



# Magnesium-promoted reductive acylation of aromatic conjugated ynones accompanying with transposition of the triple bond



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## ABSTRACT

Reductive acylation of aromatic conjugated ynones with acid chlorides in the presence of magnesium metal in *N,N*-dimethylformamide gave the corresponding enyne derivatives as the main compounds in moderate yields. Selective transposition of the ynone triple bond to the neighboring position was observed by allene intermediate formation. The existence of an aromatic ring of the starting material played an essential role in the reaction. Moreover, the acylation produced corresponding lactones in the presence of diacid chlorides. Final product structures were fully characterized and one product, 3,5-diphenyl-2-penten-4-yn-2-yl acetate was analyzed by single-crystal X-ray diffraction.

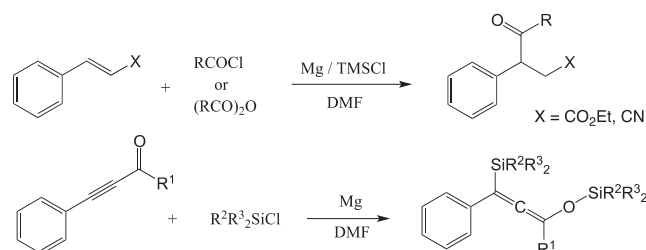
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## 1. Introduction

Ynones, key intermediates in organic chemistry, have been applied to many natural product syntheses.<sup>1</sup> Because of their bi-functional electrophilicity, ynones and their analogues can be transformed into heterocyclic compounds, such as quinoline,<sup>2</sup> pyrimidine,<sup>3</sup> pyrazole,<sup>4</sup> pyridine,<sup>5</sup> and furan,<sup>6</sup> as valuable building blocks.

We have previously reported the regioselective acylation of aromatic  $\alpha,\beta$ -unsaturated carbonyl compounds,<sup>7</sup> aromatic aldehydes,<sup>8</sup> aromatic ketones,<sup>8</sup> and styrenes<sup>9</sup> by electroreduction or magnesium-promoted reduction to give the corresponding coupling compounds in good to excellent yields. Furthermore, as a recent result, the magnesium-promoted reductive silylation of aromatic conjugated ynones has generated the corresponding allene compounds in excellent yields<sup>10</sup> (Scheme 1).

In this study, an aromatic conjugated ynone (**1**), which was easily prepared from phenylacetylene, was acetylated under the magnesium-promoted reduction conditions. Surprisingly, the reaction between ynone **1** and acid chloride (**2**) did not afford the expected allene derivative (**5**), but rather an enyne (**3**) as the main product, in which the triple bond was transposed<sup>11</sup> (Scheme 2). Small amounts of a compound derived from the carbonyl C- and O-double acylation (**4**) and allene (**5**) were detected.



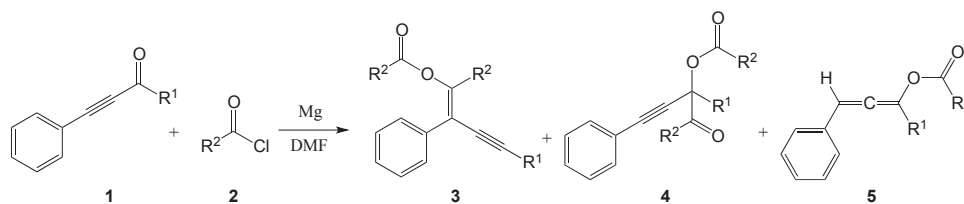
Scheme 1.

## 2. Results and discussion

Magnesium-promoted reductive coupling reactions depend on the nature of the solvent and generally require aprotic polar solvents. The starting material was consumed in aprotic polar solvents such as *N,N*-dimethylformamide (DMF), *N*-methyl-2-pyrrolidinone (NMP), and *N,N*-dimethylacetamide (DMAC). (Table 1) The reaction in DMF gave **3aa** as colorless oil in 45% yield (Table 1, entry 1). In contrast, no reaction occurred in tetrahydrofuran (THF) or acetonitrile.

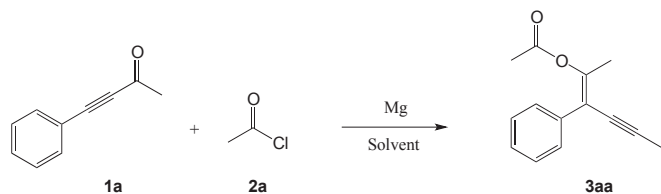
The effects of substrate concentration, reaction temperature, and ratio between acetyl chloride **2a** and magnesium in DMF were examined (Table 2). Higher substrate concentrations slightly enhanced isolated yields. However, the highest concentration (0.5 mol L<sup>-1</sup>) reduced the yield because of a striking increase in side reactions (Table 2, entries 1–4). Investigations of reaction temperature effects showed that 0 °C was appropriate for this coupling

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Scheme 2.

