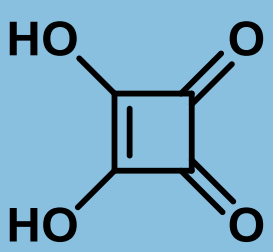
Universität Konstanz

Squaric acid derivatives – synthetic targets for ring expansion reactions



Michael Breunig

AG Gaich

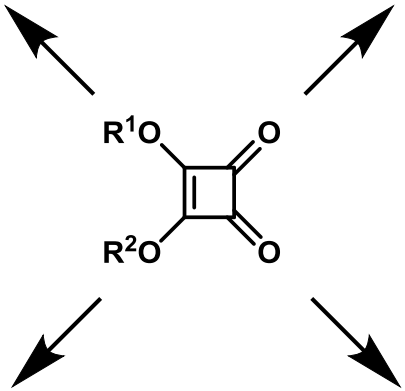
Literature Talk

29.06.16

Applications

BIOLOGY / MEDICINE

- Antitumor properties
- Protein inhibitors
- Treatment of warts



MATERIALS SCIENCE

- Conjugated polymers with low HOMO-LUMO gap

PHOTOCHEMISTRY

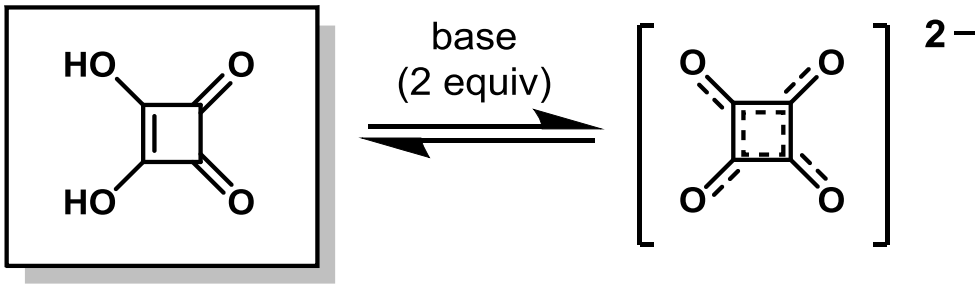
- Energy conversion in solar cells
- Squaraine dyes as photosensitizers

ORGANIC SYNTHESIS

- Ring expansions
- Total synthesis
- Methodology

C. T. Seto et al., *Org. Lett*. **2004**, *6*, 83; S. Takeda et al., *J. Am. Chem. Soc*. **2001**, *123*, 10468.
A. Ajayaghosh et al., *Org. Lett*. **2001**, *3*, 2595.
K.-Y. Law et al., *Chem. Rev*. **1993**, *93*, 449.

General background

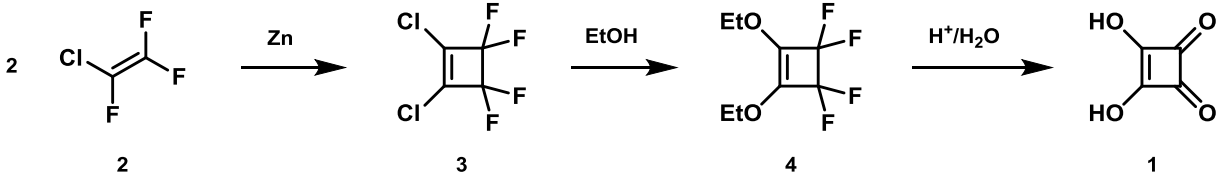


- symmetrical aromatic dianion
- pK_{a1} ~ 1.0 and pK_{a2} = 2.2
- double vinylogous carboxylic acid
- C_4 synthon

Cohen et al., *J. Am. Chem. Soc.* **1959**, *81*, 3480.

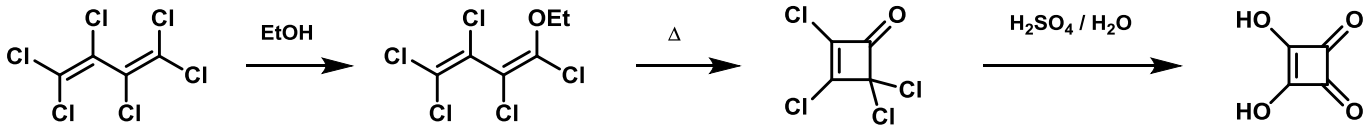
Synthesis

- First prepared by Cohen in 1959



2 3 4 1

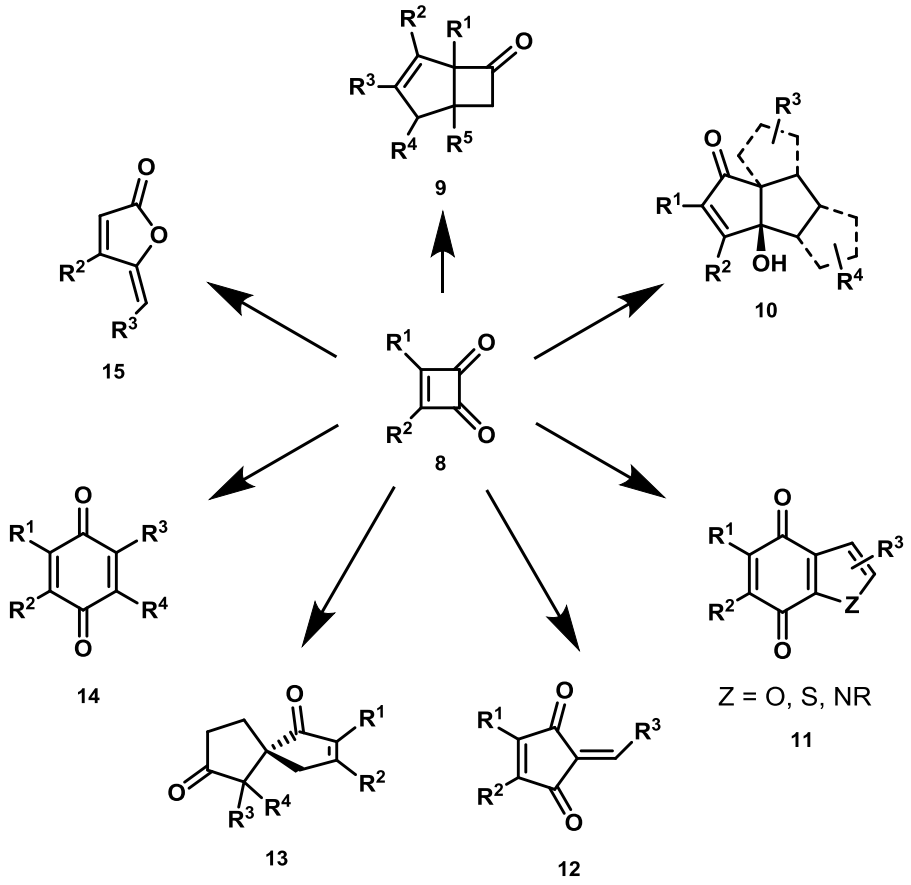
- Industrial synthesis nowadays



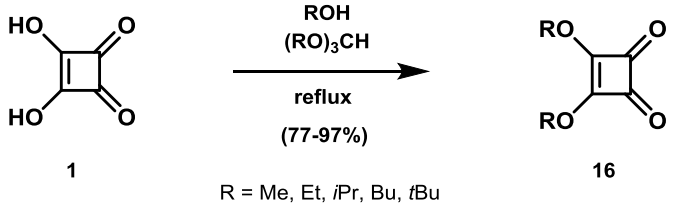
5 6 7 1

Cohen et al., *J. Am. Chem. Soc.* **1959**, *81*, 3480.
B. Jackson, US Pat., 5360937, **1993**; G. Maahs, P. Hegenberg, *Angew. Chem*. **1966**, *78*, 927.

