RCC, 03/17/14, Cyril François

Aerobic oxidation in nanomicelles of aryl alkynes, in water at room temperature

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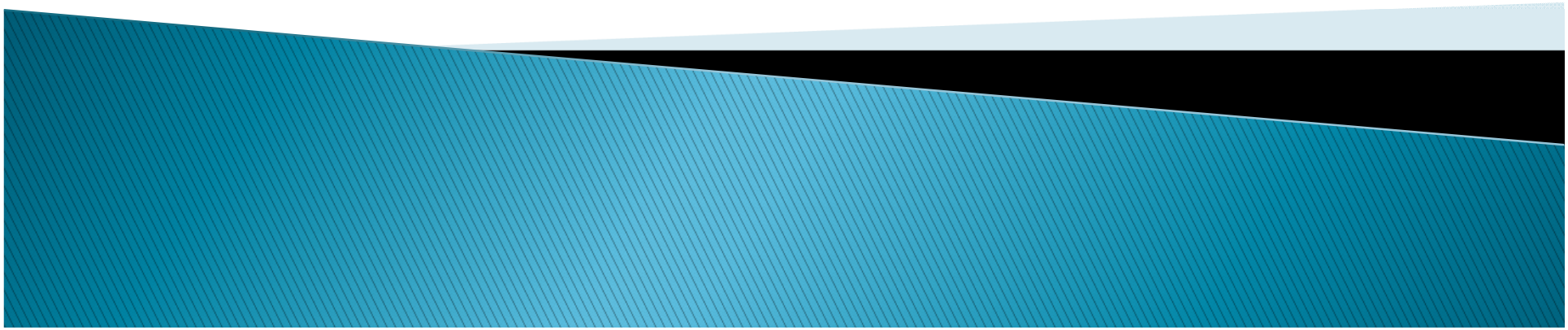
Angew. Chem. Int. Ed. 2014
DOI : 10.1002/anie.201310634

