SYNTHESIS OF MIXED BIS-AZOBENZENE FOR PHOTOSURFACTANT STUDIES

by

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In addition, the author would also like to give thanks and acknowledge the following contributions from our undergraduate students for assistance with synthesis: Dillon Zimmer, Viola Fieglein. I would also like to give thanks to my mother and grandmother, Stephanie Soltero and Julia Garcia for always supporting me through my college career.

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ABSTRACT

Photosurfactants are an emerging field of research due to their capacity for self-assembly and micellization properties. Azobenzene derivatives are of interest because not only do they have photoisomerization potential but also can be incorporated into polymers or biochemical systems due to versatile functionalization chemistry. Previous analysis of *ortho*-substituted fluorine confirms that the electron density of azobenzene can be inductively shifted from double bonded nitrogen into the *ortho*-substituted fluorine groups. Azobenzenes substituted with fluorine at the *ortho* position are of interest because they can be selectively photoisomerized by green light instead of UV light. Synthesis of a photosurfactant azobenzene with a terminal cation and anion with subsequent ionic pairing allows selective excitation of individual azobenzenes. We have synthesized a library of parent azobenzene compounds and their fluorinated derivates - this is the core of this research thesis The design of our azobenzene compounds is guided by long-range goals of studying quadrupolar effects and photocontrolled self-assembly of photosurfactants.

I. BACKGROUND

Chromophores are chemicals that absorb light typically in the near UV-visible region of the electromagnetic spectrum. Chromophores have been applied into a myriad of consumer goods and material science, such as photochromic sunglasses or solar energy storage.[1] Two common chromophores explored in research are spiropyran and azobenzene. Both of these classes of compounds exhibit photochromism. Photochromism is displayed by compounds that reversibly isomerize between two states that have different absorption spectra. This concept is displayed by the chemical phenomenon of photoisomerization. Photoisomerization is the isomerization of a compound through photoexcitation. Photoexcitation occurs when a compound is irradiated by light causing an excitation of the molecules. This photoexcitation causes an excited state of the quantum system to afford photon absorption. Photoisomerization is commonly found in retail items such as transition lenses for glasses. One of the most exciting and highly studied chromophores is azobenzene. Azobenzene undergoes photoexcitation or photoisomerization that has been applied to a large variety of materials that will be discussed within this thesis.

Azobenzene is a reversible chromophore that exhibits a *trans-cis* isomerization under UV-light irradiation. The pathway which azobenzene undergoes isomerization is through many different mechanisms. One pathway for isomerization has been theoretically modeled that an in-plane inversion may occur. The alternative direction of bond rotation is the out-of-plane rotation. Each rotation is of different energy requirements dependent on the functional groups present, especially at the *ortho*-position

of azobenzene, such as a bulky group inhibiting the in-plane rotation. The two isomerization mechanisms have been displayed below in **Figure 1**.

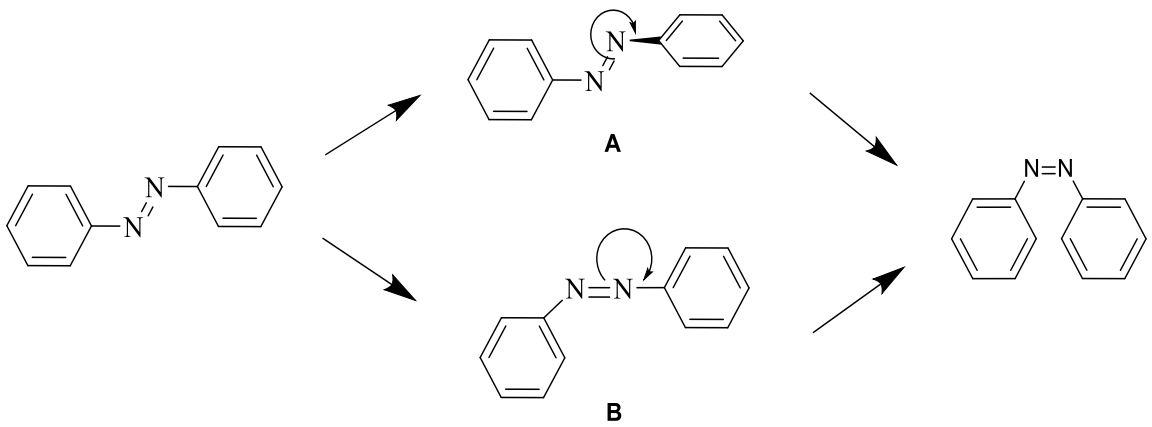


Figure 1: Azobenzene isomerization. A: Out-of-plane Rotation. B: In-plane Rotation

Due to the barriers for out-of-plane rotation, in-plane rotation has been proposed as the dominant rotation pathway for n-π* and π-π* excitation pathways.[2] One reason that the inversion mechanism is studied is to further understand the effect of functionalizing azobenzene. In this case, it has been found that electron donating groups raise the ground-state inversion height while electron withdrawing groups subsequently reduce the ground-state inversion height (a fundamental driving force for isomerization).[2] This suggests that the photoisomerization rate depends on functional groups, which may be selectively synthesized through synthetic methodology.

The mechanism which azobenzene undergoes isomerization also pertains to the reversibility of azobenzene from *cis*-to-*trans*. *Cis*-to-*trans* isomerization occurs under the influence of heat, light, and time. Firstly, it should be known that azobenzene is thermodynamically stable in the *trans* state. Thus, the thermodynamic rate of relaxation from *cis*-to-*trans* may be studied. One method for the relaxation of azobenzene is through

thermal relaxation. This relaxation can occur at room temperature and is reduced by placing a sample in cold conditions, such as isomerizing azobenzene in solution and then storing it in a freezer. Traditionally, the isomerization rate from *cis*-to-*trans* is recorded at a fixed temperature to compare different functionalized azobenzenes with one another for understanding of how functional groups effect the half-life of each *cis* isomer. However, adding heat to an azobenzene may increase the rate of isomerization back to *trans*. This has been researched to find the relative isomerization rate (k) by application of the Gibb's free energy equation found below in **Equation 1**.

$$k = \frac{k_B T}{h} e^{\frac{-\Delta G}{k_B T}} \qquad \textbf{Equation 1}$$

The Gibb's free energy equation describes the rate of isomerization for azobenzene from the *cis*-state to *trans*-state through thermal isomerization. This as seen above may be manipulated through increased temperatures. At higher temperatures, azobenzene has been shown to have a shorter half-life for the *cis*-state.[3] Simultaneously, the *cis*-state may be stabilized by keeping the sample at low temperatures such as keeping the *cis* sample within a freezer.

Azobenzene is attractive due to synthetic versatility that makes synthesis of a wide variety of compounds possible. Substituents on the azobenzene directly affect properties such as isomerization rate, *cis*-half-life, UV-Vis spectra, and the photostationary state. One example of azobenzene functionalization is the *ortho*-substitution with fluorine. [4] Tetra-*ortho*-fluoro-azobenzene exhibits a bathochromic (red) shift in the n-π* transition for the *cis*-isomer. Normally, the n-π* bands for *cis* and *trans* isomers overlap; the shift exhibited by the fluorine derivative makes it possible to selectively excite the trans isomer at visible wavelengths (500 nm, green light). *Ortho*-

fluoro substitution causes an inductive effect at the azo-bond by lowering the n-orbital energy, leading to a higher energy gap. The reason that *ortho*-fluorines increase the n-π* excitation energy is because they reduce the lone pair repulsion in the *cis*-isomer. This effect is caused by the inductive σ-electron withdrawing fluorine groups. Since this energy gap is decreased there is bathochromic shift of excitation wavelength (λ). The added advantage of visible-light photoisomerization is the possibility of *in vivo* applications, such as light sensitivity restoration within blind mice. [5] Another critical area of study for azobenzene as a surfactant is within miscellization such as study of the critical packing parameter (CPP).

These parameters are of interest to study for azobenzene due to the capacity for self-assembly within macromolecules. The self-assembly and micellization of surfactants can be characterized by consideration of the CPP. The CPP is calculated by the equation found in **Figure 2** below.

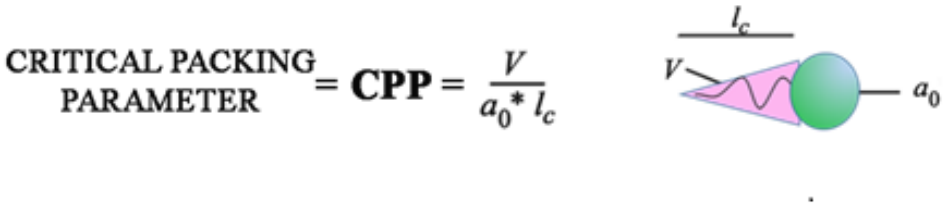


Figure 2: Critical Packing Parameter – V is surface area of cone, a_0 is surface area of hydrophilic head, and l_c is the length of the hydrophobic tail

CPP is analyzed for micelles to predict likely parameters for size, shape, and aggregation characteristics within amphiphilic systems. CPP can be applied to surfactants for understanding the structural formation when compounds aggregate. Firstly, the surface area of the tail is found. Secondly, the surface area of the head group a_0 is obtained. The

head is a hydrophilic group that is commonly a carboxylic acid or amine group. Finally, the length of the tail, l_c is observed. This tail length controls the hydrophobicity of compounds such as in long-chained detergents. The most common micelles formed are globular, cylindrical, bilayers, and vesicles.[6] When the CPP value is very small (<1/3), a cone structure is formed. These cone structures form spherical micelles upon aggregation. At larger CPP values (~1/3-1), this structure becomes less conical and more cylindrical. This is when bilayers or sandwich-shaped miscelle aggregation occurs. After the CPP has a value above 1, inversion of the cone occurs, creating an inverted miscelle structure. Surfactants are an example of a chemical that may perform miscellization, like soap during cleaning dirty dishes.

Surfactants are chemicals that lower surface tension and have an amphipathic structure composed of a hydrophilic head group with a hydrophobic tail. A common surfactant is sodium dodecyl sulfate that is commonly found in most detergents. Azobenzene is the most common chromophore in photosurfactant studies.[7, 8] Photosurfactants are a combination of a surfactant with a photoisomerizable structural unit. The self-assembly of surfactants is responsible for their detergency and will be an important consideration in our proposed research. Thus, we propose to analyze azobenzene as an amphiphilic photosurfactant.

It is suggested that within amphiphiles containing two alkyl chains (or hydrophobic tails) that the CPP value will be comparable in bilayers or vesicles relative to globular micelles or cylindrical micelles of single chained amphiphiles.[2] One example of a difunctional amphiphile is didodecyldimethylammonium bromide (DDAB) which has a larger CPP (0.6-0.8) than its single-tailed comparator of

dodecyltrimethylammonium chloride (DTAC) at 0.333.[9] This hypothetical parameter is of interest to analyze for a bis-functionalized photosurfactant. A unique bis-functionalized photosurfactant is a quaternary ammonium bis-azobenzene found below in **Figure 3**.

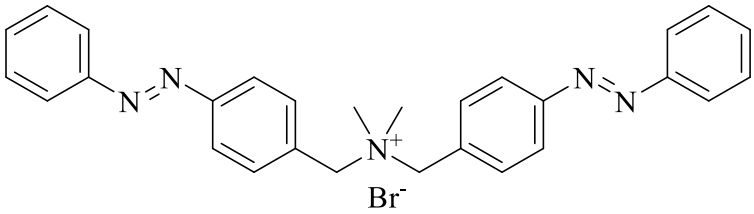


Figure 3: ***N,N-bis(azobenzene)-N,N-dimethylammonium bromide***

In a mixed bis-azobenzene system where one azobenzene is functionalized with *ortho*-fluorines, selective photoisomerization of the fluoroazobenzene will be possible and allow the study of intramolecular azobenzene interactions. We predict that quadrupolar effects may be present. Quadrupolar effects are due to energetically favorable π-stacking of electron-rich and electron-poor benzene rings. This effect may also be displayed by combining a single-chain cationic azobenzene with a single-chain anionic fluorinated azobenzene. Thus, the core hypothesis of our work is that selective photoexcitation of azobenzene ions will produce different self-assembled structures in water.

A. *UV-Visible Spectroscopy*

UV-Visible spectroscopy is the most common and useful method for characterizing the light responsive and photodynamic properties of azobenzene. Azobenzene exhibits two electronic transitions in UV-Visible spectroscopy: the $\pi - \pi^*$ transition in the UV region, and a $n - \pi^*$ transition in the visible region. The *cis* (Z)

isomer exhibits a less intense π – π* transition as well as a more intense n – π* transition compared to *trans* (E). This can be seen below in **Figure 4**.

