
Ring contraction reactions in Total synthesis

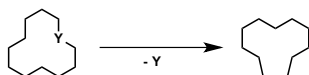
Ruben Eckermann
Gaich-Group Seminar
October 2nd, 2014

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Overview

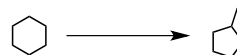
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Exclusion of one heteroatom



- Eschenmoser contraction
 - Ramberg-Bäcklund reaction
 - Photo-Fries rearrangement
 - Wittig rearrangement
 - Stevens rearrangement
 - Co-mediated O → C – contraction
 - Zr-mediated O → C – contraction
- mostly used for **macrocycles**

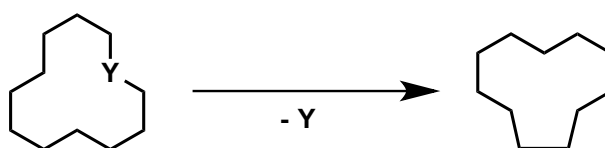
One-carbon contraction



- Wager-Meerwein/Pinacol rearrangements
 - Epoxide rearrangement
 - Favorski rearrangement
 - oxidative contractions
 - Wolff rearrangement
- mostly used for **cyclopentyl** units
- Review: L. F. Silva, Jr. *Tetrahedron* **2002**, *58*, 9137-9161

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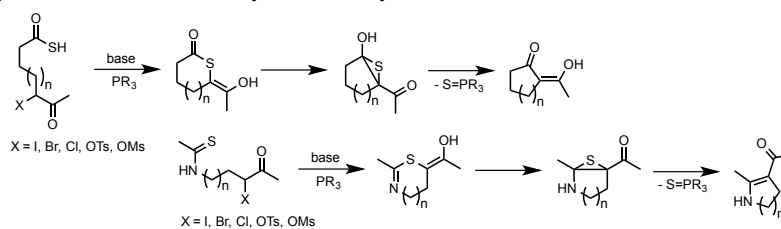
Exclusion of one heteroatom



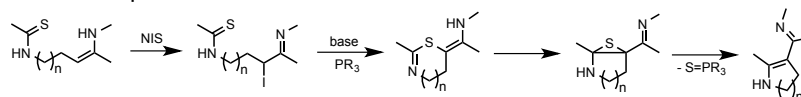
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Eschenmoser sulfide contraction

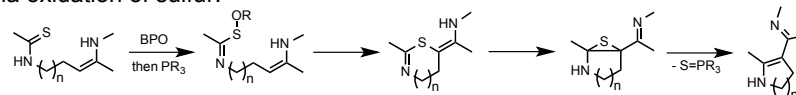
Synthesis of 1,3-dicarbonyls via S-alkylation:



via enamine prefunctionalization:



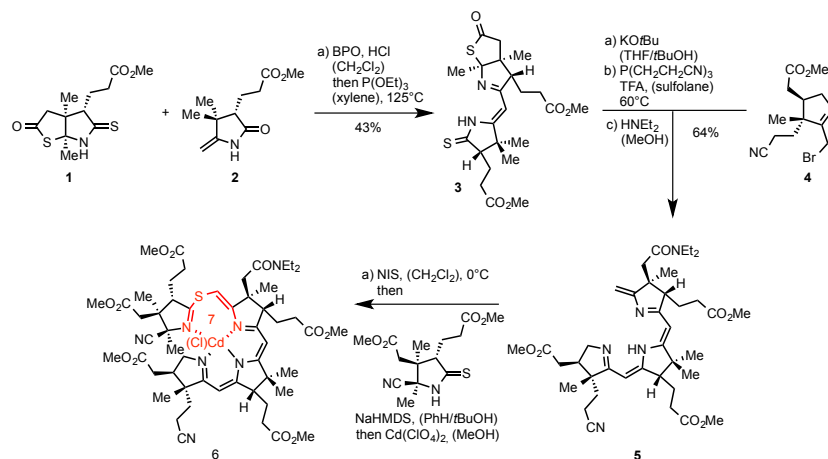
via oxidation of sulfur:



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Vitamin B₁₂ synthesis

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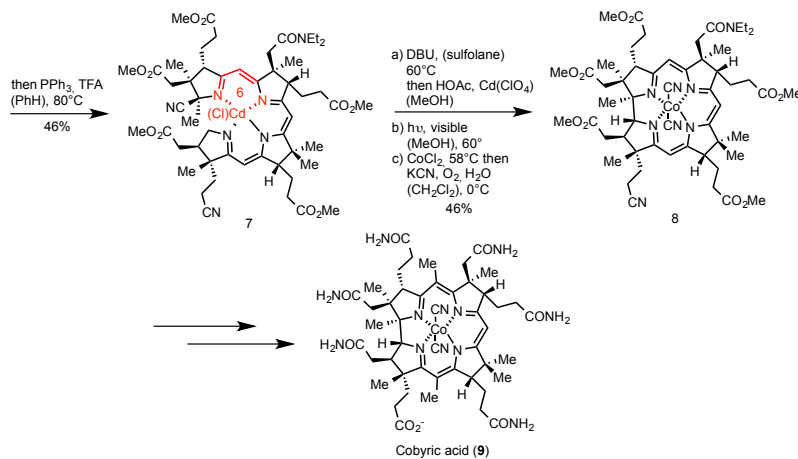