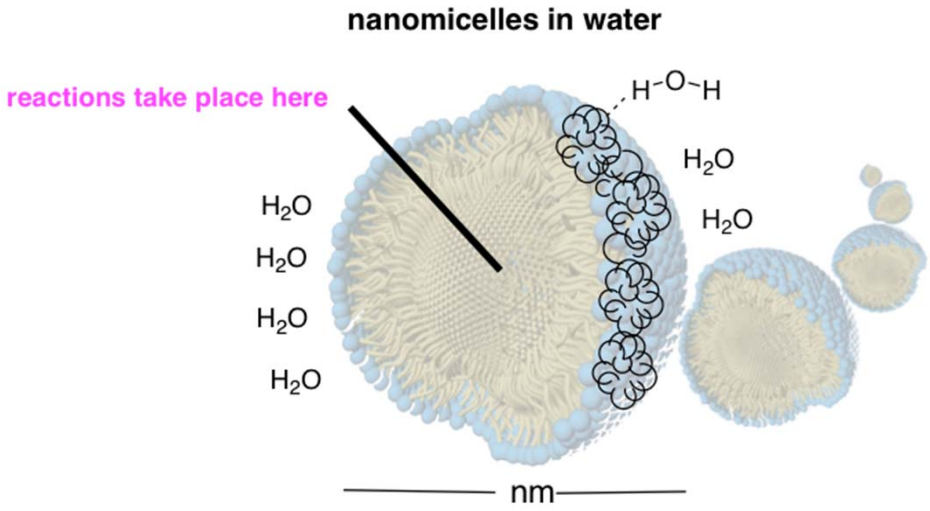


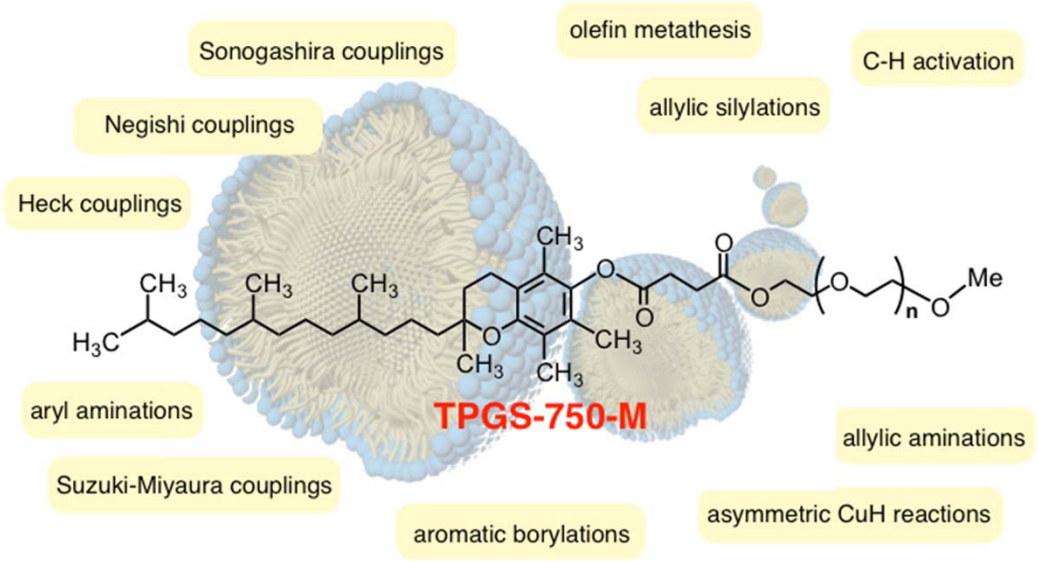
Standards of green chemistry

- Minimize organic waste
- Use cheap and non-toxic/polluting reagents
- No harsh conditions
- Often not compatible with organometallic chemistry

Previous works from Lipshutz group

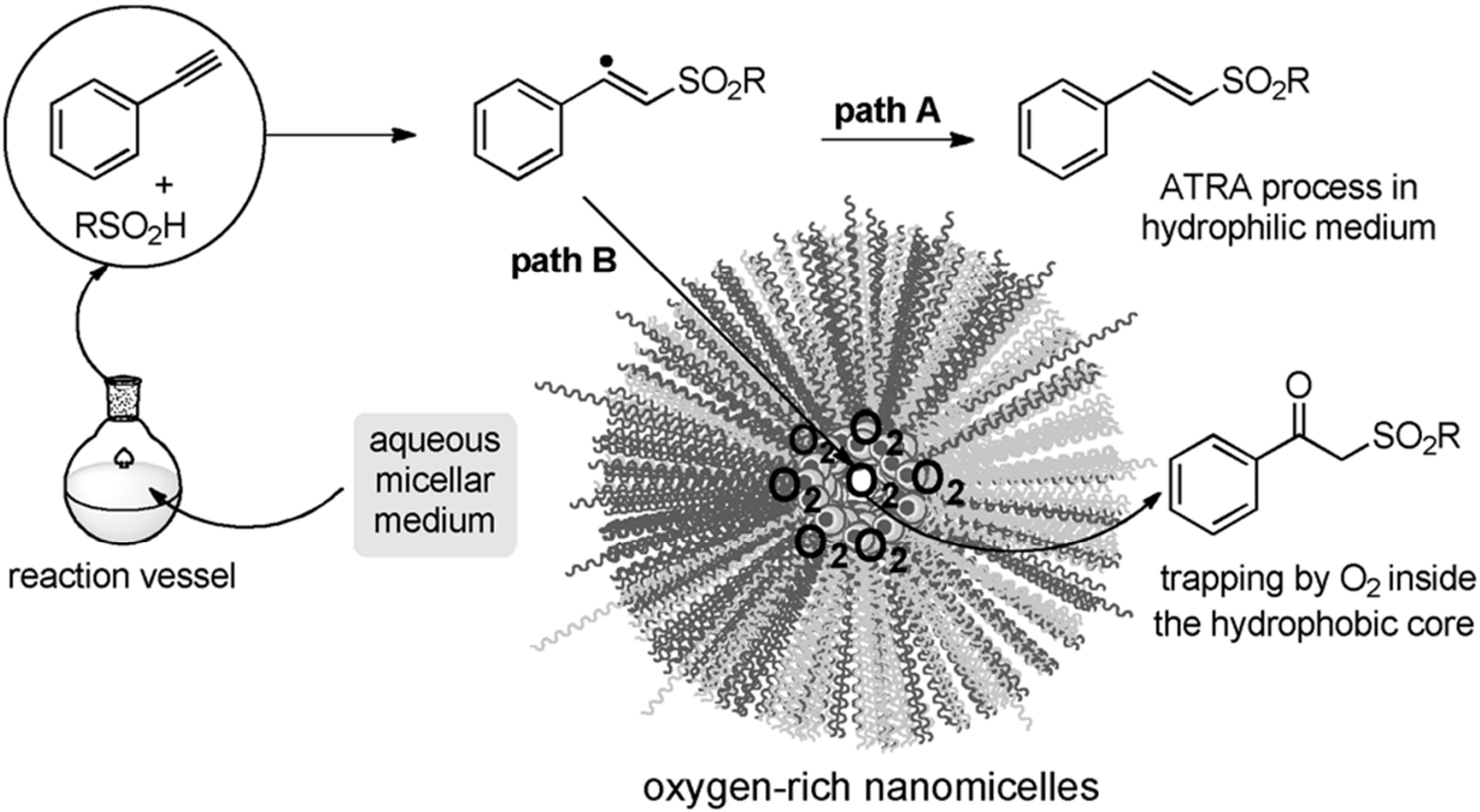
Development of organometallic chemistry in water



