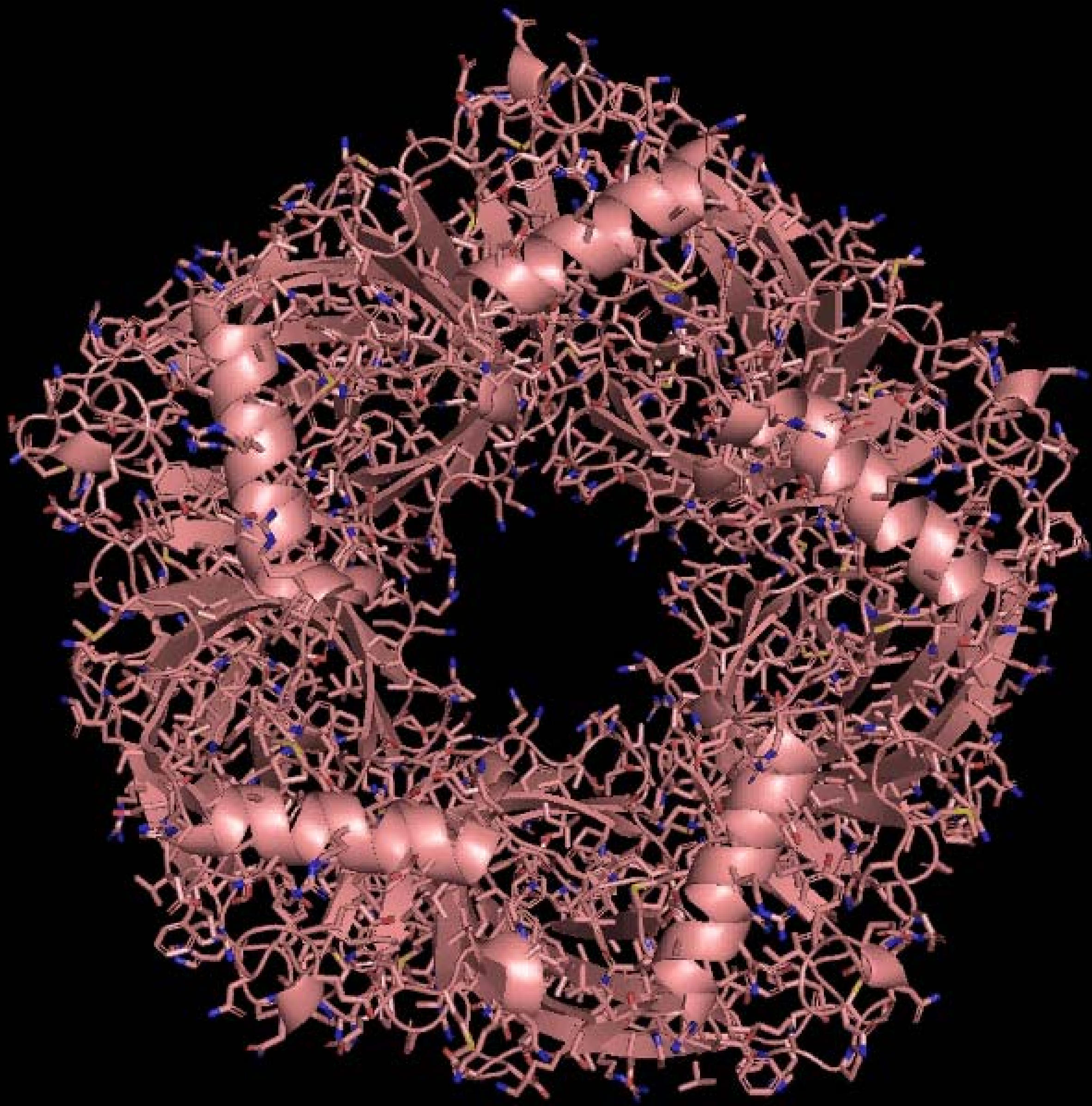
Earth a Water Planet is

blue *not green!*

Mouse AChE
Gorge Entrance View



Click chemistry -- surprises!

‘In situ’ inhibitor Synthesis
by enzymes --->

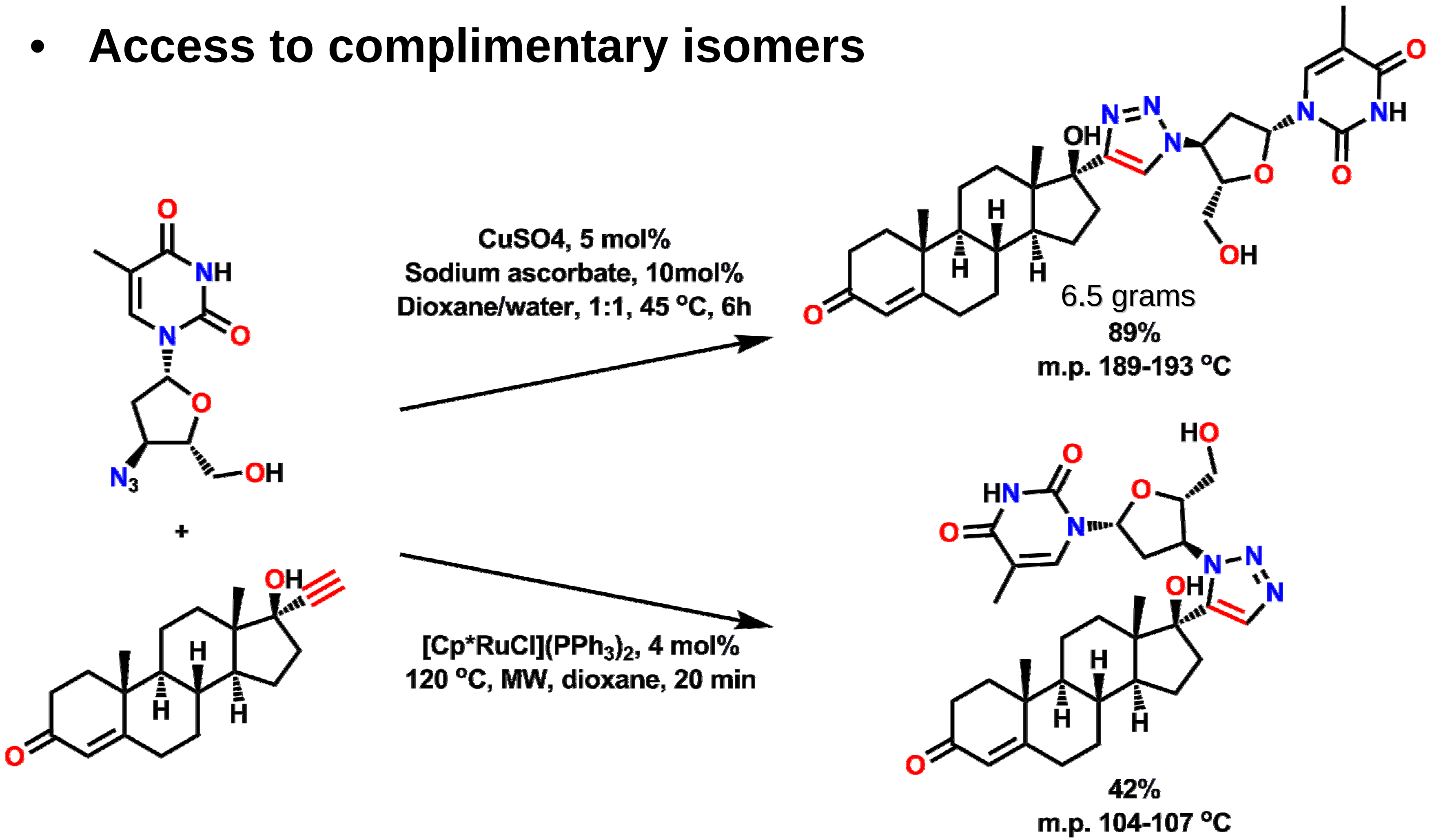
Cu(I)-catalyzed synthesis
of 1,4-triazoles --->

