Problem Session (5)

Please provide reaction mechanisms.







Problem Session (5) answer

1. Synthetic study of spongistatin by Prof. Leighton group¹⁾



- 1.1. Proposed mechanism
- 1.1.1. Palladium-catalyzed hydrosilylation²⁾



¹ Reznik, S.; Marcus, B. S.; Leighton, J. L. Chem. Sci. 2012, 3, 3326.

² Ligands were omitted for clarity.



1.1.2. Complexation with 1-2



1.1.3. Sc(OTf)₃-catalyzed crotylation







1.1.4. Fleming-Tamao oxidation









- 1.2. Regio- and cis-trans selectivity of hydrosilylation
- 1.2.1. Ojima group's results³⁾





- The hydropalladation of **1-29** regioselectively occurred to afford **1-30**, presumably because generation of tri-substituted π -allyl palladium complex (**1-30**) is more favored compared to that of di-substituted one (**1-37**).
- **Cis-trans** isomers other than **1-34** and **1-36** (i.e. **1-32** and **1-40**) was not obtained, presumably because transformation from a π -allyl palladium complex to a σ -allyl palladium complex (**1-30** \rightarrow **1-33** and **1-30** \rightarrow **1-35**) is likely to be irreversible.

³ Ojima, I.; Kumagai, M. J. Organomet. Chem. 1978, 157, 359.

1.3. Stereoselectivity of crotylation

1.3.1. Effect of the chiral auxiliary



■ The diastereoselectivity seems not to be caused by the substrate (1-41 and 1-42), but the chiral auxiliary (1-2).



Figure 1. (a) An explanation for "Strain-release Lewis acidity". (b) Structure of diazasilacyclopentane **1-51**. (c) X-ray structure of **1-51**.⁴⁾ The Si-N-Si bond angle was ~96°.

- Cyclic, strained silanes, such as diazasilacyclopentane **1-51**, exhibit much higher Lewis acidity.⁵⁾
- The silacycle spans apical and equatorial positions. The nucleophile occupies the other apical position.

⁴ Auner, N.; Penzenstadler, E.; Herdtweck, E. Z. Naturforsch. B Chem. Sci. **1992**, 47, 1377.

⁵ Denmark, S. E.; Griedel, B. D.; Coe, D. M. J. Org. Chem. **1993**, 58, 988.



Assuming chair-like transition states and equatorial orientation of R⁷, 4 transition states (TS1-TS4) are possible.



- TS-2 and TS-4 are disfavored due to repulsion between chlorine atom and Sc(OTf)₃.
- **TS-3** and **TS-4** are disfavored due to repulsion between chlorine atom and lone pair of apical N.
- \rightarrow 1-18 would be preferably obtained via TS-1.



Table 1. TS geometries from HF/6-31G* optimizations and relative energies (kcal/mol) from MP2/6-311++G** single-point energy calculations for the simplified model. Nonlabelled atoms are hydrogen. The Si-Cl distances are given.



1.4. Stereoselectivity of protonation after Fleming-Tamao oxidation



Considering the allylic strain and syn-pentane interactions, **1-21a** and **1-21b** would be the preferred conformations.



: minimized allylic strain/syn-pentane interactions

Protonation from the alpha face would be favored.

⁶ Zhang, X.; Houk, K. N.; Leighton, J. L. Angew. Chem., Int. Ed. 2005, 44, 938.

2. Asymmetric synthesis of (-)-6-epi-Garcimultiflorone A by Prof. Porco, Jr. group⁷



2.1. Proposed reaction mechanism



⁷ Wen, S.; Boyce, J. H.; Kandappa, S. K.; Sivaguru, J.; Porco, J. A., Jr. J. Am. Chem. Soc. 2019, 141, 11315.



2.2. Excited-state intramolecular proton transfer (ESIPT)^{8,9)}



⁸ Formosinho, S. J.; Arnaut, L. G. J. Photochem. Photobiol., A 1993, 75, 21.

⁹ For an example of ESIPT-related reactions in PS: 100313_PS_Ken Mukai_[3+2] dipolar cycloaddition

¹⁰ Okazaki, T.; Hirota, N.; Terazima, M. J. Chem. Phys. **1999**, *110*, 11399.

¹¹ Foster, K. L.; Baker, S.; Brousmiche, D. W.; Wan, P. J. Photochem. Photobiol., A 1999, 129, 157.

¹² Lukeman, M.; Simon, H.; Wan, P.; Wang, Y.-H. J. Org. Chem. 2015, 80, 11281.

2.3. Reactivity of a similar substrate





Figure 2. UV-vis, excitation, and phosphorescence spectra for **2-25** in 2-MeTHF. UV-vis absorption was recorded at rt. Excitation spectra were recorded by monitoring the fluorescence signal at $\lambda_{em} = 454$ nm at room temperature. Phosphorescence spectra were recorded at 77 K in 2-MeTHF glass.

- λ_{max} was ~350 nm and absorbance at 390 nm is not so high. There is a possibility that only minor tautomers of 2-25 such as 2-26b could be excited at 390 nm.
- 2.5. Deuterium-labeling study



Cyclization from **2-29-d** or **2-30-d** is likely to be faster than σ-bond rotation.



2-25a 2-25b

2.7.

1.3:1 mixture of **2-25a** and **2-25b** (**2-25**) **ble 2** The results of the Ar_{-} or O_{-} bubbling

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Table 2.	The results of the Ar- or O2-bubbling experiments			
	entry	bubbled gas	2-28	2-32
	1	Ar	7% (calc. 16% from 2-25b)	3% (calc. 7% from 2-25b)
	2	O2	7% (calc. 16% from 2-25b)	3% (calc. 7% from 2-25b)

38 °C, 12 h

O₂ bubbling did not cause an observable difference in comparison to reaction conducted under Ar, implying reaction pathway that does not contain triplet biradical pathway.

ÓМе

2-32 (from 2-25b)

ÓMe

2-28 (from 2-25b)



2-4 seems to be generated from 2-3. 2-3 might exhibit different UV-vis spectrum from that of 2-1. There is a possibility that 2-3 could be excited by irradiation of light (390 nm).