


**Project SEED 2008**


**Research Report:**


**Synthesis of (E) -and (Z)- $\alpha$ -2,5-Dimethyl-3-furylethylidene(isopropylidene)succinic Anhydride**


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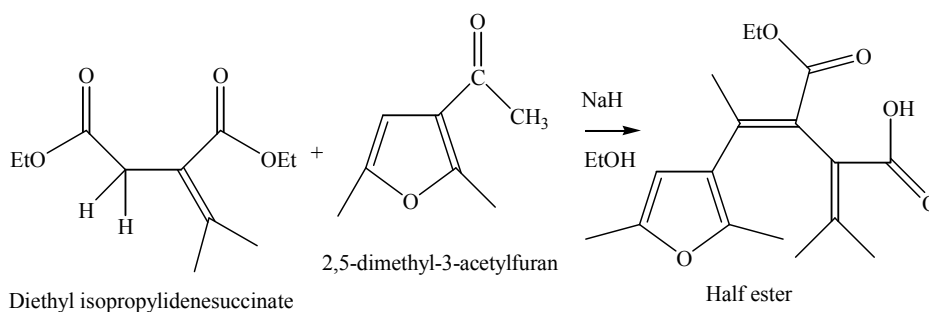
  
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## Introduction

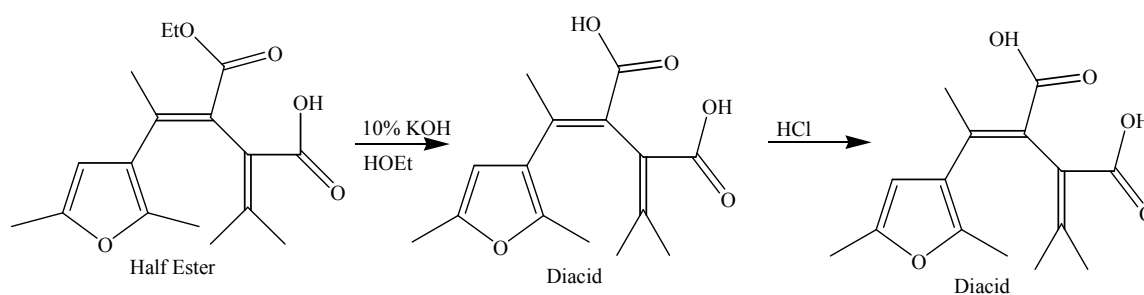
“Photochromism is defined as a reversible transformation in a chemical species between two forms having different absorption spectra by photoirradiation.”<sup>1</sup> There are various applications for photochromatic materials.<sup>1</sup> (E)- $\alpha$ -2,5-Dimethyl-3-furylethylidene(isopropylidene)succinic anhydride is a fulgide that undergoes a conversion when irradiated with light, it can be used in photochemical reaction studies. It is reported that by using ultraviolet light (E)- $\alpha$ -2,5-Dimethyl-3-furylethylidene(isopropylidene)succinic anhydride will photocyclize.

This paper discusses the preparation of (E) -and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride in three steps. In the first step half-ester was synthesized from a reaction of diethyl isopropylidene succinate and 2,5-dimethyl-3-acetylfuran using sodium hydride (NaH) in toluene. The resulting half-ester was converted to a diacid by hydrolysis using ethanolic potassium hydroxide and then protonation using hydrochloric acid (HCl). The resulting diacid was treated with acetyl chloride to yield the product. Figure 1 displays the 3 steps in this synthesis.