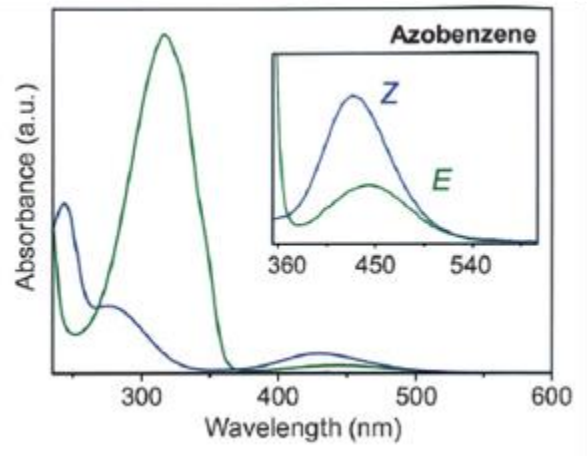


Figure 4: Photoisomerization of Tetrafluoroazobenzene.[4]

These two transitions are useful for kinetic studies of the photoisomerization.[10] After photoexcitation to *cis*, heat may be applied for reversible isomerization to the *trans* state. This reversibility by heat varies at different temperatures due to the kinetics observed from the Arrhenius equation found below in **Equation 2**.

$$k = Ae^{\frac{-E_a}{RT}} \qquad \textbf{Equation 2}$$

The Arrhenius equation implies the rate dependence from temperature, showing that the half-life of the *cis* isomer decreases as temperature increases. Researchers have reported the kinetics of isomerization for a solution of methanolic 4-methylazobenzene in an ionic liquid, BMIM (1-butyl-3-methylimidazolium hexafluorophosphate), at different temperatures to describe solvation capability of azobenzene as well as rate of reversibility.[3] Thus it has been shown how the isomerization of azobenzene is affected through modification of temperature. These measurements for kinetics as well as temperature

dependence of azobenzene's reversible *cis*-to-*trans* isomerization rates are dependent on the functional groups.

The most common functionalization of azobenzene is at the *para*-position since there are an abundance of starting materials available. To create an amphiphilic azobenzene, one may attach an ammonium tag to the *para*-position. In a study by Wegner, it was found that attaching an ammonium tag to the *para*-position decreased the thermal *cis*-to-*trans* photoisomerization rate.[8] For example, *para*-carboxylic acid substituted azobenzenes have been shown to exhibit a bathochromic shift of the $\pi - \pi^*$ peak of azobenzene.[11] Another intriguing study for *para*-functionalized azobenzene has shown that electron-withdrawing *para*-substituted azobenzenes isomerized faster than the parent azobenzene; this study also showed that *para*-nitroazobenzene induced the fastest isomerization, which can be validated by electron withdrawing theory where the nitro group may pull electron density from the azo group to the nitro group.[12] This information would indicated that *para*-functionalization of azobenzene with an electron donating group would reduce the isomerization rate of azobenzene.

Another common functionalization of azobenzene is at the *ortho*-position. One example of this is the selective *ortho*-amination with pyrrolidine of azobenzene where it was found that a strong molar absorptivity is found within the visible range and a remarkably long *cis* stability of 72 hours at 25˚C.[13] This functionalization would be important for applying azobenzene into more aqueous environments where *cis* stability is favored to increase solubility.

The *cis*-state of azobenzene is commonly studied due to the significant difference from the *trans*-state. This *cis*-state has many desirable qualities such as a dipole moment increase of 3 Debye, increase in aqueous solubility, and a decrease in the end-to-end distance because the *cis*-isomer is more compact.[4]

B. *Synthesis*

The three most common methods to synthesize azobenzene are the diazonium reaction, Baeyer-Mills reaction, and oxidative coupling.

i. Diazonium Reaction

The diazonium reaction is an ideal synthetic method for creating azobenzenes with a *para*-hydroxy functionalization, such as 4-hydroxyazobenzene seen below in **Figure 5**.

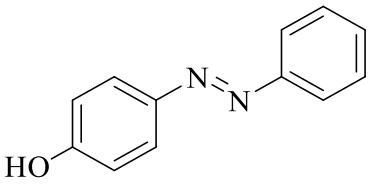


Figure 5: 4-Hydroxyazobenzene

This reaction has been used to synthesize 4-hydroxyazobenzene for antifungal activity against macrophomina phaseolina, showing the facile nature of synthesis and application of azobenzene to biological research.[13] This reaction is ideal for phenols and anilines because the electrons may delocalize from the phenolic oxygen anion (in the presence of base), facilitating the nucleophilic attack to the diazonium salt as seen below in **Figure 6**.

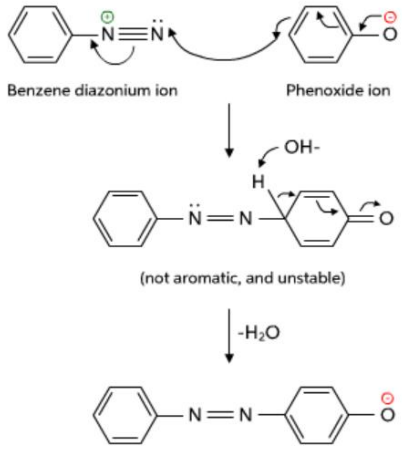


Figure 6: Mechanism of Diazonium Reaction for 4-Hydroxyazobenzene.[12]

First, an amine must be treated with an acid in the presence of sodium nitrite to produce the diazonium salt. Then, the diazonium salt may be reacted with a nucleophile in the presence of base to synthesize an azobenzene. The base is critical for the nucleophile, in the case of a phenol as the phenoxide ion, to become more nucleophilic. The diazonium reaction favors electron rich reactants as it is an electrophilic substitution reaction. Therefore, there may be limitations within synthesis through this method if the compound being coupled with the diazonium salt is very electron poor at the *para* position. Additionally, if the aniline has a highly electron-donating group at the *para* position, it may stabilize the diazonium salt leading to no reaction. Thus, it is optimal to have a diazonium salt with a neutral to electron-withdrawing *para* group and a neutral to electron-rich *para* functionalized nucleophile. As the diazonium is an aqueous reaction, some azobenzenes may be acidified at the last step to afford a pure precipitate for vacuum filtration, such as 4-benzoic-acid-azobenzene. Otherwise, azobenzene is

commonly separated by two-phase extraction with an organic solvent, then subsequently purified by column chromatography.

ii. Baeyer-Mills Reaction

The Baeyer-Mills reaction is a convenient method for azobenzene synthesis requiring a nitrosobenzene and an amine. This is the best method for synthesizing asymmetric azobenzenes. This reaction is convenient because one may choose an amine that may not be suitable for diazonium synthesis, then through an oxidation reaction with potassium peroxymonosulfate (Oxone), create the nitrosobenzene and subsequently react this with an amine. Not only is this a highly tunable reaction, but also it is a one-pot synthesis in the presence of acetic acid (AcOH) at room temperature. The use of acetic acid as a solvent facilitates easy purification by solvent removal on the rotovap followed by two-phase separation to remove residual acid. Column chromatography or recrystallization is used in the final purification step. The reaction may be depicted below in **Figure 7**.

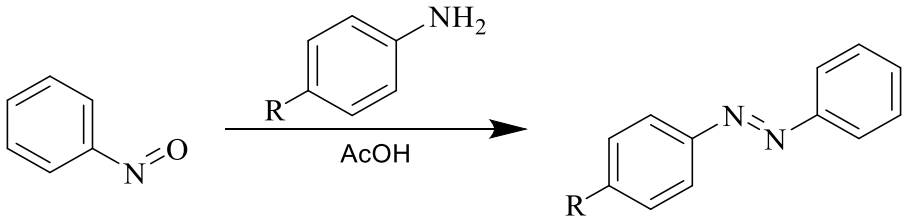


Figure 7: Baeyer-Mills Reaction

iii. Oxidation Reactions

The most traditional synthesis of azobenzene in an oxidative reaction is to utilize $KMNO_4$ with an aminobenzene in the presence of $CuSO_4*5H_2O$ or $FeSO_4*7H_2O$.[14] This

was traditionally a reagent for oxidation of amines or alcohols to carbonyls. However, in simple, more stable azobenzene structures this method is a formidable application that may be utilized at room temperature in an organic solvent such as synthesis of 4,4-dimethylazobenzene with p-toluidine.[15] However, this methodology is unfortunately not viable for many synthesis projects as it is such a strong oxidant it may oxidize other functional groups.

To resolve this issue with harsh oxidative conditions, other oxidants have been researched to substitute for $KMNO_4$. Azobenzene synthetic methodology has been recently improved by application of *N*-chlorosuccinimide (NCS) in the presence of 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) in DCM under dry ice in acetone temperatures for high yield symmetrical synthesis as seen below in **Figure 8**.[16]

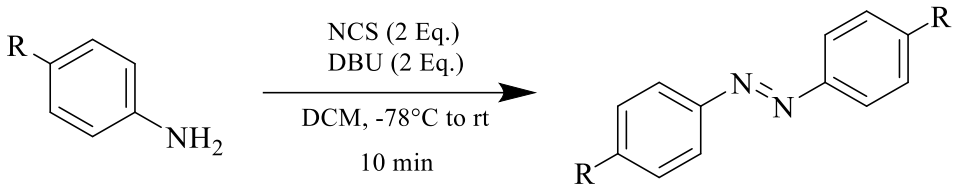


Figure 8: Symmetrical Azobenzene Synthesis by NCS and DBU.[16]

This reaction has been studied and optimized to obtain the following yields in Table 1 below.

Table 1: Azobenzene DBU Synthesis Yields. [16]

Aniline	**Yield (%)**
p-Methyl	87
p-isopropyl	66
p-acetylene	88

p-CF_3	93
p-CN	85
p-CO_2Et	82
m-CN	56
p-F	83
p-Cl	86
p-Br	59
p-I	76
m-F	75
2,4,6-F_3	70

As seen above, 17 samples of azobenzene derivatives have been synthesized and there may be future works with these reagents to afford more symmetrical azobenzenes. In comparison, the common application of $KMNO_4/7FeSO_4*7H_2O$ has previously been reported as 10-25% yield by reflux.[4] Thus, the yields above show a more bountiful synthetic technique. One benefit of the DBU reaction is only use of organic solvent (DCM). Removing $KMNO_4$ from the parent reaction can cause loss of azobenzene into the aqueous layer, especially with more polar functional groups, and is a very harsh reaction. This does not require heat, only dry ice in acetone with good yields at an extremely fast rate. Fortunately, this reaction as well is not air sensitive, so this may be performed in a fume hood without worries of air interfering in the reaction vessel.

In 1990 a bis-azobenzene was synthesized (cyclophane) with two azobenzenes bound between dimethylamino bonds.[17] This structure created a host-guest type of compound that was photoactive. The bis-azobenzene showed an incredibly low amount

of *cis*-isomerization through extensive UV light exposure. However, this study did not report a mixed system: one fluorinated azobenzene and one non-fluorinated azobenzene. Our schema to synthesize a system where each azobenzene may be photo-excited at isolated wavelengths has been described below in the experimental section. One interesting synthetic method to produce quaternary ammonium halides is through utilization of dimethylformamide in the presence of sodium carbonate with a halogenated species.[18] While successful for non-fluorinated compounds, we observed side-reactions with fluorine—containing compounds that eliminated this as a viable synthetic route. We have successfully prepared a non-fluorinated bis-azobenzene quaternary ammonium halide by this method.

C. *NMR Spectroscopy*

Azobenzene displays unique chemical shifts in the NMR for the *cis* and *trans* isomers. Because photosurfactants are usually studied in water, the aqueous solubility of azobenzene compounds is always a consideration. Complexes can be used to increase aqueous solubility: for example, a water-soluble molecular cage. *Cis*-azobenzene may be bound in a 1:1 host-guest inclusion complex of $Pd(tmeda)(NO_3)_2$ and reversibly expelled from the cage through photoexcitation to *trans* – this causes precipitation from the solution of *trans*-azobenzene.[19] A consideration for NMR analysis is the metastable state of *cis*-azobenzene. Nonetheless, isolation of a sample that has a high *cis* half-life is easy to distinguish through NMR. One may apply UV by a UV lens flashlight (or green light for fluorinated compounds) to a sample and swiftly analyze the conversion within an NMR. It should be noted that hydrogens and fluorines in *cis* azobenzene will shift within the aromatic regions due to changes in electron density. We have routinely used both ^{19}F

and ^{1}H spectroscopy in our studies. One example of the utility of ^{19}F NMR is the *trans* to *cis* isomerization of *o,o,o',o'*- tetrafluoroazobenzene where we have analyzed both isomers and they are observed as singlets that are separated by 3 ppm. Not only does ^{19}F NMR provide information for distinguishing between isomers, but also in a sample with a large number of hydrogen peaks, one may utilize ^{19}F NMR to confirm a crude sample of azobenzene has been synthesized prior to purification.

