



CN 108358838 B
2021.05.18

201810385395.X

(2006.01)

2018.04.26

CN 108358838 A

2018.08.03

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CN 104059060 A, 2014.09.24
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Synthesis and Qual i tative Structure
Acti vi ty Rel ati onshi p Eval uati ons of
Qui nol i ne-Based Bi saryl i mi dazol es as
Anti bacteri al Moti fs. Medi cal Chemi stry
(Sharjah, Uni ted Arab Emi rates) . 2016,
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1 B

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(2006.01)

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(2006.01)

24) , 2881-2885 .

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权利要求书1页 说明书11页

(2006.01)

[h]

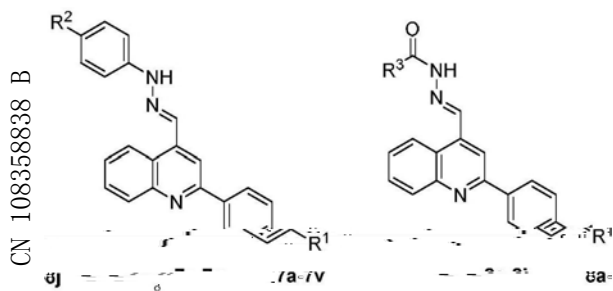
25B

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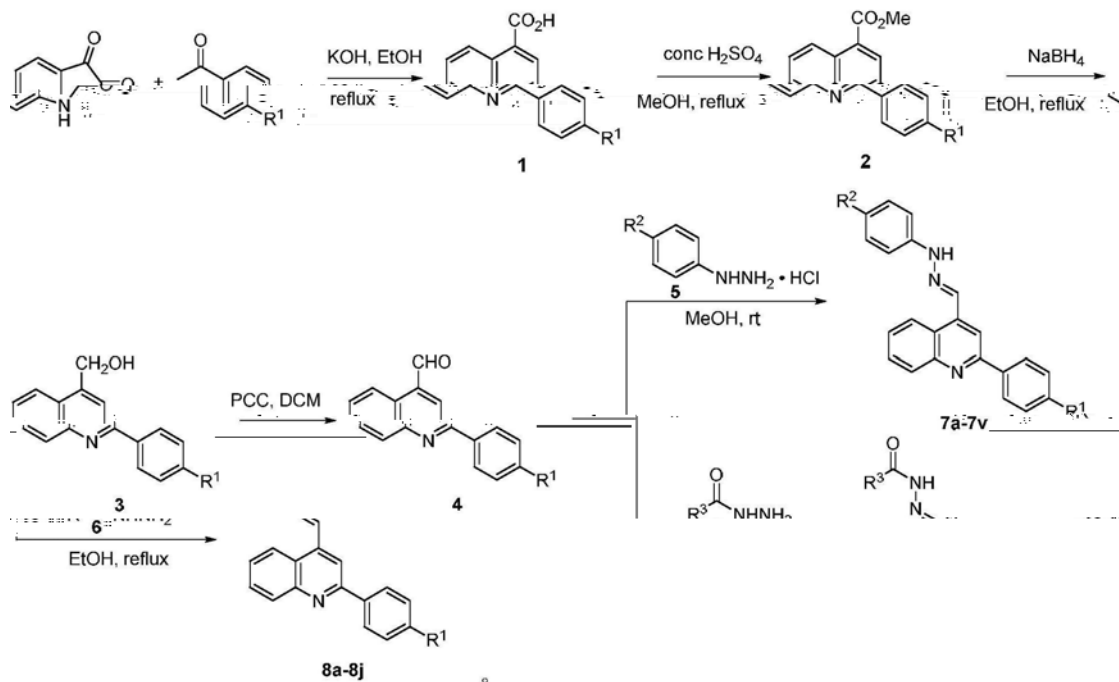
25B



7a R¹ F R² H 7b R¹ F R² OCH₃ 7c R¹ F R² CH₃ 7d R¹ F R² F 7e R¹ F R² Cl 7f R¹ F R² CN 7g R¹ F R² CF₃ 7h R¹ F R² NO₂ 7i R¹ H R² H 7j R¹ H R² NO₂ 7k R¹ H R² OCH₃ 7l R¹ H R² CH₃ 7m R¹ H R² F 7n R¹ H R² Cl 7o R¹ H R² CF₃ 7p R¹ CF₃ R² OCH₃ 7q R¹ CF₃ R² NO₂ 7r R¹ CF₃ R² CH₃ 7s R¹ CF₃ R² F 7t R¹ CF₃ R² Cl 7u R¹ CF₃ R² CF₃ 7v R¹ CF₃ R² H

