

Supplementary Information

Microwave-Assisted vs. Conventional Knoevenagel-Doebner Condensation for the Synthesis of 3-Arylacrylic Acids: a Pyridine-Rationalized Approach

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Experimental section

Base effect

Table S1. Effect of bases and base mixtures on the synthesis of acrylic acid (**2c**)

entry	Yield ^a / %				time / min
	Py (MW)	Py (CM)	TEA (MW)	TEA + Py ^b (MW)	
1	5	—	—	—	10
2	15	—	—	3	15
3	45	5	5	5	20
4	80	12	12	20	25
5	98	35	75	80	60

Conditions: compound **2c** (1 mmol), malonic acid (2 mmol), pyridine (400 μ L, ca. 50 mmol), 80 $^{\circ}$ C. CM: conventional heating, 8 h; MW: microwave irradiation, 1 h. ^aIsolated yields; ^b200 μ L triethylamine (TEA) and 200 μ L pyridine (Py).

Nuclear magnetic resonance spectra

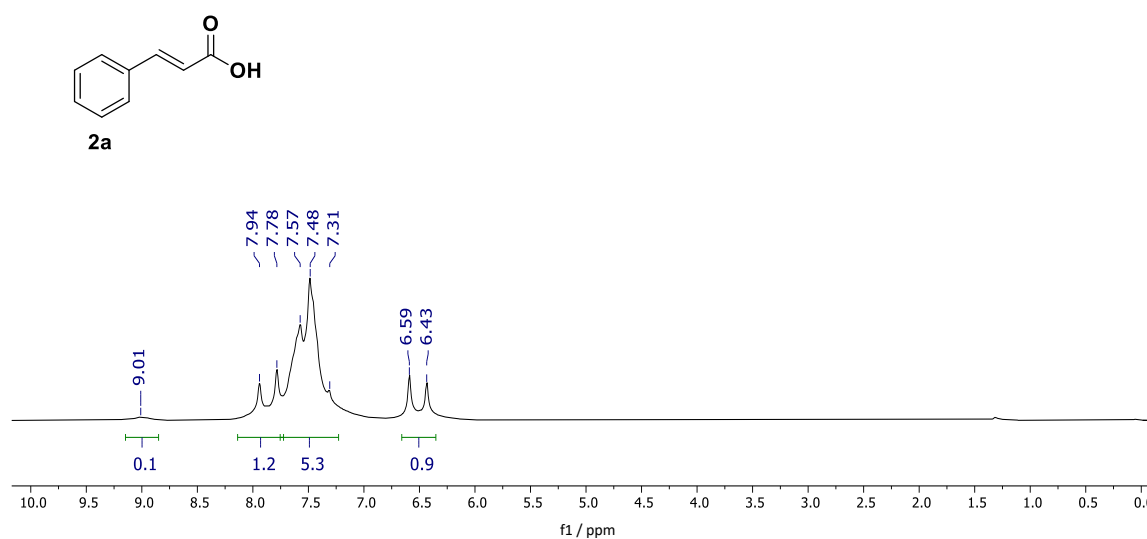


Figure S1. ¹H NMR spectrum (100 MHz, CDCl₃) of cinnamic acid (**2a**).

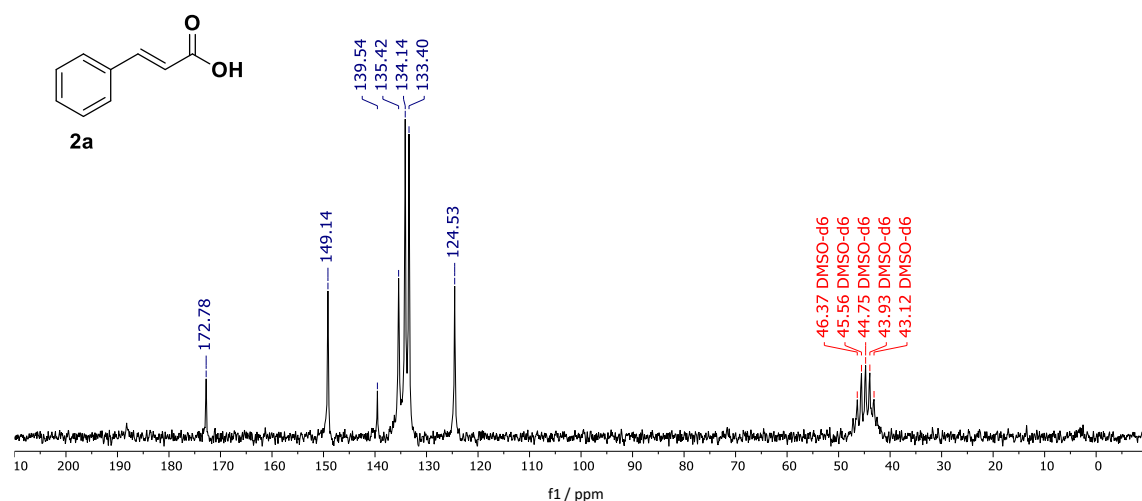


Figure S2. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆) of cinnamic acid (**2a**).

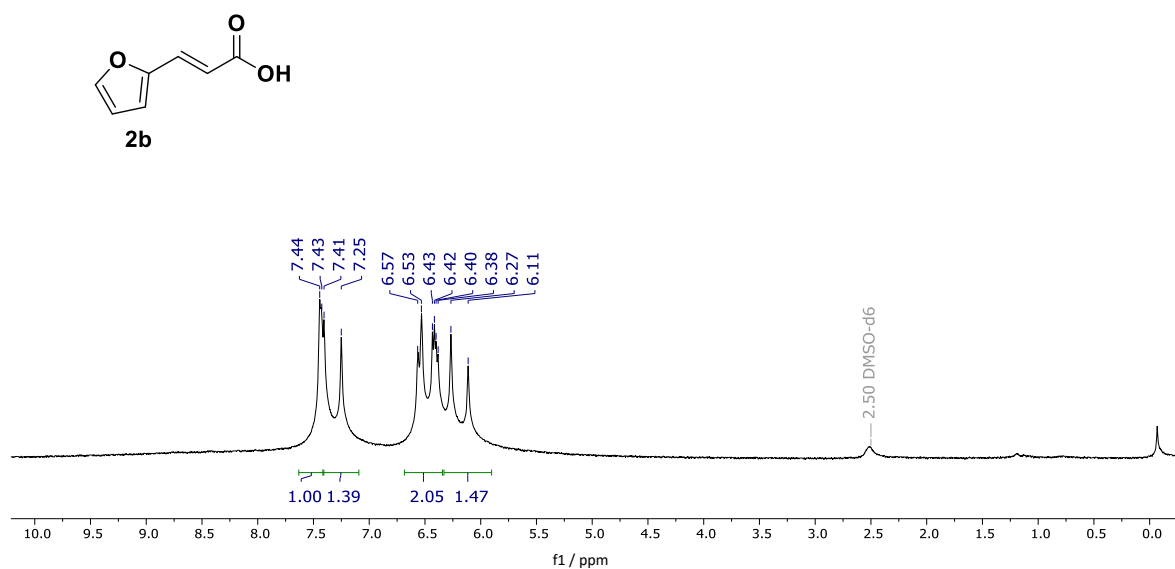


Figure S3. ¹H NMR spectrum (100 MHz, DMSO-*d*₆) of (*E*)-3-(furan-2-yl)acrylic acid (**2b**).

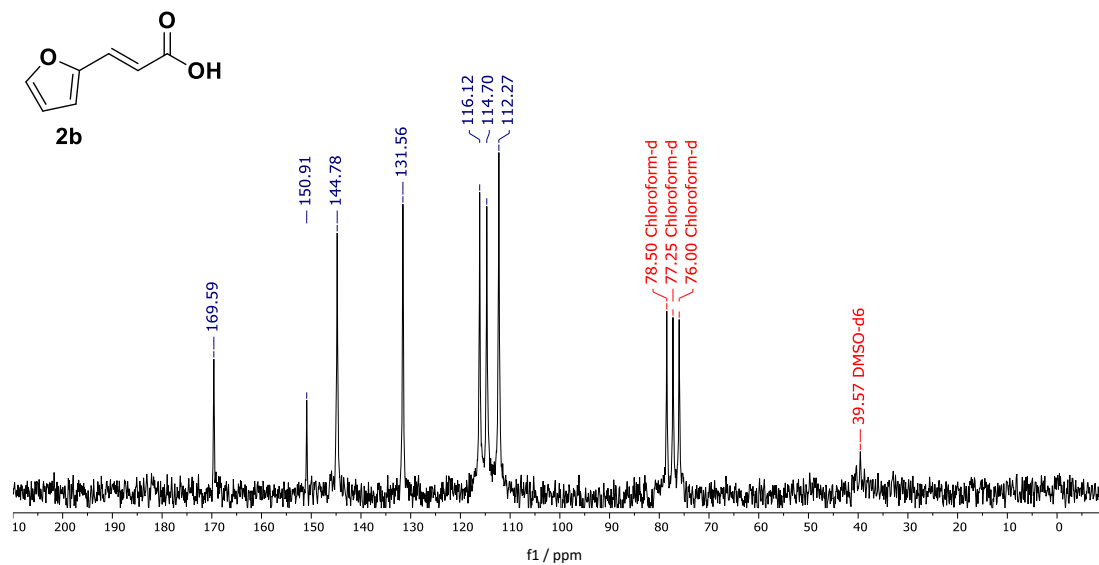


Figure S4. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆) of (*E*)-3-(furan-2-yl)acrylic acid (**2b**).

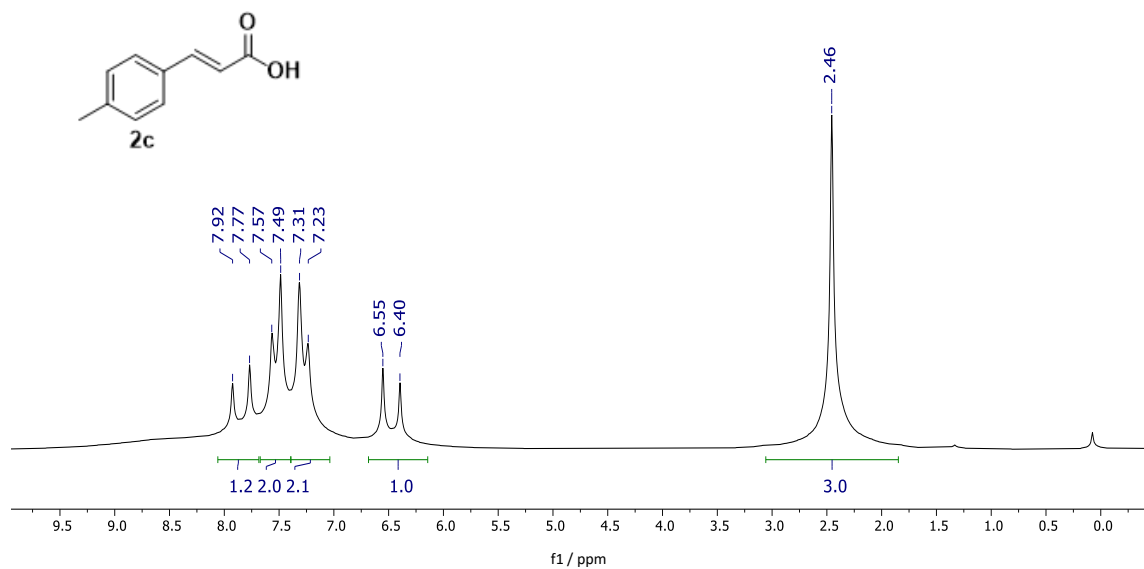


Figure S5. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(*p*-tolyl) acrylic acid (**2c**).

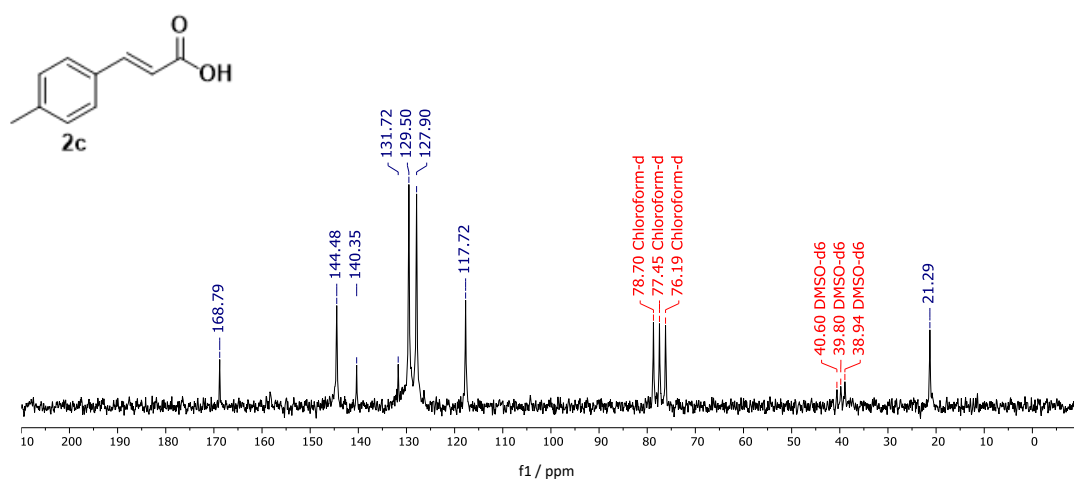


Figure S6. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(*p*-tolyl)acrylic acid (**2c**).

