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Authors: Xiao-Feng Wu, Yuya Hu, Zhiping Yin, Thomas Werner, and Anke Spannenberg

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DBU-Catalyzed Carbonylative Cyclization of Propargylic Alcohols with Elemental Sulfur

Yuya Hu,[a] Zhiping Yin,[a] Thomas Werner,[a] Anke Spannenberg,[a] Xiao-Feng Wu*[a,b]

Abstract: A novel carbonylation procedure on the cyclization of propargylic alcohols with elemental sulfur has been developed. With DBU as the catalyst, elemental sulfur and carbon monoxide can be activated and incorporated into the propargylic alcohols. Good to excellent yields of the desired sulfur containing heterocyles can be produced at room temperature.

Introduction

Sulfur-containing molecules are important moieties in general organic synthesis, and have been reported with many applications in the materials science and also pharmaceuticals.[1] Hence, numerous methodologies have been developed in recent years for their constructions. A variety of sulfuration agents, such as thiols, sulfides and their oxidized derivatives and so on have been applied.[2] Among them, sulfur powder (S_8) is considered as an ideal reagent due to its low cost, nontoxic, odorless, high stability and easy-handling characters.[3] Studies have been performed for introducing sulfur atoms into organic molecules, including multi-components coupling reactions, polymerizations and fabrication of *S*-containing organometallic complexes.[4] Not surprisingly, sulfur assisted carbonylation reactions have been studied as well.[5] Various *S*-alkyl carbonothioates, 2,4-dioxo-l,2,3,4-tetrahydroquinazolines, thiocarbamateds and etc. can be produced selectively. Among the known sulfur-containing heterocycles, 1,3-oxathiolan-2-ones are useful building blocks in organic chemistry, polymer sciences, and also present in biological active compounds such as quercetin-oxathiolanone, an effective inhibitor of xanthine oxidase.[6] Carbonylative procedures using epoxides as the substrates and catalyzed by NaH have been established as well.[7,8] Processes based on carbonyl sulfide gas (SCO) and react with various substrates have also been achieved. Herein, we wish to report our new results on the synthesis of 4-alkylidene-1,3-oxathiolan-2-ones with DBU as the catalyst. Good to excellent yields of the desired products can be formed from propargylic alcohols and sulfur powder at room temperature.

[a] Y. Hu, Z.Yin, Dr. T. Werner, Dr. A. Spannenberg, Prof. Dr. X.-F. Wu
Leibniz-Institut für Katalyse e. V. an der Universität Rostock, Albert-Einstein-Straße 29a, 18059 Rostock, Germany
E-mail: xiao-feng.wu@catalysis.de
https://www.catalysis.de/mitarbeiter/wu-xiao-feng/
[b] Prof. Dr. X.-F. Wu
Department of Chemistry, Zhejiang Sci-Tech University, Xiasha Campus, Hangzhou 310018, People's Republic of China

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Results and Discussion

Initially, we choose 2-methyl-4-phenylbut-3-yn-2-ol as the model substrate to establish this transformation. In the presence of sulfur powder, promoted by one equivalent of DBU, using toluene as reaction media at room temperature for 12 hours, 93% of the desired (*Z*)-4-benzylidene-5,5-dimethyl-1,3-oxathiolan-2-one was isolated (Table 1, entry 1). Similar amount of yield can be obtained with 0.5 equivalent of DBU (Table 1, entry 2). However, no target molecule could be detected with NEt_3, NaOAc or Na_2CO_3 as the promotor (Table 1, entries 3-5). The loading of DBU can even be decreased to 10 mol%, however, only 20% of product can be obtained with 5 mol% of DBU (Table 1, entries 6 and 7). With 10 mol% of DBU as the catalyst, decreased yield was observed under 5 bar of CO (Table 1, entry 8). In the testing of reaction solvents, improved yield can be achieved in MeCN with 97% of isolated yield while the other tested solvents were all inferior (Table 1, entries 9-13). Then we turn back to looking for possible replacer again. Due to the relatively low pK_a of DABCO, DiPEA and DMAP, no reaction occurred with them as the catalyst (Table 1, entries 14-16). However, as we expected, quantitative yield of the target product can be formed with DBN or TBD as the catalyst (Table 1, entries 17 and 18). Moreover, the chemical structure of the obtained product was confirmed by X-ray analysis as well (Figure 1).

