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Chemical fixation of CO_2/CS_2 to access iodoallenyl oxazolidinones and allenyl thiazolidine-thiones†

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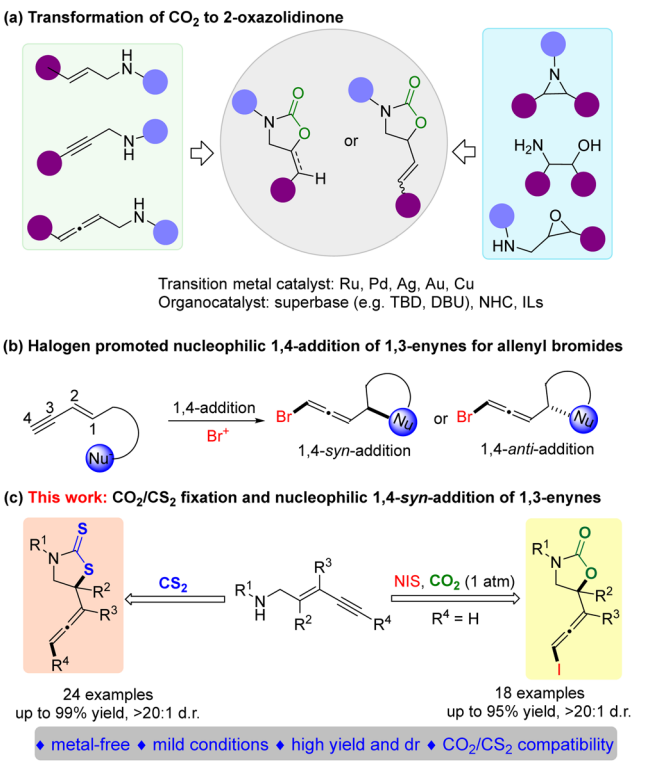
Constructing heterocyclic compounds by chemical fixation of CO_2/CS_2 as a C1 building block is a promising approach. An efficient and environmentally friendly synthetic approach has been developed using CO_2/CS_2 to prepare complicated allenyl heterocycles with high yields and diastereoselectivities in a metal-free manner under mild conditions. NIS promoted CO_2 fixation and the cyclization reaction by exclusive 1,4-*syn*-addition of 1,3-enynes rather than 1,2-addition or 3,4-addition, while CS_2 participated in unique 1,4-*syn*-hydrothiolation of 1,3-enynes to afford allenyl heterocycles with different reaction patterns.

With the increasing of the ever-growing carbon dioxide (CO_2) level in the aerosphere, a variety of approaches have been developed for CO_2 capture, storage and its utilization in the past few decades.[1] With CO_2 being an abundant, nontoxic and easily available C1 building block, the fixation and post-transformations into valuable products are very hot topics related to the effective reduction of CO_2 emissions nowadays.[2] However, chemists have achieved very limited yields for the conversion of CO_2 to carboxylic acids, (poly)carbonates, carbamates, ureas and so on.[1a,3] Therefore, efficiently recycling CO_2 into value-added products remains a formidable challenge especially under atmospheric pressure due to the thermodynamic stability and kinetic inertness of CO_2.

2-Oxazolidinones are some of the important heterocyclic compounds, and have been widely applied as chemical intermediates, chiral auxiliaries, drugs and other bioactive molecules.[4] To date, several methods were developed for constructing oxazolidinones using CO_2 as a sustainable feedstock such as carbonylations of amino alcohols with phosgene/CO_2, carbamations of unsaturated amines/epoxy amines with CO_2, coupling reactions between aziridine and CO_2, *etc.*[5–7] However, harsh reaction conditions including strong acids/bases, or high pressures, have usually been utilized to activate inert CO_2. Recently, several catalytic approaches for the carboxylative cyclization of unsaturated amines with CO_2 have been disclosed, including using transition metal catalysts based on Ru, Pd, Ag, Au, and Cu[8] and organocatalysts obtained using superbases,[9] ionic liquids[10] and N-heterocyclic carbene[11] (Scheme 1a). Additionally, halogen promoted intramolecular nucleophilic 1,4-*syn*/*anti*-addition of 1,3-enynes represents one



Scheme 1 Synthesis of oxazolidinones from CO_2. (a) Transformation of CO_2 to 2-oxazolidinone. (b) Halogen promoted nucleophilic addition. (c) CO_2/CS_2 fixation and nucleophilic addition.

