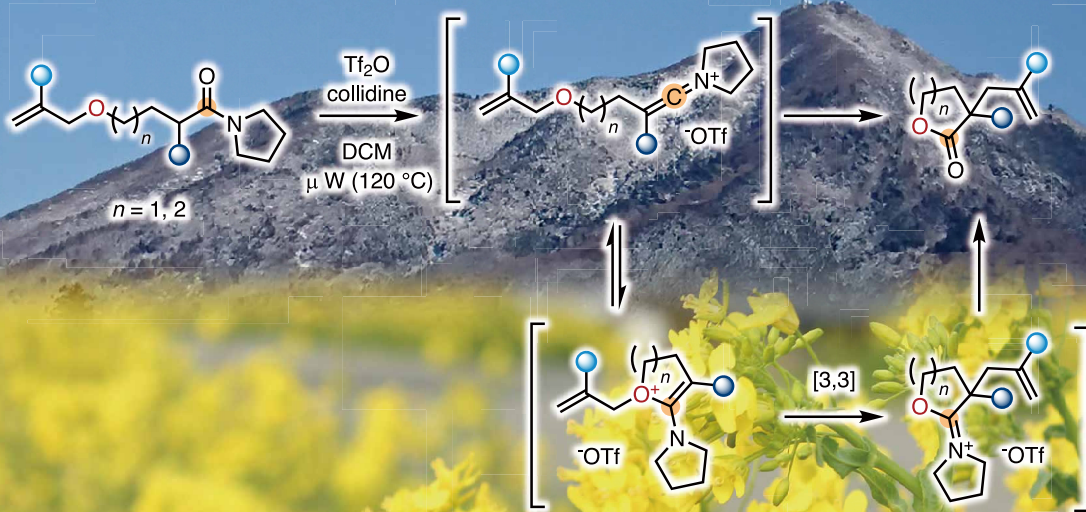


TCIメール

2021年春号 | No. 186



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in Amide Activation:

A Powerful Tool to Forge Heterocyclic Cores

Haoqi Zhang, Margaux Riomet, Nuno Maulide
Institute of Organic Chemistry,
University of Vienna, Austria

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閑話九題

高知工科大学 環境理工学群 教授 西脇 永敏

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導電性ポリマーの原料モノマー



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寄稿論文

Trifluoromethanesulfonic Anhydride in Amide Activation: A Powerful Tool to Forge Heterocyclic Cores

Haoqi Zhang, Margaux Riomet, Nuno Maulide

Institute of Organic Chemistry, University of Vienna, Währinger Strasse 38, 1090 Vienna, Austria

E-mail: maulide@univie.ac.at

Abstract

Trifluoromethanesulfonic anhydride is a powerful reagent for the activation of a wide range of functionalities. Among them, the electrophilic activation of amides is a compelling approach to access heterocycles under mild reaction conditions. Herein, we outline the most recent achievements in the construction of heterocycles *via* amide activation with trifluoromethanesulfonic anhydride.

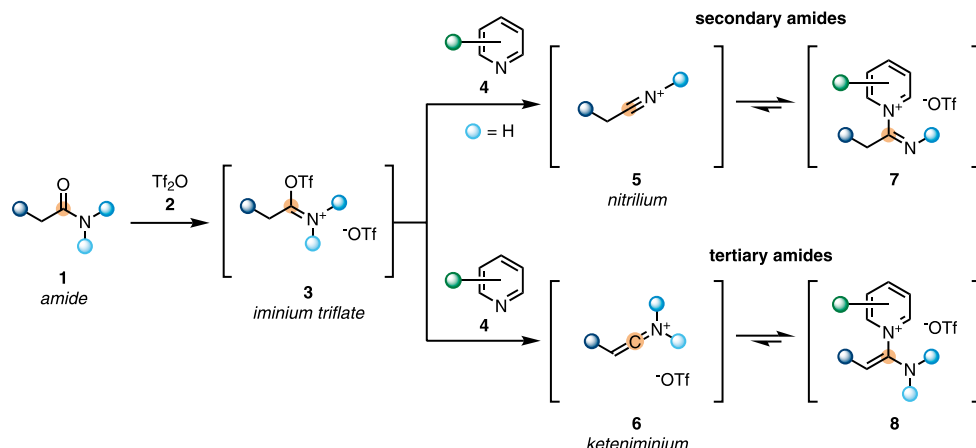
Keywords: Trifluoromethanesulfonic anhydride, triflic anhydride, amide activation, heterocycle, Umpolung

Introduction

In recent decades, trifluoromethanesulfonic anhydride, also known as triflic anhydride, has proven to be an extraordinary reagent for a broad range of transformations. Given its high affinity towards *O*-nucleophiles, reaction with alcohols, carbonyls, sulfur- phosphorus- and iodine oxides towards formation of the corresponding triflates is strongly favoured. As one of the premier leaving groups in organic chemistry, the generated triflates then open the door to various downstream transformations, including (but not limited to) substitution reactions, cross-coupling processes, redox reactions and rearrangements.^[1,2]

In this ocean of possible applications, our group has been particularly interested in the electrophilic activation of amides with triflic anhydride. Thanks to the pioneering work of Ghosez and Charette,^[3,4] it is known that the reaction can proceed through different reactive intermediates, depending on the nature of the amide **1** as well as the presence (or absence)

of a base (**Scheme 1**). When subjected to triflic anhydride **2**, amides are generally rapidly converted to the corresponding iminium triflates **3**. Further deprotonation, usually by a pyridine derivative can lead to formation of a highly electrophilic intermediate – a nitrilium ion **5** in case of secondary amides, or a keteniminium ion **6** for their tertiary counterparts. These ionic species participate in an equilibrium with the pyridine adducts **7** and **8**. Amide activation with triflic anhydride has yielded a literal cornucopia of novel transformations.^[5–7] In particular, recent years have seen its exploitation by various groups for the generation of heterocyclic cores. Due to their pervasive presence in biological and pharmaceutically relevant structures, the preparation of heterocycles remains a focal point in organic synthesis. In this short review, we will focus on recent discoveries for the formation of heterocycles *via* amide activation with triflic anhydride.



Scheme 1. Amide activation with Tf_2O and formation of different reaction intermediates.

