

Trialkylamine-Mediated Intramolecular Acylation of Alkenes with Carboxylic Acid Chlorides

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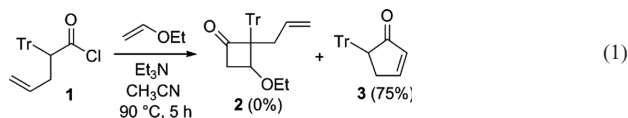
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Trialkylamine-mediated intramolecular cyclization of pent-4-enoyl chlorides was studied. Substitution with a tertiary alkyl group at the 2-position gave cyclopent-2-en-1-ones, while substitution with an aromatic group gave enol esters, which were formed by *O*-acylation of initially formed 3-chlorocyclopentanones with ketenes.

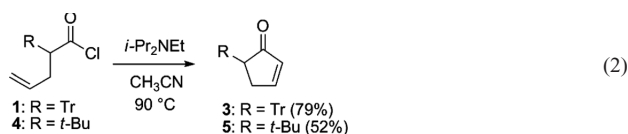
Key words intramolecular cyclization; carboxylic acid chloride; alkene; allyl ketene

During our investigation on Lewis acid-catalyzed intramolecular [4+2] cycloaddition of 2-allyl-3-ethoxycyclobutanones,^{1–4} we tried to prepare 2-allyl-3-ethoxy-2-tritylcyclobutanone **2** by [2+2] cycloaddition under standard conditions of employing 2-tritylpent-4-enoyl chloride **1**, ethyl vinyl ether, and triethylamine. However, the desired product **2** was not obtained, whereas a cyclopentenone **3** was obtained in 75% yield (Eq. 1).



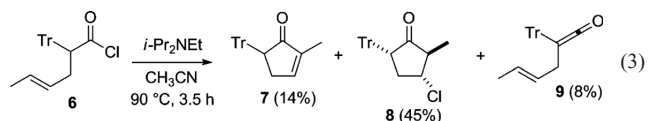
Intramolecular acylation of olefin has been conventionally carried out by Friedel–Crafts reaction of alkenyl acid chlorides by using a Lewis acid such as AlCl₃,⁵ but the observed base-promoted intramolecular cyclization has not been reported to date. We report here the scope and limitations on the present base-promoted intramolecular acylation of a carbon-carbon double bond of acid chlorides.

Investigation of reaction conditions for conversion of **1** to **3** in the absence of ethyl vinyl ether revealed that **3** was obtained in 79% yield by using 1.2 eq of ethyldiisopropylamine at 90 °C for 11 h (Eq. 2).⁶



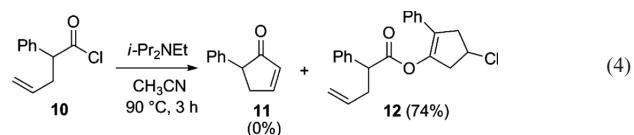
The reaction proceeded more smoothly in acetonitrile than in toluene. Carboxylic acid chloride **4** having a *t*-butyl group at the 2-position also gave the corresponding cyclopentenone **5** in 52% isolated yield (90 °C for 3 h).

Next, cyclization of an internal alkenyl group was examined by using 2-crotyl-2-tritylacetyl chloride **6**. The cyclization of **6** was found to proceed slowly, and cyclopentenone **7** was obtained in low yield (14%) (Eq. 3).



It should be noted that 3-chlorocyclopentanone **8**, which might be a precursor of **7**, was obtained in 45% yield as a single diastereomer⁷ and ketene **9** was isolated in 8% yield after preparative thin-layer chromatography on silica gel.^{8–10} The isolation of **8** and **9** suggests that an internal alkyl group retards the intramolecular cyclization due to its steric effect.

On the other hand, reaction of carboxylic acid chloride **10** bearing a phenyl group at the 2-position did not give the expected cyclopentenone **11**, whereas an enol ester **12** was obtained in 74% yield as a mixture of diastereomers (dr = 54 : 46) (Eq. 4).



