http://greensoc.chm.unipg.it

~~Novel~~ Technologies for green synthesis and catalysis

@ Chiesi

UNIVERSITÀ DI PARMA

Innovation & Sustainability in Process Chemistry

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luigi.vaccaro@unipg.it

UMBRIA: The Green Heart of Italy

Laboratory of Green Synthetic Organic Chemistry Perugia

Green S.O.C. Perugia

http://greensoc.chm.unipg.it

From a paint of

GERARDO DOTTORI
(Perugia)

With the support of

FONDAZIONE CASSA RISPARMIO PERUGIA

Laboratory of Green S.O.C. Perugia

http://greensoc.chm.unipg.it

SPRING 2024

What does Green Chemistry really mean ?

Efficient Chemistry???

Reduced Environmental Impact Chemistry???

Chemistry for a Sustainable Development???

Conscientious Chemistry???

Modern Chemistry???

What does mean “MAKING” Green Chemistry?

J. A. Linthorst, Origins and development of green chemistry
Foundation of Chemistry , 2010, 12, 55–68

EPA – US Environmental Protection Agency

THE POLLUTION PREVENTION ACT OF 1990

This was the U.S. environmental law stating that the first choice for preventing pollution is to **design industrial processes that do not lead to waste production**

This is the Green Chemistry approach

"The Congress hereby declares it to be the national policy of the United States that pollution should be prevented or reduced at the source whenever feasible; pollution that cannot be prevented should be recycled in an environmentally safe manner, whenever feasible; pollution that cannot be prevented or recycled should be treated in an environmentally safe manner whenever feasible; and disposal or other release into the environment should be employed only as a last resort and should be conducted in an environmentally safe manner"

Green chemistry is a great opportunity to improve process efficiency…

- **Mountains of solid waste are piling up—particularly in industrialized nations.**
- **Air and water pollution continue to be problems in many places.**

Most importantly attention was officially pointed on “millions of tons of pollution” and the related cost of “tens of billions of dollars per year” (Pollution Prevention Act 1990, p.617).

KEY ELEMENTS CONTRIBUTING TO WASTE/ENERGY

1. REACTION MEDIUM

2. CATALYST/additives

3. STIRRING technology (downstream management)

BIG DIFFERENCE BETWEEN ACADEMIA AND INDUSTRY

1. REACTION MEDIUM

2. CATALYST/additives

3. STIRRING technology (downstream management)

IN ACADEMIA

AREAS OF EXPERTISE TO BE PROMOTED

IN INDUSTRY

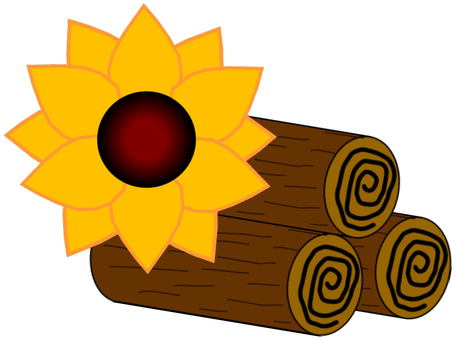
POSSIBLE SOLUTIONS TO A SPECIFIC ISSUE

CONCLUSION:

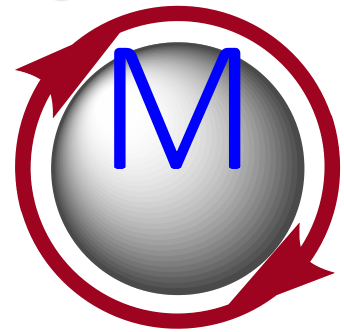
THE CONCEPT OF INTRINSICALLY GREEN DOES NOT EXIST

Safe Reaction Media

Biomass/waste valorization

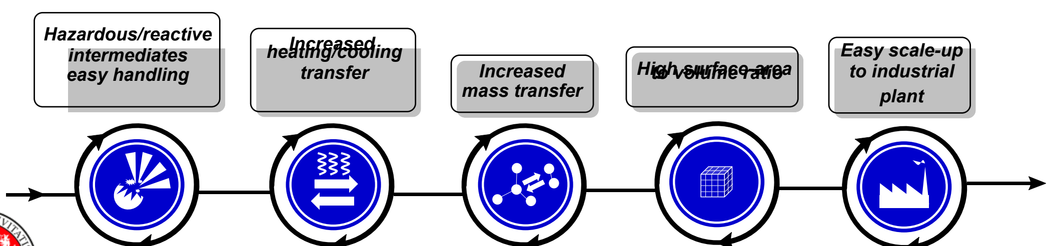


Heterogeneous Catalyst

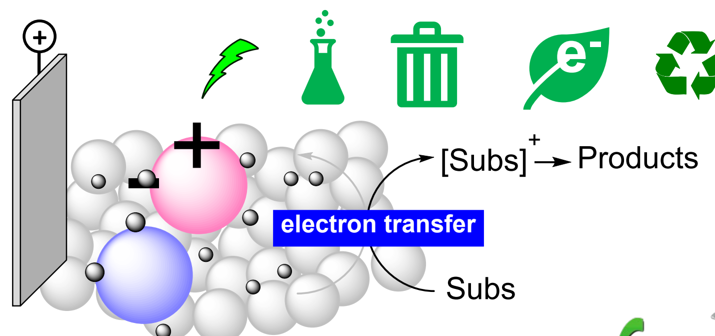


Green Assessment

Flow Chemistry



Green electrochemistry



GREEN CHEMISTRY …green metrics

12 Principles

Paul T. Anastas

Effective Mass Yield (EMY)

Tomas Hudlicky

Atom Economy

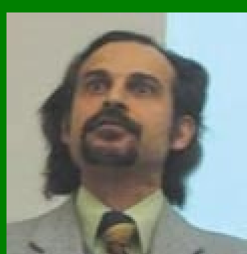
Barry M. Trost

E-Factor

Roger A. Sheldon

LCA, Eatos

Jürgen O.Metzger



E-Factors

John Andraos

Ecoscale

Koen Van Aken

Lucjan Strekowski

Luc Patiny

THE USE OF METRICS AT AN EARLY STAGE OF THE PROCESS DESIGN

HELPS TO AVOID FAILURE AT A LATER STAGE

ATTENTION
MEASURING WRONG IS ONE OF THE CURRENT SUSTAINABILITY ISSUE

NEW METRICS APPEAR EVERY DAY...

FOR THE SPECIFIC ISSUE THEY NEED TO BE DEVELOPED/ADAPTED

REACTION MEDIUM

NOVEL SAFER SOLVENTS

For a cleaner chemical production

Green S.O.C. Perugia

For more details see at http://greensoc.chm.unipg.it/

Solvent-Free Conditions (SolFC)

WATER

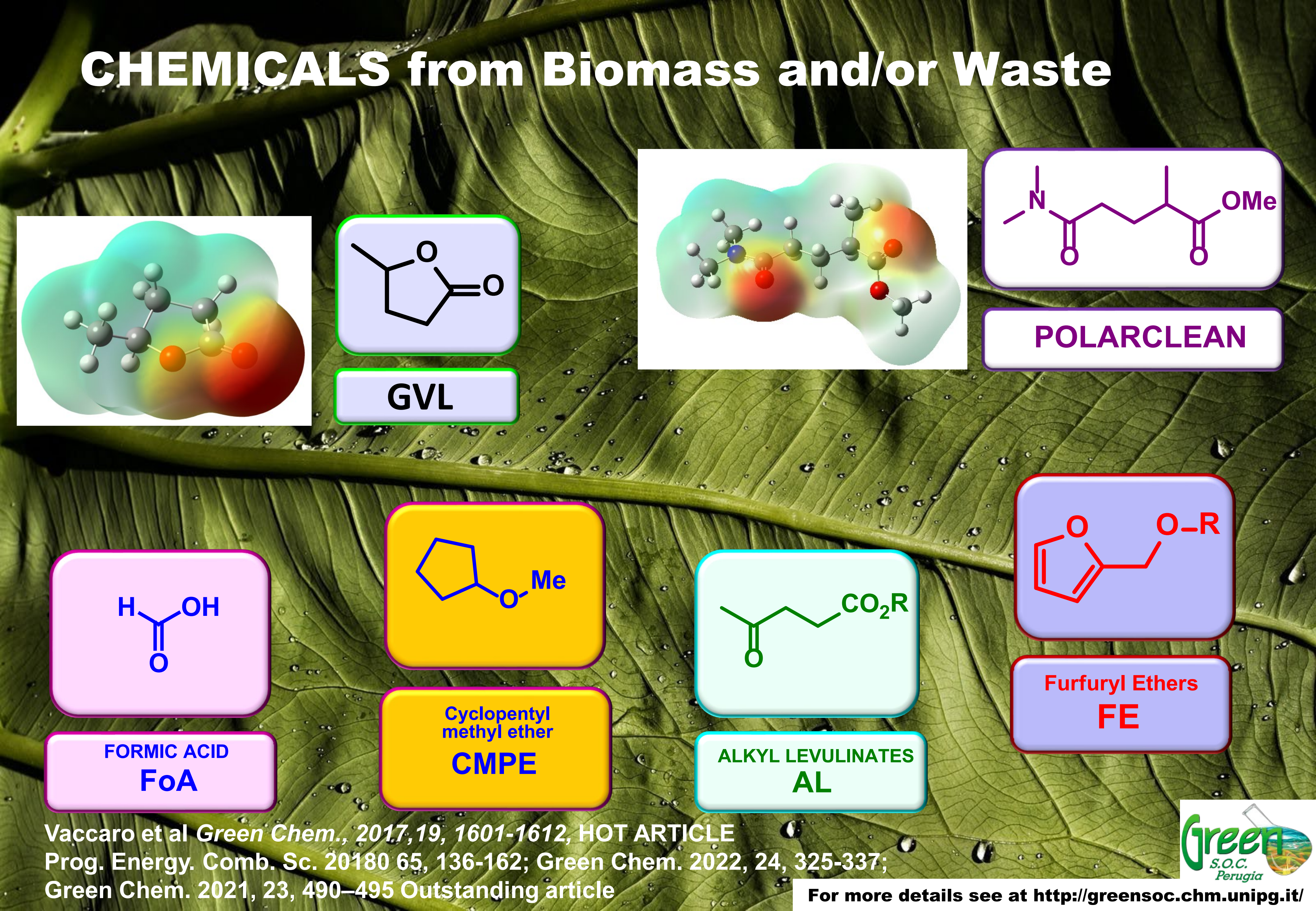
The safest NOT ALWAYS the greenest option

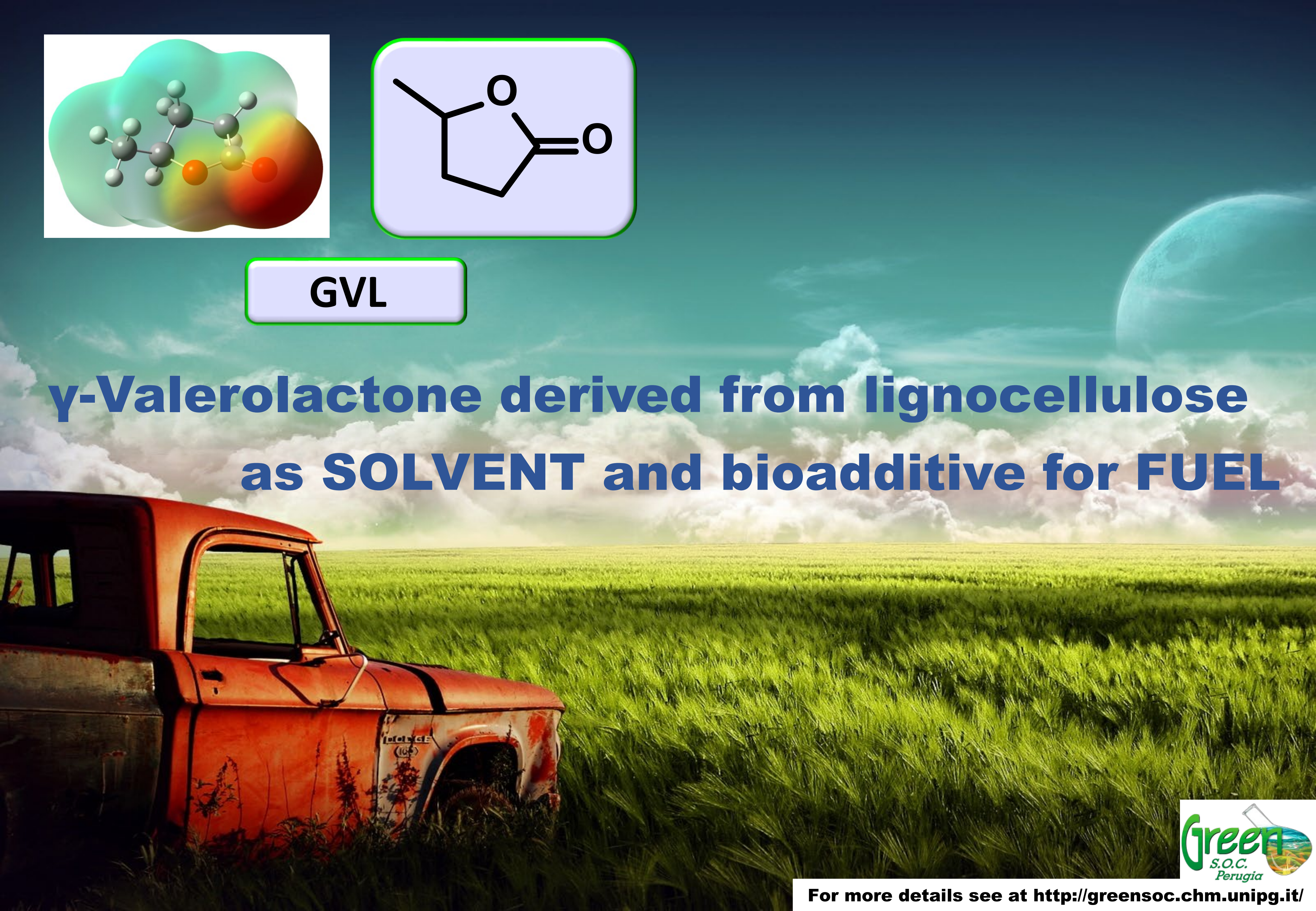
Alternative solvents from Biomass or waste

Safer organic solvents - Azeotropes

RECOVERY and REUSE must always be considered as a key issue

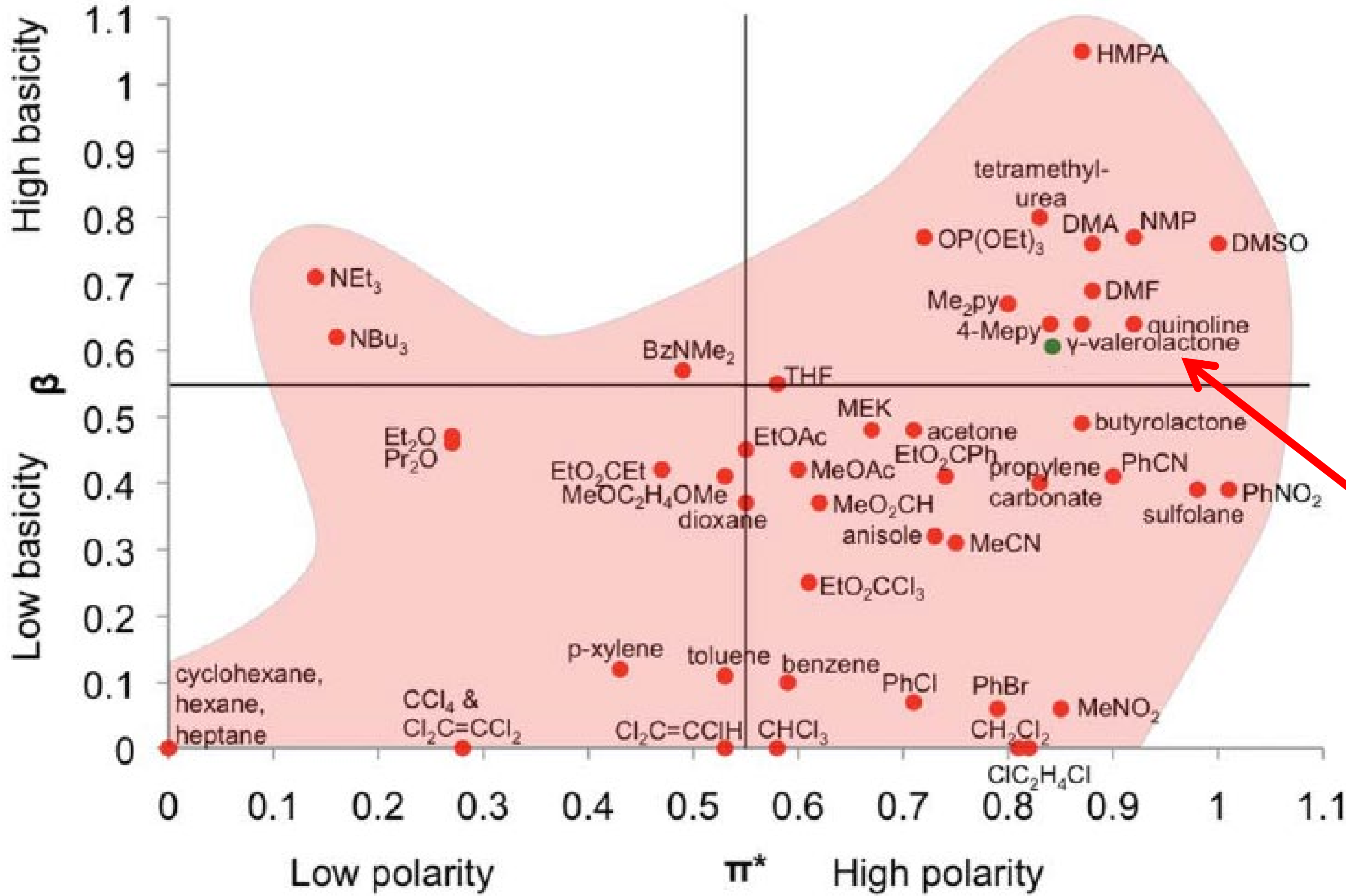
Some recent examples Vaccaro et al. Green Chem., 2017,19, 1601-1612, HOT ARTICLE; Green Chem., 2020, 22, 5937 Outstanding article; Green Chem., 2020, 22, 6240; Green Chem. 2022, 24, 9094, HOT ARTICLE; ACS Sus. Chem. Eng. 2022, 10, 9123

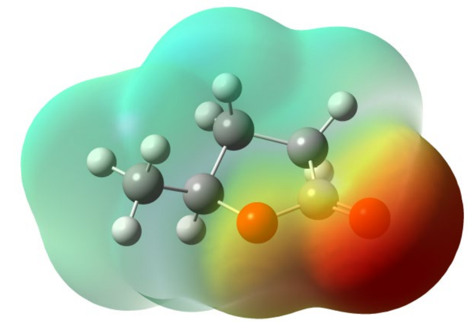

CHEMICALS from Biomass and/or Waste
O
O
GVL
N
OMe
O
O
POLARCLEAN
H
OH
O
FORMIC ACID
FoA
Me
O
Cyclopentyl
methyl ether
CMPE
CO2R
O
ALKYL LEVULINATES
AL
O
O–R
Furfuryl Ethers
FE
Vaccaro et al Green Chem., 2017,19, 1601-1612, HOT ARTICLE
Prog. Energy. Comb. Sc. 20180 65, 136-162; Green Chem. 2022, 24, 325-337;
Green Chem. 2021, 23, 490–495 Outstanding article
Green S.O.C. Perugia
For more details see at http://greensoc.chm.unipg.it/

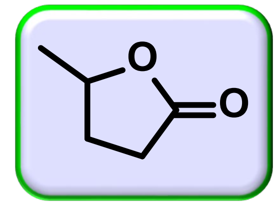

GVL
γ-Valerolactone derived from lignocellulose
as SOLVENT and bioadditive for FUEL
For more details see at http://greensoc.chm.unipg.it/

CAN GVL be a valid bioderived alternative to classic Dipolar Aprotic Media?

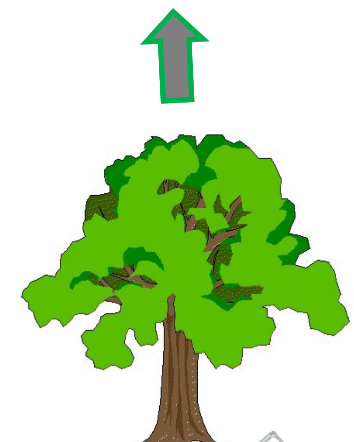
Gamma-Valerolactone - GVL



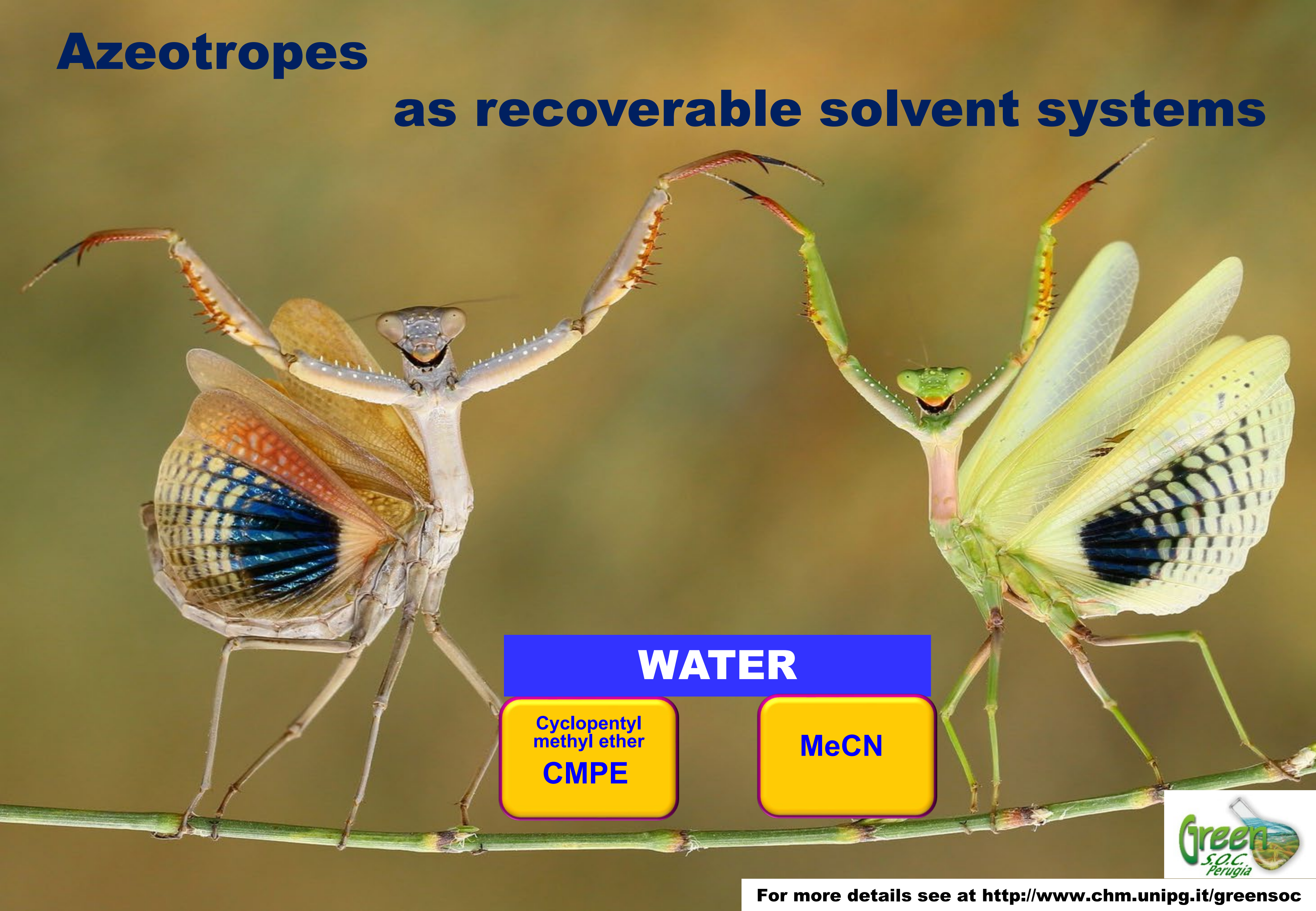




GVL



Dumesic, J. A. et al. Green Chem., 2013, 15, 584–595


Azeotropes
as recoverable solvent systems
WATER
Cyclopentyl
methyl ether
CMPE
MeCN
Green S.O.C. Perugia
For more details see at http://www.chm.unipg.it/greensoc


CATALYST
RECOVERABLE...
Green S.O.C. Perugia
For more details see at http://greensoc.chm.unipg.it/

Heterogeneous catalyst… a crucial tool to access greenness

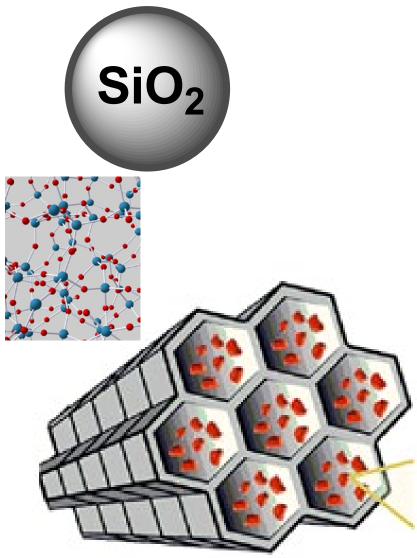
NOVEL and SAFER MEDIA, FLOW → NOVEL SUPPORTS FOR CATALYSIS

TWO MAIN DIRECTIONS

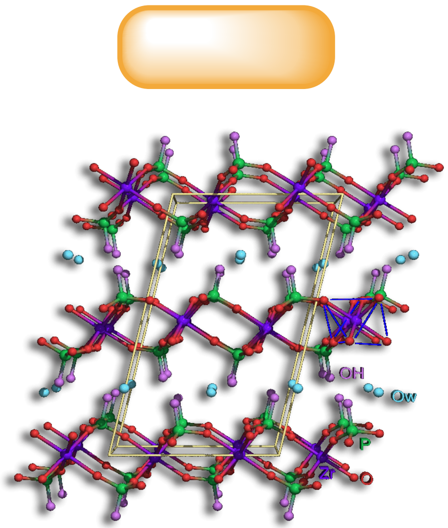
Inorganic supports

Organic Supports

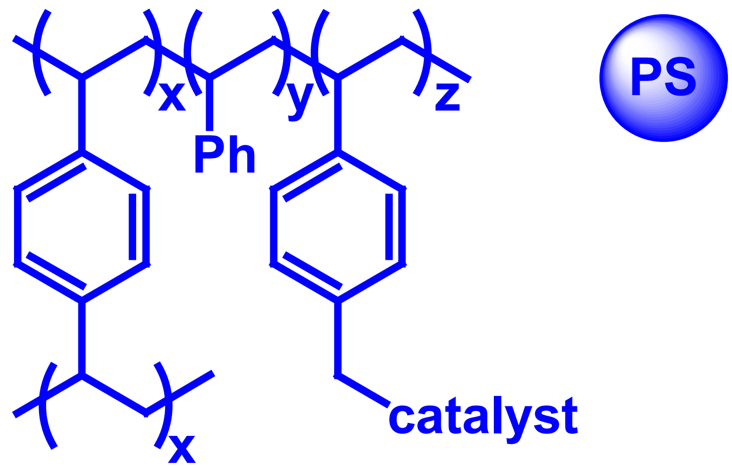
SILICA



Zr/P or MOF



Polystyrene-based supports



e.g. : Adv. Synth. Catal. 2013, *355*, 2007, J. Mol. Catal. A, Chemical 2014, 387, 57; ACS Sustainable Chem. Eng. 2014, 2, 2813; Adv. Synth. Catal. 2015, 357, 2351; ChemCatChem in press… *and work in progress*

e.g. : Chem. Commun. 2015, 51, 15990; ChemSusChem, 2020, 13, 2786; ACS SCE 2020, 8, 17154… in progress

e.g. : *Vaccaro et al. J. Catal.* 2013, 309, 260-267 , Eur. Pol. J. 2015, 73, 391-401; Green Chem. 2018, 20, 2888-2893 - ACS Sus. Chem. Eng. 2019, Green Chem., 2020, 6560–6566, ACS Sus Chem Eng 2021, 9, 5740, ACS Sustainable Chem. Eng. 2021, 9, 12196-12204; Green Chem., 2021,23, 490-495; Green Chem., 2021,23, 7210-7218 and work in progress…

NOVEL ORGANIC POLYMERIC MATERIALS FOR CATALYSIS

Vaccaro et al. J. Catal. 2013, 309, 260-267 , Green Chem. 2018, 20, 2888-2893 - ACS Sus. Chem. Eng. 2019, Green Chem., 2020, 6560–6566, ACS Sus Chem Eng 2021, 9, 5740, ACS Sustainable Chem. Eng. 2021, 9, 12196-12204; Green Chem., 2021,23, 490-495; Green Chem., 2021,23, 7210-7218and work in progress

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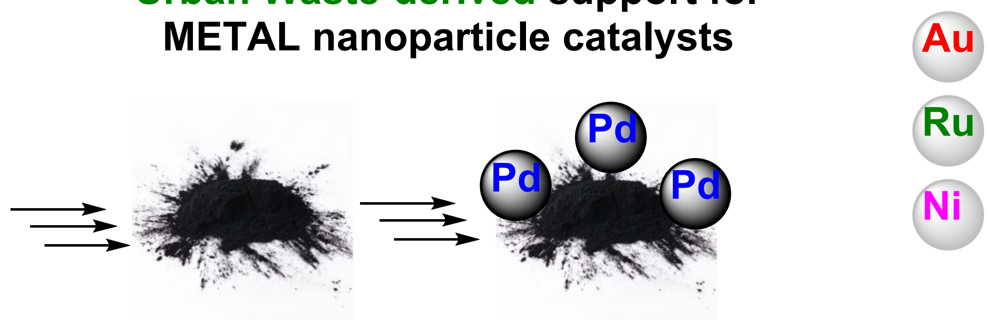
From waste valorization to circular approaches to catalysis

pine needle

Urban waste in central Italy and in several Mediterranean areas

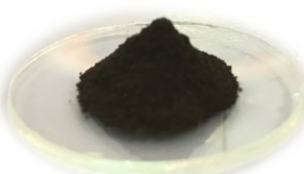
Circular economy approach

Urban Waste-derived support for METAL nanoparticle catalysts



✓ **adsorbent** for water purification

✓ **support** for heterogeneous catalyst

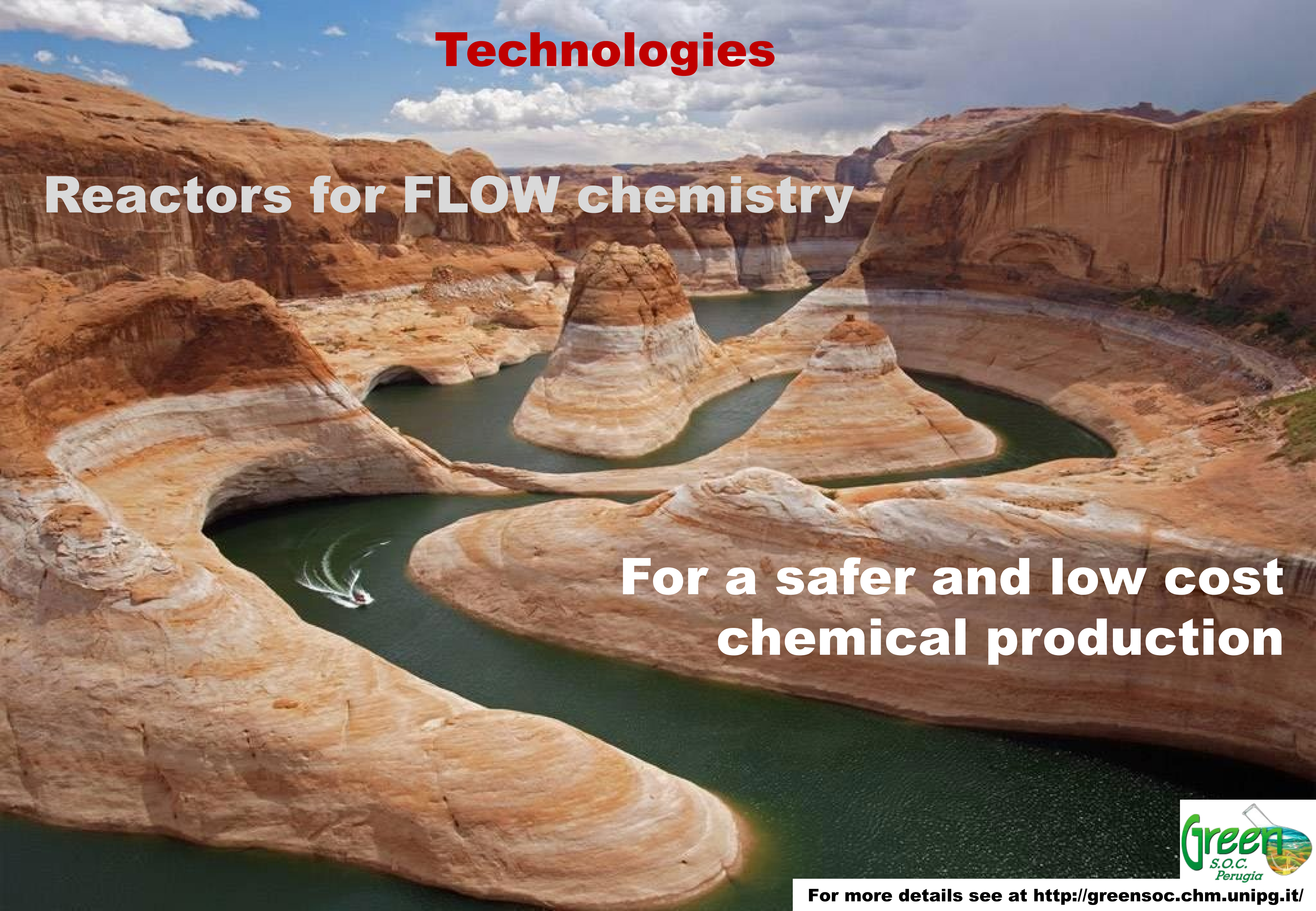


ALSO WE ARE FOCUSING ON WASTE FROM LEATHER or PHOTOVOLTAIC PANELS

L. Vaccaro et al.: *Green Chem.*, **2021**, *23*, 5887–5895; *ACS Sustainable Chem. Eng.* **2021**, *9*, 12196−12204

Technologies

Reactors for FLOW chemistry

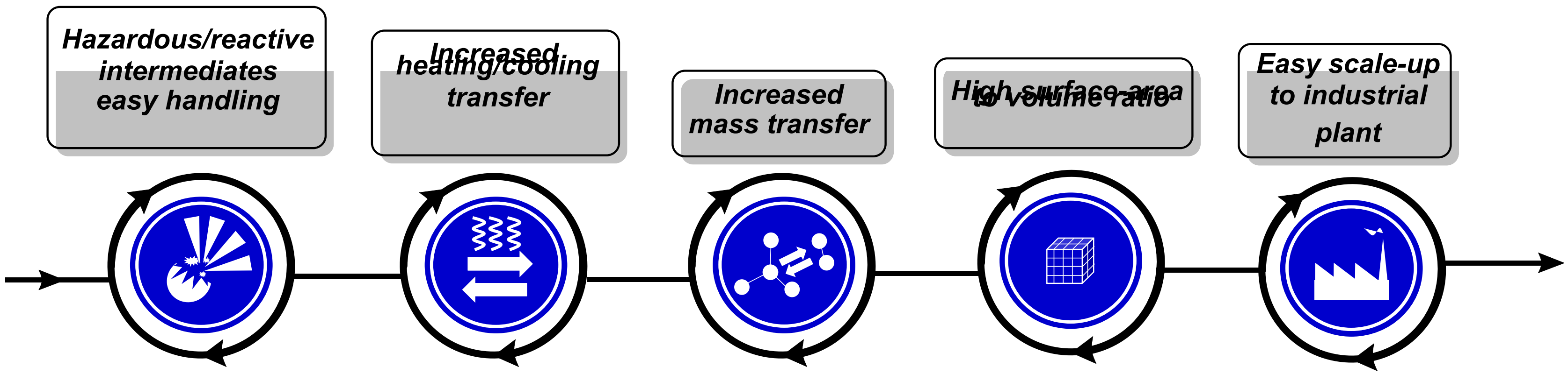


For a safer and low cost chemical production

Green S.O.C. Perugia

For more details see at http://greensoc.chm.unipg.it/

Flow chemistry and Green Chemistry



Green Chem. 2014, 16, 3680 3704

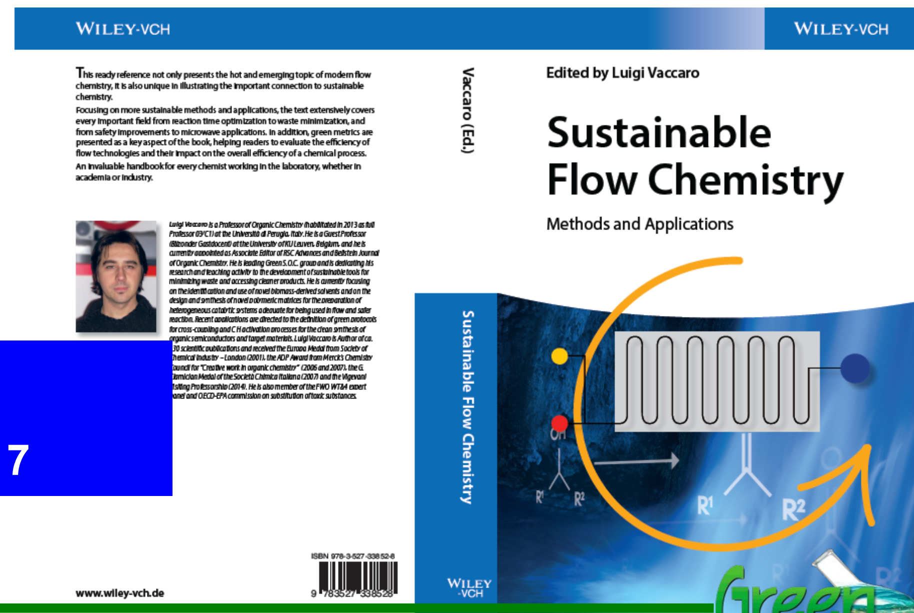
Chem. Soc. Rev., 2019, 48, 2767

Green Chem., 2020, 22, 5937-5955

Green Chem 2023, 25, 7916-7933

Sustainable flow chemistry

Editor L. Vaccaro Wiley –VCH, 2017



FLOW CHEMISTRY IS NOT INTRINSECALLY GREEN

Different approaches towards a single goal: WASTE MINIMIZATION

GREEN METRICS

Recoverable Green solvents for recoverable catalysts

Heterogeneous Catalytic Systems

FLOW REACTORS

FOCUS ON A SPECIFIC ISSUE

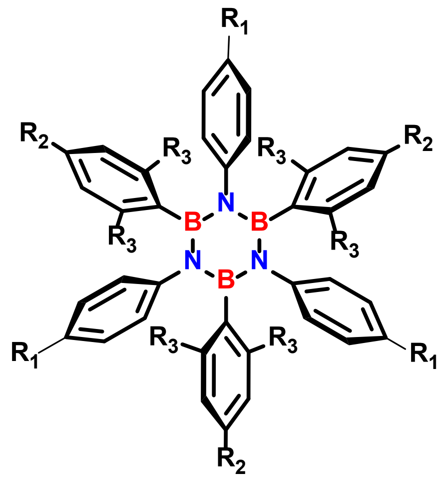
TO SITUATE A SPECIFIC

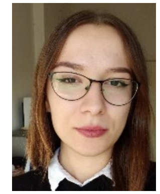
GREEN/SUSTAINABLE SOLUTION

Green functionalization of hexa-aryl borazines

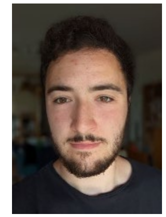
Alireza Nazari

Fan Huang, PhD





Ejdi Cela



Dario Marchionni

http://greensoc.chm.unipg.it

Hexa-aryl borazinesare valuable precursors to doped-nanographenes and doped-polyphenylenes.

They serve as a stable doping unit in materials displaying unique electronic and optical properties.

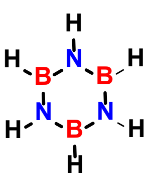
Their potential is limited by the harsh conditions generally utilized for their synthesis

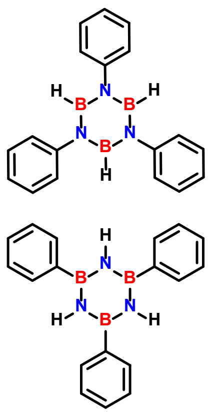
STIBNITE

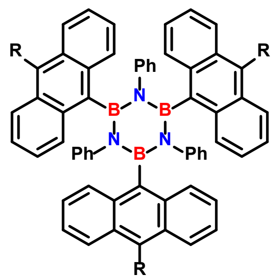
EU ITN consortium led by Prof, Bonifazi UVIE

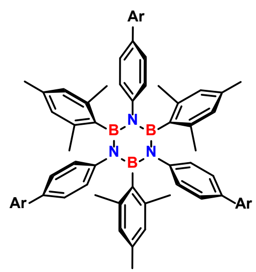
L. Vaccaro et al, *Adv. Funct. Mater. 2023* , 33, 2303635.

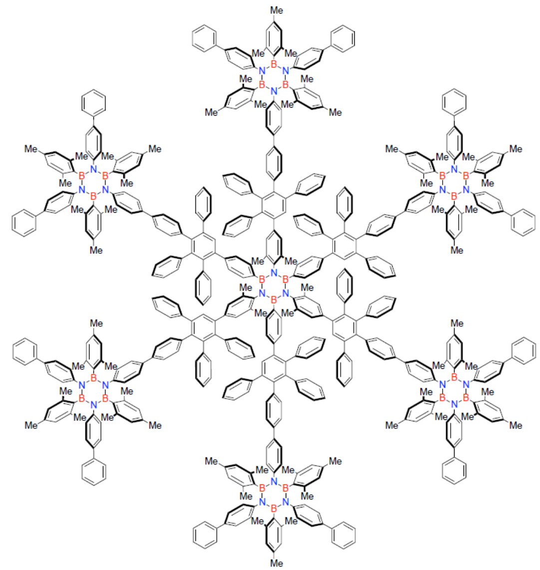
History of borazine-incorporated frameworks

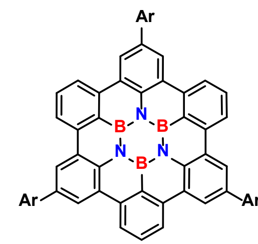


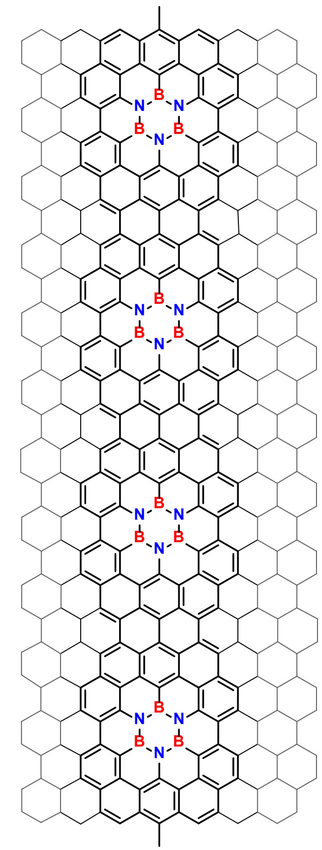












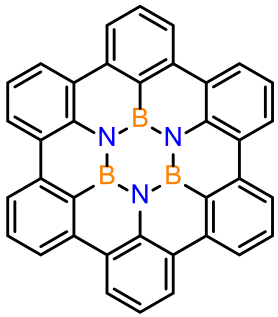
1926 | 2005 | 2005-2013 | 2017 | 2015-2017 | STiBNite

Berichte der Dtsch. Chem. Gesellschaft (A B Ser., **1926**, 59, 2215–2223. Chem. Commun., **2005**, 3547–3549, J. AM. CHEM. SOC. **2005**, 127, 14859-14866, Angew. Chem. Int. Ed. **2015**, *54*, 8284 –8286, Angew. Chem. **2017**, *129*, 4554 –4558, J. Am. Chem. Soc. **2017**, 139, 15, 5503–5519

Developing atomically precise doping

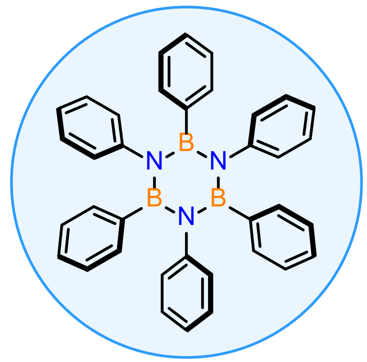
Hexaphenyl borazines as molecular precursors

Planarization

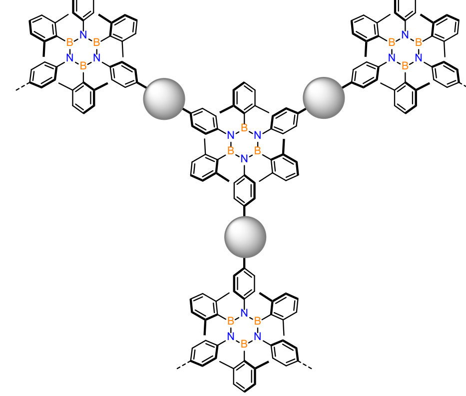


Angew. Chem. Int. Ed. 2015, *54*, 8284–8286.
Angew. Chem. 2017, *129*, 4554 –4558.

