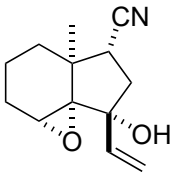
Problem Session (8)

2016/09/10 MASANORI NAGATOMO

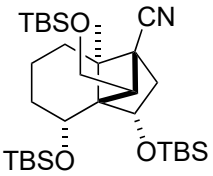
Please explain the reaction mechanisms

1.



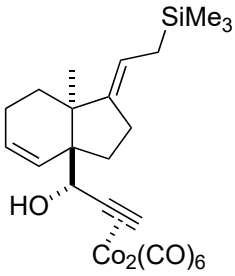
1-1

1. TMSOTf (2 eq.), 2,6-lutidine (3 eq.)
   $(CH_2Cl)_2$ (0.3 M), 45 °C, 1.5 h;
   HF·py, 0 °C, 15 min, 97%
2. DIBAL-H (3 eq.), THF (0.2 M), -78 °C, 1 h
3. TBSOTf (3 eq.), 2,6-lutidine (4.5 eq.)
   CH_2Cl_2 (0.3 M), 16 h, 93% (2 steps)
4. *m*-CPBA (4.5 eq.), $(CH_2Cl)_2$ (0.67 M), 2 d;
   Me_2C=CHMe, 20 min, 74%
5. LiN^iPr_2 (2 eq.), THF (0.1 M), 0 °C, 45 min;
   TBSCl (2 eq.), $O=P(NMe_2)_3$ (2 eq.), 1.5 h, 99%



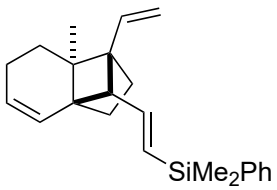
1-2

2.



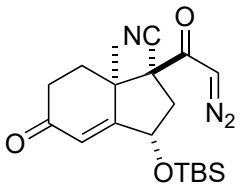
2-1

1. TMSOTf (5 eq.), $(CH_2Cl)_2$ (0.1 M), -20 °C;
   THF (6.2 M), -20 to 30 °C, 1 h, 76%
2. $HSiMe_2Ph$ (5 eq.)
   TMS—≡—TMS (6 eq.)
   $(CH_2Cl)_2$ (0.2 M), 65 °C, 1 h, 85%



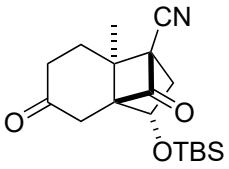
2-2

3.



3-1

1. $HN=C(NMe_2)_2$ (0.1 eq.), CH_2Cl_2 (0.07 M)
   reflux, 24 h, 47% (brsm 57%)
2. *hv* (UV), O_2, CH_2Cl_2 (0.008 M), -78 °C, 9 h
   42%



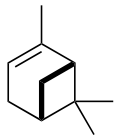
3-2

Problem Session (8)- Answer

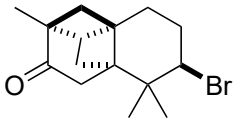
2016/09/10 MASANORI NAGATOMO

—Topic: Construction of bridged cyclobutane

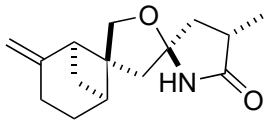
• Representative natural products having bridged cyclobutane



