

Synthesis and Purification of
3-[1-(2,5-Dimethyl-3-furanyl)ethylidene]dihydro-
4-(1-methylethylidene)-(3E)-2,5-Furandione

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08/10/2007

Date

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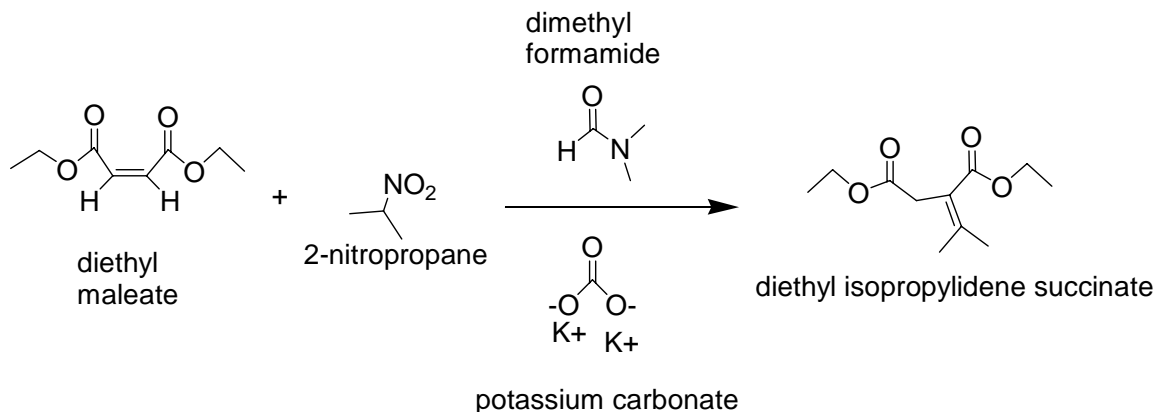
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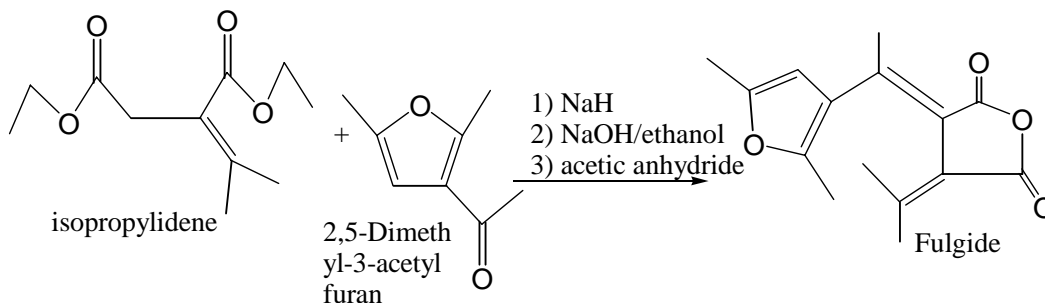
Introduction

The purpose of the experiments was to synthesize a fulgide: 3-[1-(2,5-dimethyl-3-furanyl)ethylidene]dihydro-4-(1-methylethylidene)-(3E)-2,5-furandione.

For this to work, I used two different compounds, 1 solvent, and a catalyst as the first step of the syntheses which makes diethyl isopropylidene succinate.



The next step of the synthesis was to use isopropylidene to get to the product.



The experiments was done using the many techniques including vacuum distillation, rotary evaporation, extractions, refluxing, column and thin layer chromatography.

Experimental Section

LPL07VI27-2. Thin Layer Chromatography of Fulgide

From a previous synthesis of fulgide, A TLC (thin layer chromatography) was done on the fulgide. For the solvent, hexanes and ethyl acetate were used. First, the inside of a jar was lined with paper. Solutions of 5%, 10%, 20%, 30%, and 40% of ethyl acetate in 10 mL of hexanes solution were prepared. Second, 0.5 mL of ethyl acetate was mixed with 9.5 ml of hexanes. The mixture was poured into the jar. Then a piece of TLC plate (250 mm layer, backing: aluminum, fluorescence: UV₂₅, coating: silica gel, #4420 222) was cut and a spot of the solution was placed onto it using a glass capillary. The spot was placed on a starting line drawn by pencil. The TLC paper was put into the jar and the plate developed. Once it was done, the finish line was drawn and an ultraviolet lamp was used to see the spots. Besides changing the amount of ethyl acetate for each additional TLC, the same steps were repeated for 10, 20, 30, and 40% of ethyl acetate.

