Indian Journal of Biochemistry & Biophysics
Vol. 63, September 2026, pp. 1099-1111
DOI: 10.56042/ijbb.v63i9.22771

Synthesis of imidazole derivatives and *In silico*/*in vitro* evaluation of potential antidiabetic activity

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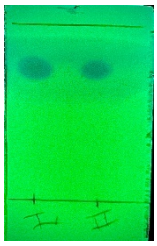
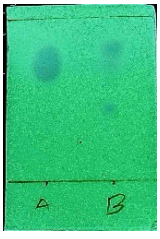
Received 15 August 2025; *revised 16 July 2025*

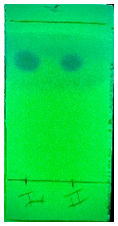
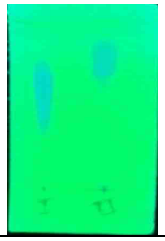
Supplementary data

Suppl. Table 1 — Physicochemical properties of synthesized compounds

Compound	Molecular Formula	M.Wt (g/mol)	Yield (%)	m.p. (°C)	Rf Value
SM-01	$C_{31}H_{28}N_4O_2$	488.8	91.54	210–212	0.90 
SM-02	$C_{31}H_{28}N_4O_2$	488.8	98.59	225–227	0.98 
SM-03	$C_{31}H_{27}ClN_4O_2$	523	84.26	215–222	0.75 

(*Contd.*)

Table 1 — Physicochemical properties of synthesized compounds (*Contd*.)

Compound	Molecular Formula	M.Wt (g/mol)	Yield (%)	m.p. (°C)	Rf Value
SM-04	$C_{31}H_{27}ClN_4O_2$	523	87.77	226–235	0.90
					
SM-05	$C_{32}H_{30}N_4O_2$	502.6	86.74	230–232	0.80
					
SM-06	$C_{31}H_{26}Cl_2N_4O_2$	557.62	95.77	230–232	0.70
					
SM-07	$C_{33}H_{30}N_4O_2$	514.6	70.42	230–232	0.60
					
SM-08	$C_{31}H_{27}BrN_4O_2$	567.48	95.77	230–232	0.70
					

Experimental Data of synthesized compound (SM01-08)

2-(2-benzylhydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-01)

Light yellow, Yield:91.54%, M.P: 210-212 °C, Rf: 0.90, ^{1}H NMR (400 Hz, $CDCl_3$): δ 3.85-4.08 (7H, 3.90 (s), 3.97 (s), 4.03 (s)), 7.12 (2H, ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.23-7.41 (5H, 7.29 (dddd, *J* = 7.7, 1.3, 0.9, 0.5 Hz), 7.32 (tt, *J* = 7.7, 1.3 Hz), 7.35 (tdd, *J* = 7.7, 1.8, 0.5 Hz)), 7.43-7.63 (6H, 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$): δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 127.2 (1C, s), 127.6-127.8 (6C, 127.6 (s), 127.7 (s), 127.7 (s)), 128.3-128.5 (4C, 128.3 (s), 128.4 (s), 128.4 (s)), 128.5-128.7 (4C, 128.6 (s), 128.6 (s)), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 137.0 (1C, s), 139.6 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{31}H_{28}N_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

2-(2-benzylhydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-02)

Yellow, Yield: 98.59%, M.P: 225-227°C, Rf: 0.98, ^{1}H NMR: δ 3.85-4.08 (7H, 3.90 (s), 3.97 (s), 4.03 (s)), 7.12 (2H, ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.23-7.41 (5H, 7.29 (dddd, *J* = 7.7, 1.3, 0.9, 0.5 Hz), 7.32 (tt, *J* = 7.7, 1.3 Hz), 7.35 (tdd, *J* = 7.7, 1.8, 0.5 Hz)), 7.43-7.63 (6H, 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$): δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 126.7 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.7 (7C, 128.4 (s), 128.4 (s), 128.5 (s), 128.6 (s), 128.6 (s)), 129.3 (1C, s), 129.5 (1C, s), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 132.4 (1C, s), 134.1 (1C, s), 137.0 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{31}H_{28}N_4O_2$ m/*z* (%), calcd. (found):488 (480.6, M-1).

2-(2-(2-chlorobenzyl) hydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-03)

Pale yellow, Yield: 84.26%, M.P: 215-217°C, Rf-0.75, ^{1}H NMR: δ 3.85-4.02 (5H, 3.90 (s), 3.97 (s)), 4.13 (2H, s), 7.05-7.38 (5H, 7.12 (ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.18 (ddd, *J* = 7.9, 7.5, 1.6 Hz), 7.31 (ddd, *J* = 8.3, 7.5, 1.5 Hz), 7.32 (ddd, *J* = 7.9, 1.5, 0.5 Hz)), 7.39-7.63 (7H, 7.45 (ddd, *J* = 8.3, 1.6, 0.5 Hz), 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$): δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 126.7 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.7 (7C, 128.4 (s), 128.4 (s), 128.5 (s), 128.6 (s), 128.6 (s)), 129.3 (1C, s), 129.5 (1C, s), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 132.4 (1C, s), 134.1 (1C, s), 137.0 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{31}H_{27}ClN_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

2-(2-(4-chlorobenzyl) hydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-04)

light yellow, Yield: 87.77%, MP: 226-228°C, Rf: 0.90, ^{1}H NMR: δ 3.85-4.06 (7H, 3.90 (s), 3.97 (s), 4.01 (s)), 7.12 (2H, ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.31 (2H, ddd, *J* = 8.3, 1.2, 0.5 Hz), 7.39-7.63 (8H, 7.45 (ddd, *J* = 8.3, 1.3, 0.5 Hz), 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$): δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.7 (8C, 128.4 (s), 128.4 (s), 128.5 (s), 128.6 (s), 128.6 (s)), 129.4 (2C, s), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 133.3 (1C, s), 137.0 (1C, s), 139.6 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{31}H_{27}ClN_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-(2-(4-methylbenzyl) hydrazineyl) ethan-1-one (SM-05)

yellow, Yield: 86.74%, MP: 230-232°C, Rf: 0.80, ^{1}H NMR: δ 2.25 (3H, s), 3.85-4.05 (7H, 3.90 (s), 3.97 (s), 4.00 (s)), 6.88-7.18 (6H, 6.94 (ddd, *J* = 8.0, 1.0, 0.5 Hz), 7.05 (ddd, *J* = 8.0, 1.2, 0.5 Hz), 7.12 (ddd, *J* = 8.7, 1.4, 0.4

Hz)), 7.43-7.63 (6H, 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$): δ 21.4 (1C, s), 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.5 (4C, 128.3 (s), 128.4 (s), 128.4 (s)), 128.5-128.8 (6C, 128.6 (s), 128.6 (s), 128.7 (s)), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 136.1 (1C, s), 137.0 (1C, s), 139.6 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{32}H_{30}N_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

2-(2-(3,4-dichlorobenzyl) hydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-06)

Light yellow, Yield: 95.77%, MP: 230-232°C, Rf: 0.70, ^{1}H NMR: δ 3.85-4.02 (7H, 3.90 (s), 3.96 (s), 3.97 (s)), 7.12 (2H, ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.28 (1H, dd, *J* = 8.2, 1.3 Hz), 7.43-7.63 (8H, 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.50 (dd, *J* = 8.2, 0.5 Hz), 7.50 (dd, *J* = 1.3, 0.5 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz, $CDCl_3$):δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 125.6 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.5 (2C, 128.4 (s), 128.4 (s)), 128.5-128.7 (4C, 128.6 (s), 128.6 (s)), 129.4 (1C, s), 129.7 (2C, s), 130.3 (1C, s), 130.5 (1C, s), 130.7 (1C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 131.9 (1C, s), 132.7 (1C, s), 137.0 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s).Mass $C_{31}H_{26}Cl_2N_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-(2-(4-vinylbenzyl) hydrazineyl) ethan-1-one (SM-07)

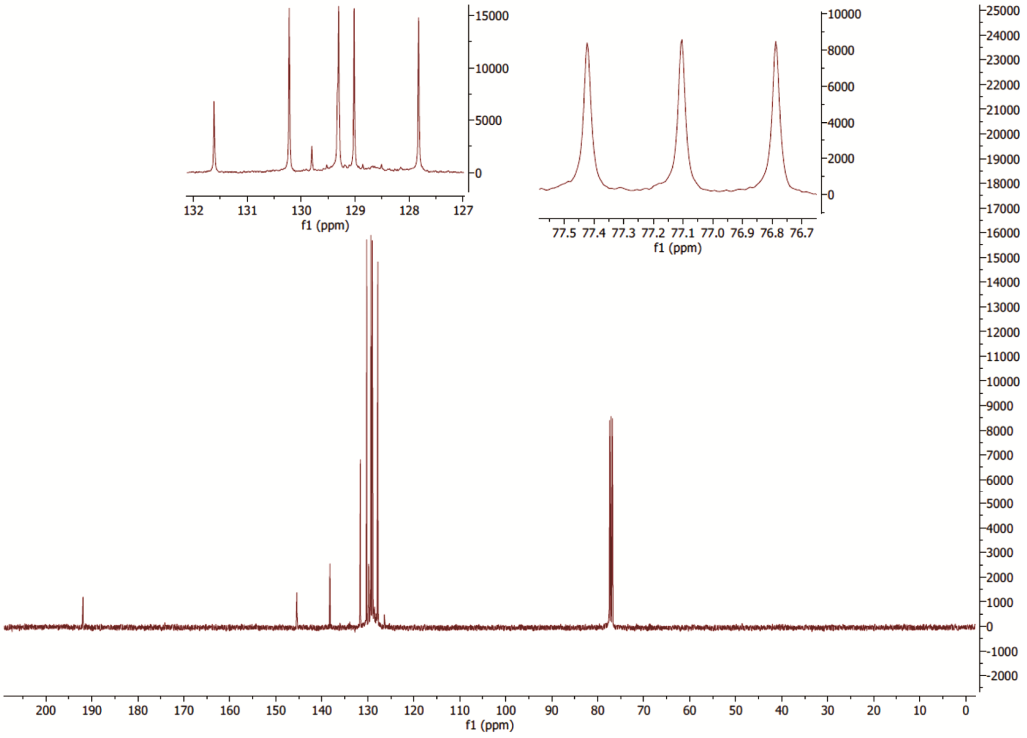
Yellow, Yield: 70.42%, MP: 230-232°C, Rf: 0.60, ^{1}H NMR: δ 3.85-4.06 (7H, 3.90 (s), 3.97 (s), 4.01 (s)), 5.14 (1H, dd, J = 11.0, 1.1 Hz), 5.85 (1H, dd, J = 18.2, 1.1 Hz), 6.84 (1H, dd, J = 18.2, 11.0 Hz), 7.05-7.18 (4H, 7.12 (ddd, J = 8.2, 1.2, 0.5 Hz), 7.12 (ddd, J = 8.7, 1.4, 0.4 Hz)), 7.26 (2H, ddd, J = 8.2, 1.8, 0.5 Hz), 7.43-7.63 (6H, 7.50 (tdd, J = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, J = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, J = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, J = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, J = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, J = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, J = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz, $CDCl_3$): δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 113.9-114.0 (3C, 113.9 (s), 114.0 (s)), 125.6 (1C, s), 127.6-127.8 (6C, 127.6 (s), 127.7 (s), 127.7 (s)), 128.3-128.5 (2C, 128.4 (s), 128.4 (s)), 128.5-128.7 (4C, 128.6 (s), 128.6 (s)), 129.4 (2C, s), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 136.3 (1C, s), 137.0 (1C, s), 137.3 (1C, s), 139.6 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{33}H_{30}N_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

