A new method for the synthesis of γ-oxobutyronitriles *via* addition of aroyl chlorides to acrylonitrile promoted by samarium metal in DMF

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Without any pretreatment or activator, metallic samarium in DMF promotes the addition of aroyl chlorides to acrylonitrile to form γ-oxobutyronitriles

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γ-Oxobutyronitriles, as well as 1,4-dicarbonyl compounds are important synthetic intermediates for the syntheses of cyclopentenones, cyclopenta-1,3-diones, butenolides, and derivatives of furan and pyrrole.[1] Therefore, a number of methodologies for their formation have appeared.[2] However, these methods generally require unusual substrates or relatively harsh reaction conditions.

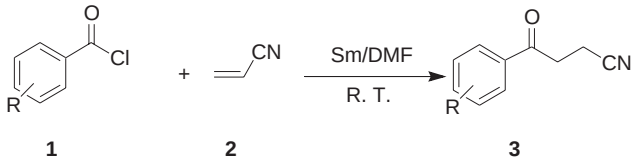
Although SmI_2 is a useful reagent,[3] its storage is difficult due to sensitivity to oxidation in air. On the other hand, metallic samarium is stable in air and has strong reducing power (Sm^{3+}/Sm= –2.41V), so that direct use of metallic samarium as a reducing agent in organic transformations has drawn the attention of many organic chemists.[4] However, in most cases, the reactions promoted by samarium are carried out in THF,[5] and the metallic samarium has to be activated or pretreated by various methods. Metallic samarium has been activated in reactions by other reagents, such as iodine, hydrochloric acid, and alkyl halides, *etc*.[5,6] Until now, few reports could be found concerning organic reactions promoted efficiently by metallic samarium without any activator or pretreatment.[7]

We have found 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 addition of aroyl chlorides 1 to acrylonitrile 2, thus affording a new method for the synthesis of γ-oxobutyronitriles 3 (Scheme 1).

Table 1 summarises our results on the addition of aroyl chlorides to acrylonitrile induced by Sm metal in DMF. It is found that the substituents in the aromatic rings in aroyl chlorides influence this reaction strongly. Electron-withdrawing groups, such as fluoro, chloro, *etc*. accelerate the reaction and lead to relatively higher yields of products 3, as shown in Table 1 (Entries 2, 4, 5 and 7). On the other hand, aroyl chlorides with electron-donating group are not favoured in this reaction. For example, with methyl groups on the aromatic rings, the reaction requires a longer time and affords the expected products in relatively lower yield (**3c** and **3f**). When the substituents on the aromatic rings are electron-rich enough (**1h** and **1i**), the desired products were not formed.

Temperature also influences the reaction remarkably. No reaction was observed below –10 °C. On the other hand, if the reaction temperature exceeded 40 °C, the yields of 1, 2-diketones, which were by-products of the reaction and resulted from the self-coupling reaction of the aroyl chloride, increased significantly. Optimisation of the reaction conditions found that the appropriate temperature for this reaction is about 15–25 °C. Attempts to extend this reaction to aliphatic acid chlorides (for example, phenylacetyl chloride, lauroyl chloride and acetyl chloride) were not successful and only complex inseparable mixtures were obtained.

Though the detailed mechanism of the above reaction has not yet been clarified, it is probable that the reaction may involve a radical mechanism (Scheme 2) based on our experimental



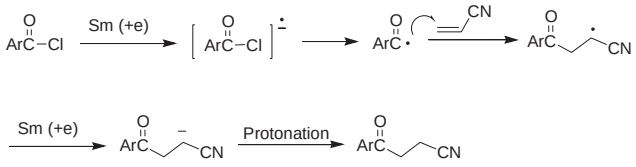
1 **2** **3**

Scheme 1

Table 1 Sm-promoted addition of acrylonitrile with aroyl chlorides

Entry	R in **1** and **3**	Reaction time (h)	Products **3**	Yield/%[a]
1	H (**1a**)	1	**3a**	76
2	4-Cl (**1b**)	1.5	**3b**	77
3	4-CH_3 (**1c**)	1.5	**3c**	57
4	4-F (**1d**)	1.5	**3d**	73
5	3-Cl (**1e**)	1.5	**3e**	68
6	3-CH_3 (**1f**)	2	**3f**	58
7	2-Cl (**1g**)	2	**3g**	63
8	4-CH_3O (**1h**)	5	—	—[b]
9	2-Furoyl chloride (**1i**)	5	—	—[b]

[a]Yield of isolated products. [b]A complex mixture was obtained.



