

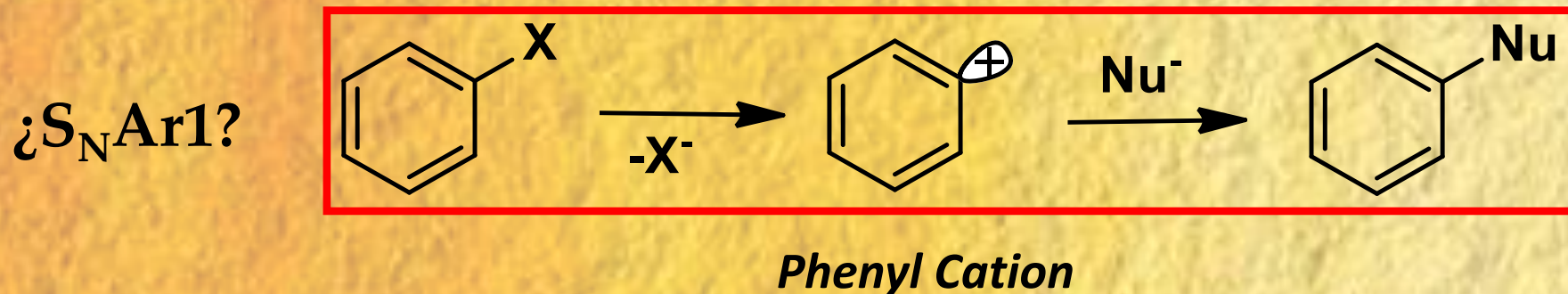
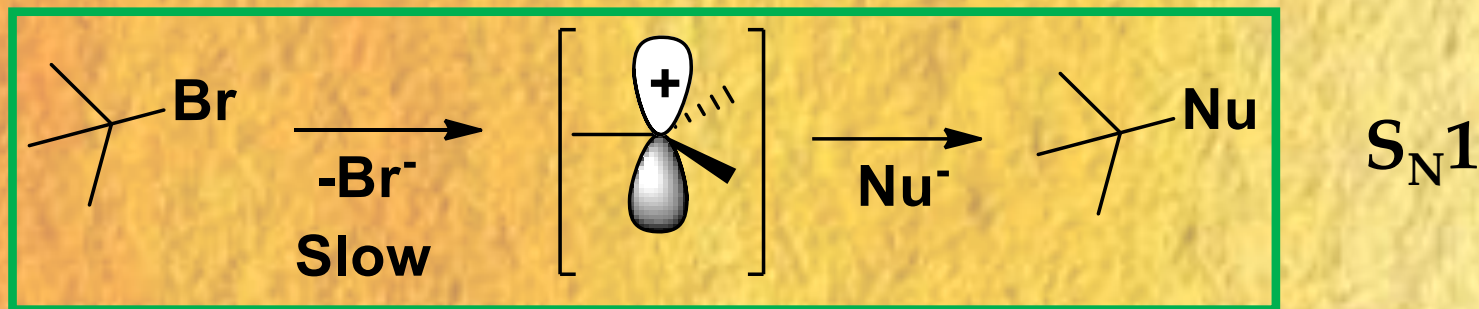


With the lights on.

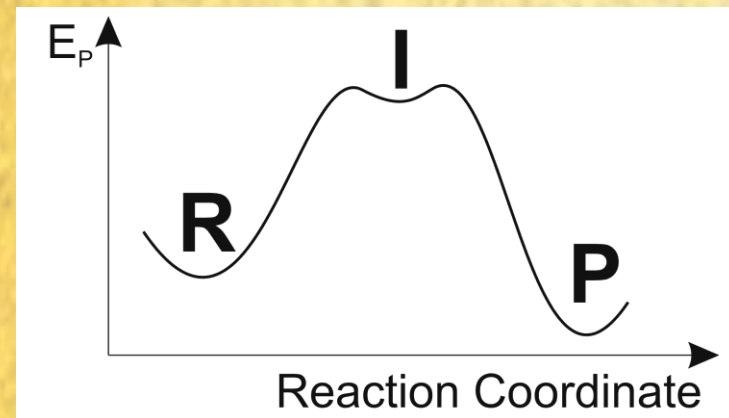
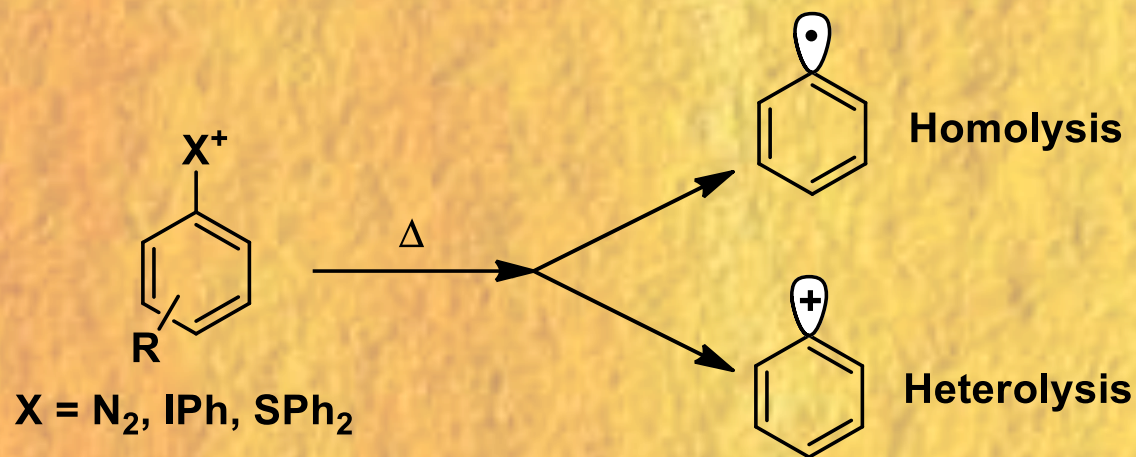
Photochemical generation of aryl cations

***PhotoGreen Lab**, Department of Chemistry, University of Pavia,
Viale Taramelli 12, 27100 Pavia, Italy*

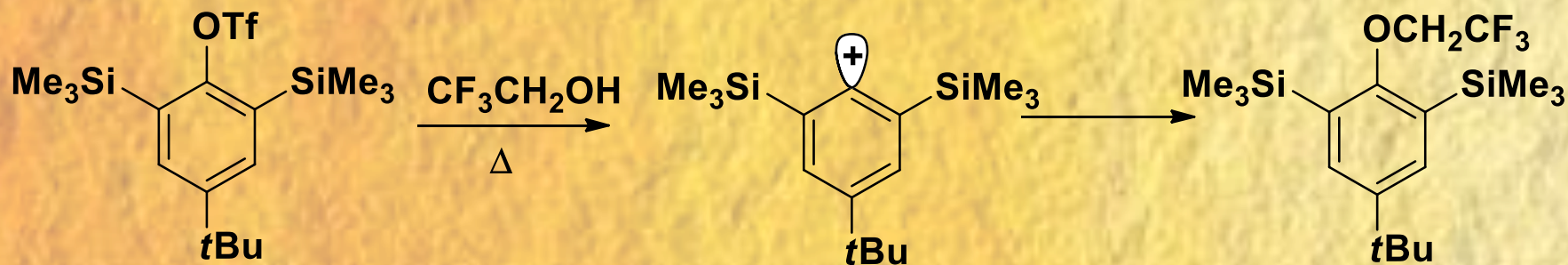
Aryl cation as intermediate in organic reactions.



Thermal generation of aryl cations.

