Supplemental Data

Tofacitinib is a mechanism-based inactivator of cytochrome P450 3A4

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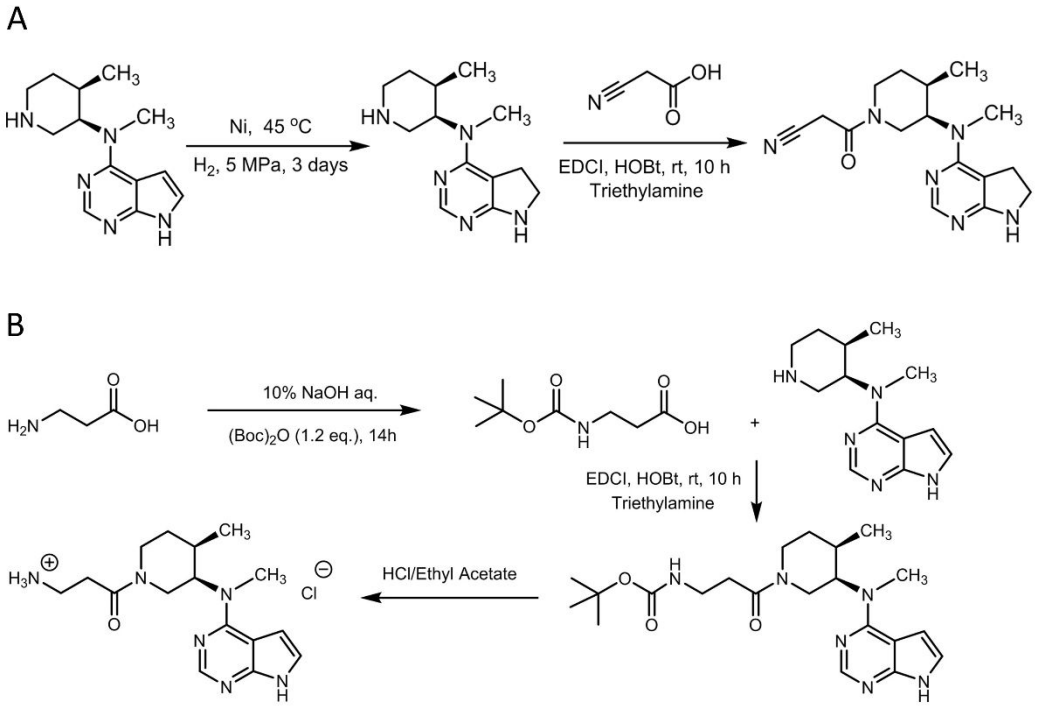
Scheme S1. Synthetic routes of analog **2** (A) and analog **3** (B) of TFT.



