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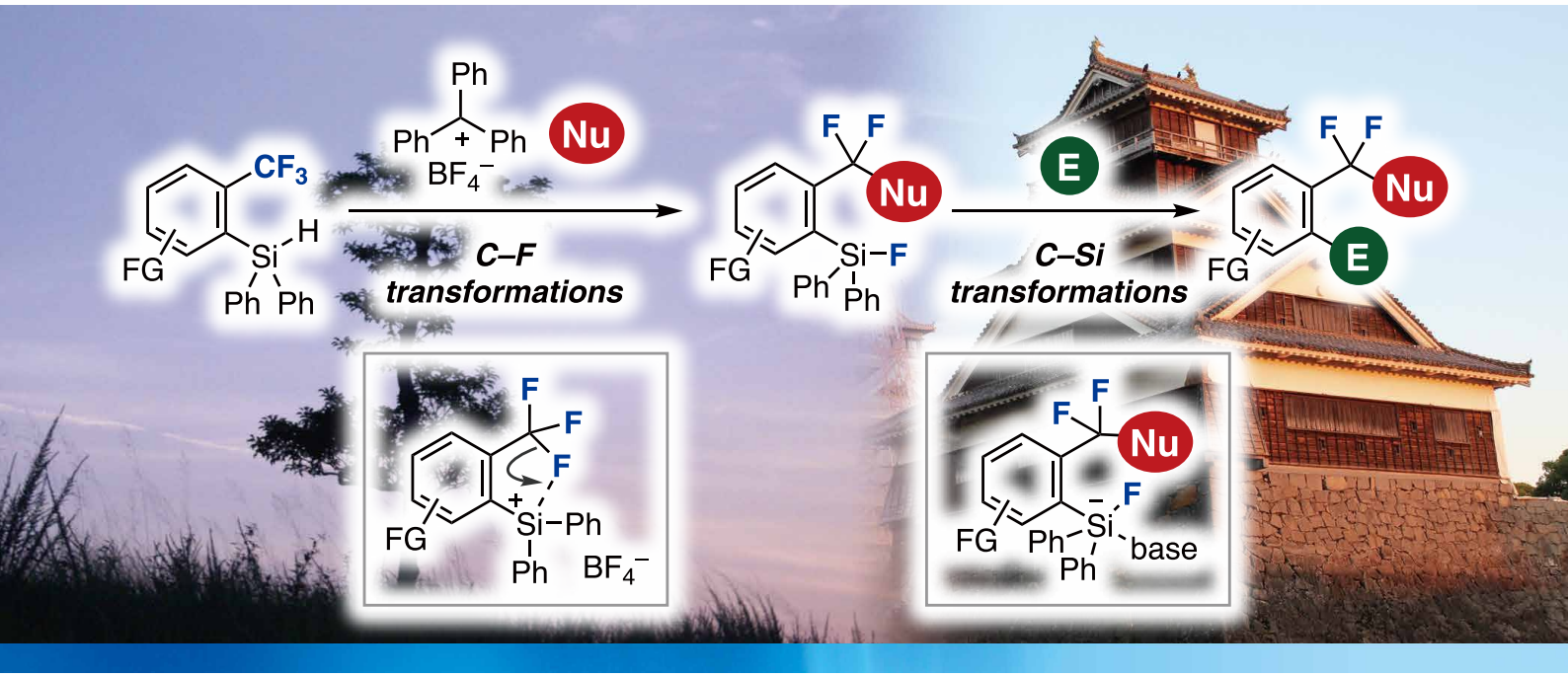

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Research Article

Selective Transformations of Aromatic Trifluoromethyl Groups

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Abstract: The trifluoromethyl group is robust, hydrophobic, and electron-withdrawing. A wide range of molecules bearing trifluoromethyl groups have thus played crucial roles in the organic synthesis of a wide range of compounds. Nonetheless, despite vigorous studies on trifluoromethyl compounds, selective transformations of the C–F bond of trifluoromethyl groups remain challenging. We recently accomplished selective transformations of the C–F bond of aromatic trifluoromethyl groups under mild conditions. In particular, transformations of a single C–F bond of *o*-hydrosilyl-substituted benzotrifluorides have been achieved. We have also developed an efficient synthetic method for diaryl ketones via C–F cleavages of benzodifluorides.

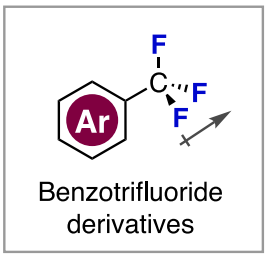
Keywords: Trifluoromethyl group, C–F bond, Silyl cations, Difluoromethylenes, Carbonyl compounds

1. Introduction

The trifluoromethyl group is a fundamental functional group in organic chemistry (**Fig. 1A**). The CF_3 group has for example played significant roles in the development of bioactive compounds owing to its uniquely robust and hydrophobic nature derived from its strong C–F bonds (**Fig. 1B**).[1,2] Since fluorine is the most electro-negative element, CF_3 groups have a significant electron-withdrawing nature. The introduction of CF_3 groups into aromatic compounds thus significantly affects the electronic properties of the compounds, which is crucial in the development of organic electronic materials and organocatalysts. The electron-withdrawing nature of aromatic CF_3 groups enables selective deprotonation at the *ortho*-position in synthetic chemistry, but the potential of benzotrifluorides in synthetic organic chemistry remains limited due to difficulties in the selective transformations of CF_3 groups.

Aromatic difluoromethylenes are similar to benzotirifluorides and play a significant role in pharmaceuticals, but progress in their utilization has been slow due to the lack of information regarding the synthesis of difluoromethylenes. Various efficient methods for installing CF_3 groups have been developed recently based on rapid improvements in organometallic chemistry. Single transformations of CF_3 groups can support the efficient synthesis of a broad range of difluoromethylenes, although such transformations require harsh conditions due to the strong C–F bonds. Transformations of CF_3 groups may result in further, facile C–F bond cleavages of CF_2 moieties due to the weaker C–F bonds, leading to the cleavage of all three C–F bonds (**Fig. 1C**).[3,4] For example, in 2008, Ozerov and coworkers reported reduction of the CF_3 group of perfluorotoluene under mild conditions via the generation of a silyl cation bearing a carborane moiety as a counterion, and all three C–F bonds of the CF_3 group were reduced (**Fig. 1D**).[3a] Difficult selective transformations of the CF_3 group and the overreactions of difluoromethylenes has hindered exploration of synthetic chemistry strategies using the CF_3 group as a one-carbon unit.[5]

A



Trifluoromethyl group

- ✓ Robust functional group
- ✓ Strong electron-withdrawing nature
- ✓ Challenging C–F transformations
  - harsh conditions for C–F cleavages
  - overreaction problems

B

	bond length (Å)	bond energy (kcal/mol)
C–H	1.10	105
C–F	1.38	110
C–Cl	1.78	84
C–Br	1.94	70

C

	bond length (Å)	bond energy (kcal/mol)
H_3C–F	1.38	110
H_2FC–F	1.36	120
HF_2C–F	1.33	128
F_3C–F	1.32	131

D

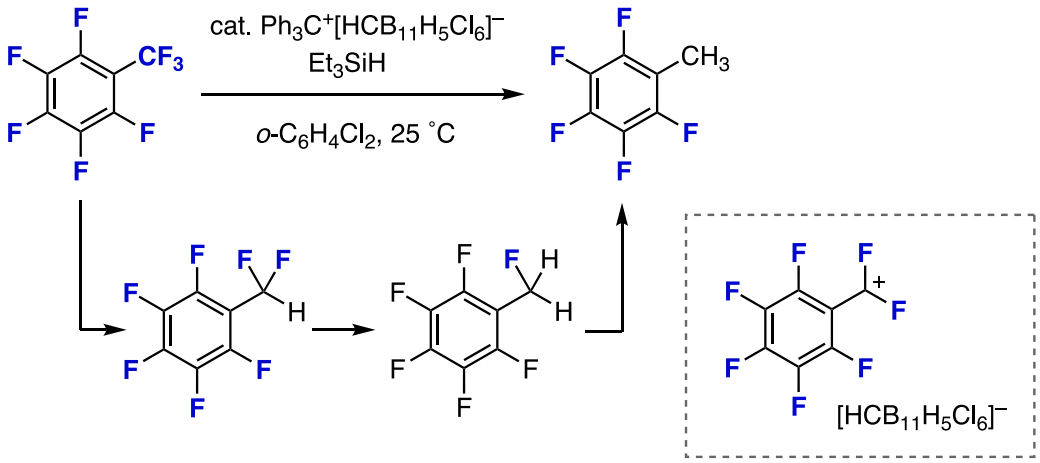


Figure 1. (A) Benzotrifluorides. (B) Carbon–hydrogen and carbon–halogen bonds. (C) Carbon–fluorine bonds. (D) Transformation of C–F bonds.

We recently found that selective transformations of the aromatic CF_3 group can proceed under mild conditions (**Fig. 2**). Indeed, 1) difluoromethylene syntheses through the activation of *ortho*-hydrosilyl groups (**Fig. 2A**)[6] and 2) ketone syntheses via arylation and carbonyl formation of CF_3 groups (**Fig. 2B**)[7] have been developed. This allowed us to demonstrate selective C–F transformations. These methods easily enabled us to expand the diversity of accessible products from simple starting materials in short steps. Herein, we summarize our recent achievements for C–F transformations of the CF_3 group.

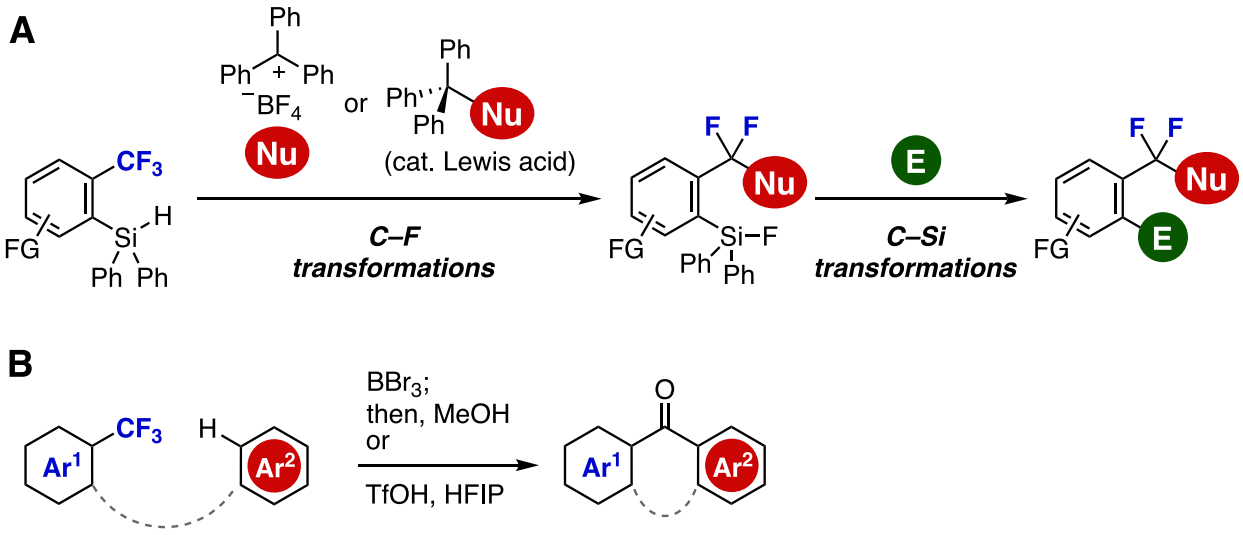


Figure 2. (A) Difluoromethylene synthesis. (B) Diaryl ketone synthesis.