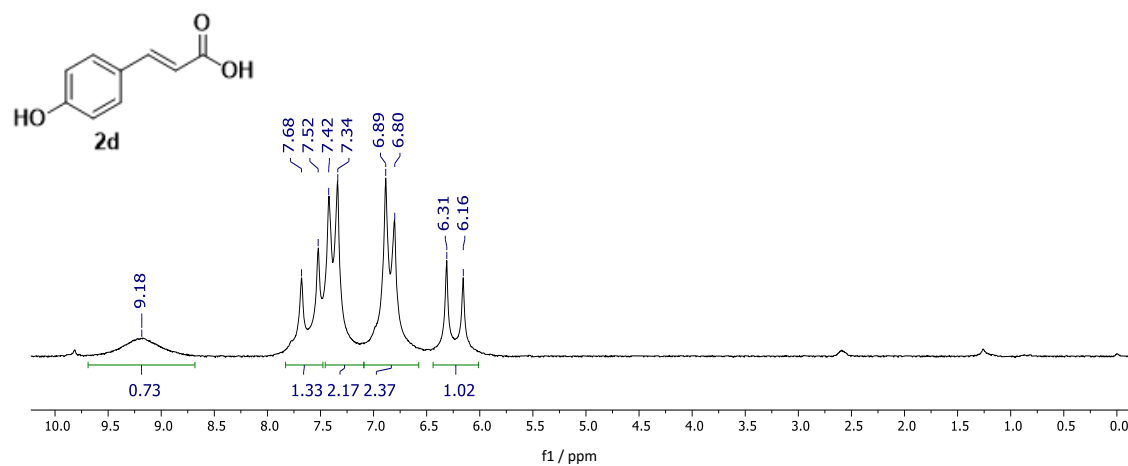


Figure S7. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-hydroxyphenyl)acrylic acid (**2d**).

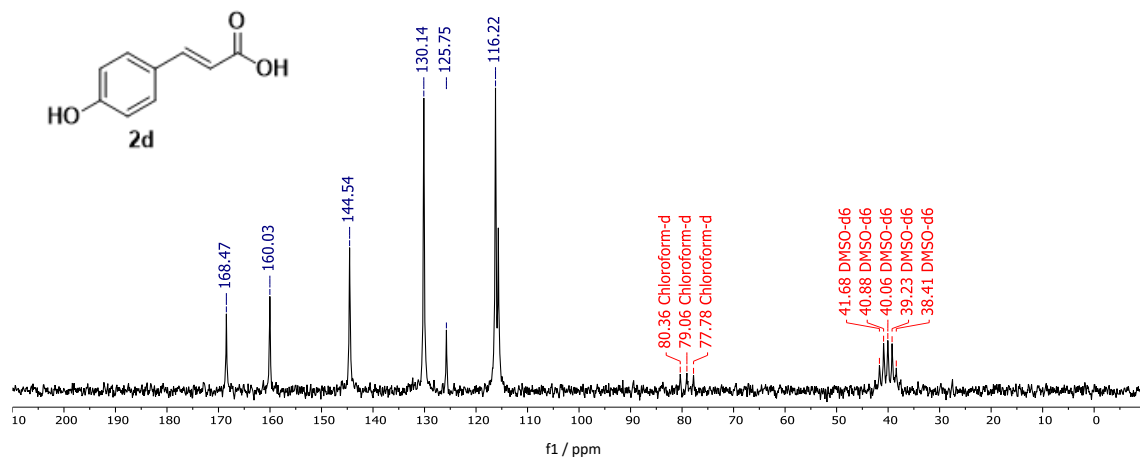


Figure S8. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-hydroxyphenyl)acrylic acid (**2d**).

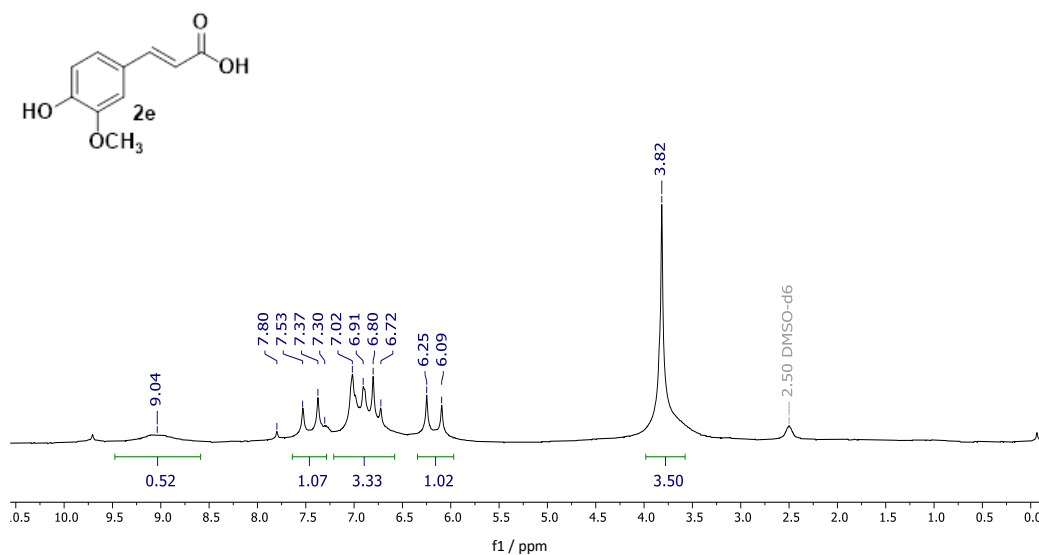


Figure S9. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylic acid (**2e**).

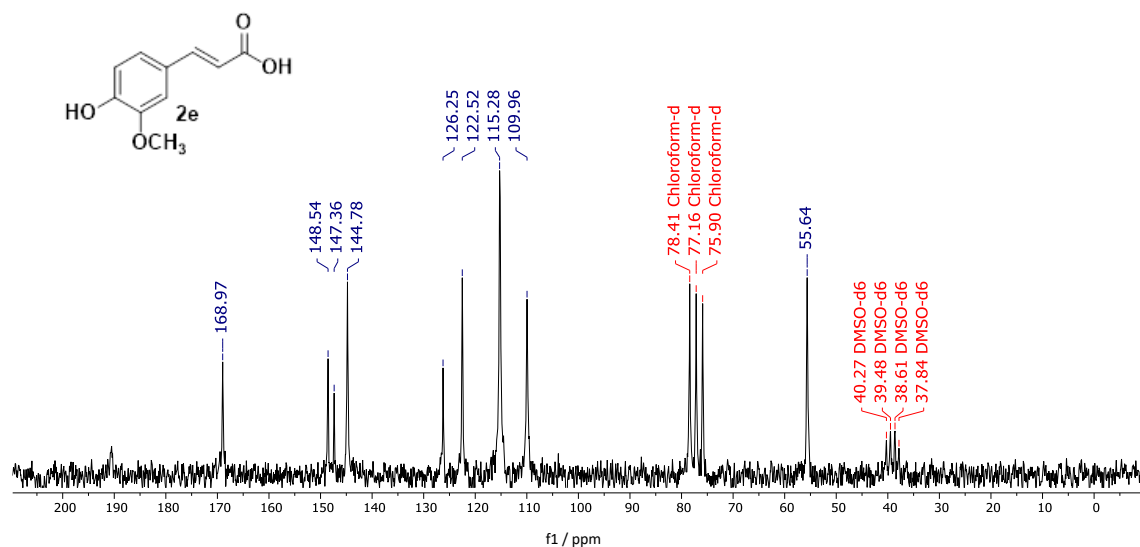


Figure S10. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-hydroxy-3-methoxyphenyl) acrylic acid (**2e**).

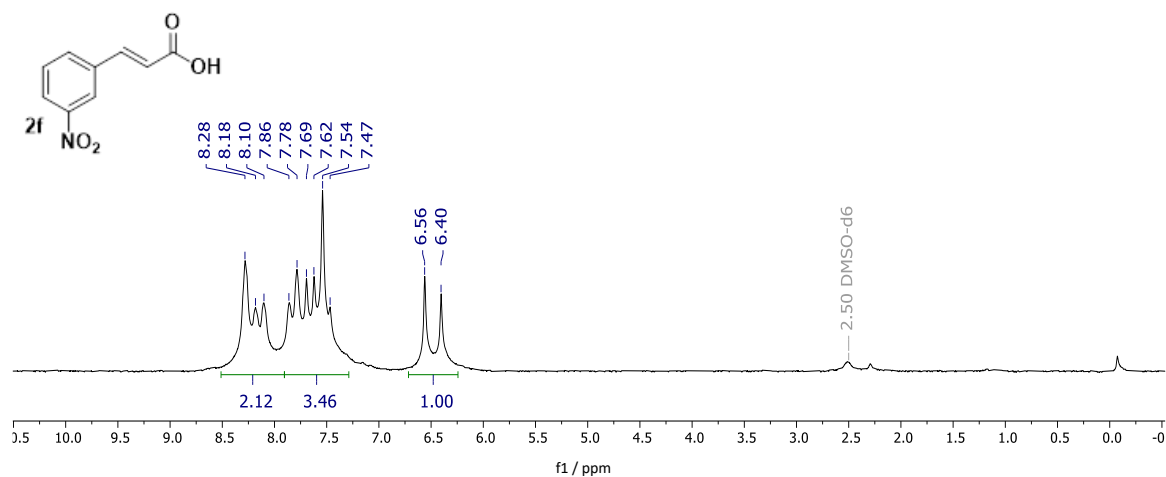


Figure S11. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(3-nitrophenyl)acrylic acid (**2f**).

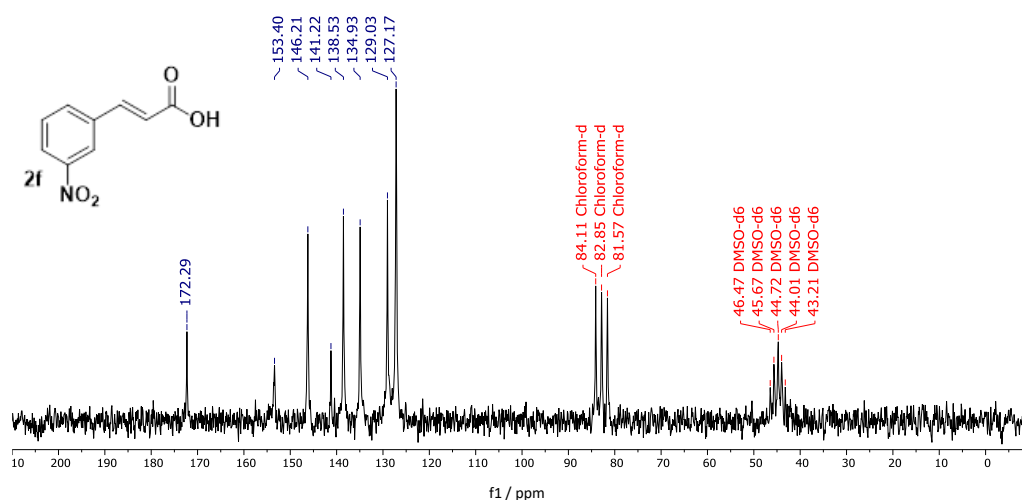


Figure S12. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(3-nitrophenyl)acrylic acid (**2f**).

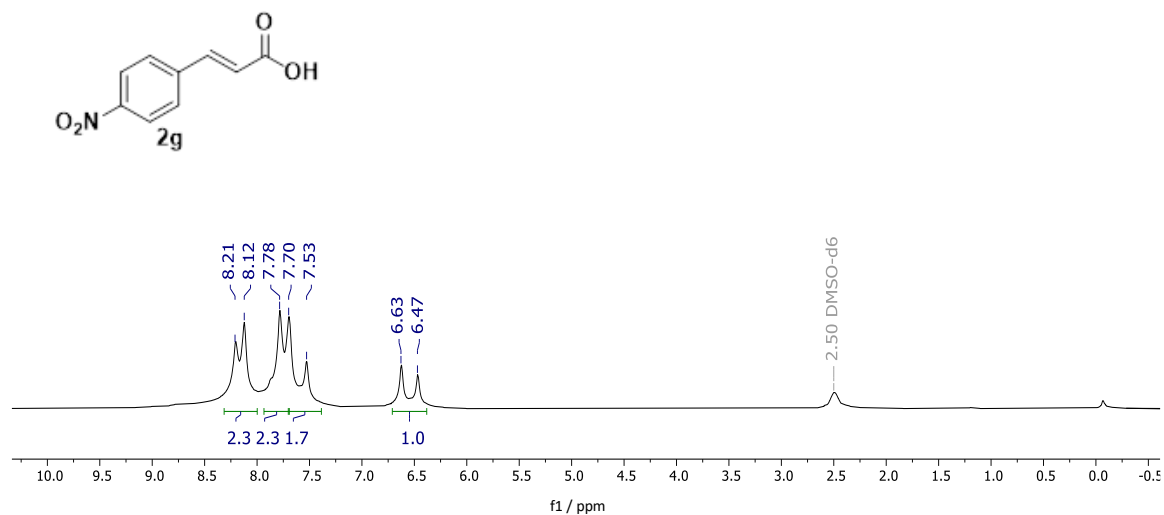


Figure S13. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of *(E)*-3-(4-nitrophenyl)acrylic acid (**2g**).

