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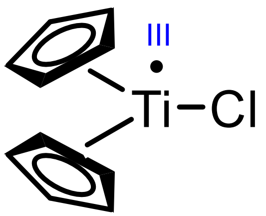
The Nugent Reagent: Cp_2TiCl

Eur. J. Org. Chem. **2015**, *21*, 4567–4591



Li Bo

2021.03.11

J. Enrique Oltra

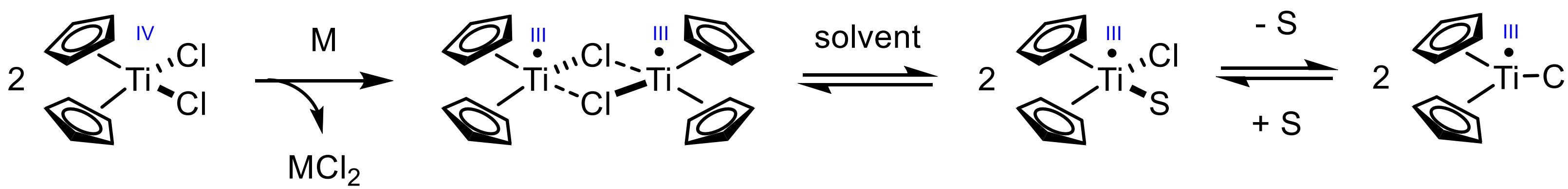
- J. Enrique Oltra was born in Quatretonda, Valencia (Spain).
- He graduated in pharmacy and in 1987 obtained his Ph.D. at the University of Granada (UGR).
- Subsequently he held a postdoctoral position at the Institut de Chimie des Substances Naturelles (CNRS) under the supervision of Prof. P. Potier.
- From 1990 to 2007 he was a lecturer at the Department of Organic Chemistry of the UGR.
- In February 2008 he was promoted to the position of Full Professor.

Content

Intrduction

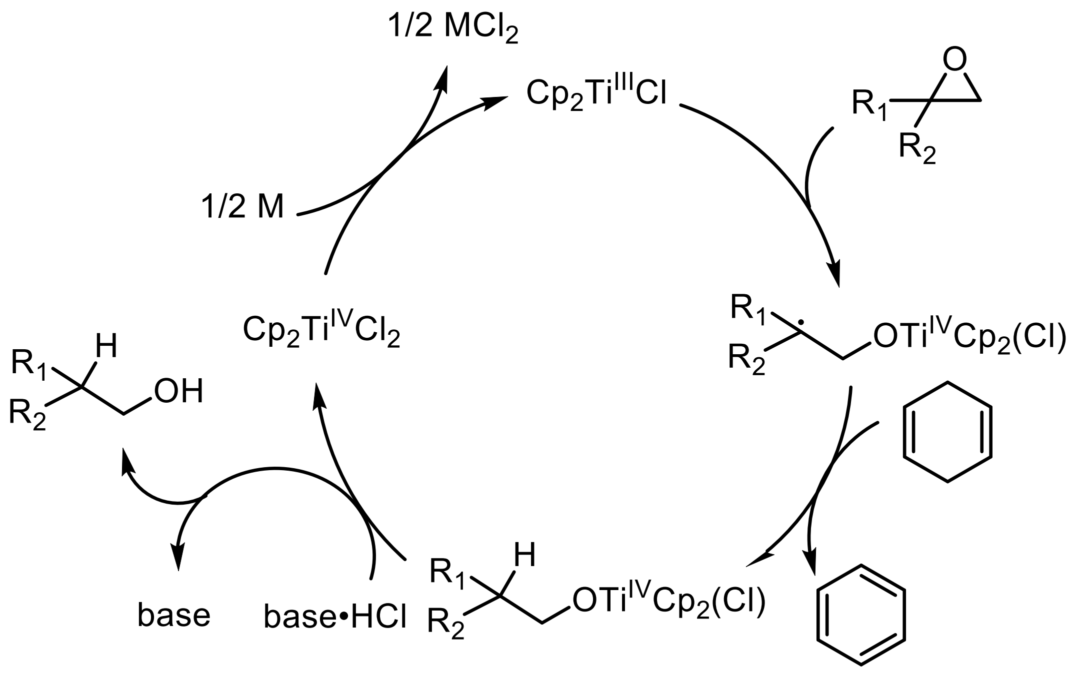
- Cp_2TiCl was synthesised for the first time by Wilkinson in 1955
- Nugent described its initial applications in radical organic chemistry in 1994

