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Amine-catalyzed formal (3 + 3) annulations of 2-(acetoxymethyl)buta-2,3-dienoate with sulfur ylides: synthesis of 4*H*-pyrans bearing a vinyl sulfide group†

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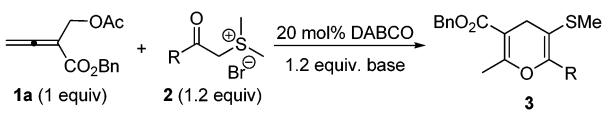
A DABCO-catalyzed (3 + 3) annulation between 2-(acetoxymethyl)buta-2,3-dienoate and sulfur ylides has been developed, which provides a facile method for the synthesis of 4*H*-pyrans bearing a vinyl sulfide group.

Sulfur ylides are an important class of reagents widely used for synthesis of epoxide, aziridine and cyclopropane.[1] In these cases, sulfur ylide exhibits dual functions: good nucleophilicity of ylide carbon to initiate addition to an electrophilic carbon center and efficient leaving ability of sulfide to ensure formation of three-membered product. However, the latter process renders the sulfur moiety being wasted. Thus, special attention has been paid to the development of novel transformations for sulfur atom transfer from ylide into product, providing an alternative method for the synthesis of organosulfur compounds.[2] In addition, organosulfur compounds have received great attention due to their special biological and chemical properties.[3] Herein, we report an amine-catalyzed synthesis of S-containing 4*H*-pyran **3** from allenoate **1a** and sulfur ylide which is generated *in situ* through the reaction of sulfonium salt **2** and a base (eqn (1)).



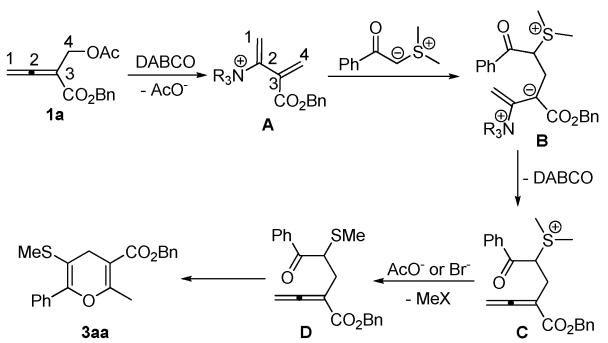
(1)

Recently, we have developed the DABCO-catalyzed annulations of allenoate **1a** with bis-nucleophiles (DBCO: 1,4-diazabicyclo[2.2.2]octane).[4] The success can be attributed to the following reasons: (1) the interaction between **1a** and catalyst readily leads to the formation of intermediate **A** *via* an addition–elimination process (Scheme 1); (2) more importantly, the 4C of intermediate **A** exhibits good electrophilicity for C-nucleophile attack. These findings lead us to envision that sulfur ylide would also be able to attack intermediate **A**, resulting in the formation of betaine intermediate **B**, containing several active functional groups and would achieve some novel transformations.

To validate the above postulation, we conducted the reaction of allenoate **1a** and Me_2S sulfonium salt **2a** in benzene solvent with the use of 20 mol% DABCO as catalyst and 1.2 equiv. K_2CO_3 as base (Table 1, entry 1). To our delight, compound **3aa** was obtained in 70% isolated yield. Thus, the sulfur atom of the ylide was successfully transferred into the product. The formation of **3aa** could be rationalized by the following sequence (Scheme 1). Contrary to expected cyclopropanation[5] for betaine intermediate **B**, it undergoes 1,2-elimination of DABCO catalyst to form intermediate **C**.[6] Subsequently, the methyl group of Me_2S sulfonium would be attacked by AcO^- or Br^- to yield intermediate **D**,[7] which is followed by intramolecular oxa-Michael addition to produce 4*H*-pyran **3aa** (Scheme 1). Unfortunately, intermediate **D** was not detected although several endeavors were made.

With these primary results in hand, we then briefly screened base and the reaction solvent in order to establish the optimized conditions (Table 1). Finally, it was found that the combination of K_2CO_3 as base and acetone as solvent afforded compound **3aa** in as high as 96% yield (Table 1, entry 7). It should be emphasized that no product **3aa** was observed without DABCO catalyst and 79% of **1a** was recovered.

