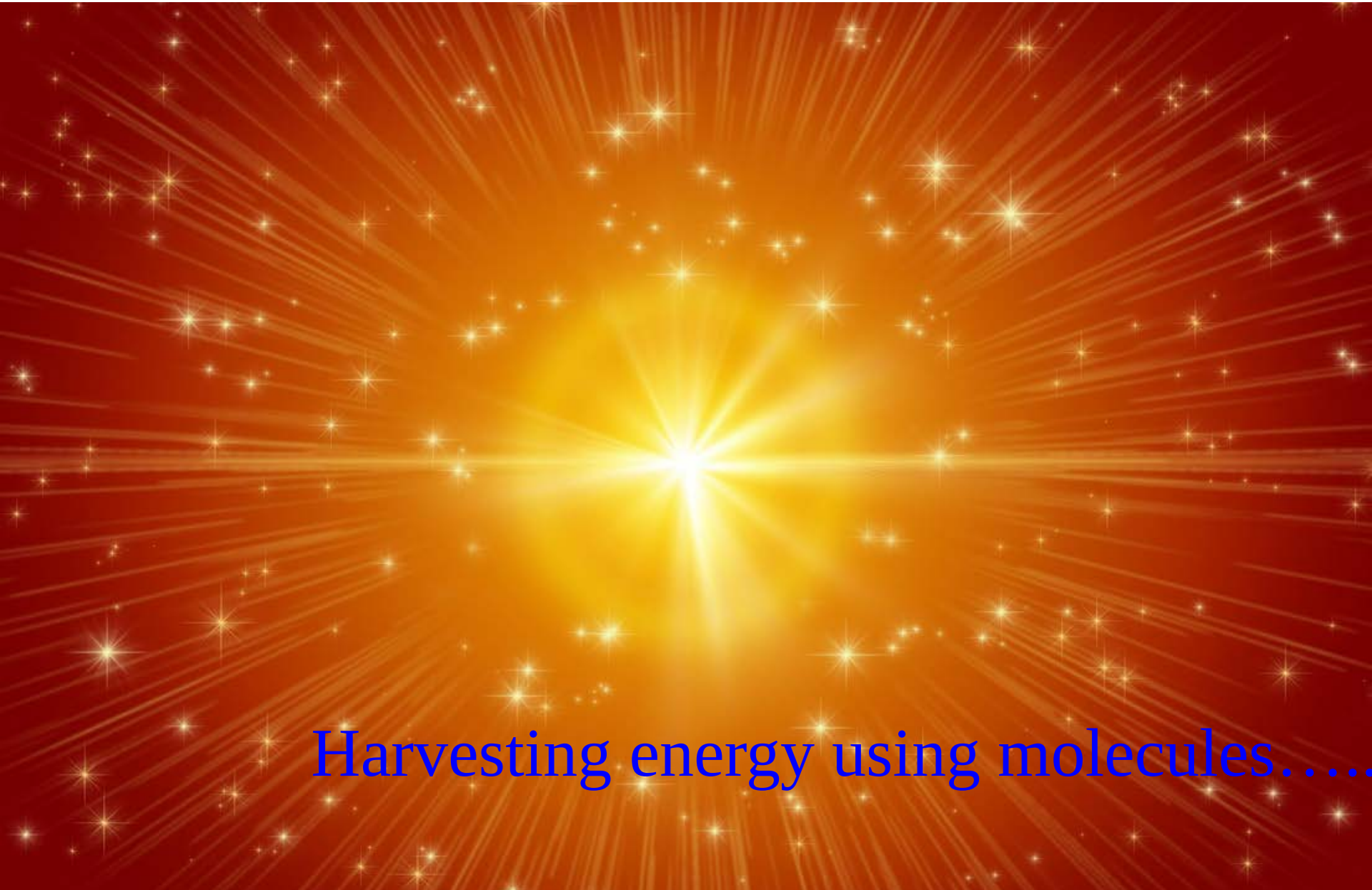
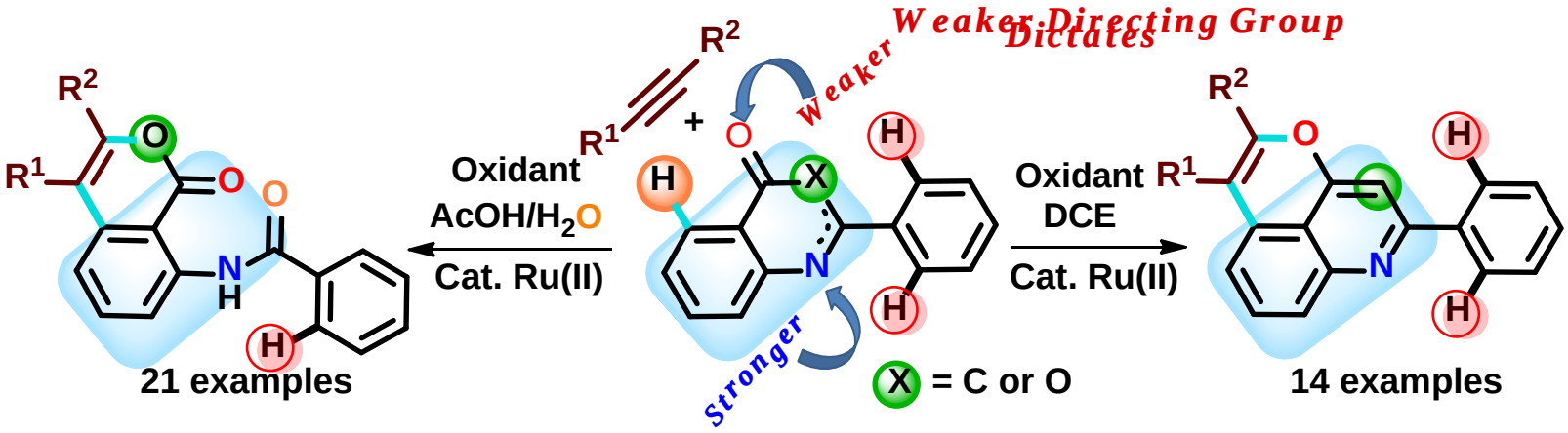
FLUORESCENT, AIEGEN AND CYTOTOXIC BEHAVIOUR OF ANNULATED POLCYCLIC HETEROAROMATICS

BHISMA K. PATEL

Light Emission: A useful yet mysterious process to the humankind……



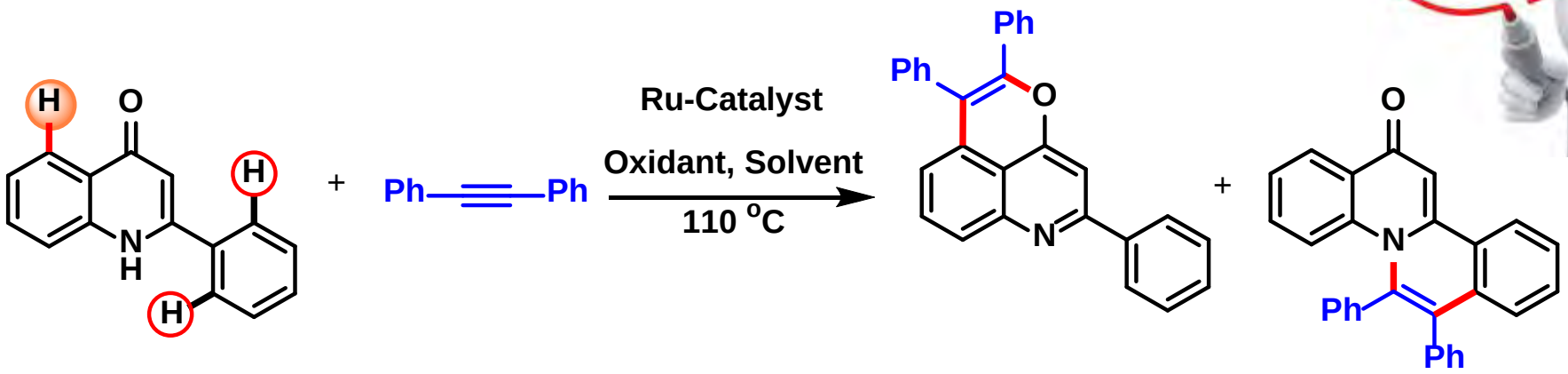
C–H/O–H Annulations of Directing Arenes *via* Weak Coordination



Org. Lett. **2015**, *17*, 5678

ACS Editors" Choice

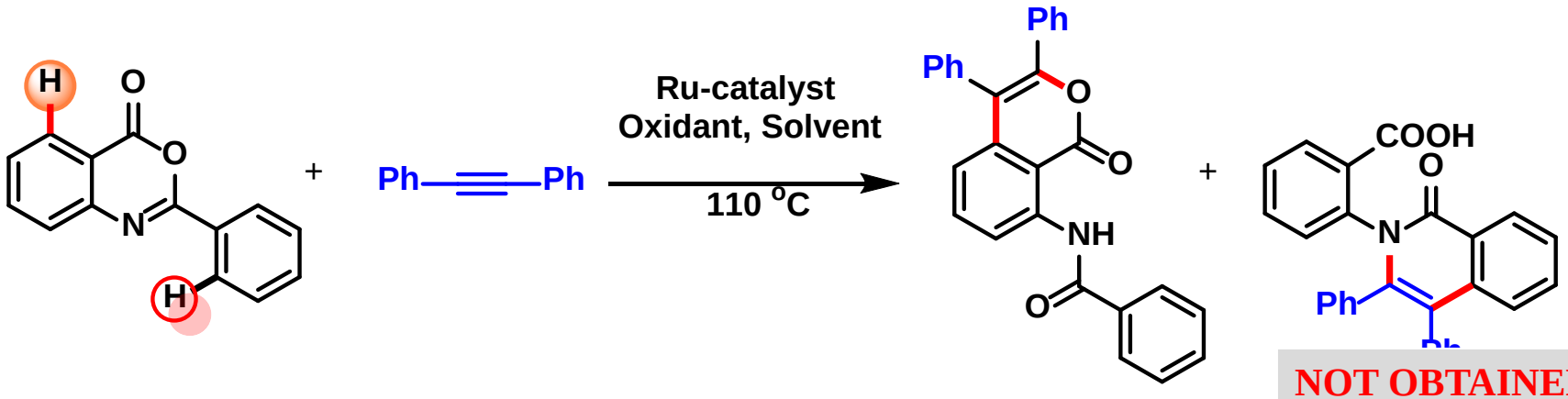
Substrate Controlled Convergent Annulation



NOT OBTAINED

Optimized Condition:

$[Ru(p\text{-cymene})Cl_2]_2$ (2.0 mol %), $Cu(OAc)_2$ (1.2 equiv), DCE, 110 °C

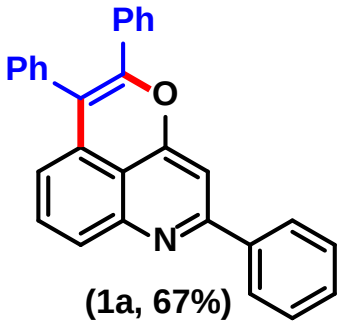


NOT OBTAINED

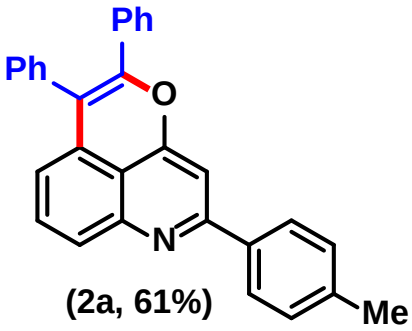
Optimized Condition:

$[Ru(p\text{-cymene})Cl_2]_2$ (2.0 mol %), AgOAc (1.2 equiv), AcOH, 110 °C

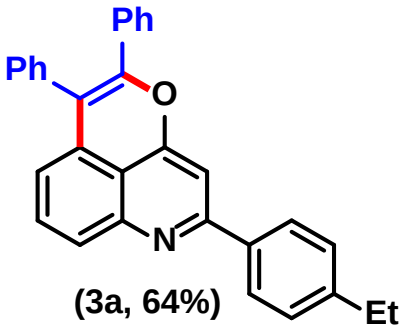
Scope of 2-Arylquinolinone for C–H/O–H Annulation



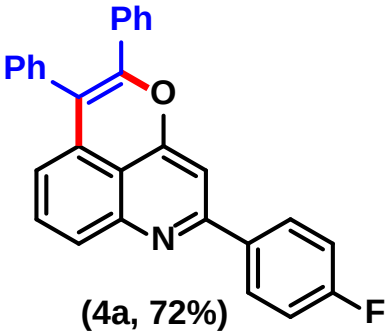
(1a, 67%)



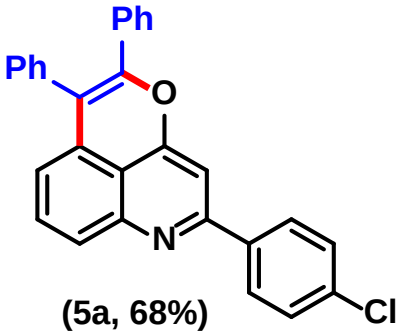
(2a, 61%)



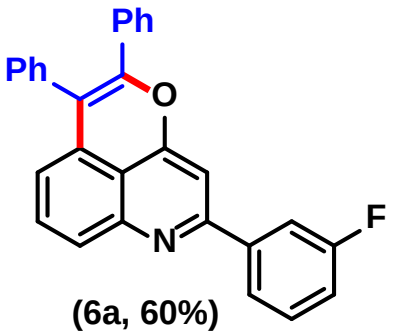
(3a, 64%)



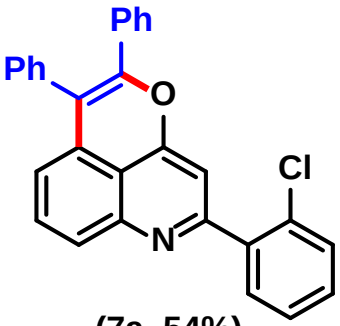
(4a, 72%)



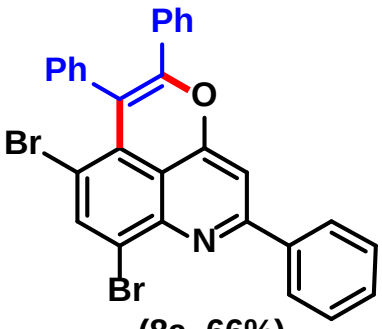
(5a, 68%)



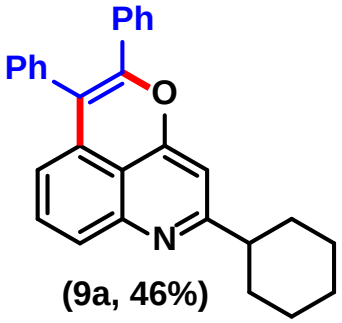
(6a, 60%)



(7a, 54%)

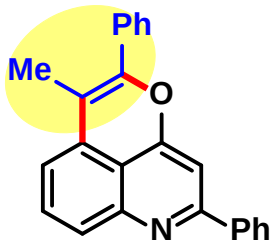


(8a, 66%)

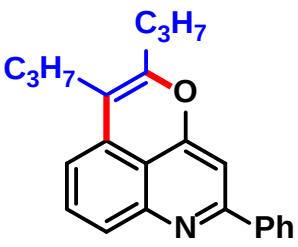


(9a, 46%)

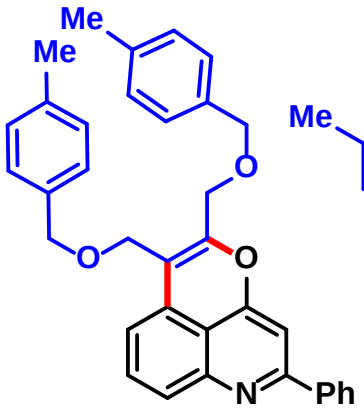
Scope of Alkynes for Annulation with 2-Phenylquinolinone



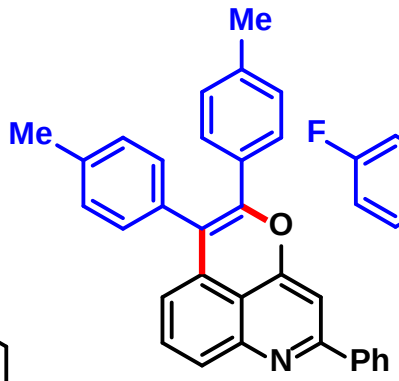
(1b, 71%)



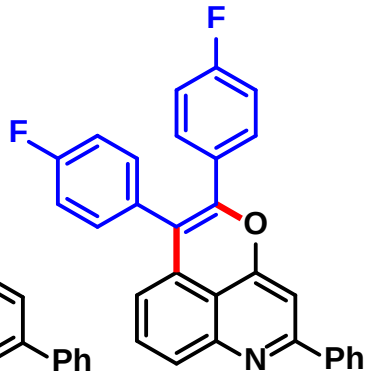
(1c, 59%)



(1c, 51%)

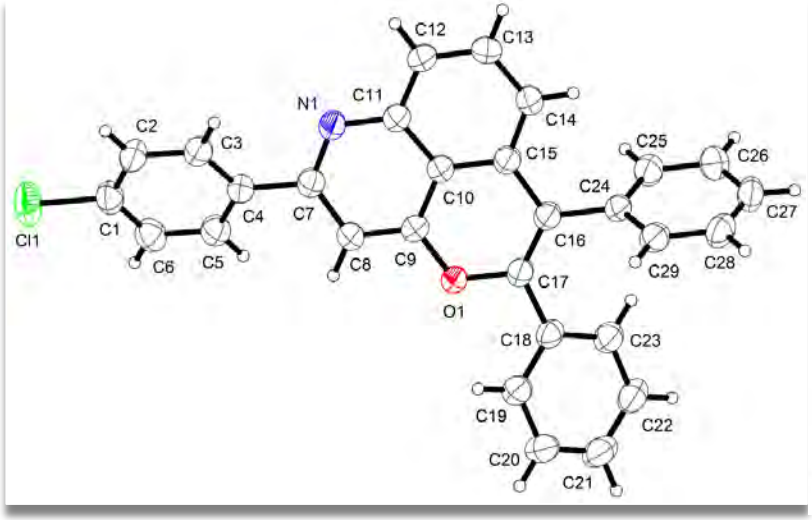


(1d, 70%)



