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Copper-catalyzed diesterification of 1,3-diene for the synthesis of allylic diester compounds

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ABSTRACT

A novel and atom economical copper-catalyzed diesterification of 1,3-dienes has been developed; the available allylic diester derivatives, which are the important intermediates for the synthesis of natural products, were attained with moderate to good yields. Preliminary mechanistic study suggests that allylic radical might be involved in this transformation.

Difunctionalization of isolated alkenes is one of classic and valuable transformations known in organic synthesis.[1] Particularly, numerous metal mediated and metal catalyzed difunctionalization reactions in the field have been developed broadly including alkene dioxygenation,[2] aminooxygenation,[3] diamination,[4] diarylation[5] and aminohalogenation.[6] Comparison with isolated alkenes, the catalytic difunctionalization of conjugated dienes has received significantly less attention.[7] Shi developed a series of important palladium and copper catalyzed diamination reactions of 1,3-dienes.[8] Diarylation and 1,2-hydrovinylation of 1,3-dienes under palladium catalysis were recently reported by Sigman.[9] Additionally, the functionalization of 1,3-dienes was also successfully employed in catalytic [4+2] cycloaddition.[10] Mechanistically, palladium-catalyzed difunctionalization of conjugated dienes generally proceeds through the generation of π-allyl palladium intermediates from Pd(0) or Pd(II) with 1,3-dienes.[11] (Scheme 1a) However, besides the formation of π-allyl metal species, copper catalyzed difunctionalization of 1,3-dienes is likely to be undergoing an allylic radical pathway.[7a,8g] Recently, our laboratory contributed a regioselective 1,2-alkylesterification of dienes to allylic esters in the presence of copper catalyst, in which we proposed that 1,3-dienes reacted with alkyl radical to afford allylic radical intermediates and subsequently coupled with other partners[12] (Scheme 1b).

To our knowledge, a more general method for the copper-catalyzed diesterification of 1,3-dienes to the corresponding allylic diester derivatives has not been demonstrated to date. Furthermore, the allylic diester derivatives could transform to diol derivatives which are key in the synthesis of natural products.[13] We herein established a new and atom economical synthetic approach for diesterification of 1,3-dienes with aryl diacyl peroxide using copper as catalyst under mild reaction conditions.

The copper-catalyzed 1,2-alkylesterification of dienes was realized in our previous work and only 11% yield of the 1,2-arylesterificated product was generated in the presence of catalytic amounts of CuTc when employing benzoyl peroxide and 2,3-dimethylbuta-1,3-diene.[12] However, the 1,2-diesterificated product could be obtained with 40% yield using 10 mol% of CuTc as catalyst in 1,4-dioxane at 80 °C for 18 h (Table 1, entry 1). With this result in hand, we conducted the reaction condition optimization while 2,3-dimethylbuta-1,3-diene **1a** and benzoic peroxide **2a** were determined as the model substrates. Initially, the yield of 1,2-diesterificated product **3a** was increased to 55% in toluene with CuTc as catalyst (Table 1, entry 2). The catalyst screening in toluene revealed that CuBr was the most reactive catalyst for this transformation compared to other copper catalysts, improving the yield further to 63% (Table 1, entry 5). Examination of solvent showed that 1,2-dichlorobenzene was the best solvent, which led to an improvement of anticipated product in 72% yield (Table 1, entry 7). Moreover, the yield of product **3a** declined with decreasing the reaction temperature from 80 °C to 60 °C (Table 1, entry 7–9). Decreasing CuBr

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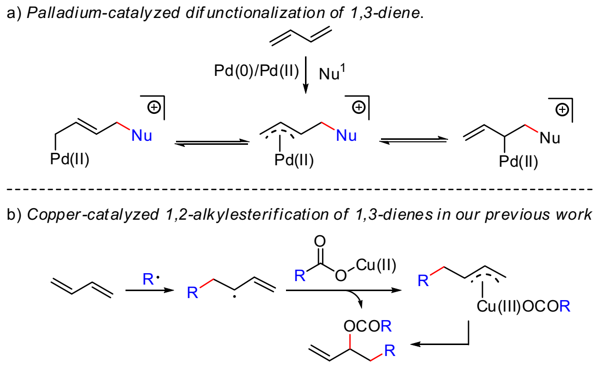


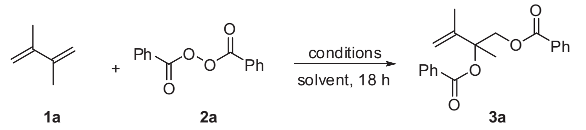
Scheme 1. Metal-catalyzed difunctionalization of 1,3-diene.

loading to 1 mol% did not affect the reactivity of the 1,2-diesterification (Table 1, entry 10), but only 10% yield of **3a** was attained without any catalyst (Table 1, entry 11).