II. EXPERIMENTAL

A. *Materials and Methods*

All solvents and reagents were purchased from Sigma-Aldrich and were used as received without additional purification. Thin-layer chromatography was performed on silica gel matrix (L x W 20 cm x 20 cm, Sigma-Aldrich) using a UV light (λ = 250 nm) to observe spots. Supelco silica gel (high purity grade, average pore size 60 Å (52-73 Å), 70-230 mesh, 63-200 µm, for column chromatography) was used for column chromatography. NMR spectra were obtained with a Bruker AV-400 NMR instrument (Bruker, Karlsruhe, Germany) with CD_3CN, $CDCl_3$, and DMSO-d_6. The signals for the deuterated solvents were calibrated to internal standards (CD_3CN: ^1H 1.94 ppm, ^{13}C 1.32 ppm and 118.26 ppm; $CDCl_3$: ^1H 7.26 ppm, ^{13}C 77.16 ppm; DMSO-d_6: ^1H 2.50 ppm, ^{13}C 39.50 ppm). The following abbreviations were applied for NMR data as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. UV-Vis molar absorbtivity was determined by a plot of concentration versus absorbance.

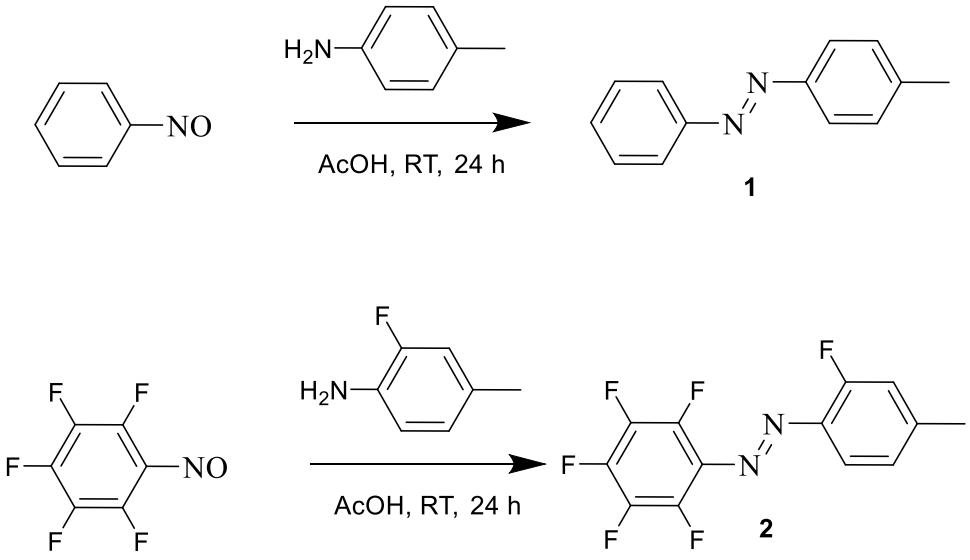
An Ocean Optics HR2000+ CCD array detector was utilized to acquire UV-Vis spectra. The light source was a DH2000 deuterium/halogen light. These components were connected using a 600 µm diameter quartz fiber optic cables. The spectral range for acquisition was set to 250-650 nm. The configuration for the detector was a 25 µm slit aperture with a grating of H1 at 300 nm. The collection parameters for acquisition were 20 scans to average, a boxcar width of 3 and an acquisition time tailored for each sample depending on the molar absorptivity and concentration. Molar absorptivity is found by the Beer-Lambert law as found below in Equation **3** where A is absorbance of a sample, ε is molar absorptivity, b is path cell length (1 cm), and C is concentration of a sample.

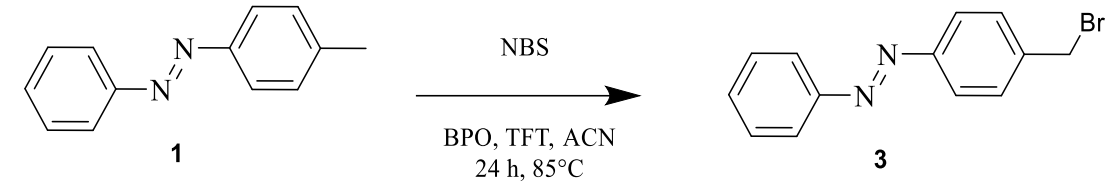
$$A = \varepsilon bC \qquad \text{Equation } \mathbf{3}$$

Irradiation of samples was performed by utilization of a XeHg Lamp with a Newport Power Supply set at 250 watts. UV and Visible wavelengths were isolated by utilizing a bandpass filter to irradiate the samples. The UV bandpass filter ranges from 200-400nm and is called 313nm FWHM 20 nm – CO674-16 from Pixelteq. The Visible bandpass filter ranges from 400-700nm and is called 575nm FWHM 100 nm – 102400159 from Pixelteq. When conducting the trans-to-cis photoisomerization, samples were irradiated until the photostationary state is obtained which corresponds to an unchanging UV-Vis spectrum.

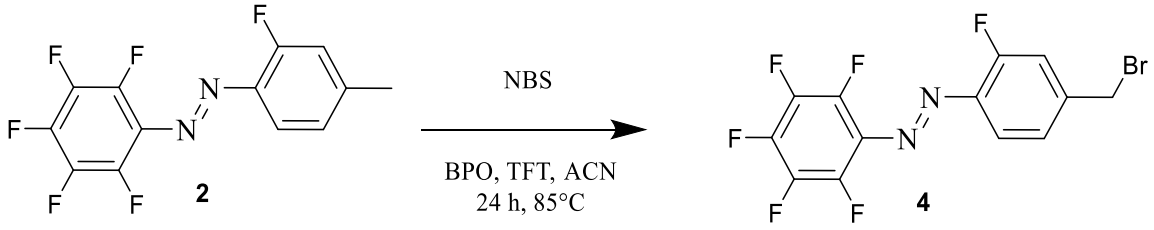
B. *Synthetic Schema*

We have synthesized a library of potential photosurfactants including bis-azobenzenes. The following image below in Figure **9** displays our synthetic schema.

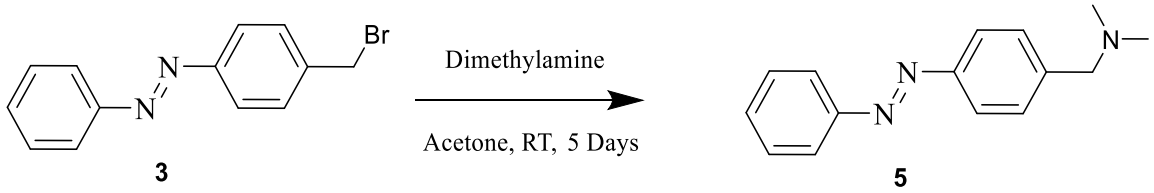



NBS
BPO, TFT, ACN
24 h, 85°C

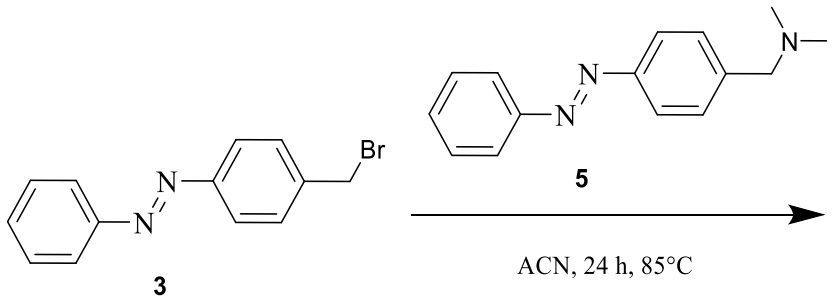
1 3


NBS
BPO, TFT, ACN
24 h, 85°C

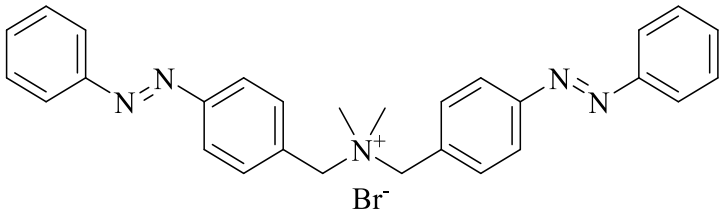
2 4


Dimethylamine
Acetone, RT, 5 Days

3 5


5
ACN, 24 h, 85°C

3



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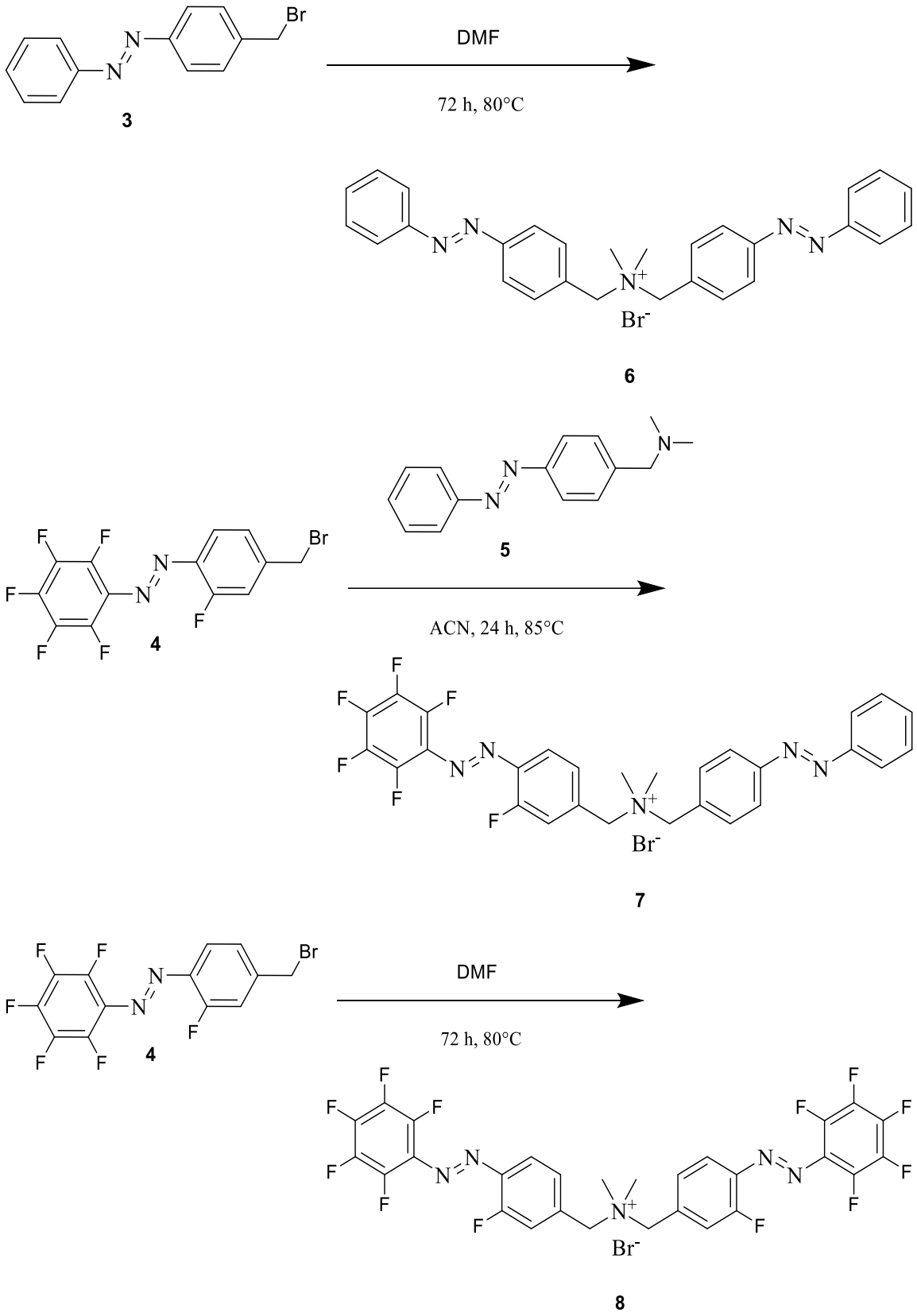
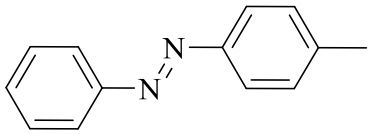


Figure 9: Full Synthetic Schema for Bis-azobenzene

C. *Synthesis*



4-Methylazobenzene **(Compound 1)**

Nitrosobenzene (4.5g, 42 mmol, 1 eq) and p-toluidine (4.5g; 42 mmol; 1 eq) were added to glacial acetic acid (AcOH) (50mL). The reaction mixture was stirred for 24 h at room temperature. After completion of reaction, the crude mixture was poured over ice to dilute acid and precipitate product. Then, the crude slurry was vacuum filtered through a Büchner funnel into a 1 L vacuum filter flask and rinsed with 500 mL of distilled water. The precipitate was purified by silica gel flash chromatography using hexanes as the eluent to afford a yellow/orange powder. Compound **1** was characterized through ^{1}H NMR in ($CDCl_3$). Experimental yield: 7.943g. Theoretical Yield: 8.242g. Percent Yield: 96.4%. The spectrum was in correspondence to a previous report on compound **1.**[20]

4-Methylazobenzene: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.98 (d, 2H), 7.94-7.91 (d, 2H), 7.58-7.48 (t, 3H), 7.37-7.35 (d, 2H), 2.47 (s, 3H). See **Figure 10**. The UV data has been studied in other literature, so it was not analyzed for this study.

