Taxane Chemistry

Konstantin Samarin

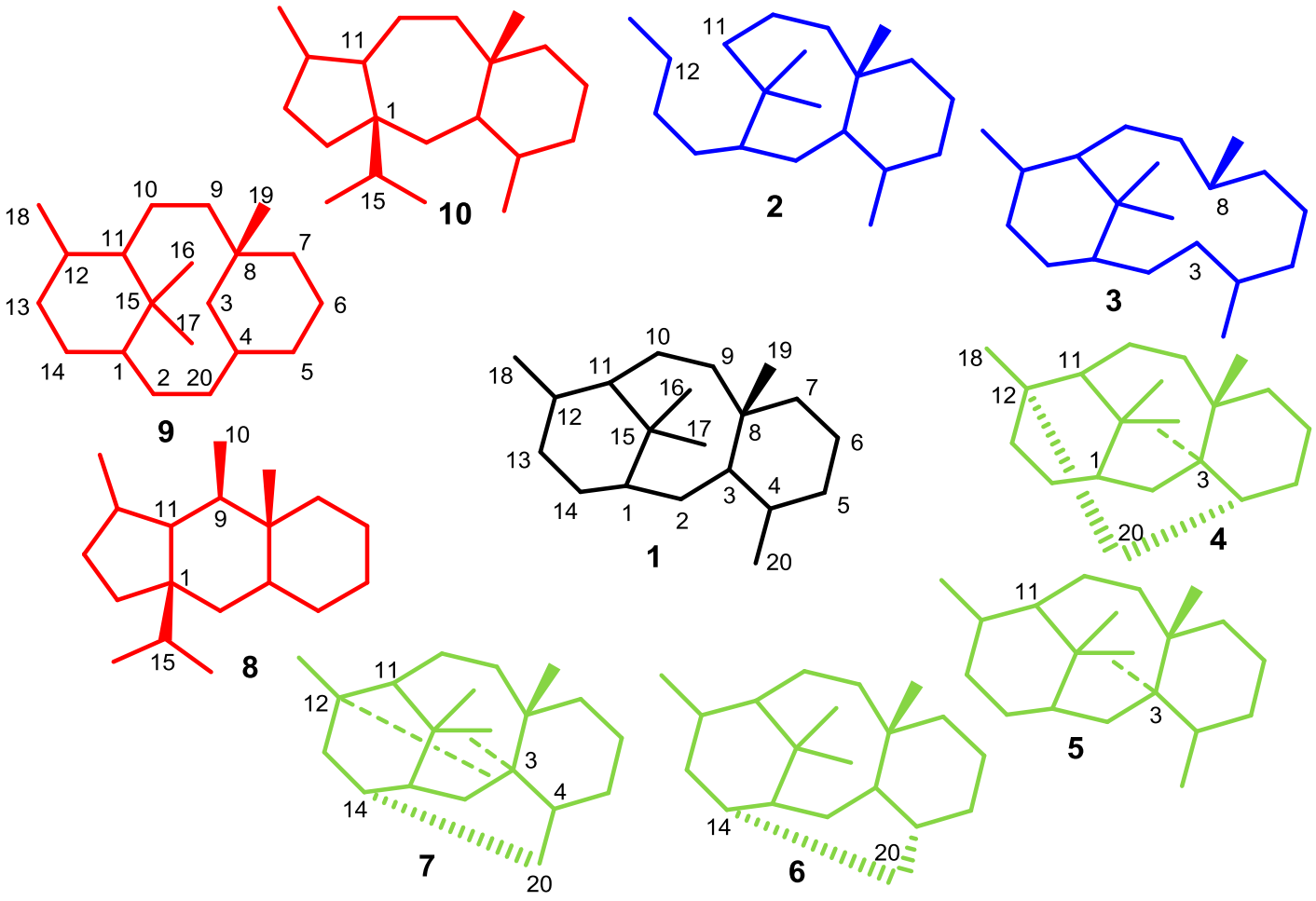
Gaich-Group Seminar

28.10.2014

Distribution of *Taxus* sp. in the world

[1] Wang Y.-F., Shi Q.-W., Dong M., Kiyota H., Gu Y.-C., Cong B. *Chem. Rev*. **2011**, *111*, 7652 – 7709

Taxane skeleton variations



[1] Wang Y.-F., Shi Q.-W., Dong M., Kiyota H., Gu Y.-C., Cong B. *Chem. Rev*. **2011**, *111*, 7652 – 7709

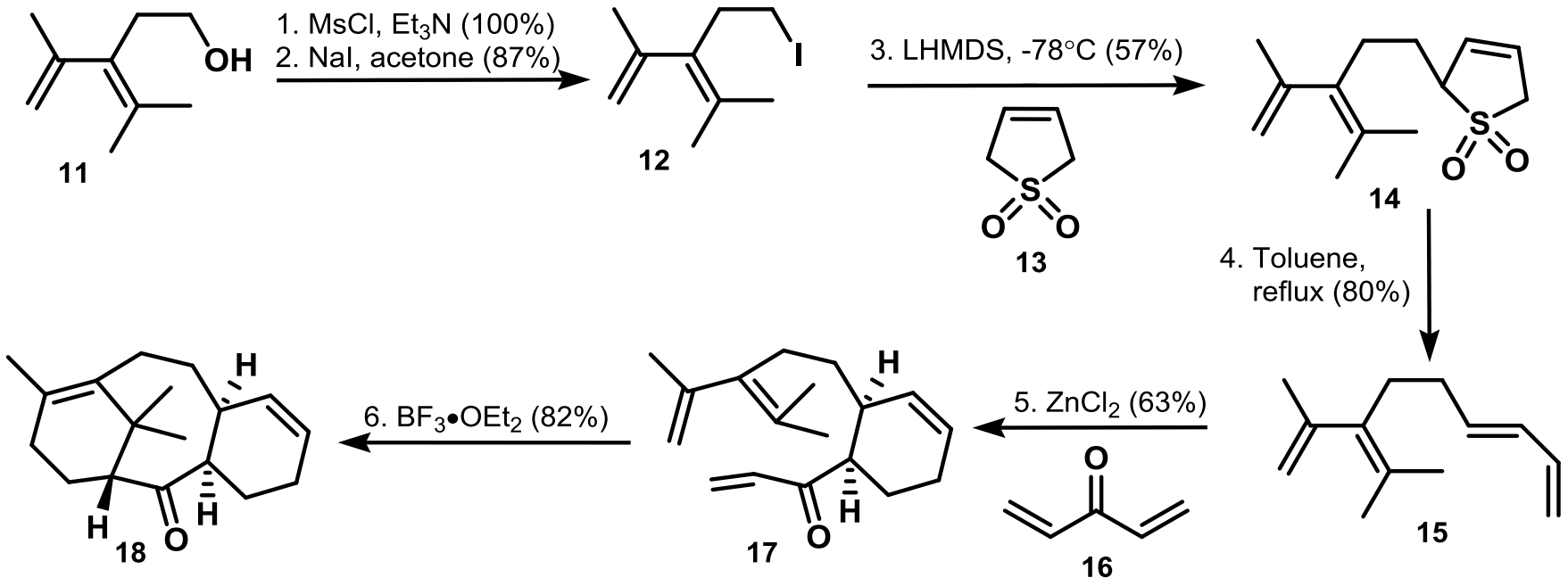
Overview

- More than 550 taxanes have been isolated to the end of 2009*.
- Total synthesis of *Taxol:*

- Holton R.A. (1994, 46 steps, linear)
- Nicolaou K.C. (1994, 40 steps, convergent, 3 parts)
- Danishefsky S.J. (1996, formal, 53 steps, convergent, 2 parts)
- Wender P.A. (1997, formal, 40 steps, linear)
- Kuwajima I. (1988, 66 steps, convergent, 3 parts)
- Mukaiyama T. (1999, 61 steps, linear)

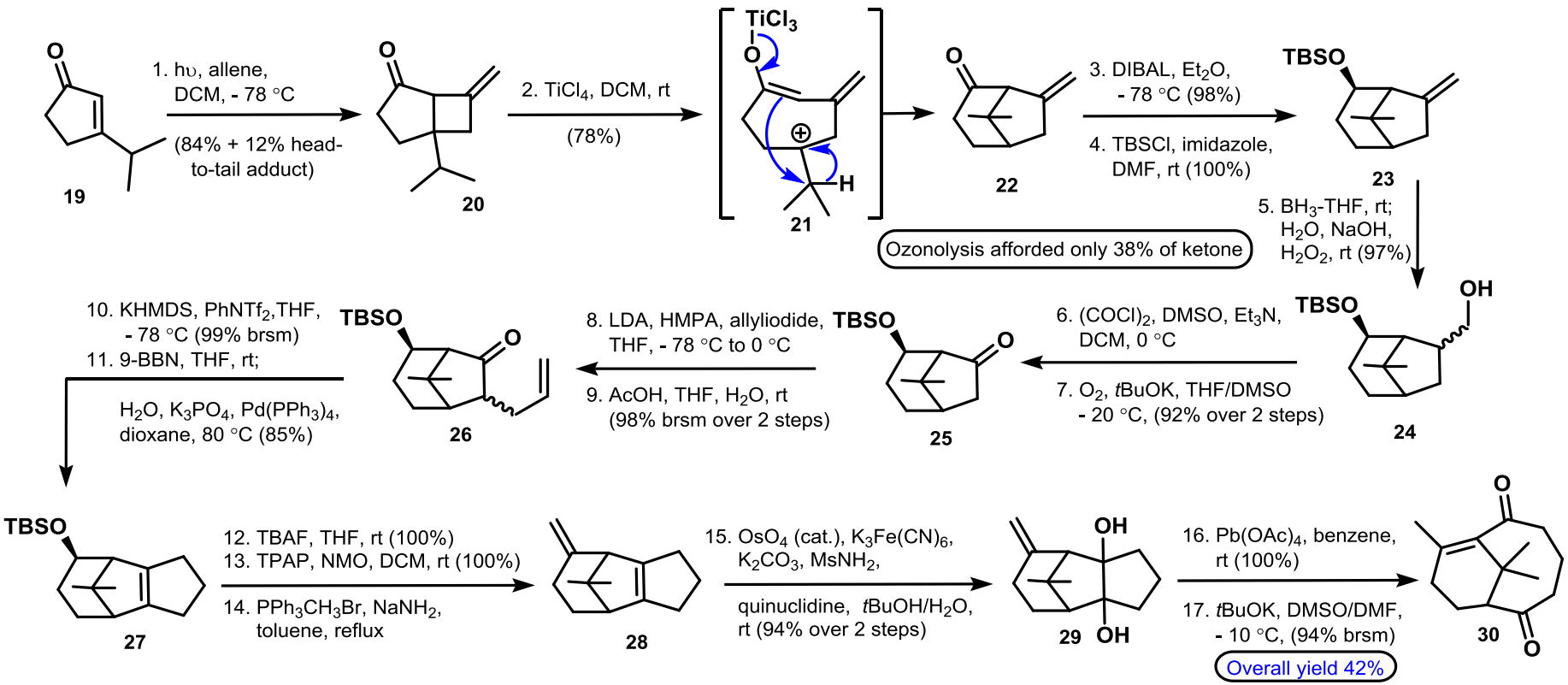
[1] Wang Y.-F., Shi Q.-W., Dong M., Kiyota H., Gu Y.-C., Cong B. *Chem. Rev*. **2011**, *111*, 7652 – 7709

Double Diels-Alder approach



[2] Winkler J. D., Kim H. S., Kim, S. *Tetrahedron Lett*. **1995**, *36*, 687 – 690

