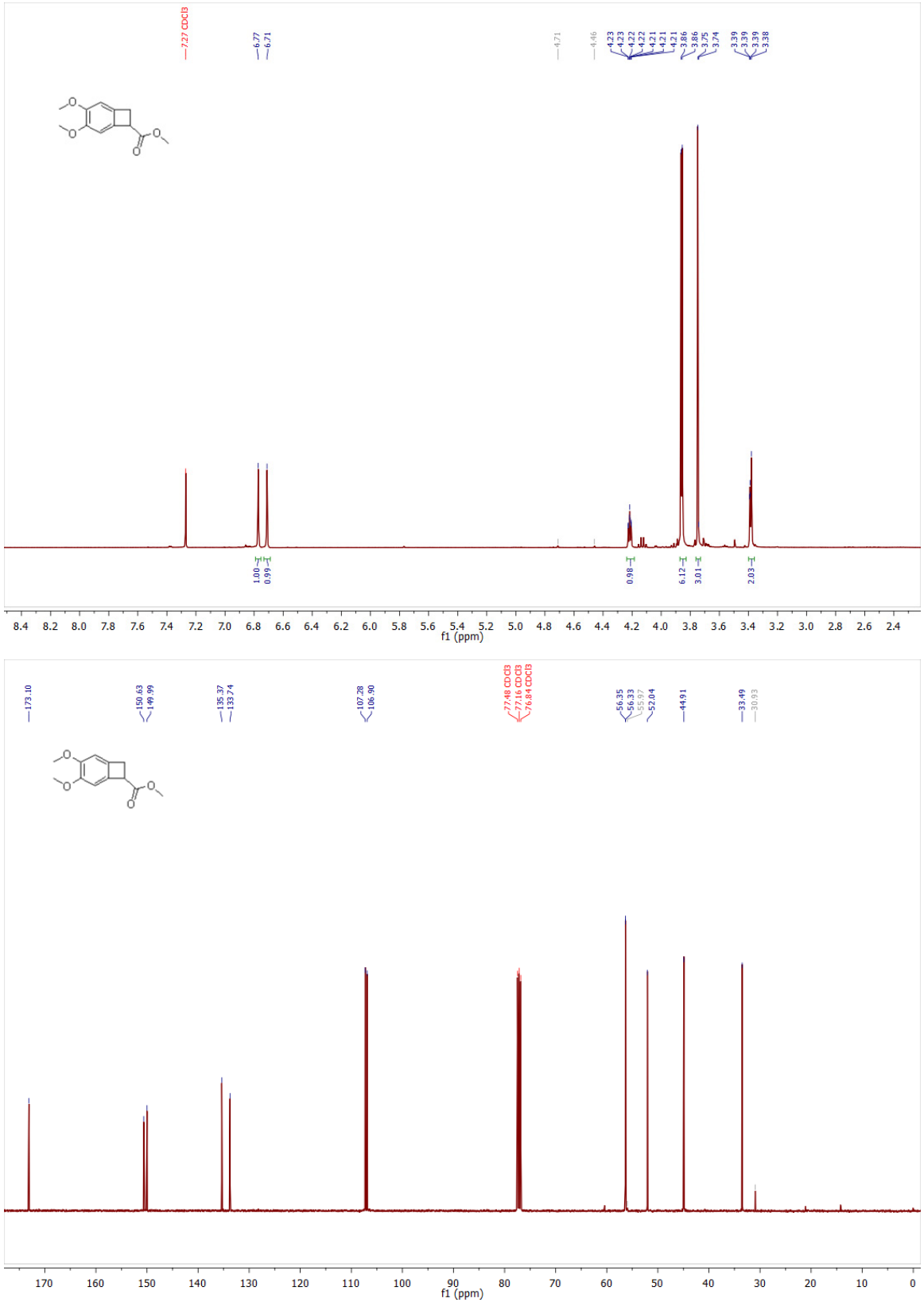


Figure S1. ^{1}H-NMR and ^{13}C-NMR of compound **7.**

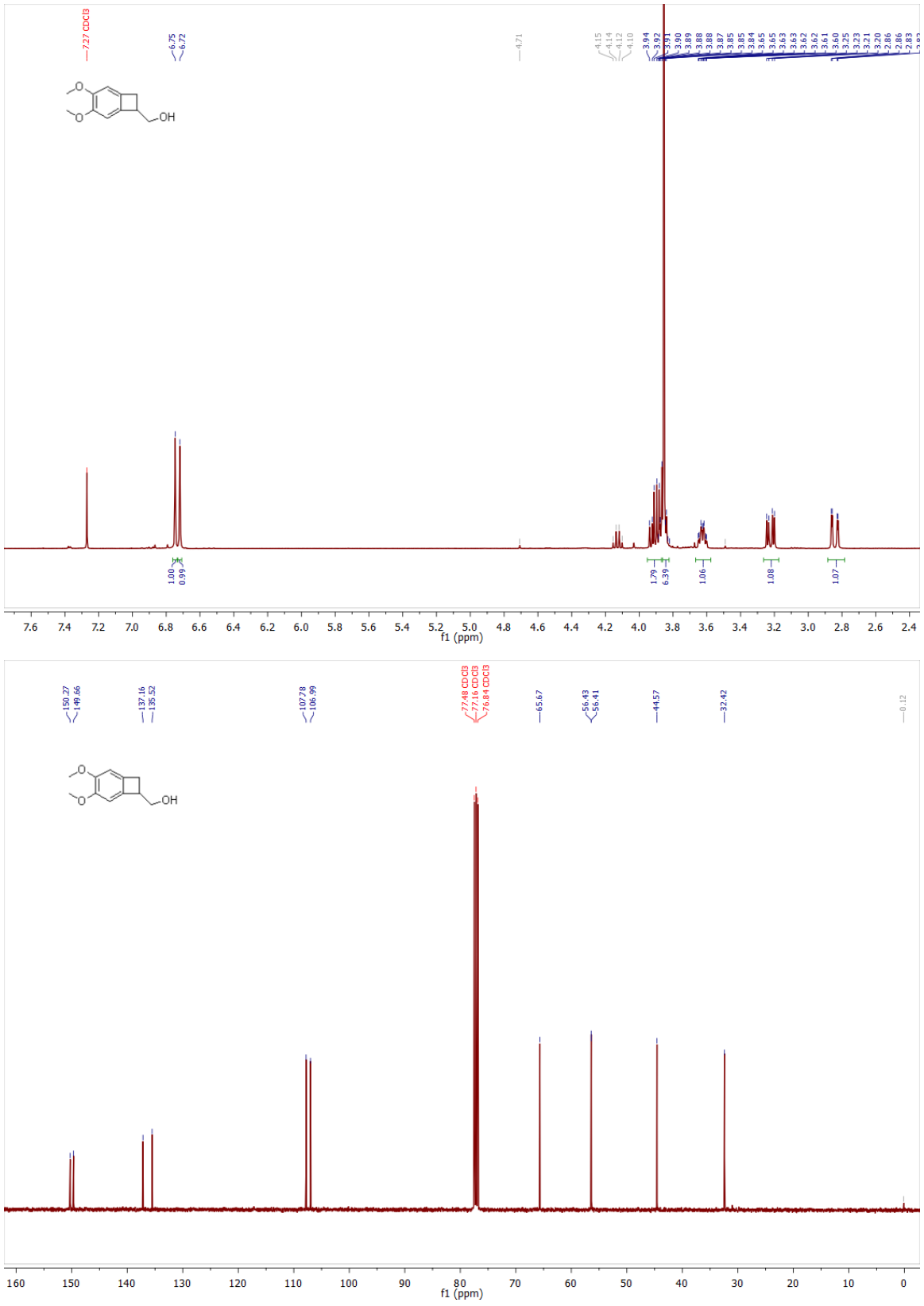


