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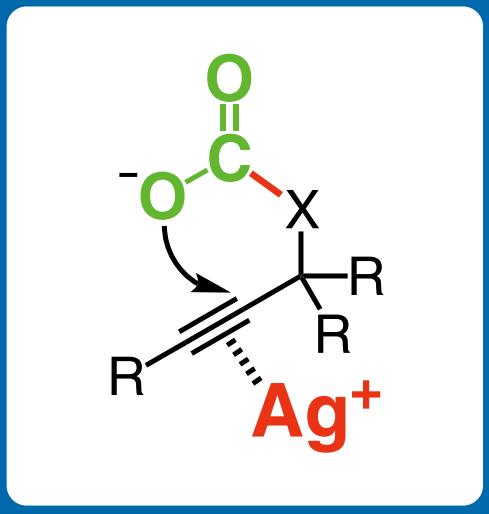

CONTENTS

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Research Article

Silver-Catalyzed CO_2 Incorporation Reactions

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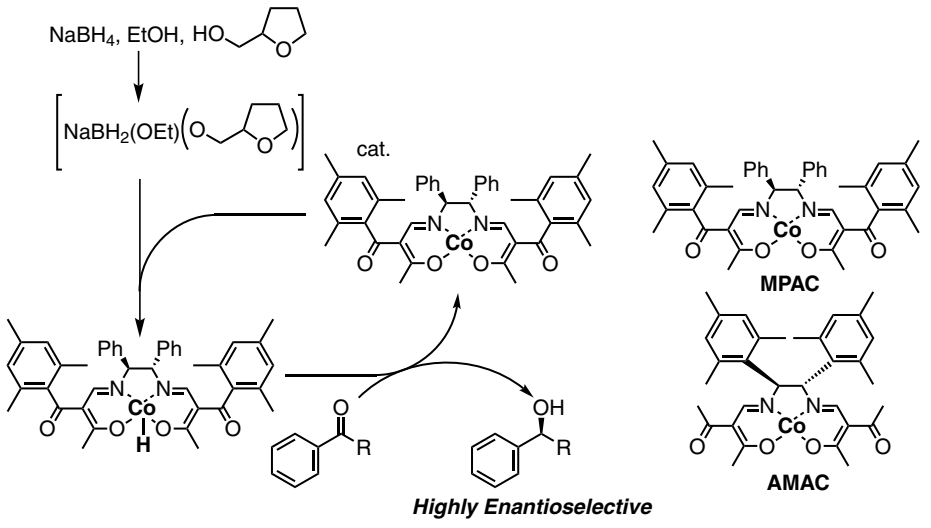
Abstract: Silver-catalyzed reactions are some of the important methodologies in organic chemistry. For the sequential carboxylation and cyclization of alkyne derivatives, such as propargyl alcohols and amines, using carbon dioxide, silver catalysts show significant reactivity under mild conditions unlike other transition metals. Related silver-catalyzed C–C bond forming reactions with carbon dioxide have also provided the synthetic methods of the corresponding carboxylic acid derivatives.

Keywords: Carbon dioxide, Silver catalyst, Alkyne, Cyclic carbonate, Heterocycle

1. Introduction

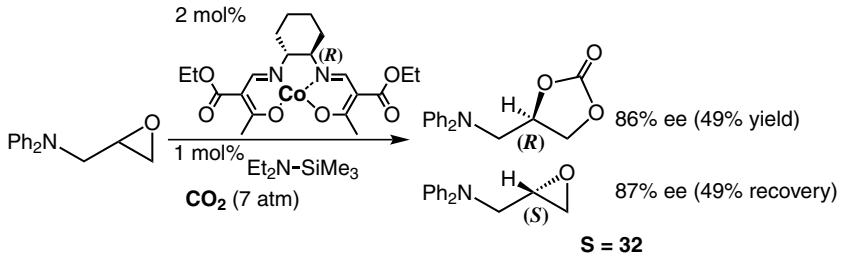
Although the authenticity of temperature data which is the basis of "global warming theory" that the average temperature of the earth is rising unprecedented is suspected, it is fact that the concentration of carbon dioxide in the atmosphere is increasing. There is no choice but to commit a cause for human activity that depends on energy from fossil fuels. In chemistry, oxidation of hydrocarbons releases energy to exhaust the most oxidized carbon dioxide ultimately. This is the unique and basic principle of combustion of fossil fuels, metabolism of life body, fuel cells, *etc*. The challenges of the future are not to merely reduce carbon dioxide emissions, but to convert the energy from fossil fuel base to various resources, although much attention on carbon dioxide due to a powerful greenhouse effect. In industry, because carbon dioxide is provided abundantly on reasonable cost and it is non-toxic in itself, research as an organic synthetic resource is also active. The commercial production of salicylic acid by the Kolbe-Schmitt reaction is one of the most famous practical processes, and recently synthesis of dimethyl carbonate



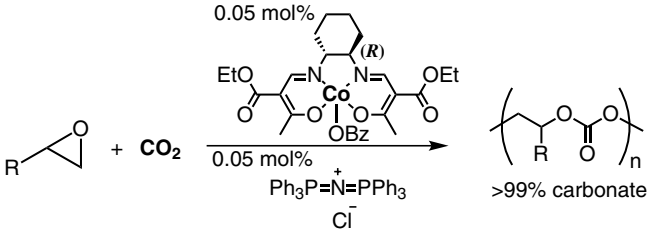
Scheme 1. Enantioselective borohydride reduction

by reaction with methanol has been reported. Cyclic carbonates obtained from the reaction of epoxide and carbon dioxide are expected as polymer precursors such as polycarbonate, as aprotic polar solvents or synthetic intermediates. However, these reactions require severe reaction conditions of high pressure and high temperature including supercritical conditions due to the stability of carbon dioxide, and are limited to the industrial production purpose of simple compounds. The reactions under milder conditions are required for advanced molecular transformation such as synthesis of more complicated structure with high stereoselectivity.

From our research group, optically active cobalt(II) complexes with a conventional reductant; sodium borohydride, have been proposed as an effective system for the catalytic enantioselective reduction of ketone and imine derivatives to afford the corresponding secondary alcohols and amines in high-to-excellent yields with high enantioselectivities[1] (Scheme 1). These cobalt complexes could be employed as the catalyst for enantioselective cyclopropanation of styrene derivatives with diazoacetates.[2] During mechanistic researches, density functional calculations on the hetero-Diels–Alder reaction catalyzed by 3-oxobutylideneaminatocobalt complexes revealed that axial coordination of an aldehyde as a Lewis base induces a spin transition in the catalytic cycle.[3] The Lewis acidity of the complex is increased, and the enantioselectivity improved. Based on these considerations, in the presence of a catalytic amount of optically active cobalt complexes and amine bases, racemic glycidols reacted with gaseous carbon dioxide to afford the optically active cyclic carbonate along with the optically active starting epoxide[4] (Scheme2). The alternating copolymerization of propylene oxide/ alkylene oxide and carbon dioxide has been developed.[5] The ratio-controlled incorporation of the poly(alkylene carbonate) units could improve the thermal properties, such as the glass-transition temperature and thermal degradation temperature, of the obtained polycarbonates[6] (Scheme 3).



Scheme 2. Enantioselective CO_2 fixation catalyzed by cobalt complex



Scheme 3. Polycarbonate with cobalt complex catalyst

2. Silver-Catalyzed Carboxylation of Propargyl Alcohols

In 2007, we reported the silver-catalyzed carboxylation and cyclization of propargyl alcohols under mild reaction conditions.[7,8,9] The study indicated that the combined use of silver acetate and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was an efficient catalyst system for the incorporation of carbon dioxide into various propargyl alcohols to afford the corresponding cyclic carbonates in high-to-excellent yields, though other transition-metals including copper, gold, rhodium, mercury, platinum, and palladium were not effective at room temperature. It was also noted that this catalytic system could be applied to the aryl- and alkyl-substituted internal alkynes even under mild reaction conditions (Scheme 4). The *exo*-alkenyl cyclic carbonates were obtained as the sole isomers and the geometry of the C–C double bond was confirmed to be the *Z* isomer by X-ray single crystal structure analysis or NOE. These results suggested that the silver catalyst activates the C–C triple bond from the opposite side of the carbonate to promote *anti*-addition through 5-*exo*-dig cyclization.

