The Toad Suck Institute for Green Organic Chemistry

Development of a Green Organic Chemistry Laboratory at Hendrix College, Conway, Arkansas

We began microscale labs around 1988, for green reasons.

We began "green chemistry" in 2001, as follows.

- "The unexamined reaction is not worth running."
- Does the experiment teach something that is indispensable?
- Is there a greener way to do it?
- University of Oregon, Green Chem. in Educ. Workshop

"An Asymptotic Approach to the Development of a Green Organic Chemistry Laboratory"*

"…the goal of making a chemical product or process 'environmentally benign' is a mere statement of the ethic of continuous improvement more than it is a metric by which to measure improvement."

"Green Chemistry, Theory and Practice", P.T. Anastas and J. C. Warner, Oxford University Press, 1998.)

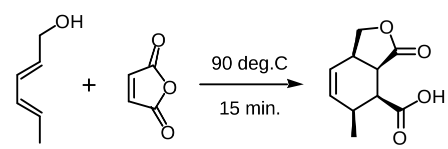
J. Chem. Educ.* **2004, *81*, 1187-1190 (August)

The Ideal Synthesis-P. Wender

"The ideal synthesis may be defined as one in which the target molecule is prepared from readily available starting materials in one simple, safe, environmentally-acceptable, and resource-effective operation that proceeds quickly and in quantitative yield."

P.A. Wender & B. L. Miller, in "Organic Synthesis: Theory and Applications", T. Hudlicky, Ed., *Greenwich: JAI Press*, 1993, 2, 27-66.

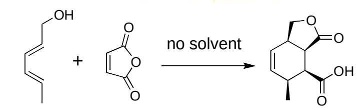
Diels-Alder/Nucl. Acyl Subst.



McDaniel, K.F.; Weekly, R. M. *J. Chem. Educ.* **1997**, *74*, 1465.
- original procedure calls for reflux in toluene
- all protons visible in 300 MHz NMR in acetone-d_6
- proton NMR assignments by COSY
- diastereotopic hydrogens

Solventless Green Evolution

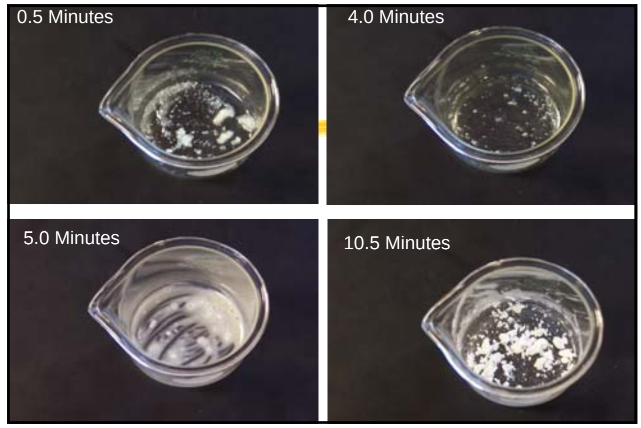
K. Tanaka, *Solvent-free Organic Synthesis*; Wiley-VCH: Weinheim, 2003



Three variations :

1. 90 ^{o}C, 15 min, no solvent;
2. microwave, reduced power, 30 sec., no solvent;
3. manual mixing, RT, no solvent, 11 min.

Mechanistic study: M. N. Paddon-Row, M. S. Sherburn *et al.*, *Org. Biomol. Chem.* 2005, *3*, 1302-1307.



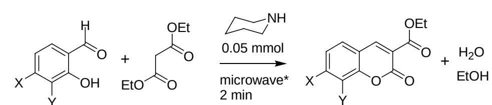
Intramolecular Reactions

"We all know that enforced propinquity often leads on to greater intimacy." (The closer we hold reagents together, the more likely they are to react.)