2-(2-(2-bromobenzyl) hydrazineyl)-1-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl) ethan-1-one (SM-08)

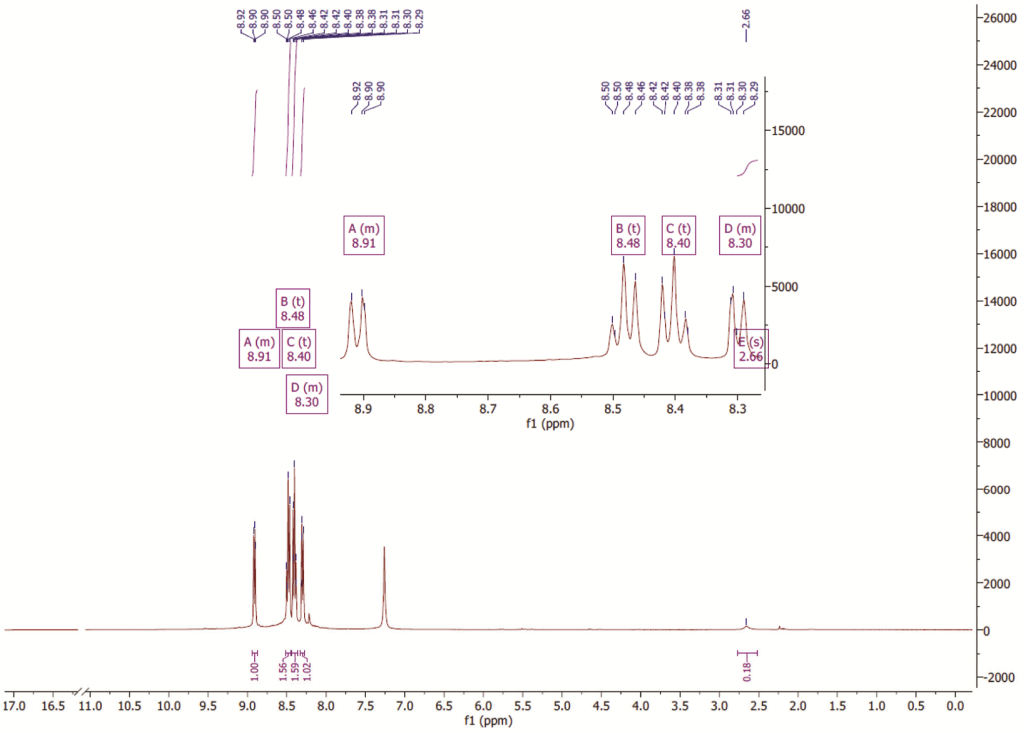
Pale yellow, Yield: 95.77%, MP: 230-232°C, Rf: 0.70, ^{1}H NMR: δ 3.85-4.02 (5H, 3.90 (s), 3.97 (s)), 4.11 (2H, s), 6.93 (1H, ddd, *J* = 8.1, 7.7, 1.7 Hz), 7.05-7.32 (4H, 7.12 (ddd, *J* = 8.7, 1.4, 0.4 Hz), 7.22 (ddd, *J* = 8.1, 7.7, 1.3 Hz), 7.26 (ddd, *J* = 8.1, 1.3, 0.5 Hz)), 7.40-7.63 (7H, 7.46 (ddd, *J* = 8.1, 1.7, 0.5 Hz), 7.50 (tdd, *J* = 7.4, 1.9, 1.4 Hz), 7.52 (dddd, *J* = 7.5, 6.1, 1.4, 1.3 Hz), 7.55 (dddd, *J* = 7.4, 6.8, 1.7, 0.5 Hz), 7.56 (dddd, *J* = 8.1, 7.4, 1.6, 0.4 Hz)), 7.70 (2H, ddd, *J* = 8.7, 1.9, 0.4 Hz), 7.91-8.13 (4H, 7.98 (dddd, *J* = 8.1, 1.7, 1.5, 0.4 Hz), 8.07 (dddd, *J* = 7.4, 1.6, 1.4, 0.5 Hz)). ^{13}C NMR (100 Hz,$CDCl_3$) **:** δ 43.4 (1C, s), 48.9 (1C, s), 55.3 (1C, s), 114.0 (2C, s), 123.9 (1C, s), 125.6 (1C, s), 126.7 (1C, s), 127.7-127.8 (4C, 127.7 (s), 127.7 (s)), 128.3-128.5 (3C, 128.3 (s), 128.4 (s), 128.4 (s)), 128.5-128.7 (4C, 128.6 (s), 128.6 (s)), 129.3 (1C, s), 129.7 (2C, s), 130.9-131.1 (2C, 131.0 (s), 131.0 (s)), 132.4 (1C, s), 132.8 (1C, s), 137.0 (1C, s), 141.6 (1C, s), 153.6 (1C, s), 160.3 (1C, s), 168.6 (1C, s). Mass $C_{31}H_{27}BrN_4O_2$ m/*z* (%), calcd. (found):488 (482.3, M-1).

Spectroscopic analysis

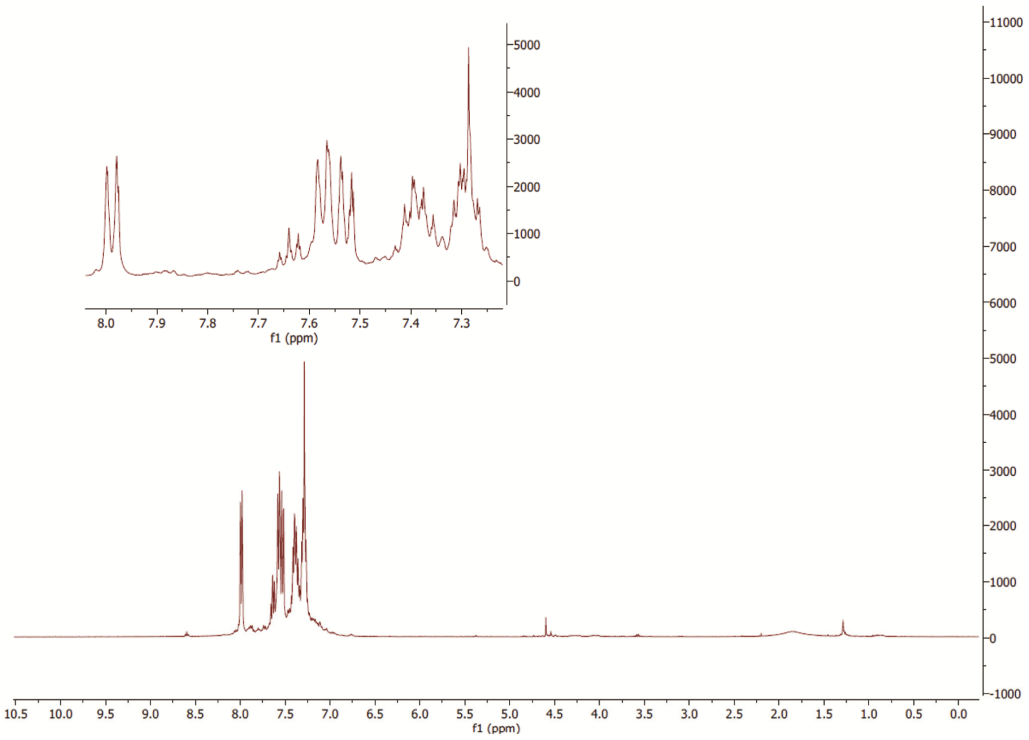
NMR (H & C) SM-01 TO SM-08



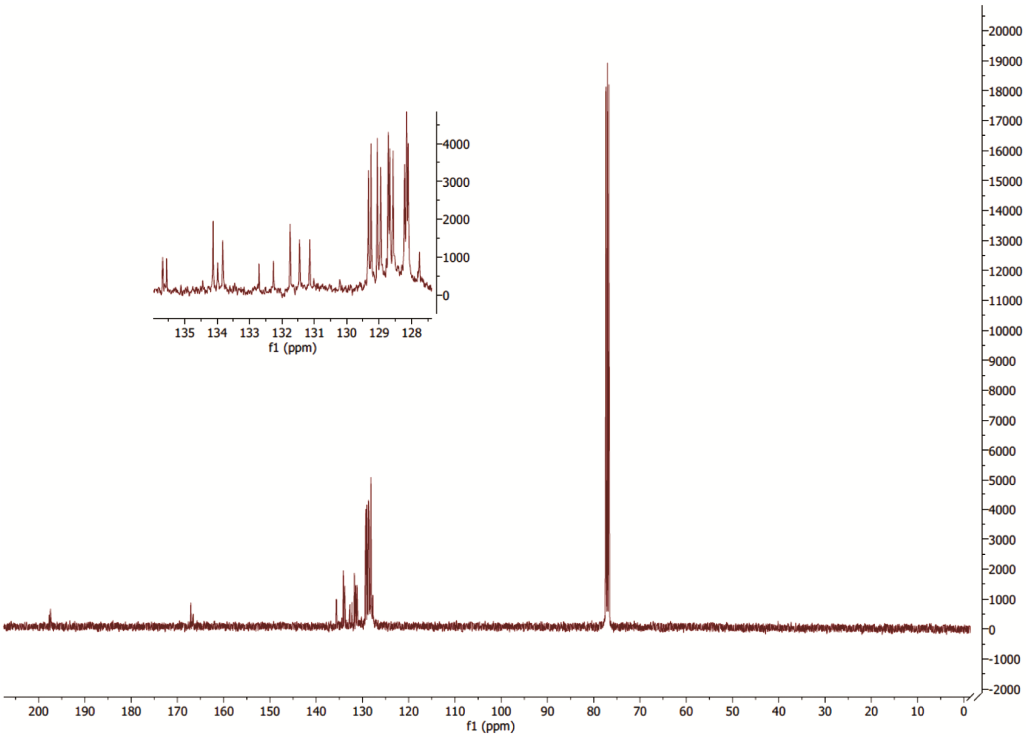
Suppl. Fig. S1a — 13C-NMR Spectrum of compound (SM-01)



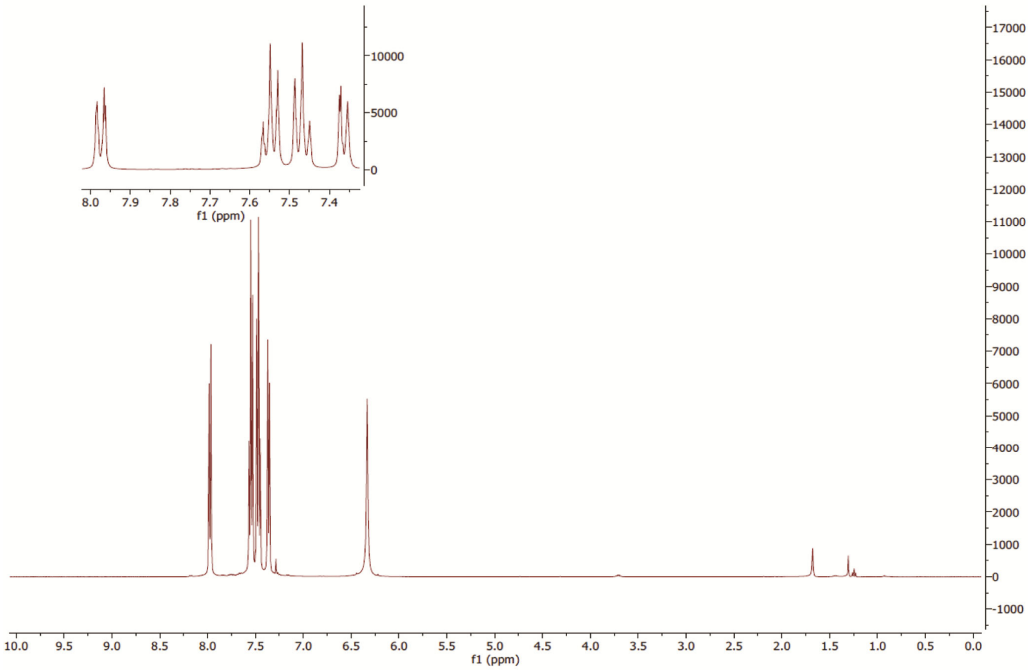
Suppl. Fig. S1b — 1H-NMR Spectrum of compound (SM-01)



