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An unexpected Lewis acids-catalyzed tandem ring-opening rearrangement of vinylcyclopropane ketone with aryl aldehyde

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ABSTRACT

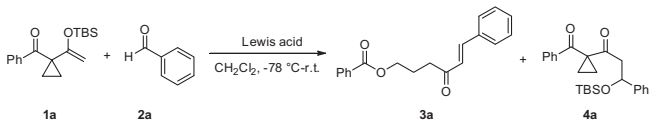
A novel tandem reaction of vinylcyclopropane ketone with benzaldehyde has been successfully developed. This provides a new method for the preparation of γ-oxo-hexenone derivatives from easily accessible starting materials.

Vinyl cyclopropanes (VCPs) are useful C_5 synthons in organic synthesis. Typical reactions of VCPs being applied in organic synthesis include rearrangements to cyclopentenes and transition metal-catalyzed cycloadditions.[1,2] During our exploration for development of novel acid-catalyzed polar formal cycloadditions of activated cyclopropanes for the construction of cyclic skeletons, we observed an unexpected tandem process of VCP ketone **1a** with benzaldehyde, which led to γ-oxo-hexenone **4a** (Table 1). Because γ-oxo-hexenones are useful intermediates in organic synthesis,[3,4] we started to explore this novel reaction.

Under catalysis of $Sc(OTf)_3$, reaction of **1a** with benzaldehyde **2a** was carried out from −70 °C to room temperature. The reaction was sluggish but finally gave **4a** after 5 days (Table 1, entry 1). The structure of **4a** was confirmed by X-ray crystallographic analysis (Fig. 1).[5,6] Various Lewis acids were screened and the results are listed in Table 1. In some cases, a Mukaiyama–Aldol product **3a** was obtained. We found that when it was first carried out at −70 °C for 2 h under catalysis of $Sc(OTf)_3$ and was then carried out at rt for additional 54 h under catalysis of TMSOTf, the reaction was accelerated with a better yield (entry 11). This reaction condition was selected for further investigation.

The scope of substrates **2** was then explored (Table 2). We found that both electron-rich and electron-deficient benzaldehydes worked well with moderate to excellent yields (entries 2–9).

Table 1
Screening of Lewis acids for optimal condition[a]



Entry	Cat.[a]	Time	Yield
1	$Sc(OTf)_3$	5 d	**3a** 66%
2	$Yb(OTf)_3$	9 d	**3a** 17%, **4a** 26%
3	BF_3Et_2O	2 d	**3a** 31%
4	$SnCl_4$	10 d	**3a** 34%
5	$TiCl_4$	15 d	**4a** 59%
6	$ZnCl_2$	13 d	**3a** 5%, **4a** 33%
7	$Sn(OTf)_2$	3 d	**3a** 16%
8	$Zn(OTf)_2$	13 d	**4a** 26%
9	$Cu(OTf)_2$	2 d	**3a** 7%
10	TMSOTf	15 h	—
11	$Sc(OTf)_3$ + TMSOTf[b]	56 h	**3a** 75%

[a] General condition: **1a** (0.66 mmol), **2a** (0.55 mmol), Lewis acids (0.2 equiv), and CH_2Cl_2 (10 mL) were mixed and stirred from −70 °C to rt.
[b] The reaction was first carried out at −70 °C for 2 h under catalysis of $Sc(OTf)_3$ (0.2 equiv), and then at rt for 54 h under catalysis of TMSOTf (0.2 equiv).

Benzaldehyde substituted with NO_2, 2-furaldehyde and aliphatic butyraldehyde did not give the corresponding products.

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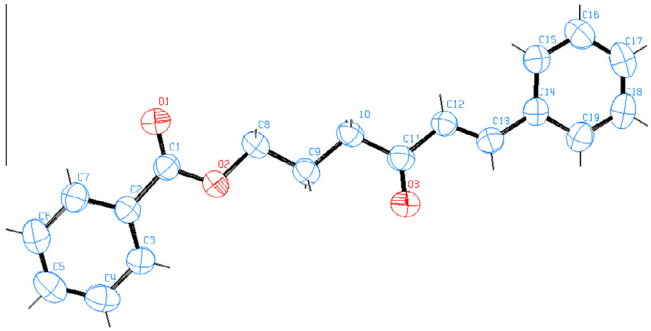
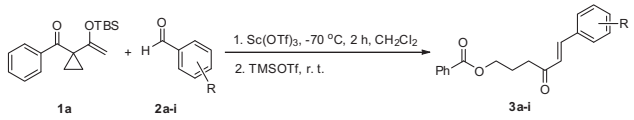