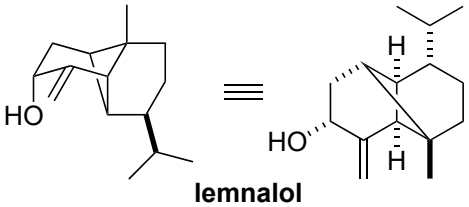
(*1R*,*5R*)-α-pinene



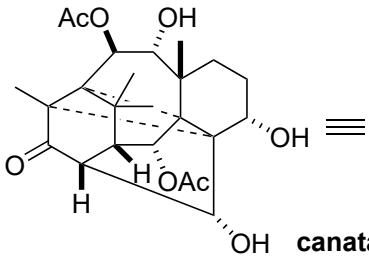
aplydactone



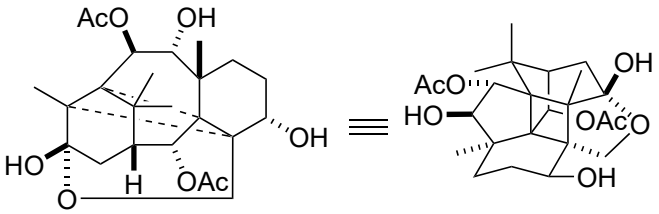
sporulaminal A



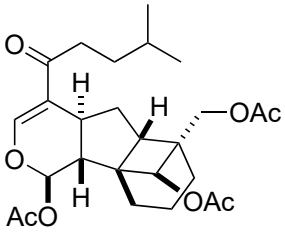
lemnalol



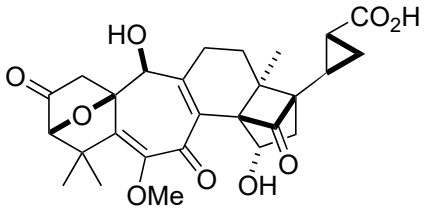
canataxpropellane



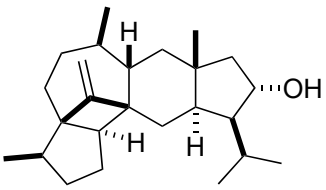
taxpropellane



plumisclerin A



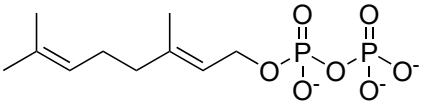
solanoeclepin A



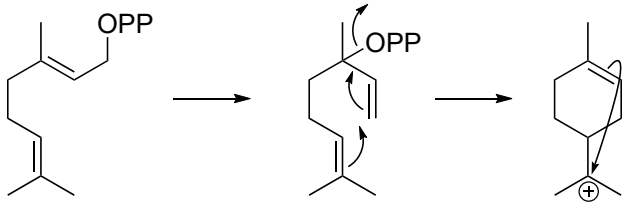
astellatol

• Proposed biosynthetic pathway

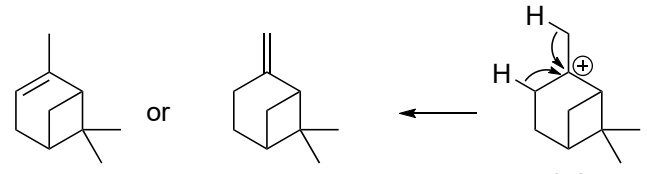
–pinene



geranyl pyrophosphate