Hexaphenylborazine

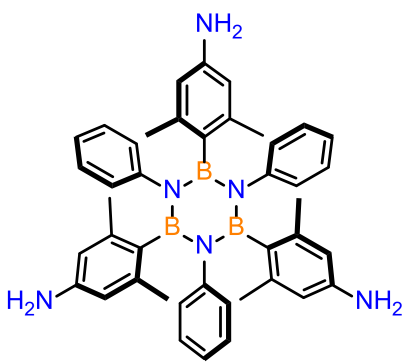


MOFs



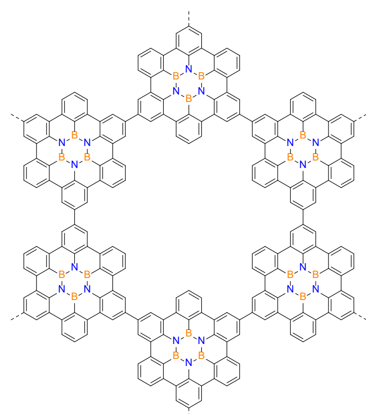
Chemistry – A European Journal, 2021, *27*, 4124–4133.

Functionalization



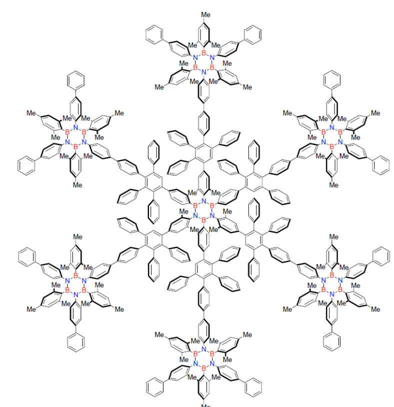
J. Org. Chem., 2019, *84*, 9101–9116.

On surface assembly



ACS Nano, 2015, *9*, 9228–9235.

Polyphenylenes



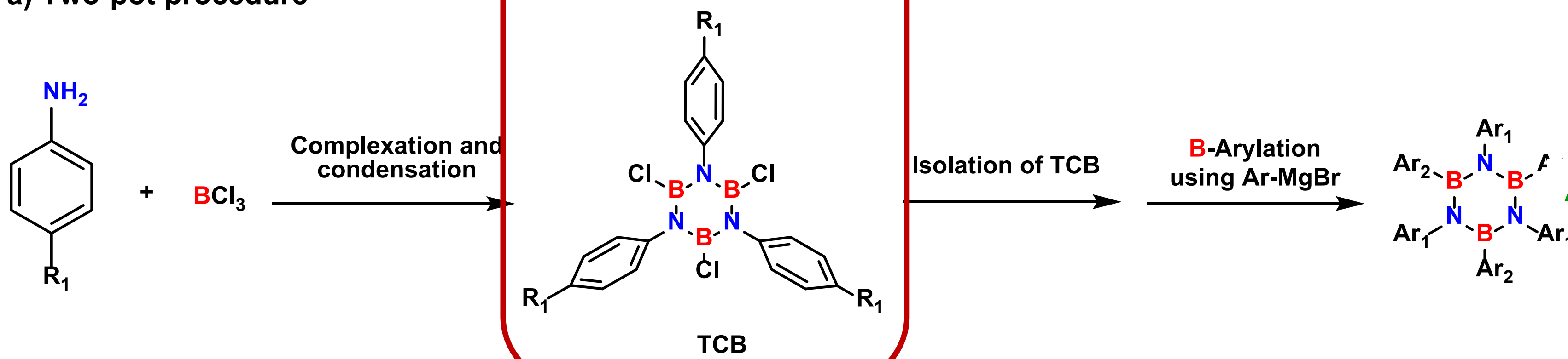
J. Am. Chem. Soc. 2017, *139*, 15, 5503–5519

Continuous-flow waste minimized synthesis of hexaaryl borazines

STIBNITE

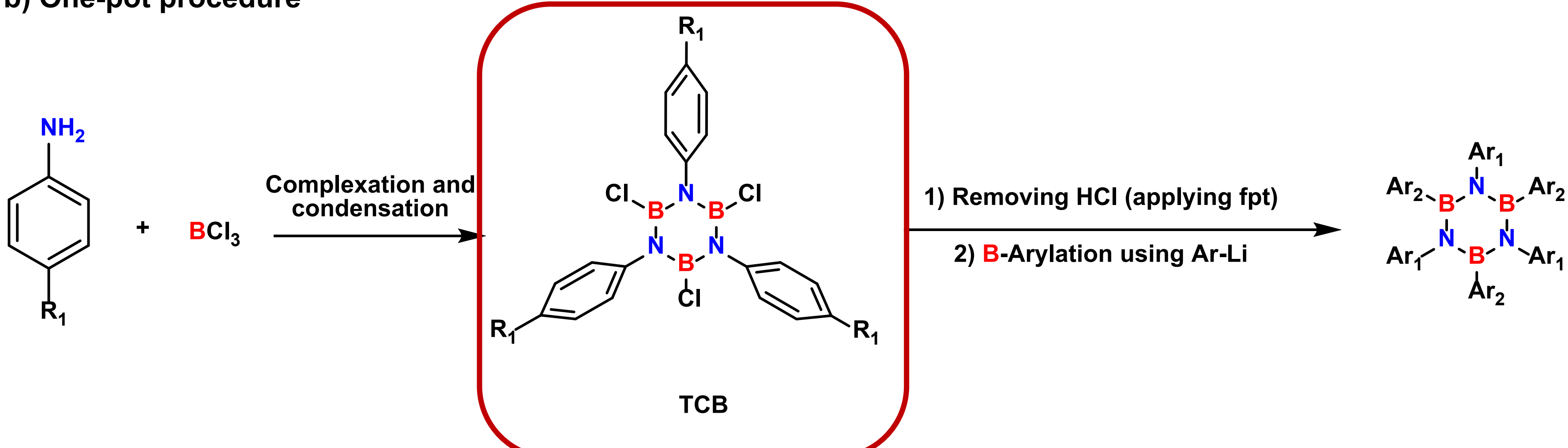
✓ traditional methods

a) Two-pot procedure



Alireza Nazari

b) One-pot procedure



S. Yamaguchi et al, *J. Am. Chem. Soc.*, 2005, 127, 14859–14866

D. Bonifazi et al, *J. Am. Chem. Soc.*, 2017, 139, 5503–5519

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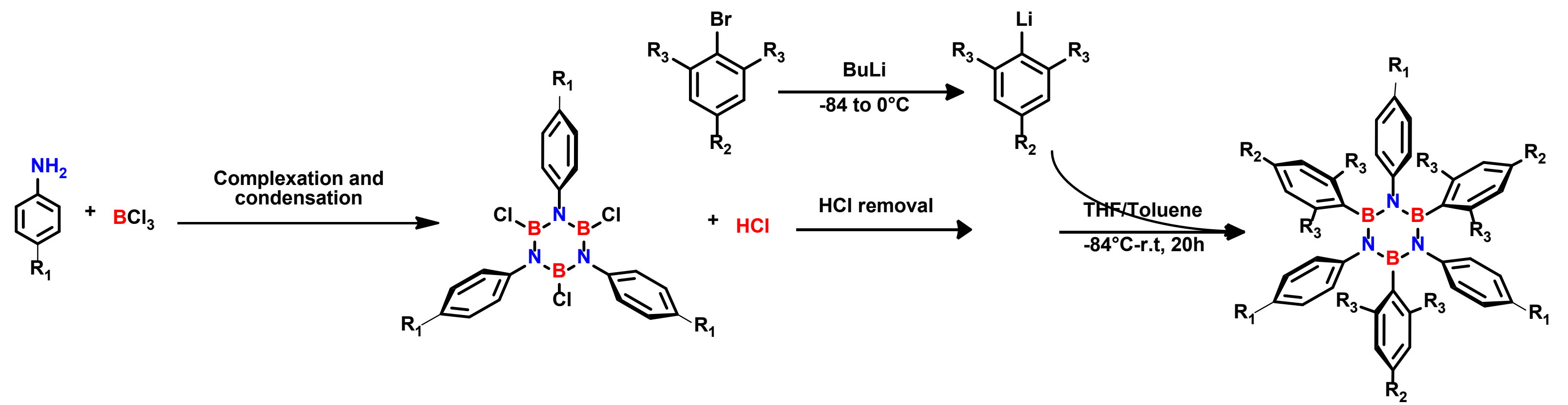
Boron Arylation of Boron Halide under Continuous Flow conditions: An Efficient Method for the Synthesis of Hexaaryl-Substituted Borazines

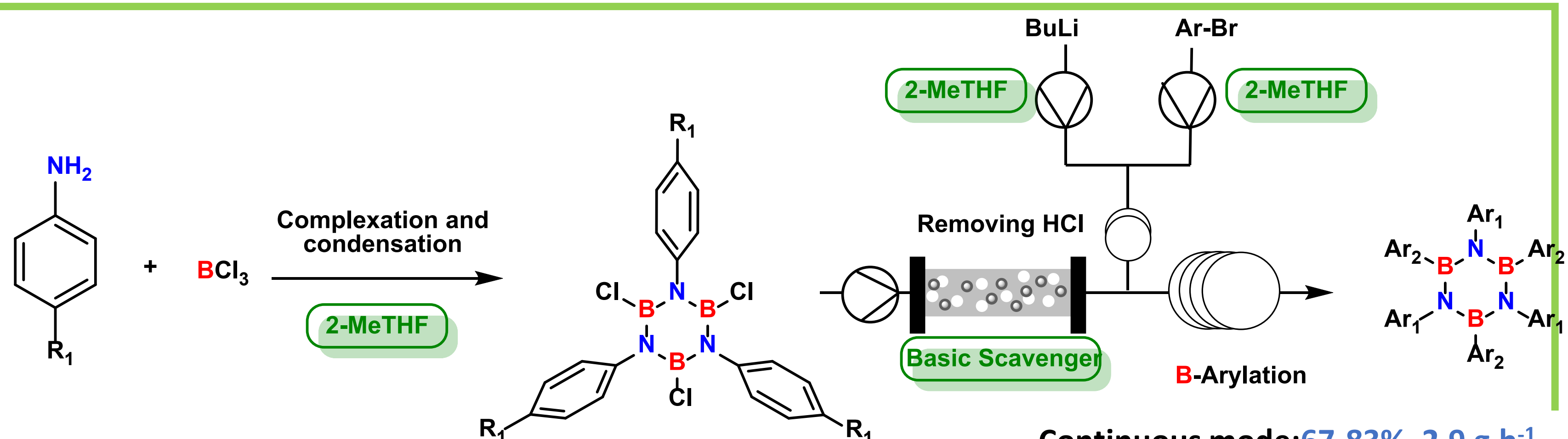
STIBNITE

Principal method



Novel method

Alireza Nazari



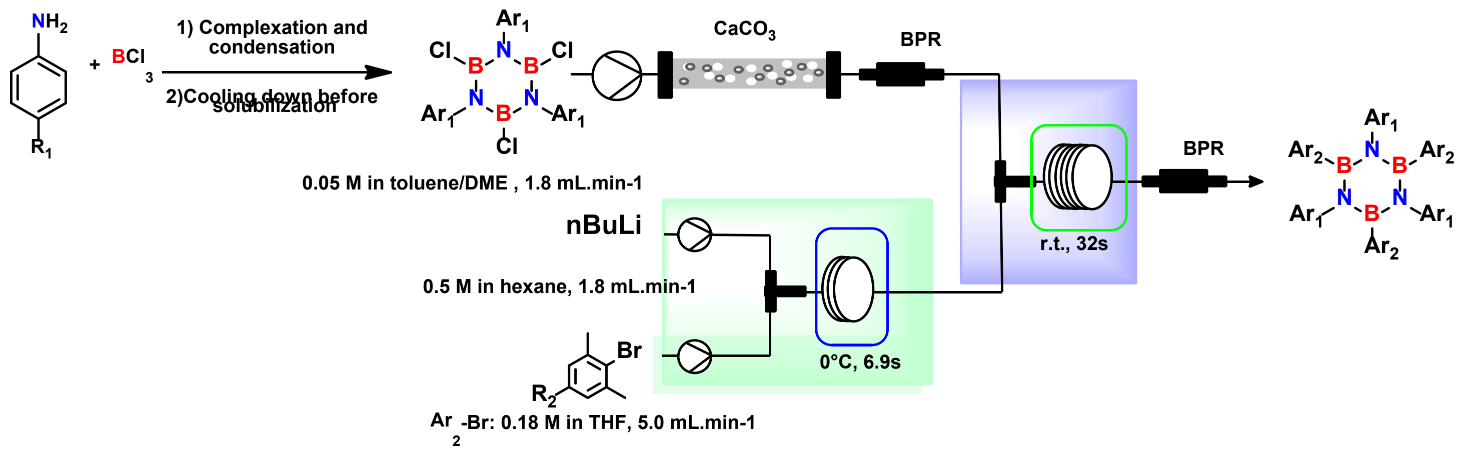
TCB

Continuous mode: 67-83%, 2.9 g.h^{-1}

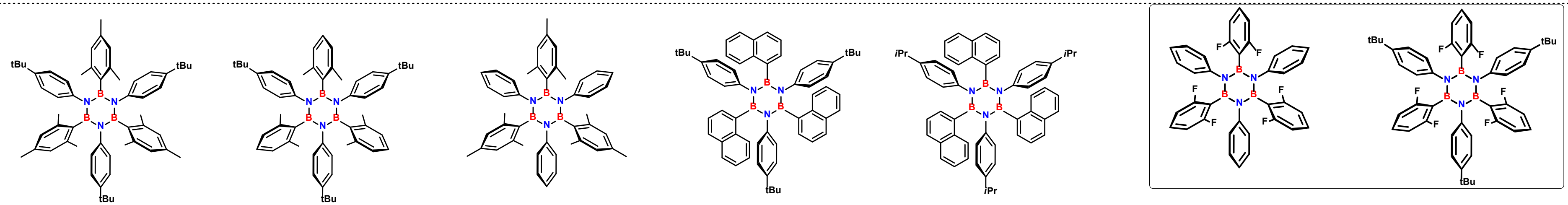
Batch process: 49%, 0.016 g.h^{-1}

Continuous-flow waste minimized synthesis of hexaaryl borazines

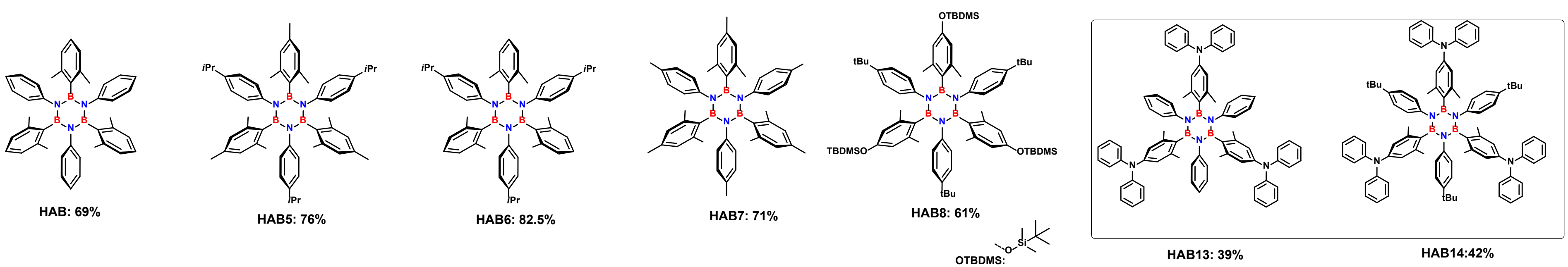
✓ OUR APPROACH



Alireza Nazari



HAB1: 74% HAB2: 79% HAB3: 76% HAB9: 52% HAB10: 44% HAB11: 48% HAB 12: 59%



HAB: 69% HAB5: 76% HAB6: 82.5% HAB7: 71% HAB8: 61% HAB13: 39% HAB14:42%

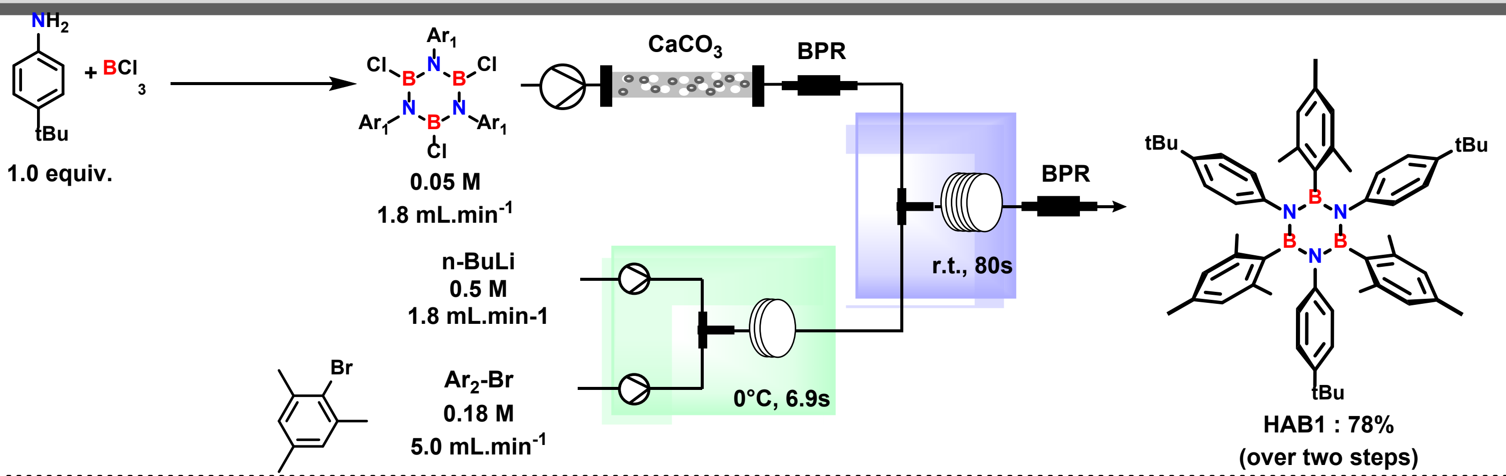
OTBDMS:

L. Vaccaro et al, *Green Chem.* 2024, 26,7059–7066 hot article

Continuous-flow waste minimized synthesis of hexaaryl borazines

STIBNITE

✓ OUR APPROACH



Alireza Nazari

	E-factor:	BI - SHI	Time (h)	Yield (%)
This work (smalle scale)	55	0.95 - 0.74	18.5	74
This work (larger scale)	45	0.95 - 0.74	19.5	78
Bonifazi (2013)	278	0.71 - 0.68	41.0	40
Yamaguchi (2005)	89	0.72 - 0.74	39.0	70
Groszos (1958)	79	0.49 - 0.44	17.0	48

Gram scale synthesis and more…

NOT mg

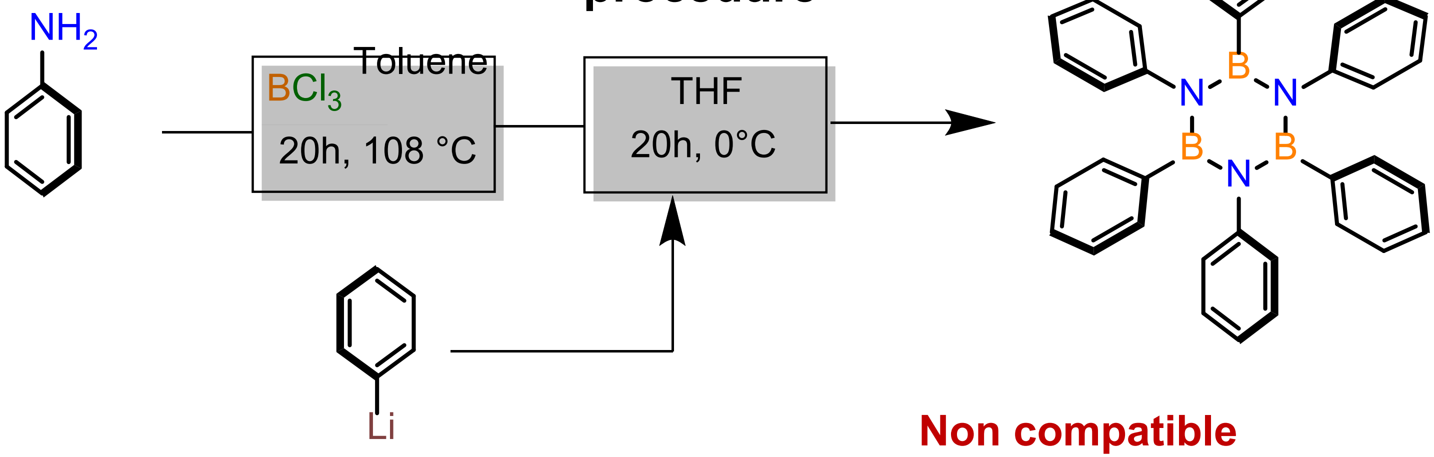
L. Vaccaro et al, *Green Chem.* 2024, 26,7059–7066 hot article

Green S.O.C. Perugia

Molecular borazines

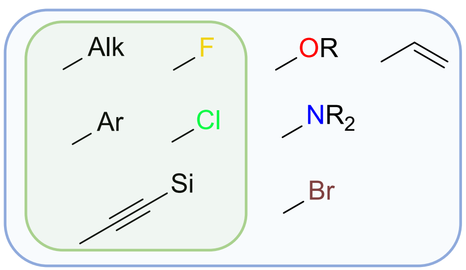
The need for post-synthetic functionalization

Standard synthetic procedure

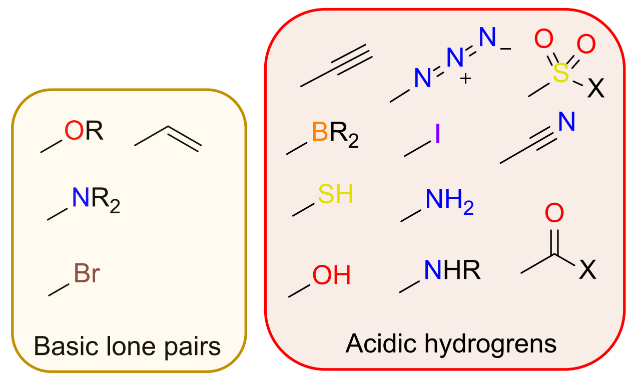


Non compatible

Compatible



N ring **B ring**



N ring incompatible

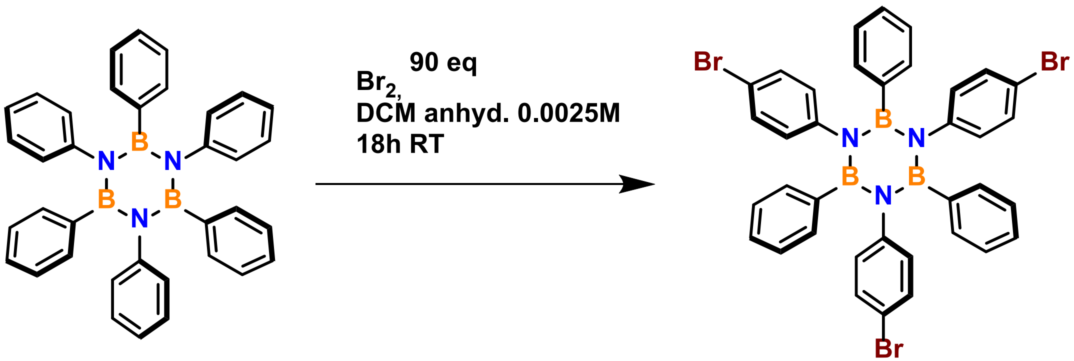
Any ring incompatible

Molecular borazines

The need for post-synthetic functionalization

1b) Bromination on the *N*-aryl ring

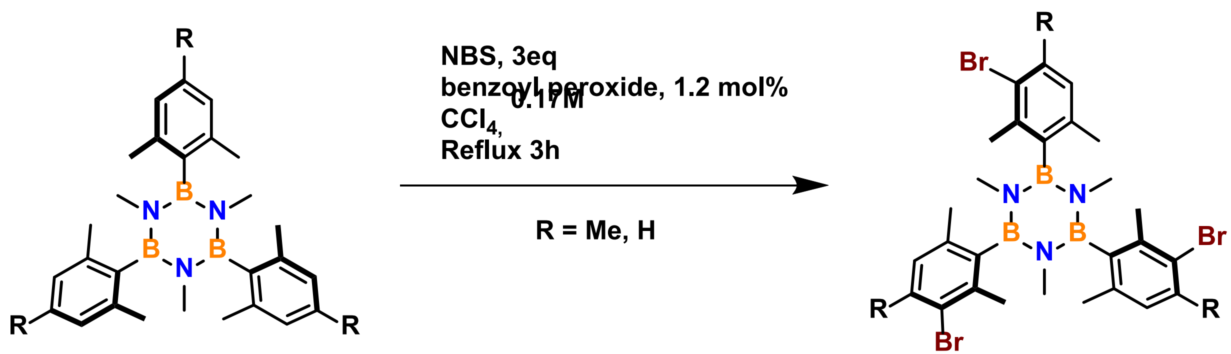
H. F. Bettinger et al., ChemPlusChem 2013, 78, 988–994.



35%

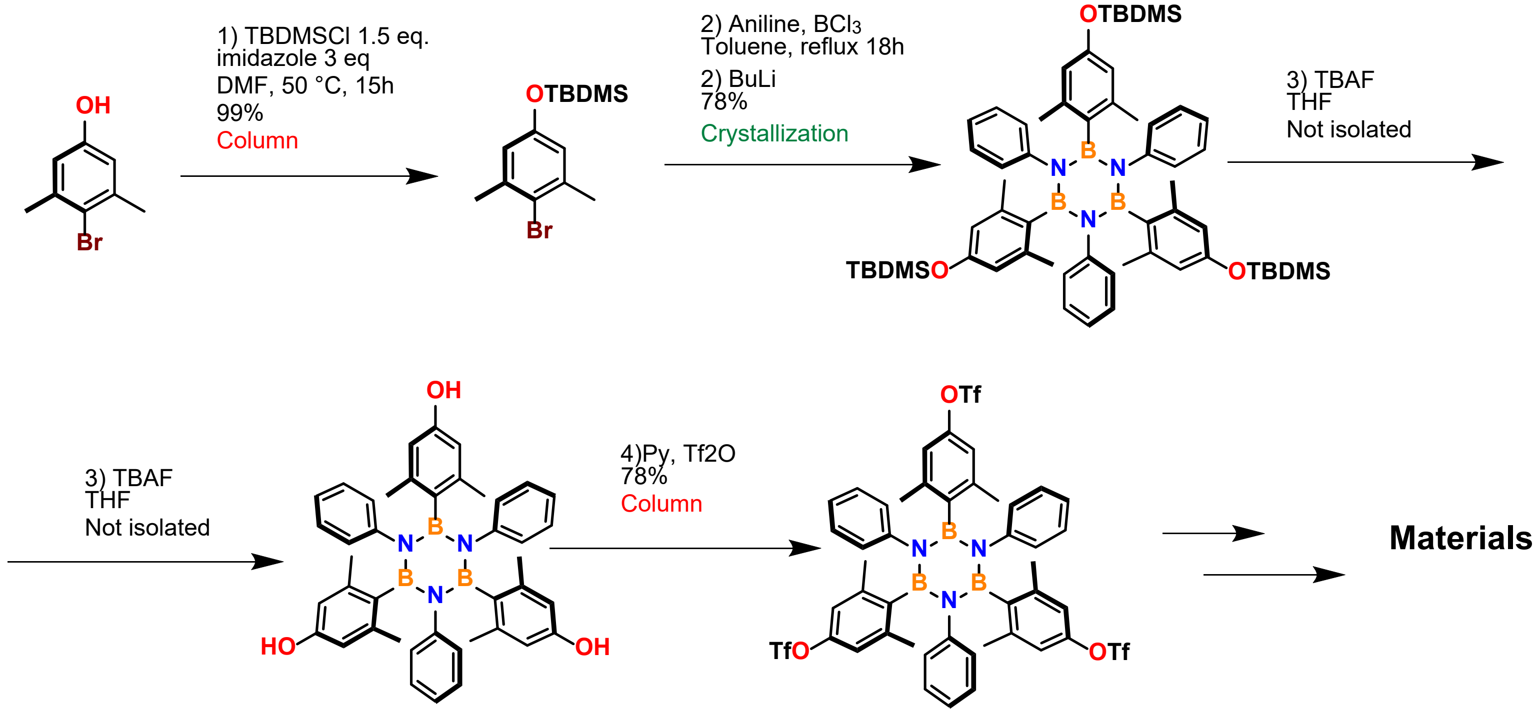
1c) Friedel-Crafts chemistry on the *B*-aryl ring

K. Nagasawa, Inorg. Chem. 1966, 5, 442–445.



WHY halogenation?

Standard procedure to access pseudohalide functionality for cross couplings

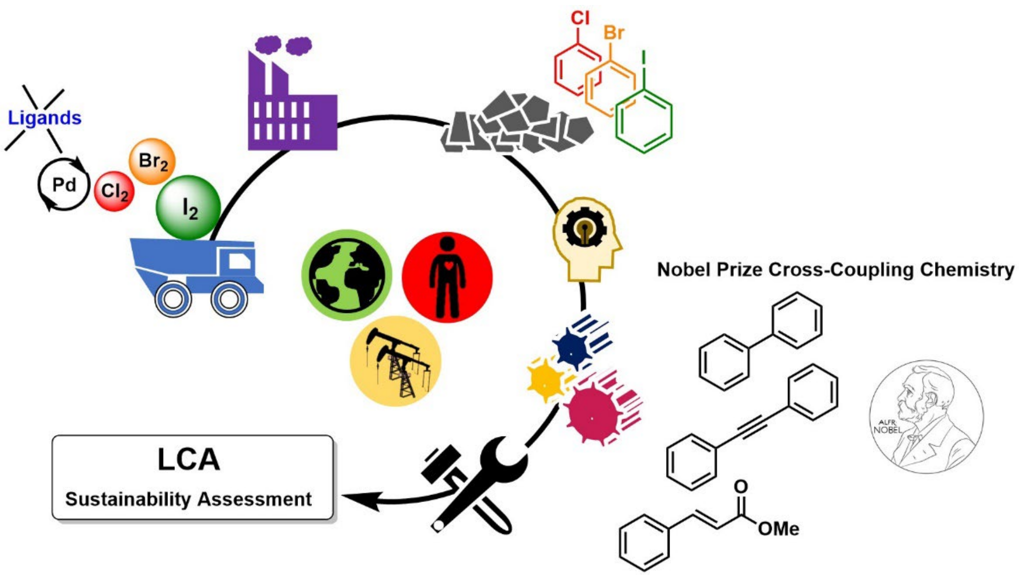


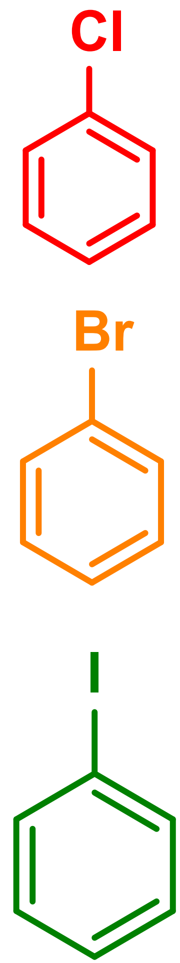
Can halogenation work in a single step?

J. Am. Chem. Soc. 2017, 139, 5503–5519
Chemistry – A European Journal 2018, 24, 9565–9571
J. Org. Chem. 2019, 84, 9101.

Iodination more sustainable alternative to bromination and chlorination

The sustainability impact of Nobel Prize Chemistry: life cycle assessment of C–C cross-coupling reactions





Poorly reactive

Highly efficient catalytic systems are needed

REMIND CHLORINE-FREE CHEMISTRY CONCEPT

Bromide or Iodide are

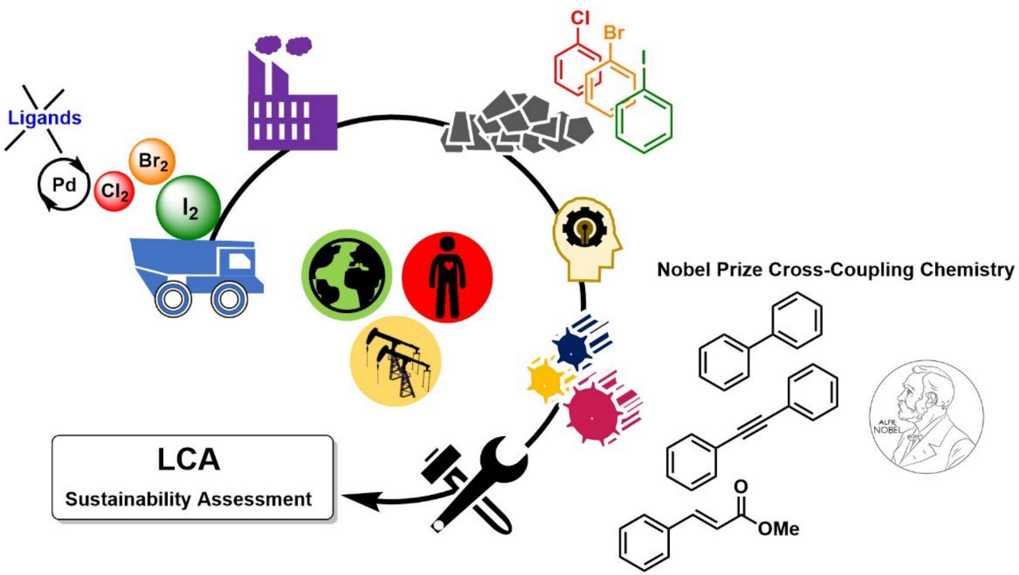
More reactive and also Cheaper

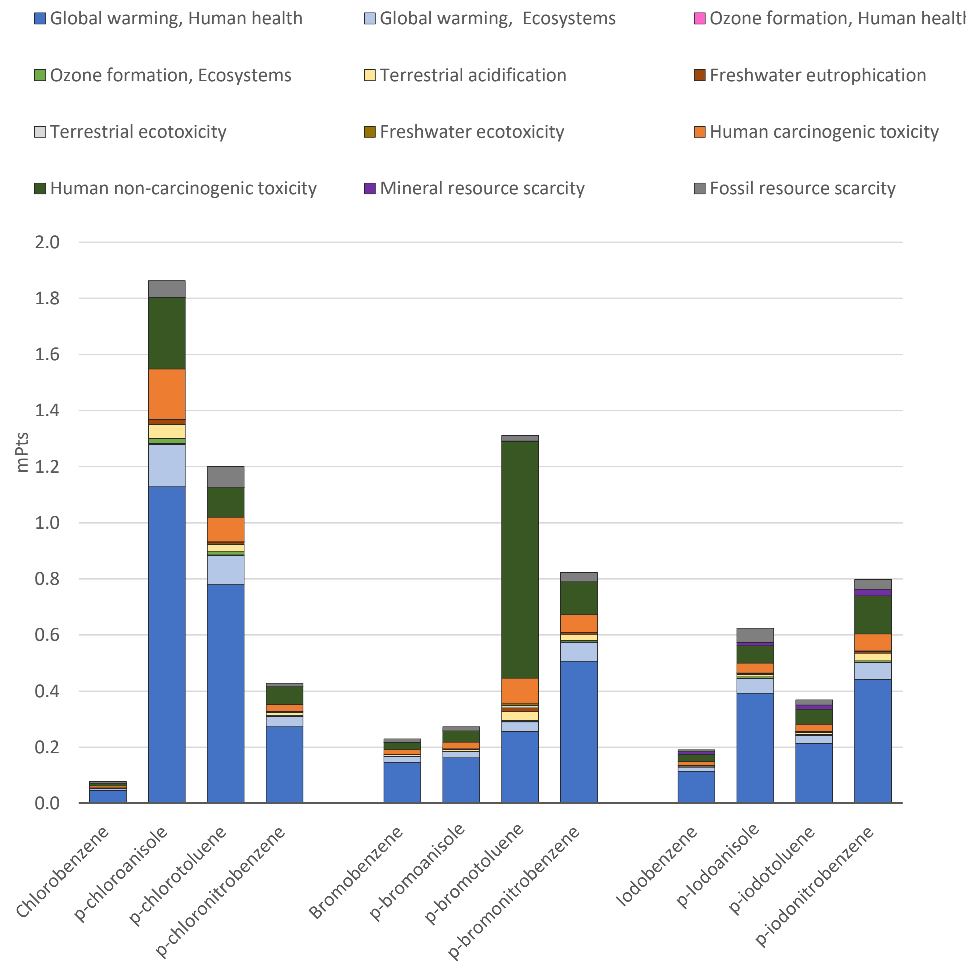
(simpler catalytic systems can be sufficient for their reactivity

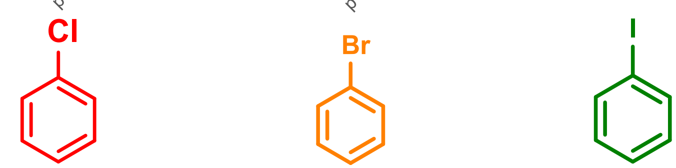
Depending on the type of reactions (Heck, Sonogashira, Suzuki…) bromides or iodides are more adequate

Iodination more sustainable alternative to bromination and chlorination

The sustainability impact of Nobel Prize Chemistry: life cycle assessment of C–C cross-coupling reactions



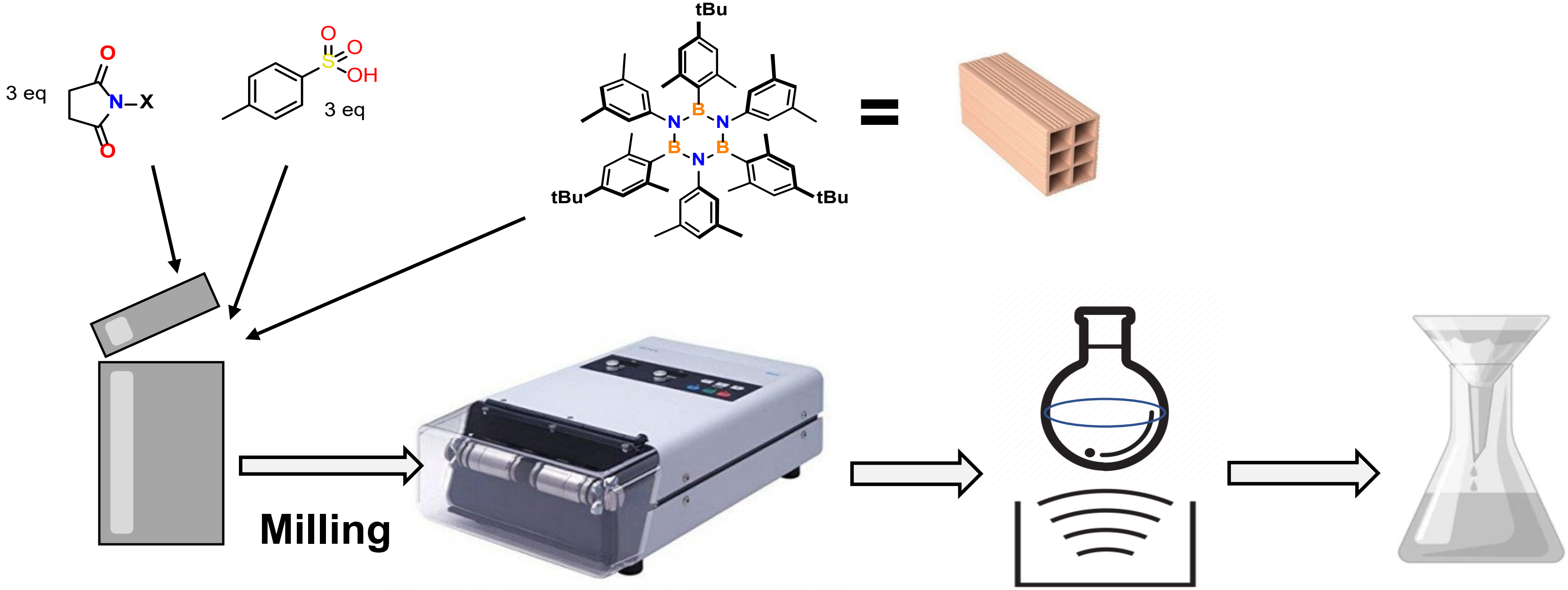


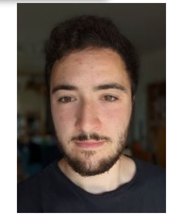


Green Chem., 2024, 25 9760-9778, **HOT ARTICLE**

Iodination of ORGANIC BORAZINES

A solvent-free approach using Ball Billing

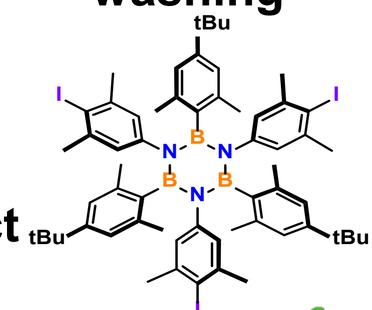




Dario

Overall solvent consumption 1 mmol scale: 12 mL MeOH
Solvent recovery by distillation: 9.7 mL
<u>E-Factor: 2.4</u>

Pure product

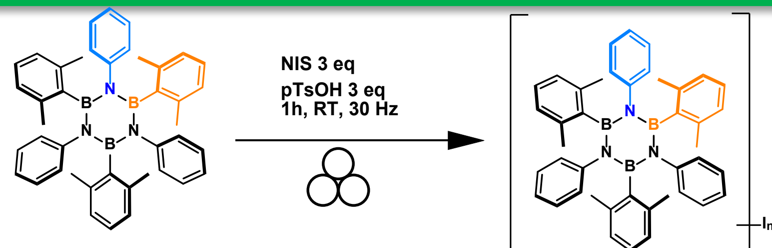


Vaccaro et al *Adv Synth Catal* 2024, 366, 494−501. *and*

Green Chem., 2024, DOI: 10.1039/D4GC00699B **HOT ARTICLE selected for front cover image**

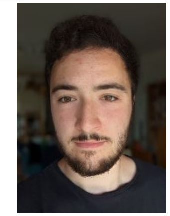
Iodination of ORGANIC BORAZINES

Substrate scope

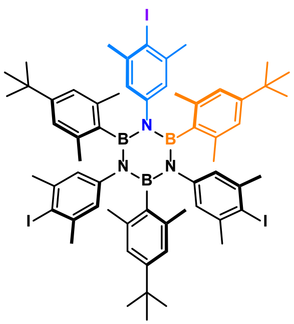


1-7, 9

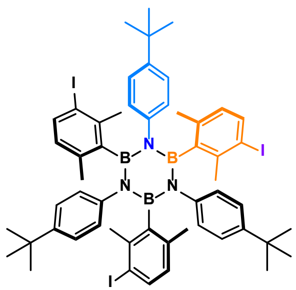
11-20



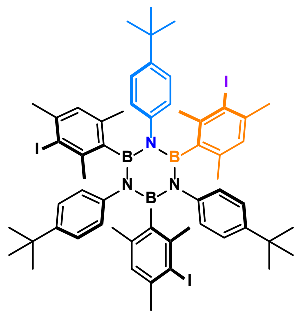
Dario



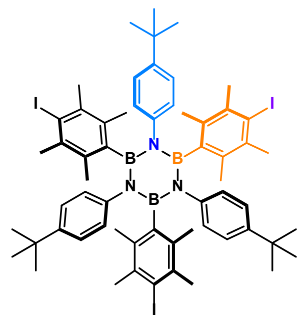
11 - 90%



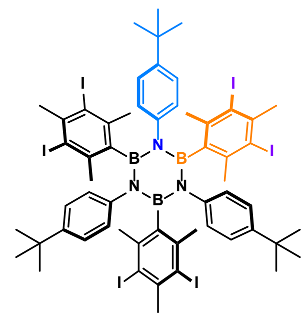
12 - 76% (cis+trans)