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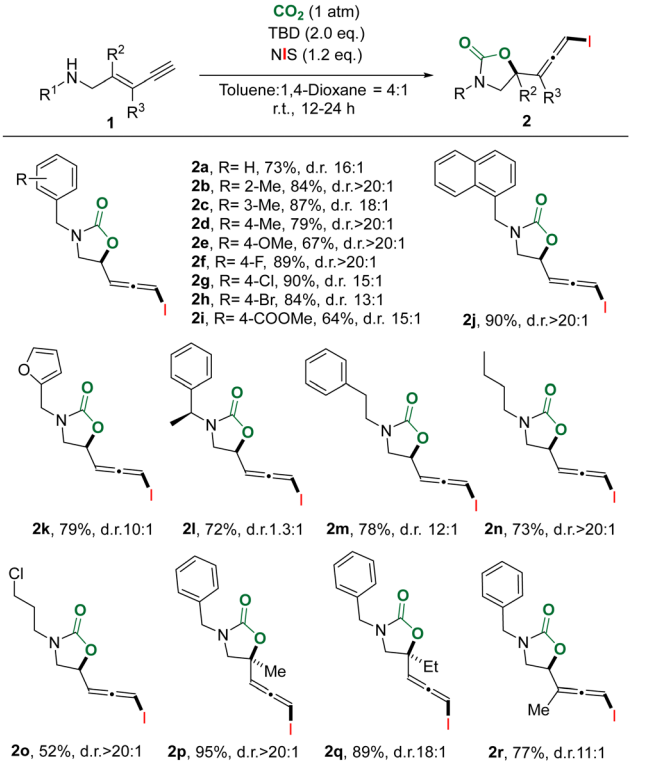
of the powerful approaches for the stereoselective introduction of allenyl bromides (Scheme 1b).[12] Allenes are attractive molecules, and serve as versatile synthons for preparation of a variety of bioactive compounds.[13] Therefore, we envisioned that 1,3-enynes could efficiently activate CO_2 to undergo nucleophilic 1,4-addition rather than 1,2-addition or 3,4-addition promoted by halogen. Such a designed reaction can not only afford important haloallenyl-containing 2-oxazolidones from simple starting materials, but also expand the diversity of CO_2 transformations (Scheme 1c).

Carbon disulfide (CS_2) as an isoelectronic analogue of carbon dioxide is extensively used to prepare versatile organosulfur compounds due to its low cost, stability, and easy availability. A thiazolidine-2-thione skeleton is a useful intermediate in the fields of medicine, agriculture, and fine chemicals.[14] Although the synthetic methods for the preparation of thiazolidine-2-thiones using CS_2 have been reported,[15–17] the reaction between CS_2 and 1,3-enynes to afford allenes is still unprecedented. Compared to CO_2, CS_2 is considered to be more reactive due to the weaker C=S double bond.[18] Thus, we rationalized that CS_2 could rapidly react with 1,3-enynes even without additional electrophilic reagents. Herein, we proposed a concept for chemical fixation of CO_2/CS_2 for converting these C1 building blocks to unique iodoallenyl 2-oxazolidones or allenyl thiazolidine-2-thiones by exclusive 1,4-*syn*-addition of 1,3-enynes.