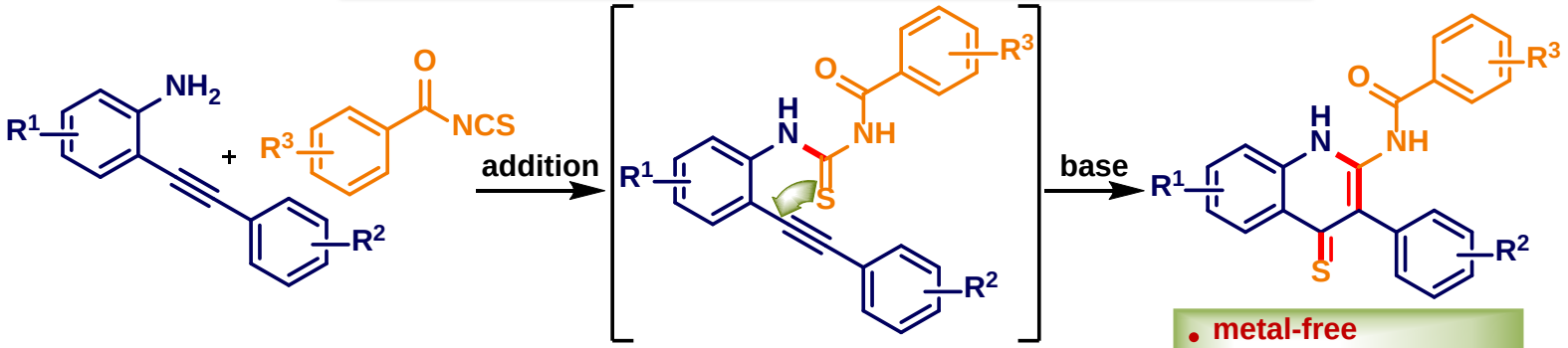
(1e, 77%)

Crystal structure:

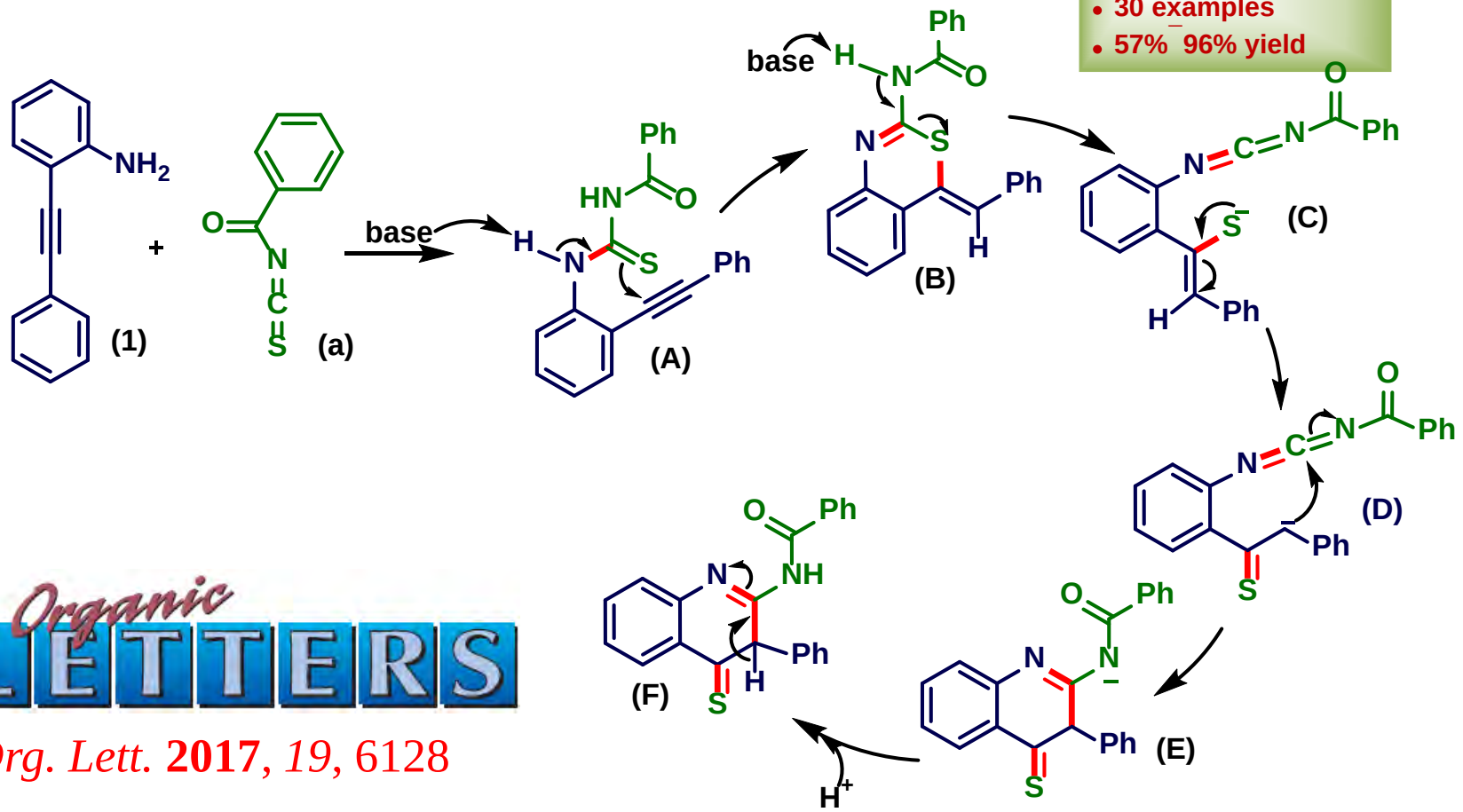


ORTEP view of 5a

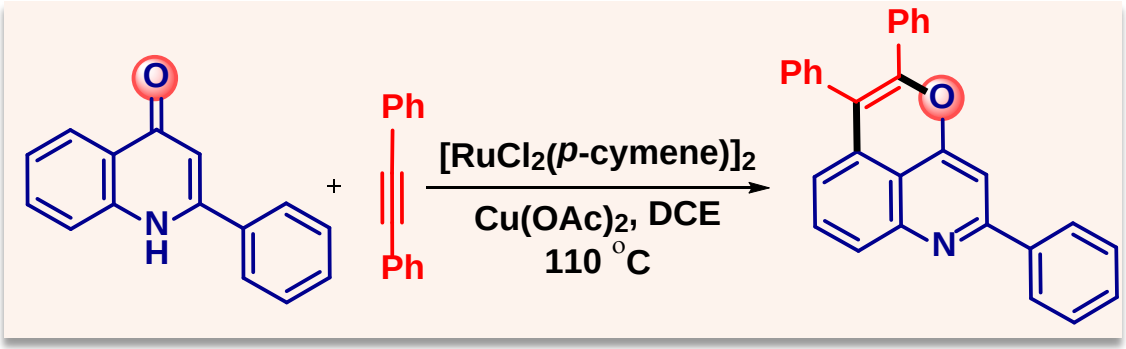
Synthesis of Quinoline-4(1*H*)-thiones



- metal-free
- 100% atom economy
- 30 examples
- 57% – 96% yield



Org. Lett. **2017**, *19*, 6128



Weak co-ordinating site dominates over the strong

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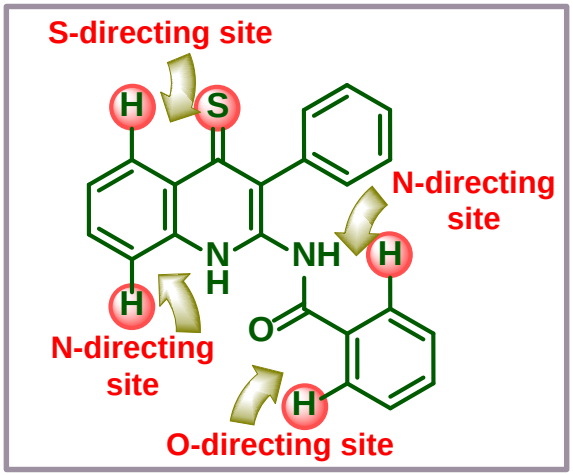
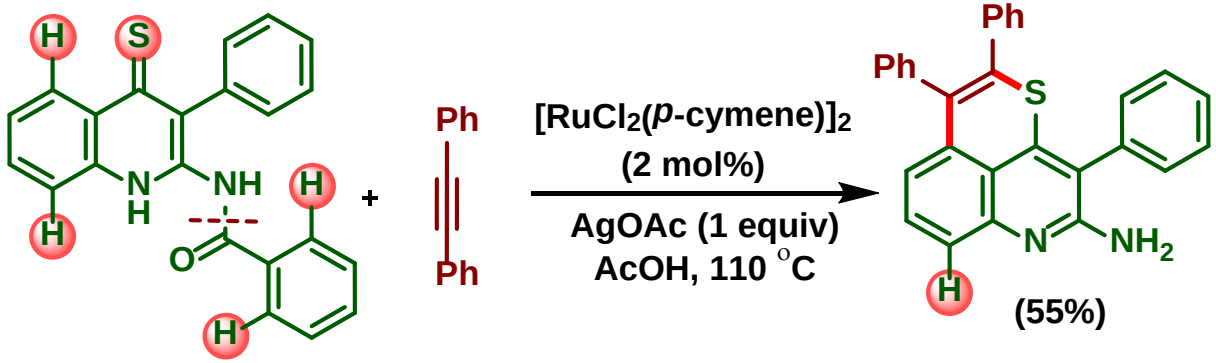
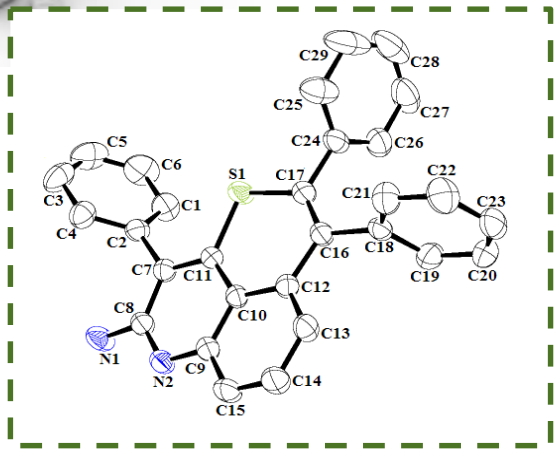


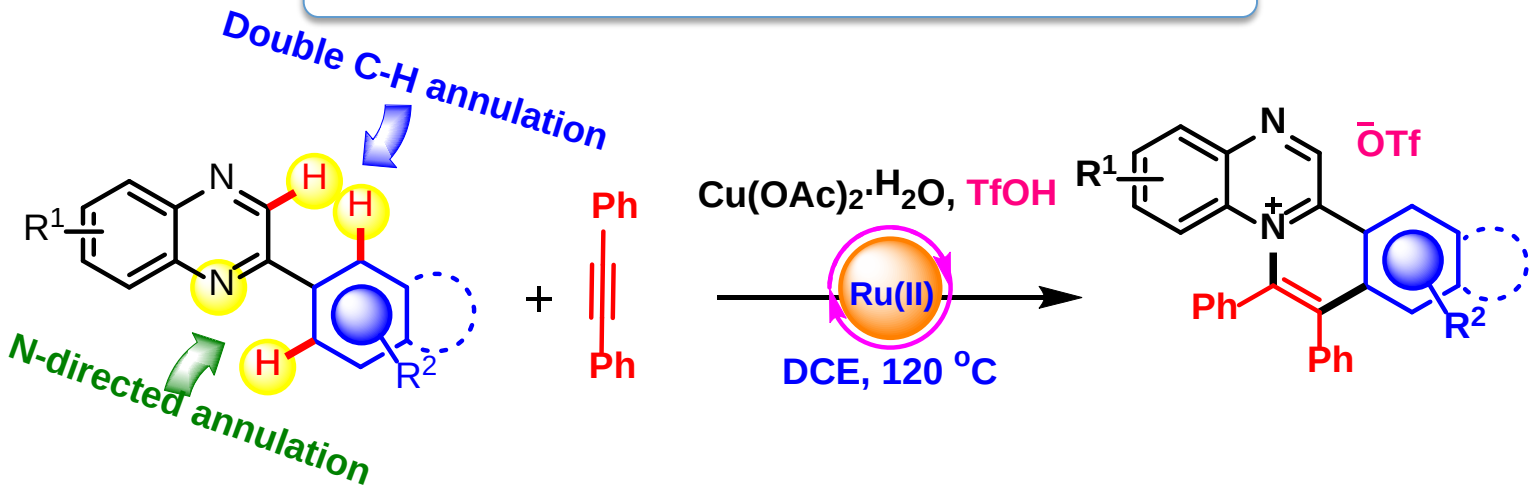


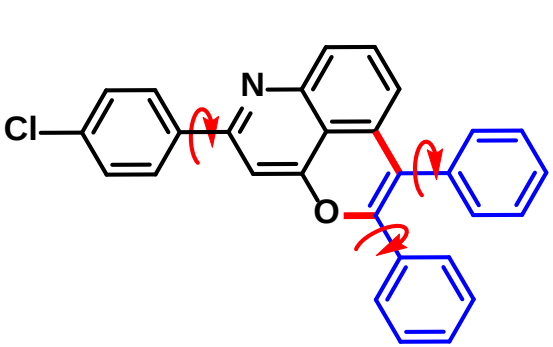


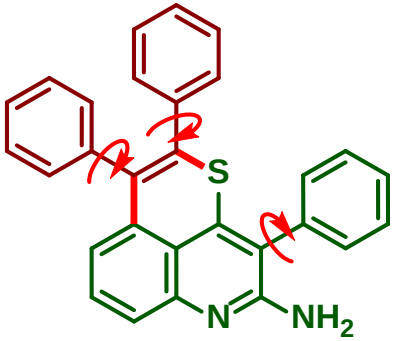
Again Weak Coordination Dictates.

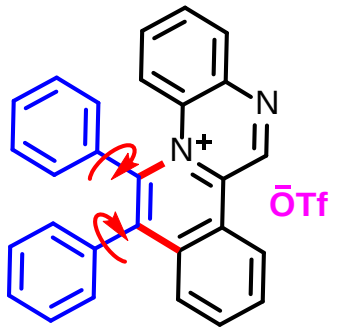
The first example of C-H, S-H annulation

