SUPPLEMNTARY INFORMATION

Amantadine and Rimantadine Analogues—Single-Crystal Analysis and Anti-Coronaviral Activity

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Table S1. Bond Lengths for **1R**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O4	C3	1.247(9)	C8	C9	1.542(12)
N2	C2	1.460(9)	C9	C15	1.484(13)
N2	C3	1.315(9)	C9	C10	1.535(13)
N6A	C18A	1.497(17)	C14	C13	1.516(12)
N6A	C5A	1.480(14)	C15	C13	1.507(14)
N6A	C7A	1.508(15)	C16	C11	1.548(14)
C1	C2	1.537(11)	C13	C12	1.502(16)
C1	C8	1.513(10)	C10	C11	1.499(16)
C1	C14	1.515(10)	C11	C12	1.495(16)
C1	C16	1.526(10)	C5B	N6B	1.50(2)
C2	C17	1.516(12)	C7B	N6B	1.50(2)
C3	C5A	1.521(12)	C18B	N6B	1.55(2)
C3	C5B	1.55(3)			

Table S2. Bond Lengths for **2A**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O4	C3	1.227(4)	C2	C17	1.519(5)
N2	C3	1.330(4)	C8	C9	1.517(5)
N2	C2	1.461(4)	C9	C10	1.522(5)
N6	C5	1.466(5)	C9	C15	1.530(6)
N6	C7	1.475(5)	C11	C16	1.527(6)
C3	C5	1.513(4)	C11	C10	1.516(6)
C1	C2	1.551(5)	C11	C12	1.521(7)
C1	C8	1.529(5)	C14	C13	1.529(5)
C1	C16	1.533(5)	C12	C13	1.523(7)
C1	C14	1.534(4)	C13	C15	1.523(7)

Table S3. Bond Lengths for **2R**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O4	C3	1.225(12)	C11	C10	1.536(13)
N2	C1	1.483(11)	N6	C5	1.411(15)
N2	C3	1.315(13)	N6	C7	1.456(14)
C1	C8	1.544(12)	C13	C12	1.524(13)
C1	C15	1.508(12)	C13	C16	1.497(14)
C1	C16	1.536(12)	C13	C14	1.491(14)
C3	C5	1.525(12)	C8	C9	1.546(13)
C11	C15	1.522(12)	C9	C10	1.516(14)
C11	C12	1.530(13)	C9	C14	1.530(12)

Table S4. Bond Angles for **1R**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	N2	C2	124.2(7)	C15	C9	C8	109.9(7)
C18A	N6A	C7A	108.3(13)	C15	C9	C10	109.2(9)
C5A	N6A	C18A	110.7(13)	C10	C9	C8	108.2(8)
C5A	N6A	C7A	111.2(10)	C1	C14	C13	112.1(7)
C8	C1	C2	112.3(6)	C9	C15	C13	110.4(8)
C8	C1	C14	108.0(7)	C1	C16	C11	110.4(8)
C8	C1	C16	107.9(7)	C15	C13	C14	108.9(8)
C14	C1	C2	110.4(6)	C12	C13	C14	110.1(10)
C14	C1	C16	108.0(8)	C12	C13	C15	108.5(8)
C16	C1	C2	110.1(6)	N6A	C5A	C3	109.0(10)
N2	C2	C1	112.9(6)	C11	C10	C9	109.7(7)
N2	C2	C17	108.3(7)	C10	C11	C16	108.4(10)
C17	C2	C1	114.9(7)	C12	C11	C16	110.9(9)
O4	C3	N2	125.3(7)	C12	C11	C10	109.0(9)
O4	C3	C5A	119.8(7)	C11	C12	C13	110.0(9)
O4	C3	C5B	111.6(14)	N6B	C5B	C3	109(3)
N2	C3	C5A	114.0(7)	C5B	N6B	C7B	123(4)
N2	C3	C5B	113.4(13)	C5B	N6B	C18B	107(3)
C1	C8	C9	110.9(7)	C7B	N6B	C18B	113(4)