In the reactions mentioned above, the silver-catalyzed reaction of propargyl alcohols with carbon dioxide selectively afforded the corresponding cyclic carbonates in a toluene solution (path **a** in Scheme 4), while in DMF, the corresponding α,β-unsaturated carbonyl compounds, generated via a Meyer–Schuster type reaction, were detected. In polar solvent, the β-carbon of propargyl alcohol would be alternatively attacked

to promote the [3,3]-sigmatropic rearrangement into the allene-enolate. The α,β-unsaturated carbonyl compounds would result from the release of carbon dioxide[10] (path **b** in Scheme 4).

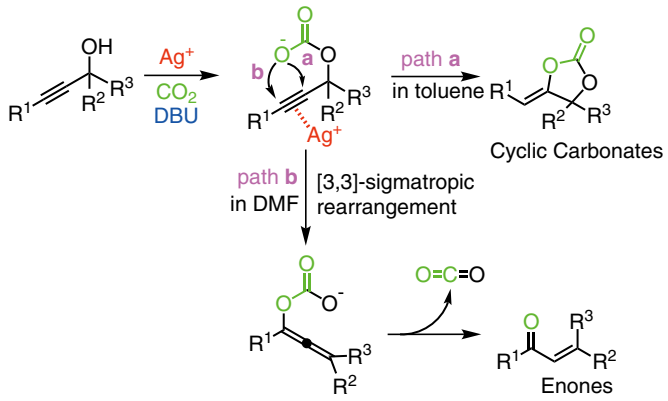
The computational approach for the reaction mechanism was performed.[11] As a model substrate, 2-methyl-3-pentyn-2-ol was adopted for the representative of propargylic alcohol, and 1-methyl-1,4,5,6-tetrahydropyrimidine for the DBU base. The calculations suggested that carboxylate with silver catalyst would be formed as an active species, although the reaction pathway was not clear. We then analyzed the cyclization mechanism from the active species. Although the activation energy between the two pathways did not reverse in the calculation of the model substrate, this observation shows that the polarity of the solvent was crucial for the ratio between the cyclic carbonate and the enone, and this tendency was consistent with the fact that the carbonate was preferentially obtained in the nonpolar solvent, while the enone was predominantly formed in the polar solvent.

On the basis of the reaction mechanism, we developed the asymmetric carbon dioxide incorporation into bispropargyl alcohols with desymmetrization by the combination of silver acetate and the chiral Schiff base ligand L* to afford the corresponding cyclic carbonates with good-to-excellent enantiomeric excess[12] (Scheme 5).

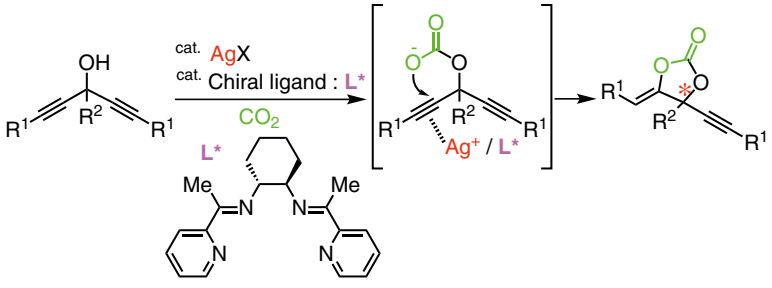
3. Carboxylation with C–C Bond Formation

3-1. Cobalt-Catalyzed Reductive Carboxylation

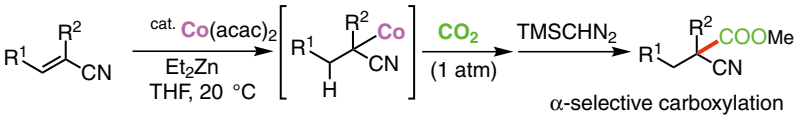
In the presence of a catalytic amount of bis(acetylacetonato) cobalt(II), the reductive carboxylation of α,β-unsaturated carbonyl compounds with carbon dioxide was studied. From this laboratory, the combined use of cobalt(II) complexes with various reductants, such as 2-propanol,[13] silanes,[14] and sodium borohydride,[15] was examined. Isayama and Mukaiyama reported the reductive aldol reaction from α,β-unsaturated nitriles catalyzed by bis(acetylacetonato)cobalt(II) and phenylsilane in 1989.[16] The reaction mechanism is presumed to be as follows: phenylsilane could act on the cobalt complex as a reducing agent to generate "cobalt hydride." Its 1,4-addition to an α,β-unsaturated nitrile would afford the corresponding cobalt enolate equivalent, which would produce the cobalt alkoxide of the aldol adduct by a nucleophilic attack on the electrophile such as aldehydes and ketones. The screening of various reducing agent revealed that diethylzinc effectively afforded the corresponding α-carboxylates in high yield and high regioselectivity from α,β-unsaturated nitriles[17] and *N*-methylanilides.[18]



Scheme 4. Reaction pathways of propargylic alcohol with CO_2



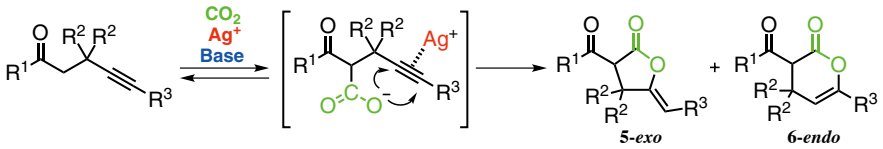
Scheme 5. Enantioselective chemical incorporation of CO_2 into bispropargylic alcohols



Scheme 6. Cobalt-catalyzed reductive carboxylation

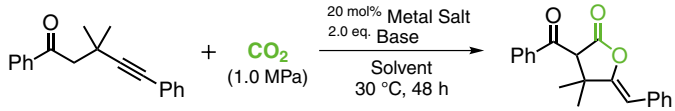
3-2. C–C Bond formation between Enolate and Carbon Dioxide

Propargyl alcohols and propargyl amines were converted to the corresponding cyclic carbonates and oxazolidinones in the presence of silver catalyst. To incorporate carbon dioxide into organic molecules, the formation of C–C bonds between the substrate and carbon dioxide is important. Cyclization following C–C bond forming carboxylation can afford the corresponding lactones that are not easily decarboxylated. In this section, the silver-catalyzed C–C bond forming carboxylation and cyclization reactions are described. Enolate has been a promising reagent for the C–C bond forming reactions in organic chemistry. The reactions of an enolate with carbon dioxide produce the corresponding β-ketocarboxylic acids. Due to its thermodynamic instability, however, β-ketocarboxylic acid would easily revert to the starting material.[19] Therefore, careful treatment or subsequent reduction of the product was required.



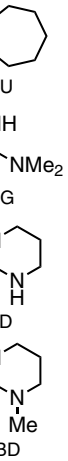
Scheme 7. C–C Bond formation with CO_2

Table 1. Examination of reaction conditions



Entry	Metal Salt	Base	Solvent	Yield / %[a]
1	none	DBU	DMSO	0
2	$Pd(OAc)_2$	DBU	DMSO	trace
3	$Cu(OTf)_2$	DBU	DMSO	0
4	CuBr	DBU	DMSO	0
5	AuCl	DBU	DMSO	0
6	$(Ph_3P)AuCl$	DBU	DMSO	trace
7	AgOAc	DBU	DMSO	22
8	AgOBz	DBU	DMSO	40
9	AgOBz	TMG	DMSO	7
10	AgOBz	TBD	DMSO	3
11	AgOBz	MTBD	DMSO	48
12	AgOBz	MTBD	DMF	72
13[b]	AgOBz	MTBD	DMF	91

[a] Isolated yield. [b] 4 eq. MTBD, 25 °C.