2. Selective transformations of trifluoromethyl groups by *ortho*-hydrosilyl groups

2-1. Monoallylation of trifluoromethyl groups[6a]

The C–F transformation is challenging due to the robustness of trifluoromethyl groups, in which overreactions by further C–F transformations take place easily. We addressed this issue by designing a new reaction utilizing an *ortho*-hydrosilyl group of benzotrifluorides. Installation of the "dual-use" silyl group enabled us to achieve difluoromethylene synthesis from benzotrifluorides since 1) hydrosilyl groups can be used as precursors to generate silyl cations for C–F cleavage and 2) the resulting fluorosilyl group can be used in various transformations due to smooth activation with a base (**Fig. 3A**). We conceived that treatment of *o*-hydrosilyl-substituted benzotrifluorides with a trityl cation supports C–F transformations via generation of a silyl cation by hydride abstraction from the hydrosilyl group, fluoride abstraction from a neighboring trifluoromethyl group, and nucleophilic attack with nucleophiles. The resulting fluorosilyl group can be activated with bases owing to the electro-negative fluoro group, allowing us to achieve a wide range of C–Si bond transformations. Thus, selective transformations of various difluoromethylenes can be accomplished from simple benzotrifluorides, nucleophiles, and electrophiles in two steps.

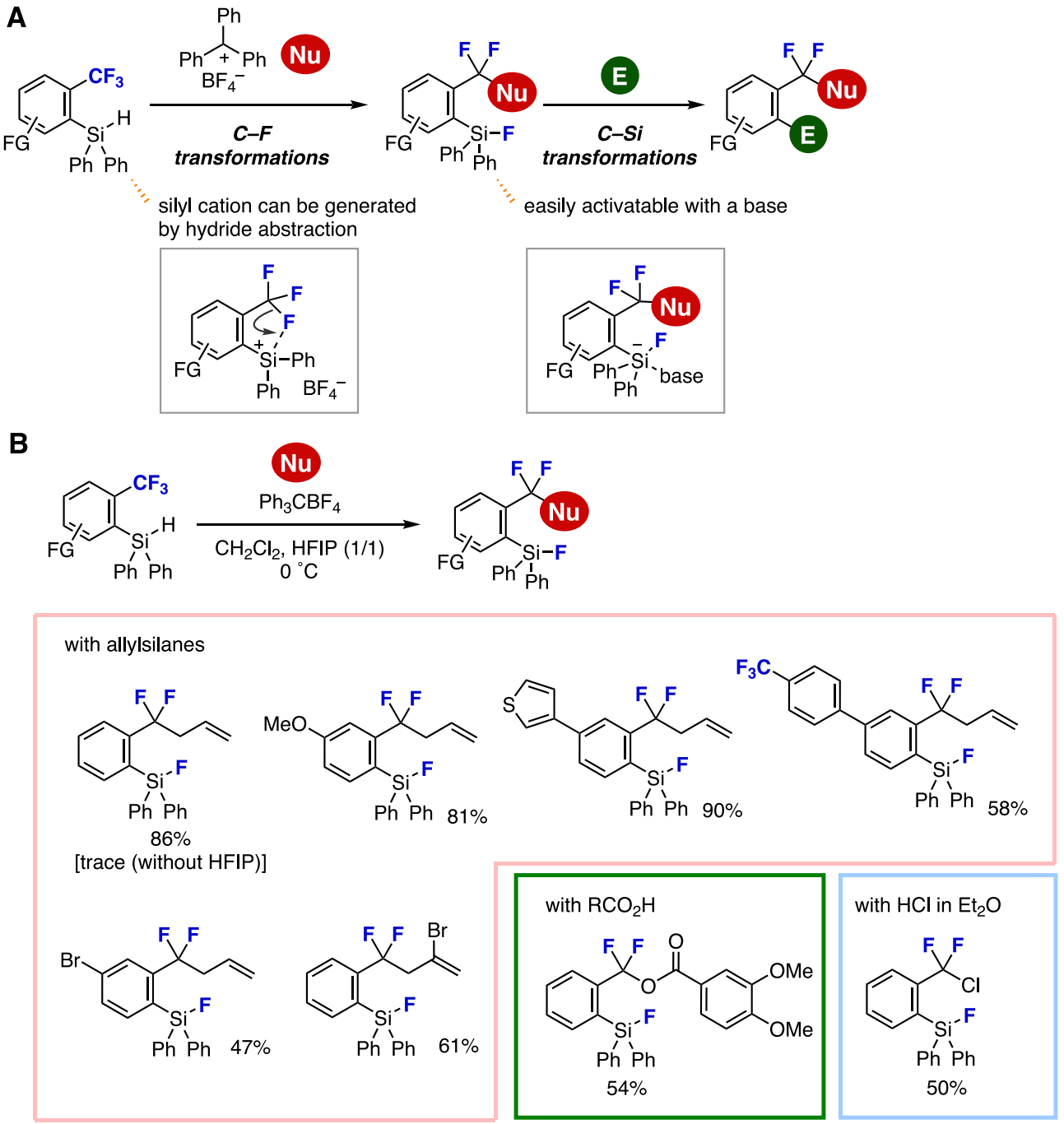


Figure 3. (A) C–F transformations using the *ortho*-hydrosilyl group (B) Examples of single C–F transformations.

The desired C–F transformations were challenging due to the unstable silyl cation intermediates. We succeeded in the single C–F allylation of *o*-diphenylsilyl-substituted benzotrifluorides by using a trityl cation in the presence of allylsilanes (**Fig. 3B**). The key to this success was the choice of solvents: dichloromethane and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP),[10] which significantly stabilized the unstable cationic intermediates. Of note, no side products arising from further C–F transformations were observed in this reaction. We succeeded in the synthesis of various monoallylated products without damaging a range of functional groups, as well as achieving C–F carboxylation and chlorination. The transformations of fluorosilyl groups are described in section 2-4.

2-2. Single thiolation of trifluoromethyl groups using all-in-one reagents[6b]

Treatment of *o*-(diphenylsilyl)benzotrifluoride with a trityl cation in the presence of 4-methoxybenzenethiol afforded a trithiolated product in high yield through further thiolation of monothiolated product (**Fig. 4A**, upper). To solve this problem, we designed a reaction via the activation of trityl sulfides[11] with Lewis acid catalysts (**Fig. 4B**). The activation of trityl sulfides generating thiolate ions and trityl cations would result in the single thiolation of benzotrifluorides since the generation of HBF_4 can be prevented in this system using trityl sulfides instead of thiols. Indeed, treatment of *o*-(diphenylsilyl)benzotrifluorides with a catalytic amount of $Yb(OTf)_3$ in the presence of trityl sulfides provided the desired monothiolated product in good yield (**Fig. 4A**, lower), where trithiolated product by overreactions through further C–F cleavage was not detected. We clarified that trityl cation was generated in equilibrium by treating trityl sulfides with a catalytic amount of $Yb(OTf)_3$. We accomplished the synthesis of diverse difluorobenzyl sulfides by the single thiolation of *o*-silylbenzotrifluorides.

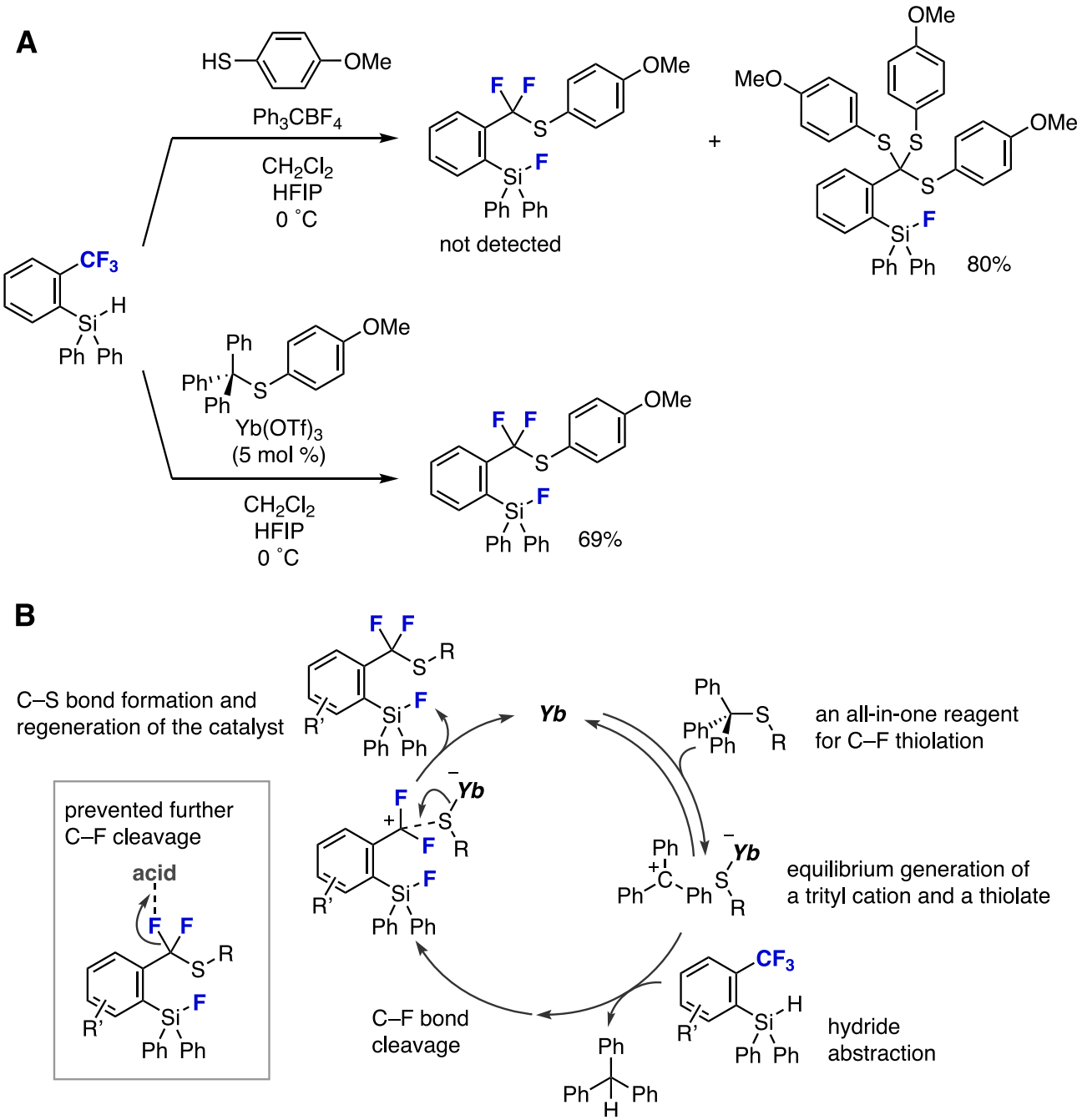


Figure 4. (A) Thiolations of *o*-(diphenylsilyl)benzotrifluoride. (B) Plausible mechanism.

