

Supporting Information For

Synthesis of new derivatives of berberine canagliflozin and study on their antibacterial activity and mechanism

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B90C0919/1

¹H NMR (400 MHz, Chloroform-*d*) δ 7.14 (s, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 2H), 5.99 – 5.88 (m, 3H), 5.75 (s, 1H), 5.35 – 5.27 (m, 2H), 3.87 (s, 3H), 3.71 – 3.59 (m, 1H), 3.48 (dt, *J* = 11.1, 4.9 Hz, 1H), 3.01 – 2.71 (m, 3H), 2.45 (dd, *J* = 16.6, 4.6 Hz, 1H).

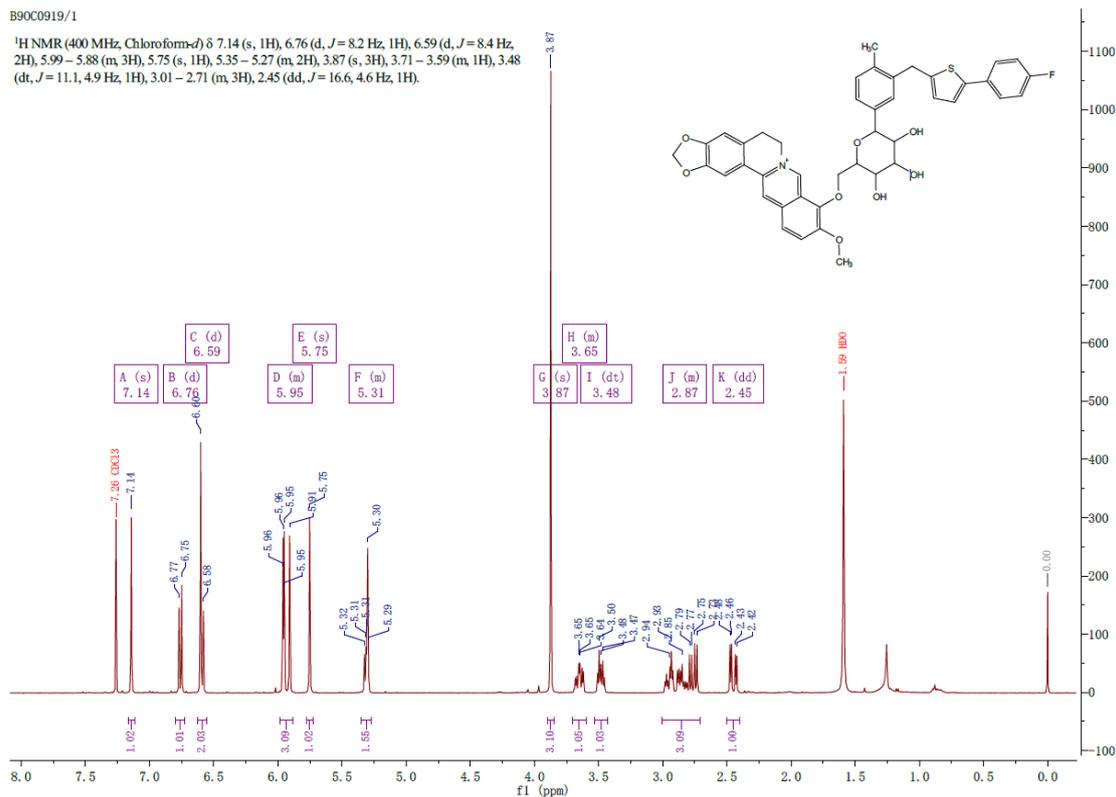


Figure S 1 ¹H NMR spectra of compound B90C

B90C0919-2C/2

¹³C NMR (101 MHz, Chloroform-*d*) δ 165.49, 150.39, 148.69, 147.63, 144.40, 140.43, 137.60, 134.72, 130.62, 129.64, 127.47, 123.58, 119.17, 115.43, 114.91, 110.89, 108.11, 108.06, 104.89, 104.38, 103.71, 101.63, 101.22, 95.30, 77.36, 56.84, 56.42, 55.09, 47.95, 39.25, 30.62, 29.84, 28.54, 18.61.

