Fluorination of Quercetin Using Various Methods

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Abstract

Quercetin is a naturally available compound and has been reported to have pharmaceutical properties. In the present project, fluorination of quercetin will be carried out using Selectfluor and the products will be characterized. Reaction conditions will vary from room temperature, sonicator, and sand-bath. The reaction will be conducted using traditional and microwave methods, and the products and yields will be compared.

Introduction

Quercetin powder and structure (CITE)

Flavonoids function in the body as antioxidants, regulating cellular activity and removing toxic free radicals (1). One example of a flavonoid is the antioxidant Quercetin. Quercetin is a compound known as a dietary flavonoid (2). While the fluorination of other flavonoids has been well documented, there is no research on the fluorination of quercetin (3). Quercetin as a pure powder is yellow (4). The structure of the compound is polyphenolic with OH groups attached at positions 3, 5, 7, 3′, and 4′ (4)

Present work and designing strategy

- **The objective of present study and design.**
  - Objective 1: To determine if this compound can be fluorinated
  - Objective 2: What happens to this compound when it is reacted under different conditions?
  - Does heat cause the fluorinated compound to decompose?

The objective of this present study is to perform the fluorination of the antioxidant quercetin under different reaction conditions in order to compare the products of the reaction.
Lastly, the products will be characterized using TLC, fluorine NMR, and IR.

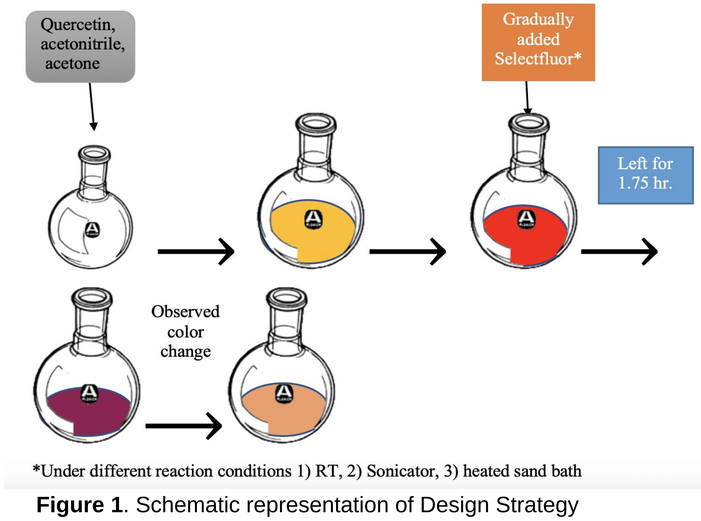

Figure 1. Schematic representation of Design Strategy

Methods

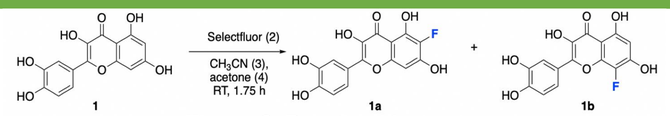

Figure 2. Reaction Mechanism

Quercetin, acetonitrile and acetone are added to 100 mL round bottom flask as Figure 1 shows. To the stirring yellow suspension is added Selectfluor in small portions over a 10 min period. Upon initial addition of Selectfluor, the solution slowly turns deep red and continues to darken while adding the remaining fluorinating agent. The reaction mixture is capped and stirred for 1.75 h. This experiment was run 3 times under different conditions. The general reaction was the same the first run was at room temperature, the second run was performed using a sonicator, and the third run was performed using a sand bath at 60-70 degrees Celsius. After the reaction was finished, the products of the reaction were characterized the TLC.

Figure 3: a) Room Temperature, b) Sonicator, c) Sand Bath

Results and discussion

After the reaction was finished as described, the product from the first run was subjected to vacuum distillation in order to remove any of the acetonitrile solvent from the flask. After the solvent was removed from the flask, only a solid residue remained.

Next, a separatory funnel was used in order to remove any remaining Selectfluor, since this fluorinating agent is not soluble in nonpolar solvents. Once the aqueous layer and the organic layer were appropriately separated, the organic layer (containing the fluorinated quercetin product) was placed on the rotary evaporator in order to once again remove any solvent. The product residue was dark brown and gummy, so cyclohexane and ethyl acetate were added in order for recrystallization to occur. Since recrystallization was unsuccessful, column chromatography was utilized in order to separate the contents of the first run.

TLC plates were used along the way in order to test for the presence of product (or possibly multiple products).

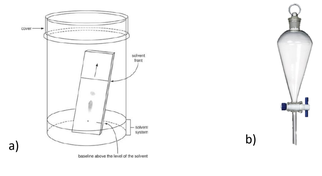

Figure 4: a) Thin Layer Chromatography Set up, and b) Separatory Funnel Set up

Results and discussion

Date	Title	Rf Value
1/29/2021	FOQ Run #1 vs Starting Material Quercetin	Quercetin: 0.78 FOQ: 2 spots at 0.47, 0.63
2/5/21	FOQ Run #1 vs. Dr. Sloops Product from last semester	Dr. Sloop: 0.75 FOQ Run #1: 3 spots at 0.52, 0.91, 0.97
2/5/21	FOQ Run #1 vs. FOQ Run #2	Run #1: 2 spots at 0.45, 0.67 Run #2: 0.42
2/11/21	FOQ Run #2 vs Dr. Sloop's Product from last semester	Dr. Sloop: 2 spots 0.41, 0.58 FOQ Run #2: 0.37
2/18/21	FOQ Run #1 (After Distillation) vs. Starting Quercetin	FOQ Run #1 (After distillation): 0.65 Quercetin: 0.77
3/01/2021	FOQ Run #3 vs. Starting Quercetin	FOQ Run #3: 0.61 Quercetin: 0.78

Figure 4: All samples from Thin Layer Chromatography in a mixture of 30 hexane: 70 ethyl acetate. Key: FOQ: Fluorination of Quercetin, Run #1: Attempt #1 from 1/29/2021, Run #2: Attempt #2 from 2/5/2021, Run #3: Attempt #3 from 3/01/2021

The different spots on the TLC plates indicate multiple products form when the reaction is performed at room temperature. However, the fact that the same sample will form or lose spots suggests that the products decompose over time. This may indicate that fluorinated quercetin is unstable at temperatures above 20 ^{o}C for prolonged periods of time. Additionally, fluorine is UV sensitive, which may have played a role in the decomposition of products.

Conclusions

In the future, the products from all 3 attempts should be characterized using Fluorine NMR and IR. More care should be taken in future attempts in order to protect the samples from UV damage, as well as maintain a tight control on the temperature to which the samples are exposed. Pure quercetin has many biochemical properties including anti-carcinogenic, anti-inflammatory and antiviral activities; and more research should be conducted in the future to determine if the fluorination of quercetin produces stable products.

References

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Acknowledgments

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