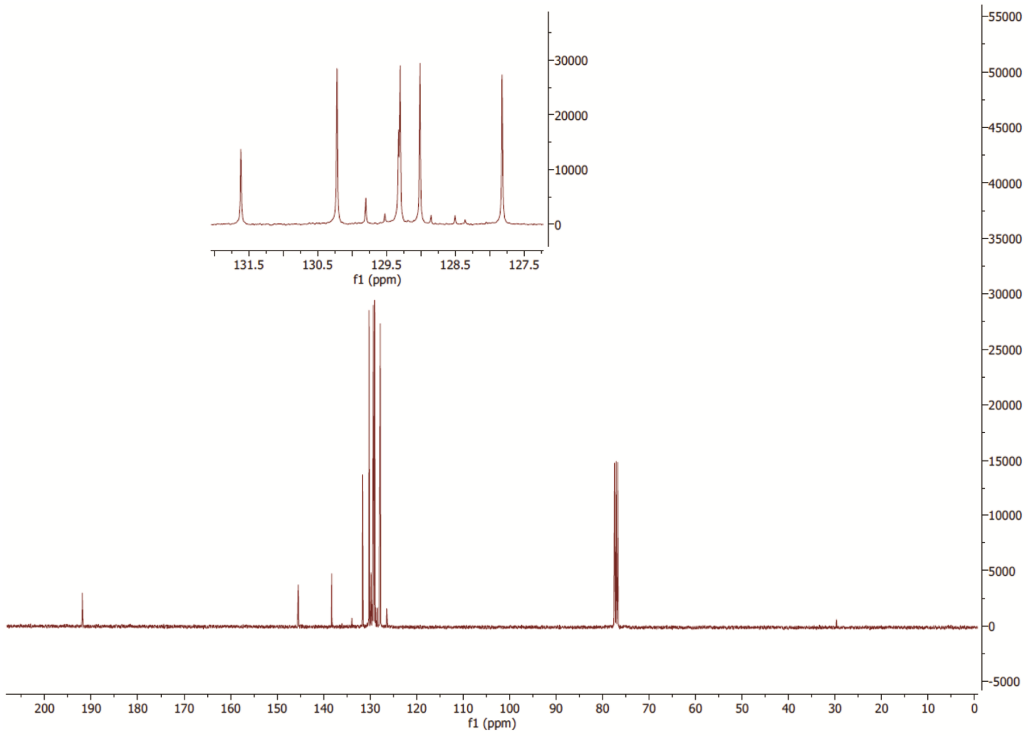
Suppl. Fig. S1c — 1H-NMR Spectrum of compound (SM-02)



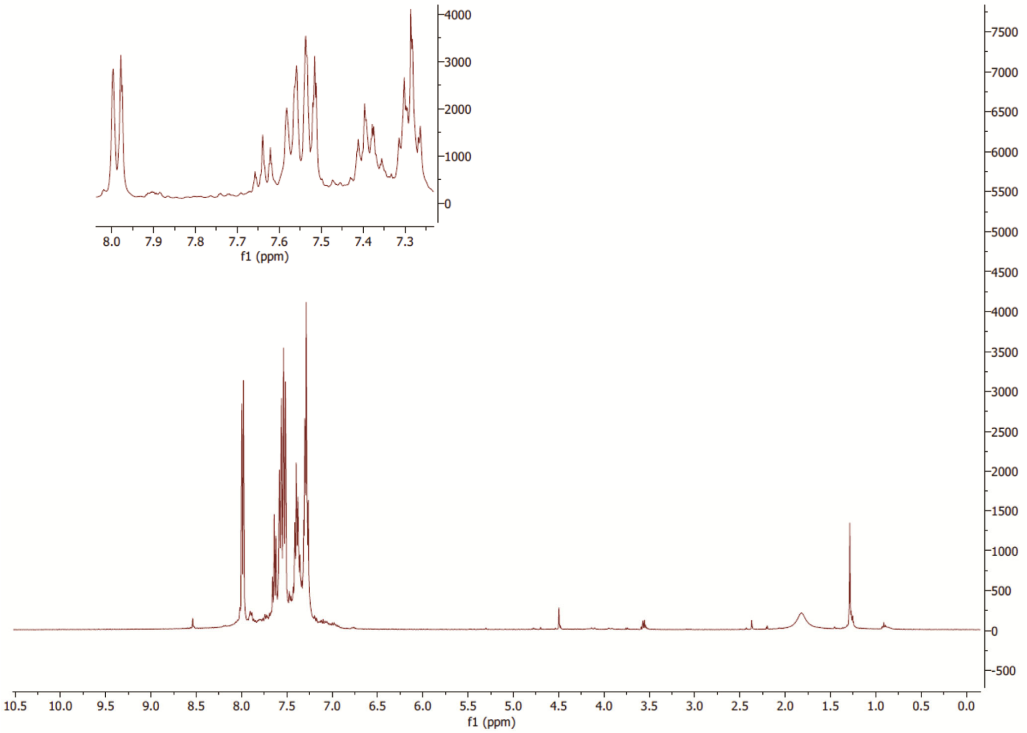
Suppl. Fig. S1d — 13C-NMR Spectrum of compound (SM-02)



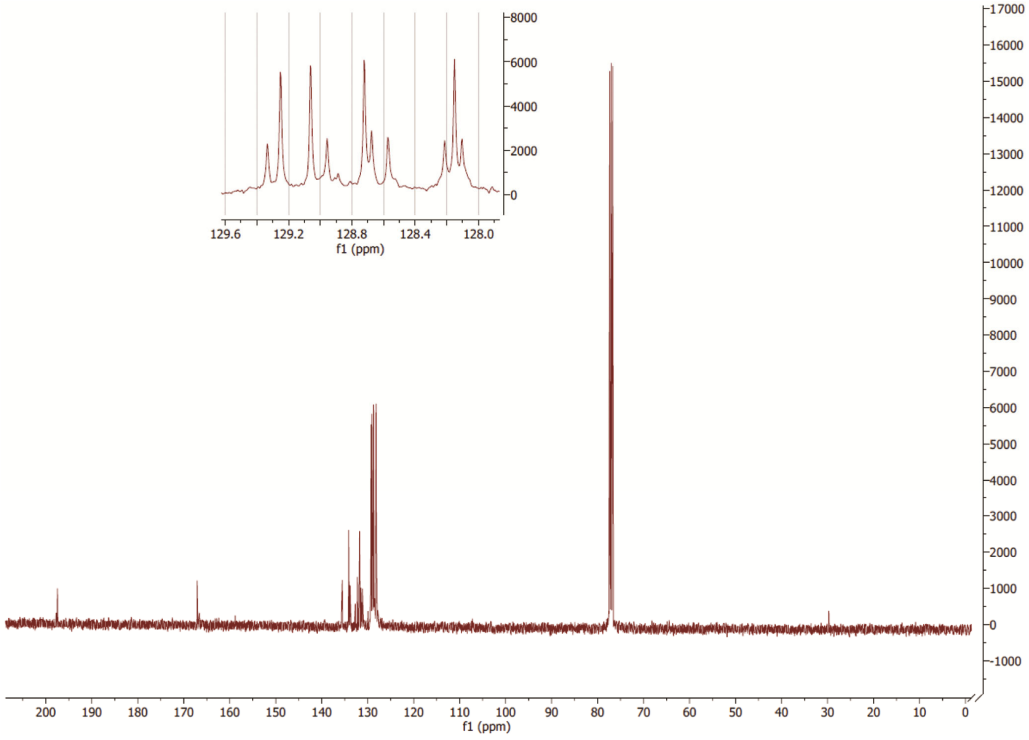
Suppl. Fig. S1e — 1H-NMR Spectrum of compound (SM-03)



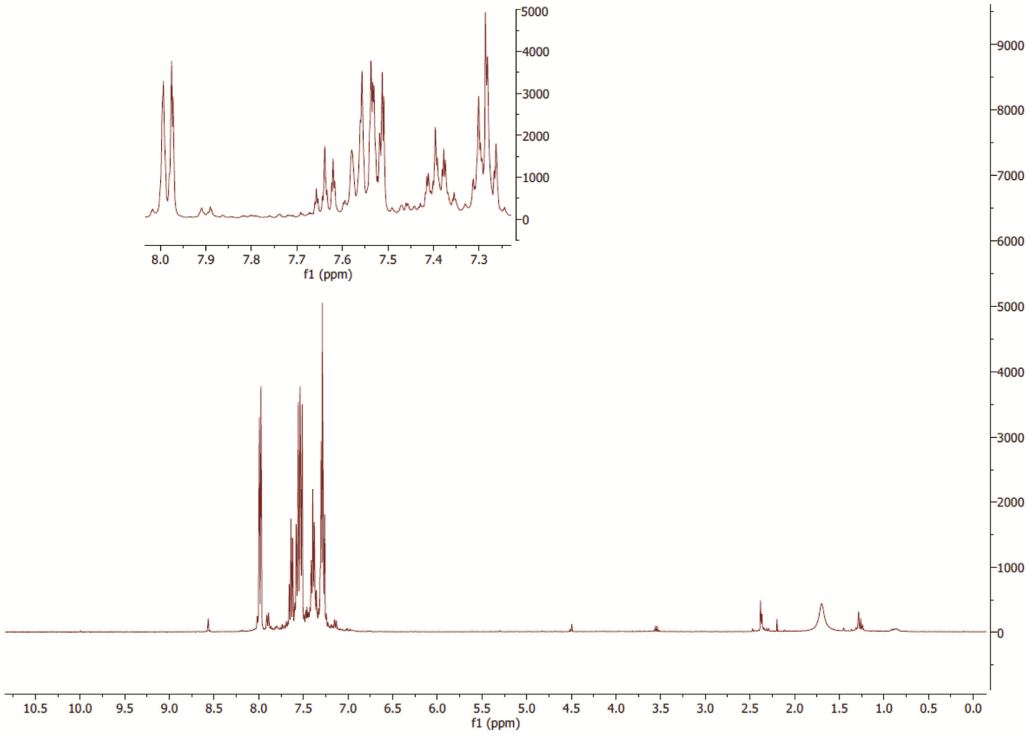
Suppl. Fig. S1f — 13C-NMR Spectrum of compound (SM-03)