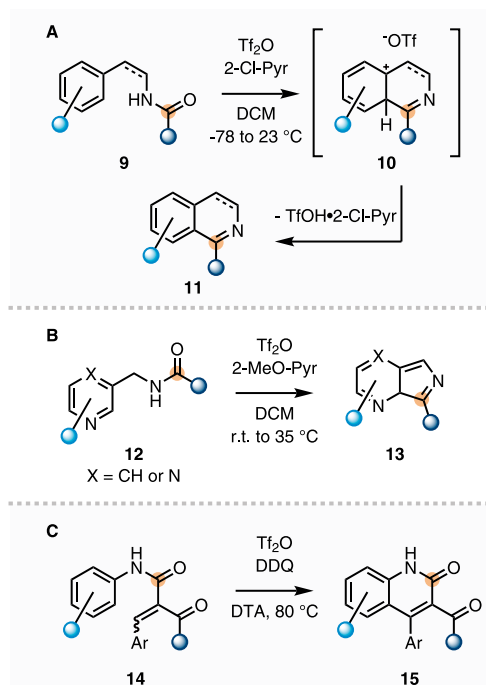
Activation of Secondary Amides with Triflic Anhydride

Intramolecular Annulations

The susceptibility of amides for nucleophilic attacks after activation with triflic anhydride was explored for a range of cyclisation processes. Movassaghi *et al.* showcased its utility for a Bischler-Napieralski type process (Scheme 2A).^[8] After amide activation, the intermediate underwent intramolecular SE_{Ar} reaction; rearomatization then resulted in **isoquinolines 11** and their 3,4-dihydro derivatives. In comparison to classical Bischler-Napieralski conditions using POCl_3 , elevated reaction temperatures could be avoided, while acid-sensitive substrates were well tolerated. As an alternative approach, Hendrickson's reagent, obtained from triphenylphosphine oxide and triflic anhydride, was employed in the same transformation to further exacerbate oxophilicity in the amide activation event.^[9]

As an extension of this mild cyclodehydration reaction, the activation of *N*-(2-pyridinylmethyl)-benzamides **12** with triflic anhydride resulted in formation of bicyclic **imidazo[1,5-*a*]pyridines 13** (Scheme 2B). By utilising an electron richer base in form of 2-methoxy-pyridine in conjunction with mild heating, the conversion could be further increased.^[10] In contrast, amide activation in presence of a conjugated C-C double bond (**14**) led to increased

β -electrophilicity as showcased in the intramolecular cyclisation of *N*-aryl cinnamyl amides **15** (Scheme 2C).^[11] 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was employed as an additional oxidant to decrease the reaction time and improve selectivity towards poly-substituted **quinolin-2(1*H*)-ones 15**.

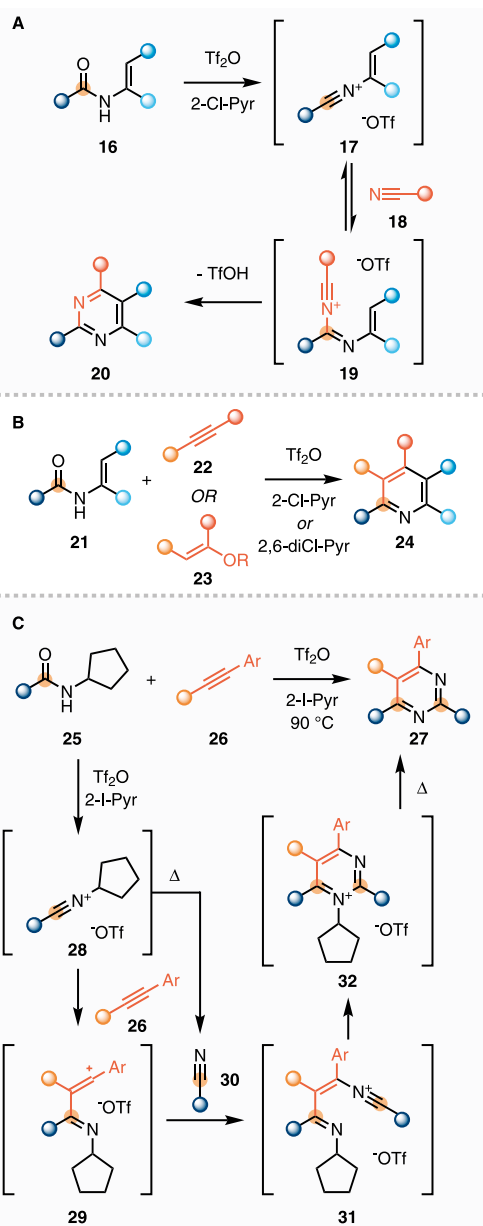


Scheme 2. Intramolecular annulations of activated secondary amides. A: isoquinolines. B: imidazo[1,5-*a*]pyridines. C: quinolin-2(1*H*)-ones (DTA = *N,N*-dimethyl trifluoroacetamide).

Intermolecular Annulations

The activation of amides opens the doorway to a broad range of external nucleophiles. The nucleophilic addition of a nitrile **18** to the *in-situ* formed nitrilium ion **17** led to the formation of a new nitrilium species **19** (Scheme 3A).^[12,13] In presence of an *N*-vinyl or *N*-aryl moiety, Movassaghi showed that this reactive intermediate further underwent an electrocyclisation event, convergently yielding **pyrimidine** derivatives **20**. Similarly, the reaction with alkynes **22** or enol-ethers **23** proceeded with formation of corresponding cations followed by cyclisation and aromatization to **pyridine** and **quinoline** derivatives **24** (Scheme 3B).^[14–16]