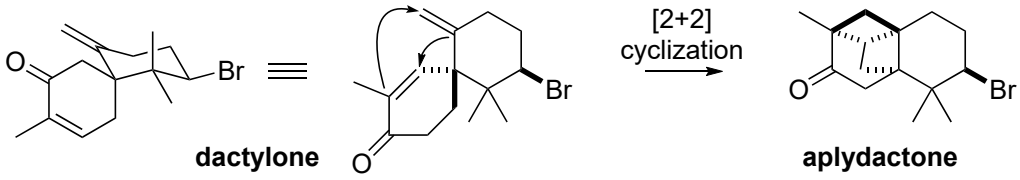


linaloyl pyrophosphate **0-1**



α-pinene **β-pinene** **0-2**

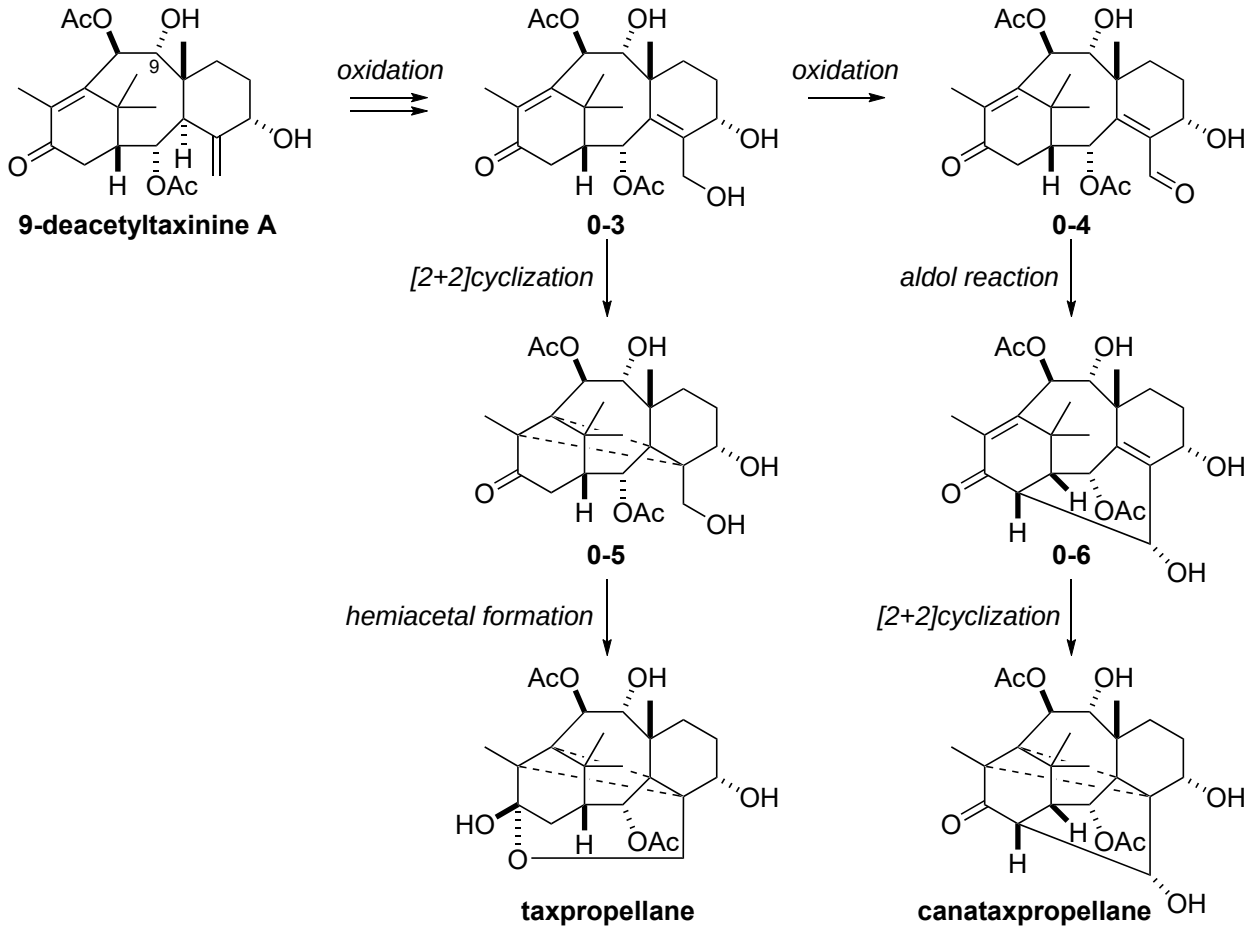
–aplydactone



dactylone **aplydactone**

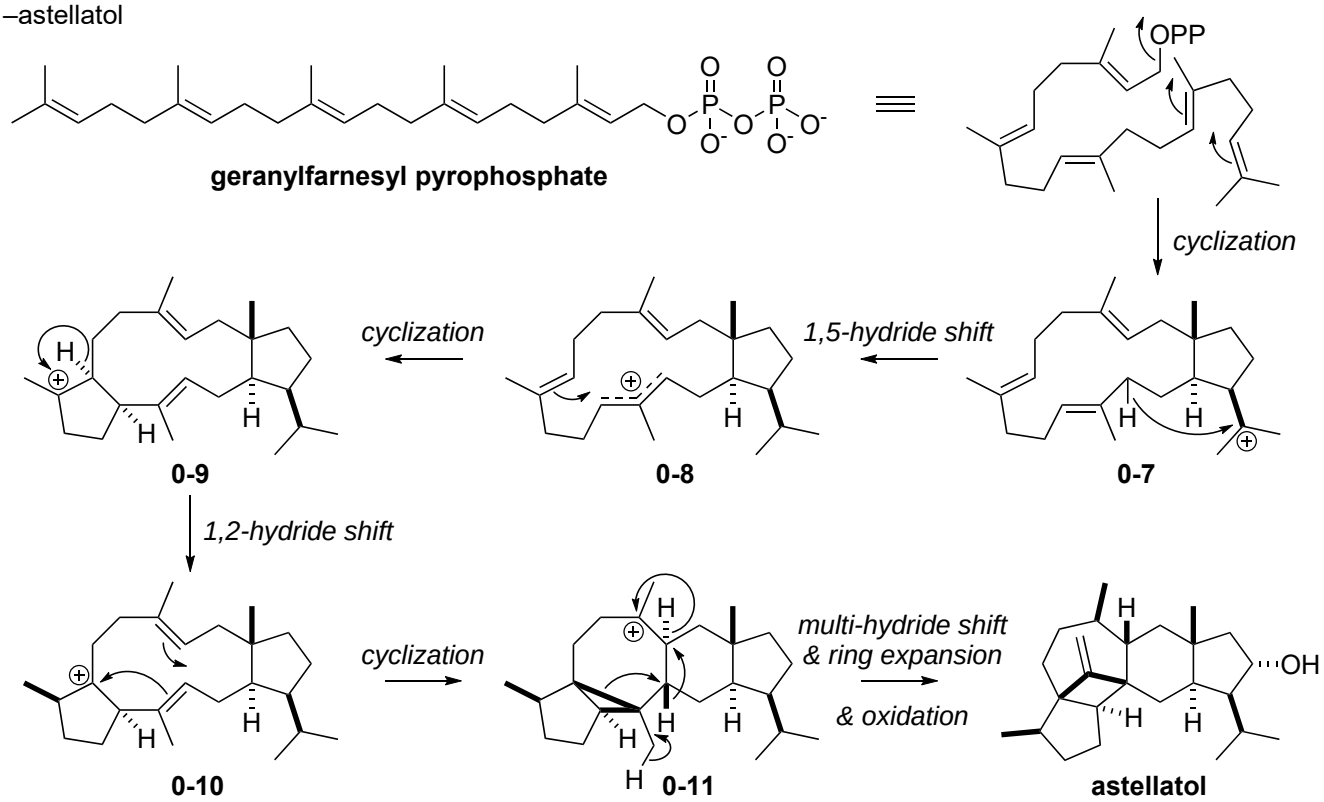
V.A. Stonik et al. *J. Am. Chem. Soc.* **2001**, *123*, 504.

–canataxpropellane and taxpropellane



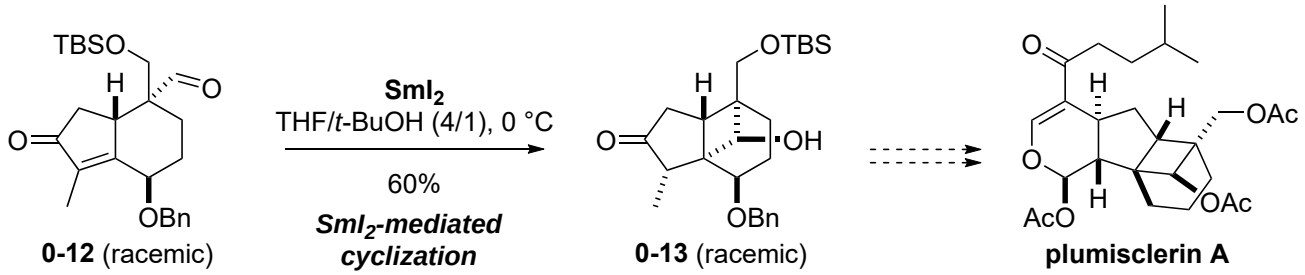
H. Kiyota et al. *Eur. J. Org. Chem.* **2008**, 5414. H. Kiyota et al. *Tetrahedron Lett.* **2007**, *48*, 2721.

–astellatol

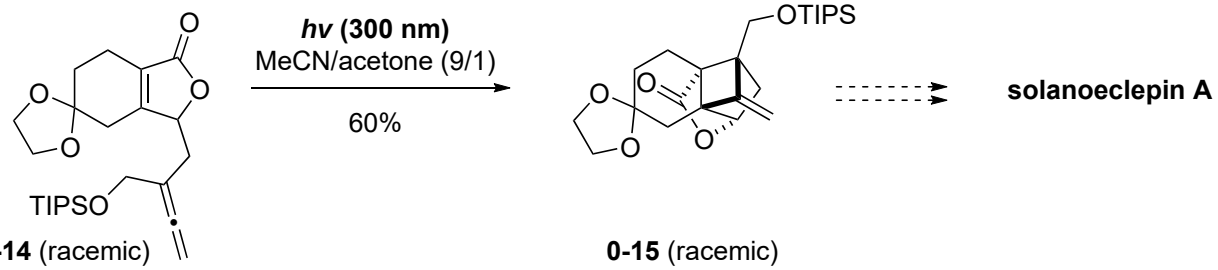


H. Oikawa et al. *J. Am. Chem. Soc.* **2015**, *137*, 11846.

• In many case.....



