Supporting Information (5 pages)

Discovery of Boron-conjugated 4-Anilinoquinazoline as a Prolonged Inhibitor of EGFR Tyrosine Kinase

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1. Molecular Docking and Quantum Mechanical Simulations

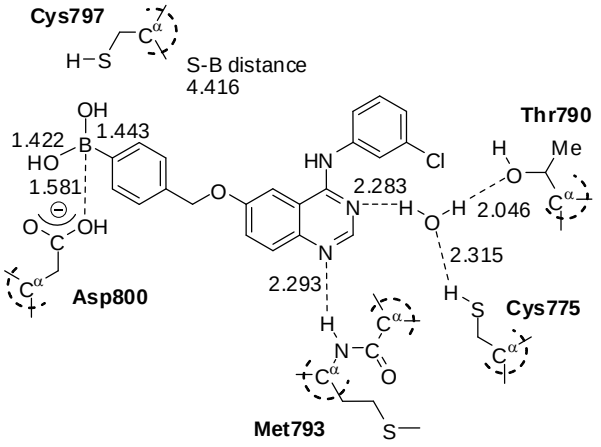


Fig. S1 QM/MM optimized geometries for an EGFR-compound **7d** docking mode (model 1).

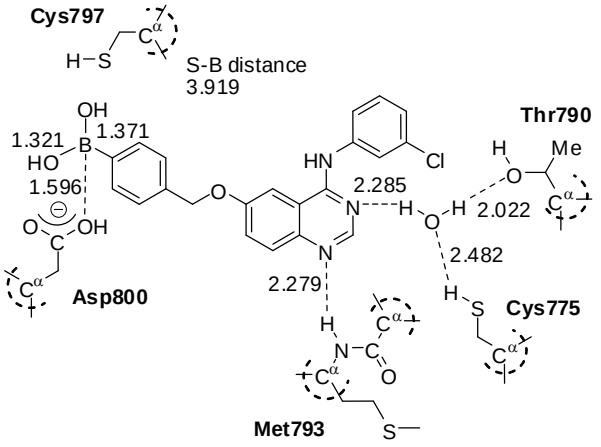


Fig. S2 QM/MM optimized geometries for an EGFR-compound **7d** docking mode (model 2).

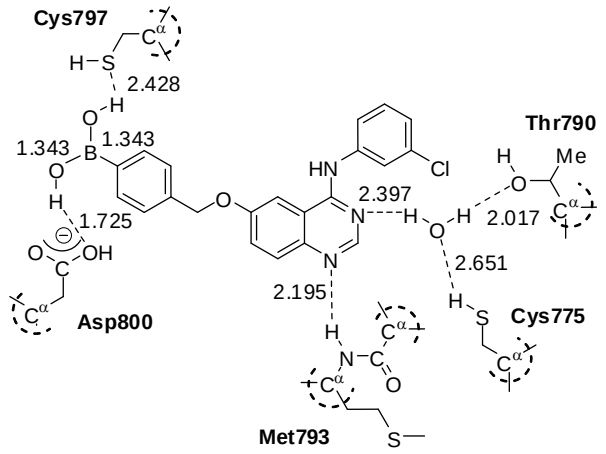
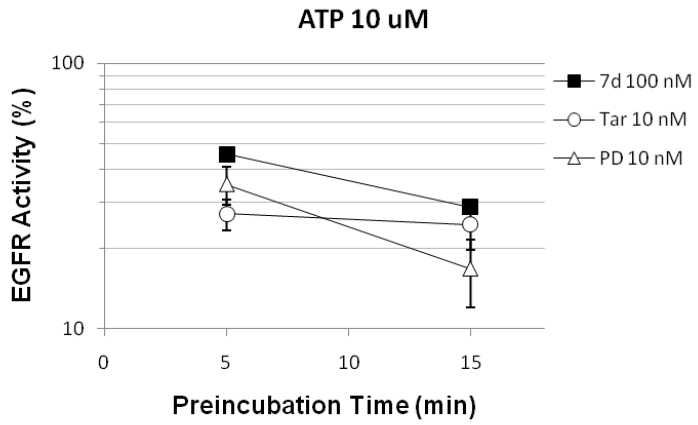