To test the concept, we began our investigation by using **1a** as the model substrate, and treated with DBU and NIS under 1 atm CO_2 in $CHCl_3$ at room temperature. The iodoallenyl oxazolidinone product **2a** was obtained in 28% yield with 1 : 1 dr (Table S1, ESI,† entry 1). Then, various bases were screened (Table S1, ESI,† entries 2–6). TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) could provide better combined yield and diastereoselectivity, generating product **2a** in 48% isolated yield and 3 : 1 dr. Next, different solvents and binary mixed solvents were explored and best results were obtained using a toluene/1,4-dioxane (4 : 1) system (Table S1, entry 25, see the ESI† for optimization details).[19]

With the optimal reaction conditions in hand, we investigated the substitution effect on the amines and alkenes for the substrate scope (Table 1). Various changes at nitrogen and alkene substituents could be well tolerated. For the diverse substituents of nitrogen, no obvious electronic effects were observed in most cases. The *ortho*-, *meta*- and *para*-methylbenzyl substrates provided desired products (**2b–2d**) with a high yield (79–87%) and dr (18 : 1 to > 20 : 1). These results indicate that different substituted patterns may affect the reactivity. The more electron-donating *para*-methoxy group gave the desired product (**2e**) in 67% with excellent dr (> 20 : 1). Therefore, more *para*-substituted substrates were examined for this CO_2 chemical fixation. *para*-Halo-substrates also showed high yields (84–90%) even though the diastereoselectivities from fluoro- to chloro- and bromo- slightly decreased (**2f–2h**). The desirable product (**2i**) was afforded in moderate yield and dr for the more electron-withdrawing ester substrate. To our delight, sterically demanding 1-naphthylmethyl carbamate (**2j**) was acquired in excellent yield (90%) and diastereoselectivity (dr > 20 : 1). In contrast, a lower dr was observed for

Table 1 Substrate scope for iodoallenyl oxazolidinones[a]

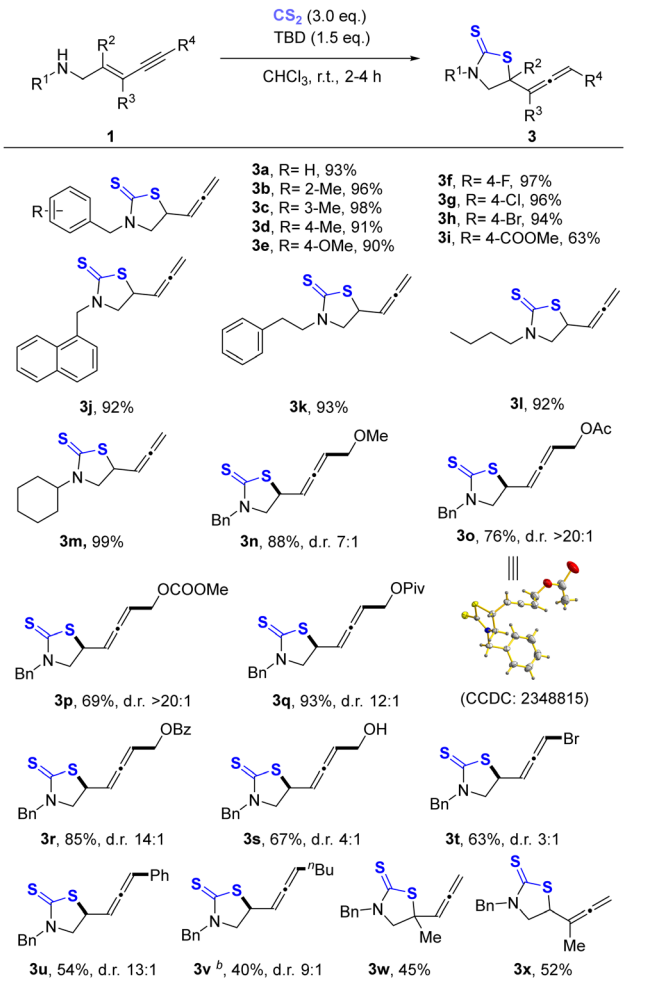


[a] Standard reaction conditions: **1** (0.1 mmol), TBD (0.2 mmol) and toluene:1,4-dioxane (2 mL, 4 : 1) were stirred for 10 min under a CO_2 atmosphere (1 atm) at rt before NIS (0.12 mmol) was added, then the mixture was stirred for 12–24 h with a CO_2 balloon (1 atm).