2-3. Single chlorination of trifluoromethyl groups using all-in-one reagents[6c]

Single thiolation of benzotrifluorides required Lewis acid catalysts due to the C–S bond strength of trityl sulfides. In contrast, treatment of *o*-(diphenylsilyl) benzotrifluoride with trityl chloride in chlorobenzene and HFIP resulted in the single C–F chlorination without catalysts (**Fig. 5A**). A wide variety of difluoromethylenes were synthesized without further C–F transformations (**Fig. 5B**). We also accomplished single bromination and thiocyanation of *o*-silylbenzotrifluorides. The resulting α,α-difluorobenzyl chlorides are useful synthetic intermediates for diverse benzodifluorides by various transformations.[12] While synthesizable α,α-difluorobenzyl chlorides by conventional methods were strictly limited, our method enabled us to prepare a wide variety of highly functionalized α,α-difluorobenzyl chlorides. Therefore, this study will serve in organofluorine chemistry. Transformations of the chloro group are shown in section 2-4.

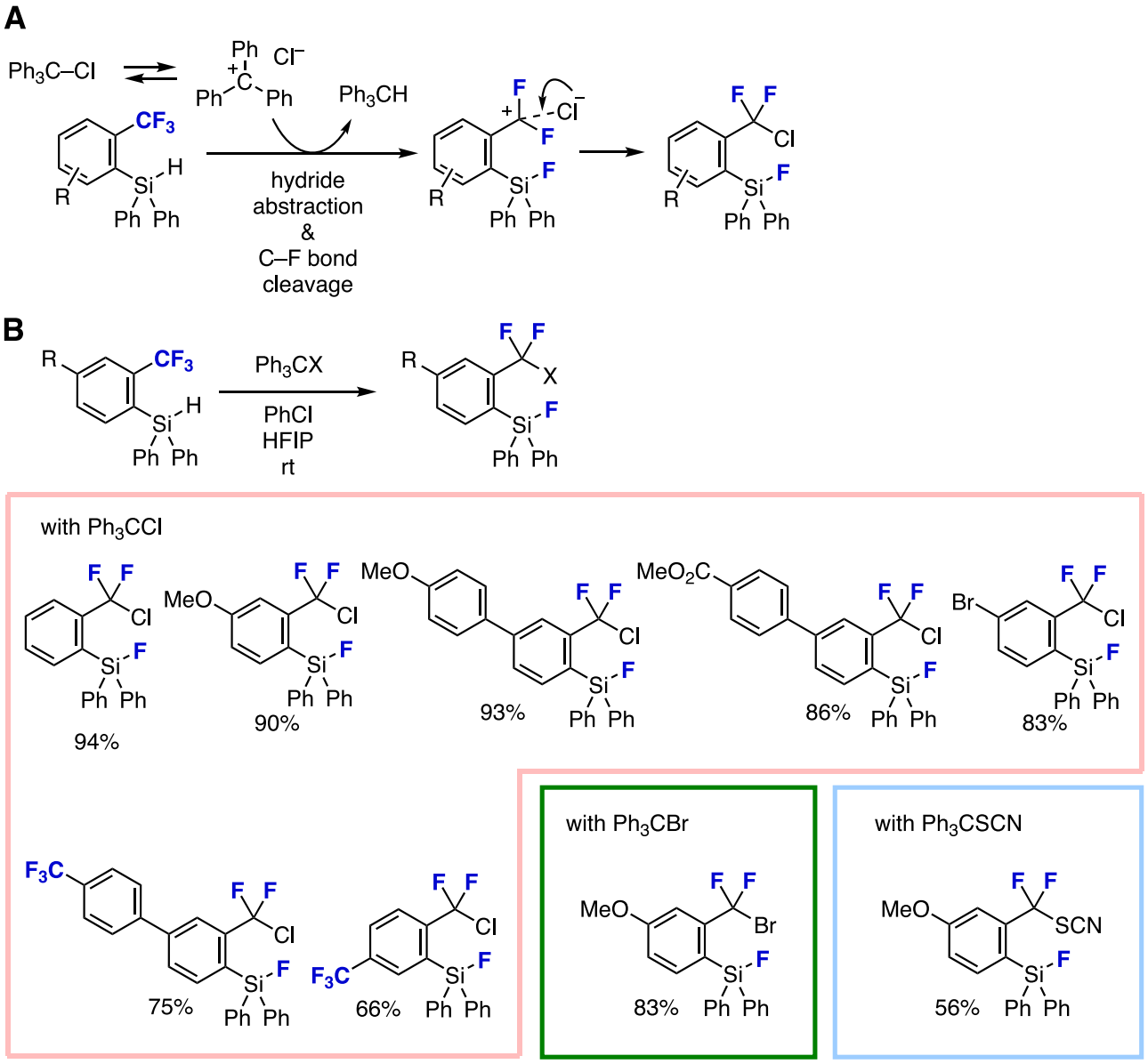


Figure 5. (A) Single chlorination of benzotrifluorides. (B) Product examples.

2-4. Difluoromethylene synthesis by C–Si transformations[6a–6c]

Since silyl groups bearing electron-negative atoms can be activated easily with bases, we succeeded in installing a wide variety of functional groups by C–Si transformations (**Fig. 6**). For example, desilylprotonation of *o*-fluorosilyl-substituted benzodifluorides with tetrabutylammonium fluoride without damaging difluoromethylene moieties. We accomplished C–Si arylation when performing palladium-catalyzed Hiyama cross-coupling[9] of *o*-fluorosilyl-substituted benzodifluorides with aryl iodides. In contrast, no reaction proceeded when using hydrosilanes instead of fluorosilanes owing to the difficult activation with bases. In addition, desilylhalogenations were achieved by treatment of fluorosilanes with *N*-halosuccinimides in the presence of silver fluoride.[13] These C–Si transformations allowed us to synthesize difluoromethylenes having a wide variety of functional groups at the *ortho*-position. These results clearly show that the "dual-use" silyl groups of benzotrifluorides enabled not only selective C–F transformations but also diversifications of products by further C–Si transformations.

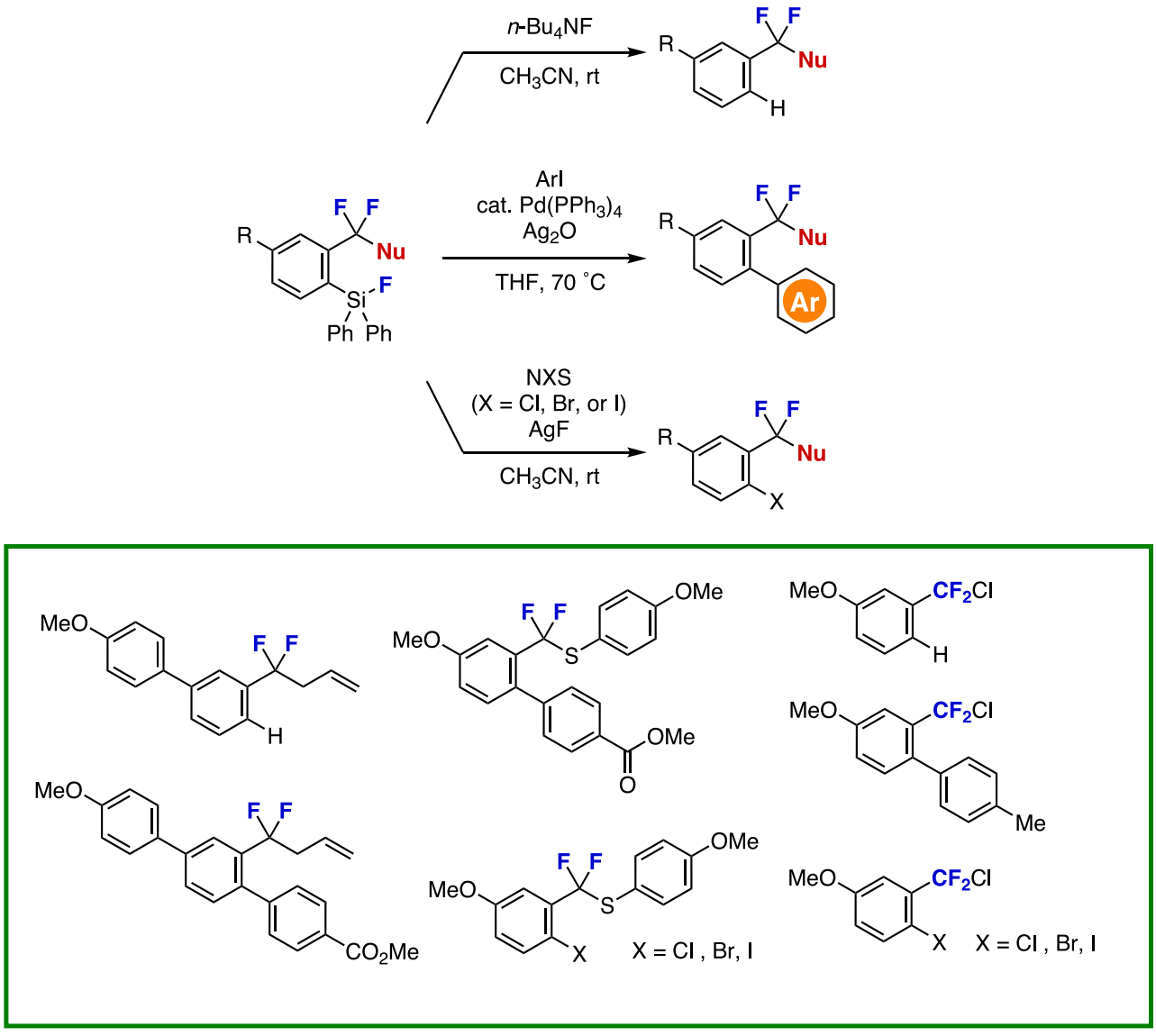


Figure 6. Transformations of fluorosilyl groups (NXS = *N*-halosuccimide (X = Cl, Br, I))

Good transformability of α,α-difluorobenzyl chlorides allowed us to synthesize diverse organofluorines through single C–F chlorination of benzotrifluorides (**Fig. 7**). For instance, after the C–F monochlorination of *o*-(diphenylsilyl)benzotrifluoride, desilylbromination was achieved without the purification of the reaction mixture of intermediates (**Fig. 7A**). We also succeeded in the synthesis of various difluorobenzyl ethers by substitution of chlorides with phenols under basic conditions (**Fig. 7B**). Radical C–C formation was accomplished by treatment of difluorobenzyl fluorides with samarium iodide in the presence of styrene as a radical acceptor (**Fig. 7C**). Studies on transformations of α,α-difluorobenzyl chlorides were immature and their contribution to synthetic chemistry was quite limited due to the poor accessibility before our studies. Contrastingly, we found that various transformations of α,α-difluorobenzyl chlorides obviously serve in the organofluorine synthesis.