- green crystalline powder
- mild single-electron-transfer (SET) reagent



M = Zn, Mn

Catalytic cycle



M = Mn, Zn

$R_1 = CH_3$, $R_2 = CH_2CH_2Ph$

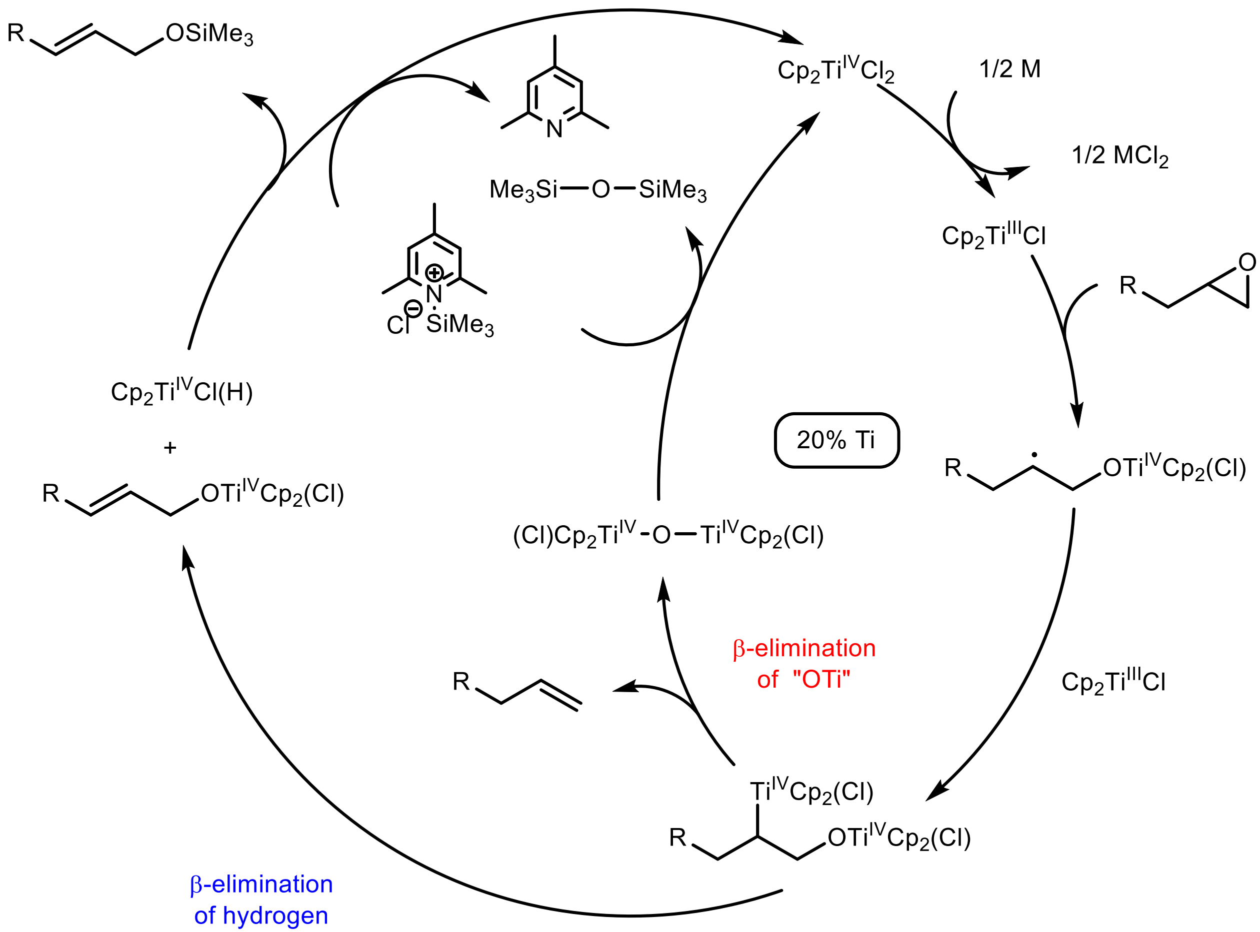
base = 2,4,6-collidine

yield: 88%

Catalytic Cp_2TiCl-mediated epoxide opening with use of 2,4,6-collidine·HCl

A. Gansäuer, M. Pierobon, H. Bluhm, *Angew. Chem. Int. Ed*. **1998**, *37*, 101

Catalytic cycle



Catalytic Cp_2TiCl-mediated epoxide opening with use of TMSCl/2,4,6-collidine

A. F. Barrero, A. Rosales, J. M. Cuerva, J. E. Oltra, *Org.Lett*. **2003**, *5*, 1935

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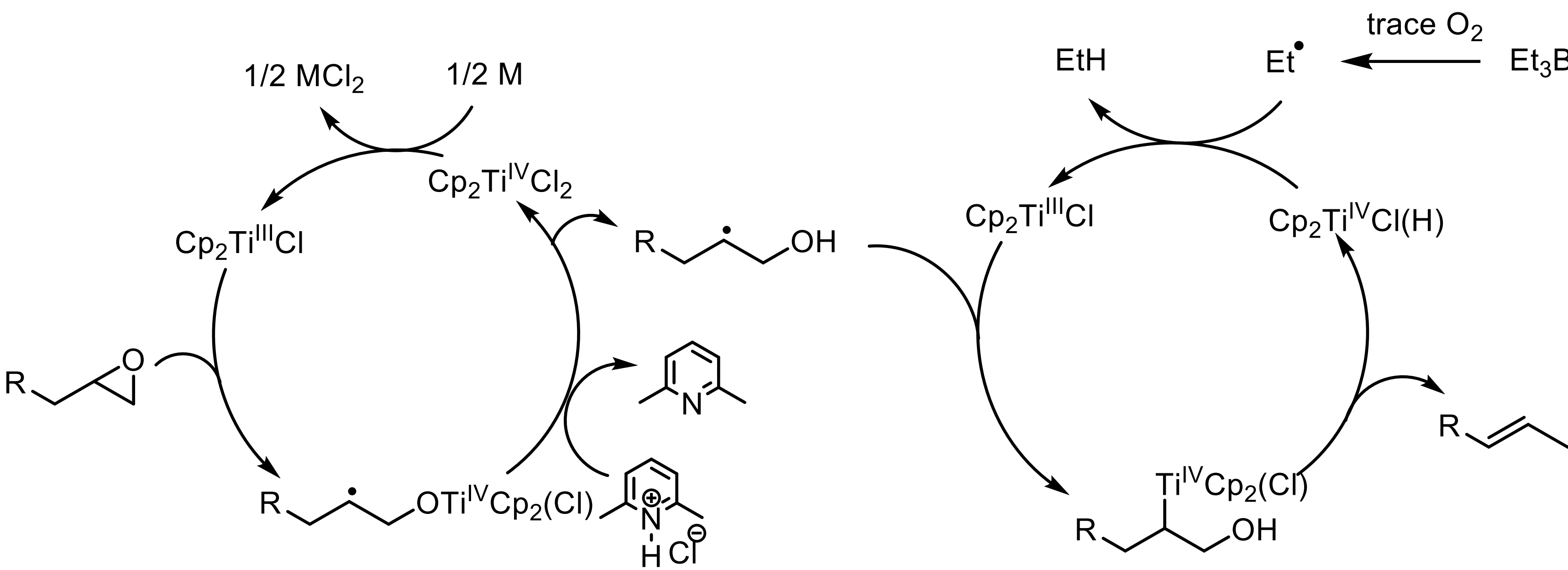
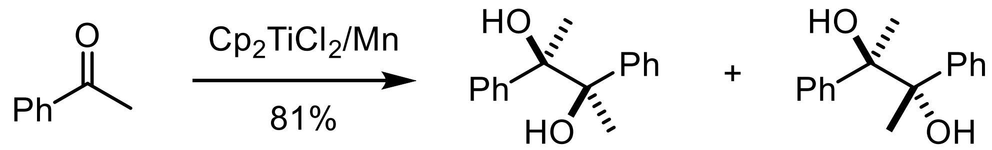
Catalytic cycle

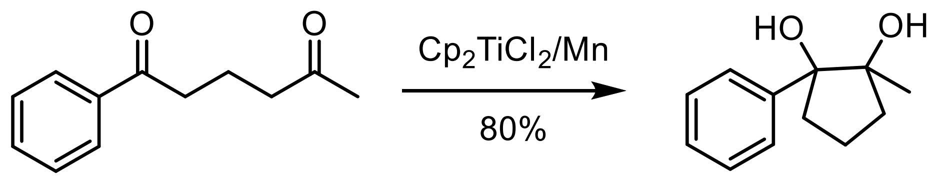


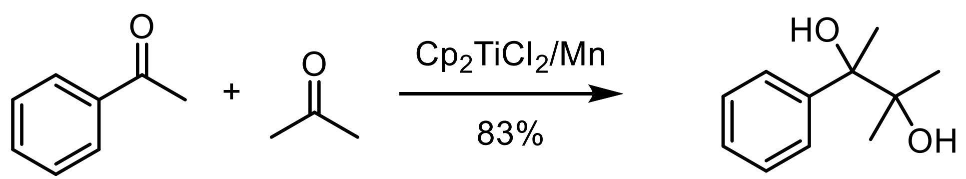
Catalytic Cp_2TiCl-mediated epoxide opening with use of Et_3B/2,6-lutidine hydrochloride