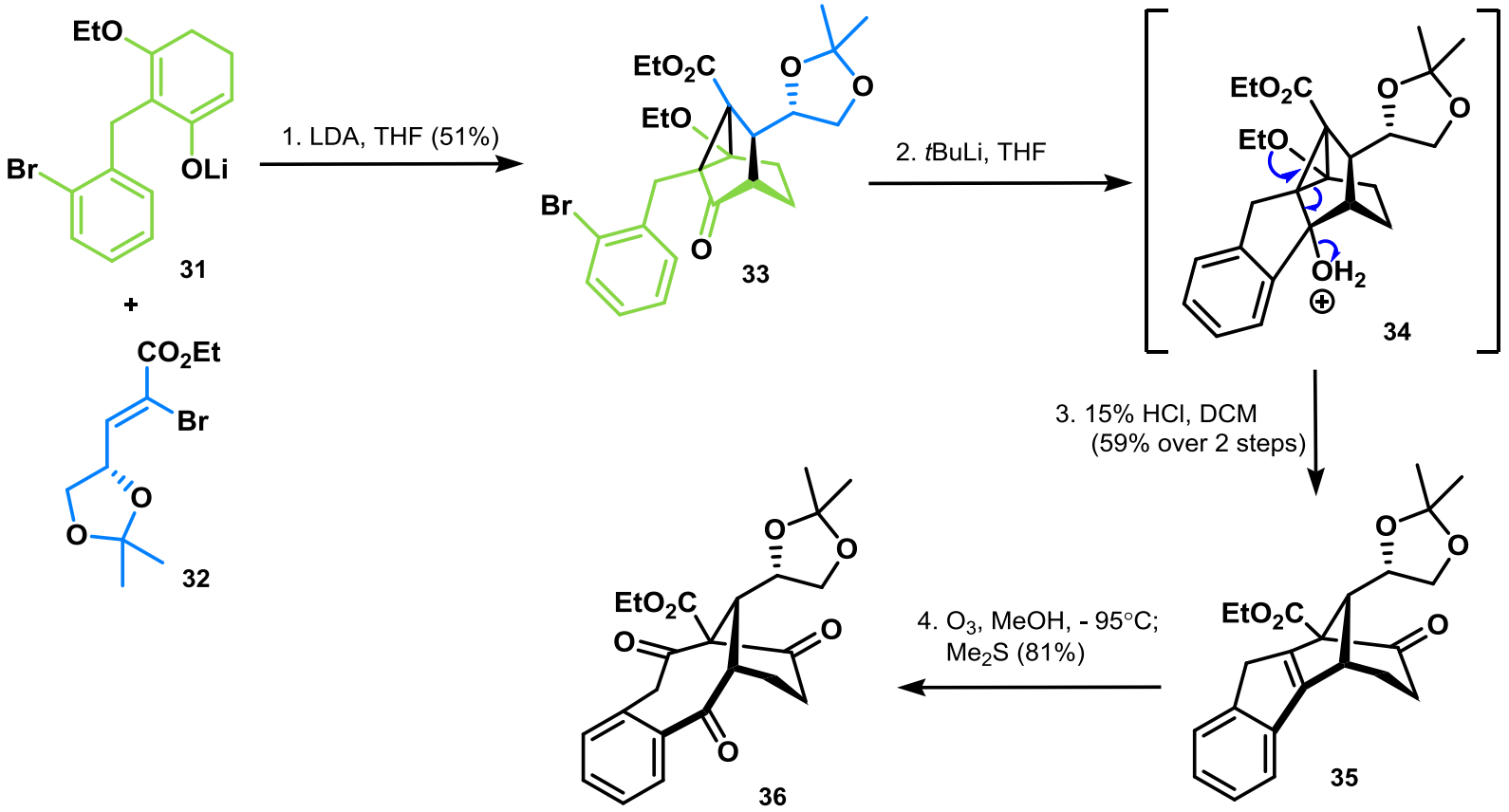
[2+2]/carbocationic rearrangement approach



[3] Shimada Y., Nakamura M., Suzuki T., Matsui J., Tatsumi R., Tsutsumi K., Morimoto T., Kurosawa H., Kakiuchi K. *Tetrahedron Lett*. **2003**, *44*, 1401 – 1403

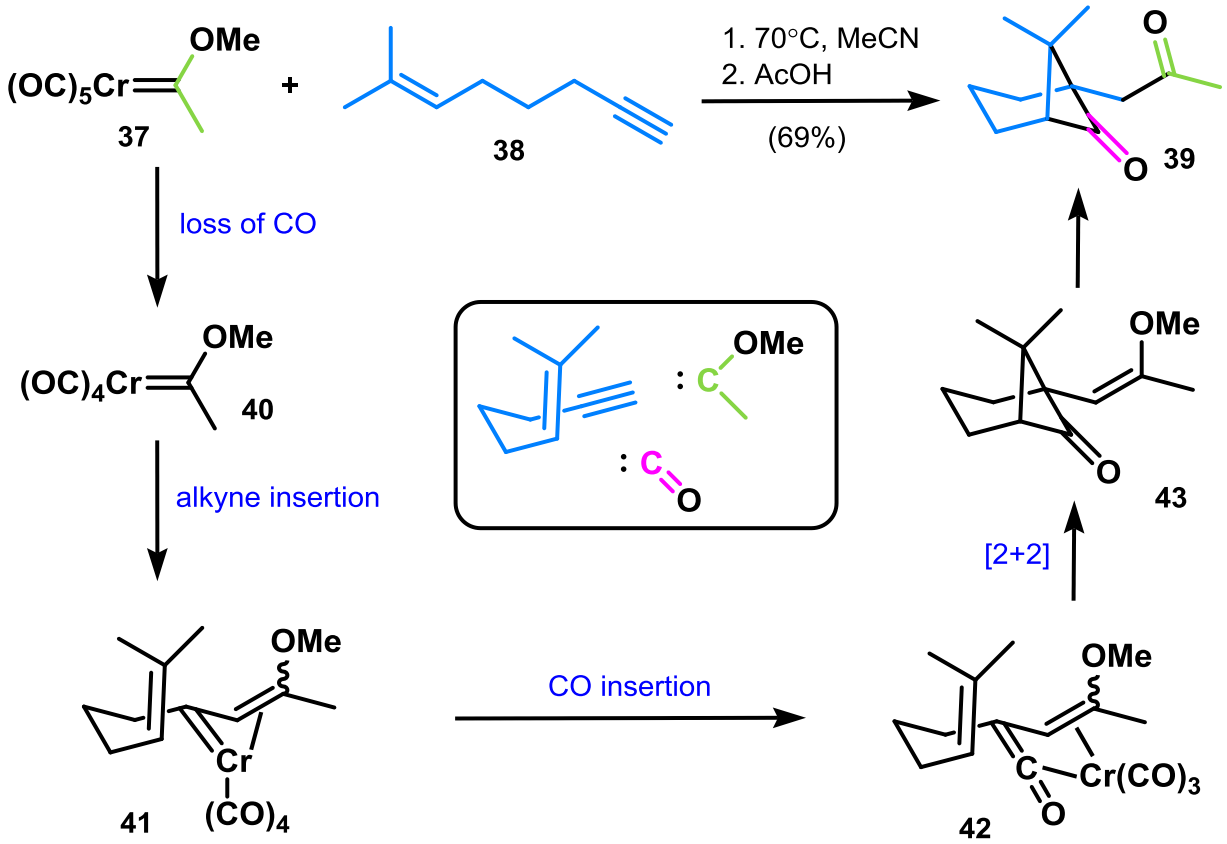
[4] Enomoto T., Morimoto T., Ueno M., Matsukubo T., Shimada Y., Tsutsumi K., Shirai R., Kakiuchi K. *Tetrahedron*. **2008**, *64*, 4051 – 4059 (installation of C ring)

Double Michael addition/ Sn2 substitution - domino process



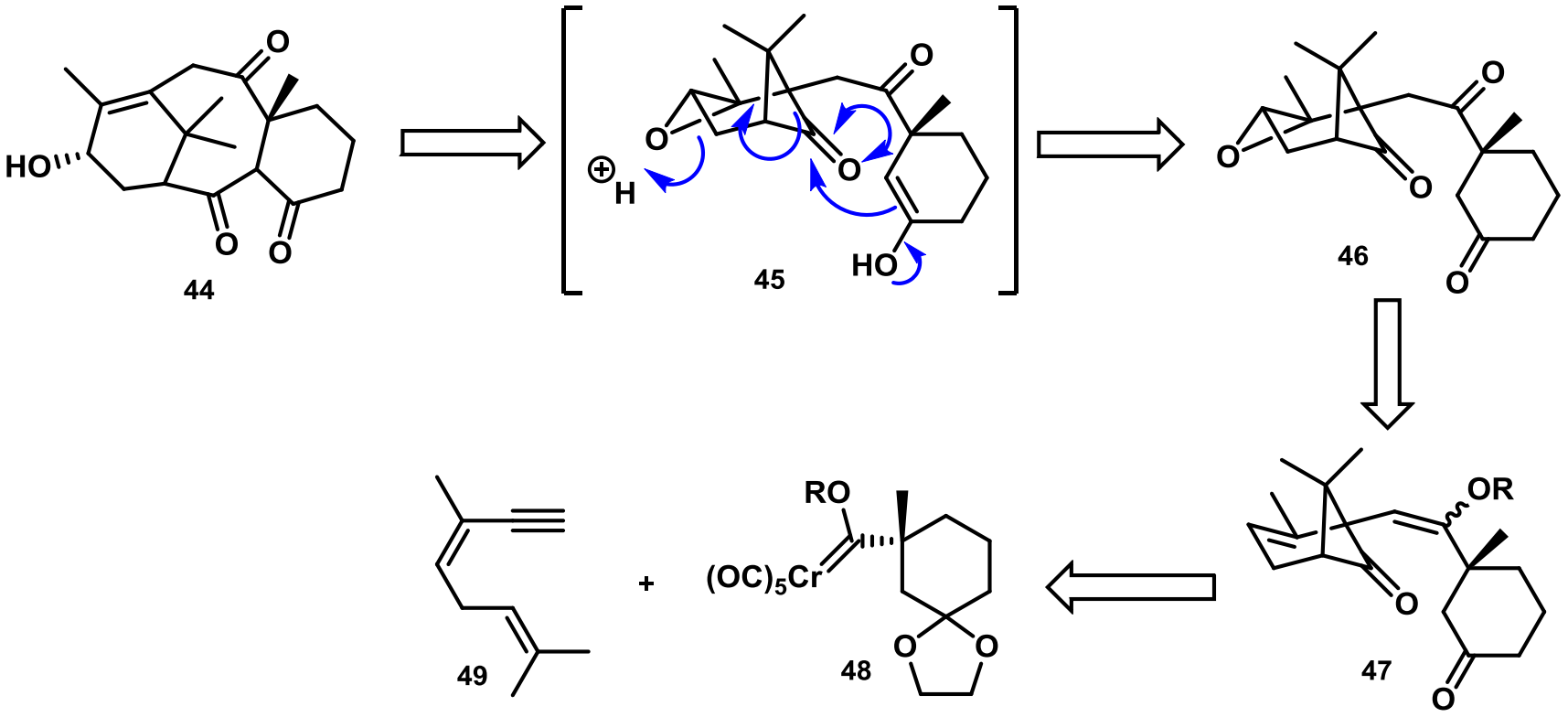
[5] Gutke H.-J., Braun N. A., Spitzner D. *Tetrahedron*. **2004**, *60*, 8137 – 8141