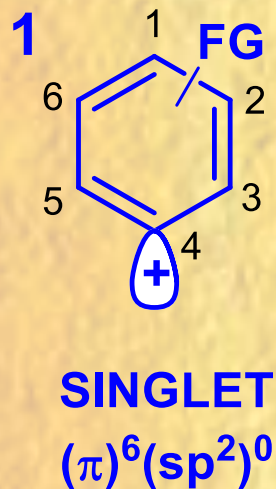
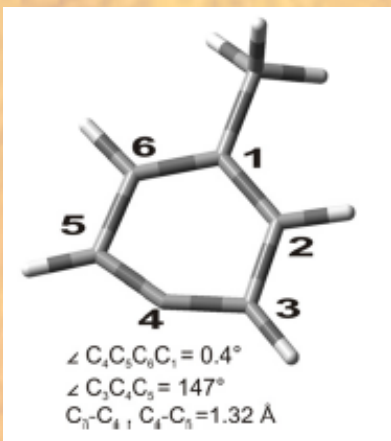


E. S. Lewis *J. Am. Chem. Soc.*, **1958**, *80*, 1371.

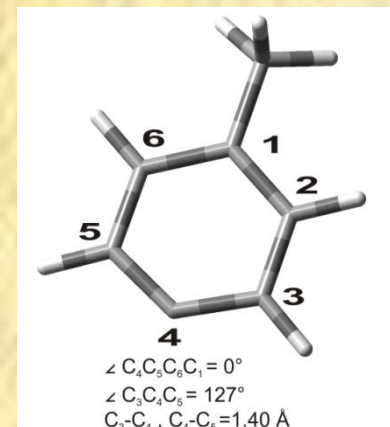


Y. Himeshima, H. Kobayashi, T. Sonoda, *J. Am. Chem. Soc.* **1985**, *107*, 5286

Aryl cations as new reactive intermediates



FG = CH₃



FG = CH₃

Non selective Electrophile

- Addition to the solvent

Chemoselective Electrophile

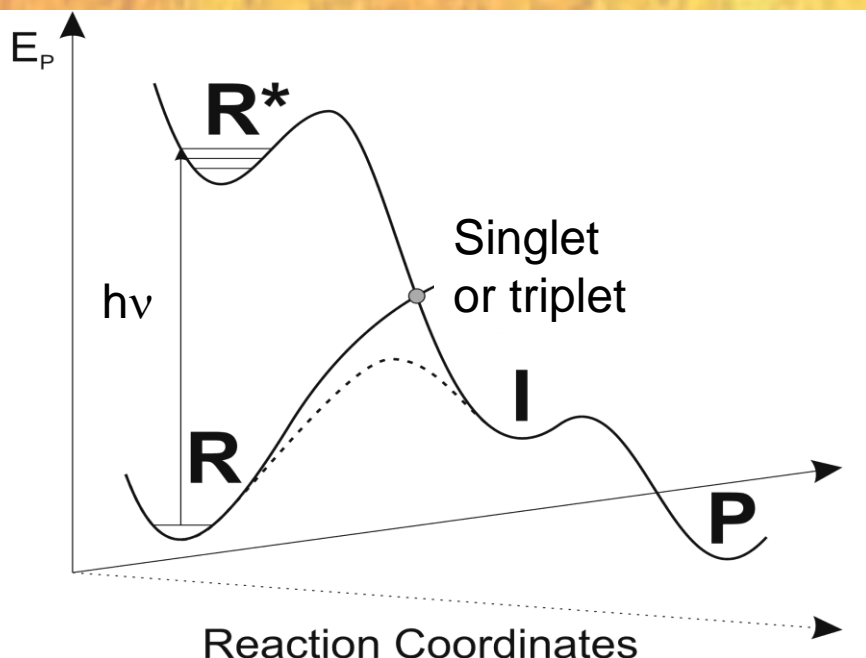
- NO Addition to the solvent

- Hydrogen abstraction from the solvent

- Reaction with π nucleophiles

(olefins, alkynes and (hetero)aromatics).

Advantages of the photochemical approach.

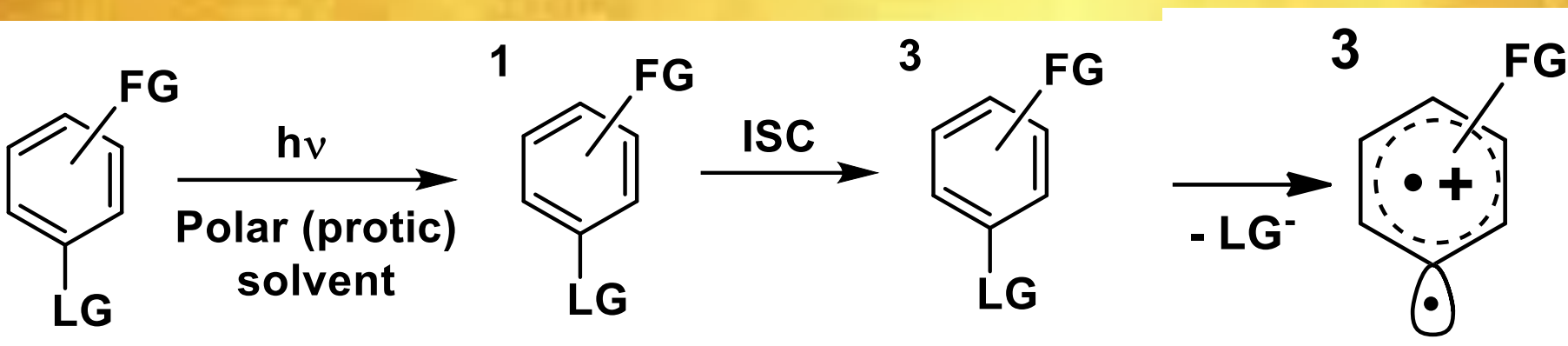


1. Mild conditions

2. Photon as green reagent

3. Different spin states accessible

Triplet Phenyl cations from aryl halides and esters

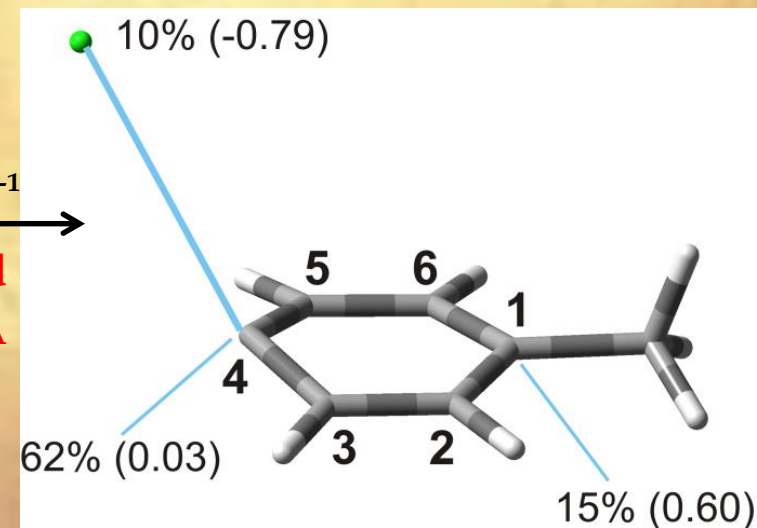
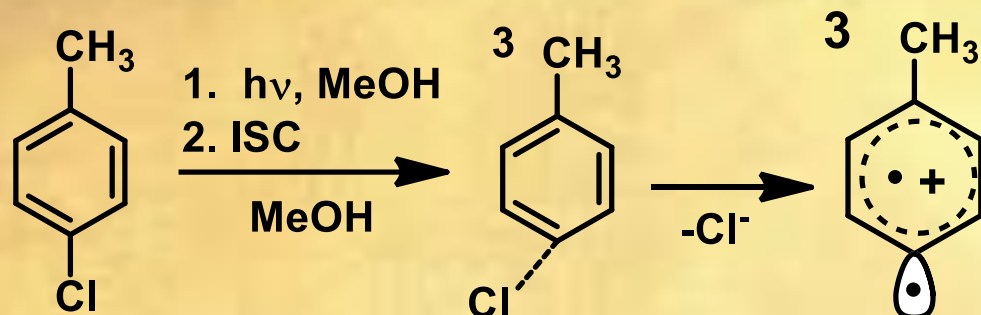


LG (Leaving group) = Cl, F, OSO_2R , $OP(O)(OEt)_2$, OSO_3R
FG (Functional group) = OMe, NMe_2 , OH, SMe, Alkyl

Conditions for the photochemical generation of triplet phenyl cations:

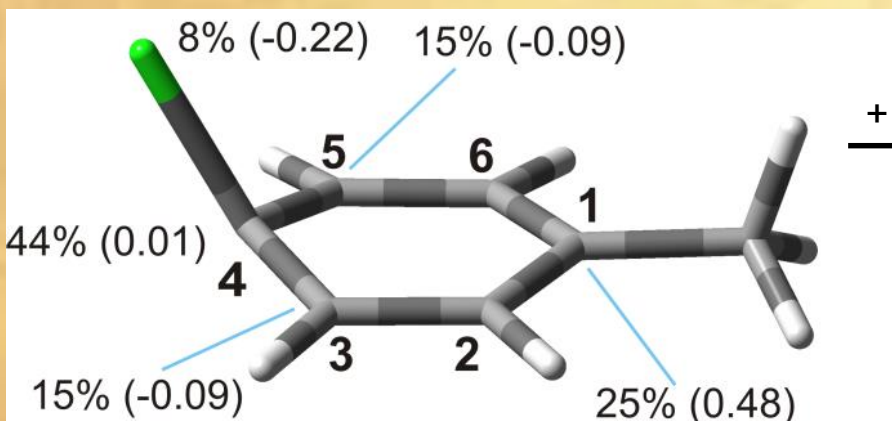
1. The photoheterolytic cleavage must arise from the triplet excited state (efficient ISC required).
2. Reactions have to be carried out in polar solvents ($AcOEt$, MeCN, CH_3OH , H_2O , CF_3CH_2OH).