S. Fuse, M. Hanochi, T. Doi, T. Takahashi, *Tetrahedron Lett*. **2004**, *45*, 1961

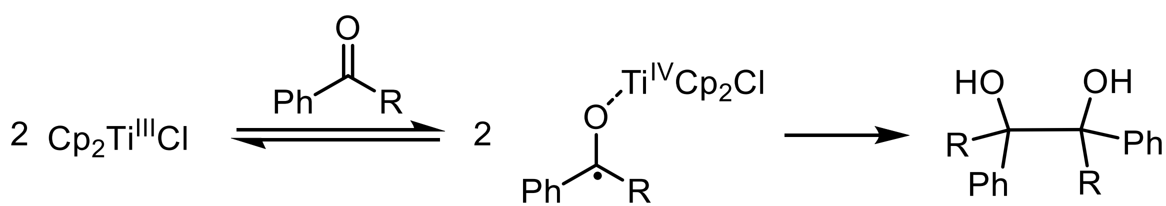
Pinacol coupling





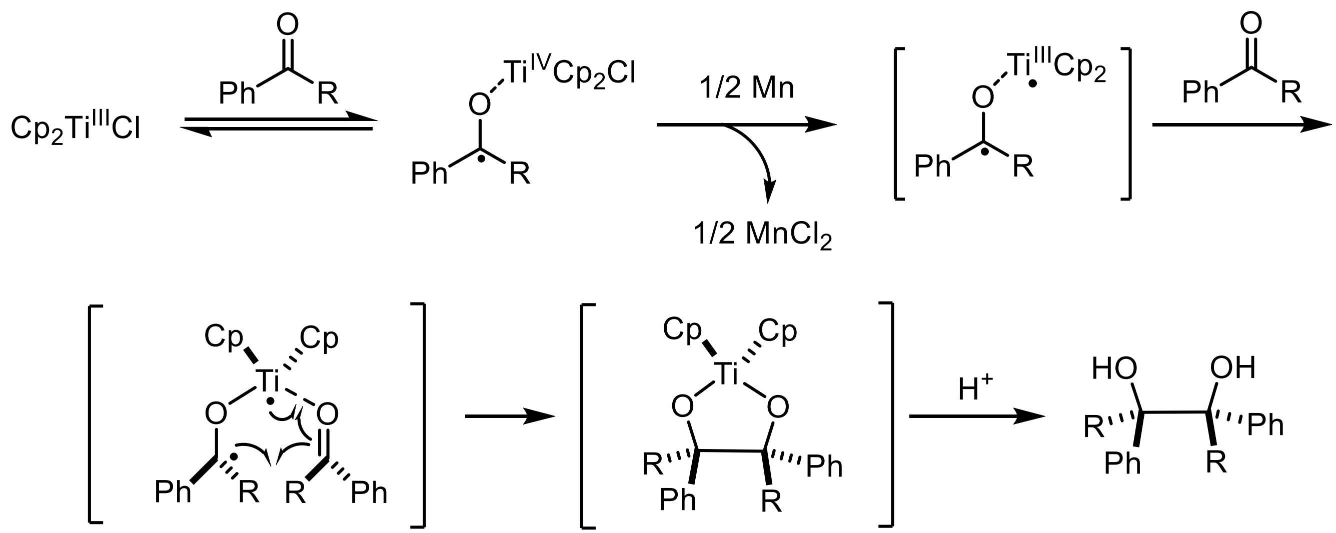


Mechanism A

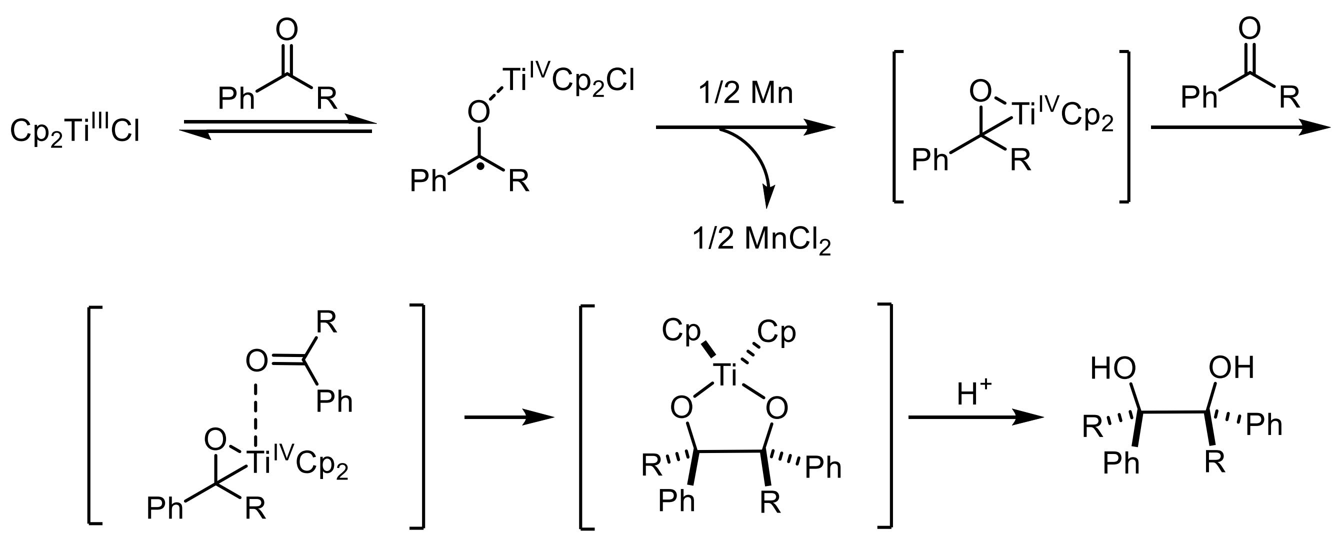


Pinacol coupling

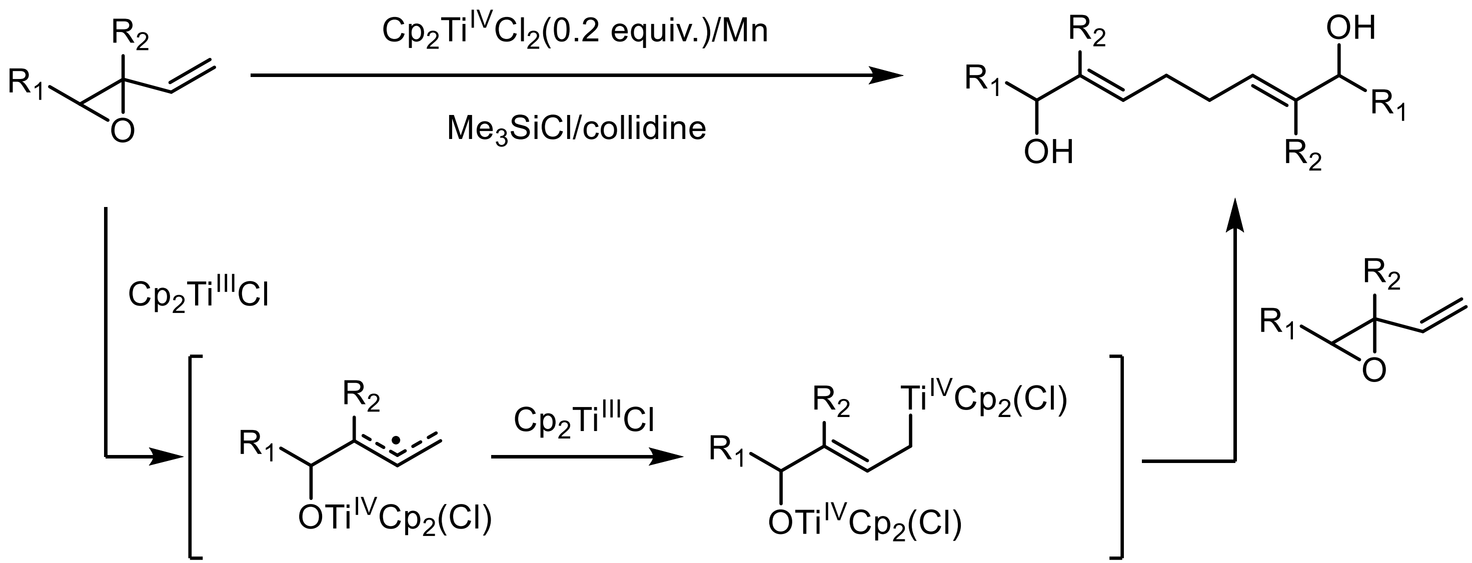
Mechanism B



Mechanism C



Homocoupling of Vinyl Epoxides



A. F. Barrero, J. F. Quílez del Moral, E. M. Sánchez, J. F. Arteaga, *Org. Lett*. **2006**, *8*, 669

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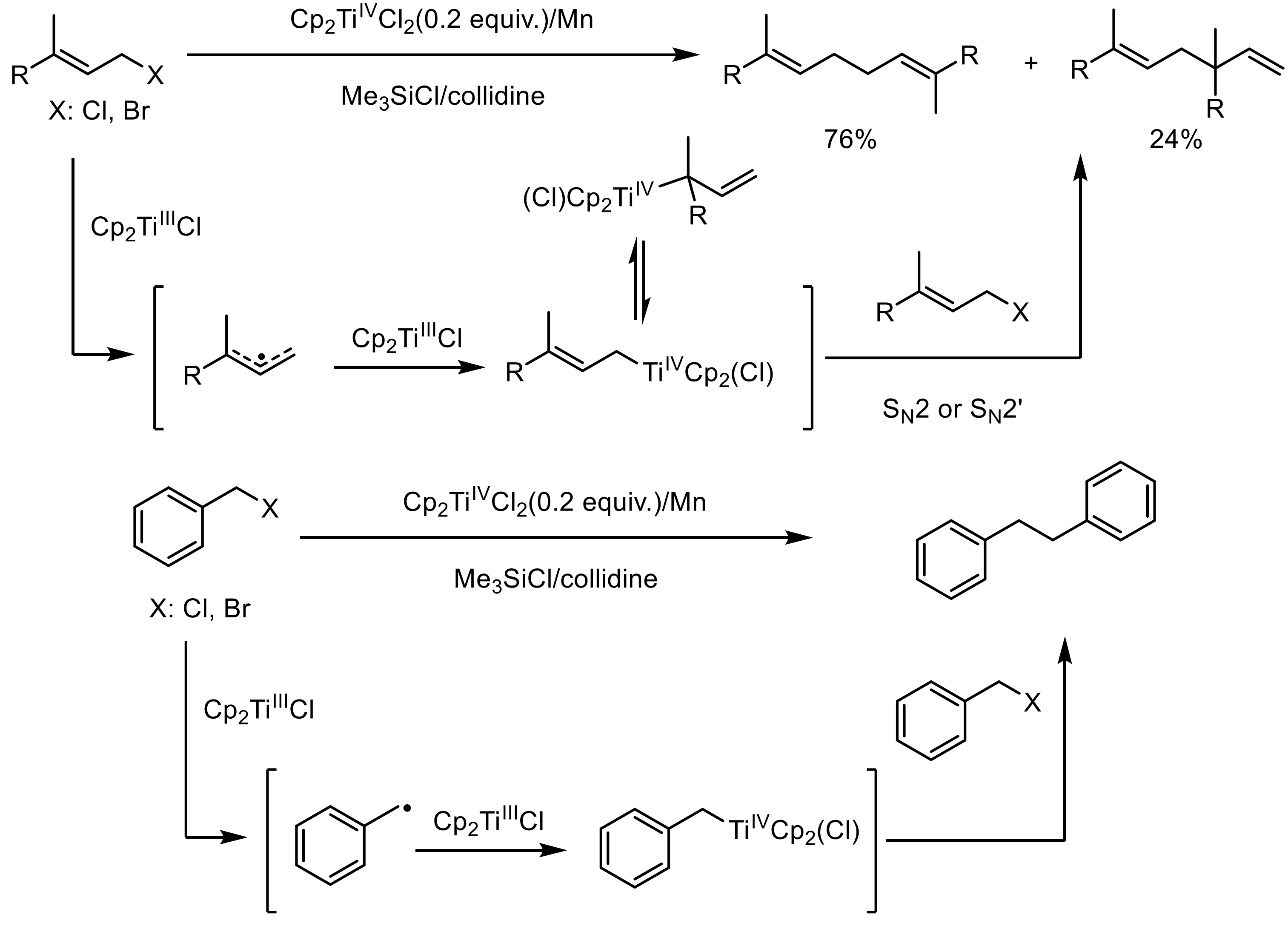
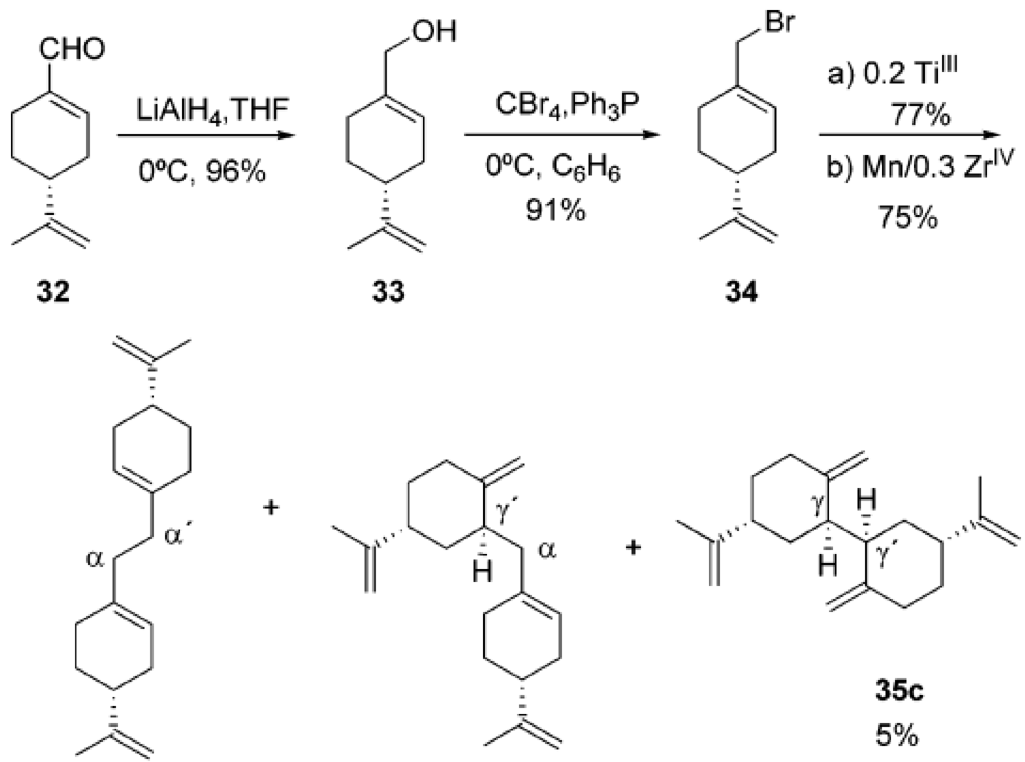
Homocoupling of Allyl Halides and Benzyl Halides



SCHEME 5. Homocoupling Reaction of (*R*)-Perillyl Bromide (34): Synthesis of the Advanced Intermediate 36



35a

42% using Ti^{III}

48% using Mn/Zr^{IV}

35b

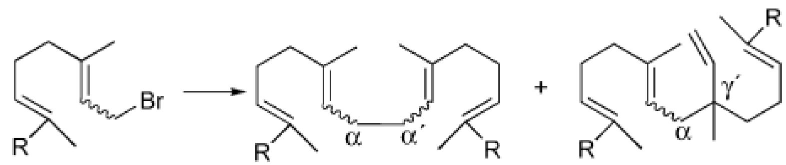
31% using Ti^{III}

24% using Mn/Zr^{IV}

35c

5%

Homocoupling of Allyl Halides and Benzyl Halides



