



Hydroquinones as Halogen-Bonding Catalyst for Radical Perfluoroalkylation Reactions

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Light Mediated Reactions

- A reaction that is promoted by light is known as a photochemical reaction
- This chemical reaction is initiated by the absorption of energy in the form of light
- The absorption of light creates an excited state that leads to a reaction that changes the molecules' physical and chemical state from their original form

Visible light is a renewable, clean, and abundant source of energy

- The absorption of the wavelength is from 400nm – 700nm

These reactions are very attractive to researchers because this design of chemical products/processes minimizes the environmental impact of chemical synthesis (AKA green chemistry)

- This process is beneficial because it reduces the amount of toxic and polluting waste, decreasing the chemical disruptions of ecosystems

- This ultimately reduces the pollution that could decrease human health, the environment, and natural resources

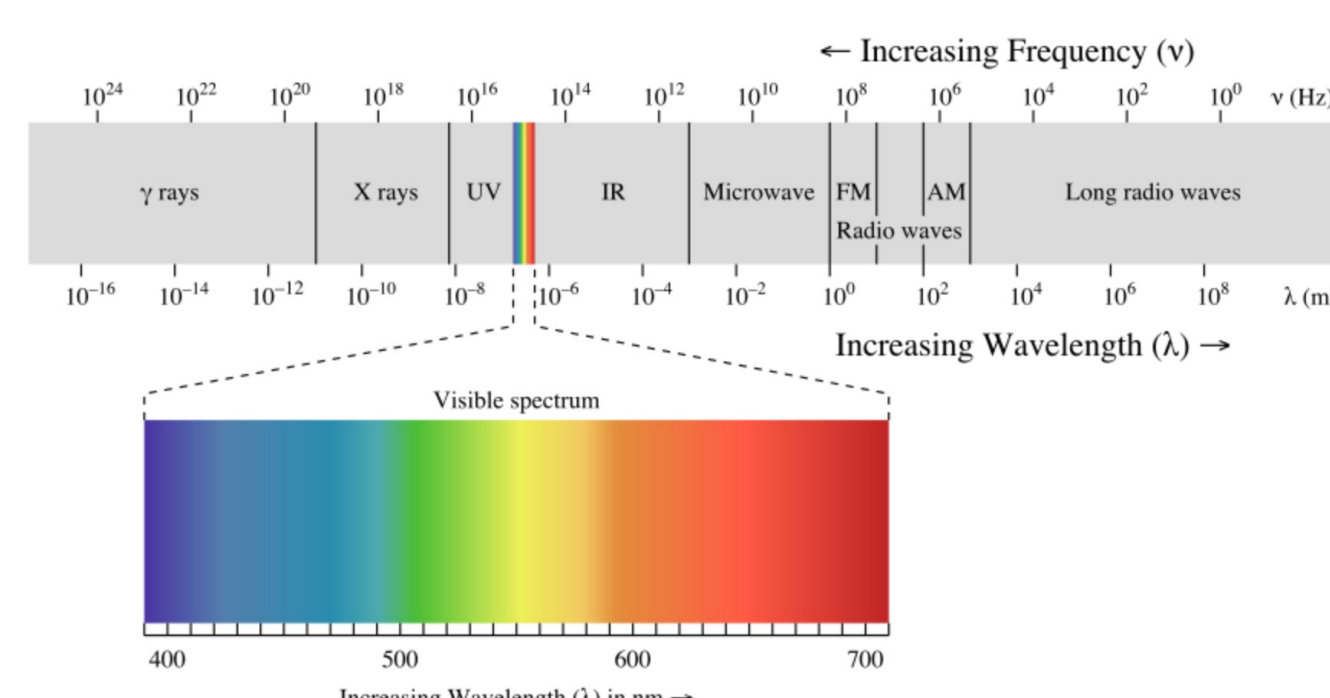


Figure 1. The Electromagnetic Spectrum

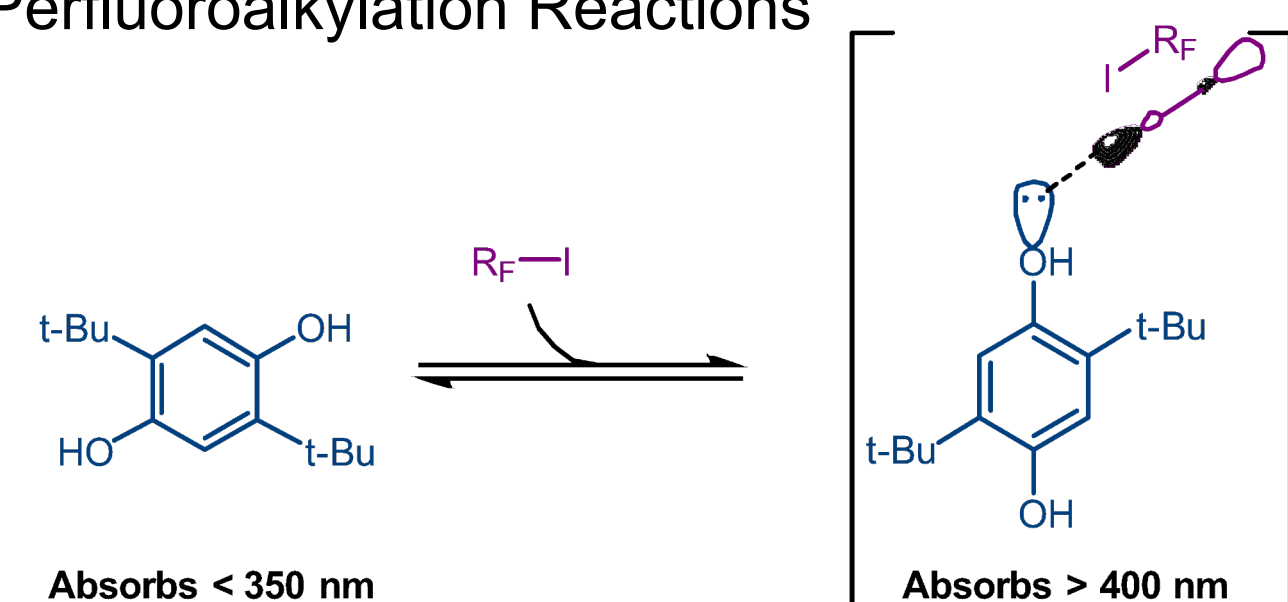
Charge-Transfer Complexes (CTCs)

- The generation of a new ground state aggregate by the association of an electron-rich substrate, also known as the donor, along with an electron-poor substrate, which is known as the acceptor

- The CTC (also known as Electron Donor-Acceptor Complex) is often able to absorb in the visible light region, whereas the individual substrates do not, providing an alternative strategy for performing visible-light-mediated reactions