07VI26-2. Experiment 4; First step of synthesis; isopropylidene

Dimethyl formamide (120 mL, 1.54 mol), 2-nitropropane (28 mL, 0.31 moles), diethyl maleate (32 mL, 0.197 moles), potassium carbonate (30 g, 0.217 mol) were placed in a 3-necked 500-mL round bottom flask. The flask containing the solution was placed on a heating mantle that was balanced on a heating ring and ring stand. The solution refluxed for 5 hours. Once it was done boiling, a drop of sample was taken and put into a vial with 40 drops of acetone to take a GCMS (Gas Chromatography Mass Spectroscopy).

Next the product was taken and an extraction was done 3 times using 80 mL of ethyl ether. After the product was done from the extraction, the solvent was removed by rotary evaporation. Once that was done, a vacuum distillation proceeded. We came out with four different samples at four different temperatures.

07VI28-4. Column Chromatography of Fulgide

In this experiment, a column chromatography was going to take place. A column (100 mL), beaker, hexane, ethyl acetate, silica gel, research sand, funnel, nitrogen gas, a mantle, and 55 test tubes were gathered. Half an inch of sand was poured into the column. Using the beaker, silica gel and hexanes were mixed until a slightly thick gel formed which was poured into the column until $\frac{3}{4}$ full. Another $\frac{1}{2}$ inch of sand was added. The crude fulgide was added on top of the sand, and about 75 mL of hexanes. Then nitrogen was used to push solution down. The column started and the product poured into test tubes.

07VII9-1; 07VII10. Column Chromatography of fulgide

Column chromatography was done on a larger amount of crude fulgide. About 30 mL of hexanes were added into the column and then $\frac{1}{2}$ inch of sand was added that was then packed down using nitrogen gas. Next more hexanes were added, and the silica gel was added until the column was about $\frac{3}{4}$ full. Again nitrogen was used to pack that down too. The hexanes were again added and another $\frac{1}{2}$ inch of sand was added to the column. That was packed down once added. Once that was done, the fulgide was added, and 100 mL of hexanes was added. Now the column was ready to pour into the test tubes.

07VII19-2 Experiment 5; First step of synthesis

This experiment was a repeat of experiment 4 but in a bigger quantity. This time the experiment was multiplied by 8 times the original amount. 56 mL of 2-nitropropane (0.621 moles), 64 mL of diethyl maleate (0.39 moles), 240 mL of dimethyl formamide, and 60 g of potassium carbonate (0.43 moles) were used. First the 60 g of potassium carbonate was added into a 1000-mL three-necked round bottom flask and the rest was added after that. The solution refluxed for 5 hours and a GCMS was taken. After the GCMS, an extraction of the solution was done twice using 200 mL of ethyl ether and 100 mL of water. After the extraction the solvent was evaporated, and a vacuum distillation was done. There were 5 samples that came from the distillation. A GCMS was taken of every sample.