Figure S2. ^{1}H-NMR and ^{13}C-NMR of compound **4.**

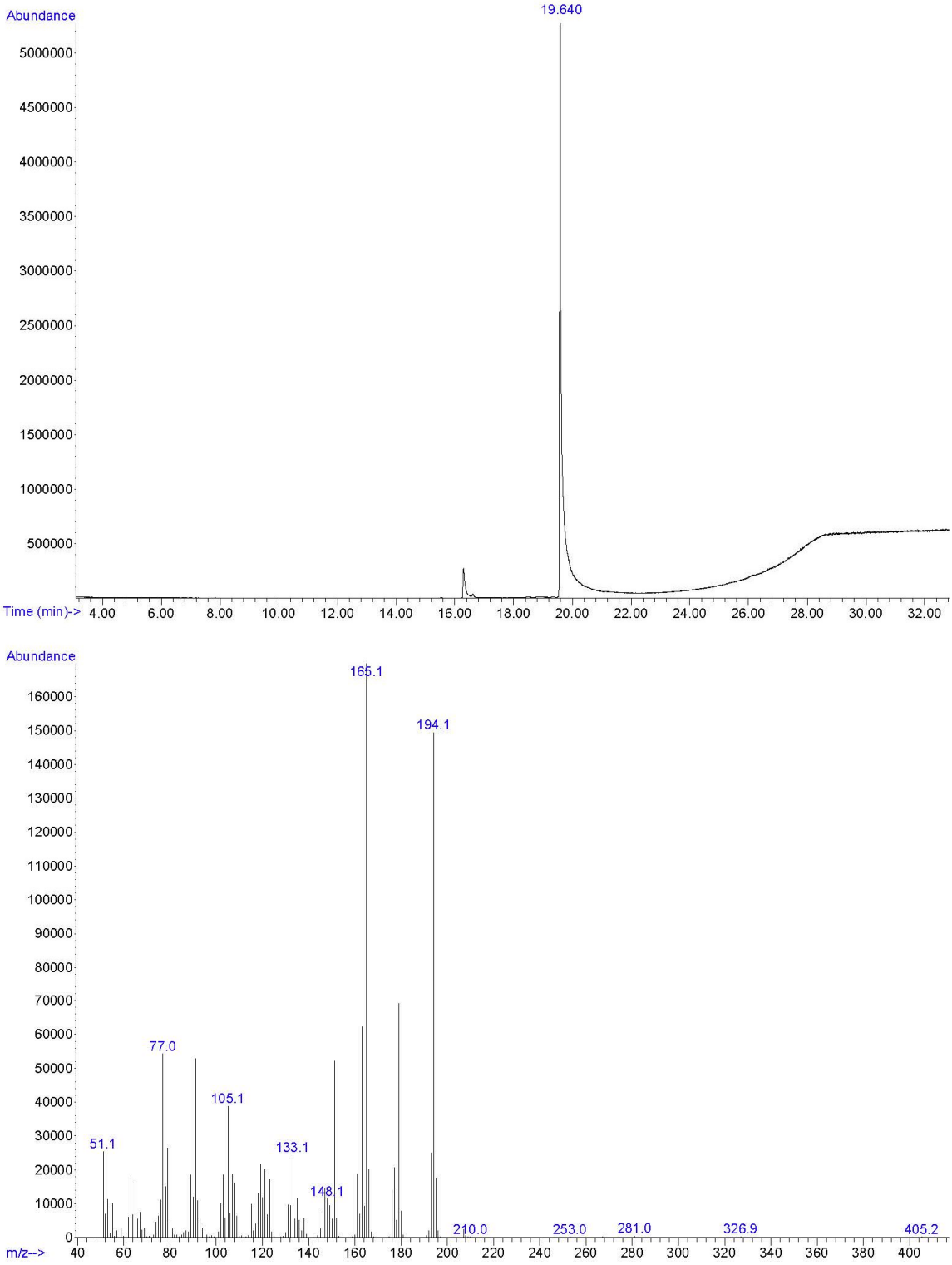


Figure S3. GC-MS of compound **4.**

