

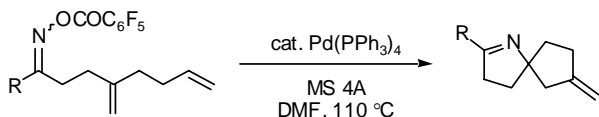
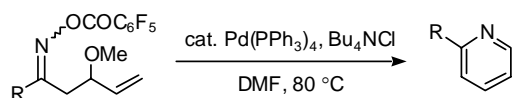
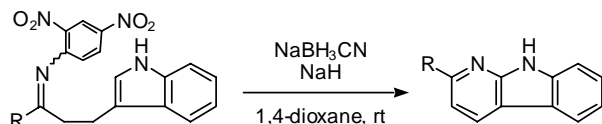
SYNTHETIC ORGANIC CHEMISTRY

Annual Research Review

(1) "Construction of Nitrogen-Containing Heterocyclic Systems via Intramolecular Cyclization of Oxime Derivatives"

In contrast to the well-known Beckmann rearrangement, novel substitution-type reactions on the oxime nitrogen atoms were found in our laboratory, providing various heterocycles and amines. Treatment of *O*-2,4-dinitrophenyl oximes having an olefin moiety with a one-electron reductant generates alkylideneaminyl radical species, which in turn readily add to an intramolecular unsaturated bond to give the corresponding cyclization products including α -carboline.

O-Acyl oxime derivatives were found to react with palladium(0) complex to generate alkylideneamino-palladium(II) species, which underwent the Mizoroki-Heck-type cyclization (amino-Heck reaction) with an intramolecular unsaturation to give pyrroles. On treatment of β -alkoxy γ,δ -unsaturated ketone oximes with palladium(0), 5-*exo* cyclization products, pyrroles or 6-*endo* cyclization products, pyridines are selectively obtained depending on the conditions. Furthermore, 1-azaspiro[4,4]nonane system is directly constructed from dienyl ketone oximes by palladium-catalyzed cascade amino-Heck reaction.



A-1) *Chem. Lett.*, **2001**, 146-147

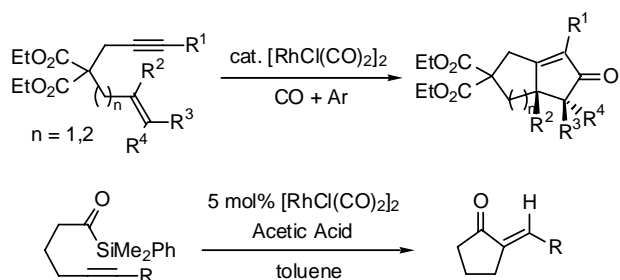
A-3) *Chem. Lett.*, **2001**, 526-527

A-4) *Synlett*, **2001**, 974-976

(2) "Rhodium-Catalyzed Formations of Unsaturated Cyclic Ketones"

A rhodium carbonyl complex, $[\text{RhCl}(\text{CO})_2]_2$ was found to catalyze intramolecular Pauson-Khand type reactions. By the use of the catalyst, cyclopentenone derivatives are prepared

from various 1,7- and 1,6-enynes under atmospheric pressure of CO. This rhodium-catalyzed reaction is accelerated by reducing the partial pressure of CO to less than 1 atm. Furthermore, the rhodium complex also catalyzes the cyclization of 5- and 6-alkynoyl silanes in the presence of acetic acid to afford α -alkylidenecyclopentanones and -cyclohexanones. The reaction seems to proceed *via* transmetalation between the acylsilane moiety and a rhodium(I) complex.

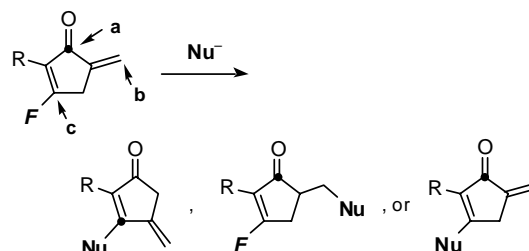


A-2) *J. Organomet. Chem.*, **624**, 73-87 (2001)

A-7) *Chem. Lett.*, **2001**, 1210-1211

(3) "Regioselective Synthesis of Highly Substituted 2-Cyclopentenones from Cross-Conjugated Dienone System"