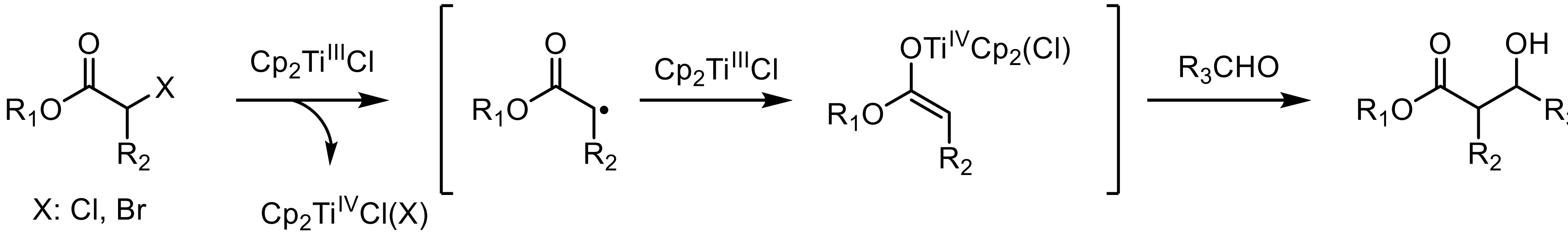
4a (*E*) R = CH_3
4b (*Z*) R = CH_3
4c (2*E*,6*E*) R = COOMe
4d (2*E*,6*Z*) R = COOMe

5a R = CH_3
5b R = CH_3
5c R = COOMe
5d R = COOMe

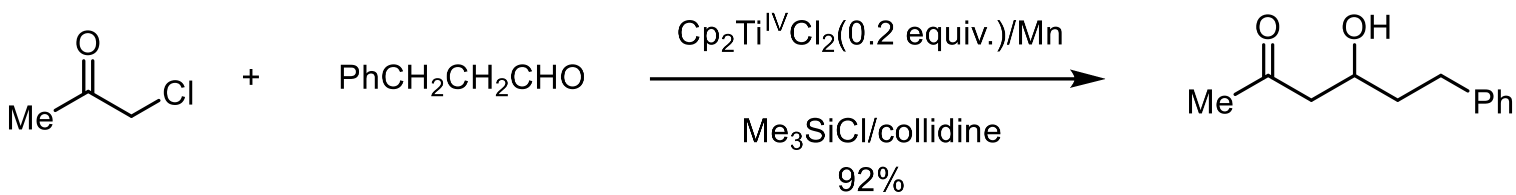
entry	allylic bromide	equiv of Cp_2TiCl_2[b]	time (min)	ratio[c] $\alpha,\alpha':\alpha,\gamma'$[d]	compd	yield[e] (%)
1	**4a**	3	2	70:30	**5a**	80
2	**4a**	0.2	15	64:36	**5a**	89
3	**4b**	3	2	74:26	**5b**	70
4	**4b**	0.2	15	73:27	**5b**	90
5	**4c**	3	2	77:23	**5c**	84
6	**4c**	0.2	10	74:26	**5c**	85
7	**4d**	3	2	85:15	**5d**	60
8	**4d**	0.2	10	81:19	**5d**	64
9[f]	**4c**	3	10	85:15	**5c**	67
10[g]	**4d**	0.05	20	78:22	**5d**	55

A. F. Barrero, *Org. Lett*. **2005**, *7*, 2301

Reformatsky reaction



J. D. Parrish, D. R. Shelton, R. D. Little, *Org. Lett*. **2003**, *5*, 3615



R. E. Estévez, M. Paradas, A. Millán, T. Jiménez, R. Robles, J. M. Cuerva, J. E. Oltra, *J. Org. Chem*. **2008**, *73*, 1616

