

Kinetic study and characterization of the Wittig reaction between 4-(nitrobenzyl) triphenylphosphonium bromide, potassium hydroxide (KOH) and benzaldehyde

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Introduction

Known for its wide range of applications and versatility, the Wittig reaction is used in organic syntheses and especially in the manufacturing of vitamins and pharmaceuticals [1,2]. The general mechanism consists of a carbonyl group from an aldehyde or ketone reacting with a phosphonium ylide to create a mixture of cis- and trans-alkenes [3]. A phosphonium salt can be used to create the ylide, which must be formed using a base.

In this study, we analyzed the reaction between 4-(nitrobenzyl) triphenylphosphonium bromide (NBTP), potassium hydroxide (KOH), and benzaldehyde using ethanol as a solvent. The ylide formed is red in color, and when benzaldehyde was added to the solution, the color faded, indicating the progression of the reaction. Using UV-vis spectroscopy, we performed a kinetic study to determine the pseudo reaction order with respect to the ylide disappearance for the Wittig reaction with excess benzaldehyde. Characterization of the formed ylide and products was completed using Raman spectroscopy and FTIR spectroscopy.

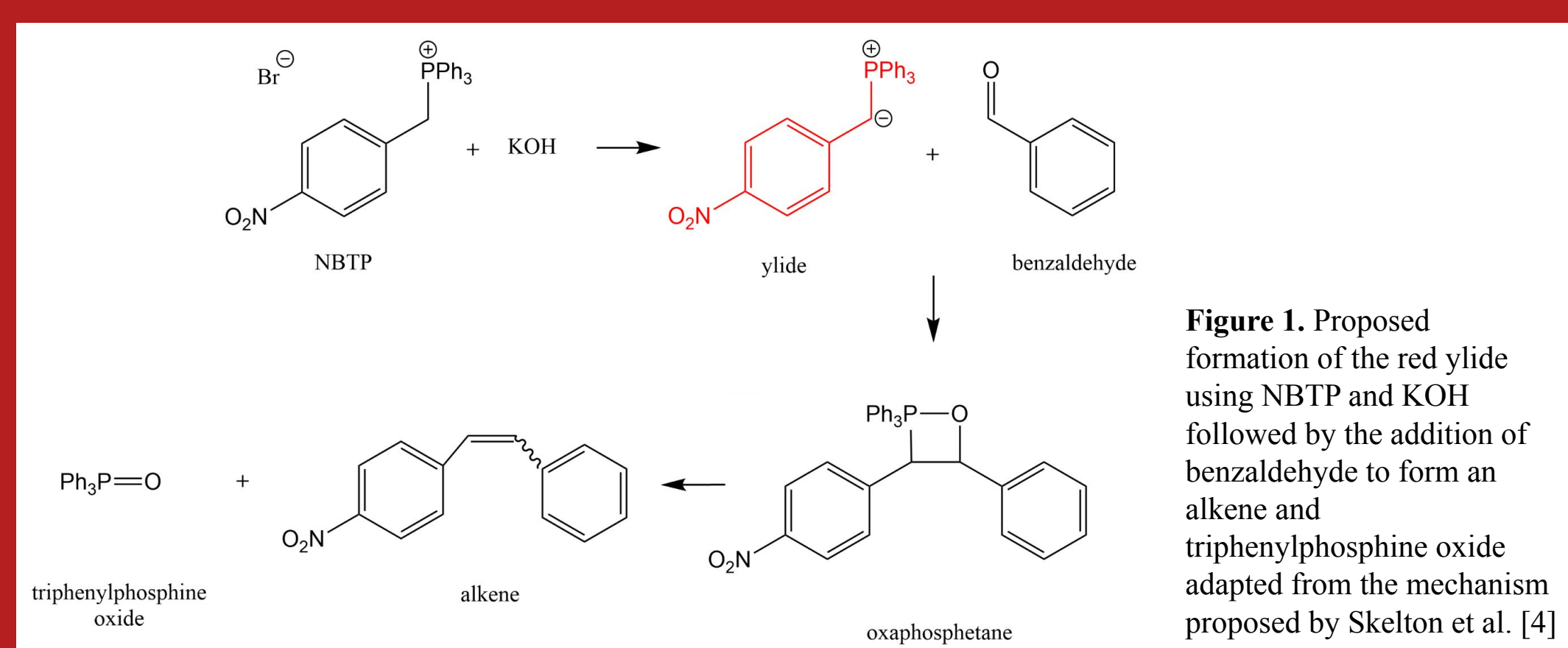
Current Wittig reactions employed for pharmaceutical production often include hazardous reactants, byproducts, and reaction conditions. In order to establish green chemistry models for alternate, environmentally-safer processes, a wealth of kinetic data currently undiscovered must be further investigated. Our study seeks to further characterize common species involved in Wittig reactions and their kinetic parameters to make way for future modeling of green alternatives to the use of Wittig reactions for pharmaceutical manufacturing.