Under the optimized reaction conditions, the scope of aryl diacyl peroxide **2** was investigated with 2,3-dimethylbuta-1,3-diene **1a** (Table 2). A range of electron-withdrawing substituted benzoic peroxides were examined, such as *p*-F, *p*-Cl, and *p*-Br groups, which reacted smoothly and afforded the corresponding products **3b–d** in good yields (Table 2, entry 1–3). Additionally, moderate to good yields (46–73%) of the 1,2-diesterificated products **3e–i** with electron-donating groups were obtained. The lower yield of product **3g** might be due to the steric effect of the *o*-Me group. Moreover, the 2-Nap group substituted peroxide **2j** was also tolerated in the difunctionalized transformation, gave 57% yield of adduct **3j**. It is noteworthy that the addition of peroxide **2** to 2,3-dimethylbuta-1,3-diene **1a** provided a majority of 1,2-diesterificated products and only trace amounts of 1,4-diesterificated products. Unfortunately, alkyl diacyl peroxide could not participate in the difunctionalization under the optimized reaction conditions (Table 2, entry 10).

We next studied the reactivity of a variety of 1,3-diene **1** in the copper-catalyzed diesterification with benzoic peroxide **2a** (Table 3). 2-Methyl-3-butadiene **1b** provided the 1,2-difunctionalized adduct **4** in 52% yield, which was added to the C=C bond with methyl group. 1,2- and 1,4-Difunctionalized products of 1,3-butadiene **1c** were generated in 26% and 22% yields separately when increasing the catalyst loading to 10 mol% (**5** and **6**). Interestingly, the *E*/*Z* selectivity of 3-methyl-1,3-pentadiene **1d** did not affect the product, which gave 61% yield of diastereoselective 1,2-additon product **7** (d.r. = 1.8:1) and 19% yield of 1,4-additon product **8**. The long-chain alkyl group substituted 1,3-diene **1e** and **1f** led to the generation of 1,2-adducts with 70% and 76% yields, respectively. The functional group such as tert-butyldimethylsilyloxy (TBSO) was also well-tolerated in the catalysis, gave rise to the

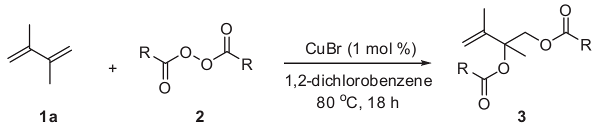
Table 1
Optimization of reaction conditions[a]

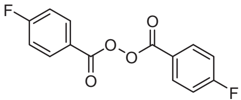
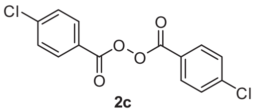
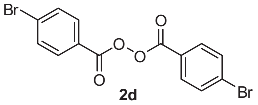
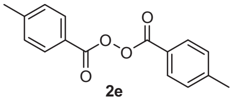
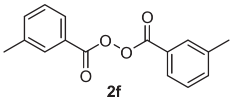
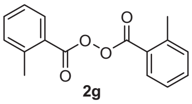
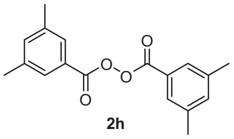
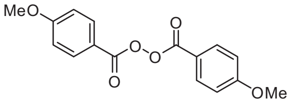
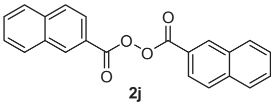
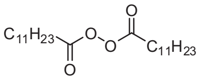


Entry	Catalyst (mol%)	Solvent	Temp (°C)	Yield[b] (%)
1	CuTc (10)	1,4-Dioxane	80	40
2	CuTc (10)	Toluene	80	55
3	Cu(OAc)$_2$ (10)	Toluene	80	62
4	CuBr·SMe$_2$ (10)	Toluene	80	54
5	CuBr (10)	Toluene	80	63
6	CuBr (10)	PhCF$_3$	80	62
7	CuBr (10)	1,2-Dichlorobenzene	80	72
8	CuBr (10)	1,2-Dichlorobenzene	70	62
9	CuBr (10)	1,2-Dichlorobenzene	60	32
10	CuBr (1)	1,2-Dichlorobenzene	80	72
11	None	1,2-Dichlorobenzene	80	10

[a] Reaction conditions: 2,3-dimethylbuta-1,3-diene **1a** (3.0 mmol), benzoic peroxide **2a** (1.0 mmol), solvent (2.0 mL), 18 h, under argon atmosphere.
[b] Isolated yield.