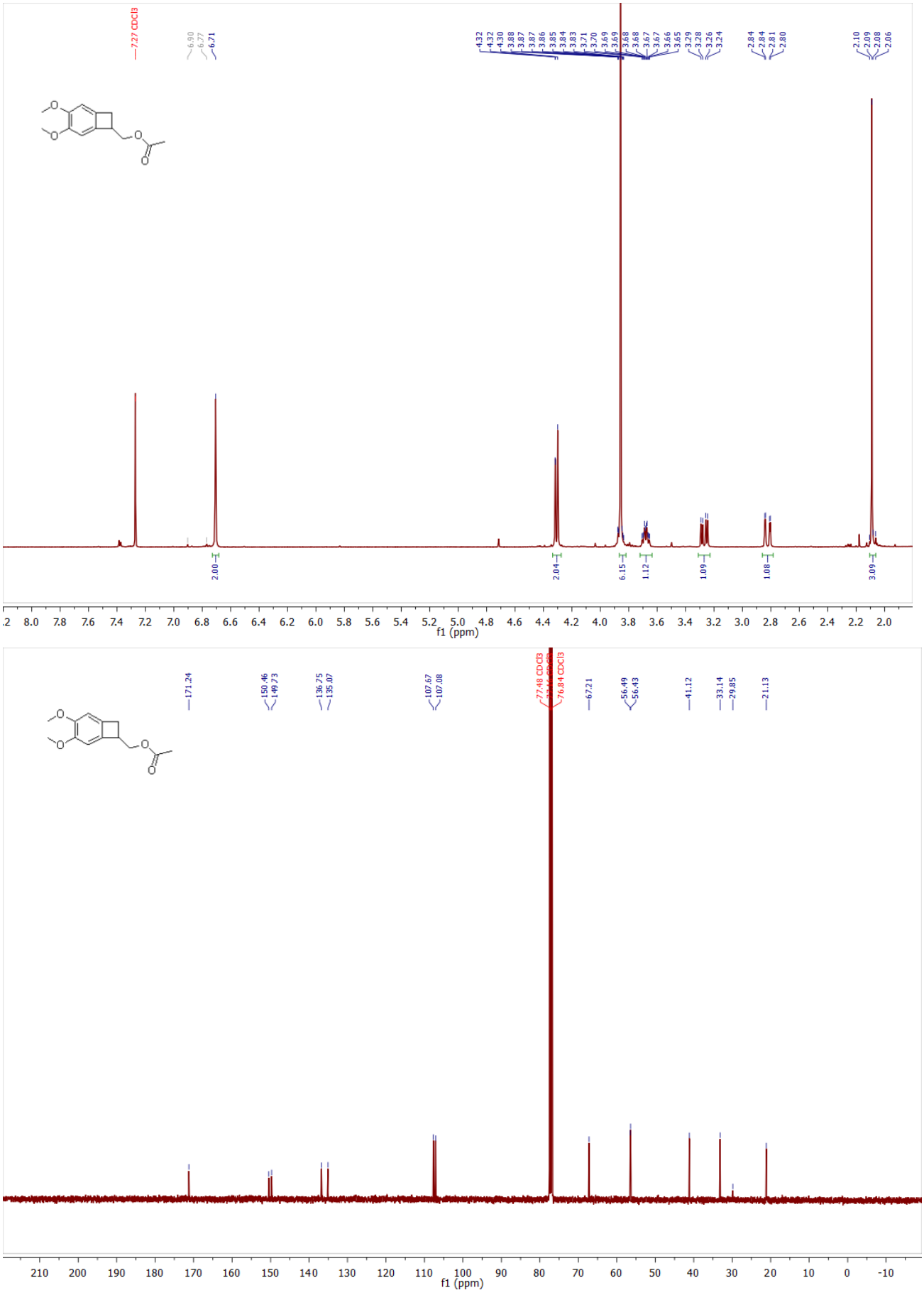


Figure S4. ^{1}H-NMR and ^{13}C-NMR of compound **5.**

