JOC*Note*

Reaction of 2,3-Allenoates with $TsNBr_2$ in the Presence of Base: A Facile Highly Stereoselective Synthesis of (1*E*,2*E*)-3-Bromo-4-oxo-*N*′-tosyl-2-alkenoxylimidic Acid Ethyl Esters

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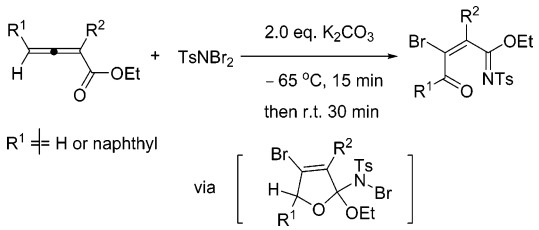

A novel reaction pathway of 2,3-allenoates with an electrophile ($TsNBr_2$) in the presence of K_2CO_3 to produce (1*E*,2*E*)-3-bromo-4-oxo-*N*′-tosyl-2-alkenoxylimidic acid ethyl esters is reported. The reaction proceeds in a highly stereoselective fashion. A plausible mechanism to rationalize this reaction is also proposed.

Allenes, featured by the presence of two orthogonal π-bonds, show unique reactivity in organic synthesis.[1] In the past decades, much attention has been paid to the study of their reactivity, especially on the control of the relative selectivity and their potential synthetic utilities.[2−5] Researchers have found that both regioselective and stereoselective addition to allenes can be tuned by introducing various nucleophilic functionalities at the α-carbon atom.[4] Recently, 2,3-allenoates, a readily accessible class of allenes, have exhibited great potential in the synthesis of many compounds with biological and synthetic importance.[5] Generally, the attached ester groups facilitate the regio- and stereoselective addition to the two double bonds, and two kinds of reaction pathways of 2,3-allenoates have been disclosed for reactions with electrophiles so far: (1) selective addition to the β,γ-double bond to give stereodefined functionalized vinyl compounds (type a, Scheme 1);[6,7d] (2) interaction of 2,3-allenoates with electrophiles followed by participation of the ester carbonyl group to form cyclic cations. Further reaction with nucleophiles yields unstable cyclic intermediates which evolve to the final products (type b, Scheme 1). As for the reaction pathway type b, most cases give γ-butenolides as the products of electrophilic cyclization in the presence of water,[7] and scarcely any other nucleophile has been reported.

The utility of *N*,*N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) as a Br^+ source has attracted our interest recently because of its simplicity and efficiency.[8] This reagent could provide a sulfonamide as the nucleophilic counterpart to construct a carbon−nitrogen bond, thus serving as a good aminobromination reagent in organic synthesis.[9] Although much work has been done in aminobromination, hydrobromination, and alkoxybromination of the C=C unsaturated bond using $TsNBr_2$ in the past,[9,10] the interaction with allenes has not been studied and

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SCHEME 1. Reaction Pathways of 2,3-Allenoates with Electrophiles

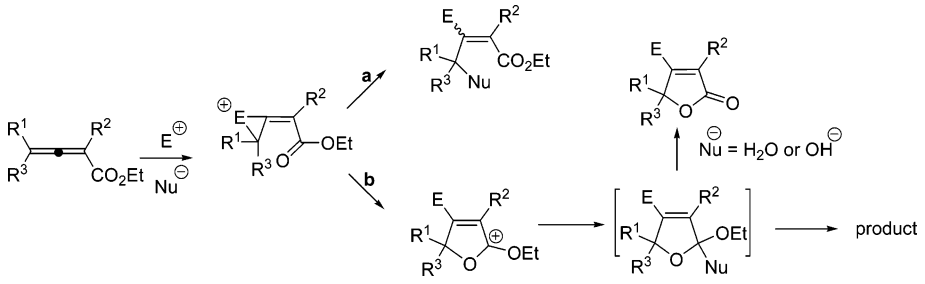
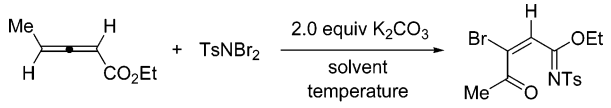