Under the optimized conditions, the substrate scope was further investigated and the results are summarized in Table 2. The reaction worked well for allenoate **1a** with various aromatic ketone-stabilized sulfonium salts **2a–2i**; good to excellent yields were attainable, regardless of the electronic nature and the



Scheme 1 Proposal for the formation of compound **3aa** (NR_3 = DABCO).

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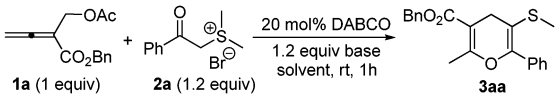
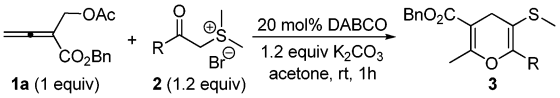
Table 1 Optimization of reaction conditions



Entry	Base	Solvent	Yield[b] (%)
1	K_2CO_3	Benzene	70
2	Cs_2CO_3	Benzene	59
3	K_2CO_3	PhMe	27
4	K_2CO_3	CH_2Cl_2	88
5	K_2CO_3	MeCN	62
6	K_2CO_3	DMF	47
7	**K_2CO_3**	**Acetone**	**96**
8	Na_2CO_3	Acetone	88

[a] *Reaction conditions*: to a solution of **2a** (0.12 mmol, 1.2 equiv.), base (0.12 mmol, 1.2 equiv.), DABCO (0.02 mmol, 20 mol%) in the specified solvent (1.3 mL), was slowly added the solution of **1** (0.10 mmol, 1.0 equiv.) in the same solvent (1.3 mL) over 20 min. [b] Isolated yield.

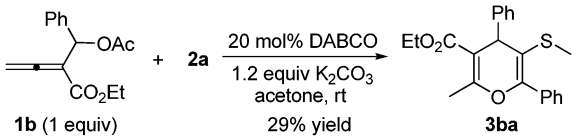
Table 2 Reaction scope



Entry	**2** (R)	**3**	Yield[b] (%)
1	**2a** (Ph)	**3aa**	96
2	**2b** (4-BrC_6H_4)	**3ab**	86
3	**2c** (4-$NO_2C_6H_4$)	**3ac**	75
4	**2d** (4-ClC_6H_4)	**3ad**	84
5	**2e** (4-MeC_6H_4)	**3ae**	84
6	**2f** (3-$NO_2C_6H_4$)	**3af**	83
7	**2g** (2-furyl)	**3ag**	88
8	**2h** (2,4-$Me_2C_6H_3$)	**3ah**	80
9	**2i** (3,4-$Me_2C_6H_3$)	**3ai**	91
10[c]	**2j** (Me)	**3aj**	17

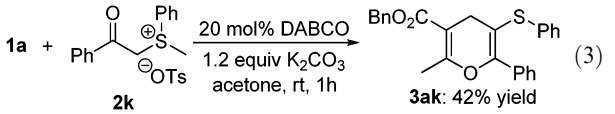
[a] *Reaction conditions*: to a solution of **2** (0.12 mmol, 1.2 equiv.), K_2CO_3 (0.12 mmol, 1.2 equiv.), DABCO (0.02 mmol, 20 mol%) in acetone (1.3 mL), was slowly added a solution of **1** (0.10 mmol, 1.0 equiv.) in acetone (1.3 mL) over 20 min. [b] Isolated yield. [c] Reaction time: 24 h.

substitution pattern of the aryl groups (Table 2, entries 1–9). However, the reaction of methyl ketone-stabilized sulfonium salt **2j** was found to be very sluggish and only 17% isolated yield of **3aj** was obtained even with a prolonged reaction time (Table 1, entry 10).

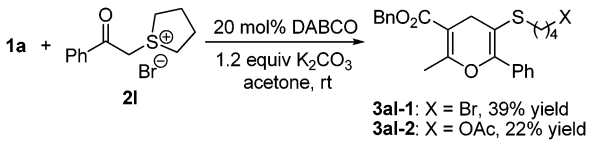


(2)

The transformation could be extended to β′-substituted substrate **1b**, which afforded the corresponding 4-substituted 4*H*-pyran **3ba** in 29% yield (eqn (2)). The low yield was likely due to the steric hindrance imposed by phenyl substituent. On the other hand, PhSME sulfonium **2k** also reacted well with **1a** to give product **3ak** in 42% yield (eqn (3)). When tetrahydrothiophene sulfonium salt **2l** was employed, ring-opened products **3al-1** and **3al-2** were isolated in 39 and 22% yield, respectively (eqn (4)). In view of ready availability of allenoate **1a** and sulfonium salts, the transformation provides convenient access to organosulfur compounds under mild conditions.



