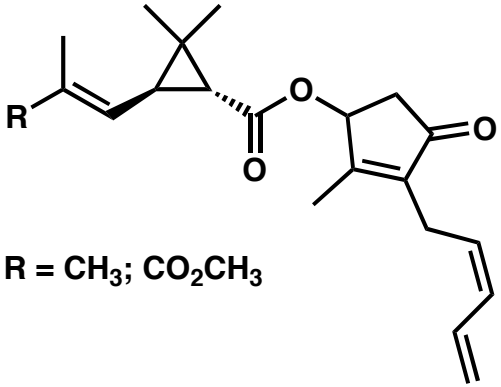
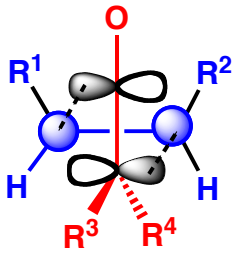


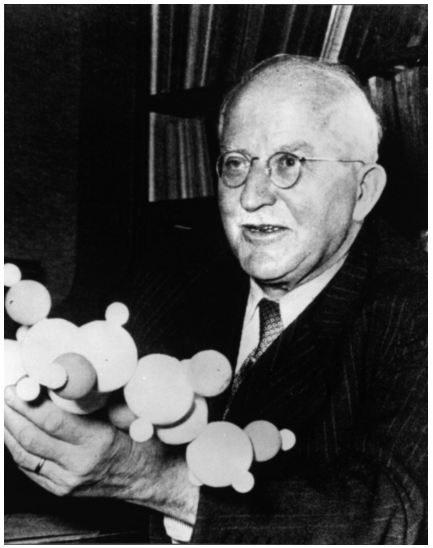


Herrmann Staudinger: From Organic to Macromolecular Chemistry

April, 11, 2011

Christian Grünanger

$$\frac{\eta_{sp}}{c} = K_m \bullet M$$



International Historic Landmark of Chemistry

Origin of Polymeric Sciences

review: Mühlhaupt, R. *Angew. Chem. Int. Ed.* **2004**, *43*, 1054-1063.

Overview

** March 23, 1881 in Worms*

1903:	*PhD from University of Halle*	*malonate addition to unsaturated compounds*
1903-1907:	*Habilitation with J. Thiele at University of Strasbourg*	*ketene chemistry*
1907-1912:	*Asstistant Professor at Technical University of Karlsruhe*	*oxalyl chloride, aliphatic diazo compounds, carbene reactions, new organophosphorus compounds, biofunctional small molecules, preparation and polymerization of isoprene and butadiene*
1912-1926:	*Professor at ETH Zürich*	
1926-1956:	*Professor at Albert-Ludwigs-University, Freiburg*	*development of the concept of macromolecules*

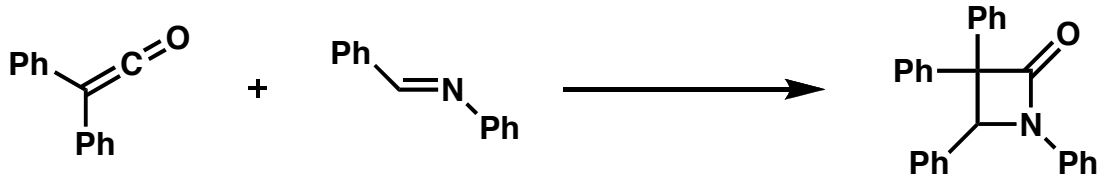
+ September 8, 1965 in Freiburg

Ketenes: Isolation and Identification

1905:

Staudinger, H. *Ber. Dtsch. Chem. Ges.* **1905**, *38*, 1735 - 1739.

1907:

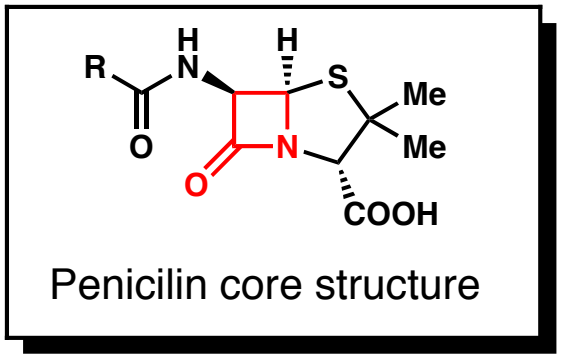


also describes β-lactones and cyclobutanones

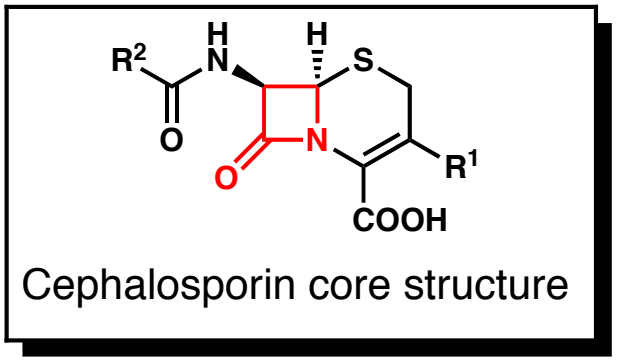
Staudinger, H. *Justus Liebigs Ann. Chem.* **1907**, *356*, 51-123.

Ketenes: Importance for β-Lactam Synthesis

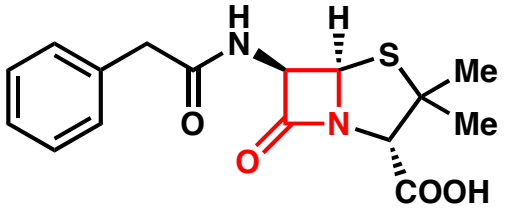
1928: A. Fleming: Discovery of Penicillin