Fischer Carbene mediated alkyne insertion/carbonylation/[2+2] – domino process



[6] Kim O.K., Wulff W.D., Jiang W. *J. Org. Chem*. **1993**, *58*, 5571 – 5573

Fischer Carbene mediated alkyne insertion/carbonylation/[2+2] – domino process



[7] Jiang W., Fuertes M. J., Wulff W.D. *Tetrahedron*. **2000**, *56*, 2183 – 2194

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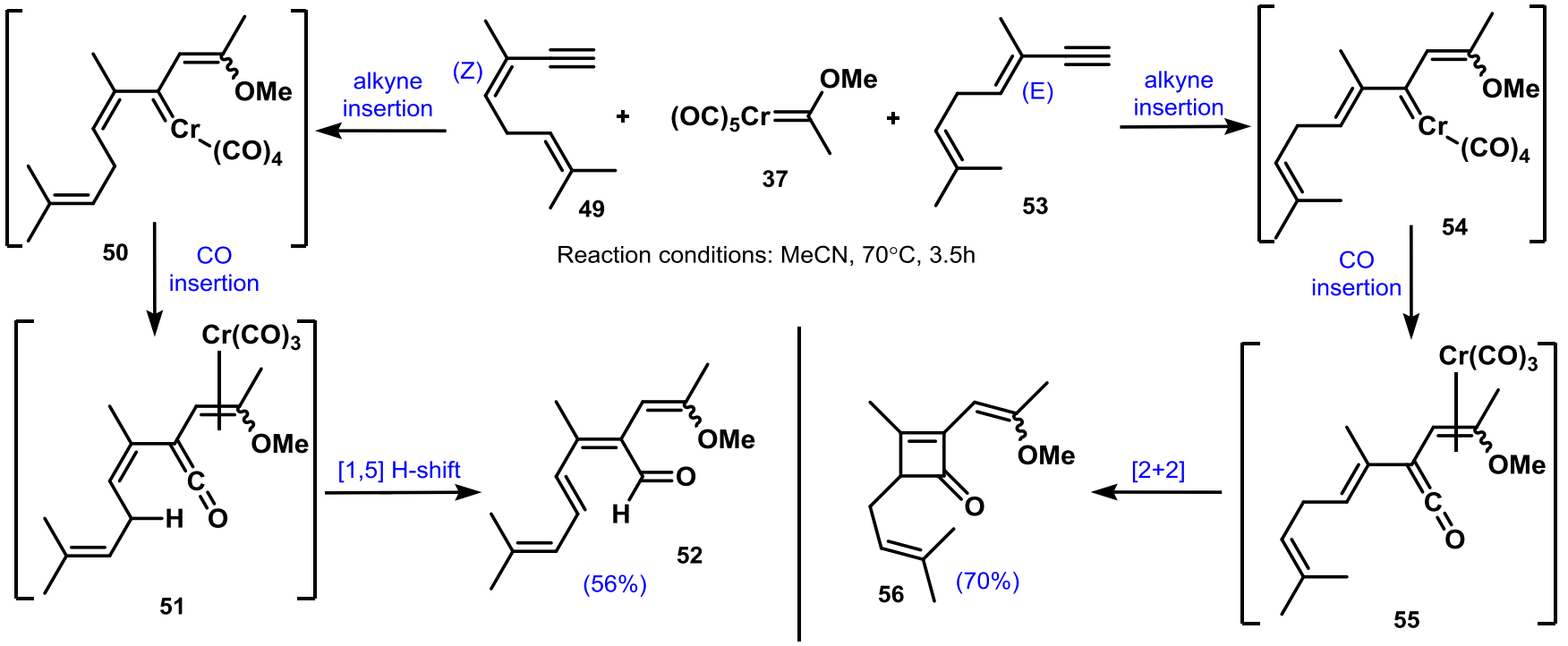

[7] Jiang W., Fuertes M. J., Wulff W.D. *Tetrahedron*. **2000**, *56*, 2183 – 2194

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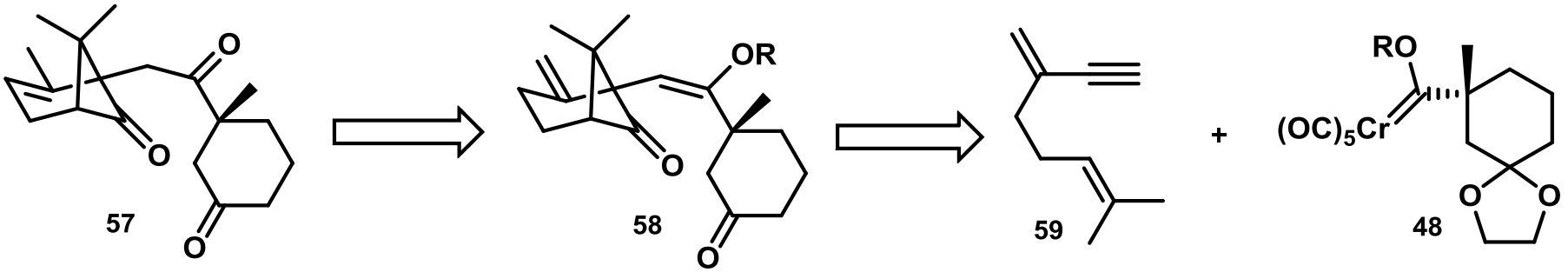
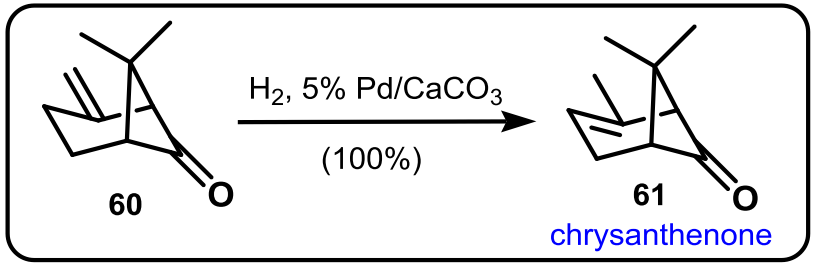
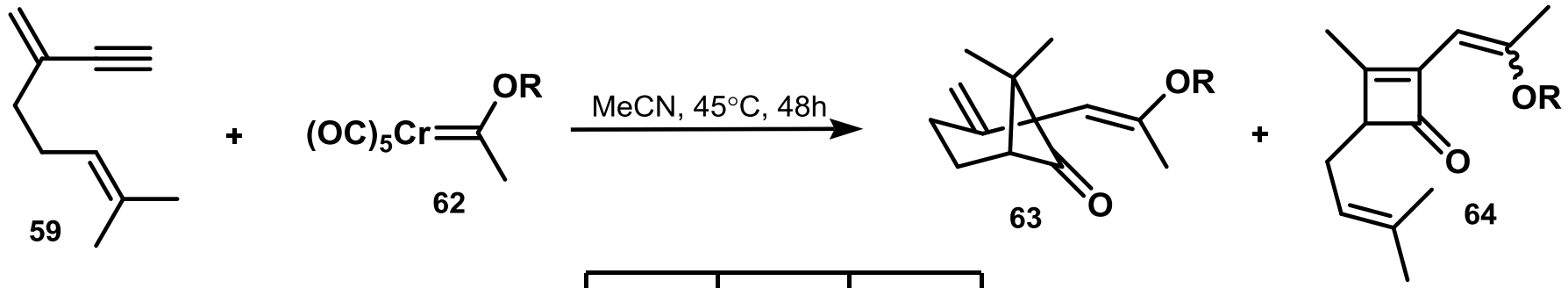




[7] Jiang W., Fuertes M. J., Wulff W.D. *Tetrahedron*. **2000**, *56*, 2183 – 2194
[8] Kulkarni Y. S., Snider B. B. *J. Org. Chem*. **1985**, *50*, 2809 – 2810

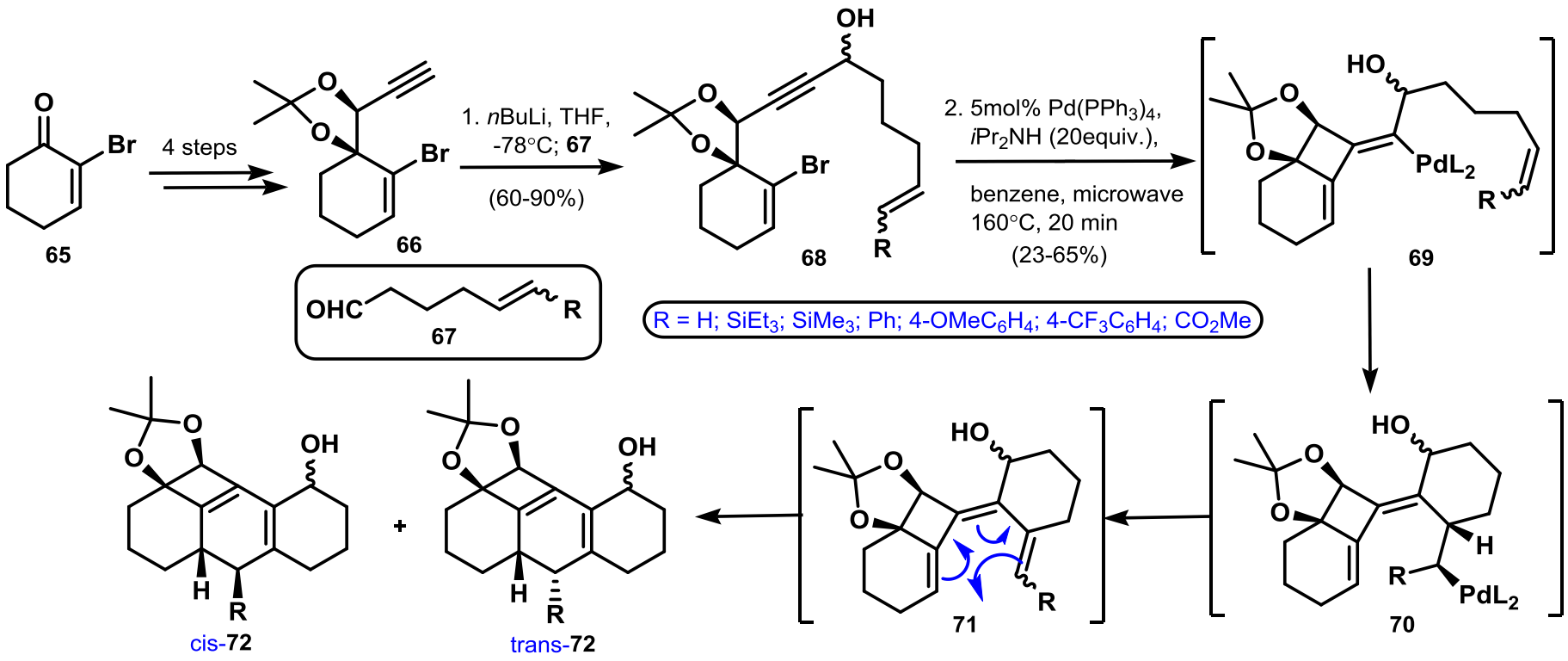
Fischer Carbene mediated alkyne insertion/carbonylation/[2+2] – domino process



R	Yield (%)	Ratio
MOM	84	2.8
Ph(OMe)	82	1.4
PhH	87	4.3
PhBr	78	7.3
$PhCF_3$	76	7.0

