Supplementary Information

Development of selective RyR2 inhibitors with a parabanic acid pharmacophore

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1. ¹H-NMR and ¹³C-NMR charts for synthesized new compounds

Compound: 4



¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)





¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)





¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)





¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)



¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹H-NMR spectrum (400 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (100 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

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¹H-NMR spectrum (400 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (100 MHz, Acetone-*d*₆, 298 K)

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¹³C-NMR spectrum (100 MHz, Acetone-*d*₆, 298 K)

¹H-NMR spectrum (400 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (100 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹H-NMR spectrum (400 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (125 MHz, Acetone-*d*₆, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹H-NMR spectrum (400 MHz, CDCl₃, 298 K)

1 1

190 180 170 160 150 140 130 120 110 100 90

80 70

60 50 40 30 20

ppm

¹H-NMR spectrum (400 MHz, CDCl₃, 298 K)

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

¹³C-NMR spectrum (125 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

¹³C-NMR spectrum (100 MHz, CDCl₃, 298 K)

2. Fitting curves of synthesized compounds for RyR2 inhibiton

3. HPLC charts and conditions for compounds 1 and 18

HPLC conditions for compound **1**

Column: GL Sciences 5020-01732 (Particle size 5 μ m, Inner diameter 4.6 ϕ , Length 250 mm) Solvent: CH₃CM-H₂O gradient solvent containing 0.1%TFA

Speed: 1.0 mL/min

Conditions: 30-90% CH₃CN over 35 min, then 95% CH₃CN containing 0.1% TFA wash for 15 min Detection: UV absorbance at 220 nm

Purity: 97%

HPLC conditions for compound 18

Column: GL Sciences 5020-01732 (Particle size 5 μ m, Inner diameter 4.6 ϕ , Length 250 mm) Solvent: CH₃CM-H₂O gradient solvent containing 0.1%TFA

Speed: 1.0 mL/min

Conditions: 30-90% CH₃CN over 35 min, then 95% CH₃CN containing 0.1%TFA wash for 15 min Detection: UV absorbance at 220 nm

Purity: 99%