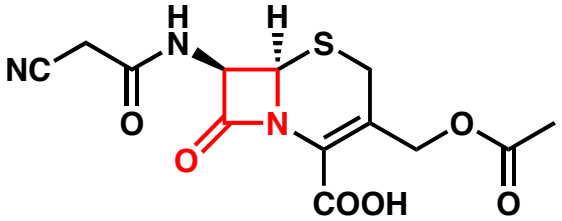
Penicilin core structure



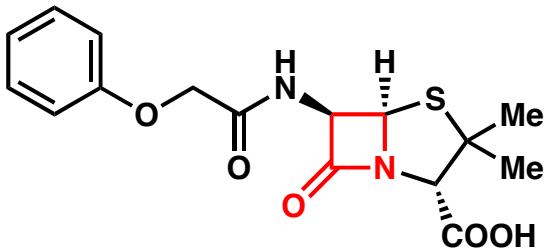
Cephalosporin core structure



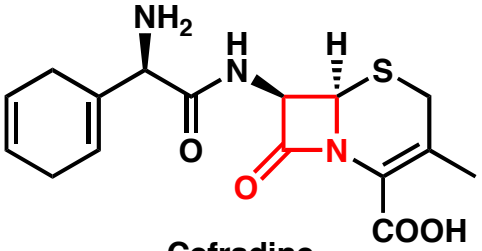
Benzylpenicillin, Penicillin G



Cefacetril



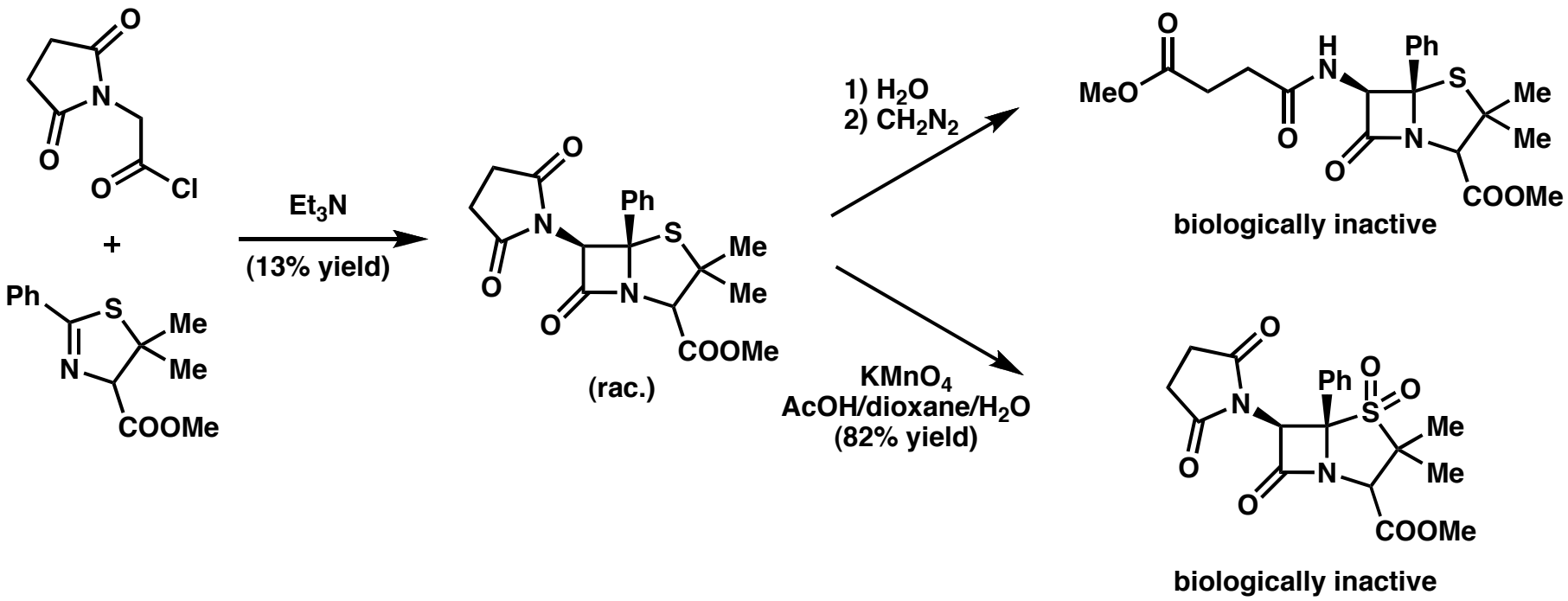
Phenoxymethylpenicillin, Penicillin V



Cefradine

β-Lactams in Total Synthesis

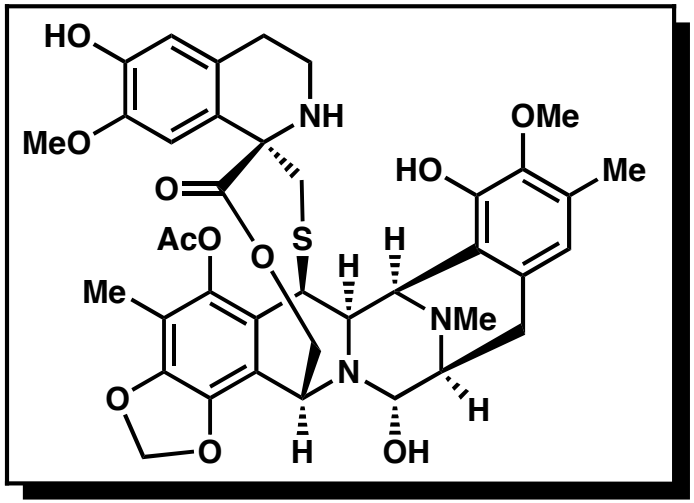
First synthetic penicillin structure

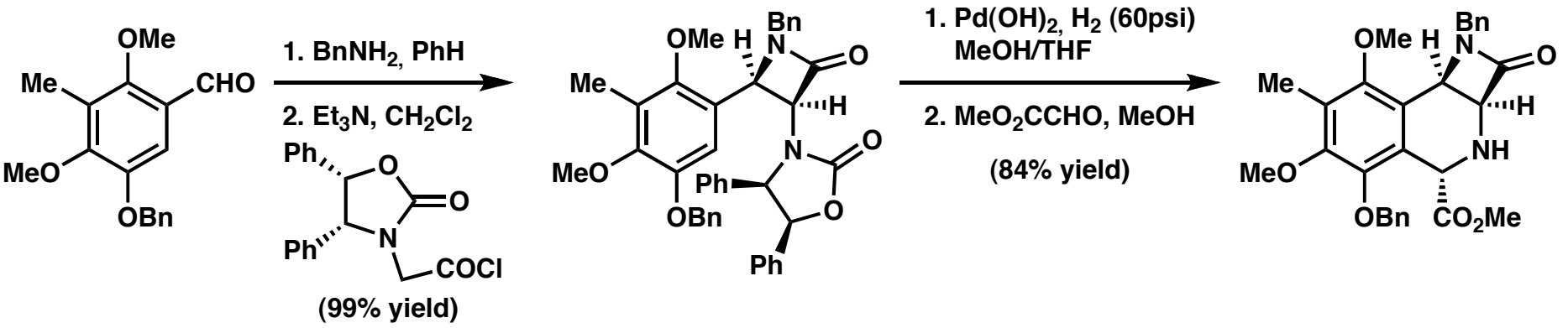


Sheehan, J. C.; Buhle, E. L.; Corey, E. J.; Laubach, G. D.; Ryan, J. J. *J. Am. Chem. Soc.* **1950**, *72*, 3828-3829.

β-Lactams in Total Synthesis

Synthetic Studies on Ecteinascidin-743

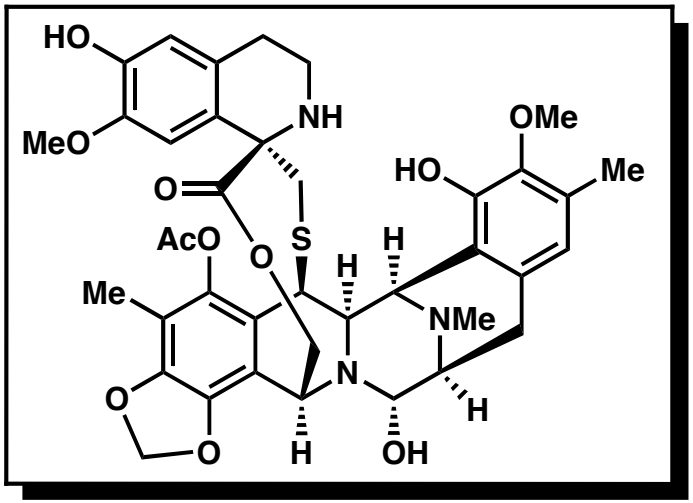


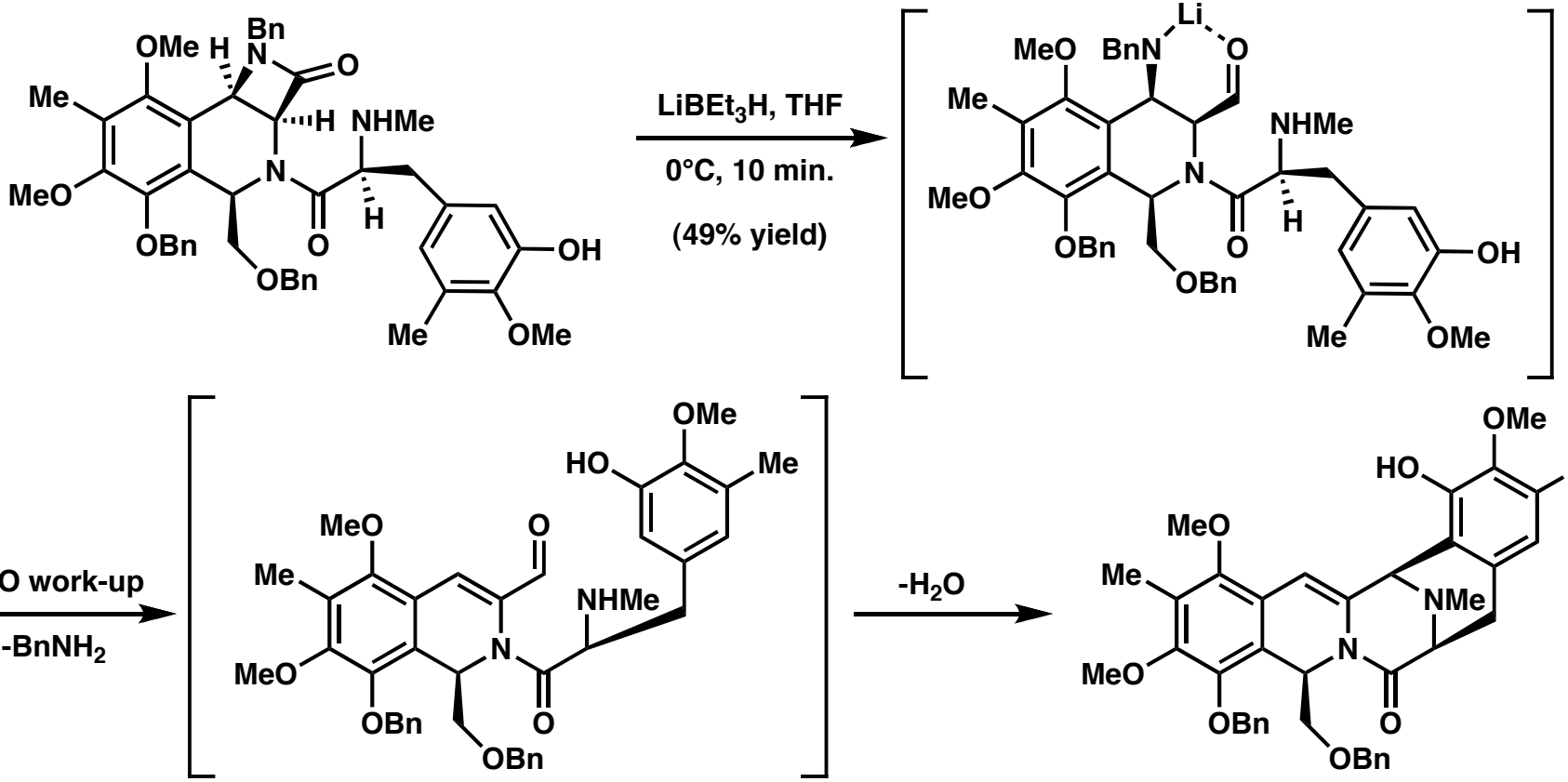


Jin, W.; Metobo, S.; Williams, R. M.; *Org. Lett.* **2003**, *5*, 2095-2098.