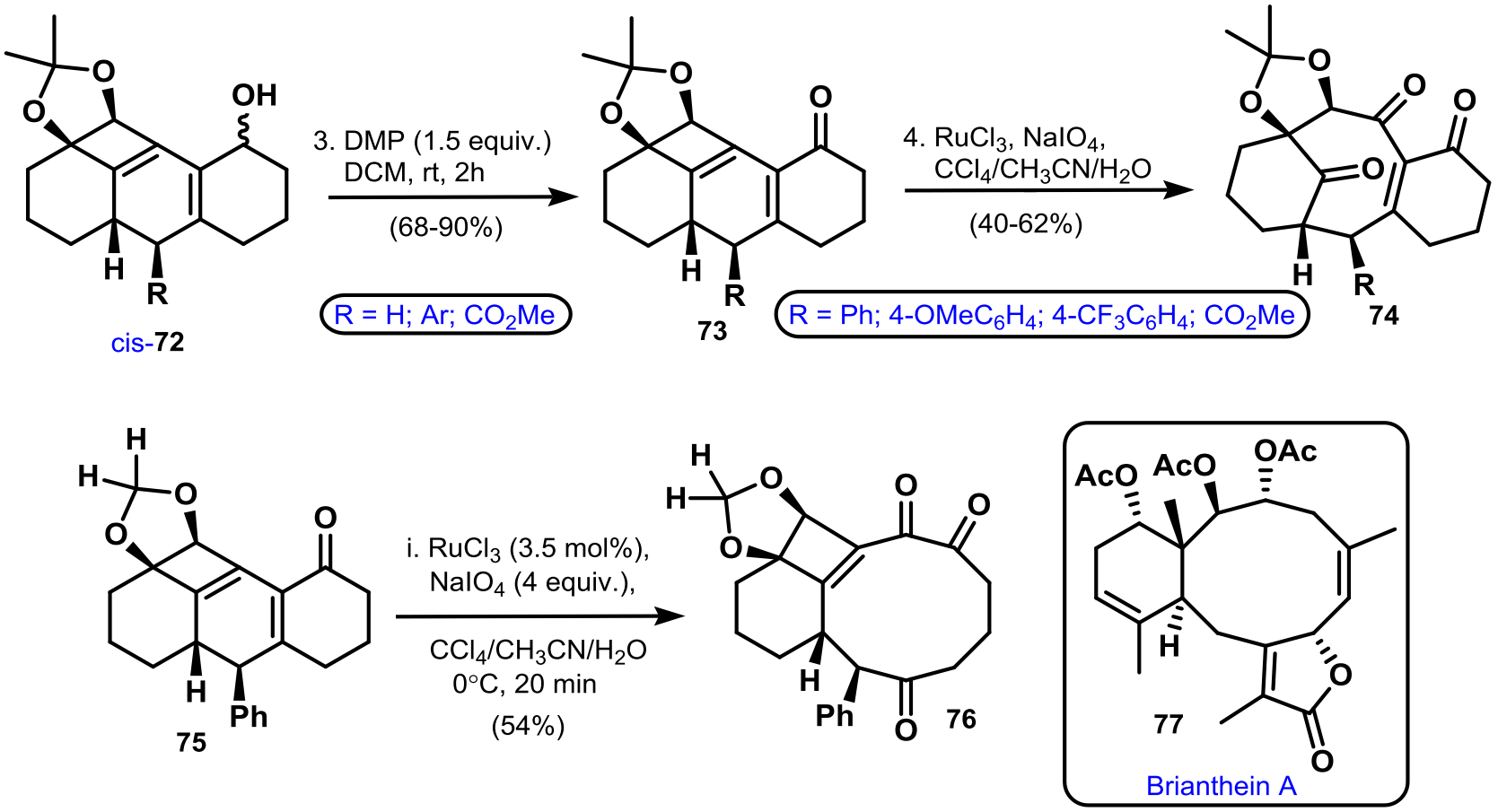
[7] Jiang W., Fuertes M. J., Wulff W.D. *Tetrahedron*. **2000**, *56*, 2183 – 2194

Palladium-mediated cyclocarbo-palladation/ intramolecular Heck/6π-electrocyclization domino process



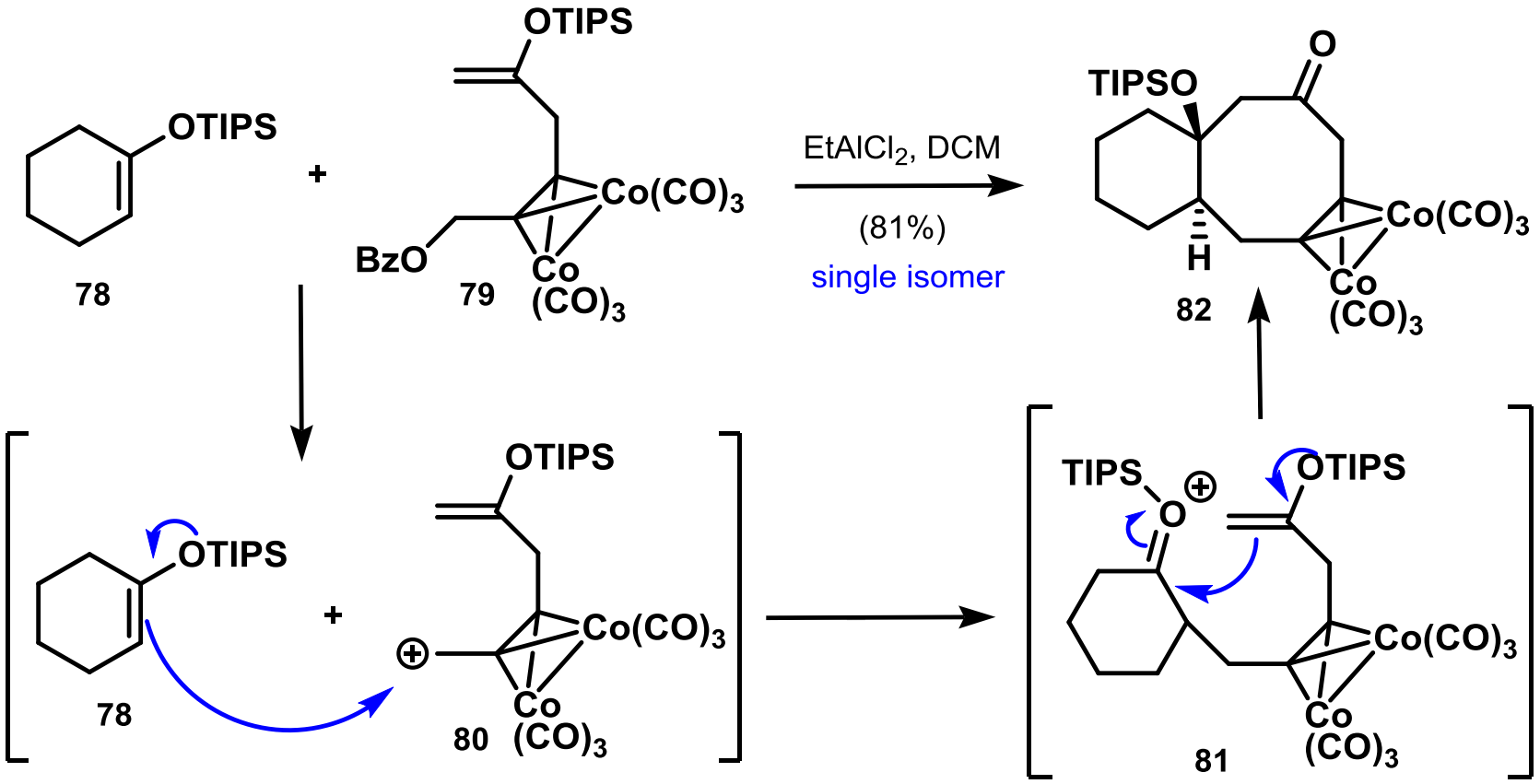
[9] Petrignet J., Boudhar A., Blond G., Suffert J. *Angew. Chem. Int. Ed.*. **2011**, *50*, 3285 – 3289

Palladium-mediated domino process



[9] Petrignet J., Boudhar A., Blond G., Suffert J. *Angew. Chem. Int. Ed.*. **2011**, *50*, 3285 – 3289
[10] Aoki S., Okano M., Matsui K., Itoh T., Satari R., Akiyama S.-I., Kobayashi M. *Tetrahedron*, **2001**, *57*, 8951 – 8957 (Brianthein A)

Formal intermolecular [6+2]-cycloaddition



[11] Mitachi K., Shimizu T., Miyashita M., Tanino K. *Tetrahedron Lett*. **2010**, *51*, 3983 – 3986

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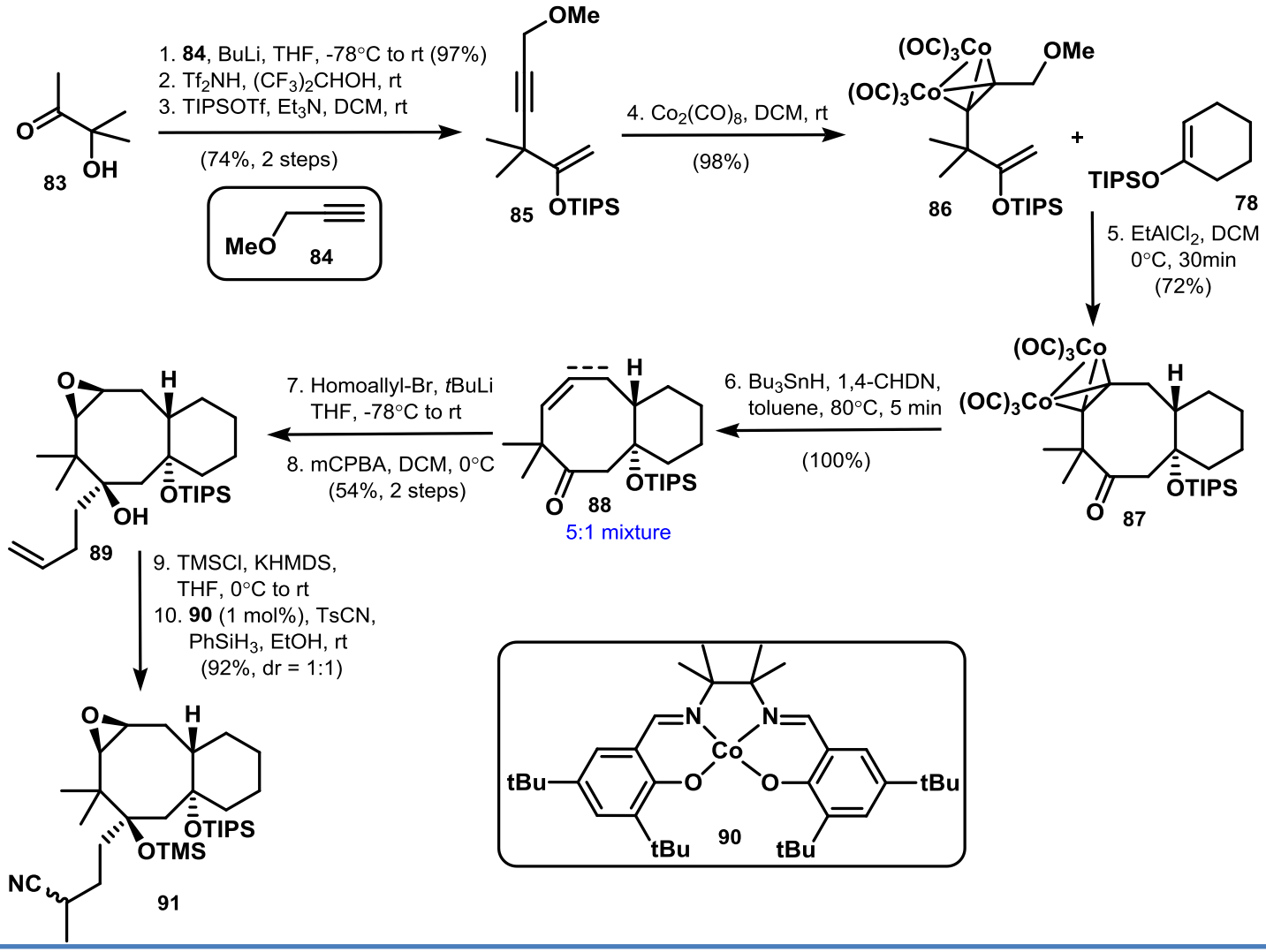