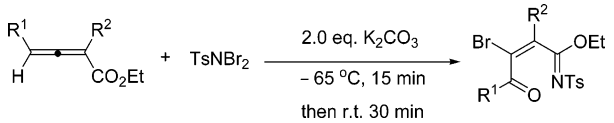
TABLE 1. Optimization of the Reaction Conditions of 2,3-Allenoates with $TsNBr_2$[a]



entry	solvent	temp (°C)	**2a** (%)[b]
1[c]	CH_2Cl_2	25	32[d] (30[e])
2	CH_2Cl_2	25	34
3	CH_2Cl_2	0	41
4	CH_2Cl_2	−40	64
5	**CH_2Cl_2**	**−65**	**81**
6	CH_2Cl_2	−80	81
7	MeCN[f]	−65	80
9	toluene	−65	−
10	THF	−65	56

[a] All of the reactions were kept stirring for 15 min at the specified temperature, and then allowed to warm to room temperature and stirred for 30 min more. [b] Isolated yields. [c] No base was added. [d] The reaction mixture was quenched with saturated potassium carbonate solution. [e] The reaction mixture was quenched with saturated sodium thiosulfate solution. [f] MeCN was distilled three times from P_2O_5.

TABLE 2. Reaction of Various 2,3-Allenoates with $TsNBr_2$ in the Presence of K_2CO_3[a]



entry	R^1	R^2	**2**	yield[b]
1	Me	H (**1a**)	**2a**	81
2	Me	Bn (**1b**)	**2b**	77
3	Et	H (**1c**)	**2c**	82
4	Et	Me (**1d**)	**2d**	75
5	Et	Bn (**1e**)	**2e**	83
6	*n*-Bu	H (**1f**)	**2f**	85
7	*n*-Bu	Me (**1g**)	**2g**	87
8	*n*-Bu	Bn (**1h**)	**2h**	91
9	*n*-Bu	n−Bu (**1i**)	**2i**	93
10	*n*-C_7H_{15}	H (**1j**)	**2j**	87
11	*n*-C_7H_{15}	Me (**1k**)	**2k**	83
12	*n*-C_7H_{15}	Bn (**1l**)	**2l**	71
13[c]	Ph	H (**1m**)	**2m**	61
14	Ph	Bn (**1n**)	**2n**	71
15	Ph	n−Bu (**1o**)	**2o**	66
16	H	Bn (**1p**)		*d*
17[c]	H	Me (**1q**)		*d*

[a] All of the reactions were carried out on a scale of 0.5 mmol in dry CH_2Cl_2. [b] Isolated yields. [c] The reaction mixture was kept stirring at −80 °C for 20 min. [d] No identifiable products were obtained.

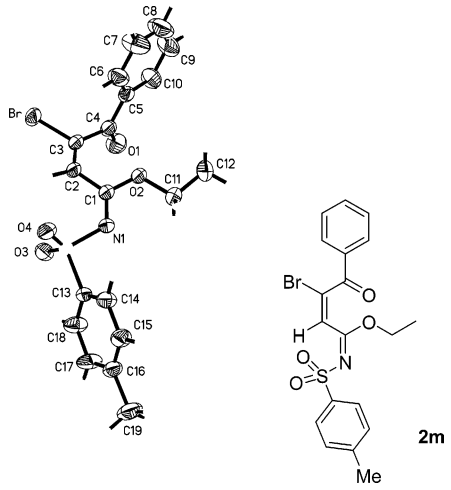


FIGURE 1. ORTEP representation of the product **2m**.

remains unclear. In this paper, we wish to present our research results on the reaction of 2,3-allenoates with $TsNBr_2$. In the presence of K_2CO_3 as the base, $TsNBr_2$ treatment provides a novel method to prepare (1*E*,2*E*)-3-bromo-4-oxo-*N*′-tosyl-2-alkenoxylimidic acid ethyl esters.