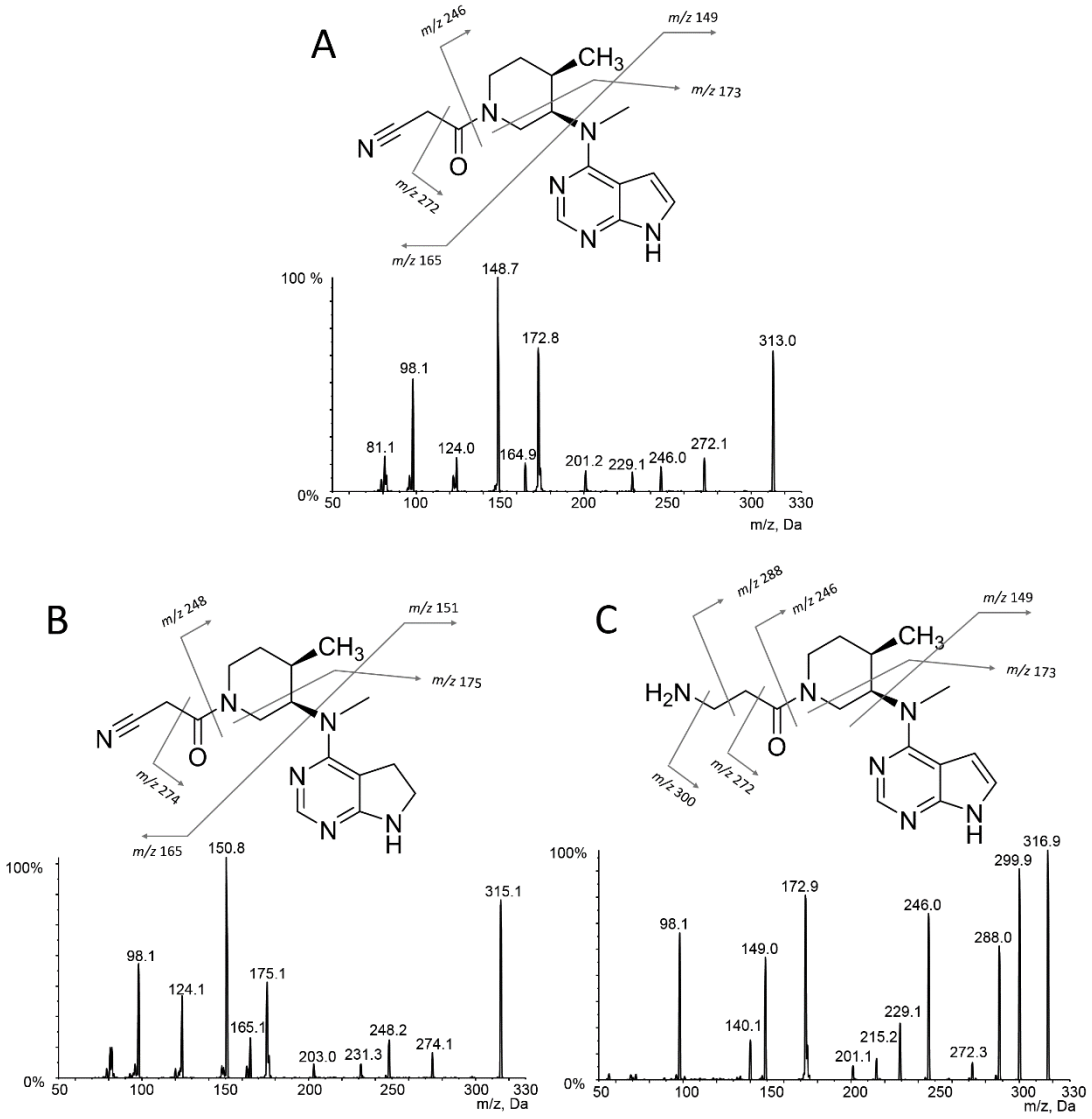


Figure S1. Tandem mass spectrometric spectra of TFT and TFT analogs. The MS/MS spectra of TFT and TFT analogs were obtained by MS_2 scanning. MS/MS spectrum of TFT provides fingerprint fragment ions at *m*/*z* 313, 272, 246, 229, 201, 173, 165, 149, and 98 (A)； MS/MS spectrum of analog **2** provides fingerprint fragment ions at *m*/*z* 315, 274, 248, 231, 203, 175, 165, 151, and 98 (B); MS/MS spectrum of analog **3** provides fingerprint fragment ions at *m*/*z* 317, 300, 288, 272, 246, 229, 201, 173, 149, and 98 (C).

