

Quantitative Evaluation of Lewis Acidity in Solution —Fluorescent Lewis Adduct Method—

2026.01.10 Literature Seminar

M1 Dan Matsubara

Contents

- 1. Introduction**
- 2. Fluorescent Lewis Adduct (FLA) Method**
- 3. Solvent Effects on the Strength of Lewis Acids
(main paper)**

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Lewis Acids

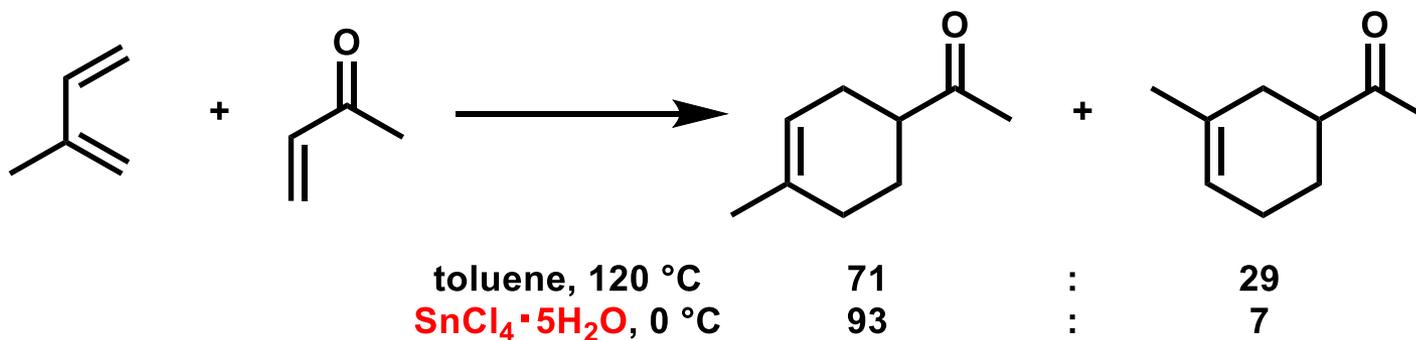
Lewis acid: an electron pair acceptor

- Ex) 1. Boron compounds: $\text{BF}_3 \cdot \text{OEt}_2$, $\text{B}(\text{C}_6\text{F}_5)_3$
2. Metal cations: AlCl_3 , $\text{Sc}(\text{OTf})_3$
3. Cationic species: TMSOTf

Friedel-Crafts Acylation

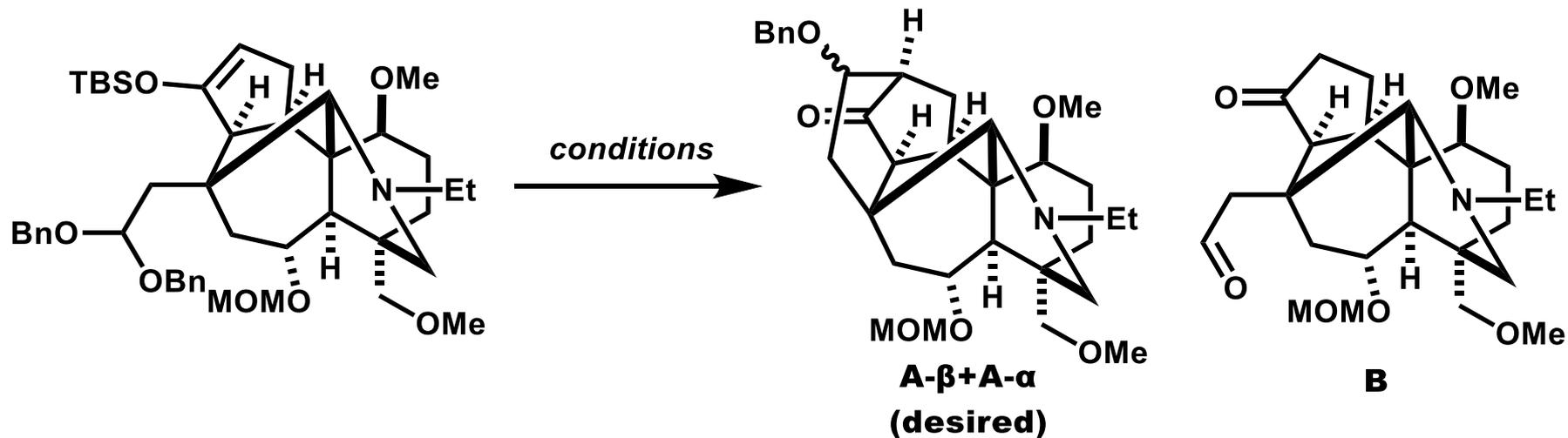


Diels-Alder reaction

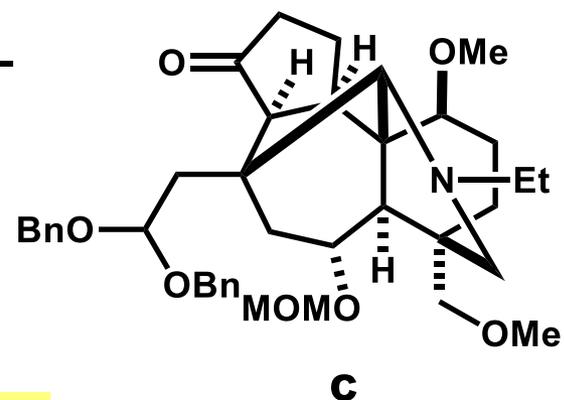


The Use of Lewis Acids in Total Synthesis

Ex) Mukaiyama aldol reaction (Total synthesis of Puberline C)



entry	conditions	A-β+A-α	B	C
1	SnCl₄ (4 equiv), MS 4A, CH ₂ Cl ₂ -78 to -40 to -20 °C	7.1% (1 : 0)	28%	0%
2	SnCl₄ in CH ₂ Cl ₂ (3 equiv) ZnCl₂ in MeCN (3 equiv) MS 4A, toluene -78 to -25 °C	decomposed		
3	SnCl₄ in CH ₂ Cl ₂ (3+3+3 equiv) ZnCl₂ in Et₂O (3+3+3 equiv) MS 4A, toluene -78 to -25 °C	22%(4.2 : 1)	19%	10%



Brønsted Acids vs. Lewis Acids

Brønsted Acids

Lewis Acids (LA)

Definition of strength

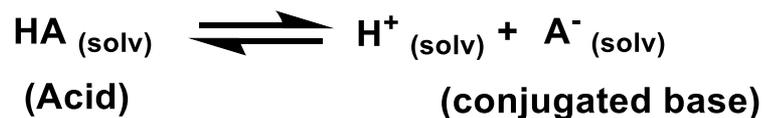
The ability to donate a proton (H^+)

The strength of **Lewis acid-base binding**

Unified scale

pK_a

Absence



$$K_{a,S} = \frac{[\text{H}^+, S][\text{A}^-, S]}{[\text{HA}, S]}$$

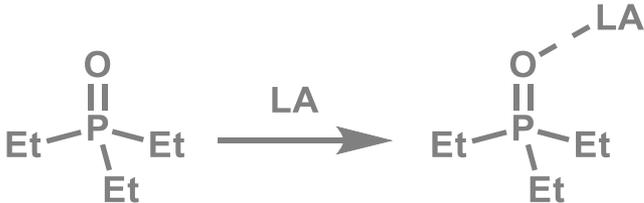
[X]: the concentration of X

$$\text{pK}_{a,S} = -\log K_{a,S}$$

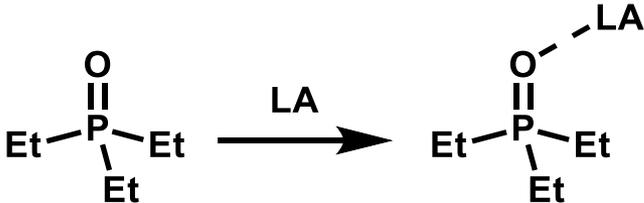
Lewis acidity depends on

- Lewis base
- Solvent
- Environment

How to evaluate "Lewis Acidity"

