聲明

本檔案之內容僅供下載人自學或推廣化學教育之非營利目的使用。並請於使用時註明出處。[如本頁取材自○○○教授演講內容]。

綠色耦聯反應
回顧近年新型態耦聯反應之進展

國立中興大學
National Chung Hsing University

Chin-Fa Lee
李進發
November 22, 2014

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1. Condensed Principles of Green Chemistry

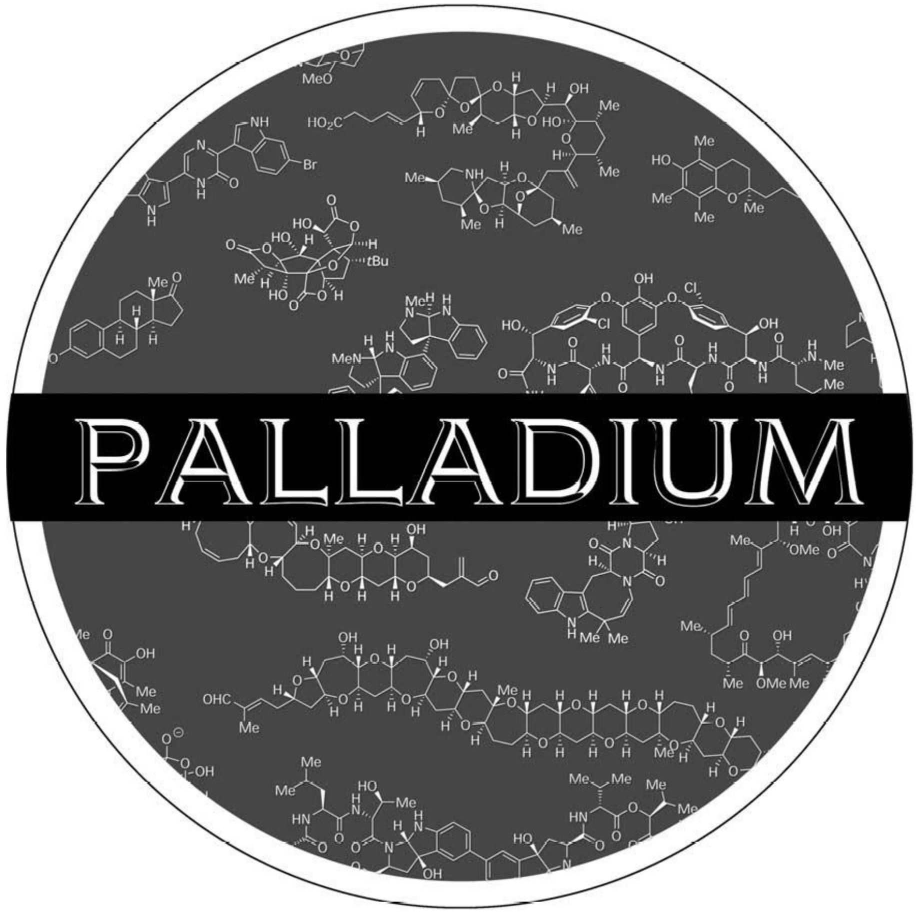
Twelve principles of green chemistry written in the form of a mnemonic:
PRODUCTIVELY

P – Prevent wastes
R – Renewable materials
O – Omit derivatization steps
D – Degradable chemical products
U – Use safe synthetic methods
C – Catalytic reagents
T – Temperature, Pressure ambient
I – In–Process Monitoring
V – Very few auxiliary substances
E – E-factor, maximize feed in product
L – Low toxicity of chemical products
Y – Yes, it is safe

Tang, S. L. Y. ; Smith, R. L.; Poliakoff, M. *Green Chem.*, **2005**, *7*, 761-762

2. Transition-Metal-Catalyzed Cross-Coupling Reactions

Palladium-Catalyzed Cross-Coupling Reactions in Total Synthesis



Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442-4489.

Coupling Reactions

A **coupling reaction** in organic chemistry is a catch-all term for a variety of reactions where two hydrocarbon fragments are coupled with the aid of a metal catalyst with formation of a new carbon-carbon bond in the product.

Cross-couplings involve reactions between two different partners and **homo-couplings** couple two identical partners.

$$R^1-X + R^2-M \xrightarrow{\text{Catalyst}} R^1-R^2 + M-X$$

Coupling reactions mainly includes:

Heck reaction

Negishi coupling

Suzuki reaction

Hiyama coupling

Buchwald-Hartwig reaction

Stille cross coupling

Kumada coupling

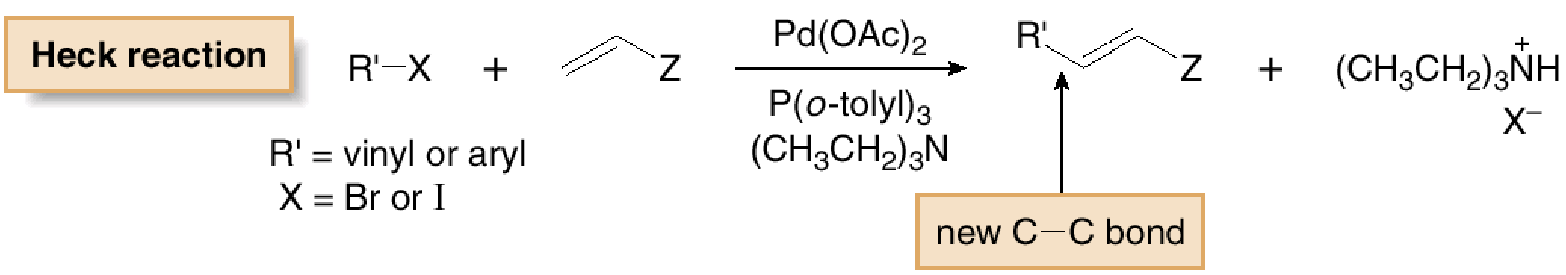
Fukuyama Reaction

Ullmann reaction

Carbon-Carbon Bond-Forming Reactions

The Heck Reaction:

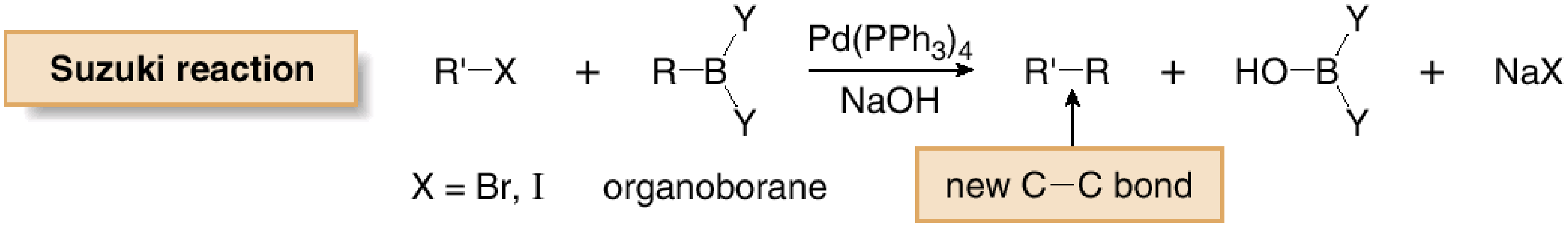
- The Heck reaction is a Pd-catalyzed coupling of a vinyl or aryl halide with an alkene to form a more highly substituted alkene with a new C—C bond.
- Palladium(II) acetate $[Pd(OAc)_2]$ in the presence of a triarylphosphine $[P(o\text{-tolyl})_3]$ is the typical catalyst.
- The reaction is carried out in the presence of a base such as triethylamine.
- The Heck reaction is a substitution in which one H atom of the alkene starting material is replaced by the R' group of the vinyl or aryl halide.



Carbon-Carbon Bond-Forming Reactions

The Suzuki Reaction:

- The Suzuki reaction is a palladium-catalyzed coupling of a vinyl or aryl halide (R'X) with an organoborane (RBY_2) to form a product (R—R') with a new C—C bond.
- $Pd(PPh_3)_4$ is the typical palladium catalyst.
- The reaction is carried out in the presence of a base such as NaOH or $NaOCH_2CH_3$.
- The halogen is usually Br or I.
- The Suzuki reaction is completely stereospecific.



Carbon-Carbon Bond-Forming Reactions

The Negishi Coupling:

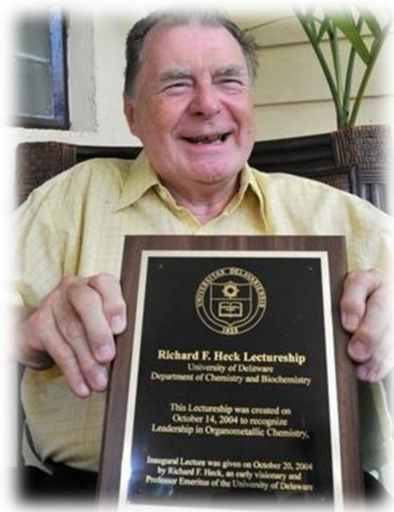
Negishi Coupling, published in 1977, was the first reaction that allowed the preparation of unsymmetrical biaryls in good yields. The versatile nickel- or palladium-catalyzed coupling of organozinc compounds with various halides (aryl, vinyl, benzyl, or allyl) has a broad scope, and is not restricted to the formation of biaryls.

$$R^1\text{-}X + R^2\text{-}ZnX \xrightarrow{\textit{catalyst}} R^1\text{-}R^2 + ZnX_2$$

R^1 = alkenyl, aryl, allyl, benzyl, propargyl

R^2 = alkenyl, aryl, alkynyl, alkyl, benzyl, allyl

THE NOBEL PRIZE IN CHEMISTRY 2010



Richard F. Heck

University of Delaware, Newark, DE, USA,

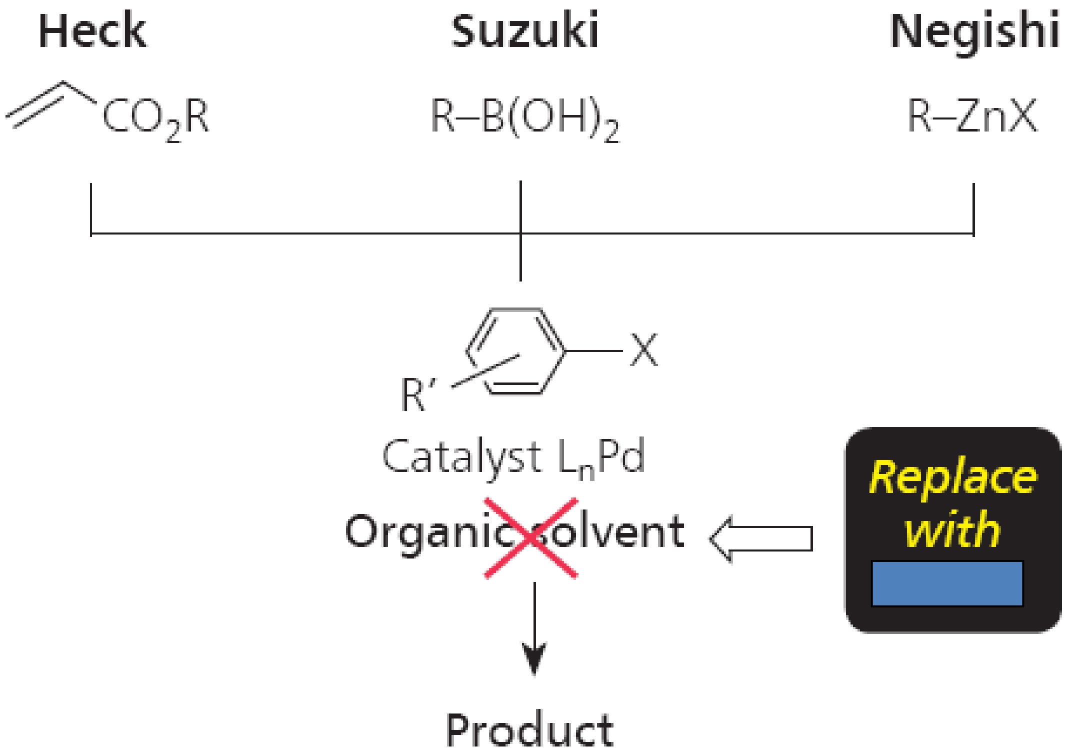
Akira Suzuki

Hokkaido University, Sapporo, Japan

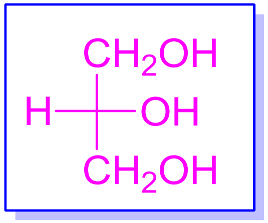
Ei-ichi Negishi

Purdue University, West Lafayette, IN, USA

Transition-Metal-Catalyzed Cross-Couplings Going



Glycerol as a Solvent



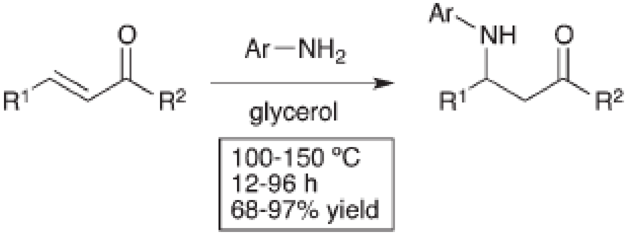
丙三醇，是一種多元醇，是能溶解許多有機和無機化合物，包括過渡金屬錯合物，使用於許多不同的領域，如化妝品，藥品或食品行業中，它主要用作保濕劑，增稠劑，潤滑劑，增甜劑或抗冷凍機。

García, J. I. ; García-Marín, H.; Pires, E. *Green Chem*., **2014**, *16*, 1007–1033

Glycerol as a Solvent

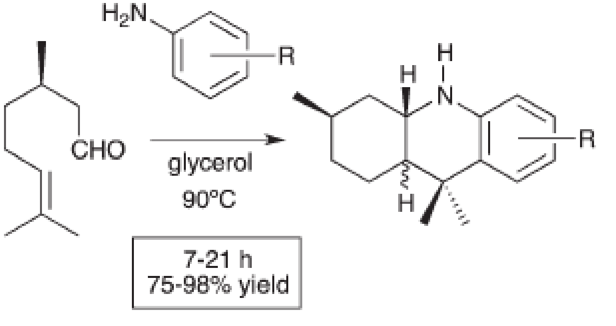
Non-catalyzed organic synthesis

Glycerol has been used as a solvent for aza-Michael addition of aromatic amines to electron-deficient α,β-unsaturated ketones.



Ying, A.; Zhang, Q.; Li, H.; Shen, G.; Gong, W.; He, M. *Res. Chem. Intermed*., **2013**, *39*, 517–525.

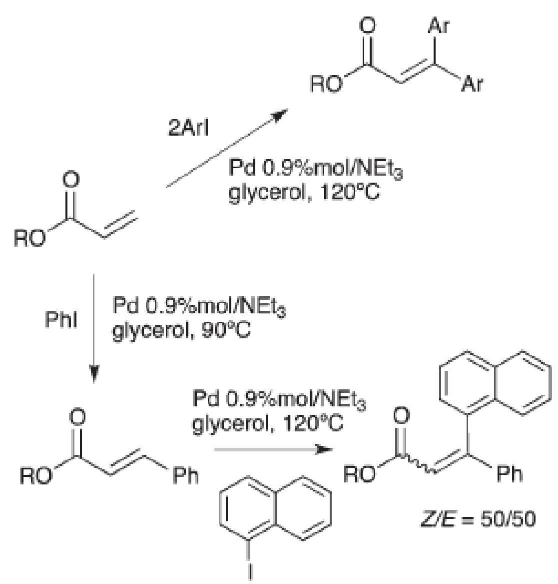
Synthesis of octahydroacridines via one-pot imine condensation/hetero-Diels–Alder reaction of (R)- citronellal with substituted arylamines



Nascimento, J. E. R.; Barcellos, A. M.; Sachini, M.; Perin, G.; Lenardão, E. J.; Alves, D.; Jacob, R. G.; Missau, F. *Tetrahedron Lett.*, *2011*, **52**, 2571–2574.

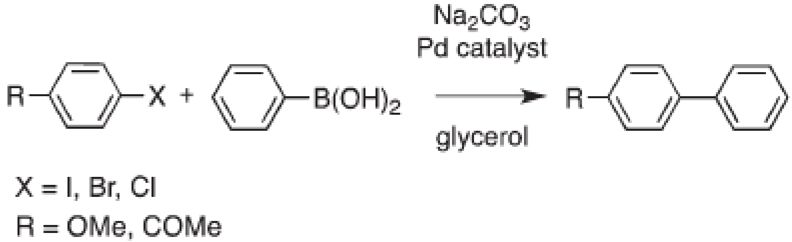
Glycerol as a Solvent

Mizoroki–Heck reaction:
Palladium nanoparticles catalyzed diarylation of acrylate derivatives



Delample, M.; Villandier, N.; Douliez, J.-P.; Camy, S.; Condoret, J.-S.; Pouilloux, Y.; Barrault, J.; Jérôme, F. *Green Chem.*, **2010**, *12*, 804–808.