Table S5. Bond Angles for **2A**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	N2	C2	123.9(3)	N6	C5	C3	110.1(3)
C5	N6	C7	113.2(3)	C8	C9	C10	109.3(3)
O4	C3	N2	125.0(3)	C8	C9	C15	109.0(3)
O4	C3	C5	120.4(3)	C10	C9	C15	109.9(3)
N2	C3	C5	114.5(3)	C10	C11	C16	109.2(3)
C8	C1	C2	109.8(3)	C10	C11	C12	110.1(4)
C8	C1	C16	107.2(3)	C12	C11	C16	109.0(3)
C8	C1	C14	108.7(3)	C11	C16	C1	110.6(3)
C16	C1	C2	109.3(3)	C13	C14	C1	110.1(3)
C16	C1	C14	109.1(3)	C11	C10	C9	109.3(3)
C14	C1	C2	112.6(3)	C11	C12	C13	109.8(3)
N2	C2	C1	111.4(3)	C12	C13	C14	109.2(4)
N2	C2	C17	108.3(3)	C12	C13	C15	109.9(4)
C17	C2	C1	116.2(3)	C15	C13	C14	109.3(3)
C9	C8	C1	111.2(3)	C13	C15	C9	109.3(4)

Table S6. Bond Angles for **2R**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	N2	C1	123.8(7)	C16	C13	C12	109.7(7)
N2	C1	C8	106.3(7)	C14	C13	C12	109.4(8)
N2	C1	C15	112.2(7)	C14	C13	C16	109.7(8)
N2	C1	C16	111.5(7)	C1	C8	C9	108.7(7)
C15	C1	C8	108.5(7)	C10	C9	C8	108.7(7)
C15	C1	C16	110.3(7)	C10	C9	C14	110.1(8)
C16	C1	C8	107.9(7)	C14	C9	C8	109.7(7)
O4	C3	N2	127.6(8)	C1	C15	C11	110.6(7)
O4	C3	C5	117.1(9)	C13	C12	C11	109.6(7)
N2	C3	C5	115.2(8)	C13	C16	C1	110.7(7)
C15	C11	C12	109.2(7)	C9	C10	C11	109.1(7)
C15	C11	C10	108.6(8)	C13	C14	C9	110.2(8)
C12	C11	C10	109.8(7)	N6	C5	C3	111.6(9)
C5	N6	C7	117.4(9)				

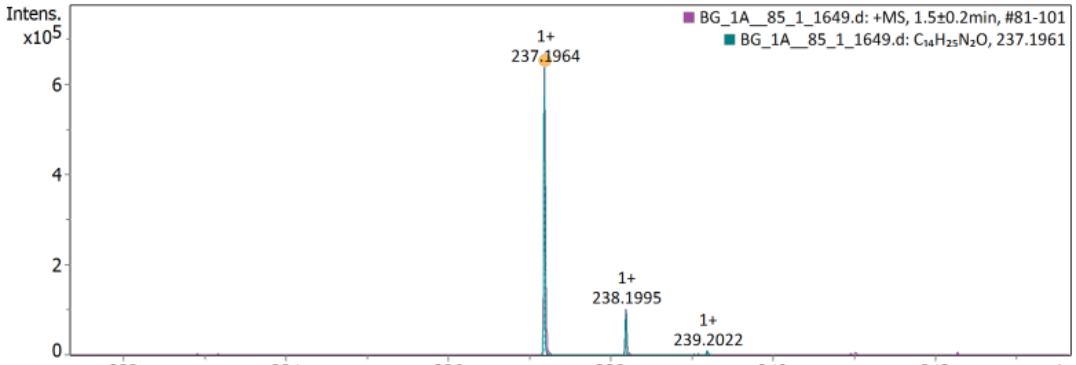
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Martin\BG\Ivanka\BG_1A__85_1_1649.d	Acquisition Date	07-Apr-22 12:25:35
Method	HR_Low_MeOH_pos.m	Operator	Demo User
Sample Name	BG_1A_	Instrument	compact 8255754.20121
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e¯ Conf	N-Rule	Adduct
237.196359	1	C14H25N2O	100.00	237.196140	-0.2	-0.9	0.7	4.0	even	ok	M+H

