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Communication

Cyclopropanation of active methylene compounds with β-alkoxycarbonyl vinylsulfonium salts

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ABSTRACT

An efficient synthesis of β-alkoxycarbonyl vinylsulfonium salts had been developed. Their reaction with indene-1,3-diones and other active methylene compounds provided cyclopropane carboxylates in good yields. A tentative reaction mechanism was proposed.

Vinylsulfonium salts are a class of special Michael acceptors with diversified reactivities. They had been used as efficient ethylene transfer reagents for the synthesis of various valuable products. Their reactions with amino aldehydes or ketones generated heterocyclic epoxides [1]. They were also used to react with bisheteroatomic nucleophiles for the preparation of heterocyclic compounds [2]. The reaction of vinylsulfonium salts with active methylene compounds or primary amines provided cyclopropanes and aziridines [3]. In addition, 1-butadienyl-sulfonium salts were applied for the synthesis of epoxides *via* the conjugate addition and subsequent intramolecular cyclization [4]. Huang and co-workers explored the applications of allenic sulfonium salts for the synthesis of fused heterocycles [5]. Recently, we developed an annulation reaction of vinylsulfonium salts with β-naphthols and 1,4-hydroxycoumarins. A series of dihydrofuran derivatives were prepared in moderate to good yields [6]. Despite these progresses, only few functionalized vinylsulfonium salts were prepared and applied to new synthetic reactions [1f,3b,3c]. Their reactivities and synthetic potentials remain to be explored. As a continuous effort to explore the new synthetic applications of vinylsulfonium salts, herein we report the first synthesis of β-alkoxycarbonyl vinylsulfonium salts and their application for the cyclopropanation of active methylene compounds. A variety of cyclopropane carboxylates could be prepared in good yields.

The synthesis of β-alkoxycarbonyl vinylsulfonium salts **1a-1c** is showed in Scheme 1. The conjugate addition of thiophenol to propiolates provided 3-(phenylthio)acrylates in good yields [7]. The further phenylation with diphenyliodonium triflate gave β-alkyloxycarbonyl vinylsulfonium salts **1a-1c** [8]. Only *Z*-isomers were detected for **1a-1b**, but a small amount of *E*-isomer was observed for **1c**. The experiment details please see Supporting information.

The reaction of **1a** with 1,3-indenedione **2a** was examined and the results are summarized in Table 1. The reaction underwent smoothly in the presence of organic bases DBU (1,5-diazabicyclo [4.3.0]non-5-ene), TMG (tetramethylguanidine) and Et_3N, but lower yields were obtained with DABCO (1, 4-diazabicyclo[2.2.2] octane) and DMAP ((4-dimethylamino-pyridine) (Table 1, entries 1–5). Inorganic bases are also efficient (Table 1, entries 6–10). Considering the yield and convenient work-up, Et_3N was selected for the further study. The optimal amount of Et_3N was identified as 2 equiv. More or less amount of Et_3N led to decreased yields (Table 1, entries 11 and 12). The effect of reaction solvent was also examined (Table 1, entries 13–22). The reaction occurred in various organic solvents. The best yield was achieved in $CHCl_3$.

The reactions of **1b** and **1c** with **2a** were also examined (Scheme 2). The good reactivity was observed for **1b**, but **1c** is less reactive probably due to the increased steric hindrance. The product **3ac** was obtained in 49% yield as a mixture of *trans*/*cis* isomers.

The reaction of a series of 1,3-indene-diones **2a-h** with **1a** were examined and the results are summarized in Table 2. The substitutions on the benzene ring with 4-Cl and 4-F were tolerated

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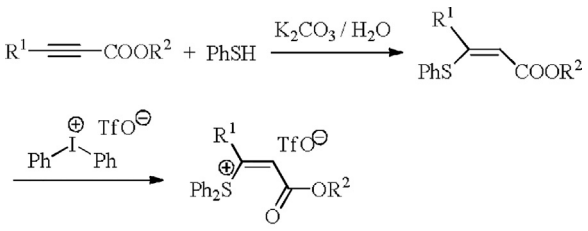
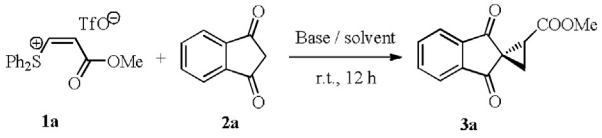


1a, R^1 = H, R^2 = Me (*Z*), 71.6%
1b, R^1 = H, R^2 = Bn (*Z*), 56.7%
1c, R^1 = Me, R^2 = Me (*Z*/*E*=3:1), 65.8%

Scheme 1. Synthesis of *β*-alkoxycarbonyl vinylsulfonium salts **1a-1c**.