Ru(II)-catalyzed synthesis
of 1,5-triazoles --->

enhanced reactivity
‘on water’ (***not in it***) ---->

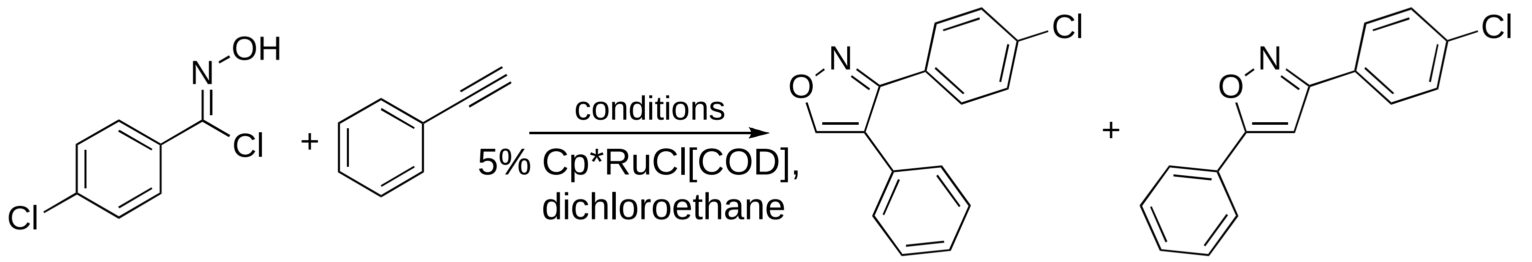
Cu and Ru "Fusion" Reactions

- **Access to complimentary isomers**

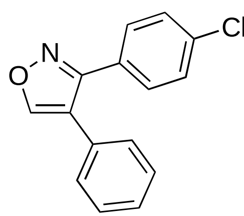


Jeroen Wassenaar & Lars Rasmussen, unpublished results

Ru-catalyzed nitrile oxide-alkyne cycloadditions



A:**B**



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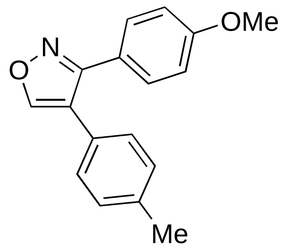

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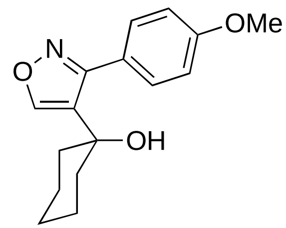

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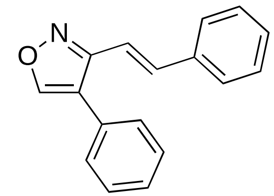

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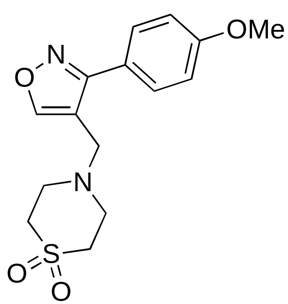

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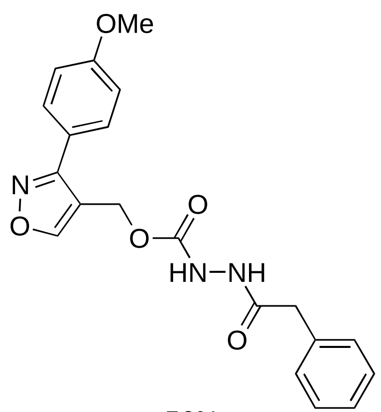

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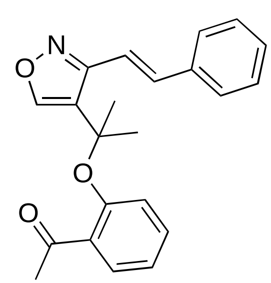


93%

unpublished results,
Scott Grecian and
Valery Fokin

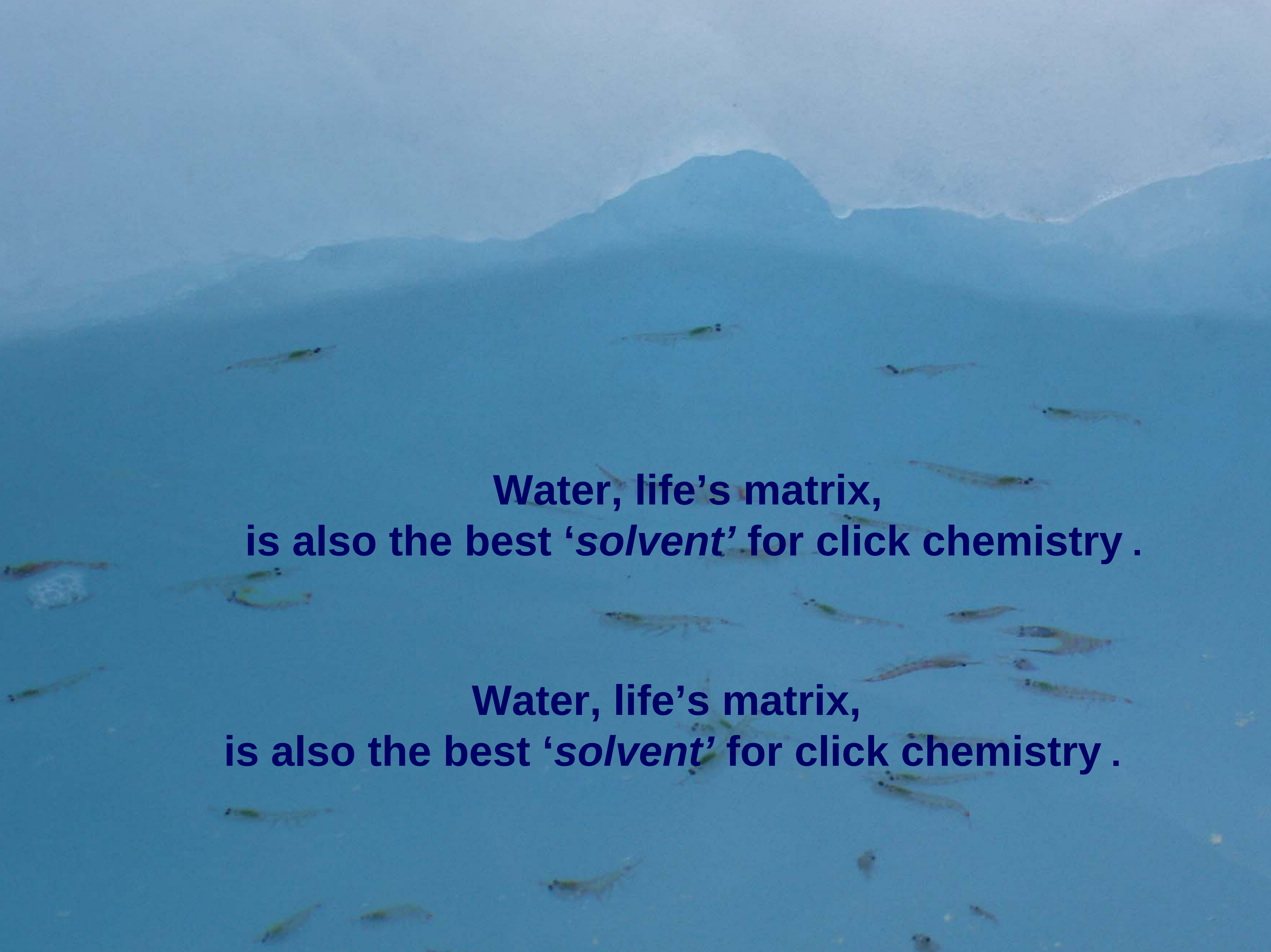
Click chemistry -- surprises!

'In situ' inhibitor Synthesis
by enzymes --->

Cu(I)-catalyzed synthesis
of 1,4-triazoles --->

Ru(II)-catalyzed synthesis
of 1,5-triazoles --->

enhanced reactivity
'on water' (***not in it***) ---->


Water, life’s matrix,
is also the best ‘*solvent’* for click chemistry .
Water, life’s matrix,
is also the best ‘*solvent’* for click chemistry .

Orig Life Evol Biosph (2007) 37:67–82
DOI 10.1007/s11084-006-9018-5

BIOMEDICAL VIGNETTE

Mineral Surface Directed Membrane Assembly

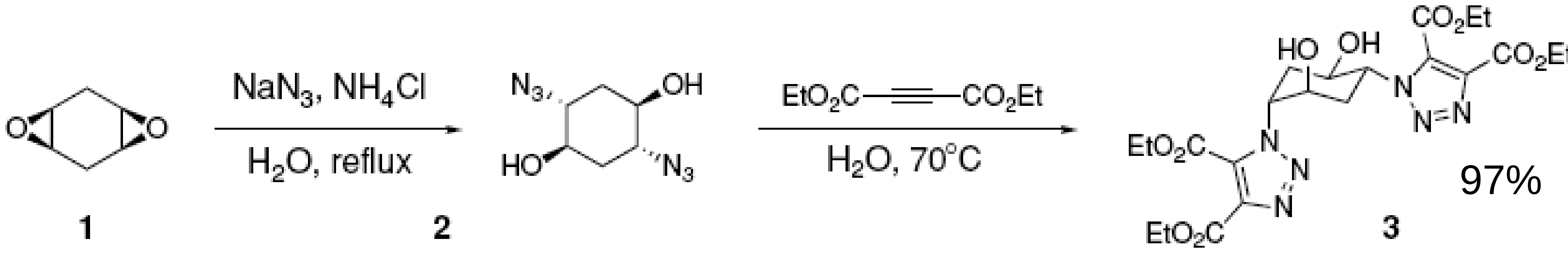
Martin M. Hanczyc • Sheref S. Mansy • Jack W. Szostak