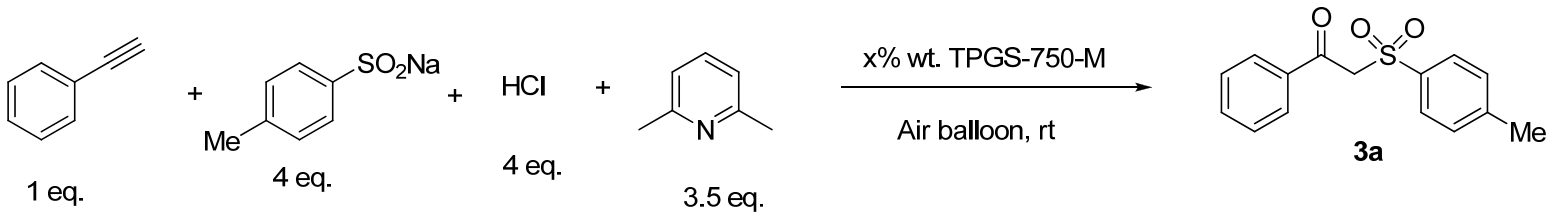


A step towards sustainability

Overview


+
RSO_2H
reaction vessel
aqueous micellar medium
SO_2R
path A
SO_2R
ATRA process in hydrophilic medium
path B
O_2
oxygen-rich nanomicelles
O
SO_2R
trapping by O_2 inside the hydrophobic core

Optimization of the reaction



1 eq. + 4 eq. + 4 eq. + 3.5 eq.

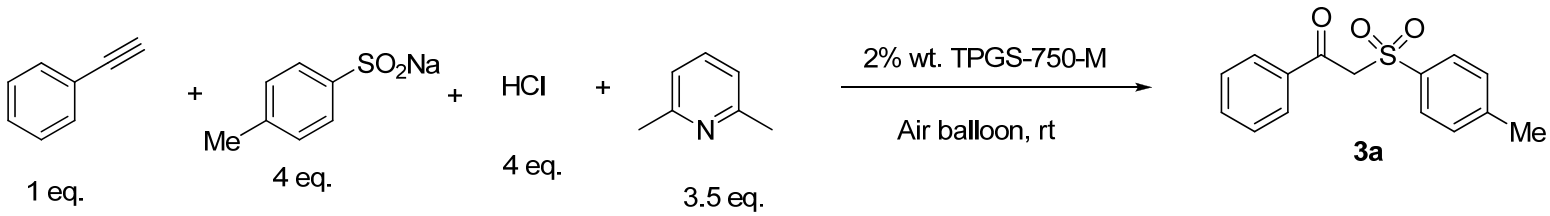
3a

2e. Effect of surfactant conc. in water

Entry	% (w/w) of TPGS-750M	Time (h)	% yield 3
1	0.5	25	10
2	1.0	25	12
3	**2.0**	**6.5**	**84**
4	3.0	6*	50
5	4.0	6*	30

*extending a reaction time up to 24 h didn't improve the yields.
Other reaction conditions are: 1 mmol, 0.3 M phenylacetylene in TPGS-750M solution in water, 4.0 mmol sodium *p*-toluenesulfinate), 4.0 mmol HCl , and 3.5 mmol 2,6- lutidine (except phenylacetylene, all reagents were added in two portions in 80 min interval), RT, air balloon.