Triplet Phenyl cations from aryl halides and esters



+ 15.6 Kcal mol⁻¹

Ar-Cl bond
up to 4.00 Å

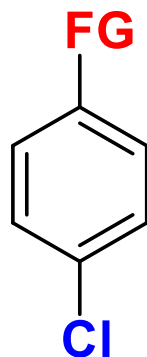


MeOH bulk, UB3LYP/6-311+G(2d,p)

Photogeneration of triplet phenyl cation ($^3\text{Ar}^+$)

Decrease the likelihood of
photoheterolysis

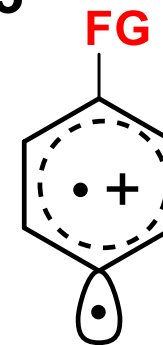
3



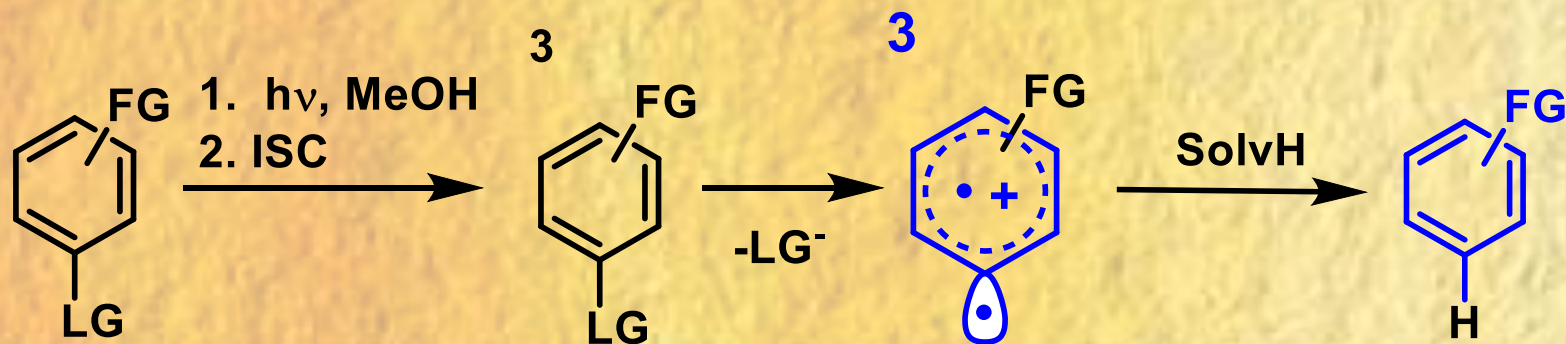
- 1, **FG** = NMe_2
- 2, **FG** = NH_2
- 3, **FG** = OH
- 4, **FG** = OMe
- 5, **FG** = CH_2SiMe_3
- 6, **FG** = Me
- 7, **FG** = Et
- 8, **FG** = $i\text{Pr}$
- 9, **FG** = $t\text{Bu}$
- 10, **FG** = SiMe_3
- 11, **FG** = H

$-\text{Cl}^-$

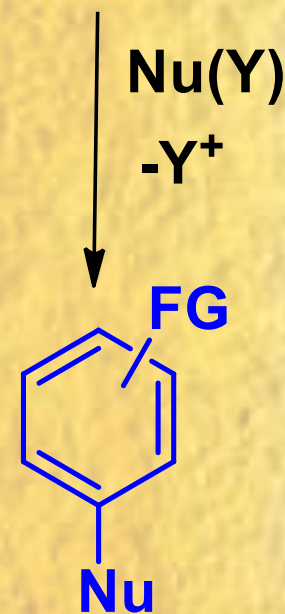
3



Triplet Phenyl cations from aryl halides and esters

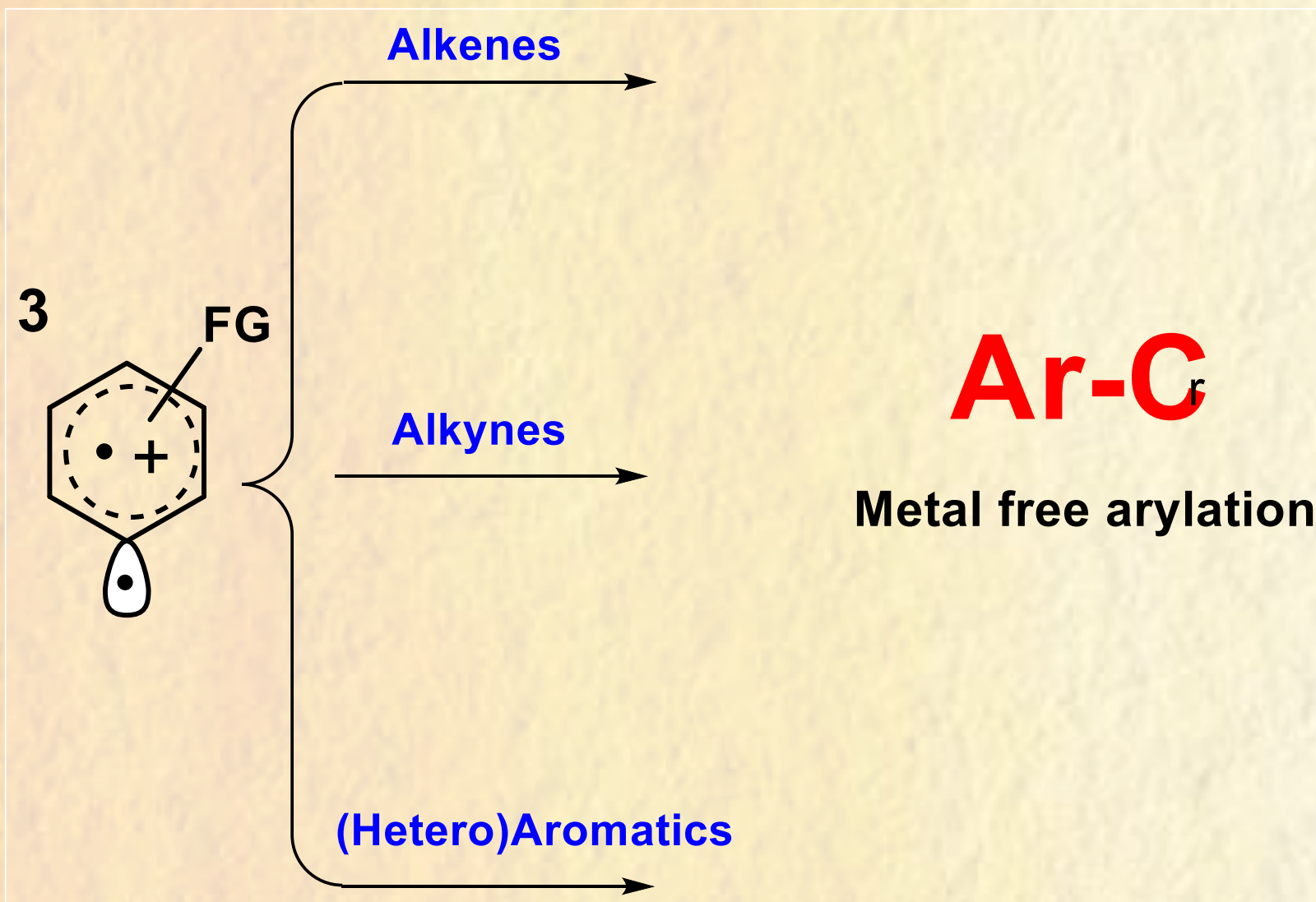


Triplet phenyl cation is always the first generated intermediate. Its reactivity depends on both the nature and the position of the functional group.

