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# SYNTHESIS OF A POTENTIAL ANTITUBERCULOSIS DRUG FROM THE PLANT *PIPER SANCTUM*

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**Abstract**

**Mycobacterium tuberculosis, the bacterium responsible for causing tuberculosis, is one of the leading causes of death from infectious disease worldwide. Mass screening of natural products has led to the discovery of new compounds that exhibit bioactivity against active and latent tuberculosis infection. One example is the compound 2-oxo-14-(3',4'-methylenedioxyphenyl)tetradecane which was isolated from the plant *Piper sanctum*. The research in this article discusses the first synthesis of this natural product. The compound is prepared in eight steps in a 17% overall yield. Further studies will hopefully illuminate the specific mechanism of action behind this compound's observed antitubercular activity.**

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## Introduction

*Mycobacterium tuberculosis*, the pathogen responsible for causing tuberculosis, is a major global health concern. In 2020, it was estimated that 10 million people were infected with tuberculosis resulting in 1.2-1.3 million deaths.[1] While there is an existing protocol for tuberculosis therapy,[2] the appearance of new extensively drug-resistant tuberculosis, multidrug-resistant tuberculosis, and HIV/AIDS-tuberculosis coinfection has led to increased research on the development of new drugs to treat this pandemic.[3] A focal point for the discovery of novel antituberculosis agents is natural products. One plant of interest is the evergreen shrub *Piper sanctum* found in Mexico and Central America.

*Piper sanctum* has been used traditionally as both a spice and a home remedy in Mexico. The leaves have an anise-like aroma and are used to wrap tamales and other foods. The plant's leaves can also be steeped to make tea and this beverage is often used to treat respiratory ailments.[4,5] Because of its medicinal properties, *Piper sanctum* is commonly referred to as "hoja santa" or the "sacred herb".[5,6]

In 2004, researchers performed mass screenings of *Piper sanctum* extracts to identify compounds with bioactivity against *Myobacterium tuberculosis*.[5] Of the 14 molecules isolated in this study, 2-oxo-14-(3',4'-methylenedioxyphenyl)tetradecane (**1**) was one compound that exhibited promising activity against the bacterium with a minimal inhibitory concentration (MIC) of 6.25 μg/mL (**Figure 1**).[5]

Inspection of the literature illustrates that compound **1** has never been synthesized. In addition, no studies have been performed that provide insight into this compound's mechanism of action. Because of its structure, it is hypothesized that compound **1** could potentially be a 1,4-dihydroxy-2-naphthoate prenyltransferase (MenA) inhibitor.[3,7,8] The aromatic ring attached to a lengthy alkyl side chain mimics some previously reported compounds that have been shown to inhibit MenA.[7]

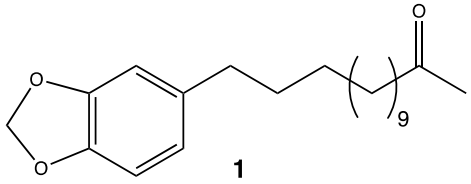



**Figure 1**. 2-oxo-14-(3',4'-methylenedioxyphenyl)tetradecane

In the menaquinone biosynthetic pathway, the enzyme MenA catalyzes a decarboxylative prenylation of 1,4-dihydroxy-2-naphthoate (**2**) to prepare dimethylmenaquinone (**3**). Dimethylmenaquinone (**3**) is then transformed to menaquinone (**4**) by S-adenosyl-L-methionine (MenG) (**Figure 2**).[8] Menaquinone plays an essential role in the electron transport chain of mycobacteria, cycling between menaquinone (**4**) and menaquinol (**5**) to transfer electrons in the production of adenosine triphosphate (ATP) (**Figure 2**).[8] Similar to mammalian cells, ATP is the primary chemical energy source for bacteria. Inhibitors of MenA have been shown to initiate significant growth inhibition of Gram-positive bacteria.[7,9] Because menaquinone biosynthesis does not occur in human cells, MenA inhibitors have become an exciting target for the development of novel, selective antibacterial drugs.