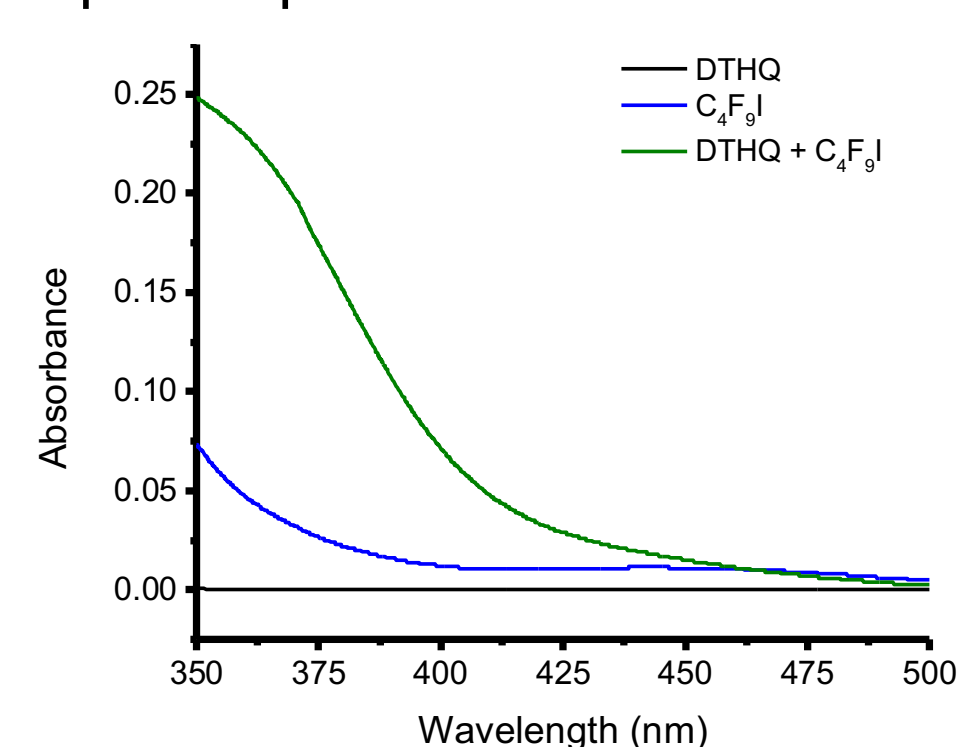
- In previous work, the Pitre Lab found that substituted hydroquinones are able to form a CTC with perfluoroalkyl iodides to promote the radical perfluoroalkylation of electron-rich (hetero)arenes

Scheme 2. Catalytic Halogen-Bonding Complex for Perfluoroalkylation Reactions



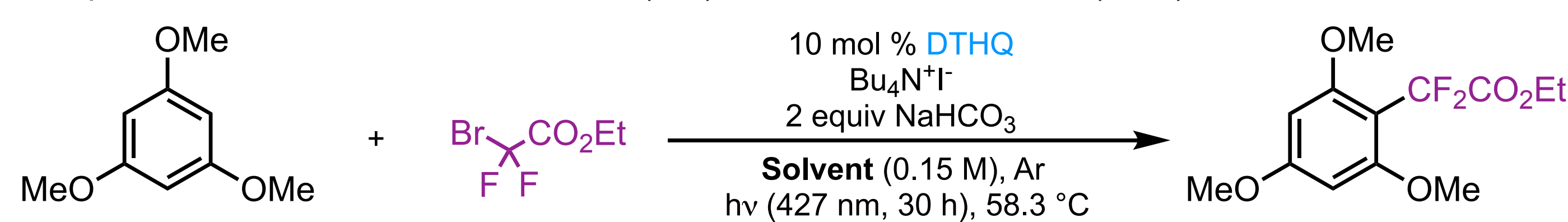
Tasnim, T.; Ryan C.; Christensen, M. L.; Fennell, C. J.; Pitre, S. P. *Org. Lett.* **2022**, *24*, 446–450.