Class	Global Lewis Acidity (gLA)	Effective Lewis Acidity (eLA)
Principle	The thermodynamic affinity of for a given Lewis base (the IUPAC definition of Lewis Acidity)	The change in the properties of the Lewis base upon binding
Method	<p>ex) Fluoride-Ion Affinity (FIA)</p> $\text{F}^- \xrightarrow{\text{LA}} \text{LA}-\text{F}^-$	<p>ex) Gutmann-Beckett (GB) method</p> 
Measured quantity	the enthalpy change (<i>in silico</i>)	the magnitude of the downfield shift in ^{31}P NMR
Advantages	<ul style="list-style-type: none"> • a unified scale (fixed Lewis base: F^-) 	<ul style="list-style-type: none"> • Experimentally accessible • Reflects Lewis acid behavior in solution
Limitations	<ul style="list-style-type: none"> • Strong dependence on the Lewis base (hard F^- donor) • Does not reflect real reaction conditions • Limited applicability to metal-based and cationic Lewis acids 	<ul style="list-style-type: none"> • Strong dependence on the Lewis base (hard $\text{P}=\text{O}$ donor) • Sensitive to binding equilibria and incomplete adduct formation • Limited applicability to metal-based and cationic Lewis acids

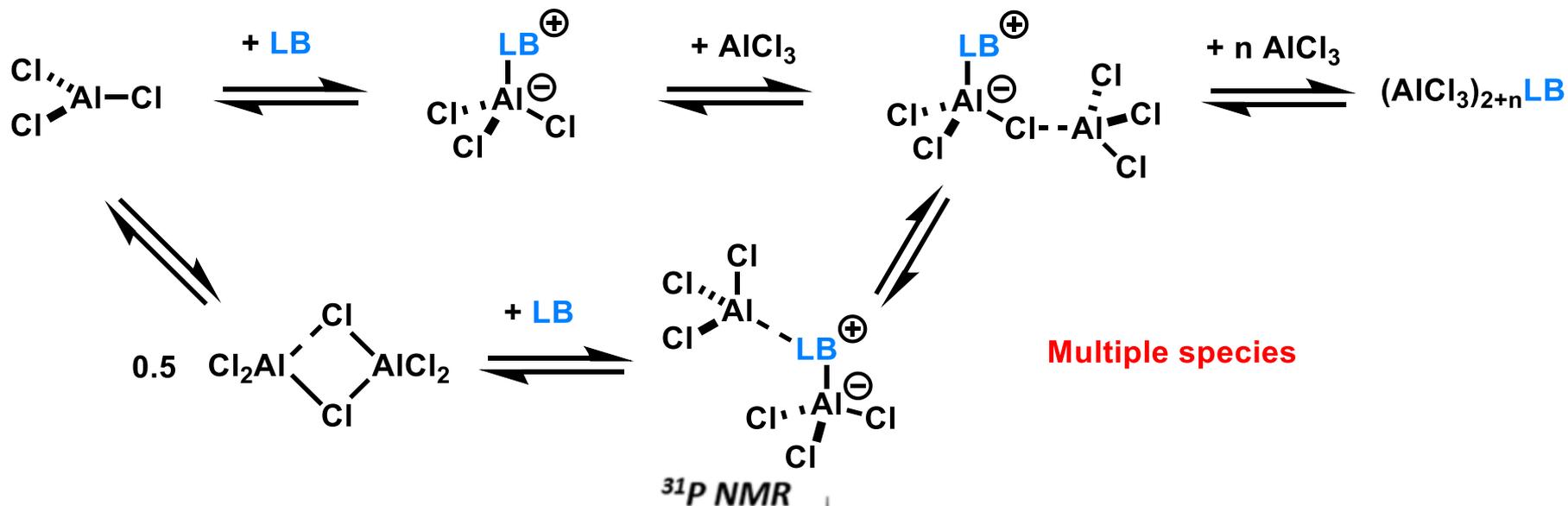
How to evaluate "Lewis Acidity"

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Method	ex) Fluoride-Ion Affinity (FIA) $\text{F}^- \xrightarrow{\text{LA}} \text{LA}-\text{F}^-$	ex) Gutmann-Beckett (GB) method 
Measured quantity	the enthalpy change (<i>in silico</i>)	the magnitude of the downfield shift in ^{31}P NMR
Advantages	<ul style="list-style-type: none"> • a unified scale (fixed Lewis base: F^-) • Widely applicable through computational methods 	<ul style="list-style-type: none"> • Experimentally accessible • Reflects Lewis acid behavior in solution
Limitations	<ul style="list-style-type: none"> • Strong dependence on the Lewis base (hard F^- donor) • Does not reflect real reaction conditions • Limited applicability to metal-based and cationic Lewis acids 	<ul style="list-style-type: none"> • Strong dependence on the Lewis base (hard $\text{P}=\text{O}$ donor) • Sensitive to binding equilibria and incomplete adduct formation • Limited applicability to metal-based and cationic Lewis acids

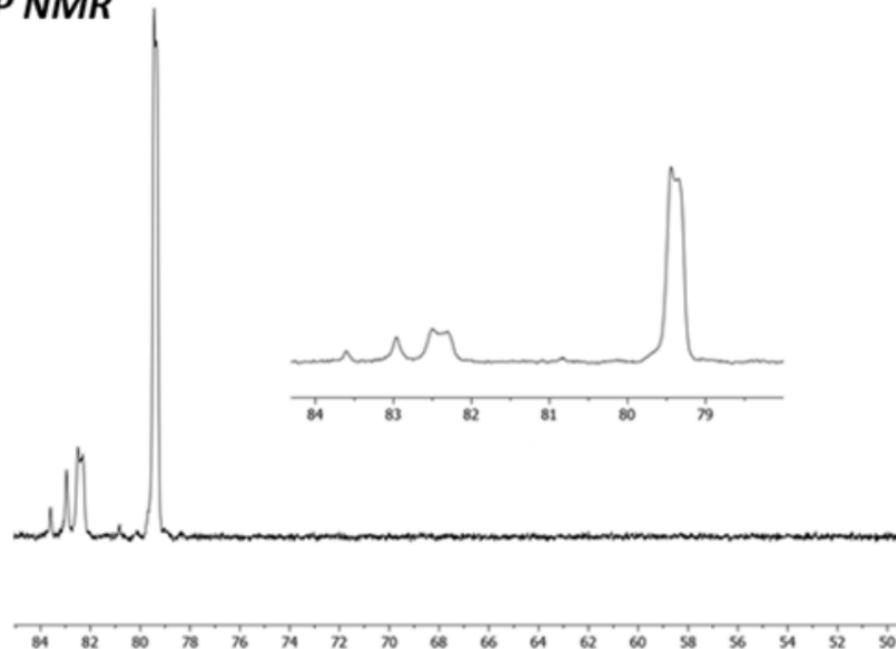
1) Beckett, M.A.; Strickland, G.C.; Holland, J.R.; Sukumar Varma, K. *Polymer*, **1996**, 37, 4629–4631.

2) Mayer, U.; Gutmann, V.; Gerger, W. *Monatsh. Chem.* **1975**, 106, 1235–1257.

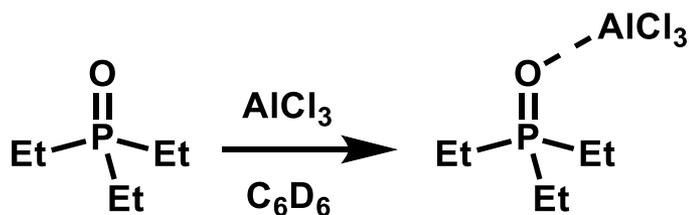
Limitation of GB Method



^{31}P NMR



GB method



Not properly evaluated by GB methods



Fluorescent Lewis Adduct (FLA) method

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(main paper)

Introduction of Prof. Thomas Baumgartner

Educational and Professional Careers:

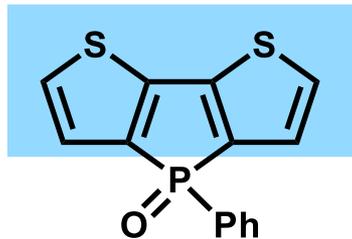
-1996 Dipl. Chem. (MSc) @ University of Bonn (Prof. Edgar Niecke)
1996-1998 PhD @ University of Bonn (Prof. Edgar Niecke)
1998-1999 Research Associate @ University of Bonn (Prof. Edgar Niecke)
1999-2002 Postdoctoral Fellow @ the University of Toronto (Prof. Ian Manners)
2002-2003 Habilitand @ Johannes Gutenberg-University, Mainz (Prof. Jun Okuda)
2003-2006 Habilitand @ RWTH Aachen University (Prof. Jun Okuda)
2006-2009 Assistant Professor @ University of Calgary
2009-2013 Associate Professor @ University of Calgary
2013-2017 Full Professor @ University of Calgary
2017- Full Professor @ York Univeristy