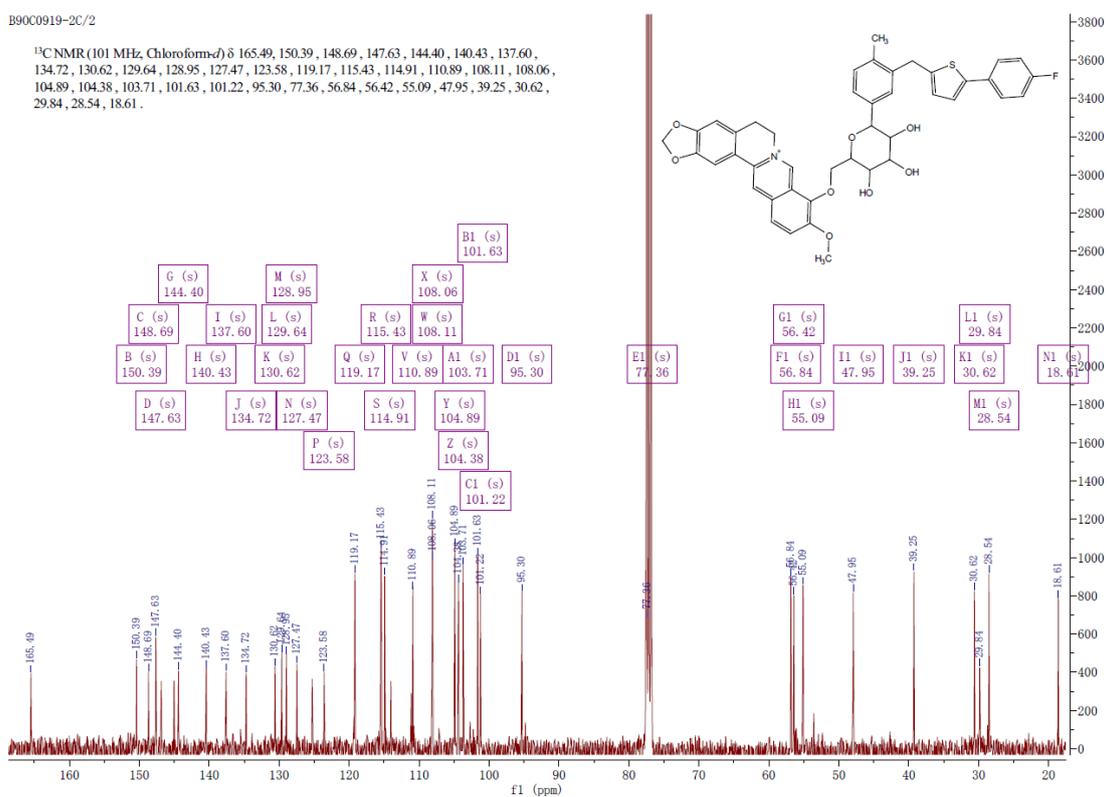


Figure S 2 ¹³C NMR spectra of compound B90C

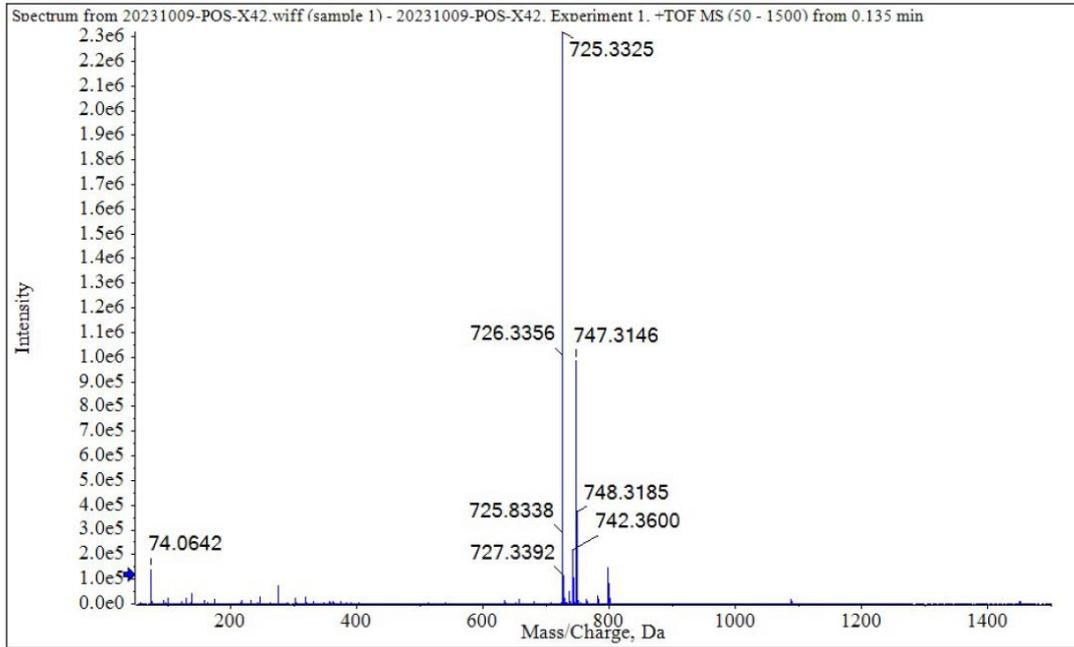


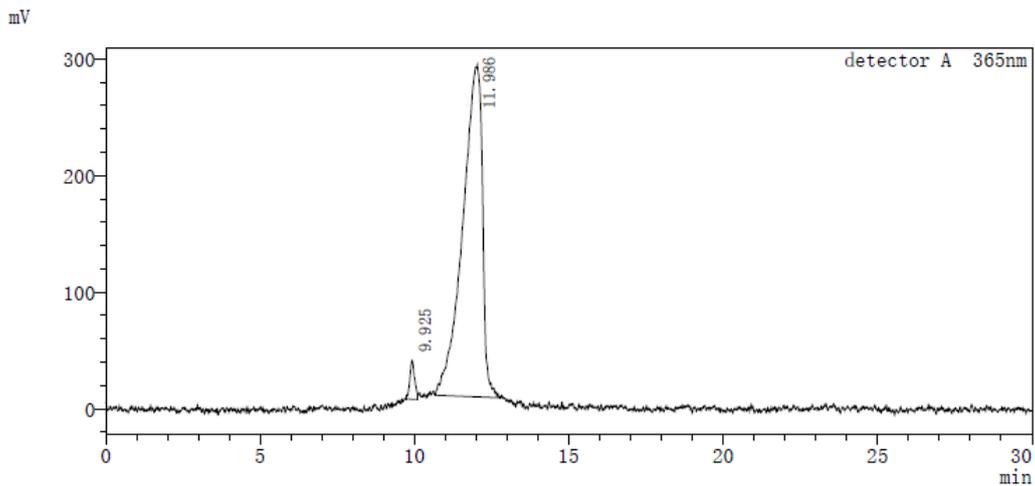
Figure S 3 MS spectra of compound B9OC

SHIMADZU
LabSolutions Analysis report

<Sample Information>

Sample : b9oca365nm
 Sample ID : 01
 Inj. Volume : 10 uL
 Acquisition Date : 2023/9/13 10:37:25