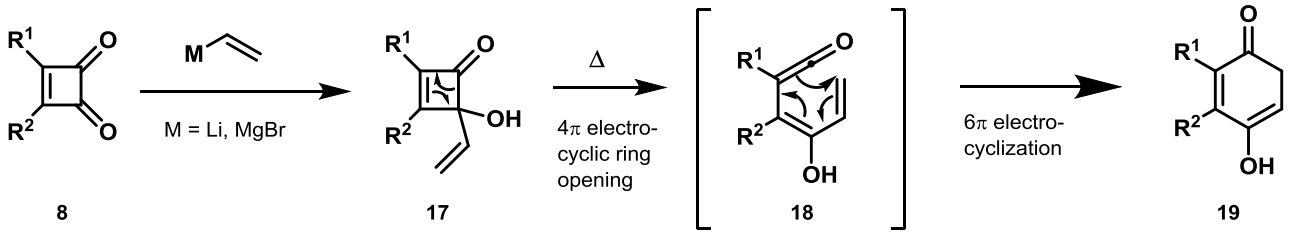
Scope of ring expansions



Dialkyl squarates

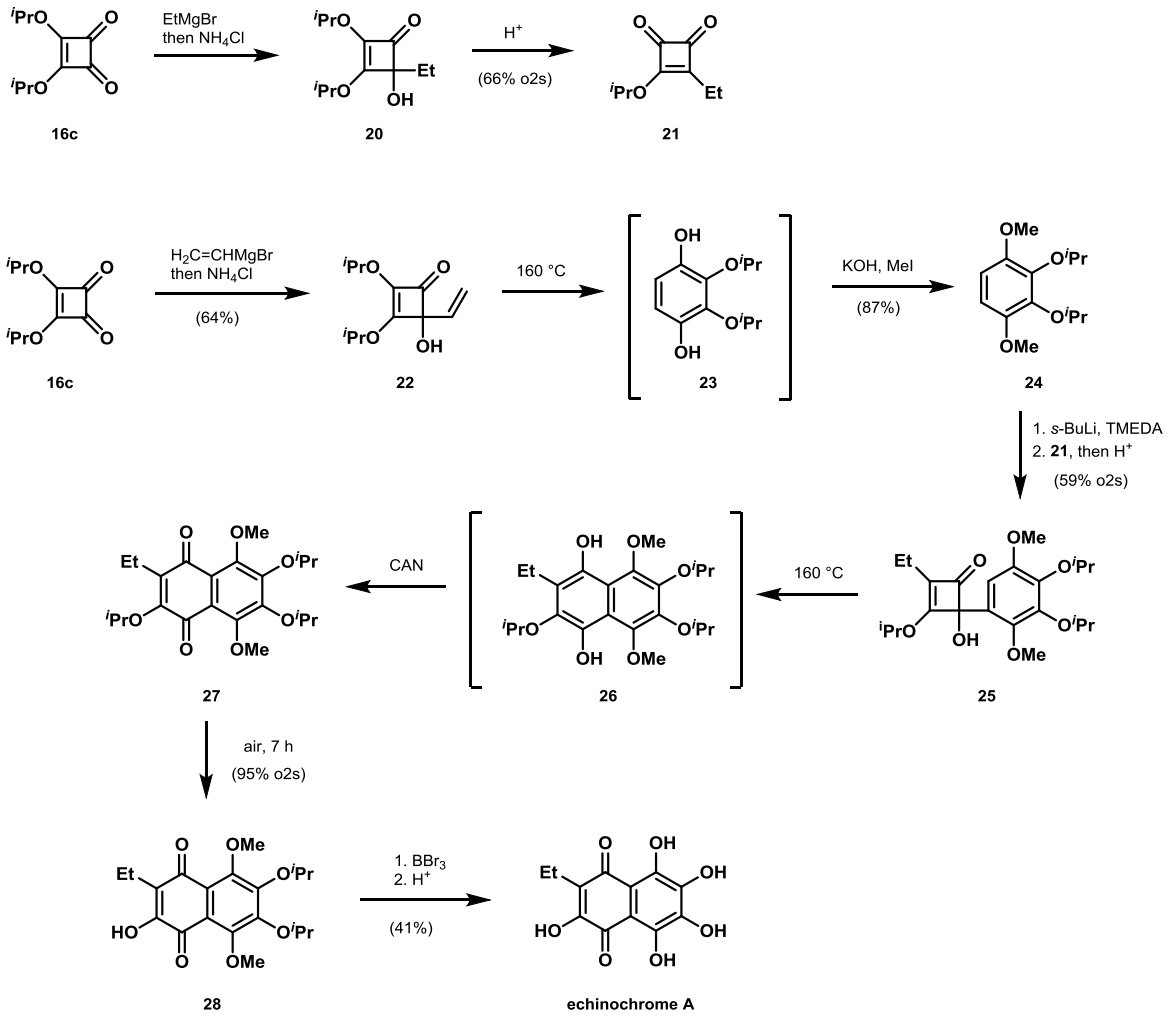


- Squarate esters are highly strained
- Electrophilic reagents: 1,2- and 1,4 addition
- Good solubility in most organic solvents
- Highly oxygenated building blocks



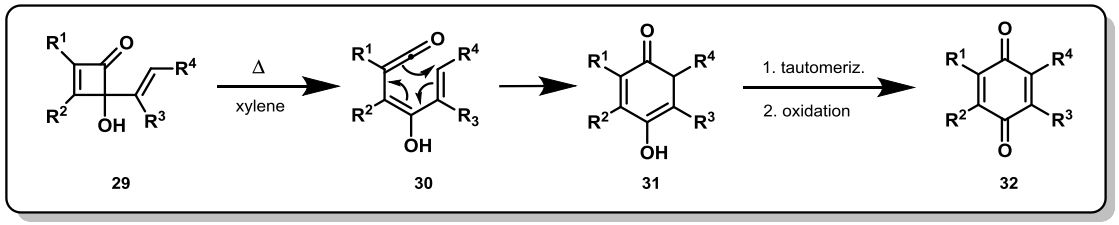
Moore et al., *Synth. Commun.* **1997**, *27*, 2177.
L. Paquette, *Eur. J. Org. Chem.* **1998**, 1709.

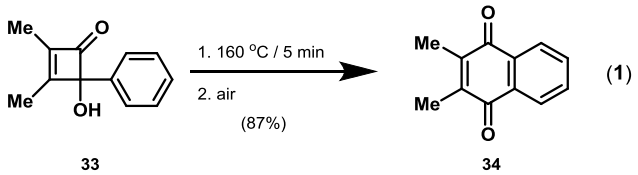
Echinochrome A



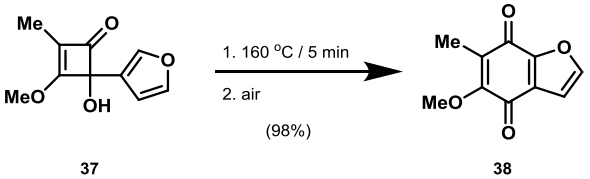
E. Pena-Cabrera, L. S. Liebeskind, *J. Org. Chem.* **2001**, *67*, 1689.

Ring-fused quinones





(1)



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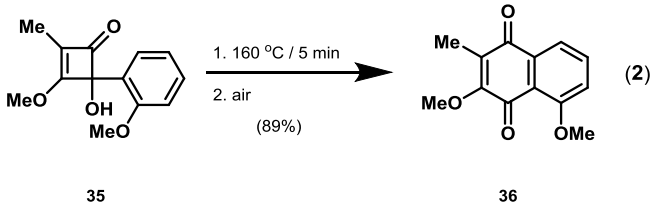
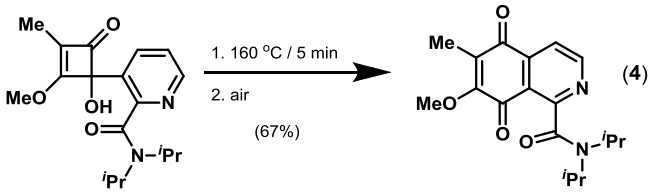