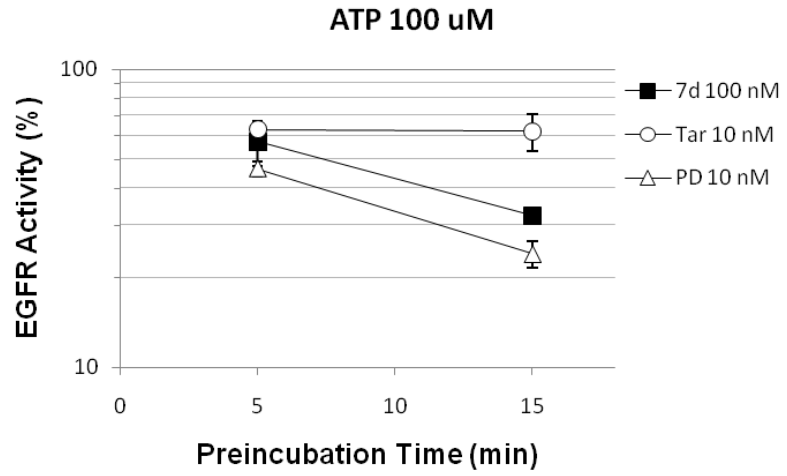
Fig. S3. QM/MM optimized geometries for an EGFR-compound **7d** docking mode (model 3).

2. Additional *in vitro* irreversible inhibition study of EGFR tyrosine kinase activity

(A)



(B)



(C)

	ATP (uM)	EGFR Activity (%)	
		5 min	15 min
7d (100 nM)	10	45.6±0.8	28.7±1.2
	100	57.1±9.8	32.3±1.6
Tar (10 nM)	10	27.0±3.6	24.7±4.9
	100	62.8±1.6	61.9±8.6
PD (10 nM)	10	34.9±5.7	16.8±4.9
	100	46.4±2.6	24.0±2.4

Fig. S4. Effects of ATP concentration on *in vitro* preincubation-time-dependent EGFR inhibition by compound **7d**. EGFR was incubated in kinase assay buffer with 100 nM compound **7d**, 10 nM Tarceva (Tar), or 10 nM PD168393 (PD). After incubation for 5 and 15 min, kinase assay was initiated by adding 10 μM ATP (A) or 100 μM ATP (B), and phosphorylation of the poly(Glu:Tyr) substrate was detected. (C) Percent of EGFR activity represent mean±s.d.

