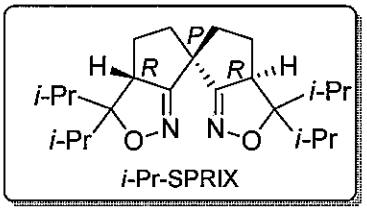
Form 3

Synopsis of Thesis

Title: Development of Novel Enantioselective Cyclative Functionalization of Alkenes and Alkynes: Pd(II/IV) and Pd(0/II) Catalysis Using SPRIX Ligand

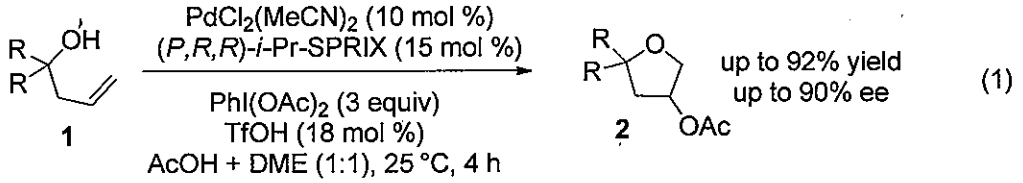
(アルケンならびにアルキンを基質とする新規エナンチオ選択的環化的官能基化反応の開発：SPRIX配位子を活用するPd(II/IV)触媒とPd(0/II)触媒)

Name of Applicant: Dhage Yogesh Daulat



Part A: Catalytic reactions through a Pd(II)/Pd(IV) cycle have received considerable attention in synthetic organic chemistry because they provide attractive access to novel organic compounds that are complementary to those obtained in conventional Pd(0)/Pd(II) processes. Our group have succeeded in the development of an enantioselective Pd(II)/Pd(IV) catalysis by utilizing a chiral ligand *i*-Pr-SPRIX.[1] To further develop an enantioselective Pd(II)/Pd(IV) catalysis, I focused on olefin oxidation reported by Song and Dong, in which homoallyl alcohols **1** were cyclized in a formal 5-*endo*-*trig* mode to give acetoxylated tetrahydrofuran derivatives **2**.[2] Herein I report an enantioselective cyclative acetoxylation of **1** promoted by Pd–*i*-Pr-SPRIX catalyst under Pd(II)/Pd(IV) redox conditions.[3]

After screening of reaction parameters, I eventually found that the addition of catalytic amount of triflic acid (TfOH) served as a key role for achieving high enantioselectivity. Thus, the reaction proceeded by treatment of **1** with 10 mol % of $PdCl_2(MeCN)_2$, 15 mol % of (*P,R,R*)-*i*-Pr-SPRIX, and 18 mol % of TfOH in the presence of 3 equiv of $PhI(OAc)_2$ in a 1:1 mixture of AcOH–dimethoxyethane (DME) at 25 °C for 4 h to afford **2** in moderate to good yields with up to 90% ee. The detailed study on the reaction pathway of this enantioselective transformation has also been investigated.



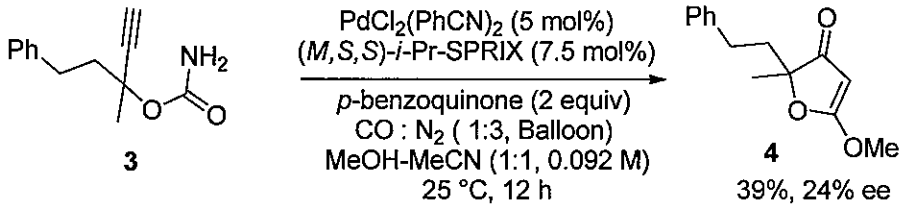
(1)

Part B: The part B is related to the application of SPRIX ligand in asymmetric carbonylative cyclization of propargyl carbamates **3** in order to synthesis the chiral 5-methoxy-3(*2H*)-furanone **4**. 3(2H)-Furanones are structural motifs that are widely present in natural products and medicinally important agents. Due to the importance of the chiral furanones in biologically active compounds, the asymmetric construction of furanones or its derivatives is demanding and challenging task.

The extreme optimization of reaction conditions revealed that (*M,S,S*)-*i*-Pr-SPRIX ligand could induce low enantioselectivity and moderate yield of **4**.

The treatment of **3** with 5 mol % of $PdCl_2(PhCN)_2$, 7.5 mol % of (*M,S,S*)-*i*-Pr-SPRIX, and 2 equiv of *p*-BQ, in presence of CO: N_2 (1:3), in a 1:1 mixture of MeOH–MeCN (Acetonitrile) at 25 °C for 12 h, afforded **4** in 39% yield and 24% ee (eq 2).

The complete study on racemic synthesis of 5-methoxy-3(*2H*)-furanone was developed by Prof. Kato and coworkers.[4]



(2)

References:

1) (a) Tsujihara, T.; Takenaka, K.; Onitsuka, K.; Hatanaka, M.; Sasai, H. *J. Am. Chem. Soc.* **2009**, *131*, 3452. (b) Takenaka, K.; Hashimoto, S.; Takizawa, S.; Sasai, H. *Adv. Synth. Catal.* **2011**, *353*, 1067.
2) Li, Y.; Song, D.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 2962.
3) Takenaka, K.; Dhage, Y. D.; Sasai, H. *Chem. Commun.* **2013**, *49*, 11224.
4) Kusakabe, T.; Takahashi, T.; Shen, R.; Ikeda, A.; Dhage, Y. D.; Kanno, Y.; Inouye, Y.; Sasai, H.; Mochida, T.; Kato. K. *Angew. Chem. Int. Ed.* **2013**, *52*, 7845.

様式 7

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

Yogesh D. Dhage は、Pd-Spiro bis(isoxazoline)錯体（Pd-SPRIX）を触媒とするアルケニルアルコール類のエナンチオ選択的環化反応を見いだしている。本反応は、これまで報告例の非常に少ない四価の Pd が反応に関与する Pd(II/IV)触媒系であり、3－オキシテトラヒドロフラン誘導体が高収率かつ高エナンチオ選択的に得られる。効率的な反応の促進にはトリフロロメタンスルホン酸の添加が必須であり、NMR 等を駆使した反応機構の解析を行った結果、触媒活性種の構造を提示することにも成功している。本研究成果は 2013 年発行の Chem. Commun.誌に速報として発表している。本環化反応は、Pd-SPRIX 触媒を用いないとエナンチオ選択的に進行しない新規反応であり、光学活性な生物活性物質の合成に有用であると期待できる。

本申請者は、Pd 触媒を用いるプロパルギルカルバメートのカルボニル化反応も検討し、一酸化炭素と窒素を混合した条件下において、比較的効率よく反応が進行することも見いだしている。よって本論文は、博士（理学）の学位論文として十分価値あるものと認める。