Methodology

- Stock solutions created: 0.1 M NBTP & 0.2 M KOH (in ethanol)
- Serial dilutions to obtain 0.01 M NBTP & 0.01 M KOH
- 0.10 M benzaldehyde was made from a 9.8 M stock solution, diluted with ethanol.
- To collect the absorbance spectra, 47.2 μL of both 0.01 M NBTP and 0.01 M KOH were pipetted into a microplate. After 20 min, 5.6 μL of 0.10 M benzaldehyde were added.
- The same procedure was followed to obtain the FTIR spectra of the ylide and product.
- To prepare the ylide and product samples for Raman analysis, 236 μL of 0.05 M NBTP, 236 μL of 0.05 M KOH, and 28 μL of 0.5 M benzaldehyde were mixed. Both samples were stored in the fume hood until dry.

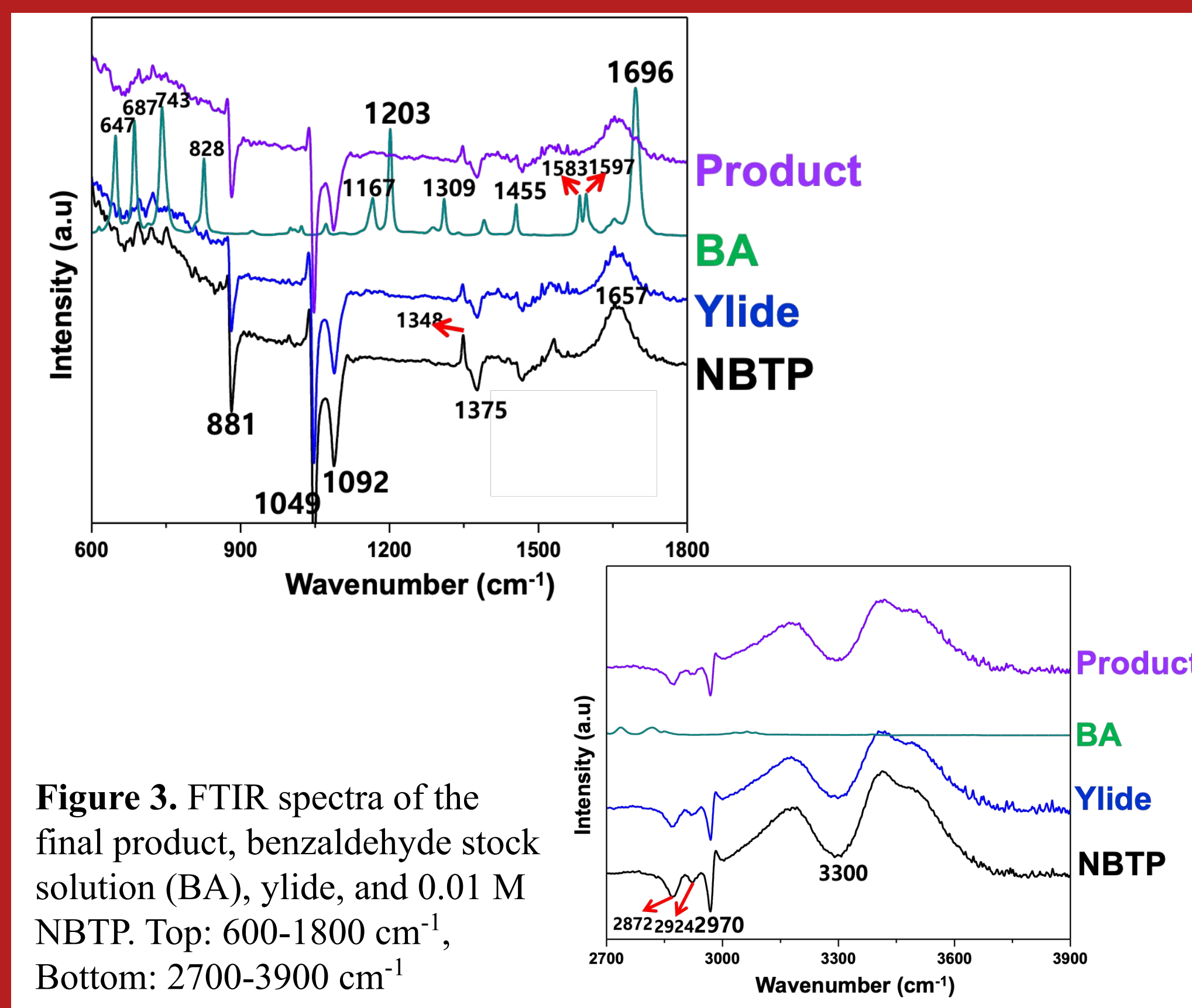
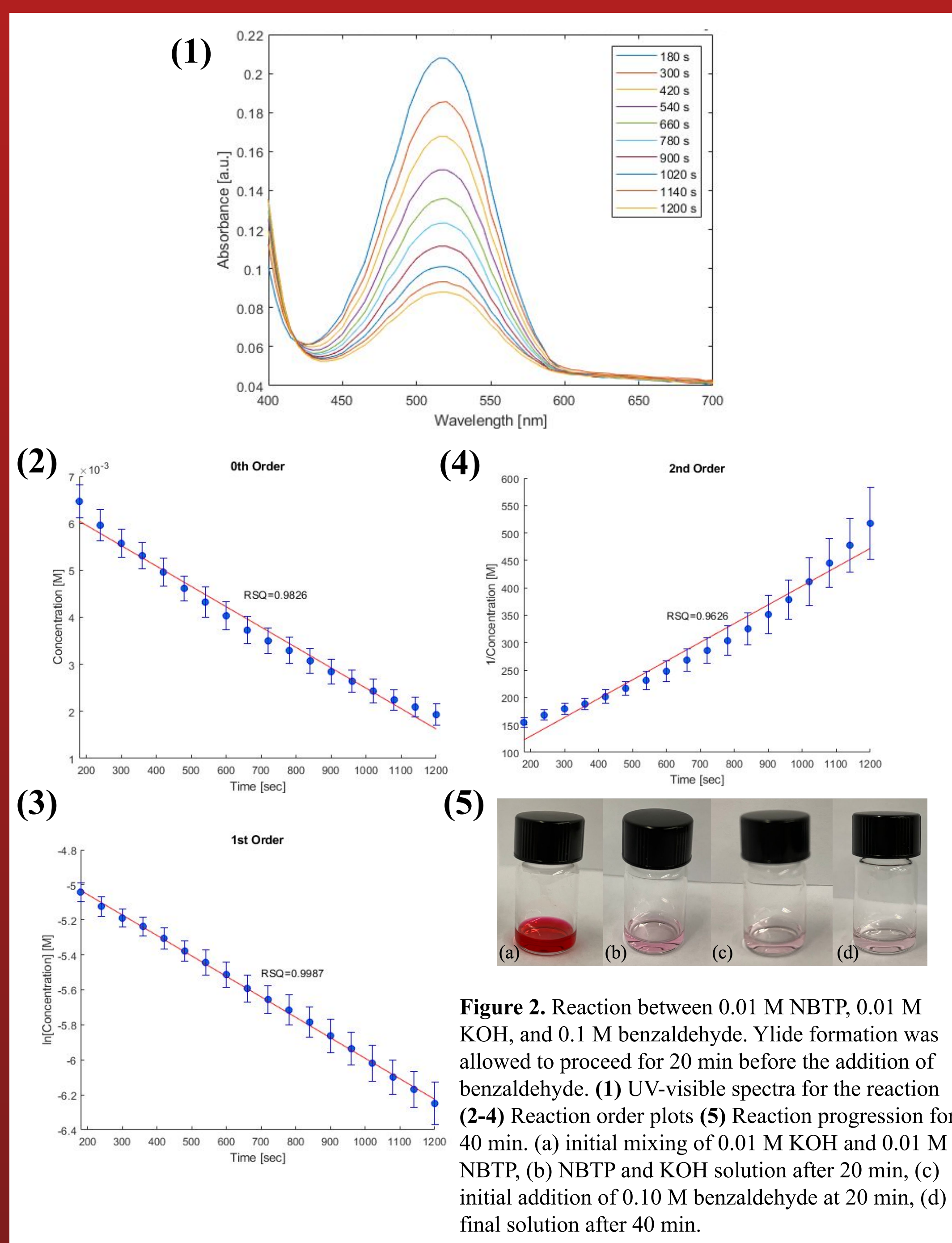
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UV-Visible (UV-vis) Spectroscopy