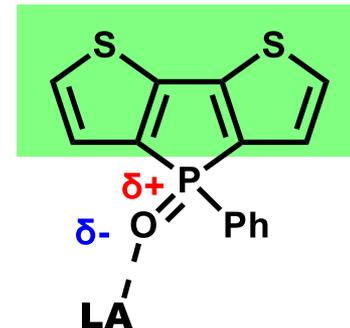
Research Topic:

Organophosphorus Chemistry

Working Hypothesis



fluorescent P=O probe



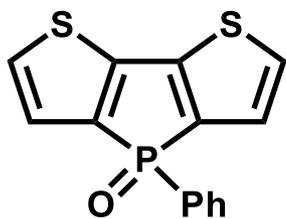
fluorescent P=O probe
bound to a Lewis acid

Change in P=O polarization

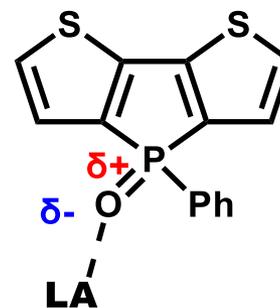
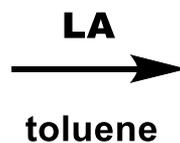


Change in fluorescence

Verification of Working Hypothesis



1



1-LA

Lewis Acid	λ_{abs} (nm)	λ_{em} (nm)	ϵ ($\text{M}^{-1}\text{cm}^{-1}$) (ϕ)	^{31}P δ (ppm)	Stokes Shift (cm^{-1})	$\Delta \lambda_{\text{em}}$ (nm)
None	366	446	5,600 (0.74)	14.2	4,900	-
BPh_3^{a}	355	452	15,000 (0.90)	21.5	6,045	6
$\text{B}(\text{C}_6\text{F}_5)_3^{\text{b}}$	389	509	5,100 (0.89)	30.2	6,061	63

^a 2000 equiv

^b 5 equiv

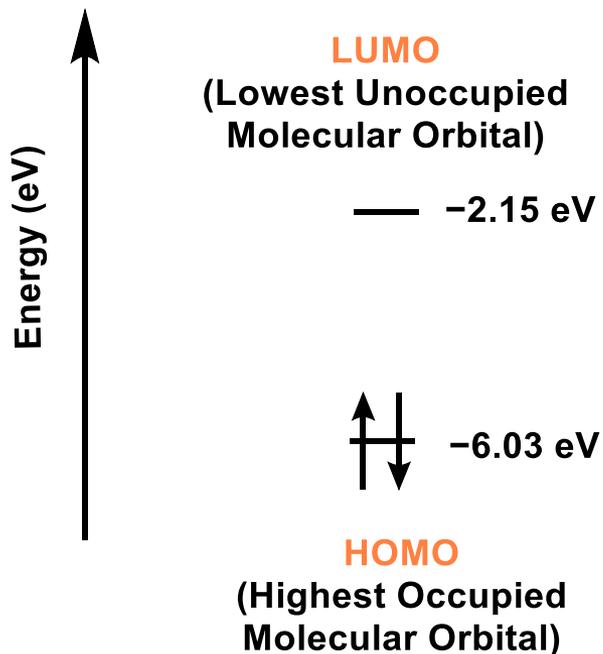
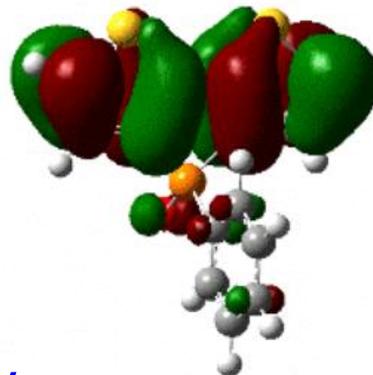
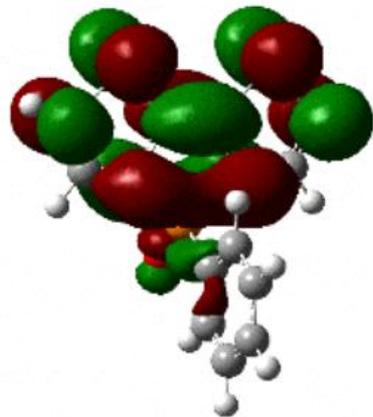
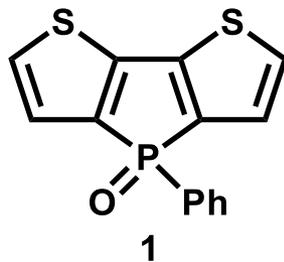


probe 1

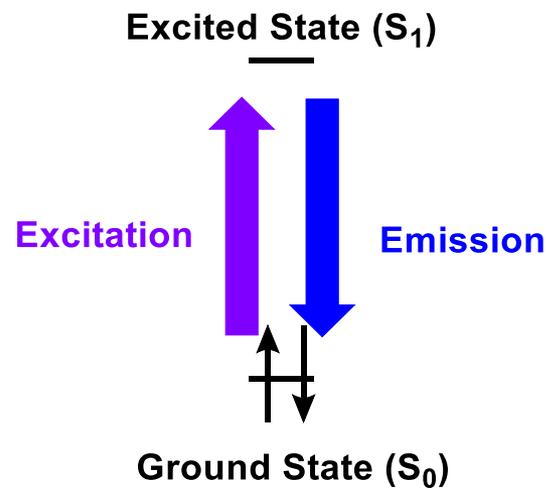


probe 1- $\text{B}(\text{C}_6\text{F}_5)_3$

Properties of Probe 1



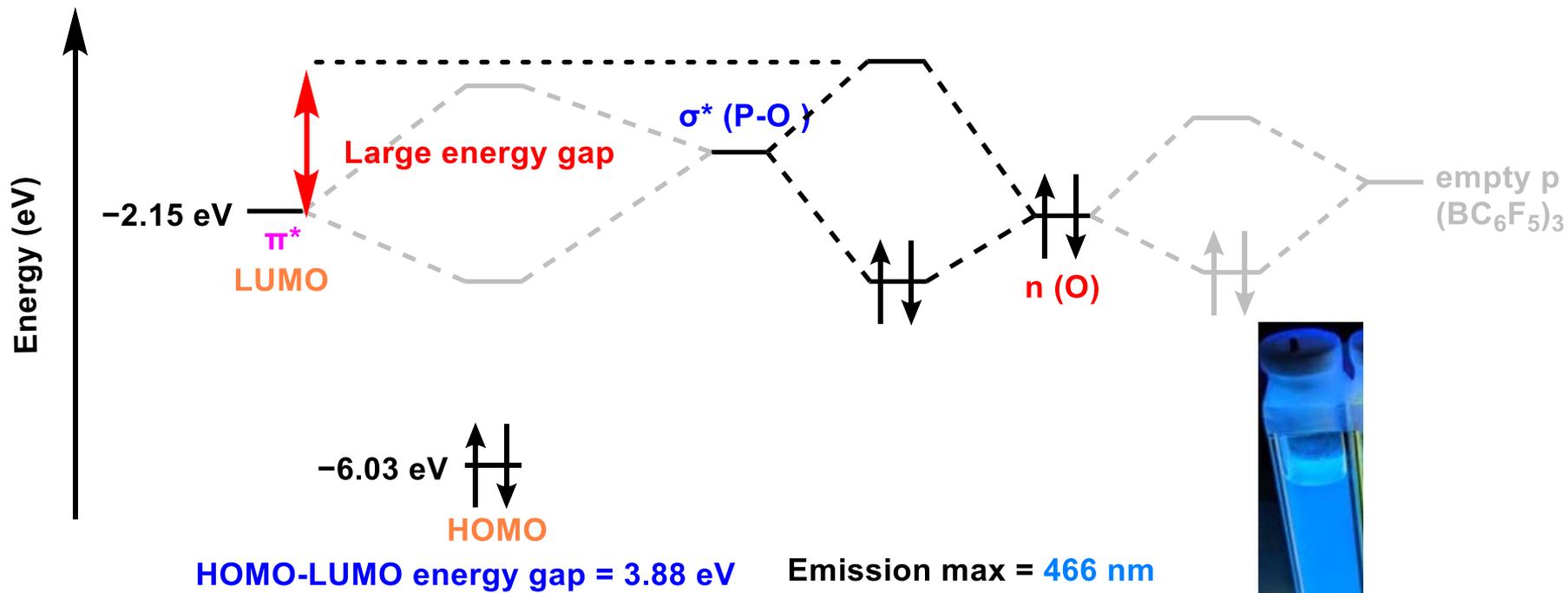
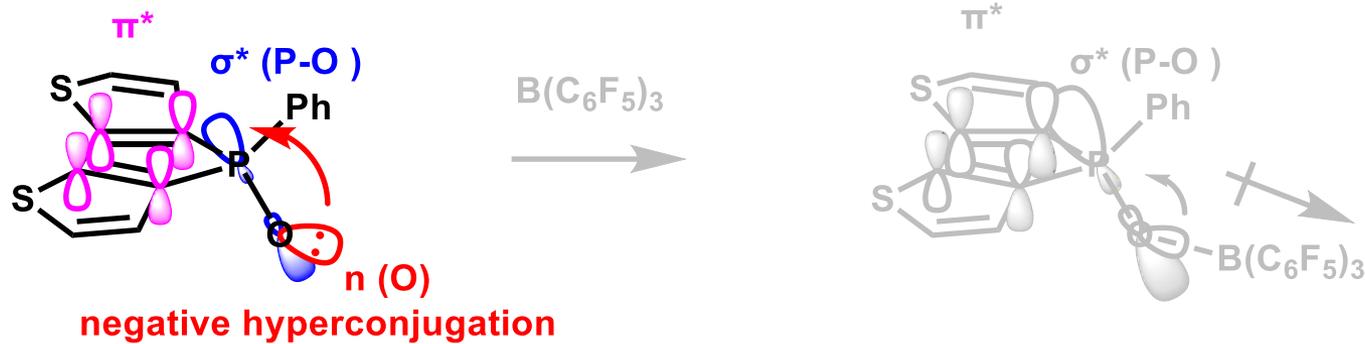
* Principle of Fluorescence