<Chromatogram>



<Chromatogram peak table>

detector A 365nm

number	retention time	peak area	hight	concentration
1	9.925	353117	32886	2.743 %
2	11.986	12519188	282176	97.257 %
总计		12872305	315063	

Figure S 4 The purity of B9OC from HPLC

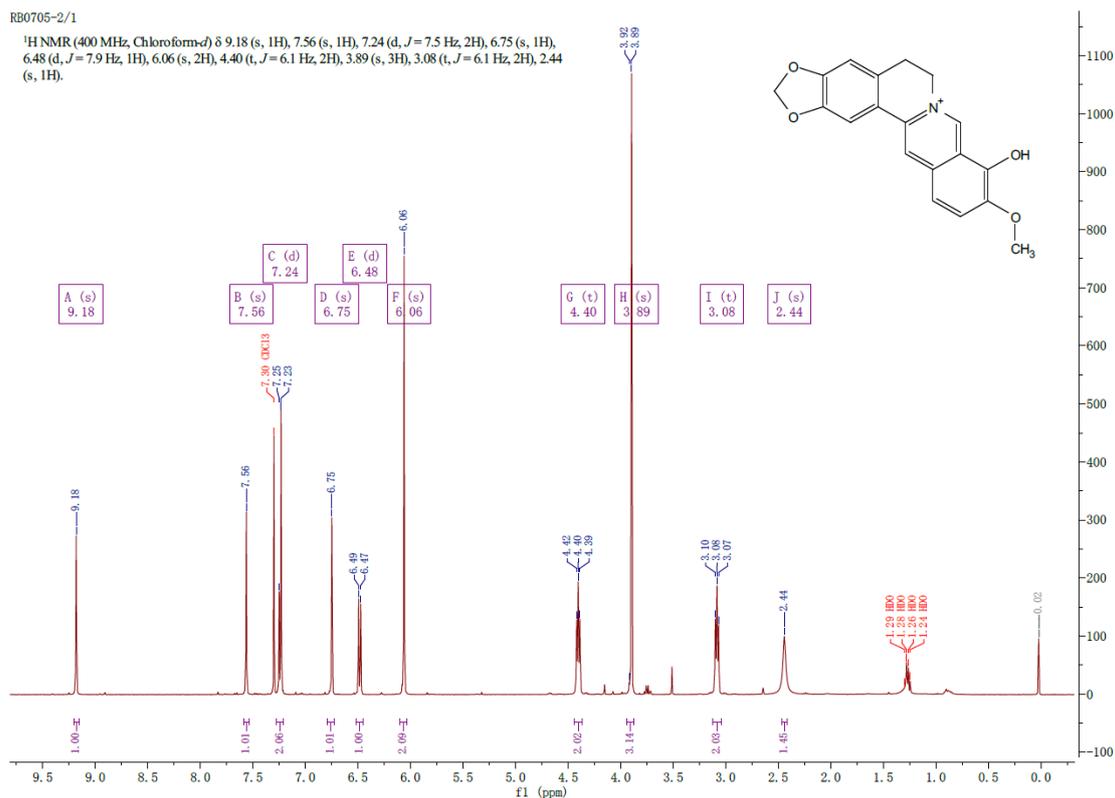


Figure S 5 ^1H NMR spectra of compound Berberubine

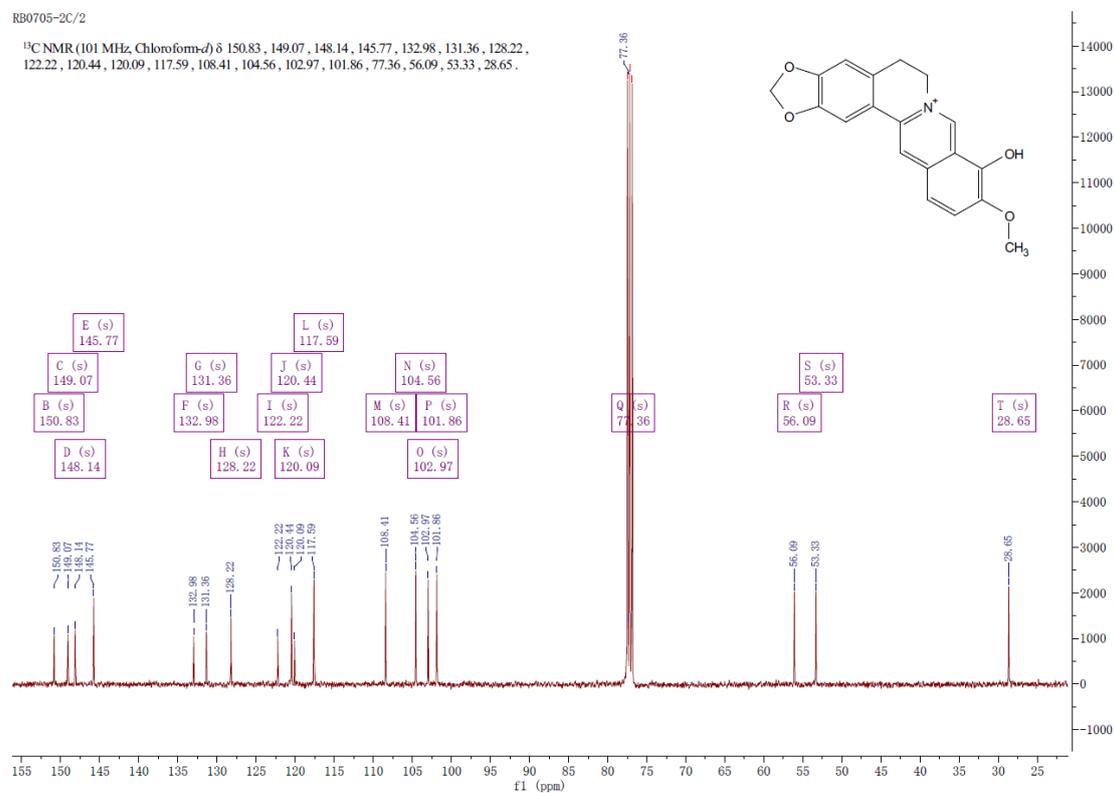


Figure S 6 ^{13}C NMR spectra of compound Berberubine

BRC0914/1

$^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.46 – 7.38 (m, 2H), 7.25 – 7.11 (m, 3H), 7.08 – 6.92 (m, 3H), 6.63 (d, $J = 3.6$ Hz, 1H), 5.30 (s, 2H), 4.43 (s, 1H), 4.15 – 4.07 (m, 3H), 4.02 (d, $J = 12.4$ Hz, 1H), 3.69 – 3.56 (m, 4H), 3.44 (dd, $J = 8.7, 3.3$ Hz, 2H), 3.07 (d, $J = 3.7$ Hz, 1H), 2.27 (s, 3H).

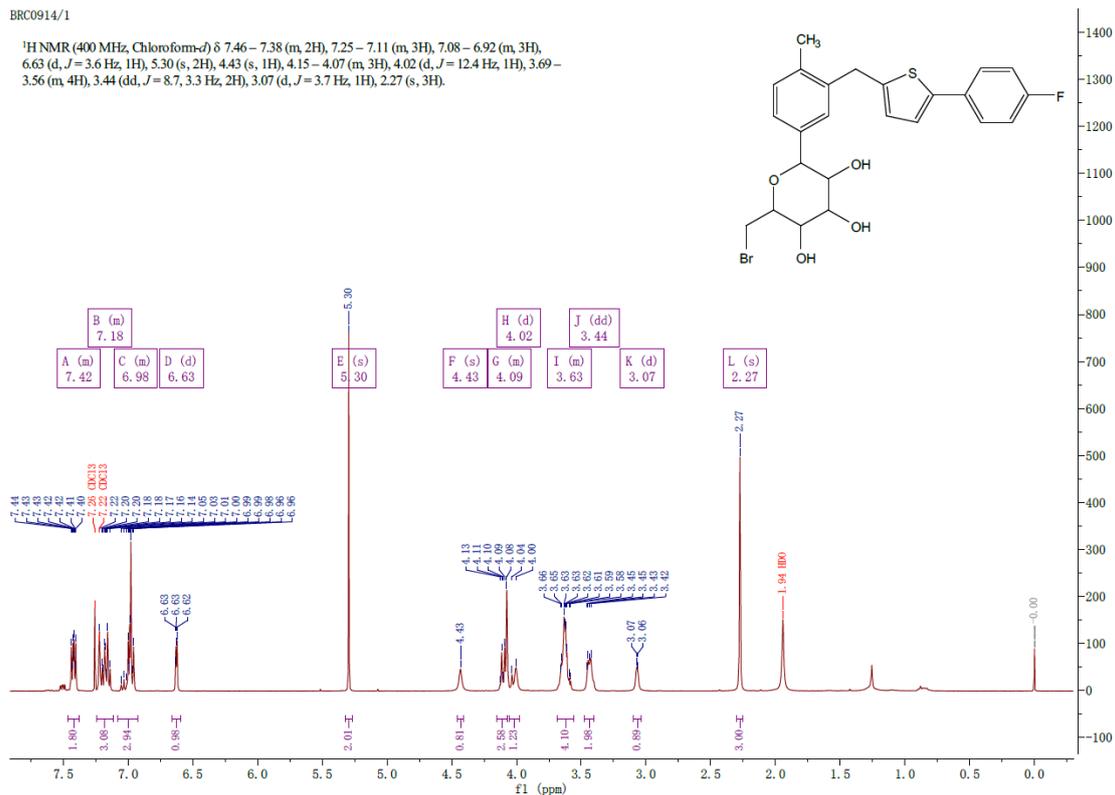


Figure S 7 $^1\text{H NMR}$ spectra of compound Canagliflozin bromide

BRC0914C/2

$^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 143.05, 141.68, 138.57, 137.12, 135.95, 130.97, 130.81, 128.82, 127.26, 127.18, 126.18, 125.85, 122.85, 115.96, 115.74, 81.44, 77.72, 77.36, 75.32, 71.94, 53.58, 34.25, 33.65, 19.43.