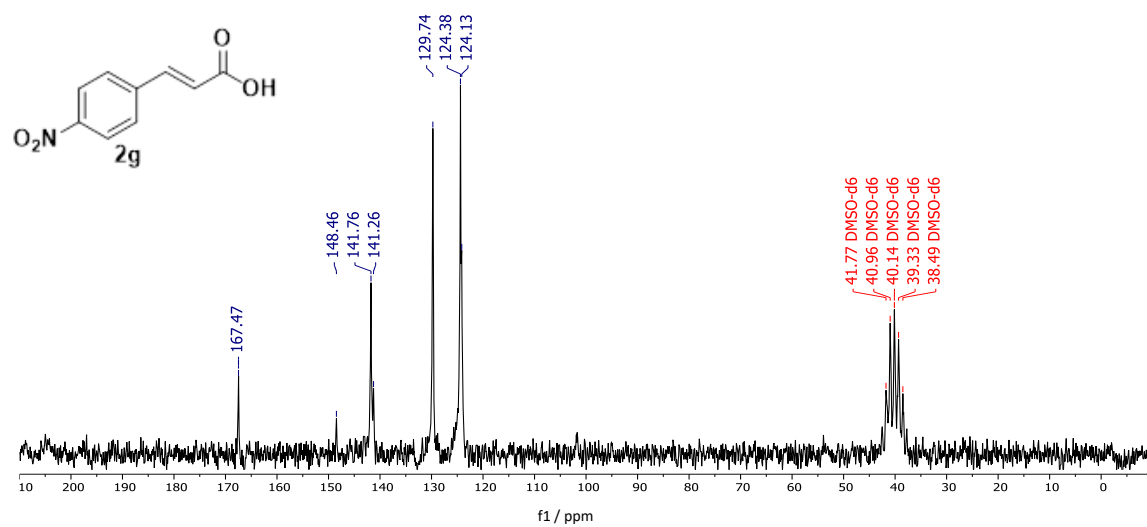


Figure S14. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of *(E)*-3-(4-nitrophenyl)acrylic acid (**2g**).

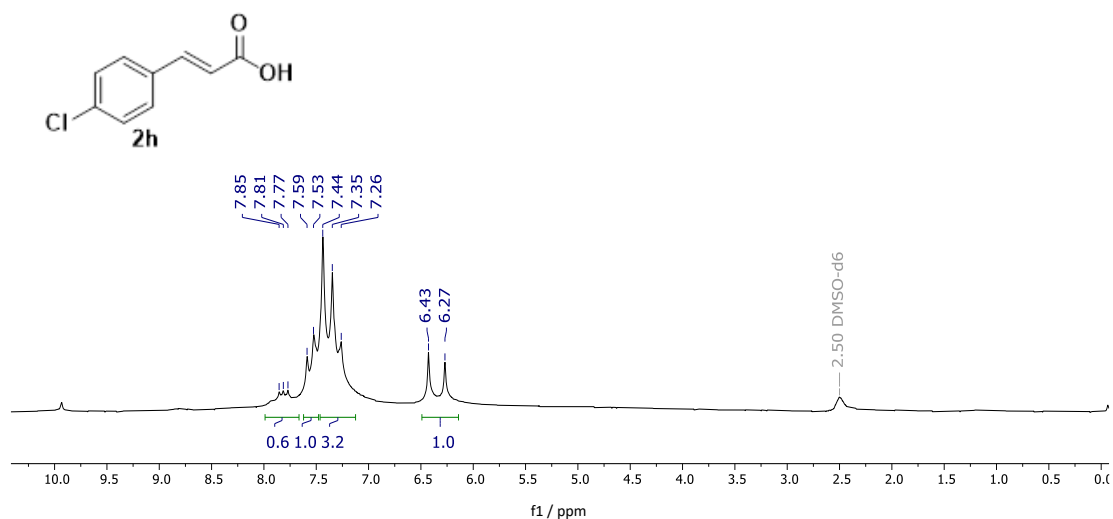


Figure S15. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-chlorophenyl)acrylic acid (**2h**).

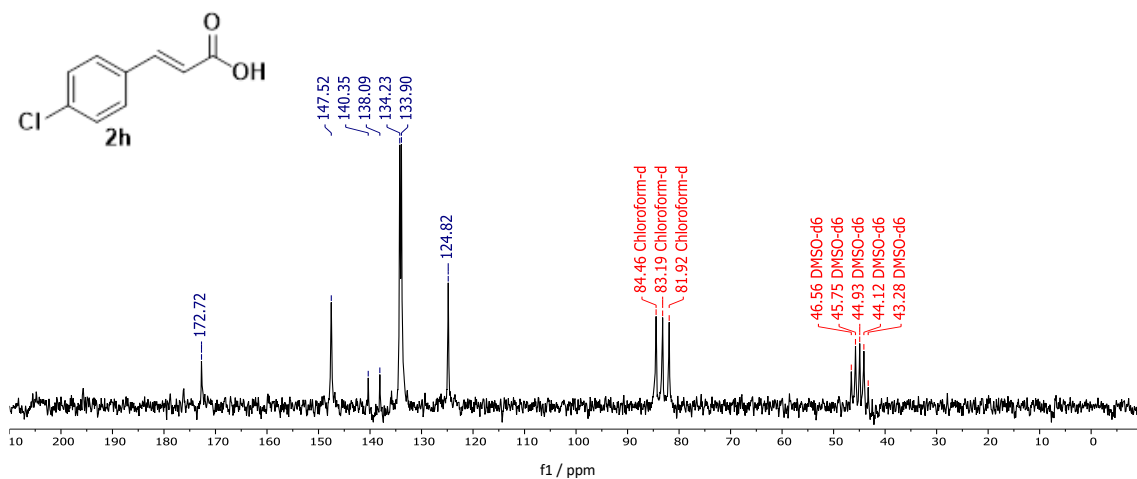


Figure S16. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(4-chlorophenyl)acrylic acid (**2h**).

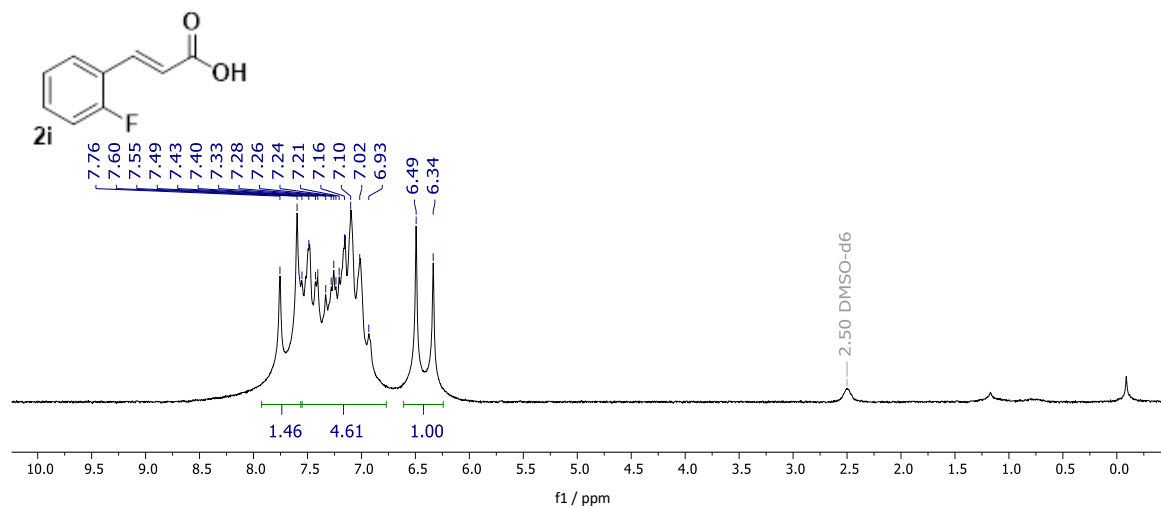


Figure S17. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(2-fluorophenyl)acrylic acid (**2i**).¹

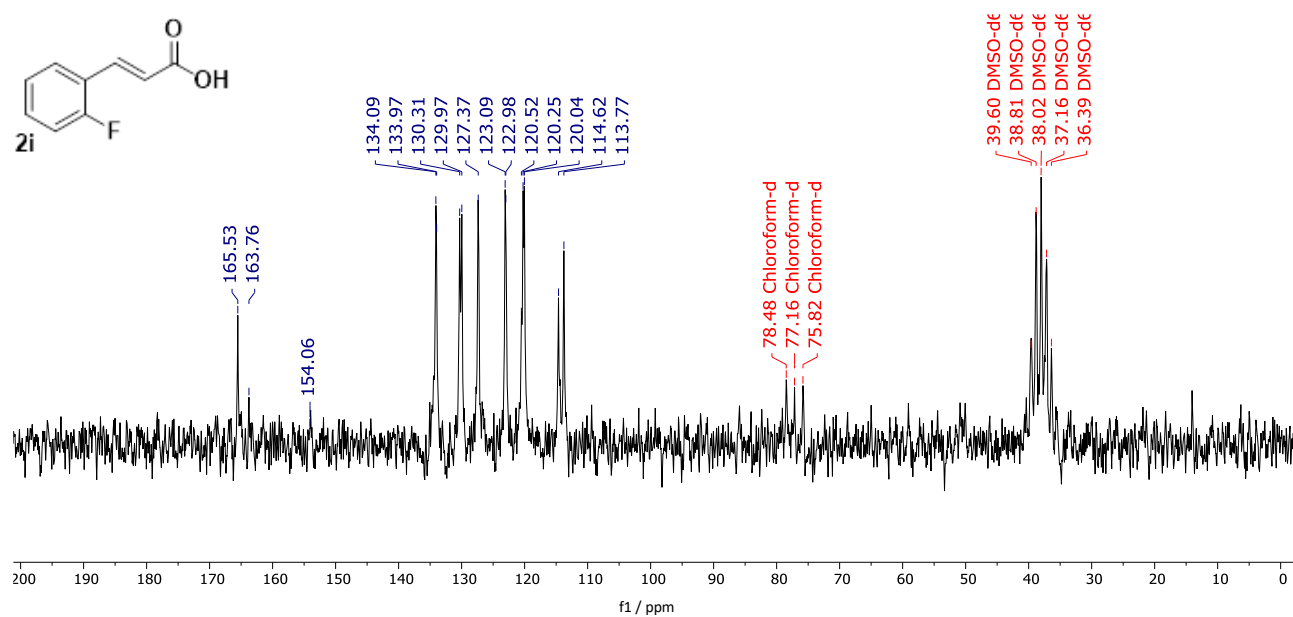


Figure S18. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (*E*)-3-(2-fluorophenyl)acrylic acid (**2i**).¹

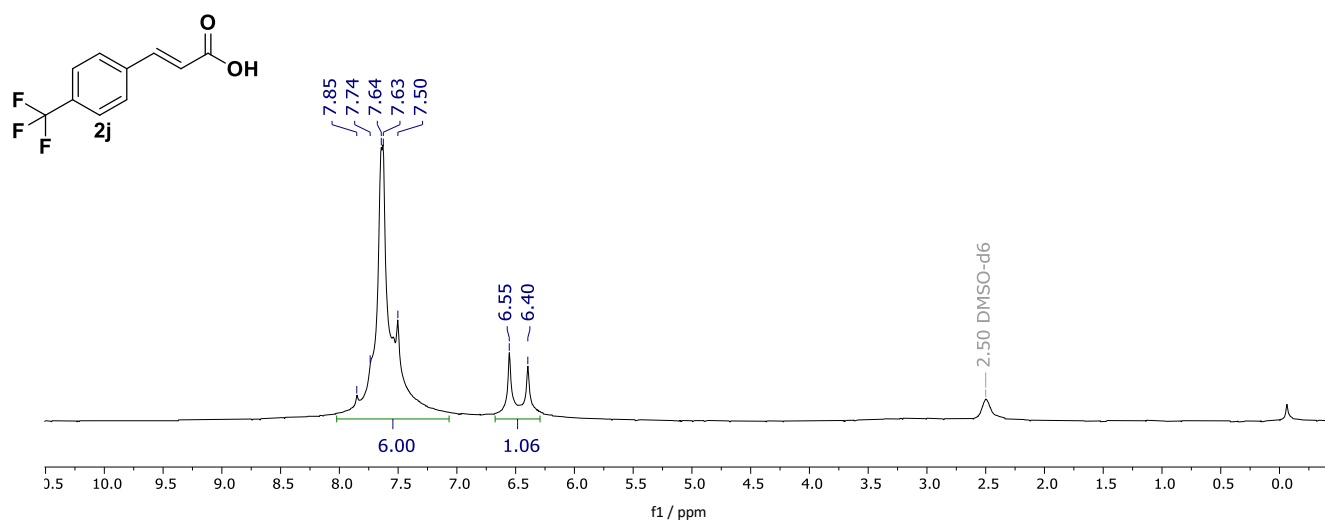


Figure S19. ¹H NMR spectrum (100 MHz, DMSO-*d*₆) of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylic acid (**2j**).²

