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論　文　名	「Synthetic Studies on Novel Anionic and Transition Metal-Catalyzed Reactions（アニオン種および遷移金属錯体種を活用した合成反応に関する研究）」
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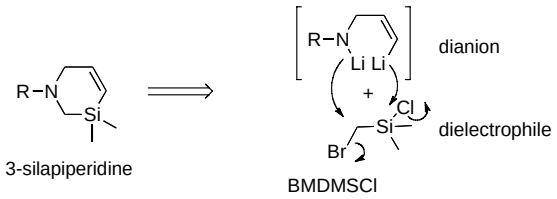
論文要旨

This manuscript will deal with three research area that were studied during this thesis: a strategy employing anionic chemistry as a tool for the synthesis of 3-silapiperidines will be presented, as well as mechanistic studies about 1,5-enynes cycloisomerizations and the synthesis of resorcinols by carbonylative cyclization of vinylpropargylic pivalates.

1) Towards the synthesis of 3-silapiperidines

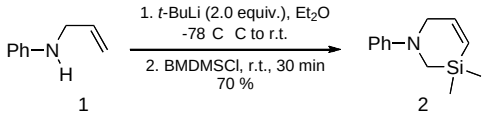
I have developed a new method for the synthesis of 3-silapiperidines starting from secondary allylamines. *N*-silylated allylamines are known to form *cis*-vinylic dianions upon the action of lithium reagent.[1] Therefore, the strategy for the synthesis of silapiperidines relies on the reactivity of the dielectrophilic reagent (bromomethyl)dimethylsilyl chloride (BMDMSCl) with a dianionic species derived from an allylamine (Scheme 1).

The most electrophilic site (at the silicon atom of BMDMSCl) would first undergo the nucleophilic attack of the most basic anion (at the vinylic position of allylamine), followed by a second nucleophilic substitution to form the heterocycle.



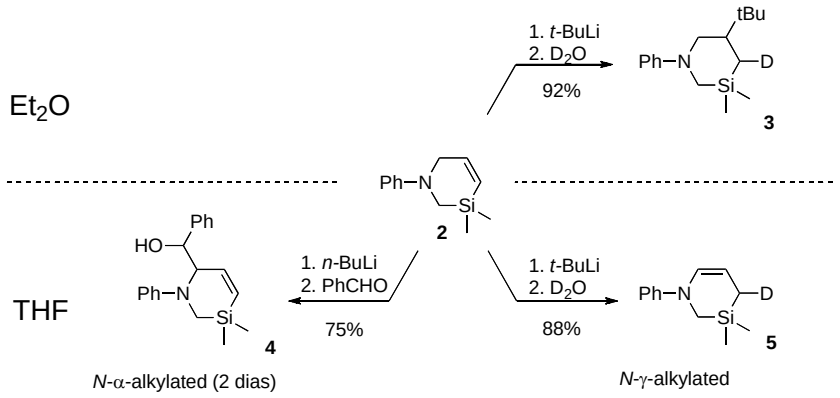
Scheme 1. strategy for the preparation of 3-silapiperidines

It was found that deprotonation of *N*-phenylallylamine **1** with two equivalents of *n*-BuLi or *t*-BuLi followed by the reaction with BMDMSCl gave the expected 3-silapiperidine **2** in 70% yield (Scheme 2).