β-Lactams in Total Synthesis

Synthetic Studies on Ecteinascidin-743

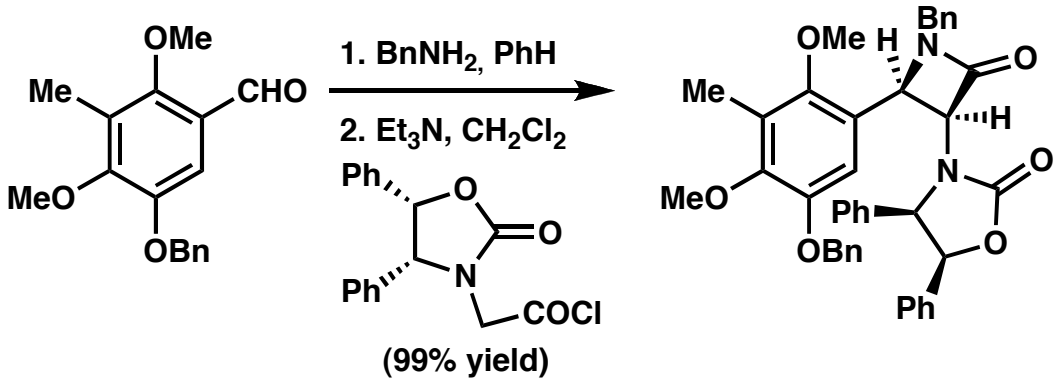


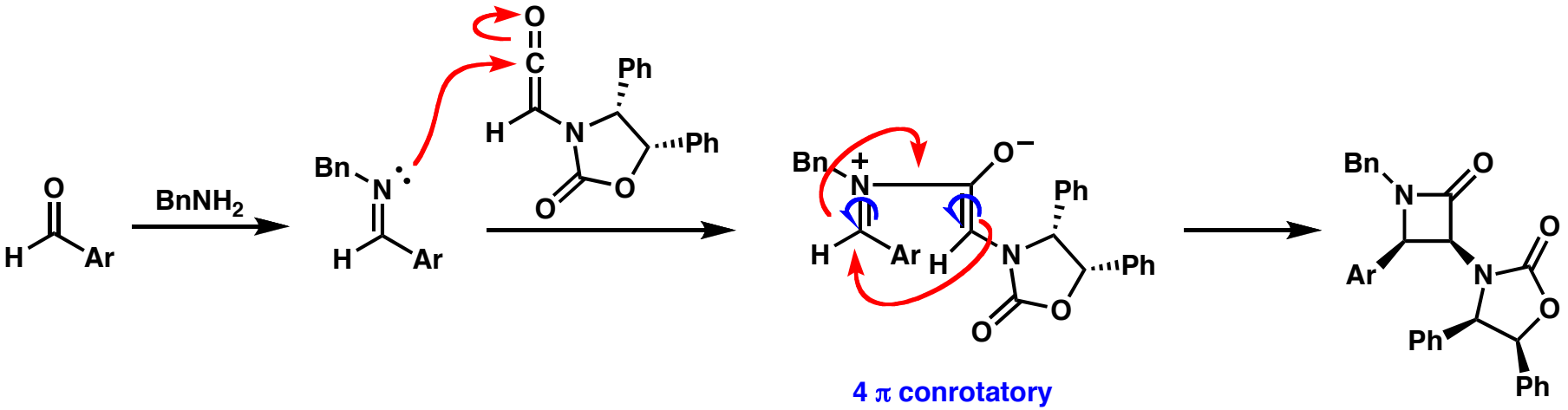


Jin, W.; Metobo, S.; Williams, R. M.; *Org. Lett.* **2003**, *5*, 2095-2098.

β-Lactams in Total Synthesis

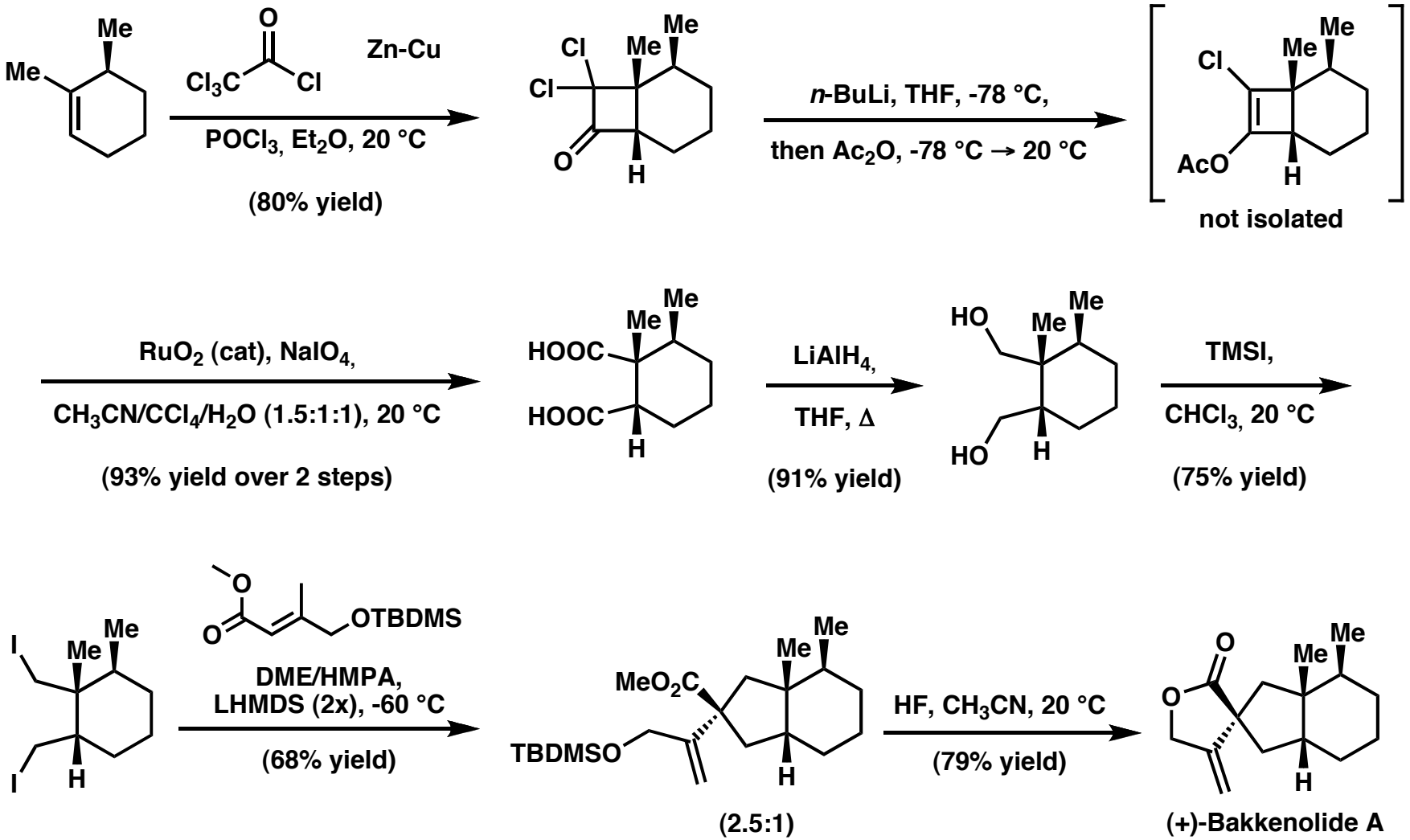
Synthetic Studies on Ecteinascidin-743 - Origin of Diastereoselectivity





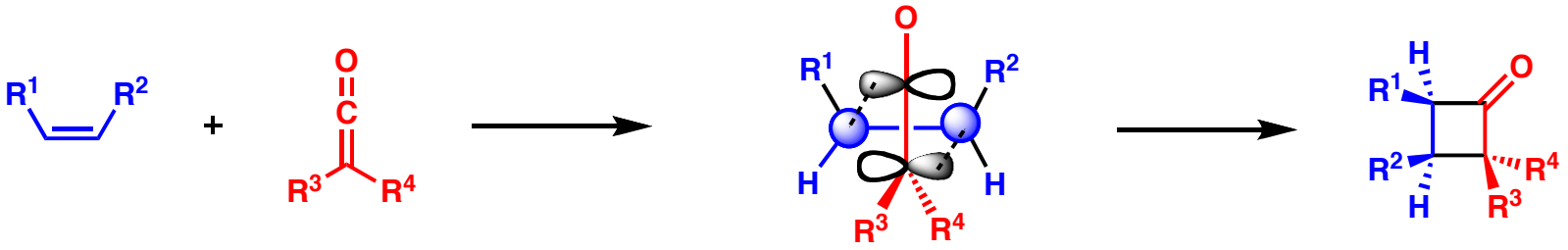
for mechanistic studies: Venturini, A.; González, J. *J. Org. Chem.* **2002**, *67*, 9089-9092.

Cyclobutanones in Total Synthesis



Brocksom, T. J.; Coelho, F.; Deprés, J.-P.; Greene, A. E.; Freire de Lima, M. E.; Hamelin, O.; Hartmann, B.; Kanazawa, A. M.; Wang, Y. *J. Am. Chem. Soc.* **2002**, *124*, 15313-15325.

Reactivity of Ketenes with Alkenes



LUMO of ketene: antarafacial

HOMO of alkene: suprafacial

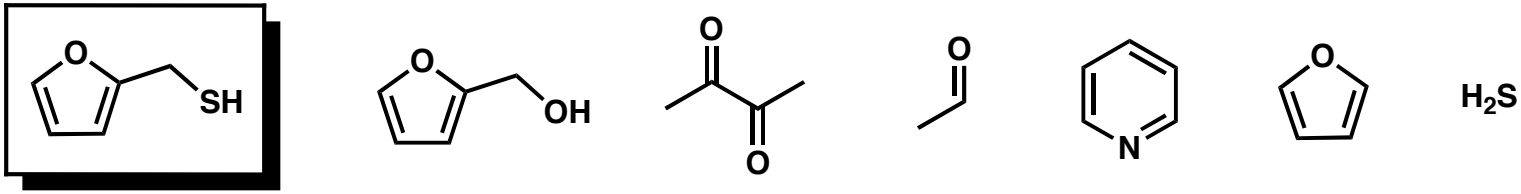
Huisgen, R.; Mayr, H. *Tet. Lett.,* **1975**, *16*, 2969-2972.

Coffee break?

Isolation of Coffee and Pepper flavors

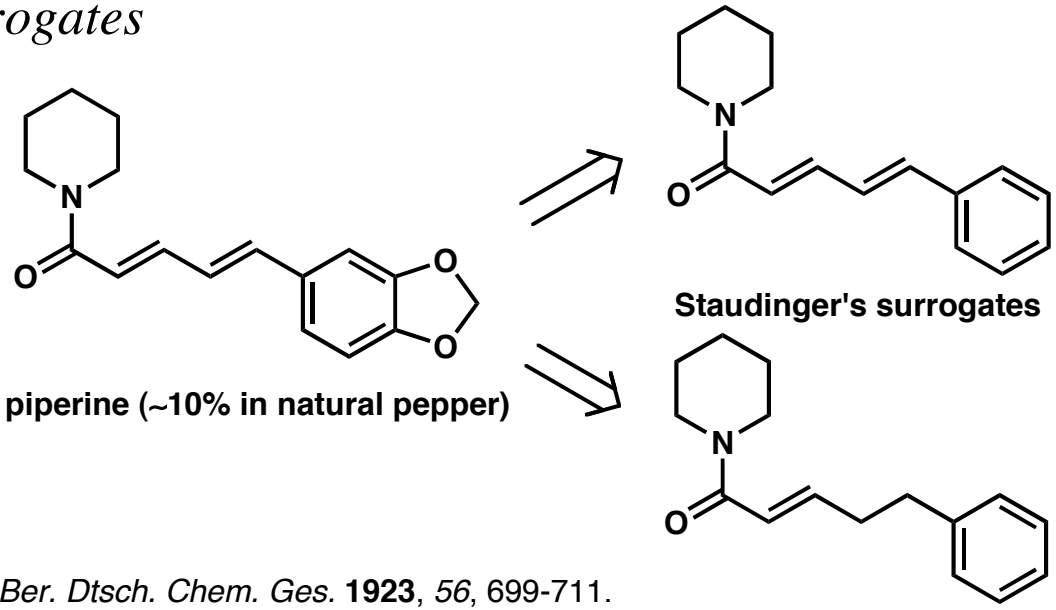
~1914-1918 due to shortage of coffee during WWI

Coffee: Isolation of 70 compounds



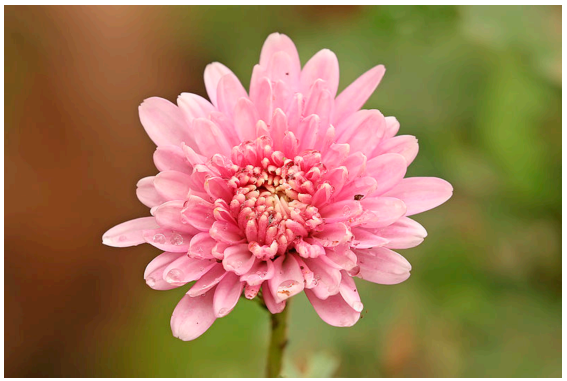
Reichstein, T.; Staudinger, H. *Angew. Chem.* **1950**, *62*, 292.
Johnston, W. R.; Frey, C. N.; *J. Am. Chem. Soc.* **1938**, *60*, 1624-1627.