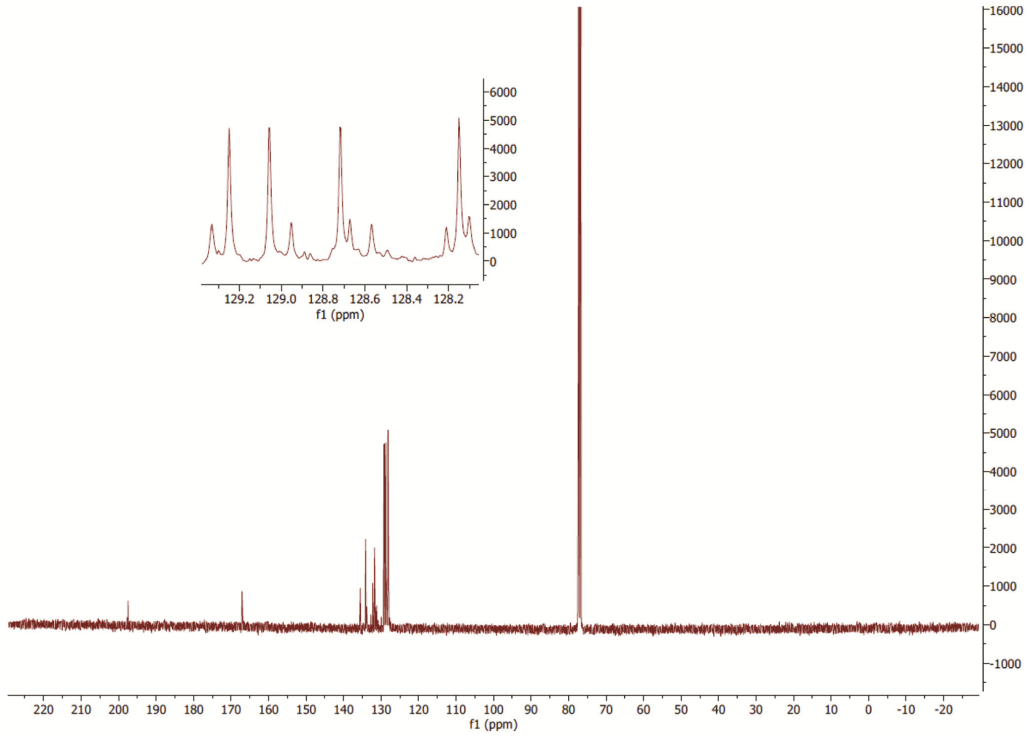
Suppl. Fig. S1g — 1H-NMR Spectrum of compound (SM-04)



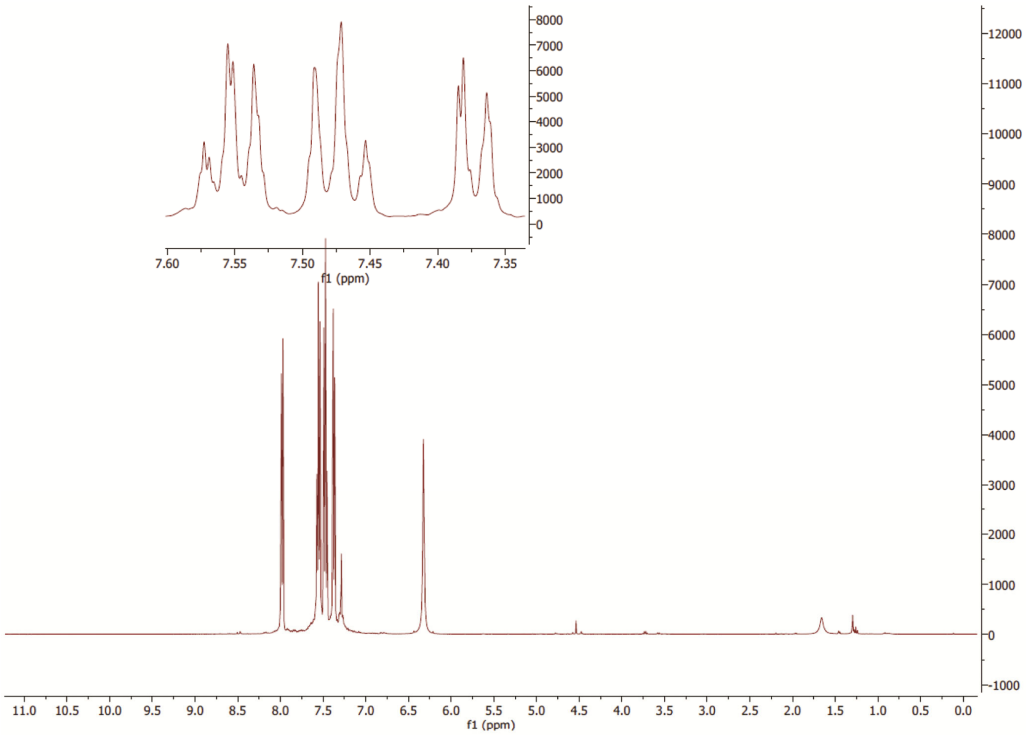
Suppl. Fig. S1h — 13C-NMR Spectrum of compound (SM-04)



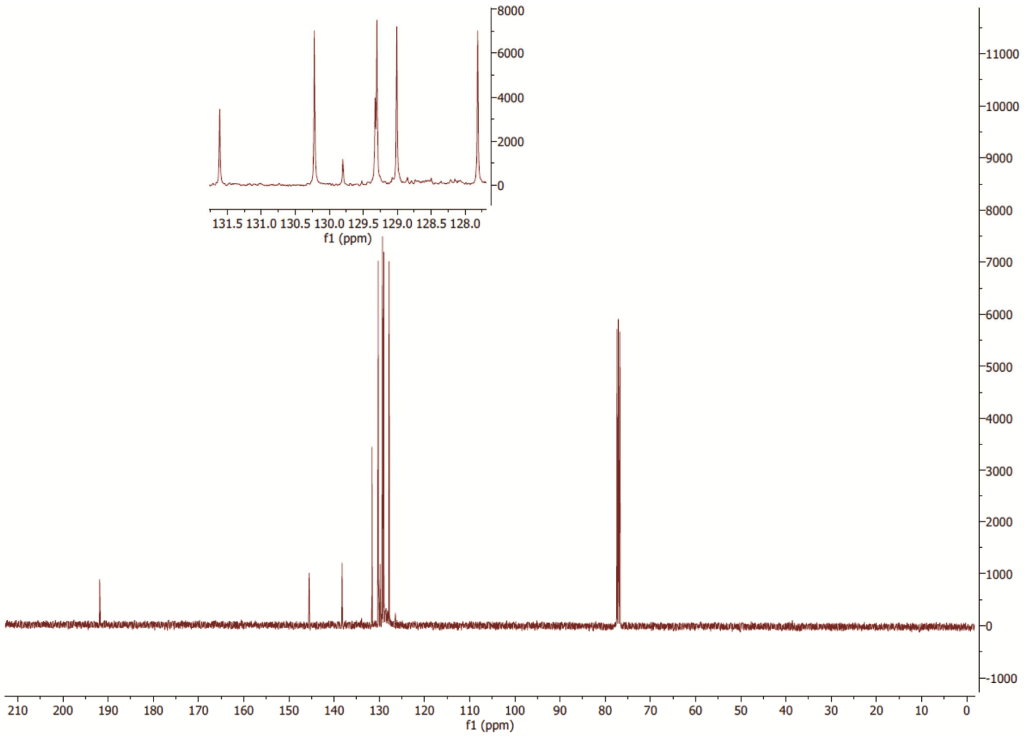
Suppl. Fig. S1i — 1H-NMR Spectrum of compound (SM-05)



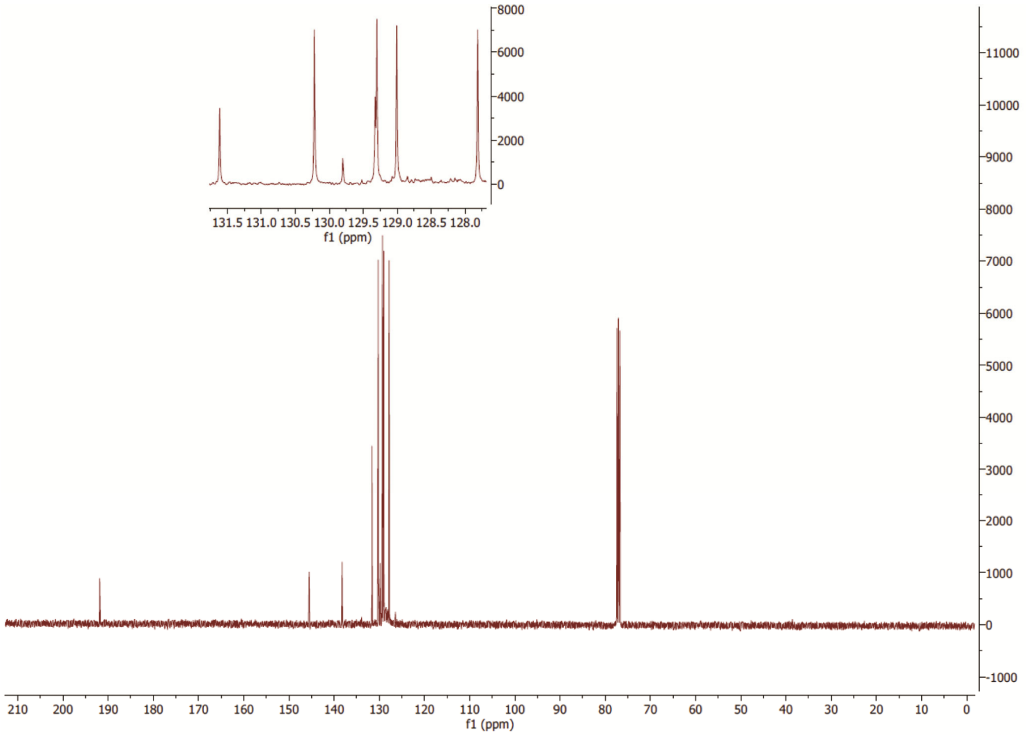
Suppl. Fig. S1j — 13C-NMR Spectrum of compound (SM-05)



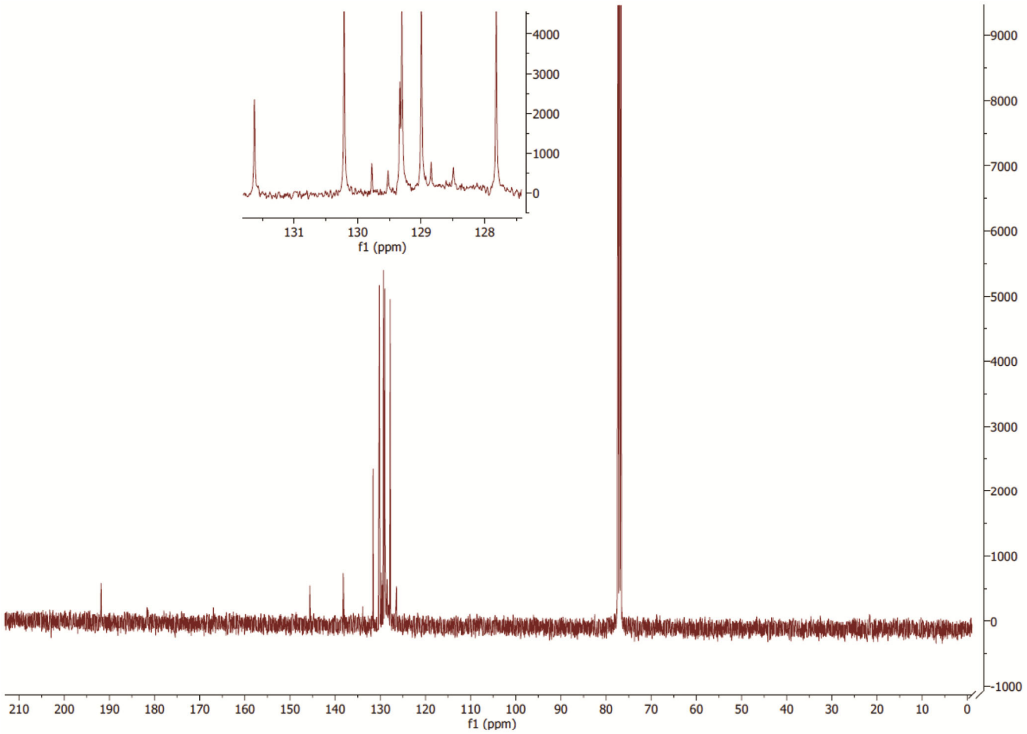
Suppl. Fig. S1k — 1H-NMR Spectrum of compound (SM-06)



