

Title: Substituted Imidazole of 5-Fluoro-2-[4-[(2-phenyl-1H-imidazol-5-yl)methyl]-1-piperazinyl]pyrimidine
Inactivates Cytochrome P450 2D6 by Protein Adduction
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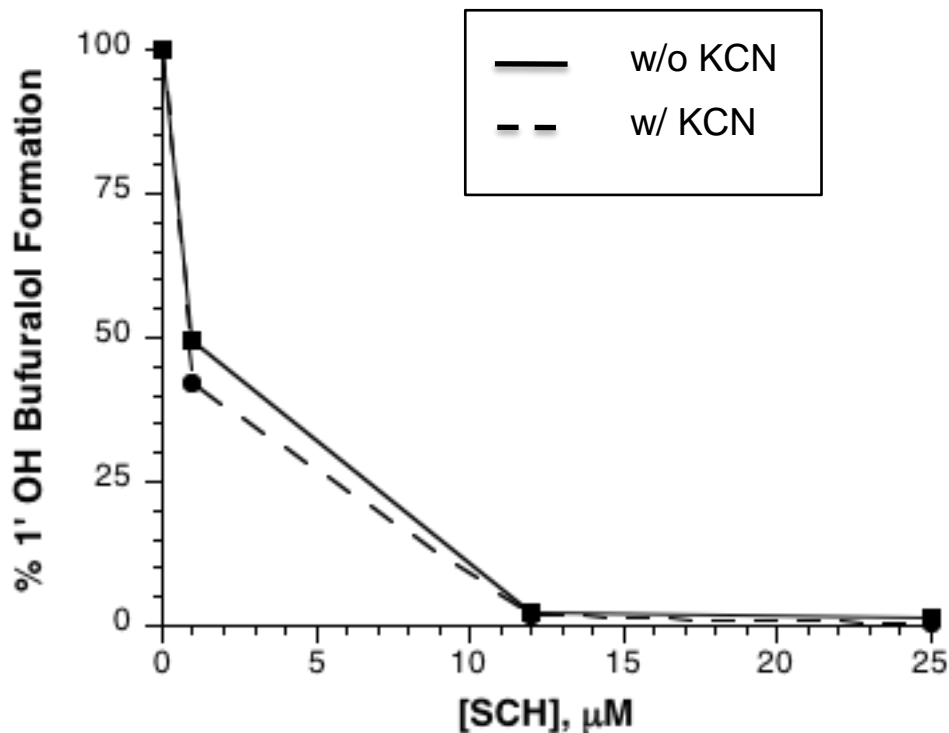


Figure S3. Analysis of possible imminium ion formation. Cyanide trapping assays were performed using primary reaction mixtures containing 0-25 μM SCH 66712, 20 pmol CYP2D6 Supersomes and 2 mM potassium cyanide in 100 mM potassium phosphate, pH 7.4. Reactions were preincubated in a 37 $^{\circ}\text{C}$ shaking water bath and after three minutes were initiated by the addition of 1 mM NADPH. After 30 minutes, aliquots were removed and added to secondary reaction mixtures containing 100 μM bufuralol and 1 mM NADPH in 100 mM potassium phosphate, pH 7.4, in a final volume of 200 μL . Secondary reactions (in duplicate) were incubated for 10 minutes at 37 $^{\circ}\text{C}$ and quenched with 15 μL 70% perchloric acid. Reaction mixtures were centrifuged (2000 \times g, 5 min) to remove the precipitated enzyme and aliquots of the recovered supernatants were directly injected onto HPLC for analysis.