We reported *fluorine-directed* Nazarov cyclizations of 2,2-difluorovinyl vinyl ketones to afford 3-fluoro-5-methylene-2-cyclopentenone, which is an attractive synthetic intermediate for the preparation of cyclopentenones because of its highly functionalized structure, a cross-conjugated dienone system with a vinylic fluorine. The fluorinated cyclopentenone is treated with appropriate nucleophiles and Lewis acids to undergo regioselective (a) 1,2-addition, (b) exocyclic 1,4-addition, and (c) endocyclic 1,4-addition, leading to a variety of highly substituted cyclopentenones including cyclopentanoid antibiotic methylenomycin B analogues.



a: 1,2-Addition b: *exo*-1,4-Addition c: *endo*-1,4-Addition & Elimination
& 1,3-CO Transposition

A-10) *Org. Lett.*, **3**, 2345-2348 (2001)

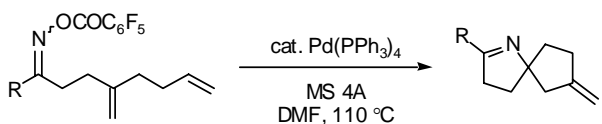
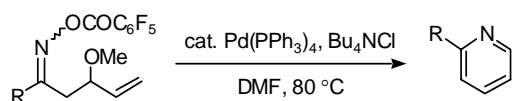
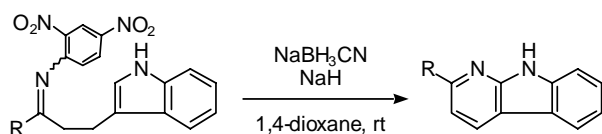
有機合成化学研究室

研究レビュー

(1) オキシム化合物の分子内環化を利用する含窒素ヘテロ環の構築

オキシム化合物は一般にBeckmann転位反応を起こし易いが、我々は転位反応に代わり、オキシムの窒素原子上で置換形式の反応を進行させ、ヘテロ環化合物やアミン類の合成を達成している。この方法論の展開として、オキシムに一電子還元剤や低原子価金属を作用させて窒素ラジカル種や窒素金属種を発生させ、分子内のオレフィンと反応させることによって環化を行い、各種含窒素ヘテロ環骨格の構築に成功した。

分子内に不飽和結合部を有する*O*-2,4-ジニトロフェニルオキシムに一電子還元剤を作用させると、生じたアミルラジカル種が分子内の不飽和結合に付加し、環化生成物である α -カルボリン類等を効率良く与える。また、*O*-アシルオキシムと0価パラジウムとの反応では、アミノパラジウム種を経由してMizoroki-Heck型反応が進行する。すなわち、 γ,δ -不飽和オキシムにパラジウム触媒を作用させるとアミノHeck反応が進行し、条件を選ぶことにより5-*exo*環化生成物であるピロール類あるいは6-*endo*環化生成物であるピリジン類を各々選択的に合成できる。さらに連続環化により、ジエニルケトンオキシムから一挙に1-アザスピロ[4,4]ノナン骨格も構築できる。



A-1) *Chem. Lett.*, **2001**, 146-147

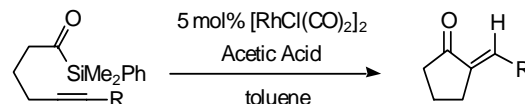
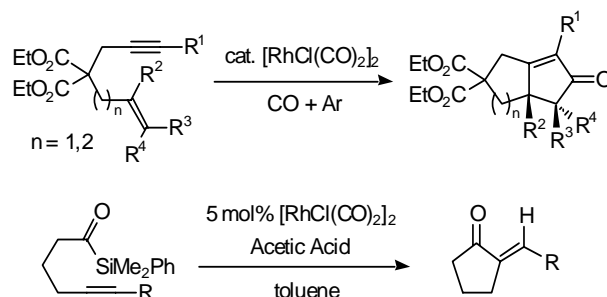
A-3) *Chem. Lett.*, **2001**, 526-527

A-4) *Synlett*, **2001**, 974-976

(2) ロジウム(I)カルボニル錯体を触媒として用いる環状不飽和ケトンの合成

我々は、ロジウム(I)カルボニル錯体が分子内Pauson-Khand反応に有効な触媒になることを見出した。この反応は様々な置換様式の1,6-および1,7-エンインに対して適用でき、環状エンインが得られる。また、一酸化炭素の分圧を1気圧以下にすることで反応が促進されることも明らかにした。

さらに、この触媒が分子内にアルキン部位を有するアシルシランの環化反応にも利用できることがわかった。反応は従来例のないアシルシラン部位とロジウム(I)錯体との間の金属交換を経て進行すると考えられ、様々な不飽和環状ケトンが得られる。