The objective of this research was to synthesize compound **1** (**Figure 1**). It was envisioned that compound **1** could be prepared in eight steps from commercially available piperonal (**6**)

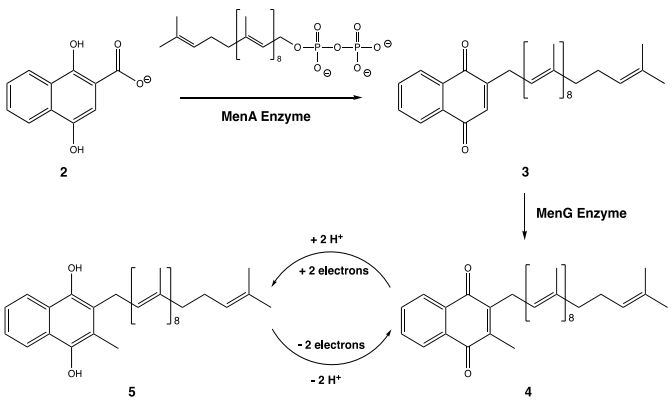



**Figure 2**. Menaquinone (**4**) Mediated Electron Transport

and 1,12-dodecanediol (**7**) (**Scheme 1**). The first five steps of this sequence were recently published as an Advanced Organic Chemistry laboratory for undergraduate students.[10] In this laboratory, compound **13** and four analogues incorporating different aromatic rings were prepared. This paper illustrates how these compounds could be further transformed to prepare the desired antituberculosis drug targets, focusing exclusively on the natural product, compound **1**.

## Experimental Methods

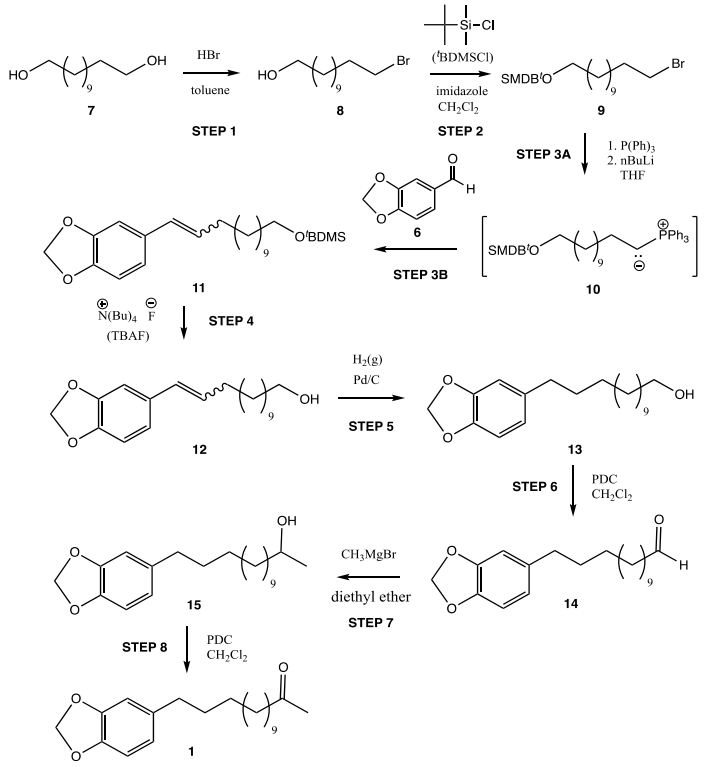
Column chromatography was performed using 230-400 mesh silica gel. Nuclear magnetic resonance (NMR) was recorded on a JEOL 400 MHz NMR spectrometer. Gas chromatography-mass spectrometry (GC-MS) was carried out on an Agilent Technologies 7890/5975C gas chromatograph-mass spectrometer. The GC column (30 m x 0.25 mm) has a 0.25 mm polydimethylsiloxane (PDMS) with 5% phenyl substitution stationary phase. The GC oven conditions are listed below for each step. All starting materials were purchased from Millipore Sigma and used as received.

