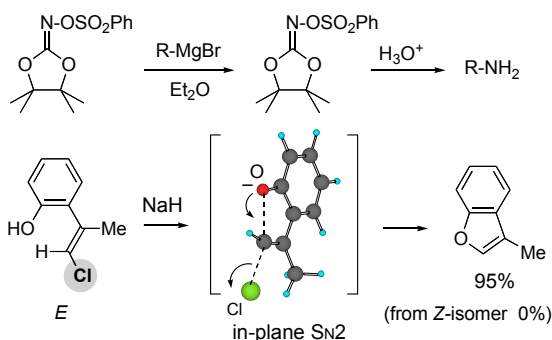


SYNTHETIC ORGANIC CHEMISTRY

Annual Research Highlights

(1) “Development of new synthetic methods based on the substitution at sp^2 atoms”

Previously, we found that the nucleophilic substitution on sp^2 nitrogen of oximes easily occurred in an S_N2 manner. Based on these findings, we have developed new amination methods with oximes: Spiro[indoline-3,2'-pyrrolidine] derivatives are synthesized from β -3-indolyl ketones. A 1,3-dioxolan-2-one *O*-sulfonyloxime functions as a good electrophilic amination reagent. Various aza-heterocycles are synthesized by a radical chain reaction of oximes with an iron-diene complex moiety and amino-Heck reactions. Although nucleophilic substitution on sp^2 carbon is known to hardly occur, we have proved that the substitution proceeds under certain circumstances by experimental and theoretical studies.



1-2) *Chem. Lett.*, **33**, 26–27 (2004).

1-3) *Bull. Chem. Soc. Jpn.*, **77**, 575–584 (2004).

1-5) *Bull. Chem. Soc. Jpn.*, **77**, 785–796 (2004).

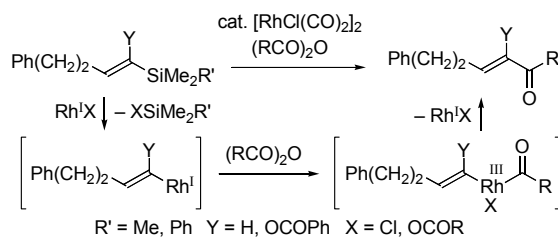
1-7) *Org. Lett.*, **6**, 2461–2463 (2004).

1-8) *Org. Lett.*, **6**, 4619–4621 (2004).

(2) “Rhodium-catalyzed desilylative acylation of vinylsilanes with acid anhydrides”

We have been studying on development of a new catalytic system including activation of organosilicon compounds directed towards organic synthesis. The first catalytic desilylative acylation of vinylsilanes has been achieved by the use of rhodium(I) carbonyl complex $[\text{RhCl}(\text{CO})_2]_2$ and acid anhydrides to give α,β -unsaturated ketones. The reaction includes a transmetalation step, which proceeds without formation of silicates. This catalytic system was applied to the acylation of α -acyloxy vinylsilanes to afford α -acyloxy enones,

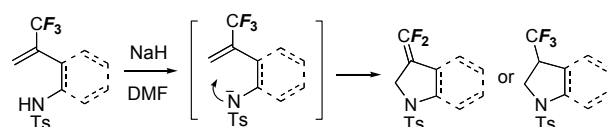
which were converted to unsymmetrical α -diketones or their regioselectively protected monoacetals.



1-4) *Chem. Lett.*, **33**, 424–425 (2004).

(3) “Construction of fluorinated heterocycles via the nucleophilic cyclization of fluoroalkenes”

5-endo-trig Cyclization has long been considered to be a disfavored process according to Baldwin's rules. Especially, nucleophile-driven ones have rarely been observed in synthetic chemistry. We have already found that this type of cyclization were effected by using the properties of *gem*-difluoroalkenes. Taking advantage of the reactivity toward nucleophilic addition and substitution for the fluorines of 2-trifluoromethyl-1-alkenes, we have succeeded in nucleophilic *5-endo-trig* cyclization of trifluoromethylalkenes bearing a nucleophile on the homoallylic position. The cyclizations efficiently provide 5- and 6-membered heterocycles bearing a CF_3 -, CF_2H -, or $\text{CF}_2=$ group.



1-9) *Chem. Lett.*, **33**, 590–591 (2004).

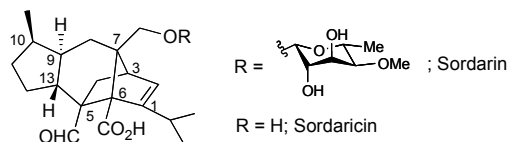
1-11) *Synlett*, **2004**, 1219–1222 (2004).

1-13) *Chem. Lett.*, **33**, 1206–1207 (2004).

1-14) *Chem. Lett.*, **33**, 1354–1355 (2004).

