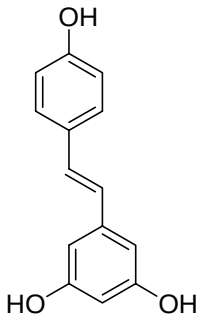
Total Synthesis of Resveratrol-Based Natural Products: A Chemoselective Solution

Scott Snyder and co-workers

Angew. Chem. Int. Ed. Earlyview



Resveratrol

-A phytoalexin produced by plants under attack or some type of stress (bacteria/fungi).

-Commonly associated with red wine and grape skins.

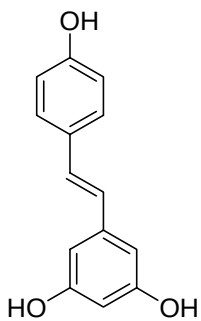
-Not present in white wine or grape juice.

-Concentration of ~100 μM in red wine.

-Believed to be the support of the “French Paradox” by some.

-Resveratrol has demonstrated anticancer, antiviral, neuroprotective, anti-aging and anti-inflammatory effects.

David Waller @ Wipf Group



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Jang and co-workers *Science* **1997**, *275*, 218.
http://en.wikipedia.org/wiki/Resveratrol
Howitz and co-workers Nature 2003, 425, 191.

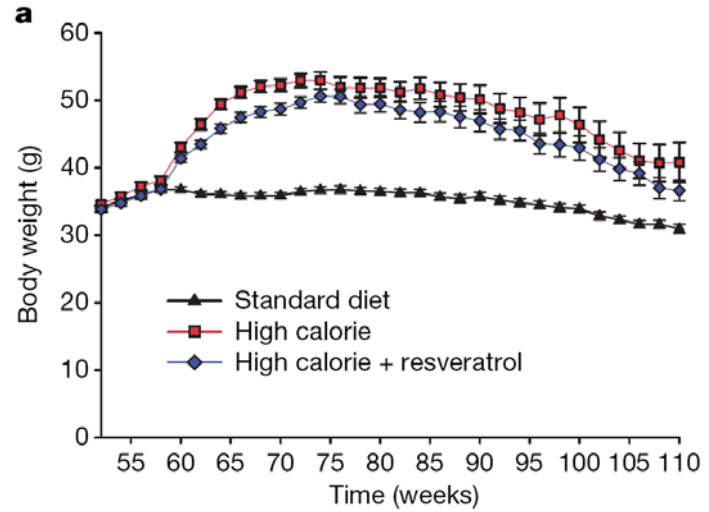
Resveratrol – Anti-aging Properties

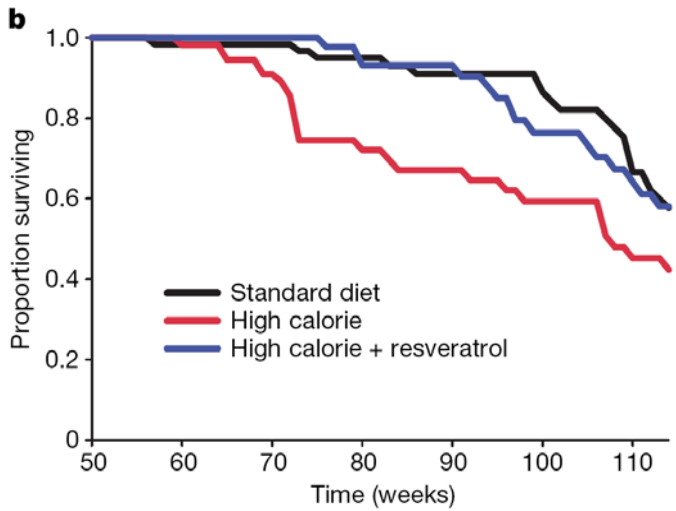
-Lifespan extension is dependent on Sir2 activation

-Sir2 is a deacetlyase “proposed to underlie the beneficial effects of calorie restriction”.

-In this study, resveratrol shifts the physiology of middle-aged mice on a high-calorie diet towards that of a standard diet and significantly increases their lifespan.