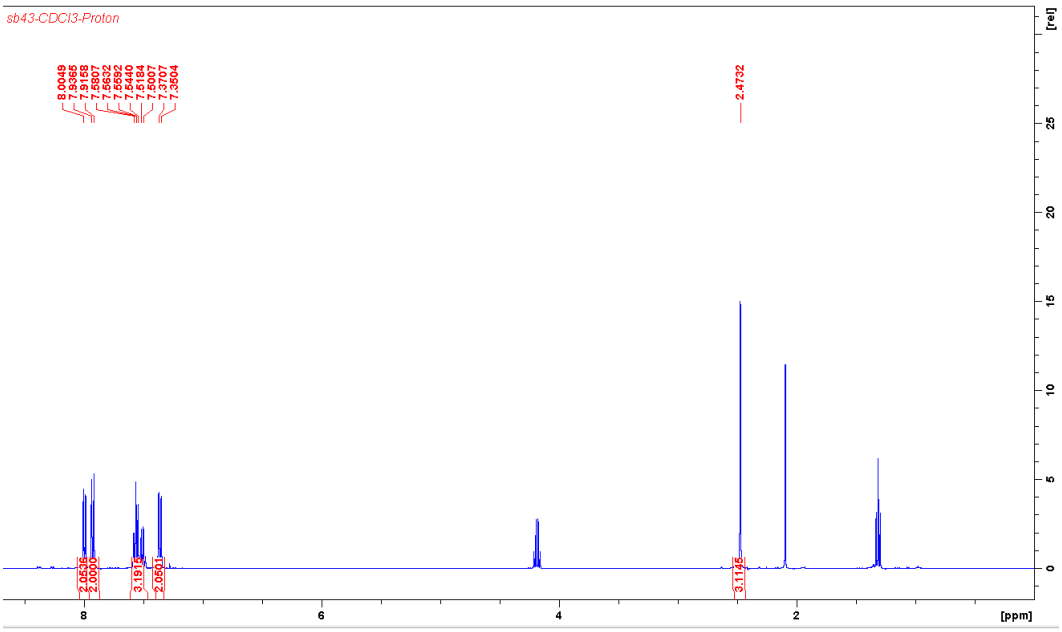
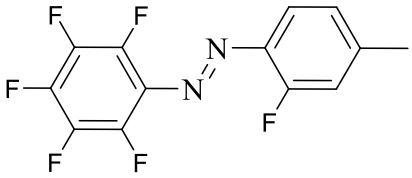


Figure 10: ^{1}H NMR of Compound 1



1-(2-Fluoro-4-methylphenyl)-2-(pentafluorophenyl)diazene **(Compound 2)**

Pentafluoro-nitrosobenzene (13.937g; 70.7 mmol, 1 eq) and 2-fluoro-4-methylaniline (18.758 g; 70 mmol; 1 eq) were added to glacial acetic acid (AcOH) (50mL). The reaction mixture was stirred for 24 h at room temperature. After completion of reaction, the crude mixture was poured over ice to dilute acid and precipitate product. Then, the crude slurry was vacuum filtered through a Büchner funnel into a 1 L vacuum filter flask and rinsed with 500 mL of distilled water. The precipitate was purified by silica gel flash chromatography using hexanes as the eluent to afford orange oily crystals. Compound **2** was characterized through ^{1}H NMR in ($CDCl_3$) and ^{19}F NMR in ($CDCl_3$). The spectra were evaluated through predictive NMR analysis using Chemdraw Ultra 12 as the

compound has not been reported. Experimental yield: 7.6g Theoretical Yield: 21.5g Percent Yield: 35%

1-(2-Fluoro-4-methylphenyl)-2-(pentafluorophenyl)diazene: ^{1}H NMR (400 MHz. $CDCl_3$) δ 7.67 (t, 1H), 7.15-7.12 (d, 1H), 7.08-7.05 (d, 1H), 2.47 (s, 3H). ^{19}F NMR (400 MHz, $CDCl_3$) δ -123.04 (s, 1F), -150.17 to -150.21 (d, 2F), -152.54 to -152.66 (t, 1F), -162.11 to -162.21 (t, 2F). See **Figures 11** and **12**.

UV-Vis (*trans* isomer in DMSO): λ_{max} (π-π*) = 327 nm; ε = 12,800 L mol^{-1} cm^{-1}. See **Figures 13** and **14**.

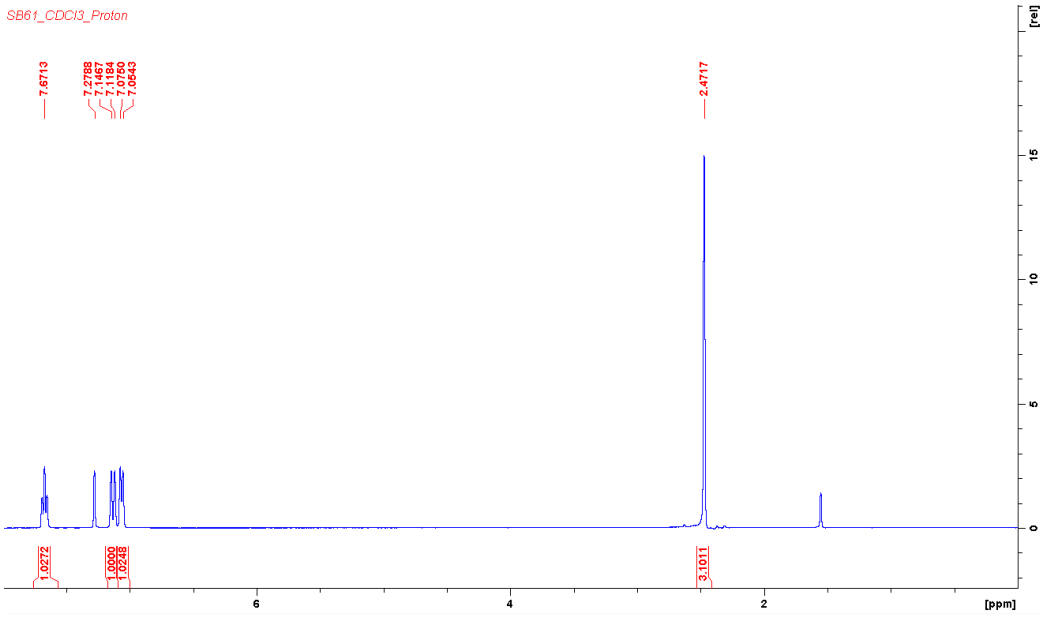


Figure 11: ^{1}H NMR of Compound 2

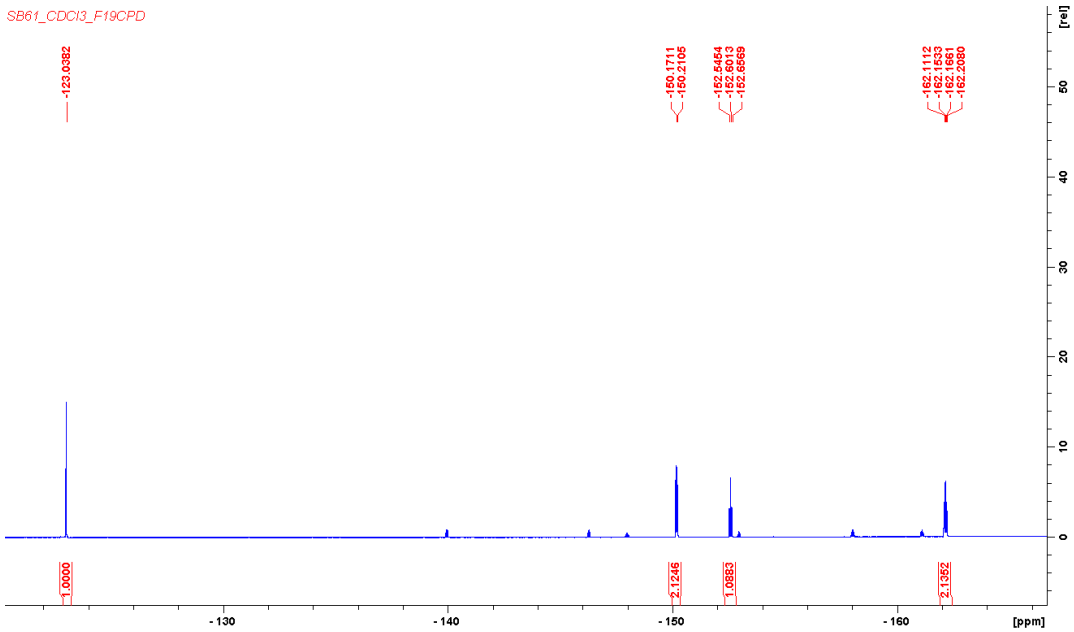


Figure 12: ^{19}F NMR of Compound 2

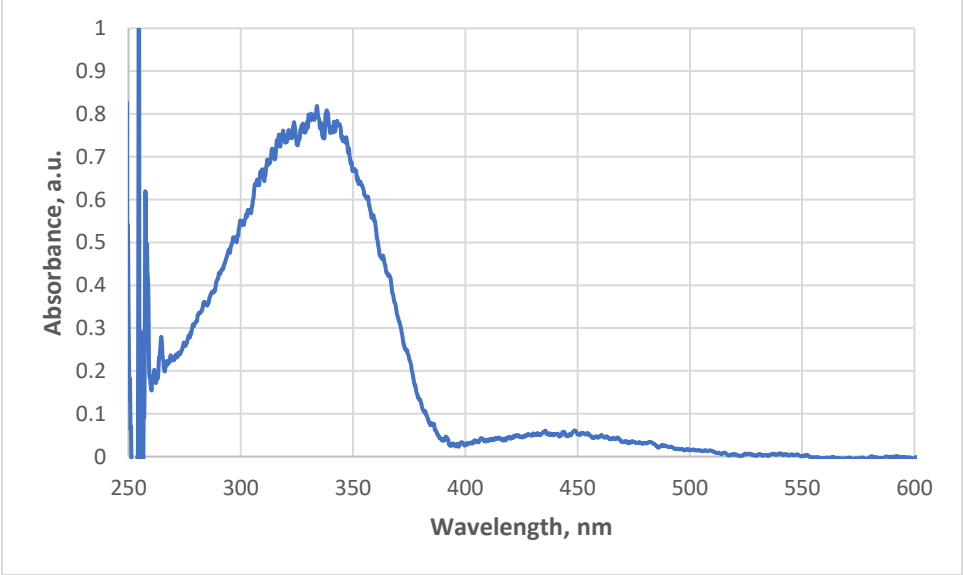


Figure 13: UV/Vis Spectra of Compound 2 (*trans*)

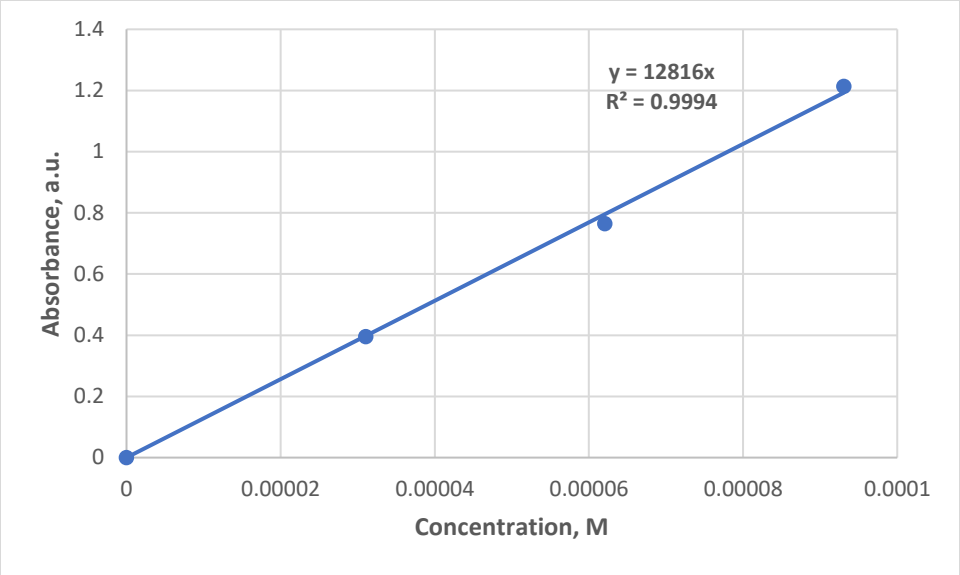
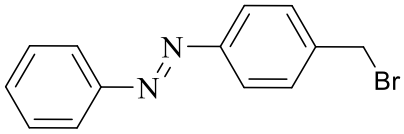