**Table 1**  
Solvent effects on the reaction between aromatic ynone (**1a**) and acetyl chloride (**2a**)



Entry	Solvent	Isolated yield (%)
1	DMF	45
2	NMP	Trace <sup>a</sup>
3	DMAc	Trace <sup>a</sup>
4	THF	No reaction
5	CH <sub>3</sub> CN	No reaction

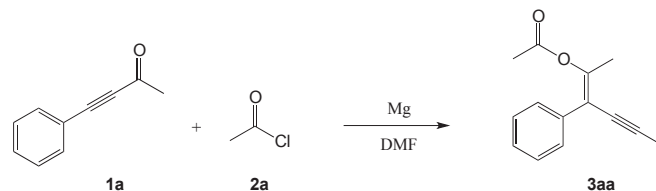
Mg (4 equiv), solvent (40 mL), **2a** (8 equiv), **1a** (5 mmol), 3–6 h, N<sub>2</sub> atmosphere.

<sup>a</sup> Determined by gas chromatography.

reaction. A large amount of starting material was recovered at  $-15\text{ }^{\circ}\text{C}$  although the reaction time was extended to 30 h (Table 2, entry 5). In contrast, too many side reactions occurred at  $30\text{ }^{\circ}\text{C}$ , giving the desired product in low yield (Table 2, entry 6). Further exploration on Mg and acetyl chloride ratios showed that 8 equiv of acetyl chloride **2a** and 4 equiv of magnesium produced the best results (Table 2, entries 3 and 7–12).

Next, various ynones **1** and acyl chloride **2** were allowed to react in the presence of magnesium metal under these optimized conditions (Table 3). Acyl chlorides comprising short-chain and branched alkyl groups were tolerated, giving rise to the desired compounds **3aa–3ae** in moderate yield (Table 3, entries 1–5).

**Table 2**  
Optimization of the reaction conditions



Entry	Substrates concn (mol L <sup>-1</sup> )	Temperature (°C)	<b>2a</b> <sup>a</sup> (equiv)	Mg <sup>a</sup> (equiv)	Isolated yield (%)
1	0.13	0	8	4	45
2	0.25	0	8	4	51
3	0.33	0	8	4	58
4	0.50	0	8	4	45
5	0.33	$-15$	8	4	35 <sup>b</sup>
6	0.33	30	8	4	30
7	0.33	0	6	4	16
8	0.33	0	8	5	47
9	0.33	0	6	3	51
10	0.33	0	10	5	30
11	0.33	0	4	2	Trace
12	0.33	0	8	3	26

<sup>a</sup> No reaction occurred in the absence of magnesium turnings or acetyl chloride **2a**.

<sup>b</sup> 30 h.

Compound **3af**, which bears two chlorine moieties, was prepared in 40% yield with the survival of the carbon–chlorine bond (Table 3, entry 6). Nevertheless, a complex mixture was detected instead of the desired compound when benzoyl chloride (**2g**) was used, suggesting that the acyl chloride may undergo decomposition via magnesium metal-induced reduction (Table 3, entry 7). Interestingly, an acid chloride bearing a bulky substituent, such as a cyclohexyl group (**2h**), did not generate the desired compound because of steric hindrance (Table 3, entry 8).

The tolerance of the R<sup>1</sup> substituent of aromatic conjugated ynones **1b–1g** was investigated (Table 3, entries 9–14). Ynones with an alkyl group, such as ethyl, *n*-butyl, cyclohexyl, and  $\beta$ -phenylethyl substituents, gave the desired compounds in moderate yields (Table 3, entries 9–11 and 13). Interestingly, no byproduct **4** formed in entry 11 because of steric hindrance between cyclohexyl group and acetyl chloride. In addition, aromatic substituents, such as phenyl (**1e**) and 2-furanyl groups (**1g**), did not significantly impact the acylation and readily generated the corresponding coupling compounds (**3ea** and **3ga**) in moderate yields (Table 3, entries 12 and 14). Unfortunately, this coupling reaction failed when an aromatic conjugated ester was used as a reactant (Table 3, entry 15). As suggested previously, allene derivatives are unstable. In particular, those derived from aromatic conjugated esters exhibit high instability because of their ketene acetal structure, which may result in unsuccessful reactions.<sup>10</sup>

Nuclear Overhauser effect experiments of several desired compounds **3** suggested that the structures of **3** would be single *E*-isomers. Crystallization of compound **3ea** confirmed its precise structure to be *E*-isomer through the use of single-crystal X-ray diffraction<sup>12</sup> (Fig. 1).

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