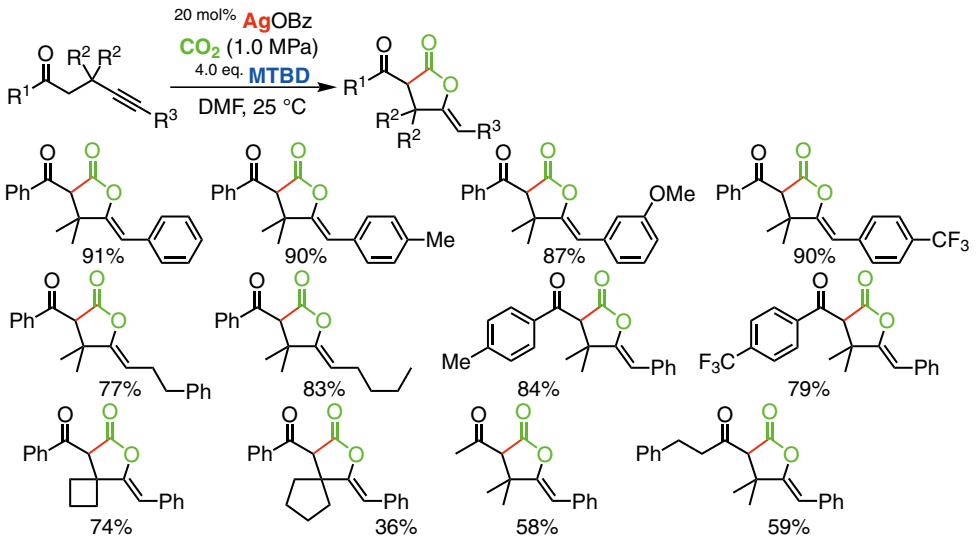


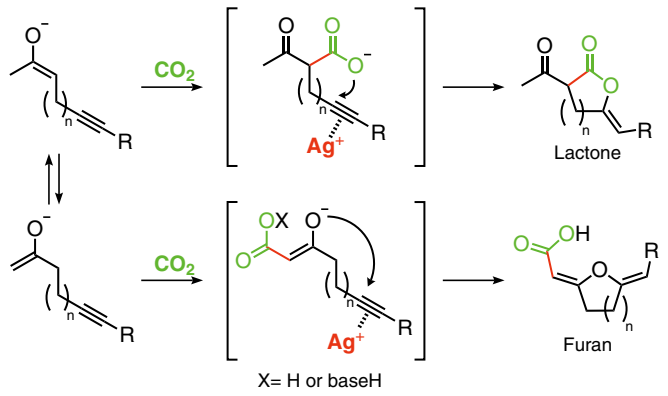
Figure 1. Silver-catalyzed CO_2 incorporation with C–C bond formation

A tandem reaction for the conversion of β-ketocarboxylic acid into a stable compound is one of the most reasonable methods for the reaction of an enolate and carbon dioxide. We reported that β-ketocarboxylate was trapped by the silver-activated C–C triple bond to afford the corresponding stable 5-membered lactone in a one-pot synthesis (Scheme 7).

Several metal catalysts were investigated for the reaction of the model substrate, in DMSO in the presence of DBU (2.0 equiv) under 1.0 MPa CO_2 pressure (Table 1). The reactions did not proceed in the absence of the metal salt. Palladium, copper, and gold(I) salts, which were expected to activate the C–C triple bond, hardly worked for this reaction. Among the catalysts tested, a silver salt was the most effective catalyst for this reaction to produce the γ-lactone. Taking into account the acidity of a proton of the substrate, several bases were screened. In the previous work, amidine-type bases such as DBU were effectively employed to afford the cyclic carbonates in high yield. Based on these results, various amine bases, such as TBD and MTBD, were examined. When MTBD was employed as a base, the product was obtained in good yield, whereas TBD was not an effective base for this reaction. In the preliminary examination of solvents, nonprotic polar solvents were found to promote the reaction smoothly. Several nonprotic polar solvents were next examined. As a result, DMF was found to be the most suitable as the reaction in this solvent afforded the product in the highest yield. Under the optimized conditions the product was obtained in 91% yield at 25 °C in 48 h.[20]

A good scope of substrates under the optimized reaction conditions was indicated (Figure 1). Both aromatic and aliphatic ketones were suitable for this reaction.

Interestingly, during the reaction optimization of the alkyne-containing aliphatic ketones, not only the corresponding lactone derivatives, but also furan derivatives containing a carboxyl group were detected. Based on the structure of the furan, it was assumed that the ketone carbonyl of the β-ketocarboxylic acid was trapped on the C–C triple bond activated by the silver catalyst unlike in our previous studies. This result inspired us to examine the C–C bond forming reaction with carbon dioxide to successively construct a carboxyl group and a furan skeleton. It was postulated that dihydro-isobenzofuran derivatives



Scheme 8. Silver-catalyzed cyclization affords furan derivatives

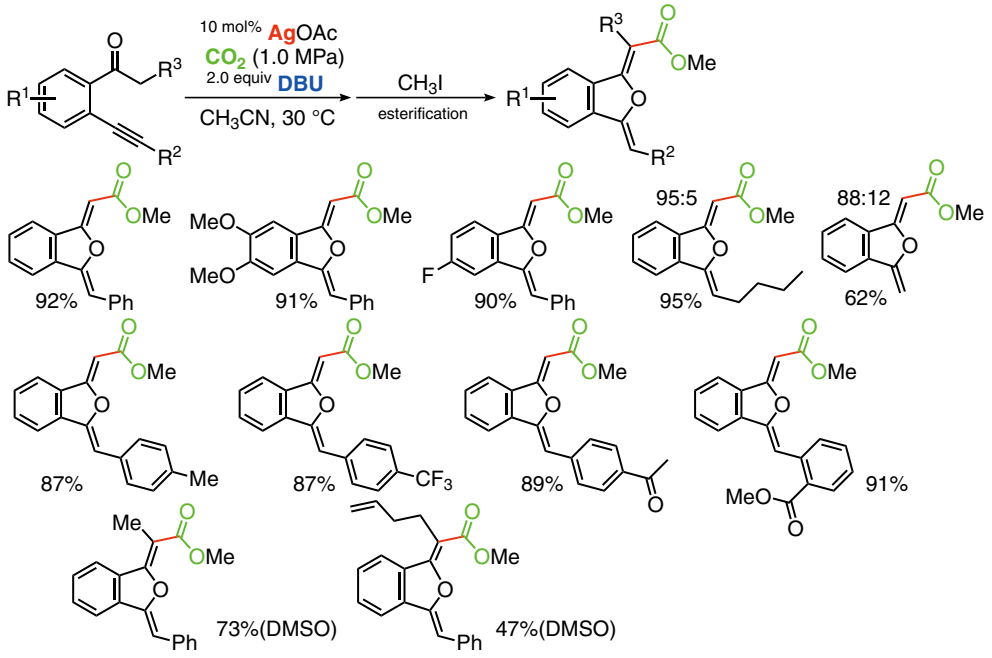


Figure 2. Silver-catalyzed cyclization of several *o*-alkynylacetophenones

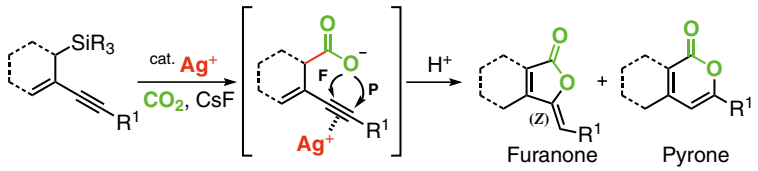
bearing a carboxyl group could be obtained by the 5-*exo*-dig regioselective cyclization of *o*-alkynyl-acetophenone and carbon dioxide using the silver-catalytic system (Scheme 8).

Unfortunately, the purification of the product was not successful using the standard methods, such as back extraction and silica gel column chromatography, though the product could be isolated by recrystallization. In order to obtain the corresponding ester, esterification was attempted. It was found that the carboxylate could be esterified with methyl iodide in a one-pot synthesis to give the corresponding methyl ester in 92% yield.[21] The substrate scope of the silver-catalyzed cyclization under the optimized reaction conditions was shown in Figure 2. The geometries of the two C–C double bonds were suggested to be *Z* isomers based on NOE experiments.

Recently, the silver-catalyzed cascade carboxylation and cyclization of the trimethyl(2-methylenebut-3-yn-1-yl)-silane derivatives were developed. The allylsilane compound is one of the useful reagents for new C–C bond formation. For example, Hosomi–Sakurai allylation has been used to provide homoallyl alcohols, which are an important framework for the total synthesis of natural products and medicinal compounds. Though allylsilane compounds have the additional potential for carbon dioxide incorporation, few systems involving the Lewis acid mediated carboxylation have been reported. The present reaction was promoted by a silver salt and CsF to afford the corresponding 2-furanones and 2-pyrones in good-to-high yields[22] (Scheme 9).