Figure 14: Molar Absorptivity of Compound 2 (*trans*)



***1-[4-(Bromomethyl)phenyl]-2-phenyldiazene* (Compound 3)**

4-Methylazobenzene (Compound **1)** (7.943g; 40 mmol; 1 eq), benzoyl peroxide (BPO) (0.500g; 4.2 mmol; 0.1 eq), and N-bromosuccinimide (NBS) (10.13g; 56 mmol; 1.4 eq) was added to a solution of 50 mL α,α,α-trifluorotoluene. The reaction mixture was stirred and refluxed for 48 h at 80°C. The crude solution was reduced on rotovap to a solid. This solid was extracted by ethyl ether (3 x 25 mL) and decanted into a 500 mL separatory funnel. The remaining solid was discarded. The organic solution was washed by 1N HCl (2 x 20 mL), 1 N NaOH (2 x 20 mL), distilled water (2 x 20 mL), Brine (1 x 20mL), and finally dried over Sodium Sulfate. The crude organic layer was reduced by rotovap and then purified by column chromatography. (Hexane to 5% Toluene: Hexane to 25% Toluene: Hexane). The product was validated by proton NMR to reference.[21] Experimental yield: 11.18g. Theoretical yield: 13.12g. Percent Yield: 85.2%.

1-[4-(Bromomethyl)phenyl]-2-phenyldiazene:^{1}H NMR (400 MHz. $CDCl_3$) δ 7.97-7.49 (m, 9H), 4.58 (s, 2H). See **Figure 15**.

UV-Vis (*trans* isomer in DMSO): λ_{max} = 332 nm; ε = 18,000 L mol^{-1} cm^{-1}. See **Figures 16** and **17**.

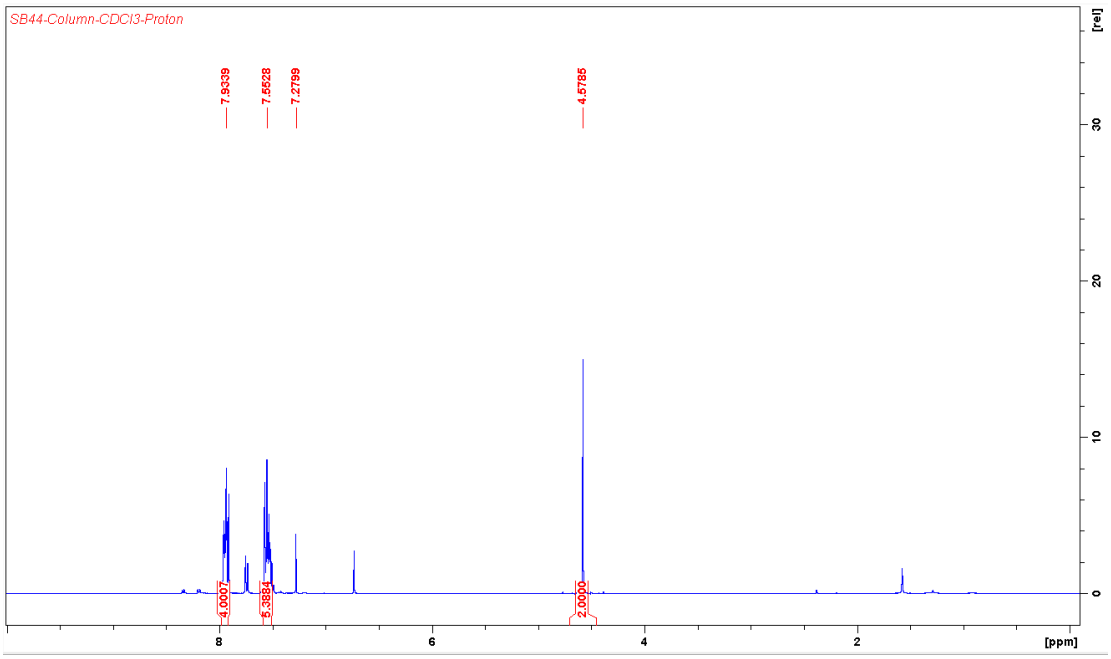


Figure 15: ^{1}H NMR of Compound 3

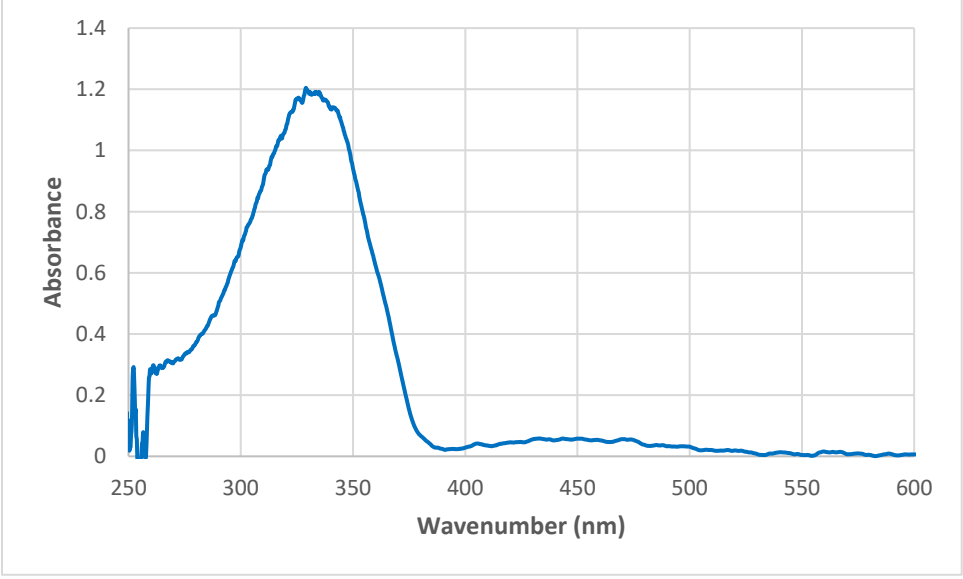


Figure 16: UV/Vis Spectra of Compound 3 (*trans)*

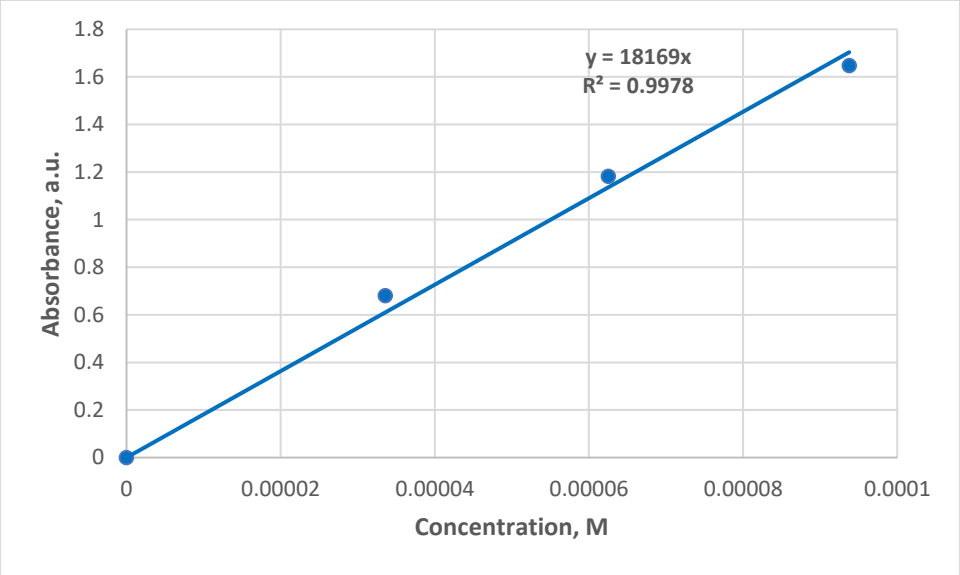
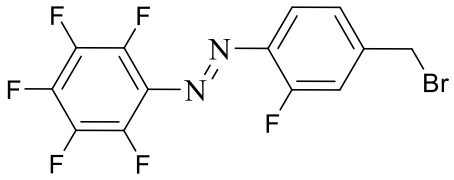


Figure 17: Molar Absorptivity of Compound 3 (*trans)*



***1-(4-(Bromomethyl)-2-fluorophenyl)-2-(pentafluorophenyl)diazene* (Compound 4)**

1-(2-Fluoro-4-methylphenyl)-2-(pentafluorophenyl)diazene (Compound **2**) (1g; 3.29 mmol; 1 eq), benzoyl peroxide (BPO) (0.100g; 0.33 mmol; 0.1 eq), and N-bromosuccinimide (NBS) (1.18g; 80 mmol; 2 eq) was added to a solution of 50 mL α,α,α-trifluorotoluene. The reaction mixture was stirred and refluxed for 48 h at 80°C. The crude solution was reduced on rotovap to a solid. This solid was extracted by ethyl ether (3 x 25 mL) and decanted into a 500 mL separatory funnel. The remaining solid was discarded. The organic solution was washed by 1N HCl (2 x 20 mL), 1 N NaOH (2 x 20 mL), distilled water (2 x 20 mL), Brine (1 x 20mL), and finally dried over Sodium Sulfate. The crude organic layer was reduced by rotovap and then purified by column chromatography. (Hexane to 5% Toluene: Hexane to 25% Toluene: Hexane). The

reaction schema was followed by traditional bromination found in reference, however the novel product was evaluated through predictive NMR analysis using Chemdraw Ultra 12 as the compound has not been reported.[21]

Experimental yield: 0.6767 g. Theoretical yield: 1.260g. Percent Yield: 54%.

1-(4-(Bromomethyl)-2-fluorophenyl)-2-(pentafluorophenyl)diazene: ^{1}H NMR (400 MHz. $CDCl_3$) δ 7.78-7.74 (t, J = , 1H), 7.60-7.57 (m, J = , 9H), 7.47-7.34 (m, J = , 1H), 6.65 (s, 1H), 4.52 (s, 2H). See **Figure 18**.

UV-Vis (*trans* isomer in DMSO): λ_{max} = 329 nm; ε = 15,200 L mol^{-1} cm^{-1}. See **Figures 19** and **20**.