--R. B. Woodward

(Quoted in K. B. Sharpless, *Chem. Brit.* **1986**, 22, 38-44)

Soventless Microwave-Assisted Coumarin Synthesis



0.5 mmol 0.5 mmol

*Panasonic Inverter Technology Dr. R.Varma, US EPA

a. X=Y=H
b. X=OMe, Y=H
c. X=H, Y = OMe

[Heinrich Emil Albert Knoevenagel (1865-1921)]

1. Grind at RT, no solvent; T. Sugino, K. Tanaka *Chemistry Lett.* **2001**, *30*, 110-111.
2. Meldrum's acid; 10 hr reflux in H_2O, no catalyst; R. Maggi et al. *Green Chem.* **2001**, *3*, 173-174.
3. Microwave, no solvent; D. Bogdal Politechnika Krakowska, Poland (Google)

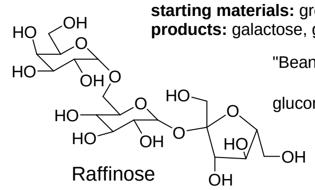
A Truly Green Starting Material

A Green Tale of Three Enzymes

"Chemistry and Flatulence: An Introductory Enzyme Experiment"

J. R. Hardee et al. *J. Chem. Educ.* **2000**, *77*, 498-500.

starting materials: green peas, glucose, water
products: galactose, glucose, fructose



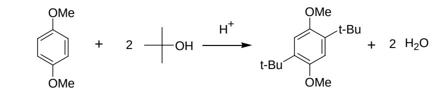
Raffinose

"Beano" (α-galactosidase, sucrase)

glucometer strips (glucose oxidase)

D-glucose + O_2 ⟶ D-gluconolactone + H_2O_2

Green Metrics: "Atom Economy" is not the Whole Story



$C_8H_{10}O_2$-138 $C_4H_{10}O$-74 $C_{16}H_{26}O_2$-250

1. **% atom economy** = (250/(138 + 74 + 74)) x 100 = **87.4%**
2. Suppose the purified yield is 50%:
   % atom effciency = 87.4% x50 = **43.7%**
3. 120 mg 1,4-dimethoxybenzene; 155 mg t-BuOH; 920 mg H_2SO_4; recrystallization solvent (70% *i*-PrOH/H_2O), 1.5 mL =1.287 g
   Effective mass yield = mass of desired product / mass of all reactants, solvents etc.-mass of prod. X 100

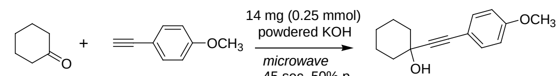
   = 109 mg / 2897.5 mg x 100 = **3.76 %**

Microwave in a Microfuge

VWR SuperClear polypropylene Micro-centrifuge Tubes, vol. 1.7 mL (cat.no. 20170-355), in a 10 mL Pyrex beaker

WARNING: DON'T OVERHEAT! (~30 sec, 50% power)

Microwave-assisted, Solvent-free Addition of 4-Ethynylanisole to Cyclohexanone



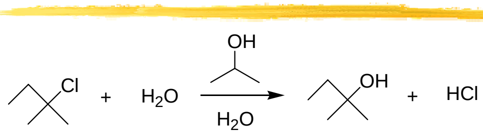
26 μL (0.25 mmol) 28 μL (0.25 mmol)

Reaction vessel: 1.7 mL microfuge tube

Workup: Add 400 μL of sat'd. brine, mix, centrifuge, wash solid with H_2O and dry

Reference: Adapted from H. Miyamoto, S. Yasaka, and K. Tanaka, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 185-186. (See also: K. Tanaka *Solvent-free Organic Synthesis*; Wiley-VCH: Weinheim, 2003; p 43.)

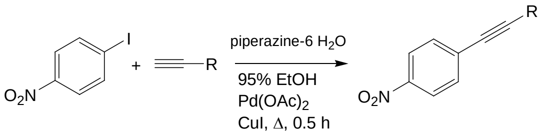
Chemical Kinetics: Evidence for the Sn1 Mechanism; Green Solvent Effect on Rate

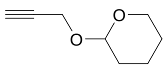


- Determination of rate constants for different solvent mixes;
- Titration using microburets; 118 μL of t-pentyl chloride, 10 mL of solvent.

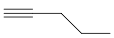
Adapted from: a. *Modern Experimental Organic Chemistry*, Roberts *et al.*, 4th Ed., Saunders, NY, 1985; b. *Chemistry in the Laboratory*, Postma *et al.*, 5th Ed., Freeman, NY, 2000.

Sonogashira Coupling





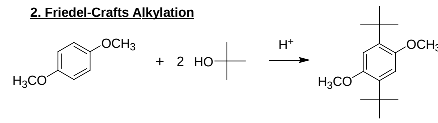
T. E. Goodwin, E. M. Hurst, A. S. Ross
J. Chem. Educ. **1999**, *76*, 74-75.