[12] Hanada R., Mitachi K., Tanino K. *Tetrahedron Lett.*, **2014**, *55*, 1097 – 1099

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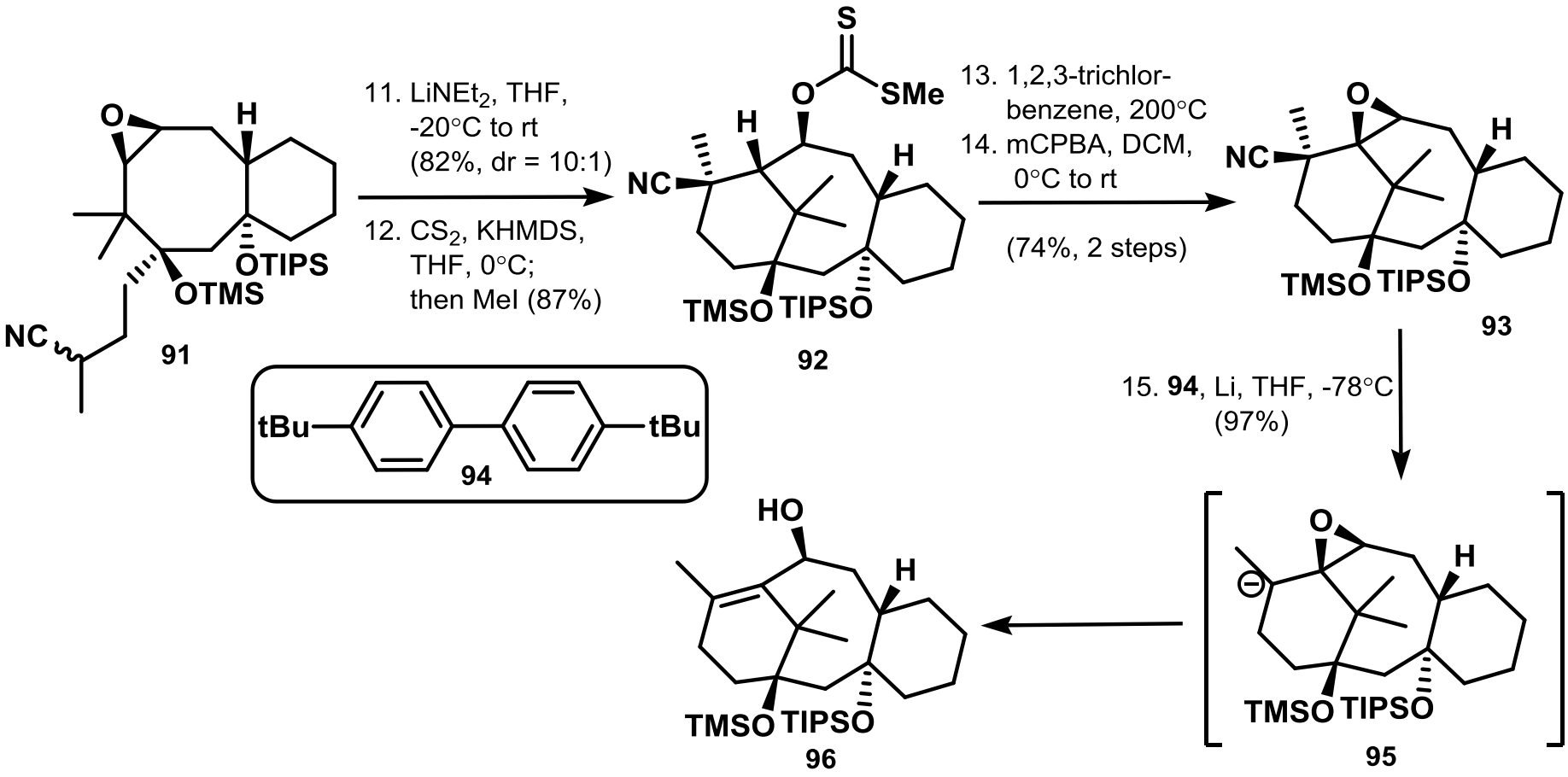
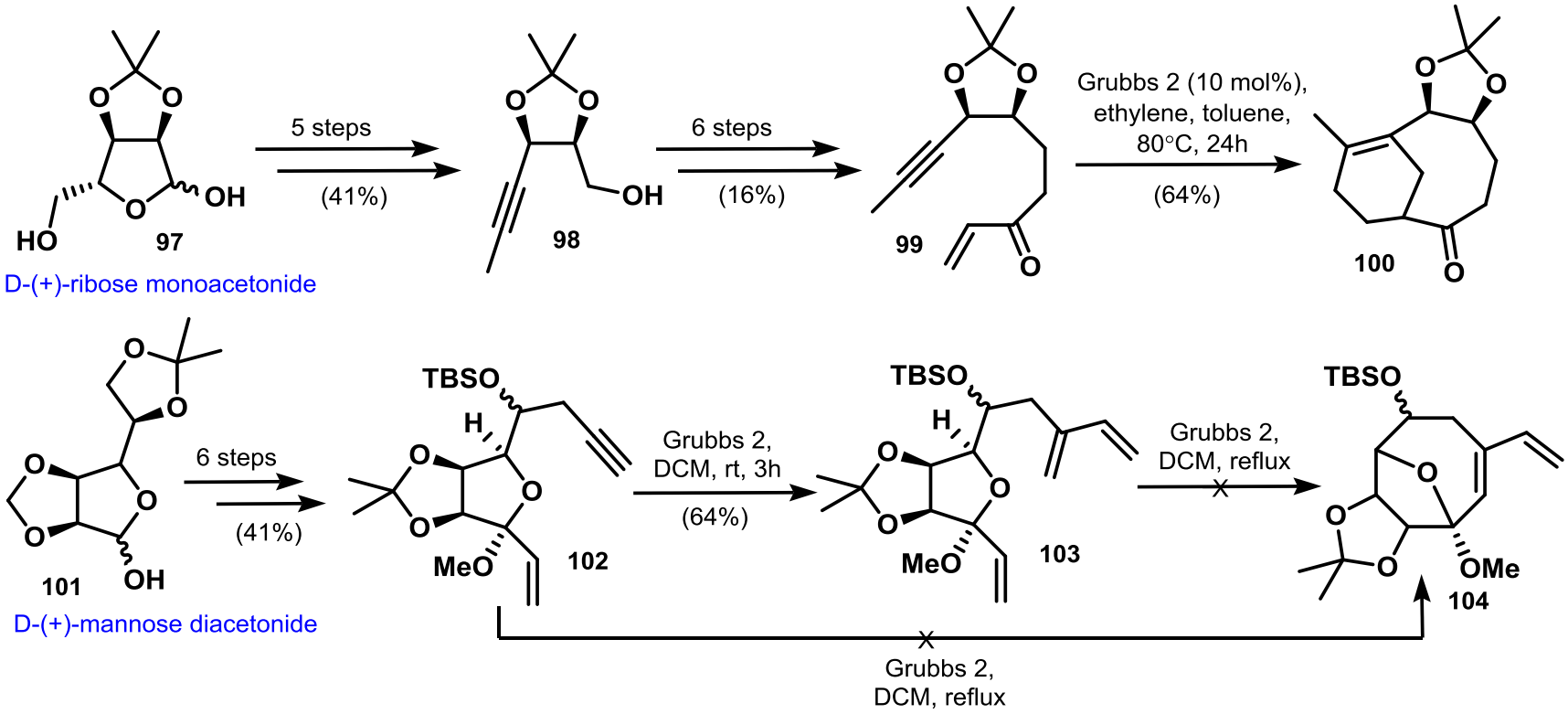


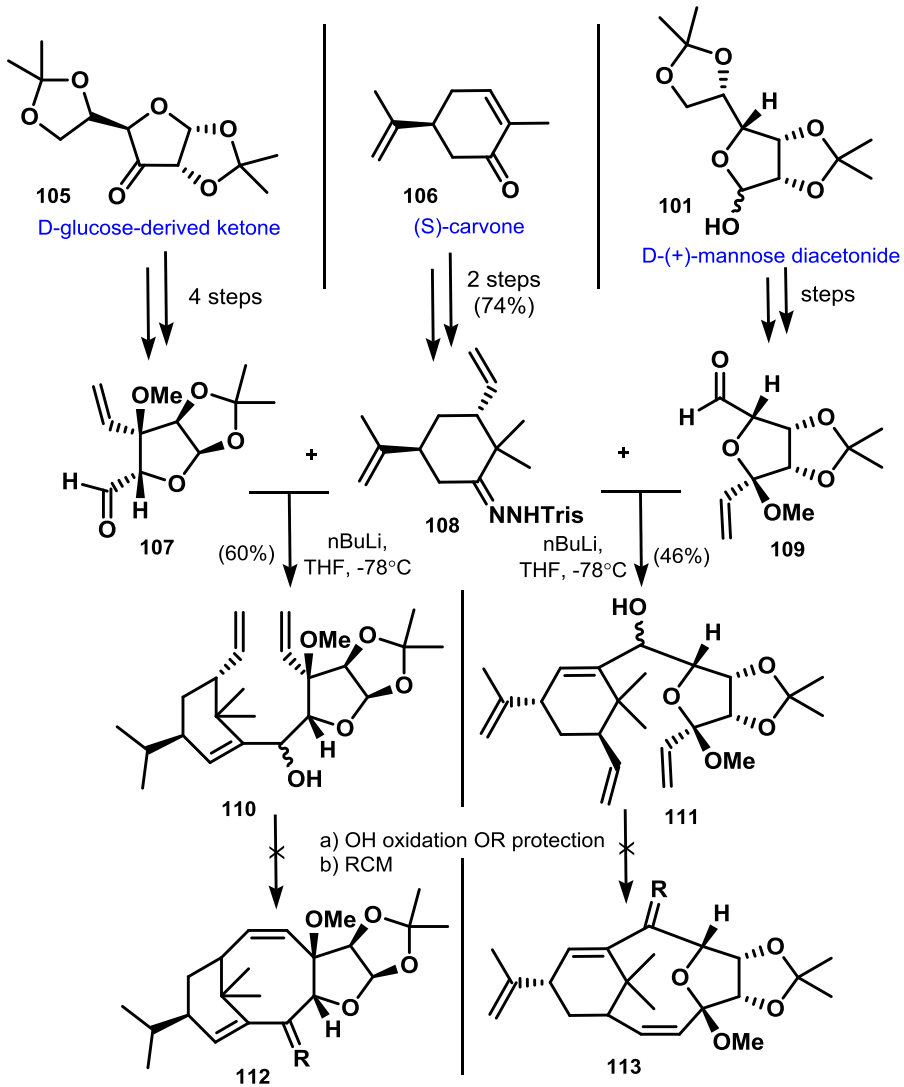
[12] Hanada R., Mitachi K., Tanino K. *Tetrahedron Lett*., **2014**, *55*, 1097 – 1099