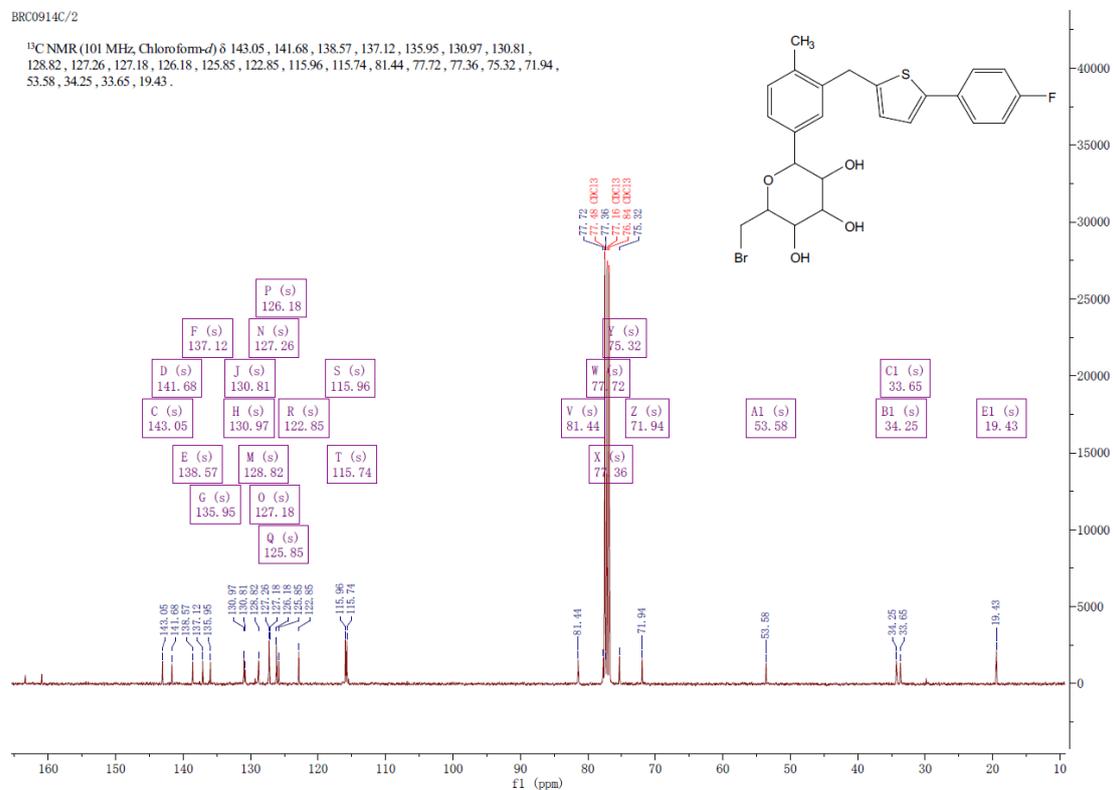


Figure S 8 $^{13}\text{C NMR}$ spectra of compound Canagliflozin bromide

B90BU1020/1

^1H NMR (400 MHz, Chloroform-*d*) δ 10.29 (s, 1H), 8.36 (s, 1H), 7.91 (d, J =9.0 Hz, 1H), 7.74 (d, J =9.0 Hz, 1H), 7.36 (s, 1H), 6.77 (s, 1H), 6.04 (s, 2H), 5.32 (t, J =6.3 Hz, 2H), 4.45 (t, J =6.8 Hz, 2H), 4.01 (s, 3H), 3.31 (t, J =6.3 Hz, 2H), 1.99 (p, J =6.9 Hz, 3H), 1.57 (q, J =7.5 Hz, 3H), 1.24 (s, 3H), 1.01 (t, J =7.4 Hz, 4H).

