

## Michael Addition Reaction of Alkenyl Trichloroacetates Catalyzed by Dibutyltin Dimethoxide

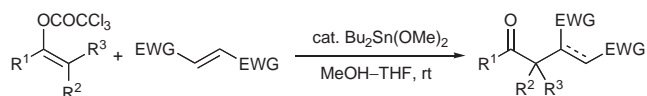
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The Michael addition of alkenyl trichloroacetates to *p*-benzoquinone was achieved using dibutyltin dimethoxide as a catalyst in a mixed solvent consisting of THF and MeOH. Various monoalkylated benzoquinone derivatives were obtained from cyclic and acyclic trichloroacetates in moderate yield. *trans*- $\beta$ -Nitrostyrene was also a favorable electrophile in this catalytic process, which gave an expected Michael adduct.

The Michael addition of enolates to  $\alpha,\beta$ -unsaturated carbonyl compounds is a beneficial method to prepare 1,5-diketones.<sup>1</sup> Since the 1,5-dicarbonyl moiety is not only found in many natural products, but is also capable of being transformed into  $\beta$ -hydroxycyclohexanones and other useful compounds, efficient ways of obtaining this structure are desired for organic synthesis.<sup>2</sup> Numerous examples of the Lewis acid-catalyzed Mukaiyama-type Michael addition of silyl enolates to enones have so far been reported,<sup>3</sup> however the method has difficulty in applying to acid-labile substrates. We report here a novel conjugate addition reaction of alkenyl trichloroacetates to Michael acceptors catalyzed by dibutyltin dimethoxide under almost neutral reaction conditions (Scheme 1).

We have previously shown that dibutyltin dimethoxide [Bu<sub>2</sub>Sn(OMe)<sub>2</sub>] behaves as a catalyst in aldol reaction of alkenyl trichloroacetates with aldehydes in the presence of methanol.<sup>4</sup> In this reaction, a nucleophilic attack of methoxide ion of the tin reagent to the alkenyl esters efficiently generates the corresponding tin enolates. We envisioned that this tin dimethoxide might promote the Michael addition reaction of alkenyl trichloroacetates to  $\alpha,\beta$ -unsaturated carbonyl compounds via a formation of tin enolates.<sup>5</sup> Thus, we initially examined the reaction of cyclohexanone-derived alkenyl trichloroacetate **1a** with chalcone in the presence of a stoichiometric amount of Bu<sub>2</sub>Sn(OMe)<sub>2</sub> at room temperature for 2 h, however the targeted Michael adduct was not obtained at all. Then, we tested various Michael acceptors and among them, *p*-benzoquinone (**2**) showed remarkable reactivity toward an in situ generated tin enolate, and unexpected monosubstituted benzoquinone derivative **3a**, which is considered to be formed by the Michael addition reaction and subsequent oxidation by coexisting *p*-benzoquinone (**2**), was obtained in 43% yield (Entry 1, Table 1). Furthermore, the same compound was given in moderate yield under the influence of a catalytic amount of the tin methoxide and an excess amount of



**Scheme 1.** Dibutyltin dimethoxide catalyzed conjugate addition reaction of alkenyl trichloroacetates to Michael acceptors.

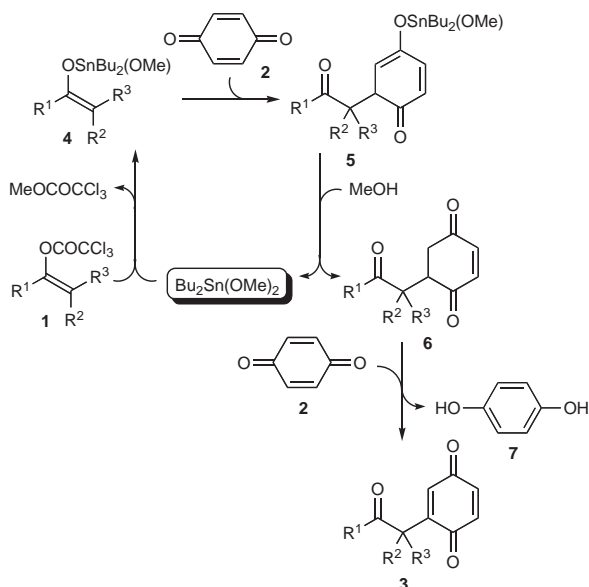
**Table 1.** Catalytic Michael addition of various alkenyl trichloroacetates **1** to *p*-benzoquinone (**2**)<sup>a</sup>

Entry	Alkenyl trichloroacetate	Product	Yield/% <sup>b</sup>
1 <sup>c</sup>		<b>3a</b>	43
2	<b>1a</b>	<b>3a</b>	46
3		<b>3b</b>	42
4		<b>3c</b>	39
5		<b>3d</b>	23
6		<b>3e</b>	35

<sup>a</sup>An alkenyl trichloroacetate **1** (1.1 equiv) reacted with 1 equiv of *p*-benzoquinone (**2**). <sup>b</sup>Isolated yield based on **2** (1 mmol). <sup>c</sup>The reaction was performed using 100 mol % of Bu<sub>2</sub>Sn(OMe)<sub>2</sub> without MeOH for 2 h.