### Step 1: Synthesis of Half Ester



## Step 2: Synthesis of Diacid



## Step 3: Synthesis of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride

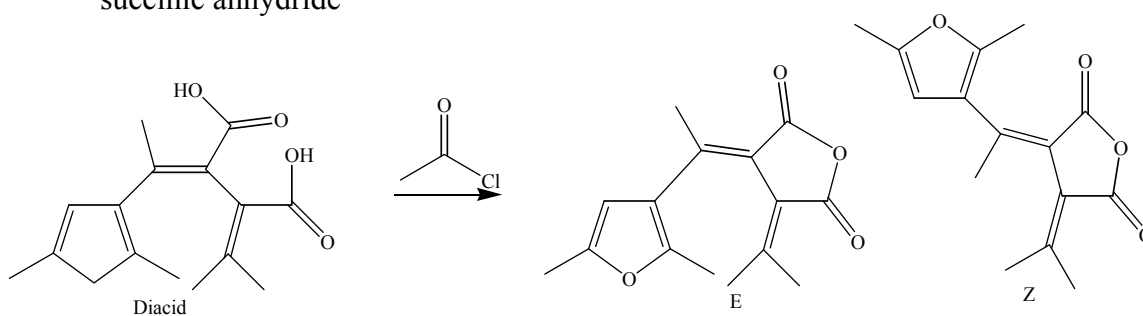


Figure 1: synthesis of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride.

## Experimental Section

### Materials and methods

**Chemicals:** Hydrochloric acid (HCl, 5M), Potassium hydroxide (certified A.C.S Pellets), Toluene and Magnesium Sulfate ( $\text{MgSO}_4$ , anhydrous) were purchased from Fisher Scientific. 2,5-dimethyl-3-acetylfuran (98%), Toluene (99.8% anhydrous) and Sodium Hydride (NaH, 100%) were purchased from Sigma Aldrich. Ethyl alcohol (200 proof) was purchased from Pharmco. Diethylisopropylidene succinate was synthesized from a previous experiment (LL07VII23). Acetyl Chloride (98%) was purchased from Merck.

### **Synthesis of Half Ester**

2,5-dimethyl-3-acetylfuran (2.8 g, 0.0203 moles) and diethylisopropylidenesuccinate (4.4 g, 0.0206 moles) were weighed into 2 different beakers. Inside the glove box NaH (1.018 g, 0.0424 moles) was weighed and added into a 100 mL 3-neck round bottom flask, and anhydrous toluene was added (40 mL). After withdrawing the flask out of the glove box, equipped with a condenser it was lowered into a 60 °C water bath. Into the reaction flask 2,5-dimethyl-3-acetylfuran, diethylisopropylidenesuccinate, and a catalytic amount of absolute ethyl alcohol was added. After heating for an hour a sample was taken out and dissolved in 5M HCl for GCMS analysis. The sample separated into an aqueous and organic layer, GCMS was done for both layers. Upon reaction completion, the reaction mixture was poured on an ice bath and allowed to melt. The solution was poured into a separatory funnel and a liquid- liquid extraction was done 3 times using H<sub>2</sub>O (100 mL). After distinguishing the organic (top) and aqueous (bottom) layers the aqueous layer's pH level was analyzed. The pH level of the solution was basic so 5M HCl was used to turn the solution into an acid. A liquid-liquid extraction was done 3 times using toluene (35 mL). The toluene layers were combined and MgSO<sub>4</sub> was added. The solution was left in the fume hood overnight wrapped in foil with the lights off. After removing solution from the fume hood the solution was vacuum filtered to remove the MgSO<sub>4</sub>. In 100 mL pear shaped flask aliquots of the solution were evaporated using rotovaped. A sample was taken and GCMS analysis was done. The synthesis of half ester was repeated four times.

### **Synthesis of Diacid**

The synthesis of diacid was repeated 4 times using various amounts of reagents. Refer to table 1 for the amounts of the reagents used. Potassium hydroxide pellets (KOH) (2.508

g) were dissolved in a mixture of ethyl alcohol (EtOH) (28.5 mL) and water (1.5 mL) and was put into a 25 mL volumetric flask. The KOH/EtOH mixture was added to a 50 mL flask containing the prepared half ester (2.507 g). The reflux apparatus was assembled and temperature was gradually increased to 78 °C. At 78 °C there was no boiling of the reaction mixture, but experiment was continued. Temperature was allowed to cool to room temperature and the solution mixture was poured into an empty flask. 5M HCl acid was added to the solution, and a pH test was performed to verify acidity. The reaction mixture was vacuum filtered twice and extracted three times using toluene (35 mL). The reaction mixture was dried with MgSO<sub>4</sub> overnight. The solution was vacuum filtered to remove the MgSO<sub>4</sub> and the toluene was evaporated using rotovaped.