## GC-MS Oven Conditions

| **Step 1** | **Step 2** | **Steps 4 - 8** |
|---|---|---|
| 150°C for 2 m | 150°C for 2 m | 170°C for 2 m |
| Ramp:20°C/m to 250°C. | Ramp:20 °C/m to 250°C. | Ramp:40°C/m to 250°C |
| Hold @ 250°C for 1 m | Hold @ 250°C for 2 m | Hold @ 250°C for 8 m |

### *Step 1: Mono-Bromination*[10]

Commercially available 1,12-dodecanediol **7** (2.00 g, 9.90 mmol) was placed into a 100 mL round bottom flask and dissolved in toluene solvent (25 mL). Hydrobromic acid (48 wt% in water) (4.50 mL, 39.8 mmol) was added to the flask and the resulting biphasic mixture was heated at reflux in a 125 °C oil bath for exactly 30 minutes. The reaction mixture was cooled to room temperature, diluted with brine (25 mL), and extracted two times with hexanes (30 mL x 2). The organic layers were combined, dried over magnesium sulfate, filtered, and concentrated. Mono-brominated product **8** was isolated as a white solid (1.84 g, 70.5%). Three products, mono-brominated product **8**, 1,12-dibromododecane, and diol **7**, were observed by gas chromatography-mass spectrometry (GC-MS). The ratio of the products prepared were determined by GC to be 83.2 mono-brominated product **8** (Retention time (RT) = 6.10 min): 4.78 di-brominated product (RT = 6.63 min): 1.00 diol **7** (5.48 min). These numbers correspond to a 93.5% purity of product **8**. Compound **8** was carried directly into the next step without further purification. $^1$H NMR (400 MHz, $CDCl_3$) δ 3.62 (t, $J$ = 6.8 Hz, 2H), 3.39 (t, $J$ = 6.8 Hz, 2H), 1.84 (tt, $J$ = 6.8, 6.8 Hz, 2H), 1.55 (tt, $J$ = 6.8. 6.8 Hz, 2H), 1.43 – 1.21 (m, 17H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 63.2, 34.2, 32.9, 32.9, 29.7, 29.6, 29.6, 29.5 (2C), 28.8, 28.2, 25.8. GC-MS RT = 6.093 min, ($M^+$-46) = 218/220 (loss of water and ethylene).




**Scheme 1.** Synthesis of Compound **1**

### *Step 2: Silyl Protection*[10]

Crude product **8** (1.84 g, 6.94 mmol) was dissolved in dichloromethane (25 mL) and subsequently treated with *tert*-butyldimethylsilyl chloride (1.15 g, 7.60 mmol) and imidazole (0.57 g, 8.3 mmol). The reaction mixture was allowed to stir for one hour at room temperature. The resulting mixture was quenched with brine (25 mL) and extracted twice with diethyl ether (40 mL x 2). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated to provide silyl ether **9** as a colorless oil (2.40 g, 91.2%). The ratio of products prepared was determined by GC to be 32.8 silyl ether **9** (RT = 7.81 min): 1.00 dibrominated product (RT = 6.63 min). These numbers correspond to a 97.0% purity of product **9**. Compound **9** was carried directly into the next step without further purification. $^1$H NMR (400 MHz, $CDCl_3$) δ 3.58 (t, $J$ = 6.8 Hz, 2H), 3.38 (t, $J$ = 6.8 Hz, 2H), 1.83 (tt, $J$ = 6.8, 6.8 Hz, 2H), 1.49 (tt, $J$ = 6.8, 6.8 Hz, 2H), 1.42 (tt, $J$ = 6.8, 6.8 Hz, 2H), 1.32 – 1.21 (m, 14H), 0.87 (s, 9H), 0.03 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 63.4, 34.0, 33.0, 32.9, 29.7, 29.6, 29.6, 29.5 (2C), 28.9, 28.3, 26.1 (3C), 25.9, 18.4, -5.2 (2C). GC-MS RT = 7.803 min, ($M^+$-57) = 321/323 (loss of *tert*-butyl).