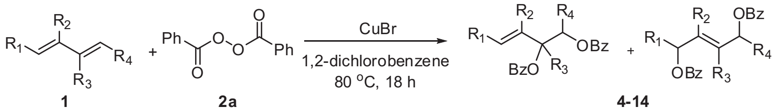
Table 2
Substrate scope of aryl diacyl peroxides[a]

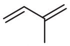
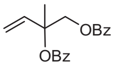
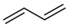
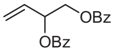
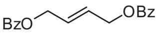
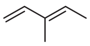
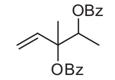
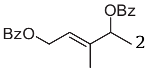
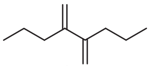
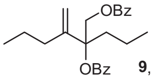
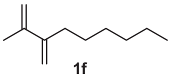
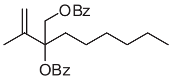
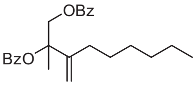
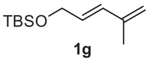
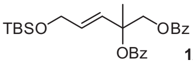
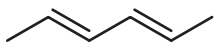
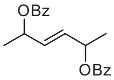
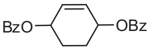


Entry	Peroxide **2**	Product and yield[b]
1	 **2b**	**3b**, 70%
2	 **2c**	**3c**, 71%
3	 **2d**	**3d**, 65%
4	 **2e**	**3e**, 67%
5	 **2f**	**3f**, 60%
6	 **2g**	**3g**, 46%
7	 **2h**	**3h**, 53%
8	 **2i**	**3i**, 73%
9	 **2j**	**3j**, 57%
10	 **2k**	**3k**, NR

[a] Reaction conditions: 2,3-dimethylbuta-1,3-diene **1a** (1.5 mmol), aryl diacyl peroxide **2** (0.5 mmol), CuBr (1 mol%), 1,2-dichlorobenzene (1.5 mL), 80 °C, 18 h, under argon atmosphere.
[b] Isolated yield.

Table 3
Substrate scope of 1,3-dienes[a]



Entry	1,3-Diene **1**	Product and yield[b]
1	 **1b**	 **4**, 52%
2[c]	 **1c**	 **5**, 26%  **6**, 22%
3	 **1d**, *E*/*Z* = 1.76 : 1	 **7**, 61% (d.r. = 1.8 : 1)[d]  **8**, 19%
4	 **1e**	 **9**, 70%
5	 **1f**	 **10** 76% (1 : 1)  **11**
6	 **1g**	 **12**, 53%
7	 **1h**	 **13**, 48%
8[e]	 **1i**	 **14**, 32%

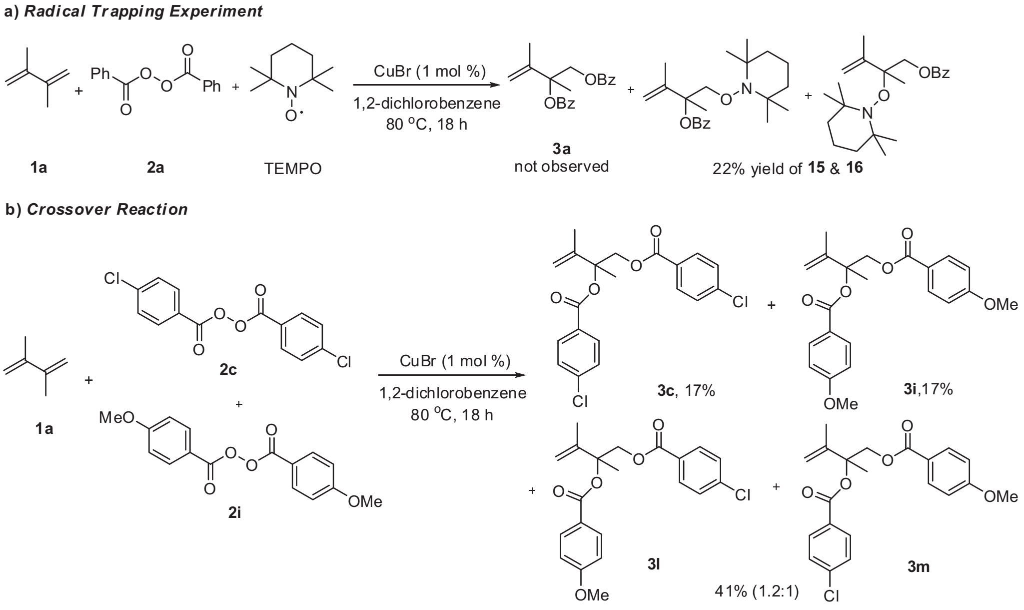
[d] The d.r. value of **7** was determined by ^{1}H NMR.