Figure 4. Absorption Spectra Between DTHQ and C₄F₉I

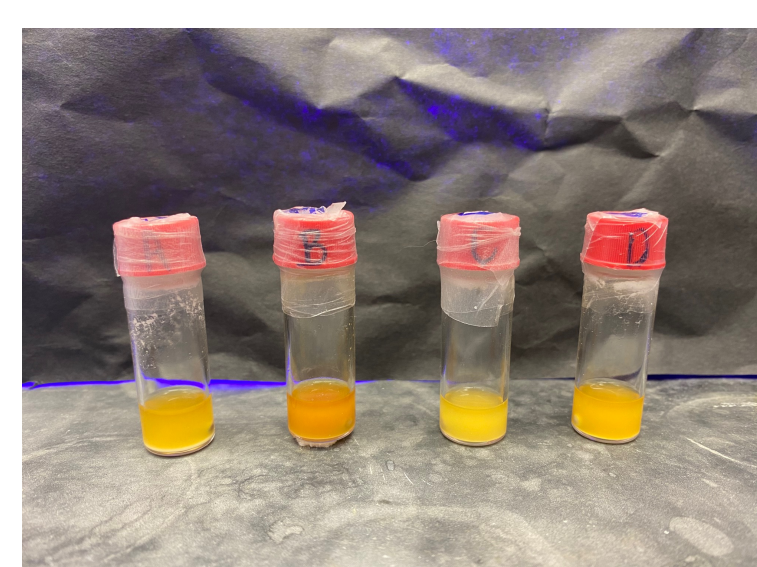
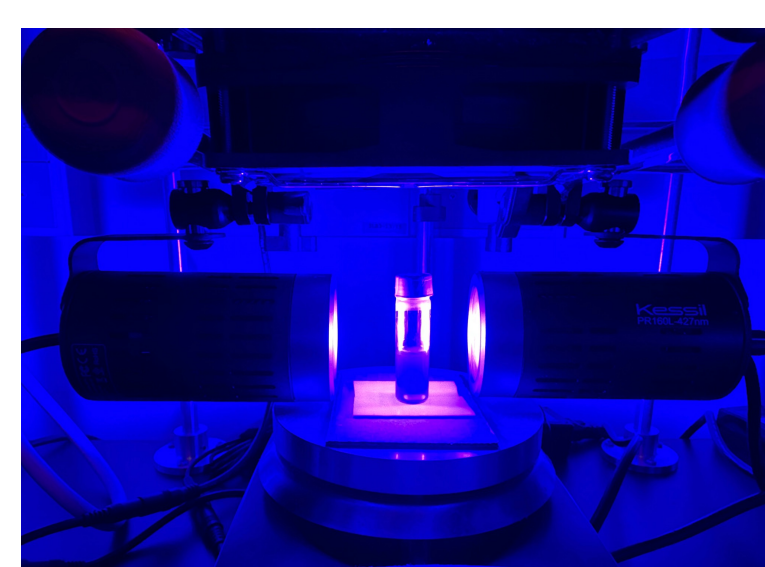


Reaction Optimization

Table 1. Optimization of Reaction Conditions (1-6) and Control Reactions (7-12)



Entry	Bu ₄ N ⁺ I ⁻	Solvent	Time (hours)	Yield
1	1 equiv	Acetone	30	84%
2	1 equiv	DMSO	30	Quantitative
3	20 mol%	DMSO	30	75%
4	20 mol%	DMSO	6	54%
5	20 mol%	DMSO	18	65%
6	20 mol%	DMSO	24	87%
7	-	DMSO	24	31% (without Bu ₄ N ⁺ I ⁻)
8	20 mol%	DMSO	24	26% (without Base/NaHCO ₃)
9	20 mol%	DMSO	24	22% (without degassing/ under air)
10	20 mol%	DMSO	24	Trace (without irradiation)
11	20 mol%	DMSO	24	11% (without DTHQ)
12	20 mol%	DMSO	24	89% (r. t.)