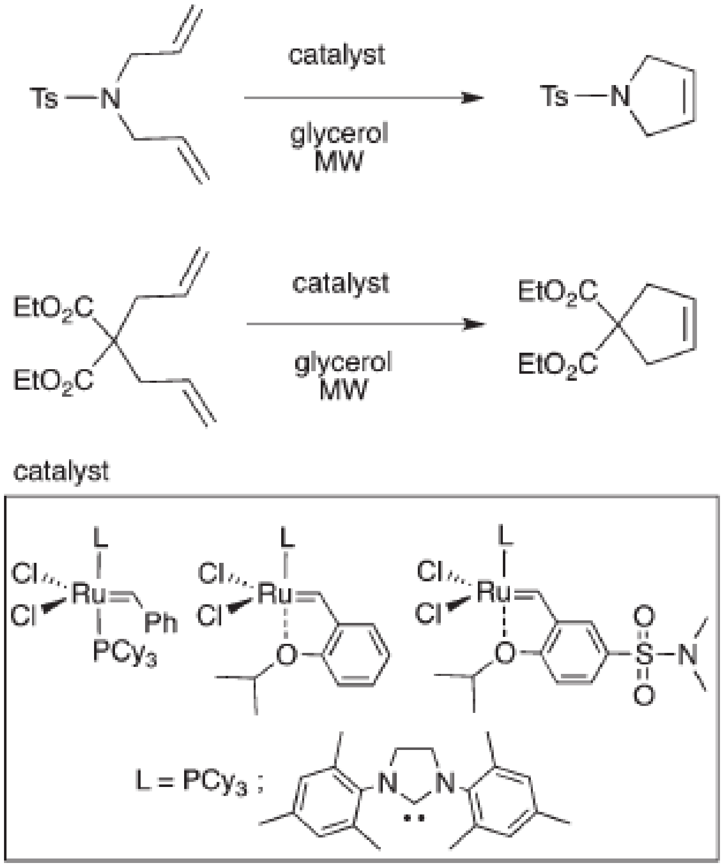
Palladium-catalyzed Suzuki cross-coupling reaction



Cravotto, G.; Orio, L.; Gaudino, E. C.; Martina, K. ; Tavor, D.; Wolfson, A. *ChemSusChem*, **2011**, *4*, 1130–1134.

Glycerol as a Solvent

Transition-Metal-Catalyzed organic synthesis

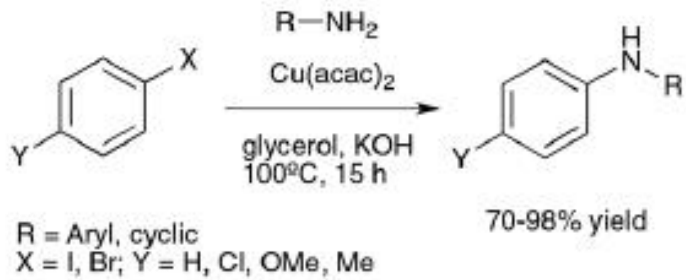


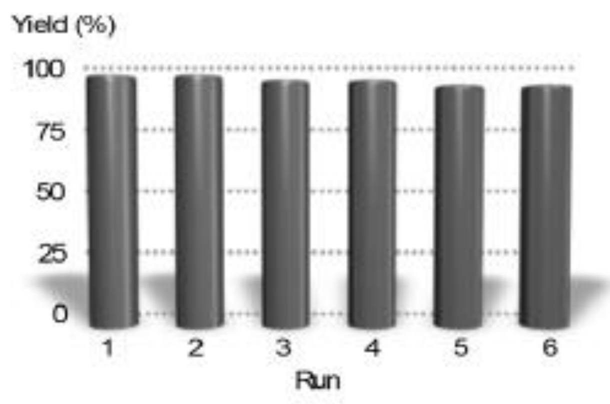
Bakhrou, N.; Lamaty, F. ; Martinez, J.; Colacino, E. *Tetrahedron Lett.*, **2010**, *51*, 3935–3937

Glycerol as a Solvent

Transition-Metal-Catalyzed organic synthesis

$Cu(acac)_2$ catalyzed Coupling reaction of aryl halides with amines



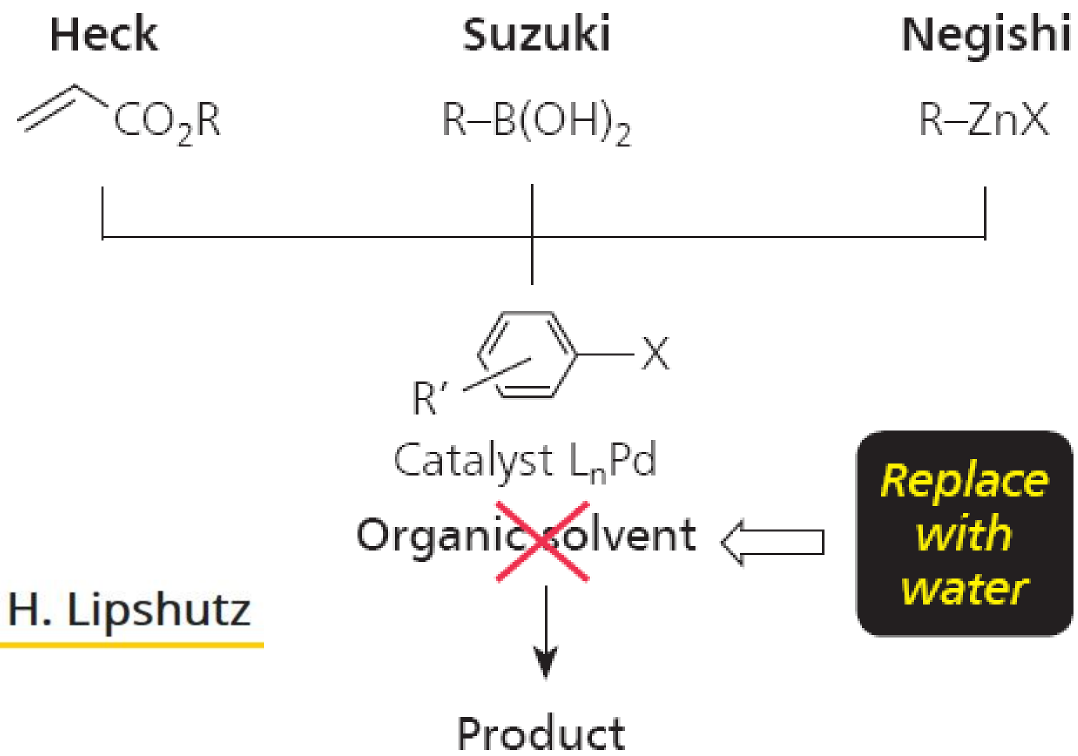


Recycling experiments (X = I, Y = H, R = Ph)

They reported that the glycerol catalytic phase could readily be separated from the reaction mixture and reused for several runs without any loss in catalytic efficiency.

Khatri, P. K.; Jain, S. L. *Tetrahedron Lett.*, **2013**, *54*, 2740–2743.

Transition-Metal-Catalyzed Cross-Couplings Going Green: in *Water* at Room Temperature



Professor Bruce H. Lipshutz

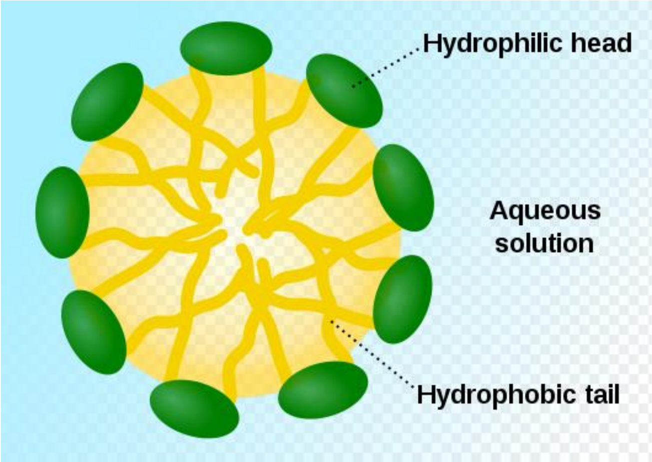
Presidential Green Chemistry Challenge Award, June 20, 2011

University of California, Santa Barbara

Reactions in Micellar Systems

Micelles are kind of amphiphiles molecules consisting of a hydrophilic head group and a hydrophobic lipophilic tail, and are thus able to interact with both polar and nonpolar compounds. When the hydrophobic tail reaches a certain chain length, the amphiphiles reduce the unusually high surface tension of water and are referred to as tensides (or surfactants).

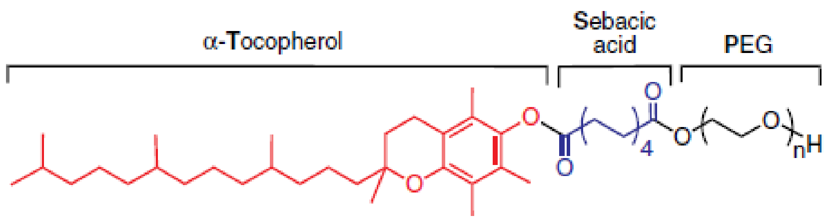
Micelles are especially simple spherical supramolecules, which are formed by amphiphiles in water or media similar to water. A micellar system appears to be homogeneous since these aggregates are of colloidal size; however, in reality the absorbed reactants are in a microheterogeneous two-phase system.



http://en.wikipedia.org/wiki/Micelle

Dwars, T.; Paetzold, E.; Oehme, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 7174

Various Micellar Systems



1

Figure 1. Structure of the Nonionic Amphiphile PTS (**1**, n = ca. 13).

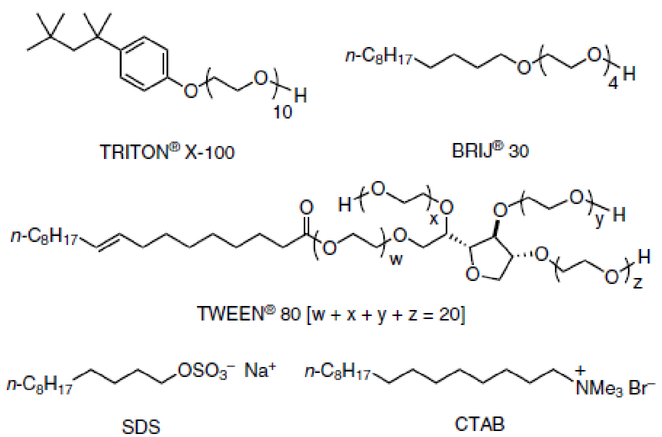


Figure 2. Commonly Used Nonionic and Ionic Surfactants.
(Ref. 17–20)

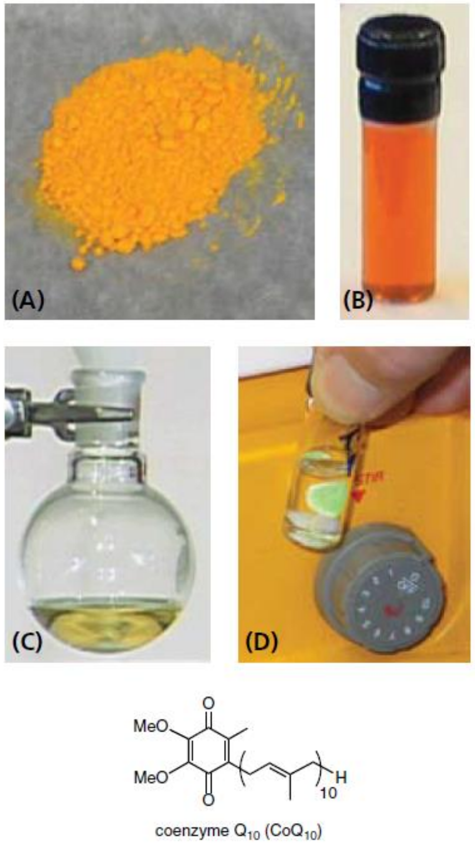
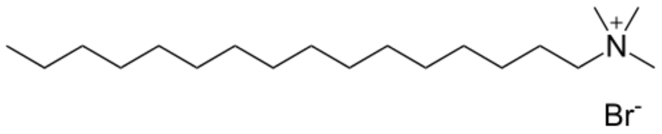
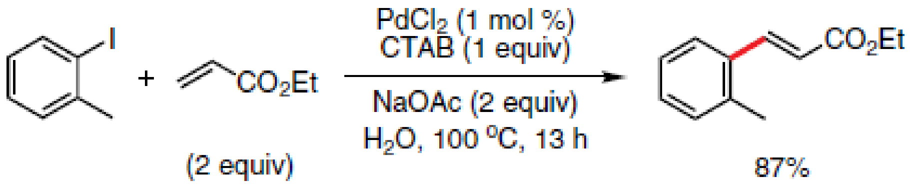


Figure 4. (A) Pure, Water-Insoluble Coenzyme Q_{10}. (B) Solution of 50 mg/mL CoQ_{10} in PTS–H_2O. (C) Neat PTS. (D) Solution of TAXOL® in PTS–H_2O (10 mg/mL). (Photos © B. H. Lipshutz.)

Lipshutz, B. H.; Ghorai , S. *Aldrichimica Acta*, **2008**, *41*, 59.

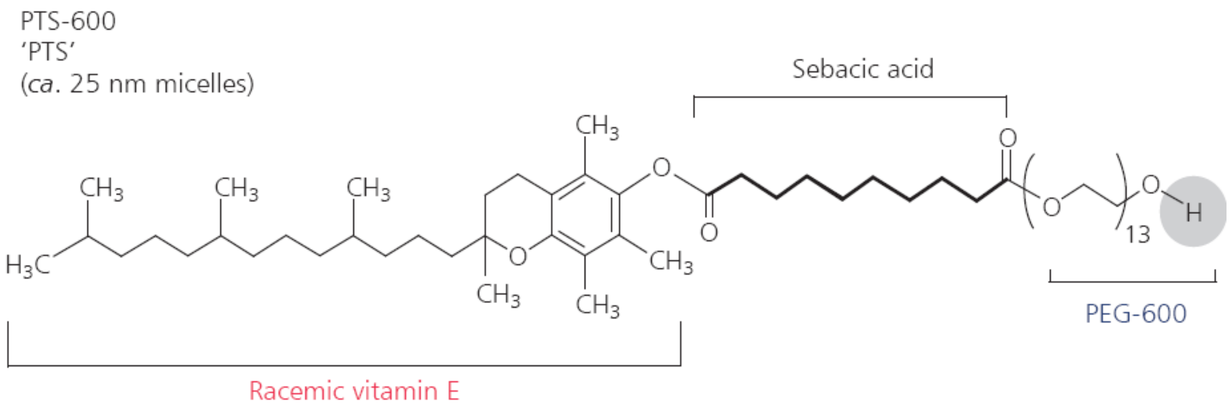
Use of CTAB





Bhattacharya, S.; Srivastava, A.; Sengupta, S. *Tetrahedron Lett*. **2005**, *46*, 3557

Polyoxyethanyl α-tocopheryl sebacate (PTS)



Sale by sigma-aldrich
100ML = $ 348.00
In general used as
15 wt% in Water

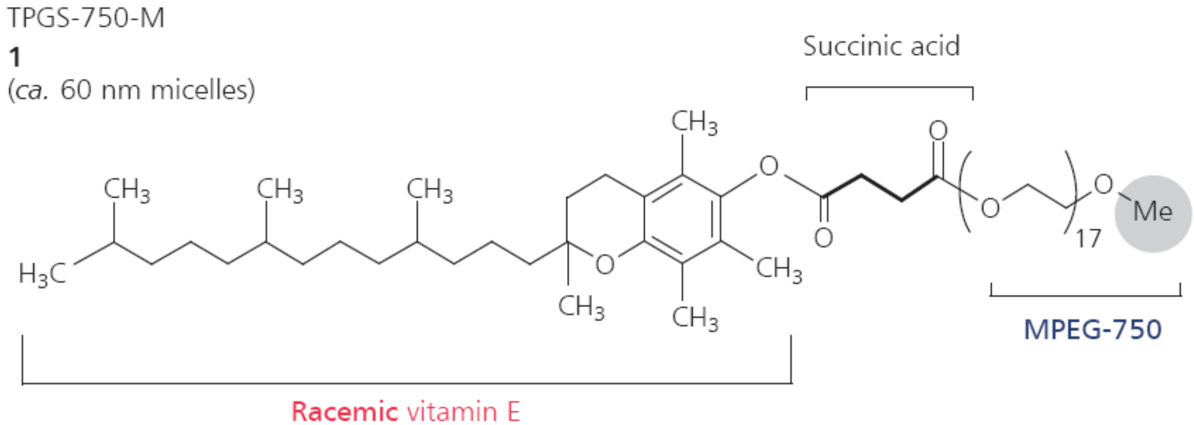
B. H. Lipshutz and S. Ghorai, *Aldrichim. Acta*, **2008**, *41*, 59

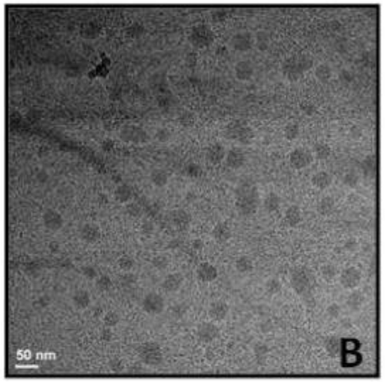
PTS (or PTS-600) is a nonionic amphiphile recently introduced by Professor Bruce Lipshutz of UC-Santa Barbara that is proving to be a versatile "solubilizer" for organic molecules in water.