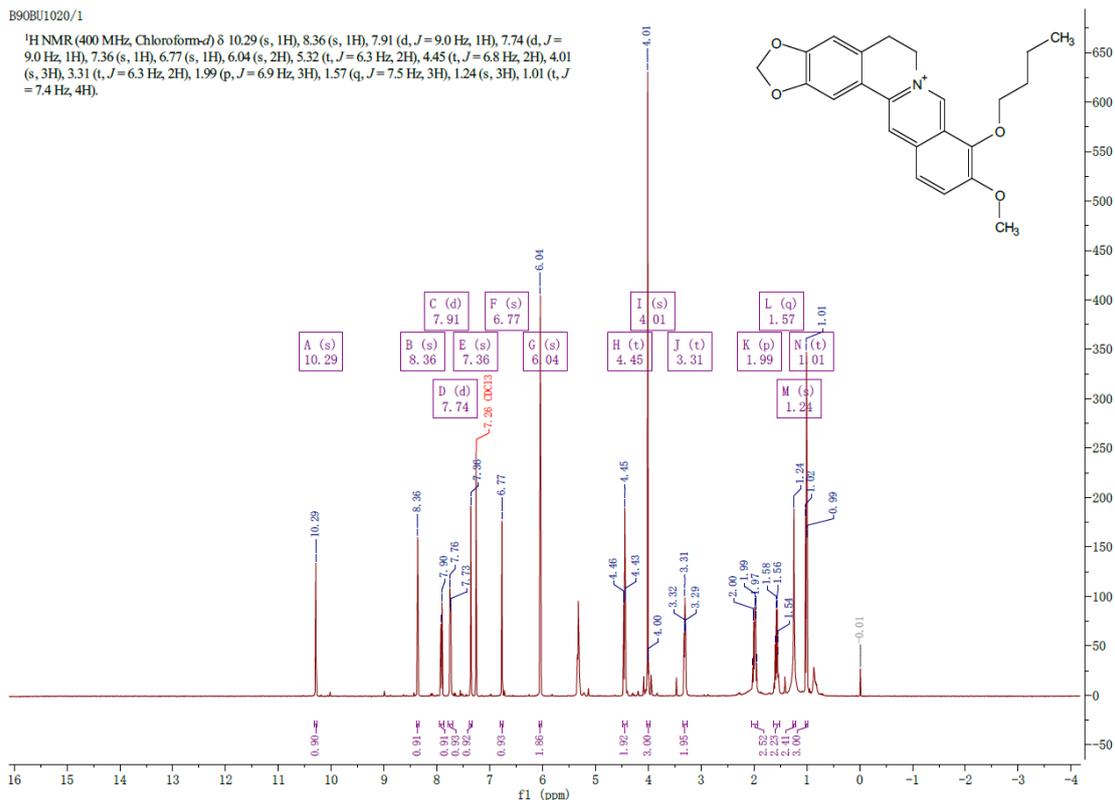


Figure S 9 ^1H NMR spectra of compound B90BU

B90BU1020C/2

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.75, 148.39, 146.76, 137.68, 133.48, 130.62, 126.11, 123.02, 122.49, 120.38, 119.85, 108.61, 105.42, 102.22, 77.36, 75.46, 57.09, 56.21, 32.33, 29.83, 27.79, 19.22, 14.09.