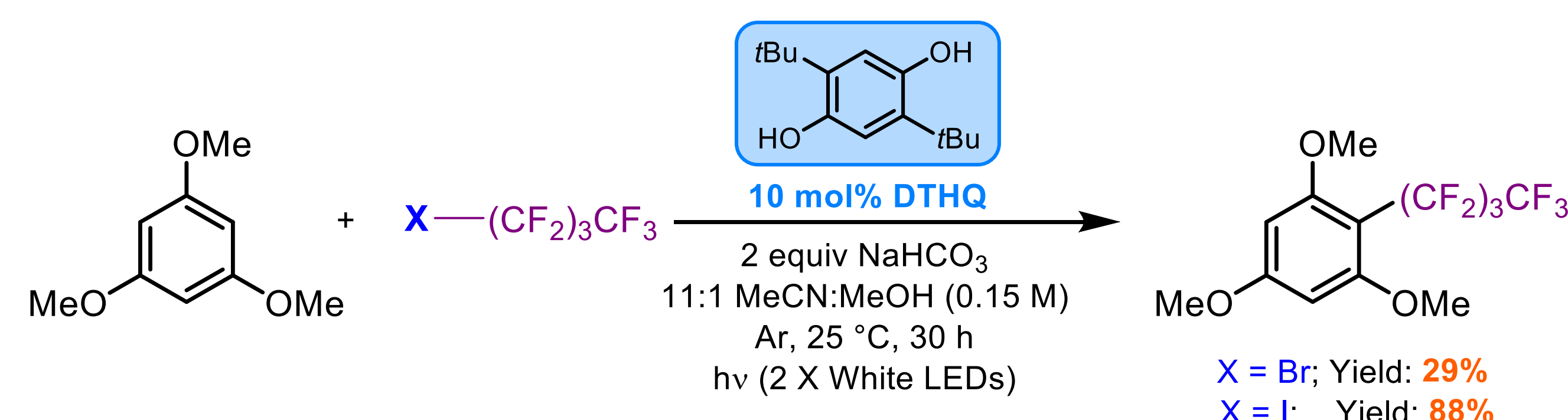
Halogen-Bonding

- A halogen bond occurs when there is evidence of a non-covalent interaction between an electrophilic halogen substituent and the Lewis base
- Halogen-based Lewis acid is the halogen-bond donor
- Lewis acid: a molecule that can accept a pair of electrons
- The interaction angle is approx. 180 degrees
- Strength of halogen bonding (X = I > Br > Cl > F)

- In previous work, perfluoroalkyl iodides resulted in higher yields compared to the corresponding bromides owing to bromides being less effective at forming halogen-bonds

- The goal of this work is to develop a method to engage alkyl bromides and chlorides using halogen-bonding photocatalysis by performing an *in situ* Finkelstein reaction with an iodide salt

Scheme 1. Perfluoroalkylation of (Hetero)arenes



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Figure 3. 180 Degree Interaction Angle