Lipophilic substrates and catalysts can efficiently enter the 25 nm micelles formed by PTS in water leading to cross-coupling reactions such as metathesis, Suzuki-Miyaura, and Heck reactions at room temperature.

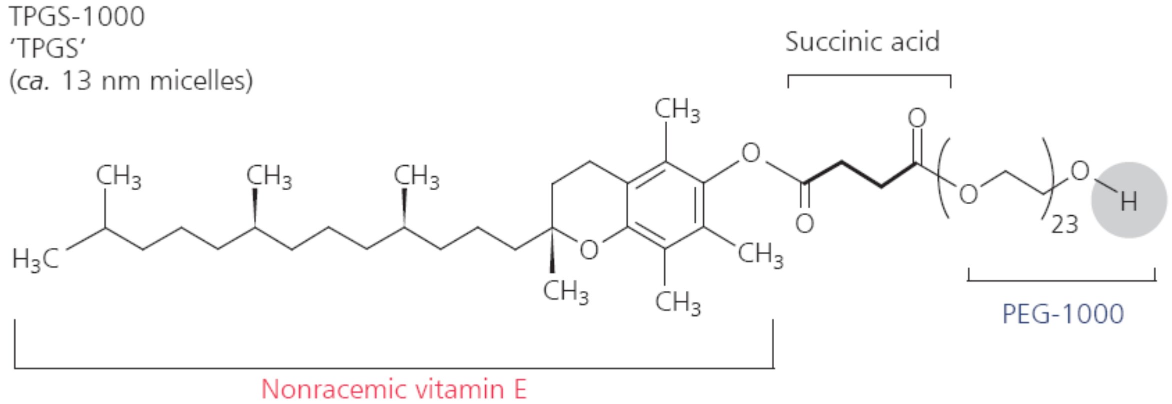
Importantly, there is no need for a co-solvent to enhance solubility of water-insoluble substrates in these reactions.

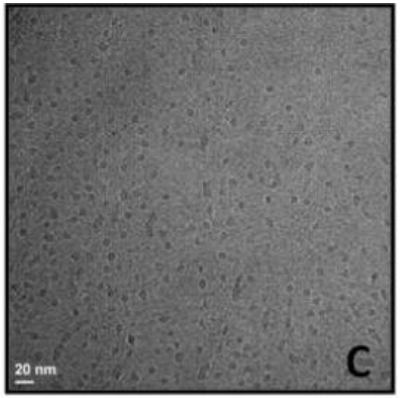
TPGS-1000 和 TPGS-750-M 之間的結構差異



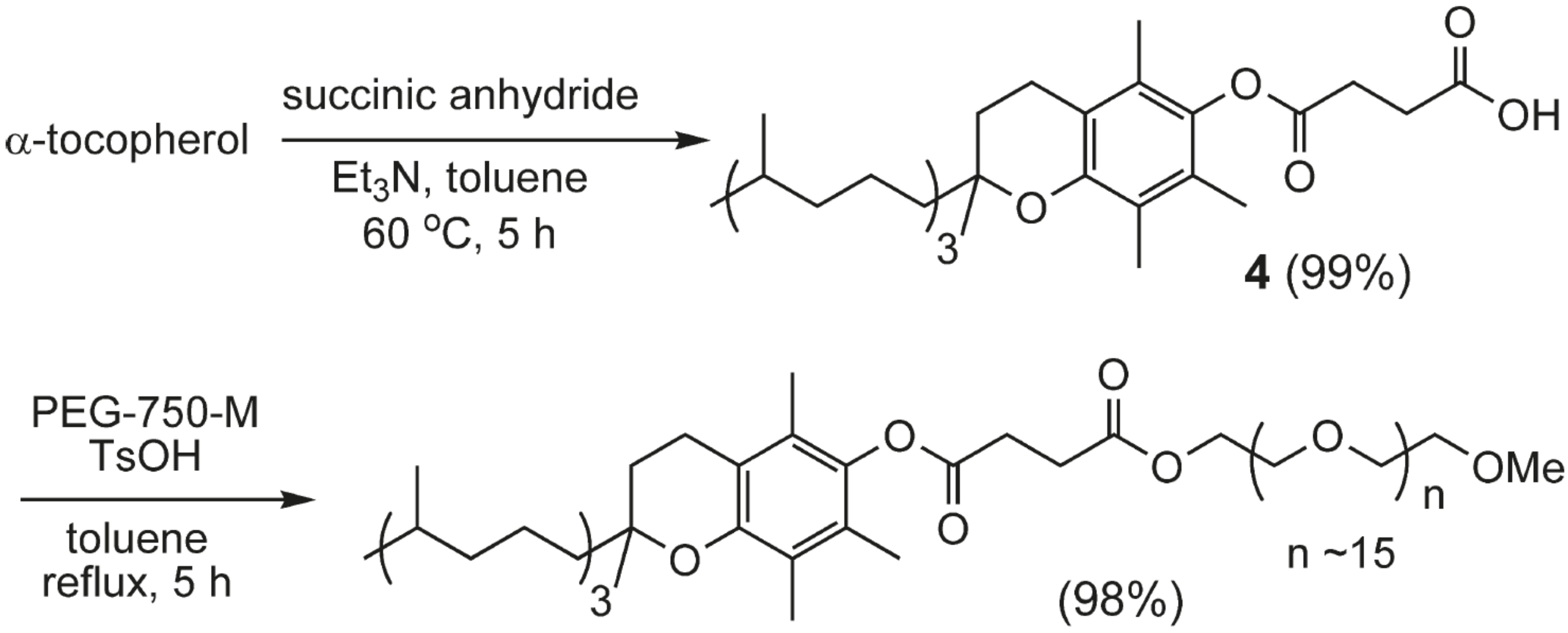


B. H. Lipshutz, S. Ghorai, A. R. Abela, R. Moser, T. Nishikata, C. Duplais, A. Krasovskiy, R. D. Gaston and R. C. Gadwood, *J. Org. Chem.*, **2011**, 76, (11), 4379





J. D. Cawley and M. H. Stern, Eastman Kodak Company, 'Water-Soluble Tocopherol Derivatives', *US Patent* 2,680,749; 1954



2; TPGS-750-M (MW ~ 1262)

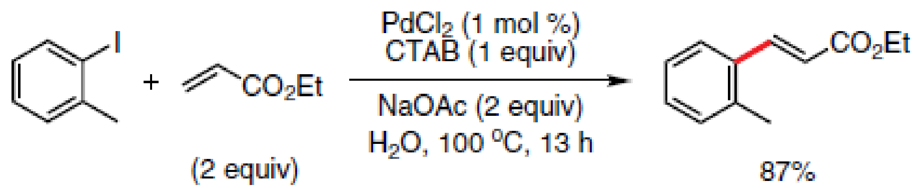
Synthesis of TPGS-1000步驟同上(將PEG-750-M改成PEG-750-M)

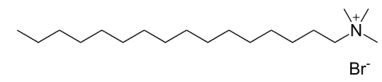
Bruce H. Lipshutz, B. H. *et al. J. Org. Chem*. **2011**, *76*, 4379.

Synthetic Chemistry in Micellar Systems

Heck Coupling

Use of CTAB

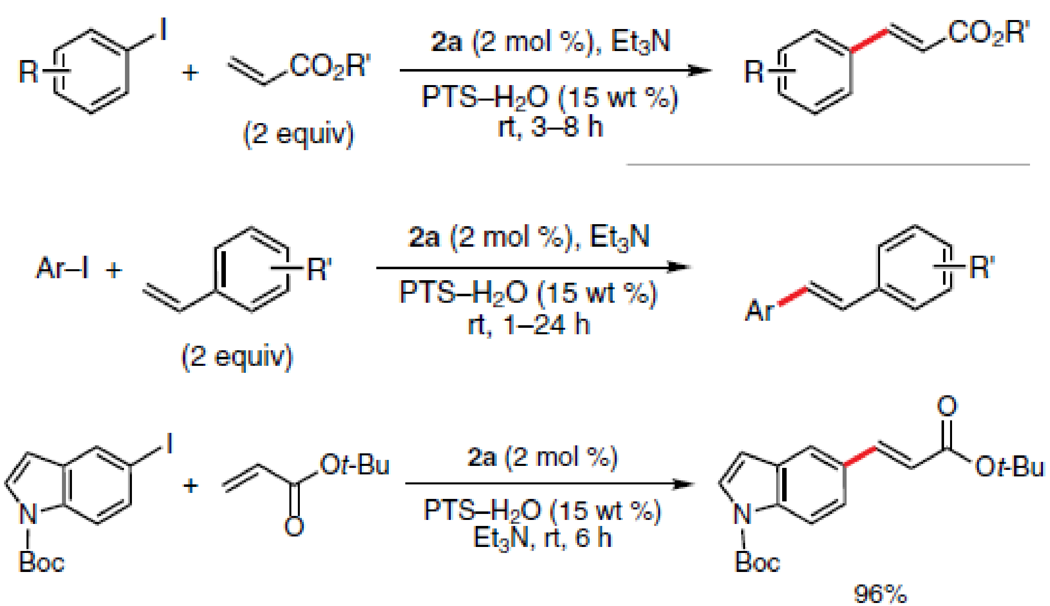


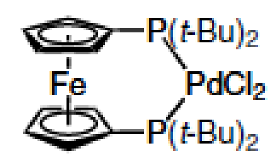


CTAB

Bhattacharya, S.; Srivastava, A.; Sengupta, S. *Tetrahedron Lett.* **2005**, *46*, 3557.

Use of PTS-H_2O as Solvent





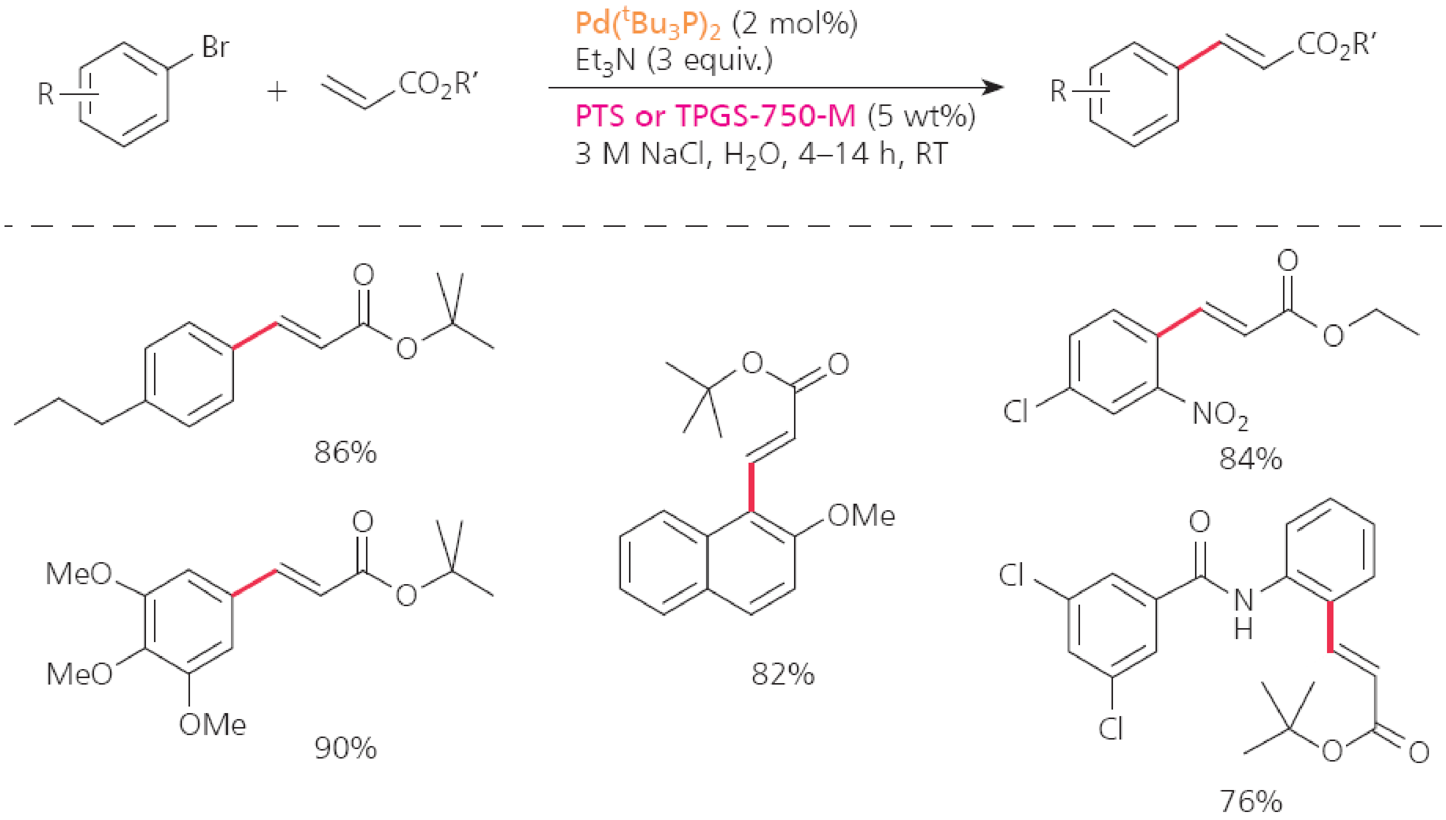
2a
[Pd(dtbpf)Cl_2]

Lipshutz, B. H.; Taft, B. R. *Org. Lett.* **2008**, *10*, 1329.

Synthetic Chemistry in Micellar Systems

Heck Coupling

Use of PTS-600 or TPGS-750-M

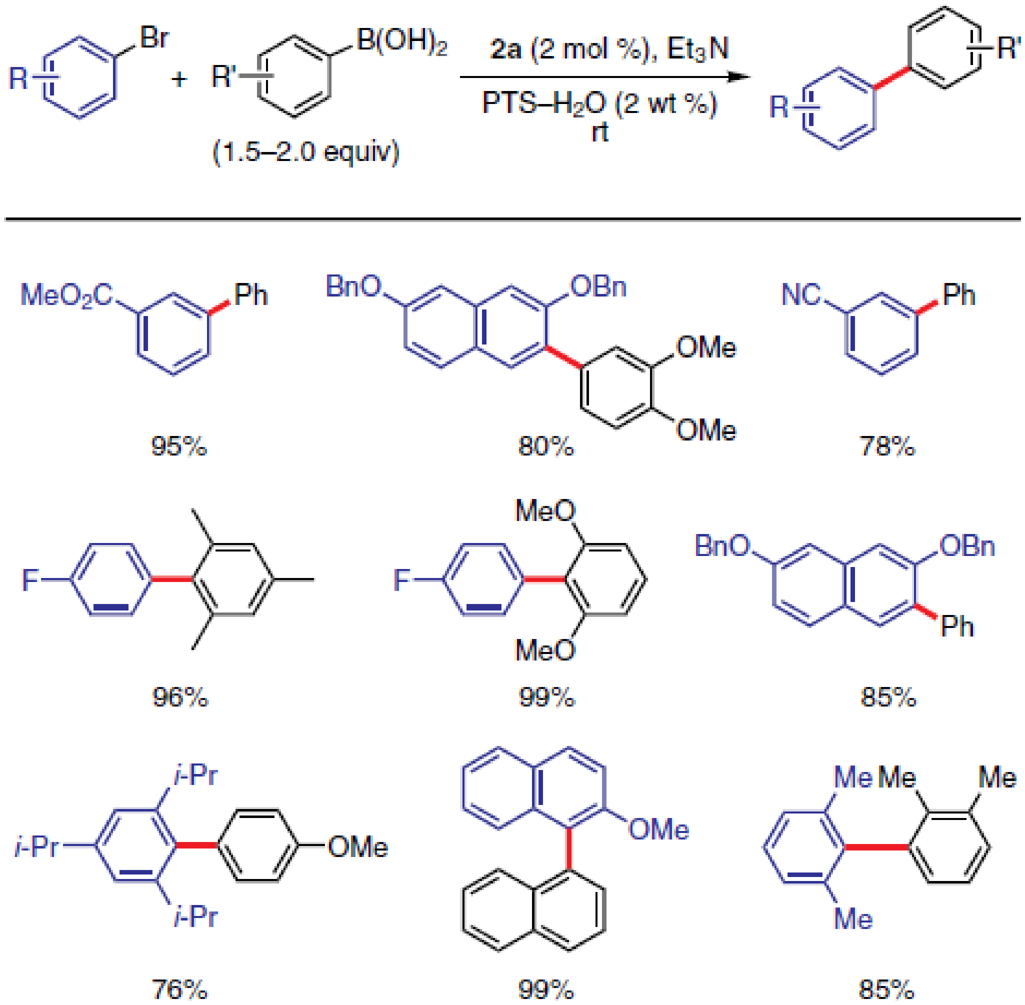


Bruce H. Lipshutz*, Benjamin R. Taft, Alexander R. Abela *Platinum Metals Rev.*, **2012**, *56*, (2), 62–74

Synthetic Chemistry in Micellar Systems

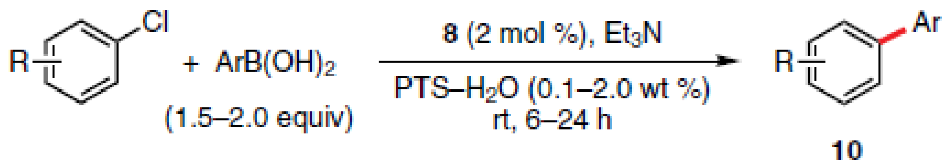
Suzuki–Miyaura Coupling

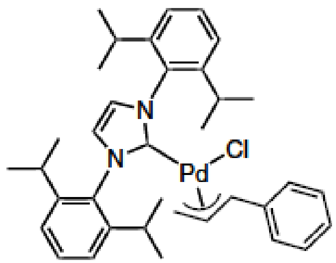
Use of PTS-H_2O as Solvent



Lipshutz, B. H.; Petersen, T. B.; Abela, A. R. *Org. Lett.* **2008**, *10*, 1333.