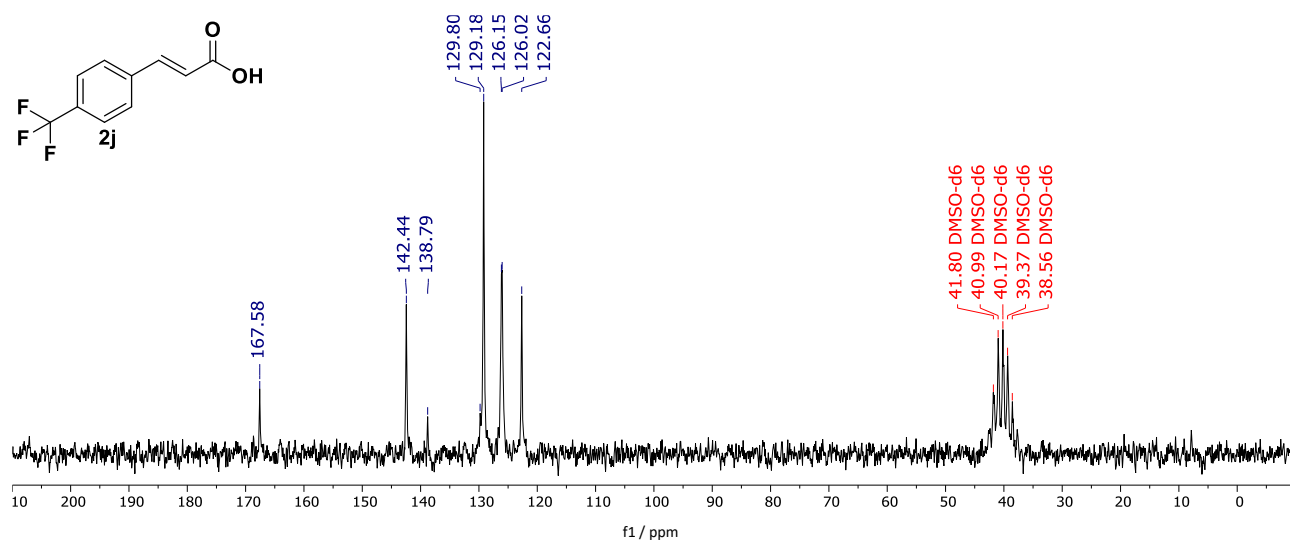


Figure S20. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆) of (*E*)-3-(4-(trifluoromethyl)phenyl) acrylic acid (**2j**).²

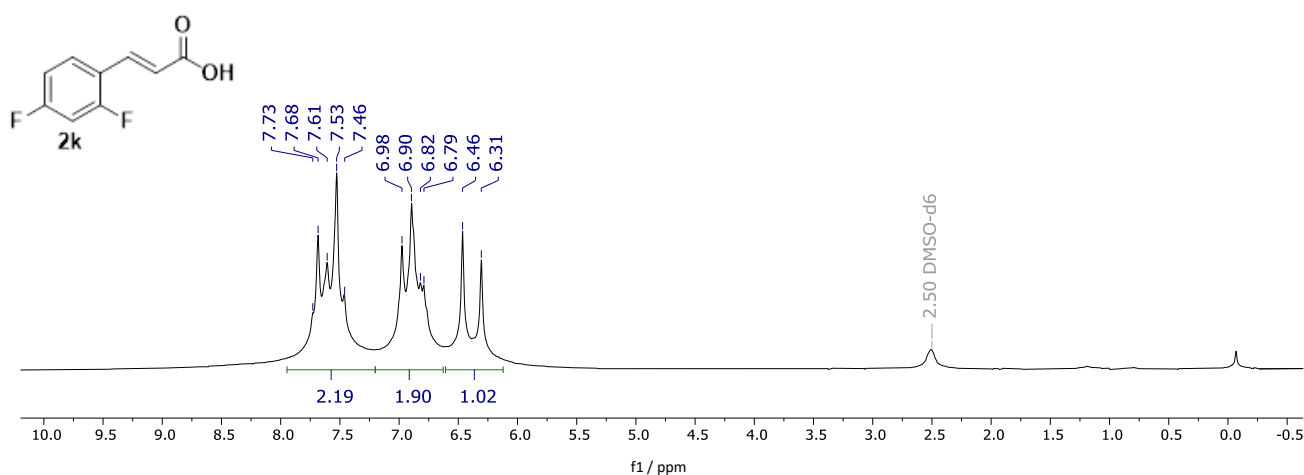


Figure S21. ¹H NMR spectrum (100 MHz, DMSO-*d*₆) of (*E*)-3-(2,4-difluorophenyl) acrylic acid (**2k**).¹

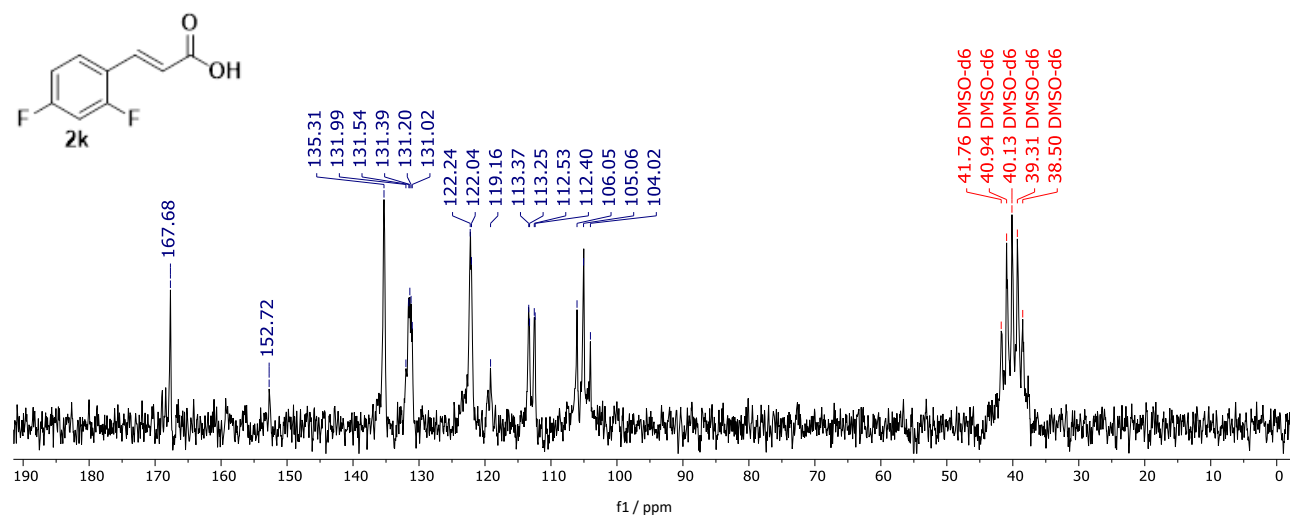


Figure S22. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆) of (*E*)-3-(2,4-difluorophenyl) acrylic acid (**2k**).¹

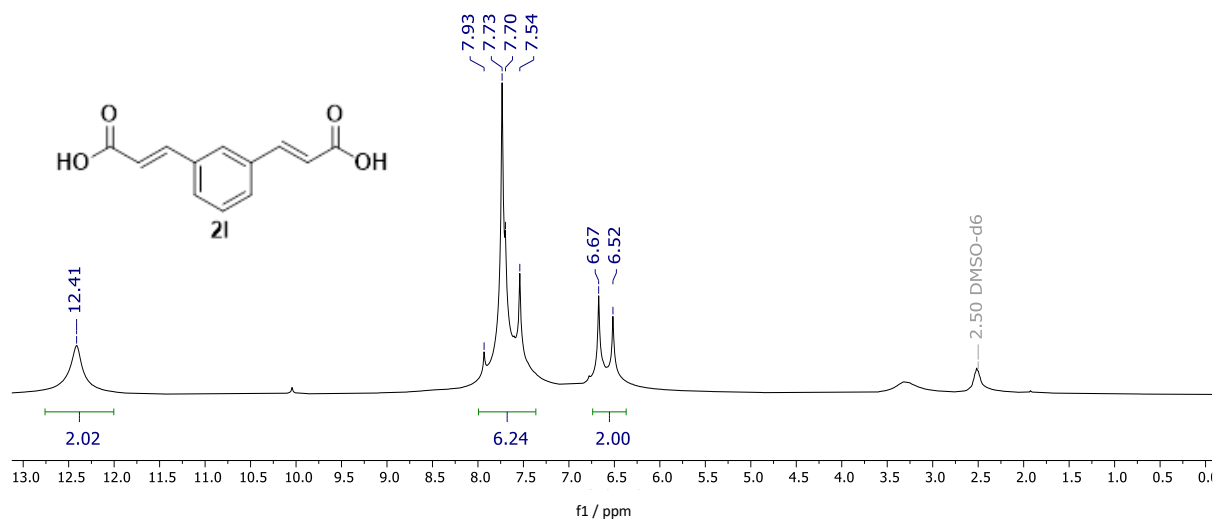


Figure S23. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (**2E,2'E**)-3,3'-(1,3-phenylene) diacrylic acid (**2I**).

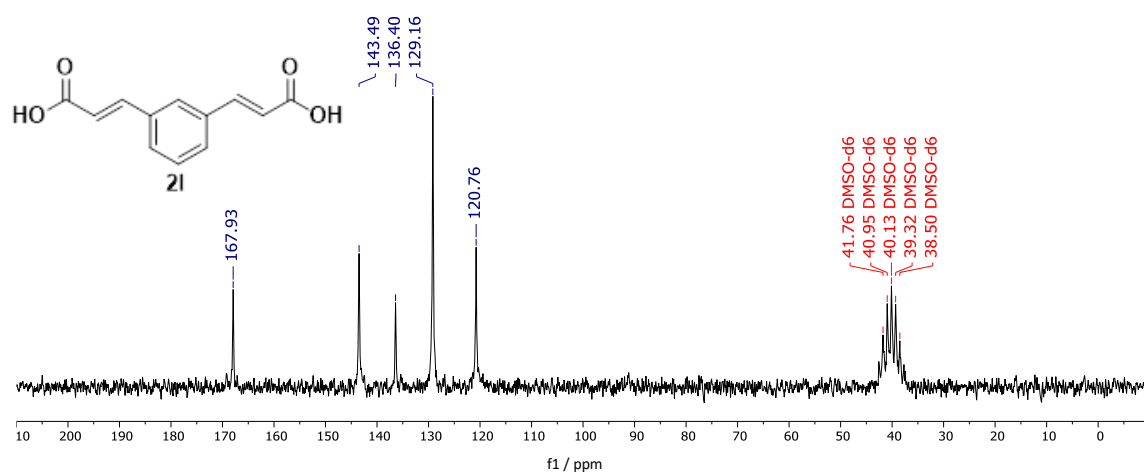


Figure S24. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (**2E,2'E**)-3,3'-(1,3-phenylene) diacrylic acid (**2I**).