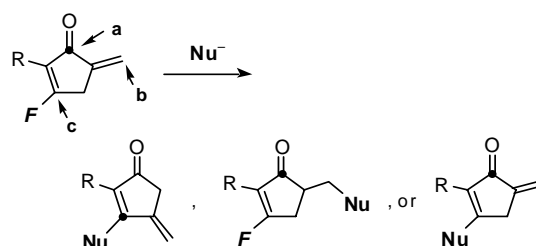


A-2) *J. Organomet. Chem.*, **624**, 73-87 (2001)

A-7) *Chem. Lett.*, **2001**, 1210-1211

(3) 多置換シクロペンテン類の選択的合成

先に我々は、フッ素の特性を利用した選択的Nazarov環化によって、交差共役系を有する含フッ素シクロペンテン骨格の構築に成功している。この化合物は、多様な反応性により有用な合成中間体となる。すなわち、適当な求核剤とルイス酸を選ぶことにより、(a) 1,3-カルボニル転位を伴う1,2-付加、(b) *exo*-1,4-付加、あるいは(c) フッ素の脱離を伴う*endo*-1,4-付加のいずれかを選択的に進行させ、methylenomycin B 類縁体を含む種々の置換シクロペンテンへと誘導できる。



a: 1,2-Addition b: *exo*-1,4-Addition c: *endo*-1,4-Addition & 1,3-CO Transposition & Elimination

A-10) *Org. Lett.*, **3**, 2345-2348 (2001)

A. Original Papers

- 1) A. Ono and K. Narasaka: "Synthesis of α -Carbolines from β -(3-Indolyl) Ketone *O*-2,4-Dinitrophenyloximes", *Chem. Lett.*, **2001**, 146–147.
- 2) T. Kobayashi, Y. Koga, and K. Narasaka "The Rhodium-Catalyzed Pauson-Khand Reaction", *J. Organomet. Chem.*, **624**, 73–87 (2001).
- 3) H. Tsutsui and K. Narasaka: "Synthesis of Pyridine and Isoquinoline Derivatives by the Palladium-Catalyzed Cyclization of Olefinic Ketone *O*-Pentafluorobenzoyloximes", *Chem. Lett.*, **2001**, 526–527.
- 4) M. Kitamura, S. Zaman, and K. Narasaka: "Synthesis of Spiro Imines from Oximes by Palladium-Catalyzed Cascade Reaction", *Synlett*, **2001**, 974–976.
- 5) T. Mikami and K. Narasaka: "Photochemical Transformation of γ,δ -Unsaturated Ketone *O*-(*p*-Cyanophenyl)oximes to 3,4-Dihydro-2*H*-pyrrole Derivatives", *C. R. Acad. Sci. Paris, Chimie/Chemistry*, **4**, 477–485 (2001).
- 6) (Y. Fukuda), (M. Ishibashi), (A. Terasaki), (T. Kondow), (K. Osoda), and K. Narasaka: "Anionic Polymerization of an Acrylonitrile Trimer Studied by Photoelectron Spectroscopy", *J. Phys. Chem., A*, **105**, 7180–7184 (2001).
- 7) M. Yamane, T. Amemiya, and K. Narasaka: "Rhodium(I)-Catalyzed Acylation of Alkyne with Acylsilane: Transformation of 5- or 6-Alkynoylsilane to α -Alkylidenecycloalkanone", *Chem. Lett.*, **2001**, 1210–1211.
- 8) Y. Wada, J. Ichikawa, (T. Katsume), (T. Nohiro), (T. Okauchi), and (T. Minami): "Intramolecular Cyclizations of *o*-Substituted β,β -Difluorostyrenes: Synthesis of 3-Fluorinated Isochromenes and Isothiochromenes", *Chem Bull. Chem. Soc. Jpn.*, **74**, 971–977 (2001).
- 9) J. Ichikawa: "Control over Reactivity of Intermediates by Fluorine Substituent", *J. Synth. Org. Chem., Jpn.*, **59**, 428–429 (2001).
- 10) J. Ichikawa, M. Fujiwara, (S. Miyazaki), (M. Ikemoto), (T. Okauchi), and (T. Minami): "Regioselective Nucleophilic Additions to Cross-Conjugated Dienone System Bearing β -Fluorine: A Versatile Approach to Highly Substituted 2-Cyclopentenones", *Org. Lett.*, **3**, 2345–2348 (2001).

C. Proceedings

- 1) J. Ichikawa, Y. Wada, and T. Mori: "Synthesis of 3-Fluorinated Quinoline Derivative *via* Intramolecular Substitution of *o*-Substituted β,β -Difluorostyrenes", 18th International Congress of Heterocyclic Chemistry (18th ICHC), July, 2001 (Yokohama).