Synthesis of triazole derivatives of lawsone of interest in cancer of head and neck

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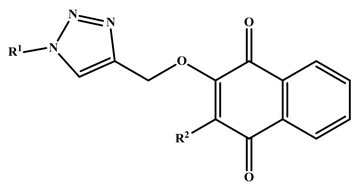
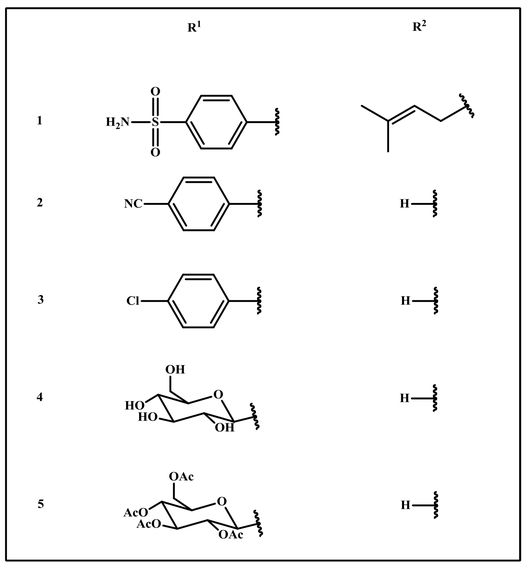
INTRODUCTION

As part of a project aimed at designing and synthesizing potential inhibitors of three enzymes overexpressed in head and neck cancers (2GS2, 1DDF, 1D2Q), four triazole derivatives of lawsone (2-hydroxy-1,4-naphtalenedione) and a derivative of lapachol (2-hydroxy-3-(3-methyl-2-buten-1-yl)-1,4-naphthalenedione) stood out as the most promising in a virtual screening study of an in-house chemical library. Based on this, these five triazoles (structures shown below) were synthesized to assess their activity against head and neck cancer cell lines.



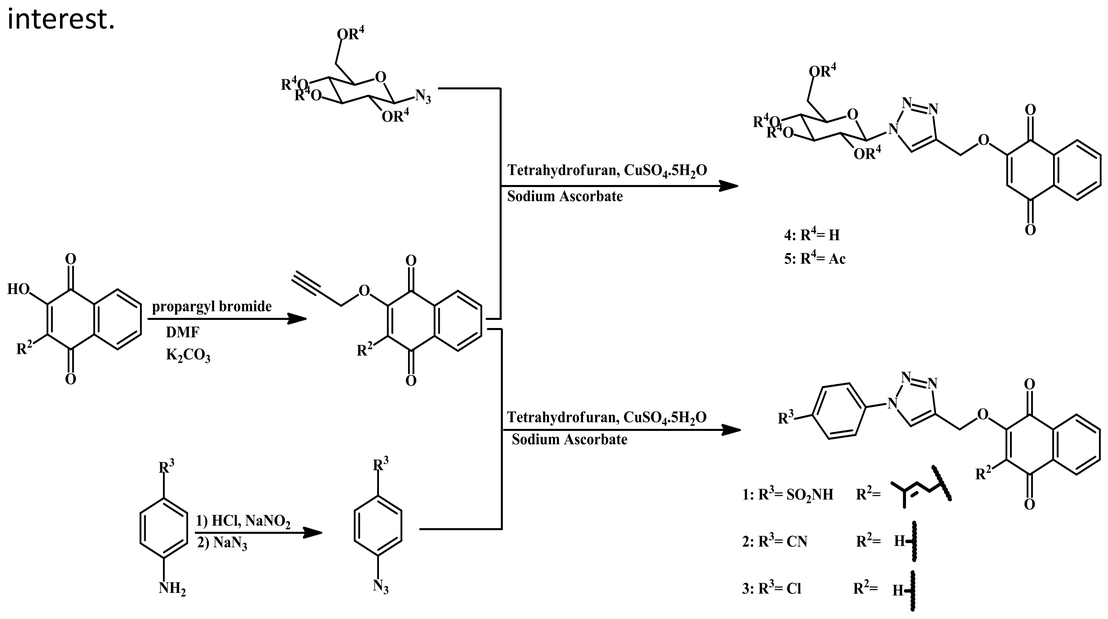


OBJECTIVE

The objective of this work was to synthesize four triazoles derived from lawsone and one from lapachol, to assess their efficiency when exposed to head and neck cancer cell lines.

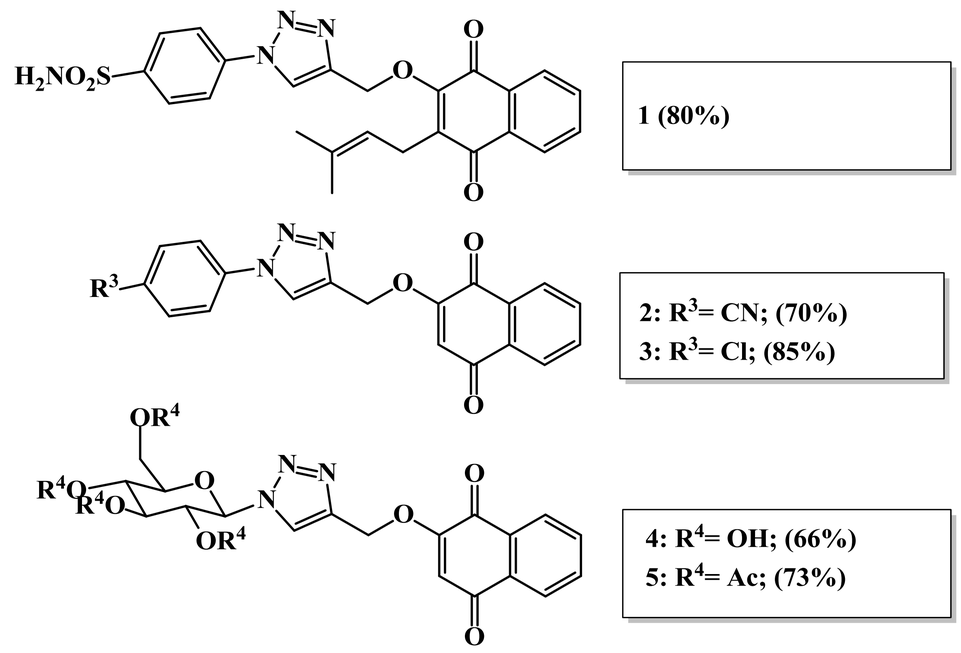
METHODOLOGY

The synthesis was carried out as follows. Initially, the propargyl ethers of lawsone and lapachol were obtained by reacting lawsone or lapachol with propargyl bromide in alkaline medium. In parallel, the aromatic azides were prepared by diazotization of suitably substituted anilines followed by reacting the corresponding diazonium salts with sodium azide. The peracetylated D-glucosylazide and the corresponding deacetylated derivative were available in the laboratory. Finally, the azido-alkyne cycloaddition reaction ("click" reaction) between lawsone or lapachol propargyl ether and the corresponding azides provided the triazole derivatives of interest.



RESULTS

O-propargyllawsone and *O*-propargyllapachol were obtained in 70% and 80% yield, respectively. The azides were obtained in general yield of *circa* 90%. The triazoles were obtained with yields in the range of 60-85%, as shown below.



CONCLUSION

The five triazoles were obtained in good yields. All compounds were characterized by ^{1}HNMR and ^{13}CNMR techniques.

REFERENCES

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