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Synthesis and Pharmacological Evaluation of Phenstatin Analogues

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Combretastatin A-4 (CA-4), a natural product isolated from *Combretum caffrum*, is one of the potent antimitotic agents which inhibit the polymerization of tubulin by binding to the colchicine site and changing the shape of the endothelial cells lining the blood vessels and thus arresting cell life cycle in G_2/M phase. Although mounting synthetic CA-4 analogous have been reported and come up with certain antitumor candidates in clinic trial. Still, searching safe and more potent antitumor agent is a mainstream and interesting topic. Here, a type of new trimethoxybenzoyl quinone derivatives based on the structural feature of phenstatin, a carbonyl-linked analogue of CA-4, was delicately manipulated. For the preparation of these derivatives, 5-bromo-1,2,3-trimethoxy benzene was first treated with magnesium turnings followed by aldehyde in situ to give alcohol intermediate. The subsequent oxidation and amination provide a series of quinone derivatives. All the synthesized compounds were tested in vitro for the growth inhibition of KB cell line. The results indicated that only N1-P2 showed moderate cytotoxicity on KB cells with IC_{50} of 1.8 μM.