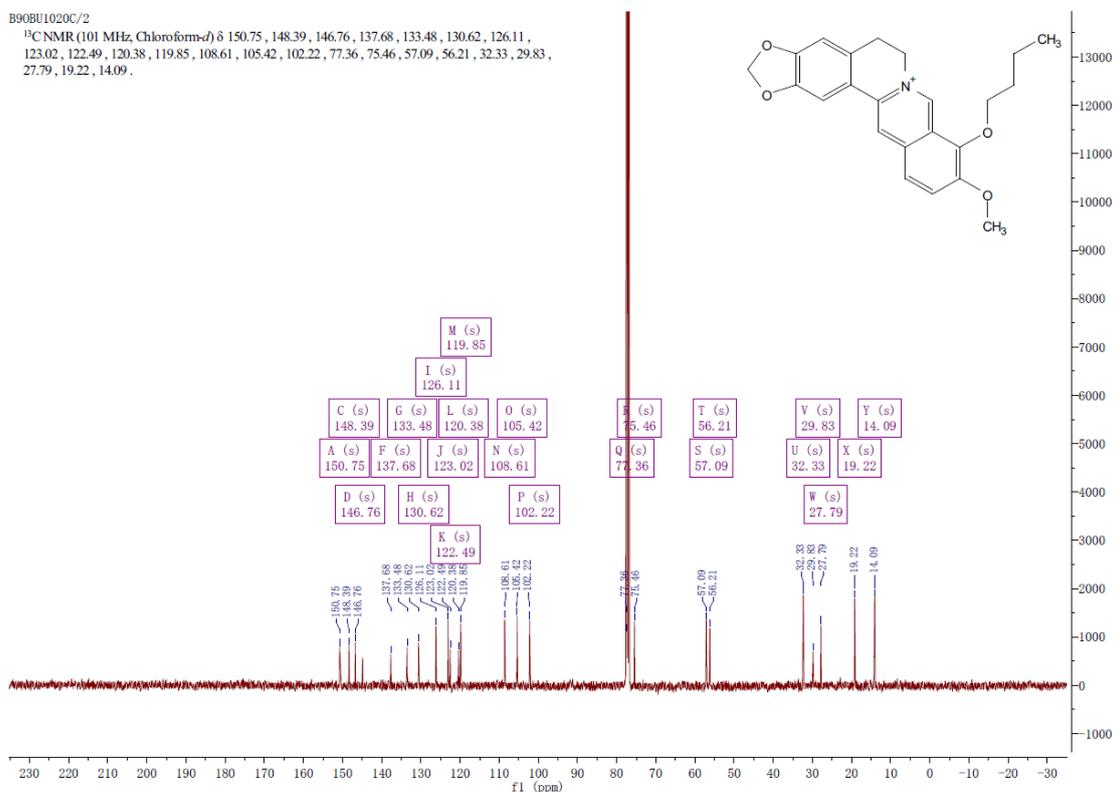


Figure S 10 ^{13}C NMR spectra of compound B90BU

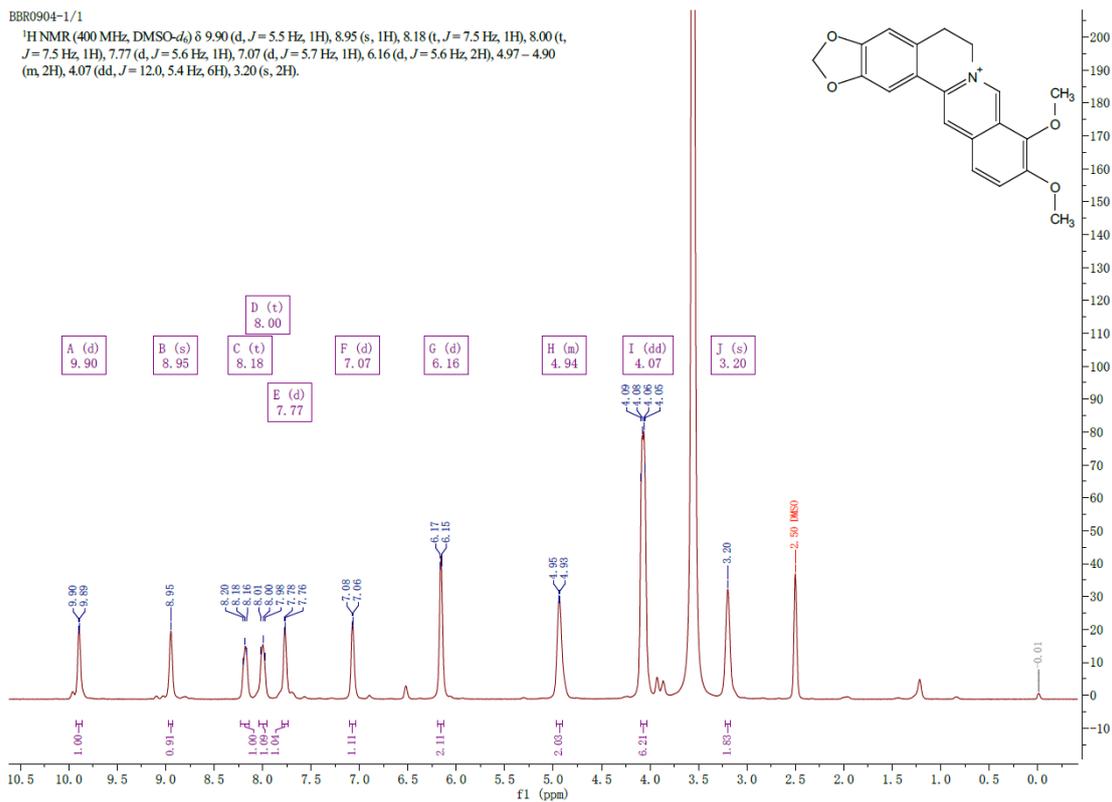


Figure S 11 ¹H NMR spectra of compound BBR

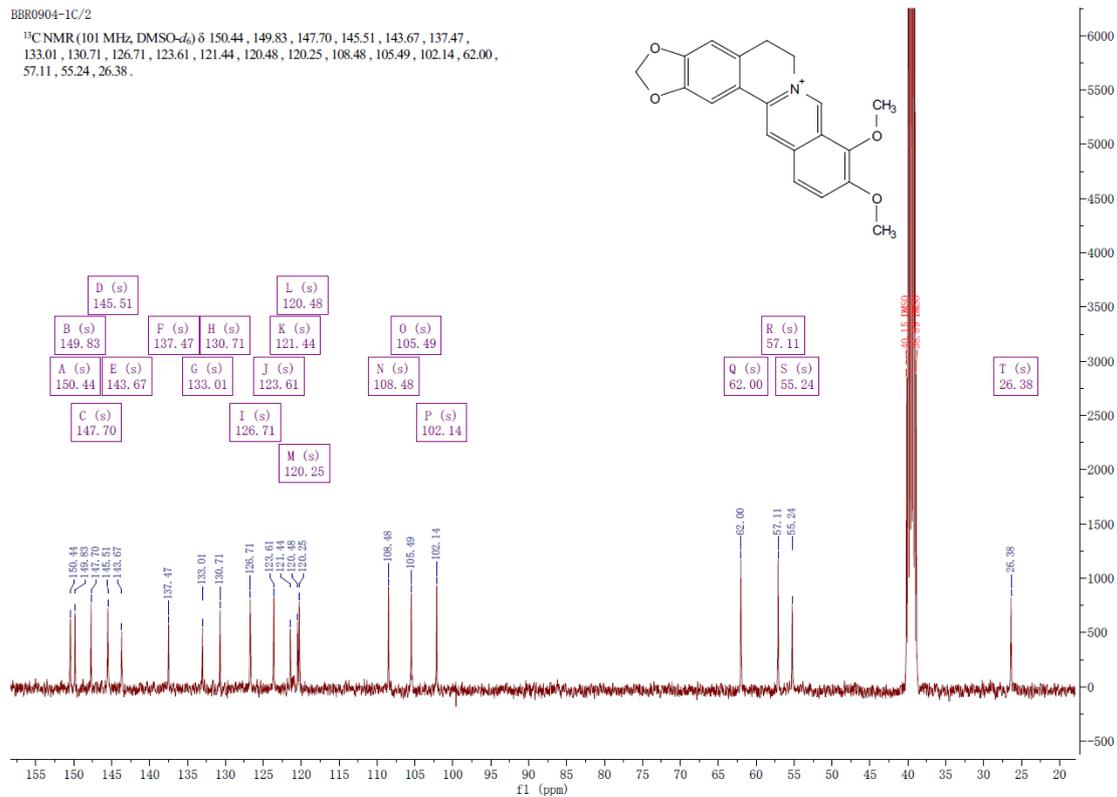


Figure S 12 ¹³C NMR spectra of compound BBR

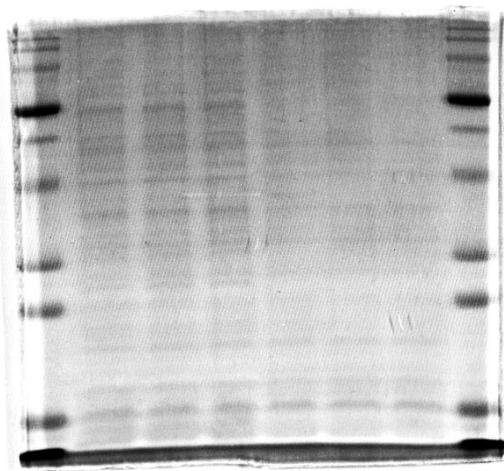


Figure S 13 Western blot images for PBS-B9OC

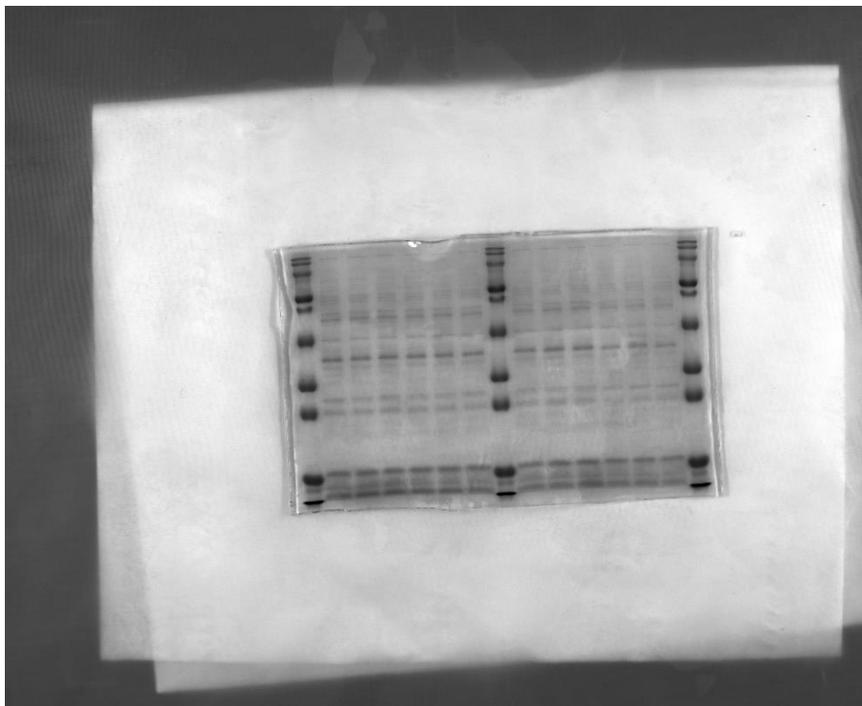
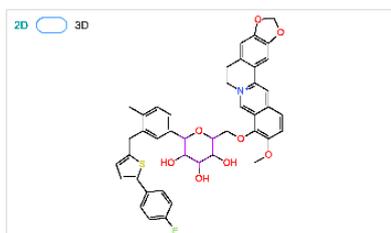


Figure S 14 Western blot images for PBS-BBR-CAN-BBR+CAN



Basic Properties

Formula	C ₂₉ H ₂₉ FNO ₆ S ⁺
Molecular Weight	748.85
Fraction Csp ³	0.28
Num. of Heavy Atoms	54
Num. Rotatable Bonds	8
Num. H-bond Acceptors	9
Num. H-bond Donors	3
TPSA	110.72
CLogP	6.46
Ring Count	9
Aromatic Ring Count	6
PAINS	0 alert
LogD	3.23
pKa	▼
Strongest Acidic pKa	7.19
Strongest Basic pKa	n/a.

CYP Induction Probability 0.27

CYP Inhibition Probability ▼

1A2	0.48
2C19	0.9
2C9	0.83
2D6	0.76
3A4	0.99

Excretion Properties

Human Clearance 0.4

Absorption Properties

Solubility ▼

Thermodynamic Solubility, Log(S, mol/L)	-3.09
ESOL_Kinetic, Log(S, mol/L)	-4.42
Solubility _{ds1}	0.95
Solubility _{ds10}	0.91
Solubility _{ds100}	0.86