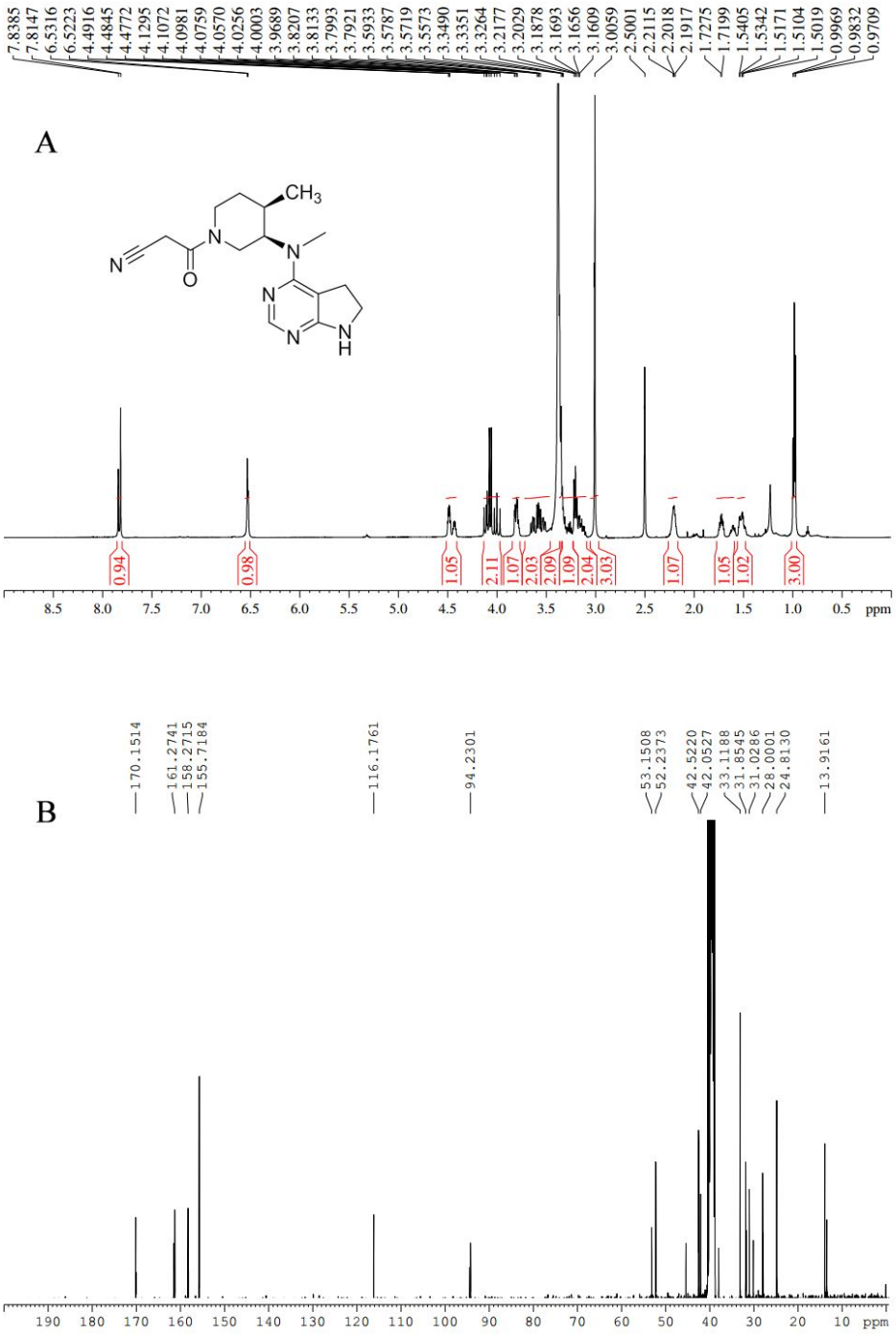


Figure S2. ^{1}H NMR (A) and ^{13}C NMR (B) spectra of TFT analog **2**. ^{1}H NMR (600 MHz，DMSO-*d*6) δ 7.84 and 7.81 (d, 1H), 6.53 and 6.52 (d, 1H), 4.50-4.42 (m, 1H), 4.13-3.97 (m, 2H), 3.82-3.77 (m, 1H), 3.66-3.51 (m, 2H), 3.35 (s, 2H), 3.34-3.24 (m, 1H), 3.22-3.10 (m, 2H), 3.01 (s, 3H), 2.26-2.18 (m, 1H), 1.75-1.58 (m, 1H), 1.54-1.45 (m, 1H), and 1.00-0.97 (m, 3H). ^{13}C NMR (400 MHz, D_2O): δ 170.2, 161.3, 158.3, 155.7, 116.2, 94.2, 53.2, 52.2, 42.5, 42.1, 33.1, 31.9, 31.0, 28.0, 24.8, and 13.9.