Scheme 2

results and the previous reports.[8-10] The reaction must be initiated with first formation of the aroyl radical and subsequent attack of the aroyl radical on acrylonitrile. An alternative mechanism involving initial electron transfers from samarium metal to acrylonitrile first to form the corresponding radical can be excluded, since no product resulting from the self-coupling of acrylonitrile was obtained. In addition, the fact that the reaction only worked for aroyl chlorides but not for aliphatic acyl chlorides can be interpreted by the proposed mechanism. An aroyl radical is much more stable than an aliphatic acyl radical, and so an aroyl radical can be formed more easily under such reaction conditions. Finally, as a solvent with strong polarity, DMF may play an important role in stabilising the intermediates, dissolving samarium salts etc, thus assisting the reaction to proceed smoothly. It should be pointed out that this Sm-promoted addition of aroyl chlorides to acrylonitrile did not occur in THF, even the self-coupling reaction of aroyl chlorides hardly proceeded with THF as the reaction medium.[11]

In conclusion, Sm-promoted radical addition of aroyl chlorides to acrylonitrile offers an efficient and convenient method for the syntheses of γ-oxobutyronitriles. With simple equipment and material, short reaction times, a facile operation procedure, mild reaction conditions, and a high

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potential for large-scale preparation, this reaction seems to offer one of the most promising methods for the synthesis of compounds that may be expected to be formed in such a reaction system. Furthermore, because the direct use of samarium in organic synthesis without any activator is rarely reported, this reaction may be of some significance in this research area.

Experimental

General: Melting points were uncorrected. Infrared spectra were recorded on an IR-408 spectrometer in KBr or as a thin film with absorption maxima in cm^{-1}. ^1H NMR spectra were determined in a Bruker AC–400 spectrometer as $CDCl_3$ solutions. *J* values are in Hertz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on an HP 5989B MS spectrometer. Microanalysis was carried out on an EA 1110 instrument. DMF was redistilled and dried by molecular sieves before use. The reaction was monitored by TLC, and the products were isolated by silica gel column chromatography using ethyl acetate and cyclohexane (1 : 6) as eluant.

Typical procedure for the synthesis of 4-aryl-4-oxobutyronitriles: To a mixture of Sm powder (1 mmol), acrylonitrile (4 mmol) in freshly distilled 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 in 30 minutes and an exothermic reaction was observed. After being stirred for a given time (Table 1, the reaction was monitored by TLC), the reaction was quenched with dilute HCl (0.1 mol/l, 5 ml) and extracted with ether (3×30 ml). The organic phase was washed with water (20 ml), saturated brine (15 ml), and dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure to give the crude product, which was purified to afford methyl γ-oxo-benzenebutyronitrile in 76% yield.

4-Oxo-4-phenylbutyronitrile (**3a**): Light yellow solid. m.p. 73–74 °C (lit. 76 °C)[12a]. ν_{max}(KBr)/cm^{-1}: 3061 2937, 2249, 1684, 1596, 1447. δ_H($CDCl_3$): 7.95–7.97 (2H, m), 7.60–7.64 (1H, m), 7.48–7.52 (2H, m), 3.37–3.41 (2H, t, *J* = 7.1), 2.77–2.80 (2H, t, *J* = 7.1). *m/z*(%): 159 (M^+, 3.47), 105 (100.00), 77 (69.76), 54 (7.06). Anal. $C_{10}H_9NO$. Calcd. C, 75.45; H, 5.70; N, 8.80. Found C, 75.52; H, 5.83; N, 8.76 %.

4-(4-Chlorophenyl)-4-oxobutyronitrile (**3b**): Light yellow solid. m.p. 75–77 °C (lit. 72–73 °C)[12b]. ν_{max}(KBr)/cm^{-1}: 3091 2957, 2251, 1676, 1591, 1573. δ_H($CDCl_3$): 7.88–7.92 (2H, m), 7.46–7.50 (2H, m), 3.34–3.37 (2H, t, *J* = 7.0), 2.76–2.80 (2H, t, *J* = 7.0). *m/z*(%): 195 (M^++2, 2.01), 193 (M^+, 6.05), 158 (0.56), 139 (100.00), 111 (43.94), 54 (7.06). Anal. $C_{10}H_8ClNO$. C, 62.03; H, 4.16; N, 7.23. Found C, 62.11; H, 4.18; N, 7.26 %.

