

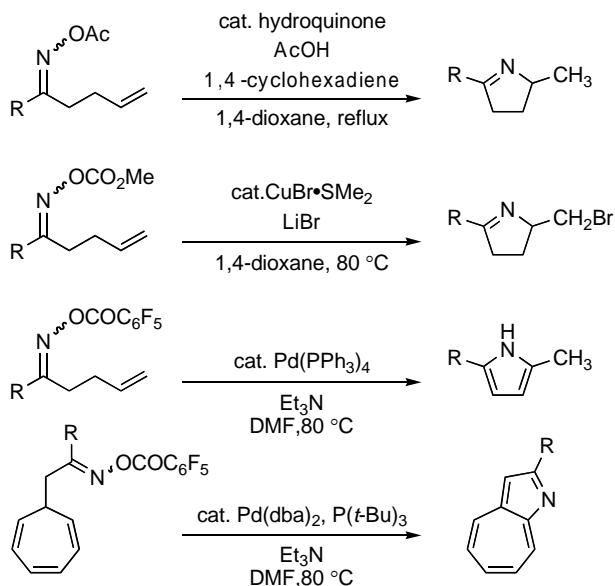
SYNTHETIC ORGANIC CHEMISTRY

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 oxime nitrogen atoms were found in our laboratory, providing various heterocycles. Treatment of *O*-substituted oximes having an olefin moiety with a one-electron reductant generates alkylideneaminy radical species, which in turn readily add to an intramolecular unsaturated bond to give the corresponding cyclization products. 3,4-Dihydro-2*H*-pyrrole derivatives are synthesized from γ,δ -unsaturated ketone *O*-acetyloximes or *O*-methoxy-carbonyloximes on treatment with cat. hydroquinone or Cu(I) salt, respectively.

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. For example, treatment of cycloheptatrienylmethyl ketone oximes with palladium(0) affords 1-azaazulenes in good yield.



A-1) *Chem. Lett.*, **2002**, 144–145

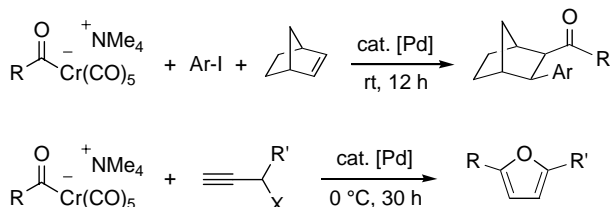
A-2) *Chem. Lett.*, **2002**, 606–607

A-3) *Bull. Chem. Soc. Jpn.*, **75**, 1451–1460

A-4) *Chem. Lett.*, **2002**, 782–783

(2) "Palladium-Catalyzed Preparation of Carbonyl Compounds by Using Acylchromates as Acyl Donors"

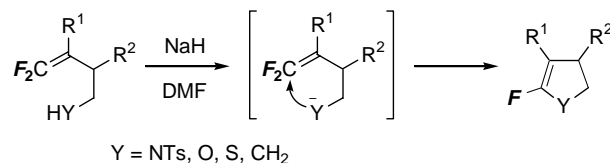
We have been studying on a novel catalytic acylation reaction in which the key intermediate is acylpalladium(II) complexes generated via transmetalation between palladium(II) and acylchromates. This methodology was applied to palladium-catalyzed acylation of alkenes. When reactive alkenes such as norbornene and allenes are treated with aryl iodides, acylchromates, and a catalytic amount of a palladium complex, aryl acylation of the alkenes proceeds at room temperature. Multi-substituted furans are prepared by employing the palladium-catalyzed reaction of acylchromates with propargyl halides. The reaction proceeds via allenyl ketone intermediates.