A. Eschenmoser, C. E. Winter, *Science* **1977**, *196*, 1410 - 1420

5

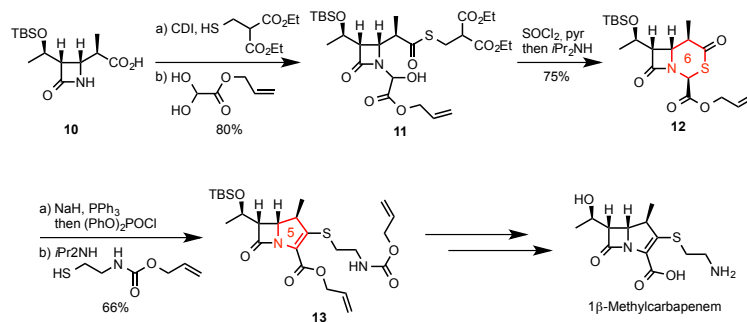
Vitamin B₁₂ synthesis

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A. Eschenmoser, C. E. Winter, *Science* **1977**, *196*, 1410 - 1420

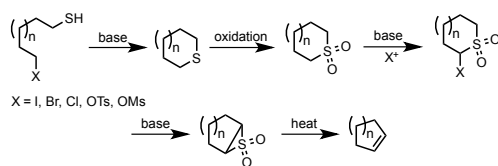
6

1 β -MethylcarbapenemGaich-Group Seminar
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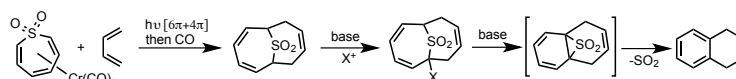
7

Ramberg-Bäcklund rearrangementGaich-Group Seminar
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via S-alkylation/oxidation:



via cycloaddition:



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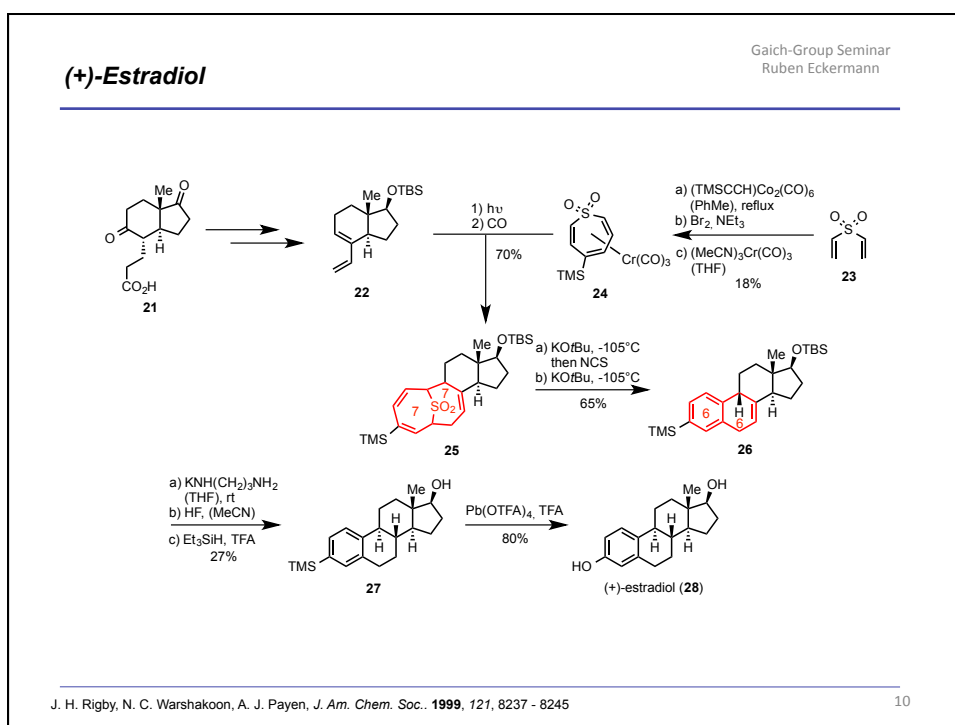
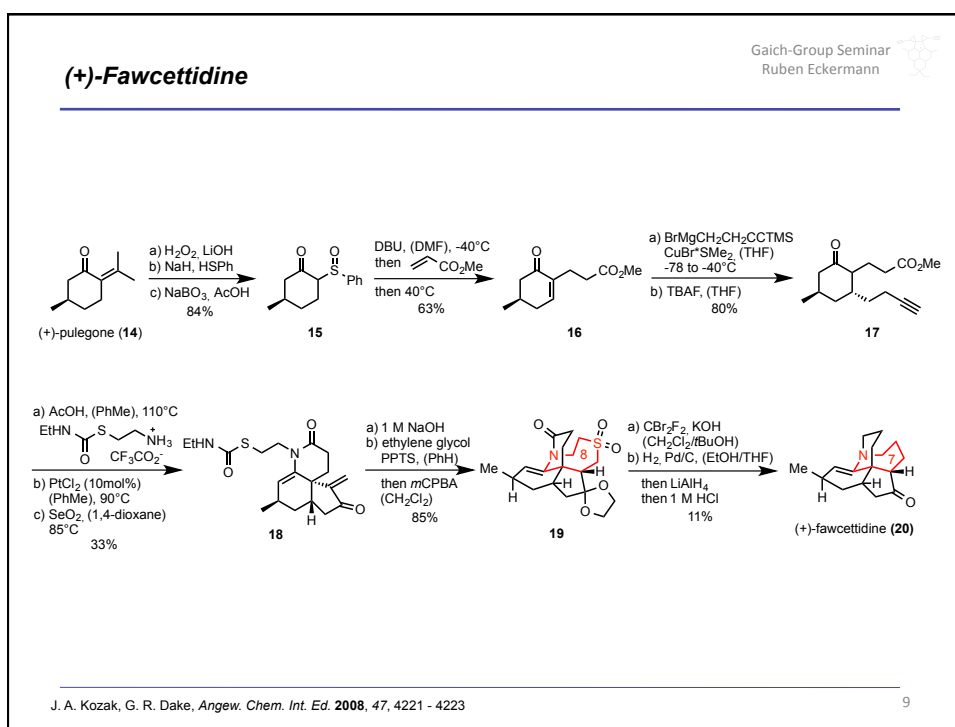
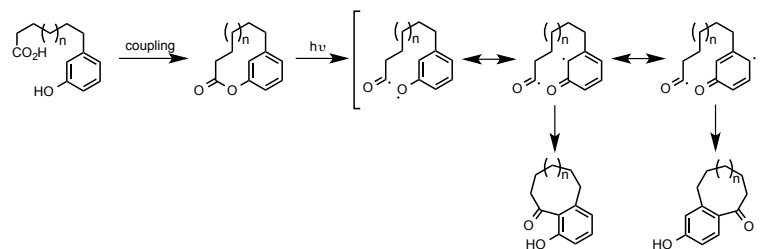