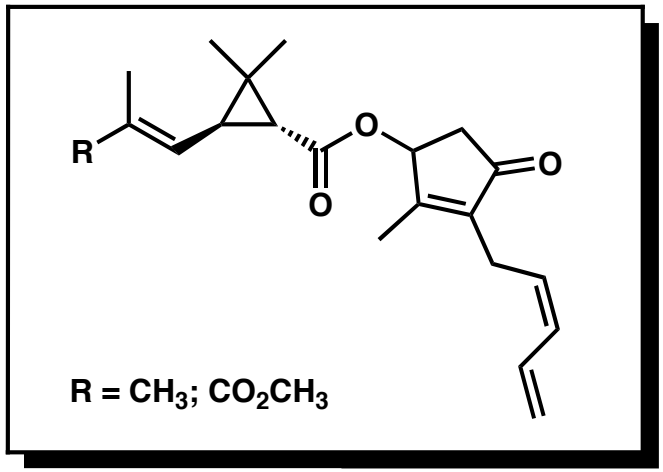
Pepper: Search for surrogates



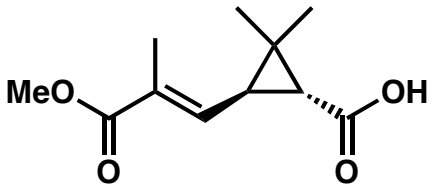
a) Staudinger, H.; Schneider, H. *Ber. Dtsch. Chem. Ges.* **1923**, *56*, 699-711.
b) Staudinger, H.; Müller, F.; *Ber. Dtsch. Chem. Ges.* **1923**, *56*, 711-715.

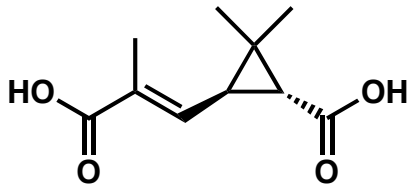
Identification of Pyrethrins as active ingredients of Dalmatian insect-powder

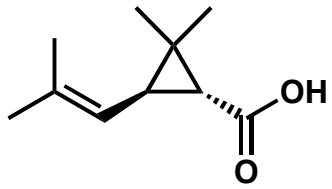


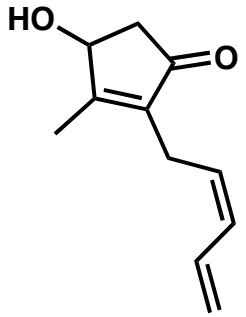


NaOH (aq.)



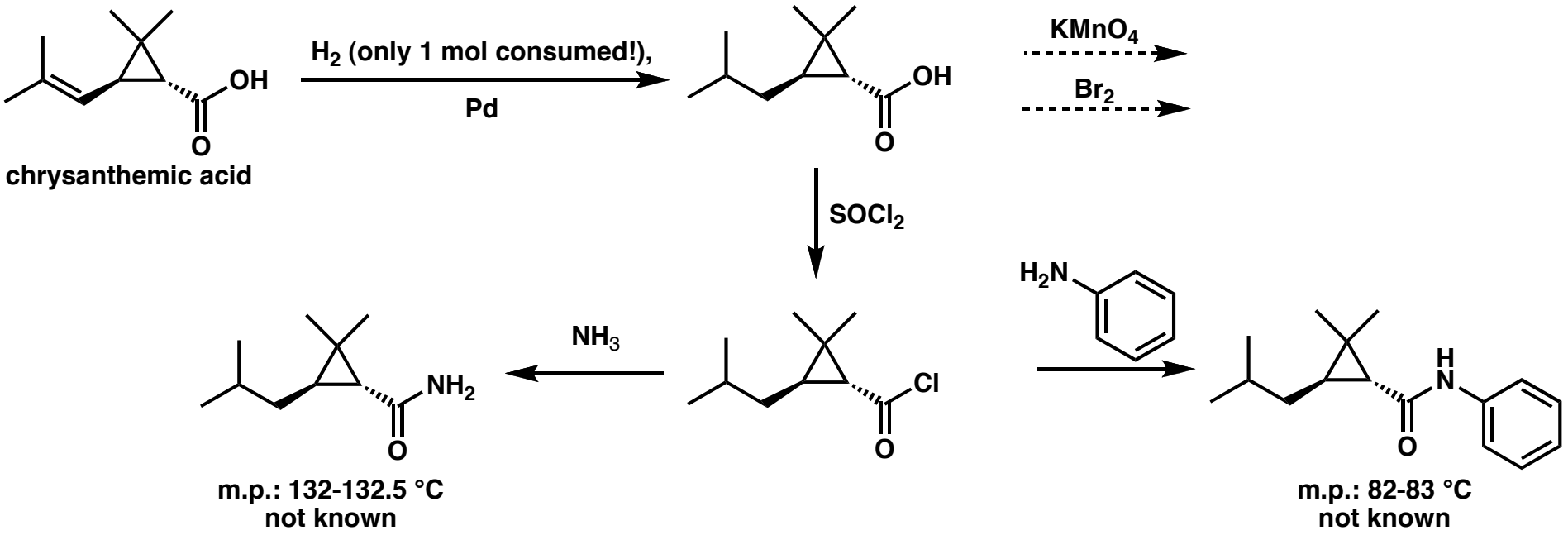


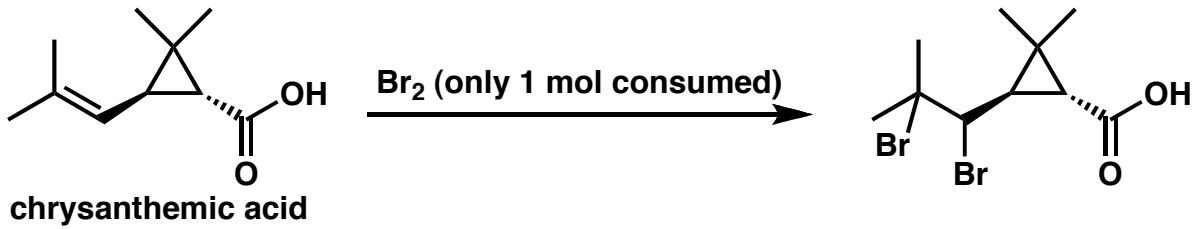




a) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 201-211.
b) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 212-235.

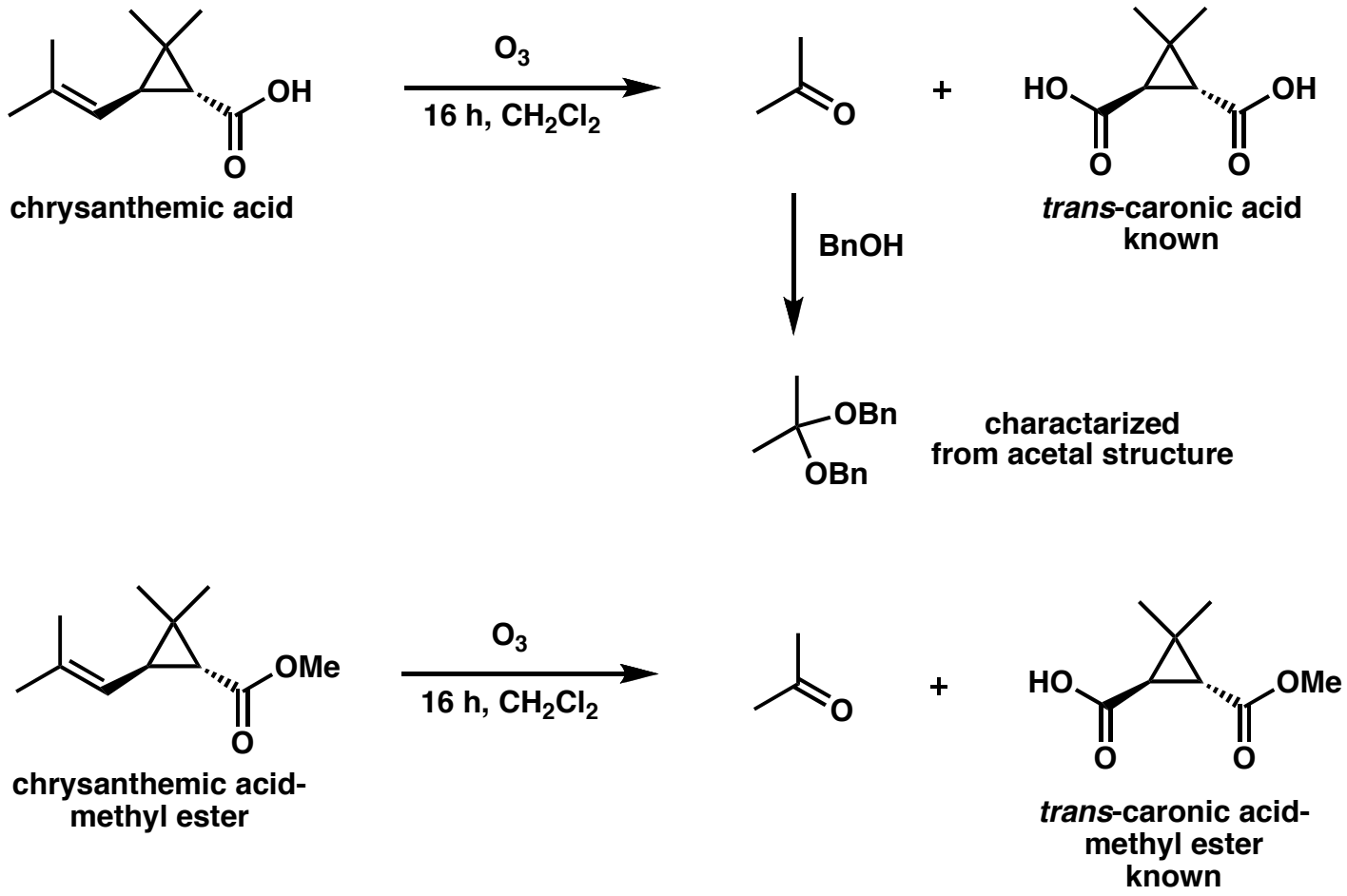
Identification of Pyrethrins





a) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 201-211.
b) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 212-235.