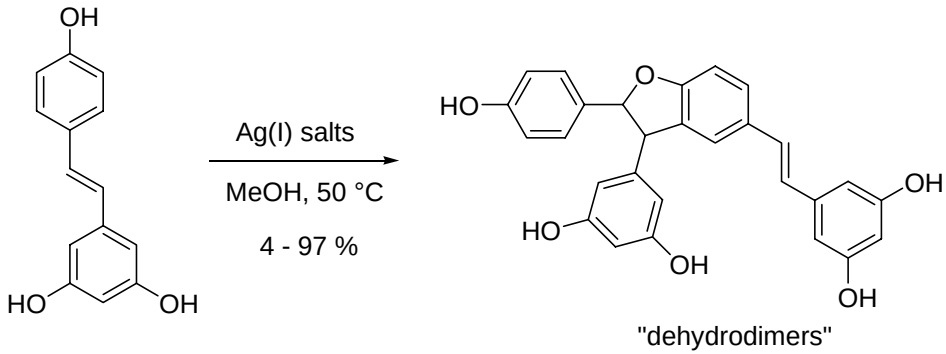
Fatty liver disease





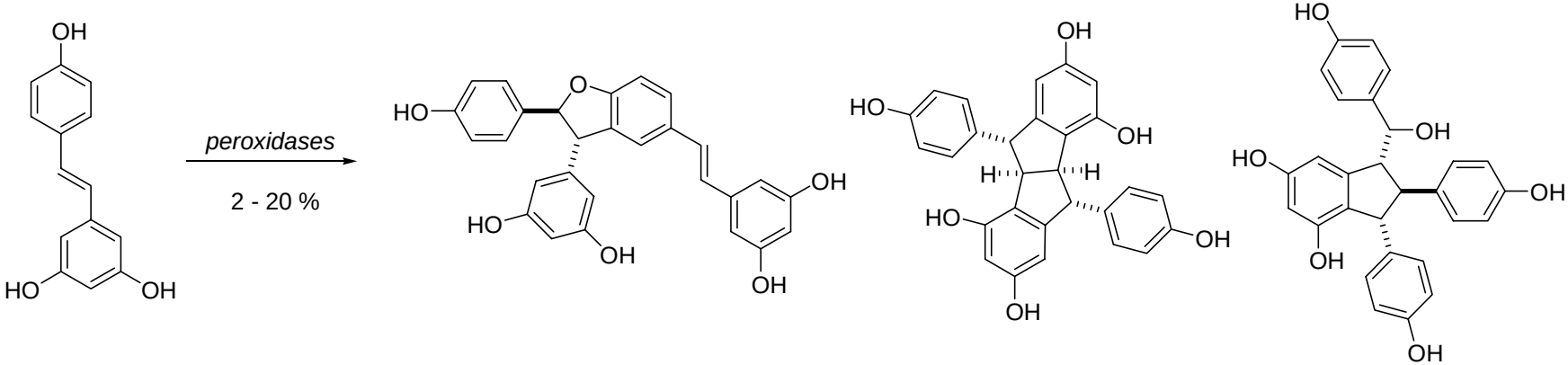
Baur and co-workers *Nature* **2006**, *444*, 337-342

Previous Synthetic Efforts at Resveratrol Family: A Sampling



-Lack of selectivity

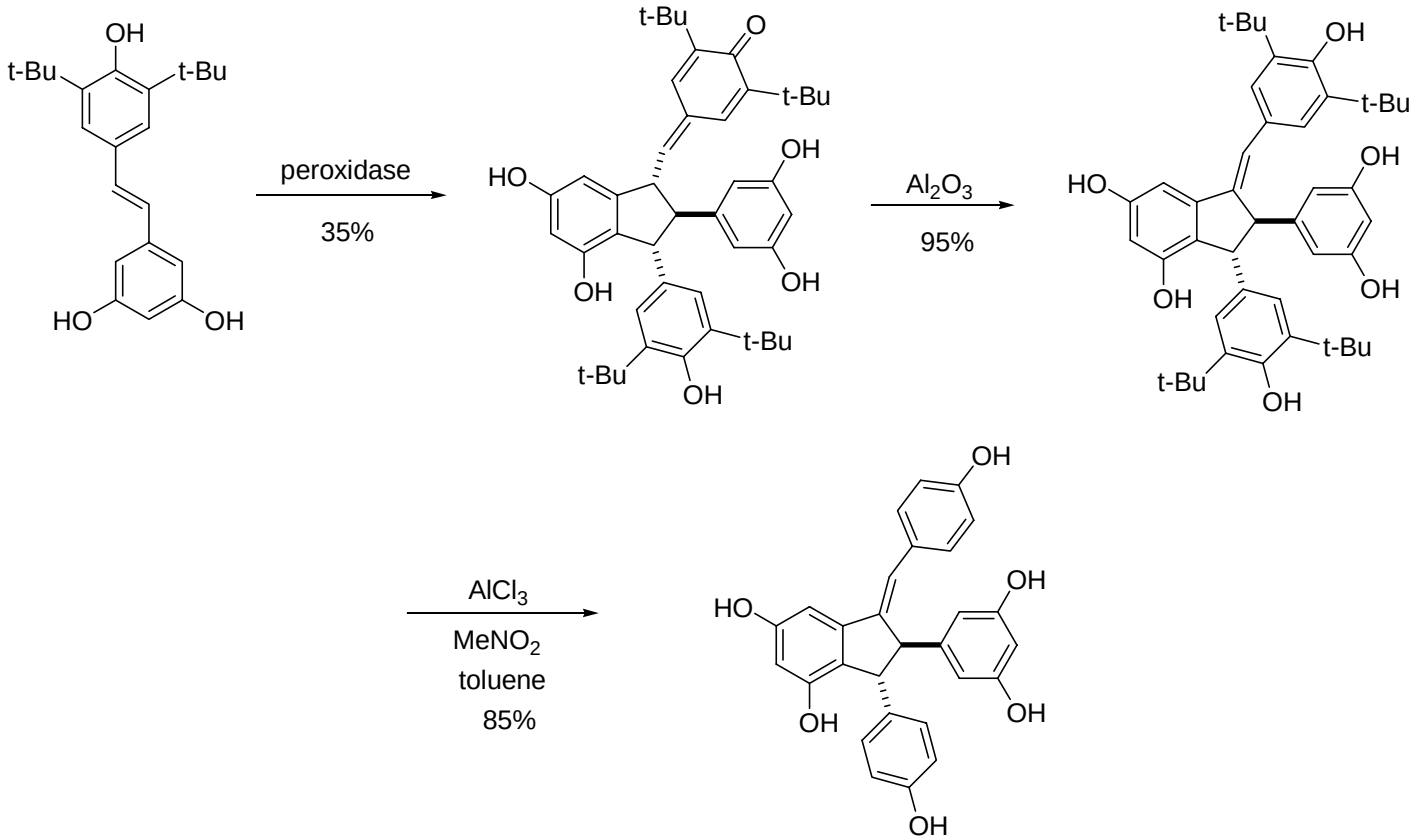
Sako and co-workers *J. Org. Chem.* **2004**, *69*, 2598-2600



