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Synthesis of novel aromatic quinols for colon and renal cancers

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Synthesis of Novel Aromatic Quinols for Colon and Renal Cancers

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Introduction

❖ **Colon Cancer**

- The third most common cancer in USA
- More than 1 million Americans currently living with colon cancer
- 148,810 new cases expected in 2010
- 50,000 deaths annually

❖ **Renal Cancer**

- Approximately 58,000 people diagnosed in USA annually
- Seventh most common cancer and tenth most common cause of cancer related death in men
- A disease of the kidneys in which cells grow uncontrollably and form a tumor

❖ **Risk Factors**

- Smoking
- Gender, race, and age
- Nutrition and weight
- Hypertension
- Overuse of certain medications

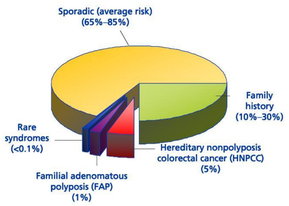
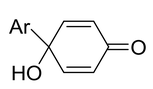


Figure 1. Facts related to colorectal and renal cancers

Application

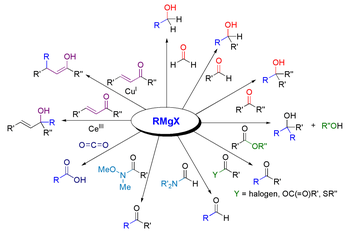
❖ **Aromatic quinols have demonstrated *in vitro* antitumor activity**

- Abnormal tyrosine protein kinase (PTKs) cause many human cancers
- Aromatic quinols shown to be PTK inhibitors
- They have longer half lives
- Rapid bioactivity



❖ **Grignard Reaction**

- The addition of an organomagnesium halide to a ketone or aldehyde to form a tertiary or secondary alcohol



❖ **Examples of Aromatic Quinols**

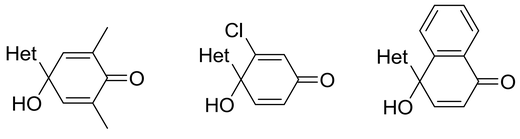
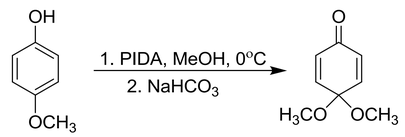


Figure 2. Three heteroaromatic quinols showing antitumor activity.

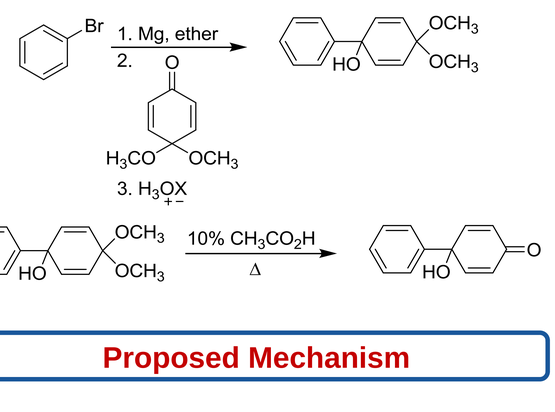
- These heteroaromatic quinols demonstrated GI50 values at 0.36μM, 0.46μM and 0.74μM respectively
- GI50 values indicate 50% of cancerous cell growth inhibition at the specified concentrations

Reaction Scheme

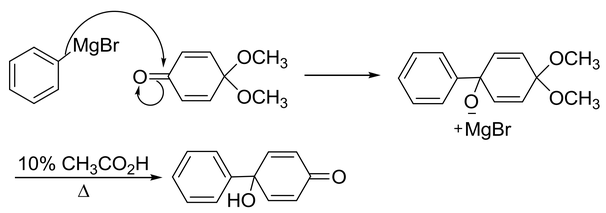
Scheme 1. Preparation of 4,4-dimethoxy-2,5-cyclohexadien-1-one



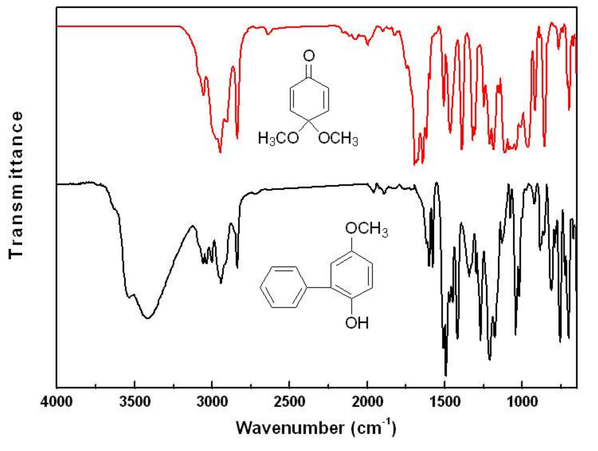
Scheme 2. Preparation of 4-hydroxy-4-phenyl-2,5-cyclohexadien-1-one



