様　式　Ｃ－１９、Ｆ－１９－１、Ｚ－１９　（共通）

科学研究費助成事業　　研究成果報告書

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研究課題名（和文）Repurposing the novel DATB catalyst for the direct catalytic cross-coupling of carboxylic acids

研究課題名（英文）Repurposing the novel DATB catalyst for the direct catalytic cross-coupling of carboxylic acids

研究代表者

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交付決定額（研究期間全体）：（直接経費）　　3,200,000円

研究成果の概要（和文）：初めは、DATB触媒を遷移金属と組み合わせることで新しい反応経路にアクセスできると予想していました。しかし、1年にわたる無数の試みにもかかわらず、この目標を達成することはできませんでした。そのため、DATBの構造の変更がその反応性にどのような影響を与えるかを探るために、計画を変更しました。私たちのアイデアの一つは、N(BOH)2を含む分子の合成、特性の解析、そして触媒活性のテストでした。幸運なことに、私たちはこの試みに成功し、DATB触媒よりもさらに触媒活性の高い棚上安定化化合物を生成しました。この研究は「Org. Lett. (2023, 25, 4, 694-697)」で発表されました。

研究成果の学術的意義や社会的意義
One of the most frequently encountered reactions in chemistry, especially in medicinal chemistry, is that of amide bond formation. The 'traditional' methods to achieve this transformation necessarily occur with concurrent production of waste materials. This project uncovered a new catalytic method.

研究成果の概要（英文）：We had initially anticipated that the DATB catalyst could be used in tandem with transition metals to access novel reaction pathways. However. despite countless attempts over the course of a year, we we never successful in achieving this goal. As such, we changed modified our plan to exploring how changes to the structure of DATB could alter its reactivity. One of our ideas was to synthesize, characterize and test the catalytic activity of N(BOH)2-containing molecules. While this moiety is structurally similar to DATB, no synthetic pathways to produce it were present in the literature. Fortunately, we were successful in our endevour, producing a shelf-stable compound that was even more catalytically active than the DATB catalyst. The work was published in Org. Lett. (2023, 25, 4, 694-697). This novel catalytically-active moiety likely provides a novel mode of action for amide activation, which warrants further investigation.

研究分野：Catalysis

キーワード：DATB　Catalyst　Boron　Amide bond　Synthesis

研究開始当初の背景

Background at the beginning of the research

Although amide bonds are seen to be ubiquitous in organic chemistry, the main route to this functional group continues to be stoichiometric activation of a carboxylic acid prior to coupling with an amine, resulting in a large amount of waste material. Various boron-containing compounds have been identified as promising catalysts for this transformation, including the recently discovered heterocycle DATB (1,3-dioxa-5-aza-2,4,6-triborinane) – a powerful catalyst with unique mode of action. The novel mode of activation of carboxylic acids could perceivably also be applied to the synthesis of molecules distinct from amides, giving access to a range of otherwise difficult to synthesize materials.

研究の目的

Purpose of research

1) We were seeking to expand the already broad chemical reactivity of carboxylic acids in order to provide rapid access to useful building blocks for chemical synthesis. To mediate this process, we hypothesized that the novel catalyst 'DATB', discovered in our laboratory, could be re-purposed from amide bond synthesis to be used in C-C bond formation reactions.
2) We were looking to improve the catalytic activity of the compound 'DATB', which was discovered in our laboratory. Since the compound was discovered recently, there appeared to be scope to modify its structure to investigate how it would affect its reactivity.

研究の方法

Method of research

1) We initially conducted experiments probing whether a combination of carboxylic acids of varying reactivity, various types of transition metals with an assortment of ligands, and various coupling partners, in the presence of the catalyst DATB, would provide a synthetic shortcut to a variety of otherwise difficult to access chemicals. We then conducted similar

experiments with the carboxylic acid reactive partner ideally being transformed to an activated amide in situ as a reactive partner, and finally attempted the use such reactive amides, synthesized and purified prior to the reaction, instead of starting with a carboxylic acid.

2) We designed and attempted the synthesis of DATB derivative compounds, and following their synthesis, investigated their reactivity compared with the parent compound, as judged by their ability catalyze a standard dehydrative amide bond formation reaction.

研究成果

Research results

When it was found that the original DATB catalyst was not sufficiently powerful to activate carboxylic acids for incorporation into transition metal catalytic pathways, new catalyst designs were considered. The synthesis of these new compounds was found to be very challenging, with even simple modifications preventing the formation of the DATB heterocycle. Despite considerable effort, only a few compounds containing the DATB heterocycle were able to be synthesized, and they were found to have comparatively poor catalytic properties.

It was then hypothesized that molecules containing a N(BOH)2 moiety, which is structurally related to DATB, would be able to activate carboxylic acids in a similar manner. This functional group was not known in the literature, and it took many design iterations and considerable effort to find a synthetic pathway to a compound containing it. Fortunately, we were successful in our endeavor, producing a shelf-stable compound that was even more catalytically active than the DATB catalyst. The work was published in Org. Lett. (2023, 25, 4, 694-697). This novel catalytically active moiety likely provides a novel mode of action for amide activation, which warrants further investigation.

５．主な発表論文等

〔雑誌論文〕　計1件（うち査読付論文　1件／うち国際共著　0件／うちオープンアクセス　0件）

１．著者名 Opie Christopher R.、Noda Hidetoshi、Shibasaki Masakatsu、Kumagai Naoya	４．巻 25
２．論文標題 Less Is More: N(BOH)2 Configuration Exhibits Higher Reactivity than the B3NO2 Heterocycle in Catalytic Dehydrative Amide Formation	５．発行年 2023年
３．雑誌名 Organic Letters	６．最初と最後の頁 694～697
掲載論文のDOI（デジタルオブジェクト識別子） 10.1021/acs.orglett.2c04382	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

〔学会発表〕　計1件（うち招待講演　0件／うち国際学会　0件）

１．発表者名 Christopher Roderick Opie, Nobuaki Kashiwagi, Hidetoshi Noda, Ryosuke Tsutsumi, Masakatsu Shibasaki, Naoya Kumagai
２．発表標題 The Synthesis and Isolation of Novel Bis-Hydroxyboranes and DATB-containing molecules
３．学会等名 The 142nd Annual Meeting of the Pharmaceutical Society of Japan (Nagoya)
４．発表年 2022年

〔図書〕　計0件

〔産業財産権〕

〔その他〕

微生物化学研究所HP https://www.bikaken.or.jp/

６．研究組織

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考

７．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計0件

８．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関