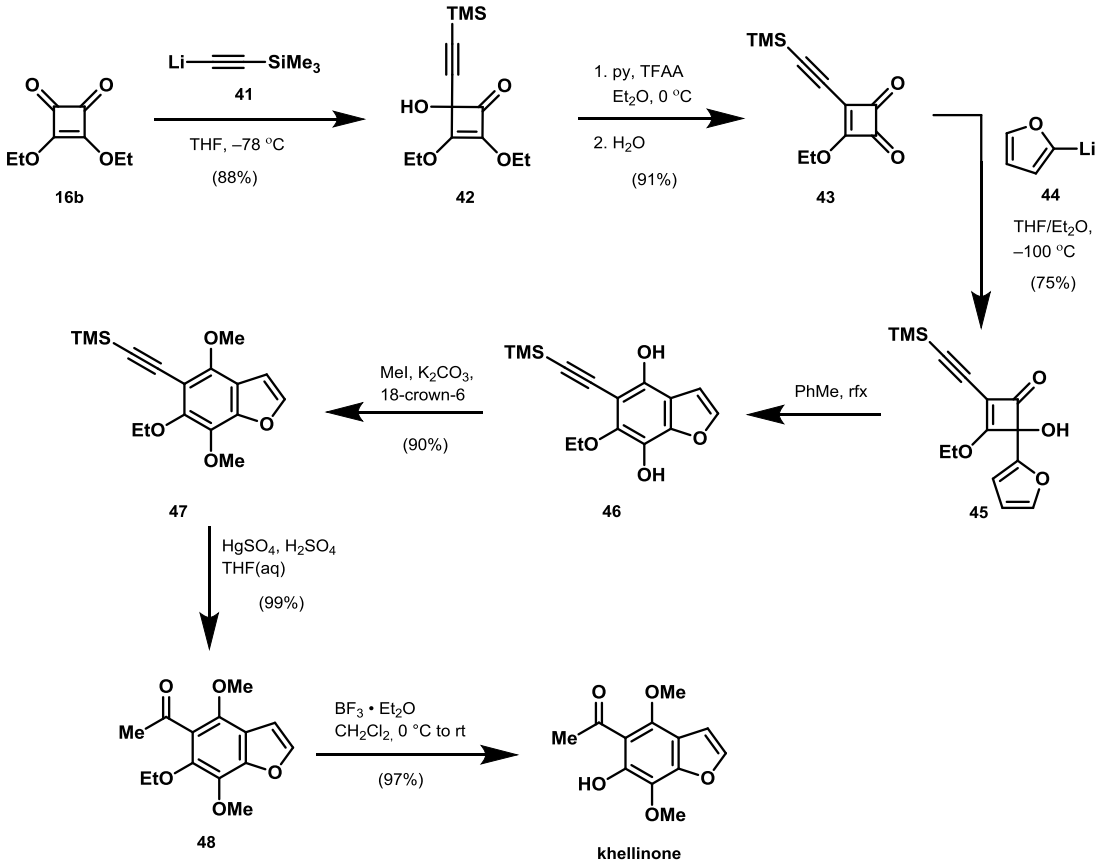
(2)



(4)

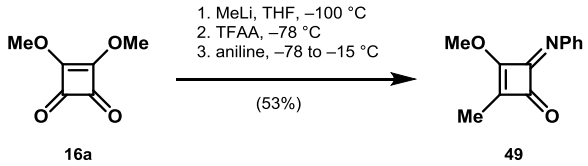
L. S. Liebeskind, *Tetrahedron* **1989**, *45*, 3053.

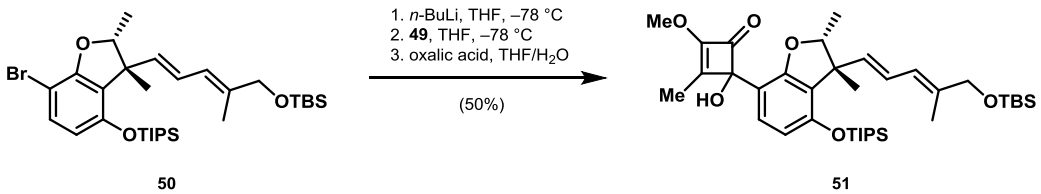
Khellinone

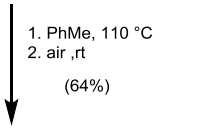


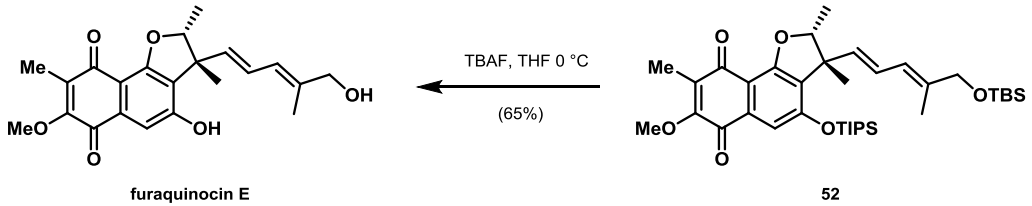
H. W. Moore, *J. Org. Chem.* **1987**, *52*, 3491.