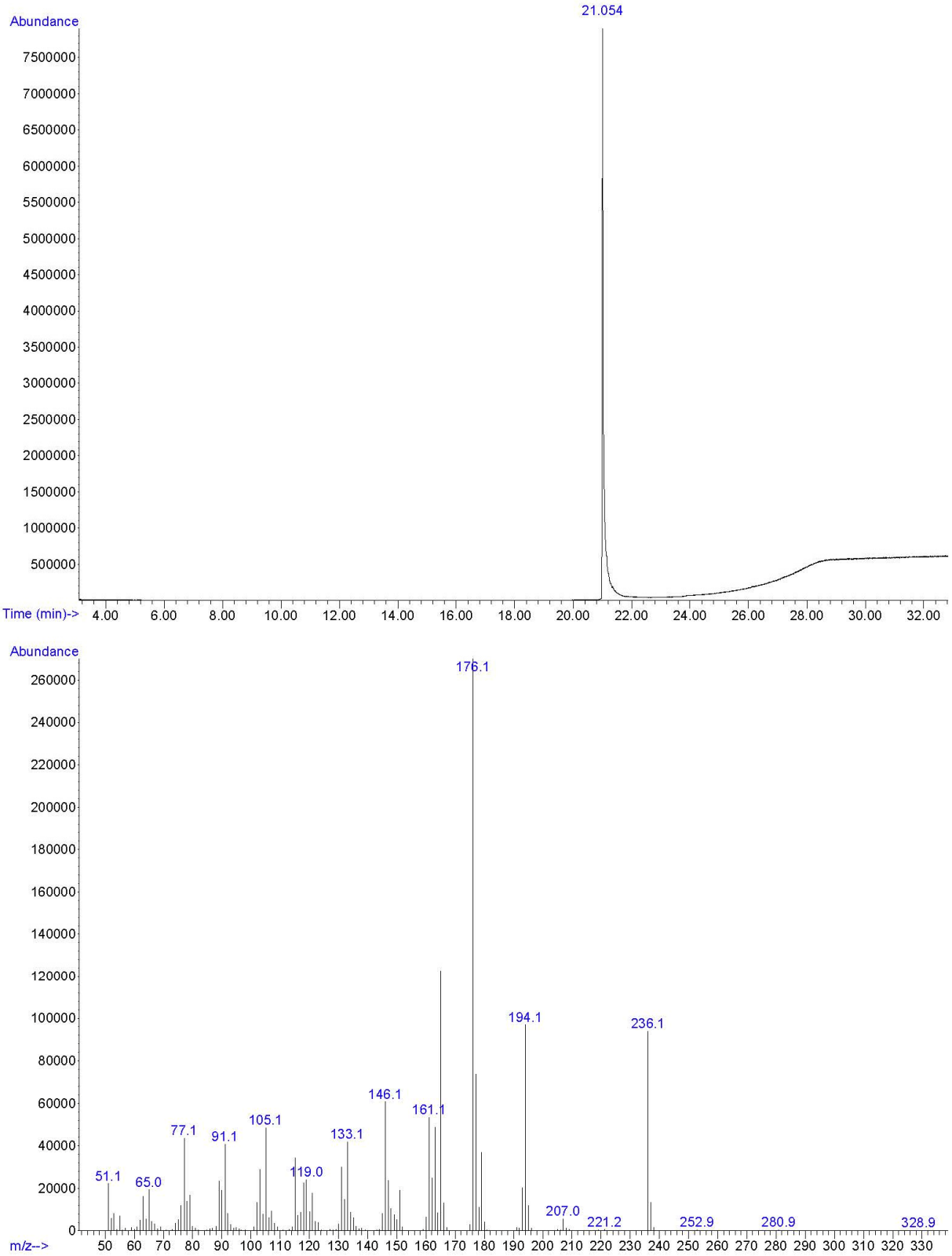


Figure S5. GC-MS of compound **5.**

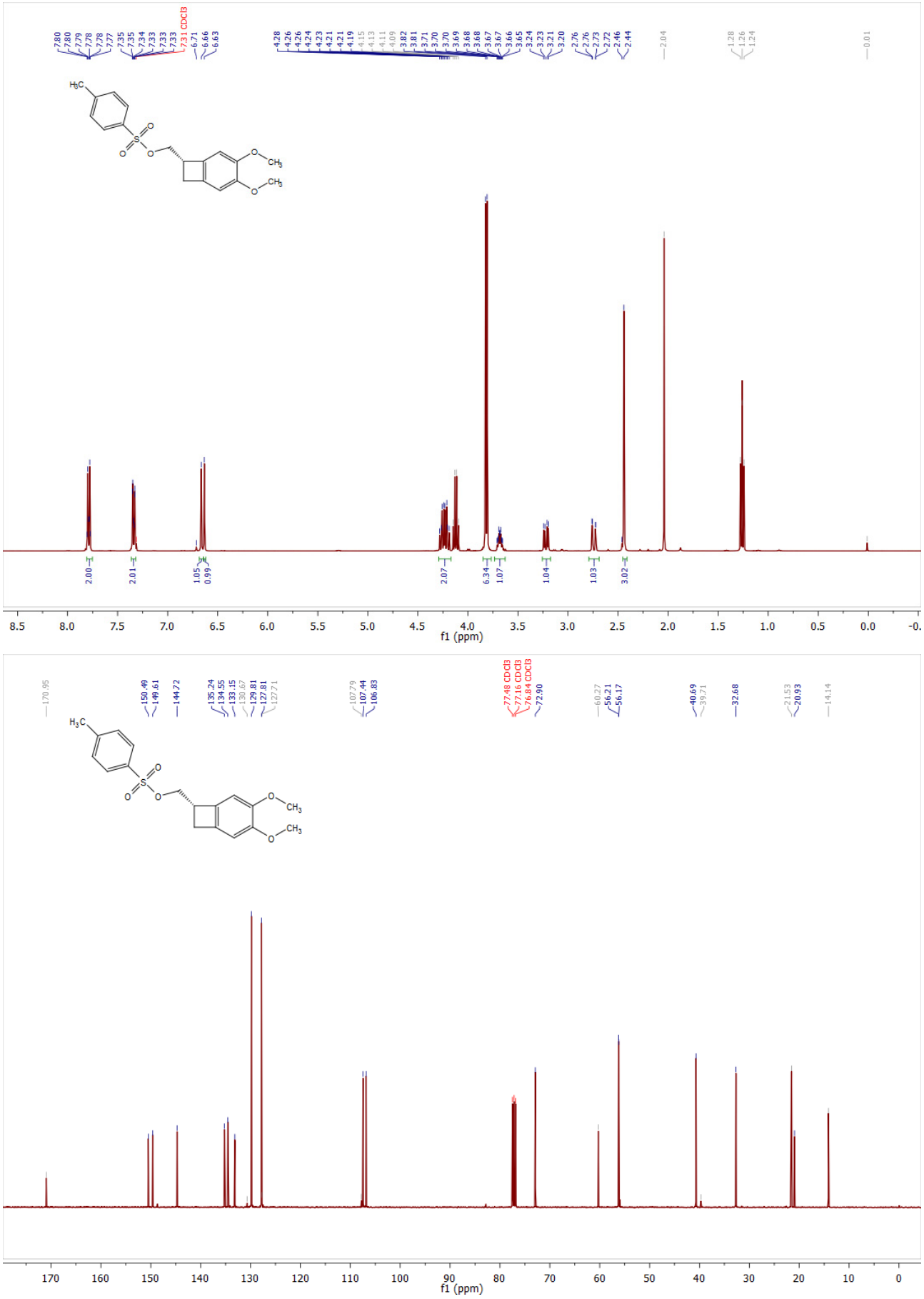


Figure S6. ^{1}H-NMR and ^{13}C-NMR of compound **(*S*)-8.**

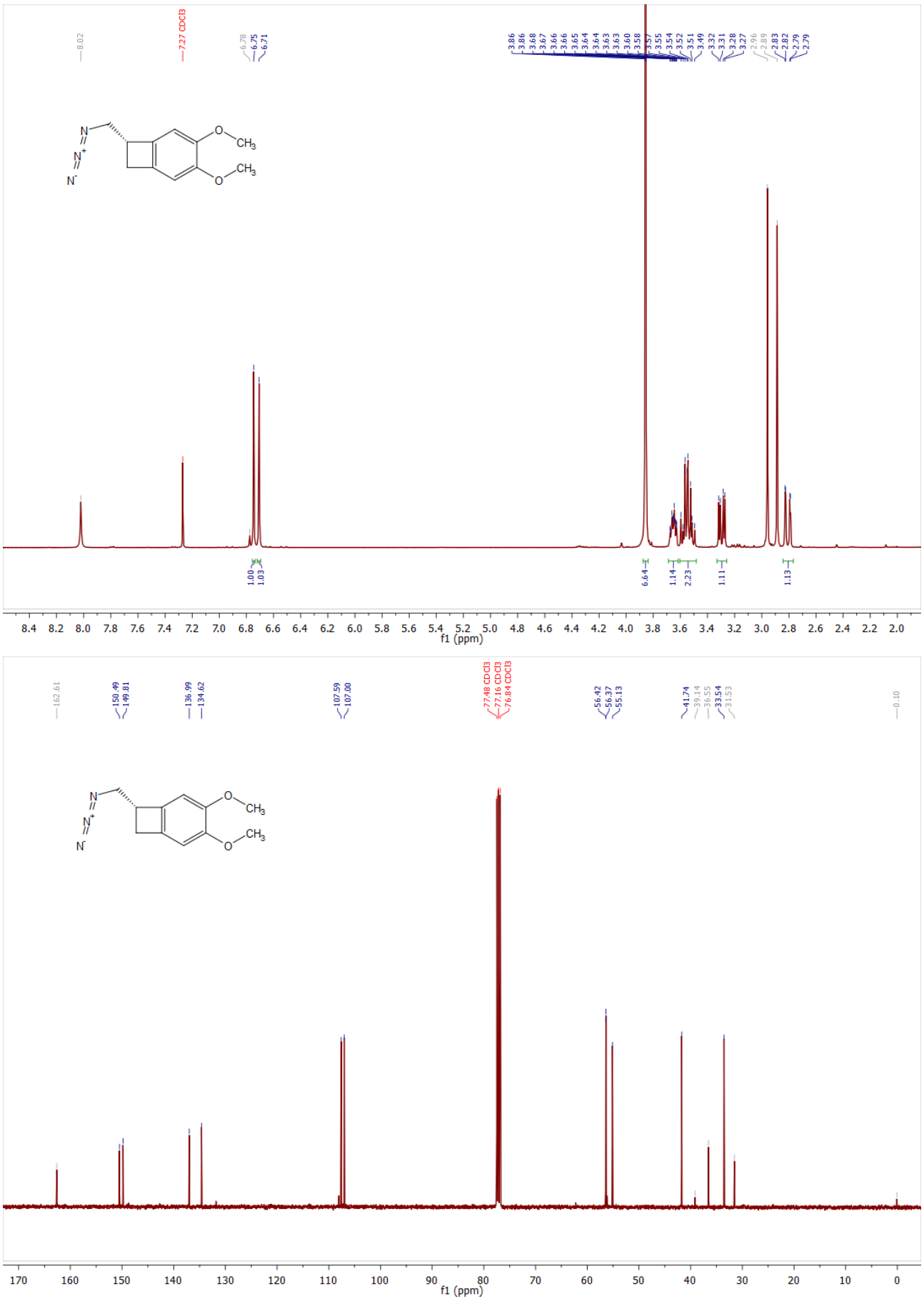


Figure S7. ^{1}H-NMR and ^{13}C-NMR of compound **(*S*)-9.**

