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A new strategy for the synthesis of α,β-diaroylpropionates promoted by samarium metal in DMF

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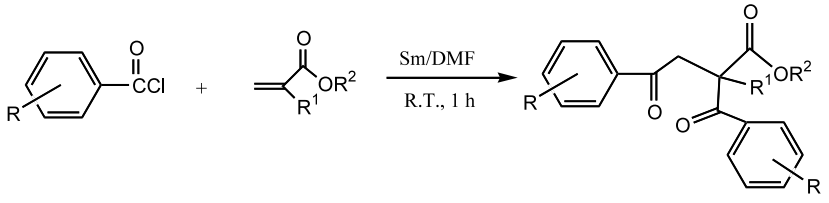
Abstract—When promoted by samarium in DMF, aroyl chlorides react readily with acrylates to afford α,β-diaroylpropionates in good to excellent yields without pretreating or activating the metallic samarium.

The direct use of metallic samarium as a reducing agent in organic transformations has attracted the attention of many organic chemists.[1] However, in most cases, the reactions promoted by samarium are usually carried out in THF,[2] and metallic samarium has to be activated or pretreated by various methods so as to ensure the reactions proceed smoothly. Generally, metallic samarium is activated for reaction by other reagents, such as iodine, hydrochloric acid, and alkyl halides, etc.[2,3] Until now, few precedents have appeared in the literature using metallic samarium without any activator or pretreatment.[4]

1,4-Dicarbonyl compounds, constitute key intermediates in various natural product syntheses, and are important synthetic precursors of cyclopentenones, cyclopenta-1,3-diones, butenolides, and derivatives of furan and pyrrole,[5] and a number of methods for their synthesis have been developed.[6] 1,3-Dicarbonyl compounds have also been widely used in organic synthesis. However, the syntheses of 2-alkoxycarbonyl 1,4-diketones are rarely reported, and only a few methods are available which required unusual substrates and relatively harsh reaction conditions.[7]

Here we wish to report that when *N*,*N*-dimethylformamide (DMF) is used as a solvent instead of THF, metallic samarium, without the need to be activated or pretreated, can promote the reactions of acrylates **2** with aroyl chlorides **1**, affording a conceptually new strategy for the synthesis of 2-alkoxycarbonyl 1,4-diketones **3** (Scheme 1).

As a result of direct use of metallic samarium without activator, simple equipment and material, short reaction times, facile operation procedures, mild reaction conditions, and high potential for large-scale preparations, this reaction type seems to offer one of the most promising methods for the synthesis of the target compounds.



1 **2** **3**

Scheme 1.

Keywords: samarium; DMF; aroyl chloride; acrylate; α,β-diaroylpropionate.
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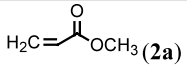
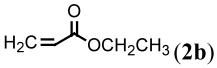
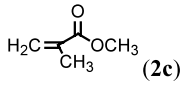
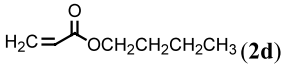
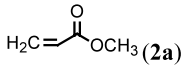
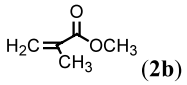
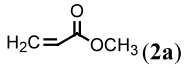
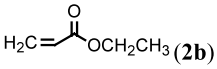
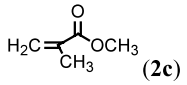
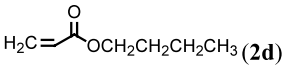
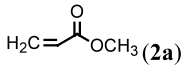
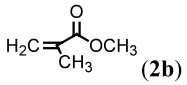
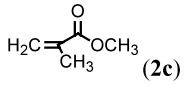
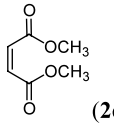
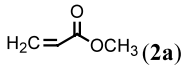
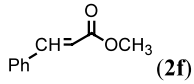
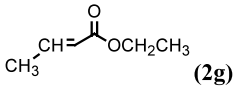
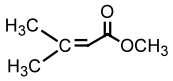
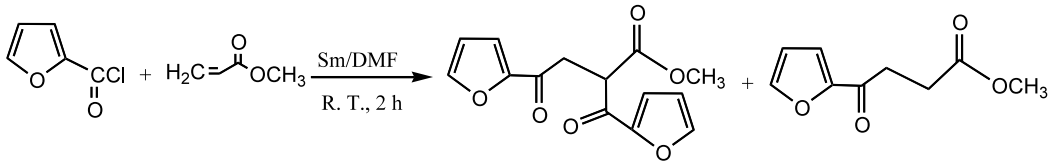
Table 1. Sm-promoted carbon–carbon double bond addition products of acrylates with aroyl chlorides

Entry	R in **1**	Substituted acrylate **2**	Isolated yield (%) of **3**[a]
1	H	 (**2a**)	91(**3a**)
2	H	 (**2b**)	93(**3b**)
3	H	 (**2c**)	84(**3c**)
4	H	 (**2d**)	81(**3d**)
5	4-CH_3-	 (**2a**)	86(**3e**)
6	4-CH_3-	 (**2b**)	79(**3f**)
7	4-Cl-	 (**2a**)	78(**3g**)
8	4-Cl-	 (**2b**)	77(**3h**)
9	4-Cl-	 (**2c**)	72(**3i**)
10	4-Cl-	 (**2d**)	90(**3j**)
11	4-F-	 (**2a**)	82(**3k**)
12	4-F-	 (**2b**)	88(**3l**)
13	3-Cl-	 (**2c**)	63(**3m**)
14	4-F-	 (**2e**)	46(**3n**)[b]
15	H[c]	 (**2a**)	31(**3o**) 29(**3p**)[d]
16	H	 (**2f**)	—[e]
17	4-F-	 (**2g**)	—[e]
18	H	 (**2h**)	—[f]

[a] Isolated yields based on aroyl chlorides. [b] A pair of inseparable diastereoisomers were obtained. [c] Furan-2-carbonyl chloride was used as substrate. [d] **3p** is a 1,4-addition product. [e] The resulting residue was a complicated mixture which defied further separation and identification. [f] Only self-coupling products of aroyl chloride were obtained.