Furaquinocin E



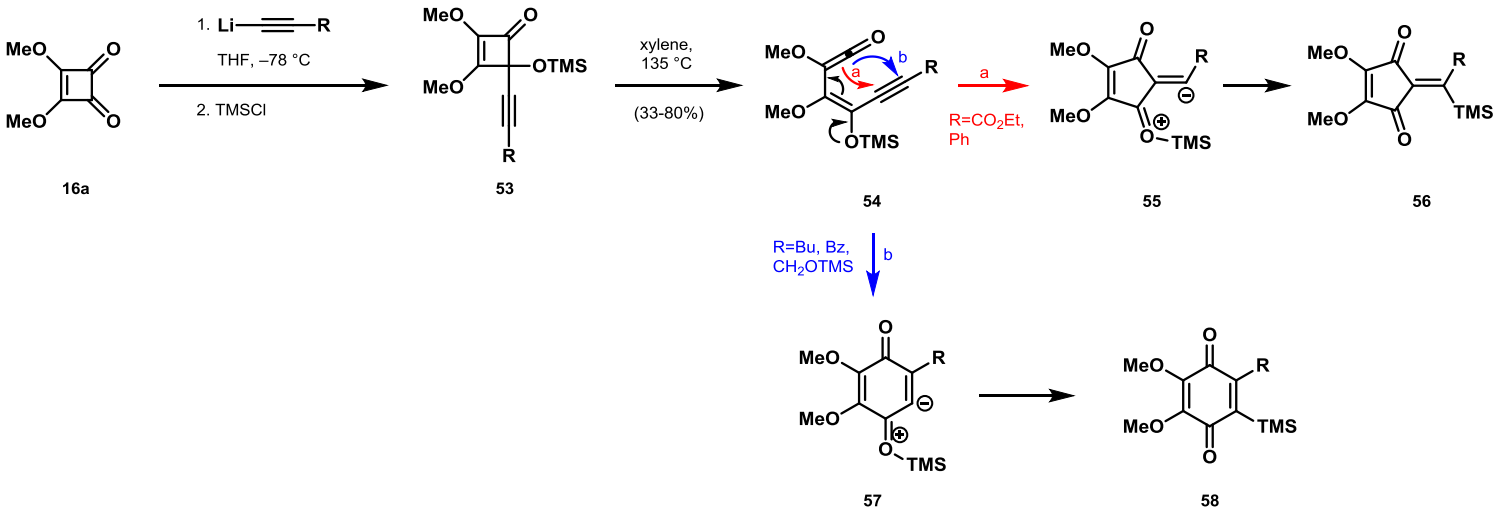






B. M. Trost et al., *J. Am. Chem. Soc.* **2003**, *125*, 13155.

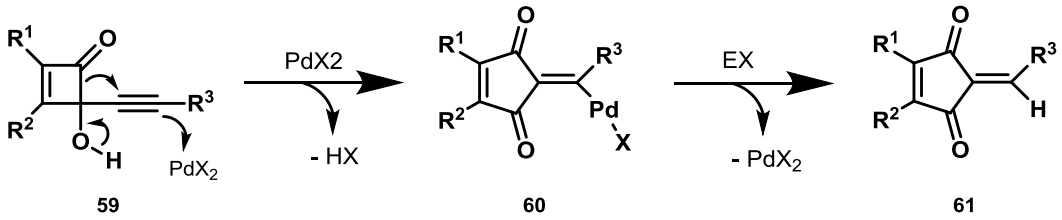
Quinone vs. cyclopentenedione

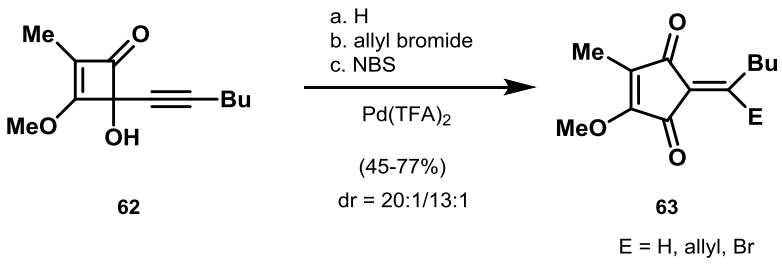


16a 53 54 55 56 57 58

H. W. Moore et al., *J. Am. Chem. Soc.* **1985**, *107*, 3393.

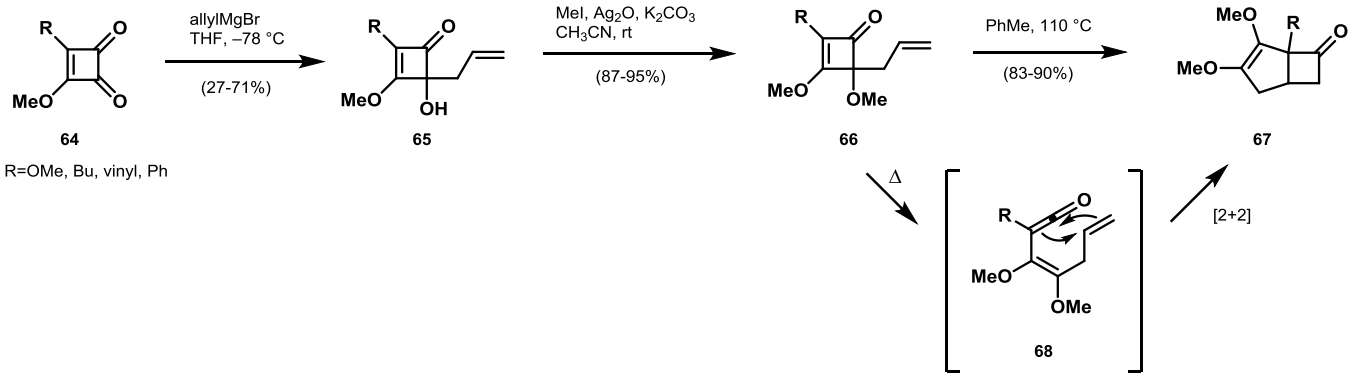
Cyclopentenediones via Pd(II) catalysis





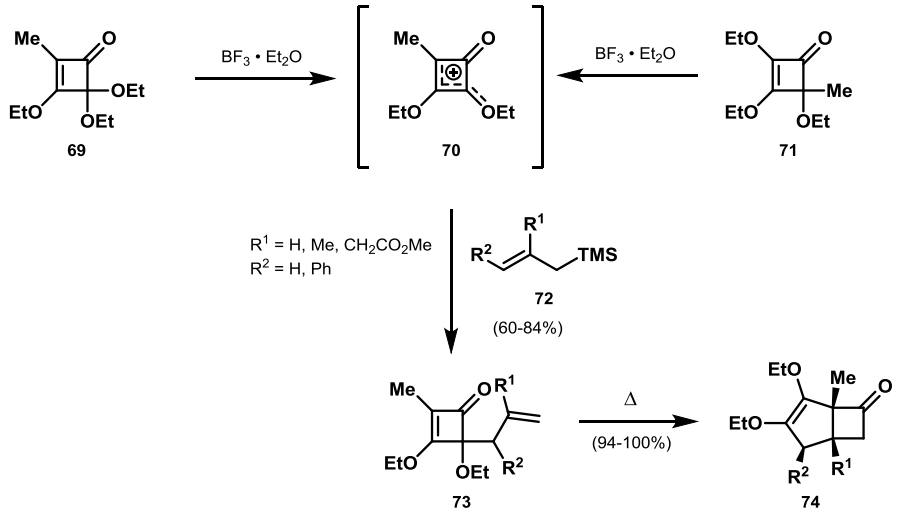
L. S. Liebeskind et al., *J. Am Chem. Soc.* **1987**, *109*, 7908.

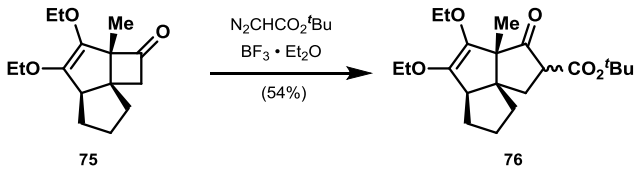
Bicyclo[3.2.0]heptenones



H. W. Moore et al., *J. Org. Chem.* **1991**, *56*, 6094.

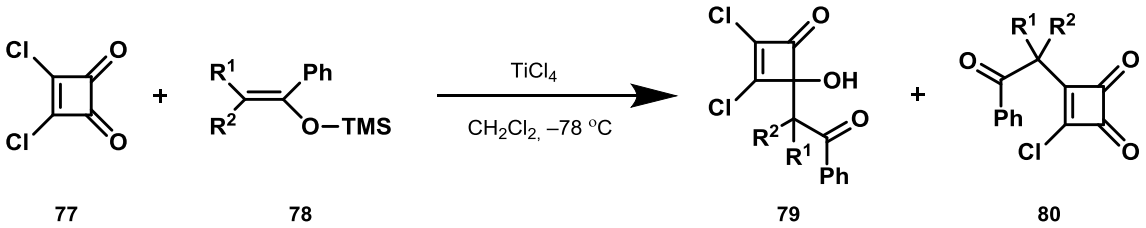
Bicyclo[3.2.0]heptenones / triquinanes





H. W. Moore et al., *J. Org. Chem.* **1991**, *56*, 6094.
S. Eguchi et al., *Synlett* **1998**, *11*, 1167.

Silylenol ethers: 1,2- vs 1,4-addition

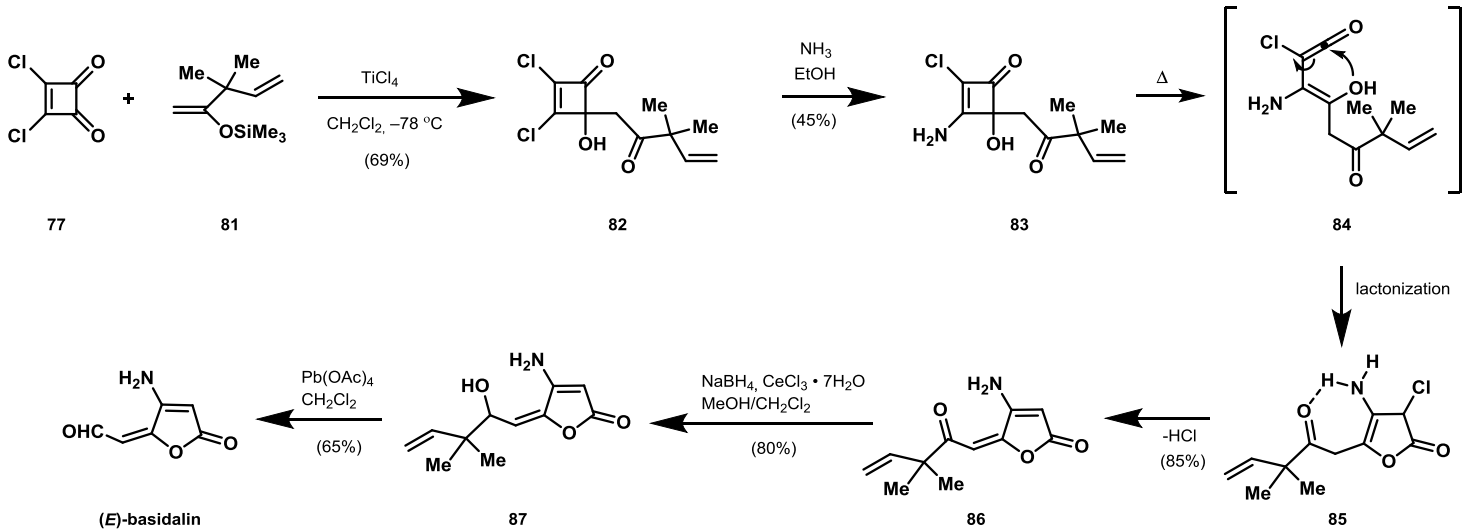


77 **78** **79** **80**

	1,2-addition	1,4-addition
R^1=R^2=H:	52%	-----
R^1=Me, R^2=H:	38%	-----
R^1=R^2=Me:	7%	82%