Suzuki–Miyaura Cross-Couplings of Aryl Chlorides in PTS–H_2O



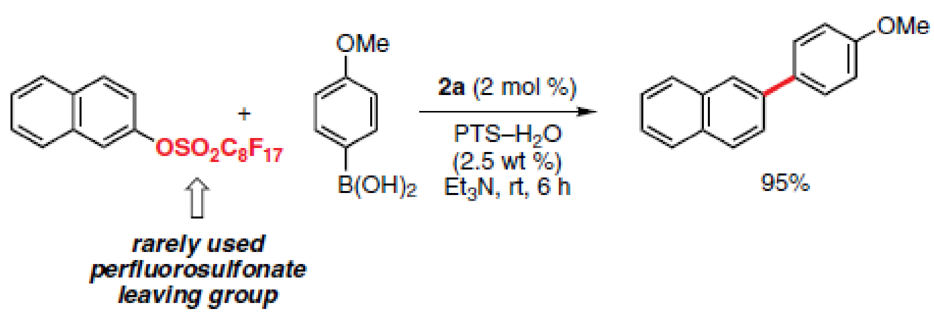


8, NEOLYST® CX31

10	R	Ar	Yield
a	2-MeO	Ph	100%
b	2,6-Me_2	4-$MeOC_6H_4$	99%
c	4-NC	2,4-$F_2C_6H_3$	96%
d	2,6-Me_2	1-Np	100%

Lipshutz, B. H.; Petersen, T. B.; Abela, A. R. *Org. Lett.* **2008**, *10*, 1333.

Phenol-based leaving groups such perfluorooctanesulfonate moiety, $C_8F_{17}SO_2$– represent another opportunity in PTS-assisted Suzuki–Miyaura couplings.

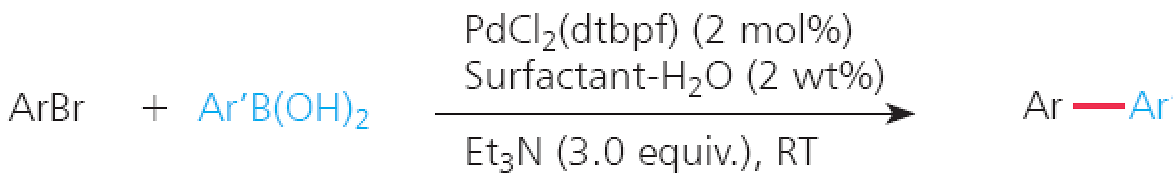


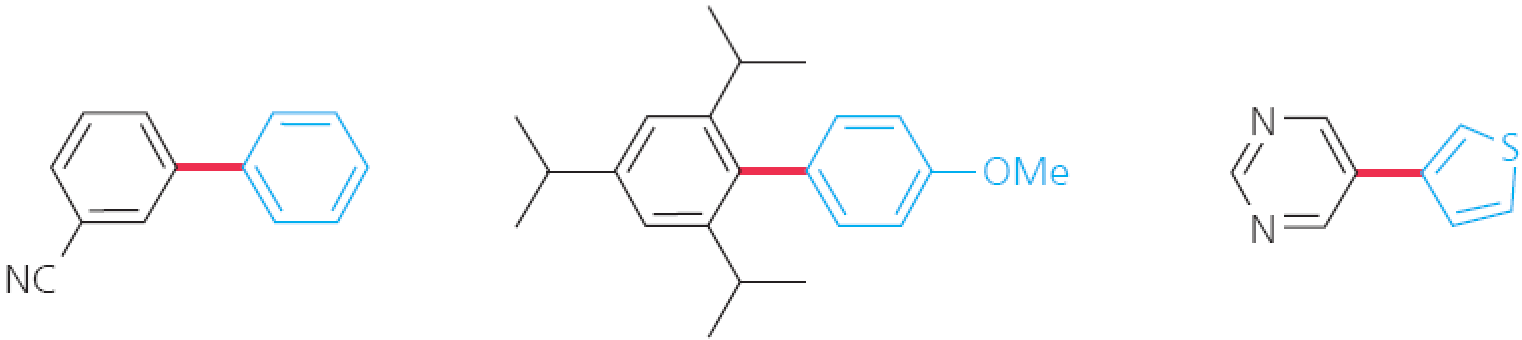
Zhang, W.; Chen, C. H.-T.; Lu, Y.; Nagashima, T. *Org. Lett.* **2004**, *6*, 1473

Synthetic Chemistry in Micellar Systems

Suzuki–Miyaura Coupling

Use of TPGS-750-M, PTS as Solvent





93% (2 h)
(TPGS-750-M)

88% (24 h)
(TPGS-750-M)

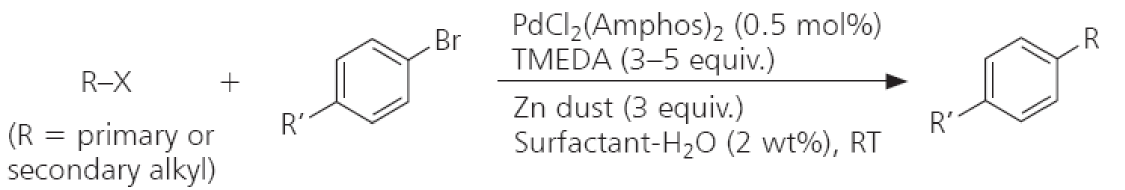
99% (6 h)
(PTS)

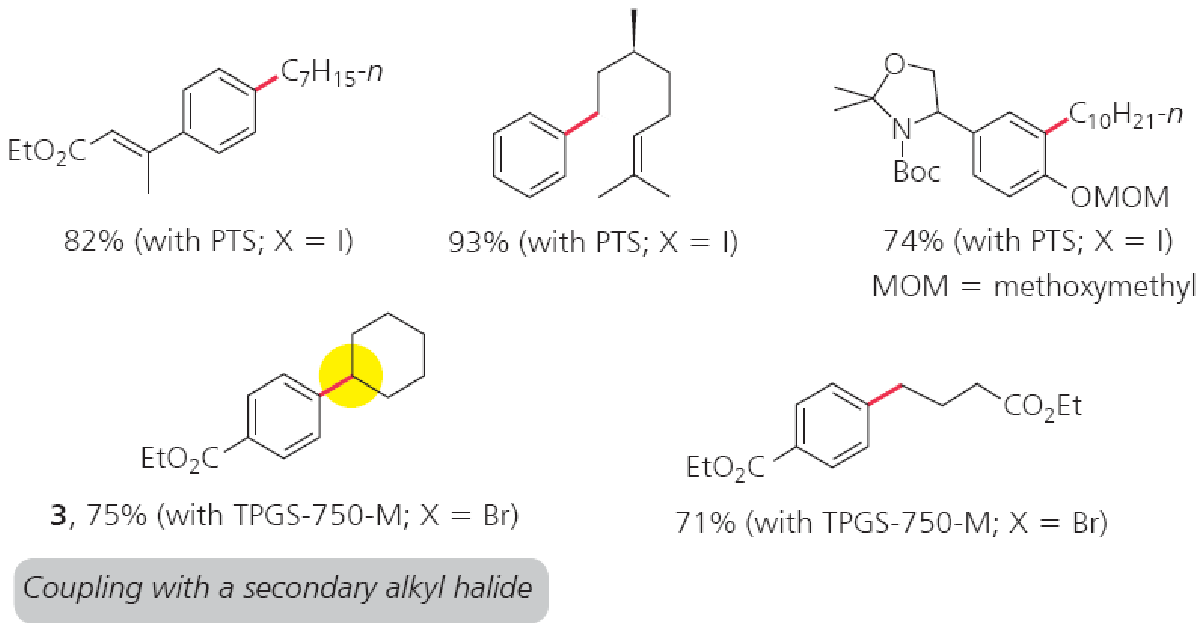
T. J. Colacot and H. A. Shea, *Org. Lett.*, **2004**, *6*, (21), 3731

Synthetic Chemistry in Micellar Systems

Negishi-Like Couplings in Water

Use of TPGS-750-M, PTS



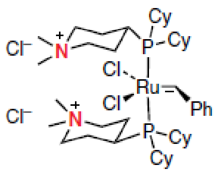


A. Krasovskiy, C. Duplais and B. H. Lipshutz, *J. Am. Chem. Soc.*, **2009**, *131, (43), 15592*

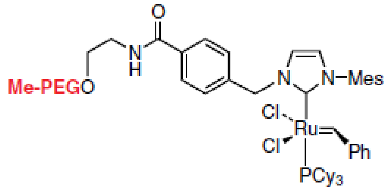
Synthetic Chemistry in Micellar Systems

Olefin Metathesis

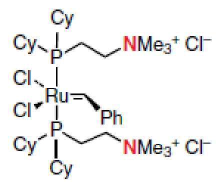
Representative Water-Soluble Catalysts for Metathesis



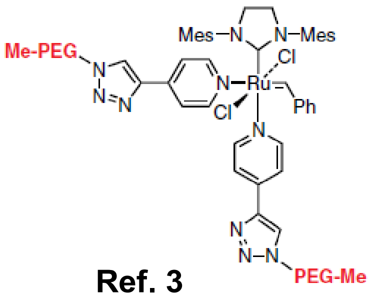
Ref. 1



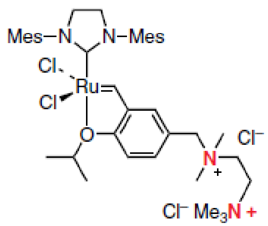
Ref. 2



Ref. 1



Ref. 3



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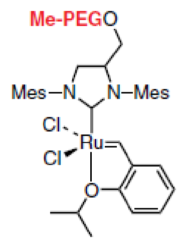


Ref. 5

1. Mohr, B.; Lynn, D. M.; Grubbs, R. H. *Organometallics* **1996**, *15*, 4317. (b) Kirkland, T. A.; Lynn, D. M.; Grubbs, R. H. *J. Org. Chem.* **1998**, *63*, 9904. (c) Lynn, D. M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 3187.
2. Gallivan, J. P.; Jordan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **2005**, *46*, 2577.
3. Samanta, D.; Kratz, K.; Zhang, X.; Emrick, T. *Macromolecules* **2008**, *41*, 530.
4. Jordan, J. P.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5152.
5. Hong, S. H.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 3508.

Literature Reports on RCM Reactions in Water

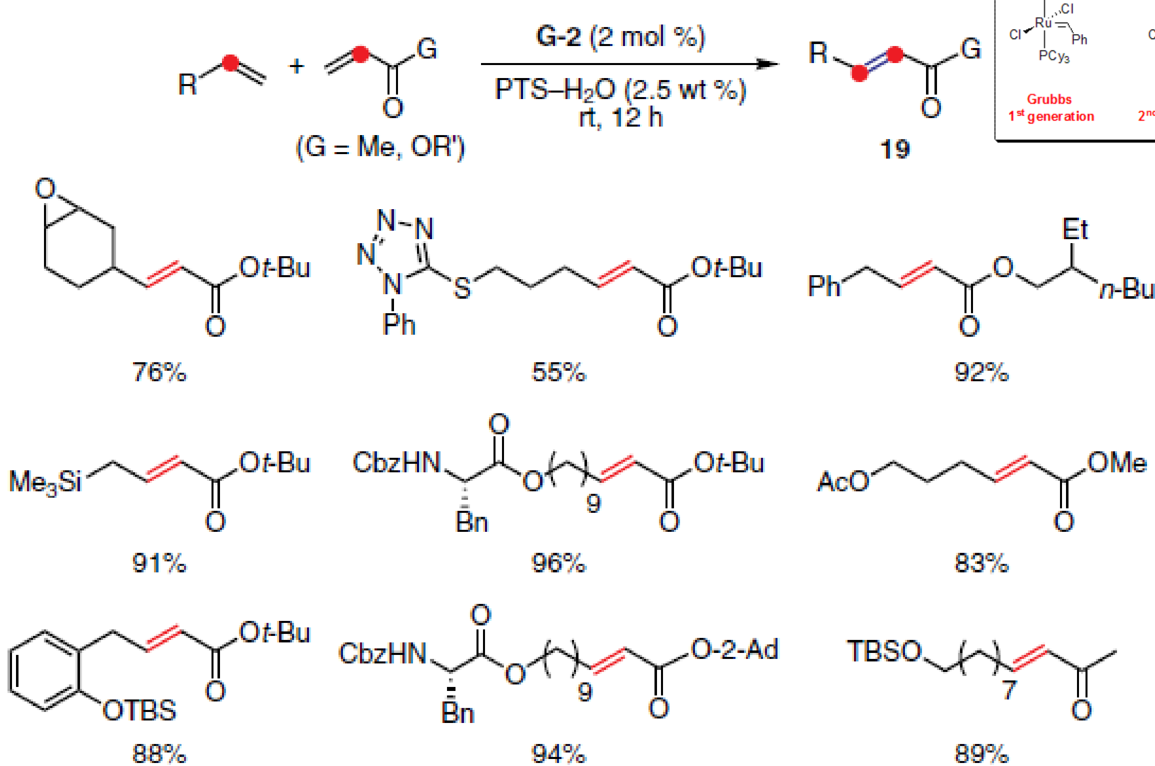
Year	Catalyst	Additive	Examples	Comments	Senior Author
1998	**13**	-	2	5–60% conversions, 5–10 mol % catalyst, degassed H_2O, 45 °C under argon, ring size: 5	Grubbs
2002	Grubbs 1st Gen	SDS[a]	8	23–100% conversions, 5 mol % catalyst, degassed H_2O, 25 °C under N_2, 0.5 h, 0.05 M SDS, ring sizes: 5 and 6	Sinou
2004	**20**	-	1	90% conversion, 1 mol % catalyst, degassed H_2O, 25 °C under N_2, 1 h, ring size: 5	Weberskirch
2006	**15**	-	5	5–95% conversions, 5 mol % catalyst, degassed H_2O, 25 °C under argon, 12–36 h, ring sizes: 5 and 6	Grubbs
2007	**21**	DTAC[b]	1	91% conversion, 25 °C, 3.5 h, 0.048 M DTAC, ring size: 5	Mingotaud
2007	**14**	–	5	5–95% conversions, 5 mol % catalyst, degassed H_2O, 30–45 °C, under argon, 24 h, ring sizes: 5 and 6	Grubbs
2008	Grubbs 2nd Gen	–	5	65–99% yields, 5 mol % catalyst, 40 °C ultrasonication, 5 h, ring sizes: 5 and 6	Grela
2008	**22**	–	4	95–99% conversions, 5 mol % catalyst, 25 °C, 5–24 h, ring size: 5	Grela

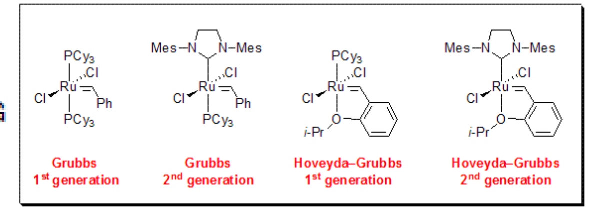
[a] SDS = sodium dodecyl sulfate. [b] DTAC = dodecyltrimethylammonium chloride.