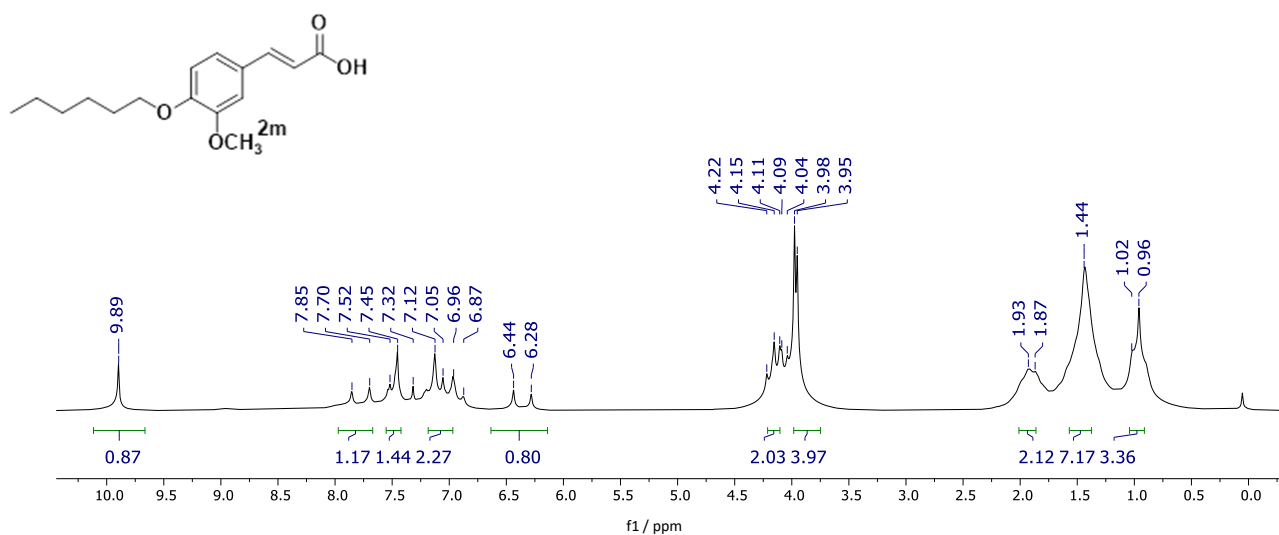


Figure S25. ¹H NMR spectrum (100 MHz, DMSO-*d*₆ and CDCl₃) of (E)-3-(4-(hexyloxy)-3-methoxyphenyl)acrylic acid (2m).

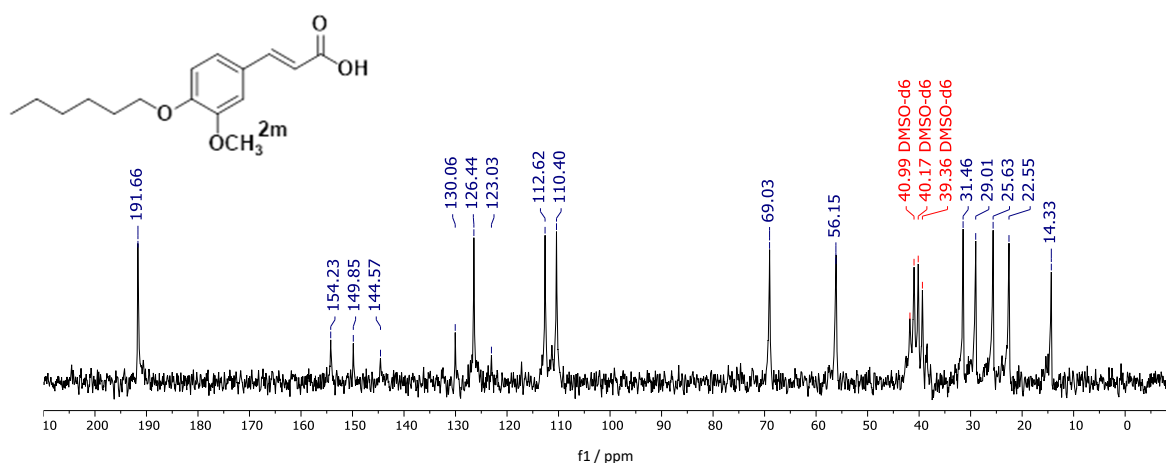


Figure S26. ¹³C NMR spectrum (25 MHz, DMSO-*d*₆ and CDCl₃) of (E)-3-(4-(hexyloxy)-3-methoxyphenyl)acrylic acid (2m).

Mass spectra

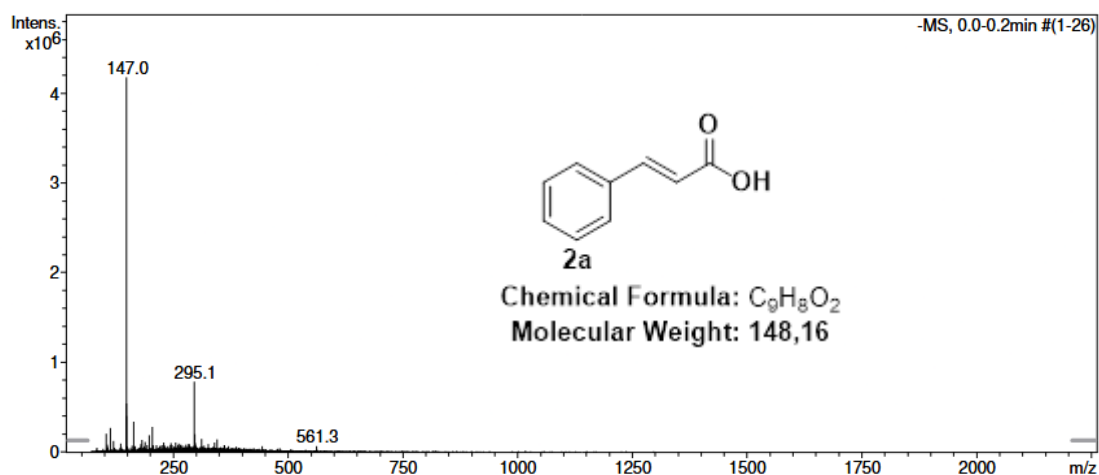


Figure S27. Mass spectrum (negative mode) of cinnamic acid (**2a**).

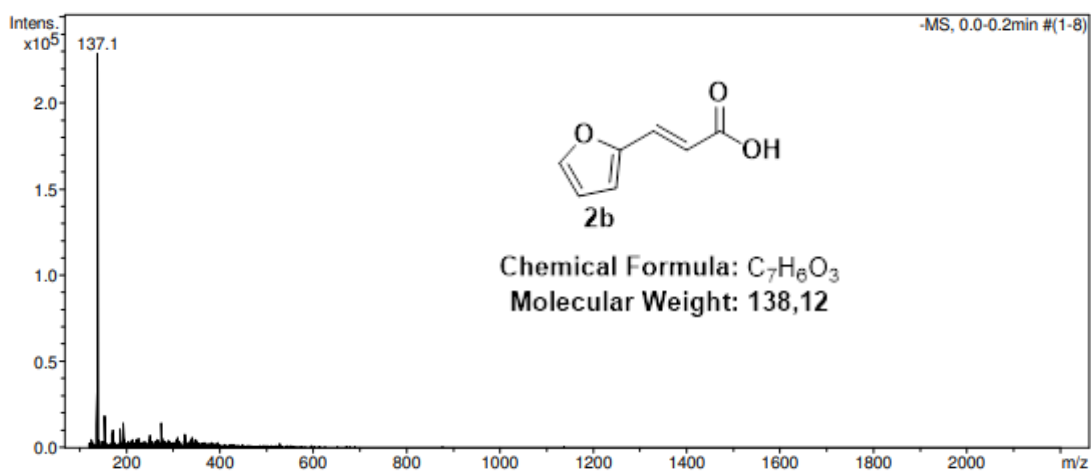


Figure S28. Mass spectrum (negative mode) of (*E*)-3-(furan-2-yl)acrylic acid (**2b**).

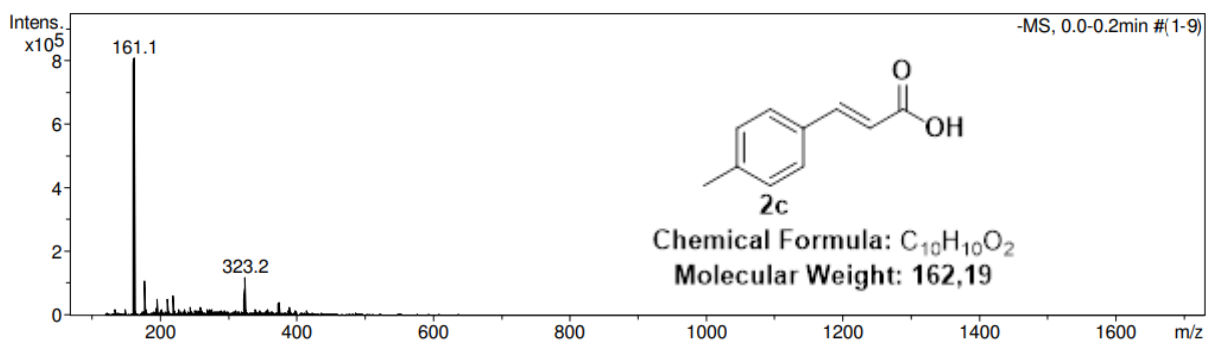


Figure S29. Mass spectrum (negative mode) of (*E*)-3-(*p*-tolyl)acrylic acid (**2c**).

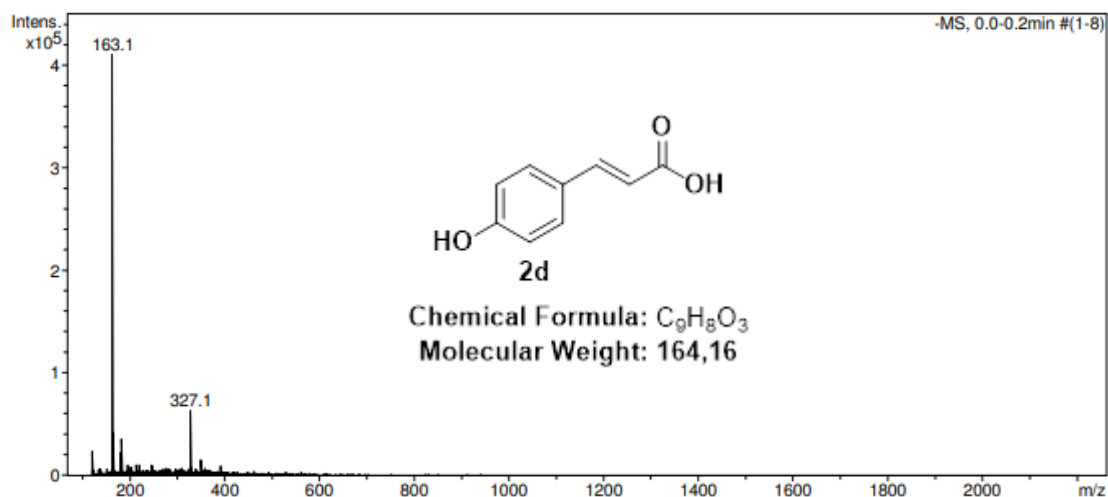


Figure S30. Mass spectrum (negative mode) of (*E*)-3-(4-hydroxyphenyl)acrylic acid (**2d**).

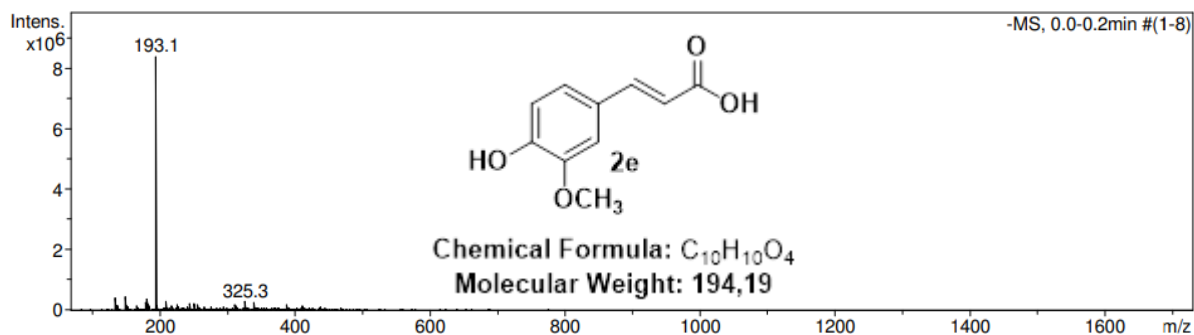


Figure S31. Mass spectrum (negative mode) of (*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylic acid (**2e**).

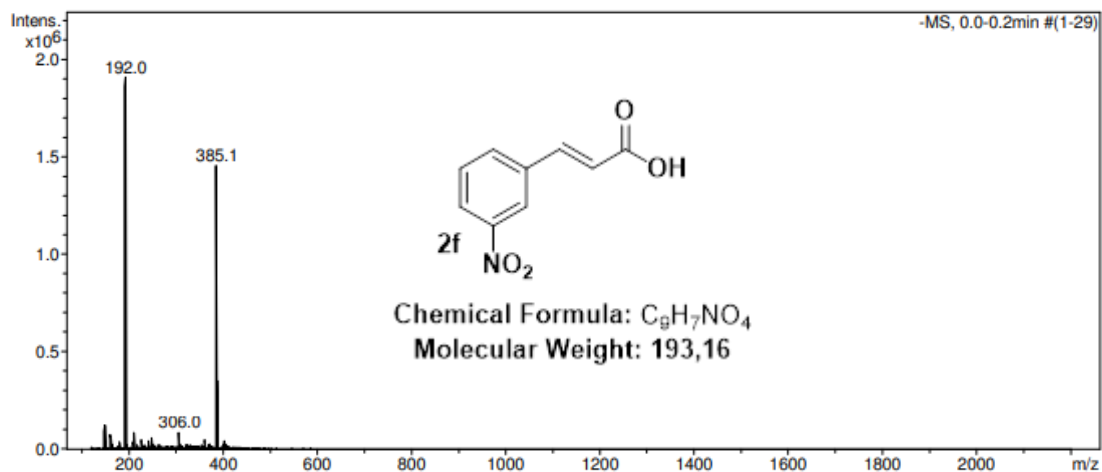


Figure S32. Mass spectrum (negative mode) of (*E*)-3-(3-nitrophenyl)acrylic acid (**2f**).

