

Supplementary Materials: Addition of vindoline to p-benzoquinone: regiochemistry, stereochemistry and symmetry considerations

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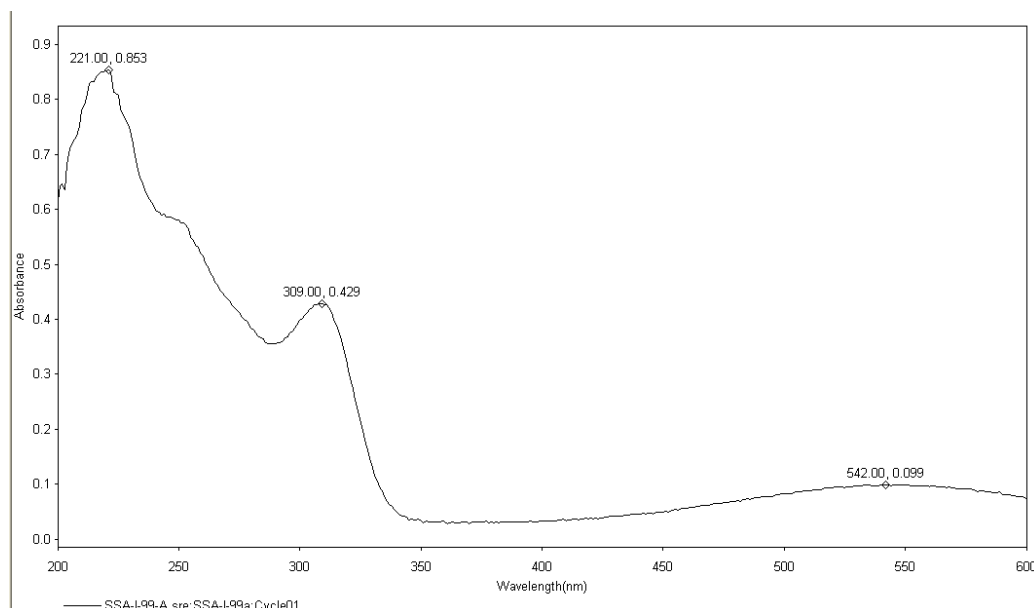


Figure S1: UV spectrum of compound **3**

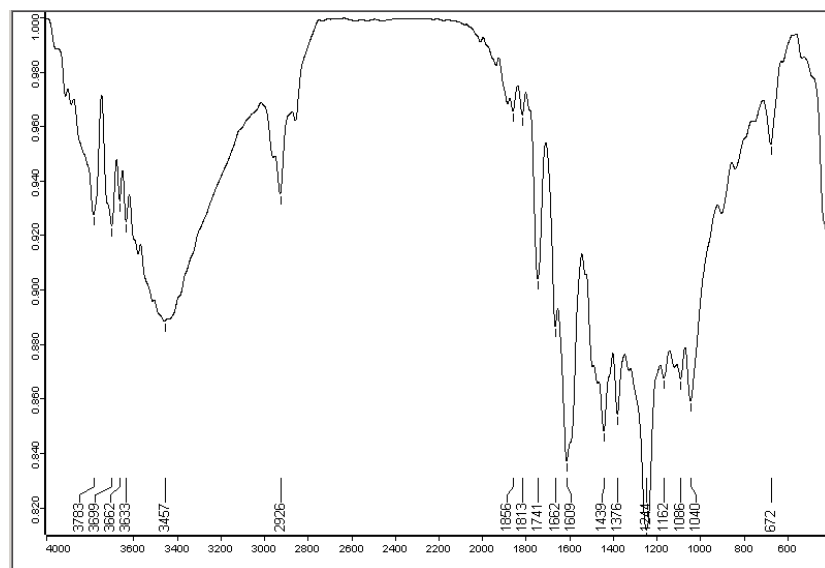


Figure S2: IR spectrum of compound **3**

Lower formula:

Upper formula:

Note: for m < 2000 the elements C, H, N, and O are considered implicitly.

Adducts, pos. ☐ Collect adducts

Adducts, neg.

Measured m/z Tolerance: ppm Charge:

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdB	e ⁻ Conf	N-Rule
563.2403	1	C ₃₁ H ₃₅ N ₂ O ₈	563.2388	-2.6	194.2	1	100.00	15.5	even	ok
563.2403	2	C ₂₈ H ₂₇ N ₁₂ O ₂	563.2374	-5.0	195.2	2	31.47	21.5	even	ok
563.2403	3	C ₂₀ H ₃₅ N ₈ O ₁₁	563.2420	3.0	243.5	3	0.95	7.5	even	ok

☐ Automatically locate monoisotopic peak Maximum number of formulae

☒ Check rings plus double bonds Minimum Maximum

Electron configuration

☒ Filter H/C element ratio Minimum H/C: Maximum H/C:

☒ Estimate carbon number ☒ Generate immediately

Figure S3: HRESI-MS spectrum of compound **3**

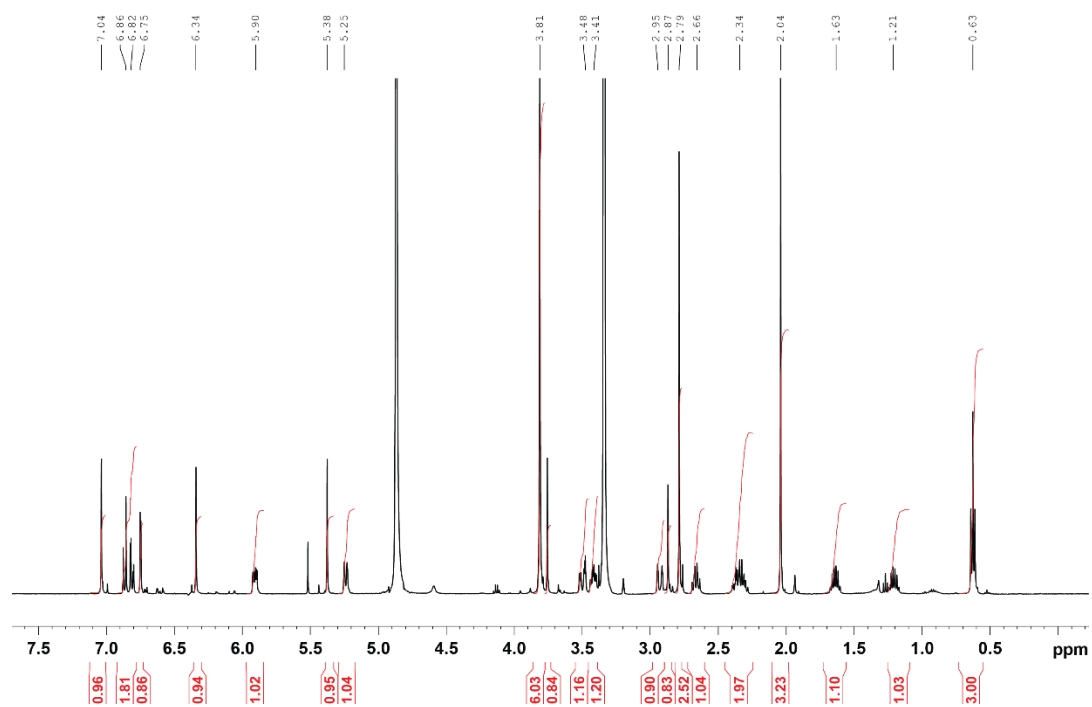


Figure S4: ¹H NMR spectrum of compound **3**

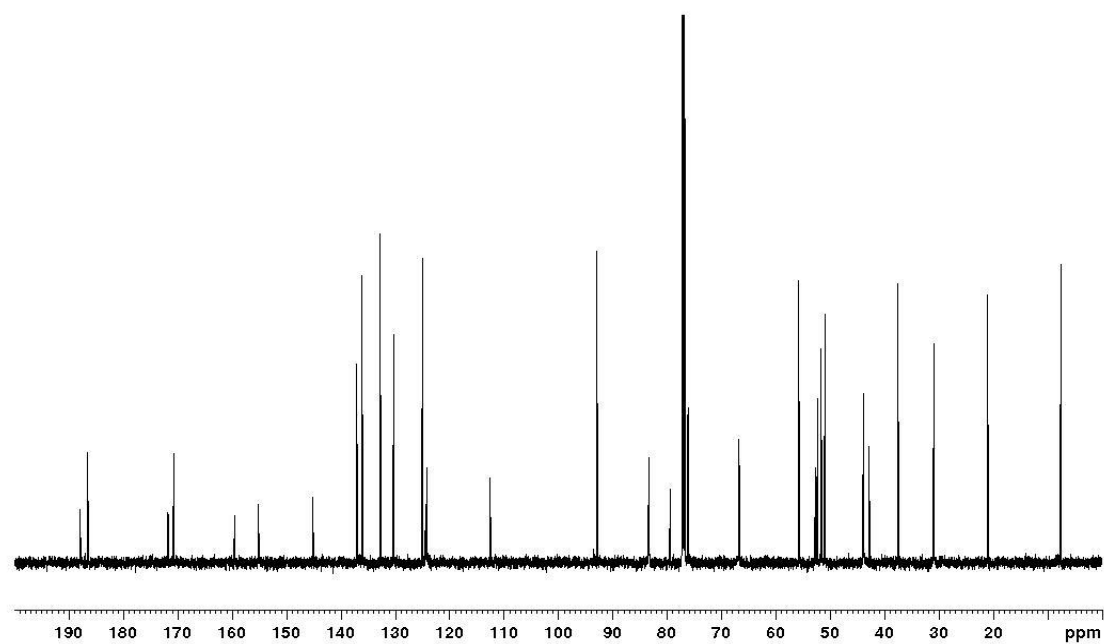


Figure S5: ^{13}C NMR spectrum of compound **3**

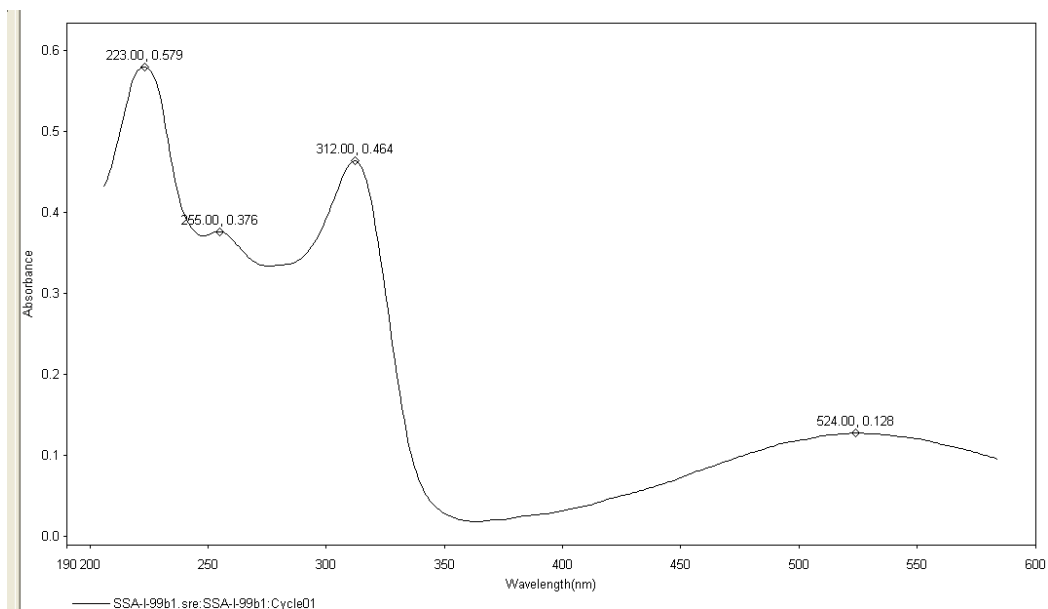


Figure S6: UV spectrum of compound **4**

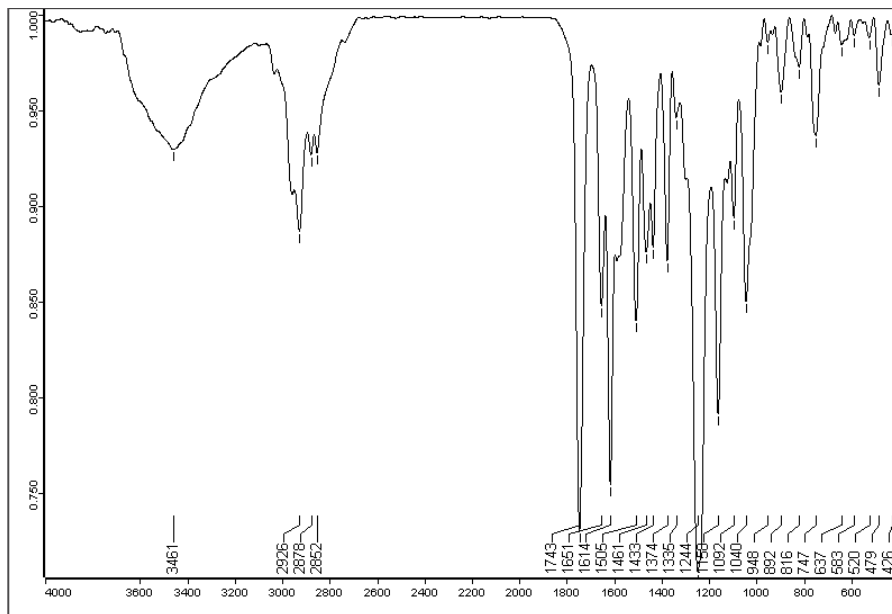


Figure S7: IR spectrum of compound **4**

Lower formula:

Upper formula:

Note: for m < 2000 the elements C, H, N, and O are considered implicitly.

Adducts, pos. ☐ Collect adducts

Adducts, neg.

Measured m/z Tolerance: mDa Charge:

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e ⁻ Conf	N-Rule
1017.4494	1	C ₅₇ H ₆₁ N ₈ O ₁₀	1017.4505	1.1	38.3	1	69.45	31.5	even	ok
1017.4494	2	C ₅₉ H ₆₃ N ₅ O ₁₁	1017.4519	2.4	40.1	2	24.87	31.0	odd	ok
1017.4494	3	C ₆₀ H ₅₉ N ₉ O ₇	1017.4532	3.8	40.6	3	6.43	36.0	odd	ok
1017.4494	4	C ₅₆ H ₆₅ N ₄ O ₁₄	1017.4492	-0.2	42.7	4	100.00	26.5	even	ok
1017.4494	5	C ₅₈ H ₆₇ N ₁₀ O ₁₅	1017.4505	1.1	42.8	5	61.14	26.0	odd	ok

☐ Automatically locate monoisotopic peak Maximum number of formulae

☒ Check rings plus double bonds Minimum Maximum

Electron configuration

☒ Filter H/C element ratio Minimum H/C: Maximum H/C:

☒ Estimate carbon number ☒ Generate immediately

Figure S8: HRESI-MS spectrum of compound **4**

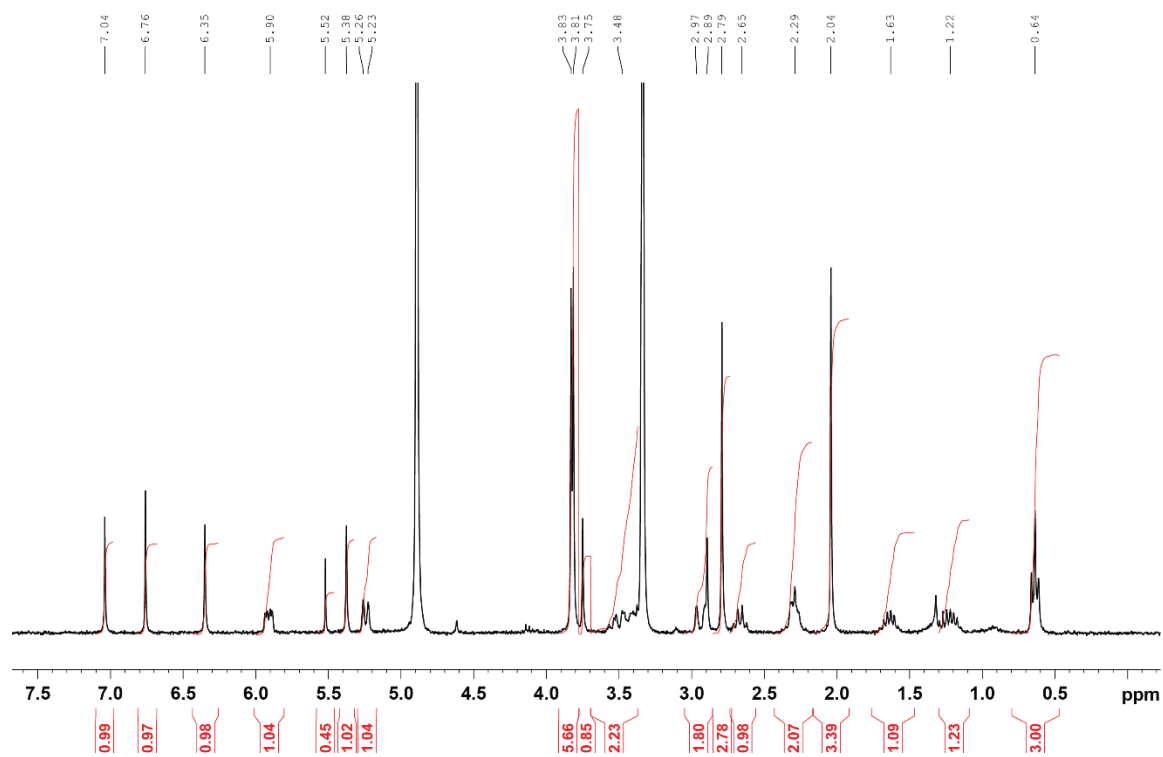


Figure S9: ^1H NMR spectrum of compound **4**

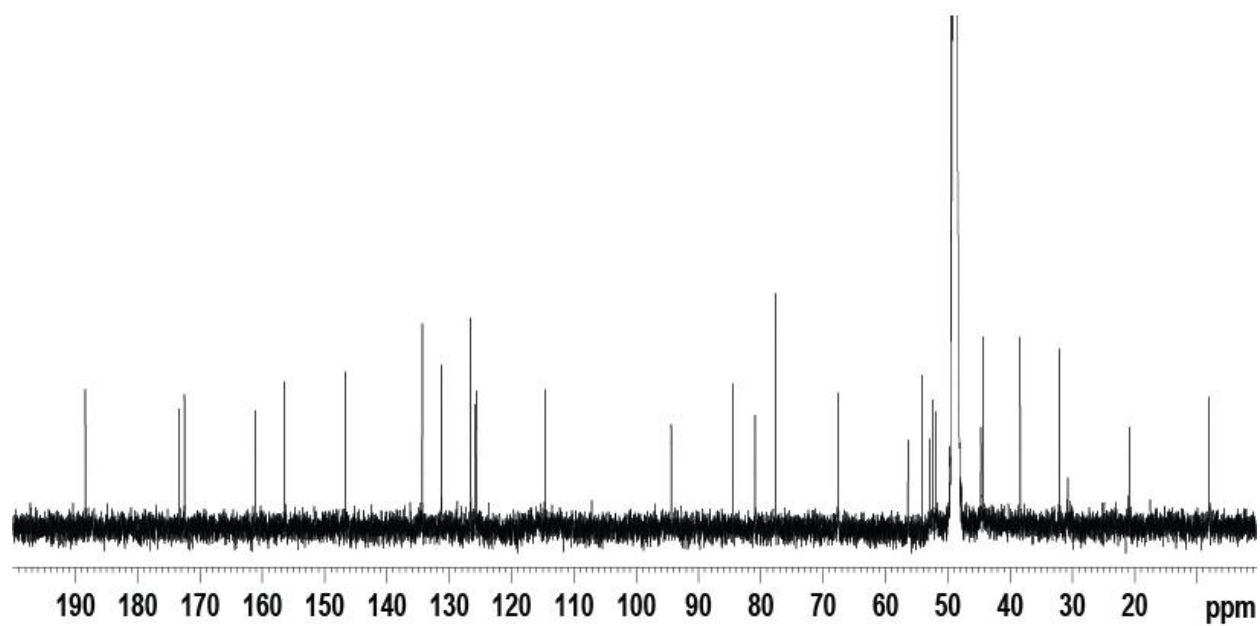


Figure S10: ^{13}C NMR spectrum of compound **4**

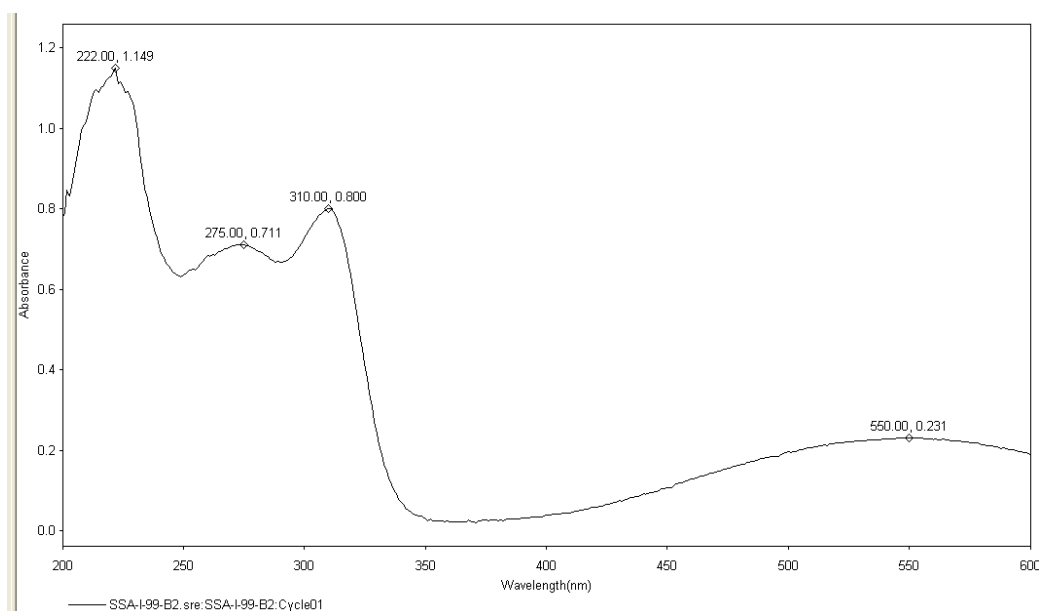


Figure S11: UV spectrum of compound **5**

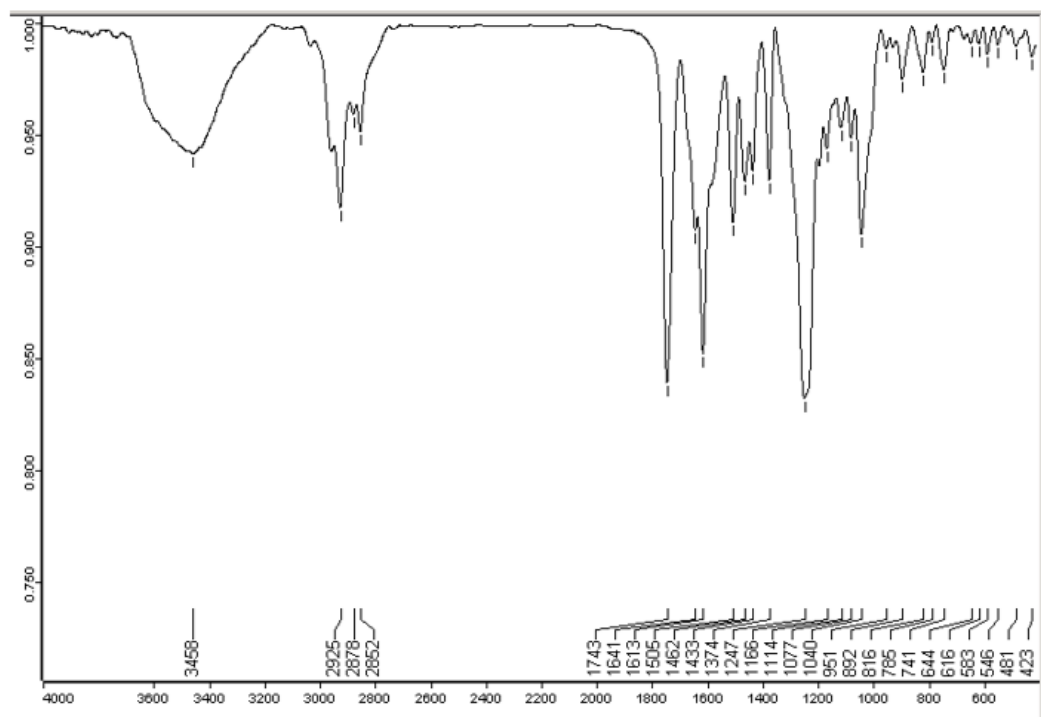


Figure S12: IR spectrum of compound **5**

Lower formula:

Upper formula:

Note: for m < 2000 the elements C, H, N, and O are considered implicitly.

Adducts, pos. ☐ Collect adducts

Adducts, neg.