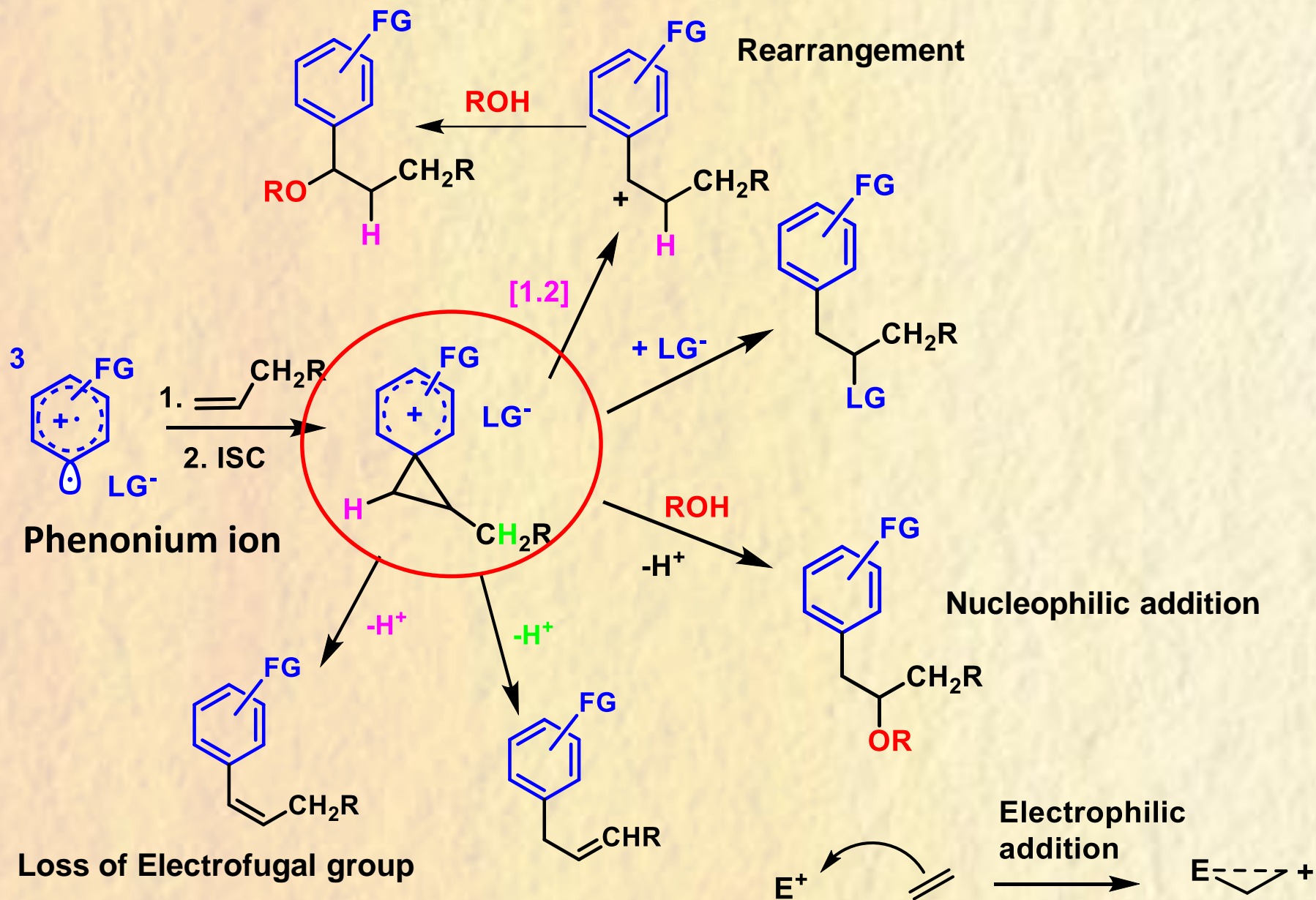


$Nu(Y) = \pi$ -bond nucleophile

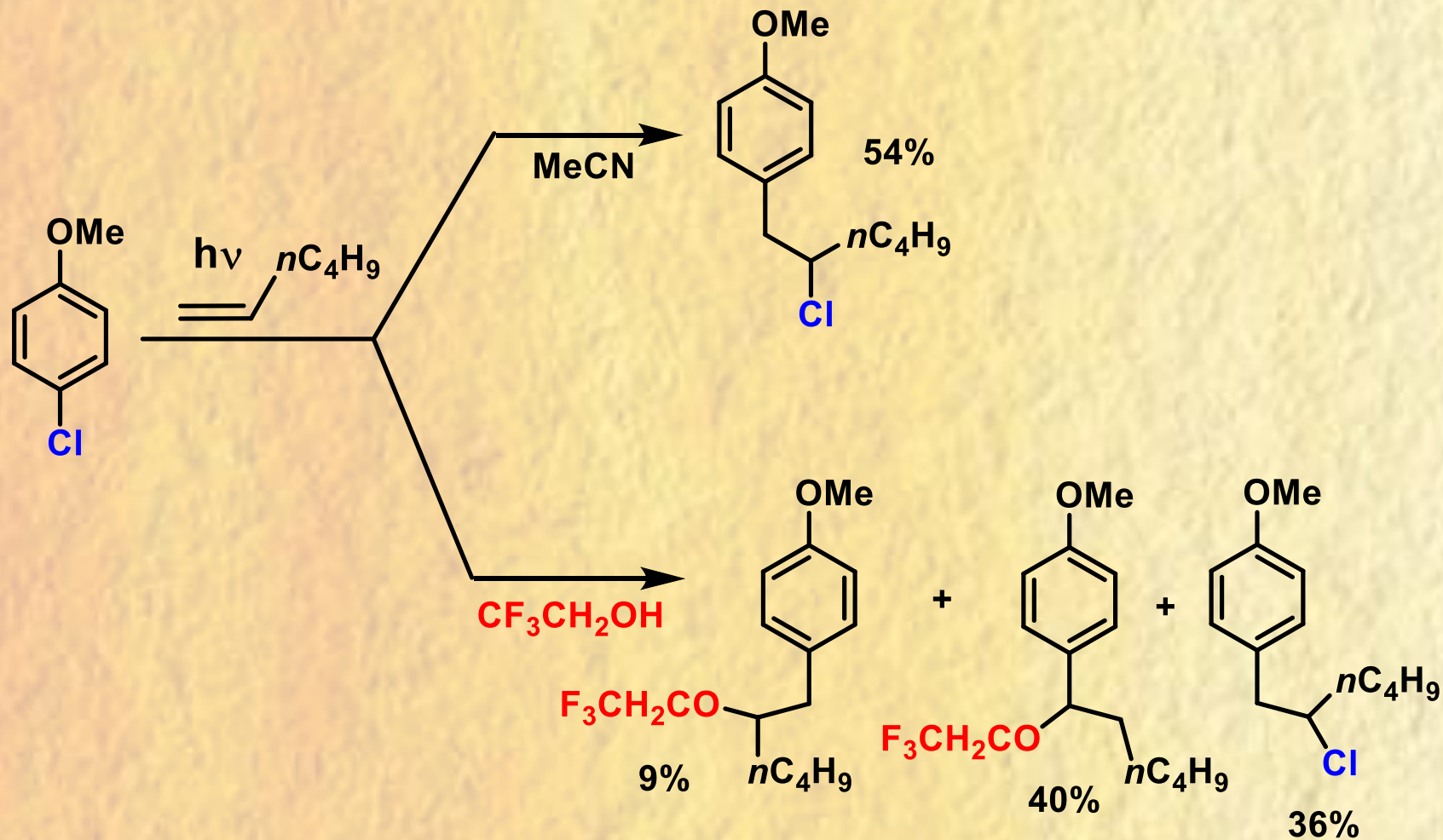
Triplet Phenyl Cations: synthetic applications



Reactivity of phenyl cations with alkenes. Observed pathways



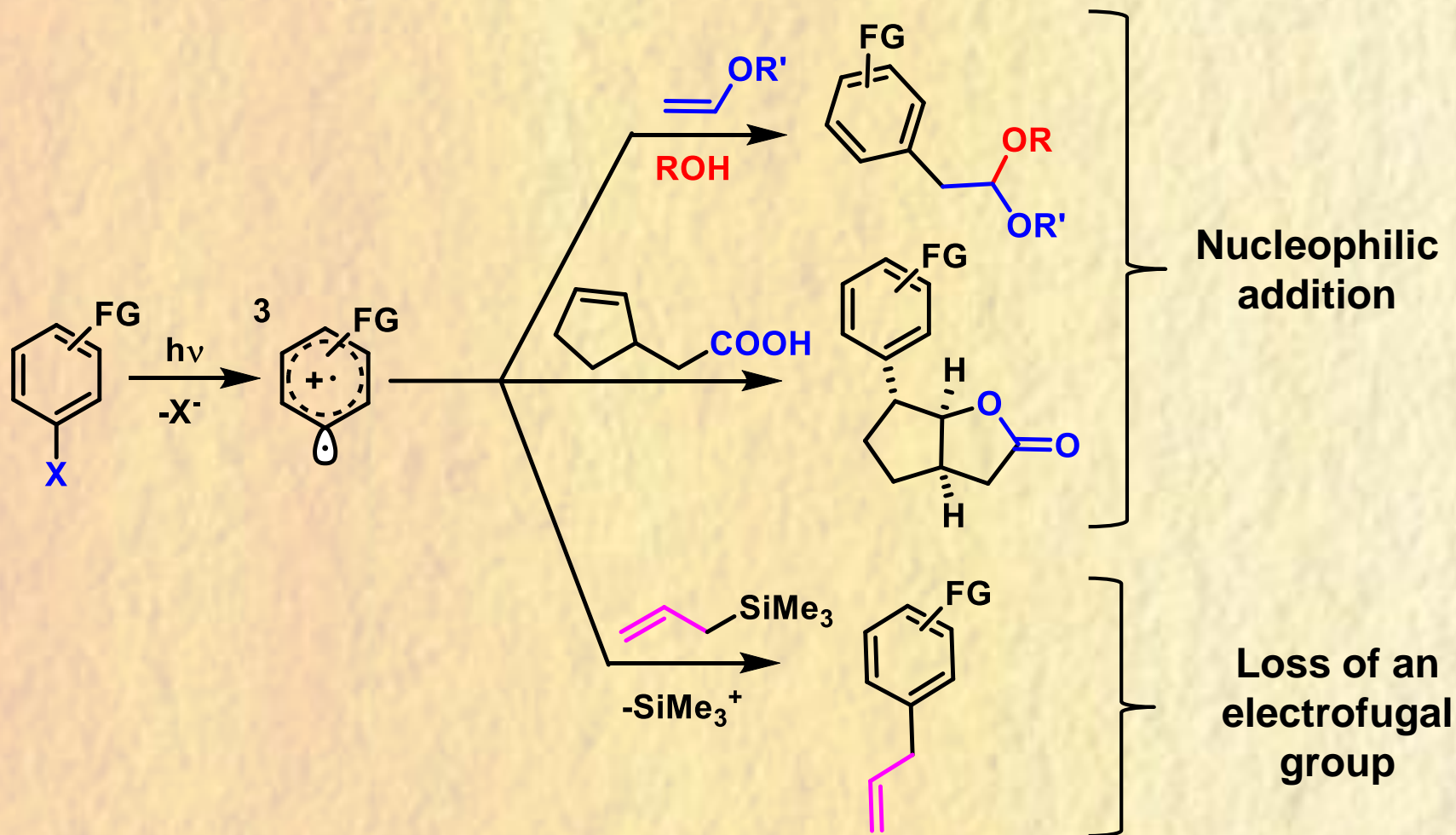
Poor chemoselectivity with unfunctionalized alkenes