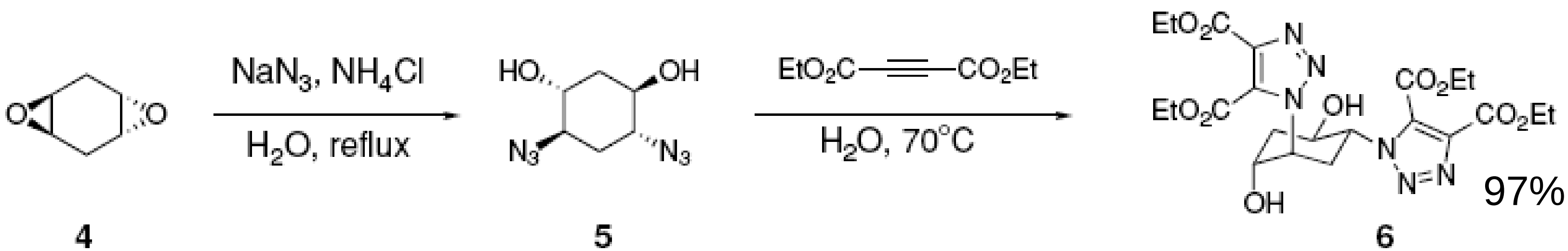
An interesting paper on how it is specifically the mineral surfaces which assemble and release the free floating bilayer lipid vesicles.

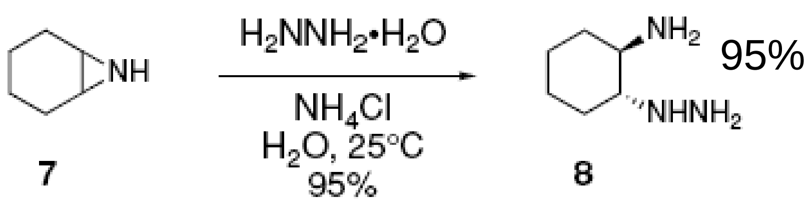
Rocks, especially 'grease' covered ones are ubiquitous in 'modern' origin of life scenarios.

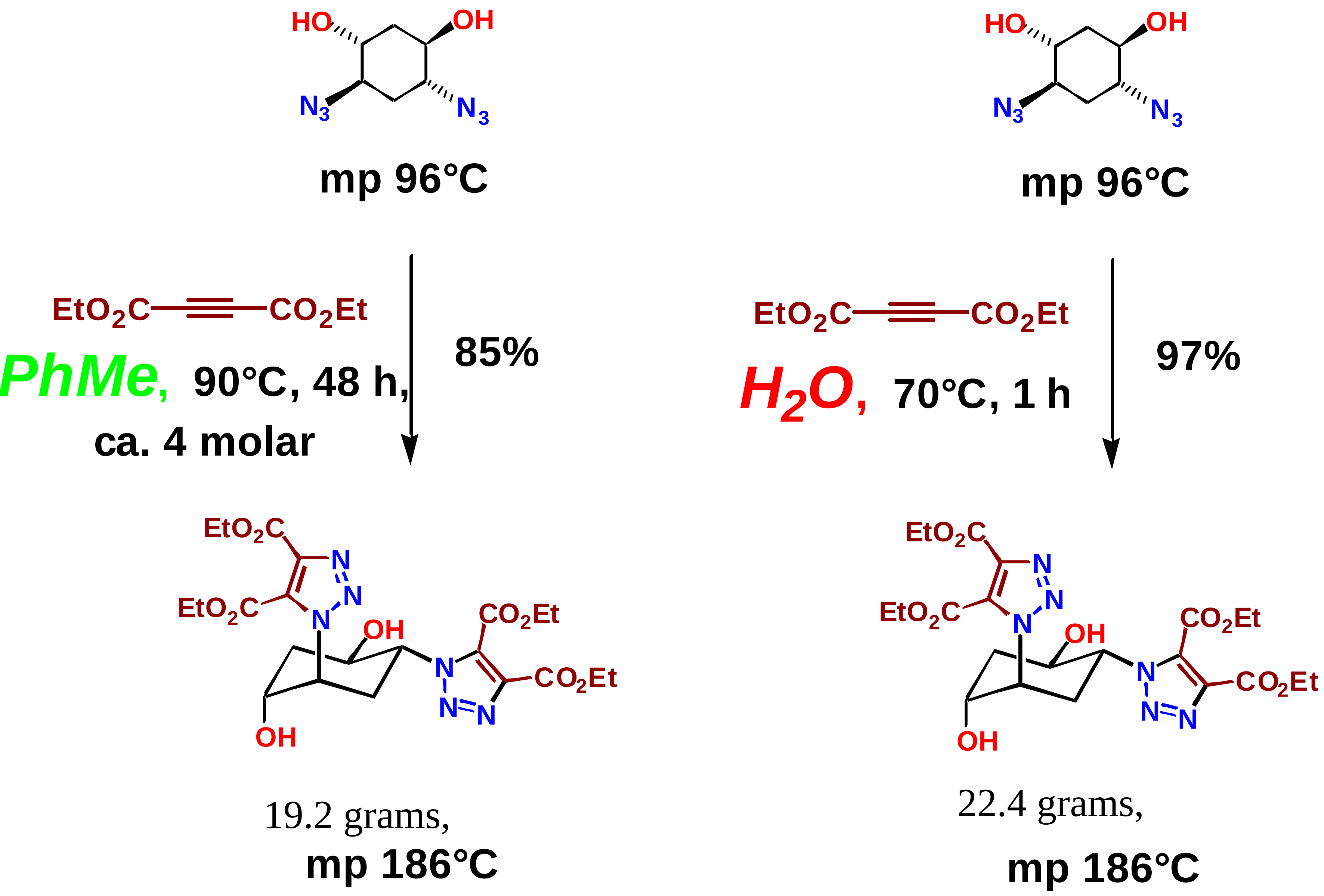

80
60
40
20

Epoxide and aziridine openings --
in aqueous suspension, i.e.
***'on'** water* **not 'in'** water







