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Synthesis of indenes by ytterbium-catalyzed carboalkoxylation/Friedel–Crafts reaction of arylidenecyclopropanes with acetals

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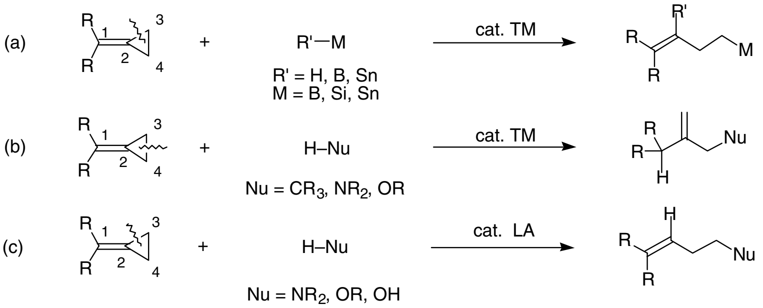
Abstract—Ytterbium-catalyzed tandem carboalkoxylation/Friedel–Crafts reaction of arylidenecyclopropanes **1** with acetals **2** afforded the corresponding indene derivatives **3** in good to high yields. For example, in the presence of 10 mol % of $Yb(OTf)_3$ the reaction of 1-phenylbenzylidenecyclopropane **1a** with the dimethyl acetals of benzaldehyde **2a**, *p*-tolualdehyde **2b**, and *p*-anisaldehyde **2c** gave 1,3-diphenyl-2-(2-methoxyethyl)indene **3a**, 2-(2-methoxyethyl)-3-phenyl-1-(*p*-tolyl)indene **3b**, and 1-(*p*-anisyl)-2-(2-methoxyethyl)-3-phenylindene **3c** in 82%, 80%, and 80% yields, respectively.

Methylenecyclopropanes have been widely utilized as a four carbon unit in organic synthesis.[1] Recently, transition metal-catalyzed addition to methylenecyclopropanes has been widely investigated and become a powerful tool to construct new carbon–carbon and carbon–heteroatom bonds.[2] The addition of metal hydrides, such as H–Sn[3] and H–Si,[4] and bismetallic compounds, such as B–B[5] and B–Si,[6] to methylenecyclopropanes proceeds through ring opening at the proximal bond between C2 and C3 (Scheme 1, type a). The addition of pronucleophiles, such as active methynes,[7] amines,[8] alcohols,[9] and hetero-aromatics,[10] proceeds via distal bond cleavage between C3 and C4 (type b), to give the allylated pronucleophiles. Lewis acidic transition metal-catalyzed addition of pronucleophiles, such as alcohols,[11] water,[12] amines,[13] and aromatic rings,[14] to methylenecyclopropanes have also been reported (type c).[15] These reactions proceed predominantly through proximal bond cleavage, affording the homoallylated pronucleophiles. To the best of our knowledge, however, the catalytic addition of a carbon–oxygen bond, so-called *carboalkoxylation*, to methylenecyclopropanes is not known. Herein, we report that the ytterbium-catalyzed tandem carboalkoxylation/



Scheme 1. Catalytic addition to methylenecyclopropanes.

Keywords: Indene; Lewis acid catalysis; Ytterbium triflate; *exo*-Methylenecyclopropane; Carboalkoxylation; Friedel–Craft reaction; Ytterbium catalyzed reaction.

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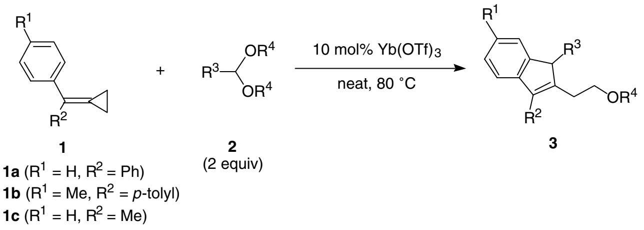
Friedel–Crafts reaction of arylidenecyclopropanes **1** with acetals **2** gives the corresponding indenes **3** in good to high yields (Eq. 1).



(1)