Table-1: Synthesis of diacid with varying reagent ratio.

Trials	Reagents				Amount of product assumed to be Diacid (g)	Percent Yield (%)	Observation
	KOH (g)	Half Ester (g)	Water (mL)	Ethyl Alcohol (mL)			
1	2.508	2.507	1.5	28.5	0.77 g	33.7	brown solid
2	5.028	2.1	2.5	47.5	2.16 g	94.9	brown solid
3	5.002	All	2.5	47.5	2.4 g	105	brown solid
4	5	2.5	45 mL ethanol		Not Determined	Not Determined	brown solid

### Synthesis of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride

Acetyl chloride was added to diacid in a reaction flask and the reflux apparatus was assembled. The temperature was increased to 60 °C and allowed to reflux for 2 ½ hours.

The reaction was allowed to cool to room temperature. To neutralize the reaction a

solution of saturated sodium bicarbonate and deionized water was added. A liquid-liquid extraction was done using toluene. The organic (top) and aqueous (bottom) layers produced from the extraction were analyzed by GCMS. The solution was left overnight to dry in  $\text{MgSO}_4$ . The solution was vacuum filtered to remove the  $\text{MgSO}_4$  and the toluene was evaporated. NMR analysis was done on the reaction mixture. The reaction mixture was precipitated using 1:1 hexanes/chloroform (final volume 10 mL) and the product was placed in the freezer for crystallization.

### **(E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride**

#### **Testing using Thin Layer Chromatography (TLC)**

Three previously prepared samples were tested to distinguish between the (E) and (Z) isomers. Each sample was placed in a test tube labeled A, B, and C. Ethyl acetate was added to each test tube to dissolve the crystals. Initially a solution of 50% ethyl acetate/hexane was prepared in a jar. A small sheet of paper towel was placed in the jar and the lid was fastened. A 7 cm long thin layer silica gel plate was cut and a horizontal line was marked off 1 cm from the bottom. A spot of each sample was positioned on the line using a capillary tube. The plate was placed into the jar containing the solvent, and the top was fastened. When the solvent reached about  $\frac{3}{4}$  the way, the plate was taken out and a line was drawn to recognize the solvent front. The spots on the plate was observed using UV light.

### **(E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride**

#### **Testing using Column Chromatography and TLC**

After removing (E)- and (Z)- $\alpha$ -2,5-Dimethyl-3-furylethylidene(isopropylidene) succinic anhydride from the freezer, some of the solvent was evaporated. Column

chromatography was done using 50% ethyl acetate/ hexane. At the end of the column chromatography 19 fractions were collected. After completing the column chromatography each sample was tested using thin layer chromatography silica gel plates. Initially a mixture of 50% ethyl acetate/ hexane was prepared in a jar. Then 10 mL of the mixture was measured out into separate jars and the lip was fastened. Five 7 cm thin layer silica gel plates were cut and on each plate a horizontal line of 1 cm was marked off from the bottom. A spot of each fraction was positioned on the line using a capillary tube. Under each fraction the corresponding number was written. The plates were placed into the jars containing the solvent, and the tops were fastened. As the solvent reached about  $\frac{3}{4}$  the way, the plates were taken out and a line was drawn to recognize the solvent front. The spots on the plates were observed using UV light. Fraction 6 was evaporated using the rotovap. Fractions 7 and 8 were mixed and evaporated using the rotovap. Fractions 3, 4, and 5 were mixed and evaporated the rotovap. Fractions 9-19 were mixed and evaporated using the rotovap. After evaporation NMR analysis was done of each fraction mixture.

