Determination of the Rate Constant for H Atom Abstraction by Phenyl Radicals for THF

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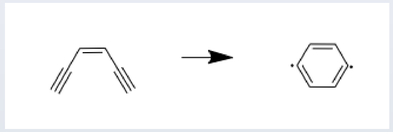
Introduction

Phenyl radicals (Ph•) are efficient hydrogen atom abstractors and this may have biological significance.[1] For example, some powerful anticancer drugs, including the enediynes, are believed to function by forming radicals that abstract hydrogen from the deoxyribose unit in DNA which leads to strand cleavage.[2]



However, the factors that control hydrogen atom abstraction, like the rate constant, are not well understood. This is largely due to the difficulty in examining reactions of highly reactive polyatomic radicals while under well-defined conditions. In experiments reported by Kenttamaa and coworkers[2], selected charged phenyl radicals were reacted with a variety of hydrogen donors in order to gain insight on the different structural features that make polyatomic radicals efficient in hydrogen atom abstraction from organic molecules. They specifically used tetrahydrofuran (THF) as a model for the deoxyribose rings of DNA. However, their methodology did not allow the determination of the absolute rate constants. Our research used competitive kinetics to determine the rate constant (k_H) for hydrogen atom abstraction by phenyl radicals from THF.

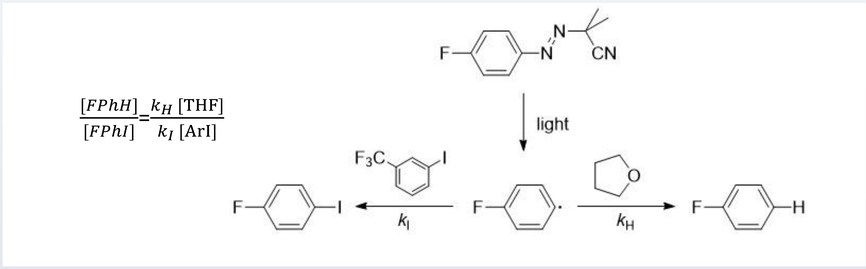
p-Fluorophenylazoisobutyronitrile (FPAIN) was used as a photochemical source of p-fluorophenyl radicals that can be tracked using ^{19}F NMR. The p-fluorophenyl radicals (FPh·) were allowed to react with THF and 3-iodobenzotrifluoride (ArI) to yield fluorobenzene (FPhH) and p-iodofluorobenzene (FPhI) (Scheme 1). The reaction of phenyl radicals with the iodoarene was used as a kinetic reference point (k_I = 2.2 x 10^8 M^{-1} s^{-1}) which allows the determination of k_H through a graphical analysis (Scheme 1). We assumed that the products are formed irreversibly, and the relative yields (FPhH/FPhI) are therefore controlled by the rates as shown in the Scheme 1 equation.

Experimental

Competitive Kinetics. Varying masses of 3-iodobenzotrifluoride and the FPAIN (0.1 mmol) were added to a 1.00 mL volumetric flask. THF was added to the meniscus line and its mass recorded. This solution was transferred to an NMR tube and ^{19}F and ^{1}H NMR were taken before and after 1-3 hour photolysis using a 65-W compact fluorescent bulb at 22 ± 1 °C. Temperature was kept constant using an oil bath which can be seen in Figure 3. Parameters for ^{19}F NMR were X offset = -100 ppm, X sweep = 150 ppm, and X points = 131072. C_6F_6 was used as a chemical shift standard with the NMR in un-locked “no-D mode”.

Introduction

Scheme 1: Competitive Kinetics with THF and ArI



Results and Discussion

Figure 1: ^{19}F NMR of expt 1 showing iodoarene (ArI), FPAIN, fluorobenzene (FPhH), and 4-fluoroiodobenzene (FPhI)