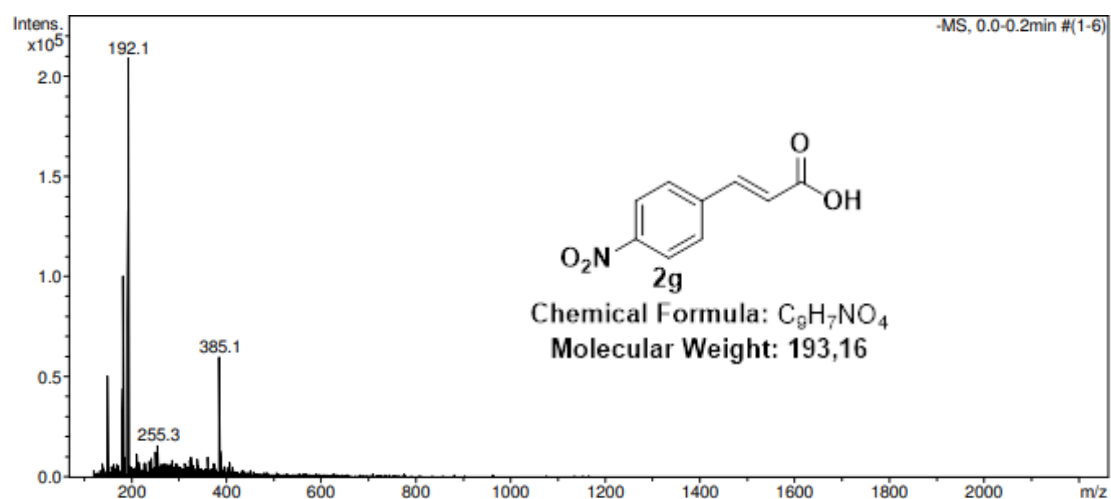


Figure S33. Mass spectrum (negative mode) of (*E*)-3-(4-nitrophenyl)acrylic acid (**2g**).

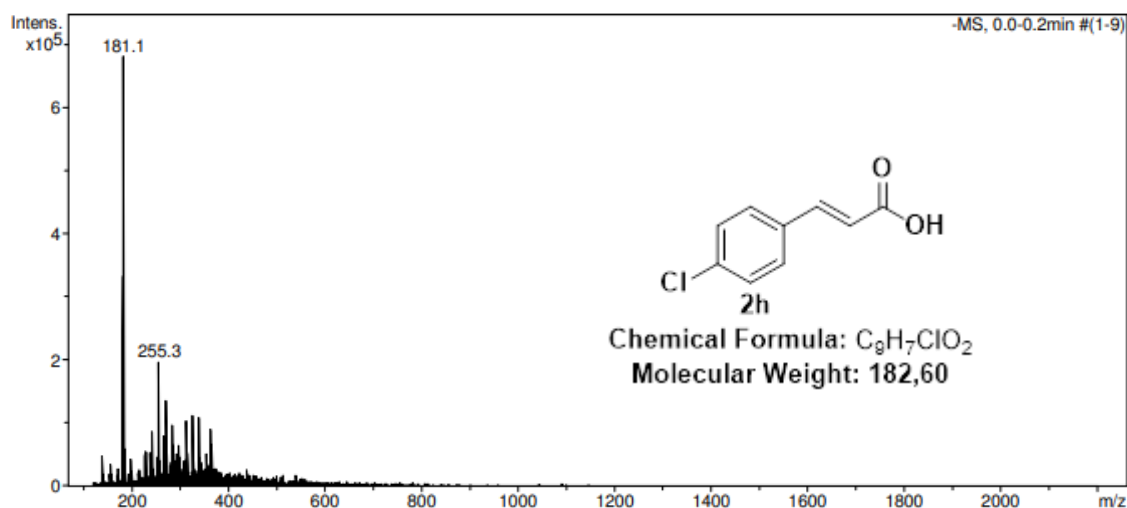


Figure S34. Mass spectrum (negative mode) of (*E*)-3-(4-chlorophenyl)acrylic acid (**2h**).

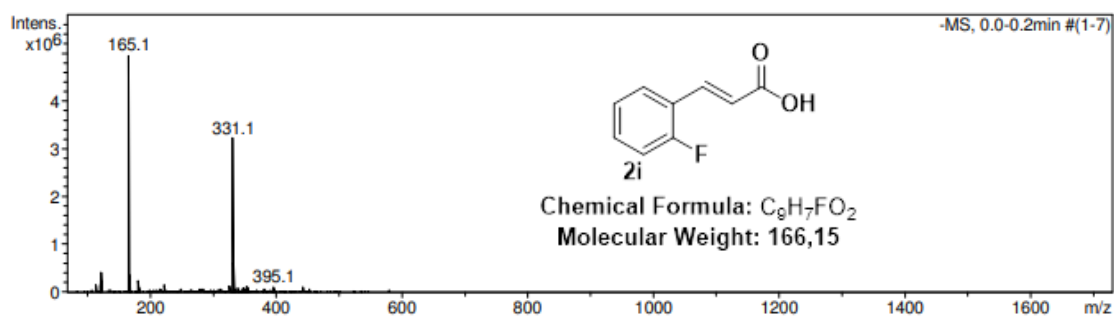


Figure S35. Mass spectrum (negative mode) of (*E*)-3-(2-fluorophenyl)acrylic acid (**2i**).

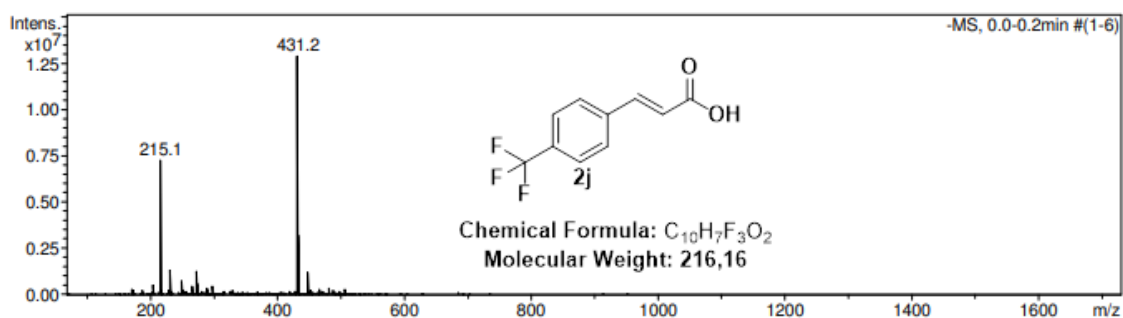


Figure S36. Mass spectrum (negative mode) of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylic acid (**2j**).

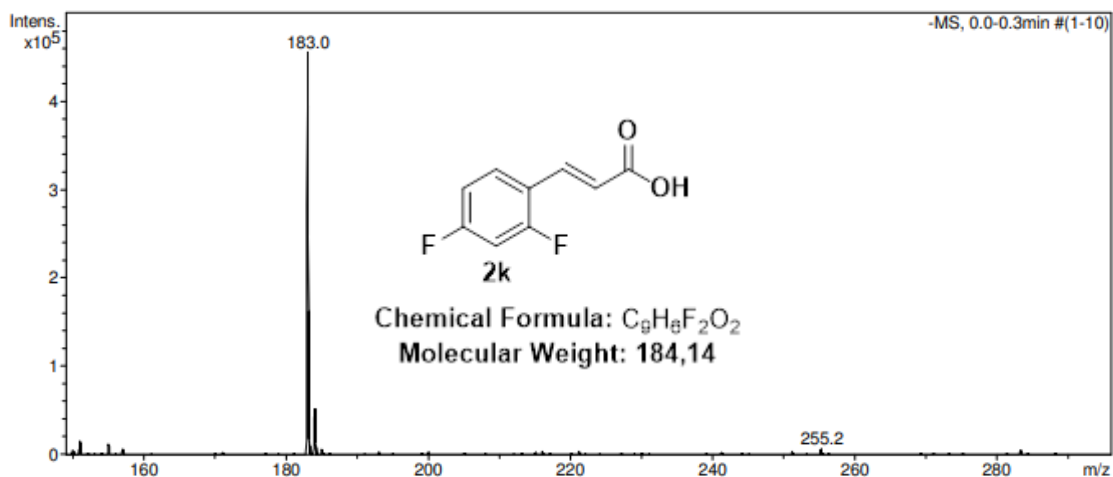


Figure S37. Mass spectrum (negative mode) of (*E*)-3-(2,4-difluorophenyl)acrylic acid (**2k**).

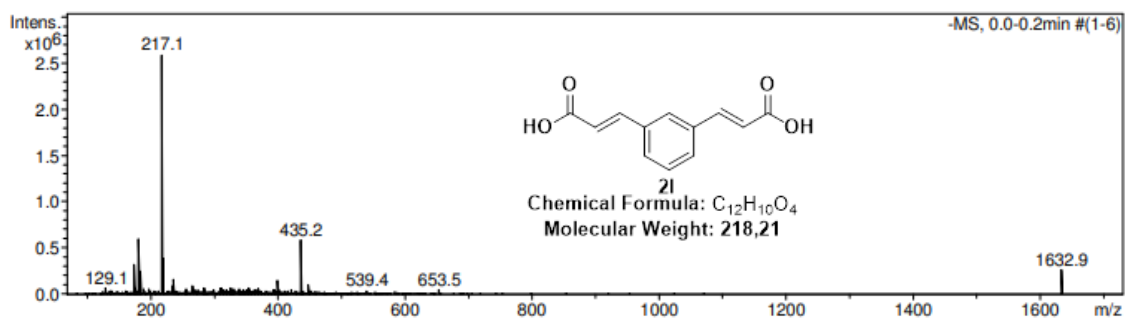


Figure S38. Mass spectrum (negative mode) of (*2E,2'E*)-3,3'-(1,3-phenylene)diacrylic acid (**2l**).

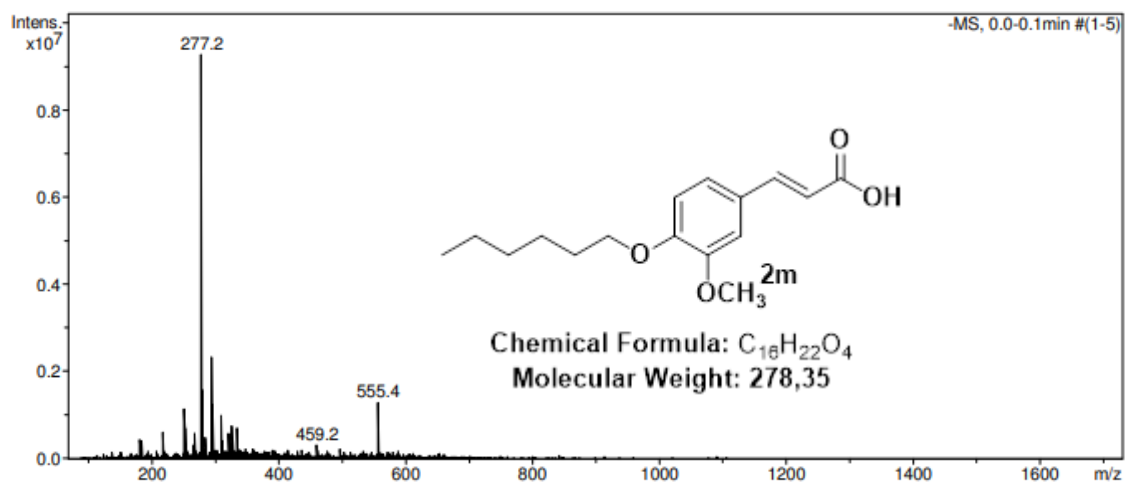


Figure S39. Mass spectrum (negative mode) of (*E*)-3-(4-(hexyloxy)-3-methoxyphenyl)acrylic (**2m**).