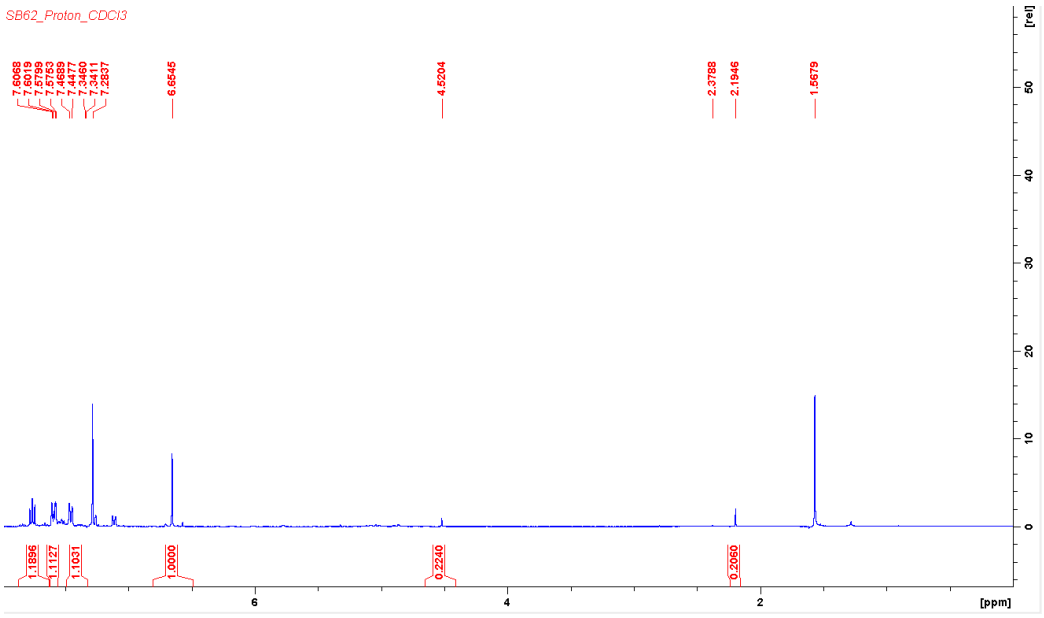


Figure 18: ^{1}H NMR of Compound 4

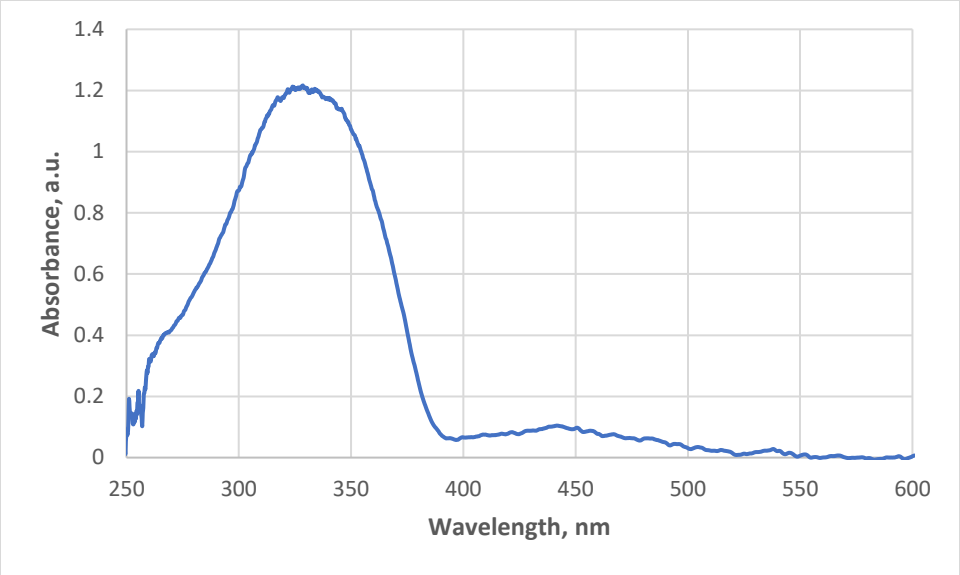


Figure 19: UV/Vis Spectra of Compound 4 (*trans)*

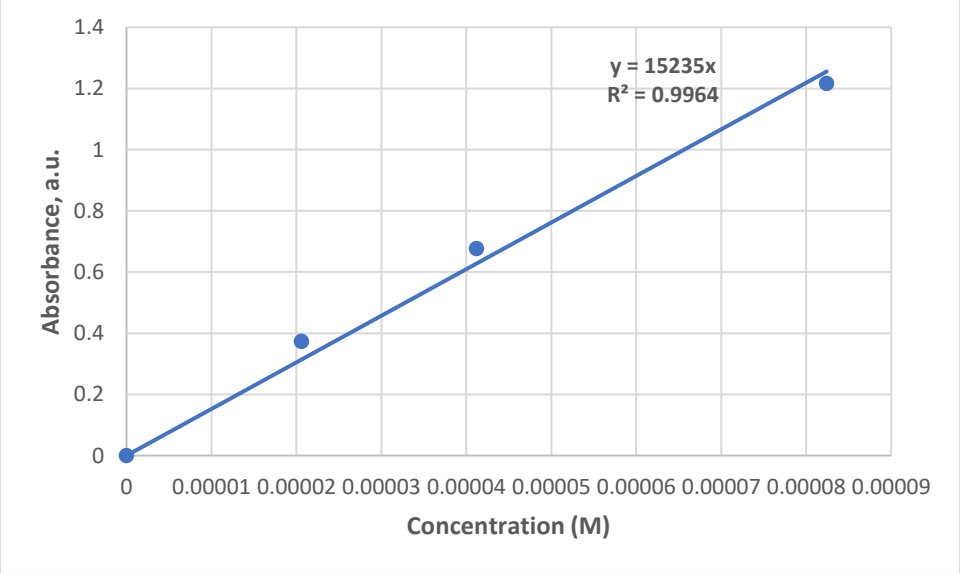
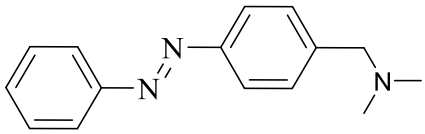


Figure 20: Molar Absorptivity of Compound 4 (*trans)*



***4-(N,N-Dimethyl)benzylazobenzene* (Compound 5)**

1-[4-(Bromomethyl)phenyl]-2-phenyldiazene (2.1g; 6.4 mmol; 1 eq) and dimethylamine in H_2O (40%) (15 mL; 118 mmol; 20 eq) was added into 50 mL acetone, then stirred for 5 days at room temperature. The solution was then reduced under pressure on a rotary evaporator. The crude material was then recrystallized by 50 mL of toluene and precipitated to afford a red powder. The product was validated through proton NMR by reference.[22] Experimental yield: 1.18g. Theoretical Yield: 2.37g. Percent Yield: 50%. *4-(N,N-Dimethyl)benzylazobenzene*: ^{1}H NMR (400 MHz. $CDCl_3$) δ 11.94 (s, 1H), 8.06-7.53 (m, J = , 9H), 4.34-4.33 (d, 2H), 2.86-2.74 (d, 6H). See **Figure 21**.

The UV data has been studied in other literature, so it was not analyzed for this study.

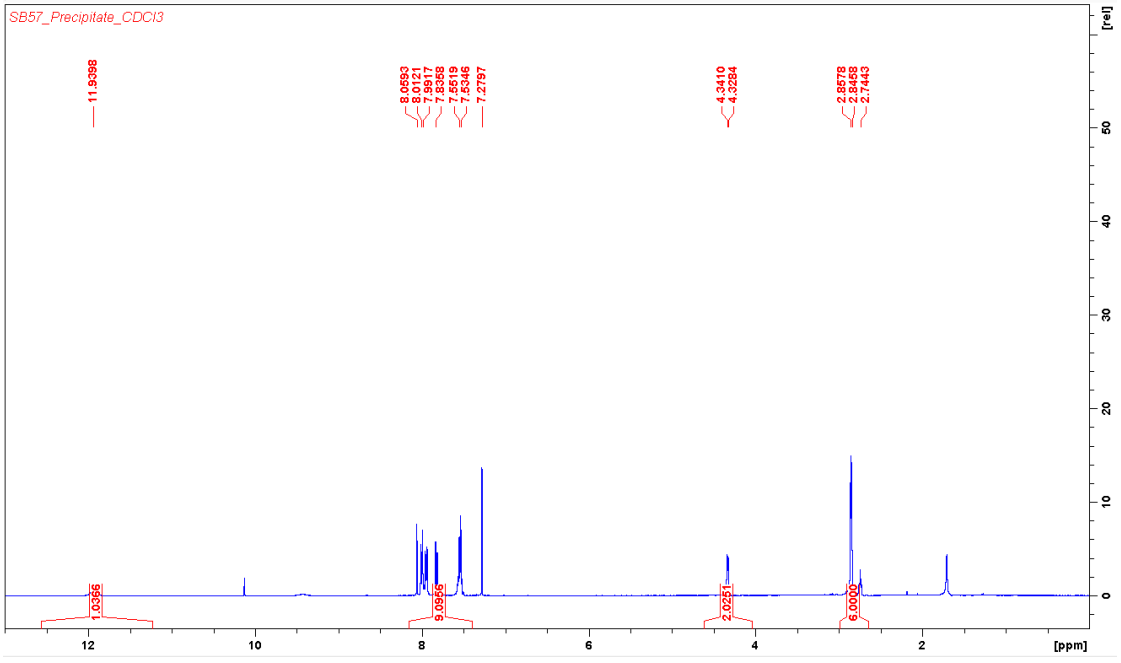
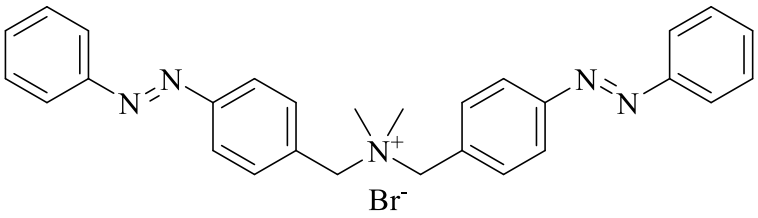


Figure 21: ^{1}H NMR of Compound 5



N,N-bis(azobenzene)-N,N-dimethylammonium bromide **(Compound 6)**

1-[4-(Bromomethyl)phenyl]-2-phenyldiazene (440 mg; 1.6 mmol; 1 eq) and *4-(N,N-Dimethyl)benzylazobenzene* (500 mg; 1.6 mmol; 1 eq) was added into 25 mL of acetonitrile, then stirred under nitrogen for 24 h. The solution was cooled in the freezer for 1 hour. A yellow precipitate was formed, filtered, and rinsed by 25 mL of acetonitrile. Experimental yield: 364 mg. Theoretical yield: 819 mg. Percent yield: 44.4%.

A method for purification of the crude *N,N-bis(azobenzene)-N,N-dimethylammonium bromide* is to perform column chromatography. Firstly, pure chloroform or dichloromethane is run to remove starting material. Then, methanol is applied to remove any excess starting material. Finally, a solution of 15% Ammonium Hydroxide: 50% Methanol: 35% Distilled H_2O is run through the column to elute the product. The product was validated by proton NMR to reference.[18]

N,N-bis(azobenzene)-N,N-dimethylammonium bromide: ^{1}H NMR (400 MHz. $CDCl_3$) δ 8.03-7.63 (m, J = , 18 H), 4.78 (s, J = , 4H), 3.01 (s, J = , 6H). ^{13}C NMR (500 MHz, DMSO) δ 153, 152, 135, 132, 131, 130, 123, 67, 49. See Figures **22** and **23**.

UV-Vis (*trans* isomer in DMSO): λ_{max} = 327 nm; ε = 28,300 L mol^{-1} cm^{-1}. See Figures **24** and **25**.