We initially examined the reaction of ethyl penta-2,3-dienoate with $TsNBr_2$ in CH_2Cl_2 at room temperature. The reaction proceeded very quickly (within 1 min). After quenching the reaction mixture with saturated sodium thiosulfate solution, we were pleased to isolate (1*E*,2*E*)-3-bromo-4-oxo-*N*′-tosylpent-2-enoxylimidic acid ethyl ester **2a** in 30% yield along with some unidentified mixture. When treating the reaction mixture with saturated potassium carbonate solution or directly adding 2.0 equiv of dry potassium carbonate into the reaction system, we got similar results. Considering the usefulness of the *N*-tosylimidic esters in organic synthesis,[11] we then tried to optimize the reaction conditions to get a useful synthesis of these products. Our experimental results show that the temperature effect played an important role in improving the product yields and suppressing side reactions. The results are summarized in Table 1. At −65 °C, a solution of **1a** in CH_2Cl_2 was added to a mixture of $TsNBr_2$ in the presence of 2.0 equiv of K_2CO_3. After being stirred at −65 °C for 15 min, the reaction was slowly warmed to room temperature and then kept stirring for another

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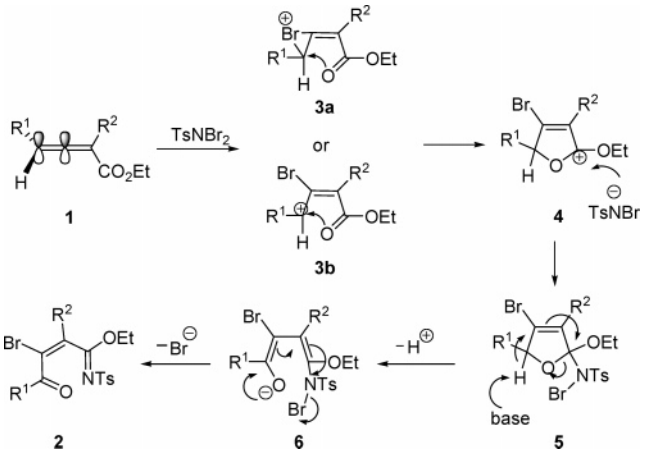
SCHEME 2



30 min. With a general workup, the product (1*E*,2*E*)-3-bromo-4-oxo-*N*′-tosylpent-2-enoxylimidic acid ethyl ester **2a** was obtained exclusively in 81% yield (entry 5, Table 1). However, when the reaction was directly carried out at room temperature or 0 °C, unidentified products were observed in low yields (entries 2 and 3, Table 1). When the reaction was conducted at a much lower temperature following a similar procedure (entry 6, Table 1), the yield was not improved significantly. Our further investigations prove that dry MeCN was also a good solvent for the reaction (entry 7, Table 1), but solvents such as toluene and THF did not work very well (entries 9 and 10, Table 1).

With the optimized conditions in hand, we next examined the reaction of various 2,3-allenoates with $TsNBr_2$ in the presence of K_2CO_3. The results summarized in Table 2 indicate that when R^1 = alkyl, R^2 = H, alkyl, or Bn, the reaction proceeded smoothly to give the products in good yields. Slightly lower yields were observed when R^1 = Ph (entries 13−15, Table 2). However, the reaction failed to furnish the corresponding products when R^1 = H (entries 16 and 17, Table 2). All of the products were characterized by spectroscopic methods, and finally the stereochemistry was established by the X-ray diffraction analysis of **2m** (Figure 1).

A plausible mechanism to rationalize this reaction is outlined in Scheme 2. The bromonium ion generated from $TsNBr_2$ first reacts with the relatively electron-rich C═C bond to produce the intermediate **3a** or **3b**.[12] The participation of the ester carbonyl group may facilitate the formation of a cyclic cation **4**, which then accepts the nucleophilic attack of $[TsNBr]^-$ to produce cyclic intermediate **5**. In the presence of K_2CO_3, the unstable **5** may lose a proton to yield intermediate **6**, which further evolves into the final product **2** with a bromine anion departure.