Scheme 2. Preparation of 3-silapiperidines

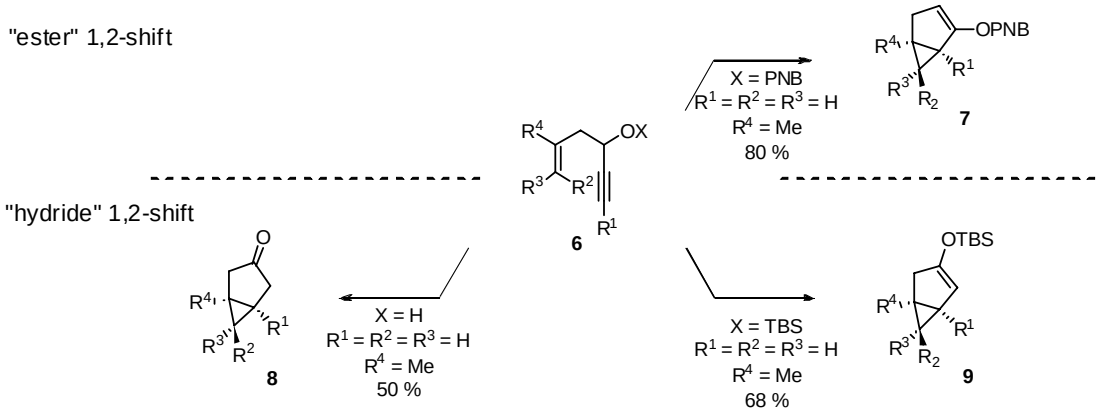
I was then interested in the functionalization of the silapiperidine **2**, therefore this compound was submitted to deprotonation with one equivalent of strong base. Subsequent addition of an electrophile afforded diversely functionalized products (Scheme 3). Besides, the reactivity of the alkyllithium reagent was solvent-dependant, and there were two alkylation sites depending on the electrophile. Silapiperidine **2** underwent conjugate addition of the alkyllithium reagent in diethyl ether to yield saturated silacycles such as **3**. On the other hand, when the reaction was carried out in tetrahydrofuran, products resulting from alkylation at the α-position or the γ-position of the nitrogen (such as **4** and **5** respectively) were formed and reflected the ambident character of the intermediate anion.



Scheme 3. Reaction of 3-silapiperidine **2**

2) Platinum(II)-catalyzed cycloisomerization of 1,5-enynes

Enynes skeletal rearrangements have been in full rise since the seminal reports of Trost in the early 1980's.[2] In particular, transition metal-catalyzed cycloisomerizations of enynes gave facile access to a broad variety of polycyclic structures. Our group was interested in the reactivity of platinum and gold salts and the possibility of these catalysts to promote novel cycloisomerization reactions. For this purpose, I studied the reaction of 1,5-enynes. These substrates led to cycloadducts possessing a cyclopropane moiety and highlighted the importance of the substitution at the propargylic position.



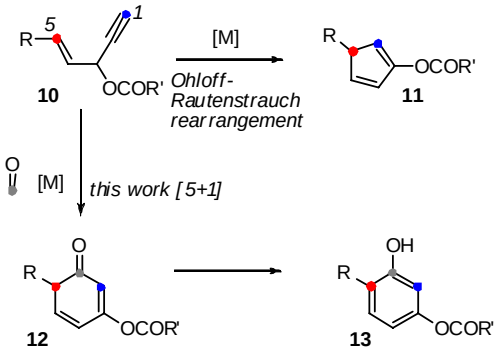
Scheme 4. Cycloisomerization of 1,5-enynes

Propargylic alcohol or silylated ether would undergo the hydride migration to form bicyclic structures of type **8** and **9** whereas a 1,2-shift of the ester would occur in case of a substrate with a *para*-nitrobenzoate moiety at the propargylic position (Scheme 4).

3) Synthesis of functionalized resorcinols from 1,4-enyne esters by [5+1] cycloaddition

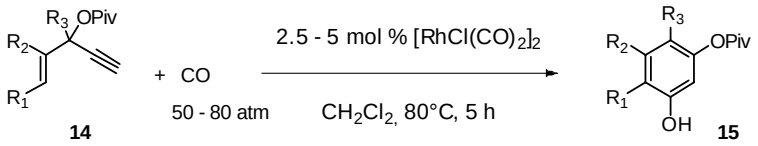
Metal-catalyzed carbonylative cycloaddition have widely been studied since a discovery of a coupling reaction between an alkyne, an alkene and carbon monoxide, which affords cyclopentenones, in the early 1970's by Pauson and Khand.[4] The purpose of this work is to develop a new carbonylative cycloaddition leading to resorcinol derivatives by combining enyne cycloisomerization and carbonylation (Scheme 5).