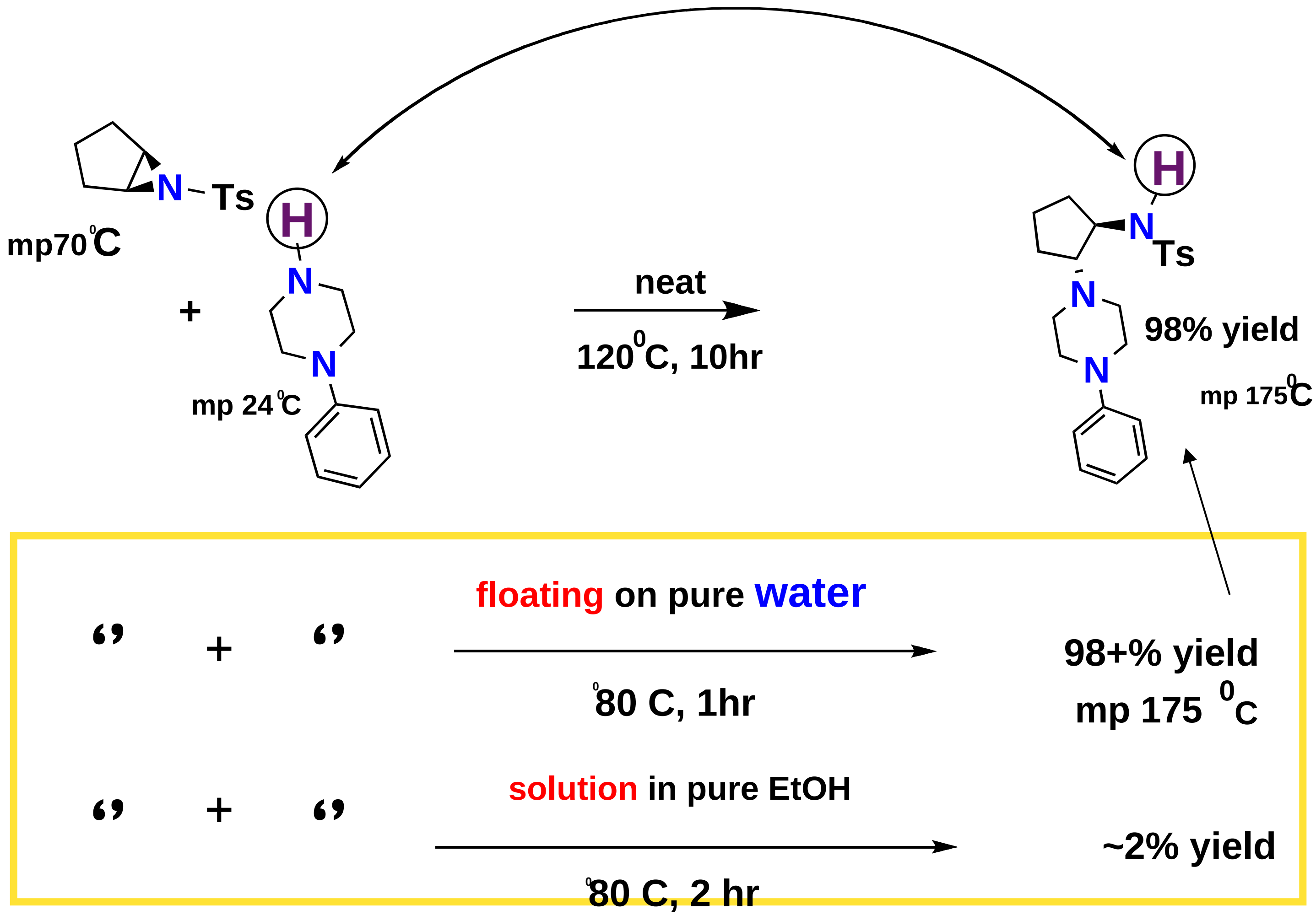


HO
OH
N3
N3
mp 96°C
EtO2C
CO2Et
PhMe,
90°C, 48 h,
ca. 4 molar
85%
EtO2C
N
N
EtO2C
N
OH
CO2Et
N
CO2Et
N
N
OH
19.2 grams,
mp 186°C
HO
OH
N3
N3
mp 96°C
EtO2C
CO2Et
H2O,
70°C, 1 h
97%
EtO2C
N
N
EtO2C
N
OH
CO2Et
N
CO2Et
N
N
OH
22.4 grams,
mp 186°C

The Best Click Reactions are simple "Fusions"

Curiously, they always proceed best

Floating on Pure Water



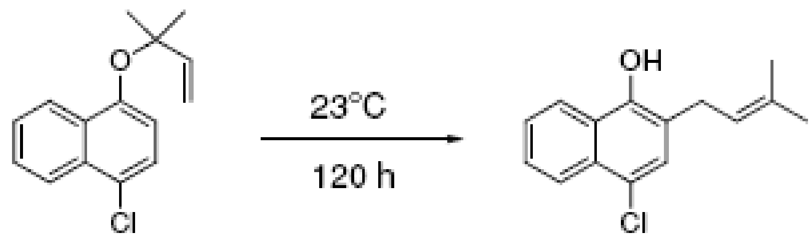
Chapter 11

Chemistry 'On Water' – Organic Synthesis in Aqueous Suspension

Sridhar Narayan, Valery V. Fokin, and K. Barry Sharpless

in "Organic Synthesis in Water: Principles, Strategies and Applications",
U. M. Lindstrom, ed., Blackwell Publishing,
Oxford, UK, 2007.

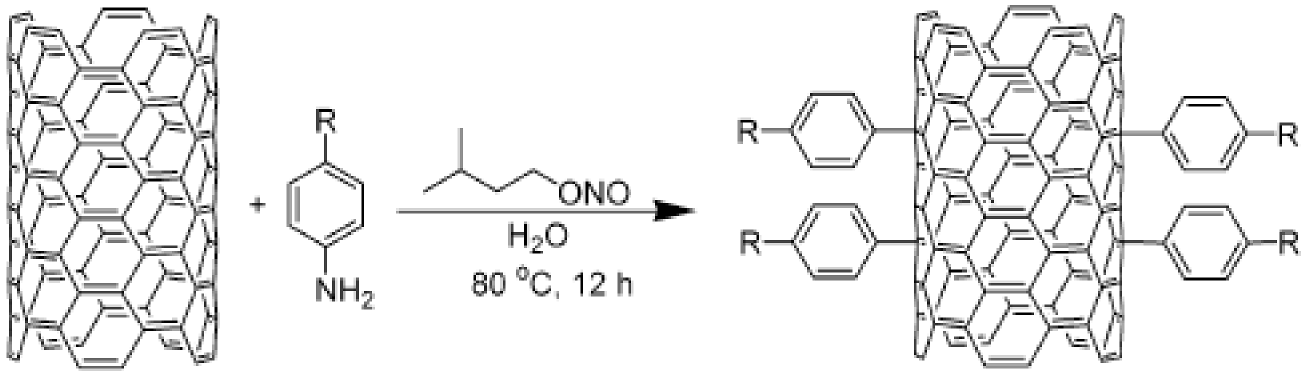
Figure 11.16 'On water' acceleration of an aromatic Claisen rearrangement.



50 **51**

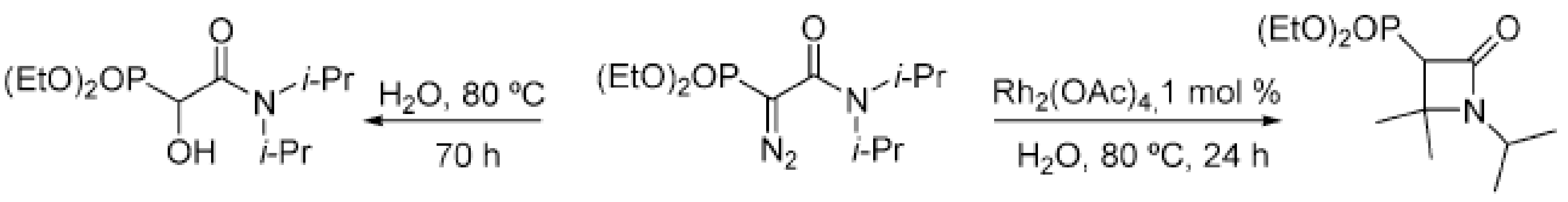
Solvent	Yield
Toluene	16%
DMF	21%
CH_3CN	27%
MeOH	56%
None	73%
H_2O	100%

• Functionalization of SWNTs 'on water' with vigorous stirring performed by Tour



R = F, Cl, Br, I, SO_3H, CO_2H, NO_2, *t*-butyl, *n*-butyl, methyl ester

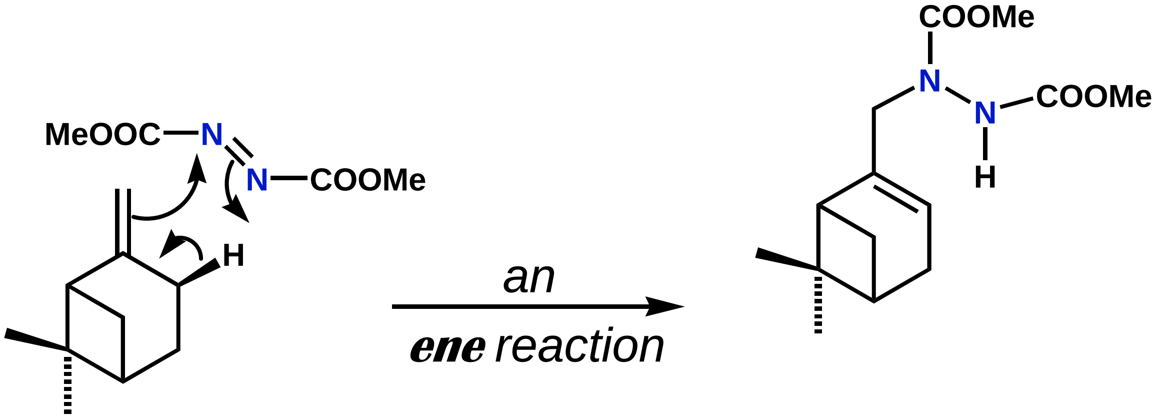
• Preferential Rh(II) carbenoid intramolecular C-H vs O-H insertion in water shown by Afonso

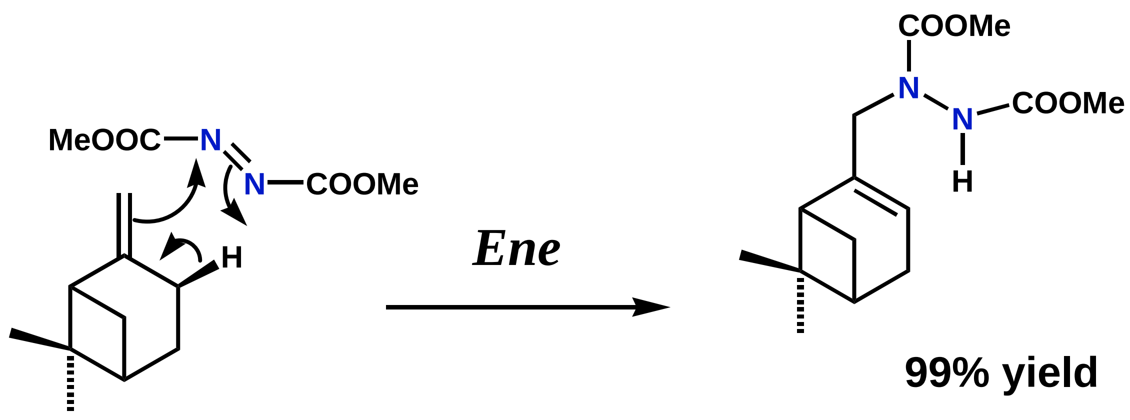


4a (>97 %)[a] **1a** **2a** (>97 %)[a]