S. Protti, D. Dondi, M. Mella, M. Fagnoni, A. Albini, *Eur. J. Org. Chem.* **2011**, 3229.

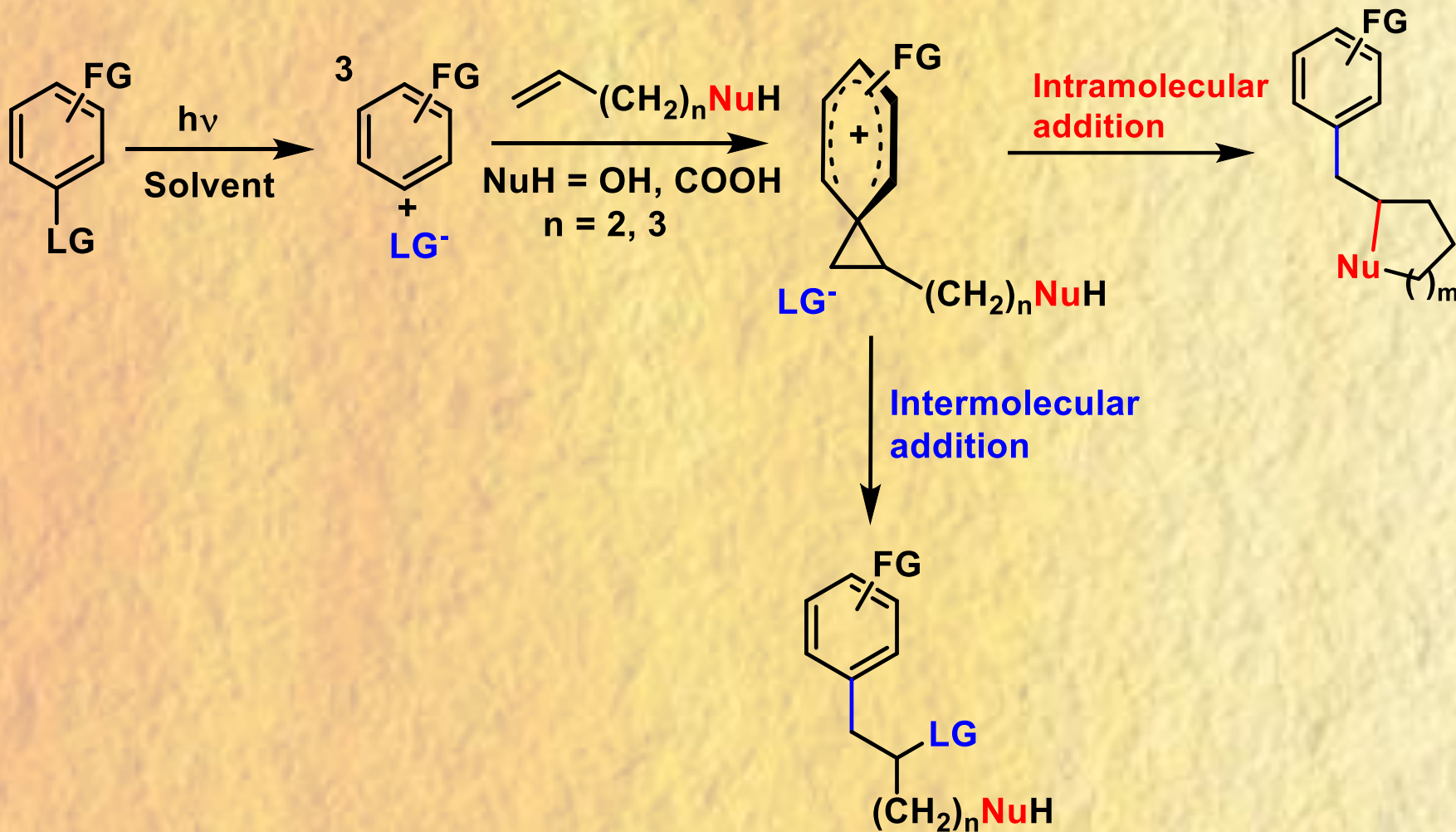
S. Protti, M. Fagnoni, M. Mella, A. Albini, *J. Org. Chem.* **2004**, 69, 3465.

Metal-free arylations via triplet phenyl cation

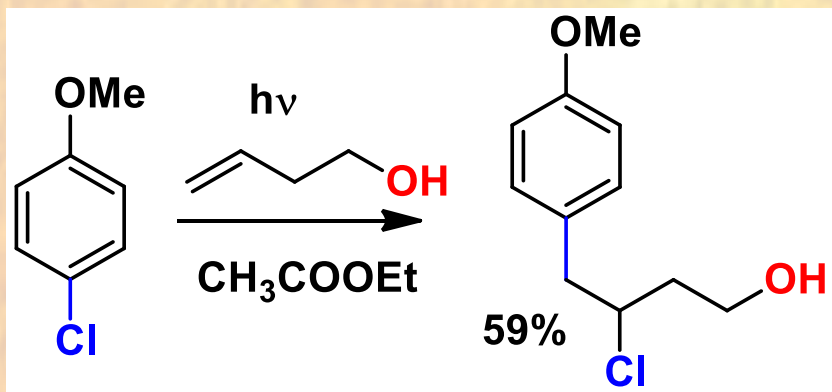


S. Lazzaroni, S. Protti, M. Fagnoni, A. Albini, *Org. Lett.* **2009**, *11*, 349; H. Qrareya, C. Raviola, S. Protti, M. Fagnoni, A. Albini, *J. Org. Chem.* **2013**, *78*, 6016. S. Protti, M. Fagnoni, A. Albini, *J. Am. Chem. Soc.* **2006**, *128*, 10670. C. Raviola, V. Canevari, S. Protti, A. Albini, M. Fagnoni, *Green Chem.* **2013**, *15*, 444.