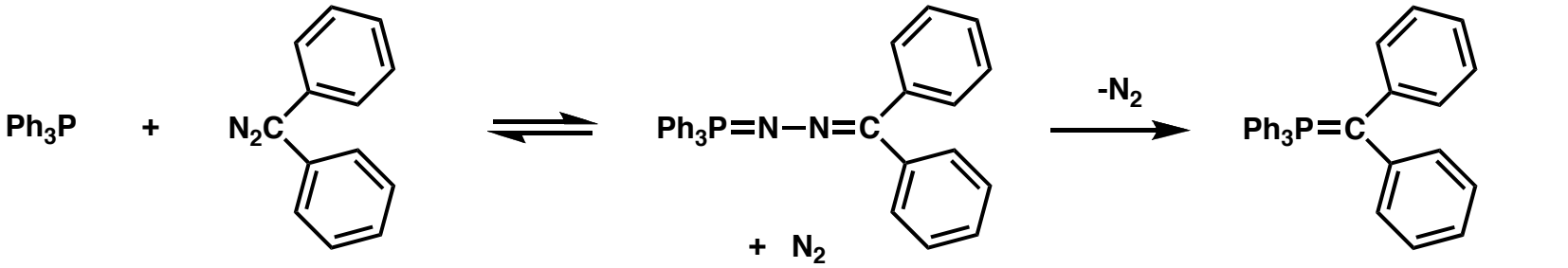
Identification of Pyrethrins

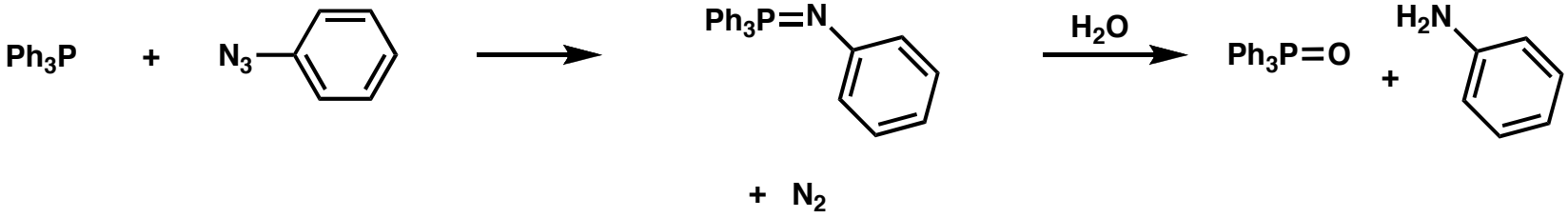


a) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 201-211.
b) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 212-235.

The Staudinger reaction: early development

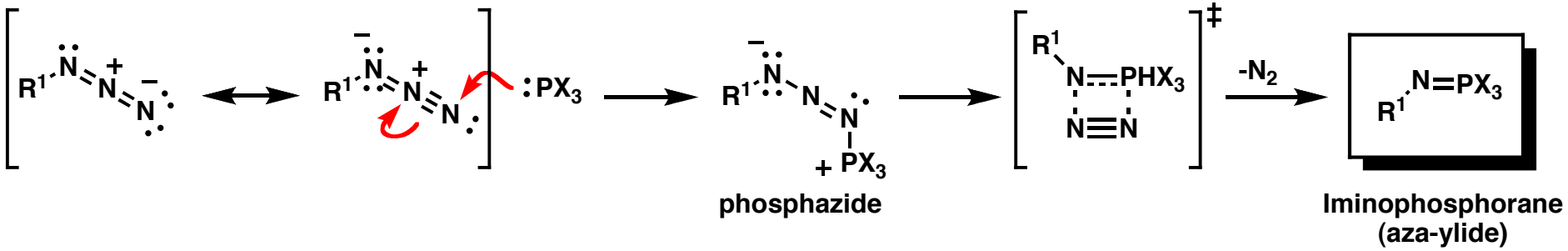
1919:

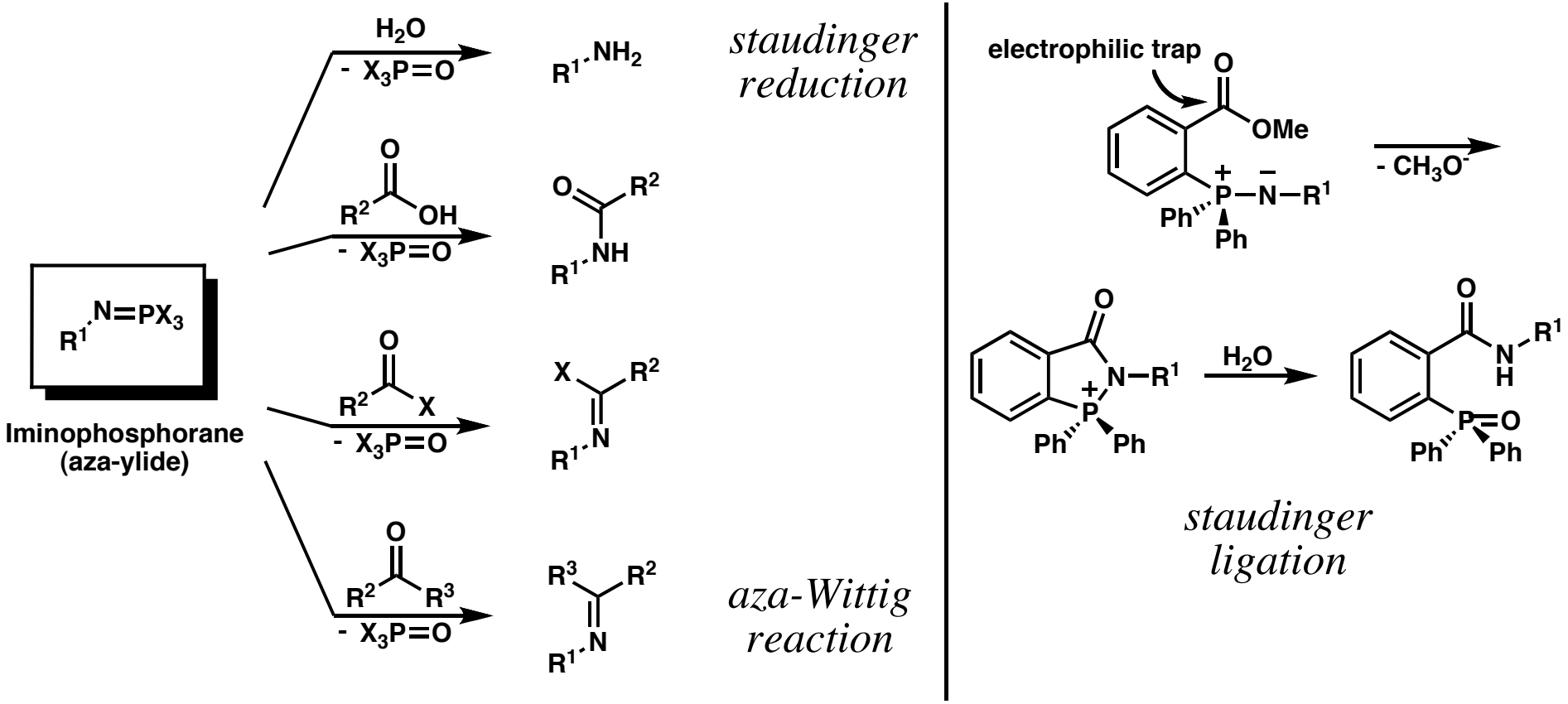




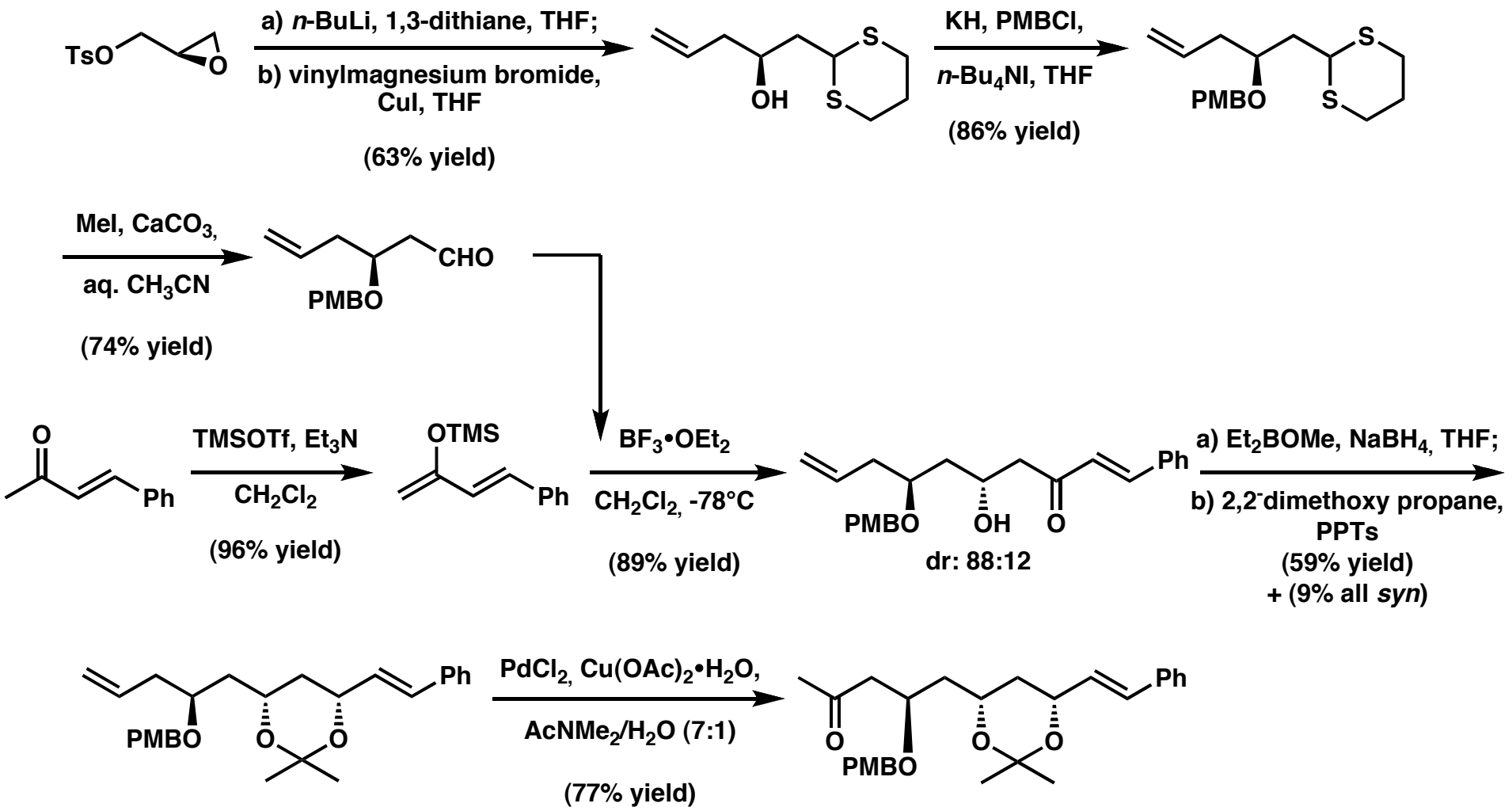
a) Staudinger, H.; Meyer, J. *Helv. Chim. Acta.*, **1919**, *2*, 619-635.
b) Staudinger, H.; Meyer, J. *Helv. Chim. Acta.*, **1919**, *2*, 635-646.
c) Staudinger, H.; Hauser, E. *Helv. Chim. Acta.*, **1921**, *4*, 861-886.

The Staudinger reaction: mechanism and applications



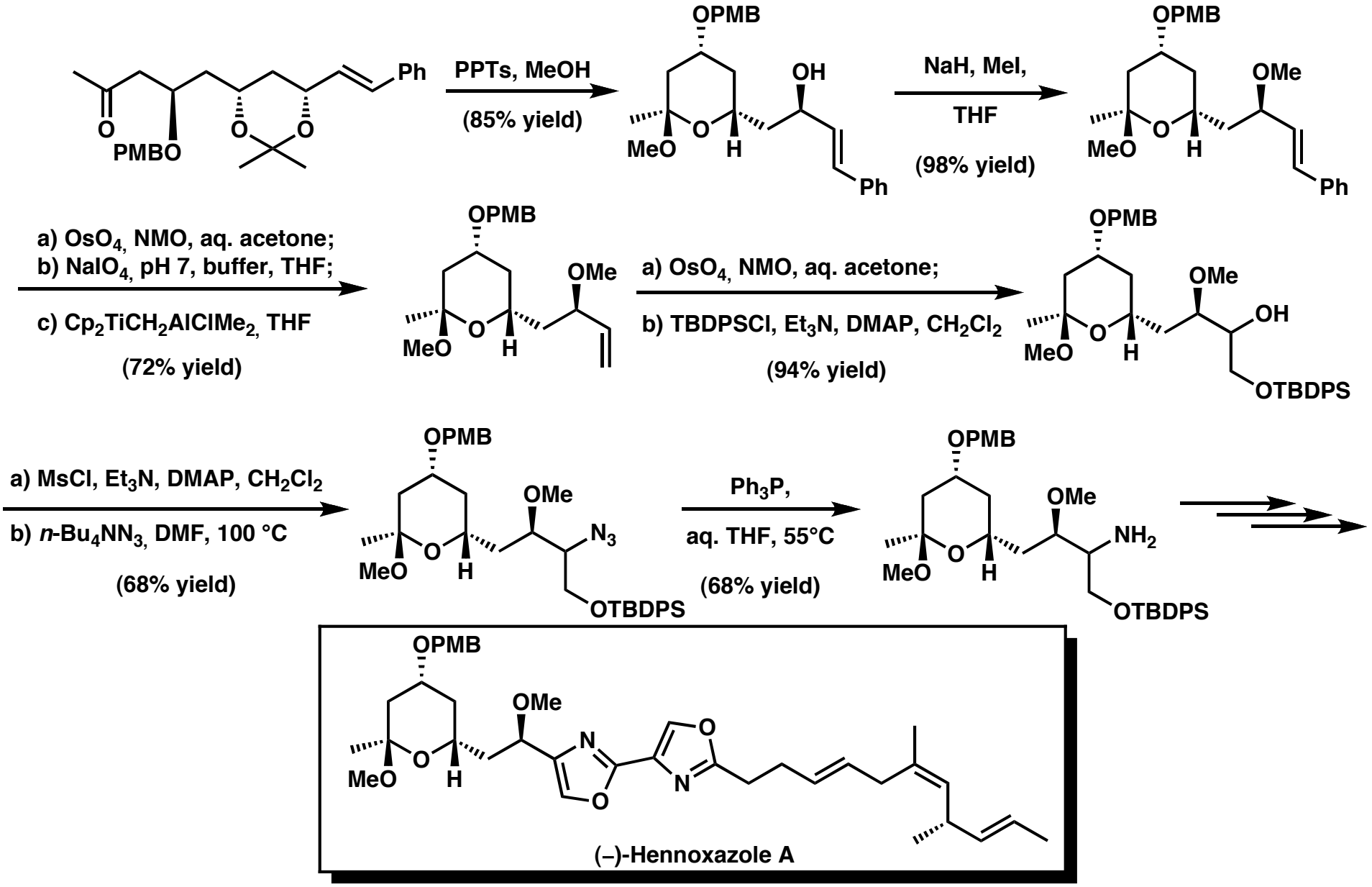


Staudinger reduction: Synthetic application



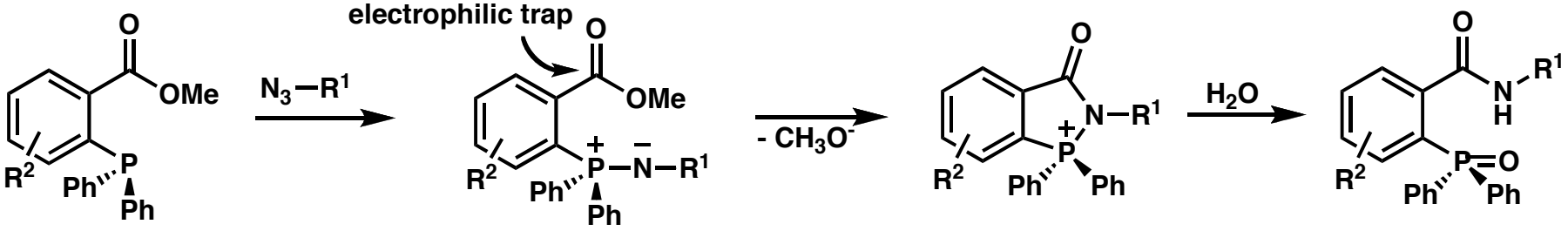
Yokokawa, F.; Asano, T.; Shioiri, T. *Org. Lett.* **2002**, *2*, 4169-4172.

Staudinger reduction: Synthetic application



Yokokawa, F.; Asano, T.; Shioiri, T. *Org. Lett.* **2002**, *2*, 4169-4172.