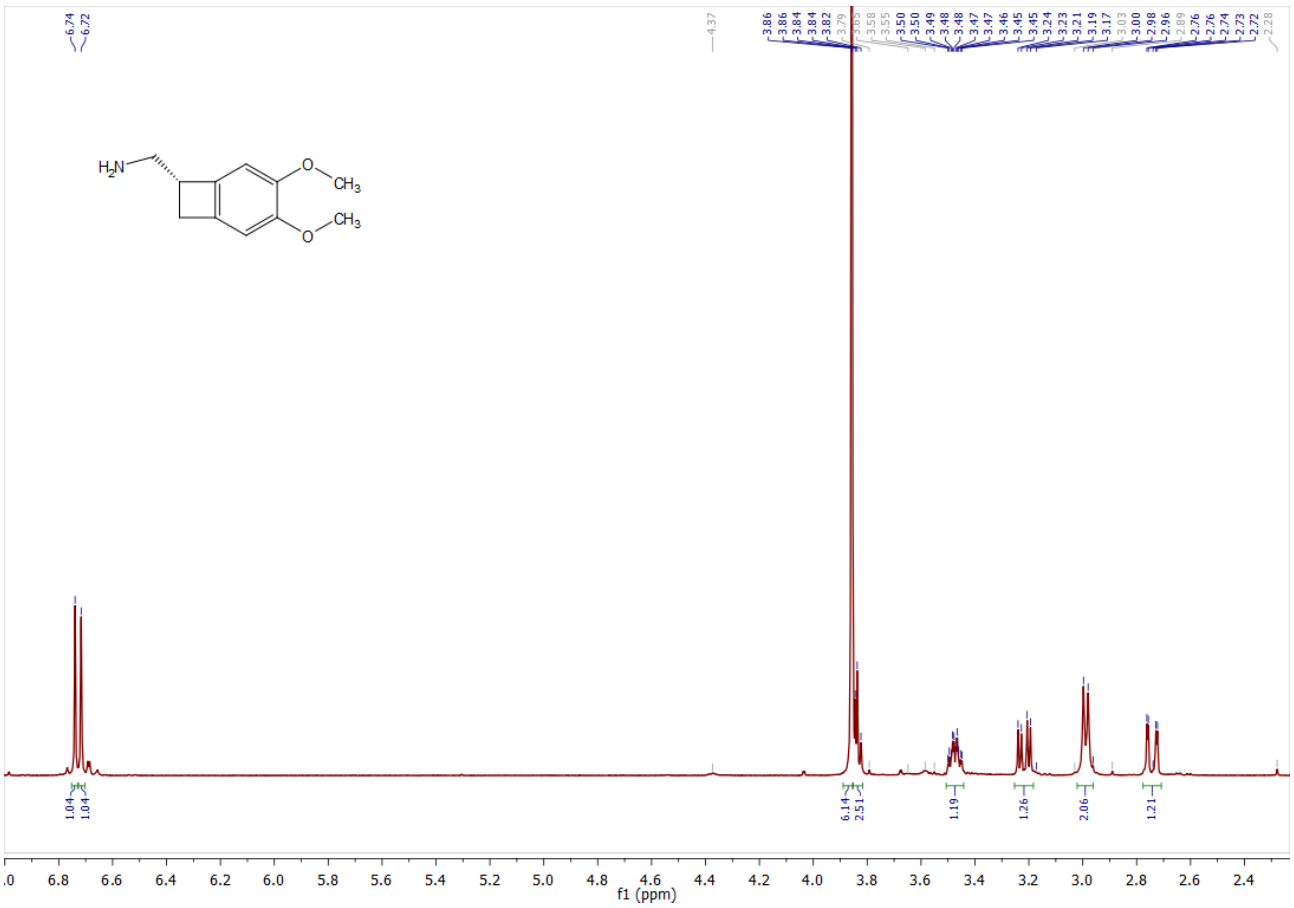
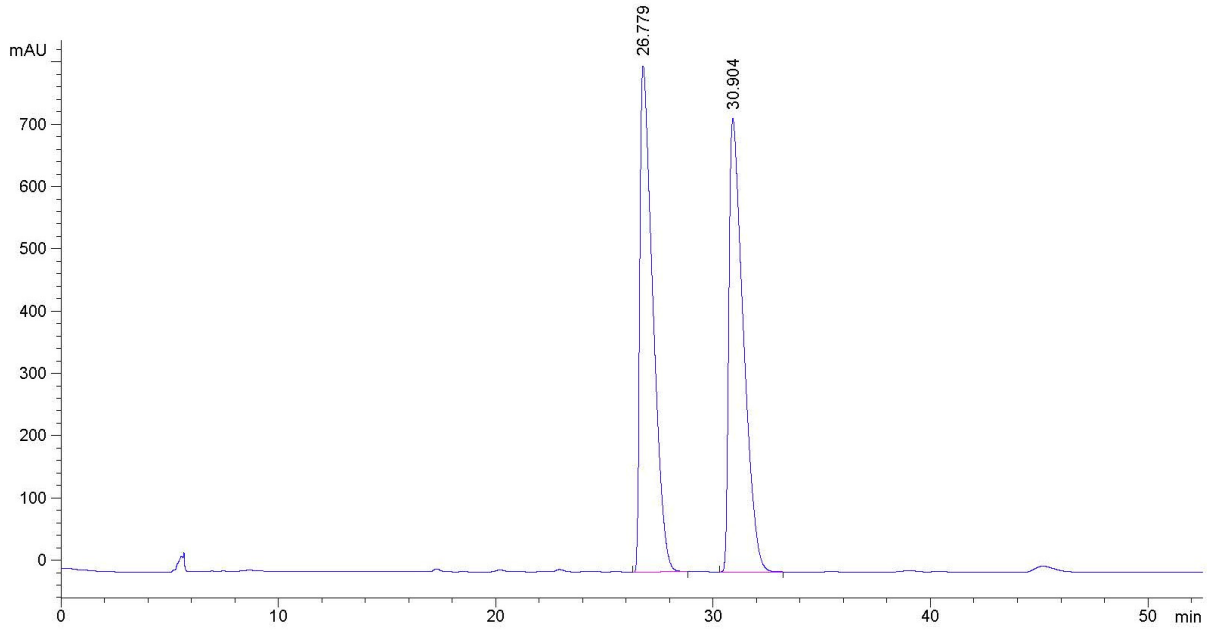
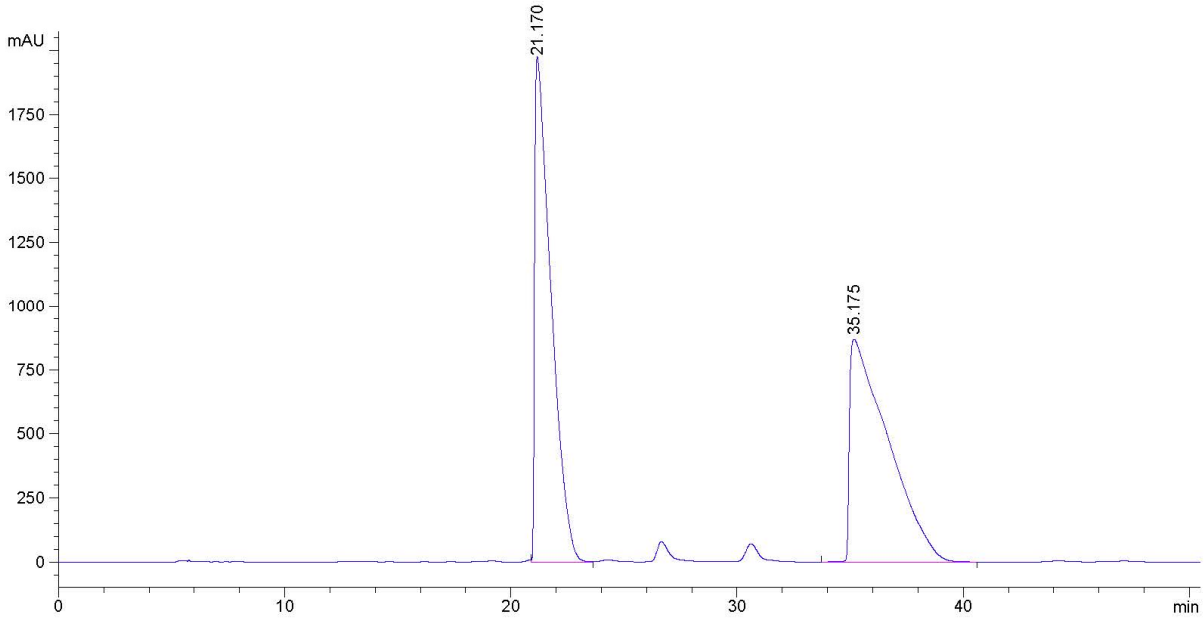