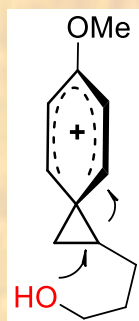
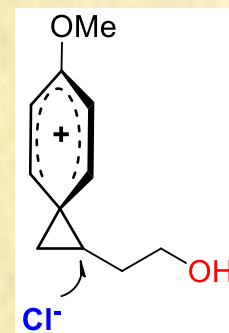
Intramolecular/intermolecular addition of a nucleophile



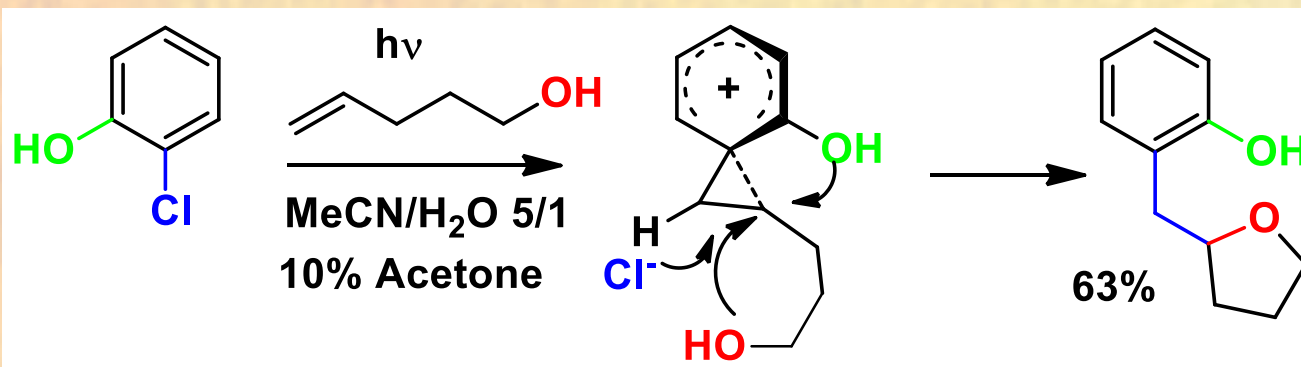
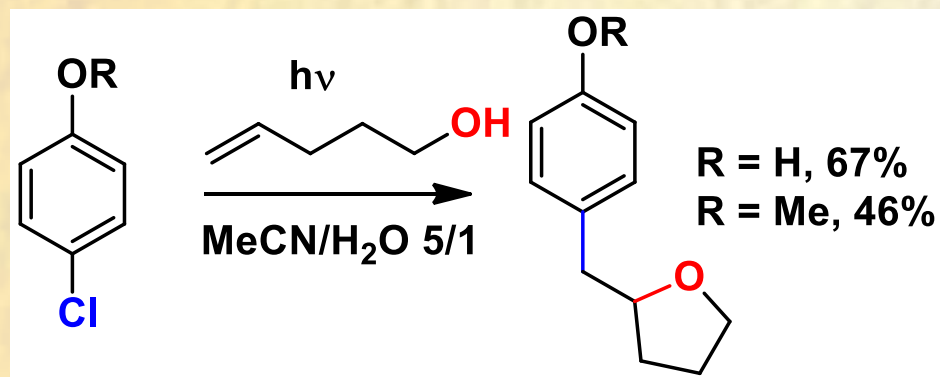
Intramolecular/intermolecular addition of a nucleophile



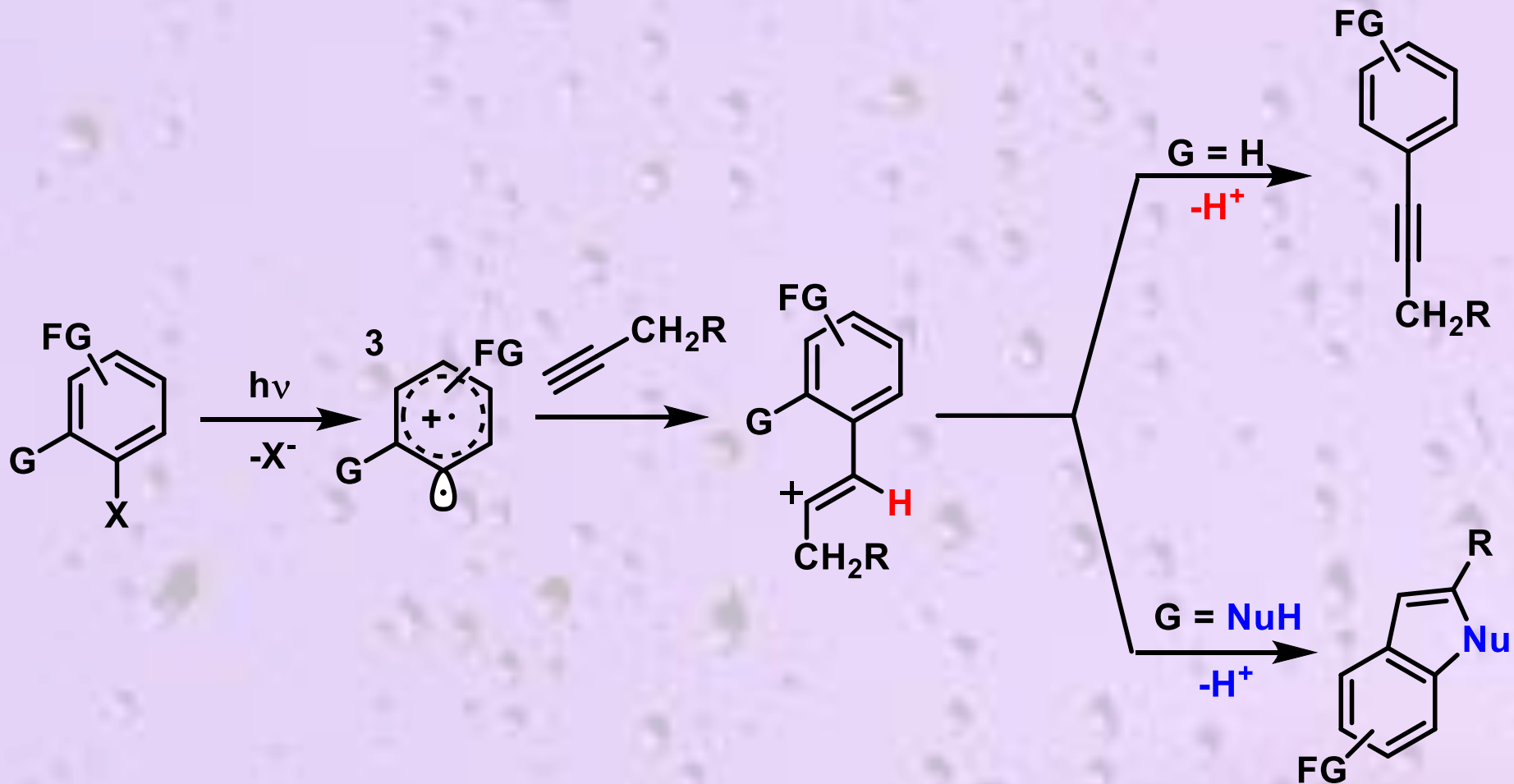
Polar solvent
Intimate ion pair



Protic solvent
solvated ion pair



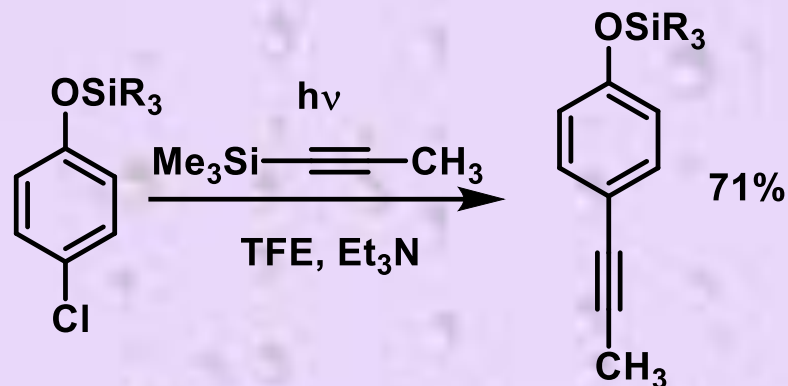
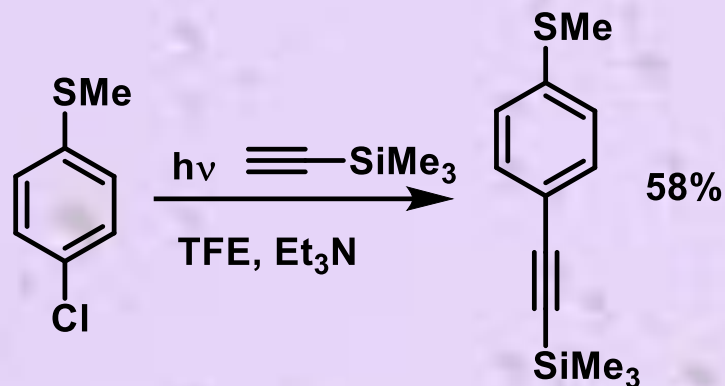
Reactivity of phenyl cations with alkynes: synthesis of arylalkynes