## **Results**

### **GCMS analysis of Half Ester**

During the synthesis of half ester GCMS analysis was performed on the starting material, then during the reaction, after extraction and finally after evaporating. Table-1 lists the retention time (min) and molecular ion ( $M^+$ ) of the GCMS analysis. The first GCMS spectrum was taken to determine the retention time of the starting material. The second GCMS was taken 53 minutes into the reaction. The spectra of the organic layer indicated that some starting material was still there and that product was starting to form. GCMS

after the reaction was complete showed fewer amounts of the starting material and new peaks for the product. GCMS taken after drying and evaporating the product showed not peaks of the starting materials and one peak which indicated the half-ester product.

Table-2: GC/MS results of half-ester synthesis.

Condition	RT (min)	M+	Compound
Starting material in toluene	5.01	168	Diethylisopropylidenesuccinate
Starting material in toluene	3.17	138	2,5-dimethyl-3-acetylfuran
53 min into reaction	3.19	138	2,5-dimethyl-3-acetylfuran
53 min into reaction	5.04	168	Diethylisopropylidenesuccinate
53 min into reaction	8.31	306	Half Ester
53 min into reaction	7.75	306	Half Ester
After extraction	7.72	306	Half Ester
After evaporating	7.66	306	Half Ester

### NMR analysis of Diacid

Table 3 has the tentative assignments of the diacid isomers based on the known assignments of the E, Z fulgide products.<sup>2</sup>

Table-3: NMR shift assignments for E, Z diacids using Figure 2

Peak	Assignment
1.63	1
1.90	8
1.91	11
2.07	3
2.12	2
2.17	4
2.23	9
2.28	10
2.35	7
2.38	5
5.73	6
5.89	12

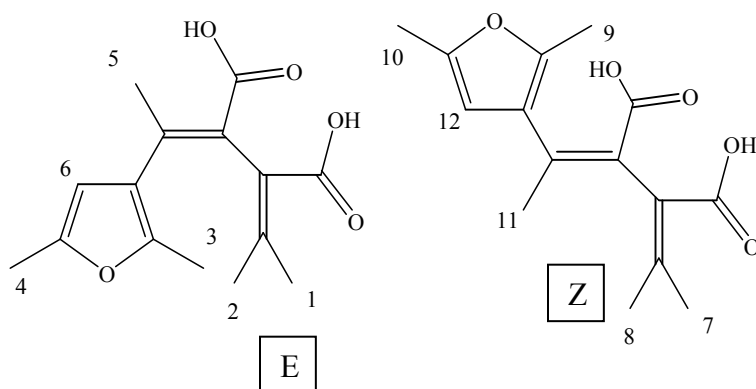


Figure-2: molecular structure of (E) and (Z) isomers of diacid.

### **NMR Data of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride**

Table 4 has chemical shift assignments based on the known assignments of the E, Z fulgide products.<sup>4</sup>

Table-4: NMR chemical shift assignment of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene-(isopropylidene) anhydride using Figure 3

Peak	Assignment
1.35	14
1.94	20
1.10	15
2.10	21
2.20	24
2.25	16
2.28	23
2.34	13
2.41	19
2.57	18
5.91	17
5.97	22

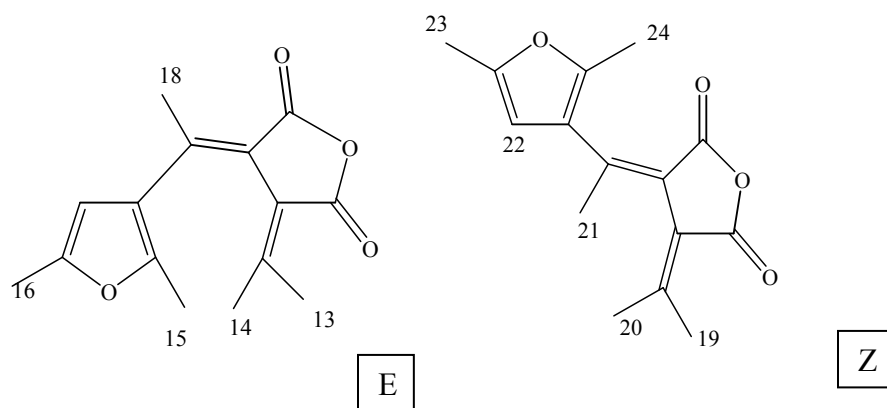


Figure-3: molecular structure of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene) anhydride.