Figure S8. ^{1}H-NMR of compound **(*S*)-2.**



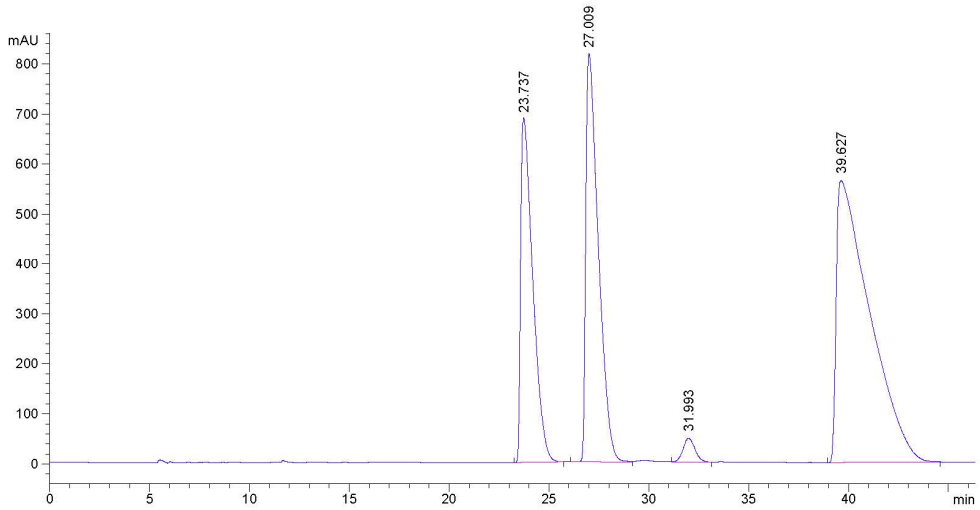
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.779	BB	0.6168	3.37164e4	812.43353	50.0808
2	30.904	BB	0.6857	3.36076e4	728.19586	49.9192

Figure S9. HPLC chromatogram of racemic alcohol **4.**



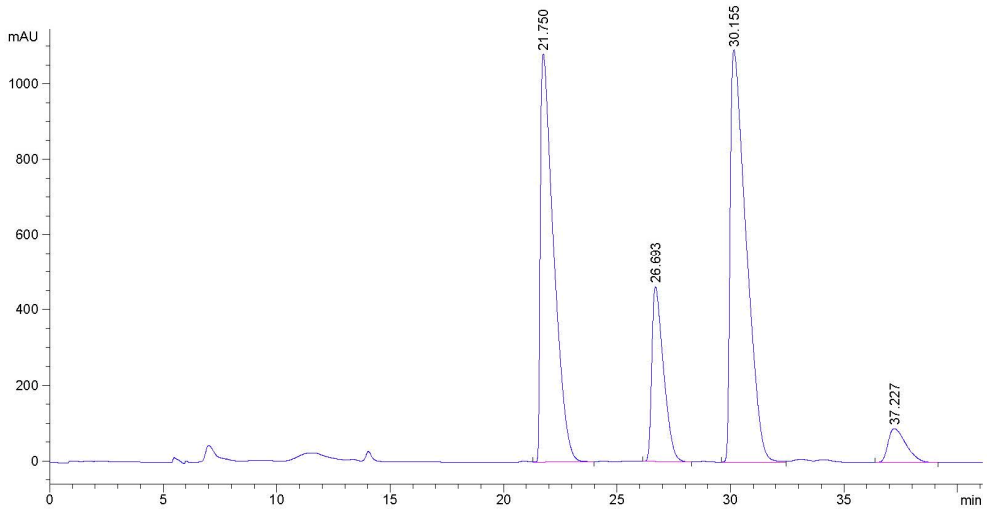
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.170	VB	0.6988	9.87800e4	1974.64697	49.1024
2	35.175	BB	1.5457	1.02392e5	867.77368	50.8976

Figure S10. HPLC chromatogram of racemic ester **5.**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.737	BB	0.6310	2.90019e4	689.01306	21.9582
2	27.009	BB	0.6436	3.56266e4	815.85181	26.9740
3	31.993	BB	0.6429	1992.09119	47.72762	1.5083
4	39.627	BB	1.4984	6.54569e4	564.57288	49.5595

Figure S11. HPLC chromatogram of enantioenriched alcohol **(*S*)-4** (96:4 e.r.). Biocatalytic conditions refer to hydrolysis of racemic ester **5** with *Lipase PS (Amano)* for 30 min (entry 5, Table 2 in the manuscript). From the optical rotatory power of the isolated species, it was deduced the following attributions: rt = 23.737 min: **(*S*)-5**; rt = 27.009 min: **(*S*)-4**; rt = 31.993 min: **(*R*)-4**; rt = 39.627 min: **(*R*)-5**.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.750	VB	0.5757	4.39381e4	1082.26843	37.0212
2	26.693	BB	0.5251	1.64487e4	461.56760	13.8593
3	30.155	BB	0.7156	5.33618e4	1092.51465	44.9614
4	37.227	BB	0.8192	4934.95313	89.56704	4.1581

Figure S12. HPLC chromatogram of enantioenriched ester **(*S*)-5** (90:10 e.r.). Biocatalytic conditions refer to acetylation of racemic alcohol **4** with *Lipase PS (Amano)* for 60 min (entry 5, Table 1 in the manuscript). From the optical rotatory power of the isolated species, it was deduced the following attributions: rt = 21.750 min: **(*S*)-5**; rt = 26.693 min: **(*S*)-4**; rt = 30.155 min: **(*R*)-4**; rt = 37.227 min: **(*R*)-5**.