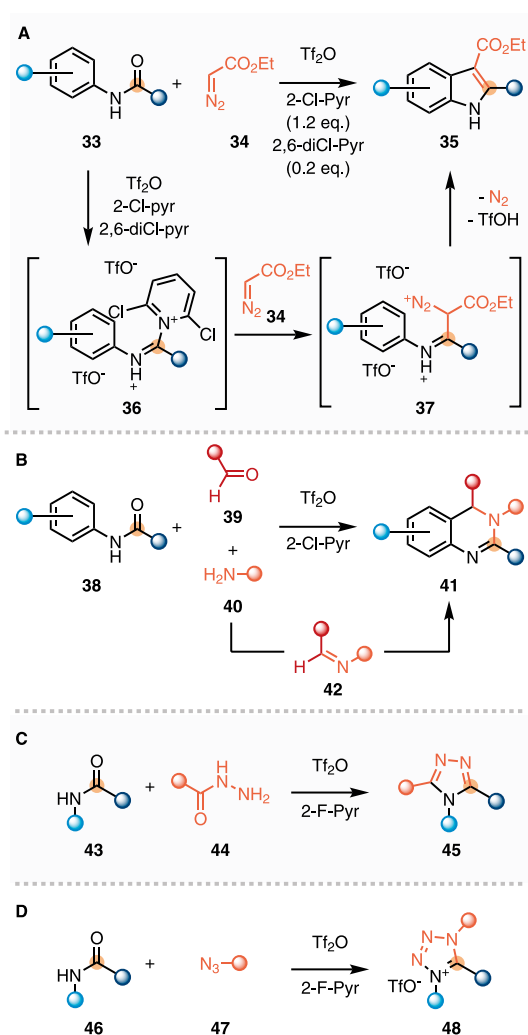
In complementary fashion, our group investigated the transformation with alkynes **26** in absence of *N*-vinyl or *N*-aryl functionality on the amide substrate **25** (Scheme 3C). In comparison to the former approaches, the reaction was conducted at elevated temperature and with an excess of amide starting material, resulting in poly-substituted **pyrimidine** derivatives **27**. Comparable to the previous reaction, a vinylation intermediate **29** is formed after addition of the alkyne substrate **26**. Fuelled by the high reaction temperatures, the initial nitrilium species also partially underwent fragmentation to the corresponding nitrile **30**, which subsequently attacked the vinylation intermediate. Ensuing cyclisation and dealkylation eventually resulted in formation of the heterocyclic core **27**.^[17]



Scheme 3. Intermolecular annulations of activated secondary amides. **A:** **pyrimidines** via nitriles. **B:** **pyridines** and **quinolines** via alkynes and enols. **C:** **pyrimidines** via formal (2+2+2) with alkynes.

Furthermore, the use of ethyl diazoacetate **34** as nucleophile in conjunction with *N*-aryl amides **33**, Wang and coworkers achieved a concise, single step synthesis of **indoles 35** (Scheme 4A).^[18] Of particular note was the necessity for catalytic amounts of 2,6-dichloropyridine in addition to the usual 2-chloropyridine. The authors reasoned this as the consequence of reversible formation of a highly electrophilic species **36**, which could be further intercepted by ethyl diazoacetate **34**. The resulting intermediate **37** underwent a Friedel-Crafts type cyclisation releasing nitrogen gas and producing the indole core **35** after tautomerization. Moreover, the activation of *N*-aryl amides with triflic anhydride was exploited for an one-pot Pictet-Spengler-like cyclisation (Scheme 4B).^[19] This domino process started with the *in-situ* condensation of aldehyde **39** and amine **40** to imine **42**, followed by nucleophilic attack thereof on the activated amide, prior to electrophilic aromatic substitution to obtain **3,4-dihydroquinazolines 41**.

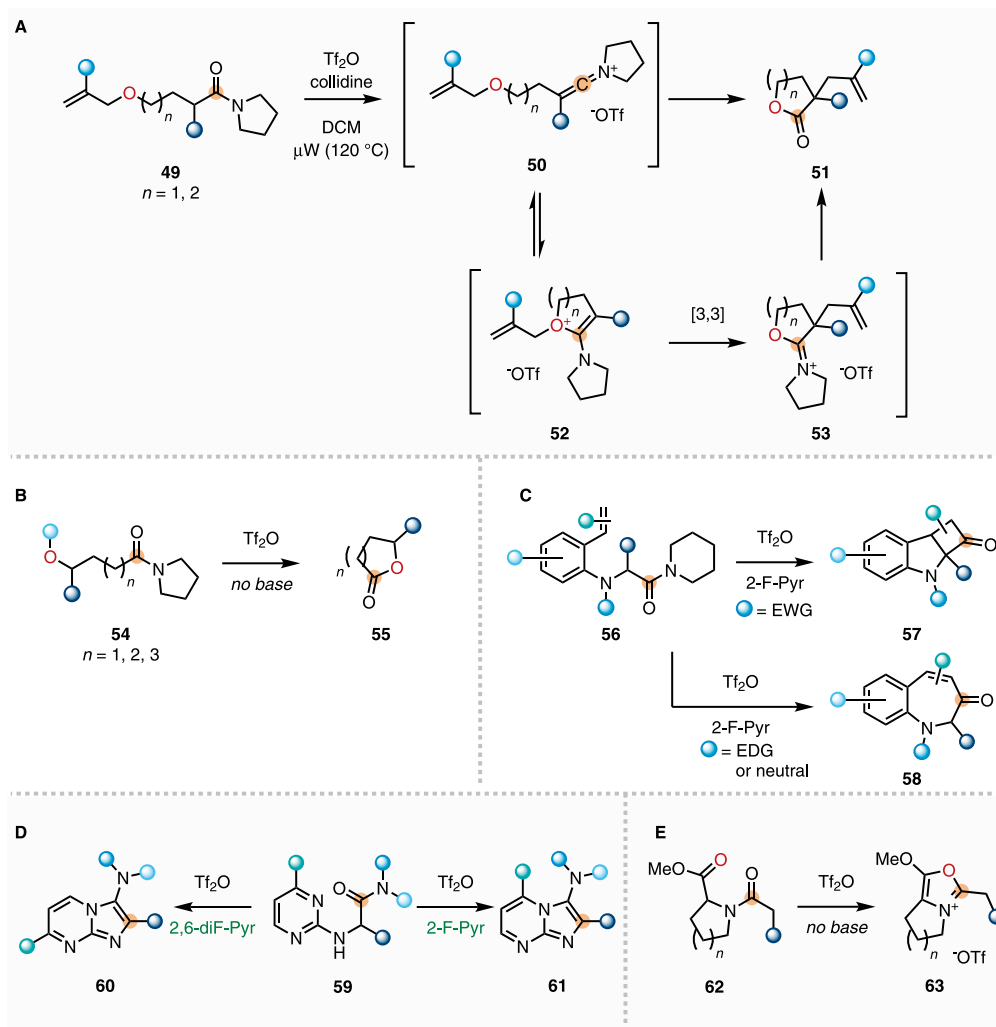
In absence of *N*-aryl or *N*-vinyl moieties, the cyclisation event can also be realized by condensation of the former amide nitrogen. This approach was employed for the synthesis of highly substituted **1,2,4-triazoles 45** (Scheme 4C).^[20] Here, the attack of hydrazide **44** on activated amide **43** was followed by cyclodehydration to forge the heterocyclic core. In parallel, our group has realized the regioselective synthesis of **tetrazolium** scaffolds **48** through a formal [3 + 2] cyclisation (Scheme 4D).^[21] Computational studies revealed a stepwise mechanism initiated by the nucleophilic attack of azide **47** on the nitrilium intermediate, followed by annulation to the final heterocycle.