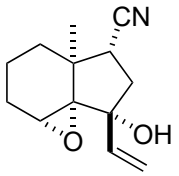
Z.-J. Yao et al. *Org. Lett.* **2015**, *17*, 3379.



H. Hiemstra et al. *Eur. J. Org. Chem.* **2006**, 127.

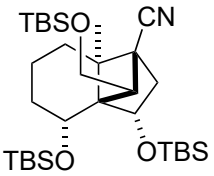
• Answer

1.



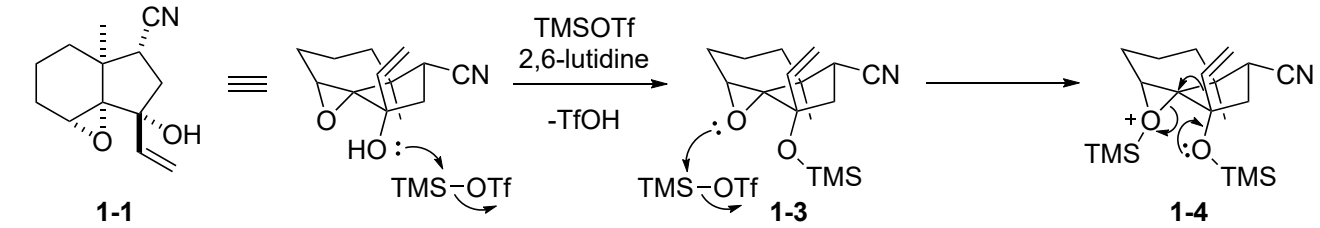
1-1

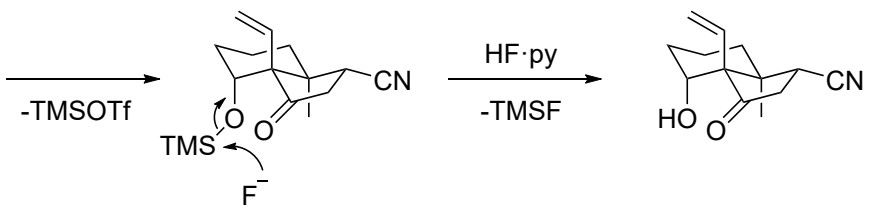
1. TMSOTf (2 eq.), 2,6-lutidine (3 eq.)
   $(CH_2Cl)_2$ (0.3 M), 45 °C, 1.5 h;
   HF·py, 0 °C, 15 min, 97%
2. DIBAL-H (3 eq.), THF (0.2 M), -78 °C, 1 h
3. TBSOTf (3 eq.), 2,6-lutidine (4.5 eq.)
   CH_2Cl_2 (0.3 M), 16 h, 93% (2 steps)
4. *m*-CPBA (4.5 eq.), $(CH_2Cl)_2$ (0.67 M), 2 d;
   Me_2C=CHMe, 20 min, 74%
5. LiN^{i}Pr$_2$ (2 eq.), THF (0.1 M), 0 °C, 45 min;
   TBSCl (2 eq.), O=P(NMe_2)$_3$ (2 eq.), 1.5 h, 99%