13 - 84% (cis+trans)

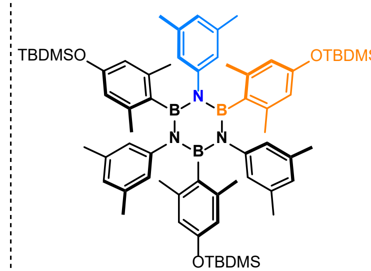


14 - 83%

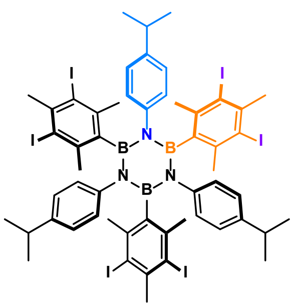


15 - 53%[a]

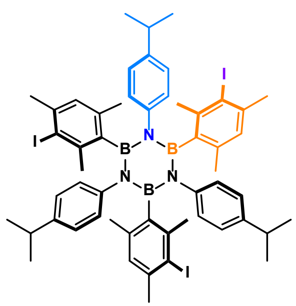
Unsuccesful substrates



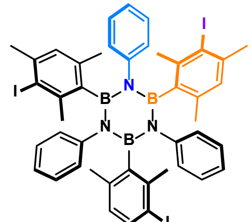
8[c]



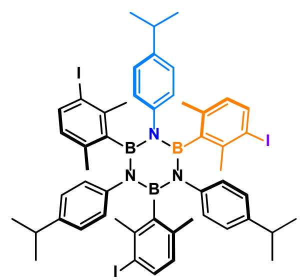
16 - 45%[a]



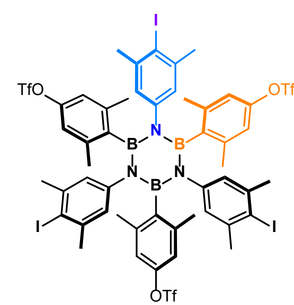
17 - 94% (cis+trans)



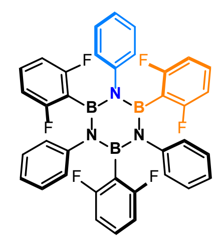
18 - 89% (cis+trans)



19 - 85% (cis+trans)



20 - 59%[b]

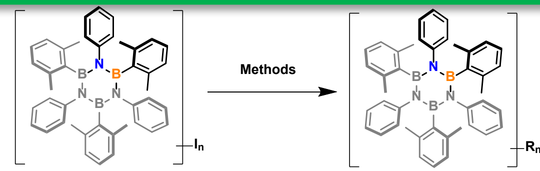


10[c]

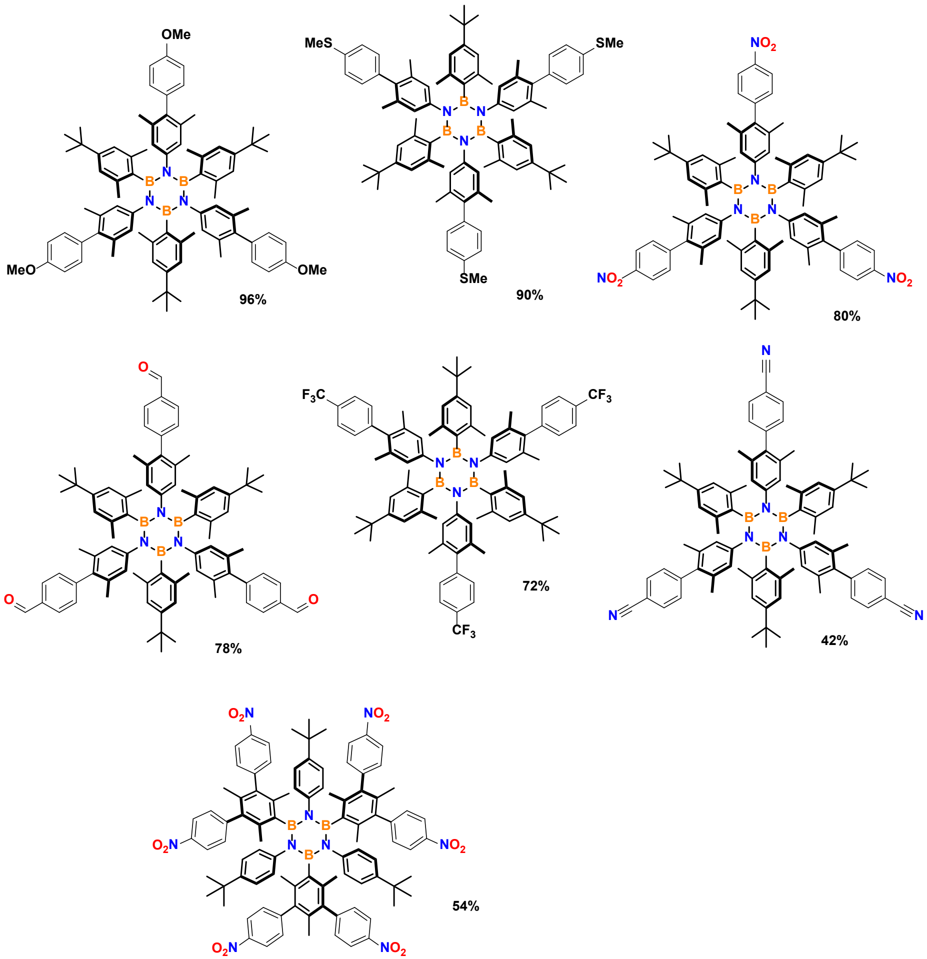
Vaccaro et al *Adv Synth Catal* 2024, 366, 494−501. ***and***

Green Chem., 2024, DOI: 10.1039/D4GC00699B **HOT ARTICLE selected for front cover image**

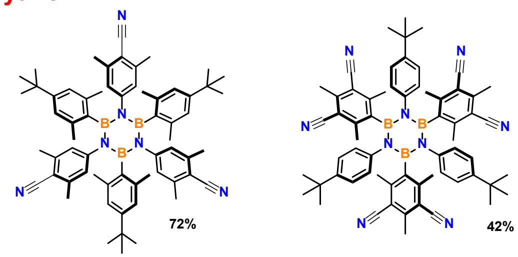
Cross-couplings and cyanation of iodinated borazines



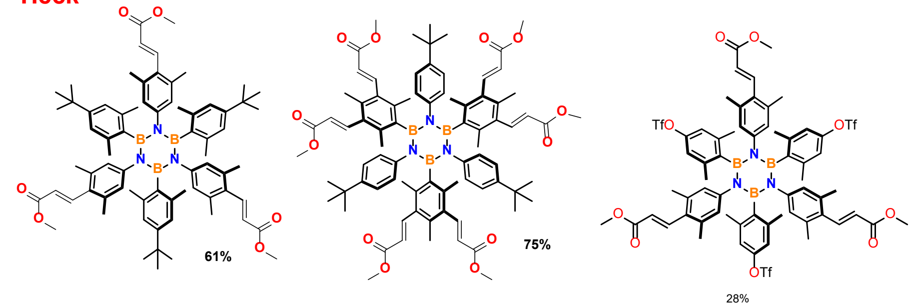
Suzuki



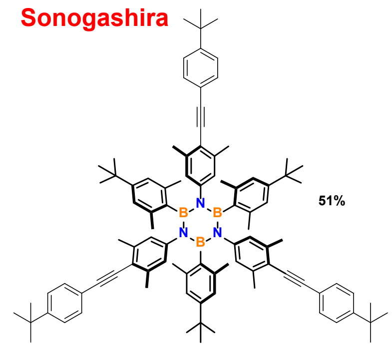
Cyano



Heck



Sonogashira



Vaccaro et al *Adv Synth Catal* 2024, 366, 494−501. ***and***

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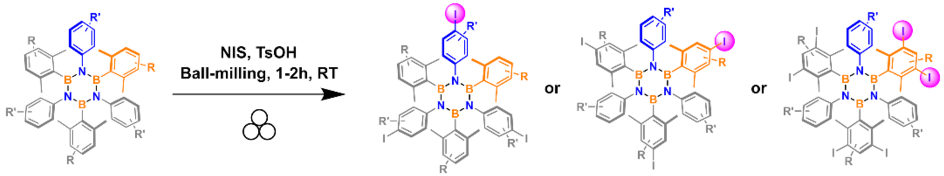
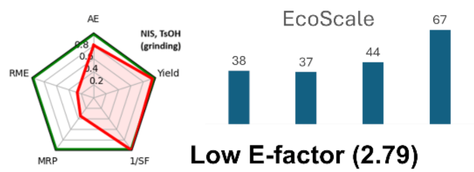
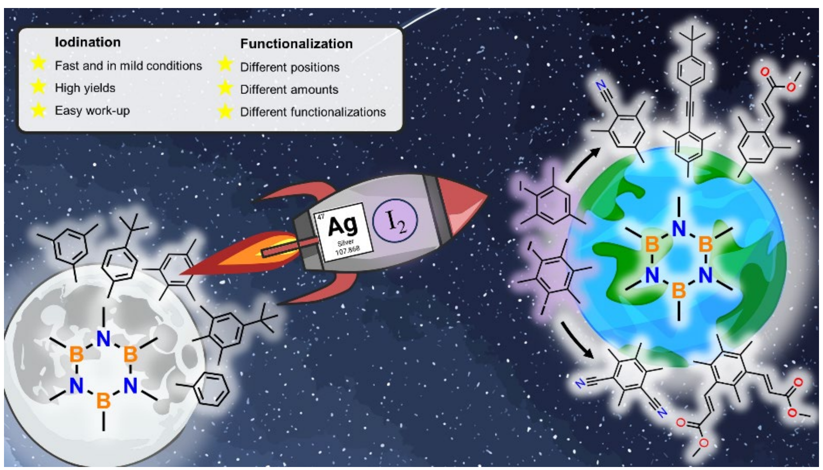
A solvent-free approach using Ball Billing

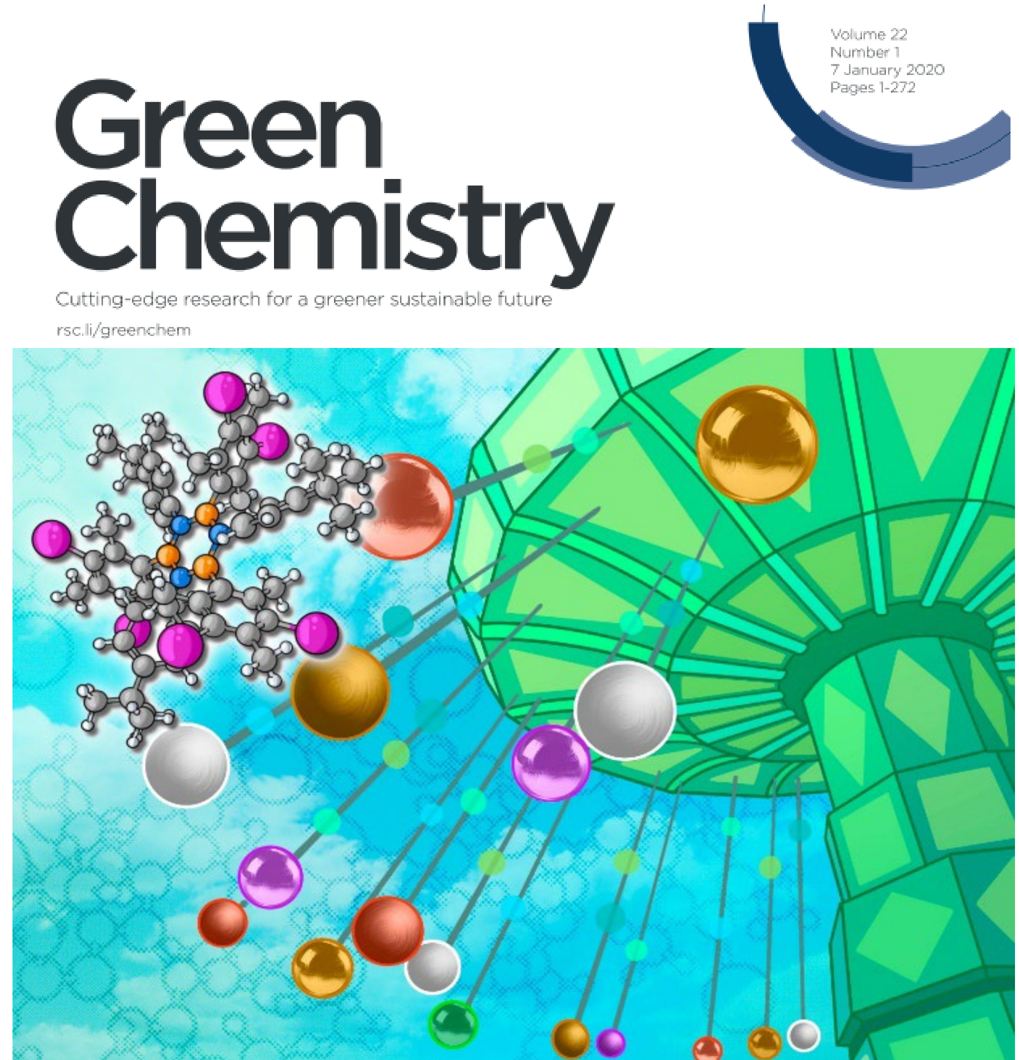


Green metrics evaluation and optimization



- **Work-up solvent recovery**
- **High yields for multiple processes**
- **Column-free product isolation**
- ***N*- and *B*-ring selective iodination**
- **Short reaction time**



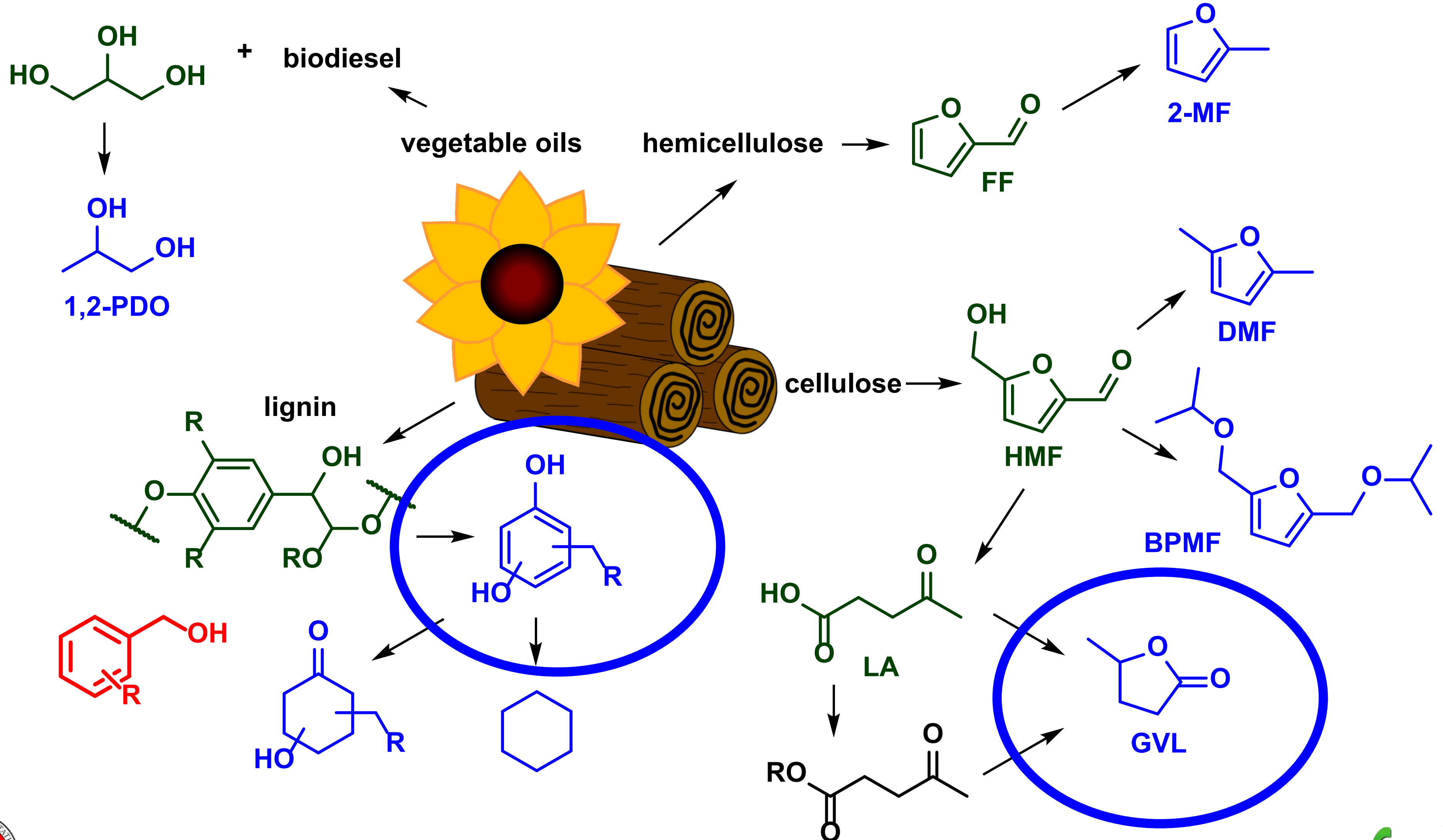


Vaccaro et al *Adv Synth Catal* 2024, 366, 494−501. *and*

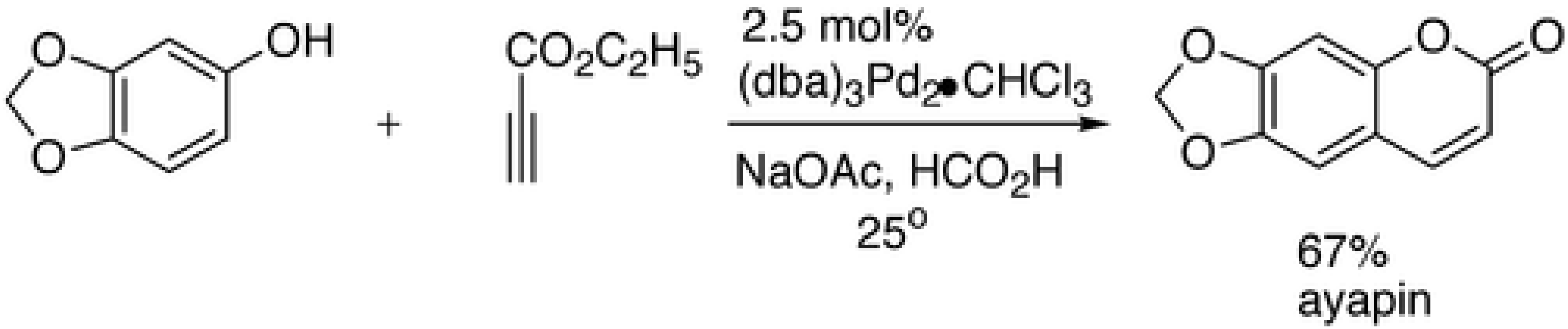
Green Chem., 2024, DOI: 10.1039/D4GC00699B **HOT ARTICLE selected for front cover image**

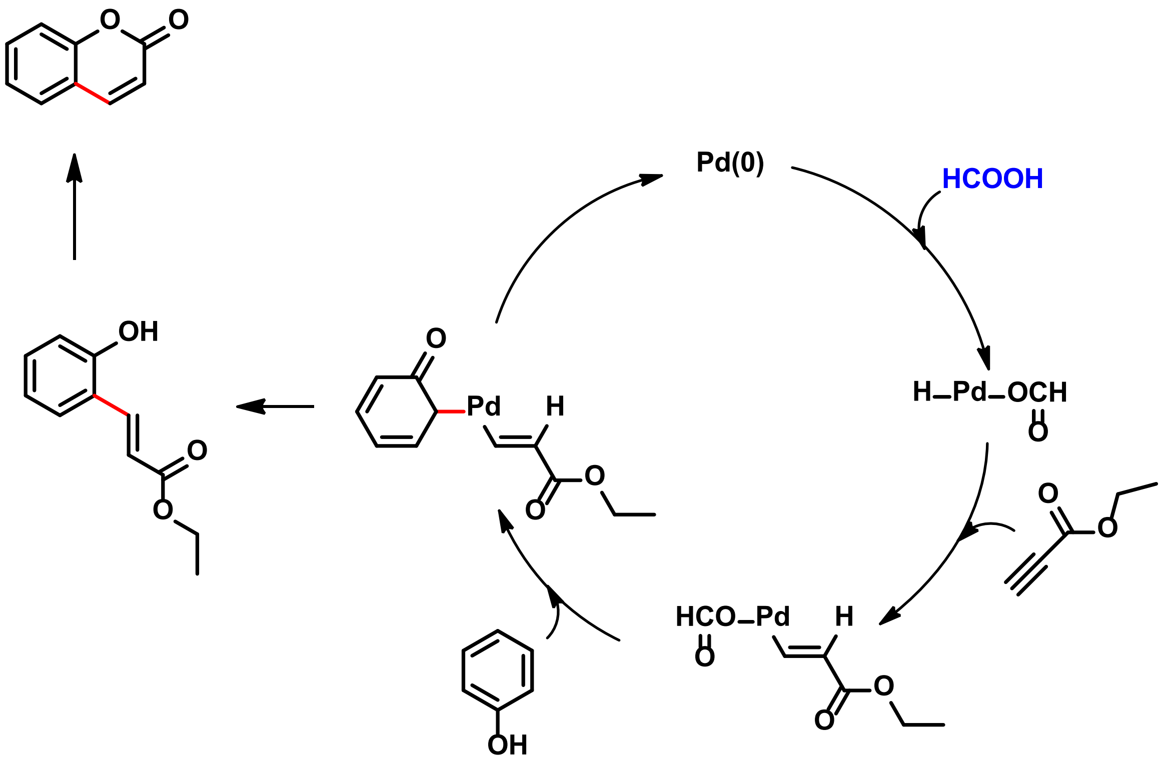
✓Biomass as source

N2 O2 H2



Accessing coumarins from phenols – Trost/Toste reaction



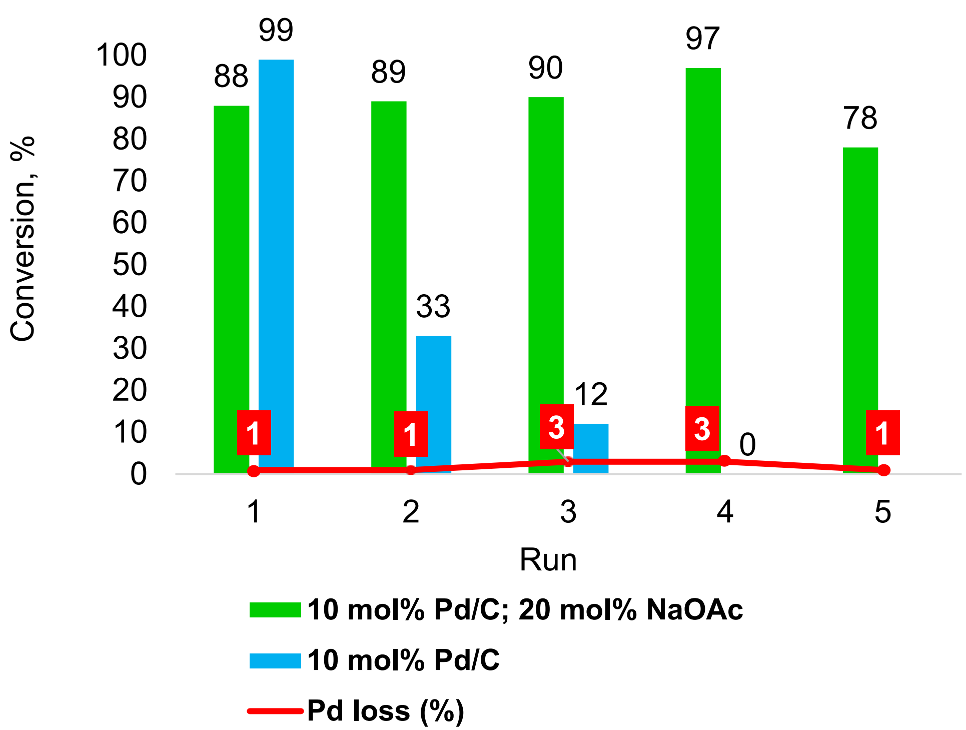


B. M. Trost, F. D. Toste, K.Greenman *J. Am. Chem. Soc.*, 2003, *125*, 4518-4526

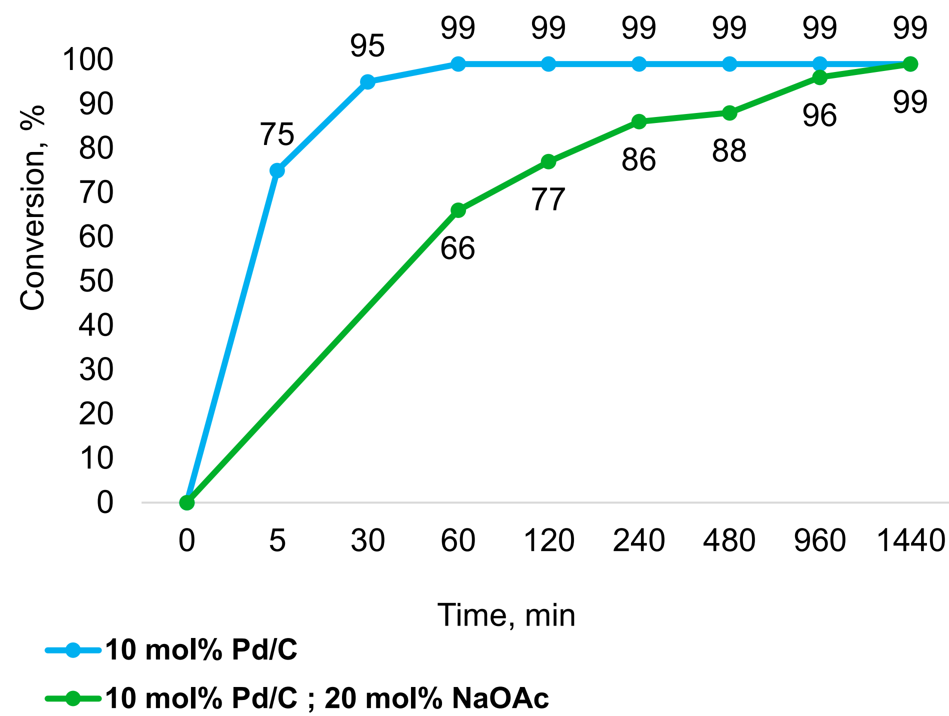
Results and Discussion

Catalytic test

Recycle of Pd/C



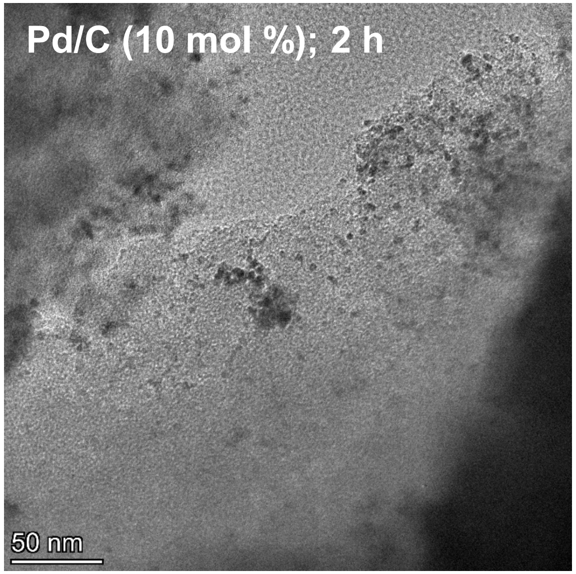
Kinetic test

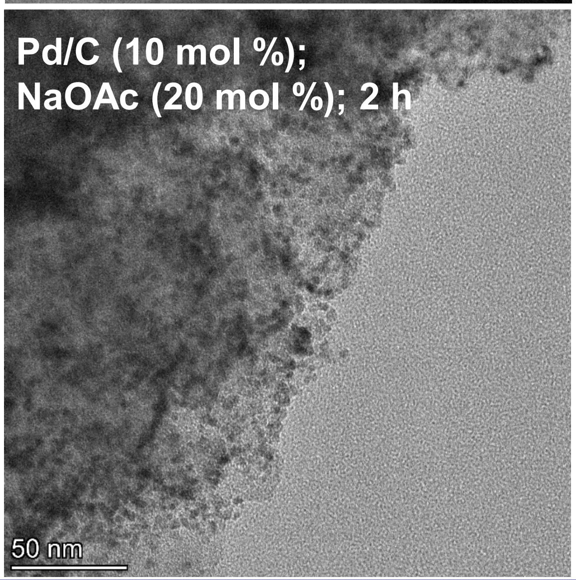


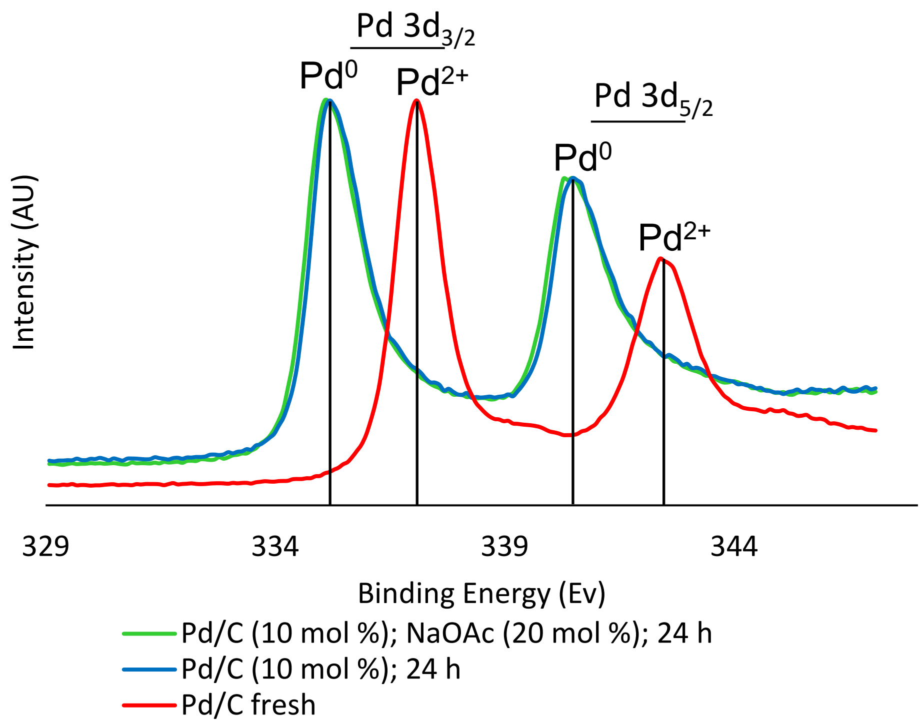
L. Vaccaro, C.-J. Li et al. *Green Chem. 2022, 24, 9094 9100*

Results and Discussion

TEM and XPS analysis

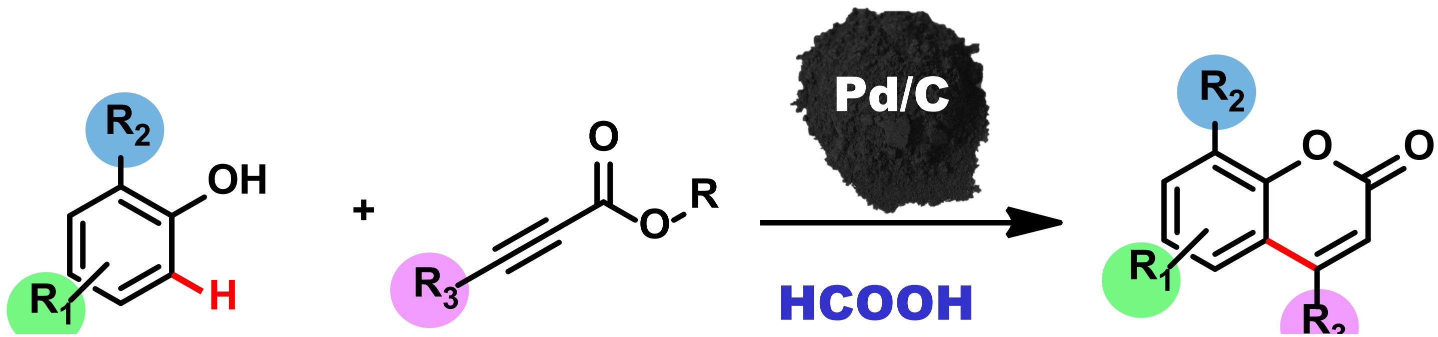


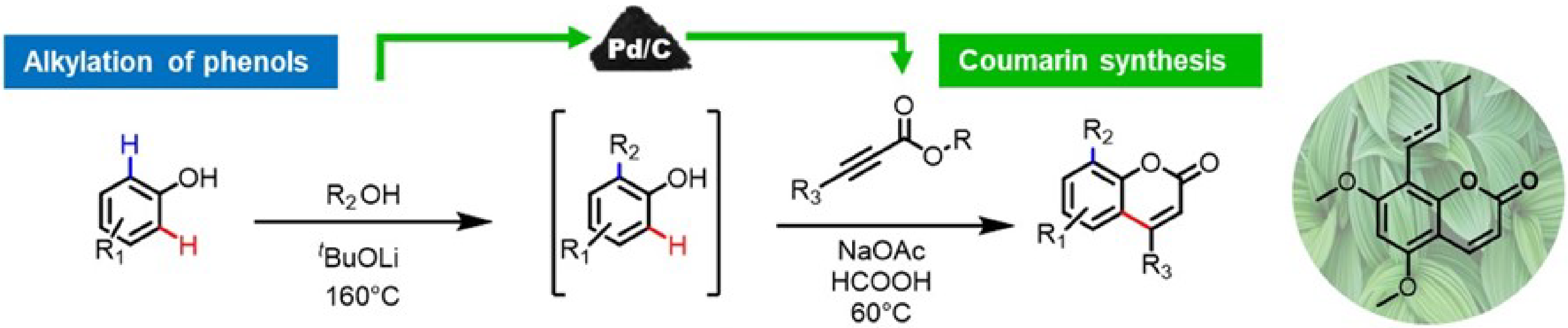




L. Vaccaro, C.-J. Li et al. *Green Chem. in press DOI: 10.1039/D2GC03579K*

PHENOL VALORISATION: Accessing coumarins via Heterogeneous catalysis





- Solvent-free reaction conditions
- Short reaction times
- One-pot catalytic methodology
- Recyclable Pd/C
- First example of Pd/C for coumarin synthesis

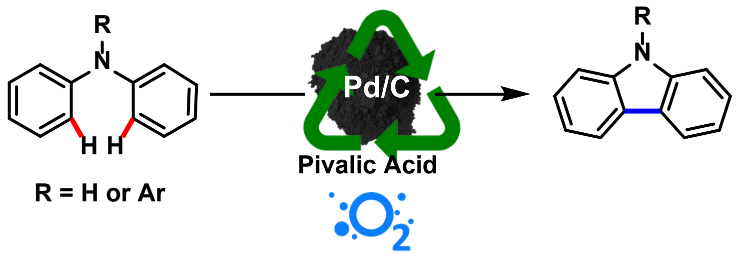
Osthole derivatives

McGill UNIVERSITY **Prof. C.-J. Li**

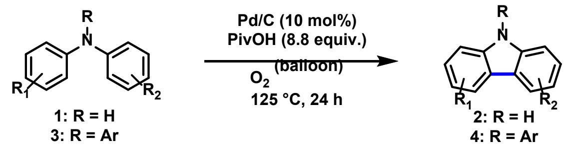
First report of coumarins synthesis from phenols via C–H functionalization catalysed by a heterogeneous catalyst

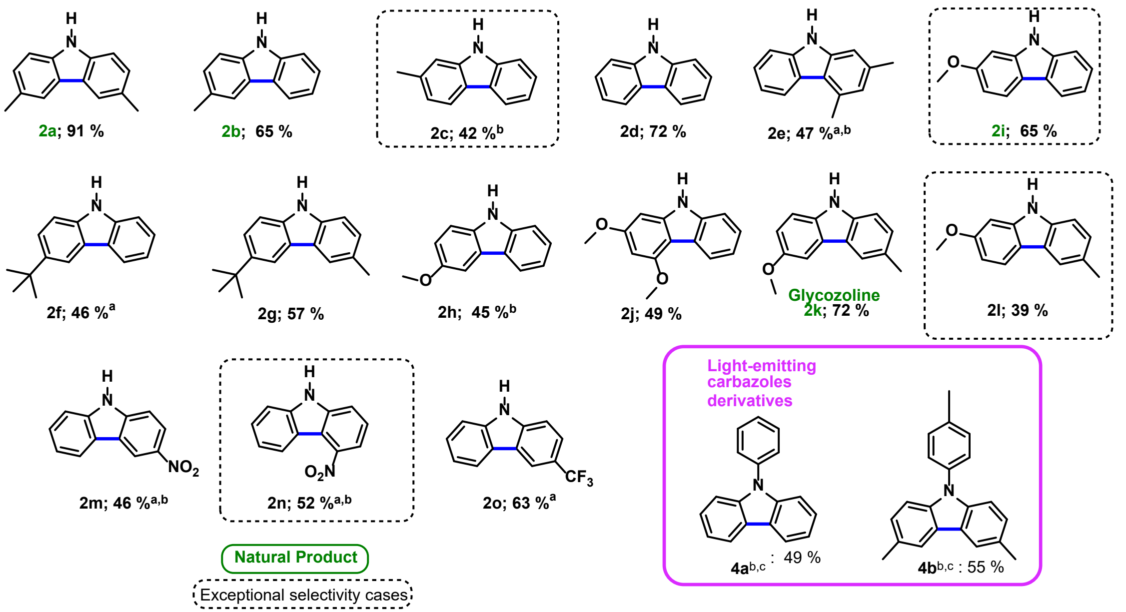
L. Vaccaro, C.-J. Li et al. *Green Chem. 2022, 24, 9094 9100 HOT ARTICLE*

From PHENOLS to arylamines and to Carbazoles via C–H/C–H Oxidative Functionalization/Cyclization of Arylamines



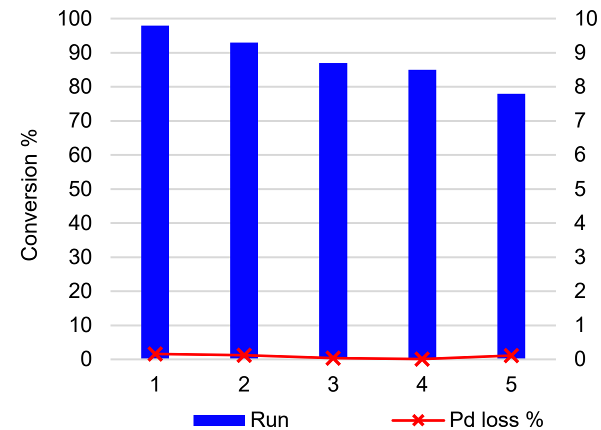
- Heterogeneous catalyst
- Recycle of the catalyst
- Oxygen ballooon as oxidant
- Solvent free condition
- Facile and safer process
- Minimized E-Factor

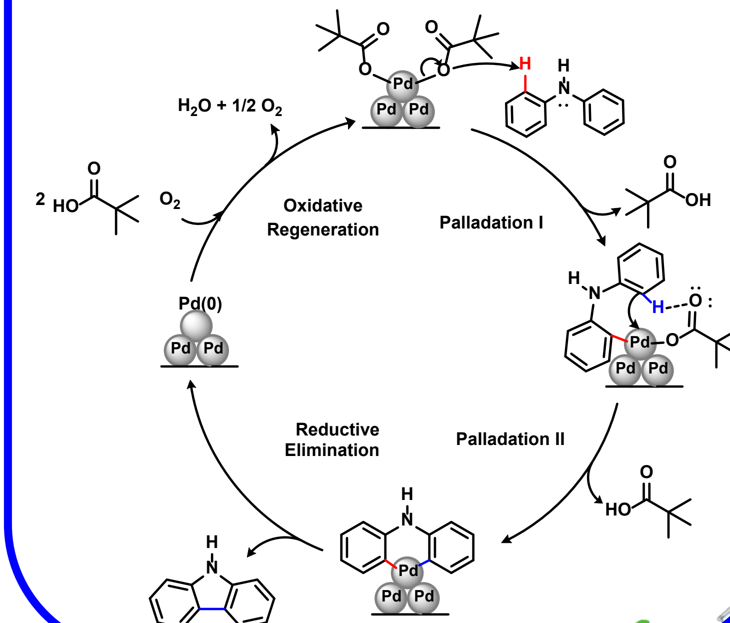




Reaction conditions: **1** (0.5 mmol); Pd/C (10 mol%), PivOH (8.8 equiv.), O_2 balloon, 125 °C, 24 h. [a]140°C. [b]Chromatographic column is required due to incomplete conversion of starting material. [c]**3** (0.5 mmol); Pd/C (25 mol%), PivOH (8.8 equiv.), O_2 balloon, 140 °C, 24 h.