Photo-Fries rearrangement

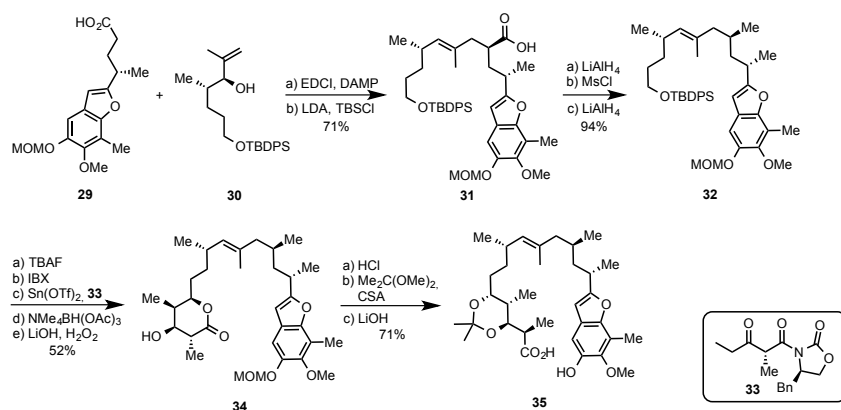
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Kendomycin

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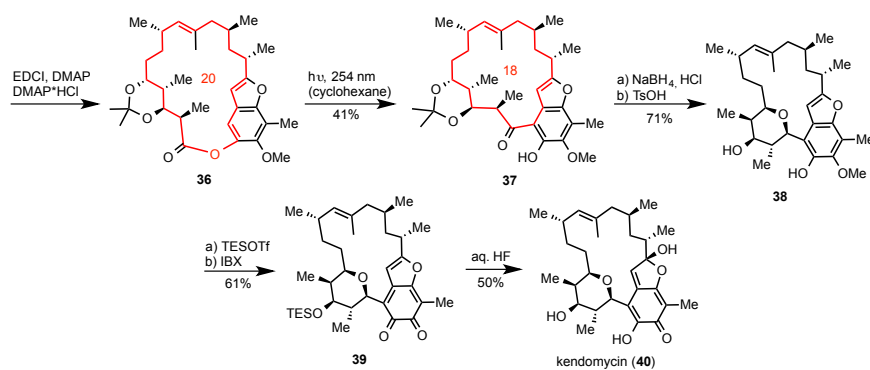


H. J. Martin, T. Magauer, J. Mulzer, *Angew. Chem. Int. Ed.* **2010**, *49*, 5614 - 5626

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Kendomycin

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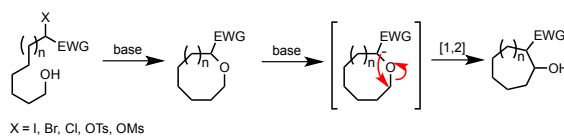
H. J. Martin, T. Magauer, J. Mulzer, *Angew. Chem. Int. Ed.* **2010**, *49*, 5614 - 5626