8a R¹ F R³ = ; 8b R¹ F R³ = ; 8c R¹ F R³ Ph 8d R¹ F R³ o-ClPh-
 8e R¹ H R³ = ; 8f R¹ H R³ = ; 8g R¹ F R³ o-ClPh- 8h R¹ F R³ Ph 8i R¹ CF₃ R³ = ; 8j R¹ CF₃ R³ = .

2. 1



CA A Cancer Journal for Clinicians			2017
1688780	600920		2016 1 25
CA A Cancer Journal for Clinicians			2015
[1]	2015	429.2	281.4

[2]

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[10]

[11]

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4-(2-

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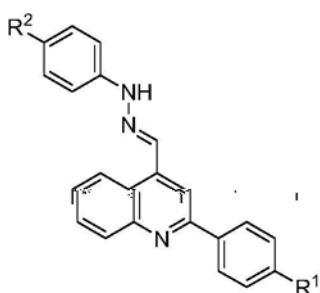
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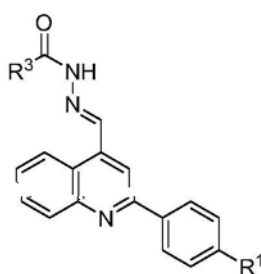
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





7a-7v





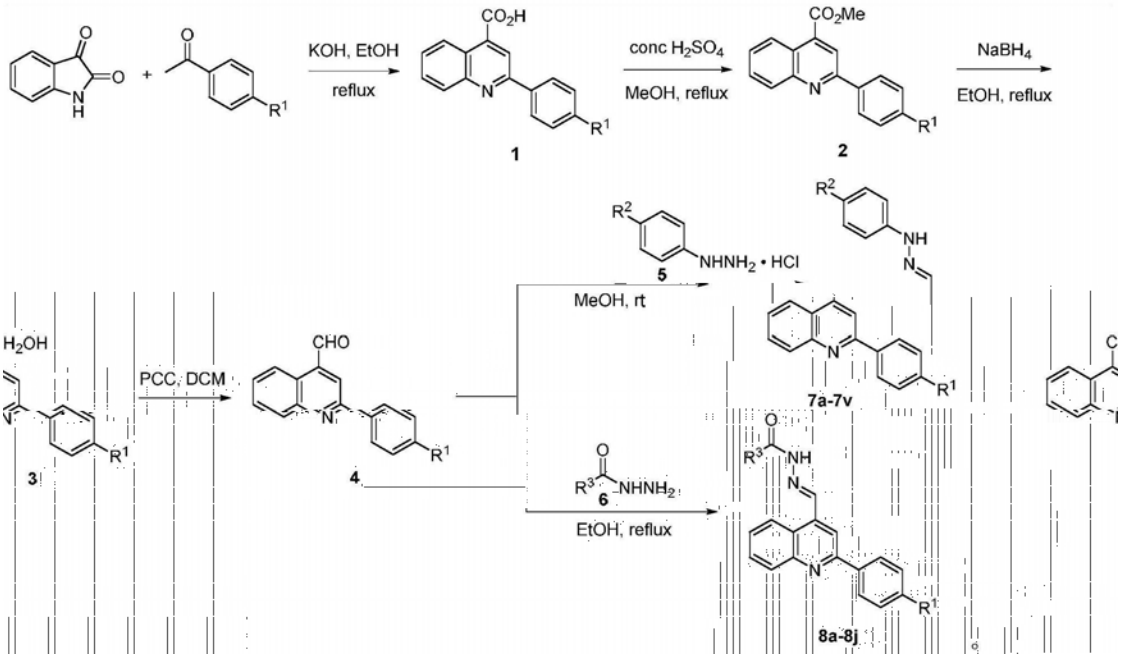
8a-8j

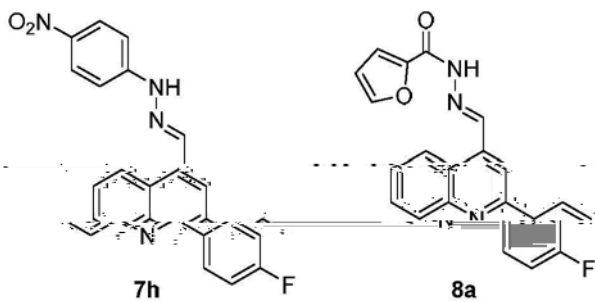
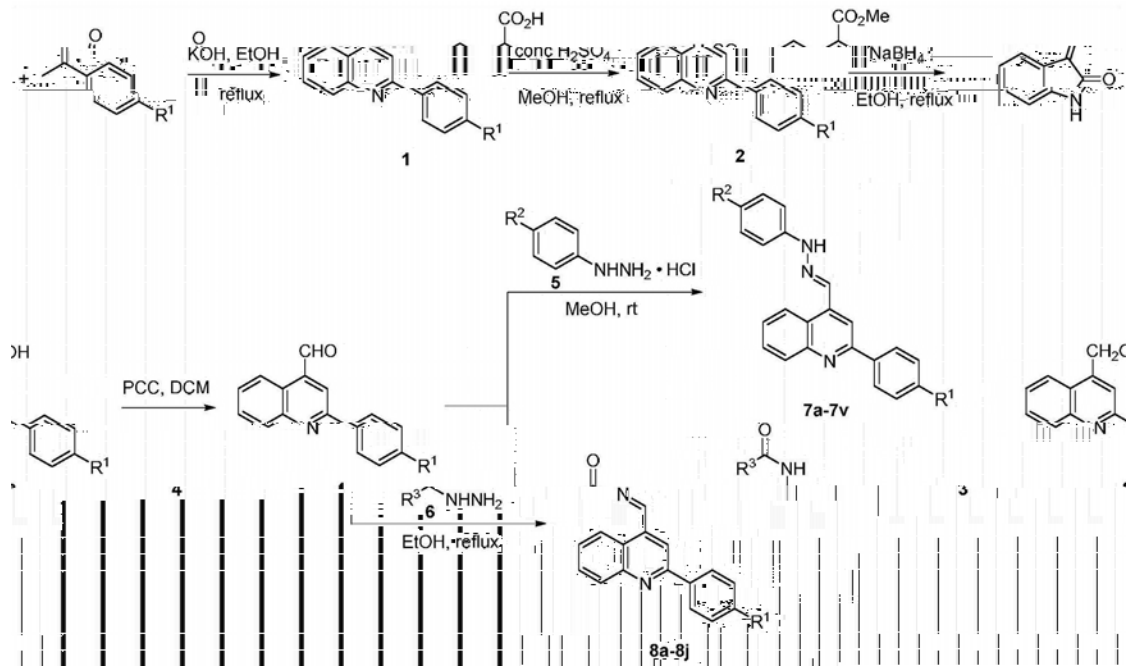
7a R¹ F R² H 7b R¹ F R² OCH₃ 7c R¹ F R² CH₃ 7d R¹ F R² F 7e R¹ F R² Cl 7f R¹ F R² CN 7g R¹ F R² CF₃ 7h R¹ F R² NO₂ 7i R¹ H R² H 7j R¹ H R² NO₂ 7k R¹ H R² OCH₃ 7l R¹ H R² CH₃ 7m R¹ H R² F 7n R¹ H R² Cl 7o R¹ H R² CF₃ 7p R¹ CF₃ R² OCH₃ 7q R¹ CF₃ R² NO₂ 7r R¹ CF₃ R² CH₃ 7s R¹ CF₃ R² F 7t R¹ CF₃ R² Cl 7u R¹ CF₃ R² CF₃ 7v R¹ CF₃ R² H