Catalyst recycle



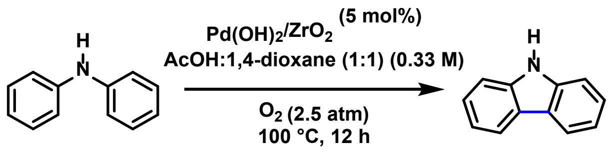


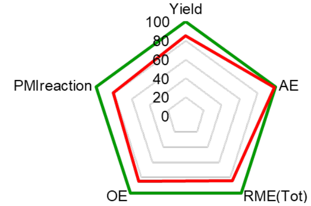
Prof. C.-J. Li

ACS Sustainable Chem. Eng. **2024**, 12, 22, 8562–8572

Green assessment

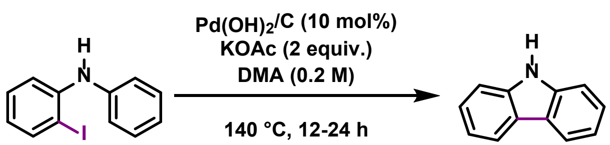
1) *Appl. Catal. B: Environ.*, **2014**, *150-151*, 523-531

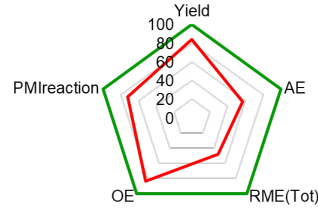




Solvent	Acetic acid 1,4-dioxane
Energy	100°C
Heath & Safety	
1,4-dioxane (H350)	
acetic acid, O_2 under pressure	

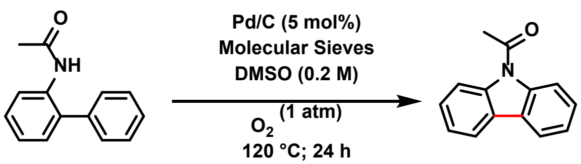
2) *J. Org. Chem.* **2005**, *70*, 7578-7584

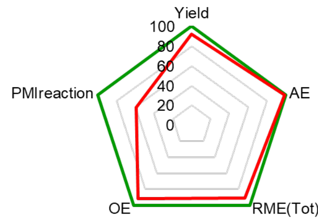




Solvent	DMA
Energy	140°C
Heath & Safety	
DMA (H360D)	
Potassium acetate	

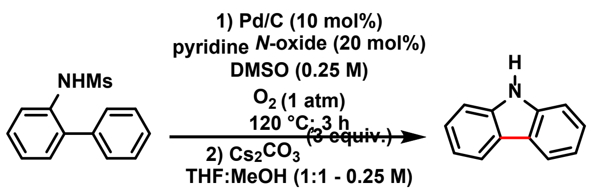
3) *Chem. Commun.* **2014**, *50*, 9049-9052

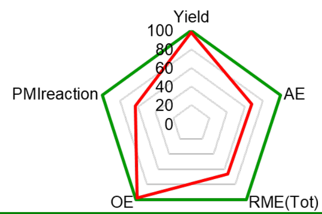




Solvent	DMSO
Energy	120°C
Health & Safety	
O_2 atmosphere, DMSO	

4) *Adv. Synth. Catal.* **2016**, *358*, 3145-3151



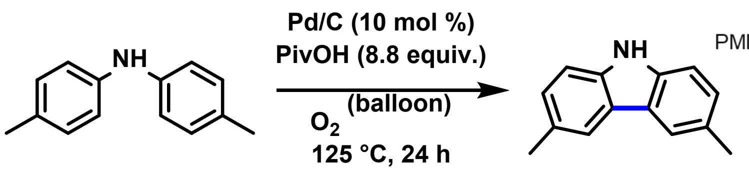


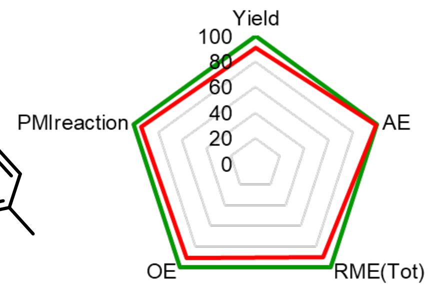
Solvent	DMSO THF MeOH
Energy	120°C
Health & Safety	
THF (H351), MeOH (H301, H311, H331)	
DMSO, Cs_2CO_3, Pyridine *N*-oxide, O_2 atmosphere	

McGill UNIVERSITY

Prof. C.-J. Li

THIS WORK





Solvent	SolFC
Energy	125°C
Health & Safety	
pivalic acid, O_2 atmosphere	

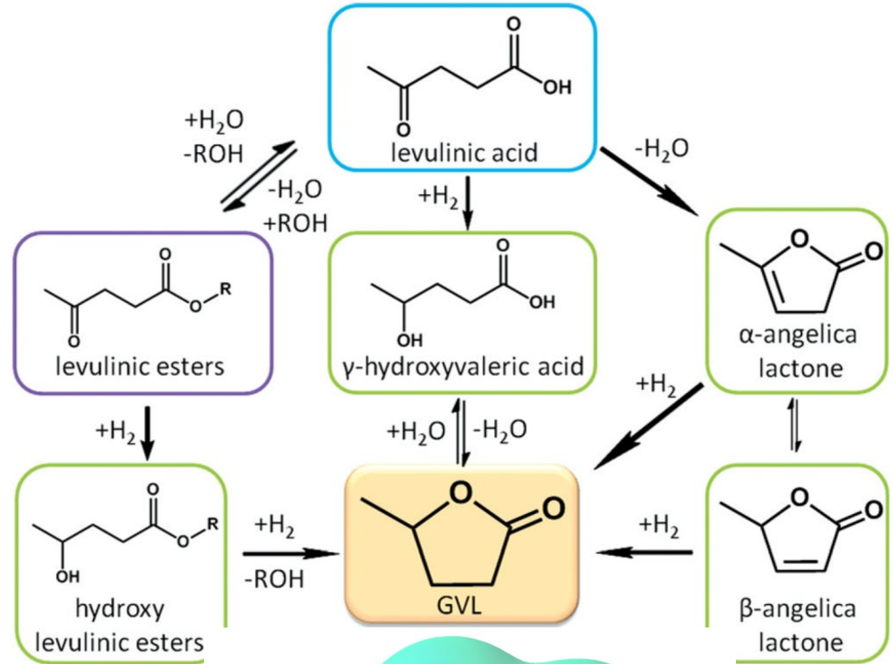
ACS Sustainable Chem. Eng. **2024**, *12*, 22, 8562–8572

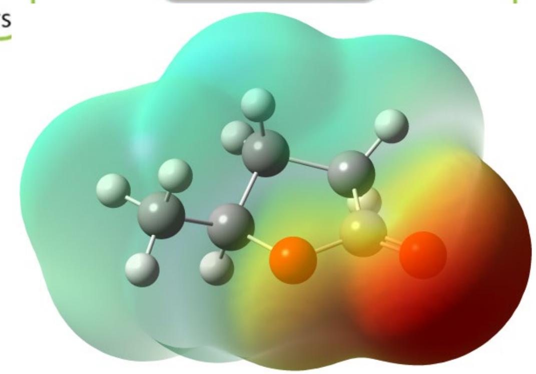
Green S.O.C. Perugia

Alternative solvents from Biomasses

Property	Value
CAS-No	108-29-2
Formula	$C_5H_8O_2$
MW (g mol^{-1})	100.112
Refractive index (n20/D	1.432
Density (g mL^{-1})	1.05
Flash point (°C)	96
Melting point (°C)	−31
Boiling point (°C)	207–208
Solubility in water (%)	100
ΔH_{vap} (kJ mol^{-1})	54.8
$\Delta_c H^\circ_{liquid}$ (kJ mol^{-1})	−2649.6

γ-Valerolactone - GVL





Boling points and polarity of dipolar aprotic solvents

NMP	**202 °C**	**ε = 32**
Dimethyl sulfoxide	**189 °C**	**ε = 48**
Dimethyl formamide	**153 °C**	**ε = 36.7**
Dimethyl acetamide	**165 °C**	**ε = 32**
Acetonitrile	**82 °C**	**ε = 37**
GVL	**207 °C**	**ε = 36.5**

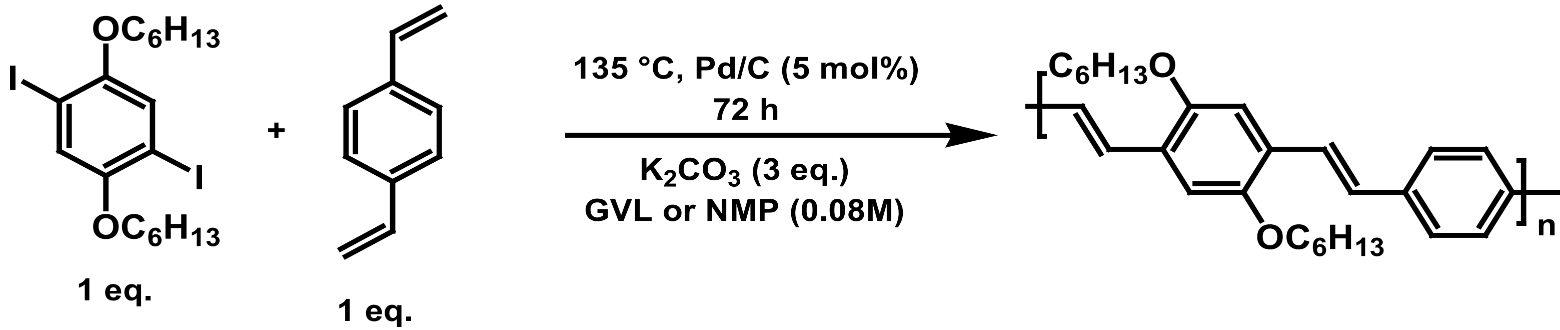
γ-Valerolactone - GVL

Dumesic, J. A. et al. Green Chem., 2013, 15, 584–595

GVL as medium for Pd-catalyzed couplings

✓ Heck Reaction in the Co-polymerization Reaction and Device Performance

CHIARA



GIACOMO

Medium	M_n (KDa)	M_w (KDa)	PDI	Pd (ppm)
GVL	8.14	16.27	1.99	**6**
NMP	16.43	36.98	1.99	**860**

Medium	J_{sc} (mA cm^{-2})	Voc (V)	FF (%)	PCE (%)	μ × 10^{-3} (cm^2 V^{-1}s^{-1})	I_{on}/I_{off}
GVL	2.4	0.92	33.7	0.73	1.01	1500
NMP	3.8	0.91	36.1	1.26	1.21	200
GVL[b]	1.6	0.75	33.8	0.39	0.90	1400

[a] Average of ~5 devices. [b] $Pd(PPh_3)_4$ was added to achieve ~800 ppm of Pd.

Green Chem. 2015, *17*, 365-372

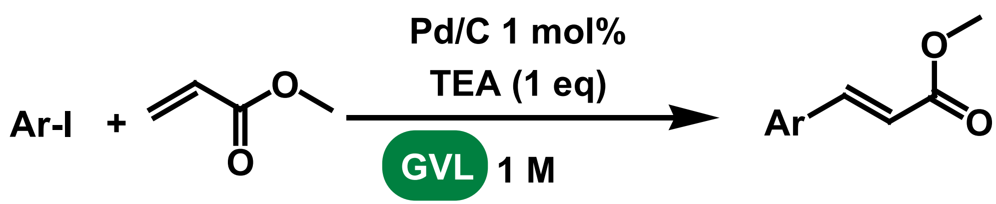
Dr. Antonio Facchetti
Flexterra Inc, USA
Organic semiconductors

GVL as medium for Pd-catalyzed couplings

WHY and HOW an alternative a reaction medium should be used?

… HOW to exploit unconventional medium properties to obtain more efficient chemical results?

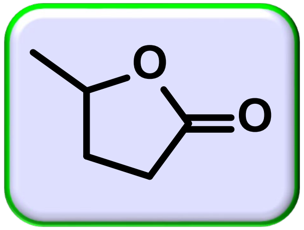
✓ Heck Reaction



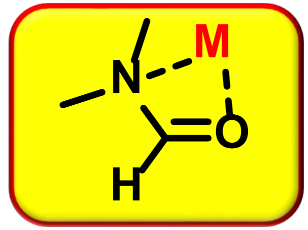
Medium	T (°C)	Time (h)	Pd content (ppm)
GVL	150	1	7.7
NMP	150	10 min	835
DMF	150	10 min	50
GVL	180	30 min	6.3
GVL	200	20 min	3.9
NMP	200	5 min	279

Green Chem. 2015, *17*, 365-372

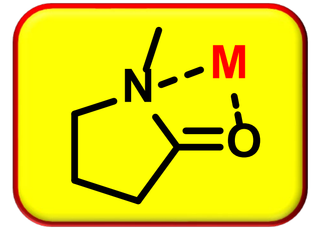
GVL as medium for Pd-catalyzed couplings



GVL

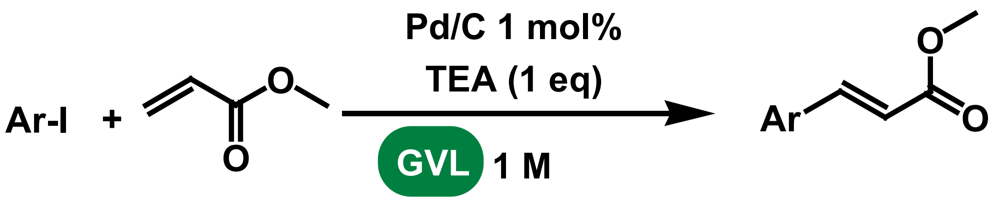


DMF



NMP

✓ Heck Reaction



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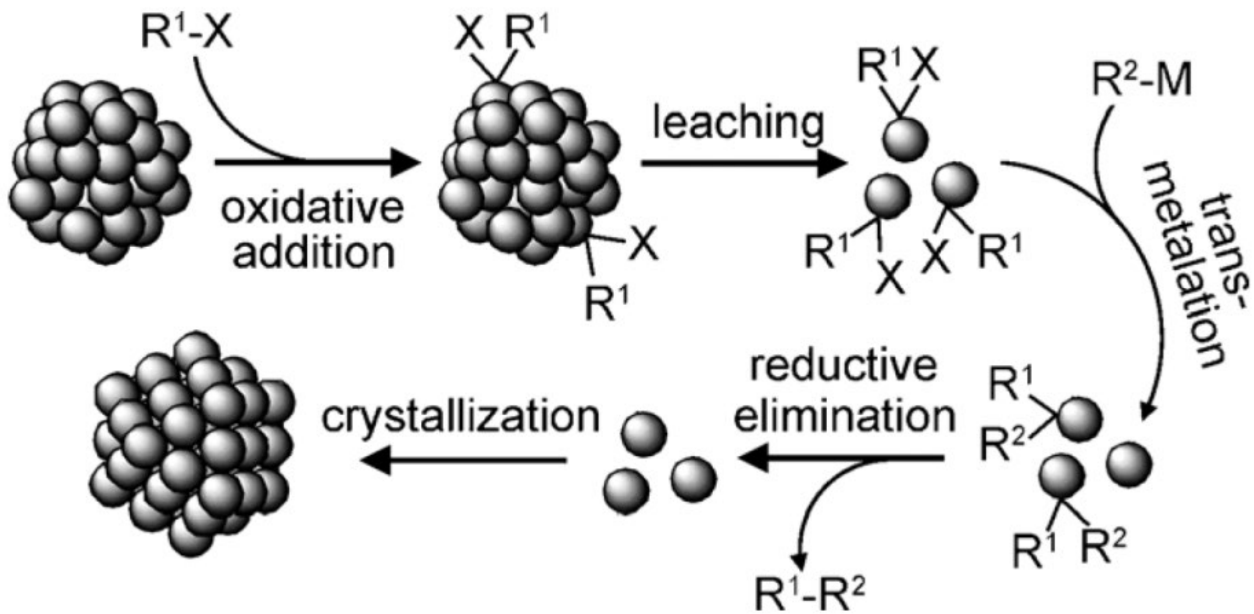
NMP	200	5 min	279

PALLADIUM *Release and Catch* catalytic system

During the process after oxidative addition “Heterogeneous Palladium” is released and after reductive elimination it «re-precipitates».

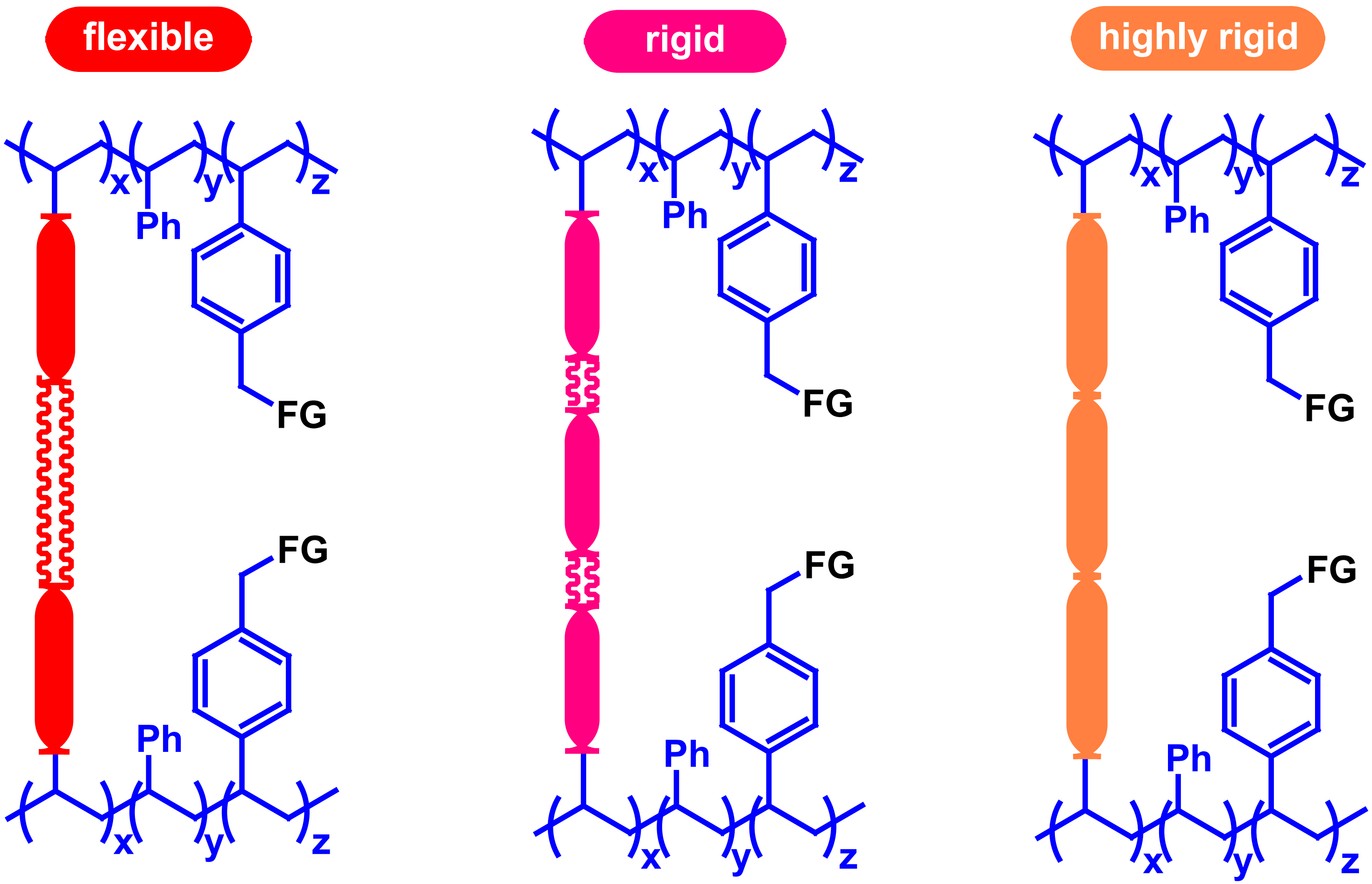
This phenomenon depends on the reaction medium, on the base, on the type of support, and on temperature



Y. Li et al. Chem. Eur. J. 2012, 18, 9813 – 9817

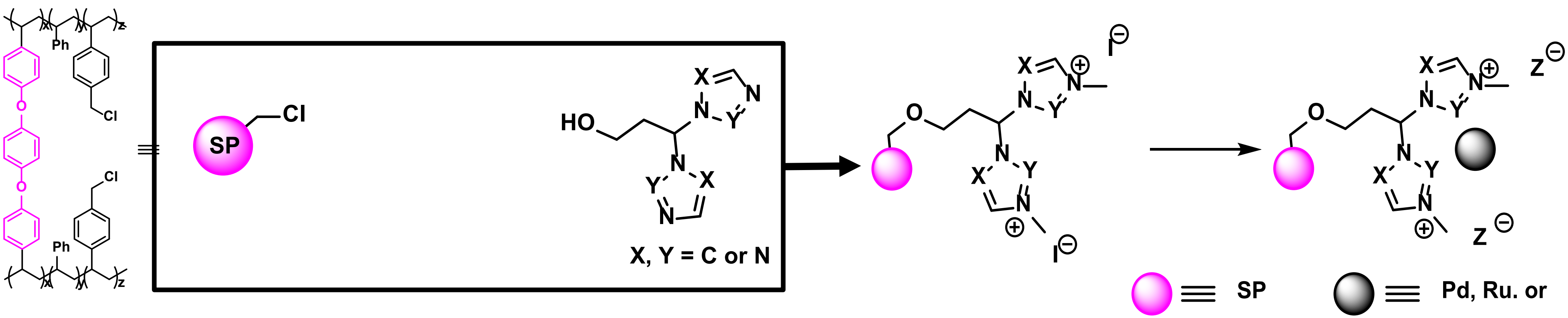
E. Garcia-Verdugo, S. V. Luis et al. Adv. Synth. Catal. 2010, 352, 3013 – 3021

ORGANIC SUPPORTS… polystyrenes

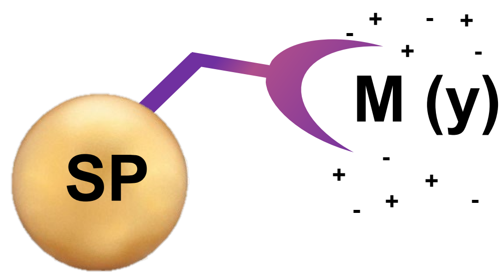


POLI-TAG – POLymeric-supported Ionic TAGs

Novel catalyst design



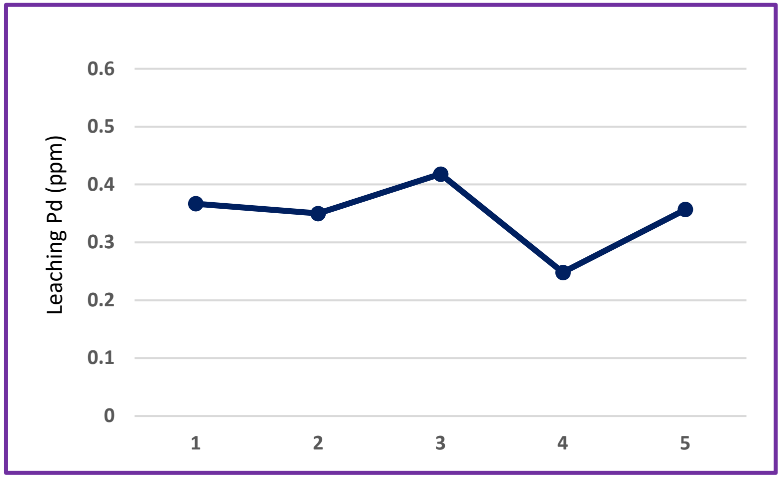
- **Novel** class of heterogeneous catalytic systems
- **Tunable properties** (support, loading, pincer-type ligand, metal)
- **Tailor-made** catalysts



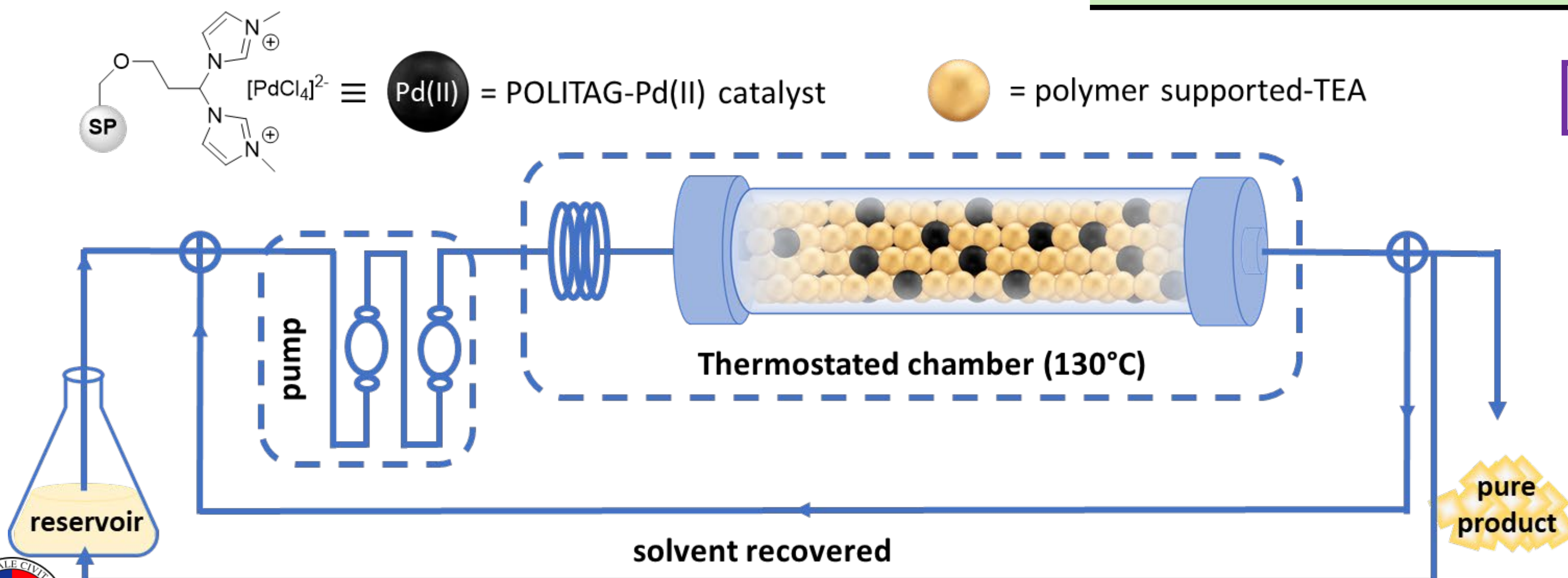
L. Vaccaro et al.: *Mol. Catal.*, **2021**, *509*, 111613; *ChemSusChem* **2021**, *14*, 3359 – 3366; *Green Chem.*, **2020**, *22*, 6560 – 6566; *ACS Sustainable Chem. Eng*. **2021**, *9*, 5740–5749; *Green Chem.*, **2019**, *21*, 355 – 360

POLI-TAG-L1-Pd(II)-L

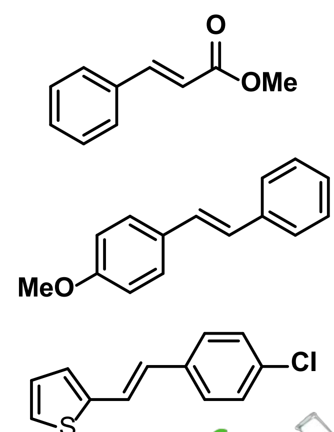
✓Recycling and flow



Run	Pd leaching (ppm)
1	**0.37**
2	**0.35**
3	**0.42**
4	**0.25**
5	**0.36**
flow	**0.05**



2.4 < E-factor < 5



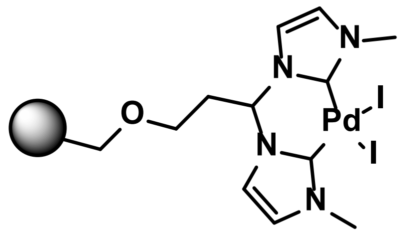
Green Chem., 2018,20, 2888-2893 - ACS Sus. Chem. Eng. 2019, 7, 6939−6946 and work in progress

POLI-TAG-L1-Pd(II)-L and POLI-TAG-L2-Pd(0)-M

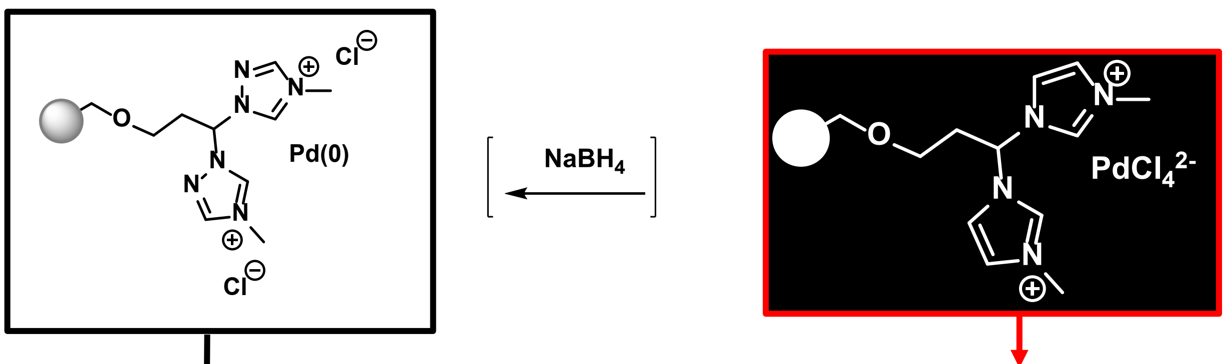
Federica

OUR POLITAG SYSTEMS DO EFFECTIVELY WORK TO CATCH PALLADIUM

“It doesn't matter whether the cat is black or white, as long as it catches mice”



Polymer Supported-NHC-Pd(II)



POLI-TAG-L2-Pd(0)-L

Pd(0) loading: **16 wt%**

POLI-TAG-L1-Pd(II)-L

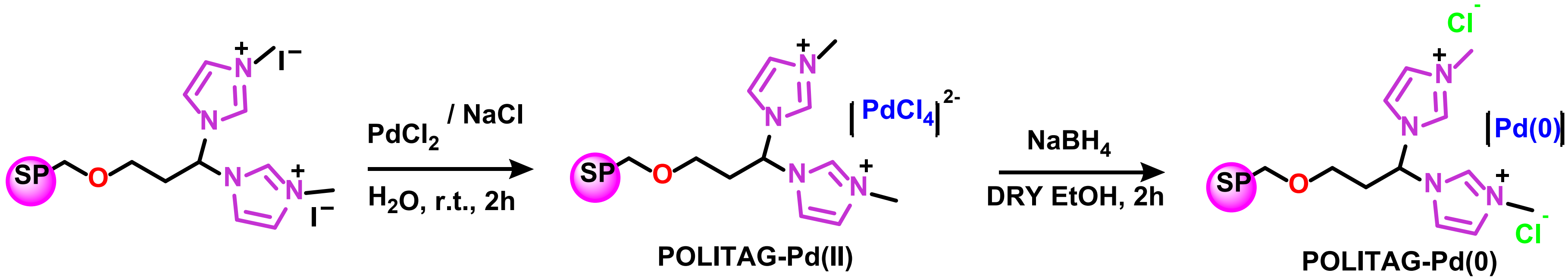
Pd(II) loading: 3 wt %

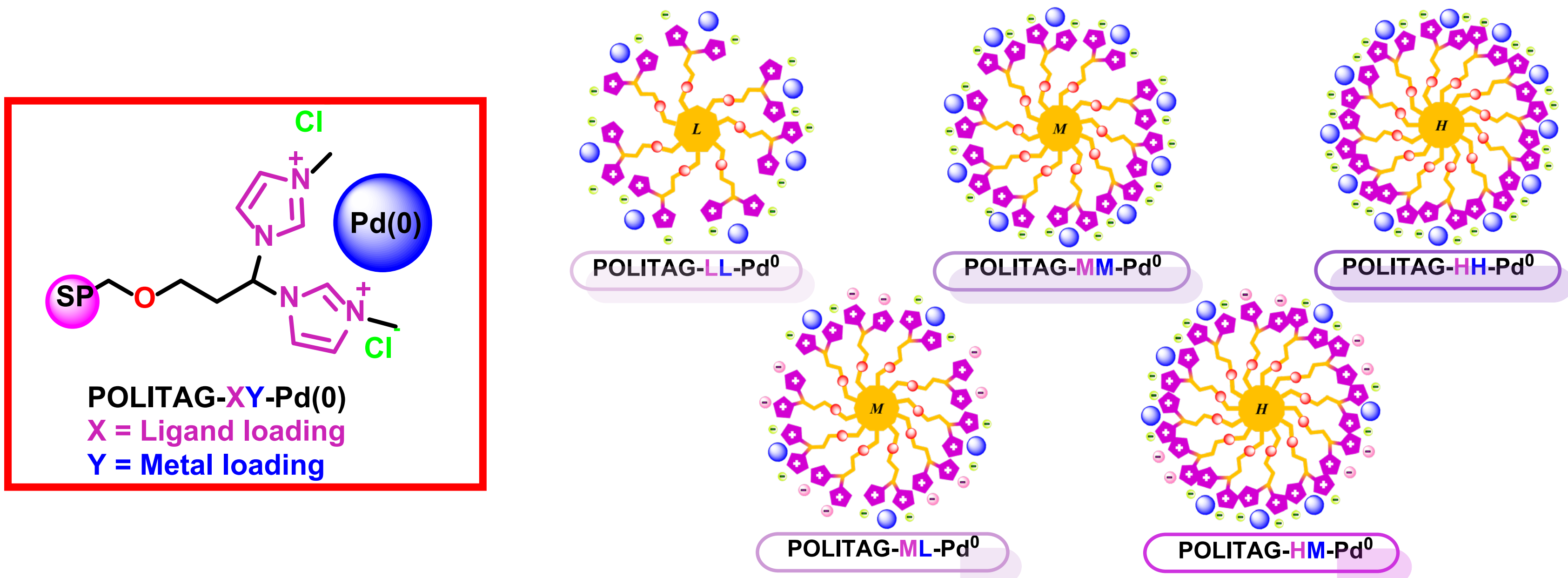
Green Chem., 2021, 23, 5887 ChemSusChem 2022, 15, e202102736 Hot Topic: C-H Activation; ACS Sustainable Chem. Eng. 2022, 10, 11, 376 and work in progress

Green S.O.C. Perugia

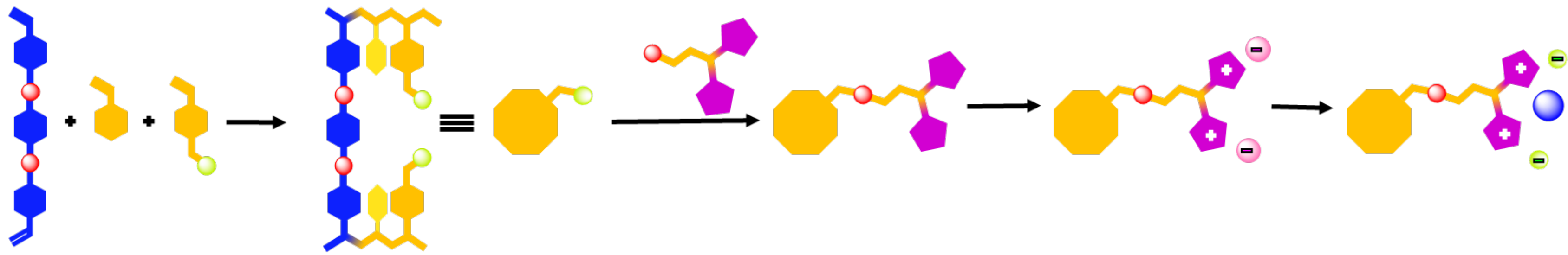
HIGHLY EFFICIENT POLI-TAG CATALYSTS

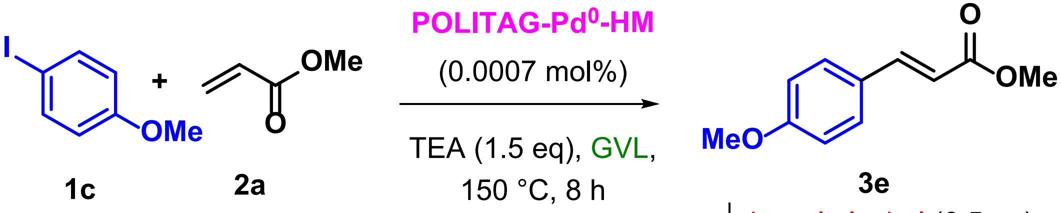
➢ Synthesis of POLITAG-X

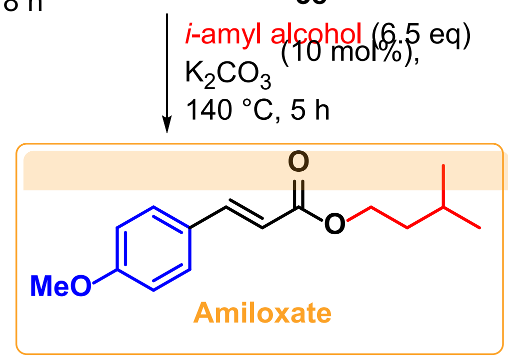




HIGHLY EFFICIENT POLI-TAG CATALYSTS



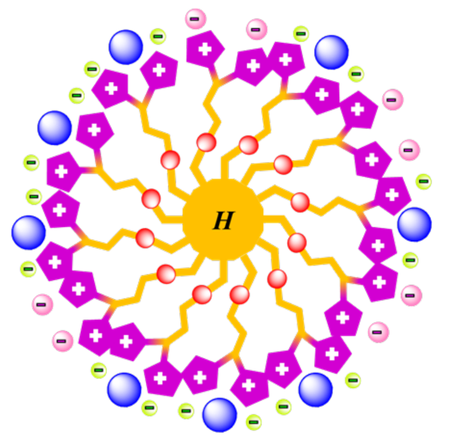




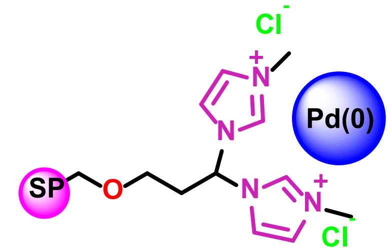
E-factor 1st step = 12.7

E-factor 2nd step = 5.2

total E-factor = 26.9



POLITAG-HM-Pd(0)



POLITAG-XY-Pd(0)
X = Ligand loading
Y = Metal loading

ACS SCE 2022, 10, 12386−12393

high TOF value: 26786 h-1 using only 0.0007 mol% of Pd in γ-valerolactone (GVL) as green reaction medium

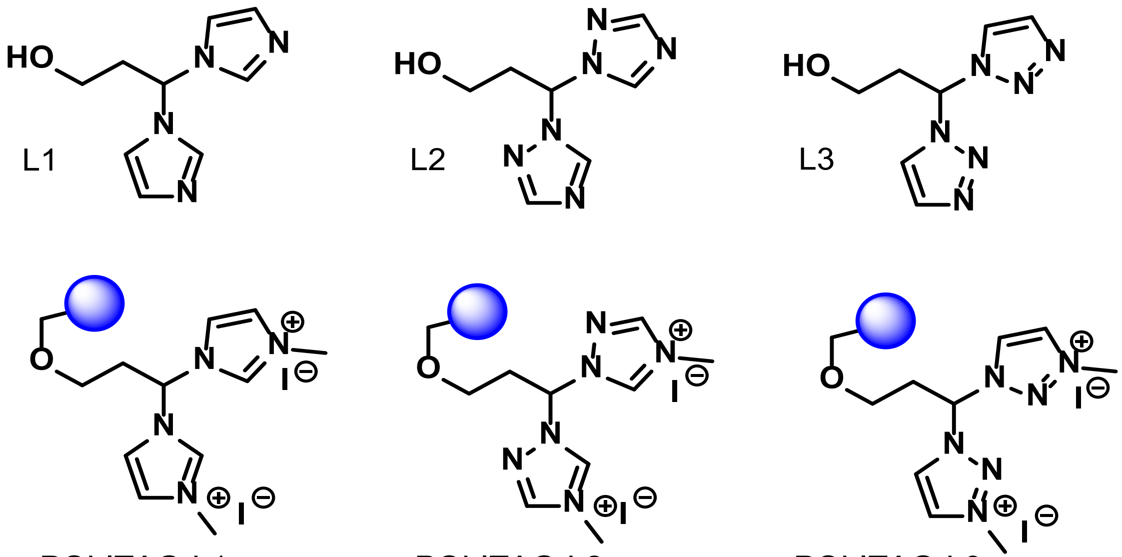
ACS SCE in press, ChemSusChem 2022, 15, e202102736 Hot Topic: C-H Activation; ACS Sustainable Chem. Eng. 2022, 10, 11, 3766–3776; Mol. Catal, 2022, 522, 112211; *Green Chem.*, 2020, 22, 6560–6566; ChemSusChem 2021, 14, 3359 –3366 and work in progress

POLITAG catalysts for the decoration of quinolines via C–H activation

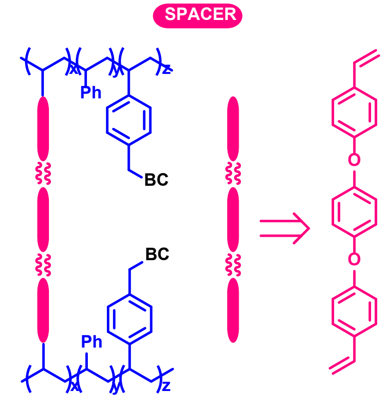
✓ POLITAG-catalysts

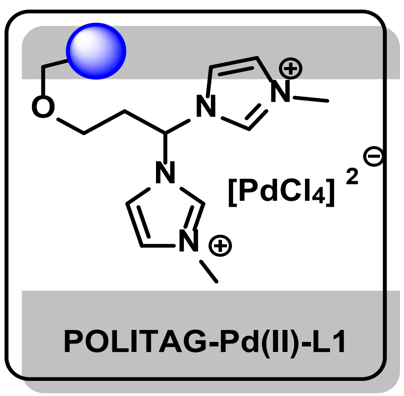
Federica

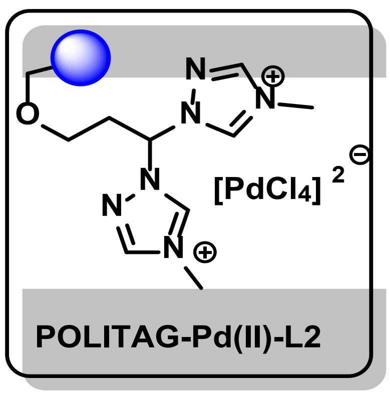
Daniele

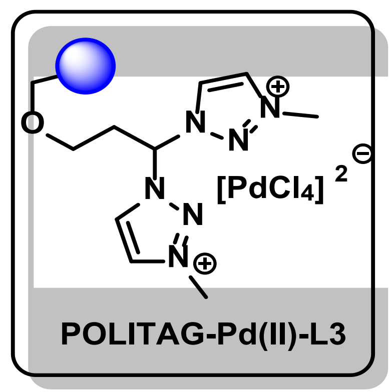


POLITAG-L1 POLITAG-L2 POLITAG-L3









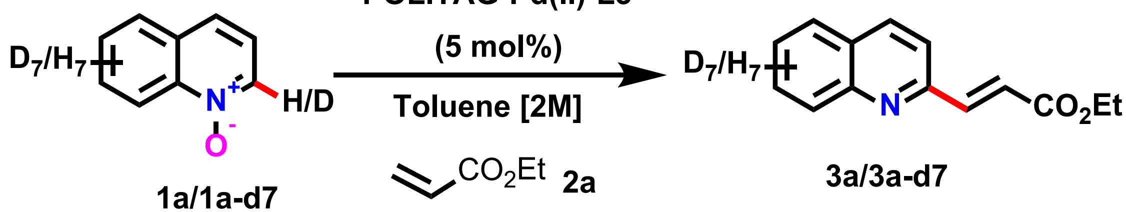
L. Vaccaro et al. *Green Chem.*, 2020, *22*, 6560–6566; Green Chem. 2019, *21*, 355; ACS SCE. 2019, *7*, 6939

POLITAG catalysts for the decoration of quinolines via C–H activation

✓ Mechanistic Investigation

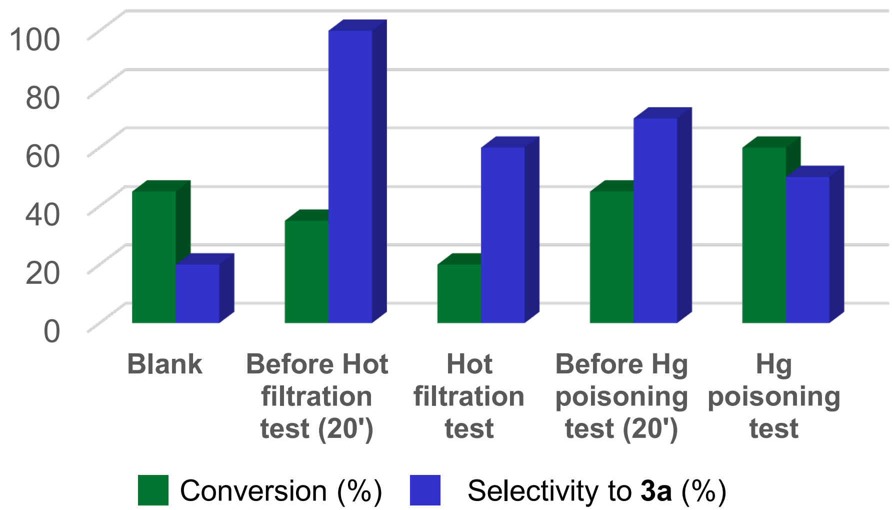
Is it C–H activation?