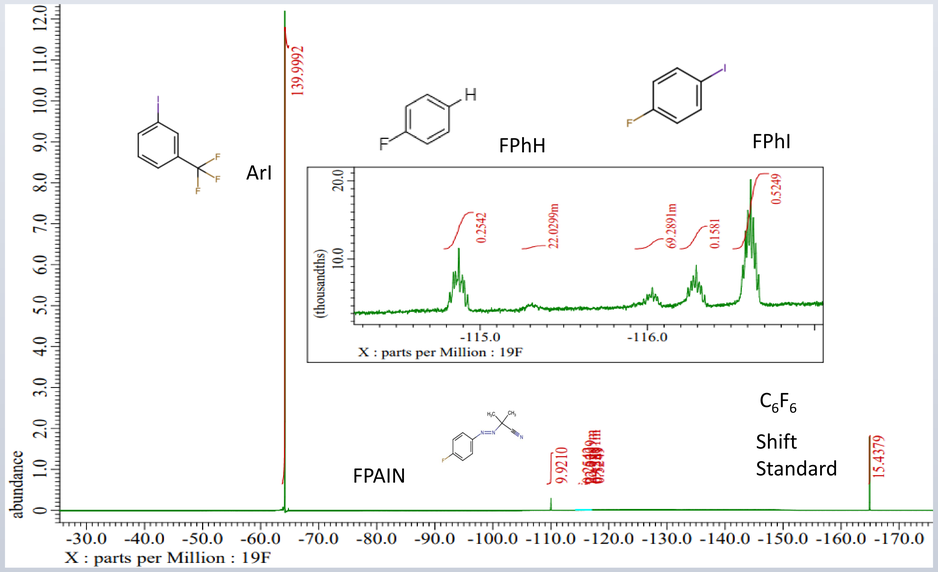


Figure 2: [FPhH]/[FPhI] vs [THF]/[ArI]

y = 0.0474x + 0, R^2 = 0.9983

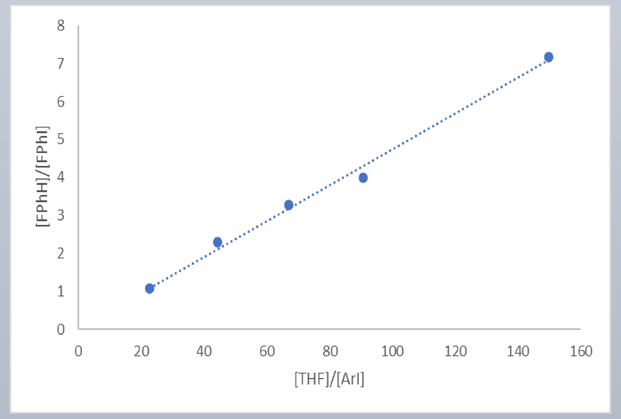
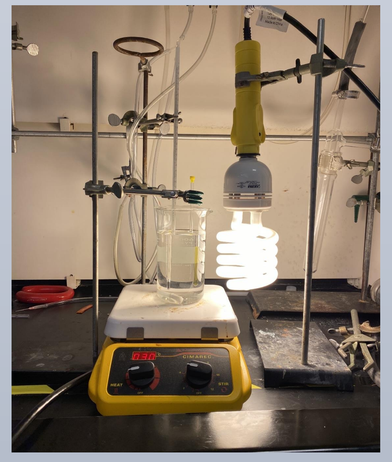


Figure 3: Oil bath and lamp set up for photolysis



Results and Discussion

Visible irradiation of FPAIN and 3-iodobenzotrifluoride (ArI) in tetrahydrofuran gave rise to two new peaks in the ^{19}F NMR (Scheme 1, Figure 2) at –114.9 and -116.3 ppm which were identified as fluorobenzene (FPhH) and p-iodofluorobenzene (FPhI) based on the pure compounds’ chemical shifts (Figure 1). This was reaffirmed by obtaining NMR spectra of the predicted products and by using C_6F_6 shift standard. (Peaks formed at -115.9, 116.6, and -115.3 have not been identified.) The formation of FPhI comes about due to the reaction of the p-fluorophenyl radicals (FPh·) with the iodoarene (ArI) and the formation of fluorobenzene (FPhH) is due to the FPh· abstracting hydrogen from THF (Scheme 1).

Integration of these peaks gives product ratios [FPhH]/[FPhI] that can be plotted versus the reactant concentration ratios [THF]/[ArI] (with the intercept set to zero) to give an excellent linear correlation, R^2 = 0.9983 (Figure 1). The slope of the best fit line (0.0474) gives the rate constant ratio k_H/k_I (Scheme 1). Using our previously determined value of k_I = 2.2 x 10^8 M^{-1}s^{-1} and multiplying by k_H/k_I we can find the desired rate constant for H abstraction from THF, k_H = 1.0 x 10^7 M^{-1}s^{-1}. The result compares favorably with the literature value determined by Scaiano and coworkers[3] using laser flash photolysis (k_H = 4.8 x 10^6 M^{-1} s^{-1}). The discrepancy may be partly due to the effect of the fluorine on phenyl radical reactivity; however, we have other evidence in our lab that suggest fluorophenyl and phenyl react similarly.

Conclusion

Visible radiation of FPAIN is a convenient way to make phenyl radicals that can be tracked by ^{19}F NMR. Using competitive kinetics, we found k_H for THF (k_H = 1.0 x 10^7 M^{-1} s^{-1}). The result agrees well with the previous measurement and should contribute toward a better understanding of how phenyl radicals react with DNA.

Future Work

Future experiments will include looking at biomolecules like purine and pyrimidine bases, as well as other small molecules such as water and acetonitrile and determining their rate constant when reacting with phenyl radicals. We would like to explore phenyl radical double bond addition reactions with the previously mentioned bases.

References

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