Heteroarene Directed Annulations

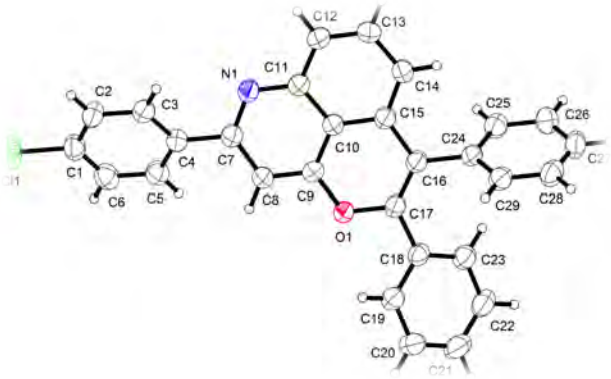


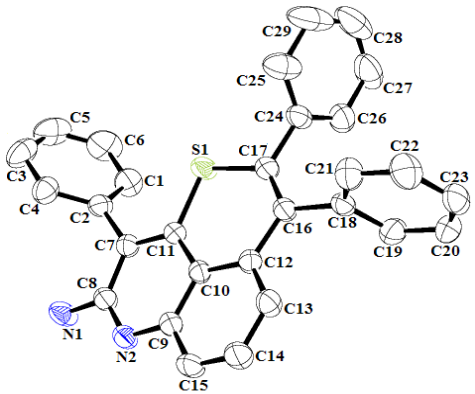


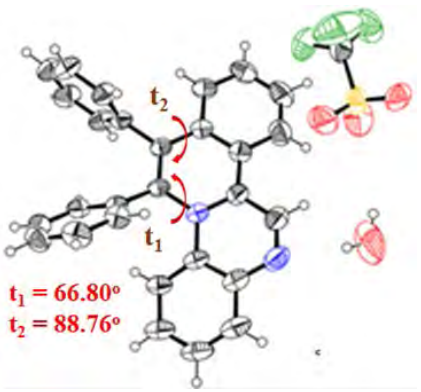


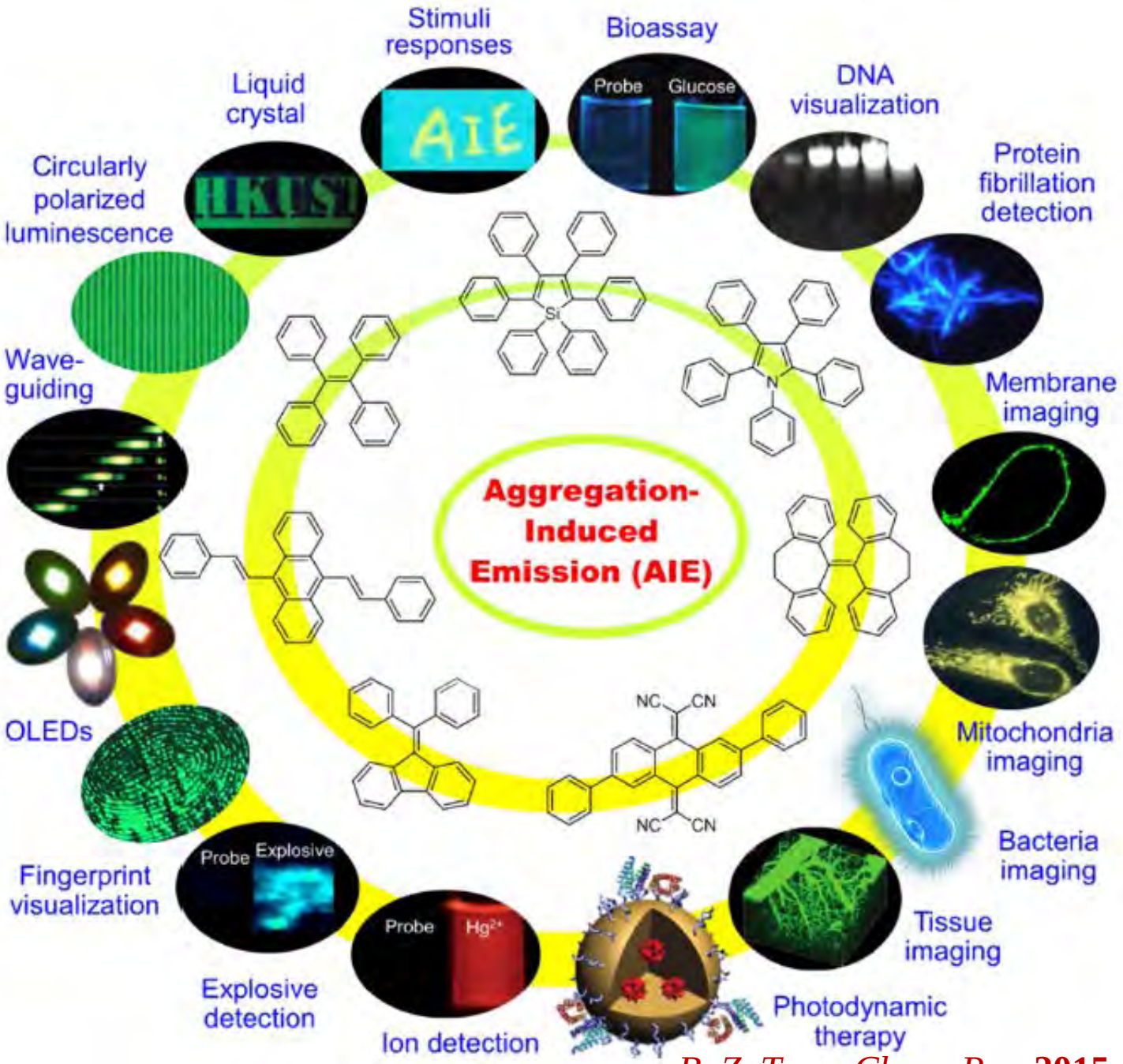


HIGHLY FLUORESCENT MOLECULES









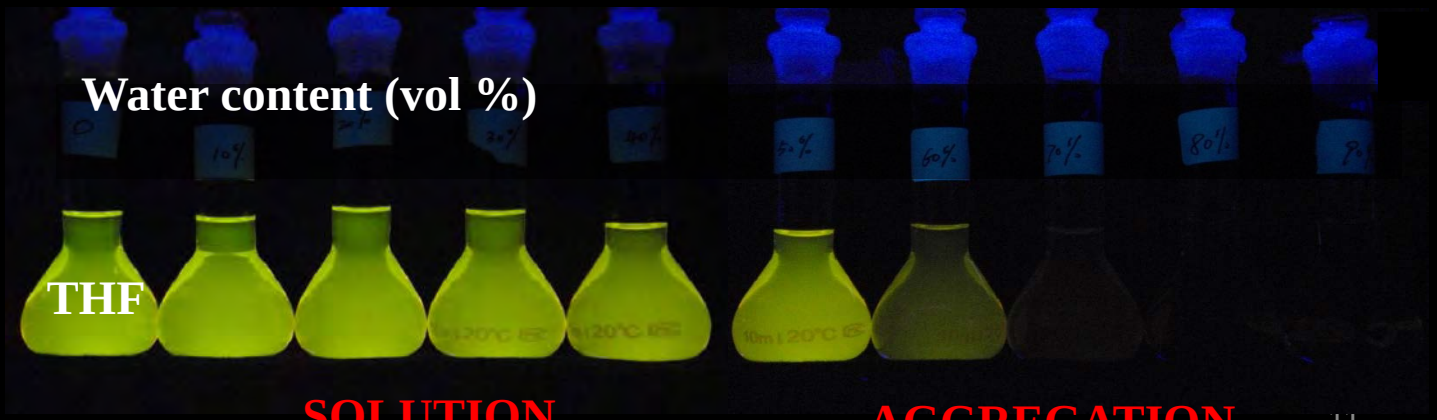
B. Z. Tang, Chem. Rev. **2015**, *115*, 11718

An Issue in the Field

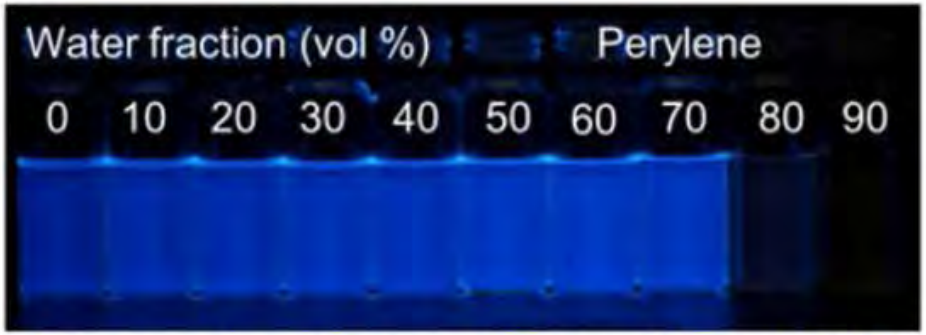
Concentration Cause Quenching

- First discovered by Förster in 1954
- Now a general belief in the area

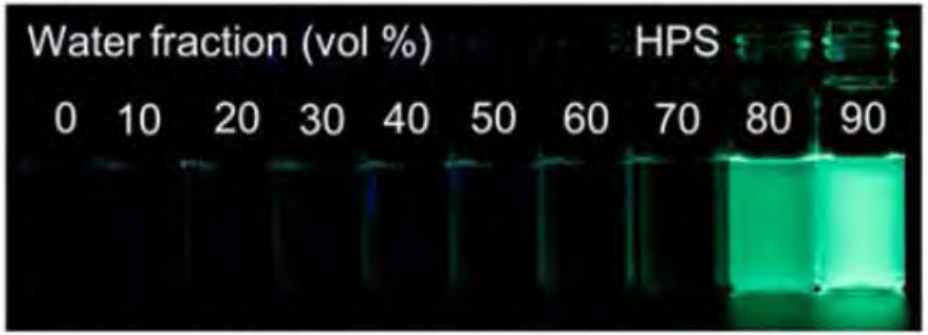
- A molecule quenches its own fluorescence at high concentration, partially due to **aggregate** formation (hence aggregation-caused quenching or ACQ).
- **Common** organic dyes show marked concentration quenching effects.



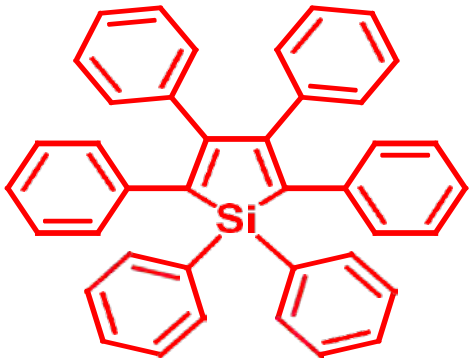
An Anti-ACQ Photophysical Phenomenon



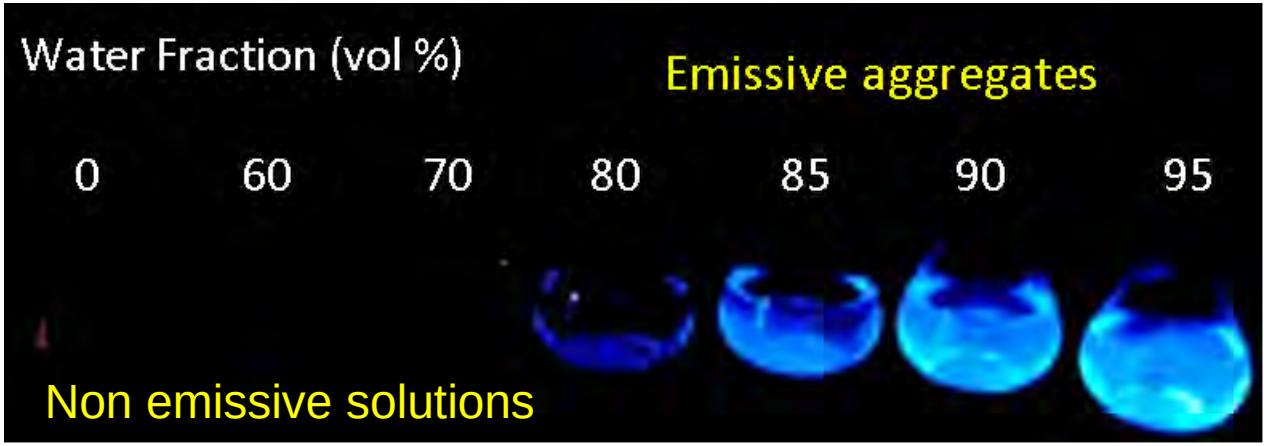
Aggregation-Caused Quenching (ACQ)



Aggregation-Induced Emission (AIE)

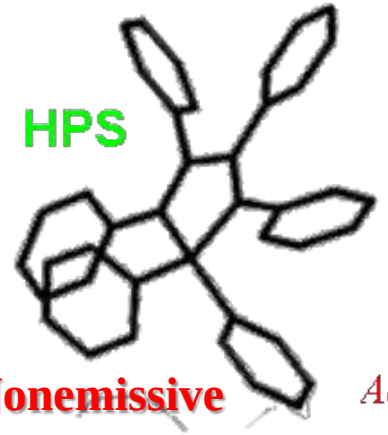


1,1,2,3,4,5-Hexaphenylsilole (HPS)



B. Z. Tang, Chem. Commun. **2001**, 1740

Restriction of Intramolecular Rotations (RIR)



Nonemissive

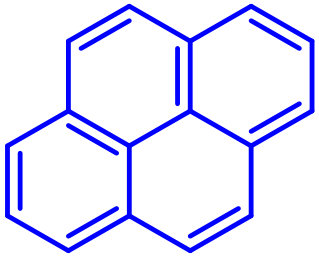
Restriction of intramolecular Rotations (RIR)

AIE

Acc. Chem. Res. **2013**, *46*,

Emissive (on)

- Dynamic intramolecular rotations in the solution state
- Intramolecular motions restricted in the aggregate state
- Propeller-shape prevents π-π interaction in the aggregates



Emissive

π-stacking interactions

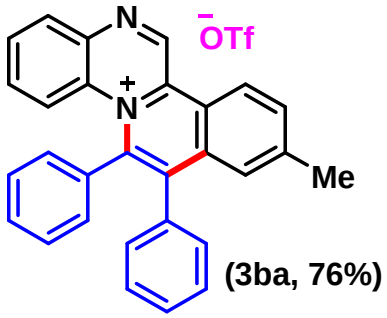
Aggregation caused quenching (ACQ)

Nonemissive (off)

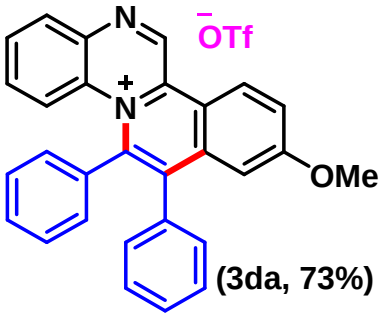
Emissive (on)

Pol-AIE **Pol-AIEE** **Pol-ACQ**

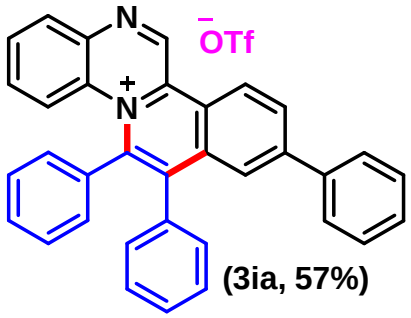
Representative Examples



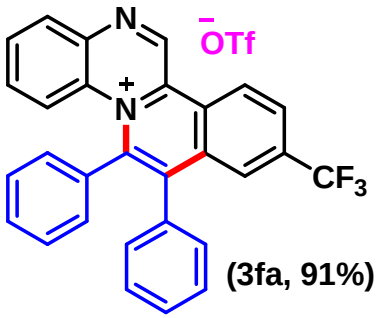
(3ba, 76%)



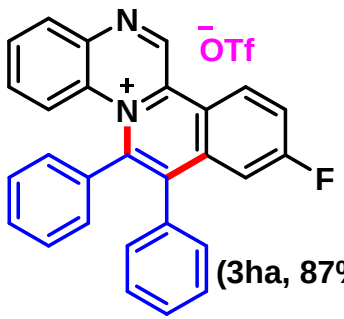
(3da, 73%)



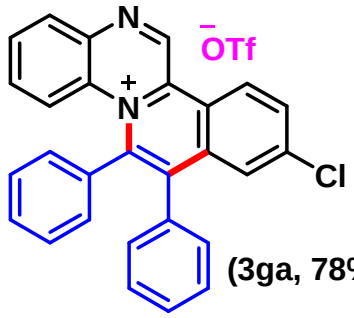
(3ia, 57%)



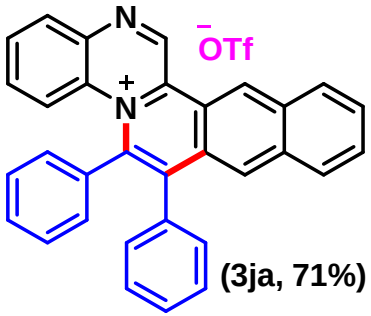
(3fa, 91%)



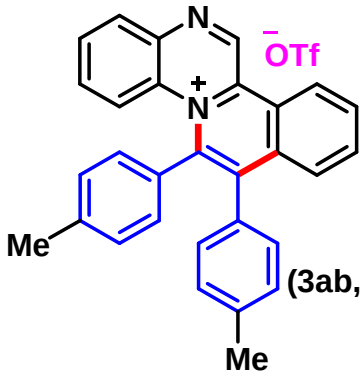
(3ha, 87%)



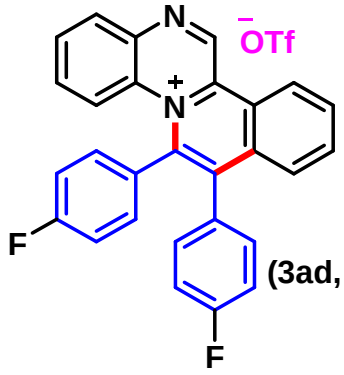
(3ga, 78%)



(3ja, 71%)

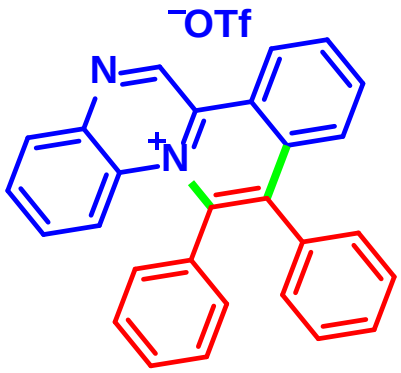


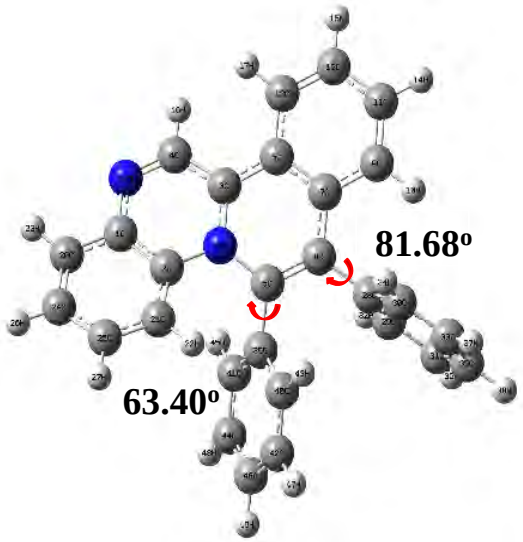
(3ab, 71%)



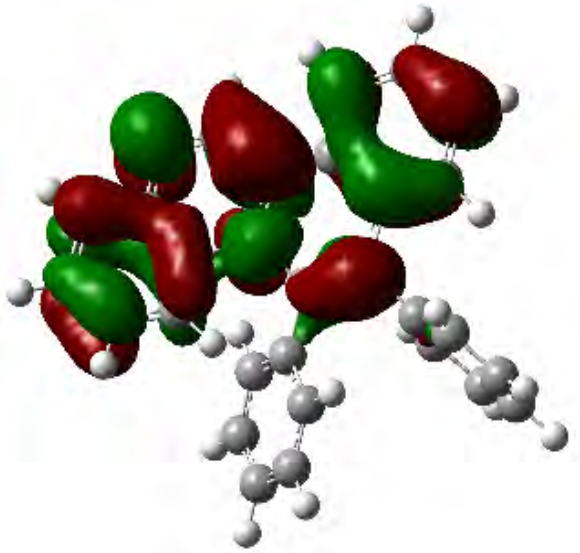
(3ad, 80%)

Theoretical Investigations



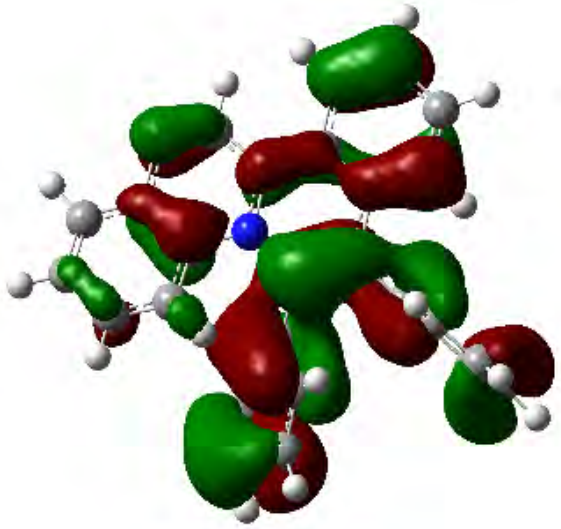


E_{LUMO} = -3.48 eV



$\Delta E_{(LUMO - HOMO)}$ = 3.30 eV

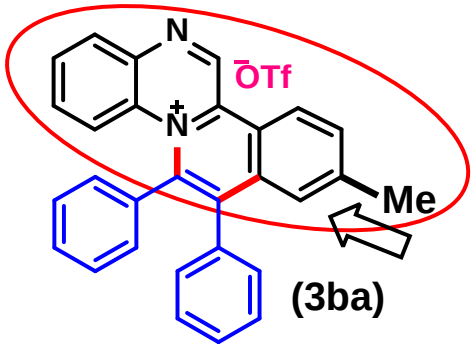
E_{HOMO} = -6.78 eV



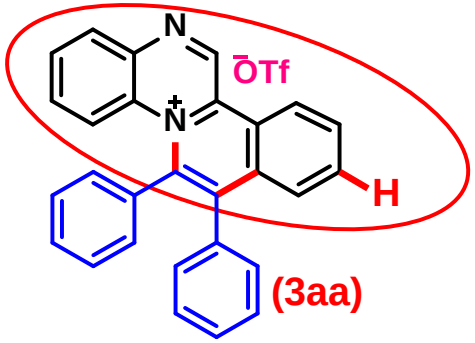
Geometry and electronic structure calculated using B3LYP/6-31G(d,p) level basic set using Gaussian 09

Can the Colour be Tuned?

