



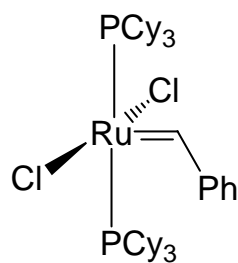
The Efficient Application of Metathesis in Pharmaceuticals and Fine Chemicals

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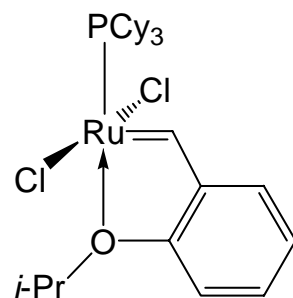
Outline

1. Olefins and Metathesis Catalysts
2. Ring Closing Metathesis in Pharmaceutical Applications
3. Cross Metathesis in Fine Chemical Applications
4. Insect Pheromones from Seed Oils
5. Materia's Building Blocks
6. Wrap up and Conclusions

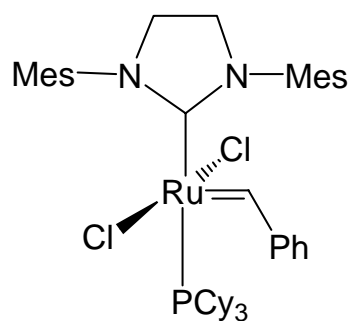
Primary Metathesis Catalysts



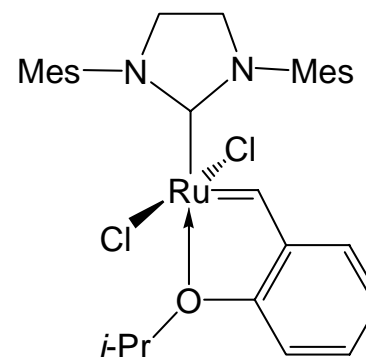
C823



C601



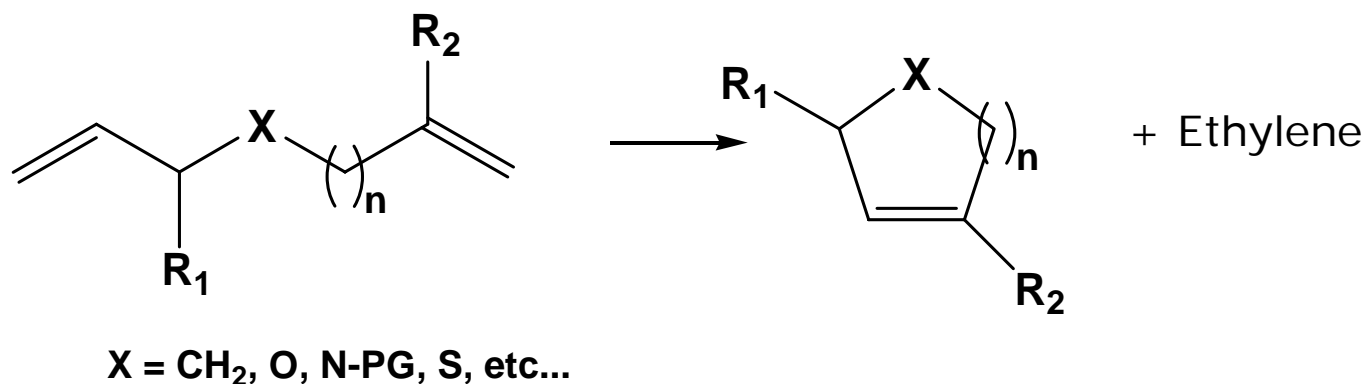