A-5) *Phosphorus, Sulfur and Silicon*, **177**, 2105 (2002)

(3) "Construction of Ring-Fluorinated Hetero- and Carbocycles via the Nucleophilic 5-endo-trig Cyclization of *gem*-Difluoroalkenes"

5-endo-trig Cyclization has long been considered to be a disfavored process in accord with Baldwin's rules. Especially, nucleophile-driven one has rarely been observed in synthetic chemistry. By using the properties of *gem*-difluoroalkenes: the highly polarized C–C double bond and the remarkable reactivity toward nucleophilic substitution for their fluorines *via* addition–elimination processes, we have succeeded in nucleophilic *5-endo-trig* cyclization of difluoroalkenes bearing *N*-, *O*-, *S*-, or *C*-nucleophiles on the homoallylic position. The cyclizations efficiently provide ring-fluorinated hetero- and carbocycles.



A-9) *Synthesis*, **2002**, 1917–1936

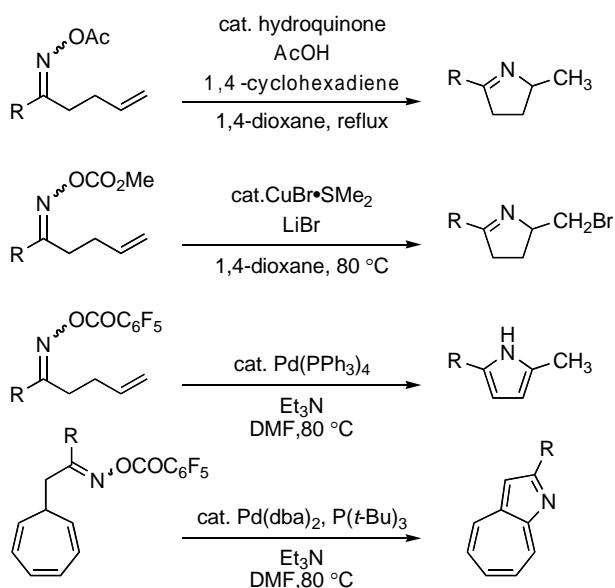
有機合成化学研究室

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

我々は、オキシムで一般に起こり易いBeckmann転位反応に代わり、そ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*-アセチルオキシムや*O*-メトキシカルボニルオキシムにそれぞれ触媒量の臭化銅(I)やヒドロキノンを作用させると、生じたアミラジカル種が分子内の不飽和結合に付加し、環化生成物であるジヒドロピロール誘導体を各々収率良く与える。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經由して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、ピロール類や1-アザブレン類が合成できる。



A-1) *Chem. Lett.*, **2002**, 144–145

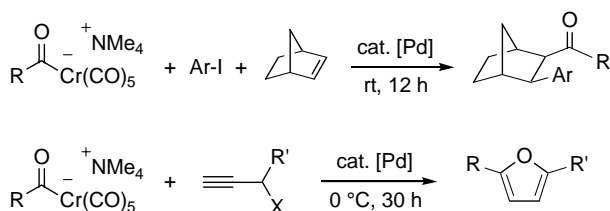
A-2) *Chem. Lett.*, **2002**, 606–607

A-3) *Bull. Chem. Soc. Jpn.*, **75**, 1451–1460

A-4) *Chem. Lett.*, **2002**, 782–783

(2) アシルクロマト錯体をアシル源として用いるカルボニル化合物の触媒的合成

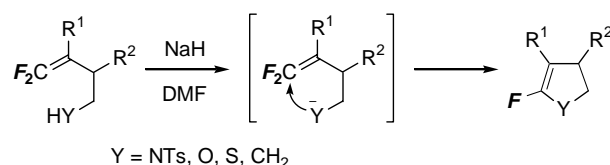
我々は、アシルクロマト錯体と二価パラジウム錯体との金属交換反応によるアシルパラジウム(II)錯体の調製を鍵として、触媒的な新規アシル化反応を開発している。この反応を応用し、ハロゲン化アリアルを用いて、通常困難であるノルボルネンなどのアルケンの触媒的カルボ-アシル化法を開発した。また、アシルクロマト錯体にパラジウム(0)触媒とハロゲン化プロパルギルを作用させると、アレニルケトンを経由して、穏やかな反応条件下に高収率で多置換フランが合成できる。



