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Indium-mediated reductive coupling of acyl cyanides: a convenient synthesis of 1,2-diketones

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Abstract

The indium-mediated reductive coupling of acyl cyanides afforded the corresponding 1,2-diketones in moderate to good yields under neutral and mild conditions. © 2000 Elsevier Science Ltd. All rights reserved.

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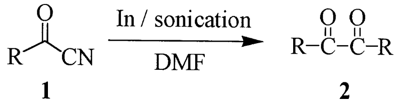
Indium-mediated reactions[1] have gained much attention over the last decade in a variety of reactions such as cyclopropanations,[2] Reformatsky reactions,[3] allylation reactions of carbonyl compounds,[4] or aldimines.[5] In particular, the reductive coupling of carbonyl derivatives is one of the most valuable methods for establishing carbon–carbon bonds. It has recently been found that aromatic aldehydes[6] and aldimines[7] are transformed into pinacols and vicinal diamines, respectively, with indium. However, to our knowledge, there is no report on the reductive coupling of acyl cyanides by the use of indium. Although the reductive coupling of acyl cyanides[8] or acid chlorides[9] mediated by SmI_2 to give 1,2-diketones was described in the literature, these methods have been somewhat limited because they are very sensitive to air and moisture. We have discovered that indium is effective for the reductive coupling reaction of acyl cyanides to afford the corresponding 1,2-diketones under neutral and mild conditions. The reaction does not require exclusion of oxygen or anhydrous conditions as required by SmI_2 for effecting the same transformation (Eq. (1)). Due to their utility in organic synthesis and their biological activities, 1,2-diketones have attracted considerable interest and several important preparative methods for 1,2-diketones have been developed.[10]



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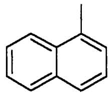
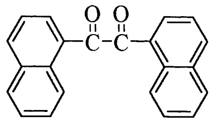
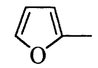
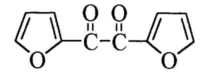
Herein we wish to report a simple, convenient procedure for the coupling of acyl cyanides to form 1,2-diketones using indium under sonication.[11] The reaction proceeds efficiently in moderate to good yields at room temperature. However, it was found that acyl chlorides reacted under the same conditions to give complex mixtures. Any significant self-coupling of acyl chlorides to give 1,2-diketones was not observed.

In a typical experimental procedure, a mixture of benzoyl cyanide (0.25 g, 1.9 mmol) and indium powder (100 mesh, 0.33 g, 2.9 mmol) in DMF (2 mL) was stirred at room temperature under sonication for a certain period of time until completion of the reaction (TLC). The reaction mixture was quenched with a few drops of water and extracted with diethyl ether. Evaporation of the solvent followed by purification via silica gel chromatography afforded benzil in 62% yield. Table 1 indicates the results of the reductive coupling of acyl cyanides using indium. The furfuroyl cyanide was also reductively coupled to give 1,2-diketone (entry 12), but the application of this approach to aliphatic acyl cyanide proved unsuccessful and only recovered starting material was isolated (entries 9 and 10).

Table 1
Reductive coupling of acyl cyanides with indium

Entry	Acyl Cyanide **1** R	Reaction Time (hr)	1,2-Diketone **2**	Yield(%)*
1	Ph	8	$(PhCO)_2$	62
2	$4\text{-}CH_3C_6H_4$	6	$(4\text{-}CH_3C_6H_4CO)_2$	78
3	$2\text{-}CH_3C_6H_4$	8	$(2\text{-}CH_3C_6H_4CO)_2$	73
4	4-*t*-BuC_6H_4	10	(4-*t*-$BuC_6H_4CO)_2$	73
5	$4\text{-}CH_3OC_6H_4$	8	$(4\text{-}CH_3OC_6H_4CO)_2$	67
6	$2\text{-}ClC_6H_4$	12	$(2\text{-}ClC_6H_4CO)_2$	61
7	$2\text{-}BrC_6H_4$	12	$(2\text{-}BrC_6H_4CO)_2$	60
8	$4\text{-}BrC_6H_4$	12	$(4\text{-}BrC_6H_4CO)_2$	62
9	$CH_3(CH_2)_8$	12	—	0
10	Cyclohexyl	12	—	0
11		12		68
12		8		70

*Isolated yields.

In the course of the process, substituents such as methoxy, chloro, or bromo groups (entries 5–8) are not affected. All products obtained showed NMR, IR and mass spectral data compatible with the structure. The structures of known compounds were determined by comparison of their spectral data with those previously reported.[12]

Indium metal has some reducing power ($In^{+3}/In = -0.34$ V) in solution and the choice of the solvent is critical in the indium-mediated reaction. The reaction was carried out in several solvents but failed in THF, THF/H_2O, DMF/H_2O, CH_3CN and water. DMF has been found to be the most suitable solvent for the reaction. Presumably, indium is somewhat more reactive in an organic solvent like DMF. It is speculated that the present reductive coupling reaction mediated by indium goes through a single electron transfer (SET) process like other metal-mediated reactions. Although the mechanism of the reaction is not yet clear, we assume that indium may transfer one electron to RCOCN to form the radical anion intermediate $(RCOCN)^{\bullet-}$, which was cleaved into $RCO^{\bullet}$ and CN^{-} and the coupling of the radical $RCO^{\bullet}$ gives 1,2-diketones **2**. Another equally likely mechanism is that the radical anion intermediate $(RCOCN)^{\bullet-}$ can dimerize to give the dialkoxide, which slowly decomposes to 1,2-diketones **2**.

In conclusion, we have demonstrated that the reductive coupling reaction of acyl cyanides using indium provides a simple and convenient method for the synthesis of 1,2-diketones under neutral and mild reaction conditions. Further investigation on the extension of the reaction and the mechanistic detail is currently in progress.

Acknowledgements

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