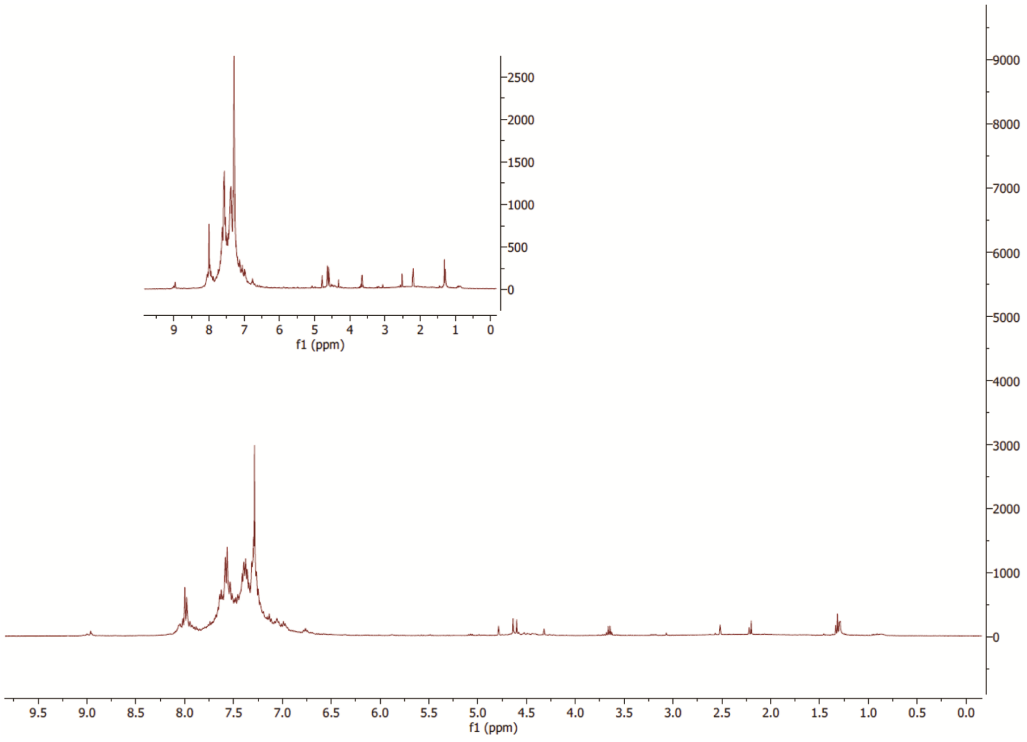
Suppl. Fig. S1l — 13C-NMR Spectrum of compound (SM-06)



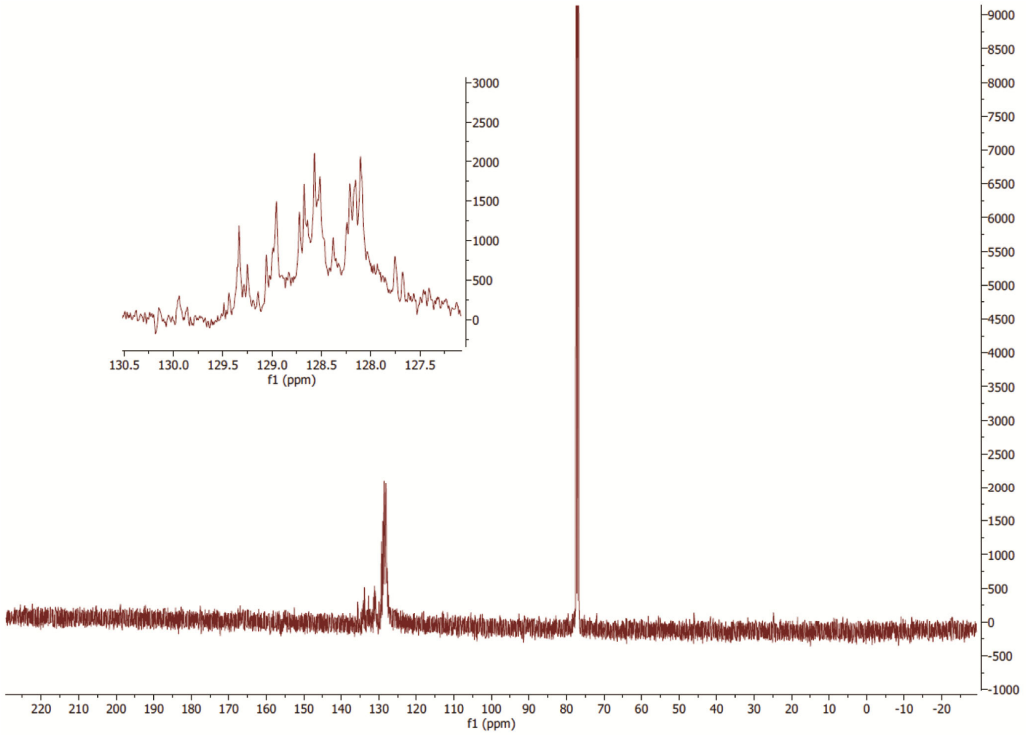
Suppl. Fig. S1m — 1H-NMR Spectrum of compound (SM-07)



Suppl. Fig. S1n — 13C-NMR Spectrum of compound (SM-07)

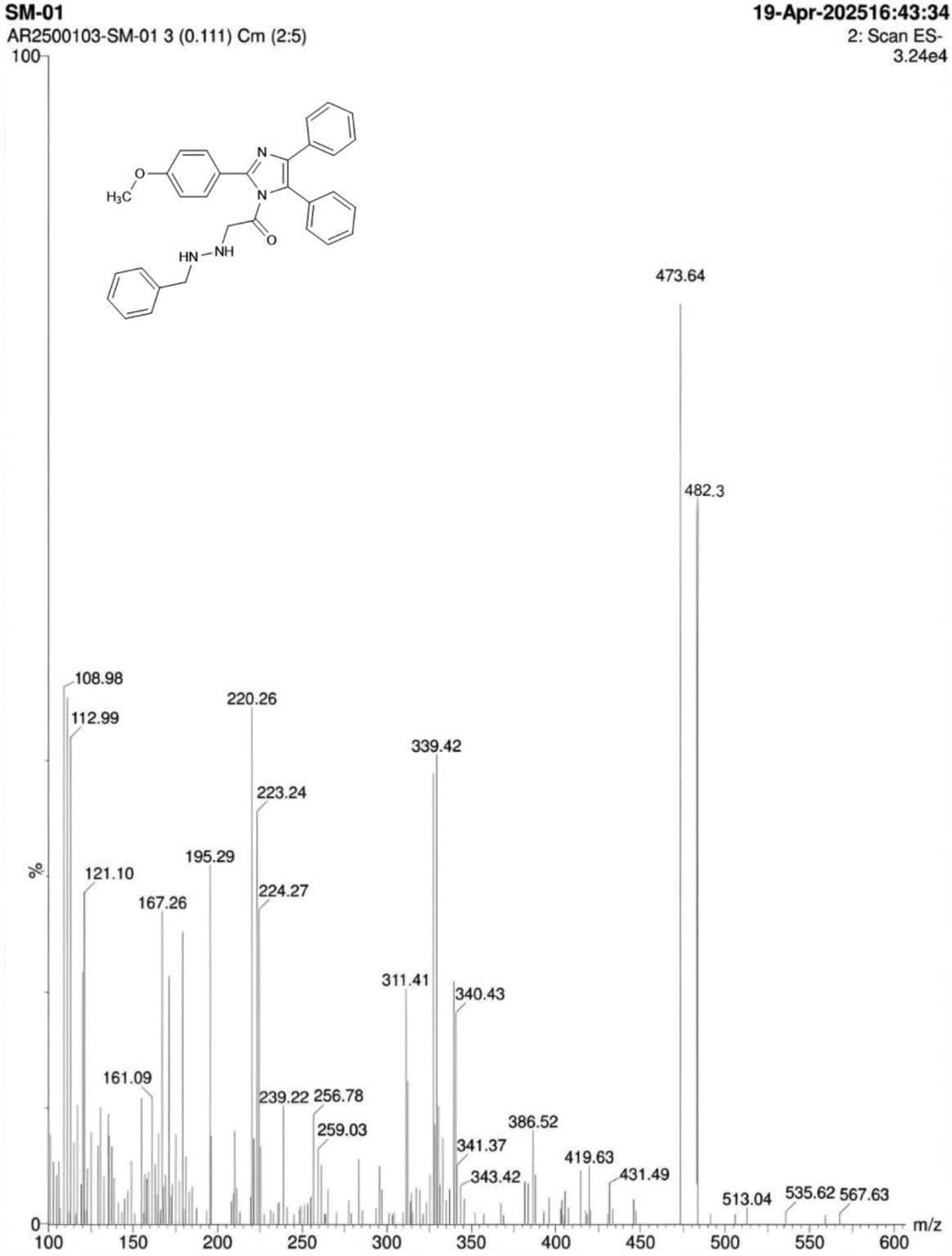


Suppl. Fig. S1o — 1H-NMR Spectrum of compound (SM-08)

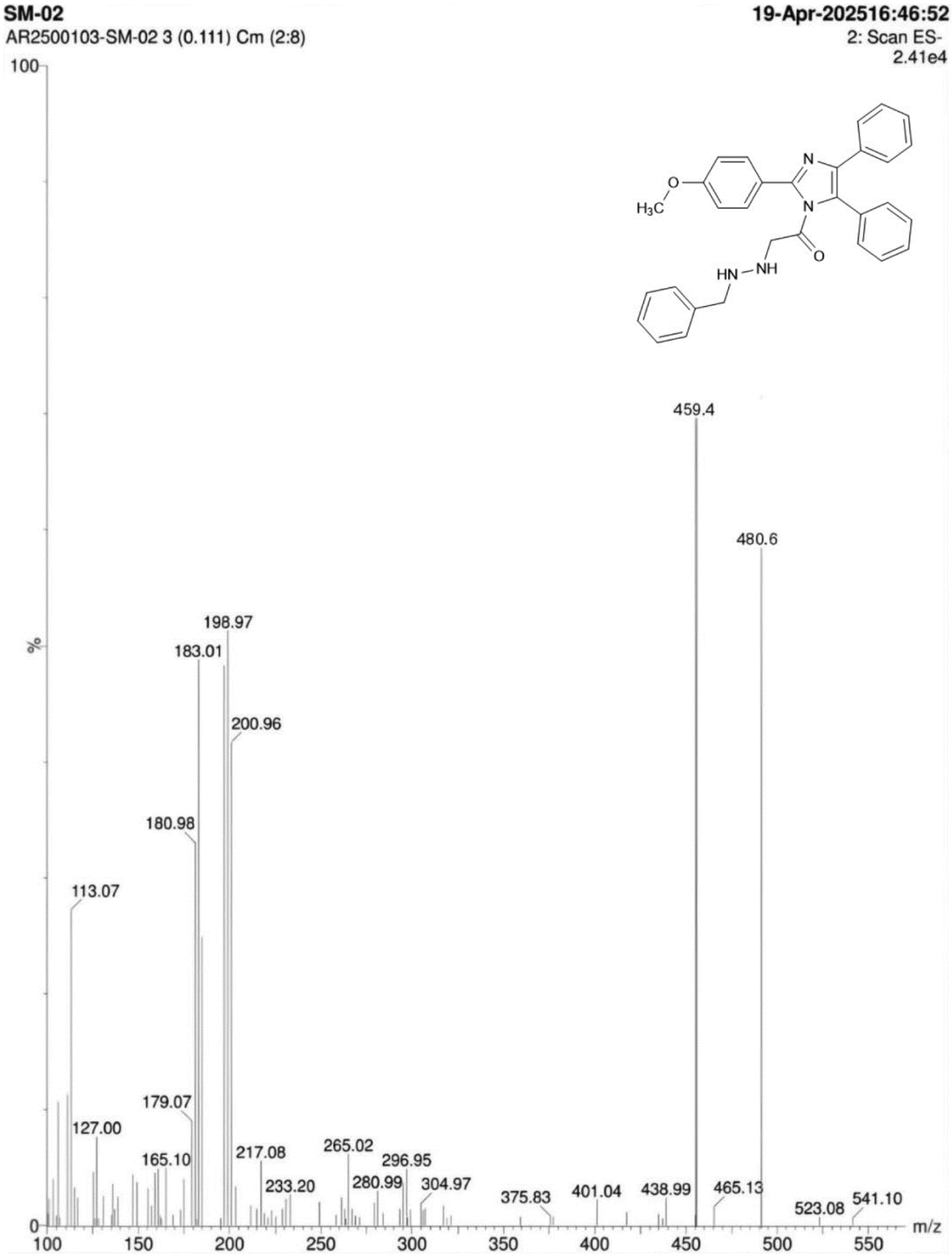


Suppl. Fig. S1p — 13C-NMR Spectrum of compound (SM-08)