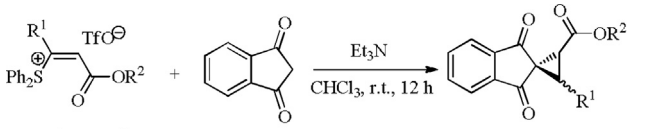
Table 1
Optimization of reaction conditions.[a]



Entry	Base	Solvent	Yield (%)[b]
1	DBU	CH_2Cl_2	82
2	TMG	CH_2Cl_2	86
3	Et_3N	CH_2Cl_2	86
4	DABCO	CH_2Cl_2	64
5	DMAP	CH_2Cl_2	48
6	K_2CO_3	CH_2Cl_2	79
7	Na_2CO_3	CH_2Cl_2	76
8	Cs_2CO_3	CH_2Cl_2	67
9	Na_3PO_4	CH_2Cl_2	54
10	KOH	CH_2Cl_2	64
11[c]	Et_3N	CH_2Cl_2	61
12[d]	Et_3N	CH_2Cl_2	85
13	Et_3N	Toluene	55
14	Et_3N	$CHCl_3$	94
15	Et_3N	$ClCH_2CH_2Cl$	90
16	Et_3N	Et_2O	72
17	Et_3N	THF	83
18	Et_3N	EtOAc	84
19	Et_3N	Acetone	85
20	Et_3N	CH_3CN	76
21	Et_3N	DMSO	70
22	Et_3N	DMF	56

[a] Conditions: the reactions were performed with **1a** (0.24 mmol), **2a** (0.2 mmol), base (0.4 mmol), solvent (4 mL).
[b] Isolated yields.
[c] Et_3N (0.2 mmol) was used.
[d] Et_3N (0.6 mmol) was used.

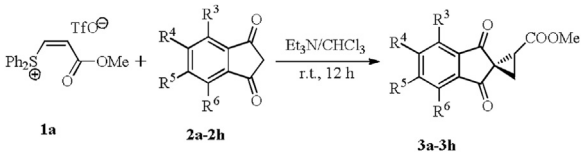
well. Excellent yields were obtained for the products **3b**-**3c**. The 4-NO_2 substituted **2d** afforded a lower yield. The substitutions with 5-Cl, 5-Br and 5-Me led to slightly lower yields. Due to the different direction of the ester group with 4- or 5-substituent, products **3b**-**g** consisted of two diastereoisomers. The ratios were determined by ^{1}H NMR spectra. The reaction of 4,5,6,7-tetrachcloro-1,3-indenedione **2h** provided the product **3h** in a good yield.



1b, R^1 = H, R^2 = Bn
1c, R^1 = Me, R^2 = Me
2a
3ab, 93%
3ac, 49% (*trans*/*cis* = 3:1)

Scheme 2. The reactions of **1b** or **1c** with **2a**. Conditions: **1b/1c** (0.24 mmol), **2a** (0.2 mmol), Et_3N (0.4 mmol), and $CHCl_3$ (4 mL). Isolated yields.

Table 2
The reaction of 1,3-indene-diones **2a-h** with **1a**.[a]



Entry	R^3	R^4	R^5	R^6	Product	Yield (%)[b,c]
1	H	H	H	H	**3a**	94
2	Cl	H	H	H	**3b**	90 (1:1.3)
3	F	H	H	H	**3c**	92 (1:1.1)
4	NO_2	H	H	H	**3d**	62 (1:1.3)
5	H	Cl	H	H	**3e**	82 (1:1)
6	H	Br	H	H	**3f**	80 (1:1)
7	H	Me	H	H	**3g**	88 (1:1)
8	Cl	Cl	Cl	Cl	**3h**	81

[a] Conditions: the reactions were performed with **1a** (0.24 mmol), **2a-h** (0.2 mmol), Et_3N (0.4 mmol), $CHCl_3$ (4 mL).
[b] Isolated yields.
[c] The diastereoisomeric ratios in the brackets were determined by ^{1}H NMR.