Synthetic Chemistry in Micellar Systems

Olefin Metathesis

Use of PTS-H_2O as Solvent



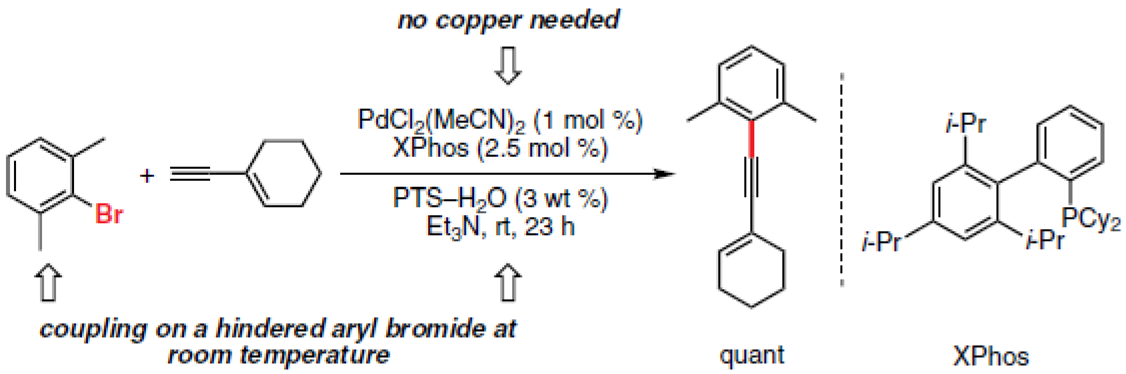


No special precautions are needed with respect to either solvent degassing or protection of reactions from air. Purification follows from established protocols (vide supra) usually involving simple filtration of reaction mixtures through a silica gel plug, followed by a standard extractive workup.

Lipshutz, B. H.; Aguinaldo, G. T.; Ghorai, S.; Voigtritter, K. *Org. Lett.* **2008**, *10*, 1325.

Synthetic Chemistry in Micellar Systems

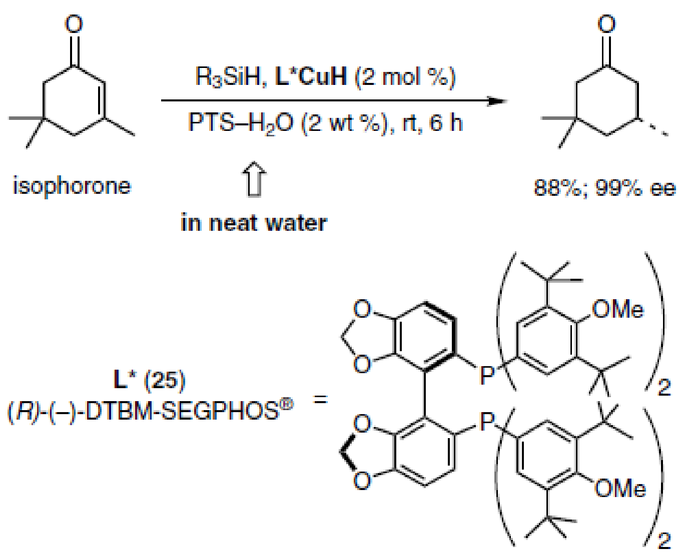
Sonogashira coupling in PTS–H_2O



Lipshutz, B. H.; Chung, D. W.; Rich, B. *Org. Lett.* **2008**, *10*, 3793.

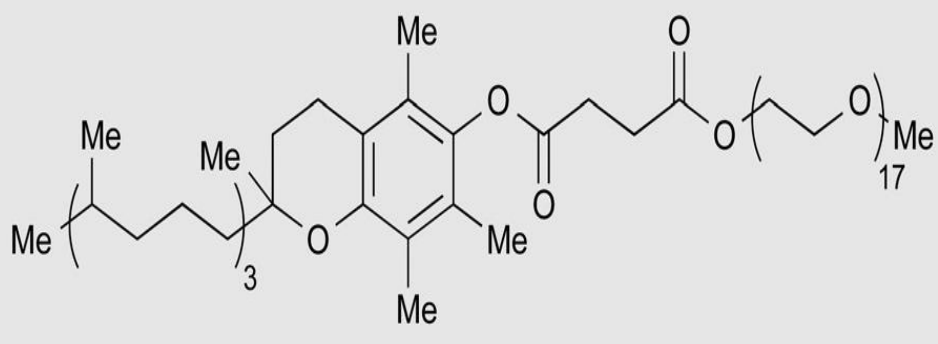
Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5993.

Asymmetric Hydrosilylation in PTS–H_2O



Lipshutz, B. H.; Ghorai, S. *Aldrichimica Acta*, **2008**, *41*, 59.

Application of TPGS-750-M as Solvent in Organic synthesis



TPGS-750-M (1) is the lead surfactant for many transition metal-catalyzed cross-couplings reactions.

This replaced its first generation precursor PTS.

They can be obtained from commercial suppliers.

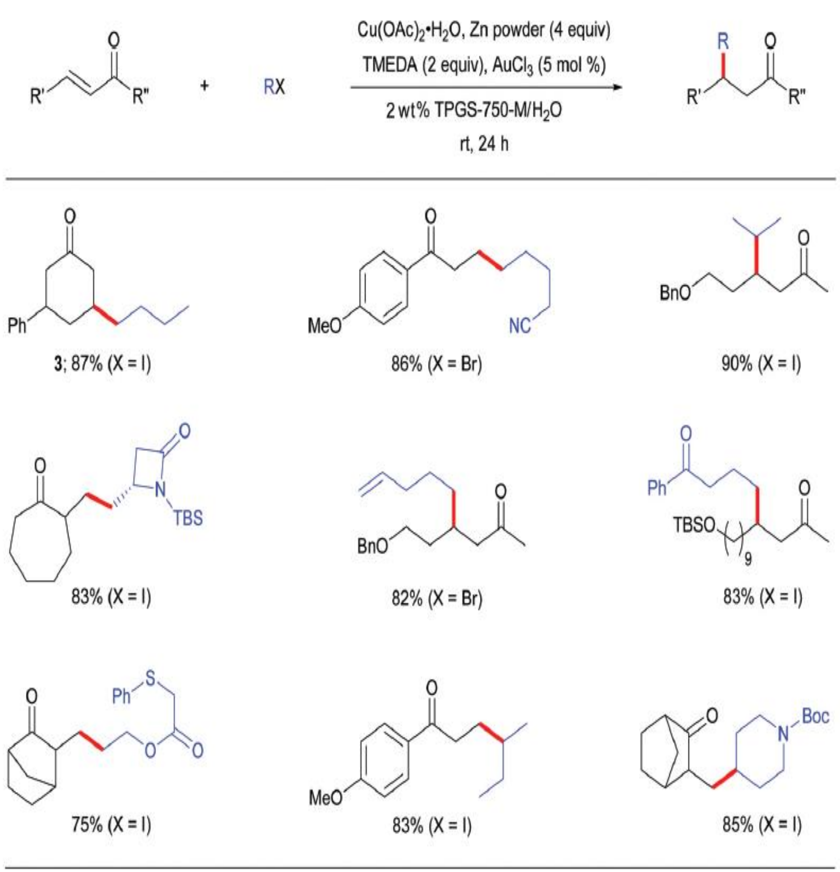
As has been shown in just about every reaction studied in either medium, these amphiphiles provide a synthetically more attractive outcome than identical reactions run in most other surfactants that might be chosen simply by virtue of expedience.

The impetus for development of second generation TPGS-750-M was predicated on the observation that micelles averaging 50–60 nm, as determined by Dynamic Light Scattering (DLS), appeared to afford yields that are equal to, or better than, those seen with PTS (average size 23 nm).

B. H. Lipshutz, S. Ghorai, A. R. Abela, R. Moser,T. Nishikata, C. Duplais, A. Krasovskiy, R. D. Gaston and R. C. Gadwood, *J. Org. Chem.*, **2011**, *76*, *4379*.

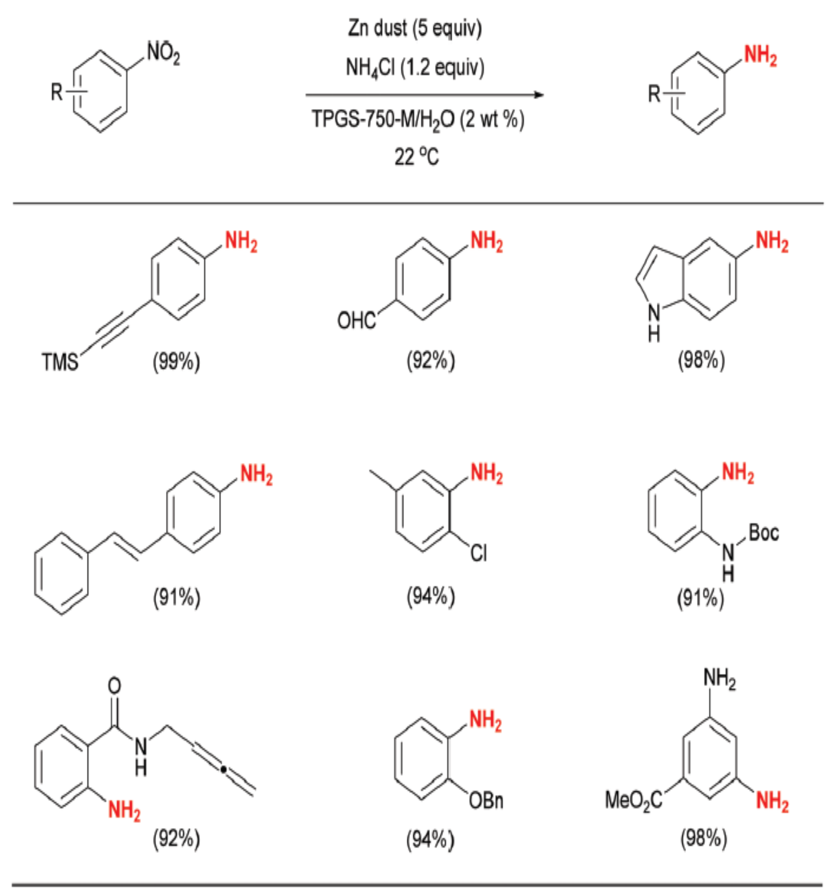
Application of TPGS-750-M as Solvent in Organic synthesis

Conjugate additions of alkyl halides to enones using TPGS-750-M



Bruce H. Lipshutz and Subir Ghoraib *Green Chem.*, **2014**, *16*, 3660–3679

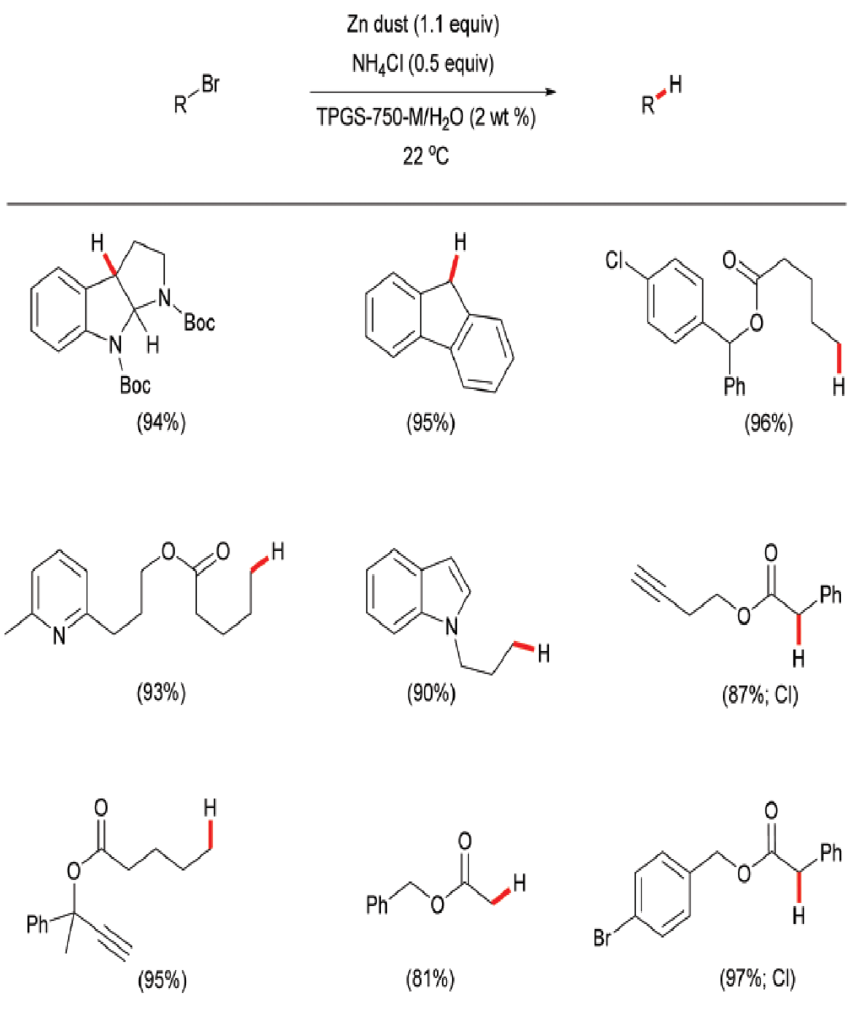
Zn mediated reductions of nitro-aromatics in water at room temperature



S. M. Kelly and B. H. Lipshutz, *Org. Lett.*, **2014**, *16*, 98.

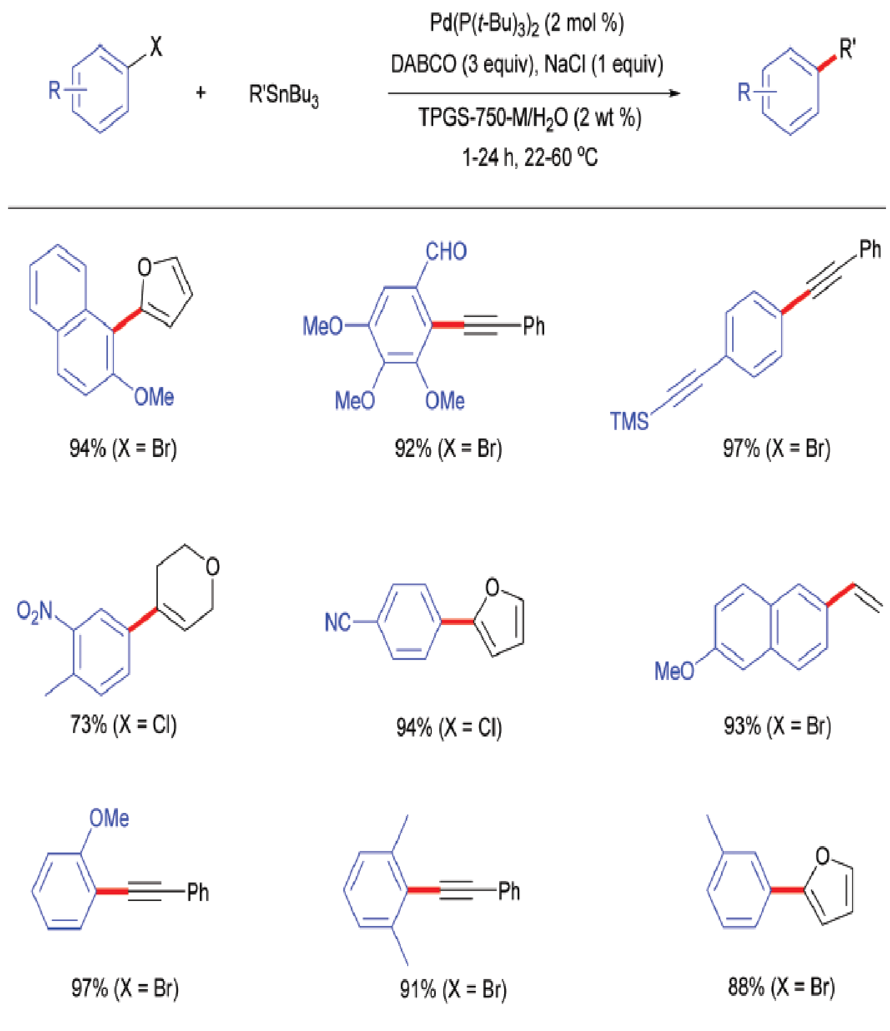
Application of TPGS-750-M as Solvent in Organic synthesis

Zn-mediated reductions of alkyl halides at room temperature.