IntermolecularKIE (independentreaction and one pot)



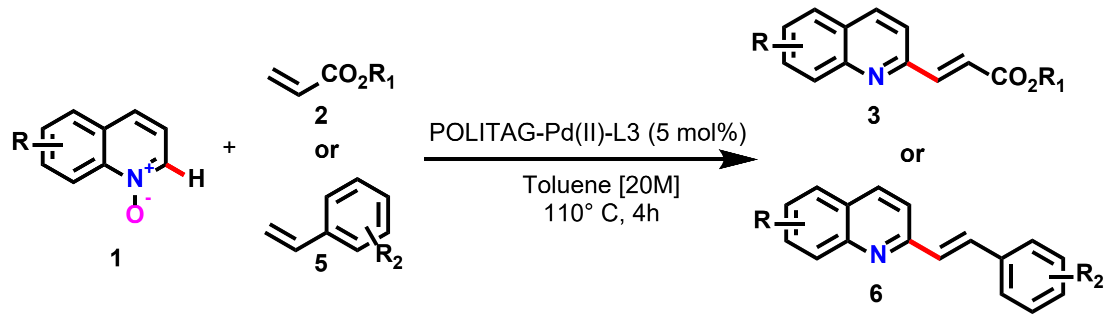
$k_H/k_D = 1.5$

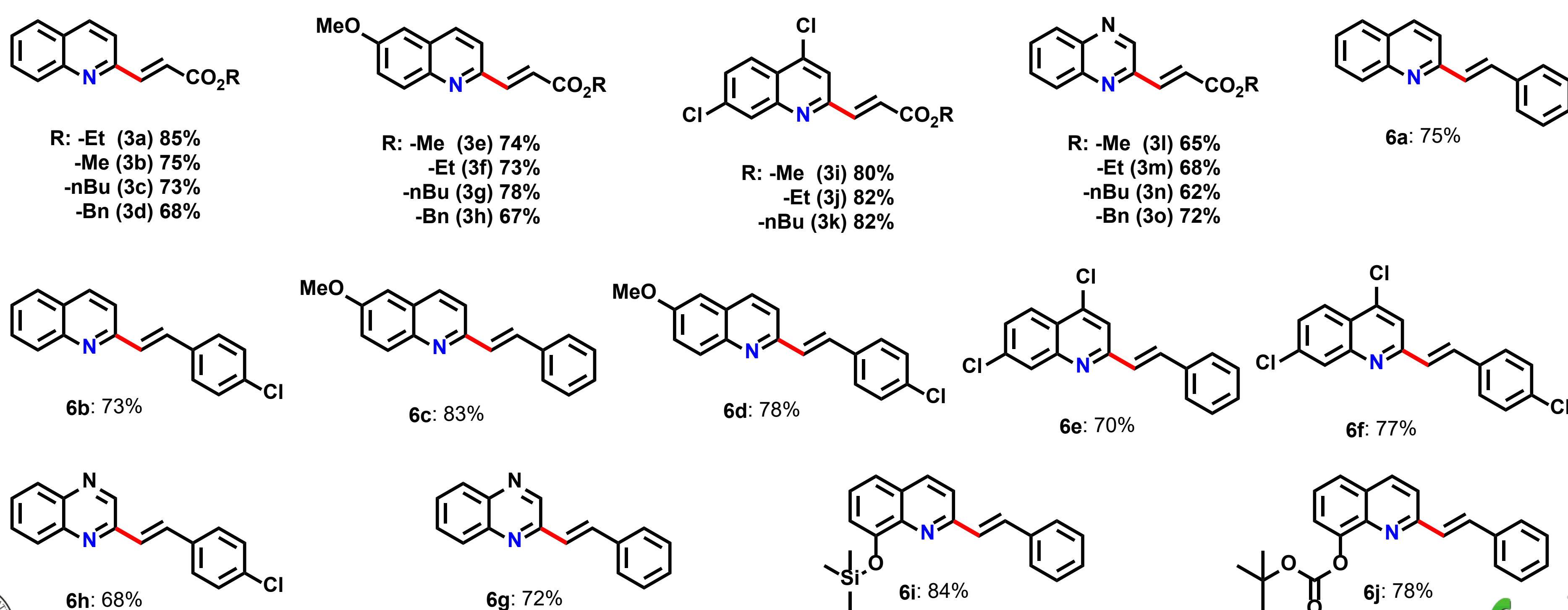
Is it Heterogeneous catalysis?



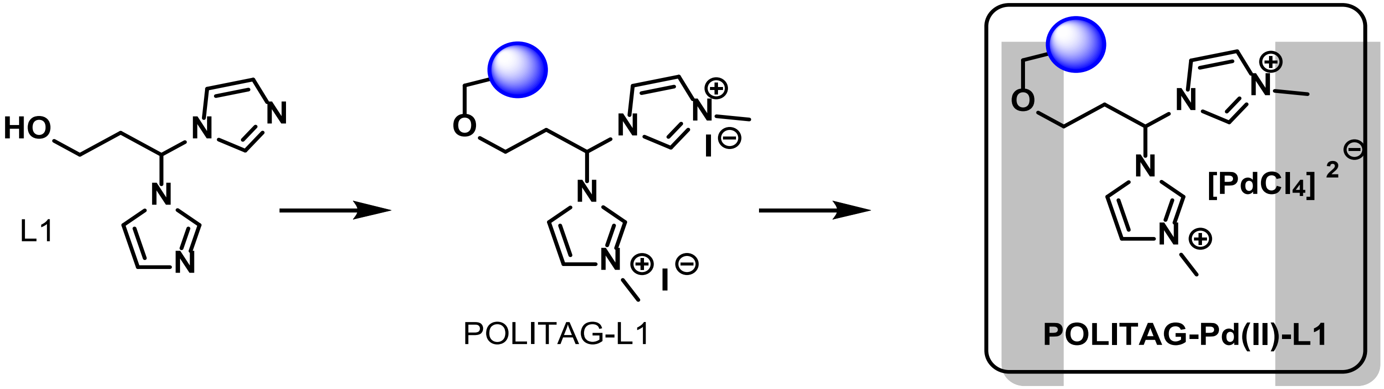
POLITAG catalysts for the decoration of quinolines via C–H activation

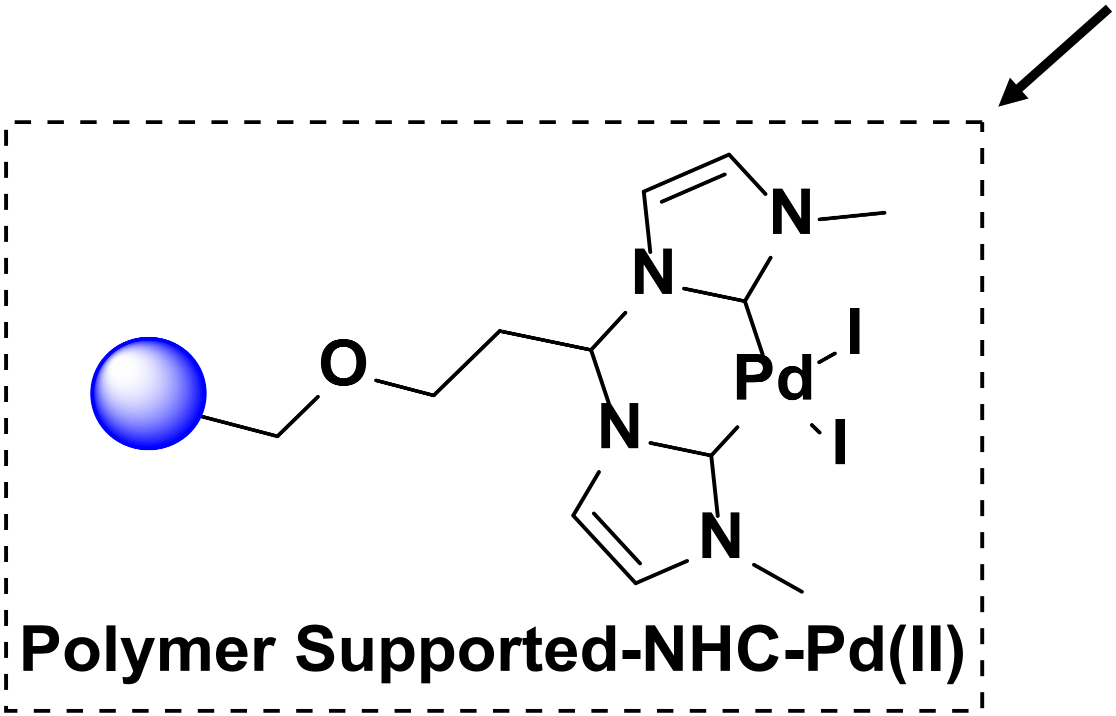
✓ Substrate scope

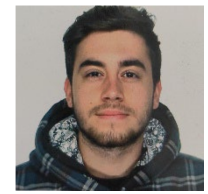




POLITAG carbene: heterogeneous NHC systems for C(sp3)–H activation



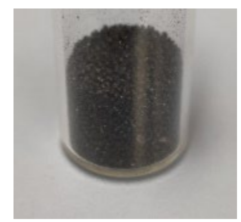




Francesco M.

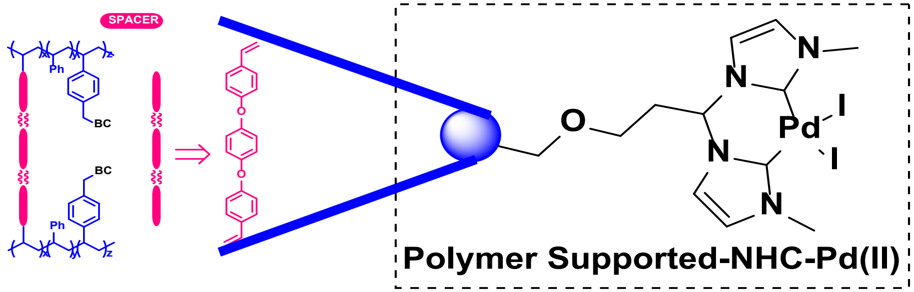
Tommaso

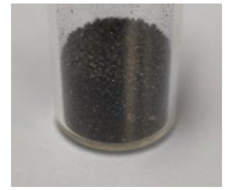
Tian



ChemSusChem 2022, 15, e202102736 Hot Topic: C-H Activation; ACS Sustainable Chem. Eng. 2022, 10, 11, 3766–3776; Mol. Catal, 2022, 522, 112211

POLITAG carbene: heterogeneous NHC systems for C(sp3)–H activation



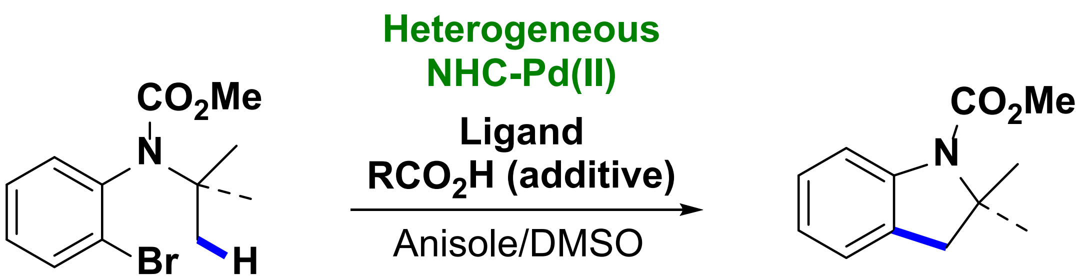


University of Basel

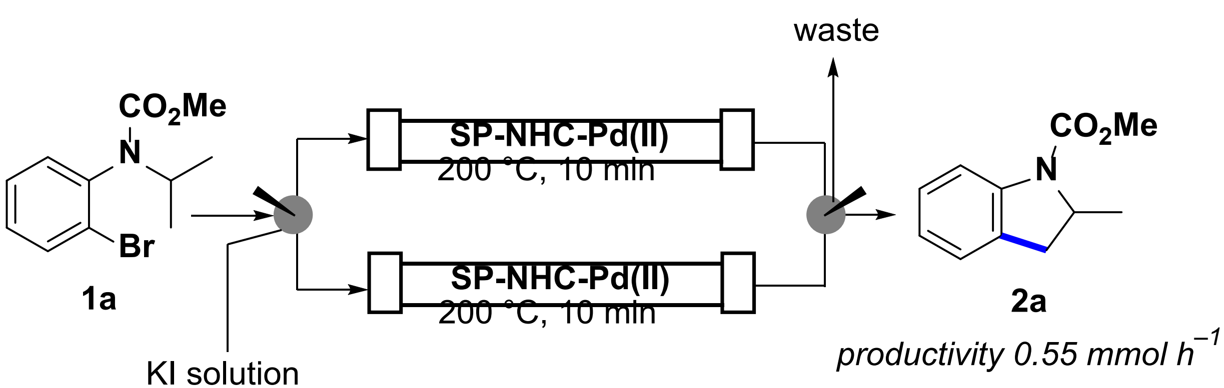
Prof. Olivier Baudoin
University of Basel

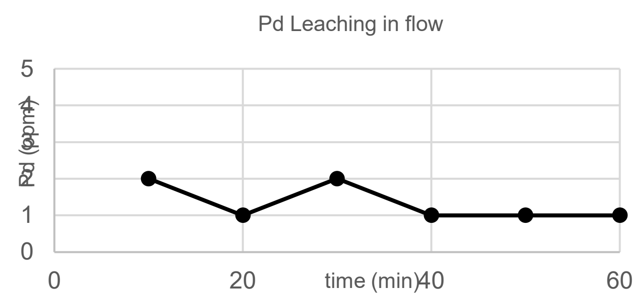
IOANNIS

Synthesis of indolines



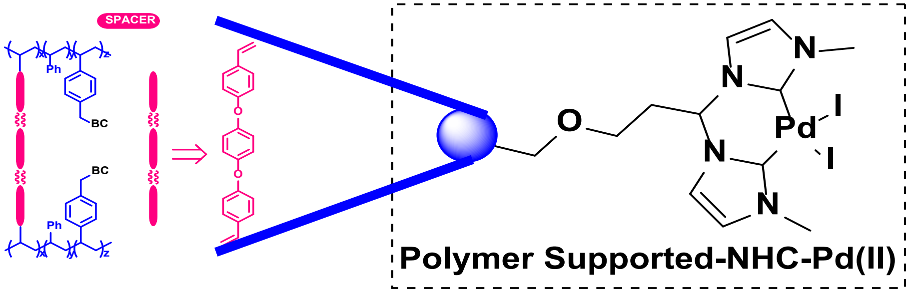
18 examples – 40-91% yields

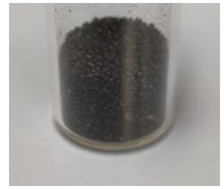


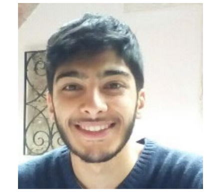


ChemSusChem 2022, 15, e202102736 hot topic C-H activation

POLITAG carbene: heterogeneous NHC systems for C(sp3)–H activation



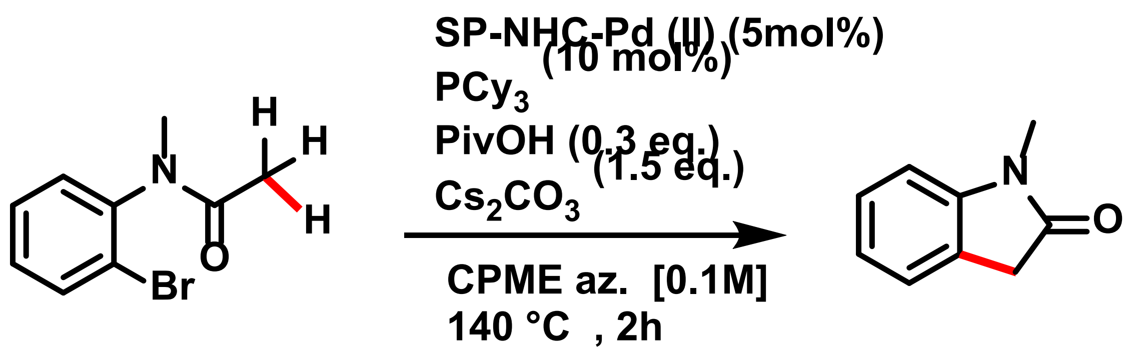


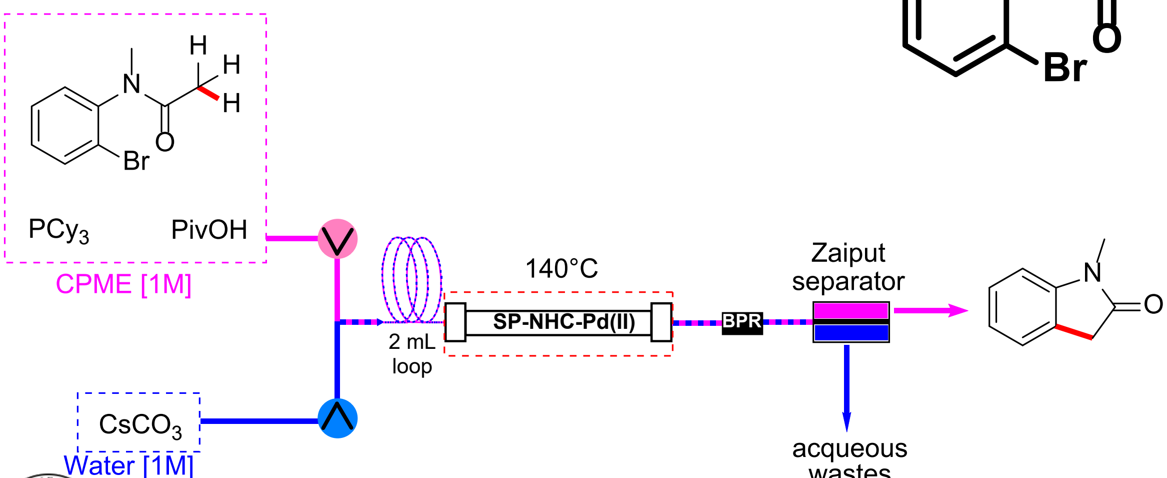


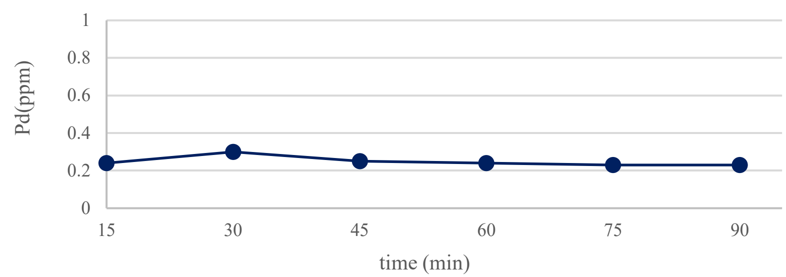
IOANNIS NIHAD

Synthesis of oxindoles

20 examples – 85-94% yields

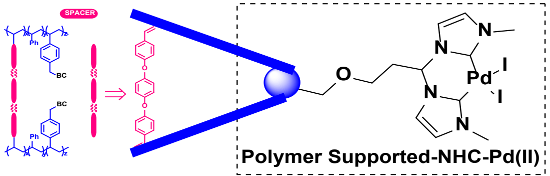


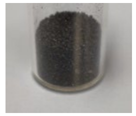




ACS Sustainable Chem. Eng. 2022, 10, 11, 3766–3776

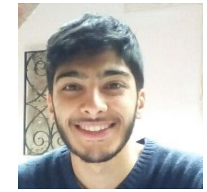
POLITAG carbene: heterogeneous NHC systems for C(sp3)–H activation





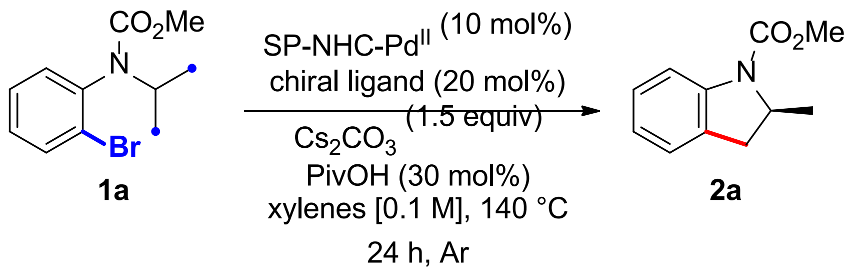
University of Basel

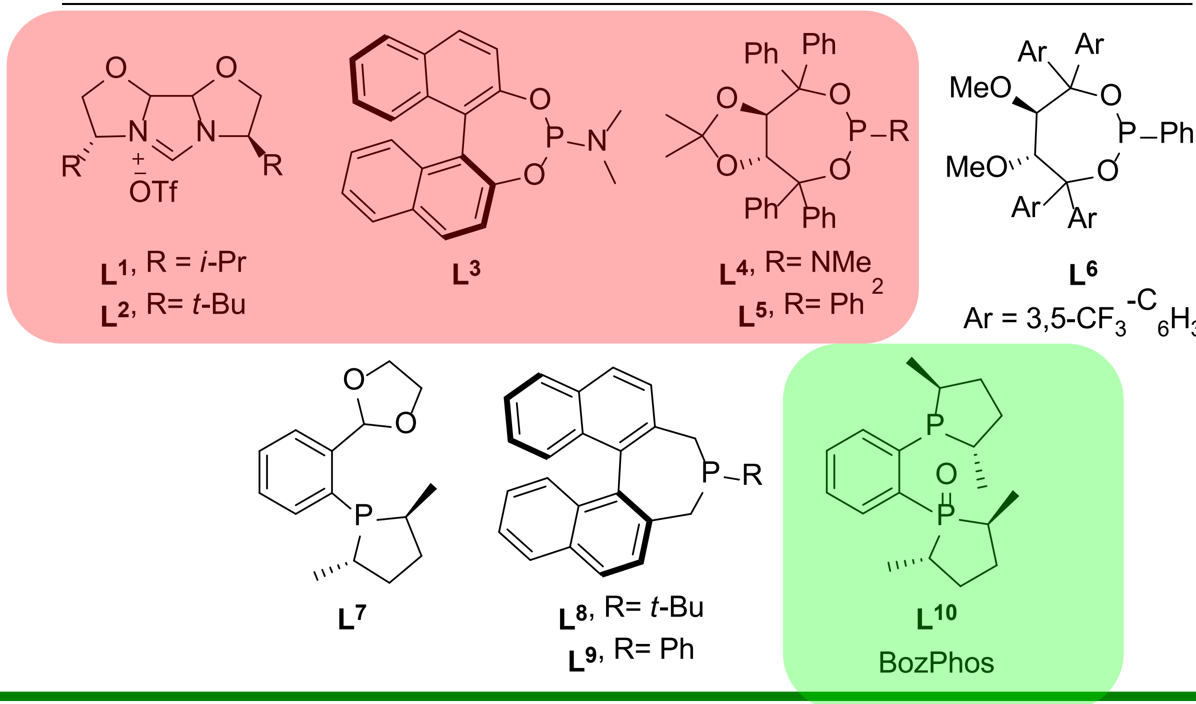
Prof. Olivier Baudoin
University of Basel



NIHAD

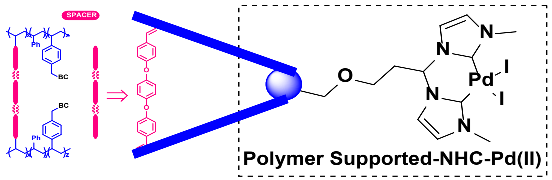
enantioselective C–H arylation

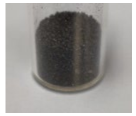




ChemSusChem 2023, 16, e202102736 hot topic C-H activation

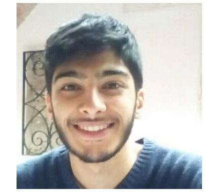
POLITAG carbene: heterogeneous NHC systems for C(sp3)–H activation





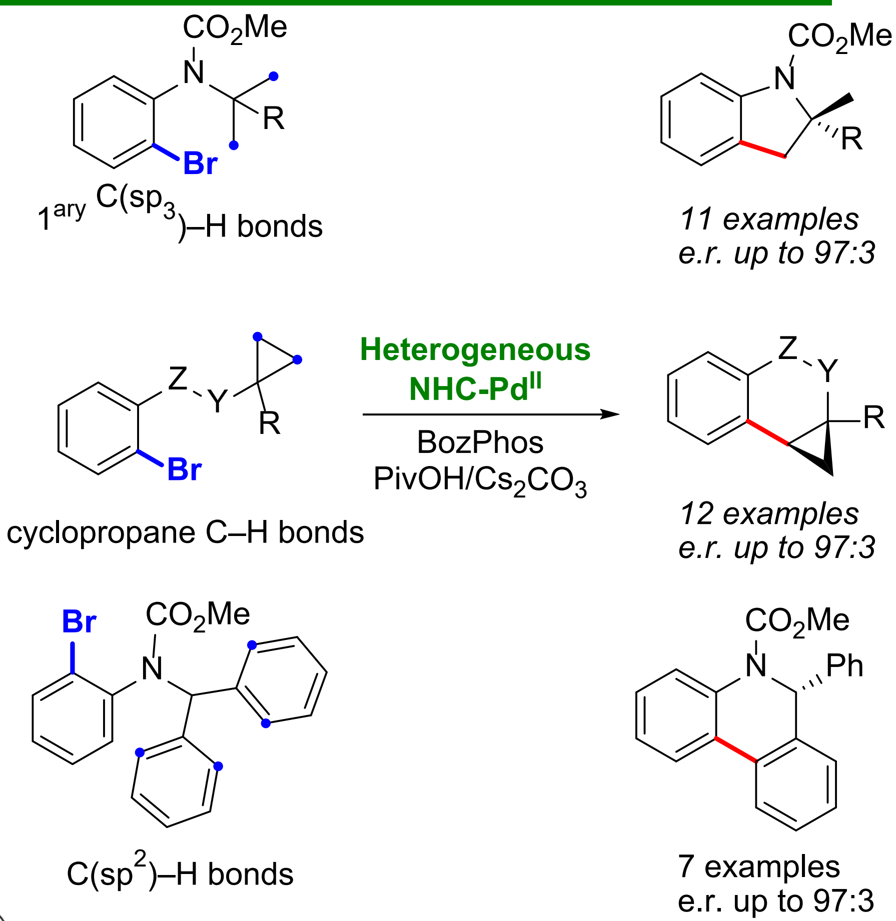
University of Basel

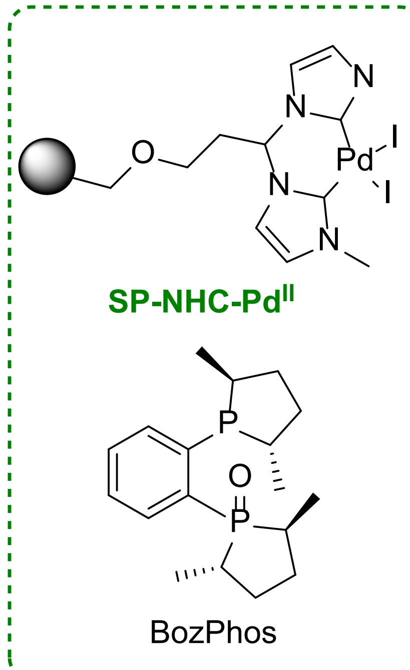
Prof. Olivier Baudoin
University of Basel



NIHAD

enantioselective C–H arylation





- *versatile chiral ligand*
- *recyclable heterogeneous catalyst*
- *high yields and enantioselectivities*

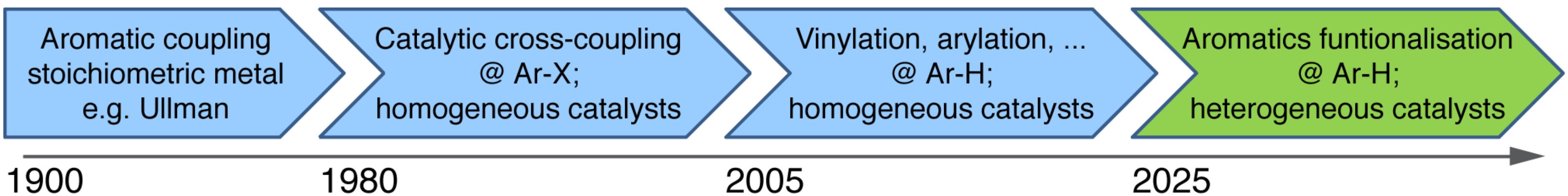
ChemSusChem 2023, 16, e202102736 hot topic C-H activation

Cross-Couplings / C-H functionalizations

Fundamental tools for the synthesis of Active Pharmaceutical Ingredients

H-CCAT

H-CCAT: **Solid Catalysts for activation of aromatic C-H bonds**



DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

Johnson & Johnson

JANSSEN
PHARMACEUTICA

JM
Johnson Matthey

ProfMOF

Axel'One

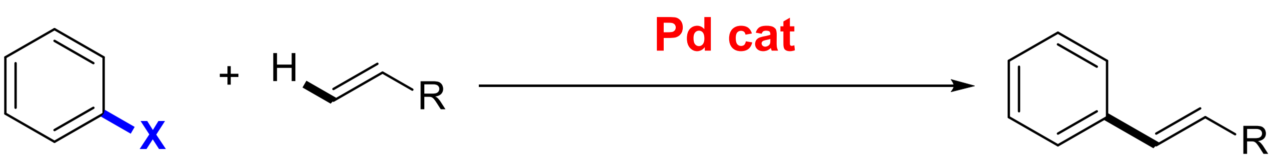
SiKÉMIA
materials surface functionalization

Heck-Mirozoki vs Fujiwara-Moritani reactions

Cross-couplings vs C–H functionalization

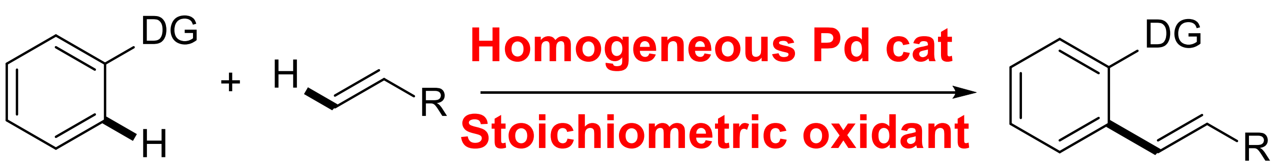
H-CCAT: **Solid Catalysts for activation of aromatic C-H bonds**

Heck-Mirozoki reaction (Heck alkenylation)



Fujiwara-Moritani Reaction

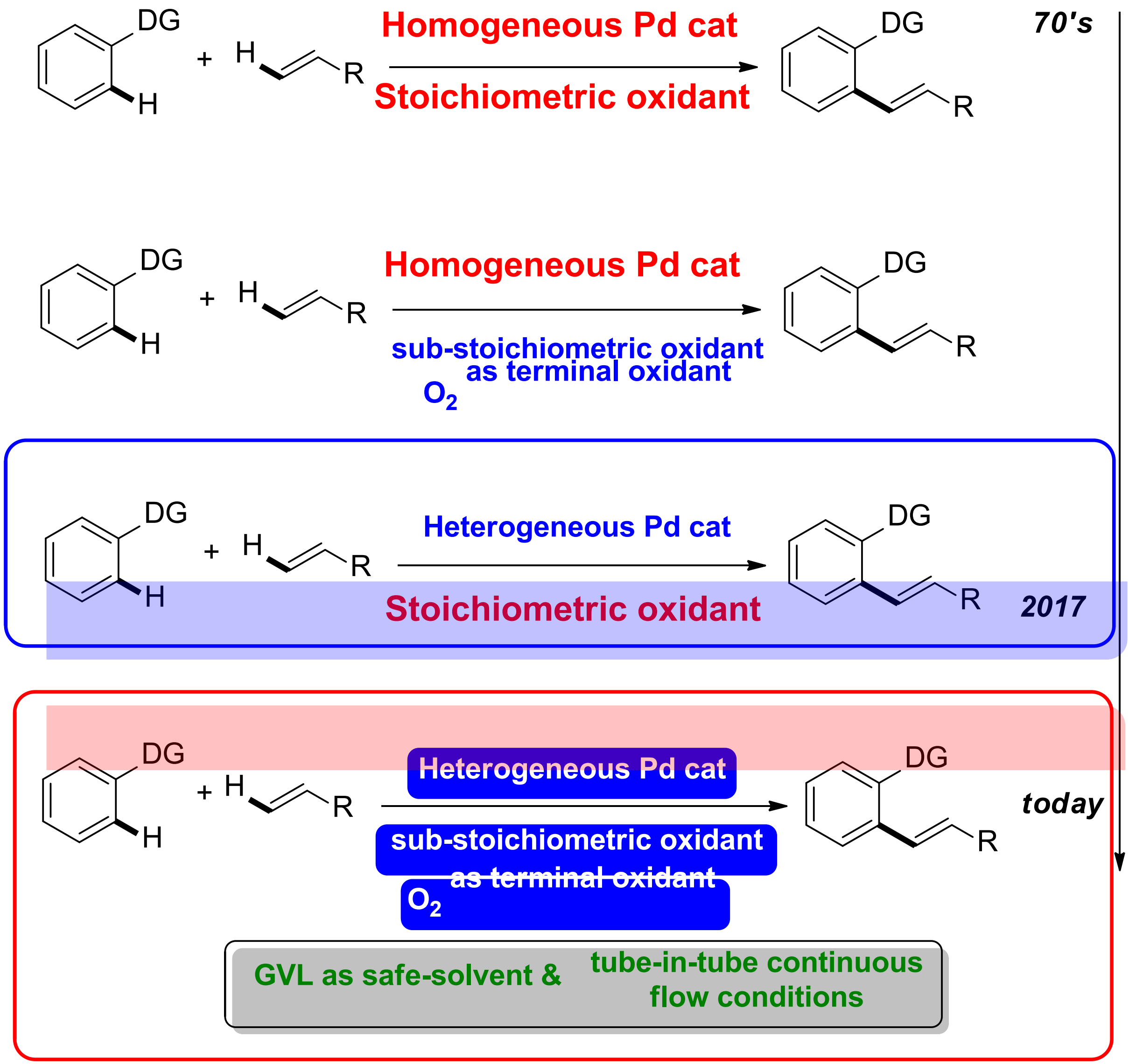
(C-H functionalization - Oxidative Heck alkenylation)



I. Moritani, Y. Fujiwara, *Tetrahedron Lett.*, 1967, 8, 111

Towards Aerobic Fujiwara-Moritani reaction

Previous work



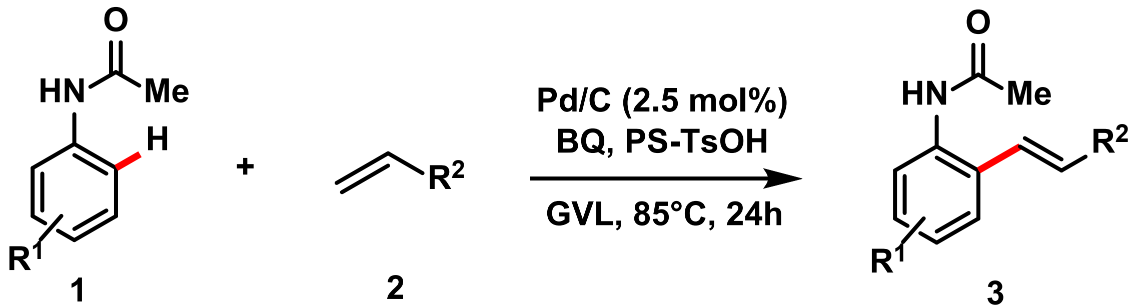
I. Moritani, Y. Fujiwara, *Tetrahedron Lett.*, 1967, 8, 111

Among others: P. W. N. M. van Leeuwen et al, JACS., 2002, 1586; K. Tanaka et al, Chem. Eur. J., 2015, 9053; C. Bolm et al , ANIE 2015, 7414; K. K. M. Hii et al, React. Chem. Eng., 2020, 1104

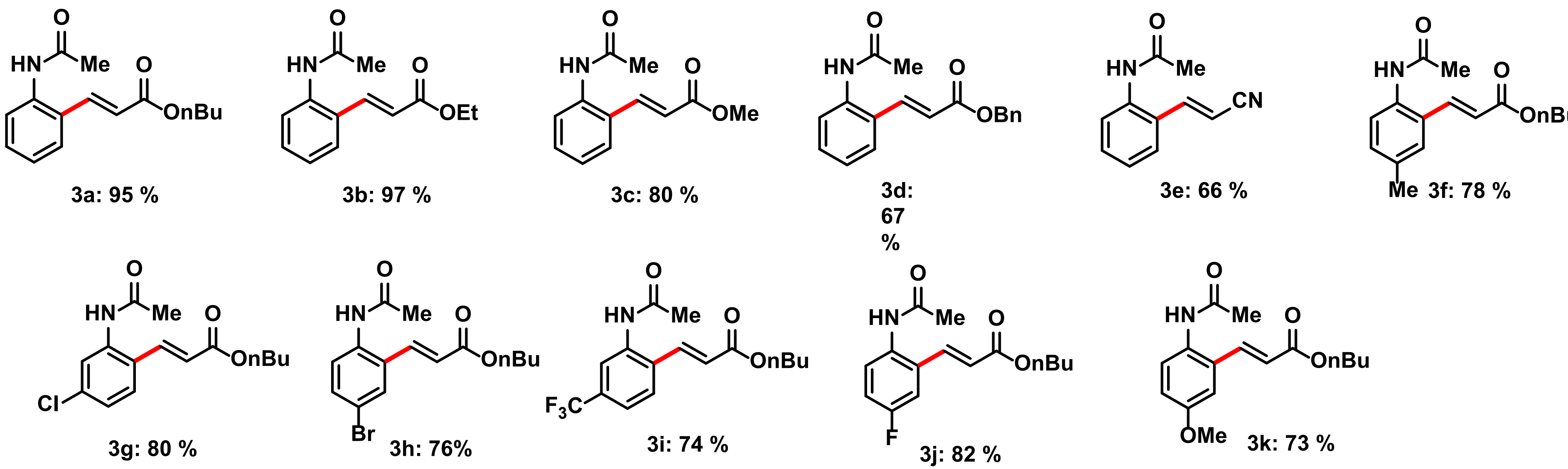
L. Vaccaro et al. Green Chem. 2017, *19*, 2510

GVL and heterogeneous catalysts in C–H activation processes

✓ Heterogeneous Palladium-Catalyzed Oxidative C–H Alkenylations… Fujiwara-Moritani reaction



FRANCESCO



Vaccaro et al Green Chem. 2017, *19*, 2510; HIGHLIGHTED in *SYNFACTS 2017 13(09) 1000*

GVL and heterogeneous catalysts in C–H activation processes

✓ Pd/C catalyzed Fujiwara-Moritani reaction

✓EXPERIMENTS SUGGEST THAT THE ACTIVE CATALYTIC SPECIES IS HETEROGENEOUS IN NATURE

➢ **Hot-filtration/mercury poisoning test** suggest a possible heterogeneous catalysis

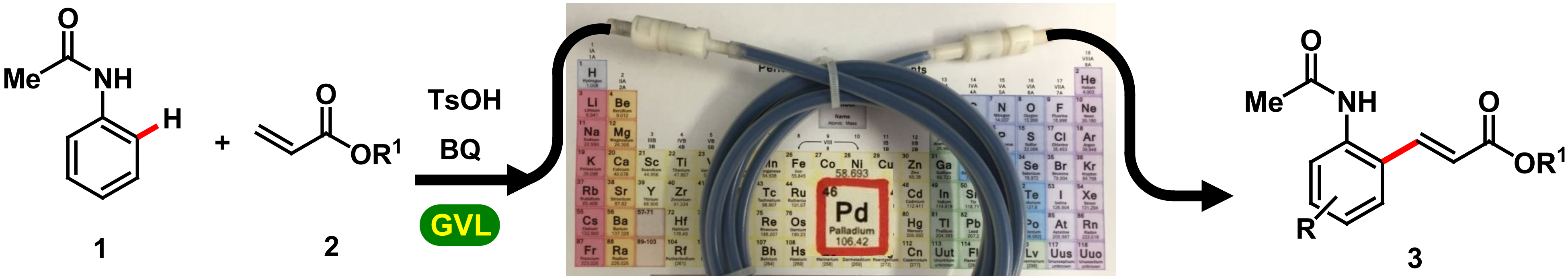
A "release and catch" mechanism is probably more likely, given the reaction conditions and the well-known mechanism of the FM reaction.