8a R¹ F R³ ; 8b R¹ F R³ ; 8c R¹ F R³ Ph 8d R¹ F R³ o-

o-Ph- 8e R¹ H R³ ; 8f R¹ H R³ ; 8g R¹ F R³ o-Ph- 8h R¹ F R³

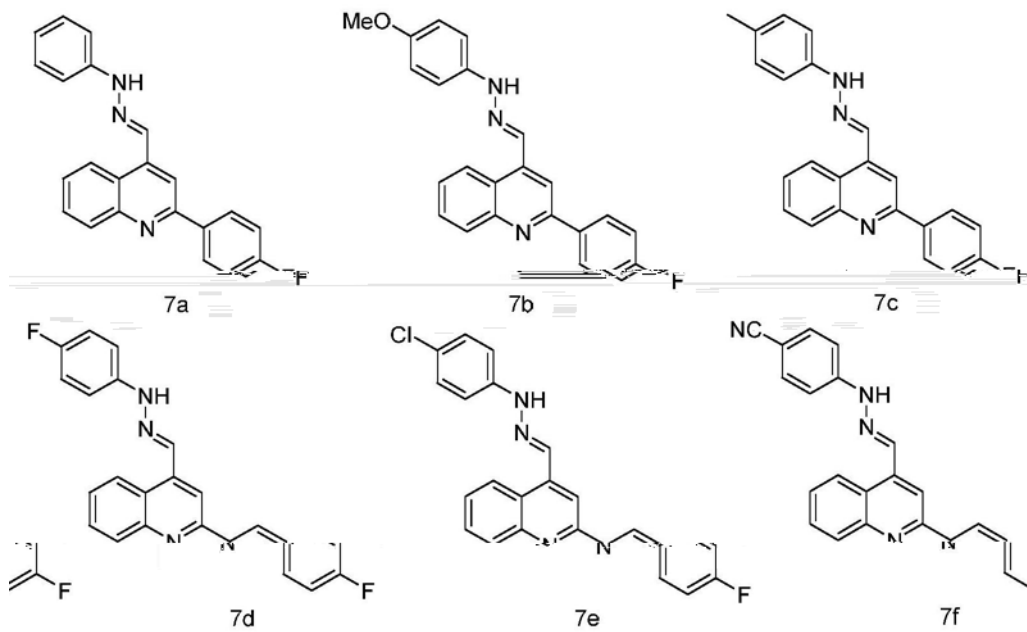
Ph 8i R¹ CF₃ R³ ; 8j R¹ CF₃ R³ .

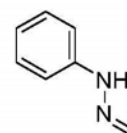
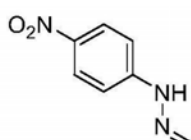
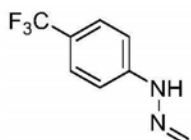




1.1	2-(4- 250mL 35mL 2M)	-4- 50mmol 80	1a 2,3- 60mmol	4- TLC	20mL
					1a	85
1.2	2-(4- 100mL 5mL)	-4- 20mmol PH	2a 2-(4- TLC	-4- (5×30mL)	20mL 20mL /
150/1)		2a	87			
1.3	2-(4- 100mL 50mL 50mL)	-4- 15mmol TLC	3a 2-(4- TLC	-4-)	45mmol 3a 92
1.4	2-(4- 250mL)	-4- 13mmol	4a (2-(4-)	-4-)	26mmol

100mL
 30
 1.5 (E)-2-(4-)-4-((2-(4-))) 7h
 25mL 0.15mmol (2-(4-) -4-) 4a 4-
 5mL TLC
 10mL, 7h
 1.6 (E)-N'-((2-(4-) -4-)) -2- 8a
 25mL 0.15mmol (2-(4-) -4-) 4a 2-
 5mL 80 TLC
 10mL 8a





(E)-2-(4-(trifluoromethyl)phenyl)-4-((2-nitrophenyl)imino)pyridine (7a): mp. 116-118 °C. $^1\text{H NMR}$ (600 MHz, DMSO-d_6) 11.00 (s, 1H), 8.75 (d, J = 8.3 Hz, 1H), 8.54 (s, 1H), 8.38 (dd, J = 8.7, 5.6 Hz, 2H), 8.32 (s, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.81 (t, J = 7.1 Hz,

1H), 7.70(dd, J 11.2, 3.9 Hz, 1H), 7.40(t, J 8.8 Hz, 2H), 7.32(t, J 7.8 Hz, 2H), 7.24(d, J 7.7 Hz, 2H), 6.87(t, J 7.2 Hz, 1H). HRMS(ESI) m/z cal cd. for C₂₆H₁₆FN₃([M+H]⁺) 342.1401, found: 342.1401

(E)-2-(4-)-4-((2-(4-))) (7b):