07VII26-1 Vacuum Filtration of fulgide

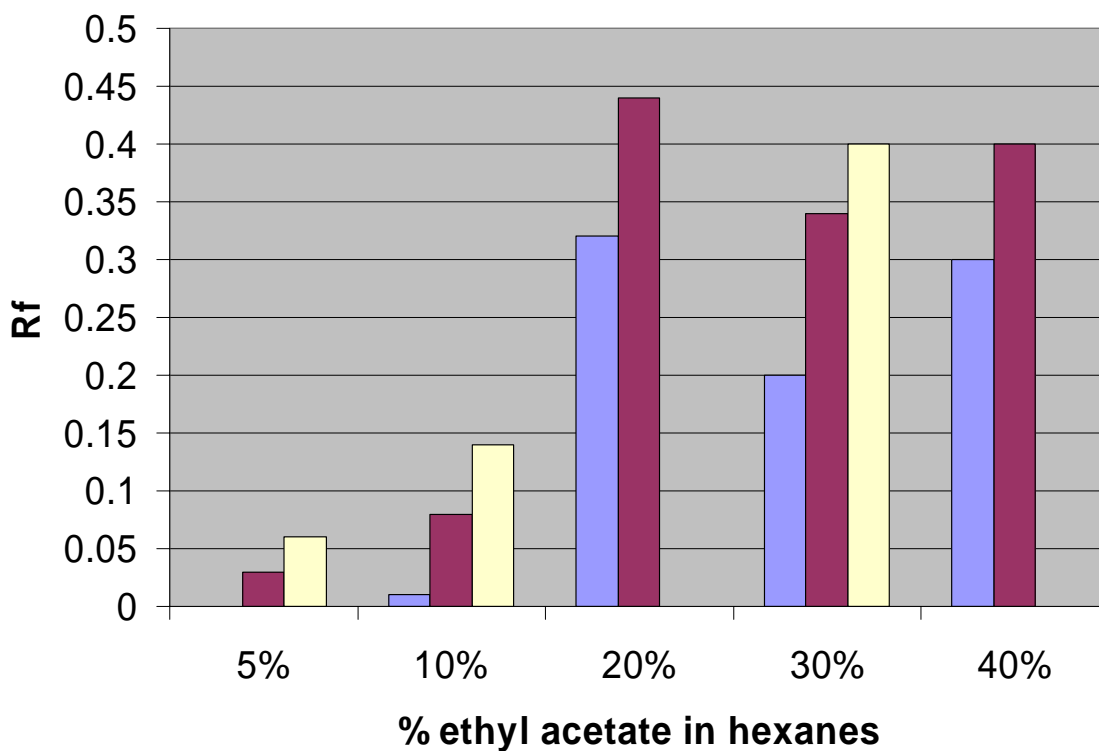
From the product of the fulgide from the column chromatography (07VII10), a vacuum filtration was done. The product had formed some crystals while in the freezer. A plastic funnel, sheet of typing paper, vacuum flask, filter paper, rubber stopper, vial, and hexanes were the materials needed. The flask was hooked up to a trap and an aspirator, and a stopper with the funnel was put on. The aspirator was turned on after adding the filter paper into the funnel. A hand was put over the funnel to make sure there was suction. Hexanes were then poured into the funnel followed by the product. After the filtration was done, there were crystals left on the filter paper. The crystals were placed on typing paper. The paper was then used to transfer the crystals into a vial. The remainder of the filtrate was rotary evaporated to 1/3 of its original size and placed back into the freezer.

Results

LPL07VI27-2: Thin Layer Chromatography of Fulgide

For the 5% ethyl acetate in hexane, I observed, using the UV light, that the spots did not travel far. So when the 10% was done I observed that the spot went further and so on for 20, 30, and 40% (See figure 1)

Figure 1. Retention Factors for Crude Fulgide in Ethyl Acetate and Hexanes



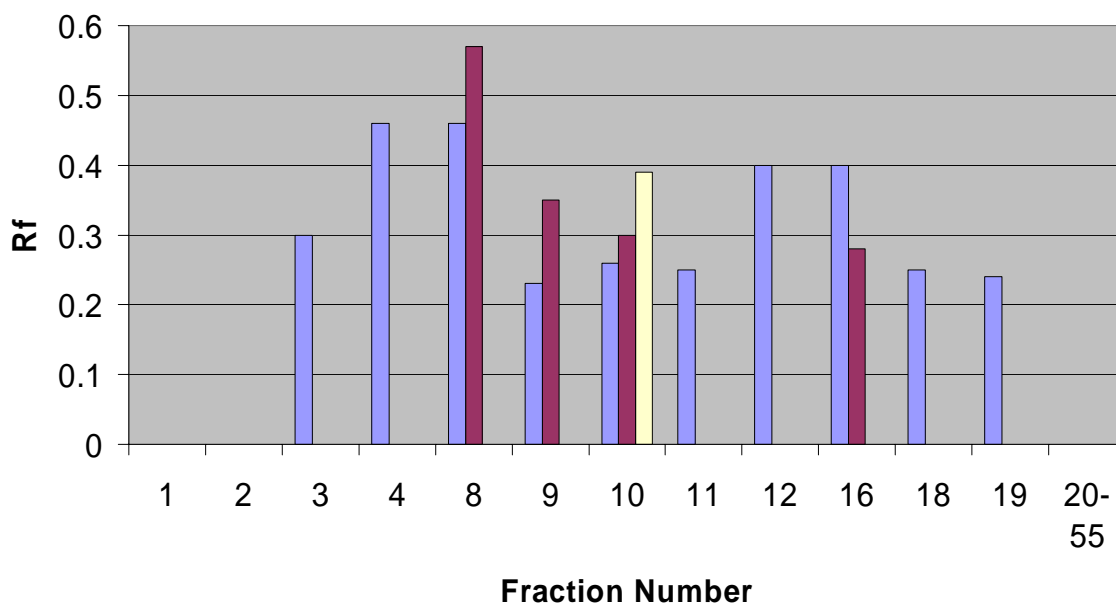
07VI26-2 Experiment 4; First step of synthesis results