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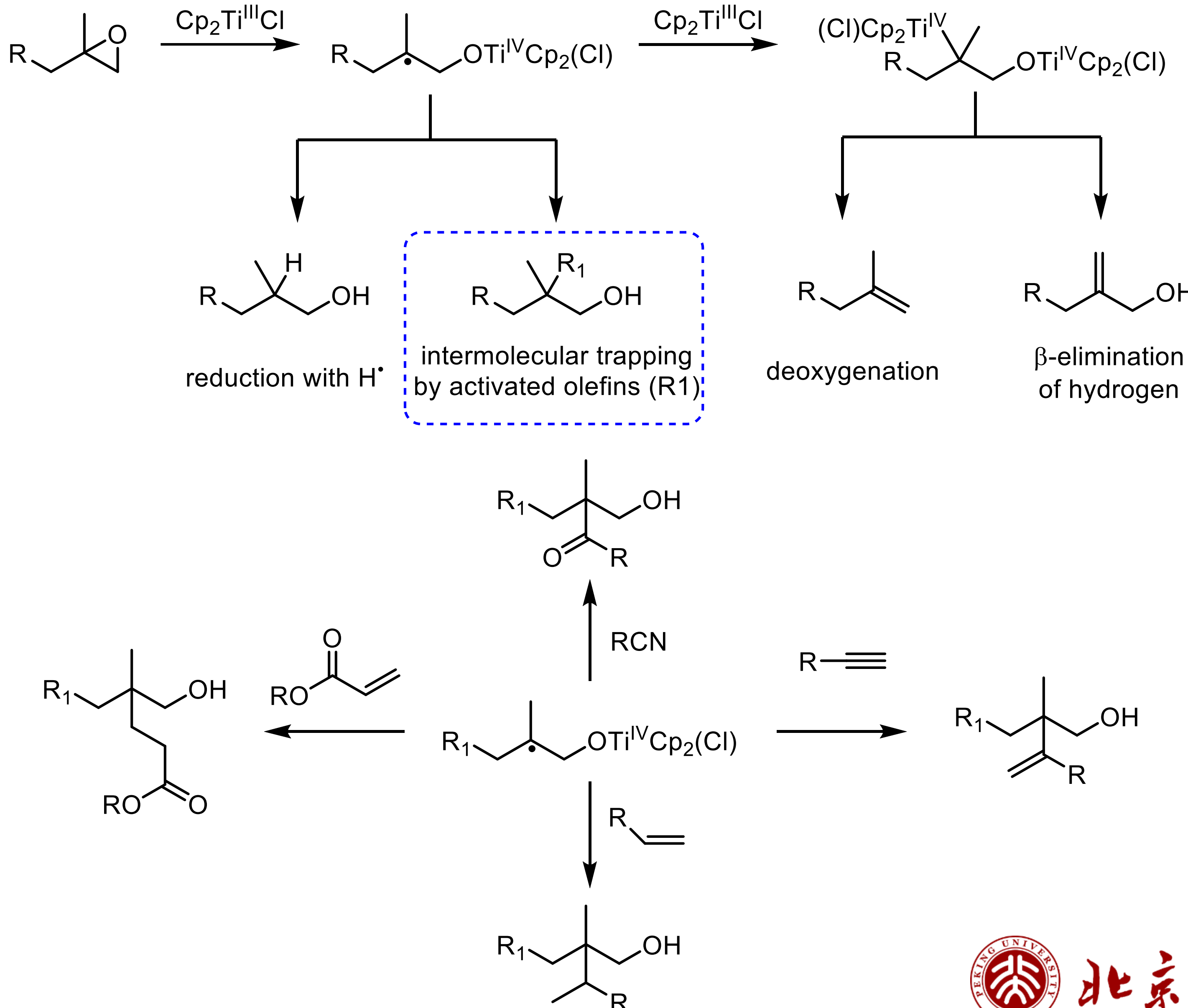
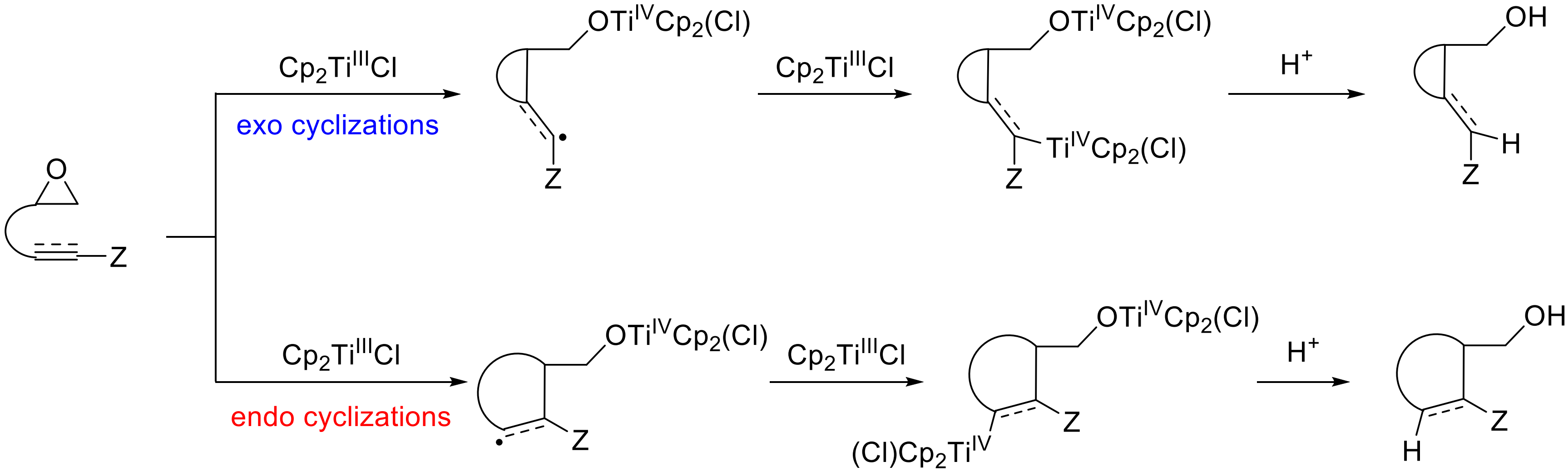
Radical Ring-Opening of Epoxides