- Absorbance spectra for the reaction progression of 0.01 M NBTP, 0.01 M KOH, and 0.10 M benzaldehyde.
 - The only peak observed in the spectra occurred at 515 nm.
 - NBTP, KOH, and benzaldehyde all did not show any peaks near this wavelength, indicating formation of the ylide.
- Zero, first, and second order plots were created from the same reaction.
 - Reaction seems to follow a first order rate law for the disappearance of the ylide, based on the linear trend of the data in the plot.
 - Absorbance values reflect a 40% conversion of the ylide into the alkene product.



Fourier Transform Infrared (FTIR) Spectroscopy

- Characteristic peaks shared by 0.01 M NBTP and ylide:
 - Bending and stretching of C-O bonds (1049, 1090~1092, & 1375~1377 cm^{-1})
 - Bending and stretching of C-H bonds (1657~1659 [aromatic bending], 2870~2872, 2924, 2970~2972 cm^{-1})
 - Nitro group present in both samples (1348~1350 cm^{-1})
- Characteristic peaks in the benzaldehyde spectrum:
 - C=O stretching (~1696 cm^{-1}) in the benzaldehyde structure only
 - Aldehydic C-H bending and C=C stretching (~1203 cm^{-1})
- Characteristic peaks in the alkene spectrum:
 - Nitro group present at ~1348 cm^{-1}