Furthermore, the reactions of **1a** with a series of active methylene compounds **4a-g** were examined and the results are summarized in Table 3. 1,3-Cyclohexanedione **4a** afforded the expected product **5a** in an excellent yield. 1,3-Diphenylpropane-1,3-dione **4b** showed low reactivity. The reaction of acetoacetone **4c** provided the product **5c** in a moderate yield. *α*-Cyano acetophenone **4d** showed good reactivity. The product **5d** was obtained in an excellent yield. The reaction of diethyl malonate **4e** is not satisfactory. The product **5e** was obtained in a poor yield. On the other hand, the reaction of coumarin **4f** and its analogue **4g** did not afford the expected products, instead *O*-vinyl products **5f** and **5g** were obtained in low yields. Ethyl *α*-cyanoacetate **4h** and the substrate **4i** were found to be unreactive (For the details of synthetic procedures, see Supporting information).

A tentative reaction mechanism was proposed (Scheme 3). The deprotonation of 1,3-indenedione **2a** with Et_3N gives the enolate anion. The conjugate addition of the anion to **1a** generates the sulfur ylide **A**. After the second deprotonation of 1,3-indenedione, the intermediate **B** is formed. Subsequent cyclization provides the product **3a** and eliminates diphenylsulfide.

The reduction of the product **3a** was studied (Scheme 4). The reaction with $NaBH_4$ afforded the complicated stereoisomers of the alcohols. The treatment with Et_3SiH gave selectively the mono-decarbonyl product **6** [9]. The ester group obviously shielded the carbonyl group on the same side. Only the carbonyl group on the opposite was reduced. The further reduction of **6** with $NaBH_4$ provided the alcohol **7** as a mixture of two diastereoisomers (details in Supporting information).

We have developed an efficient synthetic route of *β*-alkoxycarbonyl vinylsulfonium salts. Their reactions with indene-1,3-diones and other active methylene compounds were studied. A series of cyclopropane carboxylates were prepared in good yields. The characterization data of all products are posited in Supporting information. A tentative reaction mechanism was proposed. Further applications of *β*-alkoxycarbonyl vinylsulfonium salts to new synthetic reactions are currently underway.

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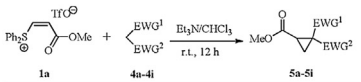
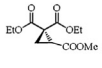
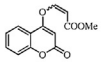
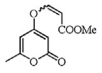
Table 3
The reaction of **1a** with active methylene compounds **4a-i**.[a]



1a 4a–4i 5a-5i

Entry	Substrate	Product/yield (%)[b]
1	 4a	 5a, 89%
2	 4b	 5b, 20%
3	 4c	 5c, 63%
4	 4d	 5d, 83%
5	 4e	 5e, 16%
6	 4f	 5f, 35% yield, *Z*/*E* = 1/1.8[c]
7	 4g	 5g, 35% yield, *Z*/*E* =1/1.2[c]
8	 4h	/
9	 4i	/

[a]Conditions: the reactions were performed with **4a**-**4i** (0.2 mmol), **1a** (0.24 mmol), Et_3N (0.4 mmol), $CHCl_3$ (4 mL).
[b]Isolated yields.
[c]Determined by ^1H NMR.

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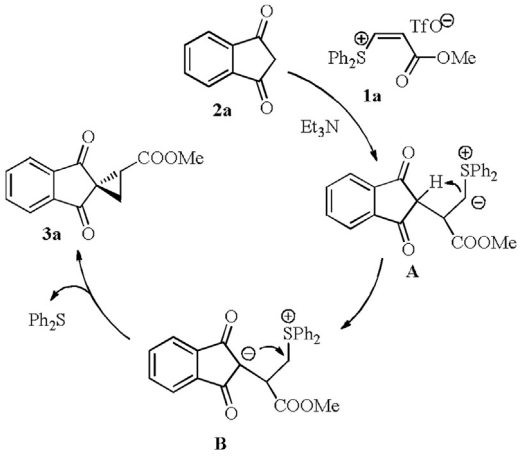
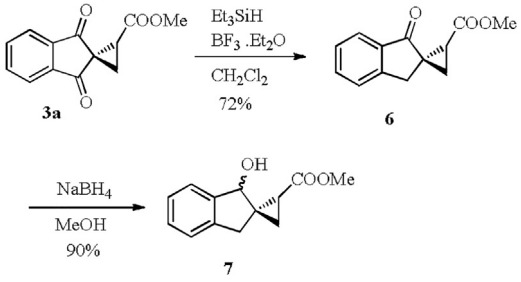
Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.cclet.2018.08.021.



Scheme 3. Proposed reaction mechanism.



Scheme 4. Reduction of the product **3a**.

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