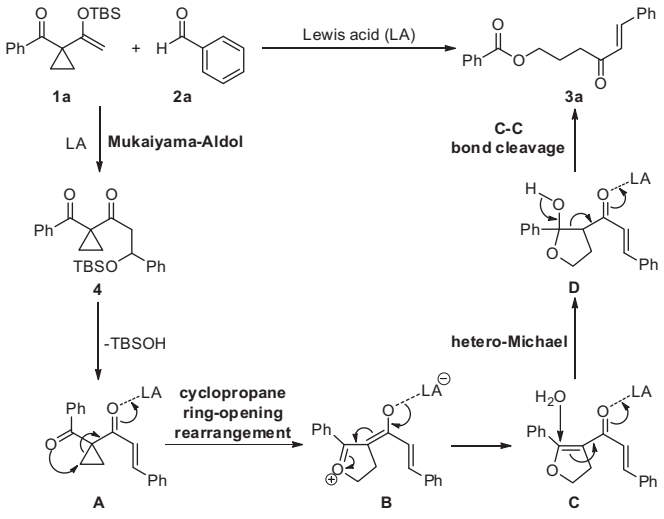
Figure 1. X-ray crystal structure of **3a**.

Table 2
Reactions of vinylcyclopropane ketone **1a** with benzaldehydes **2**[a]



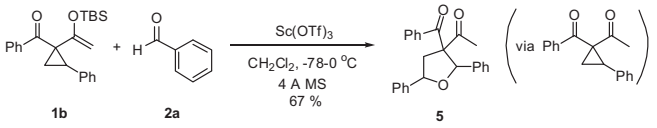
Entry	R	Time (h)	Yield[b]
1	**2a** H	56	**3a** 75%
2	**2b** *p*-Cl	53	**3b** 84%
3	**2c** *p*-Br	56	**3c** 42%
4	**2d** *p*-F	62	**3d** 63%
5	**2e** *p*-Me	48	**3e** 93%
6	**2f** *o*-Cl	67	**3f** 38%
7	**2g** *p*-tBu	60	**3g** 61%
8	**2h** *p*-MeO	51	**3h** 61%
9	**2i** *m*-MeO	51	**3i** 47%

[a] General addition: **1a** (0.66 mmol), **2a** (0.55 mmol), Lewis acids (0.2 equiv), and CH_2Cl_2 (10 mL). The reaction was first carried out at −70 °C for 2 h under catalysis of $Sc(OTf)_3$ (0.2 equiv), and then at rt for 54 h under catalysis of TMSOTf (0.2 equiv).
[b] Isolated yields.



Scheme 1. Proposed mechanism.

Depending on the above results, a possible mechanism was proposed for the tandem reactions (Scheme 1). Under catalysis of Lewis acids, the tandem process was initiated by a Mukaiyama–Aldol reaction which was followed by an elimination of TBSOH to give cyclopropane 1,1-diketone A.[7] A ring-opening rearrangement



Scheme 2.

of A gave 2,3-dihydrofuran C.[8] Probably due to the contaminating water in the reaction mixture, C was then transferred to **3a** through a hetero-Michael reaction and C–C bond cleavage process.

When substrate **1b** was employed in the reaction with **2a**, instead of the γ-oxo-hexenone product, tetrahydrofuran **5** was obtained (Scheme 2). This was probably due to the hydrolysis of enol silyl ether to cyclopropane 1,1-diketone, with the donor-activation of a phenyl group which underwent a subsequent [3+2] cycloaddition with **2a**.[9]

In summary, we have developed a novel tandem reaction of vinylcyclopropane ketone with benzaldehyde. This method provides a new strategy for the preparation of γ-oxo-hexenone derivatives from the easily accessible starting materials.

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Supplementary data

Supplementary data (experimental procedures and spectral data for all new products) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.03.035.

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6. Physical data for compound **3a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.3 Hz, 2H), 7.62–7.35 (m, 10H), 6.76 (d, J = 16.2 Hz, 1H), 4.41 (t, J = 6.3 Hz, 2H), 2.86 (t, J = 7.2 Hz, 2H), 2.19 (p, J = 6.7 Hz, 2H). ^{13}C NMR (101 MHz,) δ 199.06, 166.54, 142.73, 134.36, 132.94, 130.52, 129.55, 128.93, 128.35, 128.27, 125.98, 64.24, 37.19, 23.31.IR (neat): ν = 2964, 2897, 1709, 1689, 1612, 1450, 1314, 1283, 1127, 1041, 977, 762, 713, 684 cm^{-1}; HRMS (ESI) Calcd For $C_{19}H_{18}O_3Na$ $(M+Na)^+$: 317.1148; found: 317.1148.
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