2a **3o** (31%) **3p** (29%)

Scheme 2.

A typical procedure is as follows: to a mixture of Sm powder (1 mmol), methyl acrylate (4 mmol) in freshly distilled *N*,*N*-dimethylformamide (DMF, 10 mL), benzoyl chloride (2 mmol, freshly distilled) was added at room temperature with magnetic stirring under a nitrogen atmosphere. The resulting solution turned yellow–green within 15 min and an exothermic reaction was observed. After the completion of the reaction (about 1 h), a routine workup of the reaction mixture followed by column chromatography afforded methyl α,β-dibenzoylpropionate in 91% yield.

A variety of 2-alkoxycarbonyl 1,4-diketones **3** were obtained in good to excellent yields in the Sm/DMF system, as shown in Table 1.[8] Notably, in this Sm-promoted reaction, when an α-substituted acrylate was used as the substrate (for example, methyl α-methylacrylate, **2c**), the reaction still afforded compounds **3c**, **3f**, **3i**, **3l** and **3m** smoothly as the major products. However, the reaction is strongly influenced by the substituent on the β-position of the acrylate, and attempts to extend this reaction to methyl cinnamate (**2f**), ethyl crotonate (**2g**) and methyl β-dimethylacrylate (**2h**) were in vain. Only substrate **2e**, perhaps due to its double activation, could afford the corresponding product **3n** in 46% yield.

Interestingly, carbon–carbon double bond addition product **3o** and the 1,4-addition product **3p** were obtained simultaneously in a ratio of about 1:1 when furan-2-carbonyl chloride was used (Scheme 2). However, when aliphatic acid chlorides (such as phenylacetyl chloride, lauroyl chloride and acetyl chloride) were used instead of aroyl chlorides, the reaction did not occur at all. The temperature also influences the reaction. Hardly any reaction was observed after 2 h when the reaction temperature was below −10°C, and by-products formed by self-coupling of the aroyl chloride increased when the reaction temperature exceeded 40°C. Generally, the ideal temperature is about 15–25°C.

The mechanism of the reaction is not clear. From experimental results, we suggest that the reaction involves a radical mechanism. Because aroyl radicals are much more stable than acyl radicals, aroyl radicals may be formed in the presence of Sm whereas aliphatic acyl radicals are not. On the other hand, DMF may play an important role in stabilizing the intermediates as a solvent with strong polarity and excellent solubility, dissolving the samarium salts, etc. because the reaction does not occur in THF, indeed, even self-coupling products from the aroyl chloride are rarely formed.[9]

In conclusion, the Sm-promoted carbon–carbon double bond addition of acrylates with aroyl chlorides offers a facile, efficient, convenient and novel method for the synthesis of useful polycarbonyl compounds in good to excellent yields from very simple starting materials. Furthermore, because the direct use of metallic samarium in organic synthesis without any activator is rarely reported, this reaction may have additional significance.

Acknowledgements

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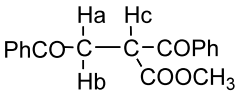
8. All of the products obtained in this study were characterized (^{1}H, ^{13}C NMR, MS, IR, EA). For example, **methyl α,β-dibenzoylpropionate (3a)**: White solid. Mp 77–78°C. ν_{max} (KBr)/cm^{-1}: 2955, 1736, 1683, 1595, 1581, 1451. δ_H ($CDCl_3$): 8.09–8.11 (2H, m), 7.99–8.01 (2H, m), 7.57–7.63 (2H, m), 7.45–7.53 (4H, m), 5.13–5.17 (1H, q, Hc, Jcb = 7.5, Jca = 6.1), 3.80–3.87 (1H, q, Hb, Jbc = 7.5, Jba = 18.3), 3.71–3.77 (1H, q, Ha, Jab = 18.3, Jac = 6.1), 3.71 (3H, s).



^{13}C NMR δ ($CDCl_3$): 196.30, 194.17, 169.25, 135.54, 135.49, 133.12, 133.01, 128.45, 128.24, 128.14, 127.70, 52.27, 48.01, 37.79. m/z (%): 297 (M^++1, 0.10), 296 (M^+, 0.06), 279 (M^+–17, 0.47), 265 (0.59), 191 (1.58), 105 (100.00), 77 (43.65). Anal. $C_{18}H_{16}O_4$. Calcd: C, 72.96; H, 5.44. Found: C, 72.83; H, 5.40%; **methyl α,β-dibenzoyl-α-methylpropionate (3c)**: White solid. Mp: 69–70°C. ν_{max} (KBr)/cm^{-1}: 2948, 1734, 1692, 1682, 1596, 1580, 1462, 1449. δ_H ($CDCl_3$): 7.96–7.98 (2H, m), 7.83–7.85 (2H, m), 7.39–7.59 (6H, m), 3.84 (2H, s), 3.71 (3H, s), 1.73 (3H, s). ^{13}C NMR δ ($CDCl_3$): 197.89, 196.90, 173.52, 136.86, 136.49, 133.37, 132.32, 128.65, 128.48, 128.43, 128.13, 56.16, 52.85, 45.64, 21.84. m/z (%): 293 (M^+–17, 0.20), 279 (0.17), 205 (1.46), 105 (100.00), 77 (44.97). Anal. $C_{19}H_{18}O_4$. Calcd: C, 73.53; H, 5.85. Found: C, 73.49; H, 5.86%.

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