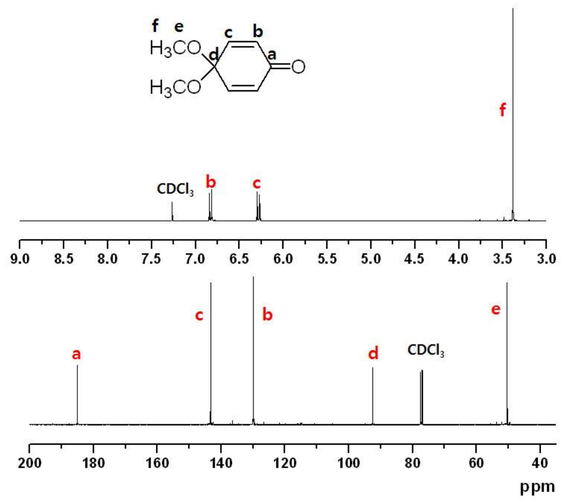
Proposed Mechanism



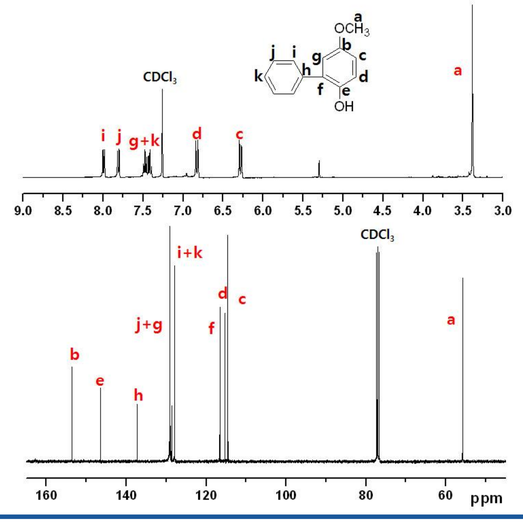
FT-IR Spectroscopy



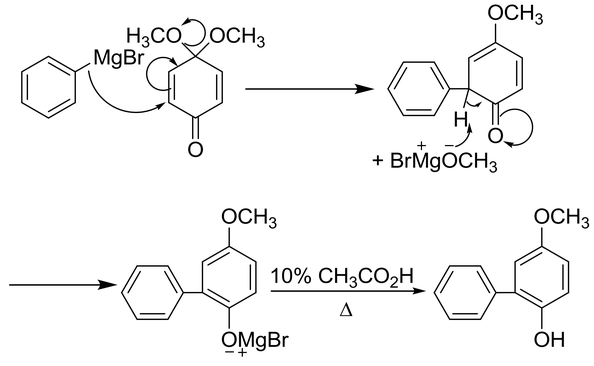
NMR Spectroscopy of Quinone



NMR Spectroscopy of Aromatic Quinol



Suggested Mechanism

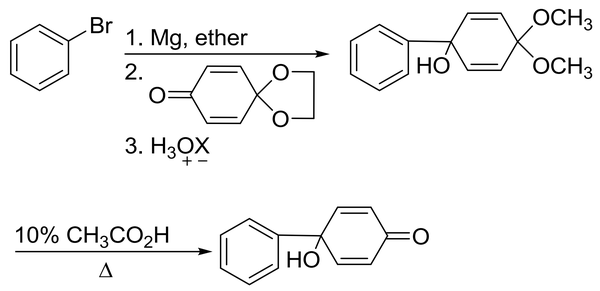


Conclusion

- FT-IR, ^{1}H, and ^{13}C spectroscopic data indicate that the synthesized molecule didn't match the desired product
- The suggested mechanism is consistent with the data from spectroscopy and reported references
- Formation of the unexpected product may be due to the resulting thermodynamic stability of the aromatic π electron system over the diene product

Future Work

- Future research should incorporate various protecting groups, such as cyclic ketals or thioketals, to avoid the directing effects of methoxy substituents which are known to result in syntheses of unexpected products.



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Acknowledgements

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