Figure S1. Mass Spectrum for **1A**

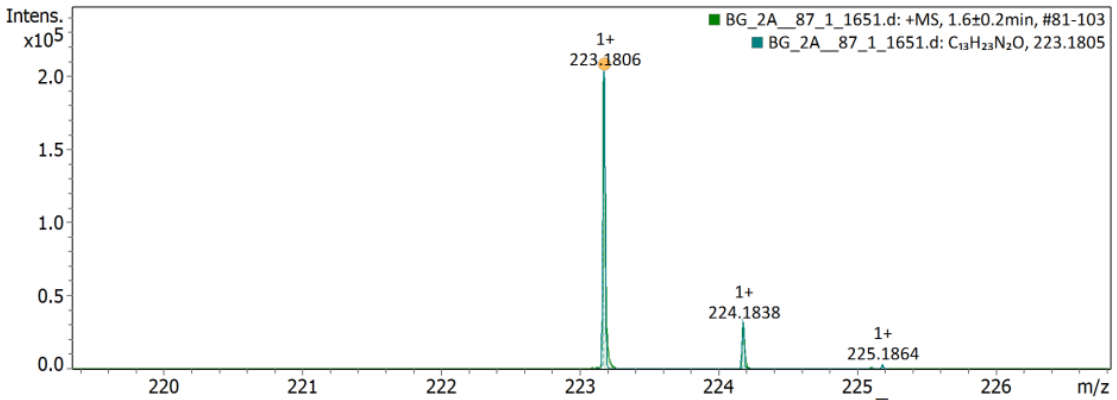
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Martin\BG\Ivanka\BG_2A__87_1_1651.d	Acquisition Date	07-Apr-22 12:33:28
Method	HR_Low_MeOH_pos.m	Operator	Demo User
Sample Name	BG_2A_	Instrument	compact 8255754.20121
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
223.180616	1	C13H23N2O	100.00	223.180490	-0.1	-0.6	0.4	4.0	even	ok	M+H

Figure S2. Mass Spectrum for **2A**

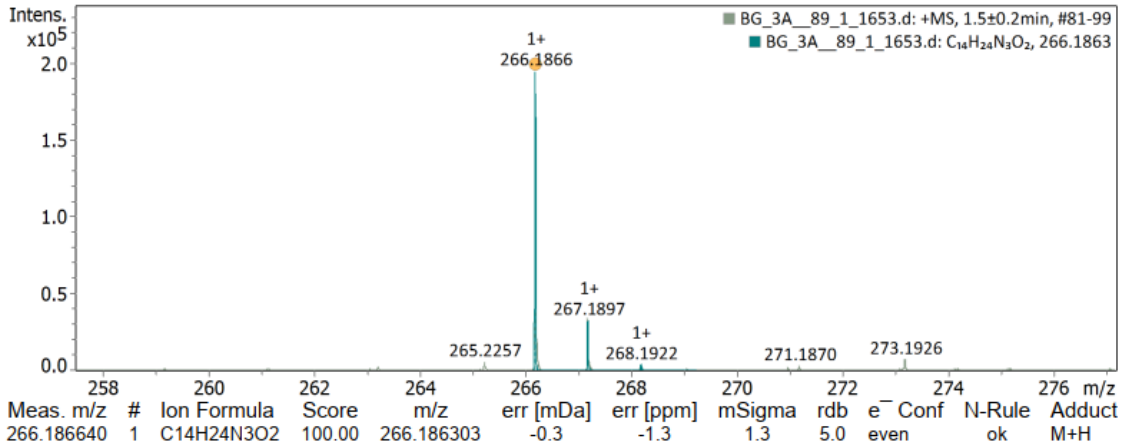
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Martin\BG\Ivanka\BG_3A__89_1_1653.d	Acquisition Date	07-Apr-22 12:41:19
Method	HR_Low_MeOH_pos.m	Operator	Demo User
Sample Name	BG_3A_	Instrument	compact 8255754.20121
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
266.186640	1	C14H24N3O2	100.00	266.186303	-0.3	-1.3	1.3	5.0	even	ok	M+H

Figure S3. Mass Spectrum for **3A**

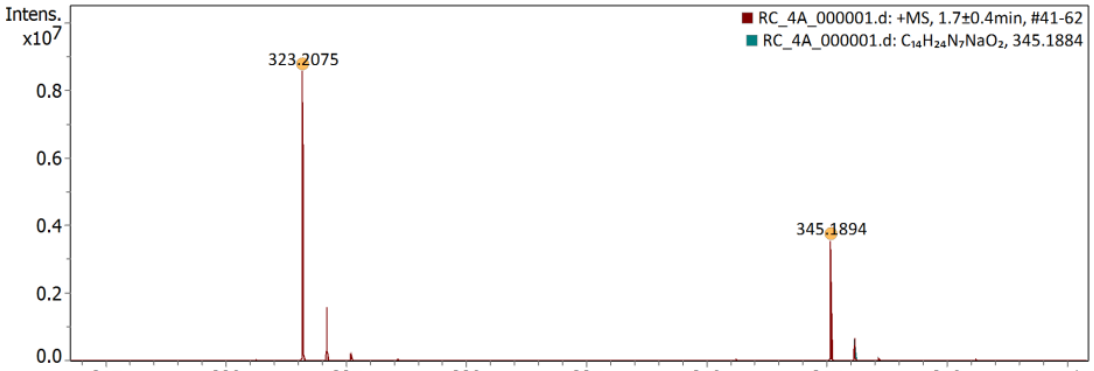
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\HRMS\RC_4A_000001.d	Acquisition Date	10-Jun-22 12:52:29
Method	bg_low_1.m	Operator	Demo User
Sample Name	RC_4A_	Instrument	compact 8255754.20121
Comment	H2O		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	3000 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	2.9 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
323.2075	1	C16H27N4O3	323.2078	0.3	0.9	2.2	1	100.00	6.0	even	ok	M+H
345.1894	1	C16H26N4NaO3	345.1897	0.3	1.0	1.8	1	100.00	6.0	even	ok	M+Na