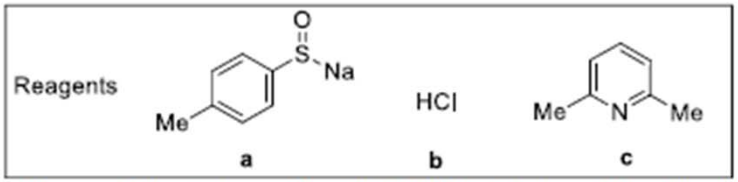
Optimization of the reaction



1 eq. + 4 eq. + 4 eq. + 3.5 eq.

3a

2i. Effect of a portion-wise addition of reagents on yield



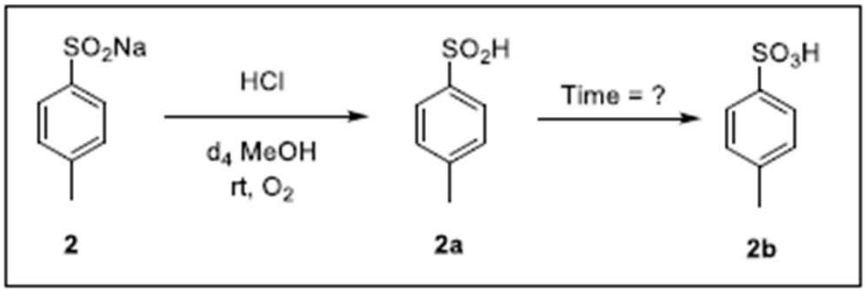
Conditions: Mixing, and then stirring **a** and **b** in TPGS-750M for 3-4 minutes followed by addition of **c**

Entry	a (mmol.)	b (mmol.)	c (mmol.)	% yield **14**
1	4.0	4.0	3.5	40
*2	2.0	2.0	1.75	84
#3	1.0	1.0	0.9	70

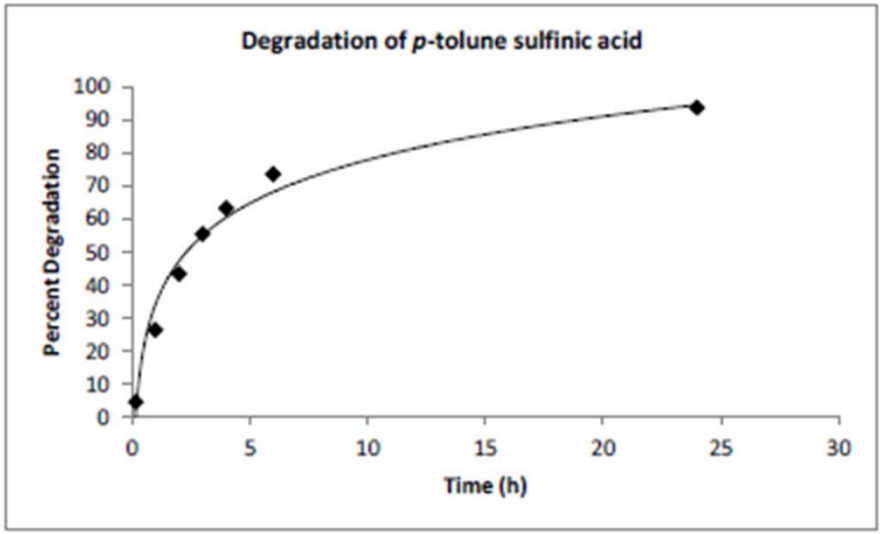
*after 80 minutes of first addition, same amounts of reagents were sequentially added.
a, **b**, and **c** were added four times after each 80 minutes intervals.
Other reaction conditions: 1 mmol, 0.3M phenylacetylene in 2% surfactant, 4.0 mmol sodium *p*- toluenesulfinate), 4.0 mmol HCl, 3.5 mmol 2,6-lutidine (all these reagents were added in two portions in 80 min interval), RT, air balloon, 6 h.