Kaliappan metathesis approach



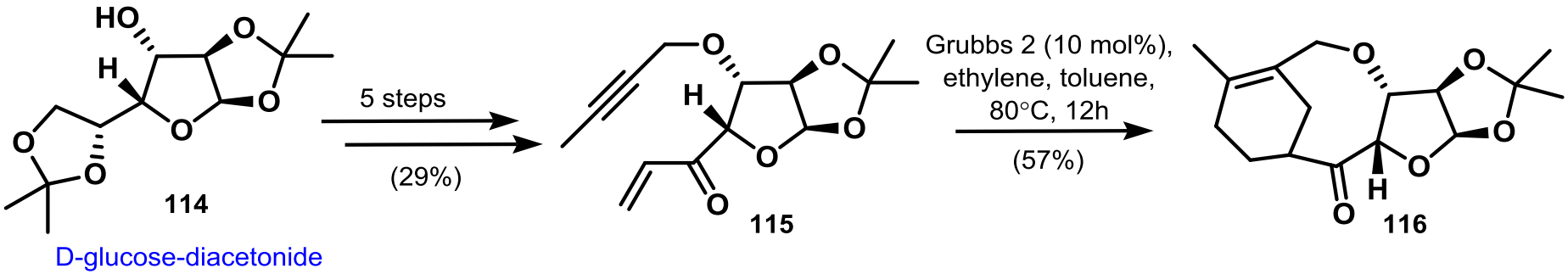
[13] Kaliappan K.P., Ravikumar V., Pujari S. *J. Chem. Sci*. **2008**, *120*, 205 – 216

Kaliappan metathesis approach



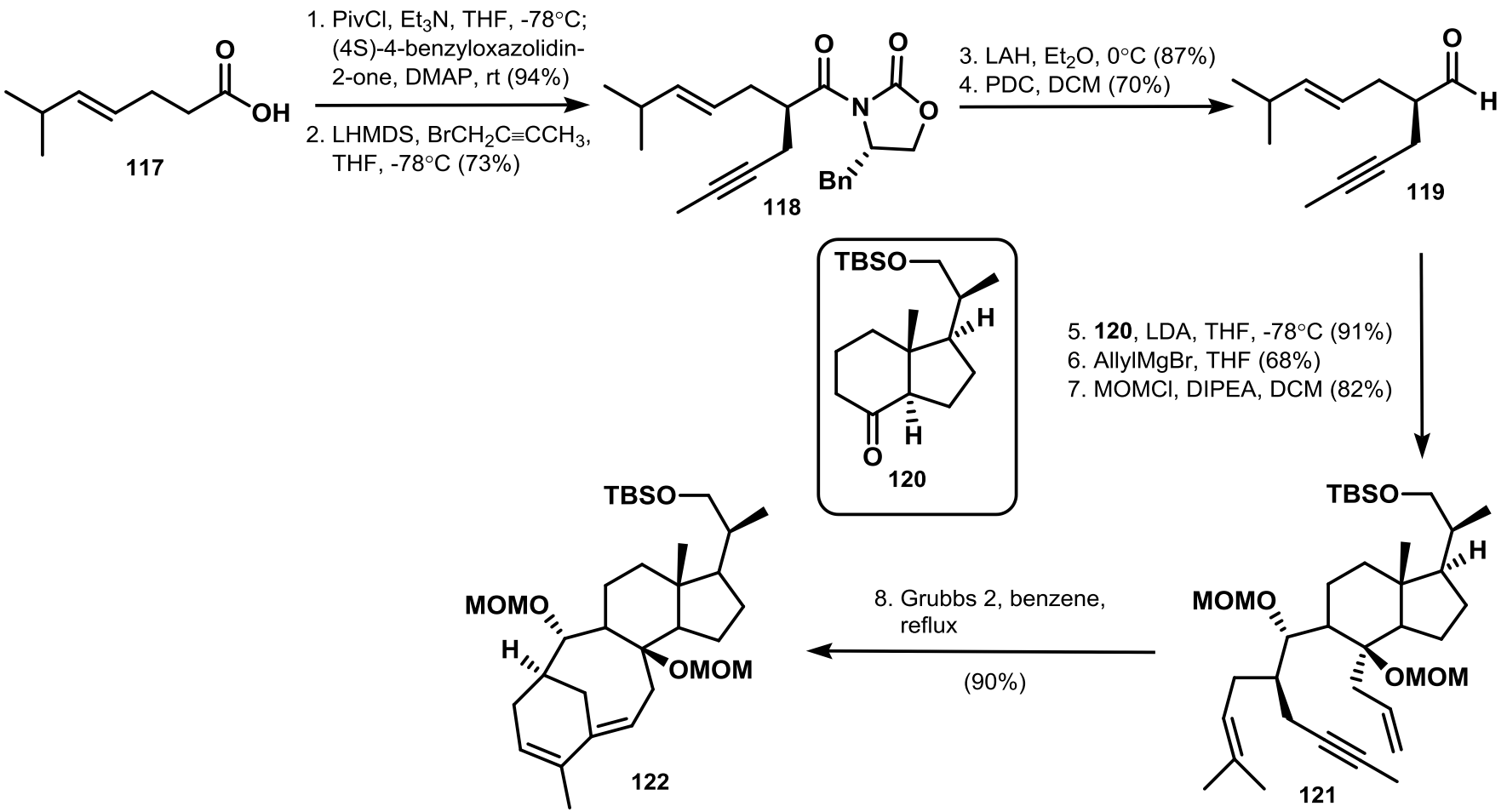
[14] Nandurdikar R.S., Subrahmanyam A.V., Kaliappan K.P. Eur. *J. Org. Chem*. **2010**, 2788 – 2799

Kaliappan metathesis approach



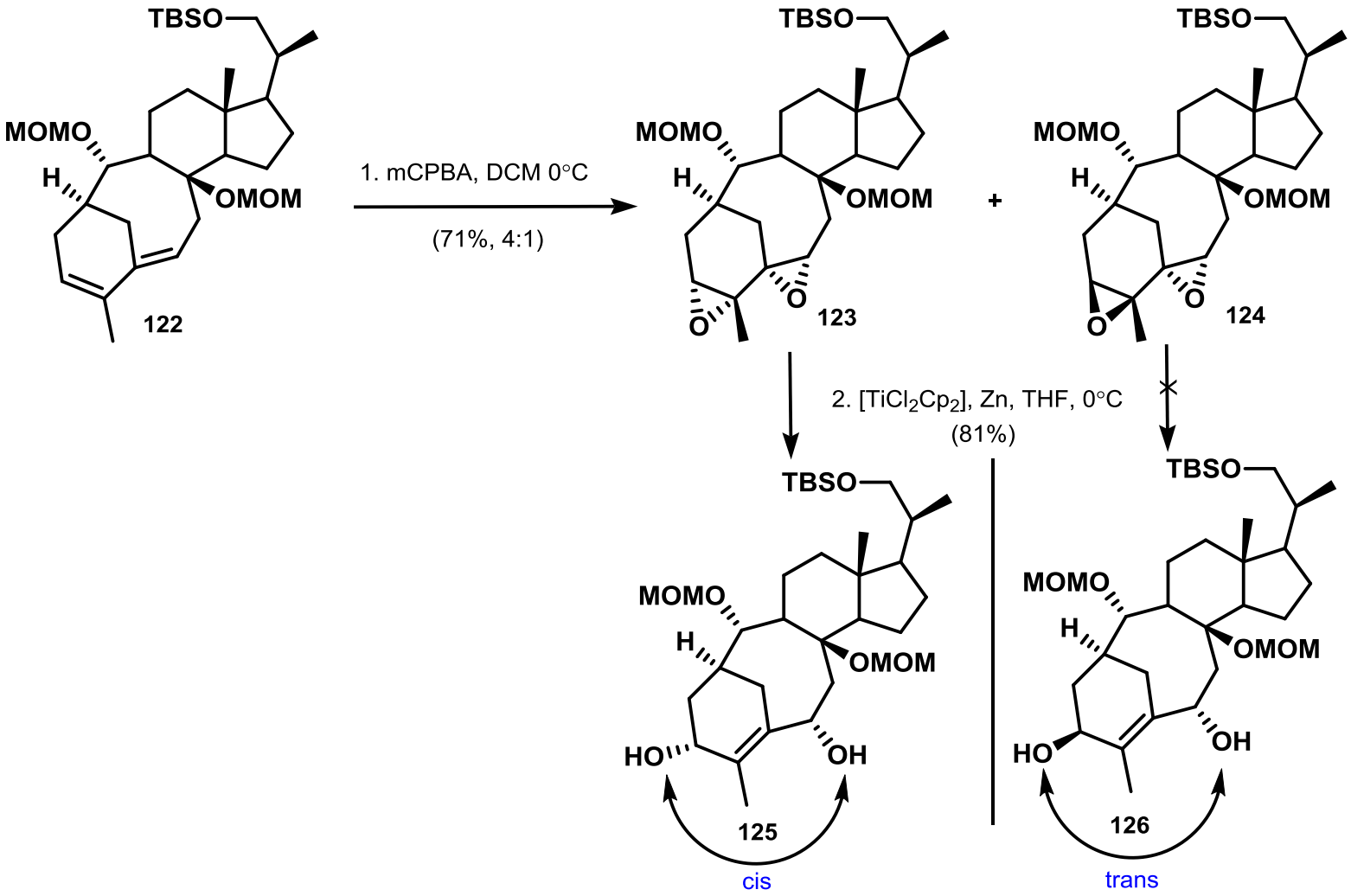
[14] Nandurdikar R.S., Subrahmanyam A.V., Kaliappan K.P. Eur. *J. Org. Chem*. **2010**, 2788 – 2799

Grantja metathesis approach



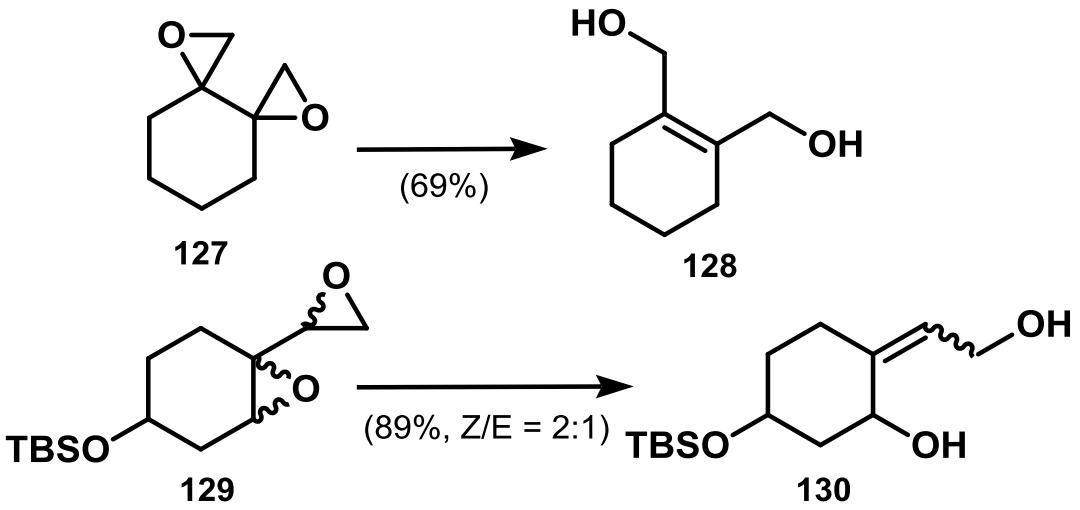
[15] Aldegunda M.J., Garcia-Fandino R., Castedo L., Granja J.R. *Chem. Eur. J.* **2007**, *13*, 5135 – 5150

Grantja metathesis approach



[16] Aldegunda M.J., Castedo L., Granja J.R. *Chem. Eur. J*. **2009**, *15*, 4785 – 4787