The results are summarized in Table 1. In the presence of 10 mol% of $Yb(OTf)_3$, the reaction of 1-phenylbenzylidenecyclopropane **1a** and 2 equiv of benzaldehyde dimethyl acetal **2a** proceeded at 80 °C without solvent for 1 h and 1,3-diphenyl-2-(2-methoxyethyl)indene **3a** was obtained in 82% yield (entry 1). In this reaction the homoallylic ether **4** was obtained as a byproduct in 5% yield. $Sc(OTf)_3$ promoted the reaction of **1a** and **2a** as well, giving **3a** in 80% yield The reaction of **1a** and **2a** using $AgBF_4$ as catalyst was much slower (24 h, 76% yield). The reaction of **1a** and **2a** using $Zn(OTf)_2$, $Sn(OTf)_2$, $Cu(OTf)_2$, or $La(OTf)_3$ afforded **3a** in a lower yield and $Cu(OAc)_2$ and $PdCl_2$ did not promote the reaction at all. The reaction of **1a** and **2a** in solvents, such as 1,2-dichloroethane or toluene, gave only a trace amount of **3a** and considerable amounts of the starting materials were recovered. The reaction of **1a** and **2a** did not proceed at 30 °C; it took 12 h to complete the reaction of **1a** and **2a** at 50 °C, affording **3a** in 70% yield. The reaction of 1 equiv of **2a** with **1a** gave **3a** in 60% yield. The dimethyl acetals of *p*-tolualdehyde **2b**, *p*-anisaldehyde **2c**, and *p*-trifluoromethylbenzaldehyde **2d** reacted with **1a** and the corresponding indene derivatives **3b–d** were obtained in 80%, 80%, and 73% yields, respectively (entries 2–4). The reaction of **1a** with 2-naphthylaldehyde dimethyl acetal **2e** afforded **3e** in 69% yield (entry 5). The reaction of the diethyl or dibutyl acetal of benzaldehyde (**2f** or **2g**) proceeded much more slowly and it took 24 h for completion; the corresponding indenes **3f** or **3g** were obtained in 71% and 85% yields, respectively (entries 6 and 7). The reaction of bis(*p*-tolyl)methylenecyclopropane **1b** with **2a** produced **3h** in a high yield, while the reaction of 1-methylbenzylidenecyclopropane **1c** with **2a** gave **3i** in a lower yield (entries 8 and 9). The reaction of bis[*m*-(trifluoromethyl)benzyl]methylenecyclopropane **1d** and **2a** gave a 2:1 mixture of **3j** and **3j′** (Eq. 2).

Table 1. $Yb(OTf)_3$-catalyzed tandem carboalkoxylation/Friedel–Crafts reaction of arylidenecyclopropanes **1** with acetals **2**[a]

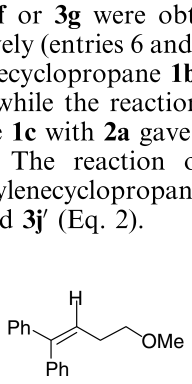
Entry	1	2	R^3	R^4	3	Yield (%)
1	**1a**	**2a**	Ph	Me	**3a**	82[b]
2	**1a**	**2b**	*p*-Tolyl	Me	**3b**	80[b]
3	**1a**	**2c**	*p*-Anisyl	Me	**3c**	80[b]
4	**1a**	**2d**	p-$CF_3C_6H_4$	Me	**3d**	73
5[c]	**1a**	**2e**	2-Naphthyl	Me	**3e**	69
6[d]	**1a**	**2f**	Ph	Et	**3f**	71
7[d]	**1a**	**2g**	Ph	Bu	**3g**	85
8	**1b**	**2a**	Ph	Me	**3h**	80
9	**1c**	**2a**	Ph	Me	**3i**	42

[a] The reaction of **1** (0.5 mmol) and **2** (1 mmol) was carried out in the presence of 10 mol% of $Yb(OTf)_3$ without solvent at 80 °C for 1 h.

[b] A trace amount (5–6%) of the homoallylic ether **4** was obtained as a byproduct.

[c] For 6 h.

[d] For 24 h.



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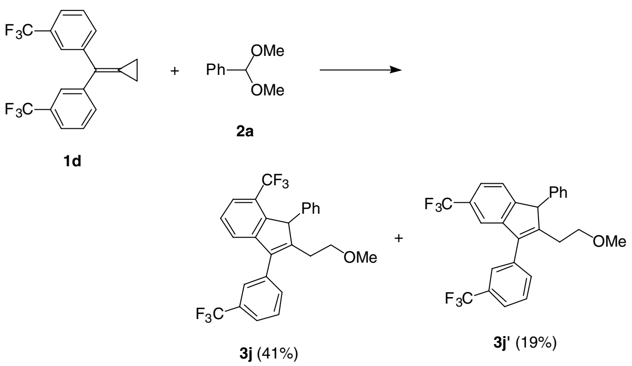


(2)

The structures of compounds **3** were confirmed by spectroscopic methods. Furthermore, the structure of **3e** was unambiguously determined by an X-ray crystallographic analysis.[16] The ORTEP drawing of **3e** is shown in Figure 1.