### *Step 3: Ylide Preparation and Wittig Reaction*[10]

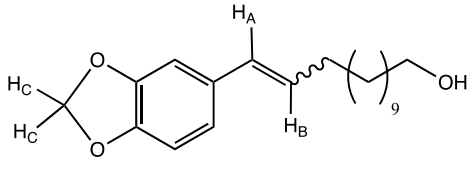
Crude silyl ether **9** (2.40 g, 6.34 mmol) was treated with triphenylphosphine (1.83 g, 6.96 mmol) and heated, with a reflux condenser attached, at 125 °C for one hour. This reaction was performed with no solvent and a stir bar was used to mix the melted solution (the melting point of triphenylphosphine is 80 °C). The reflux condenser was not necessary for this step of the reaction. It was placed on the reaction flask in preparation for adding tetrahydrofuran (THF) solvent to the hot solution in the subsequent step. The resultant solution was removed from the oil bath and THF (15 mL) was added through the reflux condenser. The THF was added to the hot reaction mixture to prevent the reaction from solidifying. The reaction mixture was then placed in an ice bath and cooled to 0 °C. The reflux condenser was removed and the flask was sealed with a rubber septum. An empty needle was placed through the septum to serve as a vent. *n*-Butyllithium (*n*BuLi) (3.0 mL of 2.5 M in hexanes, 7.5 equivalents) was slowly added. The reaction mixture turns reddish orange; the color represents the formation of ylide **10**. The flask was removed from the ice bath and the colored solution was allowed to stir for 15 minutes as it warmed to room

temperature. Piperonal (**6**) (0.98 g, 6.5 mmol) was added to the ylide and the reaction was stirred for an additional 20 minutes. 1.0 M HCl (aq) was added to the reaction mixture until a pH of 4 was achieved. The reaction mixture was diluted with distilled water and extracted twice with diethyl ether (40 mL x 2). The organic layers were combined, dried over magnesium sulfate, filtered, and concentrated. The crude product was spotted on a thin layer chromatography (TLC) plate against piperonal (**6**) using 20% ethyl acetate in hexanes as the elution solvent. The TLC plate was visualized with short wave UV light and stained with potassium permanganate. TLC analysis illustrated the presence of piperonal (**6**) starting material ($R_f$ = 0.32), the Wittig reaction product **11** ($R_f$ = 0.69), and the deprotected Wittig reaction product **12** ($R_f$ = 0.16). The crude product was carried directly into step 4 so that all of product **11** could be transformed to product **12**.

***Step 4: Silyl Ether Deprotection***[10]

The crude step 3 product (assumed a theoretical yield of product **11**, 6.34 mmol) was treated with tetrabutylammonium fluoride (TBAF) (13.0 mL of 1.0 M in THF, 13.0 mmol). No additional solvent was added. The reaction was allowed to stir for one hour at room temperature. The resulting solution was diluted with saturated ammonium chloride (aqueous) (20 mL) and extracted twice with diethyl ether (50 mL x 2). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The crude product **12** was purified by column chromatography (30% ethyl acetate in hexanes). The *trans* and *cis* isomers of alcohol **12** were effectively separated from the other impurities produced during steps 3 and 4 and isolated as a white solid (1.32 g, 65.4% yield over the two steps). The purified product was a heavy mixture of *trans*:*cis* isomers. Integration of the isomers of alcohol **12** observed on the GC trace ($RT_{trans}$ = 11.836 min, $M^+$ = 318; $RT_{cis}$ = 9.976 min, $M^+$ = 318) allowed for determination of the *trans*:*cis* ratio to be 2.0: 1.0. However, GC-MS did not conclusively determine which stereoisomer was the major product (although it was hypothesized that the *trans* isomer would have a higher boiling point and therefore be the peak with the highest retention time). The *trans* and *cis* stereochemistry was irrefutably determined by looking at coupling constants on the $^1$H NMR spectrum (**Figure 3**). Integration of the specific peaks identified as *cis* and *trans* isomers illustrated a 2.1: 1.00 *trans*:*cis* ratio and corroborated the data obtained by GC-MS.