### NMR Data of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene)succinic anhydride after Column Chromatography and TLC

These are the tentative assignments based on the known assignments of the E, Z fulgide products.<sup>4</sup>

Table-5: NMR chemical shift assignment of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene) anhydride using Figure 3

Fractions 3-5	
Peak	Assignment
1.34	14
1.98	20
2.03	15
2.09	21
2.23	13
2.32	13
2.57	18
5.93	17

Table-6: NMR chemical shift assignment of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furyl-ethylidene(isopropylidene) anhydride using Figure 3

Fraction 6	
Peak	Assignment
1.98	20
2.01	15
2.07	21
2.19	24
2.25	16
2.35	13
2.41	19
2.56	18
5.91	17
5.96	22

Table-7: NMR chemical shift assignment of (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene) anhydride using Figure 3

Fractions 7-8	
Peak	Assignment
1.34	14
1.98	20
2.01	15
2.10	21
2.25	16
2.35	13
2.43	19
2.57	18

## **Conclusions and Overview**

The compound (E)- and (Z)- $\alpha$ -2,5-dimethyl-3-furylethylidene(isopropylidene) anhydride was achieved in 3 steps. Several techniques such as evaporation using rotovaping, vacuum filtration, and liquid- liquid extractions were used during the synthesis and purification steps. A proton NMR spectrum displayed the necessary information for making the peak assignments for the compound; therefore column chromatography was performed to separate the two isomers. Unfortunately this method

did not successfully separate the isomers; however, it purified the (E) and (Z) isomers of any side products. NMR analysis performed on the fractions from the column chromatography separation helped distinguish between working samples and non working samples for future work. In future work, fractions 3-8 which contain both isomers will be mixed. Then using column chromatography equipped with a gradient solvent system ranging from 5% ethyl acetate/ hexane to 50% ethyl acetate/ hexane the isolation of the isomers will be attempted. After collecting the fractions, TLC will help to determine which fractions contain which isomer. After combining the fractions that contain the same isomers and evaporating the solvent the fractions would then be placed in the freezer with 50:50 chloroform/ hexane. After the formation of crystals, UV light should be used to convert the (Z) isomer to the (E) isomer.

I had an outstanding time this summer, but I don't believe that my experience in this program would have been the same if it wasn't for my wonderful mentor, Dr. Burkey. At the beginning of this program when I first looked into the lab I was terrified, but after Dr. Burkey showed us around it became very interesting. Every Friday Dr. Burkey scheduled for him and each Project SEED student to have a meeting to discuss what we had done in the lab that week. During these meetings we each had to talk about what we did during the week of working in the lab. I was so scared, but by the end of these meetings, I would realized that these meetings wasn't just for us to understand each other projects, but it was also to help him help us to understand our own projects. Occasionally Dr. Burkey would help me around the lab with suggestions that he felt would better my reaction. Sometimes he would meet with me to help me understand all

of my data. He would discuss with me the steps that he felt would increase the yield of the next synthesis. I am very honored to been given this opportunity with a great mentor.

### **Acknowledgment**

I would like to thank Dr. Burkey for the opportunity to participate in Project SEED. I would also like to give special thanks to **Karen L. Mosley, Daniel G. Abebe, and Kristie Ruddick** for helping me throughout this very outstanding experience.

## Sources:

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<sup>1</sup> Tsivgoulis, G. M. "New Photochromic materials." Department of Polymer Chemistry. 1995. University of Groningen. 15 July. 2008  
<http://www.mariecurie.org/annals/volume1/tsivgoulis.pdf>.

<sup>2</sup> Deblauwe, V.; Smets, G. *Makromol. Chem.* **1988**, 89, 2503-12.