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Design and Synthesis of 1,2-Naphthoquinone Derivatives

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ABSTRACT

Chagas disease (CD), also known as American trypanosomiasis, is a serious parasitic infection caused by the protozoan parasite *Trypanosoma cruzi*.[1] Although benznidazole and nifurtimox are currently the standard treatments for Chagas disease, their limitations in terms of side effects and efficacy in the chronic phase highlight the urgent need for continued research and innovation in the field of CD treatment.[2, 3] Aryloxy-1,4-naphthoquinones **1a-b** (**Figure**) have been reported in the literature[4] as potential inhibitors of the protozoan *Trypanosoma cruzi*, presenting promising IC_{50} values. As part of our research program focused on the discovery of new inhibitors of *Trypanosoma cruzi*, we report the synthesis of several aryloxy-1,2-naphthoquinones **2a-g** via the nucleophilic substitution reaction of the sodium-4-sulfonate salt 1,2-naphthoquinone **3** with the corresponding phenols **4a-g** (**Scheme**). The **2a-g** series was strategically designed by replacing the 1,4-quinonoid core, present in the antiparasitic compounds **1a-b**,[4] with a 1,2-quinonoid ring (**Figure**).

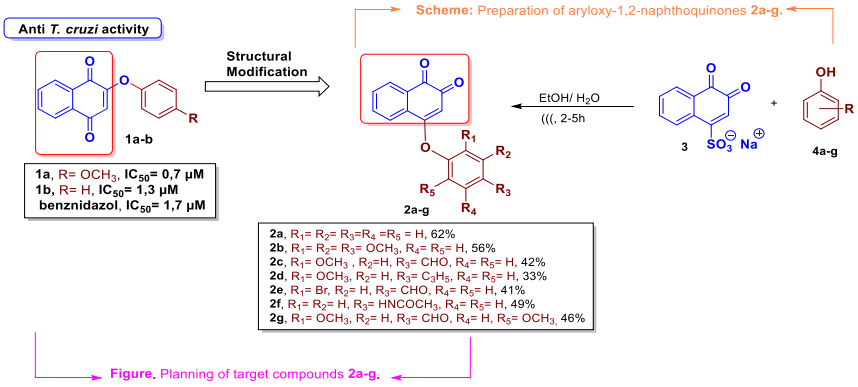

Figure. Planning of target compounds **2a-g.**

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