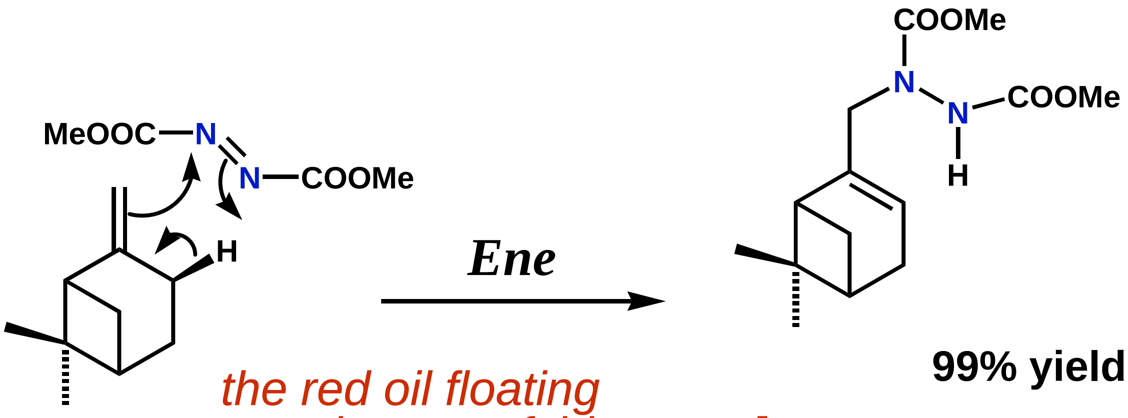
observe dramatic
rate accelerations
for *insoluble reactants*
“on water”, NOT in water!

S. Narayan, J. Muldoon, H.C Kolb,
M.G. Finn, V.V. Fokin, K. B. Sharpless,
Angew. Chem. Int. Ed. 2005, 44, 3275.




MeOOC
N
N
COOMe
H
Ene
COOMe
N
N
COOMe
H
99% yield

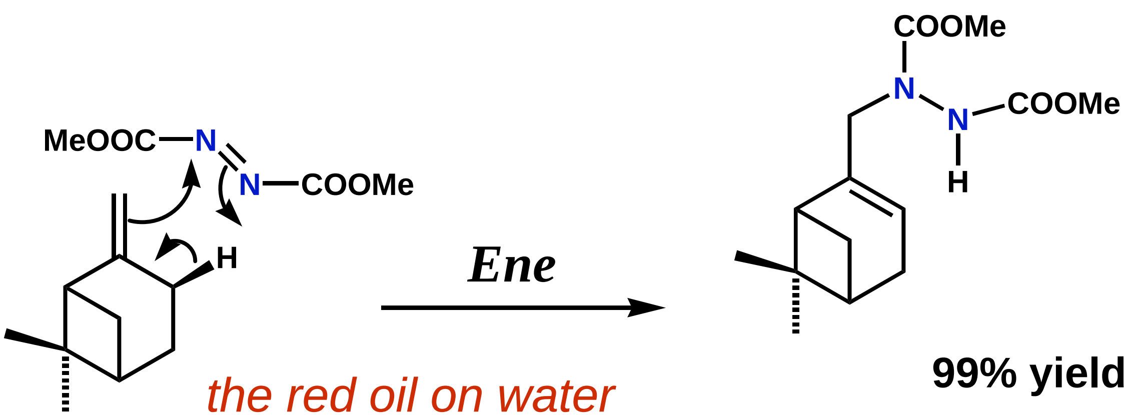
Provided with an
'oil' water-interface,
this '*ene*' reaction needs
just 30 minutes to complete
at room temperature.



*the red oil floating
on water at time zero{vide supra]
is a 'neat' equimolar solution
of the two reactants
(~4.5**M** in each component)*

Provided with an
'oil' water-interface,
this '*ene*' reaction finishes
in 30 minutes
at room temperature.

Whereas, in the
absence of water
the reaction is
7O times slower!

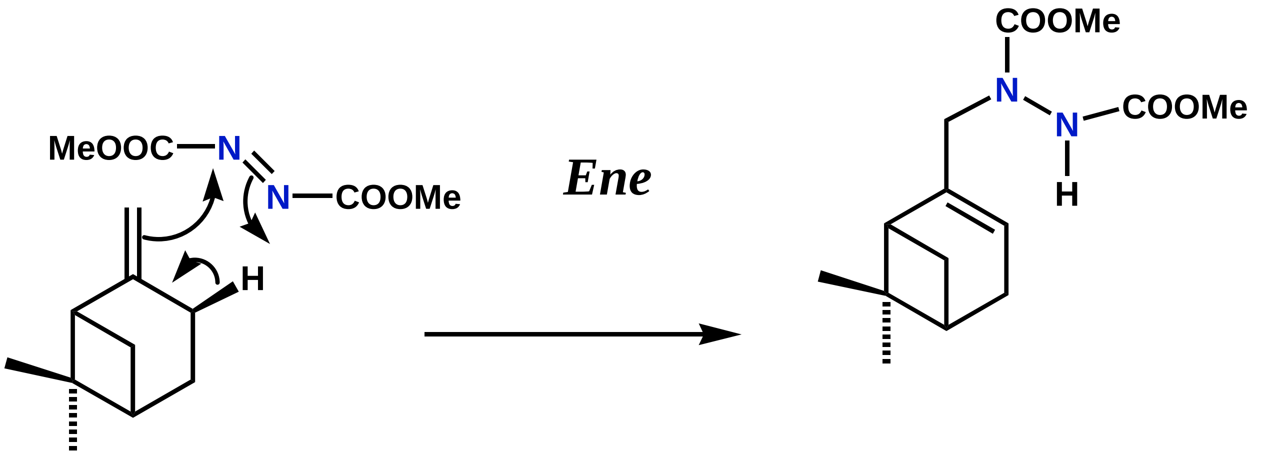


the red oil on water
'time zero' {vide supra]
is a 'neat' equimolar solution
of the two reactants
*(~4.5**M** in each component)*

99% yield

Our *accidental* discovery that click reactions can be strongly accelerated at oil-water interfaces, has ‘found’ a fascinating rationale in a new theory from Jung and Marcus:

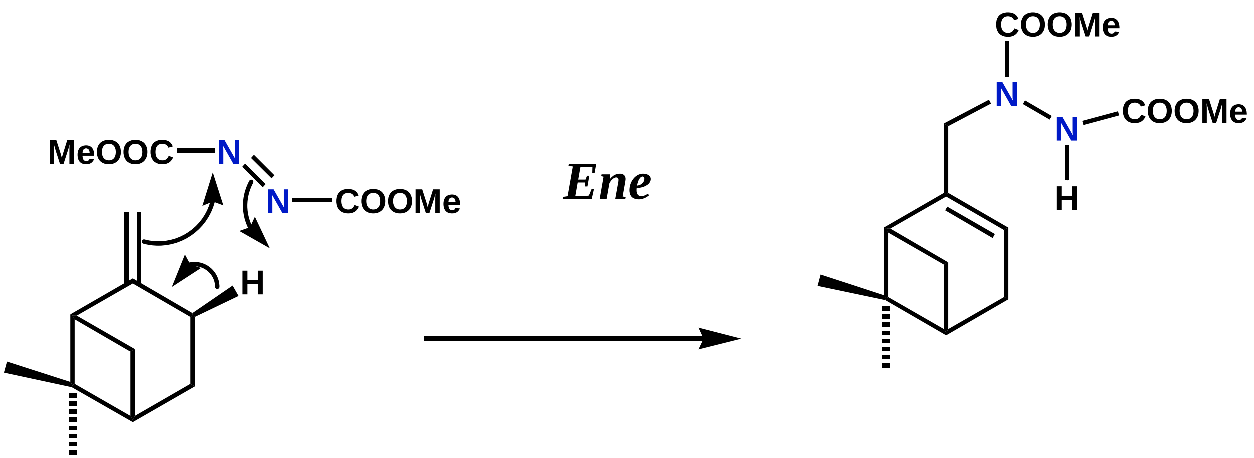
{Yousung Jung and Rudy Marcus, ***JACS***,*129*, 5492-5502 (**2007**)}



Our accidental discovery that click reactions can be strongly accelerated at oil-water interfaces, has 'found' a fascinating rationale in a new theory from Jung and Marcus:

{Yousung Jung and Rudy Marcus, ***JACS***,*129*, 5492-5502 (**2007**)}

In fact, their theory is much more 'interesting' than the phenomenon itself !