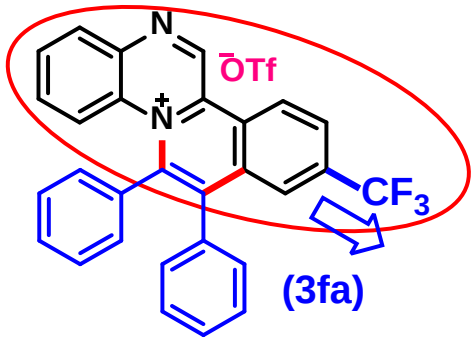
Substituents on the LUMO



(3ba)



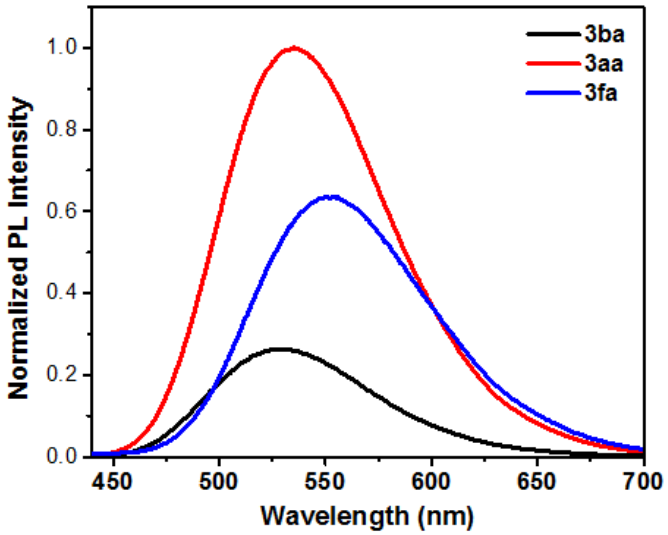
(3aa)

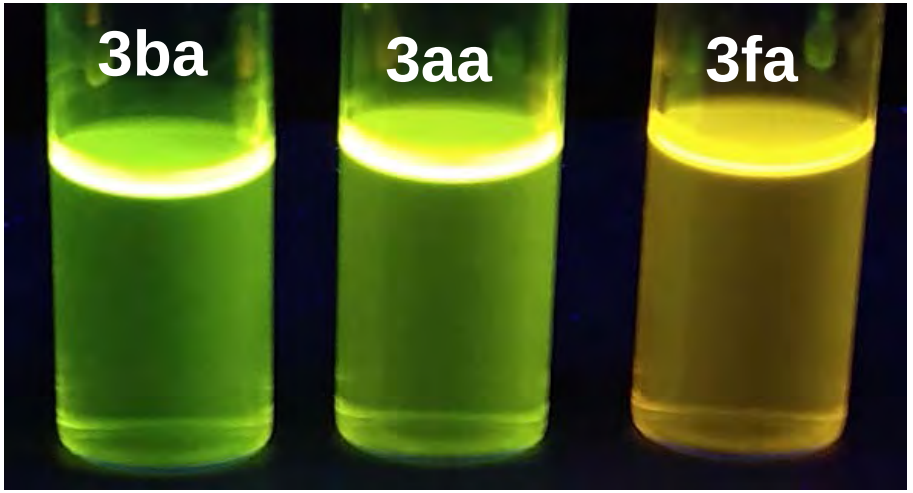


(3fa)

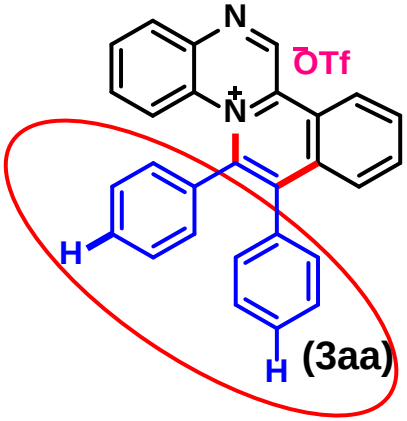
$\Delta E_{(LUMO-HOMO)}$ = 3.36 > 3.30 > 3.22 eV

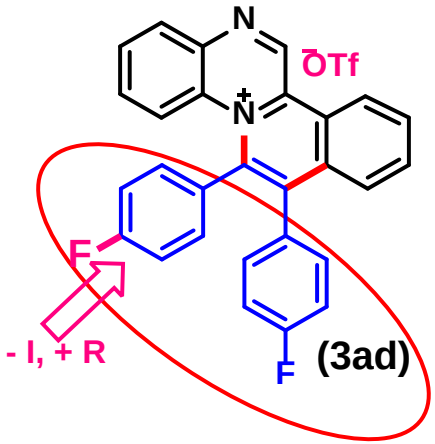
$\lambda_{max,em}$ = 529 < 535 < 554 nm

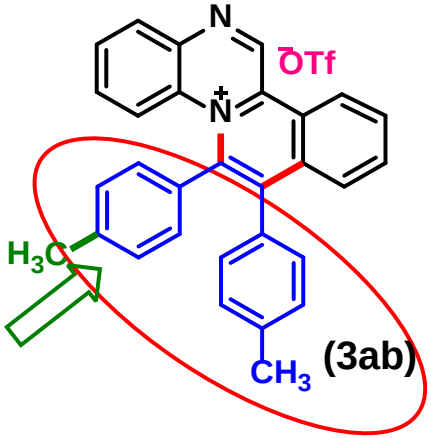




Substituents on the HOMO

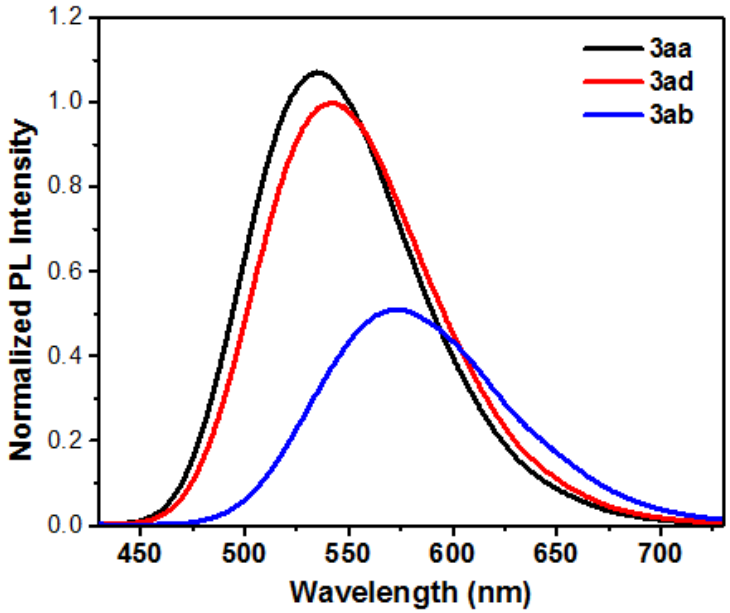


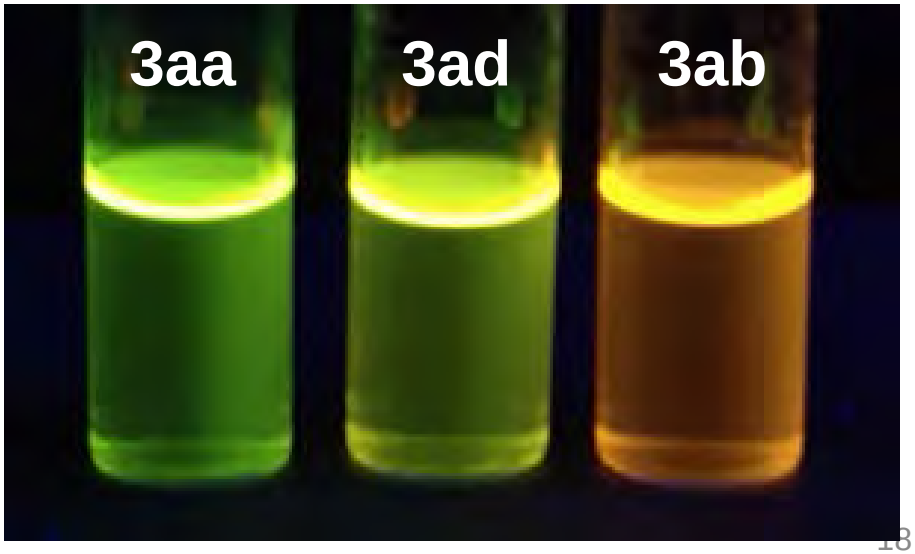




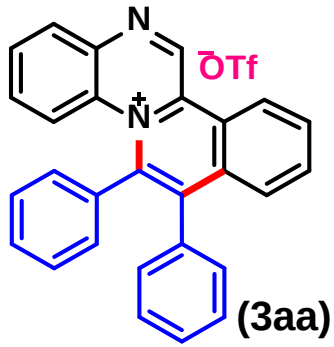
$\Delta E_{(LUMO-HOMO)}$ = **3.30** > **3.21** > **3.09 eV**

$\lambda_{max,em}$ = **535** < **542** < **571 nm**

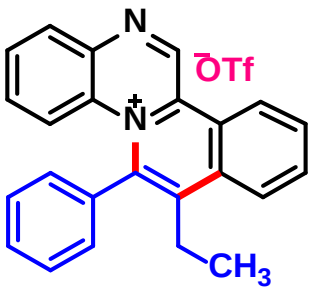




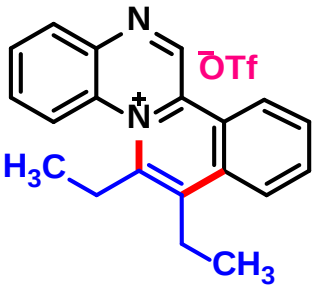
Replacement of Phenyl with Alkyl Group



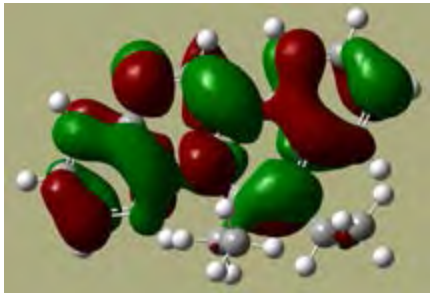
(3aa)

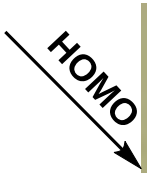


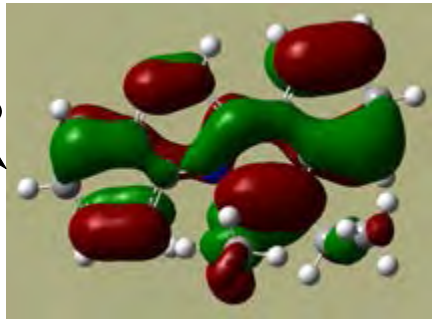
(3ag)



(3ah)

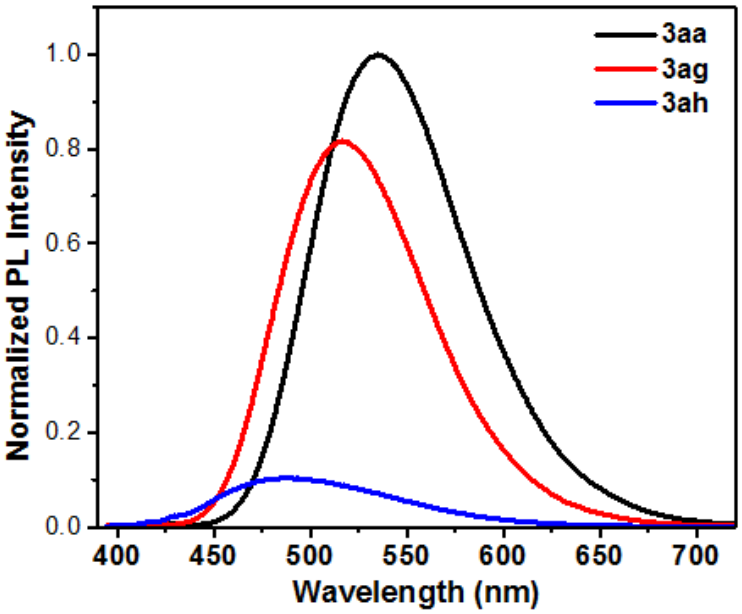






$\Delta E_{(LUMO-HOMO)}$ = 3.30 < 3.43 < 3.48 eV

$\lambda_{max,em}$ = 535 > 515 > 488 nm



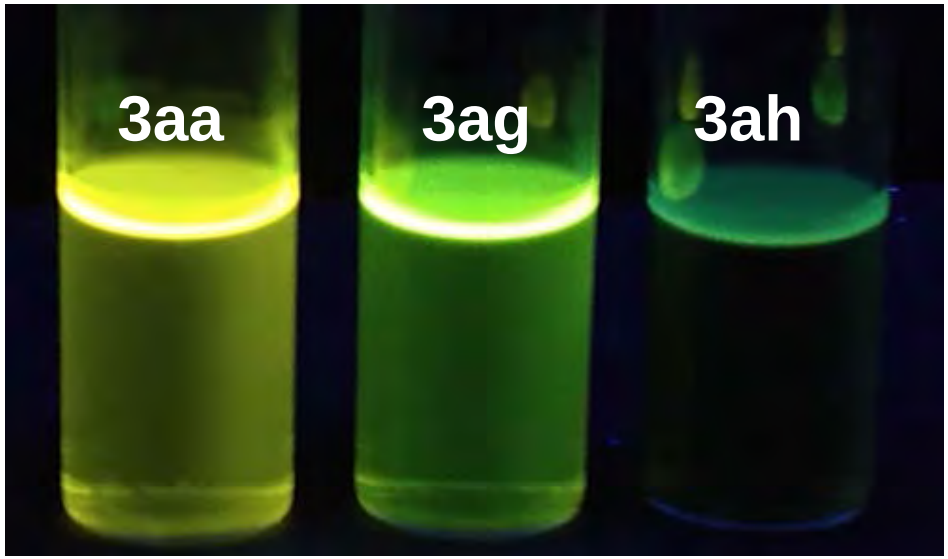
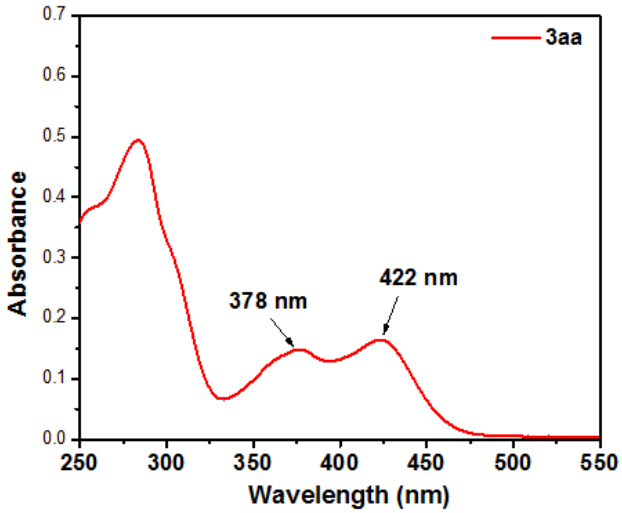
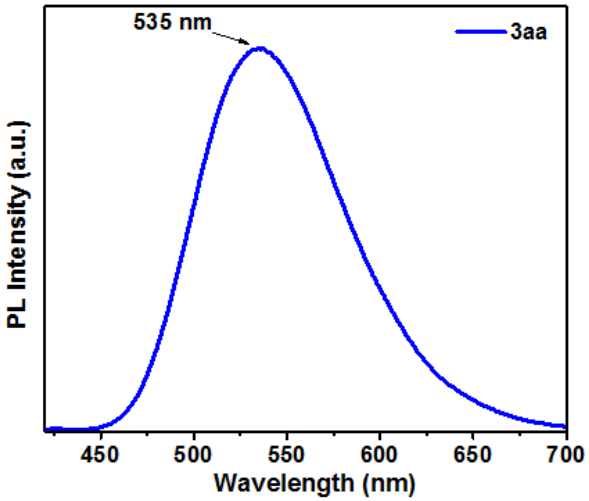
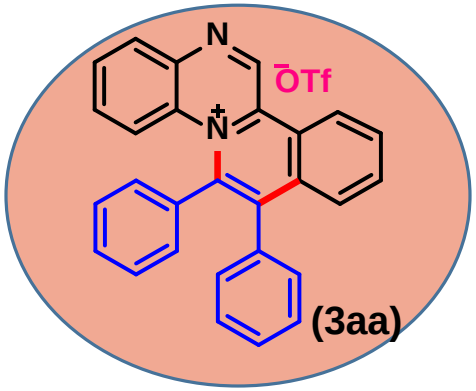
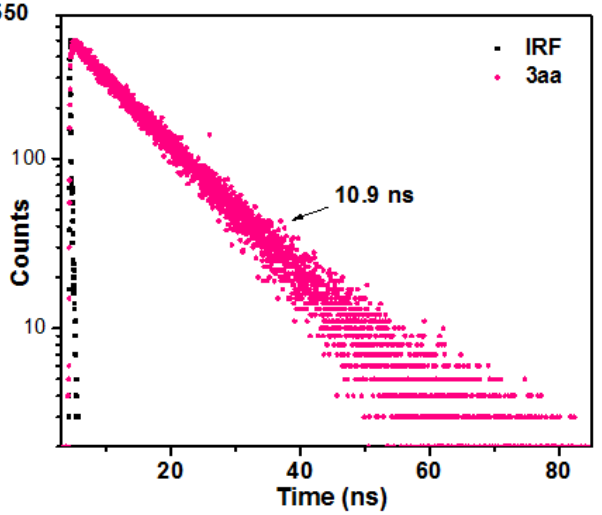