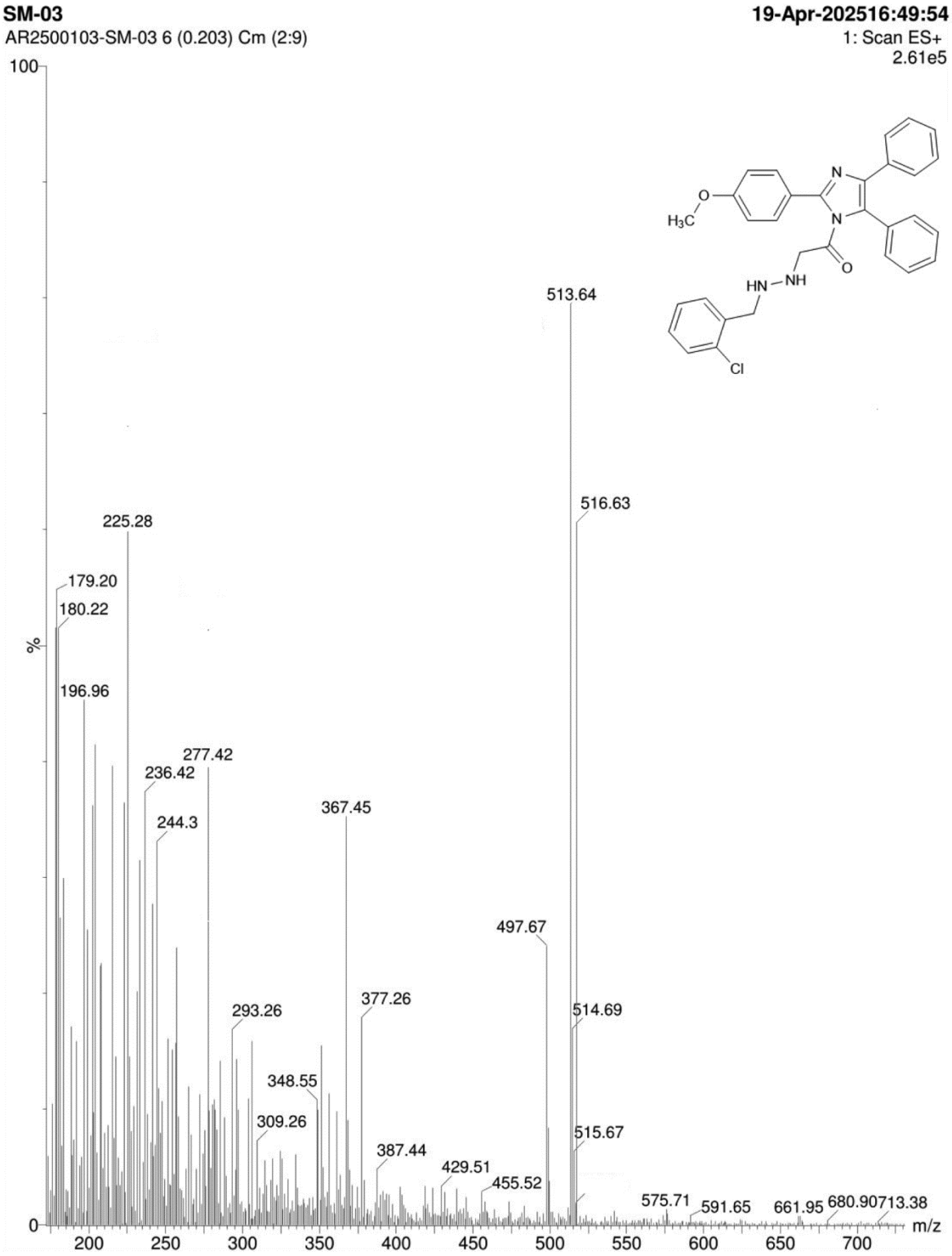
Mass Spectra SM-01 TO SM-08



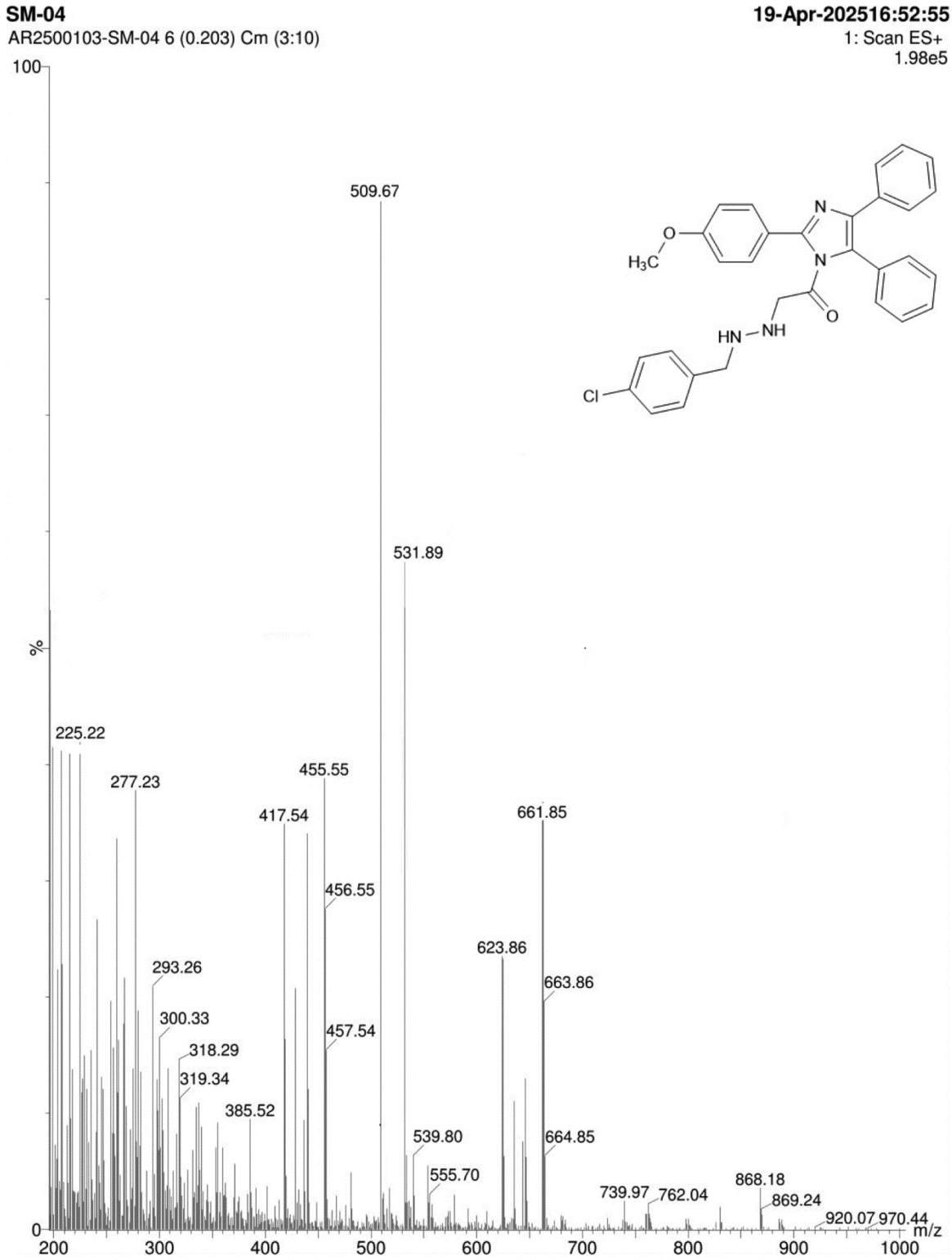
Suppl. Fig. S2a — Mass Spectrum of compound (SM-01)



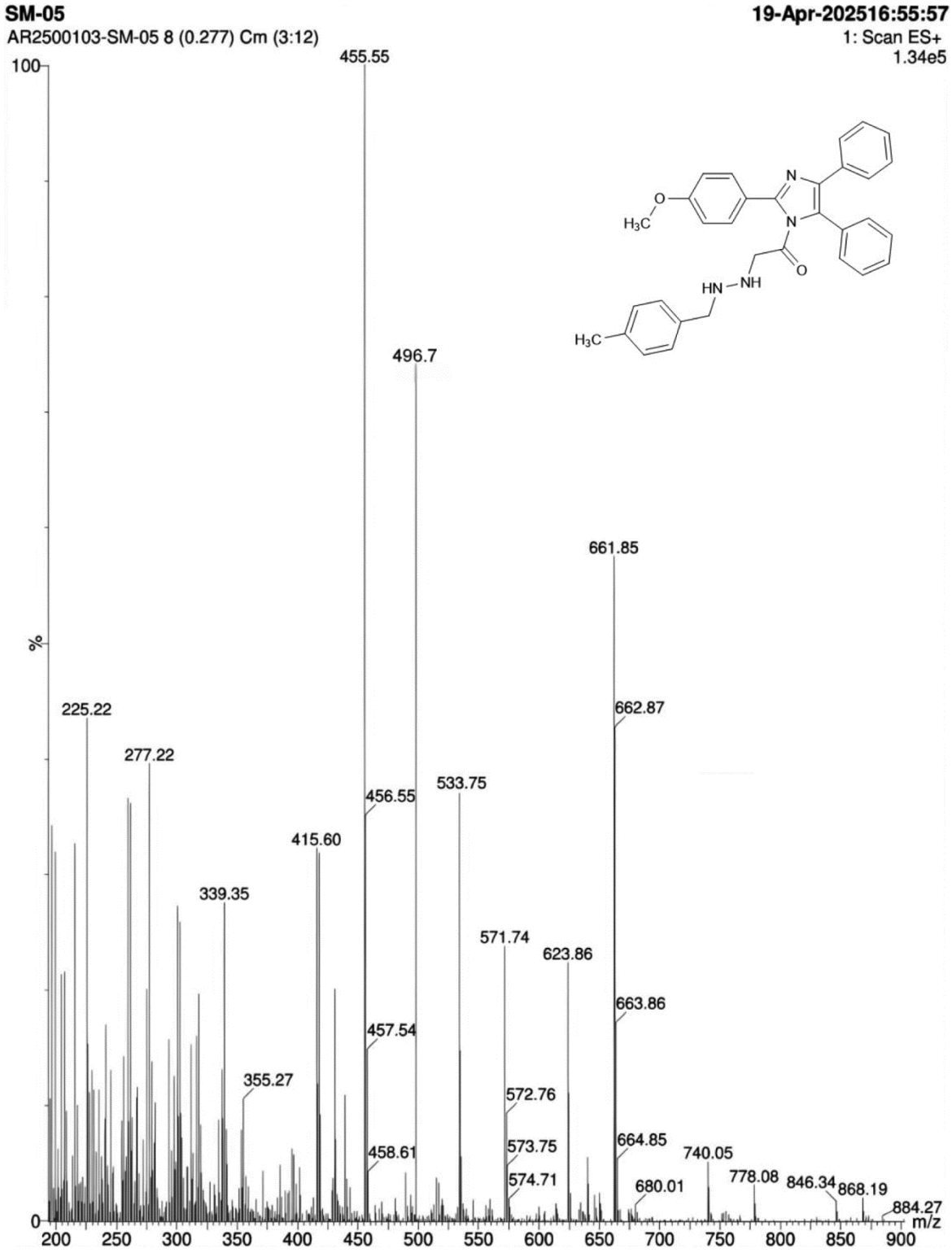
Suppl. Fig. S2b — Mass Spectrum of compound (SM-02)