P. Knochel, H. Leuser, L.-Z. Gong, S. Perrone and F. F. Kneisel, in *Handbook of Functionalized Organometallics, ed. P. Knochel, Wiley-VCH*, Weinheim, **2005**, *ch. 7, p. 251.*

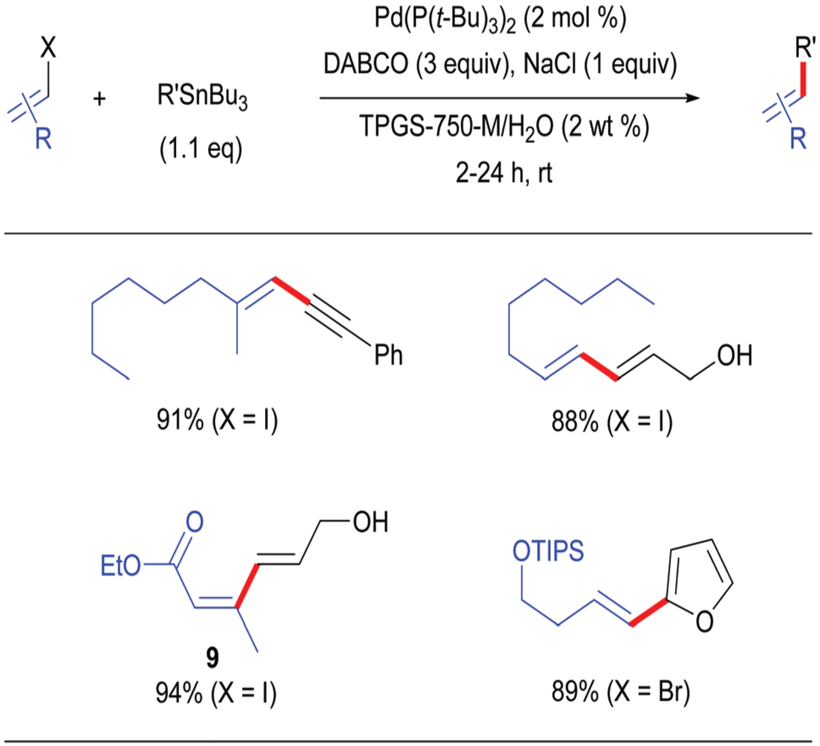
Stille couplings of aryl halides in water



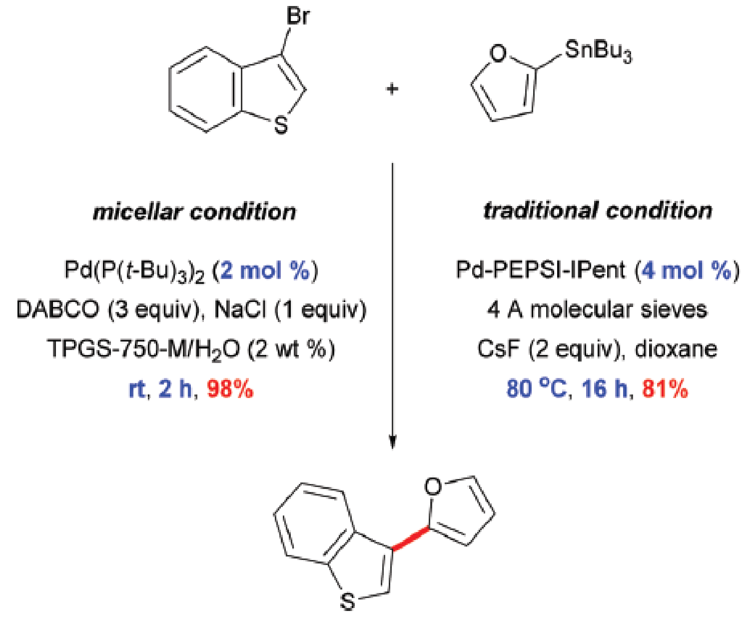
B. H. Lipshutz, R. Moser and K. R. Voigtritter, *Isr. J. Chem.*,**2010**, *50*, 691.

Application of TPGS-750-M as Solvent in Organic synthesis

Stille couplings of alkenyl halides in water at room temperature.



Comparison of Stille couplings in micellar vs. traditional conditions.

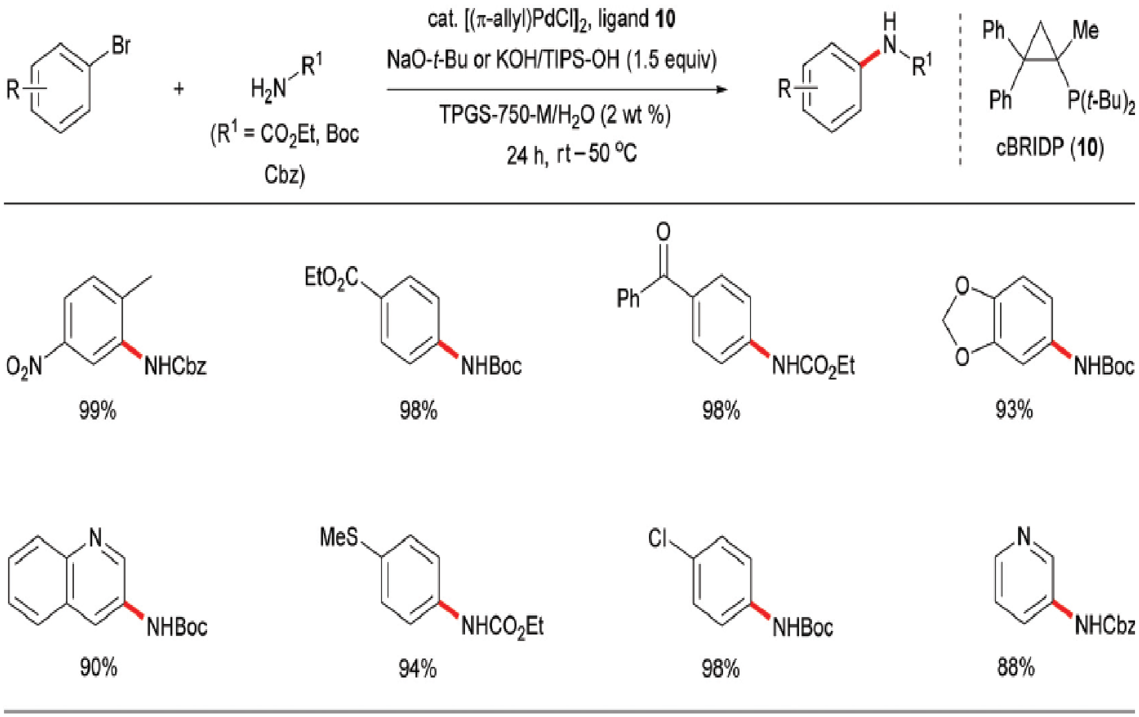


V. Farina and G. P. Roth, *Tetrahedron Lett*., **1991**, *32*, 4243.

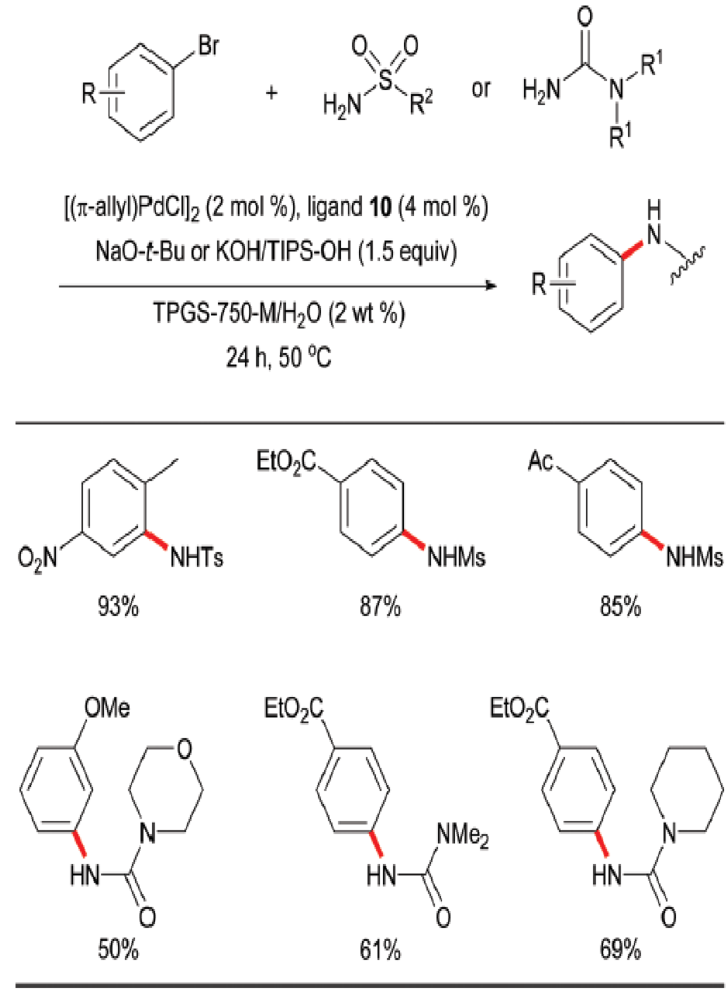
M. Dowlut, D. Mallik and M. G. Organ, *Chem. – Eur. J.*, **2010**, *16*, 4279.

Application of TPGS-750-M as Solvent in Organic synthesis

Aminations of aromatic and heteroaromatic rings



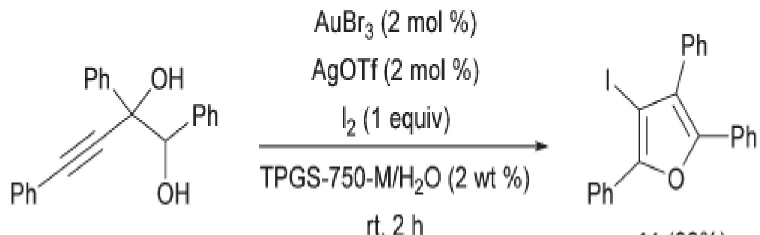
N. A. Isley, S. Dobarco and B. H. Lipshutz, *Green Chem.*,**2014**, *16*, 1480.



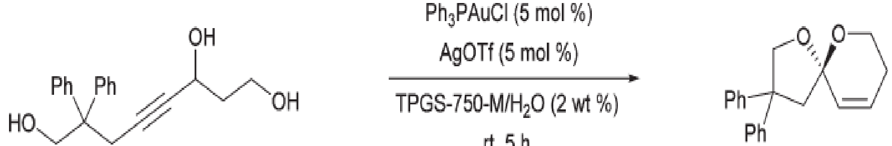
J. Yin and S. L. Buchwald, *Org. Lett.*, **2000**, *2*, 1101

Application of TPGS-750-M as Solvent in Organic synthesis

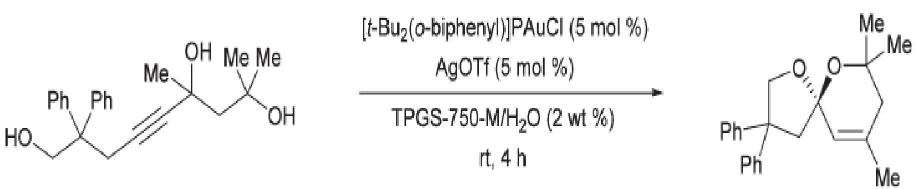
Au-catalyzed cyclodehydrations in water



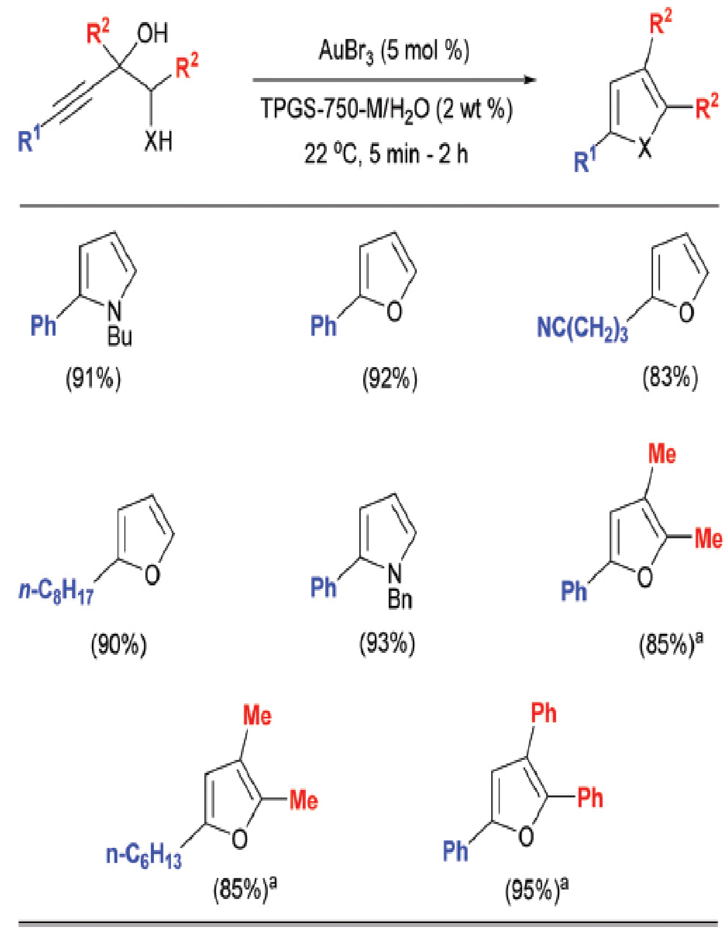
11 (93%)



12 (89%)

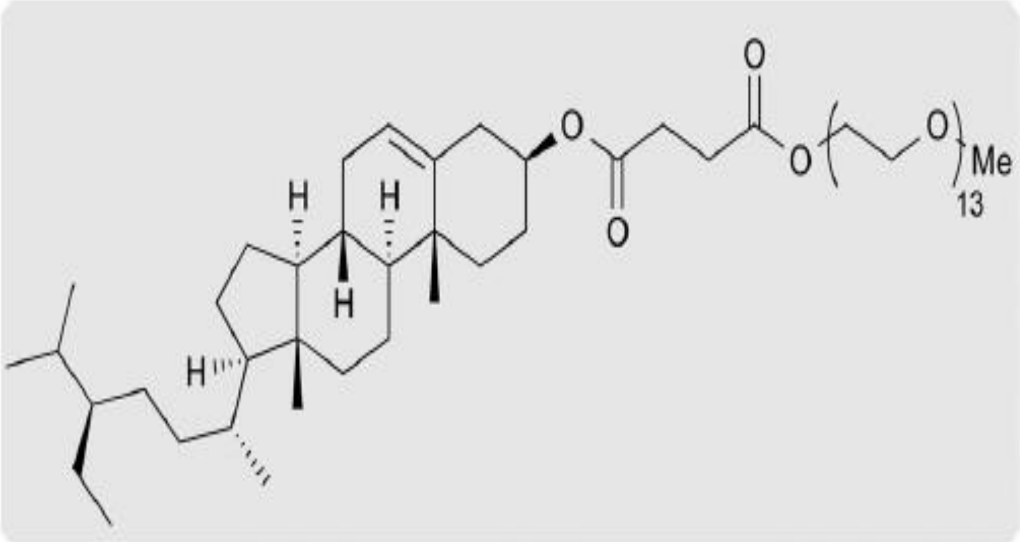


13 (46%)



S. R. K. Minkler, N. A. Isley, D. J. Lippincott, N. Krause and B. H. Lipshutz, *Org. Lett.*, **2014**, *16*, 724.

“Nok.” a third generation designer surfactant(SPGS-550-M)

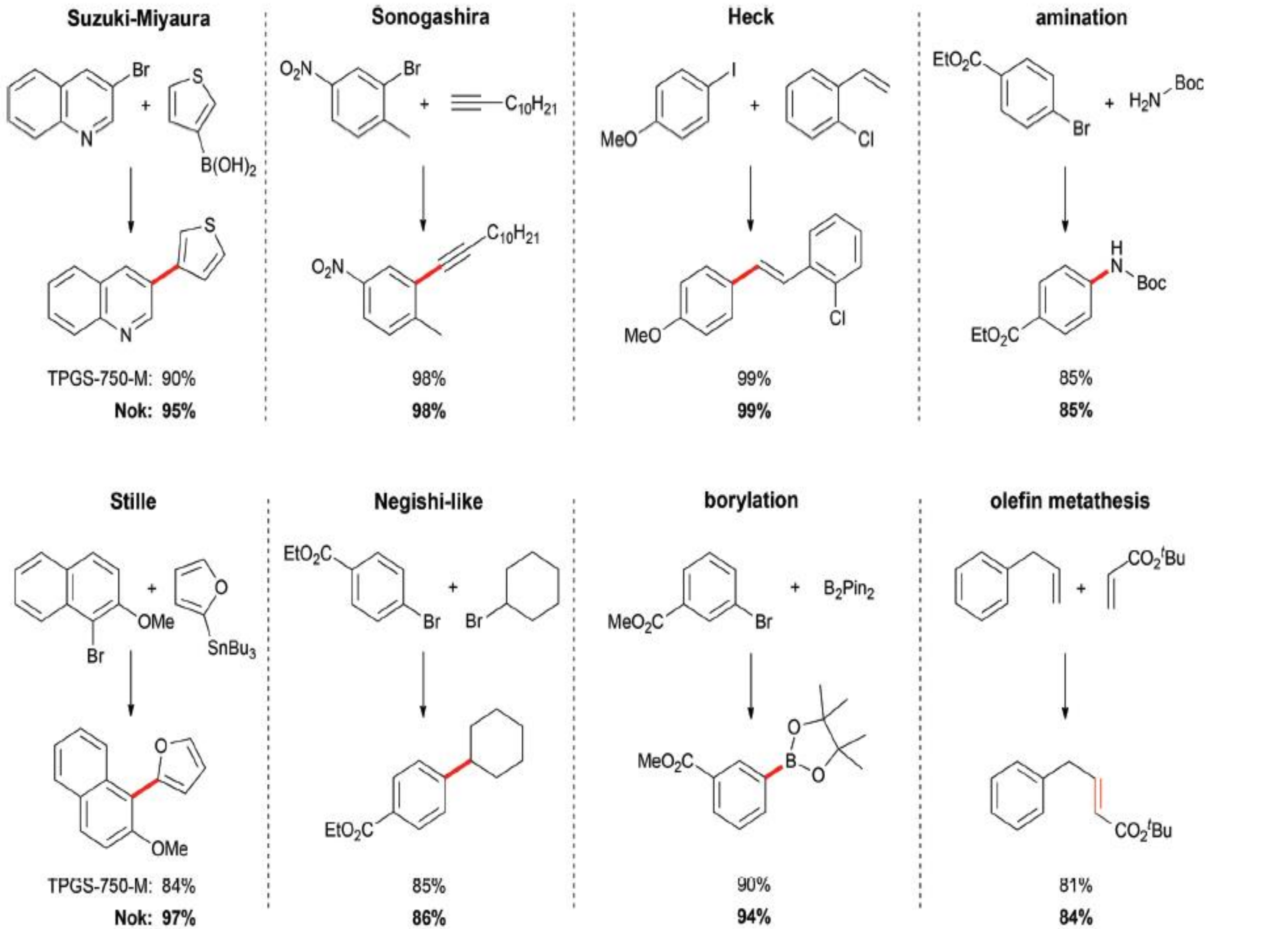


SPGS-550-M was found empirically that better results were obtained when the surfactant incorporated MPEG-550, rather than MPEG-750.