C848



C627

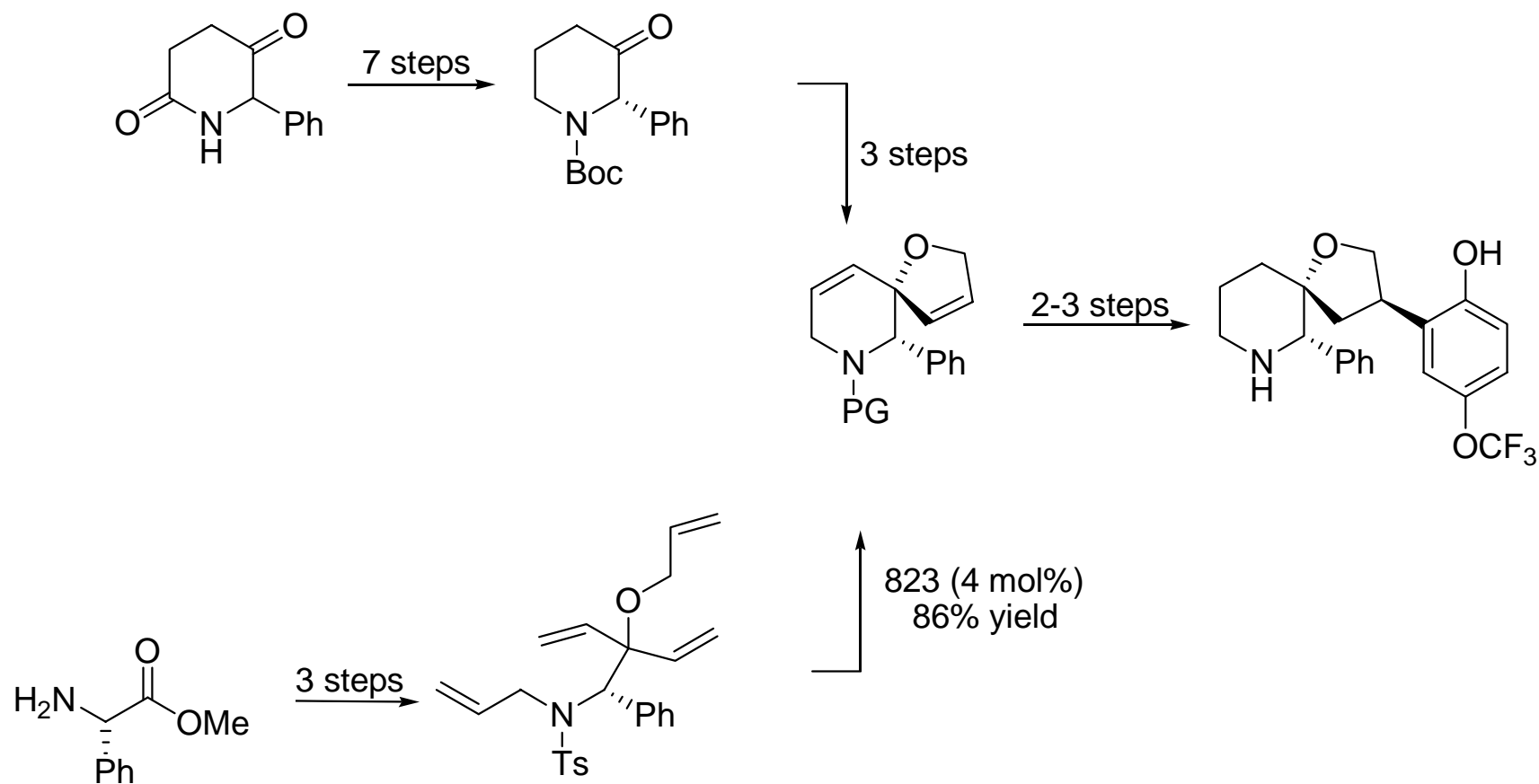
- 30+ proprietary catalysts currently available (11 through Aldrich)
- No single catalyst works best for all reactions
- Materia works with partners to develop optimal reaction conditions

Ring Closing Metathesis in Pharmaceutical Applications

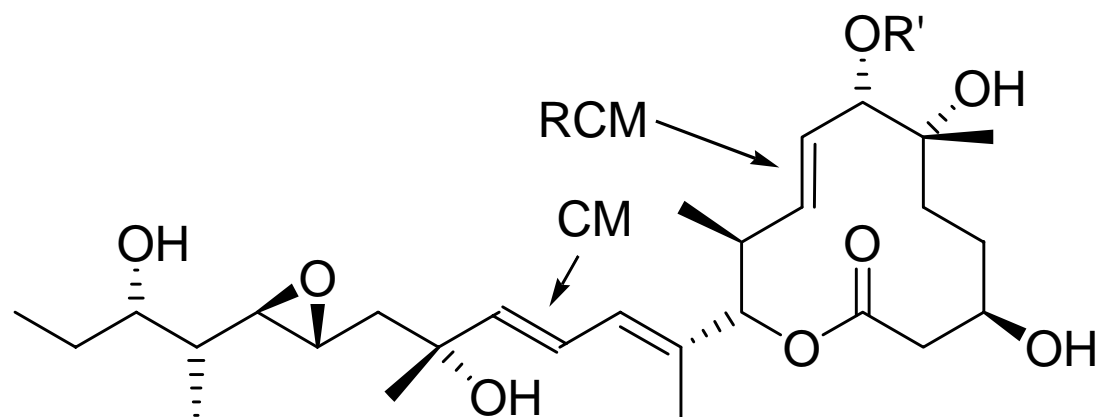


- RCM is an efficient method in the formation of medium to large rings
- Medium rings yield cis-double bonds and can be run more concentrated
- Large rings yield trans-double bonds and need to be run more dilute
- Ring low strain facilitates otherwise non-favorable metathesis reactions