Table 1. Carbonylative cyclization of propargylic alcohol.[a]

1a **2a** *(Z-isomer)*

Entry	Base	Solvent	Yield[b]
1	DBU (1 equiv.)	Toluene	93%[c]
2	DBU (50 mol%)	Toluene	93%
3	NEt_3 (50 mol%)	Toluene	0
4	NaOAc (50 mol%)	Toluene	0
5	Na_2CO_3 (50 mol%)	Toluene	0
6	DBU (10 mol%)	Toluene	88%
7	DBU (5 mol%)	Toluene	20%
8	DBU (10 mol%)	Toluene	47%[d]
9	DBU (10 mol%)	DMSO	34%
10	DBU (10 mol%)	THF	43%

11	DBU (10 mol%)	DMF	21%
12	DBU (10 mol%)	*t*BuOH	8%
13	DBU (10 mol%)	MeCN	97%[c]
14	DABCO (10 mol%)	MeCN	0
15	DiPEA (10 mol%)	MeCN	0
16	DMAP (10 mol%)	MeCN	0
17	DBN (10 mol%)	MeCN	98%
18	TBD (10 mol%)	MeCN	98%

[a] Reaction conditions: **1a** (0.5 mmol), S_8 (0.25 mmol), base, solvent (2 mL), 25 °C, CO (10 bar), 12 h. [b] Yield of **2a** was determined by GC using tetradecane as internal standard. [c] Isolated yield. [d] CO (5 bar). DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene. DABCO: 1,4-diazabicyclo[2.2.2]octane. DiPEA: *N*-ethyldiisopropylamine. DMAP: *N*,*N*-dimethylpyridin-4-amine. DBN: 1,5-diazabicyclo[4.3.0]non-5-ene. TBD: 1,3,4,6,7,8-hexahydro-2*H*-pyrimido[1,2-*a*]pyrimidine.

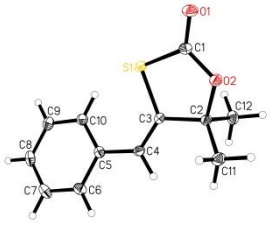
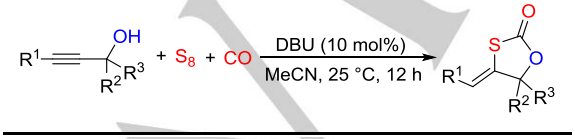
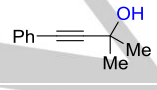
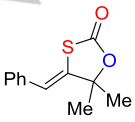
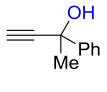
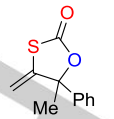
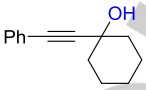
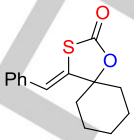
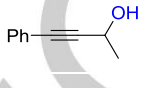
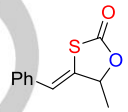
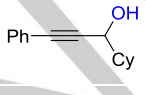
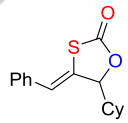
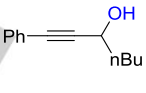
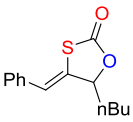
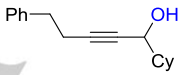
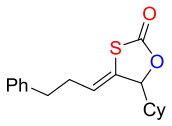
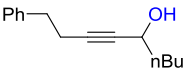
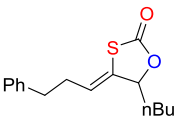
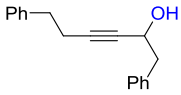
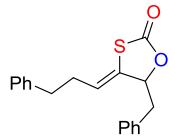
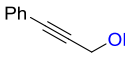
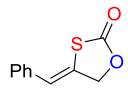