Measured m/z Tolerance: ppm Charge:

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e ⁻ Conf	N-Rule
1017.4493	1	C53H57N14O8	1017.4478	-1.5	34.4	1	52.12	32.5	even	ok
1017.4493	2	C54H53N18O4	1017.4492	-0.2	37.2	2	100.00	37.5	even	ok
1017.4493	3	C56H65N4O14	1017.4492	-0.2	40.6	3	91.69	26.5	even	ok

☐ Automatically locate monoisotopic peak Maximum number of formulae

☒ Check rings plus double bonds Minimum Maximum

Electron configuration

☒ Filter H/C element ratio Minimum H/C: Maximum H/C:

☒ Estimate carbon number ☒ Generate immediately

Figure S13: HRESI-MS spectrum of compound **5**

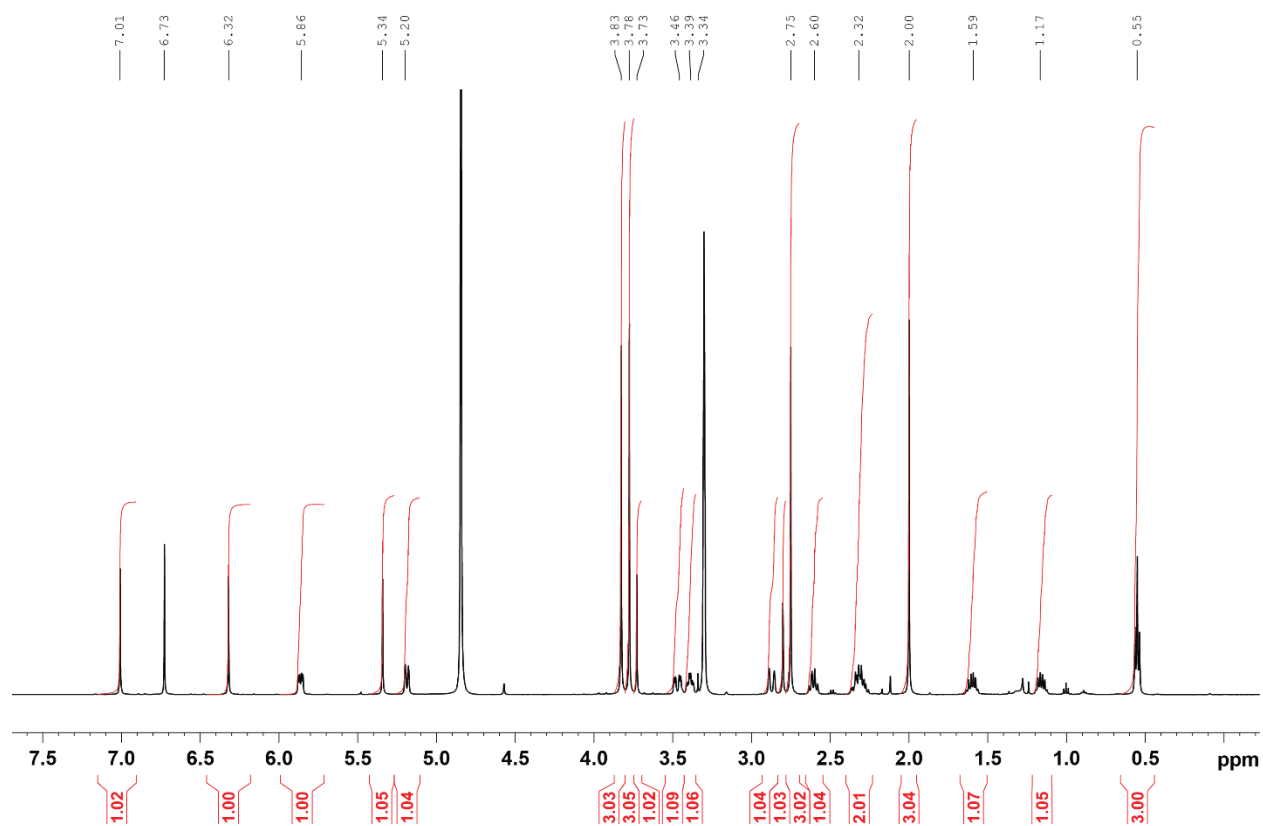


Figure S14: ¹H NMR spectrum of compound **5** (peak at 5.5 ppm is CH₂Cl₂).