When aromatic ring-substituted alkynes were used, 2-furanone derivatives were selectively obtained via 5-*exo*-dig cyclization, whereas the reaction of the alkyl-substituted alkynes produced 2-pyrone derivatives with high selectivity (Figure 3).

Tetronic acids, or 4-hydroxy-5*H*-furan-2-ones, are found in a range of natural products and are considered as important scaffolds for the construction of bioactive and pharmaceutical compounds. Although several methods for the synthesis of their derivatives have been reported, multiple steps are generally required. In this section, we report that a readily prepared conjugated ynone has been employed as a carbon nucleophile to synthesize tetronic acid derivatives using CO_2 in the presence of a silver catalyst (Scheme 10).



Scheme 9. Carboxylation of allylsilanes

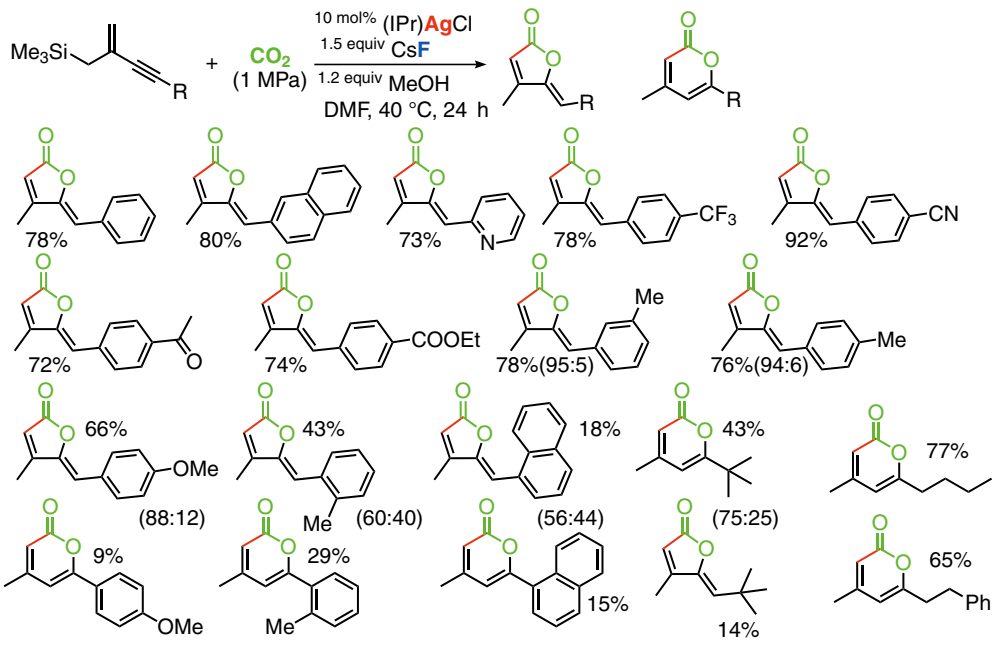
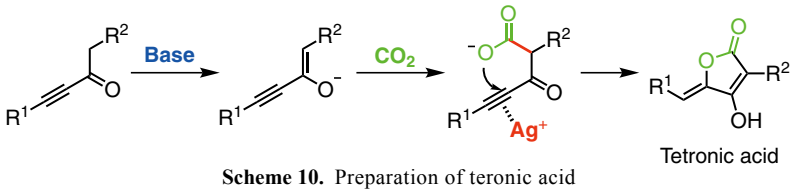


Figure 3. Carboxylation of allylsilanes



Scheme 10. Preparation of teronic acid

Various organic bases were examined first. Under 2.0 MPa pressure of CO_2, the ynone was treated with organic bases in the presence of a catalytic amount of silver acetate in 1,2-dichloromethane. When triethylamine or *N*-methylimidazole was employed, no reaction occurred, and the ynone was quantitatively recovered. The use of 1,5,7-triazabicyclo[4.4.0]-dec-5-ene (TBD), DBU, and 7-methyl-1,5,7-triazabicyclo[4.4.0]-dec-5-ene (MTBD) were found effective against the 5-*exo*-dig cyclization to afford the tetronic acid in 74%, 86%, and 90% yields, respectively.[23]

The optimized conditions were applied to various ynones. The substrates bearing phenyl, *o*-tolyl, *m*-tolyl, and *p*-tolyl groups were converted to the corresponding tetronic acids in 92%, 88%, 74%, and 87% yield, respectively. When substrates with no substituent or bearing an *n*-hexyl group were employed, the 5-*exo*-dig cyclization proceeded to afford the corresponding tetronic acids in 95% and 97% yield, respectively. On the other hand, when the reactions of substrates bearing isopropyl and cyclohexyl groups were examined, 6-*endo*-dig cyclization occurred versus the 5-*exo*-dig cyclization to afford the tetronic acids and the hydroxypyrones (Figure 4).

This protocol was applied to the synthesis of aspulvinone E (Scheme 11). The internal alkyne, which is a precursor for the CO_2 incorporation reaction, was prepared from the reaction of ethyl (4-methoxyphenyl)acetate with the lithium acetylide, generated from (4-methoxyphenyl)acetylene with *n*-BuLi. The silver-catalyzed intramolecular cyclization involving the CO_2 fixation proceeded to afford the corresponding product in 73% yield. After demethylation, aspulvinone E was obtained in 98% isolated yield. Overall, the synthesis of aspulvinone E was achieved in three steps from commercially available materials. In one previous report, six steps including Dieckmann cyclization were required to synthesize aspulvinone E. Therefore, our protocol can be regarded as noteworthy in terms of step-economy.

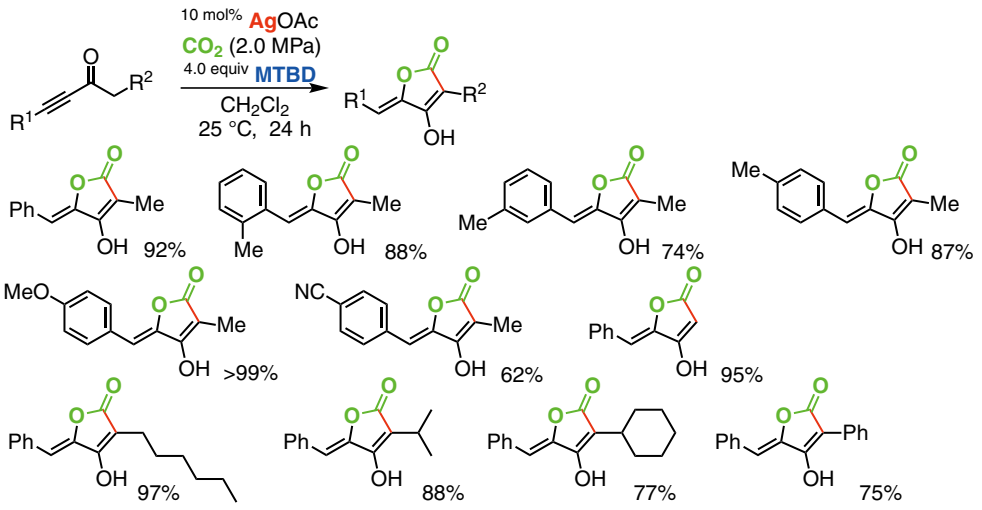
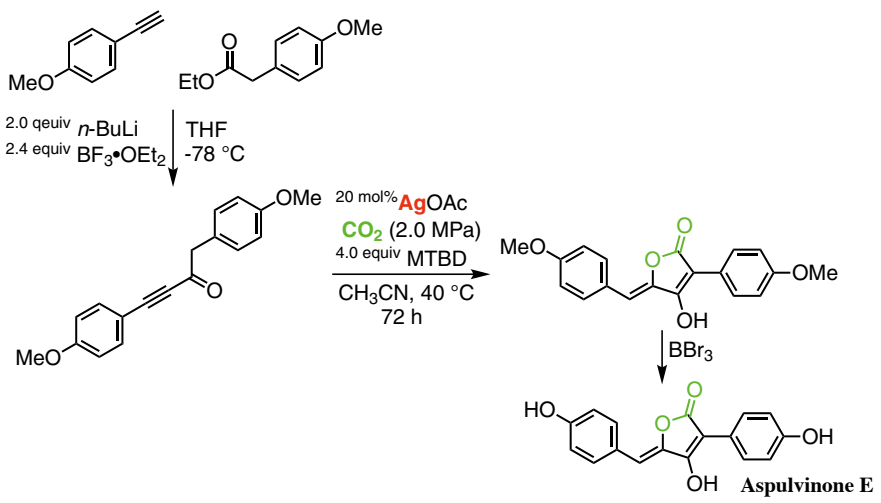