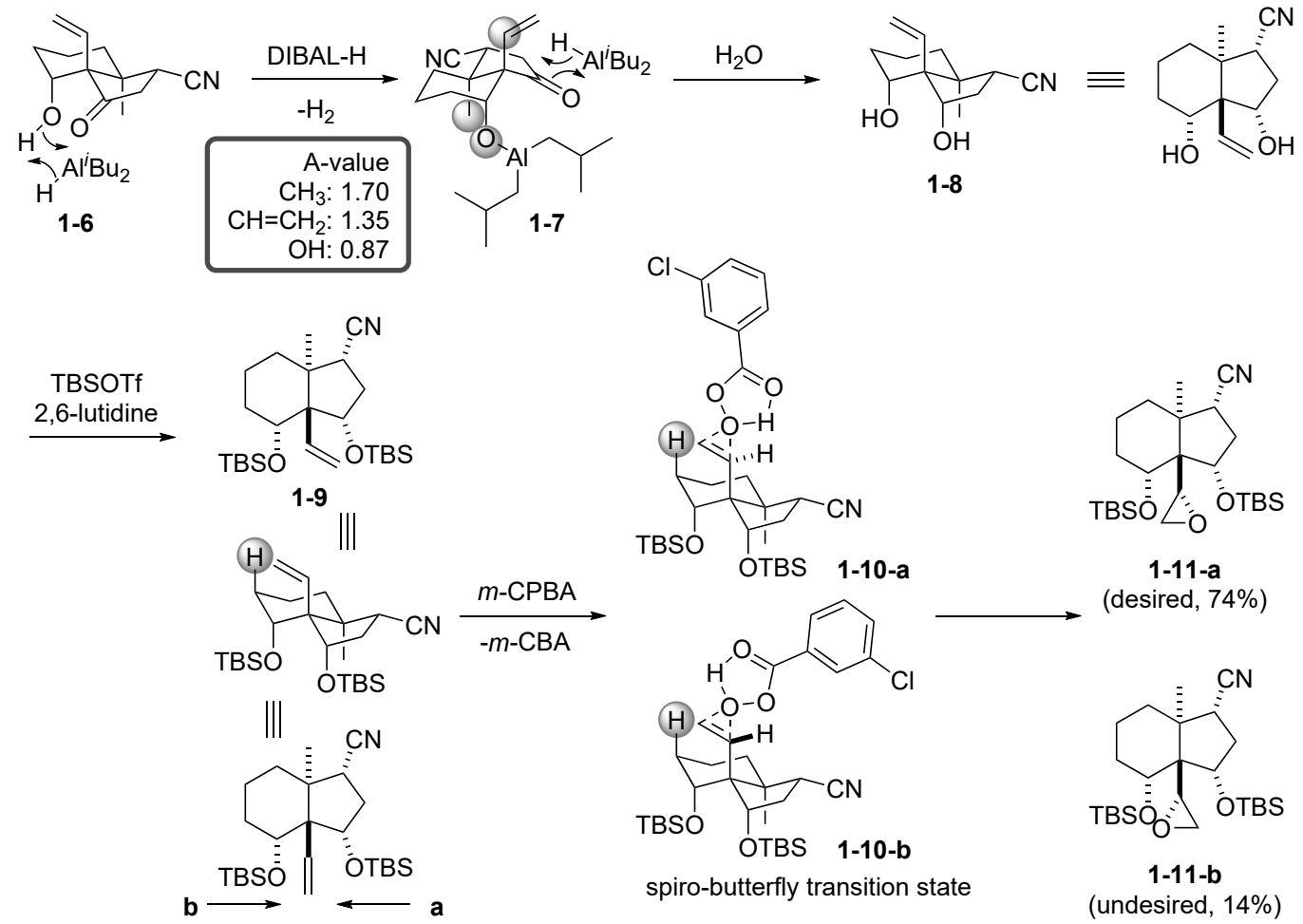


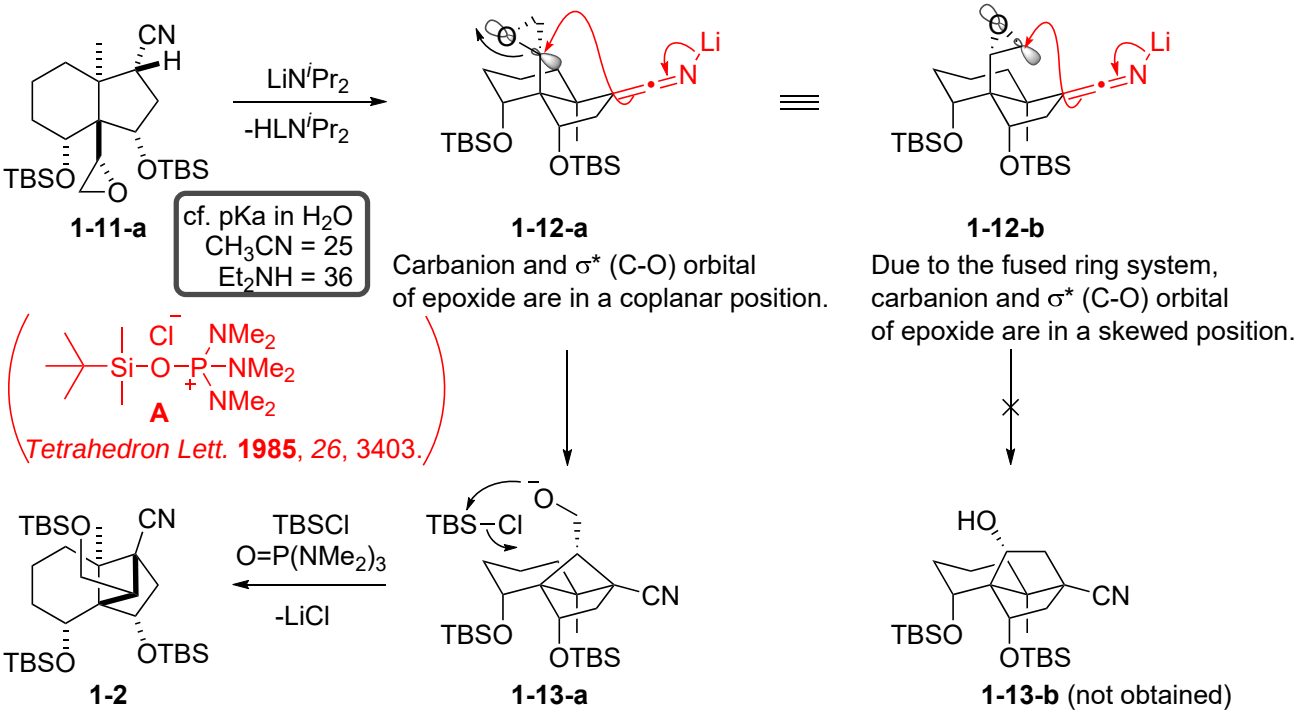
1-2

"Total synthesis of solanoeclepin A"
K. Tanino, M. Takahashi, Y. Tomata, H. Tokura, T. Uehara, T. Narabu, M. Miyashita *Nature Chem.* **2011**, *3*, 484.





