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Indium-Catalyzed [2 + 2] Cycloaddition of Allylsilanes to Internal Alkynones

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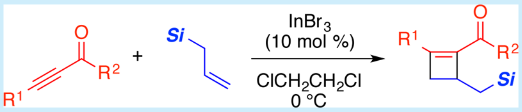
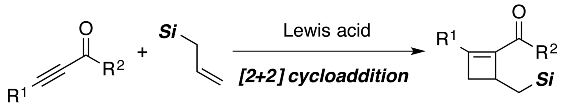
Supporting Information

ABSTRACT: We have developed an indium-catalyzed [2 + 2] cycloaddition of allylsilanes to alkynones leading to selective cyclobutenone formation. The resulting cyclobutenones were readily converted to the oxidized products by Tamao−Fleming oxidation or the ring-opened products by an electrocyclic reaction.



Small-ring molecules are generally used as highly reactive synthetic intermediates because of their ring-strain energy.[1] Of such molecules, cyclobutenes are useful compounds because they readily undergo stereoregular electrocyclic ring-opening reactions to afford the corresponding 1,3-dienes.[2] The most direct and efficient method for preparing cyclobutenes is [2 + 2] cycloaddition of alkenes with alkynes that proceeds by photoirradiation,[3] transition metal catalysis,[4] or Lewis acid catalysis.[5] Of various alkenes, allylsilanes are often used as the allyl synthons in Lewis acid mediated allylation reactions such as Mukaiyama− or Sakurai−Hosomi-type reactions.[6] For [2 + 2] cycloaddition, there have been a few reports on Lewis acid mediated reactions of allylsilanes with electron-deficient alkynes. In such reports, there remain three points requiring improvement: (1) a stoichiometric Lewis acid such as $TiCl_4$ is required, (2) the scope of alkynes is limited to terminal alkynes, and (3) a further [2 + 2] cycloaddition may occur depending on the reaction conditions (Scheme 1),[7] in which the substrate scope is limited because only terminal alkynes can be applied.[7] Therefore, it is important to develop a [2 + 2] cycloaddition reaction with internal alkynes to provide synthetic diversity.

Scheme 1. Lewis Acid Mediated [2 + 2] Cycloaddition Reaction of Alkenes with Alkynones

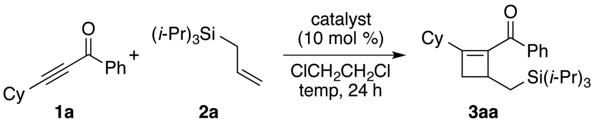


Existing Problem
· stoichiometric amount of Lewis acid is required
· applicable only for terminal alkynes
· difficult to supress further cycloaddition
Planned work
· catalytic cycloaddition
· application to internal alkynes

Meanwhile, we have studied the direct addition reactions of alkenes to α,β-unsaturated ketones controlled by the orbital−interaction effect of silicon substituents and have reported an acid-catalyzed direct conjugate addition of styrene derivatives to β-silylenones, as well as a scandium-catalyzed [3 + 2] cycloaddition reaction of allylsilanes to β-silylenones.[8] In this paper, we report an indium-catalyzed [2 + 2] cycloaddition reaction of allylsilanes to internal conjugated alkynones.

First, the reaction of alkynone **1a** and allyltriisopropylsilane **2a** in 1,2-dichloroethane was performed in the presence of various acid catalysts. Although Me_3SiOTf and HOTf were effective in the conjugate alkenylation that we have previously reported, they exhibited no catalytic activity, in the present reaction (Table 1, entries 1 and 2). Scandium(III) triflate, which is the best catalyst for the previous report on [3 + 2] cycloaddition, showed high catalytic activity, but gave only a 7%

Table 1. Lewis Acid Catalyzed [2 + 2] Cycloaddition of Allylsilane 2a with Alkynone 1a[a]



entry	catalyst	temp (°C)	**1a** conv (%)[b]	**3aa** yield (%)[b]
1	Me_3SiOTf	25	0	0
2	HOTf	25	6	0
3	$Sc(OTf)_3$	25	66	7
4	$Al(OTf)_3$	25	71	17
5	$Ga(OTf)_3$	25	79	38
6	$In(OTf)_3$	25	78	61
7	$InCl_3$	25	66	47
8	$InBr_3$	0	96	81 (73)[c]
9	InI_3	−40	98	58
10	$In(NTf_2)_3$	−40	84	53
11	$TiCl_4$ (1.0 equiv)	0	100	16
12	Me_2AlCl (1.0 equiv)	0	2	2

[a] Reactions were carried out with alkynone **1a** (0.20 mmol), allylsilane **2a** (0.40 mmol), and catalyst (20 μmol) in $ClCH_2CH_2Cl$ (1.5 mL). [b] Determined by ^1H NMR. [c] Isolated yield.