(4) “Synthetic study of Sordarin”

Sordarin, consisting of a sugar part and tetracyclic diterpene core with *trans*-perhydroindene and bicyclo[2.2.1]-heptene frameworks, is a good candidate for antifungal reagent. We have achieved the synthesis of its aglycon by oxidative radical cyclization and intramolecular allylation as key steps.



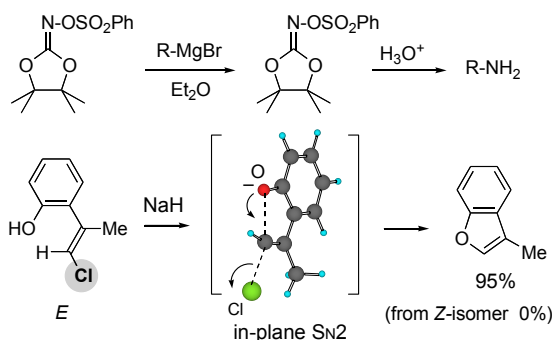
1-6) *Chem. Lett.*, **33**, 942–943 (2004).

有機合成化学研究室

研究ハイライト

(1) sp^2 原子上的置換反応を利用する合成反応の開発

先に我々は、オキシムの sp^2 窒素原子上で S_N2 型の置換反応が進行することを見出し、種々のアミノ化反応に展開している。これにより、スピロ[インドリン-3,2'-ピロリジン]の合成法を開発し、また1,3-ジオキソラン-2-オン *O*-スルホニルオキシムが優れた求電子的アミノ化剤となることを見出した。さらに、オキシムを用いる新しいラジカル連鎖反応や、アミノ-Heck反応により、各種含窒素ヘテロ環骨格の構築にも成功した。また、従来進行しないとされた sp^2 炭素原子上的 S_N2 型置換反応が起こりうることを実験化学的、理論化学的に証明した。



1-2) *Chem. Lett.*, **33**, 26–27 (2004).

1-3) *Bull. Chem. Soc. Jpn.*, **77**, 575–584 (2004).

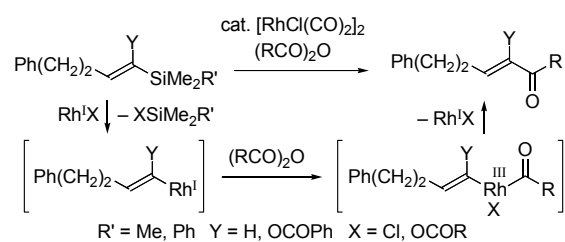
1-5) *Bull. Chem. Soc. Jpn.*, **77**, 785–796 (2004).

1-7) *Org. Lett.*, **6**, 2461–2463 (2004).

1-8) *Org. Lett.*, **6**, 4619–4621 (2004).

(2) ロジウム(I)錯体を用いるビニルシランの触媒的脱シリルアシル化

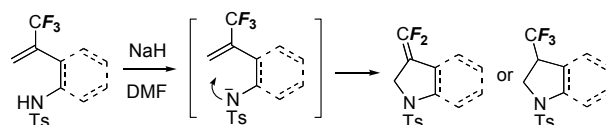
遷移金属触媒による有機ケイ素化合物の新規活性化法とそれを用いる有機合成反応の開発を目指して研究を行うなかで、ロジウム(I)カルボニル錯体がビニルシランとの金属交換に活性を示すことを見出し、ビニルシランの触媒的脱シリルアシル化を達成した。この反応は、従来のシリカートを經由するものとは異なる新規な金属交換過程を含んでいる。また、酸素官能基化されたビニルシランのアシル化に応用し、有用な合成中間体である α -ジケトンやその位置選択的保護体が簡便に合成できることを示した。



1-4) *Chem. Lett.*, **33**, 424–425 (2004).

(3) フルオロアルケン類の求核的環化による含フッ素ヘテロ環の構築

5-*endo-trig*環化はBaldwin則で不利とされ、殊に求核的反応の例は極めて希だが、我々は*gem*-ジフルオロアルケンで本環化が進行することを見出し、応用展開している。さらに、トリフルオロメチルビニル化合物が付加やフッ素の脱離を伴う置換を起こし易い点に着目し、ホモアリル位に求核部位を導入した2-トリフルオロメチル-1-アルケンを用いることによって、新たな求核的5-*endo-trig*環化を達成した。この反応では、 CF_3 基や CF_2H 基、 $CF_2=$ 基を有する各種ヘテロ環が良好な収率で得られ、また本手法により六員環も構築できる。



1-9) *Chem. Lett.*, **33**, 590–591 (2004).

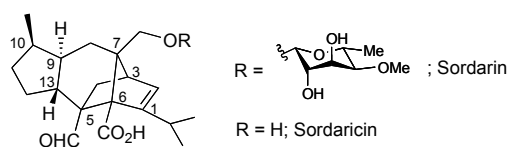
1-11) *Synlett*, **2004**, 1219–1222 (2004).

1-13) *Chem. Lett.*, **33**, 1206–1207 (2004).

1-14) *Chem. Lett.*, **33**, 1354–1355 (2004).