The first fraction, which was 0.872 g, distilled at a temp of 33 °C. Fraction 2, 3.352 g, distilled at 60 °C. Fraction 3, 5.640 g, yield 13.36% distilled at 84 °C. Fraction 4, 19.289 g, yield 45.7% distilled at 110 °C. Since 3 and 4 had the highest boiling points, I took a GCMS of them which indicated they were very pure isopropylidene.

07VI28-4 Column Chromatography of Fulgide

Fifty-five fractions eluted from the column were collected in test tubes. Every fourth test tube was analyzed by TLC (See Figure 2). Test tube 1 had nothing show up. At fraction 4 and 8 the spots were at the same RF = 0.46. At number 12 and 16, they were the same RF (0.4) but lower than 4 and 8. The spot for fraction 18 did not move from the starting line and from fractions 20 on up, a spot did not show up on a TLC. I took TLC's of fractions 2, 3, 9, 10, 11, 18 and 19. Fraction 2 had nothing but number 3 was the same as 4 through 8. Fractions 9 and 10 had two spots at RF = 0.24 and 0.33. From these results, fractions with the similar compounds were 4-8, 10-11, 12-16, 18-19 but fractions 8,9 10, and 16 had other components. Fractions 9-10, 19-55 were discarded.

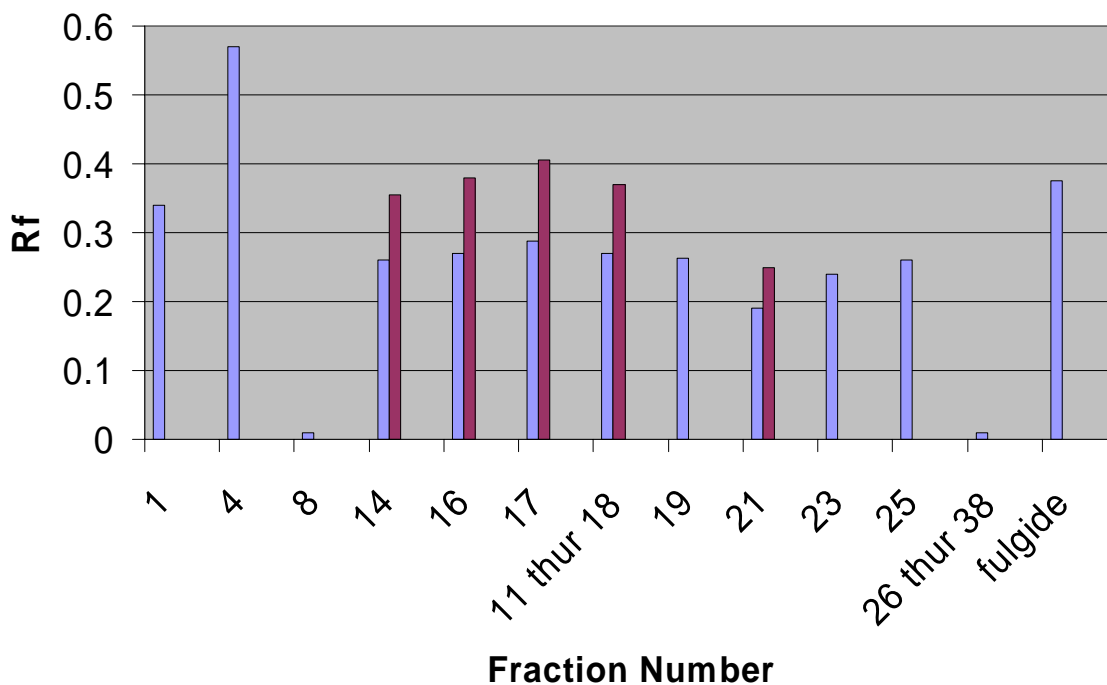
Figure 2. Retention Factors for Chromatograph Fractions from Experiment 07VI28-4