Figure 4. Preparation of various tetronic acid derivatives



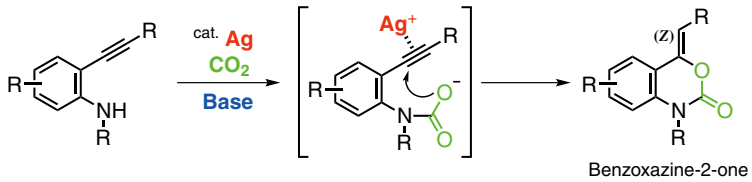
Scheme 11. Facile approach to Aspulvinone E

3-3. Rearrangement for Hydroxylquinolin-2-one and Tetramic Acid

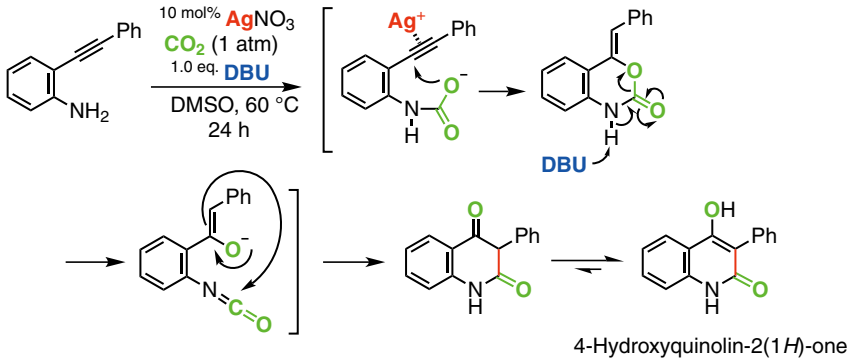
It was found that a silver catalyst successfully promoted the incorporation of CO_2 into *o*-alkynylanilines to afford the corresponding benzoxazine-2-ones bearing (*Z*)-*exo*-olefin *via* 6-*exo*-dig cyclization at the activated C–C triple bond.[24]

During the optimization for the primary *o*-alkynylaniline, a side-product was detected. Based on several analytical results, such as X-ray single crystal structure analysis, ^{1}H NMR, ^{13}C NMR and mass spectrometry, the side-product was identified to be 4-hydroxyquinolin-2(1*H*)-one. The possible reaction mechanism is shown in Scheme 13.

First, the corresponding benzoxazin-2-one would be generated from the *o*-alkynylaniline and carbon dioxide catalyzed by the silver catalyst. In the second step, the benzoxazine would immediately be deprotonated by the DBU base to generate the isocyanate and the enolate from the C–O bond cleavage of the carbamate functionality. The enolate would then attack the carbon atom of the isocyanate to afford the 1,3-diketone intermediate, which would produce the corresponding 4-hydroxyquinolin-2(1*H*)-one after enolization. Isotopic labeling experiments with $C^{18}O_2$ were conducted to reveal that the quinoline contained carbon dioxide. In addition, in situ IR measurement of the reaction of the benzoxazin-2-one and DBU was carried out. After DBU was added to the THF solution of the benzoxazine, absorption at 2150 cm^{-1} assigned as isocyanate group was observed. This result would also support the proposed reaction mechanism (Figure 5).



Scheme 12. Silver-catalyzed CO_2 incorporation into *o*-alkynylanilines



Scheme 13. Rearrangement reaction *via* isocyanate

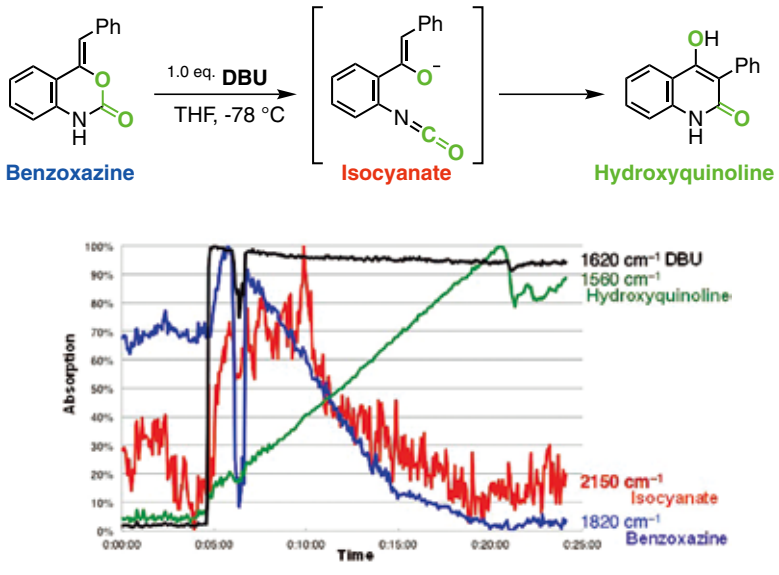


Figure 5. Isocyanate absorption region (2150 cm^{-1}) was detected by *in situ* IR measurement

Under the optimized reaction conditions, various *o*-alkynylaniline derivatives were applied to the C–C bond-forming carbon dioxide incorporation reaction. The reactivity of the enolate intermediates was not influenced by steric or electronic effect. Various substrates could be subjected to the optimized reaction conditions and smoothly transformed into the corresponding quinoline derivatives in high yields[25] (Figure 6).

The cyclization and rearrangement system was applied to propargyl amines for the synthesis of tetramic acid. Tetramic acid structures are found in natural products known for their biological activity. For example, reutericyclin[26] inhibits Gram-positive bacteria, and discodermide[27] inhibits the growth of Candida fungi. In addition, spirotetramat has been used as an agricultural chemical.[28] This rearrangement mentioned-above was expected to be applicable to five-membered ring compounds to enable synthesis of tetramic acid derivatives from the corresponding primary propargylic amines (Scheme 14).

The optimized reaction conditions were applied to reactions involving various primary propargylic amine derivatives[29] (Figure 7). In the presence of 0.5 mol% of $AgNO_3$ and 2.0 equiv of DBU under atmospheric pressure of carbon dioxide in MeCN, various propargylic amines were converted into the corresponding tetramic acids in high yield.

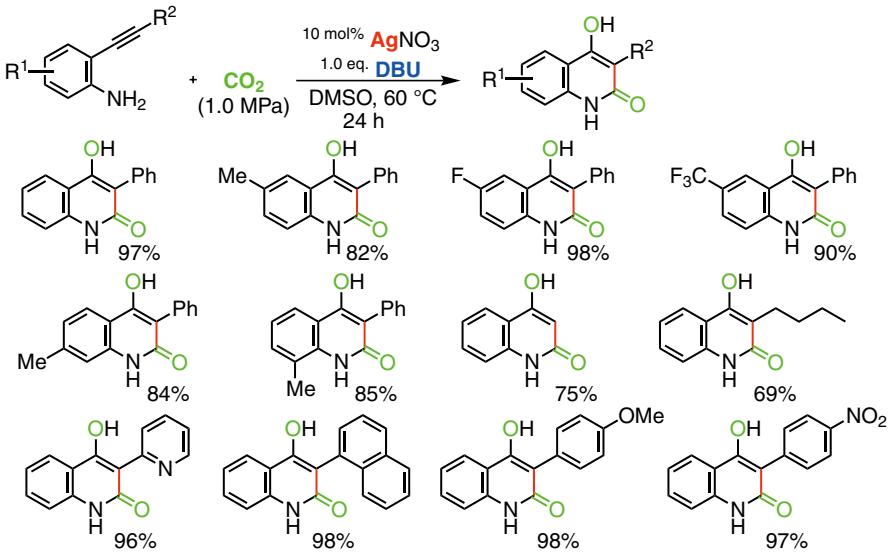
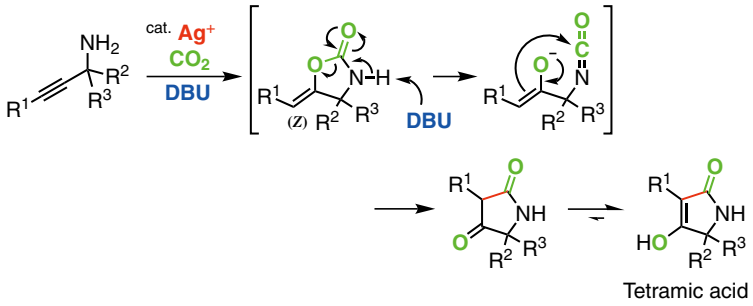