Optimization of the reaction

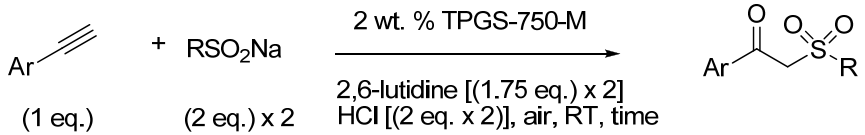
2j. Aerobic autoxidation of *p*-toluene sulfinic acid (2)

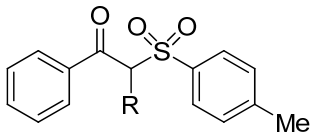


Conditions: Sulfinic acid (20 mg, 1 equiv.), HCl (9 µL, 1 equiv.), d_4-MeOH, O_2 ballon, rt. Reaction performed in NMR tube.

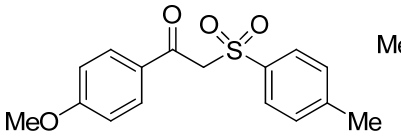


Scope of the reaction

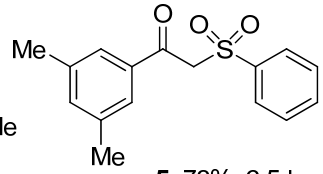




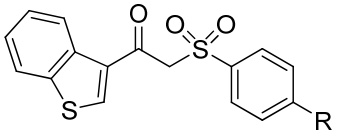
3a, R = H, 82%, 6 h
3b, R = Me, 78%, 9 h
3c, R = Et, 69%, 10 h



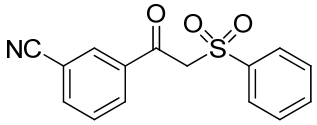
4, 71%, 7 h



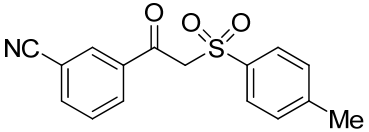
5, 78%, 6.5 h



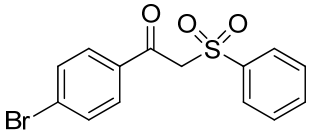
6a, R = H, 76%, 6.5 h
6b, R = Me, 78%, 6.0 h



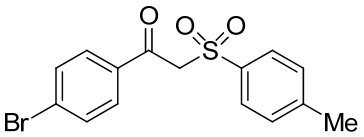
7, 69%, 9 h



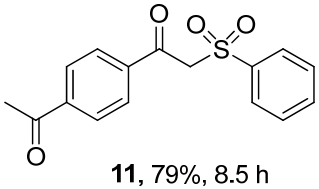
8, 71%, 8.5 h



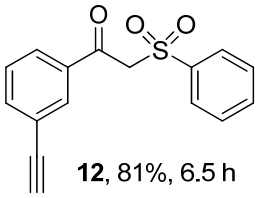
9, 71%, 8.5 h



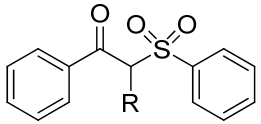
10, 75%, 8.5 h



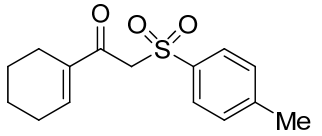
11, 79%, 8.5 h



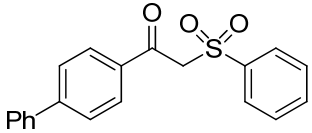
12, 81%, 6.5 h



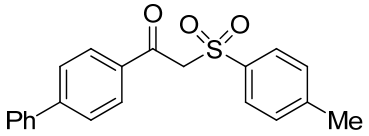
13a, R = H, 84%, 6 h
13b, R = Me, 76%, 10 h