HOMO-LUMO energy gap = 3.88 eV

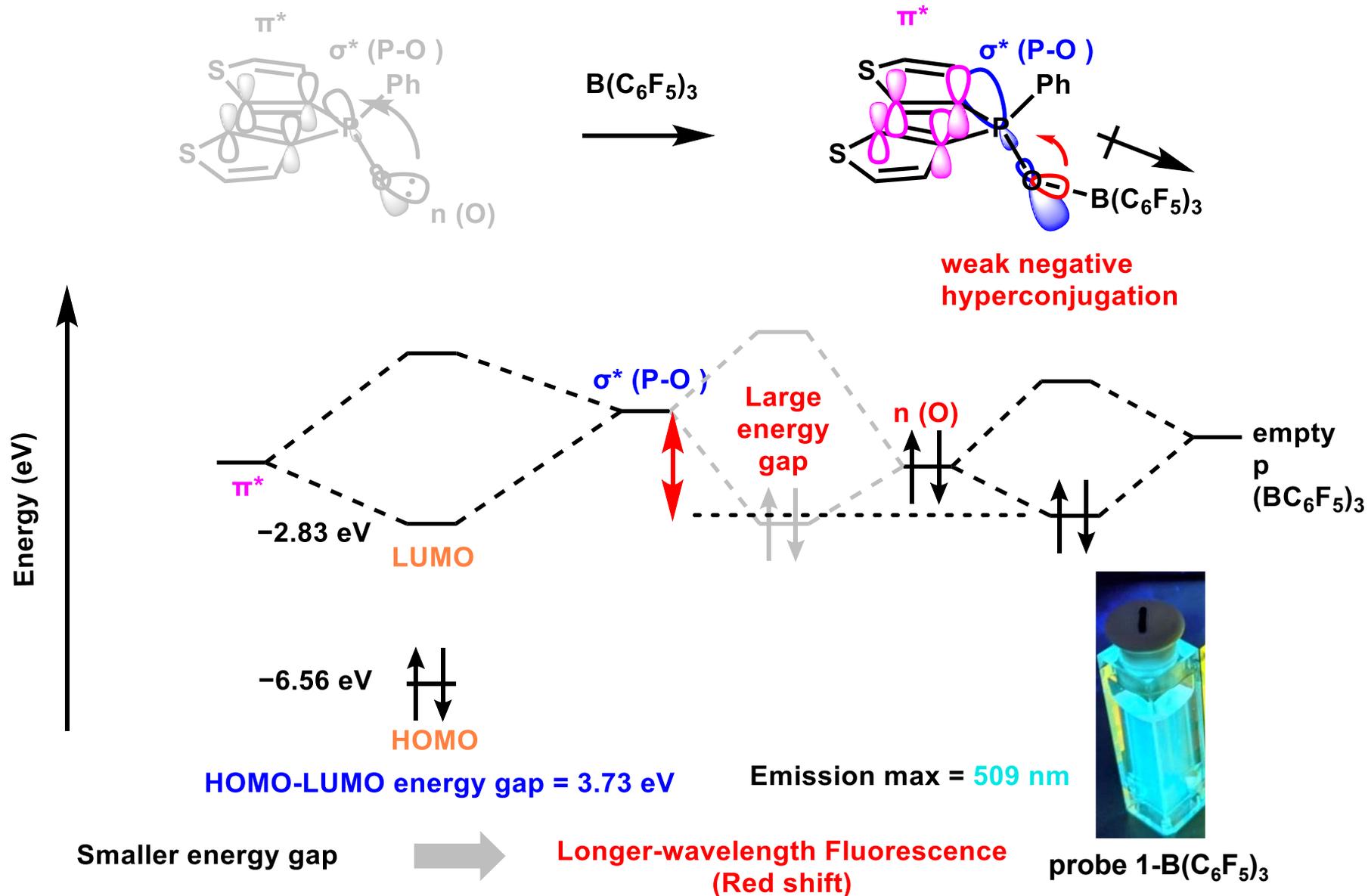
DFT calculations were performed at the B3LYP/6-31G8d) level of theory

Principle of FLA (1)