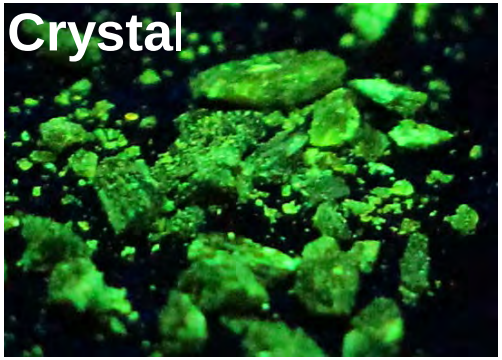
Photo Physical Properties

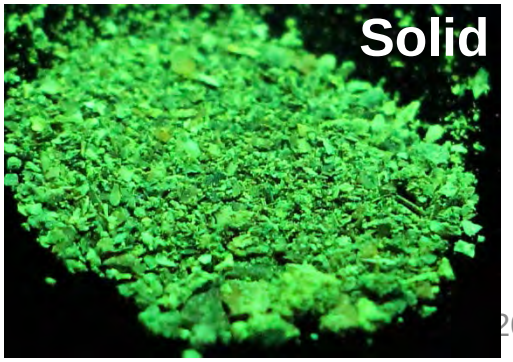




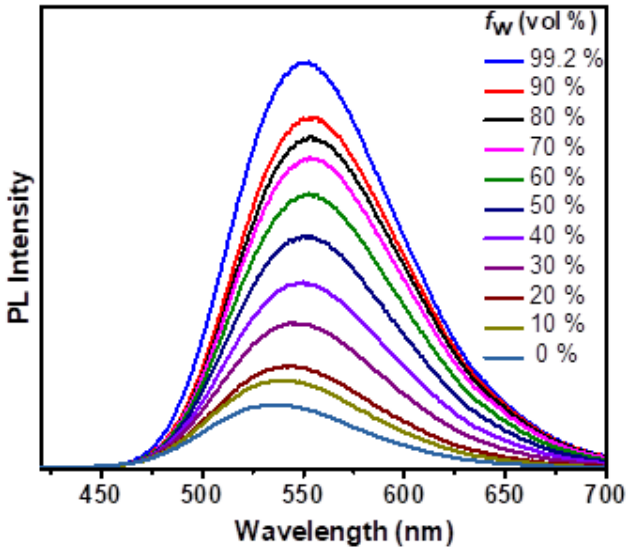




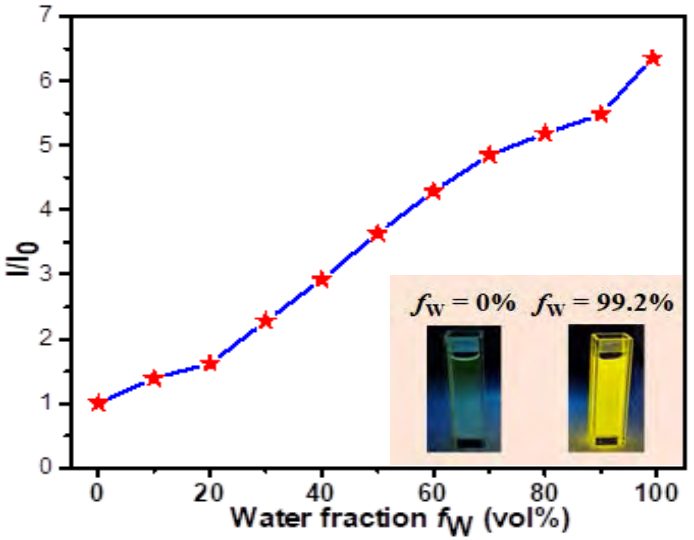




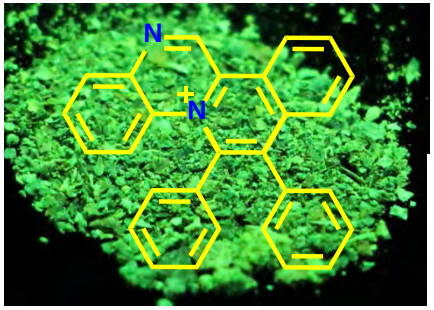
AIEE Investigation

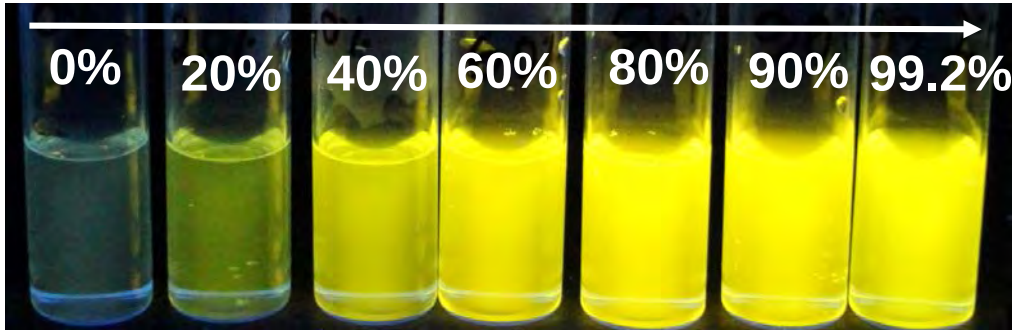


PL titration with varying f_W in DMF

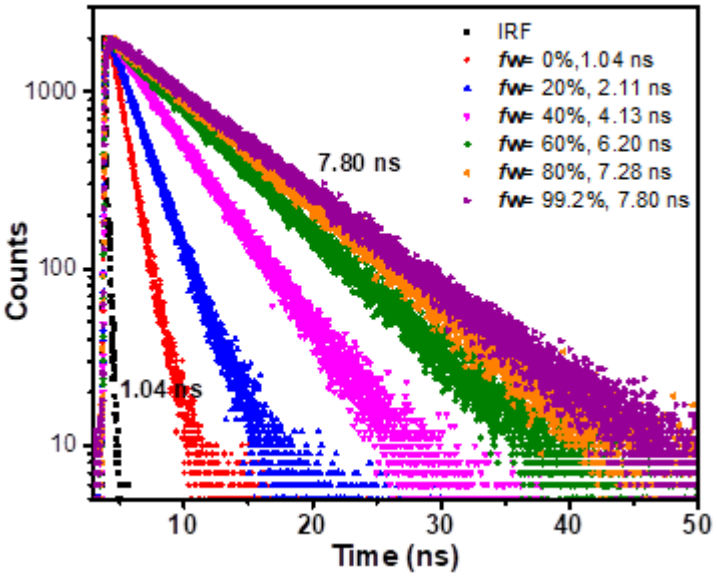


Relative intensity versus f_W in DMF



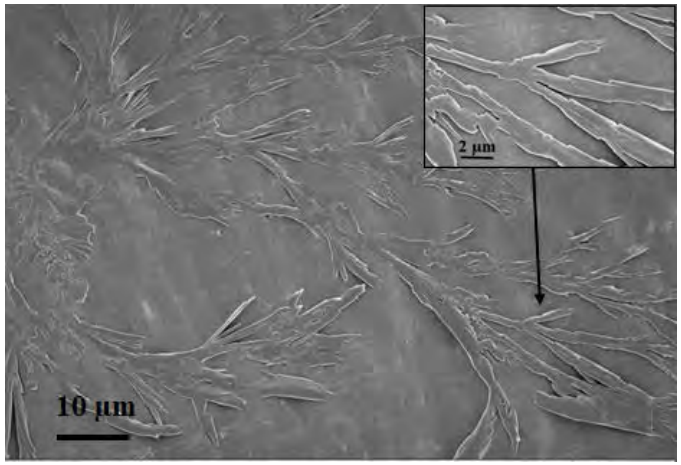


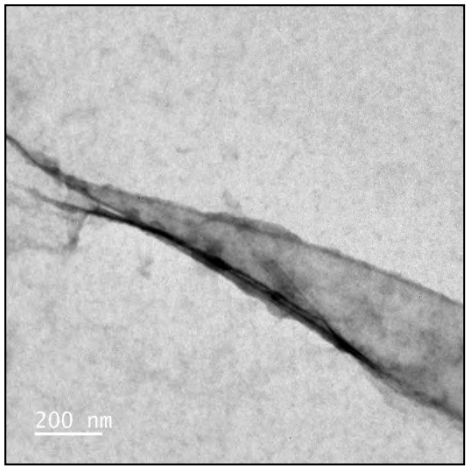
Fluorescence photographs in DMF/water at 365 nm

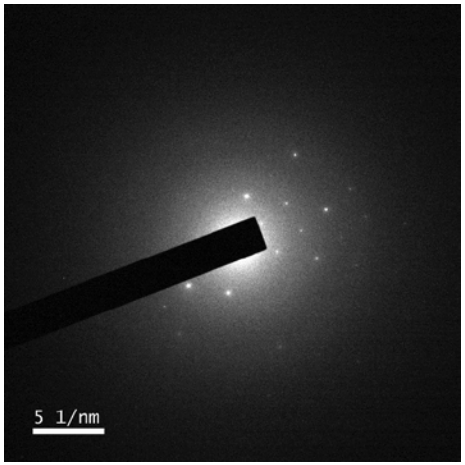


TRPL spectra with varying f_W in DMF

Morphological Investigation

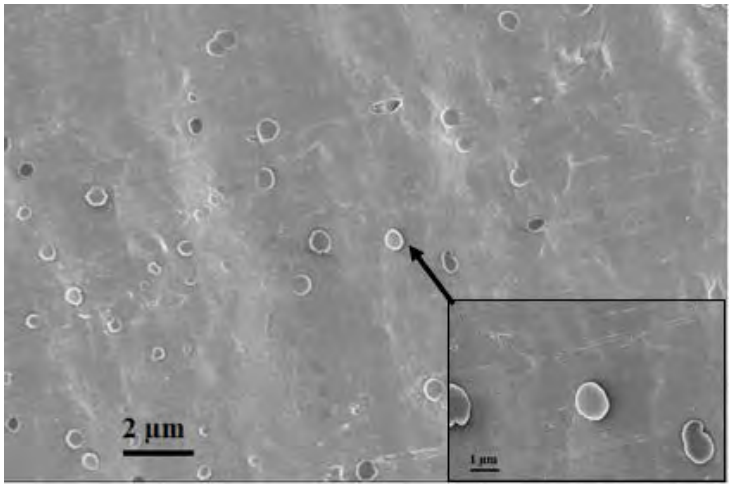


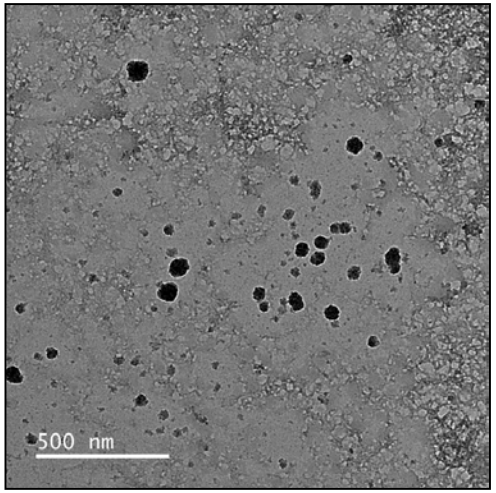




FESEM and TEM images of crystalline aggregates at f_w 99.2% (80 μM)

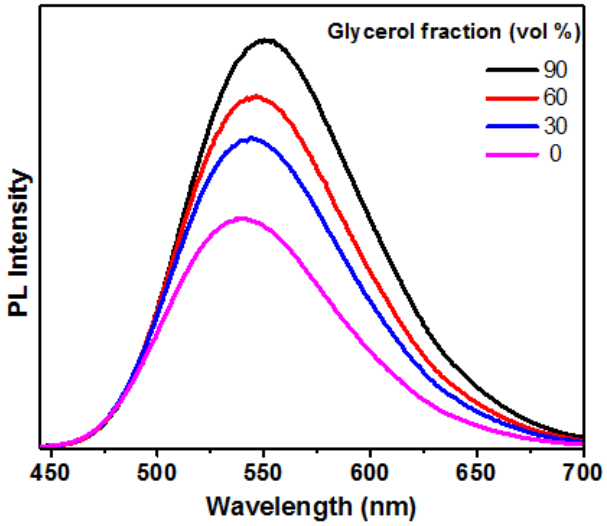
SAED pattern in TEM



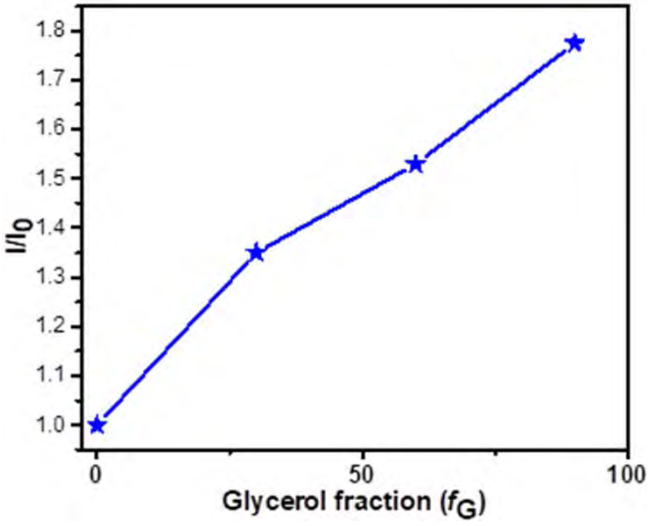


FESEM and TEM images of distorted spherical aggregates at f_w 99.6% (40 μM)