Radical Ring-Opening of Epoxides



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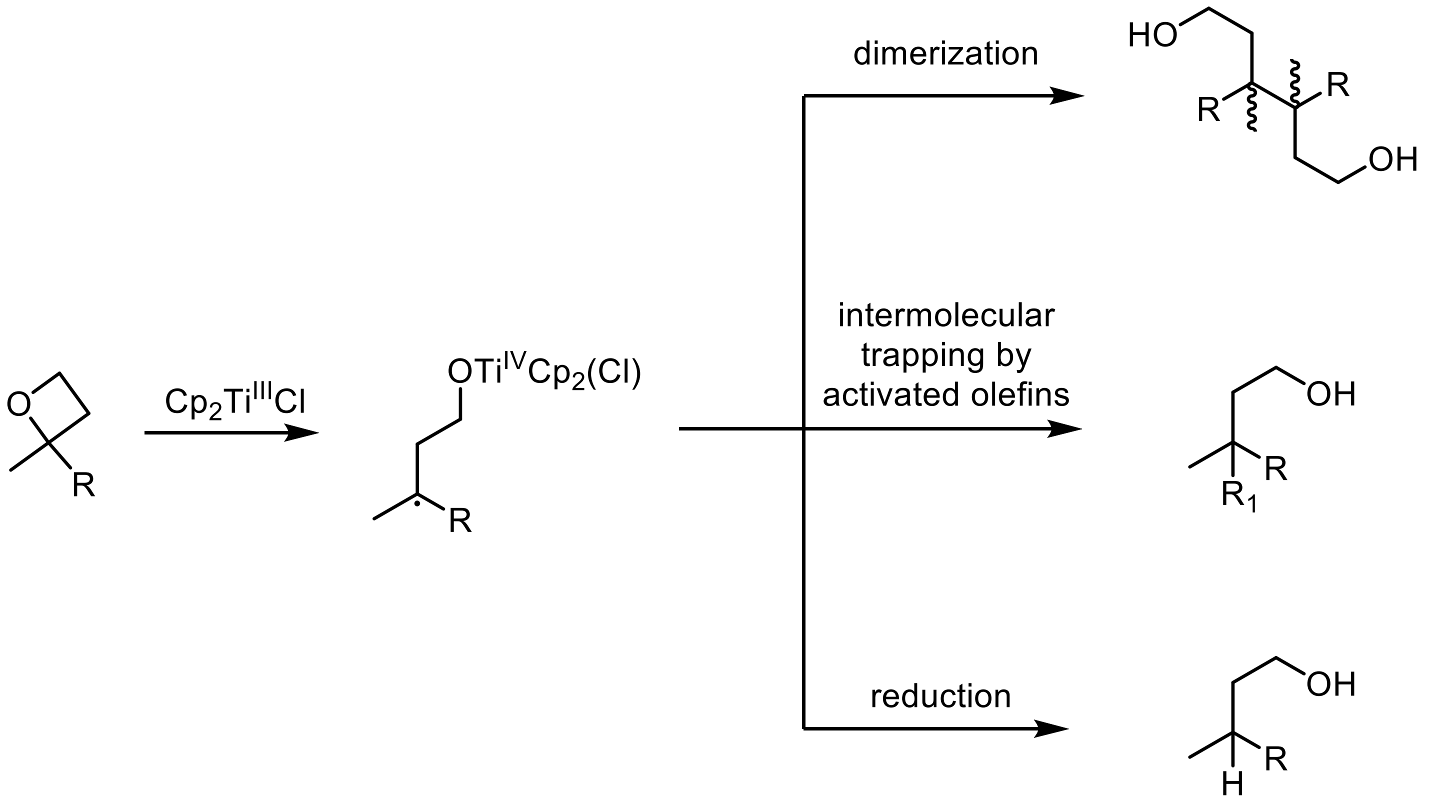
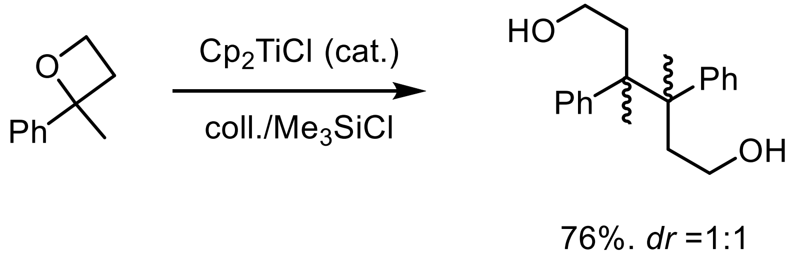
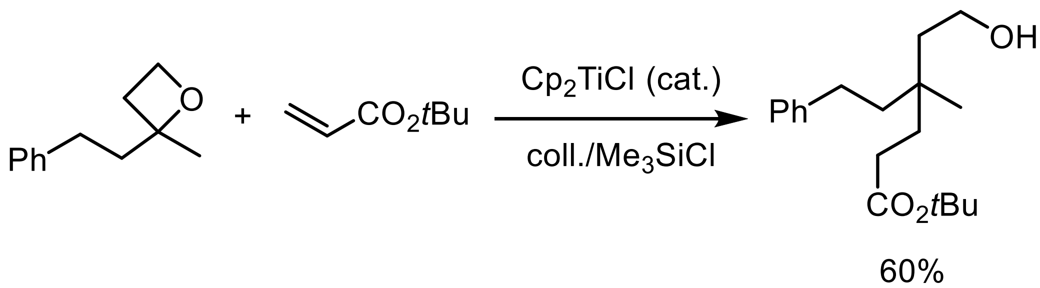
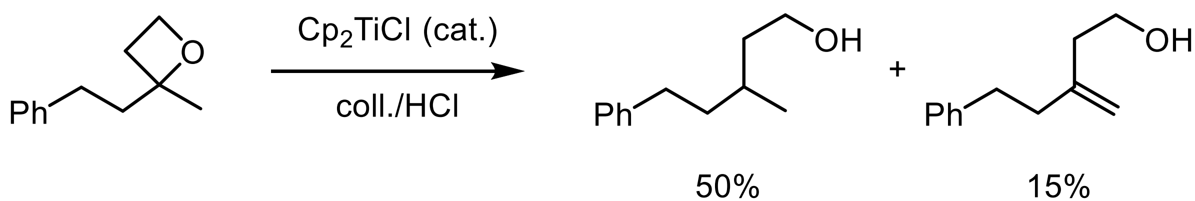
Radical Ring-Opening of Oxetanes