4-Oxo-4-p-tolylbutyronitrile (**3c**): White solid. m.p. 80–83 °C (lit. 74–76 °C)[12c]. ν_{max}(KBr)/cm^{-1}: 2971, 2251, 1682, 1612, 1576, 1517. δ_H($CDCl_3$): 7.85–7.87 (2H, m), 7.29–7.30 (2H, m), 3.35–3.38 (2H, t, *J* = 7.2), 2.76–2.79 (2H, t, *J* = 7.2), 2.44 (3H, s). *m/z*(%): 173 (M^+, 3.71), 158 (0.46), 119 (100.00), 91 (32.49), 54 (4.06). Anal. $C_{11}H_{11}NO$. Calcd. C, 76.28; H, 6.40; N, 8.09. Found C, 76.19; H, 6.42; N, 8.08 %.

4-(4-Fluorophenyl)-4-oxobutyronitrile (**3d**): Light yellow solid. m.p. 82–85 °C. ν_{max}(KBr)/cm^{-1}: 2950, 2251, 1687, 1601, 1510. δ_H($CDCl_3$): 8.00–8.03 (2H, m), 7.20–7.22 (2H, m), 3.36–3.40 (2H, t, *J* = 7.2), 2.78–2.82 (2H, t, *J* = 7.2). *m/z*(%): 177 (M^+, 4.03), 158 (0.58), 123 (100.00), 95 (18.08), 54 (2.06). Anal. $C_{10}H_8FNO$. Calcd. C, 67.79; H, 4.55; N, 7.91. Found C, 67.81; H,4.56; N, 7.90 %.

4-(3-Chlorophenyl)-4-oxobutyronitrile (**3e**): Light yellow oil. δ_{max}(film)/cm^{-1}: 3072 2924, 2250, 1692, 1595, 1574. δ_H($CDCl_3$): 8.10 (1H, s), 7.42–8.02 (3H, m), 3.36–3.40 (2H, t, *J* = 7.2), 2.78–2.82 (2H, t, *J* = 7.2). *m/z*(%): 195 (M^++2, 2.44), 193 (M^+, 7.25), 158 (6.62), 139 (100.00), 111 (44.49), 54 (9.40). Anal. $C_{10}H_8ClNO$. C, 62.03; H, 4.16; N, 7.23. Found C, 62.09; H, 4.17; N, 7.22 %.

4-Oxo-4-m-tolylbutyronitrile (**3f**): Colourless oil. ν_{max}(film)/cm^{-1}: 2925, 2250, 1687, 1608, 1589. δ_H($CDCl_3$): 7.93 (1H, s), 7.37–7.79 (3H, m), 3.38–3.41 (2H, t, *J* = 7.2), 2.78–2.81 (2H, t, *J* = 7.2), 2.45 (3H, s). *m/z*(%): 173 (M^+, 9.36), 158 (0.65), 119 (100.00), 91 (52.77), 54 (7.63). Anal. $C_{11}H_{11}NO$. Calcd. C, 76.28; H, 6.40; N, 8.09. Found C, 76.39; H, 6.39; N, 8.07 %.

4-(2-Chlorophenyl)-4-oxobutyronitrile (**3g**): Light yellow oil. ν_{max}(film)/cm^{-1}: 2922, 2251, 1701, 1590, 1470. δ_H($CDCl_3$): 7.57–7.60 (1H, m), 7.46–7.47 (2H, m), 7.38–7.40 (1H, m), 3.38–3.42 (2H, t, *J* = 7.2), 2.77–2.81 (2H, t, *J* = 7.2). *m/z*(%): 195 (M^++2, 1.91), 193 (M^+, 5.60), 158 (0.30), 139 (100.00), 111 (17.04), 54 (8.77). Anal. $C_{10}H_8ClNO$. C, 62.03; H, 4.16; N, 7.23. Found C, 62.20; H, 4.17; N, 7.22 %.

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