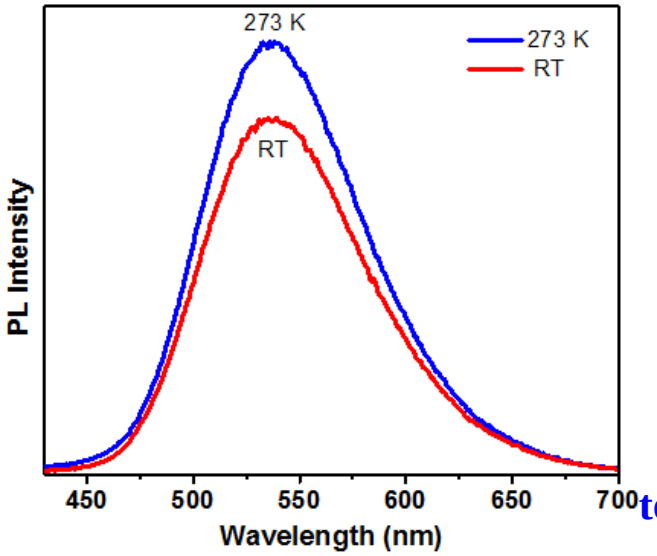
Visco- and Thermochromism



PL titration with varying f_G in MeOH



Relative intensity versus f_W in DMF



PL titration with varying temperature in DMF solvent

- **Increased in viscosity and lowering of temperature cause restriction in intramolecular motion that offers enhanced emission intensity in aggregated state**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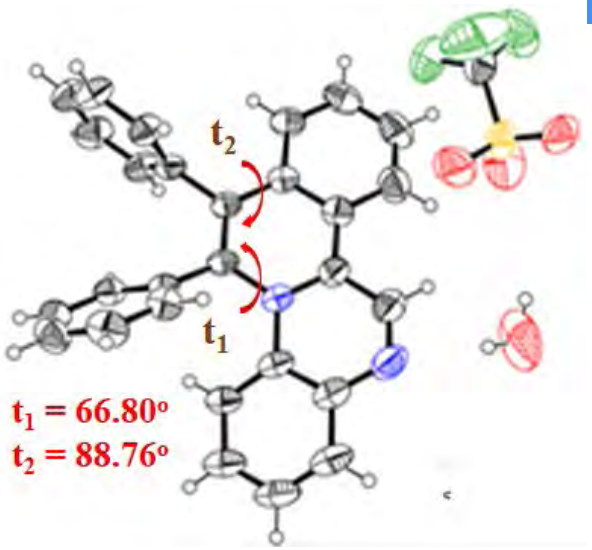
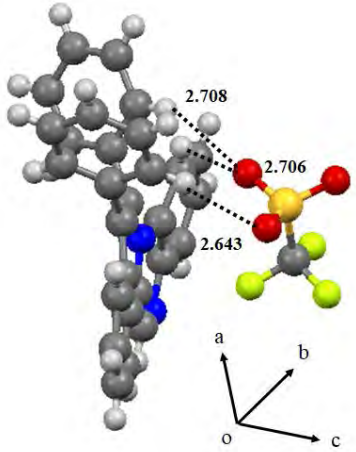
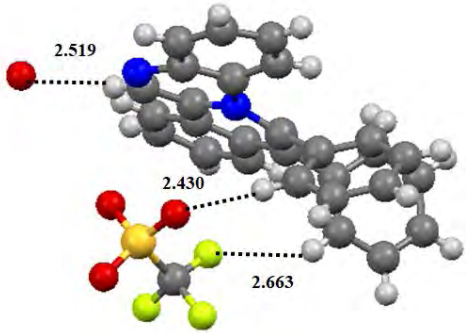
Crystal Packing

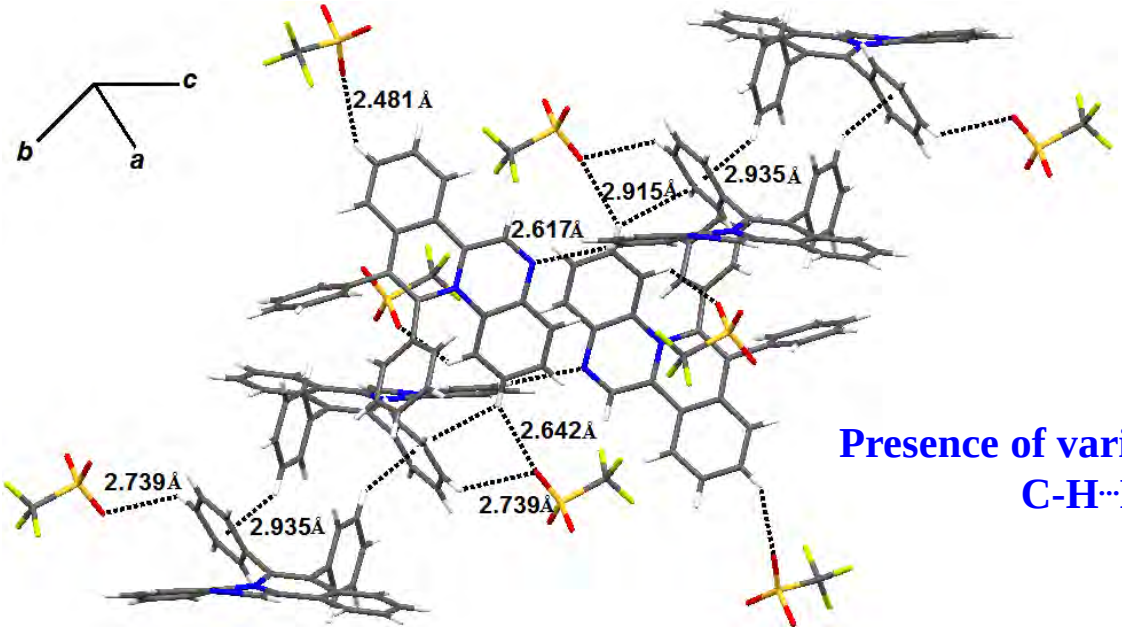


ORTEP view of 3aa with torsional angles

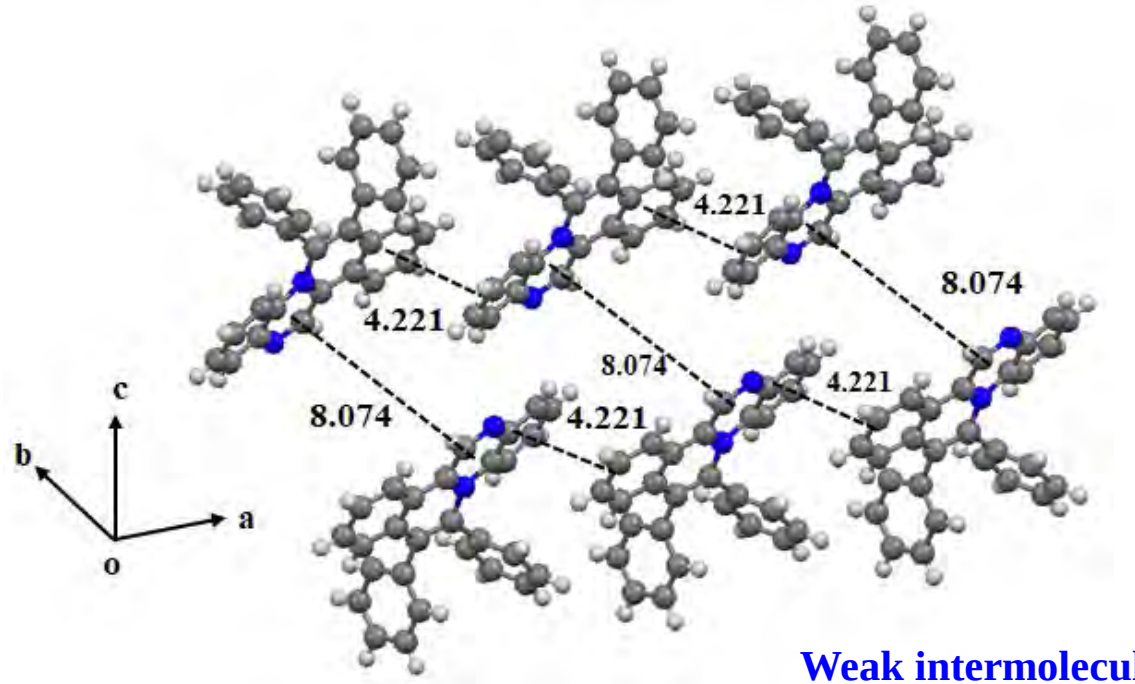


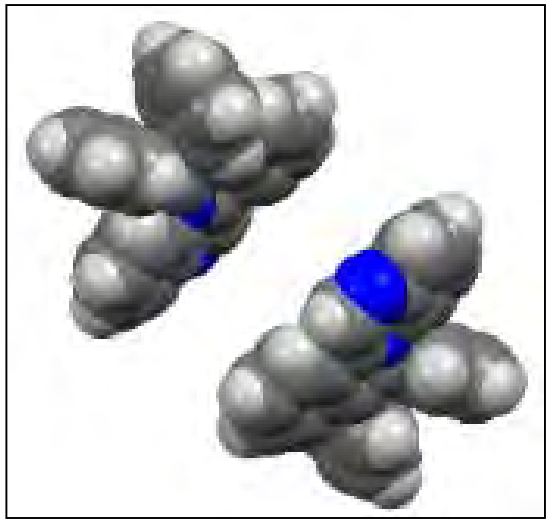


Existence of strong H-bonding interactions

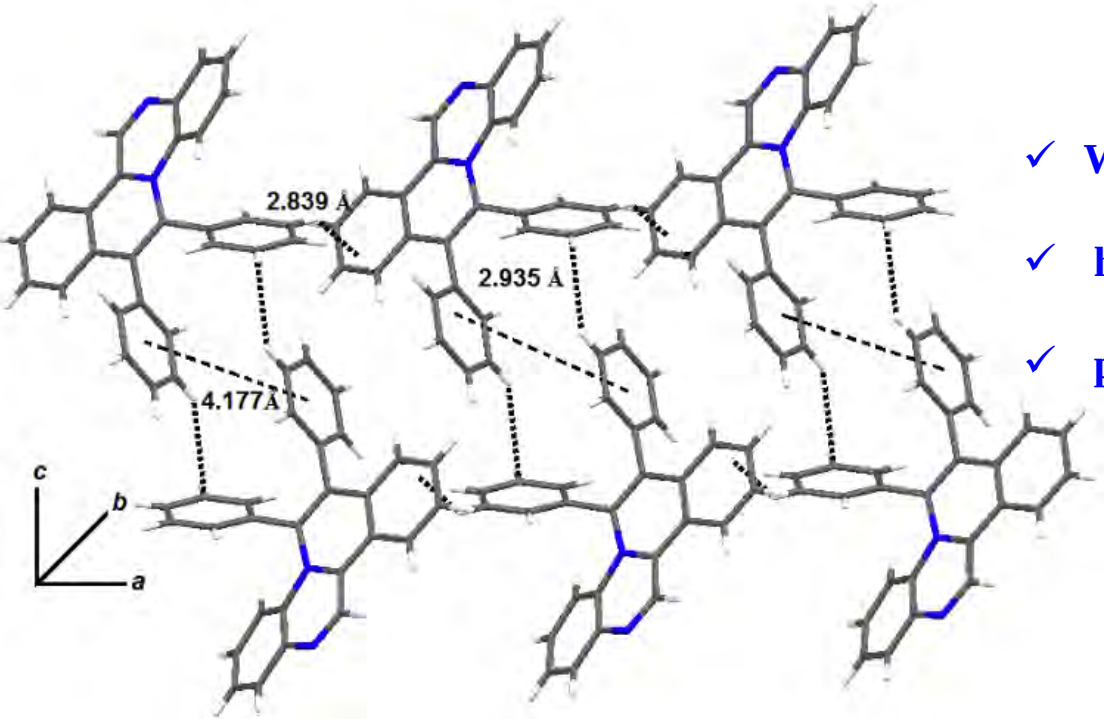


Presence of various non-covalent interactions including C-H···N, C-H···π, C-H···O and C-H···F





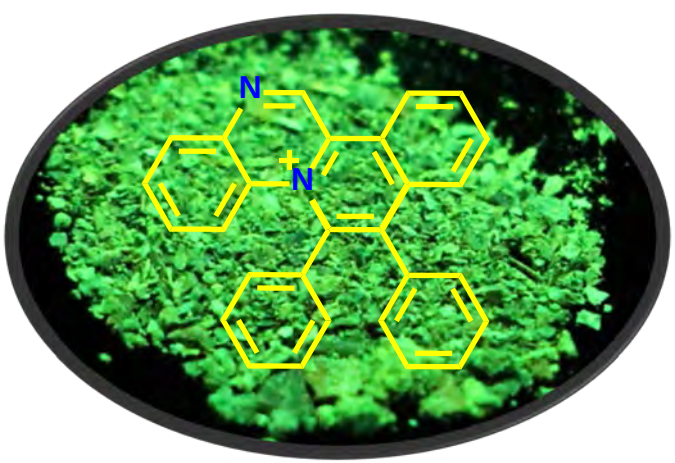
Weak intermolecular π-π interactions (8.074 – 4.177 A°)



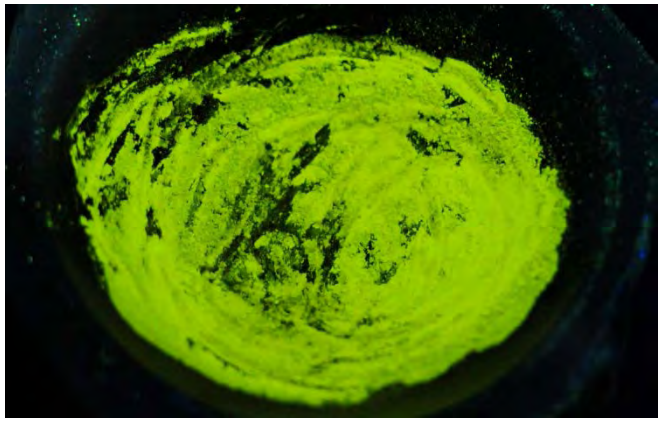
- ✓ **Weak π-π interactions**
- ✓ **highly twisted conformation**
- ✓ **presence of various non-covalent interactions**

Mechanochromism

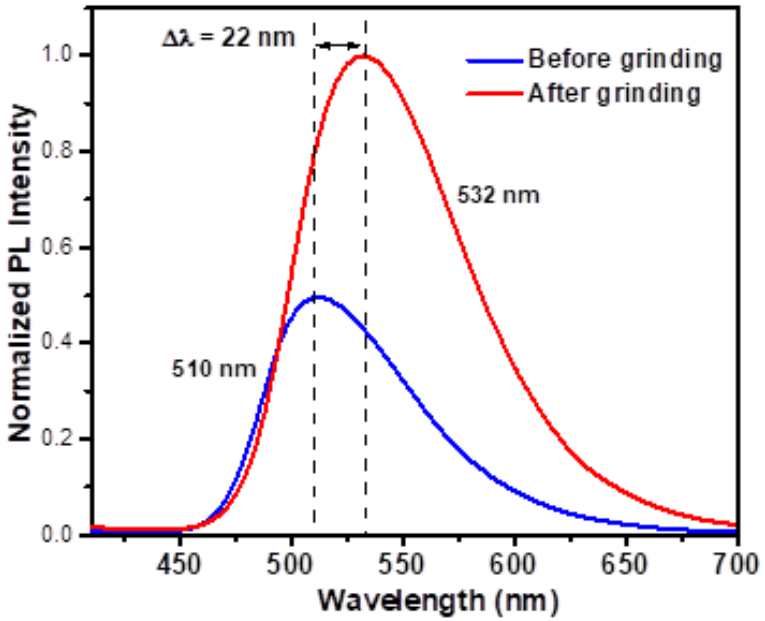
Pristine



Ground



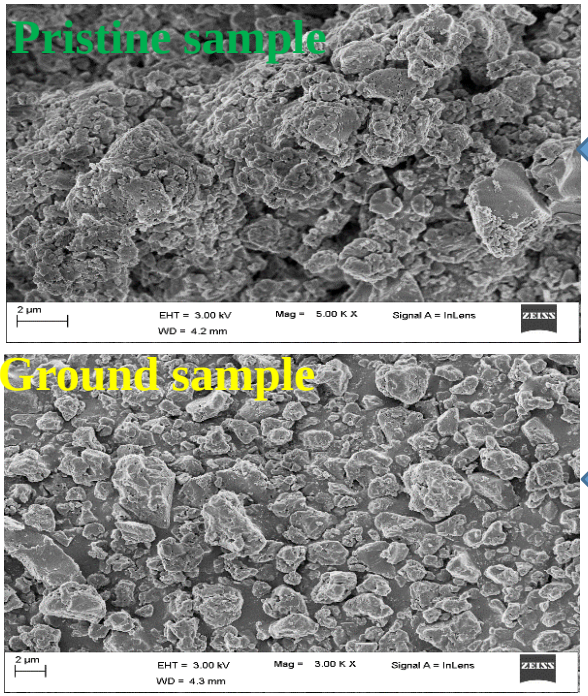
Colour transition from green to yellowish green upon grinding in mortar-pestle (in UV 365 nm)

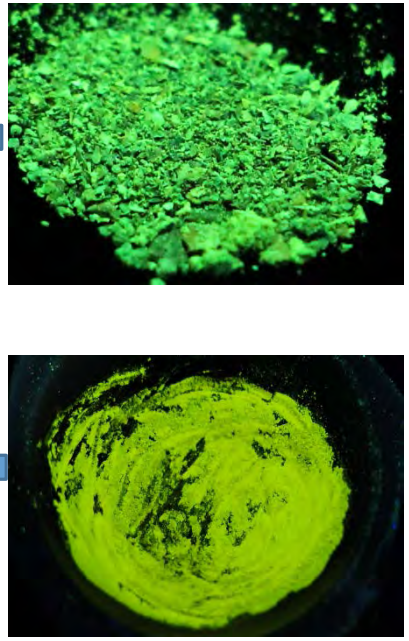


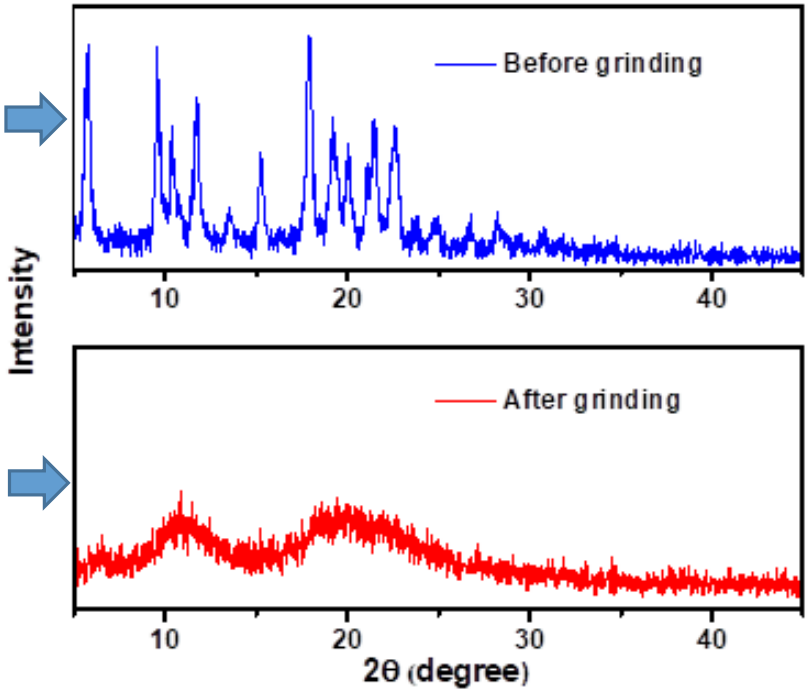
Is due to weak crystal packing and twisted D-A conformation