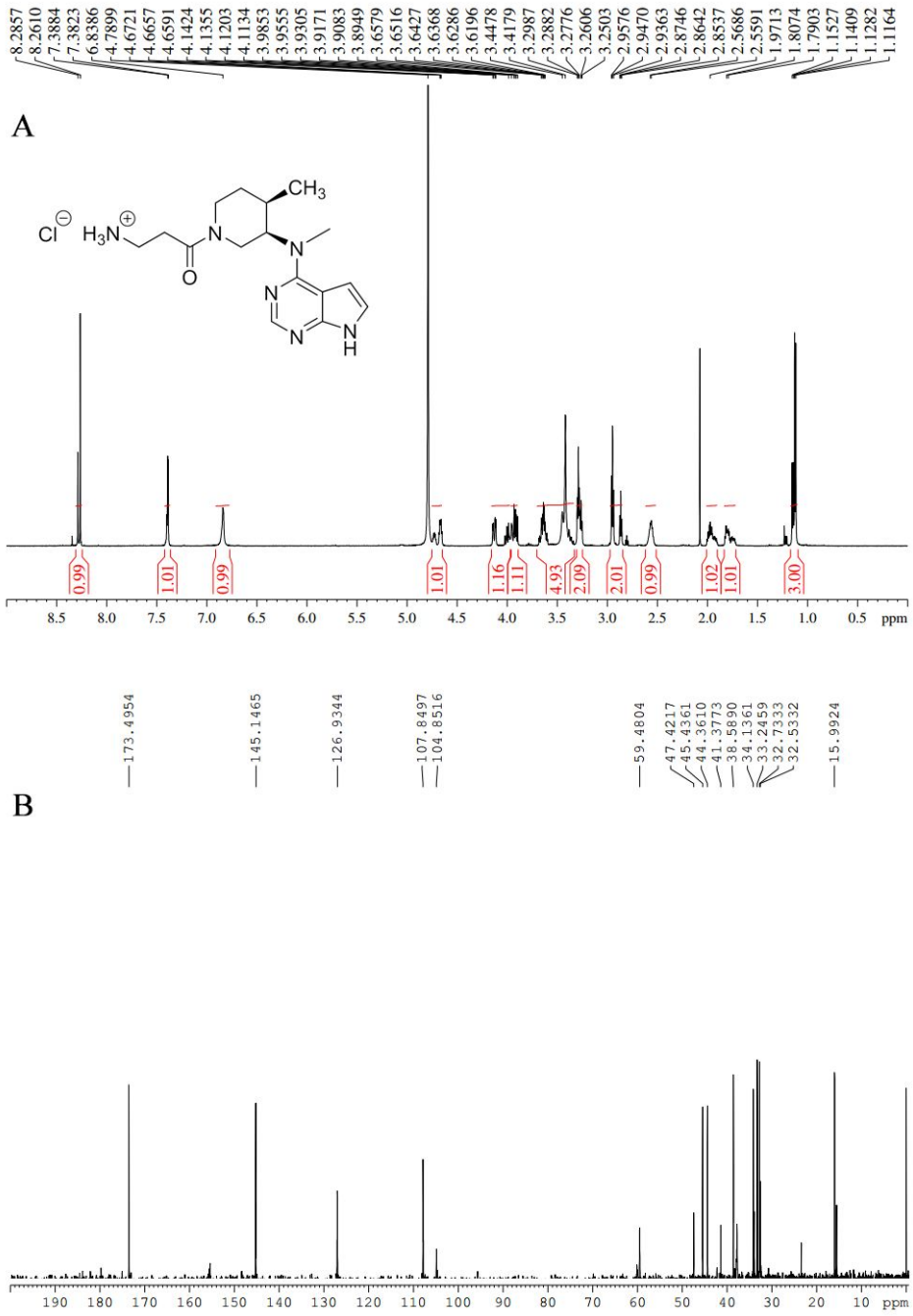


Figure S3. ^{1}H NMR (A) and ^{13}C NMR (B) spectra of TFT analog **3**. ^{1}H NMR (600 MHz, D_2O) δ 8.29 and 8.26 (d, 1H), 7.39 and 7.38 (d, 1H), 6.84 (s, 1H), 4.79-4.65 (m, 1H), 4.14-3.98 (m, 1H), 3.96-3.89 (m, 1H), 3.68-3.36 (m, 2H), 3.42 (s, 3H), 3.30-3.25 (m, 2H), 2.96-2.85 (m, 2H), 2.57-2.55 (m, 1H), 2.00-1.90 (m, 1H), 1.82-1.73 (m, 1H), and 1.15-1.12 (m, 3H). ^{13}C NMR (400 MHz, D_2O): δ 173.5, 145.1, 126.9, 107.8, 104.9, 59.5, 47.4, 45.4, 44.4, 41.4, 38.6, 34.1, 33.2, 32.7, 32.5, and 16.0.