-Low yields and selectivities

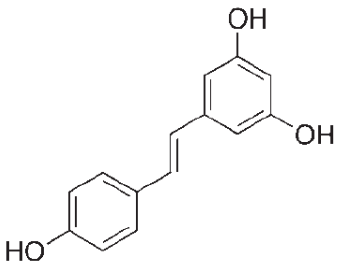
Niwa and co-workers *Tetrahedron* **2005**, *61*, 10285

Previous Synthetic Efforts at Resveratrol Family: An Engineered, Yet Successful, Approach

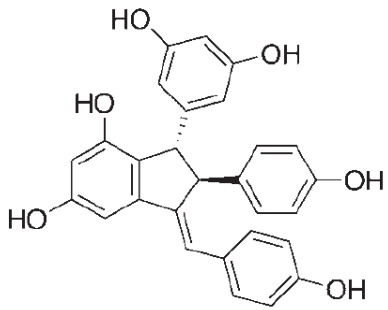


Hou and co-workers *ACIE* **2006**, *45*, 7609-7611

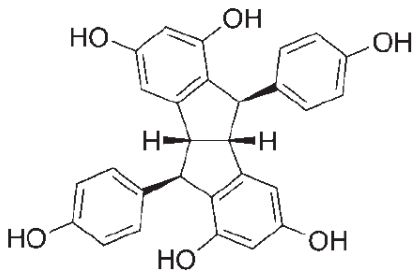
The Resveratrol Family



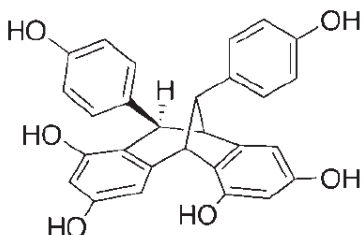
1: resveratrol



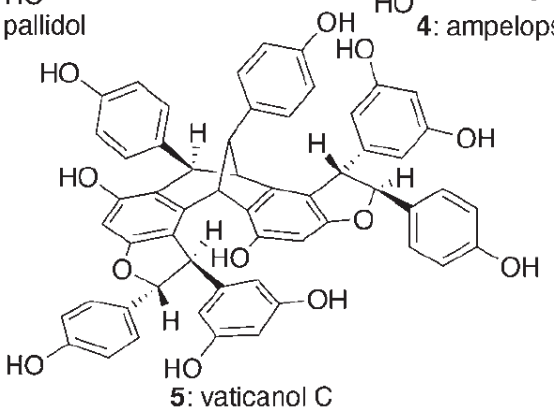
2: ampelopsin D



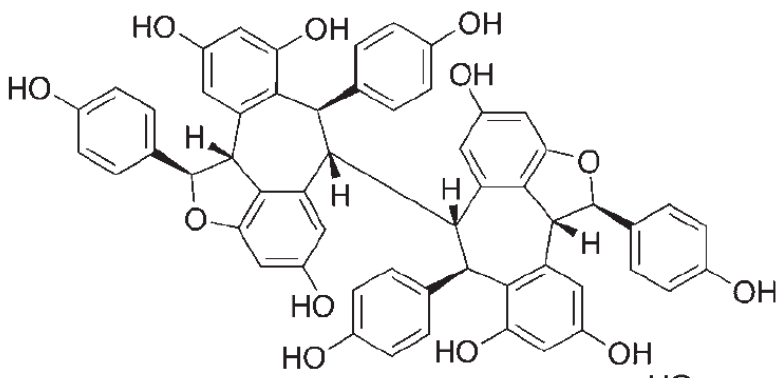
3: pallidol



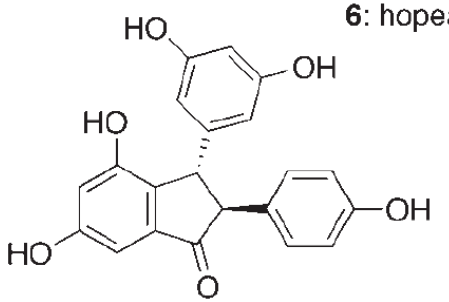
4: ampelopsin F



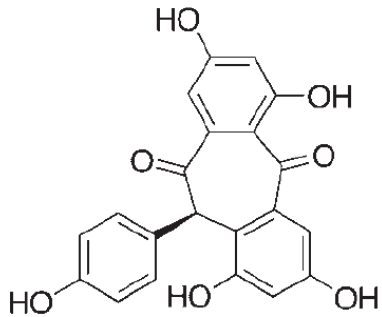