Radical Ring-Opening of Oxetanes

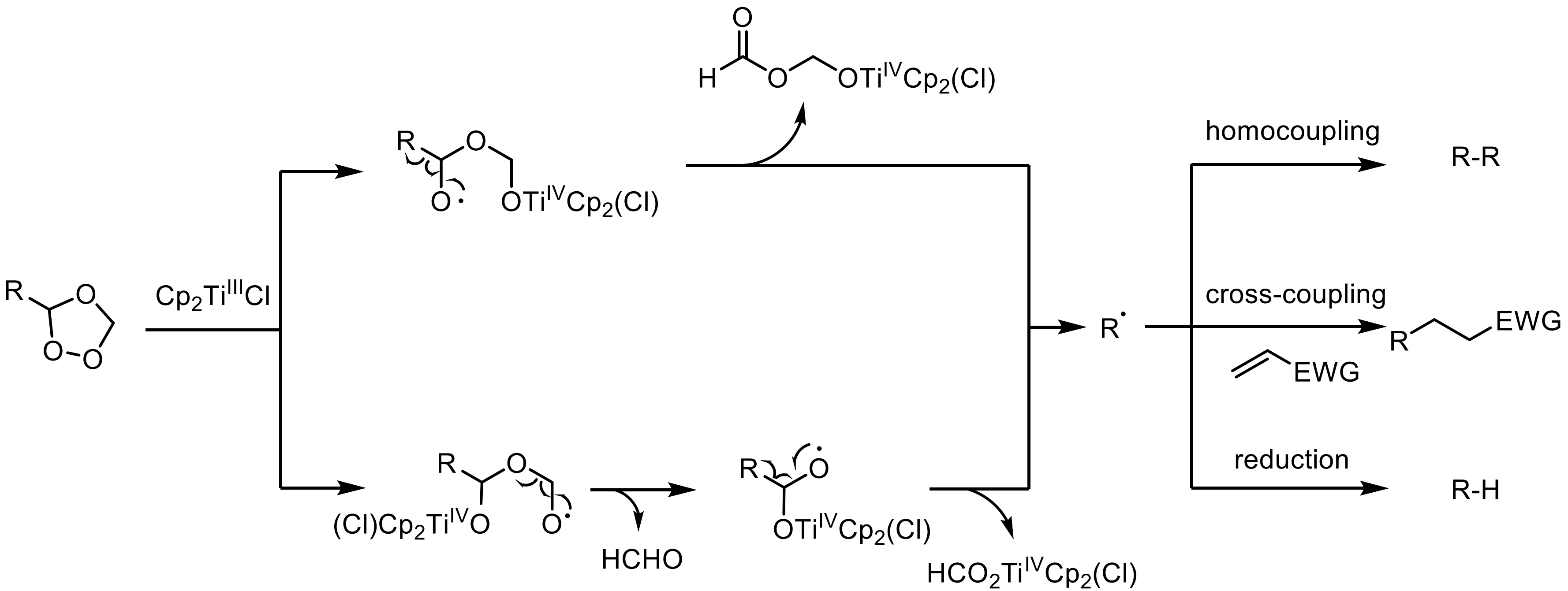




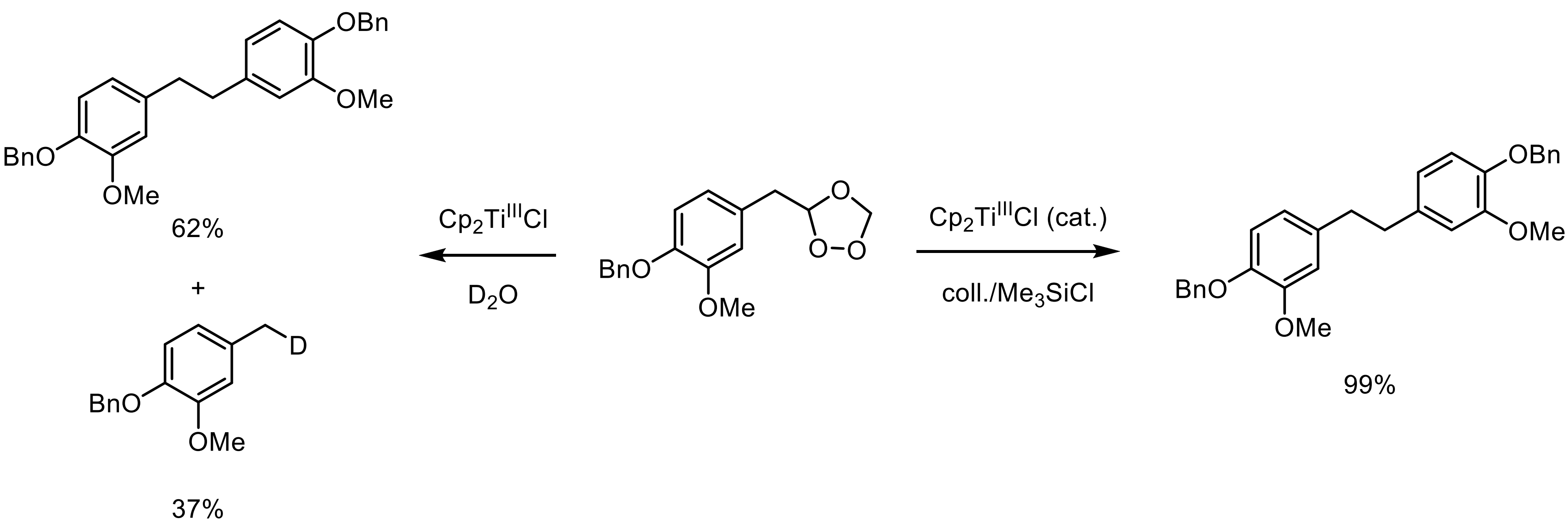


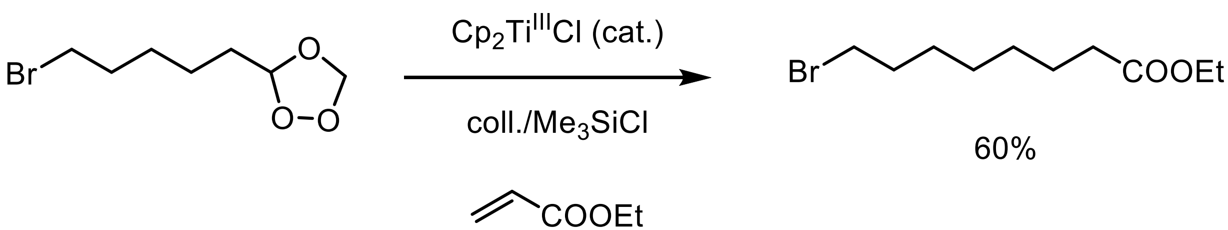
A. Gansäuer, *Tetrahedron*, **2008**, *64*, 11839

Radical Ring-Opening of Ozonides



Radical Ring-Opening of Ozonides





A. Rosales, *J. Org. Chem*. **2012**, *77*, 4171

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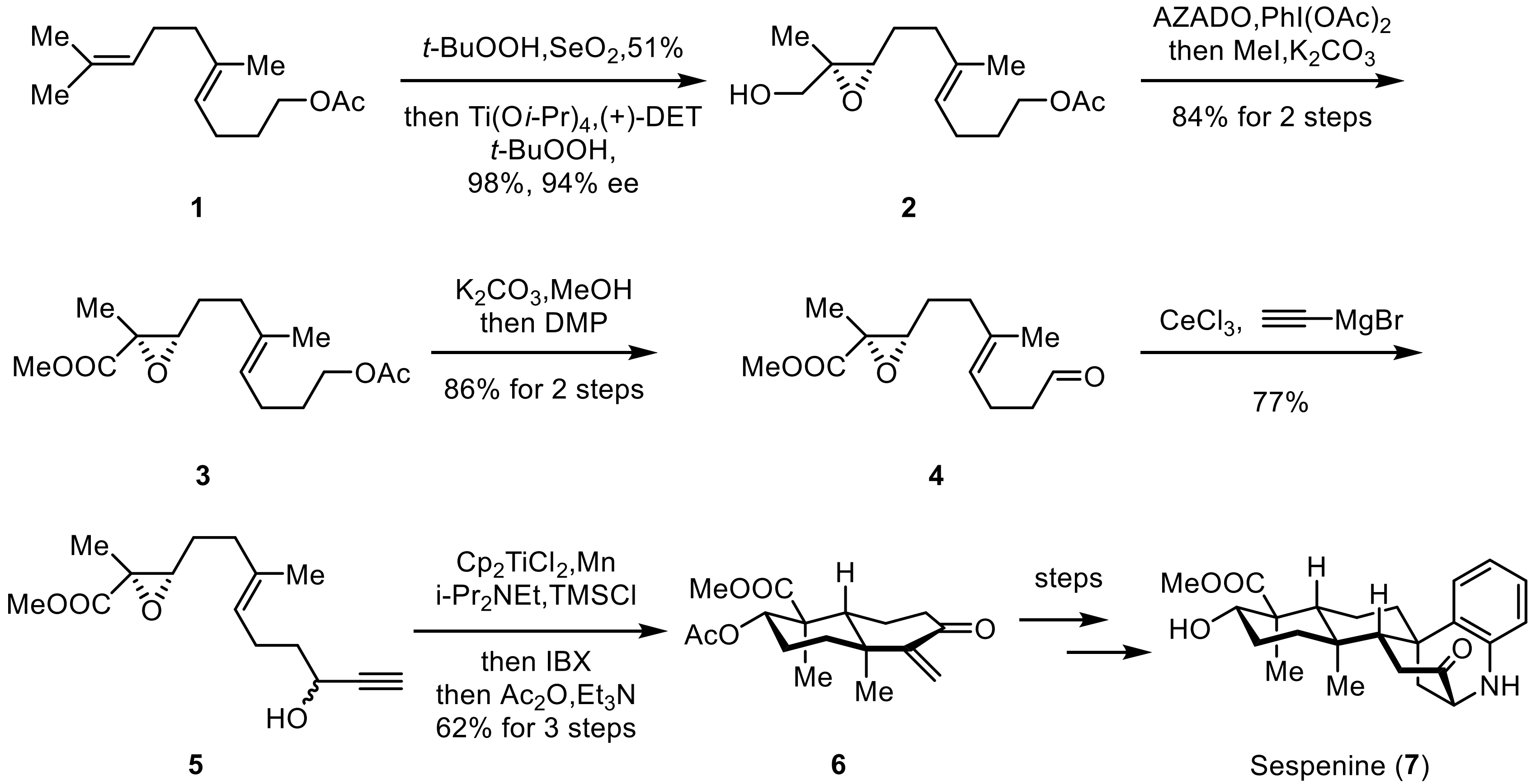
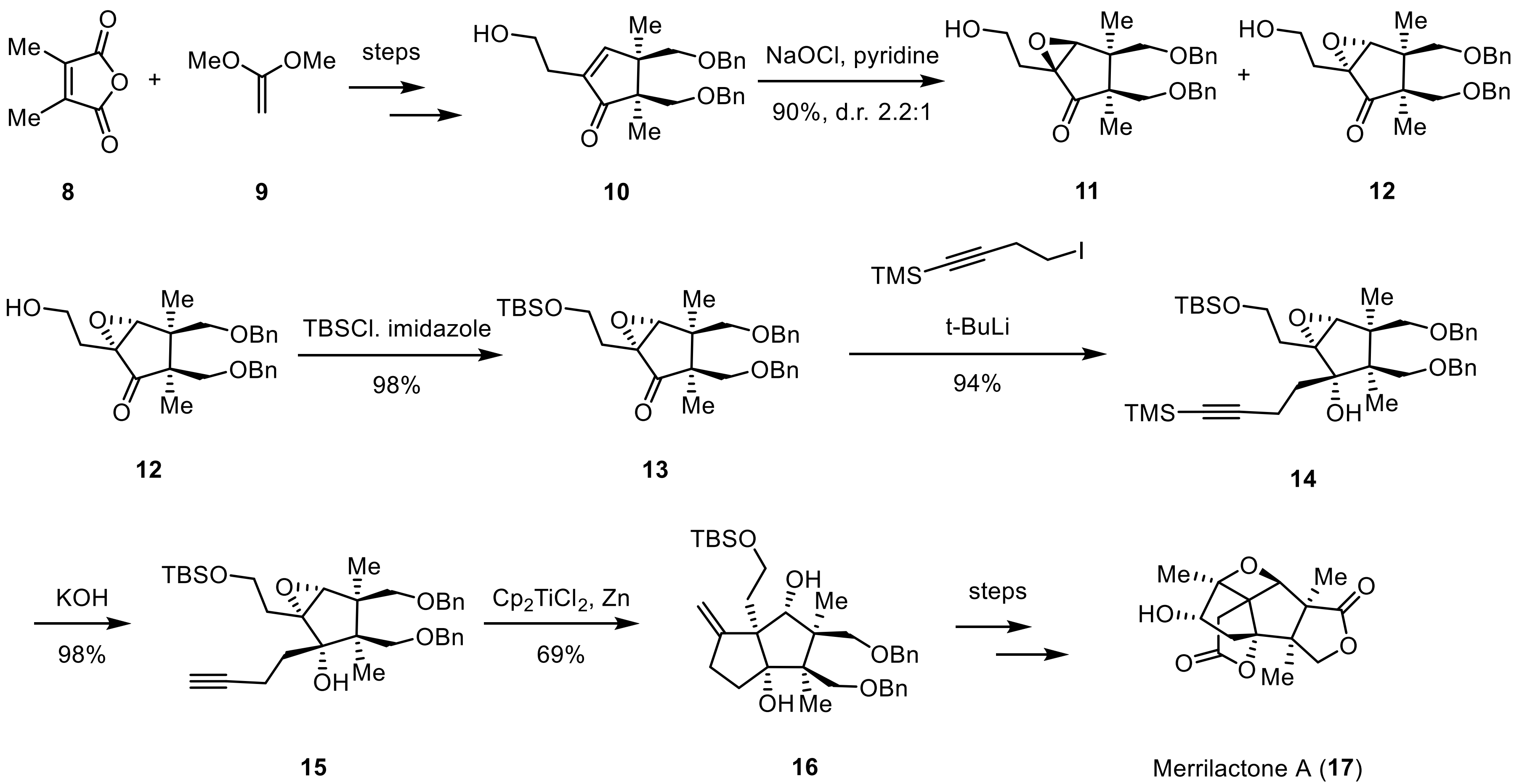
Applications in total synthesis