Effects of substituents on the aryl group of 2-arylpent-4-enoyl chlorides **13** were then investigated to clarify the scope and limitations of the formation of a novel dimerization product **14** (Table 1). Substitution of a *p*-chloro group gave enol ester **14a** in 59% yield (entry 1) while enol esters **14b, c** bearing *p*-methyl and *p*-methoxy groups, which were found to be hydrolyzed more easily during purification by column chromatography on silica gel, were obtained in moderate to low yields (entries 2, 3). Thus, substitution of the aryl group with an electron-withdrawing group gave enol esters **14** more efficiently partly because of the increased stability of **14** against hydrolysis.¹¹

Methanolysis of the obtained enol ester **14a** in the presence of an equimolar amount of 4-(dimethylamino)pyridine (DMAP) gave methyl ester **15** and cyclopentenone **16** in 90% and 64% yields, respectively (Eq. 5).

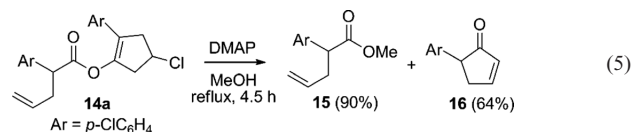


Table 1. Cyclization of 2-Arylpent-4-enoyl Chlorides

Entry	X	14	% yield ^{a)}
1	Cl	14a	59 ^{b)}
2	Me	14b	50
3	MeO	14c	20

^{a)} Determined by ¹H-NMR analysis unless otherwise noted (% yield = mol of **14**/2 × mol of **13**). ^{b)} Isolated yield.

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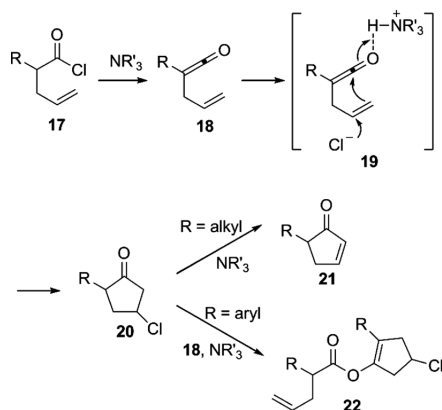


Chart 1. Proposed Mechanism for Trialkylamine-Promoted Intramolecular Acylation of Alkenes with Carboxylic Acid Chlorides

A proposed mechanism for the present amine-mediated intramolecular cyclization is shown in Chart 1. Treatment of carboxylic acid chloride **17** with trialkylamine gives ketene **18**, and intramolecular attack of the alkenyl group to the ketene carbonyl group which is activated by ammonium ion¹²⁾ gives 3-chloropentanone **20** via a transition state **19**.¹³⁾ When R is an alkyl group, dehydrochlorination with a base proceeds to give cyclopentenone **21**. The presence of an aryl group as R makes ketone **20** more enolizable, and enol ester **22** is formed by *O*-acylation of **20** with ketene **18**.

In summary, we have found that treatment of pent-4-enoyl chlorides with trialkylamine gave intramolecular cyclized products. The structure of products strongly depended on the substituent at the 2-position: a tertiary alkyl group¹⁴⁾ gave cyclopentenones, whereas an aryl group gave enol esters. The present study gives new aspects in the chemistry of allyl ketenes.^{15,16)}

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References and Notes

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- Yields of intramolecular cyclized products described here are based on the corresponding carboxylic acids. Conversion of carboxylic acids to carboxylic acid chlorides was carried out by using oxalyl chloride.
- The stereochemistry of compound **8** was determined by NOE experiments.
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- The electron-withdrawing group might increase the acidity at the α -position of **20**.
- Allyl trityl ketene was isolated in 32% yield by treatment of **1** with ethyldiisopropylamine at 90 °C for 5 min. Cyclization of isolated allyl trityl ketene in the absence of any additives took place very slowly (in acetonitrile, 90 °C, 7 d) to afford **3** in only 31% yield. On the other hand, cyclization of allyl trityl ketene in the presence of diisopropylethylamine hydrochloride took place smoothly to afford **3** in 67% yield (in acetonitrile, 90 °C, 11 h).
- Otherwise, ring cleavage of a bicyclo[2.1.0]pentan-2-one derivative, which might be formed by intramolecular [2+2] cycloaddition of **18**, may proceed to give **20**, though bicyclo[2.1.0]pentan-2-ones were not isolated in this study.
- Substitution with diphenylmethyl or benzyl groups at the 2-position (R of **17**) gave the corresponding cyclopentenones **21** in 14% and 7% yields, respectively. Therefore, substitution of a tertiary alkyl group is required for efficient cyclization to a cyclopentenone derivative **21**.
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