5: vaticanol C



6: hopeaphenol



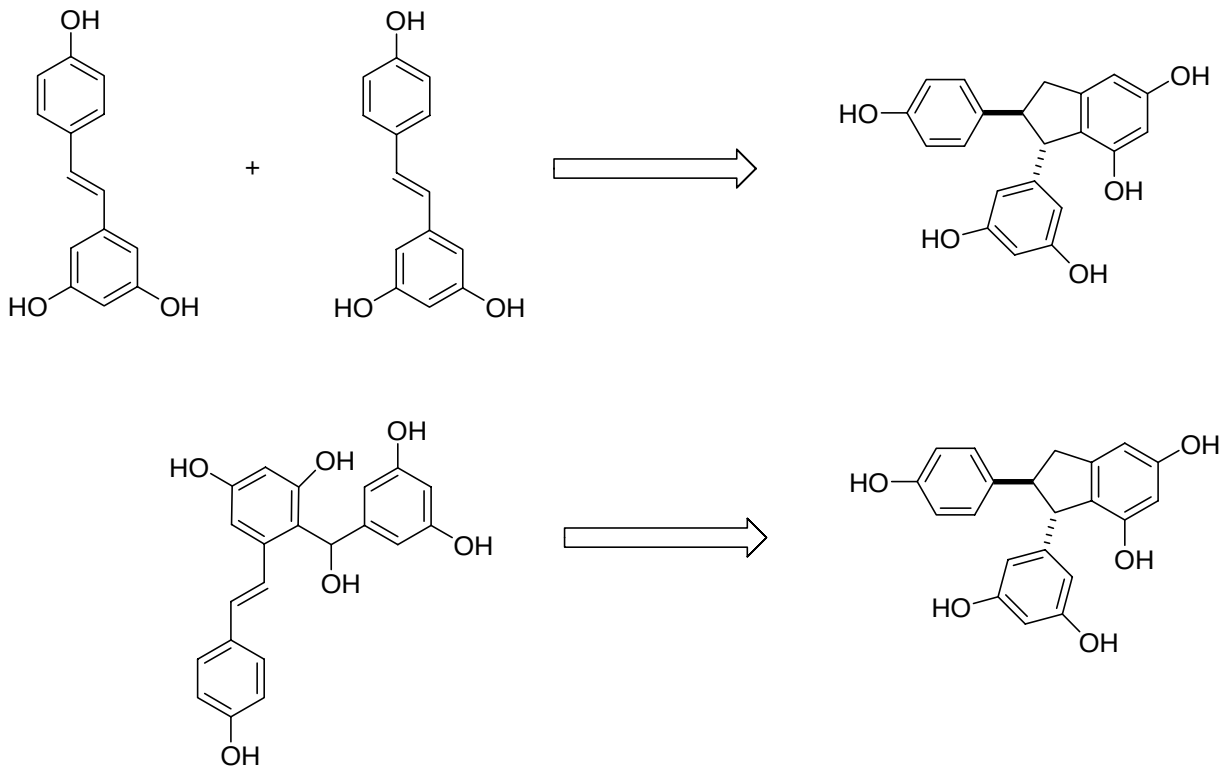
7: paucifloral F



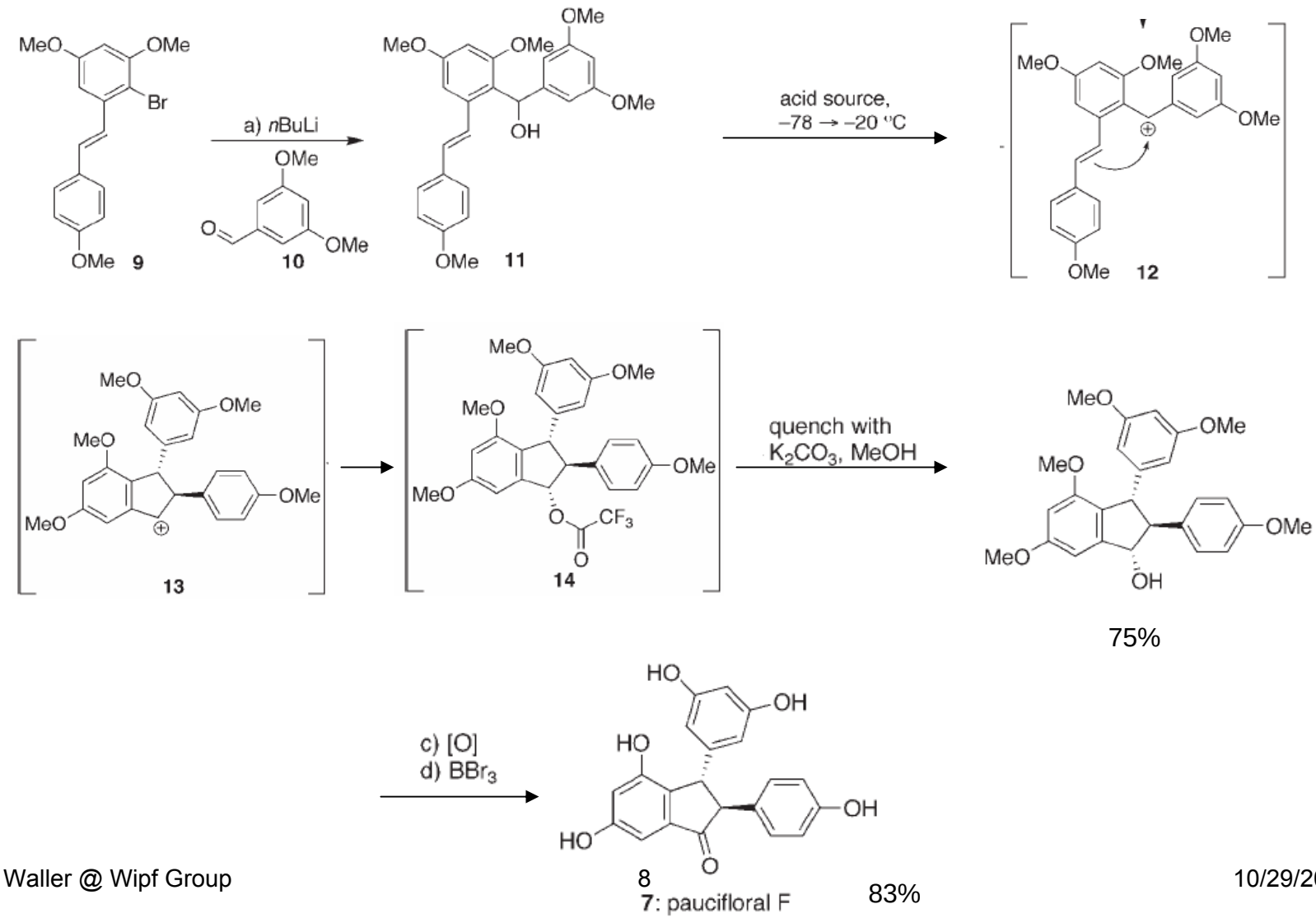
8: diptoindonesin A

A clue that more than one biological precursor exists?

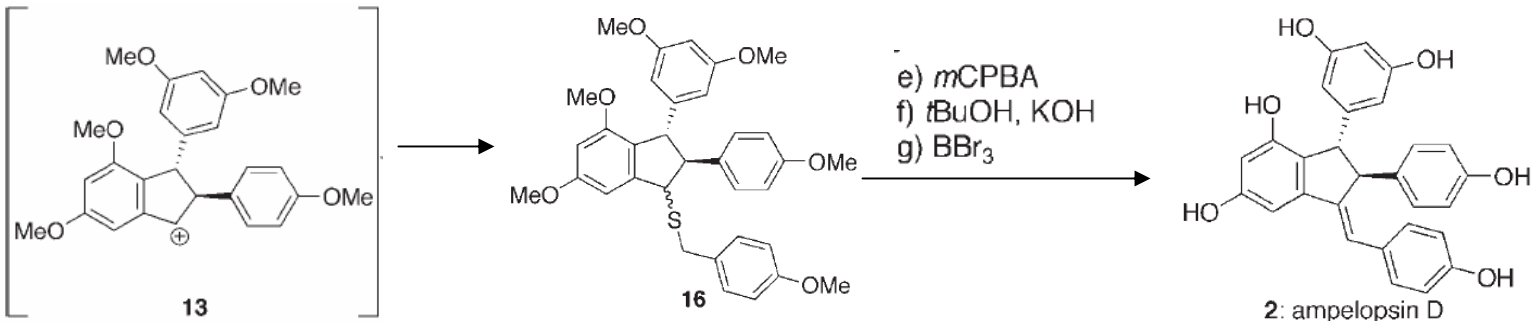
Hypothesis: Triaryl Precursor Allows Synthetic Access To Resveratrol Family