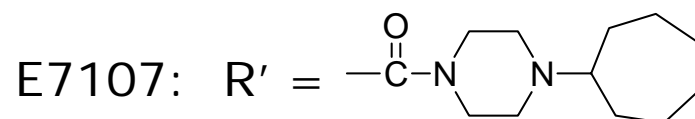
Comparing Synthetic Routes I: Merck's NK-1 Inflammation Drug



Eisai's Synthesis of Macrolide Pladienolides III

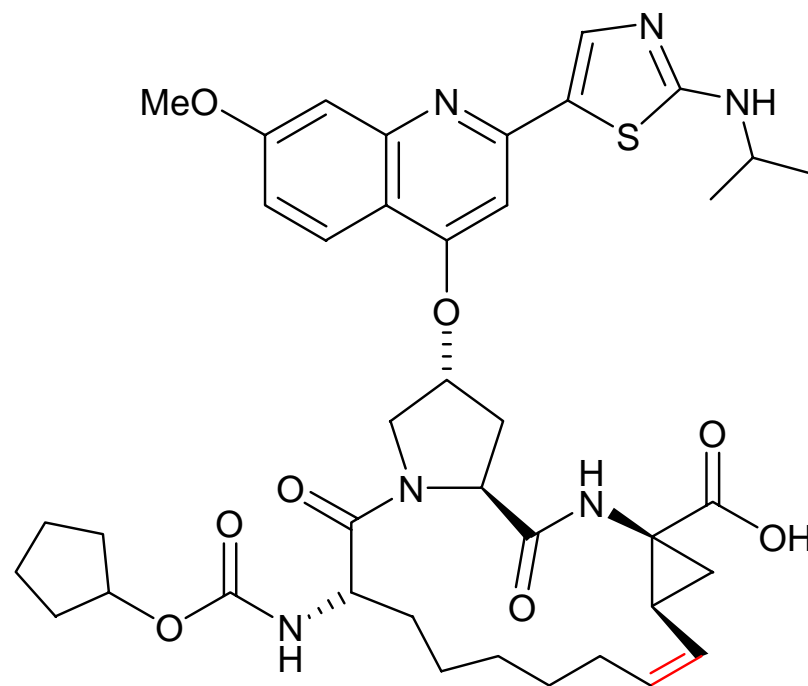


Pladienolide D: $R' = H$



Produce Pladienolide D and E7107 by cross metathesis, traditional Julia-Kocienski olefination techniques failed.