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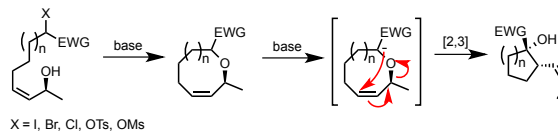
Wittig rearrangement

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[1,2] - rearrangement:

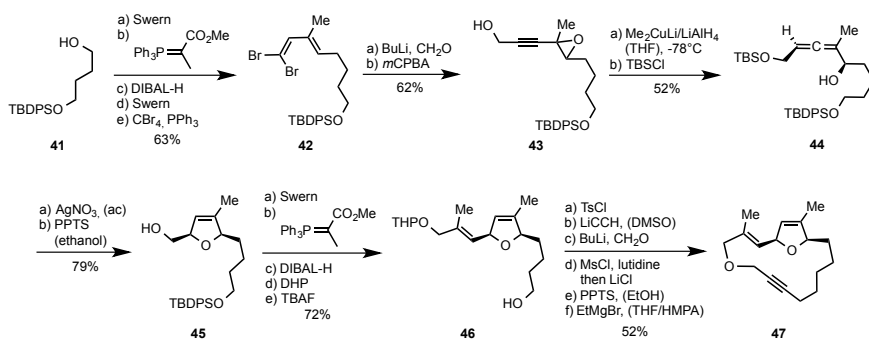


[2,3] - rearrangement:



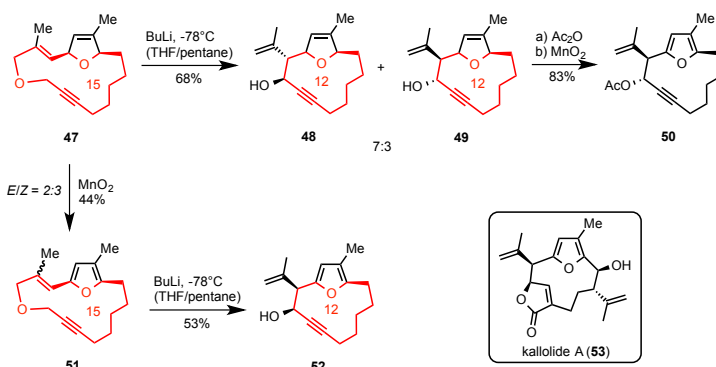
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Kallolide A ring system

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Kallolide A ring system

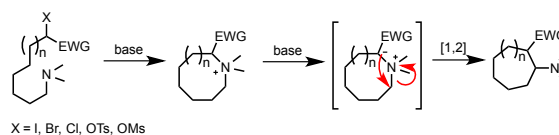
Gaich-Group Seminar
Ruben EckermannJ. A. Marshall, B. Yu, *J. Org. Chem.* **1994**, *59*, 324 - 331

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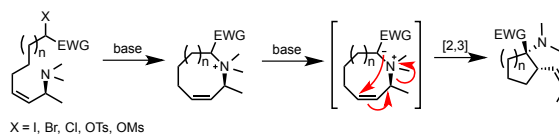
Stevens rearrangement

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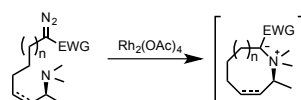
[1,2] - rearrangement:



[2,3] - rearrangement:



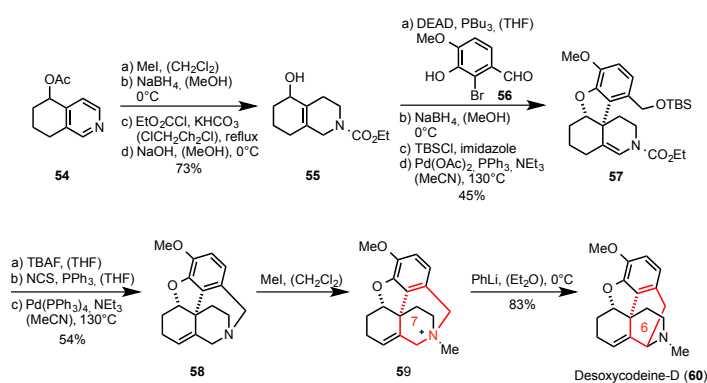
via diazo-compound:



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(±)-Desoxycodein-D

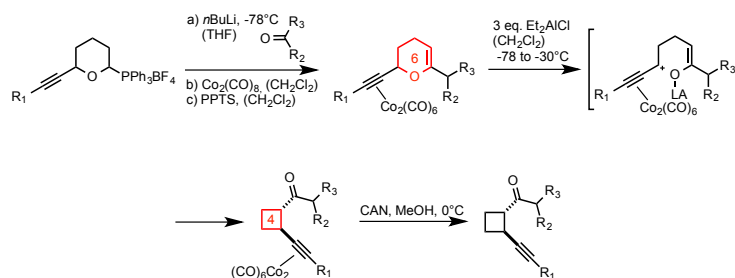
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J.-P. Liou, C.-Y. Cheng, *Tet. Lett.* **2000**, *41*, 915 - 918

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Co - mediated O → C contraction