the heterocyclic product (**2k**) obtained from the furan-2-methyl-substrate. Besides the benzyl group, other alkyl substituted substrates, especially for enantiomerically pure methyl benzyl amine, could also provide corresponding products (**2l–2o**) in moderate to good yields and dr values. Upon substitution of the alkene near amine by a methyl or an ethyl group, quaternary carbon-containing allenyl oxazolidinones were obtained in very high yields and dr (**2p**, **2q**). In the case of substitution of the olefin away from amine by a methyl group, the product (**2r**) with a trisubstituted iodoallene was afforded in 77% yield and 11 : 1 dr. Unfortunately, neither aryl-substituted substrates nor strongly electron-withdrawing substituents on the amine generated desirable products. These results suggest that the nucleophilicity of nitrogen is very crucial to this transformation. Mixtures of 1,2-addition and 1,4-addition products were obtained using the internal alkynyl substrates (see the ESI† for details).

Encouraged by the successful iodoallenylation of (*E*)-*N*-benzylpent-2-en-4-yn-1-amine (**1a**) and CO_2, the model reaction of CS_2 with **1a** was also carefully examined. In contrast, hydrothiolation of 1,3-enyne can proceed smoothly without any activation by electrophilic halogen. It may be due to more suitable nucleophilicity of dithiocarbamate than that of carbamate for this transformation because *S* was generally considered as a softer nucleophile to preferentially react with a comparable electrophile of 1,3-enyne. Desired allenyl thiazolidine-2-thione

Table 2 Substrate scope for allenyl thiazolidine-2-thiones[a]



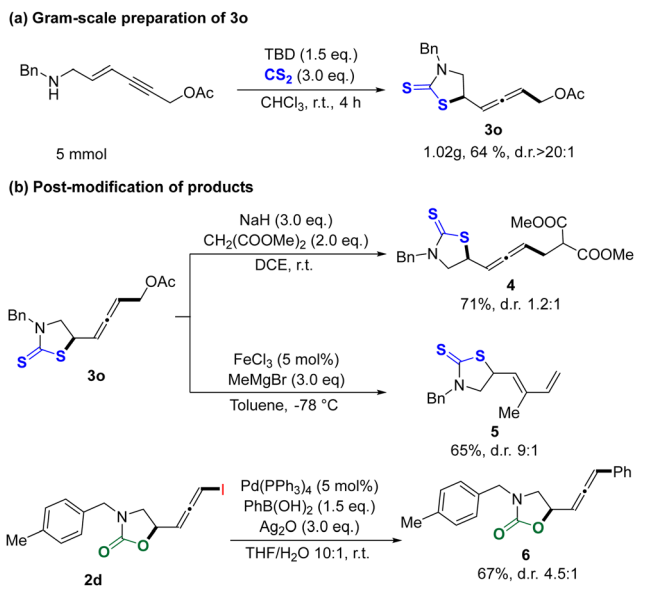
[a] Standard reaction conditions: to an oven-dried vial equipped with a stir bar were added **1** (0.1 mmol), TBD (0.15 mmol) and $CHCl_3$ (1 mL), then CS_2 (0.3 mmol) was added to the mixture and stirred for 2–4 h at rt. [b] 0.3 mmol substrate and DBU (3.0 eq.) reaction for 12 h.

3a was achieved in 96% yield by the combination of 1.5 equiv. TBD and 3.0 equiv. CS_2 in $CHCl_3$ at room temperature for 4 h. For more optimal details, please see the ESI.†