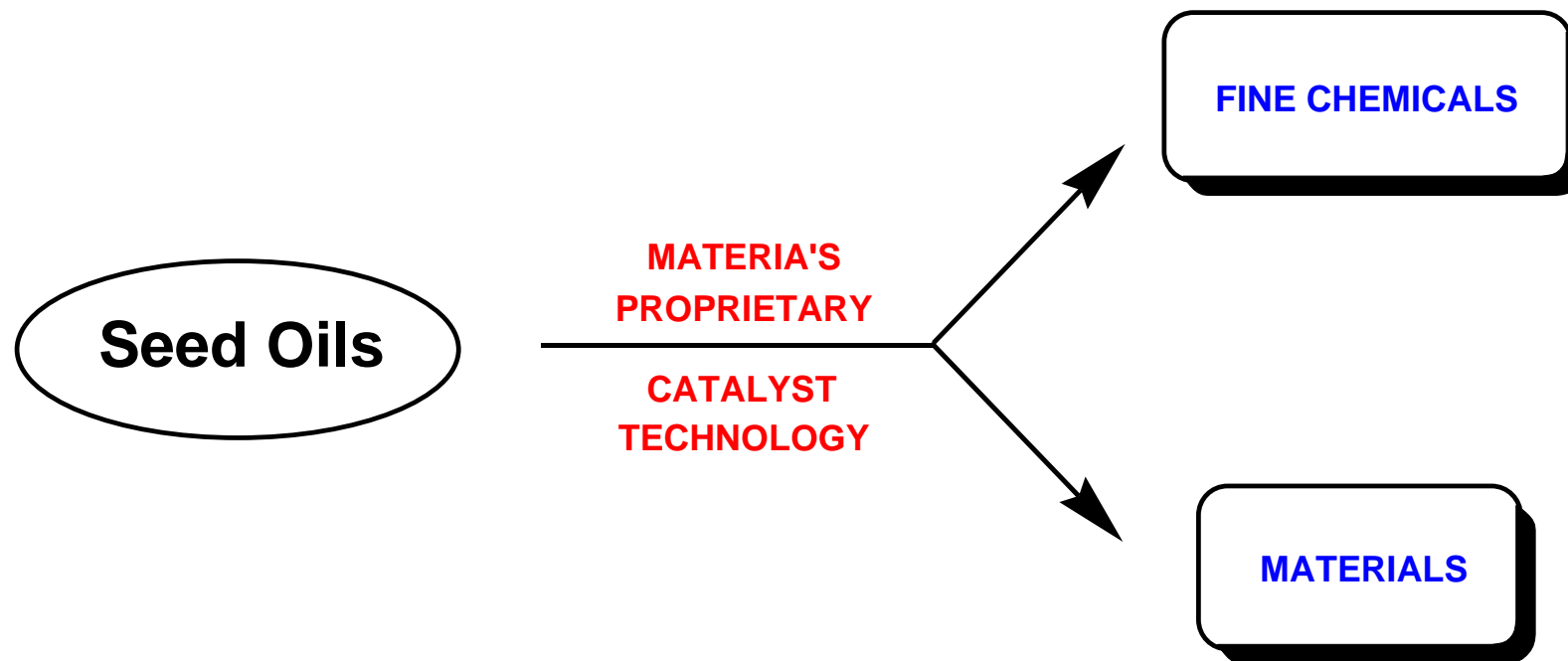
Boehringer Ingelheim's HCV NS3 Serine Protease Inhibitor



BILN 2061

Metathesis intermediate produced on 400 Kg scale

A Successful Collaboration: Seed Oils to Chemicals



Opportunities to use metathesized seed oils
to displace petroleum based products.

Cargill/Materia Collaboration

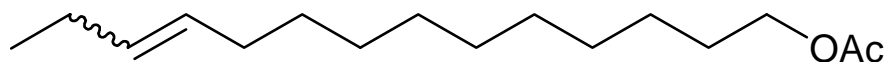
- Production of Methyl 9-Decenoate and 1-Decene
 - Main effort - ethenolysis of Soybean oil* (SBO)
 - Delivered >10x improvement in production efficiency
 - Secondary benefit - self metathesized products yielded new product opportunities
- Production of new materials: Hydrogenated Metathesized Soybean Oil wax (HMSBO)
 - HMSBO eliminates microcrystalline defects in current soy wax
 - Delivered defect-free and otherwise superior alternative
 - Biorenewable alternative to petroleum



Insect Pheromones from Seed Oils

Pheromones from Jojoba Oil

Omnivorous Leafroller Pheromone



82:18 E:Z-11-Tetradecenyl Acetate

Light Brown Apple Moth
Pheromone

E-11-Tetradecenyl Acetate and
E,E-9,11-Tetradecadienyl Acetate

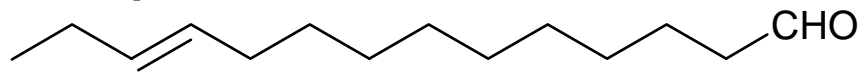


Sparganothis Pheromone

E-11-Tetradecenyl Acetate

Jojoba plant

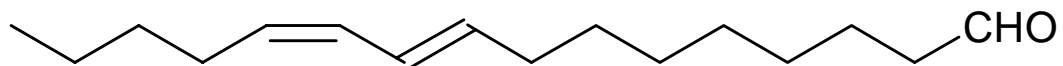
E. Sprucebud Worm Pheromone



E-11-Tetradecenal

Pheromones from Soybean Oil

Pecan Nutcase Bearer Pheromone

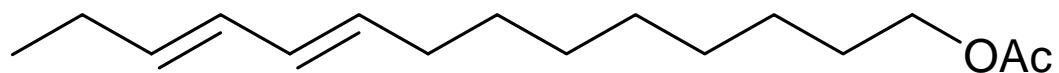


E9,Z11-Hexadecadienal



Soybeans

LBAM minor component



E,E-9,11-Tetradecadienyl Acetate