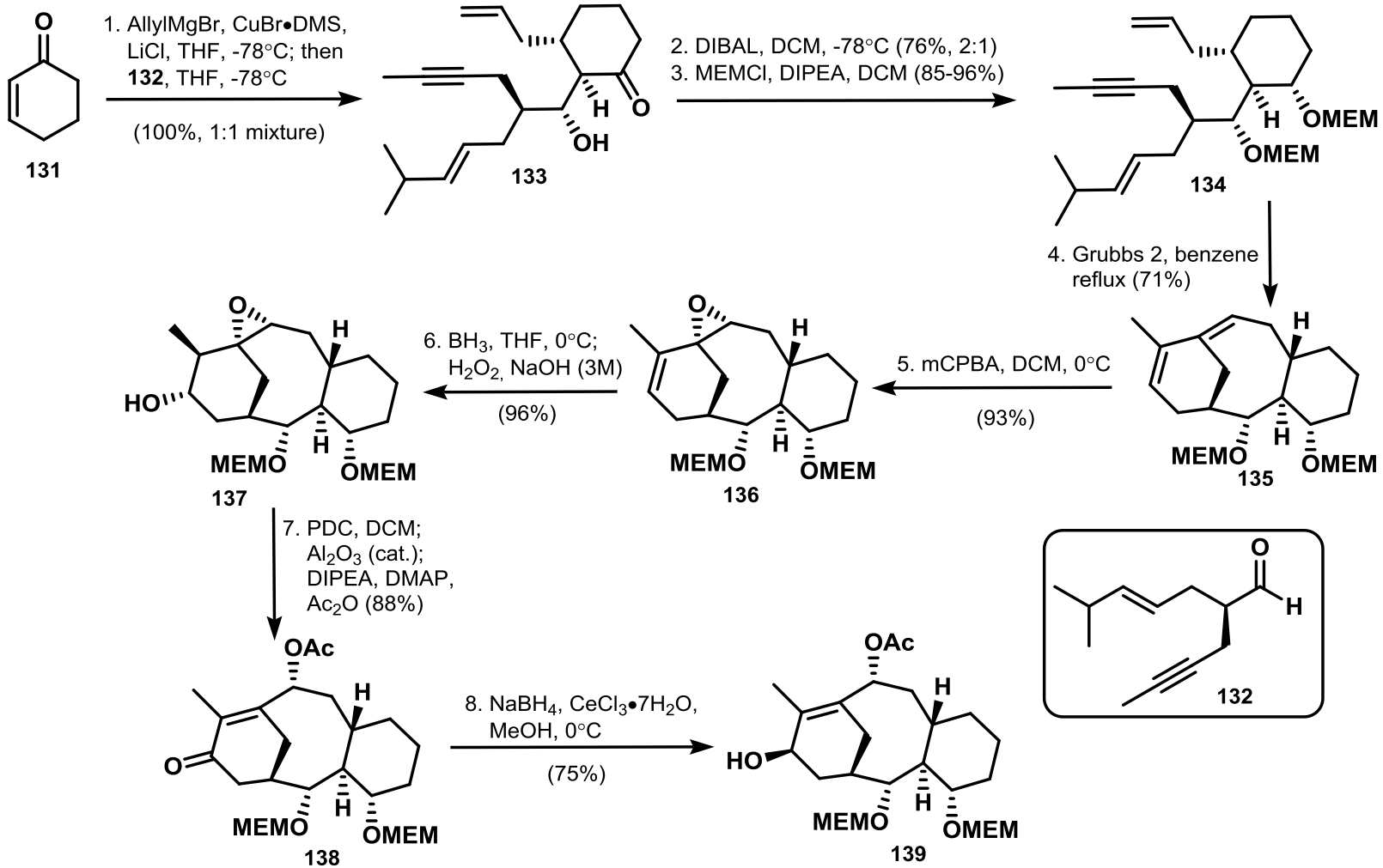
Construction of the alk-2-ene-1,4-diol system from dienes



Reaction conditions: 0.05 M in THF, [{$TiClCp_2$}$_2$] (0.2 M in THF, 1 equiv.), 0°C

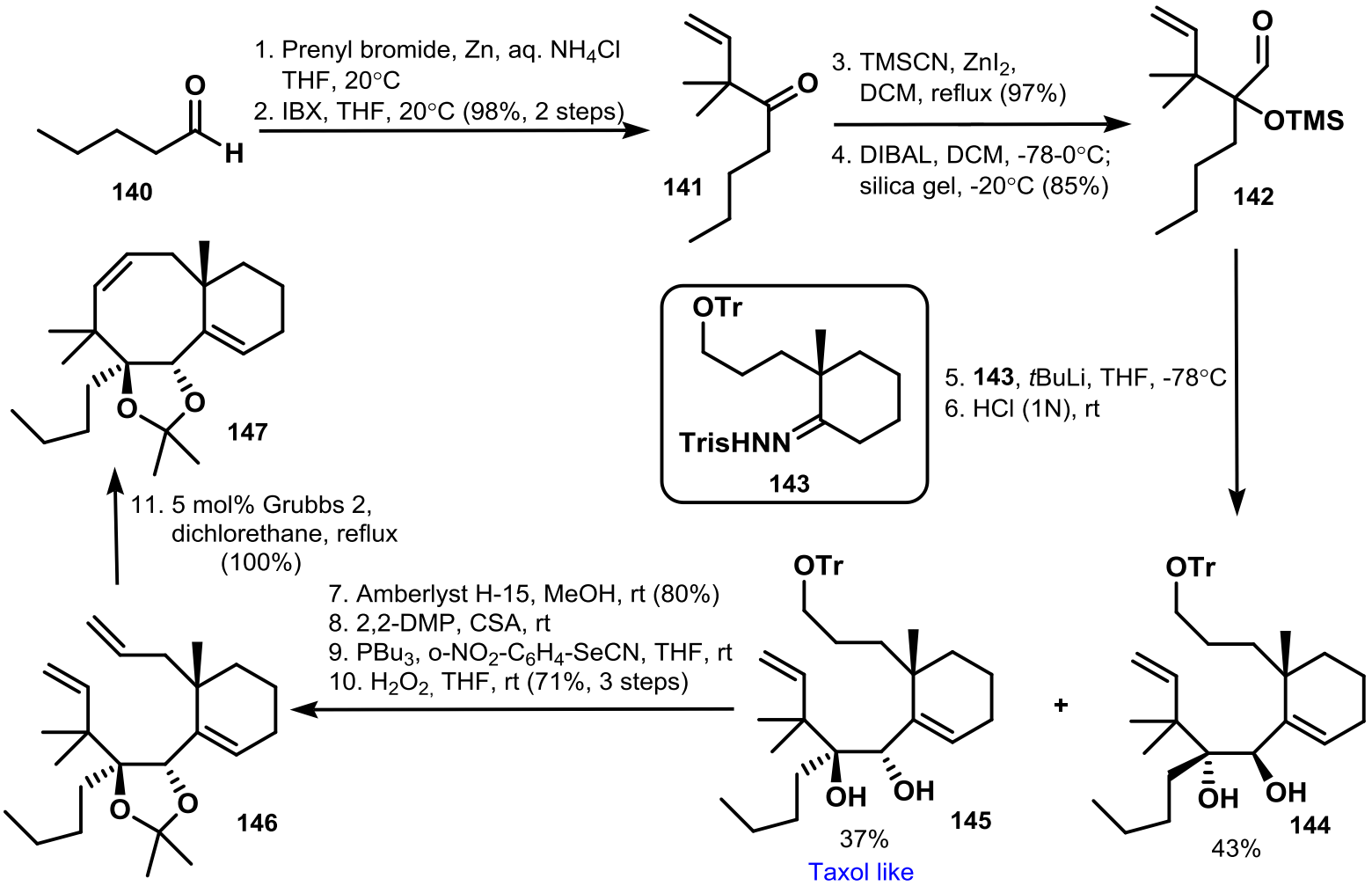
[16] Aldegunda M.J., Castedo L., Granja J.R. *Chem. Eur. J*. **2009**, *15*, 4785 – 4787

Grantja metathesis approach



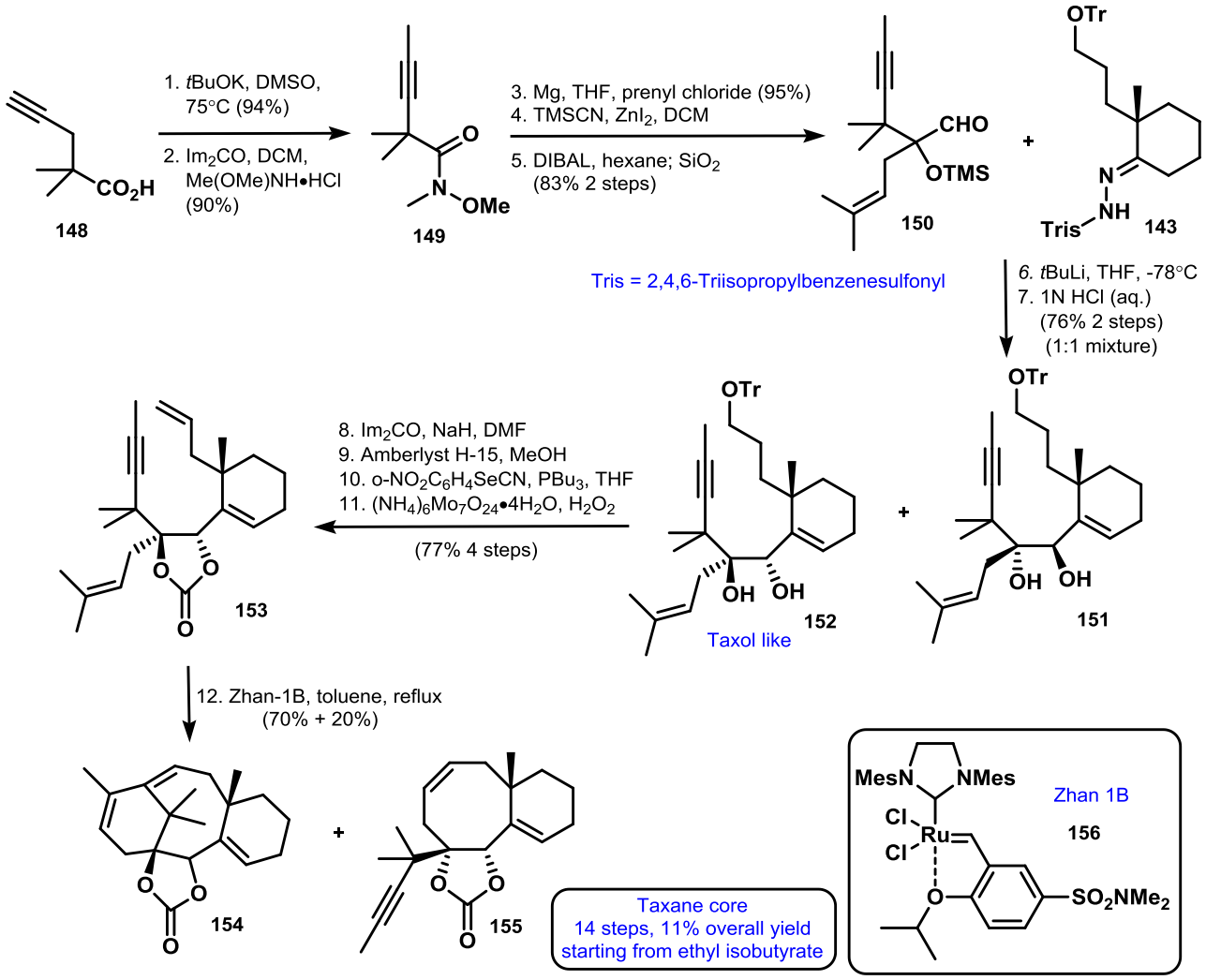
[17] Aldegunda M.J., Castedo L., Granja J.R. *Org. Lett*. **2008**, *10*, 3789 – 3792