07VII9-1; 07VII10 Column Chromatography of Fulgide (Large Scale)

I ran a TLC for fractions 1,4, 8, 14, 16, 17, 11-18, 19, 21, 23, 25, 26-38, and fulgide. (See Figure 3). All TLC were done using 20% ethyl acetate in hexanes solution.

Figure 3. Retention Factors for Chromatography of Fulgide (Large Scale) 07VII9; 07VII10



07VII19-2 Experiment 5; GCMS of 1st Step of Large Scale Synthesis

Fraction 1 came out at 43 °C, Fraction 2 came out at 43-99 ° C, Fraction 3 at 98-101 °C,. Fraction 4 at 98-101 °C, and. Fraction 5 at 101 °C. A GCMS spectrum was taken of every sample using acetone as a solvent. In fractions 3 and 4, there was pure product. In fraction 5, there was some product but with other components. Fractions 3 and 4 were combined into two containers because their GCMS were the same. The mass of fraction 3 and 4 was 47.698 g and a 56.5% yield. The remainder of fraction 4 was in

the other container, and it had a mass of 7.406 g and a 8.8% yield. The total mass for the product was 55.104 g and total 65.3% yield.

Discussion

LPL07VI27-2: Thin Layer Chromatography of Fulgide

For the 5% ethyl acetate in hexane, I observed, using the UV light, that the spots did not travel far. I think that there was not enough ethyl acetate. So it seems that the ethyl acetate is a better solvent for the TLC of the fulgide.

07VI28-4 Column Chromatography of Fulgide

From this, I may have two different products. It seems that compounds in fractions 4 and 8 are the same and likewise for 12 and 16. So now I had to see if the compounds between those are also the same. So I did another TLC. I took TLC's of fractions 2, 3, 9, 10, 11, 18 and 19. Fraction 2 had nothing to show up just like fraction 1 but fraction 3 was the same as fractions 4 through 8 so the compounds were the same. Fraction 9 had two spots and fraction 10 had 3 spots. One spot had an RF of like that for fractions 4-8 and the other had an RF like that of fractions 12-16. This means at fractions 9 and 10 is where the two different compounds were cross eluting together. Fraction 11 had the same RF as fractions 12-16 meaning they contained the same compound. Since I did not see anything in fraction 20, I had to figure out what fraction between 16 and 20 had similar RF values. I took a TLC of fraction 18 and a spot showed up the same RF as fractions 12-16. The TLC on fraction 19 was barely showing up.

07VII9-1; 07VII10 Column Chromatography of Fulgide (large scale)

It seemed as if the entire product was coming through the first few test tubes because RF for fraction 1 was the same as that for fulgide. For the first spots of fractions

14, 16, 17, 18, and 19, they seem to be the same because their R_Fs are very similar. Fractions 23 and 25 also had similar R_Fs. The second spots of fractions 14, 16, 17, and 18, were also had similar R_Fs, meaning they had similar compounds. So fractions 1-14 and 15-19 were combined and evaporated most of the solvent. Solutions were cooled in a freezer.

Summary and Conclusions

During the time span of the experiments, I synthesized isopropylidene, which had a yield of 65.3%. I also purified the fulgide. During this, I learned many different methods of purification. I learned how to use rotary evaporation, fractional vacuum distillation, vacuum filtration, and column chromatography. Thin layer chromatography was another method I learned while doing the experiments. All of these methods contributed to the synthesis of diethyl isopropylidene succinate and purification of fulgide.