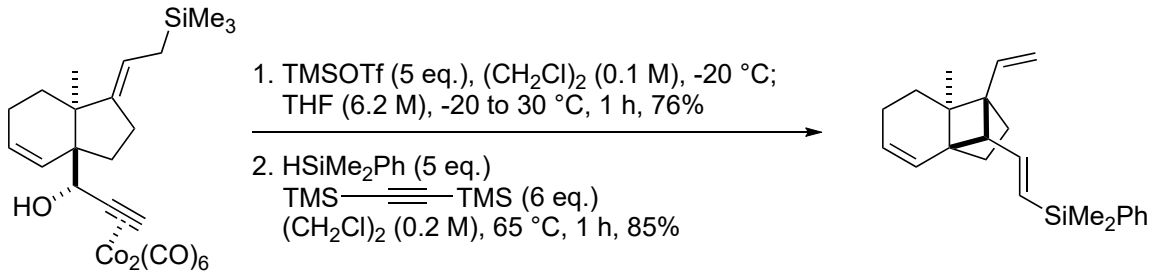




Presumably because HMPA solvated Li-cations, it accelerated S_N2 reactions by generating more "naked" alkoxide.
In addition, the more electrophilic silane salt **A** might be generated in situ.

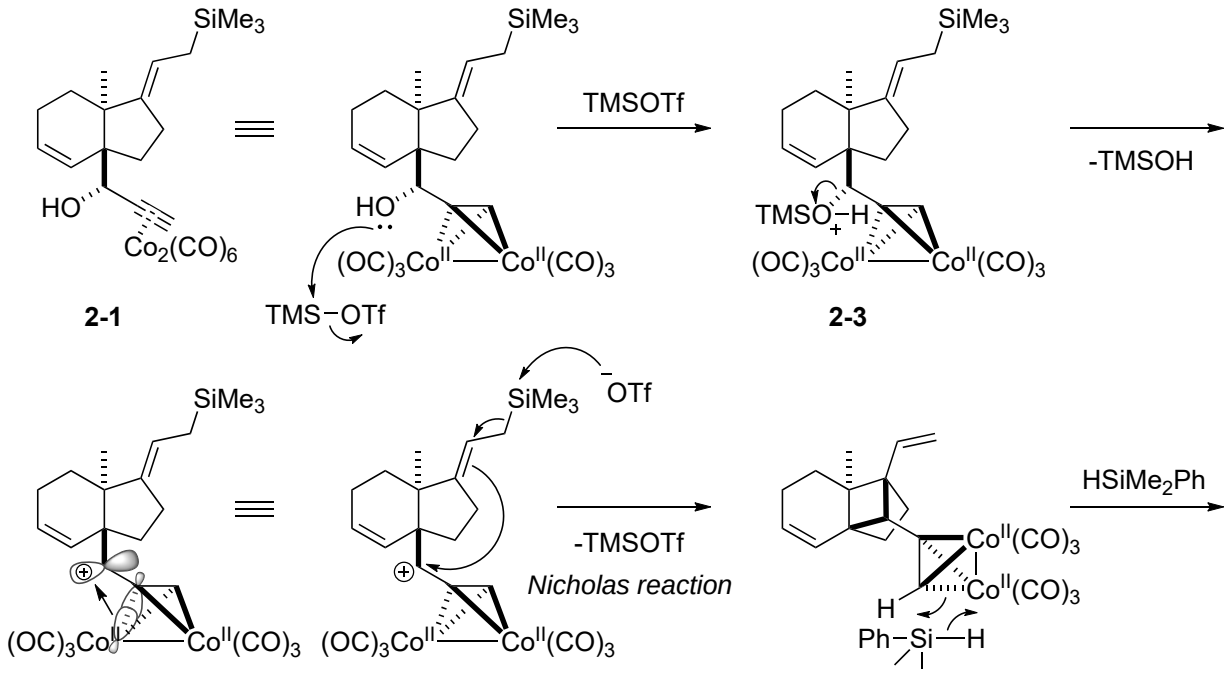
–For the detail of solanoeclepin A and its total synthesis, see also;
110910_LS_Shunichiroh_KATOH_Total_Synthesis_of_Solanoeclepin_A.pdf

2.



2-1 **2-2**

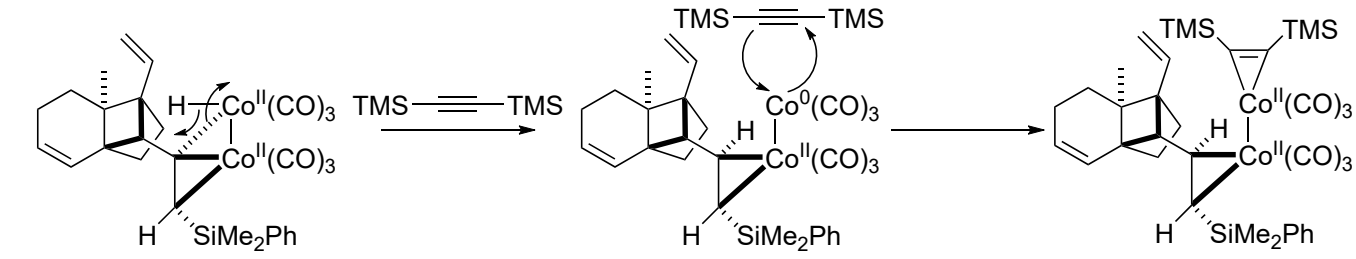
"Cobalt-Mediated Synthesis of the Tricyclo[5.2.1.0^{1,6}]decene Framework in Solanoeclepin A"
K.-W. Tsao, C.-Y. Cheng, M. Isobe *Org. Lett.* **2012**, *14*, 5274.