A plausible mechanism for this reaction is illustrated in Scheme 2. The acetal group of **2** would coordinate to

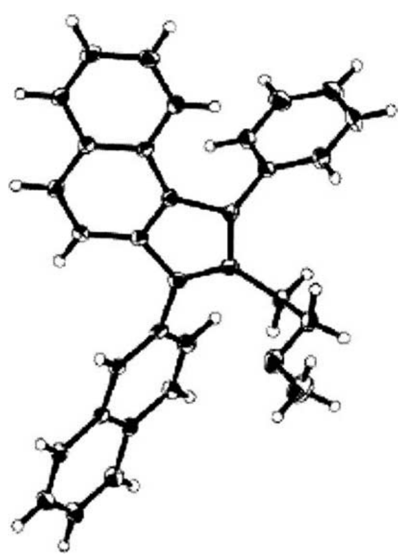
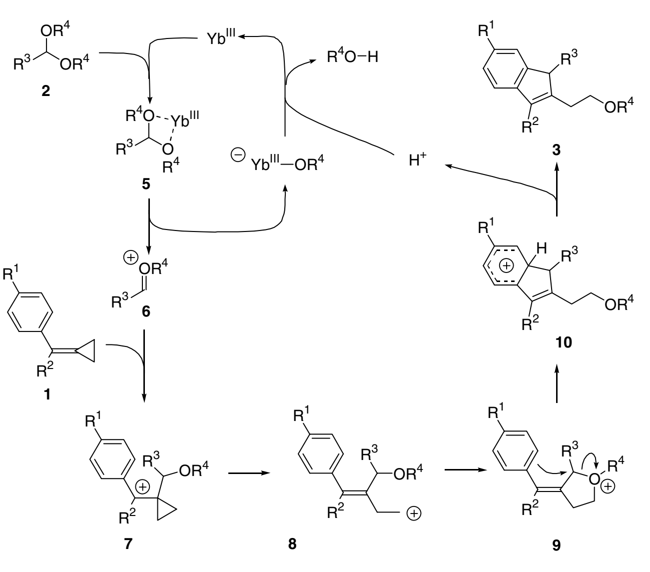


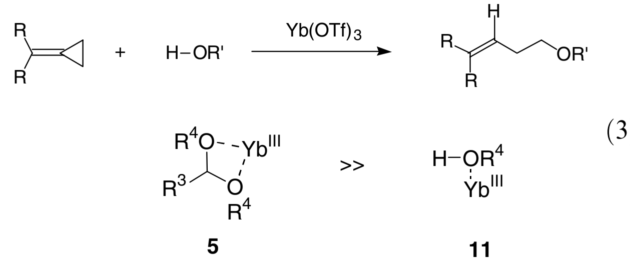
Figure 1. ORTEP drawing of **3e**.



Scheme 2.

ytterbium as shown in **5** and elimination of ytterbium alkoxide from **5** would give the oxonium cation **6**. Nucleophilic attack of the arylidenecyclopropane **1** to **6** would lead to the cyclopropylcarbinyl cation **7**. Cyclopropylcarbinyl-homoallyl rearrangement would take place and following intramolecular electrophilic attack of the resulting homoallyl cation of **8** to the alkoxy group would lead to the cyclic oxonium intermediate **9**. Friedel–Crafts type cyclization would then give the product **3**.

Recently, Shi and Xu reported that the Yb(OTf)$_3$-catalyzed addition of alcohols to methylenecyclopropanes gave the corresponding homoallylic ethers in good to high yields (Eq. 3).[11] The present reaction produces 1 equiv of R^{4}OH as a byproduct. However, only a trace amount of the homoallylic ether **4** was obtained in the reaction of **1a** and **2a**. Perhaps, the coordination of Yb(OTf)$_3$ to the acetal moiety of **2** is much preferable to that to the alcohol **11** since the acetal group can coordinate to Yb(III) strongly in a bidentate manner through two oxygen atoms as shown by structure **5** in Scheme 2.



(3)

Recently we demonstrated the palladium-catalyzed *intramolecular* carboalkoxylation of alkynes with acetals.[17] The present reaction is regarded as the first *intermolecular* carboalkoxylation reaction of carbon–carbon multiple bonds with acetals.

In conclusion, we are in a position to synthesize multifunctionalized indenes in a direct and atom economic manner. The present methodology may be useful for the synthesis of various indene frameworks,[18] which are often found in research areas, such as biochemistry,[19] coordination chemistry,[20] and polymer science.[21]

General experimental procedure for the reaction of arylidenecyclopropane **1a** *and benzaldehyde dimethyl acetal* **2a**. To the arylidenecyclopropane **1a** (103 mg, 0.5 mmol) and Yb(OTf)$_3$ (31 mg, 0.05 mmol) was added benzaldehyde dimethyl acetal **2a** (0.15 mL, 1.0 mmol) under an Ar atmosphere in a pressure vial and the mixture was stirred at 80 °C for 1 h. After completion of the reaction, which was monitored by GC, the mixture was filtered through a short silica column with ethyl acetate as eluent. Purification of the crude product by silica gel column chromatography using a mixture of hexane and ethyl acetate (10:1) as eluent afforded the indene **3a** in 82% yield.

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