Figure S4. Mass Spectrum for **4A**

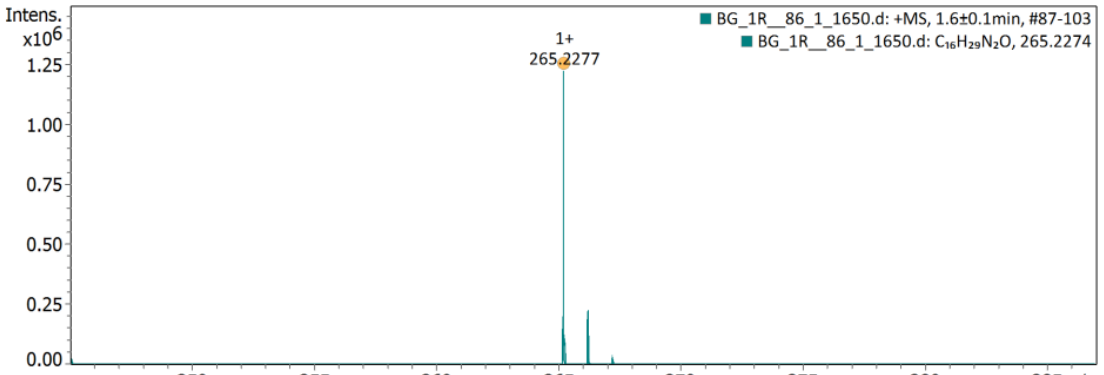
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Martin\BG\Ivanka\BG_1R__86_1_1650.d	Acquisition Date	07-Apr-22 12:29:32
Method	HR_Low_MeOH_pos.m	Operator	Demo User
Sample Name	BG_1R_	Instrument	compact 8255754.20121
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e¯ Conf	N-Rule	Adduct
265.227677	1	C16H29N2O	100.00	265.227440	-0.2	-0.9	1.2	4.0	even	ok	M+H

Figure S5. Mass Spectrum for **1R**

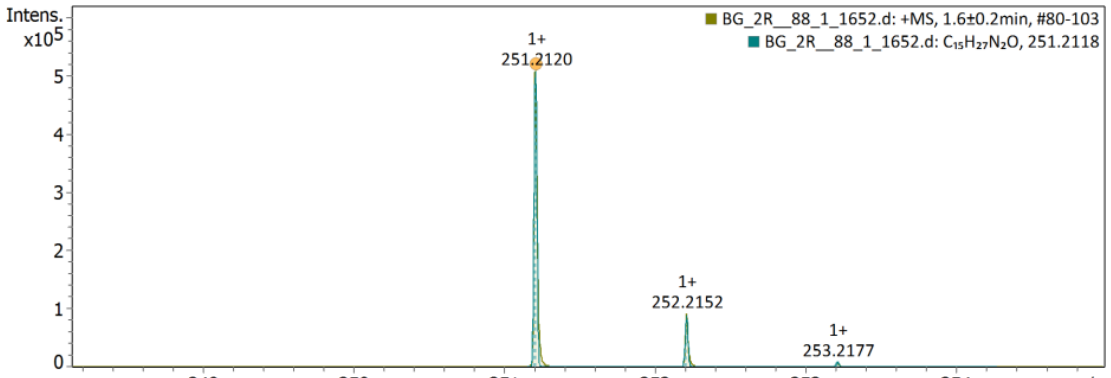
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Martin\BG\Ivanka\BG_2R__88_1_1652.d	Acquisition Date	07-Apr-22 12:37:24
Method	HR_Low_MeOH_pos.m	Operator	Demo User
Sample Name	BG_2R_	Instrument	compact 8255754.20121
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
251.211961	1	C15H27N2O	100.00	251.211790	-0.2	-0.7	4.3	4.0	even	ok	M+H