85 .mp. 220-222 ¹H NMR(400MHz, DMSO-d₆) 11.70(s, 1H), 8.73(d, J 8.4 Hz, 1H), 8.54(s, 1H), 8.34(s, 1H), 8.25(dd, J 15.9, 7.3 Hz, 3H), 7.99(t, J 7.7 Hz, 1H), 7.82(t, J 7.7 Hz, 1H), 7.51(t, J 8.8 Hz, 2H), 7.29(d, J 8.9 Hz, 2H), 6.96(d, J 8.9 Hz, 2H), 3.74(s, 3H). HRMS(ESI) m/z cal cd. for C₂₃H₁₈FN₃O([M+H]⁺) 372.1507, found: 372.1508

(E)-2-(4-)-4-((2-(4-))) (7c):

71 .mp. 216-218 ¹H NMR(400MHz, DMSO-d₆) 11.69(s, 1H), 8.73(d, J 8.5 Hz, 1H), 8.61(s, 1H), 8.33(dd, J 19.2, 10.5 Hz, 4H), 7.98(t, J 7.4 Hz, 1H), 7.83(t, J 7.4 Hz, 1H), 7.52(t, J 8.6 Hz, 2H), 7.24(d, J 8.1 Hz, 2H), 7.16(d, J 8.2 Hz, 2H), 2.27(s, 3H). HRMS(ESI) m/z cal cd. for C₂₃H₁₈FN₃([M+H]⁺) 356.1558, found: 356.1556

(E)-2-(4-)-4-((2-(4-))) (7d):

63 .mp. 127-129 ¹H NMR(400MHz, DMSO-d₆) 11.36(s, 1H), 8.73(d, J 8.5 Hz, 1H), 8.62(s, 1H), 8.41-8.35(m 3H), 8.11(d, J 7.9 Hz, 1H), 7.85-7.80(m 1H), 7.72-7.68(m 1H), 7.64(d, J 8.5 Hz, 2H), 7.44-7.35(m 5H). HRMS(ESI) m/z cal cd. for C₂₂H₁₅F₂N₃([M+H]⁺) 360.1307, found: 360.1316

(E)-2-(4-)-4-((2-(4-))) (7e):

79 .mp. 248-250 ¹H NMR(400MHz, DMSO-d₆) 11.63(s, 1H), 8.79-8.58(m 2H), 8.49-8.19(m 4H), 7.95(s, 1H), 7.81(s, 1H), 7.49(s, 2H), 7.35(d, J 18.2 Hz, 4H). HRMS(ESI) m/z cal cd. for C₂₂H₁₅FN₃([M+H]⁺) 376.1011, found: 376.1011

(E)-4-(2-((2-(4-) -4-)))) (7f):

64 .mp. 250-252 ¹H NMR(400MHz, DMSO-d₆) 11.63(s, 1H), 8.72(d, J 8.1 Hz, 1H), 8.63(s, 1H), 8.38(d, J 27.8 Hz, 3H), 8.25(s, 1H), 7.95(s, 1H), 7.81(s, 1H), 7.49(s, 2H), 7.35(d, J 18.2 Hz, 4H). HRMS(ESI) m/z cal cd. for C₂₃H₁₅FN₄([M+H]⁺) 367.1354, found: 367.1359

(E)-2-(4-)-4-((2-(4-))) (7g):

78 .mp. 238-240 ¹H NMR(400MHz, DMSO-d₆) 11.76(s, 1H), 8.80-8.65(m 2H), 8.43(s, 1H), 8.41-8.30(m 2H), 8.23(s, 1H), 7.93(s, 1H), 7.80(s, 1H), 7.66(d, J 8.4 Hz, 2H), 7.45(dd, J 23.5, 8.2 Hz, 4H). HRMS(ESI) m/z cal cd. for C₂₃H₁₅F₄N₃([M+H]⁺) 410.1275, found: 410.1275

(E)-2-(4-)-4-((2-(4-))) (7h):

69 .mp. 234-236 ¹H NMR(400MHz, DMSO-d₆) 11.76(s, 1H), 8.72(d, J 6.8 Hz, 2H), 8.39(dd, J 8.0, 4.9 Hz, 3H), 8.22(d, J 9.2 Hz, 2H), 8.13(d, J 8.3 Hz, 1H), 7.84(t, J 7.4 Hz, 1H), 7.73(t, J 7.4 Hz, 1H), 7.47-7.29(m 4H). ¹³C NMR(101MHz, DMSO) 154.8, 150.0, 148.5, 139.4, 139.0, 138.8, 130.1, 130.0, 129.6, 129.5, 127.4, 126.2, 124.2, 123.5, 116.3, 115.9, 115.7, 112.2. HRMS(ESI) m/z cal cd. for C₂₂H₁₅FN₄O₂([M+H]⁺) 387.1252, found: 387.1262