MeOH<sup>6</sup> (Entry 2). According to this catalytic procedure, various alkenyl trichloroacetates **1b–1e** were transformed into the corresponding benzoquinone derivatives **3b–3e** (Entries 3–6).<sup>7</sup> Not only cyclic substrates **1a–1d**, but acyclic **1e** also afforded the adduct **3e**. Use of fully substituted 1-trichloroacetoxycyclohexene **1d** resulted in a lower yield (Entry 5). Noteworthy is the fact that a significant amount of hydroquinone formed in these reactions, for example, the reduced compound was isolated in 43% yield in the case of Entry 2, which is good evidence for occurrence of the above-mentioned oxidation of the Michael adduct by *p*-benzoquinone (**2**). However, even when **1a** was treated with 2 equiv of **2**, the isolated yield of **3a** was not improved (38% yield based on **1a**).

A plausible catalytic mechanism of the Michael addition reaction is shown in Figure 1. First, an alkenyl trichloroacetate **1** reacts with Bu<sub>2</sub>Sn(OMe)<sub>2</sub> generating the dibutylmethoxytin enolate **4** and methyl trichloroacetate. Then, conjugate addition of the tin enolate **4** to *p*-benzoquinone (**2**) occurs to produce the tin enolate of Michael adduct **5**. Protonation of **5** by MeOH affords the Michael product **6** as an intermediate and regenerates the tin dimethoxide. Finally, oxidation of **6** with *p*-benzoquinone (**2**) results in the formation of the benzoquinone derivative **3**



**Figure 1.** A plausible reaction mechanism for the Michael addition of alkenyl trichloroacetates **1** to *p*-benzoquinone (**2**) catalyzed by  $\text{Bu}_2\text{Sn}(\text{OMe})_2$ .

**Table 2.** Michael addition of alkenyl trichloroacetate **1a** to *trans*- $\beta$ -nitrostyrene (**8**) promoted by  $\text{Bu}_2\text{Sn}(\text{OMe})_2$ <sup>a</sup>

Entry	$\text{Bu}_2\text{Sn}(\text{OMe})_2$ /mol %	Solvent	Temp /°C	Additive	Yield /% <sup>b</sup>
1	100	THF	rt	—	63
2	100	DMF	rt	—	79
3	100	THF	-20	$\text{Bu}_4\text{NBr}$ (1 equiv)	93
4	20	DMF	rt	—	38
5	20	DMF	rt	MeOH (5 equiv)	28
6	20	THF	-20	$\text{Bu}_4\text{NBr}$ (1 equiv) MeOH (5 equiv)	28

<sup>a</sup>Alkenyl trichloroacetate **1a** (1.1 equiv) reacted with 1 equiv of *trans*- $\beta$ -nitrostyrene (**8**). <sup>b</sup>Isolated yield based on **8**.

accompanied by hydroquinone (**7**).

Next, we attempted the tin methoxide-catalyzed Michael addition of alkenyl trichloroacetate **1a** to  $\beta$ -nitrostyrene (**8**) and the results are summarized in Table 2. First, we studied solvent effect in the stoichiometric reaction and found that DMF was superior to THF for obtaining the desired Michael adduct **9** in satisfactory yield (Entries 1 and 2). However, the reaction took place more effectively in THF even at  $-20^\circ\text{C}$  when tetrabutylammonium bromide was used as an additive (Entry 3).<sup>5f</sup> As a consequence, two kinds of solvent system (DMF, and THF with  $\text{Bu}_4\text{NBr}$ ) were applied to the catalytic version, however, the reactions were sluggish even in the presence of MeOH (Entries 5 and 6) and highest yield (38% yield) was attained when the reaction was performed in DMF without MeOH (Entry 4).

In summary, we have demonstrated an application of  $\text{Bu}_2\text{Sn}(\text{OMe})_2$  as a catalyst for the conjugate addition of alkenyl trichloroacetates to Michael acceptors. The catalytic reaction with *p*-benzoquinone proceeds smoothly at room temperature

to give monosubstituted benzoquinones in moderate yields owing to the Michael addition and subsequent oxidation. In the reaction of  $\beta$ -nitrostyrene, a typical Michael adduct is predominantly formed. These procedures are operationally simple employing readily available chemicals and can be performed under almost neutral conditions.

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This paper is dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday.

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- In the absence of MeOH, the reaction did not occur catalytically.
- General procedure for the preparation of **3**: Alkenyl trichloroacetate **1** (1.1 mmol) and *p*-benzoquinone (**2**, 1.0 mmol) were dissolved in dry THF (3 mL) under argon atmosphere and then dibutyltin dimethoxide (0.06 mmol) was added to the resulting solution at room temperature. To the mixture was added dropwise MeOH (10 mmol). After being stirred for 1 h at this temperature, the mixture was treated with MeOH (2 mL), brine (2 mL), and solid KF (ca. 1 g) at ambient temperature for 30 min. The resulting precipitate was filtered off. Then, the filtrate was dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo after filtration. The residual crude product was purified by column chromatography on silica gel to give the benzoquinone derivative **3**.