

Design and Synthesis of Potent in Vitro and in Vivo Anticancer Agents Based on 1-(3',4',5'-Trimethoxyphenyl)-2-Aryl-1*H*-Imidazole

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SUPPORTING INFORMATION

Detailed characterization of synthesized compounds **3b** and **3c**. S2

Figure 1s S3

Figure 2s S4

Characterization for compounds **3b** and **3c**.

2-(4'-Methoxyphenyl)-1-(3',4',5'-trimethoxyphenyl)-1*H*-imidazole (3b). Following general procedure A, the crude residue was purified by flash chromatography, using ethyl acetate as eluent, to furnish **3b** as a yellow oil. Yield: 71%. ¹H-NMR (CDCl₃) δ: 3.72 (s, 6H), 3.78 (s, 3H), 3.87 (s, 3H), 6.42 (s, 2H), 6.78 (d, J=8.8 Hz, 2H), 7.11 (d, J=1.2 Hz, 1H), 7.19 (d, J=1.2 Hz, 1H), 7.35 (d, J=8.8 Hz, 2H). ¹³C-NMR (CDCl₃) δ: 55.32, 56.34 (2C), 61.14, 103.63 (2C), 113.66 (2C), 122.51, 122.99, 128.77, 129.87 (2C), 134.44, 137.74, 146.73, 153.61 (2C), 159.73. MS (ESI): [M+1]⁺=341.1. Anal. (C₁₉H₂₀N₂O₄) C, H, N.

1-(3',4',5'-Trimethoxyphenyl)-2-(naphthalen-2'-yl)-1*H*-imidazole (3c). Following general procedure A, the crude residue was purified by flash chromatography, using ethyl acetate-petroleum ether 8-2 as eluent, to furnish **3c** as a white solid. Yield: 69%, mp 137-139 °C. ¹H-NMR (CDCl₃) δ: 3.69 (s, 6H), 3.89 (s, 3H), 6.49 (s, 2H), 7.20 (d, J=1.2 Hz, 1H), 7.29 (d, J=1.2 Hz, 1H), 7.30 (m, 3H), 7.74 (m, 3H), 8.00 (s, 1H). ¹³C-NMR (CDCl₃) δ: 56.37 (2C), 61.19, 103.71 (2C), 123.18 (2C), 125.78, 126.40, 126.66, 127.67, 127.73, 127.99, 128.52, 129.22, 132.97, 133.12, 134.35, 137.78, 146.82, 153.71 (2C). MS (ESI): [M]⁺=360.8. Anal. (C₂₂H₂₀N₂O₃) C, H, N.

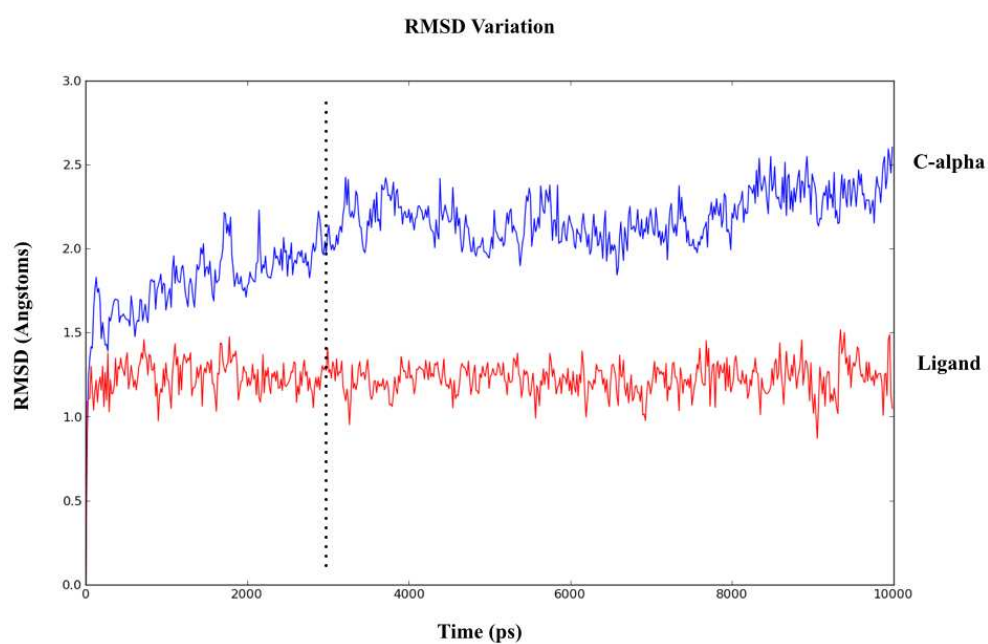


Figure 1S: Plots of RMSD (Angstroms) values against simulation time (picoseconds) for protein-**4k** complex. After 3ns of equilibration, the protein reaches the stability (C-alpha RMSD variation), while **4k** maintain its initial stable conformation during all the simulation.

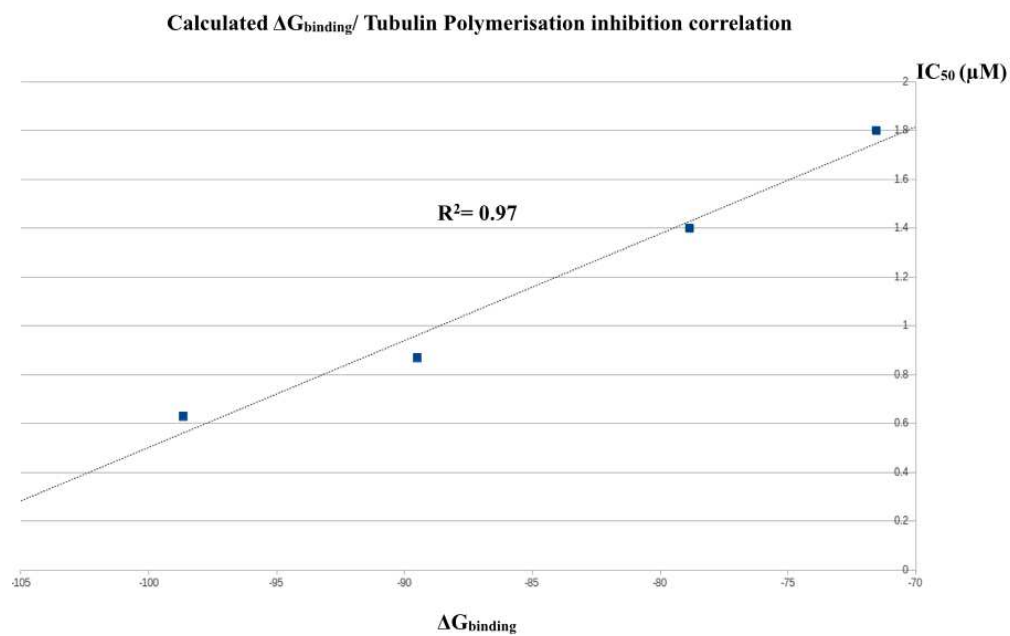


Figure 2S. Linear relation between the calculated ligand-interaction energies and inhibition of tubulin polymerization IC₅₀ values.