During grinding twists the two Ph rings which adopts a coplanar conformation with quinoxaline core leading to the extended conjugation there by shifting the emission toward red

Morphological Transformation





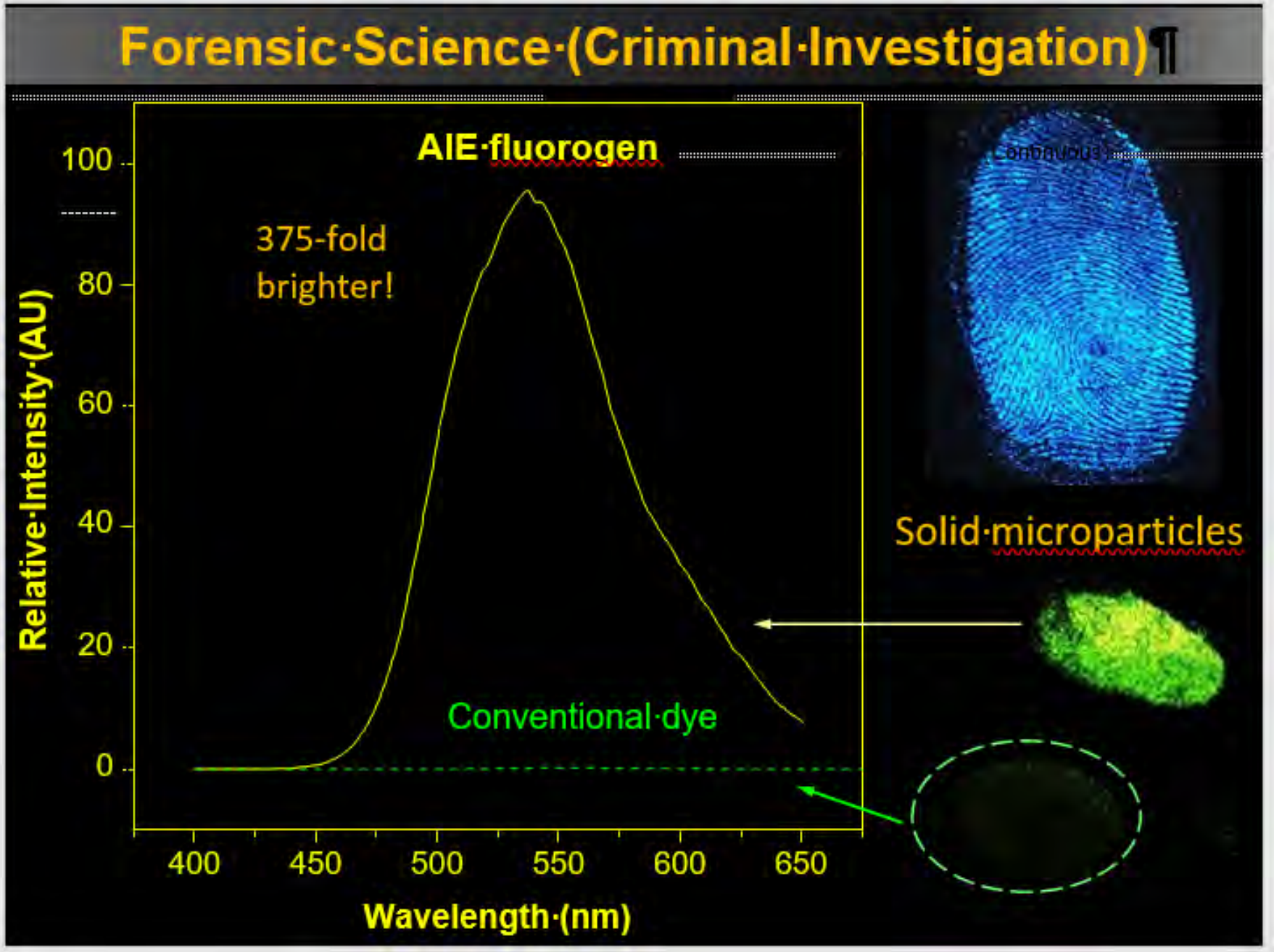


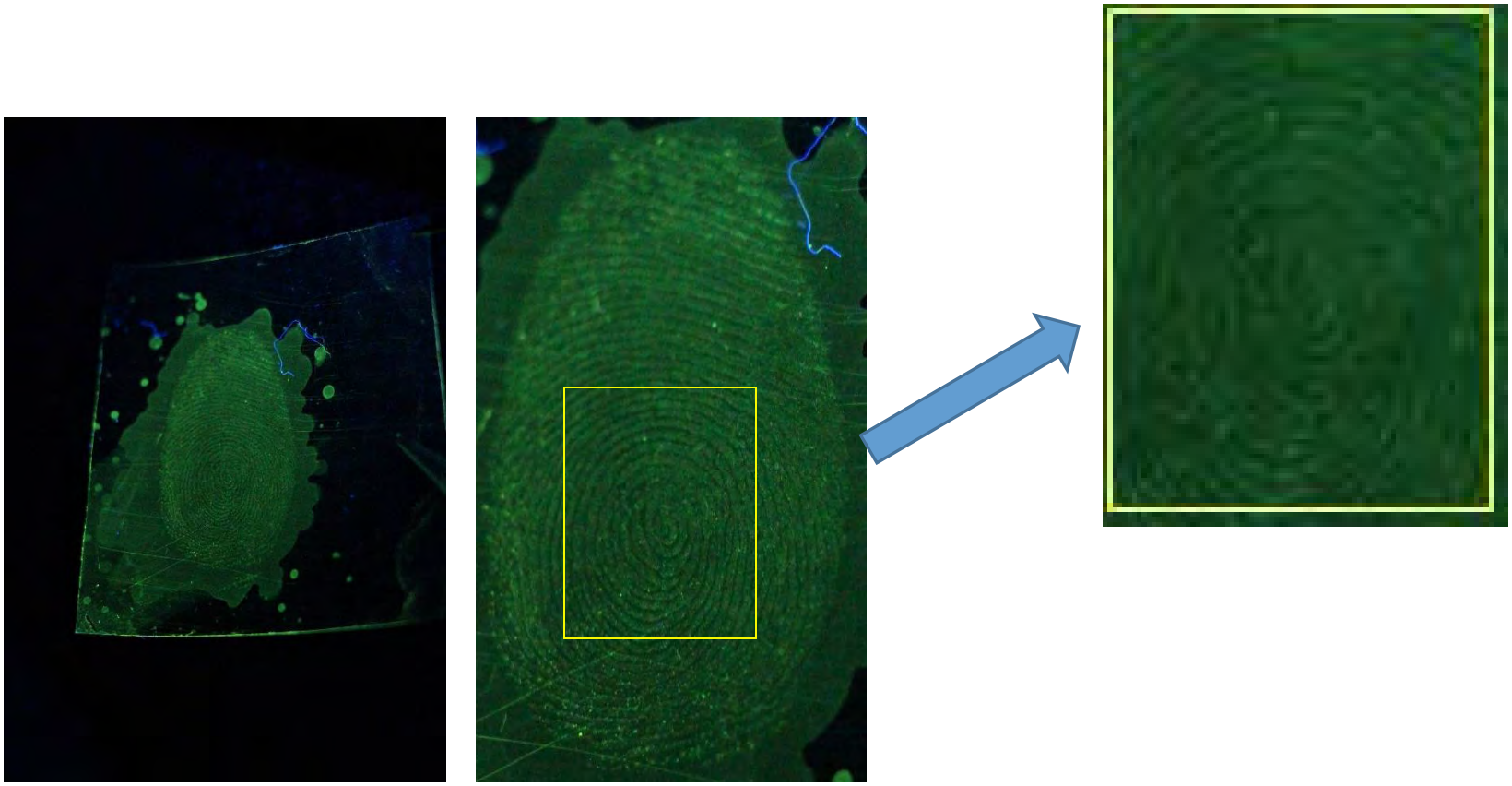
FESEM images of Pristine and Ground sample

PXRD patterns of Pristine and Ground sample

PXRD pattern confirms the transformation from crystalline to amorphous state during grinding

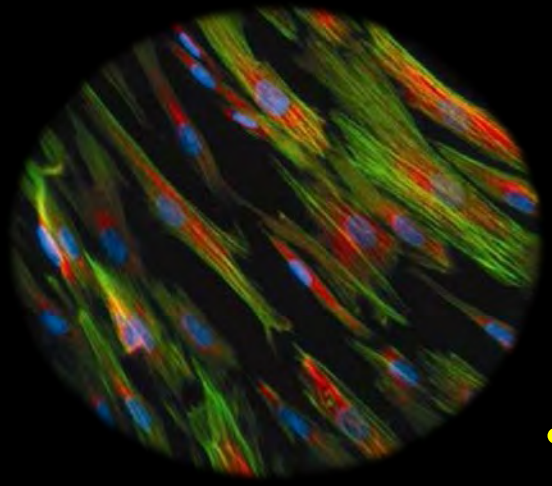
Forensic·Science·(Criminal·Investigation)¶

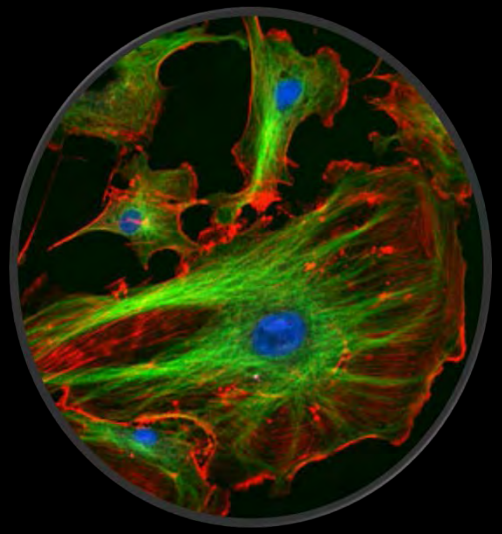




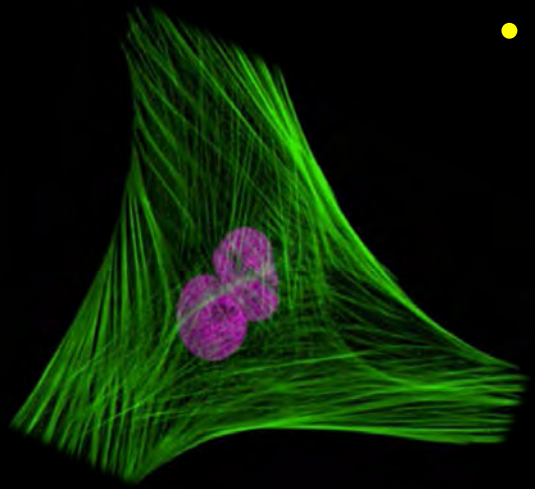
Fluorescence images of Fingerprints on adhesive tape stained with 3aa in 70:30 H_2O-MeOH solvent. Concentration = 1 mM

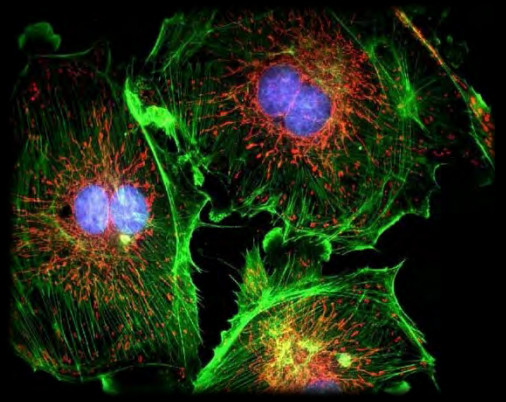
Fluorescent Bioprobes



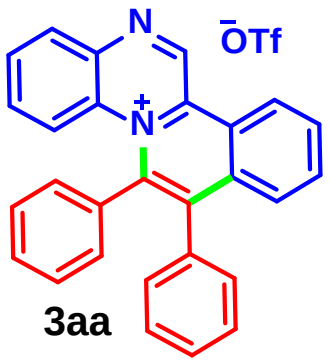


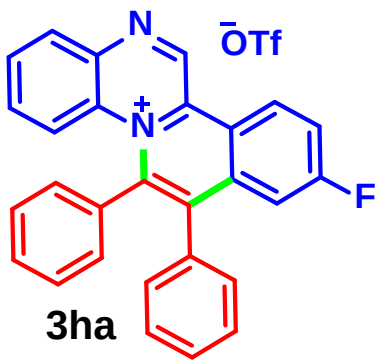
- Fast response
- Sensitive
- Low cytoxicity
- In-situ visualization
- Simple operation
- Excellent penetration

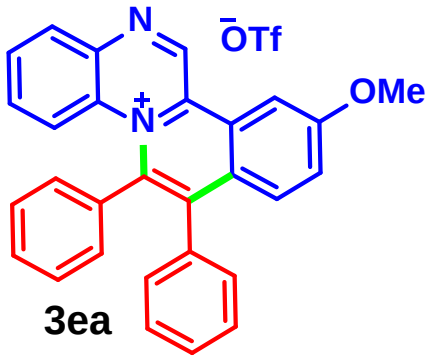


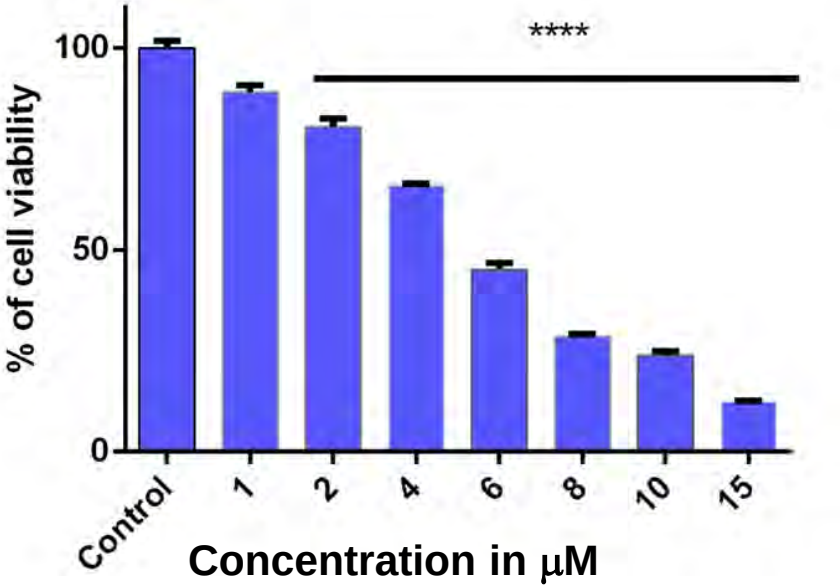


Are they bio-compatible?