(4) Sordarinの合成研究

Sordarinは、*trans*-ペルヒドロインデンとノルボルネンを含む四環性ジテルペン骨格に糖が結合した構造を有し、真菌感染症のリード化合物として注目される。我々は、ラジカル環化と分子内アリル化を利用してそのアグリコン合成に成功した。



1-6) *Chem. Lett.*, **33**, 942–943 (2004).

1. 原著論文

(1) Refereed Journals

- 1) T. Azemi, M. Kitamura, and K. Narasaka, "Transformation of 1,5- and 1,6-dienes to carbocycles by hydrozirconation and oxidation with cerium(IV) compounds" *Tetrahedron*, **60**, 1339–1344 (2004).
- 2) K. Tanaka, Y. Mori, and K. Narasaka, "Synthesis of Spiro[indoline-3,2'-pyrrolidine] Derivatives from β -3-Indolyl Ketone Oximes" *Chem. Lett.*, **33**, 26–27 (2004).
- 3) K. Tanaka, N. Yukimura, and K. Narasaka, "Radical Cyclization of *O*-Pentafluorobenzoyloximes Having a (Cyclohexadiene)Fe(CO)₃ Moiety" *Bull. Chem. Soc. Jpn.*, **77**, 575–584 (2004).
- 4) M. Yamane, K. Uera, and K. Narasaka, "Rhodium-Catalyzed Acylation of Vinylsilanes with Acid Anhydrides: Application to the Transformation of α -Acyloxy Vinylsilanes to Unsymmetrical 1,2-Diketones" *Chem. Lett.*, **33**, 424–425 (2004).
- 5) S. Chiba, M. Kitamura, O. Saku, and K. Narasaka, "Synthesis of 1-Azaazulenes from Cycloheptatrienylmethyl Ketone *O*-Pentafluorobenzoyloximes by Palladium-catalyzed Cyclization and Oxidation" *Bull. Chem. Soc. Jpn.*, **77**, 785–796 (2004).
- 6) M. Kitamura, S. Chiba, and K. Narasaka, "Synthesis of (\pm)-Sordaricin" *Chem. Lett.*, **33**, 942–943 (2004).
- 7) K. Ando, M. Kitamura, K. Miura, and K. Narasaka, "Theoretical and Experimental Study on the In-Plane S_N2-Type Substitution Reaction of Haloalkenes with Inversion of Configuration at the sp² Carbon" *Org. Lett.*, **6**, 2461–2463 (2004).
- 8) M. Kitamura, T. Suga, S. Chiba, and K. Narasaka, "Synthesis of Primary Amines by the Electrophilic Amination of Grignard Reagents with 1,3-Dioxolan-2-one *O*-Sulfonyloxime" *Org. Lett.*, **6**, 4619–4621 (2004).
- 9) T. Mori and J. Ichikawa, "KCN-Catalyzed C–C Bond Formation between Imine and *gem*-Difluoroalkene Moieties: A Facile Synthesis of 2,4-Disubstituted 3-Fluoroquinolines" *Chem. Lett.*, **33**, 590–591 (2004).
- 10) J. Ichikawa, H. Miyazaki, K. Sakoda, and Y. Wada, "Ring-Fluorinated Naphthalene and Indene Synthesis via 6- and 5-*endo-trig* Cyclizations of *gem*-Difluoroalkenes by Carbon Nucleophiles" *J. Fluorine Chem.*, **125**, 585–593 (2004).
- 11) J. Ichikawa, T. Mori, H. Miyazaki, and Y. Wada, "C–C Bond Formation between Isocyanide and β,β -Difluoroalkene Moieties via Electron Transfer: Fluorinated Quinoline and Biquinoline Syntheses" *Synlett*, **2004**, 1219–1222 (2004).
- 12) T. Saitoh, N. Jimbo, and J. Ichikawa, "A Novel Synthesis of *syn* and *anti* β -Hydroxy Dithioacetals, Masked Cross-Aldols between Aldehydes" *Chem. Lett.*, **33**, 1032–1033 (2004).
- 13) T. Mori and J. Ichikawa, "4-Difluoromethylated Quinoline Synthesis via Intramolecular S_N2' Reaction of α -Trifluoromethylstyrenes Bearing Imine Moieties" *Chem. Lett.*, **33**, 1206–1207 (2004).
- 14) J. Ichikawa, T. Mori, and Y. Iwai, "A New Class of Substrates for the Nucleophilic 5-*endo-trig* Cyclization, 1-Trifluoromethylvinyl Compounds: Syntheses of Indoline and Pyrrolidine Derivatives" *Chem. Lett.*, **33**, 1354–1355 (2004).
- 15) T. Saitoh, S. Yoshida, and J. Ichikawa, "1,8-Bis(diphenylmethyl) naphthalenediyl Dication as an Organic Oxidant: Synthesis of Benzidines via Self-Coupling of *N,N*-Dialkylanilines" *Org. Lett.*, **6**, 4563–4565 (2004).