The Staudinger Ligation: Introduction

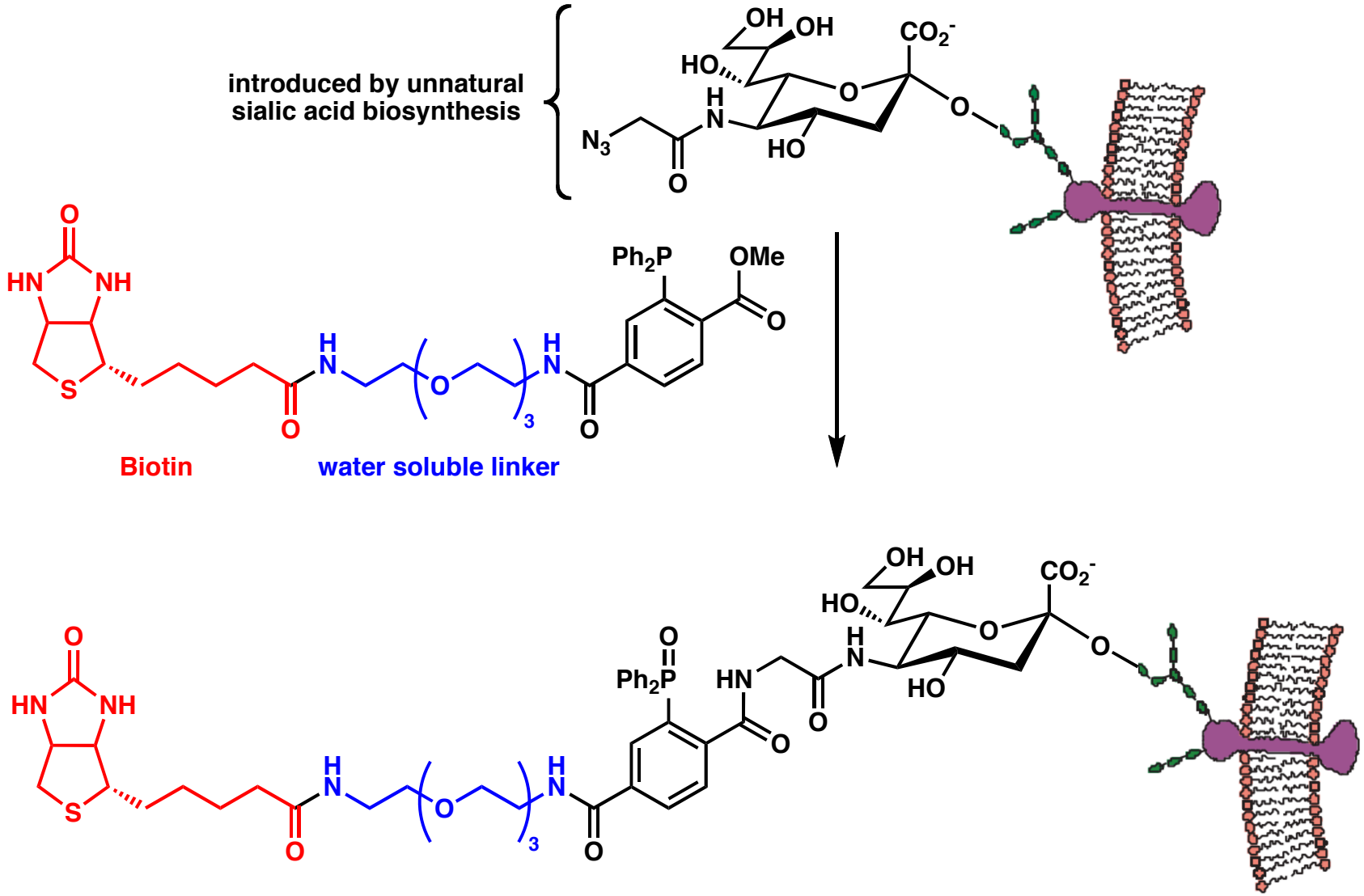


Clue: Coupling of abiotic reagents (phosphines and azides) under biocompatible conditions

$\Longrightarrow$ *Phosphine oxide and R^2 is only present and covalently bound at reaction position*

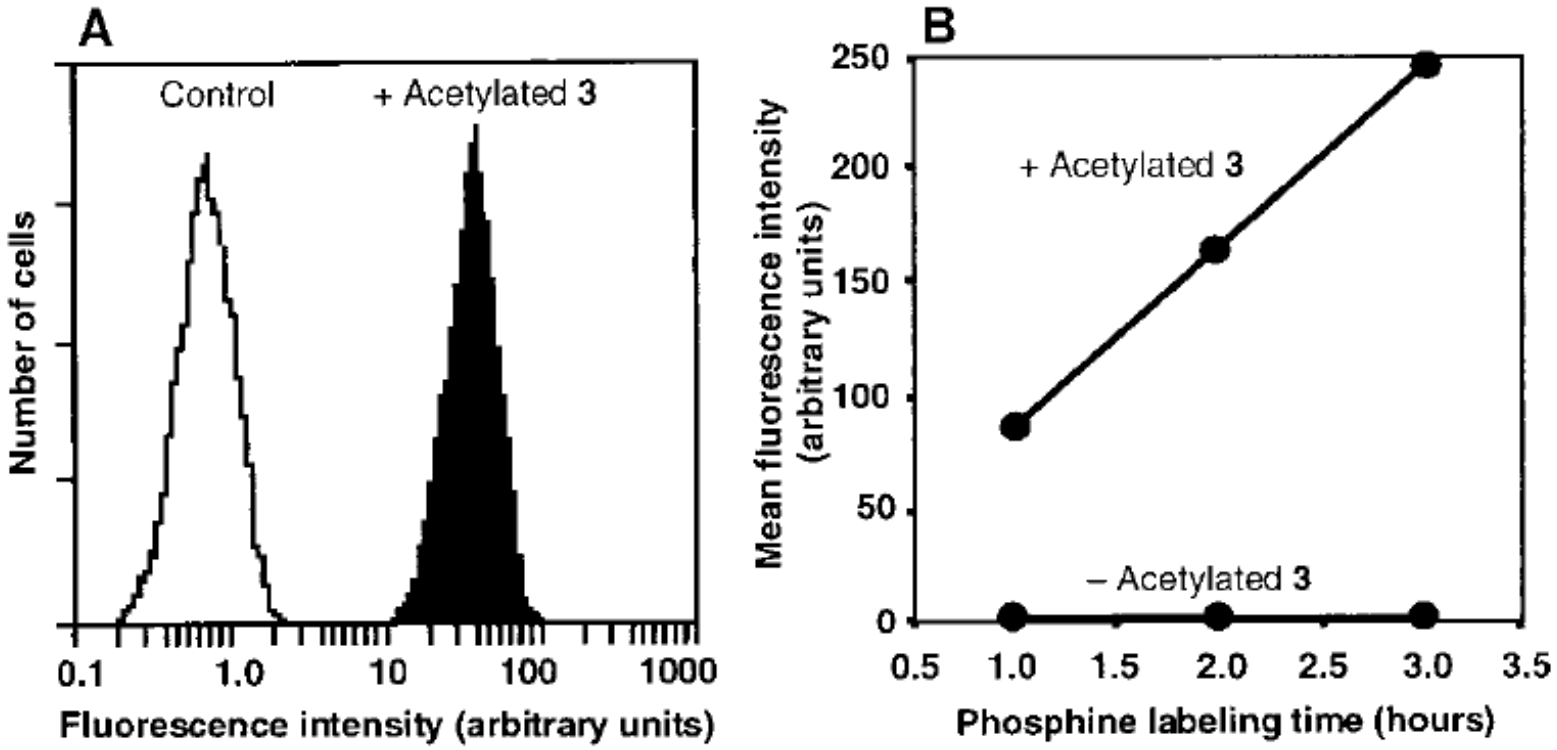
$\Longrightarrow$ *Allows examination of biological processes*

Staudinger ligation on cell surfaces



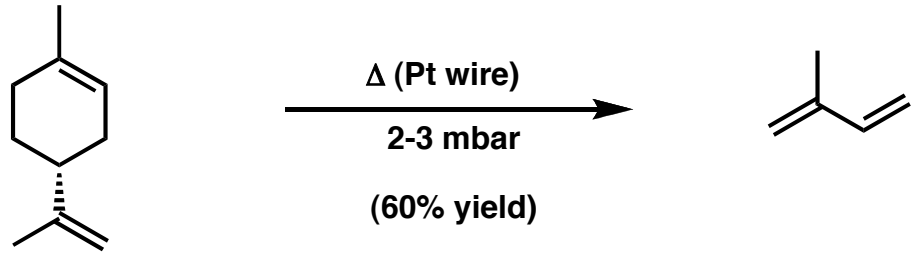
Saxon, E.; Bertozzi, C. R. *Science* **2000**, *287*, 2007-2010.

Staudinger ligation on cell surfaces



Saxon, E.; Bertozzi, C. R. *Science* **2000**, *287*, 2007-2010.

Pyrolysis of 6-membered rings: one of the first industrial routes to 1,3-dienes

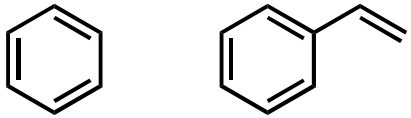


Staudinger, H.; Klever, H. W. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 2212-2215.

Definition of the word "polymer"

before ca. 1920-1930:

1833: Berzelius[a]: compounds of the same chemical composition that exhibit very different properties. = isomers, homologues



1866: Berthelot[b] reports the formation of the "polymers" benzene and styrene upon heating acetylene

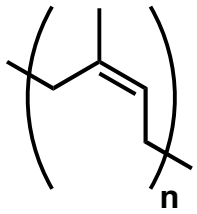
The concept of macromolecules was not accepted

ca. 1930: The community accepted Staudingers concept of macromolecules
polymers = macromolecules

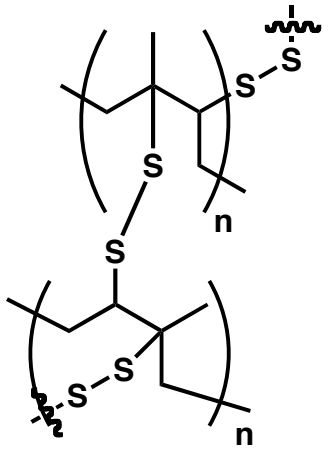
a) Berzelius, J. *Jahresber. Fortsch. Phys. Wissensch.* **1833**, *12*, 63.
b) Berthelot, P. E. M. *Bull. Soc. Chim. Fr.* **1866**, *6*, 268.

1920: known polymers - structure unknown

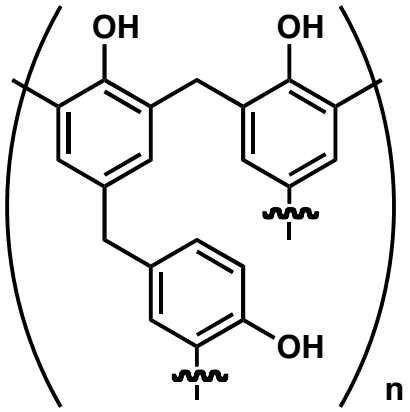
natural rubber:



vulcanized rubber:



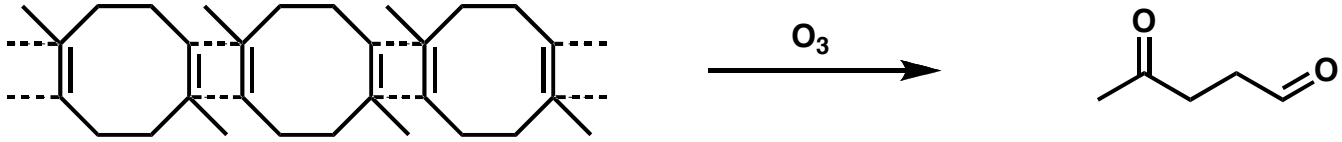
bakelite:



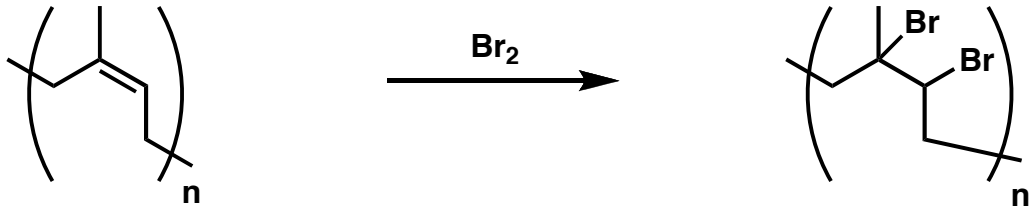
and others

Proposed wrong structures and misleading experiments

1902: Harries' proposal for natural rubber.[a] self-assembly of dimethylcyclooctadiene



1914: Pickles' bromination of natural rubber.[b] First proposal of covalent bonds between isoprene monomer molecules. Underestimation of molecular weight.

