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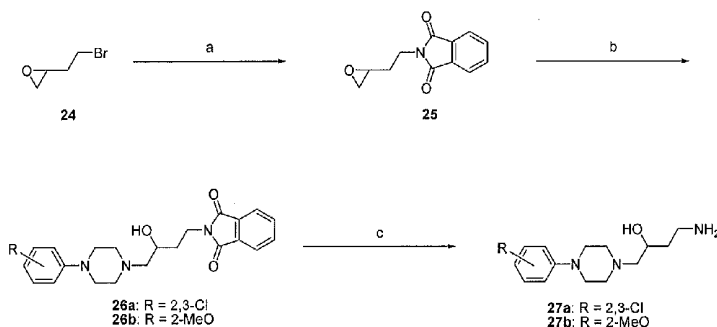
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(54) Title: 4-PHENYLPYPERAZINE DERIVATIVES WITH FUNCTIONALIZED LINKERS AS DOPAMINE D₃ RECEPTOR SELECTIVE LIGANDS AND METHODS OF USESynthesis of the 3-hydroxyl amines 27^a

Figure 1



^a Reagents and conditions: (a) phthalimid potassium salt, DMF, microwave, 100 °C, 20 min; (b) 1-(2,3-dichlorophenyl)- or 1-(2-methoxyphenyl)-piperazine, 2-PrOH, microwave, 90 °C, 20 min; (c) hydrazine, ethanol, microwave, 90 °C, 20 min.

(57) Abstract: Dopamine D₃ receptor antagonists and partial agonists are known to modulate the reinforcing and drug-seeking effects induced by cocaine and other abused substances. By introducing functionality into the butylamide linking chain of the 4-phenylpiperazine class of ligands, improved D₃ receptor affinity and selectivity, as well as water solubility, is achieved. A series of linking-chain derivatives are disclosed wherein functionality such as OH or OAc groups have been introduced into the linking chain. In general, these modifications are well tolerated at D₃ receptors and achieve high selectivity over D₂ and D₄ receptors.