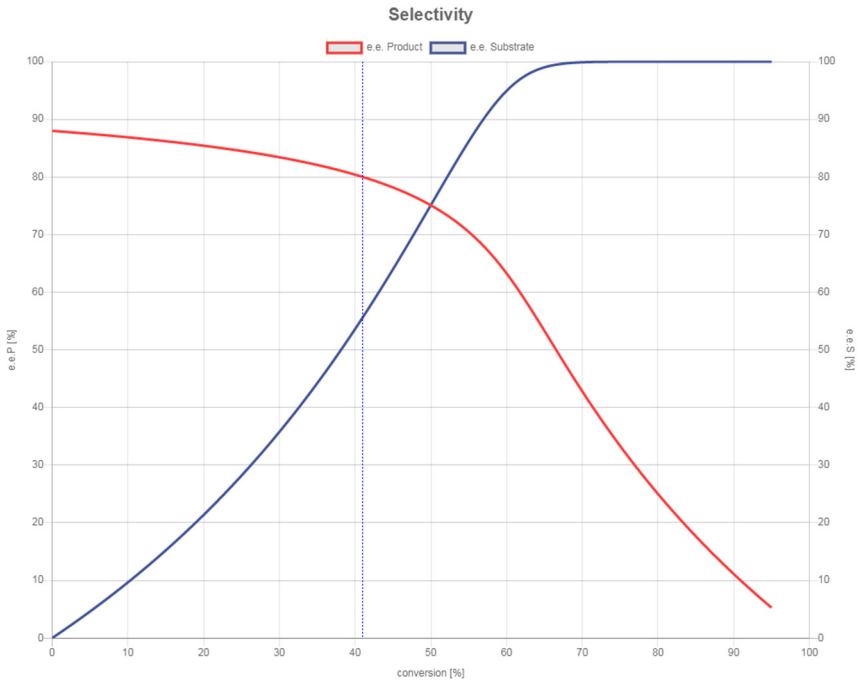


Figure S13. Selectivity profile for the acylation of **4** with *Lipase PS (Amano)*(reaction time 1h, conversion 41%, e.r 90:10) as calculated with the web-based "enantio" tool [1].

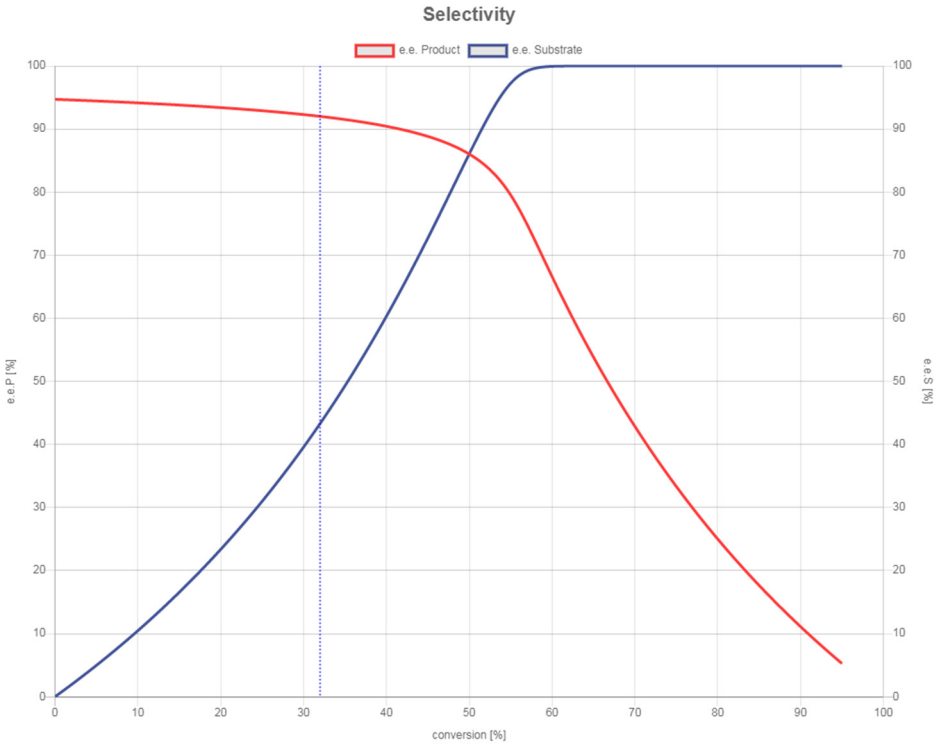


Figure S14. Selectivity profile for the hydrolysis of **5** with *Lipase PS (Amano)* (reaction time 0.5h, conversion 32%, e.r 96:4) as calculated with the web-based "enantio" tool [1].

This program can be used for the calculation of the selectivity of a kinetic resolution of a racemate, expressed as the "Enantiomeric Ratio"—the E-value (synonym for the selectivity "s"). The calculations are valid for irreversible reactions. For more detailed information on the theoretical background and of the merits and limits of the method see [2, 3].

References

1. Biocatalysis Tools Available online: http://biocatalysis.uni-graz.at/biocatalysis-tools/enantio (accessed on Dec 30, 2020).
2. Straathof, A.J.J.; Jongejan, J.A. The enantiomeric ratio: origin, determination and prediction. *Enzyme Microb. Technol*. **1997**, *21*, 559–571, doi:10.1016/S0141-0229(97)00066-5.
3. Faber, K. *Biotransformations in Organic Chemistry*; 7th edition; Springer Berlin Heidelberg: Heidelberg, Germany, **2018**, pp. 39–43.