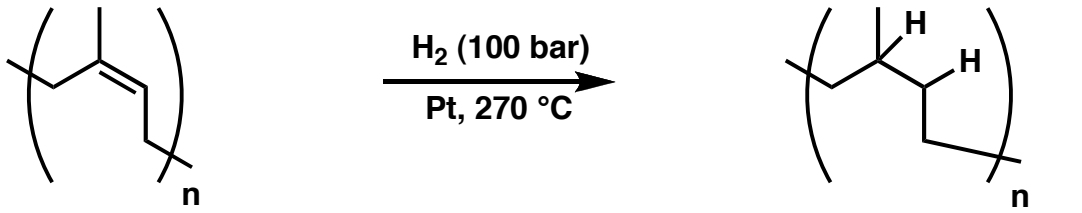


1923: Brills cristallographic work on silk fibroin[c]: protein molecules M = 500 - 600 g/mol

a) Harries, C. *Ber. Dtsch. Chem. Ges.* **1902**, *35*, 3256.
b) Pickles, S. S. *J. Chem. Soc.* **1910**, *97*, 1085.
c) Brill, R. *Justus Liebigs Ann. Chem.* **1923**, *434*, 204.

First experimental evidence

1922[a]*:*



similar characteristics

n ?

a) Staudinger, H.; Fritschi, J. *Helv. Chim. Acta* **1922**, *5*, 785-806.

Final evidence: Staudingers viscosity law

for molecules in highly diluted solution (no interaction of molecules):

Einsteins viscosity law: $\eta_{sp} = K \frac{c \bullet N_L}{M} \varphi$

η_{sp} = specific viscosity
K = constant (depending on solvent, substance)
N_L = Avogadro (Loschmidt) - constant
φ = volume of particle

for one and the same substance in different concentrations: $K \frac{N_L}{M} \varphi = K'$

$$\frac{\eta_{sp}}{c} = K'$$

Glucose

c (g/mol)	η_{sp}	η_{sp}/c	
1.00	0.027	0.027	
2.11	0.062	0.029	
4.63	0.131	0.028	
10.20	0.316	0.031	↓ association of molecules
15.72	0.619	0.039	
20.14	0.901	0.045	
24.03	1.216	0.056	

Staudinger, H.; Heuer, W. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 222-234.

Final evidence: Staudingers viscosity law

for polystyrene (polymerized by heating, $\overline{M_W} > 10000$:

$$\frac{\eta_{sp}}{c} = K'$$

polystyrene

c (g/mol)	η_{sp}	η_{sp}/c
0.125	0.54	4.32
0.25	1.21	4.84
0.5	3.05	6.10
0.75	5.69	7.58
1.0	9.25	9.25
1.5	31.00	20.66
2.0	59.5	29.75

association ?

Einsteins viscosity law: $\eta_{sp} = K \frac{c \bullet N_L}{M} \varphi$

η_{sp} = specific viscosity
K = constant (depending on solvent, substance)
N_L = Avogadro (Loschmidt) - constant
φ = volume of particle

what is the volume of a macromolecule?

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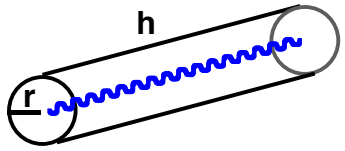
Final evidence: Staudingers viscosity law

$$\eta_{sp} = K \frac{c \bullet N_L}{M} \varphi$$

macromolecule considered to be a cylinder:

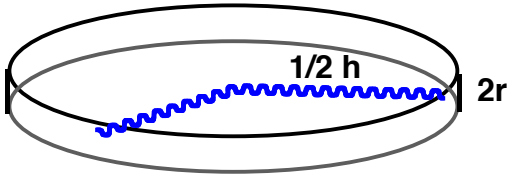


h = length of molecule
r = "radius" of chain

$$\varphi = r^2 \pi h \Longrightarrow \eta_{sp} = K \frac{c \bullet N_L \bullet r^2 \pi h}{M}$$

$$\Longrightarrow \eta_{sp} = K' c$$ *does not apply!*

macromolecule allowed to move in volume:



$$\varphi = \frac{1}{2} r \pi h^2 \Longrightarrow \eta_{sp} = K \frac{c \bullet N_L \bullet r \pi h^2}{2 M}$$

$$\Longrightarrow \eta_{sp} = K' c h = K_m \bullet c \bullet M$$

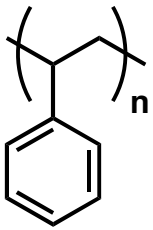
$$\Longrightarrow \boxed{\frac{\eta_{sp}}{c} = K_m \bullet M}$$ *does apply!*

Staudinger, H.; Heuer, W. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 222-234.

Final evidence: Staudingers viscosity law

polystyrenes, polymerized by heating

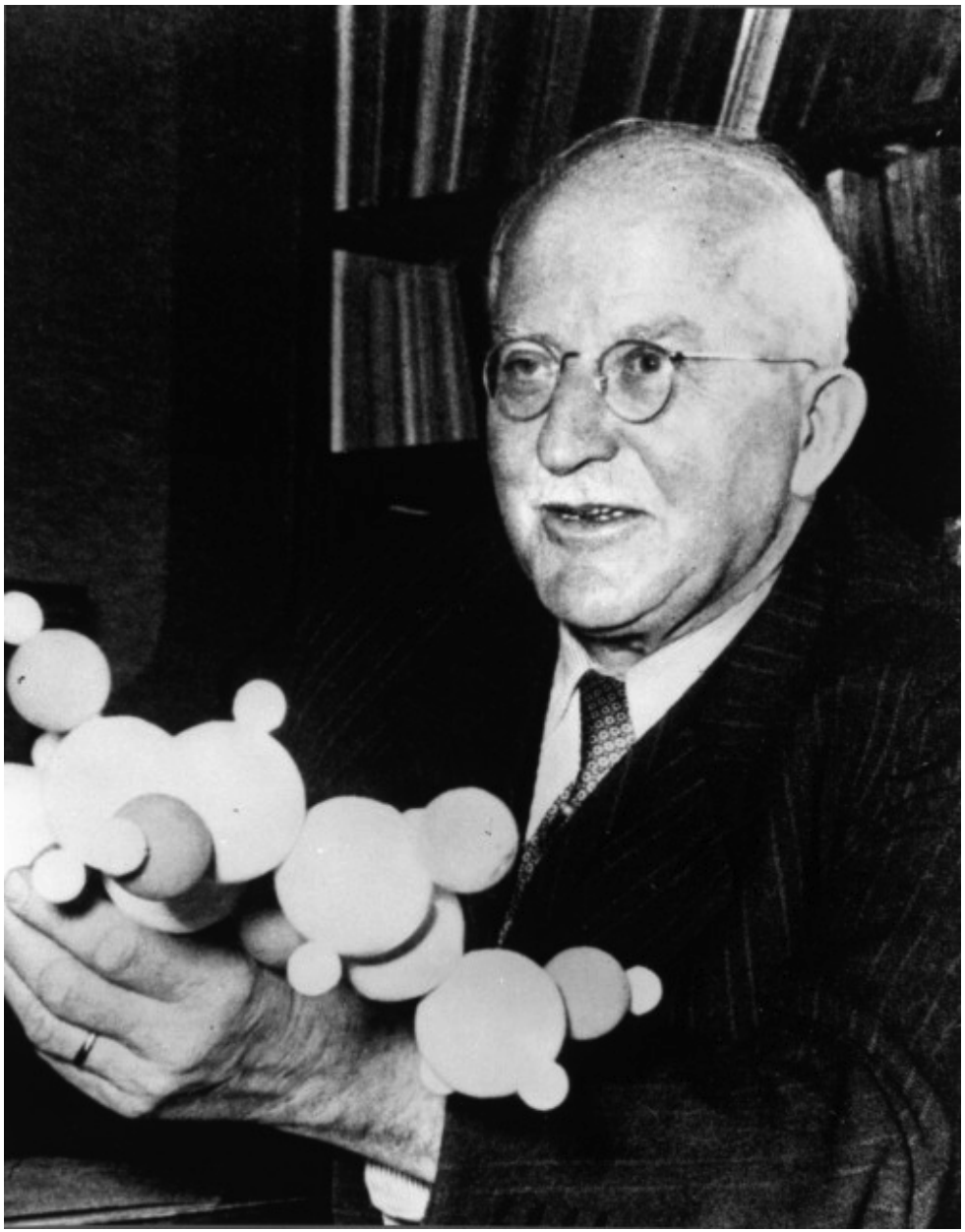
$$\frac{\eta_{sp}}{c} = K_m \bullet M$$



polymerization conditions	$\frac{\eta_{sp}}{c}$	M ($K_m = 0.25 \bullet 10^{-3}$)
6 h 260 °C	3.365	13400
12 h 150 °C	12.26	49000
53 d 100 °C	22.6	90500
17 d 65 °C	30.3	121000
cold	56.0	200000

Staudinger, H.; Heuer, W. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 222-234.

1953: Nobel prize in Chemistry



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