[a] Reaction conditions: 1,3-diene **1** (1.5 mmol), benzoic peroxide **2a** (0.5 mmol), CuBr (5 mol%), 1,2-dichlorobenzene (1.5 mL), 80 °C, 18 h, under argon atmosphere.

[b] Isolated yield.

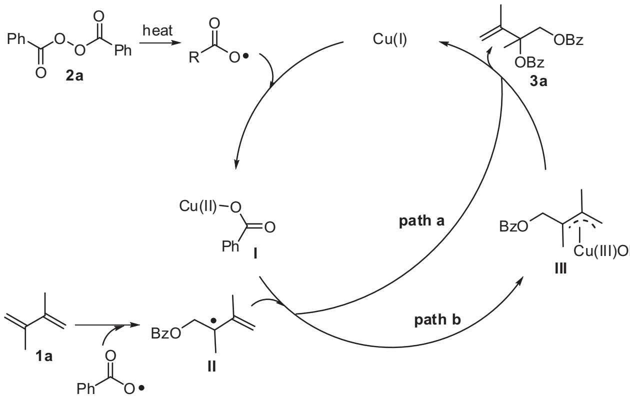
[c] 1,3-Butadiene was bubbled into a solution of **2a** and CuBr (10 mol%) in 1,2-dichlorobenzene (2 mL) for 12 h.

[e] CuBr (10 mol%).


a) *Radical Trapping Experiment*

b) *Crossover Reaction*

Scheme 2. Initial mechanism studies.



Scheme 3. Possible pathway.

desired product **12** in 53% yield. Moreover, different from terminal 1,3-dienes **1b**–**1g**, only 1,4-diesterificated product **13** and **14** were obtained when employing the internal 1,3-diene **1h** and **1i** under the same reaction conditions.

In order to propose a possible mechanism for the diesterification of 1,3-diene, two experiments were proceeded (Scheme 2). TEMPO was used to trap the radical species under the standard reaction conditions (Scheme 2a). In this step, although the product **3a** was not observed, the mixture of **15** and **16** was attained with 22% yield due to the addition of TEMPO. This result suggested that allylic radical species might be involved in the process of the transformation. A crossover reaction between electron-withdrawing and electron-donating substituted benzoic peroxide was also conducted, which indicated that the electronic properties of benzoic peroxide has not apparently influence on the radical involved difunctionalization of 1,3-diene (Scheme 2b). Also, this result suggested that the two esterification steps are separate, intermolecular events.

Based on our previous work and the initial experiment results of mechanism, the proposed catalytic two pathways are presented in Scheme 3. Initially, the Cu(I) species is oxidized by benzoic radical, generated from heating of benzoic peroxide **2a**, to afford Cu(II) benzoic species **I**. In path a, Cu(II) benzoic species **I** transfer benzoic group to the allylic radical **II**, which stems from the addition of benzoic radical to 2,3-dimethylbuta-1,3-diene **1a**, giving the desired product **3a** and regenerate the Cu(I). Alternatively, Cu(III) species **III** is generated from Cu(II) benzoic species **I** and allylic radical **II**. The reductive elimination of Cu(III) species **III** leads to the formation of diesterificated product **3a** and regeneration of Cu(I) (path b).

In conclusion, we have established the first copper-catalyzed diesterification of 1,3-dienes with various aryl diacyl peroxides, affording a range of 1,2- or 1,4-difunctionalized compound in moderate to good yields. Although integrated mechanistic studies have to investigate in future, the preliminary experiment demonstrated that allylic radical species might participate in the diesterification of 1,3-diene. Moreover, this method promises to serve as a novel strategy for the difunctionalization of 1,3-dienes to provide allylic diester molecules.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2016.06.087.

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