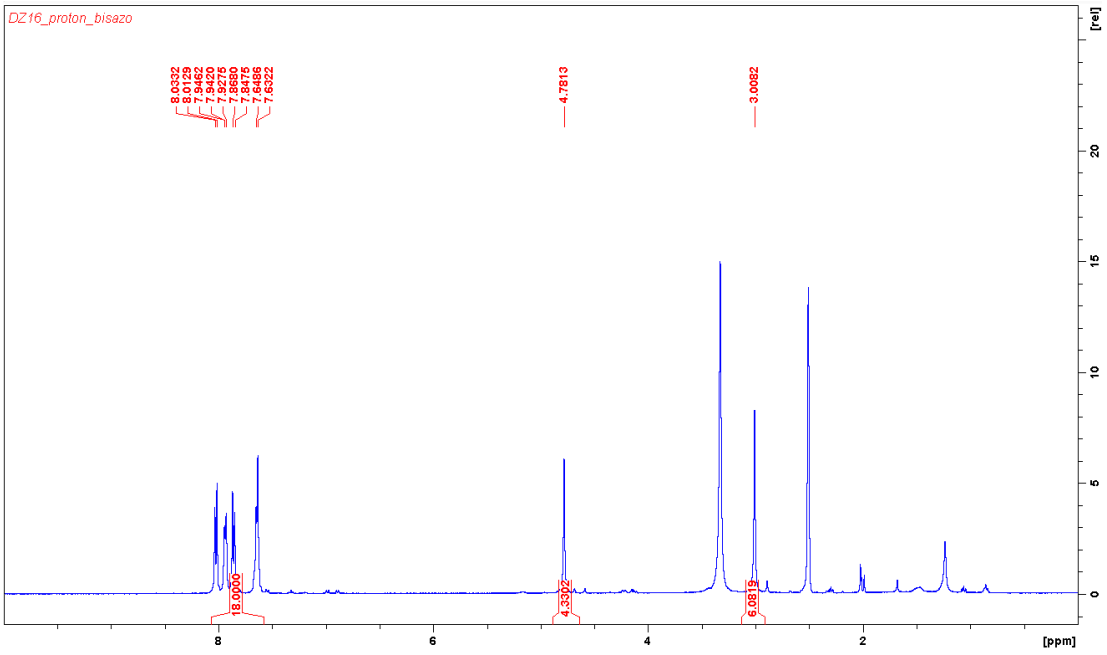


Figure 22: ^{1}H NMR of Compound 6

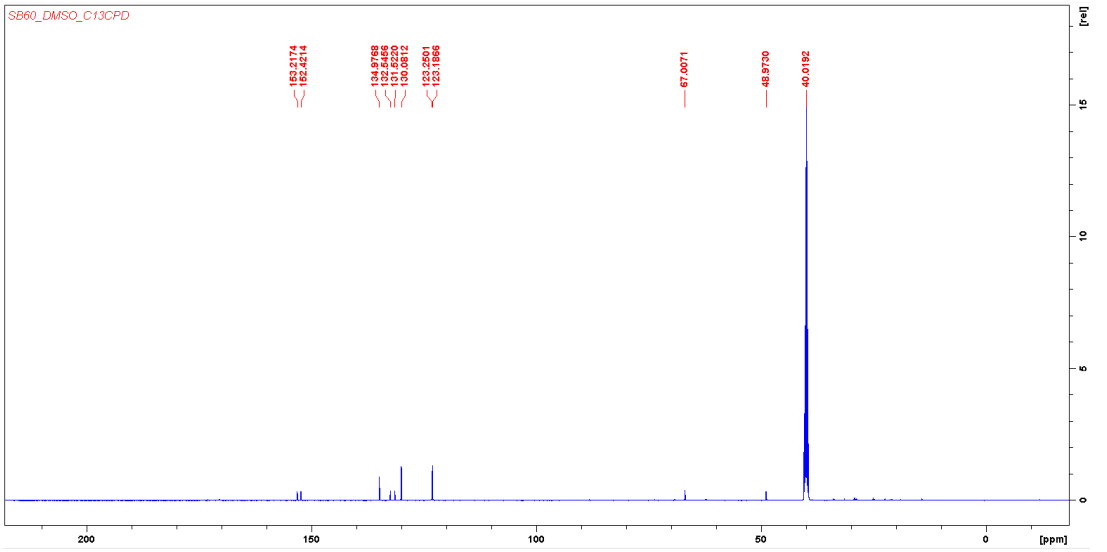


Figure 23: ^{13}C NMR of Compound 6

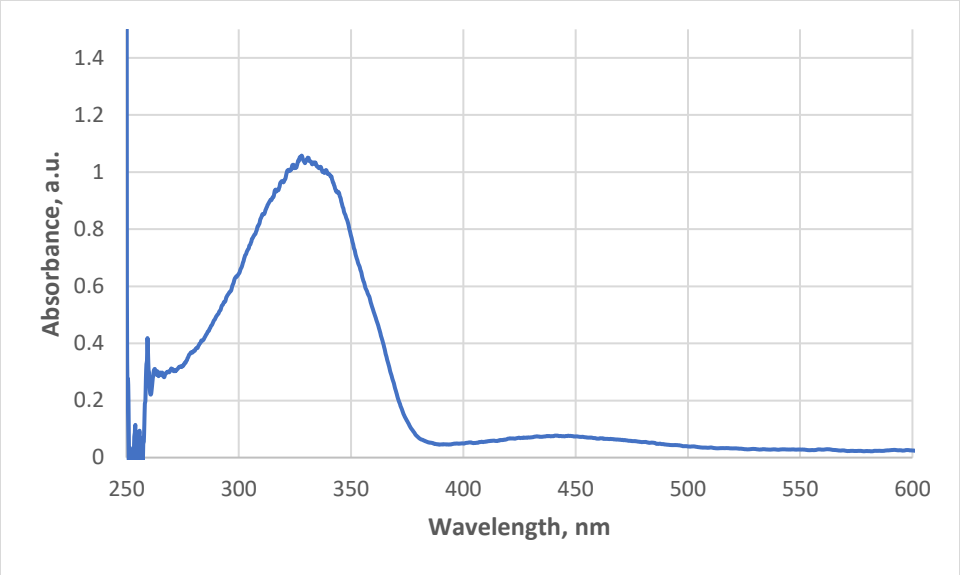


Figure 24: UV/Vis Spectra of Compound 6 (*trans*)

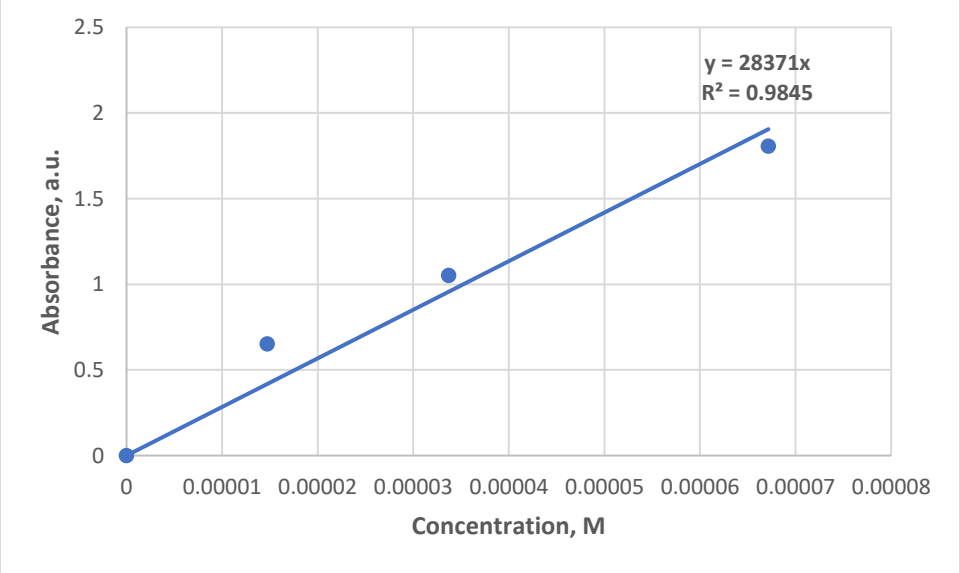
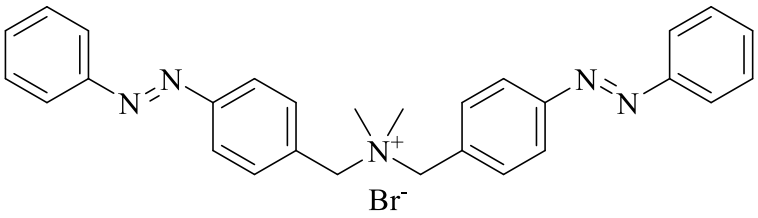
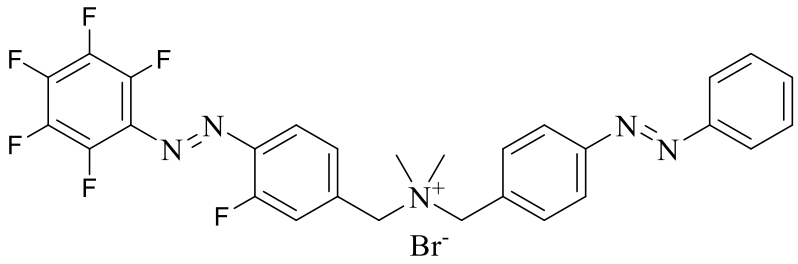


Figure 25: Molar Absorptivity of Compound 6 (*trans*)



N,N-bis(azobenzene)-N,N-dimethylammonium bromide **(Compound 6)**

Alternative Synthesis of Compound 6: *1-[4-(Bromomethyl)phenyl]-2-phenyldiazene* (350 mg; 1.27 mmol; 1 eq) was added with K_2CO_3 (552 mg; 4 mmol; 1 eq) into 20mL of dimethylformamide (DMF), then stirred with reflux at 80°C for 72 h. The crude solution was poured into a 500 mL Erlenmeyer flask and stirred with 200 mL of toluene. Decolorizing carbon was added to the solution, boiled, and stirred for 5 minutes. Then, the solution was cooled to room temperature followed by filtration in a Cellite plug to remove all solids. Xylenes (20 mL) were added into the solution to assist azeotrope of DMF and the solution was reduced under pressure on a rotovap at high heat. The crude oily solid was then added to 25 mL of hot hexanes. The solution was then added to the freezer to precipitate overnight. The product was filtered and rinsed by 100 mL of cold hexanes, then dried to afford an orange powder. The proton NMR results were validated by reference.[18]



N-(3-fluoro-4-(pentafluorophenyl)diazenyl)benzyl)-N,N-dimethyl-1-(4-phenyldiazenyl)phenyl)methanaminium bromide **(Compound 7)**

1-(4-(Bromomethyl)-2-fluorophenyl)-2-(pentafluorophenyl)diazene (0.250g; 0.6527 mmol; 1 eq) was added into 20 mL of acetonitrile in a 50 mL pressure vessel. *1-[4-(Bromomethyl)phenyl]-2-phenyldiazene* (0.200g; 0.783 mmol; 1.2 eq) was added into the solution, then refluxed at 85°C for 24 hours. The crude solution was then removed of solvents under pressure by rotary evaporator. Then, the crude material was dissolved into silica gel and column chromatography was performed. The elution gradient was as follows: 500 mL Hexane, 500 mL Methanol, and 250 mL of Methanol: (15%) Ammonium Hydroxide: DI H_2O. The elution of the Methanol: Ammonium Hydroxide: DI H_2O was acquired for the purified product. This elution was reduced under pressure on the rotary evaporator to afford a red powder. The spectra were evaluated through predictive NMR analysis using Chemdraw Ultra 12 as the compound has not been reported.

N-(3-fluoro-4-(pentafluorophenyl)diazenyl)benzyl)-N,N-dimethyl-1-(4-phenyldiazenyl)phenyl)methanaminium bromide: ^{1}H NMR (400 MHz, ACN) δ 7.88-6.78 (m, J = , 12 H), 3.74-3.26 (d, J = , 4H), 2.36 (s, J = , 6H). ^{13}C NMR (500 MHz, ACN) δ 153, 140, 132, 131, 130, 129, 128, 123, 121, 118, 77, 74, 69, 63, 29. ^{19}F NMR (400 MHz,

ACN) δ -123.33 (s, J = , 1F), -151.29 to -151.33 (d, J= , 2F), -152.46 to -152.57 (t, J= , 2F), -163.98 to -164.07 (t, J = , 1F). See Figures **26** and **27**.

UV-Vis (*trans* isomer in DMSO): λ_{max} = 330 nm; ε = 23,300 L mol^{-1} cm^{-1}. See Figures **28** and **29**.