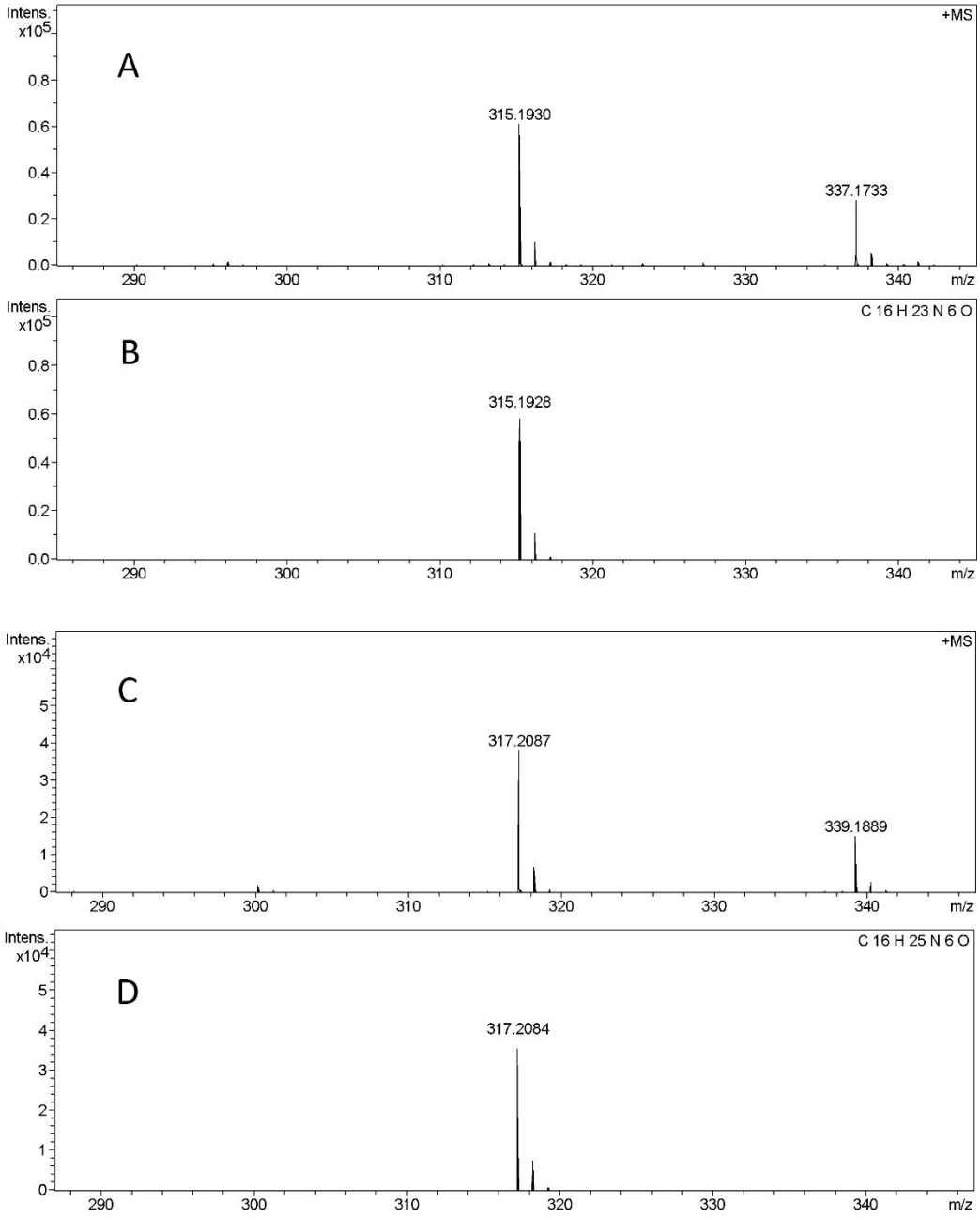


Figure S4. High resolution mass spectra of TFT analogs. A hybrid quadruple time-of-flight (Q-TOF) MS system (microQ-TOF; Bruker Corporation, Billerica, MA) was applied to analyze synthetic TFT analogs. Analog **2** showed protonated molecule ion $[M+H]^+$ at *m*/*z* 315.1930 in positive ion mode (A), which matches the elemental composition of $[M+H]^+$ $C_{16}H_{22}N_6O_1H$ (*m*/*z* 315.1928) with relative error 0.5 ppm (B). Analog **3** showed protonated molecule ion $[M+H]^+$ at *m*/*z* 317.2087 in positive ion mode (C), which matches the elemental composition of $[M+H]^+$ $C_{16}H_{24}N_6O_1H$ (*m*/*z* 317.2084) with relative error 0.8 ppm (D).