G. M. Lampman, Western Washington Univ. 2005.

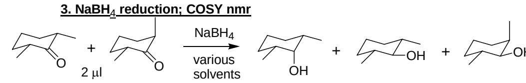
Molecular Modeling (Spartan)

1. Solventless, RT Diels-Alder reaction, Hendrix College
2. Friedel-Crafts Alkylation



J. R. Mohrig et al., "Experimental Organic Chemistry", Freeman, NY, 1998.

3. $NaBH_4$ reduction; COSY nmr



a. C.M. Garner, *J. Chem. Educ.* **1993**, *70*, A310; b. B.A. Hathaway, *J. Chem. Educ.* **1998**, *75*, 1623; c. T.E. Goodwin, J. M. Meacham, M.E. Smith, *Can J. Chem.* **1998**, *76*, 1308

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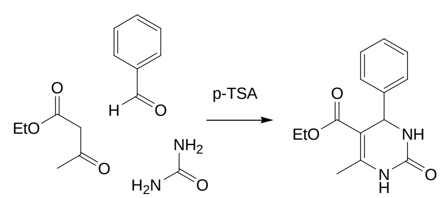
- Research Corporation ($)
- ACS-PRF ($)
- Anonymous Hendrix alumnus ($)
- Riddle's Elephant Sanctuary (www.elephantsanctuary.org)

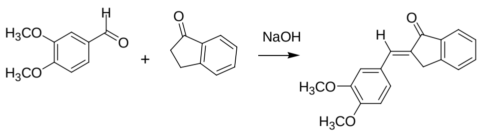
The End

Grindstone Chemistry-Ajay Bose



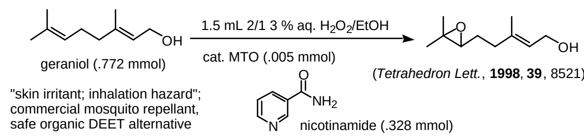
(Biginelli three component condensation
--grind 10 min with no solvent, room temp.)

Solventless Aldol Condensation

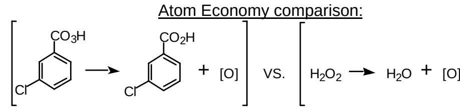


1. K. M. Doxsee, J. E. Hutchison, "Green Organic Chemistry", Thomson-Brooks/Cole, 2004.
2. G. Rothenberg, A. P. Downie, C.L. Raston, J. L. Scott, *J. Am. Chem. Soc.* **2001**, *123*, 8701.

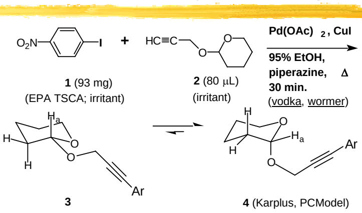
A Green Epoxidation



Atom Economy comparison:



Palladium-catalyzed coupling



Goodwin, T. E.; Hurst*, E. M.; Ross*, A. S.
***J. Chem. Educ.* 1999, *76* , 74-75.**
(*undergraduates)

The Ideal Synthesis-P. Wender

"Progress in the advancement of synthesis can be measured by parameters such as the step count, overall yield, selectivity, cost, scale, resource requirements, waste stream, development time, execution time and personnel."

P.A. Wender et al., *Chemistry & Industry* 1997, *19*, 765-769.

Green Organic Chemistry: An Elephantine Task

Temporal Gland Secretion

GREEN EDUCATION: Discuss experiments with students

- Explain experiment choices and rejections
- MSDS discussions (**caffeine**: "toxic if swallowed; irritating to eyes, respiratory system, and skin; target organs: central nervous system, heart")-**risk assessment**
- use natural products and familiar chemicals (vodka, rubbing alcohol)

Why Green Chemistry?

- **It's the right thing to do**, for the environment, for our students, for ourselves.
- **It makes you feel good** about being a chemist.
- **It's great p.r.** Students like it, as do administrators, public officials, the media, and (we hope) granting agencies.

Two Simple Questions and a Warning

- What's green about it?
- What's not green about it?
- Pasteur pipets, disposable gloves, etc.