Figure 1. X-ray crystal structure analysis of product 2a.[9]

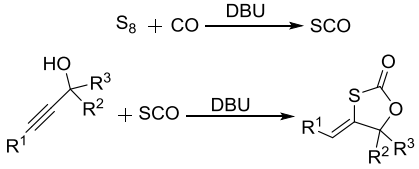
With the best reaction conditions in our hand, different substituted propargylic alcohols were tested with DBU as the catalyst subsequently (Table 2). To our delight, good to excellent yields of various 4-alkylidene-1,3-oxathiolan-2-ones were obtained from the corresponding propargylic alcohols successfully. Both secondary and tertiary alcohols are applicable. However, no desired product could be detected with primary propargylic alcohol, such as 3-phenylprop-2-yn-1-ol. The substrate added decomposed. Concerning the reaction pathway, based on literature,[5,7] we believe the reaction proceeds via the *in suit* formation of SCO from CO and S_8 (Scheme 1).

Table 2. DBU-catalyzed carbonylative cyclization of propargylic alcohols.[a]



Entry	Substrate	Product	Yield
1			97%
2			91%
3			98%
4			75%
5			74%
6			85%
7			73%
8			71%
9			61%
10			0%

[a] Reaction conditions: DBU (10 mol%), propargylic alcohols (0.5 mmol), S_8 (0.25 mmol), MeCN (2 mL), CO (10 bar), 25 °C, 12 h, isolated yield.



Scheme 1. Proposed reaction mechanism.

Conclusions

In conclusion, in this short communication, we described our new results on DBU-catalyzed carbonylative cyclization of propargylic alcohols with elemental sulfur. The desired 4-alkylidene-1,3-oxathiolan-2-ones were produced in good to excellent yields at room temperature.

Experimental Section

Under an open atmosphere, a 4 mL screw-cap vial was charged with elemental sulfur (S_8, 0.25 mmol), propargylic alcohol (0.50 mmol), MeCN (2 mL), DBU (10 mol%) and an oven-dried stirring bar. The vial was closed by Teflon septum and phenolic cap and purged with Ar through a needle. Then the vial was fixed in an alloy plate and put into Paar 4560 series autoclave (300 mL). At room temperature, the autoclave was flushed with carbon monoxide for three times and 10 bar of carbon monoxide was charged. The autoclave was placed on a heating plate equipped with magnetic stirring and an aluminum block. The reaction was stirred at room temperature for 24 hours. Afterwards, the autoclave was removed and the pressure was carefully released. After removal of solvent under reduced pressure, pure product was obtained by column chromatography on silica gel (eluent: pentane/ethyl acetate = 50:1).

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Keywords: carbonylation • cyclization • sulfur • heterocycle synthesis • 1,3-oxathiolan-2-ones

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[9] CCDC 1559823 contains the supplementary crystallographic data for this paper. Displacement ellipsoids correspond to 30% probability. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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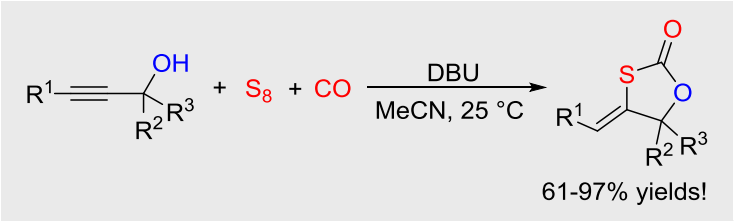

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Carbonylation

*Yuya Hu, Zhiping Yin, Thomas Werner, Anke Spannenberg, Xiao-Feng Wu**

Page No. – Page No.

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