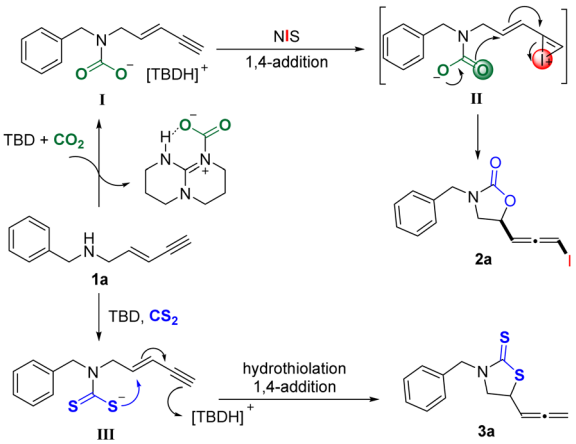
The substrate scope for TBD-promoted hydrothiolation of various 1,3-enynes with CS_2 is explored in Table 2. It shows that most of the changes for benzyl amine substrates were allowed, and the target products (**3a–3h**) were obtained in excellent yields (>**90%**). However, for the strong electron-withdrawing ester group substituted substrate, the product **3i** was obtained in 63% yield. Besides the benzyl group, other substituents on the nitrogen including the naphthyl methyl, phenylethyl, *n*-butyl or cyclohexyl group provided corresponding products (**3j–3m**) in excellent yields (>**90%**) as well. In addition, the activated internal alkyne substrates can be well compatible for such hydrothiolation. Disubstituted allenes (**3n–3s**) containing ether, ester and free hydroxyl groups were obtained in moderate to good yields and dr values. Unfortunately, the desired bromoallene **3t** was isolated in 63% yield and 3 : 1 dr. The results (**3u**, **3v**) for aryl and alkyl substituted internal alkyne were unsatisfactory, despite extending the reaction time to 12 h, which may be attributed to the decreased electrophilicity and bulky steric hindrance of 1,3-enynes. With the substitution of alkene by the methyl group, the target products (**3w**, **3x**) were obtained in 45% and 52% yields, respectively. This may also be influenced by steric hindrance and electrophilicity of the substrate. Remarkably, some products undergoing 1,2-addition were also observed (see the ESI† for details).

Subsequently, the gram scale synthesis and applicability for such chemical fixation of CO_2/CS_2 are shown in Scheme 2. As shown in Scheme 2a, allene **3o** was smoothly synthesized by gram scale (1.02 g) in 64% yield with >20 : 1 dr. To highlight the synthetic utilities of present transformation, several post-modifications of the representative products are shown in Scheme 2b. Allene **3o** containing –OAc as a leaving group could be applied in the Pd-catalyzed Tsuji–Trost reaction with dimethyl malonate as a nucleophile to obtain a new allene **4** with 71% yield and 1.2 : 1 dr.[20] $FeCl_3$ could promote the nucleophilic addition to allene **3o** with MeMgBr as a nucleophile to afford thiazolidine-2-thione **5** containing conjugated diene substitution.[21] Moreover, the Suzuki cross-coupling of iodoallene **2d** with phenylboronic acid was also performed to give desired product **6** in 67% yield.[22]

The reaction mechanism is proposed in Scheme 3 on the basis of the current results and literature.[9,12] Initially, the nucleophilic addition of **1a** to the TBD-CO_2 adduct was carried out to obtain the carbamate intermediate **I**, followed by NIS activation of the alkyne moiety of 1,3-enyne to generate iodonium interm **II**. Then, the 1,4-*syn*-addition of 1,3-enyne with carbamate occurred to give the product **2a**. Similarly, **1a** and CS_2 underwent the nucleophilic addition in the presence of TBD to give intermediate **III**. The hydrothiolation reaction would be immediately performed to form product **3a** by 1,4-*syn*-addition of 1,3-enyne with dithiocarbamate.



Scheme 2 Synthetic applications and post-modifications.



Scheme 3 Proposed mechanism for chemical fixation of CO_2/CS_2.

In summary, a tandem CO_2/CS_2 fixation and cyclization reaction was developed to prepare iodoallenyl oxazolidinones and allenyl thiazolidine-thiones and their derivatives with high yields and diastereoselectivities. The remarkable advantages of this strategy include a metal-free manner, mild reaction conditions, high atom-economy and wide substrate scope. Moreover, the two types of allenyl heterocyclic compounds are valuable building blocks for the synthesis of multifunctional molecules or natural products in the future.

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Data availability

The data supporting this article have been included as part of the ESI.†

Conflicts of interest

There are no conflicts to declare.

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