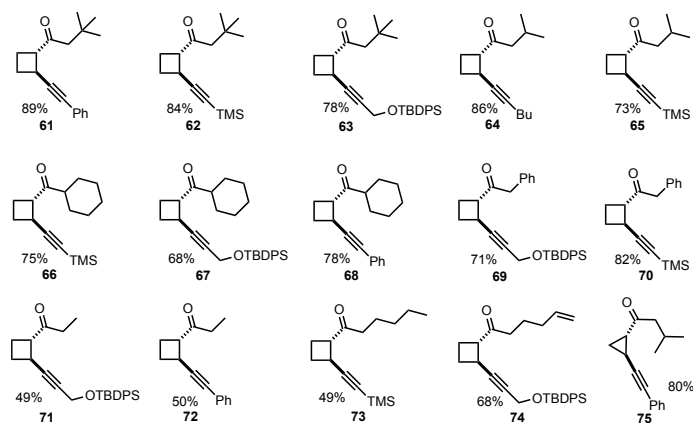
Gaich-Group Seminar
Ruben EckermannS. J. Meek, F. Pradaux, E. H. Demont, J. P. A. Harrity, *Org. Lett.* **2006**, *8*, 5597 - 5600

19

Co - mediated O → C contraction

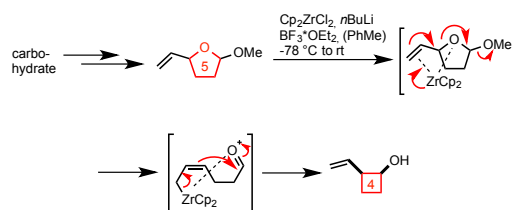
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Substrate scope:

S. J. Meek, F. Pradaux, E. H. Demont, J. P. A. Harrity, *Org. Lett.* **2006**, *8*, 5597 - 5600

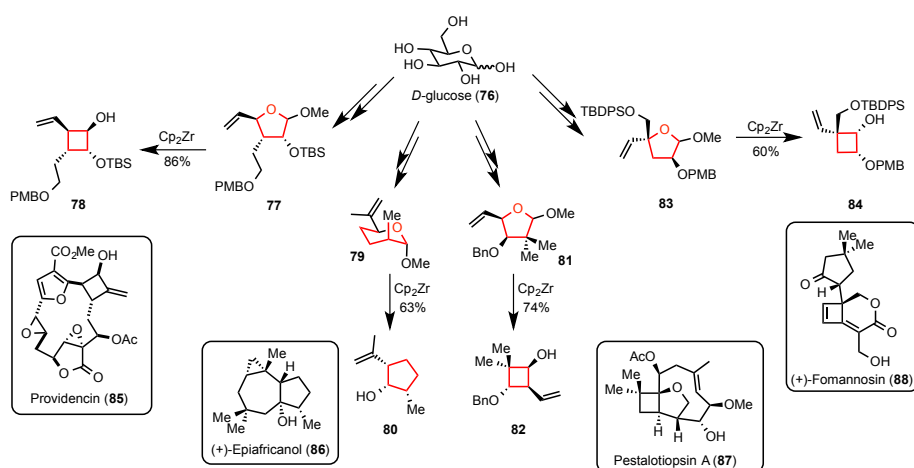
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Zr - mediated O → C contraction

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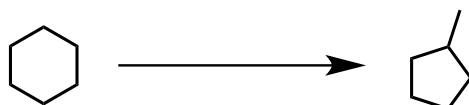
Zr - mediated O → C contraction

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- a) L. A. Paquette, X. Peng, J. Yang, *Angew. Chem. Int. Ed.* **2007**, *46*, 7817 – 7819 b) L. A. Paquette, G. D. Parker, T. Tei, S. Dong, *J. Org. Chem.* **2007**, *72*, 7125 – 7134 c) L. A. Paquette, R. M. Arbit, J.-A. Funel, S. Bolshakov, *Synthesis* **2002**, *14*, 2105 – 2109 d) J. D. White, S. Jana, *J. Org. Chem.* **2014**, *79*, 700 – 710

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One-carbon contraction

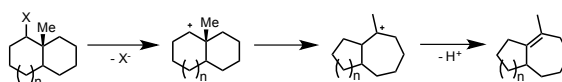


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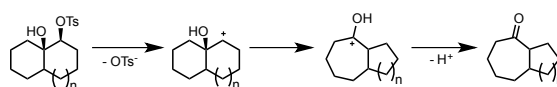
Wagner – Meerwein / Pinacol rearrangement

- rearrangement of cationic intermediates
- mostly ring contraction / expansion sequence

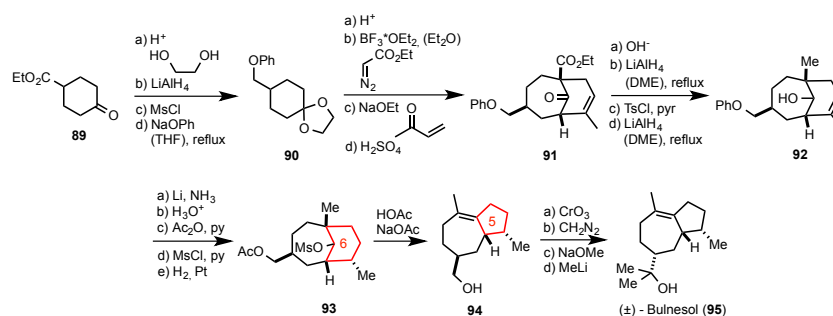
Wagner – Meerwein rearrangement:



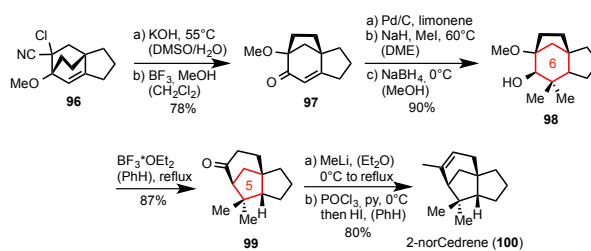
Pinacol rearrangement:



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(±) - BulnesolGaich-Group Seminar
Ruben EckermannJ. A. Marshall, J. J. Partridge, *Tetrahedron*. **1969**, 25, 2159 - 2192

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2-norCedreneGaich-Group Seminar
Ruben EckermannH. K. Hariprakash, G. S. R. SubbaRao, *Tet. Lett.* **1997**, 38, 5343 - 5346

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Epoxide rearrangement

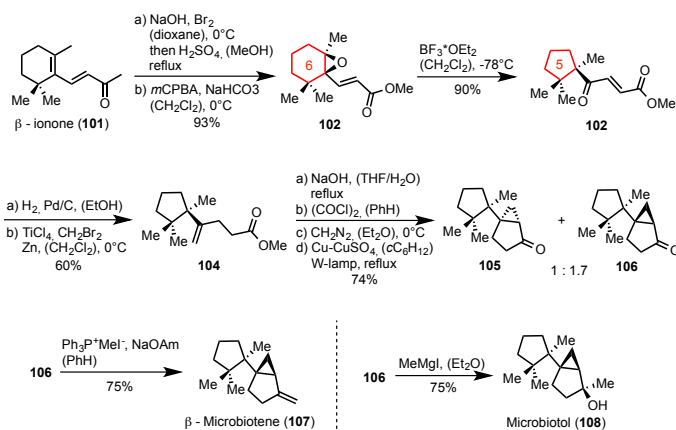
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β - Microbiotene & Microbiotol

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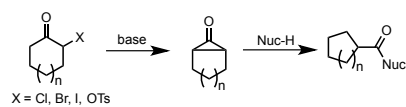
a) A. Srikrishna, S. A. Nagamani, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 3393 – 3394 b) A. Srikrishna, D. B. Ramachary, *Tet. Lett.* **1999**, 40, 6669 - 6670

28

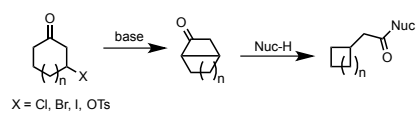
Favorski rearrangement

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Favorski rearrangement:



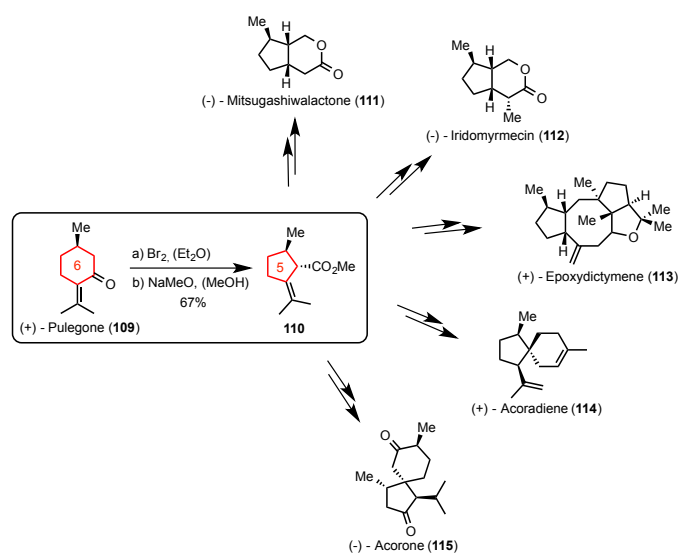
Homo-Favorski rearrangement:



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ex (+) - Pulegone

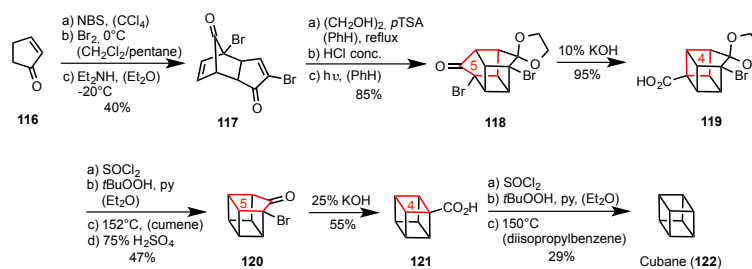
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L. F. Silva, Jr., *Tetrahedron* **2002**, *58*, 9137 - 9161