Divergent Approach to Resveratrol Family

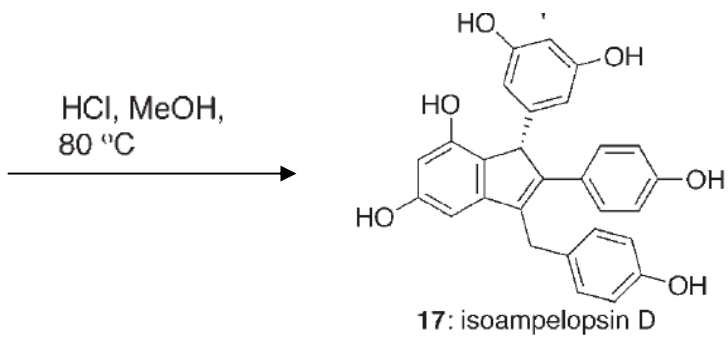


Divergent Approach to Resveratrol Family



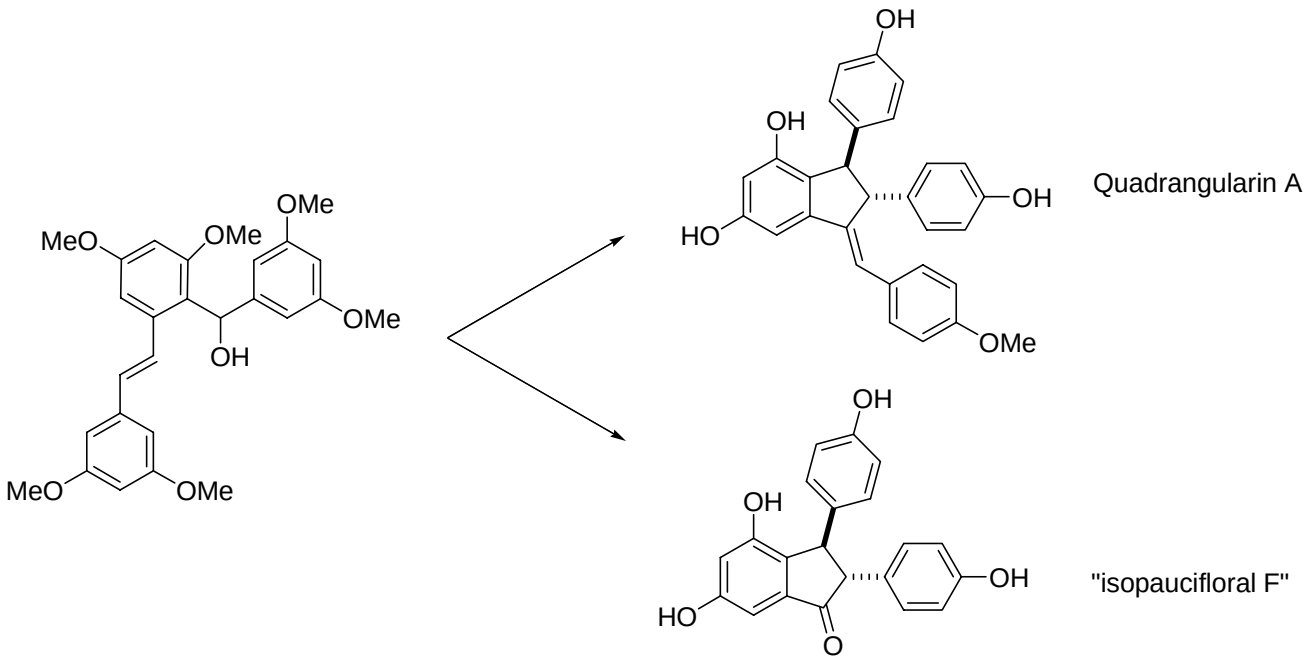
57%

31% overall