$^1$H NMR (400 MHz, $CDCl_3$) **Hydrogen A:** δ 6.26 (d, *J*=15.8 Hz, 1H) *trans;* δ 6.27 (d, *J*=11.8 Hz, 1H) *cis.* **Hydrogen B:** δ 6.02 (dt, *J*=15.8, 6.8 Hz, 1H) *trans;* δ 5.54 (dt, *J*=11.8, 7.6 Hz, 1H) *cis.* **Hydrogen C:** δ 5.89 (s, 2H) *trans*; δ 5.91 (s, 2H) *cis*. Ratio of *trans*:*cis* determined to be 2.1:1.0 by $^1$H NMR integration. GC-MS RT = 9.976 min, $M^+$ = 318 (*cis*); RT = 11.836 min, $M^+$ = 318 (*trans*). Ratio of *trans*:*cis* determined to be 2.0:1.0 by GC peak integration.




**12**

**Figure 3**. Hydrogens Integrated on $^1$H NMR to Determine *Trans:Cis* Ratio

***Step 5: Hydrogenation***[10]

*Trans* and *cis* alkenes **12** (1.32 g, 4.15 mmol) were dissolved in methanol (10.0 mL) and treated with 10% palladium/charcoal (by weight) (0.44 g, 0.41 mmol Pd). A hydrogen balloon was inserted into the flask and the reaction was purged of air through a vented septum. The hydrogen balloon was refilled and the flask was allowed to stir for 20 hours. The resulting palladium/charcoal slurry was filtered through a thin layer of silica gel over Celite over sand. The filtration funnel was rinsed thoroughly with ethyl acetate (approximately 75 mL). Concentration of the filtrate provided alcohol **13** as a white solid (0.77 g, 58%). $^1$H NMR (400 MHz, $CDCl_3$) δ 6.68 (d, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 1.6 Hz, 1H), 6.58 (dd, *J* = 7.6, 1.6 Hz, 1H), 5.87 (s, 2H), 3.59 (t, *J* = 6.8 Hz, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.20 (br s, 1H), 1.60 - 1.50 (m, 4H), 1.36 - 1.18 (m 18H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.4, 136.9, 121.1, 108.9, 108.1, 100.7, 62.9, 35.8, 32.8, 31.9, 29.7 (3C), 29.7 (2C), 29.6, 29.6, 29.3, 25.9. GC-MS RT = 10.189 min, $M^+$ = 320.

***Step 6: Oxidation***

Alcohol **13** (0.750 g, 2.34 mmol) was dissolved in dichloromethane (11 mL) and one scoop of 4 Angstrom molecular sieves was added to the reaction flask. Pyridinium dichromate (PDC) (1.33 g, 3.53 mmol) was added in one portion and the reaction was purged with nitrogen gas. A nitrogen filled balloon was inserted into the flask and the reaction was stirred at room temperature for 24 hours. The resulting brown mixture was vacuum filtered through thin layers of sand (bottom), silica gel, and celite (top). The filter was rinsed thoroughly with ethyl acetate (200 mL). The filtrate was concentrated on a rotoevaporator. The product, aldehyde **14**, appeared as a dark brown oil. The brown appearance of the product was attributed to some chromium reagent that passed through the filter. GC-MS of the crude product illustrated that aldehyde **14** was prepared with minimal by-products. Product **14** was stored under nitrogen gas and not characterized or purified further due to concerns about air oxidation of the aldehyde to a carboxylic acid. The crude product was carried directly into the next step. GC-MS RT = 9.271 min, $M^+$ = 318.