3. ^{1}H NMR spectra for compounds 2-4

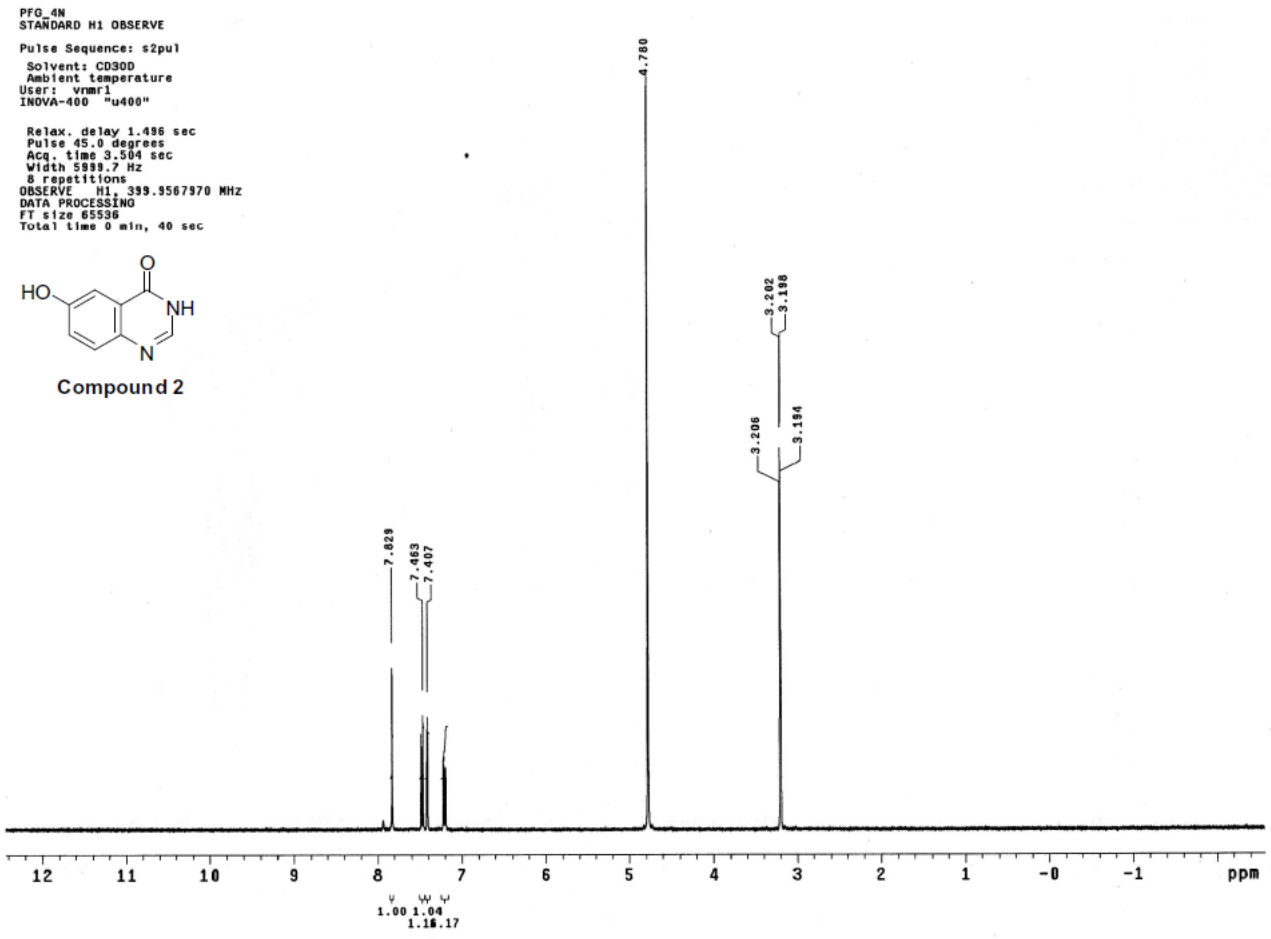


Fig. S5. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2**.

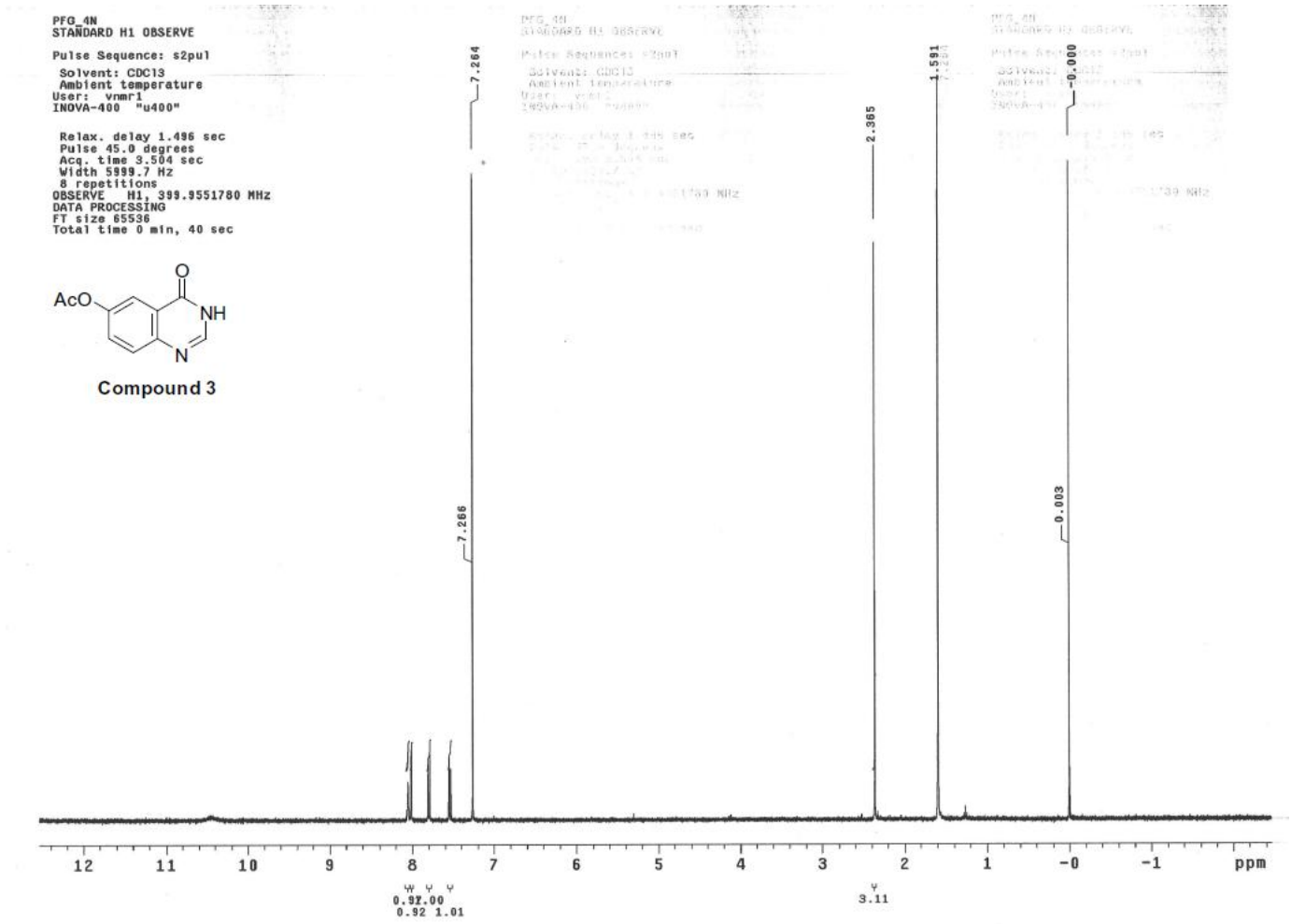


Fig. S6. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **3**.