==== Shimadzu LCsolution Analysis Report ====

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Sample ID : Emmanuel
Tray# : 1
Vial # : 1
Injection Volume : 20 µL
Data File Name : 2c_diluido2.lcd
Method File Name : Isocratico, 1.0 mL, 20 min - ACN_H2O_85_20.lcm
Batch File Name :
Report File Name : Default.lcr
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Data Processed : 11/05/2026 13:20:41

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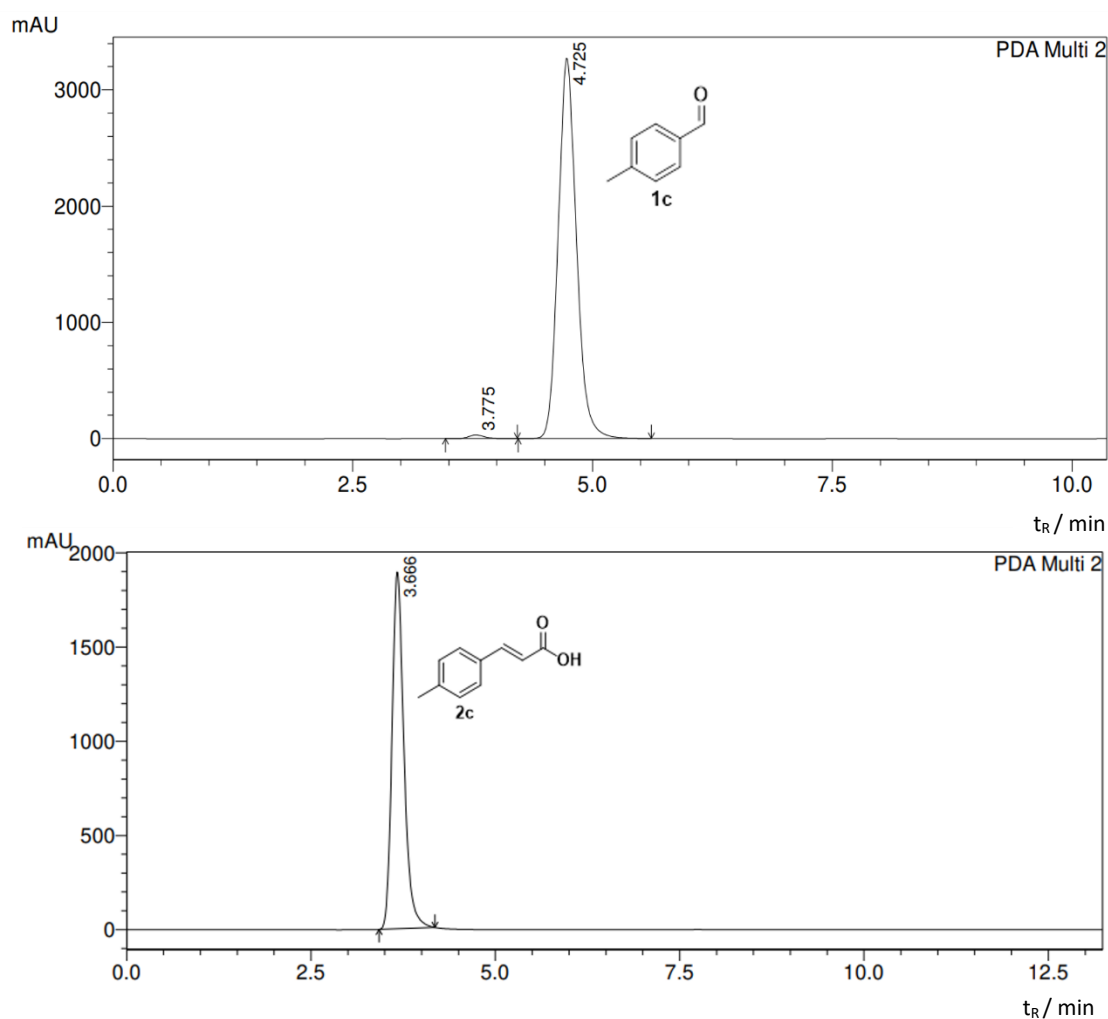


Figure S40. Comparative chromatogram of the retention time of reagent **1c** (t_R 4.725 min) and compound **2c** (t_R 3.666 min) at 254 nm.

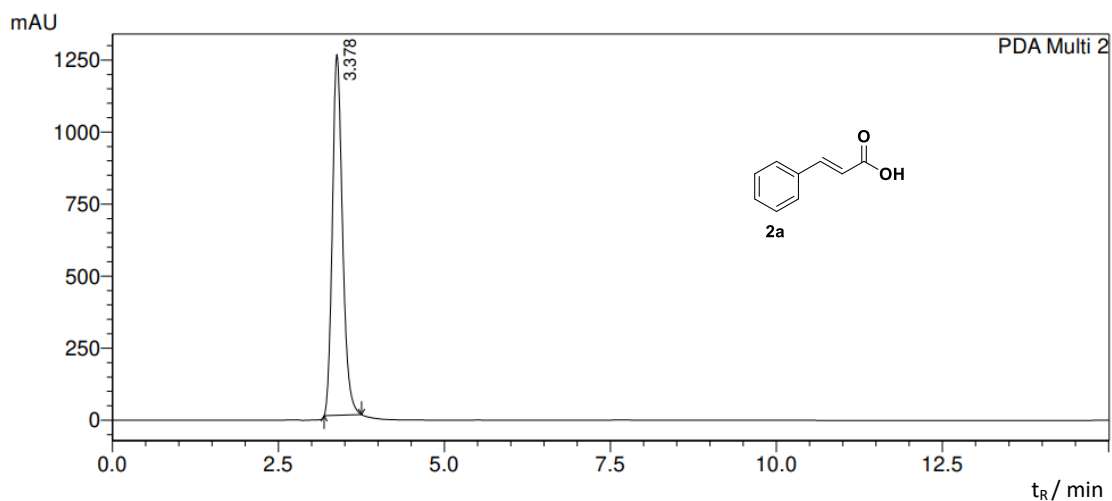


Figure S41. Chromatogram of compound **2a** at 254 nm and t_R 3.378 min.

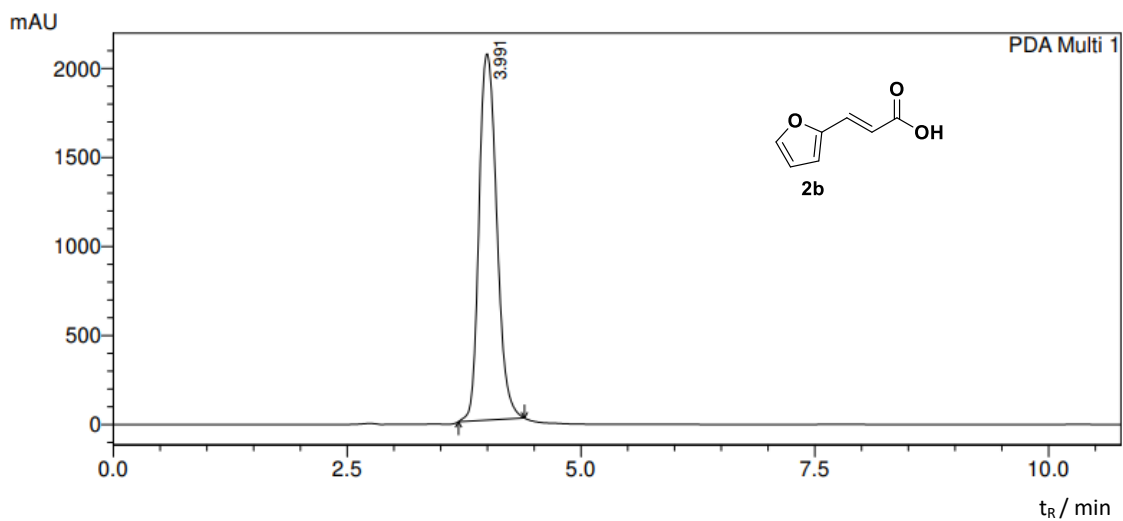


Figure S42. Chromatogram of compound **2b** at 220 nm and t_R 3.99 min.

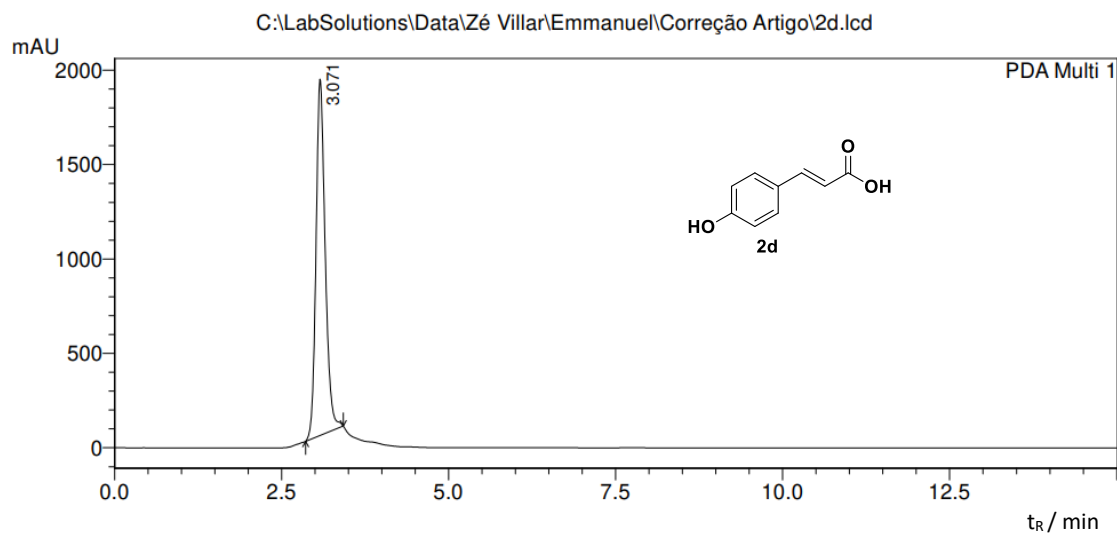


Figure S43. Chromatogram of compound **2d** at 220 nm and t_R 3.071 min.

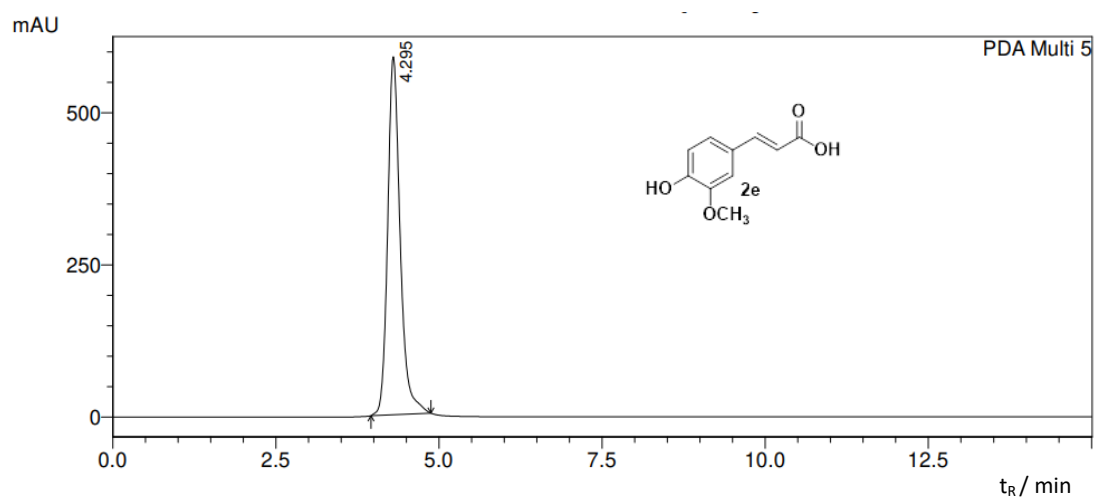


Figure S44. Chromatogram of compound **2e** at 254 nm and t_R 4.295 min.

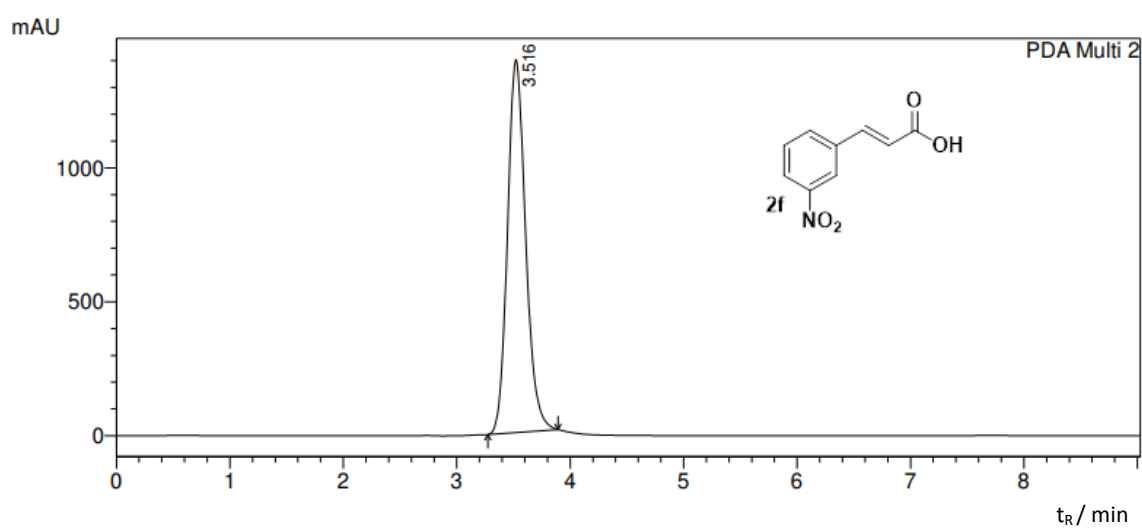


Figure S45. Chromatogram of compound **2f** at 254 nm and t_R 3.51 min.