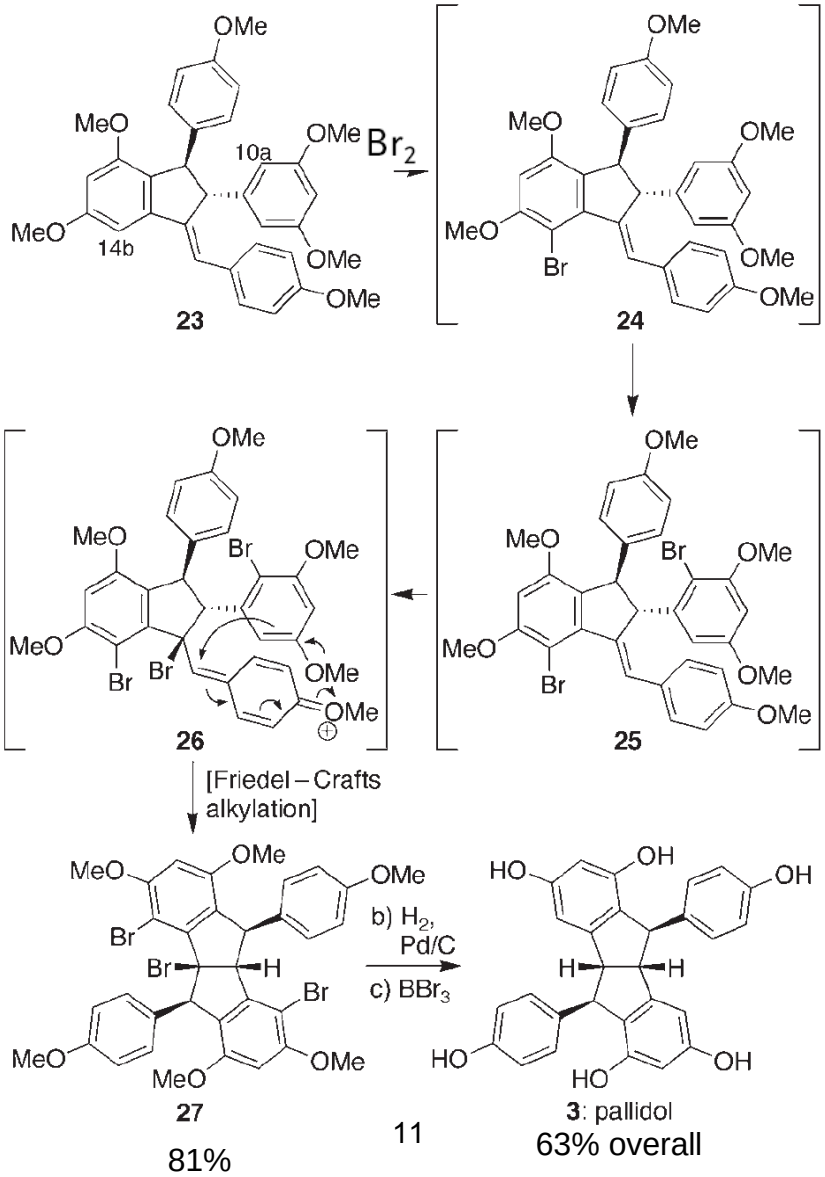
96%

Divergent Approach to Resveratrol Family



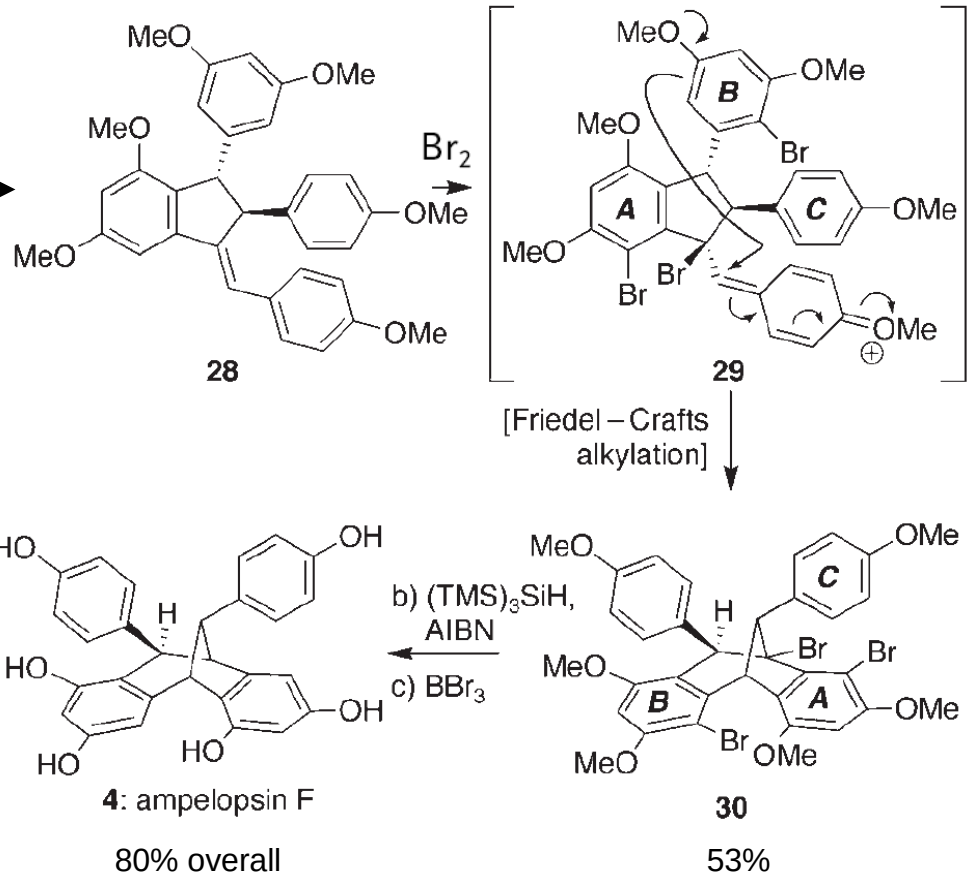
Divergent Approach to Resveratrol Family: Advance In Complexity