Striking rate acceleration of organic reactions "on water"

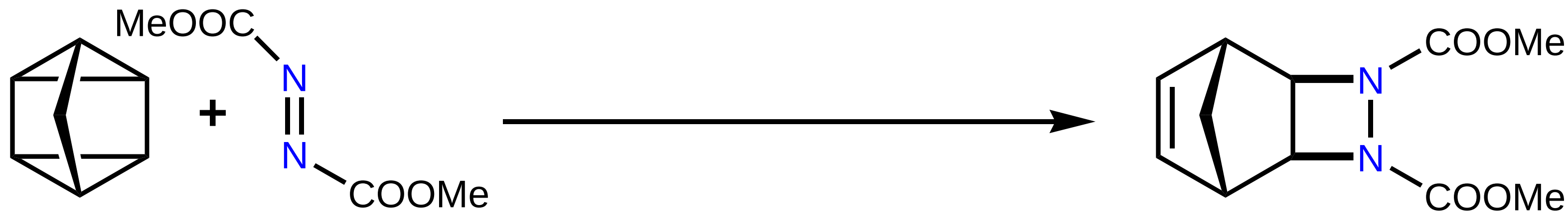
Yousung Jung and Rudolph A. Marcus

Noyes Chemical Physics Laboratory

California Institute of Technology

Yousung Jung and Rudy Marcus,
JACS, **2007**,*129*, 5492

The Best Click Reactions are simple "Fusions", and they always proceed best Floating on Water.



quadricyclane

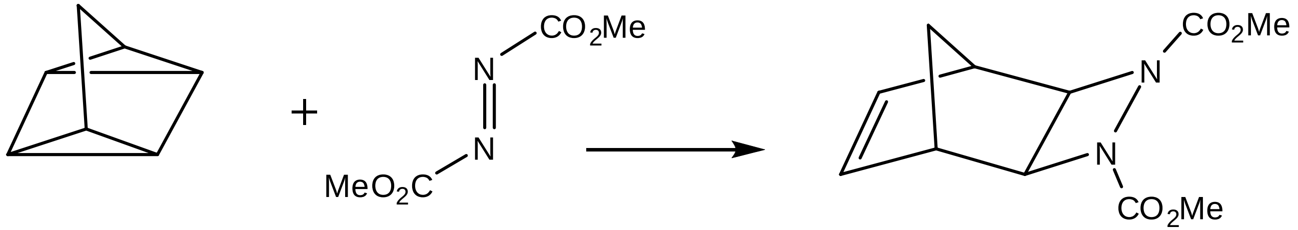
neat, cooled to 0°C → No detectible product after 2 hrs

floating "on" ice-water, hence also at 0°C → complete in 1 hr, yield ~100%, and the product layer is found under the ice-water

$MeOH \cdot H_2O$, 23 °C (homogeneous) → ~ 4 hr to completion 70% yield

Here, floating the neat reactants on water provides a rate acceleration of at least 500-fold over the neat reaction!

Experiment: reaction time data

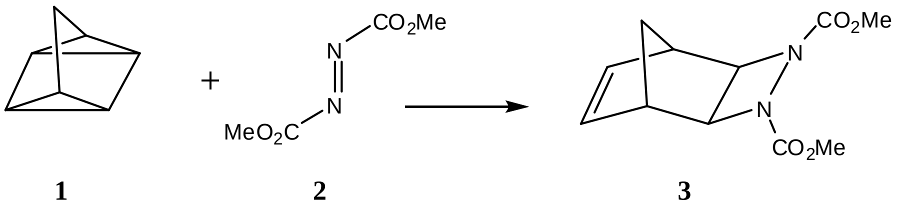


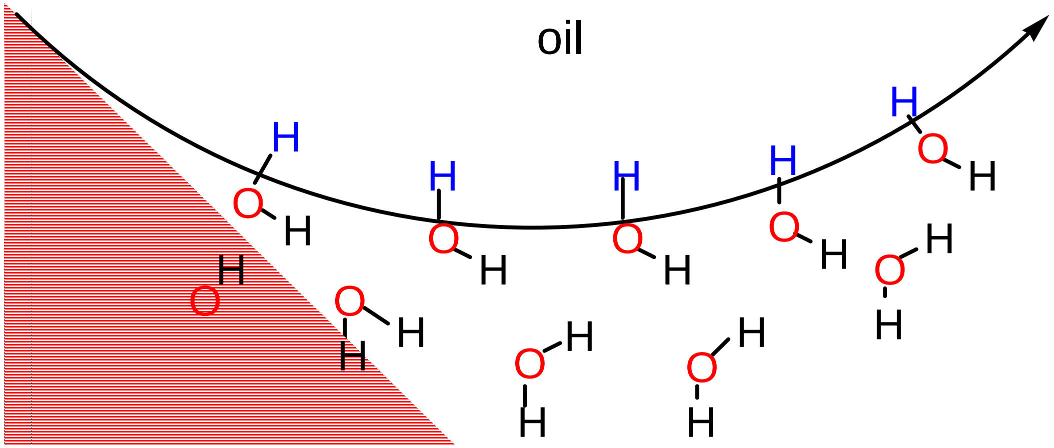
1 **2** **3**

Solvent	Conc. [M]	Time to completion
MeOH/H_2O (3:1 homogeneous)	2	4 h
Neat (solvent-free)	4.53	48 h
on H_2O (heterogeneous)	**4.53**	**10 min**
MeOH/H_2O (1:1 heterogeneous)	4.53	10 min

Sharpless and co-workers, *Angew. Chem. Int. Ed*. 44, 3275 (2005)
Klijn & Engberts, *Nature* 435, 746 (2005)

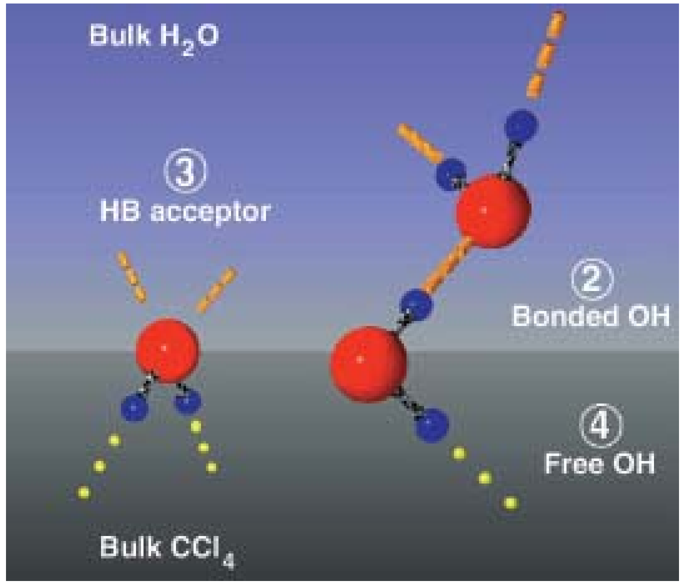
Working hypothesis





Key aspect: interfacial water structure

Aqueous hydrophobic interface

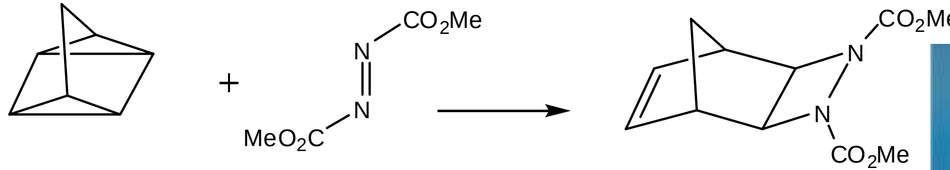


Water

Oil

J. A. McCammon, P. J. Rossky, *J. Chem Phys.* **80**(*9*), 4448 (**1984**)
Shen et al, *Science* 264, 826 (**1994**)
Richmond et al, *Science* 292, 908 (**2001**)
Saykally et al, *J. Phys.-Condens. Mat*. 14, L221 (**2002**)
Mundy & Kuo, *Science* 303, 658 (**2004**)

Starting from this view of interfacial water structure, Rudy Marcus and Yousung Jung have derived a compelling rationale for the the unique "on water" reactivity effects!



1 2 3

The goal

is to understand the rate at the interface,
which as Marcus and Jung show,
can be more than ***100,000 times faster***
than the rate in the neat-oil phase.
consisting of the 1:1 mixture of the
two, water insoluble reaction partners.
The latter of these *two rates*
is the background rate in both systems -- water
interface present and water interface absent.

“They” open with a stunning move, thinks kbs.

One needs to factor out and compare the kinetics
for the three reaction ‘situations’,
namely **neat, homogeneous, and interfacial**.