In this context, I focused my attention on the Pd(II)- or the Pt(II)-catalyzed rearrangement of 1-ethynyl-2-propenyl acetates **10** which give cyclopentadienyl acetates **11**.[5] I anticipated that under carbonylation conditions, CO might be intercepted to give transient **12,** which would eventually lead to the aromatic system of resorcinols **13**.



Scheme 5. Strategy for carbonylative [5+1]-cycloaddition

I found that $[RhCl(CO)_2]_2$ was an efficient catalyst for this reaction. When the reaction of vinylpropargylic pivalates of type **14** was carried out in the presence of a catalytic amount of rhodium catalyst under carbon monoxide pressure, resorcinol derivatives **15** were obtained (Scheme 6). A subsequent saponification of one of the cyclized compound led to the formation of a bioactive molecule.[6]



Scheme 6. Rh-catalyzed [5+1]-cycloaddition of 1,4-enynes with CO

4) Summary

This manuscript is divided into three parts. Initially, the synthesis and functionalization of 3-silapiperidines using dianionic chemistry is presented. Then, platinum and rhodium-catalyzed reactions of propargylic esters are outlined: the formation of [3.1.0] – bicyclic systems by $PtCl_2$-catalyzed cycloisomerization of enynes-1,5 in concomitance to the mechanistic pathways, and the preparation of functionalized resorcinols by $[RhCl(CO)_2]_2$-catalyzed carbonylation of vinylpropargyl pivalates were studied. The results obtained from these studies would provide new methods for the preparation of various cyclic comounds.

審査結果の要旨

本論文は、アニオン種および遷移金属錯体を活用した、有用環状化合物の新規合成法について述べている。その研究の成果として、ジアニオン種を活用したシラピペリジン骨格の新規合成法、白金触媒を用いた 1,5-エンイン類からの多環性化合物の一段合成法、ロジウム触媒を用いたエンインエステル類と一酸化炭素との[5+1]付加環化によるレゾルシノール類の新規合成法の開発を行なっている。また、天然物や天然物の鍵合成中間体の合成も達成しており、これらの反応の有用性を実証している。主な内容は以下のとおりである。

複素環化合物は多くの生理活性物質に含まれるが、その１つの炭素をケイ素に置き換えたケイ素類縁体は、しばしば元となる生理活性物質より高い生理活性を示す。このことからケイ素を含む含窒素複素環化合物の新規合成法の開発は重要な研究課題の一つであるが、本研究では、アリルアミンから容易に調製可能なジアニオン種と容易に入手可能なブロモメチルクロロシランからのシラピペリジンの一段合成に成功している。得られたシラピペリジンの官能基化の検討も行なわれており、生理活性化合物の合成への応用研究が期待される。

また、白金触媒をもちいたプロパルギル化合物の環化異性化反応により多環性化合物の一段合成法を見いだし、Sabinene や *trans*-Sabinene hydrate などの天然物の鍵合成中間体である Sabinaketone の合成も達成している。さらに、反応機構に関する知見を得るとともに不斉合成への展開も行なわれている。

レゾルシノール骨格は多くの生理活性物質に含まれる骨格であるが、ロジウム触媒を用いたエンインエステル類と一酸化炭素との[5+1]付加環化反応による効率的合成法の開発に成功している。本反応では、これまでにほとんど報告例のないプロパルギルエステル類の 1,2-転位を伴ったカルボニル化を達成しており、今後の応用的研究が期待される。また、天然物である Olivetol の前駆体合成を行なうことで本反応の合成反応としての有用性も示している。

以上のように、本論文は、アニオン種および遷移金属触媒を用いた環状化合物の新規合成法の開発を行なっているが、新規反応開発とともに天然物やその鍵合成中間体等の有用化合物の合成を行ない、それら新規反応の有用性を実証している点で高く評価できる。

本委員会は、本論文の審査、最終試験の結果に基づき、博士（理学）の学位を授与することを適当と認める。