Scheme 4. Attack of various nucleophiles on nitrilium ion and subsequent cyclisation. **A:** indoles via ethyldiazoacetate. **B:** 3,4-dihydroquinazolines via Pictet-Spengler-like cyclisation. **C:** 1,2,4-triazoles via hydrazines. **D:** tetrazolium ions via azides.

Activation of Tertiary Amides with Triflic Anhydride

Intramolecular Annulations



Scheme 5. Intramolecular cyclisations initiated by activation of tertiary amides. **A:** lactones by rearrangement of ethers. **B:** lactones by attack of alcohol derivatives. **C:** benzazepinones with alkenes. **D:** base dependent regio-selective formation of pyrimidines. **E:** oxazolium ions in absence of base.

Compared to the aforementioned secondary amides, the activation of tertiary derivatives with triflic anhydride in presence of a weak nucleophilic base typically forms keteniminium ions as reactive intermediates. Our group investigated the reactivity of tertiary amides **49** carrying an inbuilt ether moiety (Scheme 5A).^[22] After formation of intermediate **50**, the reaction favoured the nucleophilic attack of the ether oxygen and formation of oxonium

ion **52**. The intermediate subsequently underwent a [3,3]-sigmatropic rearrangement, leading to intermediate **53**. Further hydrolysis resulted in functionalised 5- and 6-membered lactones **51**. Complementary to this work, the direct use of alcohols or ether derivatives **54**, non-amenable to sigmatropic rearrangement, produced the 5-, 6- and 7-membered heterocycles **55** (Scheme 5B).^[23] For this approach, the absence of the usual base was crucial to avoid

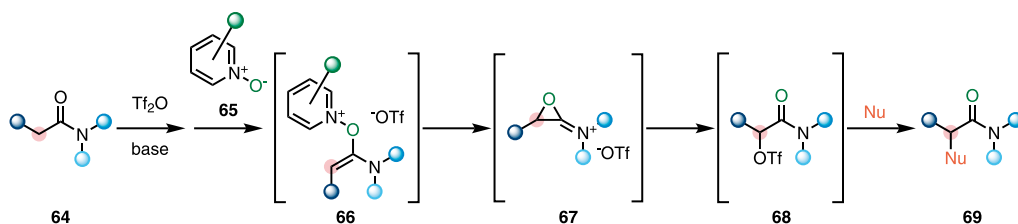
formation of elimination products. The competition between the [2+2] cycloaddition and nucleophilic pathways with alkenes was further investigated by De Mesmaeker and coworkers with α -aminoamides **56** (Scheme 5C).^[24] In presence of an electron-withdrawing substituent on the amino nitrogen **56**, the [2+2] cyclisation was favoured. With electron-neutral or -donating substituents on **56**, amide activation promoted the nucleophilic attack of the styryl group and ultimately yielded **benzazepinones 58**.

Additionally, the susceptibility of keteniminium ions towards intramolecular capture was showcased in the synthesis of 3-amino-**thiophene** derivatives^[25–27] and aminoimidazo-**pyrimidines 60** and **61** (Scheme 5D).^[28] In the latter reaction, the nature of the base played a paramount role in the regioselectivity. The authors hypothesised that the 2-fluoropyridine-promoted reaction kinetically favoured the cyclisation to pyrimidine **60**. On the other hand, 2,6-difluoropyridine primary acted as a buffer for the *in situ* generated triflic acid and thus supported the formation of the thermodynamic product **61**. Our group further investigated the role of the pyridine base during regio- and chemoselective cyclisation of amide **62** to bicyclic alkoxy **oxazolium** ions **63** (Scheme 5E).^[29]

To our surprise, the addition of a base suppressed the reaction and only starting material was recovered. In stark contrast, the absence of base quantitatively yielded the desired heterocycle.

α -Umpolung of Amides with Triflic Anhydride

In all presented cases above, the electrophilic activation of amides yields a highly electrophilic amide carbon. Under suitable conditions, this reactivity can also be transferred to the usually nucleophilic α -carbon. This concept was recently investigated by our group in the α -Umpolung of amides (Scheme 6). Following activation with triflic anhydride, the keteniminium intermediate can be intercepted by a pyridine-*N*-oxide derivative **65**, forming the adduct **66**. It is noteworthy that this species possesses electrophilic character at what was formerly the α -carbon to the amide functionality in the starting amide **64**. Postulated fragmentation to the epoxide **67** allows attack at the α -carbon by triflate ion. In contrast to the starting amide **64**, the resulting reactive key intermediate **68** is now susceptible toward nucleophiles at the α -position, opening up a broad range of new transformations.