A-5) *Phosphorus, Sulfur and Silicon*, **177**, 2105 (2002)

(3) ジフルオロオレフィンの求核的 5-endo-trig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、殊に求核的な反応の例は極めて希である。我々は、*gem*-ジフルオロオレフィンが極度に分極した二重結合を備えるとともに、付加-脱離を經由するフッ素の置換を起こし易い点に着目し、ホモアリル位に窒素、酸素、硫黄、炭素の求核部位を導入したジフルオロオレフィンを用いることによって、求核的な5-endo-trig環化を達成した。この反応では、環炭素をフッ素化した各種ヘテロ環および炭素環が良好な収率で得られる。



A-9) *Synthesis*, **2002**, 1917–1936

A. Original Papers

- 1) M. Yoshida, M. Kitamura, and K. Narasaka: "Synthesis of 3,4-Dihydro-2*H*-pyrroles from γ,δ -Unsaturated Ketone *O*-Acetyloximes", *Chem. Lett.*, **2002**, 144–145.
- 2) M. Kitamura, S. Chiba, O. Saku, and K. Narasaka: "Palladium-Catalyzed Synthesis of 1-Azaazulenes from Cycloheptatrienylmethyl Ketone *O*-Pentafluorobenzoyl Oximes", *Chem. Lett.*, **2002**, 606–607.
- 3) H. Tsutsui, M. Kitamura, and K. Narasaka: "Synthesis of Pyrrole Derivatives by Palladium-Catalyzed Cyclization of γ,δ -Unsaturated Ketone *O*-Pentafluorobenzoyloximes", *Bull. Chem. Soc. Jpn.*, **75**, 1451–1460 (2002).
- 4) Y. Koganemaru, M. Kitamura, and K. Narasaka: "Synthesis of Dihydropyrrole Derivatives by Copper-Catalyzed Cyclization of γ,δ -Unsaturated Ketone-*O*-Methoxycarbonyloximes", *Chem. Lett.*, **2002**, 784–785.
- 5) M. Yamane, Y. Kubota, and K. Narasaka: "Palladium-Catalyzed Aryl-Acylation of Alkene", *Phosphorus, Sulfur and Silicon*, **177**, 2105 (2002).
- 6) H. Yanagisawa, K. Miura, K. Narasaka, and (K. Ando): "Intramolecular Substitution Reaction of Alkylidene-Lithium Carbenoids: Regioselective Synthesis of Indenes", *Helv. Chim. Acta*, **85**, 3130–3135 (2002).
- 7) (K. Ohmori), M. Kitamura, (Y. Ishikawa), (H. Kato), (M. Oorui), and (K. Suzuki), "Semi Pinacol Strategy for Constructing B-Ring of Pradimicin-Benanomicin Antibiotics", *Tetrahedron Lett.*, **43**, 7023–7026 (2002).
- 8) J. Ichikawa, K. Sakoda, and Y. Wada: "The 5-*endo-trig* Cyclization of *gem*-Difluoroolefins with sp^3 Carbon Nucleophiles: Synthesis of 1-Fluorocyclopentenes", *Chem. Lett.*, **2002**, 282–283.
- 9) J. Ichikawa, Y. Wada, M. Fujiwara, and K. Sakoda: "The Nucleophilic 5-*endo-trig* Cyclization of 1,1-Difluoro-1-alkenes: Ring-Fluorinated Hetero- and Carbocycle Synthesis and Remarkable Effect of the Vinylic Fluorines on the Disfavored Process", *Synthesis* (Feature Article), **2002**, 1917–1936.
- 10) J. Ichikawa, T. Saitoh, (T. Tada), and (T. Mukaiyama): "A Convenient Method for Carbon Extension of Acetals and Aldehydes by the Use of Ketenedithioacetal and Nucleophiles", *Chem. Lett.*, **2002**, 996–997.