Figure 6. CO_2 Incorporation through intramolecular rearrangement with *o*-alkynylanilines



Scheme 14. CO_2 Incorporation and intramolecular rearrangement into propargylic amines

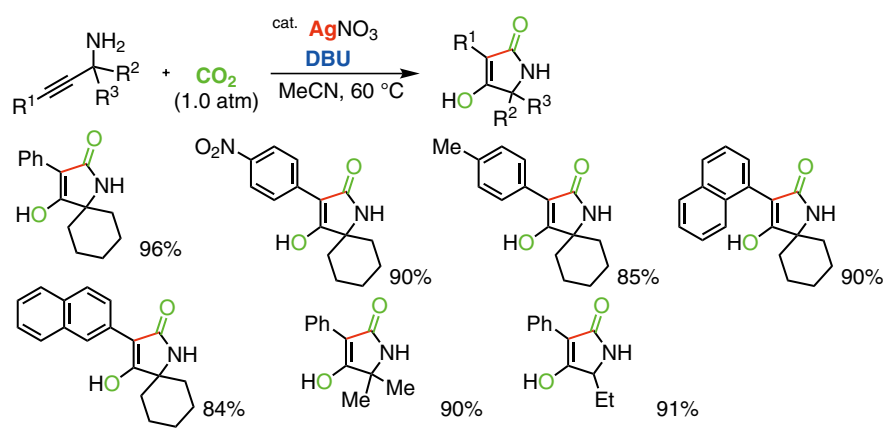


Figure 7. CO_2 Incorporation into various propargylic amines

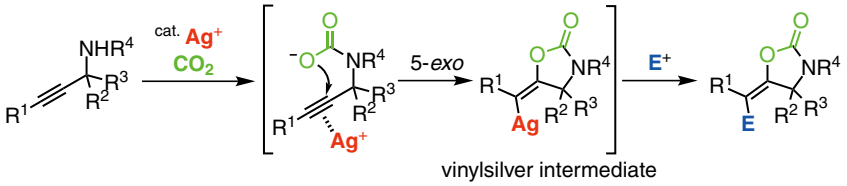
3-4. Three-Component Reaction of Propargylic Amines for Preparation of (*E*)-Halovinyloxazolidinones

The oxazolidinone preparation from carbon dioxide is one of the most attractive synthetic methods. We reported that carbon dioxide incorporation into various propargylic amines proceeded to give the corresponding oxazolidinone derivatives in high yields under mild reaction conditions, i.e., 2 mol% of AgOAc and 1.0 atm of carbon dioxide. Through the reaction, a vinylsilver intermediate was expected to be stereoselectively generated as a result of the *anti*-addition of carbamate to the C–C triple bond activated by silver salts. It is reasonable to assume that the silver ion in the intermediate would be stereospecifically replaced by a proton to produce (*Z*)-alkenyloxazolidinone and regenerate the silver catalyst. This plausible mechanism suggested that in the presence of appropriate electrophiles (E^+), the C(vinyl)–Ag bond could be stereospecifically trapped by the electrophiles instead of the proton to afford the corresponding oxazolidinones containing the C(vinyl)–E bond with high geometry control (Scheme 15).

For the initial screening, the propargylic amine was employed as the starting material using 10 mol% AgOAc in DMSO under a 2.0 MPa CO_2 atmosphere. The halonium ions were first examined using the corresponding succinimides. In the case of *N*-chlorosuccinimide and *N*-bromosuccinimide, the corresponding oxazolidinone was not obtained. When *N*-iodosuccinimide (NIS) was employed, the propargylic amine was completely consumed in 24 h to produce the oxazolidinone bearing the iodovinyl group in 92% yield.[30]

The halonium ion is typically employed as an activator for alkenes and alkynes for halocyclization, such as halolactonization. Therefore, it was a concern that, without silver catalysts, NIS itself promoted the cyclization to afford the oxazolidinone. In the absence of AgOAc, the oxazolidinone was obtained in 10% yield along with a 20% yield of the imine. The imine was supposed to be produced by the oxidation of benzylamine by the iodonium ion. When iodine was employed instead of NIS, the reaction did not afford the oxazolidinone at all. It was assumed that the iodo-cyclization pathway was not dominant in the present silver-catalyzed reaction and that the vinylsilver intermediate could be trapped by the iodonium ion to stereoselectively afford corresponding (*E*)-oxazolidinones.[31] The scope of the substrates was investigated under the optimized reaction conditions (Figure 8).

Next the bromination was examined. Initially, *N*-bromosuccinimide was employed under the similar reaction conditions as iodination reaction. However, the corresponding (*E*)-bromovinyloxazolidinone was not obtained at all and the corresponding imine was isolated in 18% yield. In order to suppress the imine formation, various organic bases were examined. It was found that the use of 1,1,3,3-tetramethylguanidine (TMG) afforded the brominated product. After screening of reaction solvents, when CH_3CN was employed for this reaction, the yield and selectivity significantly increased to 68% with the formation of the protonated product in 2% yield. The *N*-aryl guanidine substituted by an electron-withdrawing group such as the 4-CF_3 and 4-CN groups, gave the brominated product selectively. With the optimized reaction conditions, the scope of the propargylic amines for the silver-catalyzed three-component reaction was next examined using the 4-CNC_6H_4-TMG[32] (Figure 9).