	Run 1	Run 2	Run 3	Run 4	Run 5
Yield	95%	95%	94%	93%	87%
Pd leaching (ppm)	4.0	3.7	3.8	4.1	4.2

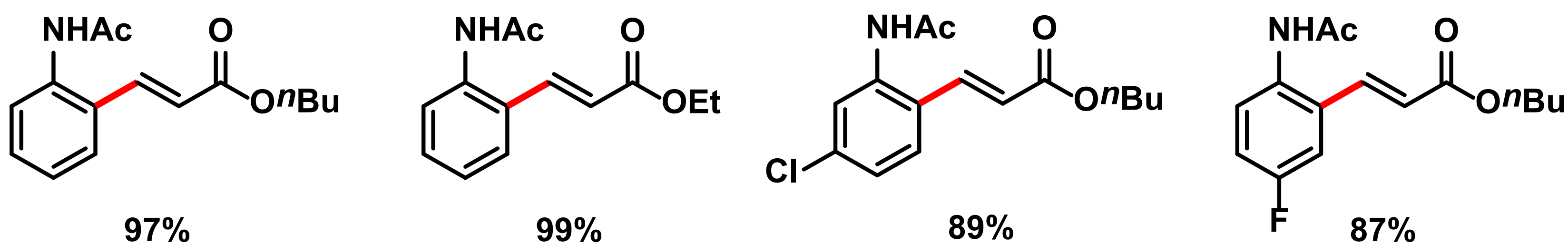
Vaccaro et al Green Chem. 2017, *19*, 2510; HIGHLIGHTED in *SYNFACTS 2017 13(09) 1000*

GVL and heterogeneous catalysts in C–H activation processes

✓ Heterogeneous Palladium-Catalyzed Fujiwara-Moritani reaction in Continuous-Flow

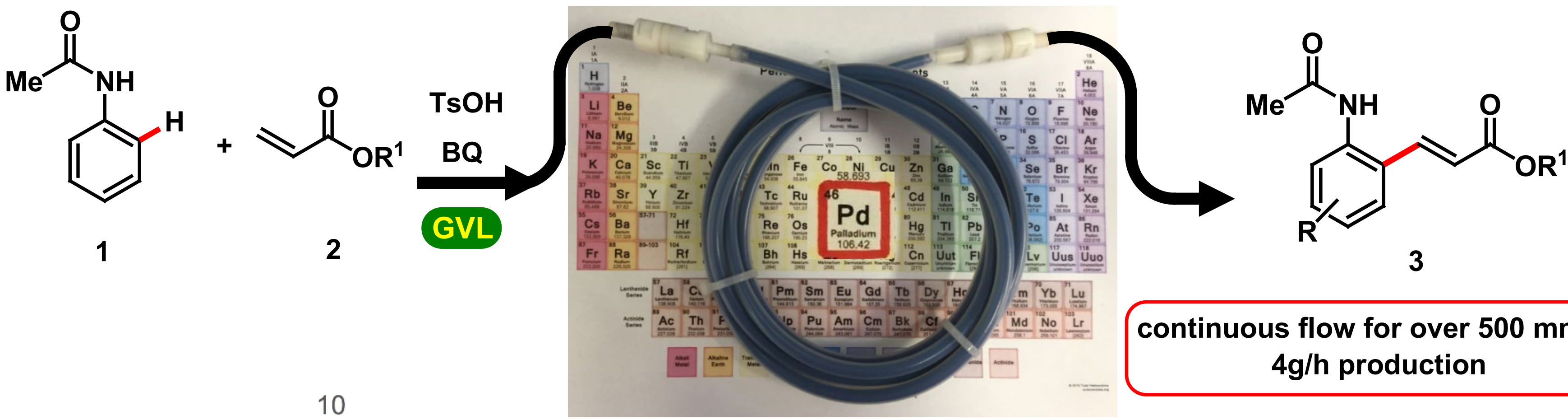


continuous flow for over 500 mmol
4g/h production

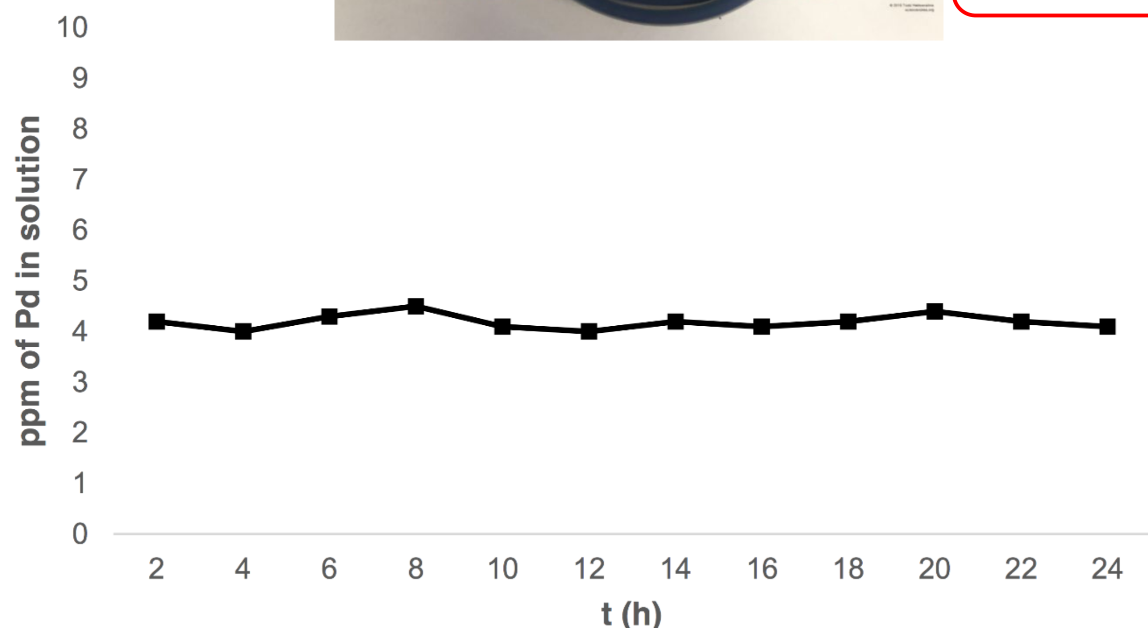


GVL and heterogeneous catalysts in C–H activation processes

✓ Heterogeneous Palladium-Catalyzed Fujiwara-Moritani reaction in Continuous-Flow



continuous flow for over 500 mmol
4g/h production

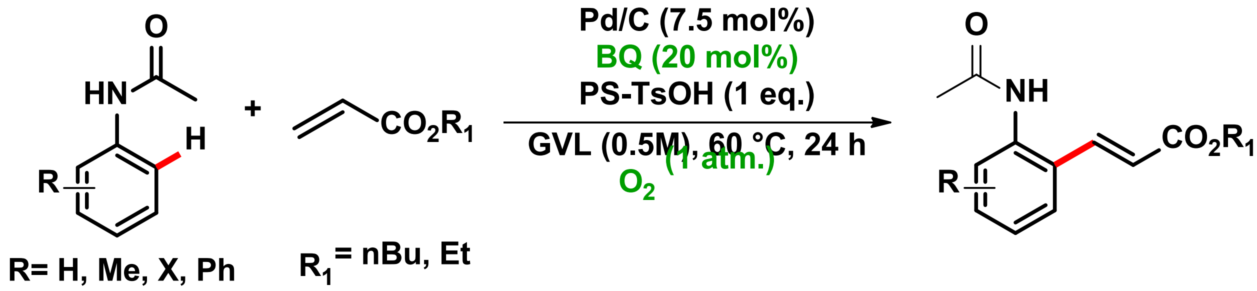


Vaccaro et al Green Chem. 2017, *19*, 2510; HIGHLIGHTED in *SYNFACTS 2017 13(09) 1000*

Towards Aerobic Fujiwara-Moritani reaction

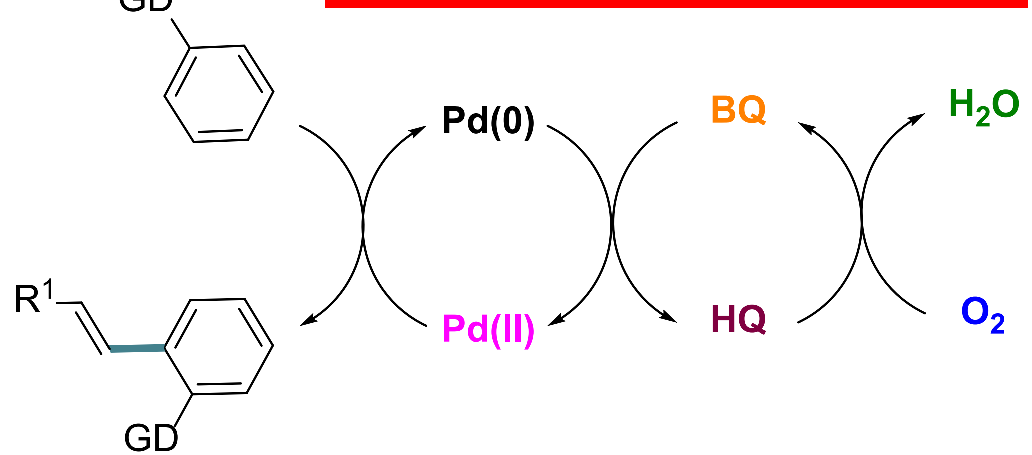
✓ Pd/C-Catalyzed Aerobic Oxidative ortho-C-H olefination of anilides in biomass derived γ-valerolactone

O_2



IOANNIS

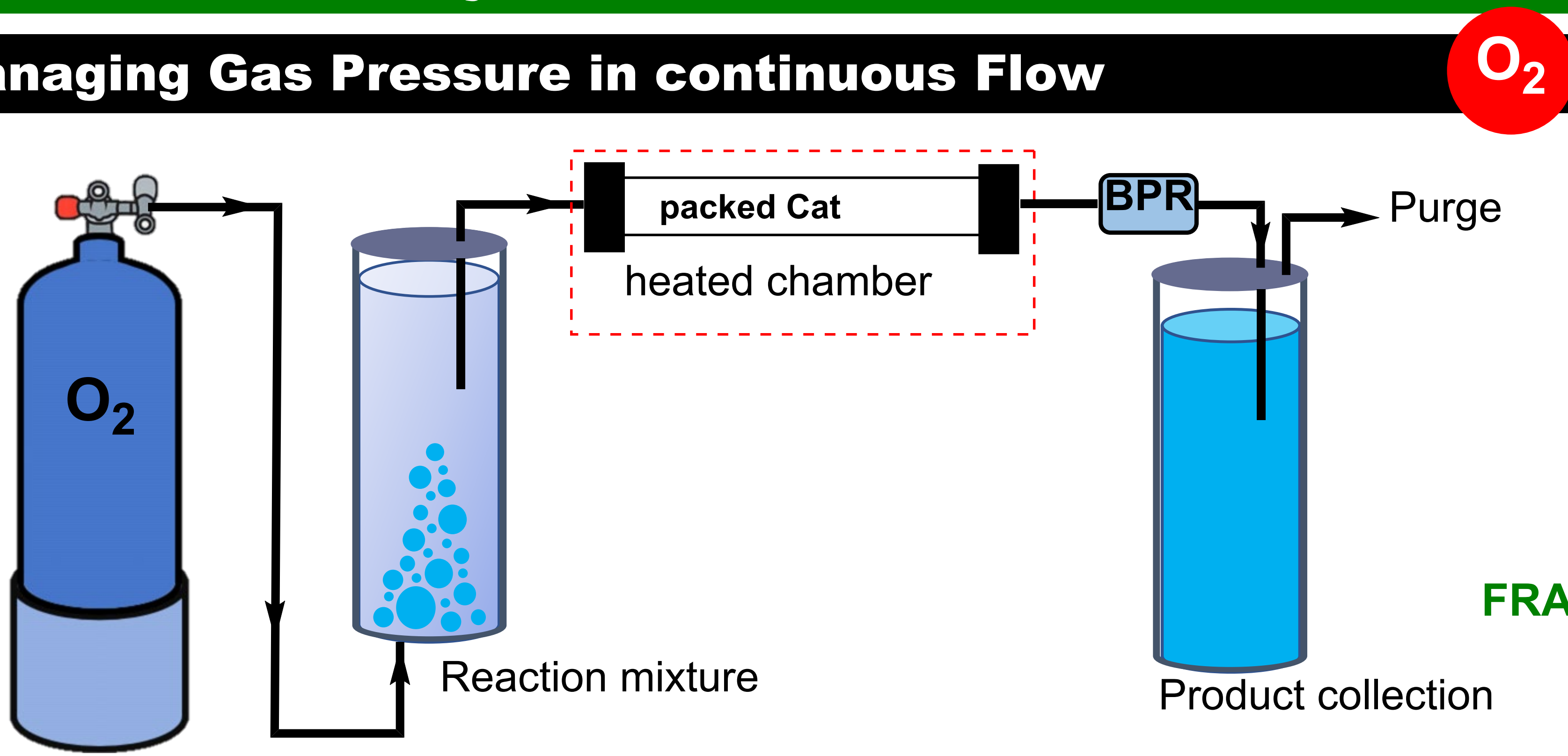
Aimig at the use of O_2 as terminal oxidant



Green S.O.C. Perugia

Towards Aerobic Fujiwara-Moritani reaction

Managing Gas Pressure in continuous Flow



IOANNIS

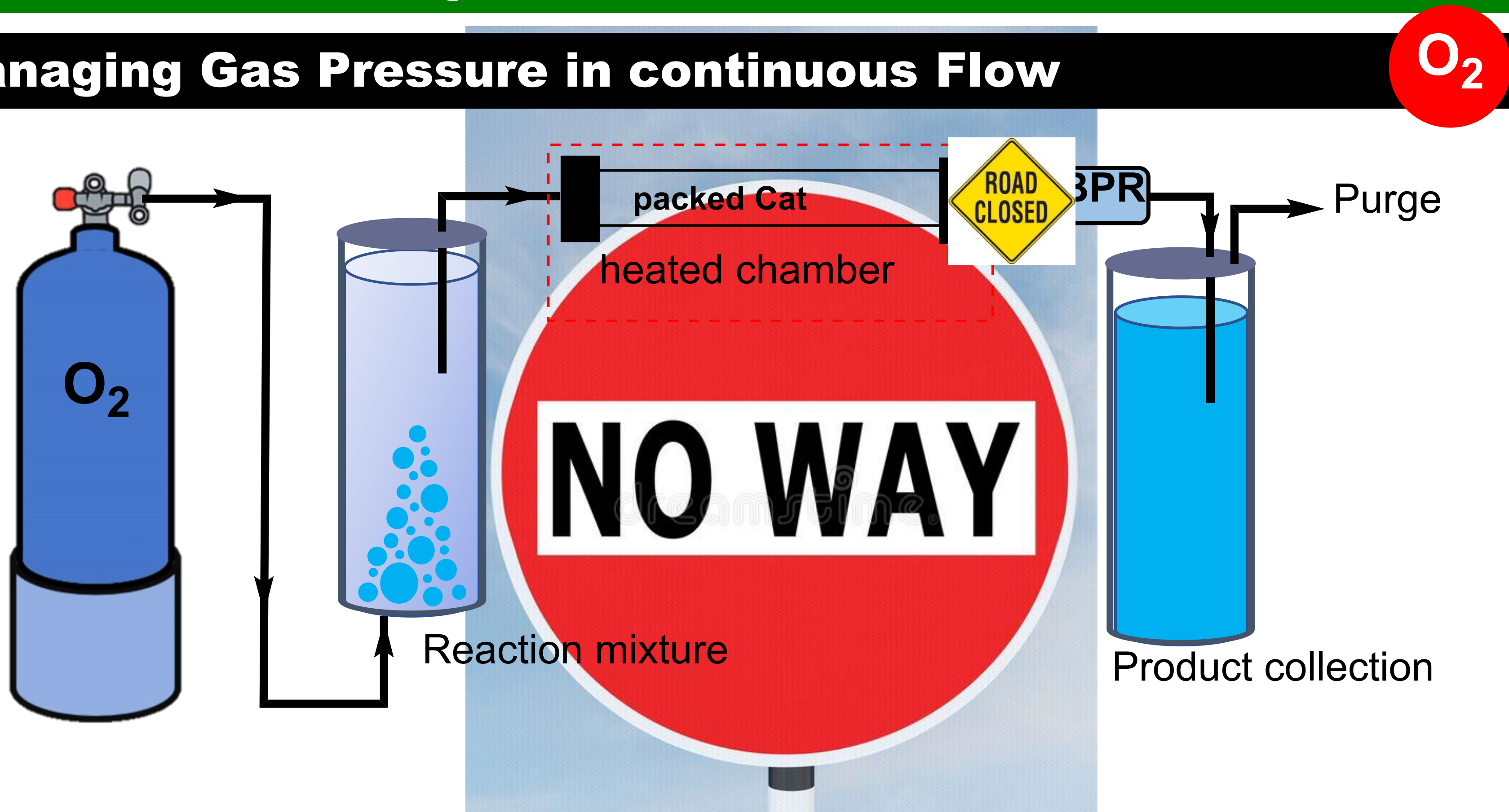
FRANCESCO M

Direct Oxygen flow using a packed heterogeneous catalyst was unsaccessful in the Fujiwara-Moritani Reaction

Very poor conversions when using 20 mol% of benzoquininone and 1-5 bar of oxygen

Towards Aerobic Fujiwara-Moritani reaction

Managing Gas Pressure in continuous Flow



IOANNIS

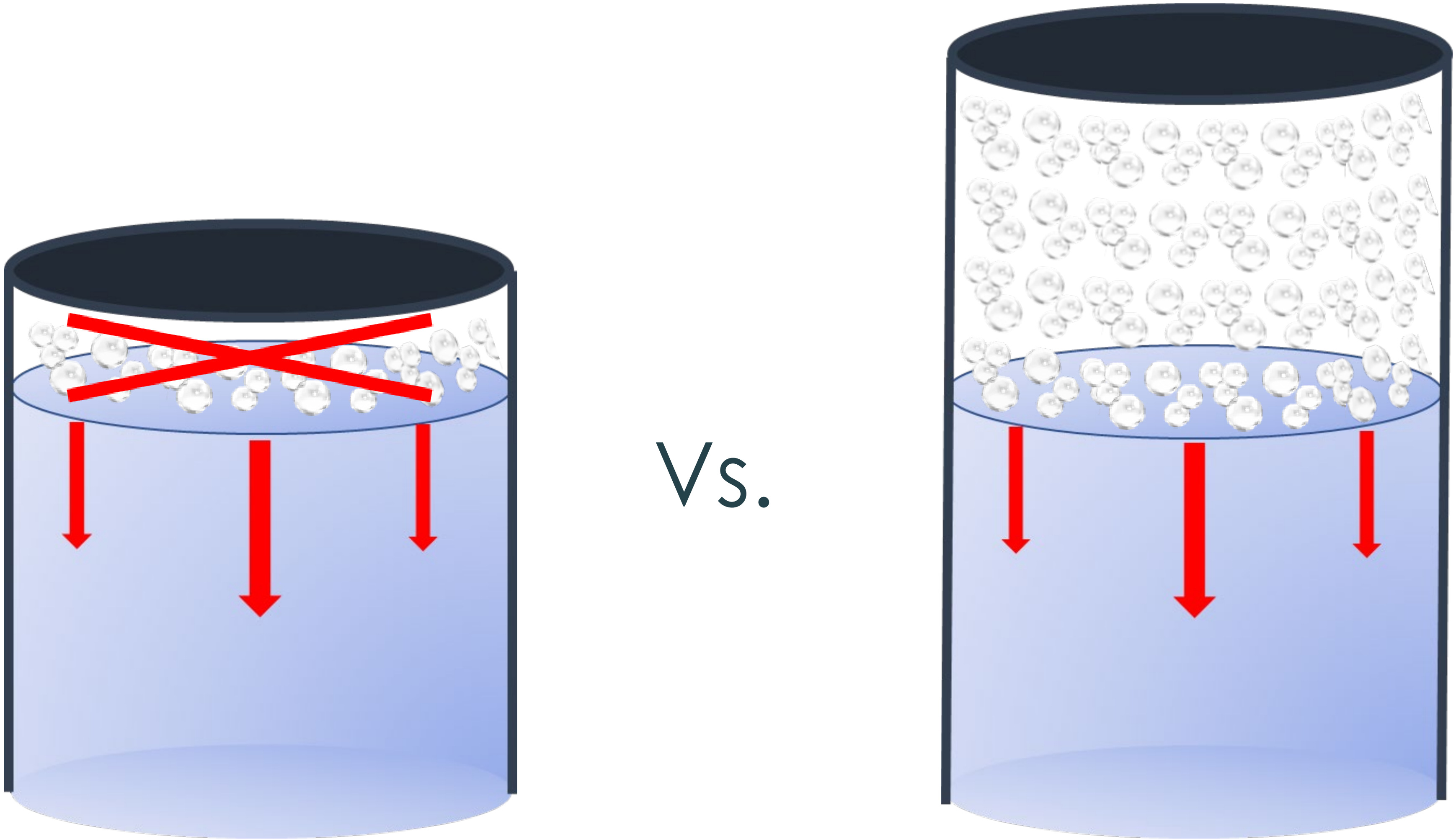
Direct Oxygen flow using a packed heterogeneous catalyst was unsaccessful in the Fujiwara-Moritani Reaction

Very poor conversions when using 20 mol% of benzoquininone and 1-5 bar of oxygen

Green Chem., 2021, 23, 6576–6582

Towards Aerobic Fujiwara-Moritani reaction

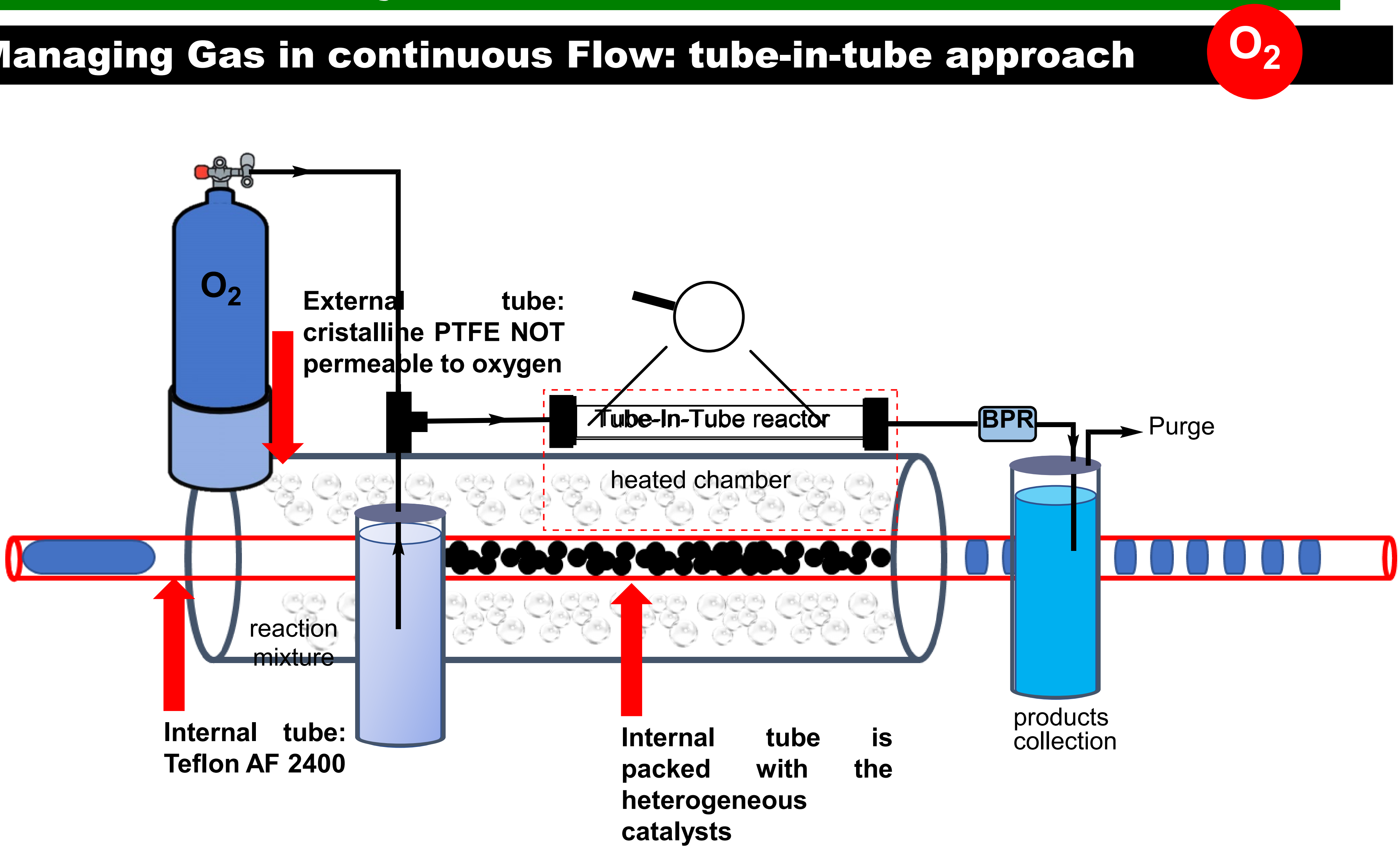
Managing Gas in continuous Flow: head space



Better results with larger head space

Towards Aerobic Fujiwara-Moritani reaction

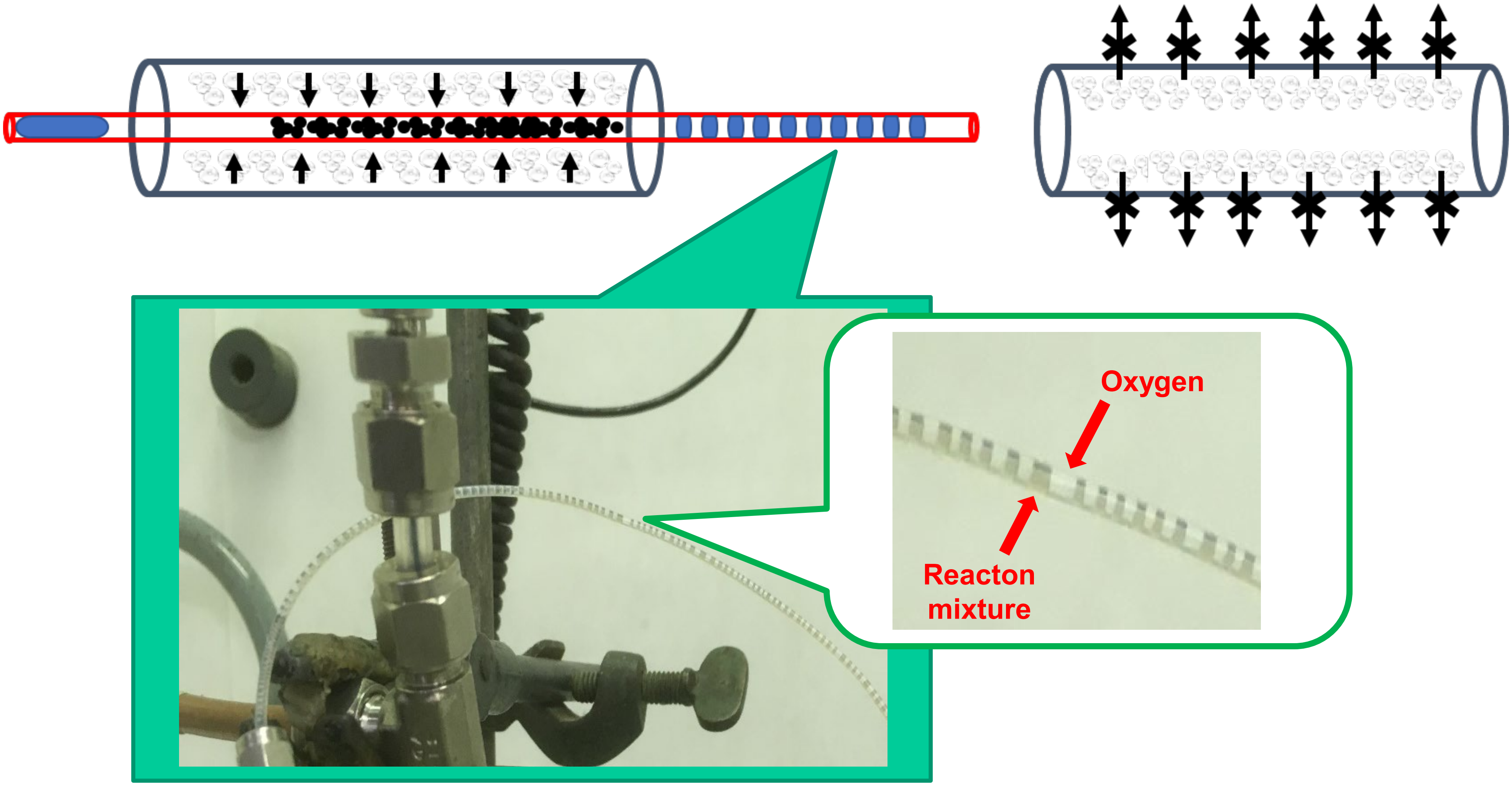
Managing Gas in continuous Flow: tube-in-tube approach



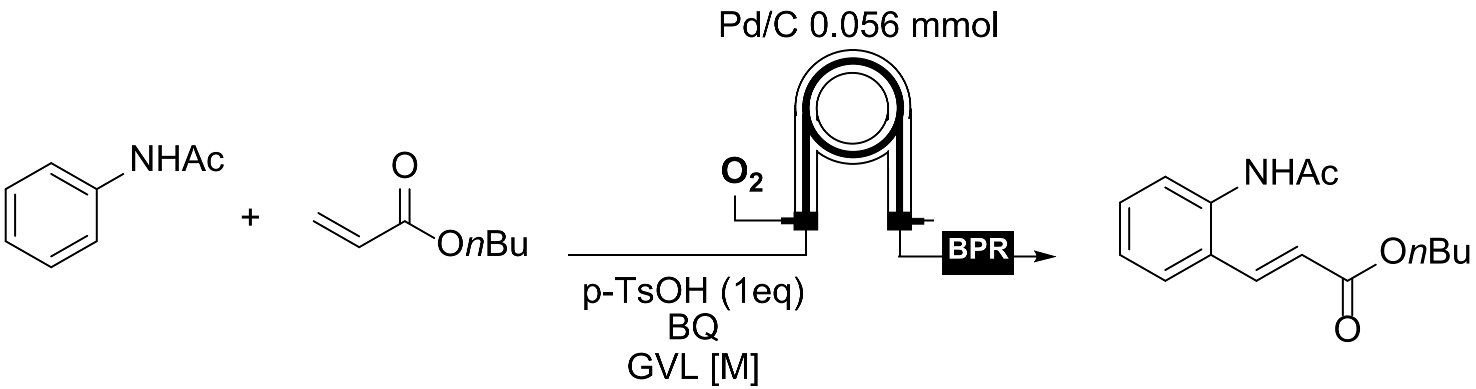
Towards Aerobic Fujiwara-Moritani reaction

Managing Gas in continuous Flow: tube-in-tube approach

O_2



Aerobic Fujiwara-Moritani reaction



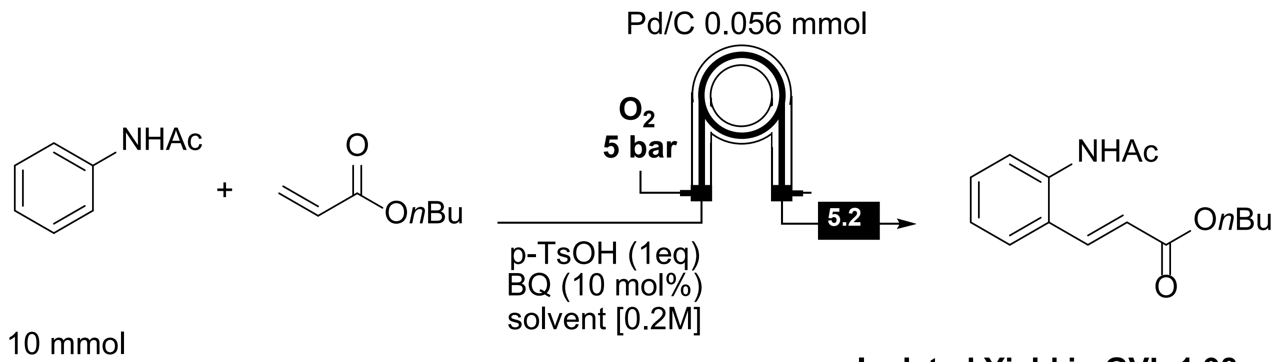
Entry	BQ (mol %)	Residence time (min)	C (%)
1	**10**	**200**	**77 (75)**
2	**7.5**	**200**	**77 (74)**
4	**5**	**200**	**75 (72)**
6	2.5	200	47 (44)
8	0	200	20 (17)

Isolated yields in parentheses

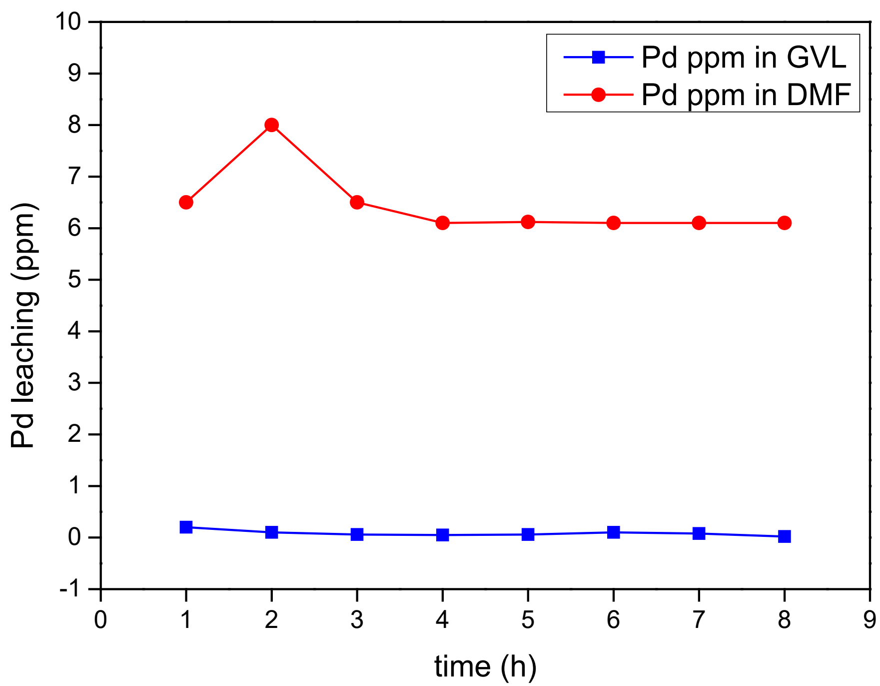
Towards Aerobic Fujiwara-Moritani reaction

Managing Gas in continuous Flow: tube-in-tube approach

O_2



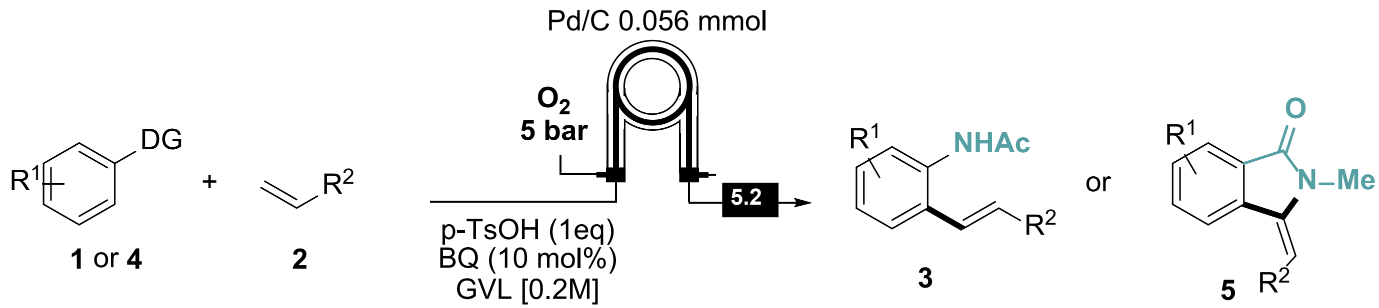
Isolated Yield in GVL 1.98 g (75 %)
Isolated Yield in DMF 1.34 g (51%)



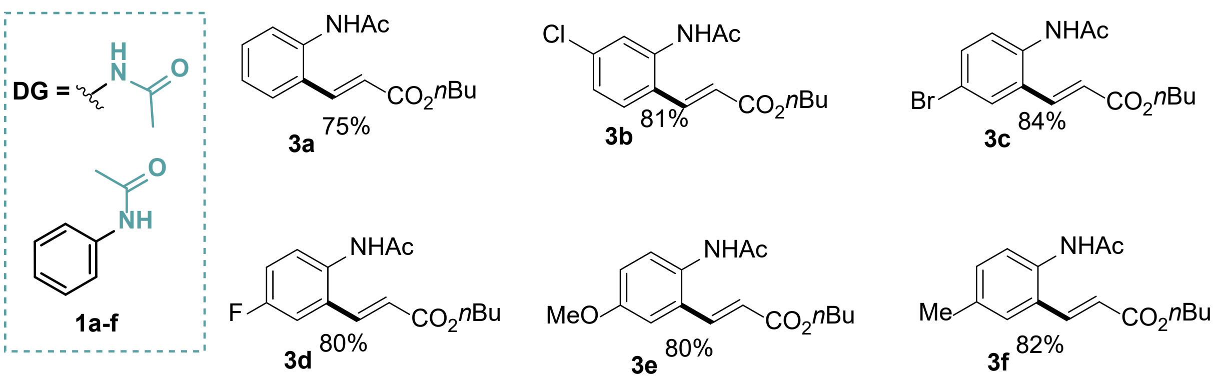
Ca. 6 ppm in DMF

0.2–0.02 ppm in GVL

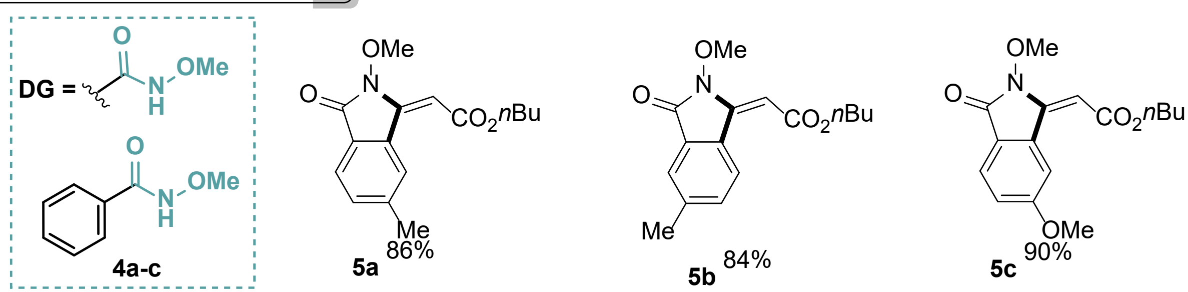
Aerobic Fujiwara-Moritani reaction



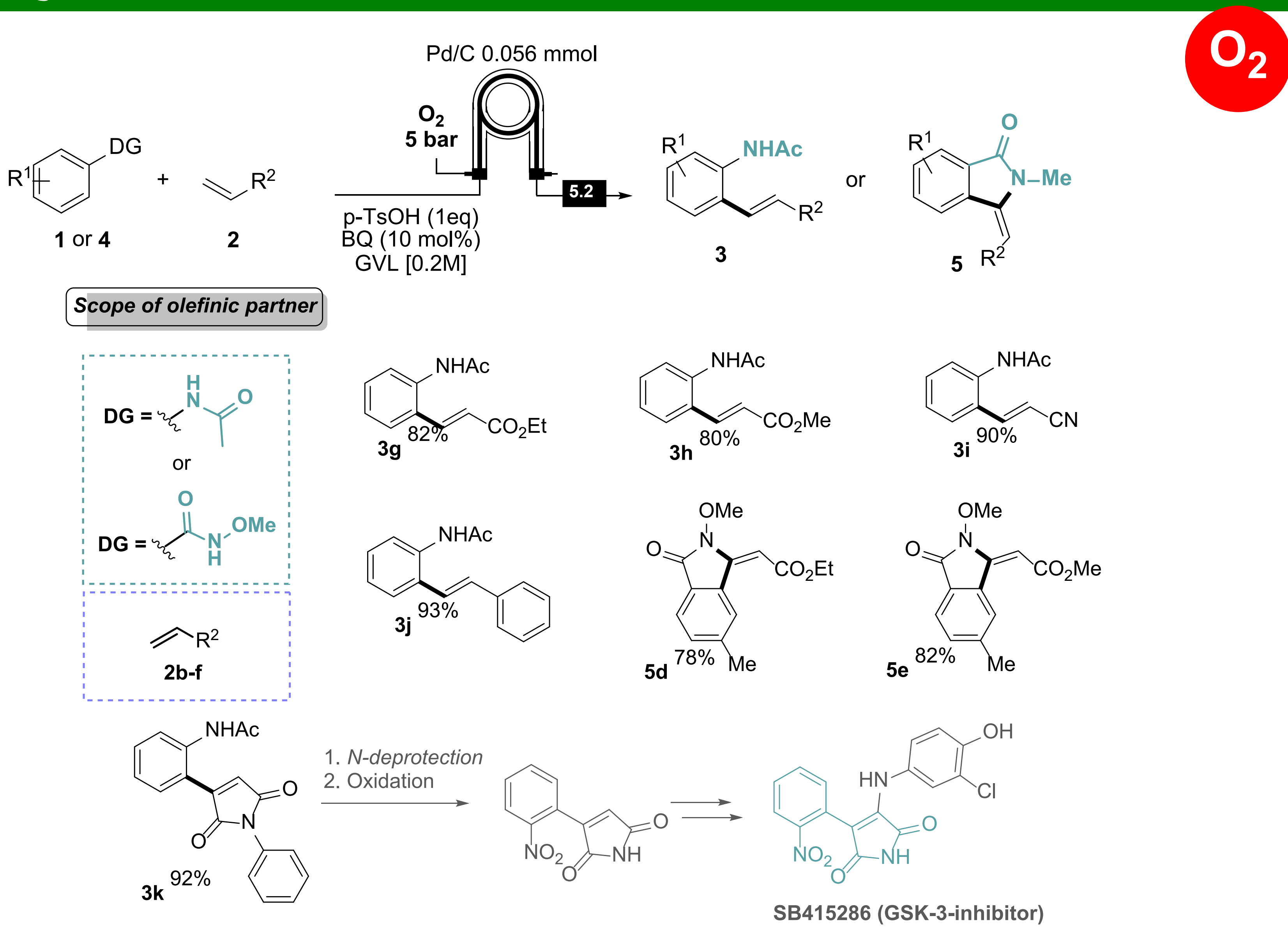
Scope of acetanilides



Scope of N-methoxy benzamides

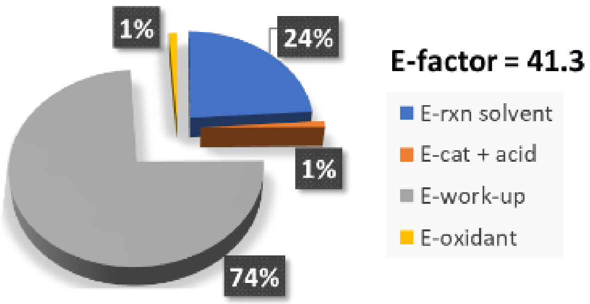


Aerobic Fujiwara-Moritani reaction

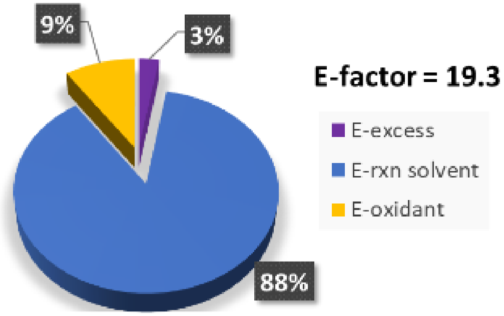


Fujiwara-Moritani reaction comparison with known protocols

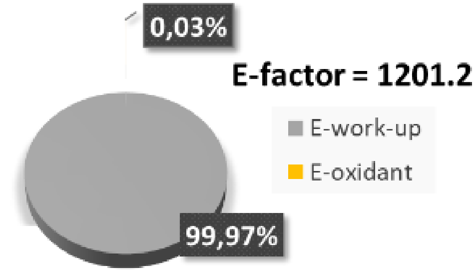
J. Am. Chem. Soc. 2002, **124**, 1586-1587



Org. Lett., **12**, 2010, 1972-1975



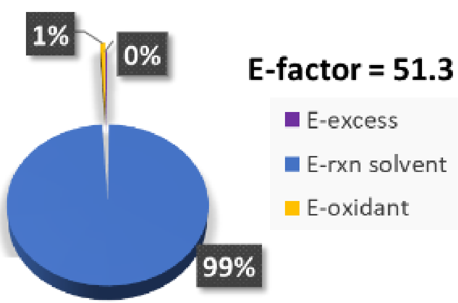
Angew. Chem. Int. Ed. 2015, **54**, 7414 –7417



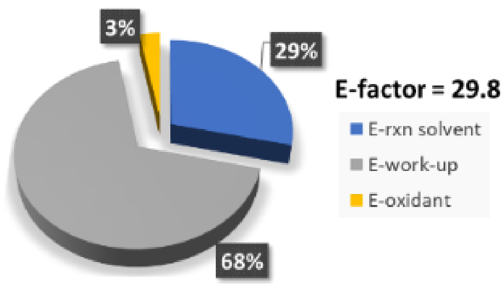
Our work

E-factor: 3.0

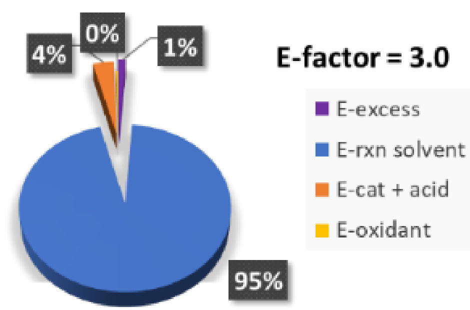
React. Chem. Eng., 2020, **5**, 1104-1111



Green Chem., 2017, **19**, 2510–2514 ***(Flow)***



This work



Our protocol in flow using stoichiometric benzoquinone

Our protocol in flow using Oxygen and 10% of benzoquinone

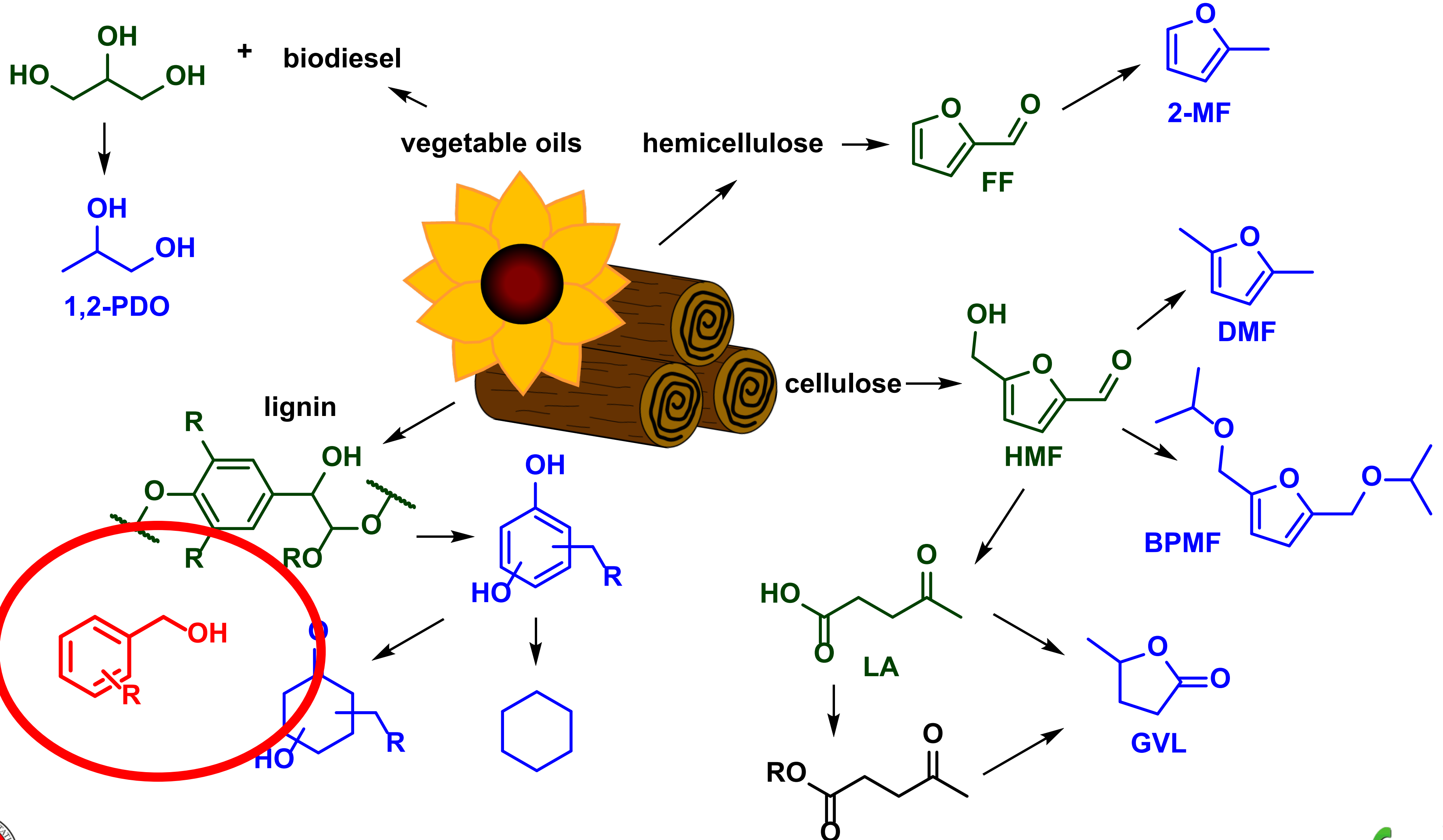
Fujiwara-Moritani reaction comparison with known protocols