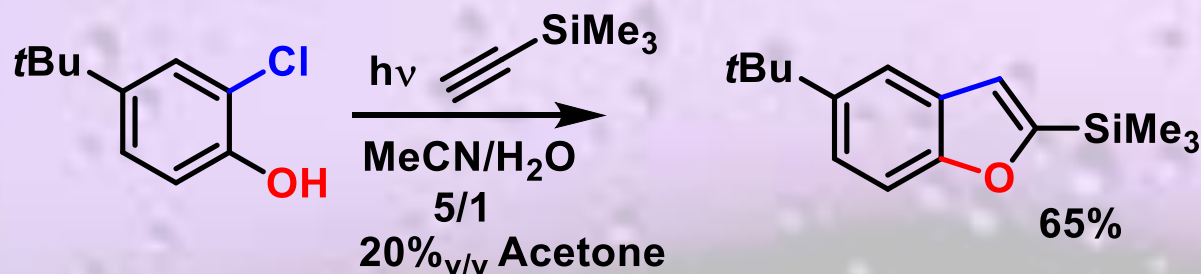
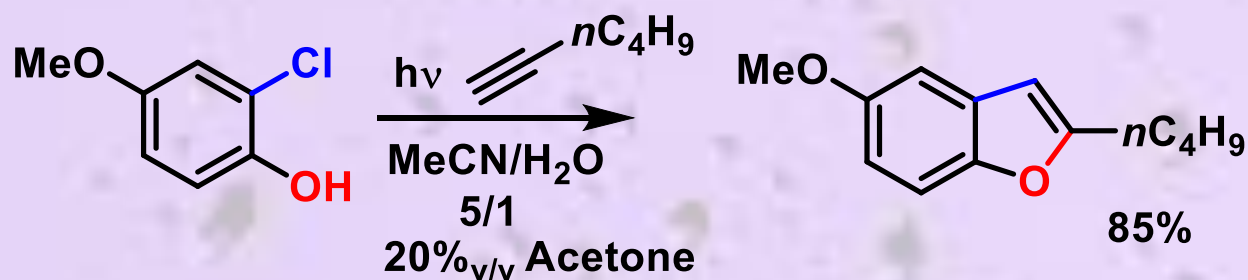
S. Protti, M. Fagnoni, A. Albini, *J. Org. Chem.* **2012**, 77, 6473.

S. Protti, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2005**, 44, 5675

Reactivity of phenyl cations with alkynes: synthesis of arylalkynes



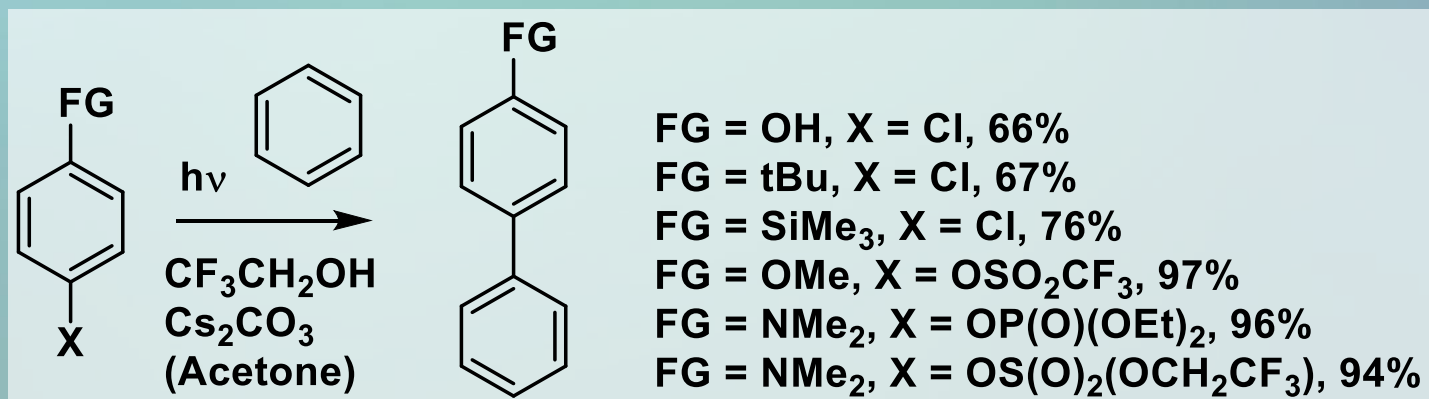
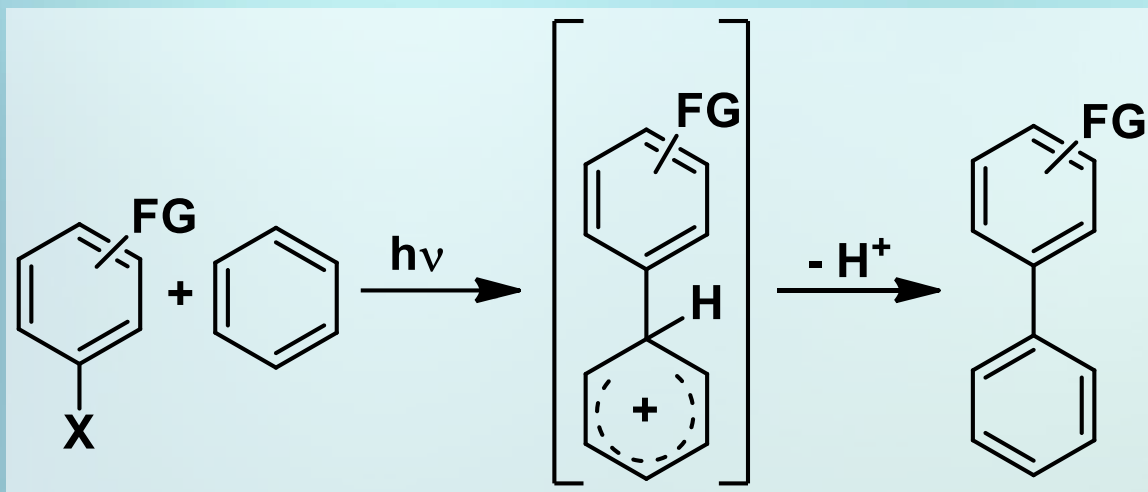
A transition **metal-free Sonogashira** reaction.



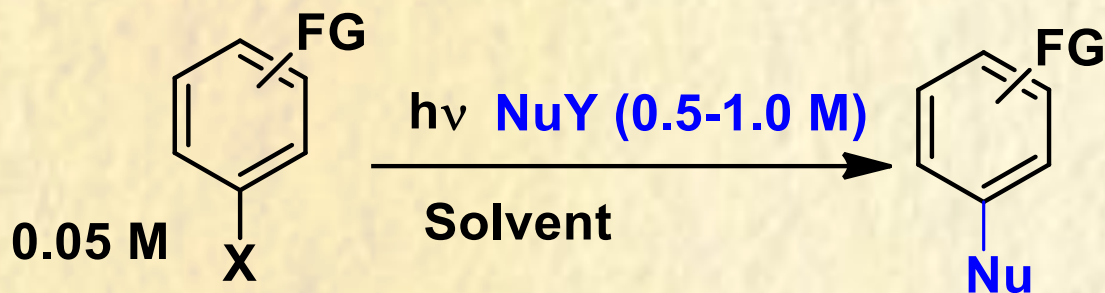
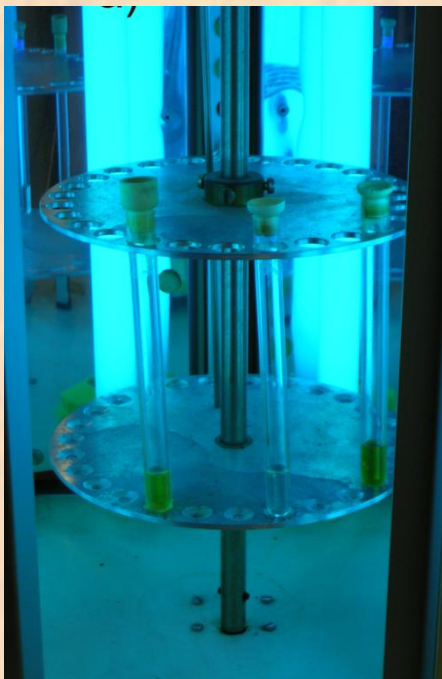
S. Protti, M. Fagnoni, A. Albini, *J. Org. Chem.* **2012**, 77, 6473.