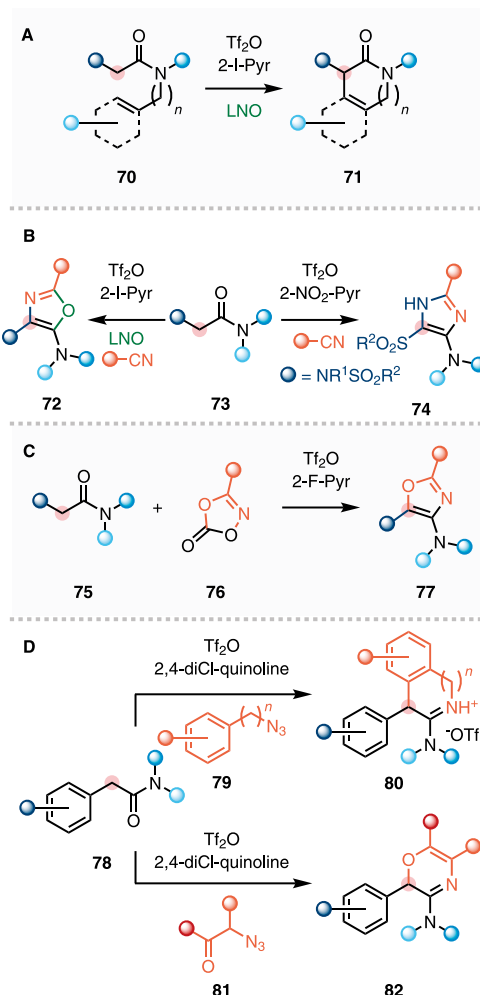
Scheme 6. Umpolung of amides with triflic anhydride and *N*-oxides

Our group utilised this electrophilic Umpolung of amides for an intramolecular, metal-free C-C coupling reaction (Scheme 7A).^[30] As opposed to previously discussed transformations originating from a Friedel-Crafts-like cyclisation, the activation of amide **70** and subsequent Umpolung by lutidine *N*-oxide resulted in C-C coupling at the α -carbon, ultimately affording a broad range of **pyridinone** and **isoquinolinone** derivatives **71**.

Further investigation revealed that the absence of an internal nucleophile in nitrile solvents leads to a different reaction mode (Scheme 7B).^[31] Instead of the formation of the triflate intermediate, the *in-situ* formed epoxide was attacked by the ubiquitous solvent, resulting in the annulation product **74**. By exchanging acetonitrile to alternative nitriles, a broad palette of amino-**oxazoles** could be synthesised.

Additionally, the employment of an *N*-sulfonyl functionality at the amide α -position resulted in a mechanistically intriguing rearrangement sequence. In absence of the competing *N*-oxide, the transformation involved migration of the sulfonyl group, consequently yielding **imidazole** derivatives **72** as the final products. In a similar fashion, using 1,4,2-dioxazol-5-ones (as both Umpolung-reagent and nucleophilic substrate), an alternative direct synthesis of amino-**oxazole** scaffolds **77** was achieved (**Scheme 7C**).^[32]

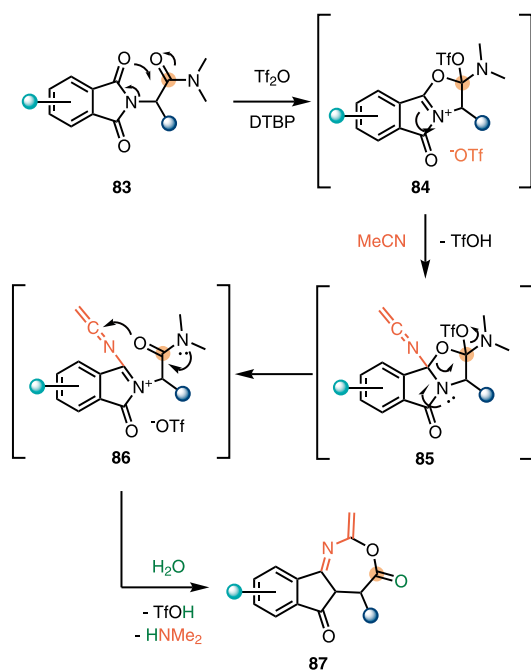
By taking this concept further, arylalkylazides **79** were investigated as Umpolung reagents and nucleophiles to forge heterocycles. In presence of a bulky, weak nucleophilic base, such as 2,4-dichloroquinoline, addition of arylalkylazide **79** resulted in a domino cyclisation event (**Scheme 7D**).^[33] Depending on the chain length of the azides, 6- or 7-membered **cyclic amidiniums 80** were accessible. By interchanging the arene functionality with other nucleophiles such as ketones or esters, an efficient synthesis of functionalised **oxazines/oxazinones 82** was achieved.



Scheme 7. Heterocycle formation by Umpolung of amides. **A:** pyridinone and isoquinolinone derivatives by C-C coupling. **B:** imidazoles and oxazoles via nitriles. **C:** oxazoles with 1,4,2-dioxazol-5-ones as the Umpolung-reagent. **D:** cyclic amidiniums and oxazine derivatives with azides and cascade cyclisation.

Miscellaneous

In addition to the discussed methodologies, the mild activation of amides with triflic anhydride also allows unusual reactivity *en route* to heterocycles. In an example from our own work, the presence of a phthalimide functionality on the α -branched amide **83** led to an unexpected rearrangement reaction with acetonitrile (Scheme 8).^[34] In contrast to the usual conditions, 2,6-di-*tert*-butylpyridine (DTBP) was used as a base. We hypothesized that this base would not add to the activated amide, thus favouring cyclisation to **84**. A nucleophilic attack followed by deprotonation of acetonitrile might then afford intermediate **85**. Subsequent ring opening to **86**, followed by 7-membered ring closure and hydrolysis resulted in novel heterocyclic scaffolds **87**.



Scheme 8. Synthesis of novel heterocycles by a cascade rearrangement reaction.

Conclusion

The electrophilic activation of amides with triflic anhydride provides a mild and sustainable approach to forge heterocyclic cores. Depending on the nature of the amides and the presence or absence of base additives, highly reactive intermediates in form of vinyl- triflates, nitrilium ions or keteniminium ions are accessible. Each of these species offers new pathways for functionalisation and annulation, leading to a wide palette of heterocycles. By using suitable reacting partners, such as *N*-oxides or azides, the α -Umpolung of amides is enabled. This in turn opens the door to an array of powerful transformations, including C-C bond formation, α -oxidation and mechanistically intriguing rearrangement reactions. The breadth of recent examples of heterocycle formation highlights the utility of triflic anhydride for electrophilic amide activation and outlines its potential for the future discovery of further, hitherto unknown transformations.

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執筆者紹介

**Haoqi Zhang**

B.Sc., M.Sc.

Institute of Organic Chemistry, University of Vienna

Haoqi Zhang is a Ph.D. student in the group of Professor Nuno Maulide at the University of Vienna, where he received his MSc degree in 2020 working on electrophilic Umpolung of amides for the construction of cyclic amidines and oxazines. For his Ph.D. thesis, he remained at the Maulide Group and his current interest lies in natural product synthesis and drug design.