***Step 7: Grignard Reaction***

Aldehyde **14** (assumed a theoretical yield of product **14** from step 6, 2.34 mmol) was dissolved in diethyl ether (5 mL). The resulting solution, under nitrogen gas, was treated with methylmagnesium bromide (4.0 mL of 3.0 M in diethyl ether, 12 mmol). The reaction was allowed to stir for 90 minutes before being placed in an ice bath and carefully quenched with saturated aqueous ammonium chloride (50 mL). The reaction mixture was extracted two times with diethyl ether (2 x 50 mL) and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated on a rotoevaporator. Crude alcohol **15** was isolated as a white solid with some brown discoloring due to the continued presence of some chromium reagent from step 6. Because of this chromium impurity, the product was carried directly into step 8 without calculating a percent yield. It was anticipated that the percent yield for the last three steps would be calculated after the final product **1** was isolated and purified. Characterization of crude alcohol **15** illustrated a very pure product. $^1$H NMR (400 MHz, $CDCl_3$) δ 6.70 (d, *J* = 8.0 Hz, 1H), 6.66 (s, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.89 (s, 2H), 3.83 - 3.72 (m, 1H), 2.50 (t, J = 8.0 Hz, 2H), 1.60 – 1.49 (m, 2H), 1.49 – 1.17 (m, 24H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.4, 136.9, 121.1, 108.9, 108.1, 100.7, 68.3, 39.5, 35.8, 31.8,

29.7 (4C), 29.7 (2C), 29.6, 29.3, 25.9, 23.6. GC-MS RT = 10.552 min, $M^+$ = 334.

***Step 8: Oxidation***

Grignard reaction product **15** (assumed a theoretical yield of product **15** from step 7, 2.34 mmol) was dissolved in dichloromethane (10 mL) and treated with pyridinium dichromate (PDC) (1.32 g, 3.51 mmol). The reaction mixture was stirred at room temperature for 24 hours. The reaction was not run under nitrogen gas like step 6 because there was no fear of over-oxidation of the secondary alcohol. The resulting mixture was vacuum filtered through a funnel containing thin layers of sand (bottom), silica gel, and celite (top). The filter was rinsed thoroughly with ethyl acetate (300 mL). Concentration of the filtrate on a rotoevaporator provided a crude white solid with some brown color present due to chromium impurities (0.576 g, 74.1% crude). GC-MS analysis of the crude product indicated the presence of desired product **1** (RT = 10.582 min, $M^+$ = 332) and two minor impurities, aldehyde **14** (RT = 9.253 min, $M^+$ = 318) and a presumed tertiary alcohol product prepared from excess Grignard reagent addition to a carboxylic acid impurity from step 6 (RT = 11.023 min, $M^+$ = 348). The crude product was purified by silica gel flash column chromatography (80:20 hexanes: ethyl acetate). The thin-layer chromatography (TLC) plates were observed by short wave UV light and stained with potassium permanganate. The spot at $R_f$ = 0.354 was isolated as product **1**. Minor impurities were observed at $R_f$ = 0.530 and $R_f$ = 0.202. These spots were not collected. Pure compound **1** was isolated as a white solid (0.547 g, 70.4% over three steps, steps 6, 7, and 8). $^1$H NMR (400 MHz, $CDCl_3$) δ 6.69 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 1.6 Hz, 1H), 6.59 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.88 (s, 2H), 2.49 (t, *J* = 8.0 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.10 (s, 3H), 1.59 – 1.48 (m, 4H), 1.32 – 1.19 (m, 16H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 209.4, 147.5, 145.4, 136.9, 121.1, 108.9, 108.1, 100.7, 43.9, 35.8, 31.8, 29.9, 29.7, 29.7 (2C), 29.6, 29.5, 29.5, 29.3 (2C), 23.9. GC-MS RT = 10.721 min, $M^+$ = 332.

**Results and Discussion**

The first step in the synthesis of 2-oxo-14-(3',4'-methylenedioxyphenyl)tetradecane (compound **1**, **Figure 1**) was mono-bromination of commercially available 1,12-dodecanediol (**7**).[10] This reaction was time sensitive. If the reaction was heated at reflux for too short of a time, poor conversion of diol **7** to mono-bromide **8** was observed. If the reaction was heated for an extended period, significant formation of the undesired di-bromide product, 1,12-dibromododecane, was detected by gas chromatography-mass spectrometry (GC-MS). The optimal reaction time was found to be exactly 30 minutes. After heating at reflux for 30 minutes, the percentage of products was determined to be 93.5% mono-brominated product **8**, 5.4% di-brominated product, and 1.1% diol **7**. These numbers were calculated by integrating the area under the corresponding GC peaks. The crude product was carried directly into step 2 without further purification.