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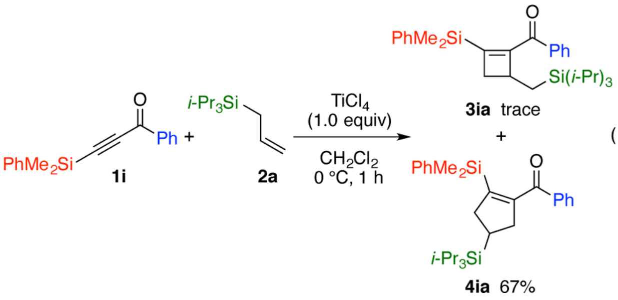
yield of the target cyclobutene. As a result of screening other metal(III) triflate salts, indium(III) triflate was proven to be the most effective catalyst in the [2 + 2] cycloaddition reaction (entries 4–6). Then, we examined other indium salts and suitable reaction temperatures (entries 7–10). While indium(III) chloride showed low catalytic activity, indium(III) bromide served as the most effective catalyst at 0 °C and gave the cycloadduct in 73% isolated yield. In the case of indium(III) iodide or bis(triflyl)imide, yields of the product were lower even at low temperature (−40 °C) because of their high reactivity. Other typical Lewis acids, such as $TiCl_4$ and Me_2AlCl, gave the cycloadduct in only very low yields even when the stoichiometric amount of these reagents was used.[9]

Various combinations of alkynones and allylsilanes afforded the corresponding cyclobutenones in high yields under the optimized reaction conditions (Scheme 2). As a terminal substituent of alkynes, the cyclohexyl group at R^1 could be altered to both *n*-butyl and *tert*-butyl groups (**3ba** and **3ca**).[10] These results show the suitability of various alkyl groups, including primary, secondary, and tertiary alkyl groups. The cycloadducts were obtained in good yields when the alkynones possess various aromatic and heteroaromatic rings such as benzene, napthalene, thiophene, and benzofuran (**3da**–**3ga**). As a silyl substituent of allylsilanes, the *tert*-butyldiphenylsilyl group (t-$BuPh_2Si$) and triphenylsilyl group (Ph_3Si), which can be used for further transformations such as Tamao–Fleming oxidation, could also be applied (**3db** and **3dc**).[11] The scope of alkynones was also expanded to *β*-silylalkynones. The reaction of alkynone **1h** with allylsilane **2b** gave the cycloadduct **3hb** selectively, while the reaction of alkynone **1i** and allylsilane **2a** underwent [3 + 2] cycloaddition involving the rearrangement of a silyl group in addition to the main [2 + 2] cycloaddition reaction, resulting in a mixture of two products, **3ia** and **4ia**, in a total yield of 87% with a ratio of ca. 1.4:1. In our previous report, the *β*-silicon substituents on the *α*,*β*-unsaturated carbonyl compounds exerted a remarkable influence on the product selectivity and also affected the selectivity in the present reaction.[8,12]

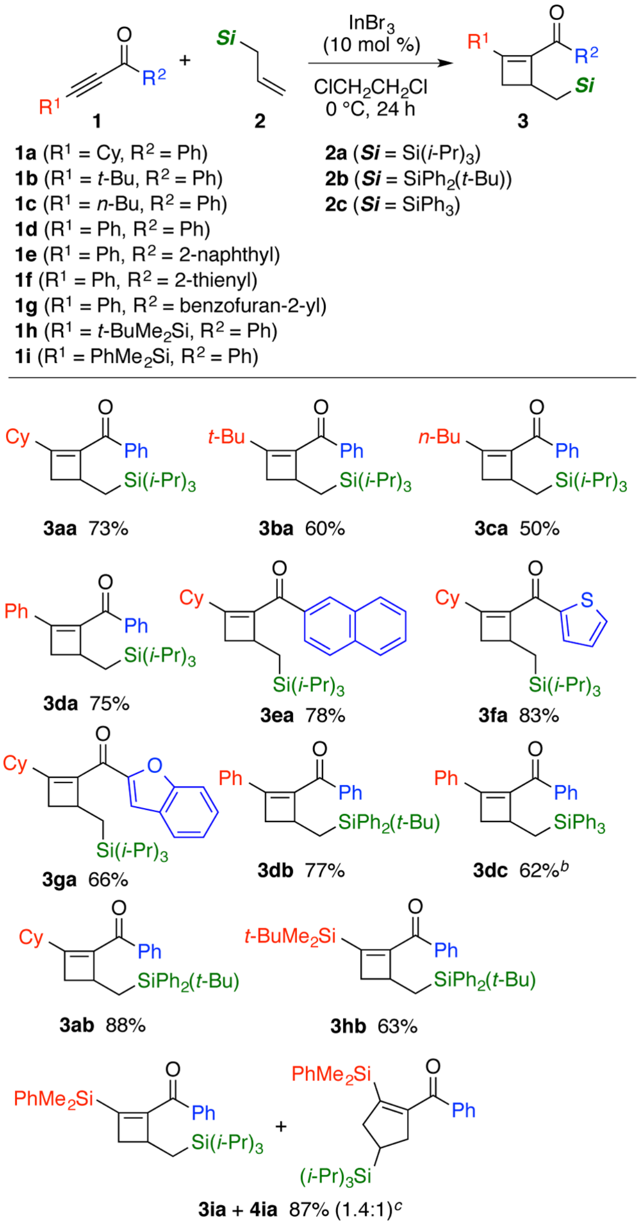
It is worth noting that the selectivity of the cycloaddition pathway was switched by using a stoichiometric amount of $TiCl_4$, and the [3 + 2] cycloaddition product **4ia** was selectively obtained in 67% yield (eq 1).[13]