Permethylated Quadrangularin

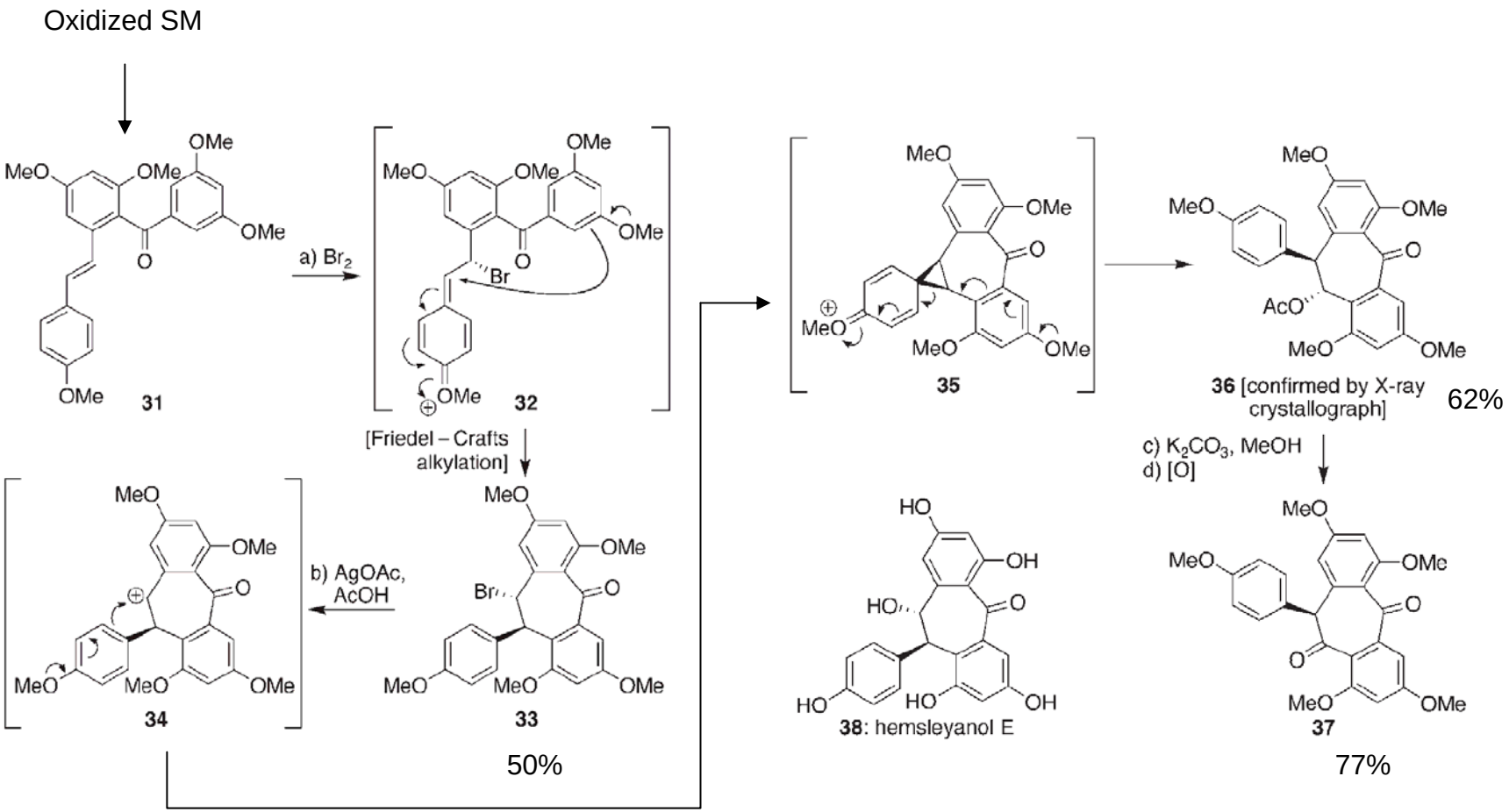


Divergent Approach to Resveratrol Family: Advance in Complexity

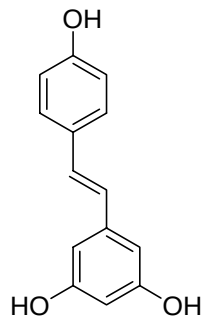
Permethylated Ampelopson D



Divergent Approach to Resveratrol Family: Unnatural Substitution Patterns



Conclusions



-A divergent approach to the resveratrol family has been described.

-A triaryl precursor has been utilized to access diverse substitution patterns.

-New access to “unnatural” family members is available through substituent shifts.

-Investigations into the family are ongoing.