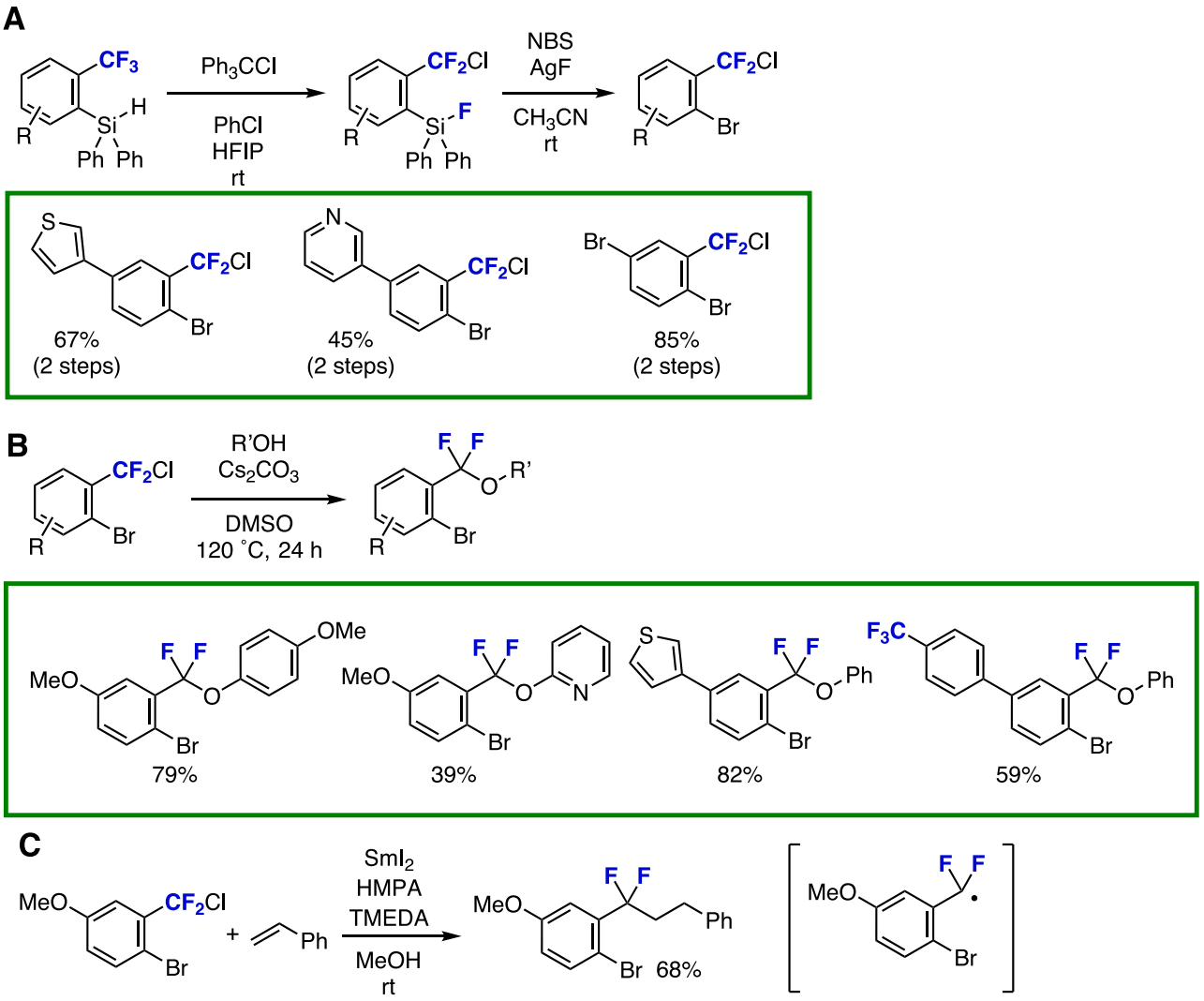


Figure 7. (A) Difluorobenzyl chloride synthesis. (B) Difluorobenzyl ether synthesis. (C) Radical addition using difluorobenzyl chloride. (DMSO = dimethyl sulfoxide; HMPA = hexamethylphosphoric triamide; TMEDA = *N*,*N*,*N*',*N*'-tetramethylethylenediamine)

2-5. Sequential transformations via reduction of fluorosilyl groups[6d]

We achieved the preparation of highly functionalized benzyl fluorides by the reduction of fluorosilyl group to reproduce the hydrosilyl group and following selective C–F transformations (**Fig. 8A**). Treatment of fluorosilanes with lithium aluminum hydride afforded hydrosilanes leaving difluoromethylene moieties untouched (**Fig. 8B**). Then, a single C–F transformation of the difluoromethylene moiety in the resulting hydrosilanes took place triggered by the second generation of a silyl cation (**Fig. 8C**). Indeed, treatment of difluoromethylenes with LAH in THF at 0 °C provided the corresponding hydrosilanes in high yields. When *o*-hydrosilyl-substituted difluoromethylenes were treated with trityl chloride, single chlorination of difluoromethylenes took place smoothly (**Fig. 8D**). We also succeeded in the synthesis of fluorobutadienes by desilylbromination of the fluorosilyl group and subsequent elimination with a base. Thus, we have developed a new method to prepare highly functionalized benzyl fluorides via the reduction of fluorosilyl group to regenerate hydrosilyl group and following single C–F transformations.

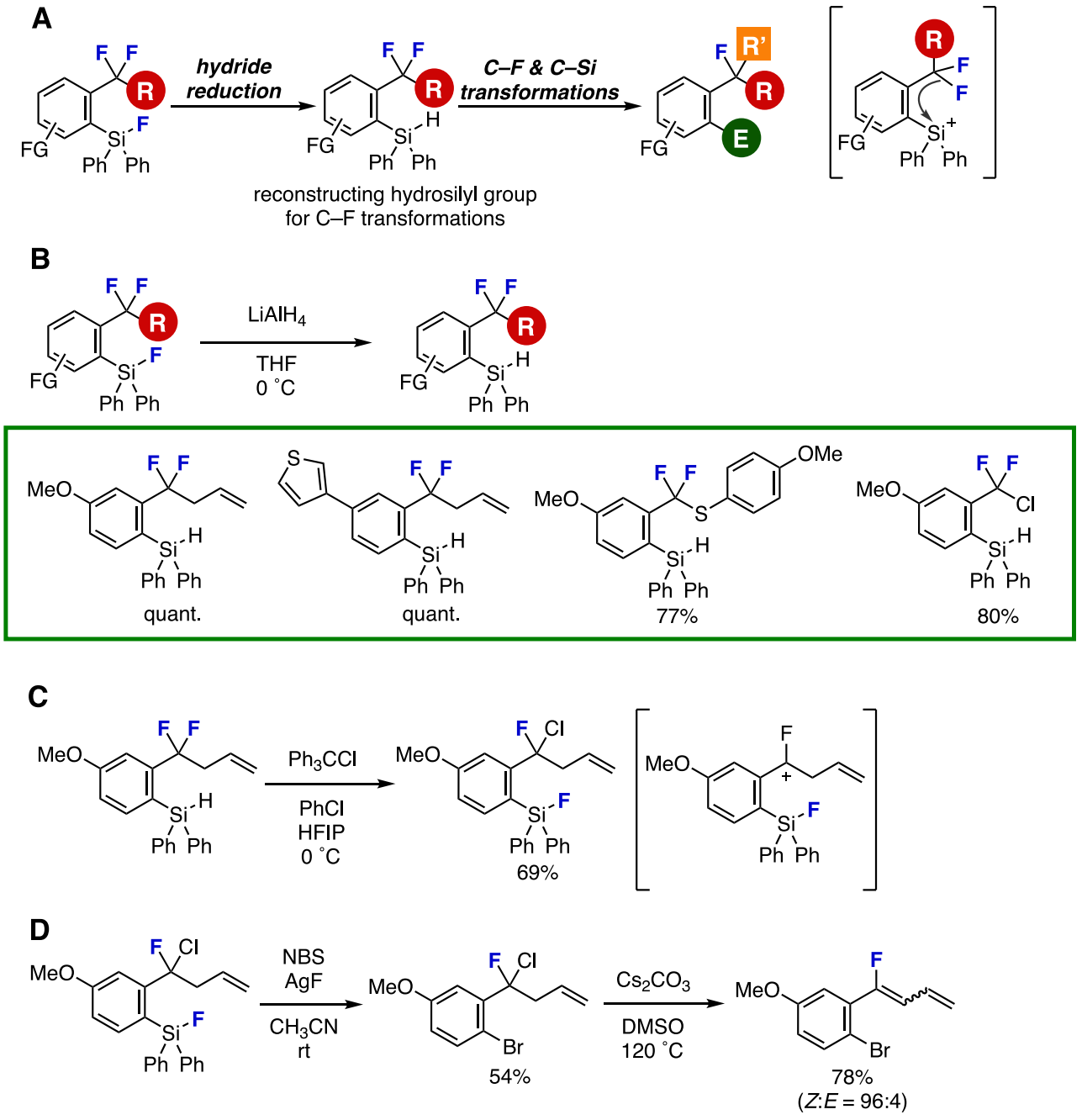


Figure 8. (A) Benzyl fluoride synthesis through regeneration of hydrosilyl group. (B) Reduction of fluorosilyl group. (C) Single C–F chlorination. (D) Fluorobutadiene synthesis.

3. Synthesis of carbonyl compounds by C–F transformations of trifluoromethyl group

3-1. Ketone synthesis using boron tribromide[7a]

Transformations of trifluoromethyl groups under mild conditions would allow us to synthesize diverse aromatic compounds having various functional groups. It is worth noting that the synthesis of benzotrifluoride derivatives can be performed under harsh conditions due to the robustness of the trifluoromethyl group. For example, *ortho*-deprotonation of benzotrifluorides enables us to synthesize various derivatives with a wide range of electrophiles. Thus, transformations utilizing trifluoromethyl group as a one-carbon unit will significantly contribute to the synthetic chemistry, which is advantageous over nucleophile-susceptible one-carbon units such as esters.

We have developed a facile method to synthesize ketones by electrophilic aromatic substitution and formation of carbonyl group via C–F cleavage using boron tribromide (**Fig. 9A**, upper). Indeed, the treatment of benzotrifluorides in dichloromethane with boron tribromide in the presence of arenes including mesitylene followed by the addition of methanol, furnished benzophenone derivatives in good yields. In contrast, C–C bond formation did not take place before the addition of methanol, in which the formation of the tribromomethyl group from the trifluoromethyl group proceeded.[15] When using water instead of methanol, the desired ketone was not observed (**Fig. 9A**, lower). These results show that C–C bond formation was realized through the activation with Lewis acids generated in situ from boron tribromide and methanol.

Selective transformations of trifluoromethyl group were accomplished without damaging highly reactive functional groups by virtue of the mild reactivity of boron tribromide (**Fig. 9B**). It is worth noting that we succeeded in the efficient arylation of trifluoromethyl group via C–F cleavages keeping triflusilyl, iodo, triflyloxy, and thio groups, which were reactive with acids, bases, transition metals, oxidants, etc.

We achieved the efficient preparation of cyclic ketones such as thioxanthones via intramolecular arylation (**Fig. 9C**). Of note, it is easy to achieve various functionalizations through selective lithiation at the 2-position of 3-bromobenzotrifluoride. Indeed, the selective deprotonation followed by arylthiolation and subsequent cyclization through C–F cleavages proceeded smoothly to afford a broad range of thioxanthones in good yields.