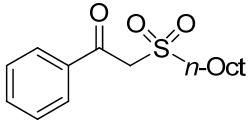
14, 62%, 7.5 h



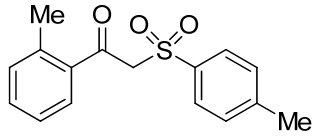
15, 71%, 8.5 h



16, 69%, 6.0 h

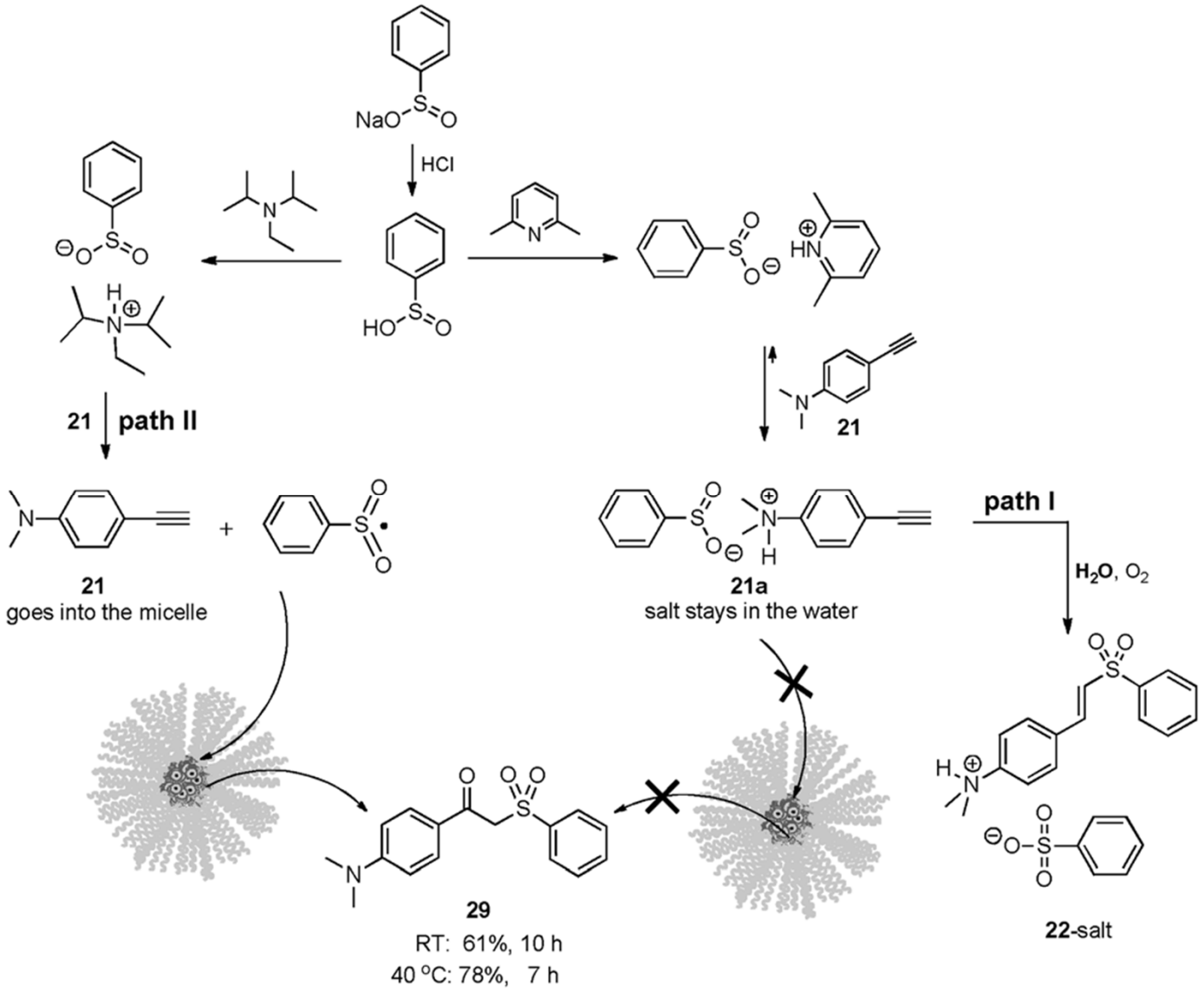


17, 77%, 8.0 h

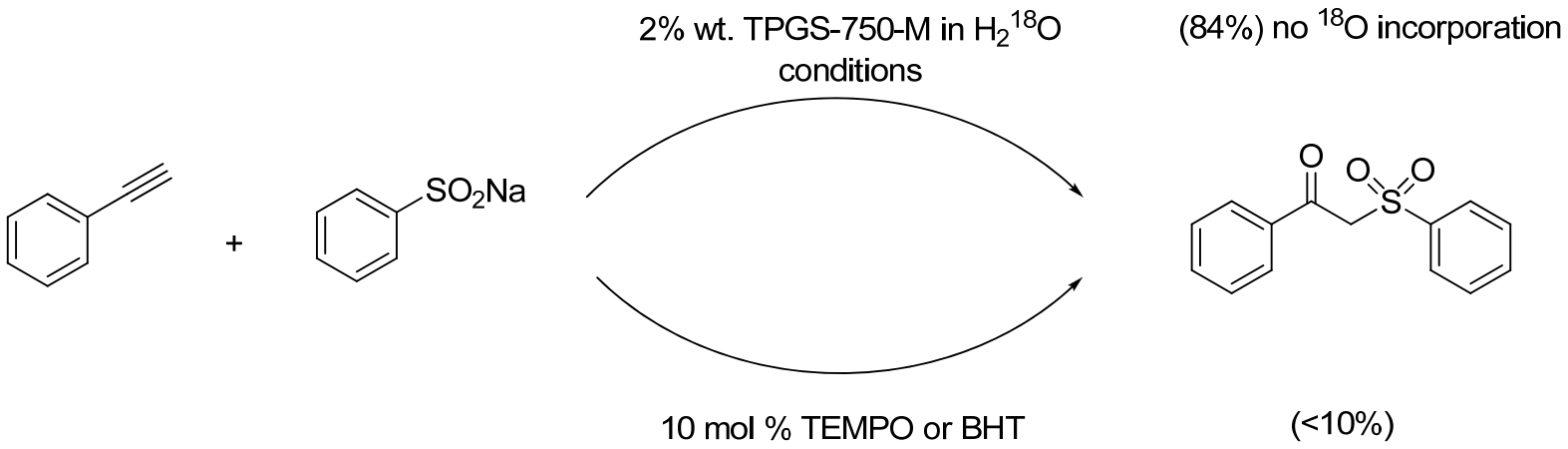


18, 76%, 8 h