Figure S6. Mass Spectrum for **2R**

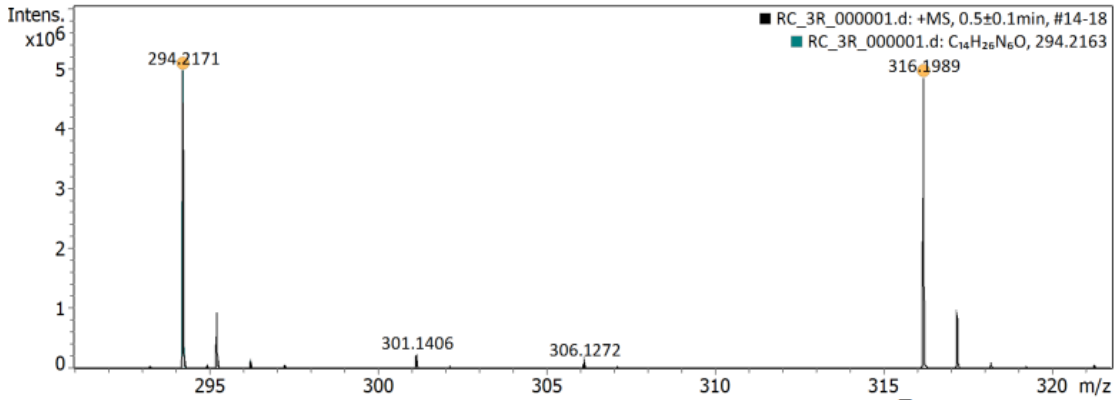
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\HRMS\RC_3R_000001.d	Acquisition Date	10-Jun-22 12:18:12
Method	bg_low_1.m	Operator	Demo User
Sample Name	RC_3R_	Instrument	compact 8255754.20121
Comment	H2O		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	3000 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	2.9 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule	Adduct
294.2171	1	C16H28N3O2	294.2176	0.5	1.7	0.8	1	100.00	5.0	even	ok	M+H
316.1989	1	C16H27N3NaO2	316.1995	0.6	2.0	0.5	1	100.00	5.0	even	ok	M+Na

Figure S7. Mass Spectrum for **3R**

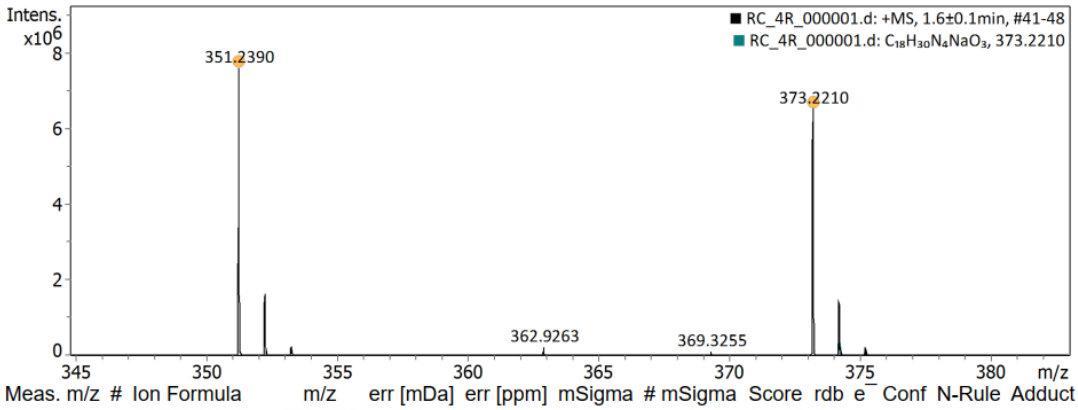
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\HRMS\RC_4R_000001.d	Acquisition Date	10-Jun-22 12:41:12
Method	bg_low_1.m	Operator	Demo User
Sample Name	RC_4R_	Instrument	compact 8255754.20121
Comment	H2O		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Negative	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	2800 V	Set Dry Heater	220 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	2.9 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
351.2390	1	C18H31N4O3	351.2391	0.1	0.2	0.6	1	100.00	6.0	even	ok	M+H
373.2210	1	C18H30N4NaO3	373.2210	0.0	0.0	2.3	1	100.00	6.0	even	ok	M+Na

Figure S8. Mass Spectrum for **4R**