Scheme 15. Three-component reaction of propargylic amine, CO_2 and electrophile

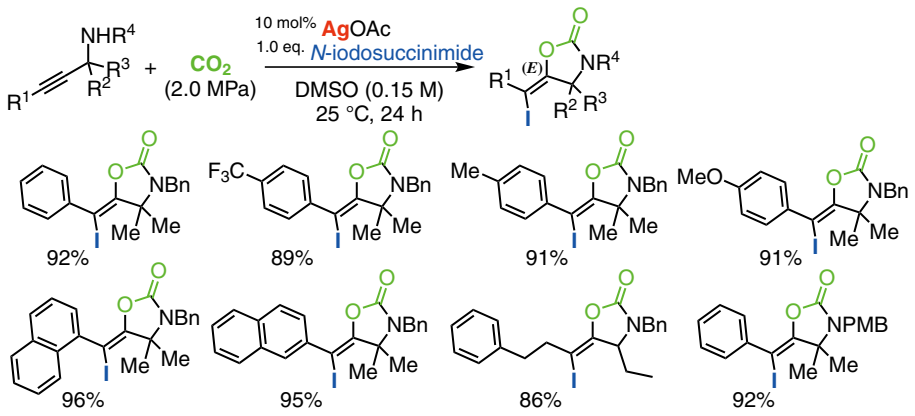


Figure 8. Three-components iodination of propargylic amines

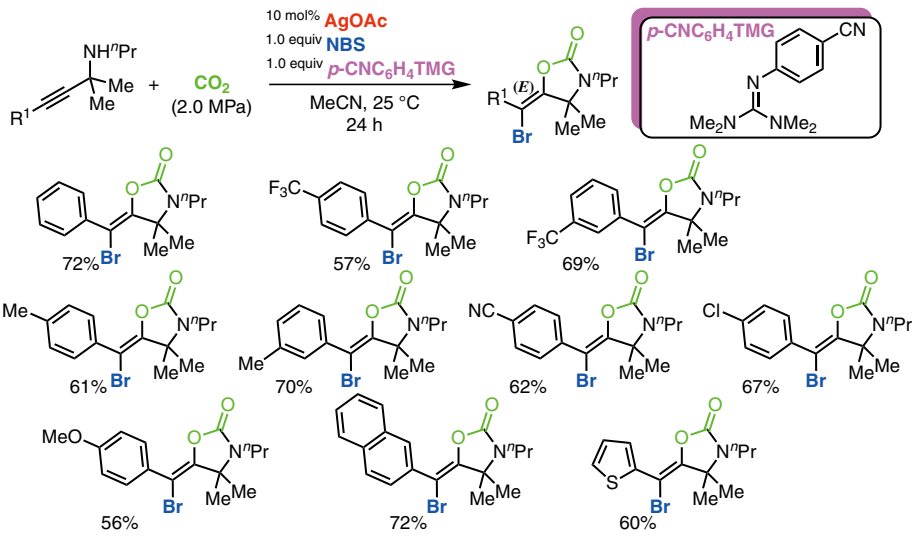


Figure 9. Three-components bromination of propargylic amines

4. Conclusion

Initially, I considered carbon dioxide was an inactive molecule due to its high thermodynamic stability, but the reactions introduced in this paper are performed under rather mild conditions at the maximum 2 MPa CO_2 pressure and 60 °C. In addition, the nucleophilic addition reaction with carbon dioxide sufficiently proceeded not only with an alcoholic oxygen atom or a nitrogen atom of an amino group but also with the enolate generated by an organic base or the carbanion equivalent generated from an organic silane compound in the presence of a fluoride ion, to afford the corresponding cyclized products. In particular, the reaction between an enolate and carbon dioxide is a reverse reaction of the decarboxylation step of the acetoacetic ester synthesis method. It was shown that decarboxylation could be sufficiently suppressed by stabilizing with lactone formation by an appropriate trap of thermally unstable β-ketocarboxylic acid with the alkyne activated in the presence of the silver catalyst. In other reactions, though it should be considered that the silver catalyst or the organic base could activate carbon dioxide, the cyclization step was effective to suppress decarboxylation.

Carbon dioxide is a safe and inexpensive C1 synthesis unit. Conventionally, highly toxic compounds such as phosgene have been applied to the same purpose. I hope that the above-mentioned reactions will replace those dangerous processes for the synthesis of heterocyclic compounds.

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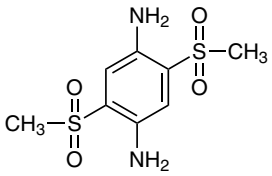
[Award] 1993 Chemical Society of Japan Award for Young Chemist, 2010 SSOCJ Nissan Chemical Industries Award for Novel Reaction & Method 2009.
[Research Interests] Organic synthesis, Asymmetric reaction
[Contact] E-mail: yamada@chem.keio.ac.jp

TCI Related Products

B1844	(*R*)-MPAC [= (1*R*,2*R*)-*N*,*N*'-Bis[3-oxo-2-(2,4,6-trimethylbenzoyl)butylidene]-1,2-diphenylethylenediaminato Cobalt(II)]			100mg
B1845	(*S*)-MPAC [= (1*S*,2*S*)-*N*,*N*'-Bis[3-oxo-2-(2,4,6-trimethylbenzoyl)butylidene]-1,2-diphenylethylenediaminato Cobalt(II)]			100mg
B2314	(*R*)-AMAC [= (1*R*,2*R*)-*N*,*N*'-Bis(2-acetyl-3-oxo-2-butenylidene)-1,2-dimesitylethylenediaminato Cobalt(II)]			100mg
B2315	(*S*)-AMAC [= (1*S*,2*S*)-*N*,*N*'-Bis(2-acetyl-3-oxo-2-butenylidene)-1,2-dimesitylethylenediaminato Cobalt(II)]			100mg
D1270	DBU (= 1,8-Diazabicyclo[5.4.0]-7-undecene)	25g	100g	500g
T0148	TMG (= 1,1,3,3-Tetramethylguanidine)	25mL	100mL	500mL
T1982	TBD (= 1,5,7-Triazabicyclo[4.4.0]dec-5-ene)		5g	25g
M1443	MTBD (= 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene)		1g	5g
B0656	NBS (= *N*-Bromosuccinimide)	25g	100g	500g

Green-Fluorescent Dye with Extremely Small Molecular Size

B5419 BMeS-*p*-A (1) **200mg 1g**



BMeS-*p*-A (**1**)

BMeS-*p*-A (**1**) is a novel synthetic dye. Due to its unique and symmetrical molecular design, **1** shows green fluorescence despite its small molecular size (Table1). **1** shows large Stokes shifts up to 140 nm due to a large conformation change in the excited-state.

The absorption and fluorescence properties of **1** are independent of pH, solvents, or concentration (Figure1, 2). **1** additionally shows high photo-stability. The unique and robust qualities of **1** could be expected to be applied to a variety of applications.

Table 1. Optical properties of BMeS-*p*-A

Solvent	λ^{max}_{abs} (nm)	λ^{max}_{em} (nm)	Stokes shift (nm)	ε ($M^{-1}cm^{-1}$)	ϕ
THF	384	490	106	4170	0.51
MeOH	385	505	120	3990	0.47
DMSO	394	509	115	4360	0.70
Water	377	517	140	3820	0.64
Powder	380	477	97	—	0.69

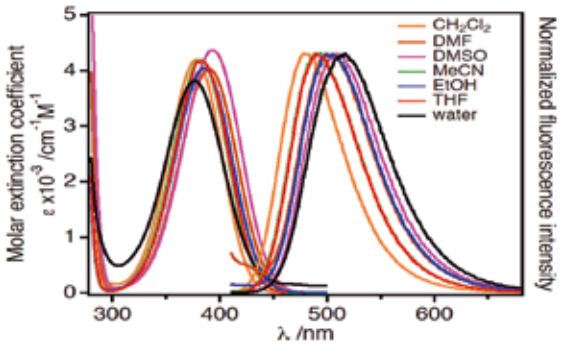


Figure 1. Absorption and fluorescence spectra of BMeS-*p*-A in various solvents

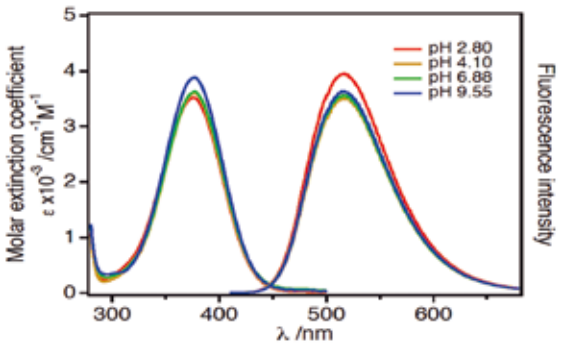


Figure 2. Absorption and fluorescence spectra of BMeS-*p*-A under various pH conditions

This material was produced by collaboration with Prof. Hiroshi Katagiri at Yamagata University.

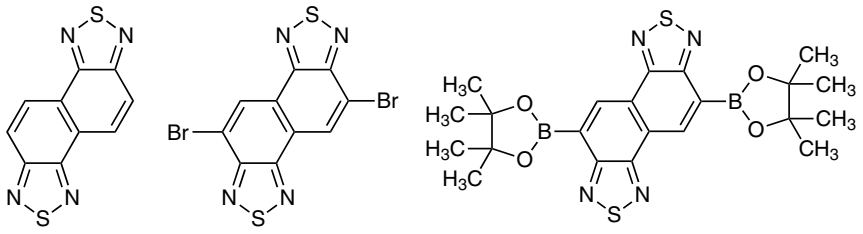
Reference

1) T. Beppu, K. Tomiguchi, A. Masuhara, Y.-J. Pu, H. Katagiri, *Angew. Chem. Int. Ed.* **2015**, *54*, 7332.