Determination of reaction pathway



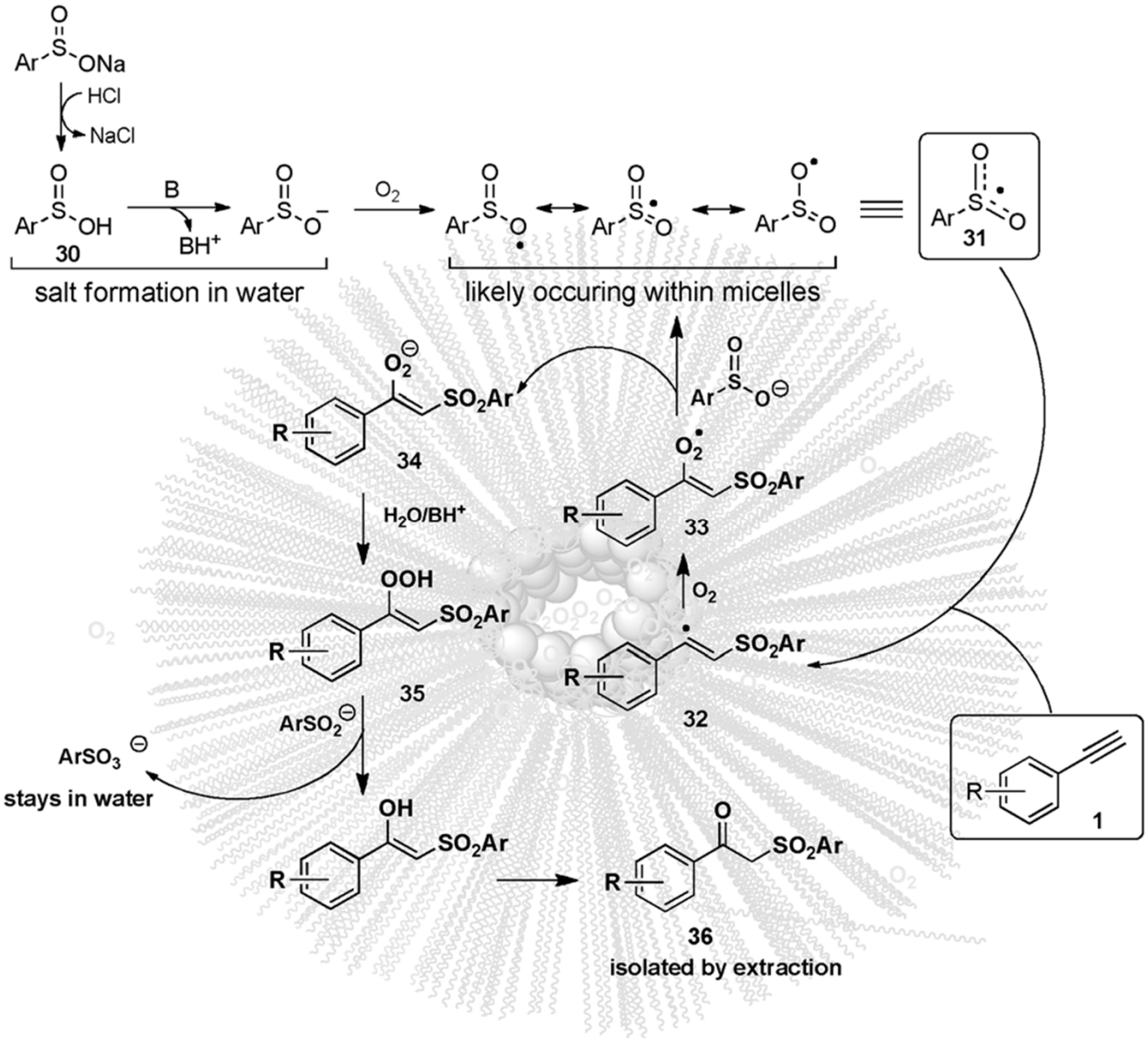
Additional experiments



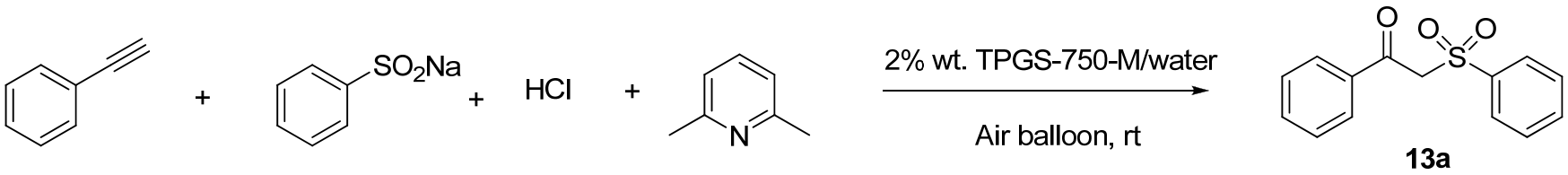
The O atom comes from O_2

Radical pathway is involved

Postulated mechanism



Environmental friendliness



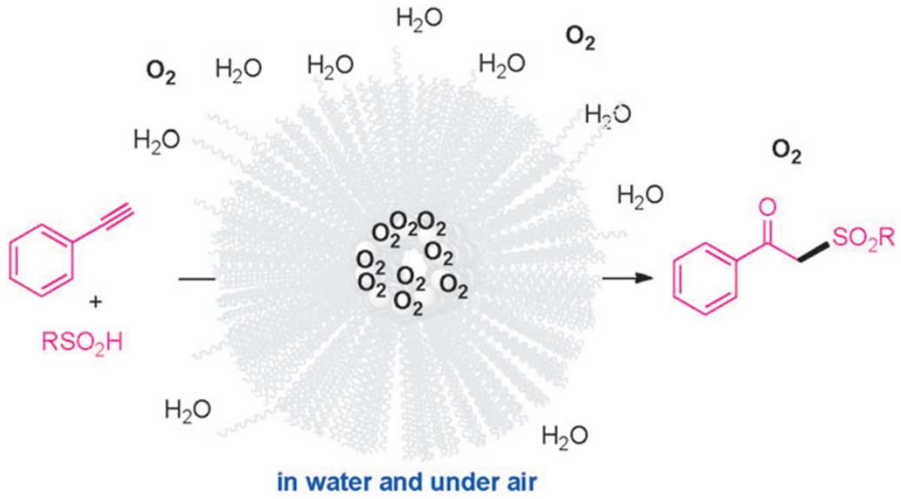
13a

Recycling of the reaction medium

Run	Yield of 13a (%)
1st	78
2nd	70
3rd	53

$$\text{E factor} = \frac{mass\ of\ organic\ waste}{mass\ of\ product} = 5.3$$

Conclusion



- « green » process
- Scope not so broad
- Some mechanistic points remain unclear