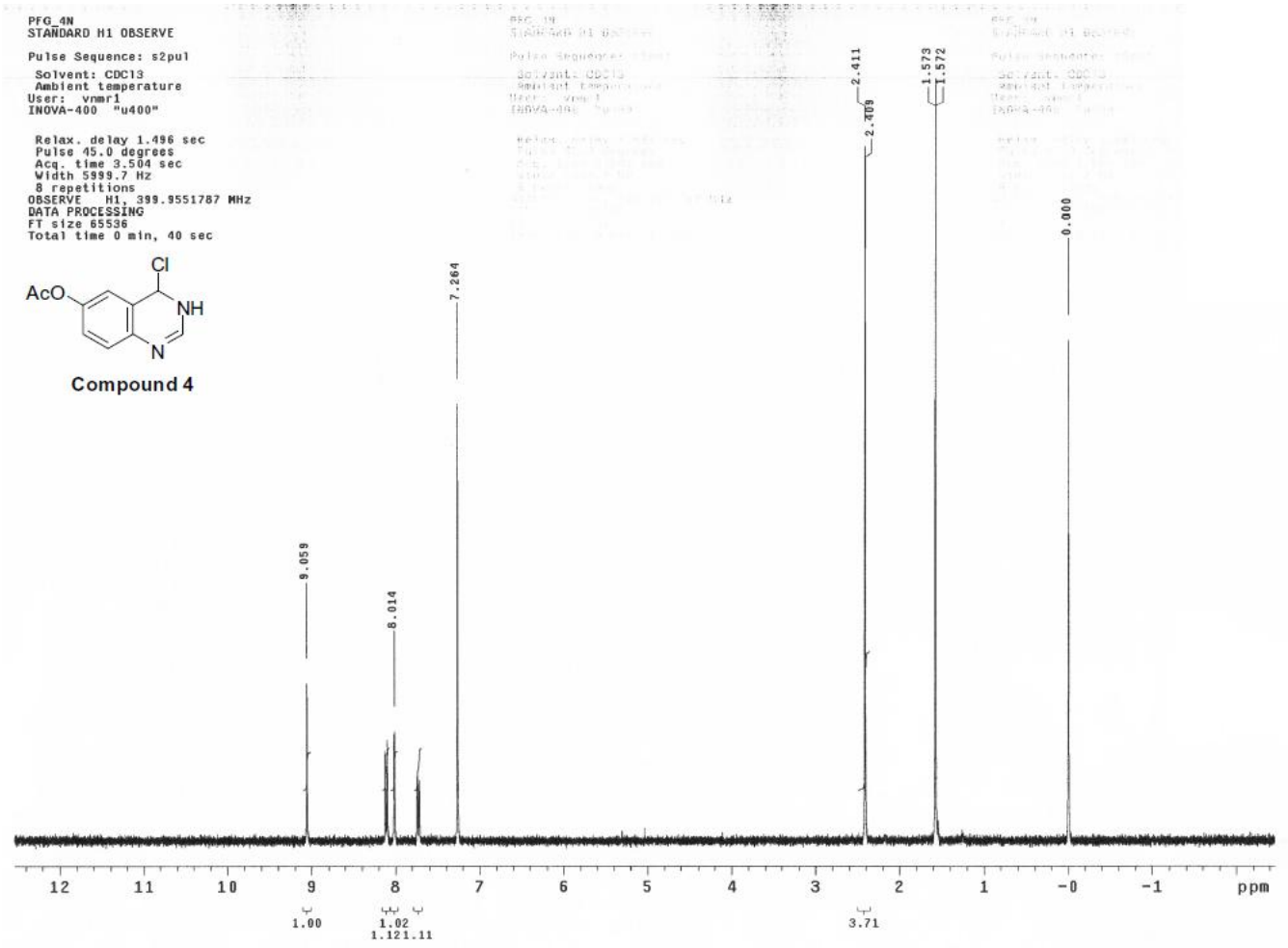


Fig. S7. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **4**.