This new micelle-forming compound, which according to the common nomenclature would be “SPGS-550-M” (SPGS = Sitosteryl PolyoxyGlyceryl Succinate), has been named “Nok”.

P. Klumphu and B. H. Lipshutz, *J. Org. Chem.*, **2014**, *79*, 888.

Cross-couplings in TPGS-750-M–H_2O vs. Nok–H_2O

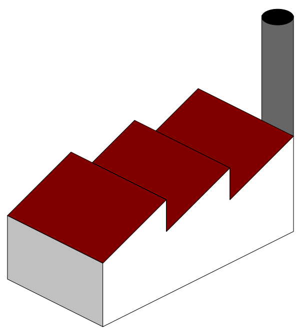


Bruce H. Lipshutz* and Subir Ghorai, *Green Chem.*, **2014**, *16*, 3660

3. C-S Coupling Reaction

Preparation of phenols from CsOH and aryl iodides using CuO on mesoporous silica

$$\text{Ar-I} + \text{CsOH} \xrightarrow{\text{CuO on Mesoporous silica}} \text{Ar-OH}$$



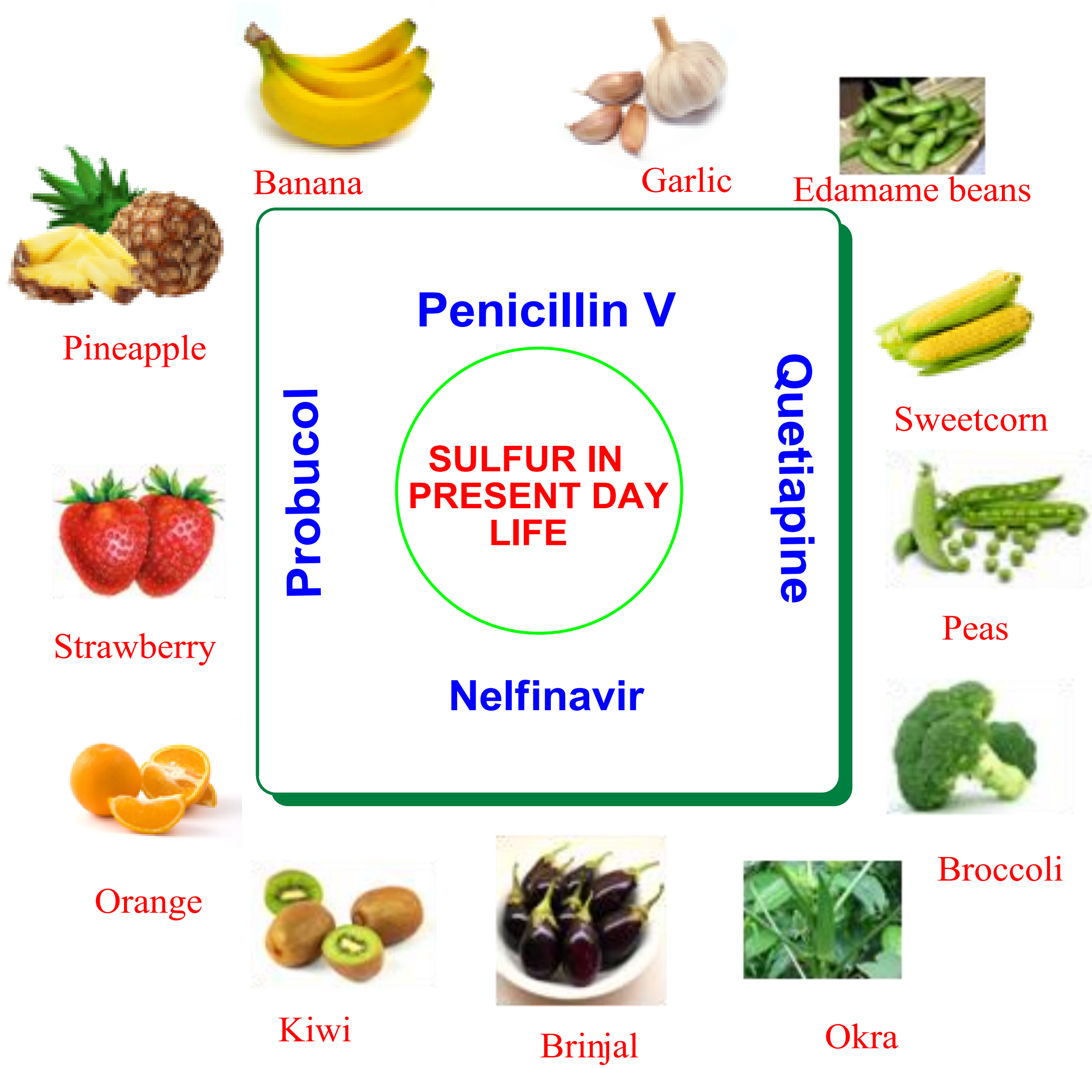
+

IC industry

rice husks (稻殼)

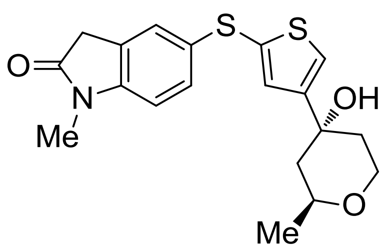
Chan, C.-C.; Chen, Y.-W.; Su, C.-S.; Lin, H.-P.; Lee, C.-F. *Eur. J. Org. Chem.* **2012**, 7288-7293.

Sulfur-Containing Molecules

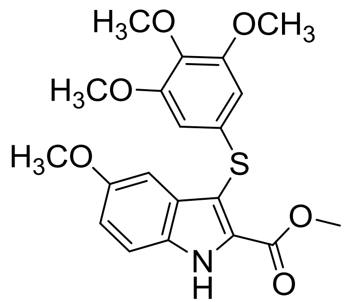


Lee, C.-F.; Liu, Y.-C.; Badsara, S. S. *Chem. Asian. J.* **2014**, *9*, 706-722 (Focus Review).

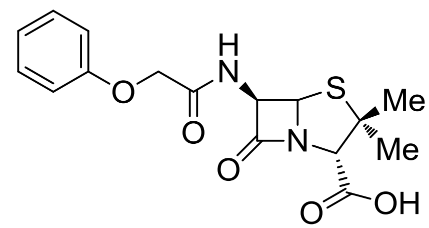
Biologically active thioethers being used as drugs or drug candidates



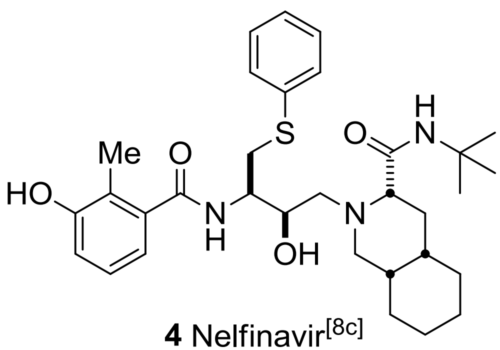
1 AZD44071[8a]



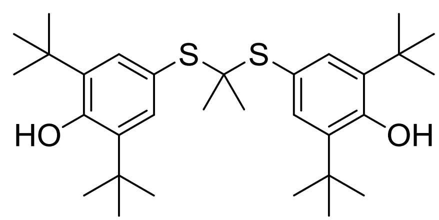
2 ATI2



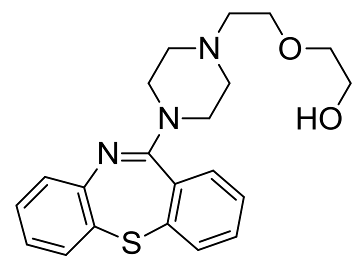
3 Penicillin V[8b]



4 Nelfinavir[8c]

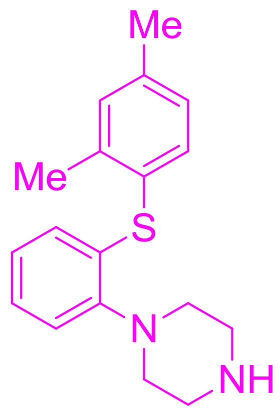


5 Probucol



6 Quetiapine[8d]

Brintellix (Vortioxetine) : Durg

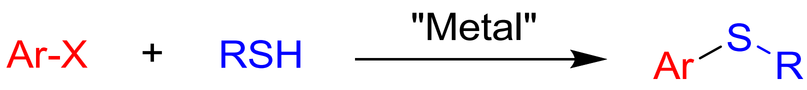


- **Approved by US FDA in Sepetmeber 2013**
- **It is an inhibitor of serotonin (5-HT) reuptake and is indicated for major depression.**
- **It is also an agonist of 5-HT1A receptors, a partial agonist of 5-HT18 receptor and an antagonist of 5-HT3 and 5-HT7 receptor.**
  Also helps patients think, concentrate and remember better.

- **It is considered the first and only compound with thispersticular combination of pharamcodynamic activity.**

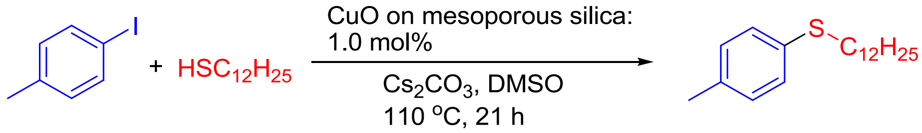
Last summer, Lundbeck reported it was recruiting more than 200 sales reps to help market the drug, which is expected to reap peak sales of $ 1.5 billion.

1.



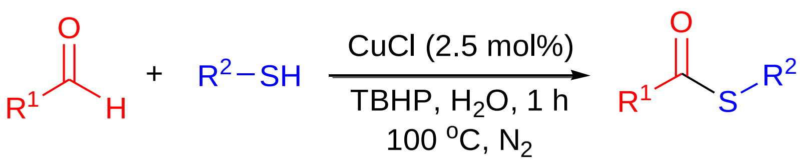
By Iron: *Chem. Commun.* **2009**, 4450;
J. Org. Chem. **2012**, *77*, 6100.
By Copper: *Eur. J. Org. Chem.* **2011**, 1776;
Org. Lett. **2011**, *13*, 5204;
Eur. J. Org. Chem. **2011**, 1776;
Synlett **2013**, 2320.
By Rhodium: *Tetrahedron Lett.* **2012**, *53*, 4365.
By Manganese: *Chem. Asian. J.* **2013**, *8*, 1029.
Chem. Asian. J. **2013**, *9*, 706 (Focus Review).

2.



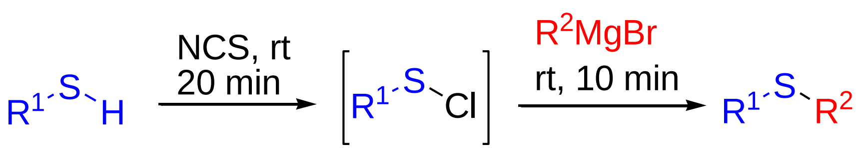
Chem. Commun. **2010**, *46*, 282.

3.



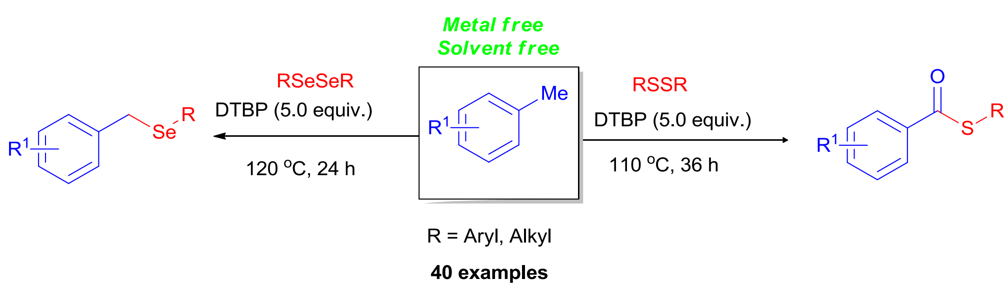
Green Chem. **2013**, *15*, 2476;
Green Chem. **2014**, *16*, 264;
J. Org. Chem. **2014**, 79, 4561;
20*RSC Adv.* **14**, *4*, 41237.

4.



J. Org. Chem. **2012**, 77, 10369.

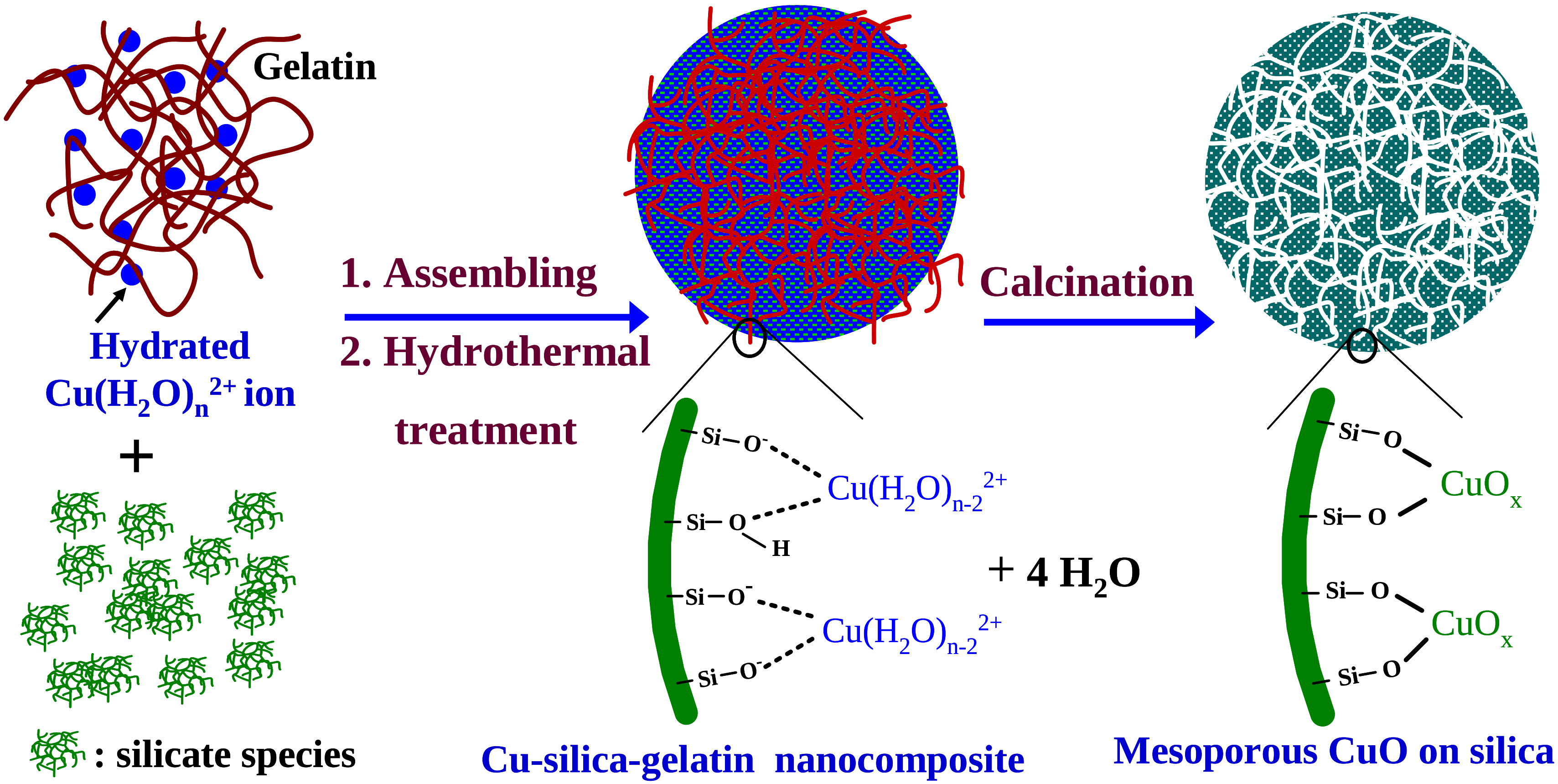
5.