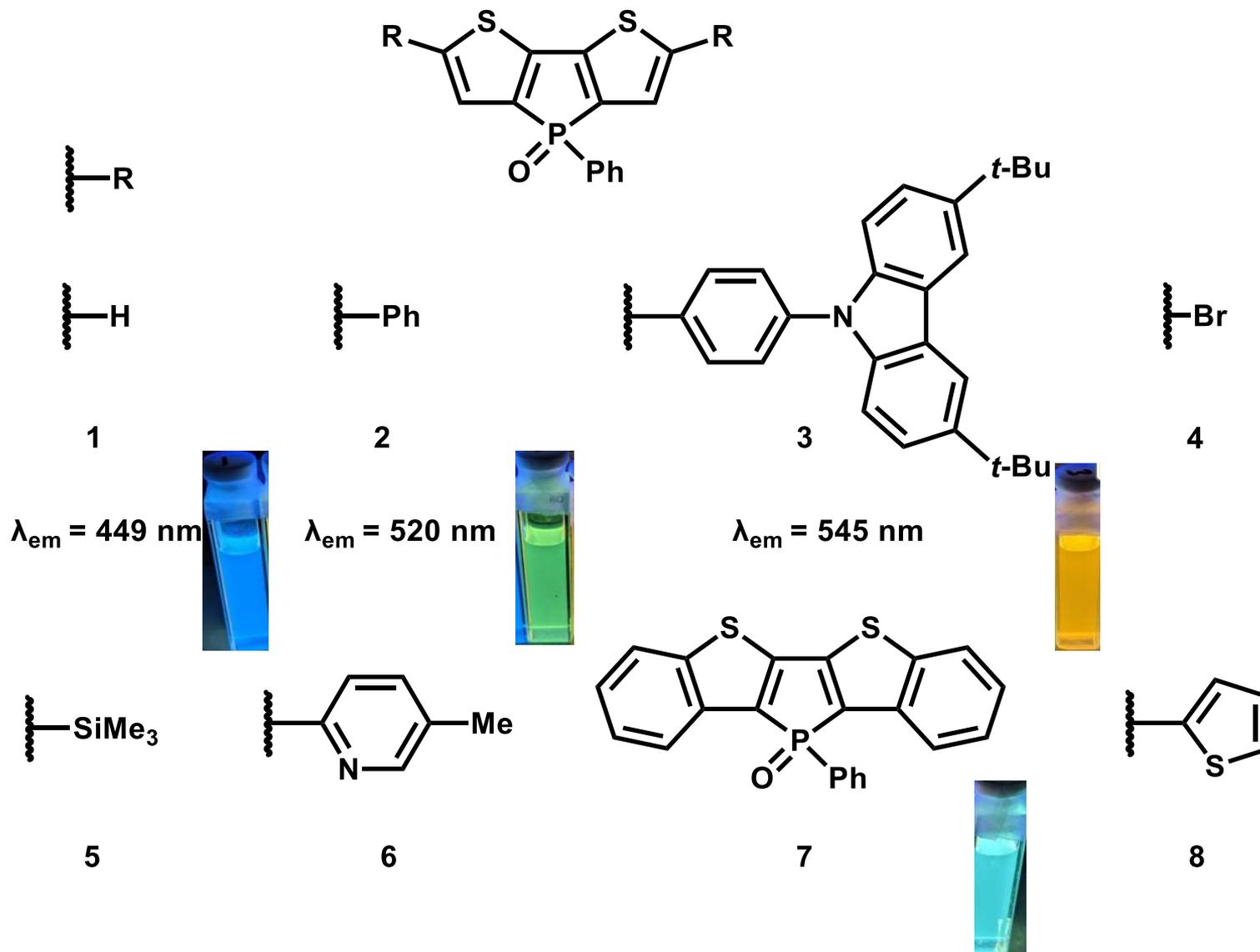


probe 1

Principle of FLA (2)



Design of Lewis Base Probes



The different π -Conjugated backbones



The different Lewis basicities

Limitation of Single-Probe Evaluation

1. Differences in emission max for probes 1, 2 and 3 upon binding to Lewis acids

	$B(C_6F_5)_3$	$B(p-C_6F_4H)_3$
1	63 nm	63 nm
2	77 nm	76 nm
3	86 nm	82 nm

$$\Delta\lambda_{em} = \lambda_{em} (LA) - \lambda_{em} (\text{none}) \quad \text{Negligible difference in emission maxima}$$

2. Differences in fluorescence of probes 1 and 3 upon binding to Lewis acids



1- $B(C_6F_5)_3$

1- $B(p-C_6F_4H)_3$



3- $B(C_6F_5)_3$

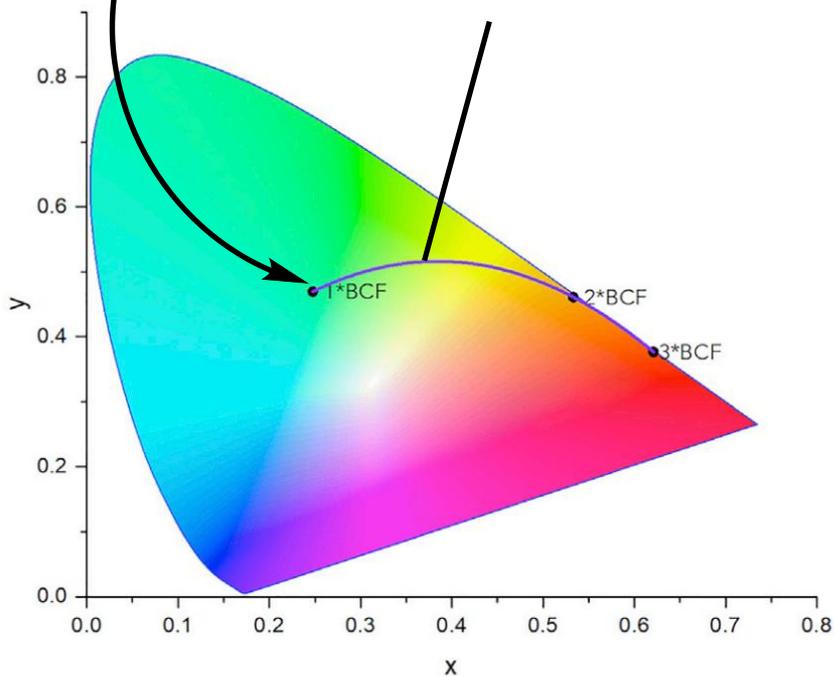
3- $B(p-C_6F_4H)_3$

Clearly different in color

Color-Based, Multi-Probe Approach



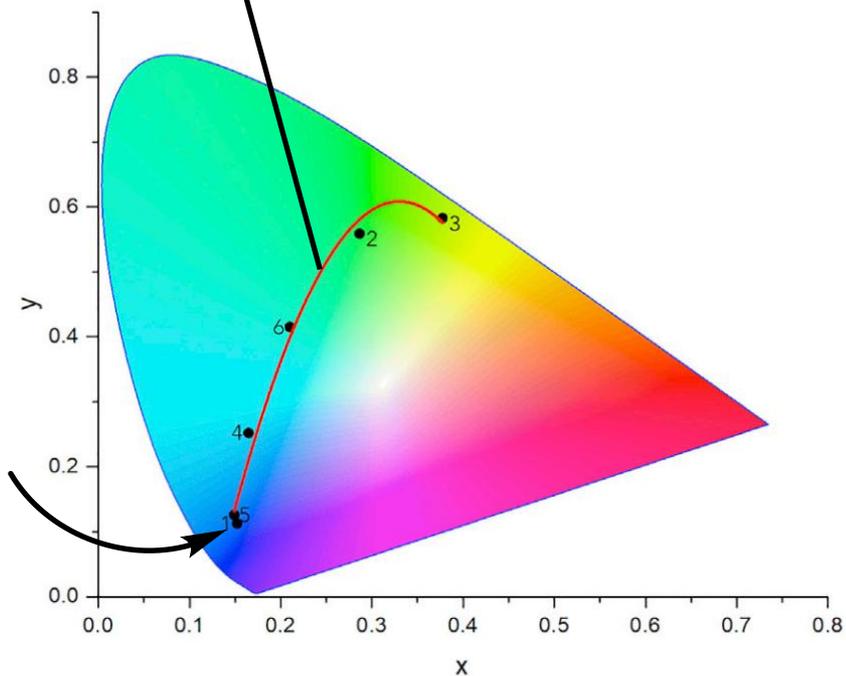
the chromaticity of the $B(C_6F_5)_3$ adduct with a theoretical probe



$$Y = -2.49445x^2 + 1.92859x + 0.14293$$

Chromaticity trend of adduct of $B(C_6F_5)_3$ with probes

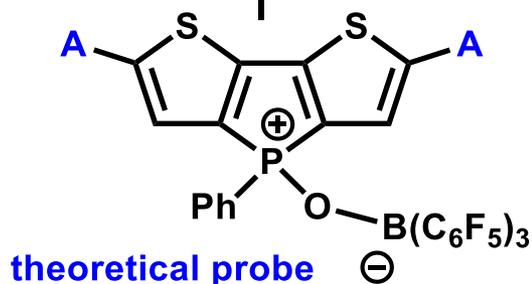
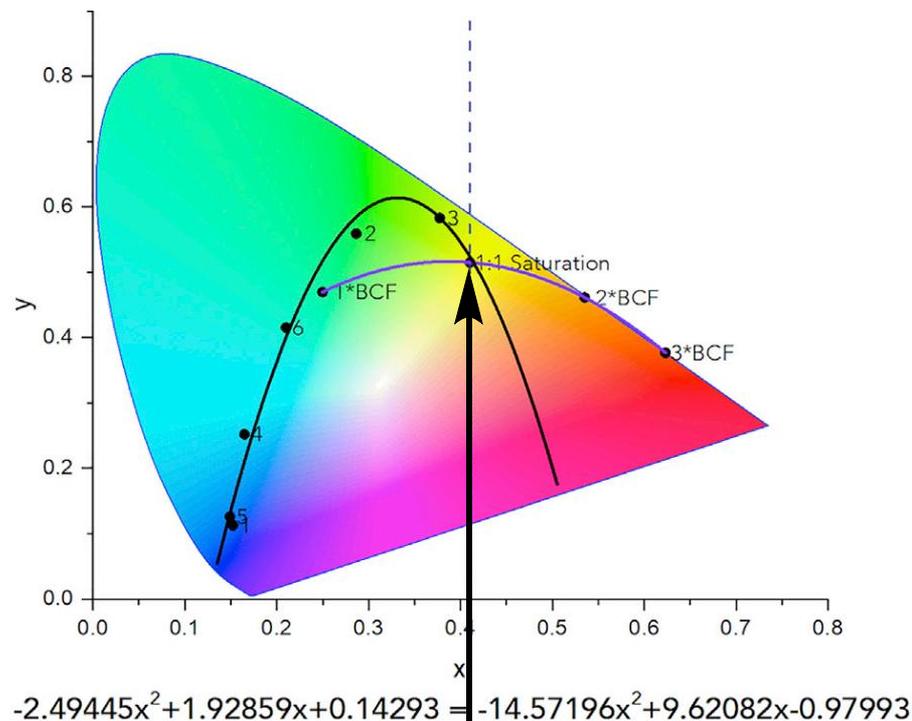
the chromaticity of a theoretical probe of specific Lewis basicity