**Margaux Riomet**

Dipl.-Ing. Dr., M.Sc.

Institute of Organic Chemistry, University of Vienna

Margaux Riomet currently occupies a postdoctoral position in the research group of Professor Nuno Maulide at the University of Vienna. She studied chemistry at Ecole Nationale Supérieure de Chimie de Paris where she completed her Engineering Degree and Msc degree in 2015 in partnership with Université Pierre et Marie Curie. In 2018, she obtained her PhD degree under the supervision of Dr. Frédéric Taran at CEA Saclay. Her Ph. D. work was dedicated to the chemistry of iminosydnone and their applications in biology. Her current research interests combine the development of new methodologies for synthesis and the design of molecular objects for live cell imaging.

**Nuno Maulide**

Professor, Ph.D.

Institute of Organic Chemistry, University of Vienna

Nuno Maulide is a Full Professor and Chair of Organic Synthesis at the University of Vienna. He obtained a Ph.D. in 2007 at the Université catholique de Louvain under the supervision of Prof. István E. Markó. Subsequently, he joined the group of Prof. Barry M. Trost at Stanford University for a post-doctoral stay in 2007-2008. In 2009, he started his independent career as a Max-Planck-Research Group Leader at the Max-Planck Institut für Kohlenforschung. In 2013, he moved to his current position as a Full Professor at the University of Vienna. Since 2018, he is an Adjunct PI at CeMM. He is a member of the Board of Editors for Organic Synthesis (2018) as well as an Associate Editor of Organic Letters (2018) and JACS AU (2020). For his research, he received numerous awards, including the recent Tetrahedron Young Investigator Award (2020), Springer Heterocyclic Chemistry Award (2018) and 3 ERC Grants. Nuno Maulide was named Scientist of the Year in Austria (2019) and is an elected Corresponding Member of the Austrian Academy of Sciences (2018).

関連製品

Trifluoromethanesulfonic Anhydride (Tf ₂ O)	10g 6,900円	25g 12,200円	250g 59,900円	T1100
2-Chloropyridine (2-Cl-Pyr)	25g 2,000円	100g 3,500円	500g 9,700円	C0279
2-Methoxypyridine (2-MeO-Pyr)			25mL 3,000円	M0788
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)		25g 12,100円	250g 63,800円	D1070
N,N-dimethyl trifluoroacetamide (DTA)		5g 4,200円	25g 12,700円	T3262
2-Fluoropyridine (2-F-Pyr)		25g 7,900円	100g 23,600円	F0217
2,6-Dichloropyridine (2,6-diCl-Pyr)		25g 2,100円	500g 15,200円	D0410
2-Iodopyridine (2-I-Pyr)		5g 7,000円	25g 23,000円	I0533
2,4-Dichloroquinoline (2,4-diCl-quinoline)		5g 11,400円	25g 38,800円	D4452
2,6-Di-tert-butylpyridine (DTBP)		5g 10,900円	25g 37,800円	D1804

化学よもやま話

閑話九題

高知工科大学 環境理工学群 教授 西脇 永敏

閑話とは暇に任せてする無駄話です。この度、大学の研究室における閑話を3回に亘って連載することになりました。学生さんにとって、1つでも参考になるものがあれば幸いです。今回は溶媒に関するお話にお付き合い下さい。

その1 エチル基降臨

文子さんが反応を仕込んでいた。TLC（薄層クロマトグラフィー）で反応追跡すると、原料のスポットが徐々に消失し、生成物のスポットが新たに現れていた。文子さんは早速に溶媒を減圧留去して、反応混合物のNMRを測定したところ、エチル基のシグナルが観察された。どこにもエチル基を有する試薬を使っていないにも拘らず、である。訳が分からなくなって先生に相談したところ、「クロロホルムを溶媒に使った?」と訊かれた。「はい」と答えると、先生は「やっぱり」と納得したが、文子さんには何のことかさっぱり分からないままであった。

⇒ クロロホルムのようなハロゲン含有溶媒は、毒性の観点から工業的には使用がかなり制限されています。とはいえ有能な溶媒ですので、大学の研究室で依然として使用されています。その一方で、特異な反応を引き起こすことがあります。その原因の1つが含まれている微量の酸であり、もう1つが安定剤として含まれているエタノールで、クロロホルムが分解してホスゲンが発生するのを防いでいます。エタノールは反応性が高い化合物ですので、反応に関与することがたまにあります。しかし、身に覚えのないシグナルが現れると焦りますよね。

その2 だまそう（DMSO）と思っても、その手には・・・

瑞紀くんが合成した新規化合物のスペクトルデータを集めていた。 ^1H NMRを測定すると、目的とする化合物の構造に矛盾のないスペクトルが得られた。しかし、重クロロホルムに対する溶解性がそれほど高くはなく、 ^{13}C NMRまでは測定できなかった。そこで、溶媒を重DMSO（ジメチルスルホキシド）に替えて ^{13}C NMRを測定すると、考えていた構造とは矛盾するスペクトルが得られた。そこで、 ^{13}C NMRの測定に用いた試料を用いて ^1H NMRを測定してみると、そこには全く異なったシグナルが観察されたのであった。

⇒ DMSO は高極性の溶媒で極性化合物の多くを溶解してくれます。ただ、高沸点で留去が困難なところが難点ですが。NMR 用の溶媒には比較的安価な重クロロホルムが用いられますが、難溶性の化合物の場合には重 DMSO が用いられます。しかし、溶媒に溶かしただけで、何も変化しないというのは勝手な思い込みで、周りの極性が変われば構造が変化してしまうこともあります。面倒臭がらずに、それぞれの溶媒でデータを収集しなければなりません。逆にそのような小さな変化を見逃さないようにすれば、新しいテーマの展開に繋がることもあるかもしれません。