Ref	Yield	RME	MRP
J. Am. Chem. Soc., 2002, 124, 1586.	85%	2.4%	0.027
Org. Lett., 2010, 12, 1972;	85%	4.9%	0.083
J. Am. Chem. Soc., 2010, 132, 9982	98%	5.7%	0.071
J. Am. Chem. Soc., 2010, 132, 9982 under air	97%	6.1%	0.077
Adv. Synth. Catal., 2011, 353, 2988–2998	76%	0.6%	0.012
Chem. Eur. J., 2015, 21, 9053	82%	4.1%	0.084
Angew. Chem., Int. Ed., 2015, 54, 7414	71%	0.1%	0.001
React. Chem. Eng., 2020, 5, 1104	91%	1.9%	0.023
Tetrahedron 2018, 74, 3879	80%	0.1%	0.002
OUR Green Chem., 2017, 19, 2510 BATCH	95%	2.5%	0.027
OUR Green Chem., 2017, 19, 2510, FLOW	97%	3.2%	0.035
OUR Oxygen TUBE-IN-TUBE FLOW	75%	25.8%	0.428

RME = Reaction Mass Efficiency; MRP: Mass Recovery Parameter

✓Biomass upgrading – hydrogenation/oxidation reactions

N_2 O_2 H_2



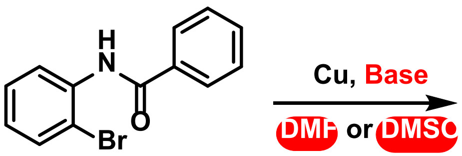
L. Vaccaro et al. *ACS Sustainable Chem. Eng.* **2021**, *9*, 9604−9624

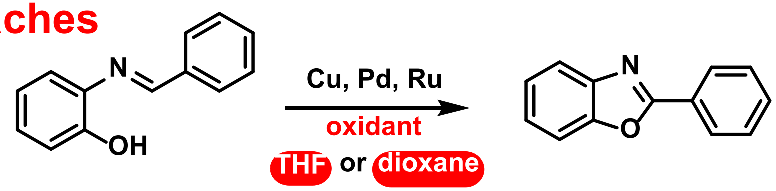
Oxidative C–H activation in Continuous Flow

Synthesis of 2-aryl benzoxazoles

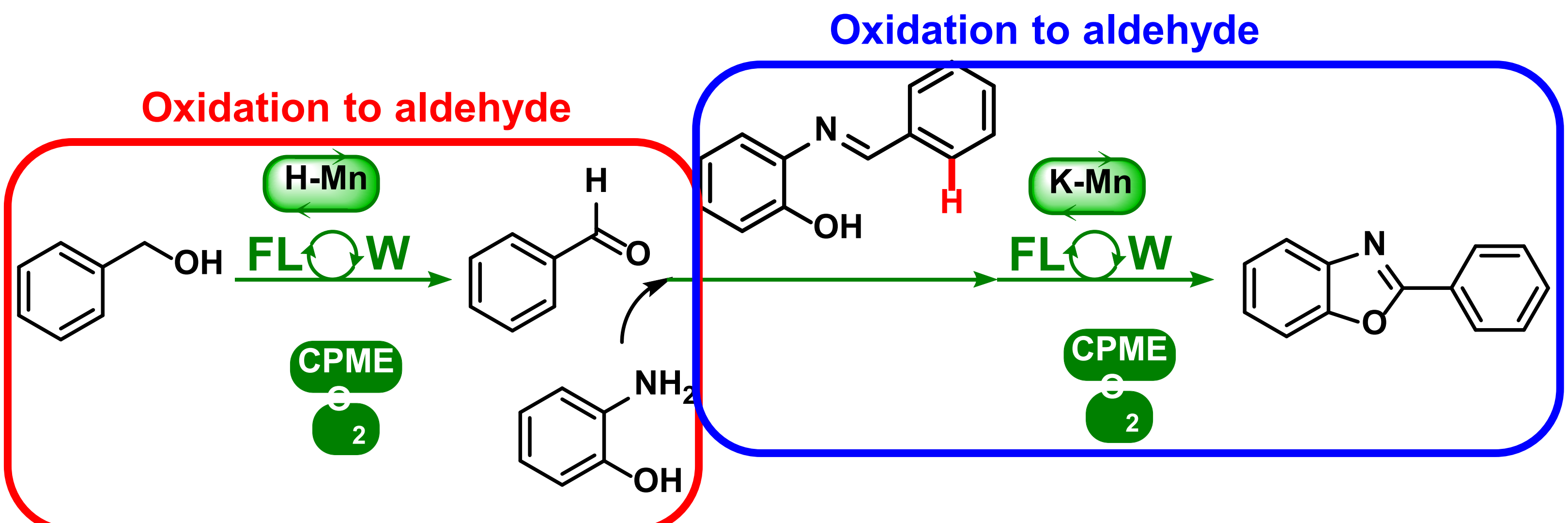
N_2 O_2

Literature approaches



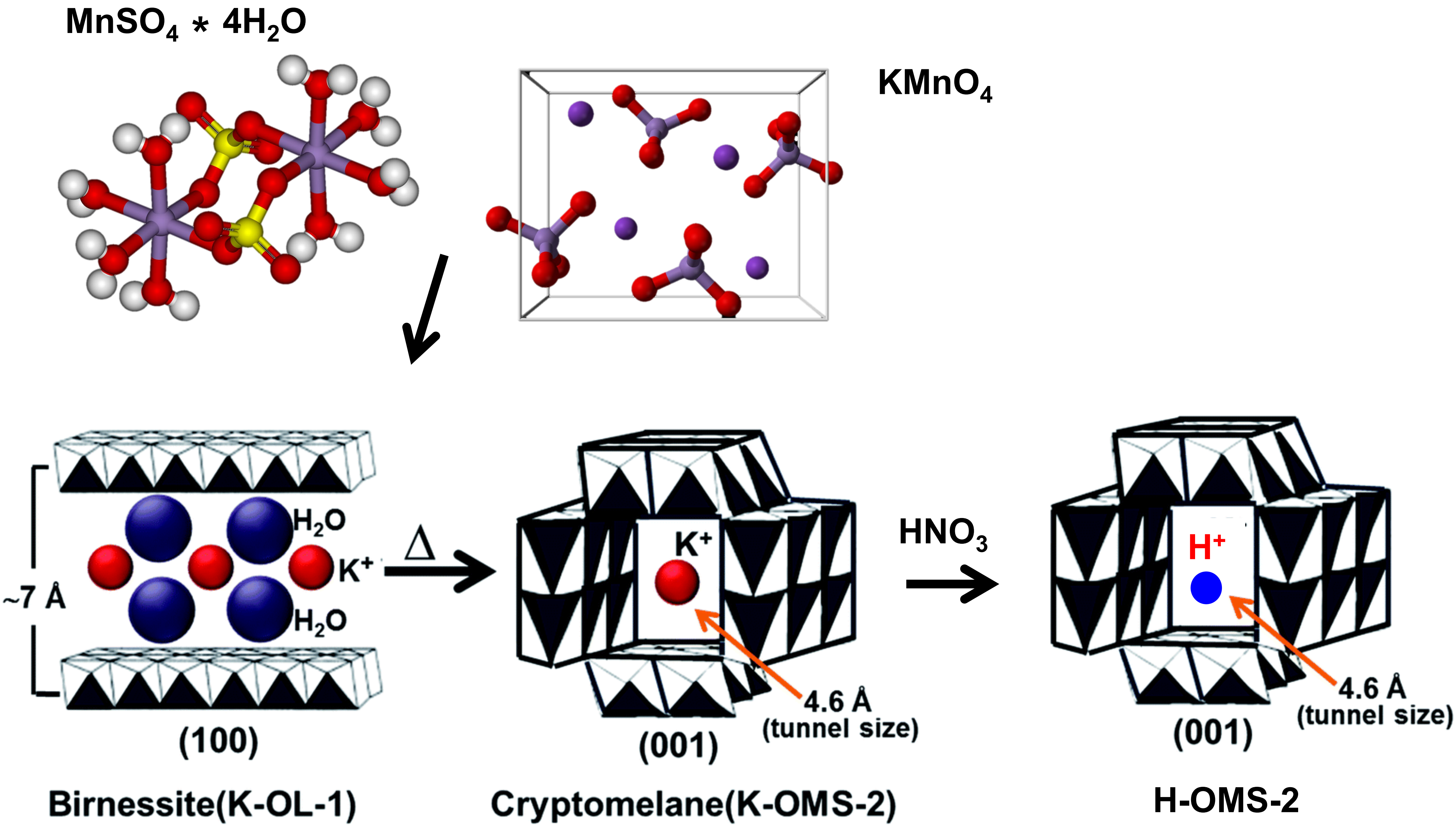


- Use of halides leading to salt waste
- Generally toxic solvents used as reaction medium
- Dangerous peroxides from ether/oxidant mix



- Recoverable heterogeneous Mn-catalysts
- CPME as peroxide stable solvent
- low E-factor
- continuous flow procedure

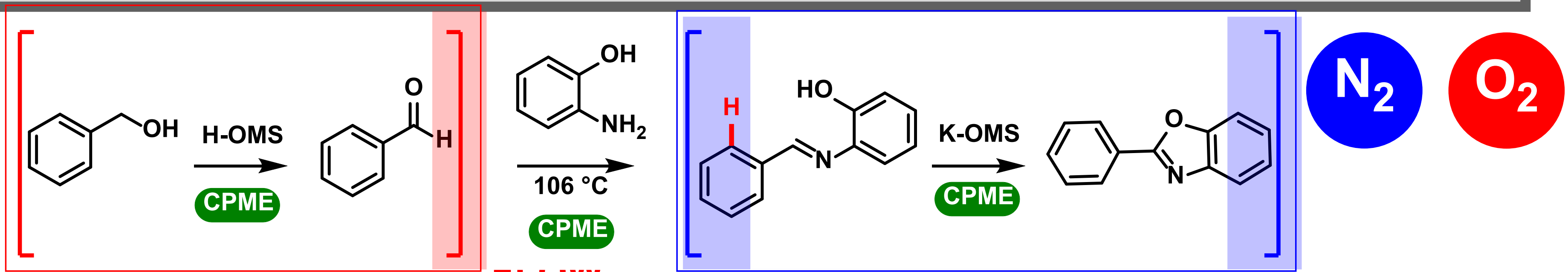
Heterogeneous Manganese catalytic systems OMS



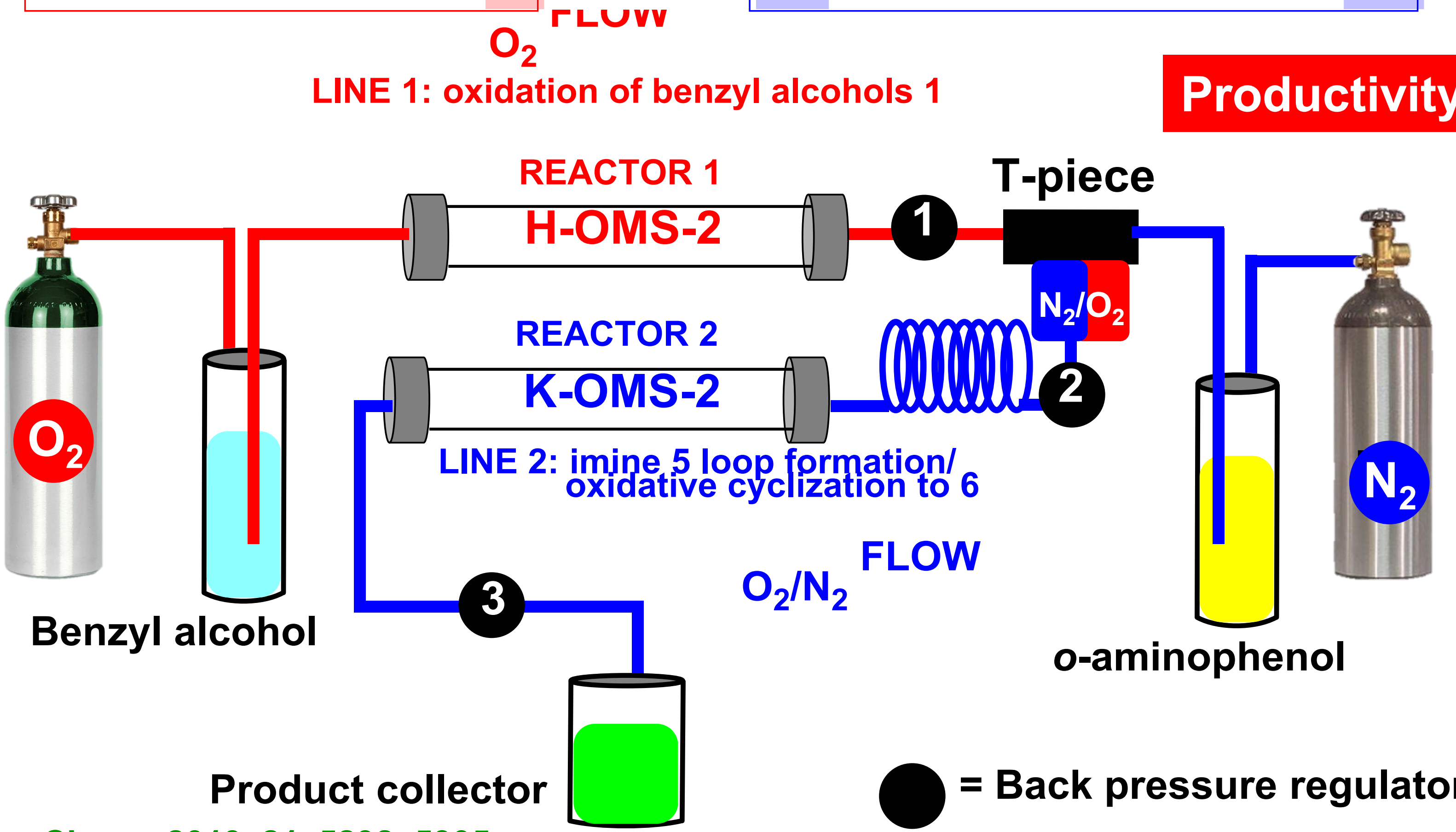
Suib S. L., et al
Angew. Chem. 2001, *113* 4410-4413; *J. Phys. Chem. C* 2008, *112*, 6786−6793; *Acc. Chem. Res.* 2008, *41*, 479−487.

Oxidative C–H activation in Continuous Flow

Pump-free continuous-flow synthesis of 2-aryl benzoxazoles



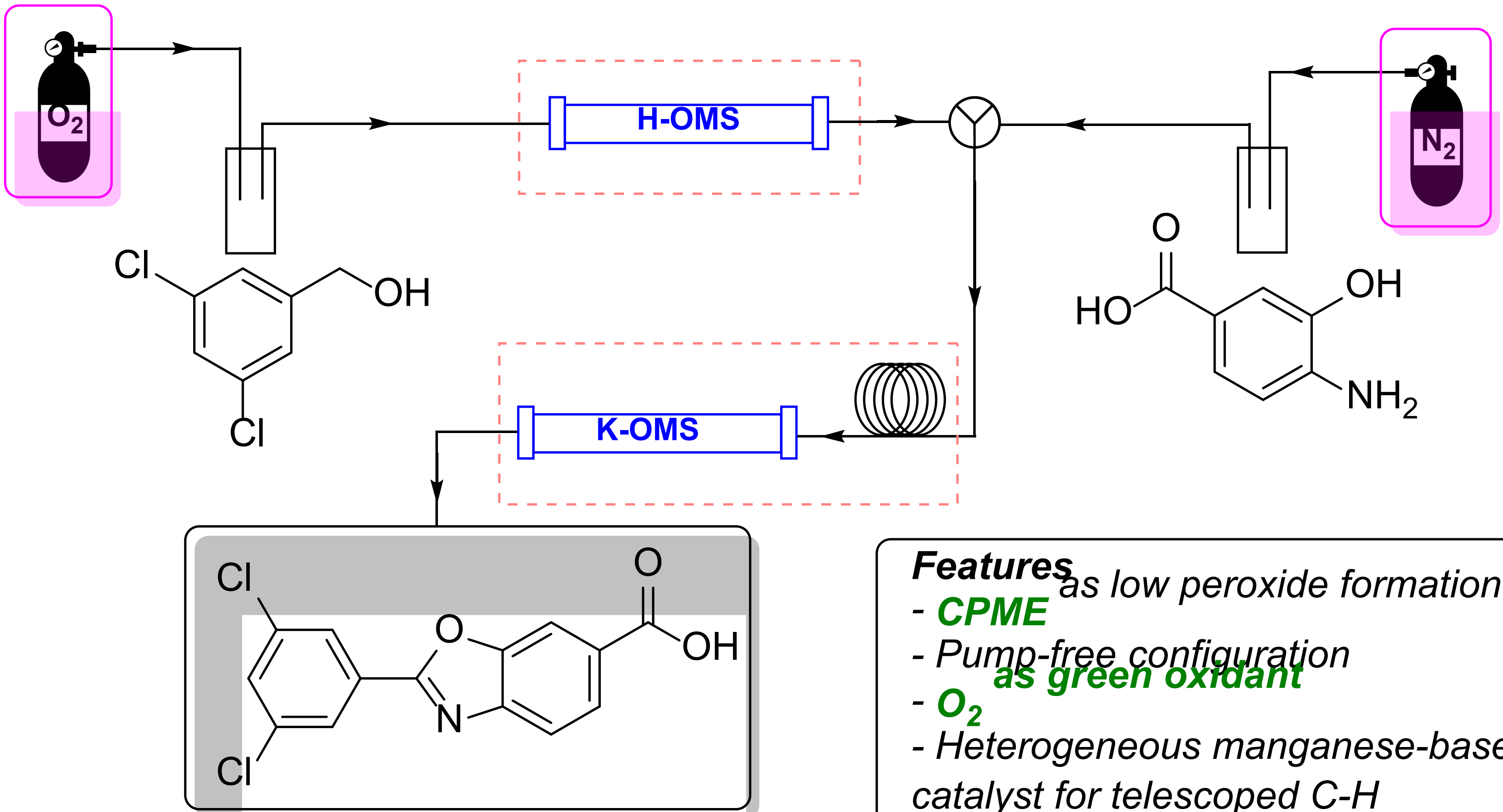
Productivity ca. 3 g/h



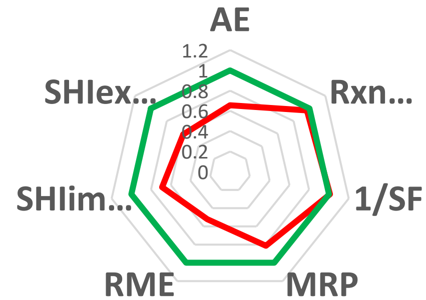
Oxidative C–H activation in Continuous Flow

Synthesis of 2-aryl benzoxazoles

N_2 O_2



tafamidis 92%



Features

- ***CPME*** *as low peroxide formation solvent*
- *Pump-free configuration*
- ***O_2*** ***as green oxidant***
- *Heterogeneous manganese-based catalyst for telescoped C-H functionalization*
- ***low E-factor***

(4.4) Tafamidis production

Oxidative C–H activation in Continuous Flow

Pump-free continuous-flow synthesis of 2-aryl benzoxazoles

Life cycle assessment of multistep benzoxazoles synthesis: from batch to waste-minimised continuous flow systems

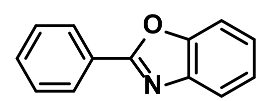
N_2 O_2

Jose Luis Osorio Osorio Tejada, Francesco Ferlin, Luigi Vaccaro and Volker Hessel

BATCH APPROACHES
- oxidative cyclization
- condensation/cyclization
- dehydrogenative coupling
- arylation of benzoxazoles

VS →

Continuous Flow Process

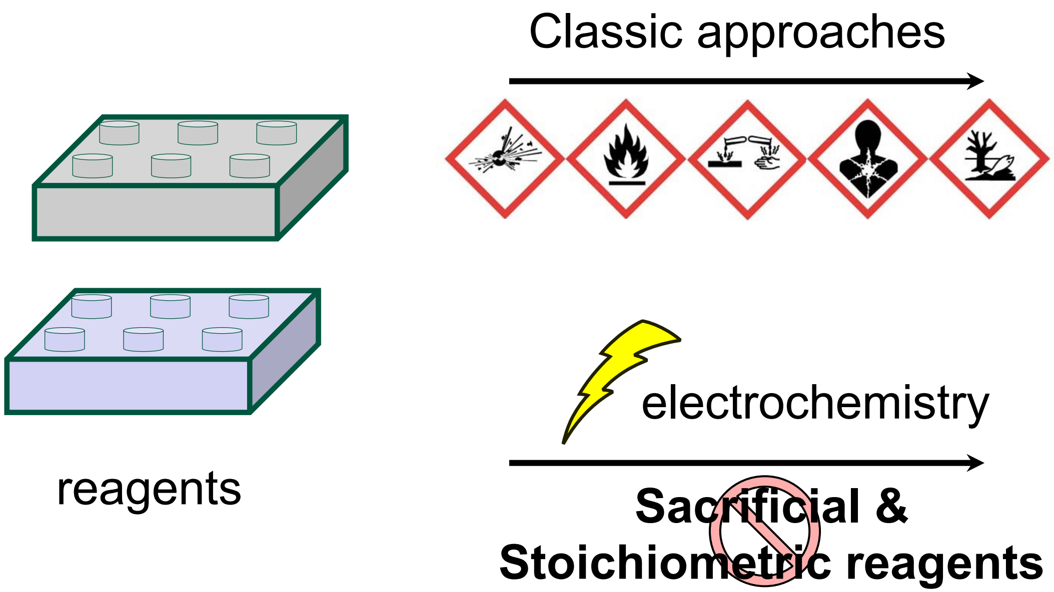


Green Chemistry, 2022, 24, 325-337

Electrosynthesis

Electrochemistry represents a valid promising synthetic methodology

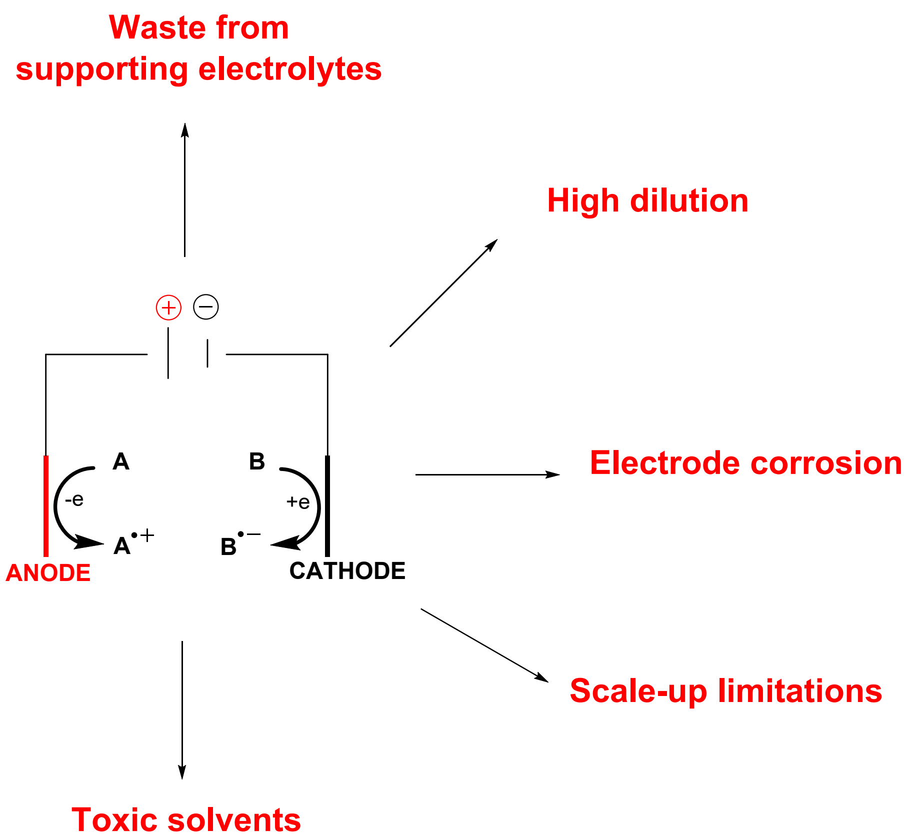
A promising alternative to organic oxidants



With an electron current as a substitute for the more classic "redox" reagents

Suggested Readings: M. Yan, Y. Kawamata, P. S. Baran, *Chem. Rev.* **2017**, 21, 13230–13319

HOW TO MINIMIZE WASTE?
HOW TO GET low E-factor



Most commonly electrolytes are used in large amounts and are chlorates or tetraalkylammonium halide salts.

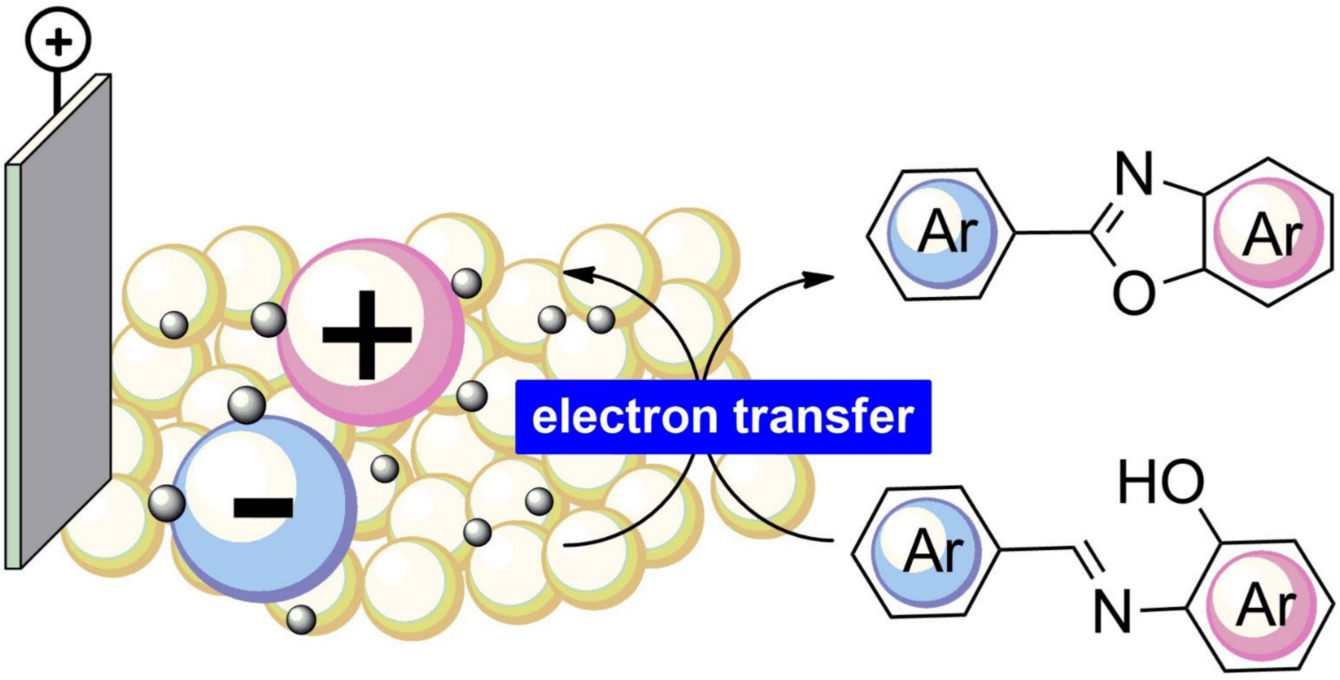
Their removal leads to the formation og halogenated aqueous waste (code 070103 of the European Waste Catalogue)

Must be eventually treated by incineration which involves a significant emission of NOx into the environment.

W. A. Arnold et al , Environ. Sci. Technol. Lett., 2020, 7, 622–631; J. Gyorgy WO2007107804A2 (2006)

SYNTHESIS of 2-aryl benzoxazoles

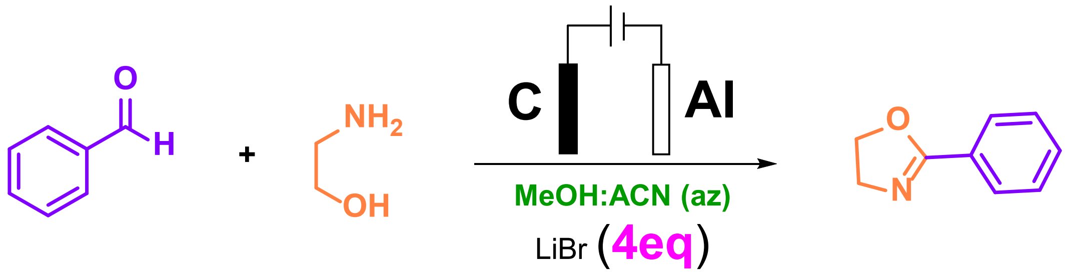
PRODUCING GREEN ENERGY USING GREEN ELECTROSYNTHESIS



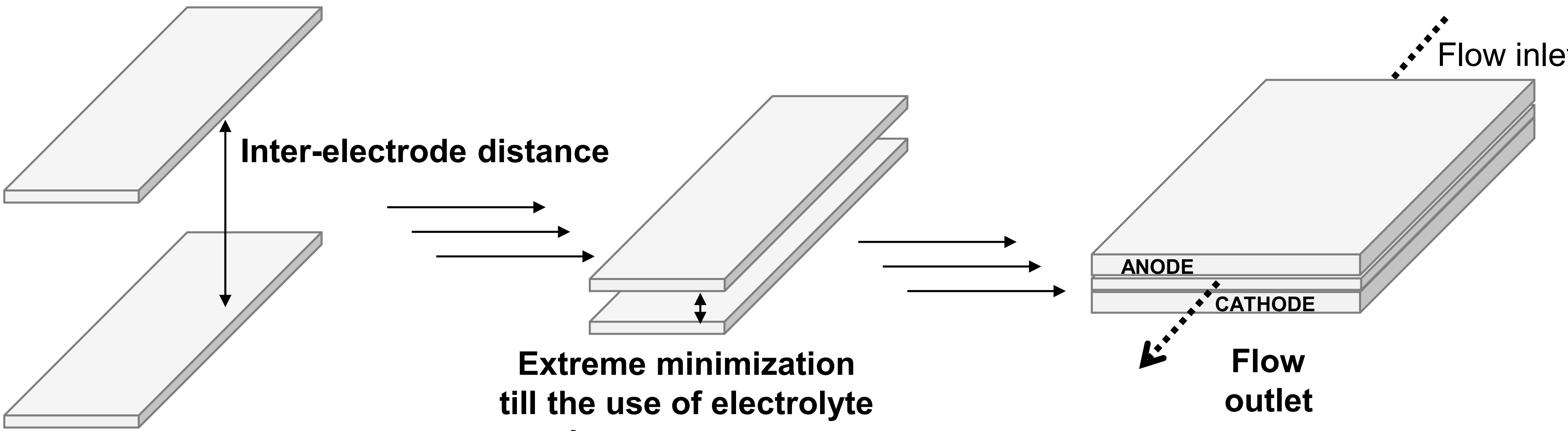
Circular Economy based approach to electrode materials

Application: Electrochemical Synthesis of Oxazoline

conductivity of the reaction mixture is also function of the inter-electrode distance



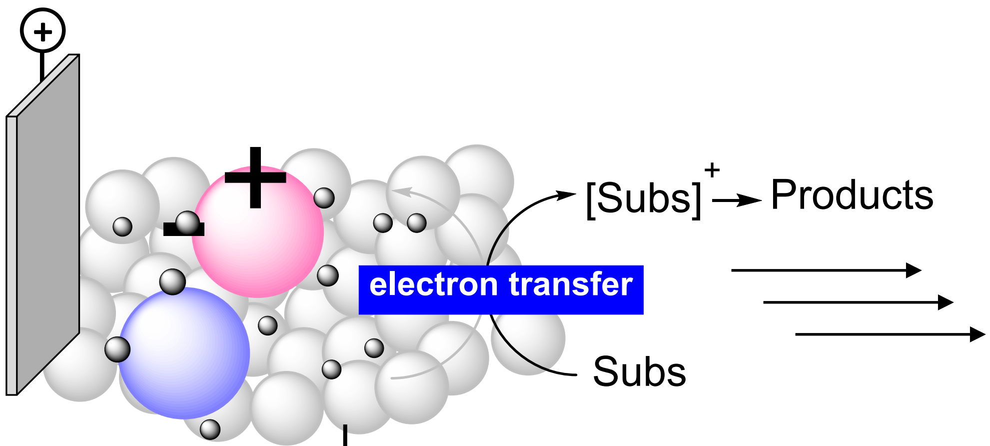
Reduce the electrolyte using customized flow electrochemical cell



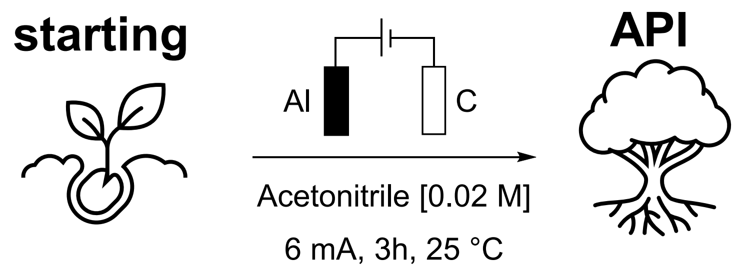
Extreme minimization till the use of electrolyte is unnecessary

SOLID electrolytes IN FLOW

Application: Electrochemical Synthesis of APIs



Development of a solid polymeric matrix which is conductive by ion-hopping mechanism



SOLID ELECTROLYTE

recovered up to 20 consecutive runs

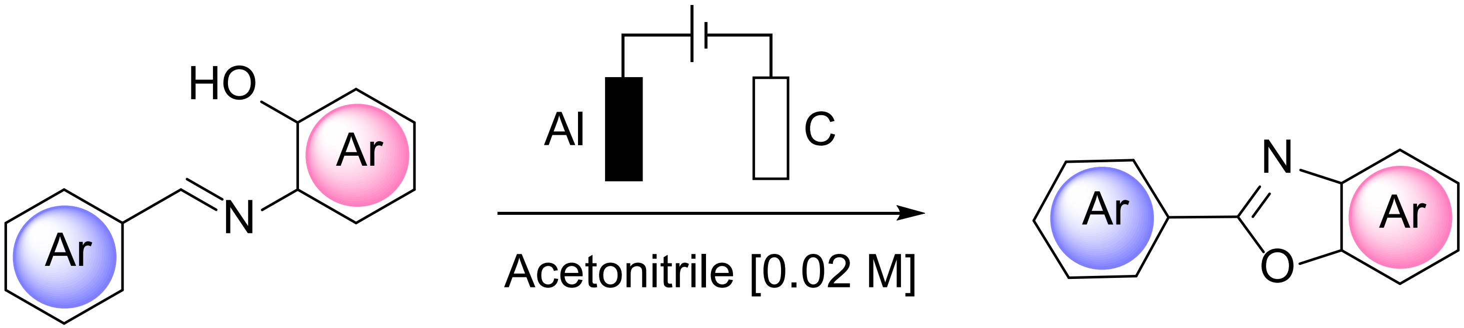
FINAL WORK-UP: JUST EVAPORATE !!!

EXTREME WASTE MINIMIZATION

Green Chemistry, 2024, 26, 6625–6633

Alternatives materials for electrolytes recovery

Application: Electrochemical Synthesis of APIs



1a → **2a**

Solid electrolyte	Recyclability	2A (%)[C]
Amberlyst 400 (Cl)	✓	>99 (92)
Amberlyst A26 (OH)	X	70
Amberlyst 900 (Cl)	✓	>99 (87)
Amberlyst 958 (Cl)	✓	>99 (90)
NH_4Cl	X	70

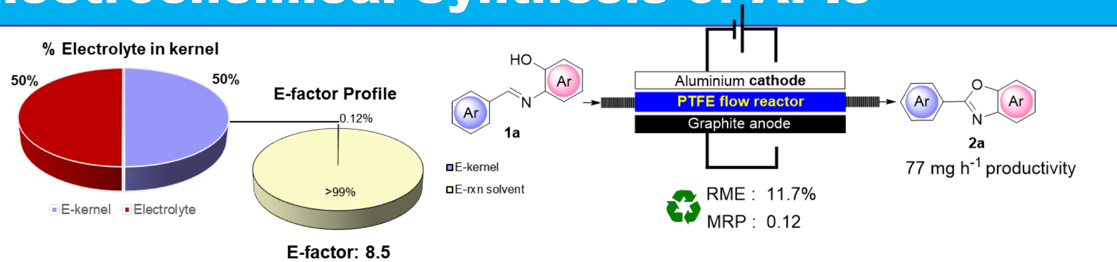
Development of a solid polymeric matrix which is conductive by ion-hopping mechanism

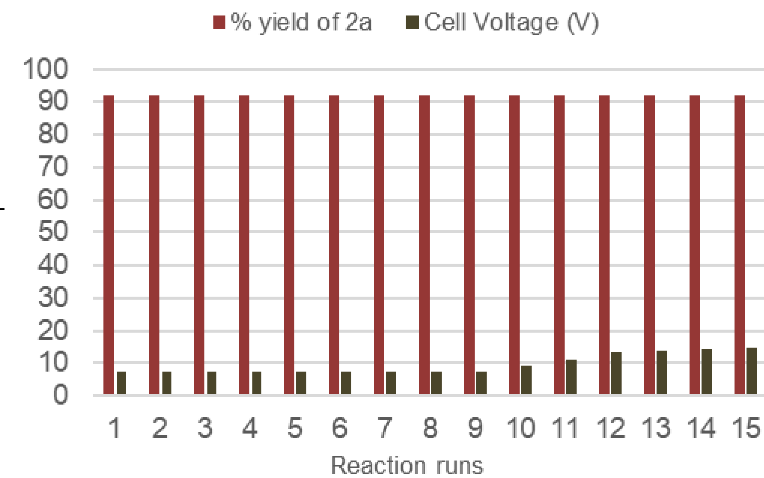
FINAL WORK-UP: JUST EVAPORATE !!!