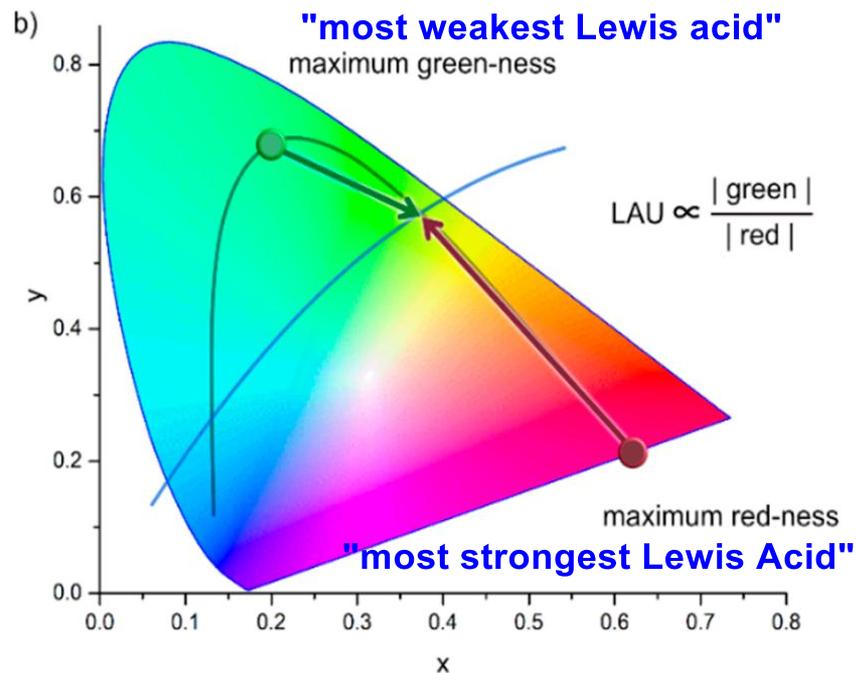
$$Y = -14.57196x^2 + 9.62082x - 0.97993$$

Chromaticity trend of probes

Lewis Acid Units (LAU)



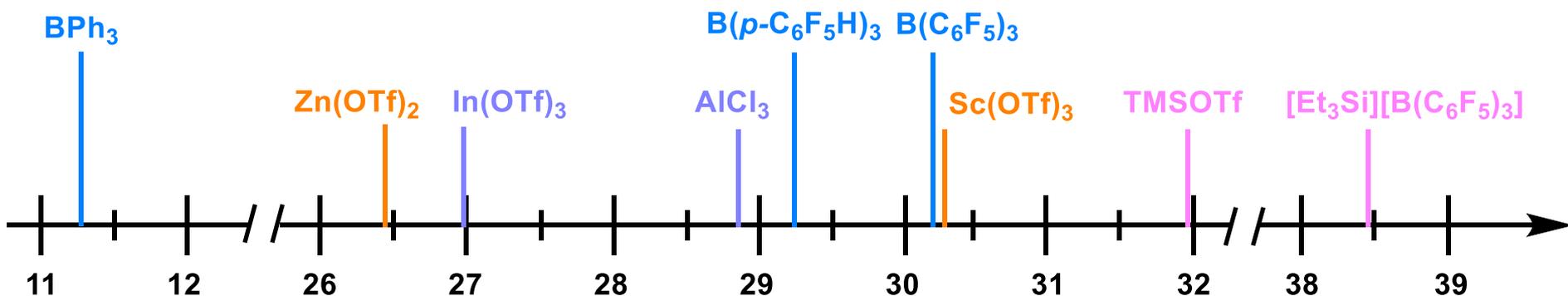
a 1:1 ratio of Lewis acid and the probe



$$strength = \frac{\sqrt{(x - 0.333)^2 + (y - 0.615)^2}}{\sqrt{(x - 0.511)^2 + (y - 0.164)^2}} \times 100$$

Lewis Acid Units (LAU)

- 1) Gaffen, J.; Bentley, J. N.; Torres, L.; Chu, C.; Baumgartner, T.; Caputo, C. *Chem*, **2019**, *5*, 1567-1583.
- 2) Bentley, J. N.; Elgadi, S.; Gaffen, J.; Demay-Drouhard, P.; Baumgartner, T.; Caputo, C. *Organometallics*, **2020**, *39*, 3645-3655.



Borane Derivative Lewis Acids

Group 13 (without B) Lewis Acids

Cationic Lewis Acids

Transition Metal Lewis Acids

} Difficult to measure by conventional eLA evaluating method such as GB method

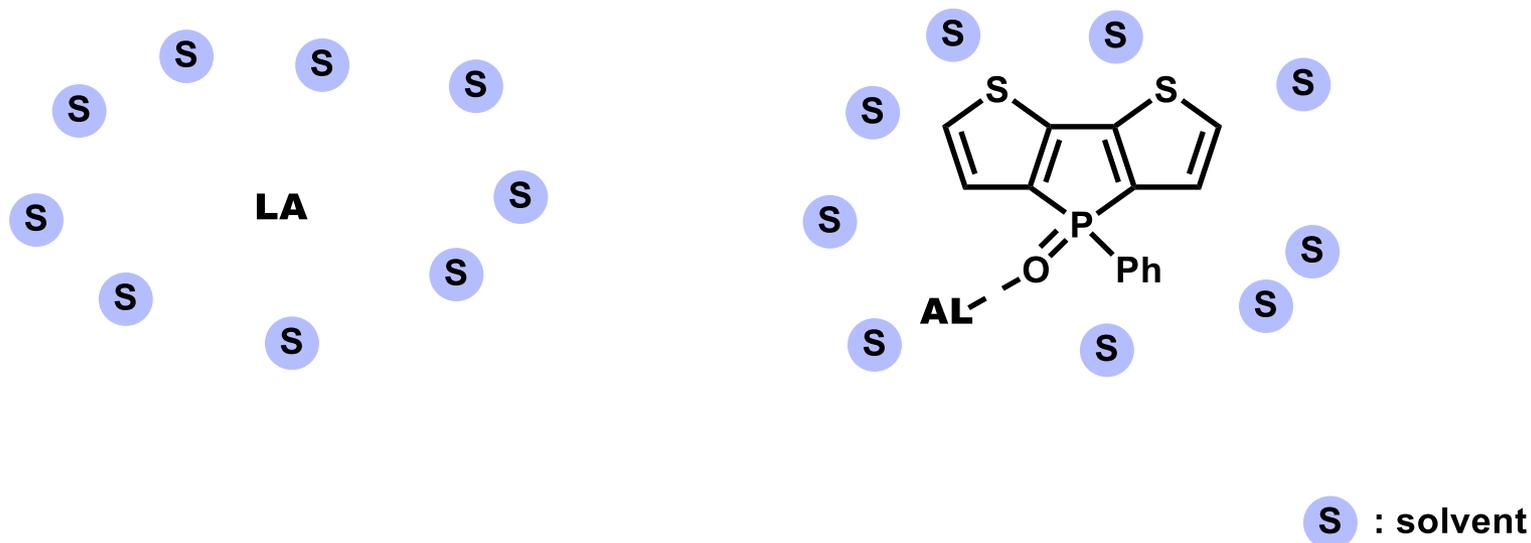
AlCl₃: All potential Lewis acid species in solution can be evaluated

Contents

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2. Fluorescent Lewis Adduct (FLA) Method
3. **Solvent Effects on the Strength of Lewis Acids
(main paper)**

Lewis Acid in solvent

Effective Lewis Acidity (eLA)



Can solvent effects on Lewis acidity be quantified?