In the second step of the sequence, the remaining alcohol functional group in mono-brominated product **8** was protected with *tert*-butyldimethylsilyl ether. The resulting product, crude silyl ether **9**, was isolated in 91% yield. One minor impurity (3.0% by GC integration) was observed in the GC spectrum. This compound was identified as 1,12-dibromododecane, which was carried into the reaction from step 1.

Crude silyl ether **9** was taken directly into step 3, the Wittig reaction. Addition of triphenylphosphine provided the phosphonium salt which was treated with *n*-butyllithium to afford phosphorus ylide **10**. Nucleophilic addition of ylide **10** to commercially available piperonal (**6**) resulted in the isolation of alkene **11**. Thin-layer chromatography analysis of the crude product illustrated the presence of piperonal (**6**), the desired Wittig reaction product **11**, and a small amount of deprotected Wittig reaction product **12**. Because the next step in the sequence was deprotection of the silyl ether, the mixture of alkene **11** and deprotected product **12** was taken directly into step 4.

Crude alkene **11** was treated with tetrabutylammonium fluoride (TBAF) and converted to deprotected product **12**. Alcohol **12** was purified by silica gel column chromatography. The purified product was determined to be a heavy mixture of *trans* and *cis* stereoisomers which could not be separated. Integration of the peaks in the GC trace and $^1$H NMR conclusively proved the *trans*:*cis* ratio to be 2.1:1.0. The two isomers were identified by their vinyl hydrogen splitting patterns. The *trans* isomer was observed to have a coupling constant of 15.8 Hz; the cis isomer's coupling constant was 11.8 Hz. The *trans*:*cis* isomers were isolated in a 65.4% yield. This was a two-step yield, the Wittig reaction (step 3) and the silyl ether deprotection (step 4). The average yield per step was approximately 81%.

In step 5, the heavy mixture of *trans*:*cis* isomers **12** was hydrogenated with hydrogen gas and palladium catalyst. Alcohol **13** was isolated as a single product and characterized by GC-MS, $^1$H NMR, and $^{13}$C NMR. Oxidation of alcohol **13** with pyridinium dichromate provided aldehyde **14** (step 6, **Scheme 1**). A percent yield was not obtained for this step because of the presence of small amounts of chromium impurity. Previous experiments in the laboratory had shown that aldehyde **14** was prone to over-oxidation, so the crude product was stored under nitrogen gas and carried directly into step 7.

Crude aldehyde **14** was treated with methylmagnesium bromide. The Grignard reaction went to completion and crude product **15** was isolated as a white solid with small amounts of brown discoloring due to the continued presence of some chromium reagent from step 6. In an effort to make this sequence as quick and inexpensive as possible, the crude product was taken directly into step 8. Oxidation of Grignard product **15** with pyridinium dichromate occurred without problems and GC-MS analysis of the crude product indicated the presence of desired compound **1** and two minor impurities, aldehyde **14** and a suspected tertiary alcohol product prepared from excess Grignard reagent addition to the carboxylic acid formed from over-oxidation of aldehyde **14**. Purification by silica gel flash column chromatography provide pure compound **1** as a white solid. The three-step yield, steps 6,7, and 8, was 70.4%.

**Conclusions**

In summary, the first reported synthesis of compound **1** was completed in eight linear steps. One of the attractive features of this synthetic sequence was the purity of all of the reaction prod-

ucts. Column chromatography only had to be performed twice during the entire sequence, after steps 4 and 8. Compound **1** was isolated in an overall yield of 17% corresponding to an average of 80% yield per step. It is anticipated that the synthesis of compound **1** will lead to further investigations into this compound's bioactivity against the bacterium, *Myobacterium tuberculosis*. Discovery of compound **1**'s mechanism of action will potentially lead to the development of a new class of drugs that can be used to treat tuberculosis.

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