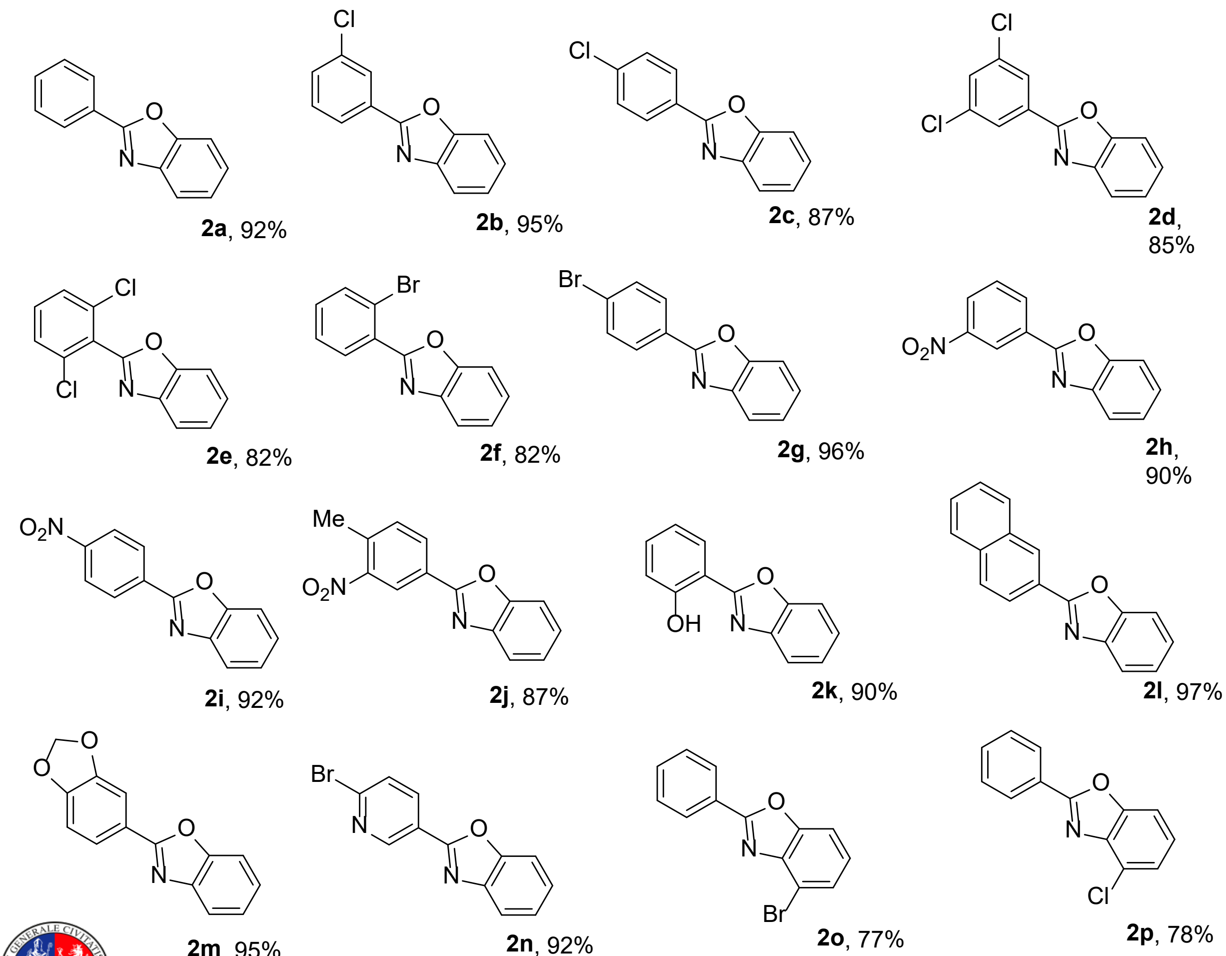
EXTREME WASTE MINIMIZATION

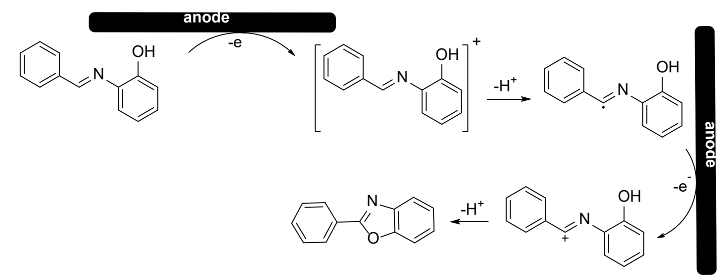
Green Chemistry, 2024, 26, 6625–6633

Electrochemical Synthesis of APIs

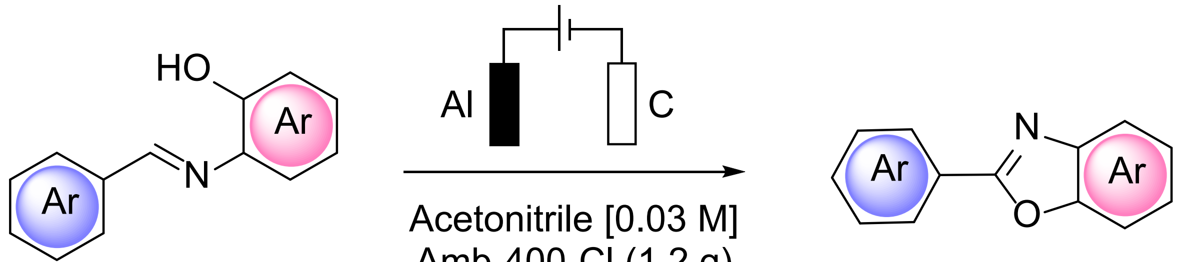






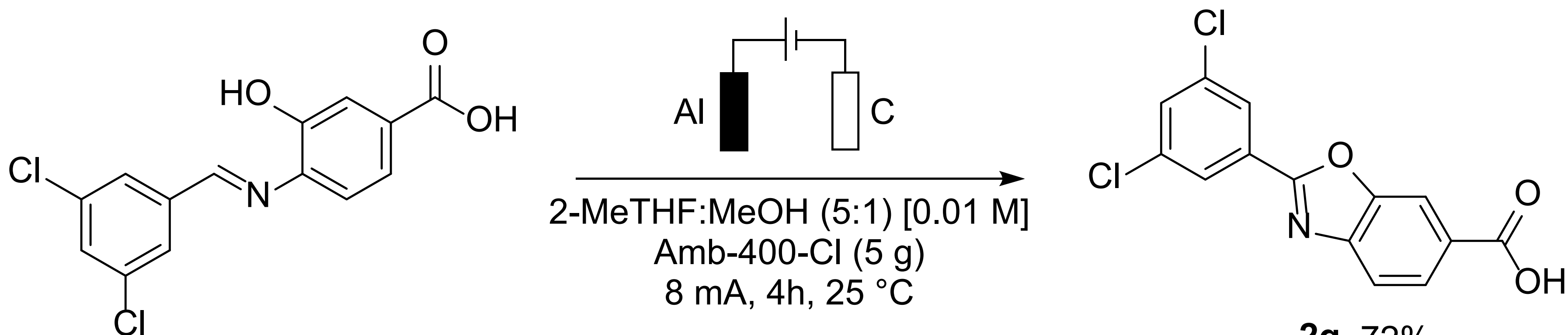


Electrochemical Synthesis of APIs



1 **2**

Concise synthesis of Tafamidis API



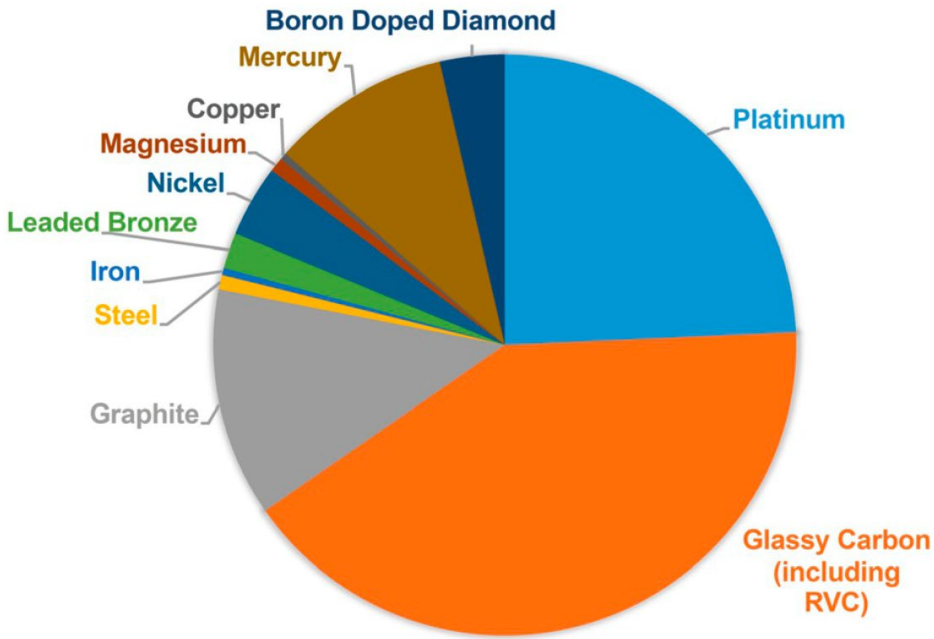
2q, 72%

Tafamidis

Our approaches to sustainable electrosynthesis

Circular Economy based electrode materials

OCCURRENCE OF ELECTRODE MATERIALS



AVERAGE PRICE (10-20 mL reactor size)

GLASSY CARBON: 70 – 300 € each

PLATINUM: 90 – 300 € each

GRAPHITE: 40 – 150 € each

ENVIRONMENTAL CONCERNS

GLASSY CARBON: wasteful and expensive methods for production

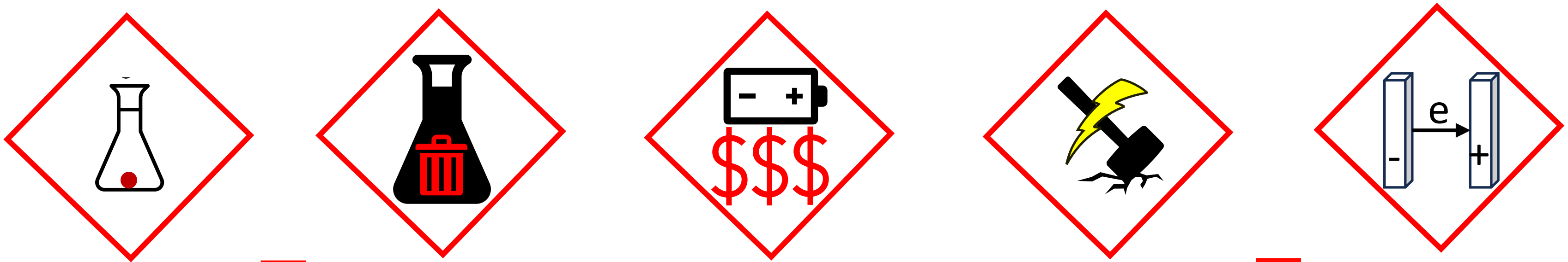
PLATINUM: resource scarcity

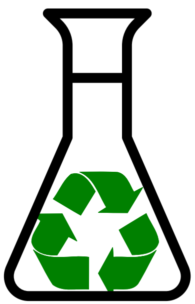
CHALLENGE

High Cost of the Electrode

Within a CIRCULAR APPROACH, waste materials can be used to build electrodes

Our approaches to sustainable electrosynthesis





safe & recoverable reaction media

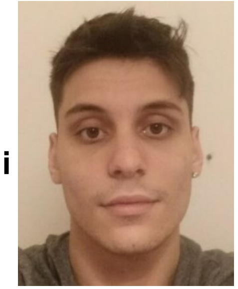
Circular-based electrode materials

Flow chemistry

Circular Economy based approach to electrode materials

Application: Electrochemical Synthesis of Oxazoline

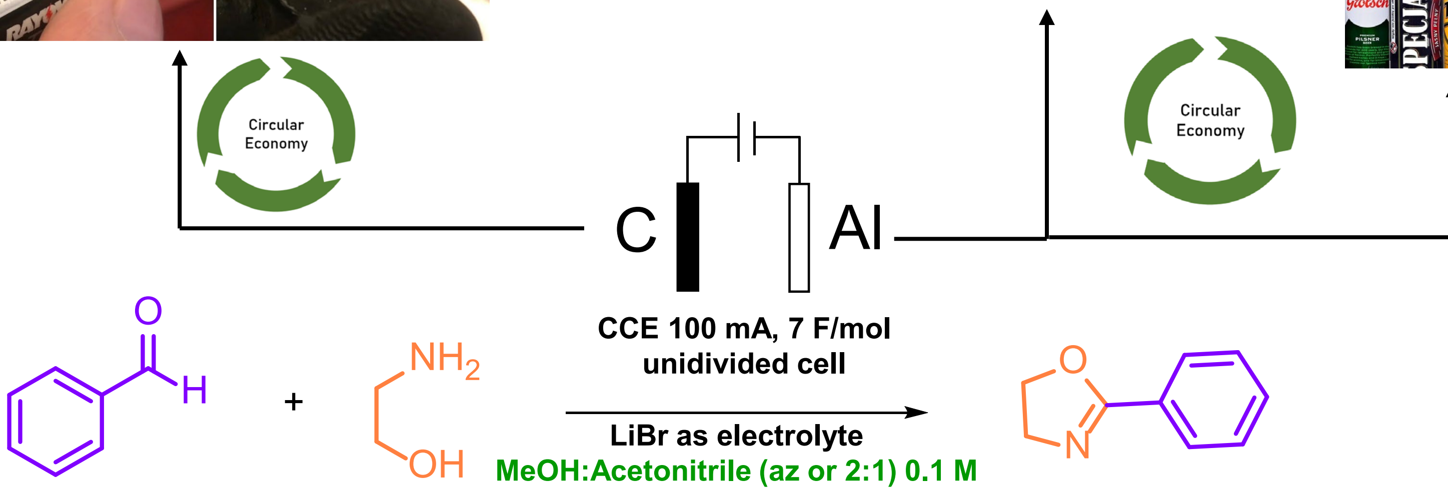
Simone T. Colangeli
Ph.D student



Inside materials of alkaline batteries (both MnO_2 paste or carbon rods)

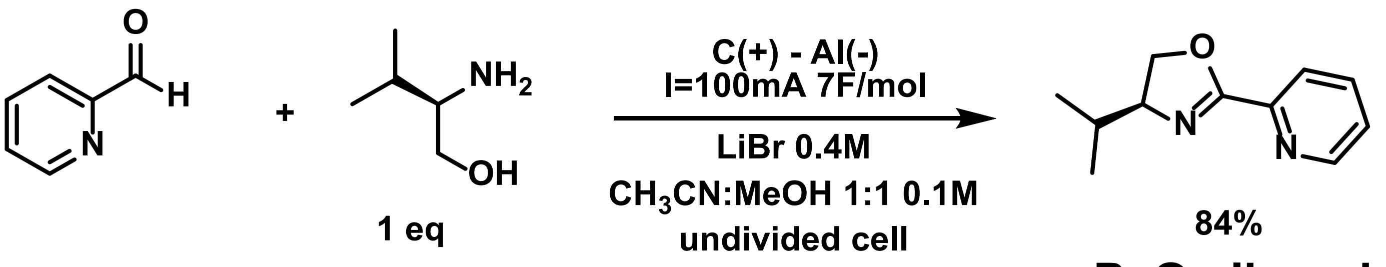
outside cover batteries

spent cans

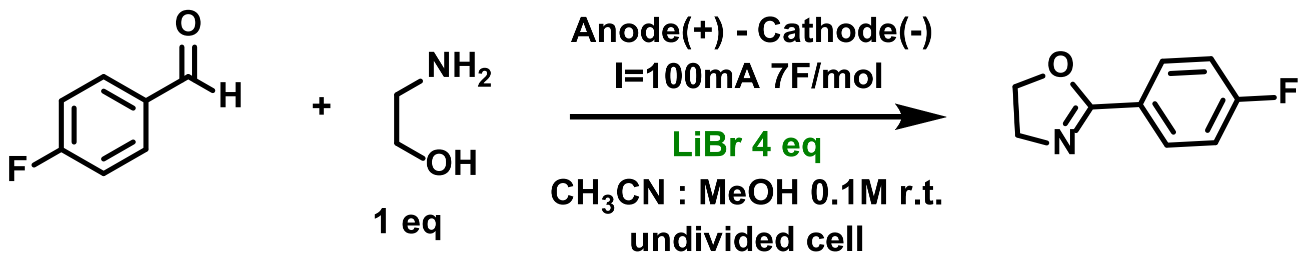


Green Chemistry, DOI: 10.1039/D4GC02564D in press

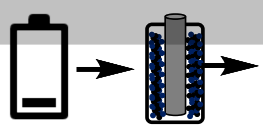
UPCYCLING OF SPENT MATERIALS & PYOX SYNTHESIS



PyOx ligand



ALKALINE BATTERIES



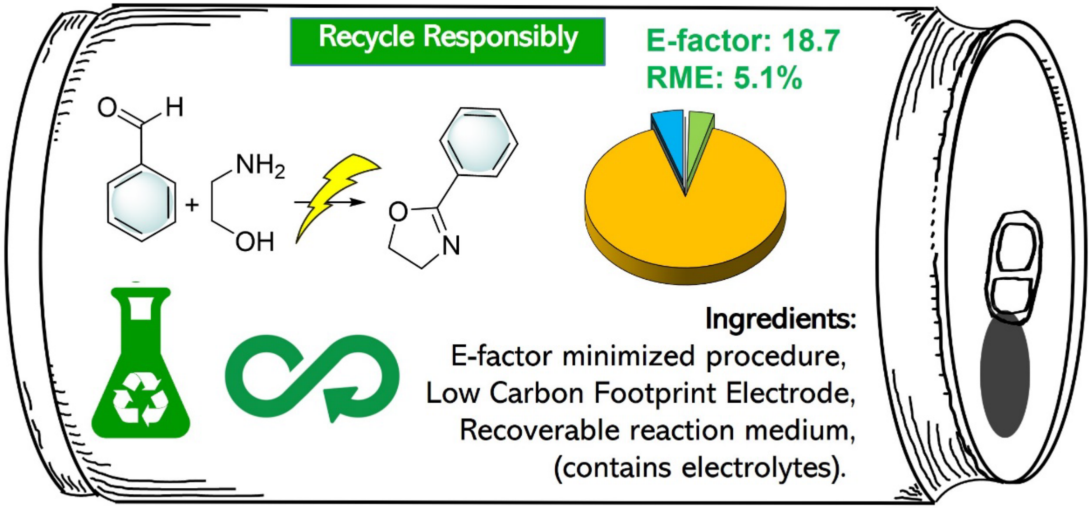
Carbon Manganese Oxide Paste (C-MaP) (+) II Stainless steel (-) **87% isolated yield**

Aluminium spent cans (-) II Graphite (+) **89% isolated yield**

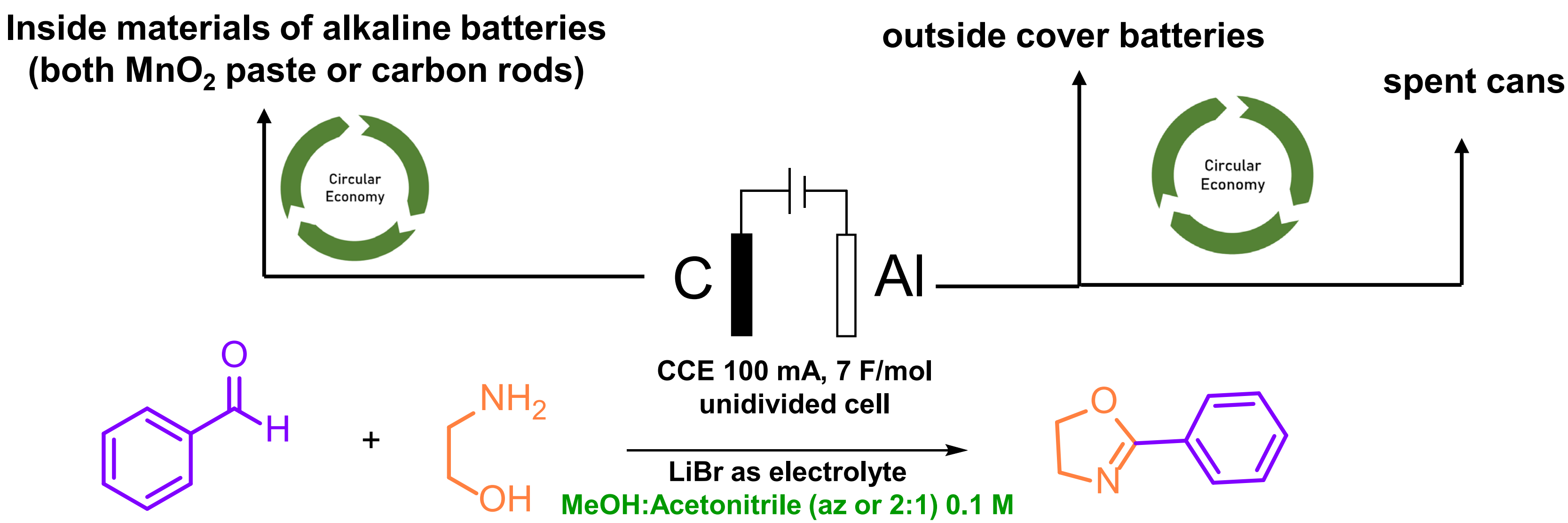
ALUMINUM CANS

Green Chemistry, DOI: 10.1039/D4GC02564D in press

SUSTAINABILITY IN A CAN...UPCYCLING OF SPENT MATERIALS



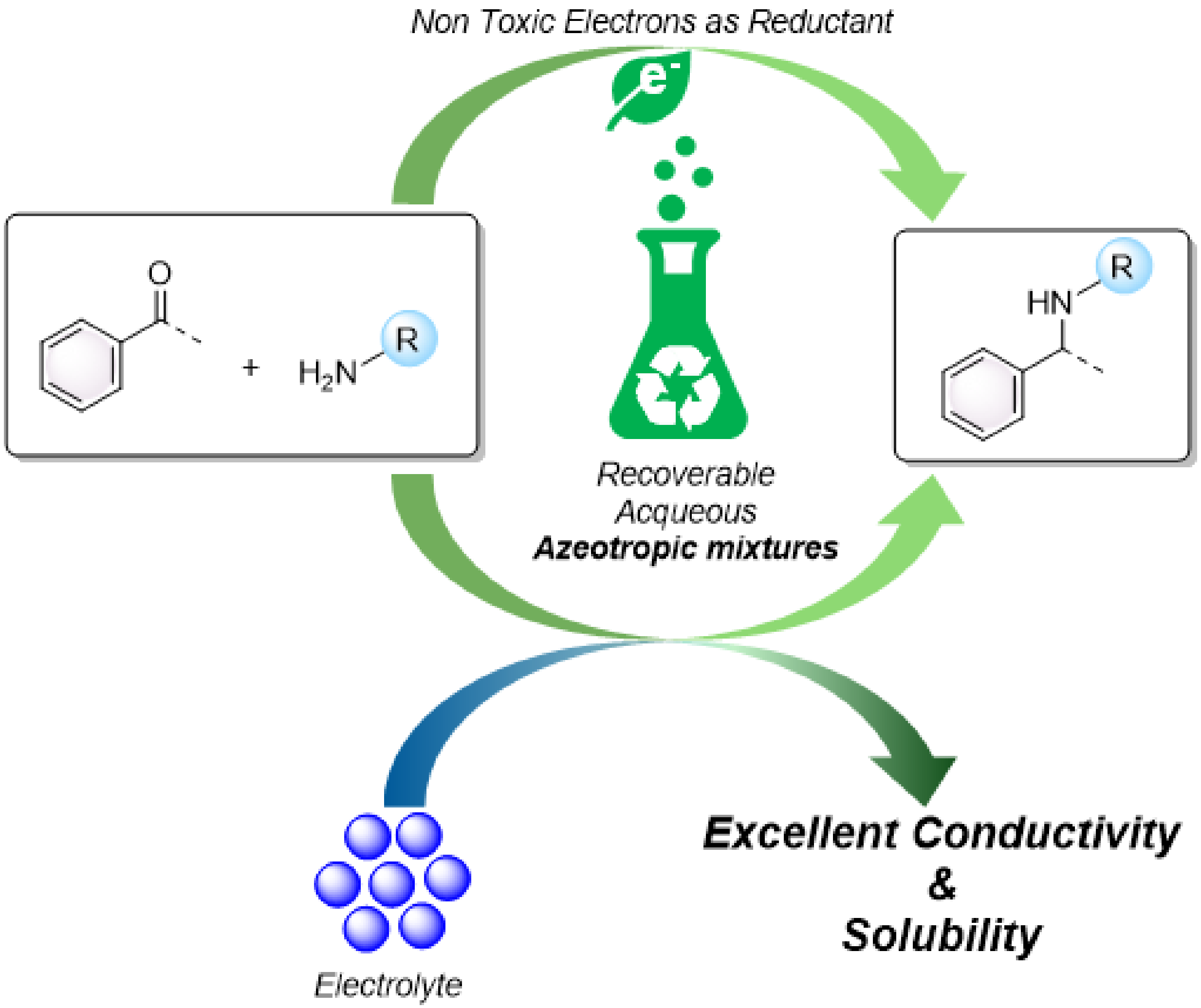
Simone T. Colangeli
Ph.D student



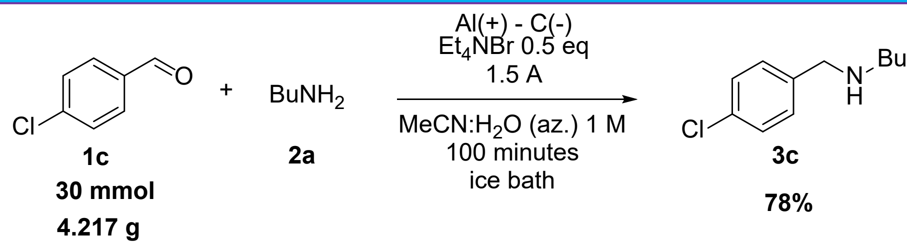
more than **20 examples**, yield 62-90%, large scale (**10 mmol**)

Green Chemistry, DOI: 10.1039/D4GC02564D in press

Electrochemical Reductive Amination



Electrochemical Reductive Amination

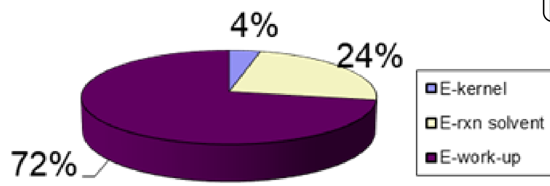


Reaction medium recovery = 82%

work-up solvent recovery = 85%

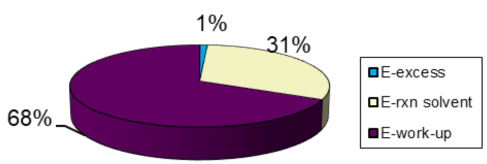
E-factor = 4.65

This work
E-factor = 4.65



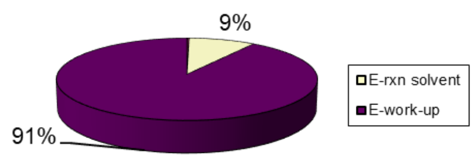
Ecoscale = 54

Org. Biomol. Chem., 2020,18, 5832
E-factor = 182.4



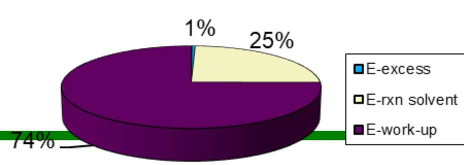
Electrochemical

Org. Lett. 2023, 25, 432
E-factor = 848.3



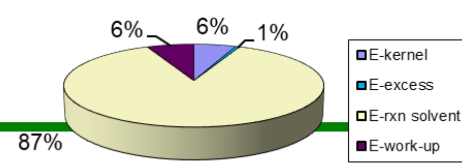
Electrochemical

J. Org. Chem. 2019, 84, 1421
E-factor = 89.9



With $NaBH_4$

Green Chem., 2021, 23, 5625
E-factor = 1.18

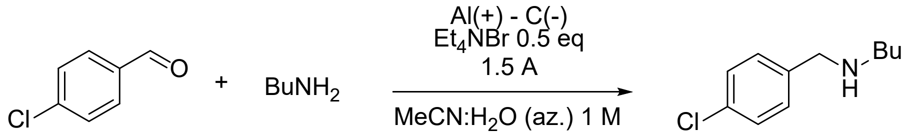


In Flow with Et_3SiH

submitted

Green S.O.C. Perugia

Electrochemical Reductive Amination

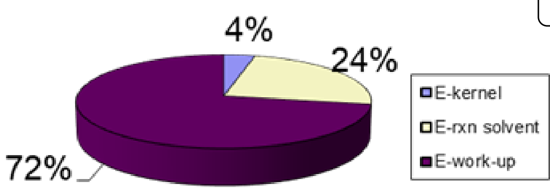


1c **30 mmol** **4.217 g** | **2a** | **3c** **78%**

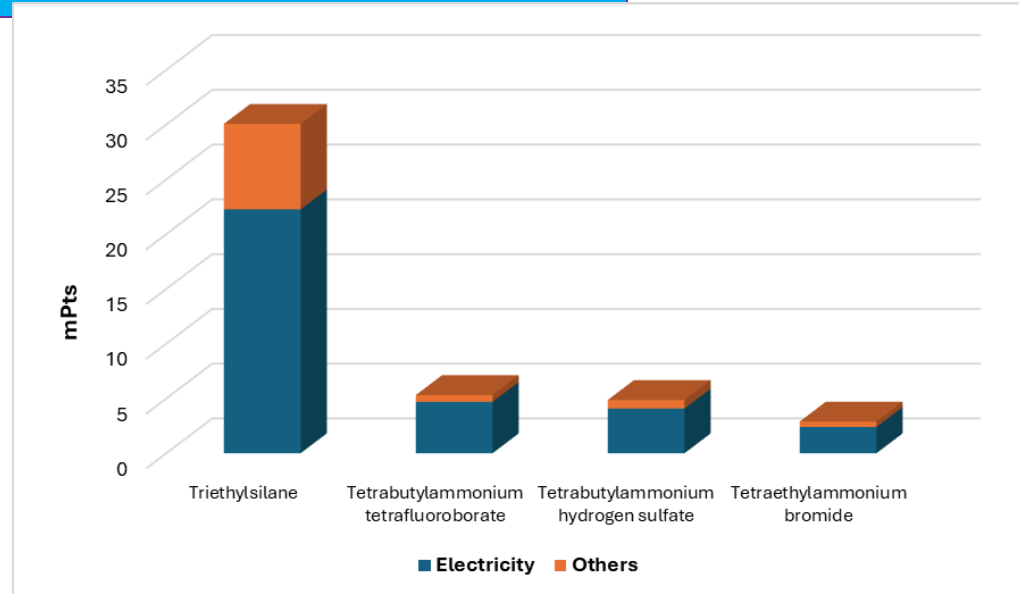
Reaction medium recovery = 82% | **work-up solvent recovery = 85%**

E-factor = 4.65

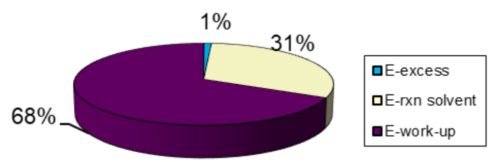
This work
E-factor = 4.65



Ecoscale = 54

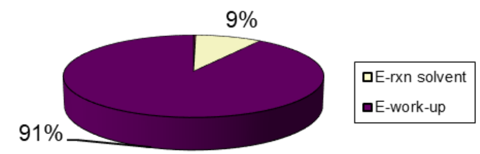


Org. Biomol. Chem., 2020,18, 5832
E-factor = 182.4



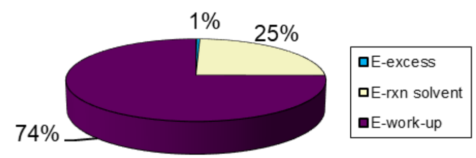
Electrochemical

Org. Lett. 2023, 25, 432
E-factor = 848.3



Electrochemical

J. Org. Chem. 2019, 84, 1421
E-factor = 89.9



With $NaBH_4$

Green Chem., 2021, 23, 5625
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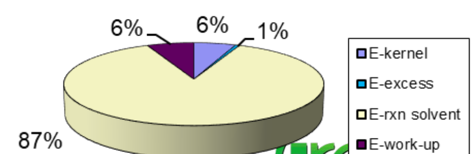
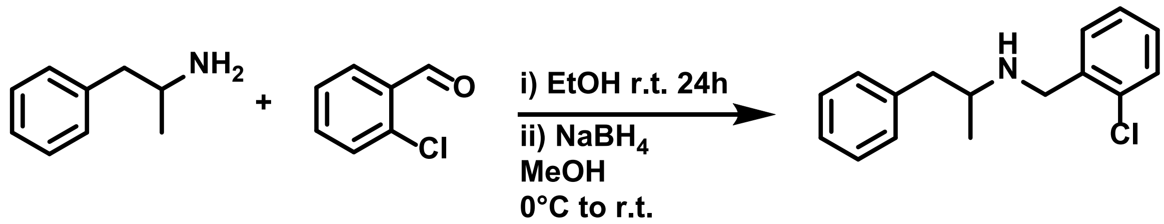


In Flow with Et_3SiH

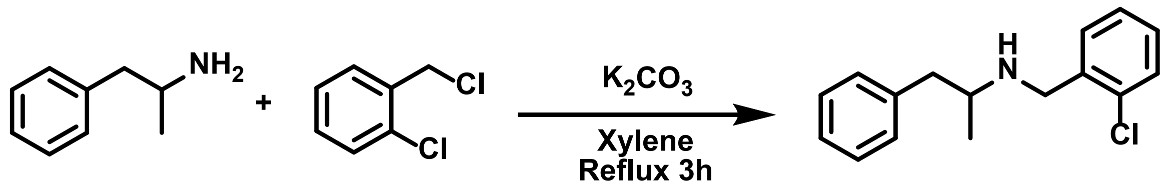
submitted

Electrochemical Reductive Amination

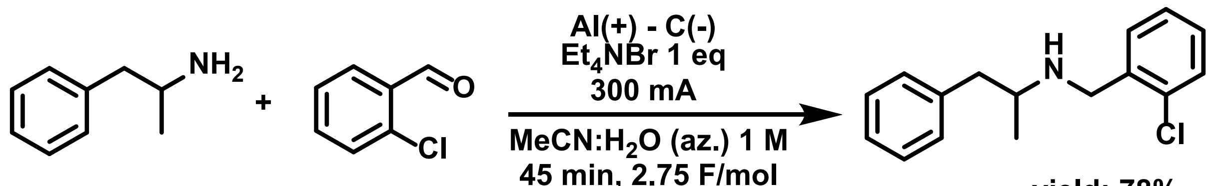
J. Liq. Chromatogr., 1990, 13, 763-777.



Pharmacol Biochem. Behav., 1997, 56, 311-316.



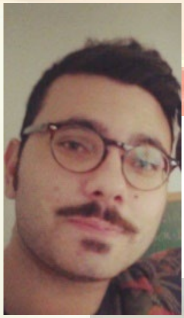
This work:



yield: 78%
E-factor: 3.69

submitted

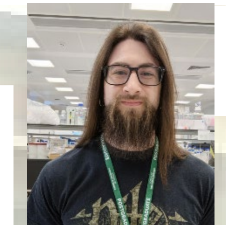
PhD and Post-DOC - Laboratory of Green S.O.C. Perugia



Francesco Ferlin,
Research Associate RTDb
Continuous-Flow Chemistry

Federica Valentini, RTDa
Novel pincer for the immobilization of Metal catalysts

Filippo Campana, RTDa
Biomass derived chemicals
Flow reactors



Matteo Bartalucci, Post-doc
MW and US flow

Dario Marchionni, PhD
BN materials funcionalization

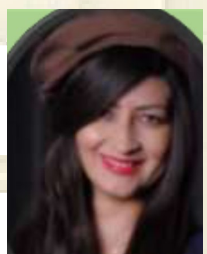
Gabriele Rossini, PhD
Green Synthesis of API

Xing Wei, PhD
Electrosynthesis in flow

Giulia Brufani, Post Doc
Heterocycles sinthesis via C-H functionalization

Fan Huang, PhD
C-H Functionalization of BN doped materials

Parvin Holakooei, PhD
Biomass valorisation strategies



Alireza Nazari, PhD
Green synthesis of B-N materials

Luca Carpisassi, Post Doc
Synthesis of API in flow

Ejdi Cela, PhD
Borazines and flow

Benedetta d’Erasmo, PhD
Novel processes for phenols valorization

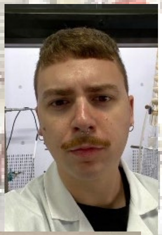
Francesco Minio, PhD
Heterogenous C(Sp3)-H functionalizaton

PhD and Master Students - Laboratory of Green S.O.C. Perugia

Simone Trastulli Colangeli, PhD
Heterocycles sinthesis via C-H functionalization

Elisa Cerza, PhD
Biomass Valorization

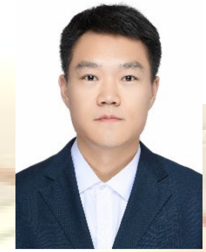
Marta Ciani, PhD
C-H functionalization



Filippo Bocerani, PhD
ADC chemistry

Edoardo Bazzica, PhD
C-H functionalization

Maria Teresa Tiberi, PhD
Phenol valorization



Tian Sang, PhD
C(Sp3)-H functionalization

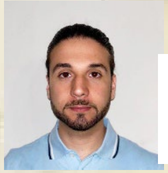
Tommaso Scarabottini, PhD
Sulfur C(Sp3)-H functionalizaton

Alessandro Maselli, PhD
Green Synthesis of APIs

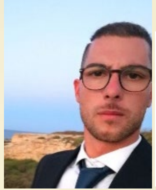
Shaomin Chen, PhD from Gu's group @ HUST Wuhan
Catalysis and phenol valorization

Daniele Gernini, CIRCC bursary
flow photochemistry

Shuang Chen, Visiting PhD Shihezi University; C-H activation



Davide Fandolfo, Master thesis
Biobased catalytic systems



Antonio Vella, PhD
Biomass valorization using safe hydrogen sources

ITALIAN PhD PROGRAMME IN CATALYSIS

26 different Italian Universities 10 International Companies

Laboratory of Green S.O.C. Perugia

Some key current collaborations

Prof. C.-J. Li,
McGill Unversity, Canada
C-H funcitonalization/phenol valorisation

Prof. Maurizio Taddei
Prof. Elena Petricci
Università degli Studi di Siena
MW/flow conditions

Prof. Lutz Ackermann
Georg-August-Universität Göttingen,
Heterogenous catalysts for C-H activation

Prof. Choongik Kim
Sogang University, Korea
Flexible Electronics Lab

Prof. Volker Hessel
University of Adelaide and University of Warwick
LCA and flow chemistry

Prof. C. Aprile
Namur University
Solid state NMR and charcterization of novel polymers

Prof. Francesco Mauriello and Emila Paone
Università di Reggio Calabria
Valorization of waste

Prof. Ping Liu,
Shihezi Unversity China
C-H funcitonalization/heterocycle synthesis

Prof. Dmitri Gelman and Prof. Raed Abu-Reziq
האוניברסיטה העברית בירושלים
The Hebrew University of Jerusalem
Metal catalyst based on pincers

Dr. Massimo Calamante,
CNR – ICCOM Firenze
materials characterization

Prof. Olivier Baudoin
University of Basel,
Csp3-Activation processes

華中科技大學化学与化工学院
School of Chemistry and Chemical Engineering , Huazhong University of Science & Technology

Prof. Yanlong Gu
Huazhong University of Science and Technology, China
New solvents and catalysis

Laboratories of Green S.O.C. & FASST

This work has been or is being supported by

Università di Perugia and MUR within:

- AMIS – Dipartimenti di Eccellenza 2018-2022
- PRIN 2022 «REWIND» – PRIN-PNRR 2023
- ECOSISTEMA PNRR – VITALITY
- ECOSISTEMA PNRR - MICS

Israeli Ministry of Science and Technology – Italian Ministry of Foreign Affairs:

- Israel-Italy Joint Innovation Program for Scientific and Technological Cooperation in R&D (prot. N. 103) and Vigevani Foundation

EU HORIZON 2020

- H-CCAT: Solid Catalysts for activation of aromatic C-H bonds
- STiBNite "Boron-Nitrogen doping".
- Green ART: GREEN ENDEAVOR IN ART RESTORATION
- Double-Active Membranes for a sustainable CO2 cycle (EIC – pathfinder)

National Science Foundation under award number CHE-0755206

American Chemical Society for the IREU grant accorded to Michael McLaughlin, Arianna Kahler-Quesada, Solliver Fusi

Etruscan Arch

Sala dei notari

Priori Palace

Thank you for the attention

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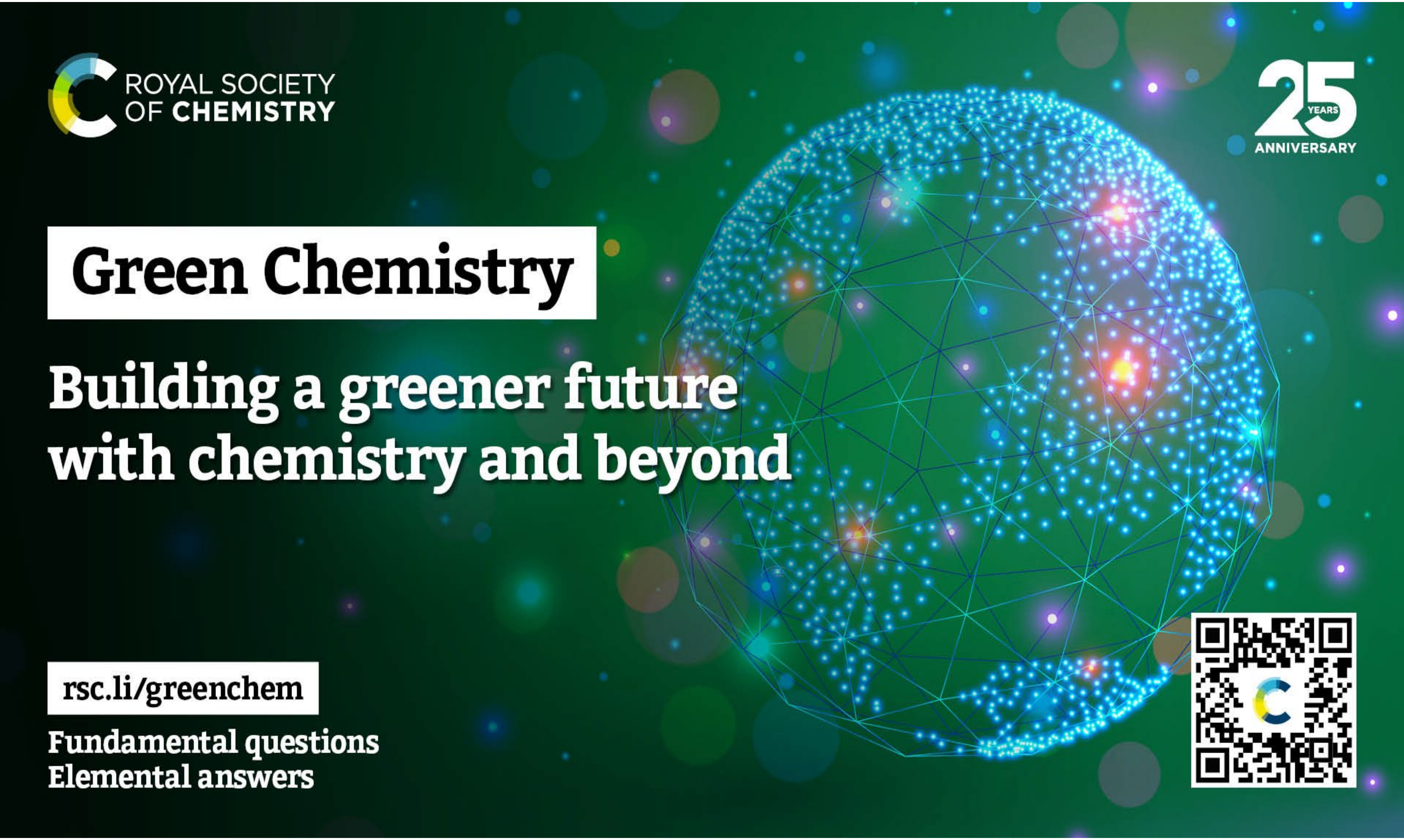
Laboratory of Green Synthetic Organic Chemistry,
Dipartimento di Chimica, Università di Perugia
Via Elce di Sotto, 8 – 06123 Perugia; Tel +39 075 5855541
luigi.vaccaro@unipg.it
http://greensoc.chm.unipg.it

Luigi Vaccaro
Laboratory of Green Synthetic Organic Chemistry,
Dipartimento di Chimica, Università di Perugia
Via Elce di Sotto, 8 – 06123 Perugia; Tel +39 075 5855541
luigi.vaccaro@unipg.it
http://greensoc.chm.unipg.it

Thank you for the attention

WINTER 2024


ROYAL SOCIETY
OF CHEMISTRY
25 YEARS
ANNIVERSARY
Green Chemistry
Building a greener future
with chemistry and beyond
rsc.li/greenchem
Fundamental questions
Elemental answers


ROYAL SOCIETY OF CHEMISTRY
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Discover the new requirement to publish in Green Chemistry

ROYAL SOCIETY OF CHEMISTRY

The Green Foundation box

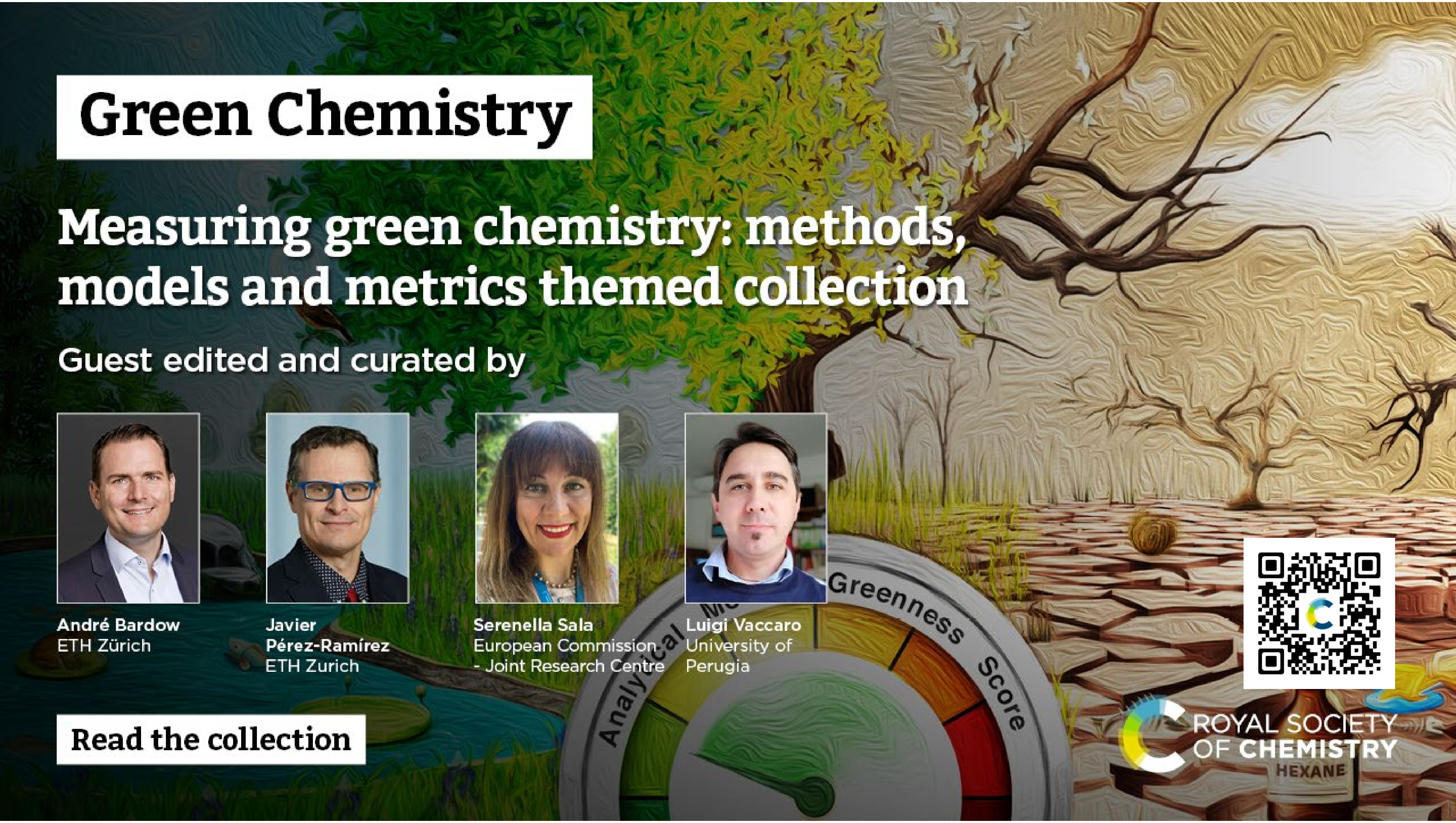
Introducing the use of a recyclable solid electrolyte for waste minimization in electrosynthesis: preparation of 2-arylbenzoxazoles under flow conditions

F. Ferlin, F. Valentini, F. Campana and L. Vaccaro

Green Chem., 2024, 26, 6625-6633. DOI:10.1039/D4GC00930D

Green foundation

1. The work introduces the use of solid electrolyte into organic electrosynthesis, and it proves that with this approach is possible to significantly reduce the waste associated to the use of stochiometric classic homogeneous electrolyte generally containing halides
2. Calculation of the green metrics (E-factors, RME, MRP) for the newly defined procedure and several literature examples, allow to quantify the specific achievement. E-factor has been reduced of ca. 82-99%. Mass of the electrolyte generally constitutes 25–68% of the entire E-kernel and in our case, we could obtain a very low value of 0.12%.
3. Future research will be dedicated to expanding the utilization of solid electrolyte in different electroassisted processes using with safe recoverable reaction media.


Green Chemistry
Measuring green chemistry: methods, models and metrics themed collection
Guest edited and curated by
André Bardow
ETH Zürich
Javier
Pérez-Ramírez
ETH Zurich
Serenella Sala
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