LAU in Various Solvents (1)

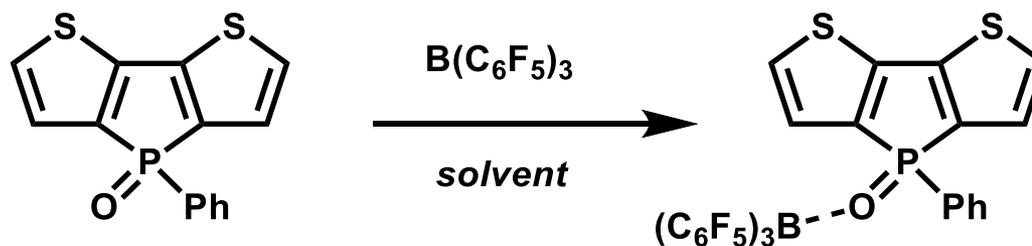
1. The properties of solvents

	toluene	PhCl	CH ₂ Cl ₂	Et ₂ O	MeCN
polarity ^a	33.9 kcal/mol	37.5 kcal/mol	41.1 kcal/mol	34.6 kcal/mol	46.0 kcal/mol
donor ability ^b	0.1 kcal/mol	1.0 kcal/mol	3.0 kcal/mol	19.2 kcal/mol	14.1 kcal/mol

^adetermined by the solvatochromism of betaine dye 30

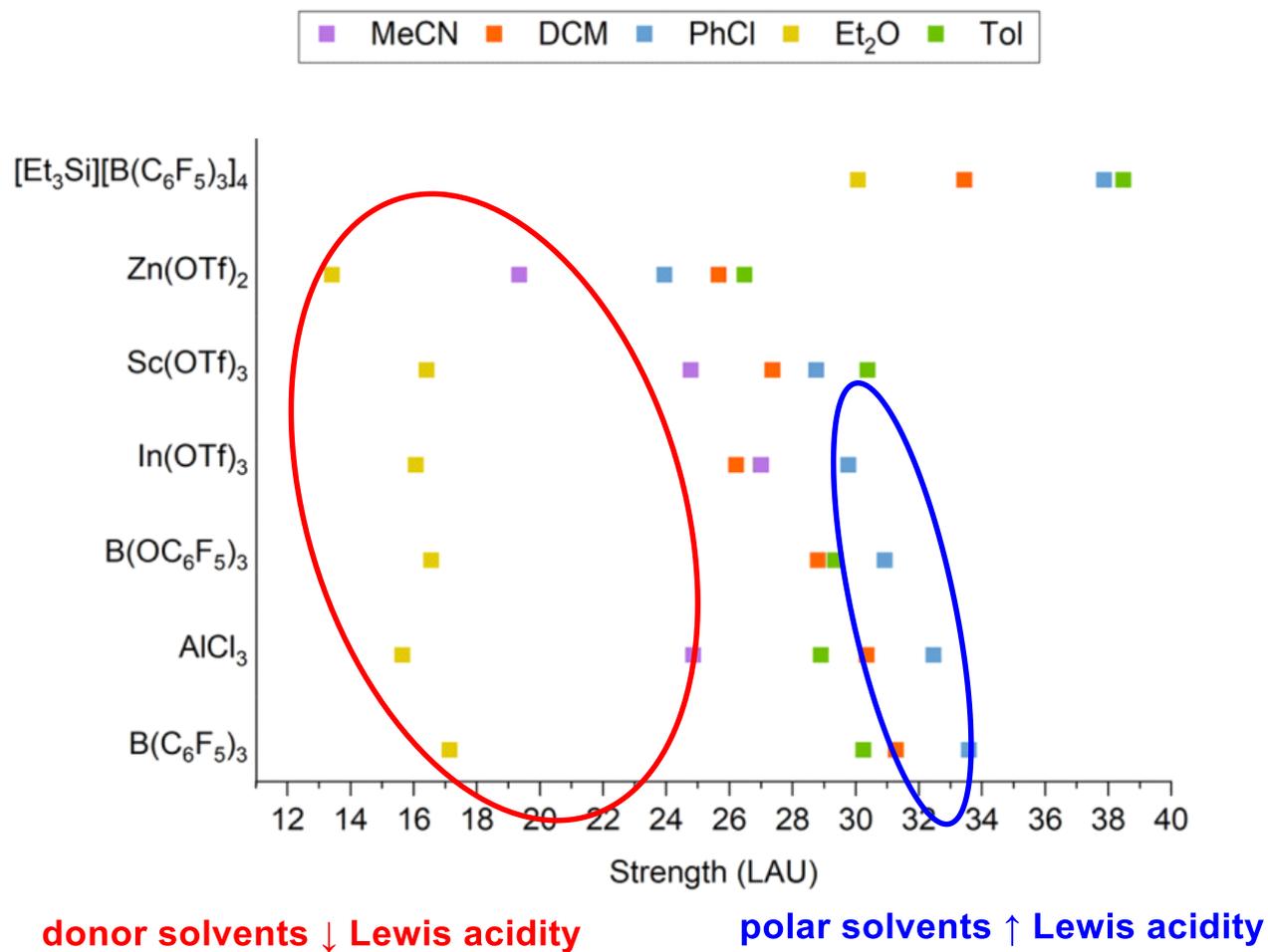
^bthe ability of a solvent to solvate the Lewis acid standard (SbCl₅)

2. The binding constants and LAU of probe 1 with B(C₆F₅)₃



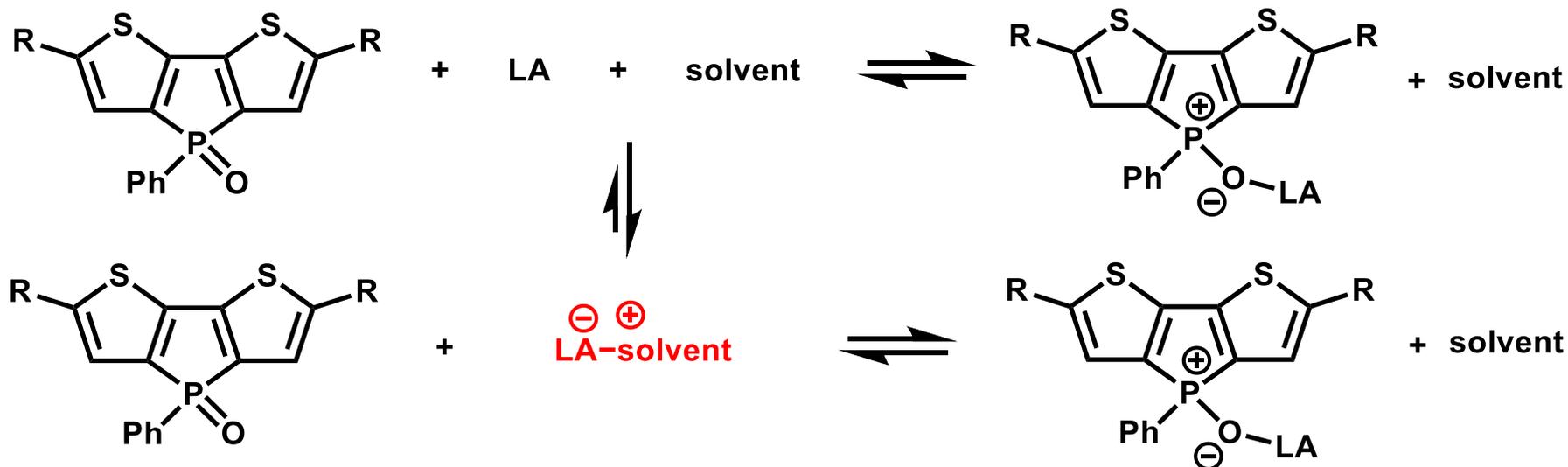
solvent	toluene	PhCl	CH ₂ Cl ₂	Et ₂ O	MeCN
binding constant	1.1 x 10 ⁵ M ⁻¹	3.1 x 10 ⁴ M ⁻¹	2.7 x 10 ⁴ M ⁻¹	2.9 x 10 ³ M ⁻¹	N.D.
LAU	30.25	33.59	31.27	17.14	N.D.

