



Indium Promoted Reductive Homocoupling of Alkyl and Aryl Halides

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Abstract : Reductive homocoupling of alkyl and aryl halides in presence of indium metal in DMF produces bialkyls and biaryls in good yields. 1,4-Diketones are obtained from α -iodoketones.

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The synthesis of bialkyls and biaryls is of considerable interest.¹⁻⁵ The classical methods for the synthesis of bialkyls and biaryls involve Wurtz¹ and Ullmann² reactions respectively. The Wurtz reaction for the coupling of alkyl halides mediated by sodium metal has serious limitations in the case of secondary alkyl halides. In addition, sodium metal has its own inconveniences. However, these difficulties have been overcome by use of other metals such as Mn, Mg etc.³ On the other hand, the Ullman reaction produces biaryls by the copper-induced reductive coupling of aryl halides. One of the major disadvantages is that, the reaction is, in general, carried out above 200°C. There are however, several modifications of this reaction involving palladium⁴ and other copper derived compounds.⁵

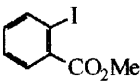
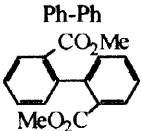
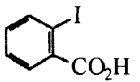
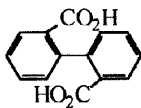
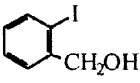
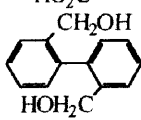
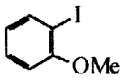
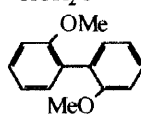
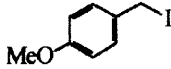
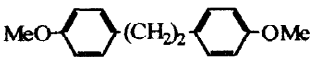
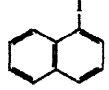
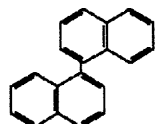
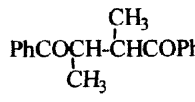

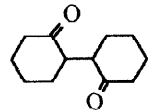
In recent times there has been increasing interest in indium-mediated transformations because of certain unique properties possessed by indium.⁶ However, although indium has been used extensively in carbonyl addition reactions,⁶ its potential in other domains has not been explored to a great extent. Because of the close resemblance of indium with magnesium, indium could also be a potential reductive coupling agent. This prompted us to initiate an investigation into indium promoted reductive coupling of alkyl and aryl halides. We have observed that both alkyl and aryl iodides undergo smooth homocoupling in DMF in the presence of indium metal to provide the corresponding dialkyls and diaryls.

The experimental procedure is very simple. A mixture of alkyl/aryl iodide (1 mmol) and indium metal (1 mmol, cut into small slices) in dry DMF (2 ml) was heated at reflux, under nitrogen, with stirring for a certain period of time (Table 1) until completion of the reaction was observed (TLC). The reaction mixture was diluted with ether and the organic phase was washed successively with water and brine and then dried (Na₂SO₄). Evaporation of solvent followed by purification by silica gel chromatography produced the homocoupled product.

A wide range of structurally varied alkyl and aryl halides underwent coupling by this procedure to furnish the corresponding bialkyls and biaryls. The results are reported in Table 1. Different types of alkyl iodides such as long chain saturated (entry 2), benzylic (entry 1) and allylic (entry 3), were coupled without any difficulty. Aryl iodides with both electron-withdrawing and electron-donating substituents underwent smooth coupling. This procedure has also been effective for the coupling of α -iodoketones to produce the corresponding 1,4-diketones (entries 11-13) which are of considerable synthetic potential.⁷ The reactions are, in general, reasonably fast and high-yielding.⁸ This procedure is found to be compatible with several sensitive functionalities such as OH, OMe, CO₂Me, CO₂H. Alkyl bromides also undergo coupling, but the process is very slow.⁹

In conclusion, this indium-promoted procedure provides a very efficient and general methodology for homocoupling of alkyl as well as aryl iodides. To the best of our knowledge this is the first report of indium-promoted direct homocoupling of both alkyl and aryl halides. Further investigations of other useful applications are in progress.

Table 1. Indium Promoted Reductive Homocoupling of Alkyl / Aryl Iodide.

entry	substrate, R-I	time(h)	product, R-R	yield (%) ^a
1	PhCH ₂ -I	8	Ph(CH ₂) ₂ Ph	89
2	CH ₃ (CH ₂) ₁₄ CH ₂ -I	12	CH ₃ (CH ₂) ₃₀ CH ₃	92
3	Ph-CH=CH-CH ₂ -I	8.5	PhCH=CH(CH ₂) ₂ CH=CHPh	80
4	Ph-I	14	Ph-Ph	78
5		12.5		82
6		15		75
7		13		78
8		11		88
9		8		90
10		13		80
11	PhCOCH ₂ -I	7	PhCO(CH ₂) ₂ COPh	60
12	PhCOCH(CH ₃)-I	8.5		57
13		8		53

^a Yields refer to pure isolated products, properly characterized by spectral data

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References and Notes

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8. In the reactions of α -iodoketones, the yields of coupled products are relatively low because of the competing reduction process.
9. Benzyl bromide took 48 h for complete coupling compared to 8 h for benzyl iodide.