(3)

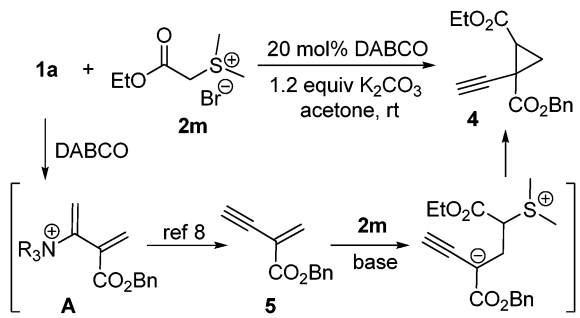


(4)

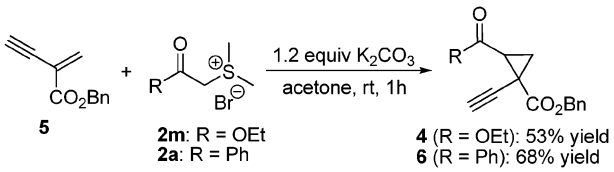
Surprisingly, the behavior of ester-stabilized sulfur ylides was found to be quite different from that of ketone-stabilized ylides. Indeed, the reaction of **1a** and **2m** under the same conditions delivered cyclopropane derivative **4** in 24% yield (Scheme 2). In 2009, Lee and co-workers found that allenoate **1a** can be readily converted into compound **5** in the presence of DABCO and base (Scheme 2).[8] Thus, **4** might be formed *via* normal cyclopropanation between **5** and the corresponding ylide derived from **2m** (Scheme 2).[9]

Indeed, compound **5**, which was independently prepared, reacted well with sulfonium salt **2m** with the assistance of K_2CO_3, affording **4** in 53% yield (Scheme 3). The reaction of **5** and **2a** also underwent smoothly to give cyclopropane **6** in 68% yield (Scheme 3). Sulfonium **2a** has a more acidic α-proton than **2m** although the corresponding ester-stabilized ylide is more reactive than the ketone-stabilized one.[10] Thus, deprotonation of **2a** is believed to be easier, to generate ketone-stabilized ylide which would readily intercept intermediate **A** to form intermediate **B** (Scheme 1). However, similar interception might not be achieved by **2m** due to its slower deprotonation. Therefore, intermediate **A** would follow a second pathway to form compound **5** in the case of **2m** (Scheme 2).

Interestingly, when Baylis–Hillmann adduct **1c**,[11] instead of **1a**, was subjected to otherwise identical conditions, organosulfur compound **3ca** was obtained, albeit in only 20% yield (eqn (5)).[12] This result led us to conclude that the allenic moiety of **D** (Scheme 1) might be beneficial for cyclization in a 6-*endo*-dig fashion, which is a favorable process according to Baldwin's rule.[13]

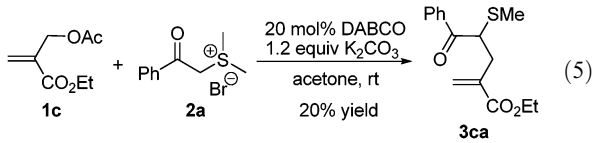


Scheme 2 Proposal for the formation of compound **4** (NR_3 = DABCO).



Scheme 3 The reaction of **5** with ylide.

In the case of **1c**, further cyclization might be interrupted likely due to the less active acrylate moiety, resulting in the isolation of acyclic compound **3ca**.



(5)

In summary, we have developed amine-catalyzed (3 + 3) annulations of allenoate **1a** and ketone-stabilized ylides under mild reaction conditions, in which the sulfur atom of the ylide was transferred into the product 4*H*-pyran. Furthermore, the allenic moiety of **1a** might provide an advantage for further cyclization in the 6-*endo*-dig fashion. We believe that these mechanistic insights would be helpful for the development of both allenoate **1a** and S-ylide related reactions.

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