LAU in Various Solvents (2)



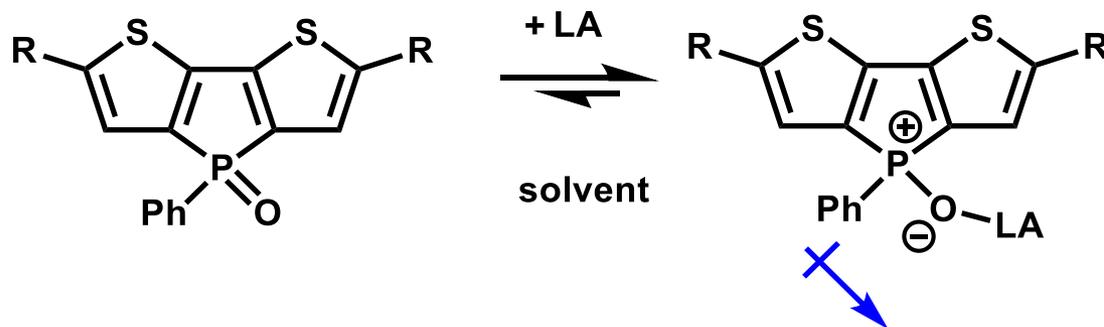
Solvent Effect Factors

1. donor solvents ↓ Lewis acidity



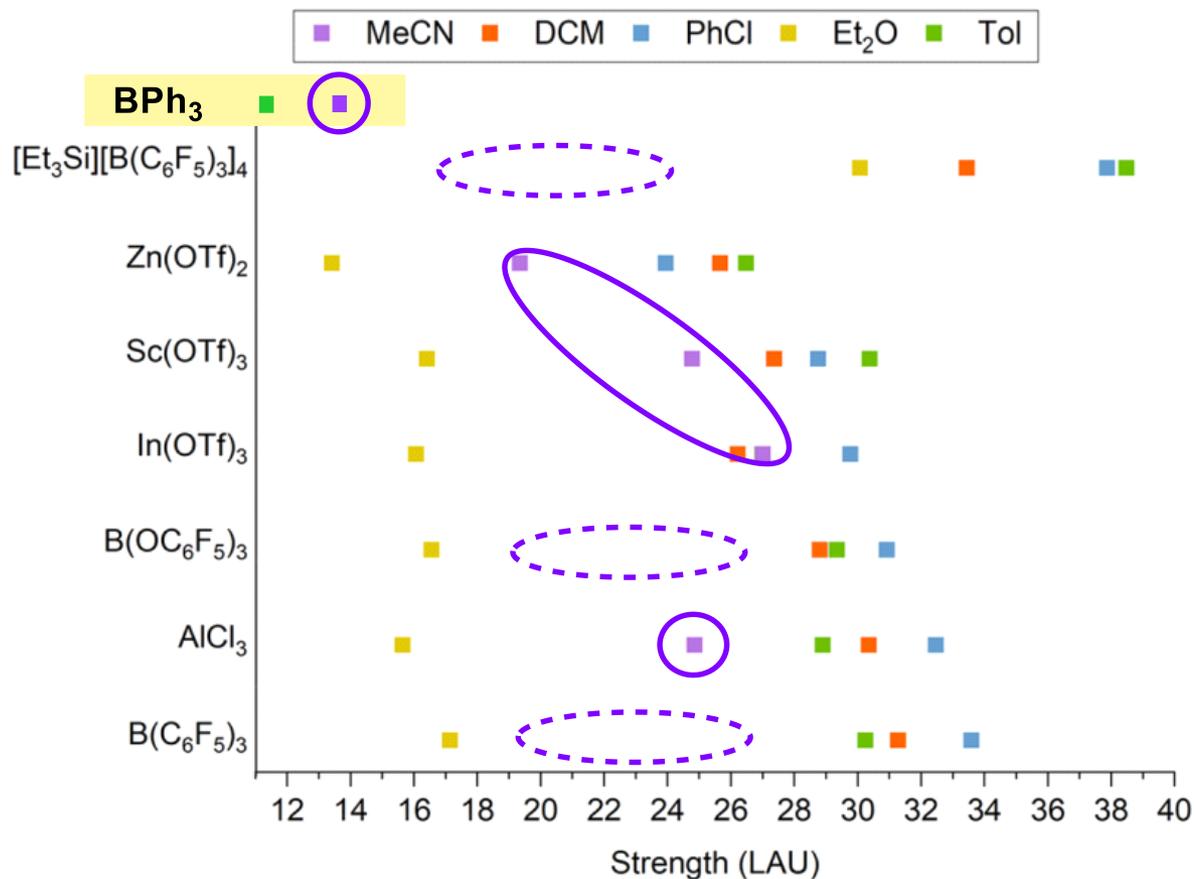
donor solvent is strongly coordinated with Lewis acid.

2. polar solvents ↑ Lewis acidity



dipole moment is stabilized by polar solvent

LAU in MeCN



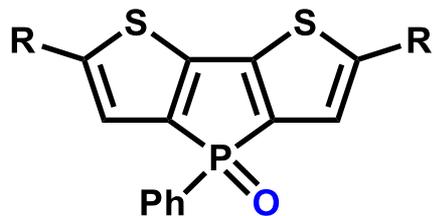
BPh₃ (weakest Lewis acid): LAU in toluene < LAU in MeCN

Cationic and Neutral borane (strong Lewis acid): LAU in MeCN is not measured at all.

AlCl₃ and triflate species: LAU in MeCN is still measurable.

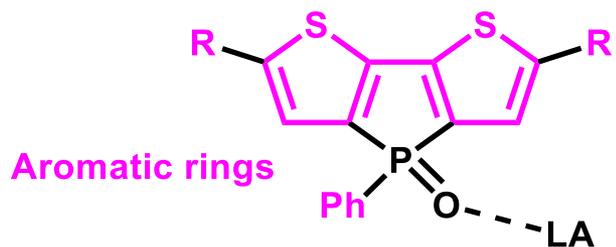
Donor vs Polarity effects depend on the Lewis acid

Limitations of FLA Method



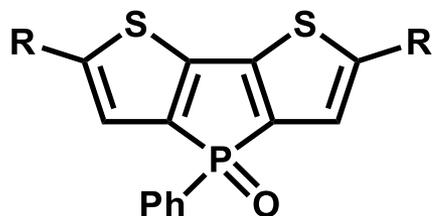
Harder Lewis base

LAU may be affected by
HSAB interaction.

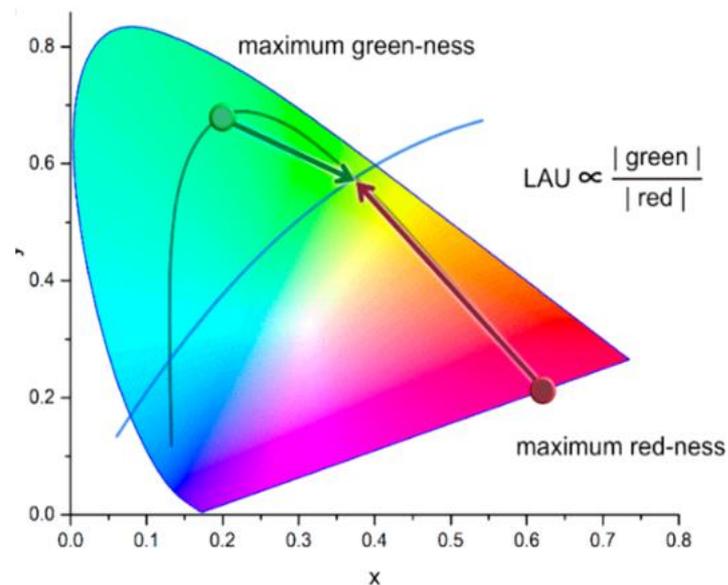


LAU may be affected by
 π - π interaction.

Summary



fluorescent P=O probes



CIE diagram

- Measures effective Lewis acidity in **solution**
- Minimizes **Lewis base dependence** using multiple probes
- Applicable to **metal-based and highly reactive Lewis acids**
- Quantifies **solvent effects** (polarity vs donor ability)
- Provides a practical, reaction-relevant acidity scale (LAU)