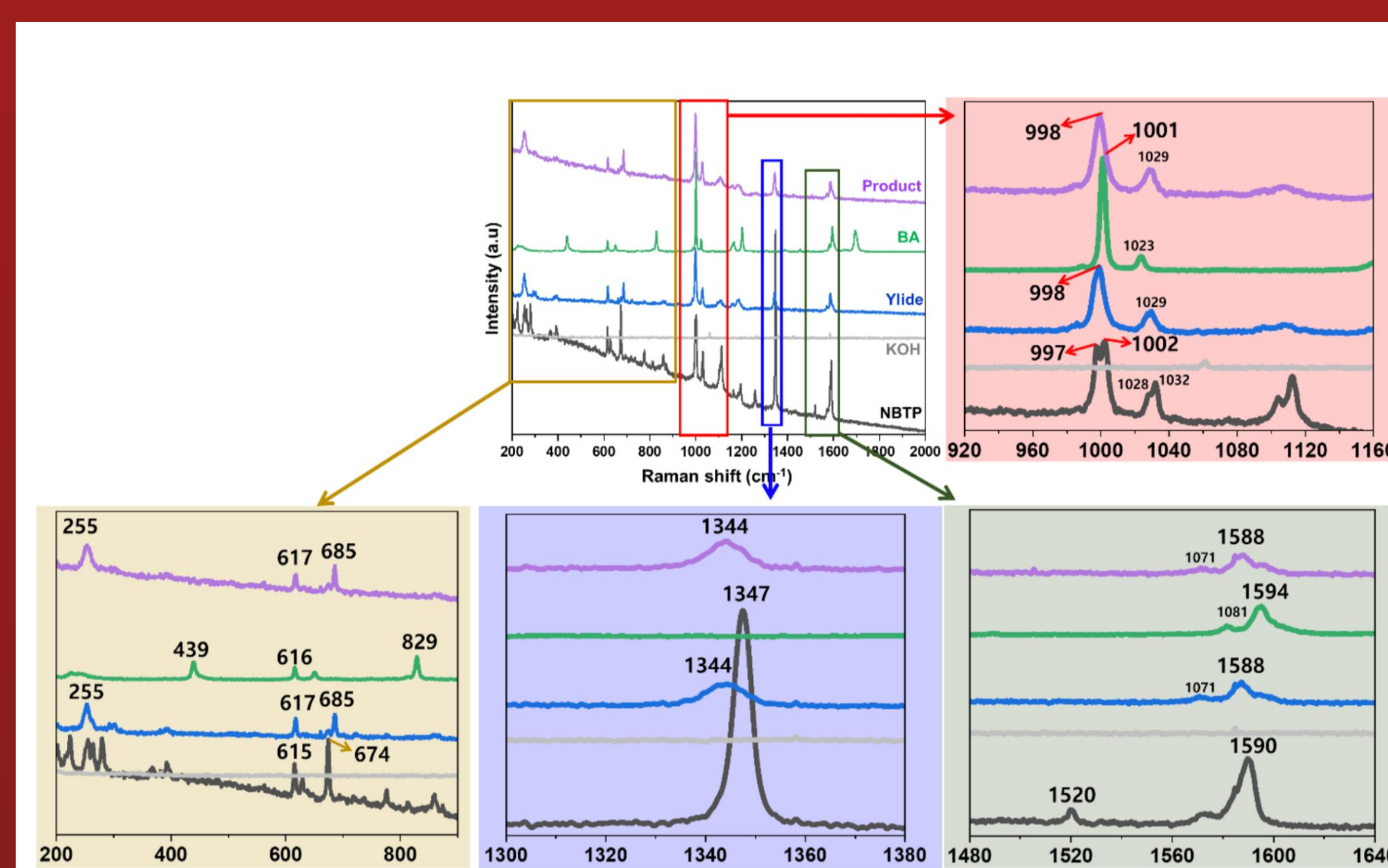


Figure 4. Raman (785 nm excitation wavelength) spectra of the product, benzaldehyde (BA), ylide, KOH, and NBTP. Highlighted regions in the Raman shift region of 200~2000 cm^{-1} include 200~900 cm^{-1} (yellow), 920~1160 cm^{-1} (red), 1300~1380 cm^{-1} (blue), and 1480~1640 cm^{-1} (green).

Raman Spectroscopy

- Peaks that were unique to benzaldehyde include those at 439, 829, and 1594 cm^{-1} , corresponding to $\text{C}_4\text{C}_7/\text{C}_3\text{C}_4$ stretching or $\text{C}_2\text{C}_3\text{C}_4$ bending within the phenyl ring, C_4C_7 stretching or $\text{C}_1\text{C}_2\text{C}_6$ bending, and C-C stretching within the phenyl ring.
- All samples except for KOH displayed peaks between 615~617 cm^{-1} , displaying bending of the phenol groups.
- Product, ylide, and NBTP peaks
 - 255 and 685 cm^{-1} : C-P-C deformation and C-P stretching, respectively.
 - 1028~1029 and 1588~1590 cm^{-1} , displaying deformation vibration of C-H on phenyl and C-C or C-N stretching, respectively.
- In the 1300~1380 cm^{-1} region, a strong peak is present in the NBTP spectrum at 1347 cm^{-1} while relatively weak peaks are shown at 1344 cm^{-1} for the product and ylide spectra.
 - The shift may be due to vibrations in aromatic moieties of NBTP.

Conclusion

In this study, characterization of fundamental Wittig reagents, a phosphonium ylide, and an alkene product is reported for a standard Wittig reaction involving NBTP, KOH, and benzaldehyde in anhydrous ethanol. Subsequent reaction order investigations were performed, suggesting a first order rate law for the disappearance of the ylide. To our knowledge, this is the first reported study characterizing a Wittig reaction using these reagents. It is the authors' hope that this can serve as a basis for future investigation and modeling into greener Wittig alternatives.

Future work pertaining to this study may involve not only investigation into greener alternative reactions but also verification of cis- and trans-alkene product yields via ¹H-NMR analysis. Multiple authors have previously reported the use of water as a medium in place of harmful lithium-based solvents typically used in Wittig syntheses. Furthermore, investigation can be made into the potential applications of the alkene product synthesized from the reported reaction between NBTP, benzaldehyde, and KOH.

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