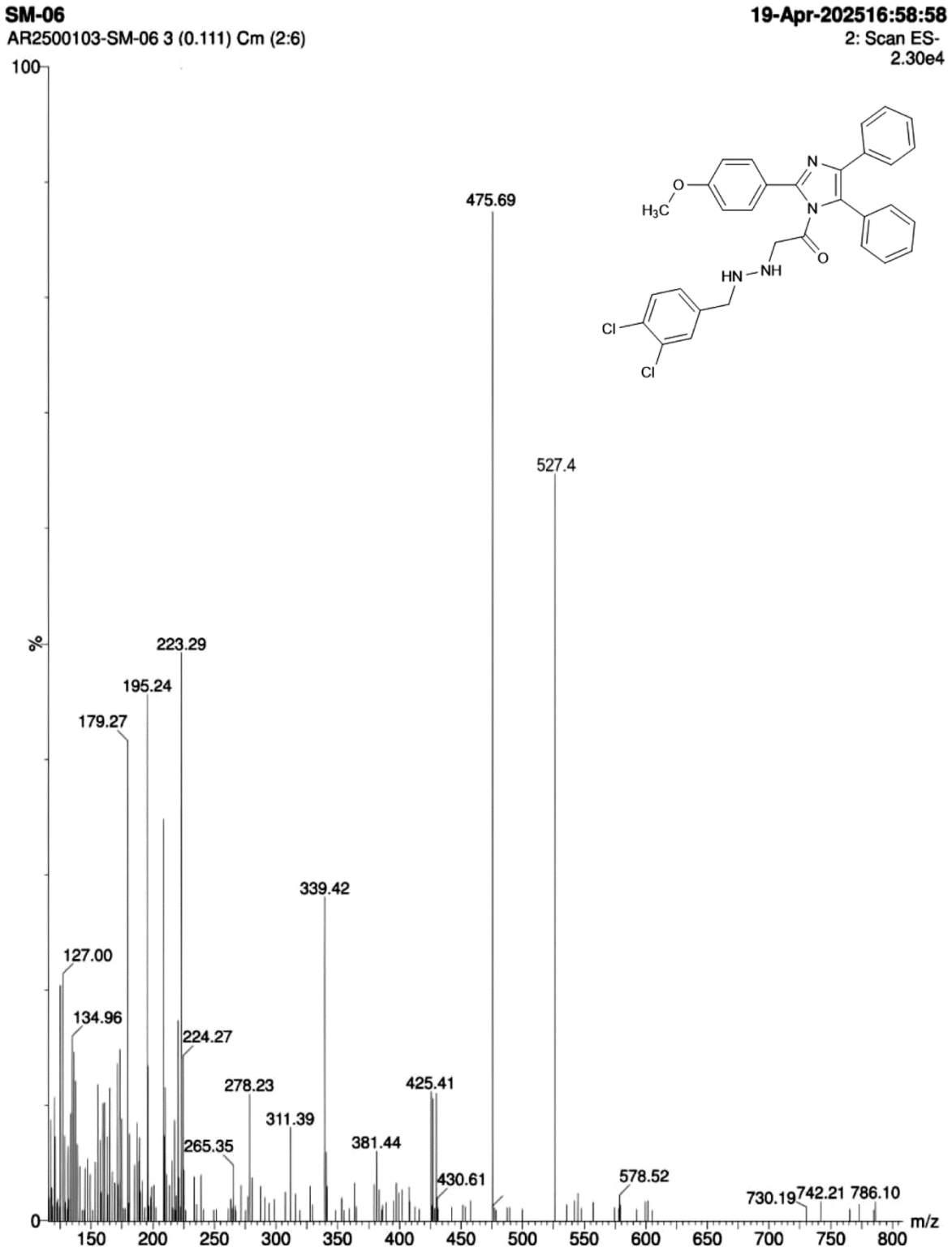
Suppl. Fig. S2c — Mass Spectrum of compound (SM-03)



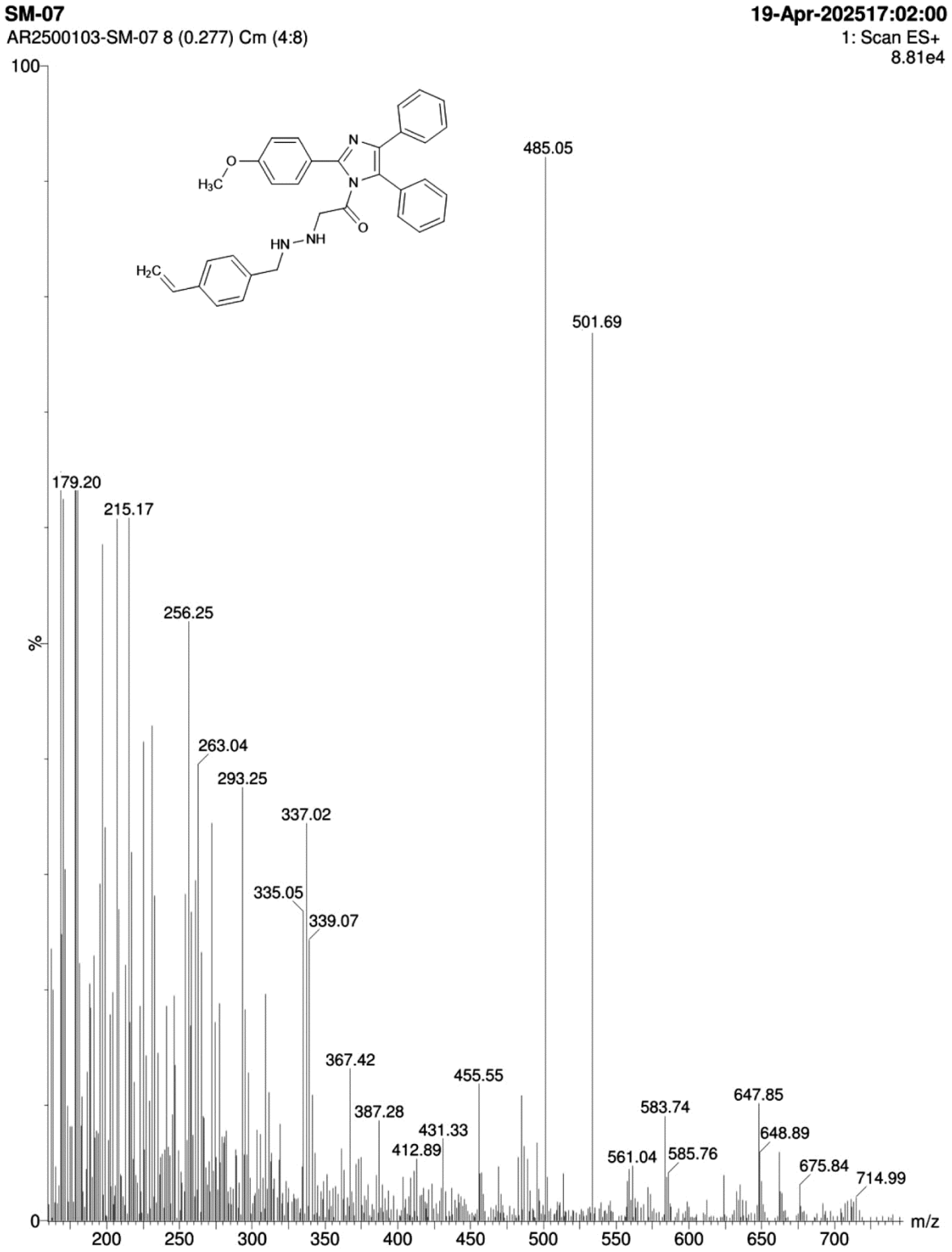
Suppl. Fig. S2d — Mass Spectrum of compound (SM-04)



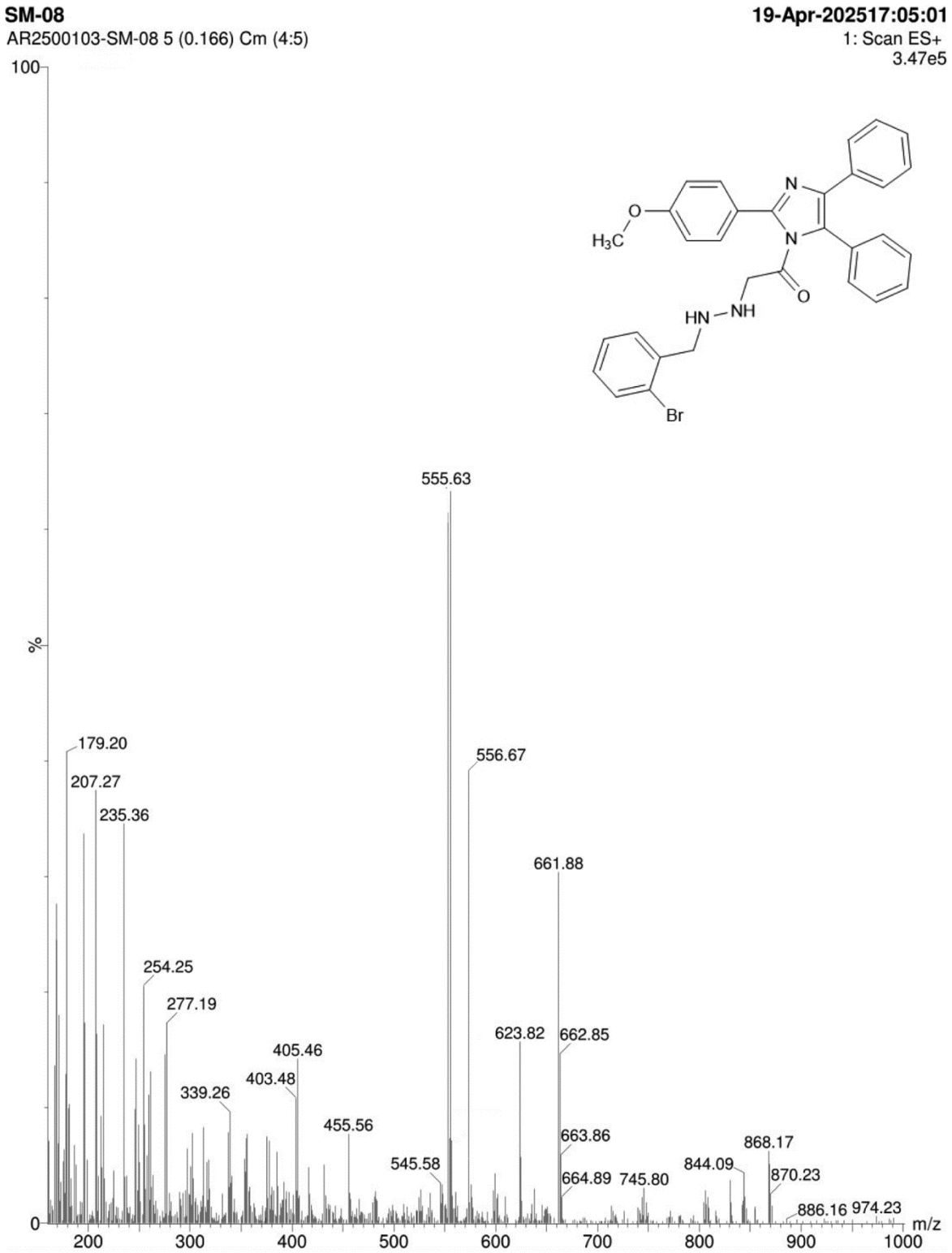
Suppl. Fig. S2e — Mass Spectrum of compound (SM-05)