Pampa	4.85
MDCK	3.43
Caco-2 Permeability(10e-6, apical to basolat...)	3.39
P-gp Substrate Probability	0.96
P-gp Inhibition Probability	0.55
Human Intestinal Absorption(HIA) Probability	0.15
Oral Bioavailability(human)	47%

Toxicity Properties

hERG Inhibition Probability	0.12
hERG Inhibition probability_cis10	0.61
hERG Inhibition probability_cis50	1
Ames Toxicity Probability	0.32
Hek293 Toxicity Probability	0.95
Hepatic Toxicity Probability	0.97
Eye Corrosion	0
Log(LD50)	2.91
Phototoxicity	0.26
Tubulin Inhibition	1
Eye Irritation	0
DILI	0.93
Genotoxicity	0.99
Carcinogenicity	0.23
Mutagenicity	0
Phospholipidosis	0.77
Reproductive Toxicity	1
TOX21 Probability ▼	
NR-AR	0.33
NR-AH-LBD	0.35
NR-AHR	0.33
NR-Aromatase	0.37
NR-ER	0.14
NR-ER-LBD	0.37
NR-PPAR-gamma	0.12
SR-ARE	0.81
SR-ATAD5	0.37
SR-HSE	0.24
SR-MMP	0.69
SR-p53	0.43

Distribution Properties

Plasma Protein Binding(human)	97%
Blood-Brain Barrier Permeability (BBBP) Pro...	0.26
Blood Brain Ratio	-0.62

Metabolism Properties

HLM-CL _{int} (μL/min/mg)	67.21
MLM-CL _{int} (μL/min/mg)	415.94
RLM-CL _{int} (μL/min/mg)	89.63

Figure S 15 ADMET Prediction of B9OC Based on Computer Aided