Useful Acceptor-Type Organic Semiconductor Building Blocks

N1105	Naphtho[1,2-*c*:5,6-*c*']bis([1,2,5]thiadiazole) (**1**)	200mg
D5288	5,10-Dibromonaphtho[1,2-*c*:5,6-*c*']bis([1,2,5]thiadiazole) (**2**)	100mg
B5470	5,10-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-naphtho[1,2-*c*:5,6-*c*']bis([1,2,5]thiadiazole) (**3**)	100mg

Naphtho[1,2-*c*:5,6-*c*']bis([1,2,5]thiadiazole) (NTz) structures (**1**–**3**) are useful electron-deficient type building blocks for organic semiconductors. Some donor–acceptor conjugated polymers containing the NTz structures exhibited better power conversion efficiency (PCE) compared with widely used 2,1,3-benzothiadiazole-based polymers in organic photovoltaic devices.[1,2] In addition, several conjugated polymers exhibiting beyond 10% PCEs were reported in 2016.[3]



1 **2** **3**

2,1,3-Benzothiadiazole

References

1) Donor–acceptor conjugated polymer based on naphtho[1,2-*c*:5,6-*c*]bis[1,2,5]thiadiazole for high-performance polymer solar cells
M. Wang, X. Hu, P. Liu, W. Li, X. Gong, F. Huang, Y. Cao, *J. Am. Chem. Soc.* **2011**, *133*, 9638.
2) Synthesis, characterization, and transistor and solar cell applications of a naphthobisthiadiazole-based semiconducting polymer
I. Osaka, M. Shimawaki, H. Mori, I. Doi, E. Miyazaki, T. Koganezawa, K. Takimiya, *J. Am. Chem. Soc.* **2012**, *134*, 3498.
3) Implication of fluorine atom on electronic properties, ordering structures, and photovoltaic performance in naphthobisthiadiazole-based semiconducting polymers
K. Kawashima, T. Fukuhara, Y. Suda, Y. Suzuki, T. Koganezawa, H. Yoshida, H. Ohkita, I. Osaka, K. Takimiya, *J. Am. Chem. Soc.* **2016**, *138*, 10265.

TCI Related Product

B0921	2,1,3-Benzothiadiazole	10g 25g

Protein Staining Reagent

C3488 Coomassie Brilliant Blue G-250 (Ready-to-use solution) [for Electrophoresis] (1) 500mL

1 is a methanol- and acetic acid-free one-component ready-to-use solution for staining proteins. After polyacrylamide gelelectrophoresis, **1** can be used for protein staining by soaking the gel in **1**.

Direction for Use :

1. After gelelectrophoresis, wash the gel with deionized water for 5 minutes three times.
2. Remove the water, add **1** till the gel is soaked and shake the gel gently for 1 hour at room temperature.
3. Remove **1** and destain the gel with deionized water for 1 hour. If high background staining is observed, destain the gel with deionized water overnight at room temperature.

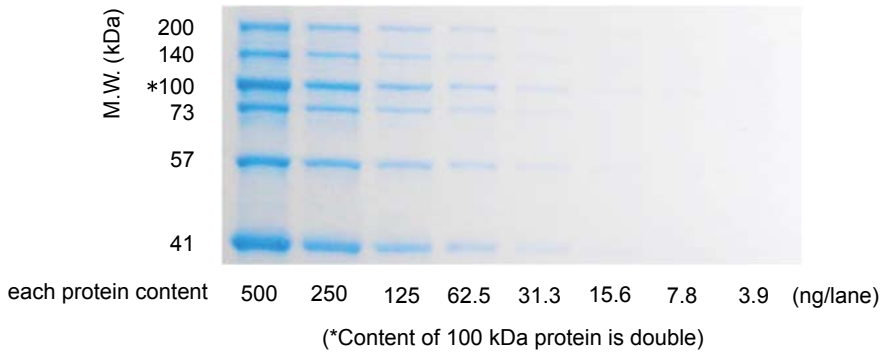


Figure. Proteins stained by the above method (destained overnight)

References

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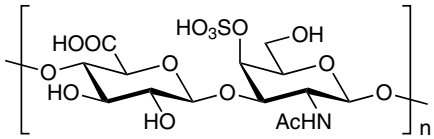
TCI Related Products

B3193	Coomassie Brilliant Blue G-250 [for Electrophoresis]	5g
B3194	Coomassie Brilliant Blue R-250 [for Electrophoresis]	5g

Monoclonal Antibody (LY111) Recognizing Chondroitin Sulfate A

A3143 Anti-Chondroitin Sulfate A Monoclonal Antibody (LY111) (1) 1 vial

The monoclonal antibody **1** binds to chondroitin sulfate A, a type of glycosaminoglycan. It has been reported that chondroitin sulfates are ubiquitous in various tissues such as cartilage, cornea, and brain, and are involved in moisture regulation and cell adhesion, as well the immune system. **1** preferentially recognizes chondroitin sulfate A, which bares a sulfate at 4-position of GalNAc (**2**).[1)]



Chondroitin Sulfate A (**2**)

Reference

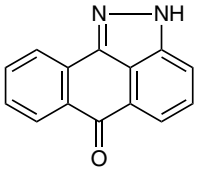
1) Structural determination of novel sulfated octasaccharides isolated from chondroitin sulfate of shark cartilage and their application for characterizing monoclonal antibody epitopes
S. S. Deepa, S. Yamada, S. Fukui, K. Sugahara, *Glycobiology* **2007**, *17*, 631.

Related Products

A2872	Anti-Chondroitin Sulfate D Monoclonal Antibody (MO-225)	1 vial
A2968	Anti-Keratan Sulfate Monoclonal Antibody (R-10G)	1 vial

c-Jun N-Terminal Kinase (JNK) Inhibitor

A2548 SP600125 (1) 25mg



1

SP600125 (**1**) is an inhibitor for JNK1, JNK2, and JNK3 with IC_{50} of 40 nM, 40 nM, and 90 nM respectively.[1)] Inhibitory constants of **1** for these JNKs are Ki = 0.19 μM. The inhibitory mechanism of **1** to the JNKs is ATP-competitive.

The selectivity of **1** was determined by crystal structural analysis using the ternary complex, JNK1-peptide fragment JIP1-**1**.[2)] JIP1 is a member of the JNK-interacting protein (JIP) family and contains a JNK binding domain (JBD), an SRC homology (SH3) domain, and a phosphotyrosine-binding (PTB) domain.[3,4)] JBD possesses the consensus sequence, R/KXXXXLXL.[5)] The sequence of peptide fragment JIP1 used in the research described above is RPKRPTTLNLF.[2)]

This product is for research purpose only.

References

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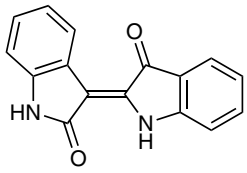
Protein Kinase Inhibitor: Indirubin

I0868 Indirubin (1) **25mg**



1

Indirubin (**1**) is an inhibitor of protein kinases (Table).[1,2] According to a crystal structure study of CDK2 in complexation with indirubin derivatives has shown that **1** interacts with the ATP-binding site of the kinase.[1] **1** also was reported to have high binding affinity with the aryl hydrocarbon receptor (AhR).[3]

In DNCB-induced mice, **1** inhibited allergic contact dermatitis by regulating T helper mediated immune system.[4]

CDK: cyclin-dependent kinase
DNCB: 1-chloro-2,4-dinitrobenzene

Table. Inhibition of kinases by indirubin

Enzyme	IC_{50} (μM)	References
CDK1/cyclin B	10	1
CDK2/cyclin A	2.2	1
CDK2/cyclin E	7.5	1
CDK4/cyclin D1	12	1
CDK5/p35	5.5	1
Casein kinase 1	8.5	1
c-Src tyrosine kinase	18	1
GSK-3β	0.6	2

This product is for research purpose only.

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1) Indirubin, the active constituent of a chinese antileukaemia medicine, inhibits cyclin-dependent kinases
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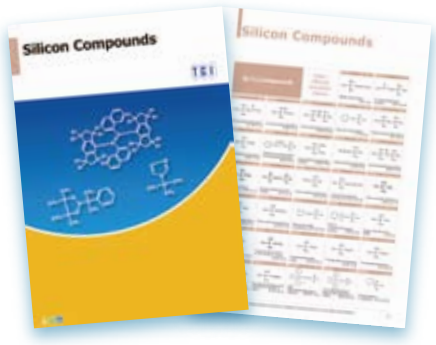

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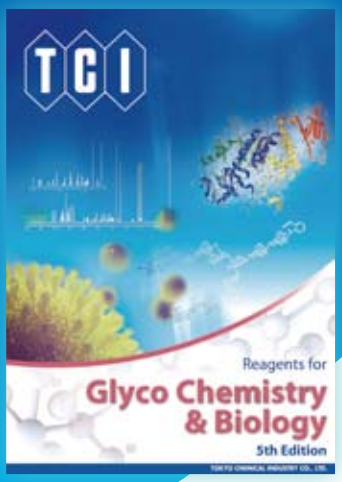

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