S. Protti, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2005**, 44, 5675

Reaction with arenes: synthesis of biaryls



The pros and cons of phenyl cations

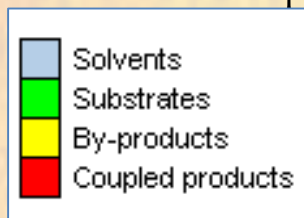
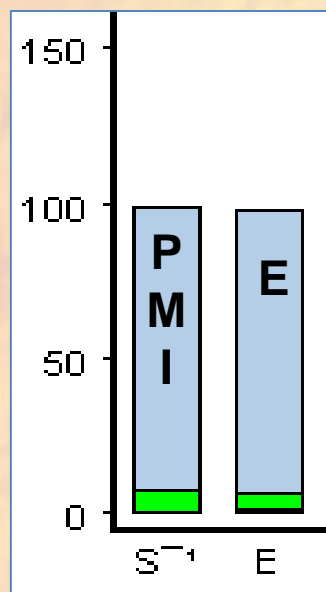


Irradiation time: 4-36 hours

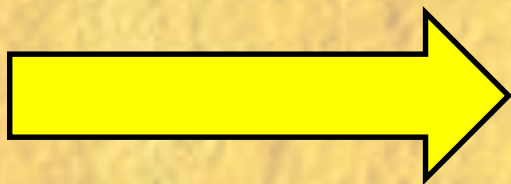
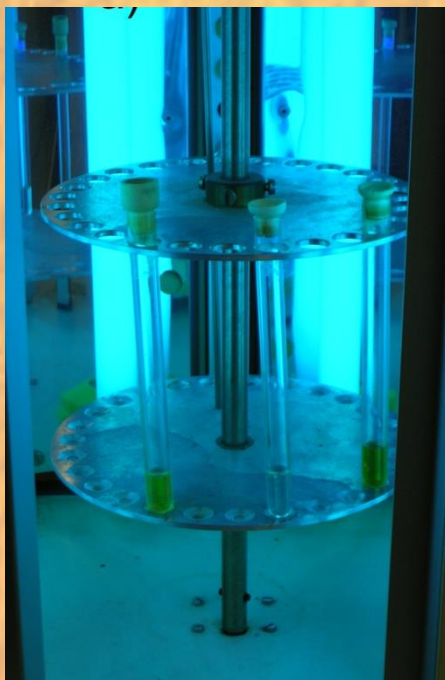
Phenyl cations are short lived intermediates
(100-400 ns)

Nucleophiles have to be used in a large excess
(up to 10-20 fold amount).

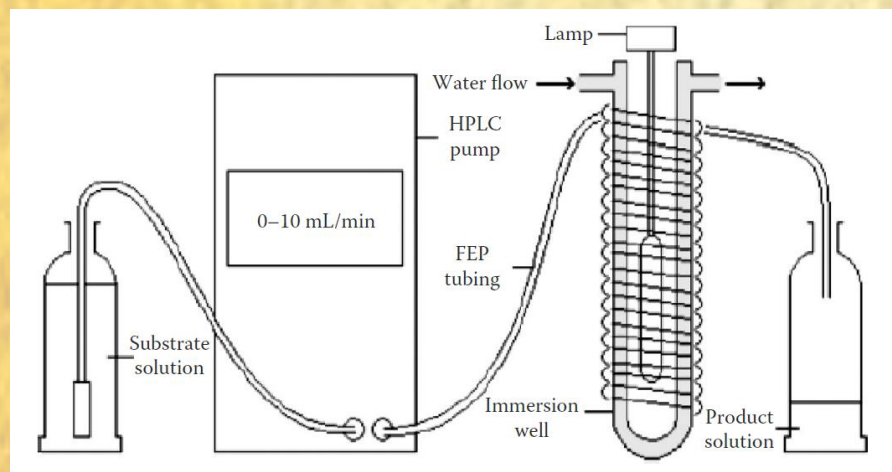
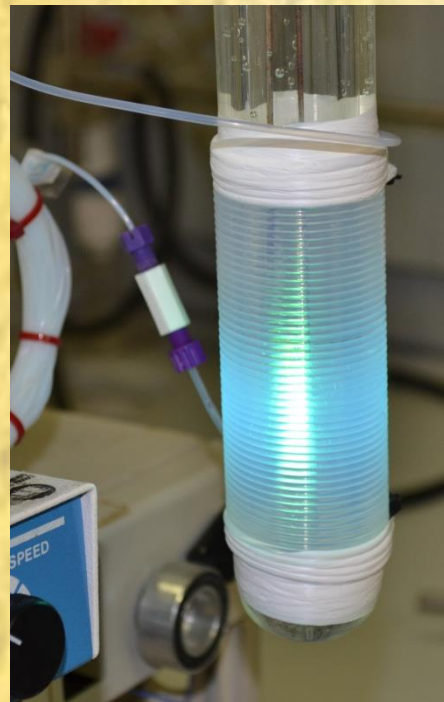
E-factor and PMI: 100-150 Kg/Kg



From batch...

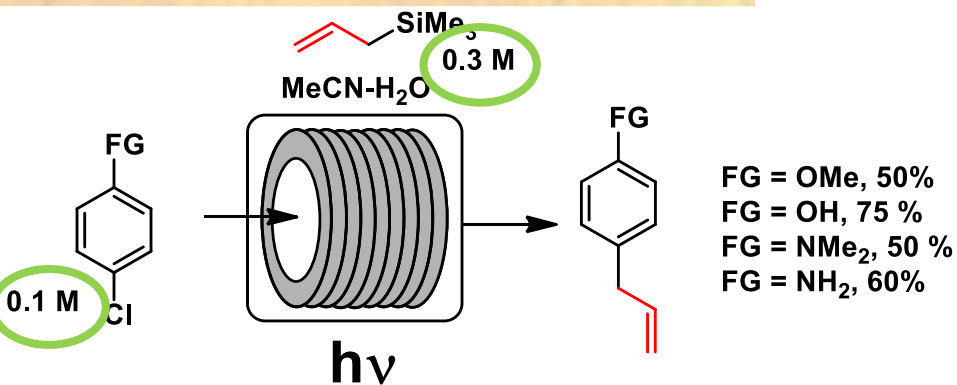
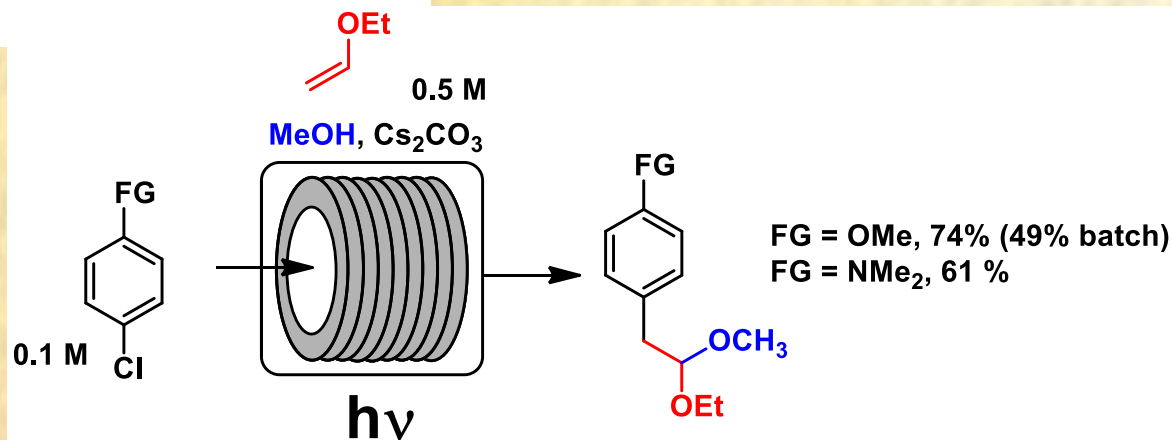
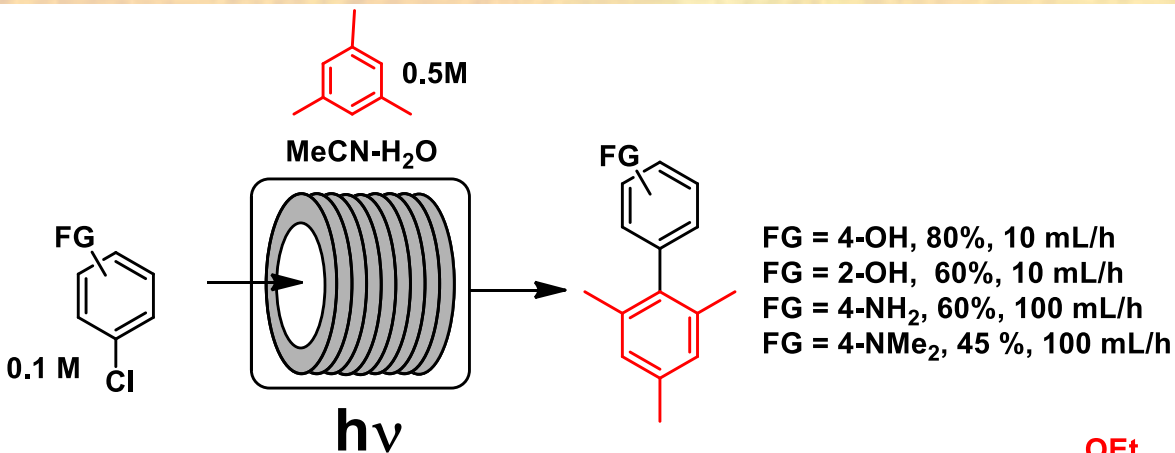


...to flow



J. P. Knowles, L. D. Elliott, K. I. Booker-Milburn,
Beilstein J. Org. Chem. 2012, 8, 2025

Photochemical arylations under flow conditions



Irradiation time: 0.5-6 hours

E-factor: down to 30 Kg/Kg