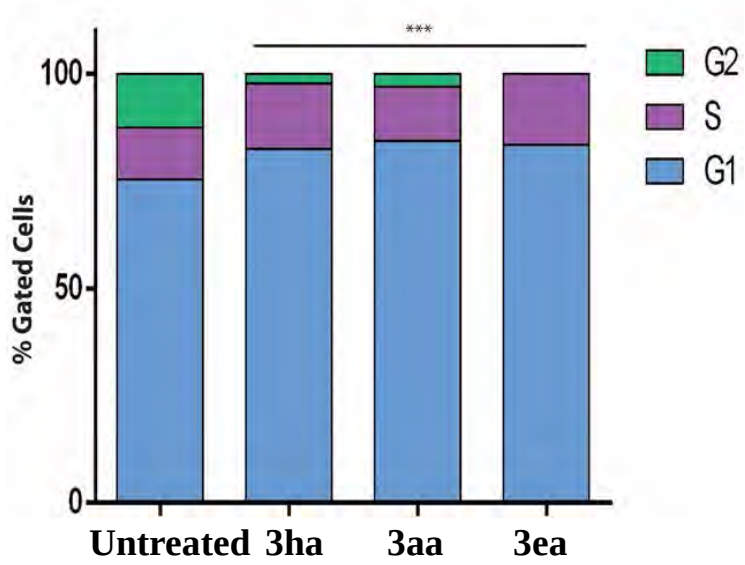




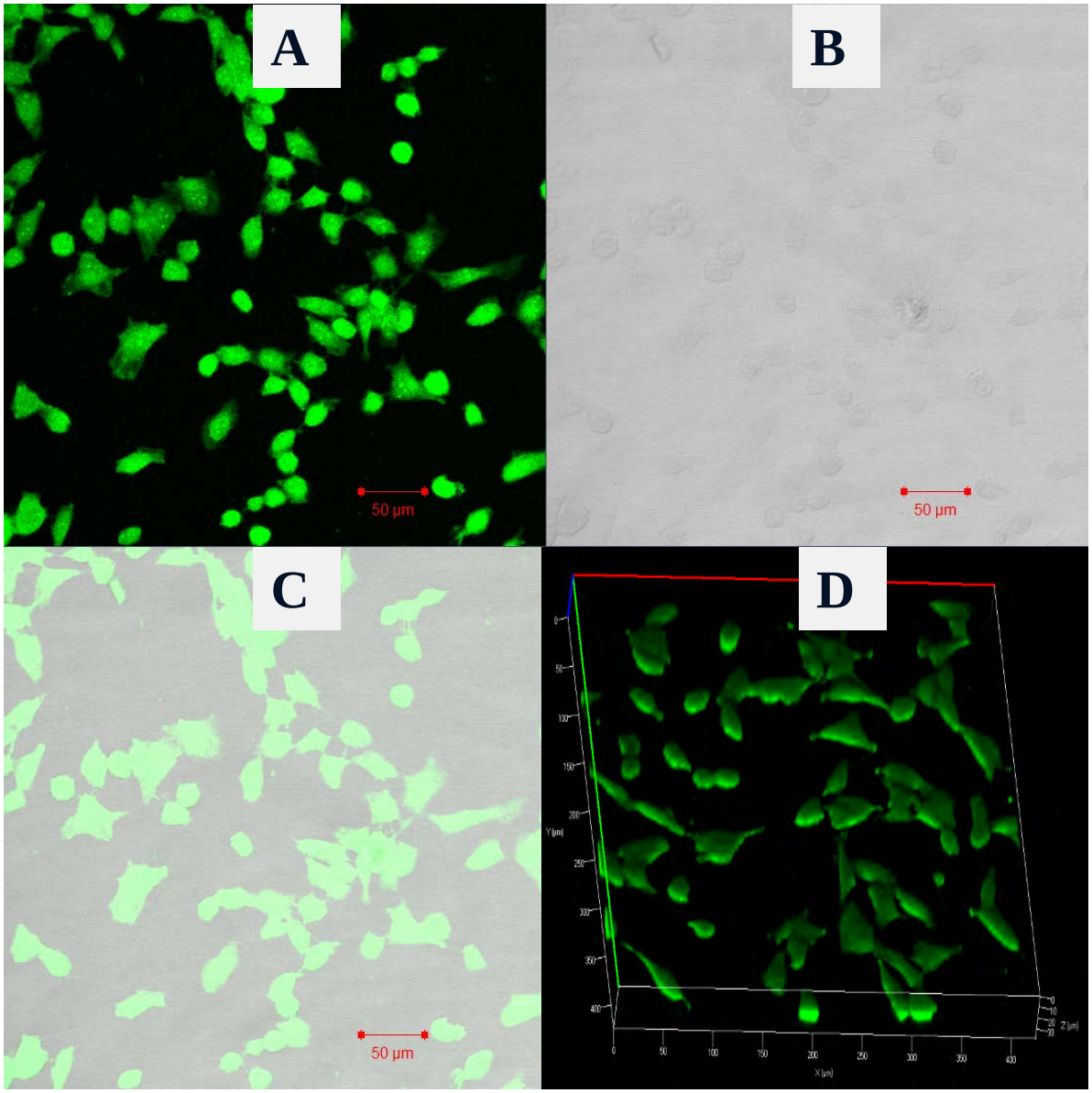


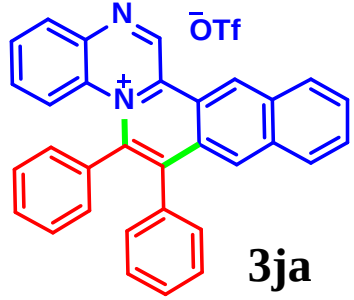


Effect of Compound 3aa in terms of reduction in percentage of viable cells as demonstrated by alamerBlue assay.



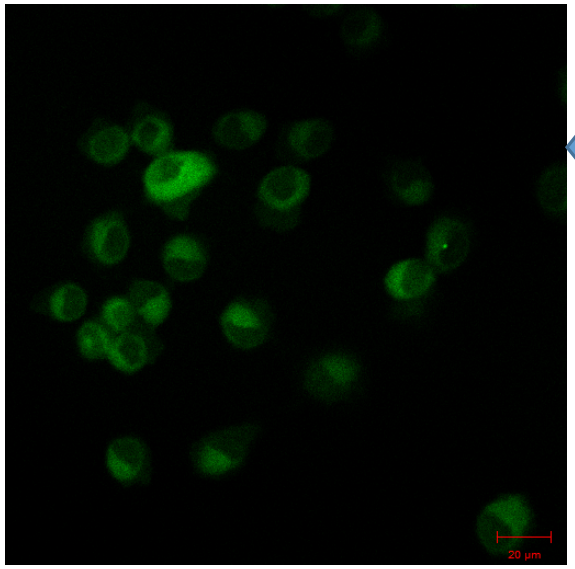
Flow cytometry based analysis of cell cycle of HeLa cells treated with compound 3ha, 3aa and 3ea which shows reduction of G2 phase

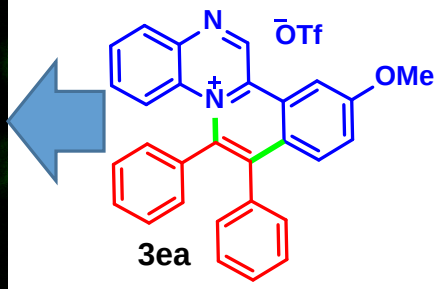




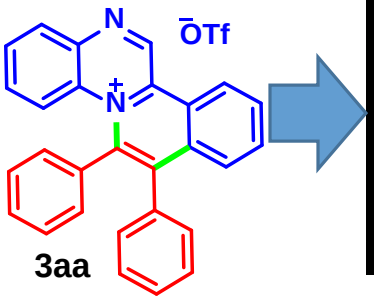
3ja

CLSM images of HeLa cell stained with 3ja, (A) Fluorescence; (B) Bright-field; (C) Merged and (D) 3D images. Cells were incubated with 200 µM of 3ja for 10 mins. Excitation: 458 nm Emission range: 480–605 nm.

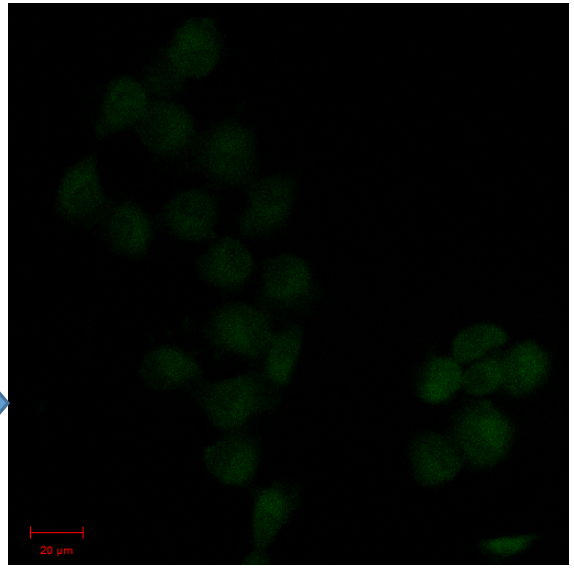


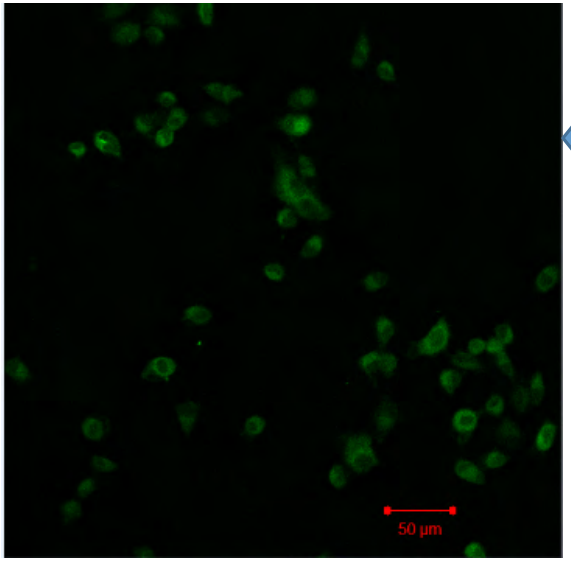


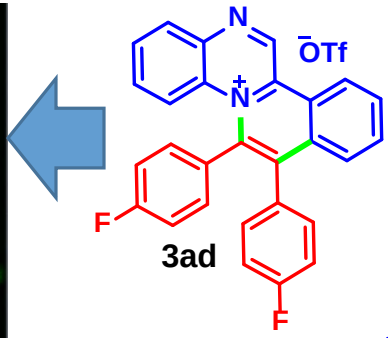
3ea



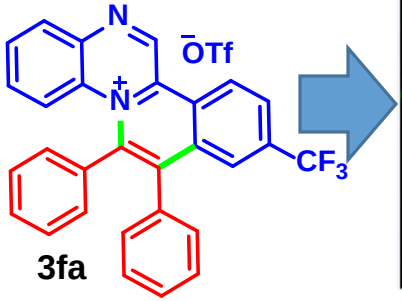
3aa



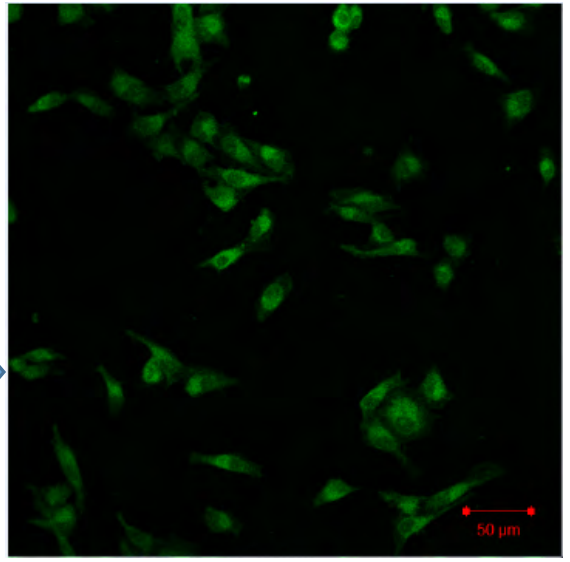




3ad

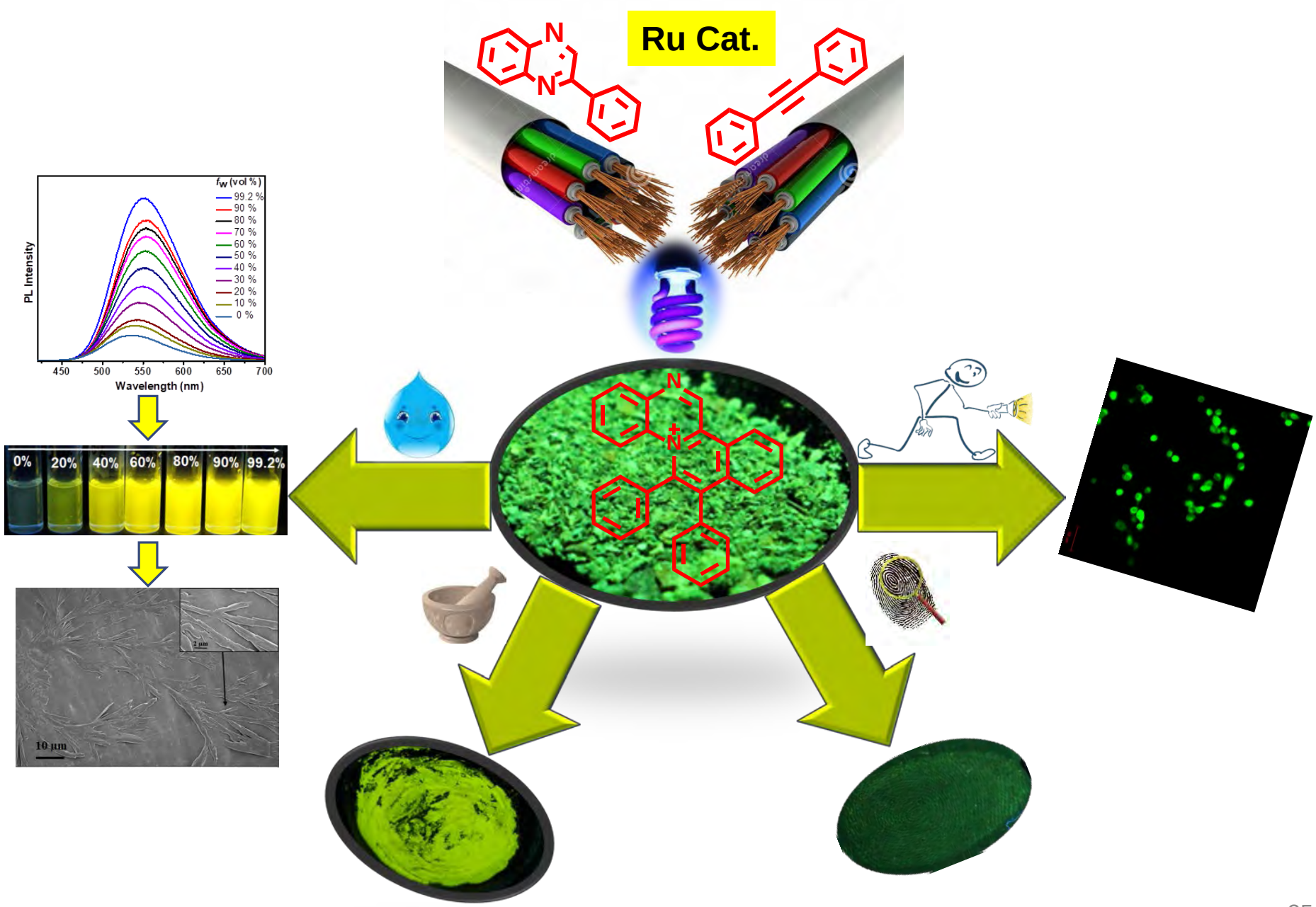


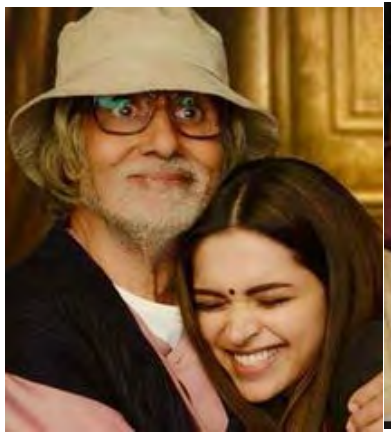
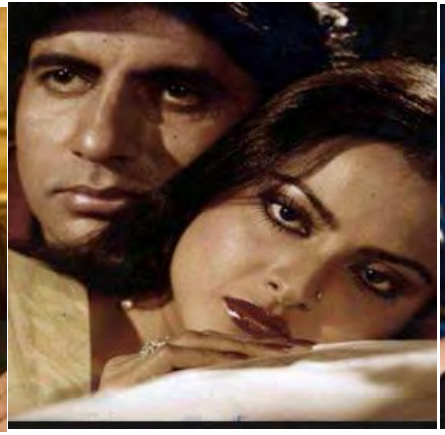
3fa

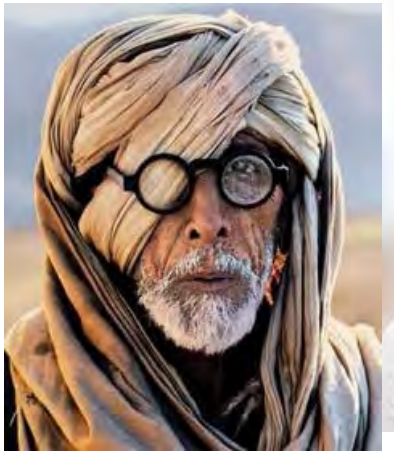


CLSM images of HeLa cell stained with 200 µM of 3ea, 3aa, 3ad, 3fa for 10 mins.

Multifunctional AIEEgen

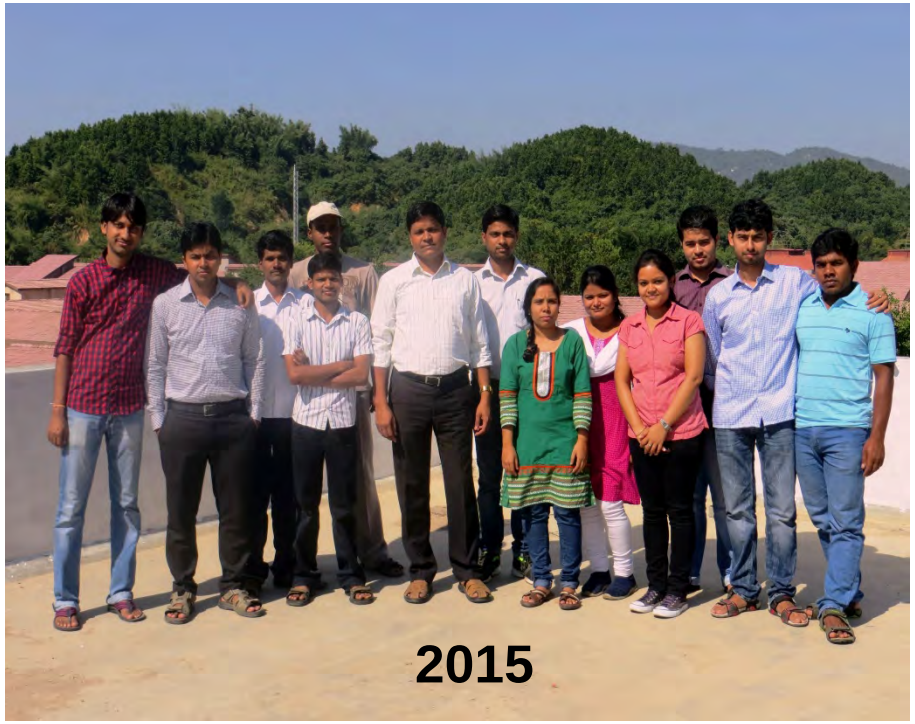







2015


2017


2018

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Department of Chemistry IIT Guwahati

THANK YOU