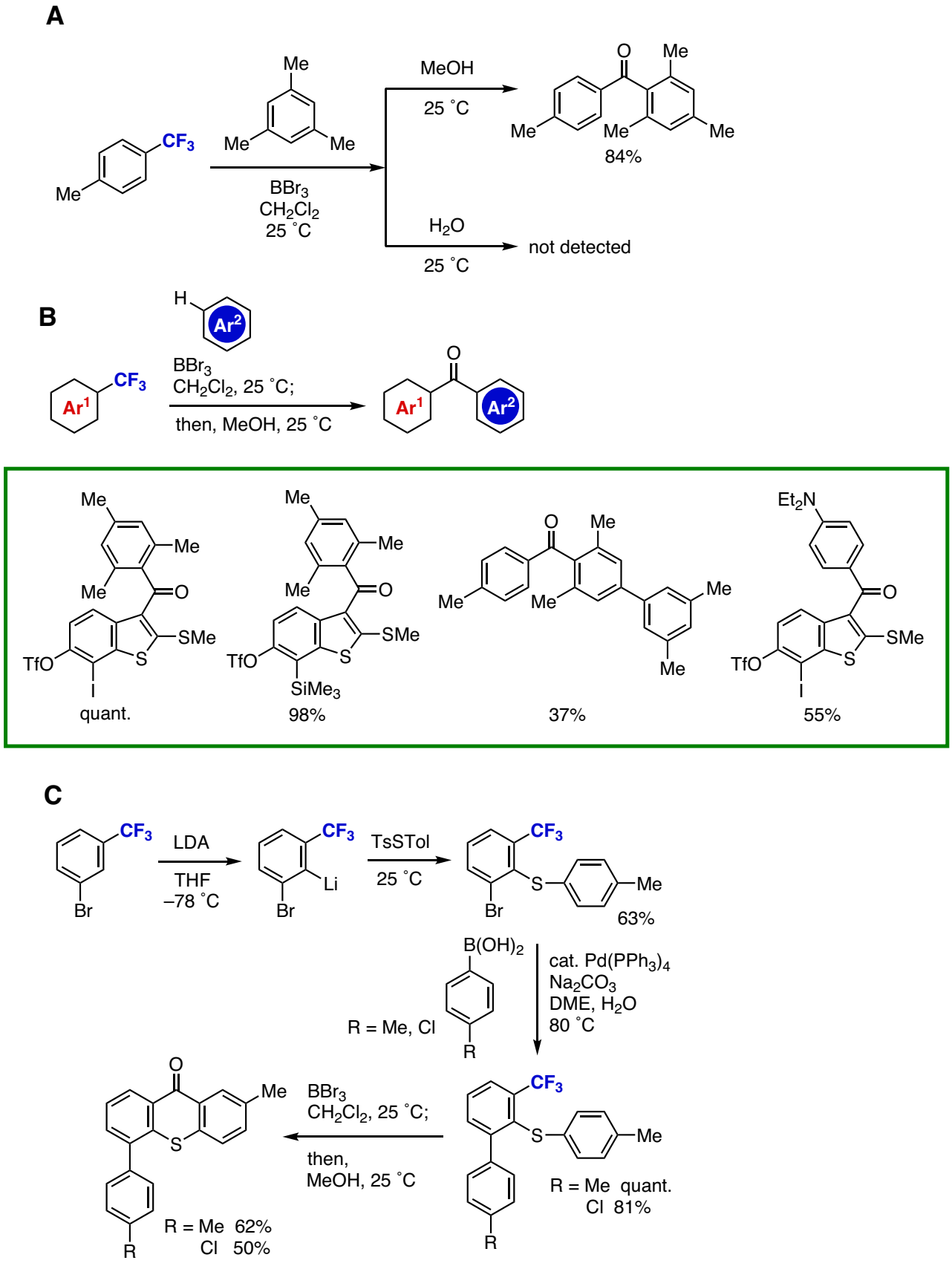


Figure 9. (A) Diaryl ketone synthesis. (B) Product examples. (C) Thioxanthone synthesis.

3-2. Cyclic ketone synthesis by cross-coupling and C–F transformation[7b]

We have developed an efficient method to synthesize various cyclic ketones through cross-coupling reactions and following C–F arylation with the carbonyl formation from *o*-bromo- or *o*-iodobenzotrifluorides (**Fig. 10A**). Indeed, after arylation or aryloxylation at the bromo or iodo group, treatment of the resulting benzotrifluoride derivatives in HFIP with trifluoromethanesuofonic acid (TfOH)[16] furnished various cyclic ketones in high yields (**Fig. 10B** and **10C**). It is worthy to note that we succeeded in the dimethoxyfluorenone synthesis from 3-methoxybenzotrifluoride via the selective deprotonation at 2-position, iodination, Suzuki–Miyaura cross-coupling, and ketone synthesis using TfOH in HFIP, where the corresponding ketone was obtained in good yield without purification of the intermediate.

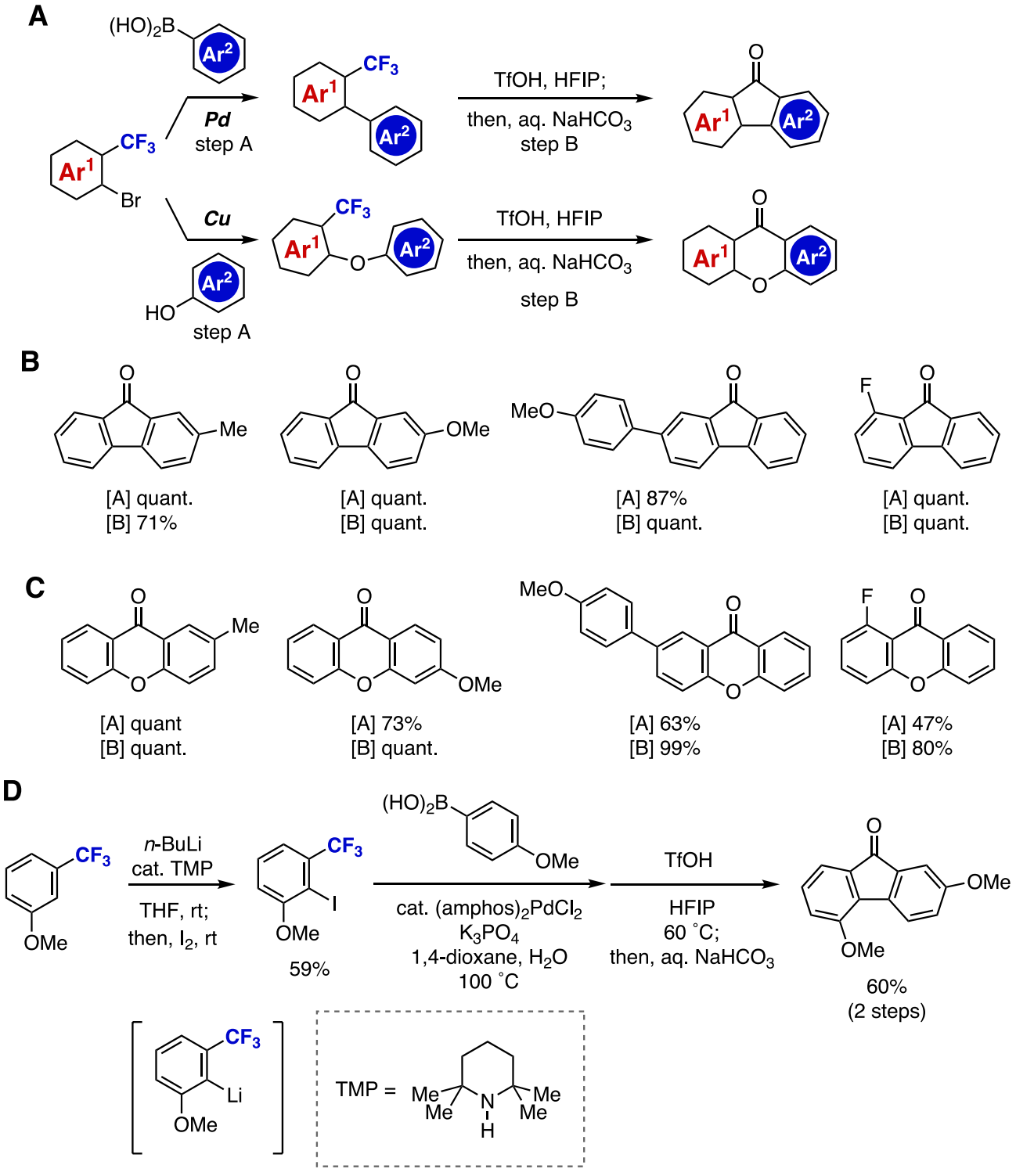


Figure 10. (A) Synthesis of fluorenones and xanthones. (B) Examples of fluorenones. (C) Examples of xanthones. (D) Fluorenone synthesis from 3-methoxybenzotrifluoride.

4. Conclusion

We have developed synthetic methods using the trifluoromethyl group. Although the trifluoromethyl group is robust under various reaction conditions, selective C–F transformations of aromatic trifluoromethyl groups can be accomplished without damaging highly reactive functional groups on the basis of proper design of substrates or choice of reagents. At the beginning of our studies, the selective C–F transformation was not a popular topic. However, diverse chemists are recently gaining attention to C–F transformations as hot topics.[17–20] Future studies such as the development of transformations based on the features of the trifluoromethyl group and synthetic methods using organofluorines which can be prepared by our methods will lead to the great advance of synthetic methodologies utilizing one-carbon units having fluorine atoms such as trifluoromethyl groups.

We clarified the reactivities of aromatic molecules bearing trifluoromethyl groups through studies on the development of novel reactions as described above. Our further studies on not only new transformations using popular functional groups but also developing new reactions and new reagents based on disclosing unpopular functional groups will expand the potential of organic chemistry.

Acknowledgement

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Suguru Yoshida received his Ph.D. from Kyoto University in 2009 under the supervision of Prof. Koichiro Oshima. From 2009 to 2010, he joined the group of Prof. Katsuhiko Tomooka at Kyushu University and that of Prof. Marcus Tius at the University of Hawaii as a postdoctoral fellow. In 2010, he became Assistant Professor at Tokyo Medical and Dental University working with Prof. Takamitsu Hosoya and was promoted to Associate Professor in 2015. He moved to Tokyo University of Science in 2021 as Associate Professor. He received the CSJ Award for Young Chemists (2017) and the Commendation for Science and Technology by MEXT (2019).

Related Products

Triphenylmethylium Tetrafluoroborate		5g	25g	T1173
Ytterbium(III) Trifluoromethanesulfonate		5g	25g	T1610
Hexamethylphosphoric Triamide (= HMPA)	25g	100g	500g	H0095
N,*N*,*N*',*N*'-Tetramethylethylenediamine (= TMEDA)	25mL	100mL	500mL	T0147
Lithium Aluminum Hydride (= LAH)		25g	100g	L0203
S-*p*-Tolyl *p*-Toluenesulfonothioate (= TsSTol)		1g	5g	T3173
Tetrakis(triphenylphosphine)palladium(0) (= $Pd(PPh_3)_4$)	1g	5g	25g	T1350
Bis[di-*tert*-butyl(4-dimethylaminophenyl)phosphine]dichloropalladium(II) (= $(amphos)_2PdCl_2$)			1g	B6255
2,2,6,6-Tetramethylpiperidine (= TMP)		25mL	250mL	T1051

Chemistry Chat

Keeping Up with Changes in Senior High School Chemistry

Toyo University Keihoku Senior High School

Hiroyuki Onuki

1. Introduction

In a previous report,[1] I described how I encountered difficulties in conducting experiments in senior high school chemistry classes. In this article, I introduce the challenges of keeping up-to-date with the latest content in senior high school chemistry, which changes occasionally.

