Synthesis of oxirane from quinones against *T. cruzi*

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INTRODUCTION

Chagas disease is an endemic disease caused by *T. cruzi*. Approximately 16 to 18 million people are infected and 50000 individuals die every year from this disease.[1] Only two drugs have been used since the 70s: nifurtimox and benznidazole. Several synthetic substances continue to be reported in the literature, [2a,b] but none of them become a new drug for a effective treatment. Our group synthesized many oxirane derivatives from quinones which showed a potent trypanocidal activity [3a,b,c]. The objective of this study is to synthesize new oxirane derivatives and evaluate them against *T. cruzi*.

RESULTS AND DISCUSSION

A solution of diazomethane in ethyl ether was added to a solution of quinone in 3:1 diethyl ether/ethanol. The reaction was carried out at room temperature for 48-120 hours. The crude product was purified by silica gel column chromatography using hexane-ethyl acetate as eluent.

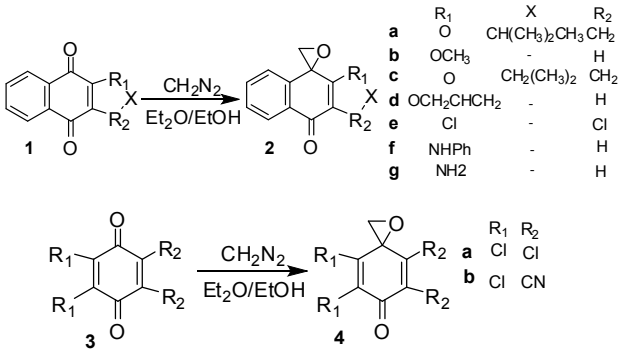

Figure 1. General scheme used for preparing oxirane from 1,4-naphthoquinones

The componds were tested against a strain of *T. cruzi* Y epimastigote forms.

Compounds 2b, 2d and 2f showed a mortality rate lower than benznidazole (Table 1). All oxirane compounds showed lower cytotoxicity than the correspondent quinones. Compound 2b appears to be the best candidate for use as a trypanocidal agent, because it shows low citotoxity. Benznidazole (control) shows IC_{50} 11.5mM and CC_{50} 40µM.

Table 1. IC_{50} quinones and they respectively oxirane derivative

quinone	IC_{50}(mM)	oxirane	IC_{50}(mM)	Yield (%)
1a	16.33	2a	16.38	70
1b	3.19	2b	1.13	80
1c	8.8	2c	19.33	60
1d	0.02	2d	0.2	35
1e	0.09	2e	9.48	52
1f	34.14	2f	2.45	65
1g	1.61	2g	19.06	69
3a	9.46	4a	7.14	74
3b	156.72	4b	26.47	50

CONCLUSION

The oxirane derivatives exhibited reduced cytotoxicity in mammalian cells compared to their corresponding quinones. Compound 2b showed a high trypanocidal activity and low cytotoxicity, compared to benznidazole. Thus, compound 2b emerges as a promising candidate for the development of a new drug for the treatment of this disease.

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