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Cubane

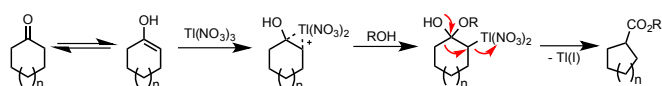
Gaich-Group Seminar
Ruben EckermannP. E. Eaton, T. W. Cole, Jr., *J. Am. Chem. Soc.* **1964**, *86*, 962 & 3157

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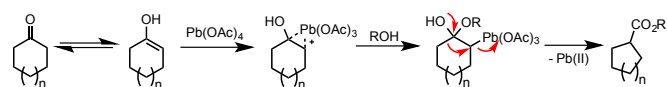
Oxidative contractions

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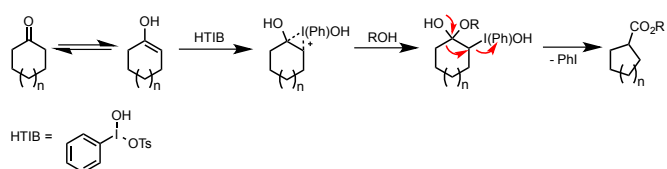
Thallium (III) – promoted:



Lead (IV) – promoted:

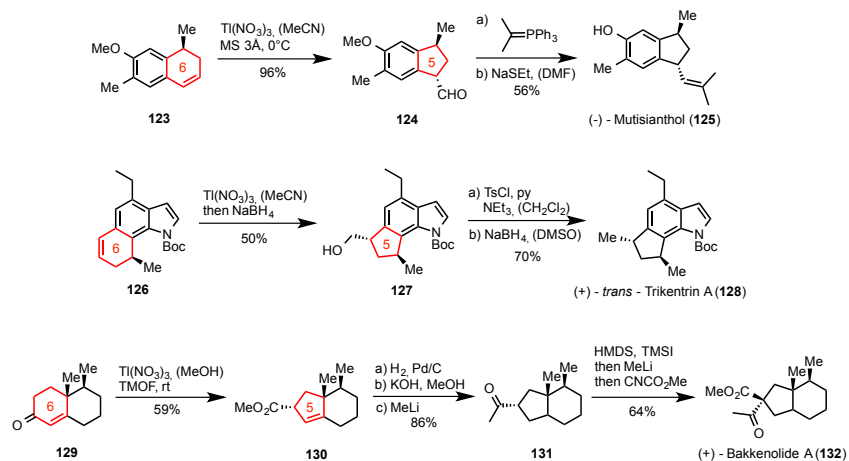


Iodine (III) – promoted:

L. F. Silva, Jr., *Tetrahedron* **2002**, *58*, 9137 - 9161

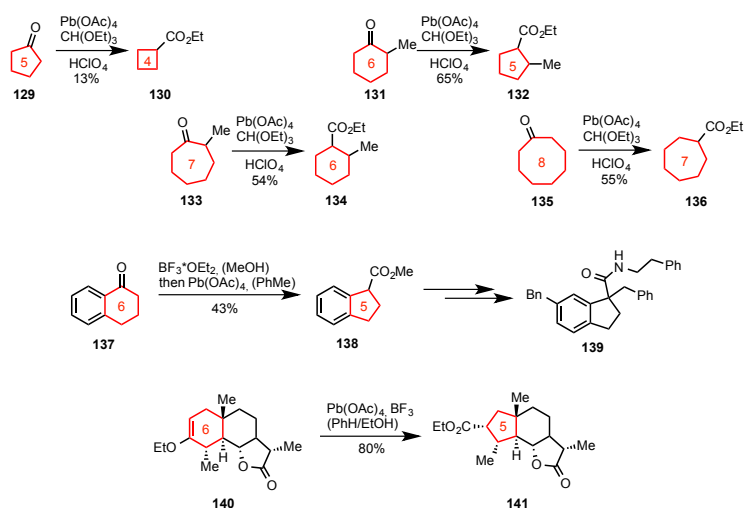
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Thallium (III) - promoted

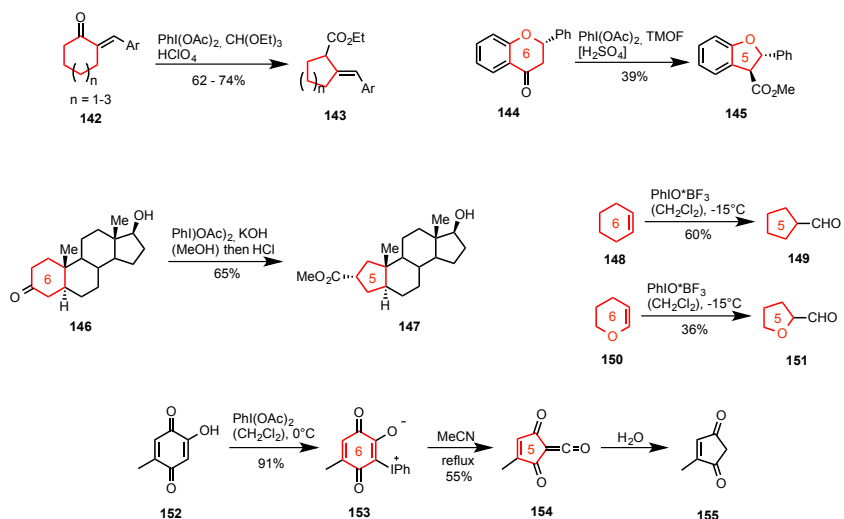
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a) V. M. T. Carneiro, H. M. C. Ferraz, T. O. Vieira, E. E. Ishikawa, L. F. Silva, Jr., *J. Org. Chem.* **2010**, *75*, 2877 – 2882 b) G. G. Bianco, H. M. C. Ferraz, A. M. Costa, L. V. Costa-Lotuf, C. Pessoa, M. O. de Moraes, M. G. Schrems, A. Pfaltz, L. F. Silva, Jr. *J. Org. Chem.* **2009**, *74*, 2561 – 2566 c) I. R. M. Tébéka, G. B. Longato, M. V. Craveiro, J. E. de Carvalho, A. L. T. G. Ruiz, L. F. Silva, Jr., *Chem. Eur. J.* **2012**, *18*, 16890 – 16901