2. Changes in Terminology

Terminology changes over time. Based on the revisions in the *Curriculum Guidelines* in Japan announced in 2018,[2] the terms used in Japanese textbooks have been significantly revised.[3,4] Teachers must pay close attention to these changes to ensure they do not overlook them when revising the guidelines.

Table 1. Changes in terminology around 2022

	Old Term	New Term
Alkali earth metals	Group 2 elements including Be and Mg	Group 2 elements including Be and Mg
Transition elements	Groups 3−11	Groups 3−12
18 Group	Inert gases	Noble gases
Reverse sublimation	(Sublimation)	Deposition
Enantiomer	Optical isomer	Enantiomer
Isomer based on double bond	Geometric isomer	*cis-trans* isomer

The teaching contents in schools are constantly changing. Hence, when I talk with people of different generations, It is interesting for me to note that they used outdated terms. For example, the terms "gram equivalent" and “normamality”: sound nostalgic.[4,5]

3. Thermochemistry

Japanese senior high school textbooks have historically described reactions involving heat exchange using thermochemical equations with an equals sign.[6] For example, the reaction for the formation of water is expressed as:

$$H_2\,(g) + \frac{1}{2}O_2\,(g) = H_2O\,(l) + 286\ kJ$$

However, from the fiscal year 2023, the textbooks have switched to thermochemical reactions that include enthalpy changes, and thus Japanese thermochemical equations are at last complied with international standards.[7] The reaction of the formation of water is now expressed as:

$$H_2\,(g) + \frac{1}{2}O_2\,(g) \rightarrow H_2O\,(l) \quad \Delta H = -286\ kJ$$

This is one of the revisions of Japanese "Galápagosized" chemical education. The previous thermochemical equations focused on energy exchange viewing from an external system, whereas the new approach describes energy exchanges from internal system.

4. Experiment: Regulations of Chemicals

Several substances have become regulated in recent years because their hazards to humans and the environment have been revealed. Examples related to senior high school classes are given below.

4.1 Mercury

After the Minamata Convention on Mercury in 2013 came into effect, schools disposed of unnecessary equipment and reagents containing mercury.[8] However, metallic mercury is indispensable for understanding the concept of pressure. The standard atmospheric pressure is described in textbooks as:

$$1.013 \times 10^5 \text{ Pa} = 760 \text{ mmHg} = 1 \text{ atm}$$

Unfortunately, many schools do not have sufficient quantities of metallic mercury, so students have to understand the relationship between atmospheric pressure and mercury in textbook only. Many students who graduated school without watching a Torricellian vacuum with their own eyes, which is a pity.

Other than metallic mercury, two mercury compounds appear in current textbooks in the following reactions:[7]

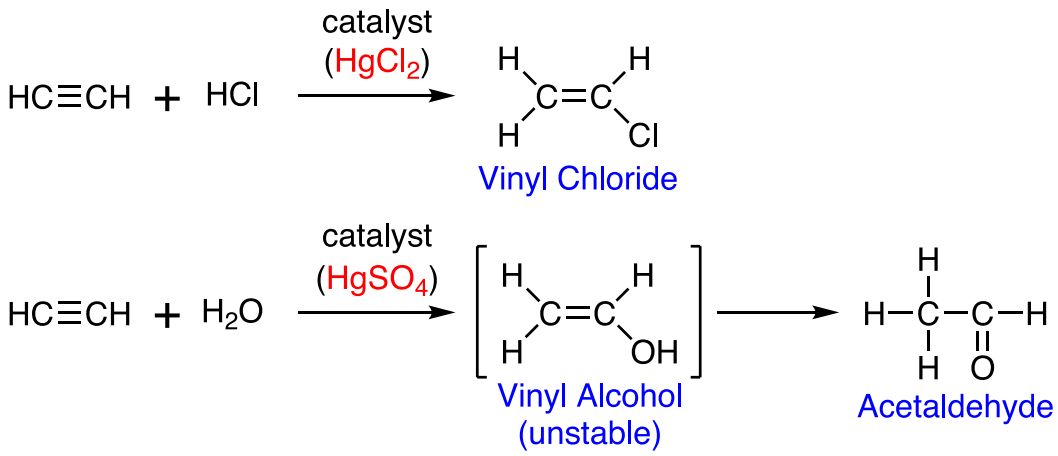

Figure 1. Mercury compounds appeared in the textbooks

Mercury compounds play important roles as catalysts for addition reactions involving triple bonds, but these compounds can cause Minamata Disease, also called "methylmercury poisoning." It is quite difficult to make students understand the harmfulness of mercury-containing substances because we cannot show these reactions or demonstrate biological toxicity directly to them.

4.2 Benzene

Benzene is carcinogenic.[9] The classic experiment "Nitration of Benzene" was removed from textbooks revised in 2017. Although "Synthesis of Azo Dyes" remains, benzene is replaced by nitrobenzene as the starting material in the laboratory. It is a pity that students cannot directly handle the basic skeleton of aromatic compounds.

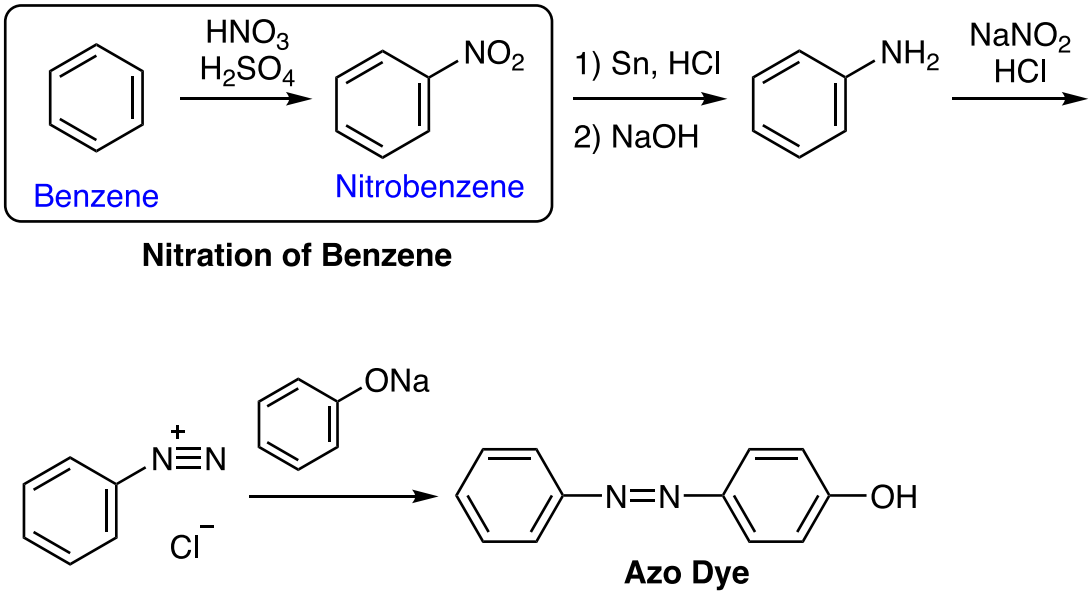

Figure 2. Synthetic route to an azo dye from benzene

4.3 Carbon Tetrachloride

As an ozone-depleting substance,[10] the use of carbon tetrachloride is limited. Students learn that its structure has a tetrahedral shape; four chloride atoms are arranged around the center carbon atom. Methane is introduced as a typical non-polar compound when studying molecular shapes and polarity. However, it is quite difficult to experimentally demonstrate that methane is non-polar because it is a gas at room temperature. Unlike methane, carbon tetrachloride is a liquid at room temperature, allowing students to visualize its non-polar properties through interactions with static electricity.[11] The following is a demonstration of polarity:

Experiment: Produce a flow of water or carbon tetrachloride from a burette, and bring an electrically charged rod close to the flow.
Result: The polar water flow is bent by the electric charge, but the non-polar carbon tetrachloride flow is not.

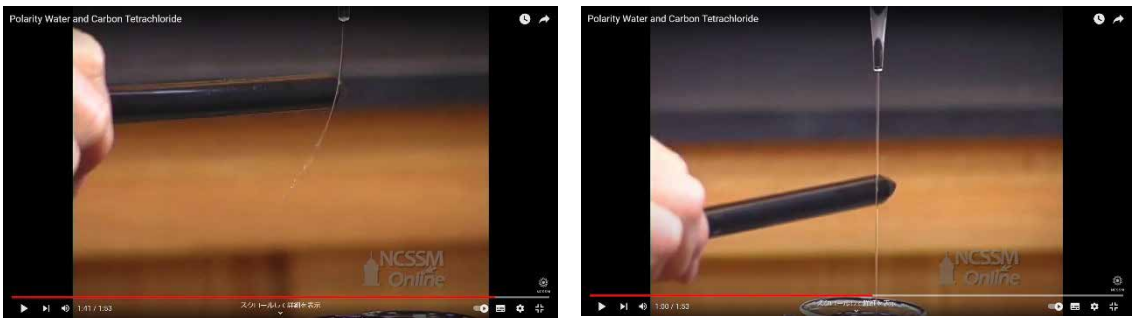

Figure 3. Flow of water (left) and carbon tetrachloride (right) near a charged rod

5. Conclusion

Due to occasional changes in content and terminology definitions in senior high school chemistry, teachers must always keep up with the latest information. Also, we have to comply the legal regulation of substances handled and their effects on the environment. Furthermore, we should not forget to update our handouts/practice problems in classrooms and experimental procedures in laboratories.

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5. One gram equivalent is an acid (or base) mass that can produce 1 mol of hydrogen ions (hydroxide ions) in a neutralization reaction. The number of gram equivalents of acid or base dissolved in 1 L of solution is called that solution's normality (symbol N). For example, one gram equivalent of sulfuric acid (molecular weight 98) is 49 g, and concentrated sulfuric acid (36 mol/L) is 18 N. This appeared in senior high school textbooks at least until 1983.
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His research interests are organic natural product chemistry, instrumental analyses, and chemical education.