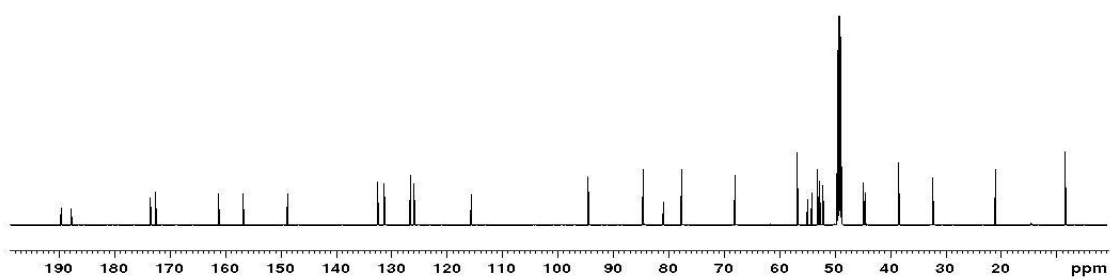


Figure S15: ^{13}C NMR spectrum of compound **5**

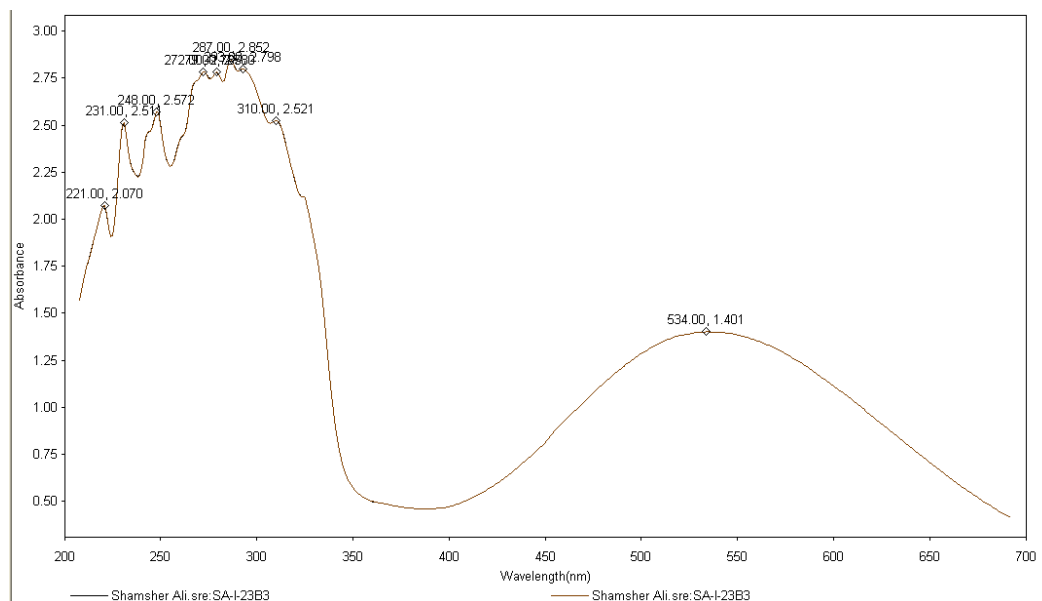


Figure-16: UV spectrum of compounds **6**

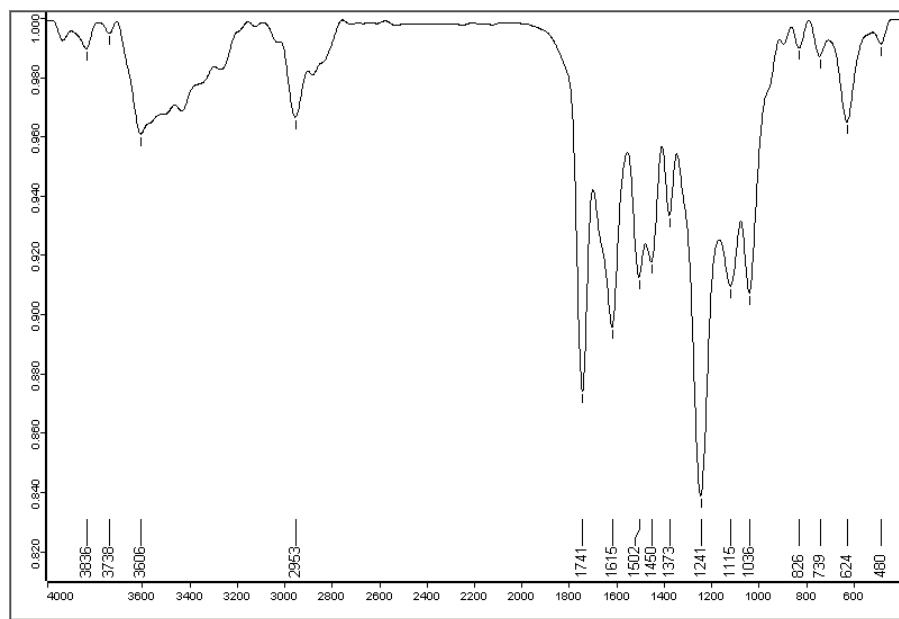


Figure S17: IR spectrum of compounds **6**

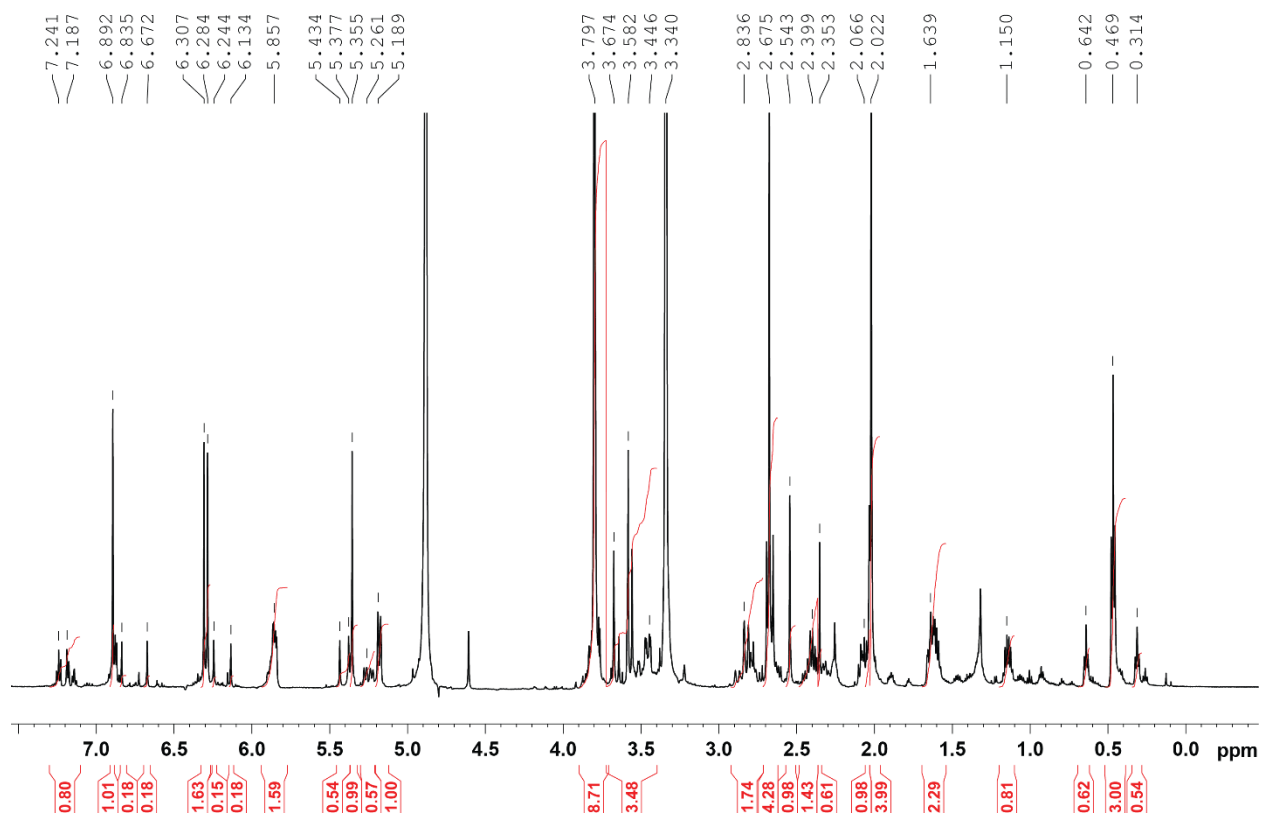


Figure S18: ¹H NMR spectrum of compounds **6**

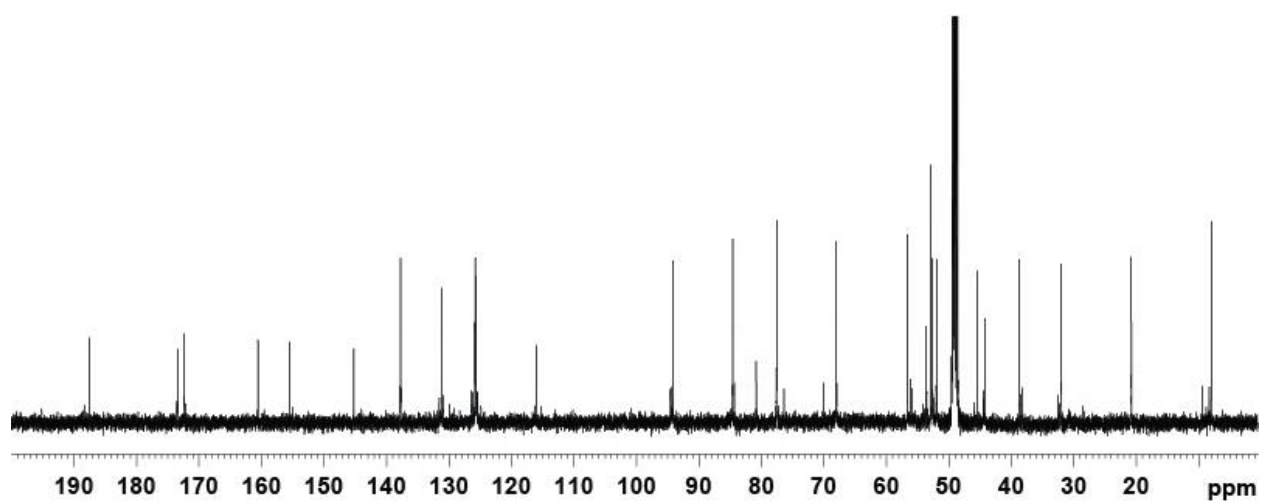


Figure S19: ¹³C NMR spectrum of compound **6**

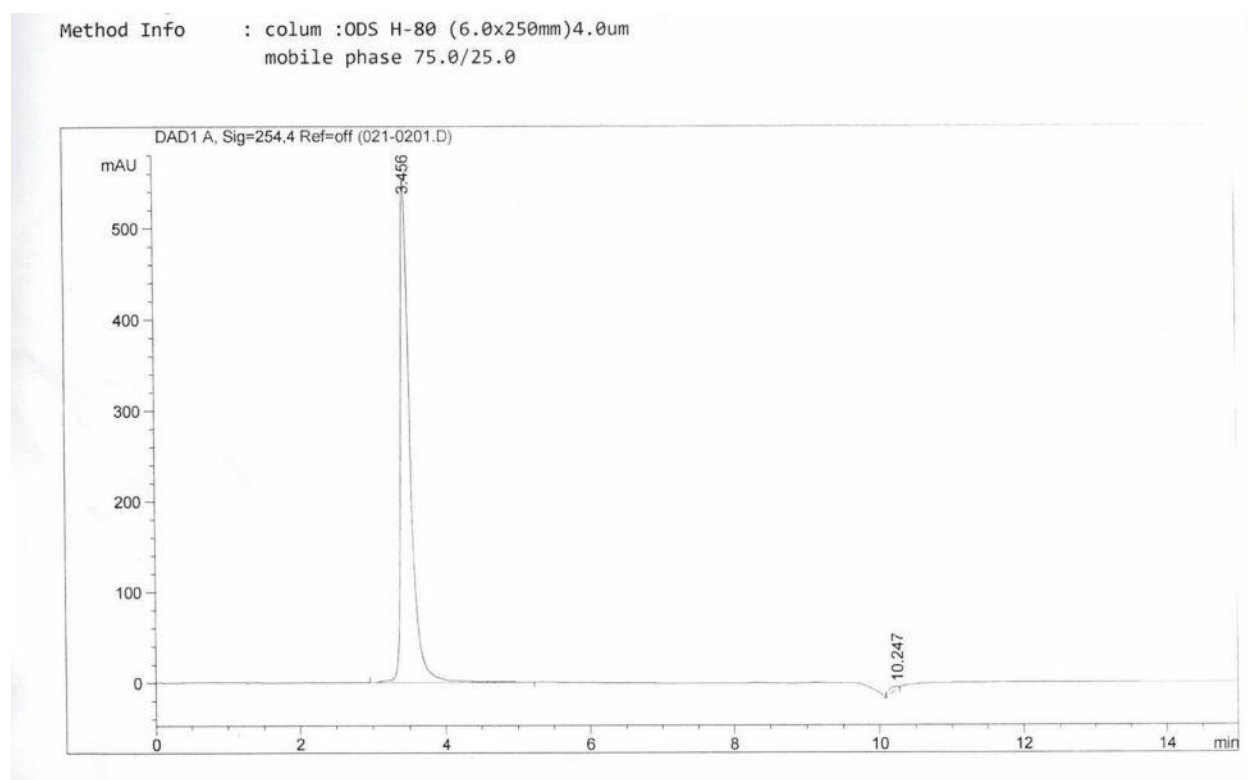


Figure S20: UPLC profile of compound **6**

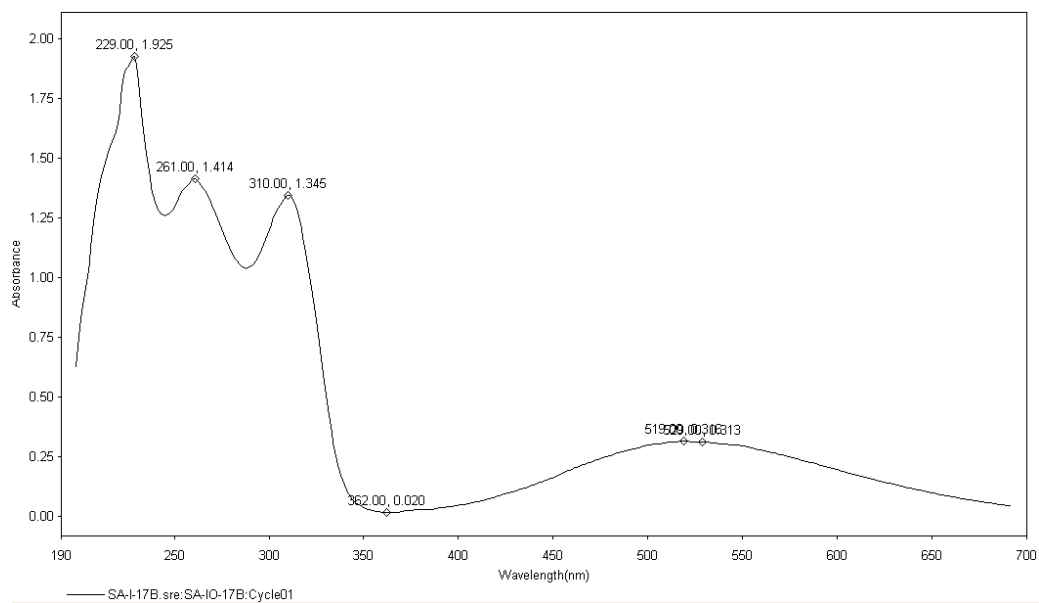


Figure S21: UV spectrum of compound **7**

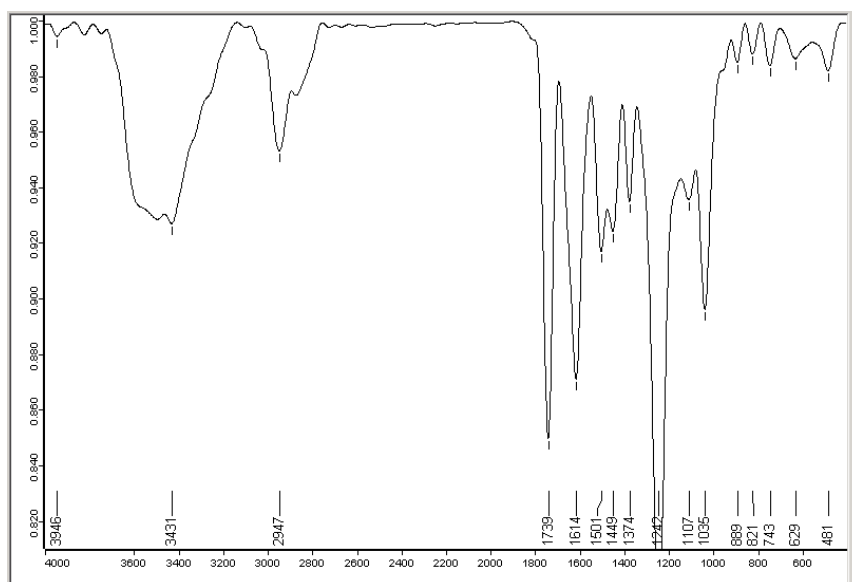


Figure S22: IR spectrum of compounds **7**

Lower formula:

Upper formula:

Note: for m < 2000 the elements C, H, N, and O are considered implicitly.

Adducts, pos. ☐ Collect adducts

Adducts, neg.

Measured m/z Tolerance: ppm Charge:

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdB	e ⁻ Conf	N-Rule
1471.6633	1	C ₈₁ H ₉₅ N ₆ O ₂₀	1471.6596	-2.5	26.7	1	100.00	37.5	even	ok
1471.6633	2	C ₈₀ H ₉₅ N ₈ O ₁₉	1471.6708	5.1	30.1	2	0.23	37.5	even	ok
1471.6633	3	C ₈₀ H ₉₉ N ₂ O ₂₄	1471.6582	-3.4	34.5	3	15.18	32.5	even	ok

☐ Automatically locate monoisotopic peak Maximum number of formulae

☒ Check rings plus double bonds Minimum Maximum

Electron configuration

☒ Filter H/C element ratio Minimum H/C: Maximum H/C:

☒ Estimate carbon number ☒ Generate immediately

Figure S23: HRESI-MS spectrum of compounds **7**

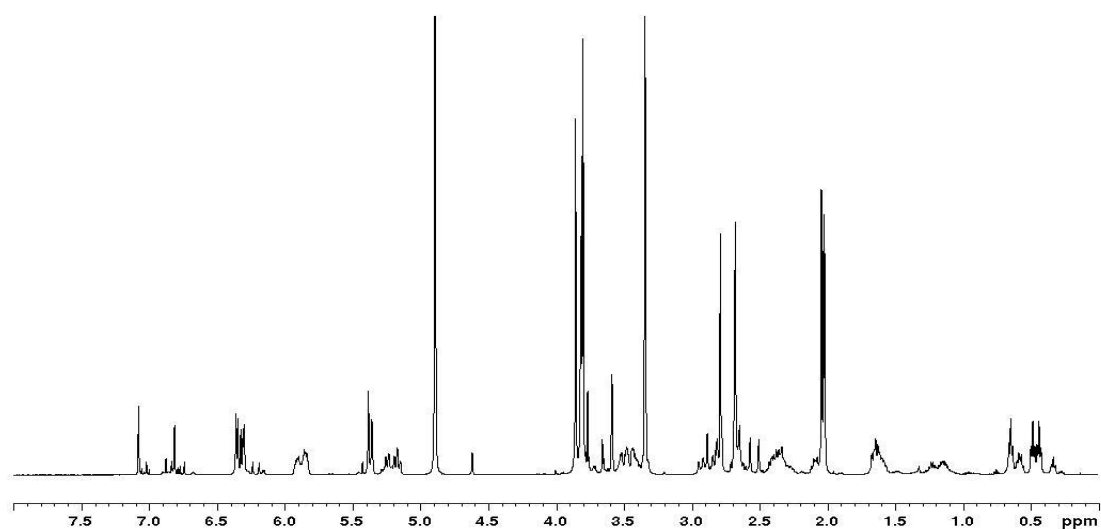


Figure S24: ^1H NMR spectrum of compounds **7**

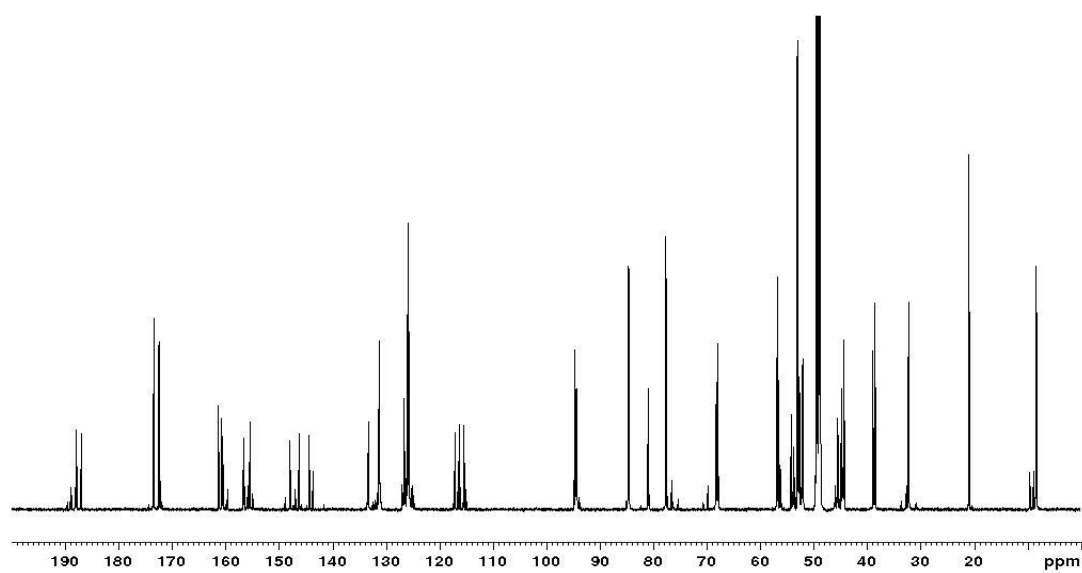


Figure S25: ^{13}C NMR spectrum of compounds **7**

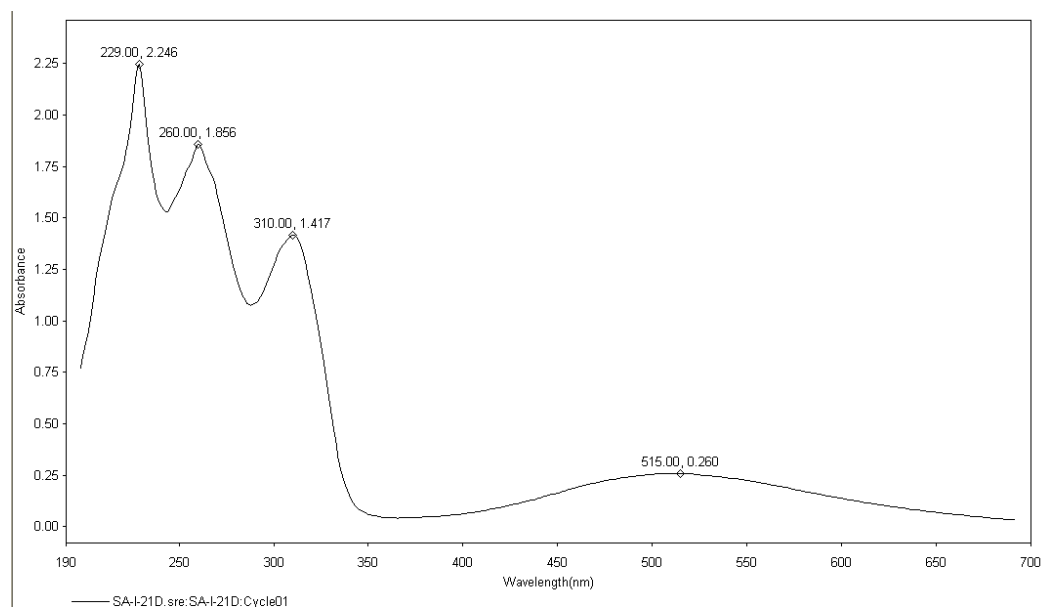


Figure S26: UV spectrum of compounds **8**

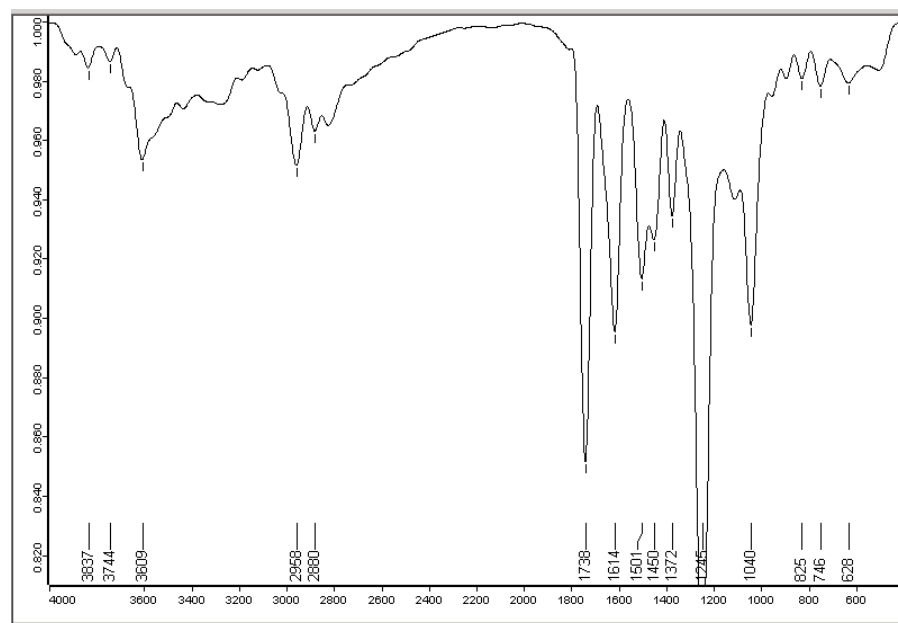


Figure S27: IR spectrum of compounds **8**

Lower formula:

Upper formula:

Note: for m < 2000 the elements C, H, N, and O are considered implicitly.

Adducts, pos. ☐ Collect adducts

Adducts, neg.

Measured m/z Tolerance: ppm Charge:

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e ⁻ Conf	N-Rule
1925.8702	1	C ₁₀₆ H ₁₂₅ N ₈ O ₂₆	1925.8700	-0.1	46.4	1	100.00	48.5	even	ok
1925.8702	2	C ₁₀₅ H ₁₂₃ N ₉ O ₂₆	1925.8574	-6.7	47.6	2	0.00	49.0	odd	ok
1925.8702	3	C ₁₀₂ H ₁₂₅ N ₈ O ₂₉	1925.8547	-8.1	52.9	3	0.00	44.5	even	ok

☐ Automatically locate monoisotopic peak Maximum number of formulae

☒ Check rings plus double bonds Minimum Maximum

Electron configuration

☒ Filter H/C element ratio Minimum H/C: Maximum H/C:

☒ Estimate carbon number ☒ Generate immediately

Figure S28: HR-ESI-MS spectrum of compounds **8**

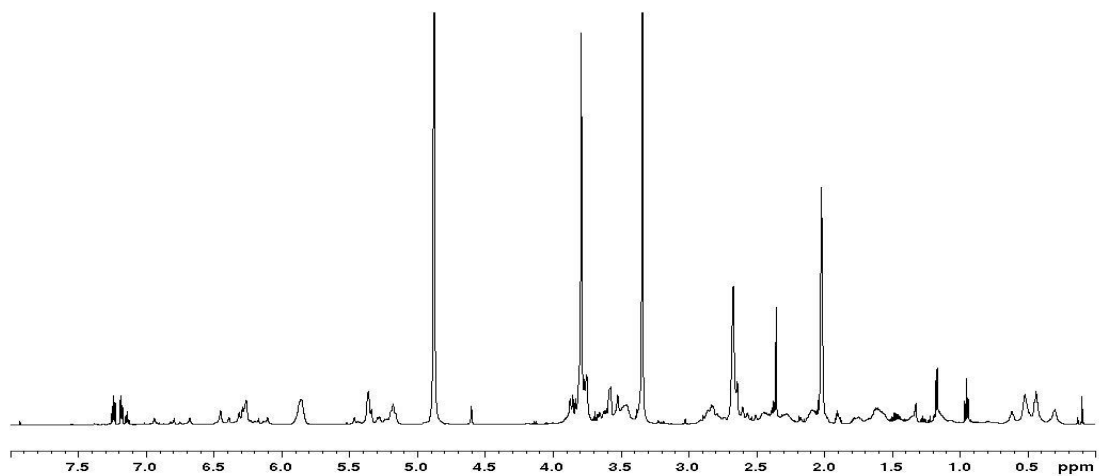


Figure S29: ^1H NMR spectrum of compounds **8**

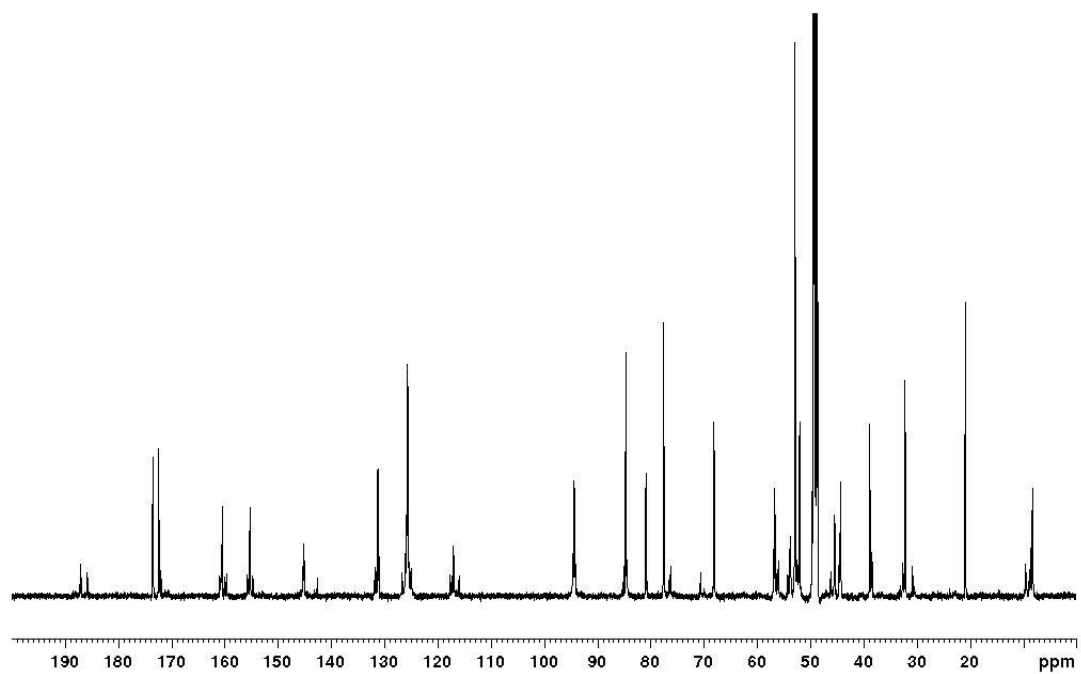


Figure S30: ^{13}C NMR spectrum of compounds **8**

Table S1: ^{13}C NMR data for compounds **1**, **3** (CDCl_3), **4**, **5** and **6a** (CD_3OD). The central spectral line of the solvent was used as a reference.

C	Vindoline 1	Mono- adduct 3	Di-adduct 4	Di-adduct 5	Gem adduct 6a
2	83.2	83.3	84.5	84.4	84.6
3	50.9	50.9	51.8	52.0	51.9
5	51.7	51.6	52.4	52.6	52.7
6	43.9	43.9	44.7	44.6	44.4
7	52.6	52.7	54.1	54.0	53.6
8	124.8	124.4	125.9	125.9	125.7
9	122.5	125.0	126.6	126.5	125.8
10	104.4	112.6	114.6	115.5	116.0
11	160.9	159.5	161.1	161.2	160.6
12	95.6	92.9	94.4	94.4	94.1
13	153.5	155.1	156.5	156.7	155.5
14	129.9	124.2	125.8	125.8	125.6
15	130.3	130.3	131.3	131.2	131.1
16	79.4	79.4	80.9	80.8	80.8
17	76.1	76.2	77.6	77.5	77.5
18	7.5	7.6	8.1	8.1	8.0
19	30.6	30.9	32.1	32.1	32.1
20	42.7	42.8	44.3	44.3	44.2
21	66.8	66.8	67.6	67.9	68.0
COOCH_3	171.7	171.8	173.4	173.4	173.4
COOC	52.0	52.3	52.9	52.9	52.9
$\text{O}\text{C}\text{OCH}_3$	170.5	170.7	172.5	172.5	172.4
OCOC	20.9	21.6	20.8	20.8	20.8
NCH_3	38.0	37.6	38.3	38.3	38.7
ArOC	55.1	55.8	56.4	56.6	56.6
1'		188.0	188.3	189.6	187.5
2'		145.1	146.7	148.7	145.2
3'		132.8	134.3	132.4	145.2
4'		186.5	188.3	187.8	187.5
5'		136.1	146.7	132.4	137.7
6'		137.0	134.3	148.7	137.7

Table S2. Energetics obtained at the DFT (M06-2X/6-311G**) level of theory, considering the methanol implicit solvent (CPCM). Values given in hartree.

	E	H° _{0K}	H° _{298K}	G° _{298K}
6a1 anti1	-1072.4627	-1072.1481	-1072.1267	-1072.1974
6a1 anti2	-1072.4626	-1072.1480	-1072.1263	-1072.1992
6b syn	-1072.4639	-1072.1490	-1072.1276	-1072.1980
TS anti1 ↔ anti2	-1072.4599	-1072.1455	-1072.1246	-1072.1953
TS anti1 ↔ syn	-1072.4300	-1072.1158	-1072.0951	-1072.1645
TS syn ↔ syn	-1072.4596	-1072.1451	-1072.1242	-1072.1242

I. Views of **6a** and **6b** isomers:

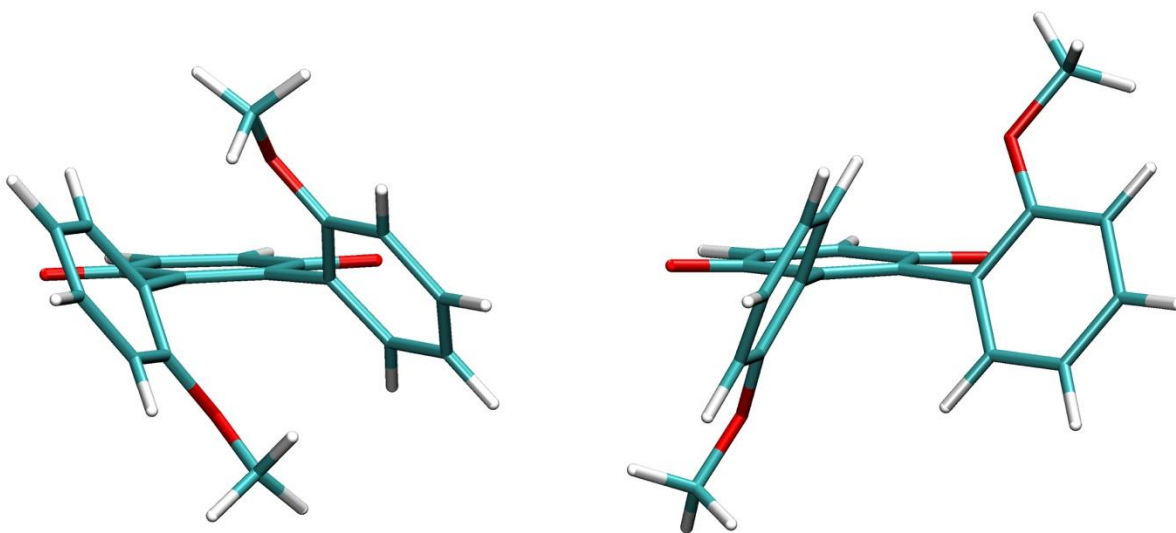


Fig. S1 **6a1** anti1 and anti2 representations (from optimized M06-2X/6-311G** geometry).

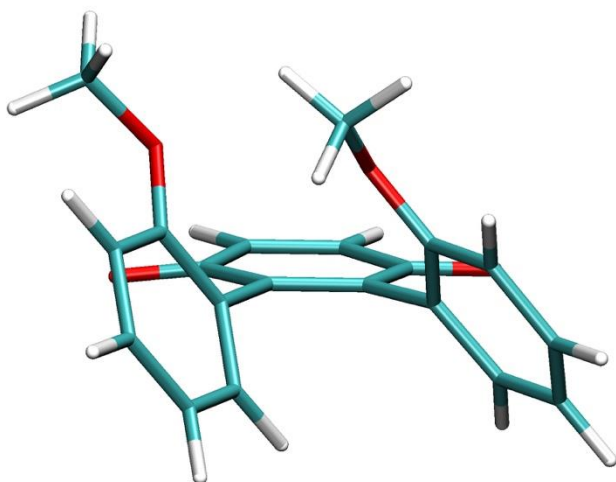


Fig. S2 6b syn representation (from optimized M06-2X/6-311G** geometry).