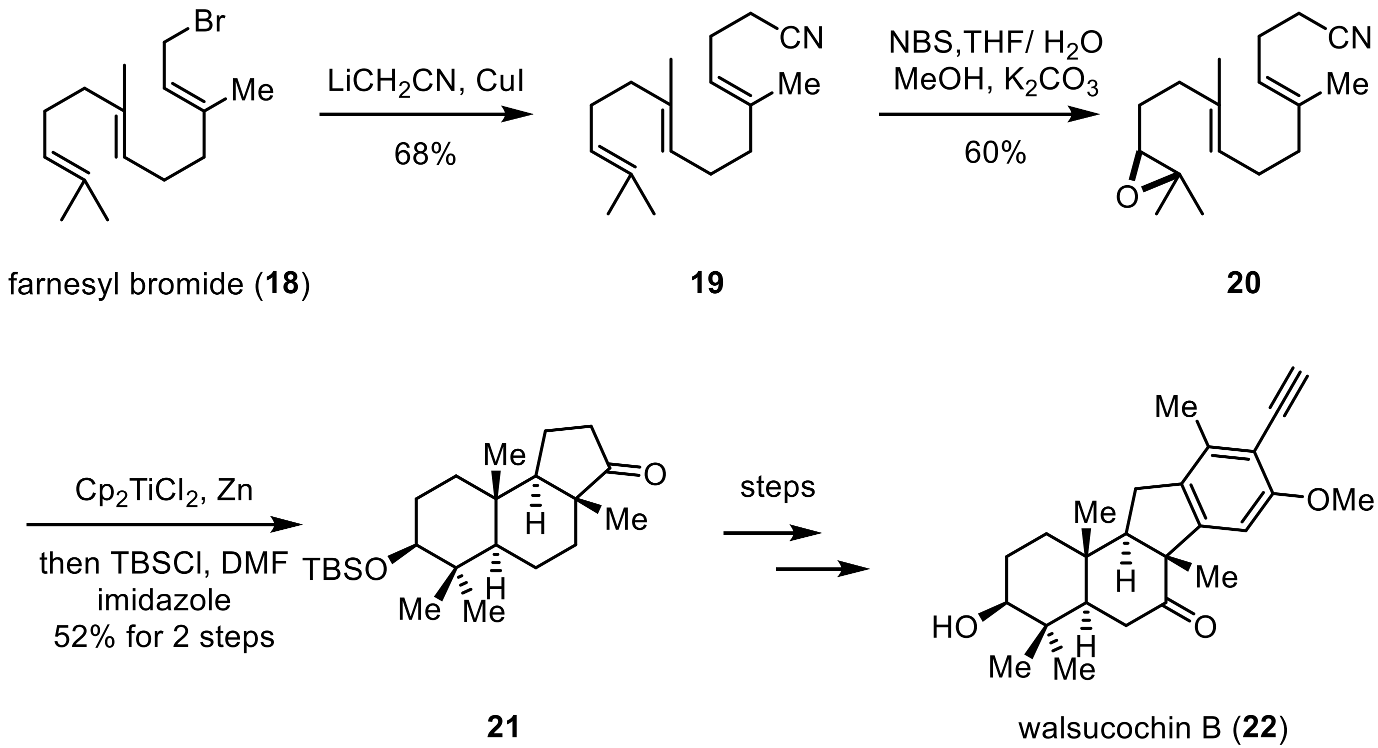
Y. Sun, P. Chen, D. Zhang, M. Baunach, C. Hertweck, A. Li, *Angew. Chem. Int. Ed*. **2014**, *53*, 9012-9016

Applications in total synthesis



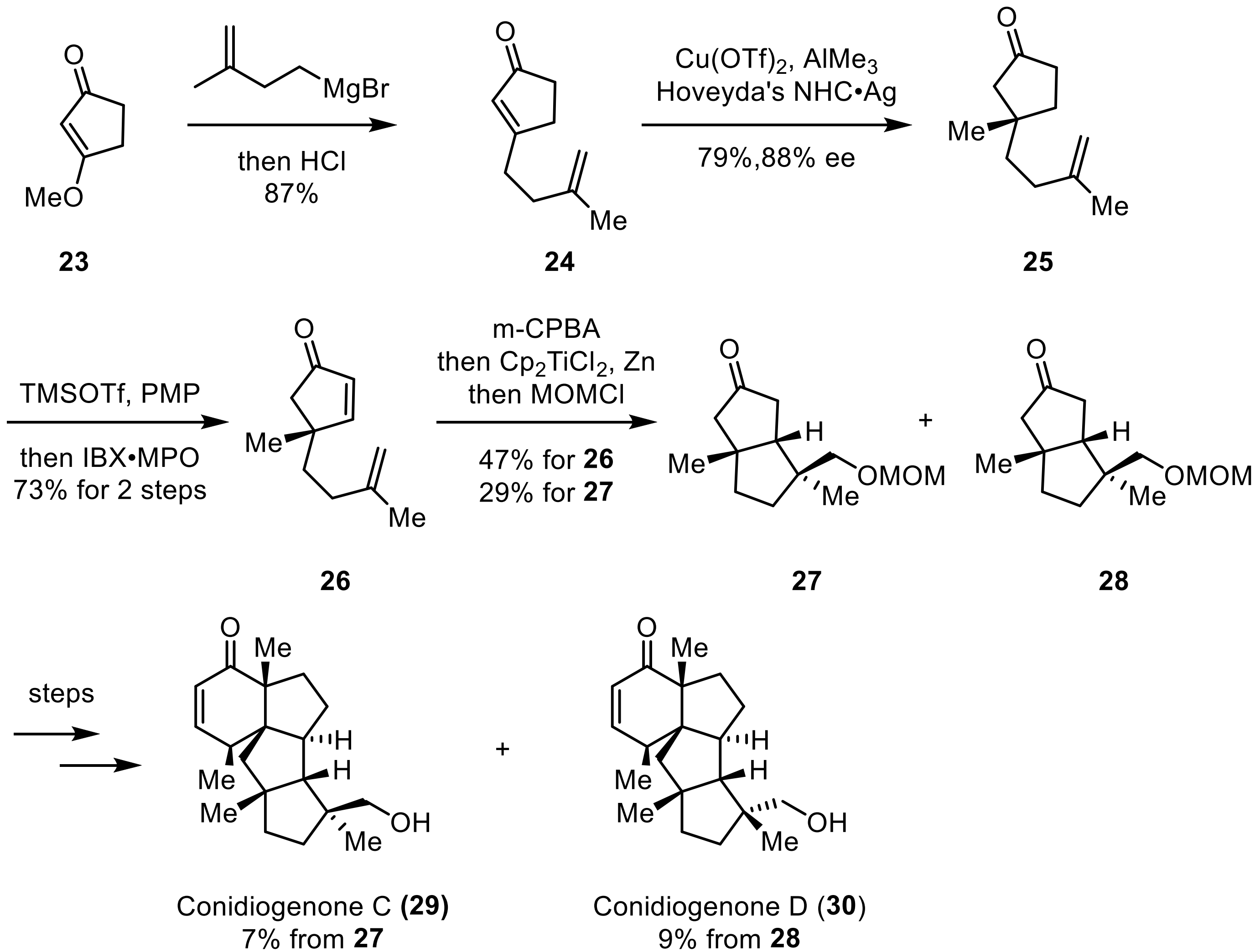
L. Shi, K. Meyer and M. F. Greaney, *Angew. Chem., Int. Ed.*, **2010**, *49*, 9250

Applications in total synthesis



X.-Y. Chen, D.-Y. Zhang, D. Xu, H. Zhou, and G. Xu, *Org. Lett*. **2020**, *22*, 6993

Applications in total synthesis



P. Hu, H. M. Chi, K. C. DeBacker, X. Gong, J. H. Keim, I. T. Hsu, S. A. Snyder, *Nature*, **2019**, *569*, 703-707.