New Products Information

Thionylimide Derivatives for Synthesis of Sulfonimidamides

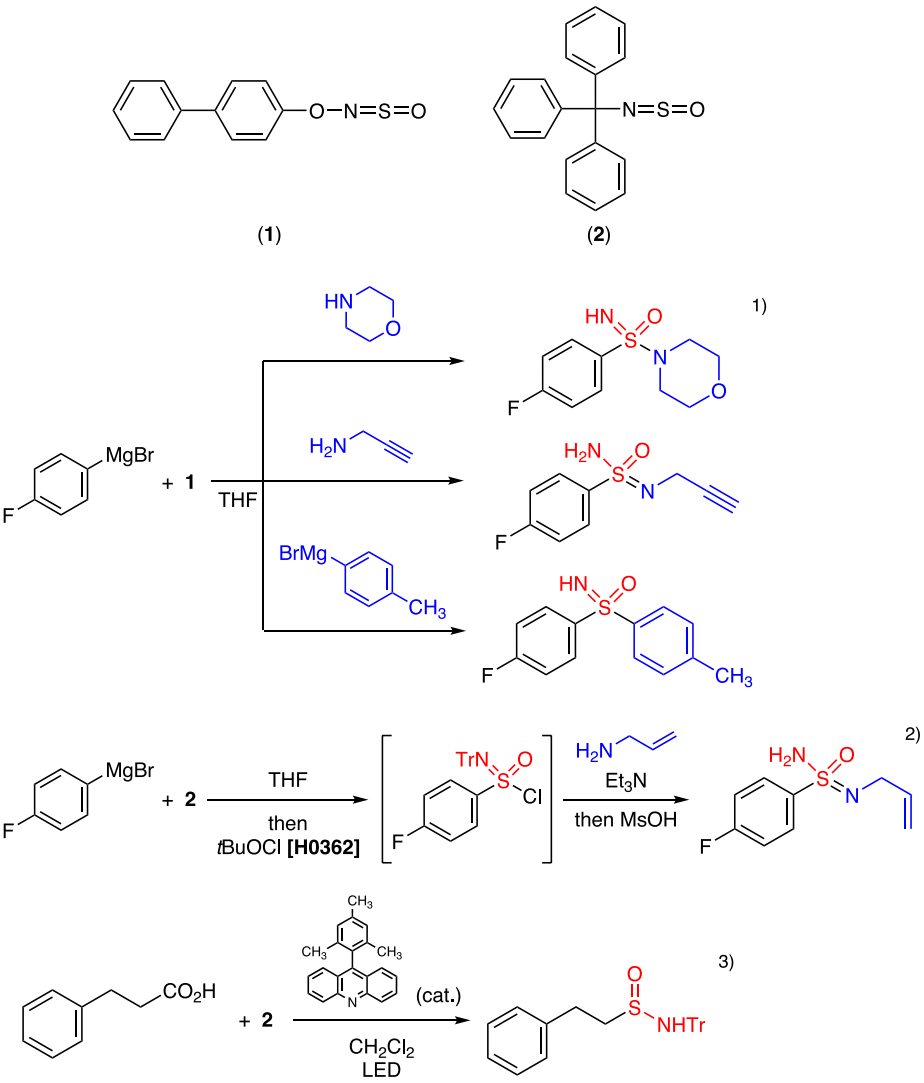
4-[(Sulfinylamino)oxy]biphenyl (= BiPhONSO) (1)

Product Number: **B6435**
1g 5g

(Triphenylmethyl)thionyl Imide (= TrNSO) (2)

Product Number: **T3773**
1g 5g

BiPhONSO (**1**) and TrNSO (**2**) are utilized in the one-pot synthesis of sulfonimidamides. **1** gives the corresponding sulfonimidamides when treated with a Grignard reagent and an amine.[1)] The substitution style of the imine moiety varies depending on whether a primary or secondary amine is used. Furthermore, when the second nucleophile is replaced by an organometallic compound, the sulfoximine is afforded. On the other hand, **2** is known to give sulfonimidamide via a chlorinated intermediate just like **1**,[2)] and is also reported to allow decarboxylative insertion of a sulfinimide moiety to carboxylic acid through a photoredox reaction.[3)]



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Related Product

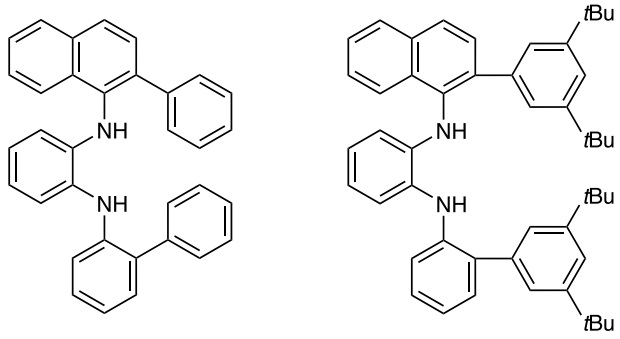
N-Sulfinyl-*tert*-butoxyamine (= *t*BuONSO)	1g	10g	U0150

Bidentate Diamine Ligands for Cu-Catalyzed C-N Coupling

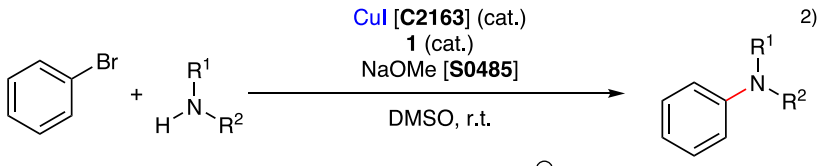
_N_-([1,1'-biphenyl]-2-yl)-_N'_-(2-phenylnaphthalen-1-yl)-benzene-1,2-diamine (1) Product Number: **B6606** **250mg 1g**

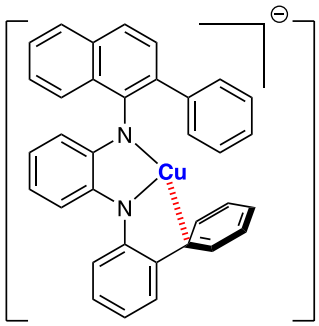
N^1-(3',5'-di-_tert_-butyl-[1,1'-biphenyl]-2-yl)-N^2-(2-(3,5-di-_tert_-butylphenyl)naphthalen-1-yl)benzene-1,2-diamine (2) Product Number: **D6240** **250mg 1g**

Amination of aromatic rings is an important reaction for the synthesis of functional compounds such as pharmaceuticals.[1] Palladium catalysts have previously been used for amination, but there have been studies on the use of copper catalysts, which have low cost, low toxicity, and are easy to remove. It was reported that C-N coupling of aryl bromides with amines is possible using diamine bidentate ligands **1** and **2** with copper salts.[2] C-N coupling of aryl bromides and primary or secondary amines proceeds at room temperature in the presence of copper iodide, **1** or **2**, and a base. Aryl bromides are also applicable to drug-like compounds containing heterocyclic rings. Ligands **1** and **2** are anionic and their high electron density accelerates oxidative addition. The catalytically active species **3** is stabilized by π-interactions with the central metal. When using aryl bromides with substituents in the *ortho*-position or bulky amines, **2** is more effective than **1** at preventing deactivation by *N*-arylation of the ligand. Furthermore, **1** has also been reported to be applicable to C-O coupling.[3]



(**1**) (**2**)





(**3**)

active Cu complex stabilized by π-interaction generated in situ

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Related Products

Copper(I) Iodide	25g	100g	500g	C2163
Sodium Methoxide		100g	500g	S0485

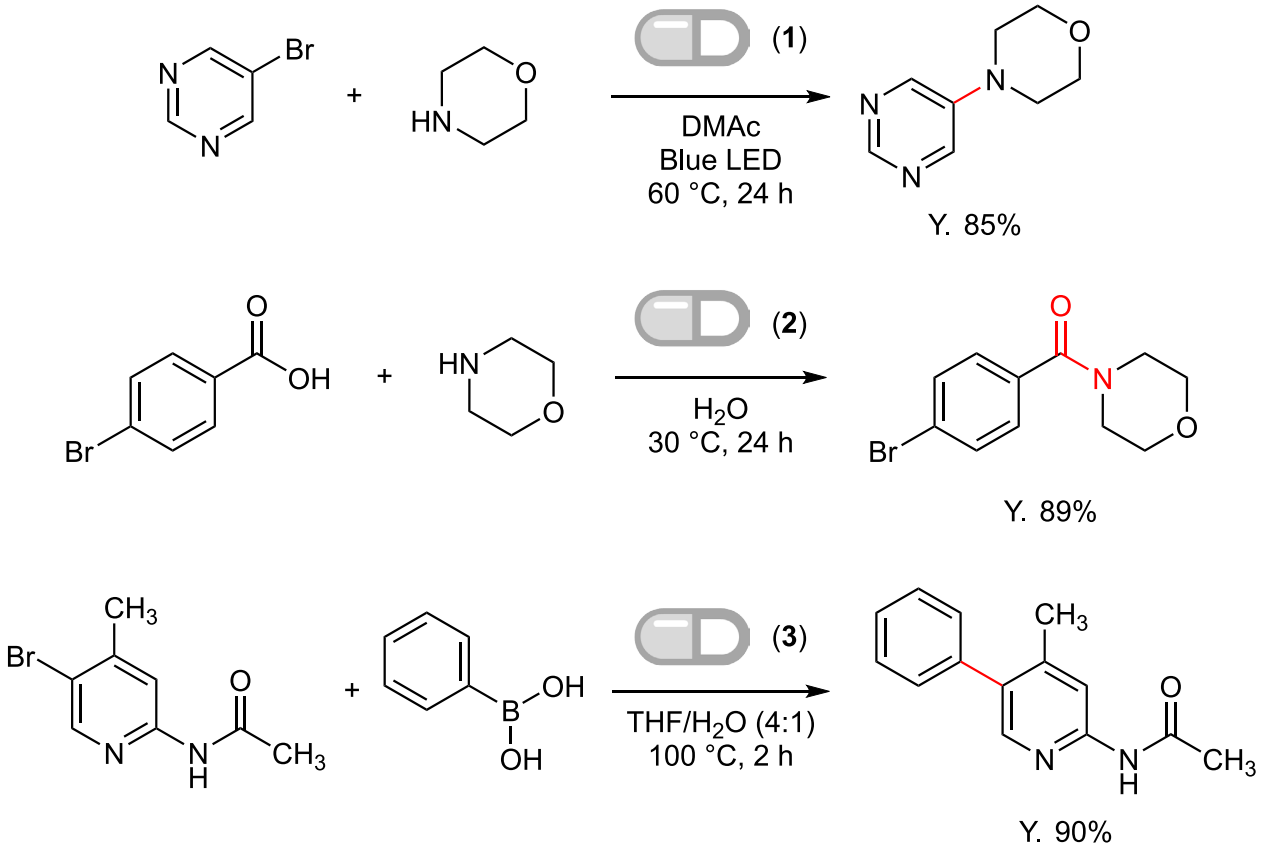
HPMC Capsule Reagents for Accelerating Synthetic Chemistry

Reagents for Metallophotoredox Cross-Coupling Reactions [$NiBr_2$(dme), [Ir[dF(CF_3)ppy]$_2$(dtbbpy)]PF_6, DABCO] (HPMC encapsulated) (1) — Product Number: **R0273** **10each**

Reagents for Condensation Reactions (EDCI·HCl, HOBt·H_2O) (HPMC encapsulated) (2) — Product Number: **R0274** **10each**

Reagents for Suzuki-Miyaura Cross-Coupling Reactions [Pd(dppf)Cl_2·CH_2Cl_2, Cs_2CO_3] (HPMC encapsulated) (3) — Product Number: **R0275** **10each**

TCI sells capsule reagents, which are synthetic reagents encapsulated in hydroxypropyl methylcellulose (HPMC) capsules. By using capsule reagents, weighing of reagents can be omitted, and reactions can be initiated simply by adding them to the reaction solution, thereby enabling rapid investigational experiments and library construction.[1-3] The lineup includes condensing reagents, reagents for photoredox reactions, and reagents for Suzuki-Miyaura cross-coupling reactions, which are frequently used in drug discovery research and synthetic organic chemistry, and the lineup is currently being expanded.