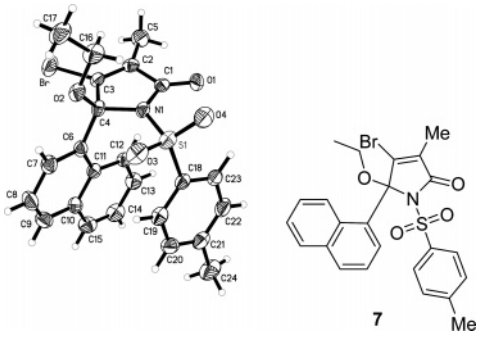


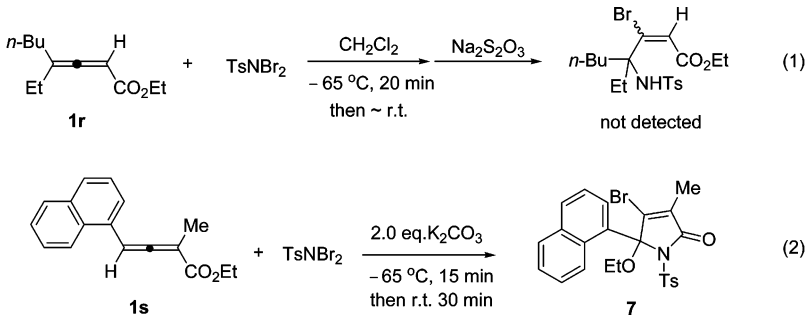
FIGURE 2. ORTEP representation of the product **7**.

The failure to get the corresponding products for the reaction of 3,3-unsubstituted 2,3-allenoates **1p** or **1q** with $TsNBr_2$ may be attributed to the fact that the stabilization of the cationic intermediate by substituents is important for the generation of **3a** or **3b**[12b,13] and the lack of neighboring group participation will result in sluggish formation of **5** (entries 16 and 17, Table 2). When 3,3-disubstituted 2,3-allenoate **1r** was applied to test its interaction with $TsNBr_2$, a mixture of unidentified products was obtained, and it is noteworthy that no aminobrominated products to the β,γ-double bond were detected even if the reaction mixture was treated with sodium thiosulfate (eq 1, Scheme 3). This may indicate that the nucleophilic attack of $[TsNBr]^-$ in the current reaction is regioselective, and the similar intermediate as **5** is quite unstable and easily decomposed. Nevertheless, when we used ethyl 2-methyl-4-(naphthalen-1-yl)buta-2,3-dienoate **1s** as substrate following the same procedure, to our surprise, an interesting and potentially very useful product,[14] 4-bromo-5-ethoxy-3-methyl-5-(naphthalen-1-yl)-1-tosyl-1H-pyrrol-2(5H)-one **7** was obtained in 48% isolated yield (eq 2, Scheme 3). As for this result, there may occur a different reaction pathway which remains to be investigated.In conclusion, we disclosed a novel reaction process of 2,3-allenoates with $TsNBr_2$ as electrophile to produce (1*E*,2*E*)-3-bromo-4-oxo-*N*′-tosyl-2-alkenoxylimidic acid ethyl esters in moderate to good yields with high stereoselectivity. The formation of 5-alkoxypyrrolin-2(5*H*)-one was observed when ethyl 2-methyl-4-(naphthalen-1-yl)buta-2,3-dienoate was used as the substrate. Further study of this reaction to determine its scope and limitations and efforts to elucidate the mechanistic details are currently underway.

Experimental Section

General Procedure for Access to (1*E*,2*E*)-3-Bromo-4-oxo-*N*′-tosyl-2-alkenoxylimidic Acid Ethyl Esters. Under an atmosphere of dry nitrogen, 2.0 equiv of K_2CO_3 (1.0 mmol) was added to a

SCHEME 3



solution of $TsNBr_2$ (0.5 mmol) in 1 mL of dry CH_2Cl_2 at −65 °C. Then a solution of 2,3-allenoate **1** (0.5 mmol) in 1 mL of CH_2Cl_2 was injected. After being stirred for 15 min at the same temperature, the cooling bath was removed and the reaction mixture was slowly warmed to room temperature and then kept stirring for another 30 min. The mixture was quenched with water and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with saturated brine and dried over anhydrous $MgSO_4$. After filtration and removal of solvent in vacuo, the residues were purified by flash silica chromatography (petroleum ether/ethyl acetate 6:1 v/v) to afford **2**.

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Supporting Information Available: General experimental details, analytical data for **2a**−**2o** and **7**, and ^1H and ^{13}C NMR spectra of these compounds. X-ray data for **4m** and **7** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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