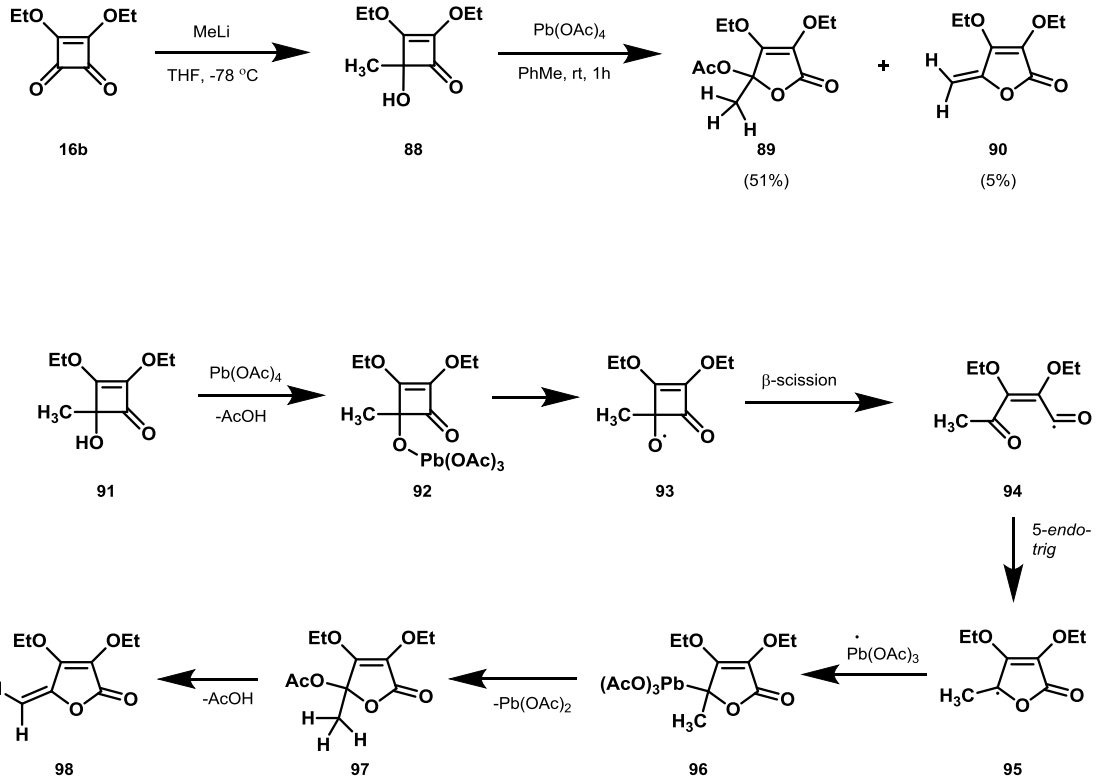
S. Eguchi et al., *J. Chem. Soc., Perkin Trans. 1* **1991**, 2272.

(*E*)-basidalin



S. Eguchi et al., *Tetrahedron* **1994**, *50*, 7783.

Radical-mediated: furanones



S. Eguchi et al., *J. Am. Chem. Soc.* **1995**, *117*, 9653.

Radical-mediated: 5-endo- vs. 5-exo-trig

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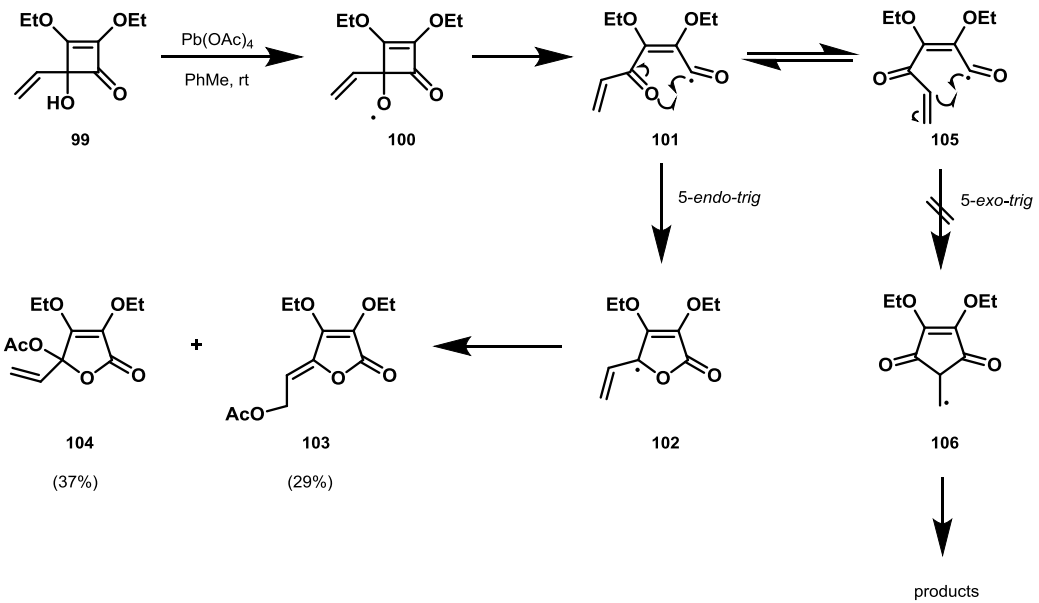
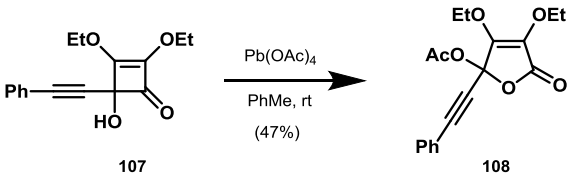
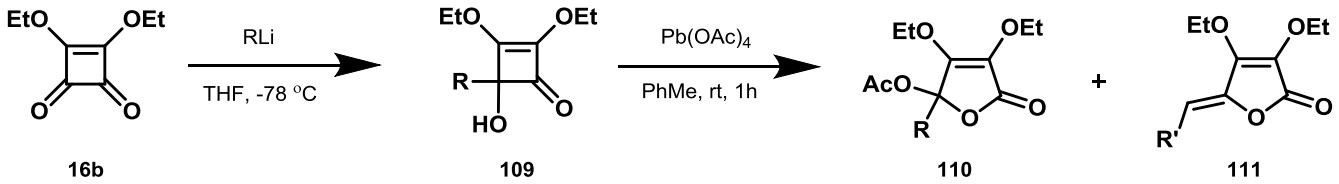
- 5-endo-trig (disfavored) vs. 5-exo-trig (favored):