その3 雲散霧消

ある梅雨空の日、文子さんがひだ折りろ紙を使って、ジエチルエーテル溶液をろ過していた。ろ過は順調に進んでいたが、ろ紙の淵にきれいな無色の結晶が析出する様子が観察された。結晶というのは化学者にとって魅力的なものである。文子さんはその結晶をスパチュラで取ろうとしたが、すくい上げた瞬間消えてなくなった。しかし、ろ紙の上には嘲笑うかのように再び結晶が析出していた。簡単に手に入らないものほど追いかけてくのが人情である。その後、文子さんはろ紙の上に現れる結晶を追いかけて、何度もトライを重ねたが、結局その努力は実を結ばれることはなかった。

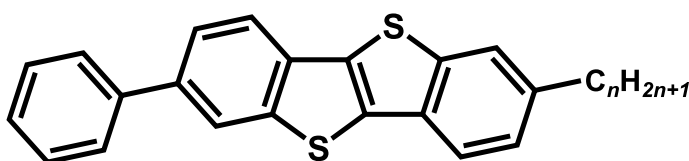
⇒ ジエチルエーテルは研究室で用いる有機溶媒の中でも低沸点、高揮発性の溶媒です。高温多湿の日にはろ過をしていますと、表面積の大きなろ紙上からどんどん揮発していきます。その際、気化熱を周囲から奪いますので、空気中の湿気がろ紙上に凝結します。そう、文子さんが取ろうとしていたのは、水の結晶だったのです。すぐに現れますけれど、取り出すと消えて無くなるのは当然ですね。しかし、何でも取って明らかにしてやろうという貪欲さは研究に必要な姿勢です。

執筆者紹介



1991年 大阪大学大学院工学研究科応用精密化学専攻博士後期課程修了,
同年 大阪教育大学教育学部助手,
2001年 同准教授,
2000—01年 デンマークオーフス大学博士研究員,
2008年 阿南工業高等専門学校准教授,
2009年 高知工科大学環境理工学群准教授,
2011年より現職

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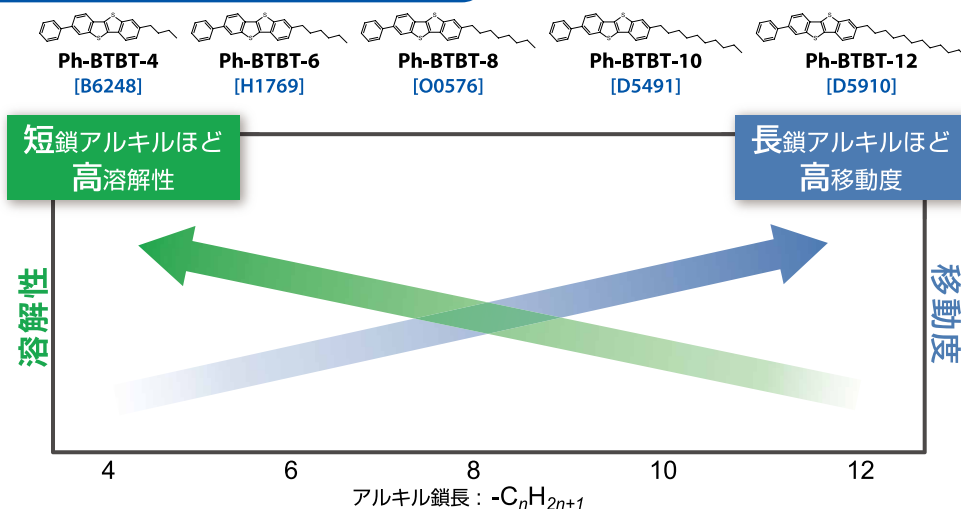
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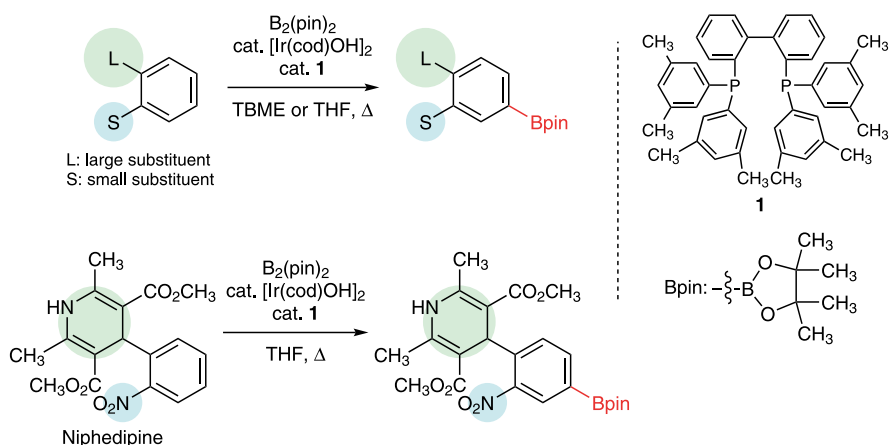


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瀬川, 伊丹らは, 2,2'-ビス[ビス(3,5-ジメチルフェニル)ホスフィノ]-1,1'-ビフェニル(1)とイリジウム塩から形成される錯体が, 位置選択的なホウ素化反応を触媒することを報告しています¹⁾。このホウ素化反応は, オルト二置換ベンゼン誘導体の, より大きな置換基に対しパラ位選択的に進行します。さらに, この反応は官能基許容性が高いため, 合成後期でのホウ素化やさらなる変換ができます。そのため創薬や機能性材料の研究に用いられることが期待されます。なお, このイリジウム錯体は一置換ベンゼンにおいてもパラ位選択的にホウ素化反応が進行することが報告されています²⁾。



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高い光透過性と安定性を備えた導電性ポリマーの原料モノマー

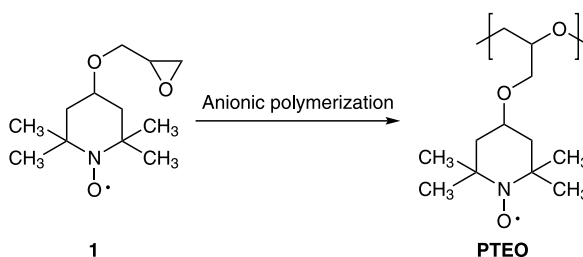
4-Glycidyloxy-2,2,6,6-tetramethylpiperidine 1-Oxyl Free Radical (**1**)