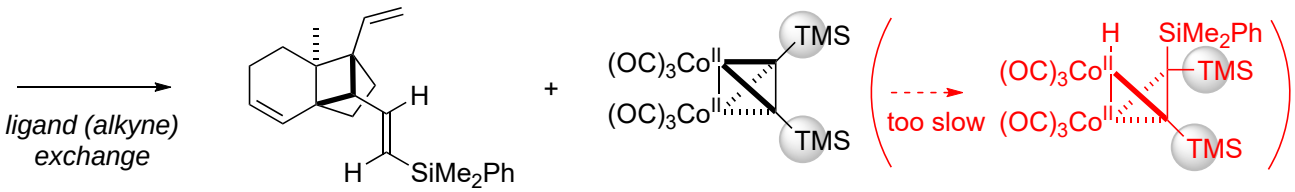
2-1 **2-3**

2-4 **2-5**

The adjacent carbocation is stabilized
by the hyper-conjugation from σ (Co-C) orbital.



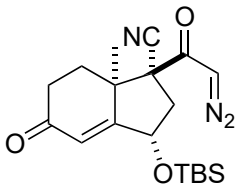
2-6 **2-7** **2-8**



2-2 **B**

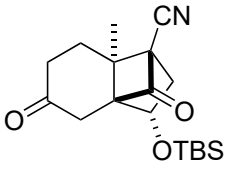
–For a deep understanding of $Co_2(CO)_8$, see also;
140729_PS_Keisuke_MASUDA_Acetylenehexacarbonyl_Dicobalt_Complex.pdf

3.



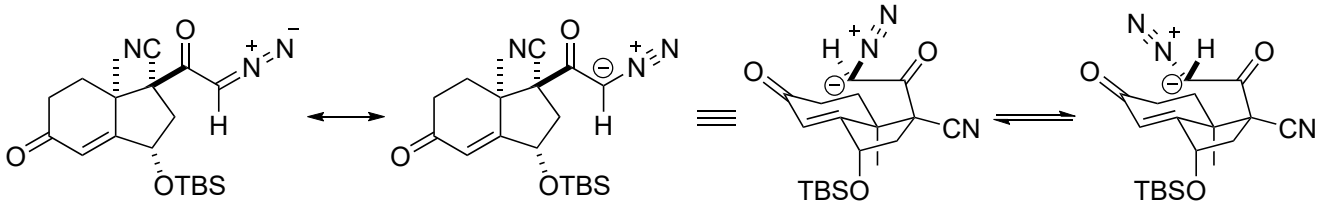
3-1

1. $HN{=}C(NMe_2)_2$ (0.1 eq.), CH_2Cl_2 (0.07 M) reflux, 24 h, 47% (brsm 57%)
2. *hv* (UV), O_2, CH_2Cl_2 (0.008 M), -78 °C, 9 h 42%

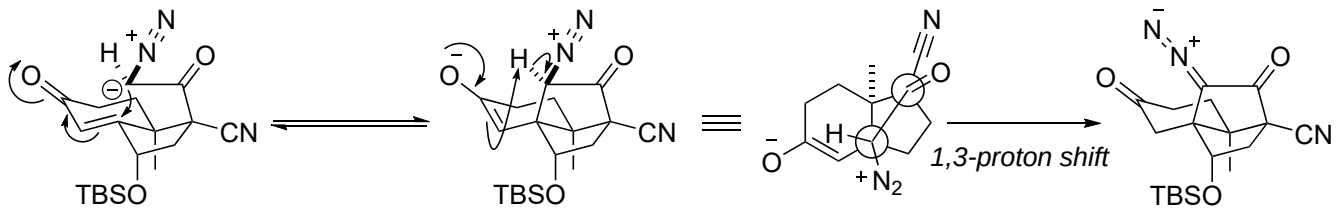


3-2

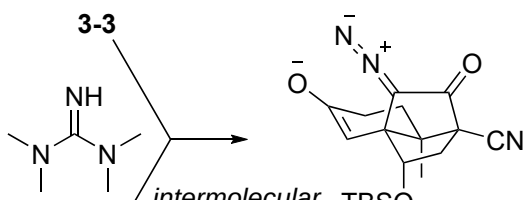
"Study toward efficient synthesis of glycocinnasperimicin D and solanoeclepin A"
Yoshifumi, Kusumoto Ph.D. Thesis, The University of Tokyo, 2011.
(Hidenori Watanabe Group)



3-1 **3-1-ab** **3-1-a** **3-1-b**



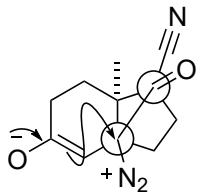
3-1-a **3-3** **3-6**



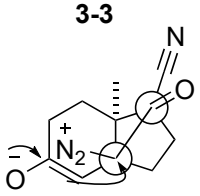
intermolecular proton transfer

3-5

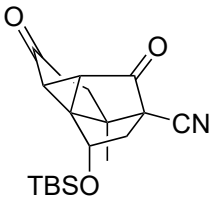
3-1-b **3-4**



3-3

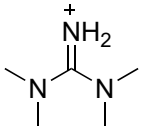


3-4

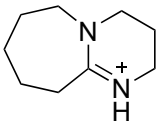


3-7
(not obtained)

pKa in H_2O

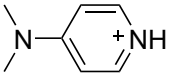


13.6

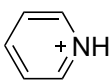


12
(estimated)