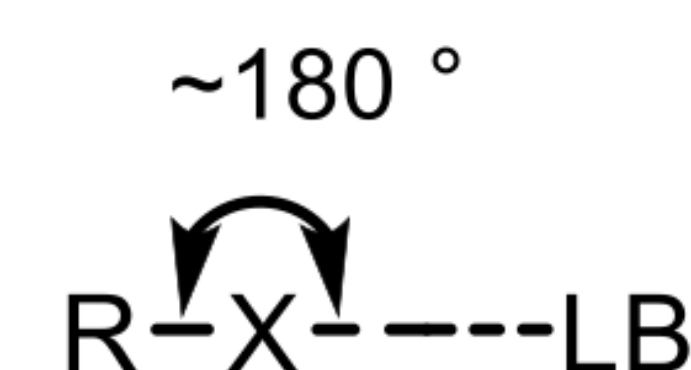
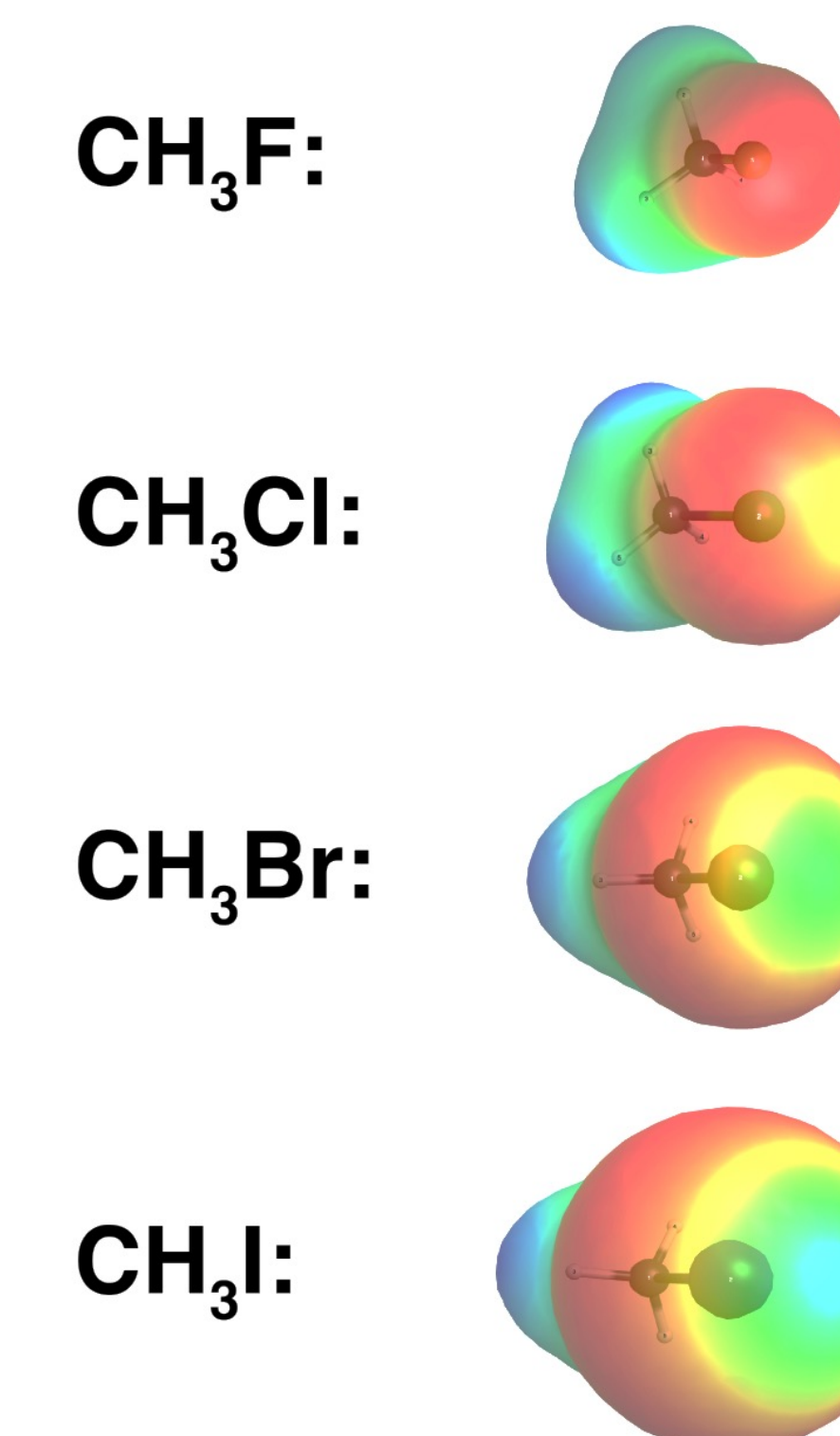