Prunet metathesis approach



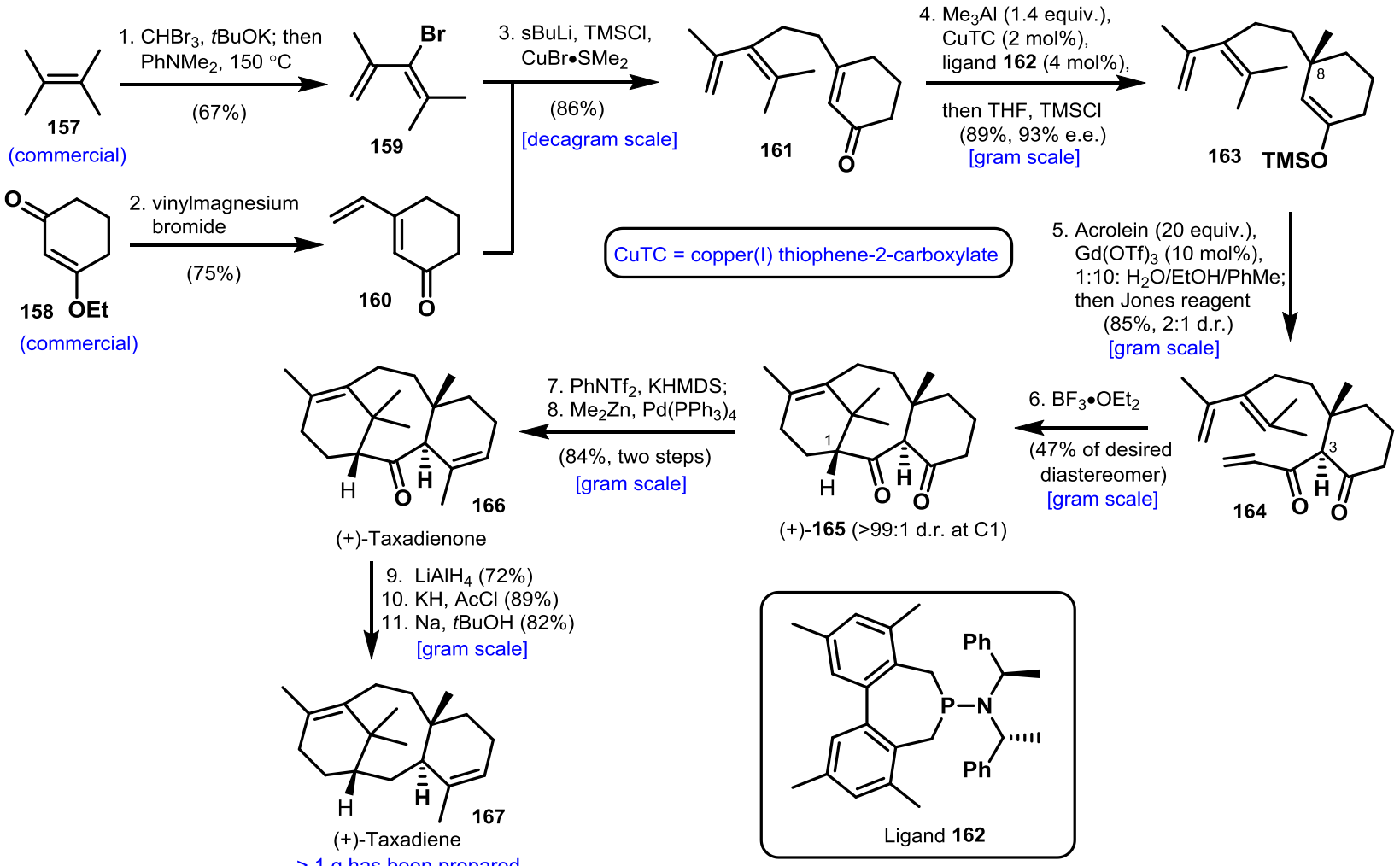
[18] Ma. C., Schiltz S., Le Goff X.F., Prunet J. *Chem. Eur. J*. **2008**, *14*, 7314 – 7323

Prunet metathesis approach



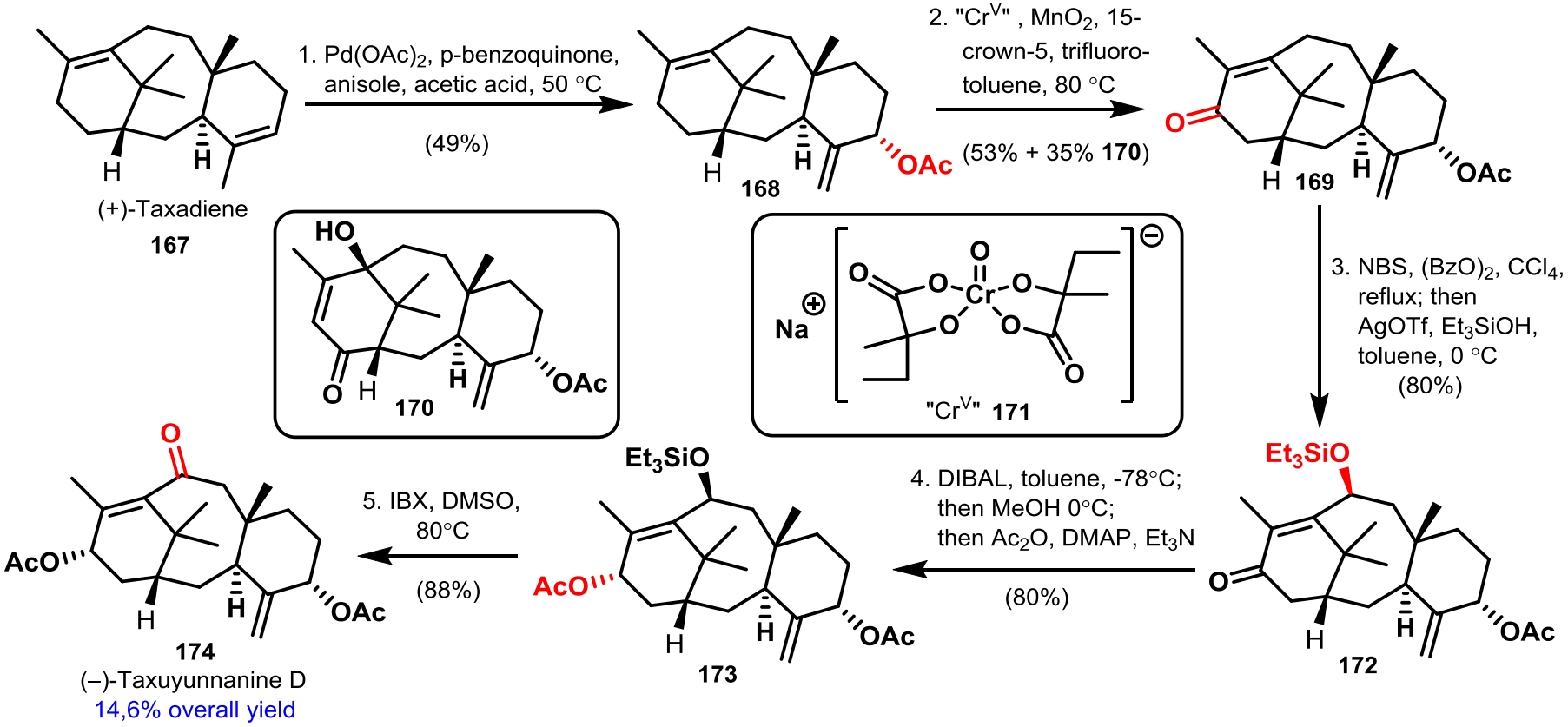
[19] Letort A., Aouzal R., Ma C., Long D.-H., Prunet J. *Org. Lett*. **2014**, *16*, 3300 – 3303

(+)-Taxadiene synthesis



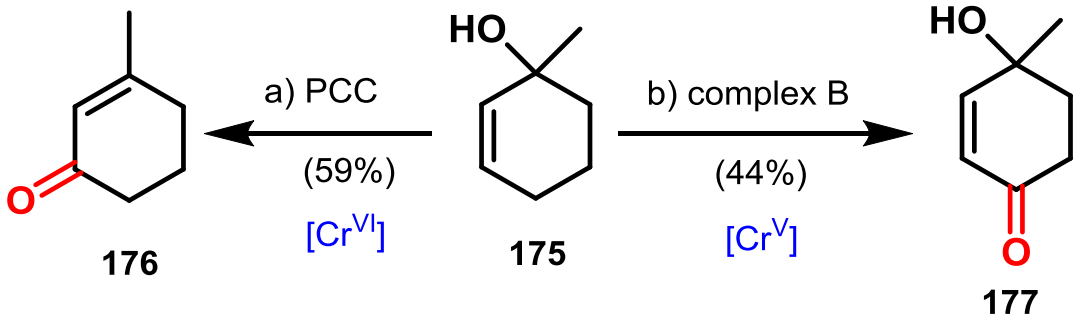
[20] Mendoza A., Ishihara Y., Baran P.S. *Nat. Chem*. **2012**, *4*, 21 – 25

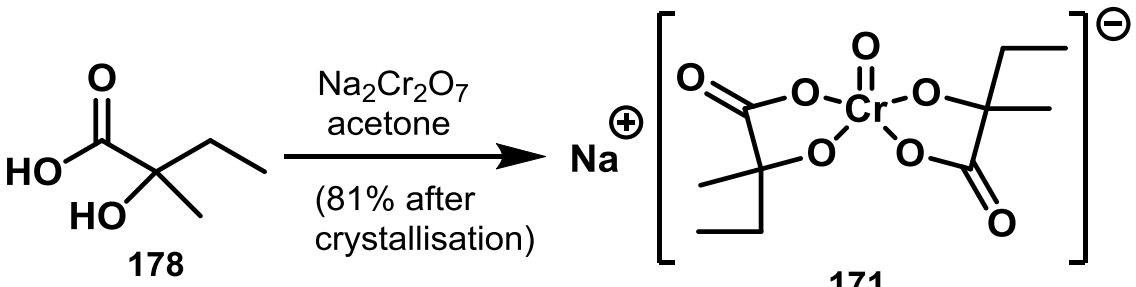
(-)-Taxuyunnanine D synthesis



[21] Wilde N.C., Isomura M., Mendoza A., Baran P.S. *J. Am. Chem. Soc.* **2014**, *136*, 4909 – 4912

Selective methylene oxidation of tertiary allylic alcohols





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available by Aldrich
CAS Number 66767-36-0
1g - 48,50 EUR

[21] Wilde N.C., Isomura M., Mendoza A., Baran P.S. *J. Am. Chem. Soc*. **2014**, *136*, 4909 – 4912
[22] Krumpolc M., Rocek J. *J. Am. Chem. Soc*. **1979**, *101*, 3206 – 3209

Further reading

1. Klingston D.G.I., Molinero A.A., Rimoldi J.M. **The Taxane Diterpenoids**. *Progress in The Chemistry of Organic Natural Products.* **1993**, *61*, 1 – 165

2. Klingston D.G.I., Jagtap P.G., Yuan H., Samala L. **The Chemistry of Taxol and Related Taxoids.** *Progress in The Chemistry of Organic Natural Products.* **2002**, *84*, 53 – 225

Thank you for attention!

Questions?