Suppl. Fig. S2f — Mass Spectrum of compound (SM-06)

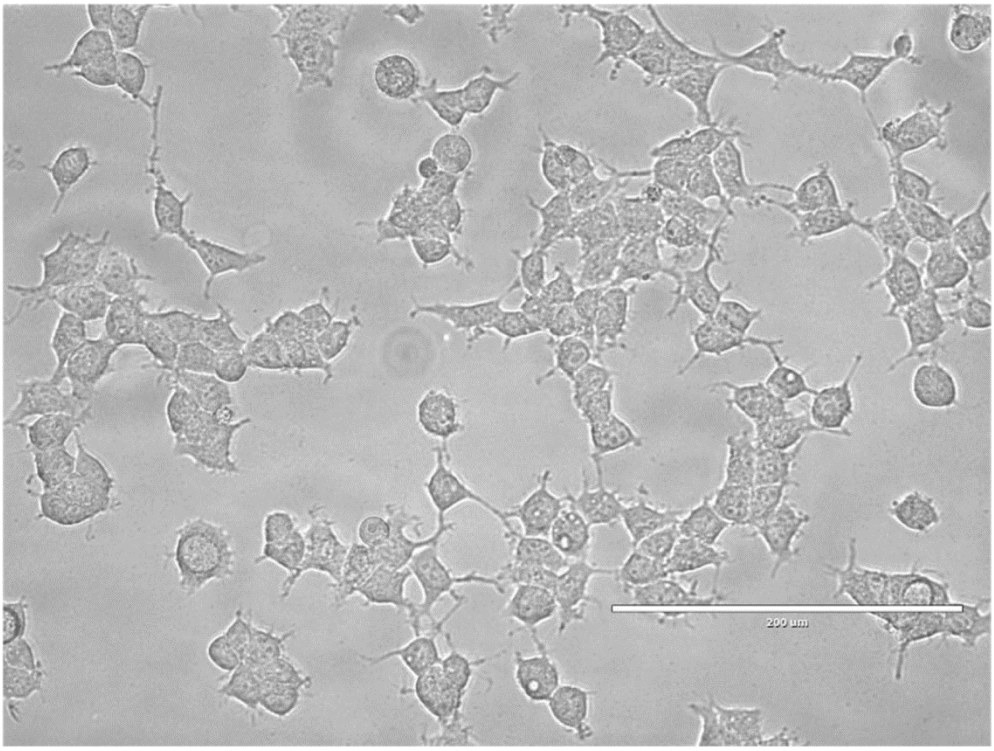


Suppl. Fig. S2g — Mass Spectrum of compound (SM-07)

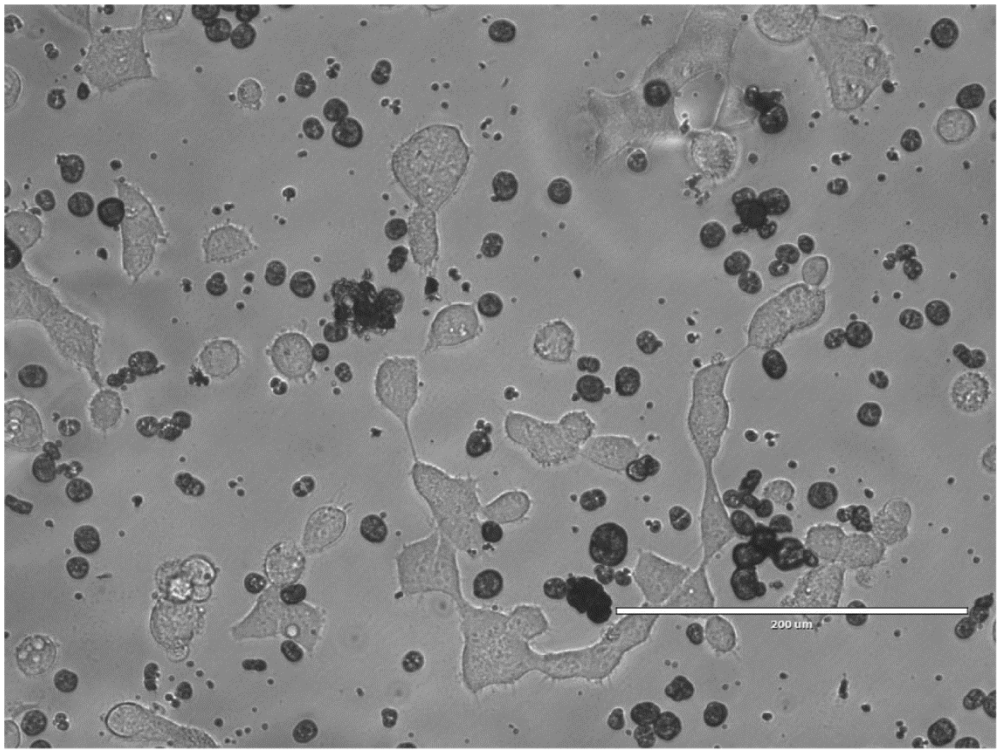


Suppl. Fig. S2h — Mass Spectrum of compound (SM-08)

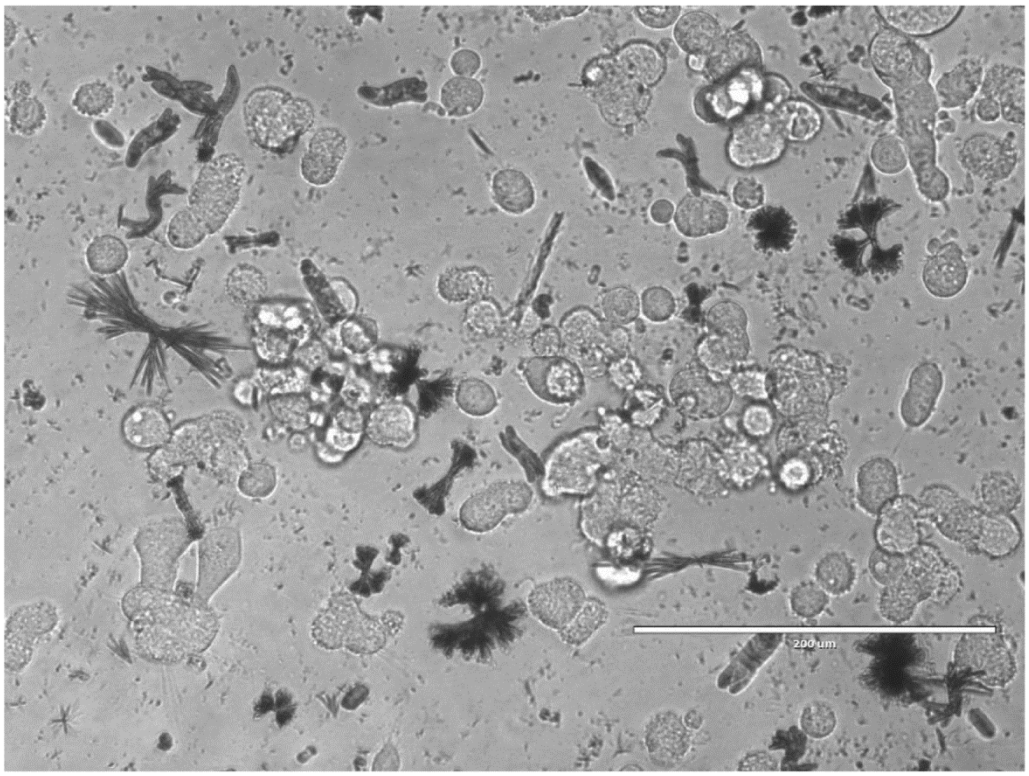
In vitro antidiabetic activity of cell line and alpha-amylase inhibition



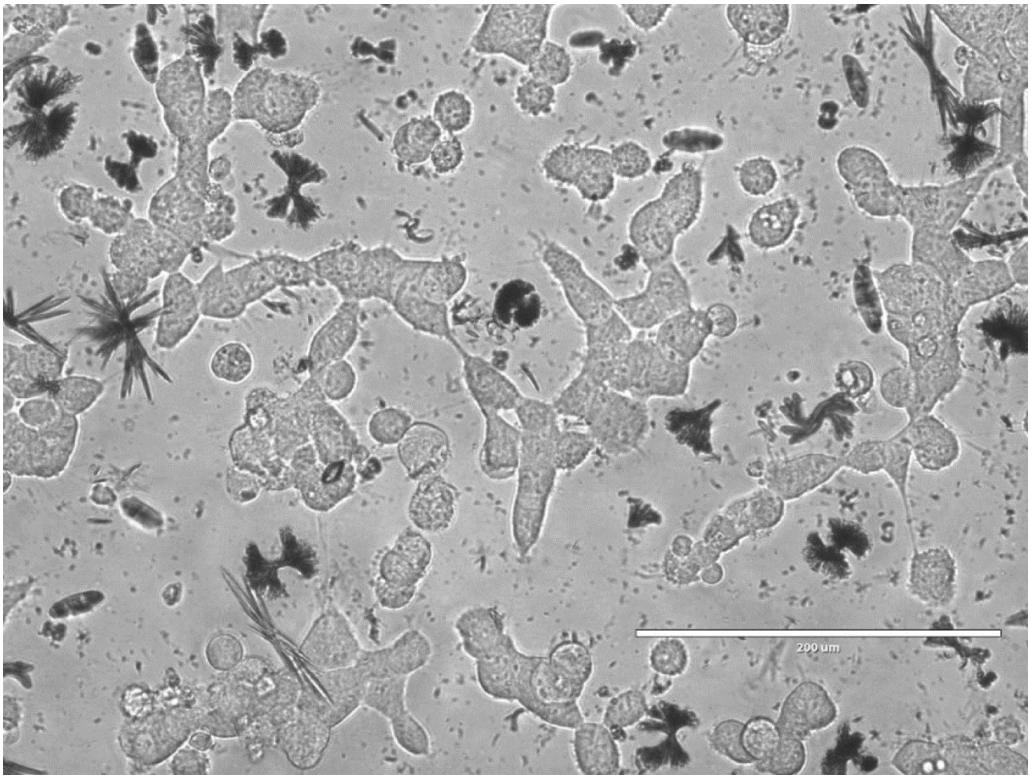
Suppl. Fig. S3a — Control



Suppl. Fig. S3b — Standard



Suppl. Fig. S3c — SM-03



Suppl. Fig. S3d — SM-04