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Related Products

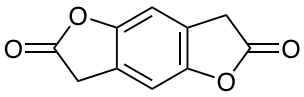
Reagents for Condensation Reactions (DMT-MM) (HPMC encapsulated)	10each	R0294
Reagents for Condensation Reactions (HATU) (HPMC encapsulated)	10each	R0295
Reagents for Condensation Reactions (1*H*-Benzotriazol-1-yloxytripyrrolidinophosphonium Hexafluorophosphate) (HPMC encapsulated)	10each	R0296

Acceptor Unit for Organic Semiconductors and Organic Conductors

3,7-Dihydrobenzo[1,2-*b*:4,5-*b*']difuran-2,6-dione (1)

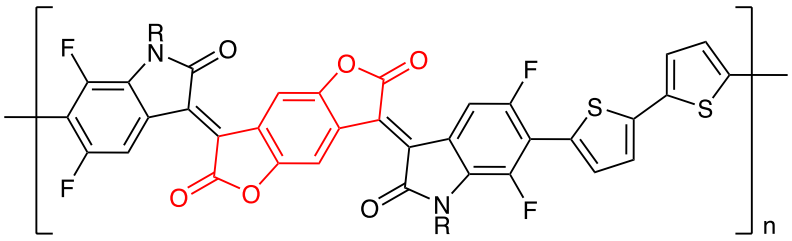
Product Number: **D6317**
1g 5g

3,7-Dihydrobenzo[1,2-*b*:4,5-*b*']difuran-2,6-dione (**1**) is an electron acceptor unit that is recently being increasingly used. Polymers combining **1** with isatin derivatives have been reported to exhibit n-type semiconducting properties with an electron mobility exceeding 1 $cm^2V^{-1}s^{-1}$ in air.[1] Among them, F4BDOPV-2T shows an extremely high electron mobility of 14.9 $cm^2V^{-1}s^{-1}$ in air.[2] Since these reports, the superiority of **1** as an acceptor unit has attracted attention, and various applications are being considered. For example, **2**, obtained by polymerizing **1**, is expected to be applied as a polymer material with excellent transparency and electrical conductivity.[3] In addition, organic thermoelectric materials with a power factor of 80 $\mu Wm^{-1}K^{-2}$, which is among the highest for organic materials, have been realized by UFBDPPV with certain dopants.[4] Further material development using **1** as a raw material with high electron accepting capacity is expected in the future.

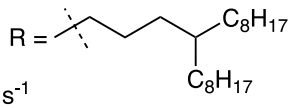


(**1**)

n-Type Organic semiconducting material

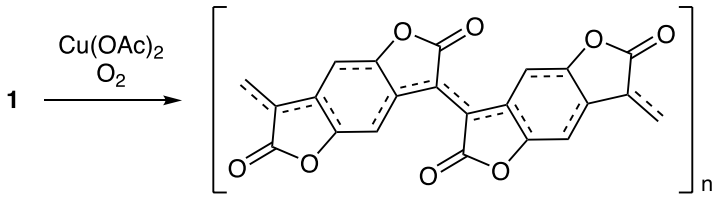


F_4BDOPV-2T



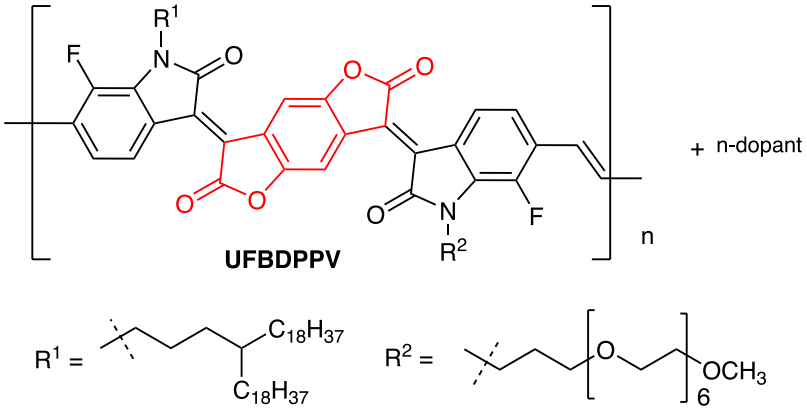
Electron mobility: 14.9 $cm^2V^{-1}s^{-1}$

Conducting material



n-doped poly-benzodifurandione (2)
low sheet resistance
high transmittance

Oorganic thermoelectric material



UFBDPPV

power factor: 80 $\mu Wm^{-1}K^{-2}$ with TAM

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Endo-type Glycohydrolytic Enzymes "Endoglycosidase"

endo-β-_N_-Acetylglucosaminidase (=Endo-M) Recombinant: from _Mucor hiemalis_ expressed in _Candida boidinii_ (100m units/vial) (1) — Product Number: **A1651** **1vial**

Endo-M-W251N Recombinant: from _Mucor hiemalis_ expressed in _Escherichia coli_ (500m units/vial) (2) — Product Number: **E1339** **1vial**

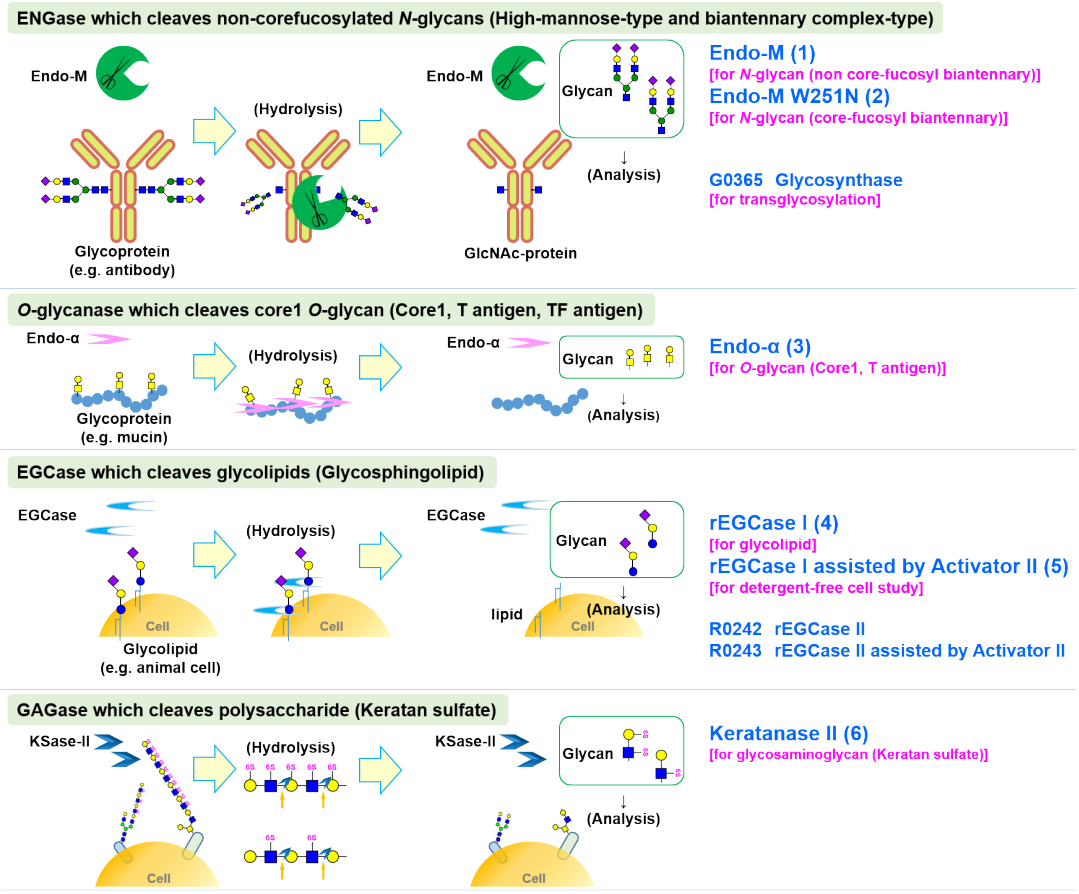
endo-β-_N_-Acetylgalactosaminidase (=Endo-α) Recombinant: from _Bifidobacterium longum_ expressed in _Escherichia coli_ (3) — Product Number: **A1844** **1vial**

rEGCase I (4) — Product Number: **R0240** **1vial**

rEGCase I assisted by Activator II (5) — Product Number: **R0241** **1vial**

Keratanase II from _Bacillus circulans_, Recombinant (6) — Product Number: **K0069** **1vial**

Two types of glycosidases are known: "exo-type" which breaks down from the terminal end of a glycan chain, and "endo-type" which cuts out oligosaccharides from the middle of a glycan chain. TCI has lined up a variety of endoglycosidases for diverse glycan analyses (**1**-**6**). They are gene-recombinant glycosidases and are already available for practical use in large quantities. Please use them as sophisticated research tools for cutting-edge glycoscience.



1 was merchandised as the fruition of NEDO project under licenses from patent-holding companies of Takara Bio Inc. and Kirin Brewery Co., LTD.

2 was commercialized under license from Ishikawa Prefectural University.

3 was merchandised as the fruition of NEDO project.

4, **5**, **R0242** and **R0243** were commercialized under license from Kyushu University.

6 was commercialized under license from Kansai Medical University.

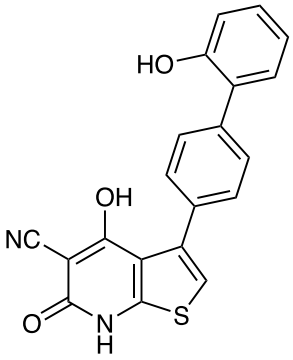
Related Products

Glycosynthase (Endo-M-N175Q) Recombinant: from *Mucor hiemalis* expressed in *Escherichia coli* (100m units/vial)	1vial	G0365
rEGCase II	1vial	R0242
rEGCase II assisted by Activator II	1vial	R0243

AMP-Activated Protein Kinase (AMPK) Activator

A 769662 (1)

Product Number: **H1552**
10mg 50mg



(**1**)

A769662 (**1**) is a cell-permeable activator of AMP-activated protein kinase (AMPK).[1] **1** was found to directly stimulate partially purified rat liver AMPK with EC_{50} = 0.8 μM and inhibited fatty acid synthesis in primary rat hepatocytes with IC_{50} = 3.2 μM.[1]

1 provided significant stimulation to purified rat liver AMPK (EC_{50} = 116 nM) and stimulation of the kinase by **1** was 50 times more potent than that by AMP.[2] The mechanism of activation of AMPK by **1** is allosteric and involves inhibiting dephosphorylation of the kinase on Thr-172.[3] **1** inhibits reprogramming of somatic cells into induced pluripotent stem cells (iPSCs)[4] and proliferation of mesenchymal stem cells.[5]

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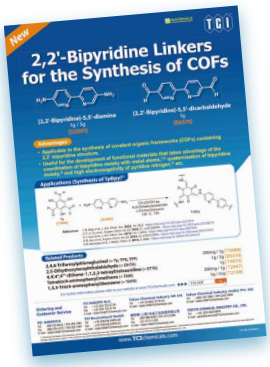
Pamphlets of TCI Products



2,2'-Bipyridine Linkers for the Synthesis of COFs

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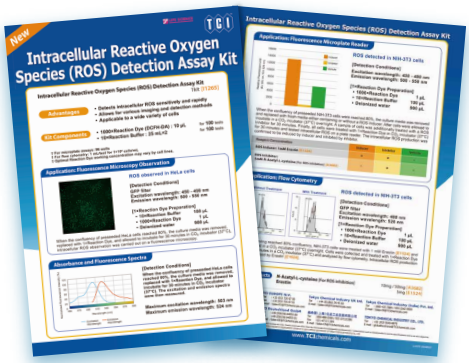
Intracellular Reactive Oxygen Species (ROS) Detection Assay Kit

https://bit.ly/3RLtH8y



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