Chem. Commun. **2014**, *50*, 11374;
Green Chem. **2014**, 16, 357 (For P-S Bond)

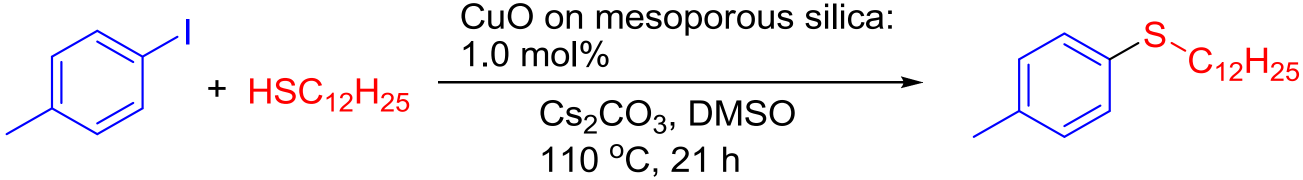
Synthesis of CuO on mesoporous silica and its applications for C-S Cross-Coupling Reaction:

Incorporation of Metal Oxides into Mesoporous Silica

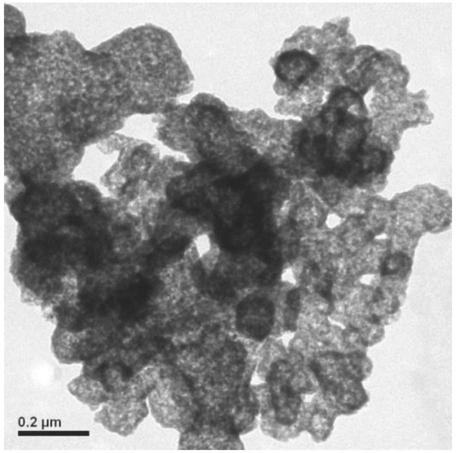


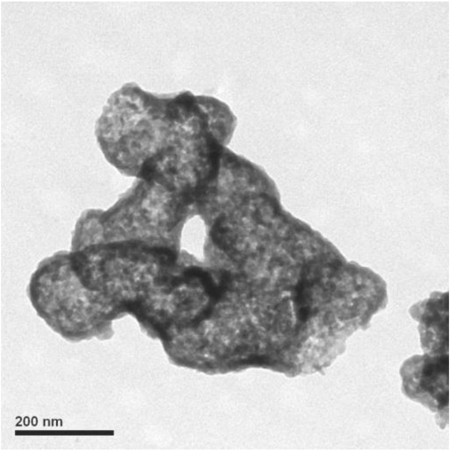
Chen, C.-K.; Chen, Y.-W.; Lin, C.-H.; Lin, H.-P.; Lee, C.-F. *Chem. Commun.* **2010**, *46*, 282-284 (Highlighted by *Synfact* **2010**, *3*, 0370).

Reuse of CuO on mesoporous silica



Run	1	2	3	4
Yield[%]	85	83	78	78





TEM images of the CuO on mesoporous silica after fourth run reaction

Chen, C.-K.; Chen, Y.-W.; Lin, C.-H.; Lin, H.-P.; Lee, C.-F. *Chem. Commun.* **2010**, *46*, 282-284 (Highlighted by *Synfact* **2010**, *3*, 0370).

Synthesis of Thioesters

Transition-Metal-Catalyzed:

Cu: Green Chem. 2013

(Top 10 most-accessed articles July–September 2013)

Fe: J. Org. Chem. 2014

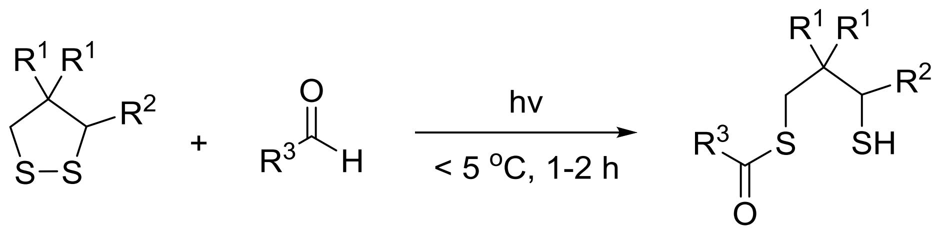
Transition-Metal-Free:

Green Chem. 2014

Chem. Commun. 2014

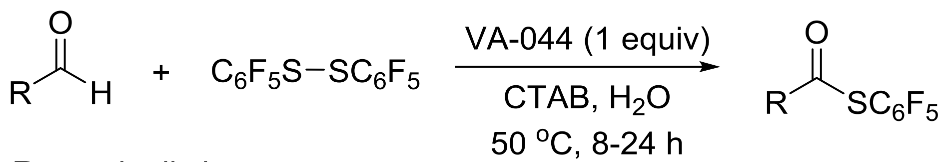
Copper-catalyzed coupling reaction of aldehydes with thiols in water

Background

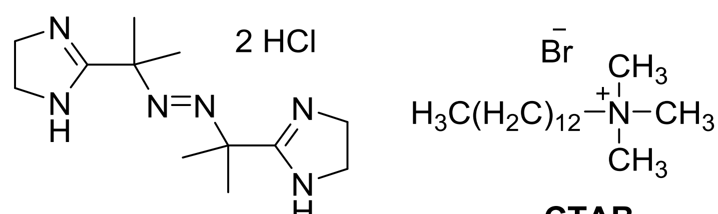


R^1 = H, Me, Et, $(CH_2)_5$
R^2 = H, $(CH_2)_4CO_2H$
R^3 = Me, Et, *i*Pr, *t*Bu, Ph

Takagi, M.; Goto, S.; Matsuda, T. *Chem. Commun.* **1976**, 92.



R = aryl, alkyl

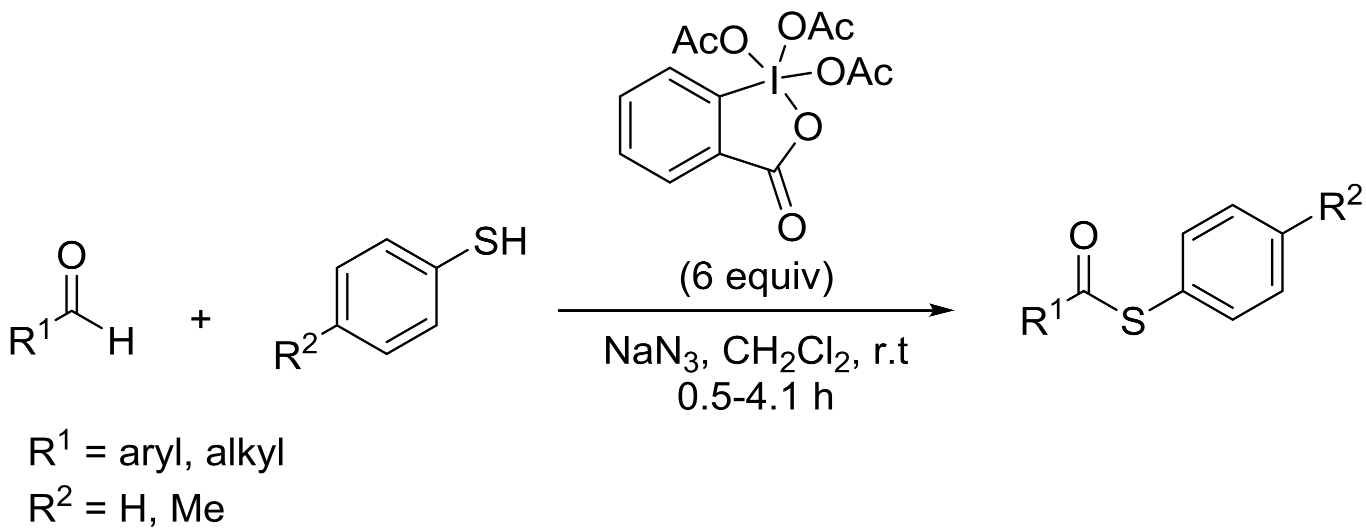


VA-044 **CTAB**

Nambu, H.; Hata, K.; Matsugi, M.; Kita, Y. *Chem. Commun.* **2002**, 1082.

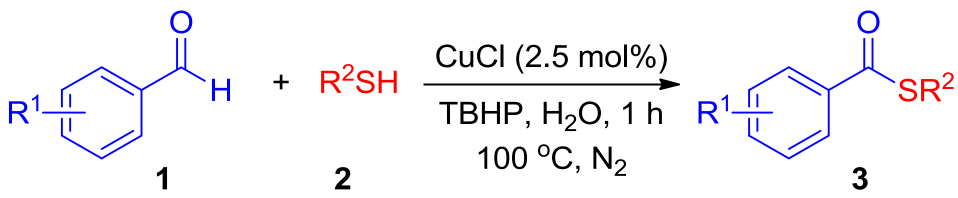
Copper-catalyzed coupling reaction of aldehydes with thiols in water

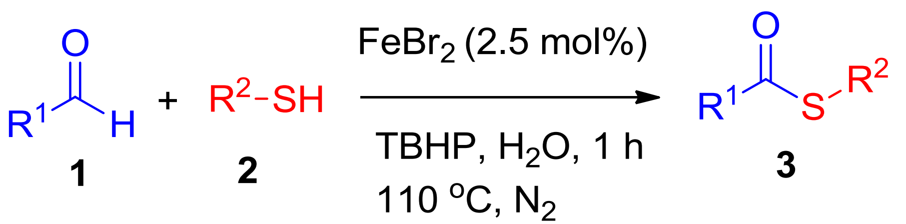
Background

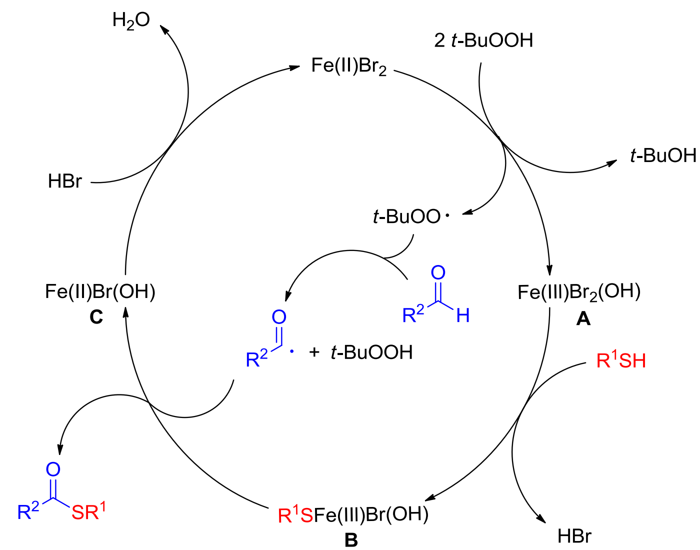


Bandgar, S. B.; Bandgar, B. P.; Korbad, B. L.; Sawant, S. S. *Tetrahedron Lett.* **2007**, *48*, 1287.

Metal-Catalyzed Synthesis of Thioesters from Thiols and Aldehydes in Water







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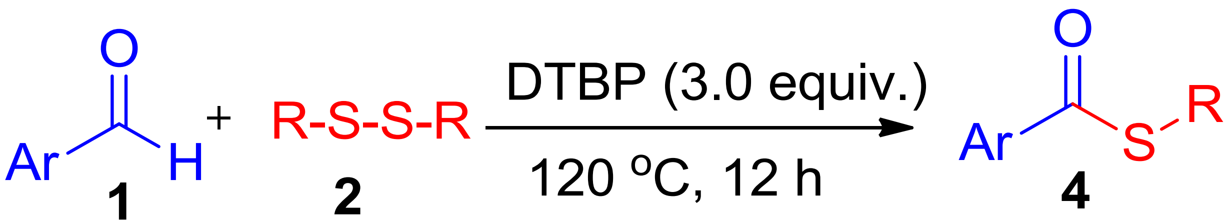
Metal-free cross-coupling reaction of aldehydes with disulfides by using DTBP as an oxidant under solvent-free conditions



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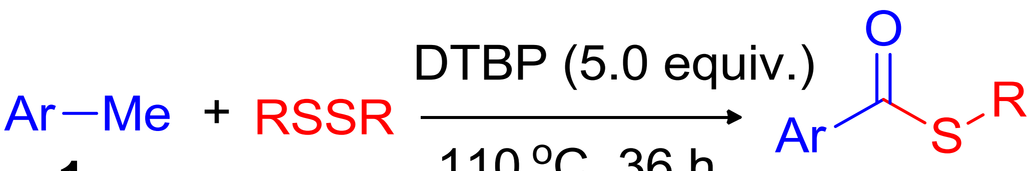
Metal-free sp^3 C-H functionalization: a novel approach for the syntheses of thioesters from methyl arenes



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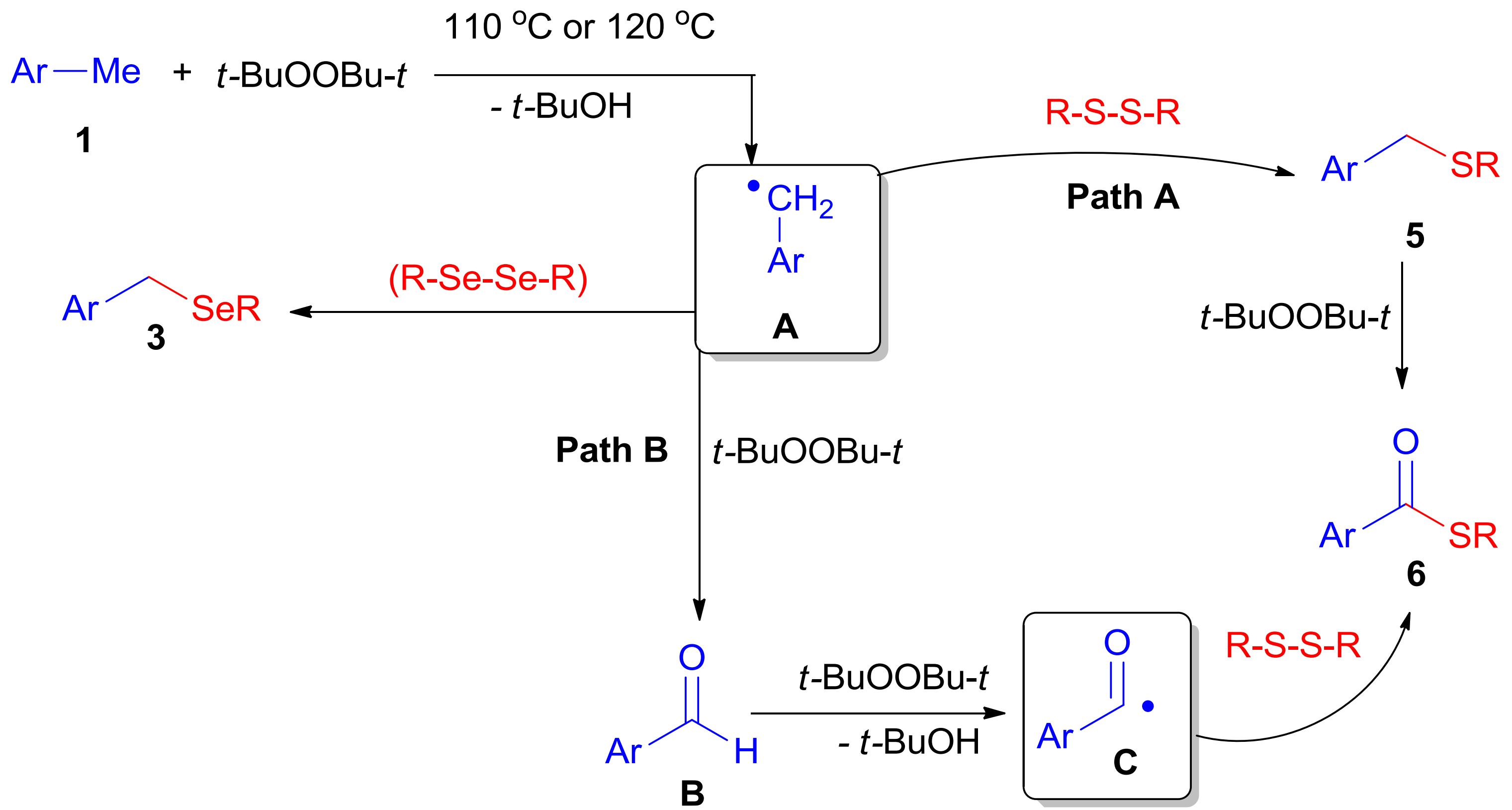
Metal-free sp^3 C-H functionalization: a novel approach for the synthesis of thioesters from methyl arenes

Plausible Mechanism



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Thank You!