製品コード: G0555

1g 5,100円 5g 17,800円

導電性ポリマーは、帯電防止材料、電極材料、蓄電池材料などの用途が期待されています¹⁾。PEDOT/PSSを始めとする導電性ポリマーは、高い電気伝導率を持たせるために化学的にドーピングされている必要があります。しかし、化学ドーピングされた π 共役ポリマーは可視光領域での光透過性に乏しいこと、ドーピングの添加量により導電性能が変化しやすいこと、ドーパントの添加により材料とデバイスの安定性を低下させることが懸念されます。そこで、ドーピングなしで高い導電率を示し、かつ、電気的に中性のポリマーを開発することは、これらの問題を解決する糸口となります。

さて、TEMPOなどの開殻構造をペンダントに有する有機ラジカルポリマーは、その高い電気的性能から近年注目を集めています。そこでBoudourisらは、4-グリシジルオキシTEMPO (**1**)をアニオン開環重合させて、有機ラジカルポリマーPTEO (poly(4-glycidyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl))を開発しました²⁾。PTEOは他の有機ラジカルポリマーに比べて1,000倍もの導電性を示し、可視領域の光透過性が高いことが明らかとなりました。そのため、これらラジカルポリマーから作られるフィルムは、高い光透過性と安定性を備えた導電性材料になることが期待されます。



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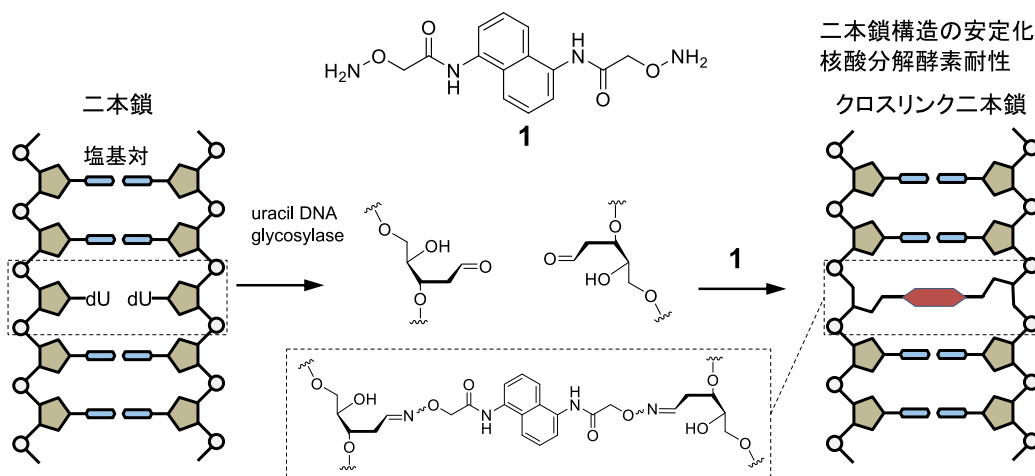
二本鎖核酸の脱塩基部位を認識して連結するジアミンクロスリンカー

***N,N'*-(Naphthalene-1,5-diyl)bis[2-(aminooxy)acetamide] (1)**

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N,N'-(ナフタレン-1,5-ジイル)ビス[2-(アミノオキシ)アセトアミド] (aoNao, **1**)は、二本鎖オリゴヌクレオチドの向かい合った脱塩基部位を共有結合し二本鎖をクロスリンクすることができます¹⁾。クロスリンクされた二本鎖は、一本鎖に解離せずに剛直な構造を形成して熱的安定性および核酸分解酵素への耐性が向上します²⁾。また、クロスリンクされた二本鎖を有するオリゴヌクレオチドは細胞内での安定性が持続するため、アンチセンス核酸などの修飾としても利用可能です^{3,4)}。さらに、**1**はオリゴヌクレオチドに限らず、一般的なクロスリンカーとしても用いることが可能です。

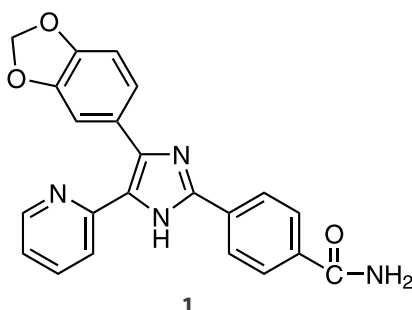


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アクチビン受容体様キナーゼ阻害剤


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SB431542 (**1**)はアクチビン受容体様キナーゼ(ALK)ファミリー-ALK4, ALK5, ALK7の特異的で強い阻害剤です¹⁾。また,**1**はTGF- β 感受性の細胞においてTGF- β の介在するSMADの活性化とフィブロネクチンとコラーゲンの発現の誘導を阻害します²⁾。

山中らが体細胞からiPS (induced pluripotent stem)細胞への再プログラミング因子を同定して以来³⁾,これらの因子の化学的代替物に関する研究も進んできました(例えば文献4,5)。**1**もマウスの線維芽細胞のiPS細胞へのリプログラミングにおいて再プログラミング因子の1つであるSox2を代替できることが報告されています⁶⁾。

本製品は試薬であり, 試験・研究用のみにご使用ください。

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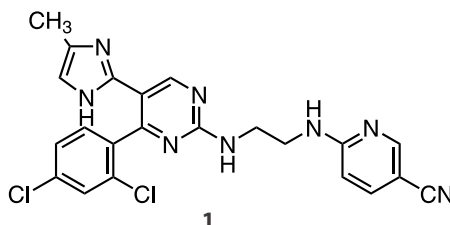
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CHIR 99021 (1)は、細胞透過性で高い選択性を有するGSK-3阻害剤¹⁾で、GSK3 α (IC₅₀ = 10 nM) と GSK3 β (6.7 nM)を阻害します²⁾。また、1はマウス胚性幹細胞の自己複製のキー化合物として使用されます³⁾。サイトカインを含まない条件で1とmTORとラパマイシンを組み合わせると、マウス及びヒト造血幹細胞を維持します⁴⁾。1の存在下では、OCT4を発現させたCD34⁺ヒト血液細胞は間葉系幹細胞(iMSCs)へ転換されます⁵⁾。

本製品は試薬であり、試験・研究用のみにご使用ください。

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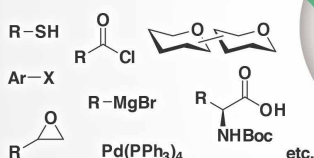
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