Et_3N 10.7

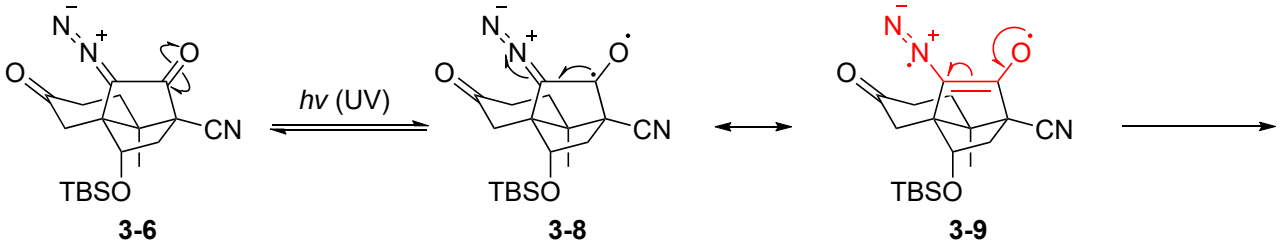


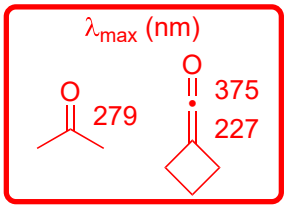
9.53

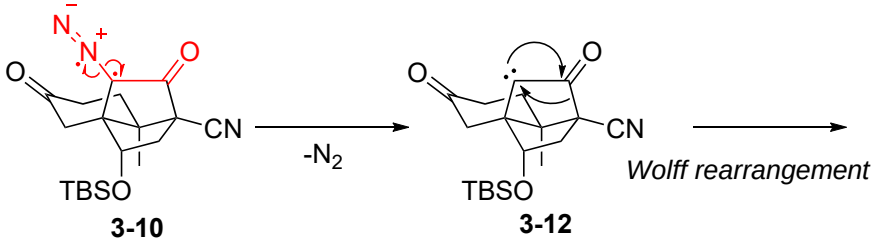


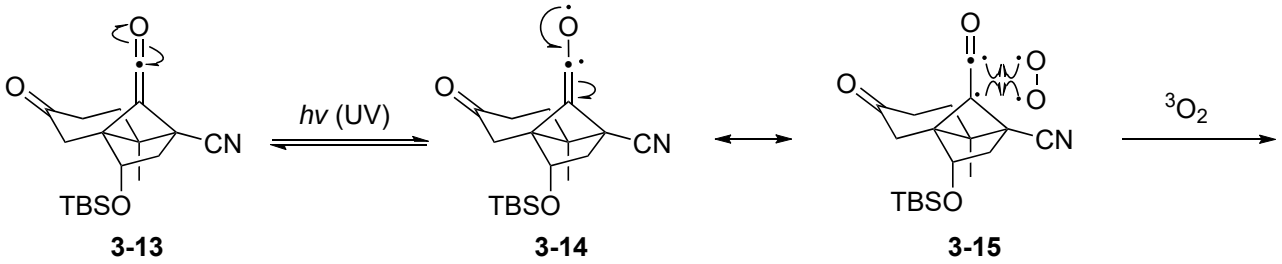
5.25

J. Org. Chem. **2002**, *67*, 1873.

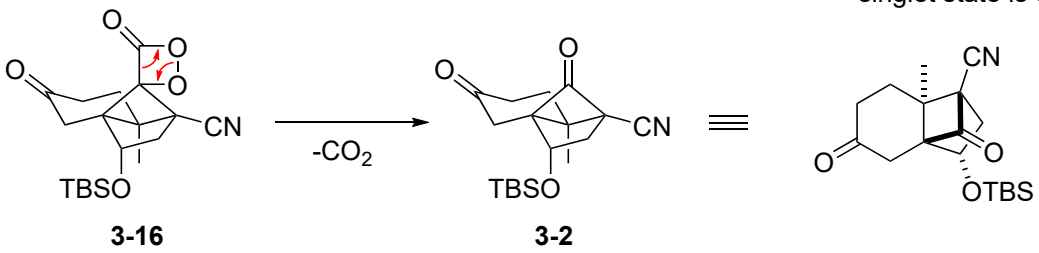




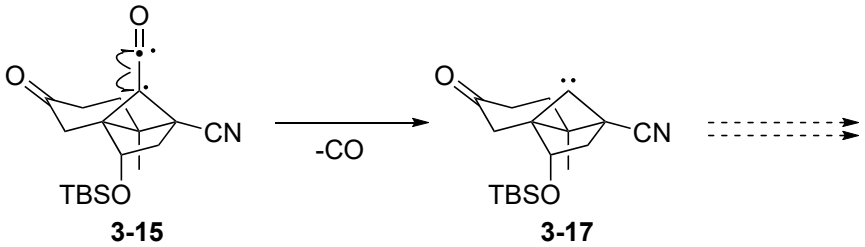




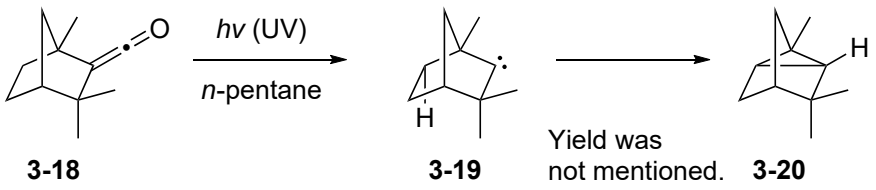
Direct excitation of O_2 from triplet to singlet state is **spin-forbidden**.

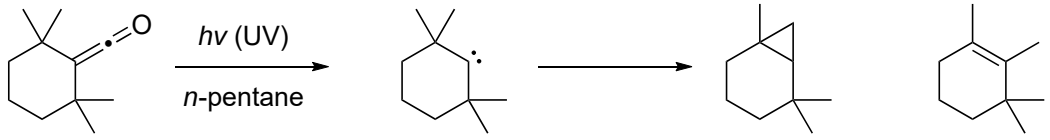


–Possible decomposition pathway...



–For example...





Angew. Chem. **1981**, *93*, 791.