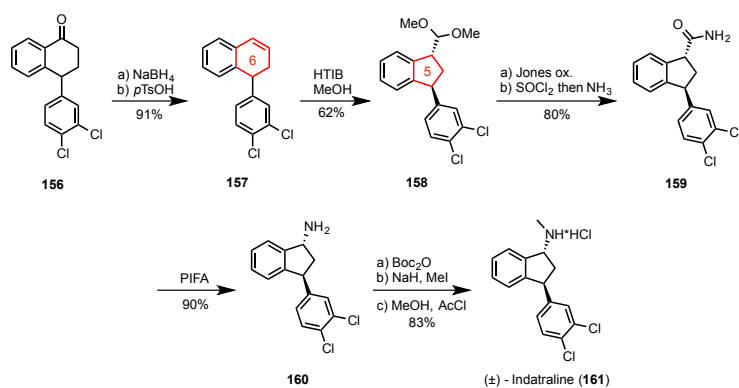
Lead (IV) - promoted

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Iodine (III) - promotedGaich-Group Seminar
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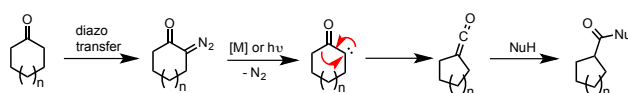
35

(±) - IndatralineGaich-Group Seminar
Ruben EckermannL. F. Silva, Jr., F. A. Siqueira, E. C. Pedrozo, F. Y. M. Vieira, A. C. Doriguetto, *Org. Lett.* **2007**, *9*, 1433 - 1436

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Wolff rearrangement

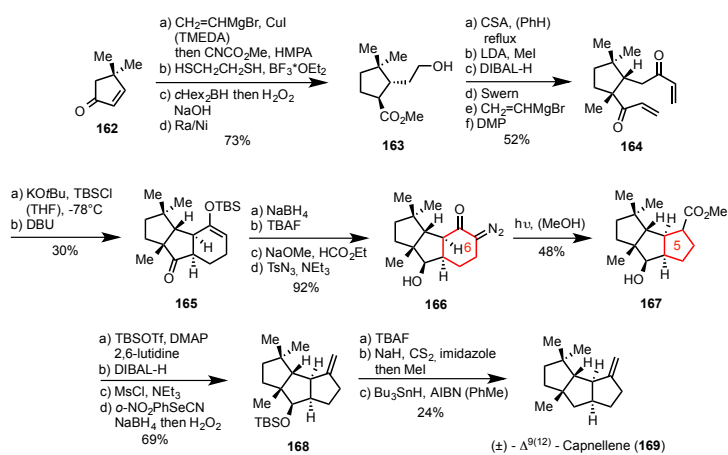
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(±) - $\Delta^9(12)$ - Capnellene

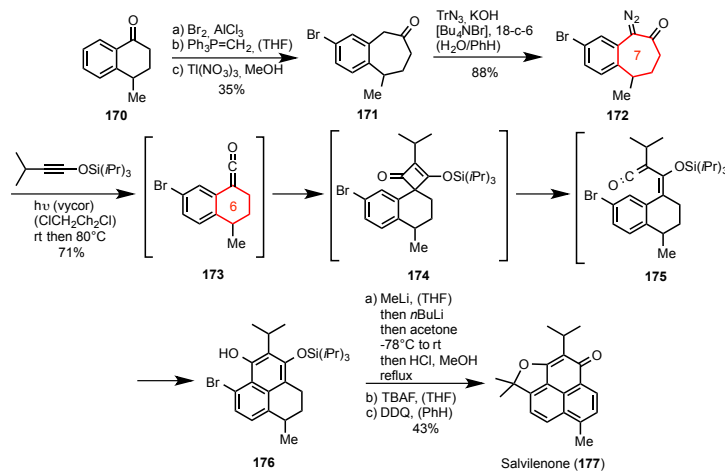
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M. Ihara, T. Suzuki, M. Katogi, N. Taniguchi, K. Fukumoto, *J. Chem. Soc., Chem. Commun.* **1991**, 646 - 647

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Salvilenone

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