S. Eguchi et al., *J. Am. Chem. Soc.* **1995**, *117*, 9653.

Radical-mediated



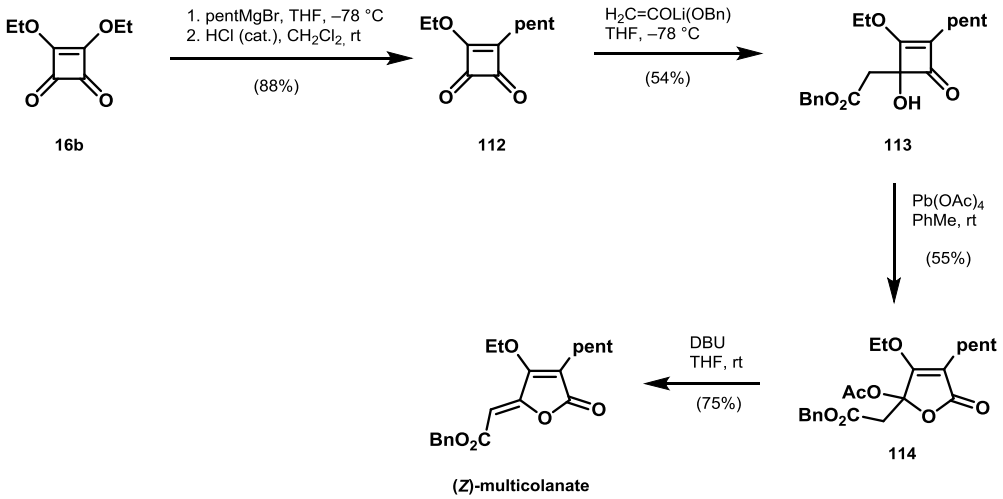
16b **109** **110** **111**

a. R=Bu, 60%
b. R=CH_2Bz, 26%
c. R=Ph, 77%
d. R=2-furyl, 38%

a. R'=Pr, 23%
b. R'=Bz, 52%

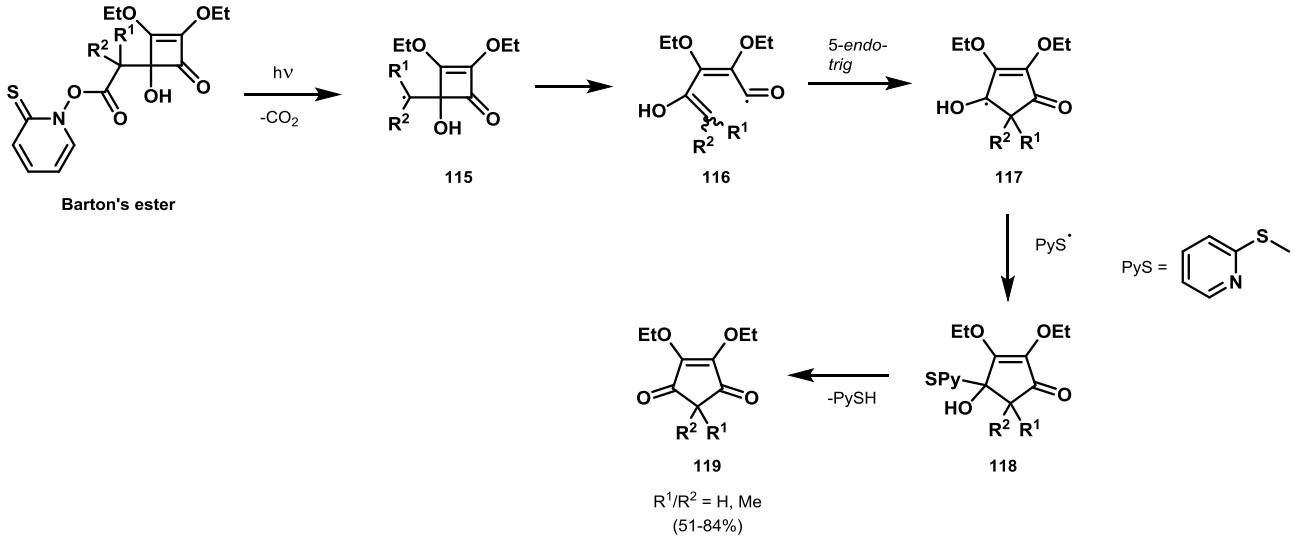
S. Eguchi et al., *J. Am. Chem. Soc.* **1995**, *117*, 9653.

(*Z*)-multicolanate



S. Eguchi et al., *J. Am. Chem. Soc.* **1995**, *117*, 9653.

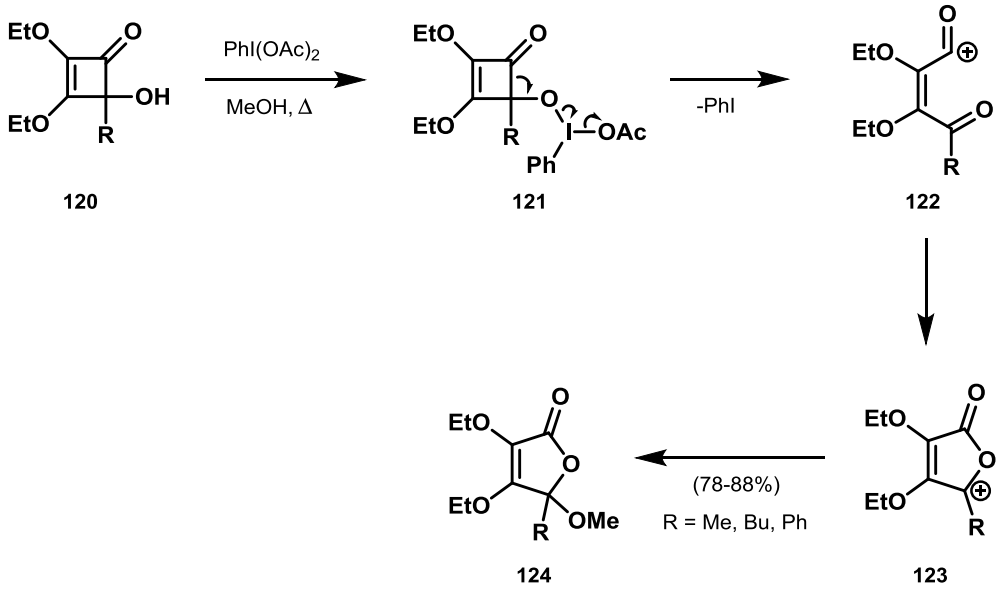
C-centered radical: cyclopentenediones



- Cyclization before keto-enol tautomerization

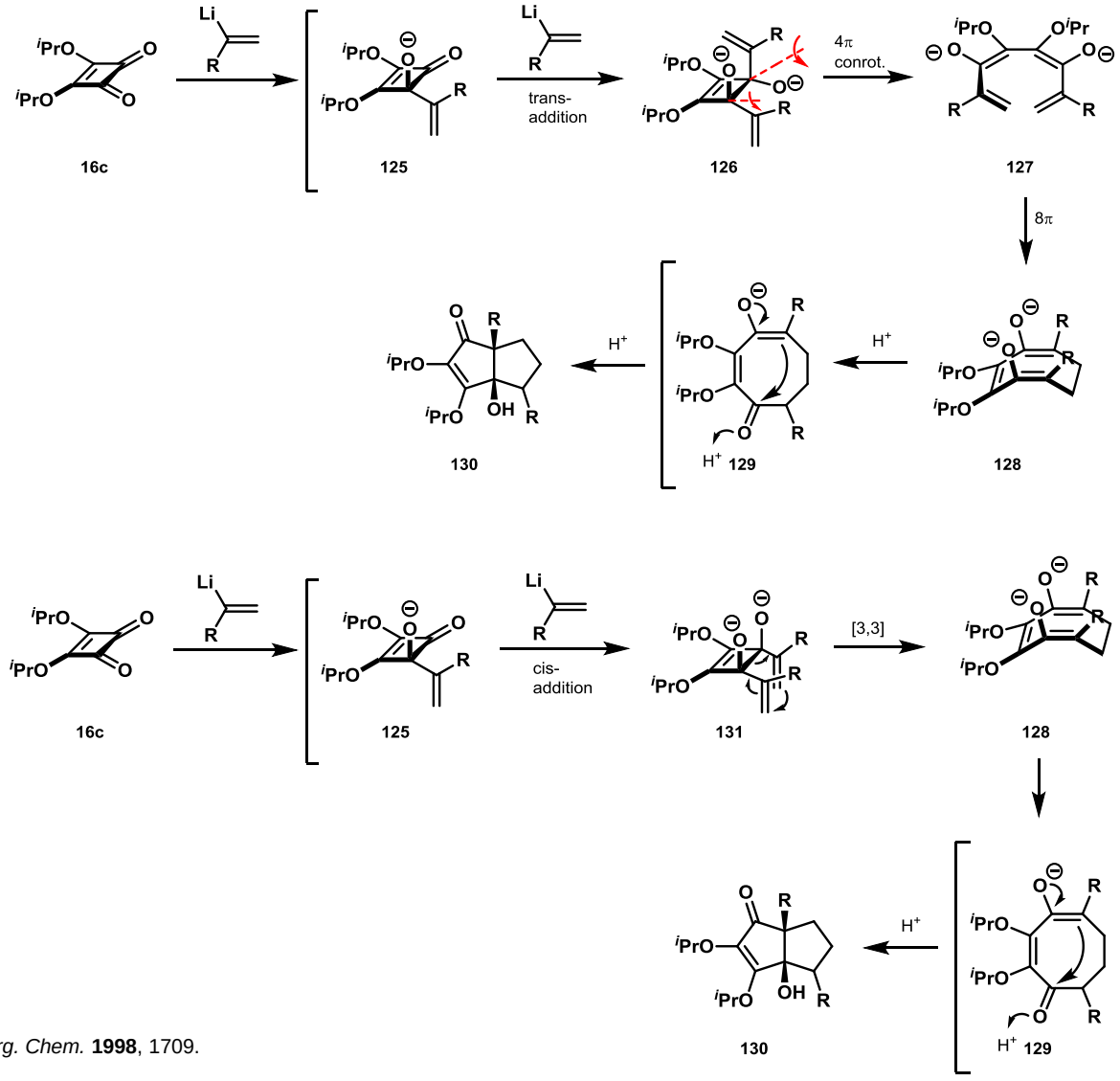
S. Eguchi et al., *J. Am. Chem. Soc.* **1995**, *117*, 9653.