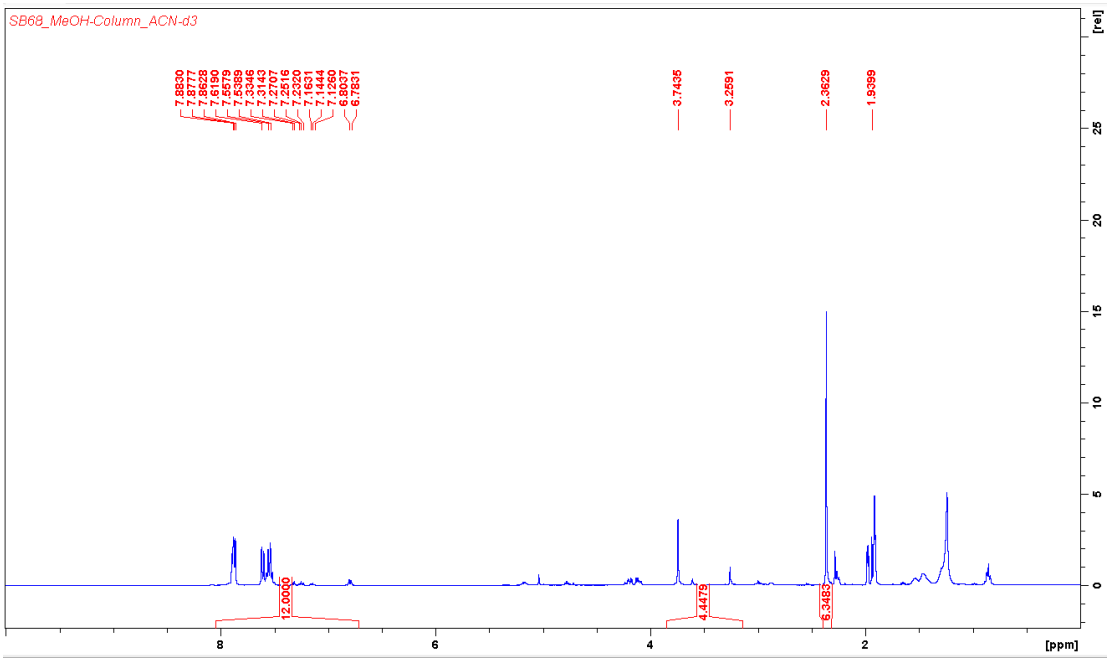


Figure 26: ^{1}H NMR of Compound 7

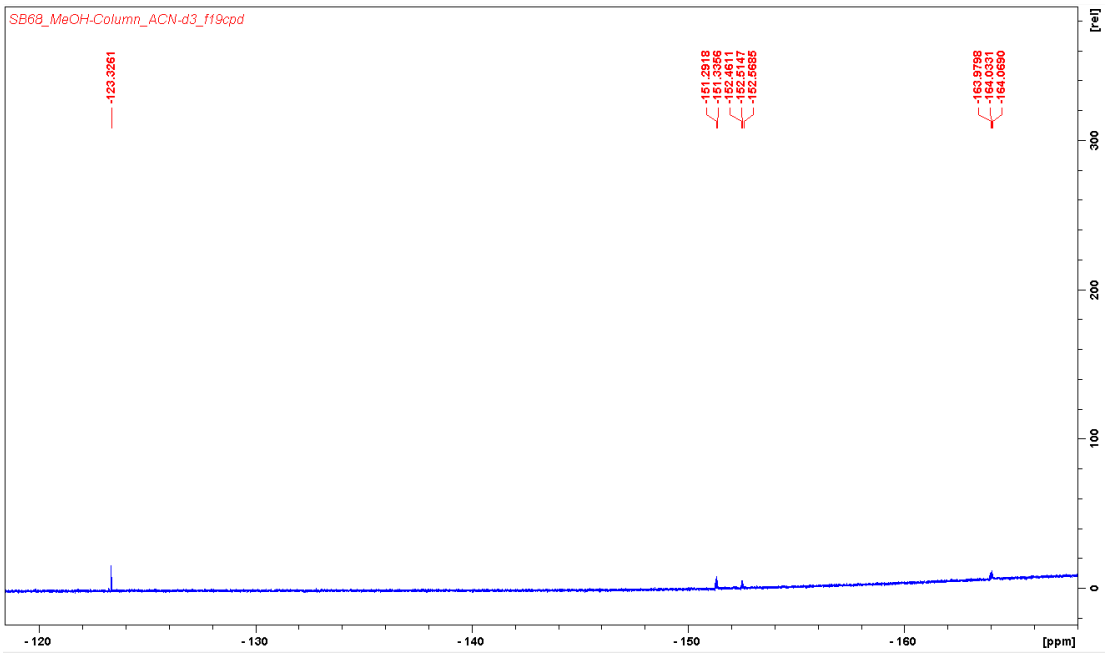


Figure 27: ^{19}F NMR of Compound 7

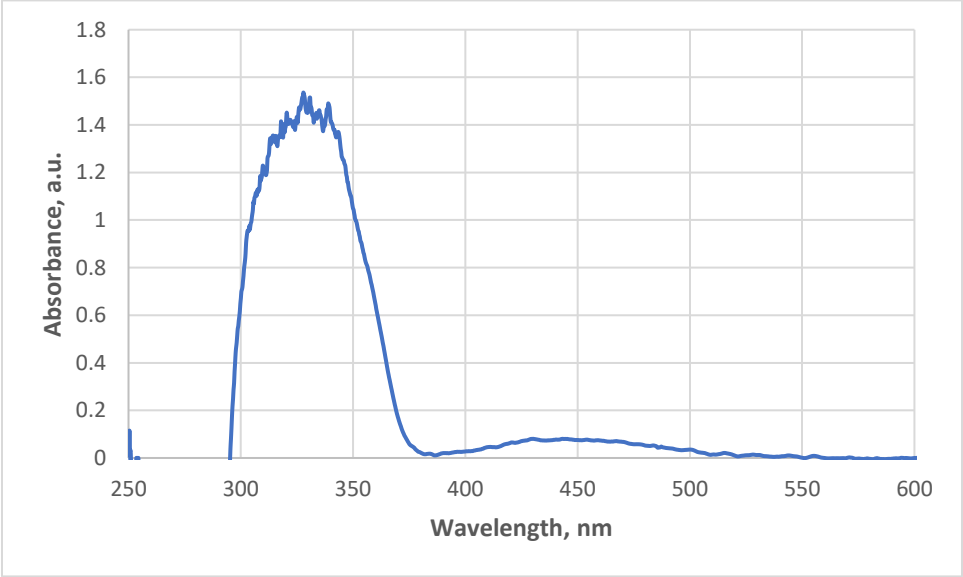


Figure 28: UV/Vis Spectra of Compound 7 (*trans)*

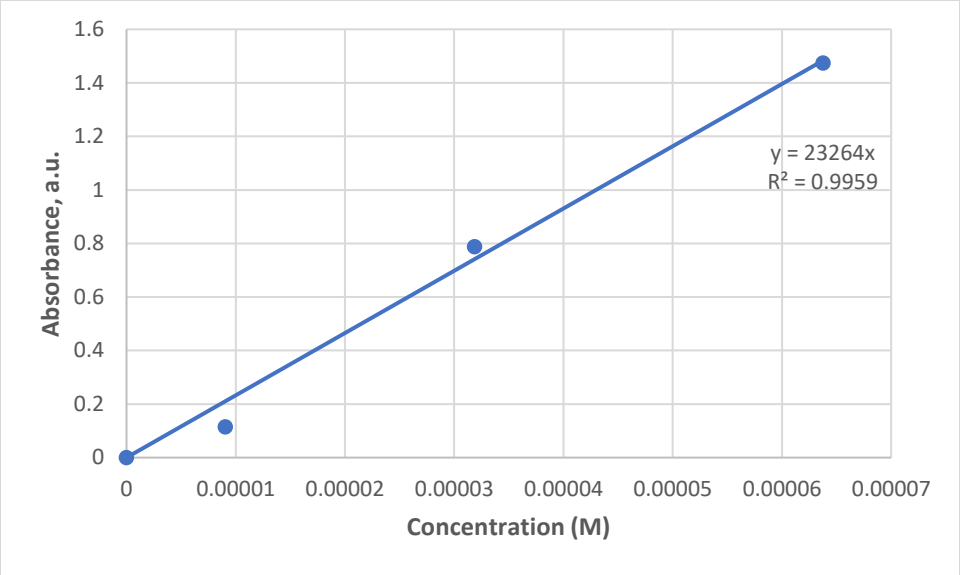
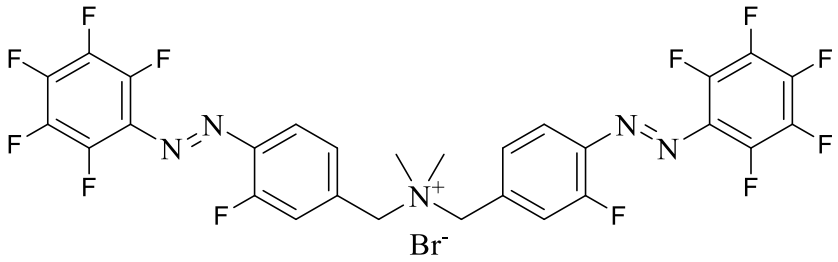


Figure 29: Molar Absorptivity of Compound 7 (*trans)*



Compound 8

1-(4-(Bromomethyl)-2-fluorophenyl)-2-(pentafluorophenyl)diazene (0.250g; 0.6527 mmol; 1 eq) was added with K_2CO_3 (552 mg; 4 mmol; 1 eq) into 20mL of dimethylformamide (DMF) in a 50 mL pressure vessel then stirred with reflux at 80°C for 72 h. The crude solution was poured into a 500 mL Erlenmeyer flask and stirred with 200 mL of toluene. Decolorizing carbon was added to the solution, boiled, and stirred for 5 minutes. Then, the solution was cooled to room temperature followed by filtration in a Cellite plug to remove all solids. Xylenes (20 mL) were added into the solution to assist azeotrope of DMF and the solution was reduced under pressure on a rotovap at high heat. The crude oily solid was then added to 25 mL of hot hexanes. The solution was then

added to the freezer to precipitate overnight. The product was filtered and rinsed by 100 mL of cold hexanes but was only given back the crude, dark brown material. The proton NMR and fluorine NMR results showed a crude product. The product was not able to be successfully purified.

III. DISCUSSION

A. *Overview*

Due to amphipathic nature of the photosurfactant targets, the crux of this thesis work was mostly purification of these ionic compounds. Therefore, the discussion describes various efforts to purify the compounds. Flash chromatography combined with recrystallization was sufficient for product purification for the majority of synthesized compounds. The purification of nonpolar synthetic intermediates was performed by column chromatography with common elution solvents. Compound **5** could be purified by simple toluene recrystallization to afford pure compound. Synthesis and purification of non-fluorinated compounds was largely successful. However, it is known that amines can displace fluorine from the aromatic azobenzene leading to mixture of products that were intractable.[13] The reaction mixtures caused streaking and multiple spots on TLC after only 10 min of stirring the reaction at 0°C. Multiple recrystallizations and column chromatography were not successful. Details on the syntheses of bis-azobenzene compounds **6,7,** and **8** are described in more detail below.

B. *Compound 6*

Purification of a bis-azobenzene was more challenging than anticipated due to the binding of a quaternary salt to the silica gel. Recrystallization did not afford pure bis-azobenzene. Through trial and error, a mixed solvent system was developed to purify a bis-azobenzene quaternary salt on column chromatography. First, hexanes were applied onto the column to remove all non-polar compounds. Then, methanol was flushed through the column to remove all polar compounds. Finally, a solution of 15%

ammonium hydroxide: 50% methanol: 35% DI H_2O was applied to afford the pure bis-azobenzene (compound **6**).

C. *Compound 7*

Fortunately, a mixed system containing fluorines on only one azobenzene and of a bis-azobenzene system was successfully synthesized (compound **7**). This synthesis was successful after coupling compound **4** to compound **5**. Afterwards, recrystallization was not successful to afford a purified compound **7**. Thus, column chromatography was applied to the system through application of hexanes, chloroform, and finally methanol to afford a pure azobenzene. This system did not require the ammonium hydroxide eluent as it is hypothesized to be more non-polar than the previous quaternary salt, or that the fluorines reduced binding affinity to silica gel.

D. *Compound 8*

We attempted synthesis of a bis-azobenzene with both azobenzenes fluorinated. Evidence of product was observed by NMR but despite numerous attempts, the product could not be purified. Preparation of quaternary compounds by reacting compound **4** with dimethylformamide for 72 h at 80°C reaction did not afford any product and we suspect the primary culprit is reactions of the aromatic fluorines.[13] Reaction of compound **5** with compound **4** afforded a crude reaction mixture containing the desired product, compound **8.** Compound **8** was verified by a slightly crude ^{19}F NMR as well as a very crude ^{1}H NMR. Despite exploration of many recrystallizing solvents, we were not able to purify compound **8**; in fact, the crude product became discolored to a tar-like color after several recrystallizations which is puzzling. Several variations of normal phase flash chromatography were unsuccessful including a variety of mixed solvent systems and

sodium bromide treated silica gel.[23] The principal difficulty was co-elution of several compounds that apparently has similar retention characteristics. On thin layer chromatography, there was a spot with low retention that we took for our product; however, flash chromatography did not cleanly separate this yellow spot.

E. *Future*

Future goals for the characterization of the azobenzene species include NMR spectroscopy such as NOESY (Nuclear Overhauser Effect Spectroscopy) to see if there is evidence of a quadrupolar effect between benzene rings of an electron deficient π-cloud on the fluorinated azobenzene that would overlap with the electron rich π-cloud of the azobenzene. Photoexcitation of the individual azobenzenes on each side of the bis-species will be performed to measure the rate of relaxation through kinetics. We hypothesize that there will be selective isomerization of the azobenzene by UV-light and the fluorinated azobenzene by green light due to the inductive effects causes by *ortho*-fluorination. Additionally, we hypothesize that the fluorinated species will have a longer half-life than the traditional azobenzene. In addition, the colloidal characterizations of each synthesized azobenzene will be performed along with mass spectrometry for further chemical verification.

IV. CONCLUSIONS

Synthesis of a *N,N-bis(azobenzene)-N,N-dimethylammonium bromide* through two synthetic methodologies was successful. A mixed system with one fluorinated azobenzene was accomplished with an effective purification technique. The synthesis of *N-(3-fluoro-4-(pentafluorophenyl)diazenyl)benzyl)-N,N-dimethyl-1-(3-fluoro-4-(pentafluorophenyl)diazenyl)benzyl)methanaminium bromide* was synthesized multiple times; however, the purification of this product was extremely difficult and unfortunately not successful. The limitations of fluorines interaction with amines in reactions has led to multiple days lost of synthesis as well as starting materials. The amination of a fluorinated benzyl bromide azobenzene was swift but quickly would turn from a brownish compound into a dark black tar-like substance. This was hypothesized that the amines were abstracting fluorines from the azobenzene rings and creating a myriad of side reactions. Thin layer chromatography showed substantial streaking in the bis-azobenzene reaction, especially for the fully fluorinated system. Not only was there a flurry of different results from the TLC, but also every column chromatography performed did not result in much separation. Many gradient systems were applied such as hexanes with toluene or hexanes with ethyl acetate. Even going to the more polar side of solvents would cause the fluorinated bis-azobenzene to elute with multiple spots. These elutions would never be a solid or powder, but more of an oil like substance with many mixed integrations in ^{1}H NMR between 3 to 6 ppm.

V. REFERENCES

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