138.3, 130.0, 129.8, 128.9, 127.5, 127.2, 124.3, 123.8, 117.4, 112.3. HRMS (ESI), m/z cal cd. for $C_{21}H_{15}N_3O_2$ ($[M+Na]^+$) 342.1237, found: 342.1247

(E)-N'-((2-(4-)) -2-) (8f): 88
 . mp. 238-240 1H NMR (400 MHz, DMSO- d_6) 12.26 (s, 1H), 9.16 (s, 1H), 8.78 (d, J 6.1 Hz, 1H), 8.35 (s, 1H), 8.28 (d, J 7.1 Hz, 2H), 8.16 (d, J 8.3 Hz, 1H), 8.02 (d, J 0.8 Hz, 1H), 7.90-7.80 (m, 1H), 7.72 (t, J 7.4 Hz, 1H), 7.55 (ddd, J 10.9, 9.6, 5.7 Hz, 3H), 7.42 (s, 1H), 6.76 (dd, J 3.5, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) 155.9, 148.4, 146.3, 138.5, 138.4, m s 2 0 m̄ .66 086 2 25 m̄ 2 2

CDC 25B
 CDC 25B CNF P CDC 25B CNF
 485nm 535nm
 CDC 25B Na₃VO₄
 (protein tyrosine
 PTP1B phosphatase) PTP1B PTP1B
 PTP1B
 PTP1B 96 384
 pN PP PTP1B 405nm
 405nm

1 7a 7v 8a 8j CDC 25B (/)

Compds	Inhibition rate(%)	Compds	Inhibition rate(%)
7a	15.14 ± 11.62	7r	86.74 ± 1.95
7b	17.19 ± 2.83	7s	18.50 ± 5.20
7c	29.17 ± 3.16	7t	83.89 ± 2.73
7d	22.64 ± 6.27	7u	80.52 ± 1.00
7e	16.57 ± 5.89	7v	74.17 ± 2.72
7f	43.37 ± 0.90	8a	2.46 ± 3.13
7g	18.42 ± 9.26	8b	12.10 ± 3.43
8c	15.07 ± 2.42	7h	25.34 ± 10.15
8d	53.85 ± 4.75	7i	16.20 ± 4.91
8e	4.10 ± 3.52	7j	80.90 ± 3.69
8f	68.55 ± 0.68	7k	60.99 ± 2.56
8g	42.85 ± 4.09	7l	53.11 ± 7.49
8h	42.62 ± 5.32	7m	7.36 ± 0.08
8i	55.00 ± 15.00	7n	25.60 ± 0.84

2 7a 7v 8a 8j PTP1B (/)

Comps	Inhibition rate(%)	Comps	Inhibition rate(%)
7a	80.64 ± 1.57	7r	78.04 ± 7.94
7b	90.50 ± 11.51	7s	83.48 ± 0.38
7c	95.45 ± 12.97	7t	73.58 ± 16.29
7d	92.07 ± 1.47	7u	97.98 ± 2.36
7e	96.34 ± 1.48	7v	94.85 ± 2.95
7f	96.40 ± 2.88	8a	83.47 ± 1.38
7g	90.68 ± 1.00	8b	76.70 ± 4.74
7h	73.33 ± 16.92	8c	86.58 ± 6.02
7i	95.03 ± 0.82	8d	93.68 ± 5.69
7j	90.25 ± 2.86	8e	96.13 ± 0.06
7k	75.16 ± 14.99	8f	91.97 ± 2.90
7l	77.40 ± 4.34	8g	87.50 ± 0.52
7m	71.72 ± 5.92	8h	92.31 ± 2.33
7n	83.77 ± 1.40	8i	92.80 ± 9.69
7o	88.67 ± 3.21	8j	93.14 ± 3.96
7p	21.61 ± 0.77		
7q	95.45 ± 12.97		

CDC 25B PTP1B
 97.98 96.40 96.34 96.13
 3.
 32 4-(2-) PTP1B
 CDC 25B PTP1B
 7p 6 PTP1B 70
 PTP1B