Cationic pathway



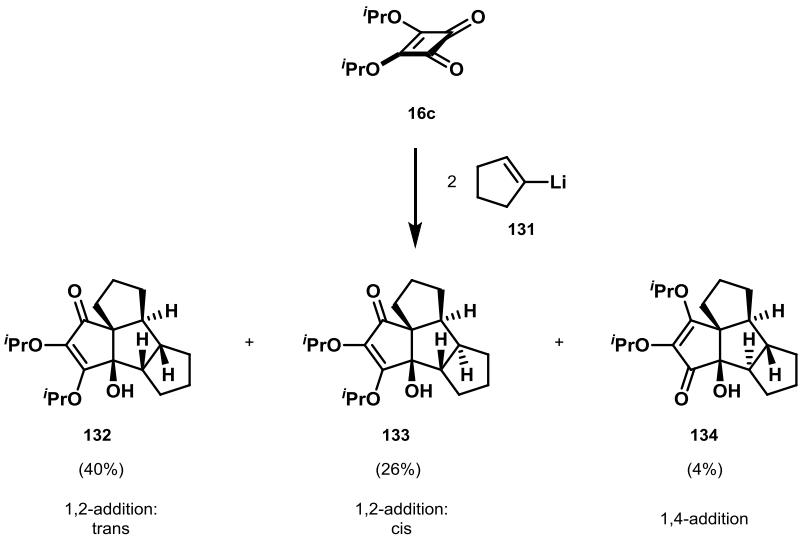
S. Eguchi et al., *Synlett* **1998**, *11*, 1167.

Double addition of vinyl-lithium

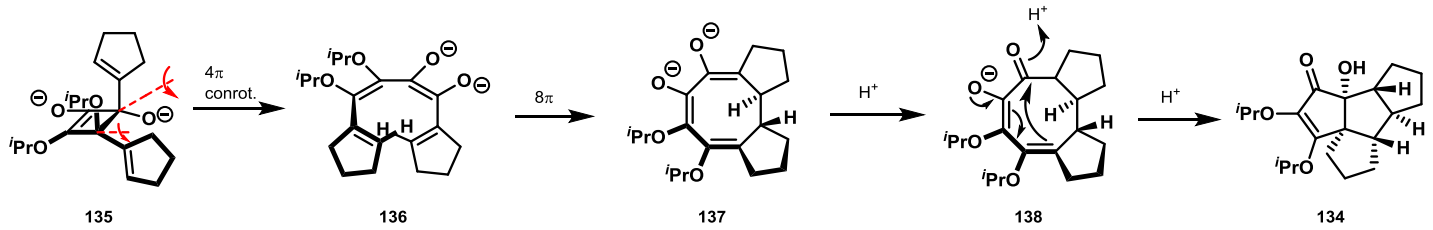


L. A. Paquette, *Eur. J. Org. Chem.* **1998**, 1709.

Polyquinanes

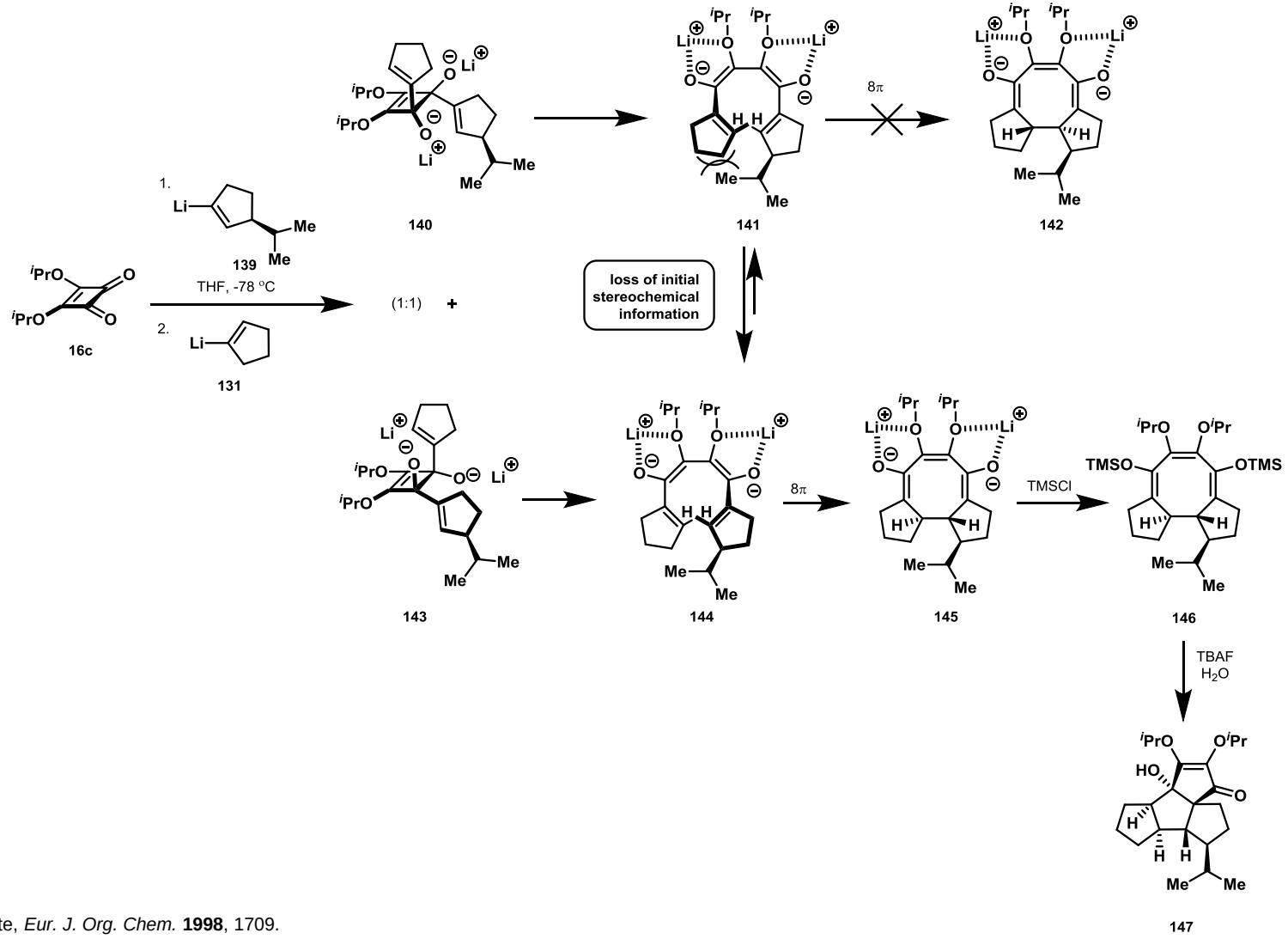


1,4-addition:



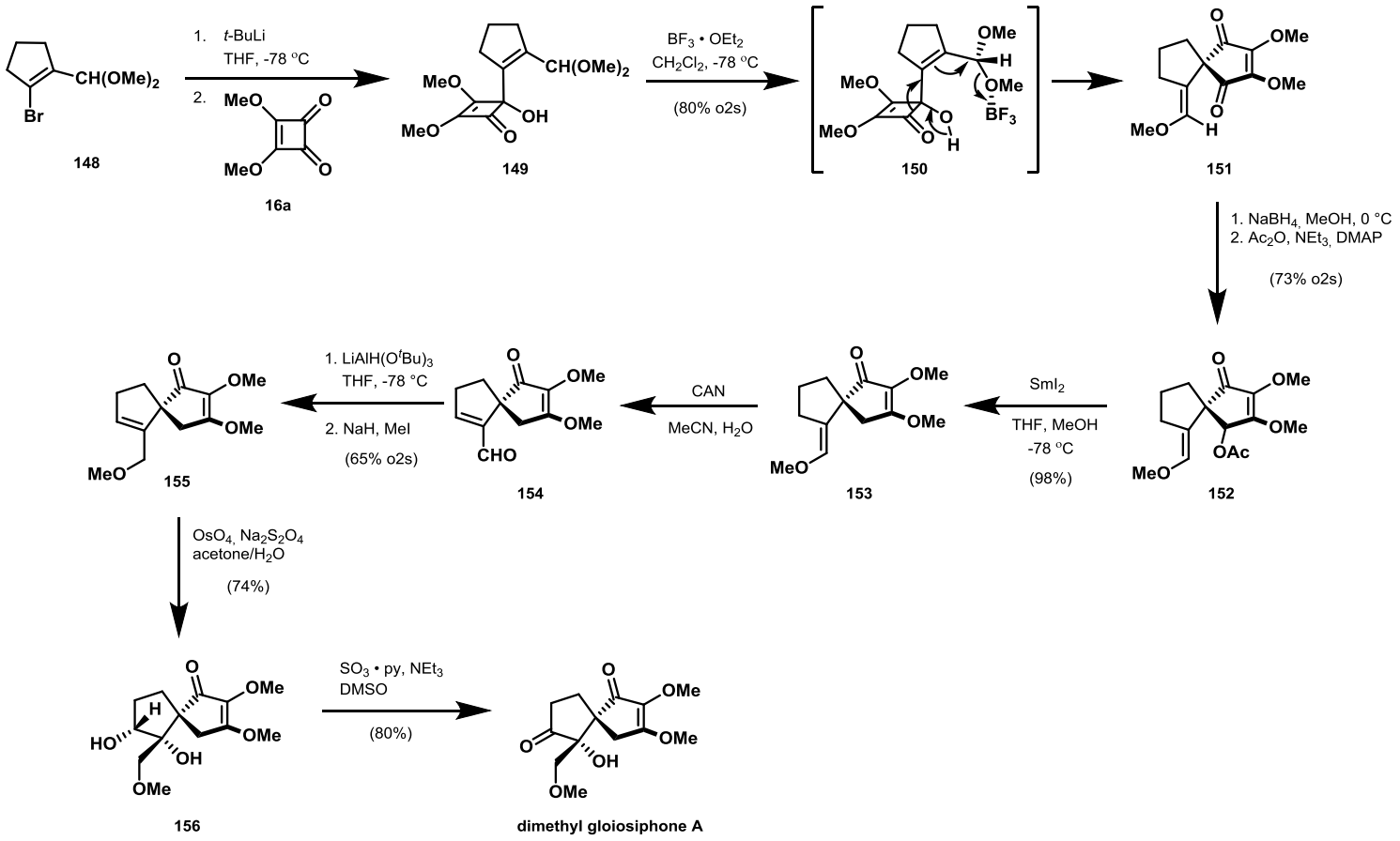
L. A. Paquette, *Eur. J. Org. Chem.* **1998**, 1709.

Stereochemical control



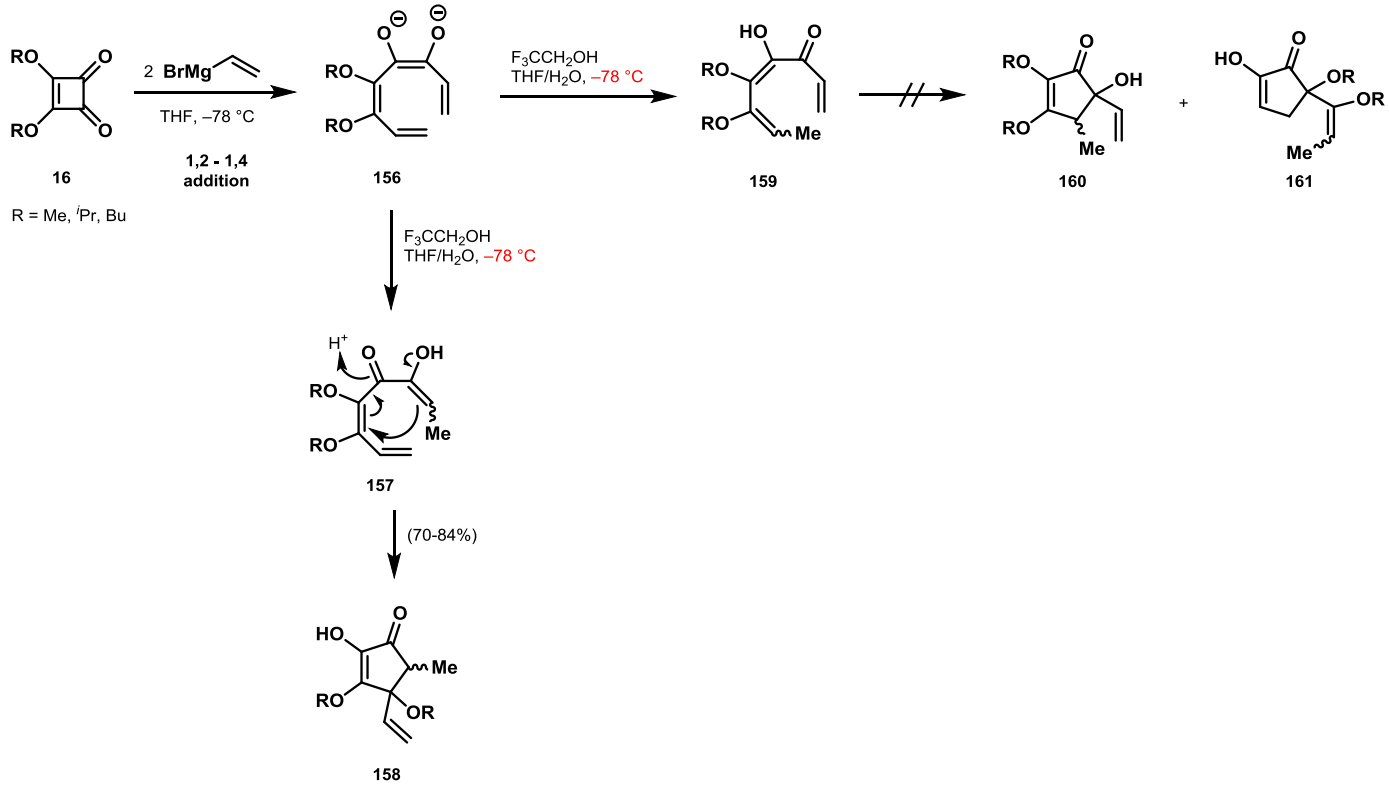
L. A. Paquette, *Eur. J. Org. Chem.* **1998**, 1709.

Dimethyl Gloiosiphone A



L. A. Paquette et al., *J. Am. Chem. Soc.* **1996**, *118*, 9456.

Highly functionalized cyclopentenones



- Protonation of octatetraene **156** at –78 ºC to prevent 8π-electrocyclization

G. Asensio et al., *J. Org. Chem.* **2012**, *77*, 6327.