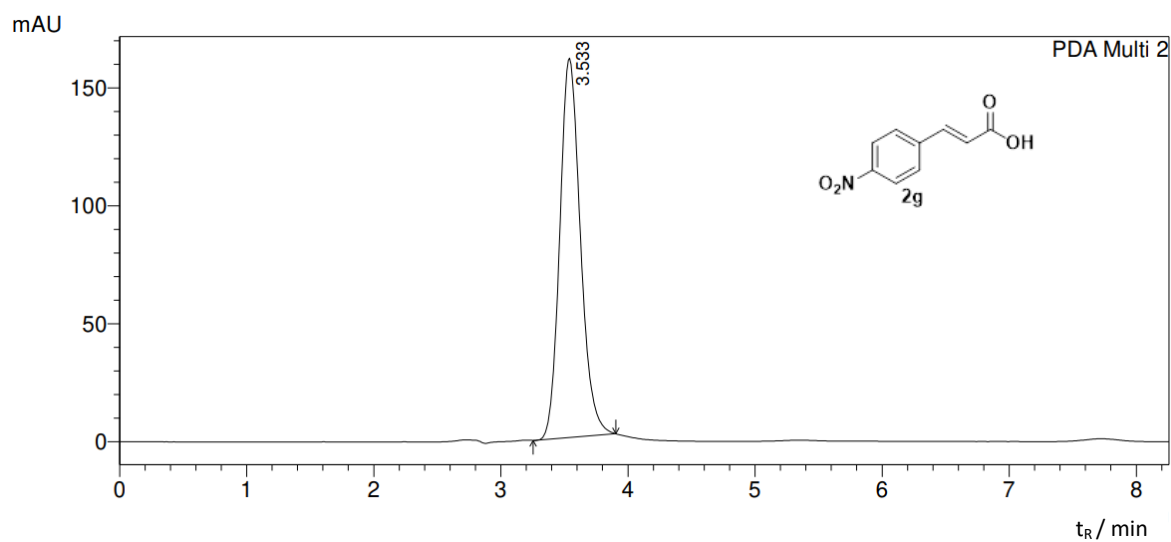


Figure S46. Chromatogram of compound **2g** at 254 nm and t_R 3.533 min.

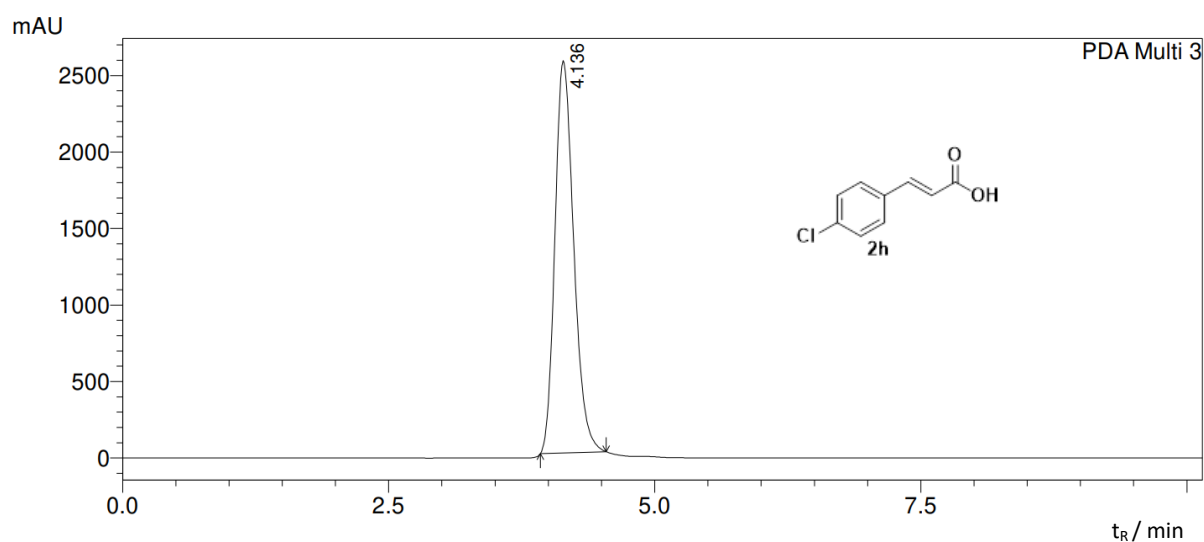


Figure S47. Chromatogram of compound **2h** at 280 nm and t_R 4.136 min.

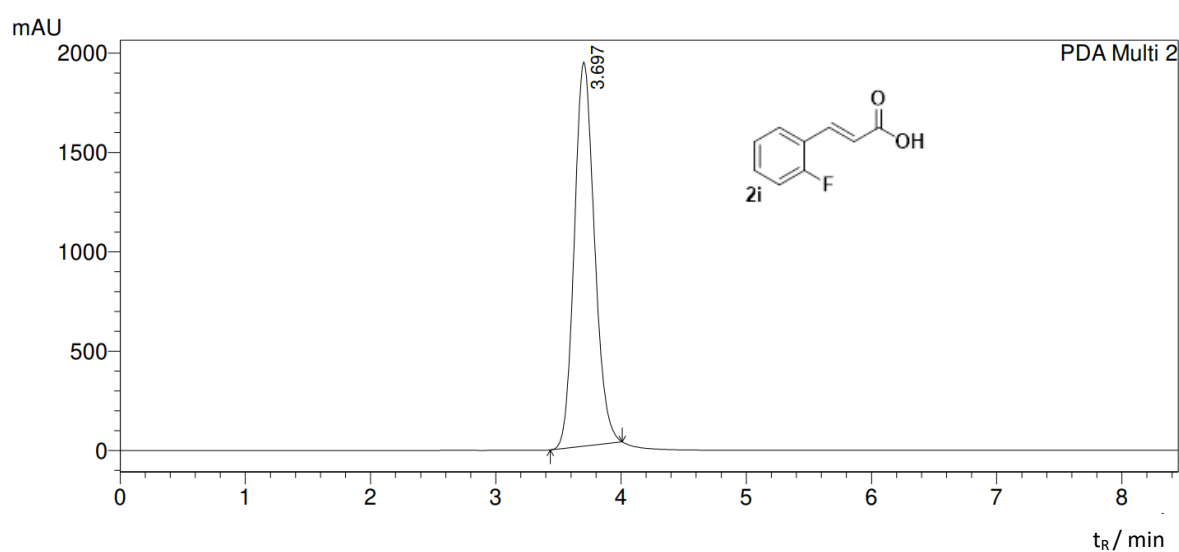


Figure S48. Chromatogram of compound **2i** at 254 nm and t_R 3.697 min.

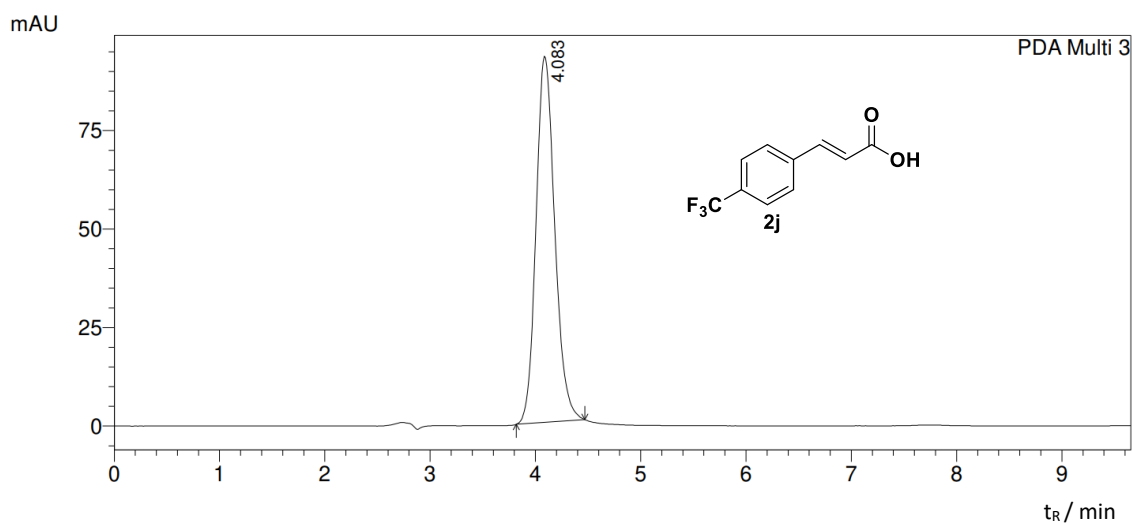


Figure S49. Chromatogram of compound **2j** at 254 nm and t_R 4.083 min.

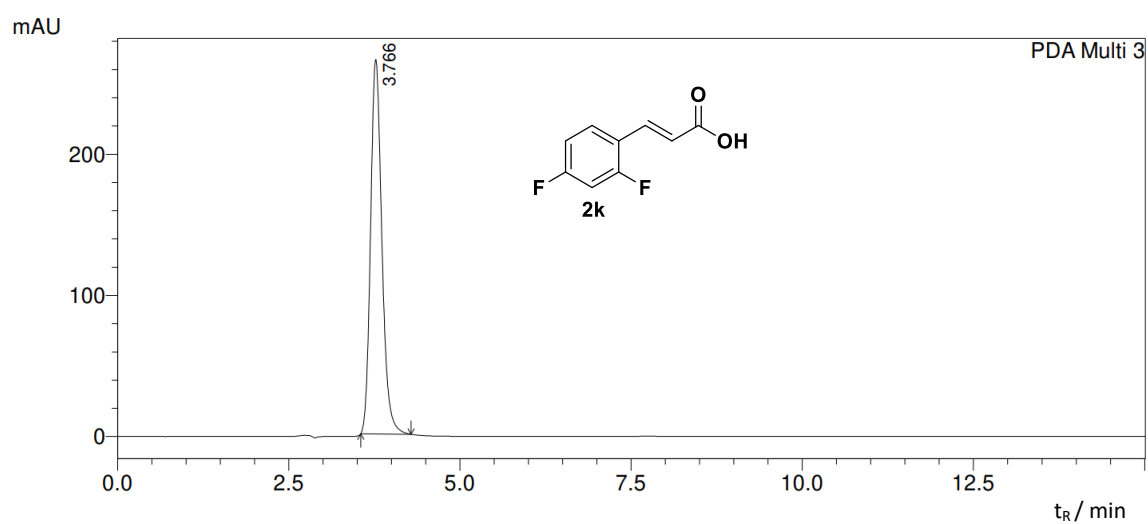


Figure S50. Chromatogram of compound **2k** at 280 nm and t_R 3.766 min.

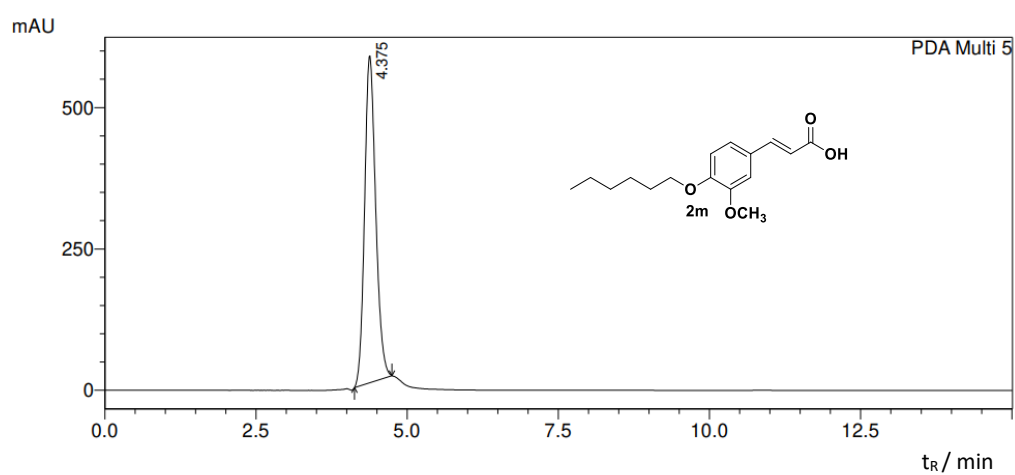


Figure S51. Chromatogram of compound **2m** at 254 nm and t_R 4.375 min.

References

1. Zhang, C.; Lu, Y.; Zhang, J.; Zang, A.; Ren, J.; Zheng, Z.; Xie, Y.; *Eur. J. Med. Chem.* **2024**, *263*, 115945. [[Crossref](#)]
2. Mori, H.; Wada, R.; Takahara, S.; Horino, Y.; Izumi, H.; Ishimoto, T.; Yoshida, T.; Mizuguchi, M.; Obita, T.; Gouda, H.; Hirono, S.; Toyooka, N.; *Bioorg. Med. Chem.* **2017**, *25*, 3736. [[Crossref](#)]