Yet how can this be done, when the rate
expressions bear incommensurable units?

But then, just a few deft, simplifying assumptions
later and
The goal
is already insight.

Experimental rate constants

Solvent	Conc. [M]	Reaction time	Rate constants (s^{-1})	
Neat	4.5	48 h	4×10^{-6}	***sec^{-1}***
Homogeneous	2	4 h	9×10^{-4}	*“*
on H_2O	**4.5**	**10 min**	0.5	*“*

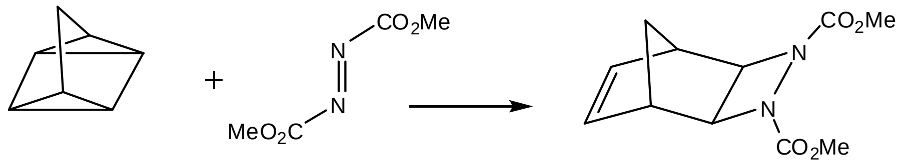
note bene:
the three reaction-types [*vide supra*] are now ‘*on the same playing field’* **= all rate constants are in *sec^{-1}***

Hence the surface reaction is ~10^5 times more efficient than neat reaction!

Jung & Marcus, *JACS*, 129, 5492 (2007)

Narayan, et al., *ACIE,* 44, 3275 (2005)

Working hypothesis



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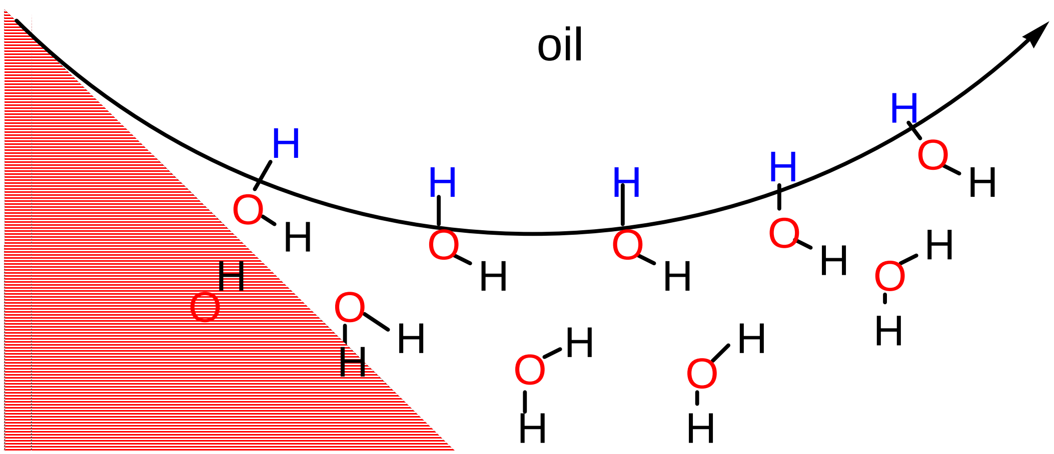
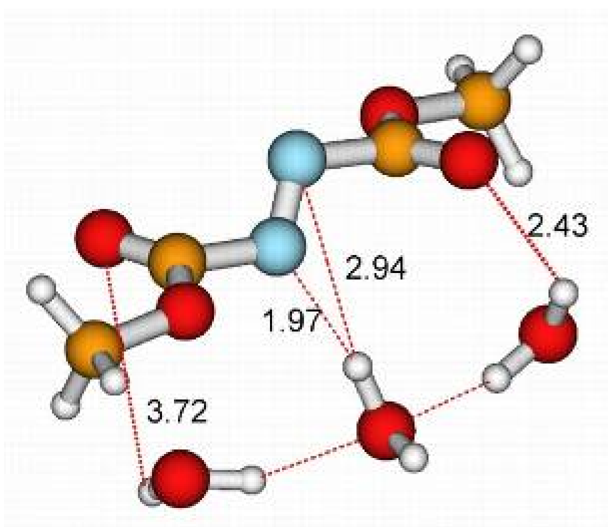


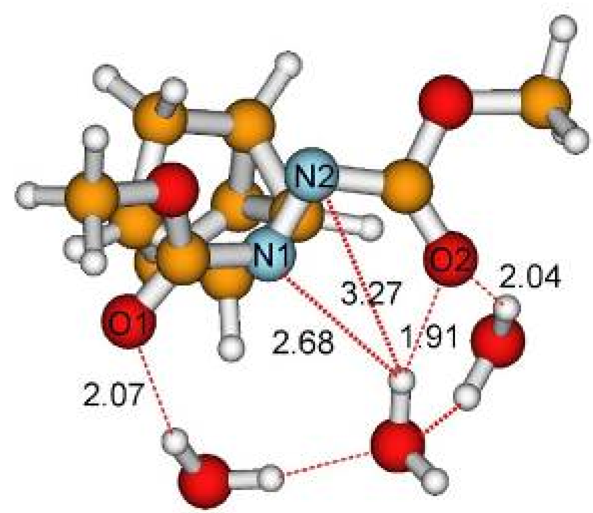
TS more polarized (stronger H-bond) than the Reactant

Atomic charges (e^-)

	N1	N2	O1	O2
Reactant DMAD	-0.17	-0.17	-0.58	-0.58
TS	-0.23	-0.31	-0.64	-0.63



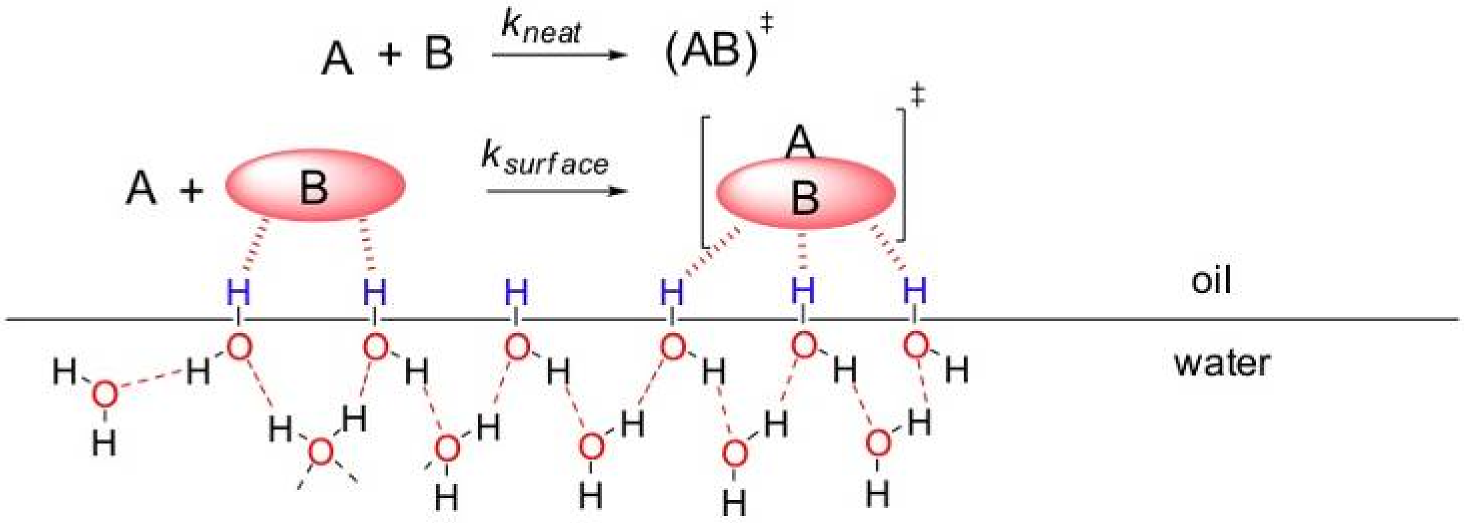
Reactant



TS

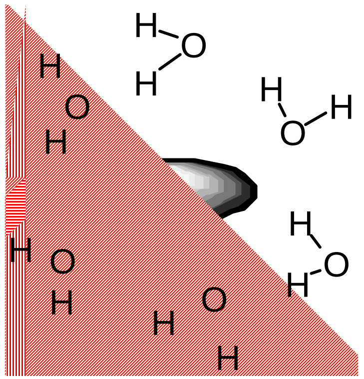
Transition state theory rate constants

Solvent	Reaction time	Experiment (s^{-1})	TST (s^{-1})
Neat	48 h	4×10^{-6}	5×10^{-7}
Homogeneous	4 h	9×10^{-4}	(next slide)
on H_2O	**10 min**	0.5	0.2