(1)

Because the cyclobutenones obtained in the present reaction have large strain energies, they are expected to undergo thermal electrocyclic reactions to afford the corresponding ring-opened products. The reaction of cycloadduct **3aa** for 2 h in refluxing toluene afforded the dienone **5aa** in 22% yield together with silylenolate **6aa** in 12% yield (eq 2). Silylenolate **6aa** was considered to be formed by the thermal sigmatropic rearrangement of **5aa** involving both C–Si bond cleavage and O–Si bond formation. Increasing the reaction time to 24 h resulted in

Scheme 2. Indium-Catalyzed [2 + 2] Cycloaddition of Allylsilanes 2 to Alkynones 1[a]



[a]Reactions were carried out with alkynone **1** (0.20 mmol), allylsilane **2** (0.40 mmol), and $InBr_3$ (20 μmol) in $ClCH_2CH_2Cl$ (1.5 mL). Isolated yields are shown. [b]Reactions were performed at 40 °C for 42 h. [c]Determined by the ^1H NMR spectrum of the mixture of **3ia** and **4ia** after column chromatography.

the selective formation of **6aa** in high yield. The silyl moiety of enolate **6aa** was readily removed by treatment with tetrabutylammonium fluoride, dienone **7aa** being obtained quantitatively as a single geometrical isomer (eq 3).

The silicon substituents on the cyclobutenones were oxidatively transformed as mentioned above. Cyclobutenone **3ab**, which possesses a $SiPh_2(t$-$Bu)$ group, was first treated with fluoroboric acid followed by aqueous hydrogen peroxide as an oxidant and KHF_2 to give alcohol **8ab** in good yield without any side reaction on the cyclobutene moiety (eq 4). It is of great interest that the generally highly reactive cyclobutene ring was tolerated under such reaction conditions.

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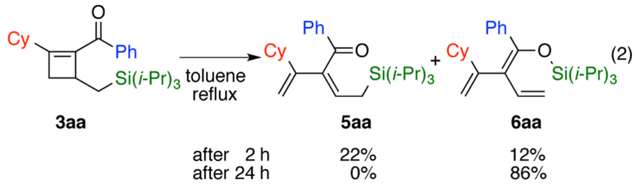

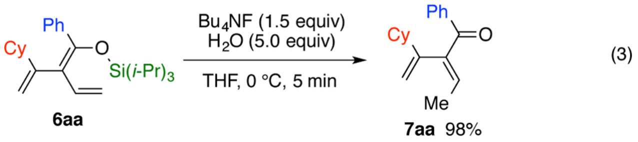

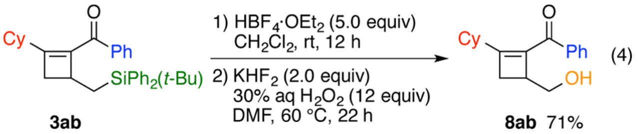

In summary, we have developed an indium-catalyzed [2 + 2] cycloaddition of allylsilanes and electron-deficient alkynes, which would serve as an efficient method for the synthesis of cyclobutenones. The selectivity of the cycloaddition mode was switched by changing the silyl substituents at the *β*-position of alkynones and the catalyst. The usefulness of the present reaction was also demonstrated by the geometry-selective thermal electrocyclic ring-opening reaction of the cyclobutenones, as well as the oxidative transformation of the silicon substituents.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b03065.

Experimental procedures and compound characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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(9) We attempted further cycloaddition of cyclobutenone **3hb** with allylsilane **2a**, but failed to obtain the desired product.

(10) In the reaction of terminal alkynone (R^1 = H), complex mixtures were obtained and the target cycloadduct was not detected.

(11) The reaction of alkynone **1a** with less hindered allyltrimethylsilane gave the [2 + 2] cycloadduct in low yield (6%).

(12) Simple alkenes such as styrene did not cause the cycloaddition with alkynones under the present conditions.

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