Figure 4. Sigma Hole Between Various Halogens



Proposed Mechanism

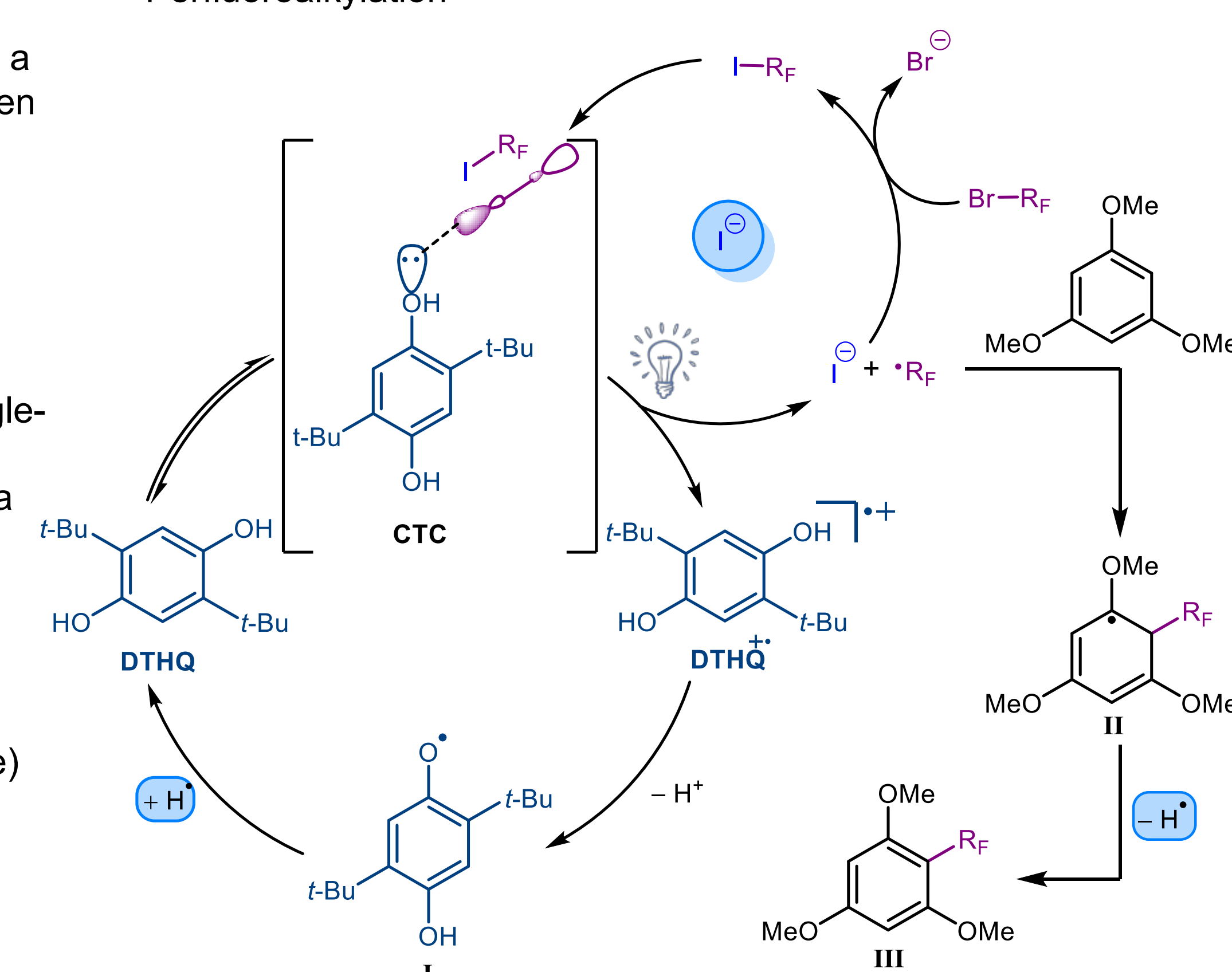
- The iodide salt and perfluoroalkyl bromide (Br-R_F) undergo a Finkelstein reaction (substitution reaction where one halogen is replaced by another). This gives off a bromide anion and generates R_F-I *in situ*.

- A CTC complex is formed initially between DTHQ and R_F-I through halogen-bonding interaction.

- The CTC is excited under 427nm irradiation leading to single-electron transfer, generating an R_F radical and a DTHQ radical cation which is subsequently deprotonated to form a phenoxy radical (I).

- Simultaneously, the R_F radical adds to electron-rich (hetero)arene to give the carbon-centered radical intermediate (II). This intermediate (II) undergoes a HAT reaction with (I) to yield the perfluoroalkylated hetero(arene) (III) and regenerate the DTHQ photocatalyst.

Scheme 3. Proposed Mechanism for the DTHQ-catalyzed Radical Perfluoroalkylation



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Conclusions and Future Directions:

- The addition of an iodide salt allows access to alkyl bromide substrates, typically poor halogen-bond donors, through a Finkelstein reaction to generate the corresponding alkyl iodide *in situ*
- Future directions include examining the substrate scope in regards to both the (hetero)arene and alkyl bromides and also extending this work to the activation of alkyl chlorides

Acknowledgements