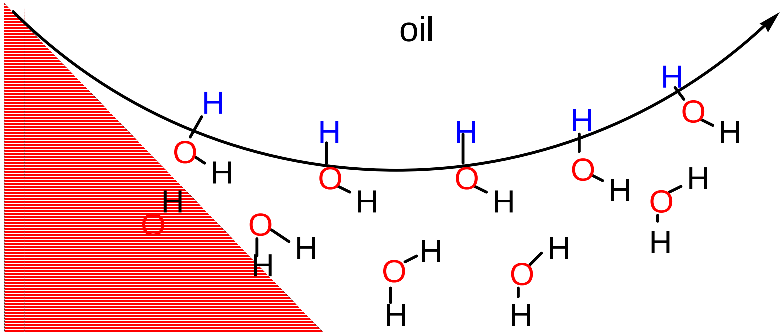


Conclusion: Interfacial H-Bond formation is the key to the rate acceleration

Aqueous homogeneous *vs*. surface reaction



Small hydrophobic solute



Hydrophobic interface

Energy required **to break the existing H bond network of water**

~ 1.5 kcal/mol per H bond (Saykally and co-workers, *Science*, **2004**)

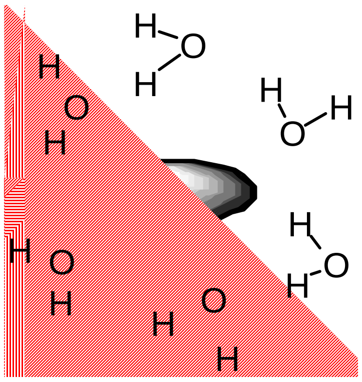
Conclusions:

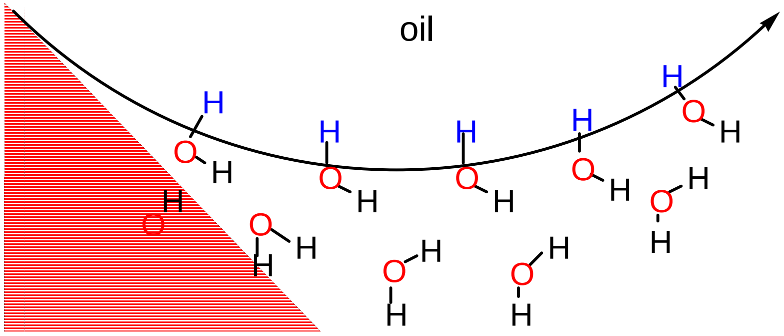
1. The surface reaction is absolutely more efficient than the neat reaction by a factor of 10^5, based on the experimental kinetic models and TST.

2. The activation barrier lowering (~7.5 kcal/mol) by the H-Bond formation with interfacial water molecules is the key.

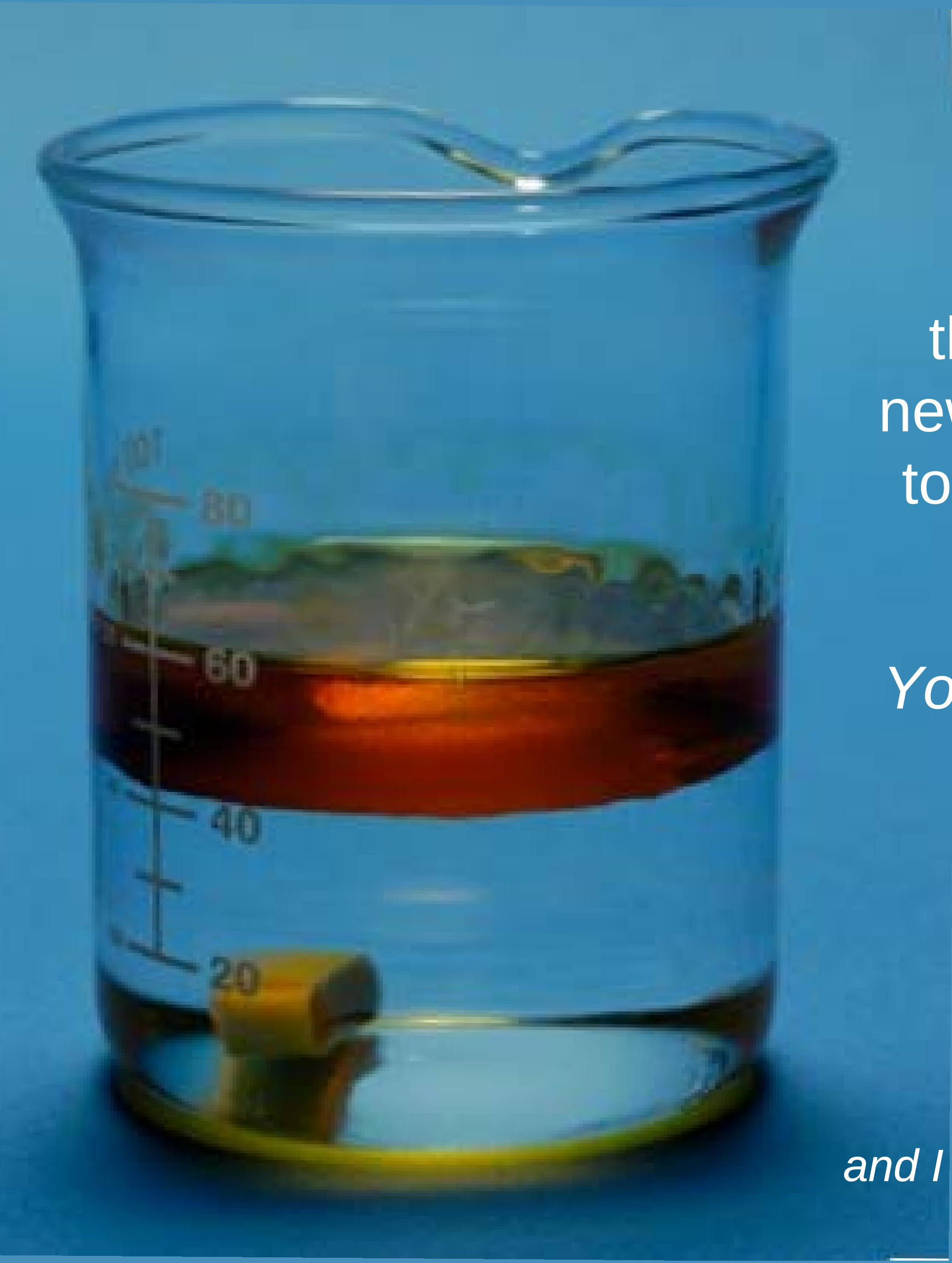
Imagine an endless field of
'dangling hydrogens', presented at the oil-water interface =
a surface
bristling with nascent H-bonds,
offered up 'for free' as a
gift from physics
and open-system thermodynamics.

Conclusions -- *continued:*





3. These *'fields' of dangling interfacial hydrogens,* likely played an important catalytic role in the origin of life
-- speculates kbs.



In short, the puzzling
oil-water interface catalysis
now has a *beautiful*
theory to explain it….. and this
new gem from Caltech sure looks
to have far reaching implications
on a planet like ours!

Yousung Jung and Rudy Marcus,
JACS, 129, 5492 (2007)

[In keeping with
our expectations for serendipity,
this ***‘reactivity enigma’*** *broke*
about a year ago, when Rudy Marcus
and I were together on a lecture tour in China]

"Science is the belief
in the ignorance of the experts."

Richard Feynman, 1966

****

Jess H. Brewer
said:

“I love [Feynman’s] phrase.

*It sums up the bare essence
of the intellectual arrogance,
the willingness to believe in one's own reasoning
regardless of what “experts" say,
that makes original science (and art) possible.”*


10^0 meters --
scale of human
companionship!

Acknowledgements

TSRI


Hartmuth Kolb

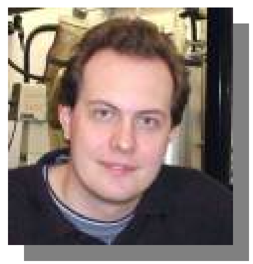

Roman Manetsch

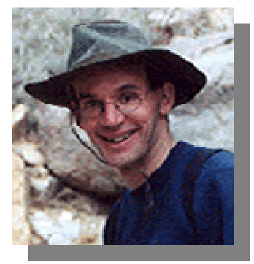

Jessica Raushel


Joseph R. Fotsing


Timo Weide

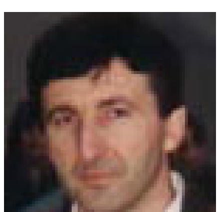

Neil Grimster


Valery Fokin


M.G. Finn

UCSD


Palmer Taylor


Zoran Radic


Todd Talley

HIV Protease

John Cappiello

Mat Whiting

John Muldoon

Carbonic Anhydrase

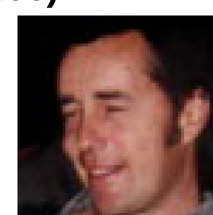
Vani Mocharla

Benoit Colasson

Stefanie Röper

Univ. de la Meditaranée (France)


Pascale Marchot


Yves Bourne